NATIONAL ACADEMY OF SCIENTIST EDUCATION

YEARBOOK 2023/24

NEMZETI TUDÓSKÉPZŐ AKADÉMIA
NATIONAL ACADEMY OF SCIENTIST EDUCATION

NEMZETI TUDÓSKÉPZŐ AKADÉMIA
NATIONAL ACADEMY OF SCIENTIST EDUCATION

NATIONAL ACADEMY OF SCIENTIST EDUCATION YEARBOOK 2023/24

A new, multigenerational education system for the 21st century 2013 – 2033

MOTTO:

"He who organizes public education, abundantly sows the seeds of culture in the loam of wide layers of people, like the Hungarian seed sower. He who cares about scientist education should be like an orchid gardener, dealing with each pot individually."

(Kuno Klebelsberg)

TABLE OF CONTENTS

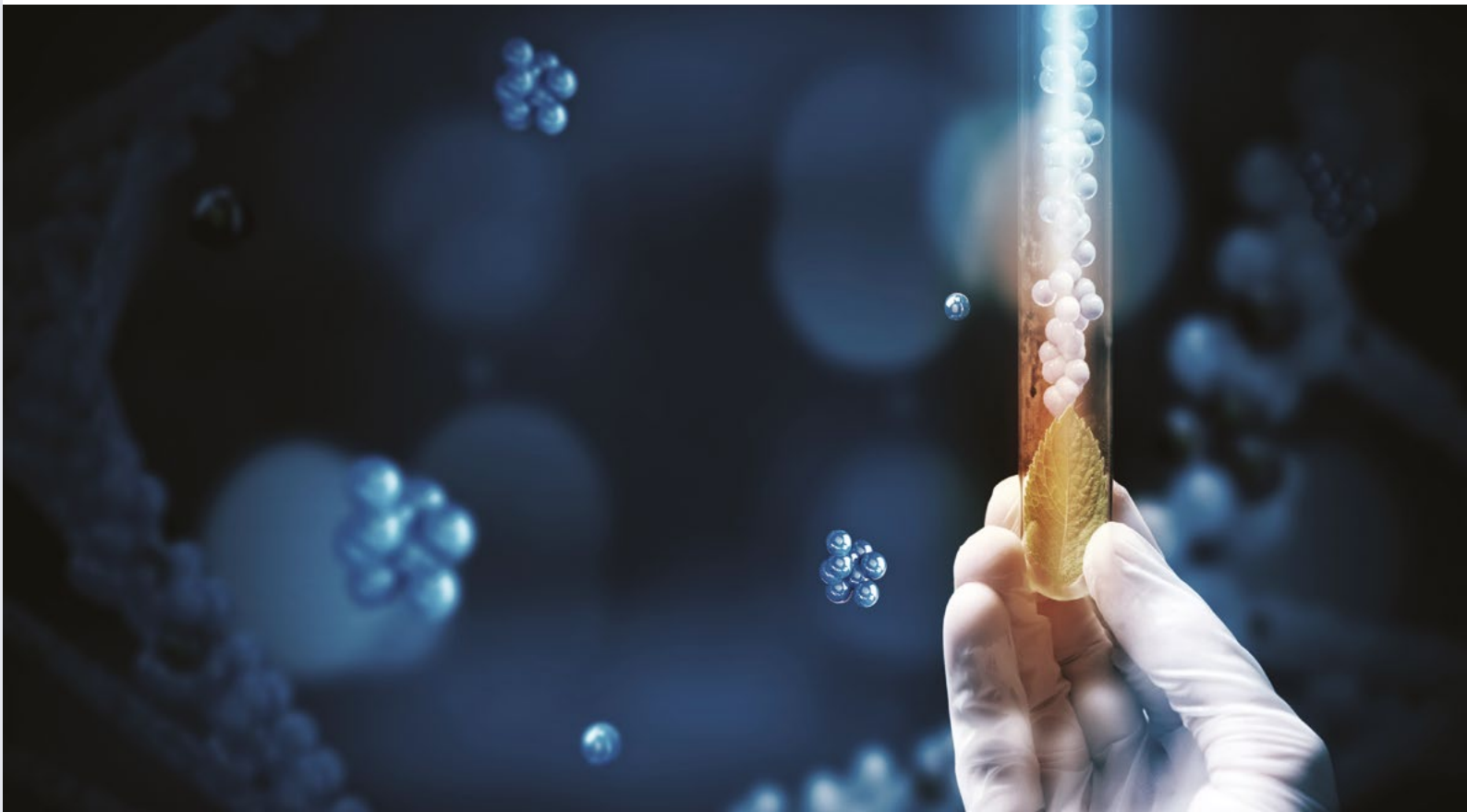
SALUTATORY

In supporting young talents, there is always the opportunity to change our future, as the science of today is the medicine of tomorrow. What we invest in talents today will create value tomorrow.

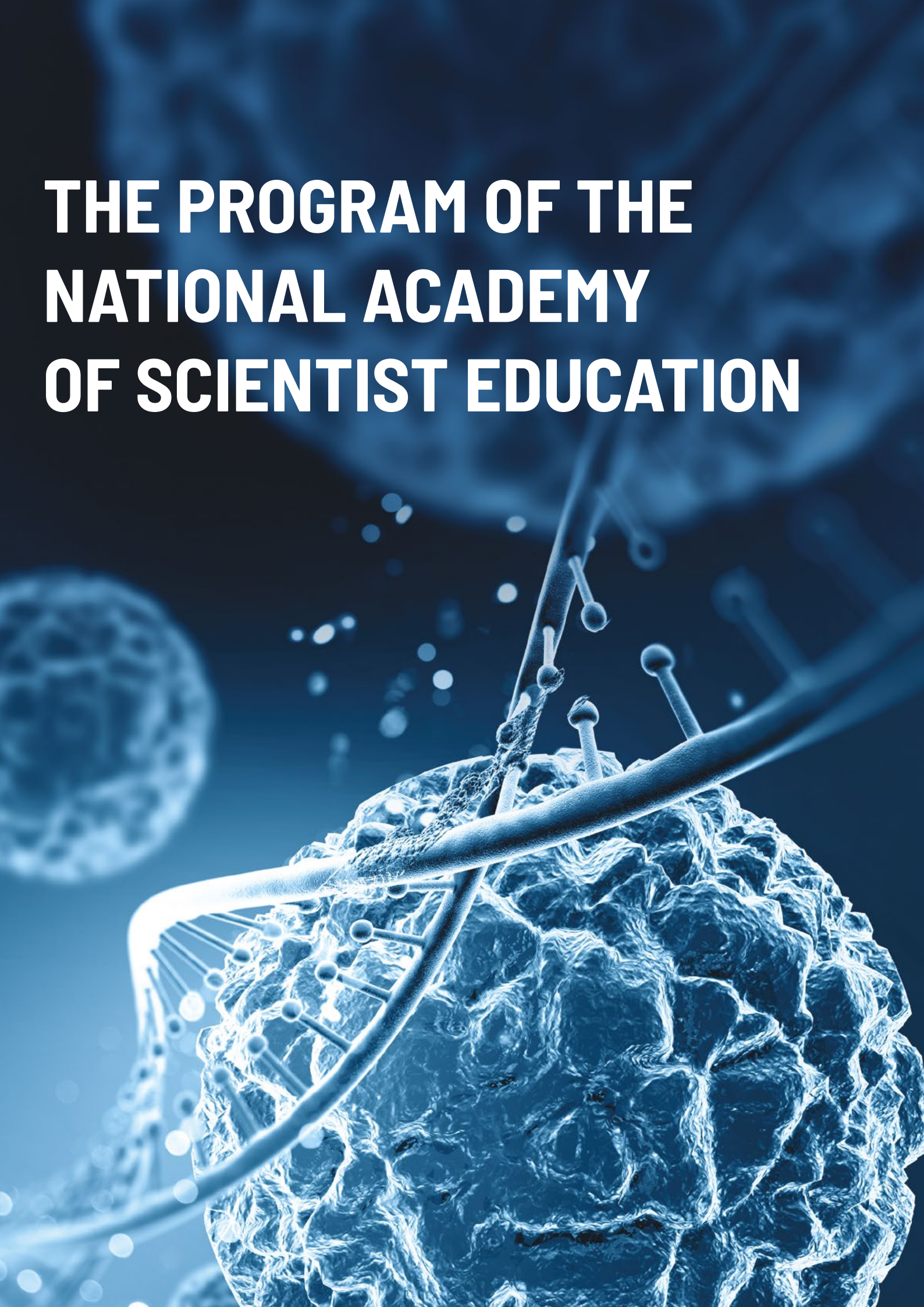
The National Academy of Scientist Education program was developed with the aim of finding the young people with whom we can research the future!

PÉTER HEGYI
Program director

ANDRÁS VARRÓ
Strategic director



THE PROGRAM OF THE NATIONAL ACADEMY OF SCIENTIST EDUCATION

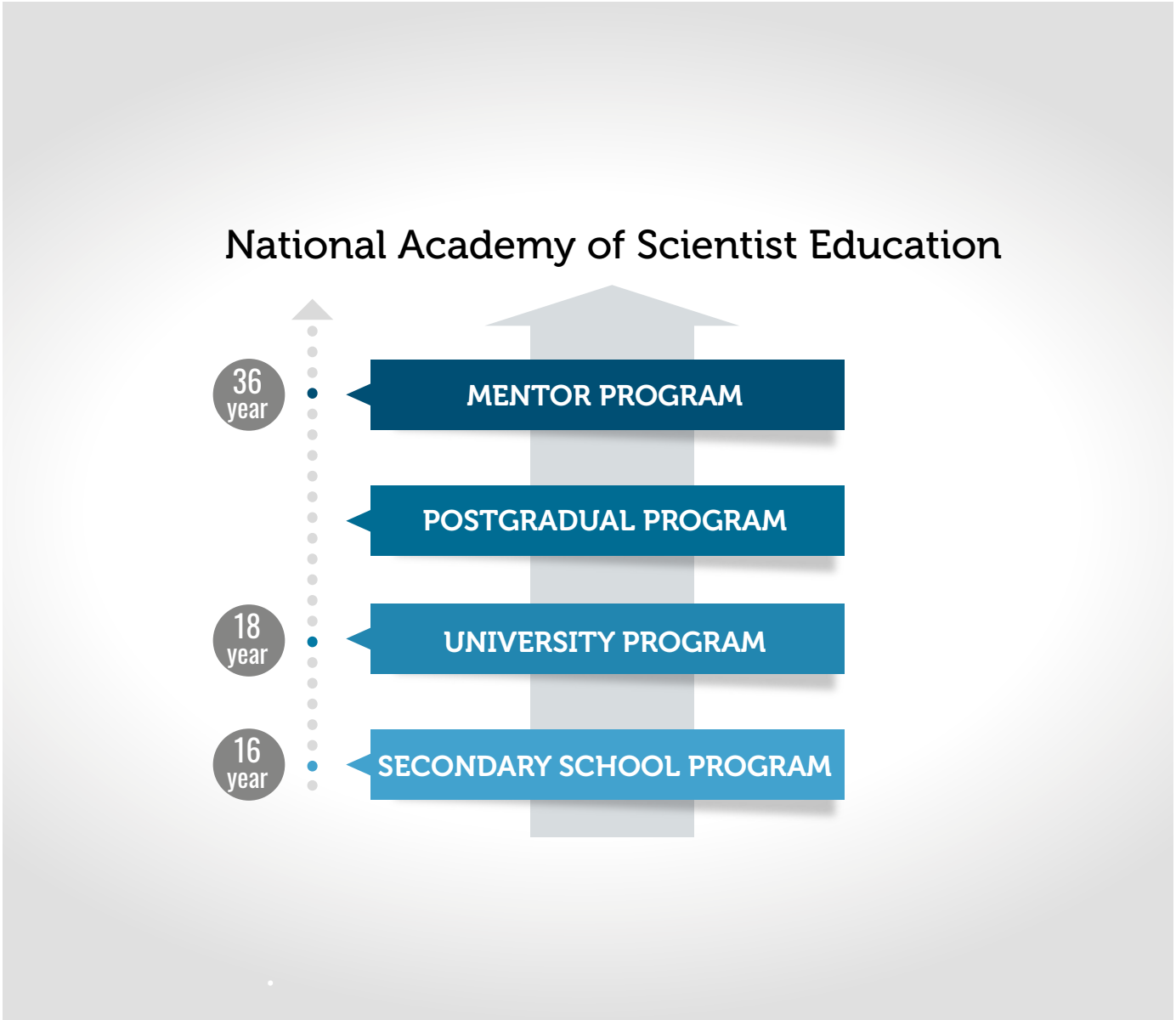


THE NATIONAL ACADEMY OF SCIENTIST EDUCATION

THE TRANSFORMATION OF THE SZEGED SCIENTISTS ACADEMY INTO THE NATIONAL ACADEMY OF SCIENTIST EDUCATION

In 2013, the Foundation for the Future of Biomedical Sciences in Szeged established the Szeged Scientists Academy. Based on the results listed over the years, it came to the point in 2021 where - with the support of the Hungarian government - the name of the Foundation was changed to **National Biomedical Foundation** and the program expanded to **National Academy of Scientist Education** (NASE) program, to include all cities with institutes of higher education in human life sciences (Budapest, Debrecen, Pécs, Szeged).

The short-term goal of the program remained to embrace talented young people interested in biomedical research, to support their scientific work, to make the career model of scientists more attractive, as well as to keep young researchers in Hungary in the long-term.



GENERAL INTRODUCTION OF THE NATIONAL ACADEMY OF SCIENTIST EDUCATION

One of the essential innovations of the educational processes of the Szeged Scientists Academy, and then of the National Academy of Scientist Education is that it guides students who are talented in research through the steps of becoming a scientist from their secondary school years.

The principal education of the secondary school pupils takes place in seven National Education Centres (in Debrecen, Gödöllő, Hódmezővásárhely, Pécs, Szeged and Szombathely) and 20 Regional Education Centres. The Regional Education Centres are led by the Szent-Györgyi Senior Teachers whose primary task is to find and mentor the pupils within their region who are particularly interested in natural sciences and are later planning to choose a research career.

The professional background to the regular theoretical and practical trainings organized by the Senior Teachers is constantly provided by the Academy.

The university **students are trained in** four cities (**Budapest, Debrecen, Pécs, Szeged**), **in six Scientific Laboratories**, at the best-equipped laboratories in the country, under the professional supervision of the **best mentors** (the so-called Szent-Györgyi Mentors). In each laboratory, a group of mentors awaits the students, who will also start research work along with their university studies. On the educational side, some university students are helped with an individual curriculum, so students can independently plan being in the laboratory when necessary for their research work. Of course, high-quality research activity cannot come at the expense of educational obligations.

The work of the Szent-Györgyi Mentors is supported by an **International Mentor Team** of nearly 60 members including outstanding researchers, even several Nobel Laureates.

The first dormitory of the Academy was opened in Szeged and has been available for the university students since September 2022.

The dormitory of the Academy in Szeged

Laboratory experiments

Eric F. Wieschaus (Nobel Laureate in Medicine, 1995) at the University of Szeged Teacher Training Secondary and Primary School

THE STUDENTS OF THE ACADEMY

Szent-Györgyi Pupils

A Szent-Györgyi Pupil can be a secondary school pupil who is already enrolled in secondary school and has an intense interest in the life sciences and related subjects (biology, chemistry). The National Academy of Scientist Education invites young people based on the recommendation of their teacher to join the Secondary School Education Program so that they might acquire the basic practical and theoretical knowledge necessary for their later research work.

A great majority of the Szent-Györgyi Puipls become Szent-Györgyi Students, and thus they take part in a 20-year training system.

Benefits:

- Laboratory training in the National and Regional Education Centres
- The opportunity to meet outstanding researchers

Project assignment under the supervision of a Szent-Györgyi Senior Teacher

Szent-Györgyi Students at the Meeting of Nobel Laureates and Talented Students

Laboratory practice under the supervision of a Szent-Györgyi Senior Teacher

Ole Petersen International Mentor and the professional leaders of the Academy with the Szent-Györgyi Students

Szent-Györgyi Students

Getting accepted and dropping out:

Students are admitted on the basis of an application and admission process in all four university cities. A prerequisite is that the young person applying to the program must be a first- or second-year student with active student status at Semmelweis University, the University of Debrecen, the University of Pécs, or the University of Szeged. Szent-Györgyi Students are primarily comprised of Szent-Györgyi Pupils. This opportunity is also announced to OKTV's (National Secondary School Academic Competition) podium finishers, thus ensuring geographical openness to the program.

Fluency in English (at least on an intermediate level) is also a prerequisite for successful admission, as well as a serious dedication to biomedical research which is to be expressed in a motivational letter.

At the end of a given academic year, students must report on their scientific progress. After the English-language "Audit" before the scientific committee, a decision is made as to whether the student will remain part of the scholarship program in the following academic year. The place of those who drop out can be taken if another student meets the entry requirements.

Students who have been admitted to the program but do not meet the expectations, or who may, in the meantime, develop in a different direction, will be dropped from the program, but later, e.g. at the beginning of each academic year, it is possible to admit older talents who reapply as academic students.

Benefits:

- Monthly scholarship
- Research opportunities in the laboratories of the best mentors in the country
- Listening to lectures by outstanding international and domestic instructors
- Dormitory accommodation in Szeged
- English language lessons
- Training in presentation techniques
- Communication training

Szent-Györgyi Students and scientific leaders at the Meeting of Nobel Laureates and talented students

THE TEACHERS OF THE ACADEMY

Szent-Györgyi Teaching Staff

The mentoring of secondary school pupils in the national and cross-border secondary school program is carried out by secondary school teachers with the titles of **Szent-Györgyi Senior Teacher** and **Szent-Györgyi Teacher**.

A **Szent-Györgyi Senior Teacher** can be a recognized authority in his region in the field of biology or chemistry education and who has decades of experience in talent development in these subjects. The National Academy of Scientist Education establishes a contractual relationship with the leading teachers who receive the title, thus helping them to devote as much of their time as possible to the organizational tasks of the talent development program. Currently, talent selection is carried out by 24 Senior Teachers covering the 19 national districts.

Their main tasks:

- Visiting partner schools in their region and maintaining continuous contact with the Szent-Györgyi Teachers there.
- Recruitment of the most talented pupils (in natural sciences) of the given region
- Mentoring pupils within their region
- Organization and conduct of laboratory practices and scientific programs for the Szent-Györgyi Pupils belonging to their area
- Participation in spring and autumn Meetings of Nobel Laureates and Talented Students
- Participation in further trainings organized by the NASE
- Recommending pupils to the National Academy of Scientist Education program, organizing, and assisting their participation

Benefits:

- They receive compensation for carrying out their duties

A **Szent-Györgyi Teacher** can be someone who effectively recognizes talents and provides them with additional knowledge in the secondary school where they teach biology or chemistry. Their pupils are regular participants in the National Secondary School Academic Competitions (OKTV), as well as in other international and national competitions, mainly in natural sciences. The faculty of the National Academy of Scientist Education is constantly growing. The Szent-Györgyi Teachers select the young people who get the opportunity to get to know the Academy's program.

Getting accepted and dropping out:

Teachers are selected on the basis of their previous talent management work. Teachers who have been admitted to the program but do not meet the requirements will lose their title and may be replaced by new teachers.

Benefits:

- Participation in further scientific trainings

Szent-Györgyi Senior Teachers with Botond Roska and the professional leaders of the Academy

Laboratory work at the Németh László Secondary and Primary School in Hódmezővásárhely under the direction of a Szent-Györgyi Teacher

Project assignment under the direction of a Szent-Györgyi Senior Teacher

THE MENTORS OF THE ACADEMY

Szent-Györgyi Mentors

The **National Academy of Scientist Education Szent-Györgyi Mentors** are researchers at one of NASE's Scientific Laboratories, who carry out internationally recognized scientific research, lead their own research group, and their publications appear in highly prestigious scientific journals.

Their main tasks:

- Academic mentoring, teaching, and topic management of students admitted to the program
- Giving students the opportunity to get involved in the activities of the research group they lead, providing them with the conditions for high-level research activity
- Holding lectures for secondary school pupils and university students
- Active participation in the seminar series to be organized for NASE students by inviting their renowned foreign collaboration partners (International Mentor)
- Participation and presentations at spring and autumn Meetings of Nobel Laureates and Talented Students
- Promoting the NASE's University Education Program

Getting accepted and dropping out:

Mentors are selected on the basis of their previous scientific or recruitment activities (in a scientific student association). Mentors who have been admitted to the program but do not meet the expectations will be dropped from the program, and new mentors may join the program in their place. The directors of the University Education Program and the Foundation decide on the invitation of mentors.

Benefits:

- They receive compensation for carrying out their duties

A certain amount of the cost of their international partner's (International Mentor) visit to Hungary will be covered in the event that, during their stay in Hungary, the International Mentor gives at least one lecture to Szent-Györgyi Students

Ole Petersen International Mentor (on the left) with the Foundation's scientific supervisors, the title "Excellent Student of the Year 2019" recipient, and the Student's Mentors

Szent-Györgyi Junior Mentors

Szent-Györgyi Mentors have the opportunity to nominate a talented, young researcher working in their laboratory, to become a Junior Mentor of a Szent-Györgyi Student, who will take an active, daily role in their education.

Their main tasks:

- They contribute to the Szent-Györgyi Student's education
- Participation at the spring and autumn Meetin*gs of Nobel Laureates and Talented Students*

Getting accepted and dropping out:

A Szent-Györgyi Junior Mentor must hold a PhD and be nominated by a Szent-Györgyi Mentor. The nomination is examined and approved by the relevant scientific supervisor. Junior Mentors who have been admitted to the program but do not meet the expectations will be dropped from the program.

Benefits:

- They receive compensation for carrying out their duties

Szent-Györgyi International Mentors

A **Szent-Györgyi International Mentor** can be researcher working in a research laboratory abroad, who carries out scientific work of considerable international reputation, leads their own research group, engages in original experimental work, the results of which are published in highly prestigious scientific journals, as well as having a scientific and research relationship (or is planning on developing one) with a Szent-Györgyi Mentor of the NASE.

Their main tasks:

- They get involved in the NASE's talent management activities, which they provide free of charge
- During their stay in Hungary, they give a lecture(s) in one or more NASE Scientific Laboratories and hold discussions with NASE Students
- They undertake the hosting of NASE Students in their own laboratories and research facilities, thus developing the young person's international contact network

Being accepted**:**

International mentors are selected based on their previous academic work. The decision to ask for their participation is decided on jointly by the directors of the University Education Program and the Foundation.

Benefits:

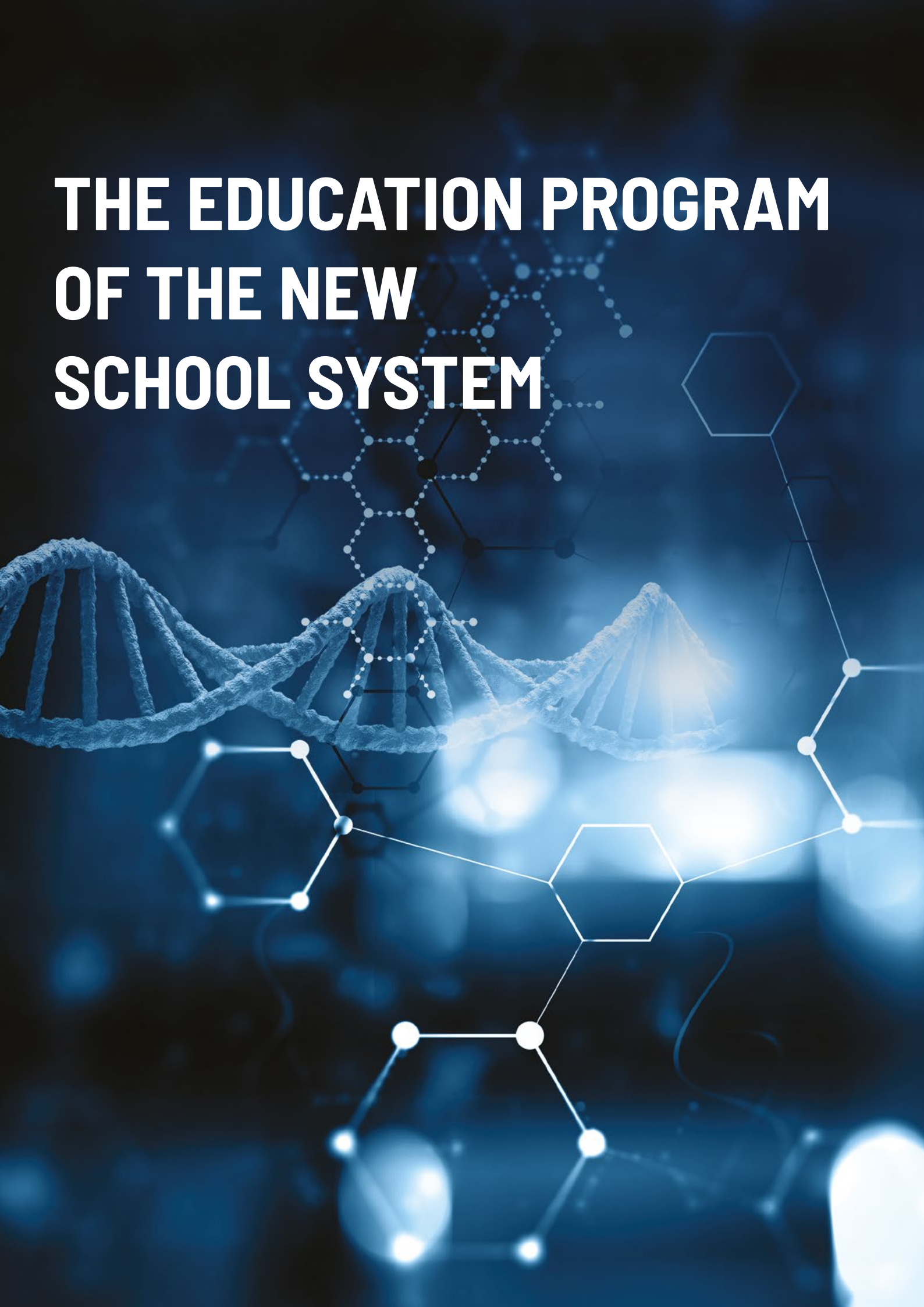
- A certain amount of their expenses when visiting their Hungarian partner (Szent-Györgyi Mentor) will be covered in the event that, during their stay in Hungary, the International Mentor gives at least one lecture to Szent-Györgyi Students
- They can recruit talented young people for their laboratories

András Varró, chairman of the Board of Trustees of the National Biomedical Foundation, and program director Péter Hegyi in front of the picture boards documenting the visits of the Nobel Laureates at the Radnóti Miklós Experimental Grammar School in Szeged

Summary

The future benefits of the new school system are invaluable. It can start a new type of school and communication channels that have not been seen, in the history of Hungarian education, since Kunó Klebelsberg. As the name of the National Biomedical Foundation reflects, the Foundation initially intends to continue its activities in the field of medical biology. In the future, the Foundation also plans to invite leading researchers from other scientific fields (e.g. chemistry, physics, mathematics, social sciences) to the Program in order to introduce them to the secondary school pupils, university students, and teachers of the Academy.

THE EDUCATION PROGRAM OF THE NEW SCHOOL SYSTEM



The program is built into the current school system and provides continuous scientific education for secondary school pupils (Szent-Györgyi Pupils) and university students (Szent-Györgyi Students).

The scientific program of the National Academy of Scientist Education is based on two main elements:

- **Secondary School Education Program**
- **University Education Program**

SECONDARY SCHOOL EDUCATION PROGRAM (SSEP)

Adrien Lengyel, Director of Secondary School Education

The first element of the NASE's education program focuses on secondary school aged pupils. The professional background of the Secondary School Education Program is given on the one hand, by the talent nurturing traditions of biology and chemistry education in Hungary, and on the other hand, represented by successful foreign examples.

The novelty of this initiative, which is unique in domestic talent management, is that it combines the development experience of professionals working in secondary schools with the expertise of university teaching staff. This makes it possible to introduce a new form of education, in which modern scientific content, with the help of the best didactic methods, ensures that hundreds of young, interested pupils can gain insight into the process of cutting-edge biomedical research and those that show some interest can join in as well.

The education plan of the program includes both, independent knowledge processing, group presentations, related discussions, conference participation, and laboratory experiments which can be carried out in several locations.

The process also includes important evaluation steps, as continuous reflections are necessary for the sake of sustainability. The teachers therefore collect the opinions and experiences of the participants after each event. Based on the accumulated information, the education program is reviewed every academic year to ensure its effectiveness by incorporating any modifications deemed necessary.

Round table discussions with the participation of Szent-Györgyi Students and Pupils at a Meeting of Nobel Laureates and Talented Students

CURRENT OPPORTUNITES FOR TALENTED SECONDARY SCHOOL PUPILS

Hungary's education system has a rich history of particularly effective talent management traditions in the fields of mathematics and natural sciences. In addition to the, now commonplace, achievements of Nobel Laureates, this is supported by the fact that talented Hungarian secondary school pupils regularly achieve resounding success in these subjects. The medals won at the International Student Olympiad and the successes in Natural Science and Technical Innovation Competitions all support the effectiveness of these traditions. In the last 8-10 years, it has also become clear that our most successful students are welcomed with open arms by the world's leading institutions of higher education. At the same time, it is also an unfortunate experience that only a small percentage of students who go abroad at this age return to their homeland, so, practically speaking, other countries benefit from the secondary school education of these pupils.

It is also important to note, that the current practices do not effectively ensure that pupils identified as talented in secondary school will have all the opportunities to become successful at university. Students entering higher education – including those who achieve success in secondary school – usually have to start all over again on the path to success. With few exceptions, the number of domestic higher education programs that allow first- and second-year students to get close to research quickly is extremely small. Excellent research ability is usually difficult to measure and recognize, even though some students with such abilities can already be identified in secondary school. The first few years of university represent a kind of loss for these students, as well as for the research groups, who could start collaborating even sooner with students if they had the appropriate preparation and capacity.

THE GOALS OF THE SECONDARY SCHOOL EDUCATION PROGRAM

When defining the goals of the program, in addition to the facts stated above, it is essential to consider the opinions of the leaders of the secondary schools and research groups. The following well-articulated goal system was compiled based on the expressed needs:

To provide an effective alternative to further education abroad

The experience gained in the analysis of the situation led the Foundation's leaders to create a special talent management program for pupils talented in the natural sciences a real viable alternative compared to the opportunities offered by foreign universities, which leads to early emigration. However, this alternative only works if the pupils learn about this option in the early stages of secondary school, before they finally decide which country they will continue their studies in.

The purpose of the program is to offer pupils involved in the system, the university program as a realistic alternative to going abroad, having special educational benefits, as well as financial and intellectual support for committed pupils.

Laboratory demonstration led by a Szent-Györgyi Student at the HUN-REN Biological Research Centre, Szeged

Laboratory visit at the HUN-REN Biological Research Centre, Szeged

Effective aid in biology education at secondary schools

The traditions of secondary school biology education in Hungary can be traced back to the exceptionally thorough work of great forerunners. At the same time, in the last few decades, with the rapid development of the sub-disciplines of biology, Hungarian biology education seems to be lagging behind top international standards. This is primarily due to the fact that the higher education system did not adequately convey the novelties of this dynamically developing science to teaching colleagues who have graduated several years ago. This lag is particularly noticeable in the case of the quantitative analysis methods of biological phenomena and certain topics, such as, molecular biology, neurobiology, cell science, the immune system, etc.

The aim of the educational program is to offer support to secondary school teachers and their pupils.

Community building and social sensitivity

An essential element of the SSEP is to identify talented pupils in places where they have not had the opportunity to join a program of this kind until now. Social equality requires, at least in the field of talent management in biology, that we somehow counterbalance the well-known effects of inequality among Hungarian secondary schools. An important educational goal of the program is also to demonstrate a socially just aspect of research success: the results one can achieve in scientific research are irrespective of gender and ethnic origin. Talented pupils in a given field usually know each other well and form a cooperative community. This confirms to them that what they are delving into is a valuable activity, thus making it possible for them to build a community based on shared values.

The aim of the program is to enforce a socially just worldview and to build a pupil community that shares these values.

Bringing together teachers working in the field of talent management

Based on the information above, perhaps it is obvious that secondary school teachers participating in talent management have a key role to play in ensuring that such a program can have a real impact. Therefore, it is the secondary school teachers that are considered to be the most important strategic partners in the SSEP. They are the ones who arouse interest in young pupils, and they are the ones whose work the program wants to help the most. It is important to emphasize that an essential aspect of the program is that each pupil can develop most effectively in their own school, with the help of their own teacher.

The goal of the program is to build a community of secondary school teachers in order to facilitate their dedicated work.

TRAINING SITES IN THE SECONDARY SCHOOL EDUCATION PROGRAM

The basic training of secondary school pupils takes place in the well-equipped, modern laboratories of the seven National Education Centres and in the twenty one Regional Education Centres.

The 7 National and the 21 Regional Education Centres

National Education Centres

National Education Centres operate in Debrecen, Gödöllő, Hódmezővásárhely, Pécs, Szombathely and two in Szeged. Their scientific work is coordinated by the head of the NEC. Their most important tasks include the management of talented pupils, introduction of new laboratory methods and tests and also the regular education of Szent-Györgyi Senior Teachers.

Schools housing central laboratories

The Specialized Laboratory for Scientific Education (TERMOSZ Laboratory) located at the **Radnóti Miklós Experimental Grammar School in Szeged**, the (SzeReTeD) Laboratory at the **University of Szeged Teacher Training Secondary and Primary School**, the laboratory of the **Nagy Lajos Grammar School of the Cistercian Order** in Pécs, the laboratory of the **ELTE Bolyai János Practice Primary and Secondary Grammar School** in Szombathely, the laboratory of the **Tóth Árpád Secondary School** in Debrecen, the laboratory of the **Premonstratensian St. Norbert Secondary School** in Gödöllő and the József Gyulai Laboratory at the **Németh László Secondary and Primary School** in Hódmezővásárhely all play an important role in the Academy's Secondary School Education concept. The support of the Hungarian government made it possible for the NASE to equip and renovate the laboratories above which are serving also the goals of the Academy. In addition to their core activities, all these secondary school laboratories serve as national centres where pupils from all over the country can conduct complex biological experiments. Furthermore, the teachers actively participating in the program also receive professional trainings in the centres, where they learn the methodology of the modern molecular biology exercises that they later perform with the Szent-Györgyi Pupils. Accordingly, NASE provides the necessary background for carrying out research and teaching tasks. During the school year, the laboratories welcome pupils and teachers who visit for several days.

National Education Centres:

RADNÓTI MIKLÓS EXPERIMENTAL GRAMMAR SCHOOL IN SZEGED
Headmaster: Anett Nagy
Szent-Györgyi Senior Teacher: Andrea Borbola

UNIVERSITY OF SZEGED TEACHER TRAINING SECONDARY AND PRIMARY SCHOOL
Headmaster: János Dobi
Szent-Györgyi Senior Teacher: István Csigér

NAGY LAJOS GRAMMAR SCHOOL OF THE CISTERCIAN ORDER IN PÉCS
Headmaster: Zsolt Nyisztor
Szent-Györgyi Senior Teacher: Eszter Dénes

ELTE BOLYAI JÁNOS PRACTICING PRIMARY AND SECONDARY GRAMMAR SCHOOL IN SZOMBATHELY
Headmaster: Zoltán Csapodi
Szent-Györgyi Senior Teachers: József Baranyai, Bence Farkas Szabó

TÓTH ÁRPÁD SECONDARY SCHOOL IN DEBRECEN
Headmaster: Amália Fenyősné Kircsi
Szent-Györgyi Senior Teacher: József Gőz

PREMONSTRATENSIAN ST. NORBERT SECONDARY SCHOOL IN GÖDÖLLŐ
Headmaster: Borbála Takácsné Elek
Szent-Györgyi Senior Teachers: Zoltán Kerényi, Zsolt Horváth

NÉMETH LÁSZLÓ SECONDARY AND PRIMARY SCHOOL IN HÓDMEZŐVÁSÁRHELY
Headmaster: László Árva
Szent-Györgyi Senior Teacher: Edit Csaláné Böngyik

Regional Education Centres:

BATTHYÁNY LAJOS HIGH SCHOOL IN NAGYKANIZSA
Headmaster: László Györek
Szent-Györgyi Senior Teacher: József Tulok

BOLYAI FARKAS HIGHSCHOOL TARGU MURES
Headmaster: Zoltán Hajdú
Szent-Györgyi Senior Teacher: Éva József

CALVINIST GRAMMAR SCHOOL OF KECSKEMÉT
Headmaster: Anna Durucz
Szent-Györgyi Senior Teachers:
Adrien Lengyel, Anna Nagy

DEÁK TÉRI LUTHERAN GYMNASIUM BUDAPEST
Headmaster: Edit Gadóné Kézdy
Szent-Györgyi Senior Teachers:
Andrea Fazakas, Zsolt Horváth

DOBÓ ISTVÁN HIGH SCHOOL IN EGER
Headmaster: Krisztián Berkes
Szent-Györgyi Senior Teacher:
Krisztina Veresné Kis

ELTE BOLYAI JÁNOS PRACTICING PRIMARY AND SECONDARY GRAMMAR SCHOOL IN SZOMBATHELY
Headmaster: Zoltán Csapodi
Szent-Györgyi Senior Teachers:
József Baranyai, Bence Farkas Szabó

ELTE TREFORT ÁGOSTON SECONDARY GRAMMAR SCHOOL – BUDAPEST
Headmaster: Zoltán Csapodi
Szent-Györgyi Senior Teachers:
Norbert Faragó, László Kutrovácz

FAZEKAS MIHALY PRIMARY AND SECONDARY GRAMMAR SCHOOL – BUDAPEST
Headmaster: Zsolt Erős-Honti
Szent-Györgyi Senior Teachers:
Zsolt Erős-Honti, Julianna Erős-Honti

FÖLDES FERENC HIGH SCHOOL – MISKOLC
Headmaster: Róbert Fazekas
Szent-Györgyi Senior Teacher: Csilla Szentesi

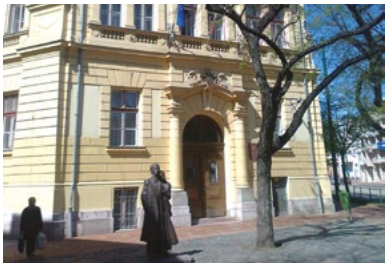
GÖDÖLLŐ REFORMED SECONDARY SCHOOL
Headmaster: Árpádné Bajusz
Szent-Györgyi Senior Teacher: Zsolt Horváth

LOVASSY LÁSZLÓ GRAMMAR SCHOOL – VESZPRÉM
Headmaster: Zoltán Schultz
Szent-Györgyi Senior Teacher: Tünde Szalainé Tóth

NAGY LAJOS GRAMMAR SCHOOL OF THE CISTERCIAN ORDER IN PÉCS
Headmaster: Zsolt Nyisztor
Szent-Györgyi Senior Teacher: Eszter Dénes

NÉMETH LÁSZLÓ SECONDARY AND PRIMARY SCHOOL IN HÓDMEZŐVÁSÁRHELY
Headmaster: László Árva
Szent-Györgyi Senior Teacher: Edit Csaláné Böngyik

PREMONSTRATENSIAN ST. NORBERT SECONDARY SCHOOL IN GÖDÖLLŐ
Headmaster: Borbála Takácsné Elek
Szent-Györgyi Senior Teacher: Zoltán Kerényi



RADNÓTI MIKLÓS EXPERIMENTAL GRAMMAR SCHOOL IN SZEGED
Headmaster: Anett Nagy
Szent-Györgyi Senior Teacher: Andrea Borbola

SZÉKESFEHÉRVÁR TELEKI BLANKA HIGH SCHOOL AND PRIMARY SCHOOL
Headmaster: Anikó Ráczné Kálmán
Szent-Györgyi Senior Teacher: Ildikó Kiss

TÁNCSICS MIHÁLY SECONDARY GRAMMAR SCHOOL OF KAPOSVÁR
Headmaster: László Vámosi
Szent-Györgyi Senior Teacher: Beatrix Bagi Kertész

TÓTH ÁRPÁD SECONDARY SCHOOL IN DEBRECEN
Headmaster: Amália Fenyősné Kircsi
Szent-Györgyi Senior Teacher: József Gőz

RÉVAI MIKLÓS HIGH SCHOOL AND COLLEGE – GYŐR
Headmaster: Péter Horváth
Szent-Györgyi Senior Teacher: József Bacher

UNIVERSITY OF SZEGED TEACHER TRAINING SECONDARY AND PRIMARY SCHOOL
Headmaster: János Dobi
Szent-Györgyi Senior Teacher: István Csigér

VARGA KATALIN SECONDARY SCHOOL, SZOLNOK
Headmaster: László Molnár
Szent-Györgyi Senior Teacher: Marianna Jeneiné Fekete

Regional Education Centres (Base Schools)

Within the NASE's Secondary School Education Program, the country is divided into 19 areas, fully covering the country. In addition, there is also a centre in Târgu Mureș, Romania. Each region belongs to a Regional Education Centre, which is under the direction of a Szent-Györgyi Senior Teacher, who, in addition to their daily work, deals with the promotion of the SSEP and the organization of local programs. The Senior Teachers maintain direct contact with the pupils belonging to the areas.

The Senior Teachers, who carry out regional coordination, regularly participate in specialized trainings, where they discuss current organizational issues and share good practices with each other, with the help of which, they can carry out development activities in their own regional centres. During the trainings, they also learn the methodology of the modern molecular biology experiments that they will have their pupils perform.

Partner schools

The priority of the Foundation is to support the talent development process in its natural environment, in secondary schools. To this end, it is essential to establish a partnership with the teachers of talented pupils, which includes recognition of their achievements and respect for the significant amount of extra work devoted to their talent management. An important part of the partnership is the fact that, along with the pupils, their teachers are also invited to every event, because the shared learning experience enables the creation of a mutually motivating situation. Being awarded the title of Szent-Györgyi Teacher in and of itself is serious incentive for secondary school teachers, as is participation in Nobel Laureate conferences, as well as access to the teaching materials and methodological guidance of the SSEP, the express purpose of which are to support the methodological development of biology education in Hungary within its own framework.

Through regular secondary school activities, pupils can get to know the outstanding scientific results of the higher education institutions participating in the national program (Budapest, Debrecen, Pécs, Szeged), all in the hopes that interested pupils will eventually choose one of these institutions as a destination for their further education and thus their development will be continuous.

Szent-Györgyi Pupils in the laboratory of a Szent-Györgyi Mentor

THE ACTIVITIES OF THE SECONDARY SCHOOL EDUCATION PROGRAM

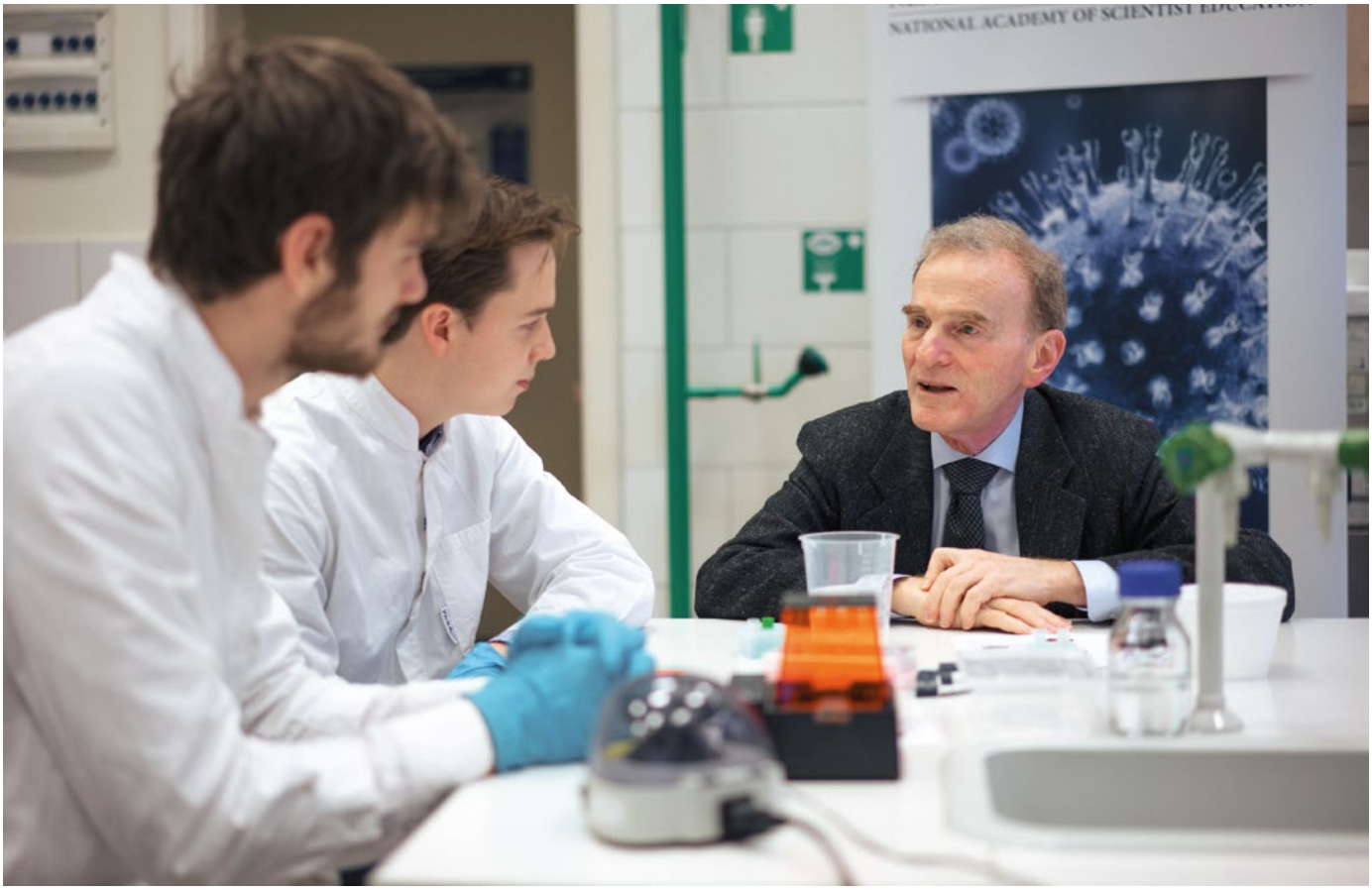
The activities of the Program were designed in such a way as to, as much as possible, achieve the set goals. The activities include theoretical education based on pupils' independent learning and group work, but great emphasis is placed on the development of practical skills. Some of the activities can be done from home, while other forms of education take place in the regional or national centres. The common goal of all activities is to impart, with the help of the most modern pedagogical methods possible, valuable knowledge that is difficult or not able to be obtained within the framework of normal public education. The content of this imparted knowledge will contribute to successful research in the future.

Processing of online course material

It's impossible to imagine modern education without online elements. eLearning gives pupils the opportunity to progress through a topic at their own pace. In order to help facilitate this, a series of teaching materials has been developed to supplement school studies, which ensure the uniformity of requirements, but at the same time also supports individual learning styles. Each topic elaborated on begins with a short theoretical summary in Hungarian, using technical terms, which is supplemented by diagrams that facilitate understanding. In addition to this, for every topic, we offer free access to English language animations and videos to process the material. Pupils also have access to multiple English language scientific publications related to each topic. Comprehension is measured by an evaluating method developed by the Szent-Györgyi Senior Teachers, on the basis of which pupils can proceed.

The range of topics is constantly expanding, so far, the following eight topics have been elaborated on:

- Basic neurological phenomena (with particular regard to processes at the cellular level)
- Membrane transport processes and channel types
- The structure and functioning of the immune system, immunological methods in biological research
- Spectroscopic methods in biomedical research
- Cellular biology (cell membranes, vesicular transport, cytoskeleton)
- Cardiology (especially in regard to the examination of heart function)
- Biomathematics and bioinformatics
- Signal transmission processes



Randy Schekman Nobel Laureate scientist at the SZeReTeD laboratory (University of Szeged Teacher Training Secondary and Primary School)

Laboratory experiments

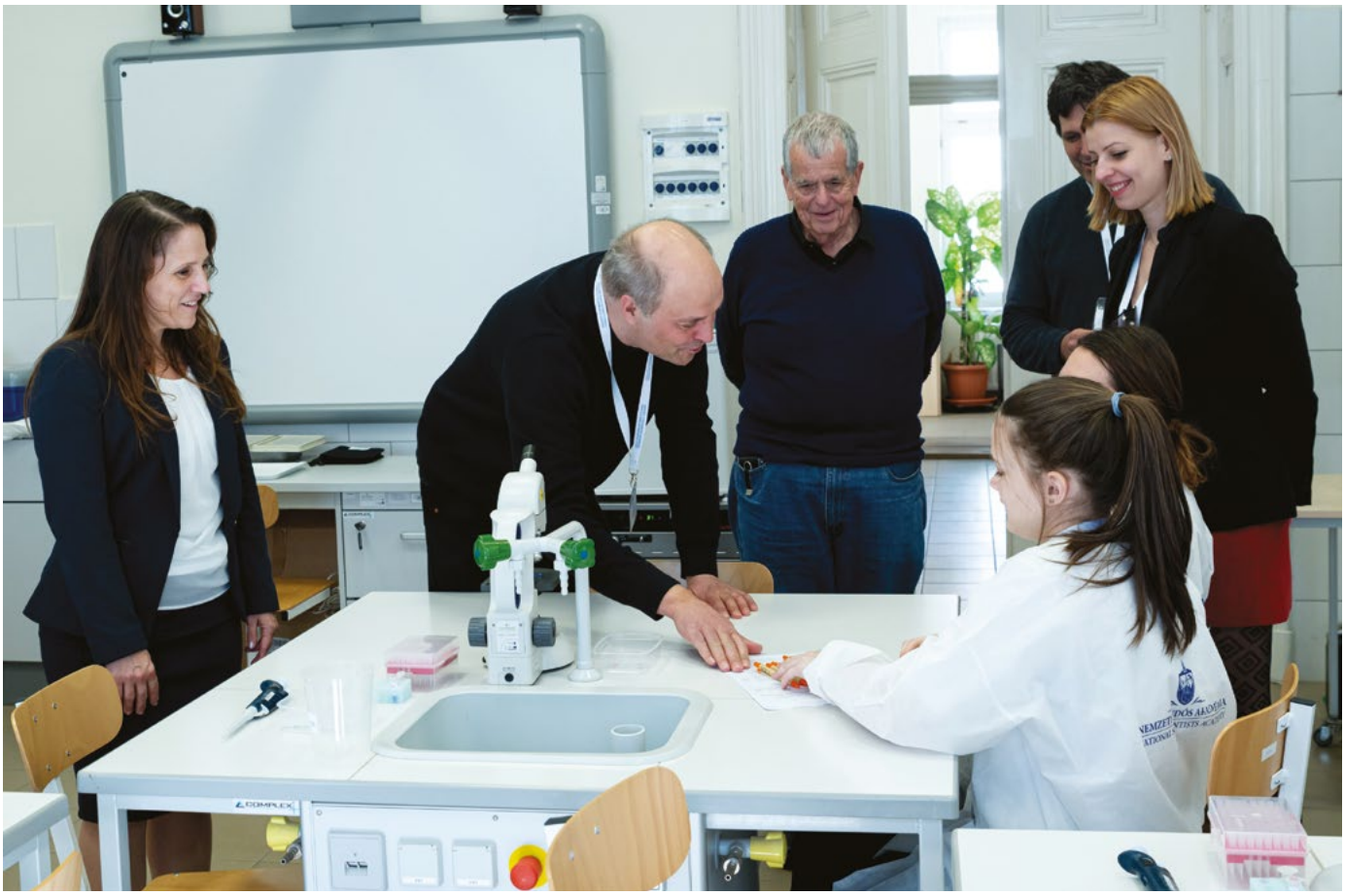
Biomedical research is largely experimental work. Pupils who are, at the very least, familiar with the basic methods of modern laboratories will be able to effectively participate in the experimental work. That is why practical preparation also plays a prominent role among the goals of the SSEP. The program's activities include two types of experiments: experiments that develop basic laboratory skills and multi-day projects.

The experiments that develop basic laboratory skills are organized and overseen by the Senior Teachers in the laboratories of the Regional Education Centres. The Senior Teachers acquire the scientific background and teaching methodology of these practices as part of specialized training courses. Acquiring the equipment needed to carry out these experiments - which is lacking most Hungarian secondary schools – results in a drastic improvement in Hungarian biology education as a whole. As a result of continuous investments, basic molecular biology experiments can be carried out at base schools for groups of up to 30 pupils at a time. Basic practical knowledge of current research includes the use of automatic pipettes, gel electrophoresis equipment, spectrophotometer upon which the correct interpretation of the information can be obtained. The transfer of this practical knowledge is practically absent from Hungarian secondary school education due to a lack of knowledge and financial resources. That is why the development of the basic molecular biology equipment of Regional Education Centres is considered an essential development in the national public education system. Not only does the NASE provide the equipment and material required for these experiments, but also the methodological knowledge necessary for their completion (in the form of workbooks and teacher's workbooks).

The content developed for the second academic year is a curriculum system which includes a theoretical introduction, tests to check their mastery, every step of the way, from preparation to execution.

Topics of experimentation to be introduced in the Regional Education Centres:

- Basics of restriction analysis; Analysis of λ-phage genetic material
- DNA investigation via PCR reaction
- Expression of GFP fluorescent protein in model organisms
- Human genetic analysis by examining the PV92 DNA segment
- Spectrophotometric protein content determination using the Bradford method



Aaron Ciechanover (in the middle) Noble Laureate scientist and Michael Brecht (on the left) German neurobiologist visiting the laboratory practice at Radnóti Miklós Experimental Grammar School in Szeged

After getting familiar with the simple methods, the pupils' knowledge becomes suitable for carrying out complex, multi-step experiments which model research processes. The short-term goal is that these experiments will be carried out, over the course of several days, by groups of pupils in the laboratories of the National Education Centres. During the development of these exercises, the emphasis was not on teaching technical execution - as the pupils who came here had already mastered it in the Regional Education Centres - but on modeling the real research process. The goal is for the pupils to be able to carry out every step of a research sub-process on site, so that they can get to know the complex process of biological research.

The complex exercises are organized around the following topics:

- The diverse application possibilities of chromatography in biological research
- Protein detection in biological research
- Complex examination of bacterial protein production
- The possibilities of using the PCR method in biological research
- Dissection and histological experiments on vertebrae organs
- Enzyme kinetic examinations

Group development programs performed in Regional Education Centres

As previously stated, Szent-Györgyi Senior Teachers working in the Regional Education Centres, play a key role in the operation of the SSEP. These occasions provide an opportunity to gather pupils from each region and have an invited Szent-Györgyi Mentor or a Szent-Györgyi Student tell them about their own research. The processing of the research report can be supplemented by a group discussion. The Senior Teachers also have the opportunity to lead other types of group sessions based on their own experience, where they present calculations or the method of essay writing to the pupils. These occasions also offer the opportunity for pupils from the same region to get to know each other and form their own communities and friendships.

Erwin Neher (who, along with Bert Sakmann, won the Nobel Prize in Medicine in 1991) and Eva-Maria Neher at TERMOSZ Laboratory (Radnóti Miklós Experimental Grammar School, Szeged)

Participation in the "Meeting of Nobel Laureates and Talented Students" conferences

In the spring and autumn of each academic year, the National Biomedical Foundation, which implements the NASE Program, organizes a conference, to which, primarily, secondary school pupils are invited.

At the spring conference, the organizers give priority to the applications of those 10th grade pupils that want to take part in the conference. At these events pupils, through the interpretation of Szent-Györgyi Students, can learn about ongoing research and their results, which, at the same time create an opportunity for secondary school pupils to get a firsthand view of the university program. The spring events also provide an opportunity to get to know the cultural diversity of the host cities, while at the same time, the secondary school central laboratories are open to guests.

The autumn conference is mainly attended by upper-year pupils (primarily 11th and 12th year) who are close to choosing a career. Accordingly, as part of the official conference program, in small groups, pupils will also have the opportunity to visit the laboratories of the Szent-Györgyi Mentors of the University Education Program accompanied by Szent-Györgyi Students, so they can see, up close, the research being carried out there. In these encounters, the pupils' questions can be answered directly by the Szent-Györgyi Mentors and Szent-Györgyi Students present.

Summer camp for young researchers

Every summer, the best performing secondary school pupils can spend a week in Szeged at a professional camp organized by the Academy, where they can join the Szent-Györgyi Mentors' research teams working in the laboratories of the University of Szeged and the HUN-REN Biological Research Centre Szeged. They also have the opportunity to participate in a variety of cultural, recreational and other professional activities during the week.

Summary

During the development of the Secondary School Education Program, the aim has always been to provide secondary school pupils and their teachers with a diverse range of modules. The offered forms of education make it possible for pupils to add valuable information to the knowledge and skills they have learned in secondary school with the help of state-of-the-art equipment and modern teaching methods.

Bert Sakmann Director General of Education (pictured second from right) at the Meeting of Nobel Laureates and Talented Students

University Education Program (UEP)

The primary task of the National Academy of Scientist Education is to provide world-class training for future researchers in Hungary. The NASE actively helps university students, from Budapest, Debrecen, Pécs, and Szeged, who are committed to science, to develop, starting in their first year, their scientific interests and enable them to get involved in scientific projects at the highest level. The NASE considers the front line of science as its reference point and sets the goal of reaching and surpassing it for its students and mentors.

At the same time, the aim of the Academy is, emphatically, not to support the cultivation of science at an average level, nor to assist studies that are part of university education. The education in the program actively complements university studies and the goal is that time spent in the laboratories of Szent-Györgyi Mentors be recognized by the universities in the form of credit points.

The education within the NASE is based on the concept of providing its students with medium and long-term scientific development starting in their university years and, optimally, getting students to the point where they are independent, research group leaders who are resource independent which, as reference, is imagined at the level of MTA Lendület and ERC Starting Grant winners. To encourage this, the long-term goal of the NASE is to provide competitive scholarships at all stages of a scientist's career (BSc, MSc, MD, or PhD student, Postdoctoral and Senior Researcher) that are superior to any alternative supported by the public sector in Hungary.

Zoltán Rakonczay,
Director of University Education

THE UNIVERSITY EDUCATION PROGRAM'S PARTNER INSTUTITIONS

The education of university students takes place in four Hungarian cities, in a total of six partner institutions, which are the following:

The NASE's Scientific Partner Institutions

University of Debrecen

With its uninterrupted history of more than four and a half centuries, the University of Debrecen is today the country's oldest continuously operating institution of higher education in the same city, and having one of the largest domestic educational complexes, it is a prominent player in the Hungarian higher education system. It also has outstanding education, research, innovation capacities and scientific results at the international level, based on which, it plays a significant role in the implementation of national strategic goals, and is also one of the 500 best universities in the world. The student community of nearly 30,000 students can increase their knowledge in 14 faculties at an institution that exhibits serious professional values. As a university of science, it has become known as an intellectual centre with the widest vertical training in Hungary, which takes part in the private sector, business life, and the socio-economic life of the local government.

University of Debrecen

The Institute of Experimental Medicine (Budapest)

The Institute of Experimental Medicine (KOKI) was founded in 1952 with the aim of carrying out high-quality research work in the field of medical sciences. By the early 2000s, the Institute had developed into one of the leading neuroscience centres in Central Europe. The focus of KOKI's activities is basic and translational research in neuroscience. The primary goal of the Institute is to contribute to the general understanding of the functioning of the nervous system, the protection of human health, more effective treatment of nervous system diseases and the development of modern technologies in all areas of neuroscience. In recent years, KOKI has been extremely successful in obtaining prestigious foreign financial resources such as the European Research Council (ERC), Howard Hughes Medical Institute or the Wellcome Trust grants. All of which have greatly contributed to the creation of new technologies and many central research units. In many cases, the discoveries made by the Institute's research groups have been published in leading scientific journals, such as Science, Nature, Nature Neuroscience or Neuron. The Institute is also dedicated to education and the training of up-and-coming researchers, which is why the Institute jointly operates a neuroscience doctoral school together with Semmelweis University.

Institute of Experimental Medicine

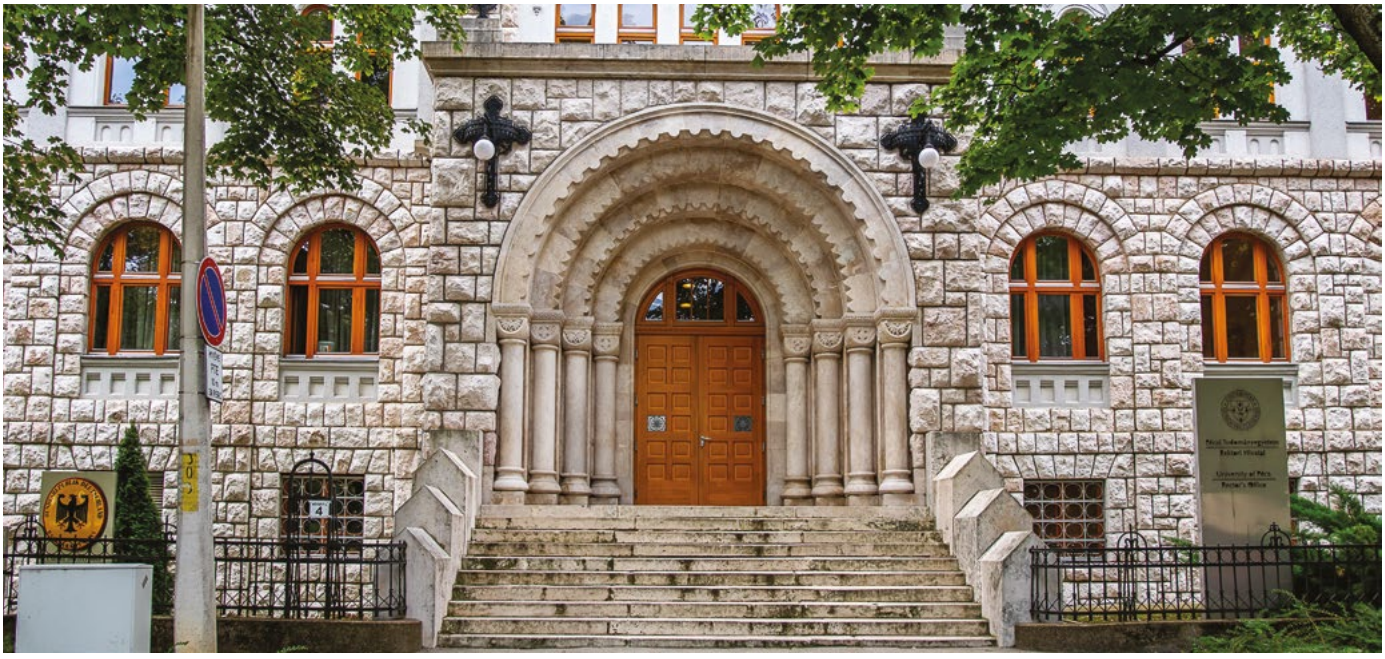
Semmelweis University (Budapest)

The more that 250-year-old Semmelweis University, which is unique in the country as a specialized university, is the leading institution of medicine and health higher education, not only in Hungary but also in the Central European region. It's three main activities are education, research-innovation, and healing; these three things make it an internationally recognized centre of knowledge. Most doctors, dentists, pharmacists, and midwives in Hungary have graduated from Semmelweis University, which is also one of the most internationally diverse universities in the world; a third of the more that 12,000 students are foreigners, coming from 97 countries around the world. Most of the country's academics work here in either the field of medicine or biomedicine, and many pioneering medical procedures were performed here in the country for the first time. The university is one of the most successful Hungarian players in international rankings: in the 2022 overall world ranking of Times Higher Education (THE), it is among the top 300 universities in the world, but it is also among the best in specialized rankings. The university is not only one of the largest healthcare institutions in the country, but it is also home to the largest number of research groups supported by the Hungarian Academy of Sciences and the National Research, Development and Innovation Office: around 300 university research groups operate here, and their research is supported by 46 international and 263 domestic grants. There are 8 doctoral schools operating at the university, and more than a thousand students are members of its Scientific Students Association.

Semmelweis University

University of Pécs

The history of higher education in Pécs dates back to 1367, when our King, Louis the Great, initiated the creation of a university in the episcopal capital, Pécs. As a result of a multi-stage integration process, the University of Pécs was created, which has now become one of the country's most famous universities with a regional leadership role. The university's 10 faculties and research centre provide high-quality education across the entire spectrum of higher education fields, 18 vocational colleges and 21 doctoral schools offer 300 courses for nearly 20,000 students. The university does a lot to ensure that it is not only an optimal choice for its talented researchers as a starting point, but also as a workplace. Its Clinical Centre is one of the largest healthcare providers in Hungary. Its three main activities are healing, education, and scientific research. The presence of a large number of Hungarian and foreign students, along with the Mediterranean atmosphere make Pécs a pleasant, bustling, and lively university city.



University of Pécs

HUN-REN Biological Research Centre Szeged

The defining institution of internationally recognized Hungarian life science research is the HUN-REN Biological Research Centre, Szeged (BRC). The four institutes of the BRC, founded in 1973 – the Institute of Biophysics, Biochemistry, Genetics and Plant Biology – employs around 260 researchers, whose work is characterized by numerous prestigious international scientific publications and patents. The researched topics cover many areas of molecular and cellular biology, which range from the industrial utilization of bacteria to the controlled breeding of cultivated plants as well as to issues of human health and environmental protection. The BRC is mainly a laboratory for basic scientific research, but BRC researchers play a prominent role in initiating the creation and management of biotechnological enterprises, as well as in performing educational tasks. The efficient operation of the BRC and the high quality of research were recognized by the European Molecular Biology Organization (EMBO) and the Centre was awarded the title of Centre of Excellence of the European Union in 2000.

HUN-REN Biological Research Centre Szeged

University of Szeged

University of Szeged

Committed to quality higher education, the University of Szeged (SZTE) is one of Hungary's leading universities. The University of Szeged was established on January 1, 2000, via the integration of the József Attila University of Szeged, the Szent-Györgyi Albert Medical University, the Szeged Food Industry College, the Juhász Gyula Teacher Training College, and the Hódmezővásárhely Agricultural College. SZTE offers hundreds of bachelors, masters, and doctoral programs, higher education vocational training, specialized trainings, and adult education programs for students and those who wish to learn. With nearly 25,000 students and around 7,000 employees (of which 2,400 are lecturers/researchers), SZTE is one of the largest organizations in the Southern Great Plain Region. Education and research are carried out at the university's 12 faculties, and health care is the responsibility of the Szent-Györgyi Albert Clinical Centre. The mission and goal of SZTE is to cultivate internationally competitive science and research and to ensure the spirit of a research university.

Meeting of Nobel Laureates and Talented Students

The common work takes place in the best-equipped laboratories at all six locations under the guidance of the best mentors (Szent-Györgyi Mentors). In each research laboratory, a group of mentors awaits students, who will, along with their university studies, also start research work in the given city.

Mentors play the most important role in the training of **Szent-Györgyi Students.** When entering the program, they all choose a Szent-Györgyi Mentor, whose research laboratory they join and participate in the ongoing work there. **Junior Mentors**, who are researchers with a doctorate degree and also work in the Mentor's laboratory, assist the Szent-Györgyi Students with their daily tasks. The **International Mentors** are internationally recognized scientists who have a close scientific and research relationship with the Szent-Györgyi Mentors.

The Bert Sakmann Dormitory

The Bert Sakmann Dormitory

The aim of the Academy is to ensure that the program's conditions meet high professional expectations, and that those participating in the program are placed in a highly motivating, quality environment.

This idea has already been realized in Szeged when the NASE's first dormitory – the **Bert Sakmann Dormitory** – was opened in the spring of 2022. In addition to several student rooms, there is also an international mentor room, where Nobel Laureates and other internationally renowned mentors can comfortably spend time in the company of young people. In addition to these rooms, a community and educational space has been created, where cultural programs, professional forums and trainings are organized for the students of the Academy. The aim of the Academy is to educate broad-minded intellectuals who, in addition to their excellent professional knowledge, will be useful members of society.

In the summer of 2022, Professor Bert Sakmann donated the original duplicate of his Nobel Prize medal and diploma to the Academy, which are exhibited in the dormitory named after him, to the delight of the visitors and the students living there.

An original duplicate of Bert Sakmann's Nobel Prize medal and diploma

OVERSIGHT OF THE ACADEMY'S UNIVERSITY EDUCATION

The oversight of the Academy's university education is provided by the **Board of Trustees** of the National Biomedical Foundation, the general director of education (**Bert Sakmann**, Nobel Prize-winning German physiologist), **the director of university education**, and the **six scientific supervisors** who oversee the six Scientific Laboratories which operate in the four university cities.

The director of education makes a proposal on the method of education, is in daily contact with the professional leaders, helps in the selection of Mentors, and participates in the Meetings of Nobel Laureates and talented students.

Students and Mentors keep in touch with the scientific supervisor overseeing the work in the given city.

The scientific supervisors coordinate the professional activities of the students and the mentors working in the Scientific Laboratories that they supervise. With their advice, they promote scientific cooperation between laboratories with different instrumentation and methodological preparation that train students.

The scientific supervisors visit the students and their mentors at their research site once per semester. The visits for the second semesters also serve as a meeting to prepare their annual work reports. Based on a comparison of the annual written and oral reports (Audit) and the system of requirements, the directors of the NASE make an annual proposal for every student and mentor as to the further payment of the scholarship and the mentor's honorarium, or its suspension or termination.

Szent-Györgyi Students with Botond Roska and the Academy's scientific supervisors

ADMISSION TO THE UNIVERSITY EDUCATION PROGRAM

Every academic year, the NASE advertises admissions to its Scientific Laboratories. The requirement for applying is that the student have active student status at an institution of higher education included in the program.

Students admitted to the program are selected in three ways:

First- or second-year undergraduate students at the University are admitted to the first year of the NASE program through an entrance exam. During the multi-step process, the examination board assesses the students' mental readiness, creativity, scientific problem-solving ability, and English language skills. The exam is organized and administered by NASE's directors responsible for secondary school and university education. To assess the candidates' English language skills, a professional English language teacher can be called in to help. The best performing students are then invited to participate in the NASE program.

The NASE also welcomes the applications of undergraduate students with scientific interests studying in the upper years of university. 2nd to 6th year undergraduate students must prove their record of excellence in scientific research in comparison with the best of their contemporaries in order to be awarded a NASE scholarship. This presupposes particularly successful participation in local and national Scientific Student Associations (SSA), as well as first and/or co-authorship in scientific publication(s).

SCIENTIFIC LABORATORY WORK

The placement of students admitted to the NASE Scientific Laboratories is coordinated and supervised by the scientific supervisors of the NASE. Students are obligated, within 3 months of admission, to discuss their selected academic topic as well as their chosen Szent-Györgyi Mentor with the scientific supervisors.

The aim of the program is for the Szent-Györgyi Mentors and the Junior Mentors to actively help the students, on a daily basis, acquire necessary laboratory skills. International Mentors (recognized researchers who publish their results in the highest quality journals) also play an important role in the training process. The short-term goal is for the international mentors to regularly take turns participating in the work of the NASE's Scientific Laboratories and dormitories, and to give lectures to the students, after which it is possible to have conversations with them.

THE NATIONAL ACADEMY OF SCIENTIST EDUCATION'S REQUIREMENTS FOR BSC, MSC AND MD STUDENTS

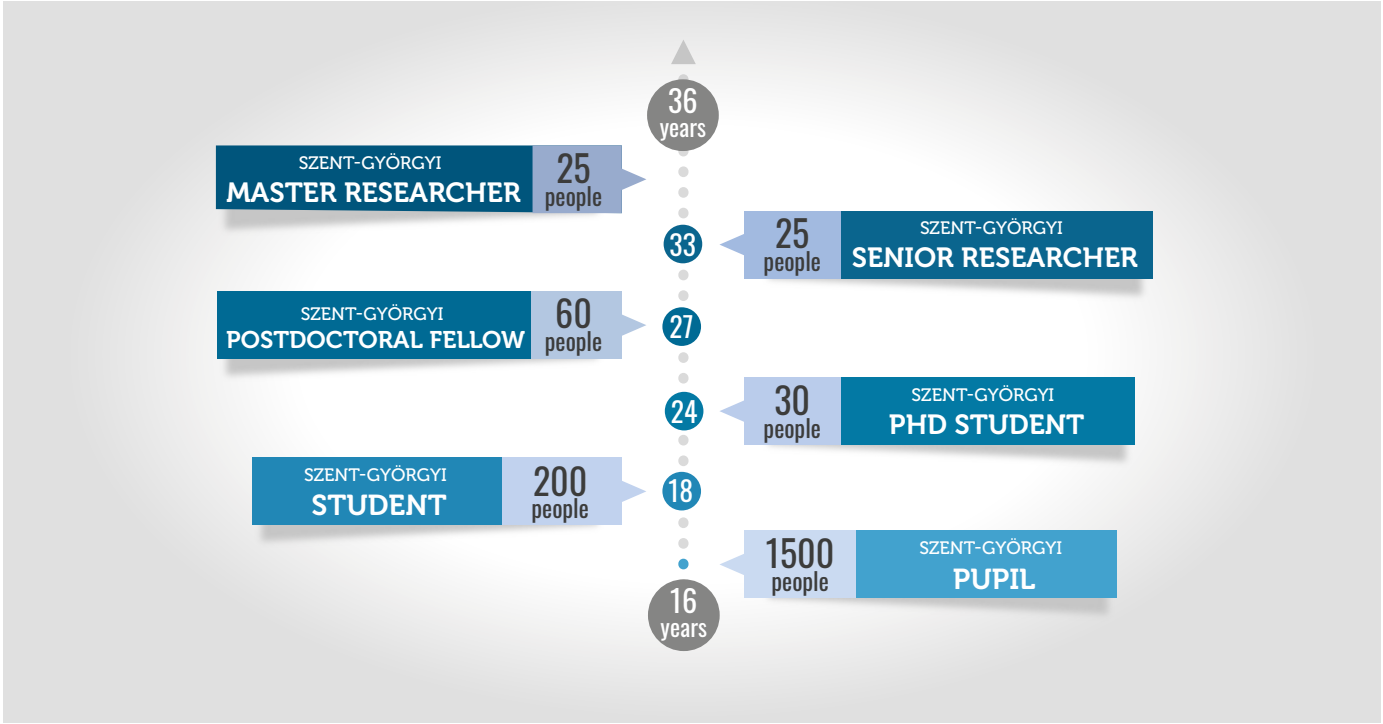
NASE Students focus on their university studies in the mornings, while in the afternoons and evenings they engage in laboratory work and have discussions with International Mentors.

Students receiving a scholarship are required, by end of the third year, to achieve co-authorship in at least one original article which is published in a journal belonging to the top 25% of the given field of study, which they must present at either a domestic or international SSA conference.

By the end of the sixth (MD) or fifth (MSc) year, it is necessary to author an article with first authorship in a journal belonging to the top 25% of the given field of study, which in most of our doctoral schools may already be formally sufficient to submit as a PhD dissertation. Accordingly, the system of requirements helps provide a MD-PhD MSc-PhD equivalent qualification during an MD/MSc education. As an alternative, the students' first author publication can be replaced by a publication with an impact factor of over 10, in which he/she is listed as a co-author and verifies his/her own results/work added to the creation of the publication in a creditable manner.

CAREER MODEL AT THE NATIONAL ACADEMY OF SCIENTIST EDUCATION

The Foundation is currently able to finance the program until the Szent-Györgyi PhD student level is reached (Szent-Györgyi Student graduates). Further stages of the career model can only be achieved with the involvement of new financial resources.



School System – The long-term plans of the National Academy of Scientist Education Program

Anna Georgina Kopasz, winning the title of the „Excellent Student of 2022". In the picture (from left to right): Péter Hegyi, Lajos Mátés, András Varró, Botond Roska, Anna Georgina Kopasz

Szent-Györgyi Student

Students admitted to the National Academy of Scientist Education receive a monthly scholarship. Students who successfully meet the above requirements will receive a certificate upon graduation. Students with a certificate can apply for the next stage or to the university's doctoral school, for PhD student status.

Szent-Györgyi PhD Student

In the first round, Szent-Györgyi Students who have received a certificate are most likely to be admitted to the PhD program of the Academy. In the longer term, the goal of the NASE is for these students to be automatically admitted to the doctoral schools of the universities. The remaining places are advertised by the NASE and filled via an application process. An applicant coming from outside the NASE program may join the scholarship system if they have published at least 2 articles in journals belonging to the top 25% of the given scientific field (in one of which they must be the first author). Students who enter the school at this level are no longer under „publication pressure" since they already meet the PhD conditions upon admission. For this reason, they can join a major, relatively long-term project which may take several years to complete. At this stage, Szent-Györgyi Students can focus on high-quality research that is exceptional, even by international standards, and also particularly beneficial to the laboratory.

The researcher must attend at least one international conference a year, and both Mentor and Student must submit a report at the end of the year. At the end of each year, the scientific supervisors along with the Board of Trustees decide whether the PhD student will retain their scholarship in the following year.

Within the four-year scholarship period, the PhD student must publish at least three articles with an IF of 5 or more, of which in at least one they are the first author. In the event that the PhD student fails to meet this criteria, they may request an extension from the Director of University Education but they must provide a detailed reason. The deadline for completion may be extended for up to 2 years but no scholarship will be given during this time. PhD Students who successfully meet the requirements will receive a certificate at the end of their PhD training.

Szent-Györgyi Postdoctoral Fellow

The postdoctoral program works on a 6-year cycle, of which the researcher spends 3-4 years in a domestic research laboratory and 2-3 years in a foreign one. The Mentor and the Postdoc can decide together which part of the cycle he/she will spend abroad. A foreign facility can only be chosen as a research site if the Board of Trustees has previously included it among the accepted foreign research laboratories (which are typically published in multidisciplinary journals). While doing their research in Hungary, the postdoctoral fellow must win an independent research grant (e.g. NRDIO).

The purpose of this period is for the Postdoctoral fellow to become independent within the 6 years and gain experience abroad that they can later assimilate at home, ideally at the same level (as a Szent-Györgyi Senior Researcher) or at the cutting edge of a particular specialized field (as a Szent-Györgyi Master Researcher).

Getting accepted and dropping out:

Szent-Györgyi PhD Students are admitted into the program in the first round. It is possible to join the program during one's studies if there is a vacancy and the candidate meets the criteria described above. The Postdoc fellow must participate in at least one international conference a year and the end of the year both Mentor and Postdoc fellow must submit a report. It is at this point that the International Mentor gets involved in the training, and thus the report must be written by all three people.

At the end of each year, the scientific supervisors along with the Board of Trustees decide whether the Postdoctoral fellow will retain their scholarship in the following year. A new student may take the place of a Postdoc who drops out of the program, provided they can meet the standards.

In six years, the researcher must publish at least three articles with an IF of above 8, of which he/she is the first author in at least one. If the Postdoc fellow does not satisfy the criteria he/she may request an extension, with detailed reasons, from the Board of Trustees. The deadline can be extended for up to three years but during that time the NASE does not provide a scholarship for that period. Postdoctoral fellows who successfully meet the criteria will get a certificate at the end of their training.

Szent-Györgyi Senior Researcher and Master Researcher

Szent-Györgyi Senior researchers and Szent-Györgyi Master researchers have at least 15 years of experience in high quality research and have received professional training at outstanding domestic and international laboratories.

Goal:

For those with serious research potential to strengthen either Hungarian scientific life or the Hungarian industrial research sector, as well as participate in the education of the next generation.

Getting accepted and dropping out:

The Master researcher or Senior researcher scholarship begins when the candidate meets the given requirements.

The title of Master researcher is conferred on those who have published articles in famous multidisciplinary newspapers (e.g., Science, Nature) as corresponding author based on research conducted in a Hungarian centre.

The title of Senior researcher is conferred on those who have published in leading specialized journals (e.g., Gastroenterology, Circulation) as corresponding author based on research conducted in a Hungarian centre. The scholarship can be awarded for up to 3 years from the publication of the given article, if the researcher in question demonstrates that he/she is conducting research which may potentially be accepted for publication in a journal of similar rank. If, during the three years, the researcher wins a substantial amount of money from an international grant (e.g, European Research Council or the Wellcome Trust), the scholarship can be extended for another 2 years.

The Senior researchers and Master researches are expected to act as Mentors at NASE, while their laboratories function as part of the program. If the researcher fails to present a publication of similar rank or to win a major grant in three years, the scholarship will cease until the candidate satisfies the above requirements.

The NASE seeks, primarily, to continue to support PhD students, Postdoctoral fellows and Senior or Master researchers from those previously supported undergraduate students to validate its educational model, however, it also considers researchers of exceptional talent and results as new recipients of scholarships during their PhD or postdoctoral studies.

Regarding the NASE's career model as a whole, we want to enforce the ever-strengthening principle of quality-based selection, which assumes a decreasing number of NASE scholarship recipients (<15 PhD students, maximum 7 postdoctoral fellows) over time.

SOCIAL LIFE

The NASE provides accommodation in its dormitory for its students in Szeged, which also provides an opportunity for interaction between students and guest lecturers/researchers/international mentors. In order to form a community of students, the NASE organizes regular scientific and other (e.g. cultural, communication) programs in Budapest, Debrecen, Pécs and Szeged.

Gala at the National Theater of Szeged

Performance of Virtuoses at the Meeting of Nobel Laureates and Talents Students Gala

AWARDS GIVEN BY THE ACADEMY

The Szent-Györgyi Talent Award

In 2013, the Foundation for the Future of Biomedical Sciences in Szeged established the Szent-Györgyl Talent Award. According to the original concept, the condition for receiving this award, is that the discovery – like in the case of the great predecessor, Albert Szent-Györgyi – has to be connected to a research carried out in Szeged and – modeled after the Nobel Prize – it has to be connected to a once-in-a-lifetime discovery.

With the establishment of the National Academy of Scientist Education, not only does outstanding research in Szeged receive recognition every year, but also in Budapest, Debrecen and Pécs.

The award winners are jointly selected by the Nobel Laureate researchers visiting the Academy's events, the scientific supervisors of the National Academy of Scientist Education's University Education Program, and the members of the Board of Trustees. The awards are presented every year in the spring on the evening of the „Meeting of Nobel Laureates and Talented Students" gala event.

Researchers awarded so far:

2013: Balázs Papp
A senior scientific associate at the Institute of Biochemistry at the Biological Research Centre, Szeged *won for his work on exploring the general properties of genetic interaction networks*.

2014: Csaba Pál
A senior scientific associate at the Institute of Biochemistry at the Biological Research Centre, Szeged *won for his work on the detailed mapping of bacterial resistance to antibiotics.*

2015: Gábor Tamás
Professor at the University of Szeged Faculty of Natural Sciences and Informatics, Institute of Biology, Department of Physiology, Organization and Neuroscience *won for the discovery of the cells responsible for slow cortical inhibition and the description of their mechanism.*

2016: Péter Hegyi
Professor at the Faculties of General Medicine of the University of Szeged and Pécs *won for his work in understanding the pathomechanism of acute alcoholic pancreatitis.*
In light of the fact that a member of the Board of Trustees received the highest professional prize in 2016, the award was not handed over. The professional achievement was recognized with a certificate.

2017: Antal Berényi
Assistant professor at the Institute of Physiology, Faculty of General Medicine, University of Szeged *won for his work exploring the principles of electrical treatment of epileptic seizures.*

Balázs Papp (in the middle), the first Talent Award winner, 2013

Csaba Pál (on the right), the 2014 award winner

Gábor Tamás (on the left), who won the award in 2015

Péter Hegyi received a certificate in 2016

Antal Berényi, the 2017 award winner

Lajos Haracska, the 2018 award winner

Dr. Péter Horváth (in the middle), winner of the 2019 Talent Award

Dr. László Nagy, winner of the 2020 Talent award

Dr. Tamás Martinek, the 2021 award winner

2018: Lajos Haracska
Research fellow at the Institute of Genetics of the Biological Research Centre, Szeged of the Hungarian Academy of Sciences *won for his research in the field of carcinogenesis, during which he described how new molecular actors influenced the stability of the genome.*

2019: Péter Horváth
Director at the Institute of Biochemistry of the Biological Research Centre, Szeged of the Hungarian Academy of Sciences *won for his publication in the January 15, 2018, edition of Nature Communications in which he and his colleagues described the technique of intelligent image-based single-cell isolation.*

2020: László Nagy
Research fellow at the Institute of Biochemistry of the Biological Research Centre, Szeged won for his outstanding research results in the topic *"Exploring the evolutionary origin of hyphae multicellularity using comparative genomic methods".*

2021: Tamás Martinek
Professor and department head at the Institute of Medicinal Chemistry of the University of Szeged for his outstanding research results in the field of *"Delivery of proteins into the cell with endocytosis-directing sequences".*

2022: Ádám Dénes
Senior research fellow at the Institute of Experimental Medicine, won for his outstanding research in the field of *"Compartment-specific modulation of neuronal and vascular responses by microglia".*

Gábor Juhász
Professor at the Biological Research Centre Szeged, won for his outstanding research in the field of *"Canonical and non-canonical roles of autophagy genes".*

Norbert Kovács
Professor at the University of Pécs, won for his outstanding research in the field of *"Deep brain stimulation to improve the quality of life for patients with movement disorders such as Parkinson's disease and dystonia".*

Attila Tóth
Professor at the University of Debrecen, won for his outstanding research in the field of *"Gains and losses upon improving cardiac contractility".*

The 2022 award winners with András Varró, the strategic director of the Foundation and the Nobel Laureate Erwin Neher (from left to right: András Varró, Ádám Dénes, Attila Tóth, Norbert Kovács, Gábor Juhász, Erwin Neher)

2023: Lóránt Székvölgyi

Head of the Lendület Genome Structure and Recombination research group at the University of Debrecen, won for his outstanding research in the field of *„Chromatin structure regulators: the story of Nodulin”.*

Gábor Kemenesi

Deputy Director of Research at the National Laboratory of Virology at the Szentágothai János Research Centre of the University of Pécs and Head of the Epidemic Prevention and Investigation Research Group, won for his outstanding research in the field of *„Isolation of infectious Lloviu virus from Screiber bats in Hungary”.*

László Csanády

Head of Semmelweis University, Institute of Biochemistry and Molecular Biology, won for his outstanding research in the field of *„Understanding the molecular background of temperature-sensitive activity of an ion channel which serves as a thermometer in the thermoregulatory center of the brain”.*

Máté Manczinger

Head of the Systems Immunology Research Group at the Biological Research Centre (Szeged), won for his outstanding research in the field of *„Investigation of generalist HLA molecules in the antitumor immune response”.*

The 2023 award winners with András Varró, the strategic director of the Foundation, Balázs Hankó (representing the Government of Hungary) and the Nobel Laureate Bruce Beutler (from left to right: András Varró, Balázs Hankó, Bruce Beutler, László Csanády, Lóránt Székvölgyi, Máté Manczinger, Gábor Kemenesi)

"Excellent Student of the Year" awardees

2018: Bernát Nógrádi
Szeged Scientists Academy 3rd year
University of Szeged, Faculty of Medicine, 3rd year

2019: Gergő Porkoláb
Szeged Scientists Academy 3rd year
University of Szeged, Faculty of Science and Informatics, Biology 3rd year

2020: Valéria Éva Meszlényi
Szeged Scientists Academy 5th year
University of Szeged, Faculty of Medicine, 6th year

2021: Márton Simon Czikkely
National Academy of Scientist Education 5th year
University of Szeged, Albert Szent-Györgyi Medical School, 5th year

2022: Anna Georgina Kopasz
National Academy of Scientist Education 6th year
University of Szeged, Faculty of Science and Informatics, Biology MSc 2nd year

2023: Gábor Orbán
National Academy of Scientist Education 6th year
Semmelweis University, Faculty of Medicine, 6th year

BERNÁT NÓGRÁDI
Excellent Student of 2018

GERGŐ PORKOLÁB
Excellent Student of 2019

VALÉRIA ÉVA MESZLÉNYI
Excellent Student of 2020

MÁRTON SIMON CZIKKELY
Excellent Student of 2021

ANNA GEORGINA KOPASZ
Excellent Student of 2022

GÁBOR ORBÁN
Excellent Student of 2023

"Excellent Pupil of the Year" awardees

2019: Gergő Bitay
Radnóti Miklós Experimental Grammar School Szeged

2020: Dominik Dobos
ELTE Bolyai János Practice Primary and Secondary Grammar School, Szombathely

2021: Botond Szikra
Táncsincs Mihály Secondary Grammar School of Kaposvár

2022: Lucien Lemaitre
Németh László Secondary and Grammar School, Hódmezővásárhely

2023: Tamás Szalay
Radnóti Miklós Experimental Grammar School Szeged

2024: Olivér Dinnyés
ELTE Bolyai János Practising Primary and Secondary Grammar School, Szombathely

GERGŐ BITAY
Excellent Pupil of 2019

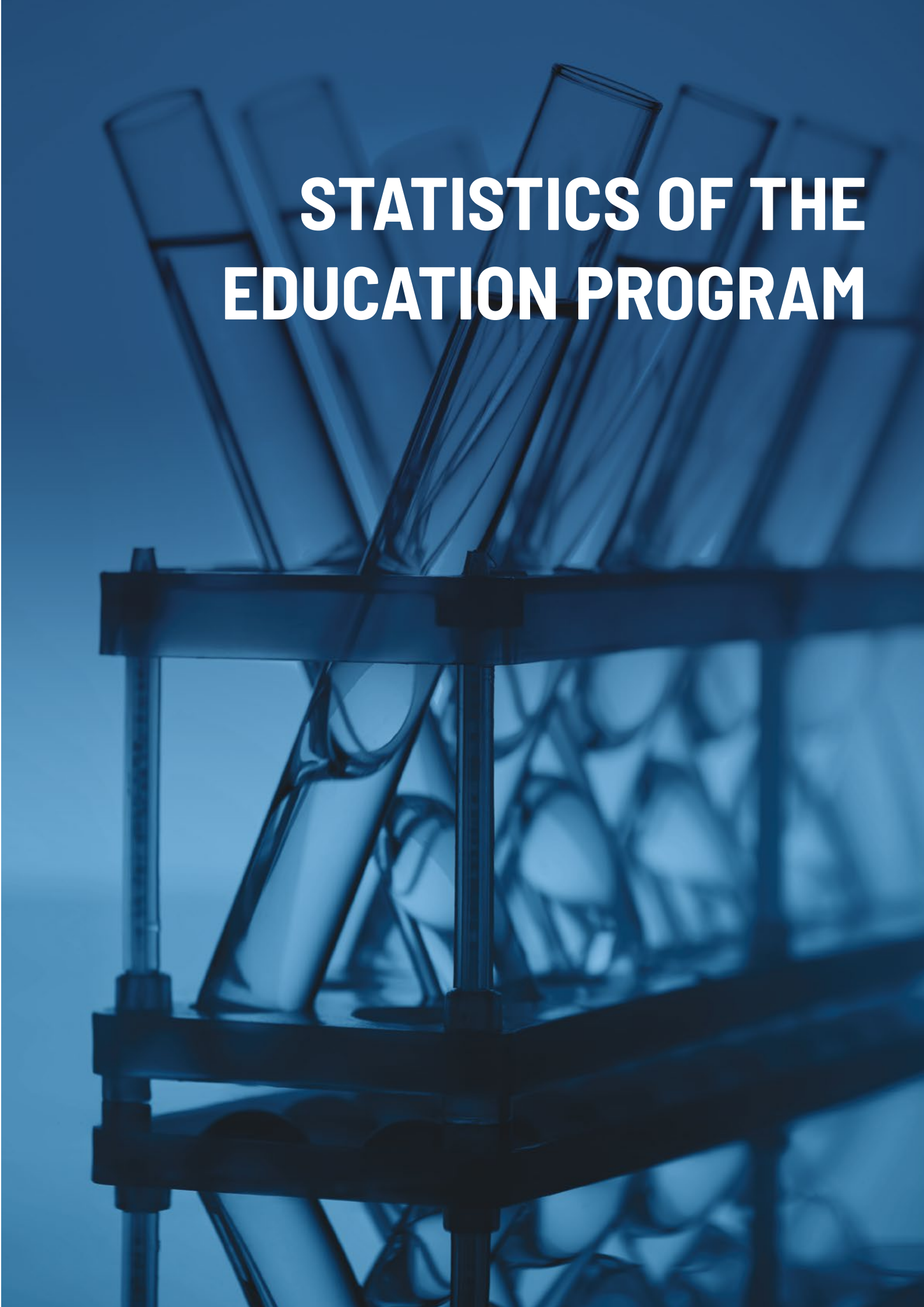
DOMINIK DOBOS
Excellent Pupil of 2020

BOTOND SZIKRA
Excellent Pupil of 2021

LUCIEN LEMAITRE
Excellent Pupil of 2022

TAMÁS SZALAY
Excellent Pupil of 2023

OLIVÉR DINNYÉS
Excellent Pupil of 2024



STATISTICS OF THE EDUCATION PROGRAM

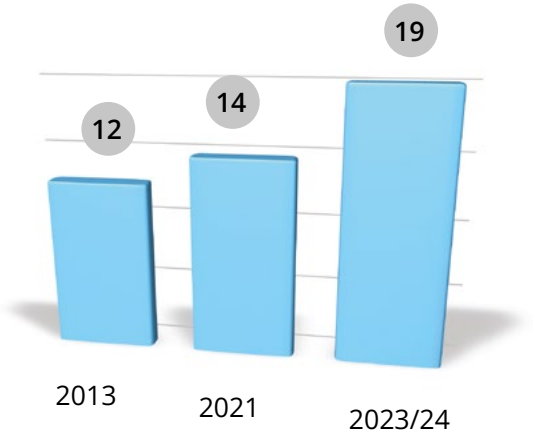
STATISTICS OF THE SECONDARY SCHOOL EDUCATION PROGRAM

Venues

In 2013, when the *Szeged Scientists Academy* was launched by the *Foundation for the Future of Biomedical Sciences in Szeged*, the 12 regions, the 3 National Training Centres and the 14 Regional Training Centres of the Secondary School Education Program provided a geographical national coverage regarding the talent management of the pupils in the field of natural sciences.

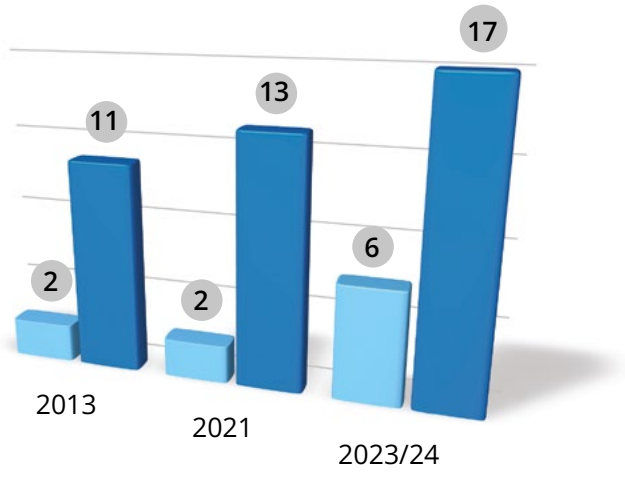
As a result of the transformation of the *Szeged Scientists Academy* to the *National Academy of Scientist Education* in 2021, the number of the regions began to increase within Hungary and in 2022 also a region beyond the border was involved in Târgu Mureș, Romania.

REGIONS

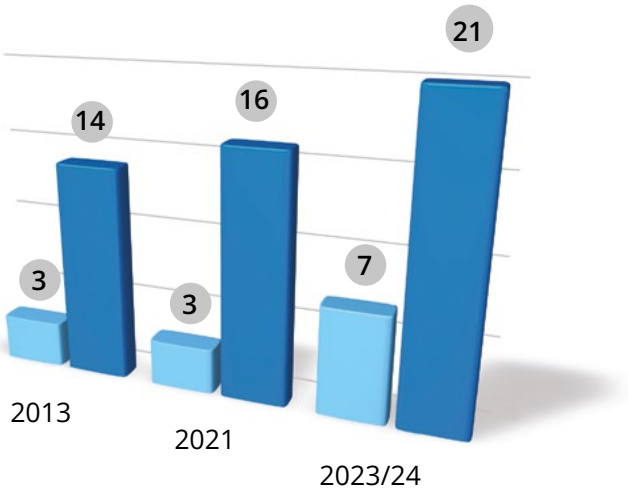


Parallel to the increase in the number of regions, the number of cities and schools involved in the implementation of the program also grew, in order to make the talent management of the pupils even more effective. Consequently, regular teacher trainings and special laboratory practices for advanced pupils can now be carried out in the 7 National Training Centres, while the 21 Regional Training Centres are responsible for the regular theoretical and practical education of the secondary school pupils.

CITIES



INSTITUTIONS

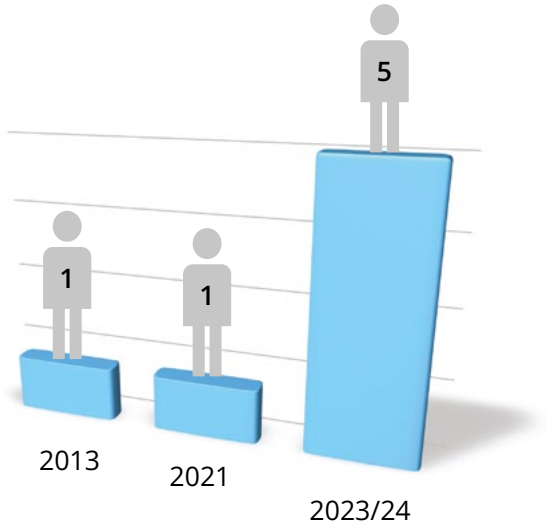


National Training Centres Regional Training Centres

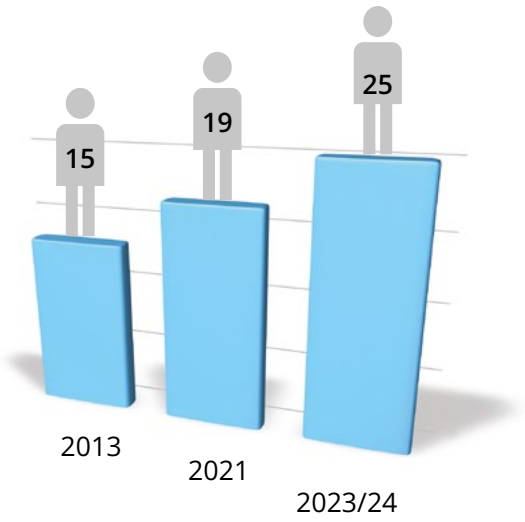
Participants

Szent-Györgyi Senior Teachers, who are recognized experts within their region in the field of biology or chemistry education, must have decades of experience in talent development in these subjects. From the very beginning, the management of the Academy was determined to involve as many experts as possible, with whom the Secondary School Program could be made even more effective and successful. As the professional work of the regions is led by the Szent-Györgyi Senior Teachers, they play a crucial role in the system.

SZENT-GYÖRGYI SENIOR TEACHERS OF THE NATIONAL TRAINING CENTRES

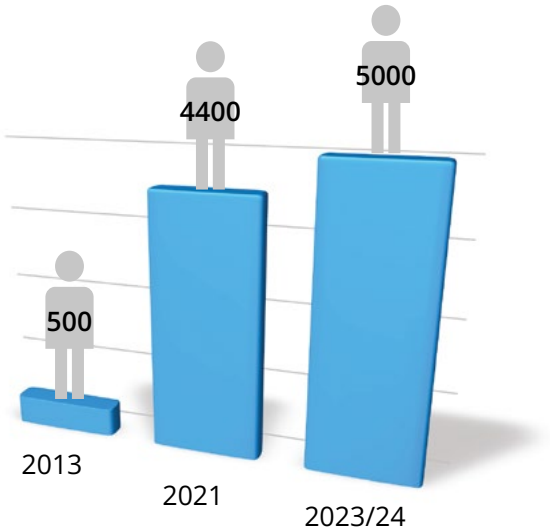


SZENT-GYÖRGYI SENIOR TEACHERS OF THE REGIONAL TRAINING CENTRES

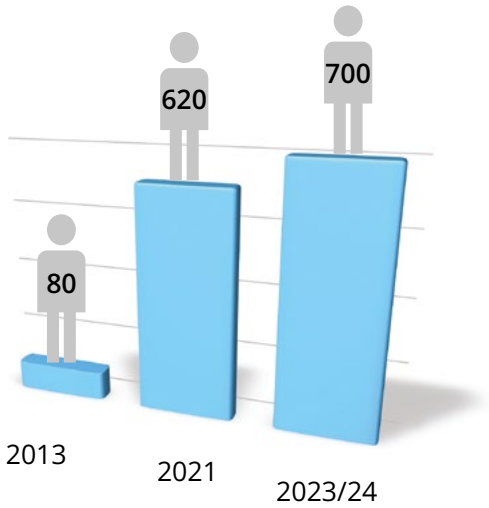


Secondary school pupils and their teachers can regularly participate in various professional programs. Since 2013, the Academy organizes two major conferences (*Meeting of Nobel Laureates and talented students*) every year, where both pupils and teachers are invited. They can also regularly attend trainings in the National and Regional Centres. The diagram below shows the total number of participants throughout the years. The exponential increase in the numbers is an outstanding success for the Academy.

SZENT-GYÖRGYI PUPILS PARTICIPATING IN PROFESSIONAL PROGRAMS

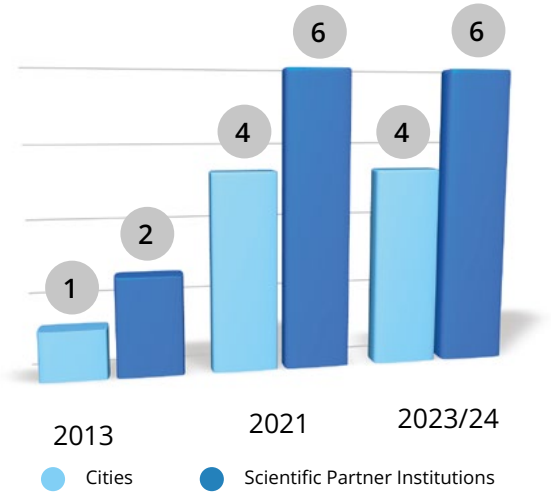


SZENT-GYÖRGYI TEACHERS PARTICIPATING IN PROFESSIONAL PROGRAMS



STATISTICS OF THE UNIVERSITY EDUCATION PROGRAM

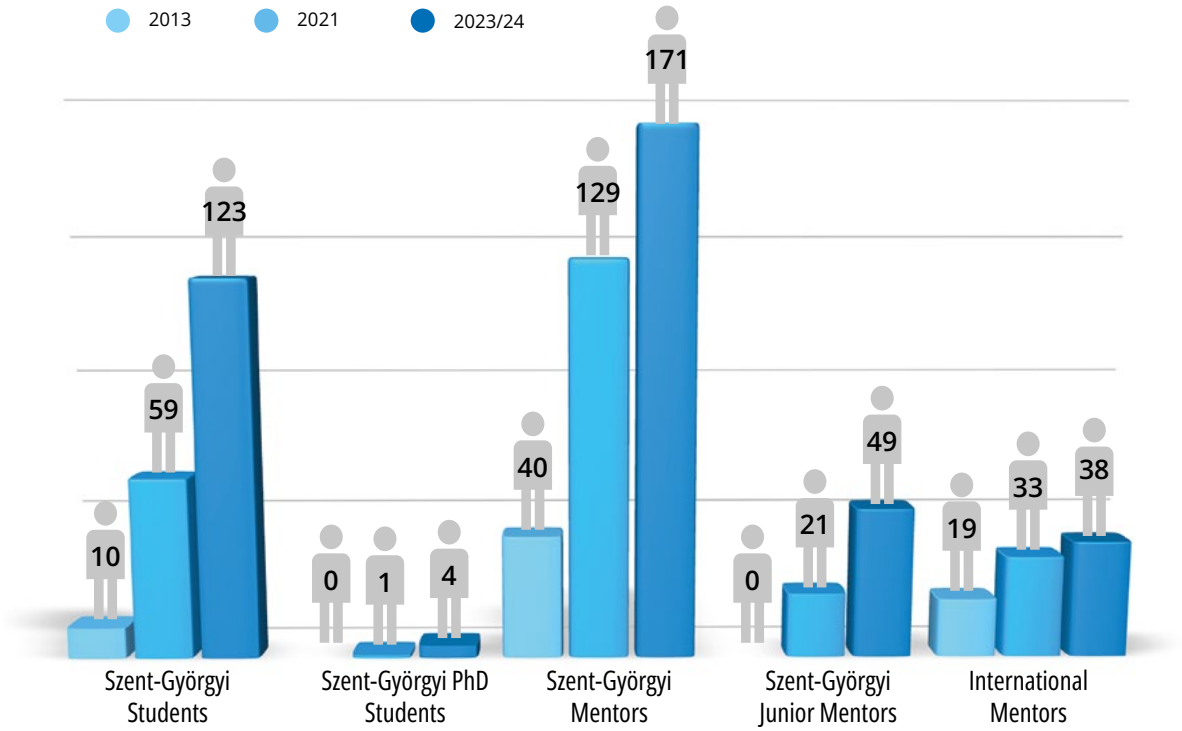
VENUES



Szeged Scientists Academy was established in 2013. In the beginning, the university program was implemented exclusively in Szeged. Based on the results listed over the years, it came to the point in 2021 where the program expanded to **National Academy of Scientist Education program,** to include all cities in the country with institutes of higher education in human life sciences. Consequently, the number of the partner institutions also increased significantly during the transformation period.

Owing to the expansion of the University Education Program in 2021, parallel to geographical growth, the number of participants in the professional program also increased significantly. The management of the Academy is determined to ensure that this growth continues unabated in the future as well.

PARTICIPANTS



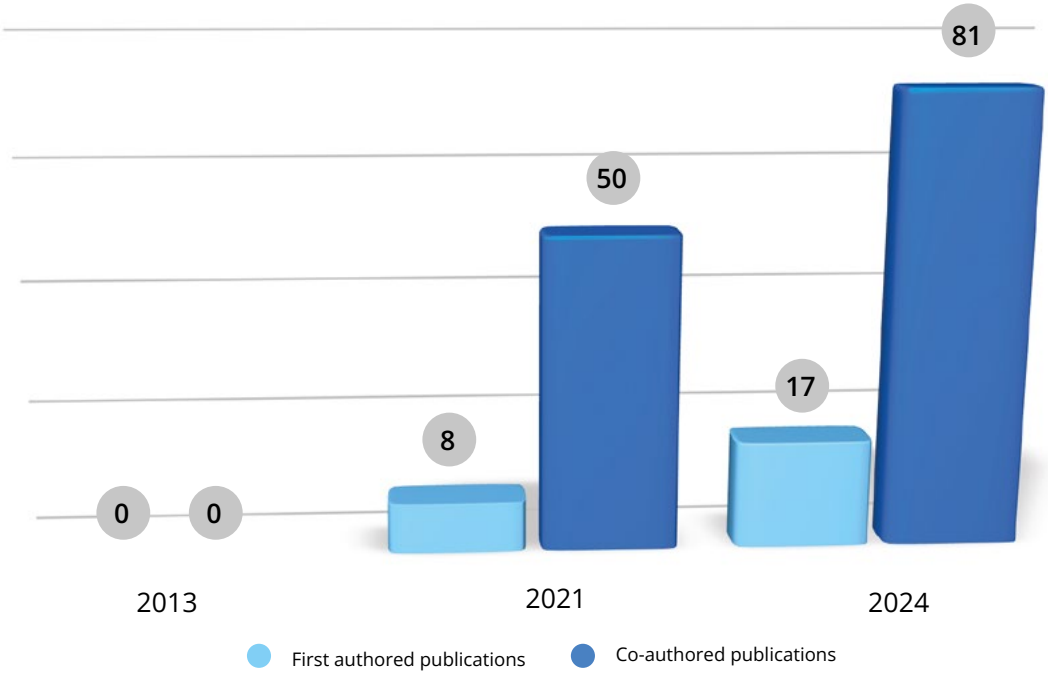
Szent-Györgyi Students performing research within the framework of the Academy need to meet the following publication requirements:

- by the end of the 30th month from the conclusion of the scholarship contract, a co-authored publication must be performed in a SciMago Q1 international journal within the field, and

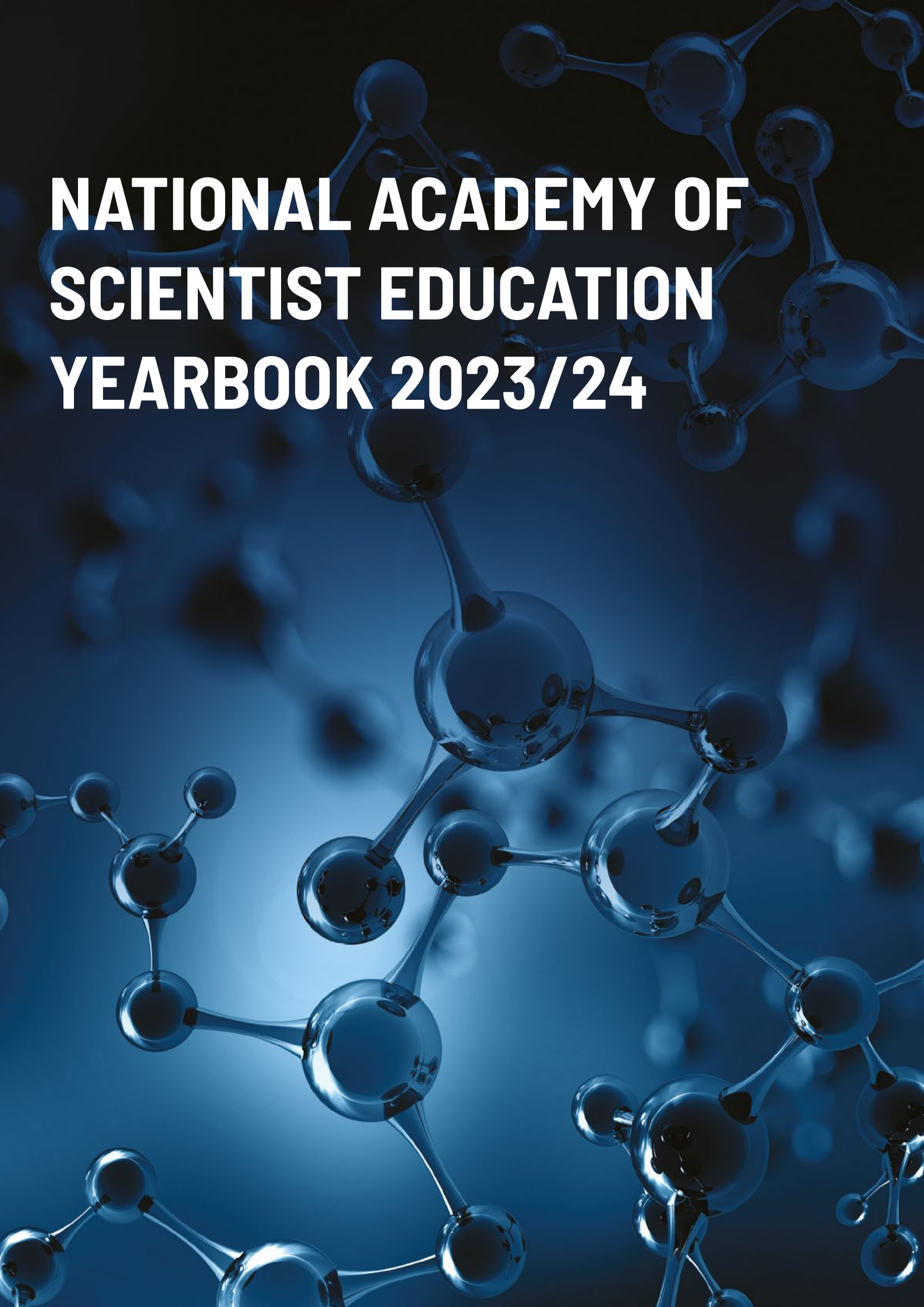
-by the time they receive their university degree, Students must be the first authors of at least one SciMago Q1 original international publication in an additional field

In accordance with preliminary expectations, as the number of students increased, so did the number of publications. It is important to note, however, that Students entering the Research Institutions joining the Program in 2021, were admitted in a progressive system.

PUBLICATIONS OF THE SZENT-GYÖRGYI STUDENTS



NATIONAL ACADEMY OF SCIENTIST EDUCATION YEARBOOK 2023/24



The members of the National Biomedical Foundation's Board of Trustees

ANDRÁS VARRÓ

Chairman of the Board of Trustees

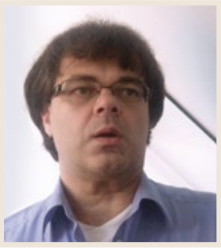
Professor of the Department of Pharmacology and Pharmacotherapy at the Albert Szent-Györgyi Medical School of the University of Szeged

PÉTER HEGYI

Professor at the Faculty of General Medicine of the Semmelweis University and the University of Pécs, professor at the Albert Szent-Györgyi Medical School of the University of Szeged

LÁSZLÓ DUX

Rector of Gál Ferenc University, professor of the Institute of Biochemistry at the Albert Szent-Györgyi Medical School of the University of Szeged



ZOLTÁN GYENGE

Dean of the Faculty of Humanities and Social Sciences at the University of Szeged

LAJOS KEMÉNY

Professor and head of the Department of Dermatology and Allergology at the Albert Szent-Györgyi Medical School of the University of Szeged

ZOLTÁN KÓNYA

Vice-Rector for Scientific Affairs and Innovation at the University of Szeged

BÉLA MERKELY

Rector of Semmelweis University

FERENC NAGY

Director General of the HUN-REN Biological Research Centre, Szeged

ZOLTÁN NUSSER

Director of the Institute of Experimental Medicine

ZSUZSANNA HELYES

Professor of the Department of Pharmacology and Pharmacotherapy at the Faculty of General Medicine of the University of Pécs

JÓZSEF TŐZSÉR

Vice-Rector responsible for health industry innovation and training development at the University of Debrecen

LÁSZLÓ VÍGH

Research Professor of the HUN-REN Biological Research Centre, Szeged

Members of the Oversight Committee

ÉVA KONDOROSI

President
Research professor at the HUN-REN Biological Research Centre, Szeged

ERIKA PINTÉR

Member
Professor and head of the Department of Pharmacology and Pharmacotherapy at the Faculty of General Medicine of the University of Pécs

PÉTER FERDINANDY

Member
Vice-Rector for science and innovation at Semmelweis University

Chief scientific leaders

BERT SAKMANN

Director general of education

Nobel Laureate cell physiologist,
Max Planck Institute für Neurobiologie,
Munich

ANDRÁS VARRÓ

Strategic director

Professor of the Department of Pharmacology and Pharmacotherapy at the Albert Szent-György Medical School of the University of Szeged

PÉTER HEGYI

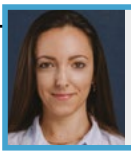
Program director

developer of the National Academy of Scientist Education (NASE) program. Professor at the Faculty of General Medicine of the Semmelweis University and the University of Pécs, professor at the Albert Szent-Györgyi Medical School of the University of Szeged

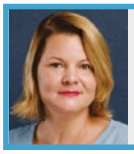
Professional and Operational implementers

ANDRÁS VARRÓ
Strategic director

ADRIEN LENGYEL
Director of Secondary School Education

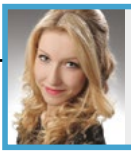


ENIKŐ GULYÁS
Training coordinator

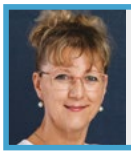


LUCA HERTELENDY-VARGA
Financial director

SÁNDOR BÁN
Pedagogical expert

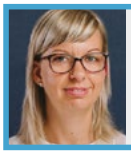


ZSÓFIA TÓTH
Training assistant



LÁSZLÓNÉ FŐDI
Financial assistant

ZSOLT NYISZTOR
Head of the National Education Centres

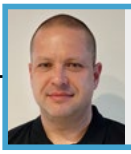


ESZTER FRICK
Financial assistant

RÓBERT KERTÉSZ
Head of the Regional Education Centres

ALICE BERECZ
Financial assistant

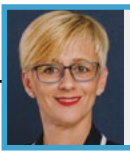
ZOLTÁN RAKONCZAY
Head of university relations

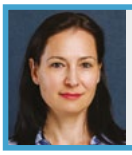


KRISZTIÁN SEBŐK
Secondary school - hospital coordinator

BERT SAKMANN
Director general of education


PÉTER HEGYI
Program director


ANITA TAKÁCS
Managing director


ÁGNES BITTERA
Marketing director


TÍMEA LEPAHIN-PAPP
Marketing coordinator

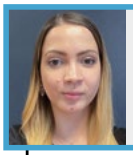

EMESE SZABÓ
Journalist


JÓZSEF TOLNAI
Website developer

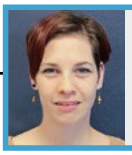

JÓZSEF ANDÓCZI-BALOG
Social and cultural program organizer


ZOLTÁN RAKONCZAY
Director of University Education


ZSUZSA PAPFALVI
Training coordinator


ÁGOTA GYŐRI
Training coordinator

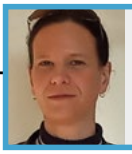

MÁRIA DELI
Scientific supervisor


JULIANNA ORBÁN
Training assistant

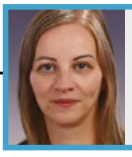

TAMÁS MARTINEK
Scientific supervisor


TÜNDE SOPRONYI
Training assistant

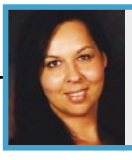

ÁDÁM DÉNES
Scientific supervisor

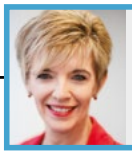

RÉKA GÉMESI
Training assistant


ATTILA MÓCSAI
Scientific supervisor


KRISZTINA KASS
Training assistant


ZOLTÁN PAPP
Scientific supervisor


RITA BALÁZS
Training assistant


ZSUZSANNA HELYES
Scientific supervisor

SECONDARY SCHOOL EDUCATION PROGRAM

Leaders of the Secondary School Education Program

ADRIEN LENGYEL

Director of Secondary School Education

Master teacher of biology and chemistry at the Calvinist Secondary School in Kecskemét

SÁNDOR BÁN

Pedagogical expert

Master teacher of biology at the Radnóti Miklós Experimental Grammar School Szeged

ZSOLT NYISZTOR

Head of the National Education Centres

Headmaster, master teacher of biology and chemistry at the Nagy Lajos Grammar School for the Cistercian Order

RÓBERT KERTÉSZ

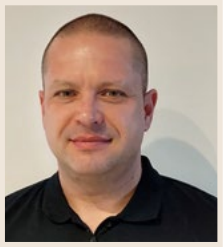
Head of the Regional Education Centres

Master teacher of biology and chemistry at the Táncsics Mihály Secondary Grammar School of Kaposvár

ZOLTÁN RAKONCZAY

Head of university relations

Professor and head of the Institute of Pathophysiology at the Albert Szent-Györgyi Medical School of the University of Szeged



KRISZTIÁN SEBŐK

Secondary school - hospital coordinator

ENIKŐ GULYÁS

Training coordinator

ZSÓFIA TÓTH

Training assistant

SZENT-GYÖRGYI SENIOR TEACHERS

ADRIEN LENGYEL

DIRECTOR OF SECONDARY SCHOOL EDUCATION

Calvinist Grammar School of Kecskemét

TEACHING CAREER IN BRIEF

Being a student at the József Attila University of Szeged, I concluded my studies as a Biology and Chemistry teacher. My first employment was at the Katona Secondary School at Kecskemét, then I changed to the Calvinistic Secondary School where I'm working up to this day. Upon launching the six-grade education program, my task was to develop the Chemistry curriculum, later I became the head of the teacher's team. We are frequent participants of the TUDOK (Annual Conference of National Scientific Students' Associations) with remarkable success. The achieved results truly enhanced my personal development. Along with a colleague, I'm organizing the Biology field trips which are quite popular amongst our students. I'm also an evaluating teacher at the advanced level final examinations. Throughout the years my main focus has been to modernize Biology education; especially reaching out for students who show interest in this field - for this achievement I received an award. Other significant professional steps were publishing textbooks and books assisting the preparation for final examinations (MAXIM publishing). These activities demand great devotion, lots of reading, consulting and many working hours, yet offer the best way for self-improvement in the dynamically changing subject of Biology. In addition, I handled full readership of a laboratory project and held advanced education to my colleagues. I find these activities both challenging and exciting. I have been working for the foundation since 2015, so our grammar school also became a basic school. The program is very attractive for students of regional high schools, today the active number covers more than a hundred students who are happy to attend our lectures and take part in laboratory classes, only here in the Kecskemét district. My work is to help as many talented students as possible find a place in our excellent universities, to take an active part in research and academic life. (I still have more research students than Szent-Györgyi.)

PUBLICATIONS

Juhász, K., **Lengyel, A.**: Biology topic papers for the 2024 matriculation examination - Maxim publishing

Juhász, K., **Lengyel, A.**: 130 topics in biology for the 2024 matriculation examination - Maxim publishing

Juhász, K., **Lengyel, A.**: Színes érettségi tételek biológiából a 2024-es érettségi követelményrendszerhez - Maxim kiadó

Cselekedeteink tüköre - / A szegedi orvosbiológiai kutatások jövőjéért / - cikk : **Lengyel Adrien** Print 2000 Nyomda 2020

Juhász K., **Vargáné L.A.** Theme Outlines for Biology Final Examination, Maxim Publishing, Szeged, 2017.

SÁNDOR BÁN

PEDAGOGICAL EXPERT

Radnóti Miklós
Experimental Grammar School Szeged

TEACHING CAREER IN BRIEF

I started my career in 1993 at the Dugonics András Piarist Grammar School, Szeged, where I taught chemistry and biology, both as part of the regular curriculum and in advanced elective courses as well as special after-school lessons. In 1998–99, I played a leading role in designing and equipping the science section of the school's new building. I was also the head of the department of biology and chemistry for four years. Since 2002, I have taught in the special biology, chemistry and mathematics programs at the Radnóti Miklós Grammar School in Szeged, mostly in small groups. Between 2005 and 2012, I headed the biology department, which developed into the most successful high school biology workshop in the country during that period, based on advanced Matura examination and competition results. My colleagues and I have also established a state-of-the-art high school molecular biology laboratory. This facility has been made available to biology teachers from other schools for in-service trainings as well as to students for selection tests for international biology competitions. My colleagues and I have attended in-service trainings in molecular biology at the EMBL laboratories in Cambridge, Heidelberg and Monterotondo on a number of occasions. Since 2009, I have been the team leader of the Hungarian national teams at the International Biology Olympiad (IBO) and mentor to our national teams at the European Union Science Olympiad (EUSO). In 2010, I won the Rátz Lifetime Achievement Award. I am currently head of the EU-funded high school science laboratory.

PUBLICATIONS

Bán S. (1998). Gondolkodás a bizonytalanról: a valószínűségi és korrelatív gondolkodás fejlődése. [Thinking about the uncertain: developing probabilistic and correlative thinking]. In Csapó B. (Ed.): Az iskolai tudás. Budapest: Osiris Kiadó.

Bán S. (2010). A tanulás természetes jellemzőinek érvényesülése az iskolai biológiaoktatásban [Implementing natural features of learning in biology instruction]. Mester és Tanítvány 28: 48-56.

Bán S et al. (Eds.). (2003). From Vandal to Voter: Active Citizenship in Europe - Analysis and Methods. Szeged-Paris: KIFE.

ZSOLT NYISZTOR

HEAD OF THE NATIONAL EDUCATION CENTRES

Nagy Lajos Grammar School of the Cistercian Order, Pécs

TEACHING CAREER IN BRIEF

I received my teaching degree in biology and chemistry at the University of Pécs. During my studies, I was engaged in an ecological study of barn owls, among other topics, as well as a molecular biology project involving the processing of samples collected in the field for taxonomic purposes. During this time, I also spent half a year in Italy as an ERASMUS student at the University of L'Aquila. In 2001, I began teaching at the Nagy Lajos Cistercian Grammar School in Pécs, where I have been a teacher ever since. I graduated from the Doctoral School of Biology and Sportbiology of University of Pécs in 2019. I studied the development of the mammalian retina. I would like to pass on to my students my enthusiasm for the sciences and the ability to wonder at the myriad beauty of the created world. I believe that Hungary should be represented among the scientific elite of the world through diligence and endurance. I consider it important for my students to leave high school not only strengthened in knowledge, but also in moral and spiritual values.

PUBLICATIONS

Nyisztor, Zs. (2015) Biológia munkafüzet 11-12. osztály [Biology workbook grades 11–12]. Pécs: Ciszterci Rend Nagy Lajos Gimnáziuma és Kollégiuma.

Nyisztor, Zs. (2015) Biológia szaktanári segédlet 11. osztály [Biology teacher's guide grade 11]. Pécs: Ciszterci Rend Nagy Lajos Gimnáziuma és Kollégiuma.

Nyisztor, Zs. (2015) Biológia szaktanári segédlet 12. osztály [Biology teacher's guide grade 12]. Pécs: Ciszterci Rend Nagy Lajos Gimnáziuma és Kollégiuma.

Nyisztor, Zs., Dénes, V., Kovács-Valasek, A., Hideg O., Berta G., Gábriel R. (2018). Pituitary adenylate cyclase activating polypeptide (PACAP1-38) exerts both pro and anti-apoptotic effects on postnatal retinal development in rat. **Neuroscience** 385, 59-66.

Denes, V., Hideg, O., **Nyisztor, Zs.**, Lakk, M., Godri, Z., Berta, G., Geck, P., Gábriel, R. (2019). The neuroprotective peptide, PACAP1-38 contributes to horizontal cell development in postnatal rat retina. Investigative **Ophtalmology and Visual Science**.

RÓBERT KERTÉSZ

HEAD OF THE REGIONAL EDUCATION CENTRES

Táncsics Mihály Secondary Grammar School of Kaposvár

TEACHING CAREER IN BRIEF

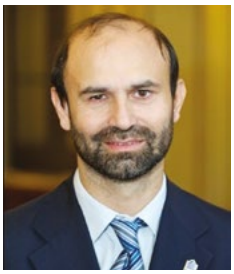
I earned my secondary school teaching degree in biology and chemisry at the József Attila University (University of Szeged) in 1993. I started working at the Department of Botany there and then moved to Kaposvár in 1997. Since then, I have been teaching biology and chemistry in the regular and specialized curricular programs at my alma mater there, Táncsics Mihály Grammar School. Since the Research area of the two-tier Matura examinations, I have participated in the work of the advanced Matura examination boards, I have corrected advanced written Matura examinations and was even requested to oversee examination marking. I passed two specialized examinations (at the University of Szeged and the Budapest University of Technology and Economics) and have incorporated the knowledge I have thus acquired into my everyday practice. In 2014, I received the rank of master teacher, so I am now also called on to provide consultations, through which I endeavour to improve the position of my scientific subjects, which are continually being pushed into the background. During my work in secondary school, I have always laid great stress on nurturing excellence – I have prepared my students for various competions in both of my subjects. I consider it important to aid my students in strengthening their own innate interest and developing their own high professional standards.

JÓZSEF BACHER

Miklós Révai High School and College, Győr

TEACHING CAREER IN BRIEF

I started my teaching career in 1997 at the Kossuth Lajos High School in Mosonmagyaróvár, Hungary. I was involved in the establishment and continuous development of the school's Öveges Laboratory, which is now enthusiastically taken over by my former students. Biology talent management has always been a priority for me. The world of field trips, summer camps and independent research has captivated my talented students. Over the years, I have built up successful collaboration with several universities (ELTE TTK, PTE ÁOK, SZE MÉK). My Master Teacher programme is also focused on biology talent management, which I have been carrying out with great success at my new workplace in Győr, Révai Miklós High School, since 2020. My colleagues and I write tenders regularly and mostly successfully to improve the equipment of the institution. The workshops and competition preparation sessions I run are very popular, and we manage to engage nearly 50-70 students per year in several age groups. Our competition results are also outstanding, not only in traditional competitions (OKTV, Árokszállásy, Szentágothai), but also in competitions based on independent research (TUDOK, Hlavay, Youth Innovation Student Olympiad) and team competitions (Bionics Academy Competition). My achievements so far have been recognised with several awards at the request of my former students.



JÓZSEF BARANYAI

ELTE Bolyai János Practice Primary and Secondary Grammar School, Szombathely

TEACHING CAREER IN BRIEF

I completed my biology degree at the József Attila University (University of Szeged) in 1994. During my university years, I was a demonstrator at the Department of Zoology, and I stayed on as an assistant lecturer after receiving my degree. I have much to thank the excellent staff at the department (Drs. Róbert Gábriel, Éva Fekete and Katalin Halasi) for my professional development. They inspired me to become an outstanding student and assistant lecturer. Soon afterward, I was invited by János Iker to the newly established Bolyai Grammar School in Szombathely and have been teaching there since then for over 20 years. I am an advocate of problem-/inquiry-based learning, but also believe that there is not one single right method: one must always dynamically adjust to the problem at hand and tailor the methods accordingly. I have worked on a number of professional boards (Hungarian National Institute for Educational Research and Development (OKI/OFI) in curriculum development, dealing with the National Curriculum etc.). I am the head of our talent center, and I am proud of all the results of all my students. In 2011, I received the Rátz Lifetime Achievement Award, and in 2013 the Bonis Bona National Talent Award.

PUBLICATIONS

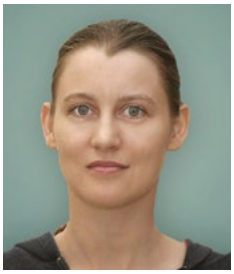
Baranyai J, Veres G. (2022). Biológia kompetencia fejlesztő feladatgyűjtemény

Baranyai J, Veres G. (2021). Biológia tankönyv 9-10.

Baranyai J, Szűcsné Kerti A. (2006). Biológia középszintű érettségi feladatgyűjtemény 10. [Intermediate biology Matura examination papers 10]. Budapest: Nemzeti Tankönyvkiadó.

Baranyai J, Szűcsné Kerti A. (2006). Biológia középszintű érettségi feladatgyűjtemény 11. [Intermediate biology Matura examination papers 11]. Budapest: Nemzeti Tankönyvkiadó.

Baranyai J, Szűcsné Kerti A. (2006). Biológia középszintű érettségi feladatgyűjtemény 12. [Intermediate biology Matura examination papers 12]. Budapest: Nemzeti Tankönyvkiadó.



ANDREA BORBOLA

Radnóti Miklós
Experimental Grammar School Szeged

TEACHING CAREER IN BRIEF

I've been an associate at the TERMOSZ Laboratory since 2014, I consider it as a prime element in my life. During my high school years I had the opportunity of assisting at the Cell Biology and Evolutional Micropaleontology Laboratory of the University of Szeged, which helped me start my scientific work. Throughout my university studies I was co-authoring several English publications, participated in an Indian-Hungarian joint research and for years I was the technical editor of the Plant Cell Biology and Development (Szeged) issue. In addition I also acquired some successful applications (Pro Renovanda Cultura Hungariae Fund – 'Students for Science' foundation).
My interests shifted towards molecular biology - starting from 2001, I carried out my PhD studies at the Genetic Institute of the Biological Research Center (Hungarian Academy of Sciences); later on I worked there as a science assistant. Next to learning the basic molecular biology techniques and elaborating new methods I also participated in several conferences. At the moment I'm teaching Biology at the Radnóti Miklós Experimental Grammar School and tending to the TERMOSZ Laboratory.

PUBLICATIONS

Kiss E, Olah B, Kalo P, Morales M, Heckmann AB, **Borbola A**, Lozsa A, Kontar K, Middleton P, Downie JA, Oldroyd GED, Endre G: (2009) Lin, a novel type of u-box/wd40 protein, controls early infection by rhizobia in legumes. **PLANT PHYSIOLOGY 151:** 1239-1249.

Borbola A: (2004) Construction of a linkage map for Medicago truncatula RIL population and its comparative analysis with other Medicago genetic maps. **ACTA BIOLOGICA SZEGEDIENSIS 48:** 51.

Kedves M, Párdutz Á and **Borbola A**: (1998) Transmission electron microscopy of X-ray irradiated teliospores of Ustilago maydis. **GRANA 37:** 29-34.

EDIT CSALÁNÉ BÖNGYIK

Németh László Secondary and Primary School, Hódmezővásárhely

TEACHING CAREER IN BRIEF

I began teaching in the Commercial and hospitality secondary school of Hódmezővásárhely in 1998, parallel with my university studies and I have been working in the Németh László Grammar School since 2015. I have been teaching biology and chemistry and during my years in the vocational secondary school my students performed well at professional competitions. I have always felt fortunate to be a teacher, I am one of the few persons whose job is their hobby. I regularly attend professional trainings and always embrace varied pedagogical methods and educational forms. Recently, I have been committed to digital pedagogy. I was teaching complex nature for a long time, I also prepared a workbook for internal use with one of my colleagues. Thanks to this I became closer to the activities of the Öveges labs and also had the opportunity to participate in the elaboration of complex labotatory workbooks. I was also engaged for two years in a teacher training for renewing STEM thinking. I gladly contribute to project writing, I am proud of my two successful National Talent Projects. I held Visible Natural Science – Digital Teaching Practice course as a trainer of MDOE from 2018. In the spring of 2020, I was invited to develop professional recommendations in line with the new NAT. In December 2020, I won the Digital Educator Award in the Tempus competition. At present, I am teaching students committed to natural sciences at each grade above 8th and also the ones who wish to perform the advanced level biology final exam.

PUBLICATIONS

(2001) K. Hernádi, I. Pálinkó, **E. Böngyik,** I. Kiricsi, Biomimetic oxygen transfer by Co and Cu complexes immobilized in porous matrices, **Studies in Surface Science and Catalysis** (https://www.sciencedirect.com/science/article/abs/pii/S0167299101818607?fbclid=IwAR0Bjxq2VFVhqnFrsiEJZDJS3EVEmpI6j-IbyL5IuL2zC7RhBZwtu6ooSo8)

(2016) Mobileszközök az oktatásban konferencia, Okostelefonokkal a természettudományos oktatásban, Debreceni Egyetemi Kiadó, Veszprém 2016

ISTVÁN CSIGÉR

University of Szeged Teacher Training Secondary and Primary School, Szeged

TEACHING CAREER IN BRIEF

I earned my degree at the József Attila University (University of Szeged) in 1985, which qualified me to teach biology and chemistry in secondary school. Right after I completed my studies, I started my career at the Vocational School for Forestry amd Water Resources Engineering and Management in Barcs, where I spent six years. I taught biology and chemistry to students in the forestry stream and chemistry and lab practice to students in the water resources engineering and management stream. In acknowledgement of my work, I received a Ministerial Commendation in 1989. In 1991, I came to my current workplace, the University of Szeged Grammar School and Primary School (previously the University of Szeged Ságvári Endre Grammar School) as a mentor teacher in biology. My basic job has been to teach biology and to train university students studying to become biology teachers (supervising student teaching and administering examinations to student teachers). I also work as the lead teacher for biology in the Szeged Regional Student Science Laboratory, established by our high school and by the University of Szeged, which supports it financially. Within the limits of reason, I endeavour to develop relationships with my high school and university students based on collegiality and respect, never compromising on quality work standards or the requirements of consistent and rigorous assessment. In acknowledgement of my teaching activities, I received the Golden Rostrum Commemorative Plaque in 2001. I first became involved in the Szeged Scientists Academy in 2012, which honored me with the title of Szent-Györgyi Teacher and then in 2016 with that of Szent-Györgyi Senior Teacher. I have endeavoured to aid the academy from the beginning to discover and cultivate young talent.

PUBLICATIONS

Csigér I, Juhász K, Vargáné Lengyel A. (2011). Biológia 11 [Biology 11]. Szeged: Maxim Könyvkiadó.

Csigér I, Juhász K, Vargáné Lengyel A. (2012). Biológia 12 [Biology 12]. Szeged: Maxim Könyvkiadó.

Csigér I, Németh E. (2005). Néhány szakmai észrevétel Lénárd Gábor Biológia II. és Biológia III. Tankönyvéről [Some observations on Gábor Lénárd's Biology II and Biology III coursebooks]. A biológia tanítása 2. szám: 7-19

ESZTER DÉNES

Nagy Lajos Grammar School of the Cistercian Order, Pécs

TEACHING CAREER IN BRIEF

In 2002, I started teaching at the first agricultural secondary school in Szentlőrinc, Hungary, in parallel with my university studies. In 2005, I graduated as a biology and environmental science teacher at the University of Pécs. During the first ten years of my teaching career, I focused on the development of pupils and talent management in parallel. Both are a source of getting my students to love biology and develop a scientific approach. I am constantly motivated by the success of my students, which encourages them to continue learning in science and methodology.

I wrote my teacher's exam in 2012, based on the intermediate level written exam and the measurement of everyday science knowledge. I wrote my teacher's exam in 2012, based on the biology intermediate written exam and the measurement of everyday science knowledge.

Between 2005 and 2016, I coordinated the Road to Science project, which created a unique science laboratory in vocational education and training, which provided the basis for professional training. I have been 'Pro Talento' awarded for my work in talent management.

Since 2006, I have been continuously involved in administering the advanced Matura examination. In 2019, I joined to the Nagy Lajos Grammar School of the Cistercian Order, where I was introduced to a whole new segment of talent management. The professional cooperation within the school and the direct knowledge of the goals of the National Academy of Science and Humanities have given my talent management work a different aspect. I consider it important to help my students achieve their goals, for which continuous professional development and network-based learning are essential.

ZSOLT ERŐS-HONTI

Fazekas Mihaly Primary and Secondary Grammar School, Budapest

TEACHING CAREER IN BRIEF

I am a research biologist with a PhD as well as having been trained as a specialized translator and secondary school biology teacher. For several years I had been working as an active reasercher at the Faculty of Horticultural Science, Szent István University. Ever since I received my teaching degree, I have been teaching biology to secondary school students (both in Hungarian and English). I participate in the nurturing excellence program at the school, preparing students for both domestic and international competitions, including the International Biology Olympiad. I also organise camps and prepare students for the Matura examination. I have developed teaching materials for public education, edited and published educational methodolgy coursebooks, and provided professional editing for materials used in public education. I participated in a Social Renewal Operational Program (TÁMOP) project dealing with the implementation of the framework curriculum in the Hungarian National Institute for Educational Research and Development (OFI), and I was also a member of a working group that harmonised the requirements of the Matura examinations with those of the framework curriculum. Since 2012, I have regularly completed assignments for the Office of Education. Currently, I am working as a biology teacher and vice principal at the Fazekas Mihály Primary and Grammar School of Budapest. As someone previously involved in higher education, it is my conviction that development and nurturing excellence should not be a process tied to particular educational phases. It should be an overarching effort. I am also convinced that success in the education system depends on effective communication between public and higher education.

PUBLICATIONS

Erős-Honti Zs. (2011). A kertészeti növények alaktana [Morphology of horticultural plants]. Egyetemi jegyzet. Budapest: BCE-KeTK.

Erős-Honti Zs. (2015). Az info-kommunikációs technológiák (IKT) alkalmazásának lehetőségei a kertészeti oktatás szakmódszertanában [Options for using Information and Communications Technology (ICT) in teaching horticulture]. In Szakmódszertani jegyzet az agrár-mérnöktanárok és -hallgatók számára (mezőgazdasági gépészet, mezőgazdaság, kertészet és parképítés) (Erős-Honti Zs, Nagy J). Budapest: BCE.

Jakucs E, **Erős-Honti Z**, Seress D, Kovács G M. (2015). Enhancing our understanding of anatomical diversity in Tomentella ectomycorrhizas: characterization of six new morphotypes. MYCORRHIZA 25(6): 419-429

NORBERT FARAGÓ

ELTE Trefort Ágoston Secondary Grammar School, Budapest

TEACHING CAREER IN BRIEF

I began my teaching career at the Terézváros Bilingual Primary and Grammar School in Budapest in 2001. I also taught biology and chemistry at a private grammar school concurrently. Since 2005, I have taught at the Trefort Ágoston School in Budapest, mostly biology. I have been a mentor teacher since 2006. In 2010, I received a certificate in mentoring candidate teachers. At school, I teach seventh- to twelfth-grade students as well as preparing the eleventh- and twelfth-grade students in advanced elective courses. Our students have achieved strong results at the Herman and Kitaibel competitions as well as at the National Secondary School Competition (OKTV) and the Árokszállásy biology and environmental protection competition. I regularly prepare students in groups for the advanced Matura examination. Since 2013, I have been head of the school's TÁMOP-funded science laboratory.

PUBLICATIONS

Faragó N., Szászné H J. (2013). Biológia lépésről lépésre [Biology step by step]. Budapest: Bölcselet Egyesület.

Czédulás K, **Faragó N,** Solymoss M, Szászné H J. (2013). Még egy lépés a biológia érettségihez [One more step toward the biology Matura examination]. Budapest: Bölcselet Egyesület.

ANDREA FAZAKAS

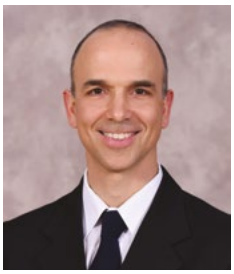
Deák Téri Lutheran Gymnasium, Budapest

TEACHING CAREER IN BRIEF

I graduated with a secondary school teaching degree in biology and chemistry at József Attila University (University of Szeged) in 1988. I began teaching at the Deák Tér Lutheran Grammar School in Budapest in 1993. I quickly learned the importance of an encouraging school atmosphere in nurturing talented students. I developed Matura examinations for the Hungarian National Institute for Educational Research and Development (OFI) between 2003 and 2006. In 2004, I attended a Training for Trainers program to implement the two-tier Matura examination, and in 2004–05, I held talks on this new system for my colleagues. I have also participated in administering the advanced Matura examination since 2005. Meanwhile, in 2005, I passed a qualifying examination to become a mentor teacher at the Faculty of Sciences, Eötvös Loránd University, Budapest. I have always been happy to mentor future teachers. I have seen five of my candidates complete their teacher training. I received the BONIS BONA for the Nation's Talent Award in 2013 in acknowledgement of my efforts in preparing students for the National Secondary School Competition (OKTV). In 2015, I applied for the master teacher rank and received it the following year. I consider it important during my work to instil a passion for biology in my students and introduce them to the logic of the natural sciences. Various extracurricular events offer excellent opportunities in that regard. During the academic year, we usually take hiking trips, mainly in the Danube–Ipoly National Park (DINP). In addition, we also visit laboratories and attend lectures organised for students by the Hungarian Academy of Sciences. During the summer holidays, I take my students to one-week ecocamps. We have already visited the Kis-Balaton, Szatmár, Őrség and Lake Velence regions in and around Hungary as well as the North Hungarian Mountains.

PUBLICATIONS

Kisfaludy A, Dombóvári L, **Fazakas A,** Lóczy D. (2008). Természettudományi Enciklopédia [Encyclopaedia of science]. Budapest: Nemzeti Tankönyvkiadó.



JÓZSEF GŐZ

Tóth Árpád Secondary School, Debrecen

TEACHING CAREER IN BRIEF

I have been teaching biology and chemistry at the Tóth Árpád Grammar School in Debrecen since 2000. During my career, I have earned a qualification in specialized Hungarian–English translation as well as passing a mentor teaching examination and receiving the title of master teacher. At my job, in addition to teaching in the specialized biology program, I also joined the Arany János Nurturing Excellence Program, the International Baccalaureate Program and the Öveges Scientific Laboratory Program, as well as being involved in grant projects and in mentoring candidate teachers. In our school we are engaged in a specialized high school program for Biology and Chemistry that enjoys the longest history in the country. An integral part of this is nurturing excellence, developing projects, and preparing students for competitions and the Matura examinations. As a Matura examiner, I operate an online database which aids in the students' preparations for the examination with items on the written part presented in a system. My main area of interest and research is the methodology of teaching biology and, within that, digital innovation. In my work, I do my best to combine the facilities of ICT and the international environment with the traditional values embodied by my workplace and the domestic professional community. In 2018, I was awarded the Szent-Györgyi Trophy by the University of Szeged, and the MESTER-M award by the MOL Foundation. As a translator I participate in the Hungarian adaptation of science education materials of Khan Academy since 2021.

PUBLICATIONS

Dobróné Tóth M, Futóné Monori E, **Gőz J**, Revákné Markóczi I. (2015). Biológiatanítás az IKT és IBL világában [Biology teaching in a world of ICT and IBL]. Debrecen: Debreceni Egyetemi Kiadó

Gőz J. (2021): A Khan Academy egy középiskolai tanár szemével. **Magyar Kémikusok Lapja 76(11):** 343-344.

ZSOLT HORVÁTH

Gödöllő Reformed Secondary School

TEACHING CAREER IN BRIEF

I received my teaching degree in biology and chemistry from the Kossuth Lajos University (University of Debrecen) in 1995 and have been working since then at the Reformed Church Grammar School in Gödöllő. During the first years of my career, I learned about the BISEL biological water quality assessment method, and in 2000 I participated in the Bioindication and Internet 2000 EU Leonardo in-service training for teachers in Belgium. Then in summer 2002, I organised the BISEL bioindication water quality assessment method 2 accredited in-service training. Between 2006 and 2008, I was asked to update high school biology coursebooks written by Gábor Lénárd and published by Nemzeti Tankönyvkiadó publishers. My tasks included editing (the Prizma series written by Mrs József Berger), preparing digital teaching materials (a CD-ROM with images, figures and experiments for the Lénárd biology coursebook series) and holding lectures (at the start-of-the-year Nemzeti Tankönyvkiadó conference). I have participated in designing biology competition items since 2008. Between 2011 and 2012, I edited digital teaching materials for chemistry and biology called Yenka and Sunflower, and I prepared a series of histological images for Mozaik Publishers. In 2015, I edited digital teaching materials entitled "The molecular cell biology of autolysis, apoptosis and cell regeneration", created by the Department of Anatomical, Cell and Developmental Biology, Eötvös Loránd University, and took part in a training for trainers on the advanced Matura examination in biology. As of 2016, my school (along with three other Hungarian high schools) has participated in a health protection program based on the TANTUdSZT contemporary teaching project, which won a teaching methodology competition announced by the Hungarian Academy of Sciences. In 2016, I had three articles published in the Eduvital column of Élet és Tudomány (Life and Science), a popular science weekly.

PUBLICATIONS

Horváth Zs. (2008). Képek, ábrák és kísérletgyűjtemény a Lénárd-féle biológia-tankönyvcsaládhoz [Images, figures and experiments for the Lénárd biology coursebook series]. Budapest: Nemzeti Tankönyvkiadó Zrt.

Horváth Zs. (2016). Fehérjebontás a sejtekben [Proteolysis in cells]. ÉLET ÉS TUDOMÁNY 71: 140-142.

Papp T, Szekeres Zs, Huoranszki Cs, **Horváth Zs.** (2016). Mindennapi kenyerünk 1-2 [Our daily bread 1–2]. ÉLET ÉS TUDOMÁNY 71: 468-470.

Horváth Zs. Biology assignments for those preparing for advanced level graduation and OKTV Mozaik Publisher, Szeged, 2019

Horváth Zs. Test maturity task sets 10 task sets with solutions and explanations Mozaik Publisher, Szeged, 2020

MARIANNA JENEINÉ FEKETE

Varga Katalin Grammar School, Szolnok

TEACHING CAREER IN BRIEF

I obtained my first degree in biology at the Károly Eszterházy Teacher Training College in Eger in 1992, and then I graduated from the University of Debrecen in 2012 as a certified biology teacher (MSc). In the meantime, thanks to the University of Debrecen, I became a Master of Arts (MA) in English in 2010. Later, in 2018, I became a qualified teacher with a specialization in mentoring. I taught in several types of schools until 2008, when I became a teacher at the Katalin Varga Secondary School in Szolnok, where I teach English and biology in Hungarian and English at intermediate and advanced levels. I participate in graduation committees of middle- and advanced-level exams, both as a member and as chairman, for biology exams in English and Hungarian. As a master teacher, I have been working as a qualifier and supervisor since January 2022. From 2009 to 2019, I was one of the implementers of the student exchange program of BIOCAMP, which was organized twice a year in Szolnok and Brussels. We worked together with the teachers of European School in Brussels. Within the framework of the program, my colleagues and I developed an English-language students' task set for internal use, which was adapted to the theme of the given year: e.g. light, water. I became the deputy head of the laboratory set up thanks to the Öveges program in 2014, where, alongside our students, we hosted practical classes in the four science subjects in a total of 12 primary schools. I became responsible for setting up the biology department in the program. In addition to organizing the in-service training of primary school teachers, my task was to introduce them to the operation of the laboratory's ICT tools and e-lab diary. From 2016, I have been regularly visiting the programs of the Szeged and National Academy of Science with my students. I became a Szent-Györgyi Teacher because I could see that lab practise, lectures in English, and especially meetings with Nobel Prize-winning scientists bring scientific research closer to my students, bring the book-like curriculum to life, and strengthen their commitment to science. As a teacher, the most important thing for me is to help students find and achieve their goals.

PUBLICATIONS

Jeneiné Fekete M: Biology Workbook 12th grade (intermediate level), Szolnok, 2014.

Jeneiné Fekete M: Teacher's Guide 12th grade (biology intermediate level), Szolnok, 2014.

Jeneiné Fekete M: Biology Workbook 11-12. grade (advanced level), Szolnok, 2014.

Jeneiné Fekete M: Teacher's Guide 11-12. grade (biology advanced level), Szolnok, 2014.

ÉVA JÓZSEF

Bolyai Farkas Highschool, Targu Mures

TEACHING CAREER IN BRIEF

I graduated from the University of Bucharest with a biology degree in 1995. I am grateful to the university because during that time, outstanding professionals guided my scientific development, I received a remarkable training in molecular biology and genetics and they provided an insight into science that defined my further development. Thanks to this I have become always open to new things and, having received a strong foundation, I have always been able to keep up with the advancement of science, knowing that my knowledge is at a certain stage and that will always be new things that need to be understood and passed on.
I began to take study trips abroad in 2003. That year I received continuative education at EMBL (European Molecular Biology Laboratory). That same year I participated in teaching workshops in Heidelberg and Jerusalem, where I got a glimpse of the current questions science was asking and the research conducted. Consequently, I went to continue this kind of work in Heidelberg in 2005 and 2007. In 2010 I gained insight into the work of EMBL and EBI (European Bioinformatics Institute) in Hinxton, where I studied bioinformatics. In 2014 I took my first steps in stuctural biology in Grenoble. Also in 2014 I obtained a master's degree in medicinal biotechnology at the University of Medicine and Pharmacy of Targu Mures. In 2020 and 2021, I also learned about the microbiome and CRISPR/cas9 technology online in the courses organized by EMBL.

These study trips have had a huge impact on my life's work. On one of my first trips I learned that these further trainings serve the purpose of preparing high school teaching how to effectively handle the rapid development of science. There are so many novelties in the various areas of science that if high school teachers cannot explain them adequately to their students, society is going to fall behind on everything that happens on the level of scientific life. This is why I aim to be a bridge between my students and the current scientific level so that my students won't have to feel left out and behind and so they understand that science isn't stagnant and they need to aquire enough knowledge so they can keep up with the pace of development.

PUBLICATIONS

Bioinformatics in public education, Teaching natural science in an up-to-date and engaging way, Lecture notes, Eötvös Lóránd University Center for Science Methodology, 2011

The theory and implementation of evolution in public education, Let's Research Together! Presentations of the conference organized by the Csíkszereda Faculty of the Sapientia Transylvanian Hungarian University, Cluj University Publishing House, 2019

To raise to life. History of the Department of Biology, 65 Years in Bolyai Highschool, Lector Publishing House, Targu Mures, 2021

ZOLTÁN JÁNOS KERÉNYI

Premonstratensian School Center, Gödöllő

TEACHING CAREER IN BRIEF

I graduated from József Attila University (University of Szeged) as both a biology teacher and a biologist with specialization in ecology. I started my teaching career in Dugonics András Piarist Grammar School in Szeged as an external teacher, then in 1998 I joined Premonstratensian St. Norbert Grammar School in Gödöllő. I was teaching in the regular curriculum for years, and I taught biology as an extracurricular activity to students applying to university and to enthusiasts as well. We launched a specialized program in biology and chemistry in 2014-15, and I played an active role in developing its content and structure as the lead of the working group. Since our school boasts a great many outstanding students, my teaching activity has become focused on working with young people with particular talent. In order to carry out this work with a truly professional manner, I attended a course at the University of Debrecen to become a talent development teacher (pedagogical professional examination), and completed 'Géniusz' in-service training as well ('Nurturing excellence among talented biology students'). One regular, preferred form of working with talented young people is the 'Path to Science' program where research teams of five students are formed to learn and improve their thinking through joint research activities on a particular subject. At the end of these projects the research teams present their results in a scientific presentation each year at ‚TUDOK' regional and national conferences. For my work in nurturing excellence, I have received Kontra György Award (2010), Bonis Bona Award (2013), Ministerial Certificate of Recognition (2016) and Pro Progressio Award (2018) so far.

PUBLICATIONS

Kerényi Z. (2004). Pilisjászfalu madárvilága [The bird world of Pilisjászfalu]. In Pilisjászfalu I. Pilisjászfalu: Pilisjászfaluért Közalapítvány.

Kerényi Z. (2011). A Gödöllői-dombság állatvilága [The animal world of the Gödöllő Hills]. In Szabó L. (Ed.): A Gödöllői-dombság természeti- és gazdaságföldrajzi viszonyai. Budapest: Agroinform Kiadó.

Kerényi Z, Ivók E. (2013). Nestsite characteristics of the European Bee-eater (Merops apiaster L.) in the Gödöllő Hills. ORNIS HUNGARICA 21(2): 23-32.

BEATRIX CSILLA BAGI KERTÉSZ

Táncsics Mihály Secondary Grammar School of Kaposvár

TEACHING CAREER IN BRIEF

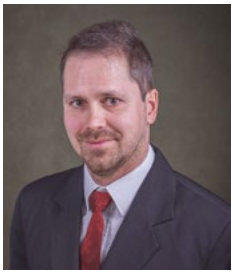
I earned my teaching degree in biology and chemistry at the József Attila University (University of Szeged) in 1993. I rounded out my degree with a postgraduate qualification in environmental protection in 1995. I taught at the Corvin Mátyás Vocational School in Hódmezővásárhely for four years, and I have been teaching in my current workplace at the Táncsics Mihály Grammar School in Kaposvár since 2001. Throughout my career, I have placed a major emphasis on nurturing excellence in my professional work. My students have achieved success at various competitions in chemistry, biology and environmental protection, many of them having gone on to study medicine, pharmacy,
biology and chemistry. I teach advanced elective courses in both my subject areas, and I was the form teacher for three of the groups in the school specializing in biology and chemistry as well as their teacher in those subjects. I have aided my students with a great deal of useful experience by regularly participating in the advanced Matura examinations in both of my subjects. I have always considered it important to learn about and apply an objective measurement of knowledge. I therefore did a specialized examination in teaching with a specialization in educational assessment at the University of Pécs in 2011. I feel responsible for the future of my academic subjects. My aim is for us to engage in a truly appealing science education in our schools at a high standard, an effort I strive to support as a consultant with a master teacher qualification. Finally, I think one needs sufficient professional humility and endurance to be successful in one's work, not only talent.

ILDIKÓ KISS

Teleki Blanka High School and Primary School, Székesfehérvár

TEACHING CAREER IN BRIEF

I graduated from the József Attila University of Szeged as a Secondary Education Biology and Chemistry major. Since 1994, I have been working at the Teleki Blanka Secondary School in Székesfehérvár where I teach both subjects in ordinary level classes and in groups preparing for the advanced level school-leaving examination. Since 2015, I have held the certificate of Master Teacher, and since 2018 I have been contributing to the operation of the institution as the head of the Biology-Chemistry department. In recent years, I have been involved in applying for and implementing several tenders, which have helped us to successfully upgrade the equipment needed for the practice-based approach of teaching Biology, Chemistry and Physics in our school.
I attach great importance to the use of methods that require the active participation of pupils and provide them with hands-on experience, both during lessons and, in extra-academic activities falling outside the realm of the normal school curriculum. Accordingly, I am an active outdoor educator and facilitator of field trips and summer nature camps organised by our school in natural environments. Learning in out-of-school settings draws the participants' attention to relevant aspects of the natural and social environment: during these events, pupils can learn about plant species and the characteristics of plant communities, and carry out botanical, zoological, anthropological, cell biological and environmental experiments and measurements. In addition to the above, I also help with the work of the Scientific Students' Association (TDK), which is a highly active scientific research group at our school. I am also involved in the preparation for the school-leaving exams every year as an examiner and a teacher marking and grading exam scripts. After their graduation, several of my students have become successful doctors, pharmacists and biologists. Moreover, from autumn 2022 as a Szent-Györgyi Senior Teacher, I also have the opportunity to guide and support students who are talented and interested. It is a great pleasure for me to shape the future through consistent engagement with bright, young minds.



LÁSZLÓ KUTROVÁCZ

ELTE Trefort Ágoston Secondary Grammar School, Budapest

TEACHING CAREER IN BRIEF

I started my teaching career in autumn 2002 at the Eötvös Loránd University Trefort Ágoston School in Budapest, where I have worked ever since. I have trained candidate teachers as a mentor teacher in chemistry there for nine years, and I have been department head since 2011. As a form teacher, I will see my second group of students complete their Matura examinations. In 2010, I received the Trefort Ágoston Certificate of Recognition from the Eötvös Loránd University Senate. In the same year, I was certified as a mentor teacher with a specialization in nurturing excellence. My goal is to shed light on the beauty and importance of scientific connections and their close ties to our everyday lives. I lay a great deal of emphasis on mentoring talented students in special after-school lessons. Two of my students have reached the National Secondary School Competition (OKTV) finals in biology and two have done so in chemistry. One of my students became a member of the national team for the International Mendeleev Chemistry Olympiad. In 2018 I received the Lórrántfy Zsuzsanna Award from the ELTE Senate, and in 2019 I received the Bonis Bona Award from the Ministry of Human Resources.

ANNA NAGY

Calvinist Grammar School of Kecskemét

TEACHING CAREER IN BRIEF

I graduated from Eötvös Loránd University with a degree in Biology-Science and Environment. During my university internship I went back to my former secondary school, the Calvinist Secondary School in Kecskemét, where I have been working ever since. I teach biology in each grades from 7-12 at the intermediate and advanced levels, and from this year onwards I also teach science. Through the teaching of biology I wish to discover with my students how exciting and wonderful the living world around us is. My colleagues and I regularly organise field trips, which are always very enjoyable. I believe it is important to transfer knowledge and values when working with students.

BENCE FARKAS SZABÓ

ELTE Bolyai János Practice Primary and Secondary Grammar School, Szombathely

TEACHING CAREER IN BRIEF

In 2016 I graduated as a biology and chemistry teacher at the University of Pécs. During my university studies, I conducted research in the Department of Experimental Zoology and Neurobiology and had the opportunity to participate in the research group of Prof. Dr. Johann Helmut Brandstätter in Erlangen for 10 months. For my achievements I received the „Student of the Year" award in 2012. On the day of my final exams, Mr. József Baranyai invited me back to my former high school to teach, so I started my teaching career right after my university studies. My school work is based on constructionist pedagogy and I use methods that help students to actively acquire knowledge. In my classes I use the flipped classroom method, problem-based teaching and Mazur's peer instruction. I am also actively participating in several projects. I am involved in the Szabó Szabolcs Foundation's Mobillab project as a Mobillab teacher. I have been contributing to the writing of the biology textbooks for NAT2020 for the Educational Authority. In 2022, I received the Richter Young Science Teacher Creative Award for my work.

PUBLICATIONS

Baranyai J., Kerényi Z., **Szabó B. F.**, Veres G., Vizkievicz A.: Gyűjtemény a biológia emelt szintű oktatásához. Oktatási Hivatal, ISBN 978-963-436-256-2

Szabó B. F. (2018). Izomorf kérdések hatása az „egymás tanítása" (peer instruction) módszer hatékonyságára, Középiskolai kémiai lapok (2498-5198): 45 pp 331-340.

TÜNDE SZALAINÉ TÓTH

Lovassy László Grammar School, Veszprém

TEACHING CAREER IN BRIEF

I have been an educator since 1982 and continue to derive great joy from my work to the present day. In addition to my daily teaching responsibilities, I have endeavoured to use and pass on my knowledge and experience at the school, municipal, county and national levels. I consider it a priority to nurture excellence: so far, 45 of my students have reached the final round of Hungary's highly respected National Secondary School Competition (OKTV) in biology, two of them won first place, two of them won second place, and 13 of them finished in the top ten. My students have achieved great success in numerous other prominent competitions for young scholars. As an acknowledgement of my work in nurturing excellence, I received the Rátz Life Achievement Award in 2014, the „Excellent Competition Preparator" title in 2017 and the MOL-Mester-M Award in 2018, as well as a Ministerial Certificate of Recognition. I have also been awarded the Ranolder Prize from the City of Veszprém and the Pro Talento Prize from the Veszprém County Institute of Education. I take part in organising county and national competitions as well as school events. I am a master teacher, consultant, board chair for the Matura examination and multiplier as well as participating in bringing grant projects to fruition. I was a form teacher for 19 years. I enjoy professional challenges, and I have worked as an educational developer in several projects for the Hungarian National Institute for Educational Research and Development (OFI). I have often published in Élet és Tudomány (Life and Science), a popular science weekly, in which studies by my students are also occasionally published. Since 2014, I have participated in the work of the National Teachers Chamber (NPK) as a national delegate, and I have been the national chair of the Man and Nature section of the Chamber since 2015.

PUBLICATIONS

Feith H, Melicher D, Máthé G, Gradvohl E, Füzi R, Darvay S, Hajdú Zs, Nagyné Horváth E, Soósné Kiss Zs, Bihariné Krekó I, Földvári-Nagy Lászlóné, Molnár E, **Szalainé Tóth T**, Urbán V, Kassay A, Falus A. (2016). Tapasztaltok és motiváltság: magyar középiskolások véleménye az egészségnevelő programokról [Experience and motivation: Hungarian high school students' views on health education programs]. ORVOSI HETILAP 2: 65-69.

Szalainé Tóth T. (2015). Megváltoztatható-e, ami génjeinkben meg van írva? [Can we change what is written in our genes?] ÉLET ÉS TUDOMÁNY 48: 1526-1528.

Szalainé Tóth T, Szűcsné Kerti A. (2017). Érettségi mintafeladatsorok biológiából (10 írásbeli emelt szintű feladatsor) [Sample Matura examinations in biology (10 advanced written examination papers)]. Szeged: Maxim Kiadó.

CSILLA SZENTESI

Földes Ferenc High School, Miskolc

TEACHING CAREER IN BRIEF

I completed my studies in biology and geography at the Kossuth Lajos University (University of Debrecen) in 1998. To this day, I have taught in my former high school, Földes Ferenc Grammar School in Miskolc. In 1998, I also completed a teaching degree in the field of environmental protection at the Eszterházy Károly College in Eger. In 2005, I passed an examination in public school management and teaching. In 1996, I joined the County Institute of Education, and I was appointed a municipal consultant in biology and environmental protection between 1998 and 2011. Since 2005, I have been a board chair for the advanced Matura examination in my subject areas and am also engaged in coordinating the corrections for the advanced written Matura examination. During my career, I have organised lectures and held practical in-service training for my colleagues in the county. I have participated in testing digital teaching materials, preparing task sheets and editing geography coursebooks as well as serving as a mentor teacher for a number of student teachers from the University of Debrecen.

As of 2015, I have also worked as a master teacher and an educational inspection and teacher certification expert. In 1997, my colleagues and I launched the Árokszállásy Biology and Environmental Protection Competition, of which I am the main organiser. My school has had a great natural sciences tradition. My work in preparing my students for the advanced Matura examination and in my capacity as a form teacher is a top priority for me. I prepare my students continuously, hold special after-school lessons, and organise fieldwork and lectures. I have received a number of certificates at national competitions through my students as well as a certificate of appreciation from the city. My greatest source of pride is my students' success and the happy smiles on their faces when they achieve their goals.

PUBLICATIONS

Szentesi Cs. (2014). Biológia munkafüzet és tanári segédlet 7.8.10. évfolyam [Biology workbook and teacher's guide for grades 7, 8 and 10]. Miskolc: Miskolc Megyei Jogú Város Önkormányzat

JÓZSEF TULOK

Batthyány Lajos High School, Nagykanizsa

TEACHING CAREER IN BRIEF

I graduated from the Biology-Physical Education department of the Berzsenyi Dániel Teacher Training College in Szombathely in 1989, and in 1996 I graduated from the biology department of the University of Pécs. After 10 years of primary school teaching, I have been teaching at Lajos Batthyány High School in Nagykanizsa since 2001.

One of my important principles in the performance of my professional duties is the teacher – student relationship based on mutual respect. I regularly take advantage of the possibilities of professional further training („Interactive whiteboard - methods for developing the competence of teachers and students"; „Talent management of doubly exceptional students"; „Self-knowledge and peer knowledge in the development of professional efficiency"). Since 2005, I have been working regularly as an advanced-level baccalaureate examiner and corrections officer.

In addition to Biology, the love of drawing and art has accompanied me since my childhood. As an appendix to my university thesis, I prepared a series of slides covering the material of high school genetics. Since the rise of information technology, I have been applying my own drawings, figures and illustrations made digitally, but the legitimacy and role of classic blackboard sketches and drawings have remained unchanged, which is why I still use them to this day.

Together with the natural science working community, we have created a professional workshop for nurturing talents, in the framework of which we coordinate our talented students not only in biology, but also in chemistry, geography, and physics, and we organize preparation sessions for them. We are in contact with the Soós Ernő Research and Development Center in Nagykanizsa, where our students regularly attend chemistry exercises. We have created a website where we can report the successes of our students, thereby motivating the students who come to our school and are interested in natural sciences. It is a great honor for me to be a part of the professional team of NTA since 2023 and to be involved in the talent management program.

KRISZTINA VERESNÉ KIS

Dobó István High School in Eger

TEACHING CAREER IN BRIEF

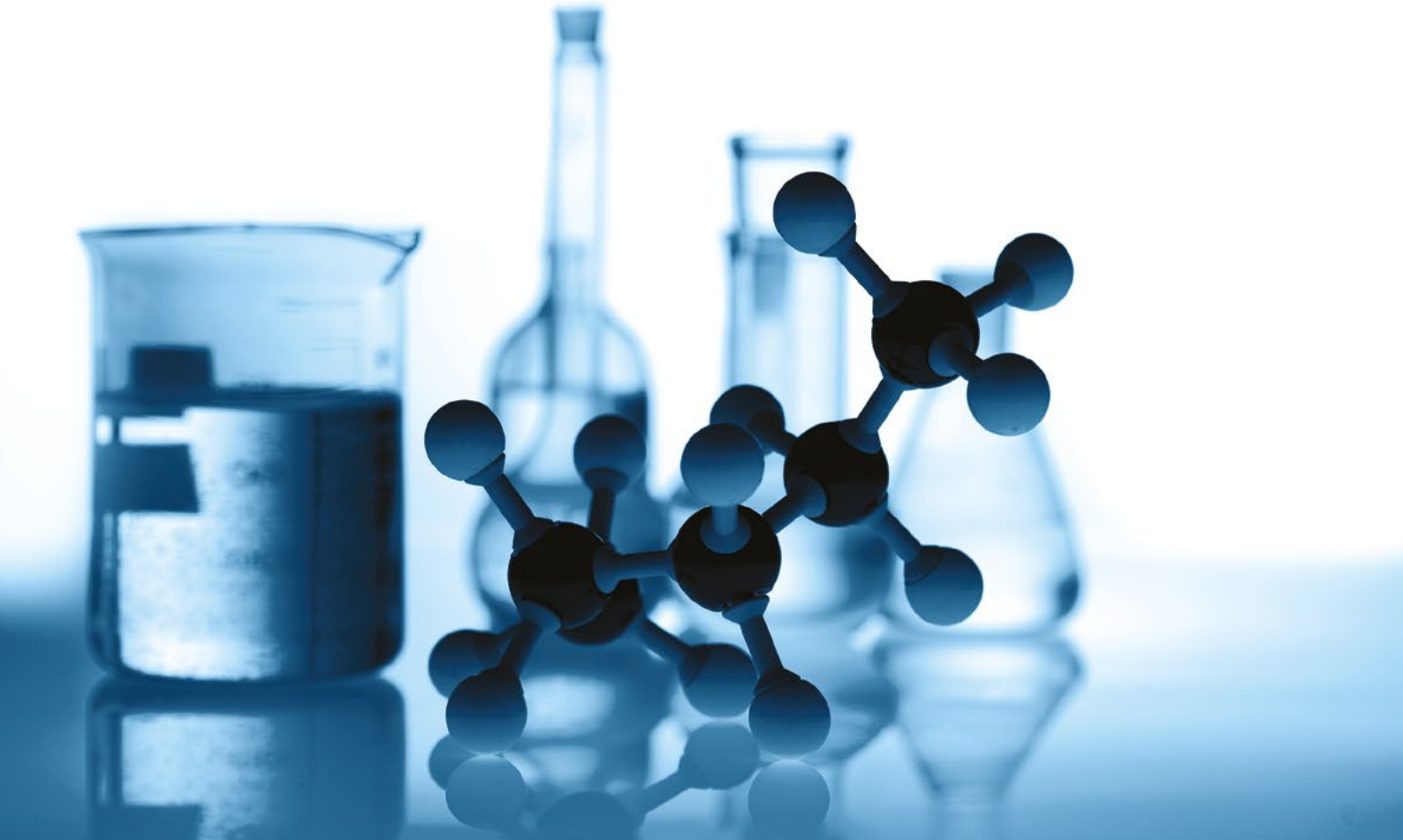
In 1992, I graduated from the biology-geography department of Kossuth Lajos University in Debrecen. I first started teaching in Miskolc at Ilona High School in Zrín, then in 1997 I moved to István Dobó High School in Egri, where I am still teaching. In 1998, I graduated from Eszterházy Károly College with a degree in environmental protection, in 2010, I obtained a mentor teacher degree, and in 2015, I obtained a talent development teacher qualification. In 2006, I took a professional exam in the field of examination chairman, expert and manager, and then in 2016 in the field of talent development teacher. In my school, I have been the leader of the biology-chemistry-geography work community since 2006. I currently coordinated the area of talent management, internal self-evaluation, eco school, and previously the finance school. In 2013, I received the Bonis Bona award and received several city and school talent management awards. I consider it a matter of my heart to embrace talented students and help them choose a career. To this end, I wrote and implemented quite a few successful applications, which helped to improve the equipment of my subjects, to implement programs and study trips that helped to develop their talents. Since 2008, I have been running the Natural Science Talent Care Workshop, and for years I have been organizing a biology competition for 8th graders with my colleagues. Carrying out the duties of the exam chairperson and the tasks of the high school graduation helps to prepare my students as well as possible for the graduation. Since 2011, I have helped quite a few students become teachers as a mentor and supervisor. Since 2016, as a master teacher, I have been performing expert tasks in the field of teacher certification and teaching supervision. In 2018-2019, on behalf of the OFI, I proofread digital teaching materials and participated in the preparation of professional materials for the laboratory of the EKE Practical School. I try to educate my students to love my subjects, to be open to learning about the ever-changing world and the latest research areas. Their success is shown by their national and international competition results.

PUBLICATIONS

In the framework of TÁMOP-3.1.3-10/2-2010-0010 „Education of natural science content with modern infrastructure, in network cooperation in the Northern Hungary region", auxiliary material entitled „Project work water tests" was prepared in 2013.

Edited by: Dr. Ágnes Horváth, Dr. Marianna Dobó: Good practices in talent management in the publication **Dr. Veresné Kis Krisztina,** Györgyi Nemcsikné Pinczés: The talent management activity of Egri Dobó István Gimnázium, published article, EKF, 2014. NTP-TÚP-13-0009 with the support of application ID number.

UNIVERSITY EDUCATION PROGRAM



Leaders of the University Education Program

ZOLTÁN RAKONCZAY

Head of university relations

Professor and head of the Institute of Pathophysiology at the Albert Szent-Györgyi Medical School of the University of Szeged

MÁRIA DELI

Scientific supervisor of the National Academy of Scientist Education (Biological Research Centre Szeged)

Director of the Institute of Biophysics, Biological Barriers Research Group at the Biological Research Centre Szeged

ÁDÁM DÉNES

Scientific supervisor of the National Academy of Scientist Education (HUN-REN Institute of Experimental Medicine)

Senior research fellow at the HUN-REN Institute of Experimental Medicine, Director of the Neuroimmunology Research Group and the Cell Biology Centre

ZSUZSANNA HELYES

Scientific supervisor of the National Academy of Scientist Education (University of Pécs)

Professor of the Department of Pharmacology and Pharmacotherapy at the Faculty of General Medicine of the University of Pécs

TAMÁS MARTINEK

Scientific supervisor of the National Academy of Scientist Education (University of Szeged)

Head of the Institute of Medical Chemistry at the Albert Szent-Györgyi Medical School of the University of Szeged

ATTILA MÓCSAI

Scientific supervisor of the National Academy of Scientist Education (Semmelweis University)

Professor of the Institute of Physiology at the Medical School of the Semmelweis University

ZOLTÁN PAPP

Scientific supervisor of the National Academy of Scientist Education (University of Debrecen)

Professor and head of the Institute of Clinical Physiology at the University of Debrecen, Deputy Dean of Science at the University of Debrecen

ZSUZSA PAPFALVI

Training coordinator

ÁGOTA GYŐRI

Training coordinator

TÜNDE SOPRONYI

Training assistant

(Semmelweis University, HUN-REN Institute of Experimental Medicine)

RÉKA GÉMESI

Training assistant

(Semmelweis University, HUN-REN Institute of Experimental Medicine)

KRISZTINA KASS

Training assistant

(University of Debrecen)

RITA LÍVIA BALÁZS

Training assistant

(University of Pécs)

JULIANNA ORBÁN

Training assistant

(University of Szeged, Biological Research Centre Szeged)

BUDAPEST
SZENT-GYÖRGYI MENTORS

LÁSZLÓ ACSÁDY

HUN-REN Institute of Experimental Medicine
Thalamus Research Group

RESEARCH AREA

The main research focus of the Thalamus Research Group is to decipher the network mechanisms of the thalamocortical circuits that underlies higher order cognition as well as its pathological and alterations. To this end we utilize cell type specific investigations at morphological, physiological and behavioral levels to reveal how nucleus specific synaptic organization of thalamic circuits provides a framework for plastic behavioral and neuronal response to environmental challenges.

SELECTED PUBLICATIONS

Acsády, L. (2018) Heartless beat or beatless heart? **Nat Neurosci 21:** 649-651.

Acsády, L., Harris, K.D. (2017) Synaptic scaling in sleep. **Science 355:** 457-457.

Acsády, L. (2017) The thalamic paradox. **Nat Neurosci 20:** 901-902.

Fiath, R., Beregszaszi, P., Horvath, D., Wittner, L., Aarts, A.A., Ruther, P., Neves, H.P., Bokor, H., **Acsady, L.**, Ulbert, I. (2016) Large-scale recording of thalamocortical circuits: in vivo electrophysiology with the two-dimensional electronic depth control silicon probe. **Journal of Neurophysiology 116:** 2312-2330.

Halassa, M.M., **Acsády, L.** (2016) Thalamic Inhibition: Diverse Sources, Diverse Scales. **Trends in Neurosciences 39:** 680-693.

ATTILA AMBRUS

Semmelweis University
Faculty of Medicine
Department of Biochemistry

RESEARCH AREA

The mitochondrion is an organelle inside the cell that serves as a powerhouse. In case the mitochondrial energy-generating processes (delivered by specific enzymes) get compromised, due to e.g. a genetic mutation that affects a key enzyme, severe clinical symptoms may arise; the generally neurological, cardiological, and/or hepatological manifestations often lead to premature death. The group of enzymes that was selected for our investigations comprises the mitochondrial alpha-keto (or 2-oxo) acid dehydrogenase multienzyme complexes (OADHc), which serve multiple pivotal roles in the energy metabolism of the mitochondrion. In the future we wish to initiate the development of enzyme replacement strategies against relevant OADHc deficiencies, where the healthy forms of the enzymes are delivered directly into the mitochondrion to replace the impaired enzymes. We also wish to design small molecule drug candidates in the near future to control the generation of harmful reactive radicals by OADHc and counteract the compromised enzymatic efficacy. Another proposed intervention approach is to reinforce by adaptor drug molecules the at times loosened obligate attachments among enzyme components in the greater enzyme complexes. For all of these approaches to be successful, first we need to investigate the relevant molecular pathomechanisms and related structures, which is part of our research program.

Selected research results will potentially be also applicable in the supplemental threatments of other neuronal disorders (like stroke, neurodegenerative disorders, etc.).

SELECTED PUBLICATIONS

Nagy, B., Polak, M., Ozohanics, O., Zambo, Z., Szabo, E., Hubert, A., Jordan, F., Novaček, J., Adam-Vizi, V., **Ambrus, A.** (2021) Structure of the dihydrolipoamide succinyltransferase (E2) component of the human alpha-ketoglutarate dehydrogenase complex (hKGDHc) revealed by cryo-EM and cross-linking mass spectrometry: Implications for the overall hKGDHc structure. **Biochim Biophys Acta (General Subjects)1865(6):** 129889.

Szabo, E., Wilk, P., Nagy, B., Zambo, Z., Bui, D., Weichsel, A., Arjunan, P., Torocsik, B., Hubert, A., Furey, W., Montfort, W.R., Jordan, F., Weiss, M.S., Adam-Vizi, V., **Ambrus, A.** (2019) Underlying molecular alterations in human dihydrolipoamide dehydrogenase deficiency revealed by structural analyses of disease-causing enzyme variants. **Hum Mol Genet 28:** 3339-3354.

Szabo, E., Mizsei, R., Wilk, P., Zambo, Z., Torocsik, B., Weiss, M.S., Adam-Vizi, V., **Ambrus, A.** (2018) Crystal structures of the disease-causing D444V mutant and the relevant wild type human dihydrolipoamide dehydrogenase. **Free Radic Biol Med 124:** 214-220.

Ambrus, A., Adam-Vizi, V. (2018) Human dihydrolipoamide dehydrogenase (E3) deficiency: novel insights into the structural basis and molecular pathomechanism. **Neurochem Int 117:** 5-14.

TAMÁS ARÁNYI

Semmelweis University
Faculty of Medicine
Department of Molecular Biology

RESEARCH AREA

1/ Our goal is to understand the role of DNA methylation in both physiological and pathological conditions. We work with conditional knockout mice to elucidate the roles of de novo methyltransferases (DNMT3a and b) in embryonic development, differentiation, maturation, and aging. We employ epigenomic methods to characterize our models.
2/ Ectopic calcification is characteristic of various rare and common diseases, such as chronic kidney disease. Loss-of-function mutations in different proteins (e.g., ABCC6) lead to rare hereditary diseases characterized by ectopic mineralization. Recently, we have identified variants causing incomplete penetrance diseases. Currently, we aim to understand the pathophysiological roles of the disease-causing proteins and epigenetic mechanisms regulating ectopic calcification processes.

SELECTED PUBLICATIONS

Jain, P., Miller-Fleming, T., Topaloudi, A, Yu, D., Drineas, P., Georgitsi, M., Yang, Z., Rizzo, R., Müller-Vahl, KR., Tumer, Z., (...) **TS-EUROTRAIN Network**; Mathews CA, Scharf JM, Hoekstra PJ, Davis LK, Paschou P. (2023). Polygenic risk score-based phenome-wide association study identifies novel association for Tourette syndrome. **Transl Psychiatry 13(1):** 69.

Tsetsos, F., Topaloudi, A., Jain, P., Yang, Z., Yu, D., Kolovos, P., Tumer, Z., Rizzo, R., Hartmann, A., Depienne, C., Worbe, Y., Müller-Vahl, KR., Cath, DC., Boomsma, DI., Wolanczyk, T., Zekanowski, C., Barta, C., (...) **TS-EUROTRAIN Network**; TIC Genetics Collaborative Group; Tischfield JA, Heiman GA, Willsey AJ, Dietrich A, Davis LK, Crowley JJ, Mathews CA, Scharf JM, Georgitsi M, Hoekstra PJ, Paschou P. (2023) Genome-wide association study points to novel locus for Gilles de la Tourette syndrome. **Biol Psychiatry Online** ahead of print.

Liang, X., **Aranyi, T.**, Zhou, J., Guan, Y., Liu, H., Susztak, K., (2023) Tet2 and Tet3 mediated cytosine hydroxymethylation in Six2 progenitor cells is critical for nephron progenitor differentiation and nephron endowment. **J Am Soc Nephrol 34(4):** 572-89.

Szeri, F., Miko, A., Navasiolava, N., Kaposi, A., Verschuere, S., Molnar, B., Li, Q., Terry, SF., Boraldi, F., Uitto, J., van de Wetering, K., Martin, L., Quaglino, D., Vanakker, OM., Tory, K., **Aranyi, T.*** (2022) The pathogenic c.1171A>G (p.Arg391Gly) and c.2359G>A (p.Val787Ile) ABCC6 variants display incomplete penetrance causing pseudoxanthoma elasticum in a subset of individuals. **Hum Mutat 43(12):** 1872-81.

Belal, S., Goudenège, D., Bocca, C., Dumont, F., Chao De La Barca, JM., Desquiret-Dumas, V., Gueguen, N., Geffroy, G., Benyahia, R., Kane, S., Khiati, S., Bris, C., **Aranyi, T.**, Stockholm, D., Inisan, A., Renaud, A., Barth, M., Simard, G., Reynier, P., Letournel, F., Lenaers, G., Bonneau, D., Chevrollier, A., Procaccio, V. (2022) Glutamate-Induced Deregulation of Krebs Cycle in Mitochondrial Encephalopathy Lactic Acidosis Syndrome Stroke-Like Episodes (MELAS) Syndrome Is Alleviated by Ketone Body Exposure. **Biomedicines 10 (7):** 1665.

CSABA BARTA

Semmelweis University
Faculty of Medicine
Department of Molecular Biology

RESEARCH AREA

The main research field of our laboratory is psychogenetics. Within these we study the genetic and epigenetic background of a number of child psychiatric disorders, so called neurodevelopmental conditions (such as Tourette syndrome, attention deficit, hyperactivity disorder /ADHD/, obsessive-compulsive disorder /OCD/) using molecular biological techniques and bioinformatic analyses. The other main research area of our group is the genetic study of different addictions. We study genetic variation associated with both substance use and dependence, as well as behavioral addictions, such as internet use, gambling, gaming, etc.) The functional role of the studied genetic variants is investigated in cell cultures derived from neural tissue, and also in some animal models (C. elegans and rodents). Apart from the above we currently have genetic and epigenetic studies on infant behavior (regulational disorder), as well as the link between type 2 diabetes and certain insulin signaling related mental disorders.

SELECTED PUBLICATIONS

Cross-Disorder Group of the Psychiatric Genomics Consortium (a total of 606 authors, incl. **Barta C**). (2019) Genomic Relationships, Novel Loci, and Pleiotropic Mechanisms across Eight Psychiatric Disorders. **Cell 179:** 1469-1482. e11.

Pagliaroli, L., Vereczkei, A., Padmanabhuni, S.S., Tárnok Zs., Farkas, L., Nagy, P., Rizzo, R., Wolanczyk, T., Szymanska, U., Kapisyzi, M., Basha, E., Koumoula, A., Androutsos, C., Tsironi, V., Karagiannidis, I., Paschou P., and **Barta, C.** (2020) Association of genetic variation in the 3'UTR of LHX6, IMMP2L and AADAC with Tourette Syndrome. **Front Neurol 11:** 803.

Pagliaroli, L., Fothi, A., Nespoli, E., Liko, I., Veto, B., Devay, P., Szeri, F., Hengerer, B., **Barta, C.,** Aranyi, T. (2021) Riluzole Administration to Rats with Levodopa-Induced Dyskinesia Leads to Loss of DNA Methylation in Neuronal Genes. **Cells 10:** 1442.

Yang, Z., Wu, H., Lee, P.H., Tsetsos, F., Davis, L.K., Yu, D., Lee, S.H., Dalsgaard, S., Haavik, J., **Barta, C.,** Zayats, T., Eapen, V., Wray, N.R., Devlin, B., Daly, M., Neale, B., Børglum, A.D., Crowley, J.J., Scharf, J., Mathews, C.A., Faraone, S.V., Franke, B., Mattheisen, M., Smoller, J.W., Paschou, P. (2021) Investigating Shared Genetic Basis Across Tourette Syndrome and Comorbid Neurodevelopmental Disorders Along the Impulsivity-Compulsivity Spectrum. **Biol Psychiatry 90:** 317-327.

Vereczkei, A., **Barta, C.,** Magi, A., Farkas, J., Eisinger, A., Király, O., Belik, A., Griffiths, M.D., Szekely, A., Sasvári-Székely, M., Urbán, R., Potenza, M.N., Badgaiyan, R.D., Blum, K., Demetrovics, Z., Kotyuk, E. (2022) FOXN3 and GDNF Polymorphisms as Common Genetic Factors of Substance Use and Addictive Behaviors. **J Pers Med 12:** 690.

ZOLTÁN BENYÓ

Semmelweis University
Faculty of Medicine
Department of Translational Medicine

RESEARCH AREA

Physiology and pathophysiology of the cardiovascular system.
Regulation of the cerebral blood flow.
Signaling pathways of the endothelium and smooth muscle.
Physiological and pathophysiological functions of lipid mediators in the cardiovascular system.
Tumor angiogenesis and metastasis formation.
Physiological control and dysfunctions of the urinary bladder.

SELECTED PUBLICATIONS

Borsodi, K., Balla, H., Molnár, P.J., Lénárt, Á., Kenessey, I., Horváth, A., Keszthelyi, A., Romics, M., Majoros, A., Nyirády, P., Offermanns, S., **Benyó, Z.** (2022) Signaling pathways mediating bradykinin-induced contraction in murine and human detrusor muscle. **Frontiers in Medicine 8:** 745638.

Thomas, M.J., Major, E., Benedek, A., Horváth, I., Máthé, D., Bergmann, R., Szász, A.M., Krenács, T., **Benyó, Z.** (2020) Suppression of metastatic melanoma growth in lung by modulated electro-hyperthermia monitored by a minimally invasive heat stress testing approach in mice. **Cancers 12:** 3872.

Dancs, P.T., Ruisanchez, E., Balogh, A., Panta, C.R., Miklós, Z., Nüsing, R.M., Aoki, J., Chun, J., Offermanns, S., Tigyi, G., **Benyó, Z.** (2017) LPA1 receptor-mediated thromboxane A2 release is responsible for lysophosphatidic acid-induced vascular smooth muscle contraction. FASEB **Journal 31:** 1547-1555.

Benyó, Z., Ruisanchez, E., Leszl-Ishiguro, M., Sándor, P., Pacher, P. (2016) Endocannabinoids in cerebrovascular regulation. **American Journal of Physiology - Heart and Circulatory Physiology, 310:** H785-H801.

Wirth, A., **Benyó, Z.,** Lukasova, M., Leutgeb, B., Wettschureck, N., Gorbey, S., Őrsy, P., Horváth, B., Maser-Gluth, C., Greiner, E., Lemmer, B., Schütz, G., Gutkind, S., Offermanns, S. (2008) G12/G13-LARG-mediated signalling in vascular smooth muscle is required for salt-induced hypertension. **Nature Medicine 14:** 64-68.

CSABA BÖDÖR

Semmelweis University
Faculty of Medicine
Department of Pathology and
Experimental Cancer Research

RESEARCH AREA

Our research focuses on better understanding of the genomic background of the malignant diseases of the hematopoietic system, i. e. leukemias and lymphomas with a special focus on identification of biomarkers and development of technologies supporting a more precise diagnosis, risk stratification and application of targeted therapies in this disease group.

SELECTED PUBLICATIONS

Bödör, C., Kotmayer, L., László. T., Takács, F., Barna, G., Kiss, R., Sebestyén, E., Nagy, T., Hegyi, L.L., Mikala, G., Fekete, S., Farkas, P., Balogh, A., Masszi, T., Demeter, J., Weisinger, J., Alizadeh, H., Kajtár, B., Kohl, Z., Szász, R., Gergely, L., Gurbity Pálfi, T., Sulák. A., Kollár, B., Egyed, M., Plander, M., Rejtő, L., Szerafin, L., Ilonczai, P., Tamáska, P., Pettendi, P., Lévai, D., Schneider, T., Sebestyén, A., Csermely, P., Matolcsy, A., Mátrai, Z., Alpár, D. (2021) Screening and monitoring of the BTKC481S mutation in a real-world cohort of patients with relapsed/refractory chronic lymphocytic leukaemia during ibrutinib therapy. **British Journal of Haematology 194:** 355-364.

Nagy, Á., Bátai, B., Balogh, A., Illés, S., Mikala, G., Nagy, N., Kiss, L., Kotmayer, L., Matolcsy, A., Alpár, D., Masszi, T., Masszi, A., **Bödör, C.** (2020) Quantitative Analysis and Monitoring of EZH2 Mutations Using Liquid Biopsy in Follicular Lymphoma. **Genes 11:** 785.

Rendeiro, AF., Krausgruber, T., Fortelny, N., Zhao, F., Penz, T., Farlik, M., Schuster, L.C., Nemc, A., Tasnády, S., Réti, M., Mátrai, Z., Alpár, D., **Bödör, C.**, Schmidl, C., Bock, C. (2020) Chromatin mapping and single-cell immune profiling define the temporal dynamics of ibrutinib response in CLL. **Nature Communications 11:** 577.

Gángó, A., Alpár, D., Galik, B., Marosvári, D., Kiss, R., Fésüs, V., Aczél, D., Eyüpoglu, E., Nagy, N., Nagy, Á., Krizsán, S., Reiniger, L., Farkas, P., Kozma, A., Ádám, E., Tasnády, S., Réti, M., Matolcsy, A., Gyenesei, A., Mátrai, Z., **Bödör, C.** (2019) Dissection of subclonal evolution by temporal mutation profiling in chronic lymphocytic leukemia patients treated with ibrutinib. **International Journal of Cancer 146:** 85-93.

Kiss, R., Alpár, D., Gángó, A., Nagy, N., Eyupoglu, E., Aczél, D., Matolcsy, A., Csomor, J., Mátrai, Z., **Bödör, C.** (2018) Spatial clonal evolution leading to ibrutinib resistance and disease progression in chronic lymphocytic leukemia. **Haematologica 104:** 38-41.

HENRIETT BUTZ

Semmelweis University, Faculty of Medicine
Department of Laboratory Medicine

National Institute of Oncology,
Department of Molecular Genetics

RESEARCH AREA

Our research interest focuses on the clinical and molecular genetics of hereditary cancer and tumor syndromes and the pathogenesis of rare cancers and tumors of the neuroendocrine system. Clinical genetic research supports the complex genetic care of cancer patients including genetic susceptibility, prevention, targeted therapy, family screening, and the implementation of novel genetic methods into the daily routine. Modern molecular genetic methods and translational research support the precise understanding of tumor pathogenesis and the identification of diagnostic, prognostic, and predictive biomarkers.

SELECTED PUBLICATIONS

Butz, H., Rácz, K., Hunyady, L., Patócs, A. (2012) Crosstalk between TGF-β signaling and the microRNA machinery. **Trends Pharmacol Sci 33:** 382-93.

Butz, H., Szabó, P.M., Nofech-Mozes, R., Rotondo, F., Kovacs, K., Mirham, L., Girgis, H., Boles, D., Patocs, A., Yousef, G.M. (2014) Integrative bioinformatics analysis reveals new prognostic biomarkers of clear cell renal cell carcinoma. **Clin Chem 60**: 1314-26.

Szabó, B., Németh, K., Mészáros, K., Krokker, L., Likó, I., Saskői, É., Németh, K., Szabó, P.T., Szücs, N., Czirják, S., Szalóki, G., Patócs, A., **Butz, H.** (2022) Aspirin Mediates Its Antitumoral Effect Through Inhibiting PTTG1 in Pituitary Adenoma. **J Clin Endocrinol Metab 107:** 3066-3079.

Kuczynski, E.A., Yin, M., Bar-Zion, A., Lee, C.R., **Butz, H.**, Man, S., Daley, F., Vermeulen, P.B., Yousef, G.M., Foster, F.S., Reynolds, A.R., Kerbel, R.S. (2016) Co-option of Liver Vessels and Not Sprouting Angiogenesis Drives Acquired Sorafenib Resistance in Hepatocellular Carcinoma. **J Natl Cancer Inst 108:** djw030.

Butz, H., Patócs, A. (2022) Mechanisms behind context-dependent role of glucocorticoids in breast cancer progression. **Cancer Metastasis Rev 41:** 803-832.

CHRISTOS CHINOPOULOS

Semmelweis University
Faculty of Medicine
Department of Biochemistry

RESEARCH AREA

Alterations in oncometabolism are substantiated by changes in protein expression 'rewiring' certain metabolic pathways, providing an excellent opportunity for cancer-specific therapeutic intervention. Identifying those proteins involved in bioenergetic pathways that are up- or downregulated in order to serve the needs of neoplasia, is crucial for beating cancer.

SELECTED PUBLICATIONS

Seyfried, T.N., Arismendi-Morillo, G., Mukherjee, P., **Chinopoulos, C.** (2020) On the Origin of ATP Synthesis in Cancer. **iScience 23:** 101761.

Chinopoulos, C. (2020) Acute sources of mitochondrial NAD+ during respiratory chain dysfunction. **Exp Neurol 327:** 113218.

Dobolyi, A., Bago, A., Palkovits, M., Nemeria, N.S., Jordan, F., Doczi, J., Ambrus, A., Adam-Vizi, V., **Chinopoulos, C.** (2020) Exclusive neuronal detection of KGDHC-specific subunits in the adult human brain cortex despite pancellular protein lysine succinylation. **Brain Struct Funct 225:** 639-667.

Chinopoulos, C. (2020) Quantification of mitochondrial DNA from peripheral tissues: Limitations in predicting the severity of neurometabolic disorders and proposal of a novel diagnostic test. **Mol Aspects Med 71:** 100834.

Chen, E., Kiebish, M.A., McDaniel, J., Niedzwiecka, K., Kucharczyk, R., Ravasz, D., Gao, F., Narain, N.R., Sarangarajan, R., Seyfried, T.N., Adam-Vizi, V., **Chinopoulos, C.** (2018) Perturbation of the yeast mitochondrial lipidome and associated membrane proteins following heterologous expression of Artemia-ANT. **Sci Rep 18:** 5915.

GÁBOR CZIRJÁK

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The main research area of our group is the study of the molecular regulatory mechanisms of potassium channels. The focus is on the background potassium channels (with two pore domains per subunit, K2P), but we also reported results on the function of voltage-gated Kv8.2 and lysosomal, unconventional TMEM175 channels. Significant results have been obtained in the detection of heterodimerization of subunits of the TASK and TREK subfamilies and in the study of the regulation of TASK and TRESK channels by signaling pathways. We are known for the first detection of the TASK-1 / TASK-3 heterodimer and the comprehensive description of the TRESK regulation by calcineurin-dependent dephosphorylation.

SELECTED PUBLICATIONS

Czirják, G., Tóth, Z.E., Enyedi, P. (2004) The two-pore domain K^+ channel, TRESK, is activated by the cytoplasmic calcium signal through calcineurin. **Journal of Biological Chemistry 279:**18550-8.

Czirják, G., Enyedi, P. (2006) Targeting of calcineurin to an NFAT-like docking site is required for the calcium-dependent activation of the background K^+ channel, TRESK. **Journal of Biological Chemistry 281:**14677-82.

Enyedi, P., **Czirják, G.** (2010) Molecular background of leak K^+ currents: two-pore domain potassium channels. **Physiological Reviews 90:** 559-605.

Braun, G., Lengyel, M., Enyedi, P., **Czirják, G.** (2015) Differential sensitivity of TREK-1, TREK-2 and TRAAK background potassium channels to the polycationic dye ruthenium red. **British Journal of Pharmacology 172:**1728-38.

Pergel, E., Veres, I., Csigi, G.I., **Czirják, G.** (2021) Translocation of TMEM175 Lysosomal Potassium Channel to the Plasma Membrane by Dynasore Compounds. **International Journal of Molecular Sciences 22:**10515.

LÁSZLÓ CSANÁDY

Semmelweis University
Faculty of Medicine
Department of Biochemistry

RESEARCH AREA

Ion channel structure-function. CFTR chloride ion channel. TRPM2 cation channel.

SELECTED PUBLICATIONS

Mihályi, C., Iordanov, I., Töröcsik, B., **Csanády, L.** (2020) Simple binding of protein kinase A, prior to phosphorylation, allows CFTR anion channels to be opened by nucleotides. **Proc Natl Acad Sci USA 117:** 21740-21746.

Liu, F., Zhang, Z., **Csanády, L.**, Gadbsy, D.C., Chen, J. (2017) Molecular stucture of the human CFTR ion channel. **Cell 169:** 85-95.

Sorum, B., Czege, D., **Csanády, L.** (2015) Timing of CFTR Pore Opening and Structure of Its Transition State. **Cell 163:** 724-733.

Tóth, B., Iordanov, I., **Csanády, L.** (2014) Putative chanzyme activity of TRPM2 cation channel is unrelated to pore gating. **Proc Natl Acad Sci USA 111:** 16949-16954.

Tóth, B., **Csanády, L.** (2012) Pore collapse underlies irreversible inactivation of TRPM2 cation channel currents. **Proc Natl Acad Sci USA 109:** 13440-13445.

GÁBOR CSUKLY

Semmelweis University
Department of Psychiatry and Psychotherapy

RESEARCH AREA

He currently leads the "Clinical Neuroscience and Neuroimaging Research Group" at Semmelweis University. The main research focus of the group is the study of emotion processing and social cognition and perception in schizophrenia and their relation to brain connectivity as measured by imaging studies. They are also investigating the early detection and prevention of dementia. Their main research methods are MR imaging and high-density EEG, as well as neuropsychological studies. The group's most recent research area is Transcranial Magnetic Stimulation (TMS), focusing on the potential of TMS treatment in treating schizophrenia.

SELECTED PUBLICATIONS

Csukly, G., Farkas, K., Fodor, T., Unoka, Z., Polner, B. (2023) Stronger coupling of emotional instability with reward processing in borderline personality disorder is predicted by schema modes. **Psychol Med**. 2023 Feb 9:1-10. doi: 10.1017/S0033291723000193. Online ahead of print. PMID: 36754994.

Becske, M., Marosi, C., Molnár, H., Fodor, Z., Tombor, L., **Csukly, G.** (2022) Distractor filtering and its electrophysiological correlates in schizophrenia. **Clin Neurophysiol.** 2022 Jan;133:71-82. doi: 10.1016/j.clinph.2021.10.009. Epub 2021 Nov 9. PMID: 34814018.

Fodor, Z., Horváth, A., Hidasi, Z., Gouw, A.A., Stam, C.J., **Csukly, G.** (2021) EEG Alpha and Beta Band Functional Connectivity and Network Structure Mark Hub Overload in Mild Cognitive Impairment During Memory Maintenance. **Front Aging Neurosci.** 2021 Oct 7;13:680200. doi: 10.3389/fnagi.2021.680200. eCollection 2021. PMID: 34690735.

Csukly, G., Szabó, Á., Polgár, P., Farkas, K., Gyebnár, G., Kozák, L.R., Stefanics. G. (2021) Fronto-thalamic structural and effective connectivity and delusions in schizophrenia: a combined DTI/DCM study. **Psychol Med.** 2021 Sep;51(12):2083-2093. doi: 10.1017/S0033291720000859. Epub 2020 Apr 24. PMID: 32329710.

Marosi, C., Fodor, Z., **Csukly, G.** (2019) From basic perception deficits to facial affect recognition impairments in schizophrenia. **Sci Rep.** 2019 Jun 20;9(1):8958. doi: 10.1038/s41598-019-45231-x.PMID: 31222063.

ÁDÁM DÉNES

HUN-REN Institute of Experimental Medicine
Laboratory of Neuroimmunology

RESEARCH AREA

Adam Denes is heading the Laboratory of Neuroimmunology and the Cell Biology Centre in the HUN-REN Institute of Experimental Medicine. His main interest is neuroinflammation and brain-immune interactions in health and disease. Their research explored the mechanisms through which inflammation inside or outside the central nervous system contributes to different forms of brain injury. They have also studied the pathways through which immune processes are controlled by the nervous system. His research group has revealed the role of microglia, the main immune cells of the brain in regulating neuronal activity and injury and the pivotal role of microglia in modulating cerebral blood flow.

SELECTED PUBLICATIONS

Császár, E., Lénárt, N., Cserép, C., Környei, Z., Fekete, R., Pósfai, B., Balázsfi, D., Hangya, B., Schwarcz, A.D., Szabadits, E., Szöllősi, D., Szigeti, K., Máthé, D., West, B.L., Sviatkó, K., Brás, A.R., Mariani, J.C., Kliewer, A., Lenkei, Z., Hricisák, L., Benyó, Z., Baranyi, M., Sperlágh, B., Menyhárt, Á., Farkas, E., **Dénes, Á.** (2022) Microglia modulate blood flow, neurovascular coupling, and hypoperfusion via purinergic actions. **J Exp Med 219:** e20211071.

Cserép, C., Pósfai, B., **Dénes, Á.** (2021). Shaping neuronal fate: functional heterogeneity of direct microglia-neuron interactions. **Neuron 109:** 222-240.

Cserép, C., Pósfai, B., Lénárt, N., Fekete, R., László, Z.I., Lele, Z., Orsolits, B., Molnár, G., Heindl, S., Schwarcz, A.D., Ujvári, K., Környei, Z., Tóth, K., Szabadits, E., Sperlágh, B., Baranyi, M., Csiba, L., Hortobágyi, T., Maglóczky, Z., Martinecz, B., Szabó, G., Erdélyi, F., Szipőcs, R., Tamkun, M.M., Gesierich, B., Duering, M., Katona, I., Liesz, A., Tamás, G., **Dénes, Á.** (2020) Microglia monitor and protect neuronal function via specialized somatic purinergic junctions. **Science 367:** 528-537.

Fekete, R., Cserép, C., Lénárt, N., Tóth, K., Orsolits, B., Martinecz, B., Méhes, E., Szabó, B., Németh, V., Gönci, B., Sperlágh, B., Boldogkői, Z., Kittel, Á., Baranyi, M., Ferenczi, S., Kovács, K., Szalay, G., Rózsa, B., Webb, C., Kovacs, G.G., Hortobágyi, T., West, B.L., Környei, Z., **Dénes, Á.** (2018) Microglia control the spread of neurotropic virus infection via P2Y12 signalling and recruit monocytes through P2Y12-independent mechanisms. **Acta Neuropathol 136:** 461-482.

Szalay, G., Martinecz, B., Lénárt, N., Környei, Z., Orsolits, B., Judák, L., Császár, E., Fekete, R., West, B.L., Katona, G., Rózsa, B., **Dénes, Á.** (2016) Microglia protect against brain injury and their selective elimination dysregulates neuronal network activity after stroke. **Nat Commun 7:** 11499.

BALÁZS ENYEDI

Semmelweis University
Department of Physiology

RESEARCH AREA

Tissue injury triggers rapid defense mechanisms against potential intruding pathogens to protect the body from the outside world within minutes. In the course of the triggered inflammatory process, chemoattractants guide leukocytes to the site of damage to serve in host defense and promote long term healing and regeneration. Our research focuses on investigating the early stages of the inflammatory processes by using molecular and cell biological tools along with transgenic zebrafish as a model system. Our main goal is to understand how cells of the damaged tissue communicate with leukocytes to trigger and regulate inflammation. To achieve this, we develop genetically encoded fluorescent biosensors using advanced molecular and genetic engineering tools. We test and optimize these tools in cell culture experiments and subsequently create transgenic zebrafish lines expressing the novel biosensors. This allows us to visualize and measure the cellular and molecular mechanisms of the inflammatory process initiated by tissue damage through confocal microscopy.

SELECTED PUBLICATIONS

Tamás, SX., Roux, BT., Vámosi, B., Dehne, FG., Török, A., Fazekas, L., **Enyedi, B.** (2023) A genetically encoded sensor for visualizing leukotriene B4 gradients in vivo. **Nat Commun.** 2023 Aug 1;14(1):4610.

Enyedi, B., Niethammer, P. (2015) Mechanisms of epithelial wound detection. **Trends Cell Biol.** 2015 Jul;25(7):398-407.

Enyedi, B., Jelcic, M., Niethammer, P. (2016) The cell nucleus serves as a mechanotransducer of tissue damage - induced inflammation. **Cell.** 2016 May 19;165(5):1160-70

Gault, WJ., **Enyedi, B.**, Niethammer, P. (2014) Osmotic surveillance mediates rapid wound closure through nucleotide release. **J. Cell Biol.** 2014 Dec 22;207(6):767-82.

Enyedi, B., Kala, S., Nikolich-Zugich, T., Niethammer, P. (2013) Tissue damage detection by osmotic surveillance. **Nat Cell Biol.** 2013 Sep;15(9):1123–1130.

HENRIETTE FARKAS

Semmelweis University
Faculty of Medicine
Department of Internal Medicine and Hematology

RESEARCH AREA

The Hungarian Angioedema Centre of Reference and Excellence (the member of the ACARE Network https://acare-network.com) at the Department of Internal Medicine and Haematology, Semmelweis University was established in 1998. Our centre is the founder and organizer of The International C1-Inhibitor deficiency and Angioedema Workshop which has taken place on 12 occasions since 1999 in Budapest, established the HAENETWORK project and Central Eastern European Angioedema Centre. Our research focuses on pathomechanism of angioedema, especially bradykinin mediated forms. Complement, molecular genetic and cell laboratories, patient registry, biobank provides the appropriate background for both clinical and basic research. We are investigating the function of plasma enzyme systems, white blood cells and endothelial cells involved in the development of angioedema, mainly in hereditary angioedema due to C1 inhibitor Deficiency. We have very good partnership and collaboration with colleagues from 44 countries.

SELECTED PUBLICATIONS

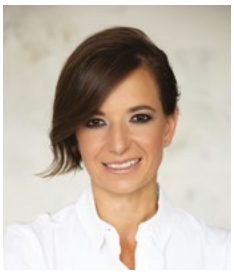
Farkas, H. et al. (2017) International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. **Allergy 72:** 300-313.

Andrási, N., Veszeli, N., Kőhalmi, K.V., Csuka, D., Temesszentandrási, Gy., Varga L., **Farkas, H.** (2018) Idiopathic Nonhistaminergic Acquired Angioedema Versus Hereditary Angioedema. **J Allergy Clin Immunol Pract 6:** 1205-1208.

Farkas, H., Kőhalmi, K.V., Visy, B., Veszeli, N., Varga, L. (2020) Clinical Characteristics and Safety of Plasma-Derived C1-Inhibitor Therapy in Children and Adolescents with Hereditary Angioedema—A Long-Term Survey. **Journal of J Allergy Clin Immunol Pract 8:** 2379-2383.

Balla, Zs., Zsilinszky, Zs., Pólai, Zs., Andrasi, N., Kőhalmi, K.V., Csuka, D., Varga, L., **Farkas, H.** (2021) The Importance of Complement Testing in Acquired Angioedema Related to Angiotensin-Converting Enzyme Inhibitors. **J Allergy Clin Immunol Pract 9 :** 947-955.

Kajdácsi, E., Veszeli, N., Mező, B., Jandrasics, Z., Kőhalmi, K.V., Ferrara, A., Cervenak, L., Varga, L., **Farkas, H.** (2021) Pathways of Neutrophil Granulocyte Activation in Hereditary Angioedema with C1 Inhibitor Deficiency. **Clin Rev Allergy Immunol 60:** 383-395.



ANDREA FEKETE

Semmelweis University
Faculty of Medicine
1st Department of Paediatrics

RESEARCH AREA

Open-angle glaucoma, diabetic keratopathy and corneal scarring are severe, non-retinal complications of diabetes. Their therapy is insufficient: POAG is treated by lowering intra-ocular pressure by medication or surgery; however, progression continues in many patients. Treatment of corneal dysfunction is largely symptomatic as well. Therefore preclinical research should aim at identifying disease mechanisms and novel antifibrotic therapies for both diseases. Renal ischemia/reperfusion injury-induced acute kidney injury develops in various clinical conditions and is the main cause of graft loss or delayed graft function following transplantation. Beside the shortage in donors, minimizing ischemia/reperfusion injury and thus improving long-term graft function remains a major and yet unsolved problem. Our aim is to characterize previously unknown molecular signaling mechanisms for the treatment of renal ischemia/reperfusion injury. By developing a new preservation solution containing Sigma-1 receptor agonists we could tackle the problem of donor shortage by optimizing the condition of expanded criteria donor grafts and extending maximum graft storage time. Idiopathic pulmonary fibrosis is the most common form of interstitial pulmonary diseases, with constantly growing incidence. The disease is associated with high mortality, as median survival after diagnosis is only 2-3 years. Main causes include environmental factors, infections and genetic factors. The latest studies suggest that fibrosis of the lungs is common among patients who recovered from the acute phase of a COVID-19 infection. Despite obvious clinical significance, the molecular mechanisms leading to fibrosis are largely unknown and currently there is no effective therapeutic agent which could prevent tissue fibrosis. Our aim is to identify the molecular pathways responsible for the protective effect of Sigma-1 receptor agonists, and thus to develop novel, effective therapies.

SELECTED PUBLICATIONS

Hodrea, J., Saeed, A., Molnar, A., Fintha, A., Barczi, A., Wagner, L.J., Szabo, A.J., **Fekete, A.**, Balogh, D.B. (2022) SGLT2 inhibitor dapagliflozin prevents atherosclerotic and cardiac complications in experimental type 1 diabetes. **Plos One 17:** 2 Paper: e0263285.

Hosszu, A., Kaucsar, T., Seeliger, E., **Fekete, A.** (2021) Animal Models of Renal Pathophysiology and DiseaseIn. Pohlmann, Andreas (szerk.) **Preclinical MRI of the Kidney: Methods and Protocols New York, USA Springer (Boston) 720:** 27-44.

Balogh, D.B., Molnar, A., Hosszu, A., Lakat, T., Hodrea, J., Szabo, A.J., Lenart, L., **Fekete, A.** (2020) Antidepressant effect in diabetes-associated depression: a novel potential of RAAS inhibition. **Psychoneuroendocrinology 118:** 104705.

Lenart, L., Balogh, D.B., Lenart, N., Barczi, A., Hosszu, A., Farkas, T., Hodrea, J., Szabo, A.J., Szigeti, K., Denes, A., **Fekete, A.** (2019) Novel therapeutic potential of angiotensin receptor 1 blockade in a rat model of diabetes-associated depression parallels altered BDNF signalling. **Diabetologia 62:** 1501-1513.

CSABA FEKETE

HUN-REN Institute of Experimental Medicine
Integrative Neuroendocrinology Research Group

RESEARCH AREA

The main research goals of our laboratory are the elucidation of the central regulatory mechanisms controlling the hypothalamic-pituitary-thyroid axis and the examination of the neuronal circuits controlling the energy homeostasis.

SELECTED PUBLICATIONS

Farkas, E., Varga, E., Kovács, B., Szilvásy-Szabó, A., Cote-Vélez, A., Péterfi, Z., Matziari, M., Tóth, M., Zelena, D., Mezriczky, Zs. et al. (2020) A glial-neuronal circuit in the median eminence regulates thyrotropin-releasing hormone-release via the endocannabinoid system. **Iscience 23:** 100921. 41 p.

Mohacsik, P., Erdelyi, F., Baranyi, M., Botz, B., Szabo, G., Toth, M., Haltrich, I., Helyes, Z., Sperlagh, B., Toth, Z. et al. (2018) A transgenic mouse model for detection of tissue-specific thyroid hormone action. **Endocrinology 159:** 1159-1171. 13 p.

Péterfi, Z., Farkas, I., Denis, R.G.P., Farkas, E., Uchigashima, M., Füzesi, T., Watanabe, M., Lechan, R.M., Liposits, Z., Luquet, S. et al. (2018) Endocannabinoid and nitric oxide systems of the hypothalamic paraventricular nucleus mediate effects of NPY on energy expenditure. **Molecular Metabolism 18:** 120-133.14 p.

Fekete, C., Lechan, R.M. (2014) Central Regulation of Pituitary-Thyroid Axis Under Physiological and Pathophysiological Conditions. **Endocrine Reviews 35:** 59-194. 36 p.

Kola, B., Farkas, I., Christ-Crain, M., Wittmann, G., Loll, F., Amin, F., Harvey-White, J., Liposits, Z., Kunos, G., Grossman, A.B. et al. (2008) The orexigenic effect of ghrelin is mediated through central activation of the endogenous cannabinoid system. **Plos One 3:** 3. Paper: e1797.

BALÁZS GEREBEN

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

Thyroid hormones (TH) are master regulators of cellular metabolism and proliferation and consequently exert a fundamental impact on brain development and function predominantly due to their impact on transcriptomic activity. The Laboratory aims to (i) identify and modulate cell-type specific molecular pathways responsible for the regulation of TH economy in the brain and coupled peripheries; (ii) translate these mechanisms to specific brain functions under physiological and pathophysiological conditions; (iii) develop transgenic approaches to assess and modulate cell-type specific TH action. They combine molecular, cell biological, anatomical and transgenic techniques to study regulation and consequences of TH signalling. (1) They study the molecular regulation of deiodinase enzymes mediating TH metabolism with special respect to the complex and tight regulation of type 2 deiodinase (D2) to identify molecular elements and protein-protein interactions allowing the rapid regulation of D2 activity along the ubiquitin/proteasome pathway and its role in the generation of tissue-specific hypothyroidism. The studies also target the regulation of the D2-encoding dio2 gene during hypothalamic response to inflammation, a phenomenon they described as a component of the pathogenesis of the nonthyroidal illness syndrome. (2) They investigate the mechanisms and biological consequences of D2 and type 3 deiodinase (D3) mediated neuro-glial coupling of TH metabolism and its impact on the hypothalamo-pituitary-thyroid axis and thyroid hormone signaling of the nervous system. (3) The Laboratory is involved in the generation of transgenic mouse models for cell-type specific modulation and assessment of TH signalling and also aims to identify human markers representing tissue TH economy. This resulted in the generation and patenting of the Thyroid Hormone Action Indicator (THAI) Mouse, allowing tissue-specific assessment of TH action in vivo.

SELECTED PUBLICATIONS

Jo, S., Fonseca, T.L., Da Costa Bocco, B.M., Fernandes, G.W., McAninch, E.A., Bolin, A.P., Da Conceição, R.R., De Castro, J.P.W., Ignacio, D.L., Egri, P., Németh, D., Fekete, C., Bernardi, M.M., Leitch, V.D., Mannan, N.S., Curry, K.F., Butterfield, N.C., Bassett, J.H.D., Williams, G.R., **Gereben, B.,** Ribeiro, M.O., Bianco, A.C. (2019) Type 2 deiodinase polymorphism causes ER stress and hypothyroidism in the brain. **J Clin Invest 129:** 230-245.

Mohácsik, P., Erdélyi, F., Baranyi, M., Botz, B., Szabó, G., Tóth, M., Haltrich, I., Helyes, Zs., Sperlágh, B., Tóth, Zs., Sinkó, R., Lechan, R.M., Bianco, A.C., Fekete, Cs., **Gereben B.** (2018) A transgenic mouse model for detection of tissue-specific thyroid hormone action. **Endocrinology 159:** 1159–1171.

Kollár, A., Kvarta, Papp, Zs., Egri, P., **Gereben, B.** (2016) Different Types Of Luciferase Reporters Show Distinct Susceptibility To T3-Evoked Down-Regulation. **Thyroid 2016 26:** 179-82.

Gereben, B., McAninch, E.A., Riberio, M.O., Bianco, A.C. (2015) Scope and limitations of iodothyronine deiodinases in hypothyroidism. **Nature Rev Endo 11:** 642-52.

ANIKÓ GÖRBE

Semmelweis University
Faculty of Medicine
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

In experimental cardiology models, several studies have already demonstrated that the reperfusion phase following cardiac oxygen deprivation activates processes that lead to further damage of myocardial tissue. However, there are protective mechanisms that can reduce the extent of damage. However, failures in clinical trials show that these mechanisms are not sufficiently effective in ischemic heart patients. Preclinical data suggest that co-morbidities such as hyperlipidemia, metabolic syndrome, diabetes mellitus-induced tissue changes and drug treatment of these diseases have a strong interfering effect. Furthermore, the presence of ischaemia/reperfusion injury and co-morbidities poses additional risks, as the hidden side effects of many drugs are only seen in such cases. Our research addresses the potential cardioprotective effects of microRNAs. The development of noncoding RNAs (such as microRNAs) as molecules of diagnostic and therapeutic value has in recent years brought them to the forefront of the pharmaceutical industry for the precision diagnosis and treatment of a number of diseases.

SELECTED PUBLICATIONS

Makkos A., Ágg B., Varga ZV., Giricz Z., Gyöngyösi M., Lukovic D., Schulz R., Barteková M., **Görbe A.**, Ferdinandy P. (2021) Molecular Network Approach Reveals Rictor as a Central Target of Cardiac ProtectomiRs. **Int J Mol Sci. 22:** 9539.

Bencsik, P., Gömöri, K., Szabados, T., Sántha, P., Helyes, Z., Jancsó, G., Ferdinandy, P., **Görbe, A.** (2020) Myocardial ischemia reperfusion injury and cardioprotection in the presence of sensory neuropathy: therapeutic options. **Br J Pharmacol 177:** 5336-5356.

Makkos, A., Ágg, B., Petrovich, B., Varga, Z.V., **Görbe, A.**, Ferdinandy, P. (2021) Systematic review and network analysis of microRNAs involved in cardioprotection against myocardial ischemia/reperfusion injury and infarction: Involvement of redox signalling. **Free Radic Biol Med 172:** 237-251.

Gömöri, K., Szabados, T., Kenyeres, É., Pipis, J., Földesi, .I, Siska, A., Dormán, G., Ferdinandy, P., **Görbe, A.**, Bencsik, P. (2020) Cardioprotective Effect of Novel Matrix Metalloproteinase Inhibitors. **Int J Mol Sci. 21:** E6990.

Pálóczi, J., Szántai, Á., Kobolák, J., Bock, I., Ruivo, E., Kiss, B., Gáspár, R., Pipis, J., Ocsovszki, I., Táncos, Z., Fehér, A., Dinnyés, A., Onódi, Z., Madonna, R., Ferdinandy, P., **Görbe, A.** (2020) Systematic analysis of different pluripotent stem cell-derived cardiac myocytes as potential testing model for cardiocytoprotection. **Vascul Pharmacol 133-134:** 106781.

BALÁZS HANGYA

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

We are interested in the neural basis of cognitive functions both in the normal and diseased brain. We are investigating how different neuron types of subcortical centres mediate cognitive processes such as attention, learning and memory. Cholinergic neurons have been associated with learning and other cognitive functions; however, their activity during behavior is unknown. Understanding how the activity of basal forebrain cholinergic neurons support learning as well as how their impairment leads to learning deficits can help understanding their role in neurodegenerative dementias. Intermingled with cholinergic neurons, the basal forebrain also contains cortically projecting long-range inhibitory neurons. To understand how the basal forebrain supports cognition, it is important to determine how cognitive functions associated with the basal forebrain are segregated among different cell types.

SELECTED PUBLICATIONS

Hegedüs, P., Heckenast, J., **Hangya, B.** (2021) Differential recruitment of ventral pallidal e-types by behaviorally salient stimuli during Pavlovian conditioning. **iScience 24:** 102377.

Király, B., Balázsfi, D., Horváth, I., Solari, N., Sviatkó, K., Lengyel, K., Birtalan, E., Babos, M., Bagaméry, G., Máthé, D., Szigeti, K., **Hangya, B.** (2020) In Vivo Localization of Chronically Implanted Electrodes and Optic Fibers in Mice. **Nat Comm 11:** 4686.

Laszlovszky, T., Schlingloff, D., Hegedüs, P., Freund, T.F., Gulyás, A., Kepecs, A., **Hangya, B.** (2020) Distinct synchronization, cortical coupling and behavioral function of two basal forebrain cholinergic neuron types. **Nat Neurosci 23:** 992-1003.

Hangya, B., Ranade, S.P., Lorenc, M., Kepecs, A. (2015) Central cholinergic neurons are rapidly recruited by reinforcement feedback. **Cell 162:** 1155–1168.

Pi, H.J., **Hangya, B.**, Kvitsiani, D., Sanders, J.I., Huang, Z.J., Kepecs, A. (2013) Cortical interneurons that specialize in disinhibitory control. **Nature 503:** 521-524.

TAMÁS HEGEDŰS

Semmelweis University
Faculty of Medicine
Department of Biophysics and Radiation Biology

RESEARCH AREA

Our research focuses on transmembrane proteins, which are associated with many diseases and are the targets of most available drugs. We are investigating ABC proteins acting as multidrug transporters to protect cells from toxic substances. We use theoretical and computational methods to understand their mechanism of function and substrate recognition. We also investigate how cystic fibrosis causing mutations in the CFTR/ABCC7 chloride channel affect protein unfolding, dynamics and function. CFTR channel opening requires phosphorylation of its disordered regulatory region. In order to understand the associated regulatory processes, we determine the intramolecular interactions of the disordered region and design a protein to counteract these interactions to achieve activation. In a similar manner, we design a small protein that binds to the C-terminus of the SARS Cov-2 Envelope transmembrane protein, inhibiting its binding to the human Pals1 protein, thus the degradation of cell-cell contacts and the development of inflammation.

SELECTED PUBLICATIONS

Hegedűs, T., Geisler, M., Lukács, G.L., Farkas, B. (2022) Ins and Outs of AlphaFold2 Transmembrane Protein Structure Predictions. **Cell Mol Life Sci 79:** 73.

Nagy, T., Tóth, Á., Telbisz, Á., Sarkadi, B., Tordai, H., Tordai, A., **Hegedűs, T.** (2021) The Transport Pathway in the ABCG2 Protein and Its Regulation Revealed by Molecular Dynamics Simulations. **Cell Mol Life Sci 78:** 2329–2339.

Csizmadia, G., Erdős, G., Tordai, H., Padányi, R., Tosatto, S., Dosztányi, Z., **Hegedűs, T.** (2020) The MemMoRF Database for Recognizing Disordered Protein Regions Interacting with Cellular Membranes. **Nucleic Acids Res 49:** D355–D360.

Veit, G., Avramescu, R., Perdomo, D., Phuan, P., Bagdany, M., Apaja, P., Borot, F., Szollosi, D., Wu, Y., Finkbeiner, W., **Hegedus, T.,** Verkman, A., és Lukacs, G. (2014) Some Gating Potentiators, Including VX-770, Diminish ΔF508-CFTR Functional Expression. **Sci Transl Med 6:** 246ra97.

ESZTER MÁRIA HORVÁTH

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

Oxidative stress is characterized by the imbalance between the release of oxygen and nitrogen-derived free radicals and oxidants and the body's antioxidant capacity. Accumulating free radicals and oxidants can damage cellular components, which play important role in the development and maintenance of several diseases. Our group examines these processes and their predictive value in physiological and pathophysiological conditions; in pregnancy and its complications, in inflammatory and in cardiovascular diseases.

SELECTED PUBLICATIONS

Lajtai, K., Tarszabó, R., Bányai, B., Péterffy, B., Gerszi, D., Ruisanchez, É., Sziva, R. E., Korsós-Novák, Á., Benkő, R., Hadjadj, L., **Horváth, E. M.** et al. (2021) Effect of Vitamin D Status on Vascular Function of the Aorta in a Rat Model PCOS. **Oxid Med Cell Longev 2021:** 8865979.

Lajtai, K., Nagy, Cs.T., Tarszabó, R., Benkő, R., Hadjadj, L., Sziva, R.E., Gerszi, D., Bányai, B., Ferdinandy, P. Nádasy, Gy.L., **Horváth, E.M.** et al. (2019) Effects of Vitamin D Deficiency on Proliferation and Autophagy of Ovarian and Liver Tissues in a Rat Model of Polycystic Ovary Syndrome. **Biomolecules 9:** 471.

Horvath, E.M., Magenheim, R., Beres, N.J., Benko, R., Pek, T., Tabak, A.G., Szabo, C. (2018) Oxidative-Nitrative Stress and Poly (ADP-Ribose) Polymerase Activation 3 Years after Pregnancy. **Oxid Med Cell Longev 2018:** 1743253.

Barany, T., Simon, A., Szabo, G., Benko, R., Mezei, Zs., Molnar, L., Becker, D., Merkely, B., Zima, E., **Horvath, E.M.** (2017) Oxidative Stress-Related Parthanatos of Circulating Mononuclear Leukocytes in Heart Failure. **Oxid Med Cell Longev 2017:** 1249614.

Horváth, E.M., Magenheim, R., Kugler, E., Vácz, G., Szigethy, A., Lévárdi, F., Kollai, M., Szabo, C., Lacza, Z. (2009) Nitrative stress and poly (ADP-ribose) polymerase activation in healthy and gestational diabetic pregnancies. **Diabetologia 52:** 1935-1943.

ERIK HRABOVSZKY

HUN-REN Institute of Experimental Medicine
Reproductive Neurobiology Research Group

RESEARCH AREA

Molecular, cellular and system biology research at the Laboratory of Reproductive Neurobiology aims to provide a deeper understanding of the central regulatory mechanisms of human reproduction. Hypothalamic secretion of gonadotropin-releasing hormone (GnRH) builds up during pubertal development. Secretory pulses of GnRH at every 30-90 minutes stimulate luteinizing and follicle stimulating hormone (LH and FSH) production in the anterior pituitary gland. These troph hormones, in turn, initiate and later maintain functions of the gonads (testes and ovaries). This laboratory combines anatomical, electrophysiological and molecular approaches to study i) the neuronal and hormonal control of pulsatile GnRH/LH secretion, ii) the mechanisms of the mid-cycle GnRH/LH surge which triggers ovulation in females, iii) the central effects of gonadal steroid hormones on neuroendocrine systems and on wider aspects of general neuronal functioning and iv) the molecular and cellular processes underlying reproductive senescence.

SELECTED PUBLICATIONS

Hrabovszky, E., Shughrue, P.J., Merchenthaler, I., Hajszán, T., Liposits, Zs., Carpenter, C.D. and Petersen, S.L. (2000) Detection of estrogen receptor-β messenger ribonucleic acid and I [estrogen] binding sites in luteinizing hormone-releasing hormone neurons of the rat brain. **Endocrinology 141:** 3506-3509.

Hrabovszky, E., Ciofi, P., Vida, B., Horvath, M.C., Keller, É., Caraty, A., Bloom, S.R., Ghatei, M.A., Dhillo, W.S., Liposits, Z. and Kallo, I. (2010) The kisspeptin system of the human hypothalamus. Sexual dimorphism and relationship with gonadotropin-releasing hormone and neurokinin B neurons. **Eur. J. Neurosci 31:** 1984-1998.

Skrapits, K., Sárvári, M., Farkas, I., Göcz, B., Takács, S., Rumpler, É., Váczi, V., Vastagh, C., Rácz, G., Matolcsy, A., Solymosi, N., Póliska, S., Tóth, B., Erdélyi, F., Szabó, G., Culler, M.D., Allet, C., Cotellessa, L., Prévot, V., Giacobini, P. and **Hrabovszky E.** (2021) The cryptic gonadotropin-releasing hormone neuronal system of human basal ganglia. **Elife 10:** e67714.

Campbell, R.E., Coolen, L.M., Hoffman, G.E. and **Hrabovszky, E.** (2022) Highlights of neuroanatomical discoveries of the mammalian gonadotropin-releasing hormone system. **J Neuroendocrinol 34:** e13115.

Göcz, B., Rumpler, É., Sárvári, M., Skrapits, K., Takács, S., Farkas, I., Csillag, V., Trinh, S.H., Bardóczi, Z., Ruska, Y., Solymosi, N., Póliska, S., Szőke, Z., Bartoloni, L., Zouaghi, Y., Messina, A., Pitteloud, N., Anderson, R.C., Millar, R.P., Quinton, R., Manchishi, S.M., Colledge, W.H. and **Hrabovszky E.** (2022) Transcriptome profiling of kisspeptin neurons from the mouse arcuate nucleus reveals new mechanisms in estrogenic control of fertility. **Proc Natl Acad Sci U S A 119:** e2113749119.

PÉTER IGAZ

Semmelweis University
Faculty of Medicine
Department of Internal Medicine and
Oncology, Department of Endocrinology

RESEARCH AREA

Studies on endocrine tumors, especially adrenal and neuroendocrine tumors. In the focus, non-coding RNAs (especially microRNAs), their pathogenic roles and utility as biomarkers are examined. Both tissue and biofluid samples are used. As biomarkers, markers of malignancy and prognosis are searched for. The clinical relevance of these studies is underlined by the diagnostic difficulties related to the adrenal and neuroendocrine tumors both in histology and clinical diagnostics.

SELECTED PUBLICATIONS

Turai, P.I., Herold, Z., Nyirő, G., Borka, K., Micsik, T., Tőke, J., Szücs, N., Tóth, M., Patócs, A., **Igaz, P.** (2022) Tissue miRNA Combinations for the Differential Diagnosis of Adrenocortical Carcinoma and Adenoma Established by Artificial Intelligence. **Cancers 14:** 895.

Decmann, A., Perge, P., Nyírő, G., Darvasi, O., Likó, I., Borka, K., Micsik, T., Tóth, Z., Bancos, I., Pezzani, R., Iacobone, M., Patócs, A., **Igaz, P.** (2018) MicroRNA expression profiling in adrenal myelolipoma. **J Clin Endocrinol Metab: 103:** 3522-3530.

Perge, P., Butz, H., Pezzani, R., Bancos, I., Nagy, Z., Pálóczi, K., Nyírő, G., Decmann, A., Pap, E., Luconi, M., Mannelli, M., Buzás, E.I., Tóth, M., Boscaro, M., Patócs, A., **Igaz, P.** (2017) Evaluation and diagnostic potential of circulating exosomal microRNAs in adrenocortical tumors. **Scientific Reports 7:** 5474.

Perge, P., Nagy, Z., Decmann, Á., Igaz, I., **Igaz, P.** (2017) Potential relevance of microRNAs in inter-species epigenetic communication, and implications for disease pathogenesis. RNA **Biology 14:** 391-401.

Szabó, P.M., Tamási, V., Molnár, V., Andrásfalvy, M., Tömböl, Z., Farkas, R., Kövesdi, K., Patócs, A., Tóth, M., Szalai, C., Falus, A., Rácz, K., **Igaz, P.** (2010) Meta-analysis of adrenocortical tumor genomics data: novel pathogenic pathways revealed. **Oncogene 29:** 3163-3172.

Tömböl, Z., Szabó, P.M., Molnár, V., Wiener, Z., Tölgyesi, G., Horányi, J., Riesz, P., Reismann, P., Patócs, A., Likó, I., Gaillard, R.C., Falus, A., Rácz, K., **Igaz, P.** (2009) Integrative molecular-bioinformatics study of human adrenocortical tumors: microRNA, tissue specific target prediction and pathway analysis. **Endocrine-Related Cancer 16:** 895-906.

ZOLTÁN PÉTER JAKUS

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The lymphatic system plays an essential role in regulating fluid balance, controlling immune cell migration and lipid absorption. Recently, other novel and unexpected functions of the system have been revealed. It is therefore critical that we understand the organ-specific functions of the lymphatic system. Our research group aims to study the organ-specific roles of the lymphatic system and lymphatic growth signaling pathways under physiological and pathological conditions using preclinical transgenic mouse models. In our experiments, we have developed a nucleoside-modified mRNA-based system that induces organ-specific lymphatic growth and reverses experimental lymphedema. We revealed that pulmonary lymphatic function and fetal breathing movements play a critical role in the preparation of the fetal lung for inflation at birth. In addition, our data suggest that the mechanical forces induced by lymphatic flow are critical factors in controlling the developmental program of meningeal lymphatics.

SELECTED PUBLICATIONS

Szőke, D., Kovács, G., Kemecsei, É., Bálint, L., Szoták-Ajtay, K., Aradi, P., Styevkóné, Dinnyés, A., Mui, B.L., Tam, Y.K., Madden, T.D., Karikó, K., Kataru, R.P., Hope, M.J., Weissman, D., Mehrara, B.J., Pardi, N., **Jakus, Z.** (2021) Nucleoside-modified VEGFC mRNA induces organ-specific lymphatic growth and reverses experimental lymphedema. **Nat Commun 12:** 3460.

Bálint, L., Ocskay, Z., Deák, B.A., Aradi, P., **Jakus, Z.** (2020) Lymph Flow Induces the Postnatal Formation of Mature and Functional Meningeal Lymphatic Vessels. **Front Immunol 10:** 3043.

Szoták-Ajtay, K,. Szőke, D., Kovács, G., Andréka, J., Brenner, G.B., Giricz, Z., Penninger, J., Kahn, M.L., **Jakus, Z.** (2020) Reduced Prenatal Pulmonary Lymphatic Function Is Observed in Clp1 K/K Embryos With Impaired Motor Functions Including Fetal Breathing Movements in Preparation of the Developing Lung for Inflation at Birth. **Front Bioeng Biotechnol 8:** 136.

Bálint, L., **Jakus, Z.** (2021) Mechanosensation and Mechanotransduction by Lymphatic Endothelial Cells Act as Important Regulators of Lymphatic Development and Function. **Int J Mol Sci 22:** 3955.

Pawlak, J.B., Bálint, L., Lim, L., Ma, W., Davis, R.B., Benyó, Z., Soares, M.J., Oliver, G., Kahn, M.L., **Jakus, Z.,** Caron, K.M. (2019) Lymphatic mimicry in maternal endothelial cells promotes placental spiral artery remodeling. **J Clin Invest 129:** 4912-4921.

KRISZTINA KÁLDI

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The circadian time-keeping system enhances the adaptive ability of the organism by preparing it to the periodical changes in the environment, and on the other hand, allows temporal separation of otherwise conflicting biochemical activities. Endogenous time measuring is organized at the cellular level and almost all mammalian cells harbour self-sustained circadian oscillators. In mammals, the suprachiasmatic nucleus is considered as the master pacemaker, that drives and synchronizes peripheral oscillators by neuronal and humoral mechanisms. Circadian rhythm disturbances are associated with an increased risk of severe health problems, including cardiovascular diseases, metabolic syndrome, diabetes mellitus, various malignancies and psychiatric diseases such as mood disorders. In the modern society the risk for circadian misalignment is increasing due to the growing demand of shift work and intense exposure to artificial light during the late evening hours. Our research group is interested in a broad field of chronobiology research including the examination of molecular clock functions, studying circadian control of the immune system and exploring human behavioral rhythms.

SELECTED PUBLICATIONS

Szőke, A., Sárkány, O., Schermann, G., Kapuy, O., Diernfellner, ACR., Brunner, M., Gyöngyösi, N., **Káldi. K.** (2023) Adaptation to glucose starvation is associated with molecular reorganization of the circadian clock in Neurospora crassa. **eLife 12:** e79765.

Ella, K., Sűdy, Á., Búr, Z., Koós, B., Kisiczki, Á., Mócsai, A., **Káldi, K.** (2022) Time restricted feeding modifies leukocyte responsiveness and improves inflammation outcome. **Front Immunol 13:** 924541.

Sűdy, Á.R., Ella, K., Bódizs, R., **Káldi, K.** (2019) Association of Social Jetlag With Sleep Quality and Autonomic Cardiac Control During Sleep in Young Healthy Men. **Front Neurosci 13:** 950.

Ella, K., Csépányi-Kömi, R., **Káldi, K.** (2016) Circadian regulation of human peripheral neutrophils. **Brain Behav Immun 57:** 209-221.

Haraszti, R.Á., Ella, K., Gyöngyösi, N., Roenneberg, T., **Káldi, K.** (2014) Social jetlag negatively correlates with academic performance in undergraduates. **Chronobiol Int 31:** 603-12.

Gyöngyösi, N., Nagy, D., Makara, K., Ella, K., **Káldi, K.** (2013) Reactive oxygen species can modulate circadian phase and period in Neurospora crassa. **Free Radic Biol Med 58**: 134-143.

Malzahn, E., * Ciprianidis, S., * **Káldi, K.** (*joint first authors), Schafmeier, T., Brunner, M. (2010) Photoadaptation in Neurospora by Competitive Interaction of Activating and Inhibitory LOV Domains. **Cell 142:** 762-772.

ISTVÁN KATONA

HUN-REN Institute of Experimental Medicine
Molecular Neurobiology Research Group

RESEARCH AREA

Synaptic junctions are major sites of communication in the brain, where chemical messenger molecules transmit information from presynaptic neurons to their postsynaptic partners. The efficacy of synaptic transmission is not constant in time and space. Instead, its plasticity is a fundamental phenomenon underlying information storage and adaptation to environmental stimuli. Although classical neurotransmitters (such as glutamate and GABA) have well characterized principal roles in mediating basal neurotransmission, emerging evidence has revealed that synapses exploit a wide array of additional messenger molecules integrated into sophisticated signaling pathways to accomplish their complex functions. Thus, the major objective of our laboratory is to identify new signaling systems regulating synaptic transmission and its plasticity. We aim to characterize the molecular architecture of these novel pathways and to elucidate their physiological roles. Ultimately, this activity is envisaged to help gain a better understanding of synaptic function and reveal new aspects of impaired synaptic activity in brain disorders.

SELECTED PUBLICATIONS

Prokop, S., Ábrányi-Balogh, P., Barti, B., Vámosi, M., Zöldi, M., Barna, L., Urbán, G.M., Tóth, A.D., Dudok, B., Egyed, A., Deng, H., Leggio, G.M., Hunyady, L., van der Stelt, M., Keserű, G.M., **Katona, I.** (2021) PharmacoSTORM nanoscale pharmacology reveals cariprazine binding on Islands of Calleja granule cells. **Nature Communications 12:** 6505.

László, Z., Lele, Z., Zöldi, M., Miczán, V., Mógor, F., Simon, G.M., Mackie, K., Kacskovics, I., Cravatt, B.F. and **Katona, I.** (2020) ABHD4-mediated developmental anoikis safeguards the embryonic brain. **Nature Communications 11:**1.

Frau, R.*, Miczan, V.*, Traccis, F., Aroni, S., Pongor, C.I., Saba, P., Serra, V., Sagheddu, C., Fanni, S., Congiu, M., Devoto, P., Cheer, J.F., **Katona, I.***, Melis, M.* (2019) Prenatal THC exposure produces a hyperdopaminergic phenotype rescued by pregnenolone. **Nature Neuroscience 22:** 1975–1985.

Barna, L., Dudok, B., Miczán, V., Horváth, A., László, Z.I., and **Katona, I.** (2016) Correlated confocal and super-resolution imaging by VividSTORM. **Nature Protocols 11:** 163-183.

Dudok, B., Barna, L., Ledri, M., Szabó, S.I., Szabadits, E., Pintér, B., Woodhams, S.G., Henstridge, C.M., Balla, GY., Nyilas, R., Varga, C., Lee, S.H., Matolcsi, M., Cervenak, J., Kacskovics, I., Watanabe, M., Sagheddu, C., Melis, M., Pistis, M., Soltesz, I. and **Katona, I.** (2015) Cell-specific STORM superresolution imaging reveals nanoscale organization of cannabinoid signaling. **Nature Neuroscience 18:** 75-86.

LAJOS KEMÉNY

Semmelweis University
Department of Physiology

RESEARCH AREA

The HCEMM-SU Translational Dermatology Research Group focuses on understanding the biology of pigment producing cells (melanocytes) and melanoma cells.
Despite recent developments in the field of immunooncology by the introduction of immune-checkpoint blockade (ICB) in the management of melanoma, resistance to ICB therapies still poses a tremendous problem. The group aims to identify novel therapeutic approaches to overcome resistance to ICB therapies. The most common resistance mechanism, the loss of antigen presentation, might offer novel vulnerabilities to antigen presentation-independent mechanisms. The group aims to find regulators and novel therapeutic targets by creating a novel mouse model of immunotherapy resistance. This novel model of ICB resistance combined with in vivo genome-wide CRISPR screen approaches will be used to identify novel targets that may be utilized to overcome ICB resistance.
Other projects in the lab focus on mechanism of pigmentation and non-apoptotic forms of cell death in melanoma.

SELECTED PUBLICATIONS

Meznerics, FA., Illés, K., Dembrovszky, F., Fehérvári, P., **Kemény, LV**., Kovács, KD., Wikonkál, NM., Csupor, D., Hegyi, P., Bánvölgyi, A. Platelet-Rich Plasma in Alopecia Areata-A Steroid-Free Treatment Modality: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. **Biomedicines 10(8):** 1829.

Hermann, AL.*, Fell, GL.*, **Kemény, LV.***, Fung, CY., Held, KD., Biggs, PJ., Rivera, PD., Bilbo, SD., Igras, V., Willers, H., Kung, J., Gheorghiu, L., Hideghéty, K., Mao, J., Woolf, CJ., Fisher, DE., β-Endorphin mediates radiation therapy fatigue. **Sci Adv 8(50):** eabn6025.

Meznerics, F.A, Fehérvári, P., Dembrovszky, F., Kovács, KD., **Kemény, LV.**, Csupor, D., Hegyi, P., Bánvölgyi, A., Platelet-Rich Plasma in Chronic Wound Management: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. **J Clin Med 11(24):** 7532.

Meznerics, FA., **Kemény, LV.**, Gunther, E., Bakó, E., Dembrovszky, F., Szabó, B., Ascsillán, A., Lutz, E., Csupor, D., Hegyi, P., Bánvölgyi, A., Nagy, G., Multi-biomarker disease activity score: an objective tool for monitoring rheumatoid arthritis? A systematic review and meta-analysis. **Rheumatology (Oxford)** 2022 Dec 28: keac715.

Gil, J., Rezeli, M., Lutz, E. G., Kim, Y., Sugihara, Y., Malm, J., Semenov, Y. R., Yu, K. H., Nguyen, N., Wan, G., **Kemény, LV.**, Kárpáti, S., Németh, I. B., & Marko-Varga, G. (2021). An Observational Study on the Molecular Profiling of Primary Melanomas Reveals a Progression Dependence on Mitochondrial Activation. **Cancers 13(23)**, 6066.

ÉVA KERESZTURI

Semmelweis University
Department of Molecular Biology

RESEARCH AREA

Molecular genetics, functional genetics, molecular biology, lipotoxicity, lipid metabolism disorders, desaturation.
Whole-genome sequencing, now routinely used, has resulted in the identification of countless human genetic variations. However, this vast amount of information can only be interpreted in the context of a functional analysis of genetic variation. Our group is working on the molecular biological characterization of conditions associated with disorders of lipid metabolism (diabetes, obesity). Our experiments focus on the central enzymes of unsaturated fatty acid synthesis, the Stearoyl-CoA desaturases (SCD). The main function of SCDs is the on-demand channeling of saturated fatty acids towards unsaturated fatty acids, making them indispensable in many physiological processes (signal transduction, energy storage, membrane fluidity). However, their abnormal function can induce pathological processes by shifting the optimal fatty acid profile. DNA modifications in SCDs can significantly affect protein function. Genetic variations filtered by our own expression data and different prediction algorithms are characterized using classical molecular biological methods. Variants that are found to be relevant are also investigated in clinical patient samples.

SELECTED PUBLICATIONS

Orosz, G., Szabó, L., Bereti, S., Zámbó, V., Csala, M., **Kereszturi, É.** (2023) Molecular Basis of Unequal Alternative Splicing of Human SCD5 and Its Alteration by Natural Genetic Variations. **Int J Mol Sci.** 2023 Mar 30;24(7):6517.

Zámbó, V., Orosz, G., Szabó, L., Tibori, K., Sipeki, S., Molnár, K., Csala, M., **Kereszturi, É.** (2022) A Single Nucleotide Polymorphism (rs3811792) Affecting Human SCD5 Promoter Activity Is Associated with Diabetes Mellitus. **Genes (Basel).** 2022 Oct 3;13(10):1784.

Tibori, K., Orosz, G., Zámbó, V., Szelényi, P., Sarnyai, F., Tamási, V., Rónai, Z., Mátyási, J., Tóth, B., Csala, M., **Kereszturi, É.** (2022) Molecular Mechanisms Underlying the Elevated Expression of a Potentially Type 2 Diabetes Mellitus Associated SCD1 Variant. **Int J Mol Sci.** 2022 Jun 2;23(11):6221.

Németh, K., Tóth, B., Sarnyai, F., Koncz, A., Lenzinger, D., **Kereszturi, É.**, Visnovitz, T., Kestecher, BM., Osteikoetxea, X., Csala, M., Buzás, EI., Tamási, V. (2023) High fat diet and PCSK9 knockout modulates lipid profile of the liver and changes the expression of lipid homeostasis related genes. **Nutr Metab (Lond).** 2023 Mar 31;20(1):19.

Sarnyai, F., **Kereszturi, É.**, Szirmai, K., Mátyási, J., Al-Hag, JI., Csizmadia, T., Lőw, P., Szelényi, P., Tamási, V., Tibori, K., Zámbó, V., Tóth, B., Csala, M. (2022) Different Metabolism and Toxicity of TRANS Fatty Acids, Elaidate and Vaccenate Compared to Cis-Oleate in HepG2 Cells. **Int J Mol Sci.** 2022 Jun 30;23(13): 7298.

KRISZTINA KOVÁCS

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

Neurobiology of stress. Regulation of the hypothalamo-pituitary-adrenocortical axis. The role of gut microbiome in the neuroendocrine regulation.

SELECTED PUBLICATIONS

Xu, L., Füredi, N., Lutter, C., Geenen, B., Pétervári, E., Balaskó, M., Dénes, Á., **Kovács, K.J.**, Gaszner, B., Kozicz, T. (2022) Leptin coordinates efferent sympathetic outflow to the white adipose tissue through the midbrain centrally-projecting Edinger-Westphal nucleus in male rats. **Neuropharmacology 205:** 108898.

Kuti, D., Winkler, Zs., Horváth, K., Juhász, B., Paholcsek, M., Stágel, A., Gulyás, G., Czeglédi, L., Ferenczi, Sz., **Kovács, K.J.** (2020) Gastrointestinal (Non-systemic) Antibiotic Rifaximin Differentially Affects Chronic Stress-induced Changes in Colon Microbiome and Gut Permeability without Effect on Behavior. **Brain Behav Immun 804:** 218.228.

Winkler, Zs., Kuti, D., Polyák, Á., Juhász, B., Gulyás, K., Lénárt, N., Dénes, Á., Ferenczi, Sz., **Kovács, K.J.** (2019) Hypoglycemia-activated Hypothalamic Microglia Impairs Glucose Counterregulatory Responses. **Sci Rep 9:** 6224.

Winkler, Z., Kuti, D., Ferenczi, S., Gulyas, K., Polyak, A., **Kovacs, K.J.** (2017) Impaired microglia fractalkine signaling affects stress reaction and coping style in mice. **Behav Brain Res 334:** 119-128.

Ferenczi, S., Szegi, K., Winkler, Z., Barna, T., **Kovacs, K.J.** (2016) Oligomannan Prebiotic Attenuates Immunological, Clinical and Behavioral Symptoms in Mouse Model of Inflammatory Bowel Disease. **Sci Rep 6:** 34132.

LÁSZLÓ KŐHIDAI

Semmelweis University
Faculty of Medicine
Department of Genetics, Cell- and Immunobiology

RESEARCH AREA

Main research fields investigated in Chemotaxis Research Group are
(i) research on cell adhesion, chemotaxis and other basic cell physiological responses;
(ii) phylogeny of cell signaling - studies in ciliated model cells;
(iii) characterization of 'Chemotaxome', the novel category of systems biology.
An underlined, ongoing project of the Research Group is to develop conjugates of drug-targeting available for different kinds of molecular delivery (chemotactic drug targeting) in tumors, atherosclerosis etc. The most significant models are unicellular eukaryotes (Tetrahymena pyriformis) as well as several mammalian tumor cell lines. The Research Group is the host of the core facility of impedance based cell analytical research infrastructure (ECIS, xCELLignece) qualified as SKI by NEKIFUT/NKTH.

SELECTED PUBLICATIONS

Kohidai, L., Vakkuri, O., Keresztesi, M., Leppaluoto, J., Csaba, G., (2002) Melatonin in the unicellular Tetrahymena pyriformis: effects of different lighting conditions. **Cell Biochem Funct 20:** 3 pp. 269-272.

Lajkó, E., Bányai, P., Zámbó, Z., Kursinszki, L., Szőke, E., **Kohidai, L.** (2015) Targeted tumor therapy by Rubia tinctorum L.: Analytical characterization of hydroxy-anthraquinones and investigation of their selective cytotoxic, adhesion and migration modulator effects on melanoma cell lines. (A2058 and HT168-M1) **Cancer Cell Int 15 Paper:** 119.

Kohidai, L., Lajko, E., Pallinger, E., Csaba, G. (2012) Verification of epigenetic inheritance in a unicellular model system: multigenerational effects of hormonal imprinting. **Cell Biol Int 36:** 10 pp. 951-959.

Kohidai, L,. Csaba, G., Laszlo, V., (1990) Persistence of receptor memory induced in tetrahymena by insulin imprinting. **Acta Microbiol Hung 37** pp. 269-275.

Kohidai, L., (1995) method for determination of chemoattraction in tetrahymena- pyriformis. **Current Microbiology 30:** 4 pp. 251-253.

ZSOLT LELE

HUN-REN Institute of Experimental Medicine
Molecular Neurobiology Research Group

RESEARCH AREA

The Laboratory of Molecular Neurobiology has 3 major projects running currently. 1.) Development and novel application of the PharmacoSTORM superresolution microscopy. 2.) The role of endocannabinoid synthesizing enzymes in the development of the central nervous system. 3.) The role of cadherin cell adhesion molecules in cortical development. Of these, the second and the third projects are under my supervision. Endocannabinoids are endogenous molecules which bind to the same receptor which Δ^9-tetrahidrocannabinol, the main psychoactive component of marijuana targets. Currently there are two main endocannabinoids anandamide and 2-AG although there are several more or less uncharacterized lipids which may belong to this category. Synthesis of these signalling molecules can occur via many pathways, at least based on biochemical and in vitro cell culture experiments. Our main targets are the potential alternative synthesizing enzymes of anandamide, and we aim to characterize their role in the development of the CNS. The other project focuses on cadherins (Ca2+ -dependent adhesion molecules) and their role in cortical development. Of the more than 100 members of the cadherin superfamily our lab focuses on the classic (ie. β-catenin-binding) cadherin family. One of our main projects is actually at the crossing point of these projects where we recently described a novel protecting mechanism in the developing embryonic cortex which we termed developmental anoikis. Our main goal is currently to describe the molecular mechanisms behind this phenomenon.

SELECTED PUBLICATIONS

László, Z.I., **Lele, Z.,** Zöldi, M., Miczán, V., Mógor, F., Simon, G.M., Mackie, K., Kacskovics, I., Cravatt, B.F., Katona. I. (2020) ABHD4-dependent developmental anoikis safeguards the embryonic brain. **Nat Commun 11:** 4363.

Cserep, C., Posfai, B., Lenart, N., Fekete, R., Laszlo, Z.I., **Lele, Z.,** Orsolits, B., Molnar, G., Heindl, S., Schwarcz, A.D. et al. (2020) Microglia monitor and protect neuronal function through specialized somatic purinergic junctions. **Science 367:** 528-537.

László, Z.I., Bercsényi, K., Mayer, M., Lefkovics, K., Szabó, G., Katona, I., **Lele, Z.** (2020) N-cadherin (Cdh2) Maintains Migration and Postmitotic Survival of Cortical Interneuron Precursors in a Cell-Type-Specific Manner. **Cereb Cortex 30:** 1318-1329.

Klinger-Gratz, P.P., Ralvenius, W.T., Neumann, E., Kato, A., Nyilas, R., **Lele, Z.,** Katona, I., Zeilhofer, H.U. (2018) Acetaminophen Relieves Inflammatory Pain through CB1 Cannabinoid Receptors in the Rostral Ventromedial Medulla. **J Neurosci 38:** 322-334.

Lefkovics, K., Mayer, M., Bercsenyi, K., Szabo, G., **Lele, Z.** (2012) Comparative analysis of type II classic cadherin mRNA distribution patterns in the developing and adult mouse somatosensory cortex and hippocampus suggests significant functional redundancy. **J Comp Neurol 520:** 1387-1405.

ZSOLT LIPOSITS

HUN-REN Institute of Experimental Medicine
Endocrine Neurobiology Research Team

RESEARCH AREA

Neuronal and hormonal regulation of reproduction.

SELECTED PUBLICATIONS

Balint, F., Csillag, V., Vastagh, C., **Liposits, Z.**, and Farkas, I. (2021) Insulin-like growth factor 1 (IGF-1) increases GABAergic neurotransmission to GnRH neurons via suppressing the retrograde tonic endocannabinoid signaling pathway in mice. **Neuroendocrinology 111:** 1219–1230.

Vastagh, C., Farkas, I., Scott, M.M., and **Liposits, Z.** (2021) Networking of glucagon-like peptide-1 axons with GnRH neurons in the basal forebrain of male mice revealed by 3DISCO-based immunocytochemistry and optogenetics. **Brain Structure & Function 226:** 105–120.

Bake, T., Le May, M.V., Edvardsson, C.E., Vogel, H., Bergström, U., Albers, M.N., Skibicka, K.P., Farkas, I., **Liposits, Z.** and Dickson, S.L. (2020) Ghrelin Receptor Stimulation of the Lateral Parabrachial Nucleus in Rats Increases Food Intake but not Food Motivation. **Obesity 28:** 1503–1511.

Leiszter, K., Galamb, O., Kalmár, A., Zsigrai, S., Valcz, G., Szigeti, K.A., Barták, B.K., Nagy, Z.B., Dank, M., **Liposits, Z**., Igaz, P., Tulassay, Z. and Molnár, B. (2020) Az ösztrogének lehetséges szerepe a vastagbéldaganatok kialakulásában. **Orvosi Hetilap 161:** 532–543.

Balla, B., Sárvári, M., Kósa, J.P., Kocsis-Deák, B., Tobiás, B., Árvai, K., Takács, I., Podani, J., **Liposits, Z**. and Lakatos, P. (2019) Long-term selective estrogen receptor-beta agonist treatment modulates gene expression in bone and bone marrow of ovariectomized rats. **Journal of Steroid Biochemistry and Molecular Biology 188:** 185–194.

JUDIT MAKARA

HUN-REN Institute of Experimental Medicine
Neuronal Signaling Research Group

RESEARCH AREA

The focus of our research is to understand the principles of information processing by neurons. Nerve cells receive thousands of synaptic inputs onto their thin and long processes called dendrites and transform the integrated information to an output signal at the cell body. Processing of inputs takes place primarily in the dendrites that express a variety of voltage dependent ion channels, allowing them to perform diverse forms of nonlinear summation and input-output transformation. Furthermore, the fine regulation of ion channel function makes this processing dynamic. We use cutting edge microscopic and electrophysiological methods in brain slices and awake behaving rodents to elucidate the basic principles and regulation of dendritic function in neurons of the hippocampus (a brain region important for episodic memory) as well as the possible roles of these cellular information processing mechanisms in learning and memory guiding behaviour.

SELECTED PUBLICATIONS

Magó, Á., Kis, N., Lükő, B, **Makara, J.K.** (2021) Distinct dendritic Ca2+ spike forms produce opposing input-output transformations in rat CA3 pyramidal cells. **eLife 10:** e74493.

Ujfalussy, B.B., **Makara, J.K.** (2020) Impact of functional synapse clusters on neuronal response selectivity. **Nature Communications 11:** 1413.

Magó, Á., Weber, J.P., Ujfalussy, B.B., **Makara, J.K.** (2020) Synaptic plasticity depends on the fine-scale input pattern in thin dendrites of CA1 pyramidal neurons. **J. Neuroscience 40:** 2593-2605.

Raus Balind, S., Magó, Á., Ahmadi, M., Kis, N., Varga-Németh, Z., Lőrincz, A., **Makara, J.K.** (2019) Diverse synaptic and dendritic mechanisms of complex spike burst generation in hippocampal CA3 pyramidal cells. **Nature Communications, 10:** 1859.

Harnett, M.T.*, **Makara, J.K.***, Spruston, N., Kath, W.L., Magee, J.C.† (2012) Synaptic amplification by dendritic spines enhances input cooperativity. **Nature, 491:** 599-602. *shared first authors.

PÁL MAUROVICH-HORVAT

Semmelweis University
Faculty of Medicine
Medical Imaging Centre

RESEARCH AREA

Our research interest focuses on non-invasive cardiovascular imaging to improve cardiovascular risk assessment and clinical outcomes. In addition, the research group conducts research projects aiming to improve diagnostic imaging efficacy using artificial intelligence techniques such as deep learning and radiomics.

SELECTED PUBLICATIONS

DISCHARGE Trial Group, **Maurovich-Horvat, P.**, Bosserdt, M., Kofoed, KF., et al. (2022) CT or Invasive Coronary Angiography in Stable Chest Pain. **N Engl J Med 386(17):** 1591-1602.

Drobni, ZD., Kolossvary, M., Karady, J., Jermendy, AL., Tarnoki, AD., Tarnoki, DL., Simon, J., Szilveszter, B., Littvay, L., Voros, S., Jermendy, G., Merkely, B., **Maurovich-Horvat, P.** (2022) Heritability of Coronary Artery Disease: Insights From a Classical Twin Study. **Circ Cardiovasc Imaging 15(3):** e013348.

Kolossváry, M., Karády, J., Kikuchi, Y., Ivanov, A., Schlett, CL., Lu MT., Foldyna, B., Merkely, B., Aerts, HJ., Hoffmann, U., **Maurovich-Horvat, P.**, (2019) Radiomics versus Visual and Histogram-based Assessment to Identify Atheromatous Lesions at Coronary CT Angiography: An ex Vivo Study. **Radiology 293(1):** 89-96.

Simon, J., Fung, K., Raisi-Estabragh, Z., Aung, N., Khanji, MY., Kolossváry, M., Merkely, B., Munroe, PB., Harvey, NC., Piechnik, SK., Neubauer, S., Petersen, SE., **Maurovich-Horvat, P.** (2022) Light to moderate coffee consumption is associated with lower risk of death: a UK Biobank study. **Eur J Prev Cardiol 29(6):** 982-991.

TAMÁS MÉSZÁROS

Semmelweis University
Department of Molecular Biology

RESEARCH AREA

Our research group is dedicated to the selection of aptamers with diagnostic and therapeutic potential, along with the development of methods related to this field. We collaborate closely with partners to explore the practicality of the aptamers we select in a variety of cellular model systems. To fulfill the protein needs for aptamer selection, our research group has fine-tuned an in vitro translation system. This system not only aids in generating the necessary proteins but also facilitates our protein functional tests, with a primary focus on mitogen-activated protein kinases.

SELECTED PUBLICATIONS

Percze, K., Tolnai, Z.J., Eleveld, M., Ou, L., Du, H., Olia, A.S., Kwong, P.D., de Jonge, M.I., **Mészáros, T.** (2023) Tryptophan-like side chain holding aptamers inhibit respiratory syncytial virus infection of lung epithelial cells. **Sci Rep 13:** 1 Paper: 9403 , 12 p.

Tolnai, Z.J., András, J., Szeitner, Z., Percze, K., Simon, L.F., Gyurcsányi, R.E., **Mészáros, T.** (2020) Spiegelmer-based sandwich assay for cardiac troponin i detection. **Int J Mol Sci 21:** 14 Paper: 4963 , 11 p.

Tolnai, Z., Harkai, Á., Szeitner, Z., Scholz, É.N., Percze, K., Gyurkovics, A., **Mészáros, T.** (2019) A simple modification increases specificity and efficiency of asymmetric PCR. **Anal Chim Acta 1047** pp. 225-230. , 6 p.

Percze, K., Szakacs, Z., Scholz, E., Andras, J., Szeitner, Z ., Kieboom, CH., Ferwerda, G., Jonge, M.I., Gyurcsanyi, R.E., **Meszaros, T.** (2017) Aptamers for respiratory syncytial virus detection. **Sci Rep 7** Paper: 42794 , 11 p.

Nagy, S.K., Darula, Z., Kallai, B.M., Bogre, L., Banhegyi, G., Medzihradszky, K.F., Horvath, G., **Meszaros, T.** (2015) Activation of AtMPK9 through autophosphorylation that makes it independent of the canonical MAPK cascades. **Biochem J 467:** 1 pp. 167-175., 9 p.

ÉVA MIKICS

HUN-REN Institute of Experimental Medicine
Laboratory of Translational Behavioural Neuroscience

RESEARCH AREA

Our lab conducts behavioral neuroscience research with a translational approach. We aim to better understand the neurobiological background of mental disorders using animal models in order to identify potential targets for novel treatment strategies. Our work is mainly focused on the long-term effects of early-life stress, i.e. how early adverse factors contribute to vulnerability for the development of specific mental disorders.

SELECTED PUBLICATIONS

Bruzsik, B., Biro, L., Zelena, D., Sipos, E., Török, B., Sarosdi, K.R., Szebik, H., **Mikics#**, E., Toth#. M. #equal contribution (2022) Neurochemically distinct populations of the bed nucleus of stria terminalis modulate innate fear response to weak threat evoked by predator odor stimuli. **Neurobiol Stress 15:** 100415.

Bruzsik, B., Biro, L., Zelena, D., Sipos, E., Szebik, H., Sarosdi, K.R., Horvath, O., Farkas, I., Csillag, V., Finszter, C.K., **Mikics#**, E., and Toth#, M. #equal contribution, (2021) Somatostatin neurons of the bed nucleus of stria terminalis enhance associative fear memory consolidation in mice. **J Neurosci 41:** 1982–1995.

Miskolczi, C., Halász, J., and **Mikics, É.** (2019) Changes in neuroplasticity following early-life social adversities. **Pediatr Res 85:** 225–233.

Mikics*¬, E., Guirado*, R., Umemori, J., Toth, M., Biro, L., Miskolczi, C., Balazsfi, D., Zelena, D., Castren, E., Haller, J., and Karpova, N. *equal contribution (2018) Social Learning Requires Plasticity Enhanced by Fluoxetine Through Prefrontal Bdnf-TrkB Signaling to Limit Aggression Induced by Post-Weaning Social Isolation. **Neuropsychopharmacology 43:** 235–245.

Mikics, É., Kruk, M., and Haller, J. (2004) Genomic and non-genomic effects of glucocorticoids on aggressive behavior in male rats. **Psychoneuroendocrinology 29:** 618–635.

ATTILA MÓCSAI

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The aim of our group is to understand the molecular mechanisms of various human diseases, laying down the foundations for new diagnostic and therapeutic approaches. Our experiments focus on the inflammatory processes that determine the pathomechanism of a large number of major human diseases. We investigate their molecular mechanisms using transgenic animal models, healthy and patient-derived human cells and tissues, state-of-the-art molecular biology and gene editing, as well as functional and imaging methods. We have close collaboration with several prominent international research groups. Our group is supported by several programmes of excellence, including the Frontline and Topical Excellence programmes, as well as the European Union's largest international rheumatology consortium.

SELECTED PUBLICATIONS

Szilveszter, K.P., Vikár, S., Horváth, Á.I., Helyes, Z., Sárdy, M. and **Mócsai, A.** (2022) Phospholipase Cγ2 is essential for experimental models of epidermolysis bullosa acquisita. **J Invest Dermatol 142:** 1114-1125.

Futosi, K., Kása, O., Szilveszter, K.P. and **Mócsai, A.** (2021) Neutrophil phospholipase Cγ2 drives autoantibody-induced arthritis through the generation of the inflammatory microenvironment. **Arthritis Rheumatol 73:** 1614-1625.

Orosz, A., Walzog, B. and **Mócsai, A.** (2021) In vivo functions of mouse neutrophils derived from HoxB8-transduced conditionally immortalized myeloid progenitors. **J Immunol 206:** 432–445.

Németh, T., Sperandio, M. and **Mócsai, A.** (2020) Neutrophils as emerging therapeutic targets. **Nat Rev Drug Discov 19:** 253-275.

Csete, D., Simon, E., Alatshan, A., Aradi, P., Dobó-Nagy, C., Jakus, Z., Benkő, S., Győri, D.S. and **Mócsai, A.** (2019) Hematopoietic or osteoclast-specific deletion of Syk leads to increased bone mass in experimental mice. **Front Immunol 10:** 937.

NÁNDOR NAGY

Semmelweis University
Faculty of Medicine
Department of Anatomy, Histology and Embryology
Stem Cells and Experimental Embryology Laboratory

RESEARCH AREA

Our research is focusing on two broad areas. Firstly, our laboratory is interested in developmental mechanisms of enteric nervous system (ENS) formation. This work is aimed at understanding the development of the ENS in normal, abnormal, and evolutionary contexts. We do this by examining the role of the extracellular environment in the embryonic gut that regulate the mechanisms of neural crest derived stem cell differentiation during intestinal morphogenesis. Secondly, our laboratory focuses on mechanisms that underlie lymphoid organ formation. This work also uses the avian embryo as the model system, and addresses cellular (stem cell migration, differentiation), molecular (Foxn1, CXCR4, Shh, BMP4 expression), immunological (IBDV and bronchitis infection) and morphological (confocal, immune electron-microscopy) aspects of the primary and secondary lymphoid organ formation. Our aim is to discover how the avian lymphoid organs are built, and how immunosuppressive diseases affect its organization.
https://semmelweis.hu/stemcell/en/about-us/

SELECTED PUBLICATIONS

Nagy, N. (Corresponding author), Kovács, T., Stavely, R., Halasy, V., Soós, A., Szőcs, E., Hotta, R., Graham, H., Goldstein, A.M. (2021) Avian ceca are required for hindgut enteric nervous system development by inhibiting neuronal differentiation via non-canonical Wnt signaling and by promoting enteric neural crest cell proliferation. **Development 148:** dev199825.

Dóra, D., Ferenczi, S., Stavely, R., Tóth, V.E., Varga, Z.V., Kovács, T., Bódi, I., Hotta, R., Kovács, K.J., Goldstein, A.M., and **Nagy, N.** (2021) Evidence of a Myenteric Plexus Barrier and Its Macrophage-Dependent Degradation During Murine Colitis: Implications in Enteric Neuroinflammation. **Cell Mol Gasrtoenterol Hepatol 12:** 1617-1641.

Nagy, N. (Corresponding author), Barad, C., Hotta, R., Bhave, S., Arciero, E., Dora, D., and Goldstein, A.M. (2018) Collagen 18 and agrin are secreted by neural crest cells to remodel their microenvironment and regulate their migration during enteric nervous system development. **Development 145:** dev160317.

Nagy, N. (Corresponding author), Barad, C., Graham, H.K., Hotta, R., Cheng, L.S., Fejszak, N., and Goldstein, A.M. (2016) Sonic hedgehog controls enteric nervous system development by patterning the extracellular matrix. **Development 143:** 264-275. IF: 5,843

Dóra, D., Fejszák, N., Goldstein, A.M., Minkó, K., **Nagy, N.** (2017). Ontogeny of ramified CD45 cells in chicken embryo and their contribution to bursal secretory dendritic cells. **Cell Tissue Res 368:** 353-370.

TAMÁS NÉMETH

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The prevalence of rheumatoid arthritis, which is an autoimmune disease and sometimes causes serious joint deformity and loss of function, is estimated to be around 0.5-1%. Despite of the fact that we can use more and more drugs in therapy, remission can not be reached for many patients, so it is important to identify new drug targets, which necessitates a better understanding of the pathogenesis. Many cell types are involved in the development of rheumatoid arthritis: in addition to resident cells in the synovium (e.g. synovial fibroblasts), cells of both the adaptive and the innate immune system (e.g. neutrophils and macrophages) are key players. The aim of the Translational Rheumatology Research Group is to study the signaling pathways of synovial fibroblasts, macrophages and neutrophils in the development and progression of autoimmune arthritis, and to inhibit the function of the identified molecules, which can contribute to the development of new therapies.

SELECTED PUBLICATIONS

Káposztás, E., Balogh, L., Mócsai, A., Kemecsei, É., Jakus, Z. and **Németh, T.** (2023) The selective inhibition of the Syk tyrosine kinase ameliorates experimental autoimmune arthritis. **Front Immunol 14:** 1279155.

Németh, T., Balogh, L., Káposztás, E., Szilveszter, K.P. and Mócsai, A. (2023) Neutrophil-specific Syk expression is crucial for skin disease in experimental epidermolysis bullosa acquisita. **J Invest Dermatol 143(7)**: 1147-1156.

Németh, T., Nagy, G. and Pap, T. (2022) Synovial fibroblasts as potential drug targets in rheumatoid arthritis, where do we stand and where shall we go? **Ann Rheum Dis 81(8):** 1055-1064.

Németh, T., Sperandio, M. and Mócsai, A. (2020) Neutrophils as emerging therapeutic targets. **Nat Rev Drug Discov 19:** 253-275.

Németh, T., Futosi, K., Sitaru, C., Ruland, J. and Mócsai A. (2016) Neutrophil-specific deletion of the CARD9 gene expression regulator suppresses autoantibody-induced inflammation in vivo. **Nat Commun 7:** 11004.

ZOLTÁN NUSSER

HUN-REN Institute of Experimental Medicine
Cellular Neurophysiology Research Group

RESEARCH AREA

The most fundamental function of nerve cells is the integration of their synaptic inputs to generate their propagating output signal, the action potential. The major aims of Dr Nusser's laboratory are to understand how identified presynaptic nerve cells release neurotransmitters; how the released transmitter molecules activate their postsynaptic receptors; and how the generated postsynaptic potentials are integrated to generate an action potential. The Laboratory of Cellular Neurophysiology focuses on the following major project areas using a variety of molecular, neuroanatomical, in vitro electrophysiological, in vitro and in vivo imaging and in silico modeling approaches: 1. Revealing the molecular, structural and functional heterogeneity of cortical excitatory and inhibitory synapses. Determine the molecular specializations underlying the functional and structural diversity of synapses, such as the probability and short-term plasticity of transmitter release, and the extent of postsynaptic receptor activation. 2. Creating a molecular map of the neuronal surface by determining the location and density of various voltage- and ligand-gated ion channel subunits in defined subcellular compartments of identified nerve cells. 3. Understanding the mechanisms underlying hippocampal network activity during behaviour.

SELECTED PUBLICATIONS

Aldahabi, M., Balint, F., Holderith, N., Lorincz, A., Reva, M., and **Nusser, Z.** (2022) Different priming states of synaptic vesicles underlie distinct release probabilities at hippocampal excitatory synapses. **Neuron 110:** 4144-4161.

Karlocai, M.R., Heredi, J., Benedek, T., Holderith, N., Lorincz, A. and **Nusser, Z.** (2021) Variability in the Munc13-1 content of excitatory release sites. **eLife 0:**e67468

Holderith, N., Heredi, J., Kis, V., and **Nusser, Z.** (2020) A high-resolution method for quantitative molecular analysis of functionally characterized synapses. **Cell Rep 32:** 107968.

Rebola, N., Reva, M., Kirizs, T., Szoboszlay, M., Lorincz, A., Moneron, G., **Nusser, Z.** and DiGregorio, D.A. (2019) Distinct nanoscale calcium channel and synaptic vesicle topographies contribute to the diversity of synaptic function. **Neuron 104:** 693-710.

Éltes, T., Kirizs, T., **Nusser, Z.** & Holderith, N. (2017) Target cell type-dependent differences in Ca^{2+} channel function underlie distinct release probabilities at hippocampal glutamatergic terminals. **J Neurosci 37:** 1910-1924.

Szoboszlay M., Lorincz, A., Lanore, F., Vervaeke, K., Silver, R. A. & **Nusser, Z.** (2016) Functional properties of dendritic gap junctions in cerebellar Golgi cells. **Neuron 90:** 1043-1056.

GÁBOR NYIRI

HUN-REN Institute of Experimental Medicine
Cerebral Cortex Research Group

RESEARCH AREA

My research group focuses on the sub-cortical control of learning and memory processes. We study these questions from synaptic-level electron microscopy studies to viral neuronal tracing methods and behavioral-level studies.

SELECTED PUBLICATIONS

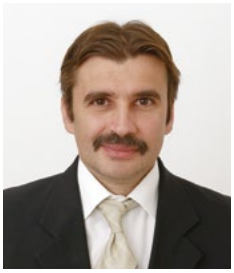
Szőnyi, A., Sos, K.E., Nyilas, R., Schlingloff, D., Domonkos, A., Takács, V.T. Pósfai, B., Hegedüs, P., Priestley, J.B.J.B., Gundlach, A.L.A.L., Gulyás, A.I.A.I., Varga, V., Losonczy, A., Freund, T.F., **Nyiri, G.** (2019) Brainstem nucleus incertus controls contextual memory formation. **Science 364.**

Szőnyi, A., Zichó, K., Barth, A.M., Gönczi, R.T.R.T., Schlingloff, D., Török, B., Sipos, E., Major, A., Bardóczi, Z., Sos, K.E.K.E., Gulyás, A.I.A.I., Varga, V., Zelena, D., Freund, T.F., **Nyiri, G.** (2019) A., Median raphe controls acquisition of negative experience in the mouse. **Science 366.**

Takács, V.T., Cserép, C., Schlingloff, D., Pósfai, B., Szőnyi, A., Sos, K.E.K.E., Környei, Z., Dénes, Á., Gulyás, A.I.A.I., Freund, T.F., Freund, T.F., **Nyiri, G.** (2018) Co-transmission of acetylcholine and GABA regulates hippocampal states. **Nat Commun. 9:** 2848.

Szabadits, E., Cserép, C., Szonyi, A., Fukazawa, Y., Shigemoto, R., Watanabe, M., Itohara, S., Freund, T.F.T.F., **Nyiri, G.** (2011) NMDA receptors in hippocampal GABAergic synapses and their role in nitric oxide signaling. **J Neurosci 31:** 5893–5904.

Szabadits, E., Cserép, C., Ludányi, A., Katona, I., Gracia-Llanes, J., Freund, T.F., **Nyiri, G.** (2007) Hippocampal GABAergic synapses possess the molecular machinery for retrograde nitric oxide signaling. **J Neurosci 27:** 8101–8111.



ATTILA PATÓCS

Semmelweis University
Faculty of Medicine
Department of Laboratory Medicine

RESEARCH AREA

Genetics, oncogentics, genomics, endocrine tumors, hereditary cancer.

SELECTED PUBLICATIONS

Patocs, A., Zhang, L., Xu, Y., Weber, F., Caldes, T., Mutter, G.L., Platzer, P., Eng, C. (2007) Breast-Cancer Stromal Cells with TP53 Mutations and Nodal Metastases. **N Engl J Med 357:** 2543-2551.

Tretter, L., **Patocs, A.,** Chinopoulos, C. (2016) Succinate, an intermediate in metabolism, signal transduction, ROS, hypoxia, and tumorigenesis. **Biochim Biophys Acta1857:** 1086-1101.

Butz, H., Rácz, K., Hunyady, L., **Patócs, A.** (2012) Crosstalk between TGF-β signaling and the microRNA machinery. **Trends Pharmacol Sci 33:** 382-393.

Ni, Y., Zbuk, K.M., Sadler, T., **Patocs, A.,** Lobo, G., Edelman, E., Platzer, P., Orloff, M.S., Waite, K.A., Eng, C. (2008) Germline mutations and variants in the succinate dehydrogenase genes in Cowden and Cowden-like syndromes. **Am J Hum Genet 83:** 261-268.

Butz, H., Likó, I., Czirják, S., Igaz, P., Khan, M.M., Zivkovic, V., Bálint, K., Korbonits, M., Rácz, K., **Patócs, A.** (2010) Down-regulation of Wee1 kinase by a specific subset of microRNA in human sporadic pituitary adenomas. **J Clin Endocinol Metab 95:** E181-E191.

KAROLINA MILENA PIRCS

Semmelweis University
Faculty of Medicine
Department of Translational Medicine

RESEARCH AREA

I am interested in how alterations in autophagy contribute to healthy ageing and the pathophysiology of age-related, chronic neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease and Huntington's disease.

SELECTED PUBLICATIONS

Pircs, K., Drouin-Ouellet, J., Horváth, V., Gil, J., Rezeli, M., Garza, R., Grassi, D.A., Sharma, Y., St-Amour, I., Harris, K., Jönsson, M.E., Johansson, P.A., Vuono, R., Fazal, S.V., Stoker, T., Hersbach, B.A., Sharma, K., Lagerwall, J., Lagerström, S., Storm, P., Hébert, S.S., Marko-Varga, Gy., Parmar, M., Barker, R.A., Jakobsson, J. (2021) Distinct subcellular autophagy impairments in induced neurons from Huntington's disease patients. **Brain** awab473 (online, ahead of print)

Brattas, P.L., Hersbach, B.A., Madsen, S., Petri, R., Jakobsson, J., **Pircs, K.** (2020) Impact of differential and time-dependent autophagy activation on therapeutic efficacy in a model of Huntington disease. **Autophagy 17:** 1316-1329.

Pircs, K., Petri, R., Madsen, S., Brattås, P.L., Vuono, R., Ottosson, R.D., St-Amour, I., Hersbach, A.B., Matusiak-Brückner, M., Hult, Lundh, S., Petersén, A., Déglon, N., Hébert, S.S., Parmar, M., Barker, A.R., Jakobsson, J. (2018) Huntingtin aggregation impairs autophagy leading to Argonaute-2 accumulation and global microRNA dysregulation. **Cell Rep 24:** 1397-1406.

Drouin-Ouellet, J., Lau, S., Brattas, P.L., Rylander, Ottosson, D., **Pircs, K.,** Grassi, D., Collins, M.L., Vuono, R., Sjöland, A.A., Westergren-Thorsson, G., Graff, C., Minthon, L., Toresson, H., Barker, A.R., Jakobsson, J., Parmar, M. (2017) REST suppression mediates neural conversion of adult human fibroblasts via microRNA dependent and independent pathways. **EMBO Mol Med 9:** 1117-1131.

FRIGYES SÁMUEL RÁCZ

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

In our study we investigate the effects of aging on neurodynamics and various aspects of cognitive functioning. Our research focuses on the identification of neurophysiological biomarkers that can potentially predict age-related changes in cognition and help better understand their biological origin. Our project has two fundamental aspects. First, we develop new analythical and computational methods that can effectively capture nontrivial features of neural dynamics. These include, but are not limited to methods for assessing the fractal properties of dynamic functional connectivity among distinct brain regions, a subfield that only recently became the focus of interest in the field of neuroscience. Second, we collect and analyze data from our population of interest, specifically healthy (i.e., no history of any neuropsychiatric disorder or any severe general medical condition), elderly individuals. Results from the elderly group are contrasted with those obtained from healthy, young (age < 40 years) adults. We record cortical activity usin electroencephalography (EEG). Measurements are first performed in resting-state (i.e., not engaging in any specific mental activity), then EEG is recorded while subjects perform three different cognitive tasks. These all put different mental skills to test, such as pattern recognition, working memory or spatial orientation and learning. Following the EEG recordings, participants are further evaluated using the standardized and validated Cambridge Neuropsychological Test Automated Battery (CANTAB). This session includes seven further tasks, each testing various aspects of cognition that are most commonly affected in conditions related to age and pathologies eventually leading to dementia. Our research therefore not only focuses on how resting-state neural activity might predict performance related to different aspects of cognition, it is also equivalently important, how the brain adapts to increased mental challange/workload, and how this adaptation might be affected at a later age.

SELECTED PUBLICATIONS

Mukli, P., Csipo, T., Lipecz, A., Stylianou, O., **Racz, F.S.**, Owens, C.D., Perry, J.W., Tarantini, S., Sorond, F.A., Kellawan, J.M. and Purebl, G., (2021) Sleep deprivation alters task related changes in functional connectivity of the frontal cortex: A near infrared spectroscopy study. **Brain and Behavior 11:** p.e02135.

Racz, F.S., Farkas, K., Stylianou, O., Kaposzta, Z., Czoch, A., Mukli, P., Csukly, G. and Eke, A. (2021) Separating scale free and oscillatory components of neural activity in schizophrenia. **Brain and Behavior 11:** p.e02047.

Kaposzta, Z., Stylianou, O., Mukli, P., Eke, A. and **Racz, F.S.** (2021) Decreased connection density and modularity of functional brain networks during back working memory paradigm. **Brain and Behavior 11:** p.e01932.

Racz, F.S., Mukli, P., Nagy, Z. and Eke, A., (2018) Multifractal dynamics of resting-state functional connectivity in the prefrontal cortex. **Physiological measurement 39:** p.024003.

ANNA SEBESTYÉN

Semmelweis University
Faculty of Medicine
Department of Pathology and Experimental Cancer Research

RESEARCH AREA

The signalling network failures of solid tumours, and their tissue heterogeneity are in the focus of our Tumour Metabolism Research Group. Our main questions are related to the regulatory role of mTOR signalling in cellular metabolism, metabolic heterogeneity and plasticity. We are characterising human cancer tissues and additionally, we can use traditional 2D cell culturing and xenograft models in our experimental research work regarding to tumour progression, therapy resistance and metastasis. Furthermore, in our new research direction we are developing and applying new in vitro 3D bioprinted cancer models.

SELECTED PUBLICATIONS

Dankó, T., Petővári, G., Raffay, R., Sztankovics, D., Moldvai, D., Vetlényi, E., Krencz, I., Rókusz, A., Sipos, K., Visnovitz, T., Pápay, J., **Sebestyén, A.** (2022) Characterisation of 3D Bioprinted Human Breast Cancer Model for In Vitro Drug and Metabolic Targeting. **Int J Mol Sci 23**(13): 7444.

Sebestyén, A., Dankó, T., Sztankovics, D., Moldvai, D., Raffay, R., Cervi, C., Krencz, I., Zsiros, V., Jeney, A., Petővári, G. (2021)The role of metabolic ecosystem in cancer progression - metabolic plasticity and mTOR hyperactivity in tumor tissues. **Cancer Metastasis Rev 40**(4): 989-1033.

Misra, S., Moro, CF., Del Chiaro, M., Pouso S., **Sebestyén, A.**, Löhr M., Björnstedt, M., Verbeke, CS. (2019) Ex vivo organotypic culture system of precision-cut slices of human pancreatic ductal adenocarcinoma. **Sci Rep 9**(1): 2133.

Hujber, Z., Horváth, G., Petővári, G., Krencz, I., Dankó, T., Mészáros, K., Rajnai, H., Szoboszlai, N., Leenders, WPJ., Jeney, A., Tretter, L., **Sebestyén, A.** (2018) GABA, glutamine, glutamate oxidation and succinic semialdehyde dehydrogenase expression in human gliomas. **J Exp Clin Cancer Res 37**(1): 271.

Nemes, K., Csóka, M., Nagy, N., Márk, Á., Váradi, Z., Dankó, T., Kovács, G., Kopper, L., **Sebestyén, A.** (2015) Expression of certain leukemia/lymphoma related microRNAs and its correlation with prognosis in childhood acute lymphoblastic leukemia. **Pathol Oncol Res 21**(3): 597-604.

BEÁTA SPERLÁGH

HUN-REN Institute of Experimental Medicine
Molecular Pharmacology Research Group

RESEARCH AREA

ATP is one of the most versatile molecule in the living cells: it is well known as the universal "energy currency", and as a building block of DNA, but it is also an important signalling substance of intercellular communication. This latter function of ATP is mediated by ionotropic P2X and metabotropic P2Y receptors. The general scientific mission of my research is to understand the ATP mediated signalling in the normal and pathological nervous system; and thereby to identify new therapeutic targets for the treatment of CNS diseases. We employ multidisciplinary approaches to study purinergic mechanisms, including studies on the release and action of ATP, mapping and identification of purinergic receptors under physiological conditions and in animal models of various neurological and psychiatric disorders and clinical studies. The main focus of our current interest is to identify the role of P2X7 receptors and the coupled signalling pathways (NLRP3-IL-1beta) in animal models of autism, schizophrenia and mood disorders as well as that of the metabotropic P2Y12 receptors in the pathophysiology of pain and Parkinson's disease.

SELECTED PUBLICATIONS

Szabó, D., Tod, P., Gölöncsér, F., Román, V., Lendvai, B., Otrokocsi, L., **Sperlágh, B.** (2022) Maternal P2X7 receptor inhibition prevents autism-like phenotype in male mouse offspring through the NLRP3-IL-1β pathway. **Brain Behav Immun 101:** 318-332.

Iring, A., Tóth, A., Baranyi, M., Otrokocsi, L., Módis, L.V., Gölöncsér, F., Varga, B., Hortobágyi, T., Bereczki, D., Dénes, Á., **Sperlágh, B.** (2022) The dualistic role of the purinergic P2Y12-receptor in an in vivo model of Parkinson's disease: Signalling pathway and novel therapeutic targets. **Pharmacol Res 176:** 106045.

Gölöncsér, F., Baranyi, M., Iring, A., Hricisák, L., Otrokocsi, L., Benyó, Z., **Sperlágh, B.** (2021) Involvement of P2Y12 receptors in a nitroglycerin-induced model of migraine in male mice. **Br J Pharmacol 178:** 4626-4645.

Horváth, G., Otrokocsi, L., Beko, K., Baranyi, M., Kittel, Á., Fritz-Ruenes, P.A., **Sperlágh, B.** (2019) P2X7 Receptors Drive Poly(I:C) Induced Autism-like Behavior in Mice. **J Neurosci 39:** 2542-2561.

Bekő, K., Koványi, B., Gölöncsér, F., Horváth, G., Dénes, Á., Környei, Z., Botz, B., Helyes, Z., Müller, C.E., **Sperlágh, B.** (2017) Contribution of platelet P2Y12 receptors to chronic Complete Freund's adjuvant-induced inflammatory pain. **J Thromb Haemost 15:** 1223-1235.

JÁNOS SZABADICS

HUN-REN Institute of Experimental Medicine
Cellular Neuropharmacology Group

RESEARCH AREA

The current theories of the broader hippocampal network explain its memory functions based on the firing of individual neurons. However, the cellular mechanisms that underlie these functions are elusive. We are interested in the functions that determine the activity of dentate gyrus granule cells (DG GC). DG GCs translate diverse inputs into highly different specific codes, which underlies the so-called pattern separation that allows us to distinguish similar events, objects. We focus on the principles that govern how single GCs extract information from the activity of single upstream neurons from the four major input pathways using direct patch clamp recordings and voltage-sensitive dye/protein imaging of single small axon terminals together with anatomical and computational approaches. The two perforant paths (PPs) that originate from the medial and lateral entorhinal cortices convey spatial context (such as the famous grid cell activity) or specific information content (for example certain objects). Inputs from hilar mossy cells distinguishes subtle differences and inputs from the hypothalamic supramammillary nucleus synchronizing GC activities during attention.

SELECTED PUBLICATIONS

Oláh, V.J., Lukacsovich, D., Winterer, J., Arszovszki, A., Lőrincz, A., Nusser, Z., Földy, C., **Szabadics, J.** (2020) Functional specification of CCK+ interneurons by alternative isoforms of Kv4.3 auxiliary subunits. **eLife, 9:** e58515.

Neubrandt, M., Oláh, V.J., Brunner, J., Marosi, E., Soltesz, I., **Szabadics, J.** (2018) Single bursts of individual granule cells functionally rearrange feed-forward inhibition. **J. Neurosci. 38:** 1711-1724.

Neubrandt, M., Oláh, V.J., Brunner, J., **Szabadics, J.** (2017) Feedforward inhibition is randomly wired from individual granule cells onto CA3 pyramidal cells. **Hippocampus 27:** 1034-1039.

Brunner J, **Szabadics J** (2016) Analogue modulation of back-propagating action potentials enables dendritic hybrid signalling. **Nat Commun 7:** 13033.

Luo, W., Egger, M., Domonkos, A., Que, L., Lukacsovich, D., Cruz-Ochoa, N.A., Szőcs, S., Seng, C., Arszovszki, A., Sipos, E., Amrein, I., Winterer, J., Lukacsovich, T., **Szabadics, J.**, Wolfer, D.P., Varga, C., Földy, C. (2021) Recurrent rewiring of the adult hippocampal mossy fiber system by a single transcriptional regulator, Id2. **Proc Natl Acad Sci USA 118:** e2108239118.

NÁNDOR SZEGEDI

Semmelweis University
Faculty of Medicine
The Hearth and Vascular Centre

RESEARCH AREA

My main research area is cardiac electrophysiology, with a highlight on catheter ablation treatment of atrial fibrillation (AF). AF is the most common sustained rhythm disorder, the invasive therapy of which is much more effective than drug treatment, but its effectiveness falls short of that of other arrhythmias. Accordingly, further developments and the evaluation of new techniques' effectiveness and safety are essential. Currently, I am mainly interested in high-energy radiofrequency ablation and electroporation.

SELECTED PUBLICATIONS

Orbán G., Salló Z., Perge P., Ábrahám P., Piros K., Nagy KV., Osztheimer I., Merkely B., Gellér L., **Szegedi N.** (2022) Characteristics of Very High-Power, Short-Duration Radiofrequency Applications. **Front Cardiovasc Med 9:** 941434.

Szegedi N., Salló Z., Perge P., Piros K., Nagy VK., Osztheimer I., Merkely B., Gellér L. (2021) The role of local impedance drop in the acute lesion efficacy during pulmonary vein isolation performed with a new contact force sensing catheter-A pilot study. **PLoS One 16(9):** e0257050.

Szegedi N., Széplaki G., Herczeg S., Tahin T., Salló Z., Nagy VK., Osztheimer I., Özcan EE., Merkely B., Gellér L. (2019) Repeat procedure is a new independent predictor of complications of atrial fibrillation ablation. **Europace 21(5):** 732-737.

Szegedi N., Vecsey-Nagy M., Simon J., Szilveszter B., Herczeg S., Kolossváry M., Idelbi H., Osztheimer I., Klaudia Nagy V., Tahin T., Széplaki G., Delgado V., Bax JJ., Maurovich-Horvat P., Merkely B., Gellér L.. (2022) Orientation of the right superior pulmonary vein affects outcome after pulmonary vein isolation. **Eur Heart J Cardiovasc Imaging 23(4):** 515-523.

Szegedi N., Simon J., Szilveszter B., Salló Z., Herczeg S., Száraz L., Kolossváry M., Orbán G., Széplaki G., Nagy KV., Mahdiui ME., Smit JM., Delgado V., Bax JJ., Maurovich-Horvat P., Merkely B., Gellér L. (2022) Abutting Left Atrial Appendage and Left Superior Pulmonary Vein Predicts Recurrence of Atrial Fibrillation After Point-by-Point Pulmonary Vein Isolation. **Front Cardiovasc Med 9:** 708298.

Salló Z., Perge P., Balogi B., Orbán G., Piros K., Herczeg S., Nagy KV., Osztheimer I., Ábrahám P., Merkely B., Gellér L., **Szegedi N.** (2022) Impact of High-Power and Very High-Power Short-Duration Radiofrequency Ablation on Procedure Characteristics and First-Pass Isolation During Pulmonary Vein Isolation. **Front Cardiovasc Med 9:** 935705

KÁLMÁN TORY

Semmelweis University
Faculty of Medicine
1st Department of Paediatrics

RESEARCH AREA

The research group formerly identified the first variant with a trans-associated mutation-dependent pathogenicity in an autosomal recessive disorder (NPHS2 R229Q) [Tory et al, Nat Genet, 2014) and a novel gene of steroid-resistant nephrotic syndrome (DKC1). They demonstrated the role of rRNA-pseudouridylation in DKC1-associated nephrotic syndrome [Balogh et al, PNAS, 2020]. The group created a novel population-genetic algorithm to identify novel incompletely penetrant variants and interallelic interactions in autosomal recessive disorders [Mikó et al, Hum Mutat, 2021]. Function and interallelic interactions of the most frequently implicated protein in steroid-resistant nephrotic syndrome, podocin, as well as the function of novel genes are studied in cell culture experiments and on a Caenorhabditis elegans model.

SELECTED PUBLICATIONS

Mikó, Á., Kaposi, A., Schnabel, K., Seidl, D., **Tory, K**. (2021) Identification of incompletely penetrant variants and interallelic interactions in autosomal recessive disorders by a population-genetic approach. **Hum Mutat 42:** 1473-87.

Balogh, E., Chandler, J.C., Varga, M., Tahoun, M.K., Menyhárd, D., Schay, G., Goncalves, T., Hamar, R., Légrádi, R., Szekeres, Á., Gribouval, O., Kleta, R., Stanescu, H., Bockenhauer, D., Kerti, A., Williams, H., Kinsler, V., Di, W.L., Curtis, D., Kolatsi-Joannou, M., Hammid, H., Szőcs, A., Perczel, K., Maka, E., Toldi, G., Sava, F., Arrondel, C., Kardos, M., Fintha, A., Hossain, A., D'Arco, F., Kaliakatsos, M., Koeglmeier, J., Mifsud, W., Mooseja, M., Faro, A., Jávorszky, E., Rudas, G.H., Saied, M., Marzouk, S., Kelen, K., Götze, J., Reusz, G., Tulassay, T., Dragon, F., Mollet, G., Motameny, S., Thiele, H., Dorval, G., Nürnberg, P., Perczel, A., Szabó, A.J., Long, D.A., Tomita, K., Antignac, C., Waters, A.M., **Tory, K.** (2020) Pseudouridylation defect due to DKC1 and NOP10 mutations cause nephrotic syndrome with cataracts, hearing impairment and enterocolitis. **Proc Natl Acad Sci USA 117:** 15137-47.

Mikó, Á.K., Menyhárd, D., Kaposi, A., Antignac, C., T**ory, K.** (2018) The mutation-dependent pathogenicity of NPHS2 R229Q: a guide for clinical assessment. **Hum Mutat 39:** 1854-60.

Stráner, P., Balogh, E., Schay, G., Arrondel, C., Mikó, Á., L'Auné, G., Benmerah, A., Perczel, A.K., Menyhárd, D., Antignac, C., Mollet, G., **Tory, K.** (2018) C-terminal oligomerization of podocin mediates interallelic interactions. **Biochim Biophys Acta Mol Basis Dis. 1864:** 2448-2457.

Tory, K., Menyhard, D.K., Woerner, S., Nevo, F., Gribouval, O., Kerti, A., Straner, P., Arrondel, C., Cong, E.H., Tulassay, T., Mollet, G., Perczel, A., Antignac, C. (2014) Mutation-dependent recessive inheritance of NPHS2-associated steroid-resistant nephrotic syndrome. **Nat Genet 46:** 299-304.

MARIANNA TÖRÖK

Semmelweis University
Faculty of Medicine
Department of Obstetrics and Gynaecology

RESEARCH AREA

Sports adaptation of different types of blood vessels and their gender differences in an animal model. Investigation of the hemodynamic effects of vitamin D deficiency and supplementation on adaptation of different types of isolated blood vessels and network adaptation. Gender differences in adaptation to vitamin D deficiency. Vascular effects of testosterone deficiency and hypertension on adaptation of resistance coronary arterioles in animal model. Correlation between vitamin D status and Polycystic Ovary Syndrome. Effect of vitamin D deficiency and supplementation on reproductive functions.

SELECTED PUBLICATIONS

Dalloul, H., Hainzl, T., Monori-Kiss, A., Hadjadj, L., Nádasy, G.L., **Török, M.**, Várbíró, Sz. (2022) Vitamin D deficiency and supplementation altered the network of the coronary arteries in a rodent model – in situ video microscopic technique. **Nutrients 14:** 2041.

Várbíró, Sz., Takács, I., Tűű, L., Nas, K., Sziva, R.E., Hetthéssy, J.R., **Török, M.** (2022) Effects of Vitamin D on Fertility, Pregnancy and Polycystic Ovary Syndrome – A Review. **Nutrients 14:** 1649.

Vezér, M., Demeter, Á., Szekeres, M., Jósvai, A., Bányai, B., Oláh, A., Balogh, F., Horváth, E.M., Radovits, T., Merkely, B., Ács, N., Nádasy, G.L., **Török, M.**, Várbíró, Sz. (2022) Sex differences in rat renal arterial responses following exercise training. **American Journal of Physiology: Heart and Circulatory Physiology 322:** H310-H318.

Merkely, P., Bakos, M., Bányai, B., Monori-Kiss, A., Horváth, E.M., Bognár, J., Benkő, R., Oláh, A., Radovits, T., Merkely, B., Ács, N., Nádasy, G.L., **Török, M.**, Várbíró, Sz. (2021) Sex differences in exercise-training-related functional and morphological adaptation of rat gracilis muscle arterioles. **Frontiers in Physiology 12:** 685664.

Török, M., Merkely, P., Monori-Kiss, A., Horváth, E.M., Sziva, R.E., Péterffy B., Jósvai, A., Sayour, A.A., Oláh, A., Radovits, T., Merkely, B.. Nándor, Á., Nádasy, L.Gy., Várbíró, Sz. (2021) Network analysis of the left anterior descending coronary arteries in swim-trained rats by an in situ video-microscopic tehcnique. **Biology of Sex Differences 12:** 17.

Jósvai, A., **Török, M.**, Mátrai, M., Hetthéssy, J., Monori-Kiss, A., Makk, J., Székács, B., Nádasy, L.Gy., Várbíró, Sz. (2020) Effects of Testosterone Deficiency and Angiotensin II-Induced Hypertension on the Biomechanics of Intramural Coronary Arteries. **Journal of Sexual Medicine 17:** 2322-2330.

BALÁZS UJFALUSSY

HUN-REN Institute of Experimental Medicine
Biological Computation Research Group

RESEARCH AREA

We are using mathematical models and computational analysis to study the neuronal basis of memory and navigation. Our goal is to understand how basic biophysical mechanisms in a specific neuronal system (the hippocampus) give rise to higher order cognitive processes. What is the effect of nonlinear dendritic processing of inputs on the dynamics of the network and thus how they influence the learning and recall of memories and ultimately the behavior of the animal? We answer similar questions using computational models in close collaborate with experimental colleagues. During the research, models are also used in a different way: during learning the neuronal network of the brain develops a model of the environment that the animal can use to interpret the incoming sensory information or to predict possible future consequences of its actions. Describing or analysing both of these models requires computational tools. We are looking for students passionate for understanding the nervous system but also interested in mathematics and programming.

SELECTED PUBLICATIONS

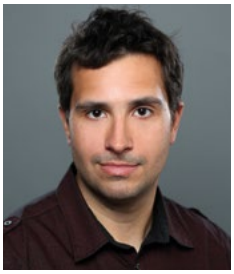
Ujfalussy, B.B., Orbán, G. (2021) Sampling motion trajectories during hippocampal theta sequences. **BioRxiv 2021.12.14.472575.**

Ujfalussy, B.B., Makara, J.K., (2020) Impact of functional synapse clusters on neuronal response selectivity. **Nature Comm 11:** 1-14.

Vágó, L., **Ujfalussy, B.B.** (2018) Robust and efficient coding with grid cells. **PLoS Computational Biology 14:** e1005922.

Ujfalussy, B.B., Makara, J.K., Lengyel, M., Branco, T. (2018) Global and multiplexed dendritic com- putations under in vivo-like conditions. **Neuron 100:** 579-592.

Ujfalussy, B.B., Branco, T., Makara J.K., Lengyel M. (2015) Dendritic nonlinearities are tuned for efficient spike-based computations in cortical circuits. **eLife 4:** e10056.



PETER UJMA

Semmelweis University
Institute of Behavioural Sciences

RESEARCH AREA

Electroencephalography, the study of sleep oscillations using scalp and invasive EEG recordings.
The differential psychology and physiology of sleep, the relationship between individual differences in sleep, anthropometric and psychological characteristics.
Intelligence research.

SELECTED PUBLICATIONS

Taji, W., Pierson, R., **Ujma, PP.** (2023). Protocol of the Budapest sleep, experiences, and traits study: An accessible resource for understanding associations between daily experiences, individual differences, and objectively measured sleep. **PLoS ONE 18(10)**: e0288909.

Ujma, P.P., Horváth, C.G., Bódizs, R. (2023). Daily rhythms, light exposure and social jetlag correlate with demographic characteristics and health in a nationally representative survey. **Sci Rep 13**, 12287.

Ujma, PP., Bódizs, R., Dresler, M., Simor, P., Purcell, S., Stone, KL., Yaffe, K., Redline, S. (2023). Multivariate prediction of cognitive performance from the sleep electroencephalogram. **Neuroimage 279,** 120319.

Ujma, PP., Szalárdy, O., Fabó, D., Erőss, L., Bódizs, R. (2021). Thalamic activity during scalp slow waves in humans.**Neuroimage 257**, 119325.

SZABOLCS VÁRBÍRÓ

Semmelweis University
Faculty of Medicine
Department of Obstetrics and Gynaecology

RESEARCH AREA

Our work group studied cardiovascular effects of female sexualsteroids in different animal models: its protective role in gender studies and in gender related cardiovascular sport adaptation studies. In pathophysiological models: cardiovascular adaptation in hypertension, menopause and polycystic ovary syndrome. In clinical studies we examine the connections of cardiovascular diseases with previous deliveries, spontaneous abortions - and its potential genetic and psychological background. During our experiments we use in vivo and in vitro observation methods: eg. treatment of vigil and anaesthetized animals - different surgical methods of experimental animals - isolation of vessels from different regions and vascular beds, the biomechanikcal and pharmacological reactivity of isolated vessels and also LAD network analysis with vascular phyciology methods and immunohystochemical analysis of hystological sections.

SELECTED PUBLICATIONS

Várbíró, S., Takács, I., Tűű, L., Nas, K., Sziva, R.E., Hetthéssy, J.R., Török, M. (2022) Effects of Vitamin D on Fertility, Pregnancy and Polycystic Ovary Syndrome-A Review. **Nutrients 14:** 1649.

Sipos, M., Gerszi, D., Dalloul, H., Bányai, B., Sziva, R.E., Kollarics, R., Magyar, P., Török, M., Ács, N., Szekeres, M., Nádasy, G.L., Hadjadj, L., Horváth, E.M., **Várbíró, S.** (2021) Vitamin D Deficiency and Gender Alter Vasoconstrictor and Vasodilator Reactivity in Rat Carotid Artery. **Int J Mol Sci 22:** 8029.

Merkely, P., Bakos, M., Bányai, B., Monori-Kiss, A., Horváth, E.M., Bognár, J., Benkő, R., Oláh, A., Radovits, T., Merkely, B., Ács, N., Nádasy, G.L., Török, M., **Várbíró, S.** (2021) Sex Differences in Exercise-Training-Related Functional and Morphological Adaptation of Rat Gracilis Muscle Arterioles. **Front Physiol 12:** 685664.

Török, M., Merkely, P., Monori-Kiss, A., Horváth, E.M., Sziva, R.E., Péterffy, B., Jósvai, A., Sayour, A.A., Oláh, A., Radovits, T., Merkely, B., Ács, N., Nádasy, G.L., **Várbíró, S.** (2021) Network analysis of the left anterior descending coronary arteries in swim-trained rats by an in situ video microscopic technique. **Biol Sex Differ 12:** 37.

Sziva, R.E., Fontányi, Z., Pál, É., Hadjadj, L., Monori-Kiss, A., Horváth, E.M., Benkő, R., Magyar, A., Heinzlmann, A., Benyó, Z., Nádasy, G.L., **Várbíró, S.** (2020) Vitamin D Deficiency Induces Elevated Oxidative and Biomechanical Damage in Coronary Arterioles in Male Rats. **Antioxidants (Basel) 9:** 997.

GÁBOR VARGA

Semmelweis University
Centre for Translational Medicine
and Faculty of Dentistry,
Department of Oral Biology

RESEARCH AREA

The main research area of Gábor Varga is to study the mechanisms that regulate the development and functioning of tissues of epithelial origin, primarily salivary glands, tooth enamel, and the pancreas at molecular level. Another direction of his research is the investigation of stem cells derived from human tooth tissue into odontogenic, osteogenic and neurogenic directions for tissue regeneration systems. In addition to his work as a theoretical researcher, he has participated in and also led numerous clinical research collaborations, including research aiming the application of saliva diagnostics for the identification of the COVID-19 disease. He actively participates in the work of the Translational Medicine Center of Semmelweis University, founded in 2021, as a vice director, and an active supervisor.

SELECTED PUBLICATIONS

Dudás C., Czumbel L.M., Kiss S., Gede N., Hegyi P., Mártha K., **Varga G**. (2023) Clinical bracket failure rates between different bonding techniques: a systematic review and meta-analysis. **Eur J Orthod 45(2):** 175-185.

Földes A., Sang-Ngoen T., Kádár K., Rácz R., Zsembery Á., DenBesten P., Steward MC., **Varga G.** (2021) Three-Dimensional Culture of Ameloblast-Originated HAT-7 Cells for Functional Modeling of Defective Tooth Enamel Formation. **Front Pharmacol 12:** 682654.

Földes A., Reider H., Varga A., Nagy KS., Perczel-Kovach K., Kis-Petik K., DenBesten P., Ballagi A., **Varga G.** (2021) Culturing and Scaling up Stem Cells of Dental Pulp Origin Using Microcarriers. **Polymers (Basel) 13(22):** 3951.

Czumbel LM., Kiss S., Farkas N., Mandel I., Hegyi A., Nagy Á., Lohinai Z., Szakács Z., Hegyi P., Steward MC., **Varga G.** (2020) Saliva as a Candidate for COVID-19 Diagnostic Testing: A Meta-Analysis. **Front Med (Lausanne) 7:** 465.

Farkasdi S., Pammer D., Rácz R., Hriczó-Koperdák G., Szabó BT., Dobó-Nagy C., Kerémi B., Blazsek J., Cuisinier F., Wu G., **Varga G.** (2019) Development of a quantitative preclinical screening model for implant osseointegration in rat tail vertebra. **Clin Oral Investig 23(7):** 2959-2973.

Bori E., Guo J., Rácz R., Burghardt B., Földes A., Kerémi B., Harada H., Steward MC., Den Besten P., Bronckers AL., **Varga G.** (2016) Evidence for Bicarbonate Secretion by Ameloblasts in a Novel Cellular Model. **J Dent Res 95(5):** 588-96.

VIKTOR VARGA

HUN-REN Institute of Experimental Medicine
Subcortical Modulation Research Group

RESEARCH AREA

We live in an ever-changing world. Our survival and well-being depend on how we can adapt to it by momentarily readjusting our actions. In order to do so, we have to filter out unimportant inputs and store only relevant information. Then, based on the combination of freshly acquired information and our memories, we select an action plan matching the actual situation. Subcortical modulation, by influencing all stages of cortical information processing, is indispensable for the selection, storage and recall of information and for carrying out the optimal action. Disruption of subcortical modulation leads to severe psychiatric illnesses. Our lab aims to unravel the operational principles of subcortical modulation. We aim to decipher the modulatory signal (or code) and how it influences information processing in target cortical circuits. We are also interested in the feedback from the cortex to subcortical regions whereby we would be able to uncover how cortical circuits control their modulation.

SELECTED PUBLICATIONS

Jelitai, M., Barth, A.M., Komlósi, F., Freund, T.F., **Varga, V.** (2021) Activity and coupling to hippocampal oscillations of median raphe GABAergic cells in awake mice. **Front Neural Circuits 15:** 784034.

Barth, A.M., Domonkos, A., Fernandez-Ruiz, A., Freund, T.F., **Varga, V.** (2018) Hippocampalnetwork dynamics during rearing episodes. **Cell Reports 23:** 1706-1715.

Domonkos, A., Ledri, L.N., Laszlovszky, T., Cserép, C., Borhegyi, Z., Papp, E., Nyiri, G., Freund, T.F., **Varga, V.** (2016) Divergent in vivo activity of serotonergic and non-serotonergic VGluT3-neurones in the median raphe region. **J Physiol (London) 594:** 3775-90.

Vandecasteele, M., **Varga, V.,** Berényi, A., Papp, E., Bartho, P., Venance, L., Freund, T.F., Buzsaki, G. (2014) Optogenetic activation of septal cholinergic neurons suppresses sharp wave ripples and enhances theta oscillations in the hippocampus. **Proc Natl Acad Sci USA 111:** 13535-13540.

Varga, V., Losonczy, A., Zemelman, B.V., Borhegyi, Z., Nyiri, G., Domonkos, A., Hangya, B.,Holderith, N., Magee, J.C., Freund, T.F. (2009) Fast synaptic subcortical control of hippocampalcircuits. **Science 326:** 449-453.

ZOLTÁN VARGA

Semmelweis University
Faculty of Medicine
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

We are aiming to explore key inflammatory mechanisms of cardiovascular (heart failure and myocardial infarction) and oncological diseases by using translational animal models, cell cultures, and human samples. We place special emphasis on studying the interection of cancer and cardiovascular comorbidities, and investigating the potential pharmacological treatment of these conditions.

SELECTED PUBLICATIONS

Onódi, Z., Visnovitz, T., Kiss, B., Hambalkó, S., Koncz, A., Ágg, B., Váradi, B., Tóth, V.É., Nagy, R.N., Gergely, T.G., Gergő, D., Makkos, A., Pelyhe, C., Varga, N., Reé, D., Apáti, Á., Leszek, P., Kovács, T., Nagy, N., Ferdinandy, P., Buzás, E.I., Görbe, A., Giricz, Z., **Varga, Z.V.** (2021) Systematic transcriptomic and phenotypic characterization ofhuman and murine cardiac myocyte cell lines and primary cardiomyocytes reveals seriouslimitations and low resemblances to adult cardiac phenotype. **J Mol Cell Cardiol 165:** 19-30.

Onódi, Z., Ruppert, M., Kucsera, D., Sayour, A.A., Tóth, V.E., Koncsos, G., Novák, J., Brenner, G.B., Makkos, A., Baranyai, T., Giricz, Z., Görbe, A., Leszek, P., Gyöngyösi, M., Horváth, I.G., Schulz, R., Merkely, B., Ferdinandy, P., Radovits, T., **Varga, Z.V.** (2021) AIM2-driven inflammasomeactivation in heartfailure. **Cardiovasc Res 117:** 2639-2651.

van Esbroeck, A.C.M., **Varga, Z.V.,** Di, X., van Rooden, E.J., Tóth, V.E., Onódi, Z., Kuśmierczyk, M., Leszek, P., Ferdinandy, P., Hankemeier, T., van der Stelt, M., Pacher, P. (2020) Activity-based protein profilingof the human failing ischemic heart revealsalterations in hydrolase activities involving theendocannabinoid system. **Pharmacol Res 151:** 104578.

Varga, Z.V., Erdelyi, K., Paloczi, J., Cinar, R., Zsengeller, Z.K., Jourdan, T., Matyas, C., Balazs, N.T., Guillot, A., Xiang, X., Mehal, A., Hasko, G., Stillman, I.E., Rosen, S., Gao, B., Kunos, G., Pacher, P. (2018) Disruption of renal arginine metabolismpromotes kidney injury in hepatorenal syndrome. **Hepatology 68:** 1519-1533.

Valenta, I., **Varga, Z.V.,** Valentine, H., Cinar, R., Horti, A., Mathews, W.B., Dannals, R.F., Steele, K., Kunos, G., Wahl R.L., Pomper, M.G., Wong, D.F., Pacher, P., Schindler, T.H. (2018) Feasibility Evaluation of MyocardialCannabinoid Type 1 Receptor Imaging inObesity: A Translational Approach. **JACC Cardiovasc Imaging 11:** 320-332.

ZOLTÁN WIENER

Semmelweis University
Department of Genetics, Cell- and Immunobiology

RESEARCH AREA

Colorectal cancer (CRC) is a leading cause of cancer-related death. Despite progress in the understanding of CRC, this disease remains a major health problem. The 5-year survival of patients with pancreatic ductal adenocarcinoma (PDAC) is extremely low, which has hardly improved in recent years. This can at least partially be attributed to the late diagnosis and the lack of early symptoms. Recent studies have shown that not only tumor cells, but also stromal cells (e.g. fibroblasts) significantly contribute to the progression of both CRC and PDAC and to bad patient survival. In the Molecular Oncobiology Research Group, we are focusing on the identification of new communication mechanisms between tumor cells and the stroma, which can form the basis of future therapeutic interventions for CRC and PDAC. One of our areas of interest is the function of extracellular vesicles (EV), representing a special form of membrane-bound cell-cell communication, and which can also be considered a molecular package. 3D organoids produced from patients play a central role in our studies. They are considered one of the most modern methods for modeling human tumors.

SELECTED PUBLICATIONS

Soós, AÁ., Kelemen, A., Orosz, A., Szvicsek, Z., Tölgyes, T., Dede, K., Bursics, A., **Wiener, Z.** (2023) High CD142 Level Marks Tumor-Promoting Fibroblasts with Targeting Potential in Colorectal Cancer. **Int J Mol Sci 24(14):** 11585.

Kelemen, A., Carmi, I., Oszvald, Á., Lőrincz, P., Petővári, G., Tölgyes, T., Dede, K., Bursics, A., Buzás, EI., **Wiener, Z.** (2021) IFITM1 expression determines extracellular vesicle uptake in colorectal cancer. **Cell Mol Life Sci 78(21-22):** 7009-7024.

Zeöld, A., Sándor, GO., Kiss, A., Soós, AÁ., Tölgyes, T., Bursics, A., Szűcs, Á., Harsányi, L., Kittel, Á., Gézsi, A., Buzás, EI., **Wiener, Z.** (2021) Shared extracellular vesicle miRNA profiles of matched ductal pancreatic adenocarcinoma organoids and blood plasma samples show the power of organoid technology. **Cell Mol Life Sci 78(6):** 3005-3020.

Oszvald, Á., Szvicsek, Z., Sándor, GO., Kelemen, A., Soós, AÁ., Pálóczi, K., Bursics, A., Dede, K., Tölgyes, T., Buzás, EI., Zeöld, A., **Wiener, Z.** (2020). Extracellular vesicles transmit epithelial growth factor activity in the intestinal stem cell niche. **Stem Cells.38(2):** 291-300.

Szvicsek, Z., Oszvald, Á., Szabó, L., Sándor, GO., Kelemen, A., Soós, AÁ., Pálóczi, K., Harsányi, L., Tölgyes, T., Dede, K., Bursics, A., Buzás, EI., Zeöld, A., **Wiener, Z.** (2019). Extracellular vesicle release from intestinal organoids is modulated by Apc mutation and other colorectal cancer progression factors. **Cell Mol Life Sci 76(12):** 2463-2476.

NIKOLETT WOHNER

Semmelweis University
Department of Biochemistry

RESEARCH AREA

Our research focuses on translational medicine in the field of thrombosis and hemostasis. Thrombi are complex structures that cannot be investigated in simplified systems, as red blood cells, leukocytes, platelets and molecules originating from these cells profoundly determine thrombus formation and thrombolysis. In our studies we use in vitro, ex vivo and in vivo methods combined with advanced microscopic technics to uncover the pathophysiology of hemostatic processes. We concentrate on the role of neutrophil extracellular traps (NETs) and their interactions with hemostatic components. Furthermore, we aim to shed light on the pathomechanism of bleeding or thrombotic complications in hematological diseases. Our results may thoroughly affect the development of new thrombolytic therapies and help to identify new thrombotic markers.

SELECTED PUBLICATIONS

Simon, B., Ceglédi, A., Dolgos, J., Farkas, P., Gaddh, M., Hankó, L., Horváth, R., Kaposi, A., Magyar, L., Masszi, T., Szederjesi, A., **Wohner, N.**, Bodó, I. (2022) Combined immunosuppression for acquired hemophilia A: CyDRi is a highly effective low-toxicity regimen. **Blood 140(18):** 1983-1992.

Wohner, N., Sebastian, S., Muczynski, V., Huskens, D., de Laat, B., de Groot, PG., Lenting, PJ. (2022) Osteoprotegerin modulates platelet adhesion to von Willebrand factor during release from endothelial cells. **J Thromb Haemost 20(3):** 755-766.

Lovas, S., Varga, G., Farkas, P., Masszi, T., **Wohner, N.**, Bereczki, Á., Adamkovich, N., Borbényi, Z., Szomor, Á., Alizadeh, H., Szaleczky, E., Wolf, K., Schneider, T., Plander, M., Szendrei, T., Csacsovszki, O., Csukly. Z., Rajnics, P., Egyed, M., Nagy, Z., Rejtő, L., Illés, Á., Mikala, G., Váróczy, L. (2019) Real-world data on the efficacy and safety of daratumumab treatment in Hungarian relapsed/refractory multiple myeloma patients. **Int J Hematol110(5):** 559-565.

Varga, G., Mikala, G., Gopcsa, L., Csukly, Z., Kollai, S., Balázs, G., Botond, T., **Wohner, N.**, Horváth, L., Szombath, G., Farkas, P., Masszi T. (2018) Multiple Myeloma of the Central Nervous System: 13 Cases and Review of the Literature. **J Oncol 2018:** 3970169.

Wohner, N., Muczynski, V., Mohamadi, A., Legendre, P., Proulle, V., Aymé, G., Christophe, OD., Lenting, PJ., Denis, CV., Casari, C. (2018) Macrophage scavenger receptor SR-AI contributes to the clearance of von Willebrand factor. **Haematologica 103(4):** 728-737.

ZOLTÁN ZÁDORI

Semmelweis University
Faculty of Medicine
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

The gastrointestinal (GI) mucosa is constantly exposed to a wide variety of luminal aggressors, including gastric acid, pepsin, bile acids and bacterial components. In order to withstand these damaging factors and maintain the integrity of mucosal barrier, several physical and chemical defense mechanisms interact in a complex manner. Numerous conditions can lead to GI ulcers by directly damaging the epithelial cells and/or by disrupting the delicate balance between aggressive and defensive factors. Our previous studies focused mainly on the pathogenesis of gastric ulcers, whereas our recent projects aim to characterize the pathogenesis of small intestinal injury (enteropathy) caused by nonsteroidal anti-inflammatory drugs (NSAIDs) or by ischemia/reperfusion. One of our main interests is to analyze the NSAID-induced changes in intestinal bacteria and bile acids, and to identify the factors contributing to alterations of the microbiota. We also aim to identify novel therapeutic options for the treatment of enteropathy.

SELECTED PUBLICATIONS

Hutka, B., Várallyay, A., László, S.B., Tóth, A.S., Scheich, B., Paku, S., Vörös, I., Pós, Z., Varga, Z.V., Norman, D.D., Balogh, A., Benyó, Z., Tigyi, G., Gyires, K., **Zádori, Z.S.** (2024) A dual role of lysophosphatidic acid type 2 receptor (LPAR2) in nonsteroidal anti-inflammatory drug-induced mouse enteropathy. **Acta Pharmacologica Sinica 45:** 339-353.

Zádori, Z.S., Király, K., Al-Khrasani, M., Gyires, K. (2023) Interactions between NSAIDs, opioids and the gut microbiota - Future perspectives in the management of inflammation and pain. **Pharmacology & Therapeutics 241:** 108327.

Hutka, B., Lázár, B., Tóth, A.S., Ágg, B., László, S.B., Makra, N., Ligeti, B., Scheich, B., Király, K., Al-Khrasani, M., Szabo, D., Ferdinandy, P., Gyires, K., **Zádori, Z.S.** (2021) The nonsteroidal anti-inflammatory drug ketorolac alters the small intestinal microbiota and bile acids without inducing intestinal damage or delaying peristalsis in the rat. **Frontiers In Pharmacology 12:** 664177.

Lázár, B., László, S.B., Hutka, B., Tóth, A.S., Mohammadzadeh, A., Berekméri, E., Ágg, B., Balogh, M., Sajtos, V., Király, K., Al-Khrasani, M., Földes, A., Varga, G., Makra, N., Ostorházi, E., Szabó, D., Ligeti, B., Kemény, Á., Helyes, Z., Ferdinandy, P., Gyires, K., **Zádori, Z.S.** (2021) A comprehensive time course and correlation analysis of indomethacin-induced inflammation, bile acid alterations and dysbiosis in the rat small intestine. **Biochemical Pharmacology 190:** 114590.

László, S.B, Lázár, B., Brenner, G.B., Makkos, A., Balogh, M., Al-Khrasani, M., Hutka, B., Mohammadzadeh, A., Kemény, Á., László, T., Scheich, B., Szabados, T., Kenyeres, É., Giricz, Z., Bencsik, P., Varga, Z.V., Novák, J., Helyes, Z., Ferdinandy, P., Gyires, K., **Zádori, Z.S.** (2020) Chronic treatment with rofecoxib but not ischemic preconditioning of the myocardium ameliorates early intestinal damage following cardiac ischemia/reperfusion injury in rats. **Biochemical Pharmacology 178:** 114099.

VIKTORIA ZSIROS

Semmelweis University
Faculty of Medicine
Department of Anatomy, Histology and Embryology

RESEARCH AREA

The role of epithelial-mesenchymal (EMT) and mesenchymal-epithelial transformation (MET) during embryogenesis, tumorigenesis and inflammation is essential. In our laboratory we proved that during Freund's adjuvant-induced inflammation rat mesenteric mesothelial cells undergo epithelial-mesenchymal transition type II (EMT). During this process the mesothelial cells produce pro-inflammatory cytokines (TGF-β, GM-CSF, TNFα, IL-6, etc.) and express their receptors. After the peak of inflammation, regeneration (MET) starts, which is mediated by intense autophagy and accompanied by non-canonical signaling pathways induced by various BMP factors.
Rapid diagnosis and early treatment of peritonitis remains a challenge in emergency medicine. Both primary and secondary peritonitis have a very high mortality rate. The main regulator of these inflammatory processes is the mesothelium, which is in the focus of our investigations. Therefore, clarifying the steps and molecular regulation of inflammation and regeneration in the mesothelial cells would facilitate the diagnosis of peritonitis, the choice of therapeutic methods, and possibly enable prevention.

SELECTED PUBLICATIONS

Zsiros, V., Katz, S., Dóczi, N., Kiss, AL. (2017) Autophagy is the key process in the re-establishment of the epitheloid phenotype during mesenchymal-epithelial transition (MET). **Exp Cell Res 352(2):** 382-392.

Katz, S., **Zsiros, V.**, Dóczi, N., Kiss, AL. (2018) Inflammation-Induced Epithelial-to-Mesenchymal Transition and GM-CSF Treatment Stimulate Mesenteric Mesothelial Cells to Transdifferentiate into Macrophages. **Inflammation 41(5):** 1825-1834.

Zsiros, V., Katz, S., Doczi, N., Kiss, AL. (2019) Endocytosis of GM-CSF receptor β is essential for signal transduction regulating mesothelial-macrophage transition. **Biochim Biophys Acta Mol Cell Res1866(9):** 1450-1462.

Katz, S., **Zsiros, V.**, Kiss, AL. (2019) Under inflammatory stimuli mesenteric mesothelial cells transdifferentiate into macrophages and produce pro-inflammatory cytokine IL-6. **Inflamm Res 68(7):** 525-528.

Zsiros, V., Kiss, AL. (2020) Cellular and molecular events of inflammation induced transdifferentiation (EMT) and regeneration (MET) in mesenteric mesothelial cells. **Inflamm Res 69(12):** 1173-1179.

Zsiros, V., Dóczi, N., Petővári, G., Pop, A., Erdei, Z., Sebestyén, AL., Kiss, A. (2023) BMP-induced non-canonical signaling is upregulated during autophagy-mediated regeneration in inflamed mesothelial cells. **Sci Rep 13(1):** 10426.

BUDAPEST
SZENT-GYÖRGYI JUNIOR MENTORS

DÓRA BALOGH

Semmelweis University
1st Department of Paediatrics

RESEARCH AREA

I am a postdoctoral fellow at the MTA-SE Lendület "Momentum" Diabetes Research Group, Semmelweis University, under the guidance of Prof. Andrea Fekete. My research interests focus on identifying novel therapeutic targets and investigating pathophysiological processes in developing chronic diabetic complications, specifically renal and cardiac fibrosis. Our research focuses on the Sigma-1 receptor and its signaling pathways. Alongside scientific tasks, I am gaining valuable insight into drug development and project management.
In addition, I recently joined the research group in the Horizon 2020 FEMaLe project, led by Dr. Attila Bokor, where we employ artificial intelligence and machine learning-based methods to reduce diagnostic delays in endometriosis.

SELECTED PUBLICATIONS

Balogh, DB., Molnar, A., Degi, A., Toth, A., Lenart, L., Saeed, A., Barczi, A., Szabo, AJ., Wagner, LJ., Reusz, G., Fekete. A. (2023) Cardioprotective and Antifibrotic Effects of Low-Dose Renin–Angiotensin–Aldosterone System Inhibitors in Type 1 Diabetic Rat Model. **Int J Mol Sci 24(23):** 17043.

Balogh, DB., Wagner, LJ., Fekete, A. (2023) An Overview of the Cardioprotective Effects of Novel Antidiabetic Classes: Focus on Inflammation, Oxidative Stress, and Fibrosis. **Int J Mol Sci 24(9):** 7789.

Hodrea, J., Saeed, A., Molnar, A., Fintha, A., Barczi, A., Wagner, LJ., Szabo, AJ., Fekete, A., **Balogh, DB.** (2022) SGLT2 inhibitor dapagliflozin prevents atherosclerotic and cardiac complications in experimental type 1 diabetes. **PLoS One 17(2):** e0263285.

Hodrea, J., *__Balogh, DB.__, Hosszu, A., Lenart, L., Besztercei, B., Koszegi, S., Sparding, N., Genovese, F., Wagner, LJ., Szabo, AJ., Fekete, A. (2020) Reduced O-GlcNAcylation and tubular hypoxia contribute to the antifibrotic effect of SGLT2 inhibitor dapagliflozin in the diabetic kidney. **Am J Physiol Renal Physiol 318(4):** F1017-F1029. J. Hodrea and D. B. Balogh contributed equally to this work.

Balogh, DB., Molnar, A., Hosszu, A., Hodrea, J., Szabo, AJ., Lenart, L., Fekete, A. (2020) Antidepressant effect in diabetes-associated depression: a novel potential of RAAS inhibition. **Psychoneuroendocrinology 118:** 104705.

LÁSZLÓ BIRÓ

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

Exposure to acute stress can lead to the emergence of behavioral disturbances that place a heavy burden on both the individual and society. Previous research indicated that the paraventricular thalamic nucleus (PVT) is a brain area that plays a key role in the modulation of fear, anxiety, and increased arousal. Calretinin-expressing neurons in the paraventricular thalamus (PVT/CR+) exhibit significant activation under acute stress. In addition, PVT/CR+ cells send selective innervation to key stress-sensitive brain regions in the forebrain, suggesting a large-scale influence on brain function and behavior. In our research, we study the neurochemical identity, topography and the functional contribution of the ascending subcortical projections targeting the PVT/CR+ neurons in stress-induced behavioral disturbances.

SELECTED PUBLICATIONS

Bruzsik, B., **Biro, L.**, Zelena, D., Sipos, E., Szebik, H., Sarosdi, K.R., Horvath, O., Farkas, I., Csillag, V., Finszter, C.K., Mikics, E., Toth, M. (2021) Somatostatin neurons of the bed nucleus of stria terminalis enhance associative fear memory consolidation in mice. **Journal of Neuroscience 41:** 1982-1995.

Biro, L., Sipos, E., Bruzsik, B., Farkas, I., Zelena, D., Balazsfi, D., Toth, M., Haller, J. (2018) Task division within the prefrontal cortex: distinct neuron populations selectively control different aspects of aggressive behavior via the hypothalamus. **Journal of Neuroscience 38:** 4065-4075.

Mikics, E., Guirado, R., Umemori, J., Toth, M., **Biro, L.**, Miskolczi, C., Balazsfi, D., Zelena, D., Castren, E., Haller, J., Karpova, NN. (2018) Social Learning Requires Plasticity Enhanced by Fluoxetine Through Prefrontal Bdnf- TrkB Signaling to Limit Aggression Induced by Post-Weaning Social Isolation. **Neuropsychopharmacology. 43:**235-245.

Biro, L., Toth, M., Sipos, E., Bruzsik, B., Tulogdi, A., Tulogdi, A., Bendahan, S., Sandi, C., Haller, J. (2017). Structural and functional alterations in the prefrontal cortex after post-weaning social isolation: relationship with species-typical and deviant aggression. **Brain structure and function 222:** 1861-1875.

ANIKÓ BOZSIK

Semmelweis University
National Institute of Oncology

RESEARCH AREA

In our department, we carry out genetic testing of germline predisposing genes for hereditary tumors. As part of routine diagnostics, we look for heritable mutations related to the clinical phenotype. We test the genetic background of cancer syndromes possessing a high degree of heredity: most often, we carry out tests in cases of familial breast and ovarian cancer, hereditary colon tumors or neuroendocrine tumor syndromes. In addition to routine diagnostics, our research activities include the functional testing of variants with unknown effects, primarily with cDNA-level tests. We also examine the correlations of known heredity with other genetic and non-genetic factors, including those affecting tumor formation, aggressiveness, and therapy response.

SELECTED PUBLICATIONS

Bozsik, A., Butz, H., Grolmusz, VK., Polgár, C., Patócs, A., Papp, J. (2023) Genome sequencing-based discovery of a novel deep intronic APC pathogenic variant causing exonization.**Eur J Hum Genet 31:** 7 pp. 841-845.

Butz, H., **Bozsik, A.**,* Grolmusz, V., Szőcs, E., Papp, J., Patócs, A. (2023) Challenging interpretation of germline TP53 variants based on the experience of a national comprehensive cancer centre. **Sci Rep 13:** 1 Paper: 14259.

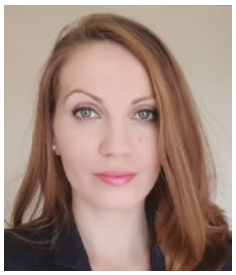
Butz, H., Nagy, P., Papp, J., **Bozsik, A.**, Grolmusz, VK., Pócza, T., Oláh, E., Patócs, A. (2023) PALB2 Variants Extend the Mutational Profile of Hungarian Patients with Breast and Ovarian Cancer. **Cancers 15:** 17 Paper: 4350.

Grolmusz, VK., Nagy, P., Likó, I., Butz, H., Pócza, T., **Bozsik, A.**, Papp, J., Oláh, E., Patócs, A. (2023) A common genetic variation in GZMB may associate with cancer risk in patients with Lynch syndrome. **Front Oncol 13** Paper: 1005066.

Pálla, S., Tőke, J.,* **Bozsik, A.**,* ; Butz, H., Papp, J., Likó, I., Kuroli, E., Bánvölgyi, A., Hamar, M., Bertherat, J. et al. (2023) Whole genome sequencing resolves 10 years diagnostic odyssey in familiar myxoma. **Sci Rep 13:** 1 Paper: 14658.

Bozsik, A., Papp, J., Grolmusz, VK., Patócs, A., Oláh, E., Butz, H. (2022) Reclassification of Five BRCA1/2 Variants with Unknown Significance Using Complex Functional Study. **Cancer Res Treat 54:** 4 pp. 970-984.

Butz, H., Lövey, J.,* Szentkereszty, M., **Bozsik, A.**, Tóth, E., Patócs, A. (2022) Case Report: A Novel Pathomechanism in PEComa by the Loss of Heterozygosity of TP53. **Front Oncol 12** Paper: 849004.



KRISZTINA ELLA

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The circadian time-keeping system enables the organism to anticipate the daily environmental changes and therefore is a crucial factor of adaptation. The endogenous rhythm is generated at the cellular level by a mechanism based on the action of interconnected transcription/translation feedback loops. The circadian system has a central pacemaker in the suprachiasmatic nucleus (SCN), which may coordinate and synchronize the peripheral oscillators present in other tissues through neuronal and humoral pathways. The main regulator of the SCN is light, but the peripheral clocks can also be modified by metabolic effects (e.g. food intake and its timing). Cellular clock function influences a wide range of physiological and pathological processes, e.g. both activity of the immune system and leukocyte migration have a characteristic circadian rhythm. Our investigations focus on the following questions: 1.) Which neural, humoral, hormonal and metabolic factors influence the circadian rhythm of immune functions? 2.) Which clock proteins control the effector functions of immune cells? 3.) What kind of individual differences can be detected in the clock function of the immune system? 4.) How does the circadian rhythm of the immune system change in different inflammatory and metabolic diseases and in sepsis? 5.) Is a cell's own molecular clock necessary for the control of rhythmic processes or is the operation of the central clock in the SCN sufficient? Understanding the regulation of the rhythmic immune system activity may help to identify therapeutic targets or design complementary therapeutic tools. For example, development of chronotherapeutic (time-dependent drug administration) strategies and design of individualised therapy for various inflammatory or other immune-related diseases could be possible.

SELECTED PUBLICATIONS

Sűdy, Á., **Ella, K.**, Bódizs, R., Káldi, K. (2019) Association of Social Jetlag With Sleep Quality and Autonomic Cardiac Control During Sleep in Young Healthy Men. **Front Neurosci 13:** 950.

Gyöngyösi, N., Szőke, A., **Ella, K.**, Káldi, K. (2017) The small G protein RAS2 is involved in the metabolic compensation of the circadian clock in the circadian model Neurospora crassa. **J Biol Chem 292:** 14929-14939.

Ella, K., Csépányi-Kömi, R., Káldi, K. (2016) Circadian regulation of human peripheral neutrophils. **Brain Behav Immun 57:** 209-221.

Haraszti, R., **Ella, K.**, Gyöngyösi, N., Roenneberg, T., Káldi, K. (2014) Social jetlag negatively correlates with academic performance in undergraduates. **Chronobiol Int 31:** 603-612.

Gyöngyösi, N., Nagy, D., Makara, K., **Ella, K.**, Káldi, K. (2013) Reactive oxygen species can modulate circadian phase and period in Neurospora crassa. **Free Radic Biol Med 58:** 134-143.

ANNA ZSUZSANNA FÖLDES

Semmelweis University
Faculty of Dentistry
Department of Oral Biology

RESEARCH AREA

Present research field: Characterisation of stem cells of dental origin, studies on tissue regeneration-, differentiation capacity and immunomodulatory effects in vitro; studies on the structural and functional differentiation of the salivary gland and its secretion and transport processes. Development of a 3D cellular model of the ameloblast, studies on its structural and functional differentiation, secretion and transport processes. Covid research. previous research field: Functional neuroanatomy of the neuroendocrine hypothalamus, mapping of stress-related CNS networks; neurobiological effects of drug withdrawal, role and effects of histamine in the regulation of feeding (nutrition).

SELECTED PUBLICATIONS

Földes, A., Reider, H., Varga, A., Nagy, K.S., Perczel-Kovach, K., Kis-Petik, K., DenBesten, P., Ballagi, A., Varga, G. (2021) Culturing and Scaling up Stem Cells of Dental Pulp Origin Using Microcarriers. **Polymers 13:** 3951.

Földes, A., Sang-Ngoen, T.*, Kádár, K., Rácz, R., Zsembery, Á., DenBesten, P., Steward, M.C., Varga, G. (2021) Three-Dimensional Culture of Ameloblast-Originated HAT-7 Cells for Functional Modeling of Defective Tooth Enamel Formation. **Front Phamracol 12:** 682654.

Földes, A., Kadar, K., Keremi, B., Zsembery, A., Gyires, K., Zádori, Z.S., Varga, G. (2016) Mesenchymal stem cells of dental origin - their potential for anti-inflammatory and regenerative actions in brain and gut damage. **Curr Neuropharmacol 14:** 914-934.

Fülöp, A.K., **Földes, A.*,** Buzás, E., Hegyi, K., Miklós, I.H., Romics, L., Kleiber, M., Nagy, A., Falus, A., Kovács, K.J. (2003) Hyperleptinemia, visceral adiposity, and decreased glucose tolerance in mice with a targeted disruption of the histidine decarboxylase gene. **Endocrinology 144:** 4306-4314.

Kovács, K.J., **Földes, A.,** Sawchenko, P.E. (2000) Glucocorticoid negative feedback selectively targets vasopressin transcription in parvocellular neurosecretory neurons. **J Neurosci 20:** 3843-3852.

KRISZTINA FUTOSI

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

Autoimmune and autoinflammatory diseases are characterized by the pathological overactivation of the immune system. In addition to acute flares, these inflammations in most cases show a chronic, progressive course and are associated with significant tissue damage, resulting in a significant deterioration in the quality of life of the affected patients. Our research group investigates the cellular and molecular mechanisms underlying the above inflammatory processes, which may contribute to a better understanding of the pathomechanism of these diseases and to identify new therapeutic targets. In our recent studies, we investigate the role of tyrosine kinase signaling pathways in the development of autoimmune arthritis, and in the urate crystal-mediated non-autoimmune gout by using genetic and pharmacological approaches. In recent years, we have identified a number of signaling molecules involved in the development of these inflammatory processes.

SELECTED PUBLICATIONS

Futosi, K., Kása, O., Szilveszter, K., Mócsai, A. (2021) Neutrophil phospholipase Cγ2 drives autoantibody-induced arthritis through the generation of the inflammatory microenvironment. **Arthritis & Rheumatology 73:** 1614-1625.

Németh, T., **Futosi, K.**, Szilveszter, K., Vilinovszki, O., Kiss-Pápai, L., Mócsai, A. (2018) Lineage-specific analysis of Syk function in autoantibody-induced arthritis. **Frontiers in Immunology 9:** 555.

Németh T., **Futosi, K.**, Sitaru, C., Ruland, J., Mócsai, A. (2016) Neutrophil-specific deletion of the CARD9 gene expression regulator suppresses autoantibody-induced inflammation in vivo. **Nature Communications 7:** 11004.

Futosi, K., Németh, T., Pick, R., Vántus, T., Walzog, B., Mócsai, A. (2012) Dasatinib inhibits pro-inflammatory functions of mature human neutrophils. **Blood 119:** 4981-4991.

MÁRTA JELITAI

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

Unraveling the fundamental operational principles of subcortical modulation.
In recent years, there has been significant progress in our understanding of brain function and the establishment of dynamically changing neuronal circuits, which form the basic elements of a 'thought'. However, still little is known about the mechanism of subcortical modulation, which are responsible for the formation of our emotions, and influence our cortical function and memory processes. We are particularly interested in the connection between the hippocampus and two of its main modulatory inputs: the medial septum (MS) and the median raphe (MR). The activity of the MR is strongly associated with the formation of negative emotions, while the MS is thought to play a pivotal role in orchestrating the activity of hippocampal coding neuronal assemblies. Given the hippocampus's crucial role in the memory formation, our project aims to investigate the effect of subcortical regulatory circuits (MS, MR) on hippocampal information processing at different contexts. We monitor neuronal activity using multichannel electrodes in awake, behaving mice and identify specific cells using optogenetic techniques.

SELECTED PUBLICATIONS

Barth M.A., **Jelitai M.***, Vasarhelyi-Nagy M.F., Varga V. (2023) Aversive stimulus-tuned responses in the CA1 of the dorsal hippocampus. **Nat Comm 14:** 1 Paper: 6841.
*: first co-author

Kiraly B., Domonkos A., **Jelitai M.**, Lopes-dos-Santos V., Martine-Bellver S., Kocsis B., Schlinloff D., Joshi A., Salib M., Fiath R., Bartho P., Ulbert I., Freund T.F., Viney T.J., Dupret D., Varga V., Hangya B. (2023) The medial septum controls hippocampal supra-theta oscillations. **Nat Comm 14:** 1 Paper: 6159.

Jelitai M., Barth M.A., Komlósi F., Freund T., Varga V.: (2021) Activity and Coupling to Hippocampal Oscillations of Median Raphe GABAergic Cells in Awake Mice. **Front Neural Circuits 15:** 17 Paper: 784034, 12 p.

Jelitai M, P. Puggioni, T. Ishikawa, A. Rinaldi, I. Duguid: (2016) Dendritic excitation-inhibition balance shapes cerebellar output during motor behavior. **Nat Commun. 7:** 13722.

Puggioni P., **Jelitai M.**, Duguid I., van Rossum MC. (2017) Extraction of synaptic input properties in vivo. **Neural Comput 29(7):** 1745-1768.

ORSOLYA LÁNG

Semmelweis University
Faculty of Medicine
Department of Genetics, Cell- and Immunobiology

RESEARCH AREA

Although many new therapeutic compounds are tested in clinical trials, the mortality rate for some tumors (e.g. pancreatic tumors, ductal adenocarcinoma) is still very high. Among the main reasons for the poor prognosis is the lack of a targeted chemotherapeutic agent and the rapid development of resistance during standard chemotherapy(gemcitabine), in which the cellular elements of the microenvironment play a critical role. The main aims of our research are (i) to identify new antitumor compounds (mainly small molecules) by impedimetric methods (ii) to identify intracellular targets of these new drug candidates; (iii) to elucidate the exact molecular mechanism of the antitumor effect on pancreatic cancer modell; (iv) to identify the molecular mechanisms of the antitumor effect on the tumor environment, e.g. immune cells and ECM composition, which may also influence both the possible development of resistance and the in vivo efficacy of the molecule.

SELECTED PUBLICATIONS

Kalabay, M., Szász, Z., **Láng, O.**, Lajkó, E., Pállinger, É., Duró, C., Jernei, T., Csámpai, A., Takács, A., Kőhidai, L. (2022) Investigation of the Antitumor Effects of Tamoxifen and Its Ferrocene-Linked Derivatives on Pancreatic and Breast Cancer Cell Lines. **Pharmaceuticals 15:** 314.

Kőhidai, Z., Takács, A., Lajkó, E., Géczi, Z., Pállinger, É., **Láng, O.**, Kőhidai, L. (2022) The effects of mouthwashes in human gingiva epithelial progenitor (HGEPp) cells. **Clin Oral Invest 26:** 4559-4574.

Takács, A., Szász, Z., Kalabay, M., Bárány, P., Csámpai, A., Hegyesi, H., **Láng, O.**, Lajkó, E., Kőhidai, L. (2021) The Synergistic Activity of Bortezomib and TIC10 against A2058 Melanoma Cells. **Pharmaceuticals 14:** 820.

Láng, O., Nagy, K.S., Láng, J., Perczel-Kovách, K., Herczegh, A., Lohinai, Z., Varga, G., Kőhidai, L. (2021) Comparative study of hyperpure chlorine dioxide with two other irrigants regarding the viability of periodontal ligament stem cells. **Clin Oral Invest 25:** 2981-2992.

Takács, A., Lajkó, E., **Láng, O.**, Istenes, I., Kőhidai, L. (2020) Alpha-lipoic acid alters the antitumor effect of bortezomib in melanoma cells in vitro. **Sci Rep 14287.**

BÁLINT NAGY

Semmelweis University
Faculty of Medicine
Department of Biochemistry

RESEARCH AREA

The mitochondrion is an organelle inside the cell that serves as a powerhouse. In case the mitochondrial energy-generating processes (delivered by specific enzymes) get compromised, due to e.g. a genetic mutation that affects a key enzyme, severe clinical symptoms may arise; the generally neurological, cardiological, and/or hepatological manifestations often lead to premature death. The group of enzymes that was selected for our investigations comprises the mitochondrial alpha-keto (or 2-oxo) acid dehydrogenase multienzyme complexes (OADHc), which serve multiple pivotal roles in the energy metabolism of the mitochondrion. In the future we wish to initiate the development of enzyme replacement strategies against
relevant OADHc deficiencies, where the healthy forms of the enzymes are delivered directly into the mitochondrion to replace the impaired enzymes. We also wish to design small molecule drug candidates in the near future to control the generation of harmful reactive radicals by OADHc and counteract the compromised enzymatic efficacy. Another proposed intervention approach is to reinforce by adaptor drug molecules the at times loosened obligate attachments among enzyme components in the greater enzyme complexes. For all of these approaches to be successful, first we need to investigate the relevant molecular pathomechanisms and related structures, which is part of our research program. Selected research results will potentially be also applicable in the supplemental treatments of other neuronal disorders.

SELECTED PUBLICATIONS

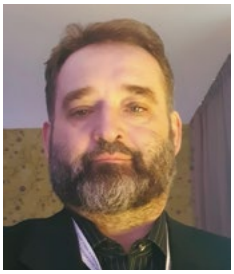
Szabo, E., Nemes-Nikodem, E., Vass, KR., Zambo, Z., Zrupko, E., Torocsik, B., Ozohanics, O., **Nagy, B.**, Ambrus, A. (2023) Structural and Biochemical Investigation of Selected Pathogenic Mutants of the Human Dihydrolipoamide Dehydrogenase. **Int J Mol Sci 24(13):** 10826.

Nemeria, NS., **Nagy, B.**, Sanchez, R., Zhang, X., Leandro, J., Ambrus, A., Houten, SM., Jordan, F. (2022) Functional Versatility of the Human 2-Oxoadipate Dehydrogenase in the L-Lysine Degradation Pathway toward Its Non-Cognate Substrate 2-Oxopimelic Acid. **Int J Mol Sci 23(15):** 8213.

Nagy, B., Polak, M., Ozohanics, O., Zambo, Z., Szabo, E., Hubert, A., Jordan, F., Novacek, J., Adam-Vizi, V., Ambrus, A. (2021) Structure of the dihydrolipoamide succinyltransferase (E2) component of the human alpha-ketoglutarate dehydrogenase complex (hKGDHc) revealed by cryo-EM and cross-linking mass spectrometry: Implications for the overall hKGDHc structure. **Biochim Biophys Acta Gen Subj 1865(6):** 129889.

Zhang, X., Nemeria, NS., Leandro, J., Houten, SM., Lazarus, MB., Gerfen, GJ., Ozohanics, O., Ambrus, A., **Nagy, B.**, Brukh, R., Jordan, F. (2020) Structure-function analyses of the G729R 2-oxoadipate dehydrogenase genetic variant associated with L-lysine metabolism disorder. **J Biol Chem 295(23):** 8078.

Szabo, E., Wilk, P., **Nagy, B.**, Zambo, Z., Bui, D., Weichsel, A., Arjunan, P., Torocsik, B., Hubert, A., Furey, W., Monfort, WR; Jordan, F., Weiss, MS., Adam-Vizi, V., Ambrus, A. (2019)Underlying molecular alterations in human dihydrolipoamide dehydrogenase deficiency revealed by structural analyses of disease-causing enzyme variants. **Hum Mol Genet 28(20):** 3339.



GÁBOR NYIRŐ

Semmelweis University
Faculty of Medicine
Department of Laboratory Medicine
Department of Internal Medicine and Oncology

RESEARCH AREA

Tumors originating from the human adrenal cortex can be divided in two groups, adrenocortical adenomas (ACA) wich are more frequent but benign and adrenocortical carcinomas (ACC) with bad prognosis but luckily also less frequent. Differenciating these two tumor types is difficult even for an experienced pathologist from postoperative tissue samples. Our research group is looking for specific molecular markers, so called microRNAs, that could help in these differentiations. The expression of microRNAs is tissue specific (thus tumor specific). They also have a role in the regulation of gene expression so their role can be regarded either tumor driver or tumor supressor. MicroRNAs are stable, they are present in (tumor)tissues, in the blood, and in other body fluids. This gives us a possibility to exploit them as minimal invasive biomarkers in diagnostics. MicroRNAs are present in neuroendocrine tumors of the gastrointestinal tract. We plan to investigate the diagnostic possibilities of microRNA expression in pancreas neuroendocrine tumors (pNET) in this project.

SELECTED PUBLICATIONS

Turai P.I., Herold, Z., **Nyirő, G.**, Borka, K., Micsik, T., Tőke, J., Szücs, N., Tóth, M., Patócs, A., Igaz, P. (2022) Tissue miRNA Combinations for the Differential Diagnosis of Adrenocortical Carcinoma and Adenoma Established by Artificial Intelligence. **Cancers Basel 11; 14:** 895.

Olah, C., Hahnen, C., Nagy, N., Musial, J., Varadi, M., **Nyiro, G.**, Gyorffy, B., Hadaschik, B., Rawitzer, J., Ting, S., Sjödahl, G., Hoffmann, M.J., Reis, H., Szarvas, T. (2021) A quantitative polymerase chain reaction based method for molecular subtype classification of urinary bladder cancer-Stromal gene expressions show higher prognostic values than intrinsic tumor genes. **Int J Cancer 1;150:** 856-867.

Turai, P.I., **Nyírő, G.**, Butz, H., Patócs, A., Igaz, P. (2021) MicroRNAs, Long Non-Coding RNAs, and Circular RNAs: Potential Biomarkers and Therapeutic Targets in Pheochromocytoma/Paraganglioma. **Cancers Basel 26;13:** 1522.

Saskői, É., Hujber, Z., **Nyírő, G.**, Likó, I., Mátyási, B., Petővári, G., Mészáros, K., Kovács, A.L., Patthy, L., Supekar, S., Fan, H., Sváb, G., Tretter, L., Sarkar, A., Nazir, A., Sebestyén, A., Patócs, A., Mehta, A., Takács-Vellai, K. (2020) The SDHB Arg230His mutation causing familial paraganglioma alters glycolysis in a new Caenorhabditis elegans model. **Dis Model Mech. 15;13:** dmm044925.

Szalay, B., Tátrai, E., **Nyírő, G.**, Vezér, T., Dura, G. (2012) Potential toxic effects of iron oxide nanoparticles in in vivo and in vitro experiments. **J Appl Toxicol 32:** 446-53.

BALÁZS PÓSFAI

Insitute of Experimental Medicine
Laboratory of Neuroimmunology

RESEARCH AREA

Microglia are the main immune-competent cells of the brain that form transient contacts with other cellular elements of the central nervous system using their evermoving processes. We set out to examine the role of microglia in basic physiological and pathological processes of the nervous system. We combine cutting-edge anatomical techniques with in vivo, ex vivo and in vitro approaches to investigate microglial contactomics, especially somatic junctions established with the cell bodies of neurons and contacts with elements of the neurovascular unit. Our experiments provide opportunity for observations ranging from population level to the subcellular, nanoscale level.

SELECTED PUBLICATIONS

Cserép, C., Schwarcz, AD., **Pósfai, B.**, László, ZI., Kellermayer, A., Környei, Z., Kisfali, M., Nyerges, M., Lele, Z., Katona, I., Dénes, Á. (2022) Microglial control of neuronal development via somatic purinergic junctions. **Cell Rep 40(12):** 111369.

Császár, E., Lénárt, N., Cserép, C., Környei, Z., Fekete, R., **Pósfai, B.**, Balázsfi, D., Hangya, B., Schwarcz, AD., Szabadits, E., Szöllősi, D., Szigeti, K., Máthé, D., West, BL., Sviatkó, K., Brás, AR., Mariani, JC., Kliewer, A., Lenkei, Z., Hricisák, L., Benyó, Z., Baranyi, M., Sperlágh, B., Menyhárt, Á., Farkas, E., Dénes, Á. (2022) Microglia modulate blood flow, neurovascular coupling, and hypoperfusion via purinergic actions. **J Exp Med 219(3):** e20211071.

Tóth, K., Lénárt, N., Berki, P., Fekete, R., Szabadits, E., **Pósfai, B.**, Cserép, C., Alatshan, A., Benkő, S., Kiss, D., Hübner, CA., Gulyás, AI., Kaila, K., Környei, Z., Dénes, Á. (2022) The NKCC1 ion transporter modulates microglial phenotype and inflammatory response to brain injury in a cell-autonomous manner. **PLoS Biology 20(1):** e3001526.

Cserép, C., **Pósfai, B.**, Dénes, Á. (2021) Shaping Neuronal Fate: Functional Heterogeneity of Direct Microglia-Neuron Interactions. **Neuron 109(2):** 222–240.

Cserép, C.[#], **Pósfai, B.**[#], Lénárt, N., Fekete, R., László, Z. I., Lele, Z., Orsolits, B., Molnár, G., Heindl, S., Schwarcz, A. D., Ujvári, K., Környei, Z., Tóth, K., Szabadits, E., Sperlágh, B., Baranyi, M., Csiba, L., Hortobágyi, T., Maglóczky, Z., Martinecz, B., Szabó, G., Erdélyi, F., Szipőcs, R., Tamkun, MM., Gesierich, B., Duering, M., Katona, I., Liesz, A., Tamás, G., Dénes, Á. (2020). Microglia monitor and protect neuronal function through specialized somatic purinergic junctions. **Science 367(6477):** 528–537.
[#] shared co-first authors

ÍRISZ SZABÓ

HUN-REN Institute of Experimental Medicine

RESEARCH AREA

Our aim is the better understanding of cognitive processes such as learning, attention and the formation of memory. The many neurons in our brain can interact with each other and thus communicate with each other with various so-called neuromodulators. The mediated information is essential for the healthy course of cognitive processes. Such important neuromodulatory systems are the dopaminergic system, the cholinergic system, the noradrenergic system and the serotonergic system. These neuromodulatory systems are implicated in almost all dementia-related or mental illnesses. In our experiments, we investigate the role of these neuromodulatory systems in the course of learning in healthy and diseased brain.

SELECTED PUBLICATIONS

Szabó Í, Varga VÉ, Dvorácskó S, Farkas AE, Körmöczi T, Berkecz R, Kecskés S, Menyhárt Á, Frank R, Hantosi D, Cozzi NV, Frecska E, Tömböly C, Krizbai IA, Bari F, Farkas E. (2021) N,N-Dimethyltryptamine attenuates spreading depolarization and restrains neurodegeneration by sigma-1 receptor activation in the ischemic rat brain. **Neuropharmacology 192:** 108612.

Körmöczi T, **Szabó Í**, Farkas E, Penke B, Janáky T, Ilisz I, Berkecz R. (2020) Heart-cutting two-dimensional liquid chromatography coupled to quadrupole-orbitrap high resolution mass spectrometry for determination of N,N-dimethyltryptamine in rat plasma and brain; Method development and application. **J Pharm Biomed Anal 191:** 113615.

Varga DP*, **Szabó Í***, Varga VÉ, Menhyárt Á, M Tóth O, Kozma M, Bálint AR, Krizbai IA, Bari F, Farkas E. (2020) The antagonism of prostaglandin FP receptors inhibits the evolution of spreading depolarization in an experimental model of global forebrain ischemia. **Neurobiol Dis 137:** 104780.

Tóth OM, Menyhárt Á, Varga VÉ, Hantosi D, Iványkovits-Kiss O, Varga DP, **Szabó Í,** Janovák L, Dékány I, Farkas E, Bari F. (2020) Chitosan nanoparticles release nimodipine in response to tissue acidosis to attenuate spreading depolarization evoked during forebrain ischemia. **Neuropharmacology 162:** 107850.

Szabó Í, M Tóth O, Török Z, Varga DP, Menyhárt Á, Frank R, Hantosi D, Hunya Á, Bari F, Horváth I, Vigh L, Farkas E. (2019) The impact of dihydropyridine derivatives on the cerebral blood flow response to somatosensory stimulation and spreading depolarization. **Br J Pharmacol 176(9):** 1222-1234.

ANDREA SZABÓ-VERECZKEI

Semmelweis University
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The main topic of my research interest is the genetic analysis of various psychiatric diseases and their possible predisposing genetic factors. My research career began with the investigation of genetic risk factors for heroin addiction at the Institute of Medical Chemistry, Molecular Biology and Pathobiochemistry at Semmelweis University (currently Department of Molecular Biology). During my work, I mainly investigated the genetic risk factors of the dopaminergic and serotonergic systems in the background of the development of heroin addiction and the success of replacement therapies. Over the years, I have participated in the genetic research of depression, obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD) and Tourette's syndrome as part of collaborations. In recent years, I have primarily been involved in examining the genetic risk factors of potentially addictive substances (alcohol, tobacco, cannabis and other drugs) and behaviors (internet use, online gaming, social media use, gambling, exercise, hair pulling, eating).

SELECTED PUBLICATIONS

Garbett, K. A., **Vereczkei, A.**, Kalman, S., Brown, J. A., Taylor, W. D., Faludi, G., et al. (2015). Coordinated Messenger RNA/MicroRNA Changes in Fibroblasts of Patients with Major Depression. **Biol Psychiatry 77(3):** 256-265.

Garbett, K. A., **Vereczkei, A.**, Kaman, S., Wang, L., Korade, Z., Shelton, R. C., et al. (2015). Fibroblasts from patients with major depressive disorder show distinct transcriptional response to metabolic stressors. **Transl Psychiatry, 5(3):** e523.

Vereczkei, A., Abdul-Rahman, O., Halmai, Z., Nagy, G., Szekely, A., Somogyi, A., et al. (2019). Association of purinergic receptor P2RX7 gene polymorphisms with depression symptoms. **Prog Neuropsychopharmacol Biol Psychiatry 92:** 207-216.

Kotyuk, E., Magi, A., Eisinger, A., Kiraly, O., **Vereczkei, A.**, Barta, C., et al. (2020). Co-occurrences of substance use and other potentially addictive behaviors: Epidemiological results from the Psychological and Genetic Factors of the Addictive Behaviors (PGA) Study. **J Behav Addic 9(2):** 272-288.

Vereczkei, A., Barta, C., Magi, A., Farkas, J., Eisinger, A., Kiraly, O., et al. (2022). FOXN3 and GDNF Polymorphisms as Common Genetic Factors of Substance Use and Addictive Behaviors. **J Pers Med 12(5):** 690.

MÁTÉ TÓTH

HUN-REN Institute of Experimental Medicine
Laboratory of Translation Behavioural Neuroscience

RESEARCH AREA

Our behavioral neuroscience research focuses on translational research questions, i.e. to explore the neurobiological mechanisms of mental disorders (mainly anxiety-affective and posttraumatic stress disorders). We use and develop clinically valid animal models of these disorders in order to explore the etiological background on multiple levels: what molecular and neural network alterations mediate pathological changes and vulnerabilities for these conditions. We apply mostly 'top-down' approach by using relevant behavioral paradigms to catch an important aspect of the disorder (e.g. fear generalization or passive coping) and then we investigate the underlying molecular and network characteristics/mechanisms by means of qPCR, immunohistochemistry, and microscopic techniques. Subsequently, we test the casual importance of these mechanisms (e.g. by chemogenetics).

SELECTED PUBLICATIONS

Bruzsik, B., Biro L., Zelena, D., Sipos, E., Szebik, H., Sárosdi, K.R., Horváth, O., Farkas, I., Csillag, V., Finszter, C.K., Mikics, E., **Tóth, M.** (2021) Somatostatin Neurons of the Bed Nucleus of Stria Terminalis Enhance Associative Fear Memory Consolidation in Mice. **J Neurosci 41(9):** 1982-1995.

Biro, L., Sipos, E., Bruzsik, B., Farkas, I., Zelena, D., Balázsfi. D.,* **Tóth, M.,** *Haller, J. (2018) Task Division within the Prefrontal Cortex: Distinct Neuron Populations Selectively Control Different Aspects of Aggressive Behavior via the Hypothalamus. **J Neurosci 38(17):** 4065-4075.

Tóth, M., Flandreau, EI., Deslauriers, J., Geyer, MA., Mansuy, IM., Merlo Pich, E., Risbrough, VB. (2016) Overexpression of Forebrain CRH During Early Life Increases Trauma Susceptibility in Adulthood. **Neuropsychopharmacology 41(6):** 1681-90.

Tóth, M., Gresack, JE., Bangasser, DA., Plona, Z., Valentino, RJ., Flandreau, EI., Mansuy, I., Merlo-Pich, E., Geyer, MA., Risbrough, V. (2014) Forebrain-Specific CRF Over-Production During Development is Sufficient to Induce Enduring Anxiety and Startle Abnormalities in Adult Mice. **Neuropsychopharmacology 39(6):** 1409-19.

Halász, J., **Tóth, M.,** Mikics, E., Hrabovszky, E., Barsy, B., Barsvári, B., Haller, J. (2007) The effect of neurokinin1 receptor blockade on territorial aggression and in a model of violent aggression. **Biol Psychiatry 63(3):** 271-8.

BUDAPEST
SZENT-GYÖRGYI STUDENTS

1ST YEAR STUDENTS

PÉTER BERKI

National Academy of Scientist Education, 1st year
Semmelweis University
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Andrea Fekete
Junior mentor: Dóra Balogh
Theme of research: Transcranial Magnetic Stimulation (TMS) in psychiatric disorders
Language: English/B2, German/C1

ÁRPÁD FÁBIÁN-KOVÁCS

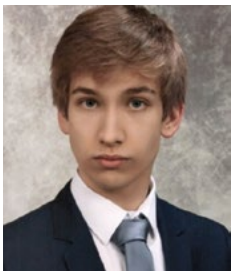
National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Gábor Csukly
Theme of research: Transcranial Magnetic Stimulation (TMS) in psychiatric disorders
Language: English/native

ÁDÁM FALUVÉGI

National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 2nd year

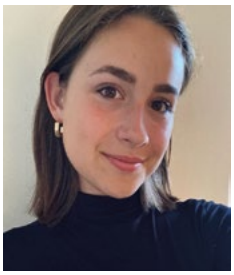
Szent-Györgyi Mentor: Judit Makara
Theme of research: Role of active dendrites in neuronal information processing
Language: English/B2-C1



SOMA FUISZ

National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Lajos Kemény
Theme of research: Investigation of mechanisms responsible for resistance against immune-based therapies in melanoma
Language: English/B2



EMMA HARSÁNYI

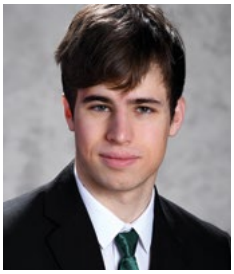
National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Judit Makara
Theme of research: Cellular mechanisms of spatial navigaton and memory in the hippocampus
Language: German/C1, English/B2

BOTOND KERTÉSZ

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

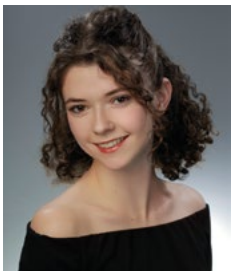
Szent-Györgyi Mentor: Attila Ambrus
Junior mentor: Bálint Nagy
Theme of research: Structure-function analysis of mitochondrial alpha-keto acid dehydrogenase complex mutations causing nervous system impairment
Language: English/B2



BENCE KORMOS

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

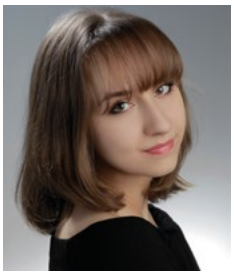
Szent-Györgyi Mentor: Zoltán Jakus
Theme of research: Characterization of the organ-specific functions of lymphatics
Language: English/B2



VIKTÓRIA KOVÁCS

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

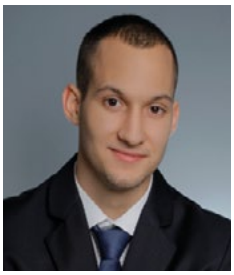
Szent-Györgyi Mentor: Attila Patócs
Junior mentor: Anikó Bozsik
Theme of research: Insilico and functional classification of genetic variants in hereditary cancer syndromes. Algorithms in variant classification od tumor suppressor genes and their application in classification. RNA based methods and their use in variant classification.
Language: English/C1, German/B2



LILI LENGYEL

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Zoltán Zádori
Theme of research: Seeking new options for the treatment of NSAID enteropathy
Language: English/C1



MARCELL MATÚZ

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Csaba Bödör
Theme of research: Genomic profiling and monitoring of B-cell lymphomas
Language: English/B2, German/B2

KOLOS NÉMETH

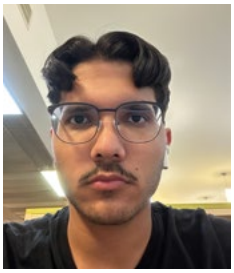
National Academy of Scientist Education, 1st year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Viktor Varga
Junior mentor: Márta Jelitai
Theme of research: Analysis of medialis septum - cortex dialogue
Language: English/C1, German/C1

BARNABÁS PAULOVITS

National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Balázs Enyedi
Theme of research: Investigating chemoattractant secretion and tissue distribution with novel biosensors
Language: English/intermediate



YAHYA SULOK

National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Balázs Hangya
Junior mentor: Írisz Szabó
Theme of research: Investigating the neural mechanisms of implicit learning
Language: English/B2, German/B2

TAMÁS SOMA SZALAY

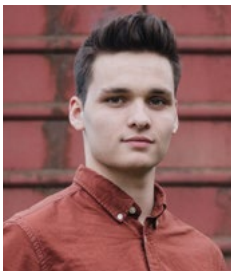
National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Attila Mócsai
Theme of research: Molecular analysis of the role of innate immunity in inflammatory disease models
Language: English/C1

ANITA VARGA

National Academy of Scientist Education, 1st year
Semmelweis University,
Faculty of Medicine, 2nd year

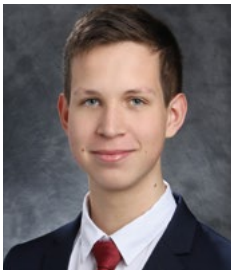
Szent-Györgyi Mentor: László Csanády
Theme of research: Molecular characterization of cystic fibrosis associated CFTR mutations
Language: English/B2, German/B2



ANDOR VIZI

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Balázs Hangya
Theme of research: The role of lateral septum in controling cognitive functions
Language: English/C1, Romanian/B2



TAMÁS ZSOLDOS

National Academy of Scientist Education, 1st year
Semmelweis University, Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Gábor Nyiri
Theme of research: Brainstem regulation of memory
Language: English/C1, German/C1

2ND YEAR STUDENTS

BÁLINT ANTAL

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Attila Patócs
Junior mentor: Henriett Butz
Specialization: molecular genetics, clinical genetics, oncogenetics
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Endocrine tumours have the highest hereditary genetic determinants. Therefore, germline genetic testing in such patients is crucial. The setting and validation of diagnostic tests is a fundamental quality assurance issue, as hereditary genetic variations do not change during the lifetime and determine the development of the disease. A reliable result improves the expected outcome of the disease by determining the risk of gene-related cancers, patients can be included in screening tests, and in some cases preventive intervention or targeted treatment is possible. It also allows screening of relatives and family planning. My research aims to apply and validate diagnostic genetic tests and their use in clinical genetic care. The results of the tests will be presented at national and international conferences and a publication is currently in progress.

AMBITIONS AND CAREER GOALS

As a curious person, I've always been interested in how the world works, which led me to want to work as a researcher in the future. I am most interested in genetics because I believe it is the blueprint of living organisms, the key to understanding life and heredity. My goal is to gain a deeper understanding of the world of genetics and to contribute to the advancement of human knowledge in this field. My long-term plans are to continue genetic research and to participate in projects that contribute to solving many health problems.

ANDRÁS BUZÁS-KAIZLER

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Éva Mikics
Junior mentor: Máté Tóth
Specialization: behavioural neurobiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Perinatal asphyxia (PA) is one of the most significant early-life insults and is responsible for the death of approximately 1 million neonates each year. Besides its role in neonatal mortality, mild-moderate PA also contributes to various neurodevelopmental disorders leading to neuropsychiatric diseases such as ADHD, autism spectrum disorder, epilepsy, and schizophrenia. Neuroinflammation plays an important role in the pathomechanism of PA, which is considered crucial for the development of long-term disorders. We aim to reveal the connection between inflammation and the emergence of neuropsychiatric diseases. For our investigation, we use rat and mouse models of asphyxia developed by our group. These models do not involve surgical interventions and do not cause focal lesions, thus providing an authentic model for examining the pathomechanisms of PA. Our findings confirmed the reliability of the rodent models and highlighted the importance of neuroinflammation. Our research may contribute to a better understanding of neuropsychiatric disorders and provide clinically relevant information regarding the treatment of PA and the prevention of its long-term effects.

AMBITIONS AND CAREER GOALS

Since my childhood, I have always wanted to know everything. Secrets are something I cannot tolerate, even if they are kept by the human body or the universe. This aspiration for understanding and knowing drives me during my studies and research. My goal is to obtain solid and comprehensive knowledge within the field of Biomedical Science so that later I can use this knowledge to help people and contribute to the development of science. I believe that there is no such thing as useless knowledge, and everything contributes to our insight. Therefore, I aim to interiorize not just the Medical Science but also every intellectual pursuit.

MÁTÉ CSEPI

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 3rd year

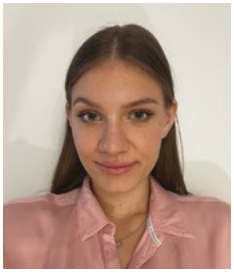
Szent-Györgyi Mentor: Tamás Hegedűs
Specialization: biophysics and bioinformatics of transmembrane proteins
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

With the development of experimental techniques, new protein sequences become available. However, the methods for determining the three-dimensional structure and the function of proteins could not keep up with this rapid development. Using prediction methods, it is possible to assign functions to the accumulating sequences. Primarily, we employ protein language models. They enable to transform amino acid sequences into vectorial representations which encode structural and functional properties of proteins, like hydrophobicity, participation in transmembrane regions, or membrane-binding abilities. Up to this point, we have worked with a specific group of membrane-binding regions named MemMoRFs (Membrane-binding Molecular Recognition Features), which are intrinsically disordered, lacking a well-defined secondary structure and gain stable secondary structural elements upon association with lipids. These proteins and regions play essential roles in numerous biological processes, including cell cycle regulation, cell signaling, and apoptosis. Our goal is to identify MemMoRFs with high confidence that will aid in enhancing our understanding of their roles in the cell or the body.

AMBITIONS AND CAREER GOALS

I am heading towards medical research and scientific discovery, guided by the Szent-Györgyi Program and my medical university studies. These two important components complement each other organically and provide an opportunity for me to delve deeper and contribute to the advancement of medical biology. By participating in TDK conferences, I aim to enhance my presentation skills. The program offers me a chance to collaborate closely with other researchers and experts. My goal is to take part in uncovering and applying the latest scientific findings in the field of healthcare.



ZSANNA GECSE

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Nándor Nagy
Specialization: stem cells, embryology, histology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The main goal of my research is the characterization of neural stem cells originated from the enteric nervous system, and a detailed understanding of their development and functioning. The enteric nervous system is responsible for the proper motility of the intestine, maintaining immune functions, and the normal rate of absorption and secretion as well. A deep knowledge of the operation of the enteric nervous system is therefore essential for a better understanding of congenital disorders such as Hirschsprung disease, in which part of the nervous elements are missing. My aim is to explore the possible stem cell therapy treatment of the disease to replace the current surgical removal of the uncolonized colon.

AMBITIONS AND CAREER GOALS

Throughout my career, I always want to focus on making people's lives better, whether it's research or clinical work. My goal is to be able to provide help for those in need with high-quality medical knowledge behind my back. During my career, I want to always stay motivated and curious about new technologies and discoveries, so that I can become better and better in the field where I will eventually deepen my knowledge.

REBEKA GELENCSÉR

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Anna Sebestyén
Specialization: experimental medical research, pathology, oncology, tumour biology
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

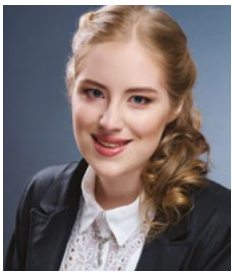
The metabolic heterogeneity of tumor tissue, the organization of the most diverse metabolic pathways and signaling pathways have long been a serious challenge in tumor therapy. Current traditional two-dimensional cell cultures do not fully enable the modeling of these complex processes, since the tumor tissue itself is a heterogeneous three-dimensional structure capable of adaptation. Based on more and more research, we can conclude that three-dimensional bioprinting can be a solution to this problem. In our research, our goals include the development of three-dimensional bioprinted tumor models, and then we can investigate the effect of several metabolic inhibitors in them, potentially finding new active pharmaceutical ingredients in order to develop more effective tumor therapy methods.

AMBITIONS AND CAREER GOALS

In addition to the desire to heal, the desire for a deeper understanding of nature led me to medicine. The research gives me the opportunity not only to develop my way of thinking, but I am confident that I can contribute to the work of my research group in order to advance biomedical research and develop new therapeutic methods by developing new model systems. The program provides me with an excellent framework for this, as they help me with scientific research work that goes beyond the academic framework already during the theoretical years of the training.

PUBLICATIONS

Moldvai, D.,[1] Sztankovics, D.,[1] Dankó, T.,[1] Szalai, F.,[1] Miyaura, R.,[1] Petővári, G.,[1] Krencz, I.,[1] **Gelencsér, R.,**[1] Sebestyén, A.,[1] (2024) Effects of 3D tissue structure on drug sensitivity - 3D bioprinted tissue mimetic structures in cancer research. **Magy Onkol.** 37768119.
Sztankovics, D.,[1] Moldvai, D.,[1] Petővári, G.,[1] **Gelencsér, R.**,[1] Krencz, I.,[1] Raffay, R.,[1] Dankó, T.,[1] Sebestyén, A.[1] (2023) 3D bioprinting and the revolution in experimental cancer model systems-A review of developing new models and experiences with in vitro 3D bioprinted breast cancer tissue-mimetic structures. **Pathol Oncol Res** 36843955.



LILLA HORVÁTH

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Henriette Farkas
Specialization: allergy and clinical immunology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Clinical characteristics of hereditary angioedema – long term study

VIOLA NAGY

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Csaba Barta
Junior mentor: Andrea Szabó-Vereczkei
Specialization: psychogenetics
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Addiction, in neurobiological terms, is a chronic disease of the brain's reward, motivation and memory centres and their interconnecting neural circuits. It is now well established that the risk of developing various substance and behavioural addictions, in addition to the undeniably significant environmental influences, can depend up to 50% on the genetic background of the individual. Identifying and studying the genes involved in this could be a key to improving the treatment and prevention of addictions, either by facilitating progress towards personalised medicine or at the level of identifying appropriate drug targets for medical treatment. Our research group is working on the genotyping of such known addiction-related genes, collected by the Genetic Addiction Risk Score (GARS), in the context of a population genetics study.

AMBITIONS AND CAREER GOALS

Since childhood, I have been fascinated by the history of medicine; the tangible results of progress that have provided precise yet simple solutions to the problems of the past. I see facilitating this kind of progress as the essential goal of biomedical research. I also wanted to be a part of this process; I wanted to do research since the beginning of my medical studies. The Szent-Györgyi programme provided the perfect background for this goal. In addition to learning practical methods, the programme helped me deepen my theoretical knowledge and has given me insight into the working conditions of researchers. All of this has only strengthened my commitment to this career path. Although I have not yet decided whether I want to work exclusively as a researcher or as a clinician as well, I know for sure that I want to continue to be actively involved in science.

ÁGNES PAKUTS

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 3rd year

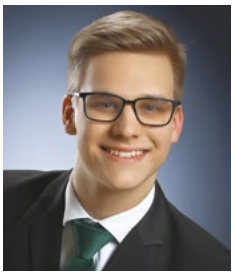
Szent-Györgyi Mentor: Eszter Horváth
Specialization: theoretical and translational medicine
Language: English/advanced, German/advanced, Italian/ intermediate, Spanish/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Polycystic ovary syndrome is amongst the most common endocrine disorders that can effect women and often cause infertility, anovulation, and polycystic ovaries. Research conducted in recent years allows us to conclude that there may be a bidirectional relationship between polycystic ovary syndrome and the development of oral and periodontal diseases. We want to examine the connection between these diseases and look for suitable therapeutic methods and tools.

AMBITIONS AND CAREER GOALS

In addition to my dental studies, I believed it to be very important to participate in research related to my future profession. I would like to gain as much knowledge and experience as possible, preferably before obtaining my medical degree. The Szent-Györgyi program is an excellent opportunity for me to be able to do meaningful work in fine educational and research institutions in addition to my academic studies.



TAMÁS SZABÓ

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Kálmán Tory
Specialization: pediatrics, genetics, nephrology, molecular biology
Language: English/advaned

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Alport syndrome is a genetic disorder which is caused by a variant occuring in the genes of type IV collagen (***COL4A3, COL4A4, COL4A5***). The inheritance of the disorder is really complex. COL4A3 and COL4A4 is located on chromosome 2 while COL4A5 is located on chromosome X. There is also a chance of dominant inheritance in the case of autosomal chromosomes. The laboratory previously published an algorithm (Mikó et al, Hum Mutat, 2021), which we use for the observation of the disorder. We would like to identify variants with incomplete penetrance. If there are such variants we would like to search interallelic interactions. Among the heterozygote variants we would like to search signs of dominant negative effect.

AMBITIONS AND CAREER GOALS

During the university I would like to get as much knowledge as I can which I think will be useful in my future career. The fact that I joined to a research group is helping me in this goal. I suppose that I gain way of thinking here which can help me solve various kinds of problems in my future.

CSONGOR GYÖRGY SZÁNTÓ

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

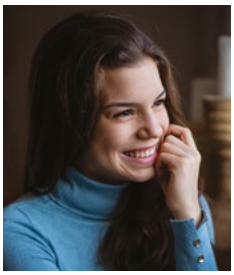
Szent-Györgyi Mentor: Krisztina Káldi
Junior mentor: Krisztina Ella
Specialization: physiology, chronobiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The circadian clock is the internal time-measuring mechanism of the organisms, which adjusts their physiological processes to the daily changes of the environment. These endogenous clocks control the metabolism and the immune system, hence their function shows daily rhythm. Our research group's main goal is to investigate the effects of TRE (Time-Restricted Eating) on the metabolism and the immune system's efficiency. The TRE, which is the restriction of food intake in the active phase of the day, has proven to be an effective method for treating and preventing diseases such as obesity or type 2 diabetes. However, we do not know much about this beneficial effect's mechanism, and about the factors that determine the most effective, personalized application of the method. Primarily we are trying to answer these questions on animal models.

AMBITIONS AND CAREER GOALS

Ever since I was a fifth grader, my goal was to become a medical doctor. I like helping others and the health of the people around me is very important to me. I have always been amazed by the workings of living systems and the study of nature. I couldn't mention any other profession that matches my personality and main interests more than this. After getting my medical degree I want to get a PhD, to have detailed knowledge on a field which I can use next to the hospital beds.



SÁRA VIDA

National Academy of Scientist Education, 2nd year
Semmelweis University
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Ádám Dénes
Junior mentor: Balázs Pósfai
Specialization: neuroimmunology
Language: English/advanced, French/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Neurological diseases are a huge burden on society. Unfortunately, current attempts at the treatment of such diseases or even at the halting of neurodegeneration are extremely expensive, and almost all fail at the clinical stage. The vast majority of such pursuits are targeted at neurons. Our lab aims to put the emphasis on the brain's resident immune cell, microglia, and understand the complexity of the human brain and the aforementioned diseases through the study of microglia cells and microglial interactions under anatomical and different pathological conditions. We assume that the study of the functioning of microglia in a neuropathological context can contribute to a better understanding of diseases and the discovery of possible therapeutic targets.

AMBITIONS AND CAREER GOALS

In the forthcoming years, I would like to successfully complete my degree in General Medicine at Semmelweis University while continuing my current research at the HUN-REN Institute of Experimental Medicine in the Neuroimmunology Research Group with the support of the National Academy of Sciences, and contribute to the advancement of our scientific knowledge. My long-term goal is to become a successful researcher. I also aim to obtain a PhD and postdoctoral degree. The knowledge one can obtain through the programme, as well as the publications and chances to participate in conferences, provide an excellent opportunity to achieve these goals.

BENCE CZUMBEL

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

3RD YEAR STUDENTS

Szent-Györgyi Mentor: Christos Chinopoulos
Junior mentor: Dóra Ravasz
Specialization: oncometabolism, mitochondriology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Hydrogen sulfide (H2S) was once considered to have only toxic properties, until it was discovered to be an endogenous signaling molecule. Mitochondria play an important role in its catabolism, in the reaction catalysed by sulfide-quinon-oxidoreductase, H2S is oxidized, coenzyme Q is reduced, thus it has a metabolic connection to the respiratory chain. Our research focuses on the effect of H2S on oxidative phosphorylation, especially if the respiratory chain works dysfunctionally (which we model by blocking different complexes of the respiratory chain and/or creating anoxic conditions).

AMBITIONS AND CAREER GOALS

My goal is to be a useful member of my research group and to gain scientific experince. As a second year medical student I have not made any definite plans regarding my future, I can see myself both as a researcher and a practicing physician, therefore, the most appealing option for me would be if my future work could somehow combine these two activities.

DORINA DEBRECZENI

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Gábor Czirják
Specialization: molecular biology and electrophysiology
Language: English/advanced, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

In my research, I investigate human TMEM175 lysosomal and TRESK two-pore potassium channels and their various mutations for their electrophysiological properties and regulatory mechanisms. The TMEM175 potassium channel plays an important role in regulating the K+ permeability of the lysosomal and endosomal membranes. This transmembrane protein has a special structure: it does not contain the P domain, which is the selectivity filter in all other known potassium channels. It is therefore questionable what is the reason for the high selectivity of TMEM175 for K+ over Na+. We also investigate the regulation of PKB, ion selectivity, and the effect of additional inhibitors (e.g., 4-aminopyridine) on TMEM175. One variant of TMEM175 (M393T) may be associated with an early onset of a neurodegenerative disease, Parkinson's disease, according to recent research. To understand this mechanism, it is particularly important to investigate the properties of the TMEM175 channel, as it may later be the target of drug treatments. K2P channels are common determinants of the regulated K + conductance of the plasma membrane, found in most animal and plant species, but are extremely structurally and functionally diverse. The TRESK K2P channel I examined is found in significant amounts in the sensory neuron subpopulations responsible for pain perception, affecting their excitability and the intensity of the response to painful stimuli. Some mutations in TRESK cause a rare form of hereditary migraine headache. In our research, we study general and direct regulatory mechanisms of the TRESK channel in heterologous systems that are likely to be independent of the cell-expressing cell type. Thus, a significant part of the mechanisms we describe provide a good basis for further studies to elucidate the role of the TRESK channel in pain perception.

AMBITIONS AND CAREER GOALS

I have been very curious and busy getting to know the complex living systems, the microscopic material world around us, and I can create something scientifically lasting. I believe that research provides an opportunity to develop a new way of thinking in addition to the material knowledge that can be acquired. One of my goals is to do research in addition to my medical work after completing my studies, as this way I may help more.

PUBLICATIONS

Debreczeni, D.,[1] Baukál, D.,[1] Pergel E.,[1] Veres, I.,[1] Czirják, G.[2] (2023) Critical contribution of the intracellular C-terminal region to TRESK channel activity is revealed by the epithelial Na+ current ratio method. **J Biol Chem**

REBEKA ÉRSEK

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: László Kőhidai
Junior mentor: Orsolya Láng
Specialization: cell physiology, drug-targeting
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Antitumor effects of novel aminophosphonate derivatives on pancreatic tumor cells.

CSENGE LILI JURENKA

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Nándor Nagy
Specialization: theoretical and translational medicine
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Hirschsprung disease is a congenital gastrointestinal disorder, that leads to problems in intestinal motility due to the partial absence of the enteric nervous system. The disorder affects 1 in 5000 newborns, and today the only therapy available is surgical removal of the affected area.
The enteric nervous system consists of neurons and glia cells derived from neural crest cells that migrate from the dorsal part of the neural tube to the intestinal wall in an early embryonic stage. The goal of my project is to block this migration in chicken embryos in vivo and create a avian organism modeling the disease. Such model could provide an opportunity to test stem cell transplantation.

AMBITIONS AND CAREER GOALS

According to my current idea of my career, my aim is to engage in both clinical and research work.

KATA KÓTA

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

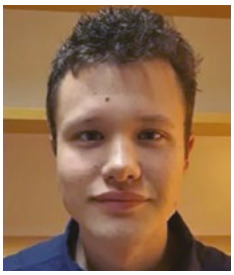
Szent-Györgyi Mentor: László Acsády
Junior mentor: László Biró
Specialization: thalamic research
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The thalamus is an especially important area in the brain, as it is the major source of inputs of the cerebral cortex, which is the top level information processor. Without the thalamus, the cortex has very little access to information from other areas of the brain. The cortex and the thalamus form a functional unit, and the disfunction of this thalamocortical system plays role in numerous neurological and psychiatric diseases. In spite of this, until recently thalamic research has been focused on a very narrow area, the relay of sensory inputs to the cortex, however all cortical areas are in connection with thalamic nuclei. Because of the lack of research, very little is known about the exact function of many thalamic nuclei so far. Our group aims to understand better this complex thalamocortical system.
A part of the group focuses on the inputs of one of the thalamic nuclei, the paraventricular nucleus (PVT). Via injecting viruses into definite areas of the brain of transgenic mice, we can visualize the axons ending in the PVT using a fluorescent or confocal microscope. This helps us determine the source of PVT inputs. Besides, we are also interested in exactly which areas of the PVT the axons from different souces end, and whether they are segregated or not. Based on this information, we can reveal the degree of integration of inputs from differnt sources in the PVT, which could help in understanding its exact function.

AMBITIONS AND CAREER GOALS

During my university years, I would like to aquire both theoretical and practical knowledge in order to become a good physician. It is equally important for me to join a scientific research group to learn about research work because and scietific techniques, because, I am convinced, this experience will be valuable later during my work.



BENDEGÚZ GÁBOR SRAMKÓ

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Karolina Pircs
Junior mentor: Anna Zsuzsanna Földes
Specialization: neurobiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

His research will focus on the isolation and reprogramming of dental pulp stem cells (DPSCs). These neural crest derived mesenchymal stem cells shows an excellent potential for neuronal fate determintation. Therefore they may provide a new source of functionally active, direct reprogrammed neurons in vitro. Bendegúz will collaborate with the Semmelweis University Department of Oral Biology in order of the isolation and charachterisation of DPSCs.

AMBITIONS AND CAREER GOALS

II think I have a subjective relationship whit biology. To observe and describe a part of life makes me a special joy, a type of enthusiasm. To deal with biology means for me to deal with living systems, which are well describable, and between them, the scientist can observe a logical system, which is the evolution. Most of these proceedings, which are making organisms be able to change their morphological structure and therefore be able to adapt to the varying environment, are manifested firstly in the level of the genes of cells. That's why my interest takes a special look at cells, they are dynamic systems, which can change their metabolism in the order of adaptation. If they aren't able to do that, their function will change inadequately for their physiological job and it can lead to diseases. I think these reasons are enough for a following medical doctor to want to know the world of cells always better and better. The human species interested me always better than everything else in biology, but maybe it is not my only one reason to study medicine. I can't imagine more beautiful cognitive behaviour, than medicine, because it is not just a type of science, it is an altruist behaviour, that helps me to be a useful member of society. I want to be an experienced doctor in science and in humane.

PUBLICATIONS

Sramkó, B.,[1,2] Földes, A.,[3] Kádár, K.,[3] Varga, G., [3] Zsembery, Á.,[3] Pircs, K. [1,2,4] (2023) The Wisdom in Teeth: Neuronal Differentiation of Dental Pulp Cells. **Cell Reprogram 25**(1): 32–44. PMID 36719998.

MÁTÉ MÁRK SZEKÉR

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Krisztina Káldi
Junior mentor: Krisztina Ella
Specialization: circadian rythm and metabolism
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The circadian rythm is a biologycal regulatory mechanism, that helps our body adapt to the changing environmental conditions throughout the day. The creation of this rythm requires a working endogenous clock, the so-called circadian clock. One of the more important regulators of the clock is the timing of food intake. Observation of epidemiologic, as well as animal experiments showed, that limiting food intake to a short time period of the day (time-restricted eating, TRE) has beneficial effects on the rythm of metabolic activities, and it can be an effective tool in preventing and treating obesity and type II diabetes. Our research group has found that in animal models TRE has a fundamental effect in the responsive capabilities of our immune system, and, overall has an anti-inflammatory effect. Our current experiments are aimed at finding out what is the connection between TRE, leukocyte function, which is determinded by bone marrow activity, and the rythm of adipose tissue function, which represents metabolic activity.

AMBITIONS AND CAREER GOALS

During my time in university, I would like to continue my scientific research within the NTA program, and I would also like to present said work in TDK conferences. While scientific work is important, I don't want to neglect my actual studies. When I'll be working as a doctor, i would still want to take part in scientific research, if I choose to not make research the main focus of my career.

BÁLINT KENDE SZEREDÁS

National Academy of Scientist Education, 3rd year
Semmelweis University
Faculty of Medicine, 3rd year

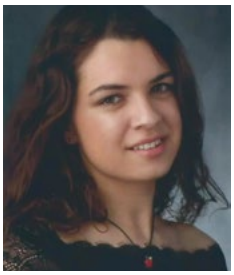
Szent-Györgyi Mentor: Péter Igaz
Junior mentor: Gábor Nyirő
Specialization: (pancreatic) neuroendocrine tumors
Language: English/advanced, Italian/intermediate, German/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

A) 2 micro-RNA. We select two of the micro-RNAs used in the literature (hsa-mir-130b-3p and hsa-mir-96-5p), which have been shown to be differentially expressed in different stages of PAN-NETs. The expression of these two miRNAs is rising in a trend between the stages and they show significant expression change. The expression of the hsa-mir-96-5p is rising according to grade, while its target, the FoxO1 shows decreasing staining in the tumors. Expected scientific results: We can validate that the expression of these two miRNAs follows well the development of the tumor, and their expression is clearly equivalent to the grade rank. And does it have diagnostic value? B) We have the opportunity to examine and probably narrow (by type and grade) a panel of 8 miRNAs, which express in every GEP-NET grade based on previous studies. This has diagnostic value. We could examine the FoxO1 expression with qRT-PCR to confirm the microscopic image. Also, we could confirm the connection of miRNA-mRNA with a functional luciferase assay.

AMBITIONS AND CAREER GOALS

Ever since I was committed to biology and medicine, research has always seemed interesting to me. I loved to find out things and understand the background of processes. However, medicine has another part, which is at least as important, where we heal people. I would like to find a combination of these, where I can do both fairly and usefully. This program gives me the opportunity to get a taste of the world of research, even this early in my studies at the university. Due to this, til my graduation I will know, which area I would like to research, and I will have a knowledge base for my PhD work. In addition, probably I will see what proportion should I share my energy and time between medical practice and research.



PETRA METTA CSIKÓS

4TH YEAR STUDENT

National Academy of Scientist Education, 4th year
Semmelweis University
Faculty of Medicine, 4th year

Szent-Györgyi Mentor: Nikolett Wohner
Specialization: biochemistry
Language: English/C1, German/B2

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Our research group is investigating the effect of tranexamic acid on thrombus formation. Tranexamic acid is a widely used antifibrinolytic agent, employed daily in various medical specialties, such as gynecology, orthopedics, and hematology. A common characteristic of antifibrinolytic agents is their potential to increase the risk of thrombosis. Surprisingly, based on our animal experimental results, tranexamic acid does not increase the risk of thrombosis and has even been reported to have a beneficial effect in acute myocardial infarction. Our research group aims to explore the molecular background of this phenomenon. Our research findings may open the door for the use of this drug in individuals with an increased risk of thromboembolism.

AMBITIONS AND CAREER GOALS

My goal is to fully immerse myself in research and extensively expand my knowledge. With this objective in view, I am enthusiastic about starting my MD-PhD studies during my fifth year as an undergraduate student. I believe that research has nurtured in me an inquisitive and analytical mindset, qualities that are paramount for both a physician and a researcher. Furthermore, I am determined to continue my engagement in research activities as a medical practitioner following the completion of my education.

5TH YEAR STUDENTS

DOROTTYA DELI

National Academy of Scientist Education, 5th year
Budapest University of Technology and Economics,Master of Science - Biomedical Engineering, 2nd year

Szent-Györgyi Mentor: Attila Mócsai
Junior mentor: Krisztina Futosi
Specialization: tyrosine-kinase signaling pathways
Language: English/B2

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Tyrosine kinases are crucial signaling components in nearly all biological processes including various aspects of signal transduction, and are major therapeutic targets in immune-mediated disorders. To facilitate the development of novel tyrosine kinase inhibitors acting on leukocytes, we have developed a rapid in vivo assay for the quantitative analysis of the effect of oral tyrosine kinase inhibitors on basal tyrosine phosphorylation in circulating mouse leukocytes. Our assay allows highly efficient analysis of the in vivo effect of orally administered tyrosine kinase inhibitors acting on leukocytes, and may be used as a suitable approach for the in vivo analysis of tyrosine kinase drug candidates.

AMBITIONS AND CAREER GOALS

We have previously shown that tyrosine kinase signaling in neutrophils play a major role in various inflammatory disease models. To facilitate the development of novel tyrosine kinase inhibitors acting on leukocytes, monocytes, eosinophils and basophil cells, we want to develope a rapid in vivo assay for the quantitative analysis of the effect of oral tyrosine kinase inhibitors on basal tyrosine phosphorylation in circulating mouse neutrophils.

PUBLICATIONS

Futosi, K., Bajza, B., **Deli, D.**, Erdélyi, A., Tusnády, S., Mócsai, A. (2023) Analysis of intracellular tyrosine phosphorylation in circulating neutrophils as a rapid assay for the in vivo effect of oral tyrosine kinase inhibitors. **Front Pharmacol 14:** 1056154.

KORNÉL MOLNÁR

National Academy of Scientist Education, 5th year
Semmelweis University
Faculty of Medicine, 5th year

Szent-Györgyi Mentor: Jakus Zoltán Péter
Specialization: vascular biology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Vaccines using messenger RNA (mRNA-LNP) technology packaged in lipid nanoparticles have recently attracted considerable scientific interest, as two vaccines against SARS-CoV-2 approved for emergency use are also based on this technology. However, processes in the immune response elicited by mRNA-LNP-based vaccines are still not fully understood. The aim of our research was to investigate the role of immune cells involved in the immune response induced by mRNA-LNP-based vaccines as well as the role of the lymphatic system in transgenic mouse models. To facilitate the success of our studies, a more detailed understanding of the processes elicited by mRNA-LNP-based vaccines may be offered in the future to increase the efficacy of these vaccines and to alleviate possible side effects.

AMBITIONS AND CAREER GOALS

My goal is to help people at the best of my ability during my future medical and research careers. To do this, it is essential to be up to date with the latest research findings in my field. The National Academy of Scienctist Education Training program is a great opportunity for me to start developing both my theoretical and practical knowledge to the highest possible level during my university years.

PUBLICATIONS

Aradi, P.,[1] Kovács, G.,[1] Kemecsei, É.,[1] **Molnár, K.**,[1] Sági, SM.,[1] Horváth, Z.,[1] Mehrara, BJ.,[2] Kataru, RP.,[2] Jakus, Z.[1] Lymphatics-dependent modulation of the sensitization and elicitation phases of contact hypersensitivity. **Journal of Investigative Dermatology**
[1]Department of Physiology, Semmelweis University School of Medicine, Budapest, Hungary
[2]Department of Surgery, Division of Plastic and Reconstructive Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
Accepted for publication

ROBERT BARTEL PIERSON

National Academy of Scientist Education, 5th year
Semmelweis University
Faculty of Medicine, 5th year

Szent-Györgyi Mentor: Péter Ujma
Specialization: sleep research, differential psychology
Language: English/native, German/B2 complex

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The study aims to define, supported by a larger number of cases and EEG measurements compared to previous publications, how personality relates to self-reported and objectively measurable chronotype and trait-level characteristics like diet, physical activity, and emotional effects. Our expected results hold scientific and clinical significance. Most importantly, our investigation would enable a finer analysis of daily events' impact on sleep. This could contribute to formulating specific recommendations for promoting better sleep, from which even a general medical practice could benefit. This is particularly relevant in a 21st-century society where sleep issues and the prevalence of insomnia reach up to 30%. These factors reduce mental and physical performance and increase the risk of mortality.

AMBITIONS AND CAREER GOALS

I aim to pivot my career towards a deeper understanding of the relationship between mental and physical health. My pathway involves pursuing a PhD, followed by a specialization in psychiatry. Subsequently, I plan to broaden my horizons by acquiring continuous academic and clinical experience, and exploring additional training opportunities to enhance the multidisciplinary approach I envision.

PUBLICATIONS

Taji, W., **Pierson, R.**, Ujma, PP. (2023) Protocol of the Budapest sleep, experiences, and traits study: An accessible resource for understanding associations between daily experiences, individual differences, and objectively measured sleep. **PLoS One 18(10)**: e0288909.

ALEXANDRA JÚLIA POP

National Academy of Scientist Education, 5th year
Semmelweis University
Faculty of Medicine, 5th year

Szent-Györgyi Mentor: Viktória Zsiros
Specialization: molecular cell biology
Language: English/C1, Romanian/conversational level

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The main aim of our research is to study the peritoneum of female rats and to understand its morphological changes. The important question behind our studies is to understand why some female rats heal more efficiently than males and what molecular mechanisms mediate this difference. Our experiments have provided statistical evidence that one of the reasons for the difference in the rate of recovery is different levels of estrogen. Our short- and long-term plans include investigating the specific effects of estrogen and its role in inflammation and regeneration. The aim of this approach is that biomarkers from the results can be potentially used to predict peritonitis. In practice, this could lead to early detection and more effective treatment of the disease. In addition, a deeper understanding of the relationship between estrogen and various molecular mechanisms may provide general applicability in therapeutic processes.

AMBITIONS AND CAREER GOALS

My research career aims to master critical thinking, with which I will be able to solve complex problems and answer related questions. Joining the Program truly supports and motivates me to continue our current research as a Ph.D. student after finishing my gradual education. I would like to apply the knowledge gained during our scientific work as a pathologist as well to become a doctor and researcher who can innovatively contribute to the improvement of medicine and people's better health.

PUBLICATIONS

Zsiros, V., Dóczi, N., Petővári, G., **Pop, A.**, Erdei, Z., Sebestyén, AL., Kiss, A. (2023) BMP-induced non-canonical signaling is upregulated during autophagy-mediated regeneration in inflamed mesothelial cells. **Sci Rep 13(1):** 10426.

RÉKA ZSÓFIA SEBESTÉNY

National Academy of Scientist Education, 5th year
Semmelweis University
Faculty of Medicine, 5th year

Szent-Györgyi Mentor: Gábor Nyiri
Specialization: neuroscience
Language: English/advanced, German/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

As a student researcher I am investigating the cortical pathways and their role in memory formation. In the brain, spatial and episodic memory cues are encoded by different small subpopulations of principal hippocampal neurons called engram cells. My goal is to gain a deeper understanding of the formation of these cell assemblies and thus understand the precise function of memory formation and recall itself. Our results are expected to contribute to a better understanding of memory processes and could help the development of treatment for memory problems.

AMBITIONS AND CAREER GOALS

My primary goal in my research career is my own professional development. I would like to become as independent of a researcher as possible and be able to realise my own ideas to the fullest. I would like to further develop my skills in stereotaxic and optical fibre surgery as well as further my knowledge in the design of behavioural experiments. My long term goal would be to write and publish my own research results.

BOGLÁRKA TÓTH

National Academy of Scientist Education, 6th year
Semmelweis University
Faculty of Medicine, 6th year

6TH YEAR STUDENTS

Szent-Györgyi Mentor: László Acsády
Specialization: neurobiology
Language: English/C1

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

There is growing evidence in the literature for the interdependent activity of the cortex and thalamus, based on this knowledge we can conclude that the thalamus is not just a simple relay site for the cortex, but they are interdependent and to maintain cortical activity thalamic input is required. Our next paper will examine frontal cortico-thalamic pathways using anatomical, electrophysiological and optogenetic behaviour experiments. Based on our research frontal cortico-thalamic pathways show major differences in anatomy, connectivity and function. In my independently performed optogenetic behavioural experiments, I examine frontal layer 5 cortico-thalamic pathways during motor learning. Based on my work (and supported by our anatomical findings), plasticity in this connection is possible, which would reshape our understanding of thalamo-cortical interactions.

AMBITIONS AND CAREER GOALS

After receiving my medical degree next year I'm planning to apply for the pre-PhD scholarship at the KOKI, where I could get an insight into 3 different laboratories' work. Either during or after my PhD I'm planning to spend a few years abroad.
I'm planning to work in research, in the field of neuroscience.

PUBLICATIONS

Hádinger, N., Bősz, E., **Tóth, B.** et al. (2023) Region-selective control of the thalamic reticular nucleus via cortical layer 5 pyramidal cells. **Nat Neurosci 26,** 116–130.

BOLDIZSÁR VÁMOSI

National Academy of Scientist Education, 6th year
Semmelweis University
Faculty of Medicine, 6th year

Szent-Györgyi Mentor: Balázs Enyedi
Specialization: physiology
Language: English/C2

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Intercellular communication is key to the body's coordinated response to tissue injury, allowing immune cells to migrate towards the wound within minutes and participate in the fight against pathogens and the coordination of wound healing. Our research aims to understand the molecular mechanisms of the response to tissue injury. This includes the development of fluorescent biosensors which are capable of real time detection of the release of mediators of the inflammatory response in living organisms. The short term goal of our research is to develop a novel system that allows us to efficiently develop new fluorescent biosensors suitable for in vivo microscopy. We hope that these new tools will help us to get closer to understanding the complex mechanisms of wound healing.

AMBITIONS AND CAREER GOALS

My aim as a doctor is to help people as much as possible with a broad perspective, empathy, social responsibility and scientific rigour. As part of this, as a clinician, I want to contribute to patient care by being well-versed in my field, effectively applying current medical knowledge, and as a researcher, I want to contribute to the advancement of medicine.

PUBLICATIONS

Tamás, S.X., Roux, B.T., **Vámosi, B**. et al. (2023) A genetically encoded sensor for visualizing leukotriene B4 gradients in vivo. **Nat Commun 14**, 4610.

BUDAPEST
SZENT-GYÖRGYI PHD STUDENTS

SIMON VIKÁR

National Academy of Scientist Education,
PhD studies 1st year

Semmelweis University School of PhD Studies
Molecular Medicine Division, 1st year

Szent-Györgyi Mentor: Attila Mócsai
Specialization: physiology, immunology, autoimmune and inflammatory diseases
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

My research encompasses the examination of the pathomechanism of bullous pemphigoid (BP), a rare autoimmune blistering. In this disease, the patients have severe pain and itching due to the developing tight blisters, but currently, for these symptoms, there is no specific therapy available. The investigation of BP pathology was made possible by a fully human ex vivo skin separation model that we previously set up, which replicated BP pathophysiology in our lab. Currently, I am using this model to assess the efficacy of various inhibitors and prospective medicinal treatments that can be further investigated in clinical investigations. With this research, I'm hoping to discover medicines that can effectively cure the severe symptoms of these individuals.

AMBITIONS AND CAREER GOALS

During my career, I want to work on the unanswered problems in rheumatology and immunology, two of the medical specialties that I find most fascinating. I'm hoping to get the chance to study and treat these critical, fascinating diseases from both a clinical and a scientific perspective. I also hope that I will be able to contribute to the body of knowledge about these diseases that is already known to humanity.

PUBLICATIONS

Vikár S, Szilveszter KP, Koszorú K, Sárdy M, Mócsai A. The Syk inhibitor entospletinib abolishes dermal-epidermal separation in a fully human ex vivo model of bullous pemphigoid. **J Invest Dermatol.** 2024 Jan 29:S0022-202X(24)00080-0. doi: 10.1016/j.jid.2024.01.009. Epub ahead of print. PMID: 38296021.

Szilveszter KP, **Vikár S**, Horváth IÁ, Helyes Zs, Sárdy M, Mócsai A: Phospholipase Cγ2 Is Essential for Experimental Models of Epidermolysis Bullosa Acquisita.

DEBRECEN
SZENT-GYÖRGYI MENTORS

ATTILA BÁCSI

University of Debrecen
Faculty of Medicine
Department of Immunology

RESEARCH AREA

Investigation of the role of reactive oxygen species in inflammatory processes. Studying how pollen-derived reactive radicals influence the function of human cells and how they affect immune responses against pollen antigens. Investigation of the interactions between the repair of oxidative DNA damage and the development of inflammation, with particular attention to the effect of the 8-oxoguanine DNA glycosylase enzyme on the activation of small molecular weight GTPases. Analysis of the interaction of signaling pathways induced by different pattern recognition receptors in human dendritic cell and macrophage subpopulations.

SELECTED PUBLICATIONS

Czimmerer, Z., Halasz, L., Daniel, B., Varga, Z., Bene, K., Domokos, A., Hoeksema, M., Shen, Z., Berger, W.K., Cseh, T., Jambrovics, K., Kolostyak, Z., Fenyvesi, F., Varadi, J., Poliska, S., Hajas, G., Szatmari, I., Glass, C.K., **Bacsi, A.**, Nagy, L. (2022) The epigenetic state of IL-4-polarized macrophages enables inflammatory cistromic expansion and extended synergistic response to TLR ligands. **Immunity 55:** 2006-2026.e6.

Tóth, M., Muzsai, S., Regulski, K., Szendi-Szatmári, T., Czimmerer, Z., Rajnavölgyi, É., Chapot-Chartier, M.,P., **Bácsi, A.** (2022) The Phagocytosis of Lacticaseibacillus casei and Its Immunomodulatory Properties on Human Monocyte-Derived Dendritic Cells Depend on the Expression of Lc-p75, a Bacterial Peptidoglycan Hydrolase. **Int J Mol Sci 23:** 7620.

Bácsi, A., Lucas, R., Sütő, M.I., Szklenár, M., Bohn, T., Rühl, R. (2022) An immune-shift induced by lycopene; from an eosinophil-dominant type towards an eosinophil/neutrophil-co-dominant type of airway inflammation. **Food Funct 13:** 6534-6544.

Mázló, A., Kovács, R., Miltner, N., Tóth, M., Veréb, Z., Szabó, K., Bacskai, I., Pázmándi, K., Apáti, Á., Bíró, T., Bene, K., Rajnavölgyi, É., **Bácsi, A.** (2021) MSC-like cells increase ability of monocyte-derived dendritic cells to polarize IL-17-/IL-10-producing T cells via CTLA-4. **iScience 24:** 102312.

Pázmándi, K., Sütő, M., Fekete, T., Varga, A., Boldizsár, E., Boldogh, I., **Bácsi, A.** (2019) Oxidized base 8-oxoguanine, a product of DNA repair processes, contributes to dendritic cell activation. **Free Radic Biol Med 143:** 209-220.

ZSUZSA BAGOLY

University of Debrecen
Faculty of Medicine
Department of Laboratory Medicine

RESEARCH AREA

Clinical research in the field of hemostasis: investigation of the underlying causes of unsuccessful thrombolysis therapy in acute ischemic stroke patients. Background: Recombinant tissue plasminogen activator (rt-PA) is currently the most important registered pharmacological treatment for the dissolution of blood clots in case of acute ischemic stroke. The therapy can be successfully used within 4.5 hours from the onset of stroke symptoms. Although the use of rt-PA is safe and effective in most cases, its main side effect is intracerebral hemorrhage with a potentially fatal outcome, which occurs in about 6-8% of patients. On the other hand, the lysis of the blood clot is only successful in about 30-40% of the patients, therefore, clinical improvement is often not achieved. Currently, little is known about why some patients develop a hemorrhagic complication while in others the same therapy will be ineffective. In our research, we examine the potential role of the blood coagulation system in the outcomes of patients. By using blood samples of acute ischemic stroke patients stored in our biobank, we can observe the level and genetic variations of the individual proteins involved in blood coagulation and compare the results with the outcome of the patients. Such observations may help to explain adverse outcomes and can serve as the basis for more effective treatments in the future.

SELECTED PUBLICATIONS

Székely, E.G., Orbán-Kálmándi, R., Szegedi, I., Katona, É., Baráth, B., Czuriga-Kovács, K.R., Lóczi, L., Vasas, N., Fekete, I., Fekete, K., Berényi, E., Oláh, L., Csiba, L., **Bagoly, Z.** (2022) Low α2-Plasmin Inhibitor Antigen Levels on Admission Are Associated With More Severe Stroke and Unfavorable Outcomes in Acute Ischemic Stroke Patients Treated With Intravenous Thrombolysis. **Front Cardiovasc Med 9:** 901286.

Lóczi, L., Orbán-Kálmándi, R., Árokszállási, T., Fekete, I., Fekete, K., Héja, M., Tóth, J., Csiba, L., **Bagoly, Z.** (2021) Thrombin generation as a predictor of outcomes in patients with non-traumatic intracerebral hemorrhage. **Front Neurol 13:** 912664.

Orbán-Kálmándi, R., Szegedi, I., Sarkady, F., Fekete, I., Fekete, K., Vasas, N., Berényi, E., Csiba, L., **Bagoly, Z.** (2021) A modified in vitro clot lysis assay predicts outcomes and safety in acute ischemic stroke patients undergoing intravenous thrombolysis. **Sci Rep 1:** 12713.

Orbán-Kálmándi, R., Árokszállási, T., Fekete, I., Fekete, K., Héja, M., Tóth, J., Sarkady, F., Csiba, L., **Bagoly, Z.** (2021) A modified in vitro clot lysis assay predicts outcomes in non-traumatic intracerebral hemorrhage stroke patients - the IRONHEART study. **Front Neurol 12:** 613441.

Székely, E.G., Czuriga-Kovács, K.R., Bereczky, Z., Katona, É., Mezei, Z.A., Nagy, A., Tóth, N.K., Berényi, E., Muszbek, L., Csiba, L., **Bagoly, Z.** (2018) Low factor XIII levels after intravenous thrombolysis predict short-term mortality in ischemic stroke patients. **Sci Rep 8:** e7662.

PÉTER BAY

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

The laboratory carries out exploratory and applied research in three main areas. We carry out investigations to understand the metabolic and non-oncological roles of PARP enzymes that were originally described as DNA repair proteins. The primary aim of these investigations is to facilitate the repurposing of clinically available, registered PARP inhibitors and to understand the role of these enzymes in cells. Oncological diseases are accompanied by changes to the composition of the bacterial communities (the microbiome) of the human body that is termed oncobiosis. The connections between tumors and the microbiome are bidirectional. Our aim is to understand the mechanisms through which neoplasias induce oncobiosis and those through which oncobiosis supports the growth and metastasis formation of tumors. We are developing diagnostic procedures in that field. Finally, in collaboration with the Department of Organic Chemistry at the University of Debrecen we are developing organic metal ion complexes with selective cytostatic property against tumors.

SELECTED PUBLICATIONS

Kovács, T., Mikó E., Ujlaki, G., Yousef, H., Csontos, V., Uray K., **Bai, P.** (2021) The involvement of oncobiosis and bacterial metabolite signaling in metastasis formation in breast cancer. **Cancer and Metastasis 40:** 1223-1249.

Szántó, M., Gupte, R., Kraus, L.W., Pacher, P., **Bai, P.** (2021) PARPs in lipid metabolism and related diseases. **Progress in Lipid Research 84:** 101117.

Kacsir, I., Sipos, A., Bényei, A., Janka, E., Buglyó, P., Somsák, L., **Bai, P.***, Bokor É.* (2022) Reactive oxygen species production is responsible for antineoplastic activity of osmium, ruthenium, iridium and rhodium half-sandwich type complexes with bidentate glycosyl heterocyclic ligands in various cancer cell models. **International Journal of Molecular Medicine 23:** 813 *shared last authors

Curtin, N., Bányai, K., Thaventhiran, J., Le, Quesne, J., Helyes, Z., **Bai, P.** (2020) Repositioning PARP inhibitors for SARS-CoV-2 infection (COVID-19); a new multi-pronged therapy for ARDS? **British Journal of Pharmacology 177:** 3635-3645.

Mikó, E., Vida, A., Kovács, T., Ujlaki, Gy., Trencsényi, Gy., Márton,J., Sári, Zs., Kovács, P., Boratkó, A., Hujber, Z., Csonka, T., Antal-Szalmás, P., Watanabe, M., Gombos, I., Csoka, B., Kiss, B., Vígh, L., Szabó, J., Méhes, G., Sebestyén, A., Goedert, J.J., **Bai, P.** (2018) Lithocholic acid, a bacterial metabolite reduces breast cancer cell proliferation and aggressiveness. BBA – **Bioenergetics 1859:** 958-974.

SZILVIA BENKŐ

University of Debrecen
Faculty of Medicine
Department of Physiology

RESEARCH AREA

Nod-like receptors are intracellular pattern recognition receptors that recognize pathogen- or danger-associated molecules and initiate cellular responses in order to protect the cell. Either directly (via inflammasome formation) or indirectly (via signal pathway), they regulate various cellular functions including pro-inflammatory cytokine secretion (like IL-1beta), cell division or cell death. NLRs function as potential therapeutic and diagnostic target since most of the already-characterized members of the family have been associated to some form of autoimmune-, autoinflammatory-, allergic- or cancer diseases. This is proven by the fact that many pharmaceutical company focuses on the molecular manipulation of NLRs by drug development. Despite of the intensive studies many questions are still open, including the cell specific function of NLRs and the molecular mechanisms that modify the functions. Our research team aims to study (1) the expression and the molecular mechanisms of the action in various macrophage subpopulations; (2) the role of skeletal muscle NLRs in the cytokine (myokine) production and insulin resistance.

SELECTED PUBLICATIONS

Tóth, K., Lénárt, N., Berki,P., Fekete, R., Szabadits, E., Pósfai, B., Cserép, C, Alatshan, A., **Benkő, S.**, Kiss, D., Hübner, C.A., Gulyás, A., Kaila, K., Környei, Z., Dénes, Á.(2022) The NKCC1 ion transporter modulates microglial phenotype and inflammatory response to brain injury in a cell-autonomous manner. **PLoS Biol 27:** 3001526.

Kovács, E.,G., Alatshan, A., Budai, M.,M., Czimmerer, Z., Bíró, E., **Benkő, S.** (2021) Caffeine Has Different Immunomodulatory Effect on the Cytokine Expression and NLRP3 Inflammasome Function in Various Human Macrophage Subpopulations. **Nutrients 13:** 2409.

Szekanecz, Z., McInnes, I.,B., Schett, G., Szamosi, S., **Benkő, S.**, Szűcs, G. (2021) Autoinflammation and autoimmunity across rheumatic and musculoskeletal diseases. **Nat Rev Rheumatol 17:** 585-595.

Alatshan, A., Kovács, G.,E., Aladdin, A., Czimmerer, Z., Tar, K., **Benkő, S.** (2020) All-Trans Retinoic Acid Enhances both the Signaling for Priming and the Glycolysis for Activation of NLRP3 Inflammasome in Human Macrophage. **Cells 9:** 1591.

Czimmerer Z, Daniel B, Horvath A, Rückerl D, Nagy G, Kiss M, Peloquin M, Budai MM, Cuaranta-Monroy I, Simandi Z, Steiner L, Nagy B Jr, Poliska S, Banko C, Bacso Z, Schulman IG, Sauer S, Deleuze JF, Allen JE, **Benko S**, Nagy L. (2018) The Transcription Factor STAT6 Mediates Direct Repression of Inflammatory Enhancers and Limits Activation of Alternatively Polarized Macrophages. **Immunity 48:** 75-90.

ANIKÓ BORBÁS

University of Debrecen
Faculty of Pharmacy
Department of Pharmaceutical Chemistry

RESEARCH AREA

Our group is engaged in the field of synthetic carbohydrate, nucleoside and antibiotic chemistry. We focuse on the production of oligosaccharides of potential antithrombotic, antiviral and antitumor effects, the synthesis of thioglycoside mimetics of biorelevant carbohydrates, the development of new types of nucleic acid analogues and the chemical modification of glycopeptide antibiotics. In the last decade, we have designed and prepared heparin-like pentasaccharides with high anticoagulant activity, and important structure-activity relationships have been revealed in the field of heparinoid anticoagulants. We applied a biocompatible conjugation reaction, the photocatalytic thiol-ene coupling reaction on unsaturated carbohydrates, and prepared a number of biologically active (antiviral, enzyme-inhibiting) glycoconjugates. Significant progress has been made in the synthesis of glycopeptide-based semisynthetic antibacterial and antiviral compounds, as well as in the design and synthesis of new nucleoside analogs with antitumor activity. Our research has recently been extended to the study of NO- and H2S-donor nonsteroidal anti-inflammatory drugs. The biological activity of our compounds is evaluated in extensive domestic and international cooperation.

SELECTED PUBLICATIONS

Debreczeni, N., Bege, M., Herczeg, M., Bereczki, I., Batta, G., Herczegh, P., **Borbás, A**. (2021) Tightly linked morpholino-nucleoside chimeras: new, compact cationic oligonucleotide analogues. **Org Biomol Chem 19:** 8711–8721.

Bereczki, I., Papp, H., Kuczmog, A., Madai, M., Nagy, V., Agócs, A., Batta, G., Milánkovits, M., Ostorházi, E Mitrović, A., Kos, J., Zsigmond, Á., Hajdú, I., Lőrincz, Z., Bajusz, D., Keserű, G.M., Hodek, J., Weber, J., Jakab, F., Herczegh, P., **Borbás, A.** (2021) Natural apocarotenoids and their synthetic glycopeptide conjugates inhibit SARS-CoV-2 replication. **Pharmaceuticals 14:** 1111.

Szűcs, Z., Naesens, L., Stevaert, A., Ostorházi, E., Batta, G., Herczegh, P., **Borbás, A.** (2020) Reprogramming of the antibacterial drug vancomycin results in potent antiviral agents devoid of antibacterial activity, **Parmaceuticals 13:** 139.

Szőke, K., Czompa,A., Lekli, I., Szabados-Fürjesi, P., Herczeg, M., Csávás, M., **Borbás, A.**, Herczegh, P., Tósaki. A. (2019) A new vasoactive hybrid aspirin containing nitrogen monoxide-releasing molsidomine moiety. **Eur J Pharm Sci 131:** 159-166.

Szűcs, Z., Kelemen, V., Thai, S.L., Csávás, M., Rőth, E., Batta, G., Stevaert, A., Vanderlinden, E., Naesens, L., Herczegh, P., **Borbás, A.** (2018) Structure-activity relationship studies of lipophilic teicoplanin pseudoaglycon derivatives as new anti-influenza virus agents. **Eur J Med Chem 157:** 1017-1030.

KATALIN GODA

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

The majority of human ABC proteins are active pumps utilizing the energy of ATP hydrolysis for exporting various compounds out of cells. Certain ABC transporters including ABCB1 and ABCG2 have extremely broad substrate spectra involving xenobiotics, endobiotics and numerous chemotherapeutic compounds applied in the treatment of various diseases. Since ABCB1 and ABCG2 are expressed in tissue barriers and in drug metabolizing and drug excreting organs (e.g., liver and kidney), they are important determinants of the pharmacokinetics of chemotherapeutic compounds. In addition, ABCB1 and ABCG2 are often overexpressed in tumour cells as well as in tumour stem cells, and therefore they are key players of the chemotherapy resistance of tumours. In view of their great physiological and medical importance, ABC transporters are important targets for pharmacological modulations. Therefore, the detailed understanding of the working mechanism of ABC proteins can promote rational drug design. On the other hand, the identification of drugs that can interact with ABCB1 or ABCG2 as substrates/inhibitors may help to avoid the emergence of drug-drug interactions upon treatment of various diseases.

SELECTED PUBLICATIONS

Gyöngy, Zs., Mocsár, G., Hegedűs, É., Stockner T., Ritter, Zs., Homolya, L., Schamberger, A.I., Orbán, I.T., Remenyik, J., Szakác,s G., **Goda, K.** (2023) Nucleotide binding is the critical regulator of ABCG2 conformational transitions. **eLife 12:** e83976.

Goda, K., Dönmez-Cakil, Y., Tarapcsák, S., Szalóki, G., Szöllősi, D., Parveen, Z., Türk, D., Szakács, G., Chiba, P., Stockner, T. (2020) Human ABCB1 with an ABCB11-like degenerate nucleotide binding site maintains transport activity by avoiding nucleotide occlusion. **PLoS Genet 16:** e1009016

Tarapcsák, S., Szalóki, G., Telbisz, Á., Gyöngy, Z., Matúz, K., Csősz, É., Nagy P., Holb, I.J, Rühl, R., Nagy, L., Szabó, G., **Goda, K.** (2017) Interactions of retinoids with the ABC transporters P-glycoprotein and Breast Cancer Resistance Protein. **Sci Rep 7:** 41376.

Bársony, O., Szalóki, G., Türk, D., Tarapcsák, S., Gutay-Tóth, Z., Bacsó, Z., Holb, I., Székvölgyi, L., Szabó, G., Csanády, L., Szakács, G., **Goda, K.** (2016) A single active catalytic site is sufficient to promote transport in P-glycoprotein. **Sci Rep 6:** 24810.

Szalóki, G., Krasznai, Z., Tóth, Á., Vízkeleti, L., Szöllősi, A., Trencsényi, G., Lajtos, I., Juhász, I., Krasznai, Z., Márián, T., Balázs, M., Szabó, G., **Goda, K.** (2014) The strong in vivo anti-tumor effect of the UIC2 monoclonal antibody is the combined result of Pgp inhibition and antibody dependent cell-mediated cytotoxicity. **PloS ONE 9:** e107875.

TIBOR HAJDÚ

University of Debrecen
Faculty of Medicine
Department of Anatomy, Histology and Embryology

RESEARCH AREA

My scientific interest is in the biology of cutaneous pigment cells (epidermal melanocytes) and their neoplastic forms (melanoma cells). My PhD thesis focused on the nuclear presence and possible functions of N-methyl-D-aspartate type glutamate receptors in melanoma cells. I also participated in several projects on cellular and molecular biology related experiments of melanocytes and melanoma cells, including the importance of different chain-length hyaluronic acids, their synthases and receptors, the effects of PACAP neuropeptide related signalling, the role of clock genes and the functions of the cytoskeleton components, called septins. After obtaining my PhD degree, I joined the Chondro-omics group of Dr. Csaba Matta and started to work on the "omics" field, focusing on cell surface proteins (the so-called surfaceome) of melanocytes and melanoma cells using proteomics, bioinformatics, and network biology methods. I'm also interested in proteomics of subcellular membranes and exosomes of pigment cells.

SELECTED PUBLICATIONS

Hajdú, T., Juhász, T., Szűcs-Somogyi, C., Rácz, K., Zákány, R. (2018) NR1 and NR3B Composed Intranuclear N-methyl-d-aspartate Receptor Complexes in Human Melanoma Cells. **Int J Mol Sci** 191929.

Hajdú, T., Kovács, P., Zsigrai, E., Takács, R., Vágó, J., Cho, S., Sasi-Szabó, L., Becsky, D., Keller-Pintér, A., Emri, G., Rácz, K., Reglődi, D., Zákány, R., Juhász, T. (2021) Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP) has inhibitory effects on melanoma cell proliferation and migration in vitro. **Front Oncol 11:** 681603.

Matta, C., Lewis, R., Fellows, C., Diszhazi, G., Almassy, J., Miosge, N., Dixon, J., Uribe, MC., May, S., Poliska, S., Barrett-Jolley, R., Fodor, J., Szentesi, P., **Hajdú, T.**, Keller-Pinter, A., Henslee ,E., Labeed, FH., Hughes, MP., Mobasheri, A. (2021) Transcriptome-based screening of ion channels and transporters in a migratory chondroprogenitor cell line isolated from late-stage osteoarthritic cartilage. **J Cell Physiol 236:** 7421-7439

Vágó, J., Katona, É., Takács, R., Dócs, K., **Hajdú, T.**, Kovács, P., Zákány, R., van der Veen, DR., Matta, C. (2022) Cyclic uniaxial mechanical load enhances chondrogenesis through entraining the molecular circadian clock. **J Pineal Res 73:** e12827.

Vágó, J., Takács, R., Kovács, P., **Hajdú, T.**, van der Veen, DR., Matta. (2023) Combining biomechanical stimulation and chronobiology: a novel approach for augmented chondrogenesis? **Front Bioeng Biotechnol 11:** 1232465.

VIKTÓRIA JENEY

University of Debrecen
Faculty of Medicine
Research Centre for Molecular Medicine

RESEARCH AREA

The major interest of our research group is soft tissue calcification, a process in which bone-like matrix deposits in the soft tissues outside of the skeletal system. Soft tissue calcification impairs the normal function of tissues and organs. The two most common types of soft tissue calcification are the vascular and the valve calcifications. Cardiovascular calcification is strongly associated with increased incidence of major cardiovascular events, such as myocardial infarction, stroke and cardiac death.
Cardiovascular calcification mostly affects the elderly, but some endemic diseases such as chronic kidney disease and type 2 diabetes largely accelerates calcification, and reduce life expectancy of these patients.
Vascular and valve calcification is driven by an osteoblastic phenotype switch of vascular smooth muscle cells and valve interstitial cells. In the past decades numerous calcification inducers and inhibitors have been identified, but many details of the molecular mechanism and the possible therapeutic interventions are still under investigation.

SELECTED PUBLICATIONS

Balogh, E., Tóth, A., Méhes, G., Trencsényi, G., Paragh, G., **Jeney, V.** (2019) Hypoxia Triggers Osteochondrogenic Differentiation of Vascular Smooth Muscle Cells in an HIF-1 (Hypoxia-Inducible Factor 1)-Dependent and Reactive Oxygen Species-Dependent Manner. **Arterioscler Thromb Vasc Biol 39:** 1088-1099.

Tóth, A., Balogh, E., **Jeney, V.** (2020) Regulation of Vascular Calcification by Reactive Oxygen Species. **Antioxidants (Basel) 8;9:** 963.

Balogh, E., Chowdhury, A., Ababneh, H,, Csiki, D.,M., Tóth, A., **Jeney, V.** (2021) Heme-Mediated Activation of the Nrf2/HO-1 Axis Attenuates Calcification of Valve Interstitial Cells. **Biomedicines 15;9:** 427.

Tóth, A., Csiki, D.,M., Nagy, B., Jr, Balogh, E., Lente, G., Ababneh, H., Szöőr, Á., **Jeney, V.** (2022) Daprodustat Accelerates High Phosphate-Induced Calcification Through the Activation of HIF-1 Signaling. **Front Pharmacol 13:** 798053.

Csiki, D.M., Ababneh, H., Tóth, A., Lente, G., Szöőr, Á., Tóth, A., Fillér, C., Juhász, T., Nagy, B., Jr, Balogh, E., **Jeney, V.** (2023) Hypoxia-inducible factor activation promotes osteogenic transition of valve interstitial cells and accelerates aortic valve calcification in a mice model of chronic kidney disease. **Front Cardiovasc Med 10:** 1168339.

TAMÁS KOVÁCS

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

Lipids actively influence the function of transmembrane proteins through direct binding or indirect effects mediated by alterations in biophysical parameters (fluidity, hydration, dipole potential) and lateral organization (lipid raft, ceramide platform microdomains) of biological membranes. Since these parameters are determined by the lipid composition of bilayers, it is reasonable to assume that they may change in diseases characterized by alterations in membrane lipid levels. Such conditions include metabolic (hypercholesterolemia), neurodegenerative (Alzheimer's disease, Parkinson's disease) and lysosomal storage disorders (Niemann-Pick type C, Gaucher's disease) as well. However, the biological roles of changes in biophysical parameters and lateral organization of membranes in the regulation of proteins and the pathomechanism of diseases are still largely unexplored. By means of the wide variety of fluorescence-based measurement techniques available at our department, we investigate the presence and roles of such alterations in the above-mentioned diseases, which can represent novel therapeutic targets, and, in addition, help to better understand these pathological conditions.

SELECTED PUBLICATIONS

Kovacs, T., Kurtan, K., Varga, Z., Nagy, P., Panyi, G., Zakany, F. (2023) Veklury® (remdesivir) formulations inhibit initial membrane-coupled events of SARS-CoV-2 infection due to their sulfobutylether-β-cyclodextrin content. **Br J Pharmacol 180(16):** 2064–2084.

Kovacs, T., Nagy, P., Panyi, G., Szente, L., Varga, Z., Zakany, F. (2022) Cyclodextrins: Only Pharmaceutical Excipients or Full-Fledged Drug Candidates? **Pharmaceutics 14(12):** 2559.

Kovacs, T,.* Zakany, F.,* Nagy, P. (2022) It Takes More than Two to Tango: Complex, Hierarchal, and Membrane-Modulated Interactions in the Regulation of Receptor Tyrosine Kinases. **Cancers (Basel) 4:** 944.

Kovacs, T., Sohajda, T., Szente, L., Nagy, P., Panyi, G., Varga, Z., Zakany, F. (2021) Cyclodextrins Exert a Ligand-like Current Inhibitory Effect on the KV1.3 Ion Channel Independent of Membrane Cholesterol Extraction. **Front Mol Biosci 8:** 735357.

Zakany, F., Szabo, M., Batta, G., Kárpáti, L., Mándity. IM., Fülöp, P., Varga, Z., Panyi, G., Nagy, P., **Kovacs, T.** (2021) An ω-3, but Not an ω-6 Polyunsaturated Fatty Acid Decreases Membrane Dipole Potential and Stimulates Endo-Lysosomal Escape of Penetratin. **Front Cell Dev Biol 9:** 647300.

ENDRE KÁROLY KRISTÓF

University of Debrecen
Faculty of Medicine
Department of Biochemistry and Molecular Biology

RESEARCH AREA

Primarily, we aim to identify the unique molecular regulators of browning in human adipose-derived stromal cells and differentiated adipocytes obtained from adipose tissues of distinct anatomical origins by analyzing the global gene expression pattern of these cells. To prove that the identified molecular elements directly regulate brown/beige differentiation or activation, the specific genes will be deleted or overexpressed. Based on the obtained gene expression data, we wish to determine the secreted cytokine and metabolite profiles of distinct human thermogenic adipose tissues and adipocytes by system biology approaches. We also intend to systematically investigate how human browning adipocytes switch off their thermogenic capacity and become dormant in response to the withdrawal of browning-inducers. Our research might open up better strategies for specific stimulation of beneficial fat browning or preventing entry into dormancy in humans, which aid weight reduction and decrease insulin resistance in obese individuals.

SELECTED PUBLICATIONS

Kristóf, E., Doan-Xuan, Q.M., Bai, P., Bacso, Z., Fésüs, L. (2015) Laser-scanning cytometry can quantify human adipocyte browning and proves effectiveness of irisin. **Scientific Reports 5:** 12540.

Kristóf, E., Doan-Xuan, Q.M., Sárvári, A.K., Klusóczki, Á., Fischer-Posovszky, P., Wabitsch, M., Bacso, Z., Bai, P., Balajthy, Z., Fésüs L. (2016) Clozapine modifies the differentiation program of human adipocytes inducing browning. **Translational Psychiatry 6:** e963.

Klusóczki, Á., Veréb, Z., Vámos, A., Fischer-Posovszky, P., Wabitsch, M., Bacso, Z., Fésüs, L., **Kristóf E.** (2019) Differentiating SGBS adipocytes respond to PPARγ stimulation, irisin and BMP7 by functional browning and beige characteristics. **Scientific Reports 9:** 5823.

Tóth, B.B., Arianti, R., Shaw, A., Vámos, A., Veréb, Z., Póliska, S., Győry, F., Bacso, Z., Fésüs, L., **Kristóf, E.** (2020) FTO intronic SNP strongly influences human neck adipocyte browning determined by tissue and PPARγ specific regulation: a transcriptome analysis. **Cells 9:** 987.

Shaw, A., Tóth, B.B., Király, R., Arianti, R., Csomós, I., Póliska, S., Vámos, A., Korponay-Szabó, I.R., Bacso, Z., Győry, F., Fésüs, L., **Kristóf, E.** (2021) Irisin stimulates the release of CXCL1 from differentiating human subcutaneous and deep-neck derived adipocytes via upregulation of NFκB pathway. **Frontiers in Cell and Developmental Biology 9:** 737872.

Vámos, A., Shaw, A., Varga, K., Csomós, I., Mocsár, G., Balajthy, Z., Lányi, C., Bacso, Z., Szatmári-Tóth, M., **Kristóf, E.** (2022) Mitophagy mediates the beige to white transition of human primary subcutaneous adipocytes ex vivo. **Pharmaceuticals (Basel) 15:** 363.

BEÁTA LONTAY

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

Post-translational modifications, such as conjugation of proteins to phosphate and methyl groups, lipids and ubiquitin, have a major impact on the biological function of proteins. For this reason, inhibiting and activating the enzymes catalyzing these modifications, other factors regulating their expression and selectively targeting these modifications may be a therapeutic strategy for a number of diseases. Our work focuses on the pathological shift in post-translational modification patterns in reproductive diseases, insulin resistance, hyperthyroidism and tumorigenesis and the pathobiochemical processes applying biochemical, molecular biological and proteomic methods. Our work will primarily focus on the Mg2+ -dependent protein phosphatase/myosin phosphatase/protein arginine methyltransferase 5 oncogenic signaling pathway that induces lung tumor formation as a diagnostic and therapeutic target.

SELECTED PUBLICATIONS

Major, E., Győry, F., Horváth, D., Keller, I., Tamás, I., Uray, K., Fülöp, P., **Lontay, B.** (2021) Smoothelin-Like Protein 1 Regulates Development and Metabolic Transformation of Skeletal Muscle in Hyperthyroidism. **Front Endocrinol 12:** 751488.

Major, E., Keller, I., Horváth, D., Tamás, I., Erdődi, F., **Lontay, B.** (2021) Smoothelin-Like Protein 1 Regulates the Thyroid Hormone-Induced Homeostasis and Remodeling of C2C12 Cells via the Modulation of Myosin Phosphatase. **Int J Mol Sci 19:** 10293.

Uray, K., Major, E., **Lontay, B.** (2020). MicroRNA Regulatory Pathways in the Control of the Actin-Myosin Cytoskeleton. **Cells 7:** 1649.

Horváth, D., Sipos, A., Major, E., Kónya, Z., Bátori, R., Dedinszki, D., Szöllősi, A., Tamás, I., Iván, J., Kiss, A., Erdődi, F., **Lontay, B.** (2018) Myosin phosphatase accelerates cutaneous wound healing by regulating migration and differentiation of epidermal keratinocytes via Akt signaling pathway in human and murine skin. **Biochim Biophys Acta Mol Basis 10:** 3268-3280.

Sipos, A., Iván, J., Bécsi, B., Darula, Z., Tamás, I., Horváth, D., Medzihradszky, K.,F., Erdődi, F., **Lontay, B.** (2017). Myosin phosphatase and RhoA-activated kinase modulate arginine methylation by the regulation of protein arginine methyltransferase 5 in hepatocellular carcinoma cells. **Sci Rep 7:** 40590.

CSABA MATTA

University of Debrecen
Faculty of Medicine
Department of Anatomy, Histology and Embryology

RESEARCH AREA

Traditional therapies for the treatment of osteoarthritis, which affects a large proportion of the population worldwide, have limited effectiveness, owing to limited regeneration of articular cartilage. Therefore, cartilage regeneration remains a major challenge, due in part to the lack of detailed knowledge of the molecular processes that regulate cartilage formation. For this reason, a number of biological therapies are currently being developed for which a more complete understanding of cartilage differentiation is essential. Our research group is interested in the biology of cartilage tissue, with particular emphasis on its formation (chondrogenesis). We aim to understand the cell surface proteome (surfaceome) of developing cartilage cells with the hope of identifying new biomarkers. We also aim to gain a better understanding of the biological clock in differentiating chondrocytes and to synchronise these clocks with mechanical stimuli. A more precise mapping of chondrogenic pathways could contribute to the development of more efficient cartilage regeneration procedures.

SELECTED PUBLICATIONS

Matta, C., Lewis, R., Fellows, C., Diszhazi, G., Almassy, J., Miosge, N., Dixon, J., Uribe, M. C., May, S., Poliska, S., Barrett-Jolley, R., Fodor, J., Szentesi, P., Hajdú, T., Keller-Pinter, A., Henslee, E., Labeed, F. H., Hughes, M. P., & Mobasheri, A. (2021) Transcriptome-based screening of ion channels and transporters in a migratory chondroprogenitor cell line isolated from late-stage osteoarthritic cartilage. **Journal of cellular physiology 236:** 7421–7439.

Alagha, M. A., Vágó, J., Katona, É., Takács, R., van der Veen, D., Zákány, R., & **Matta, C.** (2021) A Synchronized Circadian Clock Enhances Early Chondrogenesis. **Cartilage 13:** 53S–67S.

Matta, C., Juhász, T., Fodor, J., Hajdú, T., Katona, É., Szűcs-Somogyi, C., Takács, R., Vágó, J., Oláh, T., Bartók, Á., Varga, Z., Panyi, G., Csernoch, L., & Zákány, R. (2019) N-methyl-D-aspartate (NMDA) receptor expression and function is required for early chondrogenesis. **Cell communication and signaling 17:** 166.

Matta, C., Boocock, D. J., Fellows, C. R., Miosge, N., Dixon, J. E., Liddell, S., Smith, J., & Mobasheri, A. (2019) Molecular phenotyping of the surfaceome of migratory chondroprogenitors and mesenchymal stem cells using biotinylation, glycocapture and quantitative LC-MS/MS proteomic analysis. **Scientific reports 9:** 9018.

Matta, C., Fellows, C. R., Quasnichka, H., Williams, A., Jeremiasse, B., Allaway, D., & Mobasheri, A. (2021). Clusterin secretion is attenuated by the proinflammatory cytokines interleukin-1β and tumor necrosis factor-α in models of cartilage degradation. **Journal of orthopaedic research: official publication of the Orthopaedic Research Society 39:** 1017–1029.

PÉTER NAGY

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

My workgroup is interested in the role the plasma membrane plays in physiological and pathological processes. Signaling of growth factor receptors involves dimerization and the formation of larger oligomers whose composition is not only influenced by the ligand itself, but by the surrounding lipid environment as well. We study how transmembrane signals induced by peptide growth factors alter these receptor clusters, how the lipid environment bears on this process, and how it can be correlated with transmembrane signaling. Biophysical properties of the cell membrane, including its potentials, fluidity and curvature, have been recognized to play important roles in tuning cellular responses and regulating transmembrane transport. We would like to use these principles to optimize the cellular uptake of cell penetrating peptides that could potentially enable the selective treatment of cells even with membrane impermeable drugs.
More details about the research interest of my research group can be found on our web page: https://peternagygroup.com/

SELECTED PUBLICATIONS

Kovács, T., Zákány, F., **Nagy, P.** (2022) It takes more than two to tango: complex, hierarchal, and membrane-modulated interactions in the regulation of receptor tyrosine kinases.**Cancers 14:** 944.

Hajdu, T., Szabó, K., Jakab, Á., Pócsi, I., Dombrádi, V., **Nagy, P.** (2021) Biophysical experiments reveal a protective role of protein phosphatase Z1 against oxidative damage of the cell membrane in Candida albicans. **Free Rad Biol Med 176:** 222-227.

Batta, G., Kárpáti, L., Henrique, G.F., Tóth, G., Tarapcsák, S., Kovács, T., Zákány, F., Mándity, I.M., **Nagy, P.** (2021) Statin-boosted cellular uptake and endosomal escape of penetratin due to reduced membrane dipole potential. **Br J Pharmacol 178:** 3667-3681.

Hajdu, T., Váradi, T., Rebenku, I., Kovács, T., Szöllősi, J., **Nagy, P.** (2020) Comprehensive model for epidermal growth factor receptor ligand binding involving conformational states of the extracellular and the kinase domains. **Front Cell Dev Biol 8:** 776.

Szendi-Szatmári, T., Szabó, Á., Szöllősi, J., **Nagy, P.** (2019) Reducing the detrimental effects of saturation phenomena in FRET microscopy. **Anal Chem 91:** 6378-6382.

NORBERT NÉMETH

University of Debrecen
Faculty of Medicine
Department of Operative Techniques and Surgical Research

RESEARCH AREA

Hemorheological, microcirculatory and histomorphological investigations of tissue/organ ischemia-reperfusion related to surgical interventions, with comparative analysis of the detectable injuries and their preventive/therapeutic possibilities. Complex investigation of the pathomechanism of sepsis with special regard to the hemodynamic and microcirculatory changes. Examination of regeneration of micro-vascular anastomoses, setting the optimal geometry of anastomoses and shunts with the usage of agents having a positive effect on the maturation processes.

SELECTED PUBLICATIONS

Varga, Á., Mátrai, Á., Baráth, B., Deák, Á., Horváth, L., **Németh, N.** (2022) Interspecies diversity of osmotic gradient deformability of red blood cells in human and seven vertebrate animal species. **Cells 11:** 1-15.

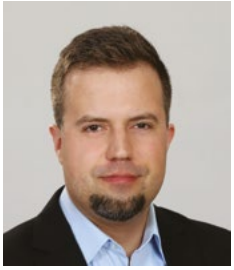
Németh, N., Pető, K., Magyar, Z., Klárik, Z., Varga, G., Oltean, M., Mantas, A., Czigány, Z., Tolba, R. (2021) Hemorheological and microcirculatory factors in liver ischemia-reperfusion injury - An update on pathophysiology, molecular mechanisms and protective strategies. **Int. J. Mol. Sci. 22:** 1-24.

Szabó, B., Fazekas, L., Ghanem, S., Godó, Z., Madar, J., Apró, A., **Németh, N.** (2020) Biomechanical comparison of microvascular anastomoses prepared by various suturing techniques. **Injury-Int. J. Care Inj. 51:** 2866-2873.

Berhés, M., **Németh, N.**, Pető, K., Deák, Á., Hajdu, E., Molnár, Á., Árkosy, P., Szabó, J., Fülesdi, B. (2019) Hemodynamic consequences of intravenously given E. coli suspension: observations in a fulminant sepsis model in pigs, a descriptive case-control study. **Eur. J. Med. Res. 24:** 1-6.

Mester, A., Magyar, Z., Molnár, Á., Somogyi, V., Tánczos, B., Pető, K., **Németh, N.** (2018) Age- and gender-related hemorheological alterations in intestinal ischemia-reperfusion in the rat. **J. Surg. Res. 225:** 68-75.

Ghanem, S., Tánczos, B., Deák, Á., Bidiga, L., **Németh, N.** (2018) Carotid-jugular fistula model to study systemic effects and fistula-related microcirculatory changes. **J. Vasc. Res. 55:** 268-277.



ATTILA OLÁH

University of Debrecen
Faculty of Medicine
Department of Physiology

RESEARCH AREA

Complex cannabinoid signaling contributes to the regulation of a number of (patho)physiological processes in human skin. These include, but are not limited to, local inflammatory processes, sebum production, pigmentation, hair growth, or differentiation of epidermal keratinocytes. Dysregulation of these processes play an important role in the pathogenesis of highly prevalent diseases (e.g., acne, hair growth disorders, atopic dermatitis, etc.). Thus, together with national and international collaborators, and industrial partners, our team aims to explore the putative therapeutic potential of the cannabinoid signaling in the above diseases. We mostly use molecular and cellular physiology approaches. In addition to the "endogenous" cannabinoids produced in our body, we also study the effects of plant-derived cannabinoids and "cannabinoid-like" compounds, as well as signaling systems that are related to the cannabinoid signaling (e.g., purinergic signaling, TRP channels, etc.). Moreover, we plan to pay special attention to the interactions between the cannabinoid signaling and the extracellular vesicle-mediated intercellular communication.

SELECTED PUBLICATIONS

Oláh, A., Tóth, B.I., Borbíró, I., Sugawara, K., Szöllősi, A.G., Czifra, G., Pál, B., Ambrus, L., Kloepper, J., Camera, E., Ludovici, M., Picardo, M., Voets, T., Zouboulis, C.C., Paus, R., Bíró, T. (2014) Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes. **J Clin Invest 124:** 3713-3724.

Oláh, A., Markovics, A., Szabó-Papp, J., Szabó, P.T., Stott, C., Zouboulis, C.C., Bíró, T. (2016) Differential effectiveness of selected non-psychotropic phytocannabinoids on human sebocyte functions implicates their introduction in dry / seborrheic skin and acne treatment. **Exp Dermatol 25:** 701-707.

Szántó, M.[#], **Oláh, A.**[#], Szöllősi, A.G., Tóth, K.F., Páyer, E., Czakó, N., Pór, Á., Kovács, I., Zouboulis, C.C., Kemény, L., Bíró, T., Tóth, B.I. (2019) Activation of TRPV3 inhibits lipogenesis and stimulates production of inflammatory mediators in human sebocytes – a putative contributor to dry skin dermatoses. **J Invest Dermatol 139:** 250-253. [#]Shared first authorship.

Tóth, K.F., Ádám, D., Bíró, T.[#], **Oláh, A.**[#,&] (2019) Cannabinoid signaling in the skin: Therapeutic potential of the "c(ut)annabinoid" system. **Molecules 24:** 918. [#]Shared last authorship. [&]Corresponding author.

Szabó, I.L., Lisztes, E., Béke, G., Tóth, K.F., Paus, R., **Oláh, A.**[#,&], Bíró, T.[#,&] (2020) The phytocannabinoid, ( )-cannabidiol, operates as a complex, differential modulator of human hair growth: Anti-inflammatory submicromolar versus hair growth inhibitory micromolar effects. **J. Invest. Dermatol 140:** 484-488. [#]Shared last authorship. [&]Shared corresponding author.

BALÁZS PÁL

University of Debrecen
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The two main profiles of the laboratory are the investigation on the pathophysiology of the brainstem cholinergic neuromodulatory actions and the age dependence of the human astrocyte-neuron communication.

The cholinergic neuromodulation of the brainstem regulates sleep-wakefulness cycles, movement and sensory gating. Loss of cholinergic neurons is related to the pathogenesis of progressive supranuclear palsy. In our research, we plan to focus on actions leading to the local degeneration of the cholinergic neurons and their consequences in behavioral tests.

We previously demonstrated that astrocytes are able to alter synaptic strength via generating NMDA receptor dependent slow inward currents. This mechanism has a strong age dependence in humans. Further research is performed for understanding its molecular background and pathophysiological significance.

SELECTED PUBLICATIONS

Csemer, A., Kovács, A., Maamrah, B., Pocsai, K., Korpás, K., Klekner, Á., Szűcs, P., Nánási, P., **Pál, B.** (2023) Astrocyte- and NMDA receptor-dependent slow inward currents differently contribute to synaptic plasticity in an age-dependent manner in mouse and human neocortex. **Aging Cell** e13939.

Maamrah, B., Pocsai, K., Bayasgalan, T., Csemer, A., **Pál, B.** (2022) KCNQ4 potassium channel subunit deletion leads to exaggerated acoustic startle reflex in mice. **Neuroreport 34:** 232-237.

Gönczi, M., Csemer, A., Szabó, L., Sztretye, M., Fodor, J., Pocsai, K., Szenthe, K., Keller-Pintér, A., Köhler, Z., Nánási, P., Szentandrássy, N., **Pál, B.**, Csernoch, L. (2022) Astaxanthin Exerts Anabolic Effects via Pleiotropic Modulation of the Excitable Tissue. **Int J Mol Sci 23:** 917.

Bayasgalan, T., Stupniki, S., Kovács, A., Csemer, A., Szentesi, P., Pocsai, K., Dionisio, L., Spitzmaul, G., **Pál, B.** (2021) Alteration of mesopontine cholinergic function by the lack of KCNQ4 subunit. **Front Cell Neurosci 26:** 15:707789.

Bayasgalan, T., Csemer, A., Kovács, A., Pocsai, K., **Pál, B.** (2021) Topographical organization of M-current on dorsal and median raphe serotonergic neurons. **Front Cell Neurosci 25:** 15: 614947.

Baksa, B., Kovács, A., Bayasgalan, T., Szentesi, P., Kőszeghy, Á., Szűcs, P., **Pál, B.** (2019) Characterization of functional subgroups among genetically identified cholinergic neurons in the pedunculopontine nucleus. **Cell Mol Life Sci 76:** 2799-2815.

GYÖRGY PANYI

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

My laboratory focuses on the electrophysiological properties of electrically non-excitable cells. We mainly study the physiological and pathophysiological role of voltage-gated ion channels, with a special emphasis on K^+ channels. One of the main goals of my research is the study of the pharmacological, biophysical and cell biology of the ion channels of immune cells. Voltage-gated K^+ channels maintain a membrane potential in these cells that allows efficient Ca^{2+} -dependent signaling pathways for antigen recognition. Among the ion channels, the role of the Kv1.3 K^+ channel stands out, but in the last decade our knowledge about the role of other K^+, Ca^{2+}, Na^+, H^+ and other channels has also expanded significantly. Disruption of the physiological activity of Kv1.3 channels may diminish or completely abolish the response of T cells to the antigen, thus, achieving immunosuppression.

SELECTED PUBLICATIONS

Naseem, M.U., Carcamo-Noriega, E., Beltran-Vidal, J., Borrego, J., Szanto,T.G., Zamudio, F.Z., Delgado-Prudencio, G., Possani, L.,D. **Panyi. G.** (2022) Cm28, a scorpion toxin having a unique primary structure, inhibits KV1.2 and KV1.3 with high affinity. **J Gen Physiol 154:** e202213146.

Csoti, A,. Del Carmen Najera Meza, R., Bogar, F., Tajti, G., Szanto, T.G., Varga, Z., Gurrola, G.B., Toth, G.K., Possani, L.D., **Panyi, G.** (2022) sVmKTx, a transcriptome analysis-based synthetic peptide analogue of Vm24, inhibits Kv1.3 channels of human T cells with improved selectivity. **Biochem pharmacol 199:** 115023.

Szanto, T.G,. Gaal, S., Karbat, I., Varga, Z., Reuveny, E., **Panyi, G.** (2021) Shaker-IR K+ channel gating in heavy water: Role of structural water molecules in inactivation. **J Gen Physiol 153:** e202012742.

Szanto, T.G., Zakany, F., Papp, F., Varga, Z., Deutsch, C.J., **Panyi, G.** (2020) The activation gate controls steady-state inactivation and recovery from inactivation in Shaker. **J Gen Physiol 152:** e20212591.

Meszaros, B., Papp, F., Mocsar, G., Kokai, E., Kovacs, K., Tajti, G., **Panyi, G.** (2020) The voltage-gated proton channel hHv1 is functionally expressed in human chorion-derived mesenchymal stem cells. **Sci Rep 10:** 7100.

ZOLTÁN PAPP

University of Debrecen
Faculty of Medicine
Department of Cardiology Division of Clinical Physiology

RESEARCH AREA

The cellular myocardial physiology laboratory, established in 2001 and unique in Hungary, provides the opportunity to study the mechanical properties of single myocardial cells obtained from human or experimental animal models of cardiovascular diseases. With the help of our sensitive mechanical measuring system, we can determine the contractile parameters of individual myocardial cells isolated from deep-frozen or even biopsy-derived myocardial tissues. Thus, the Ca2+-dependent isometric force generation of contractile proteins can be measured directly at the cellular level, and direct conclusions can be drawn about the kinetic characteristics of the actin-myosin cycle. In addition to cellular studies, the small size of the preparation (single isolated myocardial cell) allows the characterization of the composition of contractile proteins under control conditions and following enzymatic modifications (e.g., phosphorylation, degradation) or the induction of different model conditions. Thus, our experimental system is suitable for mapping cellular and subcellular changes during altered myocardial contractility in various human and experimental disease states.

SELECTED PUBLICATIONS

Bódi, B., Oláh, A., Mártha, L., Tóth, A., Radovits, T., Merkely, B., **Papp, Z.** (2021) Exercise-induced alterations of myocardial sarcomere dynamics are associated with hypophosphorylation of cardiac troponin I. **Reviews in Cardiovascular Medicine 22:** 1079-1085.

Bódi, B., Kovács, Á., Gulyás, H., Mártha, L., Tóth, A., Mátyás, C., Barta, B., Oláh, A., Merkely, B., Radovits, T., **Papp, Z.** (2021) Long-Term PDE-5A Inhibition Improves Myofilament Function in Left and Right Ventricular Cardiomyocytes through Partially Different Mechanisms in Diabetic Rat Hearts. **Antioxidants 10:** 1-13.

Bódi, B., Pilz, P., Mártha, L., Lang, M., Hamza, O., Fagyas, M., Szabó, P., Abraham, D., Tóth, A., Podesser, B., Kiss, A., **Papp, Z.** (2021) Alterations in ACE and ACE2 Activities and Cardiomyocyte Signaling Underlie Improved Myocardial Function in a Rat Model of Repeated Remote Ischemic Conditioning. **Int J Mol Sci 22:** 1-17.

Alvarado, G., Tóth, A., Csősz, É., Kalló, G., Dankó, K., Csernátony, Z., Smith, A., Gram, M., Akerström, B., Édes, I., Balla, G., **Papp, Z.**, Balla, J. (2020) Heme-Induced Oxidation of Cysteine Groups of Myofilament Proteins Leads to Contractile Dysfunction of Permeabilized Human Skeletal Muscle Fibres. **Int J Mol Sci 21:** 1-17.

Ruppert, M., Bódi, B., Korkmaz-Icöz, S., Loganathan, S., Jiang, W., Lehmann, L., Oláh, A., Barta, B., Sayour, A., Merkely, B., Karck, M., **Papp, Z.**, Szabó, G., Radovits, T. (2019) Myofilament Ca2+ sensitivity correlates with left ventricular contractility during the progression of pressure overload-induced left ventricular myocardial hypertrophy in rats. **J Mol Cell Cardio 129:** 208-218.

VALTER PÉTER PFLIEGLER

University of Debrecen
Faculty of Science and Technology
Institute of Biotechnology

RESEARCH AREA

The domestication, macro- and microevolution of Saccharomyces yeasts, especially with regard to the clades that colonize and infect humans, with the use of genomics and experimental evolution. In our group, we focus on the global diversity of the best-known and most commonly used yeast species, we define and compare the characteristics of the domesticated and wild groups of the species at the genome and phenotype levels. Certain clades of yeast are able to colonize humans and in rare cases, they can also cause infection. Thus, we are looking for the cause and modes of adaptations of isolates from human hosts by comparative studies and by using evolutionary experiments. We also use the knowledge gained to design new yeast probiotics.

SELECTED PUBLICATIONS

Imre, A., Kovács, R., Pázmándi, K., Nemes, D., Jakab, Á., Fekete, T., Rácz, H. V., Dóczi, I., Bácskay, I., Gácser, A., Kovács, K., Majoros, L., Farkas, Z., Pócsi, I., **Pfliegler, P. W.** (2021) Virulence factors and in-host selection on phenotypes in infectious probiotic yeast isolates (Saccharomyces 'boulardii'). **Journal of Fungi 7:** 746.

Rácz, H.V., Mukhtar, F., Imre, A., Rádai, Z., Gombert, A.K., Rátonyi, T., Nagy, J., Pócsi, I., **Pfliegler, W.P.** (2021) How to characterize a strain? Clonal heterogeneity in industrial Saccharomyces influences both phenotypes and heterogeneity in phenotypes. **Yeast 38:** 453-470.

Imre, A., Rácz, H.V., Antunovics, Zs., Rádai, Z., Kovács, R., Lopandic, K., Pócsi, I., **Pfliegler, W. P.** (2019): A new, rapid multiplex PCR method identifies frequent probiotic origin among clinical Saccharomyces isolates. **Microbiological Research 277:** 126298.

Pfliegler, W. P., Boros, E., Pázmándi, K., Jakab, Á., Zsuga, I., Kovács, R., Urbán, E., Antunovics, Zs., Bácsi, A., Sipiczki, M., Majoros, L., Pócsi, I. (2017) Commercial strain-derived clinical Saccharomyces cerevisiae can evolve new phenotypes without higher pathogenicity. **Molecular Nutrition & Food Research 61:** 1601099.

ZSUZSA SZONDY

University of Debrecen
Faculty of Dentistry
Department of Dental Biochemistry

RESEARCH AREA

Our research group is interested in understanding the mediobiological significance of the efferocytosis (clearance of dead cells) program. Every day 1 billion cells die in our body, mainly as part of the tissue cell turnover. But cells are dying also during infections, or tissue injury. Dead cells generated as part of the tissue turnover are cleared by tissue resident macrophages, while those generated during ipathological processes by bone marrow-derived macrophages. These cells not only engulf and degrade dead cells, but during efferocytosis an anti-inflammatory, tissue regenerating program is activated in them. If this program is disturbed, chronic inflammatory diseases and wound healing deficiencies develop. We are investigating efferocytosis in the thymus, where immature thymocytes develop, in skeletal muscle injury and the obese adipose tissue by using various genetically modified mice. Our aim is to treat chronic inflammatory diseases and wound healing more efficiently by understanding the elements of the efferocytosis program.

SZÖŐR ÁRPÁD

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

I am working on developing new generational immune and stem cell therapeutics against various types of solid tumors. Previously, I investigated the effectiveness of chimeric antigen receptor (CAR) expressing and/or bispecific T cell activating molecule (BiTE) secreting T, NK and mesenchymal stem cells on different solid tumor and leukemia models. In my current research, I am investigating and optimizing CAR and UniCAR expressing T cells that recognize the HER2 tumor-specific antigen, as well as CAR NK-92 cell lines in solid tumor models. In addition to these, I am investigating the therapeutic efficacy of the autoantigen recognizing domain expressing CAAR T cells in a murine scleroderma model.

SELECTED PUBLICATIONS

Csaplár, M., Szöllősi, J., Gottschalk, S., Vereb, G., **Szöőr, Á.** (2021) Cytolytic Activity of CAR T Cells and Maintenance of Their CD4+ Subset Is Critical for Optimal Antitumor Activity in Preclinical Solid Tumor Models. **Cancers (Basel) 17:** 4301.

Szöőr, Á., Szöllősi, J., Vereb, G. (2021) From antibodies to living drugs: quo vadis cancer immunotherapy? **Biol Futura 72:** 85-99.

Tóth, G., Szöllősi, J., Abken, H., Vereb, G., **Szöőr, Á.** (2020) A Small Number of HER2 Redirected CAR T Cells Significantly Improves Immune Response of Adoptively Transferred Mouse Lymphocytes against Human Breast Cancer Xenografts. **Int J Mol Sci 21:** 1039.

Szöőr, Á., Tóth, G., Zsebik, B., Szabó, V., Eshhar, Z., Abken, H., Vereb, G. (2020) Trastuzumab Derived HER2-specific CARs for the Treatment of Trastuzumab-Resistant Breast Cancer: CAR T Cells Penetrate and Eradicate Tumors That Are Not Accessible to Antibodies. **Cancer Lett 484:** 1-8.

Szöőr, Á., Vaidya, A., Velasquez, M., Mei, Z., Galvan, D., Torres, D., Gee, A., Heczey, A., Gottschalk, S. (2017) T Cell-Activating Mesenchymal Stem Cells as a Biotherapeutic for HCC. **Mol Ther Oncolytics 6:** 69-79.

MÓNIKA SZTRETYE

University of Debrecen
Faculty of Medicine
Department of Physiology

RESEARCH AREA

The musculoskeletal system is the active organ of movement; its main function is to move the elements that make up the body's skeleton in relation to each other, thereby changing the position of the body. The skeletal muscle is made up of skeletal muscle fibres, whose basic function is contraction in response to nerve command. In skeletal muscle, electro-mechanical coupling (ECC, Excitation-Contraction Coupling) is the conversion of an electrical signal (action potential) at the sarcolemma into a contraction response. Modifications of the finely regulated steps of ECC, such as ageing, oxidative stress, genetic causes can lead to severe muscle diseases.
The endocannabinoid system (ECS) is a widespread signalling system whose alteration is associated with an increasing number of human diseases. Increased ECS activity has been observed in degenerative muscle diseases such as Duchenne muscular dystrophy (DMD). Our current research investigates the role of skeletal muscle ECS: in the development of degenerative muscle diseases, in muscle function, in mitochondrial calcium homeostasis processes, and also its effects on regenerative processes.

SELECTED PUBLICATIONS

Kalkan, H., Panza, E., Pagano, E., Ercolano, G., Moriello, C., Piscitelli, F., **Sztretye, M.**, Capasso, R., Di, Marzo, V., Iannotti, F.A. (2023) Dysfunctional endocannabinoid CB1 receptor expression and signaling contribute to skeletal muscle cell toxicity induced by simvastatin. **Cell Death Dis 14:** 544.

Sztretye, M., Singlár, Z., Ganbat, N., Al-Gaadi, D., Szabó, K., Köhler, Z., Dux, L., Keller-Pintér, A., Csernoch, L., Szentesi, P. (2023) Unravelling the Effects of Syndecan-4 Knockdown on Skeletal Muscle Functions. **Int J Mol Sci 24:** 6933.

Singlár, Z., Ganbat, N., Szentesi, P., Osgonsandag, N., Szabó, L., Telek, A., Fodor, J., Dienes, B., Gönczi, M., Csernoch, L., **Sztretye, M.** (2022) Genetic Manipulation of CB1 Cannabinoid Receptors Reveals a Role in Maintaining Proper Skeletal Muscle Morphology and Function in Mice. **Int J Mol Sci 23:** 15653.

Singlár, Z., Szentesi, P., Fodor, J., Angyal, Á., Csernoch, L., **Sztretye, M.** (2021) Assessing the Potential of Nutraceuticals as Geroprotectors on Muscle Performance and Cognition in Aging Mice. **Antioxidants 10:** 1415.

Sztretye, M., Szabó, L., Dobrosi, N., Fodor, J., Szentesi, P., Almássy, J., Magyar, Z., Dienes, B., Csernoch, L. (2020) From Mice to Humans: an Overview of the Potentials and Limitations of Current Transgenic Mouse Models of Major Muscular Dystrophies and Congenital Myopathies. **Int J Mol Sci 21:** 8935.

ATTILA TÓTH

University of Debrecen
Faculty of Medicine
Department of Cardiology Division of Clinical Physiology

RESEARCH AREA

We deal with three areas of research in our laboratory. (1) High blood pressure affects one in three adults, but the cause is unknown in 90% of cases. The diameter of the blood vessels determines the tissue blood supply and blood pressure. We investigate the mechanisms of regulation of the vascular diameter, with particular reference to mechanisms that depend on temperature-dependent receptors and angiotensin peptides. (2) Heart failure is a high-mortality disease that is unfortunately common in Hungary. In our research, we investigate the mechanisms leading to heart failure and the mechanisms of action of new experimental drugs. (3) Cardiovascular disease is the leading cause of death. With proper medication, survival can be significantly improved. Nevertheless, less than half of patients are taking their medications properly. In addition, setting the right dose of drug is difficult and time consuming. In our research, we develop methods that are suitable for measuring the biochemical efficacy of drugs. This may make it possible to determine the optimal dose for a given patient after a simple blood draw.

SELECTED PUBLICATIONS

Fagyas, M., Bánhegyi, V., Úri, K., Enyedi, A., Lizanecz, E., Mányiné Siket, I., Mártha, L., Fülöp, G., Radovits, T., Pólos, M., Merkely, B., Kovács, Á., Szilvássy, Z., Ungvári, Z., Édes, I., Csanádi, Z. (...), **Tóth, A.** (2021) Changes in the SARS-CoV-2 cellular receptor ACE2 levels in cardiovascular patients: a potential biomarker for the stratification of COVID-19 patients. **GeroScience** [Epub ahead of print]

Bánhegyi, V., Enyedi, A., Fülöp, G., Oláh, A., Mányiné Siket, I., Váradi, C., Bottyán, K., Lódi, M., Csongrádi, A., Umar, M., Fagyas, M., Czuriga, D., Édes, I., Pólos, M., Merkely, B., Csanádi, Z., Papp, Z., Szabó, G., Radovits, T., Takács, I., **Tóth, A.** (2021) Human Tissue Angiotensin Converting Enzyme (ACE) Activity Is Regulated by Genetic Polymorphisms, Posttranslational Modifications, Endogenous Inhibitors and Secretion in the Serum, Lungs and Heart. **Cells 10:** 1708

Fagyas, M., Kertész, A., Mányiné Siket, I., Bánhegyi, V., Kracskó, B., Szegedi, A., Szokol, M., Vajda, G., Rácz, I., Gulyás, H., Szkibák, N., Rácz, V., Csanádi, Z., Papp, Z., **Tóth, A.**, Sipka, S. (2021) Level of the SARS-CoV-2 receptor ACE2 activity is highly elevated in old-aged patients with aortic stenosis: implications for ACE2 as a biomarker for the severity of COVID-19. **GeroScience 43:** 19-29.

Fülöp, G., Oláh, A., Csípő, T., Kovács, Á., Pórszász, R., Veress, R., Horváth, B., Nagy, L., Bódi, B., Fagyas, M., Helgadottir, S., Bánhegyi, V., Juhász, B., Bombicz, M., Priksz, D., Nánási, P., Merkely, B., Édes, I., Csanádi, Z., Papp, Z., Radovits, T., **Tóth, A.** (2021) Omecamtiv mecarbil evokes diastolic dysfunction and leads to periodic electromechanical alternans. **Basic Res Cardiol 116:** 24

Tóth, A., Fagyas, M., Papp, Z., Édes, I.: **Dilution based inhibition assay.** [szabadalom]

DÁNIEL TÖRŐCSIK

University of Debrecen
Faculty of Medicine
Department of Dermatology

RESEARCH AREA

The Group is a great opportunity for all who are interested in everyday skin problems such as acne and want to have a knowledge that can be translated into the real world. Our aim is to provide a knowledge that the participant could benefit from not only throughout the university years but also in post-doctoral fellowships. Moreover, we offer an exciting field of research for anyone who is interested in dermatology or in the cosmetic industry. In the nearly 10 years that we spent with research on how sebocytes moisturize the skin and how their altered lipid production leads to the development of acne. We also revealed that the changing sebaceous gland density at different parts of the body could be behind the site-specific appearance of some inflammatory skin diseases. Based on these findings we are currently investigating how sebocyte derived lipids could be therapeutically applied not only to treat dry skin but also inflammatory diseases.

SELECTED PUBLICATIONS

Seiringer, P., Hillig, C., Schäbitz, A., Jargosch, M., Pilz, A.C., Eyerich, S., Szegedi, A., Sochorová, M., Gruber, F., Zouboulis, C.C., Biedermann, T., Menden, M.P., Eyerich, K., **Törőcsik, D.** (2024) Spatial transcriptomics reveals altered lipid metabolism and inflammation-related gene expression of sebaceous glands in psoriasis and atopic dermatitis. **Front Immunol 15:** 1334844.

Kovács, D., Camera, E., Póliska, S., Cavallo, A., Maiellaro, M., Dull, K., Gruber, F., Zouboulis, C.C., Szegedi, A., **Törőcsik, D.** (2023) Linoleic Acid Induced Changes in SZ95 Sebocytes-Comparison with Palmitic Acid and Arachidonic Acid. **Nutrients 15:** 3315.

Dull, K., Lénárt, K., Dajnoki, Z., Póliska, S., Uchiyama, E., Hendrik, Z., Szegedi, A., **Törőcsik, D.** (2023) Barrier function-related genes and proteins have an altered expression in acne-involved skin. **J Eur Acad Dermatol Venereol 37:** 1415-1425.

Dull, K., Fazekas, F., Deák, D., Kovács, D., Póliska, S., Szegedi, A., Zouboulis, C.C, **Törőcsik, D.** (2021) miR-146a modulates TLR1/2 and 4 induced inflammation and links it with proliferation and lipid production via the indirect regulation of GNG7 in human SZ95 sebocytes. **Sci Rep 11:** 21510.

Törőcsik, D., Fazekas, F., Póliska, S., Gregus, A., Janka, E.A., Dull, K., Szegedi, A., Zouboulis, C.C., Kovács, D. (2021) Epidermal Growth Factor Modulates Palmitic Acid-Induced Inflammatory and Lipid Signaling Pathways in SZ95 Sebocytes. **Front Immunol 12:** 600017.

GYÖRGY TRENCSÉNYI

University of Debrecen
Faculty of Medicine
Division of Nuclear Medicine

RESEARCH AREA

With the development of molecular oncology, more and more molecular targets appear, which led to the need for new and target-specific radiopharmaceuticals. During the preclinical studies of nuclear medicine, the binding of a radionuclide-labelled molecule is examined with the PET (Positron Emission Tomography) imaging equipment. These imaging devices provide quantitative biological information and images of the internal state of the body in a non-invasive manner with high sensitivity. Our main research area is the development of radiopharmaceuticals that can efficiently identify malignancies and tumor-associated processes (e.g. neo-angiogenesis) in the living organism. The subject of our research is the development of radionuclides, which can be diagnostic or therapeutic (e.g. alpha emitter), as well as the synthesis of the targeting molecule, which binds to a receptor expressed by a tumor.

SELECTED PUBLICATIONS

Farkasinszky, G., Dénes, N., Rácz, S., Kis, A., Péli-Szabó, J., Opposits, G., Veres, G.,Balkay, L., Kertész, I., Mező, G., Hunyadi, J., **Trencsényi, G.** (2022) In Vivo imaging of Ischemia/Reperfusion-mediated Aminopeptidase N Expression in Surgical Rat Model Using Ga-NOTA-c(NGR). **In Vivo 36:** 657-666.

Kis, A., Dénes, N., Péli-Szabó, J., Arató, V., Beke, L., Matolay, O., Enyedi, K., Méhes, G., Mező, G., Bai, P., Kertész, I., **Trencsényi, G.** (2021) In Vivo Molecular Imaging of the Efficacy of Aminopeptidase N (APN/CD13) Receptor Inhibitor Treatment on Experimental Tumors Using 68Ga-NODAGA-c(NGR) Peptide. **BioMed Res Inter 2021(3):** 6642973.

Kis, A., Dénes, N., Péli-Szabó, J., Arató, V., Jószai, I., Enyedi, K., Rácz, S., Garai, I., Mező, G., Kertész, I., **Trencsényi, G.** (2020) In vivo assessment of aminopeptidase N (APN/CD13) specificity of different 68 Ga-labelled NGR derivatives using PET/MRI imaging. **Int J Pharm 589:** 119881.

Kis, A., Péli-Szabó, J., Dénes, N., Vágner, A., Nagy, G., Garai, I., Fekete, A., Szikra, D., Hajdu, I., Matolay, O., Méhes, G., Mező, G., Kertész, I., **Trencsényi, G.** (2020) In vivo Imaging of Hypoxia and Neoangiogenesis in Experimental Syngeneic Hepatocellular Carcinoma Tumor Model Using Positron Emission Tomography. **Biomed Res Int 2020(18):** 4952372.

Trencsényi, G., Kis, A., Péli-Szabó, J., Ráti, Á., Csige, K., Fenyvesi, É., Szente, L., Malanga, M., Méhes, G., Emri, M., Kertész, I., Vecsernyés, M., Fenyvesi, F., Hajdu, I. (2020) In vivo preclinical evaluation of the new 68Ga-labeled beta-cyclodextrin in prostaglandin E2 (PGE2) positive tumor model using positron emission tomography. **Int J Pharm 576(4):** 118954.

GYÖRGY VÁMOSI

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

1. Interleukin-2 and -15 receptor function
Interleukin-2 and -15 are cytokines that play a key role in the regulation of T lymphocyte life processes. IL-2 is responsible for the expansion of T cells clones specific for a pathogen, and for the apoptotic cell death of T cells after elimination of the infection. It also plays an important role in maintaining peripheral immune tolerance. IL-15, on the other hand, inhibits apoptosis and is responsible for the long-term survival of memory T cells and thus for the development of immunological memory. Both cytokines and their receptors play a role in lymphoma and autoimmune diseases and in the anti-cancer immune response, thus serving as drug targets or adjuvants.
Our aims:
a) To elucidate the molecular basis of immunological memory by investigating the appearance and role of the IL-15 receptor in the cell nucleus.
b) We have shown that the IL-2 receptor is preassembled and signals inside the cell, and that this intracrine signalling explains the ineffectiveness of antilymphoma antibody therapies. We are investigating the mechanism of intracrine signalling and would like to extend the investigation of this phenomenon to additional membrane receptors.

2. Investigating the function of nuclear receptors
Nuclear receptors are dimeric transcription factors that activate in the presence of a ligand and inhibit in the absence of their ligand the transcription of their target genes. They regulate many biological processes, such as cell division, differentiation, cell death, metabolism and immune responses. Therefore, about 10% of all prescribed drugs target nuclear receptors. The repression or activation complex is composed of the nuclear receptor dimer, the ligand(s), the corepressor or coactivator protein and the DNA response element located in the regulatory region of the target gene. We study their assembly using modern fluorescence microscopy and genomic methods. Based on our previous studies, we have demonstrated the competition of nuclear receptors for genomic binding sites or for a common heterodimerization partner, which may explain the side effects of some ligand therapies targeting nuclear receptors.

SELECTED PUBLICATIONS

Kenesei, Á., Volkó, J., Szalóki, N., Mocsár, G., Jambrovics, K., Balajthy, Z., Bodnár, B., Tóth, K., Waldmann, T.,A., **Vámosi, G.** (2021) IL-15 trans-presentation is an autonomous, antigen independent process. **J Immunol. 10:** 2489-2500.

Fadel, L., Rehó, B., Volkó, J., Bojcsuk, D., Kolostyák, Z., Nagy, G., Müller, G., Simándi, Z., Hegedüs, É., Szabó, G., Tóth, K., Nagy, L., **Vámosi, G.** (2020) Agonist binding directs dynamic competition among nuclear receptors for heterodimerizationwith retinoid X receptor. **J Biol Chem. 295:** 10045-10061.

ZOLTÁN VARGA

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

My main research profile is the study of plasma membrane ion channels, especially the structure-function relationship and pharmacological properties of voltage-gated K+ (Kv) channels. We have studied the function of human T cell Kv channels with non-peptide and scorpion-venom-derived peptide toxin inhibitors. We have identified numerous peptide toxin inhibitors of these channels and performed their biophysical characterization and selectivity profiling. We have made targeted mutations in one such toxin to improve its selectivity while maintaining its high affinity for potential therapeutic use. We also study Kv channel gating at the molecular level, such as the communication between the voltage-sensing and the pore domains, and the factors that may influence this, like the cholesterol content of the membrane. For that purpose I introduced the Voltage-Clamp Fluorometry technique to our lab. Our new research focus is the physiological and pathophysiological role of the Hv1 proton channel, e.g. in the calcification of vascular smooth muscle cells, and the development of inhibitors of this channel with therapeutic potential.

SELECTED PUBLICATIONS

Fehér, Á., Pócsi, M., Papp, F., Szántó, G., Csóti, Á., Fejes, Z., Nagy, B., Nemes, B., **Varga, Z.** (2022) Functional Voltage-Gated Sodium Channels Are Present in the Human B Cell Membrane. **Cells 7:** 1225.

Varga, Z., Tajti, G., Panyi, G. (2021) The Kv1.3 K+ channel in the immune system and its „precision pharmacology" using peptide toxins. **Biol Futura 72:** 75-83.

Zákány, F., Kovács, T., Panyi, G., **Varga, Z.** (2020) Direct and indirect cholesterol effects on membrane proteins with special focus on potassium channels. **Biochim Biophys ActaMol Cell Biol Lipids 1865:** 158706.

Zákány, F., Pap, P., Papp, F., Kovács, T., Nagy, P., Péter, M., Szente, L., Panyi, G., **Varga, Z.** (2019) Determining the target of membrane sterols on voltage-gated potassium channels. **Biochim Biophys Acta Mol Cell Biol Lipids 1864:** 312-325.

GYÖRGY VEREB

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

Developing and optimizing novel therapies against solid tumors and autoimmune diseases based on genetically reprogrammed immune cells, particularly using chimeric antigen receptors (CAR) and chimeric autoantigen receptors (CAAR) in T and NK cells. As a mechanistic background, the molecular assembly and function of immune synapses recruited by various CARs that contain versatile costimulatory domains and/or drive additional signaling pathways through other ectopic genes or RNA interference is also being explored.

Exploitation for diagnosis, prognosis, or therapeutic targeting of the interactions of receptor tyrosine kinases and integrins. Developing microscopic and other spectroscopic/cytometric methods for the quantitative analysis of molecular interactions and signaling processes in situ in cells and tissues with a view to migrate these methods to histopathology diagnostics.

Understanding the molecular dynamics of the corneal limbal stem cell niche, defining non-invasive in vivo imaging modalities that correlate with age or disease-related limbal stem cell deficiency (LSCD) and creating improved methodologies for regenerating corneas with LSCD (in cooperation with the Department of Ophthalmology, University of Debrecen).

SELECTED PUBLICATIONS

Csaplár, M., Szöllősi, J., Gottschalk, S., **Vereb, G***., Szöőr, Á*. (2021) Cytolytic Activity of CAR T Cells and Maintenance of Their CD4+ Subset Is Critical for Optimal Antitumor Activity in Preclinical Solid Tumor Models. **Cancers 13:** 1-19.

Szöőr, Á., Tóth, G., Zsebik, B., Szabó, V., Eshhar, Z., Abken, H., **Vereb, G.** (2020) Trastuzumab Derived HER2-specific CARs for the Treatment of Trastuzumab-Resistant Breast Cancer: CAR T Cells Penetrate and Eradicate Tumors That Are Not Accessible to Antibodies. **Cancer Lett 484:** 1-8.

Tóth, G., Szöőr, Á., Simon, L., Yarden, Y., Szöllősi, J., **Vereb, G.** (2016) The combination of trastuzumab and pertuzumab administered at approved doses may delay development of trastuzumab resistance by additively enhancing antibody-dependent cell-mediated cytotoxicity. **mAbs 8:** 1361-1370.

Petrás, M., Lajtos, T., Friedländer, E., Klekner, Á., Pintye, É., Feuerstein, B., Szöllősi, J., **Vereb, G.** (2013) Molecular interactions of ErbB1 (EGFR) and integrin-β1 in astrocytoma frozen sections predict clinical outcome and correlate with Akt-mediated in vitro radioresistance. **Neuro-Oncology 15:** 1027-1040.

Takács, L., Tóth, E., Losonczy, G., Szántó, A., Bahr-Ivacevic, T., Benes, V., Berta, A., **Vereb, G.** (2011) Differentially Expressed Genes Associated with Human Limbal Epithelial Phenotypes: New Molecules That Potentially Facilitate Selection of Stem Cell-Enriched Populations. Invest. **Ophthalmol Vis Sci 52:** 1252-1260.

LÁSZLÓ VIRÁG

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

The main profile of our research group is to investigate the relationship between oxidative stress and poly-ADP-ribosylation of proteins in different cellular systems and animal models. A common feature of living organisms is the generation of various free radicals and other reactive intermediates from the oxygen consumed during cellular respiration. These oxygen derivatives may have an important cellular regulatory role, but in pathological conditions, such as inflammation, ischemia-reperfusion injuryn (e.g. in myocardial infarction or stroke), their overproduction cannot be counteracted by the antioxidant system and they cause tissue damage. In addition to the peroxidation of lipids and the oxidation of proteins, oxidative damage also leads to DNA breaks, which are mainly recognized by the enzyme poly(ADP-ribose) polymerase-1 (PARP1), which marks DNA breaks with NAD-derived ADP-ribose polymers to initiate DNA repair. Through its role in DNA damage sensing, the enzyme is a survival factor, but when DNA damage is irreparably severe, PARP1 overactivation triggers a poly(ADP-ribose)-dependent cell death pathway termed parthanathos. In addition to this dual role in cell death, PARP1 also has several functions independent of DNA breakage e.g. in transcriptional regulation. ADP-ribosylation by the 17-members of the PARP enzyme family regulates almost all cellular functions. Our research group is working on diverse and multifaceted research projects, including the study of redox balance and the role of PARP enzymes in tissue macrophages, therapeutic resistance of tumor cells, cell death models, inflammatory processes and tumor-host interactions. An integral part of our research program is the identification of molecules with high-throughput screening that interfere with the above processes.

SELECTED PUBLICATIONS

Garcia,Soriano, F*.,**Virág, L*.**, Jagtap, P., Szabó. E., Mabley, JG., Liaudet, L., Marton, A., Hoyt, DG., Murthy, KG.,Salzman, AL., Southan, GJ., Szabó, C. (2001) Diabetic endothelial dysfunction: the role of poly(ADP-ribose) polymerase activation. **Nat Med. 7:** 108-13.(*shared first authors)

Erdély,i K., Bai, P., Kovács, I., Szabó, E., Mocsár, G., Kakuk, A., Szabó, C., Gergely, P., **Virág, L.** (2009) Dual role ofpoly (ADP-ribose) glycohydrolase in the regulation of cell death in oxidatively stressed A549 cells. **FASEB J 23:** 3553-63.

Géhl, Z., Bakondi, E., Resch, M.D., Hegedűs, C., Kovács, K., Lakatos, P., Szabó, A., Nagy,Z., **Virág, L.** (2016) Diabetes-induced oxidative stress in the vitreous humor. **Redox Biol 9:** 100-103.

Kiss, A., Ráduly, A.P., Regdon, Z., Polgár, Z., Tarapcsák, S., Sturniolo, I., El-Hamoly, T., **Virág, L*.**, Hegedűs, C*. (2020) Targeting Nuclear NAD+ Synthesis Inhibits DNA Repair, Impairs Metabolic Adaptation and IncreasesChemosensitivity of U-2OS Osteosarcoma Cells. **Cancers 12:** 1180. (*shared corresponding authors)

Regdon, Z., Demény, M.A., Kovács, K., Hajnády, Z., Nagy-Pénzes, M., Bakondi, E., Kiss, A., Hegedűs, C., **Virág, L.** (2021) High-content screening identifies inhibitors of oxidative stress-induced parthanatos: cytoprotective andanti-inflammatory effects of ciclopirox. **Br J Pharmacol 178:** 1095-1113.

FLORINA ZÁKÁNY

University of Debrecen
Faculty of Medicine
Department of Biophysics and Cell Biology

RESEARCH AREA

In Parkinson's disease, the progressive neuronal cell death is mainly mediated by the pathological activation of microglial cells. The voltage-gated potassium channel KV1.3 was shown to play a crucial role in this process due to a selective increase in its expression and its disease-specific phosphorylation. We found that these channels are located and phosphorylated in specific membrane microdomains. Since KV1.3 also has numerous physiological functions, such as in lymphocyte activation, fewer side effects are expected by targeting its inhibitor to these disease-specific membrane microdomains. By hampering the KV1.3-dependent pathological microglia activation with the targeted inhibitor, the amount of inflammatory cytokines produced and the rate of consequent neuronal death can be decreased. Functional consequences of KV1.3 in Parkinson's disease are investigated by molecular biological and immunological methods, confocal microscopy and flow cytometry in mouse microglial cells. To examine the effects of membrane lipids on KV1.3 gating we use two-electrode voltage-clamp fluorometry, with which the voltage-sensor and pore domains of the channel can be tracked simultaneously.

SELECTED PUBLICATIONS

Kovacs, T., Kurtan, K., Varga, Z., Nagy, P., Panyi, G., **Zakany, F.** (2023) Veklury® (remdesivir) formulations inhibit initial membrane-coupled events of SARS-CoV-2 infection due to their sulfobutylether-β-cyclodextrin content. **Br J Pharmacol 180(16):** 2064–2084.

Zakany, F., Mandity, I., Varga, Z., Panyi, G., Nagy, P., Kovacs, T. (2023) Effect of the lipid landscape on the efficacy of cell-penetrating peptides. **Cells 12:** 1700.

Kovacs,T., Nagy, P., Panyi, G., Szente, L., Varga, Z., **Zakany, F.** (2022) Cyclodextrins: Only Pharmaceutical Excipients or Full-Fledged Drug Candidates? **Pharmaceutics 14:** 2559.

Kovacs, T., Sohajda, T., Szente, L., Nagy, P., Panyi, G., Varga, Z.,* **Zakany, F.*** (2021) Cyclodextrins exert a ligand-like current inhibitory effect on the KV1.3 ion channel independent of membrane cholesterol extraction. **Front Mol Biosci 8:** 735357. *Contributed equally

Zakany, F.,* Kovacs, T.,* Panyi, G., Varga, Z. (2020) Direct and indirect cholesterol effects on membrane proteins with special focus on potassium channels. **Biochim Biophys Acta Mol Cell Biol Lipids 1865:** 158706. *Contributed equally

DEBRECEN
SZENT-GYÖRGYI JUNIOR MENTORS

MIKLÓS BEGE

University of Debrecen
Faculty of Pharmacy
Department of Pharmaceutical Chemistry

RESEARCH AREA

Synthesis of arteficial carbohydrate- and nucleoside analogues, using primarly radical thiol-ene coupling and reductive amination cyclization methods. Synthesis of new type of nucleic acids analogues e.g. cysteinyl nucleic acids, containing oligocysteine backbone instead of the natural sugar-phosphate motif. Developing new nucleoside analogs with antiviral, cytotoxic and antiprotozoa effects. Synthesis of new, fluorine containing morpholinos, with reductive amination, radical perfluoroalkyl iodode addition or N-trifluoromethylation (via dithiocarbamate). Evaluation of the Robinson-Schöpf reaction of nucleoside dialdehydes with (among others) biogene amines such as triptamine, dopamine etc. Synthesis of modified ascorbic acid derivatives.

SELECTED PUBLICATIONS

Bege, M., Singh, V., Sharma, N., Debreczeni, N., Bereczki, I., Poonam, Herczegh, P., Rathi, B., Singh, S., Borbás, A. (2023) In vitro and in vivo antiplasmodial evaluation of sugar-modified nucleoside analogues. **Sci Rep 13:** 12228.

Godoy, A. S., Nakamura, A. M., Douangamath, A., Song, Y., Noske, G. D., Gawriljuk, V. O., Fernandes, R.S., Pereira, H.D.M., Oliveira, K.I.Z., Fearon, D., Dias, A., Krojer, T., Fairhead, M., Powell, A., Dunnet, L., Brandao-Neto, J., Skyner, R., Chalk, R., Bajusz, D., **Bege, M.**, Borbás, A., Keserű, G.M., von Delft, F., Oliva, G. (2023) Allosteric regulation and crystallographic fragment screening of SARS-CoV-2 NSP15 endoribonuclease. **Nucleic Acids Res 51:** 5255-5270.

Bege, M., Kiss, A., Bereczki, I., Hodek, J., Polyák, L., Szemán-Nagy, G., Naesens, L., Weber, J., Borbás, A. (2022) Synthesis and Anticancer and Antiviral Activities of C-2′-Branched Arabinonucleosides. **Int J Mol Sci 23:** 12566.

Bege, M., Borbás, A. (2022) The Medicinal Chemistry of Artificial Nucleic Acids and Therapeutic Oligonucleotides. **J Pharm 15:** 909.

Bege, M., Bereczki, I., Molnár, D. J., Kicsák, M., Pénzes-Daku, K., Bereczky, Z., Ferenc, G., Kovács, L., Herczegh, P., Borbás, A. (2020) Synthesis and oligomerization of cysteinyl nucleosides. **Org Biomol Chem 18:** 8161-8178.

MÁTÉ ÁGOSTON DEMÉNY

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

Regulation of signaling pathways is largely achieved by dynamic chemical modification of proteins. The focus of our research lies on protein modifications through ADP-ribosylation during interaction between tumors and the immune system. As of present, one in six deaths worldwide is still due to malignant tumors. Today's medicine is pinning its best hopes on targeted molecular therapy and immunotherapy to fight cancer. An effective immune response can, indeed, eradicate malignant cells and curb metastasis. However, tumors have a number of processes that inhibit immune cell function. One of the most abundant cells in the tumor stroma are macrophages (Mφ), phagocytes that are part of the innate immune system and also play an important role in directing the adaptive immune response. Paradoxically, their presence in the tumor is usually associated with a poor prognosis, as their interaction with tumor cells results in the acquisition of a phenotype that enhances tumor vascularisation, cancer cell proliferation and resistance to chemotherapy. Both others' and our own preliminary results suggest that protein ADP-ribosylation events are involved in this reprogramming of Mφs. In the laboratory, we are using proteomic methods to identify ADP-ribosylome changes in Mφs as they switch phenotype in association with tumor cells. We are using 2D and 3D tumor cell-Mφ co-culture models to study this. We aim to identify the signaling proteins, transcription factors, metabolic enzymes that undergo modification and the ADP-ribosyltransferase enzymes responsible for their modification. We envision that targeted interference with the identified signaling pathways by manipulating ADP-ribosylation will alter the behavior of tumor Mφs in a favorable direction, which may provide the basis for new cancer therapies.

SELECTED PUBLICATIONS

Guti, E., Regdon, Z., Sturniolo, I., Kiss, A., Kovács, K., **Demény, M.**, Szöőr, Á., Vereb, G., Szöllősi, J., Hegedűs, C., Polgár, Z., Virág, L. (2022) The multitargeted receptor tyrosine kinase inhibitor sunitinib induces resistance of HER2 positive breast cancer cells to trastuzumab-mediated ADCC. **Cancer Immunol Immunother.**

Demény, M,.A., Virág, L. (2021) The PARP Enzyme Family and the Hallmarks of Cancer Part 1. Cell Intrinsic Hallmarks. **Cancers 13:** 2042.

Demény, M,.A., Virág, L. (2021)The PARP Enzyme Family and the Hallmarks of Cancer Part 2: Hallmarks Related to Cancer Host Interactions. **Cancers 13:** 2057.

Regdon, Z., **Demény, M,.A.,** Kovács, K., Hajnády, Z., Nagy-Pénzes, M., Bakondi, E., Kiss, A., Hegedűs, C., Virág, L. (2021) High-content screening identifies inhibitors of oxidative stress-induced parthanatos: cytoprotective and anti-inflammatory effects of ciclopirox. **Br J Pharmacol 178:** 1095-1113.

Sharma, R.*, **Demény, M.***, Ambrus, V., Király, S.B., Kurtán, T., Gatti-Lafranconi, P., Fuxreiter, M. (2019) Specific and Fuzzy Interactions Cooperate in Modulating Protein Half-Life. **J Mol Biol 431:** 1700-1707.

ENDRE KÓKAI

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

Studying the functional interaction between immune cells and tumour cells. Our research involves the generation of chimera antigen receptor-expressing macrophage (CAR-M) cells by lentiviral transduction that efficiently kill Her2+ tumour cells. We use THP-1 monocyte-derived cells to express CARs. Our primary objective is to optimize monocyte-CAR-M differentiation. Subsequently, we polarize the differentiated CAR-M cells into M1 phenotypic macrophages. The tumour killing ability of CAR-M cells will be studied using high-throughput confocal microscopy in a live cell model.

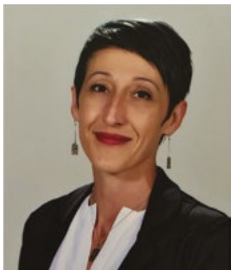
SELECTED PUBLICATIONS

Skopál, A., Kéki, T., Tóth, PÁ., Csóka, B., Koscsó, B., Német, ZH., Antonioli, L., Ivessa, A., Ciruela, F., Virág, L., Haskó, Gy., **Kókai, E.** (2022) Cathepsin D interacts with adenosine A2A receptors in mouse macrophages to modulate cell surface localization and inflammatory signalling. **J Biol Chem 298:** 101888.

Mészáros, B., Papp, F., Mocsár, G., **Kókai, E.**, Kovács, K., Tajti, G., Panyi, G. (2020) The voltage-gated proton channel hHv1 is functionally expressed in human chorion-derived mesenchymal stem cells. **Sci Rep 10:** 7100.

Hegedüs, É., **Kókai, E.**, Nánási, P., Imre, L., Halász, L., Jossé, R., Antunovics. Zs., Webb, MR., Hage, AE., Pommier, Y., Székvölgyi, L., Dombrádi, V., Szabó, G. (2018) Endogenous single-strand DNA breaks at RNA polymerase II promoters in Saccharomyces cerevisiae. **Nucleic Acids Res 46:** 10649-10668.

Csóka, B., Törő, G., Vindeirinho, J., Varga, ZV., Koscsó, B., Németh, ZH., **Kókai, E.**, Antonioli, L., Suleiman, M., Marchetti, P., Cseri, K., Deák, Á., Virág, L., Pacher, P., Bai, P., Haskó, G. (2017) A2A adenosine receptors control pancreatic dysfunction in high-fat-diet induced obesity. **FASEB J 31:** 4985-4997.



KATALIN KOVÁCS

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

Development of high throughput screening methods and molecular library screening to identify compounds that influence autophagy and other biological processes. Molecule library screening allows the investigation of existing drugs for new therapeutic purposes (drug repurposing). Our goal is to detect compounds that boost cancer cell elimination. The student will perform Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) assays. ADCC involves bridging target cells (e.g. virus-infected or cancer cells) and effector cells [e.g. natural killer (NK) cells or macrophages] with an antibody. The latter binds specifically to a cell surface antigen on the target cell while the constant region (Fc fragment) binds to the Fc receptor on the effector cells. We plan to set up assays for the quantification of cancer cell killing by NK cells and to perform high-content screening to identify ADCC enhancing drug candidates from drug libraries.

SELECTED PUBLICATIONS

Guti, E., Regdon, Z., Sturniolo, I., Kiss, A., **Kovács, K.**, Demény, M., Szöőr, Á., Vereb, G., Szöllősi, J., Hegedűs, C., Polgár, Z., Virág, L. (2022) The multitargeted receptor tyrosine kinase inhibitor sunitinib induces resistance of HER2 positive breast cancer cells to trastuzumab-mediated ADCC. **Cancer Immunol Immunother**

Regdon, Z., Robaszkiewicz, A., **Kovács, K.,** Rygielska, Ż., Hegedűs, C., Bodoor, K., Szabó, É., Virág, L. (2019) LPS protects macrophages from AIF-independent parthanatos by downregulation of PARP1 expression, induction of SOD2 expression, and a metabolic shift to aerobic glycolysis. **Free Radic Biol Med 131:** 184-196.

Kovács, K., Erdélyi, K., Hegedus, Cs., Lakatos, P., Regdon, Zs., Bai, P., Haskó, Gy., Szabó, É., Virág, L. (2012) Poly(ADP-ribosyl)ation is a survival mechanism in cigarette smoke-induced and hydrogen peroxide-mediated cell death. **Free Radic Biol Med 53:** 1680-8.

EDIT MIKÓ

University of Debrecen
Faculty of Medicine
Department of Medical Chemistry

RESEARCH AREA

Changes in the composition of the microbiome occurring during neoplasia is termed oncobiosis and the transformed microbiome is the oncobiome. Oncobiosis itself cannot induce tumors, but can promote tumor growth and metastasis formation. The oncobiome supports a set of cancer hallmarks, including avoidance of immune destruction, activation of invasion and metastasis, induction of inflammation and angiogenesis, and deregulation of cellular energetics.

Bacteria can secrete metabolites that either exert their effects locally or through the circulation reach distantly located cancer cells and influence their behavior. We identified several cytostatic bacterial metabolites in breast cancer. Bacterial metabolites are very diverse in terms of their chemical structure and include secondary bile acids that play a role in carcinogenesis. In breast cancer, secondary bile acids induce oxidative stress, reprogram cellular metabolism, leading to cytostasis, inhibition of the epithelial-mesenchymal transition and metastasis. Bacterial biosynthesis of bile acids is reduced early in breast cancer. The metabolite activated pathways are protective in breast cancer, decreased expression of markers involved in these pathways are associated with cancer progression and poor clinical prognosis. In our research the role of bile acids in carcinogenesis is primarily studied in breast cancer and pancreatic adenocarcinoma.

SELECTED PUBLICATIONS

Schwarcz, S., Kovács, P., Kovács, T., Ujlaki, G., Nyerges, P., Uray, K., Bai, P., **Mikó, E.** (2023) The pro- and antineoplastic effects of deoxycholic acid in pancreatic adenocarcinoma cell models. **Mol Biol Rep 50:** 5273-5282.

Režen, T., Rozman, D., Kovács, T., Kovács, P., Sipos, A., Bai, P., **Mikó, E.** (2022) The role of bile acids in carcinogenesis. **Cell Mol Life Sci 79:** 243.

Kovács, T, **Mikó, E.**, Ujlaki, G., Yousef, H., Csontos, V., Uray, K., Bai, P. (2021) The involvement of oncobiosis and bacterial metabolite signaling in metastasis formation in breast cancer. **Cancer Metastasis Rev 40:** 1223-1249.

Kovács, P., Csonka, T., Kovács, T., Sári, Z., Ujlaki, G., Sipos, A., Karányi, Z,, Szeőcs, D., Hegedűs, C., Uray, K., Jankó, L., Kiss, M,, Kiss, B., Laoui, D., Virág, L., Méhes, G., Bai, P., **Mikó, E.** (2019) Lithocholic Acid, a Metabolite of the Microbiome, Increases Oxidative Stress in Breast Cancer. **CANCERS (Basel). 11:** 1255.

Mikó, E., Vida, A., Kovács, T., Ujlaki, Gy., Trencsényi, Gy., Márton, J., Sári, Zs., Kovács,P., Boratkó, A., Hujber, Z., Csonka, T., Antal-Szalmás, P., Watanabe, M., Gombos, I., Csoka,B., Kiss, B., Vígh, L., Szabó, J., Méhes, G., Sebestyén, A., Goedert, JJ., Bai, P. (2018) Lithocholic acid, a bacterial metabolite reduces breast cancer cell proliferation and aggressiveness. **Biochimica et Biophysica Acta-Bioenergetics 1859:** 958-974.

DEBRECEN
SZENT-GYÖRGYI STUDENTS

1ST YEAR STUDENTS

EMÍLIA KOVÁCS

National Academy of Scientist Education, 1st year
University of Debrecen
Faculty of Medicine,1st year

Szent-Györgyi Mentor: Endre Károly Kristóf
Junior mentor: Arianti Rini
Theme of research: Examination of the molecular mechanism of thermogenesis in brown and beige adipose depots
Language: English/advanced

HENRIETTA PÉTER-PAKÓ

National Academy of Scientist Education, 1st year
University of Debrecen
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Zsuzsa Bagoly
Theme of research: Complex hemostasis investigations in patients with hemorrhagic stroke
Language: English/proficiency

ISTVÁN RÉVÉSZ

National Academy of Scientist Education, 1st year
University of Debrecen
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Péter Bay
Theme of research: Genetically modified macrophages for tumor therapy
Language: English/proficiency

LEVENTE SZOLYKA

National Academy of Scientist Education, 1st year
University of Debrecen
Faculty of Medicine, 1st year

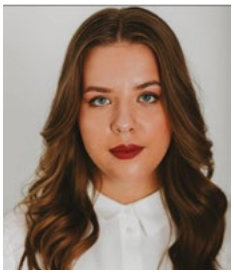
Szent-Györgyi Mentor: György Vámosi
Theme of research: The effect of dipole potential on the signalling efficiency of the interleukin-2 receptor
Language: German/intermediate

ZSIGMOND VIZI

National Academy of Scientist Education, 1st year
University of Debrecen
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Zoltán Varga
Theme of research: The role of voltage-gated sodium channels in breast carcinoma
Language: English/advanced

2ND YEAR STUDENTS



TÍMEA INGRID BÍRÓ

National Academy of Scientist Education, 2nd year
University of Debrecen
Faculty of Science and Technology, 2nd year

Szent-Györgyi Mentor: Péter Bay
Junior mentor: Edit Mikó
Specialization: Role of bacterial metabolites in breast tumours.
Language: English/proficiency Germany/intermediate, Romanian/proficiency

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

In several carcinomas, including pancreatic carcinoma, the composition of the local microbiome changes in multiple compartments, a phenomenon referred to as dysbiosis or oncobiosis. The primary objective of my research is to investigate the effects of secondary bile acids (lithocholic acid-LCA, ursodeoxycholic acid-UDCA, deoxycholic acid-DCA) as microbial metabolites on human pancreatic adenocarcinoma cells (CAPAN2 cell line). The dysbiosis associated with pancreatic cancer is an unknown and therapeutically untapped area. Our research group seeks to determine how these bacterial metabolites interfere with tumor development, cell proliferation, epithelial-mesenchymal transition, and oxidative stress processes. In my experiments, I primarily investigate in cellular systems whether bacterial metabolites are capable of influencing the function and efficacy of chemotherapeutic agents.

AMBITIONS AND CAREER GOALS

As a biochemical engineering student, my main goal is to find answers to biomedical questions through biotechnological innovations. It is important for me to be able to participate in research work within a modern and high-performance laboratory during my studies. Mentoring helps me gain an understanding of the scientific community, gradually acquiring in-depth knowledge and becoming an active member.
My aim is to combine theoretical and practical knowledge to carry out useful and successful activities for society. I hope that my research work, which currently focuses on the study of the interaction of bacterial metabolites with chemotherapy drugs, can be utilized in future therapies. I would like to participate in the application of my research results and engage in active development work alongside theoretical research.

BOGLÁRKA HARSÁNYI

National Academy of Scientist Education, 2nd year
University of Debrecen,
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Csaba Matta
Specialization: Stem cell research, differentiation, chondrogenesis
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The planned research is motivated by the fact that musculoskeletal disorders, in particular disorders of large joints such as the knee and hip, place a significant burden on health care systems worldwide. Today, cartilage replacement remains a major challenge, partly due to the lack of detailed knowledge of the molecular processes that regulate cartilage formation. For this reason, a number of biological therapeutic approaches are being developed, for which a more detailed understanding of cartilage differentiation is essential.
The central starting point for this research is that during cartilage formation, mesenchymal stem cells (MSC) and mature chondrocytes are metabolically distinct. Mature articular cartilage cells are located in a vascular tissue where nutrient availability is limited. During chondrogenesis, metabolic pathways undergo a major transformation - however, the exact mechanism of this is currently poorly understood. Understanding the differences between the metabolic pathways of cartilage progenitor cells and mature articular cartilage cells could provide a new, unexploited way to promote cartilage regeneration.

AMBITIONS AND CAREER GOALS

In the course of the above research project, I will have the opportunity to learn about the methods to answer scientific questions (RNA expression methods, protein analysis, network biology, metabolic processes) and to participate in the process of presenting the research results in the form of a scientific paper (in extenso publication). I would also like to present the research results at a scientific student conference. One of my long-term goals is to obtain a PhD degree, which I will have the opportunity to do alongside my medical studies (MD PhD).

ANNA ZSÓFIA KÁDÁR

National Academy of Scientist Education, 2nd year
University of Debrecen
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Zsuzsa Bagoly
Specialization: Clinical research in the field of hemostasis: investigation of the underlying causes of unsuccessful thrombolysis therapy in acute ischemic stroke patients.
Language: English/proficiency, German/proficiency

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

During my laboratory work, I am searching for single nucleotide polymorphisms (SNPs) that influence the outcome of blood clotting treatment in ischemic stroke. In the treatment of ischemic stroke, recombinant tissue plasminogen activator (rt-PA) infusion is administered. However, the treatment is successful in less than half of the cases, and it induces intracranial bleeding in 6-8% of patients. We assume that SNPs influence the treatment outcome, and their identification could revolutionize ischemic stroke treatment.

AMBITIONS AND CAREER GOALS

As I am a student at University of Debrecen, my first and most important goal is the succesfull graduation and succesfull researching in the field of hemostasis. After that I would like to get a PhD diplome. My greatest goal is becoming a highly educated oxyologist-emergency specialist.

KOTHALAWALA ROSEMARY CHANDRAKANTHI

National Academy of Scientist Education, 2nd year
University of Debrecen
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Tamás Kovács
Specialization: Investigation of the role of membrane organization and lipids in the functional modulation of transmembrane proteins.
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Previously, cellular membranes were considered a simple barrier, however today we know that they actively regulate and modulate various proteins and, through this, many cellular pathways. Accordingly, changes in the composition and organization of the membranes can also modify these processes. This may be particularly important in the pathogenesis of diseases that are associated with changes in the lipid composition of membranes, such as metabolic diseases (hypercholesterolemia); storage diseases (Gaucher's disease, Niemann-Pick C disease); neurodegenerative diseases (Alzheimer's, Parkinson's); tumors. Although there are already indications of this, the role played by lipid and membrane abnormalities in these conditions is still largely unexplored. By examining the membrane organization, our research group tries to learn more about the pathomechanism of these diseases, as modification of lipid levels and membrane organization can be an alternative therapeutic method or complementary therapy.

AMBITIONS AND CAREER GOALS

As a medical student my primary goal is to get a comprehensive picture of the various biomedical divisions, which I can apply in my research and later in my clinical work. During my studies I would like to put as much work in my research topic as possible, from which I can also obtain a PhD degree after receiving my diploma. I hope that the knowledge and experience acquired in the laboratory will also help me get a head start in my clinical career.

OTTÓ TATAI

National Academy of Scientist Education, 2nd year
University of Debrecen
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Attila Tóth
Specialization: Investigation of the pathomechanism of cardiovascular diseases on clinical samples.
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Investigating the pathomechanism of cardiovascular diseases on clinical samples is of paramount importance. It provides insight into the underlying biological processes that cause cardiovascular disease, which will allow improved patient outcomes. By analyzing clinical samples, we can identify biomarkers of disease, evaluate drug efficacy, and better understand the progression of disease. This information can be used to develop more personalized treatment plans and improve patient outcomes. Additionally, research into the pathomechanism of cardiovascular diseases has the potential to identify new drug targets, leading to the development of new and more effective treatments. Ultimately, investigating the pathomechanism of cardiovascular diseases on clinical samples is crucial for advancing our understanding of these conditions and improving patient care.

AMBITIONS AND CAREER GOALS

By staying up-to-date with the latest research, I will be able to provide better care for my patients and make a positive impact on their health outcomes. I also think that research can help me contribute to the medical community and advance the field of medicine. Overall, I believe that engaging in research is an important part of being a good doctor and I am excited to pursue this path.

CSONGOR VÁRÓCZY

National Academy of Scientist Education, 2nd year
University of Debrecen
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Attila Bácsi
Junior mentor: Endre Kókai
Specialization: The role of PARP enzymes in the interactions of malignant tumor cells and macrophages
Language: English/proficiency, German/proficiency

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

In the modern era of medicine, cancer research is one of the most versatile and most challenging fields that provides a vast array of opportunities for innovative experiments in molecular medicine. Furthermore, recent discoveries in connection with malignant tumors have shed light on the interaction between the immune system and tumor cells. Our research project is based on the fact, that malignant cancer cells are able to polarize macrophages that play an essential role in immune response, therefore, these macrophages will support tumor progression and metastasis formation instead of triggering anti-tumor responses. In our experiments, we simulate the tumor microenvironment using a three-dimensional spheroid model and we take cutting edge molecular biological technologies into advantage to understand the mechanisms behind macrophage polarization and to examine the role of PARP enzymes in the process.

AMBITIONS AND CAREER GOALS

As a researcher, I primarily focus on discovering molecular medicine and expanding my knowledge in connection with scientific lifestyle. From my point of view, the research project with the National Scientists Academy will help me acquire valuable knowledge about molecular biology and various essential communication skills. I really hope that my early research experience will be an ideal tool as a medical doctor to start research projects from multiple perspectives and to combine the creativity of preclinical research with the practicality of clinical research.

3RD YEAR STUDENTS

ÁKOS MÁTÉ BEDE

National Academy of Scientist Education, 3rd year
University of Debrecen, Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: László Virág
Junior mentor: Katalin Kovács
Specialization: Immunopharmacology
Language: English/advanced, Romanian/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC) involves bridging target cells (e.g. virus-infected or cancer cells) and effector cells [e.g. natural killer (NK) cells or macrophages] with an antibody. The latter binds specifically to a cell surface antigen on the target cell while the constant region (Fc fragment) binds to the Fc receptor on the effector cells. ADCC is one of the key mechanisms by which cell-based cancer therapies fight the tumor. However, these mechanisms easily burn out and boosting ADCC activity would provide therapeutic benefit in oncology. We plan to set up assays for the quantification of cancer cell killing by NK cells and to perform high-content screening to identify ADCC enhancing drug candidates from drug libraries.

AMBITIONS AND CAREER GOALS

Throughout my university education I strive to acquire deep theoretical and practical medical knowledge. My goal after graduating medical school is getting a Phd degree. I wish to become a scientist-physician, working to improve people's lives in a clinical setting as well as by conducting biomedical research.

MIKLÓS LOVAS

National Academy of Scientist Education, 3rd year
University of Debrecen, Faculty of Pharmacy, 3rd year

Szent-Györgyi Mentor: Anikó Borbás
Junior mentor: Miklós Bege
Specialization: pharmaceutical chemistry
Language: English/advanced, Spanish/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Hydrogen sulfide is widely regarded as a toxic, foul-smelling chemical, but studies have identified it as the third gasotransmitter molecule. It has been found that it plays roles in various physiological processes, and has cardioprotective, pro-apoptotic and anti-inflammatory properties. In my research project I aim to synthesize compounds that can release hydrogen-sulfide upon enzymatic hydrolysis, and study the cardioprotective properties of these compounds in ischemic rat hearts.

AMBITIONS AND CAREER GOALS

After graduating, I intend to take part in PhD education, participate in research, and also get to know different areas of pharmacy. I would like to do all this at least partly abroad, building international relations that help me grow professionally, and help building my career.

PUBLICATIONS

Tánczos, B., Vass, V., Szabó, E., **Lovas, M.**, Kattoub, Ghanem., Rasha., Bereczki, I., Borbás, A., Herczegh, P., Tósaki, Á. (2024) Effects of H2S-donor ascorbic acid derivative and ischemia/reperfusion-induced injury in isolated rat hearts. **Eur J Pharm Sci. 6:** 195:106721.
Debreczeni, N., Hotzi, J., Bege, M., **Lovas, M**., Mező, E., Bereczki, I., Herczegh, P., Kiss, L., Borbás, A. (2023) N-fluor-alkilezett morfolinok – a nukleozidanalógok új osztálya. **Chem.** 202203248.

BEÁTA VÁRKONYI

National Academy of Scientist Education, 3rd year
University of Debrecen, Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: László Virág
Junior mentor: Máté Demény
Specialization: Cell biology
Language: English, German, French

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

My research focuses on the interaction between tumour cells and macrophages. Using a co-culture system of breast cancer cells and macrophages, I investigate the role of PARP enzyme family members in the process by which the tumour reprograms tumour-associated macrophages into a tumour cell growth promoting phenotype. I plan to study the role of the post-translational protein modification process called ADP-ribosylation catalyzed by PARP enzymes, in the tumour cell-induced metabolic, transcriptional and signalling processes of macrophages. The aim and expected outcome of the research is to identify ADP-ribosylation-regulated proteins in macrophages that may be targets for reprogramming efforts towards a tumour-killing immune cell phenotype.

AMBITIONS AND CAREER GOALS

I intend to learn the research approach during my university years and then apply it in the clinic. I would like to gain experience abroad as well, which I plan to apply to my work here in Hungary. My aim is to learn as much as possible about the literature, to keep up to date with it and thus to gain a more complete picture of the challenges and achievements of the medical profession. I plan to obtain a PhD after graduating from medical school and to continue the research work I have already started.

KITTI KURTÁN

5TH YEAR STUDENT

National Academy of Scientist Education, 5th year
University of Debrecen, Faculty of Medicine, 5th year

Szent-Györgyi Mentor: Florina Zákány
Specialization: Biophysics, cell biology
Language: English/proficiency, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

My research focuses on investigating the interaction between spike proteins of different SARS-CoV-2 variants and the ACE2 receptor. Previously, we demonstrated that cholesterol-depleting cyclodextrins can alter the cell surface distribution of ACE2 and TMPRSS2 proteins essential in the initial steps of virus infection. This results in a reduced capability for the virus to bind to ACE2, subsequently decreasing its entry into the cell. Our further goal is to study the differences in the affinity of various SARS-CoV-2 variant spike proteins for ACE2. Additionally, we aim to explore how changes in the target cell membrane, especially modifications in cholesterol levels in lipid rafts, affect the affinity of SARS-CoV-2 spike proteins for ACE2 and their entry into the cell. Our results may contribute to understanding how alterations in the membrane composition of target cells and mutations in the spike protein influence the binding and entry of SARS-CoV-2 into target cells. This data can enhance our comprehension of the infection process and, consequently, aid in the development of more effective therapeutic methods.

AMBITIONS AND CAREER GOALS

My goal is to acquire extensive knowledge and experience in both research and general medical practices throughout my studies. Among my short-term plans is the completion of the MD PhD program to obtain a doctoral degree, for which the NTA training provides excellent assistance. My ambition is to become a renowned medical professional in the future. Therefore, I also consider it crucial to actively participate in research activities in the long term.

CSABA CSIKOS

6TH YEAR STUDENT

National Academy of Scientist Education, 6th year
University of Debrecen, Faculty of Medicine, 6th year

Szent-Györgyi Mentor: György Trencsényi
Specialization: Biochemistry
Language: English

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

NMNAT1 is an enzyme localized in the nucleus and it plays an important role in several biochemical processes. We are investigating the effect of NMNAT1 on the migration of tumor cells. We set up an in vitro wound healing assay with which we can examine the proliferation and migration of the cells at the same time. With this method, we may be able to find new therapeutic approches that can improve the survival rate of malignant diseases.

AMBITIONS AND CAREER GOALS

I would like to become a physician who fulfills both their professional duties and their humanitarian requirements. For this, I find it important to acquire lots of knowledge and many skills while being a medical student. Joining a research project also contributes to achieving my future goals in many ways.

PUBLICATIONS

Csikos, Cs., Vágner, A., Nagy, G., Kálmán-Szabó, I., P. Szabó, J., Toan Ngo, M., Szoboszlai, Z., Szikra, D., Krasznai, Z.T., Trencsényi, G., Garai, I. (2023) In Vivo Preclinical Assessment of the VEGF Targeting Potential of the Newly Synthesized [52Mn]Mn-DOTAGA-Bevacizumab Using Experimental Cervix Carcinoma Mouse Model. **Diagnostics (Basel): 13:** 231.

PÉCS
SZENT-GYÖRGYI MENTORS

TAMÁS ATLASZ

University of Pécs
Faculty of Sciences
Institute of Biology

RESEARCH AREA

Retinal diseases are among the leading causes of blindness. Therefore, any experimental approach that leads to a better understanding of the molecular background of these diseases, as well as the testing of groups of molecules that can reduce or potentially prevent damage, is a priority research activity. Our research focuses on the study of two posterior segment diseases of the eye (glaucoma and diabetic retinopathy) which are leading causes in the development of blindness. Our goal is to develop a new effective treatment strategy for the previously mentioned ophthalmic diseases by using different neuroprotective pharmacons, with each having distinct target points that reduce the development of the disease.

SELECTED PUBLICATIONS

Patko, E., Szabo, E., Toth, D., Tornoczky, T., Bosnyak, I., Vaczy A., **Atlasz, T.,** Reglodi, D. (2022) Distribution of PACAP and PAC1 Receptor in the Human Eye, **J Mol Neurosci**

Kvarik, T., Reglodi, D., Werling, D., Vaczy, A., Kovari, P., Szabo, E., Kovacs, K., Hashimoto, H., Ertl, T., Gyarmati, J., **Atlasz, T.** (2021) The Protective Effects of Endogenous PACAP in Oxygen-Induced Retinopathy, **J Mol Neurosci 71:** 2546–2557.

Szabó, E., Patkó, E., Váczy, A., Molitor, D., Csutak, A., Tóth, G., Reglődi, D., **Atlasz, T.** (2021) Retinoprotective Effects of PACAP Eye Drops in Microbead-Induced Glaucoma Model in Rats, **Int J Mol Sci 22:** 16.

Kovacs, K., Vaczy, A., Fekete, K., Kovari, P., **Atlasz, T.**, Reglodi, D., Gabriel, R., Gallyas, F., Sumegi, B. (2019) PARP Inhibitor Protects Against Chronic Hypoxia/Reoxygenation-Induced Retinal Injury by Regulation of MAPKs, HIF1α, Nrf2, and NFκB. **IOVS 60:** 1478–1490.

Atlasz, T., Werling, D., Song, S., Szabo, E., Vaczy, A., Kovari, P., Tamas, A., Reglodi, D., Yu, R. (2019) Retinoprotective Effects of TAT-Bound Vasoactive Intestinal Peptide and Pituitary Adenylate Cyclase Activating Polypeptide. **J Mol Neurosci 68:** 397-407.

PÉTER BALOGH

University of Pécs
Medical School
Department of Immunology and Biotechnology

RESEARCH AREA

In mice, the targeted absence of Nkx2-3 induces a number of morphological changes, mainly in the vascular pattern of the red pulp and the marginal zone. Previous research publications have described the emergence of ectopic HEV-like postcapillary venules and ectopic lymphatic vessels isolated from the systemic circulation, which show an anti-LYVE-1 positive reaction in the absence of the transcription factor Prox1.
At present, it is not clear which vascular-forming cells are affected in the modified vascular patterning, nor is it known exactly what role ectopic lymphatic vessels play in the lymphocyte migration of mutant spleens. The aim of this study is to characterise in detail the process of lymphocyte migration in the spleens of Nkx2-3-deficient mice using immunological methods and to investigate the effects of Nkx2-3 deficiency on endothelial cells.

SELECTED PUBLICATIONS

Kellermayer, Z., Vojkovics, D., Dakah, TA., Bodó, K., Botz, B., Helyes, Z., Berta, G., Kajtár, B., Schippers, A., Wagner, N., Scotto, L., O'Connor, OA., Arnold, HH., **Balogh, P.** (2019) IL-22-Independent Protection from Colitis in the Absence of Nkx2.3 Transcription Factor in Mice. **J Immunol 202:** 1833-1844.

Jia, X., Bene, J., Balázs, N., Szabó, K., Berta, G., Herczeg, R., Gyenesei, A., **Balogh, P.** (2022) Age-Associated B Cell Features of the Murine High-Grade B Cell Lymphoma Bc.DLFL1 and Its Extranodal Expansion in Abdominal Adipose Tissues. **J Immunol 280:** 2866-2876.

Gábris, F., Kiss, G., Szirmay, B., Szomor, Á., Berta, G., Jakus, Z., Kellermayer, Z., **Balogh, P.** (2023) Absence of Nkx2-3 induces ectopic lymphatic endothelial differentiation associated with impaired extramedullary stress hematopoiesis in the spleen. **Front Cell Dev Biol 11:** 1170389.

Vojkovics, D., Kellermayer, Z., Gábris, F., Schippers, A., Wagner, N., Berta, G., Farkas, K., **Balogh, P.** (2019) Differential Effects of the Absence of Nkx2-3 and MAdCAM-1 on the Distribution of Intestinal Type 3 Innate Lymphoid Cells and Postnatal SILT Formation in Mice. **Front Immunol 10:** 366.

Jia, X., Gábris, F., Jacobsen, Ó., Bedics, G., Botz, B., Helyes, Z., Kellermayer, Z., Vojkovics, D., Berta, G., Nagy, N., Jakus, Z., **Balogh, P.** (2020) Foliate Lymphoid Aggregates as Novel Forms of Serous Lymphocyte Entry Sites of Peritoneal B Cells and High-Grade B Cell Lymphomas. **J Immunol 204:** 23-36.

ÉVA BORBÉLY

University of Pécs
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Neuropeptides are important regulatory molecules of the central and peripheral nervous systems. Tachykinins represent one of the biggest family of neuropeptides, known for their wide expession throughout the brain and diverse actions in the whole body. They can influence among others pain sensation, inflammation, mood regulation and memory consolidation. HK-1, discovered in 2000, is also a member of the tachykinin family originally demonstrated in B cells. The structure of HK-1 is very similar to SP which makes the protein identification difficult and it has very similar biding properties on the NK1 receptor. We proved that HK-1 plays an important role in acute stress, acute and chronic pain conditions as well as in inflammation. The main goal of research is to unravel the expression patterns of HK-1 in the brain and stress-related organs (thymus, adrenal gland), to investigate the role of HK-1 in behavioural and structural changes characteristic for depression and its comorbidities (pain, memory disorders) and to further understand the mechanism of action of HK-1 in neuro-immune interactions.

SELECTED PUBLICATIONS

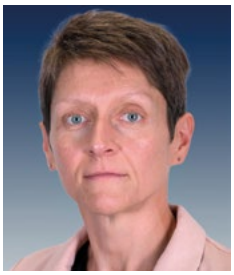
Fülöp, B., Hunyady, Á., Bencze, N., Kormos, V., Szentes, N., Dénes, Á., Lénárt, N., **Borbély, É.**, Helyes, Zs. (2023) IL-1 Mediates Chronic Stress-Induced Hyperalgesia Accompanied by Microglia and Astroglia Morphological Changes in Pain-Related Brain Regions in Mice. **Int J Mol Sci 13:** 5479.

Borbély, É., Hunyady, Á., Pohóczky, K., Payrits, M., Botz, B., Mócsai, A., Berger, A., Szőke, É., Helyes, Z. (2021) Hemokinin-1 as a Mediator of Arthritis-Related Pain via Direct Activation of Primary Sensory Neurons. **Front Pharmacol 11:** 594479.

Hunyady, Á., Hajna, Zs., Gubányi, T., Scheich, B., Kemény, Á., Gaszner, B., Borbély, É., Helyes, Z. (2019) Hemokinin-1 is an important mediator of pain in mouse models of neuropathic and inflammatory mechanisms. **Brain Res Bull 147:** 165-173.

Borbély É., Payrits M., Hunyady Á., Mező G., Pintér E. (2019) Important regulatory function of transient receptor potential ankyrin 1 receptors in age-related learning and memory alterations of mice. **Geroscience 41:** 643-654.

Borbely, E., Hajna, Z., Nabi, L., Scheich, B., Tekus, V., Laszlo, K., Ollmann, T., Kormos, V., Gaszner, B., Karadi, Z, Lénárd L., Paige C.J., Quinn J. P., Szolcsányi J., Pintér E., Keeble J., Berger A., Helyes Z. (2017) Hemokinin-1 mediates anxiolytic and anti-depressant-like actions in mice. **Brain Behav and Immun 59:** 219-232.



BEÁTA BUGYI

University of Pécs
Medical School
Department of Medical Biology

RESEARCH AREA

The actin cytoskeleton as a structural and functional unit of cells plays essential roles in virtually all cellular processes. Its functioning relies on the large inventory of actin-binding proteins and their functional couplings. Central to our research, we investigate the mechanisms underlying the functioning of the actin cytoskeleton by studying the structural features, activities, and interactions of actin and actin-binding proteins.

Our experimental approach allows us to explore the molecular relationships that regulate the organization of actin networks, so it has biomedical potential. It can contribute to a better understanding of the relevant diseases.

Our laboratory focuses on the following major research problems:

(1) Mechanisms governing the assembly of thin filaments

(2) Functional coordination of actin-microtubule cytoskeleton dynamics

SELECTED PUBLICATIONS

Telek, E., Karádi, K., Kardos, J., Kengyel, A., Fekete, Zs., Halász, H., Nyitrai, M., **Bugyi, B.**, Lukács, A. (2021) The C-terminal tail extension of myosin 16 acts as a molten globule, including intrinsically disordered regions, and interacts with the N-terminal ankyrin. **J Biol Chem 297:** 16 p.

Vemula, V., Huber, T., Ušaj, M., **Bugyi, B.**, Mansson, A. (2021) Myosin and gelsolin cooperate in actin filament severing and actomyosin motor activity. **J Biol Chem 296:** 16 p.

Bugyi, B., Kellermayer, M. (2020) The discovery of actin: "to see what everyone else has seen, and to think what nobody has thought". **J Muscle Res and Cell Motil 41:** 3-9.

Pintér, R., Huber, T., Bukovics, P., Gaszler, P., Vig, AT., Tóth, MÁ., Gazsó-Gerhát, G., Farkas, D., Migh, E., Mihály, J., **Bugyi, B.** (2020) The Activities of the Gelsolin Homology Domains of Flightless-I in Actin Dynamics. **Front Mol Biosci 7:** 18 p.

Tóth, MÁ., Majoros, KA., Vig, AT., Migh, E., Nyitrai, M., Mihály, J., **Bugyi, B.** (2016) Biochemical Activities of the Wiskott-Aldrich Syndrome Homology Region 2 Domains of Sarcomere Length Short.: WH2 domains in sarcomeric actin regulation. **J Biol Chem 291:** 667-680.

Bugyi, B., Carlier, MF. (2010) Control of actin filament treadmilling in cell motility. **Annu Rev Biophys 39:** 449-470.

BOLDIZSÁR CZÉH

University of Pécs
Szentágothai Research Centre
Structural Neurobiology Research Group

RESEARCH AREA

The physiological stress response is essential for our everyday survival, but traumatic or chronic stress represents a strong risk factor for the development of various mental and somatic disorders. The aim of our research is to investigate the functional and structural changes in the brain caused by stress. Such studies help us to understand the pathophysiology of mental disorders such as depression.
We perform clinical studies and we work also with animal models of neuropsychiatric disorders. We employ different imaging methods to examine the cellular alterations that develop under stress. Structural and functional changes in the brain are examined by magnetic resonance imaging (MRI). This method is suitable for determining the volume of different brain structures and for providing information on the microstructure of white matter structures. Functional MRI investigations are suitable for examining brain areas which are specifically activated during cognitive and emotional tasks. The in vivo imaging experiments are complemented by postmortem histological studies, in which we study morphological changes of the cells and neural networks using different microscopic methods.

SELECTED PUBLICATIONS

Nagy, S. A., Kürtös, Z., Németh, N., Perlaki, G., Csernela, E., Lakner, F. E., Dóczi, T., **Czéh, B.**, Simon, M. (2021) Childhood maltreatment results in altered deactivation of reward processing circuits in depressed patients: A functional magnetic resonance imaging study of a facial emotion recognition task. **Neurobiol Stress 15:** 100399.

Nagy, S. A., Vranesics, A., Varga, Z., Csabai, D., Bruszt, N., Bali, Z. K., Perlaki, G., Hernádi, I., Berente, Z., Miseta, A., Dóczi, T., **Czéh, B.** (2020) Stress-Induced Microstructural Alterations Correlate With the Cognitive Performance of Rats: A Longitudinal in vivo Diffusion Tensor Imaging Study. **Front Neurosci 14:** 474.

Simon, M., Németh, N., Gálber, M., Lakner, E., Csernela, E., Tényi, T., **Czéh, B.** (2019) Childhood Adversity Impairs Theory of Mind Abilities in Adult Patients With Major Depressive Disorder. **Front Psychiatry 10:** 867.

Czéh, B., Müller-Keuker, J. I., Rygula, R., Abumaria, N., Hiemke, C., Domenici, E., Fuchs, E. (2007) Chronic social stress inhibits cell proliferation in the adult medial prefrontal cortex: hemispheric asymmetry and reversal by fluoxetine treatment. **Neuropsychopharmacology 32:** 1490–1503.

Coe, C. L., Kramer, M., **Czéh, B.**, Gould, E., Reeves, A. J., Kirschbaum, C., Fuchs, E. (2003) Prenatal stress diminishes neurogenesis in the dentate gyrus of juvenile rhesus monkeys. **BiolPsychiatry 54:** 1025–1034.

Czéh, B., Michaelis, T., Watanabe, T., Frahm, J., de Biurrun, G., van Kampen, M., Bartolomucci, A., Fuchs, E. (2001) Stress-induced changes in cerebral metabolites, hippocampal volume, and cell proliferation are prevented by antidepressant treatment with tianeptine. **Proc Natl Acad Sci USA 98:** 12796–12801.

ANDRÁS GARAMI

University of Pécs
Medical School
Institute for Translational Medicine

RESEARCH AREA

Normal body temperature – which is essential for life – is maintained by various thermoregulatory mechanisms. Thermoregulatory disorders are present in many pathological conditions, e.g., febrile diseases, systemic inflammation (sepsis), organ dysfunctions (e.g., pancreatitis), heat stroke, and hypothermia. It is of utmost importance to discover the pathophysiological processes in the thermoregulatory disorders. More and more influencing factors are identified, such as the pH status and transient receptor potential channels. In our research, we aim at identifying the neural substrates and molecular mediators involved in the thermoregulatory processes mainly in different animal models, but to some extent also in human studies. Our findings can further advance the knowledge of bodily homeostasis, moreover, they can open new directions in clinical practice, most of all intensive therapy, and other sciences. Successful development of drugs designed specifically to target body temperature, could pave the road to pharmacologically controlled temperature management, thereby advancing the therapeutic approaches in clinical conditions with thermoregulatory disorders.

SELECTED PUBLICATIONS

Toldi, J., Kelava, L., Marton, S., Muhl, D., Kustan, P., Feher, Z., Maar, K., Garai, J., Pakai, E., **Garami, A.** (2023). Distinct patterns of serum and urine macrophage migration inhibitory factor kinetics predict death in sepsis: A prospective, observational clinical study. **Sci Rep 13:** 588.

Keringer, P., Furedi N., Gaszner, B., Miko, A., Pakai, E., Fekete, K., Olah, E., Kelava, L., Romanovsky, A. A., Rumbus, Z., **Garami, A.** (2022). The hyperthermic effect of central cholecystokinin is mediated by the cyclooxygenase-2 pathway. **Am J Physiol Endocrinol Metab 322:** E10–E23.

Kelava, L., Nemeth, D., Hegyi, P., Keringer, P., Kovacs, D. K., Balasko, M., Solymar, M., Pakai, E., Rumbus, Z., **Garami, A.** (2022) Dietary supplementation of transient receptor potential vanilloid-1 channel agonists reduces serum total cholesterol level: a meta-analysis of controlled human trials. **Crit Rev Food Sci Nutr 62:** 7025–7035.

Garami, A., Shimansky, Y. P., Rumbus, Z., Vizin, R., Farkas, N., Hegyi, J., Szakacs, Z., Solymar, M., Csenkey, A., Chiche, D. A., Kapil, R., Kyle, D. J., Van, Horn W. D., Hegyi, P., Romanovsky, A. A. (2020) Hyperthermia induced by transient receptor potential vanilloid-1 (TRPV1) antagonists in human clinical trials: insights from mathematical modeling and meta-analysis. **Pharmacol Ther 208:** 107474.

Pakai, E., Tekus, V., Zsiboras, Cs., Rumbus, Z., Olah, E., Keringer, P., Khidhir, N., Matics, R., Deres, L., Ordog, K., Szentes, N., Pohoczky, K., Kemeny, A., Hegyi, P., Pinter, E., **Garami, A.** (2018) The neurokinin-1 receptor contributes to the early phase of lipopolysaccharide-induced fever via stimulation of peripheral cyclooxygenase-2 protein expression in mice. **Front Immunol 9:** 166.

BALÁZS GASZNER

University of Pécs
Medical School
Institute of Anatomy

RESEARCH AREA

Animal models of depression and anxiety. Functional neuromorphological background of mood disorders. Neuropeptidergic machanisms underlying stress adaptation. The role of the corticotropin-releasing hormone peptide family in stress adaptation and energy balance: forebrain (nucleus interstitialis striae terminalis, nucleus centralis amygdalae) and hypothalamic corticotropin-releasing hormone systems, urocortin 1 (centrally projecting Edinger-Wespthal nucleus). Investigation of the neuropeptidergic mechanisms underlying the non-motor symptoms of Parkinson's disease (corticotropin-releasing hormone and related peptidergic systems, dopaminergic, serotoninergic, noradrenergic circuits). Investigation of the epigenetic and functional neuromorphological mechanisms underlying individual differences in stress adaptation ability.

SELECTED PUBLICATIONS

Kovács, L Á., Berta, G., Csernus, V., Ujvári, B., Füredi, N., **Gaszner, B.** (2019) Corticotropin-Releasing Factor-Producing Cells in the Paraventricular Nucleus of the Hypothalamus and Extended Amygdala Show Age-Dependent FOS and FOSB/DeltaFOSB Immunoreactivity in Acute and Chronic Stress Models in the Rat. **Front Aging Neurosci 274:** 19.

Gaszner, T., Farkas, J., Kun, D., Ujvári, B., Berta, G., Csernus, V., Füredi, N., Kovács, L Á., Hashimoto, H., Reglődi, D., Kormos, V., Gaszner, B. (2022) Fluoxetine treatment supports predictive validity of the three hit model of depression in male PACAP heterozygous mice and underpins the impact of early life adversity on therapeutic efficacy. **Front Endocrinol 13:** 23.

Kormos, V., Kecskés, A., Farkas, J., Gaszner, T., Csernus, V., Alomari, A., Hegedüs, D., Renner, É., Palkovits, M., Zelena, D., Helyes, Z., Pintér, E., **Gaszner, B.** (2022) Peptidergic neurons of the Edinger–Westphal nucleus express TRPA1 ion channel that is downregulated both upon chronic variable mild stress in male mice and in humans who died by suicide. **J Psychiatry Neurosci 47:** 14.

Kovács, L Á., Füredi, N., Ujvári, B., Golgol, A., **Gaszner, B.** (2022) Age-Dependent FOSB/ΔFOSB Response to Acute and Chronic Stress in the Extended Amygdala, Hypothalamic Paraventricular, Habenular, Centrally-Projecting Edinger-Westphal, and Dorsal Raphe Nuclei in Male Rats. **Front Aging Neurosci 14:** 24.

Ujvári, B., Pytel, B., Márton, Z., Bognár, M., Kovács, L Á., Farkas, J., Gaszner, T., Berta, G., Kecskés, A., Kormos, V., Farkas, B., Füredi, N., **Gaszner, B.** (2022) Neurodegeneration in the centrally-projecting Edinger–Westphal nucleus contributes to the non-motor symptoms of Parkinson's disease in the rat. **J Neuroinflammation 19:** 31.

ZSUZSANNA HELYES

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Mapping the complex mechanisms underlying chronic arthritic pain. A significant proportion of people with rheumatoid arthritis are 'difficult to treat' patients, falling into the categories of non-inflammatory and persistent inflammation. Chronic pain is the main symptom in both cases, with autoimmune, neuroinflammatory and neuropathic processes underlying central and peripheral mechanisms. As conventional analgesics are often ineffective, our aim is to understand the mechanisms of sensitisations responsible for chronic pain and to identify the key mediators and pathways involved. In mouse models of arthritis, we perform complex functional and analytical as well as morphological studies of the central nervous system (glial cell-neuron interactions, neuroinflammation). RNA isolated from peripheral blood mononuclear cells and dorsal root ganglia will be subjected to transcriptomic measurements and from plasma to metabolomic measurements, which will be evaluated using bioinformatic methods. Pain levels will be correlated with other inflammatory and immunological parameters, as well as anxiety and mood changes. Brain functional imaging studies will be performed to map changes in the activation pattern of the "pain matrix".

SELECTED PUBLICATIONS

Helyes, Z., Tékus, V., Szentes, N., Pohóczky, K., Botz, B., Kiss, T., Kemény, Á., Környei, Z., Tóth, K., Lénárt, N., Ábrahám, H., Pinteaux, E., Francis, S., Sensi, S., Dénes, Á., Goebel A. (2019) Transfer of complex regional pain syndrome to mice via human autoantibodies is mediated by interleukin-1-induced mechanisms. **Proc Natl Acad Sci USA 116:** 13067-13076.

Kecskés, A., Pohóczky, K., Kecskés, M., Varga, ZV., Kormos, V., Szőke, É., Henn-Mike, N., Fehér, M., Kun, J., Gyenesei, A., Renner, É., Palkovits, M., Ferdinandy, P., Ábrahám, IM., Gaszner, B., **Helyes Z.** (2020) Characterization of Neurons Expressing the Novel Analgesic Drug Target Somatostatin Receptor 4 in Mouse and Human Brains. **Int J Mol Sci. 21:** 7788.

Horváth, Á., Tékus, V., Bencze, N., Szentes, N., Scheich, B., Bölcskei, K., Szőke, É., Mócsai, A., Tóth-Sarudy, É., Mátyus, P., Pintér, E., **Helyes, Z.** (2018) Analgesic effects of the novel semicarbazide-sensitive amine oxidase inhibitor SZV 1287 in mouse pain models with neuropathic mechanisms: Involvement of transient receptor potential vanilloid 1 and ankyrin 1 receptors. **Pharmacol Res. 131:** 231-243.

Botz, B., Kriszta, G., Bölcskei, K., Horváth, Á.I., Mócsai, A., **Helyes, Z.** (2021) Capsaicin-Sensitive Peptidergic Sensory Nerves Are Anti-Inflammatory Gatekeepers in the Hyperacute Phase of a Mouse Rheumatoid Arthritis Model. **Int J Mol Sci. 22:** 1682.

Szentes, N., Tékus, V., Mohos, V., Borbély, É., **Helyes, Z.** (2019) Exploratory and locomotor activity, learning and memory functions in somatostatin receptor subtype 4 gene-deficient mice in relation to aging and sex. **Geroscience 41:** 631-641.

ISTVÁN HERNÁDI

University of Pécs
Faculty of Sciences
Institute of Biology

RESEARCH AREA

Investigating the neurocognitive underpinnings of ageing and neurocognitive impairment in rodents: identification of preclinical drug development strategies and development of combined cognitive enhancer therapies. The main objective of the project is to understand and model the processes underlying brain ageing and neurocognitive disorders (dementias) in rodents and to study cellular and behavioural processes in a coordinated manner in the same model. The research is carried out in two locations: our cellular biology (electrophysiology) laboratory is located at the Faculty Sciences and our small animal behavioural pharmacology laboratory is located at the Szentágothai Research Centre (SzRC). Our preclinical animal models include e.g. pharmacologically induced amnesia, natural ageing, repetitive mild traumatic brain injury and genetic (DREADD) models. Behavioural changes are investigated in state-of-the-art test packages. Our results are further utilized in both basic and applied drug discovery research. Our main long-term goal is to unravel the yet unknown mechanisms underlying neurocognitive diseases and to identify biomarkers that may later play a crucial role in the diagnosis and treatment of cognitive disorders and in the development of new drug candidates.

SELECTED PUBLICATIONS

Bali, Z. K., Bruszt, N., Kőszegi, Z., Nagy, L. V., Atlasz, T., Kovács, P., Csupor, D., Csupor-Löffler, B., **Hernádi, I.** (2022) Aconitum alkaloid songorine exerts potent gamma-aminobutyric acid-A receptor agonist action in vivo and effectively decreases anxiety without adverse sedative or psychomotor effects in the rat. **Pharmaceutics 14:** 2067.

Nagy L.V., Bali Z.K., Kapus G., Pelsőczi P., Farkas B., Lendvai B., Lévay G., **Hernádi I.** (2021) Converging Evidence on D-Amino Acid Oxidase–Dependent Enhancement of Hippocampal Firing Activity and Passive Avoidance Learning in Rats. **Int J Neuropsychopharmacol 24:** 434.

Bali Z.K., Nagy L.V., **Hernádi I.** (2017) Alpha7 nicotinic acetylcholine receptors play a predominant role in the cholinergic potentiation of N-methyl-D-aspartate evoked firing responses of hippocampal CA1 pyramidal cells. **Front Cell Neurosci 11:** 271.

Grabenhorst F., **Hernádi I.**, Schultz W. (2016) Primate amygdala neurons evaluate the progress of self-defined economic choice sequences. **Elife 12:** e18731.

Hernádi I., Grabenhorst F., Schultz W. (2015) Planning activity for internally generated reward goals in monkey amygdala neurons. **Nat Neurosci 18:** 461-469.

CSABA HETÉNYI

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Development and application of computer-aided drug design A key step in the early stages of drug design is the design of potent drug molecules. This process is now mostly carried out using computer (pharmaco-informatics) methods, which are capable of handling both large amounts of structural data and complex energy calculations. The pharmacoinformatics toolbox will be used in both target-based and ligand-based design and will be extended with new procedures in the course of the PhD work. The methods will be tested and applied in curricular areas of pharmacology such as pain management, regulation of signalling, antiviral and epigenetic-based therapies. Computational analysis of target-drug interactions: Computational docking is an indispensable tool in drug design and is widely used by pharmaceutical companies. This project focuses on the prediction of the structure and energy of drug-target interactions by computer docking. The capabilities and limitations of the method will be investigated.

SELECTED PUBLICATIONS

Zsidó, B.Z., Börzsei, R., Pintér, E., **Hetényi, C.** (2021) Prerequisite Binding Modes Determine the Dynamics of Action of Covalent Agonists of Ion Channel TRPA1. **Pharmaceuticals 14:** 988

Zsidó, B.Z., **Hetényi, C.** (2021) The role of water in ligand binding. **Curr Opin Struct Biol 67:** 1-8

Zsidó, B.Z., Börzsei, R., Szél, V., **Hetényi, C.** (2021) Determination of Ligand Binding Modes in Hydrated Viral Ion Channels to Foster Drug Design and Repositioning. **J Chem Inf Model 61:** 4011-4022

Zsidó, B.Z., **Hetényi, C.** (2020) Molecular Structure, Binding Affinity, and Biological Activity in the Epigenome. **Int J Mol Sci 21:** 4134

Horváth, I., Jeszenői, N., Bálint, M., Paragi, G, **Hetényi, C.** (2019) A fragmenting protocol with explicit hydration for calculation of binding enthalpies of targetligand complexes at a quantum mechanical level. **Int J Mol Sci 20:** 4384.

FERENC JAKAB

University of Pécs
Szentágothai Research Centre

RESEARCH AREA

Description and molecular characterisation of new viral pathogens. Emerging infectious diseases pose an extremely serious and complex challenge to humanity, but especially to the globalised world order and economy. Over the past decades, several epidemics have emerged in human populations, many of them mediated by wild animals. Two thirds of the pathogens thus emerged originate from wild animals. A striking example is the current pandemic SARS-2 coronavirus, which originates from an as yet unknown animal, but evolutionarily from bats. If we know of naturally occurring viruses with similar potential, we can use their detailed natural history to take clear and effective preventive action to avert, or at least reduce, the likelihood of their emergence in human populations. We aim at the identification of such pathogens and the development of innovative capacities for their rapid, modern and efficient testing. New viruses detected or discovered from the animal populations studied, in addition to further investigation of natural processes, transmission properties and innovative detection capacity development, may also be directly useful in other basic research lines (e.g. drug development). The National Laboratory of Virology has decades of experience in the sampling and complex virological analysis of naturally occurring zoonotic viruses.

SELECTED PUBLICATIONS

Bajusz, D., Wade, WS., Satała, G., Bojarski, AJ., Ilaš, J., Ebner, J., Grebien, F., Papp, H., **Jakab, F.**, Douangamath, A., Fearon, D., von Delft, F., Schuller, M., Ahel, I., Wakefield, A., Vajda, S., Gerencsér, J., Pallai, P., Keserű, GM. (2021) Exploring protein hotspots by optimized fragment pharmacophores. **Nat Commun 12:** 3201.

Földes, F., Madai, M., Papp, H., Kemenesi, G., Zana, B., Geiger, L., Gombos, K., Somogyi, B., Bock-Marquette, I., **Jakab, F.** (2020) Small Interfering RNAs Are Highly Effective Inhibitors of Crimean-Congo Hemorrhagic Fever Virus Replication In Vitro. **Molecules 25:** 5771.

Zana, B., Erdélyi, K., Nagy, A., Mezei, E., Nagy, O., Takács, M., Bakonyi, T., Forgách, P., Korbacska-Kutasi, O., Fehér, O., Malik, P., Ursu, K., Kertész, P., Kepner, A., Martina, M., Süli, T., Lanszki, Z., Tóth, GE., Kuczmog, A., Somogyi, B., **Jakab, F.**, Kemenesi, G. (2018) Multi-Approach Investigation Regarding the West Nile Virus Situation in Hungary. **Viruses 12:** 123.

Földes, F., Madai, M., Németh, V., Zana, B., Papp, H., Kemenesi, G., Bock-Marquette, I., Horváth, G., Herczeg, R., **Jakab, F.** (2019) Serologic survey of the Crimean-Congo haemorrhagic fever virus infection among wild rodents in Hungary. **Ticks Tick Borne Dis 10:** 101258.

Kemenesi, G., Kurucz, K., Dallos, B., Zana, B., Földes, F., Boldogh, S., Görföl, T., Carroll, MW., **Jakab, F.** (2019) Re-emergence of Lloviu virus in Miniopterus schreibersii bats, Hungary, 2016. **Emerg Microbes Infect 7:** 66.

MIKLÓS KECSKÉS

University of Pécs
Medical School
Institute of Physiology

RESEARCH AREA

The main goal of the research group is to study the expression and function of transient receptor potential (TRP) ion channels in the brain. The TRP ion channel family includes 28 members in mammals. The understanding of TRP ion channels was made possible by research on TRPV1, TRPA1 and TRPM8 channels located on peripheral nerve endings. These classic receptors play a role in cold and hot sensation, inflammatory pain sensation, but also, for example, in sensing the pungency of chili peppers. However, the expression and function of TRP ion channels in the brain is still a debate, especially regarding the expression pattern at the cellular level. Our research focuses on neurons expressing TRP ion channels from different brain areas, including the hippocampus, the amygdala and the piriform cortex.

SELECTED PUBLICATIONS

Mundrucz, L., Kecskés, A., Henn-Mike, N., Kóbor, P., Buzás, P., Vennekens, R., **Kecskés, M.** (2023) TRPM4 regulates hilar mossy cell loss in temporal lobe epilepsy. **BMC Biol 26:** 96.

Al-Omari, A.*, **Kecskés, M.***, Gaszner, B., Biró-Sütő, T., Fazekas, B., Berta, G., Kuzma, M., Pintér, E., Kormos, V. (2023) Functionally active TRPA1 ion channel is downregulated in peptidergic neurons of the Edinger-Westphal nucleus upon acute alcohol exposure. **Front Cell Dev Biol 10:** 1046559.

Vandewiele, F., Pironet, A., Jacobs, G., **Kecskés, M.**, Wegener, J., Kerselaers, S., Hendrikx, L., Verelst, J., Philippaert, K., Oosterlinck, W., Segal, A., Van Den, Broeck., Pinto, S., Priori, S.G., Lehnart, S.E., Nilius, B., Voets, T., Vennekens, R. (2022) TRPM4 inhibition by meclofenamate suppresses Ca2+-dependent triggered arrhythmias. **Eur Heart J 43:** 4195-4207.

Kecskés, A., Czéh, B., Kecskés, M. (2022) Mossy cells of the dentate gyrus: Drivers or inhibitors of epileptic seizures? **Biochim Biophys Acta Mol Cell Res. 1869:** 119279.

Kecskés, M.*, Henn-Mike, N.*, Agócs-Laboda, Á., Szőcs, S., Petykó, Z., Varga, C. (2020) Somatostatin expressing GABAergic interneurons in the medial entorhinal cortex preferentially inhibit layerIII-V pyramidal cells. **Commun Biol 3:** 754.

GÁBOR KEMENESI

University of Pécs
Faculty of Sciences
Institute of Biology

RESEARCH AREA

Research on emerging and re-emerging infectious diseases with high biosafety level (BSL3 and BSL4) as part of the OneHealth concept. Discovery, characterization and complex understanding of new viruses, assessment of their zoonotic ability (ability to jump from animal to human).

SELECTED PUBLICATIONS

Tóth, GE., Hume, AJ., Suder, EL., Zeghbib, S., Ábrahám, Á., Lanszki, Z., Varga, Z., Tauber, Z., Földes, F., Zana, B., Scaravelli, D., Scicluna, MT., Pereswiet-Soltan, A., Görföl, T., Terregino, C., De Benedictis, P., Garcia-Dorival, I., Alonso, C., Jakab, F., Mühlberger, E., Leopardi, S., **Kemenesi, G.** (2023) Isolation and genome characterization of Lloviu virus from Italian Schreibers's bats. **Sci Rep 13:** 11310.

Fletcher, P., Feldmann, F., Takada, A., Crossland, NA., Hume, AJ., Albariño, C., **Kemenesi, G.**, Feldmann, H., Mühlberger, E., Marzi, A. (2023) Pathogenicity of Lloviu and Bombali Viruses in Type I Interferon Receptor Knockout Mice. **J Infect Dis 228:** S548-S553

Kemenesi, G., Tóth, E G., Mayora-Neto, M., Scott, S., Temperton, N., Wright, E., Mühlberger, E., Adam J. Hume, Ellen L. Suder, Zana, B., Boldogh A, S., Görföl, T., Estók, P., Lanszki, Zs., Somogyi, A B., Nagy, Á., Pereszlényi, I Cs., Dudás, Cs., Földes, F., Kurucz, K., Madai, M., Zeghbib, S., Maes, P., Vanmechelen, B., Jakab, F. (2022) Isolation of infectious Lloviu virus from Schreiber's bats in Hungary. **Nat Commun 13:** 1706.

Lanszki, Zs., Tóth E. G., Schütz, É., Zeghbib, S., Rusvai, Zs., Jakab, F., **Kemenesi, G.** (2022) Complete genomic sequencing of canine distemper virus with nanopore technology during an epizootic event. **Sci Rep 12:** 4116.

Hume, J A., Heiden, B., Olejnik, J., Suder, L E., Ross, S., Scoon, A W., Bullitt, E., Ericsson, M., White, R M., Turcinovic, J., Thao, T N T., Hekman, M R., Kaserman, E J., Huang, J., Alysandratos, K D., Toth, E G., Jakab, F., Kotton, N., Wilson, A A., Emili, A., Thiel, V., Connor, H J., **Kemenesei, G.**, Cifuentes, D., Mühlberger, E. (2022) Recombinant Lloviu virus as a tool to study viral replication and host responses **PLoS Pathog.**

SÁNDOR KUNSÁGI-MÁTÉ

University of Pécs
Faculty of Pharmacy
Department of Organic and
Pharmacological Chemistry

RESEARCH AREA

The determinant role of the weak molecular interactions in the transport of bioactive molecules is associated either to their moderated adsorption onto the macromolecule's surface or also to the solubility of bioactive molecules moderated by the formation of inclusion complexes. The latter process offers too the selective and sensitive detection of bioactive molecules. Further the stereo-chemical and structural facts, the weak molecular interactions and the resulted chemical equilibria are also affected by the temperature and the molecular environment. During the last few years we described the effect of the bulk properties of the molecular environment onto the stabilities of the above mentioned inclusion complexes and also the effect of the solvent water structures have been investigated accordingly in our lab. Some cases the antioxidant, scavenging effect has been investigated regarding to the target-specific therapeutic applications. Our overall goal is to perform investigations to determine the effect of the molecular packing in the stability of drugs, to clarify the role of micro-solvation and to describe the related overall mechanisms.

SELECTED PUBLICATIONS

Preisz, Zs., **Kunsági-Máté, S.** (2021) Effect of methotrexate and its photodegradation products on the temperature induced denaturation of human serum albumin. **Spectrochim Acta A 245:**118898.

Kovács, F., Yan, H., Li, H., **Kunsági-Máté, S.** (2021) Temperature-Induced Change of Water Structure in Aqueous Solutions of Some Kosmotropic and Chaotropic Salts. **Int J Mol Sci 22:** 12896.

Preisz, Zs., Hartvig, N., Bognár, B., Kálai, T., **Kunsági-Máté, S.** (2021) Comparative EPR Study on the Scavenging Effect of Methotrexate with the Isomers of Its Photoswitchable Derivative. **Pharmaceuticals 14:** 665.

Preisz, Zs., Nagymihály, Z., Lemli, B., Kollár, L., **Kunsági-Máté, S.** (2020) Weak interaction of the antimetabolite drug methotrexate with a cavitand derivative. **Int J Mol Sci 21:** 4345.

Kovács, F., **Kunsági-Máté, S.** (2020) Change of liquid water structure under the presence of phosphate anion during changing its kosmotropic character to chaotropic along its deprotonation route. **Chem Phys Lett 756:** 137827.

KRISZTIÁN KVELL

University of Pécs
Faculty of Pharmacy
Department of Pharmaceutical Biotechnology

RESEARCH AREA

Anti-tumour effect of exercise-derived microRNAs: Regular exercise is known to protect against the development of many chronic diseases, including cancer. Our research has mapped the health protective effects of microRNAs at the molecular level. Levels of several micro-RNAs that protect against the development of tumours, including lung tumours, are elevated, based on our own data and literature. These micro-RNAs have a long-term preventive effect, but in the short term they may have an adjuvant oncotherapeutic, i.e. additional anti-tumour effect. Investigation of the toxic effects of the SARS2 viral spike protein: COVID-19 disease, caused by SARS-CoV-2, affects many tissues and organs. Although it has become known as a respiratory disease, it actually attacks the kidneys, heart/circulatory system, digestive system and central nervous system as well. Some articles have raised the toxicity of Spike protein and its degradation products in aqueous solution on cells. Our working hypothesis is that Spike protein and its degradation products released from SARS-CoV-2 viruses during infection of epithelial cells exert toxic effects. We test this working hypothesis in a conventional 2D, conventional 3D cell culture system.

SELECTED PUBLICATIONS

Garai, K., Adam, Z., Herczeg, R., Banfai, K., Gyebrovszki, A., Gyenesei, A., Pongracz, JE., Wilhelm, M., **Kvell, K.** (2021) Physical Activity as a Preventive Lifestyle Intervention Acts Through Specific Exosomal miRNA Species-Evidence From Human Short- and Long-Term Pilot Studies. **Front Physiol 12:** 658218.

Garai, K., Adam, Z., Herczeg, R., Katai, E., Nagy, T., Pal, S., Gyenesei, A., Pongracz, JE., Wilhelm, M., **Kvell K.** (2019) Artificial Neural Network Correlation and Biostatistics Evaluation of Physiological and Molecular Parameters in Healthy Young Individuals Performing Regular Exercise. **Front Physiol 10:** 1242.

Banfai, K., Ernszt, D., Pap, A., Bai, P., Garai, K., Belharazem, D., Pongracz, JE., **Kvell, K.** (2019) „Beige" Cross Talk Between the Immune System and Metabolism. **Front Endocrinol (Lausanne) 10:** 369

Banfai, K., Garai, K., Ernszt, D., Pongracz, JE., **Kvell, K.** (2019) Transgenic Exosomes for Thymus Regeneration. **Front Immunol 10:** 862

Ernszt, D., Banfai, K., Kellermayer, Z., Pap, A., Lord, JM., Pongracz, JE., **Kvell, K.** (2017) PPARgamma Deficiency Counteracts Thymic Senescence. **Front Immunol 8:** 1515.

EDINA LEMPEL

University of Pécs
Medical School
Department of Dentistry
Oral and Maxillofacial Surgery

RESEARCH AREA

Physical and biocompatibility investigations of rapid polymerized and pre-heated resin composites. According to the manufacturer's recommendation, the adequate curing of the rapid polymerized resin composites can be achieved in 3 seconds with a suitable curing unit up to 4 mm in layer thickness. However, both the layer thickness and the short exposure time could be a barrier to the proper monomer-polymer conversion. Additionally, internal stress can develop due to shrinkage of the polymerizing material, which can cause gaps at the filling/tooth interface. Insufficient polymerization may result in unreacted monomer release in the oral cavity or may diffuse to the pulp through the tubular dentin. The monomers' toxic effects are well known, although details are still being researched to this day. However, this chemical effect might be supplemented by a thermal effect, arises from both the energy, delivered by the curing unit and from the heat generated during the exothermic polymerization of the resin composite. It may cause further cell damage to pulpal cells if it exceeds the 5.5 0C threshold in the pulp. This thermal effect is even more significant in the cases of pre-heated resin composites, which are preferred because of their good adaptation ability and mechanical properties.
During our investigations, we would test the gap formation caused by the polymerization shrinkage using micro-CT; we would measure the intrapulpal manifestation of the heat generated during the polymerization; and we would examine the effects of physical and chemical stimuli on cells histomorphometric and immunohistochemical changes) on 3D pulpal tissue model.

SELECTED PUBLICATIONS

Lempel, E., Kincses, D., Szebeni, D., Jordáki, D., Lovász, BV., Szalma, J. (2022) Intrapulpal temperature changes during the cementation of ceramic veneers. **Scientific Reports 12:** 12919.

Lempel, E., Szalma, J. (2022) Effect of spray air settings of speed-increasing contra-angle handpieces on intrapulpal temperatures, drilling times, and coolant spray pattern. **Clin Oral Investig 26:** 523-533.

Kincses, D., Böddi, K., Őri, Zs., Lovász, B. V., Jeges, S., Szalma, J., Kunsági-Máté, S., **Lempel, E.** (2021) Pre-heating effect on monomer elution and degree of conversion of contemporary and thermoviscous bulk-fill resin-based dental composites. **Polymers (Basel) 13:** 3599.

Lempel, E., Őri, Zs., Kincses, D., Lovász, B. V., Kunsági-Máté, S., Szalma, J. (2021) Degree of conversion and in vitro temperature rise of pulp chamber during polymerization of flowable and sculptable conventional, bulk-fill and short-fibre reinforced resin composites. **Dental Mater 7:** 983–997.

Lempel, E., Lovász, B. V., Bihari, E., Krajczár, K., Jeges, S., Tóth, Á., Szalma, J. (2019) Long-term clinical evaluation of direct resin composite restorations in vital vs. endodontically treated posterior teeth – Retrospective study up to 13 years. **Dent Mater 35:** 1308-1318.

ERIKA PINTÉR

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Scientific interests: neuro-immuno-pharmacology, inflammation The role of capsaicin-sensitive sensory nerve endings in the regulation of microcirculation and neurogenic inflammation. Immunomodulatory effects of neurogenic inflammation. Anti-inflammatory effects of somatostatin and its analogues. Biological effects of hydrogen sulphide.

SELECTED PUBLICATIONS

Saghy, E., Sipos, E., Acs, P., Bolcskei, K., Pohoczky, K., Kemeny, A., Sandor, Z., Szoke, E., Setalo Jr. G., Komoly, S., **Pinter, E.** (2016) TRPA1 deficiency is protective in cuprizone-induced demyelination-A new target against oligodendrocyte apoptosis. **Glia 64:** 2166-2180.

Kemény, A., Kodji, X., Horváth, Sz., Komlódi, R., Szőke, E., Sándor, Z., Perkecz, A., Gyömörei, Cs., Sétáló, Gy., Kelemen, B., Biro, T., Toth, B., **Pinter, E.**, Gyulai, R. (2018) TRPA1 acts in a protective manner in imiquimod-induced psoriasiform dermatitis in mice. **J Invest Dermatol 138:** 1774-1784.

Bátai, István Z., Pápainé Sár, C., Horváth, Á., Borbély, É., Bölcskei, K., Kemény, Á., Sándor, Z., Nemes, B., Helyes, Zs., Perkecz, A., Mócsai, A., Pozsgai, G., **Pintér, E.** TRPA1 Ion Channel Determines Beneficial and Detrimental Effects of GYY4137 in Murine Serum-Transfer Arthritis. (2019) **Front Pharmacol 10:** 964.

Kriszta, G., Nemes, B., Sándor, Z., Ács, P., Komoly, S., Berente, Z., Bölcskei, K., **Pintér, E.** (2020) Investigation of Cuprizone-Induced Demyelination in mGFAP-Driven Conditional Transient Receptor Potential Ankyrin 1 (TRPA1) Receptor Knockout Mice. **Cells 9:** 81

Kántás, B., Szőke, É., Börzsei, R., Bánhegyi, P., Asghar, J., Hudhud, L., Steib, A., Hunyady, Á., Horváth, Á., Kecskés, A., Borbély, É., Hetényi, Cs., Petfő, G., **Pintér, E.** (2021) In Silico, In Vitro and In Vivo Pharmacodynamic Characterization of Novel Analgesic Drug Candidate Somatostatin SST4 Receptor Agonists **Front Pharmacol 11:** 601887.

KRISZTINA POHÓCZKY

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

My research focuses on the role of capsaicin-sensitive peptidergic sensory nerve endings, ion channels, receptors, and the sensory neuropeptides released from them, as well as neuro-immune interactions in different inflammatory diseases and chronic pain. Our research mainly involves DNA, RNA, protein-based, and cellular analyses of fresh surgical patient specimens, archived histological blocks, and in vitro cellular model systems. Endometriosis is a severe gynecological condition associated with chronic pain and infertility. Many theories have been hypothesized to explain the background of the disease, but the exact pathomechanism of the disease is not known. The adhesions and chronic abdominal pain that develop negatively affect the quality of life of patients. In our work, we investigate potential intracellular (disease-specific signaling pathways) and cellular (migration, invasion, increased survival) processes that contribute to the formation of endometriotic lesions using surgical specimens and immortalized cell lines. Hungary ranks first in Europe in terms of mortality from oral cancer. Anatomical localization, the difficulty of removing the tumor with a negative resection margin, and late diagnosis all contribute to the low survival rate. Vanilloid 1 and ankyrin 1 receptor, which are members of the Transient Receptor Ion Channels, have been hypothesized to play a role in some tumor types, and our group has demonstrated that they are functionally active in oral squamous cell carcinoma cells, but their exact role is unknown. Our main goals are to investigate the role of these receptors in this pathology using human tumor samples and the investigate the TRP-mediated effects of cigarette smoke both in human samples and and cell lines.

SELECTED PUBLICATIONS

Pohóczky, K., Kun, J., Szentes, N., Aczél, T., Urbán, P., Gyenesei, A., Bölcskei, K., Szőke, É., Sensi, S., Dénes, Á., Goebel, A., Tékus, V., Helyes, Z. (2022) Discovery of novel targets in a complex regional pain syndrome mouse model by transcriptomics: TNF and JAK-STAT pathways. **Pharmacol Res 182:** 106347.

Kissm, F., **Pohóczky, K.**, Görbe, A., Dembrovszky, F., Kiss, S., Hegyi, P., Szakó, L., Tóth, L., Somogyiné Ezer, É., Szalai, E., Helyes, Z. (2022) Addition of EGFR inhibitors to standard chemotherapy increases survival of advanced head and neck squamous cell carcinoma patients: a systematic review and meta analysis. **Oral dis 29:** 1905-1919.

Kiss, F., Kormos, K., Szőke, É., Kecskés, A., Tóth, N., Steib, A., Szállási, Á., Scheich, B., Gaszner, B., Kun, J., Fülöp, G., **Pohóczky, K.**, Helyes Z. (2021) Functional Transient Receptor Potential Ankyrin 1 and Vanilloid 1 Ion channels are overexpressed in human oral squamous cell carcinoma. **Int J Mol Sci 23:** 1921.

Kecskés, A., **Pohóczky, K**., Kecskés, M., Varga, V Z., Kormos, V., Szőke, É., Henn-Mike, N., Fehér, M., Kun, J., Gyenesei, A., Renner, É., Palkovits, M., Ferdinandy, P., Ábrahám, M I., Gaszner, B., Helyes, Z. (2020) Characterization of Neurons Expressing the Novel Analgesic Drug Target Somatostatin Receptor 4 in Mouse and Human Brains. **Int J Mol Sci 21:** 7788.

MIKLÓS POÓR

University of Pécs
Medical School
Department of Laboratory Medicine

RESEARCH AREA

I. Interaction of mycotoxins with biomolecules and with potential mycotoxin binders: Toxicokinetic studies, investigation of combinative effects, and experiments with potential mycotoxin binders (for toxin extraction, decontamination, and/or detoxification purposes). II. Interaction of natural polyphenols and their metabolites with drugs: Certain dietary supplements contain extremely high doses of polyphenols; in this project, the interaction of these polyphenols and their metabolites are examined with important proteins from the pharmacokinetic point of view (e.g., serum albumin, biotransformation enzymes, drug transporters).

SELECTED PUBLICATIONS

Poór, M., Faisal, Z., Zand, A., Bencsik, T., Lemli, B., Kunsági-Máté, S., Szente, L. (2018) Removal of zearalenone and zearalenols from aqueous solutions using insoluble beta-cyclodextrin bead polymer. **Toxins 10:** 216.

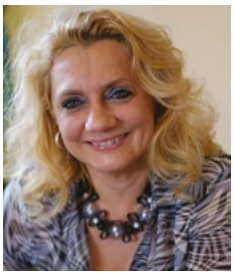
Mohos, V., Pánovics, A., Fliszár-Nyúl, E., Schilli, G., Hetényi, C., Mladěnka, P., Needs, P.W., Kroon, P.A., Pethő, G., **Poór, M.** (2019) Inhibitory effects of quercetin and its human and microbial metabolites on xanthine oxidase enzyme. **Int J Mol Sci 20:** 2681.

Faisal, Z., Garai, E., Csepregi, R., Bakos, K., Fliszár-Nyúl, E., Szente, L., Balázs, A., Cserháti, M., Kőszegi, T., Urbányi, B., Csenki, Z., **Poór, M.** (2020) Protective effects of beta-cyclodextrins vs. zearalenone-induced toxicity in HeLa cells and Tg(vtg1:mCherry) zebrafish embryos. **Chemosphere 240:** 124948.

Mohos, V., Fliszár-Nyúl, E., Ungvári, O., Bakos, É., Kuffa, K., Bencsik, T., Zsidó, B.Z., Hetényi, C., Telbisz, Á., Özvegy-Laczka, C., **Poór, M.** (2020) Effects of chrysin and its major conjugated metabolites chrysin-7-sulfate and chrysin-7-glucuronide on cytochrome P450 enzymes, and on OATP, P-gp, BCRP and MRP2 transporters. **Drug Metab and Dispos 48:** 1064-1073.

Fliszár-Nyúl, E., Szabó, Á., Szente, L., **Poór, M.** (2020) Extraction of mycotoxin alternariol from red wine and from tomato juice with beta-cyclodextrin bead polymer. **J Mol Liq 319:** 114180.

Csenki, Z., Garai, E., Faisal, Z., Csepregi, R., Garai, K., Kánainé Sipos D., Szabó, I., Kőszegi, T., Czéh, Á., Czömpöly, T., Kvell, K., **Poór, M.** (2021) The individual and combined effects of ochratoxin A with citrinin and their metabolites (ochratoxin B, ochratoxin C, and dihydrocitrinone) on 2D/3D cell cultures, and zebrafish embryo models. **Food Chem Toxicol 158:** 112674.



DÓRA REGLŐDI

University of Pécs
Medical School
Department of Anatomy

RESEARCH AREA

Investigating the effects of PACAP. Pituitary adenylate cyclase activating polypeptide (PACAP) is an anti-apoptotic, anti-inflammatory and antioxidant neuropeptide with neuroprotective and general cytoprotective effects that have been demonstrated in a number of experiments. Our group has been working for more than 15 years on mapping the physiological effects of PACAP and its protective role in in vitro and in vivo models of various pathological conditions. In the absence of endogenous PACAP, knockout (KO) mice are highly susceptible to adverse effects. Early signs of ageing are also observed due to increased oxidative stress, inflammation and apoptosis associated with the deficiency state. Our preliminary observations show increased neuronal degeneration in the brains of KO mice. In the absence of PACAP, we have described systemic tissue amyloidosis associated with aging, in addition to retinal degeneration. Our results so far suggest that the absence of PACAP accelerates several degenerative processes and leads to premature ageing. Our human, translational studies investigate PACAP expression/levels in different human tissues and biological fluids and we investigate correlations between pathological conditions and alterations in PACAP levels. These may be important for the future biomarker use of PACAP as a diagnostic and/or prognostic tool. Results can also shed light on biological functions of PACAP in the human body.

SELECTED PUBLICATIONS

Kiss, P., Banki, E., Gaszner, B., Nagy, D., Helyes, Zs., Pal, E., Reman, Gy., Toth, G., Tamas, A., **Reglodi, D.** (2021) Protective effects of PACAP in a rat model of diabetic neuropathy. **Int J Mol Sci 22:** 10691

Toth, D., Tamas, A., **Reglodi, D.** (2020) The neuroprotective and biomarker potential of PACAP in human traumatic brain injury. **Int J Mol Sci 21:** 827

Toth, D., Szabo, E., Tamas, A., Juhasz, T., Horvath, G., Fabian, E., Opper, B., Szabo, D., Maugeri, G., D'Amico, AG., D'Agata, V., Vicena, V., **Reglodi, D.** (2020) Protective effects of PACAP in peripheral organs. **Front Endocrinol 11:** 377

Reglodi, D., Jungling, A., Longuespée, R., Kriegsmann, J., Casadonte, R., Kriegsmann, M., Juhasz, T., Bardosi, A., Tamas, A., Fulop, BD., Kovacs, K., Nagy, Zs., Sparks, J., Miseta, A., Mazzucchelli, G., Hashimoto, H., Bardosi, A. (2018) Accelerated pre-senile systemic amyloidosis in PACAP knockout mice – a protective role of PACAP in age-related degenerative processes. **J Pathol 245:** 478-490

Reglodi, D., Atlasz, T., Szabo, E., Jungling, A., Tamas, A., Juhasz, T., Fulop, BD., Bardosi, A. (2018) PACAP deficiency as a model of aging. **Geroscience 40:** 437-452.

JÓZSEF SZALMA

University of Pécs
Medical School
Department of Oral and Maxillofacial Surgery

RESEARCH AREA

The research aims to reduce the complications of oral surgery interventions. One research direction deals with the heat production of hard tissue preparations. Heat effects on periodontal fibers can lead to ankylosis, those on bone can lead to thermal osteonecrosis, and heat effects on peripheral nerves can lead to neurosensory functional impairment. These thermal effects are sometimes unknown, but even if known, we must take them into account when determining the appropriate preparation methods. Our research is aimed at mapping temperatures and reducing them.

Another line of research focuses on the prevention of peripheral nerve injuries (inf. alveolar nerve, lingual nerve) associated with the removal of wisdom teeth. The precision and diagnostic/prognostic value of imaging procedures can be increased by searching for and monitoring specific radiologic signs, and by refining surgical procedures (sectioned tooth removal, coronectomy), these serious complications are more likely to be avoided, while not increasing the radiation exposure to patients.

SELECTED PUBLICATIONS

Pacheco, A., Soós, B., Lempel, E., Simon, I., Maróti, P., Möhlhenrich, SC., **Szalma J.** (2023) The effect of individual drilling sleeves ont he precision of coronectomy tooth sections. An in vitro 3D-printed jaw model experiment. Clin **Oral Investig 27:** 6769-6780.

Szalma, J., Janovics, K., Pacheco, A., Kaszás, B., Lempel, E. (2022) Pre-eruptive intracoronal resorption in "high-risk" impacted third molars: A report of four cases. **J Craniomaxillofac Surg 25:** S1010-5182.

Janovics, K., Soós, B., Tóth, Á., **Szalma J.** (2021) Is it possible to filter third molar cases with panoramic radiography in which roots surround the inferior alveolar canal? A comparison using cone-beam computed tomography. **J Craniomaxillofac Surg 49:** 971-979.

Lempel, E., **Szalma, J.** (2022) Effect of spray air settings of speed-increasing contra-angle handpieces on intrapulpal temperatures, drilling times, and coolant spray pattern. **Clin Oral Investig 26:** 523–533.

Szalma, J., Vajta, I., Lovász, BV., Kiss, C., Soós, B., Lempel, E. (2020) Identification of specific panoramic high-risk signs in impacted third molar cases where cone beam computed tomography changes the treatment decision. **J Oral Maxillofac Surg 78:** 1061-1070.

Szalma, J., Lovász, BV., Vajta, L., Soós, B., Lempel, E., Möhlhenrich, SC. (2019) The influence of the chosen in vitro bone simulation model on intraosseous temperatures and drilling times. **Sci Rep 9:** 11871.

ÉVA SZŐKE

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Pain sensation is mediated by the nocisensor Transient Receptor Potential ion channels such as the Vanilloid 1 (TRPV1) and the TRP ankyrin 1 (TRPA1). Previous discoveries on TRP channels described important structural and functional properties of these proteins, but very little is known about the function, importance and modulation opportunities of the lipid rafts surrounding them in the plasma membrane. We recently discovered that lipid raft disruption by depletion of various constituents, by methyl β-cyclodextrin (MCD), sphingomyelinase (SMase), myriocin and our carboxi-steroid compound reduced TRP activation on sensory neurons and transfected cells. We examine the potential analgesic effect of MCD, SMase, myriocin or our carboxi-steroid compound in topical dermatological formulation in in vivo mouse models. The lipid raft disruptor myriocin had an antitumor activity in a murine melanoma model. We examine the potential dual effect (antitumor and analgesic activity) of myriocin in our mouse osteosarcoma model.

SELECTED PUBLICATIONS

Szőke É, Börzsei R, Tóth DM, Lengl O, Helyes Z, Sándor Z, Szolcsányi J (2010) Effect of lipid raft disruption on TRPV1 receptor activation of trigeminal sensory neurons and transfected cell line. **Eur J Pharmacol 628:** 67-74.

Sághy É, **Szőke É**, Payrits M, Helyes Zs, Börzsei R, Erostyák J, Jánosi TZ, Sétáló Gy Jr, Szolcsányi J (2015) Evidence for the role of lipid rafts and sphingomyelin in Ca2+-gating of Transient Receptor Potential channels in trigeminal sensory neurons and peripheral nerve terminals, **Pharmacol Res 100:** 101-116.

Payrits M, Horváth Á, Biró-Sütő T, Erostyák J, Makkai G, Sághy É, Pohóczky K, Kecskés A, Kecskés M, Szolcsányi J, Helyes Z, **Szőke É.** (2020) Resolvin D1 and D2 Inhibit Transient Receptor Potential Vanilloid 1 and Ankyrin 1 Ion Channel Activation on Sensory Neurons via Lipid Raft Modification. **Int J Mol Sci 21:** 5019.

Horváth Á, Biró-Sütő T, Kántás B, Payrits M, Skoda-Földes R, Szánti-Pintér E, Helyes Z, **Szőke É** (2020) Antinociceptive Effects of Lipid Raft Disruptors, a Novel Carboxamido-Steroid and Methyl β-Cyclodextrin, in Mice by Inhibiting Transient Receptor Potential Vanilloid 1 and Ankyrin 1 Channel Activation. **Front Physiol 11:** 559109.

Horváth Á, Payrits M, Steib A, Kántás B, Biró-Sütő T, Erostyák J, Makkai G, Sághy É, Helyes Z, **Szőke É.** (2021) Analgesic effects of lipid raft disruption by sphingomyelinase and myriocin via Transient Receptor Potential Vanilloid 1 and Transient Receptor Potential Ankyrin 1 ion channel modulation. **Front Pharmacol 11:** 593319.

VALÉRIA TÉKUS

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Chronic primary pain conditions including Complex Regional Pain Syndrome (CRPS) and fibromyalgia (FM) are unmet medical needs. Despite intensive research, their aetiology and the pathophysiology are not understood, partly due to the lack of a translationally relevant animal models mimicking the main clinical symptoms and pathophysiological mechanisms.
Based on our earlier results, our research hypothesis is that neuroinflammatory mechanisms at the level of the primary sensory neurones in the dorsal root ganglia and pain-related brain regions leading to central sensitization play a crucial role in the development and maintenance CRPS and stress-related pain like FM. To identify new therapeutic options, our experiments will identify the main pathophysiological pathways and networks responsible for the chronic phase of CRPS and stress-related pain, and the role of pathogenic autoantibodies in the processes leading to the prolonged and maintenance of CRPS-related pain. We will explore the potential role of neuroinflammatory mechanisms in the chronic phase of CRPS and stress-related pain, and the role of inflammasomes and their cytokines in the brain.

SELECTED PUBLICATIONS

Pohóczky, K., Kun, J., Szentes, N., Aczél, T., Urbán, P., Gyenesei, A., Bölcskei, K., Szőke, É., Sensi, S., Dénes, Á., Goebel, A., **Tékus, V.**, Helyes, Z. (2022). Discovery of novel targets in a complex regional pain syndrome mouse model by transcriptomics: TNF and JAK-STAT pathways. **Pharmacol Res 182:** 106347.

Helyes, Z., **Tékus, V.**, Szentes, N., Pohóczky, K., Botz, B., Kiss, T., Kemény, Á., Környei, Z., Tóth, K., Lénárt, N., Ábrahám, H., Pinteaux, E., Francis, S., Sensi, S., Dénes, Á., Goebel, A. (2019) Transfer of complex regional pain syndrome to mice via human autoantibodies is mediated by interleukin-1-induced mechanisms. **Proc Natl Acad Sci U S A 116:** 13067–13076.

Tékus, V., Horváth, Á. I., Csekő, K., Szabadfi, K., Kovács-Valasek, A., Dányádi, B., Deres, L., Halmosi, R., (...) Ferdinandy, P., Pintér, E., Helyes, Z. (2021) Protective effects of the novel amine-oxidase inhibitor multi-target drug SZV 1287 on streptozotocin-induced beta cell damage and diabetic complications in rats. **Biomed Pharmacother 134:** 111105.

Horváth, Á., **Tékus, V.**, Bencze, N., Szentes, N., Scheich, B., Bölcskei, K., Szőke, É., Mócsai, A., Tóth-Sarudy, É., Mátyus, P., Pintér, E., Helyes, Z. (2018) Analgesic effects of the novel semicarbazide-sensitive amine oxidase inhibitor SZV 1287 in mouse pain models with neuropathic mechanisms: Involvement of transient receptor potential vanilloid 1 and ankyrin 1 receptors. **Pharmacol Res 131:** 231–243.

Horváth, Á. I., Szentes, N., **Tékus, V.**, Payrits, M., Szőke, É., Oláh, E., Garami, A., Fliszár-Nyúl, E., Poór, M., Sár, C., Kálai, T., Pál, S., Percze, K., Scholz, É. N., Mészáros, T., Tóth, B., Mátyus, P., Helyes, Z. (2021) Proof-of-Concept for the Analgesic Effect and Thermoregulatory Safety of Orally Administered Multi-Target Compound SZV 1287 in Mice: A Novel Drug Candidate for Neuropathic Pain. **Biomedicines 9:** 749.

DÓRA TÍMEA ZELENA

University of Pécs
Medical School
Institute of Physiology

RESEARCH AREA

1. The Role of Vasopressin in Psychiatric Disorders
Vasopressin, primarily known for regulating our body's salt-water balance, is also an important neurotransmitter in the brain. Since it plays a crucial role in stress regulation, its involvement in stress-related psychiatric disorders such as anxiety and depression has been explored. Additionally, vasopressin is important for higher cognitive functions like learning, memory, and the formation of social relationships. Disruptions in these processes have been implicated in conditions like schizophrenia and autism. Our experiments aim to investigate the role of specific brain regions in these processes. Given that both the studied disorders and vasopressin itself exhibit strong gender differences (for example, women are more prone to depression, while male animals have more vasopressin in their brains), we intend to extend our research to both genders.
2. Studying Alzheimer's Disease in Animal Models
In our aging society, the prevalence of dementia is steadily increasing, making it essential to research new therapeutic possibilities. The complexity of the disease necessitates the use of animal models. Currently, the most common models are genetically modified mouse models. In our laboratory, we aim to test new therapeutic options using a mouse model previously employed, both at the whole organism level (behavior) and at the molecular level underlying changes (molecular biology techniques, imaging). Therapeutic interventions include influencing movement and nutrition. We pay increased attention to comorbidities as well (anxiety, depression, and metabolic changes). We emphasize the potential differences between the two genders.

SELECTED PUBLICATIONS

Szőnyi, A., Zichó, K., Barth, A. M., Gönczi, R. T., Schlingloff, D., Török, B., Sipos, E., Major, A., Bardóczi, Z., Sos, K. E., Gulyás, A. I., Varga, V., **Zelena, D.**, Freund, T. F., Nyiri, G. (2019) Median raphe controls acquisition of negative experience in the mouse. **Science 366:** 8746.

Chaves, T., Török, B., Fazekas, C. L., Correia, P., Sipos, E., Várkonyi, D., Hellinger, Á., Erk, D., **Zelena, D.** (2022) Median raphe region GABAergic neurons contribute to social interest in mouse. **Life Sci. 289:** 120223.

Barabás, K., Makkai, B., Farkas, N., Horváth, H. R., Nagy, Z., Váradi, K., **Zelena, D.** (2022) Influence of COVID-19 pandemic and vaccination on the menstrual cycle: A retrospective study in Hungary. **Front Endocrinol. 13:** 974788.

Farkas, S., Szabó, A., Török, B., Sólyomvári, C., Fazekas, C. L., Bánrévi, K., Correia, P., Chaves, T., **Zelena, D.** (2022) Ovariectomy-induced hormone deprivation aggravates Aβ1-42 deposition in the basolateral amygdala and cholinergic fiber loss in the cortex but not cognitive behavioral symptoms in a triple transgenic mouse model of Alzheimer's disease. **Front Endocrinol 13:** 985424.

Keller, D., Láng, T., Cservenák, M., Puska, G., Barna, J., Csillag, V., Farkas, I., **Zelena, D.**, (...) T. B., Palkovits, M., Hasan, M. T., Grinevich, V., Dobolyi, A. (2022) A thalamo-preoptic pathway promotes social grooming in rodents. **Curr Biol. 32:** 4593-4606.

PÉCS
SZENT-GYÖRGYI JUNIOR MENTORS

ZSOLT KRISTÓF BALI

University of Pécs
Translational Neuroscience Research Group

RESEARCH AREA

Investigating the neurocognitive underpinnings of ageing and neurocognitive impairment in rodents: identification of preclinical drug development strategies and development of combined cognitive enhancer therapies. The main objective of the project is to understand and model the processes underlying brain ageing and neurocognitive disorders (dementias) in rodents and to study cellular and behavioural processes in a coordinated manner in the same model. The research is carried out in two locations: our cellular biology (electrophysiology) laboratory is located at the Faculty of Natural Sciences (Faculty of Science) and our small animal behavioural pharmacology laboratory is located at the Szentágothai Research Centre (SZKK). Our preclinical animal models include e.g. pharmacologically induced amnesia, natural ageing, repetitive mild traumatic brain injury and genetic (DREADD) models. Behavioural changes are investigated in state-of-the-art test packeges. Our results are further utilized in both basic and applied drug discovery research. Our main long-term goal is to unravel the as yet unknown mechanisms underlying neurocognitive diseases and to identify biomarkers that may later play a crucial role in the diagnosis and treatment of cognitive disorders and in the development of new drug candidates.

SELECTED PUBLICATIONS

Bruszt, N., **Bali, ZK.** Tadepalli, SA., Nagy, LV., Hernádi, I. (2021) Potentiation of cognitive enhancer effects of Alzheimer's disease medication memantine by alpha7 nicotinic acetylcholine receptor agonist PHA-543613 in the Morris water maze task. **Psychopharmacology 238:** 3273-3281.

Nagy, LV., **Bali, ZK.**, Kapus, G., Pelsőczi, P., Farkas, B., Lendvai, B., Lévay, G., Hernádi, I. (2021) Converging evidence on D-amino acid oxidase-dependent enhancement of hippocampal firing activity and passive avoidance learning in rats. **Int J Neuropsychopharmacol 24(5):** 434-445.

Tadepalli, SA., **Bali, ZK.**, Bruszt, N., Nagy, LV., Amrein, K., Fazekas, B., Büki, A., Czeiter, E., Hernádi, I. (2020) Long-term cognitive impairment without diffuse axonal injury following repetitive mild traumatic brain injury in rats. **Behav Brain Res 378:** 112268.

Bali, ZK., Bruszt, N., Tadepalli, SA., Csurgyók, R., Nagy, LV., Tompa, M., Hernádi I. (2019) Cognitive enhancer effects of low memantine doses are facilitated by an alpha7 nicotinic acetylcholine receptor agonist in scopolamine-induced amnesia in rats. **Front Pharmacol 10:** 73.

Bali, ZK., Nagy, LV., Bruszt, N., Bodó, K., Engelmann, P., Hernádi, Z., Göntér, K., Tadepalli, SA., Hernádi, I. (2023) Increased brain cytokine level associated impairment of vigilance and memory in aged rats can be alleviated by alpha7 nicotinic acetylcholine receptor agonist treatment. **Geroscience 46:** 645-664.

KITTI GARAI

University of Pécs
Faculty of Pharmacy
Department of Pharmaceutical Biotechnology

RESEARCH AREA

It has long been evident that physical exercise reduces the risk of cancer and improves treatment efficacy in tumor patients. Recent studies have shown that miRNAs are actively released into the circulation during exercise, and are deeply involved in cancer pathology. During our previous research, we detected several microRNAs that protect against the development of lung tumors. In the future, by studying the biological functions of the identified microRNAs, we will be able to better understand the regulatory network of the molecular mechanisms through which regular exercise can prevent lung carcinoma.

SELECTED PUBLICATIONS

Garai, K., Adam, Z., Herczeg, R., Banfai, K., Gyebrovszki, A., Gyenesei, A., Pongracz, J. E., Wilhelm, M., Kvell, K. (2021) Physical Activity as a Preventive Lifestyle Intervention Acts Through Specific Exosomal miRNA Species-Evidence From Human Short- and Long-Term Pilot Studies. **Front Physiol. 22:** 794940.

Garai, K., Adam, Z., Herczeg, R., Katai, E., Nagy, T., Pal, S., Gyenesei, A., Pongracz, J. E., Wilhelm, M., Kvell, K. (2019) Artificial Neural Network Correlation and Biostatistics Evaluation of Physiological and Molecular Parameters in Healthy Young Individuals Performing Regular Exercise. **Front Physiol. 10:** 1242.

ESZTER PÁKAI

University of Pécs
Medical School
Institute for Translational Medicine

RESEARCH AREA

Normal body temperature – which is essential for life – is maintained by various thermoregulatory mechanisms. Thermoregulatory disorders are present in many pathological conditions, e.g., febrile diseases, systemic inflammation (sepsis), organ dysfunctions (e.g., pancreatitis), heat stroke, and hypothermia. It is of utmost importance to discover the pathophysiological processes in the thermoregulatory disorders. More and more influencing factors are identified, such as the pH status and transient receptor potential channels. In our research, we aim at identifying the neural substrates and molecular mediators involved in the thermoregulatory processes mainly in different animal models, but to some extent also in human studies. Our findings can further advance the knowledge of bodily homeostasis, moreover, they can open new directions in clinical practice, most of all intensive therapy, and other sciences. Successful development of drugs designed specifically to target body temperature, could pave the road to pharmacologically controlled temperature management, thereby advancing the therapeutic approaches in clinical conditions with thermoregulatory disorders.

SELECTED PUBLICATIONS

Toldi, J., Kelava, L., Marton, S., Muhl, D., Kustan, P., Feher, Z., Maar, K., Garai, J., **Pakai, E.**, Garami, A. (2023) Distinct patterns of serum and urine macrophage migration inhibitory factor kinetics predict death in sepsis: a prospective, observational clinical study. **Sci Rep 13:** 588.

Kelava, L., Nemeth, D., Hegyi, P., Keringer, P., Kovacs, D. K., Balasko, M., Solymar, M., **Pakai, E.**, Rumbus, Z., Garami, A. (2022) Dietary supplementation of transient receptor potential vanilloid-1 channel agonists reduces serum total cholesterol level: a meta-analysis of controlled human trials. **Crit Rev Food Sci Nutr 62:** 7025-7035.

Keringer, P., Furedi, N., Gaszner, B., Miko, A., **Pakai, E.**, Fekete, K., Olah, E., Kelava, L., Romanovsky, A. A., Rumbus, Z., Garami, A. (2022) The hyperthermic effect of central cholecystokinin is mediated by the cyclooxygenase-2 pathway. **Am J Physiol Endocrinol Metab 322:** E10-E23.

Csenkey, A., Hargitai, E., **Pakai, E.**, Kajtar, B., Vida, L., Lorincz, A., Gergics, M., Vajda, P., Jozsa, G., Garami, A. (2022) Effectiveness of four topical treatment methods in a rat model of superficial partial-thickness burn injury: the advantages of combining zinc-hyaluronan gel with silver foam dressing. **Injury 53:** 3912-3919.

Olah, E., Rumbus, Z., Kormos, V., Tekus, V., **Pakai, E.**, Wilson, H. V., Fekete, K., Solymar, M., Kelava, L., Keringer, P., Gaszner, B., Whiteman, M., Keeble, J., Pinter, E., Garami, A. (2021) The Hypothermic Effect of Hydrogen Sulfide Is Mediated by the Transient Receptor Potential Ankyrin-1 Channel in Mice. **Pharmaceuticals 14:** 992.

ALEXANDRA VÁCZY

University of Pécs
Medical School
Department of Anatomy

RESEARCH AREA

Investigating the effects of PACAP. Pituitary adenylate cyclase activating polypeptide (PACAP) is an anti-apoptotic, anti-inflammatory and antioxidant neuropeptide with neuroprotective and general cytoprotective effects that have been demonstrated in a number of experiments. Our group has been working for more than 15 years on mapping the physiological effects of PACAP and its protective role in in vitro and in vivo models of various pathological conditions. In the absence of endogenous PACAP, knockout (KO) mice are highly susceptible to adverse effects. Early signs of ageing are also observed due to increased oxidative stress, inflammation and apoptosis associated with the deficiency state. Our preliminary observations show increased neuronal degeneration in the brains of KO mice. In the absence of PACAP, we have described systemic tissue amyloidosis associated with aging, in addition to retinal degeneration. Our results so far suggest that the absence of PACAP accelerates several degenerative processes and leads to premature ageing. Our human, translational studies investigate PACAP expression/levels in different human tissues and biological fluids and we investigate correlations between pathological conditions and alterations in PACAP levels. These may be important for the future biomarker use of PACAP as a diagnostic and/or prognostic tool. Results can also shed light on biological functions of PACAP in the human body.

SELECTED PUBLICATIONS

Patko, E., Szabo, E., Toth, D., Tornoczky, T., Bosnyak, I., **Vaczy A.**, Atlasz, T., Reglodi, D. (2022) Distribution of PACAP and PAC1 Receptor in the Human Eye, **J Mol Neurosci**

Kvarik, T., Reglodi, D., Werling, D., **Vaczy, A.**, Kovari, P., Szabo, E., Kovacs, K., Hashimoto, H., Ertl, T., Gyarmati, J., Atlasz, T. (2021) The Protective Effects of Endogenous PACAP in Oxygen-Induced Retinopathy, **J Mol Neurosci 71:** 2546–2557.

Szabó, E., Patkó, E., **Váczy, A.**, Molitor, D., Csutak, A., Tóth, G., Reglődi, D., Atlasz, T. (2021) Retinoprotective Effects of PACAP Eye Drops in Microbead-Induced Glaucoma Model in Rats, **Int J Mol Sci 22:** 16.

Kovacs, K., **Vaczy, A.**, Fekete, K., Kovari, P., Atlasz, T., Reglodi, D., Gabriel, R., Gallyas, F., Sumegi, B. (2019) PARP Inhibitor Protects Against Chronic Hypoxia/Reoxygenation-Induced Retinal Injury by Regulation of MAPKs, HIF1α, Nrf2, and NFκB. **IOVS 60:** 1478–1490.

Vaczy, A., Kovari, P., Kovacs, K., Farkas, K., Szabo, E., Kvarik, T., Kocsis, B., Fulop, B., Atlasz, T., Reglodi, D. (2018) Protective role of endogenous PACAP in inflammation-induced retinal degeneration. **Curr Pharm Des 24:** 3534–3542.

Vaczy, A., Reglodi, D., Somoskeoy, T., Kovacs, K., Lokos, E., Szabo, E., Tamas, A., Atlasz, T. (2016) The Protective Role of PAC1-Receptor Agonist Maxadilan in BCCAO-Induced Retinal Degeneration. **J Mol Neurosci 60:** 186–194.

BALÁZS ZSIDÓ

University of Pécs
Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

A key step in the early stages of drug design is the design of potent drug molecules. This process is now mostly carried out using computer (pharmaco-informatics) methods, which are capable of handling both large amounts of structural data and complex energy calculations. The pharmacoinformatics toolbox will be used in both target-based and ligand-based design and will be extended with new procedures in the course of the PhD work. The methods will be tested and applied in curricular areas of pharmacology such as pain management, regulation of signalling, antiviral and epigenetic-based therapies.

SELECTED PUBLICATIONS

Zsidó, B. Z., Börzsei, R., Pintér, E., Hetényi, C. (2021) Prerequisite Binding Modes Determine the Dynamics of Action of Covalent Agonists of Ion Channel TRPA1. **Pharmaceuticals 14:** 988

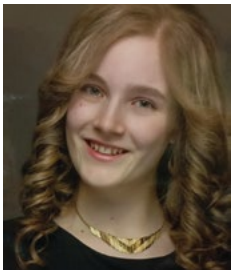
Zsidó, B. Z., Hetényi, C. (2021) The role of water in ligand binding. **Curr Opin Struct Biol 67:** 1-8

Zsidó, B. Z., Börzsei, R., Szél, V., Hetényi, C. (2021) Determination of Ligand Binding Modes in Hydrated Viral Ion Channels to Foster Drug Design and Repositioning. **J Chem Inf Model 61:** 4011-4022

Zsidó, B. Z., Hetényi, C. (2020) Molecular Structure, Binding Affinity, and Biological Activity in the Epigenome. **Int J Mol Sci 21:** 4134

PÉCS
SZENT-GYÖRGYI STUDENTS

1ST YEAR STUDENTS



ZSÓFIA HAVASI

National Academy of Scientist Education, 1st year
University of Pécs
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Balázs Gaszner
Theme of research: Neuroscience
Language: English/advanced

LEVENTE LÁNG

National Academy of Scientist Education, 1st year
University of Pécs
Faculty of Pharmacy II.
Biotechnology BSc 1st year

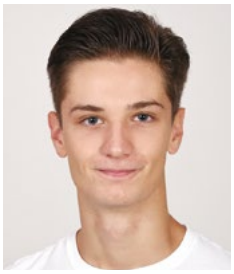
Szent-Györgyi Mentor: Gábor Kemenesi
Junior mentor: Zsófia Lanszki
Theme of research: virology
Language: English/intermediate

LÍDIA MOLNÁR

National Academy of Scientist Education, 1st year
University of Pécs
Faculty of Medicine, 1st year

Szent-Györgyi Mentor: Krisztina Pohóczky
Theme of research: molecular pharmacology, molecular biology
Language: English/advanced, German/intermediate

2ND YEAR STUDENTS



BÁLINT KISJÓS

National Academy of Scientist Education, 2nd year
University of Pécs
Faculty of Medicine, 2nd year

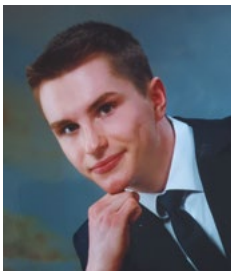
Szent-Györgyi Mentor: Krisztián Kvell
Junior mentor: Kitti Garai
Specialization: oncology, molecular biology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Regular physical activity is known to play an important role in preventing and controlling the progression of cancer and improving the effectiveness of oncotherapy. Recent research has shown that several microRNA levels are altered by exercise. These microRNAs are involved in the regulation of several biological processes responsible for the development of cancer. The aim of our work is to verify this and to map this process using multiple molecular and cellular methods.
Our research group has previously managed to detect several microRNAs that can play a role in the development of lung cancer. By studying the biological functions of the identified microRNAs in vitro, we will be able to better understand the regulatory network of molecular mechanisms by which regular exercise can prevent lung cancer.

AMBITIONS AND CAREER GOALS

As a medical student, I have a lot of studying ahead of me, but along the way, I would like to take all the opportunities I can, to help me become a better doctor. In my opinion, medical research is the most important in todays world, and I want to help it any way I can.
A balanced lifestyle is the key to success and health, because of this, after studying or doing research work, I spend time with my friends and do sports regularly.



KRISZTIÁN KLONFÁR

National Academy of Scientist Education, 2nd year
University of Pécs
Faculty of Medicine, 2nd year

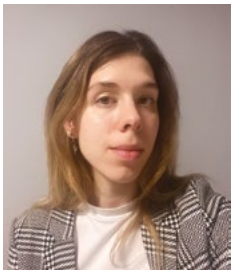
Szent-Györgyi Mentor: András Garami
Junior mentor: Eszter Pákai
Specialization: thermophysiology, thermoregulation, TRP channels, systemic inflammation
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Our research investigates the role of brain structures involved in thermoregulation and the mediators responsible for mediating these processes in animal and human studies. Currently, there is no single medicine available that is able to specifically modulate body temperature, because it is not known exactly which receptors can be directly modulated to induce controlled changes in body temperature. With our new knowledge, we have the opportunity to develop substances that act on body temperature. The short-term benefit of our research project is a better understanding of the physiological processes involved in pathologies associated with thermoregulatory disorders (e.g. fever and hypothermia associated with systemic inflammation, acute pancreatitis, heat stroke, hypothermia, etc.). In the long term, our results from the laboratory to the bedside may lay the foundations for the development of new therapeutic targets, help to better predict disease outcome based on body temperature, identify potential physical and drug means to alter body temperature and thus improve outcome and, most importantly, save lives.

AMBITIONS AND CAREER GOALS

I would like to understand and explore the mechanisms of body temperature regulation in normal and abnormal conditions. I believe that changes in body temperature have diagnostic/prognostic significance in various disease processes. In my opinion, there are no or few physiological processes that are not related to temperature in a narrow or broad sense, so my research interests are broad, and I am open to new directions of investigation.



LAURA MUNDRUCZ

National Academy of Scientist Education, 2nd year
University of Pécs
Faculty of Medicine, 2nd year

Szent-Györgyi Mentor: Miklós Kecskés
Specialization: electrophysiology
Language: English/advanced, Russian/basic, French/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Mossy cells are excitatory neurons located in the dentate gyrus of the hippocampus. They are involved in adult neurogenesis, plasticity and the formation of hippocampal oscillations. In addition, they display significant vulnerability in temporal lobe epilepsy (TLE). The function of TRPM4 ion channel - expressed specifically in mossy cells - has been previously presented by our research teem. The Transient Receptor Potential (TRP) ion channel family comprises of 28 members in mammals. These well-studies receptors play a role in several physiological processes in the peripheral nervous system. However, TRP expression in the brain is a less explored area, with specific emphasis on cellular expression patterns. Accordingly, we will monitor the function of the channel in experimental TLE model using EEG measurements, patch clamp experiments and behavioural tests. In line with the results obtained from the above mentioned techniques, we aim to clarify the cellular mechanisms underlying the death of the TLE- sensitive mossy cells. Moreover, we believe the findings will contribute greatly to the development of effective antiepileptic drugs.

AMBITIONS AND CAREER GOALS

As a Psychology BA/BSc graduate, neuroscience is a perfect addition to my previous studies. Joining my current research team has already provided several possibilities concerning scientific growth: I was familiarized with numerous modern research techniques. Given my already existing devotion towards electrophysiology, my aim is to explore as many aspects of both my and other interdisciplinary research fields as possible. I believe this will serve as a solid platform for future possibilities and that I will contribute to the work of my vibrant research environment.

PUBLICATIONS

Mundrucz, L., Kecskés, A., Henn-Mike, N., Kóbor, P., Buzás, P., Vennekens, R., Kecskés, M. (2023) TRPM4 regulates hilar mossy cell loss in temporal lobe epilepsy. **BMC Biol. 26:** 96.

DÁVID VINCE SIMON

National Academy of Scientist Education, 2nd year
University of Pécs
Faculty of Medicine, 3rd year

Szent-Györgyi Mentor: Éva Borbély
Specialization: neuropharmacology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The number of central nervous system disorders is increasing every year, with 1 in 8 people suffering from a mental disorder, according to the World Health Organisation. These include conditions such as anxiety, depression and dementia. In many cases they do not occur separately but as comorbidities of each other. Their treatment is currently a major therapeutic challenge and an important area for drug development, as the available drugs have limited efficacy and a number of serious side effects when used for prolonged periods. Through the experiments performed, we aim to elucidate the pathophysiological processes underlying these diseases and to identify new target molecules that may play a significant role in the development and exacerbation of these diseases. One of these endogenous compounds is haemokinin-1, a member of the neuropeptide family, which has been shown to play a role in acute stress responses and in the mediation of pain. The identification of its mechanism of action and target molecules may open new directions for the development of anti-anxiety/antidepressant and memory-enhancing drugs.

AMBITIONS AND CAREER GOALS

As an NASE student, I had the opportunity to participate in experiments as part of a research team and to contribute to publications and to the advancement of scientific knowledge for mankind through my active work in the lab. I would like to set my goals as follows. To extend my work as a TDK member and to fulfil the requirements of the programme as soon as possible. To present our results at various conferences and to obtain a PhD after university.

3RD YEAR STUDENTS

ANGELIKA BODÓ

National Academy of Scientist Education, 3rd year
University of Pécs, Medical School, 4th year

Szent-Györgyi Mentor: István Hernádi
Junior mentor: Zsolt Kristóf Bali
Specialization: neurobiology
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Examination of ageing and neurocognitive disorders in rodents: identification of preclinical drug development strategies and development of combined performance-enhancing therapies. In neuroscience recently, pharmacological studies are increasingly being replaced by so-called chemogenetic methods, which have the advantage of allowing selective, spatially and temporally defined manipulation of the brain area of interest. In our experiments, we aim to develop such a translational model in rodents and non-human primates using DREADD (Drug Receptors Excusively Activated by Designer Drugs) technology that reliably represents congitive impairment related to certain human pathologies, thus providing a significant role both in basic research and in the preclinical investigation of new drug candidates that enhance cognitive performance.

AMBITIONS AND CAREER GOALS

My goal is to develop, through continuous learning and experience, the knowledge base that I will later use to help advance medicine. This is why I would like to pursue a career in research after my medical degree, as I am driven by curiosity and a desire to learn, and I believe that future doctors will need to use innovative diagnostic and therapeutic methods to help their patients. I am particularly keen to promote efforts to treat the now incurable but increasingly problematic neurodegenerative diseases of the soul, such as Alzheimer's, which are a growing problem in our ageing society, and I hope that one day I will find a way to restore the hope of a long, happy and quality life for those affected.

LAJOS KARAKAI

National Academy of Scientist Education, 3rd year
University of Pécs, Medical School, 3rd year

Szent-Györgyi Mentor: Éva Szőke
Specialization: neuropharmacology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Investigation of modification of lipid rafts for analgesic and antitumor effects. We investigate the functional relationship between Transient Receptor Potential (TRP) ion channels and lipid rafts in different mouse models of acute pain and in a complex mouse osteosarcoma tumor model. Lipid rafts are specific microdomain of the cell membrane that can be disrupt through their cholesterol or sphingolipid content, thereby affecting the function of different receptors. In the acute pain model we investigate the effect of lipid raft disruption on the TRP Melastatin 3 (TRPM3) and TRP Melastatin 8 (TRPM8) ion channel , and in the chronic tumor pain model on the TRP Vanilloid 1 (TRPV1) and TRP Ankyrin 1 (TRPA1) ion channel activity, respectively.

AMBITIONS AND CAREER GOALS

Self-development in many areas of life is a close goal of mine. Of these, with a particular focus on science, where I can delve deeper into the background and learn new and exciting methods. My long-term goals are still vague, but I can see that whatever I do, I will dive into it with great enthusiasm.

ENIKŐ TARI

National Academy of Scientist Education, 3rd year
University of Pécs,
Faculty of Sciences, Biology, 4th year

Szent-Györgyi Mentor: Csaba Hetényi
Junior mentor: Balázs Zoltán Zsidó
Specialization: structural biochemistry, bioinformatics, pharmacoinformatics, bioorganic chemistry
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

It is generally recognized that carrying out drug research and the development of new pharmaceuticals is highly time and resource-consuming nowadays. This process can take up approximately 10-15 years. As a result various virtual screening techniques are now widely applied by both pharmaceutical companies and academic research groups. In this way the research is more cost-effective, and it greatly reduces the time required for the discovery of potent drugs. Throughout the research our main goal is not only to continuously expand the toolbox for drug design, but also we would like to develop and test new methods. We aim to present and publish these results in the future at conferences and scientific papers.

AMBITIONS AND CAREER GOALS

My aim is to gain as much experience and skills as possible during my university years because I believe that this is essential to become a successful researcher in the future. During these years it is important for me to continuously improve myself. In addition, I would like to work in a community where I have the opportunity to discuss my ideas and get feedback on my work.

PUBLICATIONS

Patko, E., Szabo, E., Vaczy, A., Molitor, D., **Tari, E.**, Li, L., Csutak, A., Toth, G., Reglodi, D., Atlasz, T. (2023) Protective Effects of Pituitary Adenylate-Cyclase-Activating Polypeptide on Retinal Vasculature and Molecular Responses in a Rat Model of Moderate Glaucoma. **Int J Mol Sci 24:** 13256.

KATA VÁRADI

National Academy of Scientist Education, 3rd year
University of Pécs,
Medical School, 3rd year

Szent-Györgyi Mentor: Péter Balogh
Specialization: immunology, developmental biology, morphology
Language: English/advanced, French/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Nkx2-3 is a homeodomain transcription factor that plays a crucial role in the normal ontogeny of, among others, small intestinal lymphoid tissues and the spleen. In mice, the targeted deficiency of Nkx2-3 causes morphological abnormalities, with the mutant spleen being smaller and irregular in structure. In particular, alterations in the vascular pattern of the red pulp and marginal zone and the appearance of ectopic HEV-like PNAd-positive postcapillary venules and LYVE-1/Prox1-positive lymphatic vessels are observed. It is not known at present in which vascular patterning cells the alterations are present, and the role of ectopic lymphatic vessels in the lymphocyte migration of the mutant spleen is also unknown. The aim of this study is to characterize the process of lymphocyte migration in the spleens of Nkx2-3-deficient mice and to investigate the limitation of Nkx2-3 deficiency to endothelial cells.

AMBITIONS AND CAREER GOALS

The science of today is the magic of yesterday, and the magic of today can be the science of tomorrow. And with the right skills, knowledge and tools, yesterday's idea can become tomorrow's discovery.
My goal as an undergraduate researcher is to get a closer look at the workings of the human as an extremely complex - and incredibly precise - biological system. I believe that by unravelling the precise molecular mechanisms of the 'human machine', I can contribute to the advancement of medicine and to a better understanding of our fellow human beings. I would like to make discoveries that can be passed on to future generations in the form of general knowledge, and from which they can generate their ideas themselves.

PUBLICATIONS

Barabás K, Makkai B, Farkas N, Horváth H, Nagy ZS, **Váradi K,** Zelena D. (2022) Influence of COVID-19 pandemic and vaccination on the menstrual cycle: a retrospective study in Hungary. **Frontiers in Endocrinology 13:** 9747882022.

CSENGE SÓLYOMVÁRI

4TH YEAR STUDENT

National Academy of Scientist Education, 4th year
University of Pécs
Faculty of Sciences, Biology, 4th year

Szent-Györgyi Mentor: Dóra Zelena
Junior mentor: Szidónia Farkas
Specialization: molecular biology, physiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

In our aging society the prevalence of dementia is becoming an increasingly prominent social problem. Current therapies do not halt the progression of the disease, highlighting the importance of further research. The occurrence of dementia is much more common in women, especially post-menopause, when estrogen and progesterone levels decrease. These neurosteroid hormones, as well as their precursor compounds like dehydroepiandrosterone (DHEA), have protective and anti-inflammatory effects on the nervous system. We aim to examine – with the help of a transgen mice strain - how the reduction in hormone levels during menopause affects the course of the disease, as well as the function and morphology of microglia and astrocytes. Understanding the disease better may open new possibilities for targeted therapies. Our hypothesis suggests that menopause will increase the quantity of microglia and astrocytes in the affected areas of the brain, and these cells will exhibit morphological changes, such as cell body enlargement and increased number and length of processes. In the case of treatment with estrogen and similar compounds, we expect a beneficial effect.

AMBITIONS AND CAREER GOALS

My goal is to gain as much practical knowledge as possible in my profession during my university years, which I can use in my later jobs. TDK work gives me the opportunity to be an active part of the research community and at the same time I can gain a lot of experience and build relationships. In this way, as a young, graduated biologist, I will be able to contribute more effectively to the development of science and to a life free from disease.

PUBLICATIONS

Farkas, S., Szabó, A., Török, B., **Sólyomvári, C.**, Fazekas, C. L., Bánrévi, K., Correia, P., Chaves, T., Zelena, D. (2022) Ovariectomy-induced hormone deprivation aggravates Aβ1-42 deposition in the basolateral amygdala and cholinergic fiber loss in the cortex but not cognitive behavioral symptoms in a triple transgenic mouse model of Alzheimer's disease. **Front Endocrinol 13:** 985424.

INEZ BOSNYÁK

6TH YEAR STUDENT

National Academy of Scientist Education, 6th year
University of Pécs
Medical School, 6th year

Szent-Györgyi Mentor: Dóra Reglődi
Junior mentor: Alexandra Atlaszné Váczy
Specialization: ophthalmology, neuroendocrinology, neuroscience
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The retina has very high oxygen consumption, so lack of oxygen supply can cause visual impairment. Hypoxia plays a key role in the pathogenesis of the most common vision-threatening diseases. Appropriate, side-effect free therapeutic options are not available to treat these conditions.
Hypoxic animal model is created by common carotid artery occlusion. Then we perform optical coherence tomography, electroretinography and molecular measurements.
Our aim is to find the most sensitive cell types and to understand the pathogenesis of ischemic retinopathy in time-dependent manner. Afterwards we would like to investigate the role of endogenous pituitary adenylate cyclase activating polypeptide (PACAP), which is a retinoprotective neuropeptide.
In summary, our aim is to understand the pathogenesis of ischemic retinopathy and to find new potential therapeutic targets.

AMBITIONS AND CAREER GOALS

Our research group aims to understand the pathogenesis of various common retinal diseases and to find new potential therapeutic targets. In addition, we would like to investigate the role and protective effects of PACAP in these diseases. During my university years, I would like to master as many techniques as possible and improve professionally to become the best researcher/physician I can be.

AMBITIONS AND CAREER GOALS

Koppan, M., Nagy, Zs., **Bosnyak, I.**, Reglodi, D. (2022) Female reproductive functions of the neuropeptide PACAP. **Front Endocrinol 13:** 982551.

Kiss, P., Farkas, J., Kovacs, K., Gaal, V., Biro Zs., Szabo, A., Atlasz, T., **Bosnyak I.**, Toth, G., Tamas, A., Reglodi, D. (2022) Effects of pituitary adenylate cyclase activating polypeptide (PACAP) in corneal epithelial regeneration and signal transduction in rats. **Int J Pept Res Ther 28:** 92.

Patko, E., Szabo, E., Toth, D., Tornocky, T., **Bosnyak, I.**, Vaczy, A., Atlasz, T., Reglodi, D. (2022) Distribution of PACAP and PAC1 receptor in the human eye. **J Mol Neurosci 72:** 2176–2187.

SZEGED
SZENT-GYÖRGYI MENTORS

RITA AMBRUS

University of Szeged
Faculty of Pharmacy
Institute of Pharmaceutical Technology
and Regulatory Affairs

RESEARCH AREA

Modern pharmaceutical technology is focused on formulations that are targeted to the exact site at the appropriate time, with maximum efficiency and with reduced side-effects. Nanoparticle engineering has been developed and reported for pharmaceutical applications. In this approach, poorly water-soluble compounds are formulated as nanometer-sized (< 1000 nm) drug particles. Nanoparticulate technology offers increased bioavailability, improved absorption, and the potential for drug targeting. The main question of our work how we can use and apply the prepared nanosized systems (as predispersions) in drug formulation (to reach local or systemic effect) to get effective therapies in different diseases. Therefore we should find cost-effective production by new technological processes containing the most important technological and material parameters. The aim is to reach a local and systemic effect with alternative, mainly pulmonary / nasal drug administration. There is a great need for the development of pulmonary and nasal generic formulations, as the protection of currently marketed formulations is about to expire. From a therapeutic point of view, the treatment of local asthma and Chronic Obstuctive Pulmonary Disease (COPD) / remains the main indications for inhalation therapy. However, inhalation formulations for the treatment of e.g. diabetes or schizophrenia are already available as to have systemic treatment. Many new types of nasal products were developed for systemic drug delivery are already on the market. However, the development of nasal delivery systems for the treatment of central nervous system diseases that provide rapid and effective brain pharmacon concentrations for drugs that utilize the nasal route could be a new area of research.

SELECTED PUBLICATIONS

Party, P., Bartos, Cs., Farkas, Á., Szabó-Révész, P., **Ambrus, R.** (2021) Formulation and In Vitro and In Silico Characterization of "Nano-in-Micro" Dry Powder Inhalers Containing Meloxicam. **Pharmaceutics 13:** 2 Paper: 211.

Gieszinger, P., Stefania, Csaba, N., Garcia-Fuentes, M., Prasanna, M., Gáspár, R., Sztojkov-Ivanov, A., Ducza, E., Márki, Á., Janáky, T., Kecskeméti, G., Katona, G., Szabó-Révész, P., **Ambrus, R.** (2020) Preparation and characterization of lamotrigine containing nanocapsules for nasal administration. **Eur J Pharm Biopharm 153:** pp. 177-186.

Alshweiat, A., Csóka, I., Tömösi, F., Janáky, T., Kovács, A., Gáspár, R., Sztojkov-Ivanov, A., Ducza, E., Márki, Á., Szabó-Révész, P., **Ambrus, R.** (2020) Nasal delivery of nanosuspension-based mucoadhesive formulation with improved bioavailability of loratadine: preparation, characterization, and in vivo evaluation **Int J Pharm 579:** Paper: 119166.

Ambrus R., Alshweiat A., Csóka I. Ovari G., Esmail A., Radacsi N. (2019) 3D-printed electrospinning setup for the preparation of loratadine nanofibers with enhanced physicochemical properties **Int J Pharm 567:** Paper: 118455.

ISTVÁN BACZKÓ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pharmacology and
Pharmacotherapy

RESEARCH AREA

Cardiovascular diseases lead mortality statistics worldwide. Congestive heart failure and atrial fibrillation are major contributors to cardiovascular mortality and morbidity, in addition, their prevalence is constantly increasing. The two conditions often co-exist, further increasing mortality in these patients. Despite significant improvements in their treatment in the last two decades, congestive heart failure and atrial fibrillation remain significant health care problems. Our laboratory aims at the identification of common and separate elements of electrical remodeling (changes in the expression of transmembrane ion channels and transporters in response to these conditions) in heart failure and atrial fibrillation that can serve as novel therapeutic targets with the help of different animal models of atrial fibrillation established in our laboratory with continuous clinical collaboration. Furthermore, new compounds acting on identified molecular targets are also tested in our atrial fibrillation models. Another important goal of our work is to study the mechanisms responsible for increased arrhythmia susceptibility in models of congestive heart failure, with special attention to elements of electrical remodeling. In addition, our laboratory also focuses on the unmet need for improved preclinical models for better prediction and prevention of proarrhythmic adverse effects of drugs in development in order to improve cardiovascular safety of novel compounds entering the market. In this regard, in the last 5 years, for the first time in the world, we have participated in the creation of several transgenic rabbit models of long QT syndromes.

SELECTED PUBLICATIONS

Castiglione, A., Hornyik, T., Wülfers, E.M., Giammarino, L., Eder, I., Jowais, J.J., Rieder, M., Perez-Feliz, S., Koren, G., Bősze, Z., Varró, A., Zehender, M., Brunner, M., Bode, C., Liin, S.I., Larsson, H.P., **Baczkó, I.**, Odening, K.E. (2021) Docosahexaenoic acid normalizes QT interval in LQT2 transgenic rabbit models in a genotype-specific fashion. **Europace 24:** 511-522.

Varró, A., Tomek, J., Nagy, N., Virág, L., Passini, E., Rodriguez, B., **Baczkó, I.** (2021) Cardiac transmembrane ion channels and action potentials: cellular physiology and arrhythmogenic behavior. **Physiol Rev 101:** 1083-1176.

Hornyik, T., Castiglione, A., Franke, G., Perez-Feliz, S., Major, P., Hiripi, L., Koren, G., Bősze, Z., Varró, A., Zehender, M., Brunner, M., Bode, C., **Baczkó I**.*, Odening K.E.* (2020) Transgenic LQT2, LQT5 and LQT2-5 rabbit models with decreased repolarisation reserve for prediction of drug-induced ventricular arrhythmias. **Br J Pharmacol 177:** 3744-3759. *shared senior authorship

Ferdinandy, P., **Baczkó, I.**, Bencsik, P., Giricz, Z., Görbe, A., Pacher, P., Varga, Z.V., Varró, A., Schulz, R. (2019) Definition of hidden drug cardiotoxicity: paradigm change in cardiac safety testing and its clinical implications. **Eur Heart J 40:** 1771-1777.

FERENC BARI

University of Szeged
Albert Szent-Györgyi Medical School
Faculty of Science and Informatics
Department of Medical Physics and Informatics

RESEARCH AREA

Adequate and continuous blood supply of the brain requires a very precise regulatory mechanism. Investing the properties of the cerebral microcirculation opens a unique way for understanding the details (components, dynamics) of blood flow regulation in both the healthy and the injured brain. We have been studying the major characteristics of the neurovascular coupling (enhanced neuronal activity is followed by changes in the local blood perfusion) for more than 20 years. We have obtained considerable knowledge on the nature of excitatory amino acid release and the concomitant changes in local microcirculation. We have intensively studied the vascular consequences of hypoxic-ischemic injuries and tested various, potentially neuroprotective strategies. We study cerebral microcirculation in various animal models. Our major approach is using optical methods (intravital microscopy, laser Doppler flowmetry, laser speckle contrast analysis [LASCA]). In addition, we perform *ex vivo* studies in order to characterize morphological alterations and changes in protein expression in the injured brain. Recently, we have been working on new neuroprotective approaches.
During the last years our research interest involves the question how medical informatics could help in stroke prevention and treatment of stroke victims.

SELECTED PUBLICATIONS

Clark, D., Tuor, U.I., Thompson, R., Institoris, A., Kulynych, A., Zhang, X., Kinniburgh, D.W., **Bari, F.,** Busija, D.W., Barber, P.A. (2012) Protection against recurrent stroke with resveratrol: endothelial protection. **PLOS One 7:** e47792.

Domoki, F., Zölei, D., Oláh, O., Tóth-Szűki, V., Hopp, B., **Bari, F.,** Smausz, T. (2012) Evaluation of Laser-speckle contrast image analysis techniques inthe cortical microcirculation of piglets. **Microvasc Res 83:** 311-7.

Hugyecz, M., Mracskó, E., Hertelendy, P., Farkas, E., Domoki, F., **Bari, F.** (2011) Hydrogen supplemented air inhalation reduces changes of prooxidant enzyme and gap junction protein levels after transient global cerebral ischemia in the rat hippocampus. **Brain Res 1404:** 31-8.

Mracsko, E., Hugyecz, M., Institoris, A., Farkas, E., **Bari, F.** (2010) Changes in prooxidant and antioxidant enzyme levels during cerebral hypoperfusion in rats. **Brain Res 1321:** 13-9.

Lenti, L., Domoki, F., Gáspár, T., Snipes, J.A., **Bari, F.,** Busija, D.W. (2009) N-methyl-D-aspartate induces cortical hyperemia through cortical spreading depression-dependent and independent mechanisms in rats. **Microcirculation 16:** 629-39.

ZSUZSANNA BATA-CSÖRGŐ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Dermatology and Allergology

RESEARCH AREA

Psoriasis is the most common inflammatory skin disease among Caucasians. Our research focus is on the pathomechanism of this disease. The disease is polygenic with complex pathology therefore our work has different aspects: immunology, epidermal and dermal biology, regulation of cell proliferation and differentiation and extracellular matrix biology. We are engaged in classical theory driven research, but also use large scale studies. The research group is closely related to the clinic that makes it possible to use human tissues and cells for some of our work, which enhances the clinical relevance of our results. Some of our work is more basic research, we investigate normal and pathological functions of keratinocytes, fibroblasts and melanocytes.

SELECTED PUBLICATIONS

Gál, B., Dulic, S., Kiss, M., Groma, G., Kovács, L., Kemény, L., **Bata-Csörgő, Z.** (2017) Increased circulating anti-α6-integrin autoantibodies in psoriasis and psoriatic arthritis but not in rheumatoid arthritis. **J Dermatol 44:** 370-374

Göblös, A., Danis, J., Vas, K., **Bata-Csörgő, Z.**, Kemény, L., Széll, M. (2016) Keratinocytes express functional CARD18, a negative regulator of inflammasome activation, and its altered expression in psoriasis may contribute to disease pathogenesis. **Mol Immunol 73:** 10-18.

Gubán, B., Vas, K., Balog, Z., Manczinger, M., Bebes, A., Groma, G., Széll, M., Kemény, L., **Bata-Csörgő, Z.** (2016) Abnormal regulation of fibronectin production by fibroblasts in psoriasis. **Br J Dermatol 174:** 533-41.

Belső, N., Széll, M., Pivarcsi, A., Kis, K., Kormos, B., Kenderessy, A.S., Dobozy, A., Kemény, L., **Bata-Csörgõ, Z.** (2008) Differential expression of D-type cyclins in HaCaT keratinocytes and in psoriasis. **J Invest Dermatol 128:** 634-42.

Bata-Csorgo, Z., Hammerberg, C., Voorhees, J.J., Cooper, K.D. (1995) Kinetics and regulation of human keratinocyte stem cell growth in short-term primary *ex vivo* culture. Cooperative growth factors from psoriatic lesional T lymphocytes stimulate proliferation among psoriatic uninvolved, but not normal, stem keratinocytes. **J Clin Invest 95:** 317-27.

Bata-Csorgo, Z., Hammerberg, C., Voorhees, J.J., Cooper, K.D. (1993) Flow cytometric identification of proliferative subpopulations within normal human epidermis and the localization of the primary hyperproliferative population in psoriasis. **J Exp Med 178:** 1271-81.

PÉTER BENCSIK

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Our research group, which has been operating for more than 25 years, investigates the tissue and cellular biochemical basis of myocardial stress adaptation and attempts to identify new drug targets for the development of cardioprotective drugs together with national and foreign pharmaceutical industrial partners. We focus primarily on matrix metalloproteinase-2 (MMP-2) and its possible substrate molecules, which enzyme is also found in the intra- and extracellular compartments of the heart. In the preclinical phases of drug development, we investigate the inhibitory effect of potential drug candidate molecules on MMP-2. In addition, in close collaboration with the Institute of Pharmacology at Semmelweis University, we investigate the role and expression changes of microRNAs during acute myocardial infarction. We synthesized microRNAs, which showed significant change during myocardial ischemia/reperfusion injury and test their potential cardioprotective effect by administration of these so called protectomiRs in a mouse model of acute myocardial infarction. With both of the above-mentioned therapeutic options, our aim is to develop cardioprotective drugs or therapeutic formulations that can have a positive effect on cardiac muscle even in the presence of cardiovascular risk factors, comorbidities, and already authorized and widely used other pharmacological treatments (e.g. antihyperlipidemic or antihypertensive drugs).

SELECTED PUBLICATIONS

Gömöri, K., Szabados, T., Kenyeres, É., Pipis, J., Földesi, I., Siska, A., Dormán, G., Ferdinandy, P., **Bencsik, P.** (2020) Cardioprotective effect of novel matrix metalloproteinase inhibitors. **Int J Mol Sci. 21:** 6990.

Bencsik, P., Gömöri, K., Szabados, T., Sántha, P., Helyes, Z., Jancsó, G., Ferdinandy, P., Görbe, A. (2020) Myocardial ischemia reperfusion injury and cardioprotection in the presence of sensory neuropathy: therapeutic options. **Br J Pharmacol 177:** 5336-5356.

Bencsik, P., Kiss, K., Ágg, B., Baán, J.A., Ágoston, G., Varga, A., Gömöri, K., Mendler, L., Faragó, N., Zvara, Á., Sántha, P., Puskás, L.G., Jancsó, G., Ferdinandy, P. (2019) Sensory Neuropathy Affects Cardiac miRNA Expression Network Targeting IGF-1, SLC2a-12, EIF-4e, and ULK-2 mRNAs. **Int J Mol Sci 25:** 20.

Bencsik, P., Kupai, K., Gorbe, A., Kenyeres, E., Varga, Z.V., Paloczi, J., Gaspar, R., Kovacs, L., Weber, L., Takacs, F., Hajdu, I., Fabo, G., Cseh, S., Barna, L., Csont, T., Csonka, C., Dorman, G., Ferdinandy, P. (2018) Development of Matrix Metalloproteinase-2 Inhibitors for Cardioprotection. **Front Pharmacol 9:** 296.

Kiss, K., Csonka, C., Pálóczi, J., Pipis, J., Görbe, A., Kocsis, G.F., Murlasits, Z., Sárközy, M., Szűcs, G., Holmes, C.P., Pan, Y., Bhandari, A., Csont, T., Shamloo, M., Woodburn, K.W., Ferdinandy, P.*, **Bencsik, P.** (2016) Novel, selective EPO receptor ligands lacking erythropoietic activity reduce infarct size in acute myocardial infarction in rats. **Pharmacol Res 113:** 62-70.

ANTAL BERÉNYI

University of Szeged
Albert Szent-Györgyi Medical School
Department of Physiology
MTA-SZTE 'Lendület' Oscillatory Neuronal Networks Research Group

RESEARCH AREA

Recent technical development gave a new momentum to experiments studying the brain, although the extremely complex structure of the nervous system still supplies the researchers with an endless inventory of open questions. In our research we investigate the possible therapeutic effects of Transcranial Electrical Stimulation (TES) on epileptic seizures. Particularly, we plan to develop a focused stimulation protocol both in time and space to interact only with the desired brain areas within an appropriate time-frame. To determine the appropriate focal points of stimulation, we investigate the internal dynamics of neural networks involved in seizure generation. We do this by performing a throughout analysis of networks on microscopic and mesoscopic scale with extremely high spatial and temporal resolution. The same approach is used to focus on the role of hippocampus and related circuitries in memory formation and spatial navigation. We pay special interest to the role of sensory information in this field.
Our long-term vision is to develop a closed-loop, implantable seizure suppressor device that continuously monitors the patterns of brain activity, and delivers electrical pulses in order to terminate any occurring seizures. We are hoping to translate our laboratory-stage experimental results into clinical trials within a few years.

SELECTED PUBLICATIONS

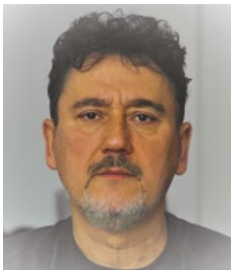
Oliva, A., Fernández-Ruiz, A, Buzsáki, G., **Berényi, A.** (2016) Role of Hippocampal CA2 Region in Triggering Sharp-Wave Ripples. **Neuron 91:** 1342-55.

Agarwal, G., Stevenson, I.H., **Berényi, A.**, Mizuseki, K., Buzsáki, G., Sommer FT. (2014) Spatially distributed local fields in the hippocampus encode rat position. **Science 344:** 626-30.

Berényi, A., Somogyvári, Z., Nagy, A.J., Roux, L., Long, J.D., Fujisawa, S., Stark, E., Leonardo, A., Harris, T.D., Buzsáki, G. (2014) Large-scale, high-density (up to 512 channels) recording of local circuits in behaving animals. **J Neurophysiol 111:** 1132-49.

Berényi, A., Belluscio, M., Mao, D., Buzsaki, G. (2012) Closed-loop control of epilepsy by transcranial electrical stimulation. **Science 337:** 735-737.

Madisen, L., Mao, T., Koch, H., Zhuo, J.M., **Berényi, A**., Fujisawa, S., Hsu, Y.W., Garcia, A.J. 3rd., Gu, X., Zanella, S., Kidney, J., Gu, H., Mao, Y., Hooks, B.M., Boyden, E.S, Buzsáki, G., Ramirez, J.M., Jones, A.R., Svoboda, K., Han, X., Turner, E.E., Zeng, H.A. (2012) Toolbox of Cre-dependent optogenetic transgenic mice for light-induced activation and silencing. **Nat Neurosci 15:** 793-802.



ZSOLT ENDRE BOLDOGKŐI

University of Szeged
Albert Szent-Györgyi Medical School
Department of Medical Biology

RESEARCH AREA

The main projects of our research group: 1. Genetic regulation in various viral families: We have been assembling the transcriptome atlases of various viruses using short- and long-read sequencing technologies. We have currently been investigating the following viruses: herpes simplex virus, pseudorabies virus, varicella-zoster virus, human cytomegalovirus, Epstein-Barr virus, vaccinia virus, influenza virus, a baculovirus, an endogenous retrovirus, a circovirus, various RNA viruses, etc. Additionally, we have been examining how the transcriptions as well as the transcription and the DNA replication are interrelated with each other. We have put forward two hypotheses for assuming a genome-wide interplay among the transcription and replication machineries, which are the Transcription Interference Network (TIN) hypothesis and the Transcription and replication Network (TRIN) hypothesis, respectively. 2. Generation of intelligent viral vectors for brain research: Application of genetically modified pseudorabies virus for tansneuronal tract-tracing, as well as analysis of neural activity using optical methods. 3. Examination of the genetic basis of major depression and suicide: high-coverage whole-exome analysis of depression. 4. Various microbiome research projects since 2019 have been launched.

SELECTED PUBLICATIONS

Tombácz, D., Prazsák, I., Szűcs, A., Dénes, B., Snyder, M., **Boldogkői, Z.** (2018) Analysis of the transcriptome of Vaccinia virus using long-read sequencing techniques. **GigaScience 7:** 139.

Tombácz, D., Prazsák, I., Moldován, N., Szűcs, A., **Boldogkői, Z.** (2018) Lytic Transcriptome Dataset of Varicella Zoster Virus Generated by Long-read Sequencing. **Front Genet 9:** 460.

Balázs, Z., Tombácz, D., Szűcs, A., Snyder, M., **Boldogkői, Z.** (2017) Long-read sequencing of the human cytomegalovirus transcriptome with the Pacific Biosciences RSII platform. **Sci Data 4**: 170194.

Tombácz, D., Maróti, Z., Kalmár, T., Csabai, Z., Balázs, Z., Takahashi, S., Palkovits, M., Snyder, M., **Boldogkői, Z.** (2017) High-coverage whole-exome sequencing identifies candidate genes for suicide in victims with major depressive disorder. **Sci Rep 7:** 7106.

Fekete, R., Cserép, C., Orsolits, B., Martinecz, B., Lénárt, N., Tóth, K., Méhes, E., Szabó, B., Németh, V., Gönci, B., Sperlágh, B., **Boldogkői, Z.,** Kittel, Á., Baranyi, M., Ferenczi, S., Kovács, K.J., Szalay, G., Rózsa, B., Webb, C., Hortobágyi, T., West, B.L., Környei, Z., Dénes, Á*. (2018) Microglia control neurotropic virus infection via P2Y12-mediated recruitment and phagocytosis. **Acta Neuropathologica 136:** 461-482.

IMRE MIKLÓS BOROS

HUN-REN Biological Research Centre,
Institute of Biochemistry
University of Szeged
Faculty of Science and Informatics
Department of Biochemistry and Molecular Biology

RESEARCH AREA

Transcription of eukaryotic genes is a multistep process that involves a large number of functionally different proteins and requires the ordered assembly of giant multiprotein complexes. In recent years the important role of chromatin structure in transcription regulation has been recognized and new directions in transcription research have been initiated. It is hoped that a better understanding of the roles of functionally distinct classes of transcription regulatory proteins and chromatin modifiers will provide keys to decipher why and how can these drive development and can be de-regulated in diseases like cancer. In joint laboratories located at the BRC and at the Biochemistry and Molecular Biology Department of SzU we use combined approaches to characterize proteins which modify chromatin structure. In one area of research we focus our studies on histone proteins used only under specific conditions for example at the very early stage of embryonic development. For these studies we use Drosophila model, as this permits us to combine genetic and cell- and molecular biology methods. Another research approaches we study gene expression changes in cancer cells. For this we use clinical samples and are primarily interested in identifying the genetic alterations that contribute tumor formation.

SELECTED PUBLICATIONS

Majoros, H.; Ujfaludi, Zs.; Borsos, B.N.; Hudacsek, V.V.; Nagy, Z.; Coin, F.; Buzas, K.; Kovács, I.; Bíró, T.; **Boros, I.M.** (2019) et al. SerpinB2 is involved in cellular response upon UV irradiation. **Scientific Reports 9:** 2753.

Ujfaludi, Zs.; Tuzesi, A.; Majoros, H.; Rothler, B.; Pankotai, T.; **Boros, I.M.** (2018) Coordinated activation of a cluster of MMP genes in response to UVB radiation. **Scientific Reports 8:** 2660.

Borsos, B.N.; Huliak, I.; Majoros, H.; Ujfaludi, Z.; Gyenis, A.; Pukler, P.; **Boros, I.M.**; Pankotai, T. (2017) Human p53 interacts with the elongating RNAPII complex and is required for the release of actinomycin D induced transcription blockage. **Scientific Reports 7:** 40960.

Pahi, Z.; Borsos, B.N.; Vedelek, B.; Shidlovskii, Y.V.; Georgieva, S.G.; **Boros, I.M.**; Pankotai, T. (2017) TAF10 and TAF10b partially redundant roles during Drosophila melanogaster morphogenesis. **Transcription 8:** 297-306.

Borsos, B.N.; Pankotai, T.; Kovacs, D.; Popescu, C.; Pahi, Z.; **Boros, I.M.** (2015) Acetylations of Ftz-F1 and histone H4K5 are required for the fine-tuning of ecdysone biosynthesis during Drosophila metamorphosis. **Developmental Biology 404:** 80-7.

Vedelek, B.; Blastyak, A.; **Boros, I.M.** (2015) Cross-Species Interaction between Rapidly Evolving Telomere-Specific Drosophila Proteins. **Plos One 10:** e0142771.

MIHÁLY BOROS

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Surgical Research

RESEARCH AREA

Surgical research can bring together many clinical disciplines and interests, ranging from cardiovascular biology to gastroenterology. The ischemia-reperfusion (I/R)-induced cellular hypoxia - reoxygenation, and subcellular oxidoreductive stress are major determinants of mortality and morbidity in many areas of clinical practice, such as sepsis or shock situations, and investigations targeting the I/R-caused microcirculatory dysfunction are essential for development of treatment strategies for several clinical pathologies. From a general perspective, it is worth pointing out that any intervention protecting microcirculation is likely to result in protection of tissue function and structure. In this scheme we have characterized the anti-inflammatory potential of membrane-forming phospholipids in I/R-induced antigenindependent inflammation, and the observation that methane formation from phosphatidylcholine metabolites occurs in ischemic systems opened up new avenues for future research. Currently we examine the possible biological roles of endogenous methane formation and whether methane - or potentially methane-releasing agents influence IR-induced microcirculatory dysfunctions and modulate the outcome of inflammation.

SELECTED PUBLICATIONS

Strifler, G., Tuboly, E., Szél, E., Kaszonyi, E., Cao, C., Kaszaki, J., Mészáros, A., **Boros, M.**, Hartmann, P. (2016) Inhaled Methane limits the mitochondrial electron transport chain dysfunction during experimental liver ischemia-reperfusion injury. **Plos One 11:** e0146363.

Boros, M., Tuboly, E., Meszaros, A., Amann, A. (2015) The role of methane in mammalian physiology-is it a gasotransmitter? **J Breath Res 9:** 014001.

Tuboly, E., Szabó, A., Garab, D., Bartha, G., Janovszky, Á., Erős, G., Szabó, A., Mohácsi, Á., Szabó, G., Kaszaki, J., Ghyczy, M., **Boros, M.** (2013) Methane biogenesis during sodium azideinduced chemical hypoxia in rats. **Am J Physiol Cell Physiol 304:** C207-214.

Boros, M., Ghyczy, M., Érces, D., Varga, G., Tőkés, T., Kupai, K., Torday, C., Kaszaki, J. (2012) The anti-inflammatory effects of methane. **Crit Care Med 40:** 1269-1278.

Ghyczy, M., Torday, C., **Boros, M.** (2003) Simultaneous generation of methane, carbon dioxide, and carbon monoxide from choline and ascorbic acid: a defensive mechanism against reductive stress? **FASEB J 17:** 1124- 1126.

PÉTER BURKOVICS

HUN-REN Biological Research Centre
Institute of Genetics

RESEARCH AREA

Duplication of the genetic material is essential for every living organism. In our laboratory, located at the Institute of Genetics in the HUN-REN Biological Research Centre, we examine the replication of eukaryotic cells. The replicative protein complex works with high speed and high fidelity, but several circumstances can interfere with this process. These could be different damage or structural barriers formed on the template DNA strand. The focus of our research interest is the replication of stable secondary structures, which formation is induced by the endogenous nucleotide sequence of the DNA. There are several types of the stable secondary structures, but our laboratory examines the replication of G-quadruplex (G4) structures. Computational analysis identified that there are more than 700,000 G4 motifs in our genome. Thus, the replication of the G4 in cells is challenging. G4 is a tetramer structure formed by stacking of guanine quartets on single-stranded nucleic acid (DNA or RNA) via Hoogsteen's base pairing. The most well examined form of G4 structures are the telomeres, which ensure the stability of the chromosome ends. Our work focuses on the replication of intrachromosomal G4 structures. Since G4 structures are very stable in physiological conditions, they can block the movement of the replicative machinery, which could lead to genome instability. On this basis, it is expected that the amount of G4-forming sequences is reduced during evolution, but the opposite is true. In E. coli and C. elegans the amount of G4-forming sequences in the genome is 0.42% and 0.89%, respectively, but in human cells 4.17% of the genome can form G4 structures that highlights the important function of G4s in the nuclear processes. Recently it has been described, that G4 structures can regulate the gene expression, the initiation of replication, the recombination and the epigenetic code. Therefore, fast end precise replication of G4 structures is essential, otherwise important nuclear functions might be damaged. For the efficient replication special DNA helicases and regulatory proteins are needed, which can synchronize the action of G4 unwinding DNA helicases and the replication apparat. In our laboratory we examine the function of these regulatory proteins.

SELECTED PUBLICATIONS

Zacheja T., Toth A., Harami G.M., Yang Q, Schwindt E., Kovács M., Paeschke K., **Burkovics, P.** (2020) Mgs1 protein supports genome stability via recognition of G-quadruplex DNA structures. **FASEB J 34:** 12646-12662.

Paeschke, K., **Burkovics, P.** (2020) Mgs1 function at G-quadruplex structures during DNA replication. **Curr Genet 67:** 225-230.

Toth, A., Hegedus, L., Juhasz, S., Haracska, L., **Burkovics, P.** (2017) The DNA-binding box of human SPARTAN contributes to the targeting of Polη to DNA damage sites. **DNA Repair (Amst). 49:** 33-42.

Burkovics, P., Dome, L., Juhasz, S., Altmannova, V., Sebesta, M., Pacesa, M., Fugger, K., Sorensen, C.S., Lee, M.Y., Haracska, L., Krejci, L. (2016) The PCNA-associated protein PARI negatively regulates homologous recombination via the inhibition of DNA repair synthesis. **Nucleic Acids Res 44:** 3176-89.

TAMÁS CSONT

University of Szeged
Albert Szent-Györgyi Medical School
Department of Biochemistry

RESEARCH AREA

Cardiovascular diseases and especially acute myocardial infarction are among the leading causes of death worldwide. Although prevention and the therapy of myocardial infarction have been significantly improved in the last decades, mortality is still unacceptably high. Therefore, development of new therapies aiming to attenuate infarct size is very relevant. Thus, our research group investigates the molecular mechanisms of infarction as well as the adaptive responses of the myocardium to ischemic stress (pre- and postconditioning) to develop novel potential therapies for the treatment of myocardial infarction. Since the risk of myocardial infarction is increased by the presence of several co-morbidities and risk factors including high cholesterol level, diabetes, obesity, hypertension, smoking, lack of exercise, kidney failure, etc., we also look at the effects of certain risk factors on the myocardium as well as on adaptive mechanisms of the heart.

SELECTED PUBLICATIONS

Sárközy, M., Szűcs, G., Fekete, V., Pipicz, M., Éder, K., Gáspár, R., Sója, A., Pipis, J., Ferdinandy, P., Csonka, C., **Csont, T.** (2016) Transcriptomic alterations in the heart of non-obese type 2 diabetic Goto-Kakizaki rats. Cardiovasc **Diabetol 15**: 110.

Pipicz, M., Varga, Z.V., Kupai, K., Gáspár, R., Kocsis, G.F., Csonka, C., **Csont, T.** (2015) Rapid ventricular pacing-induced postconditioning attenuates reperfusion injury: effects on peroxynitrite, RISK and SAFE pathways. **Br J Pharmacol 172:** 3472-83.

Varga, Z.V., Kupai, K., Szűcs, G., Gáspár, R., Pálóczi, J., Faragó, N., Zvara, A., Puskás, L.G., Rázga, Z., Tiszlavicz, L., Bencsik, P., Görbe, A., Csonka, C., Ferdinandy, P., **Csont, T.** (2013) MicroRNA-25-dependent up-regulation of NADPH oxidase 4 (NOX4) mediates hypercholesterolemia-induced oxidative/nitrative stress and subsequent dysfunction in the heart. **J Mol Cell Cardiol 62:** 111-21.

Kocsis, G.F., Sárközy, M., Bencsik, P., Pipicz, M., Varga, Z.V., Pálóczi, J., Csonka, C., Ferdinandy, P., **Csont, T.** (2012) Preconditioning protects the heart in a prolonged uremic condition. **Am J Physiol Heart Circ Physiol 303:** H1229-36.

Csont, T., Görbe, A., Bereczki, E., Szunyog, A., Aypar, E., Tóth, M.E., Varga, Z.V., Csonka, C., Fülöp, F., Sántha, M., Ferdinandy, P. (2010) Biglycan protects cardiomyocytes against hypoxia/reoxygenation injury: role of nitric oxide. **J Mol Cell Cardiol 48:** 649-52.

DEZSŐ CSUPOR

University of Szeged
Faculty of Pharmacy Institute of Clinical Pharmacy

RESEARCH AREA

My research is partly related to medicinal plants. For many years I have been involved in the quality analysis of herbal products, including qualitative and quantitative analysis of active ingredients, but also the detection of impurities and compounds used for adulteration. I also conduct preparative phytochemical research, as well as chemistry-focused research aimed at promoting rational herbal medicine use. The efficacy and safety of medicinal plants and natural compounds have been investigated in several meta-analyses and such research is ongoing. In addition to this, we are also conducting research in the field of clinical pharmacy related to the safe and rational use of medicines through the analysis of drug utilisation and efficacy and safety.

SELECTED PUBLICATIONS

Koncz, D., Tóth, B., Bahar, MA., Roza, O., **Csupor, D.** (2022) The Safety and Efficacy of Citrus aurantium (Bitter Orange) Extracts and p-Synephrine: A Systematic Review and Meta-Analysis. **Nutrients 14:** 4019

Bajtel, Á., Kiss, T., Tóth, B., Kiss, S., Hegyi, P., Vörhendi, N., Csupor-Löffler, B., Gede, N., Hohmann, J., **Csupor, D.** (2022) The Safety of Dronabinol and Nabilone: A Systematic Review and Meta-Analysis of Clinical Trials. **Pharmaceuticals 15:** 100.

Czégény, Zs., Nagy, G., Babinszki, B., Bajtel, Á., Sebestyén, Z., Kiss, T., Csupor-Löffler, B., Tóth, B., **Csupor, D.** (2021) CBD, a precursor of THC in e-cigarettes. **Sci Rep 11:** 8951.

Koncz, D., Tóth, B., Roza, O., **Csupor, D.** (2021) A Systematic Review of the European Rapid Alert System for Food and Feed: Tendencies in Illegal Food Supplements for Weight Loss. **Front Pharmacol 11:** 611361.

Mottaghipisheh, J., Kiss, T., Tóth, B., **Csupor, D.** (2020) The Prangos genus: A comprehensive review on traditional use, pharmacological activities and phytochemistry. **Phytochem Rev 19:** 1449-1470.

MÁRIA DELI

HUN-REN Biological Research Centre
Institute of Biophysics
Biological Barriers Research Group

RESEARCH AREA

Organisms are protected by biological barriers from harmful effects. These barriers also impede drug penetration. Our lab investigates methods to increase drug delivery on culture models of the blood-brain, nasal, corneal, respiratory and intestinal barriers. The pathways examined are (i) reversible opening of tight intercellular junctions by peptides or small molecules; (ii) targeting solute carriers at barriers for drug delivery by nanoparticles. Cellular toxicity of active ingredients and pharmacautical excipients are measured by a real-time impedance-based method. Double and triple co-culture models are used for experiments, and a microfluidic integrated chip has been developed in a collaborative project. Our other major research interest is the examination of blood-brain barrier injury and dysfunctions in different diseases, like Alzheimer's disease, acute pancreatitis and diabetes. The goal of these experiments is to reveal the effect of disease pathogenic factors on blood-brain barrier functions and to identify protective molecules. The protection of brain endothelial cells and the improvement of BBB functions in pathological conditions, the exploration of new approaches for drug transport/targeting to brain may have therapeutic potential in the treatment of central nervous system diseases.

SELECTED PUBLICATIONS

Mészáros, M., Porkoláb, G., Kiss, L., Pilbat, A.M., Kóta, Z., Kupihár, Z., Kéri, A., Galbács, G., Siklós, L., Tóth, A., Fülöp, L., Csete, M., Sipos, Á., Hülper, P., Sipos, P., Páli, T., Rákhely, G., Szabó-Révész, P., **Deli, M.A.**, Veszelka, S. (2018) Niosomes decorated with dual ligands targeting brain endothelial transporters increase cargo penetration across the blood-brain barrier. **Eur J Pharm Sci 123:** 228-240.

Veszelka, S., Tóth, A., Walter, F.R., Tóth, A.E., Gróf, I., Mészáros, M., Bocsik, A., Hellinger, É., Vastag, M., Rákhely, G., **Deli, M.A.** (2018) Comparison of a rat primary cell-based blood-brain barrier model with epithelial and brain endothelial cell lines: gene expression and drug transport. **Front Mol Neurosci 11:** 166.

Walter, F.R., Valkai, S., Kincses, A., Petneházi, A., Czeller, T., Veszelka, S., Ormos, P., **Deli, M.A.,** Dér, A. (2016) Versatile lab-on-a-chip tool for modeling biological barriers. **Sens Actuators B Chem 222:** 1209-1219.

Bocsik, A., Walter, F.R., Gyebrovszki, A., Fülöp, L., Blasig, I., Dabrowski, S., Ötvös, F., Tóth, A., Rákhely, G., Veszelka, S., Vastag, M., Szabó-Révész, P., **Deli, M.A.** (2016) Reversible opening of intercellular junctions of intestinal epithelial and brain endothelial cells with tight junction modulator peptides. **J Pharm Sci 105:** 754-765.

Veszelka, S., Tóth, A.E., Walter, F.R., Datki, Z., Mózes, E., Fülöp, L., Bozsó, Z., Hellinger, E., Vastag, M., Orsolits, B., Környei, Z., Penke, B., **Deli, M.A.** (2013) Docosahexaenoic acid reduces amyloid-β induced toxicity in cells of the neurovascular unit. **J Alzheimers Dis 36:** 487-501.

ANDRÁS DÉR

HUN-REN Biological Research Centre
Institute of Biophysics
Work Group of Bioelectronics

RESEARCH AREA

Bioelectronics has a double meaning in scientific literature. On the one hand, as a branch of basic biophysical sciences, it deals with electric phenomena appearing on any organization level of living systems. On the other hand, as a recently developed discipline of information technological science, it explores the potential of biological materials for application in molecular electronics. These two areas of research are in close interaction not only with each other, but also with other disciplines of basic applied sciences. Our main goal is to develop novel methods on integrated micro- and nanotechnological platforms for the investigation of light-induced processes in biological membranes, and utilize them in both branches of bioelectronic science. The most important scientific problems to be solved are, on the one hand, concerned with the investigation of electric properties of single cells and cellular interfaces, while on the other hand with the application of photochromic proteins in optoelectronics and photonics. Besides its impact on basic biophysical science, our research is expected to have utilizations in various branches of applied bioelectronics.

SELECTED PUBLICATIONS

Dér, A., Kelemen, L., Fábián, L., Taneva, S.G., Fodor, E., Páli, T., Cupane, A., Cacace, M.G., Ramsden, J.J. (2007) Interfacial Water Structure Controls Protein Conformation. **J Phys Chem B 111:** 5344-5350.

Ormos, P., Fábián L., Oroszi L., Ramsden, J.J., Wolff, E.K., **Dér, A.** (2002) Protein-based integrated optical switching and modulation. **Appl Phys Lett 80:** 4060-4062.

Dér, A., Keszthelyi, L. (eds.) (2001) Bioelectronic Applications of Photochromic Pigments, IOS Press **NATO Science Series**, Vol. 335.

Dér, A., Keszthelyi, L. (2001) Charge motion during the photocycle of bacteriorhodopsin. **Biochemistry (M) 66:** 1234-1248.

Dér, A., Oroszi, L., Kulcsár, Á., Zimányi, L., Tóth-Boconádi, R., Keszthelyi, L., Stoeckenius, W., Ormos, P. (1999) Interpretation of spatial charge displacements in bacteriorhodopsin in terms of structural changes during the photocycle. **Proc Natl Acad Sci USA 96:** 2776-2781.

ATTILA GÁCSER

University of Szeged
Faculty of Science and Informatics
Department of Microbiology

RESEARCH AREA

Infectious diseases are one the leading causes of mortality worldwide, killing millions of people every year. While bacteria and viruses cause the majority of deadly infections, notably the number of fungal diseases is increasing at an alarming rate. In fact, it is estimated that nearly as many people die annually from invasive fungal infections as from the greatly feared tuberculosis (1.4 million) or malaria (1.2 million). Our research program focuses on the most common human fungal pathogens, the opportunistic Candida species with special focus on C. parapsilosis. We investigate the basic mechanisms of fungal pathogenesis and host immunity, and we aim to improve diagnosis and identify novel biomarkers of infection. Recently, we also investigate the role of the human "mycobiome" in health and disease development and progression.

SELECTED PUBLICATIONS

Tóth, A., Zajta, E., Csonka, K., Vágvölgyi, C., Netea, M.G., **Gácser, A.** (2017) Specific pathways mediating inflammasome activation by Candida parapsilosis. **Sci Rep 7:** 43129.

Pryszcz, L.P., Nemeth, T., Saus, E., Ksiezopolska, E., Hegedusova, E., Nosek, J., Wolfe, K.H., **Gácser, A*.**, Gabaldon, T.* (2015) The Genomic Aftermath of Hybridization in the Opportunistic Pathogen Candida metapsilosis. **PLOS Genetics 11:** e1005626.

Tóth, R., Alonso, M.F., Bain, J.M., Vágvölgyi, C., Erwig, L-P., **Gácser, A.** (2015) Different Candida parapsilosis clinical isolates and lipase deficient strain trigger an altered cellular immune response. **Front Microbiol 6:** 1102.

Toth, A., Csonka, K., Jacobs, C., Vagvolgyi, C., Nosanchuk, J.D., Netea, M.G., **Gácser, A.** (2013) Candida albicans and Candida parapsilosis Induce Different T-Cell Responses in Human Peripheral Blood Mononuclear Cells. **J Infect Dis 208:** 690-698.

Lázár-Molnár, E.*, **Gácser, A**.*, Freeman, G.J., Almo, S.C., Nathenson, S.G., Nosanchuk, J.D. (2008) The PD-1/PD-L costimulatory pathway critically affects host resistance to the pathogenic fungus Histoplasma capsulatum. **Proc Natl Acad Sci USA 105:** 2658-2663.

LAJOS HARACSKA

HUN-REN Biological Research Centre
Institute of Genetics
Mutagenesis and Carcinogenesis Laboratory

RESEARCH AREA

Stalling of the DNA replication machinery, which occurs as a consequence of encountering unrepaired DNA damage, is a challenge for cells. To rescue the stalled replication fork, different DNA damage bypass mechanisms have evolved that promote replication through DNA lesions. In humans, increased error-prone bypass of DNA lesions causes increased mutagenesis and, as a consequence, a rise in the incidence of cancers. Error-free bypass processes, by contrast, keep mutagenesis low and reduce the frequency of cancers. Our research laboratory is interested in the driving forces and molecular mechanisms of mutagenesis and carcinogenesis. In particular, we investigate the following questions: What are the common roots of evolution and carcinogenesis? What are the molecular mechanisms of chromosomal rearrangements and the formation of point mutations? Why do we observe increased genome instability during carcinogenesis? What is the role of the recently described DNA repair genes in cancer suppression? Why do mutations in certain genes predispose to cancer? Which genes are commonly mutated in cancer, and how do these mutations contribute to tumour development and drug resistance? We investigate these challenging problems using human tissue culture-based reporter systems, next-generation DNA sequencing and purified proteins in reconstituted reaction pathways. Our research provides more insight into the molecular events of genome instability, carcinogenesis and has the potential to identify new tumour markers and drug targets as well as to improve personal cancer treatment.

SELECTED PUBLICATIONS

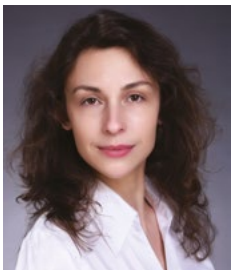
Mórocz, M., Zsigmond, E., Tóth, R., Enyedi, M.Z., Pintér, L., **Haracska, L.** (2017) DNA-dependent protease activity of human Spartan facilitates replication of DNA-protein crosslink-containing DNA. **Nucleic Acids Res 45:** 3172-3188.

Chen, J., Ai, Y., Wang, J., **Haracska, L.**, Zhuang, Z. (2010) Chemically ubiquitylated PCNA as a probe for eukaryotic translesion DNA synthesis. **Nature Chem Biol 6:** 270-2.

Blastyák, A., Pintér, L., Unk, I., Prakash, L., Prakash, S., **Haracska, L.** (2007). Yeast Rad5 protein required for postreplication repair has a DNA helicase activity specific for replication fork regression. **Molecular Cell 28:** 167-75.

Johnson, R.E., Washington, M.T., **Haracska, L.**, Prakash, S., Prakash, L. (2000) Eukaryotic polymerases ι and ζ act sequentially to bypass DNA lesions. **Nature 406:** 1015-1019.

Haracska, L., Yu, S.L., Johnson, R.E., Prakash, L., Prakash, S. (2000) Efficient and accurate replication in the presence of 7,8-dihydro-8-oxoguanine by DNA polymerase η. **Nat Gen 25:** 458-461.



PETRA HARTMANN

University of Szeged
Albert Szent-Györgyi Medical School
Department of Traumatology

RESEARCH AREA

Antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) have a potential influence on eukaryotic cells through affecting mitochondrial functions, the oxidative phosphorylation and mitochondrial reactive oxygen free radicals formation. Both drug classes are commonly used in acute and chronic inflammatory and non-inflammatory diseases of the gastrointestinal (GI) tract, where mitochondrial dysfunction can also occur. Our research group investigates the potential role of mitochondrial dysfunction in the inflamed and non-inflamed states of the digestive tract in experimental and clinical settings. We also aim at investigating the effect of drugs being commonly administered in these diseases. We perform a comprehensive analysis of in vitro doseresponse effect of antibiotics and NSAIDs using highresolution respirometry (HRR) in clinical and experimental tissue samples. In parallel, simultaneous manifestations of intramitochondrial and microcirculatory dysfunctions are monitored in a colitis model with particular interest in mucosal barrier functions and composition of the microbiome; these are examined in the presence and absence of various treatment combinations (antibiotics, antibiotics and NSAIDs, respectively).

SELECTED PUBLICATIONS

Benke, K., Jász, D.K., Szilágyi, Á.L., Baráth, B., Tuboly, E., Márton, A.R., Varga, P., Mohácsi, Á., Szabó, A., Széll, Z., Ruppert, M., Radovits, T., Szabó, G., Merkely, B., **Hartmann, P.**, Boros M. (2021) Methane supplementation improves graft function in experimental heart transplantation. **J Heart Lung Transplant 40:** 183-192.

Jász, D.K,, Szilágyi, Á.L., Tuboly, E., Baráth, B., Márton, A.R., Varga, P., Varga, G., Érces, D., Mohácsi, Á., Szabó, A., Bozó, R., Gömöri, K., Görbe, A., Boros, M., **Hartmann, P.** (2021) Reduction in hypoxia-reoxygenation-induced myocardial mitochondrial damage with exogenous methane. **J Cell Mol Med 25:** 5113-5123.

Horváth, T., Jász, D.K., Baráth, B., Poles, M.Z., Boros, M., **Hartmann, P.** (2021) Mitochondrial Consequences of Organ Preservation Techniques During Liver Transplantation. **Int J Mol Sci 22:** 2816.

Strifler, G., Tuboly, E., Görbe, A., Boros, M., Pécz, D., **Hartmann, P.** (2016) Inhaled Methane limits the mitochondrial electron transport chain dysfunction during experimental liver ischemia-reperfusion injury. **PLoS One 11:** e0146363.

Strifler, G., Tuboly, E., Szél, E., Kaszonyi, E., Cao, C., Kaszaki, J., Mészáros, A., Boros, M., **Hartmann, P.** (2016) Targeting mitochondrial dysfunction with L-alpha glycerylphosphorylcholine. **PLoS One 11:** e0166682.

PÉTER HEGYI

University of Szeged
Albert Szent-Györgyi Medical School
First Department of Medicine

RESEARCH AREA

Epithelial cells form a sheet-like contiguous layer that covers both the external and internal free surfaces of the body, e.g. the surface of skin or inner surface of hollow organs such as in the gastrointestinal tract (GIT). The epithelial cells in the GIT secrete over 10 liters of digestive fluid daily into the lumen - and after digestion - absorb the fluid and nutrients from the lumen. Derangement of this secretory process can lead to severe disorders such as cystic fibrosis or secretory diarrhoea. One of our main research interests is to understand the physiology and pathophysiology of secretory mechanisms. Most recently we have shown that epithelial fluid and ion secretion plays a crucial role in acute pancreatitis which is one of the most severe inflammatory diseases of the GI tract. Therefore, repairing the damaged secretion may lead to a new specific therapeutic way in acute pancreatitis. Besides our interest in the pancreas we work on understanding the oesophageal, gastric and colonic fluid and ion transport mechanisms.

SELECTED PUBLICATIONS

Maléth, J., Balla, Z., Kui, B., Balázs, A., Katona, M., Judák, L., Németh, I., Pallagi, P., Kemény, L.V., Rakonczay Jr, Z., Venglovecz, V., Földesi, I., Pető, Z., Somorácz, A., Borka, K., Perdomo, D., Lukacs, G.L., Gray, M.A., Monterisi, S., Zaccolo, M., Sendler, M., Mayerle, J., Kühn, J.P., Lerch, M.M., Sahin-Tóth, M., **Hegyi P.** (2015) Alcohol Disrupts Levels and Function of the Cystic Fibrosis Transmembrane Conductance Regulator to Promote Development of Pancreatitis. **Gastroenterology 148:** 427-439.e16.

Hegyi, P., Szakács, Z., Sahin-Tóth, M. (2020) Lipotoxicity and Cytokine Storm in Severe Acute Pancreatitis and COVID-19. **Gastroenterology 159:** 824-827.

Hegyi, P., Erőss, B., Izbéki, F., Párniczky, A., Szentesi, A. (2021) Accelerating the translational medicine cycle: the Academia Europaea pilot. **Nat Med 27:** 1317-1319.

Kui, B., Pintér, J., Molontay, R., Nagy, M., Farkas, N., Gede, N., Vincze, Á., Bajor, J., Gódi, S., Czimmer, J., Szabó, I., Illés, A., Sarlós, P., Hágendorn, R., Pár, G., Papp, M., Vitális, Z., Kovács, G., Fehér, E., Földi, I., Izbéki, F., Gajdán, L., Fejes, R., Németh, B.C., Török, I., Farkas, H., Mickevicius, A., Sallinen, V., Galeev, S., Ramírez-Maldonado, E., Párniczky, A., Erőss, B., Hegyi, P.J., Márta, K., Váncsa, S., Sutton, R., Szatmary, P., Latawiec, D., Halloran, C., de-Madaria, E., Pando, E., Alberti, P., Gómez-Jurado, M.J., Tantau, A., Szentesi, A., **Hegyi, P.;** Hungarian Pancreatic Study Group. (2022) EASY-APP: An artificial intelligence model and application for early and easy prediction of severity in acute pancreatitis. **Clin Transl Med 12:** e842.

Czapári, D., Váradi, A., Farkas, N., Nyári, G., Márta, K., Váncsa, S., Nagy, R., Teutsch, B., Bunduc, S., Erőss, B., Czakó, L., Vincze, Á., Izbéki, F., Papp, M., Merkely, B., Szentesi, A., **Hegyi, P.**; Hungarian Pancreatic Study Group. (2023) Detailed characteristics of post-discharge mortality in acute pancreatitis. **Gastroenterology 165:** 682-695.

JUDIT HOHMANN

University of Szeged
Faculty of Pharmacy
Department of Pharmacognosy

RESEARCH AREA

Natural products play an important role in drug discovery because of their unmatched structural diversity, amazing, and often complex structures. The aim of our group is to perform purposeful research by rational selection of plant extracts and compounds to be isolated, in order to obtain efficiently new secondary plant metabolites, which are perspective for drug discovery. Literature data, ethnomedicinal knowledge, results of screen investigations and metabolomic approaches are considered for selection of plant species. Compounds are isolated from the very complex multi-component extracts exhibiting efficacy in the used tests, with the aid of different chromatographic methods by guidance of bioassay. The structures of the purified compounds are determined by means of spectroscopic methods (NMR and MS). The biological activity is usually investigated in collaborations.

SELECTED PUBLICATIONS

Ványolós, A., Dékány, M., Kovács, B.t, Krámos, B., Bérdi, P., Zupkó, I., **Hohmann, J.**, Béni Z. (2016) Gymnopeptides A and B, cyclic octadecapeptides from the mushroom Gymnopus fusipes. **Org Lett 18:** 2688-2691.

Vasas, A., Forgo, P., Orvos, P., Tálosi, L., Csorba, A., Pinke, G., **Hohmann, J**. (2016) Myrsinane, premyrsinane, and cyclomyrsinane diterpenes from Euphorbia falcata as potassium ion channel inhibitors with selective G protein-activated inwardly rectifying ion channel (GIRK) blocking effects. **J Nat Prod 79:** 1990-2004.

Hajdu, Z., Nicolussi, S., Rau, M., Lorantfy, L., Forgo, P., **Hohmann, J.**, Csupor, D., Gertsch, J. (2014) Identification of endocannabinoid system-modulating N alkylamides from Heliopsis helianthoides var. scabra and Lepidium meyenii. **J Nat Prod 77:** 1663-1669.

Vasas, A., Rédei, D., Csupor, D., Molnar, J., **Hohmann, J.** (2012) Diterpenes from European Euphorbia species serving as prototypes for natural-product-based drug discovery. **Eur J Org Chem 2012:** 5115-5130.

Hohmann, J., Molnár, J., Rédei, D., Evanics, F., Forgo, P., Kálmán, A., Argay, G., Szabó, P. (2002) Discovery and biological evaluation of a new family of potent modulators of multidrug resistance: reversal of multidrug resistance of mouse lymphoma cells by new natural jatrophane diterpenoids isolated from Euphorbia species. **J Med Chem 45:** 2425-2431.

GYÖNGYI HORVÁTH

University of Szeged
Albert Szent-Györgyi Medical School
Department of Physiology

RESEARCH AREA

Schizophrenia is a complex neuropsychiatric disorder, with positive, and negative symptoms, and cognitive impairments. While the positive signs are well handled, the treatments of the other impairments have not been resolved.
Appropriate animal models are required to determine the exact pathomechanism of this disease and for testing new drugs. Our laboratory developed a complex (three-hit) rat model of schizophrenia, and these animals have several signs observed in schizophrenic patients, suggesting the translational relevance of this model.
The goals of our recent studies are to investigate, besides the acute behavioral test (Ambitus), the behavioral activities and cognitive functions of these animal in stress-free condition with environmental enrichment for prolonged period (Home-Manner). The analysis of the huge amount of data obtained during the experiments requires high levels of mathematics/informatics methods. This study might be appropriate not only for testing new method for the treatments of this disease, but also to characterize the effects of different drugs with addictive potential in these animals (since substance abuse is highly prevalent in schizophrenia).

SELECTED PUBLICATIONS

Horvath, G., Kertész, I., Nagy, T., Adlan, LG., Kekesi, G., Büki, A., Tuboly, G., Trencsényi, G. (2022) Caffeine-Induced Acute and Delayed Responses in Cerebral Metabolism of Control and Schizophrenia-Like Wisket Rats. **Int J Mol Sci 23(15):** 8186.

Büki, A., Kekesi, G., **Horvath, G.**, Vécsei, L. (2021) A Potential Interface between the Kynurenine Pathway and Autonomic Imbalance in Schizophrenia. **Int J Mol Sci 22(18):** 10016.

Petrovszki, Z., Adam, G., Tuboly, G., Kekesi, G., Benedek, G., Keri, S., **Horvath, G.** (2013) Characterization of gene-environment interactions by behavioral profiling of selectively bred rats: the effect of NMDA receptor inhibition and social isolation. **Behav Brain Res 240:** 134-45.

Nagy, E., Toth, K., Janositz, G., Kovacs, G., Feher-Kiss, A., Angyan, L., **Horvath, G.** (2004) Postural control in athletes participating in an ironman triathlon. **Eur J Appl Physiol 92(4-5):** 407-13.

Horvath, G. (2000) Endomorphin-1 and endomorphin-2: pharmacology of the selective endogenous mu-opioid receptor agonists. **Pharmacol Ther 88(3):** 437-63.

PÉTER HORVÁTH

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

Recent advances in light microscopy have changed the way biological research is conducted. The ability to acquire massive amounts of image data has given rise to new fields such as high content screening (HCS) or 3D imaging, which promise to open new doors both for basic research and drug discovery. However, with such massive amounts of data comes a need for automatic analysis tools. Our research concentrates on how human knowledge can be best integrated into intelligent computer algorithms for automated microscopy. To reach this goal, we have interest in image processing that is concerned with extracting biologically relevant quantitative information in 3-4-5D imaging and multi-parametric machine learning analysis that is necessary to make sense of this information. Recently, machine learning algorithms have become a popular solution for analyzing large single cell-based imaging scenarios. We concentrate on improving the state-of-the-art by detecting unusual patterns corresponding to unknown phenotypes.

SELECTED PUBLICATIONS

Pfisterer, S., Gateva, G., **Horvath, P.**, Pirhonen, J., Salo, V., Karhinen, L., Varjosalo, M., Ryhänen, S., Lappalainen, P., Ikonen, E. (2017) Role for formin-like 1-dependent acto-myosin assembly in lipid droplet dynamics and lipid storage. **Nat Commun 8:** 14858.

Horvath, P., Aulner, N., Bickle, M., Davies, A., Del Nery, E., Ebner, D., Montoya, M., Ostling, P., Pietiainen, V., Price, L., Shorte, S., Turcatti, G., von Schantz, C., Carragher, N. (2016) Screening out irrelevant cell-based models of disease. **Nat Rev Drug Discov 15:** 751–769.

Molnar, Cs., Jermyn, I., Kato, Z., Rahkama, V., Ostling, P., Mikkonen, P., Pietiainen, V., **Horvath, P. (**2016) Accurate morphology preserving segmentation of overlapping cells based on active contours. **Sci Rep 6:** 32412.

Piccinini, F., Kiss, A., **Horvath, P**. (2015) CellTracker (not only) for dummies. **Bioinformatics 32:** 955-957.

Smith, K., Li, Y., Piccinini, F., Csucs, G., Balazs, C., Bevilacqua, A., **Horvath, P.** (2015) CIDRE: an illumination-correction method for optical microscopy. **Nat Methods 12:** 404–406.

Banerjee, I., Miyake, Y., Nobs, S. P., Schneider, C., **Horvath, P.**, Kopf, M., Matthias, P., Helenius, A., Yamauchi, Y. (2014) Influenza A virus uses the aggresome processing machinery for host cell entry. **Science 346:** 473-7.

ATTILA HUNYADI

University of Szeged
Faculty of Pharmacy
Institute of Pharmacognosy

RESEARCH AREA

Cancer is a leading cause of morbidity and mortality worldwide, and it is expected that annual cancer cases will rise from 14 million in 2012 to around 22 million within the next two decades. Resistance is a major factor promoting failure of chemotherapy and there is an urgent need for new therapeutic strategies. By following a natural product inspired drug discovery strategy, our group focuses on novel chemical approaches to fight cancer and particularly multi-drug resistant cancer. In this endeavor, we aim at the preparation of nature-inspired chemical scaffolds that can act as chemo-sensitizers on resistant tumor cells, hence can be used as non-toxic adjuvants in combination with chemotherapeutics. A broad scale of interesting natural products is utilized as starting materials, e.g. well-known antioxidants, insect hormones utilized as anabolic food supplements, etc. Thanks to this and to our intensive international collaboration, an inspiring multidisciplinary working environment awaits the candidates to join our team.

SELECTED PUBLICATIONS

Fási, L., Di Meo, F., Kuo, C.Y., Stojkovic Buric, S., Martins, A., Kúsz, N., Béni, Z., Dékány, M., Balogh, G.T., Pesic, M., Wang, H.C., Trouillas, P., **Hunyadi, A.** (2019) Antioxidant-inspired drug discovery: antitumor metabolite is formed in situ from a hydroxycinnamic acid derivative upon free radical scavenging. **J Med Chem 62:** 1657-1668.

Hunyadi, A. (2019) The mechanism(s) of action of antioxidants: from scavenging reactive oxygen/nitrogen species to redox signaling and the generation of bioactive secondary metabolites. **Med Res Rev 39:** 2505-2533.

Vágvölgyi, M., Martins, A., Kulmány, Á., Zupkó, I., Gáti, T., Simon, A., Tóth, G., **Hunyadi, A.** (2018) Nitrogen-containing ecdysteroid derivatives vs. multi-drug resistance in cancer: Preparation and antitumor activity of oximes, oxime ethers and a lactam. **Eur J Med Chem 144:** 730-739.

Hunyadi, A., Herke, I., Lengyel, K., Báthori, M., Kele, Z., Simon, A., Tóth, G., Szendrei, K. (2016) Ecdysteroid containing food supplements from Cyanotis arachnoidea on the European market: evidence for spinach product counterfeiting. **Sci Rep 6:** 37322.

Csábi, J., Hsieh, T.J., Hasanpour, F., Martins, A., Kele, Z., Gáti, T., Simon, A., Tóth, G., **Hunyadi, A.** (2015) Oxidized Metabolites of 20-Hydroxyecdysone and their Activity on Skeletal Muscle Cells: Preparation of a Pair of Desmotropes with Opposite Bioactivities. **J Nat Prod 78:** 2339-2345.

GÁBOR JUHÁSZ

HUN-REN Biological Research Centre
Institute of Genetics

RESEARCH AREA

Autophagy is a fundamental catabolic pathway in eukaryotic cells. During the main route, portions of cytosol and organelles are captured into double-membrane autophagosomes, which then fuse with lysosomes to deliver their cargo for degradation and reuse. Our group is studying the role and mechanisms of autophagy mainly using the popular animal model Drosophila. We are also working on related trafficking pathways including endocytosis and crinophagy (secretory granule degradation). In recent years, we have started experiments to understand the regulation of lysosomal function.

SELECTED PUBLICATIONS

Lőrincz, P., Kenéz, L.A., Tóth, S., Kiss, V., Varga, Á., Csizmadia, T., Simon-Vecsei, Z., **Juhász, G.** (2019) Vps8 overexpression inhibits HOPS-dependent trafficking routes by out-competing Vps41/Lt. **Elife 8:** e45631.

Csizmadia, T., Lőrincz, P., Hegedűs, K., Széplaki, S., Lőw, P., **Juhász, G.** (2018) Molecular mechanisms of develop-mentally programmed crinophagy in Drosophila. **J Cell Biol 217:** 361-374.

Katheder, NS., Khezri, R., O'Farrell, F., Schultz, S.W., Jain, A., Rahman, M.M., Schink, K.O., Theodossiou, T.A., Johansen, T., **Juhász, G.**, Bilder, D., Brech, A., Stenmark, H., Rusten, T.E. (2017) Microenvironmental autophagy promotes tumour growth. **Nature 541:** 417-420.

Lorincz, P., Lakatos, Z., Varga, A., Maruzs, T., Simon-Vecsei, Z., Darula, Z., Benko, P., Csordas, G., Lippai, M., Ando, I., Hegedus, K., Medzihradszky, K., Takats, S., **Juhasz, G.** (2016) MiniCORVET is a Vps8-containing hemocyte- and nephrocyte-specific early endosomal tether in Drosophila. **Elife 5:** e14226.

Takats, S., Nagy, P., Varga, A., Pircs, K., Karpati, M., Varga, K., Kovacs, A.L., Hegedus, K., **Juhasz, G.** (2013) Autophagosomal Syntaxin17-dependent lysosomal degradation maintains neuronal function in Drosophila. **J Cell Biol 201:** 531-539.

SZILVIA JUHÁSZ

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

The microbiota thrives on all epithelial surfaces of the human body, encompassing the skin, respiratory tract, digestive tract, and urogenital tract. These microbiome communities influence the development, progression, metastasis formation, and treatment response of several cancer types. While there is limited direct evidence of causation, there is widespread recognition of the significant scientific and clinical significance of gaining a deeper molecular understanding of these interactions between microbes and cancer and how they affect cancer treatment.
To explore the microbiome's impact on the microevolution of human tumors, we apply a combination of 3D cell culture technology, analysis of mutational signatures, and profiling of the response to DNA damage. Our particular focus lies in uncovering the microbiome-related mutagenic mechanisms that accelerate the progression of cancer. We are constructing an integrated framework that enables the classification of patients based on their cancer risk and responsiveness to therapy. Furthermore, these studies will explore new pathways in the human DNA damage response system that are implicated in the evolution of cancer. Our aim is to develop biomarkers associated with the microbiome in non-cancerous patients before tumors emerge, thus revolutionizing therapeutic approaches from reactive to predictive.

SELECTED PUBLICATIONS

Réthi-Nagy, Z., Ábrahám, E., Sinka, R., **Juhász, S.***, Lipinszki, Z.* (2019) Protein Phosphatase 4 Is Required for Centrobin Function in DNA Damage Repair. **Cells 12(18):** 2219.
*Correspondence authors

Elbakry, A., **Juhász, S.**, Chan, KC., Löbrich, M. (2021) ATRX and RECQ5 define distinct homologous recombination subpathways. **Proc Natl Acad Sci U S A 118(3):** e2010370118.

Juhász, S.*, Smith, R.*, Schauer, T., Spekhardt, D., Mamar, H., Zentout, S., Chapuis, C., Huet, S., Timinszky, G. (2020) The chromatin remodeler ALC1 underlies resistance to PARP inhibitor treatment. **Science Advances 6(51):** eabb8626.
*These authors contributed equally to this work.

Juhasz, S., Elbakry, A., Mathes, A., Löbrich, M., (2018) ATRX Promotes DNA Repair Synthesis and Sister Chromatid Exchange during Homologous Recombination. **Mol Cell 71(1):** 11-24.e7.

Elbakry, A., **Juhász, S.**, Mathes, A., Löbrich, M. (2018) DNA repair synthesis and histone deposition partner during homologous recombination. **Mol Cell Oncol 5(5):** e1511210.

JÓZSEF KASZAKI

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Surgical Research

RESEARCH AREA

Sepsis remains one of the leading causes of death in the intensive care units which necessitates the development of new diagnostic tools and novel, more efficient therapeutic possibilities. The basic problem in sepsis is the discrepancy between oxygen delivery and oxygen consumption which can lead to irreversible oxygen extraction deficit and energy shortage. The cornerstone of acute care should be to prevent, assess and treat oxygen debt globally. We propose that causative factors and signs of oxygen deficit have to be examined together on microcirculatory, cellular (endothelial) and subcellular (mitochondrial) levels in different shock-affected organs (e.g. the intestine and lung) by employing sufficiently long-term, clinically relevant experimental models. With this theoretical background, the major goal of our study is to find optimal, clinically applicable manoeuvres for microcirculatory recruitment and mitochondrial resuscitation to minimize the energy deficit of organs during the septic response.

SELECTED PUBLICATIONS

Poles, M.Z., Bódi, N., Bagyánszki, M., Fekete, É., Mészáros, A.T., Varga, G., Szűcs S., Nászai, A., Kiss, L., Kozlov, A.V., Boros, M., **Kaszaki, J.** (2018) Reduction of nitrosative stress by methane: Neuroprotection through xanthine oxidoreductase inhibition in a rat model of mesenteric ischemia- reperfusion. **Free Radic Biol Med 120:** 160-169.

Érces, D., Nógrády, M., Varga, G., Szűcs, S., Mészáros, A.T., Fischer-Szatmári, T., Cao, C., Okada, N., Okada, H., Boros, M., **Kaszaki, J.** (2016) Complement C5a inhibition improves late hemodynamic and inflammatory changes in a rat model of nonocclusive mesenteric ischemia. **Surgery 159:** 960-971.

Érces, D., Nógrády, M., Nagy, E., Varga, G., Vass, A., Süveges, G., Imai, M., Okada, N., Okada, H., Boros, M., **Kaszaki, J.** (2013) Complement c5a antagonist treatment improves the acute circulatory and inflammatory consequences of experimental cardiac tamponade. **Crit Care Med 41:** 344-351.

Boros, M., Ghyczy, M., Érces, D., Varga, G., Tőkés, T., Kupai, K., Torday, Cs., **Kaszaki, J.** (2012) The anti-inflammatory effects of methane. **Crit Care Med 40:** 1269-1278.

Kaszaki, J., Érces, D., Varga, G., Szabó, A., Vécsei, L., Boros, M. (2012) Kynurenines and intestinal neurotransmission – the role of N-methyl-D-aspartate receptors. **J Neural Transm 119:** 211-223.

ANIKÓ KELLER-PINTÉR

University of Szeged
Albert Szent-Györgyi Medical School
Department of Biochemistry

RESEARCH AREA

Skeletal muscle is a highly dynamic tissue that can undergo successful regeneration upon injury, and change in size in response to exercise, aging or due to diseases (e.g. cancer cachexia, immobilization, or denervation). The muscle stem cells, satellite cells are stimulated by local damage to proliferate extensively and form myoblasts that will subsequently migrate, differentiate and fuse to form muscle fibers. Our research aims are to study (i) the signaling pathways and mechanisms in myoblast migration, differentiation, and fusion (ii) the role of exosomes in cell migration, (iii) the biology of satellite cells. Moreover, we investigate the molecular mechanisms regulating skeletal muscle mass, and we aimed to find new nanotechnological approaches for the local treatment of muscle atrophy. Skeletal muscle has an important role in whole-body metabolism, it accounts for 40% of adult human body weight, and about 90% of insulin-stimulated glucose uptake occurs in skeletal muscle. The vesicular transport of GLUT4 glucose transporters is impaired in cases of insulin resistance and type-2 diabetes mellitus leading to decreased glucose uptake of skeletal muscle and increased blood glucose level. Our further aim is to study this mechanism and to find new signaling pathways regulating glucose uptake of skeletal muscle. Our work is mainly basic research and we have strong scientific collaborations with clinicians.

SELECTED PUBLICATIONS

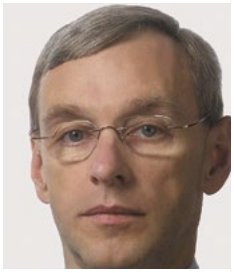
Szabo, K., Varga, D., Vegh, AG., Liu, N., Xiao, X., Xu, L., Dux, L., Erdelyi, M., Rovo, L., **Keller-Pinter, A.** (2022) Syndecan-4 affects myogenesis via Rac1-mediated actin remodeling and exhibits copy-number amplification and increased expression in human rhabdomyosarcoma tumors. **Cell Mol Life Sci 79:** 122.

Becsky, D., Szabo, K., Gyulai-Nagy, S., Gajdos, T., Bartos, Z., Balind, A., Dux, L., Horvath, P., Erdelyi, M., Homolya, L., **Keller-Pinter, A.** (2020) Syndecan-4 Modulates Cell Polarity and Migration by Influencing Centrosome Positioning and Intracellular Calcium Distribution. **Front Cell Dev Biol 15:** 575227.

Becsky, D., Gyulai-Nagy, S., Balind, A., Horvath, P., Dux, L., **Keller-Pinter, A**. (2020) Myoblast Migration and Directional Persistence Affected by Syndecan-4-Mediated Tiam-1 Expression and Distribution. **Int J Mol Sci 21:** 823.

Keller-Pinter, A., Szabo, K., Kocsis, T., Deak, F., Ocsovszki, I., Zvara, A., Puskas, L., Szilak, L., Dux, L. (2018) Syndecan-4 influences mammalian myoblast proliferation by modulating myostatin signalling and G1/S transition. **FEBS Lett 592:** 3139-3151.

Kocsis, T., Trencsenyi, G., Szabo, K., Baán, J.A., Müller, G., Mendler, L., Garai, I., Reinauer, H., Deak, F., Dux, L., **Keller- Pintér, A.** (2016) Myostatin propeptide mutation of the hypermuscular Compact mice decreases the formation of myostatin and improves insulin sensitivity. **Am J Physiol Endocrinol Metab 312:** E150-E160.



LAJOS KEMÉNY

University of Szeged
Albert Szent-Györgyi Medical School
Department of Dermatology and Allergology

RESEARCH AREA

Trillions of bacteria, fungi and viruses colonize the skin surface, collectively comprising the skin microbiome. There is a continous interaction in between the microbas and the different cells in the skin. Recent data suggest, that the skin commensal bacteria play an important role in providing a protection against more harmful bacteria, and in the regulation of skin immune system. Commensal bacteria can activate the different cells in the skin to produce inflammatory mediators. However, it is not known, how the skin cells can differentiate in between commensal and pathogenic bacterias? How do we tolerate the great number of bacteria without inducing inflammation in the skin? In special circumstances, the commensal flora has been suggested to play a role in the induction or in the maintenace of chronic inflammatory skin diseases, such as acne, rosacea or psoriasis. Important member of the skin's commensal flora is the bacterium called *Propionibacterium acnes (P. acnes)*. Even though it resides in the pilosebaceous unit of the skin, under certain circumstances it may also play an important role in the pathogenesis of acne, the most common inflammatory skin disease. We investigate how and when this commensal microbe turns pathogenic and how this bacterium influences the skin immune system.

SELECTED PUBLICATIONS

Buzas, K., Marton, A., Vizler, C., Gyukity-Sebestyen, E., Harmati, M., Nagy, K., Zvara, A., Katona, R.L., Tubak, V., Endresz, V., Németh, I., Olah, J., Vigh, L., Biro, T., **Kemeny, L**. (2016) Bacterial sepsis increases survival in metastatic melanoma: Chlamydophila pneumoniae induces macrophage polarization and tumor regression. **J Invest Dermatol 136:** 862-865.

Tax, G., Urbán, E., Palotás, Zs., **Kemény, L.**, Szabó, K. (2016**)** Propionic acid produced by Propionibacterium acnes strains contribute to their pathogenicity. **Acta Derm Venereol 93:** 43-49.

Manczinger, M., **Kemény, L**. (2013) Novel factors in the pathogenesis of psoriasis and potential drug candidates are found with systems biology approach. **Plos One 8:** e80751.

Szabó, K., **Kemény, L.** (2011) Studying the genetic predisposing factors in the pathogenesis of acne vulgaris. **Human Immunol 72:** 766–773.

Kinyó, A., Kiss-László, Z., Hambalkó, S., Bebes, A., Kiss, M., Széll, M., Bata-Csörgő, Z., Nagy, F., **Kemény, L**. (2010) COP1 contributes to UVB-induced signaling in human keratinocytes. **J Invest Dermatol 130:** 541–545.

BÁLINT KINTSES

HUN-REN Biological Research Centre
Institute of Biochemistry
Synthetic and Systems Biology Unit

RESEARCH AREA

The human body is a complex ecosystems consisting of the host and its associated microbiota made up of hundreds of beneficial commensal and disease causing pathogenic and opportunistic pathogenic bacterial species. As modern human lifestyles keep changing the ecological environment of the human microbiota at an unprecedented pace, these bacteria respond to these changes with continuous adaptation. A well known consequence of this process is the global antibiotic resistance crisis which is responsible for over 700,000 deaths annually, primarily driven by the emergence of multi-drug resistant opportunistic pathogenic bacteria. In our laboratory, we develop novel technologies in the field of synthetic biology, genomics and genome engineering for two complementary goals. First, to understand the evolutionary dynamics of antibiotic resistance development, and second, to develop novel therapeutic approaches designed to selectively target multi-drug resistant pathogenic bacteria. Beyond asking fundamental scientific questions, we are interested in the utilisation and commercialisation of our inventions.

SELECTED PUBLICATIONS

Kintses, B., Kumar, P., Jangir, PK,, Fekete, G., Számel, M., Méhi, O., Spohn, R., Daruka, L,, Martins, A., Hosseinnia, A., Gagarinova, A., Kim, S., Phanse, S., Csörgö, B., Györkei, A., Ari, E., Lázár, V., Faragó, A., Bodai, L., Nagy, I., Babu, M., Pál, C., Papp, B. (2019) Chemical-genetic profiling reveals cross-resistance and collateral sensitivity between antimicrobial peptides. **Nat Commun 10:** 5731.

Kintses, B., Méhi, O., Ari, E., Számel, M., Györkei, Á., Jangir, PK., Nagy, I., Pál, F., Fekete, G., Tengölics, R., Nyerges, Á., Likó, I., Bálint, A., Molnár, T., Bálint, B., Vásárhelyi, BM., Bustamante, M., Papp, B., Pál, C. (2019) Phylogenetic barriers to horizontal transfer of antimicrobial peptide resistance genes in the human gut microbiota. **Nature Microbiology 4: 447-458.**

Nyerges, Á., Csörgő, B., Draskovits, G., **Kintses, B.**, Szili, P., Ferenc, G., Révész, T., Ari, E., Nagy, I., Bálint, B., Vásárhelyi, BM., Bihari, P., Számel, M., Balogh, D., Papp, H., Kalapis, D., Papp, B., Pál, C. (2018) Directed evolution of multiple genomic loci allows the prediction of antibiotic resistance. **Proc Natl Acad Sci U S A 115:** E5726-E5735.

Colin, PY., **Kintses, B.**, Gielen, F., Miton, C., Fischer, G., Mahomed, M., Hyvonen, M., Morgavi, DP., Janssen, DB., Hollfelder, F. (2015) Ultrahigh-throughput Discovery of Promiscuous Enzymes by Picodroplet Functional Metagenomics. **Nature Communications 6:** 10008.

Notebaart, RA., Szappanos, B., **Kintses, B.*** , Pál, F., Györkei, Á., Bogos, B., Lázár, V., Spohn, R., Csörgő, B., Wagner, A., Ruppin, E., Pál, C., Papp, B. (2014) Network-level architecture and the evolutionary potential of underground metabolism. **Proc Natl Acad Sci U S A 111:** 11762-7.

MÓNIKA KIRICSI

University of Szeged
Faculty of Science and Informatics
Department of Biochemistry and Molecular Biology

RESEARCH AREA

The general strategy to treat cancer relies largely on traditional chemotherapy using small molecular drugs. Although conventional chemotherapy has a decent success rate it frequently causes severe side effects and can even result in the evolution of multidrug resistant cancer phenotypes. Nanoparticle based treatment of solid tumors is regarded as a novel, attractive strategy to improve cancer therapy, since approximately 10-200 nm sized materials are selectively accumulated in tumor tissues due to the passive targeting effect, where many of them, especially metallic particles can exert direct anti-cancer activity. Owing to their large surface area nanomaterials can also serve as controllable delivery platforms of various cytotoxic drugs for active tumor targeting. Our research group investigates the cellular and molecular events behind the anti-cancer activity of different types of metal nanoparticles in *in vitro* and *in vivo* animal model systems.

SELECTED PUBLICATIONS

Gopisetty, M.K., Kovács, D., Igaz, N., Rónavári, A., Bélteky, P., Rázga, Z., Venglovecz, V., Csoboz, B., Boros, I.M., Kónya, Z., **Kiricsi, M.** (2019) Endoplasmic reticulum stress: major player in size-dependent inhibition of P - glycoprotein by silver nanoparticles in multidrug-resistant breast cancer cells. **J Nanobiotechnol 17:** 9.

Huliák, I., Bodai, L., Czepán, M., Kovács, D., Szabó, A., Tiszlavicz, L., Lázár, G., Rakonczay, Z. Jr, Hegyi, P., Boros, I.M., **Kiricsi, M.** (2019) Genetic, epigenetic and transcriptional comparison of esophagus tumor-associated and adjacent normal myofibroblasts. **Oncology Rep 41:** 839-852.

Igaz, N., Kovács, D., Rázga, Z., Kónya, Z., Boros, I.M., **Kiricsi, M.** (2016) Modulating chromatin structure and DNA accessibility by deacetylase inhibition enhances the anticancer activity of silver nanoparticles. **Colloids Surf B Biointerfaces 146:** 670-7.

Kovács, D., Igaz, N., Keskeny, C., Bélteky, P., Tóth, T., Gáspár, R., Madarász, D., Rázga, Z., Kónya, Z., Boros, I.M., **Kiricsi, M.** (2016) Silver nanoparticles defeat p53-positive and p53- negative osteosarcoma cells by triggering mitochondrial stress and apoptosis. **Sci Rep 6:** 27902.

Kovács, D., Szőke, K., Igaz, N., Spengler, G., Molnár, J., Tóth, T., Madarász, D., Rázga, Z., Kónya, Z., Boros, I.M., **Kiricsi, M.** (2016) Silver nanoparticles modulate ABC transporter activity and enhance chemotherapy in multidrug resistant cancer. **Nanomedicine 12:** 601-10.

ISTVÁN KRIZBAI

HUN-REN Biological Research Centre
Institute of Biophysics

RESEARCH AREA

The central nervous system is one of the most complex and meantime the most sensitive part of our organism. For its proper function the central nervous system needs a steady state environment which is largely provided by the neurovascular unit. In this respect changes in functions of the neurovascular unit have important consequences in causing or aggravating a large number of neurological diseases. The main goal of our research is to understand the molecular mechanisms underlying the function of the neurovascular unit under physiological and pathological conditions. For this purpose, we use different in vitro models and in vivo two-photon microscopy. On the one side, we investigate the role of neurovascular unit in the formation of brain metastases and the mechanisms of migration of tumour cells into the brain. On the other hand, we investigate how cellular components of the neurovascular unit (brain endothelial cells, pericytes, astrocytes) communicate with each other in neurological disorders associated with aging and with inflammatory processes.

SELECTED PUBLICATIONS

Haskó, J., Fazakas, C., Molnár, K., Mészáros, Á., Patai, R., Szabó, G., Erdélyi, F., Nyúl-Tóth, Á., Győri, F., Kozma, M., Farkas, A.E., **Krizbai, I.A.***, Wilhelm, I.*. (2019) Response of the neurovascular unit to brain metastatic breast cancer cells. **Acta Neuropathol Commun 7:** 133. *corresponding authors

Wilhelm, I., Fazakas, C., Molnár, K., Végh, A.G., Haskó, J., **Krizbai, I.A.** (2018) Foe or friend? Janus- faces of the neurovascular unit in the formation of brain metastases. **J Cereb Blood Flow Metab 38:** 563-587.

Nyúl-Tóth, Á., Kozma, M., Nagyőszi, P., Nagy, K., Fazakas, C., Haskó, J., Molnár, K., Farkas, A.E., Végh, A.G., Váró, G., Galajda, P., Wilhelm, I., **Krizbai, I.A.** (2017) Expression of pattern recognition receptors and activation of the non-canonical inflammasome pathway in brain pericytes. **Brain Behav Immun 64:** 220-231.

Nyúl-Tóth, Á., Suciu, M., Molnár, J., Fazakas, C., Haskó, J., Herman, H., Farkas, A.E., Kaszaki, J., Hermenean, A., Wilhelm, I., **Krizbai, I.A.** (2016) Differences in the molecular structure of the blood-brain barrier in the cerebral cortex and white matter: an in silico, in vitro and ex vivo study. **Am J Physiol Heart Circ Physiol 310:** H1702-14.

Nagyőszi, P., Nyúl-Tóth, Á., Fazakas, C., Wilhelm, I., Kozma, M., Molnár J., Haskó, J., **Krizbai, I.A.** (2015) Regulation of NODlike receptors and inflammasome activation in cerebral endothelial cells. **J Neurochem 135:** 551-64.

JÓZSEF MALÉTH

University of Szeged
Albert Szent-Györgyi Medical School
First Department of Medicine

RESEARCH AREA

Epithelial cells are essential orchestrators of organ physiology by determining fluid and volume homeostasis and secreting many biologically active compounds (including enzymes and mucins). Furthermore impaired epithelial function is associated with a plethora of severe and potentially lethal diseases, such as cystic fibrosis, or acute pancreatitis, whereas malignant epithelial transformation leads to different forms of cancer. Thus, epithelial functions are extensively regulated, but the details of these regulatory pathways are not well understood. I believe that the detailed understanding of complex epithelial functions will lead to better treatment of lethal diseases therefore in my research projects I focus on the physiological and pathophysiological roles of pancreatic epithelial cells.

SELECTED PUBLICATIONS

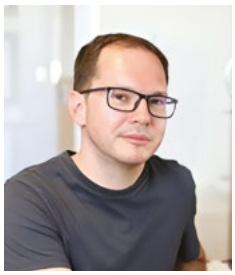
Maléth, J., Balla, Z., Kui, B., Balázs, A., Katona, M., Judák, L., Németh, I., Pallagi, P., Kemény, L.V., Rakonczay, Jr., Z., Venglovecz, V., Földesi, I., Pető, Z., Somorácz, Á., Borka, K., Perdomo, D., Lukacs, G.L., Gray, M.A., Monterisi, S., Zaccolo, M., Sendler, M., Mayerle, J., Kühn, J.P., Lerch, M.M., Sahin-Tóth, M., Hegyi, P. (2015) Alcohol Disrupts Levels and Function of the Cystic Fibrosis Transmembrane Conductance Regulator to Promote Development of Pancreatitis. **Gastroenterology 148:** 427-39.e16.

Maléth, J., Choi, S., Muallem, S., Ahuja, M. (2014) Translocation Between PI(4,5)P2-Poor and PI(4,5)P2-Rich Microdomains During Store Depletion Determines STIM1 Conformation and Orai1 Gating. **Nat Commun 17:** 5843.

Jha, A., Ahuja, M., **Maléth, J.**, Moreno, C.M., Yuan, J.P., Kim, M.S., Muallem, S. (2013) The STIM1 CTID domain determines access of SARAF to SOAR to regulate Orai1 channel function. **J Cell Biol 202:** 71-9.

Pallagi, P., Venglovecz, V., Rakonczay, Jr., Z., Borka, K, Korompay, A., Ózsvári, B., Judák, L., Sahin-Tóth, M., Geisz, A., Schnúr, A., **Maléth, J.**, Takács, T., Gray, M.A., Argent, B.E., Mayerle, J., Lerch, M.M., Wittman, T., Hegyi, P. (2011) Trypsin reduces pancreatic ductal bicarbonate secretion by inhibiting CFTR Cl^- channels and luminal anion exchangers. **Gastroenterology 141:** 2228–2239.e6.

Maléth, J., Venglovecz, V., Rázga, Zs., Tiszlavicz, L., Rakonczay, Jr., Z., Hegyi, P. (2011) The non-conjugated chenodeoxycholate induces severe mitochondrial damage and inhibits bicarbonate transport in pancreatic duct cells. **Gut 60:** 136-8.



MÁTÉ MANCZINGER

HUN-REN Biological Research Centre
Institute of Biochemistry
University of Szeged
Albert Szent-Györgyi Medical School
Department of Dermatology and Allergology

RESEARCH AREA

How does our immune system distinguish between billions of molecules? What are the main determinants of immune recognition? What factors explain that certain people are more likely to get infections or cancer, while others are protected from these diseases? My research group aims to answer these questions. We focus on the adaptive immune system, which recognizes specific molecular motifs of pathogens, cancer and our self-cells. While this system is extremely completed, it is controlled by some less complicated laws, which we intend to characterize in detail. For example, while one would expect that the immune system is more likely to recognize molecular motifs that are highly dissimilar to our self-molecules, we showed that overly high dissimilarity hinders immune recognition. Moreover, adaptive immune recognition is largely influenced by diverse genetic factors resulting in variable susceptibility to infections, cancer and autoimmune diseases. If you would like to take part in untangling the complexity of adaptive immune recognition, don't hesitate to join us!

SELECTED PUBLICATIONS

Koncz, B., Balogh, G. M., Papp, B. T., Asztalos, L., Kemény, L., & **Manczinger, M.** (2021). Self-mediated positive selection of T cells sets an obstacle to the recognition of nonself. **Proceedings of the National Academy of Sciences 118:** e2100542118.

Manczinger, M., Koncz, B., Balogh, G. M., Papp, B. T., Asztalos, L., Kemény, L., Papp, B. & Pál, C. (2021). Negative trade-off between neoantigen repertoire breadth and the specificity of HLA-I molecules shapes antitumor immunity. **Nature Cancer 2:** 950-961.

Manczinger, M., Boross, G., Kemény, L., Müller, V., Lenz, T. L., Papp, B., & Pál, C. (2019). Pathogen diversity drives the evolution of generalist MHC-II alleles in human populations. **PLoS Biology 17:** e3000131.

Manczinger, M., Kemény, L. (2018). Peptide presentation by HLA-DQ molecules is associated with the development of immune tolerance. **PeerJ 6:** e5118.

TAMÁS MARTINEK

University of Szeged
Albert Szent-Györgyi Medical School
Department of Medical Chemistry

RESEARCH AREA

The aim of our research group is to create new macromolecules from unnatural building blocks (foldamers), of which 3D structure can be predicted and programmed. Manipulating protein-protein, protein-membrane and protein-carbohydrate interactions by these chemically well defined substances is a great challenge and holds promise. While small molecule drugs can not effectively decouple macromolecule interactions in general because of their geometry, the right sized and often used antibodies have many disadvantages. We utilize foldamers as artifical self-organizing protein mimetics to modulate protein interactions, to develop diagnostic tools and novel antibacterial materials.

SELECTED PUBLICATIONS

Bhaumik K.N., Hetényi, A., Olajos, G., Martins, A., Spohn, R., Németh, L., Jojárt, B., Szili, P., Dunai, A., Jangir, P.K., Daruka, L., Földesi, I., Kata D., Pál, Cs., **Martinek, T.A.** (2022) Rationally designed foldameric adjuvants enhance antibiotic efficacy via promoting membrane hyperpolarization. **Molecular Systems Design & Engineering 7:** 21-33.

Imre, N., Hetényi A., Szabó, E., Bodnár, B., Szkalisity, A., Gróf, I., Bocsik, A., Deli M.A., Horváth, P., Czibula, Á., Monostori, É., **Martinek T.A.** (2020) Routing Nanomolar Protein Cargoes to Lipid Raf-Mediated/ Caveolar Endocytosis through a Ganglioside GM1-Specific Recognition Tag. **Advanced Science 7:** 1902621.

Hegedus, Z., Makra, I., Imre, N., Hetényi, A., Mándity, I.M., Monostori, É., **Martinek, T.A.** (2016) Foldameric probes for membrane interactions by induced β-sheet folding. **Chemical Communications 52:** 1819.

Hegedus, Z., Weber, E., Kriston-Pal, E., Makra, I., Czibula, A., Monostori, E., **Martinek, T.A.** (2013) Foldameric alpha/beta-Peptide Analogs of the beta-Sheet-Forming Antiangiogenic Anginex: Structure and Bioactivity. **Journal of the American Chemical Society 135:** 16578-16584.

Berlicki, Ł., Pilsl L., Wéber, E., Mándity, I.M., Cabrele, C., **Martinek, T.A.,** Fülöp, F., Reiser, O. (2012) Unique α,β- and α,α,β,β-peptide foldamers based on cis-β-aminocyclopentanecarboxylic acid. **Angewandte Chemie International Edition 51:** 2208-2212.

LAJOS MÁTÉS

HUN-REN Biological Research Centre
Institute of Genetics

RESEARCH AREA

Cancer is the leading cause of death in the developed world. According to estimates from the International Agency for Research on Cancer, there were 8.2 million cancer deaths in 2012 worldwide. Cancer research began as early as at the end of the 19th century, indicating the social efforts to control this devastating disease. In recent years, the tremendous advances reached in molecular biology and genomics has given further impetus to the development of this field. Among other things, the recently developed high-throughput sequencing technology platforms have generated massive amounts of genetic variation data from a huge number of cancer samples. The collected data support the concept that cancer is a disease of our genome, because in the majority of tumors tens or even hundreds of thousands of mutations have been detected. These data also show that the spontaneous mutation rate observed in normal cells is not sufficient to account for the high number of mutations found in cancers. The key feature of cancer cells, allowing them to rapidly evolve more and more new mutations, is the instability of their genetic material.
The long-term objective of our laboratory is to explore genetic alterations fuelling malignant transformation by undermining the stability of the genome.

SELECTED PUBLICATIONS

Kopasz A.G., Pusztai D.Z., Karkas R., Hudoba L., Abdullah K.S.A., Imre G., Pankotai-Bodó G., Migh E., Nagy A., Kriston A., Germán P., Bakné Drubi A., Molnár A., Fekete I., Dani V.É., Ocsovszki I., Puskás L.G., Horváth P., Sükösd F., **Mátés L.** (2022) A versatile transposon-based technology to generate loss- and gain-of-function phenotypes in the mouse liver. **BMC Biology 20:** 74.

Katter, K., Geurts, A.M., Hoffmann, O., **Mátés, L.,** Landa, V., Hiripi, L., Moreno, C., Lazar, J., Bashir, S., Zideke, V., Popova, E., Jerchowc, B., Beckerc, K., Devarajc, A., Walterj, I., Grzybowksib, M., Corbettb, M., Filhol, A.R., Hodgesb, M.R., Baderc, M., Ivics, Z., Jacob, H.J., Pravenec, M., Bősze, Z., Rülicke, T., Izsvák, Z. (2013) Transposon-mediated Transgenesis, Transgenic Rescue, and Tissue-specific Gene Expression in Rodents and Rabbit. **FASEB J 27:** 930-941.

Imre G, Takács B, Czipa E, Bakné Drubi A, Jaksa G, Latinovics D, Nagy A, Karkas R, Hudoba L, Vásárhelyi BM, Pankotai-Bodó G, Blastyák A, Hegedűs Z, Germán P, Bálint B, Abdullah KSA, Kopasz AG, Kovács A, Nagy LG, Sükösd F, Pintér L, Rülicke T, Barta E, Nagy I, Haracska L and **Mátés L.** (2023) Prolonged activity of the transposase helper may raise safety concerns during DNA transposon-based gene therapy. **Mol Ther Methods & Clin Dev 29:** 145-159.

Mátés, L., Chuah, M.K., Belay, E., Jerchow, B., Manoj, N., Acosta-Sanchez, A., Grzela, D.P., Schmitt, A., Becker, K., Matrai, J., Ma, L., Samara-Kuko, E., Gysemans, C., Pryputniewicz, D., Miskey, C., Fletcher, B., VandenDriessche, T., Ivics, Z., Izsvak, Z. (2009) Molecular evolution of a novel hyperactive Sleeping Beauty transposase enables robust stable gene transfer in vertebrates. **Nature Genet 41:** 753-761.

JÓZSEF MIHÁLY

HUN-REN Biological Research Centre
Institute of Genetics
Developmental Genetics Unit

RESEARCH AREA

Coordinated regulation of the actin and microtubule cytoskeleton is known to play a pivotal role in the growth and proper navigation of neuronal axons and dendrites that are necessary to the formation of a functional nervous system. One of our major scientific interests is to gain a better understanding of the molecular mechanisms of axonal growth and guidance by uncovering the role of the growth cone cytoskeleton regulatory proteins. In addition, we are interested in the mechanisms of myofibrillogenesis. Myofibrils are composed of repeated sarcomeres that are extremely highly ordered macromolecular assemblies where structural organization is intimately linked to their functionality as contractile units. Recently, we developed a powerful nanoscopic approach that allowed us to determine the position of 27 muscle proteins with a quasi-molecular localization precision, and by means of template based protein structure modelling, we assembled a refined I-band and H-zone model with an unparalleled scope and resolution. We aim to combine this method with genetic approaches to investigate the molecular mechanisms of sarcomere assembly during muscle development. Our studies are of potential biomedical relevance as they may help to develop more efficient neuronal regeneration methods, and to understand sarcomere assembly and function in healthy and disease conditions.

SELECTED PUBLICATIONS

Szikora, S., Gajdos, T., Novák, T., Farkas, D., Földi, I., Lenart, P., Erdélyi, M., **Mihály, J.** (2020) Nanoscopy reveals the layered organization of the sarcomeric H-zone and I-band complexes. **J Cell Biol 219: e**201907026.

Szikora, S., Földi, I., Tóth, K., Migh, E., Vig, A., Bugyi, B., Maléth, J., Hegyi, P., Kaltenecker, P., Sanchez-Soriano, N., **Mihály, J.** (2017) The formin DAAM is required for coordination of the actin and microtubule cytoskeleton in axonal growth cones. **J Cell Sci 130:** 2506-2519.

Nelson, K.S., Khan, Z., Molnár, I., **Mihály, J.,** Kaschube, M., Beitel, GJ. (2012) Drosophila Src regulates anisotropic apical surface growth to control epithelial tube size. **Nat Cell Biol 14:** 518-525.

Matusek, T., Gombos, R., Szécsényi, A., Sánchez-Soriano, N., Czibula, A., Pataki, C., Gedai, A., Prokop, A., Raskó, I., **Mihály, J.** (2008) Formin proteins of the DAAM subfamily play a role during axon growth. **J. Neurosci 28:** 13310-13319.

Boutros, M., **Mihaly, J.**, Bouwmeester, T., Mlodzik, M. (2000)Signaling specificity by Frizzled receptors in Drosophila. **Science 288:** 1825-1828.

LÁSZLÓ NAGY

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

We are interested in the general principles of genomes evolution, that of the evolution of organismal complexity, fungal development and their biotechnological applications. Fungi are the most ubiquitous microbes in modern biotechnology which, despite centuries of research, offer huge unharnessed potentials. Our research focuses on gene regulatory networks underlying fungal morphogenesis and the degradation of complex plant polysaccharides (e.g. lignocellulose). Complex plant polysaccharides, such as lignin and cellulose, are the most abundant repositories of sequestered carbon on Earth. Fungi can most efficiently reintroduce this sequestered carbon into the carbon cycle, contributing a key step to ecosystem functioning worldwide. However, the genes and gene regulatory networks that underlie the fungal decomposition of complex plant biomass are unknown. Gene regulatory networks are finely tuned circuits that regulate precise spatial and temporal expression of genes. We use modern -omics, genetic, phylogenetic and bioinformatic approaches to uncover the evolutionary origins and genetic bases of fungal morphogenesis, multicellularity and to translate basic research results into biotechnological applications.

SELECTED PUBLICATIONS

Varga, T., et al., **Nagy, G.L.** (2019) Megaphylogeny resolves global patterns of mushroom evolution. **Nat Ecol Evol 3:** 668-678.

Krizsán, K., et al., **Nagy, G.L.** (2019) A transcriptomic atlas of mushroom development highlights an independent origin of complex multicellularity. **Proc Natl Acad Sci USA 116:** 7409-7418.

Kiss, E., Hegedus, B., Varga, T., Merenyi, Z., Koszo, T., Balint, B., Prasanna, A.N., Krizsan K., Riquelme, M., Takeshita, N., **Nagy, L.G.** (2019) Comparative genomics reveals the origin of fungal hyphae and multicellularity. **Nat Commun 10:** 4080.

Nagy, G.L., Kovács, G.M., Krizsán, K. (2018) Complex multicellularity in fungi: evolutionary convergence, single origin, or both? **Biol Rev Camb Philos Soc 93:** 1778-1794.

Sipos, G., et al., **Nagy, G.L.** (2017) Genome expansion and lineage-specific genetic innovations in the forest pathogenic fungi Armillaria. **Nat Ecol Evol 1:** 1931-1941.

NORBERT NAGY

University of Szeged
Albert Szent-Györgyi Medical School,
Department of Pharmacology and
Pharmacotherapy

RESEARCH AREA

The cardiac electrophysiology investigates the electrical changes of the heart, including both the physiological and pathological functions as well as novel pharmacological interventions. The cardiovascular diseases, and especially the arrhythmias are leading cause of mortality. The arrhythmias have a complex underlying mechanism where the intracellular Ca2+ handling plays a critical role. Therefore, the main aim of our laboratory is the investigation of the physiological function of the cardiac Ca2+ handling, its role in different arrhythmias, and development of new pharmacological interventions. A novel antiarrhythmic strategy could be the selective inhibition of the cardiac Na+/ Ca2+ exchanger that may decrease the excessive Ca2+ load of the cell, additionally may have positive inotropic effect. The sinus-node as a primary rhythm generator of the heart has an extremely complex electrophysiological mechanism, at the same time, it could be involved in several types of arrhythmias. Our further aim is the investigation of the Ca2+ handling in sinus-node cells under normal as well as during pathological condition (e.g.: metabolic syndrome). It is well-known that physical activity is healthy and significantly contributes to the normal physiology of the cardiovascular system. Still, several times sudden cardiac death of competitive athletes was observed where organic disease of the heart was not found. The underlying mechanism of sudden death could be the abrupt disturbance of the normal electrophysiological function of heart, however the arrhythmia mechanism is unknown. Therefore, further aim of our Institute is to develop a reliable "athlete's heart" animal model that provides data regarding the electrophysiological changes during physical activity. Our group investigates the alterations of the Ca2+ handling in the athlete's heart.

SELECTED PUBLICATIONS

Tóth, N., Szlovák, J., Kohajda, Z., Bitay, G., Veress, R., Horváth, B., Papp, J.G., Varró, A., **Nagy, N.** (2021) The development of L-type Ca^{2+} current mediated alternans does not depend on the restitution slope in canine ventricular myocardium. **Sci Rep 11:** 16652.

Szlovák J., Tomek, J., Zhou, X., Tóth, N., Veress, R., Horváth, B., Szentandrássy, N., Levijoki, J., Papp, J.G., Herring, N., Varró, A., Eisner, D.A., Rodriguez, B., **Nagy, N.** (2021) Blockade of sodium-calcium exchanger via ORM-10962 attenuates cardiac alternans. **J Mol Cell Cardiol 153:** 111-122.

Gazdag, P., Oravecz, K., Acsai, K., Demeter-Haludka, V., Ördög, B., Szlovák, J., Kohajda, Z., Polyák, A., Barta, B.A., Oláh, A., Radovits, T., Merkely, B., Papp, J.G., Baczkó, I., Varró, A., **Nagy, N.** & Prorok, J. (2020) Increased Ca^{2+} content of the sarcoplasmic reticulum provides arrhythmogenic trigger source in swimming-induced rat athlete's heart model. **Sci Rep 10:** 19596.

Varró, A., Tomek, J, **Nagy, N.**, Virag, L., Passini, E., Rodriguez, B., Baczkó, I. (2020) Cardiac Transmembrane Ion Channels and Action Potentials: Cellular Physiology and Arrhythmogenic Behavior. **Physiol Rev 101:** 1083-1176.

ANTAL NÓGRÁDI

University of Szeged
Albert Szent-Györgyi Medical School,
Department of Anatomy, Histology and
Embryology

RESEARCH AREA

Our groups on one hand is interested in the survival and regeneration of motoneurons in case of injuries or neurodegenerative diseases. It was our group who first published that transplantation of embryonic spinal cord grafts or administration of the anti-excitotoxic compound, riluzole are able to improve the survival of the host motoneurons and induce the regeneration of their axons into the vacated ventral roots. This latter finding lead to new clinical approaches in the treatment of brachial plexus injuries.

Our other research field focuses on the rescue of injured spinal cord cell populations and the improvement of their regenerative capacity. We have isolated the secretome of a neuroectodermal cell line, NE4C which is able to induce regeneration in the injured spinal cord. The administration of this lesion-induced secretome proves to be as successful as the transplantation of the stem cells themselves. At present we use various forms of the mRNA-based gene transfer technology to induce expression of the stem cell secretome in the injured cord.

SELECTED PUBLICATIONS

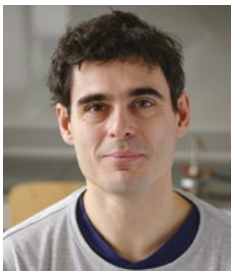
Pajer, K., Bellák, T., Grósz, T., Nógrádi, B., Patai, R., Sinkó, J., Vinay, L., Liabeuf, S., Erdélyi, M., **Nógrádi, A.** (2023) Riluzole treatment modulates KCC2 and EAAT-2 receptor expression and Ca2+ accumulation following ventral root avulsion injury. **Eur J Cell Biol 102:** 151317.

Gál, L., Bellák, T., Marton, A., Fekécs, Z., Weissman, D., Török, D., Biju, R., Vizler, C., Kristóf, R., Beattie, MB., Lin, PJC., Pardi, N., **Nógrádi, A.**, Pajer, K. (2023) Restoration of Motor Function through Delayed Intraspinal Delivery of Human IL- 10-Encoding Nucleoside-Modified mRNA after Spinal Cord Injury. **Research (Wash D C). 6:** 0056.

Molnár, K., Nógrádi, B., Kristóf, R., Mészáros, Á., Pajer, K., Siklós, L., **Nógrádi, A.**, Wilhelm, I., Krizbai, IA. (2022) Motoneuronal inflammasome activation triggers excessive neuroinflammation and impedes regeneration after sciatic nerve injury. **J Neuroinflammation 19(1):** 68.

Bellák, T., Fekécs, Z., Török, D., Táncos, Z., Nemes, C., Tézsla, Z., Gál, L., Polgári, S., Kobolák, J., Dinnyés, A., **Nógrádi, A.**, Pajer, K. (2020) Grafted human induced pluripotent stem cells improve the outcome of spinal cord injury: modulation of the lesion microenvironment. **Sci Rep 10(1):** 22414.

Simandi, Z., Pajer, K., Karolyi, K., Sieler, T., Jiang, LL., Kolostyak, Z., Sari, Z., Fekécs, Z., Pap, A., Patsalos, A., Contreras, GA., Reho, B., Papp, Z., Guo, X., Horvath, A., Kiss, G., Keresztessy, Z., Vámosi, G., Hickman, J., Xu, H., Dormann, D., Hortobagyi, T., Antal, M., **Nógrádi, A.**, Nagy, L. (2018) Arginine Methyltransferase PRMT8 Provides Cellular Stress Tolerance in Aging Motoneurons. **J Neurosci 38(35):** 7683-7700.



CSABA PÁL

HUN-REN Biological Research Centre
Institute of Biochemistry
Synthetic and Systems Biology Unit

RESEARCH AREA

We focus on bacterial pathogens and the problem of antibiotic resistance. We found that multidrug resistance mutations in bacteria simultaneously enhance sensitivity to other unrelated antibiotics (collateral sensitivity). This finding has led to the design of new antibiotic cocktails. Using bacterial genome engineering, we aim to develop novel resistance-free antibiotics. Finally, we study the evolution of adaptive immune system in response to pathogens and cancer.
More details: http://www.brc.hu/sysbiol/

SELECTED PUBLICATIONS

Kintses, B., Méhi, O., Ari, E., Számel, M., Györkei, Á., Jangir, PK., Nagy, I., Pál, F., Fekete, G., Tengölics, R., Nyerges, Á., Likó, I., Bálint, A., Molnár, T., Bálint, B., Vásárhelyi, BM., Bustamante, M., Papp, B., **Pal, C.** (2019) Phylogenetic barriers to horizontal transfer of antimicrobial peptide resistance genes in the human gut microbiota. **Nature Microbiology 4:** 447–458.

Lázár, V., Martins, A., Spohn, R., Daruka, L., Grézal, G., Fekete, G., Számel, M., Jangir, P.K., Kintses, B., Csörgő, B., Nyerges, Á, Györkei, Á., Kincses, A., Dér, A., Walter ,F.R., Deli, M.A., Urbán, E., Hegedűs, Z., Olajos G., Méhi, O., Bálint, B., Nagy, I., Martinek, T. A., PappB., **Pal C.** (2018) Antibiotic-resistant bacteria show widespread collateral sensitivity to antimicrobial peptides. **Nature Microbiology 3**: 718–731.

Pal, C., Papp, B., Pósfai, G (2014) The dawn of evolutionary genome engineering. **Nature Reviews Genetics 15:** 504- 512.

Pal, C., Macia, M., Oliver, A., Schacher, I., Buckling, A. (2007) Coevolution with viruses drives the evolution of bacterial mutation rates. **Nature 450:** 1079-81.

Pal, C., Papp, B., Lercher, MJ., Csermely, P., Oliver, SG., Laurence, D. Hurst. (2006) Chance and necessity in the evolution of minimal metabolic networks. **Nature 440:** 667- 670.

TIBOR PANKOTAI

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Pathology

RESEARCH AREA

Faithful repair of DNA double-strand breaks (DSBs) is indispensable since improper repair can lead to genome instability and subsequently to tumorigenesis. DSBs can be repaired through different pathways, and the balance between the choice of them must be tightly regulated to preserve genome integrity. DNA damage can be considered as a harmful stressor in which various biochemical pathways are activated, ensuring the proper DNA repair and cell survival. The main focus of the project is to map the signalling circuit induced by DNA damage and to understand how the malfunctional DNA repair can initiate tumorigenesis. In our experimental setup, we will use state-of-the-art biochemical technologies and genomic mapping in a human cell culture model system, and we combine these with single-cell data using super-resolution STORM microscopy. Additionally, with our experimental data, we can verify the existence and the means of DNA damage-induced cell signalization circuits and reveal the potential mechanisms of cellular communication. Although as a primary goal, the project aimed to unveil a basic research clue, identifying key steps in the repair process can help us to recognize new anti-cancer therapeutic targets, thereby also contributing to the development of novel drugs in tumor therapy.

SELECTED PUBLICATIONS

Khanam T, Muñoz I, Weiland F, Carroll T, Morgan M, Borsos BN, Pantazi V, Slean M, Novak M, Toth R, Appleton P, **Pankotai T**, Zhou H, Rouse J. (2021) CDKL5 kinase controls transcription-coupled responses to DNA damage. **EMBO J 4:** e108271.

Majoros H, Borsos BN, Ujfaludi Z, Páhi ZG, Mórocz M, Haracska L, Boros IM, **Pankotai T.** (2021) SerpinB10, a Serine Protease Inhibitor, Is Implicated in UV-Induced Cellular Response. Int **J Mol Sci 22:** 8500. DOI: 10.3390/ijms22168500.

Varga D, Majoros H, Ujfaludi Z, Erdélyi M, **Pankotai T.** (2019) Quantification of DNA damage induced repair focus formation via super-resolution dSTORM localization microscopy. **Nanoscale 11:** 14226-14236.

Caron P, **Pankotai T,** Wiegant WW, Tollenaere MAX, Furst A, Bonhomme C, Helfricht A, de Groot A, Pastink A, Vertegaal ACO, Luijsterburg MS, Soutoglou E, van Attikum H. (2019) WWP2 ubiquitylates RNA polymerase II for DNA-PK-dependent transcription arrest and repair at DNA breaks. **Genes Dev 33:** 684-704.

Borsos BN, Huliak I, Majoros H, Ujfaludi Z, Gyenis A, Pukler P, Boros IM, **Pankotai T** (2017) Human p53 interacts with the elongating RNAPII complex and is required for the release of actinomycin D induced transcription blockage. **Sci Rep 7:** 40960.

BALÁZS PAPP

HUN-REN Biological Research Centre
Institute of Biochemistry
Synthetic and Systems Biology Unit

RESEARCH AREA

Metabolism is central to life as it provides the building blocks and energy for all biological processes. While its fundamental tasks are highly conserved across all life forms, there are substantial differences in the details of how metabolism works across species and individuals. Humans are no exception. Any two of us show large metabolic differences and many diseases are known to involve changes in metabolism. However, not all metabolic differences are harmful and identifying those that impact human health is of paramount importance for medicine. Our laboratory uses computational approaches to study the variation of metabolism both within human populations and between different species. Our goal is to uncover the signatures of natural selection acting on human metabolism and thereby increase our understanding of healthy and diseased states.
For more details, see http://www.brc.hu/sysbiol/.

SELECTED PUBLICATIONS

Zampieri, M.*, Szappanos, B.*, Buchieri, M.V., Trauner, A., Piazza, I., Picotti, P., Gagneux, S., Borrell, S., Gicquel, B., Lelievre, J., **Papp, B.**, Sauer, U. (2018) High-throughput metabolomic analysis predicts mode of action of uncharacterized antimicrobial compounds. **Science Translational Medicine 10:** eaal3973.

Notebaart, R.A., Szappanos, B., Kintses, B., Pál, F., Györkei, A., Bogos, B., Lázár, V., Spohn, R., Csörgő, B., Wagner, A., Ruppin, E., Pál, C., **Papp, B.** (2014) Network-level architecture and the evolutionary potential of underground metabolism. **Proc Natl Acad Sci U S A 111:** 11762-11767.

Szappanos, B., Kovács, K., Szamecz, B., Honti, F., Costanzo, F., Baryshnikova, A., Gelius-Dietrich, G., Lercher, M.J., Jelasity, M., Myers, C.L., Andrews, B.J., Boone, C., Oliver, S.G., Pál, C., **Papp, B.** (2011) An integrated approach to characterize genetic interaction networks in yeast metabolism. **Nature Genetics 43:** 656-62.

Papp, B., Pál, C., Hurst, L.D. (2004) Metabolic network analysis of the causes and evolution of enzyme dispensability in yeast. **Nature 429:** 661-4

FERENC PETÁK

University of Szeged
Albert Szent-Györgyi Medical School
Faculty of Science and Informatics
Department of Medical Physics and Informatics

RESEARCH AREA

The cardiopulmonary research laboratory performs scientific activities in various fields of cardiopulmonary physiology and pathophysiology by using translational animal models of lung diseases and performing assessments in clinical environment. A research area is focusing on the involvement of the pulmonary hemodynamics and lung vasculature in various respiratory diseases. We clarify the mechanisms responsible for the lung function deteriorations with a particular focus on the cardiopulmonary interactions. Further research focuses on the characterization of the pulmonary consequences of general anesthesia in various animal models and in clinical environment. Improvement of patient monitoring is essential for the optimization of patient management in anesthesia and intensive care settings. Analyses of the expired gases has great importance in respiratory patient monitoring. Thus we analyze the within-breath dynamics of CO_2 exhalation by using capnography to gain insights into the ventilation-perfusion matching. Further research focuses on the pulmonary manifestations of type-2 diabetes mellitus (T2DM) that presents major public health concerns. We characterize the changes in airway function and clarify the deteriorations in the viscoelastic properties of the pulmonary parenchyma, which may be a consequence of lung volume loss, interstitial edema, proliferation, and the effect of advanced glycation endproducts and their interaction with receptors.

SELECTED PUBLICATIONS

Fodor, G.H., Bayat, S., Babik, B., Habre, W., **Petak, F.** (2018) Reversing Cholinergic Bronchoconstriction by Common Inotropic Agents: A Randomized Experimental Trial on Isolated Perfused Rat Lungs. **Anesth Analg 129:** 745-752.

Babik, B., Balogh, A.L., Sudy, R., Ivankovitsne-Kiss, O., Fodor, G.H., **Petak, F.** (2017) Levosimendan prevents bronchoconstriction and adverse respiratory tissue mechanical changes in rabbits. **Am J Physiol Lung Cell Mol Physiol. 313:** L950-L956.

Petak, F., Fodor, G.H., Babik, B., Habre, W. (2016) Airway mechanics and lung tissue viscoelasticity: effects of altered blood hematocrit in the pulmonary circulation. **J Appl Physiol 121:** 261-7.

Filep, Á., Fodor, G.H., Kun-Szabó, F., Tiszlavicz, L., Rázga, Z., Bozsó, G., Bozóki, Z., Szabó, G., **Petak, F.** (2016) Exposure to urban PM1 in rats: development of bronchial inflammation and airway hyperresponsiveness. **Respir Res 17:** 26.

Fodor, G.H., Babik, B., Czövek, D., Doras, C., Balogh, Á.L., Bayat, S., Habre, W., **Petak, F.** (2016) Fluid replacement and respiratory function: comparison of whole blood with colloid and crystalloid: A randomised animal study. **Eur J Anaesthesiol 33:** 34-41.

ZOLTÁN RAKONCZAY

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pathophysiology

RESEARCH AREA

Acute pancreatitis is a sudden inflammation of the pancreas which can have mild or severe course. Unfortunately, the latter form still has an unacceptably high mortality. The reason for this is, at least in part, due to the facts that the pathomechanism of acute pancreatitis is unclear and we have no specific treatment of the disease. The main aims of our group are to investigate the roles of various inflammatory factors, mitochondria and the recently identified pancreatic ductal cells in the development of acute pancreatitis. Our hope is to eventually open up new therapeutic possibilities in acute pancreatitis.

SELECTED PUBLICATIONS

Biczó, G., Végh, E.T., Shalbueva, N., Mareninova, O.A., Elperin, J., Lotshaw, E., Gretler, S., Lugea, A., Malla, S.R., Dawson, D., Ruchala, P., Whitelegge, J., French, S.W., Wen, L., Husain, S.Z., Gorelick, F.S., Hegyi, P., **Rakonczay Jr., Z.**, Gukovsky, I., Gukovskaya, A.S. (2018) Mitochondrial dysfunction, through impaired autophagy, leads to endoplasmic reticulum stress, deregulated lipid metabolism, and pancreatitis in animal models. **Gastroenterology 154:** 689-703.

Pallagi, P., Hegyi, P., **Rakonczay Jr., Z.** (2015) The physiology and pathophysiology of pancreatic ductal secretion: the background for clinicians. **Pancreas 44:** 1211-1233.

Pallagi, P., Balla, Z., Singh, A.K., Dósa, S., Iványi, B., Kukor, Z., Tóth, A., Riederer, B., Liu, Y.J., Engelhardt, R., Jármay, K., Szabó, A., Janovszky, Á., Perides, G., Venglovecz, V., Maléth, J., Wittmann, T., Takács, T., Gray, M.A., Gácser, A., Hegyi, P., Seidler, U., **Rakonczay Jr., Z**. (2014) The role of pancreatic ductal secretion in protection against acute pancreatitis in mice. **Crit Care Med 42:** e177-88.

Biczó, G., Hegyi, P., Dósa, S., Shalbuyeva, N., Berczi, S., Sinervirta, R., Hracskó, Z., Siska, A., Kukor, Z., Jármay, K., Venglovecz, V., Varga, I.S., Iványi, B., Alhonen, L., Wittmann, T., Gukovskaya, A., Takács, T., **Rakonczay Jr., Z.** (2011) The crucial role of early mitochondrial injury in L-lysine-induced acute pancreatitis. **Antioxid Redox Signal 15:** 2669-81.

Rakonczay Jr., Z., Hegyi P., Takács T., McCarroll J., Saluja A.K. (2008) The role of NF-κB activation in the pathogenesis of acute pancreatitis. **Gut 57:** 259-267.

MÁRTA JULIANNA SÁRKÖZY

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pathophysiology

RESEARCH AREA

Diastolic dysfunction and left ventricular hypertrophy are characteristic features of chronic heart failure in the early phases. With the progression of cardiac fibrosis, systolic dysfunction also develops leading to the late phases of chronic heart failure. Common causes of chronic heart failure are arterial hypertension, chronic kidney disease (CKD), metabolic syndrome, oncologic treatments such as chemotherapy and/or radiotherapy-induced cardiotoxicity forms. Our aim is to investigate and compare the molecular mechanisms of heart failure forms developed as a consequence of different underlying diseases. The identification of the early predictors and prevention of hypertrophy and fibrosis by the administration of protective agents are relevant research perspectives both experimentally and clinically. In our experiments, we investigate the heart function and morphology, the molecular changes in the cardiac microRNA/mRNA profiles and downstream targets as well as the circulating marker molecules, and we test new agents for the prevention of heart failure.

SELECTED PUBLICATIONS

Sárközy, M., Watzinger, S., Kovács, Z., Acar, E., Márványkövi, F., Szűcs, G., Lauber, G., Siska, A., Galla, Z., Földesi, I., Fintha, A., Kriston, A., Kovacs, F., Horváth, P., Kővári, B., Cserni, G., Krenács, T., Szabó, P., Szabó, G., Monostori, P., Zins, K., Abraham, D., Csont, T., Pokreisz, P., Podesser, BK., Kiss, A. (2023) Neuregulin-1β improves uremic cardiomyopathy and renal dysfunction in rats. **J Am Coll Cardiol Basic Trans Science 10:** 1016.

Kovács, M.G., Kovács, Z.Z.A., Varga, Z., Szűcs, G., Freiwan, M., Farkas, K., Kővári, B., Cserni, G., Kriston, A., Kovács, F., Horváth, P., Földesi, I., Csont, T., Kahán, Z., **Sárközy, M.** (2021) Investigation of the Antihypertrophic and Antifibrotic Effects of Losartan in a Rat Model of Radiation-Induced Heart Disease. **Int J Mol Sci 22:** 12963.

Kovács, Z.Z.A., Szűcs, G., Freiwan, M., Kovács, M.G., Márványkövi, F.M., Dinh, H., Siska, A., Farkas, K., Kovács, F., Kriston, A., Horváth, P., Kővári, B., Cserni, B.G., Cserni, G., Földesi, I., Csont, T., **Sárközy, M.** (2021) Comparison of the antiremodeling effects of losartan and mirabegron in a rat model of uremic cardiomyopathy. **Sci Rep 11:** 17495.

Sárközy, M., Márványkövi, F.M., Szűcs, G., Kovács, Z.Z.A., Szabó, M.R., Gáspár, R., Siska, A., Kővári, B., Cserni, G., Földesi, I., Csont, T. (2021) Ischemic preconditioning protects the heart against ischemia-reperfusion injury in chronic kidney disease in both males and females. **Biol Sex Differ 12:** 49.

Sárközy, M., Gáspár, R., Zvara, Á., Siska, A., Kővári, B., Szűcs, G., Márványkövi, F., Kovács, M.G., Diószegi, P., Bodai, L., Zsindely, N., Pipicz, M., Gömöri, K., Kiss, K., Bencsik, P., Cserni, G., Puskás, L.G., Földesi, I., Thum, T., Bátkai, S., Csont, T. (2019) Chronic kidney disease induces left ventricular overexpression of the pro-hypertrophic microRNA-212. **Sci Rep 9:** 1302.

ÁRON SZABÓ

HUN-REN Biological Research Centre
Institute of Genetics

RESEARCH AREA

Key to the long-term survival of the nervous system is its resilience towards unwanted environmental effects coupled to plasticity and regeneration following adverse events. Nerve injuries, traumatic spinal cord and brain injury, neurodegenerative diseases, viral infections, and certain chemotherapeutic agents all compromise the integrity of the nervous system. Injury, for example, results in short-term cell death and degeneration of neurites in the vicinity of the injury, which in turn may lead to inflammation and neurodegeneration that can last for years, damaging other cells. Debris and dead cells that form after injury are cleared by glial cells, which make up half of the nervous system. Without removal of debris by microglia, which represent the major phagocyte population in the brain, secondary damage may be much more sustained and severe than with normal phagocytic activity. Therefore, it is important to understand the regulation of glial phagocytosis after nerve injuries. Our working group studies glial phagocytic processes and membrane-limited degradation pathways involved in lysosomal degradation of extracellular cargoes such as axonal debris and internal cell constituents such as regulatory proteins, in the nervous system of Drosophila melanogaster or fruit fly. The ensheathing and wrapping glia of Drosophila have similar phagocytic function to microglia and use a similar phagocytic receptor as mammalian glia. The genetic toolkit and neural complexity of Drosophila allows us to obtain results that are relevant in vivo, more rapidly in contrast to those obtained in cell cultures and that are potentially translatable to mammals.

SELECTED PUBLICATIONS

Szabó, Á.*, Papin, C. *, Cornu, D., Chélot, E., Lipinszki ,Z., Udvardy, A., Redeker, V., Mayor, U., Rouyer, F. (2018) Ubiquitylation Dynamics of the Clock Cell Proteome and TIMELESS during a Circadian Cycle. **Cell Reports 23:** 2273-2282.

Alexopoulou, Z., Lang, J., Perrett, R.M., Elschami, M., Hurry, M.E., Kim, H.T., Mazaraki, D., **Szabó, Á.**, Kessler, B.M., Goldberg, A.L., Ansorge, O., Fulga, T.A., Tofaris, G.K. (2016) Deubiquitinase Usp8 regulates α-synuclein clearance and modifies its toxicity in Lewy body disease. **PNAS 113:** E4688-97.

Szabó, Á., Tofaris, G.K. (2019) Monitoring α-Synuclein Proteotoxicity in Drosophila Models. **Methods Mol Biol 1948:** 199-208.

Bhattacharjee, A. *, **Szabó, Á.***, Csizmadia, T., Laczkó-Dobos, H., Juhász, G. (2019) Understanding the importance of autophagy in human diseases using Drosophila. **J Genet Genomics 46:** 157-169.

ISTVÁN SZATMÁRI

University of Szeged
Faculty of Pharmacy
Institute of Pharmaceutical Chemistry

RESEARCH AREA

Nowadays, the majority of the approved drugs and biologically active compounds of quite complex structure contain heterocyclic moieties. Our research group focuses on the synthesis and development of potentially bioactive electron-rich aromatic carbo- and heterocycles. The transformations of potentially antitumor 8-hydroxyquinolines, indole and aza-indole derivatives, synthesis of naphtol based antibacterial compound group, and neuroprotective quinoline-carboxylic acid derivatives of elevated brain penetration make our research fields. In order to reach the target molecules, we utilize carbon-carbon coupling reactions such as aza-Friedel-Crafts and the modified Mannich-reaction. The scope of which was broadened for the starting heterocycles by our research group. The biological evaluation of the synthesised compounds are conducted in frame of different cooperations.

SELECTED PUBLICATIONS

Lőrinczi, B., Csámapi, A., Fülöp, F., **Szatmári, I.** (2021) Synthetic- and DFT modelling studies on regioselective modified Mannich reactions of hydroxy-KYNA derivatives **RSC Adv 11:** 543-554.

Hegedűs, D., Szemerédi, N., Spengler, G., **Szatmári, I.** (2022) Application of partially aromatic ortho-quionone-methides for the synthesis of novel naphthoxazines with improved antibacterial activity **Eur J Med Chem 235:** 114391.

Lőrinczi, B., Simon, P., **Szatmári, I.** (2022) Synthesis of Indole-Coupled KYNA Derivatives via C–N Bond Cleavage of Mannich Bases. **Int J Mol Sci 23:** 7152.

Csuvik, O., Szemerédi, N., Spengler, G., **Szatmári, I.** (2022) Synthesis of 4-Hydroxyquinolines as Potential Cytotoxic Agents. **Int J Mol Sci 23:** 9688.

Simon, P., Lőrinczi, B., Hetényi, A., **Szatmári, I.** (2023) Novel Eco-friendly, One-Pot Method for the Synthesis of Kynurenic Acid Ethyl Esters. **ACS Omega 8 (20):** 17966-17975.

MÁRTA SZÉLL

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Medical Genetics and the
Dermatological Research Group

RESEARCH AREA

The genome programs of the past decades have provided an enormous amount of information about the human genome and how this information is translated to the "language of life". This knowledge is essential for understanding the pathogenesis of human diseases at the molecular level and, in fact, is currently being used to develop novel diagnostics and therapeutic modalities. Our workgroup identifi es novel pathogenic mutations that result in rare monogenic human diseases. By performing functional analyses of these mutations, we attempt to understand how their mode of action leads to human disease. In another project, we investigate the genetics and molecular susceptibility factors of multifactorial human skin diseases, with a primary focus on psoriasis. We are also engaged in the investigation of non-coding RNAs. In particular, we analyze the role of the PRINS mRNA-like non-coding RNA, which was previously identifi ed by our workgroup, in cellular stress responses and in various human diseases. In the last few years our research group has joined the Hungarian Brain Research Program (NAP Project) and as the member of the clinical branch we are engaged in the identification of genetic factors in neurodegenerative human diseases. This work has already yielded several new results for the field.

SELECTED PUBLICATIONS

Tripolszki, K., Csányi, B., Nagy, D., Ratti, A., Tiloca, C., Silani, V., Kereszty, É., Török, N., Vécsei, L., Engelhardt, J.I., Klivényi, P.(5), Nagy, N., **Széll, M.** (2017) Genetic analysis of the SOD1 and C9ORF72 genes in Hungarian patients with amyotrophic lateral sclerosis. **Neurobiol Aging 53**: 195. e1-195.e5

Szell, M., Danis, J., Bata-Csorgo, Z., Kemeny, L. (2016) PRINS, a primate-specific long non-coding RNA, plays a role in the keratinocyte stress response and psoriasis pathogenesis. **Pflugers Archiv 468:** 935-943.

Szell, M., Bata-Csorgo, Z., Kemeny, L. (2008) The enigmatic world of mRNA-like ncRNAs: Their role in human evolution and in human diseases. Semin **Cancer Biol 18:** 141-148.

Sonkoly, E., Bata-Csorgo, Z., Pivarcsi, A., Polyanka, H., Kenderessy, Szabo, A., Molnar, G., Szentpali, K., Bari, L., Megyeri, K., Mandi, Y., Dobozy, A., Kemeny, L., **Szell, M.** (2005) Identifi cation and characterization of a novel, psoriasis susceptibility-related noncoding RNA gene, PRINS. **J Biol Chem 280:** 24159-24167.

Széll, M., Bata-Csorgo, Z., Koreckm, A., Pivarcsim, A., Polyánkam, H., Szeg, C., Gaál, M., Dobozy, A., Kemény, L. (2004) Proliferating keratinocytes are putative sources of the psoriasis susceptibility related EDA+ oncofoeltal fibronectin. **J Investigat Dermotol 123:** 537-546.

GÁBOR TAMÁS

University of Szeged
Albert Szent-Györgyi Medical School
Department of Physiology, Anatomy and
Neuroscience
MTA-SZTE Research Group for Cortical
Microcircuits

RESEARCH AREA

Our research is characterized by a combination of technically challenging electrophysiology, molecular biology, imaging and anatomy in pursuit of the function of cell types and their synapses in the human and rodent cerebral cortex. We discovered the cellular source (neurogliaform cells) of slow, GABAB receptor mediated inhibition in the cerebral cortex. Subsequently, we discovered the mechanism of this slow inhibition as single neuron driven nonsynaptic or volume transmission of the neurotransmitter GABA. In addition, our experiments assigned a new, excitatory role to axo-axonic cells, which were considered as the most specific inhibitory neurons of the cortex. Our commitment to cutting edge methodology recently resulted in recordings from identified interneurons in completely unaesthetized, freely behaving rodents and identified the first ripple-like oscillatory events in the neocortex and their cellular structure. We initiated a research program in 2004 for multiple patch clamp recordings in slices taken from the human cerebral cortex leading to the first recordings of human synaptic interactions and showing the existence of Hebbian networks in the human cerebral cortex.

SELECTED PUBLICATIONS

Averkin, R., Szemenyei, V., Borde, S., **Tamas, G.** (2016) Identified cellular correlates of neocortical ripple and high-gamma oscillations during spindles of natural sleep. **Neuron 92:** 916-92.

Molnar, G., Rozsa, M., Baka, J., Holderith, N., Barzo, P., Nusser, Z., **Tamas, G.** (2016) Human pyramidal to interneuron synapses are mediated by multi-vesicular release and multiple docked vesicles. **eLife 5:** e18167.

Olah, S., Fule, M., Komlosi, G., Varga, C., Baldi, R., Barzo, P. **Tamas, G.** (2009) Regulation of cortical microcircuits by unitary GABA-mediated volume transmission. **Nature 461:** 1278-81.

Szabadics, J., Varga, C., Molnar, G., Olah, S., Barzo, P., **Tamas, G.** (2006) Excitatory effect of GABAergic axo-axonic cells in cortical microcircuits. **Science 311:** 233-5.

Tamas, G., Lorincz, A., Simon, A., Szabadics, J. (2003) Identified sources and targets of slow inhibition in the neocortex. **Science 299:** 1902-1905.

GYULA TIMINSZKY

HUN-REN Biological Research Centre
Department of Genetics

RESEARCH AREA

Genome integrity is crucial for all living organisms. If damaged DNA is not promptly repaired, the mutations ultimately lead to the development of cancer. Defective repair can also cause immunodeficiency, neurodegenerative disorders and premature ageing. The range of DNA lesions require diverse signaling and repair pathways to shape the DNA damage response. This involves changes in nuclear dynamics including alterations in chromatin structure, nucleocytoplasmic transport and protein activities. ADP-ribosylation is one of the earliest post-translational modifications appearing upon DNA damage. Its effects are numerous. One of its functions is to relax chromatin at the sites of DNA damage, facilitating the access of DNA repair processes to the lesions. Our findings indicate that nuclear dynamics, mRNA metabolism and chromosome organization strongly depend on nuclear ADP-ribosylation reactions and their crosstalk with other signaling pathways. Its deregulation impairs DNA repair and is implicated in cancer. At the bedside, the inhibition of ADP-ribosylation by drugs is used to treat cancer with certain gene mutations. Our research goal is to characterize novel molecular mechanisms that regulate the DNA damage response, including nucleocytoplasmic transport, mRNA metabolism and chromatin architecture. We study novel cancer relevant mutations that are sensitive to ADP-ribosylation inhibitors, which could be potentially used to treat tumors carrying such mutations. Furthermore, we investigate the molecular basis of a novel DNA damage-induced nuclear export mechanism that regulates ADP-ribose metabolism.

SELECTED PUBLICATIONS

Smith, R., Sellou, H., Chapuis, C., Huet, S., **Timinszky, G.** (2018) CHD3 and CHD4 recruitment and chromatin remodeling activity at DNA breaks is promoted by early poly(ADP-ribose)-dependent chromatin relaxation. **Nucleic Acids Research 46:** 6087.

Singh, H.R., Nardozza, A.P., Möller, I.R., Knobloch, G., Kistemaker, H.A.V., Hassler, M., Harrer, N., Blessing, C., Eustermann, S., Kotthoff, C., Huet, S., Mueller-Planitz, F., Filippov, D.V., **Timinszky, G.**, Rand, K.D., Ladurner, A.G. (2017) A Poly-ADP-Ribose Trigger Releases the Auto-Inhibition of a Chromatin Remodeling Oncogene. **Molecular Cell 68:** 860.

Golia, B., Moeller, G.K., Jankevicius, G., Schmidt, A., Hegele, A., Preißer, J., Tran, M.L., Imhof, A., **Timinszky, G.** (2017) ATM induces MacroD2 nuclear export upon DNA damage. **Nucleic Acids Research. 45:** 244.

Czarna, A., Berndt, A., Singh, H.R., Grudziecki, A., Ladurner, A.G., **Timinszky, G.,** Kramer, A., Wolf, E. (2013) Crystal structures of Drosophila Cryptochrome and mouse. Cryptochrome1: insights into circadian function. **Cell 153:** 1394.

Jankevicius, G., Hassler, M., Golia, B., Rybin, V., Zacharias, M., **Timinszky, G.**, Ladurner, A.G. (2013) A family of macrodomain proteins reverses cellular mono-ADP-ribosylation. **Nature Structural & Molecular Biology 20:** 508.

ANDRÁS VARRÓ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Sudden cardiac death is among the leading causes of mortality worldwide. Therefore to better understand the mechanisms of sudden cardiac death and consequently to introduce effective preventive measures represent extremely important issues in the field of public health care. Sudden cardiac death may occur due to cardiac ischaemia, adverse reaction following drug treatment is associated with diseases like heart failure, congenital diseases or can develop in top athletes due to excessive exercise and/or doping. These cases can manifest due to electrophysiological malfunctions of the heart as a consequence of disturbances in cardiac transmembrane ion channel function including various types of potassium channels. Our research team focuses on investigations on the physiology and pathophysiology of these ion channels including pharmacological modulation and possible prevention of cardiac arrhythmias in general, achieving international attention worldwide.

SELECTED PUBLICATIONS

Polyák A, Topal L, Zombori-Tóth N, Prorok J, Kohajda Z, Déri S, Demeter-Haludka V, Hegyi P, Venglovecz V, Ágoston G, Husti Z, Gazdag P, Szlovák J, Árpádffy-Lovas T, Naveed M, Sarusi A, Jost N, Virág L, Nagy N, Baczkó I, Farkas AS, **Varró A.** (2023) Cardiac electrophysiological remodeling associated with in a canine model of elite execize. **Elife 12:** e80710.

Jost, N., Virág, L., Comtois, P., Ördög, Ö., Szűts, V., Seprényi, Gy., Bitay, M., Kohajda, Zs., Koncz, I., Nagy, N., Szél, T., Magyar, J., Kovács, M., Puskás, LG., Lengyel, Cs., Wettwer, E., Ravens, U., Nánási, PP., Papp, JGy., **Varró, A.**, Nattel, S. (2013) Ionic mechanisms limiting cardiac repolarization-reserve in humans compared to dogs. **J Physiol 591:** 4189-4206.

Jost, N., Nagy, N., Corici, C., Kohajda, Zs., Horváth, A., Acsai, K., Biliczki, P., Levijoki, J., Pollesello, P., Koskelainen, T., Otsomaa, L., Tóth, A., Papp, J.Gy., **Varró, A.**, Virág, L. (2013) ORM-10103, a novel specific inhibitor of the sodium/calcium exchanger, decreases early and delayed afterdepolarization in the canine heart. **Brit J Pharmacol 170:** 768-778.

Jost, N., Virág, L., Bitay, M., Takács, J., Lengyel, Cs., Biliczki, P., Nagy, Zs., Bogáts, G., Lathrop, D.A., Papp, J.Gy., **Varró, A.** (2005) Restricting excessive cardiac action potential and QT prolongation: a vital role for IKs in human ventricular muscle. **Circulation 112:** 1392-1399.

Varró, A., Baláti, B., Iost, N., Takács, J., Virág, L., Lathrop, D.A., Lengyel, C., Tálosi, L., Papp, J.Gy. (2000) The role of IKs in dog ventricular muscle and Purkinje fibre repolarisation. **J Physiol (London) 523:** 67-81.

LÁSZLÓ VÉCSEI

University of Szeged
Albert Szent-Györgyi Medical School
Department of Neurology

RESEARCH AREA

Our main research interest is the experimental and clinical investigation of the pathomechanism and possible therapeutic targets of neurological diseases. With the aid of MR imaging and electrophysiological recordings we search for the characteristic features of multiple sclerosis, Alzheimer's disease, Parkinson's disease and given headache disorders. From cerebrospinal fluid and from blood samples we determine biomarkers, which could help the diagnosis confirmation and provide details about the course of the diseases. In genetic studies, we investigate the genetic background of multiple sclerosis and Parkinson's' disease. The foundation of these experiments is our Biobank of human tissue samples, which we collect continuously. In our animal models we examine the molecular background of neurological disorders, particularly the protective effects of kynurenic acid derivatives. The kynurenine system is our main research target, which is involved in the patho-mechanism of numerous neurological disorders due to the modulatory effects on glutamatergic neurotransmission. In previous experiments, these molecules were effective in the experimental models of headache, Huntington's disease, epilepsy and stroke. Our aim is to further elucidate the mechanisms of effect and potential therapeutic value of this molecules.

SELECTED PUBLICATIONS

Vécsei, L., Szalárdy, L., Fülöp, F., Toldi J. (2013) Kynurenines in the CNS: recent advances and new questions. **Nat Rev Drug Discov 12:** 64-82.

Szpisjak, L., Zadori, D., Klivenyi, P., **Vecsei, L.** (2019) Clinical characteristics and possible drug targets in autosomal dominant spinocerebellar ataxias. **CNS Neurol Disord Drug Targets 18:** 279-293.

Fakan, B., Szalardy, L., **Vecsei, L.** (2019) Exploiting the Therapeutic potential of Endogenous Immunomodulatory Systems in Multiple Sclerosis-Special Focus on the Peroxisome Proliferator-Activated receptors (PPARs) and the Kynurenines. **Int J Mol Sci 20:** 426.

Boros, FA., Klivényi, P., Toldi, J., **Vécsei, L.** (2019) Indoleamine 2,3-dioxygenase as a novel therapeutic target for Huntington's disease. **Expert Opin Ther Targets 23:** 39-51.

Veréb, D., Szabó, N., Tuka, B., Tajti, J., Király, A., Faragó, P., Kocsis, K., Tóth, E., Kincses, B., Bagoly, T., Helyes, Z., **Vécsei, L.**, Kincses, ZT. (2018) Correlation of neurochemical and imaging markers in migraine: PACAP38 and DTI measures. **Neurology 91:** 1166-1174.

Vécsei, L., Lukács, M., Tajti, J., Fülöp, F., Toldi, J., Edvinsson, L. (2018) The therapeutic impact of new migraine discoveries. **Curr Med Chem 26:** 6261-6281.

Boros, FA., Bohár, Z., **Vécsei, L.** (2018) Genetic alterations affecting the genes encoding the enzymes of the kynurenine pathway and their association with human diseases. **Mutat Res 776:** 32-45.

Hertelendy, P., Toldi, J., Fülöp, F., **Vécsei, L.** (2018) Ischemic Stroke and Kynurenines: Medicinal Chemistry Aspects. **Curr Med Chem 25:** 5945-5957.

VIKTÓRIA VENGLOVECZ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Disruption of epithelial ion transport plays a central role in the development of many diseases, such as cystic fibrosis or diarrhea. Research in recent years has shown that altered ion transport processes are also involved in the pathomechanism of inflammatory or cancerous diseases of the esophagus (eg Barrett's esophagus or esophageal adenocarcinoma), although their role is not fully clarified. The incidence of esophageal diseases is increasing worldwide, placing a huge and costly burden on health-care systems. However, the pathomechanism of these diseases is largely unknown, which makes it difficult to develop effective therapies. The goal of our working group is to investigate the role of ion transport processes in the development and progression of esophageal diseases and to identify novel therapeutic targets that can be a promising starting point in the treatment of these diseases.

SELECTED PUBLICATIONS

Korsós, MM., Bellák, T., Becskeházi, E., Gál, E., Veréb, Z., Hegyi, P., **Venglovecz, V.** (2021) Mouse organoid culture is a suitable model to study esophageal ion transport mechanisms. **Am J Physiol-Cell Physiol 321:** C798-C811.

Becskeházi, E., Korsós, MM., Gál, E., Tiszlavicz, L., Hoyk, Zs., Deli, MA., Köhler, ZM., Keller-Pintér, A., Horváth, A., Csekő, K., Helyes, Zs., Hegyi, P., **Venglovecz, V.** (2021) Inhibition of NHE-1 increases smoke-induced proliferative activity of Barrett's esophageal cell line. **Int J Mol Sci 22:** 1058.

Becskeházi, E., Korsós, MM., Erőss, B., Hegyi, P., **Venglovecz, V.** (2020) Oesophageal ion transport mechanisms and significance under pathological conditions. **Front Physiol 11:** 855.

Laczkó, D., Rosztóczy, A., Birkás, K., Katona, M., Rakonczay, Z. Jr., Tiszlavicz, L., Róka, R., Wittmann, T., Hegyi, P., **Venglovecz, V.** (2016) Role of ion transporters in the bile acid-induced esophageal injury. **Am J Physiol Gastrointest Liver Physiol 311:** G16-31.

SZILVIA VESZELKA

HUN-REN Biological Research Centre
Institute of Biophysics

RESEARCH AREA

Pharmaceutical treatment of most disorders of the central nervous system, including neurodegenerative diseases and brain tumors, is restricted due to the poor penetration of drugs across the blood-brain barrier, the major entry route for therapeutic compounds to the central nervous system. The great majority of neuropharmaceutical candidates, hydrophilic molecules, biopharmaceuticals, and efflux transporter ligands have a low permeability across the blood-brain barrier. Biocompatible and biodegradable drug targeting systems, so-called nanocarriers hold a great promise. Nanovesicles which can encorporate drug cargos and present on their surfaces ligands for blood-brain barrier endogenous nutrient transporters achieve increased specificity and efficacy for drug delivery across the blood-brain barrier. Combination of such ligands is a novel and innovative idea which could contribute to develop systems for better treatment of central nervous system diseases.

SELECTED PUBLICATIONS

Veszelka, S., Mészáros, M., Porkoláb, G., Szecskó, A., Kondor, N., Ferenc, G., Polgár, T.F., Katona, G., Kóta, Z., Kelemen, L., Páli, T., Vigh, JP., Walter, FR., Bolognin, S., Schwamborn, J.C., Jan, J.S., Deli, M.A. (2021) A Triple Combination of Targeting Ligands Increases the Penetration of Nanoparticles across a Blood-Brain Barrier Culture Model. **Pharmaceutics 14:** 86.

Fekete, T., Mészáros, M., Szegletes, Z., Vizsnyiczai, G., Zimányi, L., Deli, M.A., **Veszelka, S.***, Kelemen, L.* (2021) Optically Manipulated Microtools to Measure Adhesion of the Nanoparticle-Targeting Ligand Glutathione to Brain Endothelial Cells. **ACS Appl Mater Interfaces 13:** 39018-39029.

Topal, G.R., Mészáros, M., Porkoláb, G., Szecskó, A., Polgár, T.F., Siklós, L., Deli, M.A., **Veszelka, S.***, Bozkir, A.* (2020) ApoE-Targeting Increases the Transfer of Solid Lipid Nanoparticles with Donepezil Cargo across a Culture Model of the Blood-Brain Barrier. **Pharmaceutics 13:** 38.

Porkoláb, G., Mészáros, M., Tóth, A., Szecskó, A., Harazin, A., Szegletes, Z., Ferenc, G., Blastyák, A., Mátés, L., Rákhely, G., Deli, M.A., **Veszelka, S.** (2020) Combination of Alanine and Glutathione as Targeting Ligands of Nanoparticles Enhances Cargo Delivery into the Cells of the Neurovascular Unit. **Pharmaceutics 12:** 635.

Mészáros, M., Porkoláb, G., Kiss, L., Pilbat, A.M, Kóta, Z., Kupihár, Z., Kéri, A., Galbács, G., Siklós, L., Tóth, A., Fülöp, L., Csete, M., Sipos, Á., Hülper, P., Sipos, P., Páli, T., Rákhely, G., Szabó-Révész, P., Deli, M.A., **Veszelka, S.** (2018) Niosomes decorated with dual ligands targeting brain endothelial transporters increase cargo penetration across the bloodbrain barrier. **Eur J Pharm Sci 123:** 228-240.

LÁSZLÓ VÍGH

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

As a "central dogma" earlier it was suggested that stress-induced protein denaturation serves as a major stress-sensing machinery, which triggers the expression of the molecular chaperone heat shock proteins (HSPs). We have introduced a new but not exclusive cellular "membrane thermosensor" model, which predicts the existence of membrane-associated stress sensing and signaling mechanisms. It proposes that changes in the physical state and composition of lipid molecular species with the concomitant destabilization/reorganization of membrane microdomains ("rafts") can serve also as "molecular switches" to operate "cellular thermometers". Using mammalian cells and the fission yeast ***(S.pombe)*** as models we intend to elucidate the mechanism of membrane-associated stress sensors, signaling pathways and the interplay and networking of potential cellular stress survival strategies. Since HSPs play a fundamental role in the pathology of several human diseases, understanding the mechanism whereby mammalian cells can elicit a stress response may also be of paramount importance for the design of novel drug molecules.

SELECTED PUBLICATIONS

Escribá, P.V., Busquets, X., Inokuchi, J.I., Balogh, G., Török, Z., Horváth, I., Harwood, J.L., **Vigh, L.** (2015) Membrane lipid therapy: Modulation of the cell membrane composition and structure as a molecular base for drug discovery and new disease treatment. **Prog Lipid Res 59:** 38-53.

Nagy, E., Balogi, Z., Gombos, I., Akerfelt, M., Björkbom, A., Balogh, G., Török, Z., Maslyanko, A., Fiszer-Kierzkowska, A., Lisowska, K., Slotte, P.J., Sistonen, L., Horváth, I., **Vigh, L.** (2007) Hyperfluidization-coupled membrane microdomain reorganization is linked to activation of the heat shock response in a murine melanoma cell line. **Proc Natl Acad Sci USA 104:** 7945-7950.

Vigh, L., Horváth, I., Maresca, B., Harwood, J.L. (2007) Can the stress protein response be controlled by ‚membrane-lipid therapy'? **Trends Biochem Sci 32:** 357-363.

Török, Z., Tsvetkova, N.M., Balogh, G., Horváth, I., Nagy, E., Pénzes, Z., Hargitai, J., Bensaude, O., Csermely, P., Crowe, J.H., Maresca, B., **Vigh, L.** (2003) Heat shock protein coinducers with no effect on protein denaturation specifically modulate the membrane lipid phase. **Proc Natl Acad Sci USA 100:** 3131-3136.

Vigh, L., Literáti, P.N., Horváth, I., Török, Z., Balogh, G., Glatz, A., Kovács, E., Boros, I., Ferdinándy, P., Farkas, B., Jaszlits, L., Jednákovits, A., Korányi, L., Maresca, B. (1997) Bimoclomol: a nontoxic, hydroxylamine derivative with stress protein-inducing activity and cytoprotective effects. **Nat Med 3:** 1150-1154.

IMOLA WILHELM

HUN-REN Biological Research Centre
Institute of Biophysics
Neurovascular Unit Research Group

RESEARCH AREA

Homeostasis and proper functioning of the central nervous system are largely determined by the coordinated action of cells of the neurovascular unit. Formed by microvascular endothelial cells, pericytes, glial cells and neurons, the neurovascular unit controls the traffic of solutes and cells between the circulation and the brain (blood-brain barrier function) and regulates cerebral blood flow in response to local neural activity (neurovascular coupling). The neurovascular unit is involved in several pathologies of the brain, including cerebral metastases and small vessel ischemic disease. Recently, we have shown that a poorly characterized cell type, namely cerebral pericytes possess significant pro-metastatic features, especially in triple negative breast cancer. In addition, we observed constriction of capillaries in the vicinity of metastatic cells and also cerebral microinfarcts, which seems to be mediated by pericytes. Therefore, on the one hand, we aim to evaluate the role of capillary pericytes in the regulation of blood supply, which is a highly debated scientific question. On the other hand, we focus on the effects of cancer cells on pericytes and other cells of the brain, to understand the mechanisms of tumour cell-induced shaping of the metastatic niche.

SELECTED PUBLICATIONS

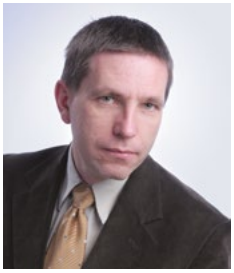
Molnár, K., Mészáros, Á., Fazakas, C., Kozma, M., Győri, F., Reisz, Z., Tiszlavicz, L., Farkas, A.E., Nyúl-Tóth, Á., Haskó, J., Krizbai, I.A., **Wilhelm, I.** (2020) Pericyte-secreted IGF2 promotes breast cancer brain metastasis formation. **Mol Oncol 14:** 2040-2057.

Haskó, J., Fazakas, C., Molnár, K., Mészáros, Á., Patai, R., Szabó, G., Erdélyi, F., Nyúl-Tóth, Á., Győri, F., Kozma, M., Farkas, A.E., Krizbai, I.A., **Wilhelm, I.** (2019) Response of the neurovascular unit to brain metastatic breast cancer cells. **Acta Neuropathol Commun 7:** 133.

Herman, H., Fazakas, C., Haskó, J., Molnár, K., Mészáros, Á., Nyúl-Tóth, Á., Szabó G, Erdélyi, F., Ardelean, A., Hermenean, A., Krizbai, I.A., **Wilhelm, I.** (2019) Paracellular and transcellular migration of metastatic cells through the cerebral endothelium. **J Cell Mol Med 23:** 2619-31.

Wilhelm, I., Fazakas, C., Molnár, K., Végh, A.G., Haskó, J., Krizbai, I.A. (2018) Foe or friend? Janus-faces of the neurovascular unit in the formation of brain metastases. **J Cereb Blood Flow Metab 38:** 563-587.

Molnár, J., Fazakas, C., Haskó, J., Sipos, O., Nagy, K., Nyúl-Tóth, Á., Farkas, A.E., Végh, A.G., Váró, G., Galajda, P., Krizbai, I.A., **Wilhelm, I.** (2016) Transmigration characteristics of breast cancer and melanoma cells through the brain endothelium: role of Rac and PI3K. **Cell Adh Migr 10:** 269-81.



ISTVÁN ZUPKÓ

University of Szeged
Faculty of Pharmacy
Department of Pharmacodynamics and Biopharmacy

RESEARCH AREA

In spite of the impressive achievements in the treatment possibilities of malignant disorders, cancers still have leading roles in mortality statistics worldwide indicating the need for novel anticancer agents. Natural products and their analogs are inexhaustible source of drugs candidates. The main aims of our group are to identify potential lead molecules by screening isolated and synthetic compounds for their anticancer properties. In vitro cell culture based studies are performed in order to characterize the cancer selectivity and the mechanism of the action of the most promising hits.

SELECTED PUBLICATIONS

Bózsity, N., Minorics, R., Szabó, J., Mernyák, E., Schneider, G., Wölfling, J., Wang, H.C., Wu, C.C., Ocsovszki, I., **Zupkó, I.** (2017) Mechanism of antiproliferative action of a new d-secoestrone-triazole derivative in cervical cancer cells and its effect on cancer cell motility. **J Steroid Biochem Mol Biol 165:** 247-57.

Molnár, J., Szebeni, J.G., Csupor-Löffler, B., Hajdú, Z., Szekeres, T., Saiko, P., Ocsovszki, I., Puskás, G.L., Hohmann, J., **Zupkó, I.** (2016) Investigation of the antiproliferative properties of natural sesquiterpenes from Artemisia asiatica and Onopordum acanthium on HL-60 cells in vitro. **Int J Mol Sci 17:** 83.

Molnár, J., Frank, É., Minorics, R., Kádár, Z., Ocsovszki, I., Schönecker, B., Wölfling, J., **Zupkó, I.** (2015) A click approach to novel D-ring-substituted 16α-triazolylestrone derivatives and characterization of their antiproliferative properties. **PLOS ONE 10:** e0118104.

Mernyák, E., Kovács, I., Minorics, R., Sere, P., Czégány, D., Sinka, I., Wölfling, J., Schneider, G., Újfaludi, Z., Boros, I., Ocsovszki, I., Varga, M., **Zupkó, I.** (2015) Synthesis of trans-16-triazolyl-13α-methyl-17-estradiol diastereomers and the effects of structural modifications on their in vitro antiproliferative activities. **J Steroid Biochem Mol Biol 150:** 123-34.

Minorics, R., Bózsity, N., Molnár, J., Wölfling, J., Mernyák, E., Schneider, G., Ocsovszki, I., **Zupkó, I.** (2015) A molecular understanding of d-homoestrone-induced G2/M cell cycle arrest in HeLa human cervical carcinoma cells. **J Cell Mol Med 19:** 2365-74.

SZEGED
SZENT-GYÖRGYI JUNIOR MENTORS

GÁBOR APJOK

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

I am a postdoctoral researcher working on the improvement of phage therapy, applying synthetic biological and genome engineering techniques, as the senior of a group of talented individuals. I am involved in projects investigating and altering the interactions between phages and the human body, the gut and the blood-brain barrier in particular. Furthermore, I regularly carry out phage hunts upon request and already isolated and provided therapeutically applicable phages to hospitals in Switzerland, Portugal and the United Kingdom.

SELECTED PUBLICATIONS

Apjok, G., Számel, M., Christodoulou, C., Seregi, V., Vásárhelyi, BM., Stirling, T., Eszenyi, B., Sári, T., Vidovics, F., Nagrand, E. et al. (2023) Characterization of antibiotic resistomes by reprogrammed bacteriophage-enabled functional metagenomics in clinical strains. **Nat Microbiol 8:** 410-423.

Visnyovszki, Á., Orosz, L., Kintses, B., Stirling, T., Vásárhelyi, BM., Ari, E., Kiss, E., Papp, B., **Apjok, G.**, Vidovics, F. et al. (2021) A covid-19 pandémiához társulóan előfordult multirezisztens acinetobacter baumannii törzsek molekuláris jellemzése. **Magyar Infektológiai és Klinikai Mikrobiológiai Társaság 48. Kongresszusa** 2021-09-30 [Debrecen, Magyarország], (előadás)

Apjok, G., Boross, G., Nyerges, A., Fekete, G., Lazar, V., Papp, B., Pal, C., Csoergo, B. (2019) Limited evolutionary conservation of multidrug resistance and collateral sensitivity. **Mol Biol Evol 38:** 3029-3029.

Dunai, A., Spohn, R., Farkas, Z., Lázár, V., Györkei, Á., **Apjok, G.**, Boross, G., Szappanos, B., Grézal, G., Faragó, A. et al. (2019) Rapid decline of bacterial drug-resistance in an antibiotic-free environment through phenotypic reversion. **ELIFE 8** Paper: e47088.

Apjok, G., Boross, G., Nyerges, Á., Fekete, G., Lázár, V., Papp, B., Pál, C., Csörgő, B. (2019) Limited evolutionary conservation of the phenotypic effects of antibiotic resistance mutations. **Mol Biol Evol 36:** 1601-1611.

Nyerges, A., Csorgo, B., Nagy, I., Balint, B., Bihari, P., Lazar, V., **Apjok, G.**, Umenhoffer, K., Bogos, B., Posfai, G. et al. (2016) A highly precise and portable genome engineering method allows comparison of mutational effects across bacterial species. **Proc Natl Acad Sci U S A 113:** 2502-2507.

RENÁTA BOZÓ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Dermatology and Allergology

RESEARCH AREA

Psoriasis is a common, chronic inflammatory, immune-mediated skin disease characterized by red, scaly patches. The psoriatic involved skin is mainly characterized by hyperproliferation of epidermal keratinocytes and infiltration of immune cells. Although nowadays the number of therapeutic options is increasing, however, there is currently no solution to prevent the recurrence of symptoms after the suspension of the therapy. The disease is characterized by the fact that the involved skin areas are well separated from the clinically uninvolved, healthy-looking skin areas. Furthermore, even a number of cellular and extracellular abnormalities are present in the uninvolved skin areas. However, the main characteristic mechanisms of involved skin such as hyperproliferation of epidermal keratinocytes and infiltration of immune cells, are not observed in uninvolved skin. Our previous studies suggest that abnormalities of the uninvolved skin on one hand can predispose to the development of symptoms, on the one hand, alterations of the uninvolved skin can be protective factors and mechanisms as well. These alterations can contribute to the special balanced, so-called pre-psoriatic condition. Studying these protective mechanisms is a novel approach in psoriasis research. Recurrence of the psoriatic lesions may potentially be prevented by a better understanding of the changes that can maintain the uninvolved state.

SELECTED PUBLICATIONS

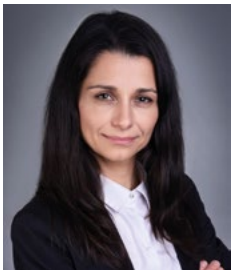
Bozó, R., Flink, L.B., Belső, N., Gubán, B., Széll, M. Kemény, L., Bata-Csörgő, Zs. (2021) Could basement membrane alterations, resembling micro-wounds at the dermo-epidermal junction in psoriatic non-lesional skin, make the skin susceptible to lesion formation? **Exp Dermatol 30:** 765-772.

Bozó, R., Danis, J., Flink, L.B., Vidács, D.L., Kemény, L., Bata-Csörgő, Zs. (2021) Stress-related regulation is abnormal in the psoriatic uninvolved skin. **LIFE-BASEL 11:** 599.

Kelemen, E.*, **Bozó, R.***, Groma, G., Bata-Csörgő, Zs., Kemény, L., Danis, J., Széll, M. (2021) The psoriatic non-lesional skin: a battlefield of constant fight between susceptibility and protective factors. **J Invest Deramtol 141:** 2785-2790.

Bozó, R., Szél, E., Danis, J., Gubán, B., Bata-Csörgő, Zs., Szabó, K., Kemény, L., Groma, G. (2020) Cartilage Oligomeric Matrix Protein Negatively Influences Keratinocyte Proliferation Via α5β1-Integrin: Potential Relevance of Altered Cartilage Oligomeric Matrix Protein Expression in Psoriasis. **J Invest Deramtol 140:** 1733-1742.e7.

Szél, E., **Bozó, R.**, Hunyadi-Gulyas, E., Manczinger, M., Szabo, K., Kemény, L., Bata-Csörgő, Zs., Groma, G. (2019) Comprehensive Proteomic Analysis Reveals Intermediate Stage of Non-Lesional Psoriatic Skin and Points out the Importance of Proteins Outside this Trend. **Sci Rep 9:** 11382.



NOÉMI CRUL-TÓTH

University of Szeged
Faculty of Pharmacy
Department of Pharmacognosy

RESEARCH AREA

Ecdysteroids are insect molting hormones synthesized by numerous plant species in a fairly high concentration, playing a complex defensive role against insect predators. It is acknowledged that ecdysteroids exert beneficial pharmacological effects in mammals including anabolic, antitumor, blood glucose and cholesterol lowering, antiarrhythmic, and neuroprotective effects, without any detectable hormonal activity. Investigating the complex role of ecdysteroids in the biota, our research team reported that phytoecdysteroids accumulate in the blood of animals (e.g. songbirds, bats) that consume herbivorous insects/caterpillars through the food chain and exert toxic effects on the blood-sucking parasites of these animals. Currently, we aim to elucidate the ecological role of these bioactive substances through the analysis of the ecdysteroid content of biological samples from insects and a variety of insectivorous animals (songbirds, bats, hedgehogs, etc.) using state-of-the-art analytical and preparative chromatographic methods.

SELECTED PUBLICATIONS

Budzynski, MA., Crul, T., Himanen, SV., **Tóth, N.**, Otvos, F., Sistonen, L., Vigh, L. (2017) Chaperone co-inducer BGP-15 inhibits histone deacetylases and enhances the heat shock response through increased chromatin accessibility. **Cell Stress & Chaperone 22(5):** 717-728.

Martins, A., **Tóth, N.**, Ványolós, A., Béni, Z., Zupkó, I., Molnár, J., Báthori, M., Hunyadi, A. (2012) Significant activity of ecdysteroids on the resistance to doxorubicin in mammalian cancer cells expressing the human ABCB1 transporter. **J Med Chem 55(11):** 5034-5043.

Tóth, N., Simon, A., Toth, G., Kele, Z., Hunyadi, A., Bathori, M. (2008) 26-Hydroxylated ecdysteroids from Silene viridiflora. **J Nat Prod 71(8):** 1461-1463.

Tóth, N., Szabó, A., Kacsala, P., Héger, J., Zádor, E. (2008) 20-Hydroxy-ecdysone increases fiber size in a muscle-specific fashion in rat. **Phytomedicine 15(9):** 691-698.

ÁRPÁD CSERNETICS

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

Transition from simple to complex multicellularity was a giant evolutionary innovation in the history of life. Mushroom-forming fungi are ideal model organisms of complex multicellularity: they start their lifecycle as unicellular spores thus developing multicellular filaments followed by formation of a complex fruiting body structures with various fungal tissues in the sexual cycle. Complex multicellularity appeared multiple times independently (convergent origins) in the fungal kingdom via unique mechanisms. In contrast, yeasts are secondarily simplified organisms with multicellular ancestors. They spend most of their life cycle as unicellular organisms but retain the genes for multicellular complexity. The potential for yeast-like growth (i.e. genetic toolkit) evolved early in fungal evolution but the transitions to yeast-like lifestyle happened much later multiple times and yeast-like growth became dominant independently in distantly related clades. To gain deeper insight into such evolutionary innovations we examine genome-evolution, differences in gene expression and reconstruct gene regulatory networks with comparative genomics and -transcriptomics and lab experiments. Investigating the genetic and molecular background of fungal plant cell wall degradation is also among our research interests. Lignocellulose decomposition is one of the most industrially exploited fungal traits (e.g. in bioethanol production). Our goal is to reconstruct gene regulatory networks that underlie plant biomass degrading fungal extracellular enzyme biosynthesis.

SELECTED PUBLICATIONS

Nagy, L.G., Varga, T., **Csernetics, Á.**, Virágh, M. (2020) Fungi took a unique evolutionary route to multicellularity: Seven key challenges for fungal multicellular life. **Fungal Biol Rev 34:** 151-169.

Nagy, G., Vaz, A.G., Szebenyi, Cs., Takó, M., Tóth, E.J., **Csernetics, Á.**, Bencsik, O., Szekeres, A., Homa, M., Ayaydin, F., Galgóczy, L., Vágvölgyi, Cs., Papp, T. (2019) CRISPR-Cas9- mediated disruption of the HMG-CoA reductase genes of Mucor circinelloides and subcellular localization of the encoded enzymes. **Fungal Genet Biol 129:** 30-39.

Homa, M., Galgóczy, L., Manikandan, P., Narendran, V., Sinka, R., **Csernetics, Á.**, Vágvölgyi, Cs., Kredics, L., Papp, T. (2018) South Indian isolates of the Fusarium solani species complex from clinical and environmental samples: identification, antifungal susceptibilities, and virulence. **Front Microbiol 9:** 1052.

Nagy, G., Szebenyi, Cs., **Csernetics, Á.**, Vaz, A.G., Tóth, E.J., Vágvölgyi, Cs., Papp, T. (2017) Development of a plasmid free CRISPR-Cas9 system for the genetic modification of Mucor circinelloides. **Sci Rep 7:** 16800.

Csernetics, Á., Nagy, G., Iturriaga, E.A., Szekeres, A., Eslava, A.P., Vágvölgyi, Cs. and Papp, T. (2011) Expression of three isoprenoid biosynthesis genes and their effects on the carotenoid production of the zygomycete Mucor circinelloides. **Fungal Genet Biol 48:** 696-703.

ILONA GRÓF

HUN-REN Biological Research Centre
Institute of Biophysics

RESEARCH AREA

Investigation of peptide carriers on culture models of biological barriers
Targeted delivery of protein drugs into cells and through biological barriers to achieve a more effective therapeutic effect is an area of intensive research. Several strategies exist already for delivery to the intracellular space, however the drugs that enter by endocytosis are unable to be effective due to entrapment in vesicles or degradation by lysosomes. We are investigating carriers that can be conjugated to a peptide or protein drug to enter cells and avoid lysosomal degradation. The aim of the research is to investigate these peptide carriers in culture models of different biological barriers for the delivery of large biomolecules. In this work, comparative study of several peptide carriers are performed on the culture model of endothelial and epithelial barriers, such as the blood-brain barrier, cornea-, lung-, and intestinal epithelium. In our experiments, we characterize the viability, integrity, and morphological changes of intercellular junctions of the cell layers. We study the intracellular localization of peptide carriers as well as their penetration through cell layers. Furthermore, passage of fluorescent proteins loaded into peptide-targeted nanoparticles through barrier models is tested. The expected results may contribute to the development of new types of carrier systems for the delivery of drugs or biopharmaceuticals across biological barriers, which may contribute to a better cure for diseases.

SELECTED PUBLICATIONS

Bocsik, A., **Gróf, I.**, Kiss, L., Ötvös, F., Zsíros, O., Daruka, L., Fülöp, L., Vastag, M., Kittel, Á., Imre, N., Martinek, T.A., Pál, C., Szabó-Révész, P., Deli, M.A. (2019) Dual Action of the PN159/KLAL/MAP Peptide: Increase of Drug Penetration across Caco-2 Intestinal Barrier Model by Modulation of Tight Junctions and Plasma Membrane Permeability. **Pharmaceutics 11:** 73.

Veszelka, S., Tóth, A., Walter, F., Tóth, A.E., **Gróf, I.**, Mészáros, M., Bocsik, A., Hellinger, É., Vastag, M., Rákhely, G., Deli, M.A. (2018) Comparison of a Rat Primary Cell-Based Blood- Brain Barrier Model With Epithelial and Brain Endothelial Cell Lines: Gene Expression and Drug Transport. **Front Mol Neurosci 11:** 166.

Imre, N., Hetényi, A., Szabó, E., Bodnár, B., Szkalisity, A., **Gróf, I.**, Bocsik, A., Deli, M.A., Horvath, P., Czibula, Á., Monostori, É., Martinek, T.A. (2020) Routing Nanomolar Protein Cargoes to Lipid Raft-Mediated/ Caveolar Endocytosis through a Ganglioside GM1-Specific Recognition Tag. **Adv Sci (Weinh) 7:** 1902621.

Gróf, I., Bocsik, A., Harazin, A., Santa-Maria, A.R., Vizsnyiczai, G., Barna, L., Kiss, L., Fur, G., Rakonczay, Z. Jr, Ambrus, R., Szabó-Révész, P., Gosselet, F., Jaikumpun, P., Szabó, H., Zsembery, Á., Deli, M.A. (2020) The E ect of Sodium Bicarbonate, a Bene cial Adjuvant Molecule in Cystic Fibrosis, on Bronchial Epithelial Cells Expressing a Wild-Type or Mutant CFTR Channel. **Int J Mol Sci 21:** 4024.

Katona, G., Sipos, B., Budai-Szucs, M., Balogh, G.T., Veszelka, S., **Gróf, I.**, Deli, M.A., Volk, B., Szabó-Révész, P., Csóka, I. (2021) Development of In Situ Gelling Meloxicam-Human Serum Albumin Nanoparticle Formulation for Nose-to- Brain Application. **Pharmaceutics 13:** 646.

ZSÓFIA HEGEDÜS

University of Szeged
Albert Szent-Györgyi Medical School
Department of Medical Chemistry

RESEARCH AREA

Protein-protein interactions (PPIs) play key role in many cellular processes including pathological conditions such as cancer progression. PPIs mediated by intrinsically disordered proteins, which fold during protein binding, are especially challenging to target. Investigating the binding mechanism and structural changes of such proteins would lead to better understanding of their function and could serve as starting points for drug discovery.
One of our approaches includes the modification of a known ligand using non-natural amino acids, which influence their binding properties and stability. In our other approach we use libraries of non-natural peptides to find binding motifs that recognize the target protein surface. Our goal is to develop methods that can be used to create high affinity and selective ligands based on the identified binding motifs. One such method is dynamic covalent chemistry where the protein acts as a selection pressure to form the best binders. Another approach is to use DNA templated synthesis to connect the binding motifs which can be identified by their DNA code.

SELECTED PUBLICATIONS

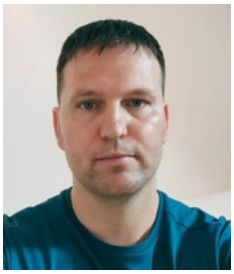
Kupihár, Z., Ferenc, G., Petrovicz, V. L., Fáy, V. R., Kovács, L., Martinek, T. A., **Hegedüs, Z.** (2023) Improved Metal-Free Approach for the Synthesis of Protected Thiol Containing Thymidine Nucleoside Phosphoramidite and Its Application for the Synthesis of Ligatable Oligonucleotide Conjugates. **Pharmaceutics. 15:** 248.

Hóbor, F., **Hegedüs, Z.**, Ibarra, A. A., Petrovicz, V. L., Bartlett, G. J., Sessions, R. B., Wilson, A. J., Edwards, T. A. (2022) Understanding p300-transcription factor interactions using sequence variation and hybridization. **RSC Chem Biol. 3:** 592-603.

Hegedüs, Z., Hóbor, F., Shoemark, D. K., Celis, S., Lian, L. Y., Trinh, C. H., Sessions R.B., Edwards, T.A., Wilson, A. J. (2021) Identification of β-strand mediated protein–protein interaction inhibitors using ligand-directed fragment ligation. **Chem Sci. 12:** 2286-2293.

Hegedus, Z., Grison, C.M., Miles, J.A., Rodriguez-Marin, S, Warriner, S.L., Webb, M.E., Wilson, A.J. (2019) A Catalytic Protein-Proteomimetic Complex: Using Aromatic Oligoamide Foldamers as Activators of RNase S. **Chem Sci. 10:** 3956-3962.

Bartus, É., **Hegedüs, Z.**, Wéber, E., Csipak, B., Szakonyi, G., Martinek, T. A. (2017) De Novo Modular Development of a Foldameric Protein–Protein Interaction Inhibitor for Separate Hot Spots: A Dynamic Covalent Assembly Approach. **ChemistryOpen 6:** 236-241.



TIBOR HORNYIK

University of Szeged
Albert Szent-Györgyi Medical School
Department of Pharmacology and Pharmacotherapy

RESEARCH AREA

Our group has been conducting research in the field of cardiac arrhythmias for decades. Our research interest includes 1) the investigation of novel antiarrhythmic drug candidates that may be used to treat atrial fibrillation, 2) studies aiming to better understand the mechanisms of sudden cardiac death in athletes, and the importance of various cardiac ionic currents that play a role in the repolarization reserve of the heart, as well as 3) developing novel animal models that can be used for more reliable prediction of drug-induced proarrhythmic side-effects. In our latest research topic we are aiming to investigate the potential cardiac electrophysiological effetcs of the 'so-called' sodium-glucose-cotransporter-2 (SGLT-2) inhibitors, a group of drugs originally used as antidiabetics, considering that these drugs have recently been recommended as first-line agents in the therapy of chronic heart failure by the latest guidelines, though, their electrophysiological effects are still not sufficiently understood.

SELECTED PUBLICATIONS

Kohajda, Z., Virág L., **Hornyik, T.**, Husti, Z., Sztojkov-Ivanov, A., Nagy, N., Horváth, A., Varga, R., Prorok, J., Szlovák, J., Tóth, N., Gazdag, P., Topal, L., Naveed, M., Árpádffy-Lovas, T., Pászti, B., Magyar, T., Koncz, I., Déri, S., Demeter-Haludka, V., Aigner, Z., Ördög, B., Patfalusi, M., Tálosi, L., Tiszlavicz, L., Földesi, I., Jost, N., Baczkó, I., Varró, A. (2022) In vivo and cellular antiarrhythmic and cardiac electrophysiological effects of desethylamiodarone in dog cardiac preparations. **Br J Pharmacol 179:** 3382-3402.

Castiglione, A.*, **Hornyik, T.***, Wülfers, EM., Giammarino, L., Edler, I., Jowais, JJ., Rieder, M., Perez-Feliz, S., Koren, G., Bősze, Z., Varró, A., Zehender, M., Brunner, M., Bode, C., Liin, SI., Larsson, HP., Baczkó, I., Odening, KE. (2022) Docosahexaenoic acid normalizes QT interval in long QT type 2 transgenic rabbit models in a genotype-specific fashion. **Europace 24:** 511-522.

Varga, RS., **Hornyik, T.**, Husti, Z., Kohajda, Z., Krajsovszky, G., Nagy, N., Jost, N., Virág, L., Tálosi, L., Mátyus, P., Varró, A., Baczkó, I. (2021) Antiarrhythmic and cardiac electrophysiological effects of SZV-270, a novel compound with combined Class I/B and Class III effects, in rabbits and dogs. **Can J Physiol Pharmacol 99:** 89-101.

Baczkó, I.*, **Hornyik, T.***, Brunner, M., Koren, G., Odening, KE. (2020) Transgenic Rabbit Models in Proarrhythmia Research. **Front Pharmacol 11:** 853.

Hornyik, T., Castiglione, A., Franke, G., Perez-Feliz, S., Major, P., Hiripi, L., Koren, G., Bősze, Z., Varró, A., Zehender, M., Brunner, M., Bode, C., Baczkó, I., Odening, KE. (2020) Transgenic LQT2, LQT5, and LQT2-5 rabbit models with decreased repolarisation reserve for prediction of drug-induced ventricular arrhythmias. **Br J Pharmacol 177:** 3744-3759.

ILDIKÓ HULIÁK

University of Szeged
Faculty of Science and Informatics

RESEARCH AREA

The tumor microenvironment (TME) has been recently recognized as a critical player in cancer progression. Beside the restructured extracellular matrix (ECM), the tumor stroma consists of numerous mesenchymal cells recruited to the TME. In addition to neoplastic cells, tumor stroma includes activated fibroblasts, various immune cells, endothelial cells, pericytes and adipocytes, which all communicate with each other. Due to these reciprocal interactions modulated by cytokines, chemokines and various growth factors, the stroma ultimately evolves into a tumor-promoting environment. Beside protein factors exosomal non-coding RNAs (miRNA, lncRNA) also facilitate tumor progression, however only a few ncRNAs were examined in relation to stromal cell – tumor cell communication. Our group investigates the involvement and the precise function of ncRNAs in tumor cell – stromal cell crosstalk.

SELECTED PUBLICATIONS

Kovács, F., **Huliák, I.**, Árva, H., Kiricsi, M., Erdős, D., Kocsis, M., Takács, G., Balogh, G.T., Frank É. (2023) Medicinal-chemistry-driven approach to 2-substituated benzoxazole-estradiol chimeras: synthesis, anticancer activity and early ADME profile. **Chem Med Chem** e202300352.

Nagy, F.I., Adamecz, D.I., Baji, Á., Kiricsi, Á., **Huliák, I.**, Rónavári, A., Kónya, Z., Frank, É., Gopisetty, M.K., Kiricsi M. (2023) Semi-synthetic dihydrotestosterone derivates modulate inherent multidrug resistance and sensitize colon cancer cells to chemotherapy. **Pharmaceutics 15:** 584.

Huliák, I., Bodai, L., Czepán, M., Kovács, D., Szabó, A., Tiszlavicz, L., Lázár, G., Rakonczay, Z. Jr, Hegyi, P., Boros, I.M., Kiricsi, M. (2019) Genetic, epigenetic and transcriptional comparison of esophagus tumor-associated and adjacent normal myofibroblasts. **Oncology Rep 41:** 839-852.

Borsos, B.N., **Huliák, I.**, Majoros, H., Újfaludi, Z., Gyenis, Á., Pukler, P., Boros, I.M., Pankotai, T. (2017) Human p53 interacts with the elongating RNAPII complex and is required for the release of actinomycin D induced transcription blockage. **Sci Rep 7:** 40960.

Huliák, I., Sike, Á., Zencir, S., Boros I.M. (2012) The objectivity of reporters: interference between physically unlinked promoters affects reporter gene expression in transient transfection experiments. **DNA Cell Biol 31:** 1580-4.

NÓRA IGAZ

University of Szeged
Faculty of Science and Informatics
Department of Biochemistry
and Molecular Biology

RESEARCH AREA

Metal nanoparticles have a great potential in cancer treatment due to a broad spectrum of anti-cancer activities. Nano-sized materials are able to accumulate in the tumor tissue owing to the fenestrated endothel of the tumor blood vessels. Moreover, the large specific surface of nanoparticles can be functionalized with tumor-specific ligands to achieve active tumor targeting. Among metal nanomaterials, silver and gold nanoparticles are the most promising entities for oncotherapeutic applications. Silver nanoparticles induce apoptosis in tumor cells by triggering the production of reactive oxygen species, whereas gold nanoparticles potentiate the efficacy of ionizing radiation, thus possess radiosensitizing activity on tumor cells. Metal nanoparticles are also excellent combinational partners of chemotherapeutic agents and of different treatment modalities. Besides the tumor-targeting activity of nanoparticles, nano-sized materials can be used to modulate the cancer promoting activity of other cell types such as cancer-associated fibroblasts and tumor-associated macrophages in the tumor microenvironment, thus we examine how metal nanoparticles affect the paracrine cross-talk between cells in the tumor tissue in order to attenuate tumor progression, invasion and dissemination.

SELECTED PUBLICATIONS

Igaz, N, Szőke, K., Kovács, D., Buhala, A., Varga, Z, Bélteky, P., Rázga, Zs., Tiszlavicz, L, Vizler, Cs., Hideghéty, K,, Kónya, Z, Kiricsi, M. (2020) Synergistic radiosensitization by gold nanoparticles and the histone deacetylase inhibitor SAHA in 2D and 3D cancer cell cultures. **Nanomaterials 10:** 158.

Kovács, D., **Igaz, N.**, Marton, A., Rónavári, A., Bélteky, P., Bodai, L., Spengler G., Tiszlavicz, L., Rázga Zs., Hegyi P., Vizler, Cs., Boros, I., Kónya, Z, Kiricsi M. (2020) Core-shell nanoparticles suppress metastasis and modify the tumoursupportive activity of cancer-associated fibroblasts **J Nanobiotechnology 18:** 18.

Szerencsés, B., **Igaz, N.**, Tóbiás, Á., Prucsi, Zs., Rónavári, A., Bélteky, P., Madarász, D., Papp, Cs., Makra, I., Vágvölgyi, Cs., Kónya Z, Pfeiffer, I., Kiricsi, M. (2020) Size-dependent activity of silver nanoparticles on the morphological switch and biofilm formation of opportunistic pathogenic yeasts. **BMC Microbiol 20:** 176.

Gopisetty, M. K., Kovács, D., **Igaz, N.**, Rónavári, A., Bélteky, P., Rázga, Zs., Venglovecz, V., Csoboz, B., Boros, I., Kónya, Z., Kiricsi, M. (2019) Endoplasmic reticulum stress: major player in size-dependent inhibition of P-glycoprotein by silver nanoparticles in multidrug-resistant breast cancer cells. **J Nanobiotechnology 17:** 9.

Rónavári, A., Kovács, D., **Igaz, N.**, Vágvölgyi, Cs., Boros, I., Kónya, Z., Pfeiffer, I., Kiricsi, M., (2017) Biological activity of green-synthesized silver nanoparticles depends on the applied natural extracts: a comprehensive study. **Int J Nanomedicine 12:** 871-883.

LÁSZLÓ JUHÁSZ

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Surgical Research

RESEARCH AREA

Functional and morphological changes within mitochondria and their altered interaction with other organelles are suggested to play a critical role in the pathogenesis of various diseases associated with life-threatening organ dysfunction. Some of them, such as sepsis and ischaemia/ reperfusion-induced injury (I/R) have more recently become an intensively developing field of basic research. Our main purpose is to investigate the underlying mitochondrial and cellular mechanisms involved in the corresponding animal model of diseases.

SELECTED PUBLICATIONS

Juhász, L., Rutai, A., Fejes, R.,Tallósy, S.P., Poles, M.Z., Szabó, A., Szatmári, I., Fülöp, F., Vécsei, L., Boros, M., Kaszaki, J. (2020) Divergent effects of the N-methyl-D-aspartate receptor antagonist kynurenic acid and the synthetic analog SZR-72 on microcirculatory and mitochondrial dysfunction in experimental sepsis. **Front Med 7:** 566582.

Nászai, A., Terhes, E., Kaszaki, J., Boros, M., **Juhász, L.** (2019) Ca(2+)N it be measured? Detection of extramitochondrial calcium movement with high-resolution fluorespirometry. **Sci Rep 9:** 19229.

Poles, M.Z., **Juhász, L.**, Boros, M. (2019) Methane and inflammation - A review (Fight fire with fire). **Intensive Care Med Exp 7:** 68.

Juhász, L., Kiss, A., Nyeső, E., Kovács, M., Seprényi, G., Kaszaki, J., Végh, Á. (2011) Is there a trigger role of peroxynitrite in the anti-arrhythmic effect of ischaemic preconditioning and peroxynitrite infusion? **Eur J Pharmacol 667:** 306-313.

Kiss, A., **Juhász, L.**, Seprényi, G., Kupai, K., Kaszaki, J., Végh, Á. (2010) The role of nitric oxide, superoxide and peroxynitrite in the anti-arrhytmic effects of preconditioning and peroxynitrite infusion in anaesthetized dogs. **Br J Pharmacol 160:** 1263-1272.

BÁLINT LŐRINCZI

University of Szeged
Faculty of Pharmacy
Institute of Pharmaceutical Chemistry

RESEARCH AREA

Our research is focused on the preparation of kinurenic acid (KYNA) derivatives with endogenous neuroprotective function by modifying their synthesis or by further transformations of the products (e.g. in modified Mannich reactions or in aza-Friedel-Crafts reactions). Furthermore, via the appropriate modifications of the KYNA synthesis, maleimide-type protein marker molecules and polycyclic phenanthrene derivatives with potential antitumor activity can also be synthesized and together with the production of iodinated benzyloxyalkylamines with antiarrhythmic activity they are also part of our research work.

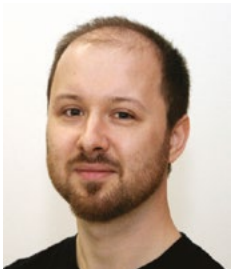
SELECTED PUBLICATIONS

Lőrinczi, B., Csámpai, A., Fülöp, F., Szatmári, I. (2020) Synthesis of New C-3 Substituted Kynurenic Acid Derivatives. **Molecules** 2020, 25, 937.

Lőrinczi, B., Csámpai, A., Fülöp, F., Szatmári, I. (2021) Synthetic- and DFT modelling studies on regioselective modified Mannich reactions of hydroxy-KYNA derivatives. **RSC Adv** 2021, 11, 543.

Lőrinczi, B., Simon, P., Szatmári, I. (2022) Synthesis of Indole-Coupled KYNA Derivatives via C–N Bond Cleavage of Mannich Bases. **Int J Mol Sci** 2022, 23, 7152.

Simon, P., **Lőrinczi, B.**, Hetényi, A., Szatmári, I. (2023) Novel Eco-friendly, One-Pot Method for the Synthesis of Kynurenic Acid Ethyl Esters. **ACS Omega** 2023, 8, 17966.



TAMÁS MARUZS

HUN-REN Biological Research Centre
Institute of Genetics

RESEARCH AREA

Organelles of eukaryotic cells represent an intricate network the members of which are connected with each other either via vesicular transport processes or permanent physical contacts. Significance of the latter type of organellar communication (the so-called membrane contact sites) has only been recognized in the last decade. The complex, dynamic endomembrane system plays a pivotal role in normal cell physiology and its proper function requires the concerted action of several proteins. Main research focus of our group is the investigation of genes and proteins involved in vesicular trafficking routes chanelling to the lysosomes, the central degradative organelles of cells. Members of the Sorting nexin (Snx) protein family play important roles in numerous points of the endolysosomal system. All Snx proteins contain the lipid-binding PX-domain that enables them to associate with organellar membranes where they utilize other protein domains to take part in versatile molecular events. However, exact cellular functions of many Snx proteins are currently unknown, and importantly, some of these proteins are involved in the pathogenesis of human diseases. Most of the Sorting nexins are evolutionarily conserved, offering the possibility to investigate their functions in model organisms. We use various fruitfly tissues to study the molecular functions of the less well-characterized Snx proteins in the endolysosomal system.

SELECTED PUBLICATIONS

Maruzs, T., Feil-Börcsök, D,. Lakatos, E., Juhász, G., Blastyák, A., Hargitai, D., Jean, S., Lőrincz, P., Juhász, G. (2023) Interaction of the sorting nexin 25 homologue Snazarus with Rab11 balances endocytic and secretory transport and maintains the ultrafiltration diaphragm in nephrocytes. **Mol Biol Cell 34(9):** ar87.

Maruzs, T., Simon-Vecsei, Z., Kiss, V., Csizmadia, T., & Juhász, G. (2019) On the fly: recent progress on autophagy and aging in Drosophila. **Front Cell Dev Biol 7:** 140.

Lőrincz, P., Lakatos, Z., Varga, A., **Maruzs, T.**, Simon-Vecsei, Z., Darula, Z., ... & Hegedűs, K. (2016). MiniCORVET is a Vps8- containing early endosomal tether in Drosophila. **Elife 5:** e14226.

Maruzs, T., Lőrincz, P., Szatmári, Z., Széplaki, S., Sándor, Z., Lakatos, Z., ... & Sass, M. (2015). Retromer ensures the degradation of autophagic cargo by maintaining lysosome function in Drosophila. Traffic 16: 1088-1107. **Mol Cell 34(9):** ar87.

Maruzs, T., Simon-Vecsei, Z., Kiss, V., Csizmadia, T., & Juhász, G. (2019). On the fly: recent progress on autophagy and aging in Drosophila. Front. **Cell Dev Biol 7:** 140.

Maruzs, T., Lőrincz, P., Szatmári, Z., Széplaki, S., Sándor, Z., Lakatos, Z., ... & Sass, M. (2015). Retromer ensures the degradation of autophagic cargo by maintaining lysosome function in Drosophila. **Traffic 16:** 1088-1107.

ERZSÉBET MERNYÁK

University of Szeged
Faculty of Pharmacy
Department of Pharmacognosy

RESEARCH AREA

Semisynthetic transformations of natural products by modern organic chemistry methods. The reactions are carried out according to the principles of green chemistry, including transition metal catalysis. We also work on the preparation of fluorescent dyes (fluorophores) suitable for the fluorescent labelling of biomolecules or nature-inspired drug candidates. We investigate the potential application of the newly synthesized fluorophores as phototeranostic agents, especially in photodynamic therapy of cancer.

SELECTED PUBLICATIONS

Mernyák, E., Kovács, I., Minorics, R., Sere, P., Czégány, D., Sinka, I., Wölfling, J., Schneider, G., Újfaludi, Z., Boros, I. et al. (2015) Synthesis of trans-16-triazolyl-13α-methyl-17-estradiol diastereomers and the effects of structural modifications on their in vitro antiproliferative activities. **J. Steroid Biochem Mol Biol** 150 pp. 123, 12 p.

Jójárt, R., Laczkó-Rigó, R., Klement, M., Kőhl, G., Kecskeméti, G., Özvegy-Laczka, C., **Mernyák, E.** (2021) Design, synthesis and biological evaluation of novel estrone phosphonates as high affinity organic anion-transporting polypeptide 2B1 (OATP2B1) inhibitors. **Bioorganic Chemistry 112** Paper: 104914, 12 p.

Traj P., Hazhmat Abdolkhaliq, A., Németh A., Dajcs, S., Trisztán, Tömösi F., Lanisnik-Rizner T., Zupkó, I., **Mernyák, E.** (2021) Transition metal-catalyzed A-ring C–H activations and C(sp^2)–C(sp^2) couplings in the 13α-estrone series and in vitro evaluation of antiproliferative properties. **J Enzyme Inhib Med Chem 36:** 1 pp. 895-902., 8 p.

Senobar Tahaei, SA., Kulmány, Á., Minorics, R., Kiss, A., Szabó, Z., Germán, P., Szebeni, GJ., Gémes, N., **Mernyák, E.**, Zupkó, I. (2023) Antiproliferative and Antimetastatic Properties of 16-Azidomethyl Substituted 3-O-Benzyl Estrone Analogs. **Int J Mol Sci 24:** 18 Paper: 13749, 16 p.)

Hlogyik, T., Laczkó-Rigó, R.,* Bakos, É., Poór, M., Kele, Z., Özvegy-Laczka, C., **Mernyák, E.** (2023) Synthesis and in vitro photodynamic activity of aza-BODIPY-based photosensitizers. **Org Biomol Chem 21:** 29 pp. 6018-6027., 10 p.

MÁRIA MÉSZÁROS

HUN-REN Biological Research Centre,
Institute of Biophysics

RESEARCH AREA

The pharmaceutical treatment of central nervous system disorders is far from satisfactory due to the poor penetration of drugs to the brain tissue. The blood-brain barrier is the major obstacle to prevent potential neuropharmaceuticals to reach their targets. Nanosized drug carriers, or nanoparticles are in the focus of research efforts to develop successful drug delivery systems for the central nervous system. Drug loading to nanoparticles alone is not enough for successful delivery of drugs to the brain. In order to elevate the permeability of nanocarriers across the blood-brain barrier a specific targeting is needed. Influx transport systems are highly expressed on the cerebral endothelium in contrast to blood vessel endothelial cells of other organs. Nanoparticles targeted by the ligands of these transporters may better dock to the luminal surface of brain microvascular endothelial cells resulting in better cellular uptake into the cells and penetration of the cargo across the blood-brain barrier. Blood-brain barrier dysfunction and inflammation play central role in the pathomechanism of many central nervous system disorders. Protection of the blood-brain barrier, the inhibition of causal factors of the brain microvascular breakdown offers an innovative therapeutic target of brain diseases. Several studies confirm that long-term treatment with non-steroidal anti-inflammatory drugs such as ibuprofen reduces the risk of Alzheimer's disease by the inhibition of inflammatory cascades. The serious peripheral side effects of long-term administration of ibuprofen limits its clinical applicability. Formulation of ibuprofen with targeted nanocarriers increases the brain specific penetration of the drug and at the same time reduces treatment doses and peripheral side-effects. The expected new results contribute to the development of new targeted nanocarrier systems for better brain delivery of drugs and to prevent and treat the diseases of central nervous system.

SELECTED PUBLICATIONS

Veszelka, S., **Mészáros, M.**, Porkoláb, G., Szecskó, A., Kondor, N., Ferenc, G., Polgár, T.F., Katona, G., Kóta, Z., Kelemen, L., Páli, T., Vigh, J.P., Walter, F.R., Bolognin, S., Schwamborn, J.C., Jan, J.S., Deli, M.A. (2022) A triple combination of targeting ligands increases the penetration of nanoparticles across a blood-brain barrier culture model. **Pharmaceutics 14:** 86.

Fekete, T., **Mészáros, M.**, Szegletes, Z., Vizsnyiczai, G., Zimányi, L., Deli, M.A., Veszelka, S., Kelemen, L. Optically manipulated microtools to measure adhesion of the nanoparticle targeting ligand glutathione to endothelial cells. (2021) **ACS Appl Mater Interfaces 13:** 39018-39029.

Topal, G.R., **Mészáros, M.**, Porkoláb, G., Szecskó, A., Polgár, T.F., Siklós, L., Deli, M.A., Veszelka, S., Bozkir, A. (2021) ApoE-Targeting Increases the Transfer of Solid Lipid Nanoparticles with Donepezil Cargo across a Culture Model of the Blood–Brain Barrier. **Pharmaceutics 13:** 38.

Porkoláb, G., **Mészáros, M.**, Tóth, A., Szecskó, A., Harazin, A., Szegletes, Z., Ferenc, G., Blastyák, A., Mátés, L., Rákhely, G., Deli, M.A., Veszelka, S. (2020) Combination of Alanine and Glutathione as Targeting Ligands of Nanoparticles Enhances Cargo Delivery into the Cells of the Neurovascular Unit. **Pharmaceutics 12:** 635.

GÁBOR MOLNÁR

University of Szeged
Faculty of Science and Informatics
Department of Physiology, Anatomy and Neuroscience
MTA-SZTE Research Group for Cortical Microcircuits

RESEARCH AREA

Since the beginning of modern neuroscience it is a primary desire to understand the human cerebral cortex. How neurons build up networks and how they are able to serve higher brain functions such as cognition, complex perception, decision-making or language is still a mystery yet to be solved. The research of human brain mainly approached with noninvasive low resolution brain-imaging technologies or scalp electrode based techniques. We still are missing the information on the intricate organization of human neuronal networks. To date substantial data have been acquired from animal models investigating the physiological mechanisms. However, research on human neural circuits are more challenging due to lack of suitable tissue. Human neurons are not "scaled-up" versions of rodent or primate neurons, but have unique structural and functional properties. Our results, apart from deepening our understanding of basic features and mechanisms neuronal circuits and connections, can also provide a basis for development of proper therapies for neurodegenerations.

SELECTED PUBLICATIONS

Cserep, C., Posfai, B., Lenart, N., Fekete, R., Laszlo, Z.I., Lele, Z., Orsolits, B., **Molnar, G.**, Heindl, S., Schwarcz, A.D., Ujvari, K., Kornyei, Z., Toth, K., Szabadits, E., Sperlagh, B., Baranyi, M., Csiba, L., Hortobagyi, T., Magloczky, Z., Martinecz, B., Szabo, G., Erdelyi, F., Szipocs, R., Tamkun, M.M., Gesierich, B., Duering, M., Katona, I., Liesz, A., Tamas, G., Denes, A. (2020) Microglia monitor and protect neuronal function through specialized somatic purinergic junctions. **Science 367:** 528-537.

Molnar, G., Rozsa, M., Baka, J., Holderith, N., Barzo, P., Nusser, Z., Tamas, G. (2016) Human pyramidal to inteiencerneuron synapses are mediated by multi-vesicular release and multiple docked vesicles. **eLife:** e18167.

Molnar, G., Farago, N., Kocsis, A.K., Rozsa, M., Lovas, S., Boldog, E., Baldi, R., Csajbok, E., Gardi, J., Puskas, L.G. , Tamas, G. (2014) GABAergic neurogliaform cells represent local sources of insulin in the cerebral cortex. **J Neurosci 34:** 1133-1137.

Molnar, G., Olah, S., Komlosi, G., Fule, M., Szabadics, J., Varga, C., Barzo, P., Tamas, G. (2008) Complex events initiated by individual spikes in the human cerebral cortex. **PLoS Biol 6:** e222.

Szabadics, J., Varga, C., **Molnar, G.**, Olah, S., Barzo, P., Tamas, G. (2006) Excitatory effect of GABAergic axo-axonic cells in cortical microcircuits. **Science 311:** 233-5.

KRISZTIÁN PAJER

University of Szeged
Albert Szent-Györgyi Medical School
Department of Anatomy, Histology and Embryology

RESEARCH AREA

I am currently an Assistant Professor of Dept. of Anatomy, Histology and Embryology at the University of Szeged. I obtained my Ph.D. degree in 2014 and joined Dr. Nógrádi's laboratory studying the cure able effect of grafted stem cells and mRNA-LNP on injured spinal cord. We described that grafted undifferentiated neuroectodermal stem cells or induced pluripotenet stem cells (iPSCs) into the injured spinal cord are able to induce significant functional recovery supported by neuroprotection and extensive axonal regeneration. The grafted stem cells produced so called lesion induced secretome. These factors were not produced by the native cultured stem cells, iPSCs or the spinal cords of injured animals. Furthermore, we provided evidence that intraspinal administration of nucleotide modified mRNA-LNP encoding human IL-10 is able to induce significant morphological and functional recovery following contusion injury in rats. I have expertise in microsurgery (spinal cord contusion injury, retrograde and anterograde labelings), histology, immunohistochemistry, cell culture methods, skeletal muscle physiology.

SELECTED PUBLICATIONS

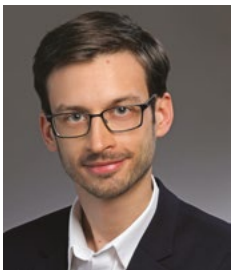
Gál, L., Bellák, T., Marton, A., Fekécs, Z., Weissman, D., Török, D., Biju, R., Vizler, C., Kristóf, R., Beattie, MB., Lin, PJC., Pardi, N., Nógrádi, A., **Pajer, K.** (2023) Restoration of Motor Function through Delayed Intraspinal Delivery of Human IL-10-Encoding Nucleoside-Modified mRNA after Spinal Cord Injury. **Research (Wash D C). 6:** 0056.

Molnár, K., Nógrádi, B., Kristóf, R., Mészáros, Á., **Pajer, K.**, Siklós, L., Nógrádi, A., Wilhelm, I., Krizbai, IA. (2022) Motoneuronal inflammasome activation triggers excessive neuroinflammation and impedes regeneration after sciatic nerve injury. **J Neuroinflammation 19(1):** 68.

Bellák, T., Fekécs, Z., Török, D., Táncos, Z., Nemes, C., Tézsla, Z., Gál, L., Polgári, S., Kobolák, J., Dinnyés, A., Nógrádi, A., **Pajer, K.** (2020) Grafted human induced pluripotent stem cells improve the outcome of spinal cord injury: modulation of the lesion microenvironment. **Sci Rep10(1):** 22414.

Pajer, K., Bellák, T., Redl, H., Nógrádi, A. (2019) Neuroectodermal Stem Cells Grafted into the Injured Spinal Cord Induce Both Axonal Regeneration and Morphological Restoration via Multiple Mechanisms. **J Neurotrauma 36(21):** 2977-2990.

Simandi, Z., **Pajer, K.**, Karolyi, K., Sieler, T., Jiang, LL., Kolostyak, Z., Sari, Z., Fekecs, Z., Pap, A., Patsalos, A., Contreras, GA., Reho, B., Papp, Z., Guo, X., Horvath, A., Kiss, G., Keresztessy, Z., Vámosi, G., Hickman, J., Xu, H., Dormann, D., Hortobagyi, T., Antal, M., Nógrádi, A., Nagy, L. (2018) Arginine Methyltransferase PRMT8 Provides Cellular Stress Tolerance in Aging Motoneurons. **J Neurosci 38(35):** 7683-7700.



MÁRTON PIPICZ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Biochemistry

RESEARCH AREA

Despite improving therapeutic options, cardiovascular diseases including myocardial infarction remain the leading cause of death. Research aiming to reduce heart damage is therefore of great importance. The heart has its own adaptive response to the cardiac injury. Various procedures can enhance this response and result in cardioprotection by reducing the injury. In addition to classical pre- and postconditioning techniques, our research group investigates pharmacological and non-pharmacological cardioprotective approaches and molecular mechanisms to alleviate cardiac injury. Certain metabolic diseases (e.g. hypercholesterolemia, diabetes) increase the risk of myocardial infarction, directly impair cardiac function and interfere with the heart's adaptive response to myocardial infarction. Our research focuses on the adverse effects of metabolic diseases as cardiovascular risk factors on cardiac function and adaptive response. We comprehensively analyse molecular changes with genomic and proteomic approaches, then we elucidate them in detail by focused studies. We also conduct experiments regarding pharmacological and non-pharmacological interventions to affect these undesirable molecular changes and to mitigate adverse cardiac effects.

SELECTED PUBLICATIONS

Pipicz, M., Kocsis, G.F., Sarvary-Arantes, L., Bencsik, P., Varga, Z.V., Ferdinandy, P., Csont, T. (2017) Low-dose endotoxin induces late preconditioning, increases peroxynitrite formation, and activates STAT3 in the rat heart. **Molecules 22:** 433.

Varga, Z.V., **Pipicz, M**., Baán, J.A., Baranyai, T., Koncsos, G., Leszek, P., Kuśmierczyk, M., Sánchez-Cabo, F., García-Pavía, P., Brenner, G.J., Giricz, Z., Csont, T., Mendler, L., Lara-Pezzi, E., Pacher, P., Ferdinandy, P. (2017) Alternative splicing of nox4 in the failing human heart. **Front Physiol 8:** 935.

Pipicz, M., Demján, V., Sárközy, M., Csont, T. (2018) Effects of cardiovascular risk factors on cardiac STAT3. **Int J Mol Sci 19:** 3572.

Szabó, M.R., Gáspár, R., **Pipicz, M.**, Zsindely, N., Diószegi, P., Sárközy, M., Bodai, L., Csont, T. (2020) Hypercholesterolemia Interferes with Induction of miR-125b-1-3p in Preconditioned Hearts. **Int J Mol Sci 21:** 3744

Demján, V., Sója, A., Kiss, T., Fejes, A., Gausz, F. D., Szűcs, G., Siska, A., Földesi, I., Tengölics, R., Darula, Z., Csupor, D., **Pipicz, M**., & Csont, T. (2021) Stellaria media tea protects against diabetes-induced cardiac dysfunction in rats without affecting glucose tolerance. **J Tradit Complement Med 12:** 250-259.

ATTILA RUTAI

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Surgical Research

RESEARCH AREA

Sepsis is one of the most challenging diseases in intensive care, with a high mortality rate despite modern, costly therapies. The septic disease process is an uncontrolled inflammatory response to infection, leading to the development of life-threatening multi-organ failure. The main difficulty in the therapy of sepsis is the heterogeneity of organ damage and the dynamic variability of the septic response, which significantly complicate the diagnosis and the use of effective OTC therapies. Nowadays, the main goal of clinical care is to eliminate the infection and, if necessary, to use organ-supportive therapies, which are not sufficient in themselves. The focus of our experiments is on new therapeutic strategies that may be able to correct the global oxygen and energy deficits that are most responsible for the development of multi-organ failure and to restore oxygen dynamic balance. In addition to reducing the inflammatory response, our therapeutic goal is to improve the function of the main elements of oxygen transport: macro- and microcirculation; and mitochondrial oxygen consumption, the key to energy production.

SELECTED PUBLICATIONS

Rutai, A., Zsikai, B., Tallósy, SP., Érces, D., Bizánc, L., Juhász, L., Poles, MZ., Sóki, J., Baaity, Z., Fejes, R., Varga, G., Földesi, I., Burián, K., Szabó, A., Boros, M., Kaszaki J. (2022) A Porcine Sepsis Model With Numerical Scoring for Early Prediction of Severity. **Front Med (Lausanne) 9:** 867796.

Tallósy, SP., Poles, MZ., **Rutai, A.**, Fejes, R., Juhász, L., Burián, K., Sóki, J., Szabó, A., Boros, M., Kaszaki, J. (2021) The microbial composition of the initial insult can predict the prognosis of experimental sepsis. **Sci Rep 11:** 22772.

Poles, MZ., Nászai, A., Gulácsi, L., Czakó, BL., Gál, KG., Glenz, RJ., Dookhun, D., **Rutai, A.**, Tallósy, SP., Szabó, A., Lőrinczi, B., Szatmári, I., Fülöp, F., Vécsei, L., Boros, M., Juhász, L., Kaszaki, J. (2021) Kynurenic Acid and Its Synthetic Derivatives Protect Against Sepsis-Associated Neutrophil Activation and Brain Mitochondrial Dysfunction in Rats. **Front Immunol 12:** 717157.

Rutai, A., Fejes, R., Juhász, L., Tallósy, SP., Poles, MZ., Földesi, I., Mészáros, AT., Szabó, A., Boros, M., Kaszaki, J. (2020) Endothelin A and B Receptors: Potential Targets for Microcirculatory-Mitochondrial Therapy in **Experimental Sepsis Shock 54:** 87-95.

Juhász, L., **Rutai, A.**, Fejes, R., Tallósy, SP., Poles, MZ., Szabó, A., Szatmári, I., Fülöp, F., Vécsei, L., Boros, M., Kaszaki, J. (2020) Divergent Effects of the N-Methyl-D-Aspartate Receptor Antagonist Kynurenic Acid and the Synthetic Analog SZR-72 on Microcirculatory and Mitochondrial Dysfunction in Experimental Sepsis. **Front Med (Lausanne) 7:** 566582.

BALÁZS SZAPPANOS

HUN-REN Biological Research Centre
Institute of Biochemistry
Synthetic and Systems Biology Unit

RESEARCH AREA

The recent emergence of the field of systems biology brought a new era in the research of evolution. The novel methods and largescale datasets enable the systematic exploration of the elements of biological systems and the interactions between them. Our group is particularly interested in studying the evolution of metabolism. By measuring the intracellular metabolite levels, that is, the metabolome in different yeasts we can assess how fast metabolism evolves and what are the driving forces behind its evolution. We are also studying the evolution of the metabolic network, that is, how can organisms gain novel enzymes and biochemical pathways to better adapt to the environmental conditions. We utilize this knowledge for strain design by discovering genetic modifications that can boost the microbial production of chemicals with industrial importance.

SELECTED PUBLICATIONS

Zampieri, M., **Szappanos, B.**, Buchieri, M.V., Trauner, A., Piazza, I., Picotti, P., Gagneux, S., Borrell, S., Gicquel, B., Lelievre, J., Papp, B., Sauer, U. (2018) High-throughput metabolomic analysis predicts mode of action of uncharacterized antimicrobial compounds. **Sci Transl Med 10:** eaal3973.

Szappanos, B., Fritzemeier, J., Csörgő, B., Lázár, V., Lu, X., Fekete, G., Bálint, B., Herczeg, R., Nagy, I., Notebaart, R.A., et al. (2016) Adaptive evolution of complex innovations through stepwise metabolic niche expansion. **Nat Commun 7:** 11607.

Notebaart, R.A., **Szappanos, B.**, Kintses, B., Pál, F., Györkei, A., Bogos, B., Lázár, V., Spohn, R., Csörgő, B., Wagner, A., Ruppin, E., Pál, C., Papp, B. (2014) Network-level architecture and the evolutionary potential of underground metabolism. **Proc Natl Acad Sci U S A 111:** 11762-11767.

Szappanos, B., Kovács, K., Szamecz, B., Honti, F., Costanzo, F., Baryshnikova, A., Gelius-Dietrich, G., Lercher, M.J., Jelasity, M., Myers, C.L., Andrews, B.J., Boone, C., Oliver, S.G., Pál, C., Papp, B. (2011) An integrated approach to characterize genetic interaction networks in yeast metabolism. **Nat Genet 43:** 656-62.

PETRA ÉVA SZILI

HUN-REN Biological Research Centre
Institute of Biochemistry
Synthetic and Systems Biology Unit

RESEARCH AREA

The spread of antibiotic resistance is one of the most pressing issues of modern healthcare. In our previous work, we developed high levels of resistance against antibiotics still in clinical development in relevant Gram-negative pathogens. Currently, the main focus of our research is to investigate the connection between the development of clinically relevant levels of resistance and changes in bacterial virulence.

SELECTED PUBLICATIONS

Nyerges, Á., Csörgő, B., Draskovits, G., Kintses, B., **Szili, P.**, Ferenc, G., Révész, T., Ari, E., Nagy, I., Balázs, B., Vásárhelyi, BM., Bihari, P., Számel, M., Balogh, D., Papp, H., Kalapis, D., Papp, B., Pál, C. (2018) Directed evolution of multiple genomic loci allows the prediction of antibiotic resistance. **Proc Natl Acad Sci 115(25):** E5726-E5735.

Szili, P., Draskovits, G., Révész, T., Bogár, F., Balogh, D., Martinek, T., Daruka, L., Spohn, R., Vásárhelyi, BM., Czikkely, M., Kintses, B., Grézal, G., Ferenc, G., Pál, C., Nyerges, Á. (2019). Rapid evolution of reduced susceptibility against a balanced dual-targeting antibiotic through stepping-stone mutations. **Antimicrob Agents Chemother 63(9):** e00207-19.

Nyerges, Á., Tomašič, T., Durcik, M., Revesz, T., **Szili, P.**, Draskovits, G., Bogar, F., Skok, Ž., Zidar, N., Ilaš, J., Zega, A., Kikelj, D., Daruka, L., Kintses, B., Vasarhelyi, B., Foldesi, I., Kata, D., Welin, M., Kimbung, R., Focht, D., Mašič, LP., Pal, C. (2020) Rational design of balanced dual-targeting antibiotics with limited resistance. **PLoS Biol 18(10):** e3000819.

DÓRA TOMBÁCZ

University of Szeged
Albert Szent-Györgyi Medical School
Department of Medical Biology

RESEARCH AREA

Genomics is the study of the structure and function of genome. The genome sequences of many organisms have now been determined. It has also been described that the mammalian genomes contain approximately 22,000 protein-coding genes, however, they only represent about 1% of the genomes. It has also been demonstrated, that almost the entire genome is transcriptionally active at both DNA strands. More and more results show that the non-protein coding RNAs have a very important role on the regulation of gene expression, on various post-transcriptional processes and on the translation. Our research projects focus on the analysis of various viruses (e. g., Herpes simplex virus, Varicella Zoster virus, Vaccinia virus, etc.). We examine the gene expression profiles and transcriptional complexity of these viruses, and also use them as model organisms for the study of our Transcriptional Interference Network (TIN) hypothesis, which propose a novel layer of genetic regulation, and is based on the interactions between the gene activities via the mechanisms of transcriptional read-through between convergent, divergent and parallel gene pairs. For these, we apply state-of-the-art sequencing and bioinformatics techniques, as well as other cutting edge technologies such as the CrispR-Cas9/dCas9 techniques, with which we generate genetically modified viruses or inducible gene expression. Our group also has bacterial- fungal- and human genomics projects (analysis of the genetic background of major depression, Alzheimer's Disease) by applying exome-, transcriptome-, methyl- and ChIP-seq techniques.

SELECTED PUBLICATIONS

Boldogkői, Z., Moldován. N., Balázs. Z., Snyder, M., **Tombácz, D.** (2019) Long-Read Sequencing - A Powerful Tool in Viral Transcriptome Research. **Trends Microbiol 27:** 578-592.

Tombácz, D., Prazsák, I., Szűcs, A., Dénes, B., Snyder, M., Boldogkői, Z. (2018) Dynamic transcriptome profiling dataset of vaccinia virus obtained from long-read sequencing techniques. **Gigascience 7:** giy139.

Tombácz, D., Sharon, D., Szűcs, A., Moldován, N., Snyder, M., Boldogkői, Z. (2018) Transcriptome-wide survey of pseudorabies virus using next- and third-generation sequencing platforms. **Sci Data 5:** 180119.

Tombácz, D., Maróti, Z., Kalmár, T., Csabai, Z., Balázs, Z., Takahashi, S., Palkovits, M., Snyder, M., Boldogkői Z. (2017) High-Coverage Whole-Exome Sequencing Identifies Candidate Genes for Suicide in Victims with Major Depressive Disorder. **Sci Rep 7:** 7106.

Boldogkői, Z., Balint. K., Awatramani. G.B., Balya, D., Busskamp,V., Viney, T.J., Lagali, P.S., Duebel, J., Pásti, E., **Tombácz, D.**, Tóth, J.S., Takács, I.F., Scherf, B.G., Roska, B. (2009) Genetically timed, activity-sensor and rainbow transsynaptic viral tools. **Nat Methods 6(2):** 127-30.

RENÁTA TÓTH

University of Szeged
Faculty of Science and Informatics
Department of Microbiology

RESEARCH AREA

Besides the bacterial flora, several fungal species are also long-term occupants of the oral microbiota. Among these, Candida are the most abundant species. Although the role of the human bacteriota and virome is well characterized, less is known about the composition of the mycobiota, let alone its role in the host. Therefore, one purpose of our project is to examine how do normal oral epithelial cells respond to the presence of commensal Candida species. We aim to explore their recognition, the corresponding signal transduction mechanisms and potential effector functions in the presence of various fungal stimuli. Since the last decade, numerous studies report alterations in the diversity of the oral microflora of immunocompromised and cancer patients (e.g. with oral squamous cell carcinoma), allowing the overgrowth of opportunistic pathogenic species (such as C. albicans and C. parapsilosis). Besides the increased probability of oral candidiasis in these patients, the abnormally altered microbiota might also influence the underlying diseases' progression. In addition to investigating the immune response regulatory effect of normal oral epithelial cells, we further aim to examine the potentially altered immunomodulatory effects of oral squamous cell carcinoma cells and to explore signaling routes that might be associated with tumor progression following fungal stimuli.

SELECTED PUBLICATIONS

Toth, R., Nosek, J., Mora-Montes, H., Gabaldon, T., Bliss, J.M., Nosanchuk J.D., Turner, S.A., Butler, G., Vagvolgyi, Cs., Gacser, A. (2019) The emergence of Candida parapsilosis: from genes to the bedside. **Clin Microbiol Rev 32:** e00111-18.

Toth, R., Cabral, V., Thuer, E., Bohner, F., Nemeth, T., Papp, Cs., Nimrichter, L., Molnar, G., Vagvolgyi, Cs., Gabaldon, T., Nosanchuk, J.D., Gacser, A. (2018) Investigation of Candida parapsilosis virulence regulatory factors during hostpathogen interaction. **Sci Rep 8:** 1346.

Toth, R., Toth, A., Vagvolgyi, Cs., Gacser, A. (2017) Candida parapsilosis secreted lipase as an important virulence factor. **Curr Protein Pept Sci 18:** 1043-1049.

Nagy, L.G., **Toth, R.**, Kiss, E., Slot, J., Gacser, A., Kovacs, G.M. (2017) Six Key Traits of Fungi: Their evolutionary origins and genetic bases. **Microbiol Spectr 5.**

Toth, R., Toth, A., Papp, Cs., Jankovics, F., Vagvolgyi, Cs., Alonso, M.F., Bain, J.M., Erwig, L.P., Gacser, A. (2014) Kinetic studies of Candida parapsilosis phagocytosis by macrophages and detection of intracellular survival mechanisms. **Front Microbiol 5:** 633.

MÁTÉ VÁGVÖLGYI

University of Szeged
Faculty of Pharmacy
Institute of Pharmacognosy

RESEARCH AREA

Bioactive natural compounds and their semi-synthetic derivatives represent a highly promising treasury of potential new drugs. Two particularly interesting naturally occurring, pharmacologically active compound groups are ecdysteroids and protoflavonoids. Ecdysteroids are present both in flora and fauna. In mammals, they are non-toxic compounds that can exert numerous beneficial non-hormonal bioactivities, such as anabolic and adaptogenic effects. Besides, our research group has discovered the particular property of notably less polar ecdysteroid derivatives to sensitize the drug resistance of both multi-drug resistant (MDR) and non-MDR cancer cells towards various chemotherapeutics. The pharmacological potential of protoflavonoids is also wide-ranging. They are intensively studied for their antitumor effects, which stem from their representatives' cytotoxic nature and their inhibitory effect on specific DNA damage response mechanisms (ATR-dependent signaling), through which they can enhance, e.g., the activity of cisplatin. Besides, considerable evidence has been revealed in recent years (e.g., inhibition of xanthine oxidase enzyme, antiviral activities) suggesting that the pharmacology of protoflavonoids might exceed their antitumor potential. The focus of our research efforts is on the structural optimization of compounds of the outlined groups with therapeutic potential, according to which semi-synthetic modifications are made on the molecules, which may result in the improvement of their chemical-physical parameters, the enhancement of their biological effects and/or the reduction of their potential disadvantageous side effects.

SELECTED PUBLICATIONS

Vágvölgyi, M., Bélteky, P., Bogdán, D., Nové, M., Spengler, G., Latif, A.D., Zupkó, I., Gáti, T., Tóth, G., Kónya, Z., Hunyadi, A. (2020) Squalenoylated Nanoparticle Pro-Drugs of Adjuvant Antitumor 11α-Hydroxyecdysteroid 2,3-Acetonides Act as Cytoprotective Agents Against Doxorubicin and Paclitaxel. **Front Pharmacol 11:** 552088.

Vágvölgyi, M., Girst, G., Kúsz, N., Ötvös, S.B., Fülöp, F., Hohmann, J., Servais, J-Y., Seguin-Devaux, C., Chang, F-R., Chen, M.S., Chang, L-K., Hunyadi, A. (2019) Less Cytotoxic Protoflavones as Antiviral Agents: Protoapigenone 1′-O-isopropyl ether Shows Improved Selectivity Against the Epstein–Barr Virus Lytic Cycle. **Int J Mol Sci 20:** 6269.

Fumagalli, G., Giorgi, G., **Vágvölgyi, M.**, Colombo, E., Christodoulou, M.S., Collico, V., Prosperi, D., Dosio, F., Hunyadi, A., Montopoli, M., Hyeraci, M., Silvani, A., Lesma, G., Dalla Via, L., Passarella, D. (2018) Heteronanoparticles by Self-Assembly of Ecdysteroid and Doxorubicin Conjugates To Overcome Cancer Resistance. **ACS Med Chem Lett 9:** 468-471.

Vágvölgyi, M., Martins, A., Kulmány, A., Zupkó, I., Gáti, T., Simon, A., Tóth, G., Hunyadi, A. (2018) Nitrogen-containing ecdysteroid derivatives vs. multi-drug resistance in cancer: Preparation and antitumor activity of oximes, oxime ethers and a lactam. **Eur J Med Chem 144:** 730-739.

GABRIELLA VARGA

University of Szeged
Albert Szent-Györgyi Medical School
Institute of Surgical Research

RESEARCH AREA

The extracorporeal circulation (ECC) can be lifesaving in conditions, accompanied by severe acute respiratory or circulatory failure, but the ECC related complications limit the application of the technique, and this reduces the group of patients who can benefit from the ECC treatment. Moreover, the complications frequently affect vital organs (kidney, brain, heart) and as a result long lasting aftercare can be necessary or in case of the most severe cases, it might even cause the death of the patient. Our main purpose is to develop and establish animal models, which will be suitable to the examination of inflammatory processes that play critical role in the pathomechanism of the ECC related complications. The other aim is to develop an innovative treatment method, the trans-oxygenator methane administration to moderate ECC associated complications.

SELECTED PUBLICATIONS

Szűcs, S., Bari, G., Ugocsai, M., Lashkarivand, R.A., Lajkó, N., Mohácsi, A., Szabó, A., Kaszaki, J., Boros, M., Érces, D., **Varga, G.** (2019) Detection of Intestinal Tissue Perfusion by RealTime Breath Methane Analysis in Rat and Pig Models of Mesenteric Circulatory Distress. **Crit Care Med 47:** e403-e411.

Bari, G., Érces, D., **Varga, G.**, Szűcs, Sz., Varga, Z., Bogáts, G., Boros, M. (2019) Methane inhalation reduces the systemic inflammatory response in a large animal model of extracorporeal circulation. **Eur J Cardiothorac Surg 56:** 135-142.

Poles, M.Z., Bódi, N., Bagyánszki, M., Fekete, É., Mészáros, A.T., **Varga, G.**, Szűcs, Sz., Nászai, A., Kiss, L., Kozlov, A.V., Boros, M., Kaszaki, J. (2018) Reduction of nitrosative stress by methane: Neuroprotection through xanthine oxidoreductase inhibition in a rat model of mesenteric ischemia-reperfusion. **Free Radic Biol Med 120:** 160-169.

Mészáros, A.T., Büki, T., Fazekas, B., Tuboly, E., Horváth, K., Poles, M.Z., Szucs, S., **Varga, G.**, Kaszaki, J., Boros, M. (2017) Inhalation of methane preserves the epithelial barrier during ischemia and reperfusion in the rat small intestine. **Surgery 161:** 1696-1709.

Boros, M., Ghyczy, M., Erces, D., **Varga, G.**, Tokes, T., Kupai, K., Torday, C., Kaszaki, J. (2012) The anti-inflammatory effects of methane. **Crit Care Med 40:** 1269-1278.

MÁTÉ VIRÁGH

HUN-REN Biological Research Centre
Institute of Biochemistry

RESEARCH AREA

During my work I focus on the genetic background of the evolution of complex multicellularity in fruiting body forming fungi. In the kingdom of Fungi, complex multicellularity emerged 8-11 times indenpendently. In fungi, the highest manifestation of complex multicellulratiy is the formation of their sexual reproductive structure, the fruiting body. Some fruting body consits of more than 30 different cell type. The molecular background of the differentiation of these cell types is, mostly unkown. The main focus of my work are the gene regulatory networks underlying the differentiation of certain cell types along with the cytoskeletal changes that determine the shape of these cells. Using comparative genomics and transcriptomics we identified several conserved regulators, that – based on their expression pattern – might play a role in fruiting body formation. I participate in the identification and functional chatracterization of these regulatrors. Furthermore, using molecular biology, histology and fluorescent microscopy I investigate the shape and the cytoskeleton of certain fruiting body cells with a special focus on the septin cytoskeleton.

SELECTED PUBLICATIONS

Merényi, Zs., **Virágh, M.**, Gluck-Thaler, E., Slot, JC., Kiss, B., Varga, T., Geösel, A., Hegedüs, B., Bálint, B., Nagy, LG. (2022) Gene age shapes the transcriptional landscape of sexual morphogenesis in mushroom forming fungi (Agaricomycetes). **Elife. 11:** e71348.

Virágh, M., Merényi, Zs., Csernetics, Á., Földi, Cs., Sahu, N., Liu, XB., Hibbett, DS., Nagy, LG. (2022) Evolutionary Morphogenesis of Sexual Fruiting Bodies in Basidiomycota: Toward a New Evo-Devo Synthesis. **Microbiol Mol Boil Rev 86:** e00019-21.

Hage, H., Miyauchi, S., **Virágh, M.**, Drula, E., Min, B., Chaduli, D., Navarro, D., Favel, A., Norest, M., Lesage-Meessen, L., Bálint, B., Merényi, Zs., Eugenio de, L., Morin, E., Martínez, TA., Baldrian, P., Štursová, M., Martynez, MJ., ... Rosso, MN. (2021) Gene family expansions and transcriptome signatures uncover fungal adaptations to wood decay. **Environ Microbiol. 23:** 5716-5732.

Nagy, LG., Varga, T., Csernetics, Á., **Virágh, M.** (2020) Fungi took a unique evolutionary route to multicellularity: Seven key challenges for fungal multicellular life. **Fungal Biology Reviews 34:** 151-169.

Kiss, E., Hegedüs, B., **Virágh, M.**, Varga, T., Merényi, Zs., Kószó, T., Bálint, B., Prasanna, AN., Krizsán, K., Kocsubé, S., Riquelme, M., Takeshita, N., Nagy GL. (2019) Comparative genomics reveals the origin of fungal hyphae and multicellularity. **Nat Commun. 10:** 4080.

Krizsán, K., Almási, É., Merényi, Zs., Sahu, N., **Virágh, M.**, Kószó, T., Mondo, S., Kiss, B., Bálint, B., Kües, U., Barry, K., Cseklye, J., Hegedüs, B., Henrissat, B., Johnson, J., Lipzen, A., Ohm, RA., Nagy, I., Pangilinan, J., ... Nagy, LG. (2019) Transcriptomic atlas of mushroom development reveals conserved genes behind complex multicellularity in fungi. **Proc Natl Acad Sci U S A. 116:** 7409-7418.

EDIT WÉBER

University of Szeged
Albert Szent-Györgyi Medical School
Department of Medical Chemistry

RESEARCH AREA

Protein-protein interactions play an important role in a number of therapeutically relevant pathophysiological processes. These interactions include large protein surfaces; hence their modulation is challenging. While small-molecule drugs cannot effectively decouple macromolecule interactions in general because of their small size, the right sized and often used antibodies have many disadvantages. Thus, proteomimetic compounds and innovative drug development strategies are required. The aim of our research group is to create new proteomimetic macromolecules from unnatural building blocks (foldamers), of which 3D structure can be predicted and programmed. Manipulating protein functions by these chemically well-defined substances is a great challenge and holds promise. We utilize foldamers as artificial self-organizing proteomimetics to modulate protein-protein interactions or to develop diagnostic tools. Our targets are proteins that have a key role in tumour development and progression. We aim to design foldamers that can bind to our target proteins and are able to inhibit their interactions, thereby modulating their function. Our goal is to construct new foldamers which can inhibit tumour growth in cells.

SELECTED PUBLICATIONS

Tököli, A., Mag, B., Bartus, É., **Wéber, E.**, Szakonyi, G., Simon, M. A; Czibula, Á., Monostori, É., Nyitray, L., Martinek, T.A. (2020) Proteomimetic surface fragments distinguish targets by function. **Chem Sci 11:** 10390.

Fenteany, G., Gaur, P., Hegedűs, L., Dudás, K., Kiss, E., **Wéber, E.**, Hackler, L., Martinek, T.A., Puskás, L., Haracska, L. (2019) Multilevel structure–activity pro ling reveals multiple green tea compound families that each modulate ubiquitin-activating enzyme and ubiquitination by a distinct mechanism. **Sci Rep 9:** 12801.

Bartus, É., Hegedüs, Z., **Wéber, E.**, Csipak, B., Szakonyi, G., Martinek, T.A. (2017) De Novo Modular Development of a Foldameric Protein-Protein Interaction Inhibitor for Separate Hot Spots: A Dynamic Covalent Assembly Approach. **Chemistryopen 6:** 236-241.

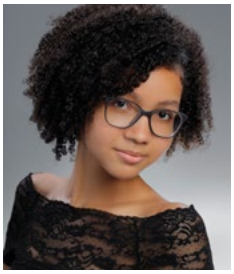
Hetényi, A., Németh, L., **Wéber, E.**, Szakonyi, G., Winter, Z., Jósvay, K., Bartus, É., Oláh, Z., Martinek, T.A. (2016) Competitive inhibition of TRPV1 – calmodulin interaction by vanilloids. **FEBS Lett 590:** 2768.

SZTE
UNIVERSITY OF SZEGED

BRC

SZEGED
SZENT-GYÖRGYI STUDENTS

1ST YEAR STUDENTS



ASAFOTEI OAKLEKIE ENÉH

National Academy of Scientist Education, 1st year
University of Szeged
Faculty of Pharmacy, 1st year

Szent-Györgyi Mentor: Judit Hohmann
Junior mentor: Noémi Crul-Tóth
Theme of research: Food-chain transfer of phytoecdysteroids: from ecological significance to human and animal health
Language: English/C2

MILÁN CSERNYÁK

National Academy of Scientist Education, 1st year
University of Szeged
Faculty of Pharmacy 1st year

Szent-Györgyi Mentor: Csaba Pál
Junior mentor: Petra Éva Szili
Theme of research: Investigation of the connection between antibiotic resistance and bacterial virulence in the case of future antibiotics
Language: English/intermediate

LILIAN KAJÁRI

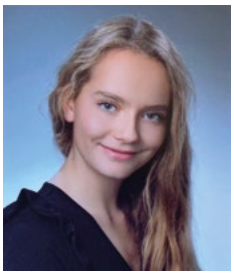
National Academy of Scientist Education, 1st year
University of Szeged
Faculty of Science and Informatics, 2nd year

Szent-Györgyi Mentor: József Maléth
Theme of research: Therapeutic approaches in the treatment of inflammatory bowel diseases associated fibrosis
Language: English/C1

BENJAMIN KOVÁCS

National Academy of Scientist Education, 1st year
University of Szeged
Faculty of Science and Informatics, 2nd year

Szent-Györgyi Mentor: Attila Hunyadi
Junior mentor: Erzsébet Mernyák
Phototheranostic synthesis based on natural compounds
Language: English/advanced



LÉNA MÉSZÁROS

National Academy of Scientist Education, 1st year
University of Szeged
Albert Szent-Györgyi Medical School 2nd year

Szent-Györgyi Mentor: Szilvia Juhász
Theme of research: The role of microbial virulence factors in the infection of human cells
Language: English/advanced

ZSOLT FERENC NAGY

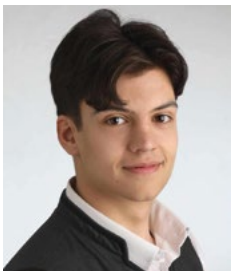
National Academy of Scientist Education, 1st year
University of Szeged
Albert Szent-Györgyi Medical School, 1st year

Szent-Györgyi Mentor: Szilvia Juhász
Theme of research: The role of microbiome in cancer development
Language: English/C1

SZABOLCS NORMAN SZATHMÁRI

National Academy of Scientist Education, 1st year
University of Szeged
Albert Szent-Györgyi Medical School 2nd year

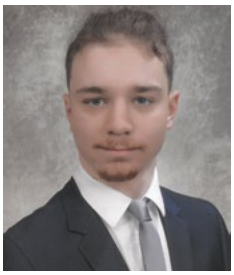
Szent-Györgyi Mentor: Antal Nógrádi
Junior mentor: Krisztián Pajer
Theme of research: mRNA therapy following spinal cord injury
Language: English/advanced



BENEDEK TARCALI

National Academy of Scientist Education, 1st year
University of Szeged
Albert Szent-Györgyi Medical School, 1st year

Szent-Györgyi Mentor: József Maléth
Theme of research: Investigation of novel therapeutic approaches in chronic pancreatitis
Language: English/intermediate



MÁRTON TILESCH

National Academy of Scientist Education, 1st year
University of Szeged
Faculty of Pharmacy, 1st year

Szent-Györgyi Mentor: István Szatmári
Junior mentor: Bálint Lőrinczi
Theme of research: Synthesis of quinoline compounds with potential MMP13 inhibitory effect
Language: English/intermediate

2ND YEAR STUDENTS

FANNI DZSUBÁK

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 2nd year

Szent-Györgyi Mentor: Tibor Pankotai
Specialization: molecular biology, bioinformatics
Language: German/advanced, English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Tumor diseases are the leading cause of death in most of the countries. In order to treat them effectively their early detection and proper, targeted treatment is crucial. In the last years with the development of DNA-based diagnostic methods it became possible to identify the mutations occurring in individual tumors. It is possible to extract DNA and RNA from non-invasive samples, such as serum diagnostics, which can be used for new generation sequencing. Our goal is to determine the gene expression patterns of individual tumor samples using methods from bioinformatics. By knowing the alterations, it is possible to apply specific and therefore more effective drug treatment. Determining the most effective treatment is of particular importance in personalized therapy, since unwanted side effects can be eliminated in this way, and as a result, the outcome of the disease can be significantly improved.

AMBITIONS AND CAREER GOALS

My main goal is that after graduating from medical university, I become a doctor with the appropriate professional knowledge, while continuing the research activity, in order to help people and contribute to their recovery. On the way to attain this, I should acquire as much knowledge as possible, which is essential for achieving my goals, and the Szent-Györgyi program provides an excellent opportunity for this.

ANDRÁS ZSOMBOR GRESCHIK

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 3rd year

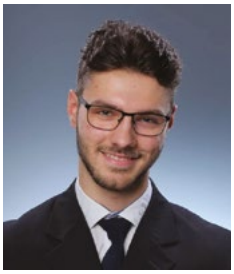
Szent-Györgyi Mentor: Márta Julianna Sárközy
Specialization: oncocardiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The significance of my research lies in investigating the cardiotoxicity and heart failure that increasingly pose a problem as side effects during oncological treatments, as well as seeking ways to prevent these symptoms. Our goal is to understand the nature of these pathological changes and compare them with the pathological changes observed in rats treated with a therapeutic substance (PIF) using onco-cardiography, histological, and molecular methods.
The expected outcome of the project is to observe a significant improvement in the cardiac abnormalities of the treated rats compared to the untreated ones (we cannot precisely estimate the exact value changes since we have not previously attempted this particular model with female animals).

AMBITIONS AND CAREER GOALS

My goal is to gain a deep understanding of the scientific problems encountered in my current project and in my future research, and to combine them with the knowledge I have acquired during my studies. Additionally, I aim to master the technical skills required for conducting research to the best of my abilities.



ANDRÁS GULYÁS

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 2nd year

Szent-Györgyi Mentor: Márta Julianna Sárközy
Specialization: biochemistry, pathophysiology
Language: English/advanced

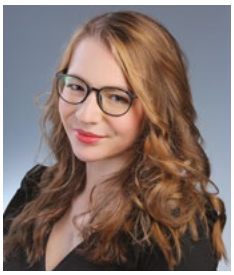
IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The prevalence of chronic kidney disease (CKD) varies between 7 and 12% in the general population worldwide. In the pre-dialysis stages of CKD, about 60% of patients are women. Cardiovascular complications, including chronic heart failure, are the leading causes of death in CKD. The CKD-associated chronic functional, structural, and electrophysiological changes of the heart are also called uremic cardiomyopathy (i.e., type 4 cardio-renal syndrome). It is characterized by diastolic dysfunction and left ventricular hypertrophy (LVH) in the heart failure with preserved ejection fraction phase (HFpEF, EF>50%) and later by more severe interstitial fibrosis and systolic dysfunction in the heart failure with reduced ejection fraction phase (HFrEF, EF<50%). However, there is no breakthrough in the therapy of uremic cardiomyopathy. Its treatment remains largely symptomatic by well-known pharmaceuticals used in other forms of heart failure (e.g., diuretics, RAAS inhibitors, etc.). Therefore, it is necessary to establish clinically relevant uremic cardiomyopathy models and to investigate the underlying molecular mechanisms for the development of preventive, diagnostic, and therapeutic strategies.

Our aim is to i) detect molecular changes (myocardial miR / mRNA targets and proteins) to identify potential new diagnostic markers and therapeutic targets and ii) test new agents potentially suitable for the prevention of the development of uremic cardiomyopathy. We hope that the findings of the present project can be used in patient care in the future.

AMBITIONS AND CAREER GOALS

My goal is to get an insight into scientific research, to deepen my knowledge in my field, to learn the necessary technics, to broaden my scope and to use the acquired experience and knowledge to develop a complex way of thinking, which I'll be able to use in medical practice. The Academy's program gives an excellent opportunity to reach these goals and I hope this helps me to become active and successful as a medical doctor and as a researcher as well in the future.



DÓRA ALEXANDRA GYÉMÁNT

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 2nd year

Szent-Györgyi Mentor: Máté Manczinger
Specialization: immunology, bioinformatics
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

One of the greatest healthcare challenges of the present time is the treatment of cancer. Our bodies contain immune cells that could potentially destroy tumors; however, certain inhibitory molecules prevent their function. During the oncology revolutionizing immunotherapy using checkpoint inhibitors, these inhibitory molecules are blocked, allowing T cells to become active and trigger an anti-tumor immune response. Indeed, while the effectiveness of immunotherapy is significantly higher than chemotherapy in many tumor types, several clinical studies have also shown that half of the patients do not respond effectively to the treatment. Since the treatment comes with high costs and, in some cases, severe side effects, there is a need to explore biomarkers that indicate the success of immunotherapy. Our goal is to utilize various databases and machine learning methods to identify factors (e.g., age, tumor stage, gender, etc.) that characterize the extent of immune selection, which can indirectly predict the success of immunotherapy.

AMBITIONS AND CAREER GOALS

During my university years, my main goal is to acquire as much knowledge and experience as possible in both research work and clinical practice. I believe that a good physician or researcher can truly excel in their own field by closely collaborating with professionals from the other discipline. During my research work, I aim to thoroughly explore a specialized field, learn efficient processing of academic literature, and also acquire relevant practical knowledge in the field of bioinformatics which will be inevitable regarding the medical and scientific field in the future.

LUCIEN LEMAITRE

National Academy of Scientist Education,
2nd year
University of Szeged
Szent-Györgyi Albert Medical School,
2nd year

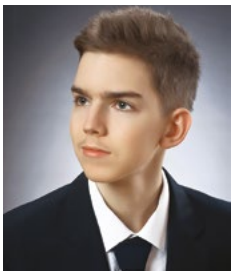
Szent-Györgyi Mentor: Mária Deli
Junior mentor: Ilona Gróf
Specialization: cell biology, pharmacology
Language: English/advanced, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

I have joined research in the fields of biomedicine and pharmacology on models of the blood-brain barrier and other biological barrier systems in the Biological Barriers Research Group. The importance of these investigations is that many drug candidates developed for the diseases of the central nervous system are inefficient because the blood-brain barrier, formed by the endothel cells of the brain capillaries, blocks drug penetration into the brain tissue. Blood-brain barrier characteristics, such as the expression of transporter proteins, display significant species variety, therefore the animal cells and models do not faithfully mimic the function of the human blood-brain barrier. In order to increase the success of preclinical drug studies, cell culture based models with a complexity close to the human blood-brain barrier are necessary. At present endothelial cell models differentiated from stem cells represent the highest level of this technology. However, the barrier function of these models is weak. The goal of my research work is to contribute to the creation of a model with complex barrier features. The new complex human blood-brain barrier model will help the investigation of drug candidates and therapeutic nanocarriers in preclinical studies.

AMBITIONS AND CAREER GOALS

As a medical student my primary aims are to obtain a medical degree, to find the most appropriate medical specialty and to do comprehensive clinical work in that field. Studying at the university and participating in basic research at the same time offer a wide range of opportunities therefore I would like to continue both activities in the future as well. For this purpose, I would like to apply for an MD-PhD programme. During my graduate and/or postgraduate studies I would also like to gain further research experience in the laboratory of one of the international mentors of the program.



CSONGOR BENCE LUDÁNYI

National Academy of Scientist Education,
2nd year
University of Szeged
Szent-Györgyi Albert Medical School,
3rd year

Szent-Györgyi Mentor: Gábor Tamás
Specialization: neurophysiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

In the vertebrate central nervous system, the cerebral cortex processes sensory information, which, combined with memory and experience, creates complex behavior. Joining the ELKH-SZTE Cortical Microcircuits Research Group, I perform electrophysiological tests on samples from rodents and on human samples originate from neurosurgical operations using the in vitro patch clamp method. Our main goal is to investigate the basic functioning and synaptic connectivity of the neuronal networks present in the cerebral cortex, especially in the connections containing inhibitory GABAergic interneurons.
The less profession-specific goal of my research is the acquisition and development of general skills such as problem-solving ability, creativity, cooperation, professional humility, and respect for my experienced mentors and colleagues.

AMBITIONS AND CAREER GOALS

As a member of the ELKH-SZTE Cortical Microcircuits Research Group, my professional goal is to learn electrophysiological methods and their application in experiments. My further aim is to acquire a critical way of thinking through conducting experiments and by having professional consultations on them, which will later advance my service as a doctor.

BENJÁMIN PASKUJ

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 3rd year

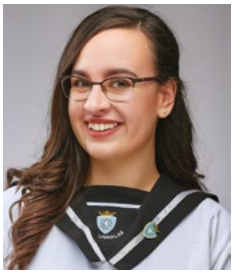
Szent-Györgyi Mentor: István Baczkó
Junior mentor: Tibor Hornyik
Specialization: cardiac electrophysiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The prevalence of heart failure can reach 10% over the age of 70 so maintaining the performance of the heart is critical. In recent years, several studies have been published on the effect of sodium-glucose cotransporter-2 (SGLT2) inhibitors, such as empagliflozin which was able to reduce the occurrence of cardiovascular mortality and heart failure by almost 25% from the presence of type 2 diabetes mellitus. Although empagliflozin is currently mainly used for the treatment of type 2 diabetes mellitus but based on clinical experience, its beneficial effect justifies experimental laboratory testing of empagliflozin.
During the cardiac electrophysiological examination of the pharmacon, we use rabbit right ventricular preparations and the measurements are performed with a standard conventional microelectrode technique. In the future we plan to use patch-clamp technique in order to understand deeper the processes. We will use other animal models and other preparations to correctly interpret the results and fully clarify the effect, if it is necessary.

AMBITIONS AND CAREER GOALS

Since cardiology has been the center of my interest based on my medical studies so far, my primary goal is a deeper understanding of the functioning of heart and the entire cardiovascular system. Through my current research, I will be able to understand a very progressive and complex field of cardiology, (cardiac electrophysiology) starting with the cellular electrical phenomena of the heart. I hope that the experience I gained during this work will contribute to use my knowledge later in both research and patient care for the benefit of patients.



ZSÓFIA ILONA PISZMAN

National Academy of Scientist Education, 2nd year
University of Szeged
Faculty of Pharmacy, 3rd year

Szent-Györgyi Mentor: Rita Ambrus
Specialization: pharmaceutical technology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Today, one of the leading causes of death worldwide are chronic lung diseases, including COPD (chronic obstructive pulmonary disease) and pneumonia, both taking millions of lives every year. Other lung diseases, such as cystic fibrosis and asthma can significantly worsen the quality of life of people suffering from the disease and shorten their life expectancy. It is key to develop effective and modern therapies for the treatment of the diseases. Nanotechnology and nanomedicines are a promising sector of innovative drug development. The goal of our research is to find new and effective therapies for the treatment of lung diseases, using nano- and micro particles and targeting pulmonal delivery. The advantages of inhalations compared to traditional oral administration are for example targeted drug delivery and lowered drug doses, therefore moderate systemic side effects.

AMBITIONS AND CAREER GOALS

As a pharmacy student, it is important to me to get to know the world of scientific research during my university studies and to acquire competences and experiences that can be beneficial later in my carrier as researcher. My goal is to contribute to the development of new and innovative formulations with my future work and research as a pharmacist, that can later be used as medicine to effectively improve patients' conditions, thus ensuring a better life for them.

DOROTTYA ANNA SZAFIÁN

National Academy of Scientist Education, 2nd year
University of Szeged
Faculty of Science and Informatics, Biology, 2nd year

Szent-Györgyi Mentor: László Nagy
Junior mentor: Máté Virágh
Specialization: fungal genomics
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Although fungi are amazing creatures, outstandingly important from a human point of view in healthcare, nutrition, or industrial fields, until now their evolution and morphogenesis is surprisingly poorly understood. Getting to know them better can open up a range of biotechnological applications. As a member of the Lendület Fungal Genomics and Evolution Group, I investigate the regulatory effect of conserved transcription factors on the development of complex multicellular structures in mushroom-forming fungi.

AMBITIONS AND CAREER GOALS

Within the framework of the program of the National Academy of Scientist Education, I can be a member of a fantastic research group that examines several different topics and uses diverse methods, of which I would like to get to know and learn as much as possible, to become a useful member of the group, and to be able to use the knowledge and experience acquired here in my future projects.

ZORKA SZOLLÁR

National Academy of Scientist Education, 2nd year
University of Szeged
Szent-Györgyi Albert Medical School, 2nd year

Szent-Györgyi Mentor: Tibor Pankotai
Specialization: molecular biology, bioinformatics
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The number of diagnosed cancer cases is increasing year by year. The emerging advanced techniques in molecular pathology provide opportunities for early diagnosis of tumors and targeted treatment of identified tumors, with the combination of these approaches ensuring the highest chances of survival. From tissue samples obtained during routine clinical procedures, as well as from non-invasive samples obtained through serum diagnostics, DNA and RNA can be isolated, which are suitable for next-generation sequencing studies. By analyzing their alterations, we can diagnose the nature of the tumor and make personalized therapeutic recommendations, determining the most effective anti-cancer drug for the patient.
The technological basis of liquid biopsy is that the DNA of deceased tumor cells enters the bloodstream. Therefore, through a simple blood draw, tumor DNA and the alterations within it can be detected from the obtained plasma. This technology allows us to detect early-stage tumors and is more cost-effective than procedures such as CT scans or MRIs. The aim of our research is to gain a better understanding of certain types of tumors through next-generation sequencing studies, thus facilitating their diagnosis and treatment.

AMBITIONS AND CAREER GOALS

In the Szent-Györgyi program, I would like to develop and acquire skills that can be useful in my future research work. I want to work towards helping people suffering from cancer and contribute to the advancement of diagnostic technologies and personalized therapies.

MÁRK VIKTOR TRESZTIÁN

National Academy of Scientist Education,
2nd year
University of Szeged
Faculty of Science and Informatics, Biology,
2nd year

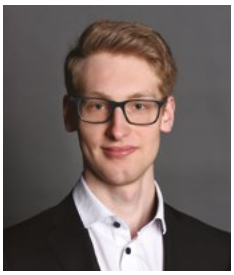
Szent-Györgyi Mentor: Tamás Martinek
Junior mentor: Zsófia Hegedüs
Specialization: pharmaceutical chemistry
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Our goal is to develop methods for the synthesis and screening of non-natural multivalent ligands, targeting protein-protein interactions that play a key role in cancer, such as the P300/HIF-1alpha interaction. This interaction regulates the hypoxic response and its inhibition leads to decreased cancer cell angiogenesis and metastasis. We designed a method where the non-natural ligands are encoded by a DNA tag and multivalent ligands can be constructed in presence of a DNA template. The DNA template allows amplification and indentification of the ligands, furthermore it can be re-used in a subsequent synthetis and selection, leading to an in vitro evolution cycle. The method can be applied to other protein targets, and the identified ligand would be therapeutically relevant in cancer.

AMBITIONS AND CAREER GOALS

My goal as a Szent-Györgyi Student is to deepen my understanding of methods to manipulate therapeutically significant protein targets. To learn and help the development of techniques, which could later be used in pharmaceutical research, techniques that are necessary for the synthesis of target proteins and ligands, their characterisation and to perform biophysical examinations.



BOTOND DÁVID VINCZE

National Academy of Scientist Education,
2nd year
University of Szeged
Szent-Györgyi Albert Medical School,
2nd year

Szent-Györgyi Mentor: Csaba Pál
Specialization: antibiotic resistance, experimental evolutionary biology
Language: German/advanced, English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

My goal is a more thorough understanding of cross-effects and resistance mechanisms between antibiotics. This will also contribute to the development of targeted therapeutic strategies and drugs that may be able to inhibit the growth and survival of multidrug resistant microorganisms.
Antibiotics are increasingly becoming ineffective against resistant microorganisms, with serious consequences for global healthcare. The results of my research can contribute to new informations about resistance mechanisms, help health professionals identify and treat resistant microorganisms, and serve as a basis for developing new antibiotics and reducing resistance, maintaining the effectiveness of antimicrobial therapies and preventing the spread of resistant microorganisms.

AMBITIONS AND CAREER GOALS

My goal is to gain knowledge beyond my university studies and to contribute to the scientific community in order to gain a deeper understanding of the field of antibiotic resistance. My short-term goal is to develop a new effective strategy for the treatment of multidrug-resistant bacteria with existing and experimental active substance, which can be crucial in the treatment of infectious diseases. I want to develop my problem-solving skills, ask better questions, and refine my data analysis and evaluation skills. These skills are essential for the foundation of my long-term goal, my research career.

3RD YEAR STUDENTS

BARBARA AMBRUS

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

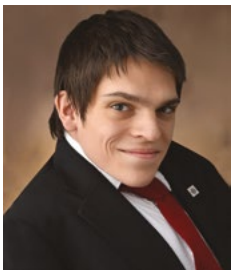
Szent-Györgyi Mentor: Zsuzsanna Bata-Csörgő
Junior mentor: Renáta Bozó
Specialization: dermatology, psoriasis
Language: English/advanced, Italian/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Psoriasis vulgaris is an immune-mediated, multifactorial, chronic skin disease, which is primarily caused be the hyperproliferation of keratinocytes and the infiltration of immune cells. There are several therapies with a short-term effect but there is no available treatment strategy which could entirely prevent the recureence/ spread of the disease. Psoriasis is characterized by well-demarcated, scaly plaques and uninvolved, healthy-looking skin, referred to as non-lesional (NL) skin. There is now strong evidence that non-lesional (NL) psoriatic skin, despite its normal appearance, represents an intermediate state between healthy and lesional skin. Extracellular matrix could play an important role in maintaining skin in NL condition, and the molecular changes in NL skin is a completely new approach. Thereby the aim of my research is to examine the changes of extracellular matrix and its regulating mechanisms in NL skin, which could be responsible for maintaining the NL phenotype. Proteases and protease inhibitors are known to play role in the regulation of extracellular matrix components, therefore our aim is to compare the expression of proteases and protease inhibitors in lesional, non-lesional and healthy skin.

AMBITIONS AND CAREER GOALS

As a member of the National Academy of Scientist Education I have the opportunity to experience all the aspects of laboratory work, along with its laborious and pleasurable side, and provides a strong background for my future career as a doctor or a researcher, both academically and socially. My long-term goal is not just to partecipate in a clinical research, but to come up with own ideas, which humankind could directly benefit from.



GERGŐ ZALÁN BIRÓ

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: Tamás Csont
Junior mentor: Márton Pipicz
Specialization: biochemistry, myocardial function
Language: English/intermediate, German/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Cardiovascular diseases are still the leading causes of death today. Obesity and its associated, or isolated metabolic disorders (eg. hypercholesterolemia, diabetes) have a negative effect on heart function and increase the risk of myocardial infarction and reduce the heart's ability to adapt to heart attack. Some findings indicate that the environmental effects on the mother can also cause alterations in the offspring, such as abnormal heart function, which may be due to epigenetic changes. However, the effects of maternal high blood cholesterol on the hearts of adult offspring have not been studied to date. One of the aims of our research group is to investigate the cardiac function of the offspring of such mothers and the adaptation of the heart to infarction in animal experiments. Furthermore, we investigate whether hypercholesterolemia causes epigenetic changes in the heart that may be associated with adverse cardiac effects, whether these are inheritable, and if so, whether they can be reversed by medication or lifestyle interventions. We hope that our research will contribute to a detailed understanding of the cardiac effects of maternal metabolic abnormalities in the offspring and to the development of treatment possibilities.

AMBITIONS AND CAREER GOALS

I would like to serve society as a specialist worthy of the title of Doctor of Medicine, both in terms of expertise and humanity. In addition to research, I am also attracted to clinical medicine, so I wish to combine the two fields during my career.

ZSOMBOR ESKÜDT

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: Áron Szabó
Specialization: drosophila genetics, glial degradation
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

One of greatest medical challenge today is the effective cure of people suffering from a neurodegenerative disease. For most of these diseases there is no therapy yet. In order to develop therapies it is important to understand which enzymes play a role in autophagic processes after nerve injury. These enzymes are evolutionary conserved, so this processes can be excellently examined in fruit flies (Drosophila melanogaster). In our model animal we can see which factors are important in STAT mediated autophagy. Our long time goal is the understanding of glial activation and to have a better view on the early transcriptional response after injury.

AMBITIONS AND CAREER GOALS

As a medical student my goal is to do research that can be well translated into human medicine. I hope that the experience gathered in the lab will make me able to work as a researcher even after graduation. Currently my most important goal is to make the best and most comprehensive article possible, out of my research topic.

BÁLINT ENDRE FEKETE

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: Bálint Kintses
Specialization: synthetic biology, genome engineering
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The emergence of antibiotic resistant pathogens is a growing threat in the global healthcare. The conventional treatments based on antibiotics are losing their efficacy. An alternative solution could be the use of bacteriophages (also phages). The host range (which bacteria can a phage infect) is determined by the proteins located on the tail end of the phage. The goal of the research is designing phages with specific tail proteins by the means of synthetic biology, so that the phage will only recognize the disease causing bacteria exclusively. To prevent the prevalence of resistance against the bacteriophage we can change these proteins while keeping the desirable properties.

AMBITIONS AND CAREER GOALS

During the Szent-Györgyi Program I got my chance to start my scientific work during my university studies. I find this instance of encounter of synthetic and microbiology rather fascinating. My goal is to be able to continue my scientific work after finishing my studies, even alongside of practising medicine.

ADÉL LÜVI

National Academy of Scientist Education,
3rd year
University of Szeged,
Faculty of Science and Informatics, Biology,
3rd year

Szent-Györgyi Mentor: Imola Wilhelm
Specialization: tumour biology
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

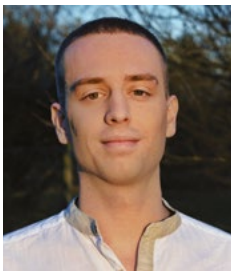
One of the most important roles of the neurovascular unit – which is built up by cerebral endothelial cells, pericytes, glial cells, and neurons – is to form the blood-brain barrier. In order to form brain metastases, tumour cells – originating principally from malignant melanoma, breast carcinoma and lung cancer – have to migrate through the blood-brain barrier, the main function of which is to prevent the penetration of toxic substances to the brain. Therefore, metastatic cells which are able to extravasate into the brain are protected from therapeutic drugs by the blood-brain barrier itself. This is the main reason why brain metastases have an extremely poor prognosis. According to our group's results, not only brain endothelial cells, but pericytes can also increase survival of the tumour cells. Currently, we are investigating whether pericytes protect tumour cells against chemotherapeutic drugs. However, not only pericytes influence the tumour cells, but this is a mutual interaction. In our experiments, we want to test how brain metastatic breast cancer cells communicate with pericytes and what changes are induced by tumour cells in pericytes to contribute to the formation of the metastatic niche. Understanding of these mechanisms may contribute to the development of novel therapeutic methods.

AMBITIONS AND CAREER GOALS

During my research work, my ambition is to contribute to the understanding of brain metastases and therefore, to help people suffering from this tumour disease. In the following years, I want to learn new methods, to improve my scientific skills, and to be a useful member of our research group with the final goal of being able to use this acquired knowledge later in my own projects.

PUBLICATIONS

Mészáros, Á., Molnár, K., Fazakas, C., Nógrádi, B., **Lüvi, A.**, Dudás, T., Tiszlavicz, L., Farkas, AE., Krizbai, IA., Wilhelm, I. (2023) Inflammasome activation in peritumoral astrocytes is a key player in breast cancer brain metastasis development. **Acta Neuropathol Commun11(1):**155.



ISTVÁN GELLÉRT MAGYARY

National Academy of Scientist Education,
3rd year
University of Szeged,
Faculty of Science and Informatics, Biology,
3rd year

Szent-Györgyi Mentor: Balázs Papp
Junior mentor: Balázs Szappanos
Specialization: systems biology, metabolomics, bioinformatics
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Recent advances in technology made metabolomics an integral part of systems biology research. Despite the surge in popularity in metabolomics, the processes governing the evolution of metabolite levels are still largely unknown. One of our lab's focuses has been the emerging field of evolutionary metabolomics, i.e. the evolution of metabolite concentrations. These previous analyses have focused on the between-species differences of metabolite concentrations with the help of data from multiple mammalian and yeast species. Among the findings were the discovery of simple molecular traits that govern the extent of evolutionary conservation. One such principle is that metabolites involved in human diseases have highly conserved concentrations between species, indicating that evolution permits less changes in metabolites that have a high health impact. Building on these findings, I will study the principles driving metabolome variation within human populations. Specifically, I will test whether the same factors govern the evolution of metabolite concentrations across species as within human populations. For my research I use a dataset of hundreds of serum metabolites from a healthy human population. Ultimately, the results will give new insights into why some metabolites are more variable between individuals than others and may inform the discovery of new biomarkers.

AMBITIONS AND CAREER GOALS

My career goal is to conduct research in the research field of personalised omics as a bioinformatician, a subfield of systems biology where the long-term goal is to help improve people's quality of life with the help of new discoveries and contribute to the early diagnoses of pathological processes. Throughout my studies I also plan on acquiring knowledge in statistics and data science and participating in relevant networking events.

GERGŐ DÁVID SVORENJ

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: Attila Gácser
Junior mentor: Renáta Tóth
Specialization: microbiology, immunology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

My research topic is based on recent observations, that inform us about the fact that besides the growing number of fungal infections, caused by Candida species, they also contribute to the progression of certain diseases. One such disease is oral squamous cell carcinoma. It has been shown that the presence of certain Candida species, such as C. albicans, the migration and potentially invasive properties of tumor cells increase following the tumor-microbe contact. The current aim of the research group, and my project as well, is to further investigate this phenomenon and to examine what molecular processes could be responsible for this effect. Identification of such processes will lead to better understanding of the complexity of microbe-tumor interactions, and may contribute to health care advancements. Understanding of these mechanisms may contribute to the development of novel therapeutic methods.

AMBITIONS AND CAREER GOALS

My ultimate aim is to achieve proper fundamentals regarding my research field, as well as to gain in-depth insights and deep knowledge into the research field of immunology and microbiology. My long-term plans enhance after every single goal achieved, the sky is the only limit. My current aim is to join the scientific community, acquire all of the basic skills needed for fundamental research, participate in a project, learn how to interpret the results and how to insert them in the current standing of the research topic.

DÓRA JULIANNA SZABÓ

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

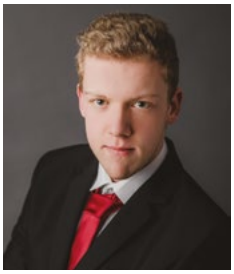
Szent-Györgyi Mentor: László Dux
Specialization: Skeletal muscle
Language: English/advanced, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Skeletal muscle demonstrates a high degree of regenerative capacity repeating the embryonic myogenic program. The empairment of this program is the cause of numerous illnesses. One of them, is the rhabdomyosarcoma, which is the most common sarcoma in childhood. Our research team works on understanding the physiological and pathological molecular background of this regeneration program. At present, syndecan-4 is observed the most, which is a transmembrane protein, that contributes to several mechanisms, like cell adhesion and migration, cell proliferation or cytokinesis, therefore tumorigenesis. By unfolding the role of syndecan-4, we could get closer to understanding the illnesses regarding the skeletal muscle, and also to their successful treatment.

AMBITIONS AND CAREER GOALS

As a Szent-Györgyi student, I have the opportunity to get an insight into the world of researches, improve in a motivating environment and broaden my knowledge, as well as challenge myself day by day. After finishing medical school, I would like to do my PhD, then work as a biomedical researcher.



NORMAN NOEL TANNER

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: Anikó Keller-Pintér
Specialization: Biochemistry
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Cell migration is absolutely necessary in the formation of the tissues, in differentiation and in regeneration. Besides that the cell migration is also an important factor in the metastasis of tumour cells. Syndecan-4 is a transmembrane protein which has a crucial role in the process that lead to efficient cell migration. The syndecan-4 is able to bind growth factors as a receptor to begin important signal transduction processes that are necessary to the cell migration. The main purpose of our research is to get a deeper understanding of the cell migration and the role of the syndecan-4 protein in this process in muscle regeneration and in rhabdomyosarcoma.

AMBITIONS AND CAREER GOALS

My greatest objective is to become a good doctor with a wide knowledge in medicine and science. To achieve that, during my university years I would like to get scientific knowledge alongside the clinical knowledge. I hope that I can use these experiences in my clinical carrier and also in research.

ISTVÁN TÓTH

National Academy of Scientist Education,
3rd year
University of Szeged,
Albert Szent-Györgyi Medical School,
3rd year

Szent-Györgyi Mentor: István Krizbai
Specialization: neuroscience
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Research in recent years supported the idea that both aging and a significant part of age-related diseases of the central nervous system are due to the inadequate functionality of the neurovascular unit that coordinates the interaction between the cerebral circulation and the functioning of the central nervous system. The physiological functioning of the nervous system requires a precisely regulated microenvironment, which is maintained by the aforementioned neurovascular unit through its two main functions (formation of the brain-blood barrier and neurovascular coupling). The main purpose of our research is to understand the functioning of the neurovascular unit more precisely in aging and age-related diseases of the brain. We plan to focus on pericytes and cerebral endothelial cells. In addition, using endothelial precursor cells we are looking for regenerative mechanisms that could provide an opportunity to maintain the functionality of neurovascular unity, thus contributing to the prevention of cognitive disabilities in elderly people.

AMBITIONS AND CAREER GOALS

During my undergraduate studies, I want to become a useful member of the research team. After completing my medical studies, I would like to get a PhD and gain experience abroad to gain as much knowledge as possible, which I can later use in my own research to become an internationally recognized researcher and help the development of science.

4TH YEAR STUDENTS

CSENGE BOCZ

National Academy of Scientist Education, 4th year
University of Szeged,
Faculty of Pharmacy, 4th year

Szent-Györgyi Mentor: Mónika Kiricsi
Junior mentor: Nóra Igaz
Specialization: nanoparticles, tumor stroma
Language: English/advanced, German/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Nowadays many people are affected by some kind of cancerous disease. Tumorcells are able to change their microenviroment, thereby creating the ideal conditions to multiply, migrate and become malignant. In this process stromal cells have a major role. These are altered functioned, cancer associated fibroblasts and immune cells. Targeting these cells is a potential therapeutic method. Nanoparticles can be used in the treatment of tumors, and they have several beneficial impacts, in contrast with the traditional cytotoxik molecules. In our research group we examine the anti-tumor effects of metal nanoparticles on stromal cells. Our goal is to get a better understanding of the communication between the cancer cells and their microenviroment, and recon the cellular and molecular events behind this process. This could provide relevant information in the fields of cancer research, and give the opportunity to develop new diagnostic techniques and treatments.

AMBITIONS AND CAREER GOALS

During my studies I would like to acquire the skills that will be really useful in my future work. I find it important to deepen my knowledge, and get a first-hand experience about what it is like to work in a laboratory and be part of a research group. My primary goal is to become a researcher and take part in the developement of novel therapeutic strategies.

DORINA KOVÁCS

National Academy of Scientist Education, 4th year
University of Szeged,
Faculty of Dentistry, 4th year

Szent-Györgyi Mentor: Bálint Kintses
Specialization: antibiotic resistance
Language: German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Testing resistance evolution with predictive screens is an imperative step of antibiotic development. These screens help to choose the lead molecules for further drug development which are less prone to resistance evolution, and thus may remain effective for years. In the laboratory of my mentor, Bálint Kintses, I'm able to join the development of a platform that accurately predicts which resistance genes will be acquired by disease-causing bacteria via horizontal gene transfer to eradicate the efficacy of a future antibiotic. We would achieve this strategic aim by testing resistance evolution in an experimental system resembling the real-life clinical environment, unlike the current technologies that use oversimplified experimental conditions. The goal is to provide a unique toolset that supports the development of promising antibiotic candidates which may remain effective for years once on the market.

AMBITIONS AND CAREER GOALS

I want to develop my theoretical and practical knowledge by taking advantage of the opportunities offered by the Szent-Györgyi program, and by learning the most possible from my Mentor. My goal is to arrange this acquired competence in the scientific research, thereby being able to cooperate in solving major scientific questions.

BENCE NAGYMIHÁLY

National Academy of Scientist Education,
4th year
University of Szeged,
Albert Szent-Györgyi Medical School,
4th year

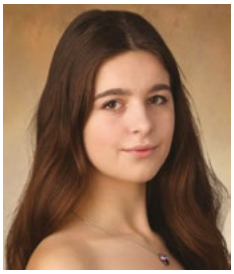
Szent-Györgyi Mentor: Tamás Martinek
Junior mentor: Edit Wéber
Specialization: Molecular biology, protein analysis techniques
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Protein-protein interactions play a role in a number of pathophysiological processes, the manipulation of which can be therapeutically beneficial. Targeting extensive protein surfaces, however, is difficult with small molecules. For this purpose, artificial agents with higher interaction surface area, e.g. protein mimetics are required. Artificial self-assembling polymers (foldamers) can inhibit protein-protein interactions. The advantages of foldamers are that they have a designable and stable secondary structure, have a larger surface area than small molecule drugs, are resistant to proteases and are less immunogenic than antibodies. We are focusing on PCNA and on Rad6 proteins. PCNA is essential for DNA replication, however, its ubiquitination promotes error-prone DNA replication and allows cancer cells to survive. Rad6 plays a role in the ubiquitination of PCNA. Our goal is to inhibit PCNA ubiquitination with foldamers by blocking the key protein-protein interactions of PCNA and Rad6. We construct the foldamers by linking small-sized, protein surface mimetic building blocks, and innovative optimisation methods, such us dissipative systems are applied. Our compounds could serve as novel anti-tumour agents.

AMBITIONS AND CAREER GOALS

During my work and studies, my aim is to acquire as much theoretical and practical knowledge as possible, so that I can later become an active participant not only in the clinical field, but also in the scientific field. The opportunities provided by the National Academy of Scientist Education will enable me to acquire scientific knowledge on which I can build and guarantee my development in the future. I would like to adopt the concepts and perspectives I have learned here, so that I can later, in my individual work, come up with my own unique ideas to influence the development of the field and use my knowledge to help people beyond the sickbed.



EMESE KINCSŐ PÁLI

National Academy of Scientist Education,
4th year
University of Szeged,
Albert Szent-Györgyi Medical School,
5th year

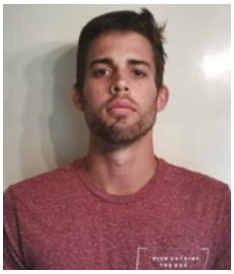
Szent-Györgyi Mentor: Szilvia Veszelka
Junior mentor: Mária Mészáros
Specialization: cell biology, pharmacology
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Cyclodextrins are versatile sugar molecules that can act both as medicines and as nanocarriers of other active ingredients. Cyclodextrins interact with lipid membranes and can selectively remove lipids from cell membranes. Some cyclodextrins are used as therapeutic drugs, while others are currently tested in clinical studies to treat human neurological diseases, including Alzheimer's disease. It is still a question whether cyclodextrins are able to cross the blood-brain barrier, the gatekeeper and protector of the central nervous system, which blocks the entry of the majority of drug molecules. The Biological Barriers Research group has an expertise in modelling and studying the blood-brain barrier. Our goal is to test different unmodified and modified cyclodextrin molecules on human cell based models of blood-brain barrier. With the help of fluorescent tags we will measure the interaction of cyclodextrins with the cells of the blood-brain barrier, namely, brain endothelial cells, pericytes and astrocytes. We will determine cellular toxicity, the entry of the cyclodextrines to the cells and using a complex model with three cell types the crossing of cyclodextrin across the barrier. These studies will help to determine if cyclodextrins need to cross the blood-brain barrier to act directly on the neuronal cells, or they can exert therapeutic effects without entering the central nervous system. Our results will help in the future therapeutic application of modified cyclodextrins in diseases.

AMBITIONS AND CAREER GOALS

In the course of my work, it is especially essential for me to accomplish activities that are useful and beneficial for society, and I have the opportunity to do so in the Biological Barriers Research Group. Drug delivery research not only has a great future ahead, but its success also promises to make human lives easier. My personal intentions include actively participating in Hungarian scientific life both as a doctor and a researcher. The possibilities provided by the Szeged Scientist Academy open unique gates to reach my goals.



DOMONKOS JÁNOS PERÉNYI

National Academy of Scientist Education,
4td year
University of Szeged,
Albert Szent-Györgyi Medical School,
5th year

Szent-Györgyi Mentor: Petra Hartmann
Junior mentor: Tamara Illésné Horváth
Specialization: mitochondrial respirational activity
Language: German/intermediate, English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The main goal of the usage of profilactic antibiotics is to prevent infections that could occur in connection with surgical interventions. Several studies have proved, that properly applied antibiotical profilaxis plays an important role in the prevention of wound-infections. However, the effect of antibiotics is not confined only to the bacterias. Depending on the concentration of the agent and the duration of the treatment, it can cause different deformities in the tissues and cells, leading to various side-effects. Effects causing mitochondrial disfunction have been proved in cases of several antibiotics, that were followed with increased reactive oxigen species (ROS) production, after which tissue-damage can emerge. To find a proper solution for these problems, we started to experience with some antibiotics that not have been used before. During our research we use the third generational ceftriaxone and the poorly absorbed rifaximine. The goal of our research is to examine the effects of these antibiotics on the mitochondrial respirational activity, and on the coupling of electron transport chain.

AMBITIONS AND CAREER GOALS

Practicing medicine always walked hand in hand with research. That is why I think it is utterly important, to take part in it during my years at the university, and get a broader perspective in disciplines. I see the scholarship of SZTA a one of a kind opportunity to develop myself, from which I hope I can make the most out of.

PUBLICATIONS

Baráth, B., Jász, D., K., Horváth, T., Baráth, B., Maróti, G., Stifler, G., Varga, G., Sándor, L., **Perényi, D.**, Tallósy, S., Donka, T., Jávor, P., Boros, M., Hartmann, P. (2022) Mitochondrial Side Effects of Surgical Prophylactic Antibiotics Ceftriaxone and Rifaximin Lead to Bowel Mucosal Damage. **Int J Mol Sci 23:** 5064

BENEDEK SZATHMÁRI

National Academy of Scientist Education,
4th year
University of Szeged,
Faculty of Science and Informatics, Biology,
4th year

Szent-Györgyi Mentor: László Nagy
Junior mentor: Árpád Csernetics
Specialization: fungal genomics
Language: English/advanced, Latin/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Fungal evolution, the investigation of which is challenging but also interesting due to great amount of convergence, is still burdened by countless unanswered questions. Our research group investigates the evolutionary biology and developmental genetics of fungi, focusing on the origin of complex multicellularity that, in contrast with other branches of the tree of life, appeared eight times independently in this clade. One of my projects is connected to the mentioned topic: I knock out genes responsible for basidium and fruiting body formation. Our aim here is to understand the origin of other fruiting body cells present around basidia better. There were also lots of simplifications in the course of fungal evolution. The group of unicellular yeasts with a reduced morphology provided some 'workstocks' for the industry, however, we know unworthily little about their evolution. I hope that with my other project, during which I investigate the density-dependent behaviour (quorum sensing) of spores of a mould species, I can also contribute to the creation of a gap-filling evolutionary concept regarding yeasts.

AMBITIONS AND CAREER GOALS

'Nothing in biology makes sense except in the light of evolution' I cannot agree more with this statement of Theodosius Dobzhansky, and my aim is to understand this overall concept. I think achieving this goal does not only require studying, but also the investigation of important problems and interesting phenomena, as well, during which one can pose, and even answer questions no one has before. Creating a complex scientific world-view built upon scepticism is crucial for me. I would like to become a broad-minded researcher with creative thoughts.

PUBLICATIONS

Nagy, L., G., Vonk, Rp., J., Künzler, M., Földi, Cs., Virágh, M., Ohm, R., A., Hennicke, F., Bálint, B., Csernetics, Á., Hegedüs, B., Hou, Z., Liu, X., Nan, S., Pareek, M., Sahu, N., **Szathmári, B.**, Varga, T., Wu, H., Yang, X., Merényi, Z. (2022) Lessons on fruiting body morphogenesis from genomes and transcriptomes of Agaricomycetes. doi: https://doi.org/10.1101/2021.12.09.471732 **Studies in Mycology (in press)**

5TH YEAR STUDENTS

GERGŐ BITAY

National Academy of Scientist Education,
5th year
University of Szeged,
Albert Szent-Györgyi Medical School,
5th year

Szent-Györgyi Mentor: Norbert Nagy
Specialization: electrophysiology, farmacology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Our research group specialises is researching the electrophysiological and pharmacological properties of the heart. We mainly focus on the spontaneous activity of the heart, Ca^{2+} - homeostasis; sudden cardiac arrest related research on athletic heart syndrome models. In our laboratory we conduct research on rabbit and dog models, both on tissue samples (conventional microelectrode technique) and on individual cells (patch-clamp). My main research involves the spontaneous activity of the sinus node: Ca^{2+} - homeostasis, sodium-calcium exchanger, small-conductance calcium-activated potassium (SK) channels. SK channels have a significant role in neurons, and due to the fact that they create a direct connection between the intracellular calcium handling and the repolarisation of the cell membrane, their role in the cardiac tissue could also be important. However, there is no consensus in the literature on the extent of their contribution to cardiac repolarisation. Because both the Ca^{2+} - homeostasis and the repolarisation are related to arrhytmias, SK channels could potentially have a major role pathophysiologically and farmacologically.

AMBITIONS AND CAREER GOALS

My ambition is to become a successful doctor and to continue with research. Furthermore, my goals are to earn a PhD and other degrees. The amount of knowledge given to us by the programme, the publications and the scientific conferences all contribute to achieve these goals.

PUBLICATIONS

Kohajda, Zs., Tóth, N., Szlovák, J., Loewe, A., **Bitay, G.**, ... Nagy, N. (2020) Novel Na+/Ca2+ Exchanger Inhibitor ORM-10962 Supports Coupled Function of Funny-Current and Na+/Ca2+ Exchanger in Pacemaking of Rabbit Sinus Node Tissue. **Front in Pharmacol 10:** 1632.

Tóth, N., Szlovák, J., Kohajda, Zs., **Bitay, G.**, Veress, R., Horváth, B., Papp, J. Gy., Varró, A., Nagy, N. (2021) The development of L-type Ca 2+ current mediated alternans does not depend on the restitution slope in canine ventricular myocardium. **Sci Rep 11:** 16652.

Bitay, G., Tóth, N., Déri, Sz., Szlovák, J., Kohajda, Zs., Varró, A., Nagy, N. (2022) The Inhibition of the Small-Conductance CA2+ -Activated Potassium Channels Decreases the Sinus Node Pacemaking during Beta-Adrenergic Activation. **Pharmaceuticals 15:** 313.

ANNA TÁCIA FÜLÖP

National Academy of Scientist Education,
5th year
University of Szeged,
Faculty of Science and Informatics,
Molecular Bionics Engineer Program,
MSc 2nd year

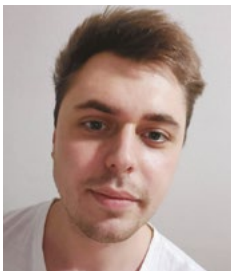
Szent-Györgyi Mentor: Máté Manczinger
Specialization: immunology, bioinformatics, bionics
Language: English/advanced, French/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

HLA molecules are essential in immune recognition, because they present short peptides to T cells. HLA-encoding genes are the most variable ones in the human genome. Using bioinformatics, we investigate the possible relationships between the peptide binding properties of different HLA variants and certain diseases (e.g. different tumours). We also aim to explain the molecular background of these associations.

AMBITIONS AND CAREER GOALS

After the current Bachelor's degree, I would like to continue my Master's degree and then to obtain a PhD degree. After graduating, I would like to join an international research team at a Hungarian university or research institute.



LEVENTE FRIGYES GULÁCSI

National Academy of Scientist Education, 5th year
University of Szeged
Szent-Györgyi Albert Medical School, 5th year

Szent-Györgyi Mentor: József Kaszaki
Junior mentor: Attila Rutai
Specialization: pathophysiology, Intensive therapy
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

During the hyperinflammatory immune response to infection, neutrophil granulocytes are activated and form neutrophil extracellular traps (NETs) composed of DNA, histones and proteases, which are used to eliminate pathogens by trapping them. At the same time, NETs can contribute to the tissue and organ damage that are characteristics of sepsis, by causing blood clotting disorders and thrombosis. Our goal is to investigate the process and therapeutic implications of neutrophil granulocyte activation and NET formation using in vitro cell lines and in vivo clinically relevant animal models. It is hypothesized that exogenous methane therapy, identified as an anti-inflammatory and ºrgan protective bioactive agent, may have a beneficial effect on NET formation.

AMBITIONS AND CAREER GOALS

My research's main goal is to gain a more detailed immunopathological understanding of the pathogenesis of sepsis. In particular, I plan to investigate the process of neutrophil extracellular trap (NET) formation associated with neutrophil granulocyte activation during the hyperinflammatory immune response and the possibilities to influence their therapeutic potential usage in in vitro cell lines and in vivo clinically relevant animal models. My long-term goal as a research physician is to achieve clinical translation of preclinical results.

PUBLICATIONS

Poles, M. Z., Nászai, A., **Gulácsi, L.**, Czakó, B. L., Gál, K. K., Glenz, R. J., Dookhun, D., Rutai, A., Tallósy, S. P., Szabó, A., Lőrinczi, B., Szatmári, I., Fülöp, F., Vécsei, L., Boros, M., Juhász, L., Kaszaki, J. (2021) Kynurenic Acid and Its Synthetic Derivatives Protect Against Sepsis-Associated Neutrophil Activation and Brain Mitochondrial Dysfunction in Rats. **Front Immunol 12:** 717157.

ZSÓFIA RITA HERNÁDI

National Academy of Scientist Education, 5th year
University of Szeged,
Faculty of Pharmacy, 5th year

Szent-Györgyi Mentor: Gyöngyi Horváth
Specialization: neuroscience
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Schizophrenia is a chronic illness with a wide range of symptoms. The main aim of current research in our laboratory is to characterise the behaviour of the "multiple hit" complex schizophrenia (Wisket) rat model in the short term (using acute behavioural tests) and long term (in large, complex housing cages). This preclinical animal model is also used to develop new therapies and explore individual drug options.

AMBITIONS AND CAREER GOALS

As a Pharmacy student, I feel that the Szent-Györgyi program offers a unique opportunity to master both research and pharmacy skills. After graduating from the University, I would like to join a doctoral school and obtain a PhD while also working as a scholarship holder at famous foreign laboratories. Finally, I would like to use my experience in independent research projects as a neuroscientist.

PUBLICATIONS

Mészáros, Á., Molnár, K., Nógrádi, B, **Hernádi, Z.** Nyúl-Tóth, Á., Wilhelm, I., Krizbai, I. A. (2020) Neurovascular Inflammaging in Health and Disease. **Cells 9(7):** 1614.

Kozma, M., Mészáros, Á., Nyúl-Tóth, Á., Molnár, K., Costea, L., **Hernádi, Z.**, Fazakas, Cs., E Farkas, A., Wilhelm, I., Krizbai, I., A. (2021) Cerebral Pericytes and Endothelial Cells Communicate through Inflammasome-Dependent Signals. **Int J Mol Sci 22(11):** 6122.

Bali, ZK., Nagy, LV., Bruszt, N., Bodó, K., Engelmann, P., **Hernádi, Z.**, Göntér, K., Tadepalli, SA., Hernádi, I. (2024) Increased brain cytokine level associated impairment of vigilance and memory in aged rats can be alleviated by alpha7 nicotinic acetylcholine receptor agonist treatment. **Geroscience 46(1):** 645-664.

GÁBOR JUHÁSZ

National Academy of Scientist Education,
5th year
University of Szeged,
Albert Szent-Györgyi Medical School,
5th year

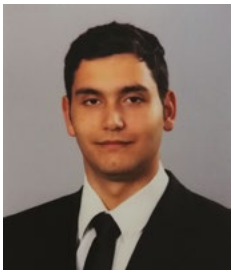
Szent-Györgyi Mentor: Gábor Juhász
Junior mentor: Tamás Maruzs
Specialization: endosomal system, membrane contact sites, drosophila genetics
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The existence of membrane contact sites, i.e. permanent physical contacts between organelles of eukaryotic cells has been known for a long time, however, understanding their functions has just begun during the last decade. The most well-characterized function of these contacts is enabling lipid transport between the contacting organelles. Interestingly, recent studies shed light on the direct role of such contacts in the endosomal system as well. During our work, we aim to investigate the function of Snx25, a known membrane contact site protein, which is involved in a human hereditary neurodegenerative disease, a distinctive type of spinocerebellar ataxia. Our results show that the mutation of the fruit fly (Drosophila melanogaster) counterpart of this gene leads to severe defects in the endosomal maturation process of the highly endocytic larval nephrocytes. As the exact mechanism of this phenomenon is currently not known, we aim to decipher the role of the Drosophila Snx25 protein in endosomal maturation using genetics and light-microscopy and our self-maintained fruit fly stocks' nephrocytes as an experimental model system.

AMBITIONS AND CAREER GOALS

My primary aim is to match the medical and scientific work. In my opinion through knowledge in all natural sciences, especially in regards to modern biology is essential to understand and discover the most effective therapies. In the near future I would like to work in the fields of genetics and cell biology. Later I intend to continue this work during my PhD study, and my task in inland and foreign laboratories in addition to my medical studies.



GÁBOR MOHÁCSI

National Academy of Scientist Education,
5th year
University of Szeged,
Albert Szent-Györgyi Medical School,
4th year

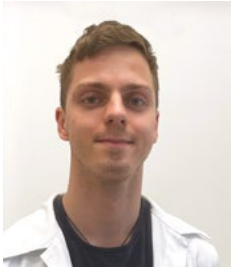
Szent-Györgyi Mentor: András Varró
Specialization: neurophysiology
Language: English/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Our aim is to understand of the mechanisms underlying cortical information processing. The two distinct type of processes are excitation and inhibition. The efferent and afferent connections of inhibitory neurons are precise and diverse. We conduct experiments in order to determine the physiologycal significance of the distinct cells. We are recording from identified interneurons in completely unaesthetized freely behaving rodents.The neurogliaform cells play an important role in neuronal inhibiton.

AMBITIONS AND CAREER GOALS

After obtaining my degree I would like to earn a PhD, as well. As a researcher I hope that I can find answers to some important questions. My dream is to develop new methods, which can be applied in clinical environments.



BENCE PÓSA

National Academy of Scientist Education,
5th year
University of Szeged,
Albert Szent-Györgyi Medical School,
4th year

Szent-Györgyi Mentor: Péter Bencsik
Specialization: Pharmacology of the Cardiovascular system
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Cardiovascular diseases are the leading cause of death in industrialised societies. The function of the heart is diverse, but the most prominent is the pump function, which is circulateing blood through the vascular system. To perform this pumping function, the heart also requires oxygenated blood, which it receives from its own private ‚coronary' circulation. Impairment of this coronary circulation results in ischaemia and death of the heart muscle, and thus impairment of pump function. MicroRNAs are RNA sequences that account for only 1% of the genome, but significantly affect the expression of other genes. In our study, we investigate the effects of myocardial ischemia, abnormal enlargement (hypertrophy) and other diseases affecting other organs (e.g. colitis) on the microRNA profile of the heart. Our aim is to identify pharmacological compounds that mimic (miRNA mimic) or inhibit (antagomiR) microRNAs, which influence the expression of microRNAs that mitigate myocardial damage and the genes/proteins they regulate, and thus have cardioprotective potential by influencing a number of processes.

AMBITIONS AND CAREER GOALS

After graduating from medical school, I would like to continue my work primarily as a clinician, but also do research. My goals are to obtain a PhD and to be actively involved in teaching and educational organisation. I believe that even as a student, we should not only treat our present patients, but also help and support our fellow doctors and students, so that we can move closer to a viable and humane professional future.

JOANNA GRACE SANDLE

National Academy of Scientist Education,
5th year
University of Szeged,
Faculty of Science and Informatics, Biology,
2nd MSc year

Szent-Györgyi Mentor: Gábor Tamás
Junior mentor: Gábor Molnár
Specialization: neurobiology, electrophysiology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

The way we percieve and process information and inputs from our environment is unique to us, humans and still most of the mechanisms which enable us to perform complex and abstract thinking are yet to be discovered. In Tamás Gábor's Research Group for Cortical Microcircuits we seek to unveil the underlying elementary mechanisms of this process on the level of synapses and neural microcircuits and the functions of different cell types in rodent and human cortical cortex. We have the excellent opportunity to compare the functions of the commonly used model animals' brain with ours by performing in vitro patch clamp in non-pathological human brain slices among other electrophysiological techniques. Our primary focus is on the role of inhibitory interneurons in such networks.

AMBITIONS AND CAREER GOALS

I endeavour to exploit the opportunities offered by Szent-Györgyi programme, broaden my understanding and learn new methods. It is of great importance to me to keep up with the developments and findings of neuroscience, and to acquire up-to-date, applicable knowledge not only in the fields of neurobiology and electrophysiology but also in borderline sciences. I want to become a useful member of a research group and be able to contribute to the development of my field of expertise.

PUBLICATIONS

Chartrand, T., Dalley, R., Close, J., Goriounova, N. A., Lee B. R., Mann, R., Miller, J. A., Molnár, G., Mukora, A., Alfiler, L., Baker, K., Bakken, T. E., Berg, J., Bertagnolli, D., Braun, T., Brouner, K., Casper, T., Csajbok, E. A., Dee, N., Egdorf, T., Enstrom, R., Galakhova, A. A., Gary, A., Gelfand, E., Goldy, J., Hadley, K., Heistek, T. S., Hill, D., Jorstad, N., Kim, L., Kocsis, A. K., Kruse, L., Kunst, M., Leon, G., Long, B., Mallory, M., McGraw, M., ... Omstead, V., Peterfi, Z., Pom, A., Potekhina, L., Rajanbabu, R., Rozsa, M., Ruiz, A., **Sandle, J.**, ... Lein, E. S. (2023) Morphoelectric and transcriptomic divergence of the layer 1 interneuron repertoire in human versus mouse neocortex. **Science 382:** eadf0805.

Iacone, Y., Morais, T. P., David, F., Delicata, F., **Sandle, J.,** Raffai, T., Parri, H. R., Weisser, J. J., Bundgaard, C., Klewe, I. V., Tamás, G., Thomsen, M. S., Crunelli, V., Lőrincz, M. L. (2021) Systemic administration of ivabradine, a hyperpolarization-activated cyclic nucleotide-gated channel inhibitor, blocks spontaneous absence seizures. **Epilepsia 62:** 1729-1743.

NOÉMI VIDA

National Academy of Scientist Education,
5th year
University of Szeged,
Albert Szent-Györgyi Medical School,
5th year

Szent-Györgyi Mentor: Mihály Boros
Junior mentor: Gabriella Varga
Specialization: diseases of systemic circulation
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Extra corporal circulation (ECC) is commonly used during several type of heart surgeries and intensive care. During extracorporal membrane oxigenization (ECMO) or cardiopulmonary bypass (CPB) the lungs are excluded from the circulation and the blood is introduced to a considerable amount of heparin. Furthermore the blood contact with the foreign surface of the CPB circuit causes an immediate inflammatory response similar to the septic systemic inflammatory response (SIRS) in which humoral and cellular factors play an essential role. The contact activation leads to intrinsic activation of the coagulation cascade and further activation of pro-inflammatory cascades, triggering a wide variety of cellular systems. If these cascade activations are dysregulated due to prolonged ECC time and further metabolic changes, significant tissue and organ damage can occur in sensitive organs such as the kidneys and intestines. In vivo animal models are used to explore the mechanisms behind these reactions, therefore in the Institute for Surgical Research, University of Szeged, a clinically relevant large animal model is used to monitor inflammatory responses during ECC. Our aim is to investigate the exact mechanism behind the ECC-induced inflammatory reactions along with the development of novel therapeutic strategies to reduce post-ECC inflammatory damage.

AMBITIONS AND CAREER GOALS

As a medical student clinical knowledge and skills are exeptionally important, however I find keeping up with scientific research and integrating them into practice is just as cruical. By working in this laboratory, I would like to deepen my knowledge in the pathophysiology of post-surgical inflammatory response and obtain surgical skills, which I will benefit from later as a practicioner.

PUBLICATIONS

Bársony, A., **Vida, N.**, Gajda, Á., Rutai, A., Mohácsi, Á., Szabó, A., Boros, M., Varga, G., Érces, D. (2020) Methane Exhalation Can Monitor the Microcirculatory Changes of the Intestinal Mucosa in a Large Animal Model of Hemorrhage and Fluid Resuscitation. **Front Med (Lausanne) 7:** 567260.

Varga, P., **Vida, N.**, Hartmann, P., Szabó, A., Mohácsi, Á., Szabó, G., Boros, M., Tuboly, E. (2019) Methanogenic potential of consumable organosulfur administration: in vitro and in vivo evidences. **PLOS One 15:** e0236578.

TIBOR DONKA

National Academy of Scientist Education,
6th year
University of Szeged
Szent-Györgyi Albert Medical School,
6th year

6TH YEAR STUDENTS

Szent-Györgyi Mentor: Petra Hartmann
Specialization: traumatology, coagulopathy, mitochondria
Language: English/advanced, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Trauma-induced coagulopathy is a major cause of mortality in polytrauma patients. During this process, many pathological pathways are activated, including the coagulation cascade. Platelets are a major player in coagulation, with mitochondria being one of their main energy carriers. In our research, we hypothesize that platelets in this study group suffer from mitochondrial dysfunction. Our studies aim at high-resolution respirometric measurements of platelet mitochondria, and in parallel, rotational viscoelastometric and aggregometric measurements. Our research will provide a deeper understanding of maladaptive platelet activations after injury, potentially leading to the discovery of new therapeutic targets in polytrauma care.

AMBITIONS AND CAREER GOALS

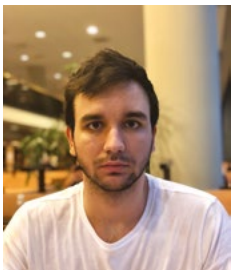
In the coming years, I would like to successfully complete the General Medicine degree at the University of Szeged, continue my ongoing research at the Traumatology Clinic with the help of the National Academy of Scientist Education, which I would like to contribute to the expansion of our scientific knowledge and the improvement of the quality of care at my level. From my ongoing research, I would like to publish my first authored article in an English journal of an appropriate level and speciality. Later, after graduation from university, I would like to pursue a Ph.D. degree in my scientific field.

PUBLICATIONS

Baráth, B., Jász, D., K., Horváth, T., Baráth, B., Maróti G., Stifler, G., Varga, G., Sándor, L., Perényi, D., Tallósy, S., **Donka, T.**, Jávor, P., Boros, M., Hartmann, P. (2022) Mitochondrial Side Effects of Surgical Prophylactic Antibiotics Ceftriaxone and Rifaximin Lead to Bowel Mucosal Damage. **Int J Mol Sci 23:** 5064.

Horváth, T., Sándor, L, Baráth, B., **Donka, T.**, Baráth, B., Mohácsi, A., Jász, DK., Hartmann, P., Boros, M. (2023) Methane Admixture Protects Liver Mitochondria and Improves Graft Function after Static Cold Storage and Reperfusion. **Antioxidants (Basel) 12:** 271.

Jávor, P., **Donka, T.**, Horváth, T., Sándor, L., Török, L., Szabó, A., Hartmann, P. (2023) Impairment of Mesenteric Perfusion as a Marker of Major Bleeding in Trauma Patients. **J Clin Med 12:** 3571.



ÁKOS HARANGOZÓ

National Academy of Scientist Education,
6th year
University of Szeged,
Albert Szent-Györgyi Medical School,
6th year

Szent-Györgyi Mentor: Zsolt Endre Boldogkői
Junior mentor: Dóra Tombácz
Specialization: genomics and gene technology
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

With modern sequencing technologies we are able to make structural and functional examination of living organisms and viruses, thus we can understand better the role of the present genes and non-coding sequences and their effect on each other. The main focus of our research group includes the genomic analysis of various human and non-human pathogenic viruses by using state of the art genome- and transcriptome sequencing methods (long- and short-read sequencing approaches). The gained genomic data is processed with the help of bioinformatical programs. Also we generate genetically modified viruses by using the CrispR-cas9/dCas9 - which is a state of the art genome editing technology capable of making very precise changes - methods for the evaluation of the effect of the gene modification on the global transcriptome.

AMBITIONS AND CAREER GOALS

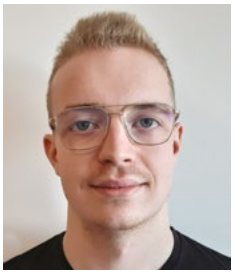
As a medical doctor I want perform medical practice and research side by side, for which this program gives the best bases. My goal with my research is to gain theoretical knowledge and practical experience which will help me in my career which hopefully will lead me to be able to help others.

PUBLICATIONS

Kakuk, B., Dörmő, Á., Csabai, Z., Kemenesi, G., Holoubek, J., Růžek, D., Prazsák, I., Dani, V. É., Dénes, B., Torma, G., Jakab, F., Tóth, G. E., Földes, F. V., Zana, B., Lanszki, Z., **Harangozó, Á.**, Fülöp, Á., Gulyás, G., Mizik, M., Kiss, A. A., ... Boldogkői, Z. (2023) In-depth Temporal Transcriptome Profiling of Monkeypox and Host Cells using Nanopore Sequencing. **Scientific Data 10(1):** 262.

Torma, G., Tombácz, D., Csabai, Z., Almsarrhad, I. A. A., Nagy, G. Á., Kakuk, B., Gulyás, G., Spires, L. M., Gupta, I., Fülöp, Á., Dörmő, Á., Prazsák, I., Mizik, M., Dani, V. É., Csányi, V., **Harangozó, Á.**, Zádori, Z., Toth, Z., & Boldogkői, Z. (2023) Identification of herpesvirus transcripts from genomic regions around the replication origins **Sci Rep 13(1):** 16395.

Tombácz, D., Dörmő, Á., Gulyás, G., Csabai, Z., Prazsák, I., Kakuk, B., **Harangozó, Á.**, Jankovics, I., Dénes, B., & Boldogkői, Z. (2022) High temporal resolution Nanopore sequencing dataset of SARS-CoV-2 and host cell RNAs. **GigaScience 11:** giac094.



ENDRE KOCSIS

National Academy of Scientist Education,
6th year
University of Szeged
Albert Szent-Györgyi Medical School,
6th year

Szent-Györgyi Mentor: Attila Hunyadi
Junior mentor: Máté Vágvölgyi
Specialization: pharmacognosy
Language: English/advanced

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

According to WHO, one in every 6 people's death (a total of 9,6 million deaths in 2018) is due to cancer, making it the second leading cause of death globally. In most cases, the cause of faliure in pharmacotherapy is originated in the tumor's apace development of resistance against cytotoxic agents, which is also called as multidrug resistance (MDR). This issue is unsolved to the present day, which calls for an urgent need for a radically new approach in enhancing our strategies. Ecdysteroids are analogs of ecdysone, a moulting hormone of arthropods, that are non-toxic and bioactive in mammals. Some of their less polar derivatives combined with a certain chemotherapeutic agent have a strong chemo-sensitizing effect on both drug susceptible and MDR cancer cell lines. The main goals of our research are the identification and semisynthetic chemical modification of new and promising lead molecules (e.g. production of fluorine substituted derivatives and their self-assembling nanostructures), as well as defining their pharmacological potential.

AMBITIONS AND CAREER GOALS

As a medical student I would like to represent the level of quality this profession requires both in my academic studies, and in my research. Apart from improving my cooperating and problem solving ability, research also provides me with an important support in leading me in the scientific literature, which sufficiently supplements my academic knowledge with comprehensive and up-to-date information. I also hope that our work can lead to results that can emerge as useful help in therapy.

PUBLICATIONS

Vágvölgyi, M., **Kocsis, E.,** Nové M., Szemerédi, N., Spengler, G., Kele, Z., Berkecz, R., Gáti, T., Tóth, G., Hunyadi, A. (2022) Divesrity-Oriented Synthesis Catalyzed by Diethylaminosulfur-Trifluoride-Preparation of New Antitumor Ecdysteroid Derivatives. **Int J Mol Sci 23:** 3447.

ÁKOS KOVÁCS

National Academy of Scientist Education,
6th year
University of Szeged,
Albert Szent-Györgyi Medical School,
6th year

Szent-Györgyi Mentor: Imre Miklós Boros
Junior mentor: Balázs Vedelek
Specialization: molecular biology, genetics
Language: English/intermediate, German/intermediate

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Early recognition is one of the most important factors in successful treatment of cancer, which ideally can be achieved through non-invasive or minimally invasive way. In case of bladder cancer, tumour cells appear in the urine, from which DNA could be purified and analysed to detect mutations specific to cancer. Mutation hotspots are in oncogenes and among them in the promoter of the telomerase reverse transcriptase, which is responsible for DNA elongation at the ends of chromosomes. The telomerase is active in embryonic cells but inactive in somatic cells, therefore the telomeres of the latter are progressively shortening, with each cell division, until they are critically shortened, that results senescence. In tumours, however the telomerase is often re-activated, therefore these cells become immortalised, so they can endlessly divide. In most cases telomerase reactivation is due to mutations at hotspots in its promoter. Our aim is to study telomerase promoter mutations in order to get answers for the following questions: Under what circumstances do the mutations appear? At which stage of carcinogenesis / tumour progression do telomerase promoter mutations appear? Is there any correlation with mutation types, appearance and bladder cancer subtypes? How do the mutations affect the course of the disease? Our long-term goal is to develop a PCR-based, simple and cost-efficient rapid test to detect the presence of potentially cancerous cells from urine targeting telomerase promoter mutation and other tumour markers.

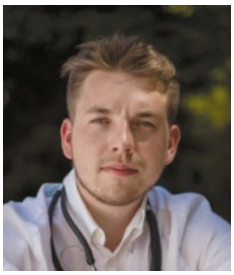
AMBITIONS AND CAREER GOALS

I would like to improve my knowledge continously in order to become as good researcher and physician as I can. With my work I hope to contribute to the advance of society that I consider the most important goal one can aim at.

PUBLICATIONS

Vedelek, B., **Kovács, Á.**, Boros, I. M. (2021) Evolutionary mode for the functional preservation of fast-evolving Drosophila telomere capping proteins. **Open Biol 11:** 210261.

SZEGED
SZENT-GYÖRGYI PHD STUDENTS



MÁRTON SIMON CZIKKELY

National Academy of Scientist Education, 1st Ph.D. year

University of Szeged,
Doctoral School of Multidisciplinary Medical Sciences, Ph.D. 1st year

Szent-Györgyi Mentor: Csaba Pál
Specialization: genetic engineering, experimental evolutionary biology, antibiotic resistance
Language: English/advanced, Spanish/advanced, German/intermediate, Latin/intermediate, Persian/basic

IMPORTANCE, AIMS, POSSIBLE OUTCOME OF RESEARCH

Pathogens seem invariably to attempt to survive the immune system of the invaded host or the pressures of applied therapies. During this accommodation process, DNA-level changes and mutations occur in the cells. These invisible, but important evolutionary processes lead to one of our biggest clinical challenges: antimicrobial resistance. Thanks to scientific advances of recent decades, it has become possible to manipulate the DNA in a precise manner, which enables a rapid and targeted examination of these very mutations. This approach offers a breakthrough in the investigation of antimicrobial resistance. A technique developed in the laboratory of my mentor, Csaba Pál, makes the rapid examination and manipulation of evolution possible with unprecedented accuracy. In our current work, we use this technique also to predict the most important resistance processes against antibiotics under development.

AMBITIONS AND CAREER GOALS

My aim is to help the fight against antibiotic resistance – a major crisis in medicine – trough the examination of its evolution in clinically important pathogens.

PUBLICATIONS

Wannier, T. M., Nyerges, A., Kuchwara, H. M., **Czikkely, M.**, Pál, C., Church G. M., et. al. (2020) Improved bacterial recombineering by parallelized protein discovery. **Proc Natl Acad Sci U S A 117:** 13689-13698.

Szili, P.§, .Draskovits§, G., Révész, T.§, **Czikkely, M.**, Pál*, Á. Nyerges, Á.,* et al. (2019) Rapid evolution of reduced susceptibility against a balanced dual-targeting antibiotic through stepping-stone mutations. A**ntimicrob Agents Chemother 63:** 00207-19.

ANNA GEORGINA KOPASZ

National Academy of Scientist Education, PhD 2nd year

University of Szeged,
Doctoral School of Multidisciplinary Medical Sciences, PhD 2nd year

Szent-Györgyi Mentor: Gyula Timinszky
Former Szent-Györgyi mentor: Lajos Mátés
Research interests: ADP-ribosylation, DNA repair
Language: English/advanced

BACKGROUND, AIMS, POSSIBLE OUTCOME OF RESEARCH

Cancer is a leading cause of morbidity and mortality globally. However, most chemotherapeutics interfere with cell division or DNA synthesis killing not only the uncontrollably multiplying cancer cells but also the proliferating healthy cells – the latter accounting for their toxicity and serious side effects. This main disadvantage emphasizes the need for drugs that specifically destroy cancer cells, ideally, without harming the healthy ones.

ADP-ribosilation is a posttranslation modification appears immediately after DNA damage. PARP1 covalently attaches ADP-ribose units to histones on the site of DNA damage generating poly(ADP-ribose) chains. Poly(ADP-ribosyl)ation (PARylation) provides a scaffold for other repair proteins and contributes to chromatin remodeling to facilitate access to the damaged DNA.

Over 15 years ago, PARP inhibitors (PARPi) were shown to selectively kill HR-defective cancer cells. Neither the many mutations cause HR-defection nor the PARP inhibitor alone kills the cell, yet, their combination is lethal – a phenomenon called synthetic lethality. Our research group completed a genome-wide CRISPR knockout screen in combination with the PARP inhibitor olaparib to identify factors that sensitize cells to PARP inhibitors when deleted. We believe our research will provide a basis to develop new drugs which enhance the sensitivity of PARP inhibitors.

AMBITIONS AND CAREER GOALS

By earning my PhD degree, I would like to master a broad range of molecular biological techniques and their biological bases. As a postdoctoral researcher, I hope I will have the chance to spend some years abroad before I can establish my own research group.

PUBLICATIONS

Kopasz, A. G., Pusztai, D. Z., Karkas, R., Hudoba, L., Abdullah, K., Imre, G., Pankotai-Bodó, G., Migh, E., Nagy, A., Kriston, A., Germán, P., Drubi, A. B., Molnár, A., Fekete, I., Dani, V. É., Ocsovszki, I., Puskás, L. G., Horváth, P., Sükösd, F., Mátés, L. (2022) A versatile transposonbased technology to generate loss- and gain-of-function phenotypes in the mouse liver. **BMC Biology 20:** 74.

Kopasz, A. G. (2021), Optimization of RNA interference-based gene silencing using a well-balanced bidirectional promoter in a somatic transgenic mouse model, Young Investigators RNA Forum, presentation and abstract.

GERGŐ PORKOLÁB

National Academy of Scientist Education,
PhD 4th year

University of Szeged,
Doctoral School of Biology, PhD 4th year

Szent-Györgyi Mentor: Mária Deli
Former Szent-Györgyi mentors: Mária Deli, Szilvia Veszelka
Research interests: cell biology, blood-brain barrier
Language: English/advanced

BACKGROUND, AIMS, POSSIBLE OUTCOME OF RESEARCH

The main goal of our research is to develop a novel drug delivery system that is capable of transporting therapeutics across the blood-brain barrier (BBB). We load the drugs into nanoparticles, which are targeted to the BBB by special molecules on their surfaces. These targeting molecules are recognised by the BBB and the drug-loaded nanoparticles – like „molecular Trojan horses – are able to enter the brain. We are also interested in developing novel, human cell-based models that enable us to investigate the interactions of nanoparticles with the BBB, as well as the healthy and diseased brain.

AMBITIONS AND CAREER GOALS

As a researcher, I would like to focus on and find solutions to relevant basic scientific problems that can potentially improve people's lives in the future.

PUBLICATIONS

Topal, G.R, Mészáros, M., **Porkoláb, G.**, Szecskó, A., Polgár, T.F, Siklós, L., Deli, M.A, Veszelka, S., Bozkir, A. (2020) ApoE-Targeting Increases the Transfer of Solid Lipid Nanoparticles with Donepezil Cargo across a Culture Model of the Blood-Brain Barrier. **Pharmaceutics 13:** 38.

Porkoláb, G., Mészáros, M., Tóth, A., Szecskó, A., Harazin, A., Szegletes, Z., Ferenc, G., Blastyák, A., Mátés, L., Rákhely, G., Deli, M.A., Veszelka, S. (2020) Combination of Alanine and Glutathione as Targeting Ligands of Nanoparticles Enhances Cargo Delivery into the Cells of the Neurovascular Unit. **Pharmaceutics 12:** 635.

Mészáros, M., **Porkoláb, G.**, Kiss, L., Pilbat, A.M., Kóta, Z., Kupihár, Z., Kéri, A., Galbács, G., Siklós, L., Tóth, A., Fülöp, L., Csete, M., Sipos, Á., Hülper, P., Sipos, P., Páli, T., Rákhely, G., Szabó-Révész, P., Deli, MA., Veszelka, S. (2018) Niosomes decorated with dual ligands targeting brain endothelial transporters increase cargo penetration across the blood-brain barrier. **Eur J Pharm Sci 123:** 228-240.

INTERNATIONAL MENTORS

IVAN AHEL

United Kingdom

Sir William Dunn School of Pathology,
University of Oxford

Contact mentor: Gyula Timinszky

DAN ANDERSSON

Sweden

Department of Medical Biochemistry
and Microbiology,
Uppsala University

Contact mentor: Csaba Pál

SUSAN BRAIN

United Kingdom

King's College London, Vascular Biology
and Inflammation Section, School of
Cardiovascular and Metabolic Medicine
& Sciences, Waterloo Campus

Contact mentor: Erika Pintér

MATTHEW CAMPBELL

Ireland

Smurfit Institute of Genetics,
Trinity College Dublin

Contact mentor: Mária Deli

FANG-RONG CHANG

China

Graduate Institute of Natural
Products,
Kaohsiung Medical University

Contact mentor: Attila Hunyadi

CHRISTIAAN DE KOCK

The Netherlands

Vrije University Amsterdam

Contact mentor: Gábor Tamás

DOBROMIR DOBREV

Germany

Institute of Pharmacology,
University Duisburg-Essen

Contact mentor: András Varró

ZSUZSANNA FABRY

United States of America

Department of Pathology and
Laboratory Medicine,
University of Wisconsin-Madison

Contact mentor: Mária Deli

TONI GABALDÓN

Spain

Bioinformatics and Genomics
Program (CRG),
ICREA Research Professor

Contact mentor: Attila Gácser

CSILLA GERGELY

France

Laboratoire Charles Coulomb
UMR 5221 CNRS – Université
Montpellier 2

Contact mentor: László Zimányi

THOMAS H. GILLINGWATER

United Kingdom

Edinburgh Medical School
Biomedical Sciences

Contact mentor: László Siklós

ANNA GUKOVSKAYA

United States of America

Department of Medicine
David Geffen School of Medicine
University of California at Los Angeles

Contact mentors:
Péter Hegyi, Zoltán Rakonczay

GYÖRGY HAJNÓCZKY

United States of America

MitoCare Center for Mitochondrial Imaging Research and Diagnostics, Thomas Jefferson University, Philadelphia

Contact mentor: Péter Hegyi

JOACHIM HEBERLE

Germany

FreieUniversität Berlin,
Department of Physics Experimental Molecular Biophysics

Contact mentor: László Zimányi

MARKUS HEIMESAAT

Germany

Department of Microbiology
Gastrointestinal Microbiology Research Group, Charité, University Medicine Berlin

Contact mentor: Mária Deli

LAURENCE D. HURST

United Kingdom

Department of Biology and Biochemistry,
The University of Bath

Contact mentor: Balázs Papp

ZOLTÁN IVICS

Germany

Division of Medical Biotechnology
Paul Ehrlich Institute,
Langen, Germany

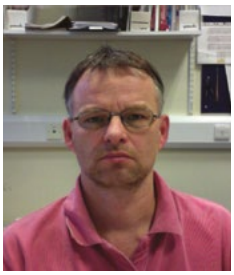
Contact mentor: Lajos Mátés

HARM H. KAMPINGA

Netherlands

Department of Cell Biology,
University of Groningen

Contact mentor: László Vígh



ENDRE KISS-TOTH

United Kingdom

The University of Sheffield,
Department of Infection,
Immunity and Cardiovascular Disease

Contact mentor: Lajos Haracska

ANDREAS LADURNER

Germany

Butenandt Institute of Physiological Chemistry LMU, Biomedical Center Faculty of Medicine, Ludwig-Maximilians-University of Munich

Contact mentor: Imre Boros

GERGELY L. LUKÁCS

Canada

Departments of Physiology and Biochemistry
McGill University, Montreal
Contact mentor: Péter Hegyi

ELEK MOLNÁR

United Kingdom

School of Physiology, Pharmacology and Neuroscience
University of Bristol
Contact mentor: László Dux

SHMUEL MUALLEM

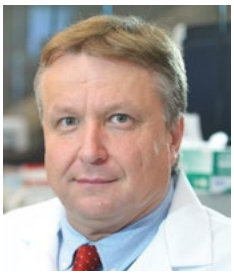
United States of America

Epithelial Signaling and Transport Section, Molecular Physiology and Therapeutics Branch, NIH NIDCR
Contact mentors:
Péter Hegyi, Zoltán Rakonczay

GEORG NAGEL

Germany

University of Würzburg
Contact mentor: András Dér



LÁSZLÓ NAGY

United States of America

Departments of Medicine and Biological Chemistry, Johns Hopkins University School of Medicine, Johns Hopkins All Children's Hospital
Contact mentor: Zsolt Boldogkői

JOSHUA D. NOSANCHUK

United States of America

Albert Einstein College of Medicine
Contact mentor: Attila Gácser

STEPHEN G. OLIVER

United Kingdom

Department of Biochemistry
University of Cambridge
Contact mentor: Balázs Papp

GÁBOR PÁPAI

France

Integrated Structural Biology, Institute of Genetics and Molecular and Cellular Biology (IGBMC)
Contact mentor: Imre Boros

ANANT P. PAREKH

United Kingdom

Department of Physiology Anatomy and Genetics
Oxford University
Contact mentors:
Péter Hegyi, Zoltán Rakonczay

OLE PETERSEN

United Kingdom

Cardiff School of Biosciences, Cardiff University
Contact mentors:
Péter Hegyi, Zoltán Rakonczay

VINCENT PROCACCIO

France

Director of the molecular diagnostic laboratory at Angers Hospital, Angers University Hospital

Contact mentor: Márta Széll

NORBERT RADÁCSI

United Kingdom

Institute for Materials and Processes, The University of Edinburgh

Contact mentor: Rita Ambrus

JEREMY J. RAMSDEN

United Kingdom

University of Buckingham, Research & Technology; Director, Henge Precision Materials Ltd; Science Director, Viridis Navitas Capital Partners Limited

Contact mentor: András Dér

BOTOND ROSKA

Switzerland

Institute of Molecular and Clinical Ophthalmology Basel

Contact mentor: Zsolt Boldogkői

MIKLÓS SAHIN-TÓTH

United States of America

Department of Surgery, University of California Los Angeles

Contact mentors: Péter Hegyi, Zoltán Rakonczay

LEA SISTONEN

Finland

Department of Biosciences, Åbo Akademi University, Turku

Contact mentor: László Vígh

ZOLTÁN UNGVÁRI

United States of America

Reynolds Oklahoma Center on Aging Department of Geriatric Medicine, University of Oklahoma Health Sciences Center

Contact mentor: Eszter Farkas

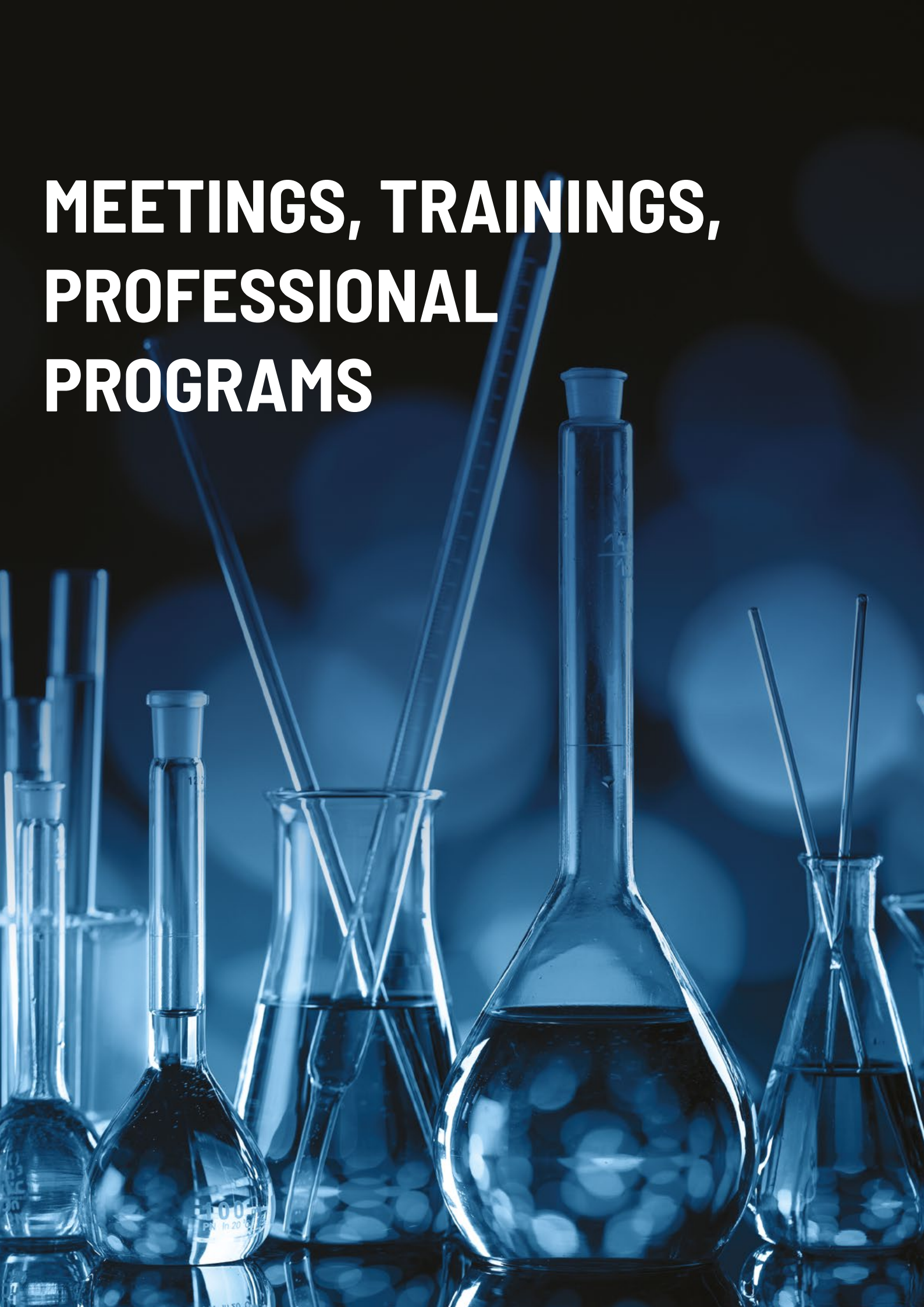
MARK VAN RANST

Belgium

Catholic University of Leuven and Rega Institute for Medical Research

Contact mentor: Péter Hegyi

MEETINGS, TRAININGS, PROFESSIONAL PROGRAMS



CONFERENCES IN 2023

XX. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

26-28 March
2023
SZEGED

NOBEL LAUREATE GUEST OF HONOR:

BRUCE ALAN BEUTLER
American immunologist and geneticist
Nobel Prize in Physiology or Medicine, 2011

2 days
6 venues
460 participants

43 secondary schools
250 Szent-Györgyi Pupils
55 Szent-Györgyi Teachers

100 Szent-Györgyi Students
40 Szent-Györgyi Mentors and Junior Mentors

XXI. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

13-15 December
2023
SZEGED

NOBEL LAUREATE GUESTS OF HONOR:

RANDY SCHEKMAN
American biochemist and cell biologist
Nobel Prize in Physiology or Medicine, 2013

THOMAS SÜDHOF
German American neuroscientist
Nobel Prize in Physiology or Medicine, 2013

INTERNATIONAL GUESTS OF HONOR:

OLE PETERSEN
Danish physician and physiologist

MIKLÓS SAHIN-TÓTH
world-renowned Hungarian expert
in the area of pancreatic disorders

2 days
4 venues
490 participants

53 secondary schools
255 Szent-Györgyi Pupils
68 Szent-Györgyi Teachers

120 Szent-Györgyi Students
20 Szent-Györgyi Mentors and Junior Mentors

TRAINING FOR SZENT-GYÖRGYI SENIOR TEACHERS

29-30 September 2023, Szeged

36 participants

TRAININGS FOR SZENT-GYÖRGYI TEACHERS

19 October 2023, Debrecen
19 October 2023, Pécs
16 February 2024, Gödöllő

29 participants

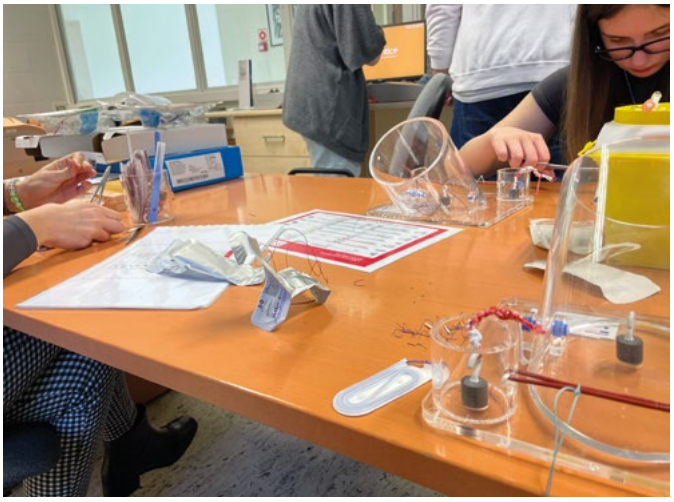
SUMMER CAMP FOR YOUNG RESEARCHERS

9-14 July 2023, Szeged

16 participants

SKILL LABORATORY PRACTICES FOR PUPILS

12 Cities
27 occasions
486 participants



VISITS OF INTERNATIONAL MENTORS

14 June 2023, Budapest

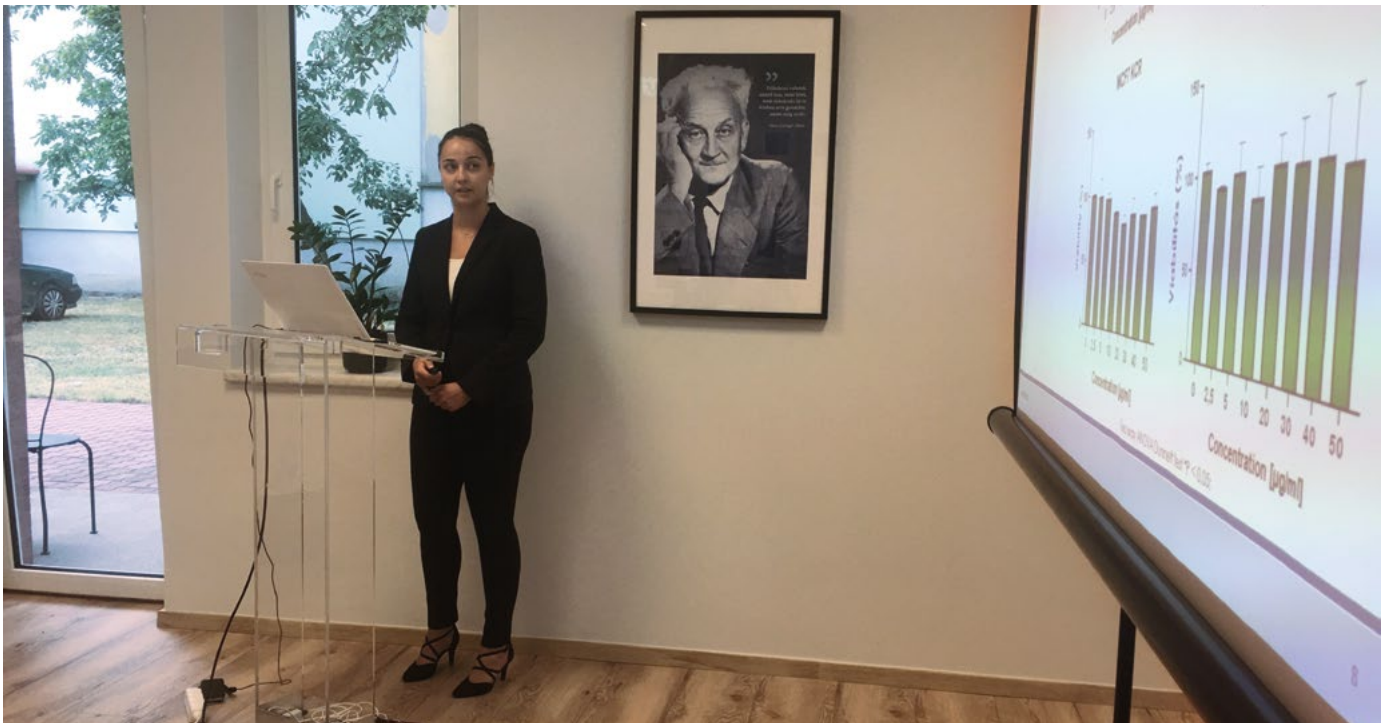
MARC VAN RANST
Belgian public health doctor and Professor of Virology at the Catholic University of Leuven and Rega Institute for Medical Research

23 September 2023, Pécs

SUSAN BRAIN
King's College London, Vascular Biology and Inflammation Section, School of Cardiovascular and Metabolic Medicine & Sciences, Waterloo Campus

PRESENTATION TECHNIQUES TRAINING

In Budapest, Debrecen, Pécs and Szeged for Szent-Györgyi Students 52 occasions



ENGLISH LANGUAGE TRAINING

In Budapest, Debrecen, Pécs and Szeged for Szent-Györgyi Students 317 occasions

UPCOMING CONFERENCES IN 2024

XXIII. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

13-15 April
2024
SZEGED

Keynote speakers:

BRIAN KOBILKA
American physiologist Nobel Prize in Physiology or Medicine, 2012

JOHN WONG EU-LI
Senior Vice President (Health Innovation and Translation) at the National University of Singapore

MARTIN MORAD
American cell biologist, professor at the University of South Carolina

DAVID EISNER
British professor of Cardiac Physiology at the University of Manchester

XXIV. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

5-7 December
2024
SZEGED

Imprint:

Published by: National Biomedical Foundation
National Academy of Scientist Education
Yearbook 2023/24

Responsible: Péter Hegyi, Program director of the National Biomedical Foundation

Contact info: www.edu-sci.org
info@edu-sci.org

Nemzeti Tudósképző Akadémia

Edited by: Ágnes Bittera, Ildikó Biró

Printed in: Szeged, 2024

The National Academy of Scientist Education Program of the National Biomedical Foundation
is implemented with the support of the Hungarian Government.