Photo: Anna Bobkó

05-07 December 2018, Szeged

XII. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

AND SZENT-GYÖRGYI SECONDARY SCHOOL COMPETITION, 2018

A joint program of the Foundation for the Future of Biomedical Sciences in Szeged, the University of Szeged and the Hungarian Academy of Sciences Biological Research Centre

SZEGEDI TUDÓS AKADÉMIA
SZEGED SCIENTISTS ACADEMY

SZEGEDI TUDÓS AKADÉMIA
SZEGED SCIENTISTS ACADEMY

VENUES

ACCOMMODATION

1 **Novotel Szeged ****** (*6721 Szeged, Maros str. 1.)*

PROGRAMS OF THE SZEGED SCIENTISTS ACADEMY

1 **Novotel Szeged ****** (*6721 Szeged, Maros str. 1.)*

2 **IH Event Center** *(6721 Szeged, Felső Tisza-part 2.)*

3 **Department of Education and Information Center**
(6722 Szeged, Ady sq. 10.)

SEMIFINAL OF THE SZENT-GYÖRGYI SECONDARY SCHOOL COMPETITION

4 **University of Szeged, Faculty of Medicine, Department of Medical Physics and Informatics, Purjesz Béla Building**
(6720 Szeged, Korányi str. 9.)

FINAL AND RESULT ANNOUNCEMENT CEREMONY OF THE SZENT-GYÖRGYI SECONDARY SCHOOL COMPETITION

5 **University of Szeged, Rector's Office**
(6720 Szeged, Dugonics sq. 13.)

GALA EVENT, DINNER RECEPTION

3 **József Attila Department of Education and Information Center**
(6722 Szeged, Ady sq. 10.)

LABORATORY VISITS

4 In the buildings of the **University of Szeged, Faculty of Medicine**
(Northern hospital garden),

6 **Institute of Surgical Research** *(Pulz str. 1.) and*

7 **Biological Research Centre** *(6726 Szeged, Temesvári ave. 62.)*

PROGRAM

05 DECEMBER 2018. Wednesday

16.00-20.00 **ARRIVAL TO NOVOTEL SZEGED, REGISTRATION**
Novotel Szeged, lobby

18.00-20.30 **DINNER FOR THE HOTEL GUESTS**
Novotel Szeged, restaurant

06 DECEMBER 2018. Thursday

07.00-09.00 **BREAKFAST** *Novotel Szeged, restaurant*

08.00-09.30 **REGISTRATION** *Novotel Szeged, lobby*

08.30-09.30 **PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS 1ST TURN**
IH Event Center, grand hall
Chairman: Dr. Márta Széll, Dr. György Lázár

- 08.30-08.45 **Zsófia Nagy:** Identifying new variants by whole exome sequencing in Hungarian patients with amyotrophic lateral sclerosis
- 08.45-09.00 **Márton Czikkely :** Application of genome engineering to study antibiotic resistance
- 09.00-09.15 **Zsófia Tóth:** LiliA: The new player of aging
- 09.15-09.30 **Gergő Porkoláb:** Targeted nanoparticles for drug delivery to the brain

Parallel program:

08.30-09.30 **SECONDARY SCHOOL STUDENTS MEET THE SZENT-GYÖRGYI UNIVERSITY STUDENTS 1ST TURN**
(round table discussions)
Novotel Szeged, Tisza Lajos Hall

10.00-11.00 **PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS 2ND TURN** ***(repetition of the 1st Turn)***
IH Event Center, grand hall
Chairman: Eszter Farkas, Mónika Kiricsi

Parallel program:

10.00-11.00 **SECONDARY SCHOOL STUDENTS MEET THE SZENT-GYÖRGYI UNIVERSITY STUDENTS 2ND TURN**
(round table discussions) repetition of the 1st Turn
Novotel Szeged, Tisza Lajos Hall

11.30-13.30 **LUNCH** *Novotel Szeged, restaurant*

14.00-16.00 **PRESENTATION OF THE SZENT-GYÖRGYI MENTORS**
József Attila Department of Education and Information Center, Congress Hall
Chairman: István Zupkó, Csaba Pál

14.00-14.15 **Dr. Eszter Farkas:** Novel approach to reducing the secondary damages following brain injuries

14.20-14.35 **Dr. Mária Deli:** Why biological barriers are important?

14.40-14.55 **Dr. Mihály Boros:** What is experimental surgery?

15.00-15.15 **Dr. Zsuzsanna Bata-Csörgő:** Investigations in Psoriasis disease

15.20-15.35 **Dr. Lajos Mátés:** Use of a mutant mouse strain in gene therapy and cancer research

15.40-15.55 **Dr. Balázs Papp:** Principles of metabolic diversity

Each presentation is followed by 5 minutes discussions.

Parallel program:

14.00-15.30 **SEMIFINAL OF THE SZENT-GYÖRGYI SECONDARY SCHOOL COMPETITION** *University of Szeged, Purjesz Béla Building*

16.00-16.30 **COFFEE BREAK**
József Attila Department of Education and Information Center, Hall

Parallel program:

16.00-16.10 **PRESS CONFERENCE** *(by invitation)*
József Attila Department of Education and Information Center, Room III.

16.30-18.45 **PLENARY SESSION**
József Attila Department of Education and Information Center, Congress Hall
Chairman: András Varró, Péter Hegyi

16.30-16.50 **Dr. Péter Hegyi:** Introduction of the Szeged Scientists Academy

16.50-17.00 **Dr. Zoltán Rakonczay:** Introduction of the university program of the Szeged Scientists Academy

17.00-17.15 **'Szent-Györgyi Student Excellence Award' Ceremony, presentation of the awarded**
Bernát Nógrádi: Autoimmunity and ultrastructural changes in amyotrophic lateral sclerosis

17.15-17.25 **Dr. László Dux:** Laudation of Dr. Kurt Wüthrich

17.30-18.45 **NOBEL LAUREATE PRESENTATION**
Kurt Wüthrich: With NMR of Biological Macromolecules to a Nobel Prize

18.45-20.00 **BREAK, PHOTOSHOOT** *(by invitation)*

20.00-20.50 **GALA PROGRAM**
József Attila Department of Education and Information Center, Congress Hall

21.00-23.00 **GALA DINNER**
József Attila Department of Education and Information Center, hall

07 DECEMBER 2018. Friday

07.00-08.30 **BREAKFAST** *Novotel Szeged, restaurant*

09.00-11.30 **SECONDARY SCHOOL PUPILS VISIT THE LABORATORIES OF THE SZENT-GYÖRGYI MENTORS**

12.00-14.00 **LUNCH**
Novotel Szeged, restaurant

14.00-15.00 **SZENT-GYÖRGYI STUDENTS MEET KURT WÜTHRICH**
Novotel Szeged, Vedres hall

15.00-16.00 **SZENT-GYÖRGYI MENTORS MEET KURT WÜTHRICH**
Novotel Szeged, Vedres hall

Parallel program:

14.30-16.00 **FINAL AND RESULT ANNOUNCEMENT CEREMONY OF THE SZENT-GYÖRGYI SECONDARY SCHOOL COMPETITION**
University of Szeged, Rector's Office

LECTURE ABSTRACTS

In the sequence of performance

ZSÓFIA NAGY

Identifying new variants by whole exome sequencing in Hungarian patients with amyotrophic lateral sclerosis

Mentor: **Dr. Márta Széll** Junior mentor: **Dr. Kornélia Tripolszki**

Introduction:

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by the loss of lower and upper motor neurons. 5-10 % of the cases show a positive family history, while the rest remain sporadic. Regarding its genetic background, more than 30 major genes have been associated to ALS so far, and more than 100 further genes have been associated with disease risk or modification.

Methods:

Our study involved 21 unrelated ALS patients of Hungarian origin. Whole exome sequencing of the samples was performed using Illumina NextSeq sequencer. Variant filtering was performed using three gene sets: ALS priority genes; ALS candidate or risk genes; and other neurogenetic diseases associated genes gene set. The identified potentially pathogenic variants have been validated via capillary sequencing.

Results:

In ALS priority genes, exome sequencing revealed 6 variants, of which 4 have not been described in literature yet. In the candidate genes 8 variants were detected and categorized as variants of uncertain significance. In the other neurogenetic diseases associated genes 6 rare variants were detected.

Discussion:

Potentially disease-causing variants in ALS priority genes have been detected in 28% (6/21) of this sporadic cohort. Our study provides further insight into the genetic etiology of this heterogenous disease.

MÁRTON CZIKKELY

Application of genome engineering to study antibiotic resistance

Mentor: **Dr. Csaba Pál**

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, mutations occur in the cells. These invisible, but important evolutionary processes lead to one of our biggest clinical challenges:

antimicrobial resistance. The emergence of drug resistance against existing antimicrobials is currently responsible for 700.000 worldwide deaths annually. According to estimations, in 2050 antimicrobial resistance is going to be a devastating problem unless we find solutions. Thanks to scientific advances of recent decades, it has become possible to manipulate the DNA in a precise manner, which enables a fast and targeted examination of these very mutations. This approach offers a breakthrough in the investigation of antimicrobial resistance. In our work we use the toolbox of evolutionary genome engineering and try to predict preclinically how resistance can evolve against an antibiotic. A technique (pORTMAGE) developed in the laboratory of my mentor, Csaba Pál, makes the rapid examination and manipulation of evolution possible with unprecedented accuracy. Our aim is the further development and utilization of this method. We also strive to be able to fully understand the evolutionary processes of accommodation, and this way to develop more resistance proof antibiotics.

ZSÓFIA TÓTH

LiliA: The new player of aging

Mentor: **Dr. Lajos Haracska**

To maintain the integrity of our genome, different DNA repair pathways have evolved ensuring the repair of damaged DNA. Mutations in DNA repair genes can result in several types of cancer, developmental diseases, and progeroid syndromes.

Progeria is a rare genetic disorder which manifests in the early appearance of aging-related phenotypes. Besides mutations in DNA repair genes (e.g. Werner, Spartan, Bloom), mutations in genes encoding the components of nuclear lamina (e.g. LaminA/C) can lead to similar symptoms, however molecular background of this is unknown. In some progeroid patients, mutation in these well-known genes cannot be identified, implying that there are yet unknown genes whose mutations may also lead to similar phenotypes. The identification of them is important for both diagnostic and scientific purposes.

In our laboratory, an undescribed protein, LiliA has been examined. It has both DNA repair- and nuclear lamina-like phenotype. During our work, we observed that, the perinuclear localization of the LiliA protein, similarly to the LaminA, changes during the mitosis. LiliA, like laminA, localizes to the end of the chromosomes, thus assisting in the separation of the sister-chromatids. From our results we concluded that this lamina-like function of LiliA is regulated by phosphorylation, just as in case of LaminA.

Based on this and our other examinazions, we can state that LiliA might be another progeroid gene, that may be the missing link in helping us understand the aging mechanisms in humans.

GERGŐ PORKOLÁB

Targeted nanoparticles for drug delivery to the brain

Mentor: **Dr. Mária Deli** Junior mentor: **Dr. Szilvia Veszelka**

Pharmaceutical treatment of central nervous system diseases is especially challenging, because the majority of therapeutic drugs are unable to reach the brain via the bloodstream. This is due to the blood-brain barrier (BBB) that is composed of brain capillary endothelial cells. The aim of our experiments was to develop a new targeted drug delivery system to transport therapeutics across the BBB. For this purpose we took advantage of nutrient transporters that are highly expressed in brain endothelial cells.

We prepared nanoparticles, so-called niosomes, of 100 nm size that can be loaded with drugs. The surface of the nanoparticles were decorated with molecules targeting brain endothelial transporters, namely the amino acid alanine, the peptide glutathione or their combination. We proved that our nanoparticles did not damage endothelial cells. The presence of targeting ligands on niosomes increased the cellular uptake of the cargo molecule in brain endothelial cells. Single and especially dual targeting also resulted in a higher permeability of the cargo across a culture model of the BBB.

Our data indicate that ligands of multiple BBB nutrient transporters can potentially be exploited for brain targeting of nanoparticles.

BERNÁT NÓGRÁDI

Autoimmunity and ultrastructural changes in amyotrophic lateral sclerosis

Mentor: **Dr. László Siklós** Junior mentor: **Dr. Roland Patai**

Amyotrophic lateral sclerosis (ALS) is the most common motor neuron disease, defined by the progressive degeneration of motor neurons and consequently the loss of motor functions. The underlying pathophysiological mechanisms form a complex system, where the different processes point towards neuronal degeneration in a self-perpetuating way. One of these mechanisms is the formation of anti-motoneuronal antibodies, outlining the importance of autoimmunity in ALS. Our research group demonstrated, that these immune-mediated processes induce severe ultrastructural changes and the elevation of intracellular calcium level, both in the spinal cord, in the cell bodies of motor neurons and in the muscles samples, in the neuro-muscular synapses. These changes are accompanied by the loss of motor neurons in the spinal cord and the regression of motor functions. Furthermore, we proved that various genetic mutations in ALS are associated with different progression of these pathophysiological aspects.

DR. ESZTER FARKAS

Novel approach to reducing the secondary damages following brain injuries

Nanoparticles are promising drug carriers, once release drugs in response to specific signals "on demand". We have demonstrated that spreading depolarization (SD) occurring in the ischemic cerebral cortex initiates acidosis. For the alleviation of SD-related brain injury, we set out to apply nanoparticles to deliver nimodipine (L-type voltage-sensitive Ca^{2+} channel antagonist) in response to decreasing tissue pH in a model of cerebral ischemia. We expected neuroprotection without undesirable side effects caused by systemic drug administration. Nimodipine (in solution, or associated to chitosan nanoparticles; 100 μM) or its vehicle was washed on the brain surface of anesthetized rats (n=35). Common carotid arteries were occluded (2VO) to create forebrain ischemia. Recurrent SDs were elicited at 15 min intervals by topical application of 1M KCl. Cerebral local field potential, blood flow (CBF) and tissue pH-variations were recorded.

Nimodipine in solution increased baseline CBF before 2VO (104±12 vs 131±43%), if carried by nanoparticles did not alter baseline CBF (105±16 vs. 107±33 %,) and caused significant CBF elevation only after tissue pH reduction associated with 2VO (pH reduction of 0.23±0.17 units overall; CBF: 60±24 vs. 35±6%, nimodipine vs. nanoparticles). Nimodipine carried by nanoparticles shortened the duration of both SD itself (106.9±65.5 vs. 54.9±37.1 s), and the associated tissue acidosis (139.5±64.7 vs. 62.6±30.8 s). Moreover, it enhanced the magnitude of SD-related hyperemia (3003.6±1793.7 vs.4543.8±2339.6 %*s).

Our data demonstrate that tissue pH-dependent, targeted drug delivery can be achieved in a model of cerebral ischemia, and may curb the metabolic burden imposed by SD on the nervous tissue.

DR. MÁRIA DELI

Why biological barriers are important?

Organisms are protected by biological barriers from harmful effects. These barriers also impede drug penetration. The Biological Barriers Research Group investigates methods to increase drug delivery on culture models of the blood-brain, nasal, lung and intestinal barriers. The pathways examined are the reversible opening of tight intercellular junctions by peptides or small molecules and targeting solute carriers at barriers for drug delivery by nanoparticles. The models are made by co-culture of two or three cell types and are investigated in microfluidic integrated chip devices, too. Our other major research interest is the examination of blood-brain barrier injury and dysfunction in different diseases, like Alzheimer's disease or diabetes. The goal of these experiments is to reveal the effect of disease pathogenic factors on 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. In our experiments in addition to cell culture, we use microfluidic chip devices, electric measurements, drug permeability assays, different microscopy techniques and molecular biological methods. The research work is supported by a large, project-based international network of cooperation partners from Japan, France, Austria, Germany, Switzerland, Italy, Luxembourg, Taiwan, Poland, Mexico and the USA.

DR. MIHÁLY BOROS

What is experimental surgery?

Experimental surgery is prototype of translational research, a process of applying basic biology tools and techniques to address basic medical problems. It comprises three main pillars: surgical research (discoveries), technical innovations (surgical technologies) and community services (surgical education). As concerns the translational aspect, Francis D. Moore, one of the greatest surgeons of the 20th century, often said that a "surgical investigator must be a bridge tender, channelling knowledge from biological science to the patient's bedside and back again". This proverbial saying clearly defines our goals and targets: to develop new scientific knowledge in specific branches of surgical pathophysiology, and an equally important aspect is to bring back the experimental results to the clinical fields of surgery. Through a concrete example, I will present this bridge, the Institute's most relevant technological repertoire (in vivo and in vitro models, surgical techniques, macro- and microcirculatory monitoring and intravital imaging possibilities, high-resolution respirometry to assess mitochondrial function, photoacoustic spectroscopy for online detection of gas concentrations), the cooperating national and international research teams, and will try to convince the audience that exogenous methane can influence the inflammatory-hemodynamic response induced by the use of a heart-lung machine in a clinically relevant large animal model.

DR. ZSUZSANNA BATA-CSÖRGŐ

Investigations in Psoriasis disease

Psoriasis is a complex immune mediated chronic disease that primarily affects the skin. Basic research has uncovered the immunological changes that are responsible for the induction and maintenance of the chronic inflammation that characterizes the skin lesions. Based on these information psoriasis was among the first chronic inflammatory diseases in which targeted biological therapies was introduced and used successfully. Unfortunately all available therapies are still symptomatic, none cures the disease. We investigate factors that distinguish the healthy skin from the healthy looking skin of patients with psoriasis, assuming that disease susceptibility is caused by abnormalities in the skin tissue homeostasis.

DR. LAJOS MÁTÉS

Use of a mutant mouse strain in gene therapy and cancer research

Our laboratory is committed to two branches of biomedical research, the development of genetic therapies and cancer research.

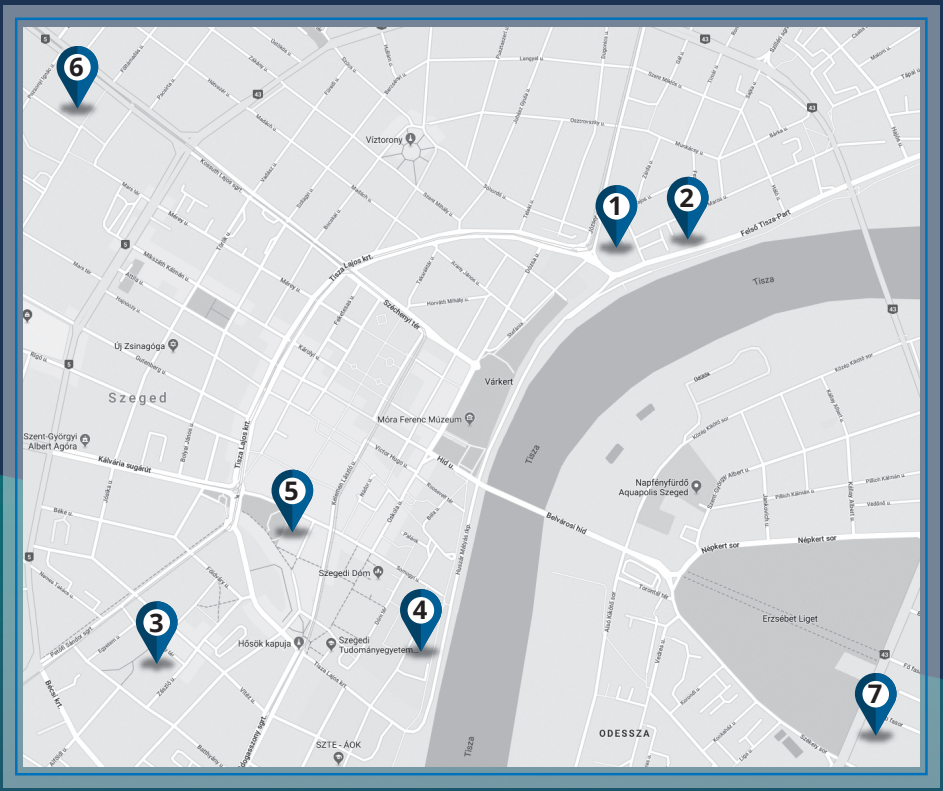
The first gene therapy clinical trials were launched more than two decades ago, due to the prior development of viral vectors, enabling highly effective gene delivery into mammalian cells. However, in the first decade of the 2000s several studies have highlighted a serious adverse effect, namely the insertional oncogenesis, induced by viral gene delivery vectors due to the activation of endogenous proto-oncogenes. Following these failures, new types of randomly integrating vectors have been needed that can be safer than the viral ones. The DNA transposon-based gene delivery vectors represent a promising new branch of randomly integrating vector development. In our laboratory, the Sleeping Beauty and piggyBac DNA transposon systems are characterized by their gene delivery efficiency and potential risk factors during the treatment of the preclinical mouse model of tyrosinemia type I.

In the field of cancer research, the primary goal of our laboratory is to identify new "driver" genes playing a role in the development of liver cancer in a somatically transgenic mouse model. Liver cancer is among the most common cancerous diseases, 70 to 80% of which are hepatocellular carcinoma. Their prognosis is very poor, with a five-year survival typically only around 10%. The identification of new „driver" genes will allow the development of new therapeutic approaches targeting those mutated proteins transcribed from these genes.

DR. BALÁZS PAPP

Principles of metabolic diversity

Metabolism is central to life as it provides the building blocks and energy for all biological processes. Recent progress in technology has allowed the precise measurement of the concentrations of numerous metabolites thereby capturing the behaviour of metabolism. Such approaches revealed large differences in metabolism between species and even between individuals of the same species, including humans. This finding raises at least two fundamental open questions: First, why do species differ in metabolic behaviour? Are all these differences useful? Second, how can we identify those metabolic variations between human individuals that cause diseases? My lab addresses these questions using state-of-the-art experimental and computational approaches. Ultimately, our work aims to uncover the general principles governing the behaviour and evolution of metabolism with implications for several fields – from the design of new metabolic pathways to identifying indicators of diseases.



1. Novotel Szeged ****
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