Photo: Balázs Papdi

2-4 December 2019

Szeged

XIV. MEETING OF NOBEL LAUREATES AND TALENTED STUDENTS

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, Szeged

SZEGEDI TUDÓS AKADÉMIA
SZEGED SCIENTISTS ACADEMY

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VENUES

ACCOMMODATION

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

REGISTRATION

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

SECONDARY SCHOOL STUDENTS MEET THE SZENT-GYÖRGYI UNIVERSITY STUDENTS, ROUND TABLE DISCUSSIONS

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

PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS

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

PRESENTATION OF SZENT-GYÖRGYI MENTORS

3 **Hunguest Hotel Forrás****** *(6726 Szeged, Szent-Györgyi Albert utca 16-24.)*

PLENARY SESSION, GALA EVENT, DINNER RECEPTION

3 **Hunguest Hotel Forrás****** *(6726 Szeged, Szent-Györgyi Albert utca 16-24.)*

LABORATORY VISITS

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

5 **Biological Research Centre, Szeged** *(6726 Szeged, Temesvári krt. 62.)*

PRESS CONFERENCE, SZENT-GYÖRGYI STUDENTS MEET THE GUESTS OF HONOR

6 **Szeged Town Hall** *(6720 Szeged, Széchenyi tér 10.)*

PROGRAM

02 DECEMBER 2019 Monday

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

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

03 DECEMBER 2019 Tuesday

07.00-08.00 **BREAKFAST**
Novotel Szeged, restaurant

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

08.30-09.30 **PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS I.**
IH Event Center, Boncz Géza hall
Chairman: Dr. György Lázár, Dr. Ferenc Nagy

- 08.30-08.45 **Valéria Meszlényi:** Increase of intracellular calcium level in Schwann cells during Wallerian degeneration
- 08.45-09.00 **Márk Harangozó:** Treatment of temporal lobe epilepsy with the electrical stimulation of the medial septum
- 09.00-09.15 **Anna Grassalkovich:** Correcting the alcohol-induced CFTR expression defect in pancreatic ductal cells
- 09.15-09.30 **Dániel Vidács:** Examination of the differentiation potential of melanocytes from human epidermis

PARALLEL PROGRAM:

08.30-09.30 **ROUND TABLE DISCUSSIONS I.**
Secondary school students meet the Szent-Györgyi university students
Novotel Szeged, Tisza hall

10.00-11.00 **PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS II.**
(repetition of PRESENTATION OF SZENT-GYÖRGYI UNIVERSITY STUDENTS I.)
IH Event Center, Boncz Géza hall
Chairman: Dr. Attila Gácser, Dr. Tamás Martinek

PARALLEL PROGRAM:

10.00-11.00 **ROUND TABLE DISCUSSIONS II.**
(repetition of ROUND TABLE DISCUSSIONS I.)
Novotel Szeged, Tisza hall

11.30-13.00 **LUNCH**
Novotel Szeged, restaurant

14.00-16.30 **REGISTRATION**
Hunguest Hotel Forrás, hall

14.30-15.50 **PRESENTATION OF SZENT-GYÖRGYI MENTORS**
Hunguest Hotel Forrás, Juhász Gyula hall
Chairman: Dr. Márta Széll, Dr. László Dux

14.30-14.45 **Dr. Péter Horváth:** Life beyond the pixels: artificial intelligence in cancer research and biology

14.50-15.05 **Dr. Zsolt Boldogkői:** Projects of Genomics and Gene Technology Research Group

15.10-15.25 **Dr. Mária Deli:** Why biological barriers are important?

15.30-15.45 **Dr. Attila Hunyadi:** Chemical studies on natural products: from insect hormones to antitumor nanoparticles

Each lecture is followed by 5 minutes of discussion.

15.50-16.30 **COFFEE BREAK**
Hunguest Hotel Forrás, conference lobby

16.30-18.40 **PLENARY SESSION**
Hunguest Hotel Forrás, Juhász Gyula hall
Chairman: Dr. András Varró, Dr. Péter Hegyi

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

16.50-17.05 **Dr. Zoltán Rakonczay:** Introduction of the University Program of the Szeged Scientists Academy

17.05-17.20 **'Szent-Györgyi Student Excellence Award 2019' Ceremony, presentation of the awardee**
Gergő Porkoláb: Interactions of targeted nanoparticles with different cell types of the brain

17.20-17.30 **Dr. Bert Sakmann's welcome speech**
17.30-17.40 **Dr. Péter Hegyi:** Laudation of Dr. Ole Petersen
17.40-18.25 **Dr. Ole Petersen:** The way of a scientist: A life experience
18.25-18.40 **Questions**

18.40-19.00 **BREAK, PHOTOSHOOT**

19.00-20.00 **GALA EVENT**
Hunguest Hotel Forrás, restaurant

20.00-22.00 **GALA DINNER**
Hunguest Hotel Forrás, restaurant

04 DECEMBER 2019 Wednesday

07.00-09.30 **BREAKFAST**
Novotel Szeged, restaurant

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

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

13.30-14.00 **PRESS CONFERENCE** (upon invitation)
Szeged Town Hall, Lechner Lajos hall

14.00-15.30 **SZENT-GYÖRGYI STUDENTS MEET DR. BERT SAKMANN AND DR. OLE PETERSEN** (upon invitation)
Szeged Town Hall, Lechner Lajos hall

LECTURE ABSTRACTS

In the sequence of performance

VALÉRIA ÉVA MESZLÉNYI

Increase of intracellular calcium level in Schwann cells during Wallerian degeneration

Mentor: **Dr. László Siklós**

Introduction: Wallerian degeneration (WD) is the process of anterograde degeneration of axon and myelin sheets following proximal nerve injury. Our aim was to study the alterations in intracellular calcium level (ICL) in Schwann cells during WD.

Methods: Calcium histochemistry was performed 12 and 24 hours after unilateral sciatic nerve axotomy on Balb/c mice (n=4/group). Samples from the sciatic and tibial nerves were removed and ICL in Schwann cells was quantified on electron microscopic images.

Results: ICL elevation could be documented 12 hours after axotomy in the tibial nerve ($p<0,001$) which could still be observed after 24 hours, however, ICL increase could be observed after 24 hours in sciatic nerve ($p<0,001$).

Discussion: Similarly to motoneurons, increased ICL was noted in Schwann cells during WD. In the future, we aim to investigate the molecular changes parallel with the increased ICL.

Financial support: Szeged Scientists Academy (EMMI, TSZ:11136-2/2019/FIRFIN), Supported by the ÚNKP-19-2 New National Excellence Program of the Ministry for Innovation and Technology

MÁRK HARANGOZÓ

Treatment of temporal lobe epilepsy with the electrical stimulation of the medial septum

Mentor: **Dr. Antal Berényi**

Epilepsy is a frequent neurological disease. The temporal lobe seizures originating from the hippocampal comissure are often drug-resistant and loss of functions due to surgical removal also urges alternative approach. The activity of certain groups of neurons can be modified by electrical stimulation to stop the seizures, but it is difficult to implement in the case of the hippocampus. Our aim is to identify small brain areas whose stimulation affects the activity of the hippocampus, thereby preventing the spreading of seizures.

We implanted stimulation and recording electrodes into rat brains. Seizures were induced by the stimulation of the hippocampal comissure. Then, we attempted to inhibit the seizures by open- and closed-loop electrical stimulations of the medial septum. Moderated seizures with electrical stimulations were compared to the control seizures.

There were no differences between the open-loop interventions and control seizures. Compared to the control cases, the severity and duration of seizures decreased, where closed-loop stimulations were used at the appropriate stages of epileptic seizures.

Based on our results, the indirect stimulation via a small brain area which is able to regulate the activity of diffuse networks, is efficient. Besides, it is important to adjust the time of the stimulation to the dynamics of the seizure, for which closed-loop system is suitable.

ANNA GRASSALKOVICH

Correcting the alcohol-induced CFTR expression defect in pancreatic ductal cells

Mentor: **Dr. Péter Hegyi** Junior Mentor: **Dr. Viktória Venglovecz**

Introduction: Acute pancreatitis (AP) is one of the most frequent gastrointestinal diseases that needs acute treatment in hospital and its mortality in severe cases can reach 30%. One of the major ethiological factors is heavy alcohol intake, which significantly decreases the cystic fibrosis transmembrane conductance regulator (CFTR) expression on the ductal epithelial cells that can lead to AP. 2 potential drugs are available to treat cystic fibrosis, which might be utilized in the treatment of alcohol-induced AP. VX-770 or Ivacaftor increases the open-state probability of the CFTR channel, whereas VX-809 or Lumacaftor restore the impaired function of CFTR. We don't have data if these 2 compounds can also be used during AP.

Aim: The main goal of our study is to test the effect of these compounds on the CFTR expression during EtOH exposure.

Methods: Intact guinea pig pancreatic ducts (PDs) were treated with different concentration of EtOH (30, 50 and 100 mM) alone and in combination with VX-770 (10 μM) and/or VX-809 (10 μM) for 12 hours. CFTR expression was evaluated by immunofluorescent staining and our images were captured by confocal microscopy.

Results: Exposure of guinea pig PDs to EtOH dose-dependently decreased the plasma membrane expression of CFTR. 10 μM VX-770 and VX-809 alone had no significant effect on the channel's expression, however, both of the compounds dose-dependently prevented the EtOH-induced CFTR damage that could be observed even after 2 hours of treatments. Co-administration of VX-770 and VX-809 also prevented the EtOH-induced (30 and 50 mM) decrease in CFTR expression, however was not able to prevent the effect of 100 mM EtOH. In addition, combination of the two drugs did not potentiate each other's effect.

Conclusion: Our findings suggest that VX-809 and VX-770 can restore the CFTR expression defect caused by alcohol. These data suggest that correcting CFTR function or expression could have therapeutic benefits in pancreatitis.

DÁNIEL LÁSZLÓ VIDÁCS

Examination of the differentiation potential of melanocytes from human epidermis

Mentor: **Dr. Zsuzsanna Bata-Csörgő** Junior Mentor: **Dr. Zoltán János Veréb**

Melanocytes are pigment producing cells which are located in the epidermis. The pigment they synthetize, called melanin is responsible for the protection against light. In our laboratory we were able to dedifferentiate these cells using a special culturing enviroment. The cells lost their ability to produce pigment and by examining several characteristics we consider them stem-like cells.

We examined cell surface markers using flow cytometry. Different antibodies were used which are conjugated with fluorescent substances in order to characterize the dedifferentiated cells' cell surface markers. While conducting flow cytometry, we use lasers, emitting light at different wavelengths, to irradiate the marked cells and detect the light emitted by them. With immunohistochemical methods we identified transcription factors that have intranuclear localization. By culturing these cells in different conditions, we could observe adipogenic, chondrogenic and osteogenic differentiation.

Our results indicate that, the melanocytes that were cultured by our novel method are in fact stem cells. We will further examine the differentiation abilities of these cells, and we also consider them as a suitable model for examining environmental carcinogenic effects.

DR. PÉTER HORVÁTH

Life beyond the pixels: artificial intelligence in cancer research and biology

In this talk I will give an overview of the computational steps in the analysis of single cell-based large-scale microscopy experiments. First, I will present a novel microscopic image correction method designed to eliminate illumination and uneven background effects which, left uncorrected, corrupt intensity-based measurements. New single-cell image segmentation methods will be presented using differential geometry, energy minimization and deep learning methods. I will discuss the Advanced Cell Classifier (ACC), a machine learning software tool capable of identifying cellular phenotypes based on features extracted from the image. It provides an interface for a user to efficiently train machine learning methods to predict various phenotypes. For cases where discrete cell-based decisions are not suitable, we propose a method to use multi-parametric regression to analyze continuous biological phenomena. To improve the learning speed and accuracy, we propose an active learning scheme that selects the most informative cell samples.

Using a combination of our newly developed methods, we introduced various single-cell isolation methods. I will show that we successfully performed DNA and RNA sequencing, and targeted electrophysiology measurements on the selected cells.

DR. ZSOLT BOLDOGKŐI

Projects of Genomics and Gene Technology Research Group

Our research group primarily works on molecular biology of viruses. There are two focuses of our investigations: the transcription regulation and construction of virus vectors for tracing brain circuitries. Our group was the first in the world in applying long-read sequencing technique for the analysis of viral transcriptomes (total RNAs). Using this method, we were able to map the transcriptome os several viruses belonging to various families, and as a result, we could multiply the number of formerly known transcripts in each case. The major aim of our investigations is to prove that the RNA polymerase reads through to adjacent and distal genes during transcription and thereby interfere with the transcription of these genes.

In another project, using molecular genetic techniques, we generate recombinant viruses, which can be applied for transneuronal tract-tracing and for the optical monitoring of neuron activity.

We also work on a project, which investigate the genetic background of major depression and suicide. In this study, we have identified several genetic variants, which contribute to the susceptibility of depression-based suicide.

We also started a project on the analysis of the molecular basis of Alzheimer disease, with a special focus on the splicing abnormalities.

In the near future, we plan to initiate projects for examining the effect of nutrition and certain disease on the microbiome.

We have modern equipments for our investigations, which include, e.g. Illumina MiSeq, tools for Oxford Nanopore Technology sequencing, PCR cyclers, real-time PCR equipments, ultracentrifuge, confocal microscopy, equipments for molecular cloning, cell culture and virology.

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. ATTILA HUNYADI

Chemical studies on natural products: from insect hormones to antitumor nanoparticles

Plant secondary metabolites represent a privileged chemical space. Such compounds have been developed during the evolution of plants with the specific aim to facilitate their adaptation to the environment through specific chemical-biological interactions. This is why (medicinal) plants can serve as a treasury of bioactive compounds including potential lead molecules for drug discovery.

In our research group, our aim is to find natural and nature-inspired compounds with high bioactivity. To this, we use a broad range of chemical approaches combining the toolkit of natural product isolation with that of modern synthetic chemistry. Techniques routinely used in our lab include a range of state-of-the-art chromatographic techniques, e.g. HPLC, supercritical fluid chromatography and centrifugal liquid-liquid partition chromatography.

Our current studies concern a wide variety of natural products, including phytoecdysteroids (insect molting hormones that have a non-hormonal anabolic effect on humans, and some of which can sensitize cancer cells to chemotherapeutics), antioxidant metabolites that may form through scavenging reactive oxygen/nitrogen species, and potent antitumor protoflavonoid derivatives. From a selected set of our compounds we also prepare self-assembling nanoparticle pro-drugs that allow targeted treatment of cells expressing high levels of LDL receptor. Bioactivity testing of the compounds is typically performed within a broad international collaboration network that includes several research groups from the Far-East and Europe.

GERGŐ PORKOLÁB

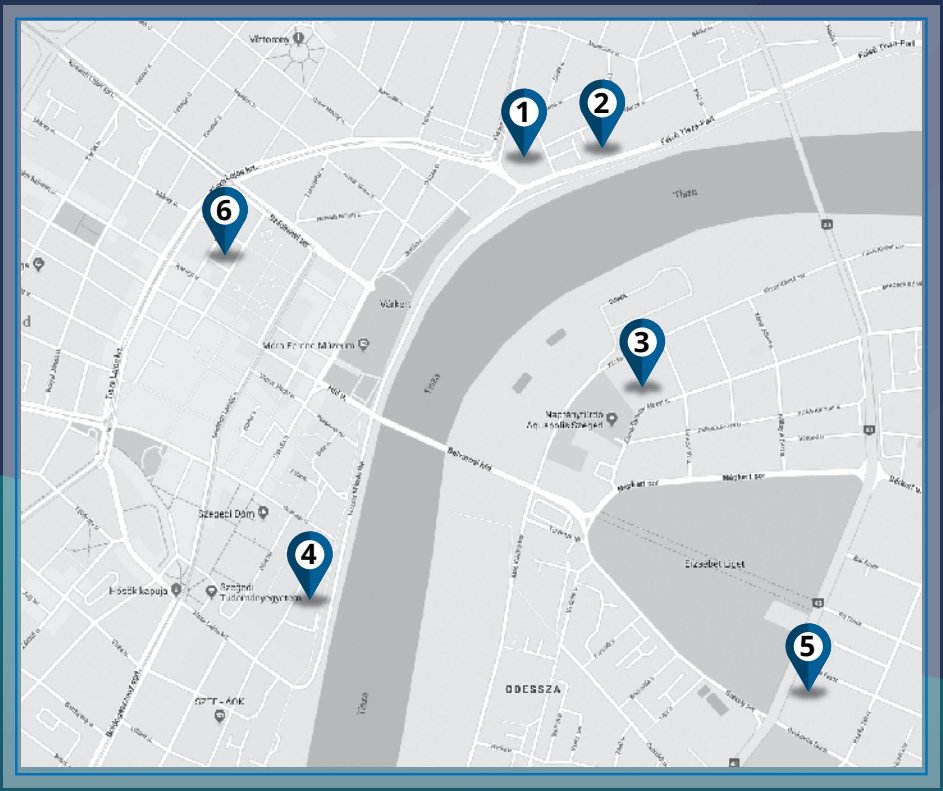
Interactions of targeted nanoparticles with different cell types of the brain

Mentor: **Dr. Maria A. Deli** Junior Mentor: **Dr. Szilvia Veszelka**

Treatment of brain diseases is especially challenging, because the majority of drugs are unable to cross the blood-brain barrier (BBB). As a solution, our research group takes the compounds to be delivered to the brain, loads them into nanoparticles (NPs) and decorates the surface of NPs with targeting molecules that are recognized by the transporters at the BBB.

The final therapeutic targets, however, are neurons – and to get to neurons, drugs have to travel trough layers of neighbouring pericytes and glial cells after crossing the BBB. Therefore it is important to develop such nanocarriers that can be recognized and taken up by multiple cell types in the brain.

First, we verified the gene expression pattern of proteins transporting the amino acid alanine in cultured brain endothelial cells, pericytes and astrocytes. Then we prepared NPs decorated with the combination of alanine and the peptide glutathione to investigate their cellular uptake. We showed that in all cell types tested, alanine-glutathione labeling of NPs resulted in a higher level of cellular uptake, compared to untargeted NPs. We also found that uptake of NPs was an active process, partially mediated by endocytosis. Our data indicates that alanine-glutathione labeling of NPs could potentially be exploited in drug delivery systems for the brain.



1. Novotel Szeged****
2. IH Event Center
3. Hunguest Hotel Forrás****
4. University of Szeged, Faculty of Medicine (Northern hospital garden)
5. Biological Research Centre, Szeged
6. Town Hall of Szeged

Sponsors of the XIV. Meeting of
Nobel Laureates and Talented Students:

Szeged Megyei Jogú Város

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