Institute
of Experimental
Medicine AS CR, v.v.i.

EU Centre of Excellence

Annual Report 2014

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Content

Introduction

In the coming years, we expect medical research to progress at an even faster and greater rate than ever before. In the Czech Republic our Institute has contributed a significant amount of research to the biomedical fields.

Recently, the Council for Research, Development and Innovation (RVVI), an advisory body to the Czech government, has approved its highest ever budget proposal for research and development (R&D) for the period 2016 to 2018. The new approach and management of the RVVI brings the promise of change. Practically speaking, this will involve the emergence of new laws concerning research, development and innovation, a prospective ministry that would be responsible for the management of science throughout the country, and the development of long-term policy frameworks and future systems for evaluating scientific work.

In 2014, the Institute of Experimental Medicine produced a number of significant results. Its scientists are continuing to work until 2018 in the following Centres of Excellence: the *Project of Excellence in the Field of Neuroscience* (primary investigator Josef Syka), the *Centre for Studies on Toxicity of Nanoparticles* (primary investigator Jan Topinka), and the *Centre for Orofacial Development and Regeneration* (primary investigator Renata Peterková). Zdeněk Zídek is the co-investigator of one of the Competence Centres of the Technological Agency of the Czech Republic (TA CR) and in the *Centre for Development of Original Drugs*. Pavel Vodička received the award for excellence from the President of the Grant Agency of the Czech Republic (GA CR), as well as further financial support for the project *Better anticipating the response of bowel and rectal cancer to chemotherapy*.

The *Research Centre for Cell Therapy and Tissue Repair received* support from the National Programme for Sustainability, Ministry of Education (NPU I), for the period 2014-19. Fully equipped laboratories are in use in the areas of tissue culturing, tissue engineering, biochemistry, molecular biology, and microbiology, and include certified grade C cleanrooms. There is ongoing basic and applied research in the field of advanced therapies using stem cells, biomaterials and nanomaterials for the treatment of severe or incurable diseases and defects. We continue to make every effort to introduce new therapeutic methods and materials into clinical trials. This is exemplified by the patented project *Atmospheric plasma source for specific use in medical bio-applications* and the registered national utility model *A source of low temperature plasma to mainly deactivate bacteria*, both contributed by the group of Šárka Kubinová, and the initiation of a clinical study concerning the safety and efficacy of the repeated administration of autologous MSCs in the treatment of ALS, sponsored by Bioinova Ltd. The research group of Evžen Amler participated in the project *New scaffold for cardiac patch*, as a result of which a European patent was registered in March 2014.

We have continued to successfully meet project objectives derived by the European Structural Funds. Examples include the project Operational Program Education for Competitiveness (OPVK) *Human Resources for Neuroscience Research* in Hradec Králové and Ústí nad Labem, supported by the European Social Fund, and the preparation of research teams for the project BIOCEV (Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University). In the context of this project, we offered an employment contract to nine post-doctorate fellows who would be able to reinforce our Institute's working groups at BIOCEV. One of our major projects, GAMA, which focuses on applied research, experimental development and innovation (from 2014 to 2019), received the support of TA CR for the commercialization of R&D outputs. The project is generally focused on bridging the critical phases of the innovation cycle – supporting applied research and the experimental development of products.

In collaboration with the Norwegian University of Trondheim, we acquired support from the Czech-Norwegian research program CZ09 for a joint project, *Biomaterials and Stem Cells in the Treatment of Stroke and Spinal Cord Injuries*, which is coordinated by Pavla Jendelová. In November 2014 we inaugurated two facilities, the *Research Centre for Genomics and Gene Mapping* and the *Centre for Advanced Imaging of Living Tissue*, financed by the Operational Program Prague Competitiveness (OPPK). These successful projects, totalling approximately 31 million CZK, have contributed significantly to the modernisation of equipment within the Institute.

The Institute is developing its own business facility, the Innovative Biomedical Centre, whilst supporting other firms within its business incubator. As part of the Acceleration Program, designed to support business in the City of Prague, three Innovation Vouchers were issued to three companies – EponaCell, Biotechinvest and ArtiCell. In 2014, the company Bioinova, 49.75% of which is owned by the Institute, continues to produce stem cells for clinical studies with the permission of the State Institute for Drug Control (SÚKL) and the European Medical Agency (EMA). In collaboration with the 2nd Medical Faculty, Charles University, Motol Hospital, Faculty Hospital Hradec Králové, and the Institute of Clinical and Experimental Medicine (IKEM), clinical studies for the treatment of amyotrophic lateral sclerosis, tendons, cartilage, bone, and diabetic foot are ongoing.

It is also our aim to emphasize the importance of education in society. In accordance with this, the Institute has organized several successful conferences, public events and international schools. Furthermore, a number of members of our research teams have participated in undergraduate teaching at the associated universities and in postgraduate training.

2014 has been a strong year for our Institute. In addition to the previously mentioned highlights, our researchers have published a total of 81 research articles in impacted journals with an average IF of 4.025. This contributes to the Institute's continual progress over the last five years, with a total of 414 publications in impacted journals with a total IF of 1629.128.

Eva Syková
Institute Director
1st Vice-Chairperson of RVVI

Focus of Activities

The Institute's research focuses on selected problems in biomedicine with particular attention paid to their application in clinical medicine. In the field of **neuroscience**, research is focused on ionic changes and diffusion parameters in the CNS during physiological and pathological states, non-synaptic transmission in the CNS, ion channels and receptors, the function of glial cells, the role of glutamate receptors and calcium ions in communication between neurons and glial cells, as well as the morphological and functional characteristics of nerve cells in the auditory system and their damage by pathological processes.

In the field of **stem cell research**, the Institute, in cooperation with the Centre for Cell Therapy and Tissue Repair, devotes significant effort to embryonic stem cells and the regulation of the cell cycle during gametogenesis and differentiation, the differentiation and implantation of neural and embryonic stem cells, the construction of tissue replacements based on hydrogels, as well as autologous chondrocytes and biodegradable matrices from unwoven nanofibres.

In the field of **cell biology**, research is concentrated on the structural-functional organization of the cell nucleus as well as on the molecular mechanisms involved in carcinogenesis and susceptibility towards neoplasia. Recent research has also been directed towards the identification of early markers indicating malignant transformations, which could be useful for early diagnostics of cancer. The molecular mechanisms involved in carcinogenesis and susceptibility towards neoplasia have also been investigated.

Other research areas include the genotoxic and embryotoxic effects of xenobiotics and the mechanisms underlying the origin of congenital defects, the origin and course of toxic reactions at cellular and tissue levels, the histochemistry and pharmacology of enzymes as markers of biochemical processes, and the effect of pharmaceuticals on the immune reaction during infectious diseases.

In the field of **biotechnological innovations** the work of the Institute has focused on technology transfer and the support of collaborations between the IEM CAS and the business sphere in the area of regenerative medicine, by means of education and joint R&D activities.

History of the Institute

The current research areas of the Institute of Experimental Medicine are a result of its **history**. Officially founded in 1975, the Institute combined four previously existing medical research laboratories. Three of these laboratories were affiliated with clinical departments of Charles University (the Departments of Plastic Surgery, Ophthalmology, and Otorhinolaryngology), whilst the fourth, oriented towards cell and tissue ultrastructures, was closely connected with the Department of Histology at the First Medical Faculty. Under the leadership of the renowned professors Burian, Kurz, Přecechtěl and Wolf, the laboratories established themselves in the world of medicine, contributing significantly to international recognition of Czechoslovak medical research. Although intellectually strong and reasonably well-equipped, the individual laboratories suffered from physical isolation and a lack of collaboration. Therefore, their consolidation into a single Institute under the Czechoslovak Academy of Sciences was mutually beneficial.

An otolaryngologist, **Prof. Vlastimil Kusák**, was appointed as the first director (1975–1984). During his leadership, the research spectrum of the Institute was extended by inviting a group of immunologists (Dr. Jiří Franěk and Dr. Karel Nouza) and by establishing a laboratory to investigate the health effects of mycotoxins in Eastern Bohemia (Olešnice, Eagle Mountains).

In the seventies and eighties the Institute's profile was crystallized, most notable by the transfer of most of the laboratories to a single building on Legerová street as well as the appointment of **Prof. Jiří Elis** as director (1984–1990). Research areas broadened to include electron microscopic investigation of the cell nucleus and nucleolus, particularly in blood cells; the morphological tracing of nucleic acids; the morphology and immunocytochemistry of the thyroid gland and pancreas; mechanisms of local immunity, cancer immunity and the graft-versus-host reaction; the bio- and histochemistry of the eye; corneal pathology and the testing of contact lenses; inner ear morphology and its change under noise; the electrophysiology of the central auditory system; the basics of genotoxicity and teratology; mechanisms and epidemiology of craniofacial malformations; and the testing of mycotoxins. While several groups and individuals succeeded in reaching a high standard of scientific work, as a whole the Institute suffered from scattered topics, a lack of internal communication and other obstacles characteristic of life in Czechoslovakia during that era.

In the beginning of the nineties the country's changing political situation and the leadership of the newly appointed director, **Prof. Richard Jelínek** (1990–1994), led to the rejuvenation of the Institute, harmonizing its scientific orientation and human capital. Its structure was reorganized on the basis of free competition for internal projects and was further strengthened by its success in obtaining grants from the Grant Agency of the Academy of Sciences. Increases were seen in both the involvement of the Institute's members in the teaching of medical students and in ecologically oriented research, particularly concerning the adverse effects of exogenous factors on organisms.

The Institute's profile further improved with the admission of two new strong scientific groups in 1991 – the Laboratory of Cellular Neurophysiology headed by Prof. Eva Syková (originally part of the Institute of Physiological Regulations), and the Laboratory of Genetic Ecotoxicology headed by Dr. Radim Šrám (a joint laboratory with the Regional Hygiene Station of Central Bohemia). Clinically oriented groups ceased to exist or were transferred to clinics. In 1993 the Institute moved to a new building in Prague-Krč, where several other biomedical institutes of the Academy of Sciences are located. In 1994, **Prof. Josef Syka** was appointed director (1994–2001), with significant changes in the Institute's organization since then focusing on its orientation and the improvement of its scientific profile.

In 2001 the Institute's current director, **Prof. Eva Syková**, was appointed and in 2002 the Institute's research program grew to its current size. At present, the Institute belongs to the biomedical group of research institutes of AS CR and is the only institute in the Czech Republic engaged in a comprehensive medical research program encompassing a number of diverse fields.

In 2015, the Institute will celebrate the 40th anniversary of its founding.

Management

Director:
Prof.
Eva Syková
MD, DSc, FCMA

Vice Director:
Assoc. Prof.
Alexandr Chvátal
DSc, MBA

Chairperson of the Council of the Institute:
Prof. Eva Syková, MD, DSc, FCMA

Chairperson of the Supervisory Board:
RNDr. Hana Sychrová, DSc, PhD

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Institute Profile

Council of the Institute

The Council is the major management body of the Institute, sharing responsibilities for the operation of the Institute with the Director. The Public Research Institutions Act stipulates the statutory duties of the Council, which involves observing the primary objectives of the Institute by setting the basic scientific orientation of research at the Institute as well as its development strategy, and by approving the Institute's budget as well as its annual report. The Council consists of both internal and external members.

Internal Members:

Prof. Eva Syková, MD, DSc, FCMA
(Chairperson of the Council)

Radim J. Šrám, MD, DSc.
(Vice-Chairperson of the Council)
Miroslava Anděrová, PhD
Assoc. Prof. Alexandr Chvátal, DSc, MBA
Assoc. Prof. Pavla Jendelová, PhD
Assoc. Prof. Miroslav Peterka, MD, DSc
Prof. Josef Syka, MD, DSc, FCMA
Pavel Vodička, MD, PhD
Zdeněk Zídek, DSc, PhD

External Members:

Prof. Stanislav Filip, MD, DSc
Milan Hájek, DSc
Assoc. Prof. Aleš Hampl, DVM, PhD
Prof. Miroslav Ryska, MD, PhD
Prof. Josef Zámečník, MD, PhD

Secretary: Petr Bažant, PhD, MBA
E-mail: bazant@biomed.cas.cz

Supervisory Board of the Institute

The Supervisory Board of the Institute is another obligatory body of the Institute mandated by law. It exercises supervisory responsibilities regarding the operation and management of the Institute and gives prior consent to intended legal actions of the Institute as defined by law (e. g., the sale or purchase of a property, the establishment of a company or other legal person and/or the holding of shares in such a company, the signing of an occupational lease etc.). The Supervisory Board meets at least two times a year.

The current Board is composed of the following members:

Hana Sychrová, DSc, PhD
(Chairperson of the Supervisory Board)

Petr Bažant, PhD, MBA
(Vice-Chairperson of the Supervisory Board)
Jiří Malý, JSD
Prof. Jiří Rubeš, DVM, PhD
Karel Filip, MD, PhD, MBA
Josef Fulka, MSc, DSc

Secretary:
Jan Prokšík, MSc
E-mail: proksik@biomed.cas.cz

Organizational Structure in 2014

EU Centre of Excellence

DIRECTOR BOARD | **VICE DIRECTOR**

COMMISSIONS | **SCIENTIC SECRETARY**

MANAGEMENT UNITS

- **Secretary Units**
- **Accounting and Economic Department**
- **Microscopy Unit**
- **Innovation Biomedical Centre**
- **Research Centre for Cell Therapy and Tissue Repair**

RESEARCH UNITS

- **Department of Neuroscience**
  Lab. of Diffusion Studies and Imaging Methods
  Lab. of Tissue Culture and Stem Cells
  Lab. of Biomaterials and Biophysical Methods
- **Department of Auditory Neuroscience**
  Laboratory of Synaptic Physiology
  Lab. of Auditory Physiology and Pathology
- **Department of Cellular Neurophysiology**
- **Department of Molecular Neurophysiology**
- **Department of Pharmacology**
- **Department of Genetic Ecotoxicology**
  Laboratory of Molecular Epidemiology
  Laboratory of Genetic Toxicology
  Laboratory of Genomics
- **Department of Teratology**
  Laboratory of Embryogenesis
  Laboratory of Odontogenesis
- **Department of the Molecular Biology of Cancer**
  Laboratory of the Genetics of Cancer
  Laboratory of DNA Repair
- **Department of Transplantation Immunology**
  Laboratory of Transplantation Immunology
  Lab. of Eye Histochemistry and Pharmacology
- **Department of Tissue Engineering**

ASSOCIATED RESEARCH CENTRES

- **Department of Neuroscience IEM AS CR and Department of Neuroscience 2nd Medical Faculty, Charles University**
- **Centre for Regenerative Medicine IEM AS CR, IKEM and Charles University**
- **Centre for Neuroregeneration and Biomedical Research IEM AS CR and Krajská zdravotní a.s. (Masaryk Hospital, Ústí nad Labem)**

Research Centres

1. Project of Excellence in the Field of Neuroscience, GA CR

Programme: GB – Projects for promotion of excellence in basic research (2012–2018)
Contractor: Institute of Physiology AS CR, v.v.i.
Principal investigator: Ladislav Vyklický, MD, DSc. Jr.
Project participants: National Institute of Mental Health, **Institute of Experimental Medicine AS CR, v.v.i.**, Charles University, 2. LF
Participant investigators: Daniela Řípová, PhD; **Prof. Josef Syka, MD, DSc, FCMA**; **Miroslava Anděrová, PhD**

Neurodegenerative disorders are common not only in the aging population, but also in young adults, becoming an increasingly serious socio-economic problem. Such etiologically heterogenous diseases lead to severe cognitive, motor and sensory deficiencies. The project aims to elucidate the pathophysiological mechanisms underlying the development of these diseases, from the genetic level up to the system level. The project will enable the creation of a network of high level scientific teams and thus promote an inter-disciplinary approach that would otherwise not be feasible based on individual projects of any single partner. Using a broad battery of methods, the mechanisms involved in regulating gene expression, membrane receptor function, inter-cellular communication, extra-cellular space modulation, and glia function will be investigated. As the research will be aimed at understanding basic processes, the output will lead to innovative and effective treatments of the diseases, e.g. using neuroactive steroids, stem cells, etc. The project will also provide a unique basis for PhD training in neuroscience.

Results in 2014

Downregulation of glutamine synthetase and glutamate transporters were reported in many neurological disorders and diseases, including Alzheimer's disease (AD). We decided to check the influence of transplanted human mesenchymal stem cells (hMSCs) on the expression of proteins of interest in specific brain regions: the hippocampus, the entorhinal cortex and the prefrontal cortex. We found a significant decrease of glutamine synthetase levels between 3xTg-AD animals (sham operated and transplanted groups) and non-transgenic controls in the hippocampus and the prefrontal cortex, suggesting the protective effect of hMSCs in AD.

Early postnatal short noise exposure (8 min, 125 dB SPL at postnatal day 14) induced permanent changes in the morphology of neurons in the central auditory system in adult rats. On the other hand, an acoustically enriched environment of moderate intensity, applied during the third and fourth week of life in rats, positively affected signal processing in the subcortical auditory nuclei in adult animals. MR morphometry and diffusion tensor imaging with a 3 T MR system demonstrated significantly worse parameters in the elderly subjects with different states of presbycusis without significant a correlation to the extent of hearing loss.

2. Centre for Studies on Toxicity of Nanoparticles, GA CR

Programme: GB – Project for promotion of excellence in basic research (2012–2018)
Contractor: Veterinary Research Institute, v.v.i.
Principal investigator: Miroslav Machala, PhD
Project participants: Institute of Chemical Process Fundamentals AS CR, v.v.i., Institute of Animal Physiology and Genetics AS CR, v.v.i.,
Institute of Analytical Chemistry AS CR, v.v.i., **Institute of Experimental Medicine AS CR, v.v.i.**, Charles University, Faculty of Science
Participant investigators: Pavel Moravec, MSc, PhD; Assoc. Prof. Omar Šedý, PhD; Zbyněk Večeřa, MSc, PhD; **Jan Topinka, DSc**; Jan Hovorka, PhD

The rapid expansion of nanomaterial production and their use in many products requires understanding the mechanisms of nanomaterial interactions with living systems. This need stems from the unique properties of nanoparticles, such as their dimensions and ability to penetrate into various tissues and cells in organisms. Some

nanoparticles are formed unintentionally as a result of anthropogenic activities (industry, traffic, local heating). The proposed interdisciplinary centre of basic research will integrate laboratories capable of performing complex studies on the toxicity mechanisms of important and widely used engineered nanoparticles, as well as anthropogenic nanoparticles in the environment, with special attention paid to heavily polluted areas of the Czech Republic. The studies will be performed on thoroughly characterized nanoparticles in order to obtain valid and comparable results on their biological action and toxicity. Such results may serve as a basis for the development of further methods to study the toxicity of nanoparticles.

Results in 2014

In 2014, the Centre achieved multiple significant priority results. The first of two major results suggests that ultrafine particles in ambient air are not major carriers of carcinogenic polycyclic aromatic hydrocarbons (cPAHs) and their genotoxicity. The second indicates that individual cPAHs induced substantially higher genotoxicity than that of their comparable concentrations in real complex mixtures in ambient air.

3. Centre for Development of Original Drugs, TA CR

Programme: Cempetence Centres (2012–2019)
Contractors: Institute of Organic Chemistry and Biochemistry AS CR, v.v.i., **Institute of Experimental Medicine AS CR, v.v.i.**, Institut of Physiology AS CR, v.v.i., Palacky University in Olomouc, LF, VŠCHT in Prague, Apigenex, Ltd, IOCB TTO Ltd, MediTox, Ltd
Principal investigator: Zdeněk Havlas, DSc, PhD
Participant investigators: **Zdeněk Zídek, DSc, PhD**; Ladislav Vyklický, MD, DSc; Assoc. Prof. Martin Valchář, PhD; Jan Zábský, MBA; Assoc. Prof. Martin Fusek, PhD; Miroslav Havránek, PhD; Assoc. Prof. Marián Hajdúch, MD, PhD

The project Centre for Development of Original Drugs is a strategic plan utilizing the results of research in medicinal chemistry and pharmacology. The goal is to enable the transfer of drug candidates into commercial practice. The project will create a structure which will be able to evolve novel drugs mainly in the pre-clinical phase. The project will increase the success rate of original drug development in the Czech Republic and will extend this field of local research and industry. The major aim of the project is evaluation of original medicinal chemistry and pharmacological data from the point of view of their transfer to commercial practice. The organization of the Centre ensures the enhancement of competitive ability of the Czech pharmaceutical industry, depending on traditional successful and recognized fields of the Czech science.

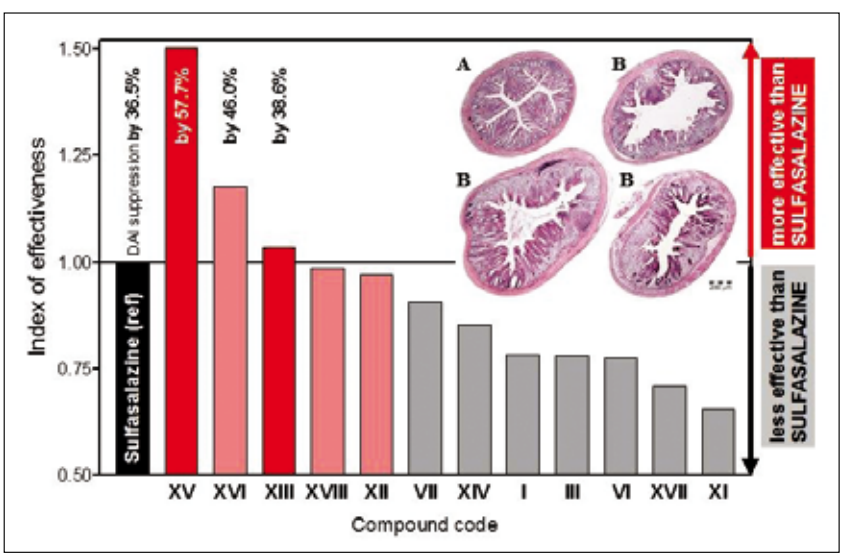

Fig: Several low-molecular weight compounds significantly suppress the severity of experimental colitis in mice. Histological sections show healthy colon (**A**) and various stages (**B**) of the disease development.

Result in 2014

Patent for substances which are expected to be used in the treatment of inflammatory diseases, especially intestinal diseases:
Patent Number: US 08883798: Pyrimidine compounds inhibiting the formation of nitric oxide and prostaglandin E2, method of production thereof and use thereof.
Patent Assignee: Institute of Organic Chemistry and Biochemistry AS CR, v.v.i., **Institute of Experimental Medicine AS CR, v.v.i.**
Inventors: Jansa, P.; Holý, A.; **Zídek, Z.**; **Kmoníčková, E.**; **Janeba, Z.**
Published: NOV 11 2014.

4. Centre of Orofacial Development and Regeneration, GA CR

Programme: GB – Projects for promotion of excellence in basic research (2014–2018)
Contractor: Institute of Experimental Medicine AS CR, v.v.i., Prague
Principal investigator: Renata Peterková, MD, PhD
Project participants: Institute of Animal Physiology and Genetics AS CR, Brno
Charles University in Prague, 1st Faculty of Medicine
Department of Stomatology, Faculty of Medicine, Masaryk University, Brno
Participant investigators: Prof. Eva Matalová, MD, PhD; Prof. Zdeněk Broukal MD, PhD; Prof. Jiří Vaněk, MD, PhD

Integration of four groups allows the complex basic research of development and regeneration of orofacial structures, mainly teeth and anchoring apparatus, from embryo to adults. Project is aimed to getting results that will contribute to elaboration of regenerative medicine methods focused on the development of biological replacements of teeth.

Development and regeneration are both creating tissues being controlled by similar genes and their products. The project will bring new results to be used in the rapidly developing area of regenerative dentistry. The results on early tooth development in animal models will help in understanding of general mechanisms of the determination of tooth type and shape, the knowledge important for engineering of tooth crowns. Odontogenic cells potentialities will be determined during ontogeny to identify cells with persisting potential to induce tooth regeneration in adults. Studies on later odontogenesis will elucidate tooth-bone interaction and the establishment of tooth fixation in the jaw by periodontal tissues. Priodont quality and possibilities of its regeneration will be studied also in human, since the quality of periodontal tissues ensuring tooth fixation is a prerequisite for successful outcome of the biological (engineered) tooth implants technologies.

Results in the first year (2014)

Lower incisor development in mice with an excess NF-κB activity. Small, supernumerary upper incisor was found documenting revival of the odontogenesis program that is suppressed under physiological conditions in mice, but stimulated in *K5-Ikkβ* mutants. (Blackburn et al, 2014). Similar small incisor is physiologically present in mouse-related group – lagomorphs.

In this study, the group of the Department of Teratology IEM AS CR was involved in morphological analyses of developing incisors in mutant and control mice using histology and 3D reconstructions.

5. Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University, BIOCEV, Ministry of Education CR

Programme: ED – Operational Programme Research and Development for Innovation (2008–2015)
Director: Prof. Pavel Martásek, MD, DSc
Project participants: Charles University, Faculty of Science and 1st Medical Faculty; Institute of Molecular Genetics AS CR; Institute of Microbiology AS CR; Institute of Macromolecular Chemistry AS CR; Institute of Physiology AS CR; **Institute of Experimental Medicine AS CR**; Institute of Biotechnology AS CR

This project aims to establish a centre of excellence, as part of the European Research Area, and guarantee the development of modern biotechnologies and biomedicine in favour of scientific progress and society. The main objective of this project is to concentrate research teams of renowned specialists with mutual professional interests, which are currently dispersed across various institutes of the Academy of Sciences of the Czech Republic and Charles University. Additionally, recruitment of young talented researchers and international experts is a necessary complement in order to establish the Biotechnology and Biomedicine Research Centre in Vestec (BIOCEV), with the ambition of creating a European Centre of Excellence.

The presence of teams providing outputs of their unique basic research and of biotech experts, who will follow the research lines with their practical applications and innovations, in a single infrastructure with top-class instrumentation, will hence fill this considerable gap in the development of biotechnology industry in the Czech Republic. Participation in the networks of European consortia of Euro-BioImaging and INFRAFRONTIER as a part of ESFRI (European Strategy Forum on Research Infrastructures) as well as collaboration with renowned European partners is an essential asset of the BIOCEV centre. The research teams will recruit young researches with international post-doctoral experience as well as top Czech and international PhD students. At the same time, new teams will be created with the aim of recruiting researchers who have succeeded in competitive funding schemes such as EMBO (European Molecular Biology Organization) or the Wellcome Trust and who have been granted support to set up a new laboratory. Generation of a new knowledge basis together with the unique BIOCEV infrastructure will provide biotech companies with exceptional means of cooperation in the form of contracted research with professional staff training in advanced biotechnology methods.

Department of Neuroscience

Head: Prof. Eva Syková, MD, DSc, FCMA
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The Department is focused on using stem cells and biomaterials in regenerative medicine, especially in the treatment of traumatic brain and spinal cord injury, neurodegenerative diseases (amyotrophic lateral sclerosis or Alzheimer disease), ischemic diabetic foot, ulcers and bone defects. The Department also studies diffusion parameters and extrasynaptic transmission in the central nervous system (CNS) during physiological and pathological states. New biophysical approaches, such as low-temperature atmospheric plasma or high-gradient magnetic field, are studied in terms of their interactions with biological systems and optimized for medical applications.

Laboratory of Tissue Culture and Stem Cells

Head of Laboratory: Assoc. Prof. Pavla Jendelová, PhD
E-mail: jendel@biomed.cas.cz | Phone: +420 241 062 828

The main topics studied in the laboratory are isolation, labelling and the use of stem cells for the treatment of brain injury, spinal cord and neurodegenerative diseases. Various types of cells (mesenchymal stem cells, neural precursor cell lines derived from fetal spinal cord, or from induced pluripotent cells) are studied, together with anti-inflammatory substances for their potential to promote the regeneration of nervous tissue. Macroporous polymeric hydrogels are used as suitable carriers for cell growth in *in vitro* cultures as well as for *in vivo* implantations facilitating the regeneration of the injured tissue. The aim of the cell therapy is to repair, replace or improve biological functions of the damaged neural tissue.

Research Scientists:
Prof. Eva Syková, MD, DSc, FCMA
Assoc. Prof. Pavla Jendelová, PhD
Takashi Amemori, DVM, PhD
Serhiy Forostyak, MD, PhD
Klára Jiráková, PhD
Lucia Urdzíková-Machová, MD, PhD
Aleš Hejčl, MD, PhD

PhD Students:
Karolína Turnovcová, MD
Jiří Růžička, MSc
Kristýna Kárová, MSc
Monika Šeneklová, MSc
Barbora Svobodová, MSc

Undergraduate Student:
Anna Kloudová

Technicians:
Michal Douděra
Linda Fedorowiczová
Pavlína Macková
Lucie Svobodová, PhD

1. Neural precursors from induced pluripotent cells (iPS-NP) significantly improve motor function in rats with spinal cord injury

Grafted cells (iPS-NP) survived well and slowly mature into different neuronal phenotypes (GABAergic, Serotonergic and motoneurons). In addition, they produced growth factors, stimulating neuronal sprouting. As a result, animals with spinal cord injury significantly improved their motor function. Rats were able to support their body weight and perform stepping, so they scored well in tests requiring movement coordination, such as beam walking.

Collaboration: Brigitte Onteniente, INSERM

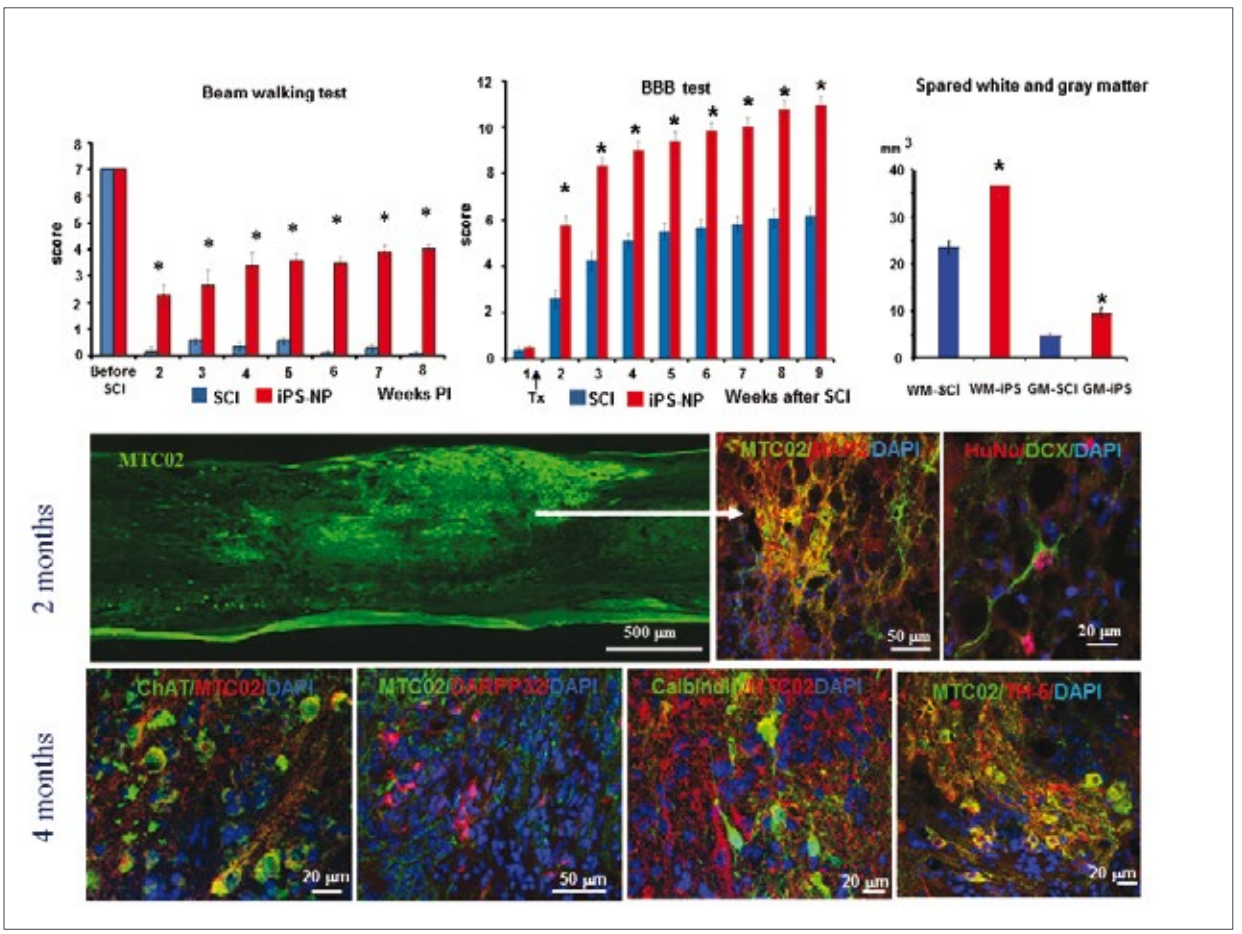

Fig: Rats implanted with neural precursors showed better functional outcome after spinal cord ijury and higher volume of spared white and grey matter. Grafted cells robustly survived in the lesion, migrated into the parenchyma and differentiated into gabaergic, dopaminergic and cholinergic neurons.

Publication:

Romanyuk N, Amemori T, Turnovcová K, Procházka P, Onteniente B, Syková E, Jendelová P, (2014): Beneficial effect of human induced pluripotent stem cell-derived neural precursors in spinal cord injury repair. Cell Transplant. [Epub ahead of print] IF 3.570

2. Mesenchymal stem cells increase lifespan of animals with amyotrofic lateral sclerosis (ALS)

We studied the effect of human mesenchymal stem cells (MSCs) in the treatment of an experimental model of ALS. We found that application of MSCs improved motor performance and muscle strength and led to an extended lifespan. MSCs partially rescued motor neuron (MN) loss and decreased apoptosis. MSCs transplantation is therefore a safe procedure able to promote CNS remodeling and regeneration.

Collaboration: Prof. James Fawcett, Cambridge, UK

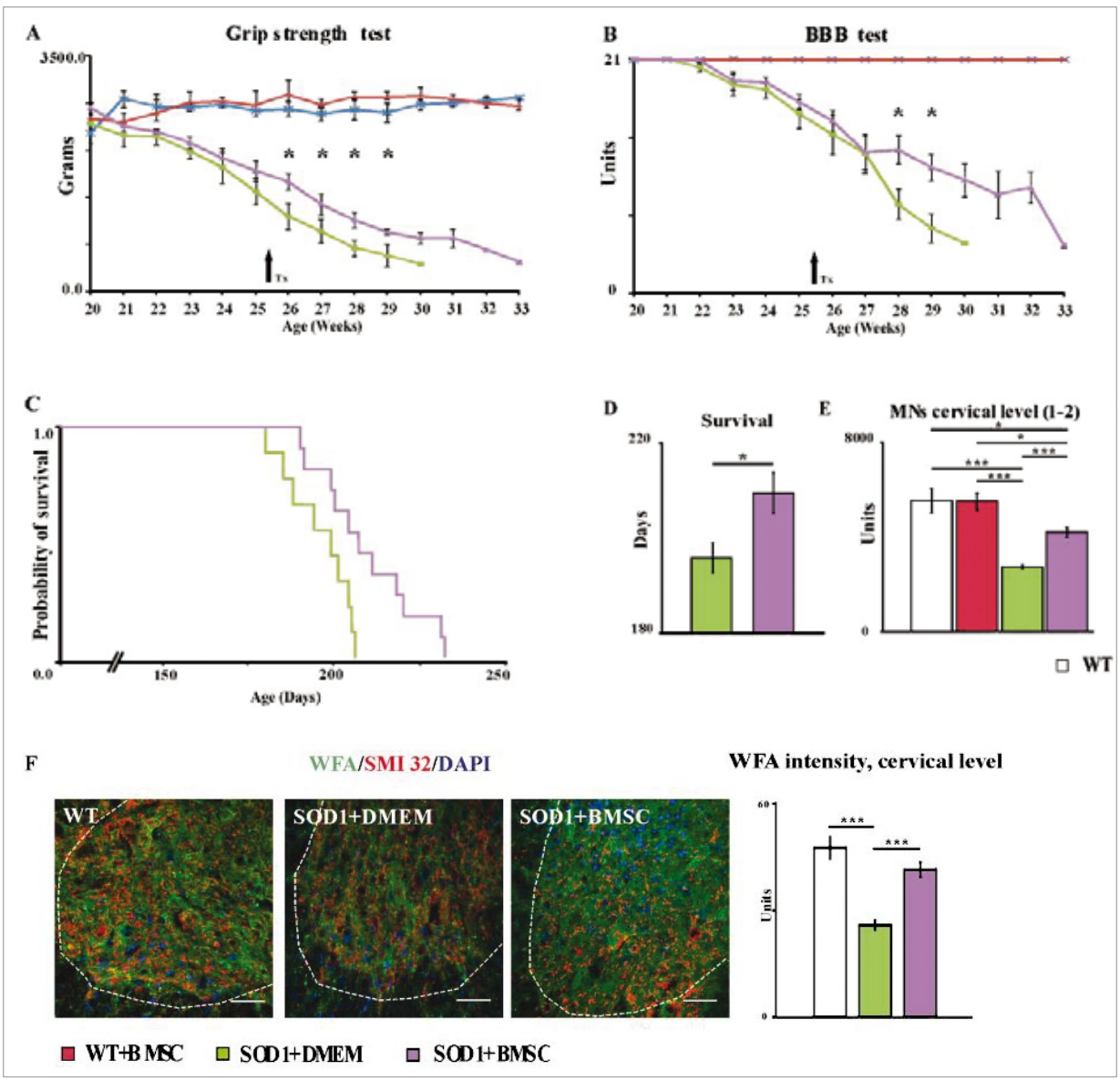

Fig: The effect of MSC application. After the appearance of first disease symptoms SOD1 rats were treated (arrow) with MSCs (intrathecally, 5×105 cells/50µl) or vehicle-injected (DMEM, 50µl). Shortly after delivery of MSCs disease progression has been slowed down shown by the digger muscle strength (**A**) and higher motor activity (**B**). MSC-treated rats lived significantly longer (**C**, **D**) and preserved higher number of ventral motor neurons (**E**) compared with vehicle-injected littermates. We found that SOD1 rats have deteriorated perineuronal nets structure around motor neurons and that application of MSCs partially preserved their structure (**F**).

Publication:

Forostyak S, Homola A, Turnovcová K, Svítil P, Jendelová P, Syková E, (2014): Intrathecal Delivery of Mesenchymal Stromal Cells Protects the Structure of Altered Perineuronal Nets in SOD1Rats and Amends the Course of ALS. Stem Cells.;32(12):3163-72. IF 7.133

Laboratory of Diffusion Studies and Imaging Methods

Head of Laboratory: Prof. Eva Syková, MD, DSc, FCMA
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The Laboratory of Diffusion Studies and Imaging Methods studies the changes in the extracellular space diffusion parameters and extrasynaptic (volume) transmission that occur during physiological and pathological states. Several animal models of pathological states and diseases attacking the CNS are used, e. g., models of chronic pain, ischemia and ischemic lesions, perinatal and early postnatal anoxia, brain edema, hydrocephalus, multiple sclerosis, Parkinson's disease, Alzheimer's disease, tumors, epilepsy, developmental disorders, aging, and brain and spinal cord injury, as well as models of CNS damage evoked by chemical or physical factors such as neurotoxins or X-irradiation. The research aims are the improvement of therapy and diagnostic methods for CNS diseases and the prevention of CNS damage.

Research Scientists:
Prof. Eva Syková, MD, DSc, FCMA
Assoc. Prof. Lýdia Vargová, MD, PhD
Ivan Voříšek, PhD
Aleš Homola, MD, PhD

PhD Students:
Lesia Dmytrenko, MSc

Technicians:
Helena Pavlíková

Important Results in 2014

1. The impact of alpha-syntrophin deletion on the changes of extracellular volume in experimental models of physiological and patological conditions

Changes in the volume of extracellular space and individual astrocytes as well as in gene expression was assesed in α-syntrophin knockout mice by real-time iontophoretic (RTI) method, 3D-confocal morphometry and RT-qPCR, respectively. The deletion of α-syntrophin altered astrocyte swelling and extracellular space volume changes during severe hypoosmotic stress, ischemia or increased K^+ concentration but not during mild (physiological) stimuli. Altered volume regulation in astrocytes plays a crucial role in edema formation and α-syntrophin thus represents a possible target for therapeutical intervention.

The results were used also in a review, which summaries current findings about the role of astrocytes and extracellular matrix in the volume transmission, neuron-glia communication and signal transfer during selected physiological and pathological states.

Collaboration: Department of Neuroscience, Charles University, 2nd Faculty of Medicine

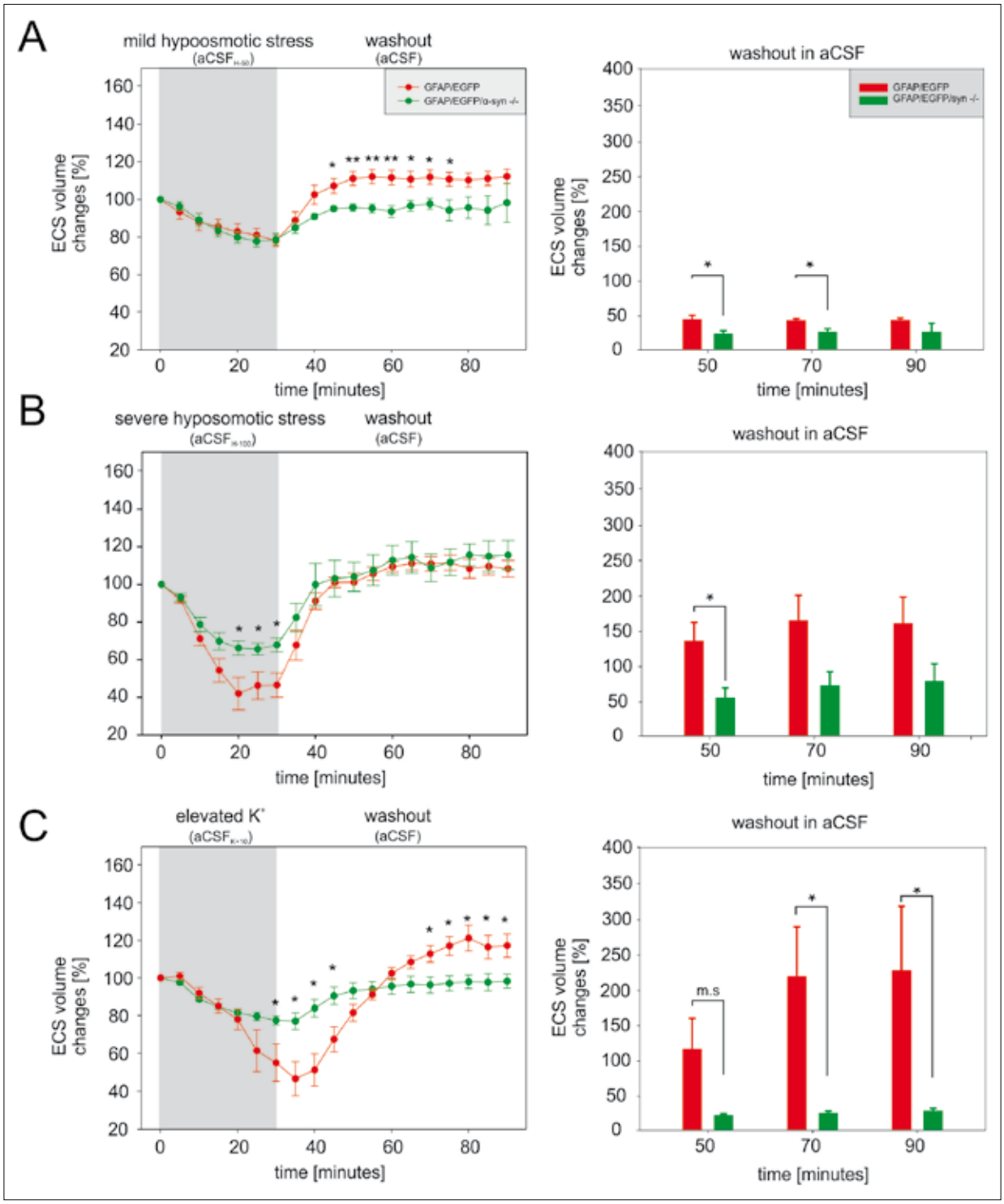

Fig. 1: The effect of hypotonic stress or elevated K^+ on the extracellular space (ECS) volume *in situ*.
The left side: The control values of all experiments were set to 100%, and the relative changes of the values of the extracellular volume fraction α were calculated at 5 min intervals during a 30 min application and a subsequent 60 min washout of mild (**A**) or severe (**B**) hypotonic stress or 10 mM K^+ (**C**). Each data point represents mean ± S.E.M. The right side: volume regulation during washout at 20 min intervals is expressed as changes in the values reached in the 30th minute of application, set as 0%. Asterisks indicate significant (*, $p<0.05$) and very significant (**, $p<0.01$) differences between GFAP/EGFP and GFAP/EGFP/α-Syn$^{-/-}$ mice.

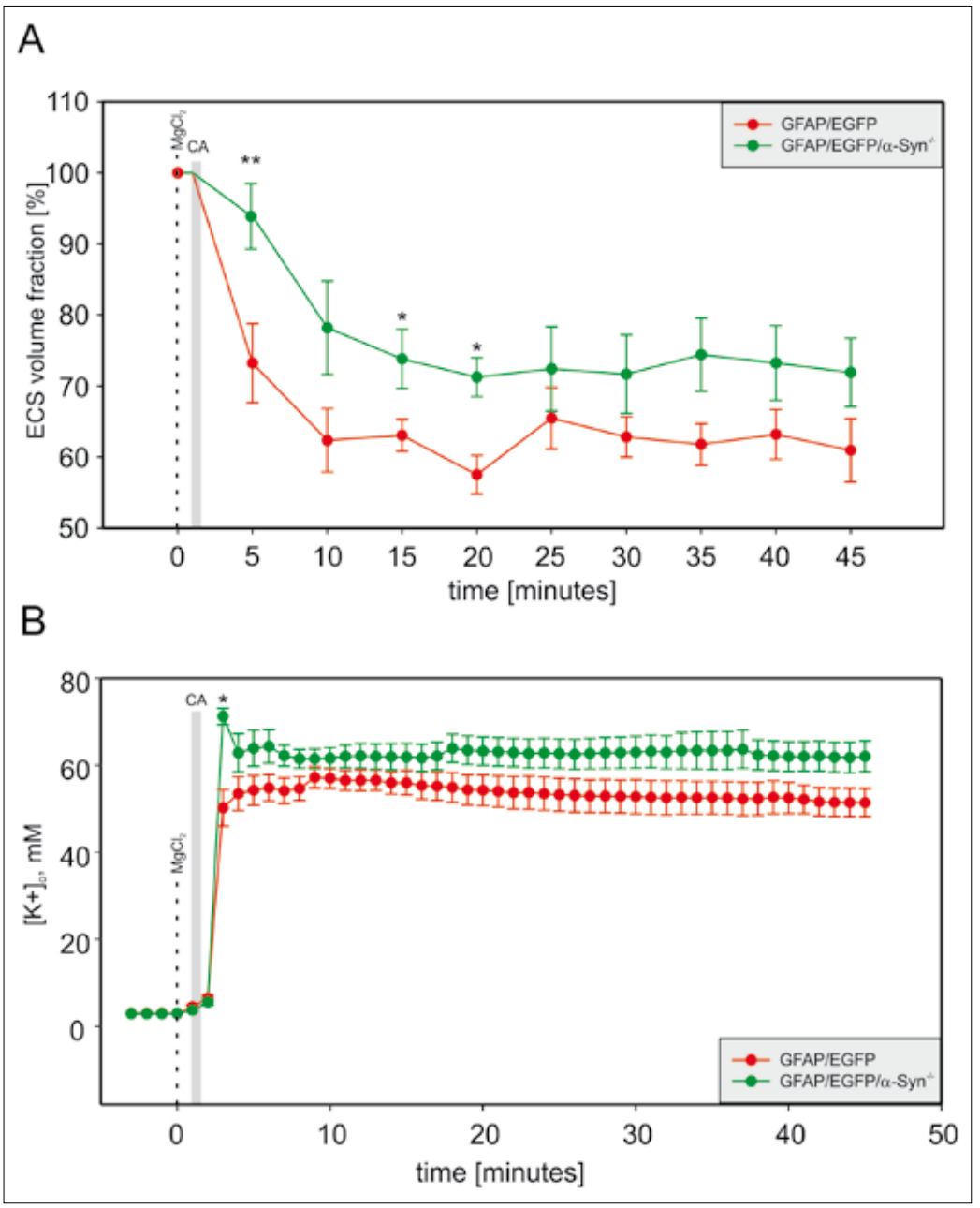

Fig. 2: Relative changes in the ECS volume fraction and $[K^+]_o$ evoked by terminal ischemia/anoxia *in vivo*. Each data point represents mean ± S.E.M, calculated at 5 min intervals for ECS volume changes and each minute for $[K^+]_o$ changes. The relative changes in the values of the ECS volume fraction α (**A**) after the onset of terminal ischemia/anoxia were significantly smaller and slower in GFAP/EGFP/α-Syn$^{-/-}$ mice than in GFAP/EGFP controls, but the final values did not differ. In contrast, the steep rise in $[K^+]o$ levels (**B**) was higher and faster in GFAP/EGFP/α-Syn$^{-/-}$ mice compared to GFAP/EGFP animals, indicating impaired homeostatic mechanisms; no difference was found in the final values. The gray bar indicates cardiac arrest (CA) and the dashed line indicates $MgCl_2$ injection. Asterisks indicate significant (*, $p<0.05$) and very significant (**, $p<0.01$) differences between GFAP/EGFP and GFAP/EGFP/α-Syn$^{-/-}$ mice.

Publications:

Anděrová M, Benešová J, Mikesová M, Džamba D, Honsa P, Kriška J, Butenko O, Novosadová V, Valihrach L, Kubista M, Dmytrenko L, Cicanič M, Vargová L, (2014): Altered Astrocytic Swelling in the Cortex of α-Syntrophin-Negative GFAP/EGFP Mice. PLoS One. 9(11):e113444. IF 3,53

Vargová L, Syková E, (2014): Astrocytes and extracellular matrix in extrasynaptic volume transmission. Philos Trans R Soc Lond B Biol Sci. 369(1654):20130608. IF 6.314

Laboratory of Biomaterials and Biophysical Methods

Head of Laboratory: Šárka Kubinová, PharmD, PhD
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The laboratory aims to develop advanced synthetic and natural biomaterials as scaffolds for regenerative medicine and tissue engineering and evaluates their functions on biological models. In collaboration with the Institute of Physics AS CR, a complex research of low-temperature plasma effects on biological systems as well as development of novel devices for medical applications is performed.

Research projects:

– Development of biomaterials for the treatment of spinal cord injury;
– Development and study of low-temperature atmospheric pressure plasma for biomedical applications;
– Controlling of stem cell fate and targeted stem cell delivery with high-gradient magnetic fields.

Research Scientist:
Šárka Kubinová, PharmD, PhD

PhD Students:
Zuzana Kočí, MSc
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Kristýna Závišková, MSc
Karel Výborný, MSc

Pre-gradual student:
Jana Dubišová, Bc

Technicians:
Linda Fedorowiczová
Lenka Uherková, MSc, PhD

Important Results in 2014

Characterization of human adipose tissue-derived stromal cells isolated from diabetic patient's distal limbs with critical ischemia

The study compares the properties of stem cells isolated from adipose tissue (ASC) in diabetic patients with critical distal limb ischemia with ASC of non-diabetic subjects. Flow cytometry confirmed the mesenchymal phenotype of diabetic ASC, however 40% of the samples revealed a high proportion of fibroblast-positive cells, which inversely correlated with the expression of CD105. In diabetic ASC, decreased osteogenic differentiation, the expression of VEGF and chemokine receptor CXCR4 was found in fibroblast-positive cells. These factors may affect the efficacy of autologous stem cell therapy in diabetic patients.

Collaboration: Institute of Clinical and Experimental Medicine

Publication:

Kočí Z, Turnovcová K, Dubský M, Baranovičová L, Holáň V, Chudíčková M, Syková E, Kubinová Š (2014): Characterization of human adipose tissue-derived stromal cells isolated from diabetic patient's distal limbs with critical ischemia.Cell Biochem Funct. 32(7):597-604. IF 2.13

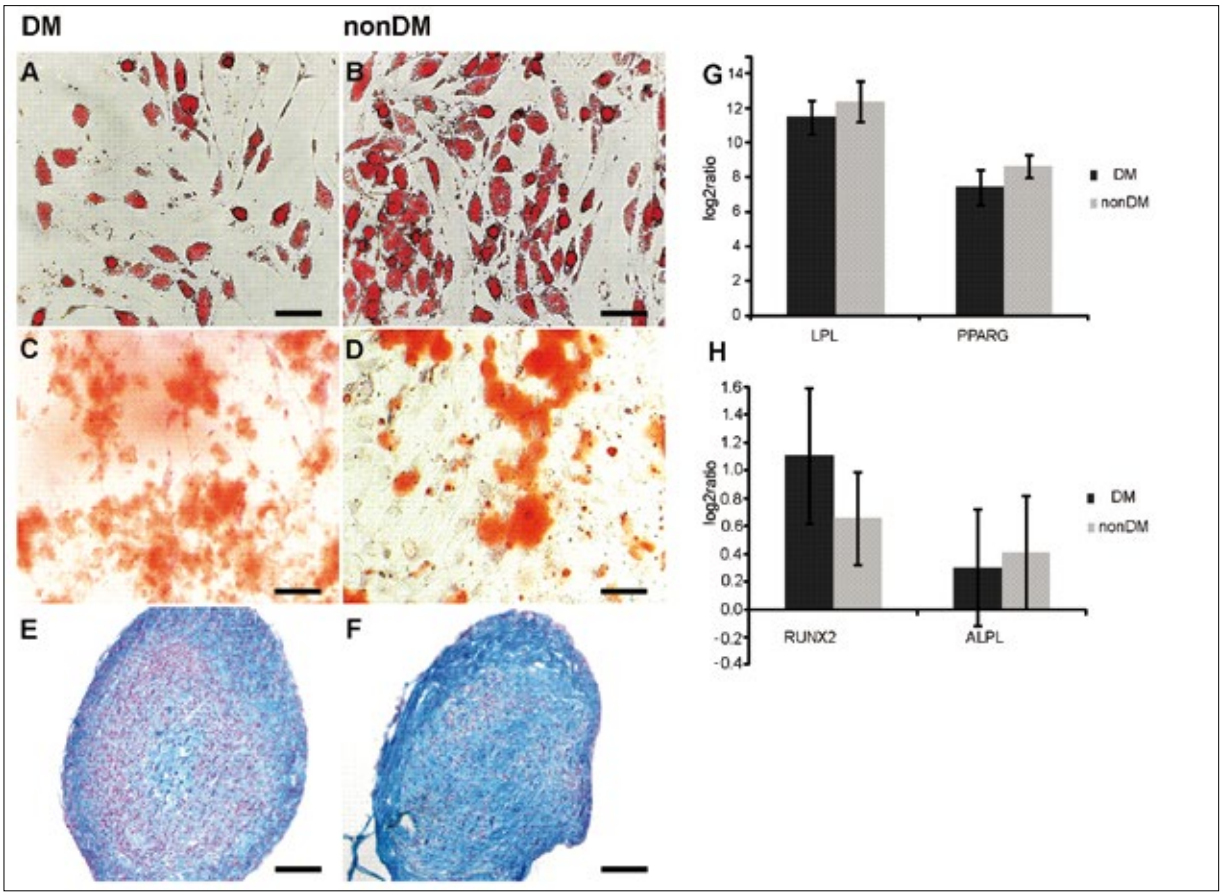

Fig: Differentiation of human adipose tissue-derived stromal cells isolated from diabetic (DM) and non-diabetic (non-DM) patients. (**A**, **B**) adipogenic; (**C**, **D**) osteogenic; (**E**, **F**) chondrogenic differentiation; (**G**, **H**) expression of adipogenic (LPL, PPARG) and osteogenic (RUNX2, ALPL) specific genes. Scale bar: 50 um. * P <0.05

Patent:
Atmospheric plasma source, particularly for use in medicinal bioapplications
PV 2013–543, no. 304 814
Institute of Physics AS CR, v.v.i., Institute of Experimental Medicine AS CR, v.v.i., Prague, CZ
Olexander Churpita MSc; Alexandr Dejneka, PhD; Assoc. Prof. Vitaly Zablotskyy, DSc; Šárka Kubinová PharmD, PhD; Prof. Eva Syková MD, DSc, FCMA

Utility model:
Low-temperature plasma source, particularly for deactivation of bacteria

Application number:
2014–30345, Registration Number: 27679

Applicant / Owner:
Institute of Physics AS CR, v.v.i., Institute of Experimental Medicine AS CR, v.v.i.

Originator:
Alexander Churpita, MSc; Alexandr Dejneka, MSc, PhD; Assoc. Prof. Vitaly Zablotskyy DSc;
Šárka Kubinova, PharmD, PhD; Prof. Eva Syková, MD, DSc, FCMA

Department of Auditory Neuroscience

Head: Prof. Josef Syka, MD, DSc, FCMA
E-mail: syka@biomed.cas.cz | Phone: +420 241 062 700

Morphological and functional characteristics of nerve cells in individual auditory nuclei under normal and pathological conditions are studied in the Department. Electrophysiological and histological data are correlated with changes in the animal behavior evaluated with behavioral tests. Audiological tests and MR imaging are used to characterize age-related changes in hearing in humans.

Laboratory of Auditory Neurophysiology

Head of Laboratory: Prof. Josef Syka, MD, DSc, FCMA
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The basic principles of the neuronal processing of simple tones and complex sounds and pathologies of the peripheral and central parts of the auditory system, appearing as a consequence of noise exposure or in conjunction with aging, are investigated in experimental animals and in human subjects using the electrophysiological, behavioral, audiometric and morphological methods. It has been demonstrated that acoustically enriched environment applied during the critical period of development in rats permanently affected signal processing in the subcortical auditory nuclei resulting in lower thresholds of neuronal responses, an increased frequency selectivity, larger response magnitudes and an increased spontaneous firing rate (Bureš et al., 2014; Fig. 1). Two-photon calcium imaging *in vivo* enabled studying of information processing in selected populations of neurons in the auditory cortex using transgenic mice. Hearing thresholds were examined over an extended frequency range 0.125–16 kHz in a large sample of men and women aged 16–70 years, to enable preparation of the standards (Jilek et al., 2014; Fig. 2). Significant atrophy in the auditory cortex of elderly subjects with different degree of presbycusis was revealed using magnetic rezonance morphometry (Profant et al., 2014). Results in human subjects were obtained in cooperation with the MR Unit, Department of Diagnostic and Interventional Radiology of the Institute for Clinical and Experimental Medicine (IKEM), Prague, and the Department of Otorhinolaryngology and Head and Neck Surgery, 1st Medical Faculty of Charles University, University Hospital Motol, Prague.

Research Scientists:
Prof. Josef Syka, MD, DSc, FCMA
Zbyněk Bureš, PhD
Jana Burianová, PhD
Jiří Lindovský, PhD
Ladislav Ouda, MD, PhD
Jiří Popelář, PhD
Oliver Profant, MD, PhD
Natalia Rybalko, PhD
Daniel Šuta, PhD
Milan Jílek, MSc

PhD Students:
Zuzana Balogová, MD
Tatyana Chumak, MD
Ondřej Novák, MSc
Ondřej Zelenka, MD

Technicians:
Jana Janoušková
Jan Setnička

Important Results in 2014

1. Age-related changes in hearing

Hearing thresholds were examined using pure-tone audiometry over the extended frequency range 0.125–16 kHz in a large sample of men and women aged 16–70 years The results could be used to normalize hearing thresholds when comparing participants differing in age and to prepare an international standard.

Magnetic resonance morphometry was used to study the state of the central auditory system in a group of elderly subjects with different degree of presbycusis. The results demonstrate significant atrophy in the auditory cortex of elderly subjects.

Collaboration: The MR Unit, Department of Diagnostic and Interventional Radiology of the Institute for Clinical and Experimental Medicine (IKEM), Prague
Department of Otorhinolaryngology and Head and Neck Surgery, 1st Medical Faculty of Charles University, University Hospital Motol, Prague

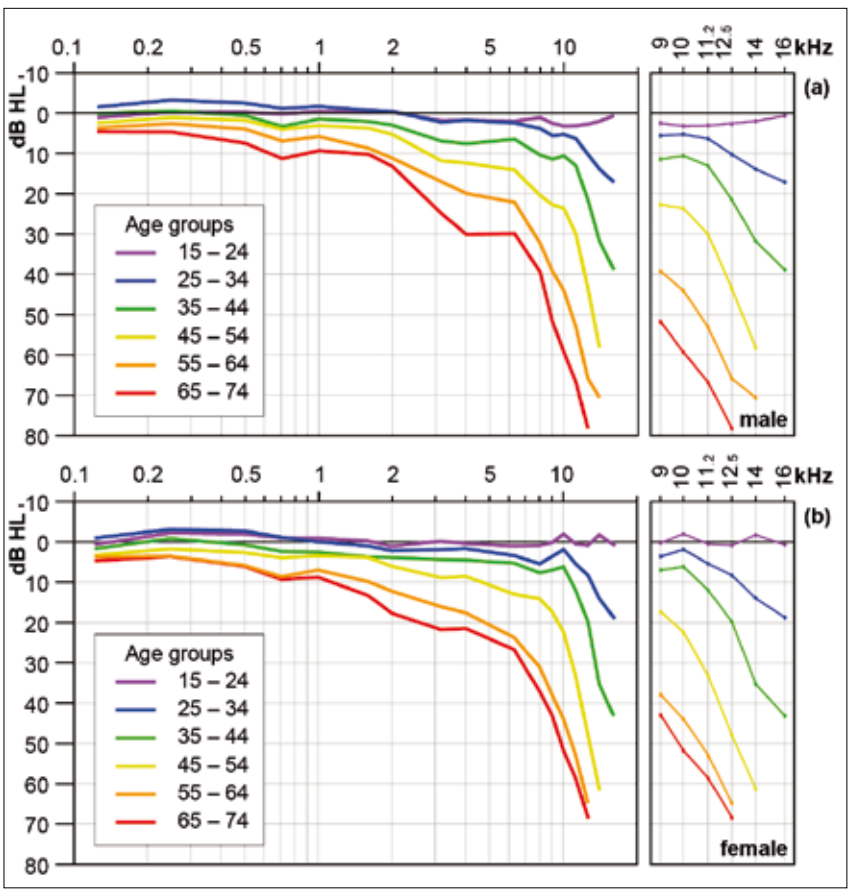

Fig: Audiograms. Average pure-tone audiograms in men (top) and women (bottom) grouped by their age in decades (the parameter is age group in years). The extended high-frequency range is zoomed for clarity.

Publication:

Jílek M, Šuta D, Syka J, (2014): Reference hearing thresholds in an extended frequency range as a function of age and their mathematical approximation. J Acoust Soc Am. 136(4):1821–1830. IF 1.555

Profant O, Škoch A, Balogová Z, Tintěra J, Hlinka J, Syka J, (2014): Diffusion tensor imaging and MR morphometry of the central auditory pathway and auditory cortex in aging. Neuroscience 260: 87–97. IF 3.327

2. Acoustical enrichment during early postnatal development in rats improves response properties of hearing function

The study explores the effects of an acoustically enriched environment applied during the critical period of development on the responsiveness of auditory neurons in rats resulting in lower excitatory thresholds at neuronal characteristic frequency, an increased frequency selectivity, larger response magnitudes, steeper rate-intensity functions and an increased spontaneous activity. Acoustically enriched environment may permanently affect signal processing in the subcortical auditory nuclei.

Collaboration: Department of Electrical Engineering and Computer Science, College of Polytechnics, Jihlava

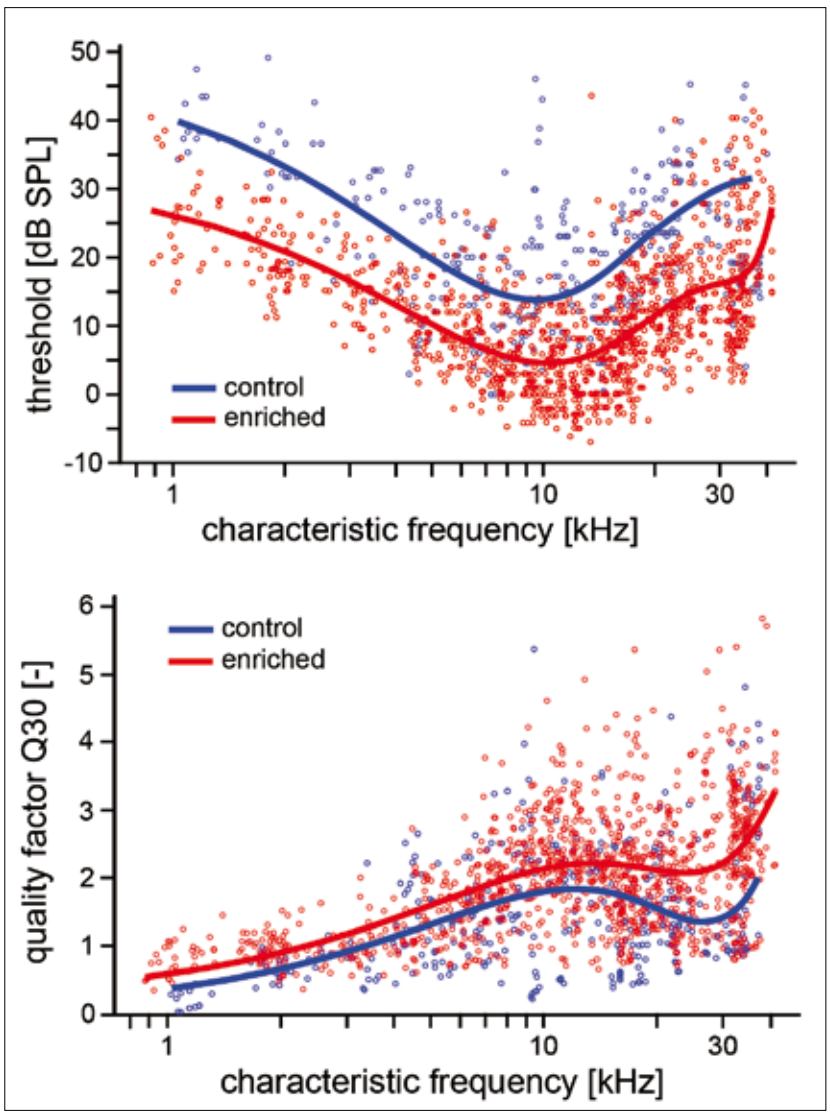

Fig: Enriched environment. Neuronal excitatory thresholds and tuning bandwidth. Top – scatter diagrams showing the dependence of the excitatory threshold on the characteristic frequency (CF) of the neurons in the control and enriched groups of rats along with fifth-order polynomial regression curves. Bottom – scatter diagrams showing the dependence of the Q30 parameter on the CF of the neurons in the control and enriched groups of rats along with fifth-order polynomial regression curves.

Publication:

Bureš Z, Bartošová J, Lindovský J, Chumak T, Popelář J, Syka J, (2014): Acoustical enrichment during early postnatal development changes response properties of inferior colliculus neurons in rats. Eur. J. Neurosci 2014, Vol. 40, pp. 3674–3683. IF 3.669

Laboratory of Synaptic Physiology

Head of Laboratory: Rostislav Tureček, PhD
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In the Laboratory of Synaptic Physiology the mechanisms underlying the plasticity of excitatory and inhibitory synaptic transmission are studied in rodent brain slices using electrophysiological and immunohistochemical techniques. The Calyx of Held synapse in the medial nucleus of the trapezoid body (MNTB) is mostly used as a model of the central type of synapse due to its large size enabling direct examination by patch-clamp technique. Recent projects in the lab are aimed at revealing the physiological roles of inhibitory transmitters, their receptors and uptake systems in the MNTB neurons. Experimental work has provided evidence of the novel excitatory nature of the classical inhibitory transmitters GABA and glycine (Tureček et al., 2014; Fig. 3). The results show that chloride-permeable glycine receptors, G-protein coupled GABA-B receptors, N-type Ca2+ channels and calcium-activated potassium conductances work in concert to support the extremely high reliability of glutamatergic synaptic transmission at MNTB neurons. Results were obtained in cooperation with the Department of Biomedicine, University of Basel, Basel, Switzerland.

Research Scientist:
Rostislav Tureček, PhD
Michaela Králíková, PhD

PhD Student:
Bohdana Hrušková, MSc
Kateryna Pysanenko, MSc

Important Result in 2014

Molecular mechanism of $GABA_B$ receptor desensitization

We studied mechanisms of KCTD12-induced desensitization of $GABA_B$ receptor activated K^+ currents. We show that the desensitization results from a dual interaction of KCTD12 with the G protein: constitutive binding stabilizes the heterotrimeric G protein at the receptor, whereas dynamic binding to the receptor-activated Gbg subunits induces desensitization by uncoupling Gbg from the effector K^+ channel. Our results show that $GABA_B$ receptors are endowed with fast and reversible desensitization by harnessing KCTD12 that intercepts Gbg signaling.

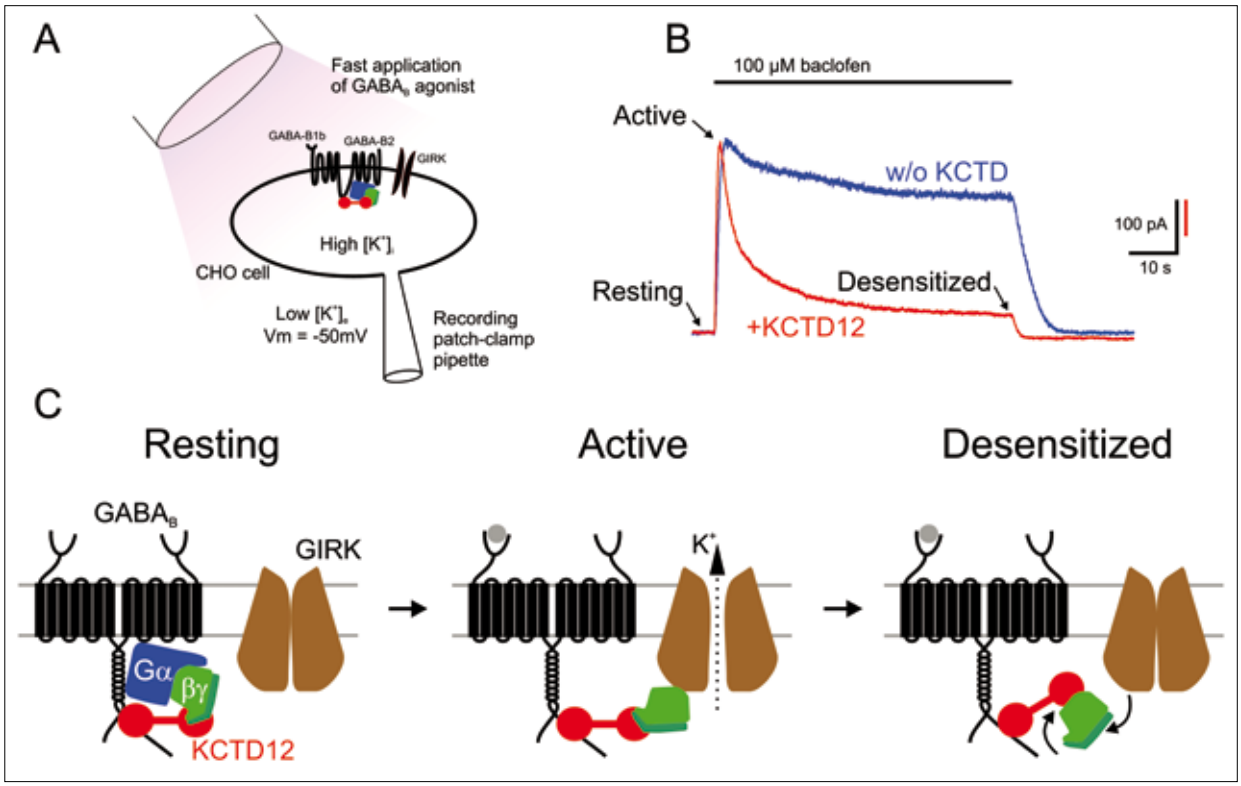

Fig: Molecular mechanism of KCTD12-induced desensitization of GABA$_B$ responses.
A, Scheme illustrates the patch-clamp recording of membrane currents mediated by G-protein activated inwardly rectifying K$^+$ channels (GIRK) from CHO cells. **B**, Representative traces of K$^+$ currents activated by GABA$_B$ agonist baclofen in CHO cells expressing GABA$_B$ receptors and GIRK channels either with or without (w/o) KCTD12. KCTD12 induces pronounced and rapid desensitization of the K$^+$ currents. **C**, Scheme illustrating a mechanism for fast desensitization of GABA$_B$-activated GIRK currents. Resting (left), active (middle), and desensitized (right) states of the current response are shown. KCTD12 constitutively assembles with GABA$_B$ receptors and the G-protein into a signaling complex (inactive state). Constitutive binding of KCTD12 to activated Gβγ allows for a transient activation of GIRK channels (active state). An activity-dependent rearrangement of KCTD12 at Gβγ leads to a shielding of the GIRK-binding site on Gβγ by KCTD12 and induces current desensitization (desensitized state).

Publication:

Tureček R, Schwenk J, Fritzius T, Ivánková K, Zolles G, Adelfinger L, Jacquier V, Besseyrias V, Gassmann M, Schulte U, Fakler B, Bettler B, (2014): Auxiliary GABA$_B$ Receptor Subunits Uncouple G Protein βγ Subunits from Effector Channels to Induce Desensitization. Neuron 82(5): 1032-1044. IF 15.982

Department of Cellular Neurophysiology

Head: Miroslava Anděrová, PhD
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The Department of Cellular Neurophysiology is focused on membrane and morphological characteristics of glial cells after ischemic brain injury and in the progression of neurodegenerative diseases, especially of Alzheimer's disease. Research is oriented towards astrocytes, both at the level of gene and protein expression, as well as at the level of astrocytic functional properties of ion channels and receptors, which are necessary for maintaining the homeostasis of ions and neurotransmitters in the extracellular environment. Another cell type which is at the centre of interest are NG2 glial cells, also called polydendrocytes, that during development and in the adult nervous tissue function primarily as precursors of oligodendrocytes, but following injury of the central nervous system they proliferate and differentiate into other cell types. The research aims to characterize their membrane properties in post-ischemic tissue and in the progression of Alzheimer's disease and to clarify the role of Wnt- and Shh-signaling pathways in proliferation/differentiation of NG2 glial cells.

Methods:
Patch-clamp method, calcium imaging, imunocyto-/imunohistochemistry, single cell RT-qPCR, FACS, induction of focal and global cerebral ischemia

Research scientists:
Miroslava Anděrová, PhD
Assoc. Prof. Alexandr Chvátal, DSc, MBA
Olena Butenko, PhD

PhD students:
Lenka Harantová, MSc
Martin Valný, MSc
Jana Turečková, MSc
Pavel Honsa, MSc
Dávid Džamba, MSc
Ján Kriška, MSc

Undergraduate students:
Denisa Koleničová
Denisa Kirdajová

Technicians:
Helena Pavliková
Markéta Hemerová, MSc

Important Results in 2014

1. Increased expression of hyperpolarization-activated cationic channels in reactive astrocytes following ischemia

Following cerebral ischemia we have identified hyperpolarization-activated (HCN) cationic channels in astrocytes. Until now, these channels were described only in neurons. Since HCN channels are mainly permeable for sodium and potassium ions, their increased expression in reactive astrocytes indicates that they may markedly influence the basic astrocytic functions in central nervous system, and consequently, an extent of nervous tissue damage following ischemia. Astrocytic HCN channels could therefore be an important therapeutic target in post-stroke therapy.

Collaboration: Institute of Biotechnology AS CR, v.v.i.

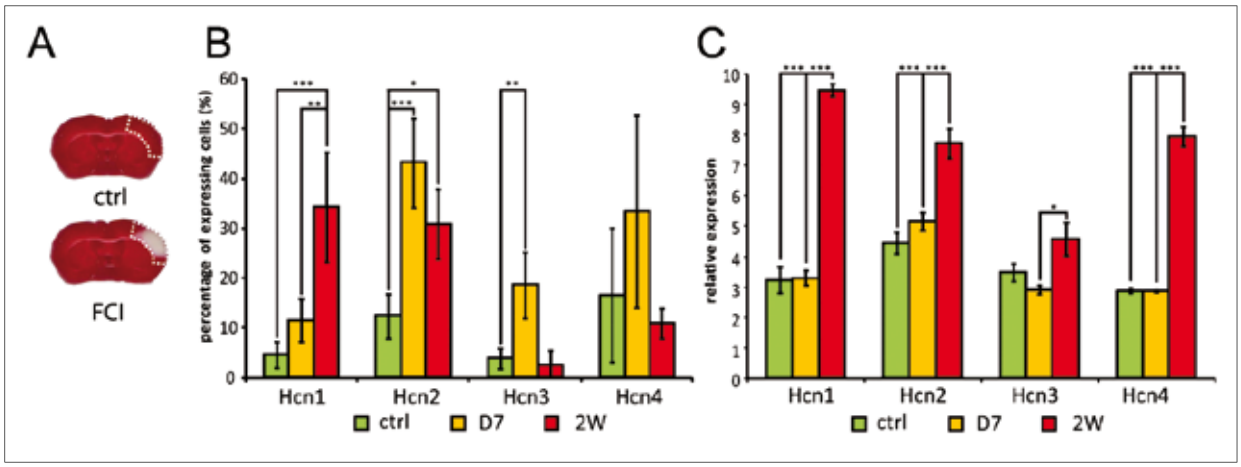


Fig.1:The expression of Hcn genes is strikingly increased in cortical astrocytes from GFAP/EGFP mice following focal cerebral ischemia – single-cell RT-qPCR profiling.
A: Scheme depicting the brain regions, which were used for EGFP+ cells isolations. These brain slices were stained with tetrazolium chloride to visualize the ischemic regions. **B**: Percentage of EGFP+ cells in the post-ischemic mouse cortex (7 and 14 days after focal cerebral ischemia; D7, 2W) expressing Hcn1, 2, 3 and 4. Note that ~30–35% of analyzed EGFP+ cells expressed Hcn1–3 genes 2W after focal cerebral ischemia (FCI). **C**:The relative expression of Hcn1–4 genes in EGFP+ cells in the control mouse cortex and in the post-ischemic cortex revealed the strong upregulation of Hcn1–4 expression 2W after FCI.
HCN1 staining in the CA1 region of the rat hippocampus in controls and five weeks after global cerebral ischemia. Brain slices were stained with anti-HCN1 antibodies and an antibody directed against glial fibrillary acidic protein (GFAP) in controls and five weeks (5W) after global cerebral ischemia (GCI). Arrowheads indicate the HCN-positive astrocytes after ischemia (s.p., stratum pyramidale; s.r., stratum radiatum). Scale bars, 50 μm.

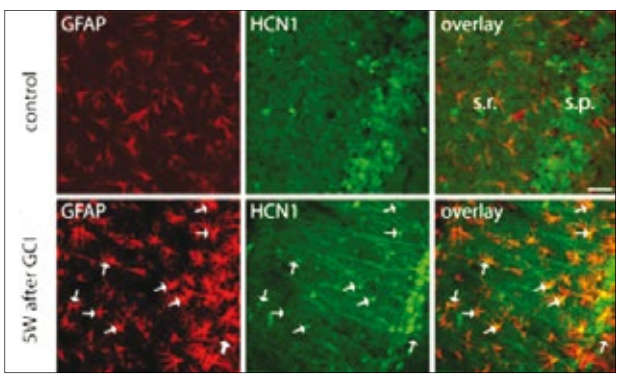


Fig.2: HCN1 staining in the CA1 region of the rat hippocampus in controls and five weeks after global cerebral ischemia.
Brain slices were stained with anti-HCN1 antibodies and an antibody directed against glial fibrillary acidic protein (GFAP) in controls and five weeks (5W) after global cerebral ischemia (GCI). Arrowheads indicate the HCN-positive astrocytes after ischemia (s.p., stratum pyramidale; s.r., stratum radiatum). Scale bars, 50 μm.

Publication:

Honsa P, Pivoňková H, Harantová L, Butenko O, Kriška J, Džamba D, Rusnaková V, Valihrach L, Kubista M. and Anděrová M, (2014): Increased expression of hyperpolarization-activated cyclic nucleotide-gated (HCN) channels in reactive astrocytes following ischemia. Glia 62 (12), 2004–2021. IF 5,466

2. Altered astrocytic swelling in the cortex of α-syntrophin-negative GFAP/EGFP mice

We have showed that knockout of α-syntrophin, which is a protein responsible for aquaporin-4 anchoring on the astrocytic membrane, affects cell swelling/volume regulation in individual astrocytes *in situ* when exposed to pathological stimuli. Astrocyte volume quantification revealed that α-syntrophin deletion results in significantly smaller/slower astrocyte swelling when induced by severe hypoosmotic stress, oxygen glucose deprivation (OGD) or 50 mM K^+.

Collaboration: Department of Neuroscience, 2nd Faculty of Medicine, Charles University in Prague
Institute of Biotechnology AS CR, v.v.i. – Prof. Mikael Kubista

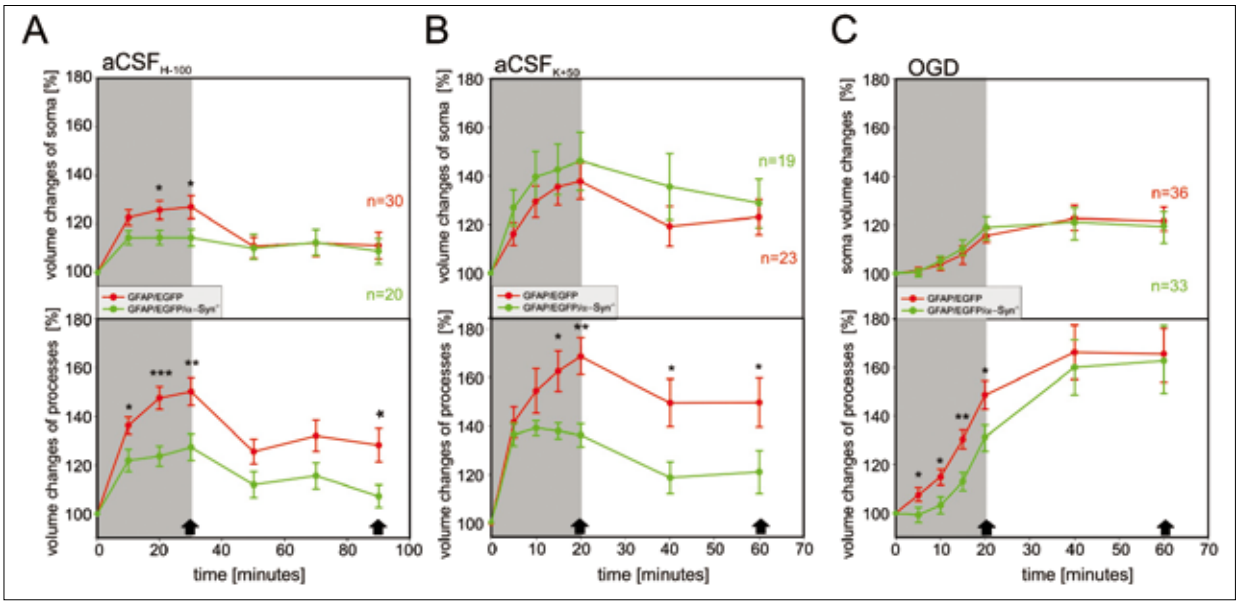


Fig.1: Volume changes in the astrocytic soma and processes during hypotonic stress, increased extracellular K^+ concentration and oxygen-glucose deprivation. (**A–C**) Time-dependent changes in the volume of the astrocytic soma (top) and processes (bottom) in GFAP/EGFP (red) and GFAP/EGFP/α-Syn$^{-/-}$ mice (green) during a 30-minute application of $aCSF_{H-100}$ (**A**), a 20-minute application of $aCSF_{K+50}$ (**B**) or 20-minute OGD (C), followed by a 60- or 40-minute washout. Asterisks indicate significant (*, $p<0.05$), very significant (**, $p<0.01$) and extremely significant (***, $p<0.001$) differences between GFAP/EGFP and GFAP/EGFP/α-Syn$^{-/-}$ mice.

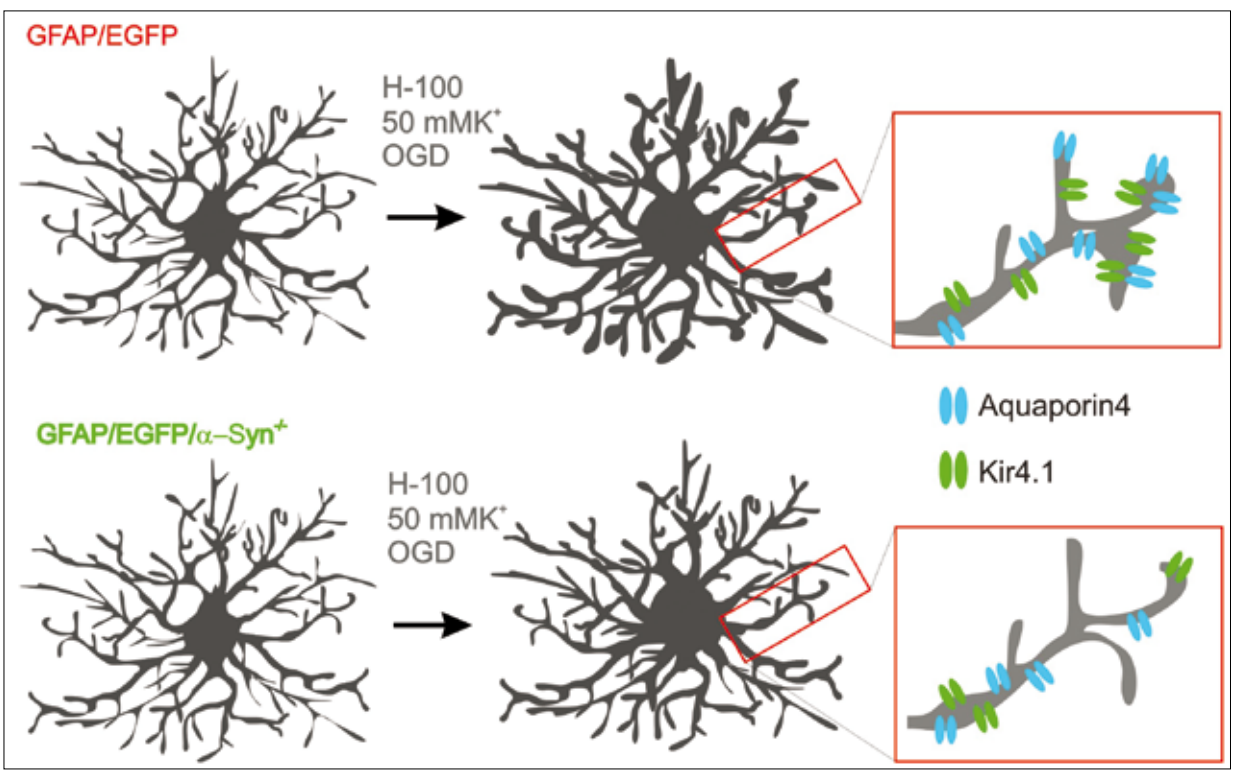


Fig. 2: The contribution of processes and cell soma to total astrocyte swelling is altered in astrocytes lacking α-syntrophin. A scheme depicting differences in swelling of astrocytic processes and cell soma in response to severe hypoosmotic stress, 50 mM K^+ and OGD (oxygen-glucose deprivation), highlighting smaller swelling of astrocytic processes in GFAP/EGFP/α-Syn$^{-/-}$ mice compared to those in GFAP/EGFP mice due to altered distribution of aquaporin4 and Kir4.1 channels.

Publication:
Anděrová M, Benešová J, Mikešová M, Džamba D, Honsa P, Kriška J, Butenko O, Novosadová V, Valihrach L, Kubista M, Dmytrenko L, Cicanič M, Vargová L (2014): Altered Astrocytic Swelling in the Cortex of α-Syntrophin-Negative GFAP/EGFP Mice, PLoS One. 9(11):e113444. IF 3.534

3. Intracellular Na^+ inhibits volume regulated anion channel in rat cortical astrocytes

Using patch clamp technique we have demonstrated that in primary cultured rat cortical astrocytes, elevations of $[Na^+]i$ reflecting those achieved during ischemia cause a marked decrease in hypotonicity-evoked current mediated by volume-regulated anion channel (VRAC). These results provide the first evidence that intracellular Na^+ dynamics can modulate astrocytic membrane conductance that controls functional processes linked to cell volume regulation and add further support to the concept that limiting astrocyte intracellular Na^+ accumulation might be a favorable strategy to counteract the development of brain edema.

Collaboration: University of Bologna, Italy, Prof. Stefano Ferroni

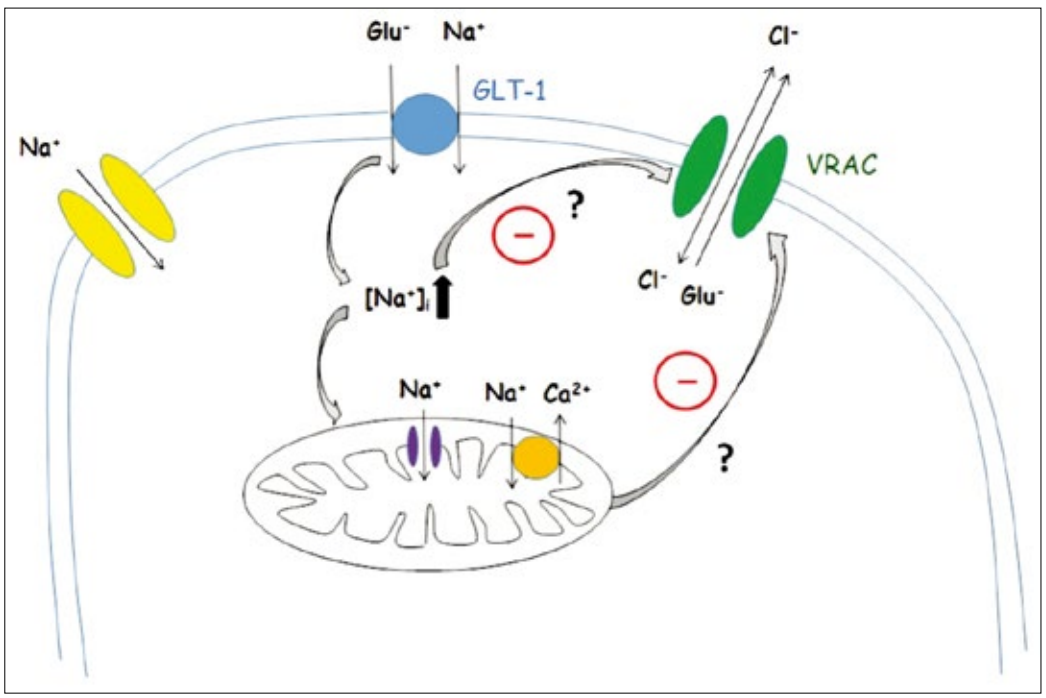
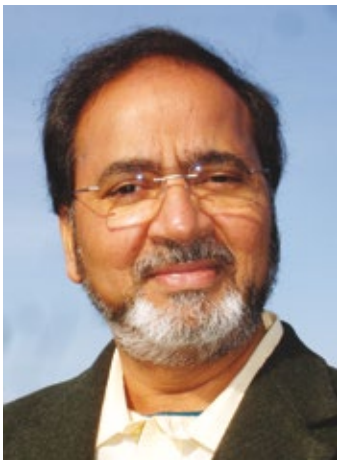


Fig: High elevation of intracellular sodium (Na^+) concentration in cultured rat astrocytes decreases the activity of volume-regulated anion channels (VRAC) measured by patch clamp technique. We speculate that in ischemic conditions intracellular Na^+ elevation either through the augmented activity of the Na^+-dependent glutamate transporter (GLT-1) or by Na^+-permeable channels could modulate the astrocytic volume and glutamate release (Glu^-) regulated by VRAC

Publication:
Minieri L, Pivoňková H, Harantová L, Anděrová M, and Ferroni S, (2014): Intracellular Na^+ inhibits volume regulated anion channel in rat cortical astrocytes, J Neurochemistry, doi: 10.1111/jnc.12962., IF 3.973

Department of Molecular Neurophysiology



Head: Govindan Dayanithi, MSc, PhD
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Phone: +420 241 062 725

The Department of Molecular Neurophysiology studies the role of vasopressin and oxytocin in the central and peripheral nervous system and their therapeutic implications for a number of human diseases. The division uses three models of transgenic rats, which allow the visualization of fluorescent vasopressin and oxytocin. These models are used to study calcium signaling and calcium homeostasis in magnocellular neurons and nerve terminals to illustrate the signaling mechanisms of vasopressin and oxytocin in DRG neurons and glial cells. Recently, within the Department, we have used a new approach to evaluate the plasticity of calcium signals in neural precursors derived from stem cells of various origins. The objective is to evaluate the pathophysiology of calcium signaling in neurons in animal models of neurodegenerative diseases and in the stem cells transplanted into the injured spinal cord.

Research Scientist:
Govindan Dayanithi, MSc, PhD
Research Director in CNRS
Tomohiko Kayano, MvD, PhD

PhD Students:
Oksana Forostyak, MD
Štěpán Kortus, MSc

Technician:
Dominika Dušková

Important Result in 2014

Full-length transient receptor potential vanilloid 1 channels mediate calcium signals and possibly contribute to osmoreception in vasopressin neurones in the rat supraoptic nukleus

The purpose of the present study was to uncover the structure and function of molecules related to the central osmoreceptorin the supraoptic nucleus (SON) of rats. For this purpose, we performed RT-PCR and immunohistochemistry for TRPV1-related molecules, and patch-clamp and imaging of the cytosolic Ca^{2+} concentration ($[Ca^{2+}]_i$) to measure responses to osmolality changes and TRPV-related drugs. Arginine vasopressin (AVP), synthesized in the SON is a key factor in systemic osmolality regulation. We found that AVP neurones in the SON possess functional full-length TRPV1. Moreover, differences between the responses to capsaicin or hyperosmolality obtained in rat SON neurones and those obtained from dorsal root ganglion neurones or TRPV1-expressing cells indicate that the osmoreceptor expressed in the SON may be a heteromultimer in which TRPV1 is co-assembled with some other, yet unidentified, molecules.

Collaboration: Prof. Izumi Shibuya, Laboratory of Veterinary Physiology, Joint Department of Veterinary Medicine, Faculty of Agriculture, Tottori University, Tottori, Japan

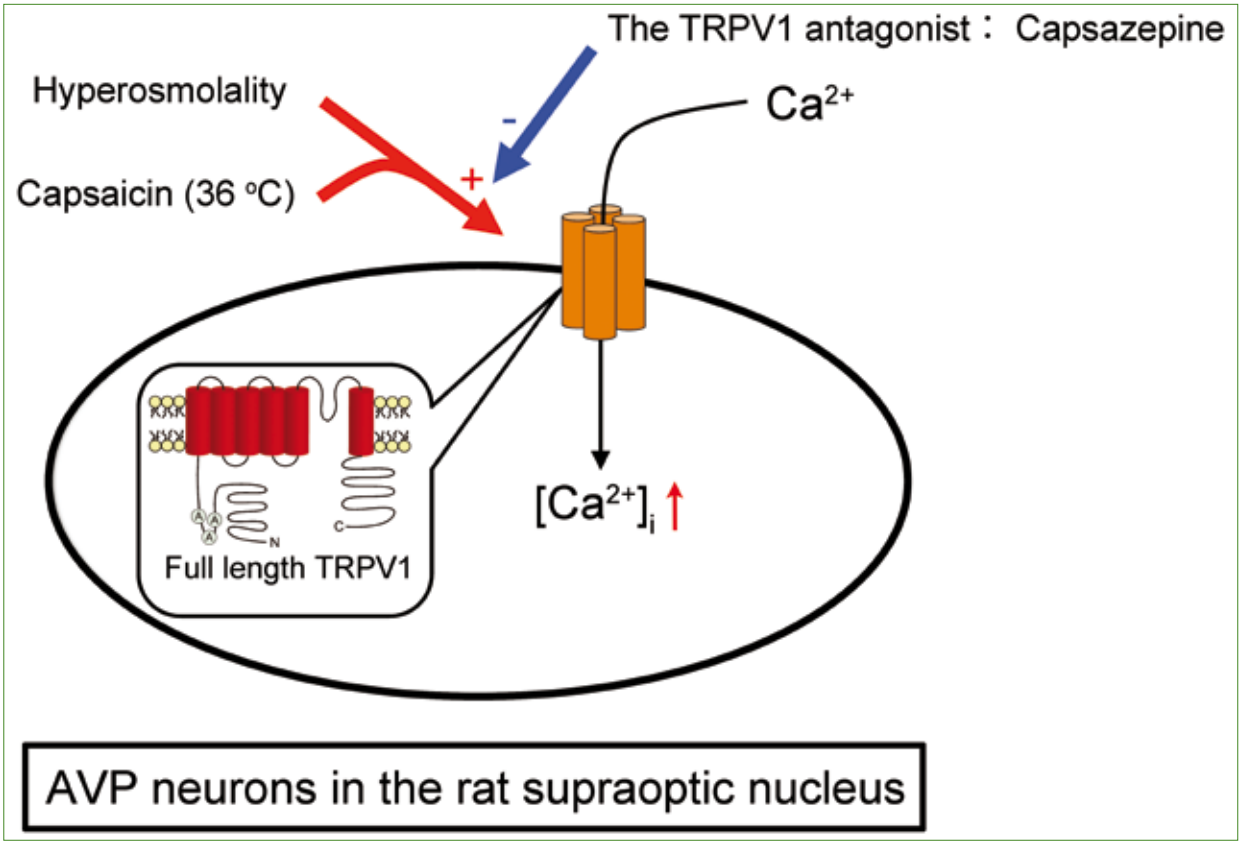

Fig: Schematic drawing showing the mechanisms of TRPV1-mediated Ca^{2+} responses in vasopressin neurons of rat supraoptic nucleus. **Highlights:** Full-length TRPV1 and a new splice variant, TRPV1_SON were expressed in the rat SON. Immunoreactivity of the N-terminal portion of TRPV1 was colocalized with that of AVP. Mannitol-induced $[Ca^{2+}]_i$ responses were observed in AVP but not in OT neurones. Mannitol-induced $[Ca^{2+}]_i$ responses were blocked by the TRPV1 antagonist CPZ and BCTC. At 36 °C, the TRPV1 agonist capsaicin evoked $[Ca^{2+}]_i$ and ionic current responses.

Publication:

Moriya T, Shibasaki R, Kayano T, Takebuchi N, Ichimura M, Kitamura N, Asano A, Hosaka YZ, Forostyak O, Verkhratsky A, Dayanithi G, Shibuya I, (2015): Full-length transient receptor potential vanilloid 1 channels mediate calcium signals and possibly contribute to osmoreception in vasopressin neurones in the rat supraoptic nucleus. Cell Calcium 57(1):25-37. IF 4.210

Department of Pharmacology

Head: Zdeněk Zídek, DSc, PhD
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Activities of the Department of Pharmacology are governed by scientific aims of the "Human Health" programme. The ultimate goal is the research and development of original low-molecular weight drugs targeting immune-related diseases. The hitherto obtained results have demonstrated immunosuppressive properties of newly synthesized derivatives of pyrimidine, and immunobiological activities of compounds of natural origin. Advanced studies are focused on the analysis of rational chemical structures and synthesis of compounds. They should facilitate transfer of experimental data to preclinical and clinical phases of research, and to commercial practice. Optimization of the structure is ensured by an immediate backward communication between chemical and biological teams of the project. An indispensable part of the studies is the determination of the safety and mechanism of drug action. The therapeutic potential of promising drug candidates is assessed using experimental models of autoimmune and inflammatory human diseases.

Research Scientist:
Zdeněk Zídek, DSc, PhD
Assoc. Prof. Eva Kmoníčková, PhD
Miloslav Kverka, MD, PhD

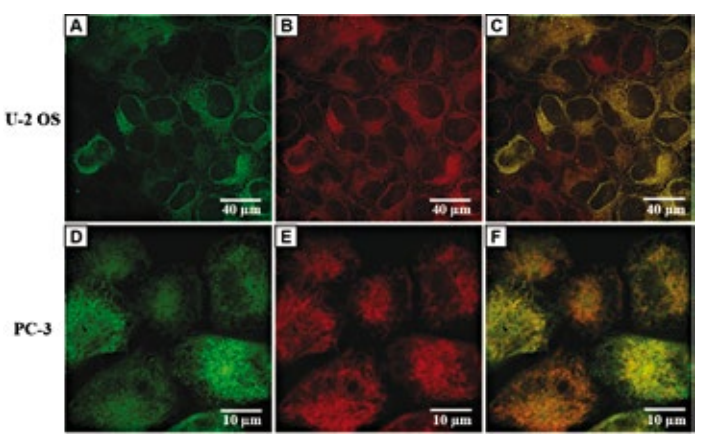
PhD Students:
Petra Kostecká, MSc
Adéla Dusilová, MSc
Silvie Rimpelová, MSc

Technician:
Jana Křížková, MSc
Eva Prchlíková

Important Results in 2014

1. Development of novel immunomodulatory drugs

We have found that sesquiterpene lactones of natural origin, thapsigargin (Tg) and trilobolide (Tb) possess immunostimulatory activity. Tg exhibits promising anticancer effects. The present study describes the method of detection of cellular uptake and intracellular distribution of these compounds. We found that Tb localizes in the endoplasmic reticulum of various cancer cell lines. The results are rational standpoint for further design of synthetic drug forms.



Collaboration: Institute of Chemical Technology in Prague

Fig: Localization of sarco-endoplasmic reticulum Ca^{2+} ATP-ase (SERCA) inhibitor trilobolide in cancer cells. Presence of trilobolide in the cells from osteosarcoma (U-2 OS, upper row) and from prostatic carcinoma (PC-3, lower row) was detected by means of its conjugation with "Bodipy" (A+D; green). Endoplasmic reticulum was labelled by ER-Tracker™ Red (B+E; red). The merge of these figures (C+F) proves the accumulation of trilobolide in endoplasmic reticulum.

Publication:
Jurášek M, Rimpelová S, Kmoníčková E, Drašar P, Ruml T, (2014): Tailor-made fluorescent trilobolide to study its biological relevance. J. Med. Chem. 57(19): 7947-7954. IF 5.480

2. Novel compounds with anti-inflammatory properties

Original poly-substituted derivatives of pyrimidine were synthesized. Their immunobiological properties were investigated using murine peritoneal cells. In dependence on the structure, the compounds proved to be inhibitors of immune-activated production of inflammatory mediators such as nitric oxide and prostaglandin E2. They are well tolerated, without signs of cytotoxicity. The compounds are candidates for treatment of chronic inflammatory diseases.

Collaboration: Institute of Organic Chemistry and Biochemistry AS CR, v.v.i.

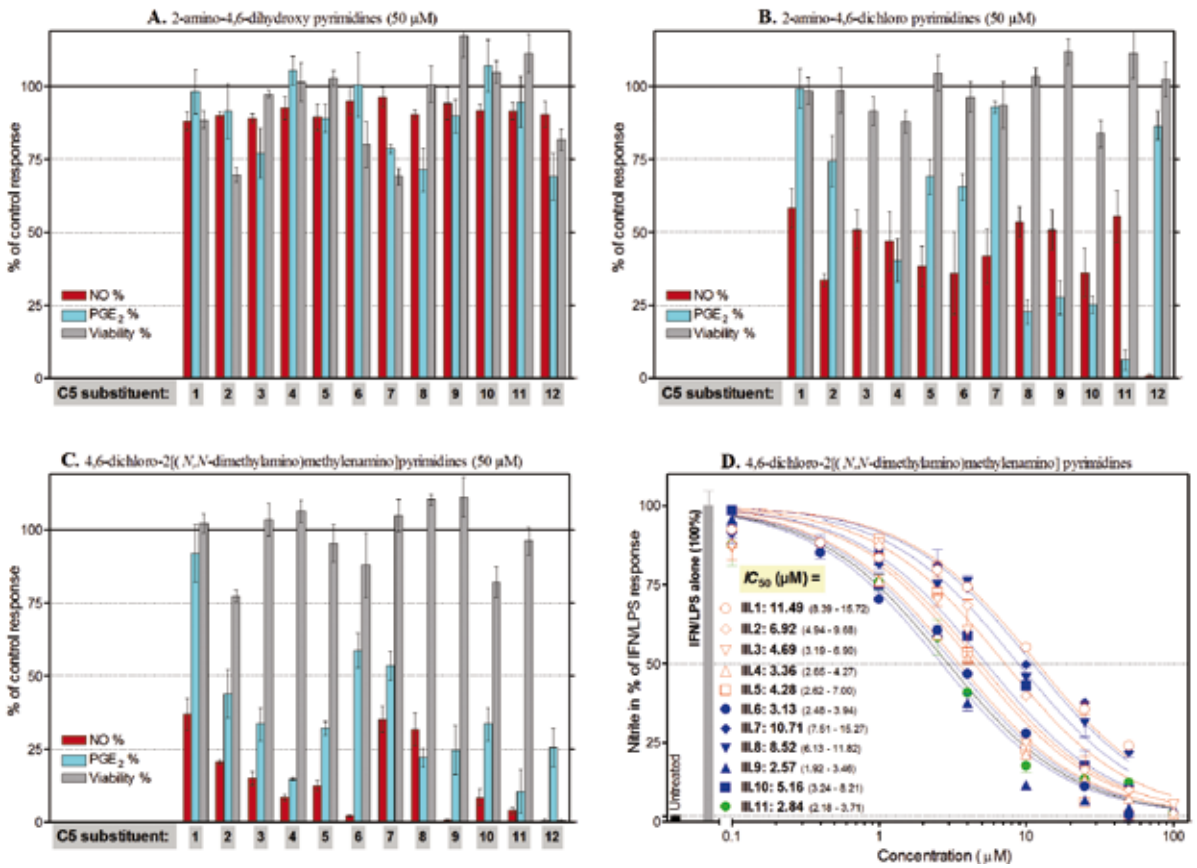


Fig: A. C4,6-hydroxy derivatives lack inhibitory activity. **B.** The intrinsic potential to suppress the production of nitric oxide (NO) and prostaglandin E2 (PGE2) is acquired by substitution of hydroxy groups with chlorine. **C.** Inhibitory activity is further enhanced by the replacement of 2-amino group with the (dimethylamino) methylenamino one. **D.** Concentrations inhibiting the NO production by 50% (IC_{50}) are approximately 5 µM.

Publications:
Jansa P, Holý A, Dračínský M, Kolman V, Janeba Z, Kostecká P, Kmoníčková E, Zídek Z, (2014): 5-Substituted 2-amino-4,6-dihydroxy- pyrimidines and 2-amino-4,6-dichloropyrimi dines: synthesis and inhibitory effects on imm- une-activated nitric oxide production. Med. Chem. Res. 23(10): 4482-4490. IF 1.612

Jansa P, Holý A, Dračínský M, Kolman V, Janeba Z, Kmoníčková E, Zídek Z, (2014): Synthesis and structure–activity relationship studies of polysubstituted pyrimidines as inhibitors of immune-activated nitric oxide production. Med. Chem. Res., DOI: 10.1007/s00044-014-1285-5. IF 1.612

Department of Genetic Ecotoxicology

Head: Radim J. Šrám, MD, DSc
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The main topic of the Department is the research of genetic damage induced by toxic and carcinogenic compounds such as polycyclic aromatic hydrocarbons and their derivatives. The effects of these chemicals are studied on cell cultures *in vitro* as well as in human translation molecular epidemiology studies and observatory epidemiological studies to analyze the impact of air pollution on human health.

Laboratory of Molecular Epidemiology

Head of Laboratory: Radim J. Šrám, MD, DSc
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The Laboratory carries out molecular epidemiology studies using biomarkers of exposure, effects and susceptibility to carcinogens and mutagens (DNA adducts, chromosome aberrations, micronuclei, DNA, proteins and lipids oxidative damage, genotyping, determination of RNA expression profiles), studies on the impact of environment to pregnancy outcomes and studies on the impact of air pollution to children health.

Research Scientists:
Radim J. Šrám, MD, DSc
Miroslav Dostál, MD, DSc
Božena Novotná, PhD
Anna Pastorková, MD, PhD
Andrea Rössnerová, PhD
Vlasta Švecová, PhD

PhD students:
Kateřina Hoňková
Yana Bagryantseva

Specialists:
Věra Topinková
Ivo Solanský

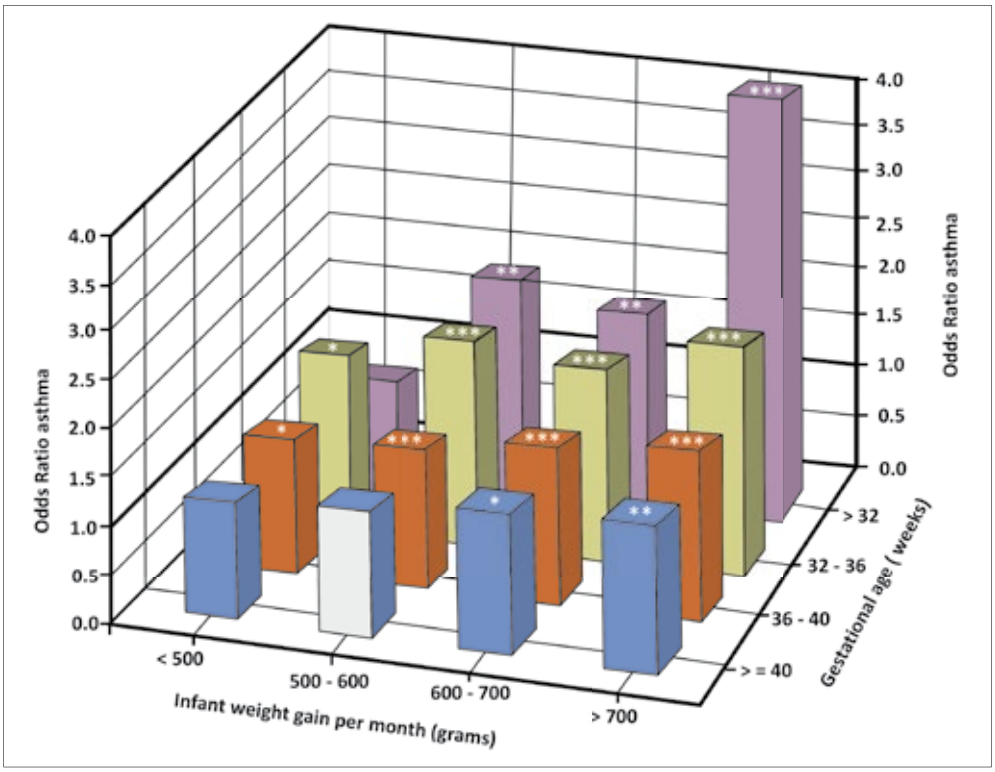
Technician:
Jolana Vaňková

Important Result in 2014

Preterm birth, infant weight gain, and childhood asthma risk: A meta-analysis of 147,000 European children

Younger gestational age at birth and higher infant weight gain were independently associated with higher risks of preschool wheezing and school-age asthma. Compared with term-born children with normal infant weight gain, we observed the highest risks of school-age asthma in children born preterm with high infant weight gain (OR 4.47; 95% CI, 2.58-7.76).

Collaboration: L. Duijts, Erasmus Medical Centre-Sophia Children's Hospital, Sp-3345, PO Box 2060, 3000 CB Rotterdam, The Netherlands



Publication:

Sonnenschein-van der Voort AM, Arends LR, de Jongste JC, Annesi-Maesano I, Arshad SH, Barros H, Basterrechea M, Bisgaard H, Chatzi L, Corpeleijn E, Correia S, Craig LC, Devereux G, Dogaru C, Dostál M, Duchen K, Eggesbø M, van der Ent CK, Fantini MP, Forastiere F, Frey U, Gehring U, Gori D, van der Gugten AC, Hanke W, Henderson AJ, Heude B, Iñiguez C, Inskip HM, Keil T, Kelleher CC, Kogevinas M, Kreiner-Møller E, Kuehni CE, Küpers LK, Lancz K, Larsen PS, Lau S, Ludvigsson J, Mommers M, Nybo Andersen AM, Palkovicova L, Pike KC, Pizzi C, Polanska K, Porta D, Richiardi L, Roberts G, Schmidt A, Šrám R, Sunyer J, Thijs C, Torrent M, Viljoen K, Wijga AH, Vrijheid M, Jaddoe VW, Duijts L: (2014) Preterm birth, infant weight gain, and childhood asthma risk: A meta-analysis of 147,000 European children. J. Allergy Clin. Immunol. 133(5): 1317–1329. IF 11.248

Laboratoy of Genetic Toxicology

Head of Laboratory: Jan Topinka, DSc, PhD

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The Laboratory studies mechanisms of genotoxic and epigenetic effects of toxic compounds bound to respirable dust particles as well as toxic effects of engineered nanoparticles. The mechanisms of genotoxicity and oxidative damage of DNA, proteins and lipids in cell cultures (A549, BEAS-2B) are studied using chip technologies.

Scientists:
Jan Topinka, DSc, PhD
Jana Schmuczerová, PhD

PhD students:
Táňa Brzicová
Jitka Štolcpartová

Specialists:
Alena Milcová
Kristýna Vrbová
Michaela Pokorná

Important Result in 2014

Analysis of gene expression changes in A549 cells induced by organic compounds from respirable air particles

We studied a toxic effects caused by the organic compounds from respirable air particels (PM2.5) in human lung A549 cells. Gene expression analysis revealed numerous deregulated genes and pathways related to activation of the aryl hydrocarbon receptor (AhR), metabolism of xenobiotics and endogenous compounds. We further identified deregulated genes involved in pro-inflammatory processes, oxidative stress response and in cancer and developmental pathways, such as TGF-β and Wnt signaling pathways. Interestingly, no DNA damage response was identified.

Collaboration: Veterinary Research Institute, Brno, Czech Technical University in Prague

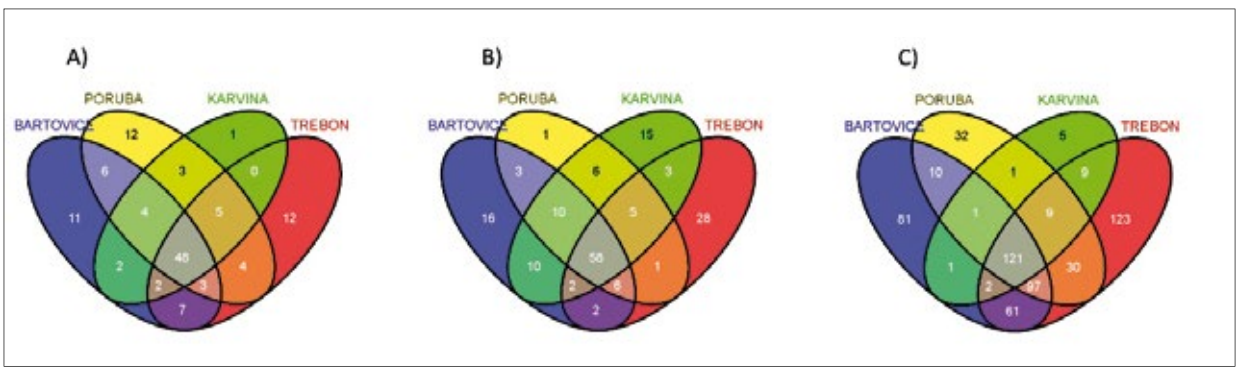

Fig: Gene expression of extractable organic matters from PM2.5. Venn diagrams representing numbers of common and locality-specific deregulated genes following 24-h treatment of A549 cells by 3 subtoxic concentrations of extractable organic matters (EOMs). EOMs were prepared by organic extraction of particulate matter <2.5 μm (PM2.5) collected in 4 localities of the Czech Republic differing by the extent and sources of the air pollution: Ostrava-Bartovice, Ostrava-Poruba, Karvina and Trebon. A549 cells were treated with the EOMs and total RNA from A549 was isolated. Global gene expression analysis was performed using whole genome Illumina chips as described in Section 2. The intersections represent the number of genes deregulated simultaneously at various localities relative to DMSO used as a solvent control (adjusted P-value < 0.05, average expression level > 4). The overlap of deregulated genes among the localities at the following concentrations: 10 μg/ml (A), 30 μg/ml (B), 60 μg/ml (C).

Publication:

Líbalová H, Krčková S, Uhlířová K, Kléma J, Cigánek M, Rössner P, Šrám RJ, Vondráček J, Machala M, Topinka J, (2014): Analysis of gene expression changes in A549 cells induced by organic compounds from respirable air particles. Mut Res Fundam Mol Mech Mutagen. Vol 770, 94–105. IF 4.44

Laboratory of Genomics

Head of Laboratory: Pavel Rössner Jr., PhD
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The laboratory studies whole-genome and gene-specific mRNA and protein expression, DNA methylation and single nucleotide polymorphisms (SNPs) in the human genome with the aim to characterize mechanisms of the toxic effects of complex mixtures in the environment.

Scientists:
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Helena Líbalová, PhD

PhD students:
Antonín Ambrož
Jitka Pavlíková

Specialist:
Zuzana Nováková

Important Result in 2014

Nonhomologous DNA end joining and chromosome aberrations in human embryonic lung fibroblasts treated with environmental pollutants

We studied the effect of environmental pollutants (carcinogenic benzo[a]pyrene (B[a]P) and organic extracts from particulate matter (PM2.5)) on DNA damage and repair. We analyzed key steps of DNA damage, including the detection of DNA breaks, DNA repair proteins, ligation (joining) of DNA ends and induction of chromosome aberrations. We found that tested compounds, particularly organic extracts, induce DNA damage followed by its repair. This, however, results in the induction of chromosome aberrations.

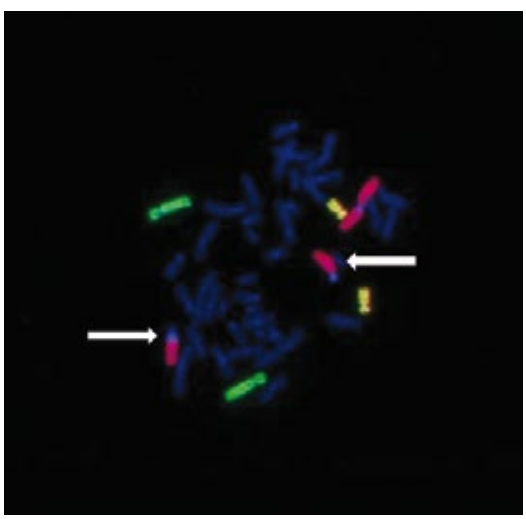
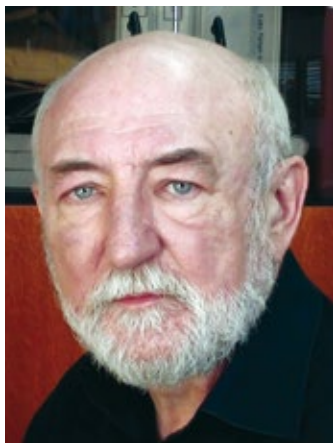


Fig: DNA damage caused by tested chemicals. The figure shows DNA damage caused by tested chemicals: reciprocal translocation between chromosome 1 and unpainted chromosome. Chromosomes 1 (red), 4 (green) and 17 (yellow) are painted in this slide; unpainted chromosomes are blue.

Publication:

Rössner P Jr, Rössnerová A, Beskid O, Tabashidze N, Líbalová H, Uhlířová K, Topinka J, Šrám RJ, (2014): Nonhomologous DNA end joining and chromosome aberrations in human embryonic lung fibroblasts treated with environmental pollutants. Mutat Res Fundam Mol Mech Mutagen, 763-764, Pages 28–38, IF 4.44

Department of Teratology



Head: Assoc. Prof. Miroslav Peterka, MD, DSc
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The main focuses of the Department of Teratology are studies on developmental abnormalities in humans as well as in experimental models. The causes and mechanisms of the inborn defect formation are studied using two experimental models (developing chick embryo and mouse odontogenesis), and using a clinical-epidemiological approach. The main target is to contribute to the knowledge about normal and abnormal development, pathogenesis of inborn defects and possibilities of their prevention.

Laboratory of Embryogenesis

Head of Laboratory: Assoc. Prof. Miroslav Peterka, MD, DSc
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In clinical-epidemiological studies, we are monitoring the incidence of orofacial clefts in the Czech population,and searching for possible causes of cleft origin using anamnestic data. Suspected inducing harmful factors, mainly the drugs used during pregnancy, are then tested experimentally. The testing of embryotoxicity is made on chick embryos using the chick embryotoxicity screening test (CHEST) method. The results of the testing are evaluated on the basis of occurrence of lethal effect, growth retardation and developmental malformations in the chick embryos.

Research Scientist:
Assoc. Prof. Miroslav Peterka, MD, DSc

Postgradual Student:
Zuzana Pavlíková, MSc

Undergraduate Student:
Klára Steklíková

Technicians:
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Simona Vojtěchová, MSc
Šárka Dvořáková

Laboratory of Odontogenesis

Head of Laboratory: Renata Peterková, MD, PhD
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The Laboratory is focused on the studies of tooth development under normal, pathological and experimental conditions. We have discovered that rudimentary tooth primordia play an important role during mouse odontogenesis. Although the rudiments disappear later prenatally, a defect in their formation can be involved in the origin of tooth anomalies. Elucidation of development and role of the rudimentary structures during odontogenesis can contribute to better understanding of tooth evolution as well as the origin of tooth anomalies. For example, an unsuppressed (revitalised) rudiment, which continues in development, can give rise to a supernumerary tooth. In this respect, such regressing or revitalising rudiments represent a natural model to study the mechanisms inhibiting or stimulating tooth development, and for testing possibilities of tooth regeneration.

Research Scientists:
Renata Peterková, MD, PhD
Mária Hovořáková, MSc, PhD
Oldřich Zahradníček, MSc, PhD
Svatava Churavá-Lagronová, MSc, PhD

Postgradual Students:
Kateřina Lochovská, MSc
Lucie Smrčková, MSc

Technicians:
Ivana Koppová
Zdena Lisá
Lenka Jandová, MSc

Important Result in 2014

Three-dimensional analysis of the early development of the dentition

The present review surveys data provided by 20 years research of odontogenesis in the laboratory mouse and in humans. Our results disprove the generally accepted concept of dentition morphogenesis, and offer new interpretations of results of studies on interactions between dental epithelium and mesenchyme, and on molecular control of tooth development in the mouse model. Such knowledge is important for future methods aimed to development of tooth biological replacements, when a tooth implant resulting from controlled differentiation of living cells will be anchored to a jaw.

Collaboration: Lesot Hervé, Institut National de la Sante et de la Recherche Medicale, UMR 1109, Team 'Osteoarticular and Dental Regenerative NanoMedicine', Strasbourg, France

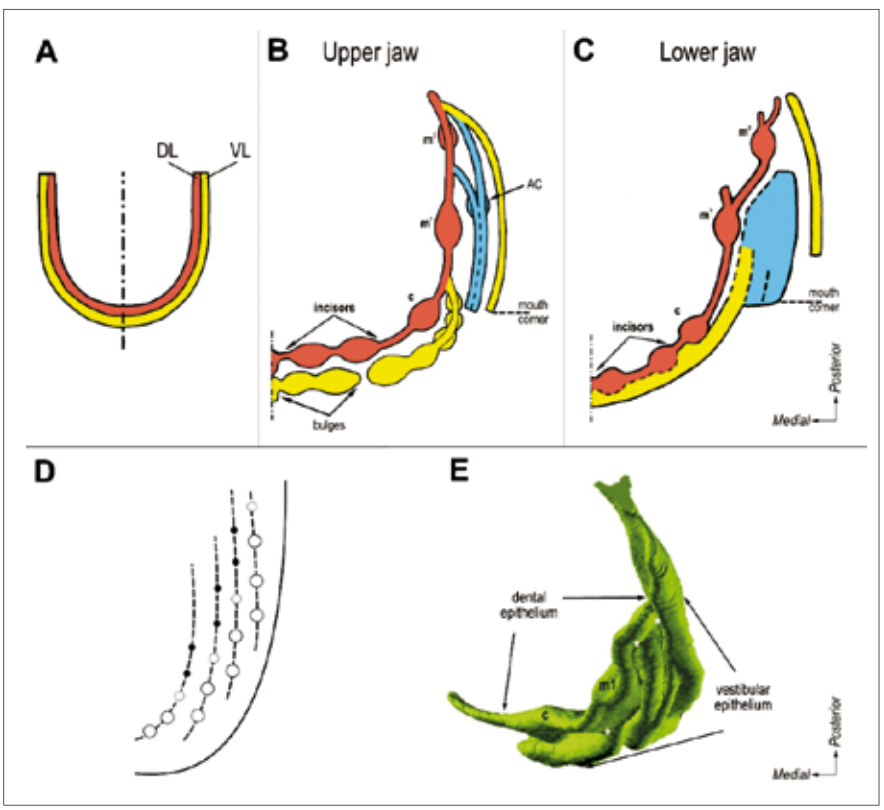

Fig. 1: Summarized data on developing dentition and oral vestibule in human and their tentative comparison with developing teeth in fishes. (**A**) Embryological textbooks present two parallel U-shaped ridges in human embryos: DL – dental lamina (giving rise to the deciduous dentition) and VL – vestibular lamina or labio-gingival band (where oral vestibule will form). (**B**) Summarization of our data by 3D reconstructions document no continuous vestibular lamina exists. Instead, a set of discontinuous epithelial structures (ridges and bulges) transiently occurs externally to the dental epithelium. Red - dental epithelium. Yellow or blue – vestibular epithelium. c, m1, m2 – the deciduous canine, first and second molar, respectively. AC – the accessory cap-shaped structure. (**D**) The schematic pattern of tooth rows ("Zahnreihen") in fishes. The empty rings and black spots indicate the older and younger teeth, respectively, new teeth are formed at the posterior end of each Zahnreihen. (**E**) Dental and vestibular epithelium in 8 weeks old human embryonic maxilla in a 3D reconstruction viewed from mesenchymal aspect. Note the reiterative fusions (white asterisks) between the dental epithelium and particular ridges of the vestibular epithelium. c, m1 – the deciduous canine and the first molar, respectively.

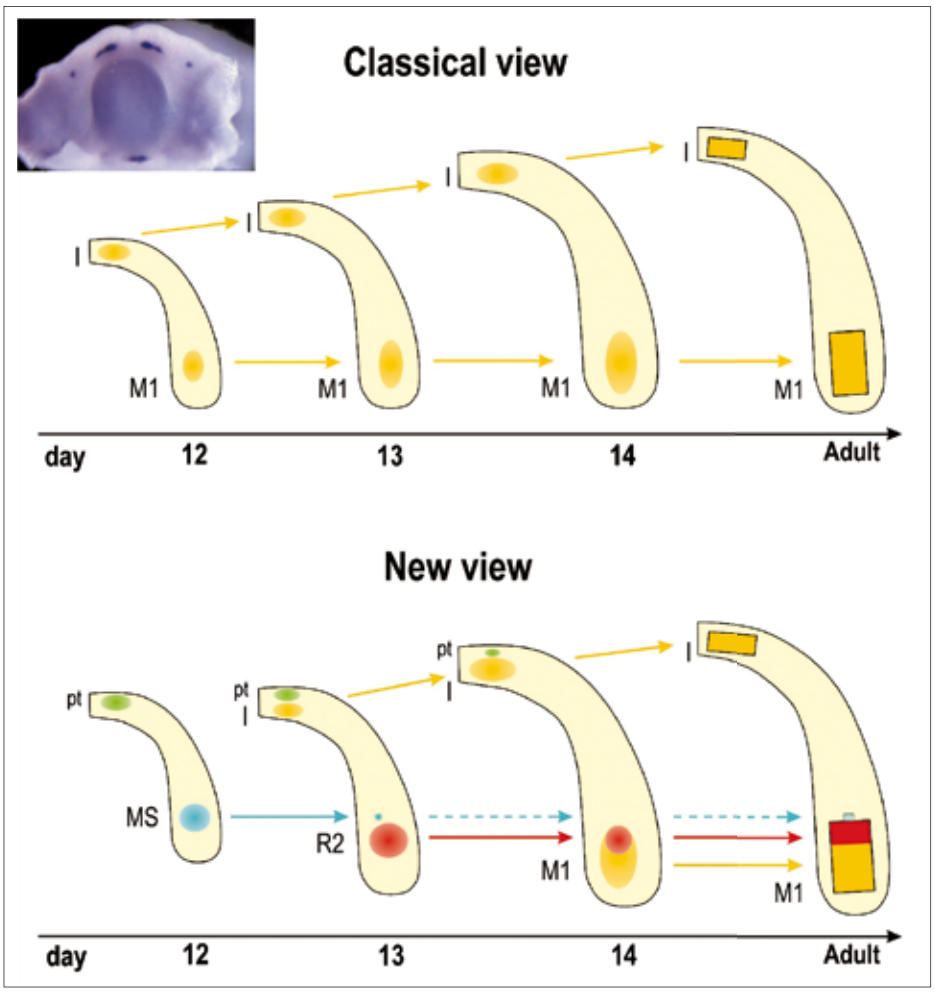

Fig. 2: Correlation between Shh signaling centres and developing teeth in the mandible of WT mice. Insert: Shh *in situ* hybridization of the whole mandible at embryonic day 12.5. Rectangles – functional teeth; round and oval shapes – Shh expression domains of developing teeth. **Classical view:** According to the literature, Shh expression is present in two signaling centres in each mandible half. The anterior one corresponds to the incisor primordium (I), the posterior one corresponds to the first molar (M1) until embryonic day 14. **New view:** According to the summary of our recent results, the Shh expression appears in several domains along the antero-posterior jaw axes of the lower jaw. The earlier-appearing domains correspond to the rudimentary tooth primordia in the incisor (pt-green) and cheek (MS-blue; R2-red) regions. Later, the primordia of functional teeth with their signaling centres appear: incisor (I-yellow), first molar (M1-yellow). The signaling centres MS, R2 and M1 appear successively in the distal direction. In adults, the functional M1 takes its origin with the contribution of R2 rudiment (red rectangle). A minor contribution of MS rudiment cannot be excluded (blue rectangle).

Publication:

Peterková R, Hovořáková M, Peterka M, Lesot H, (2014): Three-dimensional analysis of the early development of the dentition. Aust Dent J. 59 Suppl 1:55-80. IF 1.482

Department of the Molecular Biology of Cancer

Head: Pavel Vodička, MD, PhD
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In our Department we investigate molecular characteristics of solid cancers, especially of the colon, rectum, pancreas and ovaries. Within these studies we focus on the molecular-epidemiological level in order 1. to identify biomarkers of increased predisposition to tumour diseases, 2. enable early diagnostics, 3. assess individual responses to anti-tumour treatment, 4. and determine long-term prognosis. We focus mainly on the system of DNA damage repair. This extensive biological process is ensured by a minimum of six more or less independent pathways and is of a crucial importance for maintaining the structural and functional stability of DNA and thus ensures the prevention of neoplastic transformation of healthy cells. On the other hand, the activity of DNA damage repair is significantly applied also during the response of tumour cells to the impact of chemotherapeutics. The treatment by some of the most commonly used drugs proceeds via massive DNA damage and subsequent cell death. High activity of DNA repair mechanisms may contribute to resistance of cancer cells to such substances. The Department has been working with different types of biological material from a patients with cancer diseases, such as solid tissue, blood cells or plasma.

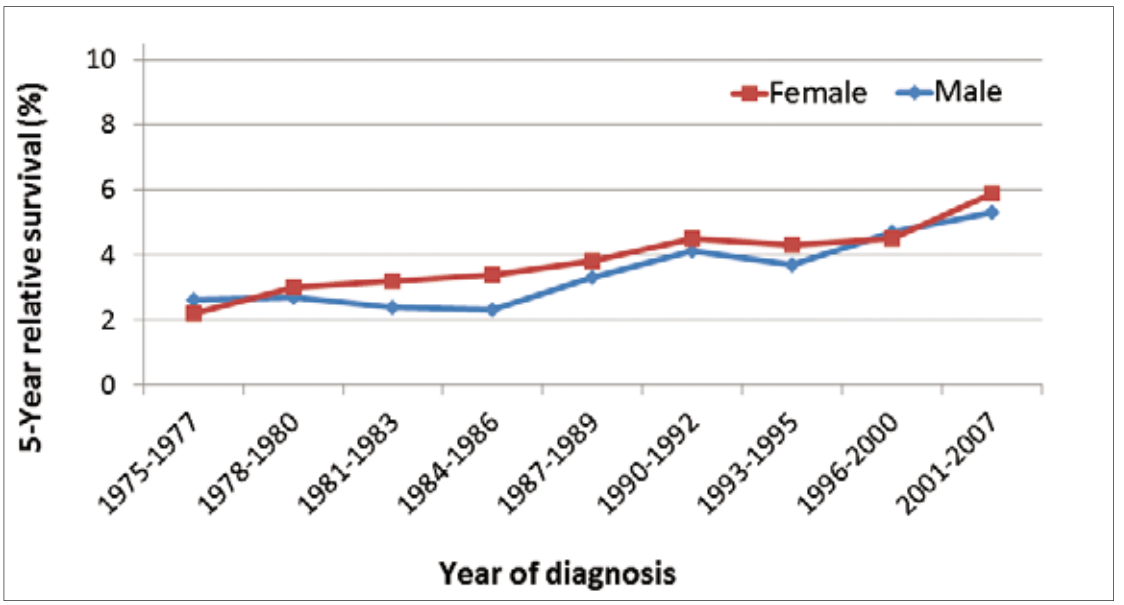
Laboratory of Tumor Genetics:
Pavel Vodička, MD, PhD
Ludmila Vodičková, MD, PhD
Veronika Vymetálková-Poláková, PhD
Petra Bendová, MSc
Linda Bártů, MSc
Alexandra Rejhová, MSc
Jiří Švec, MD, PhD
Pavel Kříž

Laboratory of DNA Repair:
Jana Slyšková, PhD
Miroslav Svoboda, MSc, PhD
Jan Král, MD
Soňa Vodénková, MSc
Michal Kroupa, MSc
Kateřina Jirásková, MSc
Andrea Čumová, MSc
Prof. Rudolf Štětina, PhD

Important Results in 2014

1. Susceptibility loci in pancreatic cancer

We have for the first time identified four new susceptibility loci, affecting the risk to pancreatic cancer. Simultaneously the relationship between pancreatic cancer and vartiants in exon 2 in TERT and telomeric PVT1 were proven. Our results add to the evidence for multifactorial pathogenesis of pancreatic cancer, which represents one of the most dreadful malignancies. Our findings contribute to understand the cause and development of the disease and to design effective therapeutical strategy.



Publication:

Wolpin BM, Rizzato C, Kraft P, Kooperberg C, Petersen GM, Wang Z, Arslan AA, Beane-Freeman L, Bracci PM, Buring J, Canzian F, Duell EJ, Gallinger S, Giles GG, Goodman GE, Goodman PJ, Jacobs EJ, Kamineni A, Klein AP, Kolonel LN, Kulke MH, Li D, Malats N, Olson SH, Risch HA, Sesso HD, Visvanathan K, White E, Zheng W, Abnet CC, Albanes D, Andriotti G, Austin MA, Barfield R, Basso D, Berndt SI, Boutron-Ruault MC, Brotzman M, Buchler MW, Bas Bueno-de-Mesquita H, Bugert P, Burdette L, Campa D, Caporaso NE, Capurso G, Chung C, Cotterchio M, Costello E, Elena J, Funel N, Gaziano M, Giese N, Giovannucci EL, Goggins M, Gorman MJ, Gross M, Haiman C, Hassan M, Helzlsouer K, Henderson BE, Holly EA, Hu N, Hunter DJ, Innocenti F, jenab M, Kaaks R, Key TJ, Khaw KT, Klein EA, Kogevinas M, Kupcinskas J, Kurtz RC, LaCroix A, Landi MT, Landi S, Le Marchand L, Mambrini A, Mannisto S, Milne RL, Nakamura Y, Oberg AL, Owzar K, Panico S, Patel AV, Peeters PH, Peters U, Piepoli A, Porta M, Real FX, Riboli E, Rothman N, Scarpa A, Shu X, Silverman DT, Soucek P, Sund M, Talar-Wojnarowska R, Taylor PR, Theodoropoulos GE, Thornquist M, Tjoenneland A, Tobias GS, Trichopoulos D, Vodička P, Wactawski-Wende J, Wentzensen N, Wu C, Yu H, Yu K, Zeleniuch-Jacquotte A, Hoover R, Hartge P, Fuchs C, Channock S, Stolzenberg-Solomon RS, Amundadottir L (2014): Genome-wide association study identifies multiple susceptibility loci for pancreatic cancer. Nature Genet. 46(9):994-1000. IF: 29.648

2. Genetic and epigenetic factors affecting colorectal cancer

In the studies shown below we addressed the effects of gene variants, long-non coding RNA, miRNA binding sites and epigenetic regulatory mechanisms on the onset, prognosis and effective therapy of colorectal cancer.

Collaboration: DKFZ Heidelberg, FRG, HUGE Turin, Italy, University in Umea, Sweden etc.

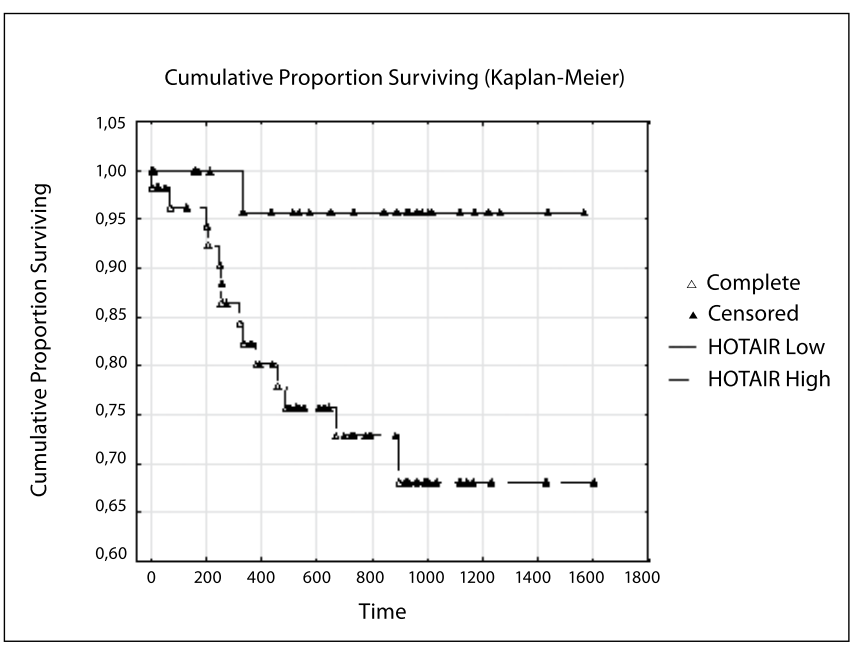


Fig: Survival analysis of patients with low and high levels of long-non-coding-RNA.

Publications:

Farkaš S, Vymětálková V, Vodičková L, Vodička P, Nilsson TK, (2014): DNA methylation changes in genes frequently mutated in colorectal cancer and in the DNA repair and Wnt/β-catenin signaling pathway genes. Epigenomics 6(2):179-91. IF 5.215

Svoboda M, Slyšková J, Schneiderová M, Makovický P, Bielik L, Levý M, Lipská L, Hemmelová B, Kala Z, Protivánková M, Vyčítal O, Liška V, Schwarzová L, Vodičková L, Vodička P, (2014): HOTAIR long non-coding RNA is a negative prognostic factor not only in primary tumors, but also in the blood of colorectal cancer patients. Carcinogenesis. 35(7):1510-5. IF 5.266

3. Mapping of DNA repair capacities

Important data have been obtained by studying DNA repair mechanisms and the genomic integrity. DNA repair capacity has been mapped in healthy subjects as well as in colorectal cancer patients, with emphasis to the prognosis and therapy. We have for the first time proven the relationship between genetic variants in *cyclin D1* and DNA damage response, homologous recombination repair process and chromosomal damage.

Collaboration: University of Oslo, Norway, DKFZ heidelberg, FRG, HUGE Turin, Italy etc.

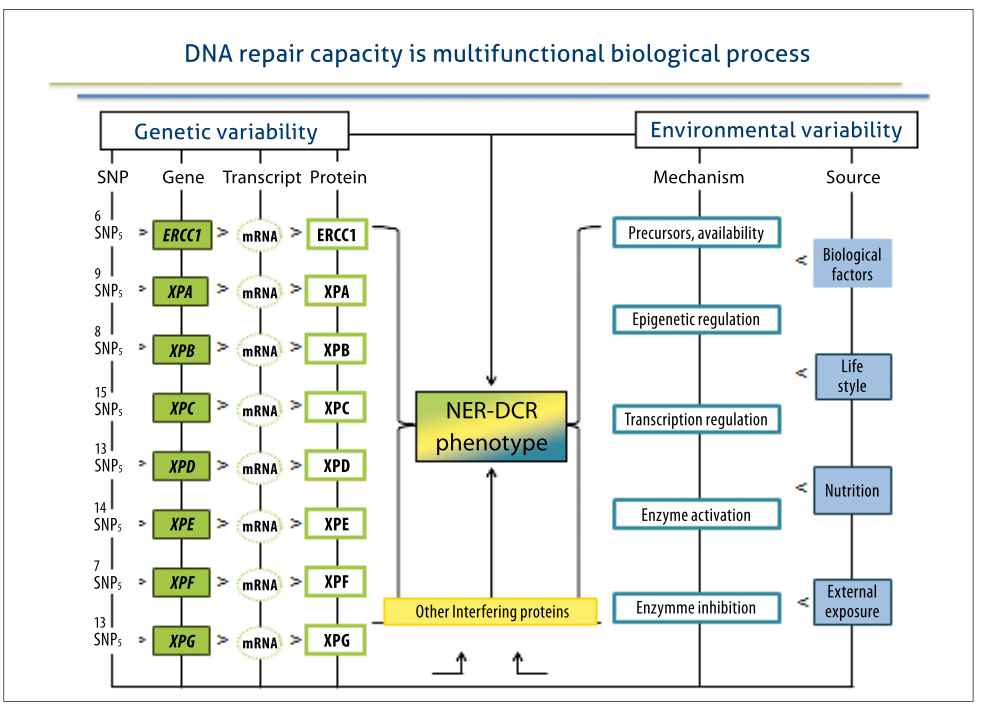


Fig: Schematic outline of factors influencing nucleotide excision repair (NER) – DNA repair capacity (DRC) phenotype.

Publications:

Slyšková J, Cordero F, Pardini B, Korenková V, Vymetálková V, Bielik L, Vodičková L, Pitule P, Liška V, Matějka VM, Levý M, Buchler T, Kubista M, Naccarati A, Vodička P (2014): Post-treatment recovery of suboptimal DNA repair capacity and gene expression levels in colorectal cancer patients. Mol Carcinog. doi: 10.1002/mc.22141. [Epub ahead of print] PubMed PMID: 24585457. IF 4.770

Hemminki K, Mušák L, Vymetálková V, Šmerhovský Z, Halašová E, Osina O, Letková L, Försti A, Vodičková L, Buchancová J, Vodička P, (2014): Cyclin D1 splice site variant triggers chromosomal aberrations in healthy humans. Leukemia. 28(3):721-2. IF 9.379

Department of Transplantation Immunology

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The research of this Department is focused on cellular and molecular mechanisms which regulate the immune response after the transplantation of stem cells. The improvment of survival of genetically distinct cells transferred for therapeutic purposes is the final aim of this research. The basic experimental model is represented by various types of stem cells which are cultured, differentiated and characterized *in vitro*. Using nanofiber scaffolds the cells are transferred onto a damaged ocular surface or skin injuries. The beneficially effects of stem cell therapy are characterized immunologically, immunohistochemically and on the level of gene expression. The results are verified in experimental preclinical models with the aim to translate the knowledge from the basic research for stem cell-based therapy in patients with a heavily damaged ocular surface.

Research workers:
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Alena Zajícová, PhD
Magdaléna Krulová, PhD

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Milada Chudičková, MSc
Peter Trošan, MSc
Michaela Pavlíková, MSc
Barbora Heřmánková, MSc

Pregraduate students:
Pavla Boháčová
Jan Kössl

Technicians:
Lucie Holáňová
Jaroslava Knížová

Important Result in 2014

The effects of cytokines on migration and therapeutic potential of mesenchymal stem cells in a model of local inflammatory reaction in damaged eye

Using a well established model of chemically damaged ocular surface in mice we showed that systemically administered mesenchymal stem cells (MSCs) selectively migrate into the site of injury and inhibit infiltration with cells of of the immune system. The ability of MSCs to inhibit local inflammatory reaction can be modulated by their preincubation with cytokines which determine the development of T and B lymphocytes and regulate the secretory capacity of MSCs. The results thus show the possibilities to use cytokine-pretreated and systemically administered MSCs for the treatment of local inflammatory reaction.

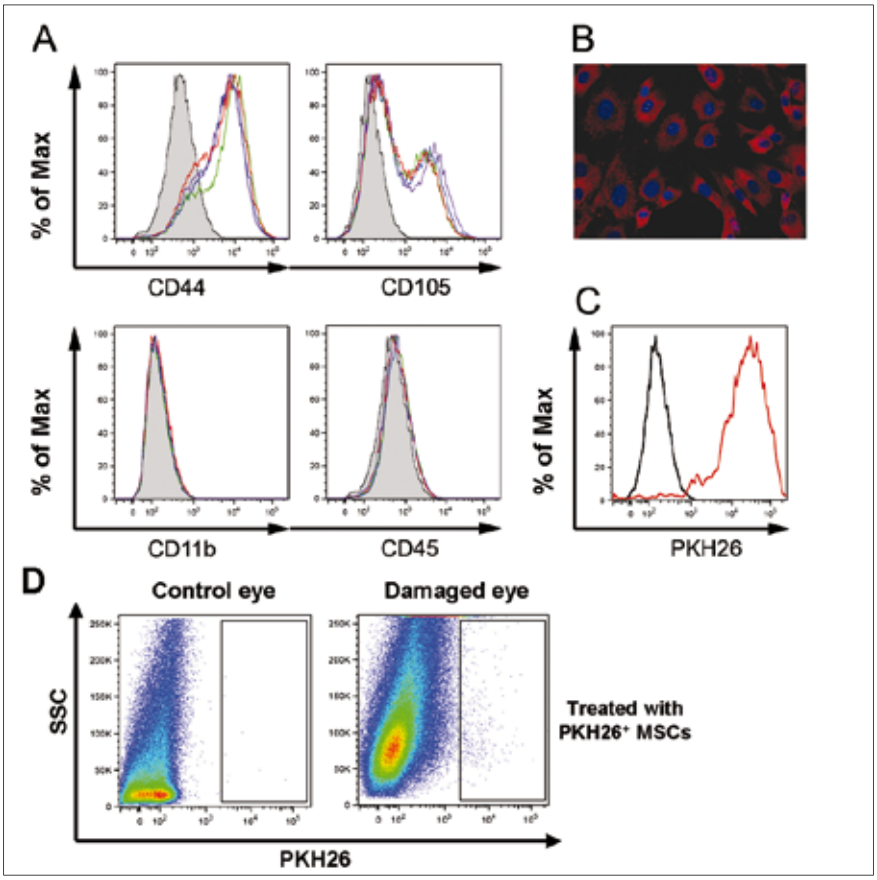

Fig: Phenotype characterization of MSCs (A), labeling of MSCs with vital dye PKH26 (**B**, **C**) and detection of labeled MSCs in the injured eye (**D**).

Publications:

Javorková E, Trošan P, Zajícová A, Krulová M, Hajková M, Holáň V, (2014): Modulation of the early inflammatory microenvironment in alkali-burned eye by systemically administered interferon treated mesenchymal stem cells. Stem Cells Dev. 23, 2490-2500. IF 4.202

Holáň V, Zajícová A, Javorková E, Trošan P, Chudičková M, Pavlíková M, Krulová M, (2014): Distinct cytokines balance the development of regulatory T cells and IL-10-producing regulatory B cells. Immunology 141, 577-586. IF 3.3735

Laboratory of Eye Histochemistry and Pharmacology

Head of Laboratory: Assoc. Prof. Jitka Čejková, MD, DSc
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The Laboratory examines the causes of non-healing lesions of the anterior eye segment in various eye injuries or diseases, and the regeneration of tissues of the anterior eye segment, particularly of the cornea, with the aim to restore visual function. For the healing of anterior eye segment lesions, special attention is devoted to developing nanofiber scaffolds as carriers of stem cells.

Research Scientists:
Assoc. Prof. Jitka Čejková, MD, DSc
Čestmír Čejka, MSc, PhD

Pre-graduated students:
Tomanová Aneta
Vašková Věrča
Švandová Ivana
Bayerová Martina

Laboratory technician:
Jana Herlová

Important Result in 2014

The importance of oxidative stress in the cornea after its Injury

Oxidative stress in the cornea has an important role in the initiation as well as propagation of corneal disturbances after its injury, e.g. after irradiation with UV rays, chemical injury, mainly after alkali burns. In the injured cornea an imbalance between oxidants and antioxidants appears, naturally occurring inhibitors of matrix metalooproteinases are inhibited. The intracorneal inflammation develops, the corneal transparency is lost and corneal neovascularization appears.

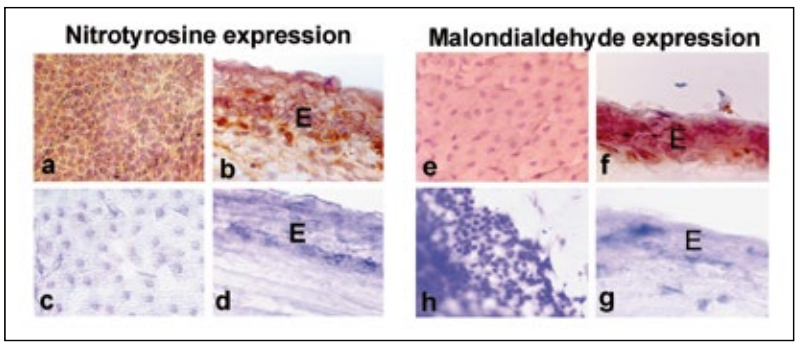

Fig 1.: Oxidative stress plays and important role in ocular diseases and injuries. Early diagnosis of oxidative stress plays the key role for choice of the mode of treatment. We found that impression cytologies of corneal epithelial cells with immunoghistochemical markers enable rapid and easy diagnostics of oxidative injuries, usable in clinical medicine. Thus the method of corneal impression cytology is not only a method suitable for the examination of severity of corneal damage, e.g. in dry eye disease as was described previously by us, however, also for sensitive detection of early corneal disturbances evoked by oxidative injury. Nitrotyrosine expression, a marker of oxidative stress, a – in corneal impression cytology after corneal injury, b- in cryostat corneal section after corneal injury, c – negative expression of nitrotyrosine in corneal imporession cytology, healthy eye, d - negative expression of nitrotyrosine in cryostat section of the cornea, healthy eye. Similarly e – h is expression of malondialdehyde, a marker of lipid peroxidation in corneal impression cytology and corneal cryostat section of injured and healthy corneas.

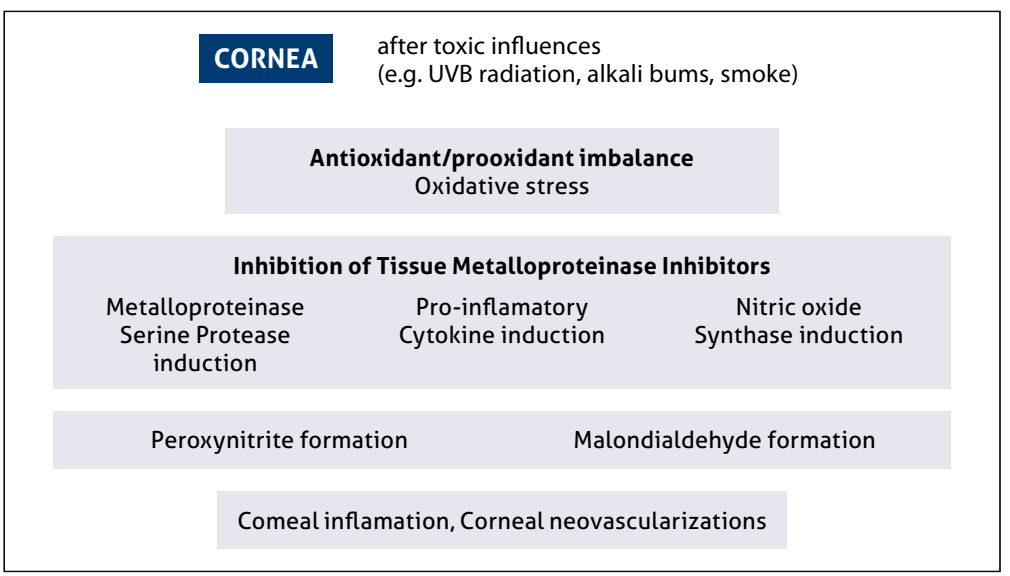

Fig 2.: The role of oxidative stress after various injuries was compared in the cornea, e.g. after UVB radiation or alkali burns. The antioxidant/prooxidant imbalance appears in the cornea (oxidative stress) leading to the inhibition of naturally existing inhibitors of metalloproteinases and serine proteases. Destructive proteases, pro-inflammatory cytokines and nitric oxide synthases are generated and activated. Nitrotyrosine and malondialdehyde (markers of oxidative stress and lipid peroxidation) occur in the cornea. The intraocular inflammation develops and cornea is vascularized.

Publication:

Čejková J, Čejka C, (2015): The role of oxidative stress in corneal diseases and injuries. Histol Histopathol. 11611– Epub. [ahead of print] IF 2.236

Department of Tissue Engineering

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The research of the Department is focused on the development of artificial tissues, mainly biodegradable scaffolds for tissue regeneration, such as nanofibers, foams, and hydrogels for the regeneration of cartilage, bone and incisional hernia. We also focus on computer modeling of protein structures. We are developing the technology of controlled drug delivery from nanofibers scaffolds with liposomes for targeted release of drugs into the defect. The work is also concentrated on the development of three-dimensional nanofibers, using novel technique of Forcespinning®. These nanofibres are more suitable for cell growth and differentiation. Moreover, high on our priority list is also the accelerated transfer of newly developed technologies and know-how into clinical practice. We are developing artificial scaffolds for the regeneration of bone and cartilage in clinical practice.

Research Scientists:
Prof. Evžen Amler, DSc, PhD
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Matej Buzgo, MSc
Martin Plencner, MSc
Dagmar Bezděková, MSc
Martin Královič, MSc
Karolína Vocetková, MD, MSc
Jana Benešová, MSc
Věra Sovková, MSc
Andrea Míčková, MSc
Gracián Tejral, MSc

Technician:
Jana Závodská

Important Results in 2014

1. Functionalized nanofibers for controlled drug delivery

The system of functionalized nanofibers with controlled drug delivery has been developed and optimized. This system has been applied for treatment of incisional hernia. Polypropylene surgical mesh was modified by PCL nanofibers covering and functionalised with adhesion of growth factors. Samples were tested *in vivo* on a rabbit model as a model for prevention of incisional hernia formation.

Collaboration: Institute of Biomedical Engineering, Czech Technical University in Prague, Kladno;
University Centre for Energy Efficient Buildings

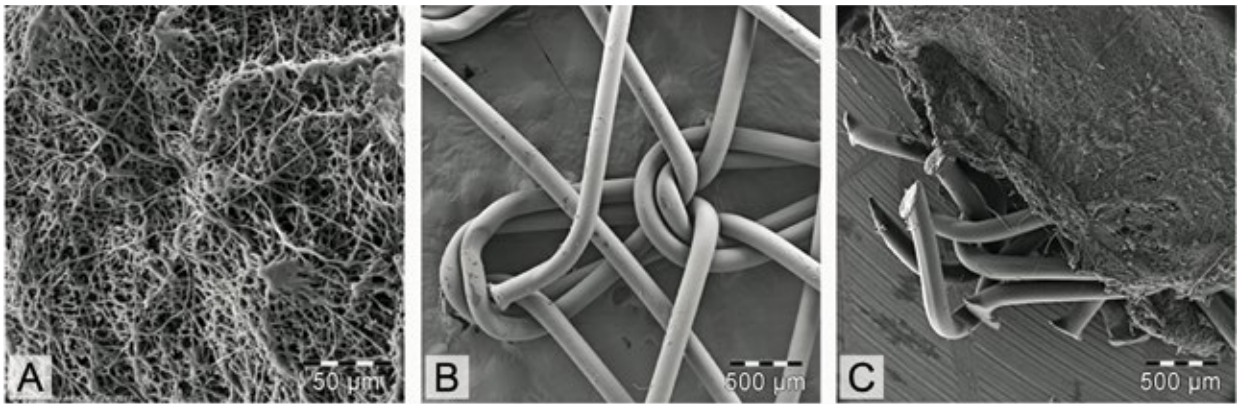

Fig: Scanning electron microscopy of the scaffolds used for the abdominal closure. Notes: (**A**) nanofibers from poly-ε-caprolactone (magnification 230×); (**B**) polypropylene mesh (magnification 18×); (**C**) polypropylene mesh functionalized with poly-ε-caprolactone nanofibers (magnification 18×).

Publication:

Amler E, Filová E, Buzgo M, Prosecká E, Rampichová M, Nečas A, Nooeaid P, Boccaccini AR, (2014): Functionalized nanofibers as drug-delivery systems for osteochondral regeneration. Nanomedicine-UK 9(7): 1083–1094, IF 5.9

2. Biomechanical testing of the repaired abdominal wall

Abdominal closure was reinforced by application of polypropylene mesh functionalized with poly-ε-caprolactone nanofibers and growth factors. This novel arrangement is going to be used for prevention of incisional hernia formation. However, the system seems to be very general and there is intended for much broader chirurgical and orthopedical application.

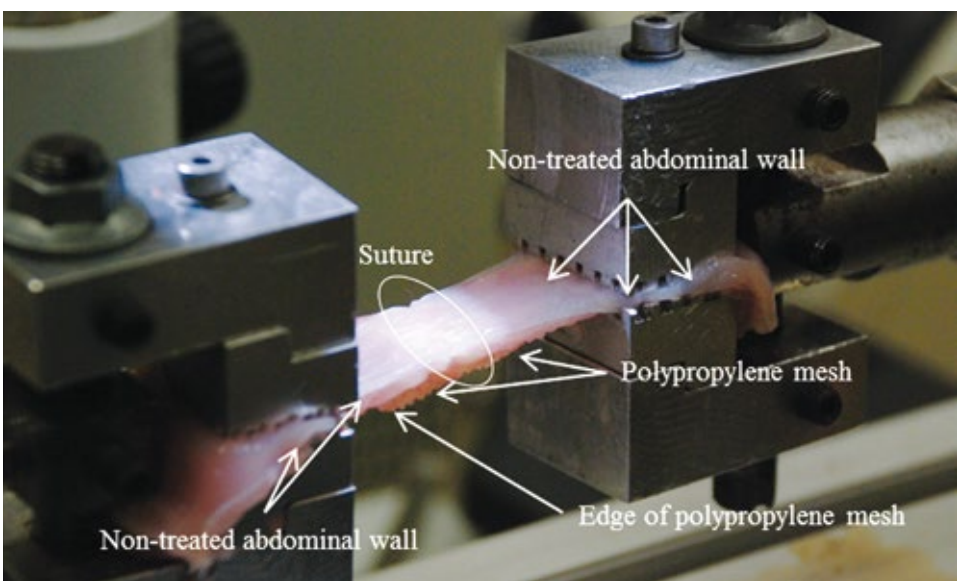

Fig. 1: Images of carriers used for closure of abdominal incision switched by scanning electron microscopy. (**A**) nanofibers of poly-ε-caprolactone (magnification × 230), (**B**) polypropylene mesh (18 × magnification), (**C**) polypropylene mesh using functionalized nanofibers of poly-ε-caprolactone.

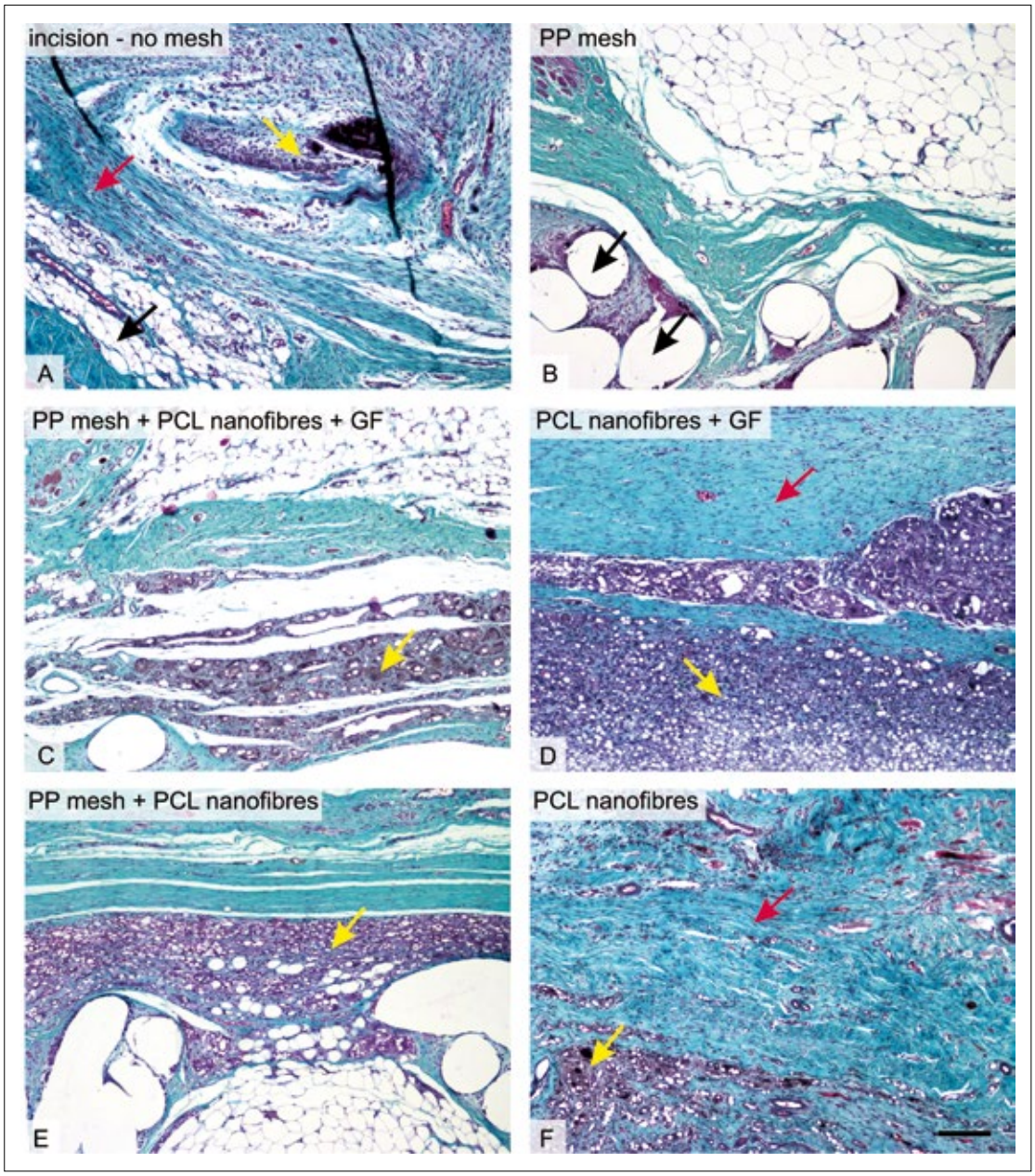

Fig. 2: Histological evaluation. Collagen, adipose tissue, and granulomatous infiltration in the scaffolds under study. In samples without any mesh (**A**), the incision was healing with a mixture of collagen (black arrow), adipose connective tissue (red arrow) and inflammatory infiltrate (yellow arrow). Samples with polypropylene (PP) mesh (**B**) had a high fraction of adipose tissue, but the spaces showing the dissolved mesh (black arrows) were surrounded by only a few inflammatory cells. Remnants of the nanofibers (**C**, **D**, **E**, **F**) were surrounded by granulomatous leukocyte-rich connective tissue (yellow arrows in **C**, **D**, **E**, **F**). The highest fraction of collagen (red arrow) was in samples of PCL nanofibers with adhered growth factors (GF) (**D**), followed by samples with no mesh (**A**) and by samples of PCL nanofibers (**F**). Low fractions of adipose tissue were found in samples of PCL nanofibers with adhered GF (**D**), samples with no mesh (**A**) and in samples of PCL nanofibers (**F**).

Publication:

Plencner M, East B, Tonar Z, Otáhal M, Prosecká E, Rampichová M, Krejčí T, Litvinec A, Buzgo M, Míčková A, Nečas A, Hoch J, Amler E, (2014): Abdominal closure reinforcement by using polypropylene mesh functionalized with poly-ε-caprolactone nanofibers and growth factors for prevention of incisional hernia formation. Int. J. Nanomed. 9: 3263-3277, IF 4.195

Microscopy Unit

Head: Jan Malínský, PhD
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We study the assembly and maintenance of cellular structures not bound by a membrane. These highly dynamic, steady state organelles engaged in specific functions communicate with their surroundings directly by diffusion, and the mechanisms controlling their structure and function are still poorly understood. Many of these compartments, such as the nucleolus or Cajal body in the cell nucleus, are easily seen under a microscope and have been known for a long time. Others have been described only recently – for instance lipid raft-based compartments in membranes. Morphological changes or the disintegration of these cellular structures often accompany pathologic phenotypes. Knowledge about the composition, formation and maintenance of these structures is limited. Thus, a great deal is open for studies using contemporary microscopy techniques, capable not only of exactly localizing cellular components, but also of detecting their movement and potential interactions at the molecular level as well.

Research Scientist:
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Postdoctoral fellow:
Vendula Strádalová, PhD

PhD Students:
Thuraya Awadová, MSc
Aleš Efenberk, MSc
Dagmar Folková, MSc
Katarína Vaškovičová, MSc

Technicians:
Tomáš Červinka, MSc
Miroslava Opekarová, PhD
Petra Veselá, MSc
Lenka Hlavínová
Jitka Eisensteinová

Important Results in 2014

1. Membrane potential governs the amount of gel-like, sphingolipd-based microdomains in the plasma

We reported the transmembrane voltage-induced lateral reorganization of sphingolipid-based, highly-ordered lipid microdomains in the plasma membrane of living cells. We found that despite the mechanism of depolarization, loss of membrane potential always leads to significant reduction of gel-like microdomains in the membrane. We suggest the voltage-induced membrane lipid reorganization to play a significant role in regulatory mechanisms such as fast cellular response to acute stress conditions.

Collaboration: Faculty of Mathematics and Physics, Charles University

Publication:

Večer J, Vesela P, Malínský J, Herman P, (2014): Sphingolipid levels crucially modulate lateral microdomain organization of plasma membrane in living yeast. FEBS Lett. 588(3):443-9. IF 3.341

Herman P, Večer J, Opekarová M, Veselá P, Jančíková I, Záhumenský J, Malínský J, (2014): Depolarization affects the lateral microdomain structure of yeast plasma membrane. FEBS J. 282(3):419-34 IF 3.986

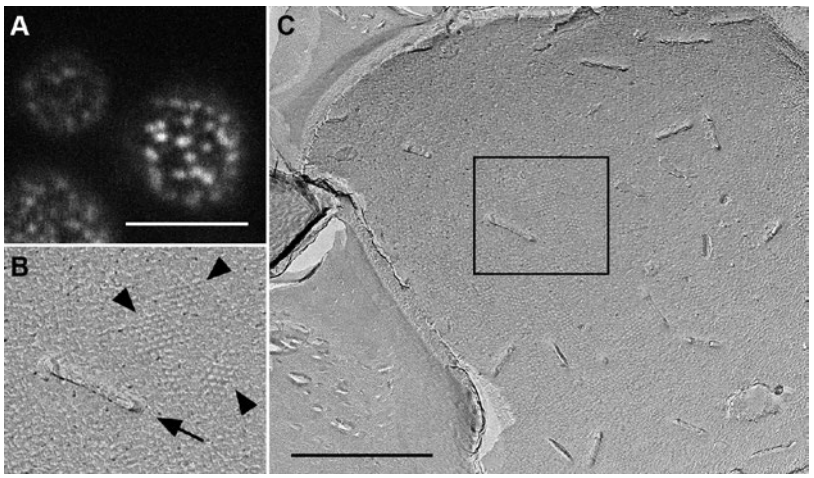
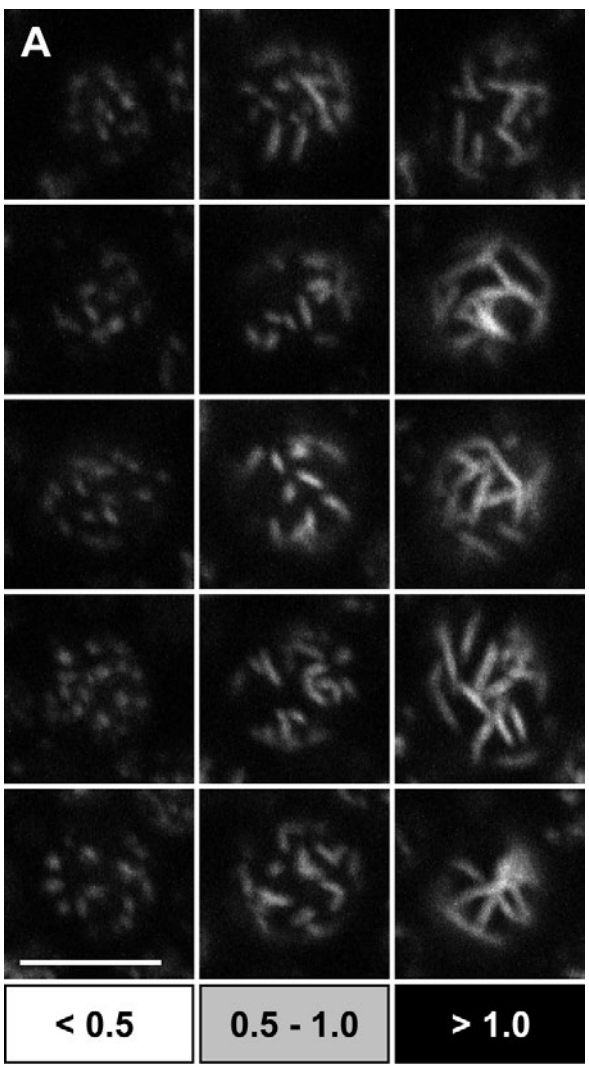


Fig:Two complementary views of microdomains in the plasma membrane. Confocal fluorescence image of the integral membrane protein distribution. The protein accumulates in specific lateral microdomains of the yeast plasma membrane (**A**). Two characteristic structures (microdomains) of the yeast plasma membrane visualized by electron microscopy: furrow-like invaginations (arrows) and hexagonal symmetry exhibiting proteolipid clusters (**B**, **C**). Scale: 5μm (**A**). 500μm (**C**).

2. Interspecies transfer of membrane microdomain

By heterologous expression of specific protein components we reconstituted the foreign plasma membrane microdomain in the host cell. We showed that the ultrastructure and function of this microdomain was preserved in the host. To the best of our knowledge, this is the first report of interspecies transfer of a functional plasma membrane microdomain.



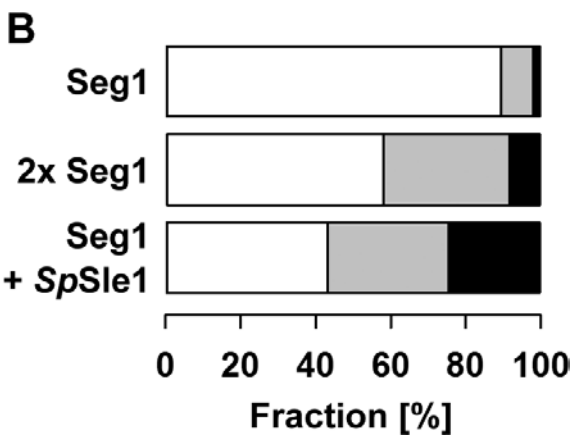


Fig: Differential stabilization of membrane compartment of Can1 (MCC) by means of specific proteins. Length of individual MCC microdomains was measured (**A**) in *S. cerevisiae* cells expressing one copy of *S. cerevisiae* SEG1 gene either alone or accompanied with another SEG1 alelle and S. pombe SLE1 gene (**B**).

Publication:

Vaskovičová K, Strádalová V, Efenberk A, Opekarová M, Malínský J, (2015): Assembly of fission yeast eisosomes in the plasma membrane of budding yeast: Import of foreign membrane microdomains. Eur J Cell Biol. 94(1):1–11. IF 3.699

Department of Technological Transfer

Head: Petr Bažant, MSc, PhD, MBA
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The Department monitors and evaluates the call for projects in domestic and foreign aid programs in business, both basic and applied research, innovation and education. In selected cases, together with other research departments of the Institute, the Department prepares project applications, contributes to the implementation of approved projects and prepares periodic monitoring reports on the progress of projects and their sustainability. The joint project between IEM AS CR and TA CR, GAMA, was approved for the years 2014–2019 in the amount of 17 mil. CZK. The department has expanded its services into the process of commercialization of new knowledge, ensuring the protection of intellectual property, and together with the Council for commercialization selects and administers proof-of-concept type projects, which are subsequently funded by the GAMA project and the Fund for the Commercialization of Knowledge, IEM. The department also plays a role in the project office, PMO, where its main purpose is to increase success in meeting the project plan, further optimizing the use of resources for the implementation of projects, planning cash flow to fund projects, and maintaining records of all completed projects.

Project manager "Commercializing knowledge IEM AS CR" within GAMA
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Project Manager EU funds:
Jan Prokšík, MSc
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Innovative Biomedical Centre (IBC)

Head: Petr Bažant, MSc, PhD, MBA
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Innovative Biomedical Centre (IBC) aids the development and successful start-up of spin-off companies based on scientific outputs from the Institute of Experimental Medicine. IBC encourages cooperation between companies, research institutes and investors.

Fig. Innovative Biomedical Centre (IBC) is situated in close proximity to the Institute in Prague 4-Krc, on the campus of the Academy of Sciences' biomedical institutes. Its construction, which took place in 2007–2008, was financed in part by EU funds.

Since 2008, IBC IEM AS CR has been a member of the Science and Technology Parks CR (www.svtp.cz).

IBC services for innovative start-ups are oriented in three, closely cooperating directions:

Promoting competitiveness in biomedicine – training in the fields of marketing, intellectual property protection, sales organization, management, financial management, project preparation, grant applicationslegal acts related to the establishment of companies, public procurement, and assistance in the implementation of good manufacturing practice. Training and coaching are arranged so that startups overcome the most common pitfalls: poorly assembled business plans and financing models, maladjusted relationships and contracts with investors, bad management firms, corporate compliance obligations under the Act, and inadequate protection of intellectual property.

Support for applied research in biomedicine – certified services under Good Manufacturing Practice: sterility tests, sampling sets production, separation and cultivation of stem cells, etc.

Business incubator for spin-off companies – services provided to othercompanies: office and laboratory rental, computer network management, purchasing management, patent and tax services, inventory management, reception, post office, administration and maintenance of real estate, business presentations, finding investors, and assistance in closing contracts. Currently, the business incubator is fully occupied.

Bioinova, Ltd.

Michael Syka, MD
Manager of clinical projects
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Tel.: +420 241 063 350
www.**bioinova.cz**

Bioinova was founded in 2008 as a spin-off company of IEM AS CR. The company focuses on the development and production of advanced-therapy medicinal products (ATMP) containing stem cells. In 2010 Bioinova obtained its Good Manufacturing Practise (AMP) lisence for the production of ATMP containing stem cells, it has also successfully passed several periodical audits of the State Institute for Drug Control (SIDC). In 2014, Bioinova was approved as the tissue establishment facility by SIDC.

Currently, Bioinova sponsors three clinical trials: **AMSC-ALS-001**, **AMSC-RC-001**, **AMSC-DSD-001** and manufactures the ATMP product for another clinical trial: **AMSC-BDT-001**.

In 2014, Michael Syka, MD, was appointed as the Manager of clinical projects for Bioinova. The CEO of the company remains Petr Bažant, MSc, PhD, MBA and Kateřina Růžičková, PhD remains the head of the quality control department. Šimona Konrádová, PhD leads the manufacture department and Petra Marková, PhD is responsible for the monitoring of clinical trials. The qualified person and chief of the quality assurance department is Ivana Drahorádová, MSc. The team is supported by Zuzana Kočí, MSc who manages applied research and preclinical studies. Cleanroom laboratory work is conducted by an experienced team of technicians: Jana Tenkrátová, Jana Káclová and Nicole Matějíčková, BS.

Clinical projects

Since its foundation, Bioinova works in tight cooperation with leading clinical centres in the Czech Republic.

In cooperation with University Hospital Motol, Bioinova conducts the clinical trial **AMSC-ALS-001** (ongoing since 2012) that aims to verify the safety and efficacy of the intrathecal administration of autologous multipotent mesenchymal stem cells in patients diagnosed with amyotrophic lateral sclerosis. In addition to 20 patients, another 6 were treated in 2014; in the first half of year 2015 three more subjects are expected to be enrolled.

Another clinical trial **AMSC-RC-001** (ongoing since 2013) focuses on using autologous multipotent mesenchymal stem cells in orthopedics to accelerate healing after rotator cuff surgery. This trial is also conducted by Bioinova in cooperation with University Hospital Motol. In addition to 3 patients, another 6 were treated in 2014; 11 more patients are planned to be enrolled in the following year.

Clinical trial **AMSC-DSD-001** (ongoing since 2013) focuses on using autologous multipotent mesenchymal stem cells in spondylosurgery to accelerate vertebral fusion in degenerative spine disease. This trial is also sponsored by Bioinova and conducted in cooperation with University Hospital Motol. In addition to 4 patients, another 5 were treated in 2014; 11 more patients are planned to be enrolled in the following year.

In the clinical trial **AMSC-BDT-001** (ongoing since 2013), Bioinova manufactures its investigational medicinal product for another sponsor – University Hospital Hradec Králové. This trial investigates the effect of the administration of autologous multipotent mesenchymal stem cells during reimplanation of hip arthroplasty. In addition to 7 subjects, another 7 were treated in 2014; 5 more patients are planned to be enrolled in the following year.

For the year 2015, Bioinova is preparing a new clinical trial to evaluate the safety and efficacy of the intrathecal administration of autologous multipotent mesenchymal stem cells in the treatment of severe spinal cord injury (grade A, B or C, according to ASIA classification).

Safety and efficacy of repeated intrathecal administration of autologous multipotent mesenchymal stem cells in patients with amyotrophic lateral sclerosis will be assessed in another clinical trial.

Also, Bioinova is designing a multi-center clinical trial which will be carried out in University Hostpital Motol, University Hospital Plzeň and Masaryk Hospital Ústí nad Labem to evaluate the safety and efficacy of the administration of autologous multipotent mesenchymal stem cells for the treatment of osteochondral lesions.

Regenerative Medicine and Tissue Engineering

Stem cell research and tissue repair provides great hope for the treatment of patients following brain and spinal cord injury, Alzheimer's disease, Parkinson's disease, diabetes, skin burns, damaged joints and arthritis, bone repair, loss of vision and hearing, as well as other incurable diseases.

The use of stem cells together with tissue engineering has brought about revolutionary possibilities for finding cures to such conditions. Studies of animal models and initial clinical studies using stem cells have demonstrated their huge potential in medicine, bringing hope to an aging population and countless patients suffering from a wide range of devastating diseases.

The core research carried out at the Institute is directed towards the study of all the currently known types of multipotent cells. We now know that both autologous and allogenic mesenchymal cells as well as embryonic, fetal, and induced pluripotent cells all have promising therapeutic effects.

Very often cell therapies need to be combined with either a natural or synthetic carrier. With this in mind fundamental multidisciplinary research in this area is necessary for the progression of future treatment.

Research Centre for Cell Therapy and Tissue Repair

Research Centre for Cell Therapy and Tissue Repair was built and put into operation by the Institute of Experimental Medicine AS CR within the Operational Programme Prague Competitiveness as part of the infrastructure for basic biomedical research and is financially supported by the National Programme sustainability Ministry of Education (NPU I – LO1309), during the period 2014–2019.

Centre builds on the successful implementation of the "Centre for Cell Therapy and Tissue Repair" (Research Centre – Ministry of Education, 1M0538, CEP12-MSM-1M-U/01:1), 2000–2004 and 2005–2011, which coordinated research and development in the field of cell therapy, cell sources and biocompatible materials and allowed the interconnection of scientific capacity and research groups in the field of cell therapy and tissue repair in the Czech Republic.

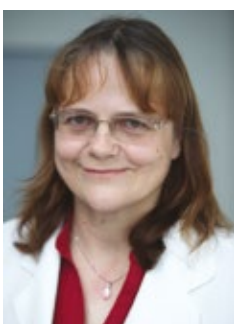
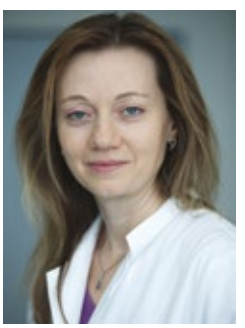
Centre is primarily focused on applied research in the field of advanced therapies using stem cells, biomaterials and nanomaterials as tools for targeted experimental treatment of diseases incurable by conventional means, including studies on the safety of these methods.

The main objectives of the Centre are based on a project implemented under the OPPK program, explained as follows:

1. To obtain a deeper knowledge of new, safe and effective treatments that offer therapies for incurable diseases and significantly shorten and/or reduce the price of current treatment.
2. The stabilization of conditions for generating high-quality scientific outputs of R&D&I, maintaining and increasing the number of jobs as well as the effective utilization, expansion, and ongoing modernization of the existing research infrastructure.
3. To strengthen interdisciplinary understanding of biomedical research by connecting the research fields of cell therapy, tissue repair, nanomaterials, functionalized nanofibers, and innovative biophysical methods.
4. To integrate the Centre into national and international structures and grant projects so as to provide additional sources for funding the further development of the Centre and strengthening its international contacts.
5. To establish and intensify the collaboration between the Centre and application sector partners such as hospitals, clinical departments, businesses, and private investors.
6. To involve undergraduate and postgraduate medical and natural sciences students into research projects in collaboration with universities and the improvement of researcher training and workforce development.

The technological facilities and infrastructure of the Centre serve as utility rooms and offer access to equipment for the four research groups at the IEM AS CR:
Department of Tissue Engineering (Prof. Evžen Amler, DSc, PhD)
Department of Transplantation Immunology (Prof. Vladimír Holáň, MD, DSc)
Department of Neuroscience (Prof. Eva Syková, MD, DSc, FCMA)
Laboratory of Stem Cell and Tissue Cultures (Assoc. Prof. Pavla Jendelová, PhD)
Laboratory of Biomaterials and Biophysical Methods (Šárka Kubinová, PharmD, PhD)



Research programs have been established on the basis of trends in global scientific development, contacts with clinicians, and the long-term research focus of the working groups in the field of cell therapy and tissue repair:

1. Study of the use of stem cells in tissue regeneration and the possibility of cell imaging using nanotechnology. Supervisor: *Assoc. Prof. Pavla Jendelová, PhD*
2. Targeted differentiation of stem cells and their use for regeneration of damaged ocular surfaces. Supervisor: *Prof. Vladimír Holáň, MD, DSc*
3. Regulation of the immune response after stem cell transplantation. Supervisor: *Prof. Vladimír Holáň, MD, DSc*
4. Preparation and characterization of functionalized nanofibers and microcapsules. Supervisor: *Prof. Evžen Amler, DSc, PhD*
5. Biological characterization of newly developed advanced materials as delivery systems of bioactive substances. Supervisor: *Prof. Evžen Amler, DSc, PhD*
6. The development of biomaterials for nerve tissue repair. Supervisor: *Šárka Kubinová, PharmD, PhD*
7. The development of biophysical methods for medical applications. Supervisor: *Šárka Kubinová, PharmD, PhD*

Introducing the new devices by Prof. Syková, director of the Institute

The opening ceremony of the Research Centre took place on April 1st, 2014 with the participation of the Deputy Prime Minister for Science, Research and Innovation, chairman RVVI **Pavel Bělobrádek**, President of the AS CR, **Prof. Jiří Drahoš** and **Prof. Eva Syková**, Director of the Institute.

Results

Zajícová A, Javorková E, Trošan E, Chudíčková M, Krulová M, Holáň V: A Low-Molecular-Weight Dialyzable Leukocyte Extract Selectively Enhances Development of CD4+RORγt+ T Cells and IL-17 Production, Folia Biologica (Praha) 2014; 60, 253-260. IF 0.778

Kočí Z, Turnovcová K, Dubský M, Baranovičová L, Holáň V, Chudíčková M, Syková E., Kubinová Š: Characterization of human adipose tissue-derived stromal cells isolated from diabetic patient's distal limbs with critical ischemia. Cell Biochem. Funct. 2014; 32(7): 597-604. IF 2.134

Zablotskyy V, Lunov O, Novotná B, Churpita O, Trošan P, Holáň V, Syková E, Dejneka A, Kubinová Š: Down-regulation of adipogenesis of mesenchymal stem cells by oscillating high-gradient magnetic fields and mechanical vibration. Appl. Phys. Lett. 2014; 105: 103702. IF 3.315

Lunov O, Zablotskyy V, Churpita O, Chanová E, Syková E, Dejneka A, Kubinová Š: Cell death induced by ozone and various non-thermal plasmas: therapeutic perspectives and limitations, Sci Rep, 2014; 4 : 7129. IF 5.078

Jelínek M, Kocourek T, Zemek J, Mikšovský J, Kubinová Š, Remsa J, Kopeček J, Jurek K: Chromium-doped DLC for implants prepared by laser-magnetron deposition. Mater Sci Eng C Mater Biol Appl. 2015;46:381-6. IF 2.736

Tukmachev D, Lunov O, Zablotskyy V, Dejneka A, Babič M, Syková E, et al. An effective strategy of magnetic stem cell delivery for spinal cord injury therapy. Nanoscale. 2015. IF 6.739

Lunov O, Churpita O, Zablotskyy V, Deyneka IG, Meshkovskii IK, Jäger A, Syková E, Kubinová Š, and Dejneka A: Non-thermal plasma mills bacteria: Scanning electron microscopy observations. Applied Physics Letters 106, 053703 (2015). IF 3.515

Other publications

Holáň V: Stem Cells and Immunity, Allergy, 2014; 4: 212–218

Syková E: stem cells and biomaterials in regenerative medicine today and tomorrow. Revue Czech Medical Academy. Vol. 10 - (2014), pp. 10 to 13 (Ed. putting dedication of the project was not allowed)

In press: Kubinová Š: New trends in neural tissue engineering, Future Neurology

Kubíková T, Filová E, Prosecká E, Plencner M, Králíčková M, Tonar Z: Histological evaluation of the effect of *in vivo* application of biomaterials for wound cartilage, bones and skin, Journal of Czech Physicians

Awards

Karolina Vocetková, MD, PhD

– Josef Hlávka Award

For the work of her diploma thesis
Award granted by Talent Foundation, Josefa, Marie and Zdeňky Hlávkových

Radim Šrám, MD, DSc

– Medal of Merit, Prague 5 District

For his work in the area of molecular epidemiology
Award granted by the City of Prague 5

Prof. Eva Syková, MD, DSc, FCMA

On Monday, September 29, 2014 Prof. Eva Syková, MD, DSc, FCMA, Director of the Institute of Experimental Medicine AS CR, was officially awarded the Silver Commemorative Medal of Charles University on the occasion of her significant lifelong contribution to science and knowledge, based on the proposal by the Rector of the University, Prof. Tomáš Zima, MD, DSc

Research Projects in 2014

Explanations:

MSM – Ministry of Education, Youth and Sports (MŠMT ČR):
ED – Operational Programme Research and Development for Innovation (OPVaVpI)
EE – Operational Programme Education for Competitiveness (OPVK)
LD – COST CZ
LH – KONTAKT II
LO – National Programme for Sustainability I
7F – EEA/Norwegian Financial Mechanism

MPO – Ministry of Industry and Trade:
FR – TIP - P – R&D Programme

MZ – Ministry of Health:
NT – Ministry of Health's – Departmental Research and Development Programme III

GAO – Czech Science Foundation (GA ČR):
GA – Standard projects
GB – Projects for promotion of excellence in basic research
GC – International projects
GP – Post-graduate (doctorate) grants

TA0 – Technology Agency of the Czech Republic (TA ČR):
TA – Programme of applied research and experimental development ALFA
TE – Competence Centres
TG – Programme of applied research, experimental development and innovations GAMA

EE2.3.20.0274 MSM

Human resources for neurosciences in the Hradec Králové and Ústí Regions

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: prof. Eva Syková, MD, DSc, FCMA
Duration: 2012–2015

EE2.3.30.0018 MSM

Development of Research Teams of IEM AS CR for the BIOCEV

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Eva Syková, MD, DSc, FCMA
Duration.: 2012–2015

Preparation of new research teams for the BIOCEV

FR-TI3/521 MPO

Technology of new magnetic nanoparticles for diagnostics and therapy in oncology

Contractor: SYNPO, a.s.
Project participant: Institute of Experimental Medicine AS CR, v.v.i., Institut of Physics AS CR,v.v.i., Institute of Chemical Technology in Prague
Investigator: Assoc. Prof. Pavla Jendelová, PhD
Duration: 2011–2015

GAP205/12/0720 GAO

Role of membrane potential in the lateral microdomain organization of the plasma membrane

Contractor: Charles University, Mathematics and Physics Faculty
Principal investigator: Assoc. Prof. Petr Heřman, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Jan Malínský, PhD
Duration: 2012–2014

GAP301/11/1568 GAO

Cellular aspects of transplantation tolerance

Contractor: Institute of Clinical and Experimental Medicine
Principal investigator: Prof. Ondřej Viklický, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Vladimír Holáň, DSc, PhD
Project participant: Institute of Molecular Genetics AS CR, v.v.i.
Duration: 2011–2014

GAP301/11/2418 GAO

Using 13C and proton MR spectroscopy to study the role of fatty acid transport and accumulation in tissues in the pathogenesis of insulin resistance

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Ivan Vořišek, PhD
Project participant: Institute of Clinical and Experimental Medicine
Investigator: Ludmila Kazdová, PhD
Duration: 2011–2015

GAP301/12/1734 GAO

Analysis of role of genetic factors in pancreatic cancer risk and prognosis

Contractor: State Health Institute Prague
Principal investigator: Pavel Souček, PhD
Project participant: Institute of Clinical and Experimental Medicine
Investigator: Assoc. Prof. Eva Honsová, MD, PhD
Project participant: University Hospital Brno
Investigator: Prof. Zdeněk Kala, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Procházka Pavel, PhD
Duration: 2012–2016

GAP302/11/0146 GAO

Role of MARVEL domain containing proteins in the geneticly encoded stress protection

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Jan Malínský, PhD
Duration: 2011–2014

GAP303/11/0131 GAO

Ectopic release of glycine – physiological role and mechanism

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Michaela Králíková – Havlíčková, PhD
Duration: 2011–2015

GAP303/11/2378 GAO

Changes in the extracellular space diffusion parameters during the development of brain edema and the role of aquaporin water-transporting proteins

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Ivan Vořišek, PhD
Duration: 2011–2016

GAP303/12/0172 GAO

Structure-activity relationship (SAR) study of immunosuppressive effects of pyrimidine analogues

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Zdeněk Zídek, DSc, PhD
Project participant: Institute of Organic Chemistry and Biochemistry AS CR, v.v.i.
Investigator: Zlatko Janeba, PhD
Duration: 2012–2016

GAP303/12/0535 GAO

Mechanisms of the anti-inflammatory effects of commensal and probiotic akteria and their role in metabolism and drug pharmacokinetics

Contractor: Institut of Microbiology AS CR, v.v.i.
Principal investigator: Tomáš Hudcovic, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Assoc. Prof. Eva Kmoníčková, PhD
Project participant: Palacký University Olomouc / Faculty of Medicine
Investigator: Assoc. Prof. Eva Anzenbacherová, PhD
Duration: 2012–2016

GAP303/12/0855 GAO

Polydendrocyte function in regeneration after ischemic brain injury – the role of Wnt signaling pathway

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Anděrová Miroslava, PhD
Duration: 2012–2015

GAP303/12/1347 GAO

Mechanisms underlying complex sound processing in the neuronal assemblies in the auditory system

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Josef Syka, MD, DSc, FCMA
Duration: 2012–2016

GAP304/10/0326 GAO

Autologous mesenchymal stem cells in rotator cuff repair enhancement – preclinical and prospective randomized clinical study

Contractor: Charles University, 2nd Faculty of Medicine
Principal investigator: Assoc. Prof. Tomáš Trč, PhD, MBA
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Eva Syková, MD, DSc, FCMA
Duration: 2010–2015

GAP304/11/0184 GAO

The potential of mesenchymal stem cells in the treatment of Alzheimer's

Contractor: Charles University, 2nd Faculty of Medicine
Principal investigator: Prof. Eva Syková, MD, DSc, FCMA
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Assoc. Prof. Pavla Jendelová, PhD
Duration: 2011–2016

GAP304/11/0189 GAO

The use of stem cells in the treatment of amyotrophic lateral sclerosis

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Assoc. Prof. Pavla Jendelová, PhD
Project participant: Charles University, 2nd Faculty of Medicine
Investigator: Aleš Homola, MD, PhD
Duration: 2011–2014

GAP304/11/0653 GAO

Targeted differentiation and transdifferentiation of limbal and mesenchymal stem cells and their therapeutic applications in preclinical models

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Vladimír Holáň, DSc, PhD
Project participant: Institute of Molecular Genetics AS CR, v.v.i.
Duration: 2011–2014

GAP304/11/1418 GAO

Differentiation of human embryonic stem cells into odontogenic lineages

Contractor: Masaryk University / Faculty of Medicine
Principal investigator: Assoc. Prof. Aleš Hampl, MVD, PhD
Project participation: Institute of Animal Physiology and Genetics AS CR, v.v.i.
Investigator: Prof. Eva Matalová, PhD
Project participation: Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2011–2014

GAP304/12/1342 GAO

Pathological changes in the central auditory system accompanying aging

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Jiří Popelář, PhD
Duration: 2012–2016

GAP304/12/1370 GAO

Superparamagnetic iron-oxide nanoparticles for cellular imaging and their effect on genotoxicity, cytotocixity and stem cell differentiation

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Assoc. Prof. Pavla Jendelová, PhD
Duration: 2012–2015

GAP304/12/1585 GAO

Molecular DNA repair characteristics in CRC tumor tissue

Contractor: Charles University, 1st Faculty of Medicine
Principal investigator: Pavel Vodička, MD, PhD
Project participant: Thomayer Hospital
Investigator: Ludmila Lipská, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Ludmila Vodičková, MD, PhD
Project participant: State Health Institute Prague
Investigator: Simona Šůsová, MSc
Project participant: Institute of Biotechnology AS CR, v.v.i.
Investigator: Vlasta Korenková, PhD
Research years: 2012–2015

GAP305/12/1766 GAO

Rudiments in the mouse model of tooth development

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Hovořáková Mária, PhD
Research years: 2012–2016

GAP503/11/0142 GAO

Genotoxic and non-genotoxic mechanisms involved in carcinogenicity of complex mixtures of air pollutants: toxicogenomic approach

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Jan Topinka, DSc, PhD
Project participant: Veterinary Research Institute
Investigator: Miroslav Machala, PhD
Duration: 2011–2015

GA13-00939S GAO

The treatment of chronic spinal cord injury using stem cells and enzymes in combination with polymer scaffolds

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Assoc. Prof. Pavla Jendelová, PhD
Project participant: Institute of Macromolecular Chemistry AS CR, v.v.i.
Investigator: Martin Přádný, PhD
Project participant: Charles University, 2nd Faculty of Medicine
Investigator: Assoc. Prof. Lýdia Vargová, MD, PhD
Duration: 2013–2016

GA13-01438S GAO

Mechanisms of toxicity of biofuel particulate emissions

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Jan Topinka, DSc, PhD
Project participant: Institute of Analytical Chemistry AS CR, v.v.i.
Investigator: Pavel Mikluška, PhD
Project participant: Czech Technical University in Prague
Investigator: Michal Vojtíšek, PhD
Duration: 2013–2015

GA13-02154S GAO

Gene expression profiling and functional characterization of glial cell subpopulations following ischemic brain injury

Contractor: Institute of Biotechnology AS CR, v. v. i.
Principal investigator: Prof. Mikael Kubista, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Miroslava Anděrová, PhD
Duration: 2013–2016

GA13-07996S GAO

Molecular mechanisms responsible for generating cellular diversity in the inner ear

Contractor: Institute of Biotechnology AS CR, v. v. i.
Principal investigator: Gabriela Pavlínková, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Josef Syka, MD, DSc, FCMA
Duration: 2013–2016

GA13-11867S GAO

The role of brain link proteins for formation and maintenance of perineuronal nets

Contractor: Charles University, 2nd Faculty of Medicine
Principal investigator: Assoc. Prof. Lýdia Vargová, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Jiří Popelář, PhD
Duration: 2013–2015

GA13-13458S GAO

Impact of air pollution to genome of newborns

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Šrám Radim, MD, DSc
Project participant: University of South Bohemia in České Budějovice, Health and Social Studies
Investigator: Miloš Velemínský, MD, PhD
Project participant: University of Chemical Industry in Prague
Investigator: Assoc. Prof. Jana Pulkrabová, PhD
Duration: 2013–2016

GA14-03540S GAO

Autologous cell based therapy for ischemic diabetic wounds: preclinical and clinical trial

Contractor: Institute of Clinical and Experimental Medicine
Principale investigator: Robert Bem, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Eva Syková, MD, DSc, FCMA
Duration: 2014–2016

GA14-12580S GAO

Treatment of severe ocular surface injuries using limbal and mesenchymal stem cells

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Vladimír Holáň, DSc, PhD
Project participant: Lexum, a.s.
Investigator: Prof. Martin Filipec, MD, PhD
Project participant: Charles University, the Faculty of Science
Investigator: Magdaléna Krulová, PhD
Duration: 2014–2016

GA14-14961S GAO

Spinal cord injury reconstruction using surface-modified biodegradable hydrogels with oriented pores seeded with mesenchymal stem cells

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal Investigator: Aleš Hejčl, MD, PhD
Project participant: Institute of Macromolecular Chemistry AS CR, v. v.i.
Investigator: Hana Macková, PhD
Duration: 2014–2016

GA14-28334S GAO

Molecular mechanism of GABA B receptor regulation by KCTD proteins

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Michaela Králíková – Havlíčková, PhD
Duration: 2014–2016

GA14-34077S GAO

Calcium homeostasis in central and peripheral oxytocin and vasopressin neurons: repercussions in osmoregulation, pregnancy, lactation and nociception

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Govindan Dayanithi, PhD
Duration: 2014–2016

GBP304/12/G069 GAO

Project of excellence in the field of neuroscience

Contractor: Institute of Physiology AS CR, v. v. i.
Principal investigator: Ladislav Vyklický Jr., MD, DSc
Project participant: The National Institute of Mental Health
Investigator: Daniela Řípová, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Josef Syka, MD, DSc, FCMA
Project participant: Charles University, 2nd Faculty of Medicine
Investigator: Miroslava Anděrová, PhD
Duration: 2012–2018

GBP503/12/G147 GAO

Centre of Studies toxic properties of nanoparticles

Contractor: Veterinary Research Institute, v.v.i.
Principal investigator: Miroslav Machala, PhD
Project participant: Institute of Chemical Process Fundamentals AS CR, v. v. i.
Investigator: Pavel Moravec, PhD
Project participant: Institute of Animal Physiology and Genetics AS CR, v. v. i.
Investigator: Assoc. Prof. Omar Šerý, PhD
Project participant: Institute of Analytical Chemistry AS CR, v. v. i.
Investigator: Zbyněk Večeřa, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Jan Topinka, DSc, PhD
Project participant: Charles University in Prague, the Faculty of Science
Investigator: Jan Hovorka, PhD
Duration: 2012–2018

GB14-37368G GAO

Centre of orofacial development and regeneration

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Renata Peterková, MD, PhD
Project participant: Institute of Animal Physiology an Genetics AS CR, v. v. i.
Investigator: Prof. Eva Matalová, PhD
Project participant: Charles University in Prague, 1st Faculty of Medicine
Investigator: Prof. Zdeněk Broukal, MD, PhD
Project participant: Masaryk University, Faculty of Medicine
Investigator: Prof. Jiří Vaněk, MD, PhD
Duration: 2014–2018

GCP303/11/J005 GAO

Neural remodeling after early sound exposures

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Josef Syka, MD, DSc, FCMA
Duration: 2011–2014

GP13-15031P GAO

The influence of anti-inflamatory agents in combination with mesenchymal stem cells on the development of traumatic spinal cord lesions in the rat

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Machová-Urdzíková Lucia, MD, PhD
Duration: 2013–2015

LD14002 MSM

Toxic effects of nanomaterials as a function of their structure and physicochemical properties

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Topinka Jan, DSc, PhD
Duration: 2014–2016

LD14050 MSM

Genetic and functional determinants of colorectal cancer and prospects to individualised therapy

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Vodička Pavel, MD, PhD
Duration: 2014 –2017

LH12024 MSM

Determining the molecular aspects of spinal cord injury, regeneration, stem cell therapy and treatment with anti-inflammatory compounds

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Assoc. Prof. Pavla Jendelová, PhD
Duration: 2012–2015

LH13061 MSM

The role of Ganoderma Lucidum in the regulation of NFkappaB-dependent DNA repair-proteasome interactions in colorectal carcinogenesis

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Vodička Pavel, MD, PhD
Duration: 2013–2015

LO1309 MSM

Cell Therapy and Tissue Repair

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Kubinová Šárka, PhaermD, PhD
Duration: 2014–2019

NT12025 MZ

Molecular-biological and histopathological characteristics of tumor infiltrating lymphocytes as instrument of prediction of risk of early colorectal cancer recurrence

Contractor: Charles University in Prague, Faculty of Medicine in Pilsen
Principal investigator: Petr Novák, MD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigators: Pavel Vodička, MD, PhD
Project participant: University Hospital in Pilsen
Investigator: Václav Liška, MD, PhD
Project participant: State Health Institute Prague
Investigators: Pavel Souček, PhD

NT12459 MZ

Possibilities of hearing preservation in patients with vestibular schwannoma

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Josef Syka, MD, DSc, FCMA
Project participant: University Hospital Motol
Investigators: Prof. Jan Betka, MD
Duration: 2011–2015

NT13424 MZ

MiR137 and its influence on the production of mucin as a potential tool in early diagnosis of colorectal cancer or colorectal cancer relapse

Contractor: Thomayer Hospital
Principal investigators: Miroslav Levý, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Vodička Pavel, MD, PhD
Duration: 2012–2015

NT13477 MZ

The use of the synthetic biomaterials in the treatment of the extensive skeletal defects in revision total hip arthroplasty

Contractor: Charles University in Prague, Faculty of Medicine in Hradec Kralové
Principale investigators: Pavel Šponer, MD, PhD
Project participant: University Hospital in Hradec Králové
Investigators: Assoc. Prof. Karel Urban, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigators: Prof. Eva Syková, MD, DSc, FCMA
Duration: 2012–2015

NT13770 MZ

Examination of DNA instability in gametes, embryos and somatic cells following oncological therapy for improvement of reproductive success in treated patients.

Contractor: University Hospital Motol
Investigators: Prof. Milan Macek Jr., MD, DSc
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Božena Novotná, PhD
Duration: 2012–2015

NT14056 MZ

Molecular and genetic biomarkers of ovarian cancer pathogenesis and resistence

Contractor: State Health Institute Prague
Principale contractor: Radka Václavíková, PhD
Project participant: University Hospital Motol
Investigator: Prof. Lukáš Rob, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Vodička Pavel, MD, PhD
Duration: 2013–2015

NT14102 MZ

A role of B lymphocytes in immune reactions after kidney transplantation

Contractor: Institute of Clinical and Experimental Medicine
Principal investigator: Prof. Ondřej Viklický, MD, PhD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Prof. Vladimír Holáň, DSc, PhD
Research duration: 2013–2015

NT14329 MZ

Evaluation of changes of molecular-biologic factors and their importance in prognosis of relapsing colorectal cancer after radical surgical treatment

Contractor: Charles University in Prague, Faculty of Medicine in Pilsen
Principal investigator: Václav Liška, MD, PhD
Project participant: University Hospital in Pilsen
Investigators: Petr Novák, MD
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigators: Pavel Vodička, MD, PhD
Project participant: State Health Institute Prague
Investigator: Pavel Souček, PhD
Duration: 2013–2015

TA04010449 TAO

Low temperature plasma in medicine

Contractor: FOTON, Ltd
Principal investigators: Jaroslav Moravec, MSc; Jiří Horáček; Tomáš Petráček, MSc
Project participant: SINDAT, Ltd
Investigator: Daniel Bezděk, MSc
Project participant: L.E.T. Optomechanika Praha, Ltd
Investigator: Tomáš Fejt, MSc
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: PharmD, Šárka Kubinová, PhD
Project participant: Institute of Physics AS CR, v.v.i.
Investigator. Alexandr Dejneka, PhD

TE01020028 TAO

Centre for Development of Original Drugs

Contractor: Institute of Organic Chemistry and Biochemistry AS CR, v. v. i.
Principal investigator: Havlas Zdeněk, DSc
Project participant: QUINTA-ANALYTICA, Ltd
Investigator: Assoc. Prof. Martin Valchář, PhD
Project participant: MediTox, Ltd
Investigator: Jan Zábský, MBA
Project participant: IOCB TTO, Ltd
Investigator: Assoc. Prof. Martin Fusek, PhD
Project participant: APIGENEX, Ltd
Investigator: Miroslav Havránek, PhD
Project participant: Institute of Physiology AS CR, v. v. i
Investigator: Ladislav Vyklický, MD, DSc
Project participant: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Zdeněk Zídek, DSc, PhD
Project participant: Palacký University Olomouc, Faculty of Medicine
Investigator: Assoc. Prof. Marián Hajdúch, MD, PhD
Project participant: Institute of Chemical Technology in Prague, Faculty of Chemical Engineering
Investigator: Prof. Vladimír Král, DSc
Duration: 2012–2019

TG 01010135 TAO

Commercialization of R & D programs in applied research, experimental development and innovation GAMA

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Prof. Eva Syková, MD, DSc, FCMA
Duration: 2014–2019

7F14057 MSM

Biomaterials and stem cells in the treatment of stroke and spinal cord injury

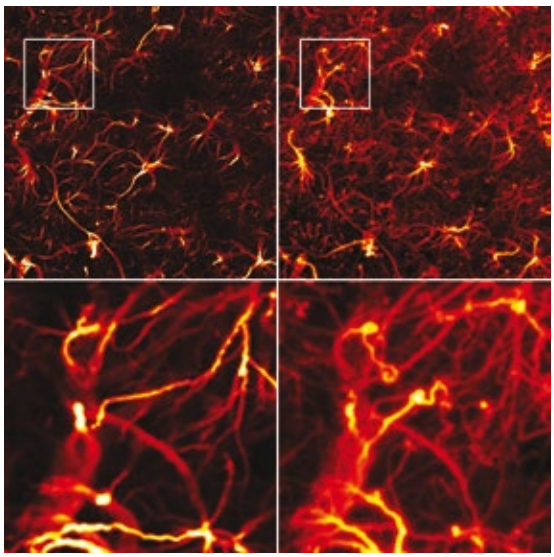
Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Investigator: Assoc. Prof. Pavla Jendelová, PhD
Project participant: Norges teknisk-naturvitenskapelige universitet
Investigator: Ioanna Sandvig, PhD
Duration: 2014–2017

Prague City Hall, Operational Programme Prague for competition (OPPK)
CZ 2.16/3.1.00/21527

Advanced imaging of living tissues

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Jan Malinský, PhD
Project summary: The objective of the project was to purchase new microscope technology to enhacement competition of the biomedical research carried out at the Institute.
Duration: 01–09/2014

Introduction of new equipment and clean rooms

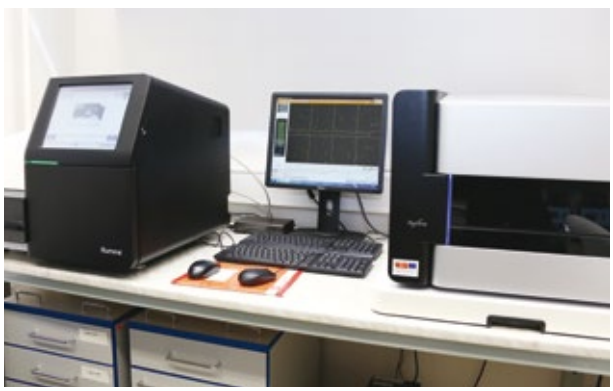


Fine network structure of astrocyte processes following the ischemic damage in rat hippocampal slice is visualized by fluorescence of the expressed glial fibrillary acidic protein. It is possible to compare the quality of image obtained by the classical confocal microscope (left) and using three-dimensional reconstruction of confocal images with enhanced dynamic contrast (right). Frames (top) indicate the fine details of vascular plexus of astrocytic processes (below). Images were obtained using a newly purchased microscope Olympus FV1200 MPE.

Prague City Hall, Operational Programme Prague for competition (OPPK)
CZ.2.16/3.1.00/21528

Research centre for genomics and proteomics

Contractor: Institute of Experimental Medicine AS CR, v.v.i.
Principal investigator: Radim Šrám, MD, DSc
Project summary: The objective of the project was to purchase new technical research equipment for the research of genomics and proteomics
Duration: 01–09/2014



System for sequencing and chip analysis

System for protein analysis

Automatic cell harvester

Publications

DEPARTMENT OF NEUROSCIENCE

Dubský, M., Jirkovská, A., Bem, R., Fejfarová, V., Pagacová, L., Němcová, A., Sixta, B., Chlupáč, J., Peregrin, J. H**., Syková, E.,** Jude, E. B.: (2014) Comparison of the effect of stem cell therapy and percutaneous transluminal angioplasty on diabetic foot disease in patients with critical limb ischemia. *Cythotherapy* 16(12): 1733–1738. IF 3.100

Dubský, M., Jirkovská, A., Bém, R., Fejfarová, V., Varga, M., Kolesar, L., Pagacova, L., **Syková, E.,** Jude, E. B.: (2014) Role of serum levels of angiogenic cytokines in assessment of angiogenesis after stem cell therapy of diabetic patients with critical limb ischemia. *Cell Transplant.* 23(12): 1517–1523. IF 3.570

Forostyak, S., Homola, A., Turnovcová, K., Svítil, P., Jendelová, P., Syková, E.: (2014) Intrathecal delivery of mesenchymal stromal cells protects the structure of altered perineuronal nets in SOD1 rats and amends the course of ALS. *Stem Cells* 32(12): 3163–3172. IF 7.133

Kelbich, P., **Hejčl, A.,** Krulichová, I. S., Procházka, J., Hanuljaková, E., Peruthová, J., Koudelková, M., Sameš, M., Krejsek, J.: (2014) Coefficient of energy balance, a new parameter for basic investigation of the cerebrospinal fluid. *Clin. Chem. Lab. Med.* 52(7): 1009–1017. IF 2.955

Kočí, Z., Turnovcová, K., Dubský, M., Baranovičová, L., **Holáň, V., Chudíčková, M., Syková, E., Kubinová, Š.:** (2014) Characterization of human adipose tissue-derived stromal cells isolated from diabetic patient's distal limbs with critical ischemia. *Cell Biochem. Funct.* 32(7): 597–604. IF 2.134

Kubinová, Š., Horák, D., **Vaněček, V.,** Plichta, Z., Proks, V., **Syková, E.:** (2014) The use of new surface-modified poly(2-hydroxyethyl methacrylate) hydrogels in tissue engineering: Treatment of the surface with fibronectin subunits versus Ac-CGGASIKVAVS-OH, cysteine, and 2-mercaptoethanol modification. *J. Biomed. Mater. Res. Part A.* 102(7): 2315–2323. IF 2.841

Lunov, O., Zablotskyy, V., Churpita, O., Chamova E., **Syková, E.,** Dejneka, A., **Kubinová, Š.:** (2014) Cell death induced by ozone and various non-thermal plasmas: therapeutic perspectives and limitations. *Sci Rep*. 4: 7129. IF 5.078

Machová - Urdziková, L., Sedláček, R., Suchy, T., **Amemori, T., Růžička, J.,** Lesný, P., Havlas, V., **Syková, E., Jendelová, P.:** (2014) Human multipotent mesenchymal stem cells improve healing after collagenase tendon injury in the rat. *Biomed. Eng. Online* 13(1): 42. IF 1.746

Machová - Urdziková, L., Růžička, J., LaBagnara, M., **Kárová, K., Kubinová, Š., Jiráková, K.,** Murali, R., **Syková, E.,** Jhanwar-Uniyal, M., **Jendelová, P.:** (2014) Human mesenchymal stem cells modulate inflammatory cytokines after spinal cord injury in rat. *Int. J. Mol. Sci.* 15(7): 11275–11293. IF 2.339

Rodríguez, J. J., Yeh, C. Y., Terzieva, S., Olabarria, M., **Kulijewicz-Nawrot, M.,** Verkhratsky, A.: (2014) Complex and region-specific changes in astroglial markers in the aging brain. *Neurobiol. Aging* 35(1): 15–23. IF 4.853

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Zablotskyy, V., Lunov, O., **Novotná, B.,** Churpita, O., **Trošan, P., Holáň, V., Syková, E.,** Dejneka, A., **Kubinová, Š.:** (2014) Down-regulation of adipogenesis of mesenchymal stem cells by oscillating high-gradient magnetic fields and mechanical vibration. *Appl. Phys. Lett.* 105(10): 103702. IF 3.315

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Tureček, R., Schwenk, J., Fritzius, T., Ivankova, K., Zolles, G., Adelfinger, L., Jacquier, V., Besseyrias, V., Gassmann, M., Schult,e U., Fakler, B., Bettler, B.: (2014) Auxiliary GABAB Receptor Subunits Uncouple G Protein βγ Subunits from Effector Channels to Induce Desensitization. *Neuron* 82(5): 1032–1044. IF 15.982

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Honsa, P., Pivoňková, H., Harantová, L., Butenko, O., Kriška, J., Džamba, D., Rusňáková, V., Valihrach, L., Kubista, M., **Anděrová, M.:** (2014) Increased expression of hyperpolarization-activated cyclic nucleotide-gated (HCN) channels in reactive astrocytes following ischemia. *Glia* 62(12): 2004–2021. IF 5.466

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DEPARTMENT OF MOLECULAR NEUROPHYSIOLOGY

Filip, S., Mokrý, J., Vávrová, J., Šinkorová, Z., Mičuda, S., Šponer, P., Filipová, A., Hrebíková, H., **Dayanithi, G.:** (2014) The peripheral chimerism of bone marrow-derived stem cells after transplantation: regeneration of GITin lrthally-irradiated mice. *J. Cell. Mol. Med.* 18(5): 832–843. IF 4.753

DEPARTMENT OF PHARMACOLOGY

Jansa, P., Holý, A., Dračínský, M., Kolman, V., Janeba, Z., **Kostecká, P., Kmoníčková, E., Zídek, Z.:** (2014) 5-Substituted 2-amino-4,6-dihydroxypyrimidines and 2-amino-4,6 dichloropyrimidines: synthesis and inhibitory effects on immune-activated nitric oxide production. *Med. Chem. Res.* 23: 4482–4490. IF 1.612

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Zídek, Z., Jansa, P., **Kmoníčková, E.:** (2014) Activation of respiratory complex II by interferongamma and its inhibition by pyrimidine derivatives. *Neuroendocrinol. Lett*. 35 (Suppl.2): 141–148. IF 0.935

DEPARTMENT OF GENETIC ECOTOXICOLOGY

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Líbalová H., Krčková, S., **Uhlířová, K.,** Klema, J., Ciganek, M., **Rössner, P. Jr., Šrám, R.,** Vondráček, J., Machala, M., **Topinka, J.:** (2014) Analysis of gene expression changes in A549 cells induced by organic compounds from respirable air particles. *Mutat. Res.-Fundam. Mol. Mech. Mutagen.* 770: 94–105. IF 4.440

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DEPARTMENT OF TERATOLOGY

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Zídek, Z., Kmoníčková, E., Janeba, Z., Kolman, V., Jansa, P.: (2014) Structure-dependent NO-, PGE2- and cytokine-inhibitory effects of pyrimidine derivatives. Proceedings of the Joint Meeting of the 8th International Symposium Nitric Oxide. s. 6-10. ISBN 978-80-971699-0-9. [Proceedings of the Joint Meeting of the 8th International Symposium Nitric Oxide: From Basic Regulations to Lifestyle-Related Diseases and The 2nd Genetic and Environmental Factors in Hypertension [0312302]. Vrsan (HR), 15.09.2014–19.09.2014]

PhD THESES DEFENDED

Burianová Jana
Effect of aging on the central portion of the auditory system of the rat.
Supervisor: Jiří Popelář, PhD / Defended: Charles University in Prague, 1st Faculty of Medicine, September 15, 2014

Butenko Olena
Expression and functional characterisation of transient receptor potential vanilloid-related channel 4 (TRPV4) in hippocampal astrocytes after ischemia/reperfusion.
Supervisor: Miroslava Anděrová, PhD / Defended: Charles University in Prague, 2nd Faculty of Medicine, April 7, 2014

Dmytrenko Lesia
Changes of the Extracellular Space Diffusion Parameters during Acute Pathological States in the Rodent Brain and the Role of AQP4 Channels in Cell Swelling.
Supervisor: Assoc. Prof. Lýdia Vargová, MD, PhD / Defended: Charles University in Prague, 2nd Faculty of Medicine, June 16, 2014

Lagronová Svatava
Časná morfogeneze dolních tvářových zubů u myší s genovými defekty.
Supervisor: Renata Peterková, MD, PhD / Defended: Charles University, the Faculty of Science, 2014

Kulijewicz Magdalena
Astrocytic changes in a mouse model of Alzheimer´s disease.
Supervisor: Prof. Eva Syková, MD, DSc, FCMA / Defended: Charles University in Prague, 2nd Faculty of Medicine, 2014

Profant Oliver
Organizace sluchové kůry a změny ve sluchovém systému u presbyakuze.
Supervisor: Prof. Josef Syka, MD, DSc, FCMA / Defended: Charles University in Prague, 2nd Faculty of Medicine, 2014

Trojanová Johana
Imunohistochemická analýza vlastností inhibičních glycinových a GABA receptorů v MNTB.
Supervisor l: Rostislav Tureček, PhD / Defended: Charles University in Prague, 2nd Faculty of Medicine, June 16, 2014

Research for Practice

The results of cooperation with business partners acquired on the basis of economic contracts

Development of a cell carrier for tissue engineering

Sponsor: EponaCell, Ltd
Application: The starting material for the development of replacement organs
Result: Development of a cell carrier for tissue engineering, two-dimensional and three-dimensional biocompatible material, toxicity tests, the influence of the material properties on cell culture growth and the proliferation ability of cell cultures on the tested material.

Procedures of stem cells manipulations

Sponsor: ArtiCell, Ltd
Application: Dentistry
Result: Developing procedures and manipulating stem cells for potential use in clinical applications, focusing on the creation of bone for dental purposes.

Treatment of damaged surface of the eye

Sponsor: BiotechInvest, Ltd
Application: Ophthalmology
Results: 1. Comparison and characterization of the ability of differentiation into cells of the corneal epithelium stem cells in the lumbar and the two types of mesenchymal stem cells (isolated from bone marrow and adipose fat) **2.** Motion possible use of differentiated mesenchymal cells to treat damaged ocular surfaces in an *in vivo* system in laboratory animals or in preclinical research.

Drug testing with the aim to improve age-related hearing dysfunction

Sponsor: Autifony, Srl Company, Verona, Italy
Application: The results suggest the possibility of improving the perception of temporal characteristics of sound in elderly individuals
Result: Old rats have impaired perception of time parameters of sound that is manifested by significantly reducing the effectiveness of prepulse inhibition of acoustic startle response in behavioral tests. This deficiency could be partially improved via the injection of Kv3.1 ion channel modulator, which is known to increase GABA-ergic inhibition in central auditory nuclei.

Professional expertises

Title	Contracting Authority
Opponent reviews of grant proposals, a total of **272**	GA CR, TA CR, AZV, IGA MZ, GA UK, the Ministry of Education, VEGA (Slovak Grant Agency), Marie Curie Individual Fellowship Horizon 2020 FNRS2014
Reviwes of Publications, a total of **63**	Editorial Board of domestic and foreign scientific journals
Opponent reviews of dissertations and doctoral theses, a total of **2**	Coresponding committees
Opponent reviews, a total of **6**	Czech Society for Experimental and Clinical Pharmacology and Toxicology

Bilateral agreements

Collaborating institutions	Country	Theme cooperation
Department of Physiology IP Pavlova, RAV, Sankt Peterburg	Russia	Neurophysiological mechanisms for detection and differentiation of audio signals in humans and animals.
US Environmental Protection Agency	NC USA	Analysis of gene-environment interactions and development of applications for risk assessment.

Patents and Utility models

Year 2014	Number	In cooperation with
Patent applications filed in the Czech Republic		
Utility models are made in the Czech Republic	1	Institute of Physics AS CR, v. v. i.
Utility models registered in the Czech Republic	1	Institute of Physics AS CR, v. v. i.
Patents filed abroad	**2**	
National patent granted	1	Institute of Macromolecular Chemistry AS CR, v. v. i.
National patent filed	1	Institute of Macromolecular Chemistry AS CR, v. v. i.

Patent No.: US8883798

Jansa P, Holý A, **Zídek Z**, **Kmoníčková E**, Janeba Z: Pyrimidine compounds inhibiting the formation of nitric oxide and prostaglandin E2, method of production thereof and use there of 2014.
Owner: Institute of Organic Chemistry and Biochemistry AS CR, v. v. i., **Institute of Experimental Medicine AS CR, v. v. i.**
Date of the Patent Acceptance: 11. 11. 2014.

The invention provides pyrimidine compounds of general formula (I), which reduce simultaneously the production of nitric oxide (NO) and prostaglandin E2 (PGE2). They have no negative effect on the viability of cells in concentrations decreasing the production of these factors by up to 50%; they are not cytotoxic. Furthermore, a method of preparation of the pyrimidine compounds of general formula (I), carrying 2-formamido group, a pharmaceutical composition comprising the substituted pyrimidine compounds according to the invention, and the use of these compounds for the treatment of inflammatory and cancer diseases are provided.

Patent No.: 304814

Churpita O, Dejneka A, Zablotskyy VA, **Kubinová Š**, **Syková E**: Atmospheric plasma source, particularly for use in medicinal bioapplications. 2014.
Owner: Institute of Physics AS CR, v. v. i., **Institute of Experimental Medicine AS CR, v. v. i.**
Date of the Patent Acceptance: 01.10. 2014.

The atmospheric plasma source, particularly for use in medicinal bioapplications according to the present invention comprises an alternating high voltage source (5) and a hollow insulation body (1) with an inlet of processing gas opening into the inside thereof. In the interior of said hollow body (1) there is arranged an internal excitation electrode (2) that is connected to the alternating high voltage source (5). In the interior of the insulation body (1) there is arranged a sandwich structure formed by layers of porous material and

consisting of the excitation electrode (2), an electrically non-conducting porous membrane (3) and an external grounding electrode (4), wherein all the components are arranged one above the other.

Patent No.: WO2014/044321 A1

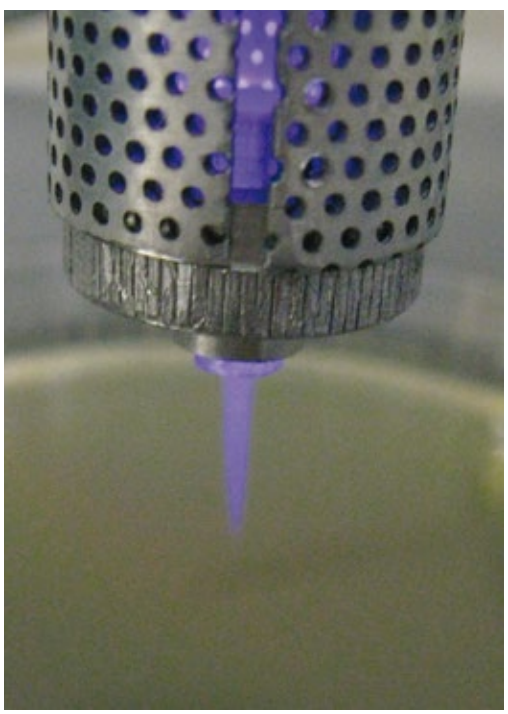
Saint-Pierre G, Herrero Gomez M, Martinez Creispera S, Saiani A, Merry C, Meade K, Guilbaud JB, Miller AF, Ciobanu C, **Amler E**, Pons Ariño A: New scaffold for cardiac patch. 2014.
Owner: Technologias Avanzadas Inspiralia S. L. – The University of Manchester – Institutul De Chimie Macromoleculara Petrui Poni, **Institute of Experimental Medicine AS CR, v. v. i.**
Date of the Patent Acceptance: 27. 03. 2014.

A biocompatible and biodegradable medical device patch actuating primarily as soft tissue structural reinforcement. The device has a layered architecture, where the primary serves as suturing layer and mechanical support to a thick porous scaffold which can be coated with a mimic-like extra cellular matrix (ECM). The device can be provided to the end user under the format of independent layers that can be cut and assembled to the specific need to the end user and patient. The layers are assembled without the need of any adhesive. Totally haemocompatible and of behavior superior to polytetrafluoroethylene used for any soft tissue repaired, the field of this invention is demonstrated for cardiovascular therapy but should not be limited to it. It is of practical relevance of vein, tendon and hernias and dermal treatments.

Utility Model No.: 27679

Churpita O, Dejneka A, Zablotskyy VA, **Syková E**, **Kubinová Š**: Low-temperature plasma source, particularly for deactivation of bacteria. 2014.
Owner: Institute of Physics AS CR, v. v. i., **Institute of Experimental Medicine AS CR, v. v. i.**
Date of the Utility Model Acceptance: 29. 12. 2014.

Technical solution falls in generating low temperature plasma and relates to the construction of low temperature plasma source, particularly for use in various medical bioapplications such as deactivation of bacteria.



Development and study of low-temperature atmospheric pressure plasma for biomedical applications

Plasma medicine is a modern and promising field combining plasma physics, life sciences and clinical medicine to implement low-temperature plasma in medical applications. Low-temperature plasmas are capable of bacterial inactivation, thus offering considerable opportunities for their use especially in medical sterilization and the treatment of wounds and multiple skin pathologies. The aim of our research is the acquisition of new knowledge about the effects of plasmas on biological systems. The mechanisms underlying these effects are being studied at the molecular, cellular and tissue levels for specific bacteria and mammalian cell cultures and tissues. The development of new low-temperature atmospheric pressure plasma devices with tightly controlled parameters and their optimization to maintain safety standards and to investigate the processes that are relevant for medical applications will also be performed. To reach the proposed goals, interdisciplinary research at the interface of plasma physics, chemistry and engineering with cell biology and medicine are being implemented.

Teaching Activities

Postgraduate education

	Number of graduates in 2014	Number of PhD students prior to December 31, 2014	Number of newly admitted students in 2014
Full-time PhD students	1	43	7
PhD students in combined and/or distance learning	5	11	4
Total	6	54	11
Foreign students	4	15	1

Education of undergraduate students

Number of bachelors	11
Number of diploma students	17
The number of undergraduate students involved in the Institute's research	23

Teaching activities of the Institute

	Summer semester 2013/2014			Winter semester 2014/2015		
The number of teaching hours during Bachelor / Master / PhD courses	148	206	44	72	450	27
Number of lectures / seminars / exercises in undergraduate programs	9	5	1	5	1	1
Number of lectures / seminars / exercises in masters programs	6	5	1	8	4	3
Number of the Institute staff involved in Bachelor / Master / PhD programs	11	3	10	10	6	5

Research cooperation between the Institute and Universities

	Institute as project promoter	Institute as project partner
Number of joint projects with the universities in 2014	10	12
The number of university employees, also employed in the Institute	7	3
The number of the Institute employees, also employed at universities	16	6

International Cooperation

Number of conferences with participating foreign scientists (Institute as organizer or co-organizer)	**3**
The number of business trips taken by the Institute researchers	**137**
– not as a part of bilateral agreements of AS CR	**123**
Number of scientists from the Institute that actively participated at international conferences	**103**
– of witch were invited lecturers	**27**
Number of posters	**72**
Number of Institute researchers as lecturers at foreign universities	**4**
Number of Institute researchers as members of the editorial boards of international journals	**25**
Number of Institute researchers with membership in international scientific governmental and non--governmental organizations (companies, committees)	**13**
The number of lectures of foreign researchers at the Institute	**14**
Number of grants and projects financed from abroad	**10**
– of which were EU programs	**9**

News in 2014

On April 1st 2014, the Deputy Prime Minister for Science, Research and Innovation, Pavel Bělobrádek, together with the President of the Academy of Sciences of the Czech Republic, Prof. Jiří Drahoš, visited the Complex of Biomedical Institutes at Krč, Prague. Accompanied by the IEM Director, Prof. Eva Syková, they also visited the clean rooms and laboratories at Innovation Biomedical Centre of the Institute.

Conferences in 2014

The Central and Eastern European Conference on Health and the Environment (CEECHE)

Organizer: Babes-Bolyai University, Romania National Institute of Environmental Health Sciences (NIEHS), USA
Contact: Eugen Gurzau, Radim Šrám, MD, DSc, Pavel Rössner, MD, PhD
Co-organizer: Institute of Experimental Medicine AS CR, v.v.i.
Date and Place of Event: Cluj, Romania, 25.–30. 5. 2014
A total of 300 participants, 250 from abroad

Quo Vadis, Scientia? Seminar on Sustainability research centres

Organizer: Committee on Education, Science, Culture, Human Rights and Petitions of the Senate PCR
Co-organizer: Institute of Experimental Medicine AS CR, v.v.i.
Contact: Prof. Eva Syková, MD, DSc, FCMA
Date and Place of Event: Prague, Senate PCR, 16. 4. 2014

SENÁT
PARLAMENTU ČESKÉ REPUBLIKY

Senator **Eva Syková**, who moderated the seminar, pointed to the fact, that European funds helped to establish nearly a dozen European Centers of Excellence and forty other regional R & D Centers. According to her, however, it is necessary to resolve the question of providing sufficient funds for the operation of these Centers responsibly, without further complicating the situation of existing institutions. Research infrastructures, built in non-Prague regions, undoubtedly serve to strengthen the competitiveness of the Czech Republic. Their establishment, however, brings additional claims on the state budget and increases the pressure on redirecting public funds outside of Prague.

Clinical studies in regenerative medicine

Organizer: Institute of Experimental Medicine AS CR, v.v.i.
Co-organizer: Society for Gene and Cell Therapy of the Czech Medical Society JEP
Contact: Prof. Eva Syková, MD, DSc, FCMA
Date and Place of Event: Prague 1, Academy of Science CR, 6. 6. 2014

Ultrafine particles pollution and health – results of the project UFIREG

Organizer: Institute of Experimental Medicine AS CR, v.v.i.
Co-organizer: Commission for Environmental AS CR
Contact: Pavel Dostál, MD, DSc; Anna Pastorková, MD, PhD
Date and Place of Event: Prague, Clarion Congress Hotel

UFIREG
Ultrafine particles – cooperation with environmental and health policy

CENTRAL EUROPE
COOPERATING FOR SUCCESS.

EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND

Cooperation between Academy of Science and Senate PCR

On the occasion of the third anniversary of the establishment of cooperation between the Senate and the Academy of Sciences of the Czech Republic initiated in 2011 by signing a joint Memorandum of permanent cooperation, representatives of both sides met in Villa Lanna in Prague during August 2014. The Assembly was opened by the President of the Academy of Science of the Czech Republic, Prof. Jiří Drahoš, and greetings were presented by the Chairman of the Senate, Milan Štěch.

From right: Vice-Presidents of the AS CR Vladimír Mareček and Pavel Baran, 1st Vice-President of the Senate and member of the Memorandum advisory group Alena Gajdůšková, President of the AS CR Jiří Drahoš, Chairman of the Senate Milan Štěch, Vice-President of the Senate Miluše Horská, Vice-President of the Committee for Education, Science, Culture, Human Rights and Petitions of the Senate Eva Syková, Vice-President of the AS CR Jan Šafanda, and member of the Memorandum advisory group Jaroslav Šebek.

International Projects and EU Framework Programs

LIFE/ENV/CZ/651 EU-IP

Innovative methods of monitoring of diesel engine exhaust toxicity in real urban traffic.

Acronym: MEDETOX
Coordinator: Institute of Experimental Medicine AS CR, v.v.i.
Principal Investigator: Jan Topinka, DSc, PhD
Duration: 2011–2016

3CE288P3 EU-OPNS

Ultrafine particles – an evidence based contribution to the development of regional and European environmental and health policy.

Acronym: UFIREG
Contractor: Technical University Dresden, Germany
Principal investigator: prof. M. Kirsch
Co-coordinator: Miroslav Dostál,MD, DSc, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2011–2014

FP7-ENV-2012-308524-2 EU-IP

Development of sensor-based Citizen´s Observatory Community for improvig quality of life in cities.

Acronym: CITI-SENSE
Financial resources: 7. EU Framework programme
Coordinator: NILU-Norway Institute for Air Research, Kjeller, Norway
Co-coordinator: Radim Šrám, MD, DSc, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2012–2016

BM1206 EU-COST

Cooperation studies on inherited susceptibility to colorectal cancer

Acronym: EUCOLONGENE
Type of cooperation: COST (Cooperation in Science and Technology)
Coordinator: Dr. Sergi Castellvi-Bel, University of Barcelona, Catalania/Spain
Co-coordinator: Pavel Vodička, MD, PhD, Institute of Experimental Medicine AS CR, v.v.i.
Participating countries: Spain, CR, Germany, UK, Sweden, Italy, Portugal, Holland, Austria, USA
Duration: 2013–2017

TD1204 EU-COST

Modelling Nanomaterial Toxicity

Acronym: MODENA
Type of cooperation: COST (Cooperation in Science and Technology)
Activity type: TD
Coordinator: Prof. Lang Tran, Institute of Occupational Medicine, Edinburgh, U.K.
Co-coordinator: Jan Topinka, DSc, PhD, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2014–2016

INFRA - 2010-1.1.31-262163 EU-IP

Quality-nano – research infrastructure

Acronym: QNANO
Financial resources: 7. EU Framework programme
Coordinator: University College Dublin, Ireland
Project manager: Jan Topinka, DSc, PhD, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2013–2015

612261 EU-CP

Targeting challenges of active ageing: innovative integrated strategies for the healing of age-related hearing loss

Acronym: TARGEAR
Financial resources: 7. EU Framework programme
Coordinator: CSIC, Spain
Co-coordinator: Prof. Josef Syka, MD, DSc, FCMA, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2014–2017

310584 EU-IP

A Common European Approach to the Regulatory Testing og Nanomaterials

Acronym: NANOREG
Financial resources: 7. EU Framework programme
Coordinator: Ministerie van Infrasructuur en Milieu, The Netherlands
Co-coordinator: Jan Topinka, DSc, PhD, Institute of Experimental Medicine AS CR, v.v.i.
Duration: 2014–2016

Brain Extracellular Matrix in Health and Disease

Acronym: Action ECMNET
Type of cooperation: COST (Cooperation in Science and Technology)
Activity type: Preparing young scientific experts in the field of neural extracellular matrix and the dissemination and popularization of knowledge concerning the extracellular matrix in the CNS on the scientific, public and political levels.
Coordinator: DZNE, Univirsity of Magdeburg, Germany; Alexandr Dityatev (Germany),
Co-coordinator: Prof. Syková, MD, DSc; L. Vargová, PhD, Institute of Experimental Medicine AS CR, v.v.i.
Participating countries: Italy, CR, Belgium, Croatia, Cyprus, Denmark, Finland, France, Germany, Greece, Italy, Netherlands, Poland, Russia, Serbia, Spain, Switzerland, Turkey,

Better Understanding the Heterogeneity of Tinnitus to Improve and Develop New Treatments

Type of cooperation: COST (Cooperation in Science and Technology)
Coordinator: University of Regensburg, Germany
Co-coordinator: Prof. Josef Syka, MD, DSc, FCMA, Institute of Experimental Medicine AS CR, v.v.i.

Foreign Scientists visited the Institute

Victoria Moreno-Manzano 5. Centro de Investigación Príncipe Felipe, Valencia	Spain	Stem Cells and Regenerative Medicine, senior scientist
Prof. Srečko Gajovič Croatian Institute for Brain Research University of Zagreb School of Medicine	Croatia	Neuroscience
Prof. Hyunok Choi Departments of Environmental Health Sciences, Epidemiology, and Biostatistics, SUNY Albany, School of Public Health, Rensselaer, NY	USA	Epidemiology
Dr. Danai Feida Department of Social Medicine, Faculty of Medicine,University of Crete	Greece	Cytogenetics
Oliver Douglas University of Connecticut Health centre, Farmington, CT	USA	Neuroanatomy
Donald Robertson University of Western Australia, Perth	Australia	Neurophysiology
David W. Smith University of Florida, Gainsville	USA	Neurophysiology of the senses
Paul P.W.W. Poon National Cheng-Kung University, Tainan	Taiwan	Neurophysiology
Miguel Diáz Gómez Medel Spain, Madrid	Spain	Audiology
Dr. Steffen Wolff Friedrich Miescher Institute for Biomedical Research, Basilej	Switzerland	Neurophysiology
Prof. Hemminki Kari DKFZ Heidelberg	Germany	Molecular Epidemiology
Prof. Izumi Shibuya Dept of Physiology, Tottori University	Japan	Calcium signaling
Prof. Carmel Caruana University of La Valetta	Malta	Radiology
Prof. Hubert Bost The Ecole Pratique des Hautes Etudes-Sorbonne, 4–14, rue Ferrus, F-75014 Paris	France	Using animal models (primates, lemurs) for the study and treatment of neurodegenerative diseases
Prof. Franco Rustichelli University of Ancona	Italy	Materials Engineering
Dr. Naccarati Alessio HUGE Turin	Italy	Genetics
Suresh Jhanwar Memorial Sloan Kettering Cancer Centre	USA	Tumor biology, senior scientist
Meena Jhanwar-Uniyal New York Medical College	USA	Molecular Biology, senior scientist
Prof. Knassmueller Siegfried University of Vienna	Austria	Genetic Toxicology
Prof. Izumi Shibuya Dept of Physiology, Tottori University	Japan	Calcium signaling and homeostasis in neurons and magnocellular terminals
Prof. Yoich Ueta Dept of Physiology, UOEH, School of Medicine, Kitakyush	Japan	Transgenic rat models for visualization of vasopressin and oxytocin in the dorsal root ganglia and glial cells
Prof. Dr. Jean- Michel Verdier INSERM 710, F-34095 Montpellier	France	Physiology and plasticity of Ca2+ signaling pathways in stem cells

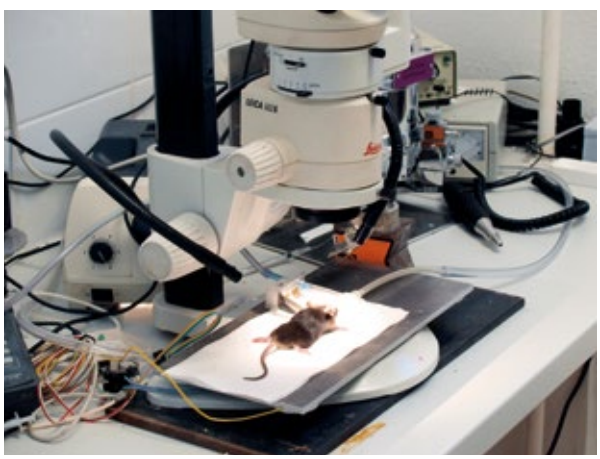
Practical Courses

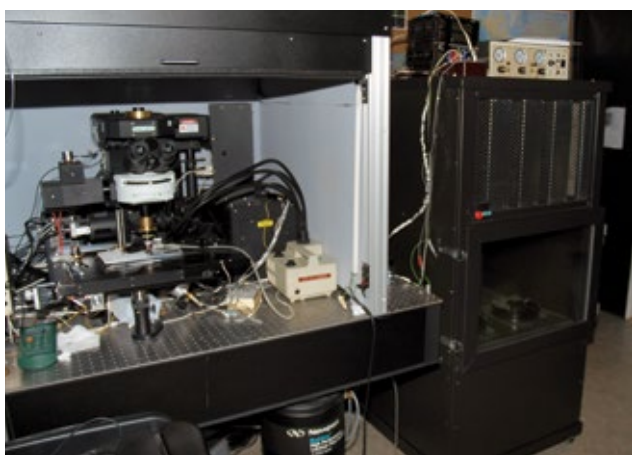
Tissue Engineering and Bionanotechnology in Regenerative Medicine

Organizer: Institute of Experimental Medicine AS CR, v.v.i.
Contact: Prof. Eva Syková MD, DSc, FCMA
Date and Place of Event: continously, Charles University in Prague, 2nd Faculty of Medicine
A total of 12 participants, 3 foreign, number of teachers: 2
Introducing bionanotechnology in regenerative medicine to medical students and participants on postgraduate programs.

Neuroscience Methods

Organizer: Institute of Experimental Medicine AS CR, v.v.i.
Date and Place of Event: in the Institute, 4.–8. 6. 2014
A total of 50 participants, 50 foreign, number of teachers: 10
Lectures and practical exercises in laboratories to demonstrate the methods used in auditory neuroscience research. Courses organized for students of University of Connecticut, USA.





New Trends in CNS Regeneration and Treatment

Organizer: Institute of Experimental Medicine AS CR, v.v.i.
Co-organizer: International Brain Research Organisation (IBRO)
Contact: Prof. Eva Syková MD, DSc, FCMA, Assoc. Prof. Pavla Jendelova, PhD
Date and Place of Event: Prague, 15.–17. 9. 2014
A total of 30 participants, 14 foreign, number of teachers: 5
Summer school for the project: OPVK Human Resources for neuroscience research in Hradec Králové and Ústí Region.




Professional collaboration with postdoctoral Master's students in the preparation of project research teams Institute of Experimental Medicine AS CR, v.v.i.

Date and Place of Event: Ongoing – Laboratory Institute in Prague 4, Kladno FBME CTU, Faculty of Medicine, Charles University in Hradec Králové.
A total of 12 participants, 4 foreign, number of teachers: 3
Three postgraduate researchers working at the IEM AS CR, professional work in the form of seminars and consultations with students on topics from the field of regenerative medicine, stem cells, biomaterials and auditory neuroscience in order to prepare the foundations for new research groups for the project BIOCEV.

Popularization Lectures

Event, date	Organizer	Description
University of the Third Age	2nd Faculty of Medicine, Charles University	Lecture by Prof. Evžen Amler, PhD
Seminar Toxicity of nanoparticles and nanotechnology safety February 20, 2014	Institute of Experimental Medicine AS CR, v.v.i., Environment Commission AS CR	Lecture by Jan Topinka, PhD, DSc Research on the toxicity of nanomaterials within the EU and the possibility of involvement of the Czech Republic
Business Club, Prague 6, February 27, 2014	Business Club	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Stem cells and regenerative medicine
Brain Awareness Week, March 10 to 14, 2014	Institute of Experimental Medicine AS CR, v.v.i., Society for Neuroscience, Academy of Sciences of the Czech Republic	15 lectures attended by 1831 people
Brain Awareness Week, March 10, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Lecture by Assoc. Prof. Alexandr Chvátal, MD, DSc: Gial cells and their role
Senate PCR, March 10, 2014	Senate PCR	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Sustainable Development in the Czech Republic – Roundtable
Brain Awareness Week, March 12, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Lecture by Prof. Josef Syka, MD, DSc, FCMA: What we now know about brain activity during perception and speech generation, reading and writing
Brain Awareness Week, March 12, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Lecture by Tomáš Hromádka, MD, PhD: Optogenetics helps uncover the secrets of activity of nerve cells
Senate PCR, March 28, 2014	Senate PCR	Prof. Eva Syková, MD, DSc, FCMA: Praha in the context of science policy – lecture, discussion and roundtable
Senate PCR, April 15, 2014	Senate PCR	Prof. Eva Syková, MD, DSc, FCMA: Sustainability of Research Centres in the Czech Republic – seminar

Senator Eva Syková at a press conference of the 15th Senate public hearing on the topic Science Centres and their importance for the development of the country.

Event, date	Organizer	Description
Learned Society Forum, April 17, 2014	Learned Society	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Where is heading our science?
Use of stem cells in the treatment of orthopedic diseases in veterinary medicine May 21, 2014	EponaCell, Ltd.	Lecture by Šárka Kubinová, PharmD, PhD
Senate PCR, May 21, 2014	Senate PCR	Prof. Eva Syková, MD, DSc, FCMA: Public-private partnerships in research, development and innovation – roundtable
Senate PCR, May 21, 2014	Senate PCR	Prof. Eva Syková, MD, DSc, FCMA: Science and business as an engine for innovation – discussion Forum
Air pollution and related impacts civilization – seminar May 22, 2014	Institute of Experimental Medicine AS CR, v.v.i., The Chamber of Deputies of the CR and AS CR	Lecture by Radim J. Šrám, MD, DSc impact of air pollution on public health Lecture by Miroslav Dostál, MD, DSc about the impact of air pollution on the incidence of the disease in children Lecture by Pavel Rössner Jr., PhD on the possible adaptation of the human organism to the adverse effects of air pollution
Kooperativa, June 24, 2014	Kooperativa	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Regenerative medicine and tissue engineering
Veterinary Medicine Practice Brno, October 3, 2014	Institute of Experimental Medicine AS CR, v.v.i., V.M.EST, a.s.	Lecture by Šárka Kubinová, PharmD, PhD
Prague Security Company, November 7, 2014	Prague Security Company	Prof. Eva Syková, MD, DSc, FCMA: What will society and human life be in the next 25 years – conference
Science and Technology Week, November 10, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Lecture by Prof. Josef Syka,MD, DSc, FCMA: What happens in the brain when we talk, write or read?
Science and Technology Week, November 12, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Lecture by Radim Šrám, MD, DSc: Effects of air pollution on public health
Open Day November 14, 2014	Institute of Experimental Medicine AS CR, v.v.i.	Educational events for the public and students, nearly 300 people visited the laboratory
Air pollution and its impact on population health – seminar November 19, 2014	Commission for Environment AS CR	Lectures Radim J. Šrám, MD, DSc: Effects of air pollution on public health Lecture by Pavel Rössner Jr., PhD: PAH exposure and pregnancy outcomes Lecture by Miroslav Dostál, MD, DSc: Ultrafine particles and Health – Project UFIREG Lecture by Vlasta Švecová, MSc, PhD: EU project CITY-SENSE: air quality monitoring with sensor technology
VII. Congress CMA, Mariánské Lázně, November 27, 2014	Czech Medical Academy	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Regenerative medicine and tissue engineering
Czech Medicine Academy, December 4, 2014	Czech Medical Academy	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Stem cells in regenerative medicine
IX. Jánskolázeňské symposium	Jánské lázně	Lecture by Prof. Eva Syková, MD, DSc, FCMA: Cell therapy – latest trends

The 16th Edition of Brain Awareness Week 2014

The brain is the most complex organ of the human body and consequently it is the subject of a vast number of studies being conducted by numerous research teams around the world. Every March, in an effort to inform the general public, Brain Awareness Week is celebrated across the USA and Europe providing a platform for scientists to communicate new findings concerning not only brain function, but also damage, disease and treatment options.

This year's Brain Awareness Week consisted of a series of public lectures presenting the latest findings in the pursuit of understanding the mysteries of the brain. As well as this the participating students and general public had the chance to learn about how best to exercise and protect their brains.

The 16th edition of this event to be held in the Czech Republic, took place from the 10th–14th March 2014, at the main building of the Academy of Sciences of the Czech Republic in Prague. Every year this event is organized by the Institute of Experimental Medicine AS CR in cooperation with the Czech Society for Neuroscience and the Centre of Administration and Operations AS CR, vvi.

The activities of Brain Awareness Week were kicked-off on Monday, March 10th with a press conference, chaired by Prof. Eva Syková, MD, DSc, FCMA, Director of the Institute of Experimental Medicine AS CR, Prof. Josef Syka, MD, DSc, FCMA, Head of the Department of Auditory Neuroscience IEM AS CR, Prof. Karel Šonka, MD, Head of the Centre for Sleep Disorders, Neurological Clinic of the 1st Medical Faculty of Charles University in Prague and General University Hospital in Prague.

Across the five-day-event, a total of 15 lectures were available to the public, attracting a total 1,831 people. The majority of the participants were made up of high-school students from across 26 schools, whilst many university students and individual members of the general public also took part.

Some of the lectures were audio/video recorded and are available online at **www.tydenmozku.cz**.

Selected Photographs

Monday, March 10
11:00 **Press Conference Brain Awareness Week**

Left to right: Karel Šonka, Eva Syková, and Josef Syka

Lectures:

Monday, March 10
09:00 **The Brain and Regenerative Medicine**, Prof. Eva Syková, MD, DSc, FCMA, Institute of Experimental Medicine AS CR, v.v.i.

11:00 **Glial cells and Their Role**, Assoc. Prof. Alexandr Chvátal, DSc, MBA, Institute of Experimental Medicine AS CR, v.v.i.

14:00 **Sleep and Dreams in Diseases of the Brain**, Prof. Karel Šonka, MD DSc, Department of Neurology, 1st Medical Faculty of Charles University and General University Hospital in Prague

Tuesday, March 11
09:00 **Time Systems and Neuropsychiatric Disorders**, Spol. Alena Sumová, MD. Institute of Physiology AS CR, v. v. i.

11:00 **Advances in the Treatment of Chronic Pain – Methods and Drugs**, Prof. Richard Rokyta MD, DSc, Department of Normal, Pathological and Clinical Physiology, 3rd Medical Faculty, Charles University, Prague

14:00 **Finding the Causes of Inherited Nerve Diseases**, Prof. Pavel Seeman, MD PhD, Department of Pediatric Neurology, 2nd Medical Faculty, Charles University and University Hospital Motol, Prague

Wednesday, March 12
09:00 **Optogenetics Helps to Uncover the Secrets of Nerve Cell Activity**, Tomáš Hromádka, MD, PhD, Institute of Experimental Medicine AS CR, v.v.i.

11:00 **What We Know Today About Brain Activity During Perception and the Generation of Speech, Reading and Writing**, Prof. Josef Syka, MD, DSc, Institute of Experimental Medicine AS CR, v.v.i.

14:00 **Neuromodulation Treatment for Movement Disorders: Control Wires to the Brain**, Assoc. Prof. Robert Jech, MD, PhD, Department of Neurology, 1st Medical Faculty of Charles University and General University Hospital, Prague

Thursday, March 13
09:00 **How Brain Networks Develops and Disappears**, Prof. Vladimír Komárek, MD, PhD, Department of Pediatric Neurology, 2nd Medical Faculty of Charles University and University Hospital Motol, Prague

11:00 **Art and Neuroscience**, Prof. Cyril Höschl MD, DSc, FRCPsych, Prague Psychiatric Centre

14:00 **Mental Disorders and Society**, Prof. Jiří Raboch, MD, DSc, Psychiatric Clinic, 1st Medical Faculty of Charles University and General University Hospital, Prague

Friday, March 14
09:00 **Memory and its Disorders**, Robert Rusina, MD, PhD, Department of Neurology, 1st Medical Faculty of Charles University and General University Hospital, Prague

11:00 **Epilepsy in the Immature Brain – Another Disease?** Assoc. Prof. PharmDr. Hana Kubová, DSc, Institute of Physiology AS CR

14:00 **Brain, Hunger and Food?** Prof. Hana Papežová, MD, PhD, Psychiatric Clinic, 1st Medical Faculty of Charles University and General University Hospital, Prague

Notes:

Tiráž
Výroční zprávu za rok 2014 vydal Ústav experimentální medicíny, v.v.i. v květnu 2015

Podklady a zpracování dat:
doc. RNDr. Alexandr Chvátal, DrSc.
a Mgr. Jana Voláková Křížová

Tisk, zlom a grafická úprava Abalon, s. r. o.
Fotografie použity s laskavým svolením Akademického bulletinu a autorky Mgr. Stanislavy Kyselové a z archívu ÚEM AV ČR.

Ústav experimentální medicíny AV ČR, v.v.i.
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