Institute
of Experimental
Medicine of the CAS

EU Centre of Excellence

2015 Annual Report

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of Experimental
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Annual Report 2015

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Content

Introduction

In the Czech Republic, the Institute of Experimental Medicine of the CAS is one of the leading biomedical research institutes and has contributed a significant amount of research to the field of biomedicine.

In the forthcoming years, we expect medical research to progress at a faster and greater rate than ever before. 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 2015, the Institute of Experimental Medicine produced a number of significant results. Its scientists continue 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 the 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 Technology Agency of the Czech Republic (TAČR) and in the Centre for the Development of Original Drugs.

The Research Centre for Cell Therapy and Tissue Repair received support from the National Program 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.

We have continued to meet the project objectives defined by the European Structural Funds. As an example, we can mention the projects of the 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 "Establishment of Research teams of IEM AS CR for BIOCEV (Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University)". Both these projects were successfully completed in 2015. One of our major current projects, GAMA, which focuses on applied research, experimental development and innovation (from 2014 to 2019), allowed for the support of the Technology Agency of the Czech Republic (TAČR) to be distributed for the commercialization of R&D outputs within the Institute's Departments. The project is

generally focused on bridging the critical phases of the innovation cycle – supporting applied research and the experimental development of products. In 2015, overall 8 partial proof of concept projects were supported from this large project.

In collaboration with the University of Trondheim in Norway, we continued to participate in the Czech-Norwegian research program CZ09 on the joint project "Biomaterials and Stem Cells in the Treatment of Stroke and Spinal Cord Injuries", which is coordinated by Pavla Jendelová.

The Institute is developing its own business facility, the Innovation Biomedical Centre, while supporting other start-up projects in its business incubator. In 2015, the company Bioinova, 42,71% of which is owned by the Institute, continued to produce stem cells for clinical trials with the approval 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 continued for the treatment of amyotrophic lateral sclerosis, tendons, cartilage, bone, and wound healing in diabetic patients with critical limb ischaemia.

It is also our aim to emphasize our contribution to education in society. In accordance with this, in 2015 the Institute organized several successful conferences, public events and international schools. Furthermore, a number of members of our research teams have participated in undergraduate teaching at associated universities and in postgraduate training.

2015 has been a e. g. substantial for our Institute. In addition to the previously mentioned highlights, our researchers have published a total of 80 research articles in impacted journals with an average IF of 3.787 and with a total IF of 302.951.

And finally, in November 2015, our Institute celebrated its 40th anniversary in the ancient Carolinum. During the gala evening, which was attended by distinguished scientific and university officials, we commemorated the Institute's history, some of the Institute's distinguished scientists and former directors. On this occasion, seven employees of the Institute were honoured with Commemorative Medals.

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 efforts 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 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 of the 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), while 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 Prof. Burian, Kurz, Přecechtěl and Wolf, the laboratories established themselves in the world of medicine, contributing significantly to the 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 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. Improvements 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, 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 the CAS and is the only institute in the Czech Republic engaged in a comprehensive medical research program encompassing a number of diverse fields.

In November 2015, the Institute celebrated its 40th anniversary in the ancient Carolinum. A gala evening was attended by distinguished scientific and university officials. Greetings from the President of the Czech Academy of Sciences, Prof. Jiří Drahoš, was presented by Prof. Eva Zažímalová, member of the Academic Board. On the occasion of the anniversary, the director of the Institute, Prof. Eva Syková, honored seven employees of the Institute with a Commemorative Medal and mentioned in her speech the importance of science as one of the main pillars of advanced societies. „Those who devote money to research, devote it to the future," emphasized Prof. Syková.

Management

Director:
Prof.
Eva Syková
MD, PhD, DSc, FCMA

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

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

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

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Institute Profile

Board of the Institute

The Board is the main governing body of the Institute, sharing responsibility for the operation of the Institute with the Director. The Act on Public Research Institutions establishes the legal obligation of the Board, which includes respect for the fundamental objectives of the Institute, adjusting the basic scientific orientation of research at the Institute, its development strategy, approving the budget as well as its annual report. The Board consists of both internal and external members.

In 2015 the Board met eight times. The Board in 2015 agreed to address a total of 22 research projects to programs of the Czech Grant Agency and the Agency for Healthcare Research, together with one research project with foreign partners. The Board also approved the annual report for 2014 and the budget for the year 2015. The Board approved the defence of 5 dissertations before the selection committees.

Internal Members:

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

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

External Members:

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

Secretary: Petr Bažant, MSc, 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 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, which was the case in 2015. Some issues were also negotiated using the per rollam procedure.

The current Supervisory Board is composed of the following members:

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

Petr Bažant, MSc, 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 2015

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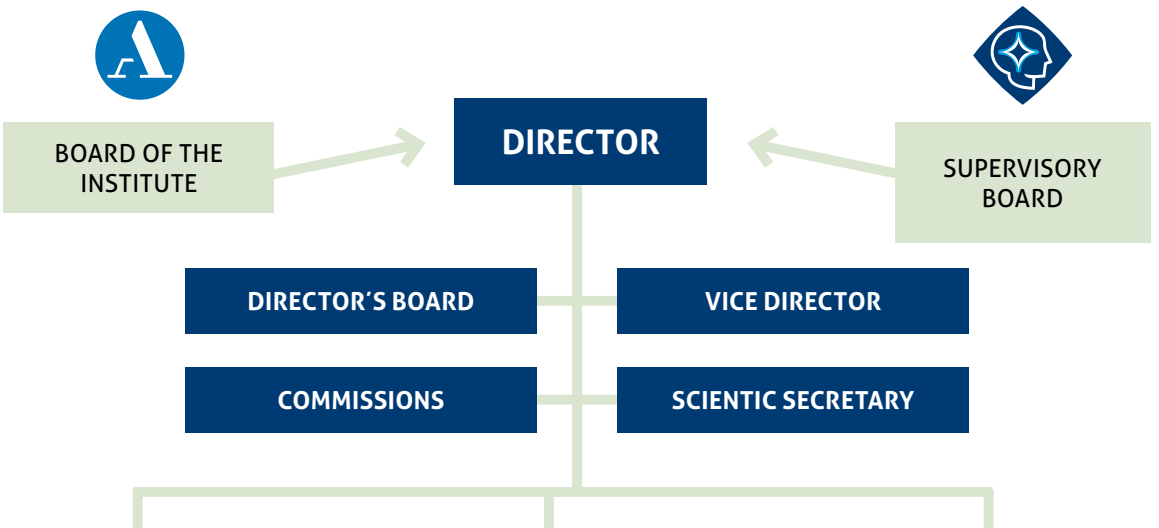


MANAGEMENT UNITS

- **Secretarial 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 CAS and Department of Neuroscience 2nd Medical Faculty, Charles University**
- **Centre for Regenerative Medicine IEM CAS, IKEM and Charles University**
- **Centre for Neuroregeneration and Biomedical Research IEM CAS 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 of the CAS
Principal investigator: Assoc. Prof. Ladislav Vyklický, MD, DSc, Jr.
Project participants: National Institute of Mental Health, **The Institute of Experimental Medicine of the CAS,** Charles University, 2nd Faculty of Medicine
Participant investigators: Daniela Řípová, PhD; **Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.**; **Miroslava Anděrová, MSc, PhD**

Neurodegenerative disorders are common not only in the aging population, but also in young adults, leading to increasingly serious socio-economic problems. 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, intercellular communication, extracellular 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 disease treatments, e.g. using neuroactive steroids, stem cells, etc. The project will also provide a unique basis for PhD training in neuroscience.

Results in 2015

Publication:
Profant O, Tintěra J, Balogová Z, Ibrahim I, Jilek M, Syka J. Functional changes in the human auditory cortex in ageing, 2015, PLoS One, 3;10(3):e0116692. IF 3.234

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
Principal investigator: Miroslav Machala, PhD
Project participants: Institute of Chemical Process Fundamentals of the CAS, Institute of Animal Physiology and Genetics of the CAS, Institute of Analytical Chemistry of the CAS, **The Institute of Experimental Medicine of the CAS**, Charles University, Faculty of Science
Participant investigators: Pavel Moravec, MSc, PhD; Assoc. Prof. Omar Šedý, PhD; Zbyněk Večeřa, MSc, PhD; **Jan Topinka, MsC, PhD, 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 2015

Publications:

1. Topinka, J., Rosssner Jr., P., Milcová, A., Schmuczerová, J., Pěnčíková, K., Rossnerová, A., Ambrož, A., Štolcpartová, J., Bendl, J., Hovorka, J., Machala, M.: Day-to-day variability of toxic events induced 1 by organic compounds bound to size segregated atmospheric aerosol, Environmental Pollution, 202 (2015) 135-145, IF 3.902

2. Pálková, L., Vondráček, L., Trilecová, L., Ciganek, M., Pěnčíková, K., Neča, J. Milcová, A., Topinka, J., Machala, M.: The aryl hydrocarbon receptor-mediated and genotoxic effects of fractionated extract of standard reference diesel exhaust particle material in pulmonary, liver and prostate cells, Toxicology *in Vitro* 29 (2015) 438–448., IF 2.903

3. Štolcpartová, J., Pechout, M., Dittrich, L., Mazač, M., Fenkl, M., Vrbová, K., Ondráček, J., Vojtíšek-Lom, M.: Internal Combustion Engines as the Main Source of Ultrafine Particles in Residential Neighborhoods: Field Measurements in the Czech Republic, Atmosphere 2015, 6, 1714-1735, IF 1.132

3. Centre for Development of Original Drugs, TA CR

Programme: Cempetence Centres (2012–2019)
Contractors: Institute of Organic Chemistry and Biochemistry of the CAS, **The Institute of Experimental Medicine of the CAS**, Institut of Physiology of the CAS, Palacky University in Olomouc, University of Chemical Technology in Prague, Apigenex, Ltd., IOCB TTO, Ltd., MediTox, Ltd.
Principal investigator: Zdeněk Havlas, PhD, DSc
Participant investigators: Zdeněk Zídek, MSc, PhD, DSc; 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 the 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 that will be able to develop 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 the field of local research and industry. The major aim of the project is to evaluate 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 the competitive ability of the Czech pharmaceutical industry, depending on traditional successful and recognized fields of Czech science.

Result in 2015

Patent Number: 305457
Jansa, P., Holý, A., Zídek, Z., Kmoníčková, E., Zlatko, J.: Pyrimidine compounds inhibiting biosynthesis of nitric oxide and prostaglandin E2, means of synthesis and usage
Responsible person: Zdeněk Zídek, MSc, PhD, DSc
Awarded: 19.8. 2015 (awarded by the Industrial Property Office of the Czech Republic). Bulletin no. 39/2015.
Usage: Treatment of diseases with overproduction of inflammatory mediators

4. Centre of Orofacial Development and Regeneration, GA CR

Programme: GB – Projects for promotion of excellence in basic research (2014–2018)
Contractor: The Institute of Experimental Medicine of the CAS
Principal investigator: Renata Peterková, MD, PhD
Project participants: Institute of Animal Physiology and Genetics of the CAS, Brno, Charles University in Prague, 1st Faculty of Medicine, Department of Stomatology, Faculty of Medicine, Masaryk University, Brno

Participant investigators: Prof. Eva Matalová, PhD; Prof. Zdeněk Broukal MD, PhD;
Prof. Lydie Izakovičová Hollá, MD, PhD.

The integration of four groups allows for complex basic research of the development and regeneration of orofacial structures, mainly teeth and anchoring apparatus, from embryo to adults. The project will contribute to the elaboration of regenerative medicine methods focused on the development of biological replacements of teeth.

Development and regeneration both create tissues controlled by similar genes and their products. The project's results will be used in the rapidly developing area of regenerative dentistry. The results on early tooth development in animal models will help in understanding the general mechanisms of the determination of tooth type and shape, knowledge important for engineering tooth crowns. Odontogenic cells potential 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 for its regeneration will also be studied in humans, since the quality of periodontal tissues ensuring tooth fixation is a prerequisite for the successful outcome of the biological (engineered) tooth implant technologies.

Results in 2015

1. Development of tooth anomalies in Spry mutant mice is accompanied by changes in the Shh expression and segmentation of dental epithelium

In Spry mutant mice, the prolongation of Shh expression in the signalling centres of premolar rudimentary tooth buds (MS and/or R2) in the mandible reflected their revival (regeneration). The prolongation of Shh expression in the signalling domain of the R2 bud – located more anteriorly in the mandible, implied the delayed start of the subsequent expression domain in the first molar (M1) and a delay in its formation in a more posterior part of the lower jaw. The manifestation of these phenomena strengthened with decreasing Spry2 gene dosage.

The whole study and the publication were realised by the Department of Teratology IEM of the CAS.

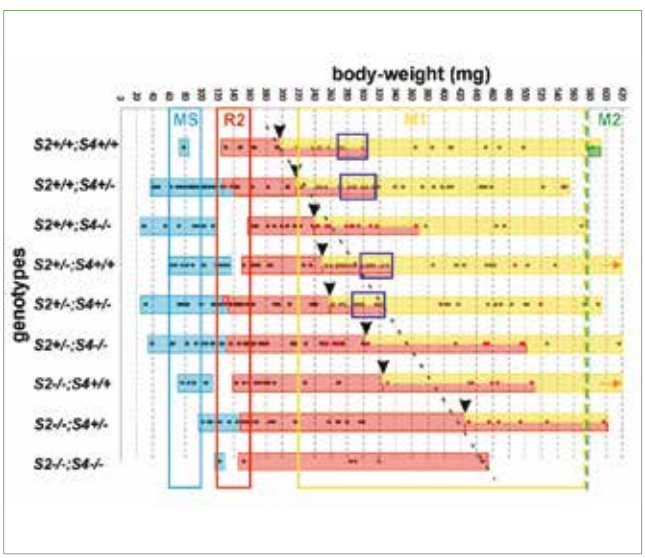


Fig. 1. Shh expression in a series of three distinct signalling domains in the cheek region of the mandible in Spry mutant mice. Shh expression sequentially appeared in a premolar rudimentary bud MS (blue bar), premolar rudimentary bud R2 (red bar) and the first molar – M1 (yellow bar) in nine various Spry2;Spry4 mouse genotypes according to embryonic body weights. Black arrowheads show the situation when the early M1 Shh signalling domain appeared and it co-existed transiently with the persisting Shh expression in R2. The oblique dashed black line suggests the trend of prolongation of Shh expression in R2 rudiment according to decreasing Spry2 gene dosage. The coloured frames (blue, red and yellow) represent referential presence of signalling domains of MS (blue), R2 (red) and M1 (yellow) observed in WT mice (according to Prochazka et al., 2010). The green dashed line is a reference line indicating the appearance of the M2 (second molar) signalling centre in the control genotype (Spry2+/+;Spry4+/+). The density of harvested embryos is shown by dots in bars.

Publication:

Lochovska, K., Peterkova, R., Pavlikova, Z., Hovorakova, M.: Sprouty gene dosage influences temporal-spatial dynamics of primary enamel knot formation. BMC Dev Biol. 2015 Apr 22;15:21. doi: 10.1186/s12861-015-0070-0. PubMed PMID: 25897685; PubMed Central PMCID: PMC4425875, IF 2.667

2. Characterisation of a new model for studies of permanently renewing dentition in reptiles

With the aim to characterise a new model for studies of permanently renewing dentition in reptiles, ten stages of embryonic development were determined in a snake (*Psammophis sibilans*) on the basis of external morphological criteria. The developmental stages were then compared with several other reptilian models. The timing and morpho-differentiation of embryonic structures such as the pharyngeal processes, eyes and scales appeared to be interspecifically conservative, while those of body pigmentation, colour and its pattern were interspecifically plastic.

The Department of Teratology IEM of the CAS was involved in designing the study, collection and documentation of data, analysis and interpretation of results, and writing the paper.

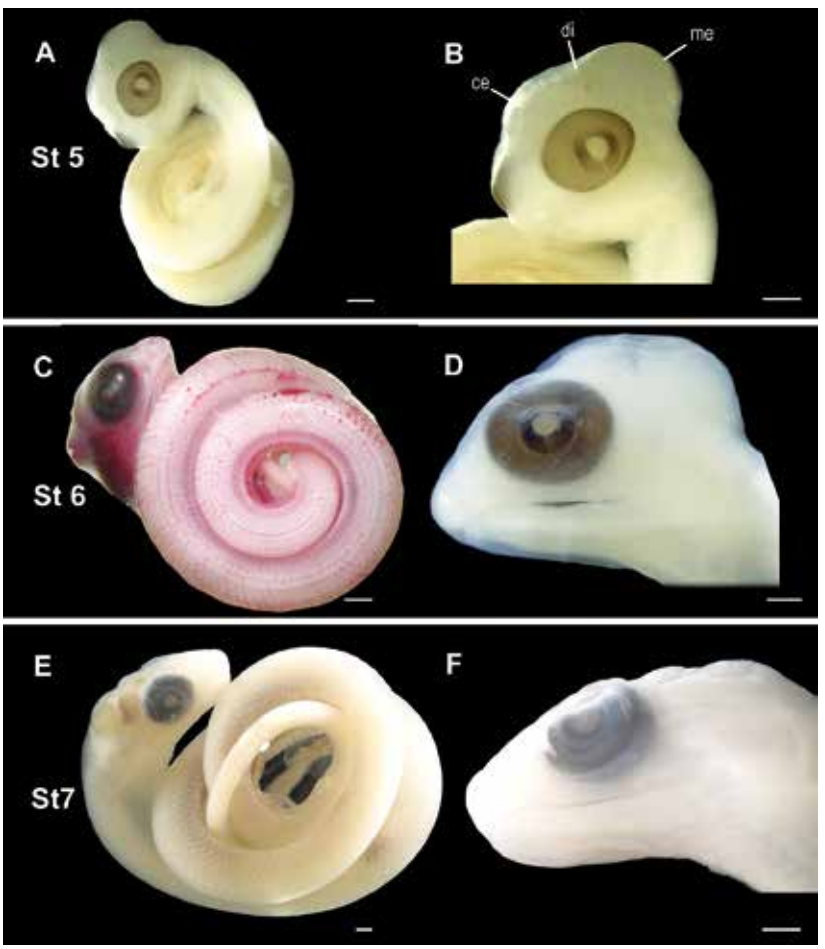


Fig. 2: Embryonic development of a snake *Psammophis sibilans* showing stages 5 – 7. (A, B) Stage 5 is characterised by increasing size of the cerebral hemispheres and by the progress in eye pigmentation. **(C, D)** Stage 6 – body scales become apparent and the brain protrudes as one broad bulge on the head. **(E, F)** Stage 7 – well developed body scales and the appearance of the first head scales. Abbreviations: ce, cerebrum; di, diencephalon; me, mesencephalon.

Publication:

Zahradnicek, O., Khannoon, E.R.: Postovipositional development of the sand snake Psammophis sibilans (Serpentes:Lamprophiidae) in comparison with other snake species. Acta Zoologica (Stockholm) *In press* (January 2016).

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

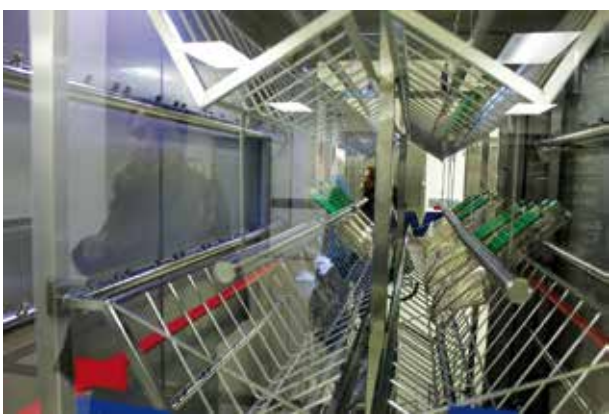
Programme: ED – Operational Programme Research and Development for Innovation (2008–2015)
Director: Prof. Pavel Martásek, MD, DSc
Project participants: Charles University, Faculty of Science and 1st Medical Faculty, Institute of Molecular Genetics of the CAS, Institute of Microbiology of the CAS, Institute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

Result in 2015:

The Construction phase of the BIOCEV Project has been completed – the BIOCEV Center is opening

Vestec, 18 December 2015 – In the presence of Deputy Minister of Education, Youth and Sports, Stanislav Štech, Rector of Charles University Tomáš Zima, Vice-President of the Czech Academy of Sciences, Vladimír Mareček, and other important guests, the implementation phase of the BIOCEV project – the Biotechnology and Biomedicine Center of the Czech Academy of Sciences and Charles University in Vestec ended today. Full operation is planned beginning January 2016. BIOCEV is currently made up of the implementation of five research programmes and the operation of six sets of research infrastructure and service laboratories. By 2020, as many as 450 researchers, including 200 post-graduate students, are supposed to work at the BIOCEV Center. The Center's objective is to learn details about organisms at the molecular level that will be used in applied research and in the development of new therapeutic procedures.

"*Cancer, cardiovascular diseases, viral and infectious diseases – all of these are among current problems of today's population. In the past, we were only able to describe these problems without being able to find their cause. Today, we can understand the cause of a disease, right down to the molecular level. Thanks to that, we are able to design a solution which, in the final phase, may lead to the development of effective medication or the discovery of a new therapeutic method, thereby saving many lives*," explained Director Pavel Martásek about the mission of the BIOCEV Center.



Prof. Josef Syka with Prof. Václav Pačes

Prof. Tomáš Zima, the Rector of Charles University

Department of Neuroscience

Head: Prof. Eva Syková, MD, PhD, DSc, FCMA

E-mail: sykova@biomed.cas.cz | Phone: +420 241 062 230

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's 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, MSc, PhD

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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, such as Alzheimer's Disease and Amytrophic lateral sclerosis (ALS). Various types of cells (mesenchymal stem cells from bone marrow, adipose tissue and Wharton jelly, neural precursor cell lines derived from fetal spinal cord, or from induced pluripotent stem 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* implants 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. Perineuronal nets are studied as markers of ALS disease progression. Balloon-induced compression lesion, spinal cord hemisection and transection are used as models of spinal cord injury, while for studies of stroke middle cerebral artery occlusion and photochemical lesion are used. The studies provide the background leading to preclinical and clinical studies. To facilitate translation of cell therapy into the clinic, magnetic nanoparticles for non-invasive *in vivo* imaging are developed and tested and their influence on cell viability, genotoxicity and differentiation potential is evaluated.

Research Scientists:
Prof. Eva Syková, MD, PhD, DSc, FCMA
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Important result in 2015

Mesenchymal stem cells reduce the working memory deficit in Alzheimer's disease model

Stem cell transplantation may have a positive influence and slow the progression of some neurodegenerative diseases. In our study, we transplanted human mesenchymal stem cells (MSCs) into the lateral ventricle of 8-month-old transgenic mice (AD-3xTg), which mimic the symptoms of Alzheimer's disease (AD). We studied the changes in the spatial reference and working memory, and the effect of transplanted MSCs on neurogenesis in the subventricular zone (SVZ). We also monitored the levels of harmful oligomer amyloid 56kDa (Ab*56), and the amount of the enzyme glutamine synthetase (GS), which is important for regulating the levels and metabolism of glutamate in the brain, in the entorhinal and prefrontal cortex and in the hippocampus, i.e. in the structures that are related with cognitive functions. In 14-month-old mice treated with MSC we observed preserved working memory, which may be a result of preserved levels of GS and significantly reduced levels of Ab*56 in the entorhinal cortex (Figure 1). These changes, observed six months after transplantation, were also accompanied by increased cell proliferation in the SVZ. Since the transplanted cells survive in the body of the recipient only for a limited period of time, it is likely that the observed effects could be even more pronounced in case of repeated administration of stem cells at regular intervals during the life spam of the 3xTg mice.

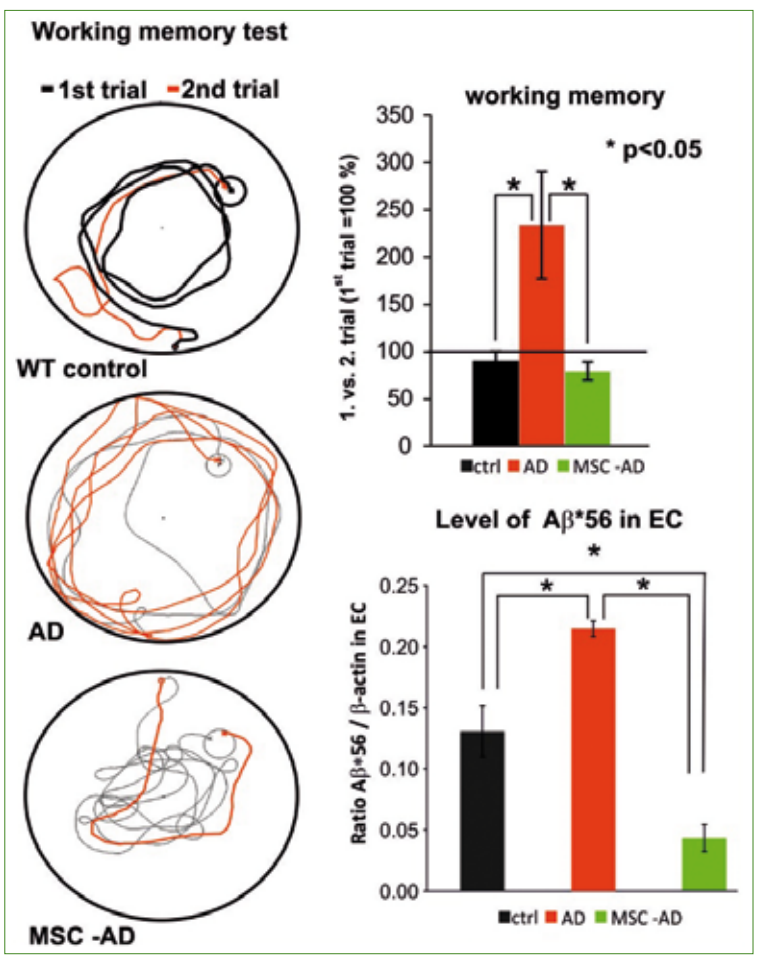

Fig: Working memory test in mice with AD. The red line represents the second trial to find the island in the water maze. The ability to remember the position of the islet is shown at the top left of the chart. AD mice had in the entorhinal cortex a reduced level of the harmful amyloid oligomer Aβ*56. The graph on the bottom right. AD – Alzheimer's disease, EC – entorhinal cortex, ctrl – control animals were age-matched.

Publication:

Ruzicka, J., Kulijewicz-Nawrot, M., Rodrigez-Arellano, J.J., Jendelova, P., Sykova, E.: Mesenchymal Stem Cells Preserve Working Memory in the 3xTg-AD Mouse Model of Alzheimer's Disease. Int J Mol Sci. 2016 Jan 25;17(2)., IF 2.863

Laboratory of Diffusion Studies and Imaging Methods

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The Laboratory of Diffusion Studies and Imaging Methods studies the changes in the extracellular space diffusion parameters and/or brain diffusivity that occur during physiological and pathological states and affect intracellular communication. Several animal models of pathological states and diseases attacking the CNS are used, e.g., models of brain ischemia and cell swelling, trauma, aging, tumors, epilepsy, Alzheimer's and Huntington's diseases, etc., with a focus on the role of glial cells and extracellular matrix. The research aims to improve therapy and diagnostic methods for CNS diseases and the prevention of CNS damage.

Research Scientists:
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Technician:
Lenka Josková

Important result in 2015

Changes in brain diffusivity in Huntington's disease patients and in the experimental R6/2 mouse model

Huntington's disease (HD) is an inherited neurodegenerative disorder with progressive impairment of motor, behavioural and cognitive functions. The clinical features of HD are closely related to the degeneration of the basal ganglia, predominantly the striatum. The main striatal output structure, the globus pallidus, strongly accumulates metalloprotein-bound iron, which was recently shown to influence the diffusion tensor scalar values. To test the hypothesis that this effect dominates in the iron-rich basal ganglia of HD patients, we examined the globus pallidus using DTI and T2 relaxometry sequences. Quantitative magnetic resonance (MR), clinical and genetic data (number of CAG repeats) were obtained from 14 HD patients. MR parameters such as the T2 relaxation rate (RR), fractional anisotropy (FA) and mean diffusivity (MD) were analysed. A positive correlation was found between RR and FA, between CAG and RR and between CAG and FA (R2=0.44). However, no correlation between MR and clinical parameters was found. Our results indicate that especially magnetic resonance FA measurements in the globus pallidus of HD patients may be strongly affected by metalloprotein-bound iron accumulation and contribute to inconsistent results of MR studies already conducted in HD. To clarify the nature of diffusivity changes in HD, we compared apparent diffusion coefficient of water (ADCW) acquired by MR with extracellular space volume fraction (α) and tortuosity (λ) measured by the iontophoretic method in the R6/2 mouse model of HD (HU) and in wild type controls (WT). In anisotropic globus pallidus, diffusion measurements were performed in the mediolateral (x), rostrocaudal (y) and ventrodorsal (z) axes. Despite structural changes in GP, diffusion anisotropy was unaffected in HU. Values of ADCW in all axes as well as values of α were significantly higher in HU than in WT, while no significant difference between WT and HU was found in the values of tortuosity. In HU globus pallidus, immunohistochemical examination showed a decreased number of NeuN positive neurons, reduction of extracellular matrix molecules and morphological changes in astrocytes (astrogliotis-like rebuilding and/or atrophy). In the somatosensory cortex, no significant differences in any of the parameters studied were found in HU. Changes in the diffusion parameters α, λ and ADCW due to structural remodelling of the HU tissue may affect synaptic as well as extrasynaptic intercellular communication and contribute to deterioration of brain functions in HD.

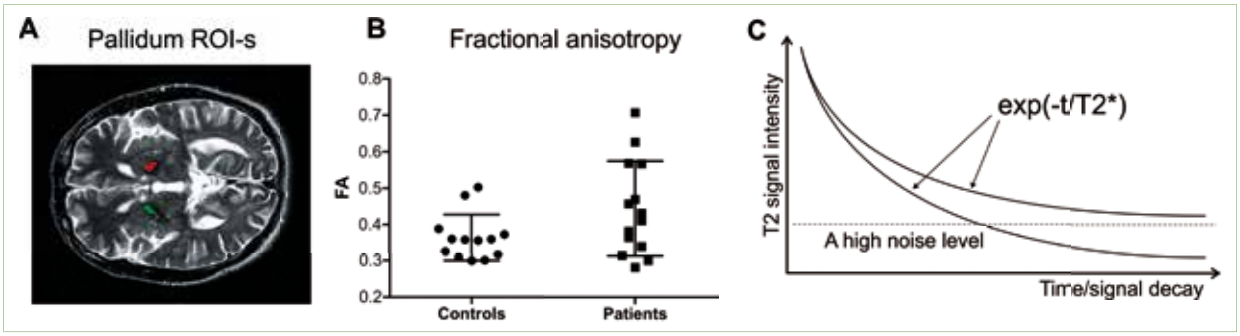

Fig. 1: A: T2-weighted image with colour-highlighted region of interest (ROI) in the globus pallidus, B: values of fractional anisotropy in healthy controls and Huntington's disease patients (HD) and C: Scheme explaining how the high level of noise affects MR measurements.
The presence of metalloprotein-bound iron induces local susceptibility differences that enhance spin dephasing, thus decreasing T2 relaxation time (1/T2 value). The regions with greater metalloprotein-bound iron content have a high level of noise, which distorts the measurements of MR parameters (C). As fractional anisotropy (FA) strongly depends on signal to noise ratio, the increased value of FA observed in the pallidum of HD subjects is likely due to error of the measurement (B).

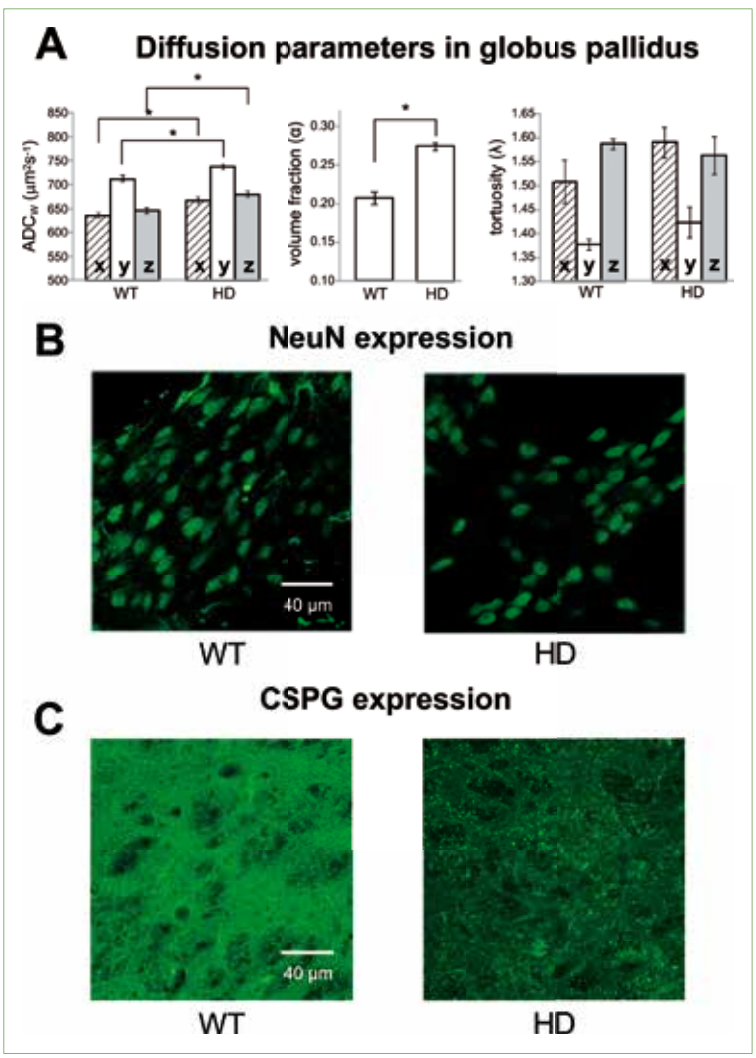

Fig. 2: Changes in brain diffusivity (A), number of neurons (B) and extracellular matrix expression (C) in globus pallidus of wild-type mice (WT) and mouse model of Huntington's disease (HD)
A: Both used diffusion methods detected anisotropic diffusion in globus pallidus of WT mice as well as in HD mice with preferential diffusion along the rostrocaudal axis. Note a significant increase in ADCW and α values in HU mice in comparison with WT ones. Data shown as means. Error bars represent the S.E.M. x – mediolateral, y – rostrocaudal and z – ventrodorsal axis. In HD mice, we found a decreased number of NeuN positive neurons (B) as well as reduction of chondroitinsulphate proteoglycan expression (C).

Publications:

Syka, M., Keller, J., Klempíř, J., Rulseh, A.M., Roth, J., Jech, R., Vorisek, I., Vymazal, J.: Correlation between relaxometry and diffusion tensor imaging in the globus pallidus of Huntington's disease patients. PLoS One. 2015 Mar 17;10(3):e0118907, IF 3.234

Vorisek, I., Syka, M., Vargova, L.: Brain diffusivity and structural changes in the R6/2 mouse model of Huntington's disease (submitted)

Laboratory of Biomaterials and Biophysical Methods

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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 of the CAS, complex research of low-temperature plasma effects on biological systems as well as the 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

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Pre-gradual student:
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Technicians:
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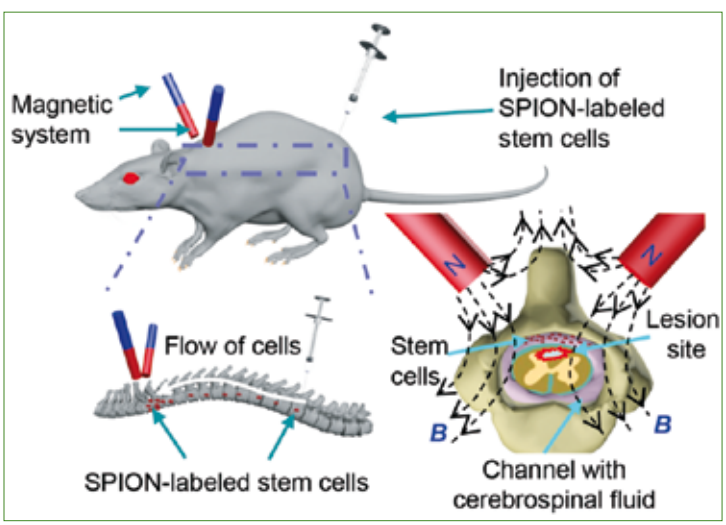
Lenka Uherková, MSc, PhD

Important result in 2015

An effective strategy of magnetic stem cell delivery for spinal cord injury therapy

In this study, we designed a magnetic system and used it to accumulate stem cells labelled with superparamagnetic iron oxide nanoparticles (SPION) at a specific site of a spinal cord injury lesion. Histological analysis of cell distribution on the spinal cord surface showed a good correlation with the calculated distribution of magnetic forces exerted onto the transplanted cells. The results suggest that focused targeting and fast delivery of stem cells can be achieved using the proposed non-invasive magnetic system.



Collaboration: Institute of Physics of the CAS

Publication:
Tukmachev, D., Lunov, O., Zablotskii, V., Dejneka, A., Babic, M., Sykova, E., Kubinova, S.: An effective strategy of magnetic stem cell delivery for spinal cord injury therapy. Nanoscale. 2015;7(9):3954-8, IF 7.39

Fig. Non-invasive magnetic system for fast and targeted cell delivery into the lesion area.

Department of Auditory Neuroscience

Head: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
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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 behaviour evaluated with behavioural tests. Audiological tests and MR imaging are used to characterize age-related changes in hearing in humans.

Laboratory of Auditory Physiology and Pathology

Head of Laboratory: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
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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 electrophysiological, behavioural, 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 us to study the 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 degrees of presbycusis was revealed using magnetic resonance 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.

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Ondřej Zelenka, MD
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Veronika Svobodová, MD

Technicians:
Jana Janoušková
Jan Setnička

Important results in 2015

1. Age-related changes in hearing

Based on MRI recordings from the auditory cortex, it seems that peripheral as well as central components of presbycusis appear to influence each other only to a limited degree. The greater extent of cortical activation in elderly subjects in comparison with young subjects, with an asymmetry towards the right side, may serve as a compensatory mechanism for the impaired processing of auditory information appearing as a consequence of ageing.

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

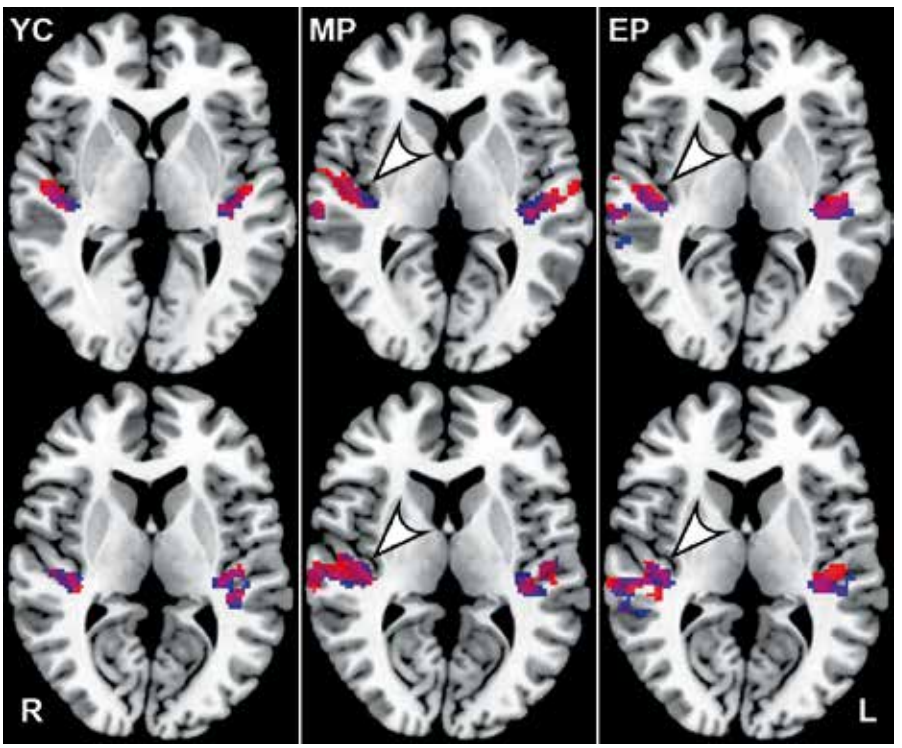

Fig: Averaged cortical activity evoked by acoustic stimulation examined by fMRI in all 3 groups.
YC – young controls, MP – mild presbycusis, EP – expressed presbycusis. Red colour – stimulation with pink noise centred at 350 Hz and 700 Hz; blue colour – stimulation with pink noise centred at 1.5 kHz, 3 kHz and 8 kHz. The arrowheads accentuate an increase in the right AC activation in both elderly groups.

Publication:

Profant O., Tintěra J., Balogová Z., Ibrahim I., Jilek M., Syka J.: (2015) Functional changes in the human auditory cortex in ageing. PLoS One. 2015 Mar 3;10(3):e011 6692, IF 3.534

2. Deterioration of the Medial Olivocochlear Efferent System Accelerates Age-Related Hearing Loss in Pax2-Isl1 Transgenic Mice

Overexpression of transcription factor ISLET1 under the Pax2 promoter in mice manifested in hyperactivity, circling behaviour, and the early onset of progressive age-related hearing loss. Early age related reduction of otoacoustic emissions (DPOAEs) was found to be conditioned by deterioration of cochlear efferent terminals. Our data provide the first evidence that the alternation of the MOC efferent system accelerates the age-related functional decline of hearing without the loss of OHCs.

Collaboration: Gabriela Pavlínková PhD, Laboratory of Molecular Pathogenetics, Institute of Biotechnology of the CAS, Prague, Prof. Bernd Fritzsch, Department of Biology, University of Iowa, Iowa City, IA, USA

Publication:

Chumak T., Bohuslavova R., Macova I., Dodd N., Buckiova D., Fritzsch B., Syka J., Pavlinkova G.: (2015) Deterioration of the Medial Olivocochlear Efferent System Accelerates Age-Related Hearing Loss in Pax2-Isl1 Transgenic Mice. Mol Neurobiol, [Epub ahead of print] DOI 10.1007/s12035-015-9215-1, IF 5.137

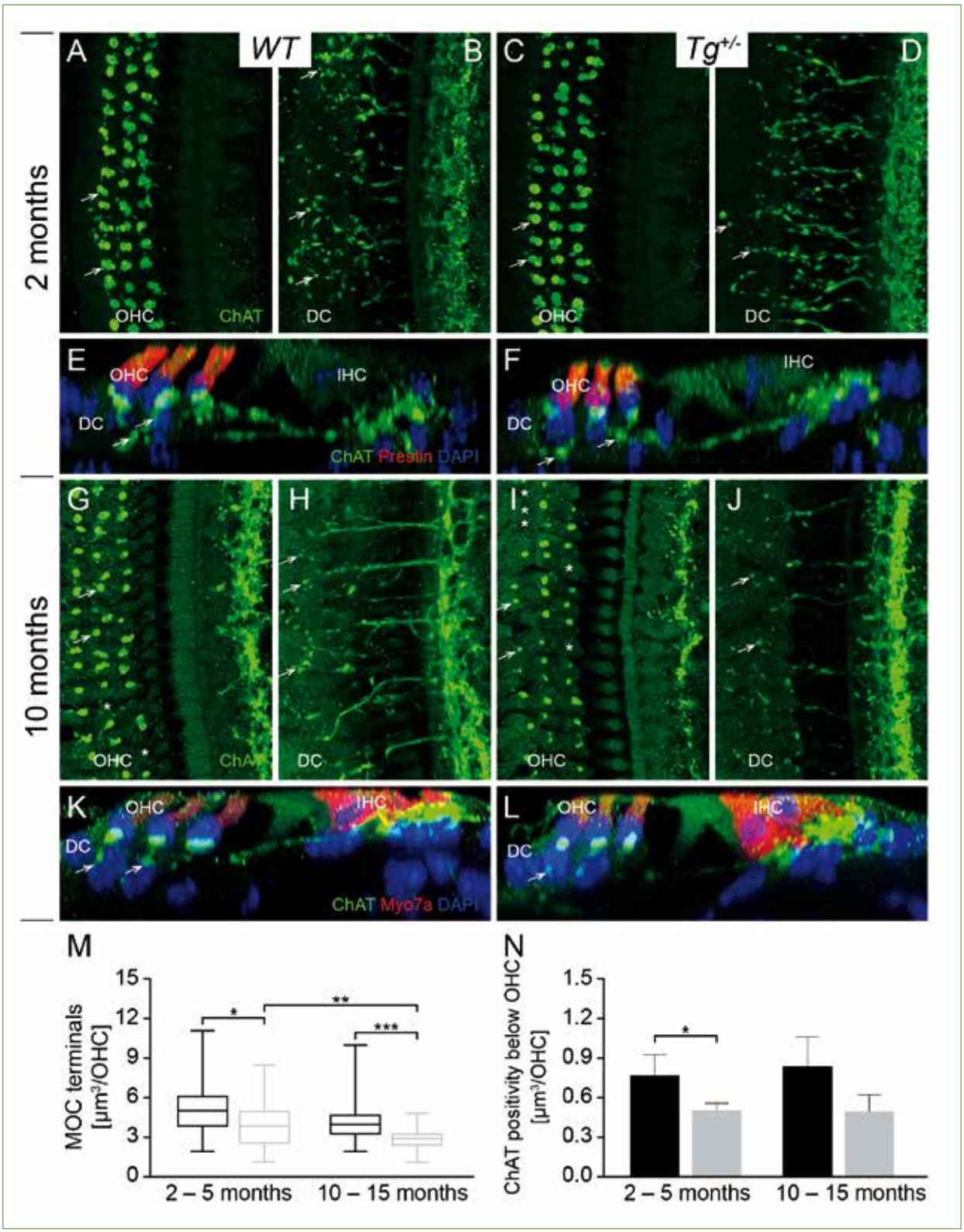

Fig. Altered efferent innervations. Despite visible similarities, the quantitative analysis shows a decrease in the volume of MOC terminals of OHCs (A, C, arrows; quantified in M) and efferent vesiculated fibres in the region of Deiters' cells (B, D, arrows; quantified in N) in young Tg+/– mice (I, M) than in WT animals (G, M). The progressive loss of efferent fibres is visible in older Tg+/– (J) compared toWT (H). In both WT and Tg+/– groups, efferent endings are missing if the OHC is lost (G, I; stars). Side view (E, F, K, L) represents the maximum projection of a focal series through the thickness of one OHC, arrows here and in B, D, H, J point out ChAT positive particles in the region of Deiters' cells. MOC medial olivocochlear efferent system, IHC inner hair cells, OHC outer hair cells, DC Deiters' cells, ChAT cholin acetyltransferaza.

Laboratory of Synaptic Physiology

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We study the mechanisms of plasticity of excitatory and inhibitory synaptic transmission by using electrophysiological and immunohistochemical techniques. Recent projects in the lab are aimed at revealing the physiological roles of inhibitory transmitters, their receptors and uptake systems in the auditory brainstem nuclei, auditory cortex or hippocampus. Particularly, we are interested in identifying proteins participating in $GABA_B$ receptor signalosome and in revealing their role in $GABA_B$-mediated inhibition in the mammalian auditory system. We would like to help to identify potential therapeutic targets for treatment of environmental noise-induced hearing disorders, like tinnitus or hyperacusis.

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Michaela Králíková, MSc, PhD

PhD Student:
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Kateryna Pysaněnko, MSc

Undergraduate student:
Adolf Melichar

Important result in 2015

1. Differential modulation of $GABA_B$ receptor-induced K^+ currents by endogenous KCTD proteins

$GABA_B$ receptors are the G-protein coupled receptors for the main inhibitory neurotransmitter in the brain, γ-aminobutyric acid (GABA). $GABA_B$ receptors regulate the excitability of most neurons in the central nervous system by modulating the activity of enzymes and ion channels. $GABA_B$ receptors associate with homo-oligomers of auxiliary KCTD 8, 12, 12b and 16 subunits that differentially regulate the receptor response by directly binding to the G-protein. We have shown distinct regulatory effects on G-protein signaling exerted by KCTD12 and 16 and provided evidence that $GABA_B$/KCTD16 complexes regulate the kinetics of late inhibitory postsynaptic currents in hippocampal neurons. In summary, our data demonstrate that simultaneous assembly of distinct KCTDs at the receptor increases the molecular complexity of native $GABA_B$ receptors.

Collaboration: Prof. Bernhard Bettler, Department of Biomedicine, Institute of Physiology, Pharmazentrum, University of Basel, Basel, Switzerland

Publication:

Raveh, A., Turecek, R. and Bettler B.: (2015). Mechanisms of Fast Desensitization of $GABA_B$ Receptor-Gated Currents. Adv. Pharmacol. 73C:145-165.

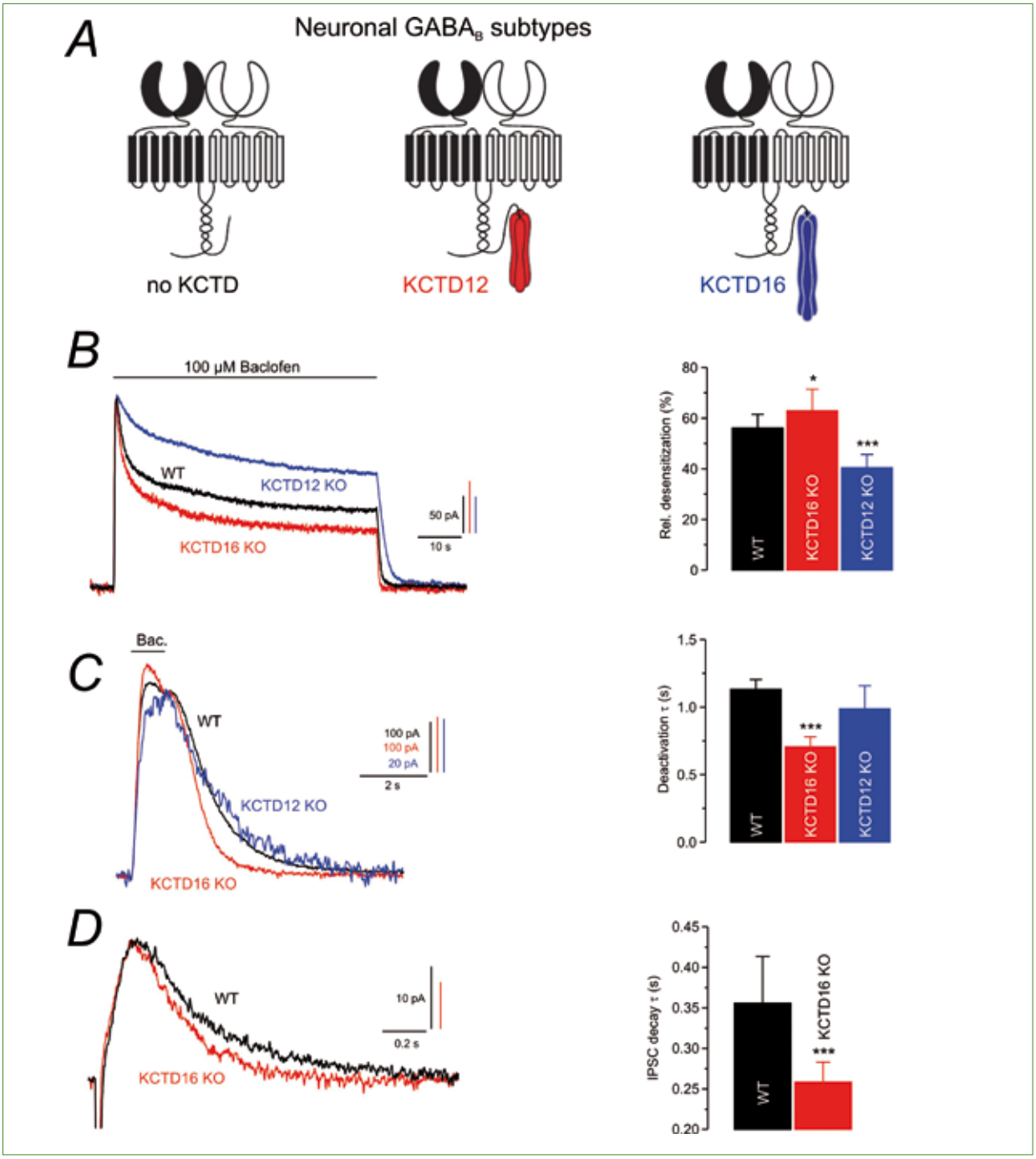

Fig. A, GABA$_B$ receptor subunit compositions in neurons. The principal subunits of GABA$_B$ receptors – GABA$_{B1}$ (black) and GABA$_{B2}$ (white) – have the prototypical seven transmembrane domains of G protein-coupled receptors. GABA$_{B2}$ associates with auxiliary KCTD12 (red) or 16 (blue) subunits. **B,** Altered GABA$_B$ receptor responses in neurons with deleted KCTD proteins. Representative traces of GABA$_B$ agonist baclofen-evoked K^+ currents recorded from cultured hippocampal neurons of WT (black), KCTD16 (red) or KCTD12 (blue) knockout mice. Deletion of KCTD12 reduces desensitization of the responses, while deletion of KCTD16 leads to slightly elevated desensitization due to higher occupancy of the receptor by KCTD12. **C,** Superimposed traces show K^+ currents evoked by 1 s-long application of baclofen to cultured hippocampal neurons isolated from WT, KCTD12 KO or KCTD16 KO mice. The bar graph summarizes the time constants obtained from a fit of the deactivation decay to a single exponential function. Note that the decay time course of the currents was significantly reduced in KCTD16 KO and unchanged in KCTD12 KO neurons, compared to WT. **D,** Examples of inhibitory postsynaptic currents (IPSCs) recorded from CA1 hippocampal neurons of WT or KCTD16 KO mice. Note faster decay kinetics of the currents obtained from KCTD16 KO neurons. The bar graph summarizes the time constants obtained from a fit of the deactivation decay of IPSCs to a single exponential function.

Department of Cellular Neurophysiology

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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 to 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-signalling pathways in proliferation/differentiation of NG2 glial cells.

Research scientists:
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Helena Pivoňková, MD, PhD

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Eliška Waloschková

Important result in 2015

Quantitative Analysis of Glutamate Receptors in Glial Cells from the Cortex of GFAP/EGFP Mice Following Ischemic Injury: Focus on NMDA Receptors

Cortical glial cells contain both ionotropic and metabotropic glutamate receptors. Despite several efforts, a comprehensive analysis of the entire family of glutamate receptors and their subunits present in glial cells is still missing. Here, we provide an overall picture of the gene expression of ionotropic (AMPA, kainate, NMDA) and the main metabotropic glutamate receptors in cortical glial cells isolated from GFAP/EGFP mice before and after focal cerebral ischemia. Employing single cell RT-qPCR, we detected the expression of genes encoding subunits of glutamate receptors in GFAP/EGFP-positive (GFAP/EGFP+) glial cells in the cortex of young adult mice. Most of the analyzed cells expressed mRNA for glutamate receptor subunits, the expression of which, in most cases, even increased after ischemic injury. Data analyses disclosed several classes of GFAP/EGFP+ glial cells with respect to glutamate receptors and revealed in what manner their expression correlates with the expression of glial markers prior to and after ischemia. Furthermore, we also examined the protein expression and functional significance of NMDA receptors in glial cells. Immunohistochemical analyses of all seven NMDA receptor subunits provided direct evidence that the GluN3A subunit is present in GFAP/EGFP+ glial cells and that its expression is increased after ischemia. *In situ* and *in vitro* Ca^{2+} imaging revealed that Ca^{2+} elevations evoked by the application of NMDA were diminished in GFAP/EGFP+ glial cells following ischemia. Our results provide a comprehensive description of glutamate receptors in cortical GFAP/EGFP+ glial cells and may serve as a basis for further research on glial cell physiology and pathophysiology.

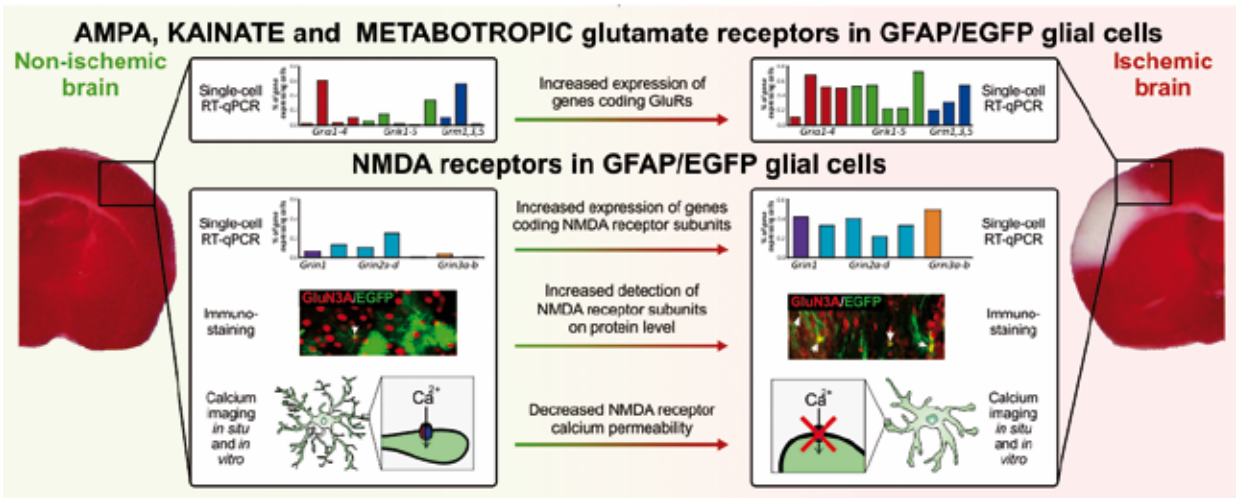


Fig.1. Focal ischemia increases expression of most of the glutamate receptors (GluRs) in GFAP/EGFP glia. As for the NMDA receptor subunits, immunohistochemical analysis confirmed their presence in GFAP/EGFP glia, and their detection was even increased after ischemic insult. The Ca^{2+} imaging results indicate diminished NMDA receptor Ca^{2+} permeability after focal ischemia, which is probably due to the involvement of GluN3A subunit.

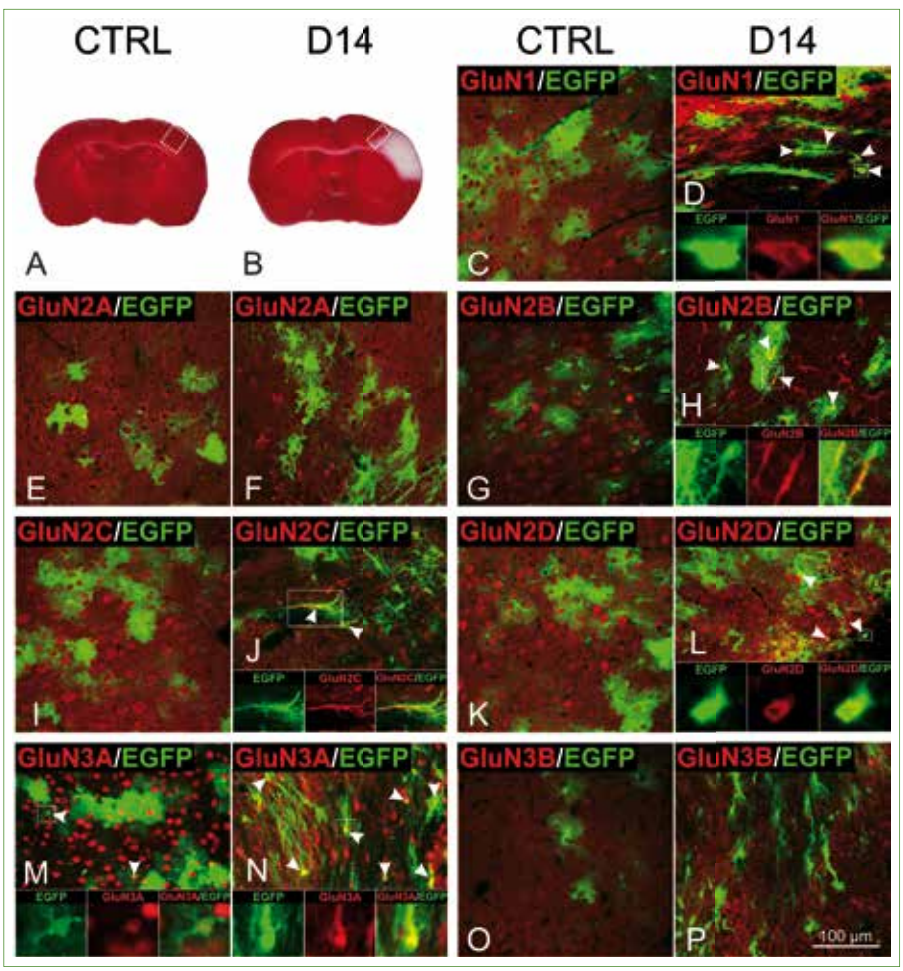
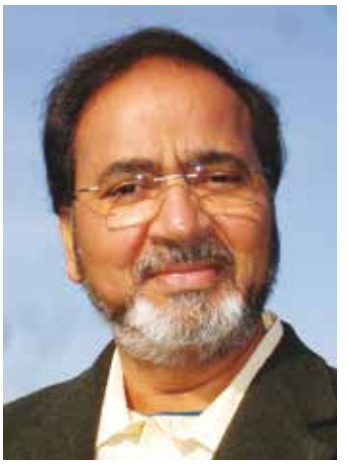


Fig.2. Immunohistochemical analysis of the GluN1, GluN2A-D and GluN3A-B subunits of the NMDA receptors in the cortex of adult GFAP/EGFP mice under control conditions (CTRL) and 14 days after MCAo (D14). Coronal brain sections from CTRL (A) and D14 (B) animals stained with triphenyltetrazolium chloride. The white colour in B indicates the volume of ischemic tissue at D14. The boxed areas indicate the regions in which the immunohistochemical analysis was performed. The arrowheads in C – P indicate the overlay of GFAP/EGFP+ cells and NMDA subunit staining – see figure insets for detailed images of cells in white rectangles. Note the overlap of the EGFP signal with GluN3A staining in CTRL tissue and GluN1, GluN2B-D and GluN3A staining at D14. The same scale bar applies to all non-inset images.

Publication:

Džamba, D., Honsa, P., Valný, M., Kriška, J., Valihrach, L., Novosadová, V., Kubista, M., Anděrová, M.: (2015) Quantitative Analysis of Glutamate Receptors in Glial Cells from the Cortex of GFAP/EGFP Mice Following Ischemic Injury: Focus on NMDA Receptors. Cell Mol Neurobiol. 35(8): 1187-1202, IF 2.506

Department of Molecular Neurophysiology



Head: Dr. Govindan Dayanithi, MSc, PhD
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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 signalling and calcium homeostasis in magnocellular neurons and nerve terminals to illustrate the signalling mechanisms of vasopressin and oxytocin in DRG neurones and glial cells. Recently, the department has also focused on the fundamental aspects of Ca^{2+} signalling mechanisms in stem cells from different species (humans, murine and non-human primate animal models for Alzheimer's disease) and of different origin obtained under different experimental conditions. This approach will lead to the development of better tools (e.g. for accurate modelling of the disease, for drug discovery or for toxicity screening) and novel approaches for cell-based therapies by improving both the differentiating potential and survival of all types of stem cells after transplantation.

Research Scientist:
Dr. Govindan Dayanithi, MSc, PhD
Research Scientist CNRS

PhD Students:
Oksana Forostyak, MD
Štěpán Kortus, MSc

Technician:
Dominika Dušková

Important results in 2015

1. Physiology of vasopressin and oxytocin and Ca^{2+} signalling in the supraoptic nucleus neurones

The magnocellular vasopressin (AVP) and oxytocin (OT) neurones of the rat supraoptic nucleus (SON) exhibit specific electrical behaviour, synthesize AVP and OT peptides, and secrete them into the neurohypophysial system in response to various physiological stimulants. The electrical activities of these neurons are regulated by the release of AVP and OT, either somato-dendritically or when applied to supraoptic neurones or slice preparations *in vitro*. In these neurones, both AVP and OT bind to specific autoreceptors, which induce distinct Ca^{2+} signals and regulate cellular events. We have recently demonstrated that freshly isolated single SON neurones from adult rats exhibited distinct spontaneous $[Ca^{2+}]_i$ oscillations. The spontaneous oscillations could be observed simultaneously in both soma and dendrites, whereas the high 50 mM K^+-induced $[Ca^{2+}]_i$ response initiates in dendrite and spreads towards the soma. The computational estimations of Ca^{2+} fluxes have also been proposed. In addition, we have also identified the major mechanisms that underlie these oscillations. To achieve this, we used Ca^{2+} imaging techniques (fast fluorescence photometry and video imaging) to measure $[Ca^{2+}]_i$ oscillations from individual neurones. These neurones were treated with various drugs targeting individual mechanisms of cellular Ca^{2+} homeostasis such as voltage-dependent-calcium-channels (VDCC; L-N-P/Q-R and T-type), endoplasmic reticulum (ER), plasma membrane Ca^{2+} pumps (PMCA) or intracellular Ca^{2+} signalling pathway.

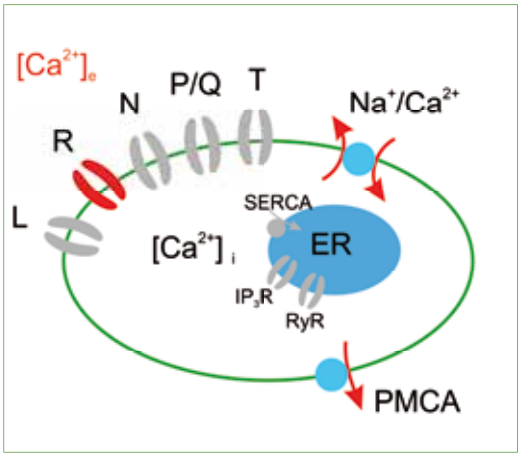

Fig. The schematic diagram shows Ca^{2+} transport mechanisms with highlights (red) of those that were identified as essential for $[Ca^{2+}]_i$ oscillations in the magnocellular neurons.

Publications:

Kortus, S., Dayanithi, G., Zapotocky, M.: Computational estimation of calcium fluxes in isolated magnocellular neurons (2015). BMC Neuroscience 16 (suppl 1): 299, IF 2.99

Kortus, S., Srinivasan, C., Forostyak, O., Ueta, Y., Sykova, E., Chvatal, A., Zapotocky, M., Verkhratsky, A., and Dayanithi, G.: Physiology of spontaneous $[Ca^{2+}]_i$ oscillations in the isolated vasopressin and oxytocin neurones of the rat supraoptic nucleus, Cell Calcium, 2016, In press, IF 3.769

Kortus, S., Srinivasan, C., Forostyak, O., Zapotocky, M., Ueta, Y., Sykova, E., Chvatal, A., Verkhratsky, A. and Dayanithi, G.: Sodium-calcium exchanger and R-type Ca^{2+} channels mediate spontaneous $[Ca^{2+}]_i$ oscillations in magnocellular neurones of the rat supraoptic nucleus, Cell Calcium, 2016, In press, IF 3.769

2. Calcium signalling in stem cells: molecular physiology and multiple roles

Stem cells (SCs) of different origins have brought hope as a potential tool for use in cell replacement therapies. Ca^{2+} signalling plays a key role in SC differentiation and proliferation, and dysregulation of Ca^{2+} homeostasis may instigate pathological scenarios. Currently, the role of ion channels and receptors in SCs is not fully understood. In recent years, we have found that (i) the pre-differentiation of human embryonic SCs (hESCs) led to the activation of Ca^{2+} signalling cascades and enhanced the functional activities of these cells; (ii) the Ca^{2+} homeostasis and the physiological properties of hESC-derived neural pre-cursors (NPs) changed during long term propagation *in vitro*; (iii) differentiation of NPs derived from human induced pluripotent SCs affects the expression of ion channels and receptors; (iv) these neuronal precursors exhibited spontaneous activity, indicating that their electrophysiological and Ca^{2+} handling properties are similar to those of mature neurones, and (v) in mesenchymal SCs isolated from the adipose tissue and bone marrow of rats the expression profile of ion channels and receptors depends not only on the differentiation conditions but also on the source from which the cells were isolated, indicating that the fate and functional properties of the differentiated cells are driven by intrinsic mechanisms. Together, identification and assignment of a unique ion channel and a Ca^{2+} handling footprint for each cell type would be necessary to qualify them as physiologically suitable for medical research, drug screening, and cell therapy.

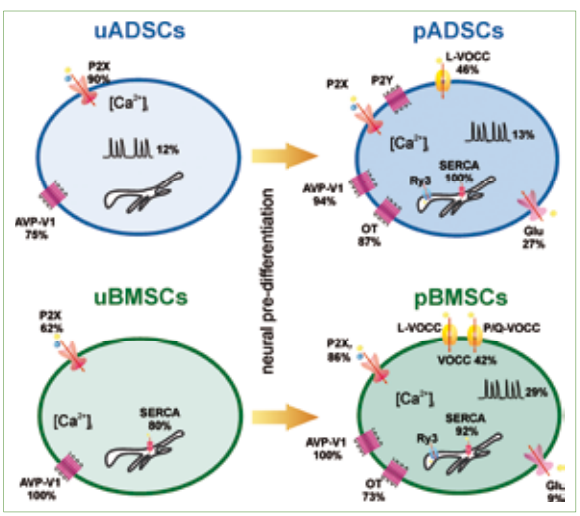

Fig. Schematic drawing showing the change in functional expression of Ca^{2+} channels and receptors linked to Ca^{2+} signalling in ADSCs and BMSCs during pre-differentiation.

Publications:

CNS regenerative medicine and stem cells. Forostyak, O., Dayanithi, G., Forostyak S.: Opera Medica et Physiologica 2016 Jan;1(1):69–76. (http://operamedphys.org/OMP_2016_01_0023).

Calcium signalling in stem cells: molecular physiology and multiple roles. Dayanithi, G. and Verkhratsky, A.: Cell Calcium-SI 'Ca^{2+} in Stem Cells' Editorial. 2016. In press, IF. 3.513

Physiology of Ca^{2+} signalling in stem cells of different origins and differentiation stages. Forostyak, O., Forostyak, S., Kortus, S., Sykova, E., Verkhratsky, A., Dayanithi, G.: Cell Calcium-SI 'Ca^{2+} in Stem Cells'. 2016. In press, IF 3.513

Department of Pharmacology

Head: Zdeněk Zídek, MSc, PhD, DSc
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Activities of the Department of Pharmacology are governed by the 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, MSc, PhD, DSc
Assoc. Prof. Eva Kmoníčková, PhD
Miloslav Kverka, MD, PhD

PhD Students:
Petra Kostecká, MSc
Adéla Dusilová, MSc

Technician:
Jana Křížková, MSc
Eva Prchlíková

Important result in 2015

Research and development of novel anti-inflammatory drugs

We have revealed a new class of pyrimidines with prominent inhibitory effects on the production of mediators of inflammation such as prostaglandin E2 and nitric oxide. The results contribute to the knowledge of the relationship between the structure and intrinsic biological activity of pyrimidines. The study is a background for the selection of lead structures with prospective beneficial effects in models of chronic inflammation.

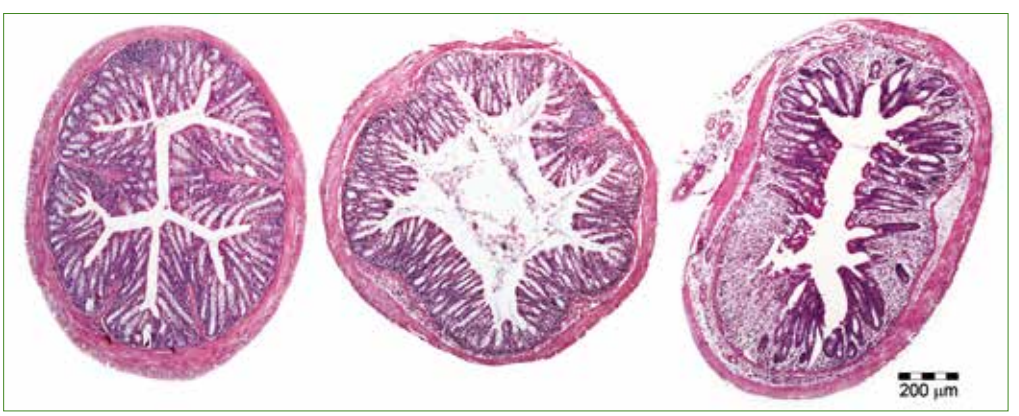

Fig. Histology of normal mouse colon (left). Severe inflammatory reaction (centre) was partially resolved after drug treatment (right).

Publication:

Jansa, P., Holý, A., Dračínský, M., Kolman, V., Janeba, Z., Kmoníčková, E., Zídek, Z.: Synthesis and structure–activity relationship studies of polysubstituted pyrimidines as inhibitors of immune-activated nitric oxide production. Med. Chem. Res., 24: 2154-2166, 2015, IF 1.402

Department of Genetic Ecotoxicology

Head: Radim J. Šrám, MD, PhD, 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, PhD, DSc
E-mail: sram@biomed.cas.cz | Phone: +420 241 062 596

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 on children's health.

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

PhD students:
Kateřina Hoňková, MSc
Jitka Pavlíková, MSc

Specialists:
Ivo Solanský, MSc
Věra Topinková, MSc

Technician:
Jolana Vaňková

Important result in 2015:

Analysis of genetic damage in lymphocytes of former uranium processing workers

The frequency of cells containing micronuclei (MN) and the presence of centromeres in the MN were analyzed in lymphocytes of men from Southern Bohemia (former workers of a former uranium processing plant "MAPE Mydlovary" and controls). No differences were found between formerly exposed workers and the control group. Moreover, former workers with X-ray examination had a significantly lower level of DNA damage than the control group. The possible reason for these results may be the adaptation of the organism.

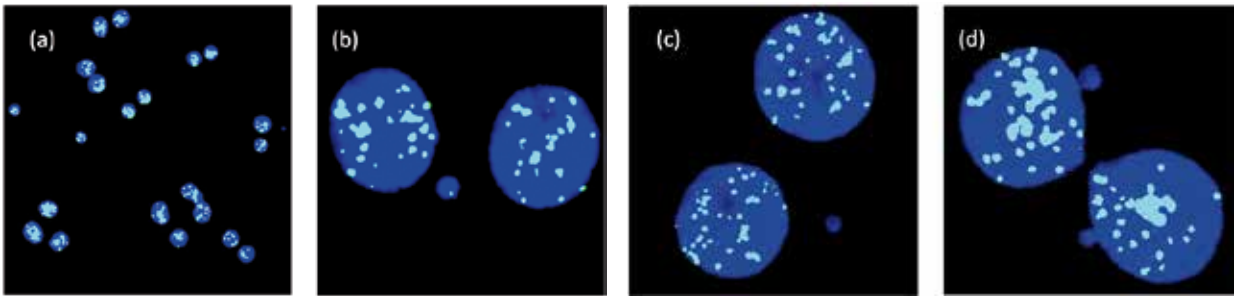

Fig. Examples of cytochalasin-B-blocked human peripheral blood lymphocytes stained with DAPI (blue) and Pan Centromeric probes with FITC (green): (a) Overall view (100x), (b) binucleated cell (BNC) with one centromere-positive (CEN+) micronucleus (MN) (1000x), (c) BNC with one centromere-negative (CEN-) MN (1000x) and (d) BNC with two MN, both CEN- (1000x).

Publication:

Zölzer, F., Havránková, R., Freitinger Skalická, Z., Rössnerová, A., Šrám, R.J.: (2015). Analysis of Genetic Damage in Lymphocytes of Former Uranium Processing Workers. Cytogenet Genome Res. 2015; 147 (1): 17-23, IF 1.561

Laboratoy of Genetic Toxicology

Head of Laboratory: Jan Topinka, MSc, PhD, DSc
E-mail: jtopinka@biomed.cas.cz | Phone: +420 241 062 675

The Laboratory studies mechanisms of genotoxic and epigenetic effects of toxic compounds bound to respirable dust particles as well as the 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, MSc, PhD, DSc

PhD students:
Táňa Brzicová, MSc
Jitka Štolcpartová, MSc

Specialists:
Alena Milcová, MSc
Michaela Pokorná, MSc
Kristýna Vrbová, MSc

Important result in 2015:

Day-to-day variability of toxic events induced by organic compounds bound to size segregated atmospheric aerosol

The temporal variability of size-segregated aerosol mass collected on a daily basis during the winter period in highly polluted districts of Ostrava city as well as toxic effects of organic compounds extracted from each size fraction were quantified. We revealed that the upper accumulation mode fraction ($0.5 < d_{ae} < 1$ μm) comprises most of the aerosol mass and contained 44% of total c-PAHs, while the ultrafine fraction (< 0.17 μm) contained only 11% of c-PAHs. DNA adduct levels and dioxin-like activity strongly correlated with both aerosol mass and c-PAH concentrations suggesting genotoxicity as a major toxic effect of organic compounds bound to size-segregated aerosol.

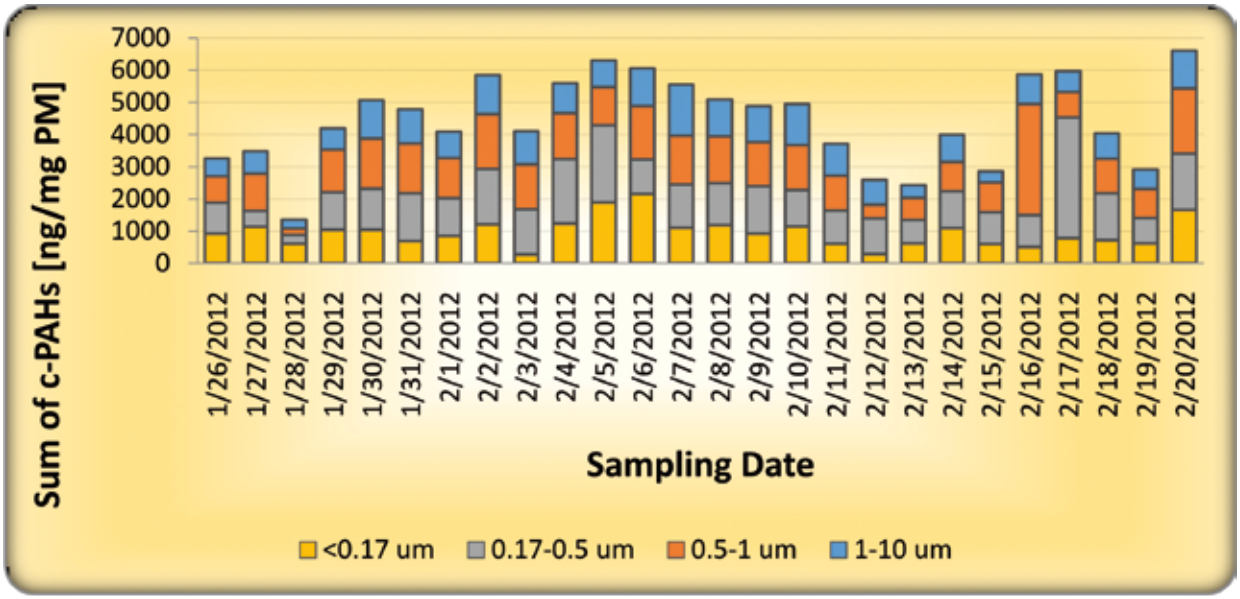

Fig. 1. Sum of c-PAH concentrations in four aerosol fractions per mg of the size fraction mass. c-PAHs include benz[a] anthracene, chrysene, benzo[k]fluoranthene, benzo[a]pyrene, dibenz[a,h]anthracene and indeno[1,2.3-cd]pyrene.

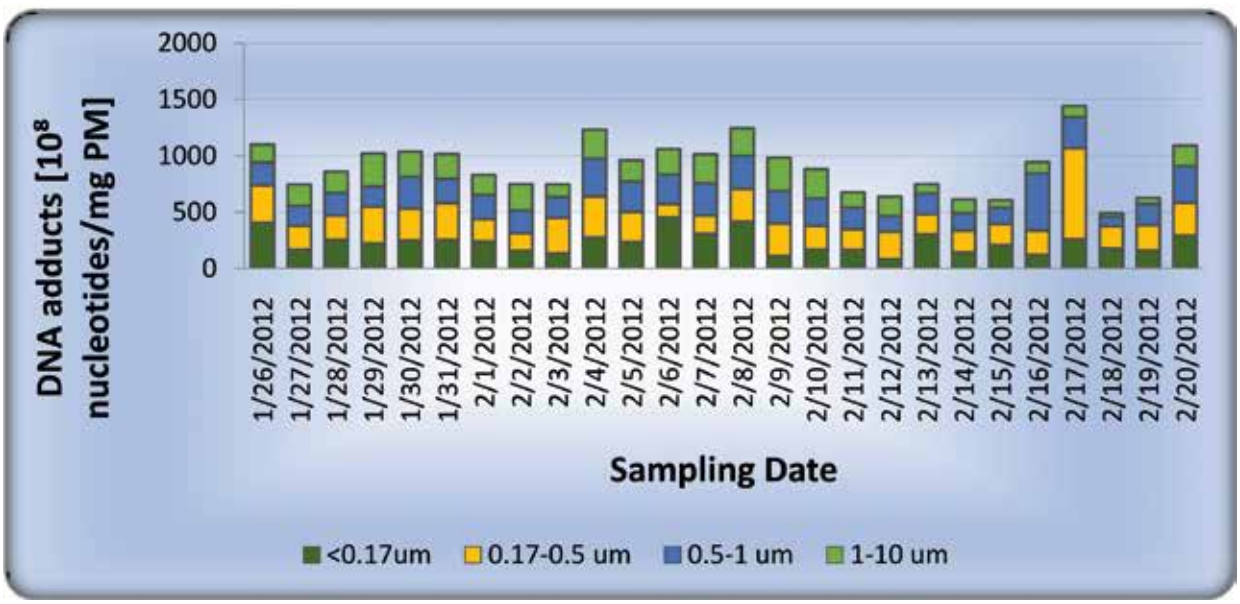

Fig.2. Total DNA adduct levels induced by organic extracts from size-segregated aerosols in an acellular system (calf thymus DNA) per mg of the size fraction mass. A strong positive correlation was found between c-PAH content in different aerosol size fractions and DNA adducts (R: 0.62 – 0.86).

Publication:

Topinka, J., Rossner Jr., P., Milcová, A., Schmuczerová, J., Pěnčíková, K., Rossnerová, A., Ambrož, A., Štolcpartová, J., Bendl, J., Hovorka, J., Machala, M.: (2015). Day-to-day variability of toxic events induced by organic compounds bound to size segregated atmospheric aerosol. Environ. Pollut. 202: 135-145, IF 3.902

Laboratory of Genomics

Head of Laboratory: Pavel Rössner, Jr., MSc, 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:
Pavel Rössner, Jr., MSc, PhD
Helena Líbalová, MSc, PhD
Veronika Vlková, MSc, PhD

PhD students:
Antonín Ambrož, MSc

Important result in 2015:

Reduced gene expression levels after chronic exposure to high concentrations of air pollutants

We analyzed the effect of air pollution on gene expression in subjects living in Prague and in the polluted Ostrava region. We expected to observe changes in the expression of DNA repair genes in subjects from the Ostrava region. Unexpectedly, the changes were found in Prague subjects, particularly in genes associated with immune response and neurodegenerative diseases. The results suggest that chronic exposure to air pollution may result in adaptation of the organism with possible negative health effects.

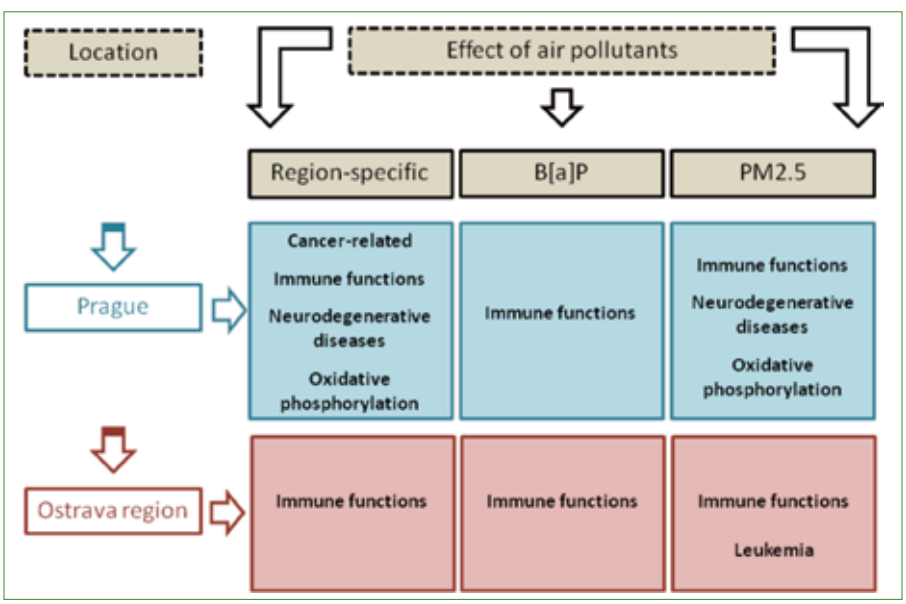
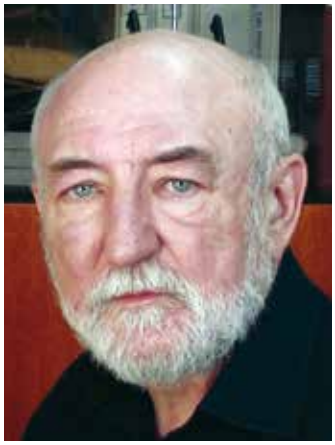


Fig. Pathways associated with air pollution in subjects from Prague and the Ostrava region. The figure shows both the pathways associated with location only and the pathways associated with exposure to air pollution (B[a]P – benzo[a]pyrene, PM2.5 – particulate matter of aerodynamic diameter < 2.5 μm).

Publication:

Rossner Jr., P., Tulupová, E., Rossnerová, A., Líbalová, H., Hoňková, K., Gmuender, H., Pastorková, A., Švecová, V., Topinka, J., Šrám, R.J.: (2015). Reduced gene expression levels after chronic exposure to high concentrations of air pollutants. Mutat Res. 780:60-70, IF 3.680

Department of Teratology



Head: Assoc. Prof. Miroslav Peterka, MD, PhD, DSc
E-mail: peterka@biomed.cas.cz | Phone: +420 241 062 604

The main focuses of the Department of Teratology is studying developmental abnormalities in humans as well as in experimental models. The causes and mechanisms of inborn defect formation are studied using two experimental models (developing chick embryo and mouse odontogenesis), and usinga clinical- epidemiological approach. The main target is to contribute to the knowledge of normal and abnormal development, pathogenesis of inborn defects and possibilities for their prevention.

Laboratory of Embryogenesis

Head of Laboratory: Assoc. Prof. Miroslav Peterka, MD, PhD, 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, PhD, DSc

Postgradual Student:
Zuzana Pavlíková, MSc

Technicians:
Petra Herlová, MSc
Simona Vojtěchová, MSc
Šárka Dvořáková

Laboratory of Odontogenesis

Head of Laboratory: Renata Peterková, MD, PhD
E-mail: repete@biomed.cas.cz | Phone: +420 241 062 232

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. Elucidating the development and role of the rudimentary structures during odontogenesis can contribute to a 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 Lagronová, MSc, PhD

PhD Students:
Lucie Horáková, MSc
Kateřina Lochovská, MSc
Klára Steklíková

Technicians:
Ivana Koppová
Zdena Lisá
Lenka Jandová, MSc
Linda Dalecká

Important result in 2015

Sprouty gene dosage influences temporal-spatial dynamics of primary enamel knot formation

In normal mice, the signalling centres of a premolar rudimentary bud and the first molar anlage fuse together to commonly form one typical signalling centre (primary enamel knot) of the first molar. With decreasing Sprouty2 and Sprouty4 gene dosages, we observed a non-fusion of the above mentioned signalling centres, with consequent formation of a supernumerary tooth primordium from the individually developing premolar bud. Our findings significantly contribute to existing knowledge about supernumerary tooth formation.

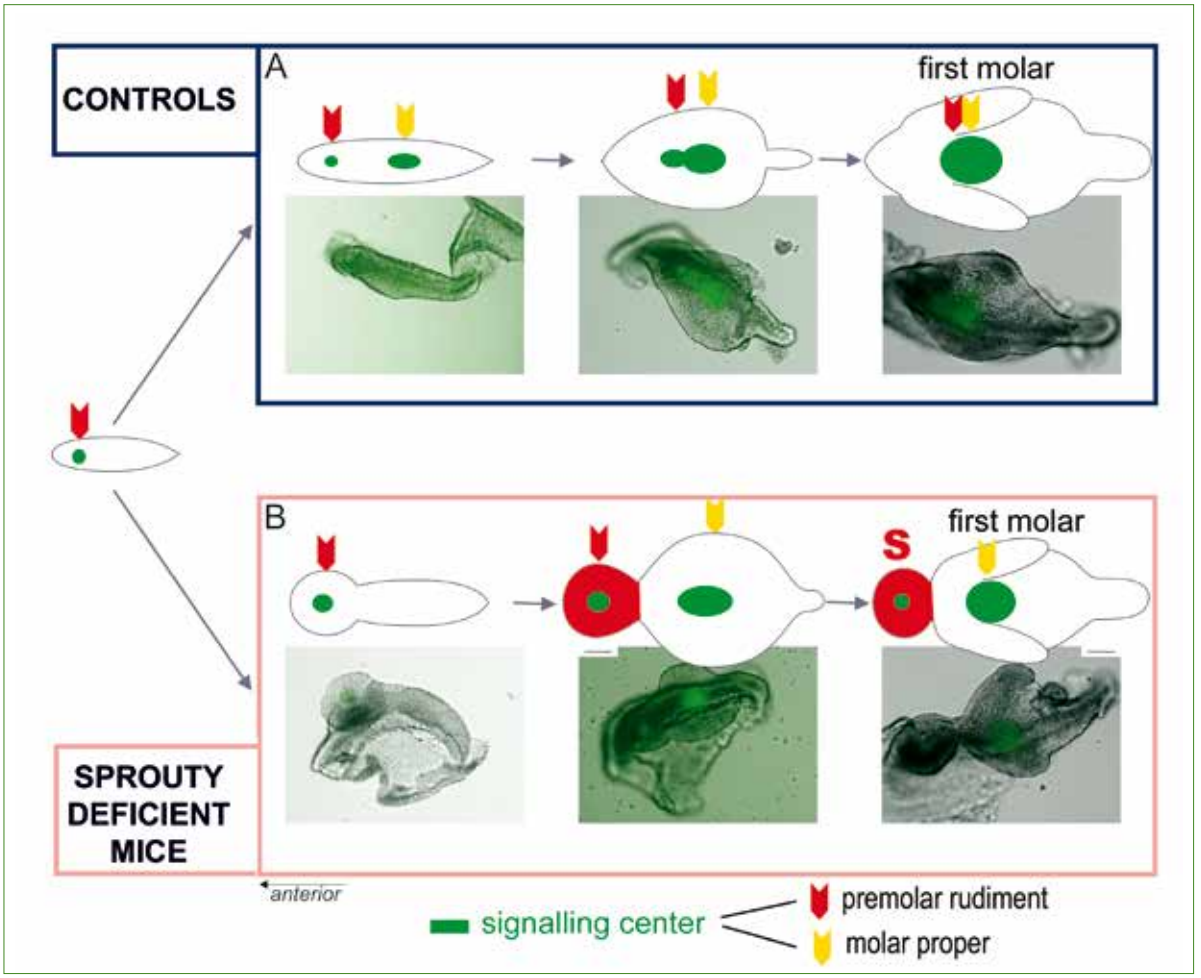

Fig. Development of a supernumerary tooth in mouse embryos.

Publication:
Lochovska, K., Peterkova, R., Pavlikova, Z., Hovorakova, M.: Sprouty gene dosage influences temporal-spatial dynamics of primary enamel knot formation. BMC Dev Biol. 2015 Apr 22;15:21. doi: 10.1186/s12861-015-0070-0, IF 2.667

Department of the Molecular Biology of Cancer

Head: Pavel Vodička, MD, PhD
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In our Department we investigate the 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 to 1. identify biomarkers of increased predisposition to tumour diseases, 2. enable early diagnostics, 3. assess individual responses to anti-tumour treatment, 4. 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 significantly changed 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. The high activity of DNA repair mechanisms may contribute to the resistance of cancer cells to such substances. The Department has been working with different types of biological material from 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 Poláková-Vymetálková, MSc, PhD
Markéta Urbanová, MSc, PhD
Petra Bendová, MSc
Kateřina Jirásková, MSc
Linda Bártů, MSc
Klára Červená, Bc
Pavel Kříž

Laboratory of DNA Repair:
Alena Opattová, MSc, PhD
Jana Slyšková, MSc, PhD
Soňa Vodenková, MSc
Alexandra Rejhová, MSc
Michal Kroupa, MSc
Andrea Čumová, MSc
Jan Král, MD
Prof. Rudolf Štětina, MSc, PhD

Important results in 2015

1. Interactions of DNA repair gene variants modulate chromosomal aberrations in healthy subjects

Numerical and structural chromosomal instability takes part in carcinogenesis. We studied functional variants in DNA repair genes in relation to chromosomal damage (CA), chromatid-type (CTA) and chromosome-type aberrations (CSA) in healthy subjects. We found significantly lower CTA frequencies associated with XPD Lys751Gln variant genotype and increased CSA linked to the RAD54L variant genotype. CAs accumulation requires complex interplay between different DNA repair pathways.

Publication:

Vodička, P., Musak, L., Frank, C., Kazimirova, A., Vymetálková, V., Barancoková, M., Smolková, B., Dzupinková, Z., Jirasková, K., Vodenková, S., Kroupa, M., Osina, O., Naccarati, A., Palitti, F., Försti, A., Dusinská, M., Vodičková, L., Hemminki, K.: (2015). Interactions of DNA repair gene variants modulate chromosomal aberrations in healthy subjects. Carcinogenesis.36(11): 1299-1306, IF 5.334

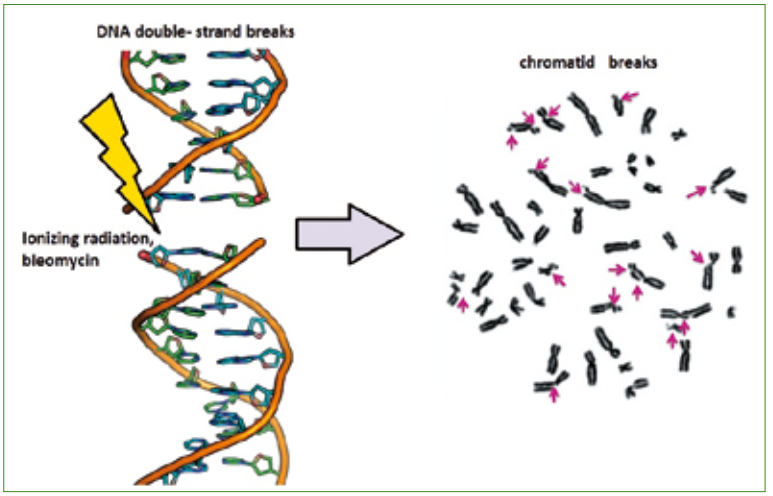

Fig. The genesis of DNA and chromosomal damage in human DNA. Many exogenous agents attack DNA and generate single-and double-strand breaks. If not repaired by DNA repair mechanisms, they may result in permanent chromosomal damage and ultimately in the onset of cancer.

2. Post-Treatment Recovery of Suboptimal DNA Repair Capacity and Gene Expression Levels in Colorectal Cancer Patients

We studied the dynamics of DNA repair in colorectal cancer patients from diagnosis to 1 year follow up, and with respect to CRC treatment. We identified a panel of blood DNA repair-related markers discerning the acute stage of the disease from the remission period. In conclusion, our results support a model in which DNA repair is altered as a result of cancer.

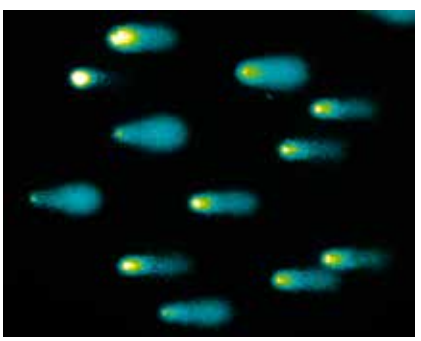

Fig. Comet assay shows the extent of DNA damage and repair. Undamaged DNA is supposed to be compact in the nucleus, damaged DNA appears as a tail of fluorescence.

Publication:

Slyšková, J., Cordero, F., Pardini, B., Korenková, V., Vymetalková, V., Bielik, L., Vodičková, L., Pitule, P., Liska, V., Matejka, V. M., Levy, 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. 54 (9): 769-778, IF 4.770

3. Polymorphisms in microRNA genes as predictors of clinical outcomes in colorectal cancer patients

Colorectal cancer (CRC) is routinely cured by a 5-fluorouracil (5-FU)-based chemotherapy. We investigated the effect of single nucleotide polymorphisms in two microRNA – encoding genes in 1,083 CRC patients recruited in the Czech Republic and we evaluated the effect of 5FU therapy on clinical outcomes. Obtained results confirm that variations in miRNA-encoding genes may be an important factor modulating CRC prognosis and predicting therapy response.

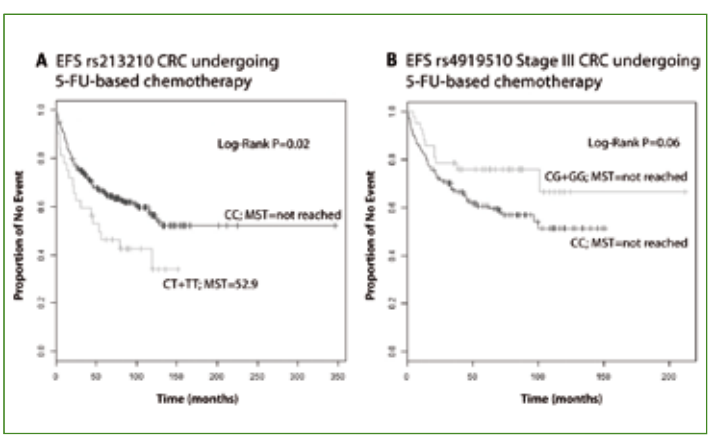

Fig. Kaplan–Meier EFS curves stratified (A) for rs213210 in all CRC patients undergoing 5-FU-based chemotherapy, and (B) for rs4919510 in stage III CRC patients undergoing 5-FU-based chemotherapy. MST, median survival time.

Publication:

Pardini, B., Rosa, F., Naccarati, A., Vymetálková, V., Ye, Y., Wu, X., di Gaetano, C., Buchler, T., Novotný, J., Matullo, G., Vodička, P.: (2015) Polymorphisms in microRNA genes as predictors of clinical outcomes in colorectal cancer patients. Carcinogenesis. 31(6): 82-86, IF 5.334

Department of Transplantation Immunology

Head: Prof. Vladimír Holáň, MSc, PhD, DSc
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The Department's research is focused on the use of stem cells in the treatment of severe injuries or so far incurable diseases, as well as on properties of non-healing lesions of the anterior eye segment after various injuries or ocular diseases.

Laboratory of of Transplantation Immunology

Head of Laboratory: Prof. Vladimír Holáň, MSc, PhD, DSc
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The Laboratory research is focused on the isolation, characterization and cultivation of stem cells and their use for treatment of severe injuries or so far incurable diseases. Stem cells are propagated in tissue cultures and using various nanofiber scaffolds transferred onto mechanically or chemically damaged ocular surface. The ability of transferred cells to inhibit a harmful inflammatory immune reaction occurring in the site of injury and to support the healing process is evaluated. The ultimate goal of the research is to get insights into the mechanisms of specific immune response after transplantation of stem cells with the aim to increase their anti-inflammatory and therapeutic potential. The experience with the study of transplantation immunity and the combination of nanotechnologies with stem cell research enables us to propose and test novel therapeutic approaches. The recent study is extended to the development of stem cell-based therapy for currently incurable serious sight-threatening retinal diseases.

Research Scientists:
Prof. Vladimír Holáň, MSc, PhD, DSc
Alena Zajícová, MSc, PhD
Eliška Javorková, MSc, PhD
Magdaléna Krulová, MSc, PhD

PhD Students:
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Michaela Hájková, MSc
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Pavla Boháčová, MSc
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Technicians:
Lucie Holáňová
Jaroslava Knížová

Undergraduate Students:
Nicole Matějčková, Bc
Julie Vacková, Bc

Important result in 2015

Comparative study on the therapeutic potential of mesenchymal stem cells and tissue-specific limbal stem cells

The ability of mesenchymal stem cells (MSC) and limbal stem cells (LSC) to produce various immunoregulatory molecules and to modulate immune response was compared. The therapeutic potential of these stem cells was evaluated in the model of treatment of chemically damaged ocular surface in the rabbit. It was found that stem cells produce a number of immunoregulatory molecules and that MSC have comparable therapeutic properties as do tissue-specific LSC. These results show evidence that MSC can replace tissue-specific LSC in the cases when LSC are absent or difficult to obtain.

Publications:

Holáň, V., Trošan, P., Čejka, Č., Javorková, E., Zajícová, A., Heřmánková, B., Chudíčková, M., Čejková, J.: A comparative study of the therapeutic potential of mesenchymal stem cells and limbal epithelial stem cells for ocular surface reconstruction. Stem Cells Translat. Med. 4, 1052-1063, 2015, IF 5.709

Heřmanková, B., Zajícová, A., Javorková, E., Chudíčková, M., Trošan, P., Hájková, M., Krulová, M., Holáň, V.: Suppression of IL-10 production by activated B cells via a cell contact-dependent cyclooxygenase-2 pathway upregulated in IFN-γ-treated mesenchymal stem cells. Immunobiology 221, 129-136, 2016, IF 3.044

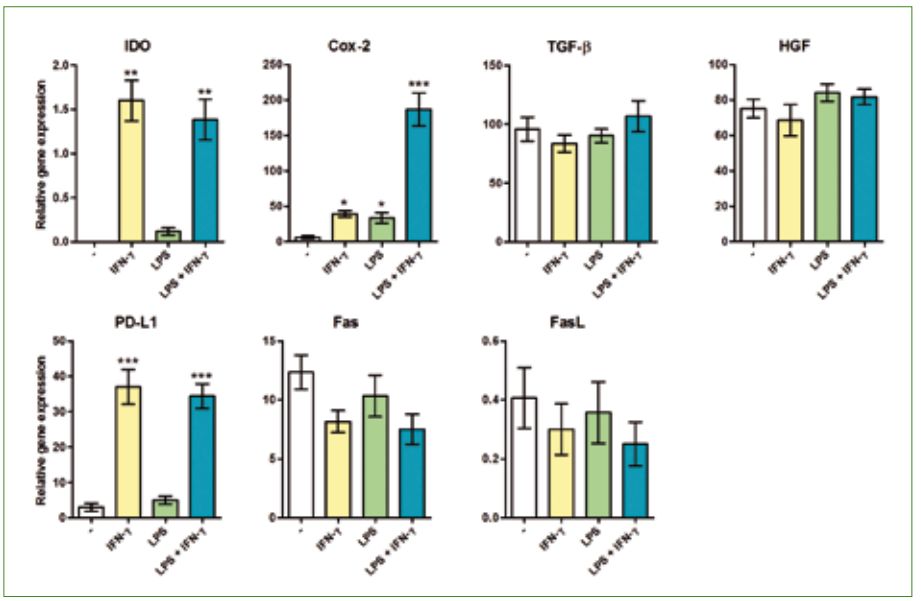

Fig.1. Characterization of MSC. The ability of MSC to express genes for immunomodulatory molecules was determined by real-time PCR. The cells were cultured untreated or were stimulated with LPS, IFN-γ with LPS plus IFN-γ.

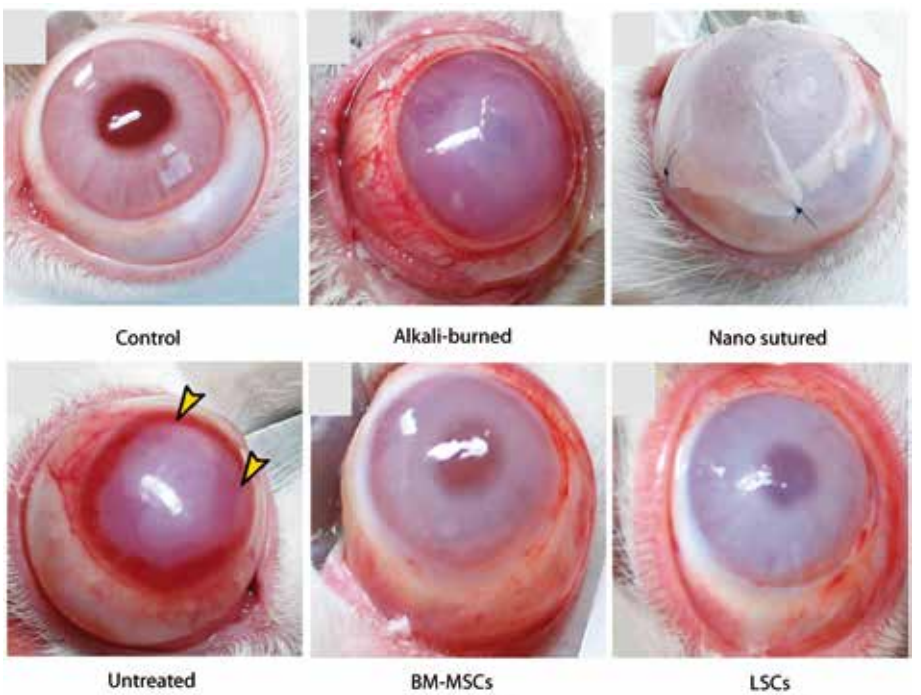

Fig.2. Therapeutic potential of MSc and LSC. Stem cells were transferred using nanofiber scaffold onto damaged ocular surface and their therapeutic potential was evaluated. The figure shows healthy rabbit eye, the eye shortly after chemical damage, damaged eye covered with nanofiber scaffold, untreated damaged eye two weeks after the injury and damaged eye treated with MSc or LSC.

Laboratory of Eye Histochemistry and Pharmacology

Head of Laboratory: Assoc. Prof. Jitka Čejková, MD, PhD, DSc
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The Laboratory examines the causes of bad healing or non-healing lesions of the anterior eye segment after various injuries or ocular diseases, and conditions necessary for regeneration of tissues of the anterior eye segment, particularly of the cornea, with the aim to restore visual functions. Great attention is devoted to the role of oxidative stress in the initiation or development of the intraocular inflammation. In regenerative processes of ocular tissues the anti-inflammatory and antioxidative effects of limbal epithelial stem cells and mesenchymal stem cells are investigated. For this reason immunohistochemical, biochemical and biophysical methods are employed.

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

Undergraduate Students:
Tomanová Aneta, Bc
Vašková Verča, Bc
Švandová Ivana, Bc
Bayerová Martina, Bc

Technician:
Jana Herlova

Important results in 2015

1. The imbalance between oxidants and antioxidants in favour of oxidants (oxidative stress) is highly involved in ocular aging processes and in many ocular diseases and injuries

The eye is directly exposed to the noxae of the external environment, such as air pollution, radiation, cigarette smoke, vapours or gases from household cleaning products, chemical burns from splashes of industrial chemicals, and danger from potential oxidative damage evoked by them.
Corneal pachymetry (the measurement of the central corneal thickness by an ultrasonic pachymeter) is a highly sensitive method for the evaluation of toxic influences to the cornea, or for the evaluation of corneal healing after the injury or disease (see graph above).

Publications:

Holáň, V., Trošan, P., Čejka, Č., Javorková, E., Zajícová, A., Heřmánková, B., Chudíčková, M., Čejková, J.: A comparative study of the therapeutic potential of mesenchymal stem cells and limbal epithelial stem cells for ocular surface reconstruction. Stem Cells Translat. Med. 4, 1052–1063, 2015, IF 5.709

Čejka, Č., Čejková, J.: Oxidative stress to the cornea, changes in corneal optical properties, and advances in treatment of corneal oxidative injuries. Oxid Med Cell Longev. 2015;2015:591530. doi: 10.1155/2015/591530. Epub 2015 Mar 11, IF 3.516

2. Severe alkali injury of the cornea leads to the loss of corneal epithelium and to the development of the intracorneal inflammation resulting in corneal neovascularization and partial or total loss of vision

Fast corneal re-epithelialization is inevitable for successful healing of the cornea with restoration of corneal transparency. Alkali injury treated with limbal epithelial stem cells or bone marrow MSCs (less with adipose mesenchymal stem cells) evoked rapid corneal re-epithelialization accompanied by suppressed intracorneal inflammation and reduced corneal neovascularization. Corneas healed with renewal of corneal transparency. Corneal hydration increased after alkali injury returned to physiological levels. This is in contrast to alkali injured untreated corneas which healed with fibrotic untransparent tissue.

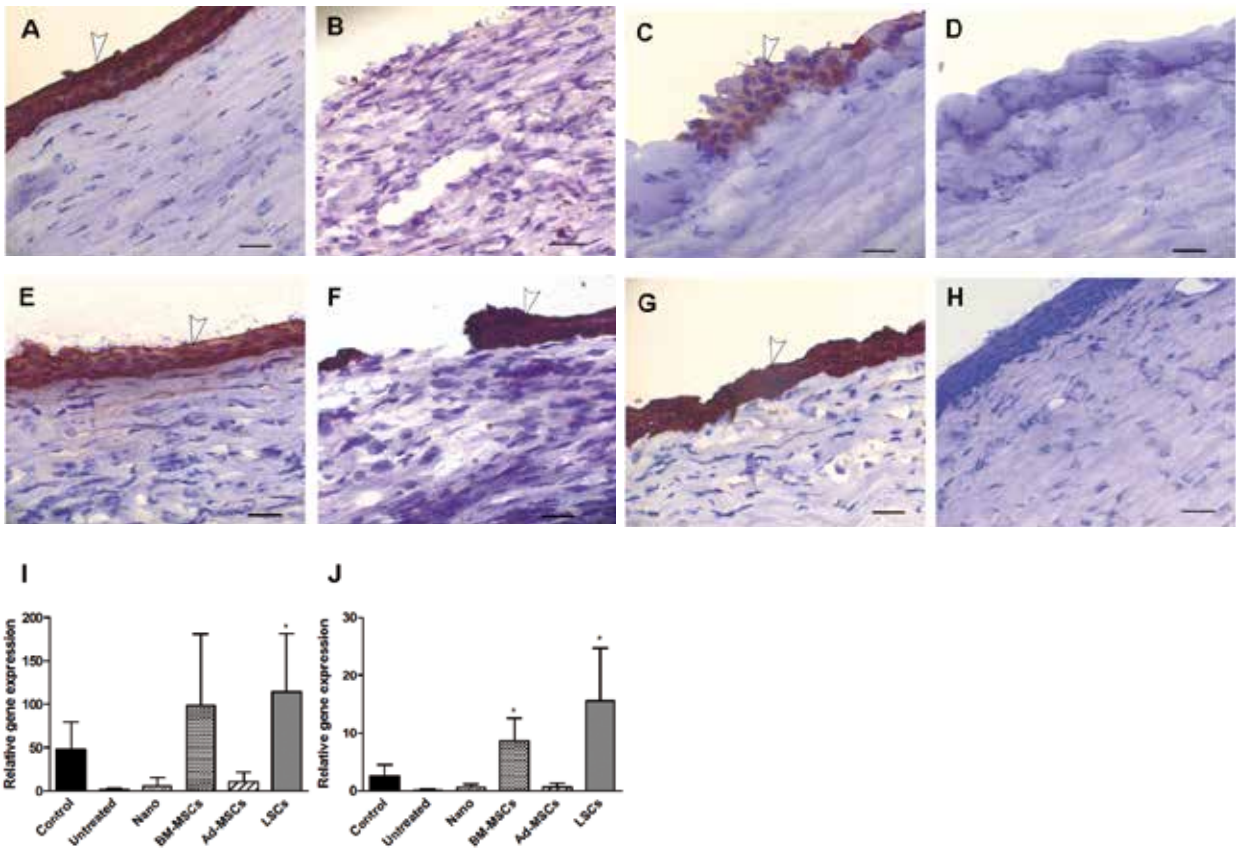

Fig.1. Corneal re-epithelialization of alkali injured and stem cell treated cornea (day 12 after the injury). Healthy cornea (A), untreated injured cornea (B), injured cornea treated with stem cell free nanofiber (C), nanofiber seeded with bone marrow-derived mesenchymal stem cell (BM-MSCs) (E), adipose tissue-derived mesenchymal stem cell (Ad-MSCs) (F) or limbal epithelial stem cell (LSCs) (G). Negative control (H). (I, J): The expression of genes for K3 (I) and K12 (J) in individual experimental groups on day 12 after injury was determined by real-time polymerase chain reaction. Each bar represents the mean +/- SD from six individual corneas. The values with an asterisk represent a statistically significant ($p < .05$) difference from the values determined in untreated injured corneas.

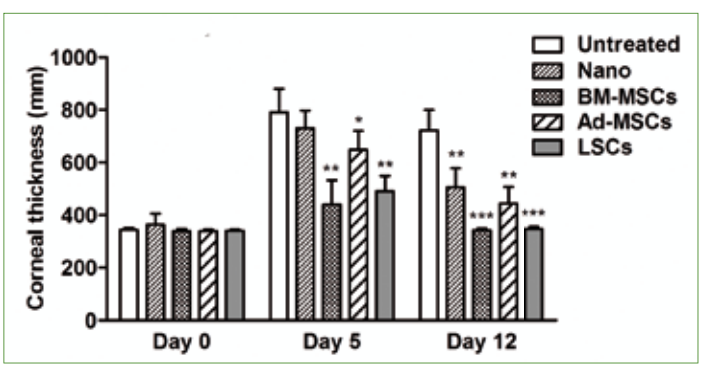

Fig.2. Corneal pachymetry. The central corneal thickness was measured in the same rabbit before injury (day 0) and on days 5 and 12 after the injury. Each bar represents the mean +/- SD from six corneas. The values with asterisks for day 5 are significantly different from those of untreated injured corneas on day 5; similarly, the values with asterisks for day 12 are significantly different from those of untreated injured corneas on day 12 (*, $p < .05$; **, $p < .01$; ***, $p < .001$). Abbreviations: Ad-MSC, adipose tissue-derived mesenchymal stem cell; BM-MSC, bone marrow-derived mesenchymal stem cell; LSC, limbal epithelial stem cell; nano, nanofiber scaffold.

Department of Tissue Engineering

Head: Prof. Evžen Amler, MSc, PhD, DSc
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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 modelling of protein structures. We develop the technology of controlled drug delivery from nanofibers scaffolds with liposomes for targeted release of drugs into the defect. Moreover, we study the surface modification of the nanofibers as well as composite blend nanofibers and its effect on cell adhesion and proliferation. The work is also concentrated on the development of three-dimensional nanofibers, using the novel technique of Forcespinning®. These nanofibers 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:
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Andrej Litvinec, MD, PhD
Eva Prosecká, MSc, PhD
Andrea Míčková, MSc, PhD
Martin Plencner, MSc, PhD

PhD Students:
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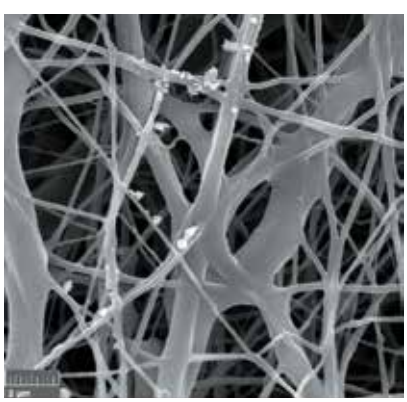
Martin Královič, MSc
Karolína Vocetková, MD
Jana Daňková, MSc
Věra Sovková, MSc
Gracián Tejral, MSc
Věra Lukášová, MSc

Undergraduate Students:
Barbora Kodedová, Bc
Veronika Blahnová, Bc
Gabriela Korbelová, Bc

Technician:
Jana Závodská

Important result in 2015

We have developed dispersion nanofibers from poly-ε-caprolactone enriched with magnetic nanoparticles prepared by needleless electrospinning



The nanofibers enhanced adhesion and osteogenic proliferation of pig MSCs and are promising for bone regeneration. (Daňková et al., 2015).

Fig. 1. Scanning electron microscopy of the poly-ε-caprolactone nanofiber scaffold with magnetic nanoparticles.
We have developed polypropylene (PP) surgical mesh coated with PCL nanofibers with adhered thrombocytes as a natural source of growth factors. The composite mesh with thrombocytes showed improved fibroblasts adhesion, proliferation, and metabolic activity compared to PP, PP coated with nanofibers, and PP functionalized with thrombocytes. The system of composite scaffold with growth factors released from thrombocytes is a promising approach for tissue engineering.

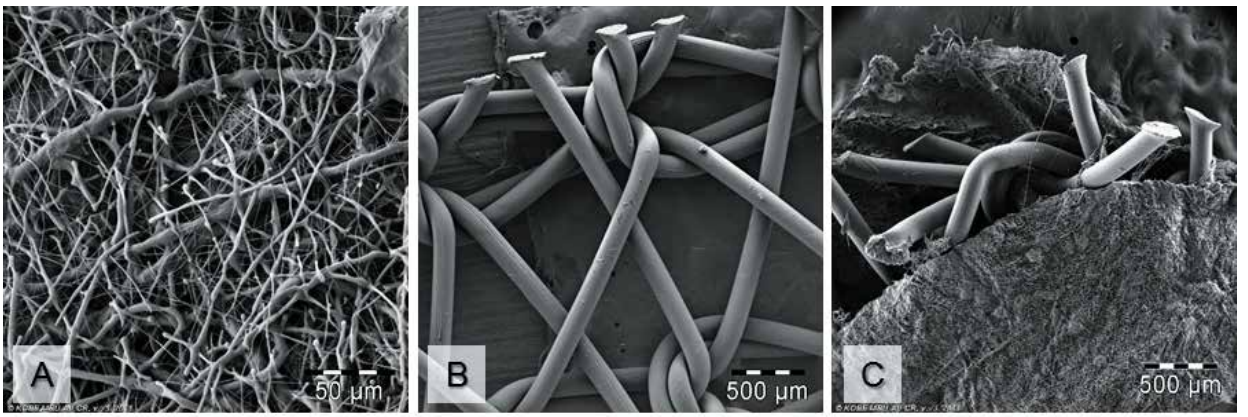


Fig. 2. Scanning electron microscopy of the implanted scaffolds. (A) PCL nanofibers; (B) PP mesh; (C) PP mesh functionalized with PCL nanofibers.
Nanofibers from polyvinyl alcohol (PVA) were functionalized by polyethylene glycol with biotin (PEG-b) linker and sequence-specific binding of avidin- antibody conjugate. PEG-b functionalized nanofibers significantly decreased nanofiber decay in a controlled manner. Moreover, the binding of anti CD-29 antibody to PEG-b linker stimulated MSCs adhesion to PVA-PEG-b nanofibers through β1-integrin receptor. The second system of the selective protein binding on the nanofiber surface represented anti-transferrin-PEG-b nanofibers.

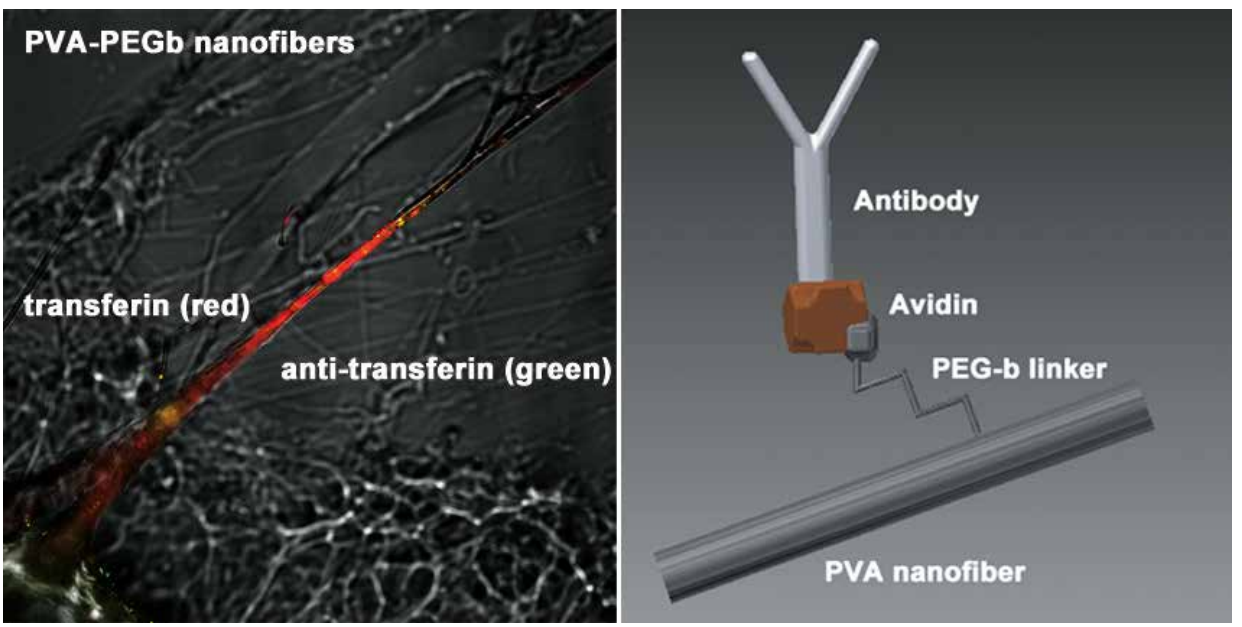


Fig. 3. Photomicrograph and schema of nanofibers from polyvinylalcohol (PVA) functionalized with polyethylene glycol with biotin (PEG-b) linker and sequence-specific binding of avidin- antibody (anti-transferin) conjugate.

Publications:

Daňková, J., Buzgo, M., Vejpravová, J., Kubíčková, S., Sovková, V., Vysloužilová, L., Mantlíková, A., Nečas, A., Amler, E.: Highly efficient mesenchymal stem cell proliferation onPCL nanofibers with embedded magnetic nanoparticles. Int J Nanomedicine. 2015 Dec 7;10:7307-17, IF 4.195

Plencner, M., Prosecká, E., Rampichová, M., East, B., Buzgo, M., Vysloužilová, L., Hoch, J., Amler, E.: 2015. Significant improvement of biocompatibility of polypropylene mesh for incisional hernia repair by using poly-ε-caprolactone nanofibers functionalized with thrombocyte-rich solution. Int J Nanomedicine. 2015 Apr 1;10:2635-2646, IF 4.195

Buzgo, M., Greplová, J., Soural, M., Bezděková, D., Míčková, A., Kofroňová, O., Benada, O., Hlaváč, J., Amler, E.: PVA immunonanofibers with controlled decay. Polymer 2015 Oct 23; 77:387-398, IF 3.562

Microscopy Unit

Head: Assoc. Prof. Jan Malínský, MSc, PhD
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We study the lateral organization of biological membranes into functional microdomains with an emphasis on their fine structure, dynamics and molecular principles of formation. Morphological changes or disintegration of these cellular structures are usually accompanied by pathological phenotypes. Taking maximum advantage of the genetically accessible yeast model, the research at the Microscopy Unit is focused on the involvement of membrane microdomains in the stress perception and adaptation, signalling and regulation of metabolic processes. Recently we described the model of general membrane structure re-organization in response to membrane depolarization as induced by environmental stimuli, pathogen or stress exposure.

Research Scientist:
Assoc. Prof. Jan Malínský, MSc, PhD
Miroslava Opekarová, MSc, PhD

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

Specialist:
Petra Veselá, MSc

Technicians:
Jitka Eisensteinová
Dagmar Folková, MSc
Lenka Hlavínová

Important results in 2015

1. Conserved 5′-3′ exoribonuclease Xrn1 is segregated at eisosomes

We have found that the main mRNA decay enzyme, 5′-3′ exoribonuclease Xrn1, accumulates at the plasma membrane-associated eisosomes after glucose exhaustion in a culture of the yeast S. cerevisiae. Plasma membrane associated localization of Xrn1 is not achieved in cells lacking the main component of eisosomes, Pil1. In contrast to the conditions, when Xrn1 accumulates in processing bodies (P-bodies), or in stress granules, Xrn1 is not accompanied by other mRNA-decay machinery components when it accumulates at eisosomes. Xrn1 is released from eisosomes after the addition of fermentable substrate. We suggest that this spatial segregation of Xrn1 from the rest of the mRNA decay machinery reflects a general regulatory mechanism, in which the key enzyme is kept separate from the rest of mRNA decay factors in resting cells but ready for immediate use when fermentable nutrients emerge and appropriate metabolism reprogramming is required.

Collaboration: Institute of Microbiology of the CAS

Fig. Localization patterns of Xrn1 during the cell culture development. Cells expressing Xrn1-GFP were observed 3 (A; log phase), 24 (B; diauxic shift), and 30 hours (C; post-diauxic shift) after the inoculation. Transversal confocal sections are presented. Bar: 5μm.

Publication:
Grousl, T., Opekarová, M., Stradalova, V., Hasek, J., Malinsky, J.: Evolutionarily Conserved 5′-3′ Exoribonuclease Xrn1 Accumulates at Plasma Membrane-Associated Eisosomes in Post-Diauxic Yeast. PLOS ONE 10(3):e0122770. Erratum in: PLOS ONE 10(4):e0126788 (2015), IF 3.234

2. Excess phosphatidylglycerol modulates mitochondrial morphology

Using fluorescence microscopy, we showed that the accumulation of phosphatidylglycerol with normal levels of cardiolipin resulted in increased fragmentation of mitochondria, while in the absence of cardiolipin, the accumulation of phosphatidylglycerol led to the formation of large mitochondrial sheets. Phosphatidylglycerol-accumulating mitochondria also exhibited increased respiration rates due to the increased activity of cytochrome c oxidase. These results indicate that excess phosphatidylglycerol or unbalanced ratios of anionic phospholipids in mitochondrial membranes have harmful consequences on mitochondrial morphology and function.

Collaboration: Institute of Animal Biochemistry and Genetics, Slovak Academy of Sciences, Ivanka pri Dunaji, Slovakia

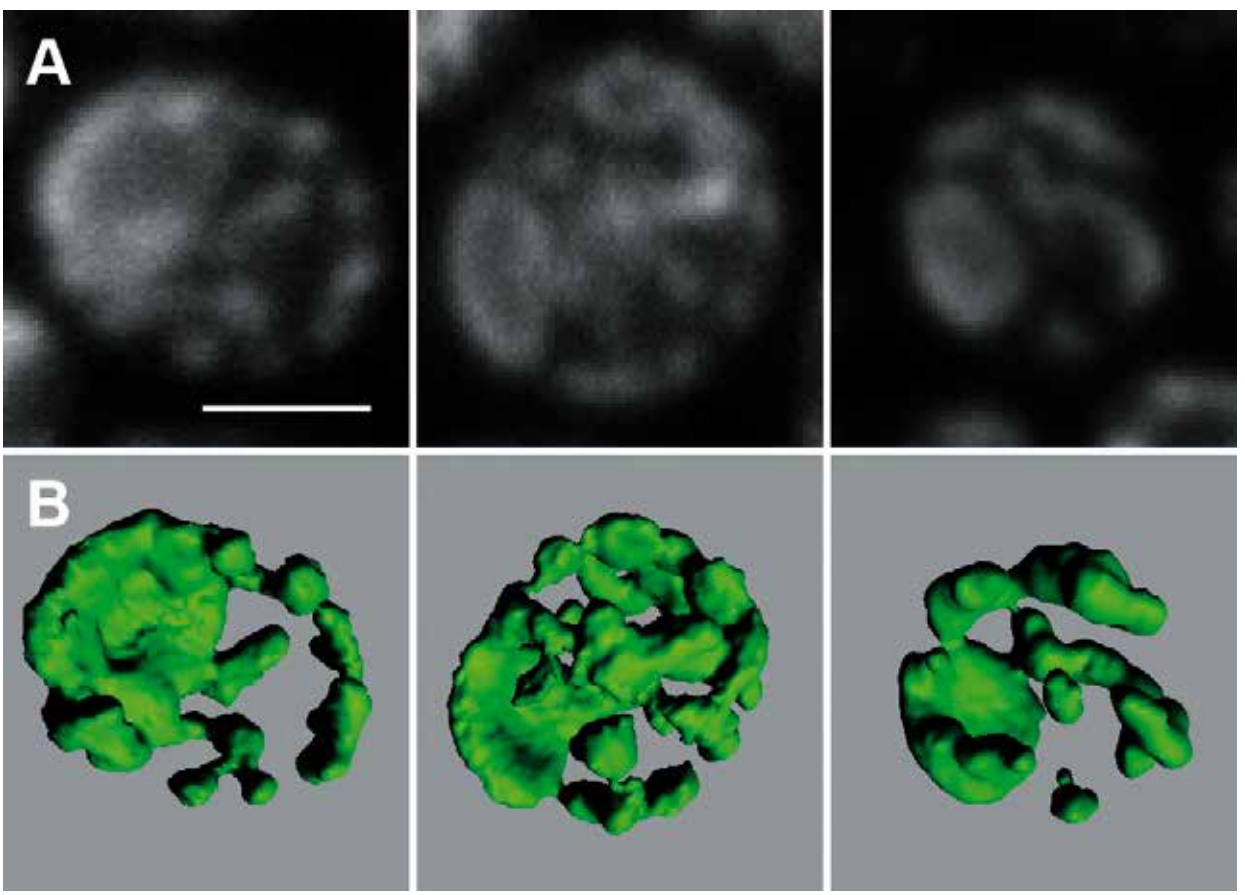

Fig. Abnormal mitochondria in cardiolipin-deficient strains of S. cerevisiae. Mitotracker Red CMX-Ros was used for mitochondrial visualization. A, three examples of cells containing Mitotracker-stained large flat sheets are presented as mean projections of five consecutive confocal sections from the cell cortex with axial spacing of 370 nm; B, isosurface projections of full 3D stacks, encompassing the whole cell. Bar: 2μm.

Publication:
Pokorna, L., Cermakova, P., Horvath, A., Baile, M.G., Claypool, S.M., Griac, P., Malinsky, J., Balazova. M.: Specific degradation of phosphatidylglycerol is necessary for proper mitochondrial morphology and function. Biochim Biophys Acta (Bioenergetics) 1857(1):34-45 (2016), IF 3.516

Department of Technological Transfer

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The Department of Technology Transfer at the IEM pursues three primary goals:

- Establishing collaborations and working relationships between industry and each of the research and creative areas of the IEM. This includes providing unique testing and evaluation services, pursuing industry sponsored research and collaborating on commercial opportunities.
- Licensing the inventions of the IEM and researchers to industry and managing the relationship between the Institute and its licensee partners.
- Serving as the economic development arm of the Institute and working with companies and entrepreneurs to leverage the resources of the IEM to the benefit of the regional and national economy.

The Department monitors and evaluates the call for projects in domestic and foreign grant programs in 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 application of the IEM project in the frame of the Czech Technology Agency (TACR) called GAMA was approved for the years 2014–2019 in a total volume of 17 million CZK.

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. In 2015, the Department assisted in the signing of two licensing agreements between the IEM and a private company and the applications of three utility models.

Project Manager EU funds:
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Innovation Biomedical Centre (IBC)

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The Innovation Biomedical Centre (IBC) aids in the development and successful start-up of spin-off companies based on scientific outputs from the Institute of Experimental Medicine. The IBC encourages cooperation between companies, research institutes and investors.

Fig. The Innovation 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, the IBC IEM of the CAS has been a member of the Science and Technology Parks CR (www.svtp.cz).

IBC activities are oriented in three, closely cooperating directions:

1. Promoting competitiveness in biomedicine (training in the fields of marketing, intellectual property protection, sales organization, management, financial management, project preparation, grant applications, legal acts related to the establishment of companies, public procurement, and assistance in the implementation of good manufacturing practice).
2. Support for applied research in biomedicine (certified services under Good Manufacturing Practice: sterility tests, sampling sets production, separation and cultivation of stem cells, etc.).
3. Business incubator for spin-off companies (help with business basics, networking activities, marketing assistance, high-speed internet access, help with accounting/financial management, access to bank loans, loan funds and guarantee programs, help with presentation skills, links to higher education resources, links to strategic partners, access to angel investors or venture capital, comprehensive business training programs, advisory boards and mentors, management team identification, help with business etiquette, technology commercialization assistance, help with regulatory compliance, intellectual property management).

Entrepreneurs who wish to enter a business incubation program must apply for admission. Acceptance criteria are based on feasible business ideas and a workable business plan.

There are also companies – virtual clients. These companies do not reside in the incubator facility. Affiliate clients may be home-based businesses or early-stage companies that have their own premises but can benefit from incubator services. Virtual clients may be too remote from an incubation facility to participate on site, and so receive counseling and other assistance electronically.

The amount of time a company spends in an incubation program can vary widely depending on a number of factors, including the type of business and the entrepreneur's level of business expertise. Life science with long research and development cycles require more time in an incubation program than manufacturing or service companies that can immediately produce and bring a product or service to market.

Bioinova, Ltd.

Bioinova was founded in 2008 as a spin-off company of the IEM of the CAS. The company focuses on the development and production of advanced-therapy medicinal products (ATMP) based on stem cells. In 2010 Bioinova obtained its Good Manufacturing Practice (GMP) license for the production of ATMP containing stem cells, it has also successfully passed several audits of the State Institute for Drug Control (SÚKL). In 2014, Bioinova was approved as a tissue establishment facility by SÚKL.
Bioinova is the sponsor of three clinical trials: AMSC-ALS-001, AMSC-RC-001, AMSC-DSD-001 and produces the ATMP for another clinical trial: AMSC-BDT-001.

In 2015, the CEO of the company remained Petr Bažant, MSc, PhD, MBA. The qualified person and the chief of the quality assurance department was Ivana Drahorádová. Michael Syka, MD worked as the pharmacovigilance and clinical projects manager. Kateřina Růžičková, PhD remained the head of the quality control department and Šimona Konrádová of the manufacturing department. Petr Rychmach and Petra Marková were responsible for the monitoring and management of the clinical trials. Tomáš Groh, PhD was appointed as PCR and FACS expert and Václav Vaněček, PhD as quality assurance expert. The team was supported by Zuzana Kočí, who focused on the preclinical studies and cell treatment innovation. Cleanroom laboratory work was conducted by an experienced team of technicians: Jana Káclová, Jana Tenkrátová, Eliška Vochomůrková and Nicole Matějčková.

Clinical projects

Since its foundation, Bioinova has worked in tight cooperation with university clinical centres on the following clinical trials: In cooperation with University Hospital Motol, Bioinova conducting the clinical trial **AMSC-ALS-001** (ongoing since 2012) that aims to verify the safety and efficacy of the intrathecal administration of autologous MSCs in patients diagnosed with ALS is mentioned above. In addition to the 26 subjects previously enrolled, the last two subjects were enrolled in the first half of 2015. A successful state regulatory authority site inspection was also performed at this time. The ongoing final data analysis started at the end of 2015 and will be presented in 2016.

The clinical trial **AMSC-DSD-001** (ongoing since 2013) focuses on using autologous MSCs in spondylosurgery to facilitate vertebral fusion in degenerative spine disease. This trial is also sponsored by Bioinova and conducted in cooperation with University Hospital Motol. In addition to 9 previously treated patients, one more subject was enrolled. Another 10 patients are planned to be enrolled in the year 2016.

Another clinical trial **AMSC-RC-001** (ongoing since 2013) focuses on using autologous MSCs in orthopedics to accelerate healing after rotator cuff surgery. This trial is also conducted by Bioinova in cooperation with University Hospital Motol. As of the end of 2015, nine subjects were enrolled. Seven subjects are planned to be enrolled in 2016.

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 MSCs on the reimplantation of hip arthroplasty. In addition to 14 previously treated subjects, 5 more patients were enrolled in 2015.

For 2016, Bioinova is preparing another phase of the ALS clinical trial to evaluate the safety and efficacy of the repeated intrathecal administration of autologous. In 2016 Bioinova will continue to prepare the multi-centre clinical trial, which is planned to be carried out in cooperation with University Hospital Motol, University Hospital Plzeň and Hospital Ústí nad Labem to evaluate the safety and efficacy of the administration of autologous MSCs 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 IEM of the CAS is directed towards the study of all the currently known types of multipotent cells. We now know that both autologous and allogenic MSCs 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

The Research Centre for Cell Therapy and Tissue Repair was built and put into operation by the Institute of Experimental Medicine of the CAS 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), for the period 2014–2019.

The 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.

The 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 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 in research projects in collaboration with universities and the improvement of researcher training and workforce development.

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, MSc, 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, MSc, PhD, DSc*
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*

The technological facilities and infrastructure of the Centre serve as utility rooms and offer access to equipment for the four research groups at the IEMof the CAS:

Department of Tissue Engineering

(Prof. Evžen Amler, MSc, PhD, DSc)

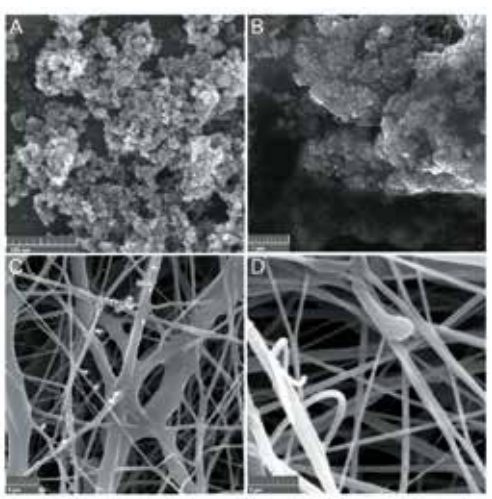
Research projects:
Development of novel functionalized nanofibers for regeneration of cartilage and bone surface functionalization of nanofibres

Results in 2015:

1. Polycaprolactone nanofibers with magnetic nanoparticles for bone regeneration

Nanofibrous scaffold made by needleless electrospinning from a mixture of poly-ε-caprolactone and magnetic particles have been developed and seeded with pig MSC. Composite nanofibers enhanced adhesion and osteogenic differentiation of MSC and is a promising scaffold for bone regeneration. (Daňková et al., 2015).

Collaborating subjects: Department of Magnetic Nanosystems, Institute of Physicsof the CAS, Prague; Department of Nonwoven Textiles, Faculty of Textile Engineering, Technical University of Liberec, Liberec



Publication:

Daňková, J., Buzgo, M., Vejpravová, J., Kubíčková, S., Sovková, V., Vysloužilová, L., Mantlíková, A., Nečas, A., Amler, E.: Highly efficient mesenchymal stem cell proliferation on poly-ε-caprolactone nanofibers with embedded magnetic nanoparticles. Int. J. Nanomed. 2015:10 Pages 7307–7317. IF 4.383

Fig. 1 A, **B** High-resolution scanning electron microscopy of the bare magnetic nanoparticles and the thawed polycaprolactone scaffold with magnetic nanoparticles (A/ magnification 65 000x, B/ magnification 20 000x); 1 **C**, **D** Scanning electron microscopy of the nanofiber scaffold with and without magnetic nanoparticles (C/ magnification 7 500x,D/ magnification 12 000x).

2. Immunonanofibres as a system of control decay and controlled cell adhesion

Nanofibers from polyvinyl alcohol (PVA) were functionalized by polyethylene glycol with biotin (PEG-b) linker and sequence-specific binding of avidin- antibody conjugate. PEG-b functionalized nanofibers significantly decreased nanofiber decay in a controlled manner. Moreover, the binding of anti CD-29 antibody to PEG-b linker stimulated MSCs adhesion to PVA-PEG-b nanofibers through β1-integrin receptor. The second system of the selective protein binding on the nanofiber surface represented anti-transferrin-PEG-b nanofibers.

Collaborating subjects: Institute of Molecular and Translational Medicine, Department of Organic Chemistry, Faculty of Science, Palacky University, Olomouc; Laboratory of Molecular Structure Character-ization, Institute of Micro-biology, Academy of Sciences of the CAS

Publication:

Buzgo, M., Greplová, J., Soural, M. Bezděková, D., Míčková, A., Kofroňová, O., Benada, O., Hlaváč, J., Amler, E.: PVA immunonanofibers with controlled decay. *Polymer* 2015 Oct 23; 77:387-398, IF 3.562

Other publications:

Rampichová, M., Vocetková, K.: "Tissue engineering" in "From functionalized nanostructures towards engineered macrostructures", eds. prof.. Carmel Caruana, Dr. Jakub Horník, Tri-state Bionanotechnology Center, e.V., Zittau, 1st edition, pp. 50-60, 2015 Chapter 2 Cell-seeded Scaffolds for Regenerative Medicine ISBN 978-80-88113-19-5 (softback), ISBN 978-80-88113-20-1 (hardback)

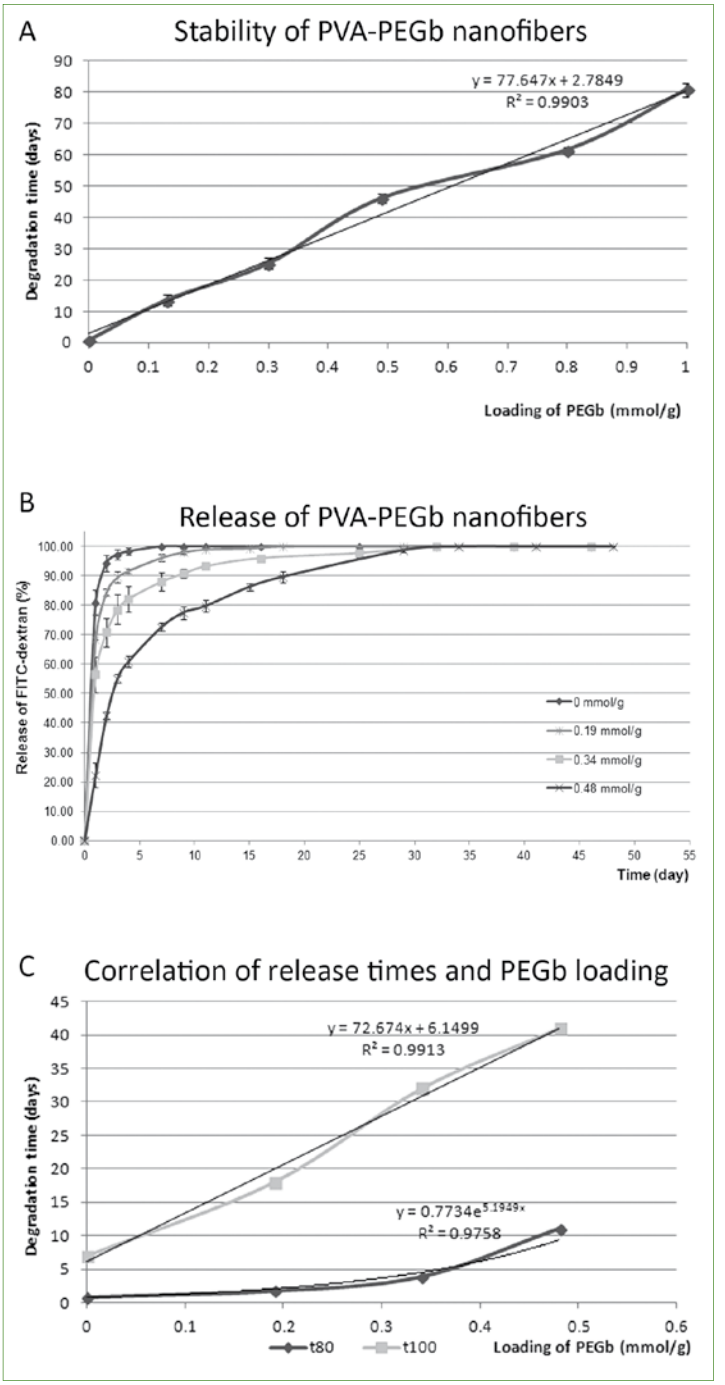
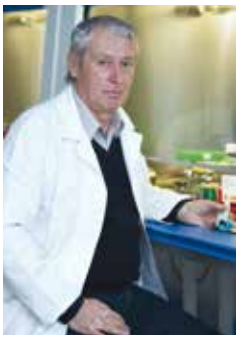


Fig. 2 Stability of modified nanofibers. (A) Determination of degradation time of PVA and PVA-PEG-b. (B) FITC-dextran was incorporated into nanofibers by blend electrospinning and the cummulative release profile was determined for unmodified PVA (0 mmol/g) and PVA modified with 0.19 mmol/g, 0.34 mmol/g, and 0.48 mmol/g PEG-b. (C) Correlation of release times and PEG-b loading.

Prosecká, E.: Bone Tissue Engineering in "From functionalized nanostructures towards engineered macrostructures", eds. prof.. Carmel Caruana, Dr. Jakub Horník, Tri-state Bionanotechnology Center, e.V., Zittau, 1st edition, pp. 99–106, 2015 Chapter 2 Cell-seeded Scaffolds for Regenerative Medicine. ISBN 978-80-88113-19-5 (softback), ISBN 978-80-88113-20-1 (hardback)

Kubíková, T., Filová, E., Prosecká, E., Plencner, M., Králíčková, M., Tonar, Z.: Histologické hodnocení vlivu *in vivo* aplikace biomateriálů na hojení chrupavky, kosti a kůže, Časopis lékařů českých, 154 (3), 110-114.



Department of Transplantation Immunology

(Prof. Vladimír Holáň, MD, DSc)

Research projects:
The therapeutic and anti-inflammatory potential of MSCs. Cell-based therapy of tissue defects or damages is often limited by the absence of available tissue-specific stem cells. To test the possibility to overcome the shortage of tissue-specific stem cells, we tested the possibility to replace them with MSCs, which can be obtained relatively easy from bone marrow or adipose tissue of the patients. Using a model of chemically induced damage of ocular surface, which is associated with the deficiency of tissue specific limbal stem cells (LSCs), we showed that MSCs can successfully replace the rare LSCs. We showed that LSCs and MSCs have comparable immunomodulatory properties and both these cell types comparably supported corneal healing, local inflammatory reaction and improved corneal transparency. The results thus showed that MSCs can effectively replace rare or absent tissue-specific LSCs.

Results in 2015:

Comparative study on the therapeutic potential of mesenchymal stem cells and tissue-specific limbal stem cells

Collaborating subjects: Faculty of Natural Science, Charles University, Prague, and European Eye Clinic Lexum, Prague

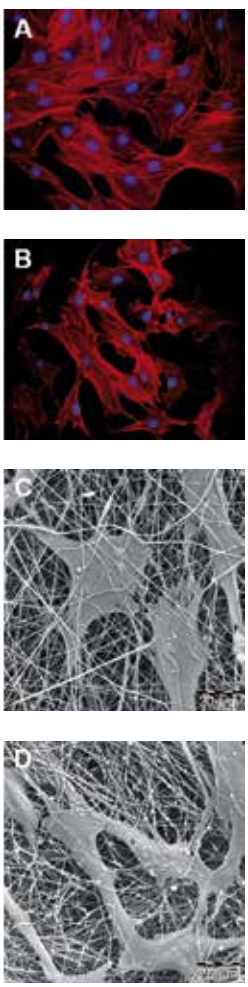


Fig. The growth of mesenchymal stem cells (MSCs) and limbal stem cells (LSCs) on plastic and nanofiber scaffolds. MSCs (**A**) or LSCs (**B**) growing on plastic were stained for F-actin with phalloidin (red filaments, nuclei – blue), or were growing on nanofiber scaffolds and the pictures were taken by scanning electron microscope (**C**, **D**).

Publication:

Holan, V., Trosan, P., Cejka, C., Javorkova, E., Zajicova, A., Hermankova, B., Chudickova, M., Cejkova, J.: A comparative study of the therapeutic potential of mesenchymal stem cells and limbal epithelial stem cells for ocular surface reconstruction. Stem Cells Translat. Med. 4, 1052-1063, 2015, IF 5.709

Other publications:

Hajkova, M., Javorkova, E., Zajicova, A., Trosan, P., Holan, V., Krulova, M.: A local application of MScs and Cyclosporine A attenuates immune response by a switch in macrophage phenotype. J. Tissue Eng. Regen. Med., 2015 Jun 29. doi: 10.1002/term.2044. [Epub ahead of print]. 2015, IF 5.199

Chudickova, M., Bruza, P., Zajicova, A.., Trosan, P., Svobodova, L., Javorkova, E., Kubinova, K., Holan, V.: Targeted neural differentiation of murine mesenchymal stem cells by a protocol simulating the inflammatory site of neural injury. J. Tissue Eng. Regen. Med., 2015 Jun 29. doi: 10.1002/term.2059. [Epub ahead of print], IF 5.199

Cejka, C., Cejkova, J., Trosan, P., Zajicova, A., Sykova, E., Holan, V.: Transfer of mesenchymal stem cells and cyclosporine A on alkalli injured rabbit cornea using nanofiber scaffolds strongly reduces corneal neovascularization and scar formation. Histol. Histopathol., in press, IF 2.096

Cejka, C., Holan, V., Trosan, P., Zajicova, A., Javorkova, E., Cejkova, J.: Favorable effect of mesenchymal stem cell treatment on the antioxidant protective mechanism in the corneal epithelium and renewal of corneal optical properties changed after alkali burns. Oxid. Med. Cell. Longev., in press, IF 3.516

Hermankova, B., Zajicova, A., Javorkova, E., Chudickova, M., Trosan, P., Hajkova, M., Krulova, M., Holan, V.: Suppression of IL-10 production by activated B cells via a cell contact-dependent cyclooxygenase-2 pathway upregulated in IFN-γ-treated mesenchymal stem cells. Immunobiology 221, 129-136, 2016, IF 3.795

Department of Neuroscience

(Prof. Eva Syková, MD, PhD, DSc, FCMA)

Laboratory of Stem Cell and Tissue Cultures

(Assoc. Prof. Pavla Jendelová, MSc, PhD)

Results in 2015:

Biological effects of silica encapsulated cobalt zinc ferrite nanoparticles in rat bone marrow mesenchymal stem cells.

Cobalt zinc ferrite nanoparticles (Co0.5Zn0.5Fe2O4+γ [CZF-NPs]) encapsulated by amorphous silica were prepared and tested in order to find a safe contrast agent and magnetic label for tracking transplanted cells within an organism using magnetic resonance imaging (MRI). No harmful effects were detected in cells exposed to the low dose of CZF-NPs. Nevertheless, the labelled cells still exhibited an adequate relaxation rate for MRI in repeated experiments and ICP-MS confirmed sufficient magnetic label concentrations inside the cells.

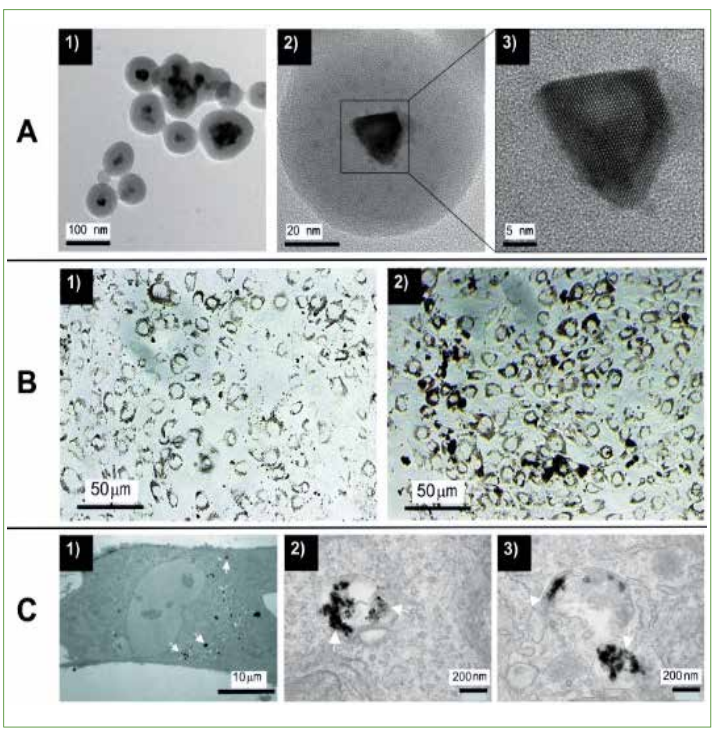


Fig. Labelling of rat bone marrow mesenchymal stem cells (MSCs) with cobalt zinc ferrite nanoparticles (CZF-NPs). (A) TEM observations of nanoparticles: low magnification image (1), high resolution-TEM image of a single particle (2) and its core (3). (B) Light microscopy images of cell cultures labelled with 0.05 mM (1) or 0.11 mM of CZF-NPs (2). (C) TEM micrographs of rat bone marrow stem cell labelled with CZF-NPs (1) and higher magnification views (2,3) showing clusters of NPs visible as black spots (white arrows) inside the endosomes/lysosomes and cytoplasm.

Publication:

Novotna, B., Turnovcova, K., Veverka, P., Rössner, P. Jr., Bagryantseva, Y., Herynek, V., Zvatora, P., Vosmanska, M., Klementova, M., Sykova, E., Jendelova, P.: The impact of silica encapsulated cobalt zinc ferrite nanoparticles on DNA, lipids and proteins of rat bone marrow mesenchymal stem cells. Nanotoxicology. 2015 Nov 18:1-9. [Epub ahead of print]

Other publications:

Lukovic, D., Moreno-Manzano, V., Lopez-Mocholi, E., Rodriguez-Jiménez, F.J., Jendelova, P., Sykova, E., Oria, M., Stojkovic, M., Erceg, S.: Complete rat spinal cord transection as a faithful model of spinal cord injury for translational cell transplantation. Sci Rep. 2015 Apr 10;5:9640.

Lukovic, D., Stojkovic, M., Moreno-Manzano, V., Jendelova, P., Sykova, E., Bhattacharya, S.S., Erceg, S.: Concise review: reactive astrocytes and stem cells in spinal cord injury: good guys or bad guys? Stem Cells. 2015 Apr;33(4):1036-41.

Romanyuk, N., Amemori, T., Turnovcova, K., Prochazka, P., Onteniente, B., Sykova, E., Jendelova, P.: Beneficial Effect of Human Induced Pluripotent Stem Cell-Derived Neural Precursors in Spinal Cord Injury Repair. Cell Transplant. 2015;24(9):1781-97

Laboratory of Biomaterials and Biophysical Methods

(Šárka Kubinová, PharmD, PhD)

Research topics:

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 Physiology of the CAS, we perform complex research on the low-temperature plasma effects on biological systems as well as develop novel devices for medical applications.

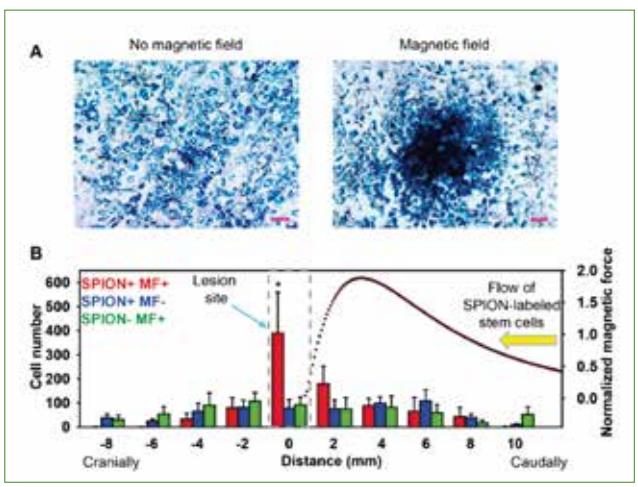
Research projects of the Laboratory:

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

Result in 2015:

An effective strategy of magnetic stem cell delivery for spinal cord injury therapy

In this study, we designed a magnetic system and used it to accumulate stem cells labelled with superparamagnetic iron oxide nanoparticles (SPION) at a specific site of a spinal cord injury lesion. Histological analysis of cell distribution on the spinal cord surface showed a good correlation with the calculated distribution of magnetic forces exerted onto the transplanted cells. The results suggest that focused targeting and fast delivery of stem cells can be achieved using the proposed non-invasive magnetic system.



Collaborating subject: Institute of Physics of the CAS

Fig. Distributions of SPION-labelled cells and non-labelled cells with and without the magnetic field. (A) Attraction of SPION-labelled cells to a cylindrical magnet *in vitro*. MSCs were labelled with SPIONs and exposed to an external magnetic field for 48 h. Cells were stained for intracellular iron using Prussian blue. Scale bar: 100 µm. (B) Numbers of the captured SPION-labelled cells and non-labelled cells in the rat model as a function of the distance from the lesion site of the SCI. After the induction of the lesion, SPION-labelled MSCs were injected intrathecally at the L5–L6 level, at a distance of 10 cm from the lesion site. Thereafter, animals were subjected to the magnetic system exposure for 2 h in longitudinal spinal cord segments. The dotted curves represent the respective magnetic gradient force distribution. Data are expressed as mean ± SEM, *P < 0.05.

Publication:

Tukmachev, D., Lunov, O., Zablotskii, V., Dejneka, A., Babic, M., Sykova, E., Kubinova, S.: An effective strategy of magnetic stem cell delivery for spinal cord injury therapy. Nanoscale. 2015;7(9):3954-8, IF 7.39

Other publications:

Jelinek, 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. 2015;46(0):381-6, IF 3.09

Lunov, O., Churpita, O., Zablotskii, V., Deyneka, I.G., Meshkovskii, I.K., Jäger, A., Syková, E., Kubinová, Š., Dejneka, A.: Non-thermal plasma mills bacteria: Scanning electron microscopy observations. Appl Phys Lett. 2015, 106, 053703, IF 3.30

Chudickova, M., Bruza, P., Zajicova, A., Trosan, P., Svobodova, L., Javorkova, E., Kubinova, S., Holan, V.: Targeted neural differentiation of murine mesenchymal stem cells by a protocol simulating the inflammatory site of neural injury. J Tissue Eng Regen Med. 2015 Jun 29. doi: 10.1002/term.2059. [Epub ahead of print], IF 5.20

Awards

Prof. Josef Syka, MD, DSc, Dr. h. c.

– Honour of the medal De Scientia et Humanitate Optime Meritis of the CAS

Medal of Merit for the Advancement of Science / Awarded by: Prof. Jiří Drahoš, MSc, DSc. Dr.h.c., chairman of the CAS

Prof. Syka is an internationally recognized scientist in the field of the neurophysiology of hearing. Throughout his career he has worked together with the Academy of Sciences of the Czech Republic. Since 1975, he has led the Auditory Neuroscience laboratory at the Institute of Experimental Medicine of the CAS. In the 90s he significantly contributed to the transformation of the Academy of Sciences and the entirety of Czech science as Deputy Chairman of the Government Council for Science and Technology Development (1993–2000). In the years 2000–2008 he was Chairman of the Grant Agency of the CR. He has also been a member of the Academic Council of the ASCR between 1992–1993 (his membership ended when he became the Director of the Institute of Experimental Medicine of the CAS, which he headed until 2000) and from 2001–2009 he also founded and became the first Chairman of the Czech Society for Neuroscience. "Hearing is an organic part of the brain. When we hear wrong, it's not just the fact that we have problems with our ears," says Profesor Syka.

– Silver commemorative medal of the Senate / For outstanding scientific work / Awarded by: Milan Štech, Chairman of the Senate of the Czech Parliament

On the occasion of the Day of Czech Statehood, the Chairman of the upper house of the Czech Parliament, Milan Stech, awarded seven people with silver commemorative medals in the name of science. The Senate President recalled that the medals are intended to show the symbolic appreciation of personalities whose work contributes to spreading the good name of the Czech Republic in the world. The laureates include personalities in the fields of science, culture, social life, sports and those who in a difficult situation have shown great personal courage. Among the physicians honored was neuro-physiologist Josef Syka for his lifetime research into hearing.

– Gold Commemorative Medal of Charles University / Awarded by: Prof. Tomáš Zima, MD, DSC, Rector of Charles University on a proposal from the 1st Faculty of Medicine

At the suggestion of the 1st Medical Faculty of Charles University on the occasion of it's jubilee, Prof. Josef Syka was awarded the gold commemorative medal of Charles University.

40th anniversary of the founding of the IEM of the CAS

On Monday, November 2, 2015 the Institute of Experimental Medicine of the CAS, EU Centre of Excellence, a major research institution in the field of basic biomedical research in the Czech Republic, celebrated its 40th anniversary with gala event in the ancient Carolinum, which was attended by distinguished guests from the scientific and university communities. A greeting from Prof. Jiri Drahos, President of the Academy of Sciences, was delivered by Prof. Eva Zažímalová, a member of the Academic Board.

– Medal of the Institute of Experimental Medicine of the CAS

Medal for Cooperation and Scientific Development

Jan Kolář
Assoc. Prof. Alexandr Chvátal, MSc, DSc, MBA
Ivana Kolářová
Zdeněk Zídek, MSc, PhD, DSc
Assoc. Prof. Miroslav Peterka, MD, PhD, DSc
Renata Peterková, MD, PhD
Dr. Govindan Dayanithi, MSc, PhD

On the occasion of the Jubilee the director of the institute, Prof. Eva Syková awarded the Commemorative Medal of Merit for cooperation and scientific development to seven colleagues at the institute and reflected on the importance of science as one of the main pillars of advanced societies. "Those who financially support research are also dedicated to the future," emphasized Prof. Syková. "It is therefore necessary to pay particular attention to the support of scientific research itself. While modern science is separated from global and national economies, it's main aim is to improve the quality of life," said Prof. Syková.

Research Projects in 2015

Explanations:

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

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

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

TAO – Technology Agency of the Czech Republic (TA ČR):
TA – Program of applied research and experimental development ALFA
TE – Competence Centres
TG – Program 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 of the CAS
Principal investigator: Prof. Eva Syková, MD, PhD, DSc, FCMA
Duration: 2012–2015

EE2.3.30.0018 MSM

Development of Research Teams of IEM of the CAS for the BIOCEV

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Prof. Eva Syková, MD, PhD, DSc, FCMA
Duration.: 2012–2015

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 of the CAS, Institute of Physics of the CAS, Institute of Chemical Technology in Prague
Investigator: Assoc. Prof. Pavla Jendelová, MSc, 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 for 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 of the CAS
Investigator: Pavel Procházka, PhD
Duration: 2012–2016

GAP303/11/0131 GAO

Ectopic release of glycine – physiological role and mechanism

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Michaela Králíková – Havlíčková, MSc, PhD
Duration: 2011–2015

GAP303/12/0172 GAO

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

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Zdeněk Zídek, MD, DSc, PhD
Project participant: Institute of Organic Chemistry and Biochemistry of the CAS
Investigator: Zlatko Janeba, PhD
Duration: 2012–2016

GAP303/12/0535 GAO

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

Contractor: Institute of Microbiology of the CAS
Principal investigator: Tomáš Hudcovic, PhD
Project participant: Institute of Experimental Medicine of the CAS
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 signalling pathway

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Miroslava Anděrová, MSc, 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 of the CAS
Principal investigator: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
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 of the CAS
Investigator: Prof. Eva Syková, MD, PhD, DSc, FCMA
Duration: 2010–2015

GAP304/12/1342 GAO

Pathological changes in the central auditory system accompanying aging

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Jiří Popelář, MSc, 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 of the CAS
Principal investigator: Assoc. Prof. Pavla Jendelová, MSc, PhD
Duration: 2012–2015

GAP304/12/1585 GAO

Molecular DNA repair characteristics in CRC tumour 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 of the CAS
Investigator: Ludmila Vodičková, MD, PhD
Project participant: State Health Institute Prague
Investigator: Simona Šůsová, MSc
Project participant: Institute of Biotechnology of the CAS
Investigator: Vlasta Korenková, PhD
Duration: 2012–2015

GAP305/12/1766 GAO

Rudiments in the mouse model of tooth development

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Mária Hovořáková, MSc, 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 of the CAS
Principal investigator: Jan Topinka, MsC, PhD, DSc
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 of the CAS
Principal investigator: Assoc. Prof. Pavla Jendelová, MSc, PhD
Project participant: Institute of Macromolecular Chemistry of the CAS
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 of the CAS
Principal investigator: Jan Topinka, MsC, PhD, DSc
Project participant: Institute of Analytical Chemistry of the CAS
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 of the CAS
Principal investigator: Prof. Mikael Kubista, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Miroslava Anděrová, MSc, PhD
Duration: 2013–2016

GA13-07996S GAO

Molecular mechanisms responsible for generating cellular diversity in the inner ear

Contractor: Institute of Biotechnology of the CAS
Principal investigator: Gabriela Pavlínková, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
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 of the CAS
Investigator: Jiří Popelář, MSc, PhD
Duration: 2013–2015

GA13-13458S GAO

Impact of air pollution to genome of newborns

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Radim Šrám, 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 for Clinical and Experimental Medicine
Principal investigator: Robert Bem, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Prof. Eva Syková, MD, PhD, 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 of the CAS
Principal investigator: Prof. Vladimír Holáň, MSc, PhD, DSc
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 of the CAS
Principal Investigator: Aleš Hejčl, MD, PhD
Project participant: Institute of Macromolecular Chemistry of the CAS
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 of the CAS
Principal investigator: Michaela Králíková – Havlíčková, MSc, 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 of the CAS
Principal investigator: Dr. Govindan Dayanithi, MSc, PhD
Duration: 2014–2016

GA15-01396S GA0

Development of tissue-specific biological scaffolds for neural tissue repair

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Šárka Kubinová, PharmD, PhD
Duration: 2015–2017

GA15-02760S GA0

Role of the aquaporin channel AQP4 in the development of cytotoxic brain edema following brain ischemia/reperfusion

Contractor: Charles University in Prague, 2nd Medical Faculty
Principal investigator: Assoc. Prof. Lýdia Vargová, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Principal investigator: Miroslava Anděrová, MSc, PhD
Duration: 2015–2017

GA15-06958S GA0

Intrathecal and intramuscular application of mesenchymal stem cells and their secretome in the treatment of amyotrophic lateral sclerosis

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Assoc. Prof. Pavla Jendelová, MSc, PhD
Project participant: Charles University in Prague, 2nd Medical Faculty
Principal investigator: Aleš Homola, MD, PhD
Duration: 2015–2017

GA15-08239S GA0

The diagnostic, predictive and prognostic role of microRNA signature in rectal cancer

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Jana Slyšková, MSc, PhD
Project participant: Institute for Clinical and Experimental Medicine
Principal investigator: Prof. Julius Špičák, MD, PhD
Project participant: Institute of Biotechnology of the CAS
Principal investigator: Vlasta Korenková, MSc, PhD
Duration: 2015–2017

GA15-10641S GA0

Specific plasma membrane microdomains in regulation of aging

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Assoc. Prof. Jan Malínský, MSc, PhD
Duration: 2015–2017

GA15-14789S GA0

Stress response to DNA damage in colorectal carcinogenesis

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Pavel Vodička, MD, PhD
Project participant: Institute of Molecular Genetics of the CAS
Principal investigator: Ladislav Anděra, MSc, PhD
Duration: 2015–2017

GA15-15697S GA0

Three-dimensional nanofibrous scaffolds with incorporated controlled drug delivery system for bone and osteochondral tissue engineering

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Prof. Franco Rustichelli
Project participant: The Czech Technical University / University Centre for Energy Efficient Buildings Principal
Investigator: Michala Rampichová, MSc, PhD
Duration: 2015–2017

GBP304/12/G069 GAO

Project of excellence in the field of neuroscience

Contractor: Institute of Physiology of the CAS
Principal investigator: Assoc. Prof. Ladislav Vyklický Jr., MD, DSc
Project participant: The National Institute of Mental Health
Investigator: Daniela Řípová, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
Project participant: Charles University, 2nd Faculty of Medicine
Investigator: Miroslava Anděrová, MSc, PhD
Duration: 2012–2018

GBP503/12/G147 GAO

Centre of Studies toxic properties of nanoparticles

Contractor: Veterinary Research Institute
Principal investigator: Miroslav Machala, PhD
Project participant: Institute of Chemical Process Fundamentals of the CAS
Investigator: Pavel Moravec, PhD
Project participant: Institute of Animal Physiology and Genetics of the CAS
Investigator: Assoc. Prof. Omar Šerý, PhD
Project participant: Institute of Analytical Chemistry of the CAS
Investigator: Zbyněk Večeřa, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Jan Topinka, MsC, PhD, DSc
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 of the CAS
Principal investigator: Renata Peterková, MD, PhD
Project participant: Institute of Animal Physiology an Genetics of the CAS
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

GP13-15031P GAO

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

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Lucia Machová-Urdzíková, 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 of the CAS
Principal investigator: Jan Topinka, DSc, PhD
Duration: 2014–2016

LD14050 MSM

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

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Pavel Vodička, 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 of the CAS
Principal investigator: Assoc. Prof. Pavla Jendelová, MSc, 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 of the CAS
Principal investigator: Pavel Vodička, MD, PhD
Duration: 2013–2015

LO1309 MSM

Cell Therapy and Tissue Repair

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Šárka Kubinová, PharmD, PhD
Duration: 2014–2019

NT12459 MZ

Possibilities of hearing preservation in patients with vestibular schwannoma

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
Project participant: University Hospital Motol
Investigator: 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 investigator: Miroslav Levý, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Pavel Vodička, MD, PhD
Duration: 2012–2015

NT13477 MZ

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

Contractor: Charles University in Prague, Faculty of Medicine in Hradec Kralové
Principal investigator: Pavel Šponer, MD, PhD
Project participant: University Hospital in Hradec Králové
Investigator: Assoc. Prof. Karel Urban, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Prof. Eva Syková, MD, PhD, 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
Investigator: Prof. Milan Macek Jr., MD, DSc
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Božena Novotná, MSc, PhD
Duration: 2012–2015

NT14056 MZ

Molecular and genetic biomarkers of ovarian cancer pathogenesis and resistance

Contractor: State Health Institute Prague
Principal contractor: Radka Václavíková, PhD
Project participant: University Hospital Motol
Investigator: Prof. Lukáš Rob, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Pavel Vodička, MD, PhD
Duration: 2013–2015

NT14102 MZ

A role of B lymphocytes in immune reactions after kidney transplantation

Contractor: Institute for Clinical and Experimental Medicine
Principal investigator: Prof. Ondřej Viklický, MD, PhD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Prof. Vladimír Holáň, MSc, PhD, DSc
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
Investigator: Petr Novák, MD
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Pavel Vodička, MD, PhD
Project participant: State Health Institute Prague
Investigator: Pavel Souček, PhD
Duration: 2013–2015

NV15-26535A MZ

The role of genetic variations in microRNA genes and in microRNA binding sites in colorectal cancer in relation to personalized therapy

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Veronika Vymetálková, MSc, PhD
Project participant: Thomayer Hospital
Principal investigator: Tomáš Büchler, MD, PhD
Duration: 2015–2018

NV15-27580A MZ

Waste perception, oxidative damage and colon microenvironment in colorectal carcinogenesis: impacts on the disease risk, prognosis and prevention

Contractor: Institute of Experimental Medicine of the CAS
Principal investigator: Pavel Vodička, MD, PhD
Project participant: University Hospital in Pilsen
Principal investigator: Václav Liška, MD, PhD
Project participant: RADANAL, Ltd
Principal investigator: Assoc. Prof. Aleš Horna, MSc, PhD
Project participant: Institute of Microbiology of the CAS
Principal investigator: Klára Klimešová, MSc, PhD
Duration: 2015–2019

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 of the CAS
Investigator: Šárka Kubinová, PharmD, PhD
Project participant: Institute of Physics of the CAS
Investigator: Alexandr Dejneka, PhD
Duration: 2014–2017

TE01020028 TAO

Centre for Development of Original Drugs

Contractor: Institute of Organic Chemistry and Biochemistry of the CAS
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 of the CAS
Investigator: Ladislav Vyklický, MD, DSc
Project participant: Institute of Experimental Medicine of the CAS
Investigator: Zdeněk Zídek, MSc, PhD, DSc
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 of the CAS
Principal investigator: Prof. Eva Syková, MD, PhD, 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 of the CAS
Investigator: Assoc. Prof. Pavla Jendelová, MSc, PhD
Project participant:
Norges teknisk-naturvitenskapelige universitet
Investigator: Ioanna Sandvig, PhD
Duration: 2014–2017

Research Infrastructures

ED CZ.1.05/1.1.00/02.0109 MSM

Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University in Vestec

Contractor: Institute of Molecular Genetics CAS
Project participant: Institute of Biotechnology CAS, Institute of Microbiology CAS, Institute of Physiology CAS, Institute of Experimental Medicine of the CAS, and Institute of Macromolecular Chemistry CAS and two faculties of Charles University in Prague (Faculty of Science and 1st Faculty of Medicine)
Investigator (IEM CAS): Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.; Assoc. Prof. Pavla Jendelová, PhD
Duration: 2012–2015



LM2015064 MSM

Czech National Node of European Infrastructure for Translation Medicine (EATRIS-CZ)

Contractor: The Palacky University, Olomouc
Principal Investigator: Assoc. Prof. Marián Hajdúch, MD, PhD
Project participants: University of Chemistry and Technology, Prague, Investigator: Prof. Vladimír Král, DSc
Institute of Organic Chemistry and Biochemistry CAS, Investigator: Prof. Martin Fusek, MSc.
Charles University, Prague, Investigator: Prof. Aleksi Šedo, MD, DSc
Institute of Macromolecular Chemistry CAS, Investigator: Dr. Petr Štěpánek, DSc
Nuclear Physics Institute CAS, Investigator: Assoc. Prof. Ondřej Lebeda, PhD
Institute of Microbiology CAS, Investigator: Radim Osička, MSc, PhD
Institue of Experimental Medicine of the CAS, Investigator: Prof. Eva Syková, MD, DSc, FCMA

International Projects and EU Framework Programs

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

Acronym: **MEDETOX**
Coordinator: Institute of Experimental Medicine of the CAS
Investigator: Jan Topinka, MSc, PhD, DSc
Duration: 2011 – 2016

COST Action MP1005 – Namabio

Type of cooperation: **COST** (Cooperation in Science and Technology)
Coordinator: Prof. Franco Rustichelli
Co- Coordinator: The Institute of Experimental Medicine of the CAS, Prof. Evžen Amler, MSc, PhD, DSc
Duration: 2011–2015

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

Acronym: **CITI-SENSE**
Coordinator: NILU-Norway Institute for Air Research, Kjeller, Norway
Co- Coordinator: Institute of Experimental Medicine of the CAS
Investigator: Radim Šrám, MD, DSc
Duration: 2012– 2016

Quality-nano research infrastructure

Acronym: **QNANO**
Coordinator: University College Dublin, Ireland
Investigator: Jan Topinka, MSc, PhD, DSc
Duration: 2014–2015

A Common European Approach to the Regulatory Testing of Nanomaterials

Acronym: **NANOREG**
Coordinator: Ministerie van Infrasructuur en Milieu, The Netherlands
Investigator: Jan Topinka, MSc, PhD, DSc
Duration: 2014–2016

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

Acronym: **TARGEAR**
Coordinator: CSIC, Španělsko
Investigator: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.
Duration: 2014–2017

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, The Institute of Experimental Medicine of the CAS
Duration: 2014–2016

Modelling Nanomaterial Toxicity

Acronym: **MODENA**
Type of cooperation: COST (Cooperation in Science and Technology)
Coordinator: Prof. Lang Tran, Institute of Occupational Medicine, Edinburgh, U.K.
Co-coordinator: Jan Topinka, MSc, PhD, DSc, Institute of Experimental Medicine of the CAS
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, University of Magdeburg, Germany; Alexandr Dityatev (Germany),
Co-coordinator: Prof. Syková, MD, DSc; L. Vargová, PhD, Institute of Experimental Medicine of the CAS

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

Acronym: **KONTAKT II**
Type of cooperation: VaVaI to support international collaboration in research and development
Coordinator: Institute of Experimental Medicine of the CAS
Co-coordinator: Assoc. Prof. Pavla Jendelová, MSc, PhD
Duration: 2011–2015

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, PhD, DSc, FCMA, Dr. h.c., Institute of Experimental Medicine of the CAS

Publications

Impacted publications that came out in late 2014 and deployed or in print for 2015

Total Number of Publications with IF	**80**
Total IF	**302.951**
Average IF per Publication	**3.787**
Other Publications without IF	**11**
Book Chapters in English	**3**
Book Chapters in Czech	**1**
Book	**1**

DEPARTMENT OF NEUROSCIENCE

Amemori, T., Jendelová, P., Růžička, J., Urdziková, L.M., Syková, E.: (2015) Alzheimer's Disease: Mechanism and Approach to Cell Therapy. *Int J Mol Sci.* 16(11):26417-26451. **IF 2.862**

Amemori, T., Růžička, J., Romanyuk, N., Jhanwar-Uniyal, M., **Syková, E., Jendelová, P.**: (2015) Comparison of intraspinal and intrathecal implantation of induced pluripotent stem cell-derived neural precursors for the treatment of spinal cord injury in rats. *Stem Cell Res Ther.* 6(1):257. **IF 3.368**

Babič, M., Schmiedtová, M., Poledne, R., **Herynek, V.,** Horák, D.: (2015) *In vivo* monitoring of rat macrophages labeled with poly(l-lysine)-iron oxide nanoparticles. *J Biomed Mater Res B Appl Biomater.* 103(6):1141-1148. **IF 2.759**

Forostyak, O., Romanyuk, N., Verkhratsky, A., **Syková, E., Dayanithi G.**: (2015) Plasticity of calcium signaling cascades in human embryonic stem cell-derived neural precursors. *Stem Cells Dev.* 22(10):1506-1521. **IF 3.727**

Havlas, V., Kotaška, J., Koníček, P., Trč, T., **Konrádová, Š., Kočí, Z., Syková, E.**: (2015) Use of cultured human autologous bone marrow stem cells in repair of a rotator cuff tear: preliminary results of a safety study. *Acta Chir Orthop Traumatol Cech.* 82(3):229-234. **IF 0.388**

Hejčl, A., **Jendelová, P.**, Sameš, M., **Syková, E.**: (2015) Experimental Treatment of Spinal Cord Injuries. *Česká Slovenská neurologie a neurochirurgie* 78(4): 377-392. **IF 0.165**

Chudičková, M., Brůža, P., **Zajícová, A., Trošan, P., Svobodová, L., Javorková, E., Kubinová, S., Holáň, V.: (2015)** Targeted neural differentiation of murine mesenchymal stem cells by a protocol simulating the inflammatory site of neural injury. *J Tissue Eng Regen Med.* IN PRESS, **IF 5.199**

Jendelová, P., Kubinová, Š., Sandvig, I., Erceg, S., Sandvig, A., Syková, E.: (2015) Current developments in cell – and biomaterial-based approaches for stroke repair. *Expert Opin Biol Ther.* 1-14. IN PRESS, **IF 3.743**

Jelínek, M., Kocourek, T., Zemek, J., Mikšovský, J., **Kubinová, Š.,** Remsa, J., Kopeček, J., Jurek, K.: (2015) Chromium-doped DLC for implants prepared by laser-magnetron deposition. *Mater. Sci. Eng. C-Mater. Biol. Appl.* 46: 381-386. **IF 3.088**

Kubinová, Š., Horák, D., **Hejčl, A.,** Plichta, Z., Kotek, J., Proks, V., **Forostyak, S., Syková, E.:** (2015) SIKVAV-modified highly superporous PHEMA scaffolds with oriented pores for spinal cord injury repair. *J Tissue Eng Regen Med.* 9(11): 1298-1309. **IF 5.199**

Lukovic, D., Moreno-Manzano, V., Lopez-Mocholi, E., Rodriguez-Jiménez, F.J., **Jendelová, P., Syková, E.,** Oria, M., Stojkovic, M., **Erceg, S.**: (2015) Complete rat spinal cord transection as a faithful model of spinal cord injury for translational cell transplantation. *Sci Rep.* 5:19640. **IF 5.578**

Lukovic, D., Stojkovic, M., Moreno-Manzano, V**., Jendelová, P., Syková, E.,** Bhattacharya, S. S., **Erceg, S.**: (2015) Reactive Astrocytes and Stem Cells in Spinal Cord Injury: Good Guys or Bad Guys? *Stem Cells.* (4): 1036-1041. **IF 6.523**

Lunov, O., Churpita, O., Zablotskii, V., Deyneka, I.G., Meshkovskii, I.K., Jäger, A., **Syková, E., Kubinová,Š.,** Dejneka, A.: (2015) Non-thermal plasma mills bacteria: Scanning electron microscopy observations. *Applied Physics Letters*. 106(5): 053703. **IF 3.302**

Lunov, O., Zablotskii, V., Churpita, O., Jäger, A., Polívka, L., **Syková, E.,** Dejneka, A., **Kubinová, Š.**: The interplay between biological and physical scenarios of bacterial death induced by non-thermal plasma. *Biomaterials*. IN PRESS. **IF 8.557**

Machová Urdzíková, L., Kárová, K., Růžička, J., Kloudová, A., Shannon, C**., Dubišová, J.,** Murali, R**., Kubinová, Š., Syková, E.,** Jhanwar-Uniyal, M**., Jendelová, P.**:The Anti-Inflammatory Compound Curcumin Enhances Locomotor and Sensory Recovery after Spinal Cord Injury in Rats by Immunomodulation *Int J Mol Sci*. 17(1): 1-15. **IF 2.862**

Novotná, B**., Turnovcová, K.,** Veverka, P., **Rössner, P. Jr., Bagryantsevá, Y.,** Herynek, V., Zvatora, P., Vosmanská, M., Klementová, M., **Syková, E., Jendelová, P.**: (2015) The impact of silica encapsulated cobalt zinc ferrite nanoparticles on DNA, lipids and proteins of rat bone marrow mesenchymal stem cells. *Nanotoxicology*. 18:1-9. IN PRESS. **IF 6.411**

Raha-Chowdhury, R., Raha, A.A., **Forostyak, S.**, Zhao, J.W., Stott, S.R., Bomford, A.: (2015) Expression and cellular localization of hepcidin mRNA and protein in normal rat brain. *BMC Neurosci*. 16:24. **IF 2.665**

Syka, M., Keller, J., Klempíř, J., Rulseh, A.M., Roth, J., Jech, R., **Vořišek, I.,** Vymazal, J.: Correlation between relaxometry and diffusion tensor imaging in the globus pallidus of Huntington's disease patients. *PLoS One*. 10(3):e0118907. **IF 3.234**

Školoudik, L., Chrobok, V., Kalfert, D., **Koči, Z., Syková, E.,** Chumak, T., Popelář, J., Syka, J., Laco, J., Dedková, J., **Dayanithi, G.**, Filip, S.:(2015) Human multipotent mesenchymal stromal cells in the treatment of postoperative temporal bone defect: an animal model. *Cell Transplant*. IN PRESS. **IF 3.127**

Tukmachev, D., Lunov, O., Zablotskii, V., Dejneka, A., Babič, M., **Syková, E., Kubinová, Š.**: (2015) An effective strategy of magnetic stem cell delivery for spinal cord injury therapy. *Nanoscale*.7(9): 3954-3958. **IF 7.394**

DEPARTMENT OF AUDITORY NEUROSCIENCE

Burianová, J., Ouda, L., Syka, J.: (2015) The influence of aging on the number of neurons and levels of non-phosporylated neurofilament proteins in the central auditory system of rats. *Front Aging Neurosci*. 7: 27. **IF 2.843**

Chovanec, M., Zvěřina, E., **Profant, O., Balogová, Z.,** Kluh, J, **Syka, J.,** Lisý, J., Merunka, I., Skřivan, J., Betka, J.: (2015) Does attempt at hearing preservation microsurgery of vestibular schwannoma affect postoperative tinnitus? *Biomed Res. Int*. 2015 783169. **IF 1.579**

Chumak, T**.,** Bohuslavová, R., Macová, I., Dodd, N**., Buckiová, D.,** Fritzsch, B., **Syka, J.,** Pavlinková, G.: (2015) Deterioration of the Medial Olivocochlear Efferent System Accelerates Age-Related Hearing Loss in Pax2-Isl1 Transgenic Mice. *Mol Neurobiol*. IN PRESS. **IF 5.137**

Chumak, T**.,** Rüttiger,L., Lee, S.C., Campanelli, D., Zuccotti, A., Singer, W., **Popelář, J.,** Gutsche, K., Geisler, H.S., Schraven, S.P., Jaumann, M., Panford-Walsh, R., Hu, J., Schimmang, T., Zimmermann, U., **Syka, J.,** Knipper, M.: (2015) BDNF in Lower Brain Parts Modifies Auditory Fiber Activity to Gain Fidelity but Increases the Risk for Generation of Central Noise After Injury. *Mol Neurobiol*. IN PRESS. **IF 5.137**

Ouda, L., Profant, O., Syka, J.: (2015) Age-related changes in the central auditory system. *Cell Tissue Res*. 361(1): 337-358. **IF 3.565**

Profant, O., Tintěra, J., **Balogová, Z.,** Ibrahim, I., **Jilek, M., Syka, J.**: (2015) Functional changes in the human auditory cortex in ageing. *PLoS One* 10(3): e0116692. **IF 3.534**

Popelář, J., Šuta, D., Lindovský, J., Bureš, Z., Pysaněnko, K., Chumak, T., Syka, J.: (2015) Cooling of the auditory cortex modifies neuronal activity in the inferior colliculus in rats. *Hear Res*. IN PRESS. **IF 2.968**

Rybalko, N., Chumak, T., Bureš, Z., Popelář, J., Šuta, D., Syka, J.: (2015) Development of the acoustic startle response in rats and its change after early acoustic trauma. *Behav. Brain Res*. 286: 212-221. **IF 3.028**

Šuta, D., Rybalko, N., Shen, D. W., **Popelář, J.,** Poon, P. W., **Syka J.**: (2015) Frequency discrimination in rats exposed to noise as juveniles. *Physiol. Behav*. 144: 60-65. **IF 2.976**

Tomková, M., Tomek, J., **Novák, O., Zelenka, O., Syka, J.,** Brom, C.: (2015) Formation and disruption of tonotopy in a large-scale model of the auditory cortex. *J Comput Neurosci*. 39(2):131-153**. IF 1.739**

DEPARTMENT OF CELLULAR NEUROPHYSIOLOGY

Džamba, D., Honsa, P., Valný, M., Kriška, J., Valihrach, L., Novosadová, V., Kubista, M., **Anděrová,M.**: (2015) Quantitative Analysis of Glutamate Receptors in Glial Cells from the Cortex of GFAP/EGFP Mice Following Ischemic Injury: Focus on NMDA Receptors. *Cell Mol Neurobiol.* 35(8): 1187-1202. **IF 2.506**

Džamba D., Harantová L., Butenko O., Anděrová, M.: (2015) Glial cells – the key elements of Alzheimer´s disease. Current Alzheimer Research IN PRESS. **IF 3.889**

Chvátal, A.: (2015) Discovering the structure of nerve tissue: Part 3: From Jan Evangelista Purkyně to Ludwig Mauthner. *J Hist Neurosci.* 19:1-35. IN PRESS. **IF 0.562**

Chvátal, A.: (2015) The dissertation on pain by Jan Křtitel Boháč published in 1746. *J Hist Neurosci.* 3:1-22. IN PRESS. **IF 0.562**

DEPARTMENT OF MOLECULAR NEUROPHYSIOLOGY

Filipová, A., Diaz-Garcia, D., Bezrouk, A., Čížková, D., Havelek, R., Vávrov,á J., **Dayanithi, G.**, Řezacová, M.: (2015) Ionizing radiation increases primary cilia incidence and induces multiciliation in C2C12 myoblasts. *Cell Biol. Int.* 39(8): 943-953. **IF 1.933**

Forostyak, O., Romanyuk, N., Verkhratsky, A., **Syková, E., Dayanithi G.**: (2015) Plasticity of calcium signaling cascades in human embryonic stem cell-derived neural precursors. *Stem Cells Dev.* 22(10):1506-1521. **IF 3.727**

Školoudik, L., Chrobok, V., Kalfert, D., **Koči, Z., Syková, E., Chumak, T., Popelář, J., Syka. J.,** Laco, J., Dedková, J., **Dayanithi, G.**, Filip, S.: (2015) Human multipotent mesenchymal stromal cells in the treatment of postoperative temporal bone defect: an animal model. Cell Transplant. IN PRESS. **IF 3.127**

DEPARTMENT OF PHARMACOLOGY

Du, Z., Hudcovic, T., Mrázek, J., Kozaková, H., Srutková, D., Schwarzer, M., Tlaskalová-Hogenová, H., Kostovcik, M., **Kverka, M.**: (2015) Development of gut inflammation in mice colonized with mucosa-associated bacteria from patients with ulcerative colitis. *Gut Pathog.* 7:32. **IF 2.281**

Harmatha, J., Vokáč, K., Buděšínský, M., **Zídek, Z., Kmoníčková, E.**: (2015) Immunobiological properties of sesquiterpene lactones obtained by chemically transformed structural modifications of trilobolide. *Fitoterapia.* 107: 90-99. **IF 2.345**

Li, Y. J., Guo, Y., Yang, Q., Weng, X. G., Yang, L., Wang, Y. J., Chen, Y., Zhang, D., Li, Q., Liu, X.C., Kan, X. X., Chen, X., Zhu, X. X., **Kmoníčková, E., Zídek, Z.**: (2015) Flavonoids casticin and chrysosplenol D from Artemisia annua L. inhibit inflammation *in vitro* and *in vivo*.*Toxicol Appl Pharmacol.* 286(3):151-158. **IF 3.705**

Potměšil, P., Holý, A., **Zídek, Z.**: (2015) Influence of Acyclic Nucleoside Phosphonate Antivirals on Gene Expression of Chemokine Receptors CCR5 and CXCR4. *Folia Biol (Praha).*61(1):1-7. **IF 1.000**

DEPARTMENT OF GENETIC ECOTOXICOLOGY

Andersen, Z. J., **Šrám, R. J.,** Ščasný, M., Gurzau, E. S., Fucic, A., Gribaldo, L., **Rossner, P. Jr., Rossnerová, A.,** Braun Kohlová, M., Máca, V., Zvěřinová,I.,Gajdosová, D., Moshammer, H., Rudnai, P., Knudsen, L. E.: (2015) Newborns health in the Danube Region: Environment, biomonitoring, interventions and economic benefits in a large prospective birth cohort study. *Environment International.* 88: 112-122. **IF 5.559**

Gallud, A., **Líbalová, H.**, Fadeel, B.: (2015) Recent nanomedicine articles of outstanding interest. *Nanomedicine (Lond)* 10 (12): 1859-1861. **IF 5.413**

Ghosh, R**., Rossner, Jr. P.**, **Hoňková, K., Dostál, M., Šrám, R.**, Hertz-Picciotto, I.: (2015) Air pollution and childhood bronchitis: Interaction with xenobiotic, immune regulatory and DNA repair genes. *Environ Int.* 87:94-100**. IF 5.559**

Hyánková, L., **Novotná, B.,** Starosta, F.: (2015) Divergent selection for shape of the growth curve in Japanese quail. 8. Effect of long-term selection on embryonic development and growth. *British poultry science* 56(2): 184-194. **IF 0.936**

Lanzinger, S., Schneider, A., Breitner, S., Stafoggia, M., Erzen, I., **Dostál, M., Pastorková, A.,** Bastian, S., Cyrys, J., Zscheppang, A., Kolodnitská, T., Peters, A.: (2015) Associations between ultrafine and fine particles and mortality in five central European cities – Results from the UFIREG study. *Environ Int.* 88:44-52. **IF 5.559**

Kabátková, M., Zapletal, O., Tylichová, Z., Neča, J., Machala, M., **Milcová, A., Topinka, J.,** Kozubík, A., Vondráček, J.: (2015) Inhibition of β-catenin signalling promotes DNA damage elicited by benzo[a]pyrene in a model of human colon cancer cells via CYP1 deregulation. *Mutagenesis.*30(4)565-576. **IF 2.793**

McCullough, L. E., Eng, S. M., Bradshaw, P. T,, Cleveland, R. J., Steck, S. E., Terry, M. B., Shen, J., Crew, K. D., **Rossner, Jr. P.,** Ahn, J., Ambrosone, C. B., Teitelbaum, S. L., Neugut, A. I., Santella, R. M., Gammon, M. D.: (2015) Genetic polymorphisms in DNA repair and oxidative stress pathways may modify the association between body size and postmenopausal breast cancer. *Ann. Epidemiol.* 25(4): 263-269. **IF 2.000**

Mordukhovich, I., Beyea, J., Herring, A.H., Hatch, M., Stellman, S.D., Teitelbaum, S.L., Richardson, D.B., Millikan, R.C., Engel, L.S., Shantakumar, S., Steck, S.E., Neugut, A.I., **Rossner, Jr. P.,** Santella, R.M., Gammon, M.D.: (2015) Vehicular Traffic-Related Polycyclic Aromatic Hydrocarbon Exposure and Breast Cancer Incidence: The Long Island Breast Cancer Study Project (LIBCSP). *Environ Health Perspect.* IN PRESS. **IF 7.977**

Novotná, B., Turnovcová, K., Veverka, P., **Rössner, P. Jr., Bagryantsevá, Y.,** Herynek, V., Zvatora, P., Vosmanská, M., Klementová, M., **Syková, E., Jendelová, P.**: (2015) The impact of silica encapsulated cobalt zinc ferrite nanoparticles on DNA, lipids and proteins of rat bone marrow mesenchymal stem cells. Nanotoxicology. Nov 18:1-9. IN PRESS. **IF 6.411**

Štolcpartová, J., Pechout, M., Dittrich, L., Mazac, M., Fenkl, M., **Vrbová, K.,** Ondráček, J., Vojtišek-Lom, M.: (2015) Internal Combustion Engines as the Main Source of Ultrafine Particles in Residential Neighborhoods: Field Measurements in the Czech Republic. *Atmosphere.* 6 (11): 1714-1735. **IF 1.132**

Pálková, L., Vondráček, J., Trilecová, L., Ciganek, M., Pěnčíková, K., Neča, J., **Milcová, A., Topinka, J.**, Machala, M.: (2015) The aryl hydrocarbon receptor-mediated and genotoxic effects of fractionated extract of standard reference diesel exhaust particle material in pulmonary, liver and prostate cells. *Toxicol. Vitro* 29(3): 438-448. **IF 2.903**

Rossner, Jr. P., Tulupová, E., Rossnerová, A., Líbalová, H., Hoňková, K., Gmuender, H., **Pastorková, A., Švecová, V., Topinka, J., Šrám, R.J.**: (2015) Reduced gene expression levels after chronic exposure to high concentrations of air pollutants. *Mutat Res.* 780:60-70I. **IF 3.680**

Topinka, J., Rossner, P. Jr., Milcová, A., Schmuczerová, J., Pěnčíková, K., **Rossnerová, A., Ambrož, A., Štolcpartová, J.,** Bendl, J., Hovorka, J., Machala, M.: (2015) Day-to-day variability of toxic events induced by organic compounds bound to size segregated atmospheric aerosol. *Environ. Pollut.* 202: 135-145. **IF 3.902**

Vojtíšek-Lom, M., Pechout, M., Dittrich, L., Beránek, V., Kotek, M., Schwarz, J., Vodička P., **Milcová, J., Rossnerová, A., Ambrož, A., Topinka, J.**: (2015) Polycyclic aromatic hydrocarbons (PAH) and their genotoxicity in exhaust emissions from a diesel engine during extended low-load operation on diesel and biodiesel fuels. *Atmos. Environ*. 109: 9-18. **IF 3.281**

Zalel, A., Yuval**, Švecová, V., Šrám, R.,** Bartoňová, A., Broday, D. M.: (2015) Modeling airborne benzo(a)pyrene concentrations in the Czech Republic. *Atmos. Environ*. 101: 166-176. **IF 3.281**

Zölzer, F., Havránková, R., Freitinger Skalická, Z., **Rössnerová, A., Šrám, R.J.**: (2015) Analysis of Genetic Damage in Lymphocytes of Former Uranium Processing Workers. *Cytogenet Genome Res.* IN PRESS. **IF 1.561**

DEPARTMENT OF TERATOLOGY

Lochovská, K., Peterková, R., Pavliková, Z., Hovoraková, M.: (2015) Sprouty gene dosage influences temporal-spatial dynamics of primary enamel knot formation. *BMC Dev Biol.* 15: 21. **IF 2.667**

Rusková, H., Bejdová, S., **Peterka, M.,** Krajíček, V., Velemínská, J.: (2015) 3-D shape analysis of palatal surface in patients with unilateral complete cleft lip and palate. *J Craniomaxillofac Surg.*42(5):e140-147. **IF 2.933**

Khannoon, E. R., **Zahradníček, O.**: (2015) Postovipositional development of the sand snake Psammophis sibilans Serpentes:Lamprophiidae) in 1 comparison with other snake species. *Acta Zoologica (Stockholm)* IN PRESS. **IF 1.258**

DEPARTMENT OF MOLECULAR BIOLOGY OF CANCER

Aherne, S.T., Madden, S.F., Hughes, D.J., Pardini, B., Naccarati, A., Levy, M., **Vodička, P.,** Neary, P., Dowling, P., Clynes, M.: (2015) Circulating miRNAs miR-34a and miR-150 associated with colorectal cancer progression. *BMC Cancer.* 15: 329. **IF 3.362**

Campa, D., Rizzato, C., Stolzenberg-Solomon, R., Pacetti, P., **Vodička, P.,** Cleary, S.P., Capurso, G., Bueno-de-Mesquita, H.B., Werner, J., Gazouli, M., Butterbach, K., Ivanauskas, A., Giese, N., Petersen, G.M., Fogar, P., Wang, Z., Bassi, C., Ryska, M., Theodoropoulos, G.E., Kooperberg, C., Li, D., Greenhalf, W., Pasquali, C., Hackert, T., Fuchs, C.S., Mohelnikova-Duchonova, B., Sperti, C., Funel, N., Dieffenbach, A.K., Wareham, N.J., Buring, J., Holcátová, I., Costello, E., Zambon, C.F., Kupcinskas, J., Risch, H.A., Kraft, P., Bracci, P.M., Pezzilli, R., Olson, S.H., Sesso, H.D., Hartge, P., Strobel, O., Małecka-Panas, E., Visvanathan, K., Arslan, A.A., Pedrazzoli, S., Souček, P., Gioffreda, D., Key, T.J., Talar-Wojnarowská, R., Scarpa, A., Mambrini, A., Jacobs, E.J., Jamroziak, K., Klein, A., Tavano, F., Bambi, F., Landi, S., Austin, M.A., **Vodičková, L.,** Brenner, H., Chanock, S.J., Delle Fave, G., Piepoli, A., Cantore, M., Zheng, W., Wolpin, B.M., Amundadottir, L.T., Canzian, F.: (2015) TERT gene harbors multiple variants associated with pancreatic cancer susceptibility. *Int J Cancer.* 1;137(9):2175-2183. **IF 5.085**

Dowling, P., Hughes, D. J., Larkin, A. M., Meiller, J., Henry, M., Meleady, P., Lynch, V., Pardini, B., Naccarati, A., Levy, M., **Vodička, P.**, Neary, P., Clynes, M.: (2015) Elevated levels of 14-3-3 proteins, serotonin, gamma enolase and pyruvate kinase identified in clinical samples from patients diagnosed with colorectal cancer. *Clin. Chim. Acta.* 441: 133-141. **IF 2.824**

Hemminki, K., Frank, C., Försti, A., Musak, L., Kazimirova, A., Barancokova, M., Horska, A., **Vymetalková, V.,** Šmerhovský, Z., **Naccarati, A.,** Souček, P., **Vodičková, L.,** Buchancová, J., Smolková, B., Dušinská, M., **Vodička, P.**: (2015) Metabolic gene variants associated with chromosomal aberrations in healthy humans. *Gene Chromosomes Cancer.* 54(4): 260-266. **IF 4.041**

Hemminki, K., Rachakonda, S., Musak, L., **Vymetálková, V.,** Halasová, E., Försti, A., **Vodičková, L.,** Buchancová, J., **Vodička, P.,** Kumar, R.: (2015) Telomere length in circulating lymphocytes: Association with chromosomal aberrations. *Gene Chromosomes Cancer.* 54(3): 194-196. **IF 4.041**

Childs, E.J., Mocci, E., Campa, D., Bracci, P.M., Gallinger, S., Goggins, M., Li, D., Neale, R.E., Olson, S.H., Scelo, G., Amundadottir, L.T., Bamlet, W.R., Bijlsma, M.F., Blackford, A., Borges, M., Brennan, P., Brenner, H., Bueno-de-Mesquita, H.B., Canzian, F., Capurso, G., Cavestro, G.M., Chaffee, K.G., Chanock, S.J., Cleary, S.P., Cotterchio, M., Foretová, L., Fuchs, C., Funel, N., Gazouli, M., Hassan, M., Herman, J.M., Holcatová, I., Holly, E.A., Hoover, R.N., Hung, R.J., Janout, V., Key, T.J., Kupcinskas, J., Kurtz, R.C., Landi, S., Lu, L., Malecka-Panas, E., Mambrini, A., Mohelniková-Duchonová, B., Neoptolemos, J.P., Oberg, A.L., Orlow, I., Pasquali, C., Pezzilli, R., Rizzato, C., Saldia, A., Scarpa, A., Stolzenberg-Solomon, R.Z., Strobel, O., Tavano, F., Vashist, Y.K., **Vodička, P.,** Wolpin, B.M., Yu, H., Petersen, G.M., Risch, H.A., Klein, A.P.: (2015) Common variation at 2p13.3, 3q29, 7p13 and 17q25.1 associated with susceptibility to pancreatic cancer. *Nat Genet.* 47(8):911-916. **IF 29.352**

Pardini, B., Rosa, F., **Naccarati, A., Vymetálková, V.,** Ye, Y., Wu, X., di Gaetano, C., Buchler, T., Novotný, J., Matullo, G., **Vodička, P.**: (2015) Polymorphisms in microRNA genes as predictors of clinical outcomes in colorectal cancer patients. *Carcinogenesis.* 31(6): 82-86. **IF 5.334**

Vodenková, S,, Polivková, Z., Musak, L., Šmerhovský, Z., Zoubková, H., Sytarová, S., Kavcová, E., Halasová, E., **Vodičková, L., Jirásková, K,, Svoboda, M.,** Ambrus, M., Hemminki, K., **Vodička, P.**: (2015) Structural chromosomal aberrations as potential risk markers in incident cancer patients. *Mutagenesis*. 30(4):557-563. **IF 2.793**

Vodička, P., Musak, L., Frank, C., Kazimirova, A., **Vymetálková, V.,** Barancoková, M., Smolková, B., Dzupinková, Z., **Jirasková, K., Vodenková, S., Kroupa, M.,** Osina, O., **Naccarati, A.,** Palitti, F., Försti, A., Dusinská, M., **Vodičková, L.,** Hemminki, K.: (2015) Interactions of DNA repair gene variants modulate chromosomal aberrations in healthy subjects. *Carcinogenesis.*36(11): 1299-1306. **IF 5.334**

Vymetálková, V., Souček, P., Kunicka, T., **Jirásková, K.,** Brynychova, V., Pardini, B., Novosadova, V., Polivkova, Z., Kubackova, K., Kozevnikovova, R., Ambrus, M., **Vodičková, L., Naccarati, A., Vodička, P.**: (2015) Genotype and Haplotype Analyses of TP53 Gene in Breast Cancer Patients: Association with Risk and Clinical Outcomes. *PLoS One.* 10(7): e0134463. **IF 3.234**

DEPARTMENT OF TRANSPLANTATION IMMUNOLOGY

Čejka, Č., Čejková, J.: (2015) Oxidative stress to the cornea, changes in corneal optical properties, and advances in treatment of corneal oxidative injuries. *Oxid Med Cell Longev.* 2015: 591530. **IF 3.516**

Čejka Č., Holáň V., Trošan P., Zajícová A., Javorková E., Čejková J.: (2015) Favorable effect of mesenchymal stem cell treatment on the antioxidant protective mechanism in the corneal epithelium and renewal of corneal optical properties changed after alkali burns. *Oxid Med Cell Longev.* IN PRESS. **IF 3.516**

Hájková, M., **Javorková, E., Zajicová, A., Trošan, P., Holáň, V., Krulová, M.**: (2015) A local application of mesenchymal stem cells and cyclosporine A attenuates immune response by a switch in macrophage phenotype. *J Tissue Eng Regen Med* IN PRESS. **IF 5.199**

Heřmánková, B., Zajícová, A., Javorková, E., Chudíčková, M., Trošan, P., Hájková, M., Krulová, M., Holáň, V.: (2015) Suppression of IL-10 production by activated B cells via a cell contact-dependent cyclooxygenase-2 pathway upregulated in IFN-γ-treated mesenchymal stem cells. *Immunobiology.* IN PRESS. **IF 3.795**

Holáň, V., Trošan, P., Čejka, Č., Javorková, E., Zajícová, A., Heřmánková, B., Chudíčková, M., Čejková, J.: (2015) A Comparative Study of the Therapeutic Potential of Mesenchymal Stem Cells and Limbal Epithelial Stem Cells for Ocular Surface Reconstruction. *Stem Cells Transl Med.* 4(9): 1052-1063**. IF 5.709**

Chudičková, M., Brůža, P., **Zajicová, A., Trošan, P., Svobodová, L., Javorková, E., Kubinová, S., Holáň, V.**: **(2015)** Targeted neural differentiation of murine mesenchymal stem cells by a protocol simulating the inflammatory site of neural injury. *J Tissue Eng Regen Med.* IN PRESS. **IF 5.199**

DEPARTMENT OF TISSUE ENGINEERING

Buzgo, M., Greplová, J., Soural, M., **Bezděková, D., Míčková, A.**, Kofroňová, O., Benada, O., Hlaváč, J., **Amler, E.**: (2015) PVA immunonanofibers with controlled decay. *Polymer.* 7: 387-398. **IF 1.653**

Daňková, J., Buzgo, M., Vejpravová, J., Kubíčková, S., **Sovková, V.,** Vysloužilová, L., Mantlíková, A., Nečas, A., **Amler, E.**: Highly efficient mesenchymal stem cell proliferation on poly-ε-caprolactone nanofibers with embedded magnetic nanoparticles. *Int J Nanomedicine.* 10:7307-17. **IF 4.383**

Erben, J., Pilarová, K., Sanetrnik, F., Chvojka, J., Jenčová, V., Blažková, L., Havlíček, J., Novák, O., Mikeš, P., **Prosecká, E.,** Lukaš, D., Kuzelová Kostaková E.: (2015) The combination of meltblown and electrospinning for bone tissue engineering. *Materials Letters* 143, 172-176. **IF 2.489**

Filová, E., Jakubcová, B., Danilová, I., Kuželová Košťáková, E., Jarošíková, T., Chernyavskiy, O., Hejda, J., Handl, M., **Beznoská, J.,** Nečas, A., Rosina, J., **Amler, E.**: (2015) Polycaprolactone foam functionalized with chitosan microparticles – a suitable scaffold for cartilage regeneration. *Physiol Res.* IN PRESS. **IF 1.293**

Plencner, M., Prosecká, E., Rampichová, M., East, B., **Buzgo, M.,** Vysloužilová, L., Hoch, J., **Amler, E.**: (2015) Significant improvement of biocompatibility of polypropylene mesh for incisional hernia repair by using poly-ε-caprolactone nanofibers functionalized with thrombocyte-rich solution. *Int J Nanomedicine.*10:2635-2646. **IF 4.383**

Sukhoruková, I.V., Sheveyko, A.N., Kiryukhantsev-Korneev,Ph.V., AnisimováN.Y., Gloushanková, N.A., Zhitnyak, I.Y., **Benešová, J., Amler, E.,** Shtanský, D.V.: (2015) Two approaches to form antibacterial surface: Doping with bactericidal element and drug loading. *Applied Surface Science.* 330:339–350. **IF 2.711**

DEPARTMENT OF MICROSCOPY UNIT

Grousl, T., **Opekarová, M., Strádalová, V.,** Hašek, J., **Malínský,** J.: (2015) Evolutionarily Conserved 5'-3' Exoribonuclease Xrn1 Accumulates at Plasma Membrane-Associated Eisosomes in Post-Diauxic Yeast. *PLoS One.* 10(3): e0122770. **IF 3.234**

Chum, T., Glatzová, D., Kvíčalová, Z., **Malínský, J.,** Brdička, T., Cebecauer, M.: (2015) The role of palmitoylation and transmembrane domain in sorting of transmembrane adaptor proteins. *J Cell Sci.* IN PRESS. **IF 5.432**

Pokorná, L., Čermáková, P., Horváth, A., Baile, M.G., Claypool, S.M., Griač, P., **Malínský, J.,** Balážová, M.: (2015) Specific degradation of phosphatidylglycerol is necessary for proper mitochondrial morphology and function. *Biochim Biophys Acta.* 1857(1): 34-45. **IF 4.381**

BOOK CHAPTERS

Rössner Jr, P., Binková, B., Rössnerová, A., Šrám, R.: Molecular Epidemiology Focused on Airborne Carcinogens. *Air Pollution and Health Effects.* London : Springer, 2015, pp. 185-203. ISBN 978-1-4471-6669-6.

Rössner Jr, P., Binková, B., Rössnerová, A., Šrám, R.: Molecular Epidemiology and Air Pollution. *Current Air Quality Issues.* Rieka : InTech, 2015, (Nejadkoorki, F.), pp. 609-643 ISBN 978-953-51-2180-0.

Raveh, A., **Tureček, R.,** Bettler, B.: Diversity and Functions of GABA Receptor: A Tribute to Hanns Mohler. In: Mechanisms of fast desensitization of GABA(B) receptor-gated currents. Part B. In *Advances in Pharmacology*. Volume 73 pp. 145-165. Eds. U. Rudolph, Elsevier, 2015. ISBN 978-0-12-802658-8.

Syka, J.: Enhancement v neurofyziologii. *Dobrý, nebo lepší život? Human enhancement.* Praha: Ústav státu a práva AV ČR, v. v. i., 2015, s. 92-102. ISBN 978-80-87439-18-0.

BOOK

Skřív, I., **Holáň, V.:** Cytokiny v klinické medicíně. Praha: Maxdorf, 2015. s. 207 ISBN 978-80-7345-427-2.

OTHER PUBLICATIONS

Chvátal, A.: (2015) Jan Křtitel Boháč (1724–1768) a jeho disertace o bolesti z roku 1746. (Jan Křtitel Boháč (1724–1768) and dissertation on pain from 1746). *Bolest* 18(1): 8-20.

Chvátal A.: (2015) Výzkum struktury nervové tkáně III: od Jana Evangelisty Purkyně (1787–1869) k Ludwigovi Mauthnerovi (1840–1894). *Československá fyziologie*. 2: 52-72.

Kubíková, T., Filová, E., Prosecká, E., Plencner, M., Králíčková, M., Tonar, Z.: (2015) Histological evaluation of biomaterials administration *in vivo* on the cartilage, bone and skin healing. *Cas Lek Cesk*.154(3):110-4.

Kubinová, Š.: (2015) New trends in spinal cord tissue engineering. *Future Neurol*. 10 (2):129-145

Neckář, P., **Syková, E.**: (2015) Stem cells in orthopaedics. *Cas Lek Cesk*. 154(3):107-9.

Svěcený, J., **Syková, E.**, Tichý, M., Laštůvka, J.: (2015) Nové možnosti terapeutické revaskularizace u ischemické choroby dolních končetin v rámci syndromu diabetické nohy autologní transplantací kmenových buněk (New options for therapeutic revascularization in lower extremity limb ischemia linked to the diabetic foot syndrome by autologous stem cell transplantation). *Cas Lek Cesk*. 154(4):161-7.

Syková, E.: (2015) Kmenové buňky v regenerativní medicine. *Ortopedie* 4: 177-181.

Šrám, R. J.: (2015) Zdravotníci bijí na poplach: dělejme něco s dopravou. *Pro-Energy Magazín.* 68-71.

Šrám, R. J., Blanka Binková: (2015) Demonstrace za čiský vzduch a Program Teplice. *Vesmír*. 94, duben, strana 236-238.

Dostál, M., Pastrková, A., Jiří Novák: (2015) Nebezpečné ultrajemné částice. *Vesmír*. 94, červenec-srpen, 445-447.

Dostál, M., Pastrková, A., Stefanie Lanzinger, Alexandra Schneider, Susane Bastian, Monika Senghaas, Ziva Erzen, Jiří Novák, Teťana Kolodnitkska, **Radim J. Šrám**, Annette Peters: (2015) Vliv ultrajemných prachových části na zdraví – projekt UFIREG. *Časopis lékařů českých.* 154 (4) 176-180.

Research for Practice

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

Physicochemical characterization of TiO2-based nanoparticles

Provider: The Ministry of Education, Youth and Sports of the CR
Partner organization: Precheza, a.s.
Project: Cytotoxicity of nanomaterials as a function of their structure and physicochemical properties. Genomics and proteomics in the study of mechanisms of the biological effects of manufactured nanoparticles.
Application: The obtained parameters are used for describing the properties of nanomaterials for testing the cytotoxicity in cell cultures.
Result: Physico-chemical characterization of 14 samples of TiO2 nanoparticles was performed using X-ray diffraction, specific surface area determination, X-ray fluorescence, and thermogravimetric analysis. Methods possible to determine the crystal size of nanomaterials to perform elemental analysis to determine water content and CO2 and possible contamination by other substances.
Publication: Brzicova, T., Stolcpartova, J., Vrbova, K., Topinka, J.: Cytotoxicity of TiO2 nanomaterials as a function of their physicochemical properties – generation of data for computational modelling. In NANOCON2015 7th International Conference (14.–16.10.2015, Brno)

Improvement of time discrimination ability of acoustical stimuli in aged rats after AUT9 application

Provider: Autifony Therapeutics Limited, London, UK
Project: The effect of AUT9 on temporal resolution in aged and young adult Fischer 344 rats.
Application: Treatment of hearing disorders in the elderly.
Result: The results indicate that AUT9 has potential in the treatment of age-related hearing impairment and supports evidence of the crucial role of Kv3.1 channels in the development of age-related temporal resolution deficit.

Bilateral agreements

Collaborating institutions	Country	Theme cooperation
Institute of Physiology I.P.Pavlova, RAV Sankt Peterburg	Russia	Neurophysiological mechanisms of detection and resolution 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
Department of Physiology, Tottori University, Prof. Izumi Shibuya	Japan	Calcium signalling and homeostasis in magnocellular neurons and terminals
Department of Physiology, UOEH, School of Medicine Kitakyushu Prof. Yoich Ueta	Japan	Transgenic rats models for visualization of vasopressin and oxytocin in the dorsal root ganglia and glial cells
INSERM U710 Prof. Jean-Michel Verdier	France	Physiology and plasticity of signalling cascades $Ca2^{+}$ in stem cells

Patents and Utility models

Year 2015	Number	In cooperation with
Utility models registered in the Czech Republic	1	
Utility models filed in the Czech Republic	2	
National patent granted	1	Institute of Macromolecular Chemistry of the CAS

Composite surgical net with nanofibrous layer

Type: National utility model application
Publication of **registration date**: 15.7.2015
Registration number: 28419
Applicant/Holder: University Hospital in Prague-Motol, Institute of Experimental Medicine of the CAS, Student Science, Ltd.
Inventor: Prof. Jiří Hoc, MD, PhD, prof. Evžen Amler, MSc, PhD, DSc, Matej Buzgo, MSc, Martin Plencner, MSc, Michala Rampichová, MSc

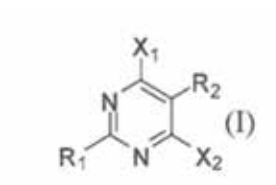
Low-temperature plasma source with possibility of contact as well as contactless application

Type: National utility model application
Application date: 6.10.2015
Registration number: 29159
Applicant/Holder: Institute of Physics of the CAS, Institute of Experimental Medicine of the CAS
Inventor: Olexander Churpita, MSc, Alexandr Dejneka, MSa, PhD, Assoc. Prof. Vitaliy Zablotskyy, PhD, DCs, Prof. Eva Syková, MD, PhD, DSc, FCMA, Šárka Kubinová, PharmD, PhD

Low-temperature plasma source, especially for plasma generation in the form of various voluminous formations

Type: National utility model application
Application date: 4.12.2015
Registration number : 29236
Applicant/Holder: Institute of Physics of the CAS, Institute of Experimental Medicine of the CAS
Inventor: Olexander Churpita, MSc, Alexandr Dejneka, MSa, PhD, Assoc. Prof. Vitaliy Zablotskyy, PhD, DCs, Prof. Eva Syková, MD, PhD, DSc, FCMA, Šárka Kubinová, PharmD, PhD

Pyrimidine compounds inhibiting formation of nitrogen monoxide and prostaglandin E2, process for their preparation and use



In the present invention, there are disclosed pyrimidine compounds that reduce production of nitrogen monoxide and at the same time prostaglandin PGE2, which, in concentrations, reduce production of these factors by 50 percent, do not have a negative affect on cell viability (are not cytotoxic). Also disclosed is a pharmaceutical composition containing such pyrimidine compounds and their use for the treatment of diseases induced by excessive production of NO and/or prostaglandin E2 or when the severity of the disease is amplified by the overproduction of NO and/or prostaglandin E2.

Type: National patent application
Application date: 28.02.2011
Publication date: 12.09.2012
Date was granted patent: 19.08.2015
Patent publication date: 30.9.2015
Applicant/Holder: Institute of Macromolecular Chemistry of the CAS, Institute of Experimental Medicine of the CAS
Inventor: Petr Jansa, MSc, Prof. Antonín Holý, MSc, PhD, DSc, Dr. hc. mult., Zdeněk Zídek, MSc, PhD, DSc, Assoc. Prof. Eva Kmoníčková, MSc, PhD, Zlatko Janeba, MSc

Teaching Activities

Postgraduate education

	Number of graduates in 2015	Number of PhD students prior to December 31, 2015	Number of newly admitted students in 2015
Full-time PhD students	2	34	8
PhD students in combined and/or distance learning	5	24	1
Total	7	58	9
Foreign students	0	14	1

Education of undergraduate students

Number of bachelors	17
Number of diploma students	15

Teaching activities of the Institute

	Summer semester 2014/2015			Winter semester 2015/2016		
The number of teaching hours during Bachelor's / Master's / PhD courses	110	138	28	62	489	28
Number of lectures / seminars / exercises in undergraduate programs	15	6	2	15	2	1
Number of lectures / seminars / exercises in Master's programs	27	2	1	32	2	3
Number of the Institute staff involved in Bachelor's / Master's / PhD programs	9	8	6	11	9	9

Research cooperation between the Institute and Universities

	Institute as project promoter		Institute as project partner	
Number of joint projects with universities in 2015 Grants/Programs	8	2	7	2

Popularization Lectures

Event, date	Organizer	Description
University of the Third Age	2nd Faculty of Medicine, Charles University	Lecture by Prof. Evžen Amler, MSc, PhD, DSc
The Ecological Exhibition, 2.12.2015	Gallery of Art Critics, Adria Palace, Prague 1	Public Lectures on the topic: Impact of environmental pollution on public health (Radim Šrám, MD, DSc) Public Lectures on the theme: Nature and Man (Andrea Rössnerová, MSc, PhD)

Event, date	Organizer	Description
Brain Awareness Week, 16.–20.3.2015	IEM of the CAS, Society for Neuroscience and Centre for Joint Activities of the CAS	Public Lectures: Prof. Josef Syka, MD, DSc, FCMA: How our brain perceives music Prof. Eva Syková, MD, PhD, DSc, FCMA: Stem cells in brain disease Assoc. Prof. Alexander Chvátal, PhD, DSc, MBA: Glial cells and their role
Science and Technology Week, 3.11.2015	Czech Academy of Science, IEM of the CAS	Open Day at the IEM of the CAS attended by 300 people
Czech Statistical Office, Prague 8, 25.6.2015	Czech Statistical Office	Lecture on the topic: The effects of environmental pollution on human health (Radim Šrám, MD, DSc)
Science and Technology Week, Carolinum, Small Auditorium, Prague 1, 3.11.2015	Czech Academy of Science, IEM of the CAS	Lecture on the topic**:** Stem cells and biomaterials in regenerative medicine (Šárka Kubinová, PharmD, PhD). Regenerative medicine uses stem cells and biomaterials for the treatment, rehabilitation or replacement of damaged organs, tissues or cells.
Science and Technology Week, Carolinum, Patriotic Hall, Prague 1, 3.11.2015	Czech Academy of Science, IEM of the CAS	Lecture on the topic: Brain, speech and music (Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.)
Science and Technology Week, Academy of Sciences, Prague 1	Czech Academy of Science, IEM of the CAS	Lecture on the topic: What should we know about air pollution (Radim Šrám, MD, DSc)
IX. Jánskolázeňské symposium, 8.1.2015	IEM of the CAS, and the city of Janské Lázně	Lecture: Prof. Eva Syková, MD, PhD, DSc, FCMA: Cell Therapy – The latest trends
Seminar, Women in research and entrepreneurship, 21.1.2015	TA CR, IEM of the CAS	Lecture by Prof. Eva Syková, MD, PhD, DSc, FCMA: Women in Science
Senate public hearing on the topic of Science Centres and their importance for the development of the Czech Republic, 12.3.2015	Senate PSP and IEM of the CAS	Contribution and participation of Prof. Eva Syková, MD, PhD, DSc, FCMA at a press conference
Debate on the topic: With organic traffic center for a better future, 16.3.2015	ČSSD Prague 4, IEM of the CAS	Prof. Eva Syková, MD, PhD, DSc, FCMA attended and contributed regarding the influence of pollution on the health of the population – Spořilov
IX. Spring Conference ČLS JEP, 25.4.2015	ČLS JEP, IEM of the CAS	Lecture by Prof. Eva Syková, MD, PhD, DSc, FCMA: Problems with stem cells

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's researchers	**105**
– not as a part of bilateral agreements of the CAS	**96**
Number of scientists from the Institute that actively participated in international conferences	**93**
Number of lectures presented at these conferences	**27**
– of which were invited lecturers	**12**
Number of posters	**71**
Number of Institute researchers as members of the editorial boards of international journals	**22**
Number of Institute researchers with membership in international scientific governmental and non-governmental organizations (companies, committees)	**9**
The number of lectures of foreign researchers at the Institute	**10**
Number of grants and projects financed from abroad	**8**
– of which were EU programs	**7**

Cooperation between Academy of Science and Senate PCR

November 18, 2015, Senator Eva Syková welcomed Taiwanese neuroscientists at the Czech Senate for a gala evening organized under the auspices of the Senate President Milan Štěch at the opening of the 10th Conference of the Czech Society for Neuroscience and the Czech-Taiwan neuroscience symposium. The guest of honor was the councilor of Taiwan in the Czech Republic, Mr. Shea-Jung Lu.

Conferences in 2015

10th Conference of the Czech Neuroscience Society together with the Czech-Taiwan Neuroscience Symposium

Date and Place of Event: 18.–19.11.2015 in Prague
Organizer: Institute of Experimental Medicine of the CAS / A total of 120 participants, 15 from abroad
Co-organizer: Czech Neuroscience Society
Contact: Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c.

European Environmental Mutagenesis and Genomics Society (EEMGS)

Date and Place of Event: 23.8.–26.8.2015 in Prague
Organizer: Institute of Experimental Medicine of the CAS / A total of 200 participants, 170 from abroad
Contact: Jan Topinka, MSc, DSc
Significant presentation: Pavel Rössner, MSc, PhD.: Oxidative damage to macromolecules in stem cells labeled with iron oxide nanoparticles

Cooperating institutions

Collaborating institution:	Topic of cooperation:
Institute of physiology I.P.Pavlova, RAV, Saint Peterburg, Russia	Neurophysiological mechanisms of detection and resolution 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
Department of Physiology, Prof. Izumi Shibuya, Tottori University-Japan	Calcium signaling and homeostasis in magnocellular neurons and nerve terminals
Department of Physiology, Prof. Yoich Ueta, UOEH School of Medicine, Kitakyushu, Japan	Models of transgenic rats in the visualization of vasopressin and oxytocin in the dorsal root ganglia and glial cells
Prof. Jean-Michel Verdier, INSERM U710, France	Physiology and plasticity cascades of Ca^{2+} signalling in stem cells

Foreign Scientists who visited the Institute

Prof. Vicenzo Desiderio University of Naples	Italy	Materials Engineering
Prof. Carmel Caruana University of La Valetta	Malta	Radiology
Meena Jhanwar –Uniyal New York Medical College	USA	Molecular Biology, senior Scientist
Suresh Jhanwar Memorial Sloan Kettering Cancer	USA	Tumor Biology
Widmar Tanner University of Regensburg, Germany Cell Biology		
Prof. Hyunok Choi Departments of Environmental Health Sciences, Epidemiology, and Biostatistics, SUNY Albany, School of Public Health, Rensselaer, NY	USA	Epidemiology
Andrej Kral ORL Clinic Hannover	Germany	ORL
Olivier Sterkers Director of Inserm/UMRS 1159, GH Pitié Salpêtrière, Paris	France	ORL and Head and Neck Surgery
Cedric Viero Department of Experimental and Clinical Pharmacology and Toxicology, Medical Faculty, Saarland University Hamburg	Germany	Cellular Pharmacology and Toxicology
Manfred Pützer Department of Computational Linguistics and Phonetics, University of Saarbrücken	Germany	Deep brain stimulation, articulation
Dr. Alessio Naccarati HUGEF Turin	Italy	Genetics
Prof. Dan Sliva University of Indianapolis	USA	Biochemistry
Prof. Guang Peng, MD Anderson Cancer Center, Houston	USA	Cancer research

Biomedical Research Campus in Prague - Krč

Practical Courses

Tissue Engineering and Regenerative Bionanotechnology

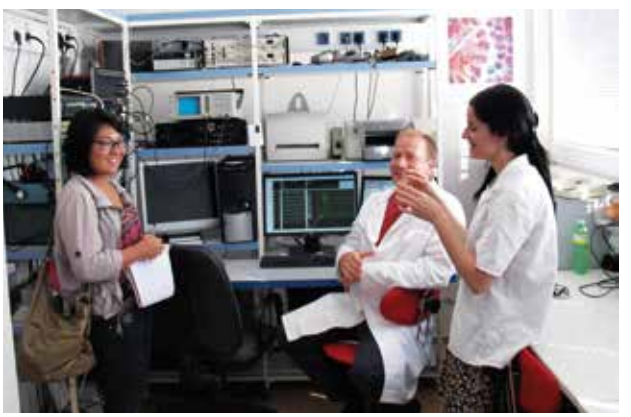
Course content: Introducing Regenerative Bionanotechnology to students of the Medicine and Postgraduate Programs
Place and date of the course: continuously, 2nd Faculty of Medicine, Charles University, Institute of Experimental Medicine of the CAS
A total of 12 participants, 3 from abroad

Training School in Auditory Neuroscience

Course content: The course was aimed at presenting the many methods currently used in auditory neuroscience. The programe consisted of theoretical lectures followed by practical demonstrations.
Place and date of the course: 12.–13.5.2015, Institute of Experimental Medicine of the CAS
A total of 16 participants, 12 from the EU program Targear, 4 from the EU program TINNET

Auditory Neuroscience Methods

Course content: A training course under the Neurobiology of Hearing 2015, organized by the University of Connecticut Health Center
Place and date of the course: 4.–5.6.2015, Prague
A total of 35 participants, 33 from abroad



Brain Awareness Week 2015 gives students insights into the world of neuroscience

In March of last year the Institute of Experimental Medicine of the CAS organized the 17th annual Brain Awareness Week lecture series, which presented the latest findings in current research in the field of neuroscience. Events in Europe were coordinated by the European Dana Alliance for the Brain (EDAB) and in the Americas by the Dana Alliance for Brain Initiatives.

Over the course of a week at the Academy of Sciences in Prague 1, thirteen presentations were made by leading experts from the Czech Republic dealing with brain activity, its treatment and functions, in order to pass on their knowledge to secondary school students and the general public. Among the major experts who spoke at the lecture series was our leading stem cells expert, Prof. Eva Syková, MD, PhD, DSc, FCMA from the Institute of Experimental Medicine of the CAS, who spoke on the topic: Stem Cells in the Treatment of Brain Diseases. Another expert, Prof. Jiří Raboch, MD, DSc, from the Psychiatric Clinic, 1st Medical Faculty, Charles University, spoke on the topic: Mental Disorders and Society. A discussion was also held after a lecture on the topic of how our brain perceives sound given by Prof. Josef Syka, MD, PhD, DSc, FCMA, Dr. h.c. also from the IEM of the CAS. Prof. Richard Rokyta, MD,DSc, President of the Czech Medical Academy, spoke on the modern treatment of chronic pain. Prof. Cyril Höschl, MD, DSc from the National Institute of Mental Health gave a lecture on the neurobiology of schizophrenia. Asoc. Prof. A. Chvátal, PhD, DSc, MBA, another scientis from IEM CAS, spoke about the role of glial cells in the CNS functions. A leading expert in multiple sclerosis, Prof. Eva Havrdová, MD, PhD, dealt with the theme of multiple sclerosis as a disease of civilization. Other experts also shared new knowledge in the field of brain research.

Listener interest often exceeded the capacity of the halls. The building of the Academy of Sciences was filled with students from Prague and high schools outside the city, who did not want to miss this unique opportunity. Lectures were attended by a total of 1,894 visitors. The media also showed considerable interest in the event. Throughout the week, reports about Brain Awareness Week appeared on Czech television and radio and in print media.

The tradition of Brain Awareness Week in the Czech Republic was established in 1998 by Prof. Josef Syka, a Czech neuroscientist engaged in hearing research. The Centre for Joint Activities of the Academy of Sciences assisted in organizing the event.

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

Presenters at the Brain Awareness Week 2015:


Prof. Eva Syková


Assoc. Prof. Alexandr Chvátal

Prof. Josef Vymazal


Prof. Robert Jech


Prof. Josef Syka


Prof. Karel Šonka


Prof. Jiří Raboch

Notes:

Tiráž
Výroční zprávu za rok 2015 vydal Ústav experimentální medicíny v květnu 2016

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

Tisk, zlom a grafická úprava Abalon, s. r. o.
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