

Premises
of the Institute
of Experimental
Medicine ASCR,
v.v.i., in Prague – Krč.



INSTITUTE OF EXPERIMENTAL MEDICINE OF THE ACADEMY OF SCIENCES OF THE CZECH REPUBLIC, v. v. i. (a public research institution)



**Institute
of Experimental
Medicine AS CR, v.v.i.**
EU Centre of Excellence

The Institute of Experimental Medicine (IEM) is a renowned centre of biomedical research, manifested by the fact that the Institute was awarded the status of an EU Centre of Excellence – MEDIPRA, by the participation of the Institute's scientists in projects of the 6th and 7th EU Framework Programmes, and by its extensive collaborations on both national and international levels. Both Czech and foreign Ph.D. students work in the Institute, funded by EU grants as well as by the Institute's core budget. The Institute supports young group leaders and is a partner in the EU project ENI-NET, bringing together leading European institutes in the field of neuroscience; it is the seat of the biomedical commission for awarding DSc. degrees; and it has the highest percentage of Ph.D. students among all the institutes of the Academy of Sciences.

The outcomes of the Institute's research, which have already been applied in practice, include those in the fields of environmental protection, neuroscience, regenerative medicine, pharmacology and diagnostic methods. Currently, the Institute comprises 12 scientific departments and laboratories:

Department of Neuroscience

(Head: Prof. MUDr. Eva Syková, DrSc.)
comprises two units. **The Laboratory of Diffusion Studies** is an internationally recognized workplace in the field of ion-selective microelectrodes and NMR measurements, whose aim is to study ionic homeostasis in the central nervous system and its diffusion parameters. Research into these topics has contributed to the understanding of extrasynaptic transmission in the central nervous system, the interpretation of MRI signals, and changes in diffusion parameters that lead to functional changes in a number of pathological conditions. **The Laboratory of Tissue Culture and Stem Cells** has achieved outcomes that enable the labelling of stem cells with superparamagnetic iron oxide nanoparticles for in vivo imaging with the aid of MRI. The research focuses on the use of adult as well as embryonic stem cells in the regeneration of damaged brain or spinal cord. A clinical study "Autologous transplantation of bone marrow stem cells in patients with a transversal spinal lesion" is carried out at the Department of Neuroscience of Motol Teaching Hospital (an IEM joint workplace) based on preclinical experiments with bone marrow cell populations. The use of stem cells for the treatment of spinal cord and

Management

Director: Prof. MUDr. Eva Syková, DrSc.
Deputy Director: Doc. RNDr. Alexandr Chvátal, DrSc.
Chairman of the IEM Council: Prof. MUDr. Eva Syková, DrSc.
Chairman of the Supervisory Board: Prof. Ing. Petr Ráb, DrSc.

Address and Contact

<http://www.iem.cas.cz>
Institute of Experimental Medicine ASCR, v.v.i.
Videňská 1083, 142 20 Prague 4 – Krč, Czech Republic
Telephone: +420 241062230, Fax: +420 241062782
Email: uemavcr@biomed.cas.cz

brain pathologies is also studied within the EU 6th Framework Programme projects RESCUE, STEMS, DIMI and ANGIOTARGETING.

Concurrently with stem cell research, the department also performs research and testing of biomaterials based on macroporous hydrogels (in cooperation with the Institute of Macromolecular Chemistry of the Academy of Sciences of the Czech Republic) and non-woven nanofibres (Technical University in Liberec, Elmarco) with the aim of making use of their ability to help bridge extensive lesions in the central nervous system and also in skin defects, including those of the diabetic foot (in cooperation with the Institute for Clinical and Experimental Medicine).

Department of Cellular Neurophysiology

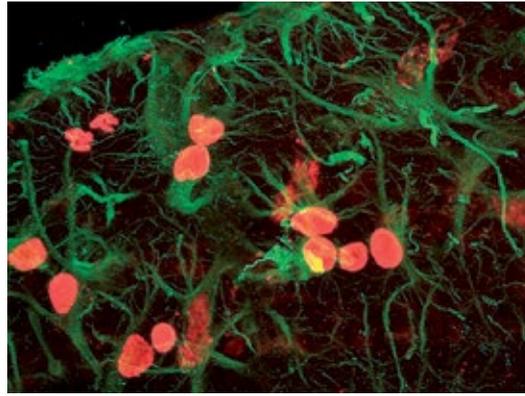
(Head: Doc. RNDr. Alexandr Chvátal, DrSc.)

is involved in several research projects focusing on the diagnosis and treatment of serious diseases of the central nervous system. The department studies the electrophysiological, morphological and immunohistochemical properties of glial cells under pathological conditions, the membrane properties of stem cells of the central nervous system in the course of their differentiation in situ and in vivo, and the role of calcium ions in the central nervous system under physiological and pathological conditions. Among the significant research outcomes has been the description of the electrophysiological, morphological and immunohistochemical properties of glial cells during anoxia and ischemia in the brain. Through the study of neuroectodermal stem cells in the course of their differentiation in nervous tissue, it was discovered that these cells develop into mature astrocytes, oligodendrocytes, and neurons. Since 2007 the department has been reinforced by Prof. Alexei Verkhratsky from the University of Manchester, whose main research focus is on glial cells and the role of calcium ions in the central nervous system.

Department of Auditory Neuroscience

(Head: Prof. MUDr. Josef Syka, DrSc.)

focuses on the ageing of the auditory system (in rats of the Fischer 344 strain and mice of the C57 strain). This



Stem cells and astrocytes in a brain lesion.
Photo © E. Syková.

research is extended by the EU project NANOEAR, which focuses on the influence of locally administered nanoparticles on the functioning of the inner ear. Another direction of research is the analysis of the coding of acoustic signals by neuronal networks in the central auditory system. The department has shown that the auditory cortex in rats has a lateralized function: the right hemisphere specialises in changes in the frequency of a sound, while the left hemisphere specialises in the temporal parameters of the sound. This knowledge alters our perception of the phylogeny of the mammalian brain. RNDr. Rostislav Tureček studies GABA and glycine receptors in the auditory pathway.

Department of Molecular Embryology

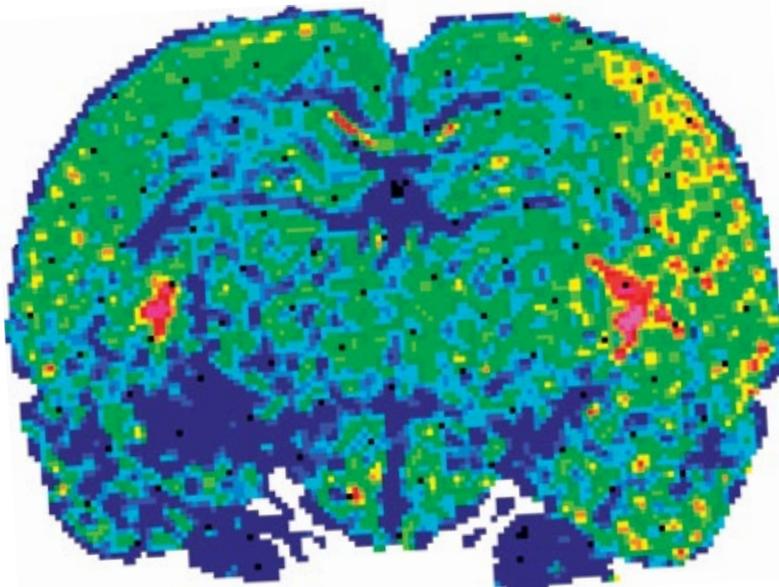
(Head: Doc. MVDr. Aleš Hampl, CSc.)

is a detached site of the IEM in Brno. Its main area of research is pluripotent stem cells, in particular human embryonic cells. The IEM is the only institution in the Czech Republic to have succeeded in isolating lines of human embryonic stem cells as early as 2003. Researchers in this department participate in two significant international projects that focus on embryonic cell research - ESTOOLS and the International Stem Cell Initiative.

Laboratory of Tissue Engineering

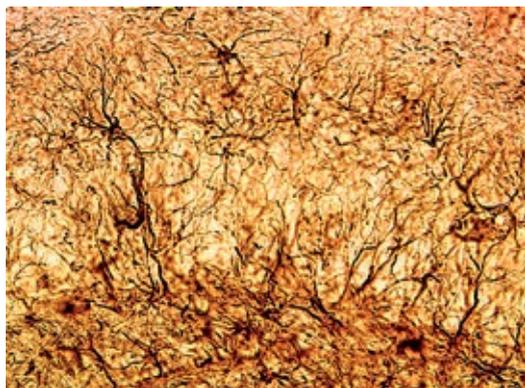
(Head: Doc. RNDr. Evžen Amler, CSc.)

was established in 2005. The main focus of its activity lies in the preparation of tissue replacements, the creation of cell carriers, especially biodegradable



Brain diffusion parameters obtained using diffusion-weighted nuclear magnetic resonance.

Altered cytoarchitecture of the hippocampus in old age. Photo © E. Syková.



ones and those based on nanofibres, the modelling of protein structures, and the search for practical applications of its research outcomes. The laboratory develops technologies for releasing bioactive substances through the use of nanofibrous carriers enriched by liposomes, which enables the controlled delivery of nutrients and pharmaceuticals directly to the location of a defect. Artificial cartilaginous replacements are prepared for clinical use in orthopaedics.

Department of Teratology

(Head: MUDr. Miroslav Peterka, DrSc.)

has demonstrated that after the Chernobyl nuclear power plant disaster, approximately 450 fewer boys were born in Bohemia in November 1986 than would have been normally expected. Further research has yielded new results regarding the presence of rudimentary teeth and tooth primordia in mammals. The rudimentary structures not only help us understand the evolutionary development of mammals, but they also represent a tool for the study of regulatory factors involved in controlled dental regeneration and for the development of live tooth replacements.

Department of Genetic Ecotoxicology

(Head: MUDr. Radim Šrám, DrSc.)

deals with molecular epidemiology and the influence of pollution on the state of the health of the population, also within EU projects. It participates in the 5th and 6th EU Framework Programmes (ECNIS, ENVIRISK and INTARESE projects) and is very active in terms of publication activities. The methods employed by the department have also been extended by the study of oxidative damage, gene expression and new genotyping methods.

Department of the Molecular Biology of Cancer

(Head: MUDr. Pavel Vodička, CSc.)

focuses on the molecular mechanisms of the origin

and development of cancer, in particular that of the large intestine and rectum. A promising approach is the use of genomics in predicting the effectiveness of antineoplastic therapy and its individualization. The department has identified a range of genes involved in DNA repair, insulin pathways as well as intra- and extracellular transporters for assessing individual risks for colorectal cancer. The link between the genotypes and phenotypes of DNA repair genes has been described. A valuable contribution has been made towards identifying new loci in the 10p14 and 8q23.3 chromosomes in relation to colorectal carcinoma.

Laboratory of Cell Biology and Microscopy Unit

(Heads: RNDr. Karel Koberna, CSc., and RNDr. Jan Malínský, Ph.D.)

has been in existence since 2006. The laboratory deals with the structure of chromatin, DNA replication, and the targeted expression and transport of bioactive molecules to human cells within the “Nanotechnologies for Society” Programme. It has described the role of the ATP-dependant chromatin remodelling complex in regulating the timing of the replication of ribosomal genes. In cooperation with the Institute of Microbiology and the University of Regensburg, the researchers of the laboratory have published a study of the role of membrane potential in forming the plasmatic membrane. A fast fluorescent microscope enables the long-term confocal imaging of live cells.

Department of Immunopharmacology

(Head: RNDr. Zdeněk Zidek, DrSc.)

assesses trends in the development of new drugs, especially immunopharmaceuticals. There is promising research into new substances that strengthen the natural defence mechanisms of an organism, which is especially important in view of the growing occurrence of resistance to antibiotics. The department has developed procedures for rational, fairly economically affordable searches for the immunostimulatory properties of substances of both synthetic and natural origin. For example, immunostimulatory virostatics producing chemokines effective against the HIV virus have been patented.

Laboratory of Eye Histochemistry and Pharmacology

(Doc. MUDr. Jitka Čejková, DrSc.)

examines the causes of poor healing of lesions of the frontal ocular segment of the eye in various ocular diseases or injuries. It seeks possibilities for prevention or treatment that enable a positive outcome; procedures are prepared that make use of stem cells in the treatment of inborn defects of the cornea.

Research workers of the Institute, Czech as well as foreign, also work in the following three research centres of the Ministry of Education:

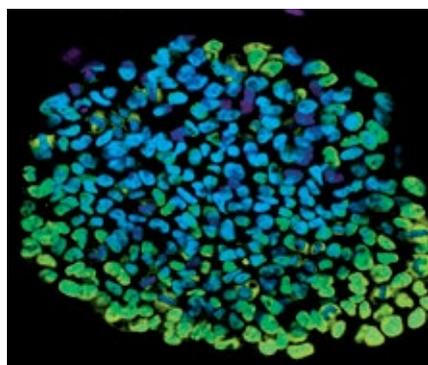
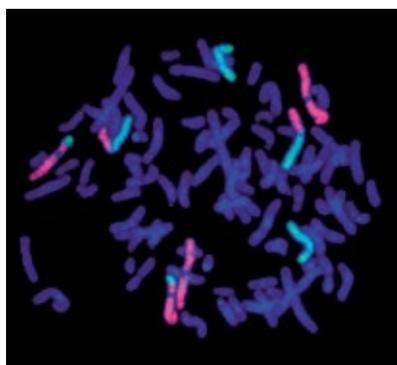
Centre for Cell Repair and Tissue Repair

(Head: Prof. Eva Syková)

combines a number of sites. Important findings have been made in stem cell transplantation in models of pathologies of the central nervous system, pancreas, liver and epidermis, the labelling of cells with

Left: Analysis of chromosome damage with the help of fluorescent probes. An example of translocation between chromosomes 1 and 4. Photo © R. Šrám.

Right: Presence of a molecular marker of undifferentiation in human embryonic stem cells (in blue) detected by indirect immunofluorescence. The transcription regulator Nanog is shown in green. Photo © A. Hampl.



superparamagnetic nanoparticles, the development of imaging methods and the development of materials for tissue repair.

New Antivirals and Antineoplastics

(Head: Dr. Zdeněk Zidek)

This department takes part in pharmacological research, for instance in the discovery of substances with immunomodulatory activity, significant in HIV therapy.

Centre for Neuroscience

(Head: Prof. Josef Syka)

joins together significant research sites in Prague in the field of neuroscience and takes part in research into the mechanisms of ionic channels, glial cells, synaptic and extrasynaptic transmission, the central mechanisms of hearing and pain, and the mechanisms underlying brain and spinal cord diseases and injuries.

Department for Technology Transfer

encourages cooperation between IEM departments and the business sphere both through training (project activities of the Centre for Support of Competitiveness in Biomedical Technologies funded from the JPD3 Programme) and research and development activities in the IBC IEM (the Innovative Biomedical Centre of the Institute of Experimental Medicine ASCR, JPD2 Programme). The IEM successfully completed the investment stage in July 2008; the operational stage follows.

The IEM is the only institute of the Academy of Sciences whose research focuses on clinical medicine with the aim of developing treatment procedures and technologies that can be applied in clinical practice. The following projects with direct clinical application are underway at the IEM:

- Bone cartilage replacement through the transplantation of expanded autologous cartilage cells in biomaterials based on biogenic macromolecules;
- The use of mesenchymal stem cells in order to speed up wound healing and their use in the treatment of spinal injuries and degenerative diseases of the central nervous system;
- Developing immunopharmaceuticals with the unique ability to stimulate interferon production, thus increasing the defence capacity of the organism against viral diseases and malignancies;
- Optimizing the properties of biomaterials based on polymer macroporous hydrogels and non-woven nanofibrous textiles for medical use;
- Developing diagnostics based on iron oxide nanoparticles designed for labelling and tracking cells in vivo with the aid of magnetic resonance;
- Using stem cells in the treatment of corneal defects, diabetes, liver failure, and ischemic heart disease.

If the outcomes of research are to be transferred to clinical practice, extensive trials are necessary. These require demanding technological facilities and are to be carried out under GLP and GMP conditions and in "clean rooms". The purpose of the IBC IEM project is to establish links with current worldwide trends in the development of biotechnologies and to make available to doctors and patients in the Czech Republic



modern treatment methods using cell therapy, tissue engineering and research outcomes in the fields of biomaterials and nanotechnologies. The task of the IBC IEM will be to support, in cooperation with private investors, the start-up of spin-off companies. In this way the IBC can create the basis for a future biomedical cluster and further extend its capacities.

The new premises of the Innovative Biomedical Centre will house the following:

- **Business incubator** for new spin-off companies that will have at their disposal all advisory services, manufacturing facilities and clean rooms with GMP status. The companies will have the opportunity to develop products of applied research.
- **Centre for Support of Competitiveness** in biomedical technologies that will focus on training and advisory activities, patent protection and the search for investment partners.
- **Centre of Applied Research** in biomedical technologies, including laboratories for applied research and development in the fields of regenerative medicine, cell therapy and pharmacology and the preparation of clinical studies.

Centre for Translational Medicine

The Institute is preparing this project from European funds within the operational programme Research and Development for Innovation. Translational medicine transfers the outcomes of basic medical research into clinical research and clinical practice. We would like to build a centre that will conduct high-quality basic medical research and, at the same time, have strong ties to innovative biotechnology practice. As regards its aim, the centre is to consist of a Centre for Regenerative Medicine, a Centre for Imaging Methods, a Centre for Cerebrovascular Diseases, a Centre for Biomedical and Biotechnological Innovations and an Administrative and Training Centre.

Conclusion

Science has always been a great and beautiful adventure, hard work and the art of experimentation, work encompassing all-round creativity, the art of not only communicating the outcomes to colleagues in expert lectures, to students and other interested persons, but also of taking an active part in the application of these outcomes in medical practice. A constant stream of new thoughts, ideas, doubts and critical assessments of the outcomes is an everyday reality in the life of a researcher. In medical research the overall picture is completed by our efforts to alleviate the suffering of the sick and improve the quality of their lives, but also by the necessity to come to terms with those ethical questions that accompany our research.