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

Premises of the Institute of Experimental Medicine AS CR, v.v.i., in Prague - Krč.

The Institute is a recognized centre of basic biomedical research and has the status of an EU Centre of Excellence – MEDIPRA. The Institute's researchers participate in projects of the 6th and 7th Framework Programmes and are engaged in extensive national and international collaborations. The Institute employs postgraduate students from abroad, who are paid either from ongoing grants or from the funds of the Institute.

The Institute supports junior group leaders and is a partner in the EU ENI-NET project, a network of excellent European neuroscience institutes. It is a seat of the Commission of Biomedicine for awarding the academic title DSc. and has the highest proportion of university graduates of all the Academy of Sciences research institutes.

The results of the IEM's research are directly applicable in neuroscience, regenerative medicine, pharmacology, teratology, environmental protection and diagnostic methods. Currently the Institute consists of 10 departments and 1 independent laboratory.

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Eva Syková, Director of the IEM, Image © J. Rasch

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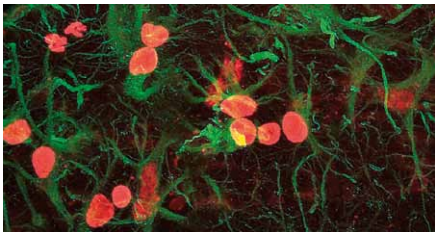
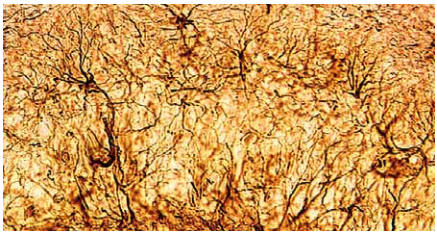


Stem cells and astrocytes in a brain lesion. Image © E. Syková.



Impaired cytoarchitecture in the aging hippocampus. Image © E. Syková

DEPARTMENT OF NEUROSCIENCE

(head: Prof. Eva Syková, MD, DSc)

consist of two units. **The Laboratory of Diffusion Studies and Imaging Methods** (E. Syková) is an internationally respected cen-ter in the field of ion-selective microelectrodes and magnetic resonance methods (MR). The main research focuses are ionic homeostasis and diffusion parameters in the central nervous system (CNS). Research in the laboratory has contributed to the understanding of extrasynaptic transmission in the CNS, to explaining the role of diffusion in a number of pathophysiological states and to the development of new MR diagnostic methods. **The Laboratory of Tissue Culture and Stem Cells**. (P. Jendelová) aims at labeling stem cells with superparamagnetic iron oxide nanoparticles for in vivo cell tracking by means of MRI. Research is focused on the use of adult and embryonic stem cells for the regeneration of the injured brain and spinal cord. Concurrently with stem cell research, the laboratory also develops and tests biomaterials based on macroporous hydrogels (in collaboration with the IMC ASCR) and nonwoven nanofibers (Technical University Liberec, Elmarco, Ltd). These materials can bridge not only CNS lesions, but also skin defects, including diabetic limbs.

The Laboratory of Eye Histochemistry and Pharmacology focuses on research into the damage and healing processes of the anterior eye segment caused by various injuries or diseases. It seeks approaches to improve healing in terms of prevention or treatment. To treat corneal injuries, methodological approaches using stem cells are being developed.

DEPARTMENT OF CELLULAR NEUROPHYSIOLOGY

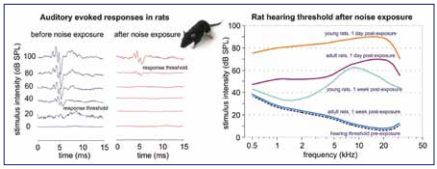
(head: Miroslava Anděrová, MSc, PhD)

focuses on research projects aimed at the diagnosis and therapy of CNS neurodegenerative deseases. Research in the **Laboratory of Molecular Neurophysiology** (A. Chvátal) is focused on the identification of the cellular and molecular mechanisms of integration in neural networks, through the characterisation of intercellular signalling pathways within neuronal-glial circuits and intracellular signalling mechanisms in neurones and glia under physiological and pathological conditions. Research in the **Laboratory of Neurobiology** (M. Anděrová) is focused on the cellular, molecular and morphological changes in neurons and glial cells during pathological states, such as ischemia or mechanical brain injury.

DEPARTMENT OF AUDITORY NEUROSCIENCE

(head: Prof. Josef Syka, MD, DSc)

consists of two units. The main research topic of the **Laboratory of Auditory Physiology and Pathophysiology** (J. Syka) is the study of the structure and function of the auditory system in animals under normal conditions and the evaluation of changes that occur during development, ageing and following the influence of various pathological factors such as noise or ototoxic drugs. Investigations in the **Laboratory of Synaptic Physiology** (R. Tureček) are aimed at studying the mechanisms of excitatory and inhibitory synaptic transmission, especially in the auditory system, with the aid of electrophysiological and immunohistochemical methods.



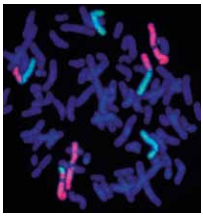
The rat hearing threshold is assessed on the basis of the recording of auditory evoked potentials from the brain. The results indicate that hearing in the early developmental period is more sensitive to injury than in adulthood.

DEPARTMENT OF MOLECULAR SIGNALLING

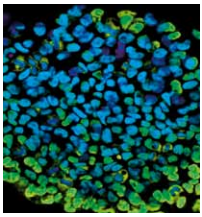
(head: Govindan Dayanithi, MSc, PhD)

focuses on the following research topics:

- molecular signalling mechanisms in excitable and non-excitable cells
- physiology of calcium signalling and calcium homeostasis in magnocellular neurones and terminals
- molecular mechanisms involved in the activation of plasma membrane calcium entry pathways with a modulatory effect on intracellular calcium release
- physiology of vasopressin and oxytocin in the central and peripheral nervous systems using newly developed transgenic rat models to visualize fluorescent vasopressin and oxytocin (vasopressin-eGFP; oxytocin-eCFP and oxytocin-mRFP1)
- physiology of vasopressin and oxytocin signalling in DRG neuron-glia interactions, nociception, pregnancy and lactation
- the physiopathology of calcium signalling in stem cells and neurodegeneration



Aanalysis of chromosomal damage using fluorescent probes. An example of translocation between chromosomes #1 and #4. Image © A.Rössnerová.



The presence of the molecular signature of nondifferentiated human embryonic stem cells (green). Image © A. Hampl.

DEPARTMENT OF TERATOLOGY

(head: Dr. Miroslav Peterka, MD, DSc)

investigates the causes and mechanisms of the origin of developmental anomalies using two experimental models (the developing chick embryo and the developing mouse dentition) and clinical-epidemiological studies. The research aim is to contribute to the knowledge of normal and pathological development, the ethiopathogenesis of developmental anomalies, and possibilities for their prevention. The origin of external malformations, especially of orofacial clefts, is the pivotal research topic of the Laboratory of Embryogenesis (M. Peterka). **The Laboratory of Odontogenesis** (R. Peterkova) focuses on tooth development under normal, pathological, and experimental conditions.

DEPARTMENT OF GENETIC ECOTOXICOLOGY

(head: Dr. Radim Šrám, MD, DrSc)

has as a major goal the study of genetic damage caused by genotoxic and carcinogenic compounds such as polycyclic aromatic hydrocarbons (PAHs), alkenes, etc. The effects of genotoxic xenobiotics are studied in cell cultures as well as in vivo by carrying out human transitional molecular epidemiologic studies and observational epidemiologic studies. **The Laboratory of Molecular Epidemiology** (R.Šrám) performs molecular epidemiology studies dealing with biomarkers of exposure to mutagens and carcinogens (DNA adducts, chromosomal aberrations, micronuclei, oxidative damage of DNA, proteins and lipids, genotyping, gene expression profiling), the outcome of pregnancies, and the health of children in relation to a polluted environment. **The Laboratory of Genetic Toxicology** (J.Topinka) is engaged in studying the genotoxic effects of xenobiotics, and oxidative damage of DNA, proteins and lipids is studied in cell cultures, such as the human hepatoma cell line HepG2 or human diploid lung fibroblasts. Further studies are concentrated on the effect of environmental pollutants on the molecular mechanisms of prostate cancer. **The Laboratory of Genomics** (P. Rössner Jr.) addresses gene expression profiles in populations exposed to polluted air, tobacco smoke and other factors, studied together with single nucleotide polymorphisms affecting metabolism, DNA repair, immunity and other biological processes.

DEPARTMENT OF THE MOLECULAR BIOLOGY OF CANCER

(head: Dr. Pavel Vodička, MD, PhD)

investigates the molecular mechanisms involved in the onset and progression of cancer, colorectal cancer in particular. **The Laboratory of DNA Repair** (P. Vodička) focuses on the molecular events included in DNA repair pathways. The DNA repair machinery plays a key role in removing damaged DNA bases and thus preventing mutagenic and carcinogenic effects. **The Laboratory of Tumour Genetics** investigates the fundamental molecular mechanisms involved in the cascade of genotoxic and carcinogenic effects in relation to exposure to xenobiotics and individual susceptibility factors. Particular attention is dedicated to discerning the role of low penetrance genes in the onset of sporadic forms of cancer, mainly colorectal cancer.

LABORATORY OF CELL BIOLOGY

(head: Dr. Karel Koberna, PhD)

studies chromatin structure, DNA replication, selective gene expression and the transport of bioactive molecules to human cells within the research programme "Nanotechnology for Society". Its researchers have described the role of the chromatin remodeling complex NoRC in the control of the replication timing of rRNA genes or the organization of human replicons.

DEPARTMENT OF PHARMACOLOGY

(head: Dr. Zdeněk Zídek, DrSc)

evaluates trends in drug research and development with special attention paid to immunomodulatory drugs. The work of the department is aimed at searching for novel compounds regulating the expression and activity of factors, mainly cytokines and nitric oxide, involved in the pathogenesis of many diseases. The research is motivated by the fact that both cytokine and anti-cytokine therapies are urgently needed in clinical practice. The department has developed original methodologies allowing quick, reliable and low-cost screening of the immunomodulatory effects of compounds of both synthetic and natural origin. Recently, agents with stimulatory effects on the production of virustatic interferon-gamma have been patented.

MICROSCOPY UNIT

(head: Dr. Jan Malinský, PhD)

is focused on the formation, distribution and dynamics of cellular structures not delimited by a membrane. A number of molecules within a cell are concentrated into specialized compartments devoid of well-defined boundaries and thus communicating by direct diffusion with their surroundings. Using current methods of microscopy, it is possible not only to localize these cellular structures but also to detect their movement and potential interactions on the level of individual molecules.

DEPARTMENT OF TECHNOLOGY TRANSFER/ INNOVATION BIOMEDICAL CENTRE

(head: Petr Bažant, PhD, MBA)

Basic scientific research outputs with high commerical potential advance to the phase of applied research or even experimental development. In the late phases of the innovation cycle, the exprectations and requirements of the target customers become more important. Therefore, it is reasonable to move those research teams dealing with experimental development closer to the customers and investors, i.e. to the Department of Technology Transfer. This is the case with the Laboratory of Tissue Engineering.

Translating basic research to clinical applications requires extensive trials using Good Laboratory Practice (GLP) and Good Manufactory Practice (GMP). The IEM has set up a successful project in the framework of the Single Programming Document for Objective 2 financed by European structural funds. The Innovation Biomedical Centre (IBC) was constructed from August 2007 to March 2008 and is equipped with a clean room facility and laboratories for applied research and scale-up technologies focused on regenerative medicine, cell therapy, biomaterials and pharmaceuticals as well as the design of clinical studies. The IBC was designed as a Business Incubator (office area, GMP-certified clean rooms) for spin-off companies. The companies housed in the incubator benefit from quality assurance and quality control services, shared consultation, patent, tax and other services and opportunities to participate in applied research projects run in the IBC facility.

LABORATORY OF TISSUE ENGINEERING

(head: Assoc. Prof. Evžen Amler, PhD)

was founded in 2005. Its main research topic is the preparation of artificial tissue, namely cartilage, as well as biodegradable composites for tissue engineering based on nanofiber scaffolds. The application of the novel technology of coaxial spinning for the production of smart nanofibers is intensively studied, especially in combination with liposomes, with the aim of developing suitable systems for controlled drug delivery. In addition, great attention is paid to accelerating the transfer of technologies and know-how to practical application. Computer modeling is also intensively employed, particularly for predicting protein structures and dynamics.

TRANSFER OF RESEARCH RESULTS INTO PRACTICE

The research activity of the Institute is oriented towards both basic research and also its application in clinical medicine. The objective of the Institute's activity is the development of medical treatments and methods applicable in many fields of clinical practice. The scientists at the Institute are working on the following projects with direct clinical impact:

- Bone cartilage replacement through the transplantation of expanded autologous cartilage cells in biomaterials based on biogenic macromolecules.

IBC IEM AS CR, archive SSČ AS CR, Image © S. Kyselová.

- The use of mesenchymal stem cells in order to accelerate wound healing and their use in the treatment of spinal injuries and degenerative diseases of the central nervous systém.
- 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 macroporous polymer hydrogels and non-woven nanofibrous textiles for medical use.
- Developing diagnostics based on iron oxide nanoparticles 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.

OTHER ONGOING PROJECTS

The IEM ASCR is maximizing the opportunities that the Structural Funds for the CR offer. An internal system to monitor, evaluate and implement projects has been created, aimed both at the development and technical improvement of physical infrastructure for research and innovation as well as for education, the popularization of research topics and the development of human resources. The new Innovation Biomedical Centre now operates as a business incubator and training center for small businesses translating the research results of the Institute into clinical practice. A project focused on the popularization of modern therapies, tissue engineering, and the therapeutic use of stem cells was implemented, followed by an educational project to expand and broaden the knowledge of researchers in preclinical and clinical testing and biomedical products quality control. The Institute, in cooperation with other research institutes and Charles University, is involved in the BIOCEV project, including a follow-up project aimed at preparing new research groups for the BIOCEV, and a new Research Center of Cell Therapy and Tissue Repair is being completed.

EU GRANTS OF THE 6TH AND 7TH FRAMEWORK PROGRAMMES

DiMI, ANGIOTARGETING, RESCUE, ENI-NET, CORTEX, STEMS, RegMedTeach, NANOEAR, EU SYNAPSE, INTARESE, ENVIRISK, AXREGEN, EdU-GLIA, BIOSCENT, Lateral membrane compartments:formation, functional relevance and genomics.