

**Evaluation of the Research and Professional Activity of the Institutes of the  
Czech Academy of Sciences (CAS)  
for the period 2010–2014**

**Final Report on the Evaluation of the Institute**

**Name of the Institute: Institute of Experimental Medicine of the CAS, v. v. i.**

**Fields, in which the Institute registered its teams:**

Basic medicine, Medical biotechnology and medical engineering

Observer representing the Academy Council of the CAS: Hana Sychrová

Observer representing the Institute: Josef Syka, substitute observer Radim Šrám

**Commission No. 9: Medical and health sciences**

Chair: Prof. Dr. Hans-Georg Joost

Date(s) of the visit of the Institute: November 20 - November 27, 2015

Programme of the visit of the Institute: see attached Minutes from the visit

Evaluated research teams:

*No. 1 - Cellular and Molecular Neurophysiology; No. 2 - Neurosciences; No. 3 -  
Molecular Biology of Cancer and Teratology; No. 4 - Transplantation Immunology,  
Tissue Engineering and Pharmacology; No. 5 - Auditory Neuroscience; No. 6 -  
Genetic Ecotoxicology*

## Introductory Statement of the Commission No. 9

The commission was very impressed by the generally high quality of biomedical research in the Academy institutes, and identified numerous strengths and opportunities (see individual reports). When we identified weaknesses, we intended to be above all, constructive, and to give external advice to the institutes for their future research strategies. However, the commission has identified structural shortcomings that might require a consideration by the Academy. These points concerned almost all institutes evaluated by the commission. Therefore, the following summary of general recommendations to CAS precedes each report on the individual institutes.

- **Coherence of the research concepts:** Most institutes and departments pursued a large number of projects that covered a very broad and diverse spectrum of themes. Many projects appeared to have little connection with others, resulting in a fragmentation of the general aims. The commission feels that diversity can be an advantage, when individual projects are of a high quality. However, when projects are not outstanding, diversity weakens the Academy institutes. In the discussion with the researchers, the commission identified the current strategy of funding as a potential reason for the fragmentation: approximately 50% of the funding comes from short-term, non-renewable grants which impairs the pursuit of important, more long-term and ambitious goals.
- **Research on humans:** The commission has asked all institutes for their translation of results into, and their participation in, human research (clinical research, epidemiology). Although there were several promising links and approaches, it seemed that this part of biomedical research needs a particular effort by the Academy. The commission realizes that linking experimental and clinical research is a very difficult task, but is convinced that a thorough discussion of this weakness must be started, and that this should lead to structural changes.
- **External advisory boards:** Most institutes lacked an external scientific advisory board. The commission considers this a particular weakness, and believes that the quality of the academy institutes could be improved by the discussion of all decisions affecting research directions in such a scientific advisory board.
- **Internal discussion and development of the research concepts:** In addition to the lack of a scientific advisory board, the commission identified the lack of other procedures that support the internal development and quality control of the scientific concepts. As an example, the commission had

expected that each institute has a forum where all projects and ideas are discussed by the principal investigators of the institutes (e.g. yearly retreats). The commission also felt that the current decision process for the initiation or termination of projects/units is suboptimal.

- **Training of PhD students within the frame of a Graduate School:** The commission concluded that the participation of students in the research programs of the institutes is overall very good. However, we note that the general training of PhD students could be improved by structures within the Academy institutes (Graduate schools) that offer a comprehensive training in all research skills, beyond the level of the respective group. Specifically, by this training, all students should become acquainted with the research of the whole institute including concepts, methods and results as well as having direct access to a combination of modern soft skills courses. Thus, building effective graduate schools would serve to strengthen the perception that studying for a PhD in a CAS institute indeed represents an attractive contemporary career option for excellent students. Indirectly, such structures would also stimulate exchange and collaboration between groups, possibly also between preclinical and clinical research. The commission learned that Graduate Schools do exist within universities, but feels that the Academy's pursuit of excellence requires a leading role of their institutes in such structures.

## **A. Evaluation of the Institute as a whole**

### **1. Introduction**

The Institute of Experimental Medicine (IEM), Czech Academy of Sciences conducts biomedical research in the fields of neuroscience, regenerative medicine, and stem cell biology as well as in the molecular biology of cancer, genetic ecotoxicology, pharmacology and teratology.

At the end of 2014, the Institute comprised 322 employees including 80 scientists, 55 PhD students and 97 technicians or supporting functions. Approximately half of the employees fall within the age group of 25-40 years. IEM currently has 10 departments, which were in part combined for this evaluation (presentation of 6 groups). The commission notes that in some these presentations there was little interaction between the combined units, creating a somewhat fragmented impression of research aims and results.

## 2. Strengths and Opportunities

The commission identified the following strengths and opportunities:

IEM is **well structured to translate basic research into clinical research and applications**. It presents with a **clear mission to devote themselves to clinical applications**.

**Sound science:** overall, experienced scientists lead the research departments. Quality of the scientific projects is reflected by high publication rate with the majority of publications scoring in the quality groups 2 and 3, as defined by the CAS. Scientific excellence is also confirmed by the ability of IEM to attract international scientists and PhD students and competitiveness in attracting grant money.

**Strong national and international partnerships.** The Institute is an internationally recognized centre in the respective fields. It has participated in numerous EU funded joint projects. The Institute has collaborations with many Czech and also international institutions. Most intense national collaborations include Charles University's First, Second and Third Medical Faculties and Faculty of Science, the Institute for Clinical and Experimental Medicine (IKEM) of the Ministry of Health, the Institute of Macromolecular Chemistry CAS, the Institute of Physics CAS, the Institute of Physiology CAS, and the Institute of Organic Chemistry and Biochemistry CAS. IEM also participated in the establishment of the Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University in Vestec (BIOCEV), which was not in operation at the time of the site visit.

**High translational potential and the infrastructure generated to do it.** IEM has created an infrastructure fostering the outreach of the most advanced translational projects to the industry. Their Innovative Biomedical Centre (IBC) serves as an incubator for early stage spinoff companies stemming from IEM research activities. ICB now hosts five spin-off companies at different stages of the development. Along with the management and infrastructure support come the training courses for the young scientists that help them to navigate in the space of biotech industry and IP protection. IEM has also put together the Research Centre for Cell therapy and Tissue repair. Within the Operational Program Prague Competitiveness (OPKK) it promotes the research and clinical applications in the field of advanced therapy medicinal products, with the focus on stem cells, biomaterials and nanomaterials. Translational potential is further emphasized by rich activity in the IP protection. Within the last five years scientists in the Institute received 117 Czech and 21 foreign grants, predominantly from the EU. The Institute also fosters research from bench to bedside.

The commission acknowledges the merit of such complex and generous infrastructure for translating the findings of IEM research activities into clinical trials.

However, the commission had no detailed insight into the structure and operations of the translational infrastructure and into the ongoing clinical trials. Also, the commission was aware of the current controversy on the efficacy of stem cell treatment e.g. in ALS which has raised ethical concerns. Because the commission had no insight into the clinical application, its review was beyond the scope of the current evaluation, and the commission focused on the evaluation of the scientific performance of IEM.

**Teaching activities-** IEM scientists have numerous teaching activities at many academic institutions with over 20 semestral courses at bachelor and master levels. IEM collaborates on the educational programs with all major Czech universities. Major focus is put on the training of PhD students as they represent a major driving force behind the experimental work. Overall, approx. 50-60 PhD students are engaged at IEM, 10-15 new students are accepted annually while 6-10, on average, defend their PhD thesis every year. Besides the scientific training, curriculum for PhD students also comprises the training in complementary skills such as publication writing, grant writing and project management. Commission also acknowledges the ability of IEM research groups to attract foreign PhD students.

### 3. Weaknesses and Threats

The commission identified several weaknesses that deserve further attention:

(1) The **age structure** is a potential threat to the Institute. While the overall age structure of the IEM seems healthy, several departmental group leaders approach or exceed the age of retirement and no clear strategy for their succession with regard to scientific directions and organizational structure of the renewal process was presented. To guide this process, the Institute needs an external advisory board (see recommendations).

(2) Despite the claimed focus on Neurosciences the presented **scope of research activities is extremely diverse and fragmented**. Although the commission recognises that diversity is inherent in the field, it thought that the diversity limits the potential for synergies between the respective departments and, in some cases, results in the existence of teams that lack the critical mass for being competitive.

(3) The commission was **unclear about how strategic decisions are made** for future direction, including a transparent, decision-making procedure followed for the future recruitments and for attracting brilliant postdocs and senior researchers.

(4) Given the extent of translational activities in several high-risk approaches, a potential threat relates to the sustainability of funding.

(5) Hypothesis-driven, deep-drilling research appears underrepresented in the Institute.

#### 4. Recommendations

- (1) The commission recommends a yearly retreat of IEM (1-2 days), where the entire faculty (all PIs) can discuss emerging fields and technologies that may influence the overall research strategy and future focus of the Institute. IEM should focus on establishing a transparent process to avoid a top-down approach in defining Institute direction.
- (2) Establish an international advisory board that would help to define and guide the future development of research and structure of the Institute. This advisory board should comprise international as well as domestic members.
- (2) IEM should define a transparent system of internal evaluation to optimize the scientific structure and output of the Institute. Effort should be made to actively look for synergies between different research teams.
- (3) IEM should establish a system of international calls for opening of new positions. Make effort to attract successful postdocs willing to return to Czech Republic and establish their own research groups.
- (5) IEM should establish a structure (graduate school) for the training of PhD students, encompassing regular seminars, data presentations and annual retreats/conferences at the Institute level.
- (6) IEM should introduce measures to enhance interaction between its units as well as with other CAS institutes. Furthermore, IEM should enhance the interaction with clinical experts in order to introduce the clinical perspective into its preclinical work.

#### 5. Detailed evaluations

##### *Declaration on the quality of the results and share in their acquisition*

The commission concludes that the quality of results of the Institute is overall **very good**. In collaborations, the contribution of the Institute plays an essential role, and the Institute is often the leading partner.

*Declaration on the involvement of students in research*

The commission considers the involvement of students in research very good, in parts excellent. Their contribution to the success of the Institute is vital and fosters a very positive and creative atmosphere.

*Declaration on societal relevance*

The commission concludes that the activities of IEM are of very high societal relevance.

*Declaration on the position in the international and national context*

The commission concludes that the position of IEM is Internationally visible, in some parts competitive, and nationally leading.

*Declaration on the vitality and sustainability*

The commission considers the vitality and sustainability of IEM high provided that the problem of age structure is resolved.

*Declaration on the strategy and plans for the future*

The commission concludes that strategy and plans for the future are convincing overall within the limitations described above.

## **B. Evaluation of the individual teams**

### **Evaluation of the Team No. 1: Cellular and Molecular Neurophysiology**

#### **1. Introduction**

The scientific team consists of two departments: Department of Cellular Neurophysiology (head Miroslava Anděrová) and Department of Molecular Neurophysiology (head Govindan Dayanithi).

#### **Department of Cellular Neurophysiology**

The Department of Cellular Neurophysiology investigates 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. A second class of cells the Department is interested in are NG2 glial cells, also known as polydendrocytes. During development and in the adult nervous tissue, these cells function primarily as precursors of oligodendrocytes, but following injury of the central nervous system they proliferate and differentiate into other cell types. The research aims to characterize their membrane properties in post-ischemic tissue and in the progression of Alzheimer's disease. An additional aim is to elucidate the role of Wnt- and Shh-signaling pathways in the proliferation/differentiation of NG2 glial cells.

Within the evaluation period the Laboratory of Cellular Neurophysiology published over 30 papers with a summary IF of 141.

#### **Department of Molecular Neurophysiology**

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 neurons and glial cells. Recently, within the Department, a new approach was used to evaluate the plasticity of calcium signals in neural precursors derived from stem cells of various origins. The objective is to evaluate the pathophysiology of calcium signalling in neurons in animal models of neurodegenerative diseases and in the stem cells transplanted into the injured spinal cord.

Within the evaluation period the Laboratory of Molecular Neurophysiology published 15 papers with a summary IF of 55.

## **2. Strengths and Opportunities**

- (1) The commission appreciates that the research effort focuses on the very important area. Both group leaders clearly have high scientific expertise and sound complementary methodological approaches.
- (2) Strong publication record given the size of the groups.
- (3) The commission considers the development of transgenic rat models a methodological strength.

## **3. Weaknesses and Threats**

- (1) The commission identified largely descriptive studies with limited hypothesis-driven input.
- (2) The presented research topics appeared to the commission to be fragmented and not connected with that of other groups. Also, an overarching research theme was not clearly presented to the commission.
- (2) The groups are involved in very few intramural or extramural collaborations. Furthermore, input from clinical experts was not apparent.

## **4. Recommendations**

- (1) The groups in the team should go beyond descriptive studies and should increase the quality of their work, thereby facilitating publications in higher profile journals.
- (2) The groups should intensify external collaborations. Joint projects could broaden the spectrum of models and experimental techniques and could thereby increase the quality of the research.
- (2) The groups should seek advice from clinical experts for improvement of the pre-clinical research with regard to models and readouts.

## **5. Detailed evaluations**

### *Declaration on the quality of the results and share in their acquisition*

The commission concludes that the overall quality of the results is very good, with the limitations described above.

*Declaration on the involvement of students in research*

Involvement of students in the research and publication activities is very good.

*Declaration on societal relevance*

Commission considers the area of research of high societal relevance.

*Declaration on the position in the international and national context*

The commission concludes that the Department is internationally visible and nationally leading.

*Declaration on the vitality and sustainability*

Research activities and scientific guidance in the current structure of the Department are sustainable.

*Declaration on the strategy and plans for the future*

The commission concludes that research strategy and future plans were not convincingly presented and should be clarified and discussed with the responsible bodies of the Institute, preferably with an external scientific advisory board.

**Evaluation of the Team No. 2: Neuroscience**

**1. Introduction**

Team No. 2 consists of three laboratories with complementary research activities.

**The Laboratory of Tissue Culture and Stem Cells**

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

**The Laboratory of Diffusion Studies and Imaging Methods** studies the changes in the extracellular space diffusion parameters and extrasynaptic (volume) transmission that occur during physiological and pathological states. Several animal models of pathological states and diseases attacking the CNS are used, e. g., models of chronic pain, ischemia and ischemic lesions, perinatal and early postnatal anoxia, brain edema, hydrocephalus, multiple sclerosis, Parkinson's disease, Alzheimer's disease, tumours, epilepsy, developmental disorders, aging, and brain and spinal cord injury, as well as models of CNS

damage evoked by chemical or physical factors such as neurotoxins or X-irradiation. The research aims are the improvement of therapy and diagnostic methods for CNS diseases and the prevention of CNS damage.

### **Laboratory of Biomaterials and Biophysical methods**

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

Overall the Neuroscience team published over 90 papers with the total IF of 352 and 5 patent applications. According to the presentation, there are 4 ongoing clinical, stem cell-therapy-based studies resulting from the preclinical research. As outlined earlier (p. 3), the review of these studies was beyond the scope of this evaluation.

Members of Neuroscience team have very extensive teaching activities at a number of academic institutions including contributions to pregraduate as well as postgraduate courses.

## **2. Strengths and Opportunities**

- (1) The commission appreciates the unique approach to study the extracellular brain volume.
- (2) The commission appreciates the focus on medically relevant projects, in particular the translational approach of the research projects to find therapies for so far untreatable diseases.
- (3) The scientific output of the team is excellent in terms of number, quality and citation impact of published papers
- (5) A particular strength is the clear push for the translational aspects and the IP protection.
- (6) There is an excellent involvement of students including graduates from the Medical Schools.

## **3. Weaknesses and Threats**

- (1) Very ambitious scope of the translational research including the performance of clinical studies under the umbrella of spin-offs is highly financially demanding. It is also demanding in terms of a strong IP position of spinoff technologies. There is a significant risk that the plans

as outlined will not find appropriate financing schemes, especially in the community of biotech investors.

(2) The commission feels that aiming at a clinical use of stem cells without a definitive proof of their pre-clinical efficacy is a very risky approach. Specifically, the commission discussed whether the team employed appropriate models and readouts to prove efficacy of the stem cell therapy in neurodegenerative diseases.

(3) IP issue resolution must be an integral part of the spin-off process, and a clear path towards a strong IP position was not defined.

#### **4. Recommendations**

(1) The team should focus on putting together a strong package of preclinical experiments to support the proof of concept of stem cell based technologies in relevant animal models with appropriate readouts.

(2) The team should carefully draft a detailed plan to attract investors for the clinical trial program.

(3) The commission recommends that the Institute increase support for the Laboratory of Biomaterials and Biophysical Methods, which currently lacks a critical mass.

#### **5. Detailed evaluations**

##### *Declaration on the quality of the results and share in their acquisition*

The commission concludes that the overall quality of the results is very good, in parts excellent, with the above-described limitations.

##### *Declaration on the involvement of students in research*

The involvement of students, including the medical graduates is very good, in parts excellent.

##### *Declaration on societal relevance*

The research activities of the Neurosciences Team are of very high relevance for the society.

##### *Declaration on the position in the international and national context*

The commission concludes that the Department is internationally visible and nationally leading.

##### *Declaration on the vitality and sustainability*

The research activities of the presented groups are sustainable provided that sufficient funding is obtained. The commission also recommends that excellence among the younger scientists should be identified and steps taken to foster their advancement in order to ensure the continuation of the programmes.

#### *Declaration on the strategy and plans for the future*

The strategy for the future was clearly presented. Presented projects are highly financially demanding, require a strong IP position. The commission feels that the orientation on the high-risk field of stem cell based therapies of neurodegenerative diseases should be counter-balanced by less risky projects.

### **Evaluation of the Team No. 3: Molecular Biology of Cancer and Teratology**

#### **1. Introduction**

For the purpose of the evaluation, two teams with distinct research topics were presented together. This combination increased the complexity of the evaluation, and, as was noted before, enhanced the impression of a too fragmented research concept. The commission tried to report its conclusions for each of the groups separately, when necessary.

#### **Molecular Biology of Cancer**

This Department investigates the molecular characteristics of solid cancers, especially of the colon, rectum, pancreas and ovaries. Here, the Department focuses 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, and (4) determine the long-term prognosis. In addition, they 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, thereby preventing the neoplastic transformation of healthy cells. On the other hand, the DNA damage repair is significantly activated during the response of tumour cells to the impact of chemotherapeutics. The treatment by some of the most commonly used drugs proceeds via massive DNA damage and subsequent cell death. High activity of DNA repair mechanisms may contribute to resistance of cancer cells to such substances. The Department has been working with different types of biological material from patients with cancer, such as solid tissue samples, blood cells or plasma.

From 2010 to 2014, the Department published a total of 61 papers, IF=262,7

## **Teratology**

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

From 2010 to 2014, the Department published a total of 19 papers, IF=60,3

### **2. Strengths and Opportunities**

- (1) Both groups investigate societally relevant research topics.
- (2) The commission appreciates the intense clinical cooperation of the Molecular Biology of Cancer group.
- (3) There is a very productive involvement of the Molecular Biology of Cancer group in international joint research collaborations.
- (4) The commission appreciates the high number of good quality papers of the Molecular Biology of Cancer Group

### **3. Weaknesses and Threats**

- (1) The commission sees the extremely competitive field of DNA repair mechanisms as a potential threat.
- (2) The relatively restricted repertoire of methods restricts the potential of the groups to gain deeper mechanistic insights.
- (3) There were no apparent synergies between the two presenting groups.
- (4) The commission noted a limited involvement of students in the Teratology group

### **4. Recommendations**

The IEM should note and discuss the lack of synergies in the activities of these two groups and consider restructuring and/or redefining the research focus of the Teratology group, preferably with guidance by an external advisory board.

### **5. Detailed evaluations**

#### *Declaration on the quality of the results and share in their acquisition*

The commission considers the quality of publications of the Molecular Biology of Cancer group as very good, in parts excellent, and good for the Teratology group.

*Declaration on the involvement of students in research*

Participation of students in research is good for the Molecular Biology of Cancer group but inadequate in Teratology group.

*Declaration on societal relevance*

The social relevance of investigated projects is high.

*Declaration on the position in the international and national context*

The Molecular Biology of Cancer group is internationally visible and nationally leading. The commission considers the Teratology group to be nationally visible.

*Declaration on the vitality and sustainability*

Vitality and sustainability of the Molecular Biology of Cancer is good. However, commission is concerned about the sustainability of the Teratology group, given the suboptimal age structure, lack of PhD students and inferior scientific output.

*Declaration on the strategy and plans for the future*

Credible and relevant strategy for the next period was presented for the Molecular Biology of Cancer group.

**Evaluation of the Team No. 4: Transplantation Immunology, Tissue Engineering and Pharmacology**

**1. Introduction**

For the purpose of the evaluation, three teams with distinct research topics and independent leadership were presented together. This combination increased the complexity of the evaluation, as it is not appropriate to draft common conclusions for independent research groups with distinct scientific performance. Therefore, the commission is reporting its conclusions for each group separately, when necessary.

**Transplantation Immunology**

The research of this Department is focused on cellular and molecular mechanisms that regulate the immune response after the transplantation of stem cells. The final aim of this research is the improvement of survival of genetically distinct cells that were transferred for therapeutic purposes. Various types of stem cells are cultured, differentiated and characterized in vitro. With nanofiber scaffolds, the cells are transferred onto a damaged ocular or skin surface. The beneficial effects of the stem cell therapy are characterized immunologically, immunohistochemically and on the level of gene expression. The results are validated in preclinical experimental models with the aim to translate the knowledge from the basic

research into a stem cell-based therapy in patients with a heavily damaged ocular surface.

From 2010 to 2014, the Department published a total of 19 papers, IF=49,1.

### **Tissue Engineering**

The research of the Department is focused on the development of biodegradable scaffolds for tissue regeneration, such as nanofibers, foams, and hydrogels for the regeneration of cartilage, bone and incisional hernia. The group also carries out computer modelling of protein structures, and improves the technology of controlled drug delivery from nanofiber scaffolds with liposomes for targeted release into the defect. In addition, the group aims at the development of three-dimensional nanofibers, using the novel technique of Forcespinning®. These nanofibres are more suitable for cell growth and differentiation. The accelerated transfer of newly developed technologies and know-how into clinical practice has a high priority.

From 2010 to 2014, the Department published a total of 24 papers, IF=68,1 patents have resulted from departmental research.

### **Pharmacology**

The ultimate goal of the Department of Pharmacology is the development of novel low-molecular weight agents for the treatment of infectious and inflammatory diseases. In the evaluated period the group demonstrated immunosuppressive properties of newly synthesized derivatives of pyrimidine, and immunological activities of compounds of natural origin. Advanced studies are focused on the analysis of chemical structures and on the activity-guided synthesis of compounds. These activities shall facilitate transfer of experimental data to preclinical and clinical phases of research, and to commercial exploitation. Optimization of the structure of agents is achieved by a close communication between chemical and biological teams of the project. An indispensable part of the studies is the investigation of the mechanism of drug action. The therapeutic potential of promising drug candidates is assessed in experimental models of autoimmune and inflammatory human diseases.

From 2010 to 2014, the Department published a total of 24 papers, IF=46,7; 1 patent has resulted from the departmental research.

## **2. Strengths and Opportunities**

- (1) There are significant synergies between the Departments Transplantation Immunology and Tissue Engineering.

- (2) Recent results of the Transplantation Immunology Department have a high translational potential.
- (3) The strong teaching activities and the extraordinary involvement of PhD students in the research are a particular strength.

### **3. Weaknesses and Threats**

- (1) In parts, the teams lack a convincing scientific performance as proven by high-quality, frequently cited publications.
- (2) The commission identified a lack of external collaborations, in particular of those that are required for translation of the results into clinical application.
- (3) The sustainability of the Department of Transplantation Immunology group might be at risk, as there is no clear plan for the succession of its chief.

### **4. Recommendations**

The commission recommends that the responsible bodies of IEM (preferably with an external advisory board) to consider reorganisation of the departments according to the existing synergies between their experimental projects, and with regard to their scientific performance.

### **5. Detailed evaluations**

#### *Declaration on the quality of the results and share in their acquisition*

Commission concludes that the presented results are overall good. Recent results on the treatment of ocular surface injuries are perceived as very good. The results of the Pharmacology group were evaluated as adequate (mean IF below 2, declining trend).

#### *Declaration on the involvement of students in research*

The involvement of students in the research activities is good for the Departments of Transplantation and Pharmacology, very good for the Department of Tissue Engineering.

#### *Declaration on societal relevance*

The commission considers the societal relevance of the Departments of Transplantation Immunology and of Tissue engineering very high.

### *Declaration on the position in the international and national context*

The commission considers the Departments of Transplantation Immunology and of Tissue engineering as internationally visible and nationally leading. The Pharmacology group is nationally visible.

### *Declaration on the vitality and sustainability*

Commission considers the sustainability of the Department of Transplantation Immunology and of Pharmacology potentially threatened because of their age structure and the lack of plan for the succession of the PI. Also, the Department of Pharmacology group did not present a convincing long-term research strategy.

### *Declaration on the strategy and plans for the future*

Strategy and plans for the future were convincing for the Departments of Transplantation Immunology and of Tissue Engineering, unclear for the Department of Pharmacology.

## **Evaluation of the Team No. 5: Auditory Neuroscience**

### **1. Introduction**

This Department investigates the nature of auditory processing by studying the characteristics of neurons in individual auditory brainstem nuclei and in the cortex under normal and pathological conditions. Electrophysiological and histological data are correlated with behavioural changes in animal experiments. Audiological tests and MR imaging are used to characterize age-related alterations of hearing in humans.

### **Laboratory of Auditory Physiology and Pathology**

The Laboratory investigates the basic principles of the neuronal processing of simple tones and complex sounds as well as the pathologies of the peripheral and central parts of the auditory system that are consequences of noise exposure or aging. These principles and pathologies are investigated in experimental animals and in human subjects with electrophysiological, behavioural, audiometric and morphological methods.

The group has demonstrated that an 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. Two-photon calcium imaging in vivo allowed studies of information processing in selected populations of neurons in the auditory cortex of transgenic mice. In human studies, 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. Significant atrophy in the

auditory cortex of elderly subjects with different degree of presbycusis was shown by magnetic resonance morphometry. 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.

### **Laboratory of Synaptic Physiology**

The Laboratory of Synaptic Physiology studies the mechanisms underlying the plasticity of excitatory and inhibitory synaptic transmission in rodent brain slices by electrophysiological and immunohistochemical techniques. The Calyx of Held synapse in the medial nucleus of the trapezoid body (MNTB) – a critical synapse in auditory processing - is being used as a model of the central type of synapse due to its large size; this allows direct investigation by the patch-clamp technique. Recent projects in the laboratory are aimed at revealing the physiological roles of inhibitory transmitters, their receptors and uptake systems in such MNTB neurons. Experimental work has provided evidence of the novel excitatory nature of the classical inhibitory transmitters GABA and glycine. The results show that chloride-permeable glycine receptors, G-protein coupled GABA-B receptors, N-type Ca<sup>2+</sup> channels and calcium-activated potassium conductance work in concert to support the extremely high reliability of glutamatergic synaptic transmission at MNTB neurons. Results were obtained in cooperation with the Department of Biomedicine, University of Basel, Basel, Switzerland.

From 2010 to 2014, the Department published a total of 36 papers, IF=192,0.

## **2. Strengths and Opportunities**

- (1) The strong, traditional Department has a clear vision and an established position in the international context.
  
- (2) The Department has a recognised high expertise in developing and performing tests of the auditory function in experimental animals. In addition, the Department employs a broad spectrum of methods and has a strong capability for developing other applications.
  
- (3) The coupling of GABA receptor signalling to potassium channels is an original result (first-author paper in *Neuron*).
  
- (4) The in-vivo application of 2-photon microscopy is unique in the Czech Republic.
  
- (6) The Department is engaged in productive international collaborations, and has a strong commitment for international training of their scientists.

(7) The Department is engaged in grant applications together with clinical centres.

### **3. Weaknesses and Threats**

As a potential threat for the Department of Auditory Neuroscience, the commission identified the age of its principal investigator, and structural changes that could result from his upcoming retirement.

### **4. Recommendations**

(1) The group of Dr. Tureček that published excellent papers in leading journals. Currently, the group lacks a critical mass and should receive more support from the institutional budget.

(2) The Department of Auditory Neuroscience should encourage young successful scientists to establish their own groups within the Department and starts their own research projects.

### **5. Detailed evaluations**

#### *Declaration on the quality of the results and share in their acquisition*

The commission concludes that the results of the Laboratory were overall very good, in part excellent. In the majority of the collaborations, the group was the leading partner; in all others it provided essential contributions.

#### *Declaration on the involvement of students in research*

Overall, the involvement of students in research and publication activities is very good.

#### *Declaration on societal relevance*

The commission considers the societal relevance very high

#### *Declaration on the position in the international and national context*

The commission concludes that the Department is internationally competitive and nationally leading.

#### *Declaration on the vitality and sustainability*

The commission considers vitality and sustainability of the group very good. Attention should be paid to the support of the newly formed group of Dr. Tureček and to the transition in the leadership of the Department in the eventuality of the retirement of Prof. Syka.

#### *Declaration on the strategy and plans for the future*

The commission concludes that research strategy, methodological improvements and future plans are convincing and demonstrate a clear vision.

## **Evaluation of the Team No. 6: Genetic Ecotoxicology**

### **1. Introduction**

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 investigated in cell culture as well as in human epidemiological studies in order to assess the impact of air pollution on human health, in particular pregnancy outcomes and child health. In addition, the genotoxic and epigenetic effects of dust particles such as diesel exhaust are studied. Methodology and readouts comprise up-to-date methods of molecular epidemiology and biomarker analysis.

From 2010 to 2014, the Department published a total of 83 papers, IF=300,1.

### **2. Strengths and Opportunities**

- (1) The impact of environmental pollutants on the epidemiology of human diseases, pregnancy outcomes and child health is a highly relevant research topic.
- (2) The team has an outstanding, documented expertise in the appropriate design and analysis of epidemiological studies and has access to large, exposed populations within the Czech Republic as well as advanced molecular methodology.
- (3) The results of the team have been published in numerous articles, and have received a high international recognition.
- (4) The team is involved in several international collaborations and EU projects.

### **3. Weaknesses and Threats**

- (1) As a potential threat for the Department, the commission identified the age of its principal investigator and structural changes that might result from his upcoming retirement.
- (2) There was no apparent interaction with other groups within the IEM or in other CAS institutes.
- (3) The Department publishes predominantly in specialized journals of toxicology, mutagenesis and environmental health; it has few highly cited papers in the evaluation period 2010-2014. The citation frequency of its

publications appeared to be lower in this than in the previous evaluation period.

#### **4. Recommendations**

(1) Efforts to integrate the group better into the Institute in order to provide synergies with other units of IEM.

(2) The Institute should make efforts to ensure the continuity of this group.

#### **5. Detailed evaluations**

##### *Declaration on the quality of the results and share in their acquisition*

The commission concludes that the results of the Laboratory were overall very good, in part excellent. In the majority of the collaborations, the group was leading partner; in all others it provided essential contributions.

##### *Declaration on the involvement of students in research*

The involvement of students in research and publication activities is adequate (only 4 defended thesis in 2010-2014).

##### *Declaration on societal relevance*

The societal relevance of this particular research area is very high.

##### *Declaration on the position in the international and national context*

The commission concludes that the Department is internationally visible and nationally leading.

##### *Declaration on the vitality and sustainability*

As a result of the age structure of the Department, it has to undergo a generational change within the next few years. The success of this change will determine the future vitality and sustainability of the Department and of its research.

##### *Declaration on the strategy and plans for the future*

The commission concludes that future research strategy, methodological improvements and research directions are convincing and demonstrate a clear vision.

**Date:** December 15, 2015

**Commission Chair:** Prof. Dr. Hans-Georg Joost