

# **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 Microbiology of the CAS, v. v. i.

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

Basic medicine

Observer representing the Academy Council of the CAS: Hana Sychrová

Observer representing the Institute: Jiří Gabriel, substitute observer Helena Tlaskalová

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

Chair: Prof. Dr. Hans-Georg Joost

Date of the visit of the Institute: November 27, 2015

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

Evaluated research teams:

*No. 17 - 151 - Laboratory of Cellular and Molecular Immunology; No. 18 - 152 - Laboratory of Tumor Immunology; No. 19 - 153 - Laboratory of Gnotobiology; No. 21 - 156 - Laboratory of Immunotherapy*

## 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 Microbiology was founded by Ivan Malek in 1962 and moved to the new campus in 1964. The Institute is one of the two biggest institutes that were evaluated by this commission (similar in size to Institute of Molecular Genetics). The organizational structure of the Institute of Microbiology comprises 22 Laboratories. In addition, there are three core facilities: the Biotechnological Pilot Plant, the Center for DNA Sequencing, and the Center Cytometry and Microscopy. Two units are not located on the campus in Prague: Algatech in Trebon and Gnotobiology in Novy Hradek.

The Institute comprises 640 employees (517 FTEs) including 495 employees in research units. The age structure appears to be well balanced: the average age of the scientists is 45 years, the average age of the lab chiefs is 52 years. The Institute of Microbiology has 153 PhD students. The Institute staff is involved in teaching 60 courses at the Charles University in Prague, which amounts to 1736 hours of teaching. As close research cooperation with the University, there are 16 joint labs and research centres at the Institute. The Institute of Microbiology tries to recruit scientists coming back from the international post docs. thus having fellows of a special scheme: "Navrat" (Returns) and several other fellowships.

The annual budget of the Institute is 353,5 Mio. KCs (173 Mio. institutional support, 169 Mio. from grants by public grant agencies, and 14.5 Mio. from industrial contracts). The commission noted that the Institute was very successful in competing for grant money. However, these grants were usually small and short-term, creating smaller and possibly underfunded projects. The number of papers has increased from 744 to 944 in this evaluation period. In addition, the Institute published in somewhat more visible journals (the average impact factor 2.9 in 2005-2009, 3.4 in 2010-2015. As compared with other institutes of the Academy, there were fewer very high quality papers in top journals.

In the future, the Institute intends to sustain large infrastructures and core facilities such as the Algae biotechnology, the cytometry and microscopy centre, and the DNA sequencing unit.

Other expensive infrastructures include ELIXIR network (Bioinformatics), C4Sys - systems biology infrastructure, Nanobiology and Structural Biology. In addition, the Institute participates in BIOCEV, which the commission considered a positive development. However, the participation in this research centre appears to be a substantial financial challenge, since its budget is not yet passed by the parliament of the Czech Republic.

Since only 4 Laboratories were evaluated in detail by this commission, the following assessment of the Institute of Microbiology is mainly based on the presentation of the whole Institute by its director, and on his answers to questions of the commission.

## **2. Strengths and Opportunities**

The commission identified as strengths and opportunities:

(1) Some core facilities have a high potential. However, some of these core facilities offer methods that require constant updating. Therefore, the Institute has to implement an efficient internal control of quality and necessity of their services.

(2) The gnotobiology facility is unique in that this technology is mastered by only 5 institutes in Europe. There are numerous international collaborations, indicating that the unit works successfully. However, the output in high-quality publication appears too low for such a group in the last few years.

(3) The research concepts of the different Laboratories comprise highly relevant topics. However, the commission had the impression that the overall research concept is in part fragmented, and would benefit from internal discussions in order to increase synergisms and cohesion.

(4) The commission identified some translational potential of the research aims and results (e.g. the polymer drug carriers). These aspects should be further strengthened, to combine with efforts to enhance human and clinical research (see below).

(5) The scientific output, as measured in the numbers of papers, is very good. However, the commission noted that not all groups succeeded to publish in high quality journals.

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

The commission identified the following weaknesses and threats:

- (1) The overall research concept of the Institute appears fragmented and not driven by joint efforts of the leading scientists to enhance cohesion and synergies.
- (2) In parts of the Institute, the quality of the scientific concepts as well as the output in terms of high-quality papers is limited and needs improvement.
- (3) The commission felt that the interest of the Institute in human and clinical research is very limited, and that there is no clear concept to connect with human research.
- (4) The commission concluded that functioning core facilities are an asset, but could become a threat when they offer costly but outdated technology and are therefore unproductive.

### **4. Recommendations**

The commission recommends that the Institute

- (1) establishes an external, international scientific advisory board,
- (2) restructures the weaker units as well as parts of the research concept based on the recommendations of that board. Such restructuring may require open calls for recruitment of new PIs.
- (3) The Institute should establish a forum for discussion of its scientific strategies among all PIs, in the format of yearly retreats and internal seminars.
- (4) The Institute should establish a quality control of its core facilities. Specifically, the necessity for the sequencing facility should be evaluated in view of commercial sequencing costs and efficiencies.

### **5. Detailed evaluations**

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

The commission concludes that the quality of the results as judged from its

publication record is fair. In most collaborative papers, the groups of the Institute provided valuable input.

*Declaration on the involvement of students in research*

The commission concludes that the involvement of students in the research is good.

*Declaration on societal relevance*

The societal relevance of the research is considered high by the commission.

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

The commission concludes that the Institute of Microbiology is internationally visible, and nationally competitive.

*Declaration on the vitality and sustainability*

The commission concludes that the vitality and sustainability of the Institute are good, in some parts very good.

*Declaration on the strategy and plans for the future*

Strategies and plans for the future of the evaluated 4 groups were considered logical and straightforward in part, but in other parts with limited innovative potential. The commission felt that the research concept of the whole Institute lacks overarching themes (mission).

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

### **Evaluation of the Team No. 17: 151 - Laboratory of Cellular and Molecular Immunology**

#### **1. Introduction**

The Laboratory is interested in the innate and adaptive immunity on mucosal surfaces under conventional and germ-free conditions, and on the study of autoimmune diseases such as celiac disease and type 1 diabetes. According to the underlying hypothesis, gut microbiota play a role in the pathogenesis of these diseases. The commission notes that these research aims are very important and also very competitive, and that it will be very difficult to prove the relevance and the causality of the associations in humans, given the complex nature and time course of the human disease (e.g. long latency period of type 1 diabetes). Another current subject of research is the barrier properties of mucosal cell surfaces. An important finding of this group is that some components of bacteria can penetrate and challenge the immune system and thereby influence the disease. The Laboratory of Cellular and Molecular Immunology uses numerous models, including human samples. It has collaborations with hospitals and hospital labs, and some projects appeared to have been inspired by clinicians.

The Laboratory comprises 13 scientific staff members (8.41 FTE) who published a total of 58 original papers in peer-reviewed journals in the evaluation period. It has established a large network of collaborations, but most of these are local or national. Five of the staff members are active as academic supervisors (4 PhD theses, 2 master and 2 bachelor students finished within the evaluation period) or giving a total of 4 courses at Charles University. The Laboratory actively pursues popularization of their research activities (TV, broadcast, seminars, etc.).

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

The commission identified as strengths and opportunities:

(1) The Laboratory addresses very relevant and timely topics.

(2) The staff members have the expertise and the critical mass to address these topics.



(3) The public outreach appears to be strong.

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

The commission identified as weaknesses and threats:

(1) Overall, there is a high heterogeneity of the aims and projects, resulting in an impression of fragmentation.

(2) Parts of the Laboratory have a low scientific output (i.e. many publications in low impact journals)

(3) The age structure (3 researchers over 70) and impending retirements are a potential threat.

### **4. Recommendations**

(1) Install new and younger members as PIs

(2) Consider the research priorities and strengthen productive groups

(3) Financing should be directed towards attracting and funding younger groups

(4) Establish more international collaborations

### **5. Detailed evaluations**

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

The commission concludes that the quality of the results is overall good.

*Declaration on the involvement of students in research*

The involvement of students is adequate, but could be increased.

*Declaration on societal relevance*

The societal relevance of the research program is considered high by the commission.

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

The commission concludes that the Laboratory is nationally and internationally visible in a field that is very competitive at the international level.

*Declaration on the vitality and sustainability*

The commission concludes that vitality and sustainability of the Laboratory in terms of funding and equipment are high, but require a particular effort in the inevitable generational change by recruitment of younger PIs.

*Declaration on the strategy and plans for the future*

The commission concludes that the scientific concept addresses the right questions, but that not all of these appeared targeted with a convincing strategy.

**Evaluation of the Team No. 18: 152 - Laboratory of Tumor Immunology**

**1. Introduction**

The Laboratory is working on drug release from polymeric delivery systems, e.g. of cytostatics. These systems reduce the toxicity of the cytostatic drug, and increase their efficacy because of an enhanced permeability and retention in the tumor tissue. It is evident that this approach has a very high potential to be translated to the clinic. Therefore, the group had started some preclinical trials with a company - but this company was bought out and the project was stopped. In addition, ongoing projects aim at the preparation of micro and nanospheres, preferably as injectable systems. A second major research topic is the immune-modulatory effect of monoclonal anti-IL2 antibodies. Some of these IL2-immunocomplexes exert a marked stimulatory effect on T cell populations, and, in combination with cytostatic agents, a strong anti-tumor activity.

As compared with other units of the Institute of Microbiology, the Laboratory is relatively small (7 researchers, 5.25 FTE). Currently, 7 doctoral, 6 master and 4 bachelor students work in the Laboratory. Three staff members are involved in academic teaching. The group lists few but essential and successful collaborations, in particular with the CAS Institute of Macromolecular Chemistry.

External funding is mainly from national sources (4 GACR-funded projects), but also from industry (SOTIO). The group published 45 original papers in recognized

journals.

## **2. Strengths and Opportunities**

The commission identified the following strengths and opportunities:

- (1) The expected results of the Laboratory have a high potential for translation into therapeutic strategies.
- (2) The research topic (enhancement of anti-tumour activity) is clearly very important.
- (3) The Laboratory employs an interdisciplinary approach for developing novel technologies and therapies.
- (4) The Laboratory seeks to obtain grants from nonpublic sources.
- (5) If the projects are successful, publication of results in excellent journals will be possible.

## **3. Weaknesses and Threats**

The commission identified the following weaknesses and threats:

- (1) The group investigates an extremely competitive research field, and may lack the critical mass to be successful in all planned projects.
- (2) The publication output is solid, but has included relatively few high-impact papers since 2010.

## **4. Recommendations**

1. The commission recommends:

- (1) The institutional support of the Laboratory should be re-considered and potentially increased to enhance its competitiveness.
- (2) The Laboratory should strengthen its ties with industry and clinical research.
- (3) The Laboratory is encouraged to actively pursue the planned international collaboration(s).

(4) The group should enhance its international visibility by efforts to increase publications in high-impact journals.

## **5. Detailed evaluations**

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

The commission concludes that the results are very good.

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

The commission concludes that the involvement of students in research is good.

### *Declaration on societal relevance*

The societal relevance of the research is considered very high by the commission.

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

The commission concludes that the Laboratory is a national leader and Internationally visible.

### *Declaration on the vitality and sustainability*

Vitality and sustainability of the Laboratory are considered good by the commission.

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

The commission concludes that strategy and plans for the future were convincing (with the above described concerns regarding the competitive field of cancer therapy), including the collaboration with the Institute of Macromolecular Chemistry.

## **Evaluation of the Team No. 19: 153 - Laboratory of Gnotobiology**

### **1. Introduction**

The Laboratory uses gnotobiotic (germ-free) animals in order to understand the interaction between microbiota and eukaryotic hosts. The commission appreciates that the Laboratory is a unique unit, because maintenance of animals under germ-free conditions is mastered in only 5 European institutes. During the evaluation period, it has become apparent that the gut microbiota have a marked impact on health and disease. Thus, the technology has a high potential to understand the underlying mechanisms in detail.

The laboratory uses gnotobiology for a broad range of themes: inflammatory bowel diseases, allergies, and the ontogeny of immunity. Furthermore, the Laboratory lists numerous collaborations with national and international partners. The commission notes that the technology is highly complex and requires a well-trained technical staff. The capacity of the technology is therefore limited, and too many projects could jeopardize their success. Thus, size and number of projects including collaborations must be planned and prioritized carefully. The Laboratory lists potentially 12 future topics that might exceed its capacity.

Total staff of the Laboratory is 41 persons including 7 researchers, 4 doctoral students, and 3 master students. The group has published 43 papers in peer-reviewed journals within the evaluation period. However, the majority was published in low-impact journals, and few higher-impact papers predominantly resulted from collaborations. External funding was obtained from public national sources, but also from 3 EU projects and one US project (PI JE Butler, University of Iowa). Members of the Laboratory are very active in popularization of their research.

## **2. Strengths and Opportunities**

The commission identified the following strengths and opportunities:

- (1) The Laboratory is a unique facility that operates and masters a technology which recently has become an important research tool.
- (2) The Laboratory has many international contacts and collaborations with highly respected groups.
- (3) The group has the potential and the critical mass for being successful in the rapidly moving field of gut microbiota.

## **3. Weaknesses and Threats**

The commission identified the following weaknesses and threats:

- 1) The scientific output in terms of papers in high-impact journals appeared low in the evaluation period.
- (2) There is concern that the Laboratory does not capitalize on many international cooperations, and that the high number of projects jeopardizes

their success.

#### **4. Recommendations**

The commission recommends that

- (1) the Laboratory adapts the number of projects to the capacity of gnotobiology in order to make better use of the resources,
- (2) prioritizes the in-house at the expense of collaborative, externally initiated projects, and
- (3) makes a particular effort to enhance the visibility of its results by publishing in higher-impact journals.

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

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

The commission concludes that the quality of results is good, with regard to journal quality and visibility as fair.

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

The commission considers the involvement of students in research as good.

##### *Declaration on societal relevance*

The commission considers the societal relevance of the research as high.

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

The commission concludes that the position of the Laboratory, with regard to the complex and important technology, is internationally visible and nationally leading.

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

The commission considers the vitality and sustainability of the Laboratory as good, with a potential for improvement.

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

The experimental strategy appeared convincing, whereas the plans for the future

were not entirely convincing because of a potential overload of non-prioritized projects.

## **Evaluation of the Team No. 21: 156 - Laboratory of Immunotherapy**

### **1. Introduction**

The Laboratory of Immunotherapy, directed by Luca Vannucci, has been established after reorganization of the Department of Immunology and Gnotobiology in 2012. The Laboratory was established to investigate the immunology of the tumor microenvironment, and comprises two senior scientists, one post-doc, two PhD students and one master degree student. The aggregate FTE are 2.04 (researchers) and 1.10 (other personnel). Thus, the Laboratory is a very small research unit.

The group uses rodent tumor models (DSS and AOM treatment) and germ-free rodents to establish a role of gut microbiota in cancer development. Furthermore, the group pursues the application of magnetic nanoparticles in experimental tumor therapy; this approach was tested in melanoma cells and melanoma-bearing mouse models. The group is very active internationally (lead by a researcher of Italian origin), is involved in many international networking activities, and has been visited by numerous distinguished guest researchers. They participate in a COST action where microwaves will be combined with electromagnetic fields, and ferromagnetic particles will be included in the therapeutic approach. The plan is to alter the tumor microenvironment by localized heating, thereby activate an immune reaction and induce apoptosis. The Laboratory is collaborating with clinicians and pathologists who are collecting data and human material.

The group published 11 papers in peer-reviewed journals, and 15 in other journals. Overall, the group published in low-impact journals. Most papers published in the evaluation period were not cited, there appeared to be only one paper which was internationally recognized (review article, cited 16 times in 3 years). Seven PhD, 2 master and 1 bachelor thesis were defended in the evaluation period. In the evaluation period, there were only 2 externally funded projects (CSF and CAS) that expired in 2012 and 2013. The group participates in one funded European consortium (COST action), and is partner of a consortium that applied for funding in the Horizon 2020 program.

## **2. Strengths and Opportunities**

The commission identified the following strengths and opportunities:

- (1) strong involvement of the senior scientists in public outreach and communication activities.
- (2) strong involvement in international networking activities.
- (3) the head of the Laboratory has numerous international connections.
- (4) Research themes are very important and, if successful, the results have a high translational potential.

## **3. Weaknesses and Threats**

The commission identified the following weaknesses and threats:

- (1) A weak scientific output; most papers published in the evaluation period were so far not cited at all.
- (2) The group lacks the critical size to be successful in a very competitive field. Given that small size, it has pursued too many diverse projects that appear underfunded.
- (3) Currently there is no funding through external grants.

## **4. Recommendations**

It is recommended that the group concentrate its resources on areas and projects, where they are competitive and can make a recognized contribution. The group needs to increase external funding and enhance its scientific output. Because of the lack of a critical mass and the low scientific output, the decision to establish the group as an independent unit (Laboratory) needs to be reconsidered.



## **5. Detailed evaluations**

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

The commission considers the quality of the results in the evaluation period fair but noted that their international recognition, as judged from the citation frequency, is low.

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

The commission concluded that the involvement of students in the research is very good but noted that the first author position was frequently taken by the senior scientists.

### *Declaration on societal relevance*

The commission considers the societal relevance of the research field high.

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

The commission concludes that the Laboratory is nationally visible.

### *Declaration on the vitality and sustainability*

Due to the lack of a critical mass, the commission considers the vitality and sustainability of the Laboratory low.

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

Strategy and plans for the future appear to be convincing. However, given that the research field is highly competitive, the commission was not entirely convinced that the group could be successful in all of the planned projects.

**Date:** December 27, 2015

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