

# **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: Biology Centre of the CAS, v. v. i.**

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

Health sciences

Observer representing the Academy Council of the CAS: Hana Sychrová

Observer representing the Institute: Vladimír Košťál, substitute observer Jaroslav Vrba

**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. 16 - Tick-borne diseases; No. 17 - Biology of disease vectors; No. 19 - Opportunistic parasitic diseases*

## 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 Biology centre in Ceske Budejovice is the largest CAS research centre outside of Prague. It comprises 19 teams in 5 institutes on the Budejovice campus: the Institutes of Entomology, Parasitology, Plant Molecular Biology, Hydrobiology and Soil Biology. In addition, it operates a field research station in Papua New Guinea. Commission No. 9 evaluated only 3 of the 19 research teams from one institute – the Institute of Parasitology. Thus, this evaluation is based mainly on materials from phase I, the director's presentation of the Biology Centre and the subsequent discussion with him and with members of the board.

The Centre encompasses 277 researchers, 85 of which are foreigners, and 100 PhD students. Forty-six percent of the budget is covered through a total of 131 external grants. The Centre has an impressive publication record of approximately 300 papers in peer-reviewed journals per year, including articles in top-quality journals. Many groups belonging to the Centre have strong international connections and collaborations. In FP7, an impressive number of 15 projects from the Centre are being funded by the European Union. The Centre has strong links with 4 domestic universities. It is also active in public outreach, as shown by its presence in the media (289 media outputs in 2014).

The mission of the Biology Centre is very general: “....to enhance the quality of life for humankind and the nature status”. Consequently, the Centre covers a very broad spectrum of research areas ranging from human diseases to environmental conservation. This broad research scope is a potential threat for the cohesion and the synergies within the Centre.

The commission noted that the Centre has established a stringent internal quality control, which has identified weaknesses and initiated measures for improvement, in particular to enhance synergies between teams.

## **2. Strengths and Opportunities**

The commission identified the following strengths and opportunities:

- (1) The quality of the research results are very good, as demonstrated by an increasing number of papers in highly recognized journals.
- (2) The Centre was very successful in applying for grants (46% of the budget covered by third-party funding; numerous EU-funded projects, one ERC advanced grant, an acceptable proportion from industry).
- (3) The Centre has an international orientation, with almost 40% of its researchers from abroad and many international links and collaborations.
- (4) The societal relevance of the research fields covered is high.
- (5) The personnel of the Centre has a healthy age structure and appears highly competent.
- (6) There are close ties with the University of South Bohemia that is located at the same campus, and with other universities. Many scientists have double appointments by both parties, university and Academy of Sciences. The Centre trains a significant number (100) of PhD students.
- (7) The Centre has established a technology transfer structure to guide translation.

## **3. Weaknesses and Threats**

- (1) The mission of the Centre is very broad. The commission had the impression that in some areas the research activities were fragmented and not cohesive. The large number of small and medium-term grants combined with the presence of certain “tangential” research directions lead the commission to conclude that the research concept of some teams is driven primarily by the possibilities to obtain grants rather than a long term quest to tackle focused scientific questions.
- (2) The commission failed to identify a forum and procedure where the research concepts could be discussed and developed among the leading scientists (PIs) with the aid of external advice. In the commission’s opinion, the existing institutional boards or the Board of the Biology Centre are not the appropriate bodies for decisions on the scientific issues.
- (3) Work on human health and diseases (e.g. in the Institute of Parasitology) requires medical expertise. However, the commission noted that there is no convincing strategy for future collaboration with clinical medicine.

(4) The commission noted the absence of a Graduate School for the training of PhD students.

#### **4. Recommendations**

(1) Intensify the discussion of the research concept within the institutes, preferably at a forum where all PIs can contribute. The aim of such a discussion should be enhance cohesion of the research plan, and to foster synergies between teams.

(2) Where necessary, the Centre should seek advice and collaboration with clinical experts. This could be achieved through membership in the advisory boards, joint research programs or joint grant applications. Not only should the translation of results be facilitated, the research plans should already be guided by the clinical perspective.

(3) The commission recommends that a discussion as to the future development of the Technology Transfer Office (which should not be just an office but rather an “incubator” for SMEs) is initiated.

(4) The commission recommends initiating a discussion on the structure and organization of PhD training with the aim to establish Graduate Schools.

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

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

The commission concludes that the quality of the results of the three evaluated teams is overall very good.

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

The involvement of students in the research is considered overall very good, in part excellent, by the commission.

##### *Declaration on societal relevance*

The societal relevance is considered very high by the commission.

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

The evaluated teams are leading in the national context, and are internationally visible, in part competitive.

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

The vitality and sustainability of the Biology Centre is considered very good by the

commission.

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

Strategy and plans for the future are in large part convincing with limitations described below in part B.

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

### **Evaluation of the Team No. 16: Tick-borne diseases**

#### **1. Introduction**

This team comprises 2 Laboratories, the Laboratory of Molecular Ecology of Vectors and Pathogens, and the Laboratory of Arbovirology. Its main research aim is the molecular biology, molecular epidemiology, and pathogenesis of tick-transmitted diseases. Pathogens such as *Borrelia burgdorferi*, the causative agent of Lyme borreliosis, and tick-borne encephalitis virus, the causative agent of tick-borne encephalitis are studied. The team tries to identify molecular and cellular factors that are involved in pathogen transmission by tick vectors, including protein-carbohydrate interactions. Proteomics and transcriptomics approaches are employed in a search for novel vaccines against Lyme borreliosis in animal models. Furthermore, tick antimicrobial and defense proteins are studied as potential lead compounds for the development of new antibiotics.

As important achievements, the team lists the discovery that the TBE virus can infect astrocytes, the identification of a promising therapeutic agent (7-Deaza-2'-C-methyladenosine), the identification of agents with anti-histaminic efficacy in tick saliva, the isolation of new *Borrelia* strains, and an in-depth evolutionary analysis of all known *Borrelia* strains.

The team consists of 8 scientists (4,91 FTEs) who have published a total of 69 papers mostly in specialized journals (e.g. parasitology) in 2010-2014. The age structure of the team appears balanced. Within the evaluation period, 6 PhD, 18 MSc, and 26 BSc thesis were defended. Four scientists of the team were involved in academic teaching. The team has numerous connections and collaborations with other groups worldwide; it is partner in one EU-funded FP7 consortium.

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

The commission identified the following strengths and opportunities:

(1) The members of the team are recognized, competent experts in the field of tick-borne diseases. The team fully masters the difficult methodology of propagation,

maintenance and handling of ticks.

(2) Because of their competence, the team has received lots of offers for international collaborations, where they give important input.

(3) The search for bioactive agents in tick saliva is a promising field and may have many implications and opportunities.

(4) The commission was impressed by the large number of students involved in research, as a consequence of the team's policy to encourage even earliest stage students to participate in the publication of high quality papers.

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

The commission identified the following weaknesses and threats:

(1) Tick borne diseases appear to be a significant public health problem in the CR. Thus, the commission had expected that the group was involved in domestic programs addressing the clinical aspects of the diseases and their treatment. However, there were only weak, if any, links with clinical research in the CR, and no strategy in place to improve this.

(2) The research program appeared to address numerous very diverse questions and fields, resulting in the impression of a fragmented program. Many topics were touched, but few were studied in depth.

(3) Considering the very broad and in part ambitious research program, the team may be too small, and may lack a critical mass of senior scientists.

(4) In the study and comparison of the different *Borrelia* strains, the focus was on structural characteristics, and it was unclear to the commission how the more important functional differences will be investigated.

(5) The plans of the team to identify novel bioactive agents in tick saliva were in large part convincing. However, it was not entirely clear, how the antihistaminic properties of lipocalin could lead to novel drugs, given the availability of very effective antihistamines. Also, the commission missed a concept for securing intellectual property and for the further translation of the results to application in humans.

### **4. Recommendations**

The commission recommends that the team



- (1) seeks contact with clinical experts with the aim to initiate collaborative projects,
- (2) puts more emphasis on the study of functional characteristics of *Borellia* strains,
- (3) reduces the diversity and fragmentation of the research program by concentrating on the most important and promising aspects,
- (4) revises its plans to analyze tick saliva, with a focus on the most promising bioactive molecules,
- (5) strengthens efforts to secure intellectual property.

## **5. Detailed evaluations**

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

The commission concludes that the results of the team are overall very good. In collaborative projects and publications, the team provided essential contributions.

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

The involvement of students in the research is considered excellent by the commission.

### *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 team is internationally visible, and leading in the national context.

### *Declaration on the vitality and sustainability*

Vitality and sustainability of the team is high but somewhat limited by the discrepancy between the size of the group and the number of projects.

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

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

## **Evaluation of the Team No. 17: Biology of disease vectors**

## 1. Introduction

The team consists of 3 Laboratories, the Laboratory of Vector Immunology (LVI), the Laboratory of Tick Transmitted Diseases (LTTD), and the Laboratory of Genomics and Proteomics of Disease Vectors (LGPDV). Its research aim is the investigation of several distinct aspects of tick biology such as (1) the immune system of ticks, (2) blood-meal digestion in ticks as a target for rational anti-tick interventions, (3) iron/heme metabolism in ticks and ferritin 2-based anti-tick vaccine, (4) laboratory transmission models as tools for the study of tick-pathogen interactions, and (5) the isolation of bioactive agents (protease inhibitors) from tick saliva. In these important fields, the groups have made breakthrough contributions such as the identification of ferritin-2 as a candidate antigen for vaccination. Furthermore, methodological progress was made by the establishment of a Lyme disease transmission model, and by employing RNA interference in *I. ricinus* nymphs. LGPD identified protease inhibitors and anticoagulants in the saliva of ticks and the sand fly, respectively, and their essential role in the feeding success. LGPDV operates a state-of-the-art high throughput system to identify bioactive compounds in tick saliva. Importantly, the research program of team 17 has a high potential for translation as demonstrated by 2 patents, and by the progress towards an anti-tick vaccine.

LVI became an independent laboratory in 2003, when the former Department of Molecular Ecology of Vectors and Pathogens was divided into several more specialized research units under the leadership of individual PIs. LTLD is a recently (2013) established laboratory which receives support from the EU-FP7 Modbiolin project. Its head, Dr. Hajdušek, returned after a three-year postdoctoral fellowship at the CNRS, Strasbourg, France. LTLD and LVI share personal staff, laboratory equipment and tightly co-operate on overlapping research projects. LGPDV was established in 2009 as an independent laboratory under the leadership of Dr. Kotsyfakis, who joined the Institute of Parasitology as the first foreign scientist awarded the J.E. Purkyně fellowship by the Academy of Sciences of the CR.

The commission notes that in this evaluation, 5 independent groups (Laboratories) that work in the area of tick-transmitted diseases were presented as 2 different teams (team 16 and 17). These teams appeared defined solely for this evaluation and did not reflect an organizational structure. We appreciate that the formation of 5 independent groups (instead of the hierarchical structure of a single department) has considerably improved the quality of research and the international visibility of the Institute of Parasitology. However, the research plan appeared somewhat fragmented and uncoordinated (see below, weaknesses and threats).

The whole team consists of 8 scientists (6 FTEs), 4 PhD and 9 undergraduate students. A total of 50 papers were published in 2010-2014, some of them in high-impact journals. The age structure of the team appears balanced. Within the

evaluation period, 1 PhD, 6 MSc, and 6 BSc thesis were defended. Three scientists of the team were involved in academic teaching. The team has excellent connections and collaborations with other groups worldwide; it is partner in several EU-funded FP7 consortia.

## **2. Strengths and Opportunities**

The commission identified the following strengths and opportunities:

- (1) The team has a strong record of publications in high impact journals. The PIs of the team are internationally recognized, the teams are involved in numerous excellent international collaborations, and receive funding from international sources.
- (2) The team employs state-of-the-art methodology, and has established new, important research tools that will considerably advance the field of disease vector biology.
- (3) The use of tick biology as a model for novel therapeutic strategies is a very innovative approach. Furthermore, the search for bioactive agents in tick saliva is a promising field and may have many implications and opportunities
- (4) The research aims have a high potential for generation of patentable results, and for translation of the results into clinical research and application.

## **3. Weaknesses and Threats**

The commission identified the following weaknesses and threats:

- (1) The research programs of the individual laboratories in teams 16 and 17 were convincing. However, viewed as a whole, they appeared fragmented and uncoordinated. Few areas of cooperation or synergies were apparent, even in areas of clear overlap (search for bioactive compounds in tick saliva by both teams). This could represent a missed opportunity.
- (2) Given the small size of the groups, and the very ambitious and broad research programs, there could be a lack of critical mass of senior scientists.
- (3) The biology of diseases vectors is highly relevant for a significant public health problem in the CR. Thus, the commission had expected that the group would be involved in domestic collaborations addressing the clinical aspects of the diseases

and their treatment. However, no convincing concept for such collaborations was presented.

(3) The project on epigenetic regulation of tick genes was not absolutely convincing, needs better justification and might be too risky.

#### **4. Recommendations.**

The commission recommends that

(1) a structure (e.g. a forum of the PIs) is established that discusses and coordinates the research program of the teams 16 and 17 in order to identify converging interests, synergies and priorities. This forum should not abolish the independence of the PIs but foster interdisciplinary collaborations and optimize the use of resources.

(2) the team seeks contact with clinical experts with the aim to initiate domestic collaborations in the translational aspects of the research program.

(3) the number of individual research projects is reduced by abandoning the weaker ones.

(4) in the search for new drugs and therapeutic approaches, efforts are concentrated on one or two of the most promising agent, and that a proof of principle for the concept is established.

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

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

The commission concludes that the results of the team are very good, in part excellent. In collaborative projects and papers, the team provides essential contributions.

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

The involvement of students in the research is considered very good by the commission.

##### *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 PIs of the team are leading in the national context, are internationally competitive, and in some aspects of the field among the leaders.

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

Vitality and sustainability are considered very good by the commission with the limitations described above. The team is possibly underfunded for the number of projects. However, we appreciate the extent of domestic and international funding which can hardly be increased without a substantial increase in scientific staff financed by the institutional budget.

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

Strategy and plans for the future were convincing with the limitations described above, and in part very ambitious and risky.

### **Evaluation of the Team No. 19: Opportunistic parasitic diseases**

#### **1. Introduction**

This team consists of two laboratories, the Laboratory of Veterinary and Medical Protistology (LVMP) and the Laboratory of Parasitic Therapy (LPT). Its current structure was the result of a major re-organization within the Institute of Parasitology in 2009 and 2010, based on the previous labs' weak structure and productivity. In 2013, the Laboratory of Parasitic Therapy was established and allocated to the team as an independent research group with only one scientist. The commission notes that formation of this team combines two groups with distinct size, aims and productivity. Therefore, the commission tried to give separate reports, where possible, for the two laboratories. However, because of the short time that the Laboratory of Parasitic Therapy has existed, the evaluation of the results and standing of the team are solely based on the track record of the Laboratory of Veterinary and Medical Protistology.

The LVMP investigates human and animal parasites of the genus *Cryptosporidium* and of the phylum *Microsporidia* (genera *Encephalitozoon* and *Enterocytozoon*). Research includes numerous areas such as parasite structure, life cycle, host-parasite relationships, host-, age- and gender-specificity, epidemiology, immune response, phylogeny and evolution. As main scientific achievements, it lists results from non-human primates, human parasitoses as well as parasitoses in other mammals, indicating a broad scope of research aims. The LPT focuses on the role of commensal gut eukaryotes on inflammatory bowel disease (IBD) with the aim to identify organisms for its prevention and therapy.

The team is a very small unit with only 4 (3.2 FTE) scientists and 2 technicians. It has a favorable age structure with none of its scientists >45 years of age. Currently, the research aims of the team are relatively broad and include numerous small projects. The publication activity of the LVMP is high and resulted in 89 papers in journals with

impact factor. LVMP is engaged in numerous international and national collaborations. It received 8 grants from public sources, among these 3 grants from Polish Science Foundations. The team is a partner in an EU-funded COST action. Since the last evaluation, the involvement of students in research was markedly improved.

## **2. Strengths and Opportunities**

(1) The research topics are extremely important for human health, veterinary medicine, farming, and also with regard to environmental aspects. There is huge public interest worldwide.

(2) The scientists of LVMP are internationally recognized experts with a strong publication record of frequently cited papers. This is a significant improvement since the last evaluation.

(3) The team is engaged in productive collaborations with 17 international partners.

(4) LMVP has introduced genetic manipulation protocols of *Cryptosporidium*; this is a new area and an important window of opportunity.

(5) LMVP has a high methodical expertise to screen for gastrointestinal pathogens. These methods and their further development could be an opportunity for commercial exploitation of the results.

## **3. Weaknesses and Threats**

(1) The team appears small for an ambitious, broad research program, and might lack the critical mass of senior scientists.

(2) The commission appreciates the numerous contacts of the team with clinics and clinical researchers that provide samples. However, we feel that the conceptual input of clinical and veterinary medicine is too low.

(3) IBD and the involvement of intestinal microbiota in its pathogenesis is a very competitive field. In addition, proof of concept is lacking that the rat model employed is relevant for studying the role of microbiota in the human disease.

## **4. Recommendations**

The commission recommends that the team strengthen contacts and collaborations

with clinical and veterinary medicine in order to get conceptual input.

## **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 very good. In collaborations, the team is frequently leading. In all other collaborations, it provides essential contributions.

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

The involvement of students in the research is considered very good by the commission.

### *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 of Medical and Veterinary Protistology is a leading group in the national context, and that it is internationally competitive.

### *Declaration on the vitality and sustainability*

Vitality and sustainability are considered good by the commission with the limitation that the high number of projects could be underfunded.

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

Strategy and plans for the future are sound with the limitations described above. The scope of the research program might be too broad for the size of the groups, and too ambitious for the Laboratory of Parasitic Therapy, given the strong competition in the IBD field.

**Date:** December 29, 2015

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