

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 Animal Physiology and Genetics 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: Michal Kubelka

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. 3 - Team of Animal Embryology; No. 4 - Experimental Animal Models

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 Animal Physiology and Genetics was founded in 1962. Its current scientific mission is the investigation of animal physiology, from advanced animal farming to biomedicine and biodiversity. The Institute lists as research topics a very broad, diverse spectrum of fields and methods: animal and human genetics, developmental biology, molecular morphogenesis, biodiversity, nutrition, microbiology and proteomics.

The Institute is one of the CAS institutes that are located outside of Prague. It is divided into 12 research units (Laboratories) and one research centre (PIGMOD), which houses, breeds and investigates experimental animal models (in particular pig models of diseases). Geographically, The Institute of Animal Physiology and Genetics is not located at one campus, its research units are scattered over three different locations (Libechov, Prague, Brno). It is apparent that such a geographical separation poses a challenge and can hinder the interaction and collaboration of individual teams. The commission concluded that this disadvantage could be overcome only by a strong scientific leadership, by a well-designed and focused research strategy and by a functioning internal organization. The main part of the Institute is located in Libechov (4 of 6 groups). Teams in Libechov and Brno focus on animal models of disease and on developmental and evolutionary biology. The remaining Laboratory in Prague investigates anaerobic microbiology, a topic that appears unrelated to the research of the other teams. Commission No. 9 evaluated two units – the unit Experimental Animal Models PIGMOD (Libechov) and the Team of Animal Embryology (Brno).

2. Strengths and Opportunities

The commission identified the following strengths and opportunities:

(1) The pig disease models (PIGMOD, Team of Experimental Animal Models) are very interesting and offer opportunities for domestic and international collaborations.

(2) The research on disease models has a high potential for translation. It has already generated strong connections to companies and institutions of applied research.

(3) The Institute as a whole comprises a very well developed, high scientific expertise in various complementary areas.

(4) There is a strong participation in academic teaching (both evaluated teams) and

in public outreach activities (particularly the team in Brno).

(5) The Institute has a good infrastructure, in part as core facilities (bioinformatics, imaging).

(6) The Institute is well connected with companies and foreign research institutes.

(7) The Institute collaborates closely with Czech universities (mainly in Prague and Brno) in research, PhD training and pre-gradual teaching.

3. Weaknesses and Threats

The commission identified the following weaknesses and threats:

(1) The structure of the Institute with its large geographical separation (4 hours drive from Libechov to Brno) is not conducive to synergies, cooperation and cohesion.

(2) The research topics of the Institute are very diverse and in part only weakly related. Consequently, the mission of the Institute (defined as “from advanced animal farming to biomedicine and biodiversity”) is extremely broad. The commission concludes that the Institute lacks the critical mass to successfully cover all topics.

(3) The commission identified few synergies, and no convincing strategy to resolve this problem.

(4) To some extent, the focus of research is mainly on the development of animal models for others and not on own, problem-oriented and challenging research. Specifically, large parts of pig model-based research are contract work for outside users. Because of this ‘outsourcing’ of the concept development, the Institute profits little from the success of the projects.

(5) The commission saw no apparent connection with the Laboratory of Anaerobic Microbiology.

(6) The age structure of the leading scientists appears suboptimal in part.

(7) The institutional budget is too low for a full operation of the PIGMOD Centre and is actually decreasing. Consequently, these projects are dependent on the external funding through contract work.

(8) The Institute lacks an independent scientific advisory board with international advisers.

(9) The commission noted an absence of strong scientific leadership and a lack of a vision for the future development of the Institute as a whole (i.e. Libechov+Prague+Brno).

4. Recommendations

(1) Strong scientific leadership and a intense discussion among all PIs is required to plan the future of the Institute, to establish a coherent research concept, to identify and harness synergistic areas, and to effectively use resources.

(2) The commission recommends that the Institute develops a strategy for the next 10 years of how to deal with its problems (suboptimal structure, geographical separation, more focused research directions, in-house interaction and synergy between groups, PI lectures etc.).

(3) The Institute should establish a Scientific Advisory Board with international participation and a strong involvement in the discussion of the research concept.

(4) The Institute should make an effort to recruit more international researchers, and to get international advice.

(5) The PIGMOD Centre should not be a unit that merely does contract research. Thus, the Institute should invest more into research initiated by the in-house scientists, and should try to capitalize more on the scientific work that is done with the animal models. Securing IP (intellectual property) should not be neglected.

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 of the Institute is good, and in part very good. In collaborative projects, the Institute makes mostly essential contributions.

Declaration on the involvement of students in research

The involvement of students in the research is adequate and in part very good (Brno).

Declaration on societal relevance

The commission concludes that the research aims of the Institute have in average societal relevance, and are in part highly relevant (specifically Brno).

Declaration on the position in the international and national context

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

Declaration on the vitality and sustainability

As a result of numerous weaknesses that are outlined above, the commission concludes that the vitality and sustainability of the Institute is relatively low.

Declaration on the strategy and plans for the future

The commission concludes that the strategy and plans for the future were not entirely convincing and require substantial improvement.

B. Evaluation of the individual teams

Evaluation of the Team No. 3: Team of Animal Embryology

1. Introduction

The Team of Animal Embryology investigates the regulatory mechanisms of embryonic and postnatal development of mammals with a focus on the development of limb and craniofacial structures and their defects. The team comprises 4 PIs, 4 postdocs, 10 PhD students and 2 master students. The age structure of the team appears well balanced. The publication activity of the team is high, showing an increase in number as well as in quality during the evaluation period.

The individual projects (research topics) appear very diverse, considering the number of PIs and the size of the team. While research on craniofacial/dental development represents a strength of the team, others such as the role of FGF signaling and limb development might be a weakness due to the high competition in an already thoroughly investigated area of research. The team is very active and also successful in applying for grants, which is considered an indicator of high quality research. However, the necessity to apply for many small, medium term grants is likely to disperse the focus of project directions. Efforts to go more deeply into the particular problem would be beneficial. The team is also successful in the development of methods. This effort has resulted in many collaborative interactions, but has apparently not led to a patent or other commercial achievements so far.

2. Strengths and Opportunities

The commission identified the following strengths and opportunities:

- (1) The team is a young group with a high, proven expertise in embryology.
- (2) The team has attracted a high number of PhD students.

(3) The productivity of the team in terms of the quality of their papers is high.

(4) The team is involved in numerous national and international collaborations, and attracted international guest scientists. This is further proof of their expertise in embryology and development.

(5) The team is very successful in obtaining grant support from national sources.

(6) The strong involvement in academic teaching is a good basis for close links with to the university and facilitates recruitment of excellent students.

3. Weaknesses and Threats

The commission identified the following weaknesses and threats:

(1) The research topics, as they were presented, appeared too diversified. The commission felt that such a fragmentation of the research activities into numerous diverse entities could jeopardize the competitiveness of the group.

(2) The team does not appear to concentrate the major part of its resources on areas of strength such as the craniofacial and dental development.

(3) According to the presentation of future strategies and plans, the group appeared to take on too many areas and distinct projects for its size and resources.

(4) The geographical separation leads to limited cooperation with other groups and to a reduced visibility within the Institute.

4. Recommendations

The commission recommends that

(1) the Institute should increase institutional funding of the team in order to support a concentration on ambitious, long-term projects,

(2) the team should prioritize the heterogeneous areas and projects, and focus on few selected topics where it can be competitive at the international level.

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 collaborations, the group has a leading role or provides essential contributions.

Declaration on the involvement of students in research

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

Declaration on societal relevance

The commission considers the societal relevance of the research very good.

Declaration on the position in the international and national context

The commission concludes that the group is internationally visible, and among the leaders in the national context.

Declaration on the vitality and sustainability

The commission considers the vitality and sustainability of the team very good.

Declaration on the strategy and plans for the future

The commission appreciates the scientific quality of the future plans of the team. However, as was outlined above, the scope appeared too broad and diverse. In addition, the commission is concerned that the scientific strategy could be driven and directed by the success of applications for small, medium-term grants.

Team 4: Experimental Animal Models

1. Introduction

This team is located in Libechov and comprises 4 distinct research units (the Laboratory of Cell Regeneration and Plasticity, the Laboratory of Applied Proteomic Applications, the Laboratory of DNA Integrity, and the Laboratory of Tumour Biology) according to the documents provided by the team. These laboratories establish and investigate various animal models for human disease, most notable several pig models that are bred and housed in the PIGMOD Centre, which, according to the organizational scheme provided by the Institute, is a separate and independent entity. Of the animal models, only the minipigs were presented to and discussed with the commission. Thus, this report is mainly based on the presentation of the PIGMOD Centre and on the written report provided by the Team 4.

The Institute indeed operates a worldwide unique facility that investigates miniature pigs as models of human disease. This includes miniature pig with surgically induced spinal chord injury, a strain with a Huntington's disease causing mutation, and a strain with hereditary melanoma susceptibility. The facility is also unique because it comprises a broad spectrum of expertise including transgenic approaches, advanced cell cultures, stem cell expertise, experimental surgery, skills of breeding etc. This unique expertise explains many productive national collaborations as well as collaborations with high-profile research groups and companies abroad. However,

these long-term collaborators that utilize the pig models determine, at least partially which models and diseases the team investigates. A typical example is the interest in neural stem cells (the team uses commercially available neural stem cells), spinal cord injury and stem cell therapy. Here the team contributes mostly the methodology and supplies the pig models to answer questions that were defined by the collaborator. The commission notes that the collaborative projects appear to be funded only partially by the external collaborator. Furthermore, the Institute is aware of the problem and lists it in the SWAT analysis. “Weaknesses: Consuming practically all disposable financial resources (from project overheads) by project PIGMOD nearly stopping the development of another part of the Institute.”

The team comprises 25 scientists and 22 other employees. For commercial activities (international patents), an application manager supports the team. The team published 63 papers in peer-reviewed, mostly lower-impact journals. During the evaluation period, 6 PhD theses, 8 master and 4 bachelor theses were defended. The team is involved in numerous international collaborations with research institutes and companies (e.g. Neuralstem Inc., San Diego), and has applied for a grant in the Horizon 2020 program as partner in a European consortium.

2. Strengths and Opportunities

The commission identified the following strengths and opportunities:

- (1) The team uses unique and valuable models of human disease and has a broad expertise in research involving animal models.
- (2) The research results of the team have a high potential for translation – e.g. methods for the treatment of spinal cord injury or melanoma.
- (3) The team has established a productive collaborative network with national as well as international partners.
- (4) The team has active interactions with biomed companies.

3. Weaknesses and Threats

The commission has identified the following weaknesses and threats:

- (1) There is a dominant focus on the development and characterization of models. The commission had the impression that research of the team is predominantly driven by the technologies and by the concepts and demands of the external collaborators.

(2) The pig models are not sufficiently financed by the collaborators. Thereby, they consume a large portion of the budget of the Institute, and require additional funding through grants from public sources.

(3) The technology driven approach may hinder work on ambitious, in-house conceived projects that are highly recognized internationally. It could be responsible for the weak record of publications in high-quality journals.

(4) The commission considers a future, potentially stricter legislation on animal (pig) experiments a serious threat for the Institute.

4. Recommendations

(1) The team Experimental Animal Models should continue to seek the advice of consultants with expertise in clinical research, in particular in the diseases that the team investigates. For example, expertise or a strong clinical partner in immunology is needed for the melanoma work.

(2) The team should make efforts to conceptually lead the important projects, and not merely provide the methodology for projects of external partners.

(3) If projects are conceptually guided by external partners, who later capitalize on the success, these partners should cover most, if not all, costs of these projects.

(4) The team should continue to focus on the translational aspects of their research.

(5) The team should make an effort to increase the number of high-quality publications.

5. Detailed evaluations

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

The commission concludes that the results of the research are overall good, in part very good. In joint projects, the team provides essential methodology.

Declaration on the involvement of students in research

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

Declaration on societal relevance

The societal relevance of the research is high.

Declaration on the position in the international and national context

The commission concludes that the methodology of the pig models is internationally visible and recognized, and nationally unique. Research directed by the team is nationally competitive, and in part internationally visible.

Declaration on the vitality and sustainability

The commission is concerned about the large geographical separation (4 hours drive) of units, which hinders cooperation and cohesion. Furthermore, it is concerned about the financial sustainability of the pig models.

Declaration on the strategy and plans for the future

The commission appreciates the scientific value of future strategy and plans as described in the documents and in the presentation of the PIGMOD Centre. However, the concept of the 4 laboratories covers a very broad range of topics, and may exceed the resources of the team. Thus, prioritization and focus may be required.

Date: December 27, 2015

Commission Chair: Prof. Dr. Hans-Georg Joost