

# **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**

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

**Chemical sciences**

Observer representing the Academy Council of the CAS: Jiri Ctyroky

Observer representing the Institute: Jiri Gabriel

### **Commission No. 4: Chemical sciences**

Chair: Dr Habil, Academician Christian Amatore

Date(s) of the visit of the Institute: November 30 - December 4, 2015

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

Evaluated research teams:

- **113 - Laboratory of Molecular Structure Characterization**
- **114 - Laboratory of Biotransformation**

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

The report presented by the Institute Director, Martin Bilej, was largely concerned with the historical development of the institute, organizational questions, and some general details (such as age structure and development, organization in departments etc.).

This multidisciplinary Institute focuses on fundamental molecular biology, encompassing structure and behavior at the cellular level and gathering an important expertise in biochemistry, physiology and molecular genetics of bacteria, yeasts, filamentous fungi and microscopic algae and immunological research. It is one of the main institutions of the Czech Republic involved in the basic microbiological research and, interestingly, also in applicative outcomes, though the primary focus is on basic research.

The Institute includes 24 basic research laboratories clustered in 7 research directions, and 3 core facilities (Center for DNA Sequencing center, Center Cytometry and Microscopy, and Biotechnological Pilot Plant) for a total of 640 employees.

Most of its teams have been evaluated by Commissions of CAS 6 (9 teams), 7 (9 teams) and 9 (4 teams) and only two teams were evaluated by this Committee (Laboratories of *Molecular Structure Characterization*, and of *Biotransformation*). Although the evaluation Committee did not gather a sufficient level of expertise to evaluate the main microbiological research directions developed by the Institute, its feeling is that the Institute completely fulfils its announced goals. In particular, it is noted that the autonomy of the Institute (since 2007) within the CAS structure has offered interesting opportunities for economical activities (production, trade and services in the fields of biology, chemistry and medical sciences) which enable efficient uses of the Institute capacities in biotechnology thanks to its pilot plants in Prague and Třeboň, and provide a sufficient internal funding for investment (construction of additional buildings and renovation of laboratories) and to offer cutting-edge scientific and technological facilities (top mass spectrometers, NMRs, flow cytometers, microscopes, sequencers *etc.*) to its scientists and students, comprising their upgrading and maintenance to remain at a high international level.

The Institute has developed and maintains long-lasting collaboration with several Czech universities based on official Association Agreements according to which the Institute's scientists teach more than 60 courses, participate in undergraduate programs and at the PhD level and act as supervisors of diploma and dissertation theses. Based on the Director's report, an remarkable number, exceeding one hundred PhD students have been trained through these accredited doctoral programs. Owing to the difficulties experienced on this matter by the other Institutes that this Committee has evaluated, this is worth noting, providing evidence for the major role played by this Institute in modern microbiology in the Czech Republic.

In conclusion, the Institute of Microbiology appears as an internationally competitive place, being among the leading ones in Europe in some of the fields (e.g., its unique facilities for breeding germ-free animals and its related aspects), giving it a perspective for future growth. In contrast with this positive conclusion and the importance of the research fields developed in the Institute, the Committee was surprised to note the rather low value of the mean impact factors of the journals in which its scientific outcomes are published since these deal with biological sciences for which IIs are generally much higher than in chemical sciences. However, the Commission has recognized that the Institute has in charge several missions of importance for the Czech Republic but that are not easily leading to publication in usually top-ranked biological journals. Nonetheless, the Commission has noted with interest that the strategies introduced by the Institute Director have already led to a significant improvement over the evaluated period (from an average IF of 2.9 in 2005-2008 to 3.6 in 2010-2014).

*Nota Bene: Since the Committee evaluated only two teams over 24 present in the Institute, it did not feel appropriate commenting on the items 1-3 beyond the overall appreciations given above.*

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

### **Evaluation of the Team: 113 - Laboratory of Molecular Structure Characterization**

#### **1. Introduction**

Within the extensive structure of the Institute of Microbiology, this group plays a very important role in providing its cutting-edge instrumentation and expertise in three different areas: (a) mass spectrometry (MS); (b) nuclear magnetic resonance (NMR) spectrometry; and (c) advanced microscopy facilities. In addition to providing valuable service and collaborative support to other teams within the Institute, the laboratory has been greatly recognized regionally for its numerous collaborations with academic and other scientific institutions in Czech Republic while maintaining in a well-balanced repartition between original researches and services. This is particularly due to its outstanding MS facilities and the expertise in structural elucidation of complex biological molecules through different techniques.

The scientists in this laboratory have been involved in virtually all aspects of “omics technologies” (proteomics, lipidomics, metabolomics, etc.) Inspiration through important biological problems has led the laboratory members to come up with technical improvements in analytical methodologies and even file patent applications. They are also involved in some contractual research and services. The portfolio of different scientific activities is very substantial. The MS facilities and researchers are outstanding and the NMR part is at least satisfactory. The microscopy facilities seem to fulfill more of a service function for the entire campus. The structural biology subgroup, which represents some of the most outstanding researchers, is in the progress of splitting and moving to the new campus in Vestec (Biotechnology and Biomedicine Center – a joint venture between the CAS and Charles University). The MS facilities include some of the most advanced and unique instrumentation in the region. The core equipment is based on the Fourier-transform MS using high-field magnets as well as advanced time-of-flight MS instruments. Among the most promising instrumental projects is imaging MS. These outstanding MS capabilities attract numerous collaborators from the campus as well as other institutions. There is also a substantial number of international collaborators (e.g., from France, New Zealand and the U.S.). The NMR spectrometric capabilities facilitate work with both large biomolecules and small (secondary metabolite) molecules using a combination

of liquid chromatography with NMR. Altogether, this is a very large team with a very favorable age distribution across the entire range. The excellent facilities and quality of scientific investigations obviously attract a large number of young scientists.

## **2. Strengths and Opportunities**

Important biological problems and excellent analytical chemistry approach are evident in numerous activities of this large team. The MS group has offered to the collaborators proteomic, peptidomic, lipidomic, glycomic and metabolomics profiling and quantitative (comparative) measurements at the highest level of MS resolution facilitated by the FTMS instruments. In response to different biological and biomedical problems of the collaborating groups, the laboratory has also developed capabilities for chemical crosslinking of proteins and hydrogen/deuterium exchange MS investigations for the studies of biomolecular interactions. Several ancillary techniques of MS were also developed through these collaborations and are documented in the analytical literature. More recently, considerable attention has been extended toward the area of biomolecular MS imaging, which is clearly a “high risk/high benefit” area necessitating breakthrough advances in sample treatment and instrumental design. The first promising results of biomedical importance were already published by the group, but future undertakings will necessitate careful strategies in view of this increasingly competitive field. The laboratory is planning very worthwhile investigations in LC-NMR and LC-MS screening efforts in the areas of “severe civilization diseases” such as asthma and diabetes. With the acquisition of new equipment in high-resolution electron scanning microscopy, this part of the laboratory will receive significant upgrade and increased role in the overall mission of the Institute. As a regional center of excellence in structural characterization, the laboratory also assumes an important function of promoting some research activities at Palacký University (Olomouc), Charles University, and Institute of Chemical Technology (Prague).

## **3. Weaknesses and Threats**

No serious weaknesses or threats are currently perceived by this Committee. The team is highly productive, having a healthy age distribution and student participation. Many interesting collaborative projects are in place. Some questions may arise in future concerning the separation of this team into the Krč and Vestec locations.

#### **4. Recommendations**

The present activities should be continued in a close collaboration style as has been done in the past period. There are no specific other recommendations at this time.

#### **5. Detailed Evaluations**

As a regional center of excellence with considerable knowledge, expertise and cutting-edge instrumentation, the team has done outstanding job in (a) developing unique analytical methodologies; (b) collaborating effectively with biological scientists and organic chemists; (c) proliferation of MS techniques to different fields of interest; (d) educating others in an important area of analytical chemistry; and (e) providing visible service activity and transfer of technologies. There were numerous scientific outputs during the evaluated period. The published work is reported in respectable journals. The pedagogical activities of the team members are outstanding, reaching numerous students at different levels. The university students seem drawn to the main areas of investigation in the laboratory. The societal relevance of these activities is quite high, including the fields of microbiology, biomedical research, disease biomarkers, biotransformations, and organic synthesis. Several senior team members are internationally recognized scientists who participate in major scientific meetings and serve on important committees and editorial boards. There are significant scientific collaborations with academic institutions domestically and internationally. Although the maintenance of instrumental capabilities and keeping up with new technologies are very expensive, the risks of limited sustainability appear minimized, given numerous directions of the field and the needs of biomedical research. The future plans and strategies appear reasonable, although it is less clear how will the research responsibilities be divided between Krč and Vestec.

## **Evaluation of the Team: 114 - Laboratory of Biotransformation**

### **1. Introduction**

The Laboratory of Biotransformation (i.e., bio-catalysis) is a large research unit covering various aspects of bioorganic chemistry, large-scale isolations of natural products, enzymatic synthesis, bioconversions, enzyme-based biotechnologies, carbohydrate synthesis, etc. Its large range of activities is further enhanced by numerous international collaborations. Informally, it is divided into subgroups: (1) glycobiology, dealing with some aspects of enzymatic biosynthesis and modifications of glycoconjugates and producing biomimetics; (2) nitrile biotransformations, dealing with bacterial and enzymatic degradation of agricultural pollutants; and (3) flavonoid and antioxidants, focusing on natural and synthetic compounds that can potentially be exploited as pharmaceuticals or food additives. Common themes among different projects in this team are the use of biocatalysts, biotransformation technologies, means to isolate compounds from biological materials, structural/functional correlations, and synthetic efforts. The researchers often need to reach outside their group to secure molecular modeling and structural characterization. Their work has multilateral practical utility in biomedical field, industrial application and bioremediation (solution of environmental problems). This team has a healthy age profile and it has secured substantial recognition in different fields. The team spans considerable range of expertise between chemistry and biology that attract a large number of foreign scientists from highly-developed countries (UK, Switzerland, Israel, etc.) leading to a very good level of international collaborations for the team .

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

The research efforts of this team are easily justified by the general importance of biocatalysis, biotechnological production, the needs for better pharmaceuticals and synthesis of bioconjugates. The key researchers in this group have also succeeded in generating an effective network of collaborators in other institutions. Their international collaborations are numerous. The screening of useful enzymes from bacterial and plant sources appear profitable in both current and future projects, as are the studies of microbiomes from the environmentally compromised areas. Glycobiology is a very promising field with the urgent needs of new knowledge, while the biosynthesis and structural modifications of glycoconjugates all promise bright

future. The team has been productive, publishing articles of both fundamental and applied nature. There has been satisfactory training of university students in the laboratory and the foreign students under the Erasmus project seem to benefit as well.

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

No fundamental weaknesses and threats are evident at this time.

### **4. Recommendations**

This is a team with focus on the problems highly relevant to biotechnology. There seems to be continuity in research goals into the next period. There are no specific recommendations at this time.

### **5. Detailed Evaluations**

The team has grown from 2010 to 2014 in the numbers of both research scientists and PhD students. The productivity has been high in terms of scientific outputs reported under this evaluation period. The program is characterized by high diversity of projects that students can choose under the direction of experienced researchers. The practical importance of the studied field should continue to attract further students. While the number of published reports is genuinely high, the quality profiles seem to favor articles with intermediate impact values due to the applied nature of many investigations. Societal relevance of this team's investigations is very high in the areas of potentially new pharmaceuticals, nutrient additives, biotechnology in general, and the attempts to clean our environment. The key team members are well-recognized scientists, nationally and internationally. They should be capable to sustain this scientifically and technologically important program into the future years. The cloning, recombinant production and isolation of new enzymes and their use in carbohydrate processing and also in the degradation of xenobiotics will remain "hot areas" for some period of time.

Fundamental studies of biocatalysts' structures and functional aspects are among the eminently worthwhile future plans for research of this team. Among the scientific successes of the institute within the evaluation period, the work on Silybin and its derivatives must be noted as efficient and original. Silybin is a natural product of interest because of (inter alia) its antioxidant and antiangiogenic properties. It may be extracted from natural products as a mixture of diastereomers, which are also usually



used in chemical applications. Using an enzymatic approach involving lipase, the group has been able to prepare diastereomerically pure Silybin A and Silybin B, by a two-step protocol (regioselective acetylation in the presence of lipase, followed by a stereoselective process with the same enzyme). With these compounds (and several derivatives) in hand, tumor angiogenesis could then be studied. Another interesting and important project involved aryl sulfotransferases in the metabolic studies of various flavonoids.

**Date:** December 23, 2015

**Commission Chair:** Dr Habil, Academician Christian Amatore