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 Organic Chemistry and Biochemistry of the CAS, v. v. i.

Fields, in which the Institute registered its teams:

Biochemistry and molecular cell biology, biophysics, virology, …

Observer representing the Academy Council of the CAS: Karel Aim
Observer representing the Institute: Substitute observer Martin Fusek

Commission No. 6: Biochemistry and molecular cell biology, biophysics, virology
Chair: Professor emeritus Morten Kielland-Brandt

Date of the visit of the Institute: November 12, 2015
Programme of the visit of the Institute: see attached Minutes from the visit

Evaluated research teams:

No.2 - Chemistry and Biology of Insulin and Insulin-like Factors (team leader Jiří Jiráček)

No.3 - Proteases of Human Pathogens (team leader Jan Konvalinka)

No.4 - Structural Biology (team leader Pavlina Řezáčová)

No.5.- Cathepsin Proteases Pathology (team leader Michael Mareš)

No.6 - Microbial Proteins (team leader Iva Pichova)

A. Evaluation of the Institute as a whole

1. Introduction

The Institute of Organic Chemistry and Biochemistry CAS, v.v.i. (IOCB) is the largest non-university chemical research institute in the Czech Republic (635 people of which 135 are PhD students, total of 500 FTEs) with long history. After World War II when the activity of universities was renewed a group of prominent chemists from the Faculty of Chemico-technological Enginering of the Czech Technical University (now University of Chemistry and Technology) created a research group under the leadership of professor František Šorm (later on the first director of the present institution). This group of these very experienced chemists moved in 1951 to the present old building (constructed in years 1923-1929). Formally the institute became a part of the Czechoslovak Academy of Sciences on January 1, 1953. The leadership of professor Šorm and his successors proved that success in science needs not only knowledge, skills and vision but also strong managing and diplomatic abilities.

The research at IOCB since its beginning is focused on organic chemistry, biochemistry and other biological disciplines, now mainly on medicinal chemistry, chemistry on natural products, synthetic methodology and molecular modelling. IOCB has nice web pages (in English and Czech) where all interesting data are available concerning research groups, institutional structure, significant results, etc.

2. Strengths and Opportunities

The strengths of IOCB are derived from the perfect leadership by its directors, their managing skills, ability to recognize new perspective research targets and always to consider possible practical applications, mainly in the field of new drugs development. Among the important strategic activities it is necessary to mention the collaboration with the US company Gilead and creation of the Gilead Sciences and IOCB Research Centre. The licence activity made possible to build new modern building and to reconstruct the old ones and to buy new equipments. In this respect IOCB became an example for all research institutions in Czech Republic. After evaluation by IAB the group structure was reorganized. One senior group ended, new junior research groups led by researchers returned from abroad were created and 6 targeted research groups were established. It is also necessary to support the successful internationalization effort focused on scientific personalities. The collaboration with Czech universities (mainly with University of Chemistry and Technology and Charles University) can serve as an example. Five professors and four associated professors are participating in regular university education. IOCB also helps to improve the research quality of other institutions by offering them qualified services. The mentioned IOCB advantages create opportunities for further successful basic research leading to practical applications (e.g. new therapeutics).

3. Weaknesses and Threats

There are no apparent weaknesses or threats.

4. Recommendations

To continue in regular research group evaluation and to try to repeat successful practical applications

5. Detailed evaluations

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

Quality of the scientific output of the IOCB is excellent as well as international collaboration and it is number one in the field of practical applications among all research institutions in Czech Republic.

Declaration on the involvement of students in research

The involvement of students in research is given by the high number of defended bachelor, master and PhD theses in collaboration with Czech universities.

Declaration on societal relevance

Societal relevance of the research pursued at the IOCB is high as it involves studies on mechanisms of HIV infection and strategy of HIV inhibition, function of nucleic acids incl. repair processes, developing of new therapeutics, widening of bioinformatics platform and in other interesting research fields. Societal relevance is also reflected in numerous presentations of the work of the IOCB teams in media.

Declaration on the position in the international and national context

Position of IOCB at the international and national level is very strong and reflects the significance of the scientific work performed by its teams and members.

Declaration on the vitality and sustainability

The Institute has, thanks to the young or relatively young research teams, a very good position in the vitality and sustainability. The support of grant and license activities was large in the past and it is possible to presume that it will continue in future.

Declaration on the strategy and plans for the future

Strategic plans for the future research were presented by the team leaders. The described research strategies for the next research period were generally precise and reasonable. Thus these plans are recommended for realization.

B. Evaluation of the individual teams

Evaluation of the Team No. 2: Jiri Jiracek - Chemistry and Biology of Insulin and Insulin-like Growth Factors

1. Introduction

Team of the Institute of Organic Chemistry and Biochemistry headed by Dr. Jiracek is oriented to the chemistry and biology of insulin and related growth factors. There are 10.97 FTE (aggregate Full Time Equivalent) workers, with almost ideal distribution of age and experience of between team members, comprising seven researchers, fourteen "other workers" employed often part-time and three former researchers.

Scientific productivity of the Team (in the last five years) is excellent as it is represented by 53 contributions with 48 papers published in journals with known impact factors (IF), three papers in proceedings, one patent and one "applied result". The journals in which the group publishes are ranging from Nature (IF 2014 37.400) and Nature Chemistry (23.297) to less impacted journals like Proteome Sci. (IF 2014 1.73). The Team publishes results in the top journals in the field and has four papers in the highest-ranking category.

The Group is involved in studies of insulin and related structures for approx. twenty years. In the field of insulin analogues, the Group was interested in modifications of amino acid 26 and on properties of amino acid residues of the insulin B chain, of the insulin like growth factor II, in conformational transitions of insulin structure, and in chemical modifications of insulin by novel methods. The Group cooperates with groups within the IOCB (Structural Biology, Theoretical Chemistry) as well as with groups from abroad (Univ. York, Walther and Eliza Hall Medical Inst., Australia).

2. Strengths and Opportunities

The strength of the team is documented by its excellent publication record. The opportunities for this group are very good as it is relatively young and focusing on modern approaches. The group has excellent international collaborations and understands the importance of translational research very well.

3. Weaknesses and Threats

No obvious weaknesses.

4. Recommendations

The group should be supported.

5. Detailed Evaluations

The documents provided and the presentation gave clear impression that the Team is pursuing a fundamental and highly important research, which is also internationally recognized. The results may in the future be of fundamental importance in biochemistry and physiology.

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

The number of original scientific papers (48) published in journals with known impact factors plus one patent, three contributions to proceedings and one "applied result", is very impressive as it includes papers in highest quality, world leading journals (Nature, Nature Chemistry, J. Biol. Chem.). Taking into account only 10.97 Full Time Equivalent positions it is an excellent productivity.

Declaration on the involvement of students in research

As it has been stated before the pedagogical work is also part of activity of this team. The students of the Faculty of Sciences (Charles U. Prague) and of the University of Chemistry and Technology Prague realize their theses there. Also, several student groups (Charles U.) are trained in terms of advanced courses of Biochemistry every year. Students also from abroad take part in the laboratory work: one from Valencia Univ. (Spain) as a student of Erasmus programme for 10 months, and one from Univ. College Dublin (one month). Head of this Team also gave a lecture at the course of Advances in Drug Discovery, Chemistry and Biology, pursued by the University of Chemistry and Technology in Prague. Since 2014, two team members teach 2 hours weekly per semester at the Charles University (Faculty of Sciences).

There are students of all three types of studies, students of the bachelor, master and doctoral (Ph.D.) programmes. They contribute to the research done in this laboratory. Recently, there were thirteen students (3 Bachelors, 1 M.A., 9 Ph.D. students) supervised by members of this team; thirteen students are also co-supervised (five bachelors, seven M.A. and one Ph.D. student). Five students of the Ph.D. programme, seven of the M.A. and seven bachelors successfully defended their theses during the last five years.

Declaration on societal relevance

The relevance of the studies realized in this laboratory is high as it is focused on the structural and functional principles important in diabetology. The team members are also active in popularization of their research (see further).

Declaration on the position in the international and national context

Overall, the position of this group in the scientific community is very well known, reflecting the importance and quality of results. Team members actively participated in preparation of the exhibition of the IOCB at the EXPO 2015 in Milano, Italy. Also, the team members gave interviews by radio as well as in the newspapers on their research. International recognition is given by the fact that the Team is involved in the grants provided by various grant agencies, local (Grant Agency of the CR) as well as international (Med. Res. Council UK grant). Also the fact that students from abroad joined the group documents their international recognition.

Declaration on the vitality and sustainability

The Team has a very good perspective as to the continuation of their work in the next period both because of its scientific productivity and ideal distribution of young and experienced members. This team is comprised of relatively young workers (ten out of 11 are in the range up to the age of 50). The main focus should be again on the funding. Focus on the patents or translational applications may help.

Declaration on the strategy and plans for the future

The research plan for the next period is clearly presented in detail in the Report and involves four most important directions of the activities of this laboratory: (i) Studies on structure-based new analogues of insulin able to bind to the insulin receptor in an optimal way, this project is currently supported also by the Medical Res. Council U.K.; (ii) studies on the metabolic and growth factor-related structural principles of insulin and growth function, supported also by the MRC U.K. and by a Czech GACR grant, both to 2017; (iii) synthesis and testing of insulin mimetic molecules of a non-peptide basis, the group already designed molecules based on insulin structural scaffold, also supported by Czech GACR project until the end of 2016; (iv) studies on structures of human insulin stored in pancreatic beta cell secretory granules by in vitro methods combined with crystallography and theoretical calculations in cooperation with York Univ. and with structural chemists of the IOCB.

Evaluation of the Team No. 3: Jan Konvalinka - Proteases of Human Pathogens

1. Introduction

The group of Jan Konvalinka reports in average about 5 research members and 11 other workers. Jan Konvalinka, as associated professor of the Charles University in Prague, where he serves as a vice-rector for science; he is also member of the Biochemistry Department. This position allows him to attract students (of various level – bachelor, master and doctoral) to work on the topics in his CAS group. Konvalinka team aims to identify, characterize and exploit enzymes, especially proteases, as therapeutic targets. They work on one well established target (HIV protease), one recently identified (glutamate carboxypeptidase II, also known as the prostate specific membrane antigen) and an emerging therapeutic target (human and mouse serine racemase).
The group has expertise in recombinant protein expression in *E.coli,* insect and mammalian cells, protein purification, assay development, enzyme kinetics, inhibitor design and synthesis.

2. Strengths and Opportunities

The big advantage of the team is a very close liaison with the Department of Biochemistry of the Charles University, which allows introducing students into well-coordinated research.

3. Weaknesses and Threats

No weaknesses are obvious.

4. Recommendations

To continue the work along the lines of the present approach and research strategy and according to stated research plans.

5. Detailed evaluations

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

The quality of research is at high level. 32 original papers in recognized impact journals, 7 chapters in scientific books, 1 scientific book and 2 patents are documented with 3/14 papers in the first decile/quartile of journal ranking, and 1/3 in the citation ranking.

Declaration on the involvement of students in research

The involvement of students in research is exemplary.

Declaration on societal relevance

The research has option to be utilized in the development of drugs for the treatment of various diseases

Declaration on the position in the international and national context

The team has very good reputation in national and international context.
Activity in the area of research popularization is very high. Jan Konvalinka wrote a popular book in Czech on viruses and anti-virus drug development (Konvalinka, J., Machala, L.: Viry pro 21. století, Praha, Academia 2011, ISBN 978-200-2021-5) that was sold in thousands of copies and critically acclaimed.
Konvalinka has been a host of two television talk shows that presented science and scientists for the public ("Čaj pro třetího" and "Interview 21"), writes often on science to major Czech newspapers ("MF Dnes", "Lidové noviny") and journals ("Vesmír"). There were many other activity mentioned in the team report.

Declaration on the vitality and sustainability

The Team has very good prognosis concerning its vitality and sustainability because majority of the team members are in the age below 30 and its ability to gain grants is also very high.

Declaration on the strategy and plans for the future

The described research strategy for next research period is very precise and reasonable. Thus, it is recommended for realization.

Evaluation of the Team No. 4: Pavlina Rezacova - Structural Biology

1. Introduction

Team of Pavlína Řezáčová is oriented on structural studies of various proteins, peptides and low molecular weight compounds of biological or medicinal importance and interest. This unit was until half of 2013 operating as a service laboratory, since that time it has been transformed into a research team with own projects; however, it is still participating in research of other groups seeking cooperation. It comprises 4.20 researchers (FTE). Scientific output of this team (in last five years) is excellent.

P. Řezáčova leads also a research team at the Institute of Molecular Genetics (IMG) focused on protein expression and crystallization (cf. the evaluation of IMG).

2. Strengths and Opportunities

The Team is highly productive, with 76 papers in peer-reviewed journals with known impact factors. As the Team focuses on the structural aspects of the proteins, peptides and active or potentially active compounds, their own research program is complemented by work in cooperation for other groups seeking the help in solving structural aspects. The Group is without any doubt highly efficient. The know-how and experience of this group is a great asset to the IOCB and other groups.
The Team collaborates with institutions abroad (U. Texas Southwestern, Dallas; Katholieke U., Leiden).

2. Weaknesses and Threats

No obvious weaknesses or threats.

3. Recommendations

The team should be supported.

5. Detailed Evaluations

Documents provided as well as the site visit gave strong impression that the Team realizes a highly interesting and internationally recognized research with fundamental importance in biochemistry and medicinal chemistry.

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

The number of original scientific papers published (76 in journals with known impact factors plus four in other journals, one book chapter and one contribution to Proceedings) is very impressive as it includes papers in journals like J Biol. Chem., Nature protocols or Blood. Taking into account only 11.75 Full Time Equivalent positions it is an excellent productivity if also a high impact factor of the journals is taken into account. According to the analysis, there are six contributions to journals with the highest impact (top decile). The only comment is that for the next evaluation, it would be informative to divide the papers to these stemming from the own research of the Group and from the cooperation on other themes.

Declaration on the involvement of students in research

As it has been stated before the students of all three types of studies, bachelor, master and doctoral (Ph.D.) programmes contribute to the research done in this laboratory.
Recently, there are ten students (3 Bachelors, 4 M.A., 3 Ph.D. students) supervised by members of this team; one student of the Ph.D. programme, one of the M.A. and two bachelors successfully defended their theses during last five years.

Declaration on societal relevance

The relevance of the studies realized in this laboratory is high as it is focused on the structural principles of processes fundamental in elucidation of various types of cancer and in finding the structural principles of potentially new drugs. However, it is probably not much recognized by the society as there is practically no activity in popularization and dissemination of the high quality results obtained.

Declaration on the position in the international and national context

Overall, the position of this group in the scientific community is well known, mirroring the importance and quality of its results. However, the outputs and extraordinary quality of the outputs are not as much recognized. Success in obtaining the funds is also a part of recognition. The Team is involved in the grants provided by various agencies, as it is stated in the Report available, there are grants covering the expenses now; it is stated also that the Team will try to maintain the financial support also in the next period.

Declaration on the vitality and sustainability

The Team has a very good perspective as to the continuation of their work in the next period. This team is comprised of relatively young workers (ten out of 12 in the range up to the age of 45). The main focus should be again on the funding, two research themes are funded now, one grant application has been submitted to help to cover the finances needed to pursue research in the third field studied, and however, three themes seem not to be funded in the near future.

Declaration on the strategy and plans for the future

The research plan for the next period is clearly outlined in the Report and involves all the most important directions of the activities of this laboratory: (i) Studies on structure-based drug design of inhibitors of human carbonic anhydrases, (ii) structural aspects of interactions of bacterial transcription repressors and (iv) of the human LEDGF/p75 transcriptional co-activator implicated in various types of human cancer and in mechanisms of HIV virus replication; (v) the fragment-based drug discovery seems to be very promising area of research with translational possibilities (also with possibility to apply for patents); (iv) structural biology of metabolic pathways (involving studies on principles of responses to insulin-like growth factors studied by another group of the IOCB) and (iv) research on the structure of cytosolic purine 5´-nucleotidase which is also a possibly druggable target as it is hyperactivated by mutations leading to relapses of acute myeloblastic leukemia after conventional therapy. Taken together, there is a perspective of this group to continue and contribute to interesting fields of research.

Evaluation of the Team No. 5: Michael Mares - Cathepsin Proteases in Pathology

1. Introduction

The quite small team is dealing with cathepsin proteases and proteolytic systems controlled by these enzymes. These enzymes are involved *e.g.* in cancer, arthritis, osteoporosis, and neurodegenerative diseases. Research is focusing on a complex approach to their roles in pathological processes and as therapeutic targets against several important parasitic diseases. Most of the outputs can have considerable impact on the population health. The research integrates protein biochemistry, functional proteomics, enzymology, protein production, 3D structure analysis and rational ligand design.

2. Strengths and Opportunities

The whole team has a very good scientific output, with 3 papers in the world leading category, 2 labelled as world excellent and two internationally recognized. Especially the quality of outputs is very good if evaluated by journal ranking. Also the citation sources are of good quality.

The research program and the grant support are very good both at national and international grant agencies.

The team has very good intramural and also international cooperation with teams focused on biology and synthesis of organic compounds.

The age structure of the Team is good for the future, consisting mostly of young scientists with sufficient amount of experienced ones. The number of students is good.

The future plans of the Team are highly innovative and have realistic research plan for 2015-

2019, and it seems most of the projects already have sufficient grant support.
Promising is the extensive collaboration with top laboratories in Czechia and abroad, which already produced a lot of good outputs. The activity of the Team in the area of research popularization is good.

3. Weaknesses and Threats
There are no obvious weaknesses and threats.

4. Recommendations
The age structure of the Team is good, enough students are involved. The aiming of research topics of the Team is convergent, intra- and extramural cooperations are well balanced, and the research of the Team is well focused. The team members should devote more energy to participate in the activities of the scientific community.

5. Detailed evaluations
Declaration on the quality of the results and share in their acquisition

The scientific output of the Team is excellent; many papers were published in journals with high IF. Three of the outputs are in the category “world leading” and two “internationally excellent”.

Declaration on the involvement of students in research

The number of students involved in the research work is very good. The pedagogical activity of the team is also satisfactory.

Declaration on societal relevance

The team has activities for research popularization.

Declaration on the position in the international and national context

The national and international collaborations are very good, and available facilities using state-of-the-art equipment and approaches allow fulfilling the plans.

Declaration on the vitality and sustainability

The Team demonstrates ability to attract funding. The strong collaborations with national and international laboratories suggest very good chances to attract national and international funding.

Declaration on the strategy and plans for the future

The research plans for the next period are realistic.

Evaluation of the Team No. 6: Iva Pichova - Microbial Proteins

1. Introduction
The team is internationally well known for its research focused on the characterization of individual proteins and enzymes that play a key role in infectivity of retroviruses. The large number of active national and international collaborations allows an interdisciplinary approach that resulted in excellent scientific productivity.

2. Strengths and Opportunities
The Team is very strong, as evidenced by high outputs score and the high ratio publications/researcher. The quality profile from Phase I, the citation profile, and the journal impact of the publications are all very good. The future research consolidates the group internationalisation.

3. Weaknesses and Threats
No obvious weaknesses.

4. Recommendations

The multidisciplinary approach should be preserved and the team contribution to the collaborative work should be highlighted. The current research is of great value and the future plans are adequate.

5. Detailed evaluations

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

The quality profile from Phase I, the citation profile, and the journal impact of the publications are very good. The ratio publications/researcher is high. However, only half of the outputs have group members as the first and/or last author.

Declaration on the involvement of students in research

There is a good number of PhD and Master students and finished theses during the period.

Declaration on societal relevance

The research subjects are highly significant for society. The group leader is an active member of several committees, councils and panels and has been involved in outreaching activities for primary school students and for the general public.

Declaration on the position in the international and national context

The Team is internationally well recognised within the field of host-pathogen interactions at a molecular level.

Declaration on the vitality and sustainability

During the evaluation period the Team has been funded by national and international grants, including one FP7 collaborative project. The future activities provide a good basis to new funding.

Declaration on the strategy and plans for the future

The plans for the future are very well described and seem well fit to the team's research profile.

Date: December 16, 2015

Commission Chair: Professor emeritus Morten Kielland-Brandt