Questionnaire
Summary of the main activities of a research institute of the Slovak Academy of Sciences

Period: January 1, 2012 – December 31, 2015

1. Basic information on the institute:

1.1. Legal name and address

Ústav molekulárnej biológie Slovenskej akadémie vied
(Institute of Molecular Biology, Slovak Academy of Sciences)
Dúbravská cesta 21, 845 51 Bratislava 45
Slovakia

1.2. URL of the institute web site

http://www.imb.savba.sk/

1.3. Executive body of the institute and its composition

Directoriat	Name	Age	Years in the position
Director	RNDr. Ján Kormanec, DrSc.	56	4
Deputy director	RNDr. Gabriela Bukovská, CSc.	58	4
Deputy director (for economy)	Ing. Anna Varcholová	63	32
Scientific secretary	Mgr. Ľuboš Kľučár, PhD.	46	8

1.4. Head of the Scientific Board

RNDr. Imrich Barák, DrSc.

1.5. Basic information on the research personnel

1.5.1. Number of employees with university degrees (PhD students included) engaged in research projects, their full time equivalent work capacity (FTE) in 2012, 2013, 2014, 2015, and average number of employees in the assessment period

	2012		2013		2014		2015		total		
	number	FTE	number	FTE	number	FTE	number	FTE	number	averaged number per year	averaged FTE
Number of employees with university degrees	59.0	43.710	57.0	43.950	47.0	42.510	49.0	40.710	**212.0**	**53.0**	**42.720**
Number of PhD students	17.0	12.880	18.0	14.740	15.0	13.820	13.0	14.150	**63.0**	**15.8**	**13.898**
Total number	76.0	56.590	75.0	58.690	62.0	56.330	62.0	54.860	**275.0**	**68.8**	**56.618**

1.5.2. Institute units/departments and their FTE employees with university degrees engaged in research and development

Research staff	2012		2013		2014		2015		average	
	No.	FTE	No.	FTE	No.	FTE	No.	FTE	No.	FTE
Institute in whole	59.0	43.710	57.0	43.950	47.0	42.510	49.0	40.710	**53.0**	**42.720**
Department of Biochemistry and Structural Biology	12.0	5.161	10.0	5.908	9.0	6.317	8.0	6.515	**9.8**	**5.975**
Department of Gene Expression	6.0	5.756	6.0	5.879	6.0	5.982	6.0	5.449	**6.0**	**5.767**
Department of Genomics and Biotechnology	13.0	10.361	13.0	10.582	11.0	10.768	11.0	9.748	**12.0**	**10.365**
Department of Microbial Genetics	8.0	6.075	8.0	6.311	6.0	4.985	8.0	5.003	**7.5**	**5.594**
Department of Microbiology	12.0	10.601	12.0	9.309	10.0	9.472	10.0	9.169	**11.0**	**9.638**
Department of Protein Biology and Evolution	5.0	4.797	5.0	4.899	5.0	4.986	6.0	4.826	**5.3**	**4.877**
Department of Molecular Apidology	3.0	0.959	3.0	1.062					**3.0**	**1.011**

1.6. Basic information on the funding of the institute

Institutional salary budget and others salary budget

Salary budget	2012	2013	2014	2015	average
Institutional Salary budget *[thousands of EUR]*	626.193	654.947	625.312	640.550	**636.751**
Other Salary budget *[thousands of EUR]*	92.432	96.970	77.367	63.417	**82.547**

1.7. Mission Statement of the Institute as presented in the Foundation Charter

1. The research activities of the Institute of Molecular Biology are focused on basic research into the molecular principles of living systems. The molecular biology of prokaryotes and eukaryotes and microbiology are the main focuses of the Institute's activity. Primary attention is paid to the biological sciences (molecular biology, microbiology, structural biology, genetics, cell biology, neuroscience, and virology), chemical sciences (mainly biochemistry and bioorganic chemistry), biotechnology (environment, industry, medicine, and agriculture), earth and environmental sciences (ecology and biodiversity), bioinformatics, biophysics, and nanotechnology.
2. The Institute offers consultation and expertise that are closely related to its main activities.
3. The Institute implements PhD education in terms of generally valid regulations.

4. The Institute requires that the results of its R&D activities be published by periodical and non-periodical presses. This is carried out according to regulations laid out by resolutions passed by the SAS Presidium.
5. The Institute offers the following enterprise activities:
    - Contractual research in molecular biology, biology, microbiology, and biotechnology
    - Provision of consultation and expertise in the fields of molecular biology, microbiology, biotechnology, and GMO
    - Synthesis of specific bio-products and standards for research and development
    - Organization of specialized seminars, conferences, and educational meetings in molecular biology, microbiology, and biotechnology

1.8. Summary of R&D activity pursued by the institute during the assessment period in both national and international contexts, (recommended 5 pages, max. 10 pages)

Over the course of its development, molecular biology has become an interdisciplinary research area, which focuses on understanding fundamental life processes at the molecular level. As a consequence, it has also contributed dramatically to recent progress in biotechnology, biomedicine, and certain environmentally related research. Accordingly, the Institute of Molecular Biology (IMB) is fully involved in these developments, applying new discoveries and ideas to both basic science and translational research. Research at IMB has a substantial national and international impact, reflecting the high quality of its research teams. Many of these have collaborations with other leading institutes from Slovakia, the EU28, and other countries from around the world. All of these are supported by international grant projects. In addition, both individuals and teams have received several prestigious scientific rewards, including the highest ones the Slovak Academy of Sciences has to offer. IMB presently includes six departments (Table 1) divided into thirteen independent laboratories which are involved in activities ranging from basic to applied research. The common goal of the research units within the institute is to better understand the molecular and cellular interactions occurring in living organisms, and to eventually predict, modify, and influence the processes that involve them. Specifically, the research activities of the Institute can be divided into five major areas:

1. Cell division and differentiation
2. Protein structure-function relationships and protein evolution
3. Microbial ecology
4. Functional genomics, bioinformatics, and biotechnology
5. Cellular and molecular biomedicine

During the last four years, the Institute has increased the level of cooperation between its various units. This has taken the form of both the sharing of technical facilities and the exchange of knowledge and expertise (in, for example, common publications, progress reports, brain-stormings, annual retreats, group meetings, journal clubs and team building activities). It should also be pointed out that massive, long-term reconstruction was recently undertaken to improve the working conditions within the Institute. Taken together, the past four years have been fruitful, not only scientifically, but also and especially with regard to the future prospective of the Institute. The following sections will describe our major achievements during the evaluation period in detail, organized according to our five main research areas aforementioned.

Table 1: Overview of the research units at IMB SAS

No.	Name of Unit	Head	Areas
#1	Department of Gene Expression	Dr. Ján Kormanec	1, 4
#2	Department of Microbial Genetics	Dr. Imrich Barák	1, 2, 4
#3	Department of Biochemistry and Structural Biology	Dr. Eva Kutejová	2, 4, 5
#4	Department of Genomics and Biotechnology	Dr. Gabriela Bukovská	2, 3, 4
#5	Department of Microbiology	Dr. Marián Farkašovský	1, 2, 3, 5
#6	Department of Protein Biology and Evolution	Dr. Štefan Janeček	2, 5

1. Cell Division and Differentiation

Cell division and differentiation is explored by *Units #1, #2,* and *#5*. *Unit #1* studies the differentiation of soil-dwelling *Streptomyces* bacteria. These organisms undergo a remarkable process of morphological differentiation connected with the production of more than 70% of the known antibiotics. The gene expression program of *Streptomyces* is extremely complex. The genome *S. coelicolor*, the best-studied representative, contains genes for 65 RNA polymerase sigma factors, including 9 close homologues of SigB, the general stress-response sigma factor. It also has 45 anti-sigma factor genes, 17 anti-anti-sigma factor genes, and 44 activating PP2C phosphatase genes. We have discovered essential roles for several stress-response sigma factors in different developmental stages and have described their contributions to the stress response. We have also elucidated the signal transduction pathways that activate SigI, SigH, and SigF, together with the roles of their corresponding anti-sigma factors and anti-anti-sigma factors. In particular, BldG, an anti-anti-sigma factor crucial for morphological differentiation and antibiotic production, was found to have a pleiotropic role in the regulation of both SigH and SigF, two sigma factors involved in regulating two discrete developmental stages, by inhibiting their respective cognate anti-sigma factors, UshX and RsfA. We have also confirmed interactions between additional sigma factors, anti-sigma factors, and anti-anti-sigma factors, all of which further illustrate the complexity of Streptomyces' regulatory processes (see also *Section 4*).

The cell division, differentiation, and programmed cell death of *Bacillus subtilis,* a common model organism, are the main research topics of *Unit #2*. Probably one of the most controversial questions about the cell division of rod-shaped bacteria concerns how the division septum is correctly placed: at mid-cell during vegetative growth but closer to one end during sporulation. In both cases, the proteins of the Min system play a central role. We have shown that the *Escherichia coli* oscillating Min system is functional when transplanted into *B. subtilis*, and that the oscillatory behaviour of this Min system inhibits sporulation. These results have allowed us to study the behaviour of *Clostridia* cell division proteins by using *B. subtilis* as a heterologous host for the first time (*see also Sections 2, 4*). *Unit #2* is also one of the leading groups in the field of bacterial sporulation. A sign of this is that it was entrusted with the organization of seven European Spores Conferences (2004–2016). The Department Head, Imrich Barák, was the main organizer of two of these meetings and a member of the organizing committee for all seven. He has also been one of the Coordinators of the Consortium of Central and Eastern European Structural Biology Groups from 2000, a member of the Bacell organization Steering group since 2011 (a European umbrella organization supporting Bacilli research), and he was the main organizer of the 2014 Bacell meeting.

The Laboratory of Molecular Microbiology in *Unit #5* also researches the fundamental principles of cell division, specifically cytokinesis, an essential event in mitosis. Cytokinesis must be spatially and temporally coordinated with nuclear migration to ensure faithful chromosome segregation. In particular, we have been studying the role of septins in cytokinesis. Septins are conserved guanosine phosphate-binding proteins present in most eukaryotic organisms. Together with the actomyosin contractile ring core components, they are crucially involved in cell division. They serve a scaffold and a diffusion barrier at the division plane, preventing the movement of proteins between the mother and daughter cells. Notably, septins have also been implicated in many human pathologies; our ultimate goal is to understand the complex septin regulatory network (see also *Section 5*).

2. Protein Structure-Function Relationships and Protein Evolution

Five of the Institute's six departments are involved in some way with research into protein structure and function. Many different approaches are used to characterize a variety of biologically important proteins. Nearly 60 different macromolecular objects have been crystallized and 37 structures determined at the Institute. *Unit #2* has studied the proteins of the *B. subtilis* spore coat, which form a layer with unique resistance properties around the spore. We have found that a small set of morphogenetic proteins controls the assembly of more than 70 different coat proteins, forming a basic scaffold for the attachment of the other spore components. In collaboration with the University of Sheffield and the Chinese Academy of Sciences, we used electron microscopy and atomic force microscopy to find that some of the

coat proteins can self-assemble to form highly organized supramolecular structures. We also identified and characterized RodZ, a new protein partner for SpoIIE, a crucial sporulation protein that links asymmetric cell division to the activation of the first compartment-specific sigma factor. RodZ is a morphogenetic protein involved in maintaining the rod cell shape; as a SpoIIE partner, it is required for asymmetric septation by stabilizing SpoIIE at the asymmetric septum formation site. Extensive structural studies of SpoIIE led to the crystallization and tertiary structure determination of its phosphatase domain (see also *Sections 1, 4*).

The Laboratory of Biochemistry and Protein Structure in *Unit #3* studies ryanodine receptors, the primary Ca^{2+} ion channels which release Ca^{2+} ions from the lumen of the sacroplasmatic reticulum into the cytosol to initiate muscle contraction. Mutations within the human ryanodine receptor 2 (hRyR2) gene are responsible for a number of severe, inherited cardiac diseases. We determined the tertiary structure of the N-terminal part of hRyR2, which includes one of the three primary mutation clusters. We generated point mutations in this region to help understand the contribution of single residues to the structure and function of hRyR2. The hRyR2 group was recognized as the best scientific group of 2014 by the Slovak Academy of Sciences. Another research subject of this Laboratory is mitochondrial ATP-dependent proteases and other components of the mitochondrial nucleoid, the large protein-DNA complex which houses most of the mitochondrial DNA. The proteases are responsible for maintaining mitochondrial homeostasis by (i) degrading damaged proteins generated by various stresses, (ii) regulating short lived proteins, (iii) assembling respiratory complexes, and (iv) stabilizing the mitochondrial nucleoid. Our main subject is the ATP-dependent Lon protease. This enzyme uses ATP hydrolysis to unfold and translocate a protein substrate to a proteolytic active site; all three processes occur in parallel. By generating several Lon point mutants, we found that its proteolytic site is connected to its ATP binding site through two adjacent loops, one with a double glycine and one containing Trp770. Substrate binding triggers movement of both loops, inducing conformational changes and enhanced ATPase and peptidase activities. We also carried out a three-dimensional reconstruction of a proteolytically-inactive hLon mutant using cryo-electron microscopy, in collaboration with the First Faculty of Medicine, Charles University, Prague, and the Institute of Microbiology (ASCR). We found that the proteolytic and ATP-binding domains (AP-domain) form a hexameric chamber, whereas the N-terminal domain is arranged as a trimer of dimers. The junction between the N-terminal domain and the AP-domain forms a narrow, trimeric channel, which is likely to be composed of coil-coiled helices. The binding of a non-hydrolyzable ATP analogue leads to a closed-ring conformation, while ADP binding causes the AP-domain to switch to a lock-washer conformation, triggering channel opening and suggesting that nucleotide-dependent rearrangements of the hLon hexamer comprise a gating mechanism for substrates entering the proteolytic chamber. In close collaboration with Department of Biochemistry and Department of Genetics, Faculty of Natural Sciences, Comenius University in Bratislava, we have also studied Mgm101, a protein crucial for mitochondrial DNA recombination, and another nucleoid component. We found species-dependent differences in its structure and DNA binding properties, and our results suggest that Mgm101 plays a role in the recombination-dependent replication of linear mtDNA and mitochondrial telomere maintenance. This Laboratory also collaborates with the Institute of Animal Biochemistry and Genetics SAS to study the protection phosphatidyl inositol transfer protein PDR16 grants against azole antifungals.

The newly formed Laboratory of Immunology (*Unit #3*) used site-directed mutagenesis to characterize the residues of the mannose 6-phosphate/insulin-like growth factor 2 receptor involved in plasminogen uptake by human macrophages. This might have an important impact on the maintenance of homeostasis (see also *Section 4, 5*).

The Laboratory of Prokaryotic Biology (*Unit #4*) studies the structure-function relationships of biotechnologically interesting proteins. Based on the tertiary structure of a complex of *Erwinia chrysanthemi* xylanase (a plant pathogenic bacterium) with its reaction product, which we recently solved, we proposed several mutations to identify the roles of individual amino-acid residues in substrate recognition and degradation. In cooperation with the Institute of Chemistry SAS, four mutant xylanases were prepared and crystallized. Modelling based on the crystal structure is in progress (see also *Sections 3, 4*). We also determined the tertiary structures of glucoamylase from *Saccharomycopsis fibuligera* and two mutants of β-glucosidase from *Zea mays,* thereby contributing to a better understanding of protein stability, activity and specificity.

These enzymes were purified in cooperation with the Laboratory of Biochemistry (*Unit #3*) and Mendel University, Brno, CR. Our study on the conformational stability of proteins was further enhanced by the tertiary structures of another three ribonuclease Sa mutants, solved at atomic resolution. In 2012 and 2014, this Laboratory also continued its tradition of organizing the two national conferences "*Proteins in our focus – Structure and function*" with the aim of bringing together proteomics researchers for discussions and collaborations.

The Laboratory of Phylogenomic Ecology in *Unit #5* studies catalytic hydroperoxidases, essential enzymes in aerobically living cells involved in the metabolism of reactive oxygen species. They are divided in peroxidases and catalases, which vary in their reactivity to peroxidic substances. In collaboration with the University of Natural Resources & Life Sciences in Vienna, Austria (BOKU, Dept. of Chemistry), we have defined four independent superfamilies of heme-containing peroxidases. This classification is based on the inferred evolutionary relationships of all peroxidase protein sequences available in international databases. These superfamilies appear to have evolved independently over the course of a long evolutionary history. In collaboration with BOKU, we have attempted to systematically investigate the structure-function relationships responsible for the typical reaction mechanism of selected microbial peroxidases from each superfamily. We have succeeded in crystallizing catalase-peroxidase 2 from the phytopathogenic fungus *Magnaporthe oryzae* and its mutants. Recently, we began investigating the still unknown family of hybrid B heme peroxidases, which may contribute significantly to the mechanism which protects important phytopathogenic fungi against oxidative stress. Understanding the mechanism of peroxidases in these pathogens and their involvement in defending against the oxidative burst of plants may help prevent agricultural losses (see also *Section 3*).

The Laboratory of Protein Evolution (*Unit #6*) has mainly been concerned with the studying the relationships between sequence, structure, function, specificity and evolution of amylolytic enzymes that operate on starch and related α-glucans using *in silico* approaches. Specifically, we have elucidated the evolution of and described the unique sequence features for several groups of α-amylases from the main α-amylase family GH13 (this is useful for assigning the enzyme specificity of hypothetical proteins). We have also identified the conserved sequence regions (the so-called sequence fingerprints) for individual enzyme specificities within a second α-amylase family, GH57. Furthermore, we have revealed the unambiguous evolutionary relatedness of α-amylase families GH57 and GH119 (including the catalytic machinery and domain fold); and finally, we have described the detailed evolutionary relationships among the 4-α-glucanotransferases from the glycoside hydrolase family GH77 (amylomaltases from borreliae and disproportionating enzyme-2 from plants). This Laboratory is one of the leading research groups worldwide in the field of amylolytic enzymes, based on more than 20 years of research experience by the Laboratory Head, Stefan Janecek. The group has established many international contacts and collaborations under several long-term projects, including the Technical University of Denmark, University of Groningen, CNRS in Gif, Gdansk University of Technology, University of Belgrade, University of Kentucky, Technology University of Malaysia, Bandung Institute of Technology and others. Štefan Janeček established and has been the main organizer of a series of international conferences on the α-amylase enzyme family, ALAMYs (http://imb.savba.sk/~janecek/Alamys/), held every third year since 2001 in Slovakia; ALAMY_6 will be held in 2016. He is also the responsible curator and co-author of several relevant α-amylase and related families in the Wikipedia-like project CAZypedia (http://www.cazypedia.org/).

3. Microbial Ecology

The scientific focus of *Unit #4's* Laboratory of Prokaryotic Biology has recently been enlarged to study enzymes involved in plant cell degradation secreted by the fungi *Trichoderma reesei* and *Schizophyllum commune*. This work is a part of its cooperation with the Institute of Chemistry, SAS. This work began with genome mining, followed by designing and preparing synthetic genes for nine enzymes, mainly xylanases and acetylesterases, all of which have been successfully expressed. In particular, the expression of an acetylesterase from *Trichoderma reesei* has been optimized and the enzyme isolated in a soluble form (see also *Sections 2, 4*).

The Laboratory of Environmental and Food Microbiology (*Unit #5*) focuses on those microbial communities responsible for the biodeterioration of cultural heritage objects, and also those responsible for the quality of traditional Slovak food (primarily cheeses and wines). This Laboratory is the first, and presently the only, one in Slovakia which performs basic and applied research into the microbial deteriogens of historical objects in order to find suitable solutions for the care and conservation of these items. In addition, the work of this group in this area during the last four years has resulted in many collaborations with many national and international institutions, operating to safeguard our cultural heritage. The Laboratory has introduced culture-independent approaches for studying food microflora in Slovakia, and the results achieved with these methods have revealed the different processes which take place during the maturation of cheese and the fermentation of wine. We have been involved in studies on the bioremediation of heavy metals, polycyclic aromatic hydrocarbons and polychlorinated biphenyls. We also cooperate with National Cheng Kung University, Dep. of Environmental Engineering (Tainan City, Taiwan) in investigating methanogenic communities in thermophilic bioreactors in order to improve the production of methane. The members of this group possess important skills for studying the microbial communities (bacteria, cyanobacteria, fungi, yeasts, algae and archaea) of various environments from the very first sampling step (e.g. the sampling of historical and artistic items must be be non-destructive), through specific cultivation methods and the detection of hydrolytic properties, to the use of nucleic acid (DNA and RNA) fingerprinting (DGGE, ARISA, T-RFLP) and high-throughput sequencing (Illumina MiSeq). Finally, this group was recognized as the best scientific group of 2015 by the Slovak Academy of Sciences.

The Laboratory of Phylogenetic Ecology (also *Unit #5*) has isolated, identified and characterized difficult to cultivate and previously uncultured bacteria from Ni-contaminated soil in southwest Slovakia. This task was achieved either using a diffusion chamber-based approach or with traditional cultivation techniques. The phylogeny of the detected bacterial species was inferred based on 16S rDNA gene sequences from the separated isolates and also by means of PCR-DGGE. We demonstrated, from a total of 108 unique prokaryotic species, that diffusion chamber cultivation produced more unique isolates of real phylogenetic novelty, leading to the *in vitro* cultivation of previously poorly cultivable species, than the more traditional methods (see also *Section 2*).

4. Functional genomics, bioinformatics and biotechnology

In an effort to identify new drug targets in human pathogens, *Unit #1* has been studying RNA polymerase sigma factors from the human pathogens *Salmonella typhimurium* and *Staphylococcus aureus*, in collaboration with several collaborators from the European research area, including ones from the U.K and Germany. RNA polymerase sigma factors have a critical role in the pathogenicity of many bacterial organisms. *Unit #1* has characterized the roles of two sigma factors, RpoE from *S. typhimurium* and SigB from *S. aureus*. Several genes belonging to the regulons controlled by these sigma factors were previously characterized in detail and found to play a crucial role in virulence and stress responses. An amino-acid residue of RpoE was found to be essential for its recognition of a specific nucleotide in its cognate promoter. In addition, a mutant with altered promoter specificity was also found. Mutated forms of this sigma factor with altered promoter specificity were introduced into the *S. typhimurium* genome and were found to initiate transcription from a large number of artificial promoters. This recognition had no significant effect upon growth, however, even under stressful conditions. In *S. aureus*, the catabolite control protein CcpE was found to have a role in tricarboxylic acid cycle activity.
Unit #1 also studies several aspects of antibiotics production, in particular, the identification, characterization, and production regulation of new antibiotics. Biotechnologically motivated research has focused on the modification of *Streptomyces* strains for better production of bioactive compounds and industrially valuable or applicable proteins. *Streptomyces* bacteria are also the main producers of bioactive natural products including many antibiotics, antitumor, antiviral, and antifungal compounds. In collaboration with *Unit #5*, we have identified a polyketide synthase gene cluster, *aur1*, in *Streptomyces aureofaciens* CCM3239 which is responsible for the production of auricin, a unique angucycline aromatic polyketide antibiotic conjugated to an amino-deoxyhexose d-forosamine. Interestingly, the *aur1* gene cluster is localized on the large (241,077 bp) linear plasmid pSA3239, together with additional gene clusters for other secondary metabolites, *e.g.* the blue pigment indigoidine. Auricin is produced

during a very narrow growth phase interval of several hours after entry into stationary phase, and is afterwards degraded into non-active metabolites (due to its instability at the high pH reached during the later stationary phase). We found that this unusual production scheme arises from a unique, strict, complex regulation mechanism, involving both feed-forward and feed-back control by auricin intermediates through several transcriptional regulators. Finally, we have also prepared and optimized a new, rapid and reliable system for large deletions in *Streptomycetes*. Using this system, we prepared a *S. lividans* strain in which three large internal antibiotic gene clusters were deleted. This strain heterologously produced the cytostatic compound mithramycin 4-fold higher than the control strain.

Because the investigation of the molecular biology of antibiotic-producing organisms is one of the most important world-wide research topics, this project has attracted many international partners from within the European research area, including partners from the U.K. The Department Head, Jan Kormanec, is an internationally recognized scientist in this field, as reflected by his invitations to international conferences and seminars. Due to his expertise in this field he was invited to join the large collaborative 7 RP project Strepsynth in 2013. At the national level, the group was selected as the top team of SAS in 2013, and was awarded "Best Project" in 2014 by SAS for their studies on the intriguing properties and regulation of auricin.

Antibiotic resistance is presently a problem in hospitals, making the production of new or modified antibiotics very important. One way to approach this is to study the biosynthetic systems which produce some of the known antibiotics. In cooperation with the Microbiological Institute in Prague, The Laboratory of Biochemistry and Structural Biology (*Unit #3*) has characterized several proteins participating in the biosynthetic pathways of lincomycin and celesticetin. The crystal structures of the S-adenosyl-l-methionine (SAM)-dependent methyltrasferase CcbJ from *Streptomyces caelestis* in the presence and absence of cofactors were solved, several point mutations were created, and docking simulations of both CcbJ–SAM–substrate and CcbJ–SAH–product complexes were made to better characterize this enzyme. We found that CcbJ is a class I methyltransferase with an open active site, allowing a number of different substrates to be accommodated (see also *Sections 2, 5*).

The Laboratory of Genomics in *Unit #4* focuses mainly on bacteriophages. They play an important role in shaping the diversity of microbial communities and in the ecology and evolution of bacterial populations. Bacteriophages and their encoded protein products are also a reservoir of potentially useful tools for many applications in biotechnology and medicine. In particular, we have pursued genomic and proteomic studies of the bacteriophages infecting industrial bacterial strains. BFK20 is a lytic corynephage infecting *Brevibacterium flavum* CCM 251. During the past four years, we have studied its replisome composition and characterized its replication proteins. Using several experimental approaches we found that the BFK20 likely has a type 2 replication module and that the phage proteins gp41 (an SF2 helicase) and gp43 (a RepA-like protein) participate in BFK20 DNA replication together with five host proteins. gp43 appears to be a hexameric multifunctional phage replication protein with primase-polymerase, NTPase and helicase activities. We have also determined and characterized the entire genome of phiBP (47,973 bp), a temperate phage of *Paenibacillus polymyxa* CCM 7400.

Bacteriophages and their lytic proteins (endolysins) are potentially a new tool to counter the alarming rise of antibiotic resistant bacteria. We isolated and characterized a new phiBP endolysin, and found it to have a typical two-domain modular structure. We confirmed its lytic and antibacterial activity against six *P. polymyxa* strains and the honeybee pathogen *P. larvae*. The presence of its cell wall-binding domain was been found to be essential for phiBP endolysin activity, which is in contrast to the BFK20 endolysin, whose catalytic activity is clearly inhibited by its cell wall binding domain.

Similarly, the Laboratory of Prokaryotic Biology studied Lytμ1/6, an endolysin encoded by bacteriophage μ1/6 of *Streptomyces aureofaciens*. This endolysin also has the typical two-domain endolysin structure, and deletion analyses and site-directed mutagenesis indicated that its N-terminal domain is responsible for its catalytic activity. We found that this endolysin is an N-acetylmuramoyl-l-alanine amidase, which is apparently unrelated to any previously known phage endolysin or bacterial autolysin catalytic domains. The predicted cell wall binding domain at the C-terminus of this endolysin is able to bind to the surface of different streptomycete cells but cannot cause lysis by itself. We have further attempted targeted design of this endolysin to extend its antibacterial activity to Gram-negative bacteria, and to produce broad spectrum

chimeric endolysins, active against both Gram-positive and Gram-negative bacteria. The expression and purification conditions of these recombinant proteins in a soluble form have been successfully optimized, and their antimicrobial activity confirmed. The bioinformatics part of this project focused on both the prediction of domains and the phylogenetic analysis of actinophage endolysins in *Streptomyces*. Predicted endolysin sequences were found in the genomes of 47 actinophages, and seven catalytic domain families were identified in these sequences. It may be mentioned here that the bioinformatics analysis of fungal proteins involved in plant cell wall degradation, mainly members of carbohydrate esterases family 16, were also performed by this laboratory, with the aim of identifying the amino acid residues residues important for substrate recognition and degradation (see also *Sections 2, 3*).

The Laboratory of Bioinformatics (*Unit #4*) mostly focuses on building and maintaining new and unique biological databases, and on cooperating with other research groups in the field of computational genomics. It maintains *phiSITE*, a database holding data on the gene expression regulation and general genomics of bacteriophages (http://www.phisite.org/). This database presently contains detailed information on more than 700 experimentally confirmed or predicted regulatory elements from 31 bacteriophages. Its integrated visualisation tool *phiGENOME* is optimised for visualising phage genomes, especially their gene regulatory elements. *phiBIOTICS* (http://www.phibiotics.org) is another in-house phage-related database which collects information on representative enzybiotics and relevant research studies on their practical application in the field of phage therapy. The accompanying tool *phiBiScan* can reliably predict potential new enzybiotics based on their primary structure. The newest addition to our collection of original databases is *viruSITE* (http://www.virusite.org), a unique viral database which was developed to bring together high-value information on viruses compiled from various sources. *viruSITE* covers the whole virus world (currently 5170 viruses) and it is focused on viral genomes, genes and proteins. The database contains information on virus taxonomy, host range, genome features, sequential relatedness, and the properties and functions of viral genes and proteins. All entries in this database are linked to numerous information resources, making *viruSITE* a comprehensive knowledge hub for viral genomics. This lab also touches the field of theoretical biology. A mathematical model simulating the interaction between bacteriophages and their bacterial hosts was developed based on other known models describing these types of interactions, but enhanced by the ability to model the system when influenced by environmental factors such as pH and temperature. This can be used for numerous estimates of growth rate, when the pH or environmental temperature are not constant. Since the model is intended for practical applications and easy accessibility, an interactive website was developed where users can run simulations with their own parameters and easily calculate and visualise the simulation results (http://www.phisite.org/model/). This lab also cooperates with a number of other research groups in Slovakia, mainly using its skills in DNA arrays and NGS data analysis. These include the study of the silkworm *Bombyx mori* neuroendocrine system (collaboration with the Insititute of Zoology SAS) and cancer research (collaboration with the Institute of Virology SAS, the Institute of Experimental Oncology SAS, and the National Institute of Oncology and Jessenius Faculty of Medicine in Martin). The group uses its broad knowledge of advanced analysis pipelines together with its available computing infrastructure to interpret the large data sets produced by these cutting edge technologies. In addition to from its research activities, the group is also involved in extensive international collaborations (running the national EMBnet node, participating in the preliminary phase of the ELIXIR consortium foundation, and participating in the COST SeqAhead project), teaching activities at Comenius University, and training Ph.D. students and young scientists (*e.g.* the DNA arrays and NGS data analysis workshop organised in 2015).

5. Cellular and molecular biomedicine

Several of the Institute's research teams pursue answers to questions about the molecular and cellular basis of life processes and how their dysfunction results in severe diseases. At the beginning of 2014, the Laboratory of Molecular Immunology was established within *Unit #3* by Vladimír Leksa at the invitation of the Scientific board of IMB following his successful research stay in Austria where he headed the Cell Migration research group at the Molecular Immunology Unit of the Institute of Hygiene and Applied Immunology (Center for Pathophysiology, Infectiology & Immunology; Medical University of Vienna), thereby reinforcing the Institute's

position in translational biomedical research. Dr. Leksa immediately began collaborations with other units within IMB and institutes of the Slovak Academy of Sciences. His research encompasses two major themes: the pericellular proteolytic system associated with human pathologies, and the molecular mechanisms underlying immune response regulation. In the last four years, he has found, first, the evidence that the mannose 6-phosphate/insulin-like growth factor 2 receptor (M6P/IGF2R) serves as a regulator of pericellular proteolysis by mediating plasminogen uptake, and second, that this receptor controls adaptive immune responses through the transporting of Lck, a primary T-cell activation kinase (see also *Section 2*).

Also in *Unit #3*, as noted above, the Laboratory of Biochemistry and Protein Structure focuses on characterizing a number of proteins important for maintaining mitochondrial homeostasis, including the Lon protease and proteins important for stabilizing mitochondrial nucleoids. Disruption of mitochondrial homeostasis has been linked to a number of pathological conditions, including cancer, neurodegeneration, aging, and inflammation; consequently, this research should grant us a clearer understanding of the basis of these diseases. Also as noted in Section 2, this Laboratory explores the molecular basis for inherited cardiac arrhythmias associated with mutations in the human RyR2 and is presently studying how these mutations influence the structure, stability and dynamics of the N-terminal domain of this protein.

As noted earlier, the main research topic of the Laboratory of Molecular Microbiology (*Unit #5*) is septins, which are implicated in several types of cancer and in neurodegenerative disorders, including hereditary neuralgic amyotrophy, Parkinson's disease, schizophrenia and bipolar disorder. There is therefore a great need to fully understand the regulatory network of septins in healthy cells. Although there have been a number of recent developments, how specific protein-protein interactions and posttranslational modifications control septin organization are still not well understood at the molecular level. In particular, how do these interactions and modifications induce changes in septin filament polymerization and the assembly of higher-order structures *in vivo*. This lab has characterized the interaction of two proteins, Gic1 and Bni5, with septins. Gic1 stabilizes septin filaments by bridging pairs or multiple filaments, forming structures which resemble railways. Similar structures have also been observed *in vitro* in the presence of Bni5. These two proteins bridge different septin subunits in distinct stages of the cell cycle. The interplay of small GTPases, accessory proteins and protein kinases was found to be crucial for regulating the formation and dissociation of septin higher-order structures during the cell cycle. Part of this project was supported by the Humboldt Foundation (see also *Section 1*).

Finally, research in *Unit #6's* Laboratory of Neurobiology focuses on the regulation of neurotransmitter transporters, particularly those for glycine, γ-aminobutyric acid, and dopamine. Sodium/chloride-dependent neurotransmitter transporters are membrane proteins which regulate neurotransmitters in brain and in some peripheral tissues. Improper functioning of them frequently causes neurological illnesses. Knowing how to inhibit them and what their regulatory pathways are may allow medical treatments to be developed which restore their physiological balance. This lab has several major recent research achievements: (1) we found that calpain-mediated cleavage of the glycine transporter GlyT1 C-terminus is regulated by phosphorylation and physically interacts with calmodulin; (2) we identified several interaction modes of the GlyT1 C-terminal PDZ interaction motifs using a collection of PDZ binding domains from MUPP1, the largest PDZ signalling protein; (3) we discovered the interesting surfactant properties of the anti-inflammatory drug diclofenac during studies of substances potentially interfering with PDZ interactions; (4) we found a potential benzophenanthridine binding pocket on human GlyT1 using molecular docking and extensive site-directed mutagenesis.

2. Partial indicators of main activities:

2.1. Research output

2.1.1. Principal types of research output of the institute: basic research/applied research, international/regional (ratios in percentage)

basic research: 90%

applied research: 10%

international research: 90%

regional research: 10%

2.1.2 List of selected publications documenting the most important results of basic research. The total number of publications listed for the assessment period should not exceed the average number of employees with university degrees engaged in research projects. The principal research outputs (max. 5, including Digital Object Identifier - DOI) should be underlined

Principal research outputs

1. Muchova, K., Chromikova, Z., Barak, I.Control of Bacillus subtilis cell shape by RodZ.(2013) *Environ. Microbiol* **15**: 3259-3271. DOI: 10.1111/1462-2920.12200 [IF2014 6.201]
2. Pangallo, D., Buckova, M., Krakova, L., Puskarova, A., Sakova, N., Grivalský, T., Chovanova, K., Zemankova, M.Biodeterioration of epoxy resin: a microbial survey through culture-independent and culture-dependent approaches.(2015) *Environ. Microbiol* **17**: 462-479. DOI: 10.1111/1462-2920.12523 [IF2014 6.201]
3. Ambro, L., Pevala, V., Ondrovicova, G., Bellova, J., Kunova, N., Kutejova, E., Bauer, J.Mutations to a glycine loop in the catalytic site of human Lon changes its protease, peptidase and ATPase activities.(2014) *FEBS J.* **281**: 1784-1797. DOI: 10.1111/febs.12740 [IF2014 4.001]
4. Mingyar, E., Feckova, L., Novakova, R., Bekeova, C., Kormanec, J.A gamma-butyrolactone autoregulator-receptor system involved in the regulation of auricin production in Streptomyces aureofaciens CCM 3239.(2015) *Appl. Microbiol. Biotechnol.* **99**(1): 309-325. DOI: 10.1007/s00253-014-6057-0 [IF2014 3.337]
5. Janecek, S., Kuchtova, A.In silico identification of catalytic residues and domain fold of the family GH119 sharing the catalytic machinery with the alpha-amylase family GH57.(2012) *FEBS Lett.* **586**(19): 3360-3366. DOI: 10.1016/j.febslet.2012.07.020 [IF2014 3.169]

Other selected publications

6. Barak, I.Open questions about the function and evolution of bacterial Min systems.(2013) *Front Microbiol* **4**: 378. DOI: 10.3389/fmicb.2013.00378 [IF2014 3.989]
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10. Jursky, F., Baliova, M., Mihalikova, A.Molecular basis for differential glycine transporters sensitivity to sanguinarine .(2012) *Toxicol. Lett.* **212**(3): 262-267. DOI: 10.1016/j.toxlet.2012.06.004 [IF2014 3.262]

11. Ambro, L., Pevala, V., Bauer, J., Kutejova, E.The influence of ATP-dependent proteases on a variety of nucleoid-associated processes.(2012) *J. Struct. Biol.* **179**: 181-192. DOI: 10.1016/j.jsb.2012.05.018 [IF2014 3.231]

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16. Sadian, Y., Gatsogiannis, C., Patasi, C., Hofnagel, O., Goody, R.S., Farkasovsky, M., Raunser, S.The role of Cdc42 and Gic1 in the regulation of septin filament formation and dissociation.(2013) *Elife* **2**: 1-26. DOI: 10.7554/eLife.01085 [IF2014 9.322]

17. Remenar, M., Karelova, E., Harichova, J., Zamocky, M., Kamlarova, A., Ferianc, P.Isolation of previously uncultivable bacteria from a nickel contaminated soil using a diffusion-chamber-based approach.(2015) *Appl. Soil Ecol* **95**: 115-127. DOI: 10.1016/j.apsoil.2015.06.013 [IF2014 2.644]

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23. Halgasova, N., Mesarosova, I., Bukovska, G.Identification of a bifunctional primase–polymerase domain of corynephage BFK20 replication protein gp43.(2012) *Virus Res.* **163**: 454-460. DOI: 10.1016/j.virusres.2011.11.005 [IF2014 2.324]

24. Solteszova, B., Halgasova, N., Bukovska, G.Interaction between phage BFK20 helicase gp41 and its host Brevibacterium flavum primase DnaG.(2015) *Virus Res.* **196**: 150-156. DOI: 10.1016/j.virusres.2014.11.022 [IF2014 2.324]

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KUTEJOVA, Eva - KUCERA, T. - MATUSKOVA, A. - JANATA, J. Mitochondrial processing peptidase. In *Handbook of Proteolytic Enzymes*. - Oxford : Elsevier Sci, 2013, p. 1435–1442. ISBN 9780123822192.

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PINAR, G. - ETTENAUER, J.D. - STERFLINGER, K. - PIOMBINO-MASCALI, D. - MAIXNER, F. - ZINK, A. - KRAKOVA, Lucia - PANGALLO, Domenico. Microbiological and molecular investigation in the Capuchin Catacombs of Palermo, Italy: Microbial deterioration risk and contamination of the indoor air. In *Science and technology for the conservation of cultural heritage*. - London : Taylor & Francis Group, 2013, p. 87–91. ISBN 978-1-138-00009-4.

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URBÁNIKOVÁ, Ľubica. Kryštalografia proteínov - význam a využitie štruktúr. In DANIELA UHRÍKOVÁ A KOL. *Biofyzika - Vybrané kapitoly : Učebnica pre vysoké školy*. Bratislava : Univerzita Komenského, Bratislavae, 2015, s. 145–174. ISBN 978-80-223-3800-4.

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BAUEROVÁ, Vladena - BAUER, Jacob - KABÁT, Peter. *Úvod do štruktúry proteinov* [elektronický zdroj]. 1. vyd. Bratislava : Veda, 2012. CD-ROM (120 s.). Názov z CD-ROM. ISBN 978-80224-1226-1.

2.1.5. List of other scientific outputs specifically important for the institute, max. 10 items

1. 7 new 3D protein structures deposited and published in PDB database during assessment period (4GHO, 4HGY, 4HGZ, 4HH4, 4J5G, 4J5K, 4JKQ)

2. Biological databases developed and maintained at the institute:
   - phiSITE, Database of Gene Regulation in Bacteriophages (http://www.phisite.org)
   - phiBIOTICS, Catalogue of Therapeutic Enzybiotics (http://www.phibiotics.org)
   - viruSITE, Integrated Database for Viral Genomics (http://www.virusite.org)

2.1.6. List of patents, patent applications, and other intellectual property rights registered abroad, incl. revenues

None

2.1.7. List of patents, patent applications, and other intellectual property rights registered in Slovakia, incl. revenues

None

2.1.8. Table of research outputs (as in annual reports).

Papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) have to be listed separately.

Scientific publications	2012			2013			2014			2015			total			
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	averaged number per year	av. No. / FTE	av. No. / salary budget
Scientific monographs and monographic studies in journals and proceedings published abroad *(AAA, ABA)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Scientific monographs and monographic studies in journals and proceedings published in Slovakia *(AAB, ABB)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Chapters in scientific monographs published abroad *(ABC)*	0.0	0.000	0.000	3.0	0.051	0.005	0.0	0.000	0.000	1.0	0.018	0.002	**4.0**	**1.0**	**0.018**	**0.002**
Chapters in scientific monographs published in Slovakia *(ABD)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Scientific papers published in journals registered in Current Contents Connect *(ADCA, ADCB, ADDA, ADDB)*	29.0	0.512	0.046	29.0	0.494	0.044	28.0	0.497	0.045	24.0	0.437	0.037	**110.0**	**27.5**	**0.486**	**0.043**
Scientific papers published in journals registered in Web of Science Core Collection and SCOPUS *(ADMA, ADMB, ADNA, ADNB)*	3.0	0.053	0.005	11.0	0.187	0.017	3.0	0.053	0.005	2.0	0.036	0.003	**19.0**	**4.8**	**0.084**	**0.007**
Scientific papers published in other foreign journals (not listed above) *(ADEA, ADEB)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Scientific papers published in other domestic journals (not listed above) *(ADFA, ADFB)*	0.0	0.000	0.000	1.0	0.017	0.002	1.0	0.018	0.002	0.0	0.000	0.000	**2.0**	**0.5**	**0.009**	**0.001**
Scientific papers published in foreign peer-reviewed proceedings *(AEC, AECA)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Scientific papers published in domestic peer-reviewed proceedings *(AED, AEDA)*	3.0	0.053	0.005	7.0	0.119	0.011	6.0	0.107	0.010	3.0	0.055	0.005	**19.0**	**4.8**	**0.084**	**0.007**
Published papers (full text) from foreign and international scientific conferences *(AFA, AFC, AFBA, AFDA)*	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	0.0	0.000	0.000	**0.0**	**0.0**	**0.000**	**0.000**
Published papers (full text) from domestic scientific conferences *(AFB, AFD, AFBB, AFDB)*	0.0	0.000	0.000	1.0	0.017	0.002	0.0	0.000	0.000	0.0	0.000	0.000	**1.0**	**0.3**	**0.004**	**0.000**

- **Supplementary information and/or comments on the scientific outputs of the institute.**

During the most recent assessment period (covering four years), 126 research papers (32 per year) were published in journals indexed by World of Science (WoS) or SCOPUS which had an average impact factor of 2.897; in the previous assessment period (which covered five years), the numbers were 142 publications (28 papers per year) in indexed journals with an average impact factor of 3.102. We have slightly increased number of publications produced per year while maintaining a moderately high IF. Most of the Institute's research is carried out using microbial model organisms (*e.g. B. subtilis*, *Streptomyces*, bacteriophages), and, consequently, the overwhelming majority of its publications appear in journals specializing in *Microbiology.* The most recent WoS median IF for this field is 2.483; the WoS median IF for, *Biochemistry and Molecular Biology*, our other main area, is 2.653.

2.2. Responses to the research outputs (citations, etc.)

2.2.1. Table with citations per annum.

Citations of papers from international collaborations in large-scale scientific projects (Dwarf team, ALICE Collaboration, ATLAS collaboration, CD Collaboration, H1 Collaboration, HADES Collaboration, and STAR Collaboration) have to be listed separately.

Citations, reviews	2011		2012		2013		2014		total		
	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	No. / FTE	number	averaged number per year	av. No. / FTE
Citations in Web of Science Core Collection (1.1, 2.1)	755.0	13.342	887.0	15.113	875.0	15.533	870.0	15.859	**3387.0**	**846.8**	**14.956**
Citations in SCOPUS (1.2, 2.2) if not listed above	57.0	1.007	75.0	1.278	67.0	1.189	105.0	1.914	**304.0**	**76.0**	**1.342**
Citations in other citation indexes and databases (not listed above) (3.2,4.2,9,10)	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	**0.0**	**0.0**	**0.000**
Other citations (not listed above) (3, 4, 3.1, 4.1)	2.0	0.035	0.0	0.000	1.0	0.018	3.0	0.055	**6.0**	**1.5**	**0.026**
Reviews (5,6)	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	**0.0**	**0.0**	**0.000**

2.2.2. List of 10 most-cited publications, with number of citations, in the assessment period (2011 – 2014).

1. (274 citations)
   Weinstock, G.M., The Honeybee Genome Sequencing Consortium (Members), Bilikova, K., Simuth, J. et al. (2006) Insights into social insects from the genome of the honeybee Apis mellifera. *Nature* **443**(7114): 931–947. doi: 10.1038/nature05260
2. (101 citations)
   MacGregor, E.A., Janecek, S., Svensson, B. (2001) Relationship of sequence and structure to specificity in the alpha-amylase family of enzymes. *Biochim. Biophys. Acta* **1546**(1): 1–20. doi: 10.1016/S0167-4838(00)00302-2
3. (89 citations)
   Sirajuddin, M., Farkasovsky, M., Hauer, F., Kuhlmann, D., Macara, I.G., Weyand, M., Stark, H., Wittinghofer, A. (2007) Structural insight into filament formation by mammalian septins. *Nature* **449**(7160): 311–315. doi: 10.1038/nature06052
4. (88 citations)
   Zamocky, M., Furtmuller, P.G., Obinger, C. (2008) Evolution of Catalases from Bacteria to Humans. *Antioxid. Redox Signal.* **10**(9): 1527–1547. doi: 10.1089/ars.2008.2046
5. (61 citations)
   Bischoff, M., Dunman, P., Kormanec, J., Macapagal, D., Murphy, E., Mounts, W., Berger-Bächi, B., Projan, S. (2004) Microarray-based analysis of the *Staphylococcus aureus* sigmaB regulon. *J. Bacteriol.* **186**(13): 4085–4099. doi: 10.1128/JB.186.13.4085-4099.2004
6. (51 citations)
   Minarik, P., Tomaskova, N., Kollarova, M., Antalík, M. (2002) Malate Dehydrogenases - Structure and Function. *Gen. Physiol. Biophys.* **21**(3): 257–265. PMID: 12537350
7. (50 citations)
   Rowley, G., Spector, M., Kormanec, J., Roberts, M. (2006) Pushing the envelope: extracytoplasmic stress responses in bacterial pathogens. *Nat. Rev. Microbiol.* **4**(5): 383–394. doi: 10.1038/nrmicro1394
8. (43 citations)
   Passardi, F., Theiler, G., Zamocky, M., Cosio, C., Rouhier, N., Teixera, F., Margis-Pinheiro, M., Ioannidis, V., Penel, C., Falquet, L., Dunand, C. (2007) PeroxiBase: The peroxidase database. *Phytochemistry* **68**(12): 1605–1611. doi: 10.1016/j.phytochem.2007.04.005
9. (41 cittions)
   Leveque, E., Janecek, S., Haye, B., Belarbi, A. (2000) Thermophilic archaeal amylolytic enzymes. *Enzyme Microb. Technol.* **26**(1): 3–14. doi: 10.1016/S0141-0229(99)00142-8
10. (39 citations)
    Vlasits, J., Jakopitsch, C., Bernroitner, M., Zamocky, M., Furtmuller, P.G., Obinger, C. (2010) Mechanisms of catalase activity of heme peroxidases. *Arch. Biochem. Biophys.* **500**(1): 74–81. doi: 10.1016/j.abb.2010.04.018

Note:

Number of citations excludes auto-citations.

2.2.3. List of most-cited authors from the Institute (at most 10 % of the research employees with university degree engaged in research projects) and their number of citations in the assessment period (2011– 2014).

1. Štefan Janeček (628 citations)
2. Ján Kormanec (549 citations)
3. Marcel Zámocký (403 citations)
4. Imrich Barák (342 citations)
5. Katarína Bíliková (338 citations)

Note:

Number of citations includes only works where the IMB SAS affiliation is given and excludes auto-citations.

- **Supplementary information and/or comments on responses to the scientific output of the institute.**

During the present assessment period the number of WoS citations increased from 2693 (539 per year) to 3387 (847 per year), which clearly indicates that recent publications are of higher quality. This also shows that the Institute's policy of publishing fewer but better articles in higher impact journals elicits a higher response from the scientific community. *(Citations from SCOPUS and other sources were not examined in the previous assessment.)*

2.3. Research status of the institute in international and national contexts

- **International/European position of the institute**

2.3.1. List of the most important research activities demonstrating the international relevance of the research performed by the institute, incl. major projects (details of projects should be supplied under Indicator 2.4). Max. 10 items.

1. The institute is a member of STREPSYNTH, a consortium for modifying the Streptomyces cell factory for the cost-effective production of biomolecules (7RP 613877)
2. The Institute was a member of the European Consortium on the genomics, proteomics and physiomics of the honeybee (6RP 37592, 7RP EU 244956)
3. The Institute hosts the Slovak National EMBnet node (http://www.embnet.sk)
4. The institute collaborates closely with the European XFEL (X-ray Free Electron Laser) in Hamburg, Germany.
5. The institute is a member of a consortium studying the role of metal homeostasis, metal reduction and sporulation in the metal resistance of Gram-positive bacteria (Scopes – Swiss Science Foundation IZ73Z0_152 527/1)
6. The Institute was a partner in the COST Action BM1006 "Next Generation Sequencing Data Analysis Network".
7. The Institute is a partner in the COST Action CM1306 "Understanding Movement and Mechanism in Molecular Machines".
8. The Institute is a member of BACELL, a platform organisation supporting Bacillus research in Europe
9. The Institute is a partner in the ESFRI programme INSTRUCT (Integrated structural biology unlocking the secrets of life), and it participated in the preliminary phase of ELIXIR (a pan-European research infrastructure for biological information).

2.3.2. List of international conferences (co)organised by the institute.

ALAMY_5 – The 5th Symposium on the Alpha-Amylase Family
20–24 October 2013, Smolenice Castle, Slovakia
Organized by: Štefan Janeček
http://imb.savba.sk/~janecek/Alamys/Alamy_5/

Bacell 2014
29–30 April 2014, Bratislava, Slovakia
Organized by: Imrich Barák

Closing COST Conference "Next Generation Sequencing: a look into the future" (COST Action BM1006 Next Generation Sequencing Data Analysis Network)
16–17 March 2015, Sheraton Hotel Bratislava, Slovakia
Organized by: Ľuboš Kľučár
http://seqahead.eu/bratislava_2015

2.3.3. List of edited proceedings from international scientific conferences.

Next Generation Sequencing: a look into the future. Final Conference & MC Meeting of COST Action BM1006.16–17 March 2015, Bratislava, Slovakia. *EMBnet.journal* **21** (Suppl. A), 2015.

2.3.4. List of journals edited/published by the institute:

2.3.4.1. WOS (IF of journals in each year of the assessment period)

Biologia (section Cellular and Molecular Biology)

Indexed in WOS, SCOPUS and other databases.

http://www.degruyter.com/view/j/biolog

IF2012 = 0.506

IF2013 = 0.696

IF2014 = 0.827

IF2015 = 0.719

2.3.4.2. SCOPUS

2.3.4.3. other databases

2.3.4.4. not included in databases

- **National position of the institute**

2.3.5. List of selected projects of national importance

1. New microbial isolates containig genes of catabolic and detoxication pathways and their use in biotechnology
   Grant agency: ASFEU
   Grant registration number: 26240220010
   Duration: 09/2009 – 02/2013
   Total Funding: 479 302 EUR
   Funding for IMB SAS: 328 605 EUR
   Responsible person at IMB SAS: Bystrík Polek - Coordinator
   Number of cooperating institutions: 2

2. Prionoses transmissible to humans: Research and development of cell model, with potential use in the application sphere
   Grant agency: ASFEU
   Grant registration number: 26240220025
   Duration: 10/2009 – 09/2012
   Total Funding: 494 082 EUR
   Funding for IMB SAS: 103 652 EUR
   Responsible person at IMB SAS: Imrich Barák
   Coordinator: Michal Novák, Institute of Neuroimunology SAS, Bratislava

Number of cooperating institutions: 2

3. Development of the diagnostic methods for the detection of tick-borne pathogens and the techniques for the preparation of the vaccine development directed against ticks
   Grant agency: ASFEU
   Grant registration number: 26240220044
   Duration: 11/2010 – 10/2013
   Total Funding: 939 915 EUR
   Funding for IMB SAS: 258 800 EUR
   Responsible person at IMB SAS: Imrich Barák - Principal investigator
   Coordinator: Dušan Žitňan, Institute of Zoology SAS
   Number of cooperating institutions: 3

4. Centre of Excellence for the use of information biomacromolecules in the prevention of diseases and for improving quality of life
   Grant agency: ASFEU
   Grant registration number: 26240120027
   Duration: 03/2010 – 03/2013
   Total Funding: 2 788 317 EUR
   Funding for IMB SAS: 0 EUR
   Responsible person at IMB SAS: Andrej Godány
   Coordinator: Marta Kollárová, Comenius University, Bratislava
   Number of cooperating institutions: 6

5. Centre of excellence for translation research in molecular medicine
   Grant agency: ASFEU
   Grant registration number: 26240120030
   Duration: 06/2010 – 05/2012
   Total Funding: 2 649 697 EUR
   Funding for IMB SAS: 10 956 EUR
   Responsible person at IMB SAS: Ján Kormanec
   Coordinator: Juraj Kopáček, Institute of Virology SAS, Bratislava
   Number of cooperating institutions: 7

6. Excellence centre for Glycomics
   Grant agency: ASFEU
   Grant registration number: 26240120031
   Duration: 11/2010 – 10/2013
   Total Funding: 3 977 975 EUR
   Funding for IMB SAS: 154 000 EUR
   Responsible person at IMB SAS: Juraj Gašperík
   Coordinator: Ján Mucha, Institute of Chemistry SAS, Bratislava
   Number of cooperating institutions: 7

7. Establishment of Competence center for research and development in molecular medicine
   Grant agency: ASFEU
   Grant registration number: ITMS 26240220071
   Duration: 10/2011 – 11/2014
   Total Funding: 6 774 791 EUR
   Funding for IMB SAS: 75 998 EUR
   Responsible person at IMB SAS: Ľubica Urbániková - Project manager
   Coordinator: Ján Turňa, Comenius University Bratislava
   Number of cooperating institutions including SR: 12

8. Lipid domains in cell division and programmed cell death in Bacillus subtilis
   Grant agency: APVV
   Registration number: APVV-00335-10

Duration: 05/2011 – 10/2014
Funding: 163 279 EUR
Principal investigator: Imrich Barák

9. Molecular mechanisms of biosynthesis, regulation, and horizontal transfer of genes responsible for production of biologically active compounds in streptomycetes
   Grant agency: APVV
   Registration number: APVV-0203-11
   Duration: 07/2012 – 12/2015
   Funding: 139 500 EUR
   Principal investigator: Ján Kormanec

10. Structural and functional characterization of human ryanodine receptor regulation and its malfunction caused by mutations
    Grant agency: APVV
    Registration number: APVV-0628-10
    Duration: 05/2011 – 10/2014
    Funding: 249 255 EUR
    Principal investigator: Jozef Ševčík

11. Assembly of protein complexes during asymmetric cell division in sporulating cells of Bacillus subtilis
    Grant agency: APVV
    Registration number: APVV-14-0181
    Duration: 07/2015 – 06/2019
    Funding: 148 475 EUR
    Principal investigator: Imrich Barák

12. Bioinformatics analysis of amylases
    Grant agency: APVV
    Registration number: LPP-0417-09
    Duration: 09/2009 – 08/2013
    Funding: 74 940 EUR
    Principal investigator: Štefan Janeček

13. New bacteriophages and phage proteins for pathogen devitalization in foods prepared by synthetic biology approach
    Grant agency: APVV
    Registration number: APVV-0098-10
    Duration: 05/2011 – 10/2014
    Funding: 90 559 EUR
    Principal investigator: Gabriela Bukovská
    Coordinator: Hana Drahovská, Faculty of Natural Sciences, Comenius University, Bratislava

14. Molecular architecture, dynamics and evolution of chromosomes in yeast mitochondria
    Grant agency: APVV
    Registration number: APVV-0123-10
    Duration: 05/2011 – 10/2014
    Funding: 80 000 EUR
    Principal investigator: Eva Kutejová
    Coordinator: Jozef Nosek, Faculty of Natural Sciences, Comenius University, Bratislava

15. Characterization of bacterial communities of Slovakian wine by molecular-biological methods
    Grant agency: APVV
    Registration number: APVV-0344-12

Duration: 10/2013 – 09/2016
Funding: 75 000 EUR
Principal investigator: Domenico Pangallo
Coordinator: Ľubica Piknová, Food Research Institute, Bratislava

16. Structure, properties and biotechnological potential of novel microbial enzymes degrading plant biomass
Grant agency: APVV
Registration number: APVV-0602-12
Duration: 10/2013 – 09/2016
Funding: 58 750 EUR
Principal investigator: Ľubica Urbániková
Coordinator: Vladimír Puchart, Institute of Chemistry SAS, Bratislava

17. Synthetic biology and production of peroxidases de novo
Grant agency: APVV
Registration number: APVV-14-0375
Duration: 07/2015 – 06/2019
Funding: 99 393 EUR
Principal investigator: Marcel Zámocký
Coordinator: Ján Turňa, Faculty of Natural Sciences, Comenius University, Bratislava

18. Complex regulation of the stress response, cell differentiation and pathogenicity in bacteria by sigma factors of RNA polymerase and their regulators
Grant agency: VEGA
Registration number: 2/0028/12
Duration: 01/2012 – 12/2015
Funding: 50 614 EUR
Principal investigator: Ján Kormanec

19. Structure and function of proteins involved in regulation of basic cell processes in Bacillus subtilis
Grant agency: VEGA
Registration number: 2/0009/13
Duration: 01/2013 – 12/2016
Funding: 47 793 EUR
Principal investigator: Imrich Barák

20. The study of replication module of corynephage BFK20
Grant agency: VEGA
Registration number: 2/0110/11
Duration: 01/2011 – 12/2013
Funding: 29 245 EUR
Principal investigator: Gabriela Bukovská

2.3.6. Projects of the Slovak Research and Development Agency (APVV)

1. Lipid domains in cell division and programmed cell death in Bacillus subtilis
Grant agency: APVV
Registration number: APVV-00335-10
Duration: 05/2011 – 10/2014
Funding: 163 279 EUR
Principal investigator: Imrich Barák

2. Molecular mechanisms of biosynthesis, regulation, and horizontal transfer of genes responsible for production of biologically active compounds in streptomycetes
Grant agency: APVV
Registration number: APVV-0203-11

Duration: 07/2012 – 12/2015
Funding: 139 500 EUR
Principal investigator: Ján Kormanec

3. Structural and functional characterization of human ryanodine receptor regulation and its malfunction caused by mutations
   Grant agency: APVV
   Registration number: APVV-0628-10
   Duration: 05/2011 – 10/2014
   Funding: 249 255 EUR
   Principal investigator: Jozef Ševčík

4. Assembly of protein complexes during asymmetric cell division in sporulating cells of Bacillus subtilis
   Grant agency: APVV
   Registration number: APVV-14-0181
   Duration: 07/2015 – 06/2019
   Funding: 148 475 EUR
   Principal investigator: Imrich Barák

5. Bioinformatics analysis of amylases
   Grant agency: APVV
   Registration number: LPP-0417-09
   Duration: 09/2009 – 08/2013
   Funding: 74 940 EUR
   Principal investigator: Štefan Janeček

6. New bacteriophages and phage proteins for pathogen devitalization in foods prepared by synthetic biology approach
   Grant agency: APVV
   Registration number: APVV-0098-10
   Duration: 05/2011 – 10/2014
   Funding: 90 559 EUR
   Principal investigator: Gabriela Bukovská
   Coordinator: Hana Drahovská, Faculty of Natural Sciences, Comenius University, Bratislava

7. Molecular architecture, dynamics and evolution of chromosomes in yeast mitochondria
   Grant agency: APVV
   Registration number: APVV-0123-10
   Duration: 05/2011 – 10/2014
   Funding: 80 000 EUR
   Principal investigator: Eva Kutejová
   Coordinator: Jozef Nosek, Faculty of Natural Sciences, Comenius University, Bratislava

8. Characterization of bacterial communities of Slovakian wine by molecular-biological methods
   Grant agency: APVV
   Registration number: APVV-0344-12
   Duration: 10/2013 – 09/2016
   Funding: 75 000 EUR
   Principal investigator: Domenico Pangallo
   Coordinator: Ľubica Piknová, Food Research Institute, Bratislava

9. Structure, properties and biotechnological potential of novel microbial enzymes degrading plant biomass
   Grant agency: APVV

Registration number: APVV-0602-12
Duration: 10/2013 – 09/2016
Funding: 58 750 EUR
Principal investigator: Ľubica Urbániková
Coordinator: Vladimír Puchart, Institute of Chemistry SAS, Bratislava

10. Synthetic biology and production of peroxidases de novo
Grant agency: APVV
Registration number: APVV-14-0375
Duration: 07/2015 – 06/2019
Funding: 99 393 EUR
Principal investigator: Marcel Zámocký
Coordinator: Ján Turňa, Faculty of Natural Sciences, Comenius University, Bratislava

2.3.7. Projects of the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA)

1. Complex regulation of the stress response, cell differentiation and pathogenicity in bacteria by sigma factors of RNA polymerase and their regulators
Grant agency: VEGA
Registration number: 2/0028/12
Duration: 01/2012 – 12/2015
Funding: 50 614 EUR
Principal investigator: Ján Kormanec

2. Structure and function of proteins involved in regulation of basic cell processes in Bacillus subtilis
Grant agency: VEGA
Registration number: 2/0009/13
Duration: 01/2013 – 12/2016
Funding: 47 793 EUR
Principal investigator: Imrich Barák

3. The study of replication module of corynephage BFK20
Grant agency: VEGA
Registration number: 2/0110/11
Duration: 01/2011 – 12/2013
Funding: 29 245 EUR
Principal investigator: Gabriela Bukovská

4. Protecting our memories: investigation into the biodeterioration of photographic and cinematographic materials
Grant agency: VEGA
Registration number: 2/0103/14
Duration: 01/2014 – 12/2016
Funding: 28 861 EUR
Principal investigator: Domenico Pangallo

5. Protein complexes in mitochondrial nucleoid
Grant agency: VEGA
Registration number: 2/0122/11
Duration: 01/2011 – 12/2013
Funding: 27 449 EUR
Principal investigator: Eva Kutejová

6. Bioinformatics studying of amylases as a base for their protein design
Grant agency: VEGA
Registration number: 2/0148/11

Duration: 01/2011 – 12/2013
Funding: 25 441 EUR
Principal investigator: Štefan Janeček

7. Characterization of functional domains of the endolysin Lytμ1/6 encoded by the Streptomyces aureofaciens phage μ1/6
   Grant agency: VEGA
   Registration number: 2/01490/11
   Duration: 01/2011 – 12/2013
   Funding: 25 497 EUR
   Principal investigator: Andrej Godány

8. Septin filaments structural changes during eukaryotic cell cycle
   Grant agency: VEGA
   Registration number: 2/0050/11
   Duration: 01/2011 – 12/2014
   Funding: 24 253 EUR
   Principal investigator: Marián Farkašovský

9. Inhibition of neurotransmitter transporters by benzophenanthridine alkaloids
   Grant agency: VEGA
   Registration number: 2/0084/13
   Duration: 01/2013 – 12/2016
   Funding: 20 576 EUR
   Principal investigator: František Jurský

10. Proteolytic system on the surface of apoptotic cells as a component of the inflammatory microenvironment
    Grant agency: VEGA
    Registration number: 2/0063/14
    Duration: 01/2014 – 12/2016
    Funding: 17 321 EUR
    Principal investigator: Vladimír Leksa

11. Integrated phage database portal
    Grant agency: VEGA
    Registration number: 2/0188/13
    Duration: 01/2013 – 12/2015
    Funding: 16 587 EUR
    Principal investigator: Ľuboš Kľučár

12. Difficult to cultivate and previously uncultured bacterial isolates in toxic metal contaminated soils: Isolation, „domestification“, characterisation and functions
    Grant agency: VEGA
    Registration number: 2/0094/13
    Duration: 01/2013 – 12/2015
    Funding: 16 185 EUR
    Principal investigator: Peter Ferianc

2.3.8. Projects of SAS Centres of Excellence

None

2.3.9. National projects supported by EU Structural Funds

1. New microbial isolates containig genes of catabolic and detoxication pathways and their use in biotechnology
   Grant agency: ASFEU
   Grant registration number: 26240220010

Duration: 09/2009 – 02/2013
Total Funding: 479 302 EUR
Funding for IMB SAS: 328 605 EUR
Responsible person at IMB SAS: Bystrík Polek - Coordinator
Number of cooperating institutions: 2

2. Prionoses transmissible to humans: Research and development of cell model, with potential use in the application sphere
Grant agency: ASFEU
Grant registration number: 26240220025
Duration: 10/2009 – 09/2012
Total Funding: 494 082 EUR
Funding for IMB SAS: 103 652 EUR
Responsible person at IMB SAS: Imrich Barák
Coordinator: Michal Novák, Institute of Neuroimunology SAS, Bratislava
Number of cooperating institutions: 2

3. Development of the diagnostic methods for the detection of tick-borne pathogens and the techniques for the preparation of the vaccine development directed against ticks
Grant agency: ASFEU
Grant registration number: 26240220044
Duration: 11/2010 – 10/2013
Total Funding: 939 915 EUR
Funding for IMB SAS: 258 800 EUR
Responsible person at IMB SAS: Imrich Barák - Principal investigator
Coordinator: Dušan Žitňan, Institute of Zoology SAS
Number of cooperating institutions: 3

4. Centre of Excellence for the use of information biomacromolecules in the prevention of diseases and for improving quality of life
Grant agency: ASFEU
Grant registration number: 26240120027
Duration: 03/2010 – 03/2013
Total Funding: 2 788 317 EUR
Funding for IMB SAS: 0 EUR
Responsible person at IMB SAS: Andrej Godány
Coordinator: Marta Kollárová, Comenius University, Bratislava
Number of cooperating institutions: 6

5. Centre of excellence for translation research in molecular medicine
Grant agency: ASFEU
Grant registration number: 26240120030
Duration: 06/2010 – 05/2012
Total Funding: 2 649 697 EUR
Funding for IMB SAS: 10 956 EUR
Responsible person at IMB SAS: Ján Kormanec
Coordinator: Juraj Kopáček, Institute of Virology SAS, Bratislava
Number of cooperating institutions: 7

6. Excellence centre for Glycomics
Grant agency: ASFEU
Grant registration number: 26240120031
Duration: 11/2010 – 10/2013
Total Funding: 3 977 975 EUR
Funding for IMB SAS: 154 000 EUR
Responsible person at IMB SAS: Juraj Gašperík
Coordinator: Ján Mucha, Institute of Chemistry SAS, Bratislava
Number of cooperating institutions: 7

7. Establishment of Competence center for research and development in molecular medicine
   Grant agency: ASFEU
   Grant registration number: ITMS 26240220071
   Duration: 10/2011 – 11/2014
   Total Funding: 6 774 791 EUR
   Funding for IMB SAS: 75 998 EUR
   Responsible person at IMB SAS: Ľubica Urbániková - Project manager
   Coordinator: Ján Turňa, Comenius University Bratislava
   Number of cooperating institutions including SR: 12

2.3.10. List of journals (published only in the Slovak language) edited/published by the institute:

2.3.10.1. WOS (IF of journals in each year of the assessment period)

2.3.10.2. SCOPUS

2.3.10.3. Other databases

2.3.10.4. Not included in databases

- **Position of individual researchers in an international context**

2.3.11. List of invited/keynote presentations at international conferences, as documented by programme or invitation letter

2012

1. Urbániková, Ľ.: Protein as the main variable in crystallization. *FEBS Practical Course, Advanced methods in macromolecular crystallization V*, Nové Hrady, Czech Republic, 22–29 Jun 2012. (invited lecture)
2. Urbániková, Ľ.: Crystallization of own proteins using commercial screening kits. *FEBS Practical Course, Advanced methods in macromolecular crystallization V*, Nové Hrady, Czech Republic, 22–29 Jun 2012. (invited lecture)

2013

1. Ambro, Ľ., Pevala, V., Bauer, J., Ondrovičová, G., Kutejová, E.: Mutation in proteolytic site of human mitochondrial Lon protease uncover the direct connection between proteolytic and ATPase domain. *8th International conference: Structure and Stability of Biomacromolecules*, Kosice, Slovakia, 10–13 Sep 2013. (invited lecture)
2. Janeček, S.: Families, subfamilies and clans of alpha-amylase and its relatedness to other starch hydrolases. *International Conference on Advances in Biotechnology & Bioinformatics*, Pune, India, 25–27 Nov 2013. (keynote lecture)
3. Janeček, S.: Sequence-specificity fingerprints of amylolytic enzymes from families GH13 and GH57. *Enzymatic and sustainable biomass valorisation*, Lund, Sweeden, 11–12 Dec 2013. (invited lecture)
4. Kormanec, J., Nováková, R., Fecková, Ľ., Rehaková, A., Mingyár, E., Homerová, D., Řežuchová, B., Sevčíková, B.: Complex regulation of the gene cluster aur1 for the angucycline antibiotic auricin in Streptomyces aureofaciens CCM3239. *First China-Europe Symposium: The biology of Actinomycete Antibiotic Production*, Beijing, China, 9–10 Apr 2013. (invited lecture)
5. Urbániková, Ľ., Vidová, B., Godány, A., Biely, P.: The Study of CE16 Acetyl Esterase from Fungus Hypocrea jecorina. *8th International conference: Structure and Stability of Biomacromolecules*, Kosice, Slovakia, 10–13 Sep 2013. (invited lecture)

2014

1. Barák, I., Muchová, K., Chromiková, Z., Makroczyová, J., Jamroškovič, J., Pavlendová, N.: Divisome and elongasome in Bacillus subtilis. *XXIV. Biochemický zjazd*, Bratislava, Slovakia, 18–21 Sep 2014. (invited lecture)
2. Urbániková, Ľ.: Protein as the main variable in crystallization. *1st FEBS-INSTRUCT crystallization course – Advanced methods in macromolecular crystallization VI*, Nove Hrady, Czech Republic, 20–27 Jun 2014. (invited lecture)
3. Urbániková, Ľ., Mesters, J.: Crystallization of own proteins using commercial screening kits. *1st FEBS-INSTRUCT crystallization course – Advanced methods in macromolecular crystallization VI*, Nove Hrady, Czech Republic, 20–27 Jun 2014. (invited lecture)

2015

1. Barák, I., Muchová, K., Chromiková, Z., Wilkinson, A.J., Valenčíková, R.: The polar septum – how to set up asymmetry during sporulation in Bacilli and Clostridia. *FEMS 2015 6th Congress of European Microbiologists*, Maastricht, The Netherlands, 5–12 Jun 2015. (invited lecture)
2. Bauerová-Hlinková, V., Borko, Ľ., Košťan, J., Hostinová, E., Gašperík, J., Zahradníková, A., Ševčík, J.: Human Cardiac Ryanodine Receptor2 – a Journey From DNA to Protein Structure.. *9th Internationa Conference Structure and Stability of Biomacromolecules*, Kosice, Slovakia, 30 Jun – 3 Jul 2015. (invited lecture)
3. Janeček, S.: Alpha-amylases from Archaea – sequences, structures and evolution. *Satellite Workshop to the CBM11 in Helsinki*, Kgs. Lyngby, Denmark, 8 May 2015. (invited lecture)
4. Janeček, S.: In silico study of enzymes involved in the metabolism of starch and glycogen in microorganisms, plants and animals. *New Horizons in Biotechnology – NHBT_2015*, Trivandrum, India, 22–25 Nov 2015. (invited lecture)
5. Pevala, V., Fricová, D., Kunová, N., Košťan, J., Bellová, J., Tomáška, Ľ., Bauer, J., Krejčí, L., Nosek, J., Kutejová, E.: The structure and DNA-binding properties of Mgm101 from a yeast *Candida parapsilosis* with a linear mitochondrial genome. *ISF Workshop on MITOCHONDRIA: Function and Dysfunction*, Kibbutz Ein-Gedi, Israel, 15–18 Feb 2015. (invited lecture)

2.3.12. List of researchers who served as members of the organising and/or programme committees

2012

1. I. Barák, 5th European Spores Conference, Royal Holloway, University of London, Egham, UK. (*organising and programme committees*)

2013

1. A. Godány, The 4th International Scientific Conference, Applied Natural Sciences 2013. Nový Smokovec, Slovakia. (*programme committee*)
2. Ľ. Kľučár, Human-Computer Interaction & Knowledge Discovery @ CD-ARES 2013, Regensburg, Germany (*programme committee*)
3. E. Kutejová, 30th International Specialized Symposium on Yeast: Cell Surface & Organelles in Yeasts, Stará Lesná, Slovakia. (*organising committee*)

2014

1. I. Barák, 6th European Spores Conference, Royal Holloway, University of London, Egham, UK. (*organising and programme committees*)
2. I. Barák, Bacell 2014 Conference, Bratislava, Slovakia. (*organising and programme committees*)
3. Ľ. Kľučár, USAB 2014, Vienna, Austria. (*programme committee*)

2015

1. Š. Janeček, New Horizons in Biotechnology. Trivandrum, India. (*organising ommittee*)
2. Ľ. Kľučár, COST Conference "Next Generation Sequencing: a look into the future", Bratislava, Slovakia. (*organising and programme committees*)

- **Position of individual researchers in a national context**

2.3.13. List of invited/keynote presentations at national conferences, as documented by programme or invitation letter

2012

1. Šimuth, J., Bíliková, K.: Na ceste k poznaniu chemického kódu dorozumievania sa vo včelstve. *XVI. Lekársky kongres naturálnej medicíny s interdisciplinárnou účasťou*, Nitra, Slovakia, 19–21 Oct 2012. (invited lecture)

2013

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2014

1. Barák, I.: Structure of proteins involved in Bacillus subtilis life cycle. *3rd Winter School of Synchrotron Radiation*, Liptovský Ján, Slovakia, 10–12 Feb 2014. (invited lecture)
2. Leksa, V.: Convergences and divergences in cellular proteolysis is controlled by the mannose 6-phosphatase/insulin-like growth factor 2 receptor (CD222). *Naše proteíny 2014 – Štruktúra a funkcia*, Bratislava, Slovakia, 15–16 Apr 2014. (invited lecture)
3. Leksa, V.: To the cell membrane and back again: The role of protein trafficking in adaptive and innate immunity. *Kuželove semináre, #96*, Bratislava, Slovakia, 21 Mar 2014. (invited lecture)

2015

1. Barák, I., Muchová, K., Krajčíková, D., Chromiková, Z., Jamroškovič, J., Makroczyová, J., Krascsenitsová, E., Valenčíková, R.: *Bacillus subtilis* as a model organism for protein structure studies by using X-ray Free Electron Laser. *X-ray for cellular imaging*, Nový Smokovec, Slovakia, 3–6 Nov 2015. (invited lecture)

2.3.14. List of researchers who served as members of organising and programme committees of national conferences

2012

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2013

1. Ľ. Urbániková, Naše proteíny 2013 – Štruktúra a funkcia. Bratisalva, Slovakia. (*organising and programme committees*)

2014

1. Ľ. Urbániková, 3. Konferencia o proteínoch – Naše proteíny 2014 – Štruktúra a funkcia. Bratisalva, Slovakia. (*organising and programme committees*)

2015

1. Ľ. Kľučár, Workshop DNA microarrays a NGS, Bratislava, Slovakia. (*organising and programme committees*)
2. M. Stano, Workshop DNA microarrays a NGS, Bratislava, Slovakia. (*organising and programme committees*)

- **Supplementary information and/or comments documenting the international and national status of the Institute**

Many scientists from the Institute are internationally recognized in their fields of research. They are members of international scientific boards and reviewers for several international grant agencies and international scientific journals. They have also organized several international conferences, and several have been invited to international conferences and seminars. The excellent scientific work of many individuals and groups have been recognized by prizes awarded during the assessment period, including a number of national prizes from the Slovak Academy of Sciences (SAS).

Professor Tony Wilkinson, from the Structural Biology Laboratory in the Department of Chemistry, York, UK, was awarded the International Prize of the Slovak Academy of Sciences in 2015 in recognition of his "outstanding work in the field of natural sciences." Professor Wilkinson has a long-standing collaboration with Dr. Imrich Barák that began in 1995. They have worked together on systems controlling bacterial development, addressing the chemical events that lead to a bacterial cell abandoning growth and forming a dormant spore which can survive adverse environmental conditions. A highlight of this work was the determination of the first structure of a protein phosphorylated on a carboxylate group and the proposal of a signalling mechanism for the wide-spread toxin-antitoxin two-component systems, which are widespread in nature.

In 2013 the Department of Gene Expression (*Unit #1;* headed by Dr. Ján Kormanec) was recognized as the top team in the whole Academy on the occasion of the 60th anniversary of SAS. In the same year the head of the Laboratory of Protein Evolution (Dr. Štefan Janeček; *Unit #6*) was awarded the SAS prize for international collaboration for his excellent results in international projects on the bioinformatic analysis of amylolytic enzymes. In 2014 the Department of Gene Expression was awarded "Best Project of SAS" for its work on the intriguing properties and regulation of auricin, a new angucycline antibiotic.

In 2015, several members of the Laboratory of Biochemistry and Protein Structure (*Unit #3*) with their collaborators from the Institute on Molecular Physiology and Genetics SAS were awarded "Best Project of SAS" for their structural and functional characterization of the ryanodine receptor 2 in relation to heart function. In addition two of our PhD students also received awards in 2015: Erik Mingyár was named a student personality of Slovakia by the Junior Chamber International-Slovakia, and Nina Kunová was awarded first place for her presentation by the Czech Society for Biochemistry and Molecular Biology at an international conference for young scientists.

Since 1999, the Institute has had a mandate from the Slovak government to serve as the National EMBnet Node (www.embnet.org). EMBnet, The Global

Bioinformatics Network, is a science-based group of collaborating nodes throughout the world. EMBnet's mission is to provide education and training in bioinformatics; to exploit network infrastructure to investigate, develop and deploy public domain software; and to assist biotechnology- and bioinformatics-related research, bridging commercial and academic sectors, promoting global cooperation through its community networks. The main activities of the National Node are education and international cooperation in the building of the necessary bio-computing infrastructure. It is also significantly involved in the activities of the Executive Editorial Board of *EMBnet.journal,* an international, open access, peer-reviewed journal. The Institute was involved in the planning stages of ELIXIR (European Life Sciences Infrastructure for Biological Information), a project funded by the EU under the European Strategy Forum on Research and Innovation (ESFRI), whose proposed activities are similar to those of the National Node.

2.4. Tables of project structure, research grants and other funding resources

- **International projects and funding**

2.4.1. Major projects within the European Research Area and other important project – Framework Programmes of the EU, ERA-NET, European Science Foundation, NATO, COST, INTAS, etc. (here and in items below please specify: type of project, title, grant number, duration, total funding and funding for the institute, responsible person in the institute and his/her status in the project, e.g. coordinator "C", work package leader "W", investigator "I"),

Start	Project title	Typ / Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Applied venomics of the species Conus consors for the production of innovative biomedical drugs. (01/2010-07/2012)	6RP / 37592	31	125 655[+]*	I J. Šimúth
	Bees in Europe and the decline of honeybee colonies. (03/2010-02/2013)	7RP / 244956	24	93 356[+]*	I K. Bíliková
	Integrated structural biology infrastructure. (04/2008-31/2015)	ESFRI / Instruct	93	20 700*	C J. Ševčík, E .Kutejová
2013	Rewiring the Streptomyces cell factory for cost-effective production of biomolecules. (12/2013-11/2018)	7RP / 613877	60	215 680*[#+]	I J. Kormanec
2014	Next Generation Sequencing Data Analysis Network. (03/2011-03/2015)	COST / BM1006	36	6 504*[+]	I Ľ. Kľučár
	Understanding Movement and Mechanism in Molecular Machines. (06/2014-06/2018)	COST / CM1306	48	4 000[+]	I Ľ. Urbániková
2015					

[+] EU funding

[#] national support (APVV)

* national support (MVTS)

2.4.2. Other international projects, incl. total funding and funding for the institute

1. The role of metal homeostasis, reduction and sporulation in the metal resistance of Gram-positive bacteria
   Grant agency: Scopes – Swiss Science Foundation
   Registration number: IZ73Z0_152527 / 1
   Duration: 04/2014 – 03/2017
   Funding: 75 000 CHF + 2855 EUR (MVTS)

Principal investigator: Imrich Barák
Coordinator: Rizlan Bernier-Latmani, EPFL Lausanne, Switzerland
Number of cooperating institutions including SR: 3

2. Mining the metagenome for modulators of cell and protein activities
Grant agency: Humboldt Foundation
Registration number: 3.4 - Fokoop - DEU/1133283
Duration: 07/2011 – 06/2014
Funding: 54 000 EUR
Principal investigator: Marán Farkašovský
Number of cooperating institutions including SR: 2

3. Exploring Microbial Diversity and Functionality in Thermophilic Bioreactors for Innovation in Biotechnology
Grant agency: SAS-MOST
Registration number: JRP 2014/3
Duration: 01/2015 – 12/2017
Funding: 75 000 EUR
Principal investigator: Domenico Pangallo
Number of cooperating institutions including SR: 2

4. Single-molecule in vivo imaging to study sporulation in Bacillus subtilis
Grant agency: The Royal Society
Registration number: IES - 2014/R3
Duration: 03/2015 – 02/2017
Funding: 9000 GBP
Principal investigator: Imrich Barák
Coordinator: Prof. Mark Leake, Department of Physics and Biology, University of York, York, UK
Number of cooperating institutions including SR: 2

5. Role of carotenoids in construction of photosynthetic complexes
Grant agency: International Visegrad Found
Registration number: IVF/21120109
Duration: 01/2012 – 12/2012
Funding: 1000 EUR
Principal investigator: Ľubica Urbániková
Coordinator: Zoltan Gombos, Biological Research Centre, HAS, Szeged, Hungary
Number of cooperating institutions including SR: 4

2.4.3. Other important, international projects and collaborations without direct funding (max. 10 projects)

1. Alpha-amylases and related enzymes from families GH13 and GH57
Duration: 01/2006 – 12/2015
Principal investigators:
Štefan Janeček, IMB SAS
Marc. J.E.C. van der Maare, Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, The Netherlands

2. Study of proteins involved in photosynthesis
Duration: 2007 – present
Principal investigators:
Ľubica Urbániková, IMB SAS
Csaba Bagyinka, Biological Research Centre, HAS, Szeged, Hungary

3. Sporulation and programmed cell death in model organism Bacillus subtilis
Duration: 2008 – present

Principal investigators:
Imrich Barák, IMB SAS
Tony Wilkinson, Structural Biology Laboratory, Department of Chemistry, York, UK

4. Mitochondrial processing peptidases
   Proteins of biosynthetic pathways of lincomycine and celesticetine
   Duration: 08/2008 – present
   Principal investigators:
   Eva Kutejová, IMB SAS
   Jiří Janata, Microbiological Institute, Academy of Sciences of Czech Republic, Prague, Czech Republic
   Department of Biochemistry and Structural Biology has closely cooperated with Microbiological Institute, Academy of Sciences of Czech Republic in Prague, where Dr.Kutejová has been involved in two project EU (IMPULS and Establishment of teams for The center of microbiology and immunology) as a head of the research group. Currently she is head of the research group Research of Natural Substances: Structure and Function in BOCEV (Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University in Vestec).

5. Crystallization and characterization of the proteins
   Duration: 12/2008 – present
   Principal investigators:
   Eva Kutejová, IMB SAS
   Kristina Djinovic-Carugo, Department for Structural and Computational Biology, Max F. Perutz Laboratories, Vienna, Austria

6. Structure-function study of beta-glucosidase, an enzyme involved into cytokinin regulation in plants.
   Duration: 2010 – present
   Principal investigators:
   Ľubica Urbániková, IMB SAS
   Břetislav Brzobohatý, Mendel University, Brno, Czech Republic,
   Pavel Mazura, CEITEC Masaryk University, Brno, Czech Republic

7. Bacillus subtili spore coat - study of formation and self assembling properties of spore coat proteins
   Duration :01/2010 - present
   Principal investigators:
   Daniela Krajčíková, IMB SAS
   Krebs Institute for Biomolecular Research, Department of Molecular Biology and Biotechnology, University of Sheffield, UK

8. Evolution of alpha-amylases and related enzymes
   Duration: 01/2011 – 12/2014 and 01/201 5– 12/2019
   Principal investigators:
   Štefan Janeček, IMB SAS
   Jean-Luc Da Lage, Laboratoire Evolution, Genomes, Comportement, Ecologie, CNRS, Gif sur Yvette, France

9. The Integral Regulatory Role of (CD222) in T cell activation (P22908)
   (funded by FWF - Austrian Science Fund)
   Duration: 01/2012 – 12/2014
   Principal investigators: Vladimír Leksa
   Vladimír Leksa, IMB SAS
   Hannes Stockinger, Center for Pathophysiology, Infectiology and Immunology, Medical University Vienna, Austria

10. Bacillus subtili spore coat - study of formation and self assembling properties of spore coat proteins
    Duration :01/2012 - present
    Principal investigators:
    Daniela Krajčíková, IMB SAS
    Jilin Tang, State Key Laboratory of Electroanalytical Chemistry, Changchun Institute of Applied Chemistry, China

- **National projects and their funding**

2.4.4. Projects supported by the Slovak Research and Development Agency (APVV)

Role of the Institute e.g. coordinator "C", investigator "I".

Start	Project title	Typ / Project number	Duration in months	*Funding for the Institute (EUR)	Role of the Institute / Responsible person
2012	Lipid domains in cell division and programmed cell death in Bacillus subtilis. (05/2011-10/2014)	APVV-00335-10	48	163,279	C I. Barák
	New bacteriophages and phage proteins for pathogen devitalization in foods prepared by synthetic biology approach. (05/2011-10/2014)	APVV-0098-10	48	90,559	I G. Bukovská
	Bioinformatics analysis of amylases. (09/2009-08/2013)	LPP-0417-09	60	74,940	C Š. Janeček
	Molecular mechanisms of biosynthesis, regulation, and horizontal transfer of genes responsible for production of biologically active compounds in streptomycetes. (07/2012-12/2015)	APVV-0203-11	42	139,500	C J. Kormanec
	Molecular architecture, dynamics and evolution of chromosomes in yeast mitochondria. (05/2011-10/2014)	APVV–0123–10	48	80,000	I E. Kutejová
	Broadening of scientific knowledge on quality and safety of Slovakian bryndza cheese using modern molecular, microbiological, and chromatographic methods. (05/2011-10/2014)	APVV-0590-10	36	62,000	I D. Pangallo
	Structure of foci and emerging diseases with emphasis on role of rodents in urban type of natural foci of diseases. (05/2011-10/2014)	APVV-0267-10	48	26,300	I I. Barák
	Structural and functional characterization of human ryanodine receptor regulation and its malfunction caused by mutations. (05/2011-10/2014)	APVV-0628-10	48	249,255	C J. Ševčík
2013	Characterization of bacterial communities of Slovakian wine by molecular-biological methods. (10/2013-9/2016).	APVV-0344-12	36	75,000	I D. Pangallo
	Structure, properties and biotechnological potential of novel microbial enzymes degrading plant biomass. (10/2013-9/2016).	APVV-0602-12	36	58,750	I Ľ. Urbániková
2014					
2015	Assembly of protein complexes during asymmetric cell division in sporulating cells of Bacillus subtilis. (07/2015-06/2019).	APVV-14-0181	48	148,475	C I. Barák
	Immune modulation by cytomegalovirus and its immunotherapeutic potential. (07/2015-06/2019)	APVV-14-0839	48	56,279	I E. Kutejová
	determine the contribution of microorganisms to organoleptic quality of bryndza cheese. (07/2015-06/2018)	APVV-14-0025	36	70,000	I D. Pangallo
	Synthetic biology and production of peroxidases de novo. (07/2015-06/2019).	APVV-14-0375	48	99,393	I M. Zámocký

*funding includes entire duration of a project

2.4.5. Projects supported by the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA) for each year, and their funding

VEGA	2012	2013	2014	2015
Number	15	14	16	17
Funding in the year (EUR)	117,920	115,258	106,785	123,557

[1]

- **Summary of funding from external resources**

2.4.6. List of projects supported by EU Structural Funds

1. New microbial isolates containig genes of catabolic and detoxication pathways and their use in biotechnology
   Grant agency: ASFEU
   Grant registration number: 26240220010
   Duration: 09/2009 – 02/2013
   Total Funding: 479 302 EUR
   Funding for IMB SAS: 328 605 EUR
   Responsible person at IMB SAS: Bystrík Polek - Coordinator
   Number of cooperating institutions: 2

2. Prionoses transmissible to humans: Research and development of cell model, with potential use in the application sphere
   Grant agency: ASFEU
   Grant registration number: 26240220025
   Duration: 10/2009 – 09/2012
   Total Funding: 494 082 EUR
   Funding for IMB SAS: 103 652 EUR
   Responsible person at IMB SAS: Imrich Barák
   Coordinator: Michal Novák, Institute of Neuroimunology SAS, Bratislava
   Number of cooperating institutions: 2

3. Development of the diagnostic methods for the detection of tick-borne pathogens and the techniques for the preparation of the vaccine development directed against ticks
   Grant agency: ASFEU
   Grant registration number: 26240220044
   Duration: 11/2010 – 10/2013
   Total Funding: 939 915 EUR
   Funding for IMB SAS: 258 800 EUR
   Responsible person at IMB SAS: Imrich Barák - Principal investigator
   Coordinator: Dušan Žitňan, Institute of Zoology SAS
   Number of cooperating institutions: 3

4. Centre of Excellence for the use of information biomacromolecules in the prevention of diseases and for improving quality of life
   Grant agency: ASFEU
   Grant registration number: 26240120027
   Duration: 03/2010 – 03/2013
   Total Funding: 2 788 317 EUR
   Funding for IMB SAS: 0 EUR
   Responsible person at IMB SAS: Andrej Godány
   Coordinator: Marta Kollárová, Comenius University, Bratislava
   Number of cooperating institutions: 6

[1] Excluding projects for the popularisation of science

5. Centre of excellence for translation research in molecular medicine
   Grant agency: ASFEU
   Grant registration number: 26240120030
   Duration: 06/2010 – 05/2012
   Total Funding: 2 649 697 EUR
   Funding for IMB SAS: 10 956 EUR
   Responsible person at IMB SAS: Ján Kormanec
   Coordinator: Juraj Kopáček, Institute of Virology SAS, Bratislava
   Number of cooperating institutions: 7

6. Excellence centre for Glycomics
   Grant agency: ASFEU
   Grant registration number: 26240120031
   Duration: 11/2010 – 10/2013
   Total Funding: 3 977 975 EUR
   Funding for IMB SAS: 154 000 EUR
   Responsible person at IMB SAS: Juraj Gašperík
   Coordinator: Ján Mucha, Institute of Chemistry SAS, Bratislava
   Number of cooperating institutions: 7

7. Establishment of Competence center for research and development in molecular medicine
   Grant agency: ASFEU
   Grant registration number: ITMS 26240220071
   Duration: 10/2011 – 11/2014
   Total Funding: 6 774 791 EUR
   Funding for IMB SAS: 75 998 EUR
   Responsible person at IMB SAS: Ľubica Urbániková - Project manager
   Coordinator: Ján Turňa, Comenius University Bratislava
   Number of cooperating institutions including SR: 12

2.4.7. Summary of external resources of the EU Structural Funds (ERDF/ESF)

Role of the Institute in the project, e.g. coordinator “C”, work package leader “W”, investigator “I”.

Start	Project title	Project number	Duration in months	Funding for the Institute (EUR)	Role of the Institute
2012	New microbial isolates containig genes of catabolic and detoxication pathways and their use in biotechnology. (09/2009-02/2013)	26240220010	48	328,605	C
	Prionoses transmissible to humans: Research and development of cell model, with potential use in the application sphere. (10/2009-09/2012)	26240220025	36	103,652	I
	Development of the diagnostic methods for the detection of tick-borne pathogens and the techniques for the preparation of the vaccine development directed against ticks. (11/2010–10/2013)	26240220044	22	258,800	I
	Centre of Excellence for the use of information biomacromolecules in the prevention of diseases and for improving quality of life. (03/2010-03/2013)	26240120027	15	0	I
	Centre of excellence for translation research in molecular medicine. (06/2010-05/2012)	26240120030	36	10,956	I
	Excellence centre for Glycomics. (11/2010-10/2013)	26240120031	48	154,000	I
	Establishment of Competence center for research and development in molecular medicine. (10/2011-11/2014)	26240220071	38	75,998	W / I
2013					
2014					
2015					

External resources	2012	2013	2014	2015	total	average
External resources (milions of EUR)	0.267	0.025	0.026	0.032	**0.350**	**0.088**
External resources transfered to coooperating research institute (milions of EUR)	0.019	0.036	0.000	0.002	**0.057**	**0.014**

- **Supplementary information and/or comments on research projects and funding sources**

During the assessment period, the ratio between external and institutional funding increased, with the greatest rise coming from international resources. The Institute collaborated in 11 internationally funded projects, including three large 6RP and 7RP collaborative research projects. The second most significant source of external funding was from 14 APVV grants and 31 VEGA grants (totals during the assessment period); in the majority of these, the Institute was the coordinator. In addition, the Institute also participated in 7 projects funded by EU Structural funds, which significantly helped in the building of new infrastructure.

2.5. PhD studies and educational activities

2.5.1. List of accredited programmes of doctoral studies, period of validity

4.2 Life science

4.2.3 Molecular Biology
in cooperation with:
Faculty of Natural Sciences, Comenius University, Bratislava (2006 – present)
(Institutional Guarantor: Ján Kormanec)

4.2.7 Microbiology
in cooperation with:
Faculty of Natural Sciences, Comenius University, Bratislava (2006 – present)
(Institutional Guarantor: Imrich Barák)

(Head of the Institutional PhD training centre: Ján Kormanec)

The Institute strongly encourages applicants for PhD study from the following research fields: molecular biology, microbiology, genetics, biochemistry, biophysics, and bioinformatics. Possible supervisors are evaluated by the Institute's Scientific Board; as of 31 December 2015, there were 28 possible PhD supervisors.

2.5.2. Summary table on doctoral studies (number of internal/external PhD students; number of foreign PhD students, number of students who successfully completed their theses, number of PhD students who quit the programme*)*

PhD study	31-12-12			31-12-13			31-12-14			31-12-15		
Number of potential PhD supervisors	26			27			27			28		
PhD students	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted
Internal	16.0	2.0	0.0	17.0	3.0	0.0	15.0	4.0	1.0	13.0	4.0	0.0
External	1.0	0.0	0.0	1.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0
Other supervised by the research employees of the institute				1.0			2.0			4.0		

2.5.3. Summary table on educational activities

Teaching	2012	2013	2014	2015
Lectures (hours/year)[2]	313	273	343	210
Practicum courses (hours/year)[2]	455	186	321	476
Supervised bachelor theses (in total)	8	6	3	12
Supervised diploma theses (in total)	15	12	8	22
Supervised PhD theses (in total)	17	19	17	17
Members in PhD committees (in total)	3	3	3	3
Members in DrSc. committees (in total)	1	0	2	2
Members in university/faculty councils (in total)	2	2	2	2
Members in habilitation/inauguration committees (in total)	0	0	0	0

2

2.5.4. List of published university textbooks

Urbániková, L.: 7 Kryštalografia proteínov – význam a využitie štruktúr, pp. 145–174 in Biofyzika – vybrané kapitoly, ed. by D. Uhríková, I. Waczuliková, A. Ziegelhöffer, T. Hianik, J. Gaburjáková, M. Gaburjáková, A. Zahradníková, L. Urbániková, M. Belicka, L. Tomášová. Univerzita Komenského v Bratislave, Bratislava 2015 (ISBN 978-80-223-3800-4)

2.5.5. Number of published academic course books

None

2.5.6. List of joint research laboratories/facilities with universities

None

- **Supplementary information and/or comments on doctoral studies and educational activities**

The Institute of Molecular Biology SAS supervises PhD students in cooperation with the Faculty of Natural Sciences, Comenius University, Bratislava, in two accredited programmes: Molecular Biology (4.2.3) and Microbiology (4.2.7). In this capacity, the Institute educated twenty-five PhD students internally and one PhD student externally during the period 1 January 2012 – 31 December 2015. During this period our research staff also supervised another four PhD students from other institutes. According to SAS regulations, our Institute can accept, on average, three PhD students per year who are funded by the SAS central budget. The number of applicants is normally around ten, so we have asked the SAS several times for an exception from this limit. It should be noted that this year we have applied for another PhD programme, 4.1.22 Biochemistry, to improve and expand our educational possibilities.

[2] Do not include time spent with bachelor, diploma or PhD students during their supervising

PhD students are active in the supervision of the bachelor and diploma thesis work of junior university students, and they also cooperate in the university's pedagogical processes. Along with other Institutional researchers, many of them present the results of our research groups at "Researcher's Night", which takes place every year in Bratislava. They participate in many doctoral student competitions and many of them have won awards.

IMB SAS hosted also PhD students from abroad. Three PhD students from University of Novi Sad, Serbia (Dragana Cucak, Aleksandra Petrović, Eleonora Bošović) visited our institute in frame of Scope – Swiss Science Foundation project for 1 or 2 months. In addition, the institute hosted also one master student Marta Golabek from Gdansk University of Technology, Gdansk, Poland for 2 months. Her stay was funded by the Erasmus programme.

2.6. Social impact

2.6.1. List of the most important results of applied research projects. Max. 10 items

1. EU Structural Funds Project (Bratislavský kraj No. 26240220010) "New microbial isolates containing genes of catabolic and detoxication pathways and their use in biotechnology" in cooperation with the Water Research Institute, Bratislava.
   (09/2009 – 09/2012)
   Principal investigators: Bystrík Polek, Peter Ferianc
   Main results: Thirty-eight difficult to cultivate and previously uncultured bacteria obtained from Ni-contaminated soil were characterized, revealing significantly high heavy-metal degradation activities. Several of these were chosen for use in bioremediation.

2. 7th FP project 244956 "Bees in Europe and the decline of honeybee colonies"
   (1/3/2010 – 28/2/2013)
   Principal investigators: Katarína Bíliková, Jozef Šimuth
   Main results: The novel compound 9-oxo-10E,12Z-octadecanoic acid, obtained from poplar tree propolis, was isolated. It exerted a significant inhibitory effect against a group of the most virulent strains of *Paenibacillus larvae* occurring in Europe. This substance has the potential to be used for practical applications.

3. 7th FP project 613877 "Rewiring the Streptomyces cell factory for cost-effective production of biomolecules (STREPSYNTH)" – the large collaborative involving several SMEs.
   (1/12/2013 – 30/11/2018)
   Principal investigator: Ján Kormanec
   Main results: We developed an efficient deletion system for *S. lividans* TK24 based on the positive selection of double-crossover events using the blue pigment producing gene *bpsA*. Using this system we prepared a triple mutant in the *act, red*, and *cda* antibiotic clusters, and removed resistance marker genes. This strain could heterologously produce the cytostatic compound mithramycin in a 4-fold higher yield.

4. SCOPES – Swiss Science Foundation IZ73Z0_152527/1 "The role of metal homeostasis, reduction and sporulation in the metal resistance of Gram-positive bacteria"
   (1/4/2014 – 31/3/2017)
   Principal investigator: Imrich Barák
   Main results: We isolated and characterized fifteen environmental, Gram-positive, endospore-forming strains, highly resistant to the presence of chromium, from soils of different origins, including highly polluted ones. One of these strains, which was characterized in more detail, is a relative of *Bacillus pseudomycoides*. We are using this strain for further molecular studies of the bacterial chromium resistance

mechanisms and will investigate its potential for the remediation of areas with heavy chromium pollution.

5. SAS-MOST JRP 2014/3 “Exploring Microbial Diversity and Functionality in Thermophilic Bioreactors for Innovation in Biotechnology.”
   (1/1/2015 – 31/12/2017)
   Principal investigator: Domenico Pangallo
   Main results: The microflora of different types of bioreactors were analyzed in order to diminish the level of polluting compounds and, consequently, increase methane production. The microflora of two different tetramethylammonium hydroxide-processing bioreactors was evaluated together with the increase in methane recovery.

6. APVV-0267-10 “Structure of foci and emerging diseases with emphasis on role of rodents in urban type of natural foci of diseases”
   (1/5/2011 – 31/10/2014)
   Principal investigator: Imrich Barák
   Main results: We prepared a specific DNA chip for detecting different tick-borne pathogens in Central Europe. In collaboration with the Institutes of Zoology, Parasitology, and Virology (all SAS), we examined ticks collected from different parts of Slovakia and inspected them for the presence of bacterial pathogens using the DNA chip.

7. APVV-0590-10 “Broadening of scientific knowledge on quality and safety of Slovakian bryndza cheese using modern molecular, microbiological, and chromatographic methods”
   (1/5/2011 – 30/4/2014)
   Principal investigator: Domenico Pangallo
   Main results: We gathered detailed information about the microbial diversity and volatile aroma-active compound profiles of Slovak bryndza cheese in order to identify those microorganisms responsible for its organoleptic properites. Using this information, we suggested some optimum starter cultures for the production of this important Slovak product.

8. APVV-0098-10 “New bacteriophages and phage proteins for pathogen devitalization in foods prepared by synthetic biology approach”
   (1/5/2011 – 31/10/2014)
   Principal investigators: Gabriela Bukovská, Andrej Godány, Ľuboš Kľučár
   Main results: We isolated, characterized and sequenced eight new bacteriophages, suitable for the inactivation of bacteria in food. We prepared recombinant endolysins, and determined their enzymatic properties and host specificity against a broad range of potentially pathogenic bacterial strains. We developed a mathematical model for the growth of phages and their hosts, including several growth parameters such as temperature and pH. This phage-host model is freely accessible to external users at http://www.phisite.org/model.

9. APVV-0344-12 “Characterization of bacterial communities of Slovakian wine by molecular-biological methods”
   (1/10/2013 – 30/9/2016)
   Principal investigator: Domenico Pangallo
   Main results: The bacterial microflora present during the microvinification of the Central European Blaufränkisch and Grüner Veltliner grapes was determined. We found that wine fermentation involved a complex bacterial community, composed of both sporadic and regularly occurring elements. These results are very interesting because they suggested that bacterial microflora should also be taken into account when regulating the *bouquet* of these two typical Central European wines.

10. APVV-14-0375 “Synthetic biology and production of peroxidases de novo”
    (1.7.2015 - 30.6.2019)

Principal investigator: Marcel Zámocký
Main results: A comprehensive knowledge on the reaction mechanism of catalytic hydroperoxidases from various microbes is applied for the construction of *de novo* synthetic heme peroxidase for efficient catalysis of diverse biopolymerization reactions without the use of recalcitrant chemicals. Bifunctional catalase-peroxidase is applied for clean room monitoring. The biotechnological SME Slovgen as technology recipient will realize these environmental biotechnologies after finishing of the project.

2.6.2. List of the most important studies commissioned for the decision-making authorities, the government and NGOs, international and foreign institutes

1. The *Laboratory of Environmental and Food Microbiology* is an important research and consulting group for several organizations concerned with the conservation and restoration of our cultural heritage. The Slovak National Library, the Slovak National Archives, and the Slovak National Gallery frequently cooperate with this laboratory. The Laboratory has developed different non-invasive microbial diagnostic protocols in order to assess the degree of deterioration of photographs, paper, books, parchment, polymeric and wooden statues and polymer materials present in historical and contemporary art collections. The Laboratory also collaborates with the Institute of Musicology, SAS, on the preservation and restoration of wooden organs. At the end of 2015, the Laboratory began another collaboration with the Betliar Museum regarding a microbial survey of the oldest surviving mummy (Žofia Šeredy) in Slovakia in order to develop a suitable strategy for its conservation.

2. Ľuboš Kľučár was appointed by the Minister for Education, Science, Research and Sport of the Slovak Republic to be a member of a thematic working group on *Information and Communication Technologies,* one of the groups established for specialised areas from the perspective of available scientific and research capacities for the *Strategy of research and innovation for intelligent specialisation of the Slovak Republic* (RIS3 SK). This group's main task is to determine the long-term strategic areas for the Operational programme *Research and innovation*, to participate in the *National plan for the use and development of research infrastructure*, and to specify the connections between RIS3 SK areas for research and economic specialisation.

3. Imrich Barák
   - Produced expert reports as one of the Coordinators of the Consortium of Central and Eastern European Structural Biology Groups (2000–present) and as a member of the SFX and XBI Consortia Management Boards at the European XFEL (X-ray Free Electron Laser) in Hamburg, Germany (member 2014–present).
   - Is a member of the Commission for Collaboration with XFEL from the Ministry of Education, Science, Research and Sport of the Slovak Republic.
   - Is a member of the Commission for coordination of activities of the Slovak Republic in the ESFRI (European Strategic Forum for Research Infrastructures) directed towards materials and physical science, with potential applications in biological and medical sciences, chemical sciences and IT (2012–present)

4. Katarína Bíliková produced an expert report: The quality of honey and bee products for the Chairman of Slovak Union of Bee-keepers (2012)

5. Gabriela Bukovská, Andrej Godány wrote experts' reports for the Ministry of Education, Science, Research and Sport of the Slovak Republic on the projects Impulses for Research and Development – applied and basic research projects (2012, 2013, 2015)

6. Peter Ferianc serves as a member of the Expert Panel on Biological Safety, Ministry of Environment of the Slovak Republic

2.6.3. List of contracts and research projects with industrial and other commercial partners, incl. revenues

1. *The Department of Microbial Genetics* has a close expert cooperation with the SME GLsystem (http://www.glsystem.sk/sk/home/). It helps with the selection and characterization of bacterial systems to effectivly utilize soil microorganisms as a substitute for chemical nitrogen fertilizers.

2. The *Department of Gene Expression* prepared a genetically manipulated Streptomyces strain with a substantially increased production level of the anticancer compound mithramycin for the Spanish biotechnological SME Entrechem (http://www.entrechem.com).

3. The project APVV-14-0375 “Synthetic biology and production of peroxidases *de novo*” in the *Laboratory of Phylogenomic Ecology* was completed in cooperation with the biotechnology SME Slovgen.

4. The *Laboratory of Prokaryotic Biology,* in cooperation with the company EL spol. s.r.o., Spišská Nová Ves, Slovakia, developed a diagnostic test for the detection of *Staphylococcus aureus* (coagulase positive) in food based on the multiplex PCR detection of toxigenic strains. The method was certified in 2013 and has been used since then in diagnostic testing.

5. The *Laboratory of Molecular Immunology* participated in project P22908 “The Integral Regulatory Role of (CD222) in T cell activation” which was funded by FWF – Austrian Science Fund
   (2010–2014)
   Principal investigator: Vladimír Leksa
   Income: 125 220 EUR per year
   In the frame of the project, the research of the Laboratory of Molecular Biology was recognized and its head was contacted by the pharmaceutical research company Pharmaxis to study a therapeutic potential of mannose 6-phosphate homologues in fibrosis mouse models. The collaboration issued to the research article.

6. *The Laboratory of Genomics* cooperates Bohemian Biotech, Ltd. (Czech Republic) in a joint consortium of Bohemian Biotech, Ltd. (Lead organization), the Faculty of Chemical and Food Technology of the Slovak Technical University, and the Institute of Molecular Biology to pursue the project “Development of biosurfactant manufacturing, technology and applications” (Trend of surfactants, their characterization and applications, submitted).

2.6.4. List of licences sold abroad and in Slovakia, incl. revenues

None

2.6.5. List of most important social discourses under the leadership or with significant participation of the institute (max. 10 items)

- In 2014, IMB SAS scientists founded an independent initiative “Science wants to live!” (http://www.vedachcezit.sk) to point out the problems of science, research and education in Slovakia in order to encourage positive changes in these areas. The initiative founders are researchers who realized that they needed to actively approach and engage in the issues of science policy in Slovkia, because these issues are not a concern of either political elite or the general public in the long term. To date, the initiative has gathered support from more than 4000 people.

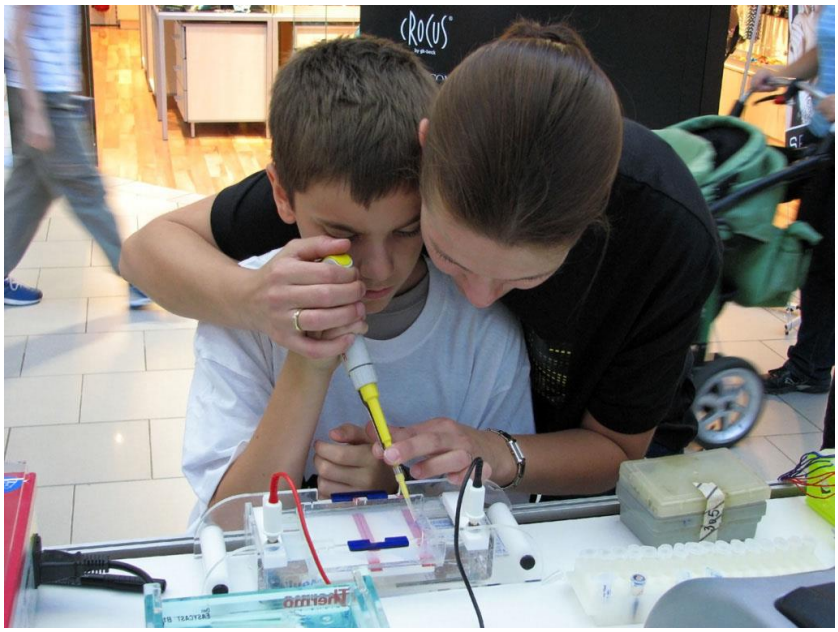
2.6.6. Summary of relevant activities, max. 300 words

In Slovakia, science is chronically underfunded and only lightly supported. The Institute's scientists expend a considerable effort every year to secure funding for projects beyond that available from academic resources. Each year they submit applications for new projects not only to national agencies, but also to research programs supported by the EU and other agencies. Several groups have tried to engage in Horizon 2020 as members of consortia, but so far unsuccessfully. Creating and establishing applied research projects with industrial or other commercial partners in Slovakia is quite difficult, owing to the relative absence of small and medium-sized biotech, pharmaceutical and biology-oriented companies. While we might have been able to transfer the results of our research into practical applications with their assistance, their absence greatly limits our ability to do so. A consequence of this is the low number of patents taken out by our researchers.

Our scientists, young researchers and PhD students regularly participate in the European Science and Technology Week (Science Week Slovakia) as well as in the scientific festival "Researcher's Night", organized every year in September, and in several other outreach activities. A detailed description is given below in section *2.7. Popularisation of Science (outreach activities)*.

2.7. Popularisation of Science (outreach activities)

2.7.1. List of the most important popularisation activities, max. 20 items



IMB SAS at the Researcher's Night.

1. Honey as medicine
   (23/2/2012, CVTI, Bratislava)
   Katarína Bíliková presented the results of her work at the "*Scientific Coffee*" event.

2. Science window open
   (29/2/2012, Gymnázium L. Sáru, Bratislava)
   Two colleagues presented a popularisation lecture at a high school: Ľuboš Ambro gave "*Mitochondria – dynamic organelles of eukaryotic cells*" and M. Stano gave "*Bacteriophages – remarkable viruses*".

3. Researcher's Night 2012
   (28/9/2012, SC Avion, Bratislava)
   We presented the stand "*DNA chips in medicine*" showing the audience the latest methods for bacterial disease detection using DNA chips. Ten researchers and PhD

students from the institute took part; the presentation was highly acclaimed by the visitors.

4. Open Doors Day 2012
   (6/11/2012, IMB SAS, Bratislava)
   As part of Science and Technology Week in the Slovak Republic, we organised a popularisation seminar with two major talks: "*Code of life*" and "*Proteins and their 3D structure*" together with a practical presentation of new methods for bacterial disease detection using DNA chips. This event, intended mainly for high school students, took place at our institute.

5. "K veci"
   (4/2/2013, RTVS, Bratislava)
   Ján Kormanec took part in a Slovak Radio talk programme focused on antibiotics and pathogenic bacteria.

6. Researcher's Night 2013
   (27/9/2013, SC Avion, Bratislava)
   We presented the stand "*World of microbes – known and unknown*" showing the marvellous life of microorganisms in soil, water, food and the human body. Twelve researchers and PhD students from the Institute took part; the presentation was highly acclaimed by the visitors.

7. Open Doors Day 2013
   (12/11/2013, IMB SAS, Bratislava)
   As part of Science and Technology Week in the Slovak Republic we organised a popularisation seminar with two major talks: "*Code of life*" and "*Why do we need to understand protein structure?*" along with a practical presentation of microorganisms living in soil, water, food and the human body. This event, mainly intended for high school students, took place at our institute.

8. Science and Technology Week in the Slovak Republic 2013
   (13/11/2013, CVTI, Bratislava)
   We have presented the stand "*World of microbes – known and unknown*" showing diverse views of the life of microorganisms in soil, water, food and the human body. Twelve researchers and PhD students from the Institute took part, and the presentation was highly acclaimed by the visitors. Two of our researchers took part at this event, which was organised by the Slovak Centre for Scientific and Technical Information.

9. When science and music influence each other
   (6/2/2014, Radio FM, Bratislava)
   Interview with Vladimír Leksa on Slovak Radio.

10. Researcher's Night 2014
    (26/9/2014, Old Market Hall, Bratislava)
    We presented the stand "*Crystals of life*". The year 2014 was chosen by UNESCO as the International Year of Crystalography and we mostly presented the applications of crystallography in modern biological research. Twelve researchers and PhD students from the institute took part, and the presentation was greatly appreciated by the visitors.

11. Science and Technology Week in the Slovak Republic 2014
    (10/11/2014, CVTI, Bratislava)
    We presented the stand "*Crystals of life*" dedicated to the *International Year of Crystalography* and showing the applications of crystallography in biomedical sciences. Two of our researchers took part at this event, organised by the Slovak Centre for Scientific and Technical Information.

12. Article in popular science magazine *Quark*
    (November 2014, *Quark* No. 11, Bratislava)
    Ján Kormanec published an article entitled “Results brings new questions. Antibiotics Auricin”.

13. Open Doors Day 2014
    (11/11/2014, ÚMB SAV, Bratislava)
    As part of Science and Technology Week in the Slovak Republic we organised a popularisation seminar with two major talks: “*Code of life*” and “*Atomic secrets of life*” together with a practical presentation dedicated to the *International Year of Crystalography* and to the application of crystallography in biomedical sciences.

14. Press Conference
    (11/12/2014, P SAV, Bratislava)
    Vladena Bauerová, Eva Hostinová, Juraj Gašperík, Alexandra Zahradníková and Jozef Ševčík presented the results of their research on the structure and function of the human ryanodine receptor 2, whose dysfunction causes heart arrhythmia. The results were published in Borko *et al.* (2013) *Protein Pept. Lett.* **20**: 1211–1216 and Borko *et al.* (2014) *Acta Crystallogr.* **D70**: 2897–2912.

15. Science without Slovakia, Slovakia without science
    (7/12/2014, *Pravda,* Bratislava)
    An essay by Vladimír Leksa assessing the attitude of the Slovak public towards science and research.

16. Researcher’s Night 2015
    (25/9/2015, Old Market Hall, Bratislava)
    We presented the stand “*World of Microbes*” showing the marvellous life of microorganisms in soil, water, food and the human body. The practical presentations were supplemented by fun contests for the youngest visitors. Fourteen researchers and PhD students from the Institute took part, and the visitors greatly enjoyed the presentation.

17. Secrets of Biology
    (October 2015)
    A series of interactive multimedia presentations in eight Slovak cities intended for elementary and high school students, presented by Erik Mingyár.

18. Science unconventionally
    (9/11/2015, Centrum vedy CVTI, Bratislava)
    We have presented the stand “*World of microbes*” showing the diverse lifestyles of microorganisms in soil, water, food and the human body. Twelve researchers and PhD students from the Institute took part; the presentation was highly acclaimed by the visitors. Two of our researchers took part at this event, organised by the Slovak Centre for Scientific and Technical Information.

19. Open Doors Day 2015
    (10/11/2015, IMB SAS, Bratislava)
    As part of Science and Technology Week in the Slovak Republic we organised a popularisation seminar with two major talks: “*Secrets of modern biology*” and “*Microorganisms like Art*” combined with a practical presentation on microorganisms living in soil, water, food and the human body.

20. Drawing with soil bacteria
    (December 2015, *Quark* No. 12, Bratislava)
    Renáta Nováková and Jana Makroczyová published an article connecting science and the visual arts.

2.7.2. Table of outreach activities according to institute annual reports

Outreach activities	2012	2013	2014	2015	total
Articles in press media/internet popularising results of science, in particular those achieved by the Institute		1	5	5	11
Appearances in telecommunication media popularising results of science, in particular those achieved by the Institute		3	5		8
Public popularisation lectures	7	7	5	4	23

- **Supplementary information and/or comments on popularisation activities, max. 300 words**

Scientists, young researchers and PhD students from the Institute regularly participated in the European Science and Technology Week (Science Week Slovakia) by organizing our annual Open Doors Day at IMB, where we explained our Institute and its scientific projects to the public. This event has become very popular, especially among high school students. We popularized our research work through lectures and we also prepared practical demonstrations of some of the basic experiments carried out at our Institute. Another scientific festival which we took part in was the “Researcher's Night” organized every year in September. We prepared demonstrations of some simple experiments in which the audience could participate: “DNA chips in medicine” (2012), “World of microorganisms – known and unknown” (2013), “Crystals of life” (2014), “World of bacteria” (2015). Our scientists and PhD students discussed different aspects of our projects with visitors. Many of our scientists (Ján Kormanec, Imrich Barák, Matej Stano, Vladimír Leksa, Renáta Nováková, Eva Kutejová, Vladena Bauerová, Erik Mingyár and others) also contributed to radio and TV programs and to other media devoted to specific scientific issues. We published responses to real public concerns in national newspapers and magazines and contributed articles about science to magazines (*e.g. Quark, Tyždeň, Zdravie*). Our scientists also repeatedly gave lectures on general or specific scientific topics either for students or at different events (exhibitions, fairs). Vladimír Leksa wrote the book *Vzdelaní Príbuzní* (Perfekt, 2013) about some of the great but forgotten scientists of Central Europe. He also blogs about science.

2.8. Background and management. Human resources and implementation of recommendations from previous assessment

2.8.1. Summary table of personnel

Personnel	2012	2013	2014	2015
All personnel	77.0	75.0	65.0	67.0
Research employees from Tab. Research staff	59.0	57.0	47.0	49.0
FTE from Tab. Research staff	43.710	43.950	42.510	40.710
Average age of research employees with university degree	44.1	43.9	46.6	46.4

2.8.1.1. Professional qualification structure (as of 31.12. 2015) FEMALE

FEMALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.									
II.a / Assoc. prof.		1	2	2	1	2	5	3	
Other researchers PhD./CSc.		2	4						
doc. / Assoc. prof.									

2.8.1.2. Professional qualification structure (as of 31.12. 2015) MALE

MALE	AGE								
Number of	< 30	31 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
DrSc. / prof.					1	2	1		
II.a / Assoc. prof.			1	2	1	1	2		1
Other researchers PhD./CSc.		1	2						
doc. / Assoc. prof.					1				1

2.8.2. Postdoctoral and mobility scheme

2.8.2.1. Postdoctoral positions supported by national and international resources

None

2.8.2.2. Postdoctoral positions supported by external funding

None

2.8.2.3. SAS stipends and SASPRO stipends

We had one unsuccessful SASPRO application during assessed period.

2.8.2.4. Internal funding - the Slovak Academy of Sciences Supporting Fund of Stefan Schwarz

Successful applicants to the Štefan Schwarz foundation:

1. M. Gabriško (01/13–01/17)
2. L. Kraková (05/13–04/17)
3. N. Labajová (01/11–03/11, 09/12–09/13, 09/15–04/18)
4. M. Stano (05/12–04/16)

2.8.3. Important research infrastructure *(max. 2 pages)*

The Institute of Molecular Biology possesses substantial research infrastructure. Each laboratory forms an independent unit with basic equipment (centrifuges, incubators,

shakers, pH meters, thermal cyclers, water baths, etc.) and the special instruments required for its particular projects. These include a microarray scanner, microplate readers, fluorescence microscopes (Olympus, Leica) equipped with digital cameras and image analysis software, an ultramicrotome for thin sectioning, a flow cytometer, special electrophoretic systems (pulsed-field gel electrophoresis, 2D electrophoresis, denaturing gradient gel electrophoresis), laminar boxes, CO_2 incubators, a vacuum concentrator, etc. All of these devices are available to all employees of the Institute. In recent years, much laboratory equipment has been updated thanks to external resources. There are also several commonly used instruments including two FPLC (Äkta Prime, Äkta FPLC), an HPLC (Shimadzu, Varian), a Dynamic Light Scattering device, a Real-time PCR machine, an automated pipetting system (epMotion), a microarrayer (Genetix), ultracentrifuges, −80°C freezers, etc. The institute has also recently established a Cell Culture Unit. This equipment is of crucial importance for research carried out at the Institute and was used also by other research groups, mainly from other institutes of SAS, Comenius University and Slovak University of Technology in Bratislava.

In 2013, the Institute's crystallization laboratory was significantly improved. Previously, it was only a small laboratory equipped with a classic trinocular stereo microscope (Zeiss, Germany) with cold light, polarisation for crystal inspection and an extended working place for conveniently manipulating them (The microscope was equipped with a 3 Mpx digital camera for crystal documentation and for transferring live images, an important feature for education and training). The laboratory has now been enlarged, fully air-conditioned, and equipped with a Rockimager RI54 automated imaging system (Formulatrix, USA). This device is complemented with a Manual UV Inspection Station (MUVIS), a stand-alone visible and UV microscope that provides a quick way to scan the plates for protein crystals. The Rockimager RI54 incubates 96-well plates with crystallisation drops and captures superior quality images under visible and polarised light at a user-defined schedule. Each plate is photographed in colour with six slices per drop in less than 4 minutes. The MUVIS allows the drops to be illuminated with UV light to quickly separate protein and salt crystals. Protein crystals fluoresce under certain wavelengths of UV light due to the presence of aromatic amino acids, but salt crystal do not. This automated crystallisation system was purchased in 2013 under Structural Funds project "Establishment of Competence centre for research and development in molecular medicine" (ITMS 26240220071, overall price 176 000 EUR). This facility has greatly enhanced our research in the field of structural biology, it was used by several our research groups and is available also to other external users.

Thanks to its international collaborations, Institute has access to much of the unique, state-of-the-art equipment available to our European partners. These include the synchrotrons in Hamburg and Grenoble (thanks to our participation in INSTRUCT), crystallographic robots at the Department for Structural and Computational Biology, Max F. Perutz Laboratories in Vienna and at BIOCEV Prague, and also to all core facilities in EMBL (the institute has collaborated with EMBL for many years, especially in the area of structural biology; it was chosen by EMBL to be the first research institute in Slovakia to host an EMBL workshop on the "*EMBL Opportunities for the Slovak Research Community*" in February 2016). Thanks to collaboration with Prof. Dr. Hannes Stockinger, the head of the Center for Pathophysiology, Infectiology & Immunology at the Medical University of Vienna, the advanced microscopy facilities of the center (single molecule tracing, confocal microscopy, state-of-the-art flow cytometry, fluorescence-activated cell sorting and image stream flow cytometry, surface-plasmon-resonance analysis Biacore optical biosensor) are also accessible. Dr. Václav Hořejší (the head of the Institute of Molecular Genetics, Academy of Sciences of the Czech Republic, Prague) has generously provided the laboratory with suitable monoclonal antibodies. International networking in bioinformatics, especially membership in EMBnet and participation in the SeqAhead COST project, allowed us to stay abreast of developments in Big Data storage and analysis. We were directly involved in the preliminary phase of the ELIXIR project, the leading EU initiative in the field of bioinformatics research and infrastructure, though to date there has been no political will to join this consortium at the national level. Our future ambition is to participate in building the National ELIXIR node.

Major improvements for research in the field of structural biology are expected in the near future from joining the European XFEL, SFX and XBI consortia. The major bottleneck for determining protein structures by crystallography is still the discovery of suitable conditions for obtaining diffraction-quality crystals. To circumvent this obstacle, we plan to use an X-ray Free Electron Laser (XFEL) to solve the structure of proteins or their complexes at the SFX (Serial Femtosecond Crystallography) end station in Hamburg, which is due to become operational in summer 2017. This facility should allow structural data to be gathered from nanocrystals, or potentially even from solutions of isolated proteins or protein complexes. The XFEL will produce coherent radiation whose X-ray brightness will be many orders of magnitude greater than that from all previous sources. IMB SAS, together with Slovak physicists, is involved in setting up the SFX and XBI (European XFEL-based Biology Infrastructure) user consortia at XFEL. Imrich Barák is a member of both the SFX and XBI Consortia Boards at European XFEL.

The Institute has a reliable computing network based on 100 Mbps and 1 Gbps Ethernet technology and structural cabling (1 Gbps for servers and internal backbone; 100 Mbps for workstations). The institute is interconnected to the SAS campus via a dedicated 1 Gbps optical line. A central PC-based server running MS Windows Server 2008 R2 OS (Primary Domain Controller) is used as the main storage and application point (users home boxes, centralised repository for documents and software, http and ftp server, DHCP and DNS server, print server, nightly backup). This central server is housed in an air-conditioned room along with 4 other Linux-based application servers, all on a UPS. These are primarily used for bioinformatics computing and also serve as the main storage and application servers for the National EMBnet Node. The main computing node possesses a 12-core Intel-based system with 128 GB RAM and an 11 TB RAID array (acquired in 2012 through ITMS project 26240220071), which provides sufficient power for most of the computing tasks required by the Institute's bioinformatics groups and was also used by other research teams nationwide and, in addition, also for training and education. The most important analysis packages include Chipster and Galaxy, used to analyse data from diverse high-throughput methods (DNA arrays, NGS, mass cytometry…). For high-demand computing jobs, access to the Slovak Infrastructure for High Performance Computing hosted at Slovak Academy of Science is provided. The Institute maintains more than one hundred PC workstations (the majority are MS Windows with a few Linux-based ones).

The Institute's real property has been also renovated. Several laboratories were reconstructed and newly equipped. In 2013 the outer shell of the main building was completely rebuilt and insulated, providing a significant reduction in energy consumption.

2.8.4. Description of how the results and suggestions of the previous assessment were taken into account

For the assessment period 2007–2011, the Institute was evaluated as category "**A**".

<u>The overall evaluation was as follows:</u>

The IMB was displayed by its director and staff as a dynamic institute with the creative atmosphere.

- Parameters of scientific performance expressed by the usual criteria showed that the Institute exceeds the average of institutes in biological field of science in the number of both publications and citations.
- Research interests documented by the research topics indicate that researchers of the Institute identified biologically relevant problems, which could not only deepen understanding of living matter but could have some application potential.
- During the evaluation period, several important findings were made by the members of the institute, such as the identification of anti-anti-sigma factor BldG, which has a key role in the differentiation in *Streptomyces*, or the discovery of lipid compartmentalization in the *Bacillus subtilis* membrane, and which pushed forward the level of knowledge in corresponding fields of science. These results appeared

after a long-term systematic analysis of important biological phenomena combined with excellent scientific imagination and methodical skills.

- The international importance of the IMB is witnessed by the cooperative projects, publications, invited lectures, etc., during the evaluation period, but also by the participation of one laboratory in the sequencing of honeybee genome, which was successfully completed.

These activities suggest that the Institute is an established and internationally credible scientific organization. As a consequence, number of finished PhD students was accepted as postdoctoral fellow in the top laboratories worldwide.

In addition to these topics, number of other important results was noticed during the evaluation procedure indicating the balanced development of Institute´s constituent laboratories, which guarantees high scientific productivity also for the future.

Comments, objections to organization's activities in the form of suggestions and specific tasks which must be performed by the organization before next regular evaluation, etc.

1. The improvement of spreading know-how by senior scientist to younger staff and PhD students by means of organization of courses.
2. The streaming of the institute´s activity towards the application sphere should be strengthened.
3. The effort should be made to provide financial support for PhD students out of the frame of regular budget.

Response to the comments

1. To improve the diffusion of skills to young scientists and PhD students, the Institute organised several conferences and courses primarily devoted to these young scientists during the present assessment period. In 2015, the institute organised a very successful two-day workshop: "Bioinformatics analysis of DNA microarray and NGS data", where, where 40 participants took part, including both the Institute's own young scientists and others from the whole of Slovakia. Each year the Institute organises the conference "Our proteins", which is primarily devoted to sharing experiences between senior and young scientists in the fields of proteomics and protein structure-function relationships. Furthermore, the Institute holds seminars about twice a month. At least once each year, each PhD student must present the results of his or her work, receiving extensive and critical discussion from senior scientists.

2. This "streaming towards application" is rather difficult in our field, since most of our projects are oriented towards basic science. Moreover, Slovakia has almost no biotechnology companies and the foreign ones are largely not interested in supporting Slovak science. Nonetheless, the development of applications is still essential, since our research is funded by public money and some of our results may in fact have practical applications. Consequently, the Institute has also been partially active in pursuing this during the assessment period. One of the main activities was the involvement of the Department of Gene expression in the large collaborative 7th FP project: "Rewiring the Streptomyces cell factory for cost-effective production of biomolecules (STREPSYNTH)" involving several SMEs. The group prepared a genetically manipulated Streptomyces strain, which produced the anticancer compound mighramycin in a substantially higher yield, which was acquired by the Spanish biotechnological SME Entrechem (http://www.entrechem.com). This development is very promising for future applications. In the previous evaluation period, the Department of Microbial Genetics developed a close expert cooperation with the Slovak SME GLsystem (www.glsystem.sk/sk/home) by helping with the selection and

characterization of bacterial systems for the effective utilization of soil microorganisms as a substitute for chemical nitrogen fertilizers. This activity was also improved through the successful funding of an applied APVV project with the title “Synthetic biology and production of peroxidases de novo”, which involved cooperation with the biotechnological SME Slovgen. Our long-running, intensive basic research on catalytic hydroperoxidases could be exploited in this applied project with the expectation of producing recombinant enzymes that might be used in various biotechnology applications in the near future. The Laboratory of Environmental and Food Microbiology cooperates very closely with several institutions responsible for safeguarding Slovak cultural heritage and property in developing and applying both culture-dependent and culture-independent microbial diagnosis systems to detect those pathogens responsible for degrading different historical objects (books, parchments, photographs, mummies, etc.). These institutions include the Slovak National Library, Slovak National Archives, Slovak National Gallery and the Betliari Museum. We also determine what microbial contaminants, especially airborne ones, are present in environment surrounding these objects. In addition, we are also trying to develop a safe, reliable and eco-friendly disinfection method for archival documents using essential oils and a method for the bio-restoration of wooden organs using proteases. This laboratory also develops new applications for testing the biodegradability of certain newly-developed polymeric foils used in agriculture (mulching foils) and packaging.

3. The Institute made efforts in this area, but the possibilities for outside funding of PhD students are rather limited. During the last evaluation period, 50% of the income of four young postdocs was drawn from the external Schwarz Fund. Additionally, they were awarded by 10% extra to their income (from the institutional budget). Several PhD students were also partially supported by external APVV projects. Three PhD students (Ľubomír Borko, Ľubomír Ambro and Eva Petrovčíková) were supported by EU Austria-Slovakia cooperation Ernst Mach Grant fellowships for short-term research stays in Austria, and two PhD students (Jana Nováková and Csilla Patasi) were supported by the Humboldt Foundation (Research group linkage program) for short-term research stays in Germany.

- **Supplementary information and/or comments on management, research infrastructure, and trends in personnel development**

After the 2011 reduction in the wage bill, the Institute’s laboratories and departments were significantly reorganised, and several inefficient scientists dismissed. However, since the final reduction was less dramatic than originally announced, this reorganization allowed the creation of a Postdoctoral fund at the Institute, enabling hiring three new young postdoctoral fellows to be hired, all of whom joined efficient laboratories. This new policy allowed the organization to not only reduce the average age of its scientists, but also allowed it to explore new fields of research. In 2014, Dr. Vladimír Leksa was hired using this fund and set up his own Laboratory of Molecular Immunology as part of the Department of Biochemistry and Structural Biology (*Unit #3*). In the same year, the Laboratory of Phylogenomic Ecology was created in the Department of Microbiology, whose newly hired head is Dr. Marcel Zámocký.

At the end of 2013, the whole Department of Molecular Apidology moved, by a delimitation procedure and after negotiations with SAS, to the Institute of Forest Ecology SAS. After delimitation from the Institute of Zoology, a new young scientist, Dr. Juraj Majtán, set up a new Laboratory of Apidology and Apitherapy, also as part of the Department of Biochemistry and Structural Biology. At present, the Institute has six departments, four of which contain a total of eleven partially-independent, grant-funded laboratories.

The current organizational structure is as follows:

Department of Gene Expression (Head: Ján Kormanec) (*Unit #1*)

Department of Microbial Genetics (Head: Dr. Imrich Barák) (*Unit #2*)

Department of Biochemistry and Structural Biology (Head: Dr. Eva Kutejová) ((*Unit #3*)

- Laboratory of Apidology and Apitherapy (Head: Dr. Juraj Majtán)
- Laboratory of Biochemistry and Protein Structure (Head: Dr. Eva Kutejová)
- Laboratory of Molecular Immunology (Head: Dr.Vladimír Leksa)

Department of Genomics and Biotechnology (Head: Dr.Gabriela Bukovská) ((*Unit #4*)

- Laboratory of Bioinformatics (Head: Dr.Ľuboš Kľučár)
- Laboratory of Genomics (Head: Dr. Gabriela Bukovská)
- Laboratory of Prokaryotic Biology (Head: Dr. Ľubica Urbániková)

Department of Microbiology (Head: Dr. Marian Farkašovský) (*Unit #5*)

- Laboratory of Environmental and Food Microbiology (Head: Dr. Domenico Pangallo)
- Laboratory of Phylogenomic Ecology (Head: Dr. Marcel Zámocký)
- Laboratory of Molecular Microbiology (Head: Dr. Marian Farkašovský)

Department of Protein Biology and Evolution (Head: Dr. Štefan Janeček) (*Unit #6*)

- Laboratory of Neurobiology (Head: Dr. Frantisek Jurský)
- Laboratory of Protein Evolution (Head: Dr. Štefan Janeček)

In 2015, two of our scientists, Dr. Marcel Zámocký and Dr. Domenico Pangallo, successfully defended their work, obtaining DrSc degrees, the highest scientific degrees in Slovakia, in Microbiology and Molecular Biology, respectively. This ensures that after the present guarantors retire, the Institute will continue to be able to maintain its PhD programmes. In addition, several our young scientists successfully obtained scientific category IIa, enabling them to become supervisors of PhD students.

3. Research strategy and future development of the institute for the next five years (2016-2020) (Recommended 3 pages, max. 5 pages)

3.1. - 3.2. Present state of the art in both the national and the international contexts. Research strategy of the institute in the national and the international contexts, objectives and methods

The overall and long-term research strategy of IMB is to acquire a broader knowledge and deeper understanding of the fundamental biological processes common to all living organisms, delineate the molecular and cellular mechanisms underlying these processes, identify and characterize their key structural determinants and interactions, and, based on these results, move towards application in biotechnology, industry, and biomedicine. In the following sections, we describe the current state-of-the-art and present the specific objectives of the Institute's individual research units as they relate to the five major research areas described above.

1. Cell Division and Differentiation

Worldwide, *Streptomyces* are extensively studied, with particular emphasis given to their regulation of antibiotic production and their complex morphological differentiation. For 25 years, *Unit #1* has been specifically studying the role of RNA polymerase sigma factors in the stress-response and differentiation. These two processes are extremely complex, as illustrated by the exceptionally large number of stress-response sigma factors and regulators. The aim of *Unit #1's* studies is to further characterize this complex regulation, specifically, the role of the complex cascade of stress response sigma factors and their regulators in *Streptomyces* differentiation.

The mechanisms of cell division and differentiation have been well-characterised in *Bacillus subtilis,* but despite intensive research, there are still crucial molecular details missing in the complex mosaic of these processes. *Unit #2's* discoveries have led to new questions in these areas, the most important being (i) how does the cell recognize, with high precision, the sites of septation at the mid-cell during vegetative growth and the cell pole during sporulation; (ii) how are these septa formed and what is the role of the protein complexes involved; and (iii) how is the highly resistant spore coat formed?

The processes of cell division vitally depend on the behaviour of cytoskeletal proteins, whose function is determined by the localization in time and space of their polymerization. In particular, different septin higher order structures are required for cell cycle progression and are crucial for basic processes like cytokinesis. The Laboratory of Molecular Microbiology (*Unit #5*) will continue its previous studies by further exploring the relationship between the structure and function of septin complexes. The results, obtained using supported lipid bilayer and fluorescence microscopy, electron microscopy, biochemical analysis and genetic approaches, are expected to further elucidate how the switch between the monomeric septin complexes, and rings, bars, gauzes or other higher-order structures regulates different processes at the cell division plane, and which proteins induce these structural changes. Experimental work will focus on how the different protein kinases are involved in regulating septin assembly in different stages of the cell cycle. A longer-term aim is to develop *in vitro* systems to reconstitute the spatial organization of septins in the presence of different accessory proteins mimicking the situation in the cell. The Laboratory will continue to collaborate with the Department of Structural Biochemistry from the Max-Planck Institute of Molecular Physiology in Dortmund.

2. Protein Structure-Function Relationships and Protein Evolution

Unit #2 is closely involved with the European X-ray Free Electron Laser (XFEL) in Hamburg, Germany. XFEL should be operational in mid-2017, and IMB SAS is a partner in setting up two consortia at XFEL: SFX/SPB (Serial Femtosecond X-ray crystallography) and XBI (XFEL Biology Infrastructure), and Imrich Barak, the head of *Unit #2*, is a member of the SFX and XBI Consortia Management Boards (2014–present). Our Institute already supports XFEL through both expertise and financing (up to 13 M EUR) through the Ministry of Education, Science, Research and Sport of the Slovak Republic. IMB will also promote the use of this state-of-art facility by Slovak scientists, especially structural biologists.

Some of the goals of the Laboratory of Biochemistry and Protein Structure (*Unit #3*) include (i) the structure-function studies of those mutations responsible for heart arrhythmias, (ii) structural studies on other hRyR2 domains, and (iii) determining the tertiary structure of the central part of hRyR2 and testing the domain switch hypothesis. Since mitochondrial dysfunctions are connected with a plethora of human disorders, the main goals of this lab involve studying those proteins involved in proper mitochondrial function (mitochondrial Lon protease, nucleoid components, and heat shock proteins) with an emphasis on their interactions and posttranslational modifications.

The Laboratory of Prokaryotic Biology (*Unit #4*) will focus on preparing all the enzymes under study, including bacteriophage tail proteins and endolysins and fungal enzymes involved in plant cell wall degradation, in quality and amounts needed for structural studies, including crystallization, structure solution and functional analysis. Mutations for improving their applicable properties and revealing the structural principles of substrate recognition, enzymatic activity and protein stability will be proposed, and mutated proteins will be prepared and studied. We will continue our long-term international collaboration with EMBL c/o DESY-Hamburg, BRC HAS Szeged, Hungary and CEITEC Brno, Czech Republic and our newer collaboration with the Institute of Chemistry, SAS, Bratislava.

The Laboratory of Protein Evolution (*Unit #6*) will continue to focus on the bioinformatics of amylolytic enzymes in an effort to contribute significantly to this field. Attention will center on individual α-amylase families, *i.e.* GH13 (with GH70 and GH77 forming the clan GH-H), both GH57 and GH119, and even GH126. Emphasis will also be given to the starch/glycogen-binding domains (*i.e.* carbohydrate-binding modules) classified as the so-called CBM families.

These *in silico* results are expected to help experimentalists, saving time and money in their efforts to, for example, design amylolytic enzymes for potential industrial use.

3. Microbial Ecology

The Laboratory of Environmental and Food Microbiology (*Unit #5*) will continue to promote its principal research pillars: food studies and cultural heritage. Food studies will mainly focus on the metatranscriptomic analysis of ewe's milk lump cheese, combined with a chemical analysis to identify the microbial producers of particular flavouring agents during its manufacture. In the area of historical and artistic objects, we will continue to use different culture approaches to isolate specific microbial groups. In order to fully identify the microflor responsible for deterioration and to improve our high-throughput sequencing analysis, various methods will be applied. Eco-friendly, safe disinfection strategies will be optimized. We would also like to apply enzymatic approaches to the restoration of wooden organs. The biodegradation properties of different and novel polymers will be assessed by implementing a new project in cooperation with the Polymer Institute, SAS. Finally, we plan to concentrate our efforts regarding waste water treatment on the bioremediation of pharmaceutical compounds and the investigation of hydrogen-producing microflora.

The Laboratory of Phylogenetic Ecology's (*Unit #5*) newest results from research into catalytic hydroperoxidases will be exploited in applied research-oriented projects. To this end, we have already begun the heterologous expression of a bifunctional catalase-peroxidase from the hyperthermostable archaeon *Archaeglobus fulgidus* in various *E. coli* producer strains with various inducers. After optimizing this expression, we will attempt, together with BOKU University, Vienna, to perform site-directed and random mutagenesis on the corresponding AfkatG gene with the aim of producing biotechnologically relevant improved biocatalysts for clean room monitoring and biopolymerization reactions. Selected genes for hybrid B heme peroxidases, manganese peroxidases, peroxidases-cyclooxygenases and peroxidase-peroxygenases will also be tested and screened for applications in selected biopolymerization and oxo-functionalization reactions. These will be heterologously expressed in the methylotrophic yeast *Pichia pastoris.* The purified recombinant enzymes obtained will be crystallized to determine their 3D structure and reaction abilities. This will provide additional knowledge of their possible physiological roles. In addition, novel bacterial isolates from heavy metal-contaminated soils will be screened to determine what hydroperoxidases they may use to survive in environmentally harsh conditions; their corresponding genes and regulatory elements will be investigated.

4. Functional genomics, bioinformatics and biotechnology

Streptomyces are the main producers of biologically active secondary metabolites, including antibiotics. *Unit #1* has characterized several gene clusters for antibiotics, most recently that for auricin. Its main goal is to produce new biologically active compounds using the biosynthetic genes of auricin and other polyketide antibiotics. We also plan to identify new secondary metabolite gene clusters and promoters by genomic and global transcriptomic analyses of *Streptomyces aureofaciens*. Finally, for biotechnological purposes, we plan to modify *Streptomyces lividans* strains to produce bioactive compounds and heterologous proteins by, for example, deleting gamma butyrolactone systems, sigma factor genes, protease genes, and antibiotic clusters.

The ability of spores to either lie dormant or germinate presents both threats and potential benefits to human health and welfare. For example, botulism and tetanus are infectious diseases transmitted by spores, spores of *Clostridium difficile* are responsible for severe hospital-acquired infections that are expensive to treat, spores of *Bacillus cereus* cause food poisoning and present a challenge to the food industry, and spores of *B. anthracis*, are a well-known concern because of their potential use as bioterrorism and biowarfare agents. In contrast, the durability of spores makes possible their use as probiotics, delivery systems for vaccines, or components of biotechnological applications. *Unit #2* is planning to investigate the self-assembly properties and tertiary structure of Cot proteins, recently discovered by this Unit, in order to understand how one of the most resistant biological layers forms and to determine their possible use in nano-biotechnology.

Bacteriophages are one of the most frequently used model organisms for studying DNA replication. The Laboratory of Genomics (*Unit #4*) will continue to study the bacteriophage BFK20 replication proteins, mainly gp41 (a putative SF2 helicase), gp43 (an SF4 type helicase) and gp44 (DNA polymerase I) together with proteins from the host cell replication machinery. A detailed description of the BFK20 replication mechanisms will widen our knowledge of DNA replication mechanisms for both corynephages and mycobacteriophages. Because phage lysins make promising anti-infective enzybiotics, and because there is growing interest in engineered lysins created by modification or rational design from natural lysins, the laboratory will continue to study the phage BFK20 and phiBP lytic proteins, with the goal of constructing recombinant endolysins with new properties and potentially important applications in medicine and biotechnology. Our specific goals are to investigate the protein-protein interactions during BFK20 infection, and analyse the phage replication proteins together with the host cell replication machinery; to construct engineered endolysins, which exhibit lytic and antibacterial activity to a broader range of bacterial strains, from bacteriophages BFK20 and phiBP; and to identify bacterial factors involved in phage-host interactions and the phage attachment and injection processes.

The Laboratory of Prokaryotic Biology (*Unit #4*) has been searching for a method to rapidly detect pathogenic bacteria (*e.g. Streptococcus*, *Staphylococcus*, *Streptomyces* and *Enterococcus*) using the receptor binding proteins of their phages (RBP, tail proteins). Its present project focuses on the *in silico* identification of RBP genes in the available genomes of bacteriophages and experimental characterization of their functions. The results should extend our knowledge about their genomic presence, their types, sequence organization, and interactions with cell wall components, thereby opening new perspectives on their use for bacterial identification. Additional *in silico* research will screen for endolysins within the available whole genome sequences of *Streptomycetal* actinophages. Functional domains and amino-acid residues involved in binding to and degrading bacterial cell walls will be identified. The tertiary structures of these proteins will be modelled and their structure-function relationships analysed. Because phage endolysins have the potential to be used as an antibiotic substitute, we will design and prepare active synthetic endolysins against both gram negative and gram positive bacteria which should be suitable for simple usage in veterinary medicine. Finally, all of these proteins will be prepared in the amounts and quality needed for crystallization and structural and functional studies. Mutations which enhance potential application properties or which reveal the structural principles of substrate recognition and enzymatic activity will be proposed and proteins containing these mutations prepared.

The Laboratory of Bioinformatics (*Unit #4*) will continue to maintain its position as one of the leading bioinformatics groups in the country, with its main focus on computational genomics. State-of-the-art techniques such as DNA arrays, NextGen sequencing and mass cytometry, require specialists able to analyse massive data sets. The lab will continue to maintain and enhance its biological databases (phiSITE, phiBIOTICS and viruSITE), with the goal of making them some of the most comprehensive resources in the field of viral genomics. In addition to its research activities, the lab will continue to be involved in educating and training in the field of computational biology. Maintaining and enhancing international cooperation and networking is an essential task, especially in this field, and continual participation in key bioinformatics collaborations (such as ELIXIR, EMBnet or Instruct) is a critical point for our future growth.

5. Cellular and molecular biomedicine

During previous research periods, the Laboratory of Molecular Immunology (*Unit #3*) provided comprehensive evidence that (i) the mannose 6-phosphate/insulin-like growth factor 2 receptor (M6P/IGF2R) functions in controlling pericellular proteolysis, vitally contributing to its tumour suppressive properties, and (ii) that M6P/IGF2R controls adaptive immune responses via transporting the primary kinase of T-cell activation, Lck, making it a promising target for modulating T-cell responses in various inflammatory diseases. In future periods, this laboratory will continue its research on both pericellular proteolytic systems and adaptive immune responses. Although this lab has only recently been established as a part of *Unit #3,* these goals arise from the continual, long-term research of its members. Its overall objectives are to delineate those mechanisms that control cell migration and T-cell activation, and

develop strategies to modulate imbalanced biological processes occurring in various human pathologies. Specific questions include: (i) could synthetic and natural peptides derived from the anti-proteolytic proteins, characterised by us, be applied to pharmacologically block the invasion of tumour cells and virulent bacteria, both of which hijack the human proteolytic system to penetrate tissue barriers; and (ii) could the intracellular protein transport machinery, we identified, be used to identify specific T-cell subsets and modulate T-cell responses when these are either insufficient or rampant? We will continue our collaboration with the Center for Pathophysiology, Infectology & Immunology at the Medical University of Vienna.

The Laboratory of Biochemistry and Structural Biology (*Unit #3*) will continue to pursue its two main themes, both of which touch on serious chronic illnesses. Much of the Laboratory's attention will be focused on the role of proteases and heat shock proteins on the function, stability, and dynamics of the mitochondrial nucleoid, taking into consideration the possible influence of post-translational modifications on these proteins. Members of the lab will also continue to study the structure and dynamics of the N-terminal part of hRyR2, and how the arrhythmia-causing mutations change these. It has recently been shown that dantrolene, a drug used to treat malignant hyperthermia, can also be used to ameliorate the effects of these arrhythmias, but the molecular details of the drug-receptor interaction remain unknown. We plan to characterize these interactions using a combination of biochemical assays, X-ray crystallography and small-angle X-ray scattering, and molecular dynamics simulation. Finally, this lab will also study the therapeutic potential of cytomegalovirus proteins and the roles of phosphatidyl inositol transfer proteins in membrane phospholipid homeostasis.

At the beginning of 2016, the Laboratory of Apidology and Apitherapy, headed by Dr. Juraj Majtan, was established at the Institute as part of *Unit #3*. The laboratory's focus is on apimedical science. The laboratory will participate in pre-clinical and clinical studies by applying novel medical devices based on honeybee products. The laboratory is linked with several biotechnological companies involved in developing commercial biomedical products, which should strengthen IMB position in the areas of application and translational medicine.

In the next five years, *Unit #6's* Laboratory of Neurobiology will continue to pursue the two most promising research lines for further elucidating the function of neurotransmitter transporters. First, the Laboratory's recent results indicate that mimicking phosphorylation on certain protein residues not only blocks the calpain cleavage sites in the cytosolic regions of certain neurotransmitter transporters, but also leads to significant transporter accumulation. We plan to verify the hypothesis that phosphorylation-regulated calpain cleavage exposes previously hidden N- and C- terminal sequences, so-called degrons, which subsequently control transporter turnover. This is a potentially new mechanism for transporter regulation. Second, we would like to extend the technique we developed to detect interactions between the short, C-terminal PDZ (postsynaptic density protein-95, discs large, zona occludens-1) motifs of neurotransmitter transporters and the multiple signalling protein MUPP1 to identify other PDZ neurotransmitter transporter interaction partners. We also plan to further characterize previously identified interactions and to discover their potential physiological significance in the regulation of neurotransmitter transporters.

Project proposals submited to 7RP or H2020	**2012**	**2013**	**2014**	**2015**
Institute as coordinator				
Institute as participant	3		2	

4. Other information relevant for the assessment

In 2013, the entire building of the Institute was renovated. The complete process took more than half a year, and during this time, the scaffold of the whole building was open and occupied by construction workers. This reconstruction substantially disrupted scientific work during this period and, since the apparent production of one year is dependent on work done in previous years, thereby diminished our apparent production during the final two years of the evaluation period.

Bratislava, 4 August 2016

RNDr. Ján Kormanec, DrSc.
Director