INSTITUTE OF MOLECULAR BIOLOGY

SLOVAK ACADEMY OF SCIENCES

Mission Statement

- research activities of the Institute of Molecular Biology are focused on **basic research of the molecular principles of living systems**
- **molecular biology and microbiology** are the main directions of the Institute's activity
- the Institute offers **consultancy and expertise** that are closely related to the main activities
- the Institute implements **PhD education** in terms of generally valid regulations
- the Institute guarantees **publication of the results** of R&D activities in periodical and non-periodical press

Scientific Departments

GENOMICS AND BIOTECHNOLOGY

Head
RNDr. Gabriela Bukovská, CSc.
Room A 318

Laboratory of Bioinformatics

Head
Mgr. Ľuboš Kľučár, PhD.
Room A 419

Laboratory of Prokaryotic Biology

Head
RNDr. Ľubica Urbániková, CSc.
Room A 105

Laboratory of Genomics

Head
RNDr. Gabriela Bukovská, CSc.
Room A 318

MICROBIOLOGY

Head
RNDr. Marián Farkašovský, CSc.
Room B 122

Lab. of Phylogenomic Ecology

Head
RNDr. Marcel Zámocký, PhD.
Room A 322

Lab. of Environ. and Food Microbiol.

vedúci laboratória
Dr. Domenico Pangallo, PhD.
Room B 16

Lab. of Molecular Microbiology

Vedúci laboratória
RNDr. Marián Farkašovský, CSc.
Room B 122

BIOCHEMISTRY AND STRUCTURAL BIOLOGY

Head
Ing. Eva Kutejová, CSc.
Room B 28

Lab. of Apidology and Apitherapy

Head
Ing. Juraj Majtán, PhD.
Room A 405

Lab. of Biochem. and Struct. Biology

Head
Ing. Eva Kutejová, CSc.
Room B 28

Lab. of Molecular Immunology

Room
Mgr. Vladimír Leksa, PhD.
Room A 206

PROTEIN BIOLOGY AND EVOLUTION

Head
Ing. Štefan Janeček, DrSc.
Room A 204

Laboratory of Protein Evolution

Head
Ing. Štefan Janeček, DrSc.
Room A 204

Laboratory of Neurobiology

Head
RNDr. František Jurský, CSc.
Room A 420

GENE EXPRESSION

Head
RNDr. Ján Kormanec, DrSc.
Room A 205

MICROBIAL GENETICS

Head
RNDr. Imrich Barák, DrSc.
Room A 221

JOURNAL BIOLOGY

Section *Cellular and Molecular Biology*

Managing Editor
Ing. Štefan Janeček, DrSc.
Room A 204

EMBnet NODE

Manager
Mgr. Ľuboš Kľučár, PhD.
Roomť A 419

General information on the research and development activity

Institute of Molecular Biology
Slovak Academy of Sciences

Research activities

- Cell division and differentiation
- Protein structure-function relationships and protein evolution
- Microbial ecology
- Functional genomics, bioinformatics and biotechnology
- Cellular and molecular biomedicine

1. Cell division and differentiation

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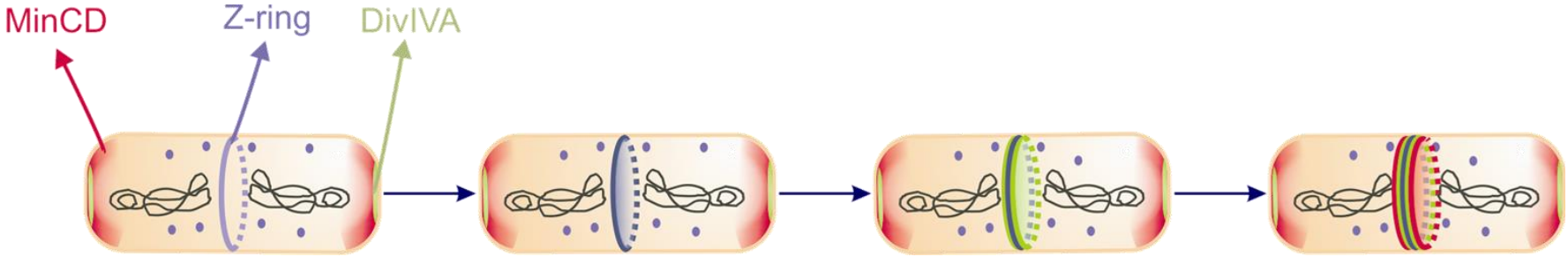
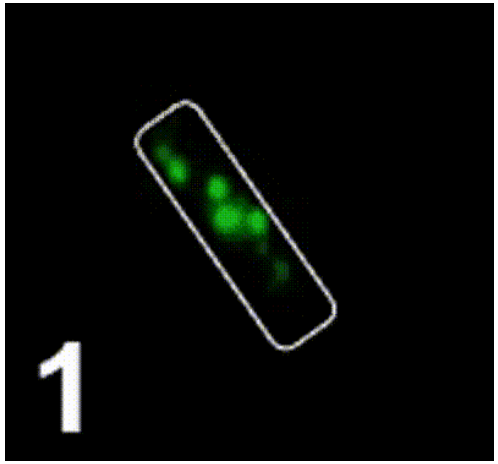
How the bacterial cells recognize the site of septation?

Min system ⇒ MinCDE and MinCD/DivIVA, MinJ

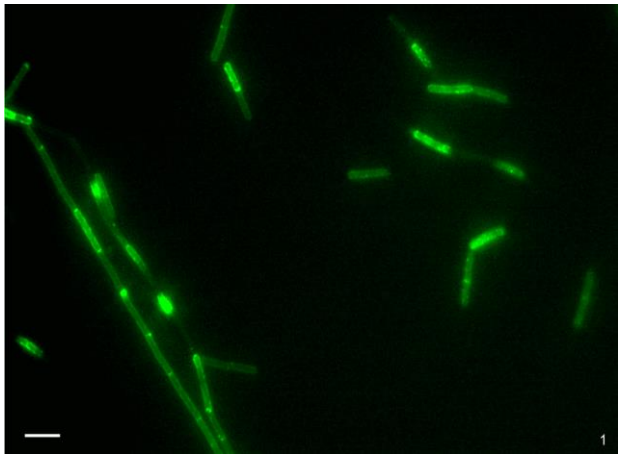


Bacillus subtilis



strain	$MinD_{Bs}$	$MinJ_{Bs}$	$MinD_{Cd}$	$MinE_{Cd}$	sporulation efficiency	oscillation	DSM plate
MO1099	$MinD_{Bs}$	$MinJ_{Bs}$	-	-	100%	-	
IB1056	-	$MinJ_{Bs}$	-	-	85 ± 2%	-	
IB1417	$MinD_{Bs}$	$MinJ_{Bs}$	$MinD_{Cd}$	$MinE_{Cd}$	32 ± 4%	+	
IB1418	-	$MinJ_{Bs}$	$MinD_{Cd}$	$MinE_{Cd}$	45 ± 4 %	+	
IB1545	-	-	-	-	97 ± 4%	-	
IB1546	-	-	$MinD_{Cd}$	$MinE_{Cd}$	0.03 ± 0.04 %	+	
IB220 *	$MinD_{Bs}$	$MinJ_{Bs}$	-	-	0.01 ± 0.004 %	-	

* *ΔSpo0A* used as negative control



Grant Projects
VEGA
APVV

Publications
J. Mol. Biol. (2012); Microbiology-SGM (2012); Int. J. Mol. Sciences (2013);
Environ. Microbiol. (2013); Front. Microbiol. (2013);

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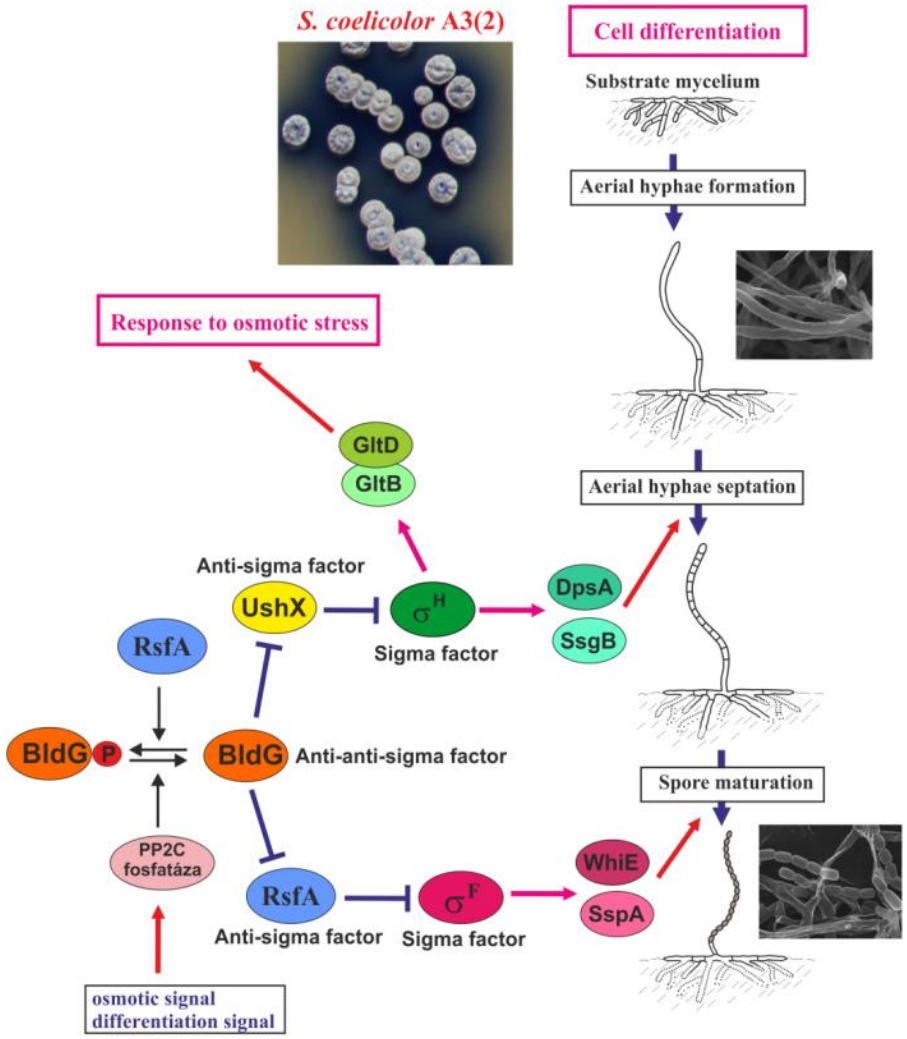
Regulation of morphological differentiation in Streptomyces

- *Streptomyces* undergo a remarkable process of morphological differentiation connected with production of antibiotics
- Remarkable amount of genes for sigma factors (65) and their regulators (anti-sigma factors, anti-anti-sigma factors)
- Revealed role of several of them in differentiation and response to stresses
- Discovery of unique signal transduction pathway activating SigH and SigF through a single anti-anti sigma factor BldG
- These two sigma factors direct expression of genes involved in regulating two discrete developmental stages and response to osmotic stress



Grant Projects
VEGA

Publications
Gene (2012)
Gene (2014)

2. Protein structure-function relationships and protein evolution

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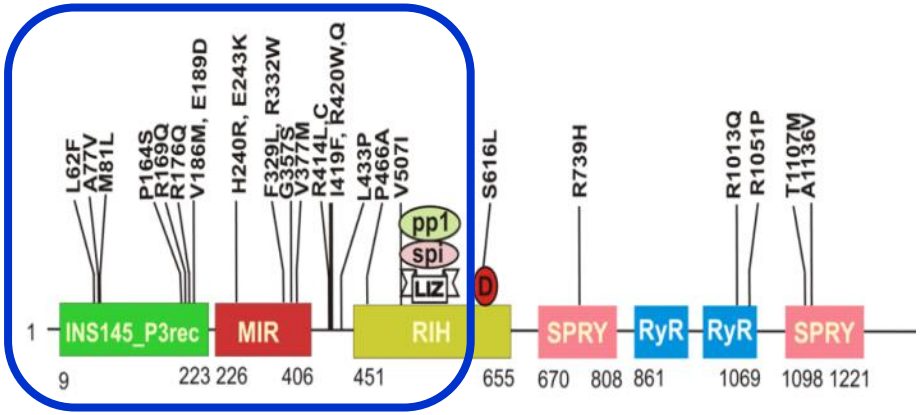
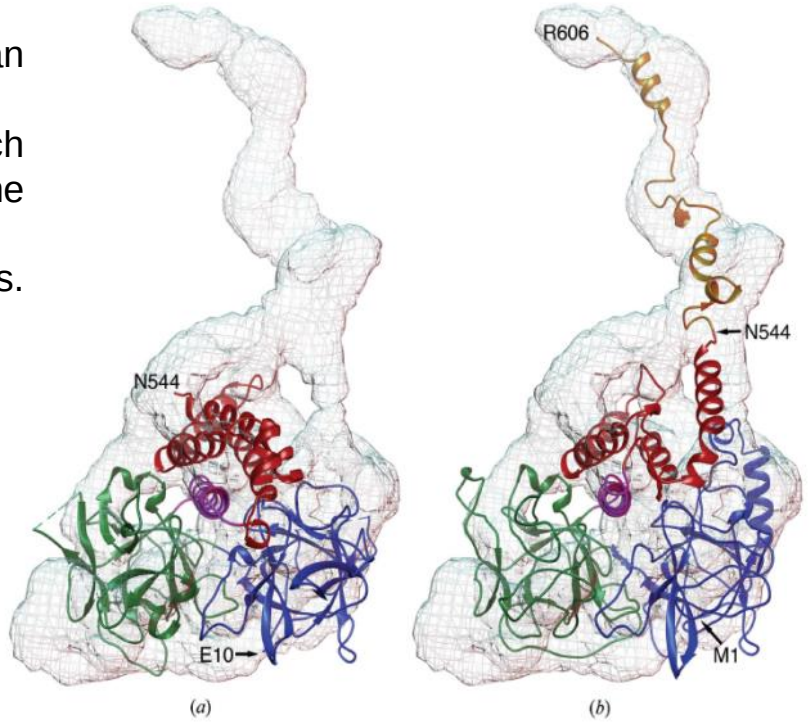
Human ryanodine receptor

- X-ray and SAXS structure of the N-terminal domain of human ryanodine receptor hRyR2
- RyR2 is a calcium release channel in myocytes which transports Ca^{2+} ions from sarcoplasmic reticulum into the cytoplasm, maintaining regular heart function
- Mutations to the human *ryr2* gene cause heart arrhythmias. One of the three mutation clusters is at the N-terminus.





SAXS structure of hRyR2 N-terminal domain (NTD) with docked crystal structure.

2015 – SAS prize awarded to a team from IMB SAS and IMFG SAS for RyR2 structural and functional studies

2014 – Press conference regarding structural and biophysical research on hRyR2 NTD

Publications

Acta Cryst. (2014)

Prot. Pept. Lett. (2013)

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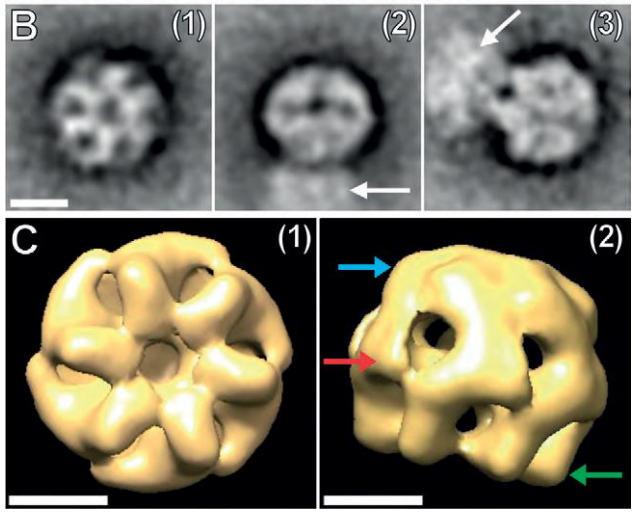
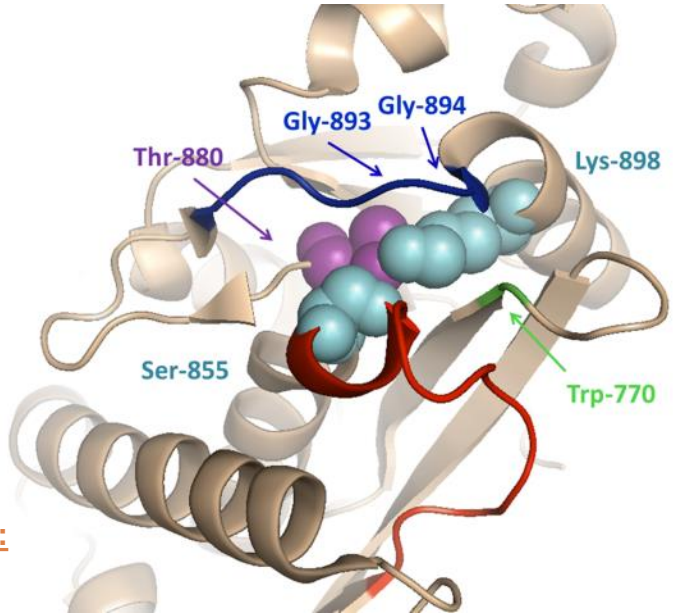
Mitochondrial ATP-dependent protease Lon

- Mitochondrial ATP-dependent protease Lon, which plays a crucial role in the maintenance of mitochondrial homeostasis. Changes in *h*Lon expression have been linked to severe diseases, including epilepsy, myopathy, paraplegia and cancer.
- 16 mutants designed, prepared and characterized. Proteolytic site connected to its ATP binding site through two loops (Gly894-894 and Trp770)
- Movement of these loops is connected with substrate binding that leads to activating ATPase hydrolysis, subsequent structural changes in proteolytic domain and degradation of the substrates
- *h*Lon is a homo-oligomer with six subunits and flexible N-domain according electron microscopy





Publications: ***FEBS J.*** **(2014);** ***J. Struct. Biol.*** **(2012)**
Folia Biologica **(2014)**

Grant projects:
APVV
VEGA

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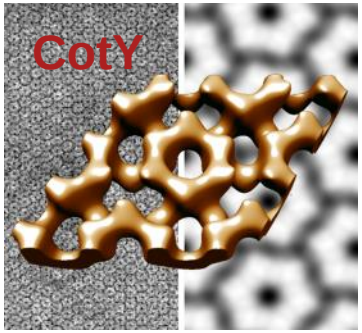
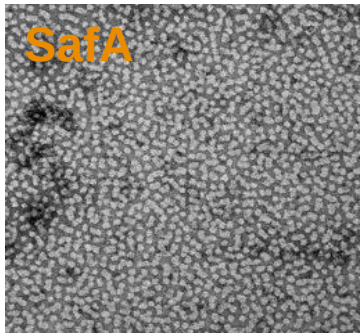
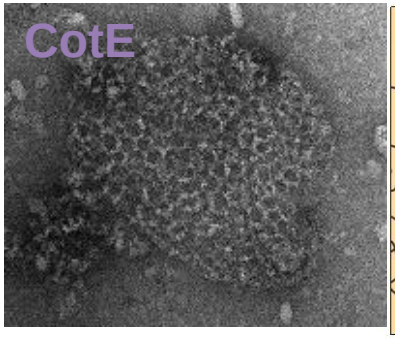
Slovak Academy of Sciences

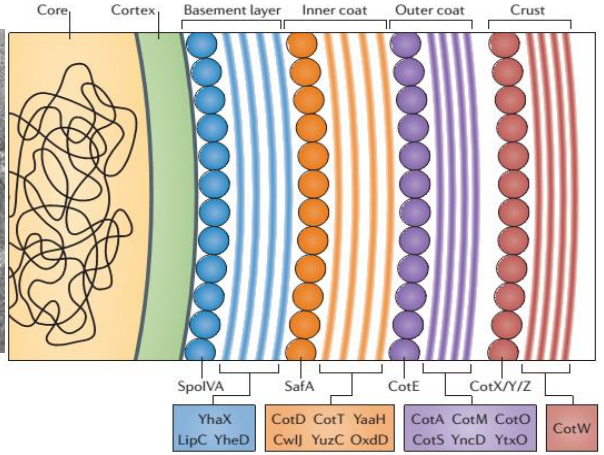
Structure of spore coat proteins

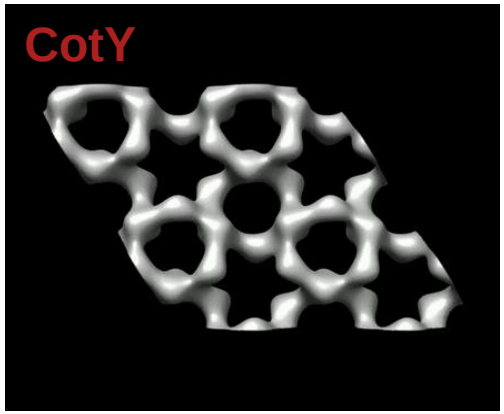
Spore coat proteins self assembly

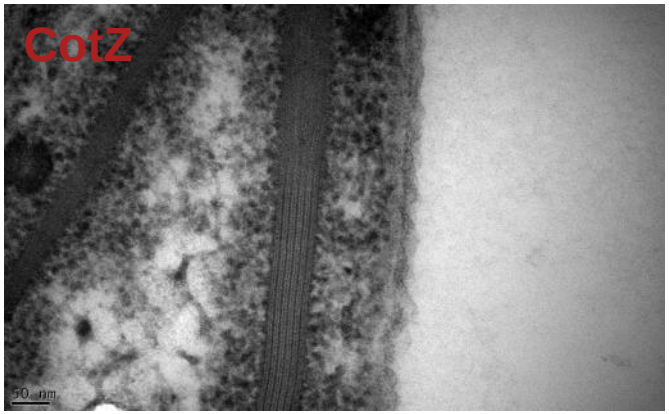


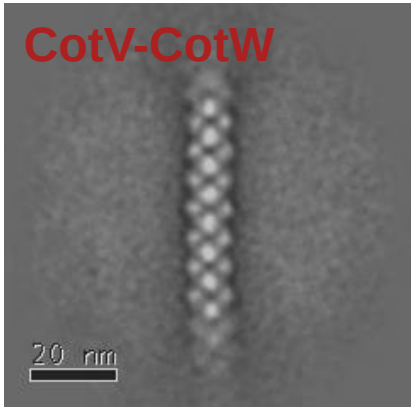












Grant Projects
VEGA; APVV; SCOPE

Publications
Chem. Asian J. 2012; J. Struct. Biol. 2013
Mol. Microbiol. 2015; J. Struct. Biol. 2015

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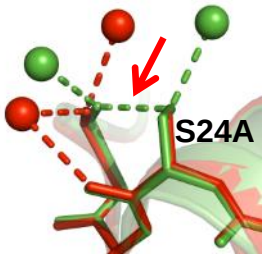
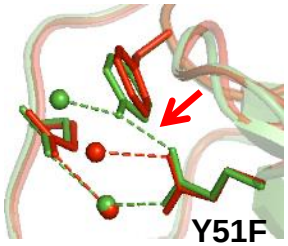
New 3D protein structures

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

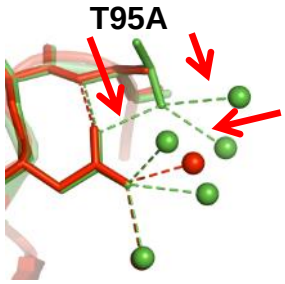
RNase Sa mutants S24A, Y51F, T95A
(PDB ID: 4GHO, 4J5K, 4J5G)

Δ(ΔG)= -0.5 kcal/mol

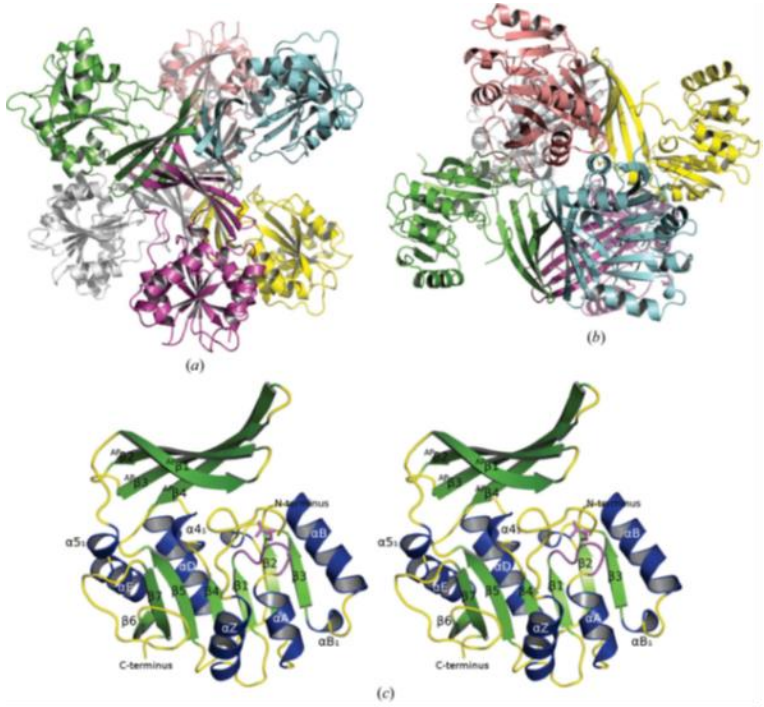




Δ(ΔG)= -2.3 kcal/mol



Δ(ΔG)= -0.3 kcal/mol



CcbJ methyltransferase X-ray structure

Publications:
Protein Sci. (2014)

Publications:
Acta Crystal. (2014)
ChemBioChem (2013)

Evaluation 2012-2015
Bratislava, November 2016

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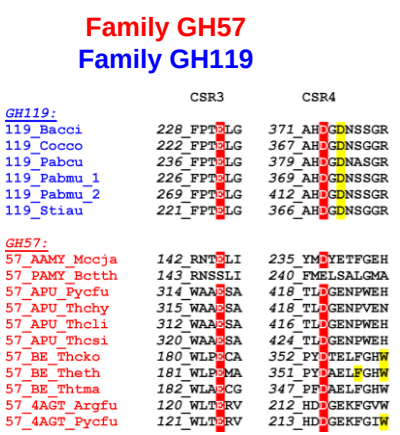
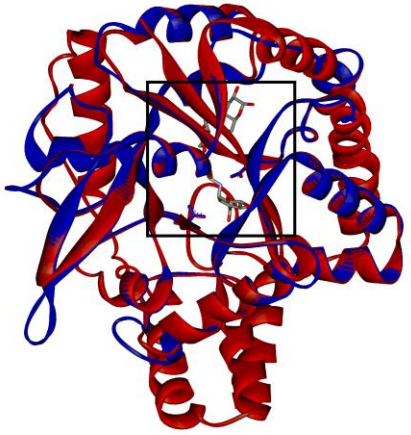
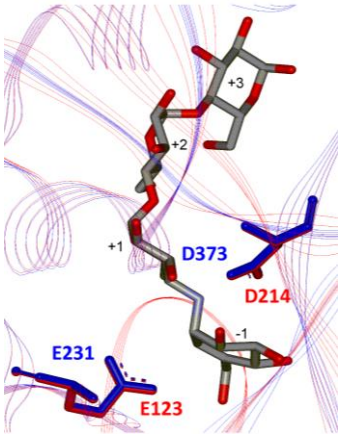
Describing evolutionary relationships in protein families
(α-amylase and glucanotransferases families)

- Identified conserved sequence regions for individual enzymes in the α-amylase family GH57 and revealed the unambiguous evolutionary relatedness between the families GH57 and GH119, including the domain fold and catalytic machinery
- Described detailed evolutionary relationships among the 4-α-glucanotransferases from the family GH77 with focus on amylomaltases from borreliae and disproportionating enzymes-2 from plants

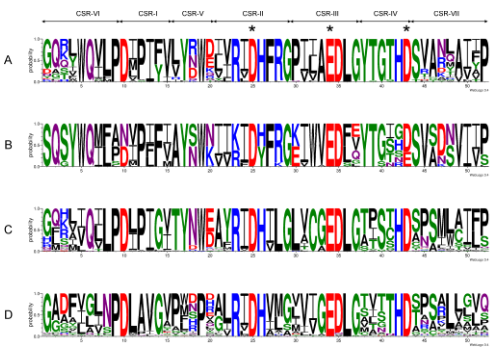
Family GH57
Family GH119

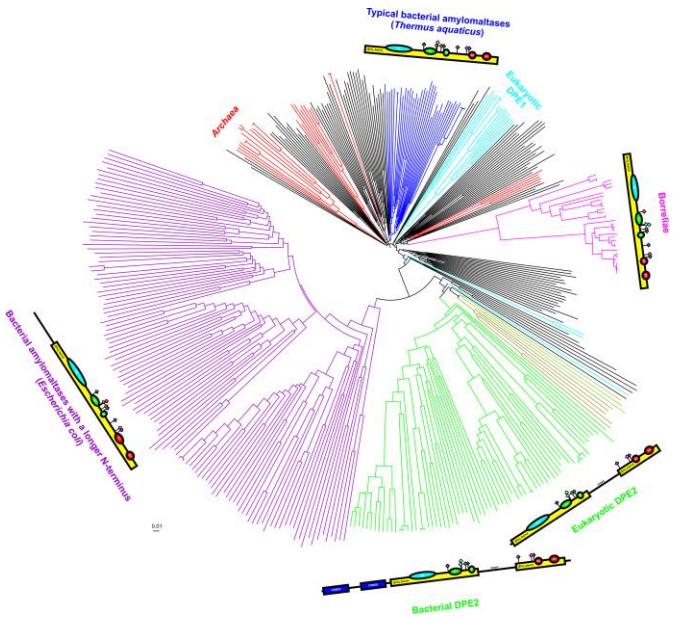






Family GH77



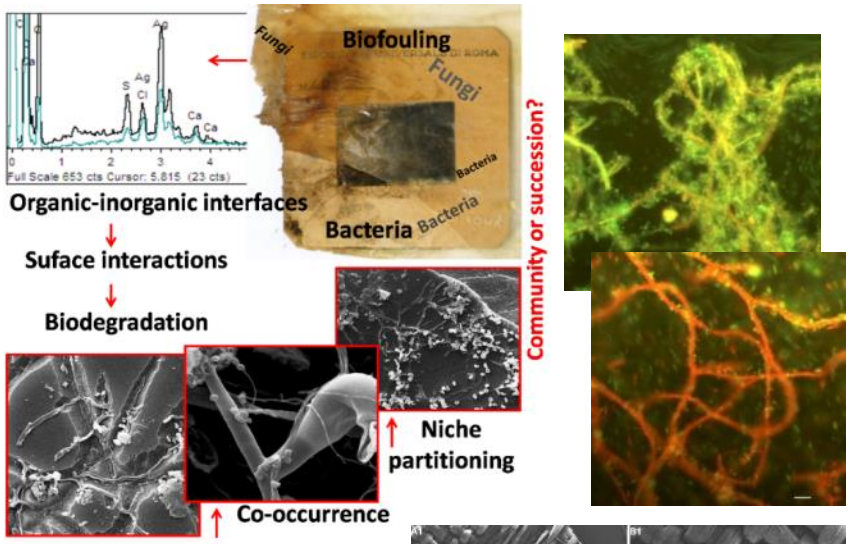


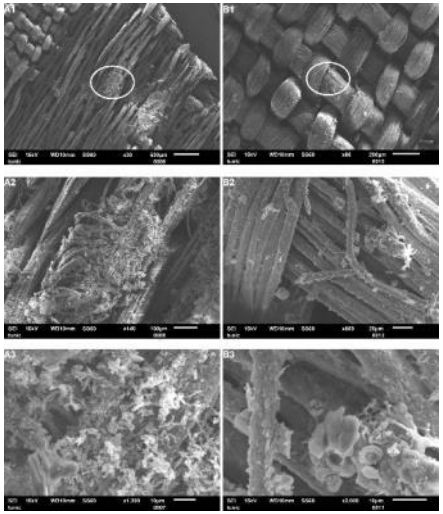
Grant Projects
APVV - LPP
VEGA

Publications
Extremophiles (2012), *FEBS Lett.* (2012)
Microbiology (2013)
Biochim. Biophys. Acta (2015)

3. Microbial ecology

Microbial diversity





- **Investigation of the microbial diversity in cultural heritage objects**
- **Investigation of the microbial diversity in bryndza-cheese and wine**
- Optimization of different non-destructive protocols for sampling, microscopic observation and material analysis
- Development of new approaches for the metatranscriptomics study of food microbial populations (Illumina MiSeq)
- Development of culture-independent strategies RNA- and DNA-based for the identification of microbiome

Grant Projects
VEGA

SAS Prize 2016

Publications
Environ. Microbiol. (2015a; 2015b)
Polym. Degrad. Stabil. (2014)
Extremophiles (2014)
Microbiol. Res.(2013)
Int. Biodeterior. Biodegrad. (2012)
World J. Microbiol. Biotechnol. (2012)

4. Functional genomics, bioinformatics and biotechnology

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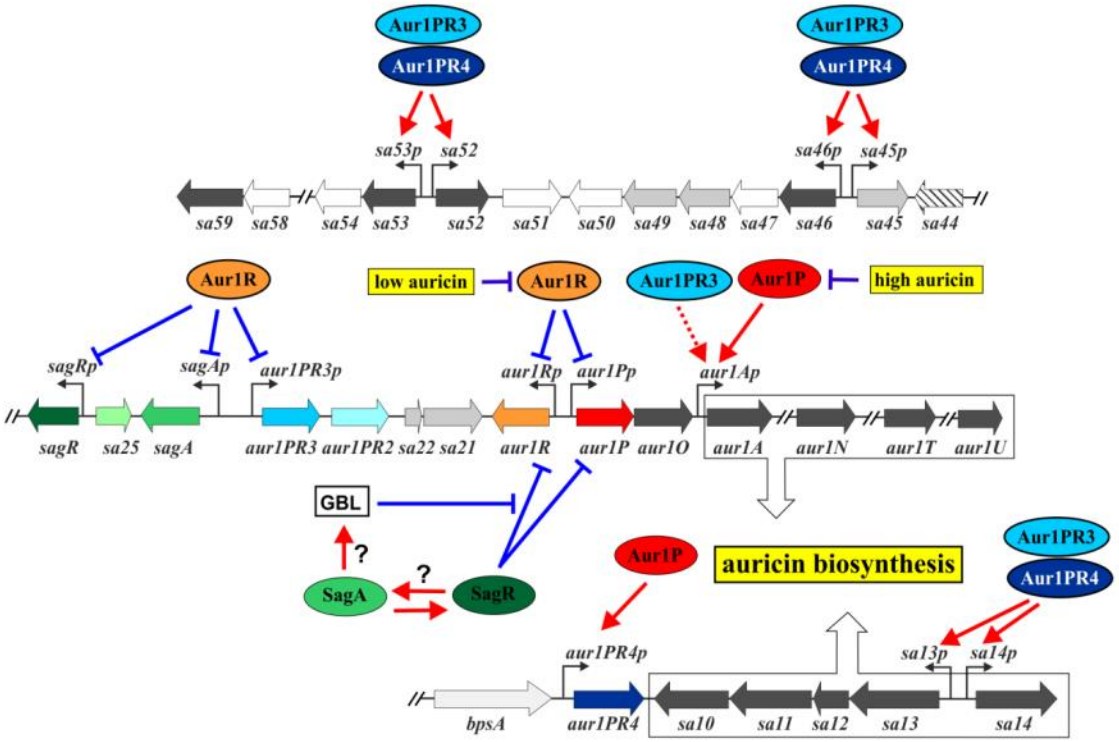
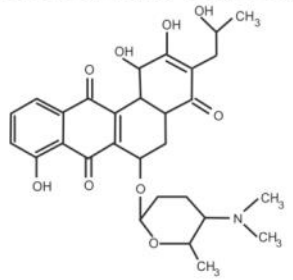
Unique polyketide antibiotic auricin

- A new gene cluster in *Streptomyces aureofaciens* responsible for the production of a unique polyketide antibiotic auricin was identified

- Auricin production arises from a unique, strict, complex regulation mechanism, involving both feed-forward and feed-back control by auricin intermediates through several transcriptional regulators at several levels



Auricin with D-forosamine; Mr=541.11973; C28H31N1O10



Grant Projects
APVV
7RP EU
SAS Prize 2014

Publications
Appl Microbiol Biotechnol (2013; 2014, 2015)
FEMS Microbiol Lett (2013a; 2013b)
Nature Chem Biol (2015)

Institute of Molecular Biology
Slovak Academy of Sciences

Bioinformatics

Biological databases

www.phisite.org

phiSITE
Database of Gene Regulation in Bacteriophages
Home | Search | Browse | Phages | Tools

www.phibiotics.org

phiBIOTICS
Catalogue of Therapeutic Enzybiotics
Home | Browse | Tools | Links

www.virusite.org

viruSITE
integrated database for viral genomics

Hardware

Linux

Software

Galaxy

CSC

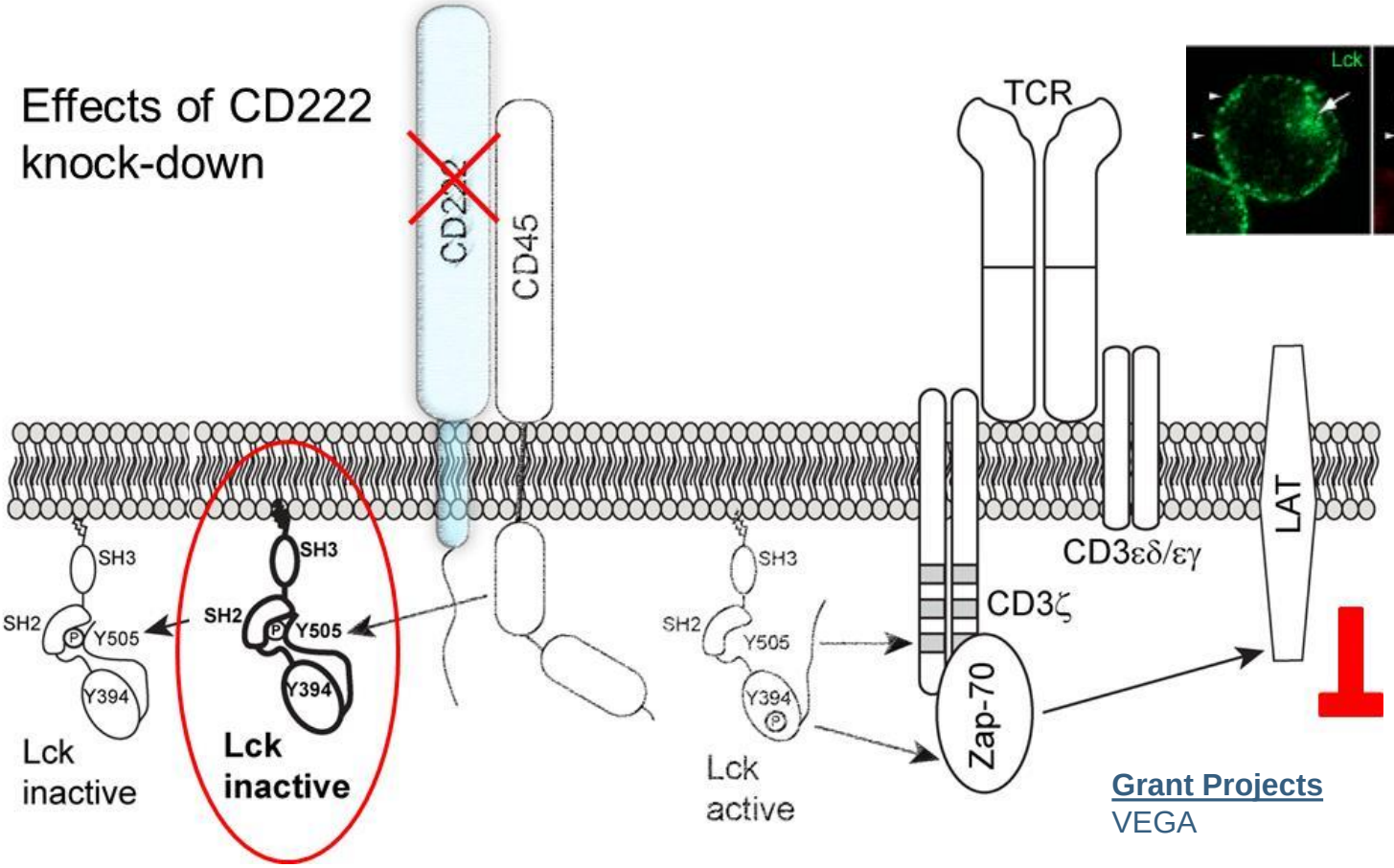
Chipster
Open source platform for data analysis

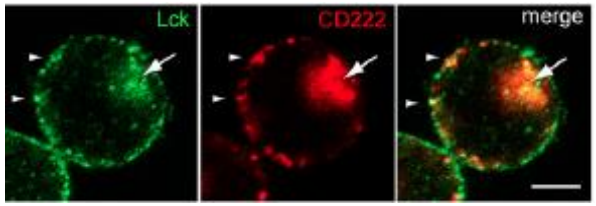
5. Cellular and molecular biomedicine

Institute of Molecular Biology
Slovak Academy of Sciences

Regulator of early T cell signalling cascade

- The Late Endosomal Transporter CD222 (cation-independent mannose 6-phosphate/insulin-like growth factor 2 receptor) is a key regulator of the early T cell signaling cascade by transporting crucial kinase Lck





Grant Projects
VEGA

Publications
J Biol Chem (2012)
J Immunol (2014)

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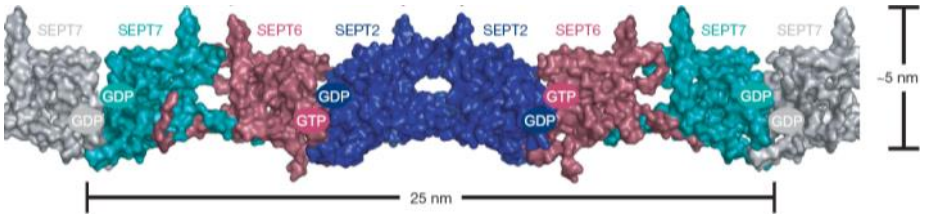
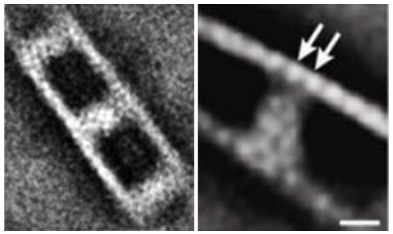
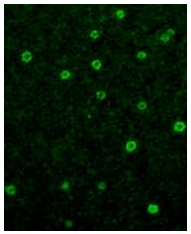
Septins – components of cytoskeleton

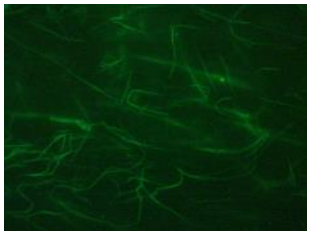
- Septins – a component of cytoskeleton, essential for cytokinesis and membrane remodelling
- Septins have been implicated in several types of cancers and in neurodegenerative disorders

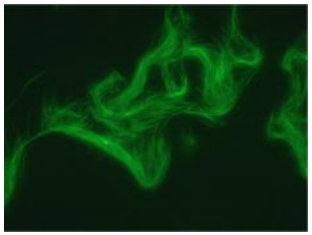


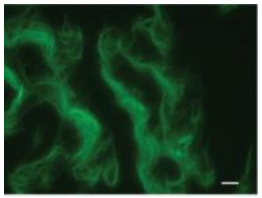
- Interactions of several yeast proteins with septins; Gic1 and Bni5 stabilize septin rings by bridging individual filaments; Elm1 kinase with Bni5 participate in septin filament disassembly; Shs1 septin trigger formation of ring structure.



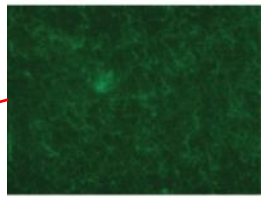




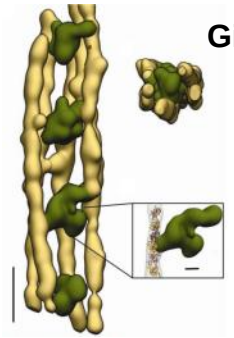




- Elm1



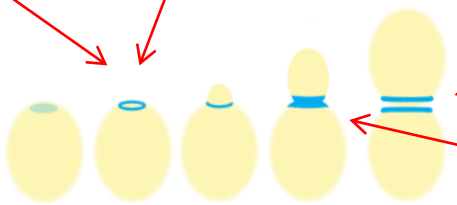
+ Elm1

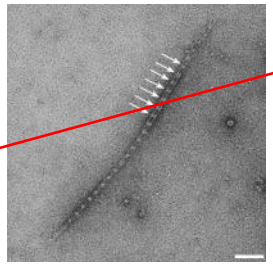


Gic1-septin

Shs1

septin





Bni5-septin

Bni5-septin

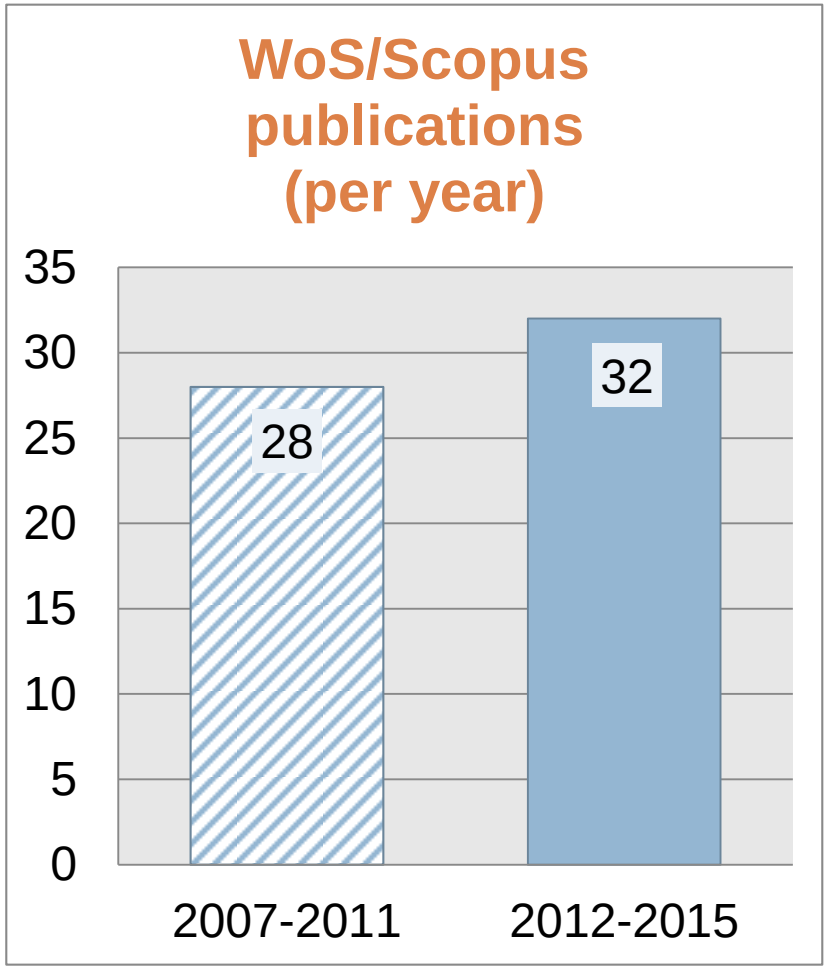
Grant Projects
VEGA
Humboldt Foundation

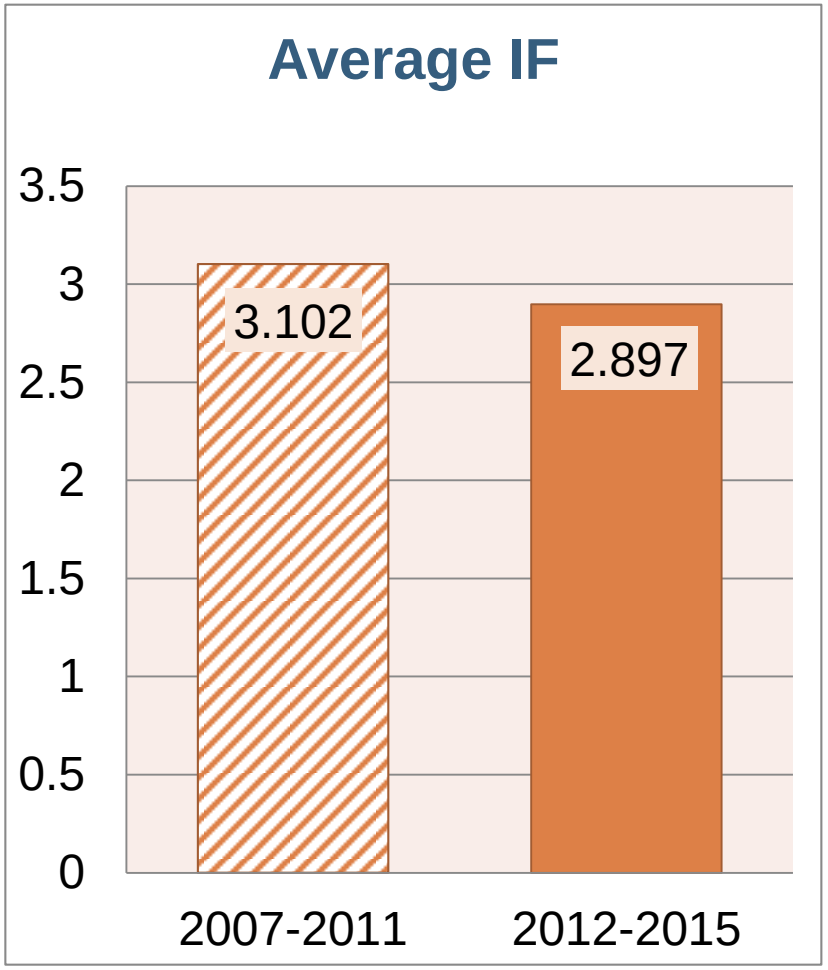
Publications
Elife (2013)
Biol Chem (2015)

Research output
and
Responses to the research outputs

Institute of Molecular Biology
Slovak Academy of Sciences

Impacted publications





MIF for Microbiology: 2.483
MIF for Biochemistry and Molecular Biology: 2.653

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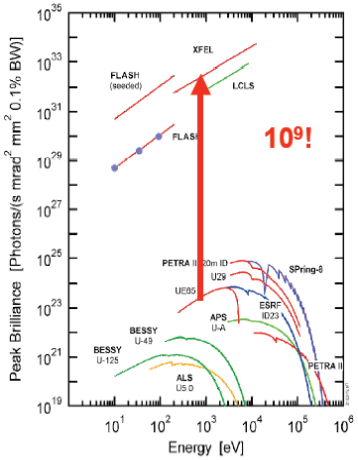
WoS citations

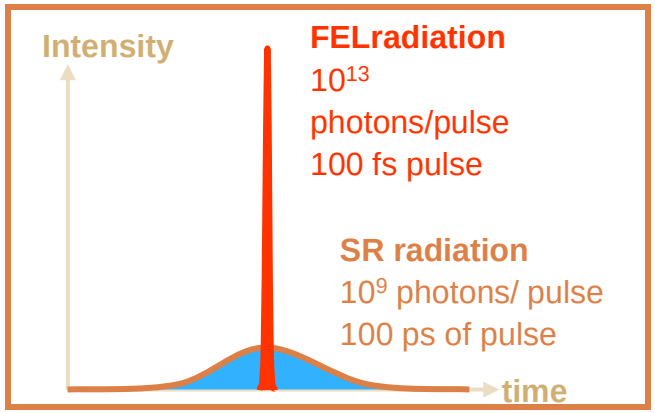
Research status of the Institute in international and national contexts

The most important research activities

- Member of one **6FP** and two **7FP** consortia
- Member of **Scopes-Swiss** Science Foundation consortium
- Partner in two **EU COST** Actions
- Partner in **ESFRI** program **INSTRUCT** (Integrated structural biology unlocking the secrets of life) and **ELIXIR** (A distributed infrastructure for life-science information)
- We host the Slovak **EMBnet** node – as a part of The Global Bioinformatics Network
- Member of **BACELL** – link together academia and industrial partners related to Bacillus subtilis research
- Partner in European **XFEL** (X-ray Free Electron Laser) in Hamburg

X-ray Free Electron Laser in Hamburg

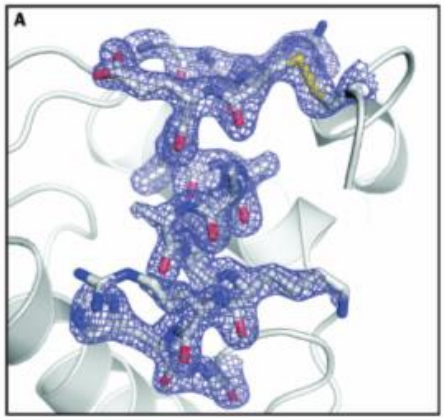




What is XFEL?

- 3.7 km laser – linear electron accelerator
- Depth of tunnels – 6 to 38 m
- Provide hard X-ray radiation
- Energy - 17.5 GeV
- Wavelength - 0.1 – 6 nm
- Frequency of flash - 100 fs
- Number of pulses / s - 27 000
- Price: 1,3 bilion €

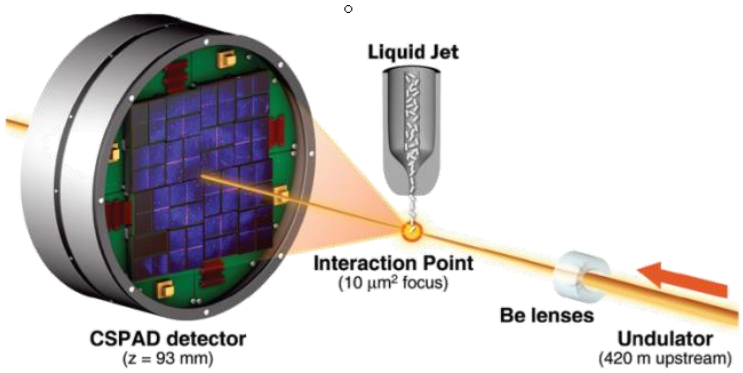
X-ray Free Electron Laser in Hamburg



X-ray Free Electron Laser (**XFEL**) in Hamburg
Serial Femtosecond Crystallography – **SFX**
XFEL-based Biology Infrastructure - **XBI**

SFX and XBI as an opportunity for Slovak structural biologists

Protein quality pre-screening center for SFX in Slovakia?



	LCLS (120 Hz)	XFEL.EU (27,000 pulses / sec)	XFEL.EU (3,000 pulses / sec)
Measurement time	14 min	3 sec	31 sec
Number of possible structures per day (1 min exchange time)	96	1.370	950
Volume of suspension	140 μL	0.5 μL	5 μL
Amount of protein	1,400 μg	5 μg	50 μg
Amount of protein with pulsed jet	10 μg	0.5 μg	5 μg

(Co)organised international conferences

2013: ALAMY_5

(The 5th Symposium on the Alpha-Amylase Family)

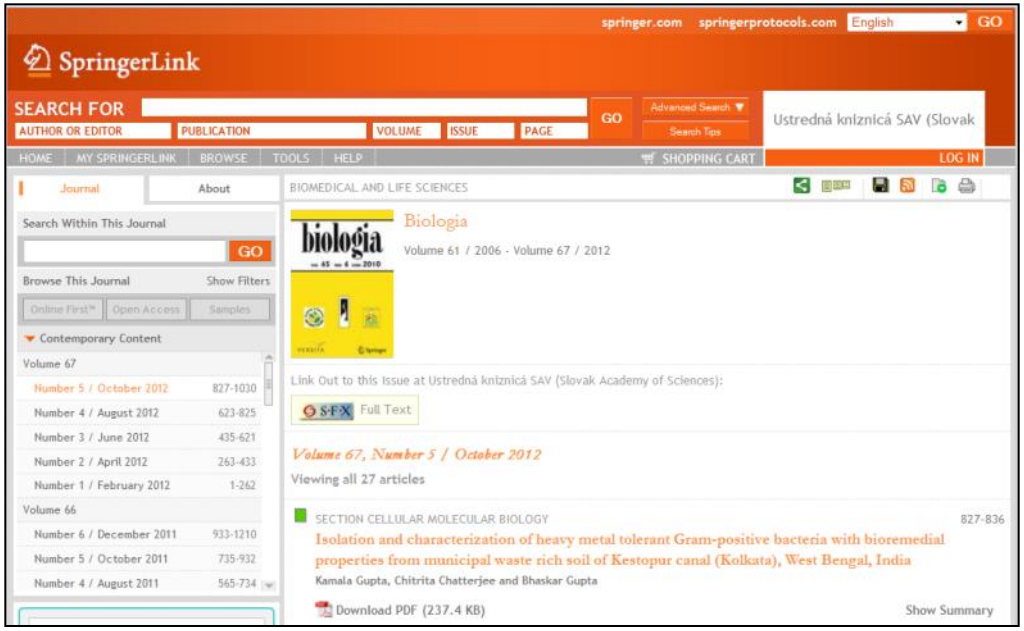
2014: Bacell 2014

(meeting organizes annually by the European *Bacillus* community)

2015: Closing **COST** Conference **"Next Generation Sequencing: a look into the future"**

COST Action BM1006: Next Generation Sequencing Data Analysis Network

Biologia (Section Cellular and Molecular Biology)



Biologia publishes high-quality research papers in the fields of microbial, plant and animal sciences.

The papers on microbial sciences cover all aspects of Bacteria, Archaea and microbial Eucarya including biochemistry, cellular and molecular biology, genomics, proteomics and bioinformatics.

Full-paper contributions should present original experimental, methodological or theoretical research. Review articles are preferably by invitation but unsolicited reviews are equally welcome.

Online content: http://www.springer.com/life+sciences/journal/11756

Indexed/abstracted: Current-Contents, Web-of-Science, Scopus, etc.

Impact Factor : 0.506 (2012), 0.696 (2013), 0.827 (2014), 0.719 (2015)

Manuscript submission: http://www.editorialmanager.com/biologia/

PhD studies and educational activities

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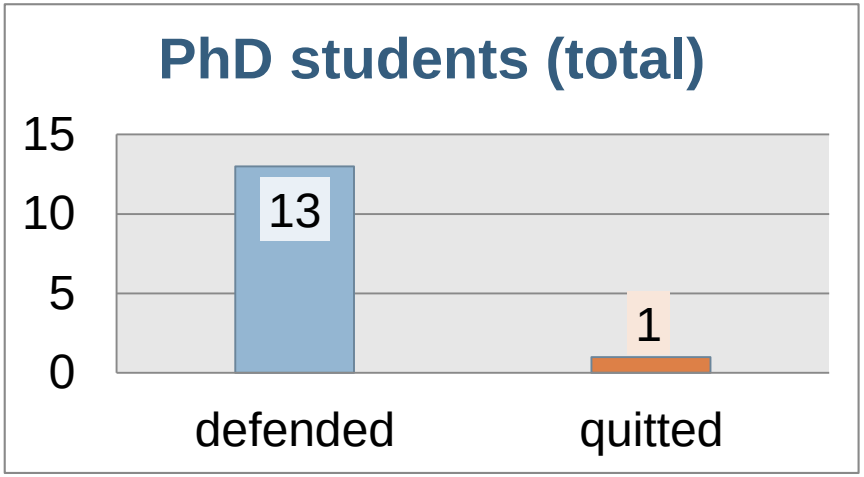
PhD studies

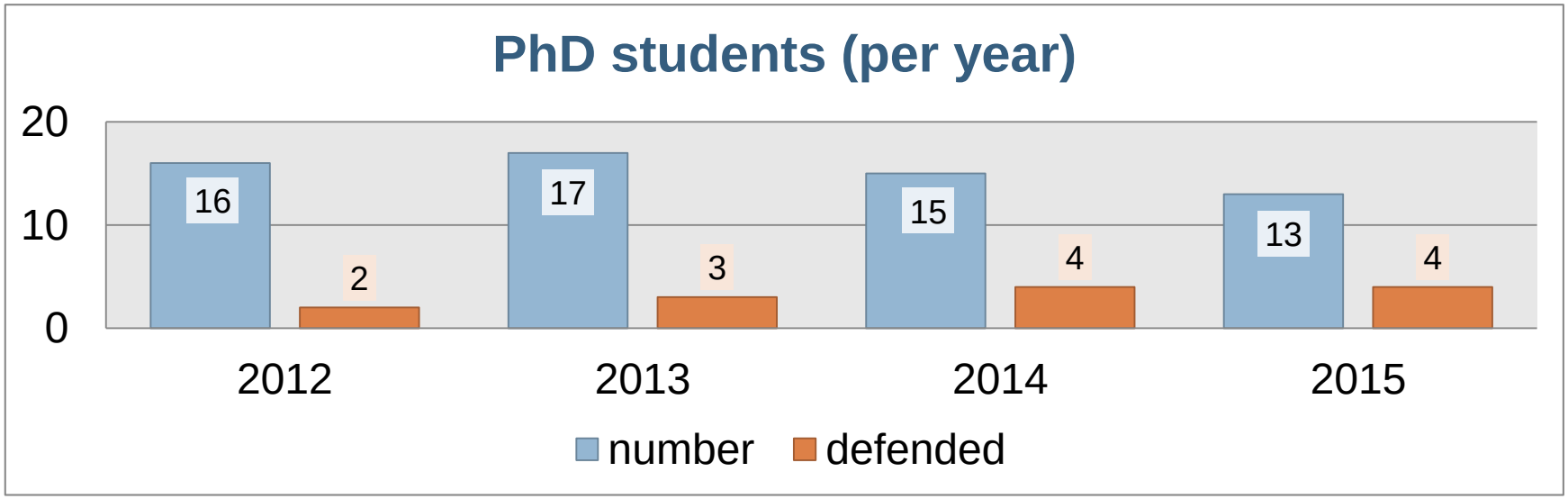
4.2.3 Molecular Biology

Comenius University

4.2.7 Microbiology

Comenius University





Pedagogical activities

Comenius University, Bratislava

Faculty of Natural Sciences
Faculty of Pharmacy
Faculty of Medicine

University of SS. Cyril and Methodius, Trnava

Faculty of Natural Sciences

Slovak University of Technology, Bratislava

Faculty of Chemical and Food Technology

	2012	2013	2014	2015
Lectures (hours/year)	313	273	343	210
Practicum courses (hours/year)	455	186	321	476
Supervised bachelor and diploma thesis	23	18	11	34

Social impact

Social impact

Important results in applied research projects

- New strains from Ni and Cr-contaminated soils useful bioremediation
- Utilization of microorganisms for nitrogen fertilizers (Slovak SME GLsystems)
- Novel compound from poplar tree propolis effective against honeybee pathogens
- Genetically-manipulated *Streptomyces* strain enabling increase production of mithramycin (Spain SME Entrechem)
- Analyzed microflora of bioreactors to decrease pollutants and increase methane production (Taiwan collaboration)
- DNA chip for detection of tick-borne pathogens
- Microbial diversity in Slovak bryndza-cheese and wine grapes to increase their taste and quality
- New bacteriophages and recombinant endolysisn for treatment of bacterial infections
- Synthetic heme peroxidase for biopolymerization reactions (Slovak SME Slovgen)

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Initiative "*Science wants to live!*"

Science and research in Slovakia face continuing insufficient funding. Among the countries of EU and OECD, Slovakia ranks lowest in financing the science. Further budget cuts (17%) for SAS were announced in 2014 for the year 2015.

Initiative ***Science wants to live!***
(www.vedachcezit.sk)

- we are informing on the pitiful situation and distortion of the system in Slovak science
- we want to provide space for ideas and comments and bring constructive suggestions for the discussion and initiate systematic changes
- we want to popularise and propagate science in the public as well as in the media and remind of the importance of science for the life of a society

Popularisation of Science (outreach activities)

Popularisation of Science

Annual **Open doors at IMB SAS** in frame of the *European Science and Technology Week*

Annual **Researcher's Night** funded by the EC

- 11 articles in press media / internet
- 8 appearances in telecommunication media
- 23 public popularisation lectures

BACKGROUND AND MANAGEMENT

Background and management

- Improved infrastructure of IMB due to the participation in 7 EU-funded projects of structural funds
- Postdoctoral fund: we have hired new young scientists and new group leaders creating two new laboratories – Dr. Leksa and Dr. Zamocky
- In 2013, the Department of Molecular Apiddology moved to IFE SAS
- In 2015, Dr. Majtan moved form IZ SAS and established a new laboratory
- 6 departments with 13 independent laboratories were established
- In 2015, two new DrSc (Zamocky and Pangallo)
- **In 2013, reconstruction of the entire building of IMB SAS**

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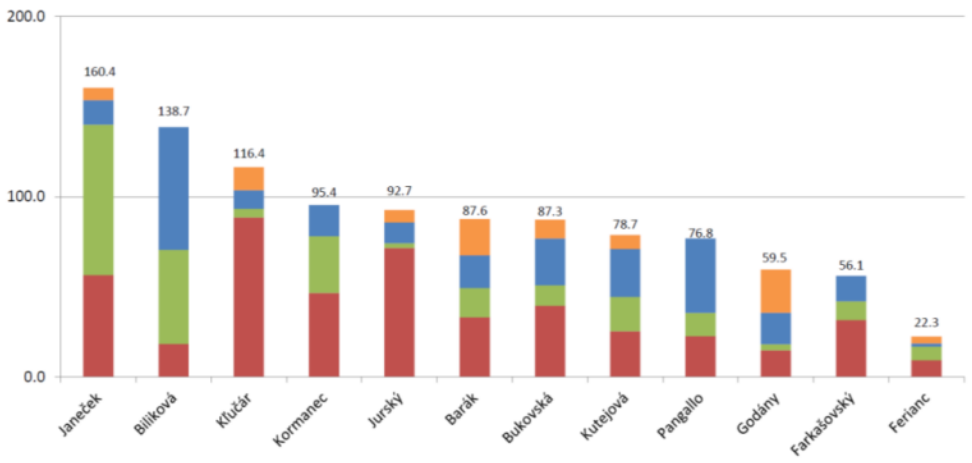
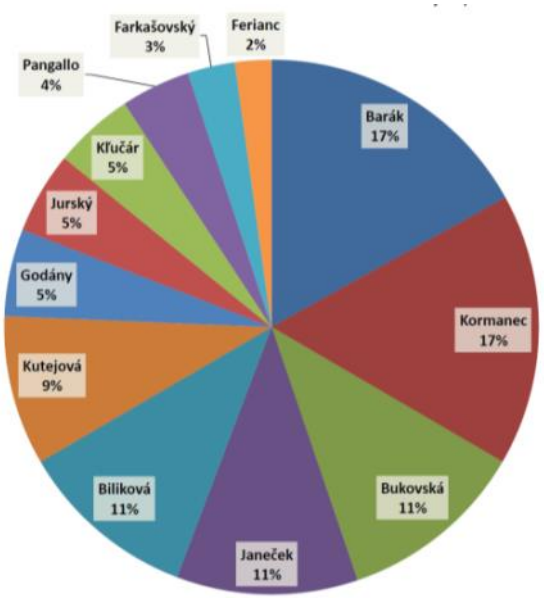
Scientific Board

- maintain internal Management Principles
- recommendation on new research employees, postdocs and PhD students
- annual evaluation of departments and laboratories





Implementation of recommendations from previous assessment

For the period of 2007-2011 the Institute was evaluated in category A

Improvement of spreading know-how by senior scientists to younger staff and PhD students by means of organization of courses

- organisation of several conferences and courses (*Bioinformatics analysis of DNA microarray and NGS data*, *Our proteins*)
- seminars to help PhD students

The streaming of the institute's activity towards the application sphere should be strengthened

- difficult in our field, almost no biotechnological companies in Slovakia, our projects are oriented toward basic research
- collaborative 7th FP project STREPSYNTH including SME, new genetically-manipulated strain prepared for one company to increase production of mithramycin
- Slovak SME GLsystems – utilisation of microorganisms for nitrogen fertilizers
- Slovak SME Slovgen – biotechnological applications of peroxidases
- Protection of cultural heritage – collaboration with Slovak National Library, Gallery and Archives

The effort should be made to provide financial support for PhD students out of the frame of regular budget

- rather limited possibilities in Slovakia, partially from external grants (APVV), foreign collaborative grants (Austria-Slovakia) and Humboldt Foundation
- 4 Postdocs co-funded by Schwartz Fund

Thank you for your attention!