Institute of Molecular Genetics of the ASCR, v. v. i.

Annual Report

2015 – 2016

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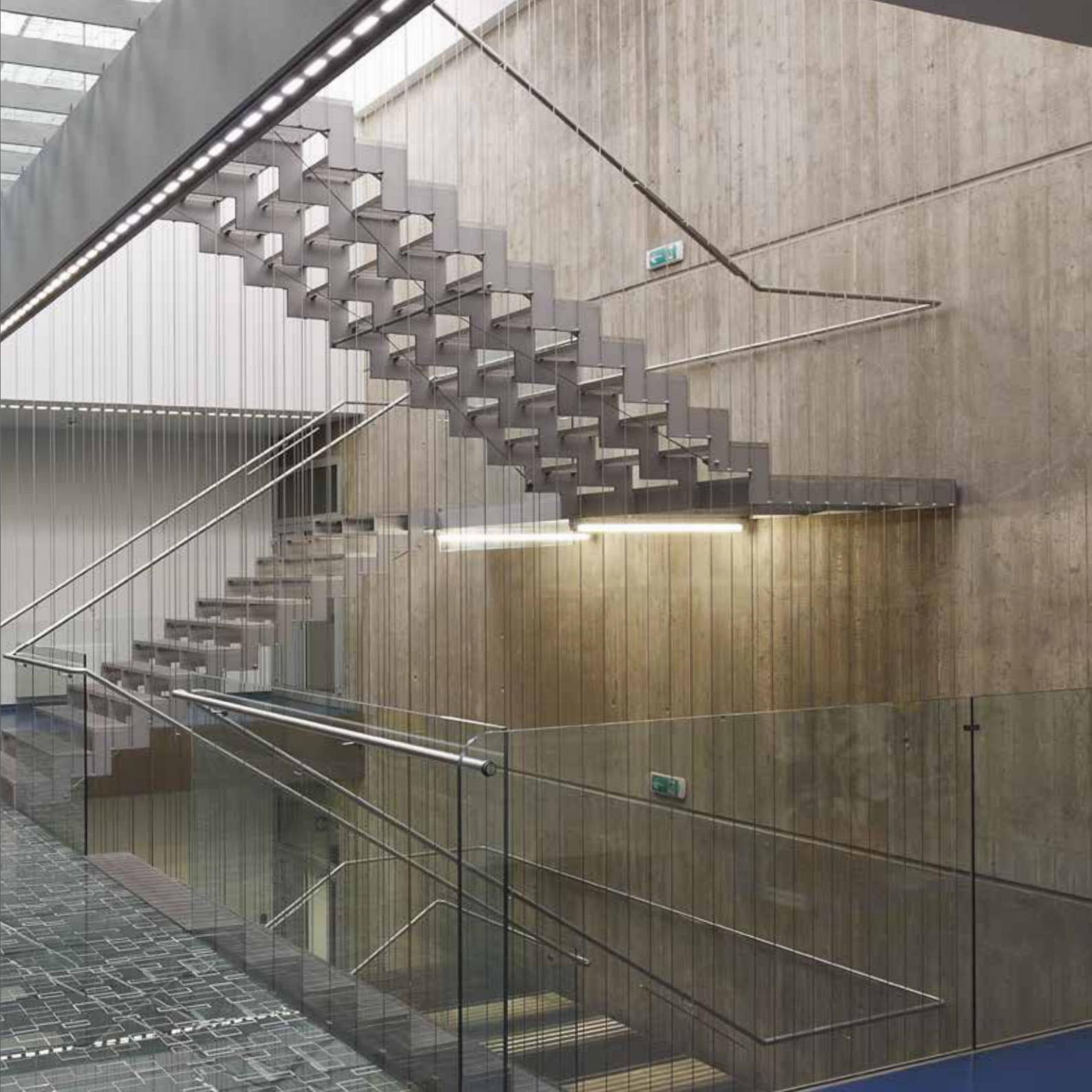


Introduction

In the past two years we were successful in what is our raison d'être – good science. We have again published a number of scientific reports in peer-reviewed international scientific journals; we have transferred a number of practically applicable products to our partner spin-off companies.

Of high importance for scientific life at our Institute was organization of many scientific seminars and lectures given by our researchers and guests. Our conference hall (bearing the name "Milan Hašek Auditorium" in honour of Milan Hašek, the founder of our Institute) hosted our annual Institute and PhD conferences and courses as well as several events organized by other on-campus institutes of the Academy.

It is gratifying that our researchers repeatedly obtain prestigious local and international grants to support their experiments aiming to reveal the still abundant secrets of cells and tissues that decide on our health or disease. The research support of our scientific groups from grant funding was again improved; the institutional part of our budget was again slightly increased. Based on very good results of our recent 5-year evaluation by international committees, our institutional budget for 2017 was increased by about 7 %, unprecedented in the past seven years.
At present, 28 research groups of the Institute are dealing with the topics covering molecular and cellular immunology, molecular and cellular oncology, cell biology of the nucleus, cytoskeleton, functional genomics and bioinformatics, study of oncogenes, molecular biology of development, structural biology and mechanisms of receptor signalling. Students represent a significant component of our scientific community; 100 doctoral students and 30 undergraduate students work on their theses in our laboratories. A number of our scientists actively work as university teachers (e.g., eight as professors and 12 as associate professors). A new round of an international call for positions of IMG Fellows took place in 2015. The successful candidates should be young researchers with extensive international postdoctoral experience who are able to secure grant support for themselves and their small independent groups, which should later develop into standard research groups. In 2015 two such position were awarded.
Although we consider basic research our highest priority, we are happy that some "by-products" of our basic research have practical importance. We collaborate with several well-prospering biotech spin-off companies that have originated at the Institute in the past years.
Of major importance is the fact the BIOCEV project (www.biocev.eu) was successfully finished by the end of 2015. Researchers and students from six Academy institutes and two faculties of Charles University have moved into the new well-equipped buildings in Vestec, including over 150 IMG employees.

The high standing of the Institute researchers is manifested by a number of recent awards and prizes, including the National Award of the Government of the Czech Republic "Czech Brains" awarded to Prof. J. Svoboda (2010) and Prof. J. Forejt (2016), the Prize of the Academy of Sciences to the teams of Prof. J. Bártek (2011), Dr. J. Hejnar (2014) and Prof. P. Svoboda (2016), František Běhounek Award to Prof. J. Bártek (2013), Silver Memorial Medal of the Senate of Parliament of the Czech Republic to Prof. J. Bártek, Prof. V. Hořejší (2013) and Dr. J. Hejnar (2015), prize of the Neuron Foundation to Prof. P. Svoboda (2014) and Dr. Jana Dobrovolná (2015), Novartis Discovery Award to Dr. M. Flemr (2014) and Dr. Lenka Kyjacová (2015). Prof. J. Forejt was holder of the prestigious five-year Academy award Premium Academiae since 2008; three Institute researchers (Prof. R. Sedláček and Prof. P. Svoboda in 2008, Dr. V. Varga in 2015) were awardees of the five-year J. E. Purkynje Fellowship, Dr. L. Macůrek and Dr. H. Fulková were awarded the Otto Wichterle fellowship in 2011 or 2015, respectively. Prof. P. Svoboda received the ERC Consolidator Grant (2015), Dr. L. Čermák was awarded the EC Marie Curie grant (2016), Dr. O. Štěpánek and Dr. V. Varga received the EMBO Installation Grants in 2015 and 2016, respectively. Three Institute scientists (Prof. J. Svoboda, Prof. V. Pačes and Prof. J. Forejt) are elected members of the Learned Society of the Czech Republic. Four Institute scientists (Prof. J. Bártek, Prof. J. Svoboda, Prof. V. Pačes and Prof. J. Forejt) are elected EMBO members. In 2016, Prof. J. Svoboda was awarded the The Neuron Award in Biology for his contribution to the world science and was elected a Foreign Associate of the National Academy of Sciences of the USA. IMG scientists serve on 30 Editorial Boards of scientific journals.

A major event in the past year was the regular evaluation of the Academy institutes by international commissions. All IMG research groups evaluated by two commissions received a very good assessment; the evaluation of the Institute as a whole contained a very pleasing sentence "The commission felt that IMG is a "Flagship" institution of Czech science and a particular asset to CAS".

The major part of our plans for the next year will be focused on successful continuation of the BIOCEV project in the newly built and well-equipped campus in Vestec and operation of three National research infrastructures (Czech Center for Phenogenomics, CZ-Openscreen a Czech-BioImaging).

Despite the funding stagnation in recent years, the development of our Institute continues successfully and I believe that our main goal of creating a stimulating environment for top research has already been achieved. Now we just have to make use of these good conditions.

Václav Hořejší
Director

A Brief History of the IMG

The Institute of Molecular Genetics, Academy of Sciences of the Czech Republic (IMG), is located on the southern outskirts of Prague, capital of the Czech Republic.

The history of the Institute started in 1953 with the establishment of the Department of Experimental Biology and Genetics of the Institute of Biology of the Czechoslovak Academy of Sciences, headed since then by Milan Hašek, co-discoverer of immunological tolerance. In 1962, the Department was transformed into the Institute of Experimental Biology and Genetics (IEBG), with Milan Hašek as its Director until 1970. The sixties of the last century were the "golden age" of the Institute, represented besides Hašek e.g. by Pavol and Juraj Ivanyi, Jan Klein, Jan Svoboda, etc. The end of the "Prague Spring" after August 1968 closed this famous era – many promising young scientists had emigrated (and were very successful at their new institutions abroad).

IMG Directors

1962 – 1970: Milan Hašek

1970: Karel Heyberger

1970 – 1977: Prokop Málek

1977 –: Josef Říman

In 1977, IEBG was re-organized and renamed Institute of Molecular Genetics of the Czechoslovak Academy of Sciences (IMG); Josef Říman was appointed its Director. Among the achievements of the otherwise difficult seventies and eighties were co-discovery of reverse transcriptase (J. Říman), discovery of virogeny (J. Svoboda) or sequencing of one of the first viral genomes (V. Pačes). After 1989, the Institute was headed by Jan Svoboda (1991-1999), Václav Pačes (1999-2005) and Václav Hořejší (2005-present). In the period 1964-2006, the Institute was divided between two distant locations. After completion of a modern new building for IMG in 2007, both parts moved together and the new premises are now hosting more than 400 employees and students.

1991 — 1999 — 2005 — 2017

Jan Svoboda

Václav Pačes

Václav Hořejší

IMG and its surroundings

The Prague-Krč campus of biomedical Academy institutes

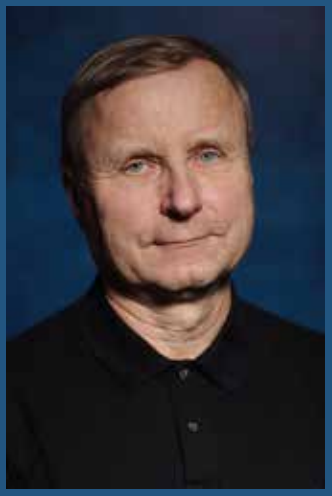
IMG is located on the campus situated in the part of Prague 4 called Krč. Five other Academy institutes share this campus – the Institute of Microbiology, Institute of Physiology, Institute of Experimental Medicine, Institute of Biotechnology and a part of the Institute of Animal Physiology and Genetics. This arrangement allows the researchers to share common infrastructure (research core facilities, guest houses, sports areas and gym, dining halls, kindergarten). The total number of on-campus researchers and students exceeds 1200.

In close proximity to this campus there is also the Institute for Clinical and Experimental Medicine (IKEM) and Thomayer Hospital. The campus lies near a major natural park (Krč forest) and is easily accessible by car or public transportation.

Prague – a city of history, culture and science

Situated on the Vltava (Moldau) River, Prague has been the political, cultural, and economic centre of the Czech state for over 1000 years. The city is home to nearly 1.2 million people. Prague is widely considered to be one of the most beautiful cities in Europe and belongs to the most visited cities on the continent. Since 1992, the historic centre of Prague has been included in the UNESCO list of World Heritage Sites. Prague also has a long-standing tradition in science. Founded in 1348, Charles University is the oldest university in central Europe. At present, Prague is the seat of eight universities, the student population being more than 100.000. There are also 54 Institutes of the Academy of Sciences and a number of other research institutions.

Institute Representatives



Václav Hořejší
Director

Petr Dráber
Deputy Director

Jiří Špička
Deputy Director for Economy

Radislav Sedláček
Deputy Director for BIOCEV Project Implementation

Miroslav Flieger
Chairman of the Supervisory Board

Vladimír Kořínek
Chairman of the Institute Council

Ilona Dita
Institute Secretary

Council of the IMG

The Council of the Institute serves as an advisory authority to the Director and decides on essential scientific and organizational issues. Its members are appointed by election and in the second term of office starting from January 2012, they are:

Vladimír Kořínek, PhD
Chairman

Zbyněk Kozmik, PhD
Vice-Chairman

Petr Bartůněk, PhD
Internal Member

Jiří Forejt, Prof, MD, DSc
Internal Member

Pavel Hozák, Prof, DSc
Internal Member

Pavlína Řezáčová (Maloy), PhD
Internal Member

Radislav Sedláček, Assoc Prof, PhD
Internal Member

David Staněk, PhD
Internal Member

External Members:

Jan Černý, Assoc Prof, PhD [Faculty of Science, Charles University, Prague]
Petr Dvořák, Prof, PhD [Faculty of Medicine, Masaryk University, Brno]
Tomáš Stopka, Assoc Prof, MD, PhD [First Faculty of Medicine, Charles University, General Faculty Hospital, Prague]
Hana Sychrová, DSc [Institute of Physiology of the ASCR, v. v. i.]

Supervisory Board

The main task of the Supervisory Board is to monitor the financial and legal matters connected with the Institute administration. Its members have been selected by the Academy of Sciences from Academy and business sphere representatives.

Miroslav Flieger, PhD
Academy Council of the ASCR
Chairman

Jiří Špička, MBA
Deputy Director,
IMG Vice-Chairman

Jan Kopečný, M.Sc., D.Sc.
IAPG AS CR

Eva Zažímalová, PhD
AC AS CR

David Štůla, BCL
Lawyer

International Scientific Advisory Board

The International Scientific Advisory Board was appointed by the Council of the IMG in January 2014. The main task of the International Scientific Advisory Board is to evaluate the research groups at IMG, provide constructive feedback and suggest future goals.

Rudi Balling
Luxembourg Centre for Systems Biomedicine, University of Luxembourg
Luxembourg, Luxembourg

Suzanne Eaton
Max Planck Institute of Molecular Cell Biology and Genetics
Dresden, Germany

Marcos Malumbres
Spanish National Cancer Research Centre
Madrid, Spain

Renée Schroeder
Max F. Perutz Laboratories
Vienna, Austria

Claudio Sunkel
Institute for Molecular and
Cell Biology
Porto, Portugal

Research Groups

Meritxell Alberich – Jorda 17
Jiří Bártek 19
Petr Bartůněk 21
Jaroslav Blahoš 23
Tomáš Brdička 25
Pavel Dráber 27
Petr Dráber 29
Dominik Filipp 31
Jiří Forejt 33
Martin Gregor 35
Jiří Hejnar 37
Václav Hořejší 39
Pavel Hozák 41
Pavel Hozák 43
Vladimír Kořínek 45
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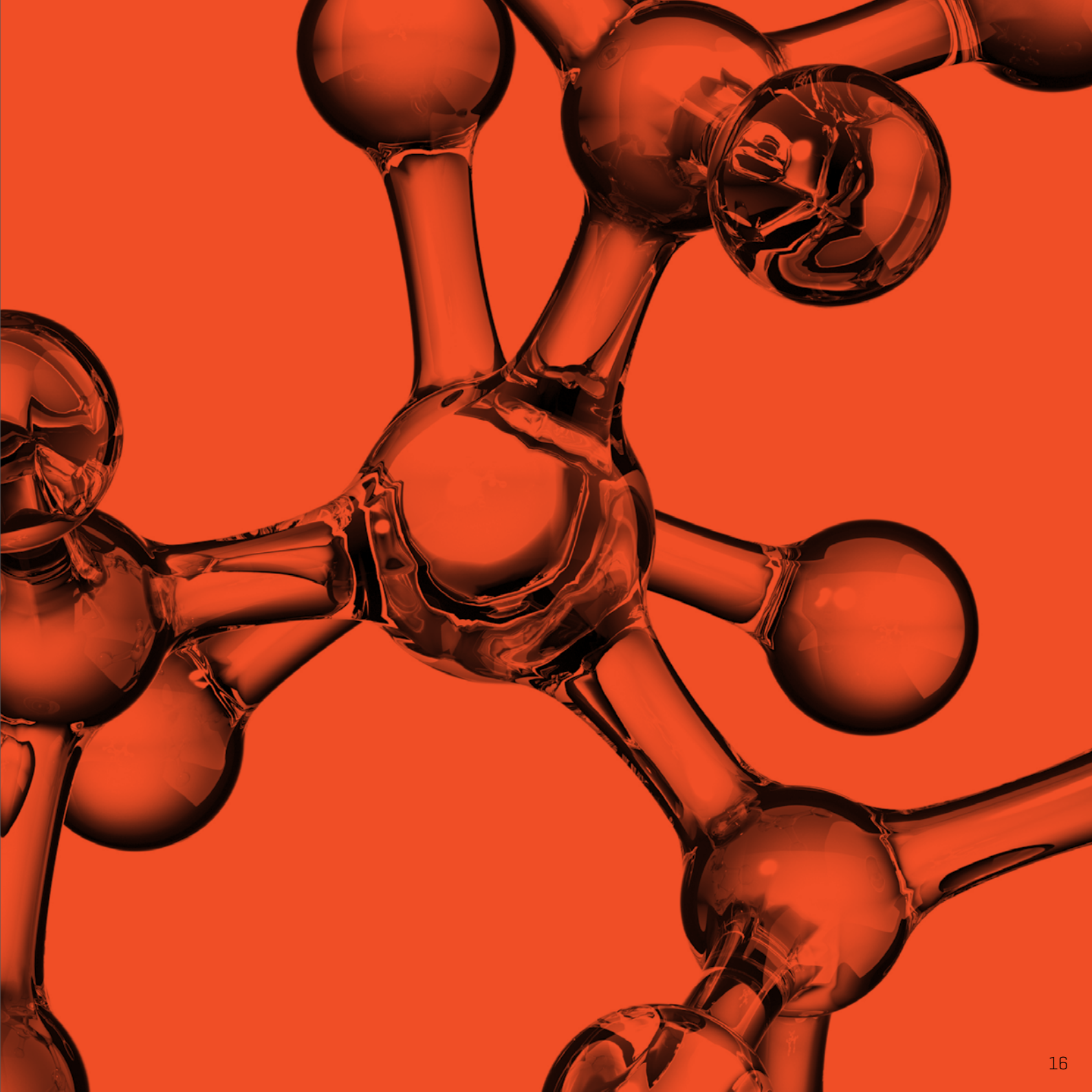
Zbyněk Kozmik 49
Zbyněk Kozmik 51
Marie Lipoldová 53
Libor Macůrek 55
Pavlína Řezáčová 57
Radislav Sedláček 59
David Staněk 61
Petr Svoboda 63
Ondřej Štěpánek 65
Zdeněk Trachtulec 67
Vladimír Varga 69
Čestmír Vlček 71



Meritxell Alberich – Jorda

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In the picture:
1. Petr Daněk | **2.** Miroslava Kardošova | **3. Meritxell Alberich-Jorda** | **4.** Polina Zjablovskaja

LABORATORY OF

HAEMATOONCOLOGY

haematopoiesis, leukaemia, haematopoietic stem cells, transcription factors

All blood cells are derived from a small population of cells called haematopoietic stem cells (HSC). HSC reside in the bone marrow, are pluripotent and can differentiate into all haematopoietic lineages. The processes of HSC maintenance, differentiation, and proliferation are tightly regulated and defects in their regulation are associated with haematopoietic disorders, such as acute myeloid leukaemia (AML). AML is a malignant haematopoietic disease that represents over 90 % of acute leukaemias in adults, and is characterized by an accumulation of immature and non-functional blood cells. AML originates from a single transformed cell, which progressively acquires additional genetic and epigenetic defects and gives rise to leukemic stem cells (LSC). The compilation of aberrations in LSC alters their normal haematopoietic program, giving rise to full-blown leukaemias. As conventional AML therapies are not efficient in eradicating the LSC, better understanding of the mechanisms regulating stem cell fate will be critical to cure this disease. In the laboratory of Haematooncology, we investigate the molecular mechanisms that control HSC and LSC. We use C/EBPα, a key transcription factor regulating HSC maintenance and myeloid differentiation, as a model to identify critical regulators in the stem cell fate. Using well-defined HSC populations and lentiviral gene transfer we investigate the role of the identified genes. We perform in vitro assays (including gene expression profiling and chromatin immunoprecipitation) and in vivo experiments (generation and analysis of murine AML models) to elucidate novel mechanisms and pathways critical for HSC fate, and determine their contribution to leukaemogenesis. Ultimately, our work will contribute to establishing knowledge for the development of better AML therapies.

Selected recent papers:

Polina Zjablovskaja, Miroslava Kardosova, Petr Danek, Pavla Angelisova, Touati Benoukraf, Tomas Kalina, Martin Balastik, Ruud Delwel, Tomas Brdicka, Daniel G. Tenen, Fréderic Fiore, Bernard Malissen,Vaclav Horejsi, and Meritxell Alberich-Jorda: EVI2B is a C/EBPα target gene required for granulocytic differentiation and functionality of hematopoietic progenitors. Submitted.

Alexander Arthur Wurm, Polina Zjablovskaja, Miroslava Kardosova, Dennis Gerloff, Daniela Bråuer-Hartmann, Christiane Katzerke, Jens-Uwe Hartmann, Stephan Fricke, Nadja Hilger, Anne-Marie Müller, Marius Bill, Daniel G. Tenen, Dietger Niederwieser, Meritxell Alberich-Jorda, Gerhard Behre. Disturbance of the C/EBPα-miR-182 balance impairs granulocytic differentiation and promotes development of acute myeloid leukemia. Submitted.

Hermanova I, Valis K, Nuskova H, Alberich-Jorda M, Fišer K, Arruabarrena Aristorena A, Fernandez-Ruiz S, Pecinova A, Niso-Santano M, Zaliova M, Novak P, Mracek T, Kroemer G, Carracedo A, Trka J and Starkova J. Pharmacological inhibition of fatty acid oxidation enhances the effect of Asparaginase in childhood acute lymphoblastic leukemia cells. **Leukemia. 2016** 30(1):209-18.


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LABORATORY OF

GENOME INTEGRITY

DNA damage response, carcinogenesis, inflammation, ageing, RecQ helicases, R-loops, gold nanoparticles

In the picture:
1. Zdeněk Hodný | **2. Jiří Bártek** | **3.** Filip Havel | **4.** Miroslav Přibyl | **5.** Jana Dobrovolná | **6.** Terezie Imrichová | **7.** Pavla Vašicová | **8.** Barbora Šalovská | **9.** Václav Urban | **10.** Martéta Vančurová | **11.** Barbora Boleslavská | **12.** Zuzana Naščáková | **13.** Blanka Mrázková

Our research is centred on cellular responses to damaged DNA (termed DNA damage response). Cells with unhealed DNA damage are mostly prevented from cell division due to activated cell cycle checkpoints; however, following unscheduled cell division, unrepaired breaks result in chromosomal instability with accompanying changes in gene dosage – the driving force of malignant transformation. We focus on 1) mechanisms of cellular response to persistent irreparable DNA damage lesions manifested as irreversible cell cycle arrest (cellular senescence); 2) mechanisms of radioresistance and chemoresistance of cancer cells; 3) role of DNA damage-induced expression of cytokines in paracrine signalling, cancer microenvironment and cell reprogramming; 4) DNA transactions mediated by RecQ DNA helicases, key players in the maintenance of genomic stability; 5) mechanisms resolving collisions between replication and transcription machineries and associated RNA:DNA hybrids referred to as R-loops; and 6) impact of the above mechanisms on cancer and ageing with the aim to find new therapeutic approaches, such as thermotherapy using targeted gold nanoparticles. Recently, we have identified the mechanism of IFNγ-induced senescence and the role of senescent cells in tumour promotion. We have described development of a stem cell-like phenotype of cancer cells in response to genotoxic stress and examined pro-survival signalling pathways responsible for radio- and chemo-resistance of cancer cells.

Selected recent papers:

Urban V, Dobrovolna J, Hühn D, Fryzelkova J, Bartek J, Janscak P: (2016) RECQ5 helicase promotes resolution of conflicts between replication and transcription in human cells. **J. Cell Biol.** 214(4), 401-15.

Burdova K, Mihaljevic B, Sturzenegger A, Chappidi N, Janscak P: (2015) The Mismatch-Binding Factor MutSβ Can Mediate ATR Activation in Response to DNA Double-Strand Breaks. **Mol. Cell** 59(4), 603-14.

Kyjacova, L., S. Hubackova, K. Krejcikova, R. Strauss, H. Hanzlikova, R. Dzijak, T. Imrichova, J. Simova, M. Reinis, J. Bartek, Z. Hodny: 2015. Radiotherapy-induced plasticity of prostate cancer mobilizes stem-like non-adherent, Erk signaling-dependent cells. **Cell Death Differ.** 22:898-911.

Hubackova, S., A. Kucerova, G. Michlits, L. Kyjacova, M. Reinis, O. Korolov, J. Bartek, and Z. Hodny: 2015. IFN[gamma] induces oxidative stress, DNA damage and tumor cell senescence via TGF[beta]/SMAD signaling-dependent induction of Nox4 and suppression of ANT2. **Oncogene.** 35:1236-1249.


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LABORATORY OF

CELL DIFFERENTIATION

haematopoietic and neural cell differentiation, zebrafish development, nuclear receptors, chemical biology

In the picture:
1. Petr Bartůněk | **2.** Michal Dvořák | **3.** Milan Gottwald | **4.** Olga Machoňová | **5.** Nikol Pavlů | **6.** Martina Zíková | **7.** Marta Dvořáková | **8.** Tereza Hojerová | **9.** Martina Šnegoňová | **10.** Justyna Kopycinska

Not in the picture:
Karolina Ditrychová | Tereza Hrušková | Jana Oltová | Ondřej Svoboda | Petr Pajer | Jana Konířová | Martin Kovář

The main interest of the laboratory is study of the molecular mechanism of cell fate determination. We have established in vitro systems to get insight into the self-renewal and differentiation of haematopoietic and neural stem cells. Neural stem cells (NSCs) are defined by their dual ability to self-renew through mitotic cell division or differentiate into the varied neural cell types of the CNS. DISP3/PTCHD2 is a sterol-sensing domain-containing protein, highly expressed in neural tissues, whose expression is regulated by thyroid hormone. We demonstrated that NSC differentiation triggered significant reduction in DISP3 expression in the resulting astrocytes, neurons and oligodendrocytes. Moreover, when DISP3 expression was disrupted, the NSC "stemness" was suppressed, leading to a larger population of cells undergoing spontaneous neuronal differentiation. Conversely, overexpression of DISP3 resulted in increased NSC proliferation and impaired cell differentiation. Our findings imply that DISP3 may help dictate the NSC cell fate to either undergo self-renewal or switch to the terminal cell differentiation programme (Konirova et al. 2016). We have extended our studies on vertebrate haematopoietic development to the zebrafish model and we have established ex vivo cultures of haematopoietic cells (Svoboda et al. 2016). These studies brought information on how haematopoietic cytokines had evolved following the diversification of teleosts and mammals from a common ancestor. Moreover, these tools enabled us to reveal the clonogenic and proliferation capacity of multipotent progenitors with respect to their mammalian haematopoietic counterparts.

Selected recent papers:

Konirova J, Oltova J, Corlett A, Kopycinska J, Kolar M, Bartunek P, Zikova M: (2016) Modulated DISP3/PTCHD2 expression influences neural stem cell fate decisions. **Sci Rep. 7**: in press.

Svoboda O, Stachura DL, Machonova O, Zon L I, Traver D, Bartunek P: Ex vivo tools for the clonal analysis of zebrafish hematopoiesis, **Nat Protocols.** 2016; 11(5):1007-20.

Hron T, Pajer P, Paces J, Bartunek P, Elleder D: Hidden genes in birds. **Genome Biol. 2015**; 16:164-167.


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LABORATORY OF

MOLECULAR PHARMACOLOGY

G-protein-coupled receptors, neurotransmitters, metabotropic glutamate receptors, cannabinoid receptors

In the picture:
1. Denisa Vozárová | **2.** Lenka Chlupisová | **3.** Alena Hájková **4.** Irina Sheveleva | **5.** Matej Gazdarica | **6. Jaroslav Blahoš**

Not in the picture:
Michaela Dvořáková

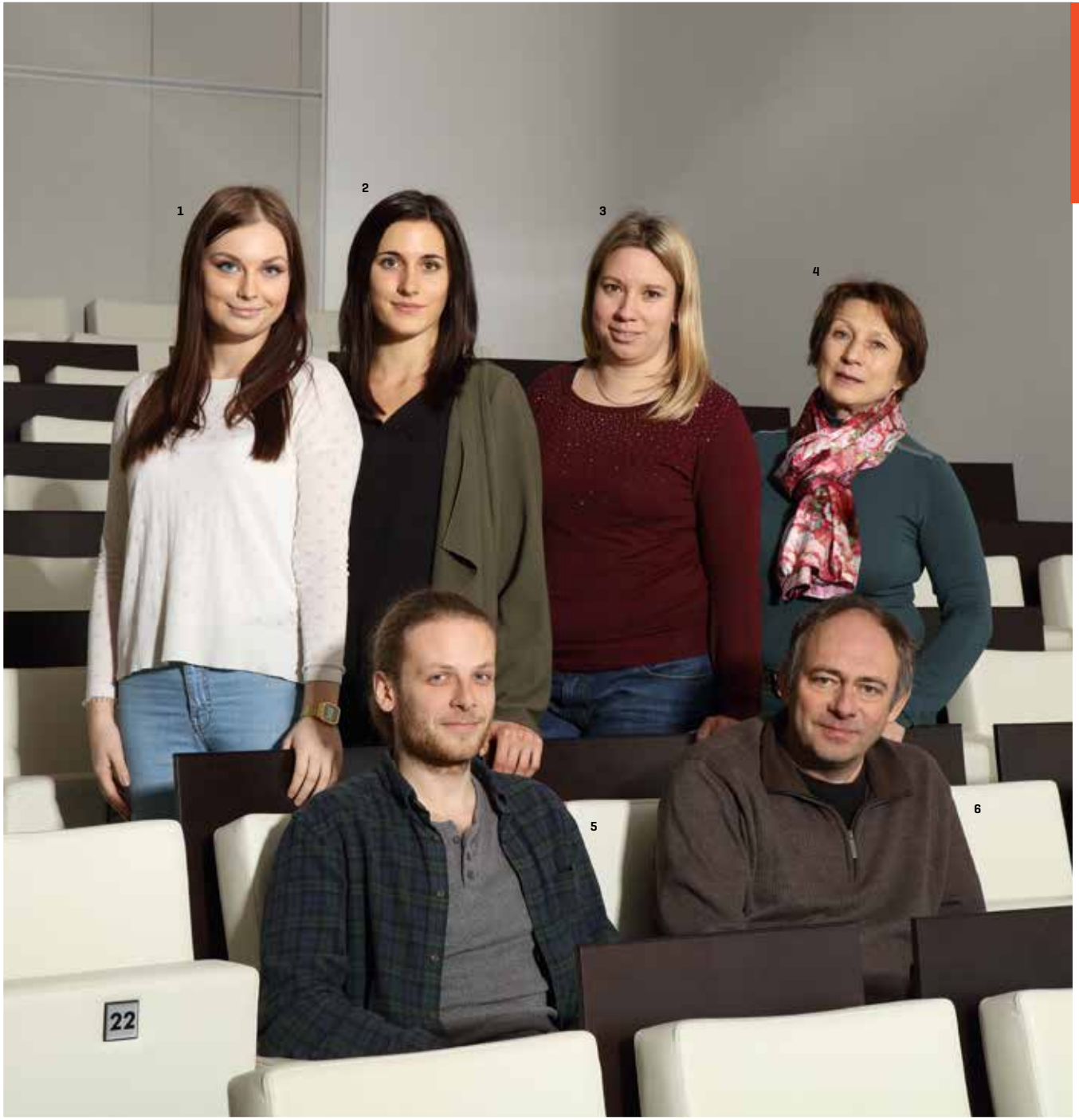
We detected a novel interacting partner of Cannabinoid Receptor 1 (CB1R). Recently, we published our data revealing that SGIP1 interferes with internalization of the activated CB1R. Moreover, this interaction affects signalling of the receptor in a biased manner. The G-protein activation was unaffected, while other pathways were modulated. Both CB1R and SGIP1 are located predominantly pre-synaptically, where the receptors show modest internalization upon agonist stimulation, while the CB1R expressed in heterologous systems are readily internalized. Genetically altered mice are now under use to reveal the SGIP1 role in this phenomenon. Overexpression of SGIP1 in animals is associated with obesity. The functional significance of the SGIP1 protein in CB1R interaction in energy homeostasis is studied in animal models.

Metabotropic glutamate receptors (mGluRs) belong to Class C-G-protein-Coupled Receptors (GPCRs) forming homodimers. Using the mutagenesis approach combined with a functional expression system we showed that within their dimeric complexes, only one subunit reaches the active state. The activation process of mGluRs is initiated by agonist binding that causes conformational changes of the extracellular ligand-binding domains. This is followed by relative movement of the transmembrane regions of the two subunits, and finally a conformational change within one of the heptahelical transmembrane domain can be transmitted to the intracellular signalling machinery. The recently resolved crystal structure of mGluR1 is in accord with our model of activation mechanism being asymmetrical, as suggested by our functional data. Recently we also disclosed that splice variants mGluR1a and mGluR1b form heterodimers in vivo. The functional relevance of the splice variant combinations in the dimeric mGluR1 complexes in vivo are now under investigation using genetically modified mice.

Selected recent papers:

Lahaie N, Kralikova M, Prézeau L, Blahos J, Bouvier M: Post-endocytotic deubiquitination and degradation of the GABAB receptor by USP14, **Journal of Biological Chemistry 2016**, Jan 27; jbc. M115.686907, Shared senior co-authorship.

Hájková A, Techlovská Š, Dvořáková M, Chambers J N, Kumpošt J, Hubálková P, Prezeau L, Blahos J: SGIP1 Alters Internalization and Modulates Signaling of Activated Cannabinoid Receptor 1 in Biased Manner, **Neuropharmacology 2016**, 107 August 2016: 201–214.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LABORATORY OF

LEUKOCYTE SIGNALLING

leukocyte signalling, membrane adaptor proteins, autoinflammation, immune responses of myeloid cells

In the picture:
1. Daniela Glatzová | **2.** Šimon Borna | **3.** Aleš Drobek | **4.** Matej Fabišík | **5. Tomáš Brdička** | **6.** Tereza Skopcová | **7.** Jarmila Králová

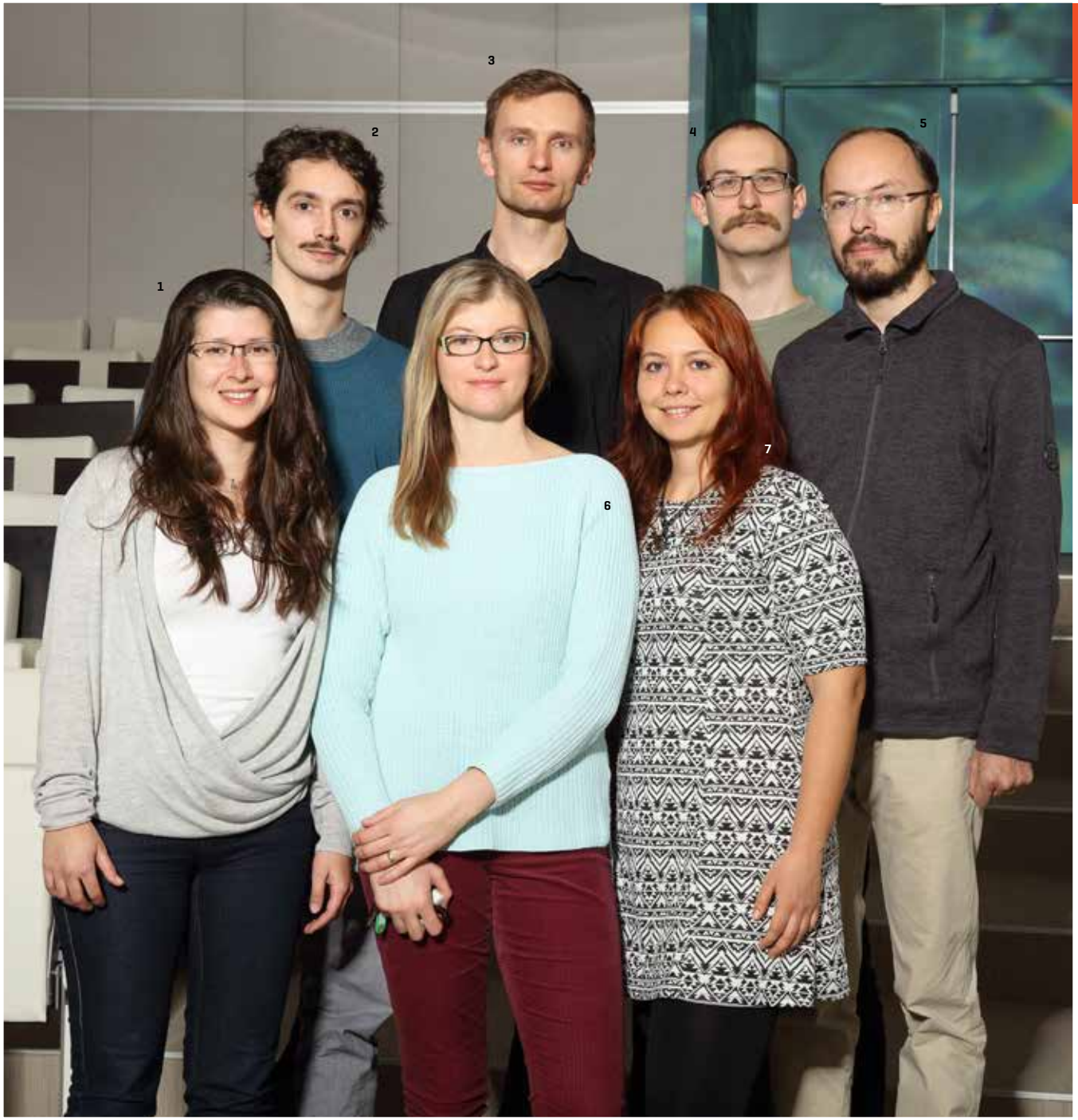
The Laboratory of Leukocyte Signalling is studying the molecular mechanisms of signal transduction downstream of various leukocyte surface receptors. Our interest has recently been focused on the membrane adaptor proteins and on the roles of these proteins in the regulation of leukocyte signalling and in leukocyte-driven pathologies. In the past several years we have been analysing several so far poorly characterized members of this family. Perhaps the most interesting is PSTPIP2. Its deficiency in mice results in an autoinflammatory disorder characterized by sterile inflammation of the bones and skin. It is similar to a human disease known as chronic recurrent multifocal osteomyelitis. We have described interactions of PSTPIP2 with negative regulators of cellular signalling Csk and SHIP1 and now are exploring further molecular mechanisms of how this protein controls inflammation. Additional projects include studies of transmembrane adaptor SCIMP in dendritic cells, which we identified as a positive regulator of signal transduction via the receptor for pathogenic fungi Dectin-1. We are also working on characterization of transmembrane adaptor LST1/A, a potential negative regulator of macrophage and osteoclast signalling, and transmembrane adaptor OPAL1, which is aberrantly expressed in childhood leukaemias and regulates activity of an important bone marrow homing receptor, CXCR4, in leukemic cells as well as in myeloid progenitors.

Selected recent papers:

Drobek A, Králová J, Skopcová T, Kucová M, Novák P, Angelisová P, Otáhal P, Alberich-Jorda M, Brdička T: PSTPIP2, a Protein Associated with Autoinflammatory Disease, Interacts with Inhibitory Enzymes SHIP1 and Csk., **J Immunol. 2015** Oct 1;195(7):3416-26.

Králová J, Fabišík M, Pokorná J, Skopcová T, Malissen B, Brdička T: The Transmembrane Adaptor Protein SCIMP Facilitates Sustained Dectin-1 Signaling in Dendritic Cells, **J Biol Chem. 2016** Aug 5;291(32):16530-40.

Chum T, Glatzová D, Kvíčalová Z, Malínský J, Brdička T, Cebecauer M: The role of palmitoylation and transmembrane domain in sorting of transmembrane adaptor proteins, **J Cell Sci. 2016** Jan 1;129(1):95-107.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LABORATORY OF

BIOLOGY OF CYTOSKELETON

modulation of microtubule organization, microtubule proteins, γ-tubulin, signal transduction

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1. Vadym Sulimenko | **2.** Tetyana Sulimenko | **3.** Vladimíra Sládková | **4.** Irena Mlchová | **5.** Ladislav Cupák | **6.** Anastasiya Klebanovych | **7. Pavel Dráber** | **8.** Zuzana Hájková | **9.** Eduarda Dráberová

Not in the picture:
Jana Uhlířová | Markéta Černohorská | Věra Vosecká

The long-term research programme of the laboratory has been focused on studying the structure-function relationships of microtubule (MT) proteins in cells under normal and pathological conditions. The organization of dynamic MT networks is controlled by MT organizing centres (MTOCs). One of the key components of MTOCs is γ-tubulin, which is necessary for nucleation of MT. Our current work focuses on understanding the modulation of MT nucleation by signal transduction molecules. Our results demonstrate that G protein-coupled receptor kinase-interacting protein 1 (GIT1), p21-activated kinase interacting exchange factor (βPIX), and p21 protein (Cdc42/Rac)-activated kinase 1 (PAK1) are in complexes with γ-tubulin in various cell lines and associate with centrosomes. Microtubule regrowth and phenotypic rescue experiments showed that GIT1 with PAK1 represent positive regulators, and βPIX a negative regulator of MT nucleation. The regulatory roles of GIT1, βPIX and PAK1 in MT nucleation correlated with recruitment of γ-tubulin to the centrosome. Moreover, in mast cells MT nucleation is modulated by Ca^{2+}, which affects γ-tubulin binding properties. We have also shown that both human γ-tubulins differ in their properties and expression during neuronal differentiation and under oxidative stress. We have demonstrated that ectopic expressions of γ-tubulin complex proteins GCP2 and GCP3 may represent novel markers in the pathobiology of gliomas.

Selected recent papers:

Černohorská M, Sulimenko V, Hájková Z, Sulimenko T, Sládková V, Vinopal S, Dráberová E, Dráber P: GIT1/βPIX signaling proteins and PAK1 kinase regulate microtubule nucleation. **BBA Mol. Cell Res.** 1863: 1282-1297, 2016.

Dráberová E, D'Agostino L, Caracciolo V, Sládková V, Sulimenko T, Sulimenko V, Sobol M, Maounis N F, Tzelepis E G, Mahera E, Křen L, Legido A, Giordano A, Mörk S, Hozák P, Dráber P, Katsetos C D: Overexpression and nucleolar localization of γ-tubulin small complex proteins GCP2 and GCP3 in glioblastoma. **J. Neuropathol. Exp. Neurol.** 74: 723-742, 2015.

Sulimenko V, Hájková Z, Černohorská M, Sulimenko T, Sládková V, Dráberová L, Vinopal S, Dráberová E, Dráber P: Microtubule nucleation in mouse bone-marrow derived mast cells is regulated by concerted action of GIT1/βPIX proteins and calcium. **J. Immunol.** 194: 4099-4111, 2015.


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LABORATORY OF

SIGNAL TRANSDUCTION

plasma membrane signalosomes, immunoreceptor signalling, ORM family regulators, mast cell

In the picture:
1. Magda Tůmová | **2.** Ivana Hálová | **3.** Viktor Bugajev | **4.** Pavol Utekal | **5.** Tomáš Paulenda | **6. Petr Dráber** | **7.** Lucie Potůčková | **8.** Lubica Dráberová | **9.** Romana Budovičová

Not in the picture:
Oleksij Redčenko

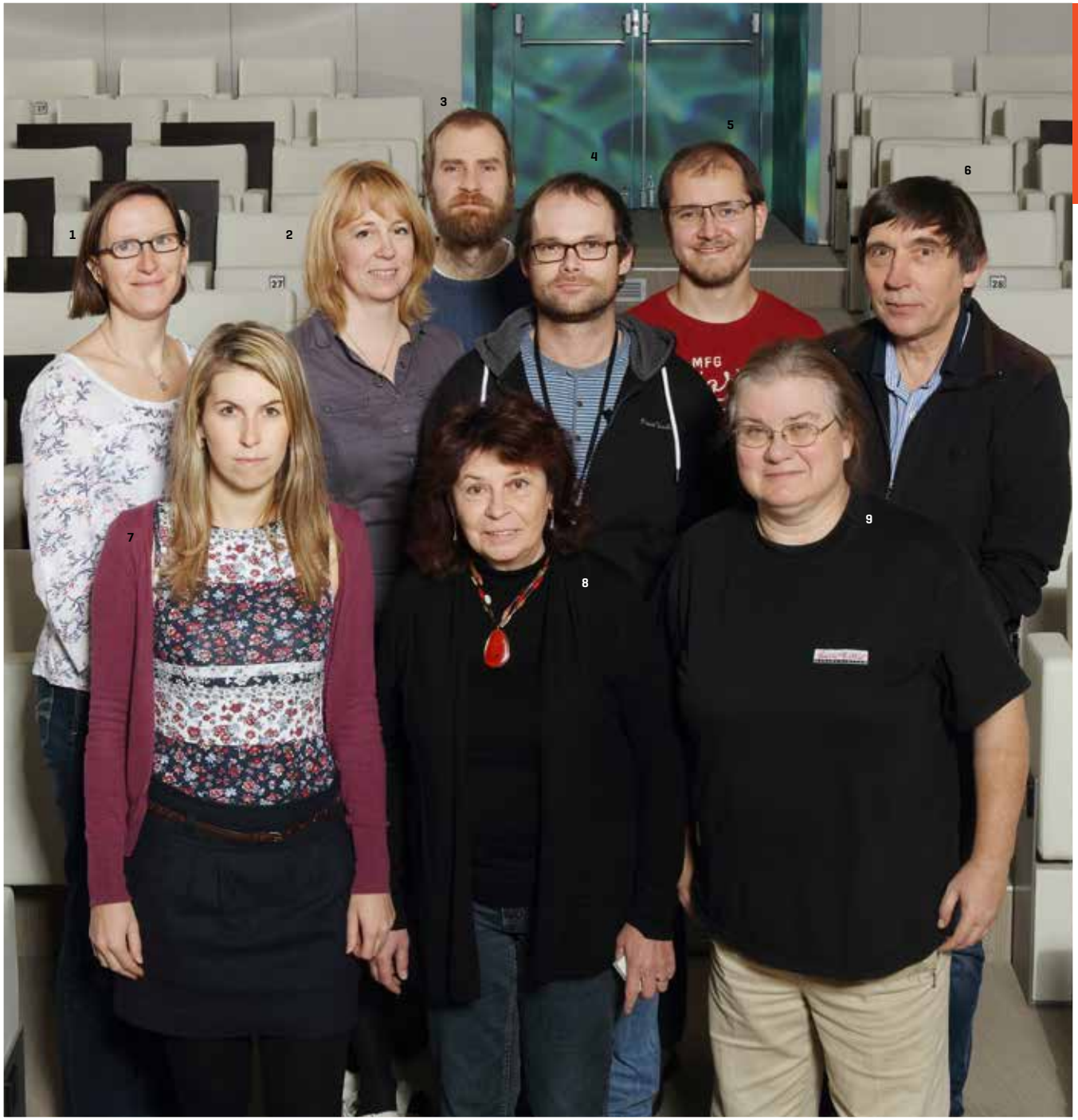
Understanding the molecular mechanisms governing signal transduction from the plasma membrane receptors to the cytoplasm remains an important research goal. High-affinity immunoglobulin E receptor (FcεRI), cKIT, and G protein-coupled receptors (GPCRs) are plasma membrane receptors involved in degranulation and/or chemotaxis of mast cells, powerful immune system modulators. Within seconds of antigen-mediated activation, mast cells release a variety of preformed biologically active compounds, followed by a wave of mediator synthesis and secretion. Increasing evidence suggests an intricate network of inhibitory and activating receptors, specific signalling pathways, and adaptor proteins whose overall signalling balance governs mast cell responsiveness to a given stimuli. In our recent studies we focused on understanding the role of plasma membrane signalosomes and selected cytoplasmic proteins during mast cells activation through FcεRI, cKit and GPCRs. To reach our goal, we used various techniques of molecular biology, immunology, immunochemistry, and immunohistochemistry. We found and described new functions of the ORMDL3 protein, galectin 3 and ethanol-sensitive plasma membrane signalosomes in mast cell activation. Our studies deepen the knowledge of the cellular and molecular mechanisms of cells involved in allergic and inflammatory diseases, a prerequisite for development of anti-allergic and anti-inflammatory drugs.

Selected recent papers:

Bambouskova, M, Polakovicova I, Halova I, Goel G, Draberova L, Bugajev V, Doan A, Utekal P, Gardet A, Xavier R J, Draber P: (2016) New regulatory roles of galectin-3 in the high-affinity IgE receptor signaling. **Mol. Cell Biol.** 36: 1366-1382.

Bugajev V, Halova I, Draberova L, Bambouskova M, Potuckova L, Draberova H, Paulenda T, Junyent S, Draber P: (2016) Negative regulatory roles of ORMDL3 in the FcεRI-triggered expression of proinflammatory mediators and chemotactic response in murine mast cells. **Cell Mol. Life Sci.** 73: 1265-1285.

Draberova L, Paulenda T, Halova I, Potuckova L, Bugajev V, Bambouskova M, Tumova M, Draber P: (2015) Ethanol inhibits high-affinity immunoglobulin E receptor (FcεRI) signaling in mast Cells by suppressing the function of FcεRI-cholesterol signalosome. **PLoS One** 10: e0144596.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LABORATORY OF

IMMUNOBIOLOGY

central and peripheral tolerance, TLRs in embryonic haematopoiesis, T-cell signalling

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Not in the picture:
Ilona Chlubnová

The main goal of our research is to elucidate the mechanism(s) guiding the process of central and peripheral immune tolerance. We investigate the role of innate immune receptors (IIRs) expressed on medullary thymic epithelial cells (mTECs) in the modification of these mechanisms. Our data showed that the set of effector molecules produced by mTECs upon IIR stimulation is quite distinct from that produced by other cells of the immune system, and thus provide evidence for a so far uncharacterized role of IIRs expressed on tolerance-inducing mTECs. We have also characterized a novel subset of functionally distinct lymph node cells with the capacity to delete self-reactive CD8+ and CD4+ T cells or mediate conversion of the latter into Tregs.

We are also very interested in the expression pattern and function of Toll-like receptors (TLRs) during the early mammalian embryogenesis. TLR2 seems to be a suitable surface marker for tracking the earliest haematopoietic progenitors in a precirculation embryo. Our newly generated transgenic mice, which enable us to perform genetic lineage tracing experiments, showed that these early TLR2-expressing progenitors contribute not only to primitive, but also to definitive haematopoiesis.

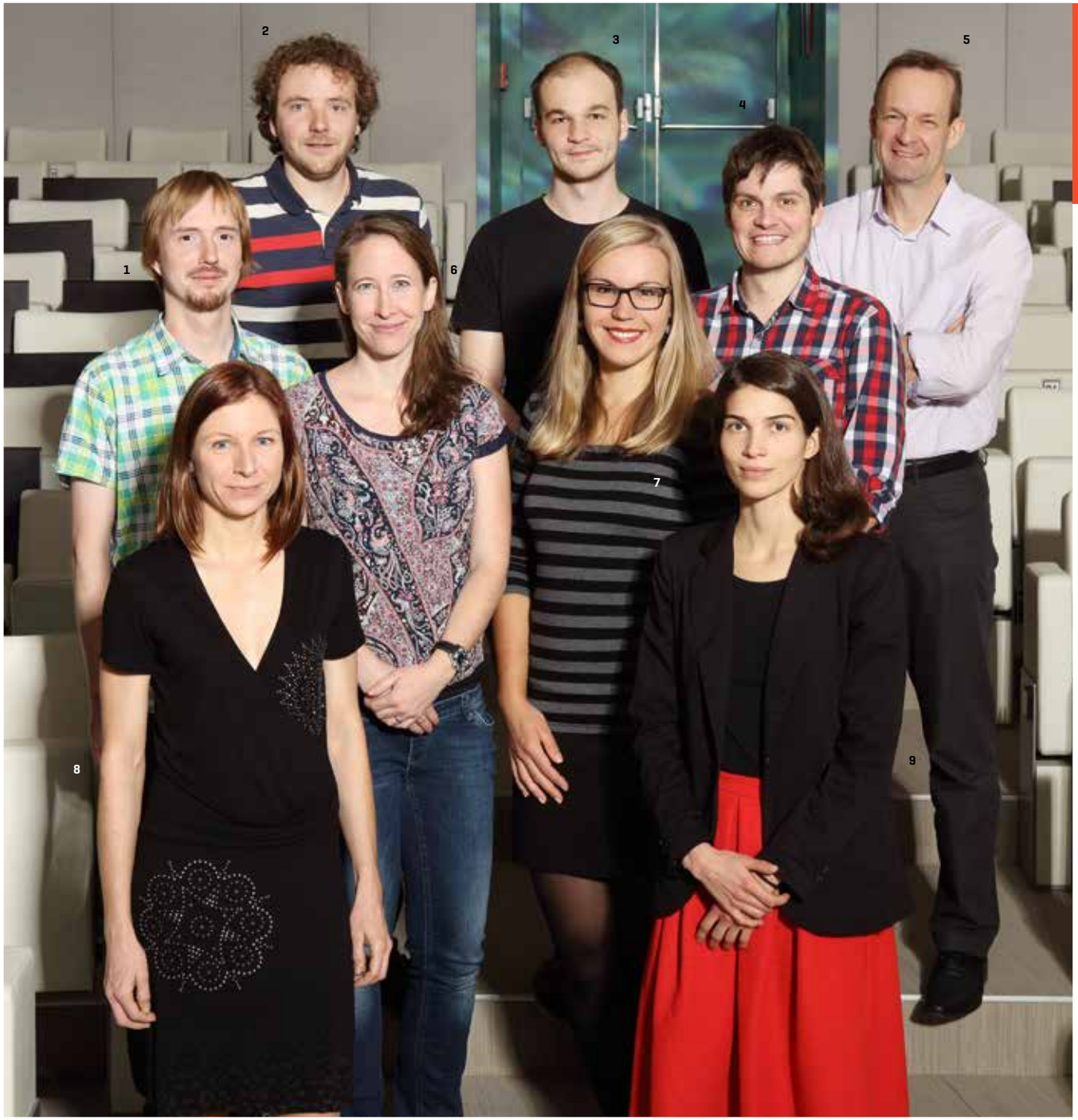
We continue in our effort to understand the biochemical events leading to the activation of T cells. We have identified several proteins involved in the regulation of Lck redistribution via linking this process to the cytoskeletal network.

Selected recent papers:

Ballek O, Valečka J, Dobešová M, Broučková A, Manning J, Řehulka P, Stulík J, Filipp D: TCR triggering induces the formation of Lck-RACK1-actinin-1 multiprotein network affecting Lck redistribution. **Front. Immunol. 2016** 7: 449.

Dobeš J, Neuwirth A, Dobešová M, Vobořil M, Balounová J, Ballek O, Lebl J, Meloni A, Krohn K, Kluger N, Ranki A, Filipp D: Gastrointestinal Autoimmunity Associated with Loss of Central Tolerance to Enteric -Defensins. **Gastroenterology 2015** 149(1):139–150.

Ballek O, Valečka J, Manning J, Filipp D: The pool of preactivated Lck in the initiation of T-cell signaling: a critical re-evaluation of the Lck standby model. **Immunol Cell Biol. 2015** 93: 384–395.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LABORATORY OF

MOUSE MOLECULAR GENETICS

hybrid sterility, Prdm9, meiotic recombination, mouse chromosome substitution strains

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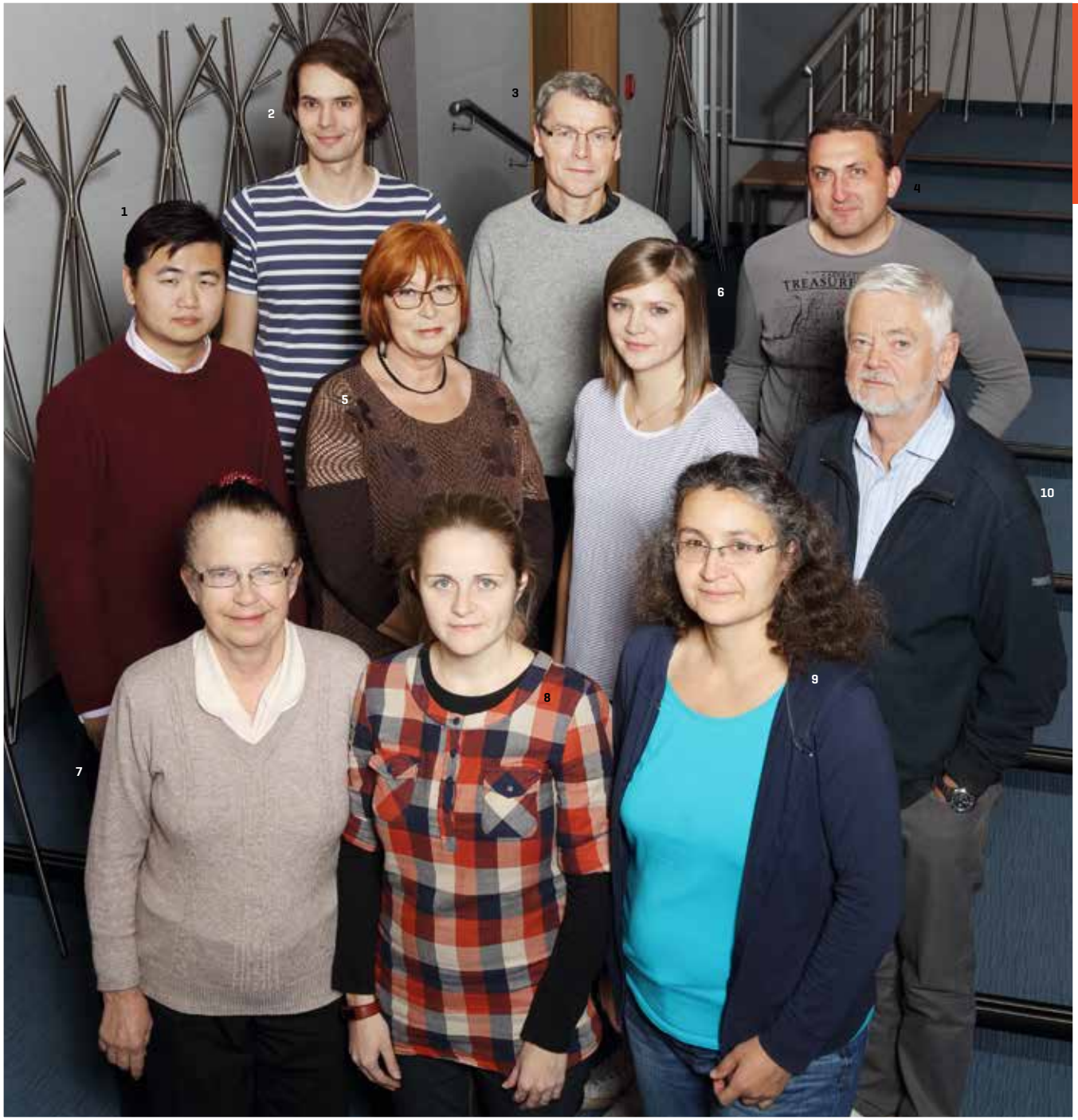
Positional cloning of the first vertebrate hybrid sterility gene Prdm9 (Meisetz), encoding a meiotic histone H3 lysine-4 tri-methyltransferase, revealed a role for epigenetics and meiotic recombination in speciation and opened a window to a systems approach to the hybrid sterility gene network. The second hybrid sterility gene, Hstx2, showing Dobzhansky-Muller incompatibility with Prdm9, was mapped to a 4.7 Mb interval on Chromosome X. The same interval of mouse Chromosome X was shown to carry a major gene regulating meiotic recombination in male but not in female hybrids.
Chromosome substitution, or consomic strains C57BL/6J-Chr # PWD/Ph/ForeJ, constructed in our laboratory are used for dissecting the genomic architecture of the sterility of Mus m. musculus x Mus m. domesticus hybrids and for many other quantitative traits of biomedical significance. Using chromosome substitution strains we have studied meiotic X-chromosome inactivation and pairing, and synapsis of homologous chromosomes in carriers of male-sterile autosomal rearrangements and in male-sterile inter-species hybrids.

Selected recent papers:

Forejt J: Genetics: Asymmetric breaks in DNA cause sterility. **Nature. 2016** Feb 11;530 (7589):167-8.

Balcova M, Faltusova B, Gergelits V, Bhattacharyya T, Mihola O, Trachtulec Z, Knopf C, Fotopulosova V, Chvatalova I, Gregorova S, Forejt J: Hybrid Sterility Locus on Chromosome X Controls Meiotic Recombination Rate in Mouse. **PLoS Genet. 2016** Apr 22;12(4):e1005906.

Forejt J: Hybrid Sterility, Mouse. In: Reference Module in Life Sciences, from Brenner's Encyclopedia of Genetics (Second Edition), **Elsevier** ISBN: xxxx, Pages xx-xx, in press 2016. (e-book).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LABORATORY OF

INTEGRATIVE BIOLOGY

simple epithelia, cytoskeleton, cell junctions, extracellular matrix, mechanotransduction

In the picture:
1. Kateřina Nepomucká | **2.** Gizem Oyman-Eyrilmez | **3.** Helena Havelková | **4.** Lenka Sarnová | **5. Martin Gregor** | **6.** Markéta Jiroušková | **7.** Alžběta Kalendová

The main research focus of our group has been centred around cytolinker-dependent regulation of the actin and intermediate filament cytoskeleton, maintenance of epithelial barrier function, adhesion-mediated signalling and cell motility.

Plectin, a ubiquitously expressed cytolinker protein, interlinks the three main components of the cytoskeleton: actin microfilaments, microtubules and intermediate filaments. In addition, plectin recruits the cytoskeleton to junctional complexes in the plasma membrane. In epithelia, plectin controls keratin cytoarchitecture and is essential for the structural integrity, mechanical strength and maintenance of the paracellular barrier function.

At the cellular level, we have recently provided evidence that intermediate filaments and plectin are crucial for cellular mechanosensing. Cells can sense their environment, such as neighbouring cells or properties of the extracellular matrix, and translate these stimuli into biochemical signals for migration, cellular transport and division. The cytoskeleton provides the physical interface between the cell and the extracellular matrix in sensing a mechanical stimulus. Previously, actin microfilaments were the only cytoskeleton component considered to be involved in mechanosensing, i.e., how the cell senses and responds to mechanical inputs.

Using advanced molecular cell biology techniques and transgenic mouse models, we are studying the role of plectin in the development, progress, and healing of various liver and intestinal diseases. Knowledge of its role in the development of liver fibrosis, cholestatic liver disease, colitis and colon cancer provides us with potential to develop new targets for treating these diseases.

Selected recent papers:

Müller M, Wetzel S, Kőhn-Gaone J, Chalupsky K, Lüllmann-Rauch R, Barikbin R, Bergmann J, Wöhner B, Zbodakova O, Leuschner I, Gregor M, Tiegs G, Rose-John S, Sedlacek R, Tirnitz-Parker J E E, Saftig P, Schmidt-Arras D: A disintegrin and metalloprotease 10 (ADAM10) is a central regulator of murine liver tissue homeostasis. **Oncotarget**, 10.18632/oncotarget.7836, 2016.

Brauer R, Tureckova J, Kanchev I, Khoylou M, Skarda J, Prochazka J, Spoutil F, Beck I M, Zbodakova O, Kasparek P, Korinek V, Chalupsky K, Karhu T, Herzig K H, Hajduch M, Gregor M, Sedlacek R: MMP-19 deficiency causes aggravation of colitis due to defects in innate immune cell function. **Mucosal Immunol.**, 9:974-85, 2015.

Song J-G, Kostan J, Drepper F, Knapp B, de Almeida Ribeiro Jr E, Konarev P V, Grishkovskaya I, Wiche G, Gregor M, Svergun D I, Warscheid B, Djinović-Carugo K: Structural insights into Ca^{2+}/calmodulin regulation of plectin 1a - integrin β4 interaction in hemidesmosomes. **Structure**, 23:558-70, 2015.


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LABORATORY OF

VIRAL AND CELLULAR GENETICS

receptors for retroviruses, retroviral vectors, endogenous retroviruses, latency of retroviruses, epigenetics

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1. Jiří Hejnar | **2.** Volodymyr Stepanets | **3.** Kryštof Štafl | **4.** Lenka Mikušová | **5.** David Přikryl | **6.** Josef Geryk | **7.** Filip Šenigl | **8.** Albert Font-Haro | **9.** Vít Karafiát | **10.** Helena Farkašová | **11.** Anna Lounková | **12.** Vladimír Pečenka | **13.** Dalibor Miklík | **14.** Tomáš Hron | **15.** Martina Slavková | **16.** Dana Kučerová | **17.** Lubomíra Pecnová | **18.** Kateřina Trejbalová | **19.** Mária Gašpareková

Retroviruses enter host cells after specific binding of retroviral envelope proteins to host cell receptors. The specificity of envelope-receptor interaction dictates the host susceptibility or resistance to certain retrovirus. Retroviruses can broaden their host range by mutations of the env gene, and vice versa, host cells develop resistance to retroviruses by mutations of genes encoding the specific receptors. Avian leukosis virus subgroup J (ALV-J), an important pathogen of domestic poultry, infects chickens and turkeys, whereas other galliform species are resistant thanks to a single amino-acid substitution in cell surface Na+/H+ exchanger (NHE1), the receptor for ALV-J. We screened the NHE1 receptor in wild bird species in order to predict the spread of ALV-J in its natural reservoirs. We identified four species of New World quails susceptible to ALV-J.
Another defence mechanism used by the host cells is inactivation of the integrated invaders at the level of transcription via DNA methylation and modifications of adjacent histones. This epigenetic regulation governs the latency of HIV, which is the major obstacle in the HIV cure. We studied the development of DNA methylation of the latent HIV-1 provirus in cell line models and in long-term-infected individuals.
Last but not least, our laboratory deals with endogenous retroviruses. When screening the newly released whole genome sequences of mammalian species using a new two-step computational procedure, we discovered a new endogenous retrovirus in the genome of Malayan colugo. These proviral sequences turned out to be the first endogenous lentivirus identified in the Euarchonta lineage, which includes primates, and represents the oldest member of the lentivirus genus.

Selected recent papers:

Plachý J, Reinišová M, Kučerová D, Šenigl F, Stepanets V, Hron T, Trejbalová K, Elleder D, Hejnar J: Identification of New World Quails Susceptible to ALV-J Infection. **J. Virol.**, in press, 2017.

Trejbalová K, Kovářová D, Blažková J, Machala L, Jilich D, Weber J, Kučerová D, Vencálek O, Hirsch I, Hejnar J: Development of 5' LTR DNA methylation of latent HIV-1 provirus in cell line models and in long-term-infected individuals. **Clin. Epigenetics**, 8: e19, 2016.

Hron T, Farkašová H, Padhi A, Pačes J, Elleder D: Life history of the oldest lentivirus: characterization of ELVgv integrations in the dermopteran genome. **Mol. Biol. Evol.** 33: 2659-2669, 2016.


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LABORATORY OF

MOLECULAR IMMUNOLOGY

membrane microdomains, chimeric antigen receptors, Evi2b (CD361)

In the picture:
1. Jana Pokorná | **2.** Eva Tvrzníková | **3. Václav Hořejší** | **4.** Pavla Angelisová

Not in the picture:
Pavel Otáhal

In 2015-2016 our laboratory was dealing with three topics:

1. Membrane rafts and immunoreceptor signalling (principal investigator Václav Hořejší)
For many years a major topic of our laboratory has been signalling molecules present in membrane rafts and their involvement in immunoreceptor signalling. In the past two years we have been working on development of novel approaches to solubilisation and biochemical characterization of these membrane microdomains using styrene-maleic acid copolymers (SMA).

2. Chimeric antigen receptors (CARs) (principal investigator Pavel Otáhal)
In collaboration with a clinical research institution we have been dealing with construction of chimeric antigen receptor constructs subsequently expressed in T lymphocytes capable of (a) specific recognition of e.g. tumour antigens, and (b) effective signalling resulting in killing of the recognized tumour cell.

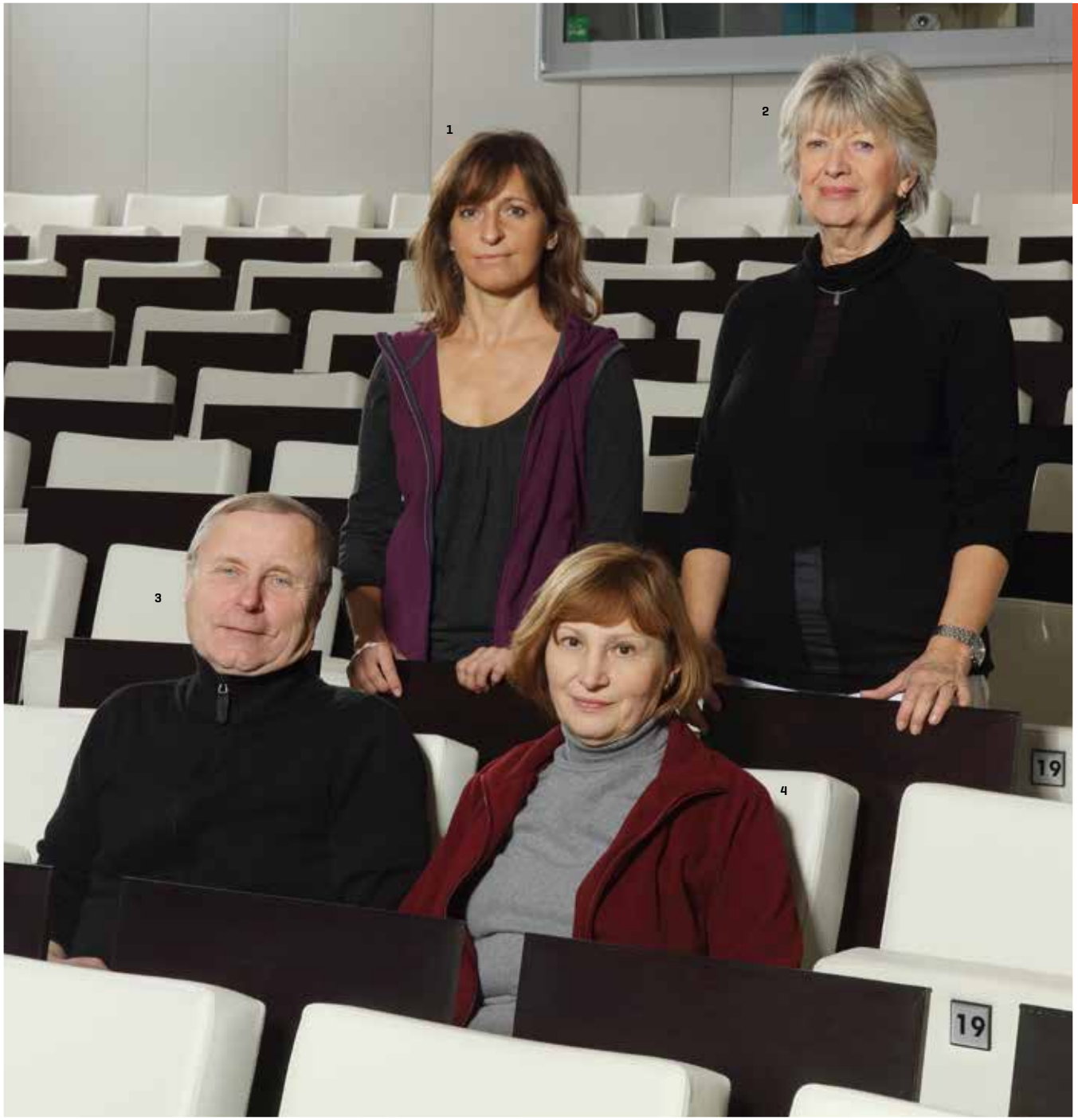
3. Leukocyte surface glycoprotein Evi2b
In collaboration with the lab of Meritxell Alberich-Jorda we have been working on elucidation of functional aspects of leukocyte surface glycoprotein Evi2b (CD361), namely its association with other leukocyte molecules.

Selected recent papers:

Zjablovskaja P, Kardosova M, Angelisova P, Benoukraf T, Kalina T, Balastik M, Delwel R, Brdicka T, Tenen D G, Fiore F, Malissen B, Horejsi V, Alberich-Jorda M: (2016) EVI2B is a C/EBP target gene required for granulocytic differentiation and functionality of hematopoietic progenitors **Cell Death Differ.**, in press.

Kralova J, Fabisik M, Pokorna J, Skopcova T, Malissen B, Brdicka T: (2016) The transmembrane adaptor protein SCIMP facilitates sustained dectin-1 signaling in dendritic cells. **J Biol. Chem.** 291: 16530-16540.

Drobek A, Kralova J, Skopcova T, Kucova M, Novák P, Angelisová P, Otahal P, Alberich-Jorda M, Brdicka T: (2015) PSTPIP2, a protein associated with autoinflammatory disease, interacts with inhibitory enzymes SHIP1 and Csk. **J. Immunol.** 195: 3416-3426.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LABORATORY OF

BIOLOGY OF THE CELL NUCLEUS

nucleus, lamins, lipids, transcription, histone deacetylases, nuclear periphery, super-resolution microscopy

In the picture:
1. Pavel Hozák | **2.** Lenka Pišlová | **3.** Lívia Uličná | **4.** Sara Eliana Lopés Escudeiro | **5.** Vlada Filimonenko | **6.** Pavel Kříž | **7.** Ilona Kalasová | **8.** Miloslava Maninová | **9.** Iva Jelínková | **10.** Jindřiška Fišerová | **11.** Jana Uhlířová | **12.** Veronika Fáberová | **13.** Margarita Sobol | **14.** Lenka Jarolímová

Cell nucleus is a fascinating organelle, where some 6 x 109 base pairs of DNA fold as a nucleoprotein complex (i.e., chromatin) into higher-order arrays so as to fit in a structure measuring only 10 μm. The machineries for transcription of genes and processing of RNA products, for accurate DNA replication, repair and recombination are precisely regulated within the nucleus. Multiple protein-protein, protein-nucleic acid, and protein-lipid interactions take place in specific microenvironments forming functional domains. Our effort concentrates around three topics:

1) Phosphoinositides (PIs) are negatively charged glycerol-based phospholipids. Growing evidence shows the importance of PIs in the nuclear functions. The PIs are implicated in pre-mRNA processing, DNA transcription and chromatin remodelling. However, these functions are still poorly understood. We therefore employ a multi-disciplinary approach in order to study the functions of nuclear lipids in transcription and chromatin remodelling.
2) Lamins are filamentous proteins forming the nuclear lamina and other poorly characterized structures in the nuclear interior. Our preliminary data reveal interactions of lamin A with phospholipid PIP2 on the surface of newly described structures – PIP2 islets. Our project will bring new data on the role of these structures in regulating nuclear order, transcription patterns and development of laminopathies.
3) Nuclear periphery represents a complex compartment of substantial importance for chromatin organization. We aim to understand the mechanism of chromatin targeting to the nuclear periphery and its consequences in gene expression and chromatin organization during the developmental processes.

Selected recent papers:

Marášek P, Dzijak R, Studenyak I, Fišerová J, Uličná L, Novák P, Hozák P: Paxillin-dependent regulation of IGF2 and H19 gene cluster expression. **J Cell Sci 2015** 128(16): 3106-16.

Venit T, Kalendová A, Petr M, Dzijak R, Pastorek L, Rohožková J, Malohlava J, Hozák P: Nuclear myosin I regulates cell membrane tension. **Sci Rep 2016** 6: 30864.


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LABORATORY OF

EPIGENETICS OF THE CELL NUCLEUS

meiosis, actin-binding proteins, chromosomal dynamics, vinculin

In the picture:
1. Robert Havalda | **2. Pavel Hozák** | **3.** Petr Flachs | **4.** Alžběta Darášová | **5.** Jana Rohožková | **6.** Lenka Hůlková

Meiosis is a key process for sexual reproduction contributing to the genetic variability of organisms. Deciphering the roles of novel components of the synaptonemal complex would therefore significantly contribute to our understanding of the molecular mechanisms and dynamics of meiotic events, and may possibly also help to explain some of the fertility deficiencies, which are a prominent medial problem affecting 10 % of humans.
Our research focuses on chromosome dynamics during gametogenesis in two eukaryotic models (C. elegans, M. musculus), where we aim to address the proteins involved in early meiotic stages during pairing and synapsis of homologous chromosomes. Identification of new players affecting meiosis during gametogenesis is clearly a very important, timely endeavour as the chromosomal dynamics and possible complications during meiotic divisions still remain incompletely understood.
In our recent results, we showed that vinculin/DEB-1 clearly participates in meiotic prophase progression. Depletion of vinculin/DEB-1 affects chromosomal pairing stabilization, attachment of chromosomes to cytoskeletal forces, and formation of the synaptonemal complex during prophase I. Our study thus revealed an unexpected role of vinculin/DEB-1 in the progression of meiotic prophase, including chromosome dynamics and pairing, the essential meiotic components. So far, the nuclear functions of vinculin/DEB-1 have not been described at all, and in this project we suggest accomplishing a systematic study using a panel of structural, molecular and genetic methods in order to reveal details about its biological functions in the cell nucleus, and in meiosis in particular.

Selected recent papers:

Vrbacký M, Kovalčíková J, Chawengsaksophak K, Beck IM, Mráček T, Nůsková H, Sedmera D, Papoušek F, Kolář F, Sobol M, Hozák P, Sedlacek R, Houštěk J: Knockout of Tmem70 alters biogenesis of ATP synthase and leads to embryonal lethality in mice. **Hum Mol Genet 2016** 25(21):4674-4685.

Venit T, Kalendová A, Petr M, Dzijak R, Pastorek L, Rohožková J, Malohlava J, Hozák P: Nuclear myosin I regulates cell membrane tension. **Sci Rep 2016** 6: 30864.


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LABORATORY OF

CELL AND DEVELOPMENTAL BIOLOGY

cancer, haematopoiesis, intestinal stem cells, JAK/STAT signalling, Wnt pathway

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Not in the picture:
Dušan Hrčkulák | Petra Burešová | Veronika Vilímková

The majority of tissues in the adult organism contain a population of tissue-specific stem cells. The proper maintenance of adult tissues is controlled by various signalling pathways that regulate the balance between the opposing processes of proliferation and differentiation. The scientific goal of our laboratory is to elucidate the molecular mechanisms influencing the behaviour of normal and transformed cells. At present, the laboratory is focused on two research themes:
1. Intestinal stem cells and cancer
Hypermethylated in cancer 1 (HIC1) represents a tumour suppressor gene frequently inactivated by DNA methylation in many types of solid tumours. We have found that the tumour-suppressive function of Hic1 in the colon is related to its inhibitory action on signalling mediated by toll-like receptor 2 (Tlr2) present on tumour cells. In the intestine, Hic1 is mainly expressed in differentiated epithelial cells and its ablation leads to increased Tlr2 production. The absence of Hic1, in a chemical-induced mouse model of carcinogenesis, resulted in larger Tlr2-positive colonic tumours that showed increased proportion of proliferating cells. We also analysed the expression of HIC1 using large datasets of human colorectal polyps and carcinomas and found that high HIC1 production distinguished a specific type of chemotherapy-responsive tumours.
2. Haematopoietic stem cells
We reported the association of gain-of-function germline mutations in Janus kinase 2 (JAK2) with a phenotype-defining mutation in myeloproliferative neoplasm. We proposed that JAK2 germline mutations may provide a clonal advantage, possibly contributing to further genomic alterations in the clone and, eventually, fatal leukemic transformation.

Selected recent papers:

Lanikova L, Babosova O, Swierczek S, Wang L, Wheeler DA, Divoky V, Korinek V, Prchal J T: Coexistence of gain-of-function JAK2 germline mutations with JAK2V617F in polycythemia vera. **Blood 2016** 128(18):2266-2270.

Janeckova L, Kolar M, Svec J, Lanikova L, Pospichalova V, Baloghova N, Vojtechova M, Sloncova E, Strnad H, Korinek V: HIC1 Expression Distinguishes Intestinal Carcinomas Sensitive to Chemotherapy. **Transl Oncol 2016** 9(2):99-107.

Janeckova L, Pospichalova V, Fafilek B, Vojtechova M, Tureckova J, Dobes J, Dubuissez M, Leprince D, Baloghova N, Horazna M, Hlavata A, Stancikova J, Sloncova E, Galuskova K, Strnad H, Korinek V: HIC1 Tumor Suppressor Loss Potentiates TLR2/NF-κB Signaling and Promotes Tissue Damage-Associated Tumorigenesis. **Mol Cancer Res 2015** 13(7):1139-48.


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Klára Klimešová

LABORATORY OF

CANCER BIOLOGY

mass spectrometry, protein stability, protein-protein interaction, ubiquitin proteasome system

The principal goal of the laboratory established in 2015 is to understand the molecular complexity of cancer formation starting from initial stages through to metastasis. In more detail, we are elucidating the role of proteasome-dependent protein degradation in various intracellular processes. Under physiologic conditions, the Ubiquitin Proteasome System (UPS) is required for precise temporal and spatial expression of a diverse repertoire of proteins. UPS is involved in the cell cycle, differentiation, or stress and immune response. The ubiquitination process is achieved via triggering an enzymatic cascade in which the ubiquitin moiety is activated by covalent linkage to E1 – the ubiquitin-activating enzyme, and transferred to E2 – the ubiquitin-conjugating enzyme. In the final step, E3 ubiquitin ligases mediate transfer of ubiquitin to the lysine residues in protein substrates, which mark them for degradation. Importantly, some ubiquitin ligases are deregulated in a wide range of disorders including cancer. In addition, many ubiquitin ligases are "orphan" since they have not yet been "paired" with specific substrate(s). Our aim is to identify substrates for selected orphan ligases. We utilize a broad spectrum of molecular biology and biochemical techniques; nevertheless, our main experimental tool is mass spectrometry analysis of ubiquitin ligase-associated proteins. In addition, to reveal biological functions of selected ligases, we employ gene editing in human cells and mice. Subsequently, the resulting cellular and mouse models are assayed to discover the involvement of the studied genes/proteins in the cell cycle control, DNA damage repair, cell migration, and invasiveness.

Selected recent papers:

Stancikova J, Krausova M, Kolar M, Fafilek B, Svec J, Sedlacek R, Neroldova M, Dobes J, Horazna M, Janeckova L, Vojtechova M, Oliverius M, Jirsa M, Korinek V: NKD1 marks intestinal and liver tumors linked to aberrant Wnt signaling. **Cellular Signalling** 27 (2): 245-56, 2015.

Hayakawa Y, Ariyama H, Stancikova J, Sakitani K, Asfaha S, Renz B W, Dubeykovskaya Z A, Shibata W, Wang H, Westphalen C B, Chen X, Takemoto Y, Kim W, Khurana S S, Tailor Y, Nagar K, Tomita H, Hara A, Sepulveda A R, Setlik W, Gershon M D, Saha S, Ding L, Shen Z, Fox J G, Friedman R A, Konieczny S F, Worthley D L, Korinek V, Wang T C: Mist1 Expressing Gastric Stem Cells Maintain the Normal and Neoplastic Gastric Epithelium and Are Supported by a Perivascular Stem Cell Niche. **Cancer Cell** 28: 1–15, 2015.

Janeckova L, Fafilek F, Krausova M, Horazna M, Vojtechova M, Alberich-Jorda M, Sloncova E, Galuskova K, Sedlacek R, Anderova M, Korinek V: Wnt signaling inhibition deprives small intestinal stem cells of clonogenic capacity. **Genesis** 54:101-14. 2016.


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LABORATORY OF

TRANSCRIPTIONAL REGULATION

development and evolution, eye, *Pax, Tcf* genes

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We are interested in studies of development and evolution of development (evo-devo). We use a combination of gain-of-function (transgenic) and loss-of-function (conditional knock-outs) approaches using laboratory mouse as a model organism to study mammalian embryonic development. We utilize several model systems including fish, amphioxus, platynereis and cnidarians to study various aspects of evo-devo, especially the evolution of eyes and gene regulatory networks.

Selected recent papers:

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Liegertová M, Pergner J, Kozmiková I, Fabian P, Pombinho AR, Strnad H, Pačes J, Vlček Č, Bartůněk P, Kozmik Z: Cubozoan genome illuminates functional diversification of opsins and photoreceptor evolution. **Sci Rep. 2015** Jul 8;5:11885. doi: 10.1038/srep11885. Erratum in: Sci Rep. 2015;5:14396.

Klimova L, Antosova B, Kuzelova A, Strnad H, Kozmik Z: Onecut1 and Onecut2 transcription factors operate downstream of Pax6 to regulate horizontal cell development. **Dev Biol. 2015** Jun 1;402(1):48-60. doi: 10.1016/j.ydbio.2015.02.023.


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LABORATORY OF

EYE BIOLOGY

eye biology, cre recombinase, transgenic mice, conditional knockout mice

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We use mouse as a model to provide novel insights into the development of the human visual system. We try to integrate several distinct approaches, especially genetics, physiology, and molecular techniques. Our current work is focused on systematic preparation of new transgenic Cre lines with defined expression in the eye tissues and their consecutive usage for systematic analysis of conditional mutants in the genes coding for transcriptional factors and components of the key signalling pathways. Mutant mice are subjected to detailed phenotyping with the aim to uncover the mechanisms underlying eye defects.

Selected recent papers:

Fujimura N: WNT/β-Catenin Signaling in Vertebrate Eye Development. **Front Cell Dev Biol. 2016** Nov 30;4:138. Review.

Antosova B, Smolikova J, Klimova L, Lachova J, Bendova M, Kozmikova I, Machon O, Kozmik Z: The gene regulatory network of lens induction is wired through Meis-dependent shadow enhancers of Pax6. **PLOS Genetics 2016** Dec 5;12(12):e1006441. doi: 10.1371/journal.pgen.1006441.


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Not in the picture:
Jarmila Vojtíšková | Yahya Sohrabi | Valeriya Volková | Monika Buddeusová | Marie Čepičková | Gabriela Jansová | Aigerim Aidarova

LABORATORY OF

MOLECULAR AND CELLULAR IMMUNOLOGY

genetics of pathogenesis of leishmaniasis, gene mapping, functional diversity, general and species-specific control

The research programme of the laboratory aims to identify the genes and molecular mechanisms involved in the control of immune response and susceptibility to complex infectious diseases. We focus on complex diseases because they are responsible for the largest part of human morbidity and mortality. They are controlled by multiple genes, and hence their pathogenesis cannot be explained by effects of a single gene with omission of others. Leishmaniasis is such a complex disease and it has served as a major paradigm of immune response to an infectious agent. We aim to identify the genes and functions controlling this disease. The disease is caused by protozoan parasites of genus *Leishmania* that multiply in macrophages. Different species of *Leishmania* induce different symptoms, but even the patients infected by the same species develop different clinical manifestations. Many phenomena observed in human leishmaniases can be investigated in the mouse. Our approach uses a combination of genetic dissection with screening of a large set of immunological and clinical parameters of the disease. We were able to dissect the complexity of the host response to *L. major,* which is characterized by many immunological and pathological parameters, by use of a special system – recombinant congenic strains of mice – and we detected and mapped more than 24 novel QTLs (quantitative trait loci) influencing the response to this parasite. We mapped seven QTLs by combination of recombinant mapping and in silico approaches to less than 1 or 2 cM. This will enable us to screen for candidate genes, detect those with altered expression after infection, and use systems analysis to identify the functional networks of genes that would define the critical pathogenetic pathways. Last but not least, we have identified diphenyleneiodonium (DPI) as an effective inhibitor of *Leishmania* parasites both in vitro and in vivo. It kills parasites more effectively than the current drugs such as amphotericin B. Moreover, DPI is also effective in killing *Trypanosoma*. The effective concentrations of the compound were non-toxic to the tested human cell lines.

Selected recent papers:

Slapničková M, Volkova V, Čepičková M, Kobets T, Šíma M, Svobodová M, Demant P, Lipoldová M: Gene-specific sex effects on eosinophil infiltration in leishmaniasis. **Biology of Sex Differences** 7:59, 2016.

Šíma M, Kocandová L, Lipoldová M: Genotyping of short tandem repeats (STRs) markers with 6 bp or higher length difference using PCR and high resolution agarose electrophoresis. **Protocol Exchange. 2015** doi:10.1038/protex.2015.054.

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LABORATORY OF

CANCER CELL BIOLOGY

cell cycle, checkpoint, DNA damage response, phosphorylation, phosphatase, tumorigenesis, oncogenic transformation

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Zuzana Líčeníková-Hořejší | Gabriela Jeníková | Jan Benada | Tomáš Liďák

Proliferation of cells is essential for keeping organisms alive and healthy, and is accomplished by passing through interphase followed by nuclear division (mitosis) and cellular division (cytokinesis). In response to DNA damage, cells temporarily stop progression through the cell cycle (checkpoint) to prevent transmission of mutations to the progeny. After completion of DNA repair, cells are allowed to re-enter the cell cycle (checkpoint recovery). Radiotherapy and chemotherapy with genotoxic pharmaceuticals represent two commonly used non-surgical strategies in the treatment of human tumours and they both rely on induction of cell death by genotoxic stress. Progression through the cell cycle and cellular responses to DNA damage are tightly controlled by interconnected signalling cascades. Malfunction of cellular checkpoints causes accumulation of mutations and can lead to the genome instability, activation of oncogenes, and eventually to malignant transformation.

In our laboratory we employ cell biology, molecular biology and biochemical approaches to identify the molecular mechanisms that control cellular responses to DNA damage. In particular, we focus on protein phosphatase PPM1D/Wip1, which is an important negative regulator of tumour suppressor p53 and controls termination of the checkpoint. Our work aims to decipher the molecular mechanisms regulating the function of PPM1D/Wip1 in human cells and in mouse models. Using chemical genetics we also evaluate PPM1D/Wip1 as a potential pharmacological target. In addition, we study the mechanisms by which Polo-like kinase 1 modulates DNA repair during mitosis. Finally, we investigate the role of CK2 kinase in folding of the large protein complexes involved in the DNA damage response.

Selected recent papers:

Pechackova S, Burdova K, Benada J, Kleiblova P, Jenikova G, Macurek L: Inhibition of WIP1 phosphatase sensitizes breast cancer cells to genotoxic stress and to MDM2 antagonist nutlin-3. **Oncotarget. 2016**; 7:14458-75.

Benada J, Burdová K, Lidak T, von Morgen P, Macurek L: Polo-like kinase 1 inhibits DNA damage response during mitosis. **Cell Cycle 2015**; 14:219-31.

Benada J, Macurek L: Targeting the Checkpoint to Kill Cancer Cells. **Biomolecules 2015**; 5:1912-37.


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LABORATORY OF

STRUCTURAL BIOLOGY

protein crystallography, human carbonic anhydrase IX, antibody engineering

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The main interests of our group are structural studies of various proteins of biological or medicinal interest using protein crystallography. We use the structural knowledge in understanding the protein function and in some projects also in modulating its function by design of specific inhibitors.
In our structure-based drug discovery project, we target enzymes from pathogenic organisms as well as human enzymes (e.g., human nucleotidases or cancer-specific carbonic anhydrase IX); the knowledge of protein structures provides a platform for the rational design of specific inhibitors.
Our group also focuses on engineering recombinant antibody fragments of potential diagnostic use. We employ several approaches aiming at practical use of recombinant antibody fragments.

Selected recent papers:

Skerlova J, Kral V, Kachala M, Fabry M, Bumba L, Svergun DI, Tosner Z, Veverka V, Rezacova P: (2015) Molecular mechanism for the action of the anti-CD44 monoclonal antibody MEM-85. **J Struct Biol** 191, 214-223.

Tesina P, Cermakova K, Horejsi M, Prochazkova K, Fabry M, Sharma S, Christ F, Demeulemeester J, Debyser Z, Rijck JD, Veverka V, Rezacova P: (2015) Multiple cellular proteins interact with LEDGF/p75 through a conserved unstructured consensus motif. **Nat Commun 6**, 7968.

Pachl P, Simak O, Rezacova P, Fabry M, Budesinsky M, Rosenberg I, Brynda J: (2015) Structure-based design of a bisphosphonate 5 '(3 ') -deoxyribonucleotidase inhibitor. **Medchemcomm 6**, 1635-1638.


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LABORATORY OF

TRANSGENIC MODELS OF DISEASES

transgenesis, disease models, embryogenesis, proteases and their inhibitors

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The laboratory has three subgroups that are interlinked by technologies used and mouse models studied to reveal gene functions in the complexity of the whole organism.
One subgroup focuses on proteases in physiology and disease, particularly on matrix metalloproteinases (MMP), a disintegrin and metalloproteinase (ADAM), and kallikreins (Klk). MMP and Klk proteases are partly responsible for controlling extracellular matrix-cell interactions affecting cell differentiation, survival, migration, and other processes. ADAM proteinases (ADAM 10, ADAM17) release ligands and their receptors from the cell surface, thus guiding bioavailability of many important regulatory molecules. We have created a number of mutants for Klk genes on the background of SPINK5, the major inhibitor of serine proteases, to reveal their complex network in the skin, especially in the development of the Netherton syndrome.
Ubiquitylation-mediated processes. Using mutant mouse models we are addressing the role of several new uncharacterized ubiquitin ligases in health and disease. A major focus of these studies is to understand the role of ubiquitylation in regulating the intestinal barrier function and to characterize links with human inflammatory bowel disease.
Early embryonic development, epigenetics, and meiosis. Using unique mouse models for the FAM208a gene we address the molecular mechanisms influencing cell fate decisions and the embryonic development, stem cell pluripotency. Other mouse models were generated to study the role of Fragile X mental retardation syndrome 1 neighbour gene (FMR1nb), especially in female reproduction during oocyte meiosis and maturation.

Selected recent papers:

Kasparek P, Ileninova Z, Haneckova R, Kanchev I, Jenickova I, Sedlacek R: A viable mouse model for Netherton syndrome based on mosaic inactivation of the Spink5 gene. **Biol Chem. 2016** Dec 1;397(12):1287-1292.

Brauer R, Tureckova J, Kanchev I, Khoylou M, Skarda J, Prochazka J, Spoutil F, Beck I M, Zbodakova O, Kasparek P, Korinek V, Chalupsky K, Karhu T, Herzig KH, Hajduch M, Gregor M, Sedlacek R: MMP-19 deficiency causes aggravation of colitis due to defects in innate immune cell function. **Mucosal Immunol. 2015** Nov 11. doi: 10.1038/mi.2015.117.

Prochazka J, Prochazkova M, Du W, Spoutil F, Tureckova J, Hoch R, Shimogori T, Sedlacek R, Rubenstein J L, Wittmann T, Klein O D: Migration of Founder Epithelial Cells Drives Proper Molar Tooth Positioning and Morphogenesis. **Dev Cell. 2015** Dec 21;35(6):713-24.


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LABORATORY OF

RNA BIOLOGY

pre-mRNA splicing, spliceosome, epigenetics, nuclear architecture, *retinitis pigmentosa*

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Our long-term interest is to determine how cells decode information stored in the genome. We focus on the molecules called mRNAs that serve as messengers between DNA and proteins. Information for protein synthesis in our genome is fragmented and the coding sequences are joined together after transcription of DNA into RNA in a process called RNA splicing. In our laboratory, we analyse how the protein-coding fragments are recognized and joined together. We mainly focus on how the nuclear environment and mainly chromatin influence RNA splicing. In addition, we study the quality control mechanisms that ensure that the splicing machinery is correctly formed on proper RNA. These studies also help us to understand why mutations in proteins that catalyse RNA splicing cause retinitis pigmentosa, a human genetic disease characterized by photoreceptor cell degeneration. As we mostly study all these processes directly in living cells, we widely employ cell culture and various microscopy techniques (e.g., super-resolution fluorescence microscopy, live cell imaging, high-content microscopy, and other).

Selected recent papers:

Bieberstein N I, Kozáková E, Huranová M, Thakur P K, Krchňáková Z, Krausová M, Carrillo-Oesterreich F, Staněk D: (2016) TALE-directed local modulation of H3K9 methylation shapes exon recognition. **Sci. Rep. 6**: 29961.

Růžičková Š, Staněk D: (2016) Mutations in spliceosomal proteins and retina degeneration. **RNA Biol.**, Jun 14: 1-9. [Epub ahead of print].

Novotný I, Malinová A, Stejskalová E, Matějů D, Klimešová K, Roithová A, Švéda M, Knejzlík Z, Staněk D: (2015) SART3-dependent accumulation of incomplete spliceosomal snRNPs in Cajal bodies. **Cell Rep. 10**: 429–440.


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LABORATORY OF

EPIGENETIC REGULATIONS

RNA degradation, dsRNA, RNAi, lncRNA, retrotransposon

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We study mechanisms governing gene expression during mammalian oocyte-to-embryo transition (OET). OET is an orchestrated process where a highly specialized cell – the oocyte – is transformed into cells that are able to give rise to a new organism. We work on three OET topics:

Maternal mRNA metabolism
OET relies on extensive post-transcriptional control of maternal mRNAs. Maternal mRNAs that are no longer needed are eliminated, while mRNAs whose products are needed for zygotic genome activation (ZGA) are maintained and translated. We particularly focus on induction of selective mRNA degradation during major developmental transitions: resumption of meiosis, fertilization, and zygotic genome activation.

Role of small RNAs during OET
We study the role of small RNA pathways (microRNA, RNA interference, and piRNA pathways) in the mammalian female germline where these three pathways co-exist. We are particularly interested in (i) variability of this co-existence across mammals, and (ii) in consequences of highly active endogenous RNA interference in somatic cells.

Role of long non-coding RNAs during OET
Long non-coding RNAs (lncRNAs) are a heterogeneous group of genome-encoded RNAs, many of which have important biological functions. In collaboration with the laboratory of Kristian Vlahovicek from the Zagreb University (bioinfo.hr), we annotate and study lncRNAs expressed during OET. This research is supported by a Marie Curie Initial Training network, RNATRAIN.

Selected recent papers:
Abe K, Yamamoto R, Franke V, Cao M, Suzuki Y, Suzuki M G, Vlahovicek K, Svoboda P, Schultz R M, Aoki F: (2015) The first murine zygotic transcription is promiscuous and uncoupled from splicing and 3' processing. **EMBO J.** 34(11):1523-37.

Svobodova E, Kubikova J, Svoboda P: (2016) Production of small RNAs by mammalian Dicer. **Pflugers Arch.** 468(6):1089-10.

Karlic R, Ganesh S, Franke V, Svobodova E, Urbanova J, Suzuki Y, Aoki F, Vlahovicek K, Svoboda P: (2017) Long non-coding RNA exchange during oocyte-to-embryo transition in mice. **DNA Research**. [Epub ahead of print] 10.1093/dnares/dsw058.


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LABORATORY OF

ADAPTIVE IMMUNITY

T cell, antigenic signalling, cell fate decision, self-tolerance, immunity

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Our group of Adaptive Immunity was established in 2016. We study T cells, a type of white blood cells that is involved in adaptive immune responses. A major task of a T cell is to discriminate between self and non-self, i.e., to avoid autoimmune reaction and fight against the invading pathogens. Our research focuses on understanding how antigenic signals determine the fate decisions of T cells during their development, homeostasis, and immune responses. We cover a wide range of processes, from molecular determinants of T-cell responses to cellular interactions in animal models of infection and autoimmunity. At the moment, we are working on three specific projects in the field of regulatory T cells, formation of self-tolerant and immune-sufficient T-cell repertoire, and origin and function of 'virtual' memory T cells. The long-term aim of our lab is to understand how T-cell receptor signals are initiated and how the primary sequence of TCR-encoding genes predetermines various T-cell fate decisions during the life-time of an individual.

Selected recent papers:

Huranova M, Stepanek O: Role of actin cytoskeleton at multiple levels of T cell activation. **AIMS Molecular Science, 2016**, 3(4): 585-596. Invited review.

Hrdinka M, Sudan K, Just S, Drobek A, Stepanek O, Schlüter D, Reinhold D, Jordan B A, Gintschel P, Schraven B, Kreutz M R: Normal Development and Function of T Cells in Proline Rich 7 (Prr7) Deficient Mice. **PLoS One. 2016** Sep 22;11(9):e0162863.

Palmer E, Drobek A, Stepanek O: Opposing effects of actin signaling and LFA-1 on establishing the affinity threshold for inducing effector T-cell responses in mice. Eur. **J. Immunol. 2016** 46: 1887–1901.


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LABORATORY OF

GERM CELL DEVELOPMENT

meiosis, genetic recombination, epigenomics, fertility, gametogenesis

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Genetic recombination is the quintessence of gametogenesis; it ensures not just the reshuffling of parental alleles and thus higher variability among the offspring, but first of all the proper segregation of chromosomes during the meiotic cell divisions and thereby fertility. The sites of meiotic double-strand DNA breaks and thus the sites of recombination are determined in many mammals by the PRDM9 (PR/SET-domain carrying 9) protein, an epigenetic factor that carries histone-3-lysine-4-methyltransferase and DNA-binding activities. This protein is essential for fertility in the laboratory mouse but not in the dog. Some, yet not all mice heterozygous for certain Prdm9 mutations display sex-specific sterility, but it is unknown whether the difference in fertility is caused by the variation in Prdm9 mutations or in the genetic background. Sterile human patients with heterozygous PRDM9 mutations have been identified, but these mutations have not been confirmed as causative. In contrast, a fertile woman carrying both copies of PRDM9 inactivated was found. We participated in production of Prdm9 mutants harbouring deletions in one of the exons encoding the catalytic PR/SET domain of both the mouse and the rat, and thus obtained a unique opportunity to analyse the precise genomic distribution of recombination sites along with the fertility of heterozygous and homozygous animals on precisely defined genetic backgrounds.

Selected recent papers:

Balcova M, Faltusova B, Gergelits V, Bhattacharyya T, Mihola O, Trachtulec Z, Knopf C, Fotopulosova V, Chvatalova I, Gregorova S, Forejt J: Hybrid Sterility Locus on Chromosome X Controls Meiotic Recombination Rate in Mouse. **PLoS Genet 2016** 12(4): e1005906. [pubmed] [doi].

Baker CL, Petkova P, Walker M, Flachs P, Mihola O, Trachtulec Z, Petkov PM, Paigen K: Multimer Formation Explains Allelic Suppression of PRDM9 Recombination Hotspots. **PLoS Genet 2015** 11(9): e1005512. [pubmed] [doi].


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LABORATORY OF

CELL MOTILITY

eukaryotic flagellum and cilium, flagellum construction, *Trypanosoma brucei*, biochemical approaches

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Martina Pružincová

In our laboratory we focus on the eukaryotic flagellum and the cilium, the organelles with motile, sensory and signalling functions. In humans the cilia are present on nearly all cell types and their malfunctions lead to pleiotropic hereditary diseases called ciliopathies. The evolutionarily conserved cytoskeletal element of the cilium, the axoneme, is a highly complex and highly organized structure. The axoneme is constructed by addition of proteins to its distal end, but how the processes of axoneme assembly are brought about is not understood. To elucidate this we take advantage of the experimental tractability of the parasitic flagellate *Trypanosoma brucei* and develop biochemical approaches for identification of proteins localizing to the distal domain of the axoneme. We study the roles of the identified proteins in the regulation of axoneme assembly and in flagellum functions, and attempt to get a mechanistic insight into their activities using in vitro reconstitution assays. Moreover, we apply the knowledge acquired studying trypanosomes to mammalian systems, such as characterizing human orthologues of the trypanosome proteins and applying the developed biochemical approaches to mammalian tissues. Understanding the processes of the axoneme assembly will help understand causes of certain ciliopathies.

Selected recent papers:

Varga V, Moreira-Leite F, Portman N, Gull K: The flagella connector of *Trypanosoma brucei* is a kinesin-powered junction distinct from the axonemal capping structure. Submitted.

Dean S, Moreira-Leite F, Varga V, Gull K: (2016) Cilium transition zone proteome reveals compartmentalisation and differential dynamics of ciliopathy complexes. **PNAS** 113(35):E5135-43.

Sunter J, Varga V, Dean S, Gull K: (2015) A dynamic coordination of flagellum and cytoplasmic cytoskeleton assembly specifies cell morphogenesis in trypanosomes. **J. Cell Sci.** 128(8), 1580-1594.


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LABORATORY OF

GENOMICS AND BIOINFORMATICS

genome analysis, transcriptome analysis, next-generation sequencing, cancer genomics

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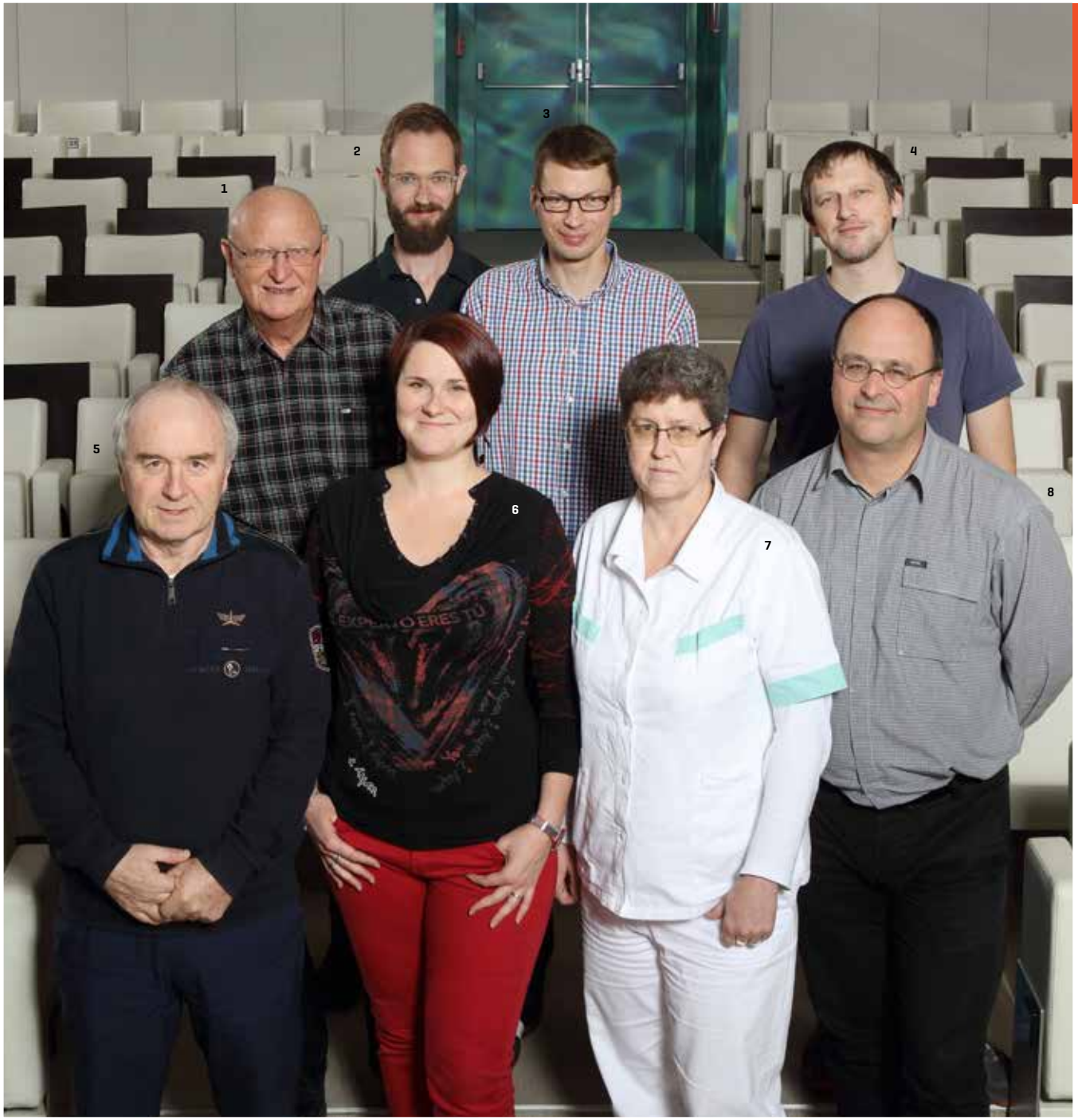
To understand the evolution of eukaryotes and the developmental processes that they regulate, it is necessary to analyse their genomes and transcriptomes. Genome sequences are the ultimate source for phylogenomics. Single-cell eukaryotes (protists) with their branching close to the root of the evolutionary tree are the best candidates for genome studies. The availability of the genomic sequences will allow inferences to be made about the gene complement of the common eukaryotic ancestor. The main interest is also focused on endosymbiotic origin of two emblematic organelles of the eukaryotic cell, the mitochondrion and the plastid. Using next-generation sequencing platforms we characterize genomes and transcriptomes of many protist species. Adding genome sequences from diverse protists to currently available eukaryotic genomes enables us to deduce, with much higher accuracy, details of many steps and processes of evolution of the eukaryotic cell. A second major topic of our group is directed towards molecular diagnostics and personalized medicine. We study intracellular interactions in malignant melanoma and in tumour-associated fibroblasts using genomics tools. We also participated in characterization of so far the oldest endogenous lentivirus found in the genome of mammalian order Dermoptera. We defined the age of this virus when it infiltrated the Dermoptera lineage and obtained evidence of the coevolution of antiviral factor TRIM5-alpha.

Selected recent papers:

Karnowska A, Vacek V, Zubáčová Z, Treitli S C, Petrželková R, Eme L, Novák L, Žárský V, Barlow L D, Herman E K, Soukal P, Hroudová M, Doležal P, Stairs C W, Roger A J, Eliáš M, Dacks J B, Vlček Č, Hampl V: A Eukaryote without a Mitochondrial Organelle. **Curr Biol 2016**, 26:1274-1284.

Ševčíková T, Klimeš V, Zbránková V, Strnad H, Hroudová M, Vlček Č, Eliáš M: A Comparative Analysis of Mitochondrial Genomes in Eustigmatophyte Algae. **Genome Biol Evol. 2016**, 8:705-722.

Hron T, Farkašová H, Padhi A, Pačes J, Elleder D: Life History of the Oldest Lentivirus: Characterization of ELVgv Integrations in the Dermopteran. **Genome. Mol Biol Evol. 2016**, 33:2659-69.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INFORMATION TECHNOLOGIES

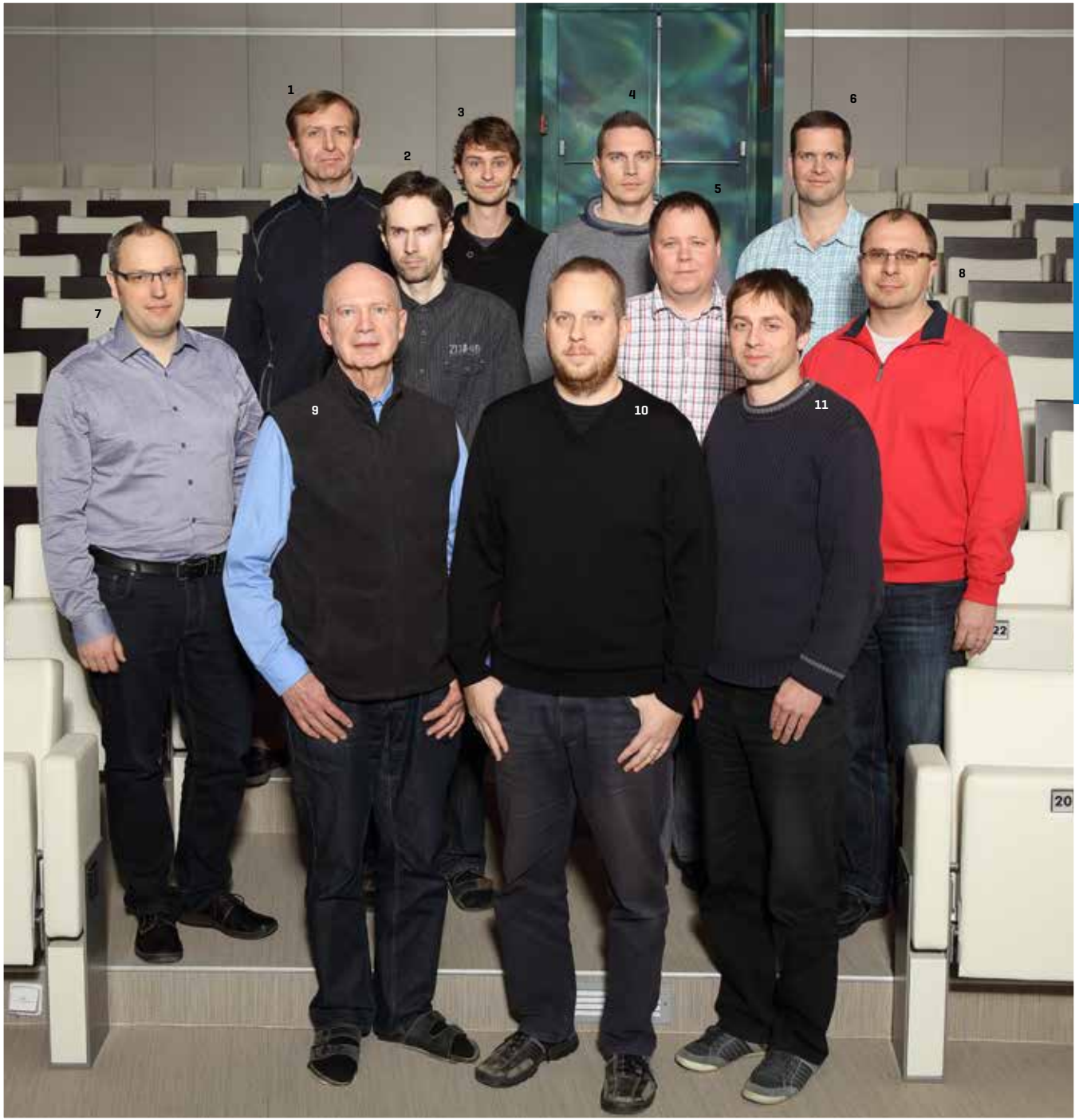
The IT department provides a wide range of information technology services to support various needs of the users at the Institute. The main tasks include:

- administration of LAN and wireless network in the img.cas.cz domain
- administration of storage area network (SAN) infrastructure, data backup and archiving
- administration of institutional servers, including e-mail and web administration
- operation of two modern data centres with UPS, air-conditioning, temperature and humidity monitoring, and fire protection system
- technical support for the end users (PC and Mac platforms, operating system and application installation, configuration) including remote support for the users in the detached sites of the Institute
- printing services
- hardware purchase consultancy
- software purchasing, license management, volume and campus license negotiations

Special support is provided to the institute facilities and research groups:

- operation of internal databases and information systems (e.g., animal tracking system, booking system)
- development of websites and web applications
- operation of the access control system and the surveillance system
- operation of the audio-visual equipment in the conference hall
- IT assistance for courses and conferences, hardware equipment providing

The IT department aims to deliver innovative services and flexible solutions using the latest technology to support modern scientific research at the Institute as well as it's smooth day-to-day operation.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GENOMICS AND BIOINFORMATICS

The facility was established in late 2005 after purchase of the Affymetrix GeneChip System and was initially operated by the staff from the Department of Mouse Molecular Genetics. Since January 2007, it has become an independent unit which provides full chip microarray services, real-time quantitative PCR service and high-throughput methods using the robotic equipment. The services are provided not only to the research groups at the Institute of Molecular Genetics, but also to other academic institutions in the Czech Republic as well as abroad. The core facility is equipped with two microarray platforms: Affymetrix GeneChip System and Illumina BeadStation 500, real-time PCR cyclers Roche LC480, JANUS robots, EnVision Plate Reader from PerkinElmer and QX200 Droplet Digital PCR System, and also with instruments for assessment of quality and quantity of the processed samples (spectrophotometer Nanodrop, Qubit Fluorometer and capillary electrophoresis Agilent Bioanalyzer 2100).


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MONOCLONAL ANTIBODIES

The facility provides preparation of mouse monoclonal antibodies including immunization using a particular immunization protocol, ELISA testing of production of specific antibodies, cloning of selected samples, freezing of cryobank samples, cultivation of cell culture supernatants, or preparation of ascitic fluid from selected clones and isotype determination of the produced antibody. Further services comprise testing of cell culture supernatants for the presence of mycoplasms and freezing of cell line banks and hybridomas.


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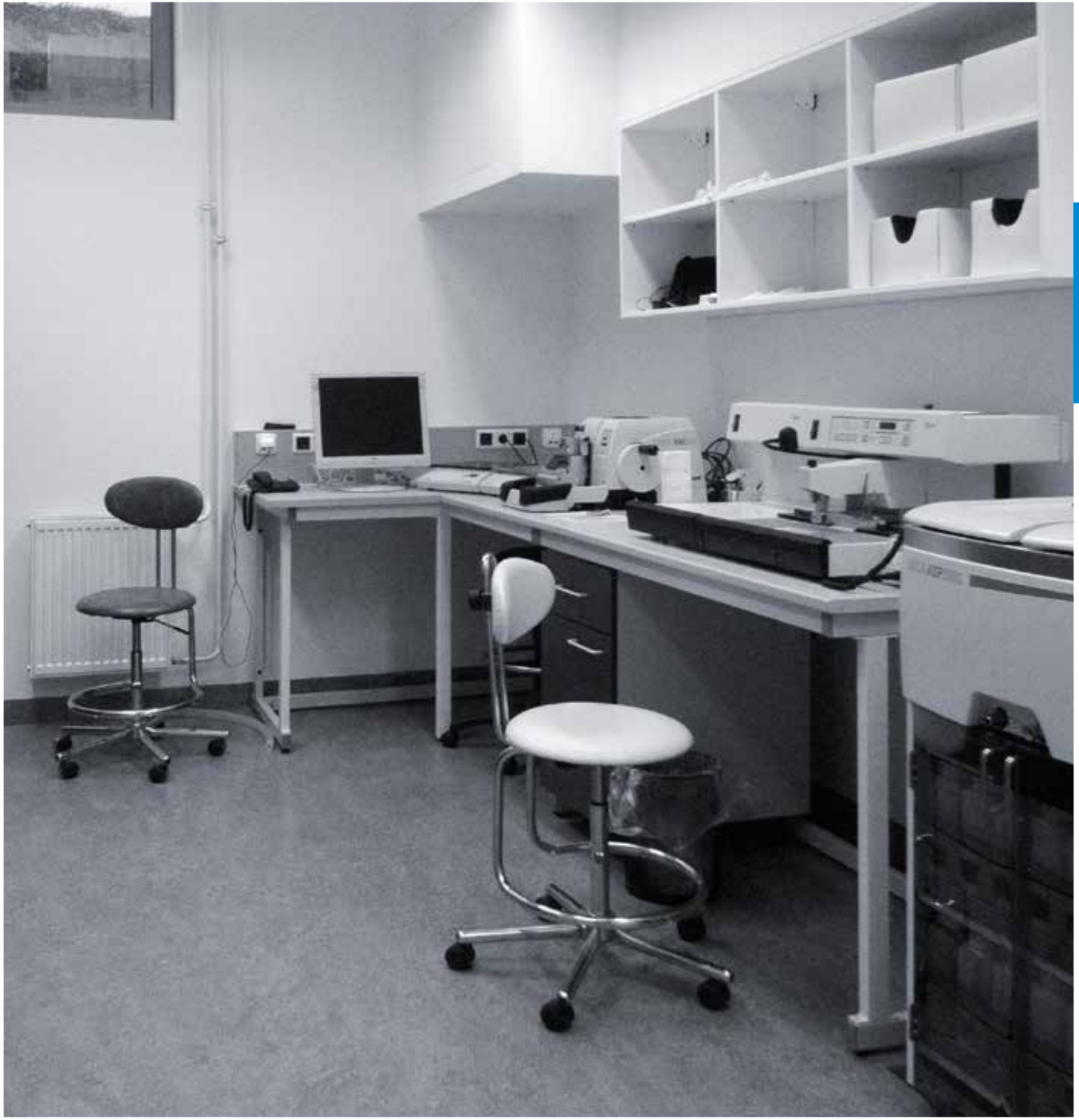
HISTOLOGICAL LABORATORY

The laboratory is equipped for preparation of paraffin blocks, tissue sectioning, deparaffination and antigen retrieval. The facility is run as a semi-self-service – tissue dehydration and paraffin embedding is handled by the staff, and all the other steps are carried out by each researcher individually. The laboratory equipment consists of a set of several Leica devices – tissue processor, paraffin-embedding station and microtomes. Tissue processor ASP200S can process up to two hundred samples in standard histological cassettes in a single run. Paraffin-embedding station EG1150H provides full comfort for creation of wax blocks. Two fully motorized rotary microtomes RM2255 are supplied with various types of blades for easy sectioning of different tissue types. All Academy researchers are welcome – after brief initial training – to use this facility.



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MEDIA AND GLASS WASHING KRČ

The service unit offers preparation of tissue culture media and solutions (ranging from redistilled deionized water and PBS through media such as RPMI, MEM varieties, HBSS, trypsin, to custom-made solutions), preparation of bacteriology media and plates (clear and with selection agents), sterilization of solutions and material (vapour sterilization, filtration of various grades), distribution of FBS, transfection agents, glass and plastic washing, decontamination of GMO and other hazardous waste (annual volume about 5,000 kg), organization of working cloth washing (more than 4,000 items per year).


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ANIMAL FACILITY (CHICKEN)

This facility is located in the village Koleč, north of Prague, about 45 km from the main campus in Prague-Krč. It mainly takes care of breeding genetically defined inbred, congenic and outbred chicken lines. The facility produces eggs, embrya and chickens needed by several research groups focusing on chicken models.


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OFFICE OF THE DIRECTOR

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Questions?
Comments?
Suggestions?

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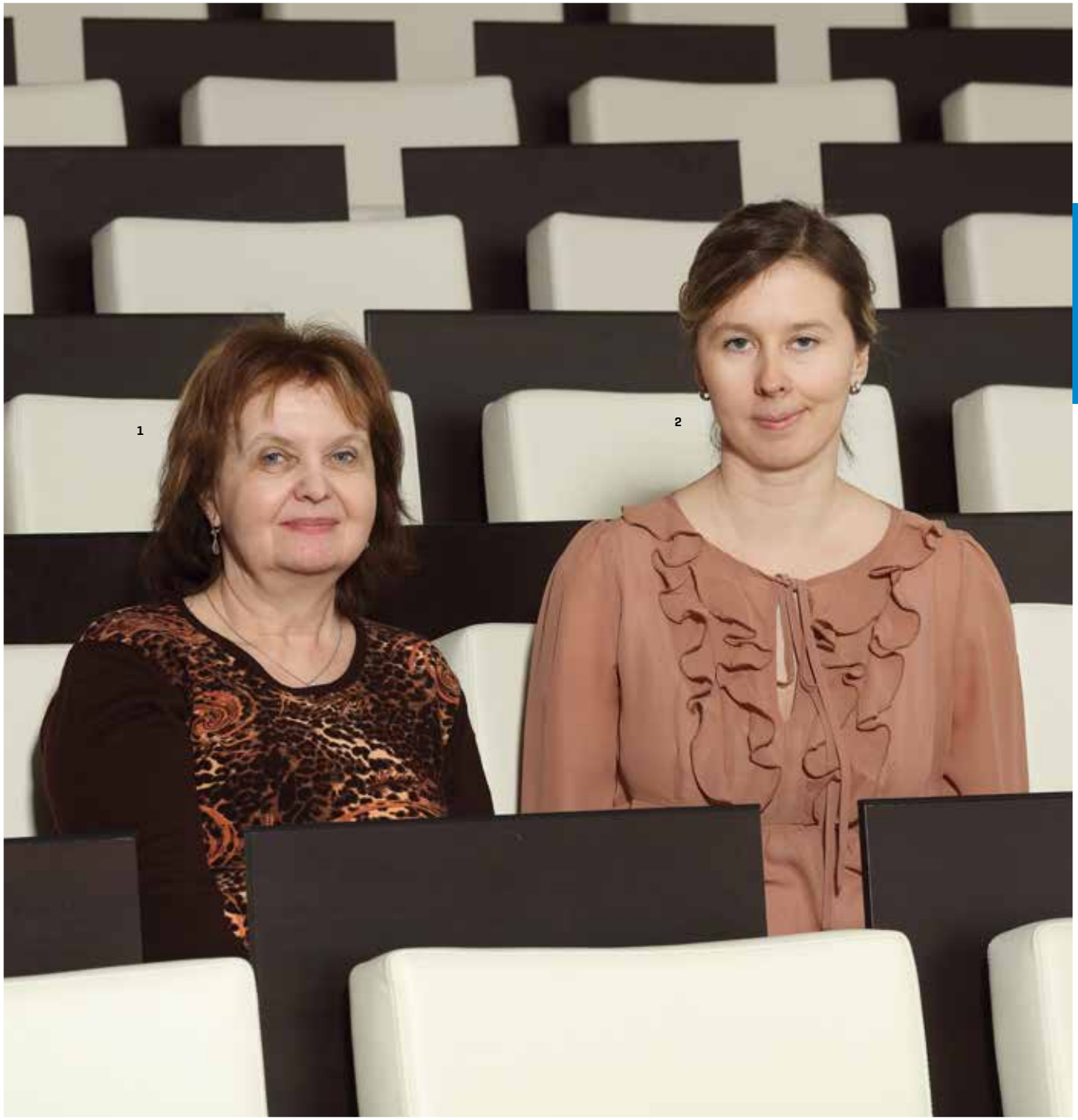
CRYOBANK KRČ

The cryobank serves for long-term storage of samples in liquid nitrogen. The current cryobank capacity is 320,000 samples, with further possible extension. The cryobank stores cell lines, hybridomas, mouse sperm and mouse embryos in liquid nitrogen or its vapours. The storage containers (LABS40K - Taylor-Wharton and 24K) are connected to the exterior liquid nitrogen container for 6,000 litres and supplied automatically. The entire cryobank system is secured by a backup energy source in case of power failure. All operations, diagnostics and monitoring of the level of liquid nitrogen in the storage containers are fully automated and controlled. Parameters (temperature, humidity, O2 concentration) and safety both in the cryobank and in the individual storage containers are followed by the monitoring system with GSM and web interface outputs.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CRYOBANK BIOCEV

The operation of the cryobank for long-term storage of samples in liquid nitrogen started in March 2016 and the cryobank is divided into two parts. The first part is situated in the main building of the BIOCEV Centre and is mainly intended for storage of cell lines and hybridomas. The second part is located in building SO-002 as a component of the transgenic and archiving module. This part of the cryobank mainly serves for preservation of mouse sperm and mouse embryos in liquid nitrogen or its vapours.

The storage containers (LABS40K, LABS80K – Taylor-Wharton and 24K) are connected to an external reservoir for liquid nitrogen with a capacity of 10,000 litres and are refilled automatically. The cryobank also includes four filling sites providing the possibility to draw liquid nitrogen into both pressure and non-pressure containers. The entire cryobank system is connected to a back-up power supply for the cases of power outage. All operations, diagnostics and checking of the liquid nitrogen level in the storage containers are fully automated and controlled. The parameters (temperature, humidity, O2 concentration) and the safety in both the cryobank and the storage containers themselves are controlled by a monitoring system connected to GSM and a web interface.

The cryobank core facility also administers production of dry ice.


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BIOCEV DIVISION

A Hot Spot of Science in the Heart of Europe
In September 2009, IMG established the BIOCEV Division. Its main task has been to ensure successful implementation of a new European scientific centre of excellence in the field of biotechnology and biomedicine, whose outputs will lead to better quality of life and to development and growth of both the knowledge economy and competitiveness of the Czech Republic.

Its implementation is a collaborative effort of six institutes of the Academy of Sciences of the Czech Republic and two faculties of Charles University in Prague. The uniqueness of the centre lies in its balanced combination of research, education and intensive cooperation with the commercial sector. Led by renowned experts, BIOCEV research teams have access to cutting-edge technologies and are an active part of major European groupings.

BIOCEV is a platform that brings together scientists, students and corporate representatives. Interaction between these groups is crucial for successful discoveries.

Pillars
TEACHING AND EDUCATION
- A wide range of educational activities and development of new graduate and postgraduate programmes of study
- Training for private sector employees
- Popularization and media coverage of biotechnology and biomedical fields

RESEARCH AND DEVELOPMENT
- Five biotechnology and biomedical research programmes: functional genomics, cell biology and virology, structural biology and protein engineering, biomaterials and tissue engineering, and development of therapeutic and diagnostic procedures
- Fully-equipped core facilities with cutting-edge instruments: Czech Centre for Phenogenomics, Centre of Molecular Structure, Imaging Methods Core Facility, OMICS Laboratory and Cryotechnologies
- Integration into the European Research Area: e.g., Infrafrontier, Instruct and the Euro-BioImaging consortium


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MEDIA AND GLASS WASHING BIOCEV

The washing unit offers washing of laboratory glass and plastic, provides central washing of working clothing, GMO waste decontamination and elimination of hazardous waste.

The media preparation unit offers preparation of cultivation media and solutions for tissue culture, preparation of bacteriological media and plates, and preparation of "custom-made" solutions. Further, the unit offers vapour sterilization of solutions and vapour or hot-air sterilization of material, as well as dry ice supplies.


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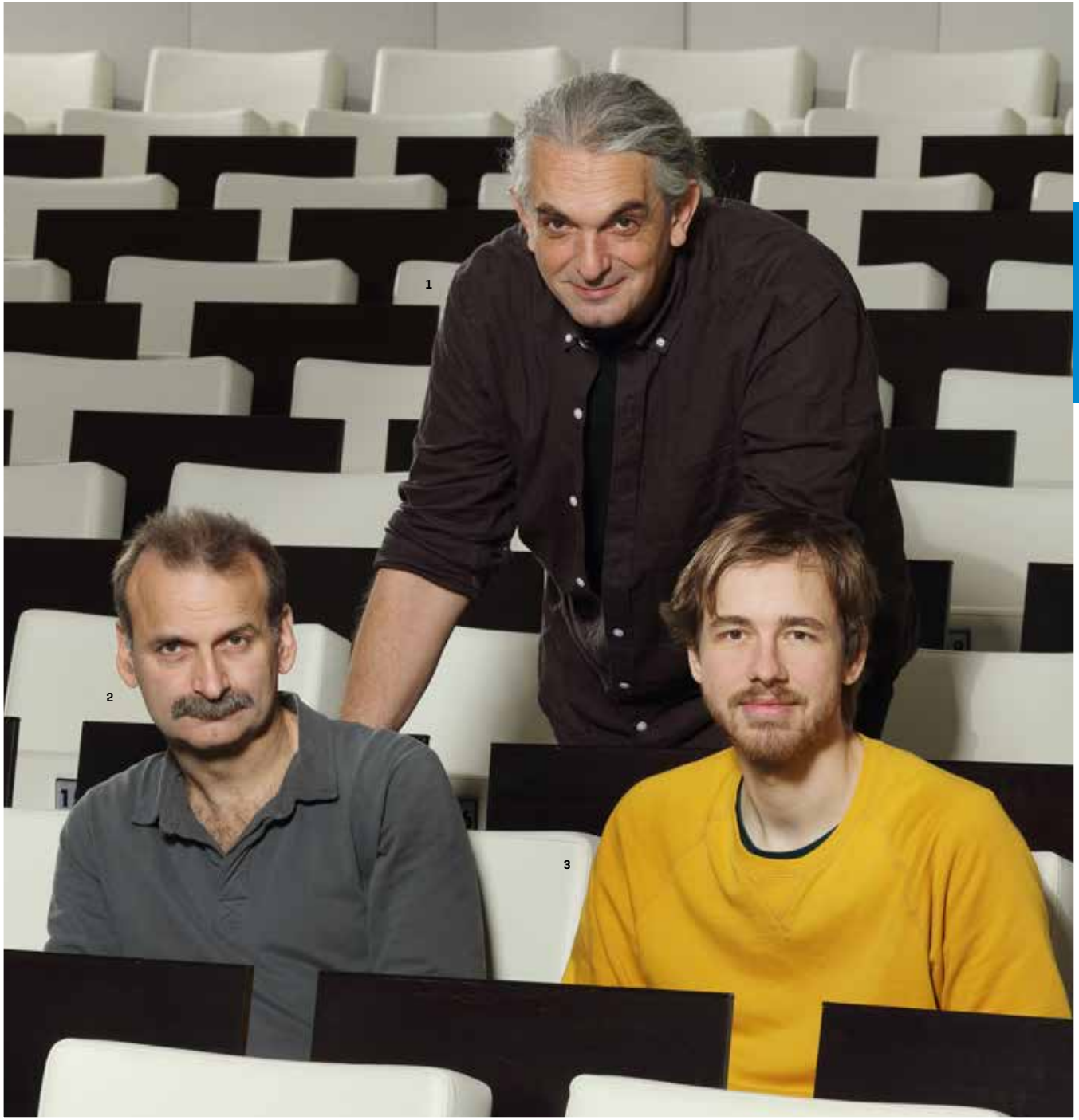
Flow Cytometry Core Facility

The facility provides methodological and instrumentation background for flow cytometry techniques. The facility is equipped with three flow cytometers – two analysers (BD FACSCalibur and BD LSRII) and one sorter. The LSRII instrument is the four-laser (405, 488, 561 and 633-nm) type with 14 fluorescence detectors. A large set of dichroic mirrors and bandpass filters are available in the laboratory, making this instrument very flexible and capable to cover most of the flow-cytometry applications. Both analysers are equipped with a HTS loader for high-throughput analysis using 96- or 384-well plates. Polychromatic high-speed cell sorter BD-Influx is equipped with five lasers (355, 405, 488, 561 and 640nm), 14 fluorescent detectors, small particle option for measuring small particles, cloning deposition unit and 6-way sorting capability. The sorter is located inside the biological safety cabinet and is fully adapted for sterile sorting. The facility is also equipped with an AutoMACS Pro (Miltenyi Biotec) magnetic separator for automatic rapid sorting of cells, as well as cell culture facilities.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Infrastructures

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CZ-OPENSCREEN 113

CZECH-BIOIMAGING
Microscopy Centre 115
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Electron Microscopy Core Facility 119

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Czech Centre for Phenogenomics

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CZECH CENTRE FOR PHENOGENOMICS – MANAGEMENT

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The Czech Centre for Phenogenomics (CCP; http://www.phenogenomics.cz/; national node of the ESFRI INFRAFRONTIER) is the only site in the Czech Republic with the expertise and capacity for large-scale generation of genetically modified mouse and rat models, and their advanced and standardized phenotyping. This expertise, together with high breeding capacity under specific pathogen-free (SPF) conditions and cryo-archiving and recovery services, provides open access to services and expertise at a level comparable to the leading research institutions in the world.
Currently, CCP is one of the largest biomedical RI in the Czech Republic with altogether more than 10,000 m^2 of space split between two research campuses: the campus of BIOCEV in Vestec and campus in Prague-Krc with academic biomedical research institutions. Based on the two campuses (but hosted only by IMG), CCP can combine the breeding capacities for animal models and effectively satisfy needs of the large research community. The new facility of CCP built in the BIOCEV campus enabled development of CCP's technologies and service quality and capacities to a highest level, comparable with the most advanced international institutions.
CCP is organized into three parts, the **Transgenic and Archiving Module (TAM)** with four specialized service subgroups (targeting, embryonic stem cells, archiving, and genotyping services). TAM provides a full portfolio of genome-editing technology using 'programmable nucleases' such as TALEN and CRISPR/Cas9. The **Animal Facility Module (AFM)** is responsible for all housing and breeding services, and the **Phenotyping Module (PM)** provides standardized phenotyping characterization of all models established or imported into CCP.


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Czech Centre for Phenogenomics

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www.phenogenomics.cz/model_generation_services
www.img.cas.cz/core-facilities/transgenic-unit

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1. Dana Kopperová | **2.** Monika Volčková | **3.** Bjoern Schuster | **4.** Jana Kopkanová | **5.** Tereza Frostová | **6.** Csilla Michaliková | **7.** Jana Ježková | **8.** Sandra Potyšová | **9.** Irena Jeníčková | **10. Inken M. Beck** | **11.** Radislav Sedláček

TRANSGENIC AND ARCHIVING MODULE

TAM provides a broad range of transgenic and archiving services, including gene targeting using classic technologies or the latest technology of programmable endonucleases, generation of transgenic animals, as well as rederivation/reanimation, and cryo-archiving of mouse strains. These procedures are highly time- and cost-demanding. Some of the projects may take longer than one year to process, which must be kept in mind when evaluating the number of services in TAM. In addition, TAM (partly in cooperation with AFM) manages animal import/export, preparation of animal cohorts on demand, genotyping, and other administrative services associated with use of genetically modified organisms within the facility. The established comprehensive technology portfolio is fully comparable with any world-class laboratory in this specific area. Moreover, CCP has invested effort into the development of new technologies, specifically the technology of "programmable nucleases" such as 'TALEN and CRISPR/Cas9'-assisted gene targeting and genome editing, which substantially improved our services in custom-tailored targeting projects, saving cost and time. Technologies provided by TAM include embryonic stem (ES) cell derivation and manipulation, development of targeting strategies and tools, generation of transgenic animals including conditional knock-out and knock-in models, genotyping, cryo-archiving, export/import/distribution, consultancy support, and administrative support (GMO licenses).


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Jan Procházka

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Czech Centre for Phenogenomics

For more information, publications and grants please visit:
www.phenogenomics.cz/phenotyping

PHENOTYPING MODULE

In the picture:
1. Jana Bieblová | **2.** Ivan Kanchev | **3.** Peter Makovický | **4.** Karel Chalupský | **5.** František Špoutil | **6.** Václav Žatečka | **7.** Ivana Švecová | **8.** Petr Macek | **9.** Cynthia Drachovsky | **10.** Trevor Epp | **11.** Attila Juhasz | **12.** Tereza Kalendová | **13.** Kateřina Koláčková | **14.** Romana Mikyšková | **15.** Kallayanee Chawengsaksophak | **16.** Barbora Singerová | **17.** Věra Mihálová | **18.** Markéta Picková | **19. Jan Procházka** | **20.** Radislav Sedláček | **21.** Šárka Suchanová | **22.** Agnieszka Kubik-Zahorodná

The phenotyping module constitutes a compendium of technologies and expertise for investigating the major physiological systems of the body. The technologies accompanying specific services are grouped into units: 1) histopathology (provides comprehensive services in processing of tissue samples including imaging and histologic evaluations), 2) metabolism, 3) clinical biochemistry and haematology, 4) cardiovascular function, 5) lung function, 6) embryology, 7) whole-body imaging and dysmorphology, and 8) neuro-behaviour and sensory function. The Units of Metabolism and Clinical Biochemistry together build the metabolomics platform. Each of the phenotyping units, with their specific sets of technology, creates a unique collection of expertise in a single location. In total, the available technologies enable collection of almost 500 parameters for each phenotyped animal, and the portfolio of services and parameters is continually developing.
The specialized modules of CCP provide open access-based services to groups and institutions from the entire Czech Republic irrespectively whether they are from the Czech Academy of Sciences or universities. Moreover, CCP also provides free access to international customers from Europe and worldwide, and the number of these customers was steadily growing in 2015-2016.


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THE GREATEST
INSPIRATION
IS THE DEADLINE

Jan Honetschläger

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Czech Centre for Phenogenomics

For more information, publications and grants please visit:
www.img.cas.cz/core-facilities/animal-facility

ANIMAL FACILITY MODULE

The Animal Facility Module is based on the newest understanding of housing and breeding of mice and rats. We have built one of the most progressive animal facilities (new building opened in 2015) in regard to logistics, versatility, and demand for animal health.
The CCP animal facility contains five individual, fully separated breeding and experimental barrier areas. Each barrier includes modern devices such as large-volume steam sterilizers and H2O2 chambers, air and wet personal areas and pass-through boxes, modern and eco-friendly HVAC (heating, ventilating and air conditioning) technology. All of these important devices help to keep the "clean" side of the SPF barrier. The animals are housed in individually ventilated cages (IVC) or digitally ventilated cages (DVC). This state-of-the-art-technology significantly improves the animal welfare level and animal facility efficiency as well as it allows detection of anomalous behaviour (sick or wounded animals), reduces animal stress and provides continuous information about the animal activity. The AFM is equipped with modern semi-automated washing technology including a tunnel cage washer, bottle washer, rack washer, and waste disposal and bedding dispensing vacuum system to increase the in-house biosecurity.
Technologies employed include housing/breeding animals in individually ventilated cages (IVC), barrier system and one-way flow of material and animals, a health monitoring system, and advanced software-assisted management of animal facility operations.

In the picture:
1. František Novotný | **2.** David Altman | **3.** Martin Herodes | **4. Jan Honetschläger** | **5.** Pavel Jína | **6.** Peter Neradil | **7.** Květa Bartošová | **8.** Václav Zikán | **9.** Antonín Čermák | **10.** Jiřina Froňková | **11.** Pavlína Pokorná | **12.** Jitka Zukálová | **13.** Ján Majerník | **14.** Nikola Dušková | **15.** Alena Babanská | **16.** Alena Vojtková | **17.** Šárka Rezková | **18.** Barbora Klimová | **19.** Daniela Hrušková | **20.** Pavla Kameníková | **21.** Daniela Kratochvílová | **22.** Stanislav Dygryn | **23.** Jaroslava Vosmíková | **24.** Jana Matoušková | **25.** Michaela Kosmáková | **26.** Romana Doubravová | **27.** Jana Vaníková | **28.** Monika Novotná | **29.** Renáta Cihelková | **30.** Dagmar Čermáková | **31.** Alexandra Hviščová | **32.** Jana Hromušková | **33.** Markéta Cibulcová | **34.** Vorlová Daniela | **35.** Veronika Repaská | **36.** Kristýna Kleiblová | **37.** Markéta Mikolášková | **38.** Nela Václavíková | **39.** Iveta Fuchsová | **40.** Gabriela Vávrová | **41.** Romana Kolaciová | **42.** Markéta Rynekrová | **43.** Zuzana Novotná | **44.** Lenka Dudaščíková | **45.** Veronika Šobíšková | **46.** Žaneta Janďourková


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CZ OPENSCREEN
National Infrastructure for Chemical Biology

For more information, publications and grants please visit:
www.openscreen.cz

In the picture:
1. Tomáš Bartoň | **2. Petr Bartůněk** | **3.** Martin Popr | **4.** David Sedlák | **5.** Tomáš Muller | **6.** Tomáš Žigo | **7.** Michal Kahle | **8.** Ctibor Škuta | **9.** Dita Franke Kidorová | **10.** Michaela Marešová | **11.** Jana Bražinová | **12.** Olga Martínková | **13.** Jarmila Králová

Not in the picture:
Jana Bartůňková | Jindřich Jindřich | Zuzana Kotrbová | Žaneta Peikerová | Antonio Pombinho | Petr Šálek

CZ-OPENSCREEN

National Infrastructure for Chemical Biology

CZ-OPENSCREEN operates the state-of-the-art technologies for research in the fields of chemical biology and provides open access to the users. Since 2010, the "CZ-OPENSCREEN National Infrastructure for Chemical Biology" has been one of the priority projects included in the Roadmap for Large Research, Development and Innovation Infrastructures in the CR. Moreover, it will serve as the national node of the ESFRI infrastructure EU-OPENSCREEN, providing access to the screening platform and to the European Chemical Biology Library. Research at CZ-OPENSCREEN is aimed at identifying new molecular probes/tools for research and new potential therapeutics. The portfolio of services includes support for seeking chemical substances with a precisely defined and specific effect in various biological systems, consultancy on assay development, assay transfer/miniaturization, high-throughput screening and high-content screening campaigns with large chemical libraries consisting of more than 85,000 compounds, confirmatory dose response assays, validation experiments in vitro, and provides standard profiling of newly synthetized chemical compounds. Cheminformatic support includes the LIMS for compound management, screening and experimental layout set-up, data visualization, data storage and mining. For more information, please visit www.openscreen.cz.


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For more information, publications and grants please visit:
www.img.cas.cz/core-facilities/microscopy-centre

In the picture:
1. Lenka Pišlová | **2.** Markéta Morská | **3. Pavel Hozák** | **4.** Karel Janoušek

MICROSCOPY CENTRE

The Microscopy Centre serves two functions:

1) Coordination of large imaging infrastructures, the CzechBioImaging as a national infrastructure (www.czech-bioimaging.cz), and the Czech participation in the EuroBioImaging (www.eurobioimaging.eu). Since January 2016, the Centre provides a national open access for users as a Czech-BioImaging node, and also international open access as part of the Prague Euro-BioImaging node candidate. All academic users are welcome to apply for Czech-BioImaging open access to enter the Centre facilities under special favourable conditions.
2) The Centre offers a wide range of state-of-the-art microscopy equipment and techniques to internal and external users. It consists of two facilities: Light Microscopy Facility and Electron Microscopy Facility. The light microscopy includes microscopy systems which range from routine fluorescence microscopes, confocal microscopes up to high-end super-resolution systems STED, SIM and STORM. Electron microscopy provides expertise and cutting edge equipment for a broad range of biological sample preparation techniques, including routine TEM observations as well as 3D electron tomography, cryo-electron microscopy and analytical electron energy-loss (EELS) analysis. The Microscopy Centre also develops new methods of image processing and analysis. The core facility widely cooperates with industry for improvement of the available methods and for intensive elaboration of new tools. All users, local and external, have full access and necessary technical support for any of the techniques and equipment, and help with image and data analysis. An important function of the Centre is also organizing user training focused on basic and advanced microscopy techniques and image analysis.


CZECH BIOIMAGING
Imaging principles of life
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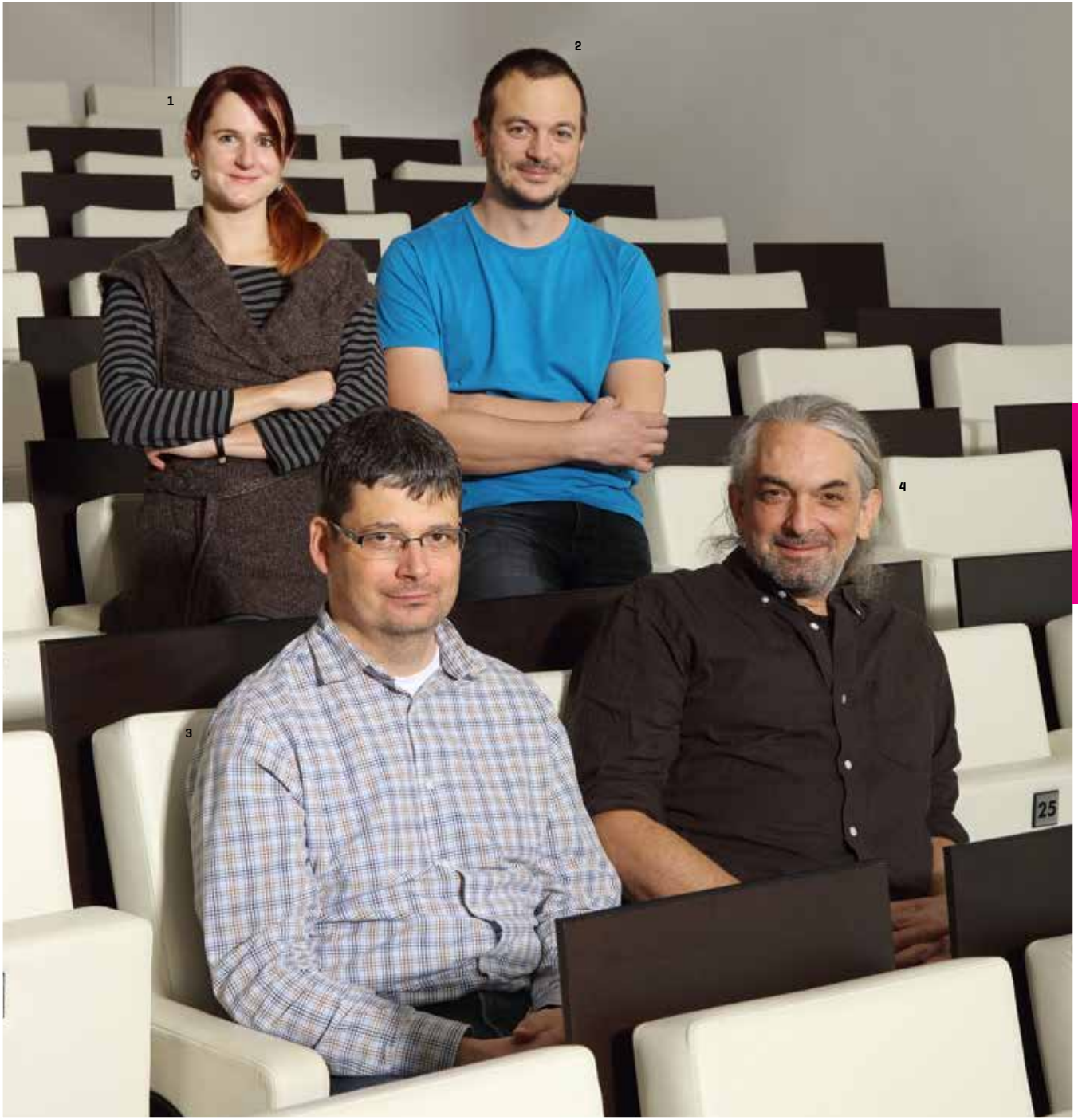
For more information, publications and grants please visit:
www.img.cas.cz/core-facilities/microscopy-centre/light-microscopy-and-flow-cytometry

In the picture:
1. Michaela Blažíková | **2.** Ivan Novotný | **3.** Martin Čapek | **4. Ondrej Horváth**

LIGHT MICROSCOPY CORE FACILITY

The facility provides methodological and instrumentation background for fluorescence microscopy techniques. The facility is equipped with a wide range of instruments, from routine fluorescence microscopes, confocal microscopes, up to high-end super-resolution microscopy systems STED, SIM and SMLM. The facility provides services for in-house research groups and as well as for a wider microscopy community on the open-access principle. Most of the instrumentation in the laboratory is available on the self-service basis, for trained users. We place strong emphasis on user education and training and provide personalized assistance to users and their projects, not only in the sense of sample preparation and image acquisition, but in data processing, reconstruction, and analysis as well. Several offline workstations for data analysis are available (Huygens Pro, MetaMorph, Fiji - ImageJ, Helicon, MatLab, SoftWorx).
The Light Microscopy Core Facility is involved in the national infrastructure for biological and medical imaging – Czech-Bioimaging. Along with the imaging facilities of the Institute of Physiology CAS, Charles University in Prague (BIOCEV) and Institute of Experimental Botany CAS, we constitute the Prague node of the Czech-Bioimaging infrastructure, which has been promoted as one of the two Czech nodes of the constructed pan-European imaging infrastructure EuroBioimaging (Advanced Light Microscopy Node Prague CZ). The Light Microscopy Core Facility provides the sponsored "Czech-Bioimaging open access" programme for both domestic and international academic users.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www.img.cas.cz/core-facilities/microscopy-centre/electron-microscopy

In the picture:
1. Jana Schrenková | **2.** Ivana Nováková | **3.** Zuzana Lubovská | **4. Vlada Filimonenko**

ELECTRON MICROSCOPY CORE FACILITY

The Electron Microscopy Core Facility provides expertise and cutting-edge equipment for a broad range of biological sample preparation and ultrastructural imaging techniques. The core facility deals with various biological samples: human and animal cell cultures, plant and animal tissues, worms, microorganisms, viruses. The sample preparation techniques include routine chemical fixation and resin embedding, high-pressure freezing, freeze-substitution, plunge-freezing, cryosectioning, and immunolabelling, including simultaneous detection of multiple targets by our self-developed methods.

A high-pressure freezing machine, two automatic freeze-substitution machines, cryo-ultramicrotomes, Vitrobot for automated plunge-freezing, and additional wet lab equipment are available. The core facility is equipped with two transmission electron microscopes (TEM) – a standard instrument for routine observation and an advanced 200 kV instrument providing the possibility of high-resolution TEM, 3D electron tomography, cryo-electron microscopy and electron energy-loss (EELS) analysis.

We collaborate with visiting scientists from the Czech Republic and the Slovak Republic. The projects include, among others: microarchitecture of lipid compartments in the cell nucleus, C. elegans meiosis, cellular mechanisms of infection and of nanoparticle uptake.

The Electron Microscopy Core Facility associated to the IMG Microscopy Centre is part of the IMG Czech-BioImaging node and Prague Euro-BioImaging node.


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BIOCEV

More than 25,000 m^2 floor space, equipped with state-of-the-art equipment and technologies, 600 researchers and students included in more than 50 research teams and 5 programmes. Biotechnology and Biomedicine Centre in Vestec (BIOCEV) is a new European scientific centre of excellence, whose outputs will lead to a better quality of life and knowledge economy.

BIOCEV

Biotechnology and Biomedicine Centre of the Academy of Sciences and Charles University in Vestec

Projects of EU-Funded Operational Programmes (Structural Funds ERDF, ESF)
Operational Programme Research and Development for Innovations

The first BIOCEV research programme (Functional Genomics) was launched in August 2012 and is headed by Assoc. Prof. Radislav Sedláček, Ph.D. Mr. Sedláček is also the Head of the Czech Centre for Phenogenomics, the largest comprehensive rodent research infrastructure in the Central Europe and BIOCEV´s core facility that participates in the worldwide network of similar facilities with the ambition to describe functions of more than 20 thousand mouse genes in the next ten years. Transgenic and gene technologies have become important experimental tools for assigning functions to genes at the level of whole complexity of the organism, creating models of genetic disorders, evaluating effects of drugs and toxins, thus helping to answer fundamental issues in basic and applied research.
The following research programmes of BIOCEV are Cellular Biology and Virology, Structural Biology and Protein Engineering, Biomaterials and Tissue Engineering, and Development of Diagnostic and Therapeutic Procedures. More details on the research programmes can be found at the project website www.biocev.eu/en/research-programme

Pillars
The uniqueness of the project lies in its balanced combination of top research integrated in five programmes, education and training of undergraduate and graduate students, and intensive cooperation with the commercial sector. Led by renowned experts, BIOCEV research teams have access to cutting-edge technologies and are an active part of major European groupings such as INFRAFRONTIER, Euro-BioImaging, Elixir or INSTRUCT.
Implementation of the BIOCEV project is a collaborative effort of six institutes of the Czech Academy of Sciences (the Institute of Molecular Genetics, the Institute of Biotechnology, the Institute of Microbiology, the Institute of Physiology, the Institute of Experimental Medicine, and the Institute of Macromolecular Chemistry) and two faculties of Charles University (the Faculty of Science and First Faculty of Medicine). The project is managed by the BIOCEV Board composed of the representatives of all these institutions. The official guarantor of the project and recipient of the funding of almost CZK 2.3 billion is the Institute of Molecular Genetics.

History
Based on completed project documentation, in July 2011 the project obtained the building authorization and in October 2011 the project was approved by the European Commission. On January 31st, 2012, the definite approval by the Czech Ministry of Education, Youth and Sports was granted. The end of 2012 was the term of the tender for the building contractor and the tenders for scientific instruments and technologies. Foundation stone ceremony was held on October 7th, 2013 and almost three years later was the official opening (June 16th, 2016). The Director of the project (Pavel Martásek) was selected in an international competition in November 2012.

Awards and Honours

2015

Balounová Jana	Award of the Czech Immunological Society – Milan Pospíšil and Mario Campa Prize for the best publication in the area of natural and anti-tumour immunity (shared 1st position)
Balounová Jana	Award of the Czech Society for Analytical Cytometry
Fulková Helena	Otto Wichterle Premium
Hejnar Jiří	Silver Memorial Medal of the Senate
Hozák Pavel	Award of the Czechoslovak Microscopic Society for outstanding merits in development of microscopic methods
Kyjacová Lenka	Novartis Discovery Award for basic research in biomedicine
Pačes Václav	Elected as Secretary General of FEBS for the period 2017-2019, invited to deliver the prestigious 14th Adrian Buzzati-Traverso lecture
Svoboda Jan	Elected as a Foreign Associate of the US National Academy of Sciences (inauguration in March 2016)

2016

Bartek Jiří	Nordic Fernström prize
Dobeš Jan	Jaroslav Šterzl Prize for a young scientist
Forejt Jiří	National award of the Czech Government "Česká hlava" (Czech Brains) for long-life research in the field of mouse genetics
Fulková Helena	Neuron Prize for young scientists
Svoboda Jan	Neuron Prize for the contribution to the world science in the field of biology
Svoboda Petr and his team	Award of the Czech Academy of Sciences for achieving outstanding scientific results in the area of "RNA interference in mammals"

Seminars and Conferences

2015

30/3-3/4	**Transmission Electron Microscopy course**
14-17/4	**Processing and Analysis of Microscopic Images in Biomedicine course**
12-13/5	**Microscopy 2015, Lednice na Moravě**
20-22/5	**XXIII Cytoskeletal Club, Vranovská Ves**
2-4/9	**Cancer EMBO YIP Meeting**
24/9	**MACS Sorting**
12-16/10	**Microscopy Methods in Biomedicine course**
2-13/11	**39th Advances in Molecular Biology and Genetics**
7-11/12	**Advanced Techniques in Fluorescence Microscopy**
26/11	**Q-PHASE – Instrument for Quantitative Phase Imaging**
27/11	**Annual IMG Conference**
30/11-5/12	**EMBO YIP PhD Course, EMBL, Heidelberg**

2016

8-12/2	**Certified qualification course of experimental design and projects of experiments**
29/2-4/3	**Elements of Science**
20/3-23/3	**Programmable Nucleases course**
20/3-23/3	**Mouse Cryopreservation Workshop**
20-23/3	**13th Transgenic Technology Meeting (TT2016)**
27-29/4	**ENIGMA2016**
3-4/5	**Microscopy Conference 2016**
6-10/6	**Processing and Analysis of Microscopic Images in Biomedicine course**
27/6-2/7	**Advanced Methods in Macromolecular Crystallization VII, the 2nd FEBS practical crystallization course in middle EU co-sponsored by INSTRUCT, Nové Hrady**
14-17/9	**Wnt Meeting 2016**
10-14/10	**Microscopy Methods in Biomedicine course**
31/10-11/11	**40th Advances in Molecular Biology and Genetics**
21-25/11	**Advanced Techniques in Fluorescence Microscopy**
28/11-2/12	**Transmission Electron Microscopy in Biomedicine**
5-7/12	**EMBO YIP PhD Course, Heidelberg**
5-9/12	**28th Workshop on Retroviral Pathogenesis, New Orleans**
9/12	**Annual IMG Conference**

Regular weekly Institute seminars – IMG speakers

2015

Iryna Kozmiková
Lucie Stegurová
Ilona Kalasová
Martin Gregor
Jarmila Králová
Antonio Pombinho
Markéta Černohorská
Nicole Bieberstein
Michaela Dvořáková
Soňa Pecháčková
Eliška Svobodová
Monika Žárská
Anna Lounková
Lucie Janečková

2016

Ondřej Ballek
Petr Tešina
Kamil Matulka
Petr Kašpárek
Lívia Uličná
Tomáš Paulenda
Anna Malinová
Aleš Drobek
Lukáš Čermák
Jana Oltová
Zuzana Hájková
Martina Slapničková
Markéta Jiroušková
Ondřej Šeda
Polina Zjablovskaja
Eliška Linhartová
Patrick Joël von Morgen
Jindřiška Fišerová
Radim Žídek
Shohag Bhattacharyya
Blanka Mrázková
Barbora Vališková
Jan Dobeš

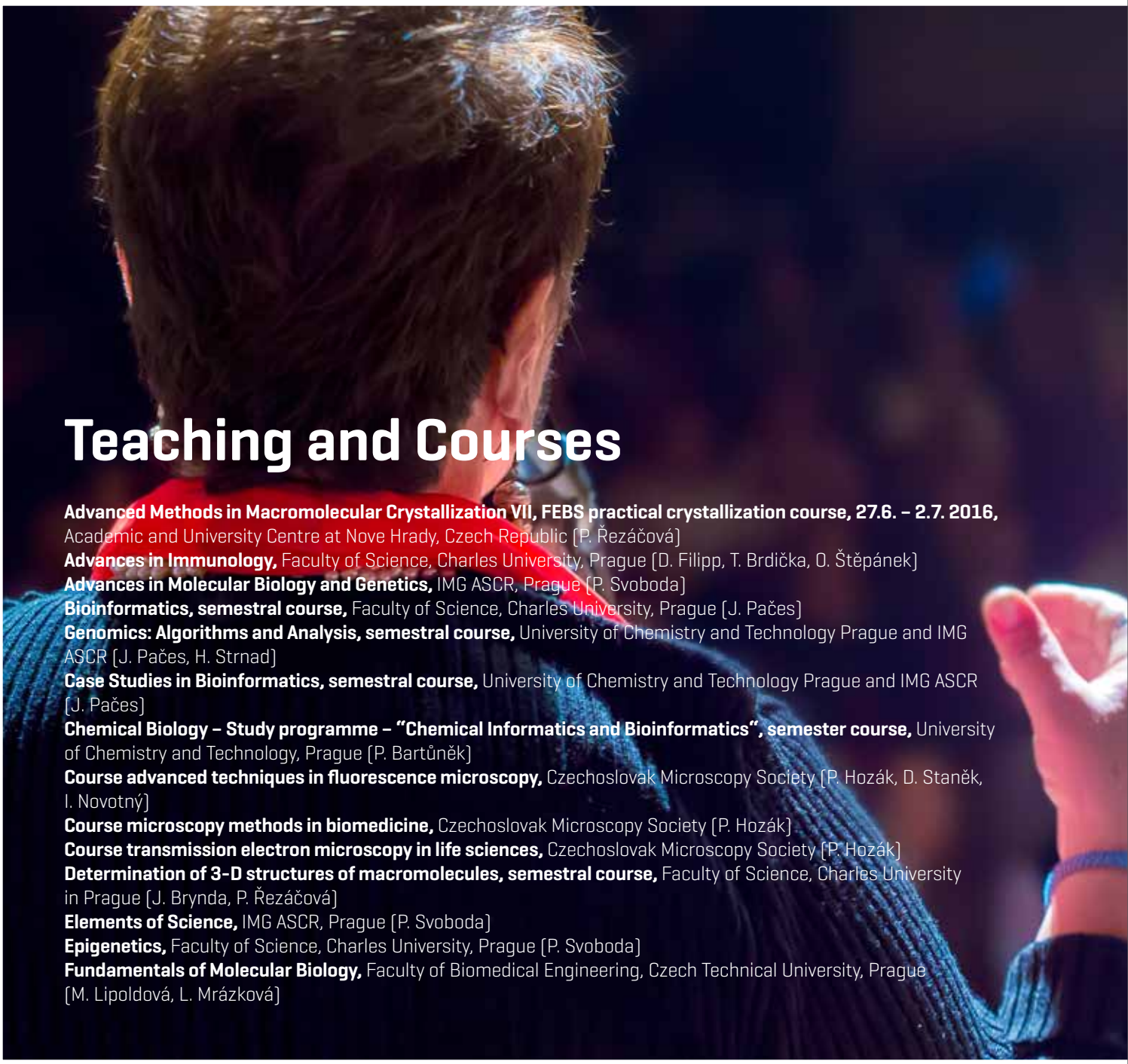
Seminar Speakers

2015

14/01/15	**Ondřej Štěpánek** [Transplantation Immunology, Department of Biomedicine University and University Hospital Basel]
11/03/15	**Benjamin Schusser** [Department of Veterinary Sciences, Ludwig Maximilian University of Munich]
18/03/15	**Arne Lindqvist** [Karolinska Institute in Stockholm]
08/04/15	**Stanislav Indik** [Institute of Virology, University of Veterinary Medicine, Vienna]
21/04/15	**Peter Sutovsky** [Animal Science and Clinical Obstetrics & Gynecology University of Missouri-Columbia Columbia, USA]
23/04/15	**Hannes Stockinger** [Department of Molecular Immunology, Institute for Hygiene and Applied Immunology Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna]
06/05/15	**Jan Konvalinka** [Institute of Organic Chemistry and Biochemistry, AS CR, Prague]
18/05/15	**Daniel G. Tenen** [Cancer Science Institute of Singapore and Harvard Medical School, Boston, USA]
20/05/15	**Kvido Stříšovský** [Institute of Organic Chemistry and Biochemistry, AS CR, Prague]
27/05/15	**Jan Kopecký** [Institute of Physiology, AS CR, Prague]
29/05/15	**Maria Jasin** [Memorial Sloan Kettering Cancer Center, New York, USA]
03/06/15	**Tomáš Valenta** [Institute of Molecular Life Sciences, University of Zürich, Switzerland]
10/06/15	**Vladimír Leksa** [Head of the Laboratory of Molecular Immunology, Institute of Molecular Immunology, Slovak Academy of Sciences]
17/06/15	**Peter Šebo** [Institute of Microbiology , AS CR, Prague]
18/06/15	**Leonid B. Margolis** [National Institute of Child Health and Human Development, National Institutes of Health, Bethesda]
24/06/15	**Michel Bouvier** [General Director of Institute for Immunology and Cancer, Department of Biochemistry and Molecular Medicine, University of Montreal]
02/07/15	**Katheleen Gardiner** [Linda Crnic Institute for Down Syndrome, University of Colorado Denver, USA]
02/09/15	**Ian Adams** [MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Western General Hospital, Edinburgh, Scotland, UK]
18/11/15	**Ondřej Vrtiška** [Editor, Journal "Vesmír"]
23/09/15	**Emil Parvanov** [The Jackson Laboratory, Bar Harbor, Maine, USA]
21/10/15	**Lukáš Chmátal** [University of Pennsylvania, Philadelphia, PA]
09/12/15	**Caren Norden** [MPI of Molecular Cell Biology and Genetics, Dresden]

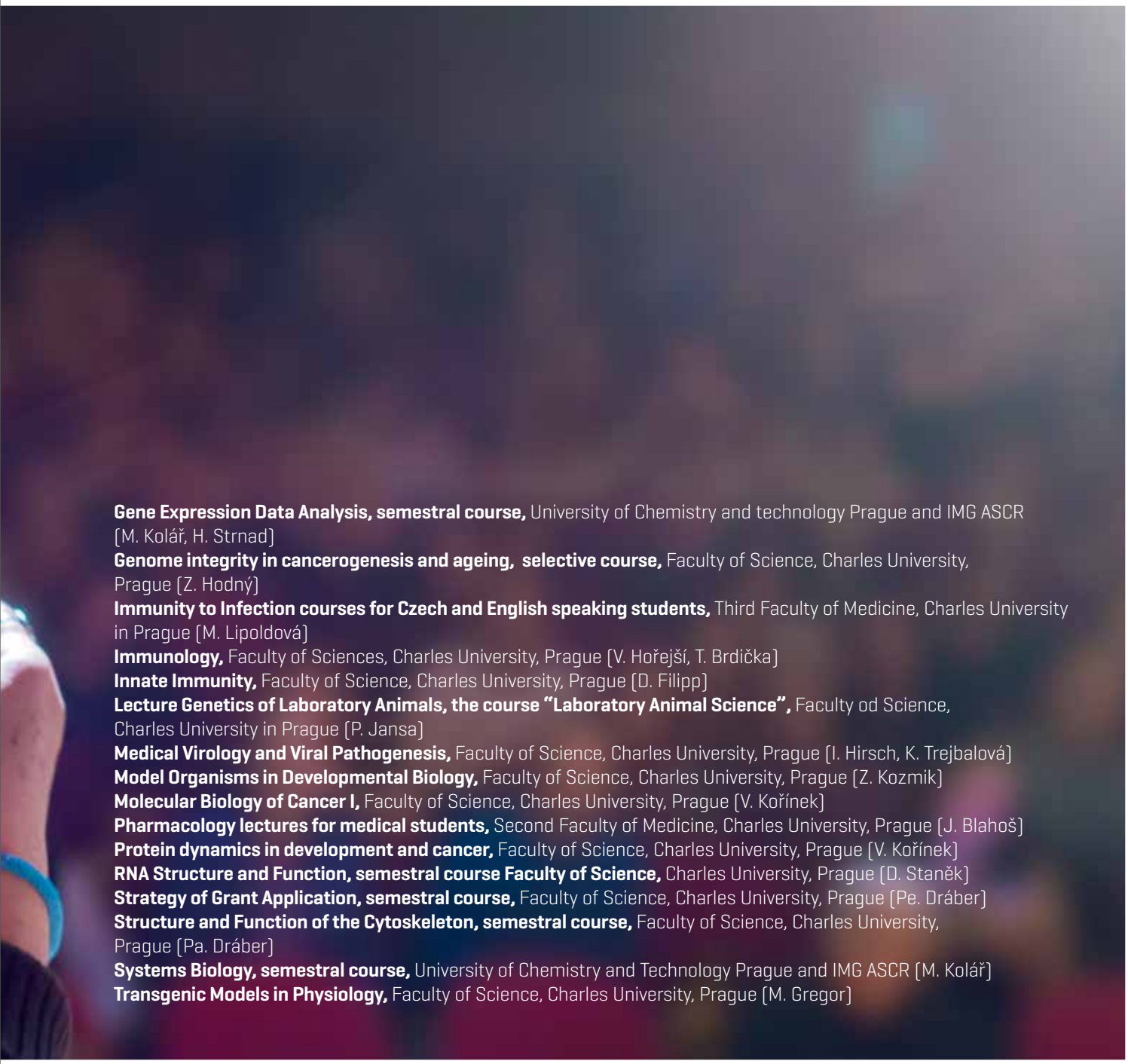
2016

27/01/16	**Ulf Andersson Ørom** (MPI of Molecular Genetics, Berlin)
10/02/16	**Nadine Vaestenhouw** (MPI of Molecular Cell Biology and Genetics, Dresden)
24/02/16	**Simon Alberti** (MPI of Molecular Cell Biology and Genetics, Dresden)
15/03/16	**Joseph Nadeau** (Pacific Northwest Diabetes Research Institute, Seattle, USA)
06/04/16	**Alessandro Vindigni** (St. Louis University School of Medicine)
11/04/16	**Susan S. Smyth** (Gill Heart Institute, Kentucky)
27/04/16	**Marina Lusic** (University Hospital Heidelberg)
04/05/16	**Joan Steitz** (Department of Molecular Biophysics and Biochemistry, Yale University)
25/05/16	**Ophir D. Klein** (University of California San Francisco)
01/06/16	**Jonathan B. Baell** (Monash University, Melbourne)
08/06/16	**Gerhard Behre** (Department for Hematology and Oncology, Universitätsklinikum Leipzig)
11/10/16	**Aleš Cvekl** (Department of Genetics and Department of Ophthalmology & Visual Sciences, Albert Einstein College of Medicine, New York, USA)
19/10/16	**Part Peterson** (University of Tartu, Faculty of Medicine, Institute of Biomedicine and Translational Medicine, Tartu, Estonia)
09/11/16	**Keith W. Caldecott** (Genome Damage and Stability Centre, University of Sussex, Brighton, United Kingdom)



Teaching and Courses

Advanced Methods in Macromolecular Crystallization VII, FEBS practical crystallization course, 27.6. – 2.7. 2016, Academic and University Centre at Nove Hrady, Czech Republic (P. Řezáčová)
Advances in Immunology, Faculty of Science, Charles University, Prague (D. Filipp, T. Brdička, O. Štěpánek)
Advances in Molecular Biology and Genetics, IMG ASCR, Prague (P. Svoboda)
Bioinformatics, semestral course, Faculty of Science, Charles University, Prague (J. Pačes)
Genomics: Algorithms and Analysis, semestral course, University of Chemistry and Technology Prague and IMG ASCR (J. Pačes, H. Strnad)
Case Studies in Bioinformatics, semestral course, University of Chemistry and Technology Prague and IMG ASCR (J. Pačes)
Chemical Biology – Study programme – "Chemical Informatics and Bioinformatics", semester course, University of Chemistry and Technology, Prague (P. Bartůněk)
Course advanced techniques in fluorescence microscopy, Czechoslovak Microscopy Society (P. Hozák, D. Staněk, I. Novotný)
Course microscopy methods in biomedicine, Czechoslovak Microscopy Society (P. Hozák)
Course transmission electron microscopy in life sciences, Czechoslovak Microscopy Society (P. Hozák)
Determination of 3-D structures of macromolecules, semestral course, Faculty of Science, Charles University in Prague (J. Brynda, P. Řezáčová)
Elements of Science, IMG ASCR, Prague (P. Svoboda)
Epigenetics, Faculty of Science, Charles University, Prague (P. Svoboda)
Fundamentals of Molecular Biology, Faculty of Biomedical Engineering, Czech Technical University, Prague (M. Lipoldová, L. Mrázková)



Gene Expression Data Analysis, semestral course, University of Chemistry and technology Prague and IMG ASCR (M. Kolář, H. Strnad)
Genome integrity in cancerogenesis and ageing, selective course, Faculty of Science, Charles University, Prague (Z. Hodný)
Immunity to Infection courses for Czech and English speaking students, Third Faculty of Medicine, Charles University in Prague (M. Lipoldová)
Immunology, Faculty of Sciences, Charles University, Prague (V. Hořejší, T. Brdička)
Innate Immunity, Faculty of Science, Charles University, Prague (D. Filipp)
Lecture Genetics of Laboratory Animals, the course "Laboratory Animal Science", Faculty od Science, Charles University in Prague (P. Jansa)
Medical Virology and Viral Pathogenesis, Faculty of Science, Charles University, Prague (I. Hirsch, K. Trejbalová)
Model Organisms in Developmental Biology, Faculty of Science, Charles University, Prague (Z. Kozmik)
Molecular Biology of Cancer I, Faculty of Science, Charles University, Prague (V. Kořínek)
Pharmacology lectures for medical students, Second Faculty of Medicine, Charles University, Prague (J. Blahoš)
Protein dynamics in development and cancer, Faculty of Science, Charles University, Prague (V. Kořínek)
RNA Structure and Function, semestral course Faculty of Science, Charles University, Prague (D. Staněk)
Strategy of Grant Application, semestral course, Faculty of Science, Charles University, Prague (Pe. Dráber)
Structure and Function of the Cytoskeleton, semestral course, Faculty of Science, Charles University, Prague (Pa. Dráber)
Systems Biology, semestral course, University of Chemistry and Technology Prague and IMG ASCR (M. Kolář)
Transgenic Models in Physiology, Faculty of Science, Charles University, Prague (M. Gregor)

PhD Programme

Students represent a significant element in our scientific community; the presence of about 100 PhD students (20 % international from both EU and non-EU countries) considerably enriches the atmosphere at the Institute and strongly contributes to its scientific output. Therefore, one of our priorities is to offer an appealing PhD programme that will attract the best students and provide them with high-quality training for a career in molecular, cell and developmental biology, immunology, genetics, and virology. The programme is based on the PhD programmes of Prague Universities, mainly Charles University and the Institute of Chemical Technology. The PhD programme and related topics are organized by our PhD Committee, which consists of four PIs (Dominik Filipp, Zbyněk Kozmik, David Staněk, Petr Svoboda) and student representatives (Lívia Uličná and Patrick Joël Von Morgen). In addition to everyday contact with their supervisors, students submit two reports to the Committee (in the second and fourth year) about their projects. This provides them with an external feedback and helps them to finish their studies on time. Further education is arranged through a number of lectures and courses organized by scientists from the Institute. PhD students also actively participate in lab meetings, journal clubs, and Institute seminars. Students can also attend English language classes, which take place directly in the IMG building. PhD students routinely present in English during lab meetings, journal clubs, and during institutional weekly seminars, which are almost exclusively given by PhD students.

Students apply to the programme through an on-line application at www.img.cas.cz/phd, where all the open PhD positions and relevant deadlines are posted. This makes our PhD programme better accessible also to students abroad, and the PhD community at our Institute is becoming more and more international. In each of the years 2015 and 2016, about 40 candidates were selected and invited for a PhD interview. The applicants gave a short presentation of their diploma thesis research in English and were briefly interviewed and assessed by a three-member committee. During the interview the applicants also visited selected laboratories and met with lab group leaders in order to find the best match. In the end, 21 students were recruited during the PhD interview procedure in 2015 and 20 in 2016.

We also aim to foster extracurricular training of our PhD students. Since 2010, we have organized a "Welcome Weekend" for the new PhD students, where they are provided with basic information about the Institute and the PhD programme. Since 2008, PhD students have also organized annual IMG PhD conferences. These have established a nice tradition of students and researchers coming together in an informal atmosphere to listen to both student talks and keynote lectures given by invited speakers.

Further information on PhD studies at the IMG can be found at www.img.cas.cz/phd.

Theses

Bachelor Theses 2016

Vojtěch Matoušek Preparation of congenic mice carrying defined genomic constructs (Supervisor: M. Lipoldová, T. Jarošíková, Faculty of Biomedical Engineering, Czech Technical University in Prague)

Diploma Theses 2015

Martina Slavková Reporter expression system for study of silencing of provirus integrated inside transcriptionally active gene (Supervisor: F. Šenigl, J. Hejnar, Faculty of Science, Charles University, Prague)

David Přikryl Study of replication and pathogenesis of retroviruses with extended host range (Supervisor: V. Pečenka, Faculty of Science, Charles University, Prague)

Jan Bartůněk The methods of biomedical research in mapping genes that modify immunological parameters in uninfected mice (Supervisor: M. Lipoldová, T. Jarošíková, Faculty of Biomedical Engineering, Czech Technical University in Prague)

Tereza Pokorná Methods of genetic engineering for genetic and functional analysis of genes that modify the response to parasite Leishmania major (Supervisor: M. Lipoldová, T. Jarošíková, Faculty of Biomedical Engineering, Czech Technical University in Prague)

Karin Heyduková The methods of biomedical research in analysis of the influence of genetic background on the functions of macrophages infected with parasite Leishmania major (M. Lipoldová, T. Jarošíková, Faculty of Biomedical Engineering, Czech Technical University in Prague)

Klára Klimešová Mapping of SART3 interactions with spliceosomal snRNPs (Supervisor: D. Staněk, Faculty of Science, Charles University, Prague)

Kašíková Lenka Characterization of the Hstx1 and Hstx2 hybrid sterility candidate genes (Supervisor: P. Jansa, Faculty of Science, Charles University, Prague)

Michaela Vaškovičová Recognition of expressed double-stranded RNAs in mammalian cells (Supervisor: P. Svoboda, Faculty of Science, Charles University, Prague)

Radek Jankele Analysis of short Argonaute isoforms from mouse oocytes (Supervisor: P. Svoboda, Faculty of Science, Charles University, Prague)

Lucie Knoblochová Role of the tumour suppressor PML in DNA damage response and cellular senescence after genotoxic stress (Supervisor: Z. Hodný, Faculty of Science, Charles University)

Eliška Davidová Role of transcription factor Snail in the mechanism of development of radioresistance in prostate carcinoma cell lines (Supervisor: Z. Hodný, Faculty of Science, Charles University, Prague)

Diploma Theses 2016

Adéla Fellnerová Chimeric antigen receptors in the treatment of haematological malignancies (Supervisor: D. Filipp, Faculty of Science, Charles University, Prague)

Petr Toman Importance of coilin-snRNP particles interaction in biogenesis of the nuclear domain named Cajal bodies (Supervisor: Z. Knejzlík, consultant: D. Staněk, Faculty of Science, Charles University, Prague)

Martin Volek Role of JARID1 family demethylases in formation of spliceosome (Supervisor: M. Stiborová, consultants: D. Staněk, N. Bieberstein, Faculty of Science, Charles University)

Kateřina Škarabellová Studies towards the biological function of ubiquitin E3 ligase RNF121 in vivo and in vitro (Supervisor: R. Sedláček, Faculty of Science, Charles University, Prague)

Erik Šebrle Posttranslational modifications affecting function of the nuclear localization signal (Supervisor: R. Sedláček, Faculty of Science, Charles University, Prague)

Radmila Hanečková Generation and analysis of double-deficient transgenic mice for kallikrein-related peptidase 5 and kallikrein-related peptidase 14 (Supervisor: R. Sedláček, Faculty of Science, Charles University, Prague)

Nikol Baloghová Characterization of tumour suppressor gene Hypermethylated in cancer 1 (Hic1) and its novel target genes in the intestinal epithelium and colorectal cancer (Supervisor: L. Janečková, Faculty of Science, Charles University, Prague)

Jana Uhlířová The role of microtubule severing ATPase katanin in modulation of glioblastoma cell motility and proliferation (Supervisor: Pa. Dráber, Faculty of Science, Charles University)

Jana Kubíková Substrate cleavage by mammalian Dicer isoforms (Supervisor: P. Svoboda, Faculty of Science, Charles University, Prague)

Ivana Dobiášová Visual system development in Platynereis dumerilii: insight from genetic engineering approach (Supervisor: Z. Kozmik, Faculty of Science, Charles University, Prague)

Alena Kučerová Role of PML in nucleolar functions (Supervisor: Z. Hodný, Faculty of Science, Charles University, Prague)

Karolína Ditrychová The role of DISP3 gene in cell proliferation (Supervisor: M. Ziková, Faculty of Science, Charles University, Prague)

Šimon Borna Analysis of the resistance of B cell antigen receptor signalling to the inhibition of Src-family kinases (Supervisor: T. Brdička)

Martina A. Poláchová Functional characterization and comparison of PPM1D/Wip1 phosphatase homologues (Supervisor: Z. Knejzlík, L. Macůrek, University of Chemistry and Technology, Prague)

Tomáš Liďák Characterization of the mechanisms of 53BP1 protein nuclear transport (Supervisor: L. Macůrek, Faculty of Science, Charles University, Prague)

PhD Theses 2015

Jan Dobeš	Novel mechanisms regulating immune tolerance and homeostasis in the intestine (Supervisor: D. Filipp, Faculty of Science, Charles University, Prague)
Pavel Marášek	Localization matters: function of paxillin and phosholipids in the cell nucleus (Supervisor: P. Hozák, Faculty of Science, Charles University, Prague)
Kateřina Bruštíková	Development of chemical regulators of microRNA and RNAi pathways (Supervisor: P. Svoboda, Faculty of Science, Charles University, Prague)
Lenka Kyjacová	Radiation-induced plasticity of prostate cancer cells (Supervisor: Z. Hodný, Faculty of Science, Charles University, Prague)
Ondřej Svoboda	Origins of vertebrate haematopoiesis (Supervisor: P. Bartůněk, Faculty of Science, Charles University, Prague)
Aleš Drobek	Regulation of leukocyte signal transduction by adapter proteins with special focus on Csk anchoring proteins (Supervisor: T. Brdička, Faculty of Science, Charles University, Prague)

PhD Theses 2016

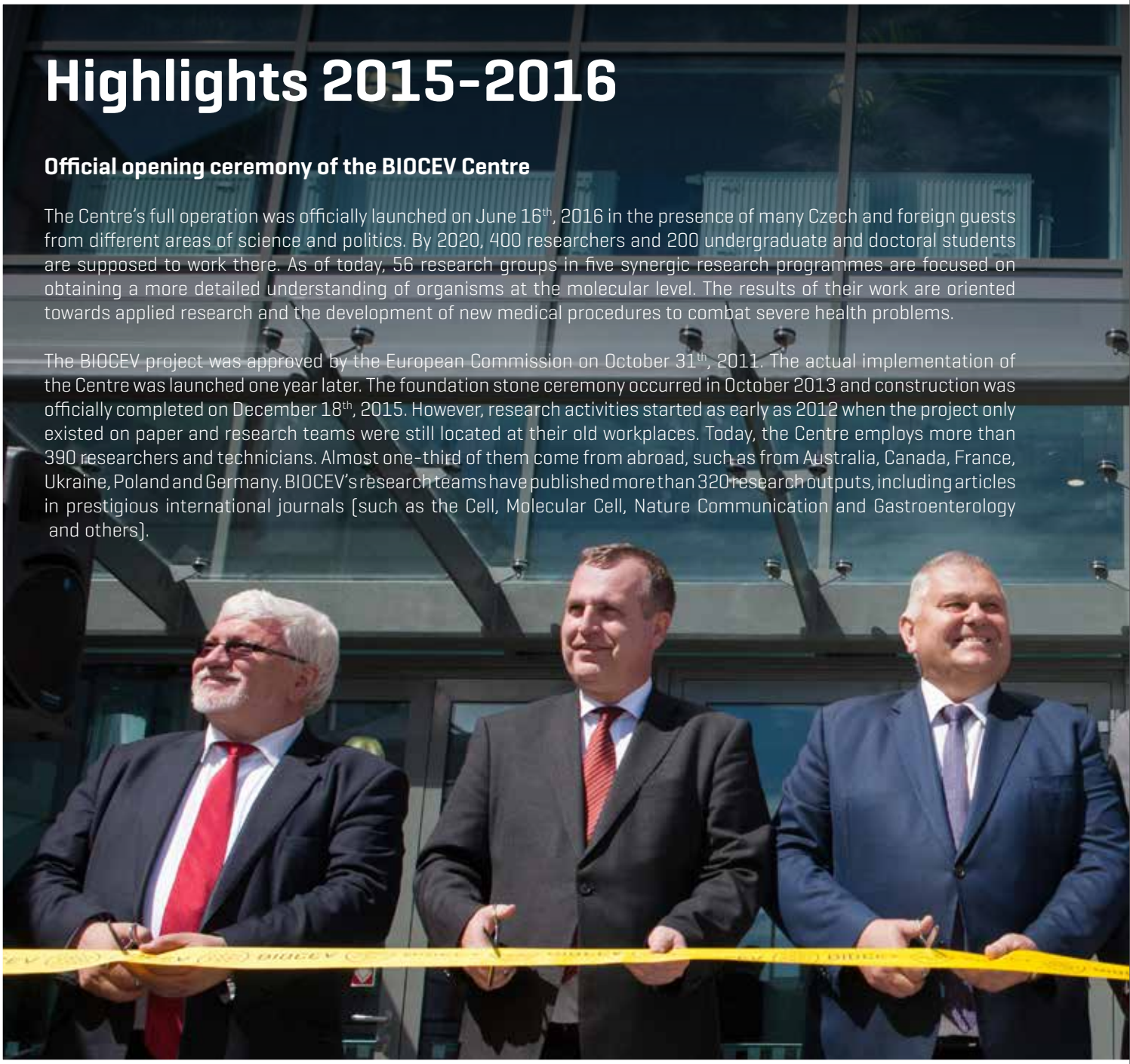
Jitka Stančíková	Molecular mechanisms of physiological renewal and cancer transformation of mammalian gastrointestinal tissues (Supervisor: V. Kořínek, Faculty of Science, Charles University, Prague)
Monika Bambousková	Molecular mechanisms of regulation of FcεRI signaling in mast cells (Supervisor: P. Dráber, Faculty of Science, Charles University, Prague)
Ilona Kalasová	Localization and function of phosphoinositides in the cell nucleus (Supervisor: P. Hozák, Faculty of Science, Charles University, Prague)
Markéta Černohorská	New regulatory mechanisms of microtubule nucleation (Supervisor: Pa. Dráber, Faculty of Science, Charles University, Prague)
Peter Fabian	The role of vent genes family in early development and brain development (Supervisor: Z. Kozmik, Faculty of Science, Charles University, Prague)
Jan Mašek	The role of transcriptional factor Tcf7l1 and Wnt/β-catenin signalling pathway during differentiation of the head ectoderm (Supervisor: Z. Kozmik, Faculty of Science, Charles University, Prague)
Lucie Žílová	The role of Pax6 transcription factor in mouse eye development (Supervisor: Z. Kozmik, Faculty of Science, Charles University, Prague)
Michaela Liegertová	Identification and characterization of main genetic components involved in phototransduction and vision of the cubozoan jellyfish Tripedalia cystophora (Z. Kozmik, Faculty of Science, Charles University, Prague)
Petr Těšina	Structural studies of LEDGF/p75 interactions (Supervisor: P. Maloy Řezáčová, Faculty of Science, Charles University, Prague)
Jakub Rídl	Metagenomic profiling of microbial consortia (Supervisor: J. Pačes, The University of Chemistry and Technology, Praque)

Highlights 2015–2016

Official opening ceremony of the BIOCEV Centre

The Centre's full operation was officially launched on June 16th, 2016 in the presence of many Czech and foreign guests from different areas of science and politics. By 2020, 400 researchers and 200 undergraduate and doctoral students are supposed to work there. As of today, 56 research groups in five synergic research programmes are focused on obtaining a more detailed understanding of organisms at the molecular level. The results of their work are oriented towards applied research and the development of new medical procedures to combat severe health problems.

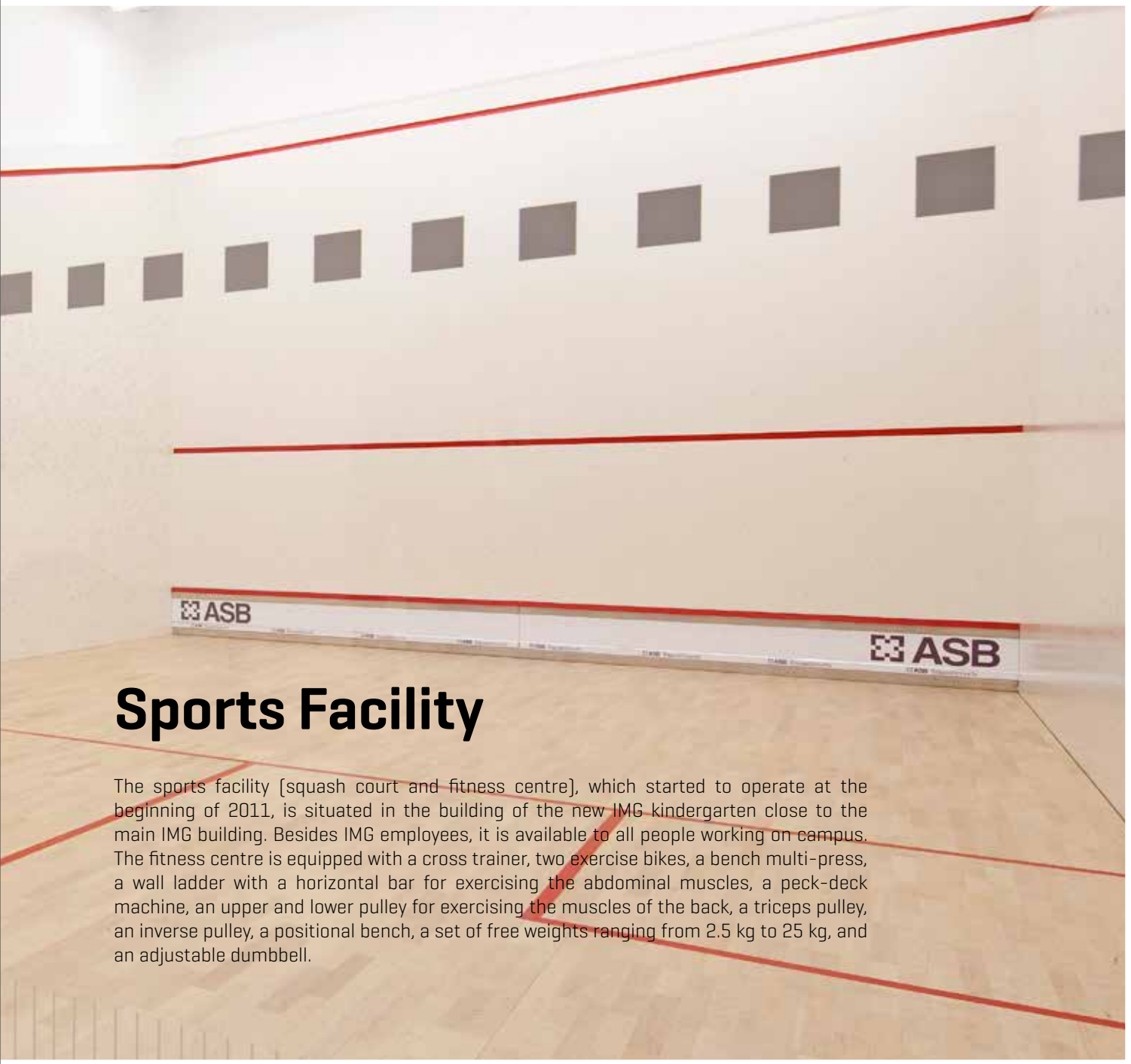
The BIOCEV project was approved by the European Commission on October 31th, 2011. The actual implementation of the Centre was launched one year later. The foundation stone ceremony occurred in October 2013 and construction was officially completed on December 18th, 2015. However, research activities started as early as 2012 when the project only existed on paper and research teams were still located at their old workplaces. Today, the Centre employs more than 390 researchers and technicians. Almost one-third of them come from abroad, such as from Australia, Canada, France, Ukraine, Poland and Germany. BIOCEV's research teams have published more than 320 research outputs, including articles in prestigious international journals (such as the Cell, Molecular Cell, Nature Communication and Gastroenterology and others).



"The journey towards Czech prosperity will run through the success of projects like BIOCEV. I believe that this more than two-billion crown investment from European and national funds will bring its benefits not only to the Czech Republic, but to the entire world as the scientific and research results accomplished by the BIOCEV centre will truly have a global impact", said **Deputy Prime Minister Pavel Bělobrádek**.

"I firmly believe that the opening of the BIOCEV centre will help the Czech research community to become a full-fledged member of the European biotechnology and biomedicine research community, improving the competitiveness of both the Czech Republic and Europe," were the words by **Minister of Education, Youth and Sports Kateřina Valachová**.

"Today, we are releasing BIOCEV into the European research sector and I believe that the centre meets all the necessary preconditions to become a major player in this respect," said **President of the Czech Academy of Sciences Jiří Drahoš**.



Sports Facility

The sports facility (squash court and fitness centre), which started to operate at the beginning of 2011, is situated in the building of the new IMG kindergarten close to the main IMG building. Besides IMG employees, it is available to all people working on campus. The fitness centre is equipped with a cross trainer, two exercise bikes, a bench multi-press, a wall ladder with a horizontal bar for exercising the abdominal muscles, a peck-deck machine, an upper and lower pulley for exercising the muscles of the back, a triceps pulley, an inverse pulley, a positional bench, a set of free weights ranging from 2.5 kg to 25 kg, and an adjustable dumbbell.

Guest House

The new guest house of the IMG, also opened in 2011, is a small two-storey building located in a quiet environment, adjacent to the kindergarten. In front of the guest house there is a small parking lot, on the other side there is an outside terrace overlooking the greenery.

Eleven rooms are available for accommodation – mostly studios. The largest unit consists of two rooms, one of which includes a kitchen area. All accommodation units have a small hallway and private bathroom, and the rooms are furnished. The kitchens are equipped with all basic appliances. Internet access is available in all rooms.

All occupants have access to a common laundry room. The maintenance and repairs of the accommodation units are provided, together with cleaning of all common areas.

Kindergarten

The kindergarten started to operate in January 2011 in a new building adjacent to the main building of the IMG. Its present capacity is 20 children aged between 2 and 6 years. It is operated by a professional company "Kindergarten of the AS CR, Ltd."

The main goal of the kindergarten is to enable parents to easily return to work. It considerably alleviates the current problem with insufficient capacity of state-run kindergartens.

The kindergarten introduces many new activities that promote comfort and professionalism for all parents and children. The kindergarten particularly supports individual approach to the child and very close cooperation with its family. It promotes active participation of the parents in the kindergarten activities and events. It aims at mutual and open communication and collaboration creating a partnership between the kindergarten and the family.

The teachers prepare a portfolio for each child: a journal containing basic information about the child, samples of his/her art and other works, a record of his/her progress, development and improvement, photos, etc. A speech therapist, optometrist and other specialists are scheduled to visit regularly.

Publications 2015-2016

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Grants 2015-2016

ALBERICH-JORDA

- MEYS, LK21307, *LK-NÁVRAT* – C/EBPgamma in normal hematopoiesis and acute myeloid leukemia: identification of molecular mechanisms involved in cell transformation, 2013–2015, *M. Alberich-Jorda*
- GACR, GA15-03796S – Function of the transmembrane protein Evi2b in hematopoiesis, 2015–2017, *M. Alberich Jorda*

BÁRTEK

- GACR, GA13-17658S – Mechanisms of radioresistance of prostate cancer cells, 2013–2016, *Z. Hodný*
- GACR, GA13-17555S – Premature cellular senescence: Mechanisms and links with cancer, 2013–2016, *J. Bártek*
- MH, NT14174 – The role of 5-azacytidine on immunoepigenetics and genotoxic stress in the treatment of myelodysplastic syndrome, 2013–2015, *J. Bártek*
- ASCR, L200521301, *CAS postdoctoral fellowship* – Role of cellular senescence in carcinogenesis and tumour resistance, 2013–2015, *S. Hubáčková*
- MEYS, LH14037, *KONTAKT II* – Identification of protein complexes associated with genotoxic RNA:DNA hybrids and their role in maintenance of genomic stability, 2014–2016, *J. Dobrovolná*
- GACR, GA14-05743S – Molecular mechanism of genomic instability caused by oncogene activation, 2014–2016, *P. Janščák*
- ASCR, L200521401, *CAS postdoctoral fellowship* – Study of molecular mechanisms suppressing genomic instability associated with transcription and replication stress, 2014–2015, *J. Dobrovolná*
- GACR, GA15-03379S – Role of oxidative stress in the interplay between cellular senescence and apoptosis, 2015–2017, *Z. Hodný*
- GACR, GA16-13967S – Plasmonic nanoparticles for theranostics with tunable optothermal properties, 2016–2018, *J. Bartek*

BARTŮNĚK

- FP7 EU, 261861, *EU-OPENSCREEN* – European Infrastructure of Open Screening Platforms for Chemical Biology, 2010–2015, *P. Bartůněk*
- GACR, GAP301/12/1478 – The role of DISP3 protein in lipid metabolism, 2012–2015, *P. Bartůněk*
- MEYS, LM2011022 – CZ-OPENSCREEN: National Infrastructure for Chemical Biology, 2012–2015, *P. Bartůněk*
- MIT, FR-TI4/802 – Development of new chemical compounds with anti-tumor activities or use in regenerative medicine, 2012–2015, *P. Bartůněk, V. Kořínek*
- TACR, TA02010212 – ReceptorX: Integrated platform for drug discovery and development, 2012–2015, *P. Bartůněk*
- MEYS, LO1220 – CZ-OPENSCREEN: National infrastructure for chemical biology, 2013–2018, *P. Bartůněk*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- MEYS, LM2015063 – National Infrastructure for Chemical Biology, 2016–2019, *P. Bartůněk*
- GACR, GA16-21024S – Red blood cells in cyprinid fish, 2016–2018, *P. Bartůněk*

BLAHOŠ

- GACR, GAP303/12/2408 – Functional Consequences of Metabotropic Glutamate Receptor 1a and 1b Splice Variants Assembly in Heterodimeric Complexes, 2012–2016, *J. Blahoš*
- GACR, GA16-24210S – Molecular Mechanism of Cannabinoid Receptor 1 Signaling Modulation by SGIP1, 2016–2018, *J. Blahoš*

BRDIČKA

- GACR, GAP302/12/1712 – Function of Csk-anchoring proteins SCIMP and PSTPIP2 in leukocyte signaling and inflammation, 2012–2015, *T. Brdička*
- MH, NT13271 – Phenotyping B- and T-cells in immunodeficiency, 2012–2015, *T. Brdička*
- GACR, GA15-06989S – Organisation and function of CD4 co-receptor on the surface of T cells at nanoscale, 2015–2017, *T. Brdička*
- GACR, GA16-07425S – Analysis of the role of transmembrane adaptor protein OPAL1 in the regulation of leukocyte receptor signaling with focus on chemokine receptor CXCR4, 2016–2018, *T. Brdička*

DRÁBER PAVEL

- GACR, GAP302/12/1673 – Role of gamma-tubulin complexes in regulation of cell cycle progression, 2012–2015, *Pa. Dráber*
- ASCR, M200521203 – Regulatory proteins of microtubules: new targets for therapy of brain tumors, 2012–2015, *Pa. Dráber*
- MEYS, LH12050, *LH-KONTAKT II* – Regulation of microtubule formation in brain cancer cells, 2012–2015, *Pa. Dráber*
- MH, NT14467 – Microtubule regulatory proteins as new biomarkers of gliomas, 2013–2015, *Pa. Dráber*
- GACR, GA15-22194S – Role of GIT-PIX signaling complex in regulation of microtubule nucleation in mast cells, 2015–2017, *Pa. Dráber*
- GACR, GA16-23702S – Role of protein phosphatases in regulation of microtubule organization in mast cells, 2016–2018, *V. Sulimenko*
- GACR, GA16-25159S – Calcium signaling to microtubules in activated mast cells, 2016–2018, *Pa. Dráber*

DRÁBER PETR

- GACR, GBP302/12/G101 – Molecular mechanisms of signaling through leukocyte receptors their role in health and disease, 2012–2018, *V. Hořejší, Pe. Dráber, D. Filipp*
- GACR, GA14-00703S – ORMDL family proteins in mast cell signaling, 2014–2016, *Pe. Dráber*
- GACR, GA14-09807S – Signaling pathways involved in mast cell chemotaxis, 2014–2016, *L. Dráberová*
- TACR, TH01010244 – MicroRNA biomarkers - new methods of quantification, 2015–2018, *Pe. Dráber*

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- GACR, GBP302/12/G101 – Molecular mechanisms of signaling through leukocyte receptors their role in health and disease, 2012–2018, *V. Hořejší, Pe. Dráber, D. Filipp*
- GACR, GP14-17194P – Synthetic oligofuranosides, their enzymatic preparation and the mode of cellular signalling, 2014–2016, *I. Chlubnová*
- ASCR, DAAD-15-15 – Aire-expressing lymph node cells in peripheral T cell tolerance, 2015–2016, *D. Filipp*
- ASCR, L200521502, *CAS postdoctoral fellowship* – Differentiation potential of early embryonic hematopoietic progenitors expressing TLR2, 2015–2016, *J. Balounová*
- GACR, GA16-26143S – Extrathymic Aire-expressing cells in peripheral T-cell tolerance, 2016–2018, *D. Filipp*

FOREJT

- GACR, GA13-08078S – Genomic architecture and molecular basis of hybrid sterility of the mouse, 2013–2017, *J. Forejt*
- GACR, GA16-01969S – Genetic Control of Genome-Wide Meiotic Recombination Rate and Homolog Recognition, 2016–2018, *J. Forejt*

GREGOR

- ASCR, L200521601, *CAS postdoctoral fellowship* – Deregulation of the epithelial cytoskeleton of the gastrointestinal tract in models of epidermolysis bullosa, 2013–2015, *A. Kalendová*
- GACR, GA15-23858S – The Impact of Liver-specific Plectin Deficiency on Pathogenesis of Liver Diseases, 2015–2017, *M. Gregor*

HEJNAR

- MA, QJ1210041 – New type of vaccine against chicken viral diseases, 2012–2016, *J. Hejnar, D. Kučerová*
- MEYS, LK11215, *LK-NÁVRAT* – Regulation of active endogenous retroviruses in the mammalian genome, 2012–2016, *D. Elleder*
- MH, NT14601 – Syncytins as markers of germ line tumors, 2013–2015, *J. Hejnar*
- GACR, GA13-37600S – Expression of fusogenic human endogenous retroviruses in germ line tumors, 2013–2015, *J. Hejnar*
- GACR, GA13-30983S – Chicken polymorphisms in retroviral receptors and their potential for cross-species transmission, 2013–2015, *J. Plachý*
- GACR, GA14-32547S – Sensing of HIV-1 by plasmacytoid dendritic cells: dichotomy of immunoreceptor signaling, 2014–2016, *I. Hirsch*
- GACR, GA14-34873S – Epigenomics of retroviral integration, 2014–2016, *J. Hejnar*
- ASCR, DAAD-15-26 – Advancing reverse genetic technologies for the chicken, 2015–2016, *J. Hejnar*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- ASCR, L200521503, *CAS postdoctoral fellowship* – Evolution of endogenous retroviruses and their role in tumorigenesis, 2015–2016, *M. Matoušková*
- GACR, GA15-22207S – Analysis of Rous sarcoma virus replication blocks in non-permissive cells and characterization of factors contributing to virus rescue, 2015–2017, *J. Svoboda*
- GACR, GA15-23993S – Gene targeting in chicken and the resistance to newly emerging retroviruses, 2015–2017, *J. Hejnar*
- GACR, GA15-24776S – Mistargeting of somatic hypermutation and its role in B cell genome instability, 2015–2017, *F. Šenigl*

HOŘEJŠÍ

- GACR, GBP302/12/G101 – Molecular mechanisms of signaling through leukocyte receptors their role in health and disease, 2012–2018, *V. Hořejší, Pe. Dráber, D. Filipp*
- MH, NT13462 – Optimization of immunotherapy and flow cytometric minimal residual disease assessment in resistant acute lymphoblastic leukaemia, 2012–2015, *P. Otáhal*

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- GACR, GA16-03403S – Vinculin / DEB-1 participation on chromosomal dynamics in gametogenesis, 2016–2018, *P. Hozák*

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- GACR, GAP305/11/2232 – Functions of myosin I and its binding partners in the cell nucleus, 2011–2015, *P. Hozák*
- MIT, FR-TI3/588 – Development of a kit for detection of mutations in structural proteins of a cell, 2011–2015, *P. Hozák*
- TACR, TE01020118 – Electron microscopy, 2012–2019, *P. Hozák*
- HFSP, RGP0017/2013 – Actin and actin-related proteins: probing their nuclear function, 2013–2017, *P. Hozák*
- MEYS, OPVK CZ.1.07/2.3.00/30.0050 – Founding the expert platform for phenotyping and imaging technologies, 2013–2015, *R. Sedláček, P. Hozák*
- MEYS, LG13035, *LG-INGO II* – Support of participation in the European Society for Histochemistry, 2013–2015, *P. Hozák*
- GACR, GA15-08738S – Phosphoinositide compartments in the cell nucleus: structure and function, 2015–2017, *P. Hozák*
- GACR, GJ15-08835Y – The role of the nuclear periphery and the active nuclear transport in chromatin organisation, 2015–2017, *J. Fišerová*
- GACR, GA16-03346S – Contribution of (pre)lamin - A phosphoinosites complexes to intranuclear order, 2016–2018, *V. Filimonenko*
- GACR, GA16-03403S – Vinculin / DEB-1 participation on chromosomal dynamics in gametogenesis, 2016–2018, *P. Hozák*

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- MEYS, LE12004, *LE-EUPRO II* – Support of the Czech participation in the pan-European research infrastructure Euro-BioImaging, 2012–2015, *P. Hozák*
- Horizon 2020, 654136, *RItrain* – Reseach Infrastructures Training Programme, 2015–2019, *P. Hozák*
- MEYS, LG15022 – Support of participation in the Society for histochemistry, 2016–2017, *P. Hozák*
- MEYS, LG15023 – Support of participation in the executive committees of the International Federation of Societies for Microscopy and the European Microscopy Society, 2016–2017, *P. Hozák*
- MEYS, CA15214, *COST Action* – An integrative action for multidisciplinary studies on cellular structural networks, 2016–2020, *P. Hozák*
- Horizon 2020, 688945, *EuBI PPII* – Euro-BioImaging Preparatory Phase II - Project, 2016–2017, *P. Hozák*
- MEYS, LM2015062 – National Infrastructure for Biological and Medical Imaging, 2016–2019, *P. Hozák*

KOŘÍNEK

- GACR, GAP305/12/2347 – Molecular mechanisms of the tumor suppressor function of the HIC1 gene, 2012–2015, *V. Kořínek*
- MEYS, OPVK CZ.1.07/2.3.00/30.0027 – Founding the Centre of Transgenic Technologies, 2012–2015, *R. Sedláček, V. Kořínek, Z. Kozmik*
- MIT, FR-TI4/802 – Development of new chemical compounds with anti-tumor activities or use in regenerative medicine, 2012–2015, *P. Bartůněk, V. Kořínek*
- GACR, GA14-33952S – Molecular mechanisms underlying cell-fate decisions in the intestine, 2014–2016, *V. Kořínek*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- MEYS, LH15223 – Molecular pathophysiology of erythroid disorders, 2015–2017, *L. Láníková*
- GACR, GJ15-18046Y – Molecular bases of clonal heterogeneity and progression of polycythemia vera, 2015–2017, *L. Láníková*
- GACR, GA15-25100S – The Wnt signaling network – novel components and regulatory mechanisms, 2015–2017, *V. Kořínek*
- GACR, GA16-06326S – Diet and microbiota as modulators of gut inflammation and colon cancer, 2016–2018, *V. Kořínek*

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- GACR, GAP305/12/2042 – The role of transcription factors Tcf in the induced cell pluripotency (iPS) and during neurogenesis, 2012–2015, *O. Machoň*
- MEYS, OPVK CZ.1.07/2.3.00/30.0027 – Founding the Centre of Transgenic Technologies, 2012–2015, *R. Sedláček, V. Kořínek, Z. Kozmik*
- MEYS, LK11214, *LK-NÁVRAT* – Genetic regulation of embryonic development of the brain and the eye, 2012–2016, *O. Machoň*
- MEYS, LH12047, *LH-KONTAKT II* – The role of alternative splicing in evolution of vertebrate body plan, 2012–2015, *Z. Kozmik*
- GACR, GP14-20839P – The role of Pituitary homeobox gene in anterior specification and left-right asymmetry in the basal chordate amphioxus, 2014–2016, *V. Soukup*
- ASCR, L200521451, *CAS postdoctoral fellowship* – Regulation of asymmetry along the left-right axis at the invertebrate-vertebrate transition, 2014–2016, *V. Soukup*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- GACR, GA15-23675S – The role of Pax6 in eye development, 2015–2017, *Z. Kozmik*
- GACR, GC15-21285J – Reconstruction of an ancestral chordate organizer: the role of Wnt/beta-catenin signaling, 2015–2017, *I. Kozmiková*

LIPOLDOVÁ

- GACR, GAP502/11/2116 – Differences in clinical course of tick-borne encephalitis in host, and their genetic determination, 2011–2015, *M. Lipoldová*
- MEYS, LH12049, *LH-KONTAKT* – New Genomic Strategy for Rapid Identification of Genes Controlling Development of Infections and Cancer, 2012–2015, *M. Lipoldová*
- GACR, GP13-41002P – Genetic control of parasite dissemination after Leishmania major infection, 2013–2015, *T. Kobets*
- GACR, GP14-35944P – Analysis of interaction between Leishmania major and macrophages of susceptible and resistant mouse strains, 2014–2015, *I. Grekov*
- GACR, GA14-30186S – Hidden relevant functional pathways in host response to Leishmania infection revealed in focused genomic constructions, 2014–2016, *M. Lipoldová*
- GACR, GA16-22346S – Strong epistatic control of development of leishmaniasis – identification of genes and mechanisms, 2016–2018, *M. Lipoldová*

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- GACR, GAP305/12/2485 – Structure and function of proteins involved in DNA damage signaling, 2012–2015, *L. Macůrek*
- GACR, GA13-18392S – Dynamics of DNA damage response in cells, 2013–2016, *L. Macůrek*
- MEYS, 7F14061, *Czech-Norwegian Research Programme* – Phosphorylation-mediated signalling in DNA damage response and cancer, 2014–2017, *L. Macůrek*
- GACR, GA14-34264S – Role of R2TP complex in DNA damage response and cell proliferation, 2014–2016, *Z. Líčeníková Hořejší*
- WCR 14-1176 – Role of PPM1D/Wip1 truncating mutations in cancer predisposition, 2014–2016, *L. Macůrek*
- MH, 16-30954A – Analysis of stromal microenvironment, molecular and immunohistochemical aspects of malignant melanoma, 2016–2019, *L. Macůrek*
- MH, 16-29959A – Bioinformatics and functional analyses of susceptibility variants supporting the NGS-based testing of hereditary cancers in the Czech Republic, 2016–2019, *L. Macůrek*
- GACR, GA16-19437S – Role of deficient checkpoint barrier in cancerogenesis, 2016–2018, *L. Macůrek*

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- GACR, GA15-05677S – Novel metallacarborane derivatives that exhibit inhibitory properties towards carbonic anhydrase enzyme and potential applicability in cancer therapy, 2015–2017, *J. Brynda*
- MIT, FV10312 – Biosensors for detection of bacterial contamination of drinking water, 2016–2019, *J. Sedláček*
- TACR, TH02030874 – Novel impedimetric biosensors for real-time groundwaters monitoring of trace xenobiotic contamination: design and evaluation, 2016–2020, *J. Sedláček*
- GACR, GA16-17207S – Polymeric drugs actively targeted by recombinant antibody fragments as therapeutic approach in treatment of GD2 positive cancers, 2016–2018, *M. Fábry*

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- MEYS, OPVK CZ.1.07/2.3.00/30.0027 – Founding the Centre of Transgenic Technologies, 2012–2015, *R. Sedláček, V. Kořínek, Z. Kozmik*
- MEYS, LK11213, *LK-NÁVRAT* – Analysis of genes Pin1 and CRMP2A and their impact on axon growth, branching and regeneration in vitro and in vivo, 2012–2016, *M. Balaštík*
- MEYS, LM2011032, *INFRAFRONTIER-CZ* – Infrafrontier-CZ/Czech Centre for Phenogenomics as a national centre of „The European infrastructure for phenotyping and archiving of model mammalian genomes": Integration of the Czech national centre into international network, 2012–2015, *R. Sedláček*
- MH, NT14461 – Senescence cells elimination in minimal residual tumour disease therapy, 2013–2015, *M. Reiniš*
- MH, NT14451 – New technology for correction of mutations in monogenetic diseases by targeted reparation of mutations using specific nucleases, 2013–2015, *R. Sedláček*
- GACR, GA13-01710S – Reactivity of pulmonary arteries in pulmonary hypertension, 2013–2017, *K. Chalupský*
- TACR, TA03011057 – Development of new methods to analyze enviromental genotoxic stress and mutagenicity of potential pharmaceutical compounds, 2013–2016, *R. Sedláček*
- MEYS, OPVK CZ.1.07/2.3.00/30.0050 – Founding the expert platform for phenotyping and imaging technologies, 2013–2015, *R. Sedláček, P. Hozák*
- FP7 EU, 334431, *AD PATHOGENESIS* – Role of CRMP2 and Pin1 in the pathogenesis of Alzheimers disease, 2013–2017, *M. Balaštík*
- FP7 EU, 312325, *Infrafrontier-I3* – Development of mouse mutant resources for functional analyses of human diseases - Enhancing the translation of research into innovation, 2013–2016, *R. Sedláček*
- GACR, GA14-10100S – Utilization of novel mouse strains for investigation of the NK cell regulatory role in development and therapy of cancer, 2014–2016, *M. Indrová*
- MEYS, LH14276, *LH - KONTAKT II* – Novel Causative Genes Identification and Functional Study for selected Mendelian Disorders, 2014–2016, *R. Sedláček*
- GACR, GA15-24769S – DNA demethylation in the IFNγ signalling pathway modulates tumour progression and tumour-cell interactions with the immune system, 2015–2017, *M. Reiniš*
- GACR, GA15-23165S – Regulation of heterochromatic gene silencing, 2015–2017, *K. Chawengsaksophak*
- Horizon 2020, 653961, *IPAD-MD* – Research Infrastructures for Phenotyping, Archiving and Distribution of Mouse Disease Models - Promoting International Cooperation and User Engagement to Enhance Biomedical Innovation, 2015–2019, *R. Sedláček*
- MEYS, LM2015040 – Czech Centre for Phenogenomics, 2016–2019, *R. Sedláček*

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- GACR, GPP301/12/P425 – Functional analysis of hBrr2 mutations linked to retinitis pigmentosa, 2012–2015, *Z. Cvačková*
- GACR, GBP305/12/G034 – Centre for RNA Biology, 2012–2018, *D. Staněk, P. Svoboda*
- MEYS, LH14033, *KONTAKT II* – Spliceosomal snRNP assembly and surveillance in Drosophila melanogaster, 2014–2016, *D. Staněk*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- ASCR, L200521501, *CAS postdoctoral fellowship* – Alternative splicing regulation by chromatin modifications, 2015–2016, *N. Bieberstein*
- GACR, GA15-00790S – Quality control of spliceosomal snRNP assembly, 2015–2017, *D. Staněk*

ŠTĚPÁNEK

- SNSF, PROMYS – T cell calculus: how T cells measure and interpret antigenic signals in health and disease, 2016–2020, *O. Štěpánek*
- EMBO, EMBO Installation Grant – Antigenic signalling and fate decisions in T cells, 2016–2018, *O. Štěpánek*
- GACR, GJ16-09208Y – T cell receptor signaling and fate decisions made by peripheral T cells in homeostasis and during inflammation, 2016–2018, *O. Štěpánek*

SVOBODA

- GACR, GBP305/12/G034 – Centre for RNA Biology, 2012–2018, *D. Staněk, P. Svoboda*
- ASCR, M200521202 – An integrative approach towards understanding mechanisms of the zygotic genome activation and establishment of pluripotency in early mammalian embryos, 2012–2015, *P. Svoboda*
- FP7 EU, 607720, *RNATRAIN* – The European non-coding RNA network, 2013–2017, *P. Svoboda*
- GACR, GA13-29531S – Development of chemical regulators of miRNA and RNAi pathways, 2013–2016, *P. Svoboda*
- MEYS, LH13084, *LH – KONTAKT II* – Post-transcriptional control of oocyte-to-zygote transition, 2013–2015, *P. Svoboda*
- MEYS, LO1419 – Biomodels for Health – Center for Model Organisms, 2015–2019, *P. Bartůněk, J. Hejnar, O. Horvath, V. Kořínek, Z. Kozmik, D. Staněk, P. Svoboda*
- Horizon 2020, ERC Consolidator Grant, 647403, *D-FENS* – Dicer-dependent defense in mammals, 2015–2020, *P. Svoboda*

TRACHTULEC

- GACR, GA14-20728S – Subspecies-specific function of meiotic genes in mouse gametogenesis, 2014–2016, *O. Mihola*
- GACR, GA16-06548S – Control of hotspots of meiotic double-strand DNA breaks in Rattus norvegicus, 2016–2018, *Z. Trachtulec*
- GACR, GA16-19158S – Effect of DNA copy number variation on fertility of the house mouse, 2016–2018, *O. Mihola*

VARGA

- ASCR, Fellowship J . E. Purkyně – Characterization of the flagellar tip domain of the protozoan *Trypanosoma brucei*; Identification and characterization of mammalian ciliary tip domain proteins, 2016–2021, *V. Varga*
- GACR, GJ16-26444Y – Identification and characterization of the eukaryotic flagellar tip domain constituents, 2016–2018, *V. Varga*

VLČEK

- GACR, GAP305/11/1061 – Evolution of parasitism:analysis of genomes and key physiological functions of free-living Mastigamoeba balamuthi and pathogenic Entamoeba histolytica, 2011–2015, *J. Pačes*
- GACR, GAP506/11/1320 – Establishment of the secondary plastid in euglenids, 2011–2015, *Č. Vlček*
- GACR, GAP304/12/1333 – Intercellular interactions in malignant melanoma – experimental study, 2012–2015, *H. Strnad*
- MH, NT13488 – Genomic analysis of tumor-associated fibroblasts in head and neck carcinoma: The basis for new generation of biologic anti-tumor therapy, 2012–2015, *H. Strnad*
- MH, NT13112 – Studies of anticancer effects of statins, 2012–2015, *H. Strnad*
- GACR, GA13-28283S – Bridging microbial community ecology and degradation of xenobiotics – the use of metagenomics to investigate microbial degradation potential, 2013–2017, *M. Kolář*
- GACR, GA13-33039S – A genomic approach to unravelling the biology and evolution of eustigmatophyte algae, 2013–2015, *V. Pačes*
- GACR, GA13-20293S – Cellular and molecular characteristics of neonatal human skin: consequences for skin healing, 2013–2016, *H. Strnad*
- GACR, GA13-24983S – Unravelling the early evolution of the eukaryotic cell through exploring the genomes of the eukaryotic superphylum Discoba, 2013–2016, *Č. Vlček*
- MEYS, LG14017 – Representation of the Czech scientific community in FEBS, IUBMB, EMBC, EMBO, ESBRA and other relevant organizations, 2014–2016, *V. Pačes*
- TACR, TE02000058 – Center of competence for molecular diagnostics and personalized medicine, 2014–2019, *V. Pačes, Č. Vlček*
- MH, NV15-28933A – Tumor microenvironment of head and neck carcinoma: Prognostic significance of extracellular matrix produced by tumor-associated fibroblasts, 2015–2018, *M. Kolář*
- MH, 16-29032A – ERK pathway activation as a prognostic tool and a prospective therapeutic target in head and neck squamous cell carcinoma and malignant melanoma, 2016–2019, *V. Pačes*
- GACR, GA16-05534S – Microenvironment of malignant melanoma as a factor of tumor aggressiveness, 2016–2018, *H. Strnad*

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