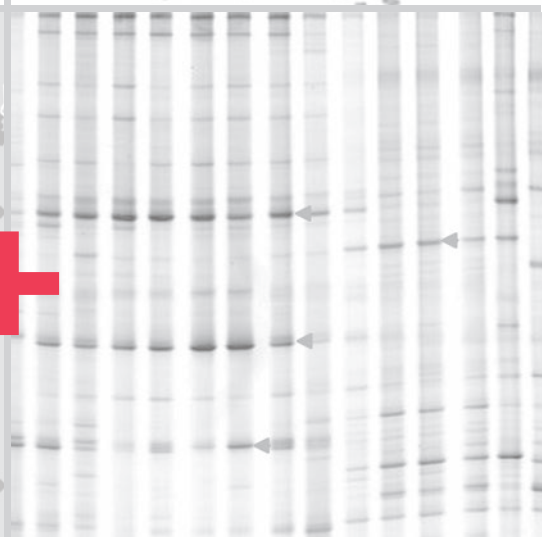
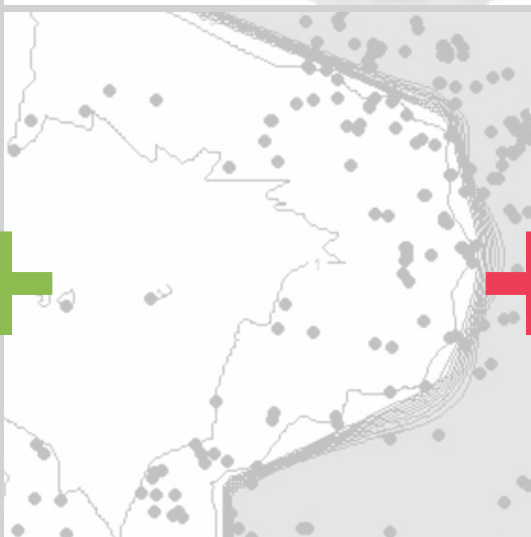
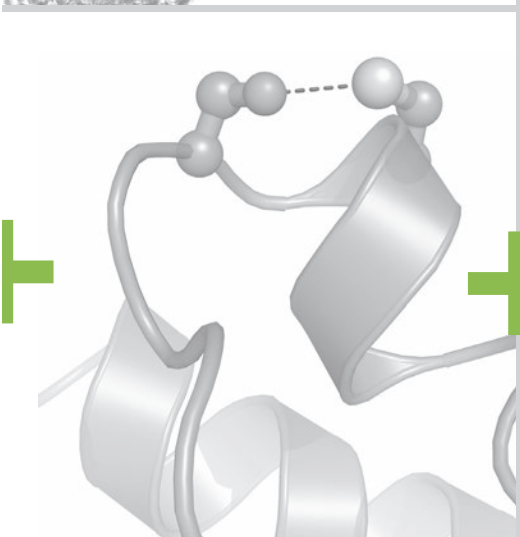
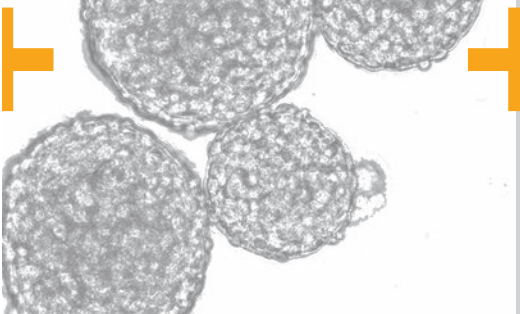


INSTITUTE OF
Animal Physiology
and Genetics
2014—2018
CZECH ACADEMY OF SCIENCES



IAPG Content

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Dear reader,

You are opening the five-year report on the IAPG activities during the period between the years 2014 and 2018. Although the Institute publishes each year annual reports and there has also been published the Bienium report in the past (covering the years 2011–2012), this is the first report covering such relatively long period of the Institute's development and providing information on scientific achievements of Institute's staff, as well as on important events occurring during this period.

I believe that information contained in this report would be interesting not only for the scientific co-workers and colleagues from other institutes and universities, but also for general public. Especially, we also aim to attract attention of young people with the hope to raise their interest in science in general, and potentially also in scientific research in our Institute.

Founded in 1963 the Institute originally oriented to farm animals, has since developed to a scientific institution utilizing the most up-to-date methods for the research of important aspects of animal physiology and genetics. At present, there are two main areas of basic research covering reproductive and developmental biology on one side and the study of biodiversity and ecology on the other side. Apart from that the Institute has also a big potential in oriented research directed to biomedical applications. This includes mainly using the pigs as animal models for the study of important neurodegenerative diseases in three laboratories of the recently established PIGMOD Centre. For this purpose the Institute is suitably situated in the countryside, but still within reach of Prague.

The period covered by this report has been also a period of a number of changes in Institute's structure – 2 laboratories were dissolved, other 4 new laboratories were established, out of 12 now existing laboratories 8 of them have new group leaders. During this period the scientists of our Institute have been relatively successful in raising funds from grant applications both on national level and from European structural funds and worldwide. Recently, we have been able to obtain two big projects from EU funds – one from Operational Programme OP VaVPI, which enabled the establishment of the PIGMOD Centre, and second from Operational Programme OP VVV, which enabled close collaboration of 6 Institute laboratories in the project of "Excellence in molecular aspects of the early development of vertebrates", and which is planned to finish in next decade. Apart from that the scientists from our Institute have been also able to obtain funds from national and international private sources in appreciable amounts.

Altogether, all these above-mentioned funds now represent more than half of the Institute's yearly budget and enabled a significant upgrade of the Institute's infrastructure (both buildings and scientific devices) on one side, and remarkable development of human resources on the other side (new postdocs and students, as well as skillful technical assistance). Our Institute has become much more international and the number of nationalities of people working on the positions of postdocs, students or senior scientists is something between 20 and 30.

The above-mentioned sources also enabled the significant improvement of the scientific achievements and the number of scientific publications, but also their quality has remarkably improved during the past few years. I am convinced that the Institute of Animal Physiology and Genetics is now in the very good shape – it has all the necessary infrastructure, as well as excellent and enthusiastic scientists on the positions of group leaders and as such has all the prerequisites for its further development and for producing groundbreaking results and excellent scientific publications in near future on the global scale.



A handwritten signature in black ink, which appears to read "Michal Kubelka".

Michal Kubelka
Director of IAPG

ČSAV - Laboratoř fyziologie a genetiky
hospodářských zvířat, Liběchov



HISTORY OF THE INSTITUTE

Upon the decision act by the late Czechoslovak Academy of Agricultural Sciences (CAAS), the laboratories in Libečov, under the name Laboratory of Reproduction Biology of Farm Animals that time, started their activities November 1, 1954.

The relatively small Libečov laboratory has gradually achieved recognized reputation among other institutions of CAAS. At the same time, many scientific contacts resulting in many cooperations in area of the reproductive biology and immunology have been established with some institutions of the Czechoslovak Academy of Sciences (CZAS).

In very important year 1962, CZAS has included into its organization three small, but the most scientifically productive research bodies, namely Laboratory of Reproduction Biology, Libečov, Department of Animal Physiology of IAP, Uhrineves, and Laboratory of radiobiology, Prague. Since January 1, 1963, CZAS has established the Laboratory of Animal Physiology and Genetics with two research departments – Department of Physiology, Uhrineves and Department of Genetics, Libečov. Later in 1969, Department of Genetics has been organized as a single, independent research body — Laboratory of Animal Genetics headed by Dr. J. Matousek and Laboratory of Animal Physiology headed by Dr. J. Bílek.

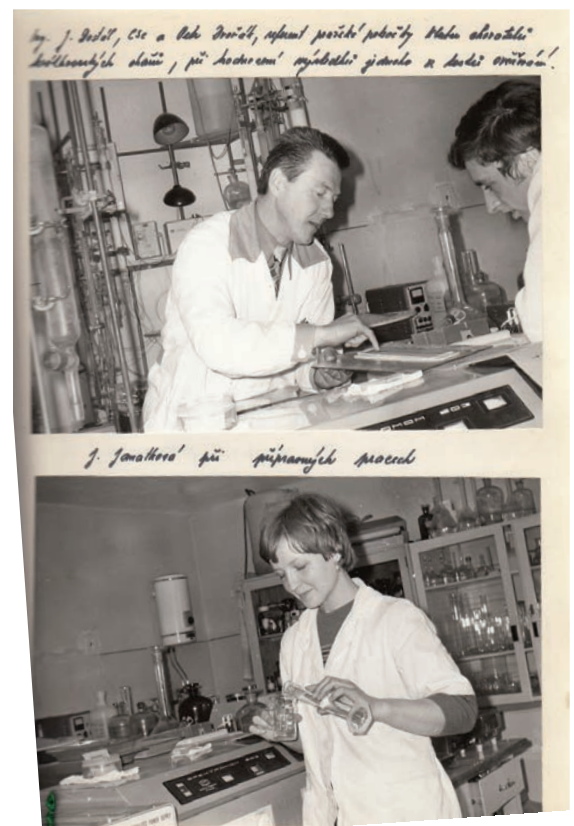
The political reasons after Russian invasion in 1968 have led to the new unification of both departments in 1972 under the name the Institute of Physiology and Genetics of Farm Animals of CZAS. February 1, 1973 was the name changed to the Institute of Physiology and Genetics of Farm Animals. The present name – the Institute of Animal Physiology and Genetics (IAPG) — was adopted since January 1, 1993 as a reflection of the first common Laboratory of Animal Physiology and Genetics.

HISTORY OF RESEARCH

The first research topics, nearly entirely focused on applied agricultural research, have been gradually changing into more basic research directions.

After period of breeding research, the female germinal cell, its fertilization, the preimplantation development of mammalian embryo, conditions of experiments with oocytes in vitro, gene expressions in early development many other related problems have been focused and studied.

This school of mammalian reproductive biology is still active and is successfully developing, bringing many basic data of present-day mammalian cloning research and regulation of cell cycle. There were running studies of hormone regulation of milk production, ruminants nutrition and gut microbiology.



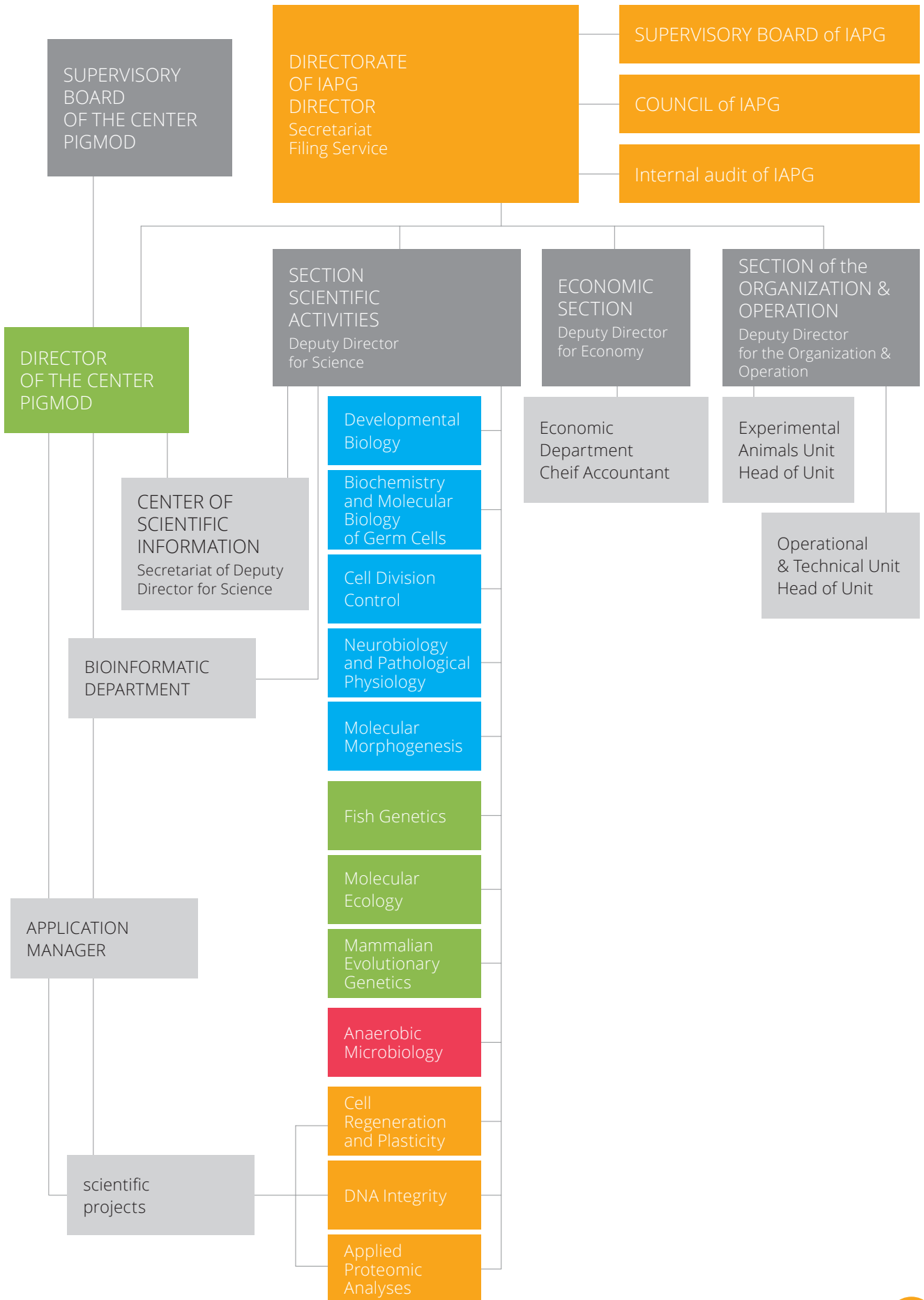


IAPG Management of Institute

Ing. Michal Kubelka, CSc.—director
Ing. Jan Kopečný, DrSc.—deputy director for science
Ing. Zdeňka Kynychová—deputy director for economy
Ing. Štěpán Hladký—deputy director for organization and operation



Organization Scheme



IAPG Councils Boards

Council of IAPG (Until 31st of January, 2017)

Internal members

prof. Ing. Petr Ráb, DrSc., dr. h. c.—chairman

RNDr. Petr Šolc, Ph.D.—deputy chairman

Ing. Jan Kopečný, DrSc.

RNDr. Petr Kotlík, Ph.D.

Ing. Michal Kubelka, CSc.

Prof. RNDr. Miloš Macholán, CSc.

MVDr. Jiří Šimůnek, CSc.

External members

doc. Ing. Pavel Kozák, Ph.D.

JUDr. Jiří Malý

doc. RNDr. Jana Pěkníková, CSc.

Prof. Ing. Vojtěch Rada, CSc.

Council of IAPG (From 1st of February, 2017)

Internal members

prof. Ing. Petr Ráb, DrSc., dr. h. c.—chairman

Mgr. Petr Vodička, Ph.D.—deputy chairman

doc. RNDr. Marcela Buchtová, Ph.D.

Ing. Zdeňka Ellederová, Ph.D.

Ing. Jan Kopečný, DrSc.

Ing. Michal Kubelka, CSc.

Ing. Andrej Šušor, Ph.D.

External members

doc. MVDr. Aleš Hampl, CSc.

RNDr. Jiří Hejnar, CSc.

Ing. Jiří Hašek, CSc.

doc. RNDr. Vladimír Krylov, Ph.D.

Supervisory Board (Until 30th of April, 2017)

RNDr. Miroslav Flieger, CSc.—chairman

RNDr. Radek Procházka, CSc.

prof. Ing. Věra Skřivanová, CSc.

doc. RNDr. Eva Zažímalová, CSc.

Ing. Martin Lhoták

Supervisory Board (From 1st of May, 2017)

prof. RNDr. Jan Zima, DrSc.—chairman

Ing. Jakub Mrázek, Ph.D.

JUDr. Jiří Malý

Ing. Petr Bobák, CSc.

prof. Mgr. Ing. Markéta Sedmíková, Ph.D.

Supervisory Board of Center PIGMOD

Ing. Jan Kopečný, DrSc.—chairman

prof. RNDr. Vladimír Holáň, DrSc.

doc. MUDr. Milan Macek sr.

RNDr. Jiří Šinkora, Ph.D.

Ing. Pavel Trefil, DrSc.



Developmental Biology

Team of Developmental Biology focuses on the animal development from gametogenesis, through oocyte fertilization up to late stages of fetuses and birth of a new organism

- To understand the processes underlying developmental defects on DNA or RNA level, chromosomal aberrations, and disruption of oocyte maturation or developmental abnormalities in fetus
- Discover new approaches contributing to the reduction of congenital defects occurrence and the disease prevention
- Investigate novel diagnostic possibilities to detect affected fetuses at early stages of development

PIGMOD

Centre PIGMOD employs minipig as a model organism, which is physiologically and genetically related to human

- To examine causes of nervous system disorders (Huntington's disease, amyotrophic lateral sclerosis, spinal cord injury and macular degeneration)
- To uncover molecular signalling underlying malignant melanoma initiation
- To study DNA quality disorders including chromosomal damage in oocytes and its effect on infertility and processes of DNA repair during neurodegeneration

IAPG Laboratories

Evolutionary Biology

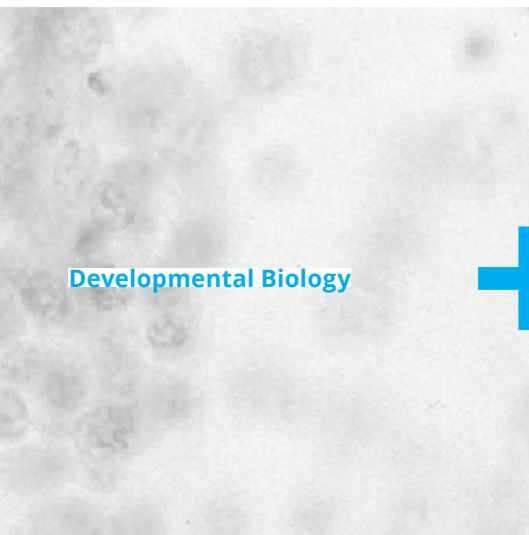
Team of Evolutionary Biology uses fish, amphibians and small vertebrates as a model species

- To investigate the ecological and evolutionary relationships between different groups of free-living animals
- To uncover genetic variation of populations of free-living vertebrates, speciation, history of their dispersion, reproductive and ecological strategies including interaction with the environment and adaptation to climate change
- Their results contribute to improvement of species conservation, environment and biodiversity protection

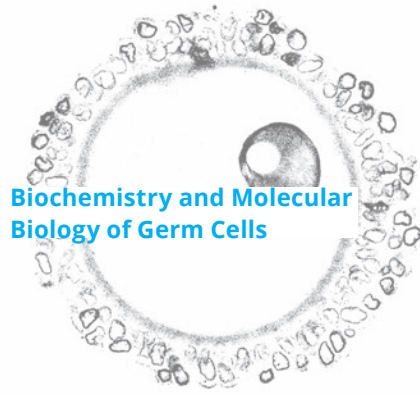
Anaerobic Microbiology

Team of Anaerobic Microbiology isolates and describes microbial species from the digestive track of humans and animals, probiotic bacteria and technologically significant xylanolytic microorganisms

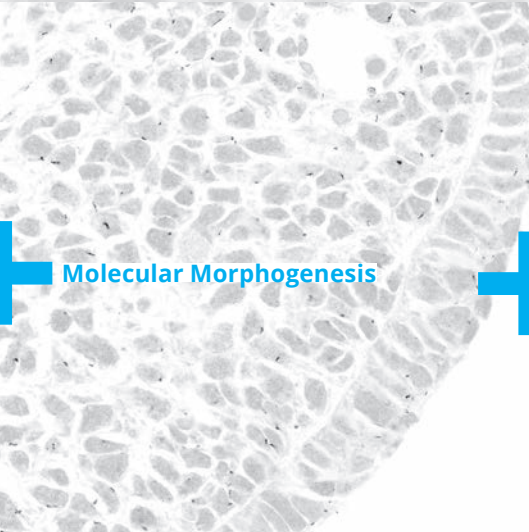
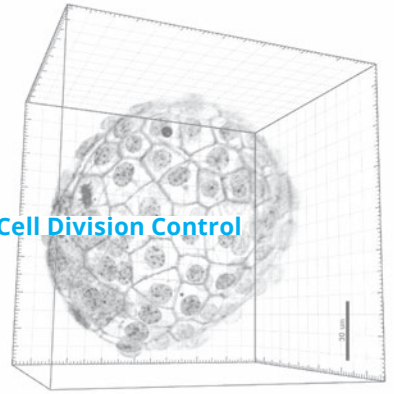
- To understand microbial diversity in relation to the nutrition and health status of the host
- To investigate diseases of the digestive tract of humans (celiac disease, IBD, cancer), "gut brains axis" (metabolic syndrome in schizophrenia, autism, Alzheimer's disease) and also the production of methane (rumen fermentation, biogas production)
- To examine the role of gastrointestinal tract microbiota in serious human diseases (celiac disease, Crohn's disease) and also to search for possible treatment (microbiota transplantation)



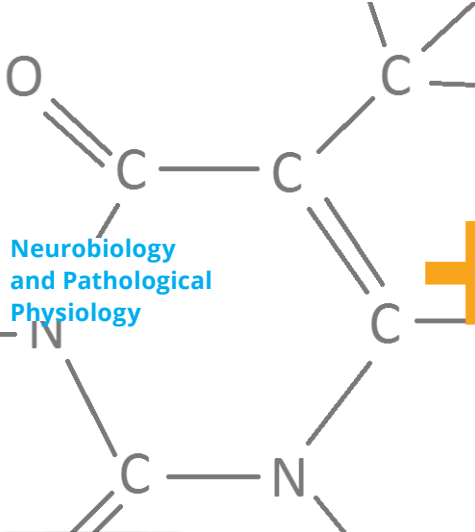
Biochemistry and Molecular Biology of Germ Cells



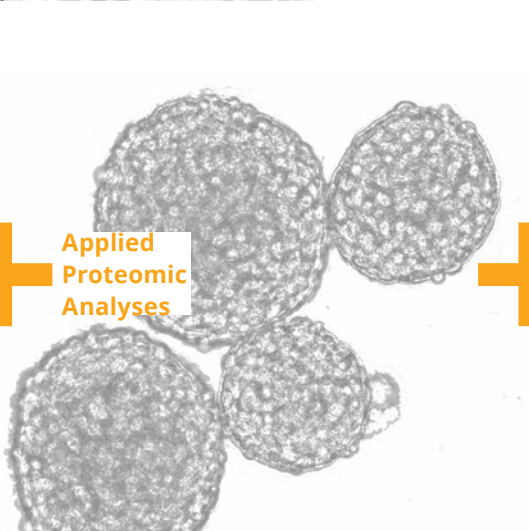
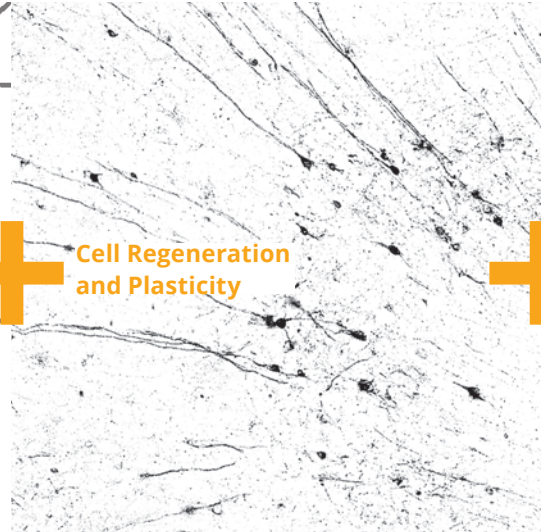
Cell Division Control



Neurobiology and Pathological Physiology



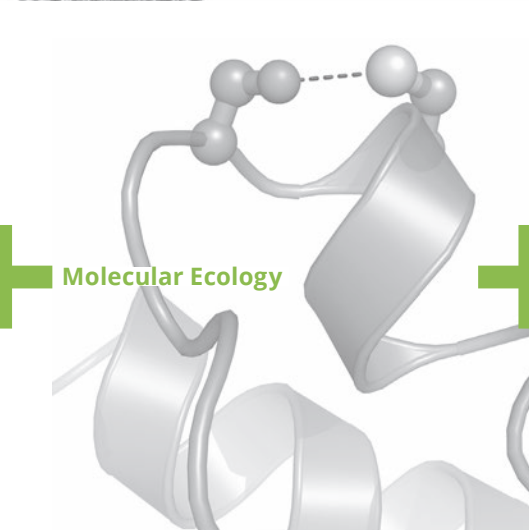
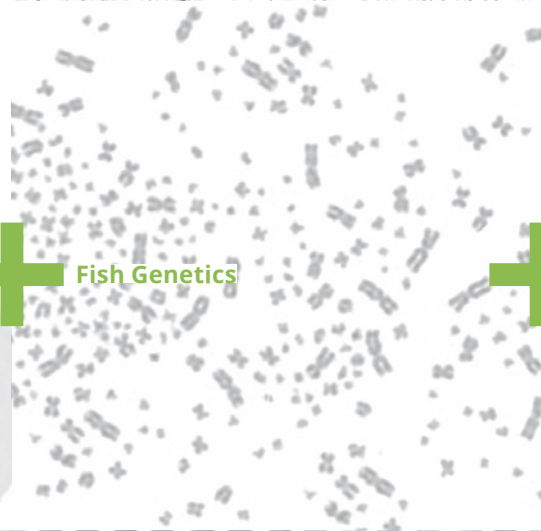
Cell Regeneration and Plasticity



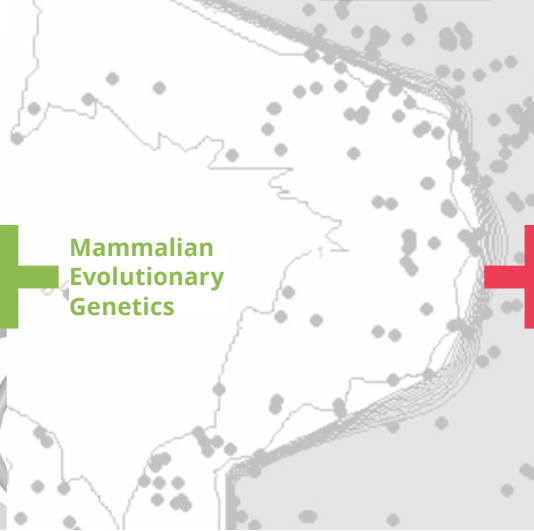
DNA Integrity



Fish Genetics



Mammalian Evolutionary Genetics



Anaerobic Microbiology





LABORATORY OF

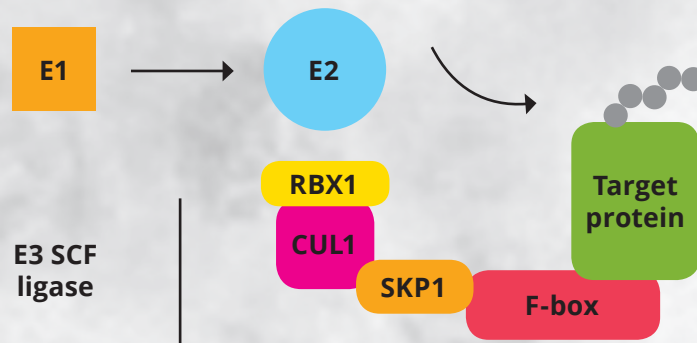
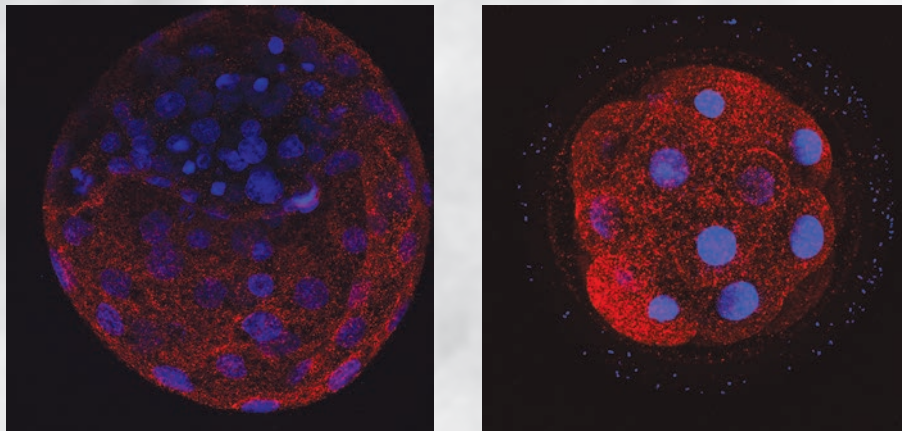
Developmental Biology

RESEARCHERS Jiří Kaňka 2 Jozef Laurinčík 7 Lucie Němcová **POSTDOCS** Ahmed Gad 1
Matej Murín 8 Tereza Toralová **Ph.D STUDENTS** Veronika Kinterová 6 Veronika Petrušková
RESEARCH ASSISTANT Jaroslava Kaňková 3 **TECHNICIAN** Monika Kopčíková 4

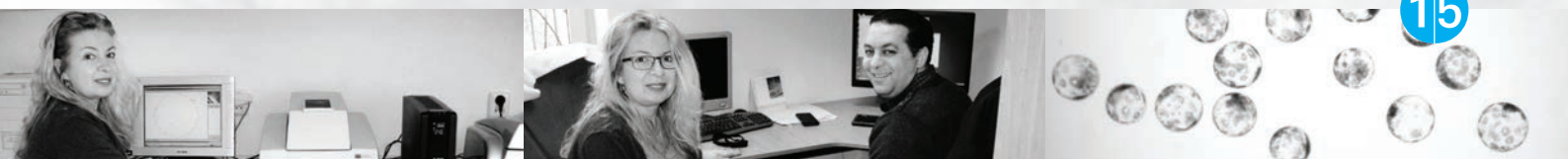
The Laboratory of Developmental Biology focuses on **gene and protein expression** during **oocyte meiotic maturation** and early **embryonic development** of mammals. We use pig and bovine oocytes and embryos cultivated *in vitro* as experimental models. Our research interests are primarily concentrated on three following areas: 1) Identification of genes and **signaling pathways** regulating oocyte maturation and developmental competence. We have been studying molecular mechanisms regulating oocyte meiotic arrest and meiotic resumption with a special attention to somatic follicular cell and oocyte intercellular communication. 2) Mechanisms of **embryonic genome activation** during the preimplantation development. Currently, our research concerns **ubiquitination** during bovine preimplantation development and its relevance to regulation of major embryonic genome activation. 3) Molecular studies on the role of oocyte **nucleolus** in regulation of early embryo development. Elegant studies in pig and mouse demonstrated that the oocyte nucleolus (nucleolar sphere) is completely essential both for completion of the oocyte meiosis and for further embryonic development. In our project, the pig oocytes and embryos will be used to study the content of the **nucleolar sphere** by proteomic and genomic approaches as well as the developmental competence conveyed by this structure.



Currently, our most important research in the area of regulation of bovine embryonic development concerns ubiquitination. We concentrate on Skp1-Cullin1-Fbox (SCF) complex, the expression of its invariant components (Cullin 1, Skp1, Rbx1) and its contribution to degradation of maternal proteins. Our up to now results have shown that embryonic expression of all these genes starts in initial stages of development. Especially cullin 1 is activated very early, already at early 8 cell stage. Genes participating in ubiquitination are usually activated at 8-cell stage, and the early activation of cullin 1 suggests its necessity for embryonic genome activation. Protein localization analysis showed interesting results especially at the blastocyst stage. There was clear concentration of protein expression and SCF complex activation to trophectoderm. These results allowed us to initiate the experiments dealing with the application of SCF complex during preimplantation development and especially in maternal protein degradation. Further, we have silenced the proteasome and SCF complex pathways with several different approaches and thus have shown that SCF complex activity and protein degradation is important for embryonic genome activation and further preimplantation development.



- We characterized the expression of SKP1-Cullin1-F-box protein complex (**SCF-complex**) and its activity profile during **bovine preimplantation development** (Benešová et al. 2016, 2017). We have silenced proteasome pathway and SCF complex pathway with several different approaches and thus have proven the necessity of SCF complex for oocyte maturation, fertilization and preimplantation development of cattle.
- Our research significantly contributed to understanding molecular mechanisms of gonadotropin-induced **maturation of pig oocytes** by identification of **genes** and **signaling pathways** activated in cumulus cells by FSH/LH and epidermal growth factor-like peptides (Blaha et al. 2015a, 2017, Procházka et al. 2017).
- We contributed to identification of a key role of **mitogen-activated protein kinase 3/1** in regulation of mammalian oocyte meiosis resumption and ovulation (Blaha et al. 2015b, Procházka and Blaha 2015).
- Members of the laboratory actively participated in **teaching** of reproductive biology at Charles University in Prague.





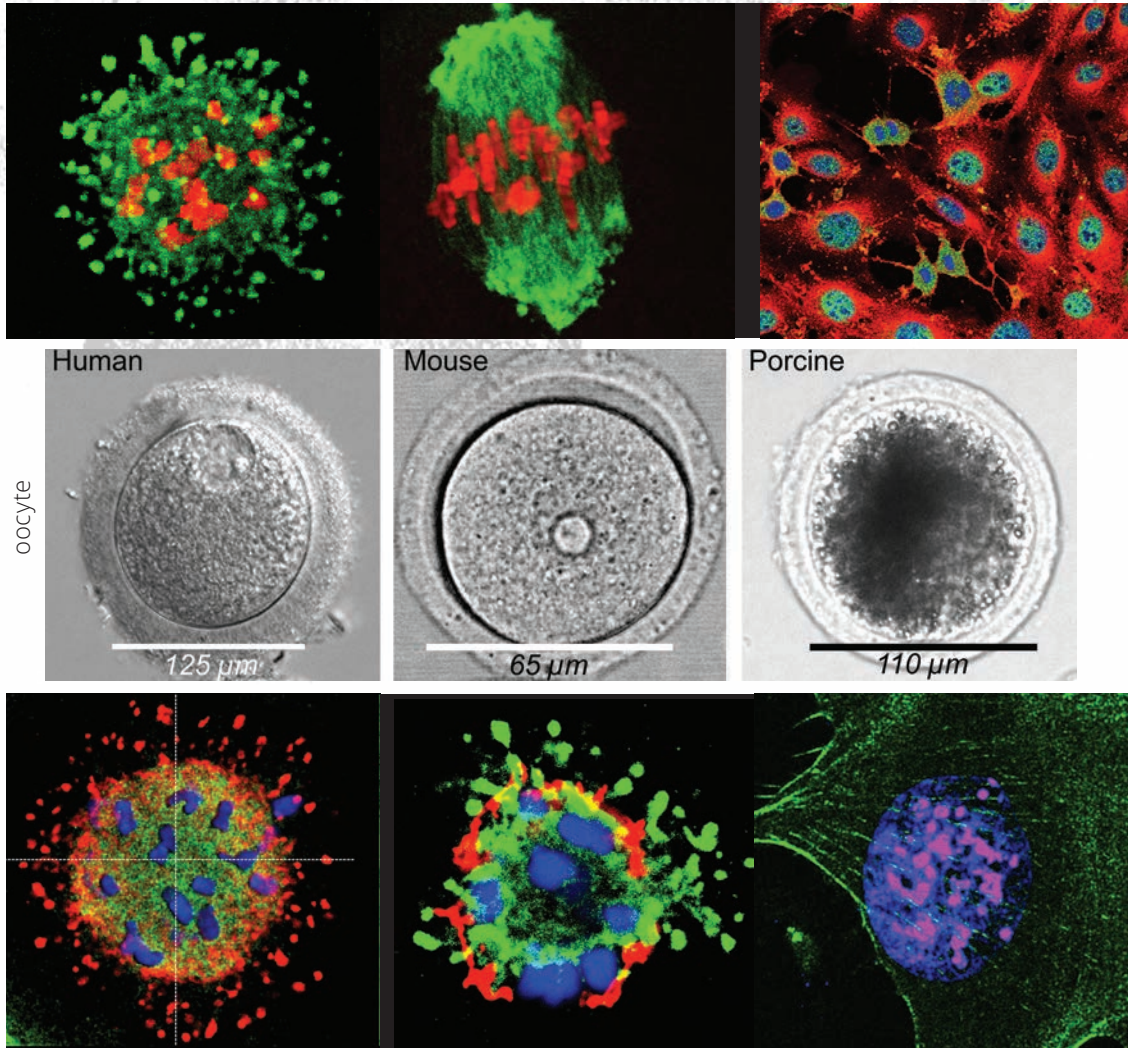
LABORATORY OF Biochemistry and Molecular Biology of Germ Cells

RESEARCHERS Jaroslav Kalous ④ Michal Kubelka ⑥ **POSTDOCS** Lenka Gahurová, Rajan Iyyappan Denisa Jansová ② **Ph.D. STUDENTS** Daria Aleshkina, Michal Dvořan, Markéta Končická ① Edgar Del Llano ⑧ Anna Tětková ⑨ **TECHNICIANS** Jaroslava Šupolíková ⑤ Markéta Hančová ⑦

We study molecular mechanisms which regulate the physiology and pathology of oocyte and embryo. In the female, meiosis results in a large cell (oocyte) that is competent for fertilization and **fundamental for supporting embryonic development**. Important characteristic of oocyte and early embryo development is the dependence on utilization of stored RNAs and proteins. In the **absence of transcription**, the oocyte and embryo development relies on **maternally synthesized RNAs**. Therefore, the regulation of gene expression is controlled almost exclusively at the level of RNA stabilization and translation. We discovered that the RNA distribution in this unique cell indicates the presence of a **novel set of regulatory mechanisms** needed to ensure that specific **gene expression** occurs **at the right time and in the right place**. Progression through both **mitotic and meiotic cycles** is controlled by the sequential activation and inactivation of a set of different protein **kinases and phosphatases**. Our team aims to uncover the **changes in timing** and the degree of **activation of the M-phase protein kinases** which are **essential for cell division** in the oogenesis and embryogenesis. These mechanisms play an important **role in the maintenance of genomic stability**. Our studies suggest **spatio-temporally regulated translational control** by the mTOR/eIF4F axis in oocyte and embryo. We investigate the translational components that are potentially **clinically relevant targets** for the development of a **healthy oocyte**.



Fluorescent images of translational regulator on the newly forming spindle. RNA binding protein is localized in the nucleus of the cells. Oocytes from various mammalian species and their size. Inactivated translational repressor 4E-BP1 after nuclear envelope breakdown. RNA is localized in the nucleus of the cell.



- We revealed a **novel mechanism** that-following the resumption of meiosis-controls **the temporal and spatial translation** of transcripts required for **genomic stability**.
- We showed that **Aurora A** kinase **do not influence CPEB1** activity and consequently synthesis of cyclin B1.
- We showed that **inactivation of 4E-BP1 promotes in situ translation** at the developing spindle.
- We described that **CDK1 influence** the **mTOR/4F** axis during oocyte meiosis.
- We unveiled that the **mTOR/4E-BP1** axis influences **similarly mouse** and **human oocyte**.
- We found that cell **nucleus** contains **abundant RNA population**.





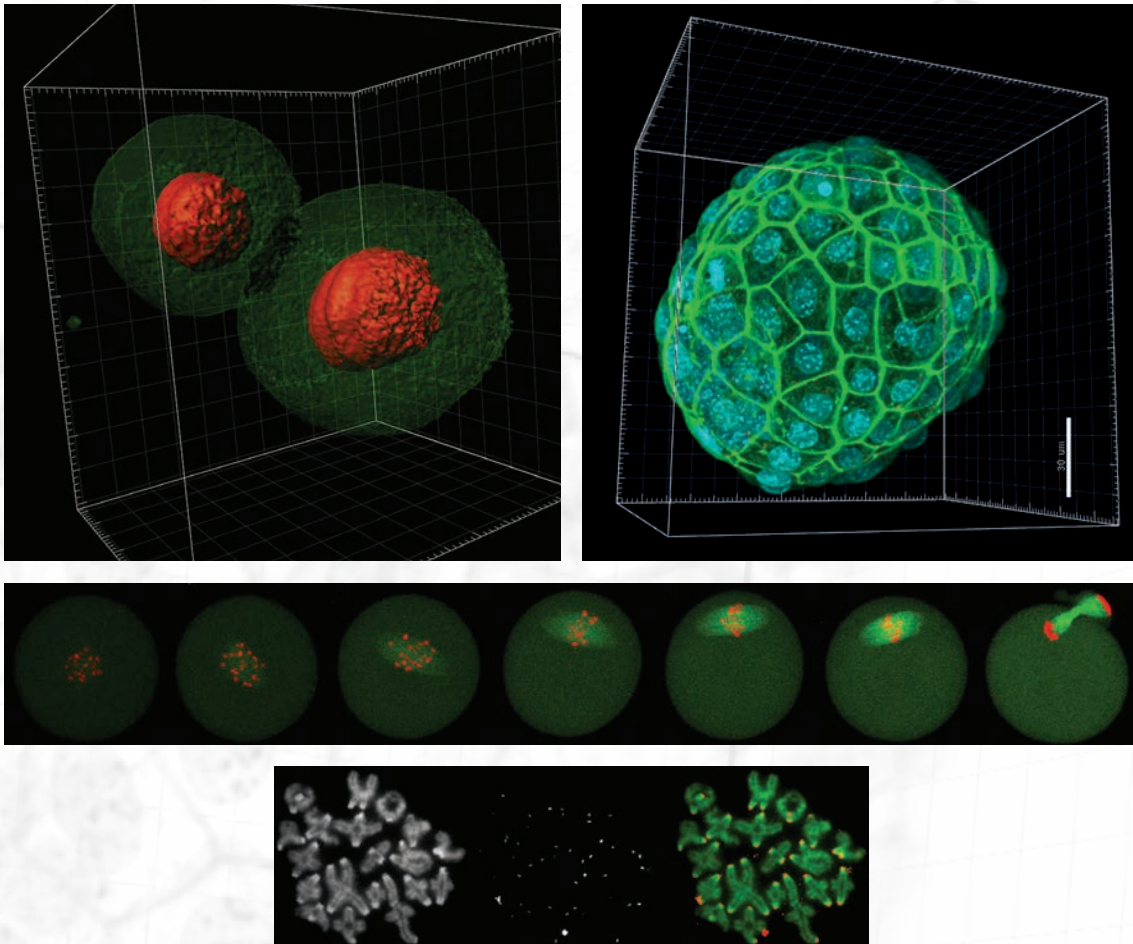
LABORATORY OF Cell Divison Control

RESEARCHER Irfan Tur **Ph.D STUDENTS** Lenka Radoňová 1 Tereza Svobodová 6 Michal Škultěty 8
DIPLOMA STUDENTS Pavla Bednářová 7 Olivie Zezulová 4 Lenka Libichová 3
BACHELOR STUDENTS Kateřina Holomková 2 Regína Gorylová

Our research is focused on cell **cycle control mechanisms** involved in monitoring **chromosome segregation** in mammalian **oocytes** and **early embryos**. Our goal is to understand the influence of **maternal aging** on chromosome segregation and increased frequency of **aneuploidy**. As model systems we use mammalian oocytes and embryos. Most of the techniques we use, such as live cell confocal microscopy, functional imaging, kinase assays or biosensors, allow to study processes at the level of individual cells. Our results are important for understanding of control mechanisms of chromosome segregation and also for understanding of pathological conditions, such as Down syndrome.



Mouse 2—cell embryo, nucleus (red) and cytoplasm (green) are visualized
 Mouse blastocyst—visualizing nuclei and borders between cells
 Assembly of the spindle and division of chromosomes in mouse oocytes
 Chromosome spreads from mouse meiosis I, chromosomes (green) with kinetochores (red)



- Discovery that **Spindle Assembly Checkpoint (SAC)** is **compromised in mammalian oocytes** (Sebestova et al., 2012) and that the premature segregation of sister chromatids shows significant differences between mouse strains (Danylevska et al. 2014).
- Our laboratory revealed important functional differences between **oocytes** matured **in vivo** and **in vitro** (Kovacovicova et al. 2016).
- We discovered that the **spindle length** is controlled by a ratio between nuclear and cytoplasmic volumes (Novakova et al. 2016).
- In collaboration with other laboratories we contributed to the discovery of **molecular mechanisms** behind **speciation in mammals** (Bhattacharyya et al., 2013) or regulation of **localized translation in mammalian oocytes** (Susor et al. 2015).
- Implementation and further development of **advanced microscopy** and micromanipulation techniques, such as microinjection, micromanipulation, multichannel live cell imaging and nuclear transfer.





LABORATORY OF

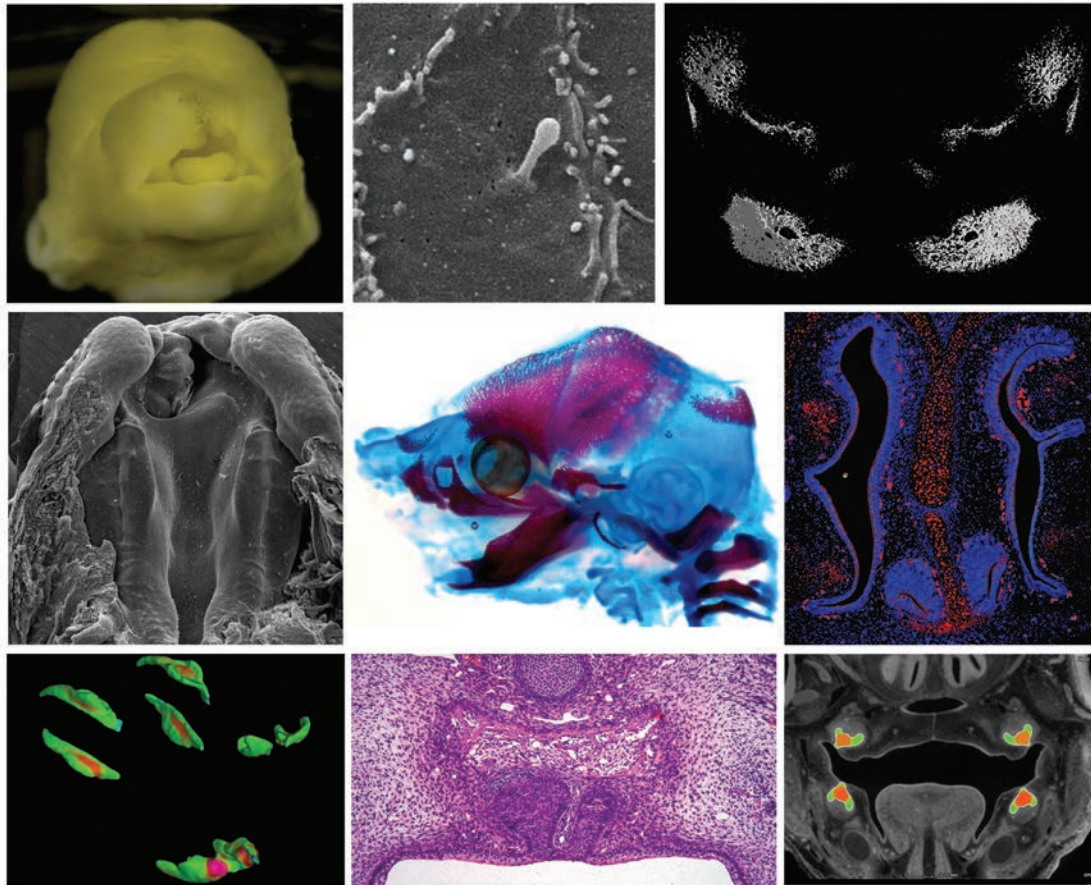
Molecular Morphogenesis

RESEARCHERS Eva Matalová ⁸ Hervé Lesot, Jan Štembírek ¹⁷ Eva Švandová **POSTDOCS** Iveta Putnová ²⁰ Eva Hrubá ¹⁴ Barbora Veselá ¹¹ Petra Celá Kolísková ³ Veronika Oralová ² **PHD STUDENTS** Marek Hampl ¹⁸ Marie Landová ⁴ Jana Dumková, Barbora Putnová ¹⁰ Jan Bobek ⁷ Alice Ramešová ⁹ Petra Nevoránková ¹⁶ Pavel Hurník, Adéla Kratochvílová ¹² Petra Bílíková ¹⁵ **MSc STUDENTS** Michael Killinger ¹³ Kristýna Olbertová ⁶ **BACHELOR STUDENTS** Lucía Bublínová, Barbora Bílková **STUDENTS** Tereza Smutná ⁵ Zuzana Ševčíková **RESEARCH ASSISTANT** Lucie Vrlíková ¹⁹ **TECHNICIAN** Veronika Jakešová

Knowledge of **developmental processes** is a key to understand causes of developmental abnormalities or to uncover the origin and diversification of lineage-specific structures during vertebrate evolution. Our laboratory focuses on fundamental morphogenetic processes in **organogenesis** with special interest in formation of **craniofacial structures** and **limb** patterning. Novel molecules and unique roles for known molecules are investigated during cell proliferation, adhesion, migration, differentiation and cell death. Particular attention is paid to hard tissues development, including teeth (**odontogenesis**) and bones (**osteogenesis**). Physiological aspects at molecular and cellular levels are investigated and related **developmental disorders** are examined. Along with increasing longevity of human population, complications related to bone and dental tissues such as osteoporosis and tooth loss become a significant medical and scientific issue. We use in vivo, ex vivo and in vitro approaches in several experimental models including mice, pig, chicken and chameleon embryos to reveal underlying developmental mechanisms. The effort of LMM is also to contribute to recent knowledge in basic and biomedical research with links to practical applications in tissue repair and regeneration.



Cleft palate development can be associated with craniofacial diseases called ciliopathies, which are caused by defective primary cilia morphology or signal transduction. We focus on transmembrane protein 107 (TMEM107) that is localized in the primary cilia and enriched at the transition zone where it acts to regulate protein content of the cilia. *Tmem107*^{-/-} mice are affected by a broad spectrum of craniofacial defects including cleft lip and palate. Palatal defects are caused by increased proliferation in mesenchyme leading to early overgrowth of palatal shelves followed by the defect in their horizontalization. Moreover, the expression of epithelial stemness marker SOX2 and mesenchymal SOX9 was altered in palatal shelves of *Tmem107*^{-/-} animals. Analysis of acetylated alpha-tubulin and IFT88 revealed region-specific changes in cilia morphology and intraflagellar transport in palatal shelves. Thus, *Tmem107* seems to be essential for proper head development and the craniofacial phenotype including expansion of the facial midline corresponds to the disruption in Hedgehog pathway activity; however interference with function of region-specific molecules such as Sox genes can explain complex tissue-specific mutant phenotype.



- We described genes that can be used to identify the **craniofacial prominences** and examined a role of several candidate genes in loss-of-function and gain-of-function experiments (Cela et al. 2013, Nimmagadda et al. 2015, Cela et al. 2016, Cela et al. 2018).
- We revealed species-specific differences in odontogenesis underlying the initiation of variable number of teeth generations and developmental processes that occur during the loss of successional **dental lamina** in monophyodont species (Dosedelova et al. 2015, Dosedelova et al. 2016, Putnova et al. 2017).
- We uncovered new non-apoptotic functions of several **caspases** and their participation in endochondral and intramembranous ossification (Svandova et al. 2014, Adamova et al. 2016, Janeckova et al. 2018).
- We demonstrated that FasL participates in MMP2 production in osteoblasts (Svandova et al. 2018).





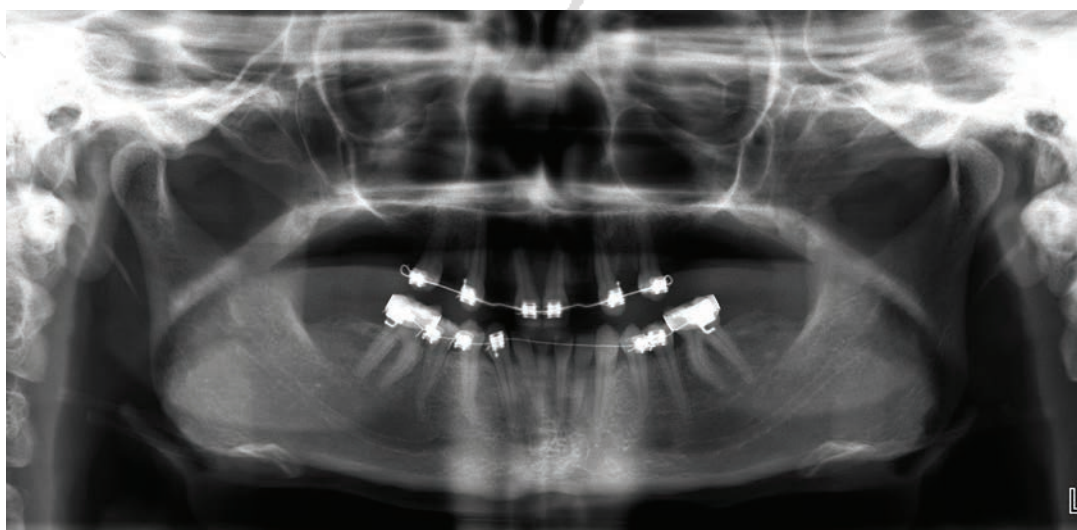
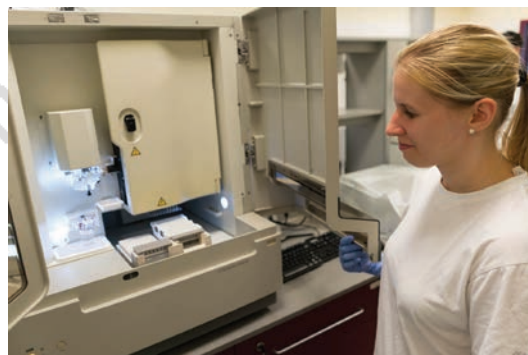
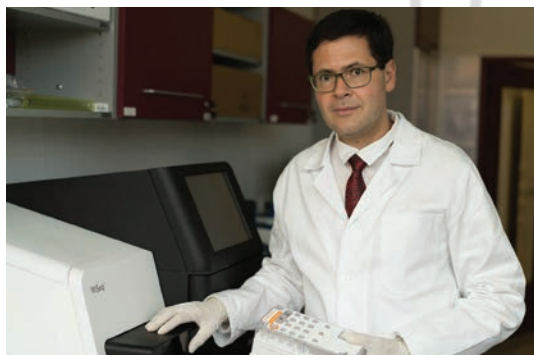
LABORATORY OF Neurobiology and Pathological Physiology

RESEARCHERS Vladimír Balcar, Pavel Kulich ¹⁰ Tomáš Zeman ⁸ Ondřej Bonczek ²
POSTDOCS Miroslav Bardelčík ¹ Peter Bielik ⁴ Laura Ewerlingová ⁷ Jan Vysloužil ⁵
RESEARCH ASSISTENTS Marie Jandová ⁶ Markéta Raclavská ³

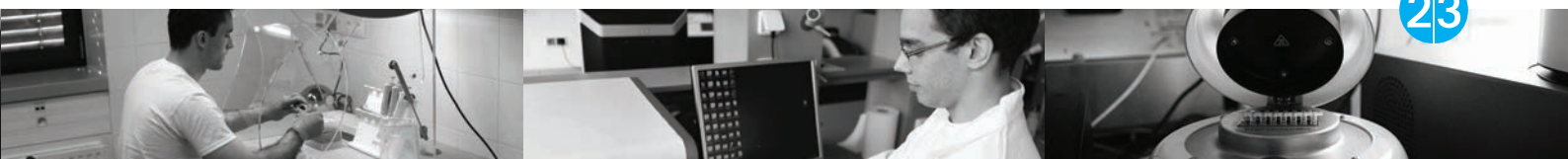
The laboratory covers a wide range of research areas dealing with molecular basis of development of diseases and selected traits. We contribute to research **of psychiatric diseases and multifactorial disorders** such as **schizophrenia, Alzheimer's disease, mild cognitive disorder, alcohol dependence, and ADHD** mostly by conducting **genetic association studies** and by identifying genes increasing susceptibility for these disorders. The fundamental aim of the research is to characterise the DNA variants that increase disease susceptibility by causing abnormalities in the structure or function of genes to create possible new treatments or prevention strategies. Particular interest is given to **CD36 gene polymorphisms**. Concurrently, we pay attention to the role of other risk factors in the pathogenesis of these diseases. In addition, laboratory is focused on studies related to the **oral sensing of fatty acids** (in relation to **obesity** and genetic variation) or to the inherited **tooth agenesis (oligodontia and hypodontia)**. Further, of great interest is the **research of the toxic effects of nanoparticles** studied on mouse models. Moreover, laboratory team conducts molecular analyses of microorganisms and study their occurrence in nature and in human body. With respect to the focus of laboratory, we utilise techniques such as NGS sequencing, capillary DNA sequencing, Real-Time PCR methods, electron microscopy.



We revealed heterozygous *g.9527G>T* mutation in the **PAX9** gene that leads to lower expression of PAX9 protein and thus could contribute to the development of tooth agenesis (Šerý et al. 2015). In the research of **tooth agenesis** we use NGS sequencing (instrument MiSeq) to reveal new mutations. In addition, capillary DNA sequencing is employed to prove NGS results.



- We have **found a relationship** between rs3211892 polymorphism of **CD36** gene and Alzheimer's disease as allele A was found to be associated with **Alzheimer's disease** (Šerý et al. 2017). In addition, we showed that Alzheimer's disease patients have significantly later onset of diabetes, hypertension and stroke in comparison with control subjects (Šerý et al. 2014).
- It was reported that rs1761667 polymorphism of **CD36** gene is associated with **variations in fatty acid taste perception** in several populations as A-allele was associated with higher lipid taste perception thresholds than G-allele in obese individuals (Daoudi et al. 2015, Mrizak et al. 2015, Sayed et al. 2015).
- Our laboratory stressed that the comorbidity between **schizophrenia and diabetes mellitus** might have **common genetic roots** and IDE gene could become new candidate gene for further research of genetic causes of schizophrenia (Ewerlingová et al. 2019).
- Our laboratory showed that **CD36** receptor may be involved in mediating the effects of vascular endothelial growth factor (VEGF) on **intraocular pressure** (IOP). As a result, these findings will help to identify the patients at risk of acutely elevated IOP following the anti-VEGF therapy (Matušková et al. 2017).





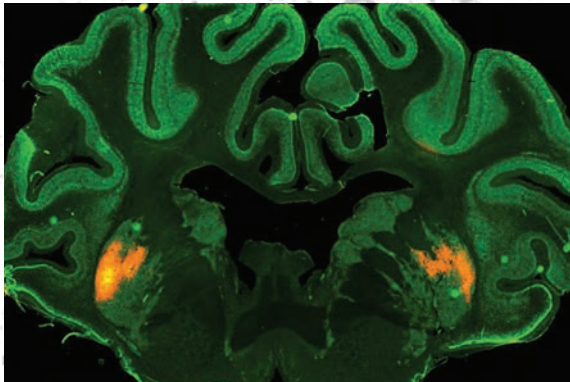
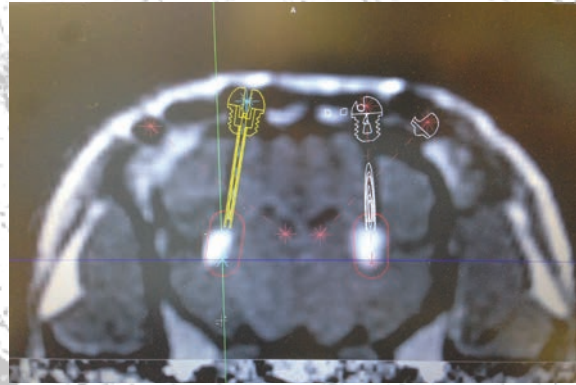
LABORATORY OF Cell Regeneration and Plasticity

RESEARCHERS Jan Motlík 1 Štefan Juhás, Jiří Klíma 10 Taras Ardan 3 Jana Juhásová, Eva Nagyová
POSTDOCS Božena Bohuslavová 5 Saskia Druťovič, Sonali Rohiwal 8 Ivona Valeková
Ph.D STUDENTS Monika Baxa, Nguyen The Duong 12 Petra Šmatlíková 4 Petra Vochozková, Lucie Zemanová
TECHNICIANS Lenka Trávníčková 11 Patrícia Jandurová 9 Irena Deylová 7 Hana Říhová 2

The main aim of our laboratory is a biomedical research using large animal model-the minipig. With the help of minipigs we study and seek treatment for various serious human diseases. Our main focus is on nervous system disorders, such as **Huntington's disease** (HD), **amyotrophic lateral sclerosis** (ALS), **spinal cord injury** and **retinopathies** (macular degeneration, Stargardt disease). But we also collaborate with medical doctors on **gastrointestinal tract diseases**. New treatments are mostly developed first on rodent models, however miniature pigs are physiologically and anatomically closer to humans and such preclinical models are essential before clinical trials in humans, including testing of new cell and gene therapies.



- 1) Our lab is equipped with the ophthalmic surgery microscope (Hi-R NEO 900A, Haag-Streit), phacoemulsifier/vitreotome (R-Evolution CR, Optikon), ophthalmic green laser (Merilas 532a, Meridian), and optical coherent tomography (OCT) (Optovue, iVue) for experimental eye surgery and noninvasive follow-up examinations.
- 2) MRI guided injection of huntingtin lowering gene therapy into striatum of transgenic minipigs for Huntington's disease.
- 3) Immunohistochemical analysis of porcine brain section after AAV5-miHTT injection
- 4) Pigs injected with miHTT-AAV5 few hours after surgery.



- We generated **transgenic minipig** model of Huntington's disease (HD), carrying N-terminal part of human mutated huntingtin to be used for basic research of HD pathological mechanisms as well as for preclinical testing of new therapies for this incurable neurodegenerative disease.
- We demonstrated broad distribution and strong human mutant **huntingtin lowering** after AAV5-miHTT **gene therapy** in a Huntington disease minipig model.
- We developed adjustable computer-controlled **compression model of spinal cord injury** in minipig. This model clinically as well as histopathologically faithfully simulate spinal cord injury in men. We implement preclinical experiments with newly established neural stem cell lines and gene therapy to introduce potential cure.
- We showed survival of syngeneic as well as allogeneic iPSC-derived neural precursors after **spinal grafting** in minipigs.
- We helped in developing a new surgical technique of **subpial application** of gene therapy.
- We helped to introduce new surgical approaches into clinical practice, such as **Natural Orifice Transluminal Endoscopic Surgery, Peroral Endoscopic Myotomy**.



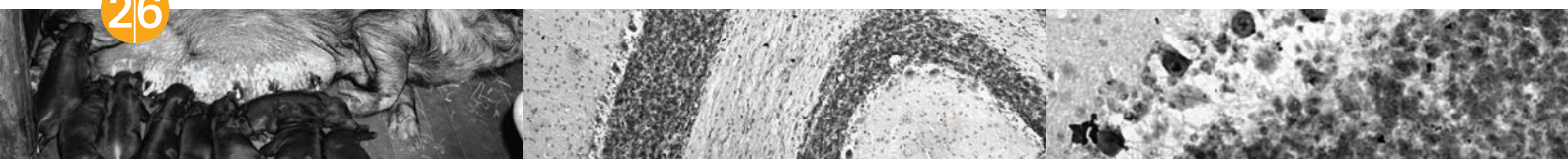


LABORATORY OF Applied Proteome Analyses

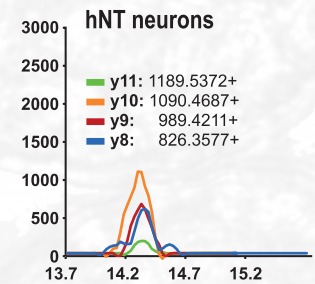
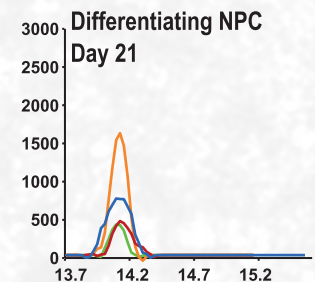
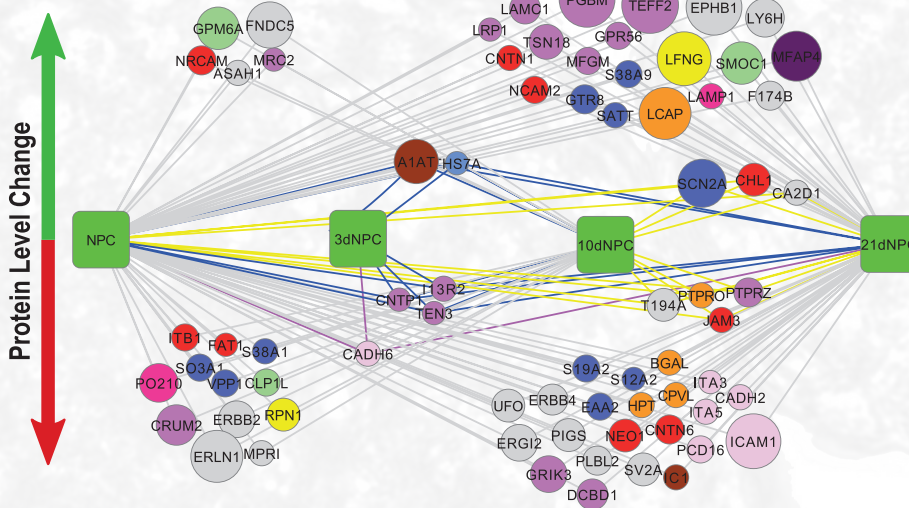
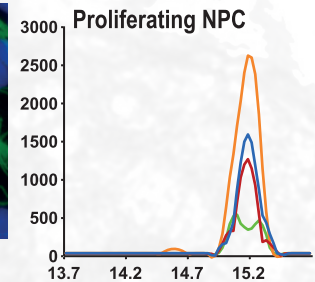
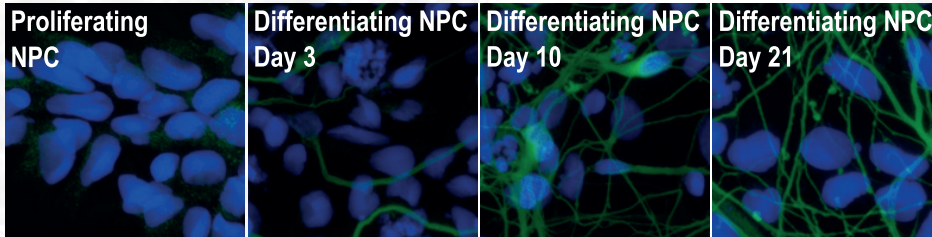
RESEARCHERS Helena Kupcová Skalníková 4 Vratislav Horák 10 **POSTDOCS** Rita Suchá, Jiřina Tylečková, Kateřina Vodičková Kepková 1 **Anna Palánová** **Ph.D STUDENTS** Martina Žižková, Jakub Červenka 2 Jana Čížková 11 Ievgeniia Poliakh 6 Petr Vaněk **RESEARCH ASSISTENTS** Jiří Klauď 3 Jaromír Novák 5 **TECHNICIANS** Jitka Klučinová 7 Jaroslava Šestáková 9

Our laboratory is using a **systems biology** approach with strong focus on **proteomics** to study biological processes connected to disease and aging. Currently, two basic themes are covered: neurobiology and cancer.

Neurobiology group studies pathology of **neurodegeneration** using animal and *in vitro* cellular models of **Huntington disease (HD)** and processes governing the differentiation of **neural stem cells (NSCs)**. **Cancer biology group** studies **cell-to-cell communication** between tumor and stromal cells and **cancer immunology** on porcine model of **malignant melanoma** developed at IAPG (Melanoma-bearing Libečov Minipig, **MeLiM**). These two research areas are connected by a common methodological approach based on the study of cell populations, their proteomes and secretomes using both antibody dependent and independent methods, including immunocyto and histochemistry, flow cytometry, multiplexed immunoassays and **mass spectrometry** based proteomics. Other common area is the use of miniature pigs as model animals, with **minipig** transgenic for fragment of mutant human **huntingtin** used as a HD model and minipig breed with hereditary malignant melanoma used as a cancer research model.



In development, neural precursor cells (NPC) differentiate into neurons and glia to form mature functional central nervous system (CNS). Deciphering the processes directing neural differentiation is important both for understanding neurodevelopmental diseases and for the use of NPC in cell therapies. One of the model systems available to study these processes is an in vitro differentiation of human NPC into mix of neurons and glia. Using mass spectrometry based proteomics we identified and quantified changes in more than 350 cell surface proteins during 20 days of in vitro differentiation of these cells. Identifying changes in cell surface proteins is especially useful, as it allows for flow cytometry based sorting of specific living cell populations for further use.



- Using 2D electrophoresis, mass spectrometry and **antibody microarrays** we analyzed changes in proteins and **signaling pathways** during differentiation of fetal porcine **neural stem cells** (Skalnikova et al. 2007, 2008).
- In collaboration with Paola Picotti group at ETH Zurich we developed mass spectrometry assay for simultaneous quantification of multiple cell processes, "**sentinel assay**" (Soste, Hrabakova et al. 2014).
- We participate in **preclinical testing** of experimental **gene therapy** for **Huntington disease**, using miRNA gene silencing with AAV vector mediated delivery (collaboration with uniQure Inc., Netherlands, Evers et al. 2018).
- In collaboration with Palacký University in Olomouc we identified proteins responsible for resistance of cancer cells to **aurora kinase** based **cytostatic** and obtained European patent EP2788504 for "Method for determination of **cancer cell sensitivity** towards aurora kinase inhibitors".
- Using the **MeLiM** (Melanoma-bearing Libechov minipig) strain, a unique large **animal cancer model**, we can in detail monitor the progression and spontaneous regression of **metastatic melanoma** and the participation of various **immune cells** and cytokines in these natural processes.





LABORATORY OF DNA Integrity

POSTDOC Dávid Drutovič 7 **Ph.D STUDENTS** Tomáš Ďuríček 2 Ivana Ferencová 3 Lucie Knoblochová 1
Michaela Vaškovičová 4 **TECHNICIAN** Ema Glöcknerová 5

Our mission is to understand how **compromised DNA/chromosome integrity** participates in the non-cancerous human diseases such as infertility or neurological disorders. Our interest in **chromosome dynamics and integrity in female meiosis** originates from the existence of the two greatly distinct cell lines in animals: *germ cells* and *somatic cells*. They have significantly different demands for the genetic stability. The germ lines must ensure transmission of the genetic information to the offsprings and must be very effective in the DNA integrity maintenance. In somatic cells, DNA repair is a compromise between growth speed, cancer risk and also the cost for DNA repair. In mammalian oocytes and early embryos we focus both on the mechanism of *chromosome segregation* as well as on *DNA damage response (DDR) on the DNA double strand breaks (DSB)*. We are also interested in **DDR in neurological Huntington's disease**. The connection of DNA damage to cancer is well known. However neurological disorders are also associated with DNA damage and compromise DNA repair, although they have completely different impact for patients in comparison to cancer. It provokes a question, how it is possible that DNA damage can lead to two completely different problems: cancer or neurodegeneration? We are interested in DSB response in cells compromised by the presence of mutated Huntingtin that is causative for Huntington's disease. Our goal is to understand problems with DSB response in Huntington's disease and help to use this knowledge both for diagnostic and therapeutic purpose.

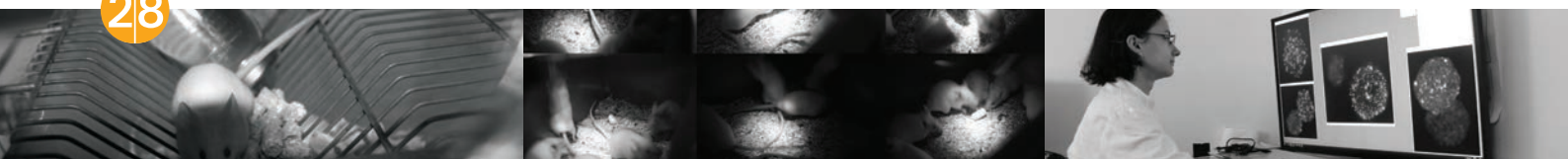
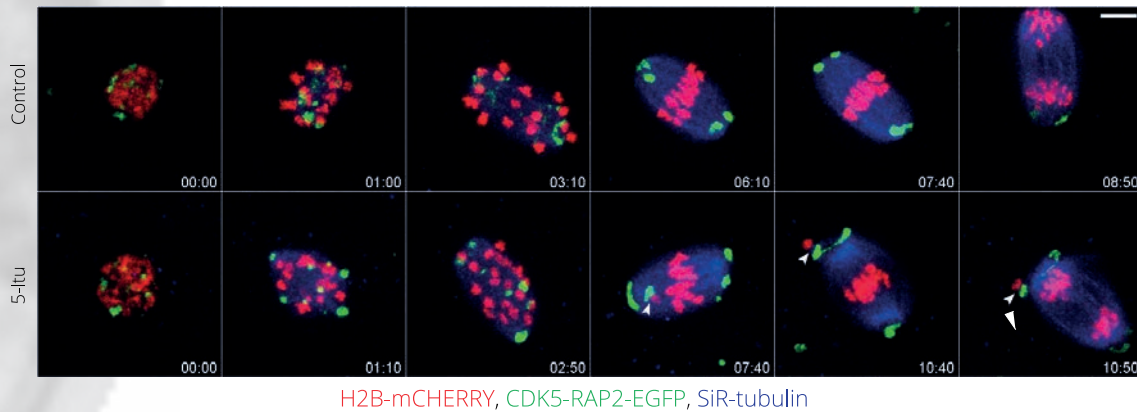
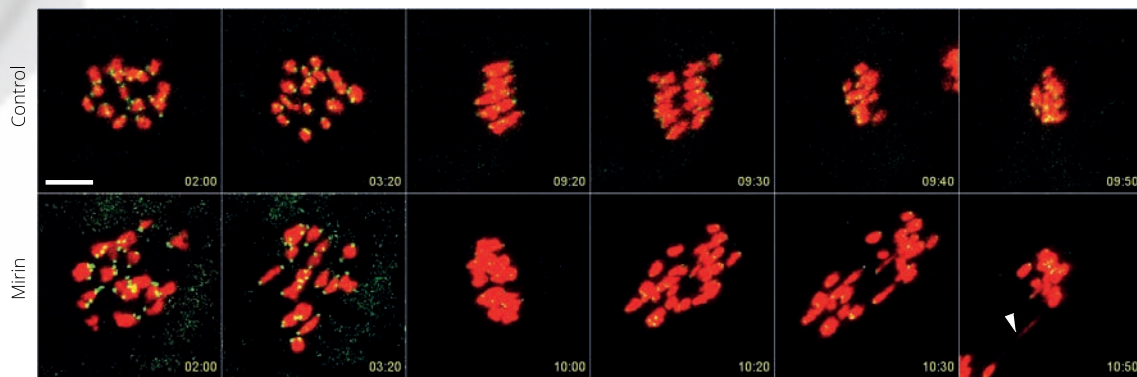


Figure 1 Spindle formation and chromosome segregation during meiosis of mouse oocyte. Oocytes express H2B-mCHERRY (chromosomes) and CDK5-RAP2-EGFP (microtubule organizing centers – MTOCs) from microinjected mRNAs. Spindles are visualized by staining with fluorogenic drug SiR-tubulin. Normal chromosome segregation (control) and defective chromosome segregation (5-Itu) when Haspin kinase was inhibited by small molecule inhibitor 5-Itu.

Figure 2 Chromosome segregation and integrity in mouse oocytes expressing H2B-mCHERRY (chromosomes) and CENPC-EGFP (kinetochores). Normal segregation of intact chromosomes in control oocyte and defective chromosome segregation associated with formation of DNA bridges in oocyte in which a genome integrity critical molecule MRE11 was inhibited by small molecule Mirin. All images represent maximum confocal z-stack projections.



H2B-mCHERRY, CDK5-RAP2-EGFP, SiR-tubulin



H2B-mCHERRY, CENPC-EGFP

- We have discovered **multiple roles of PLK1 during female meiosis** when PLK1 regulates nuclear envelope break down, spindle formation, microtubule-kinetochor attachments and it is also critical for anaphase I onset by regulation of APC/C (PLoS One. 2015 Feb 6;10(2):e0116783).
- We have shown that **during meiotic maturation oocytes are able to repair the double-strand DNA breaks** and that MRE11 nuclease is critical for chromosome integrity (Cell Cycle. 2016;15(4):546-58).
- We have uncovered requirements of **Aurora B and C** for correct **chromosome segregation** in mammalian oocytes and normal fertility. (J Cell Sci. 2016 Oct 1;129(19):3648-3660 and Curr Biol. 2018 Nov 5;28(21):3458-3468.e5.).
- We have established productive collaborations with laboratories of Dr. Karen Schindler (**Rutgers University**, New Jersey, USA) and Dr. Tomoya Kitajima (**RIKEN Center for Biosystems Dynamics Research**, Kobe, Japan).
- We are **teaching** cell cycle regulation, genome integrity and oocyte biology at **Faculty of Science and 2nd faculty of Medicine of Charles University in Prague**.





LABORATORY OF Fish Genetics

RESEARCHERS Jörg Bohlen 7 Vendula Bohlen Šlechtová 8 Lukáš Choleva 4 Janko Karel 14
Vlastimil Šlechta 19 Věra Šlechtová 10 **POSTDOCS** Marie Altmanová 13 Dmitri Dedukh 18 Marie Kaštánková 2
Zuzana Majtánová, Alexandr Sember, Krzysztof Zawierucha 17 **PHD STUDENTS** Marta Anatol 9
Oldřich Bartoš 16 Tomáš Dvořák 1 Jan Kočí 20 Jan Röslein, Alena Zikmundová 12 **TECHNICIANS** Jana Kopecká 6
Jana Machová 3 Šárka Pelikánová 5 Petra Šejnohová 11

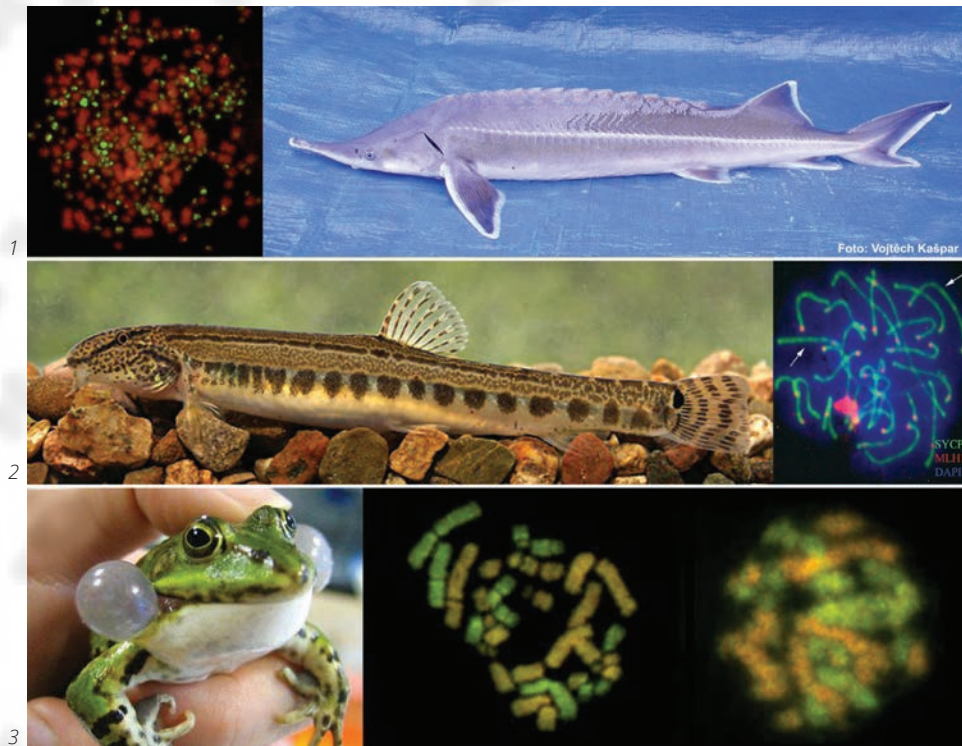
Activity of Laboratory is focused on **clonal reproduction and polyploidy in fishes and other lower vertebrates**. The long-term studies analysed hybrid asexual vertebrates using model systems of hybrid complexes of spiny loaches of the **genus *Cobitis***, fishes of the **genus *Carassius*** and also in water frogs, **genus *Pelophylax***. The issues of fish polyploidy is further developed in analysis of **hybrid polyploid sturgeons**. Related to this, we intensively analysed cytogenomics of other **basal non-teleost fishes** (gars, bowfin) and the role of transposons in fish genomes as well. Laboratory is engaged in National program of gene resources (Ministry of Agriculture) by analyses of genetic parameters fish breeds, strains and lines (common carp, tench, whitefishes, trouts, sturgeons).



1) Sturgeons, highly endangered ancient ray-finned fish lineage, experienced at least three independent whole genome duplication events. We are studying the hybrid and ploidy diversity of cultured sturgeons. Using combination of genome manipulation methods and spontaneous polyploids, we discovered the highest chromosome count among vertebrates ~ 520.

2) European spined loaches (*Cobitis*) include several morphologically and ecologically very similar species that have parapatric distribution and meet in hybrid zones. We are combining molecular phylogenetics, artificial crossing experiments, NGS sequencing and cytogenomic approaches to describe genetic background and consequences of their reproduction, **sperm-dependent parasitism — gynogenesis**, with frequent switch of sexual hosts.

3) Water frogs from Central Europe include hybrids of both sexes, collectively named *Pelophylax esculentus*. Some hybrid lineages consist of all males providing a chance to understand the origin and perpetuation of a host-parasite (egg-dependent) system compared to a common sperm-dependent parthenogenesis. Here we studied origin and perpetuation of all-male hybrid lineages. We found that these lineages were only rarely formed in the past. Therefore, modifications in meiosis turning sexual reproduction to asexual were a rare event in these hybrid tetrapods.



- Laboratory was awarded by **The Award of CAS** for outstanding results of great scientific significance entitled „Clonal vertebrates: discovery, mechanisms, biodiversity and reconstruction in model cobitoid loaches“ in 2012.
- The synthesis of clonality and polyploidy in vertebrate by **hybridization between two sexual species** was the first one in the world after 80 years since discovery of the first asexual vertebrate.
- Discovery of hemiclinal lineage with *Pelophylax esculentus* complex that **transmit male and not female genome clonally** over generation.
- Using cytogenomic analysis of two gar genera, *Atractosteus* and *Lepisosteus*, uncovered **a GC chromosomal pattern** uncharacteristic for fishes but corresponding to mammals.
- The Second Highest Chromosome Count among Vertebrates is Observed in Cultured Sturgeon, and is Associated with Genome Plasticity.
- Laboratory **contributed 5 chapters** into Fish Cytogenetic Techniques (Chondrichthyans and Teleosts), Eds: Catherine Ozouf-Costaz, Eva Pisano, Fausto Foresti, Lurdes Foresti de Almeida Toledo, CRC Press, Inc., Enfield, NH 03748, USA, 2015.





LABORATORY OF

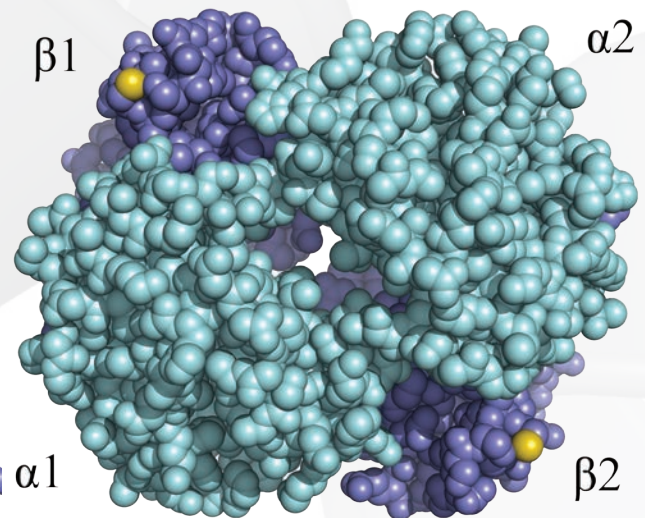
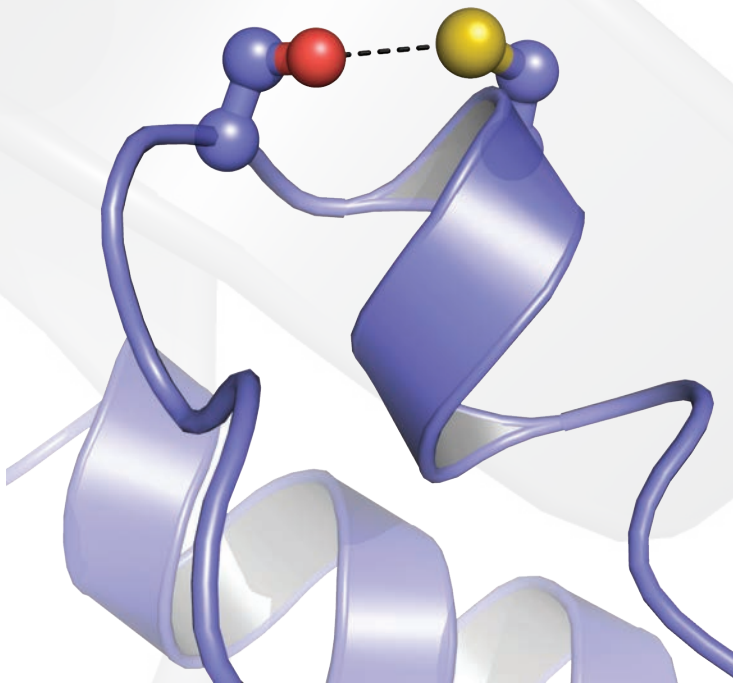
Molecular Ecology

RESEARCHERS Silvia Marková 4 Antonín Stratil 2 **POSTDOCS** Věra Dvořáková 1
Marco Alejandro Escalante **Ph.D STUDENTS** Michaela Strážnická 5 **TECHNICIAN** Petra Šejnohová 6

The major research focus of the lab is the **response of organisms to climate change**, primarily following the last ice age. By comparing genomes of **bank voles** (*Myodes glareolus*, a.k.a. *Clethrionomys glareolus*), we have provided firm evidence that an immigrant population of these small woodland mammals that arrived to Great Britain at the end of the last ice age partly replaced a pre-existing bank vole population, resulting in a genetic pattern termed the 'Celtic fringe'. With the recent projects, we are seeking to determine if such **climate-related population replacements** occurred also in other parts of the species' broad Eurasian range and to identify key **adaptations** that allowed some populations replace the others. This involves studying genes with known link to climate adaptation in other species (candidate gene approach) as well as comparing levels of population differentiation across many genes via **genome sequencing** (genome scan approach), gene expression analysis and ecological niche modelling. Such findings will be of particular relevance to population replacements in response to current climate change. We believe that disentangling the processes behind replacements that occurred in the past may help understand and ultimately predict the response of species to current and future climate change. Other our research areas are the conservation genetics and molecular systematics of **fishes, frogs and snakes**, and the evolutionary genetics of Holarctic **Daphnia**.

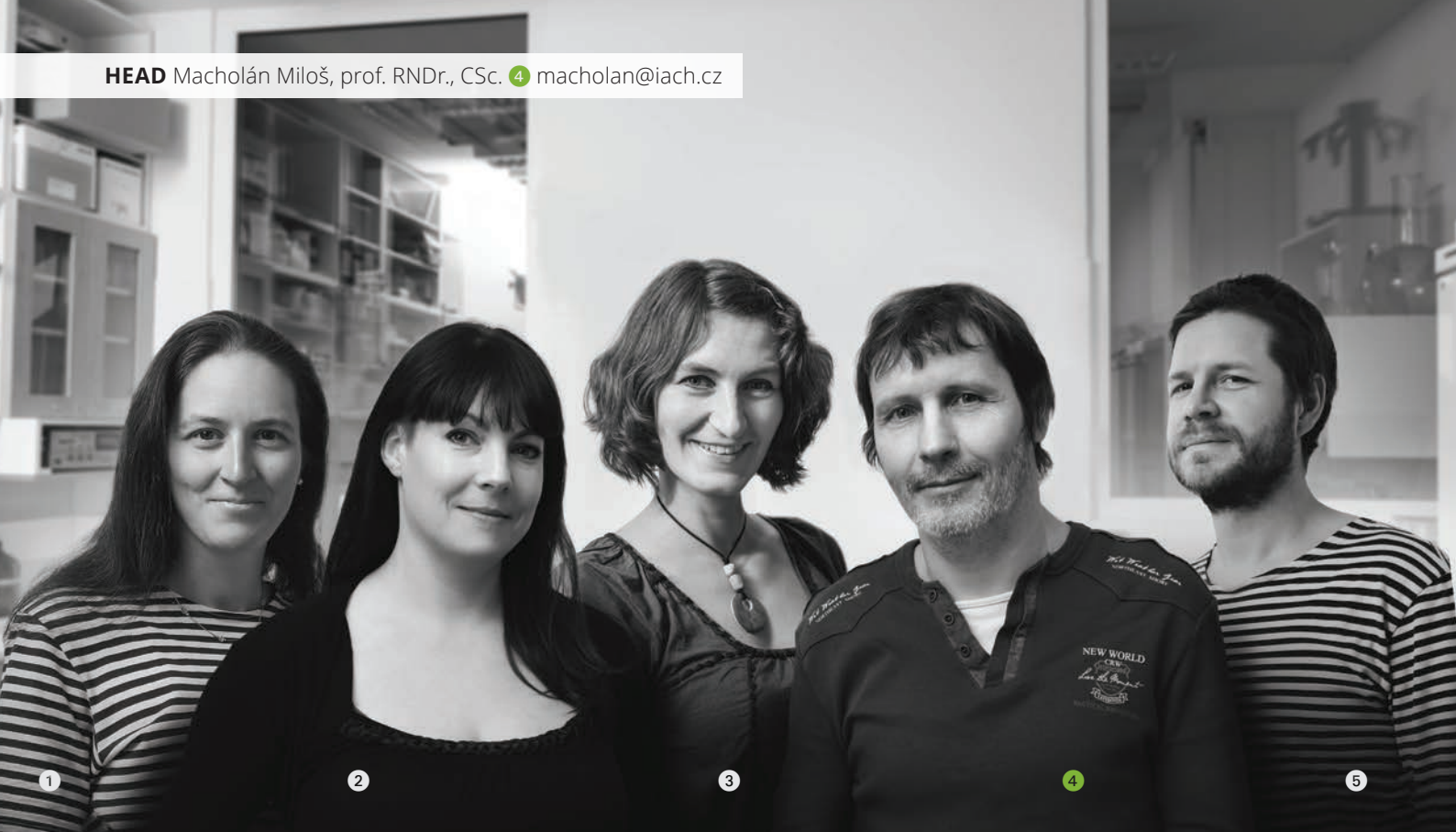


The Hb F variant of bank vole haemoglobin contains a reactive amino acid cysteine on its surface. Our functional study demonstrated that Hb F confers enhanced erythrocyte resistance to a controlled free-radical attack. The mechanistic basis is that the exposed and negatively charged side-chain sulphur atom makes the cysteine a highly reactive residue with the capacity to participate in the regeneration of the major intracellular antioxidant glutathione. Because the rate of ROS production markedly increases during energetically demanding physiological states, such as muscular activity, increased rate of growth or reproduction, or under thermal stress, the variant haemoglobin likely is advantageous under a multitude of ecological conditions.



- Using **genome sequencing**, we found evidence for a **population replacement** in the bank vole related to **the climatic change** following the last ice age.
- We discovered a mutation in **haemoglobin** of the bank vole increasing red blood cell **resistance to free radicals**, allowing a better **adaptation** to stressful environmental conditions.
- We discovered and described for science **a new species of fish** from the Danube River basin.
- We discovered a widespread **transfer of mitochondrial DNA** between species of *Daphnia* crustaceans, which shed light on the process of **ecological adaptation** in these important model organisms.
- For her diploma thesis on haemoglobin adaptation, our student Michaela Strážnická received an **Award of The Minister of the Environment**.
- For the paper describing *Barbus biharicus*, we were awarded the **Vitális Sándor Literary Prize** of the Hungarian Hydrological Society.





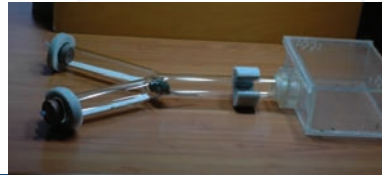
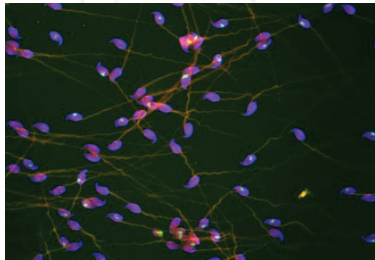
LABORATORY OF Mammalian Evolutionary Genetics

RESEARCHER Barbora Vošlajerová 3 **POSTDOC** Kristina Daniszová 2 Zuzana Hiadlovská 1
Radovan Smolinský **RESEARCHER ASSISTENTS** Ondřej Mikula 5 **TECHNICIAN** Jana Kopecká

The description and understanding of the origin and maintenance of overall biodiversity is a crucial task in contemporary biology. Our laboratory focuses on **genetic and phenotypic variation** and **evolution of mammals**, using both **wild and model species**. In the former case we focus on description of the genetic and morphological variation and **systematic relationships** among small mammals of the Palearctic and Afro-tropical zoogeographic realms. In the latter case we capitalize on the house mouse (*Mus musculus*) as a unique evolutionary model for studying factors involved in process of speciation. Our aim is to elucidate mechanisms involved in formation of prezygotic and postzygotic reproductive barriers (including so called "**speciation genes**") and to detect those parts of the genome breaking these barriers (so called "**antispeciation genes**"). For this purpose we use large number of molecular genetic techniques as well as analyses of phenotypic differences in ecology, behaviour and physiology between the two subspecies potentially affecting processes shaping hybrid zone patterns. Our results brings direct insights into the understanding of the **process of speciation**. Given the way the zone has arisen we try to supplement these data with phylogeographic mapping of the western Palearctic to reveal involvement of individual haplogroups in its origin.



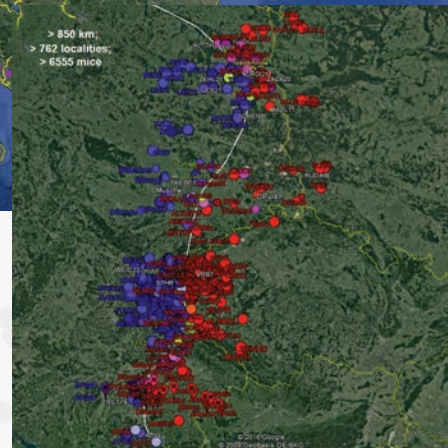
Two subspecies of the house mouse *M. m. musculus* and *M. m. domesticus* hybridize in Europe. The zone dynamics is studied across a vast area between the Baltic Sea coast and the Alps in order to distinguish random influences (colonization history, human activities, local geographic barriers, genetic drift) and deterministic factors (natural selection). We focus on both phenotype differences between the two subspecies (sexual preferences, aggression, coping with stressful conditions, exploration and dispersal, production and profiles of androgen-binding proteins, major urinary proteins, steroid hormones) and genetic processes shaping the hybrid zone patterns studied through various molecular markers (SNP, allozymes, microsatellites, sequences) and specific analyses (gene expression, gene copy number variation).



M. m. musculus



M. m. domesticus



- We revealed that differences in **social structure, behaviour and physiology** in closely related species may be crucial for dynamics of their **speciation** (Daniszová et al. 2017, Hiadlovská et al. 2013, 2014, 2015).
- We contributed to description of unique model for unravelling the role of **salivary Androgen binding proteins** in mouse communication (Chung et al. 2017).
- We brought new insights into the **evolutionary history of East African rodents** (Bryja et al. 2014, 2017).
- Members of the laboratory actively contribute to **teaching** at the universities and prepare **textbooks** and **popularisation materials** (Svoboda, Macholán 2014, Macholán 2014).





LABORATORY OF

Anaerobic Microbiology

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STUDENTS Lucie Benešová 10 Adéla Štěpánová 11 Renata Tarasová 12 Barbora Zavoloková 13
TECHNICIANS Hana Bartoňová 14 Hana Bubíková 15 Lenka Štrosová 16

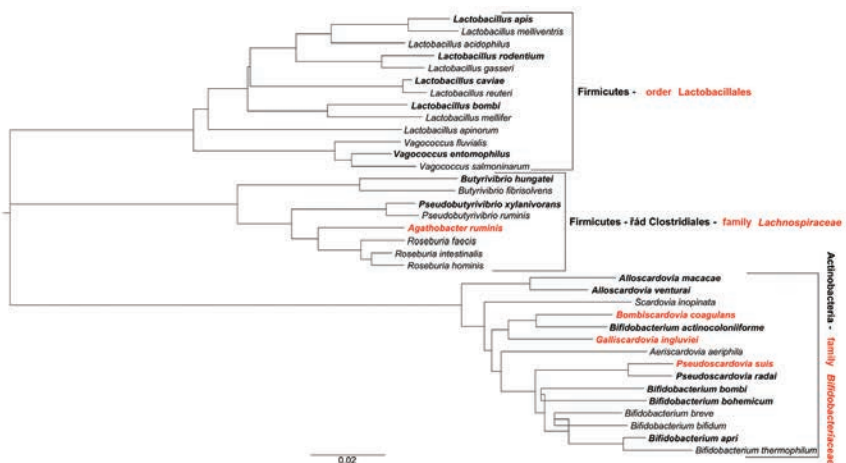
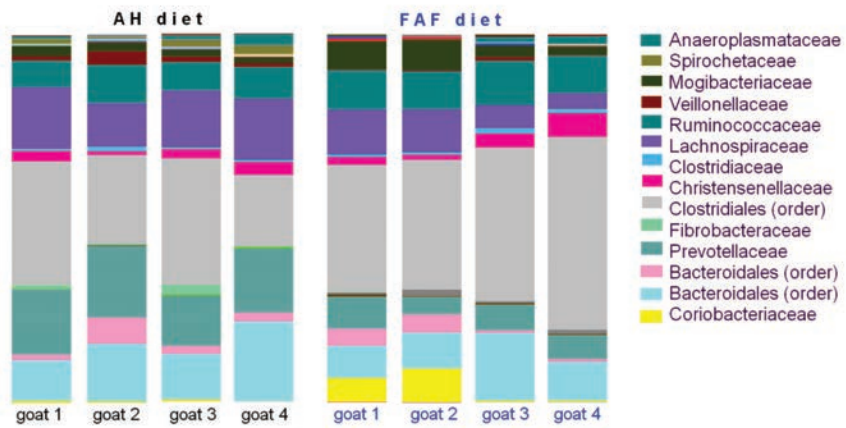
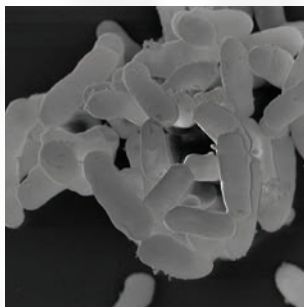
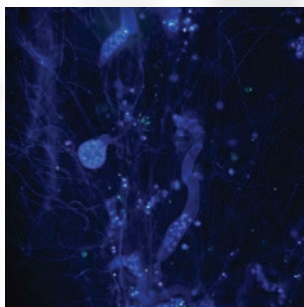
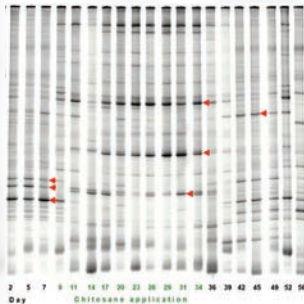
Our group has been studying anaerobic microbes for more than 40 years, with focus on human and animal gut. Animal **gut microbiota** plays irreplaceable role – it participates in nutrition processing and production of host beneficial metabolites, stimulates host's immune system and prevents contamination of pathogens. The gut microbiota is currently considered as a separate organ with its own individual and evolutionary development. It also plays a key role in many civilization disorders (obesity, diabetes, ulcer colitis, Crohn's disease, gut cancer, etc.), and also in diseases not related to gut, e.g. autism, Alzheimer's disease, stress (="gut-brain axis"). We use two main approaches to study microbiota ecosystems: microbiological with isolation and **description of new microorganisms**, and by molecular methods, when the **microbiome diversity** is analysed as a whole, without the need of cultivation.



Methodological ground of our research is isolation and description of new anaerobic bacterial and fungal taxa, and estimation of their morphology, metabolism and role in the host's ecosystem. We focus on beneficial gut bacteria (bifidobacteria, lactobacilli), and also on potentially technologically important microorganisms with high cellulolytic and xylanolytic activities (butyrate producing bacteria, anaerobic fungi). We also study phylogenetic status (classification and evaluation of evolution of organisms based on molecular markers) of family *Bifidobacteriaceae*, order *Lactobacillales* and genera *Propionibacterium*. Eighteen new microbial species and genera have already been described by our group.

Second methodological approach is the application of tools of molecular biology for description of microbial communities.

Our projects include analyses of gut microbiome from patients with inflammatory bowel diseases and estimation of treatment (biological treatment by anti-TNFalpha, prebiotics and microbiota transplantation), characterization of metabolic syndrome in schizophrenia patients and role of microbiome in "gut-brain" axis. Our lab also deals with description and alteration of microbial communities in bio-waste treatment with aim to increase efficiency of methane production, or in contrary to methane emission reduction in ruminal microbiomes.



- Large **collection** of anaerobic bacteria and fungi.
- We have isolated and **described** 18 new bacterial genera and species.
- Jiří Killer has been **awarded** by the Czechoslovak Society for Microbiology (ČSSM) as the best Czech-Slovak young microbiologist in 2015.
- Intensive **cooperation** with domestic (CAS, IKEM, IsCare) and foreign (Scotland, New Zealand, USA, Argentina) research institutes.
- Members of your laboratory actively contribute to students **teaching** at national (CULS, ChU, ICHT) and international universities (UNISS, Italy).



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IAPG Units

Supporting units are essential for the smooth running of the Institute. They take serious care for our campus, finances, animals as well as incentive atmosphere.

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Secretariat + IT

Jana Brandelová 1 Jana Zásmětová 2 Michal Horák 4

38



Secretariat Brno

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Operational and Technical Unit

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Martin Brandel 6 Edita Křováková 7 Milena Mikšová 9 Blanka Chudobová 10 Miloslava Hoření 11



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Experimental Animals Unit

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Marie Hradcová 6 Tomáš Břehovský 7 Venuše Burčová 8 Petr Jón 9

Projects

QI101A166	MZE	Biotechnology in pig husbandry and breeding	2010	2014
GAP502/11/0593	GAO	Signaling pathways and genes regulating gonadotropin-induced maturation of pig cumulus-oocyte complexes	2011	2014
GAP506/11/1792	GAO	Population structure, dispersal, and explorative behaviour in the zone of secondary contact of house mice	2011	2014
GAP506/11/1872	GAO	Adaptive genomic divergence to climatic refugia	2011	2015
GPP301/11/P081	GAO	Role of CDC25B phosphatase during cell cycle resumption: The Comparison of meiotic resumption in oocytes and G2 checkpoint recovery in somatic cells	2011	2013
GPP506/11/P596	GAO	Polyploidization as a key factor in genome evolution of basal vertebrates' lineages	2011	2013
TA01011466	TAO	Biomedical model of miniature pigs for testing of new medicaments and for new treatments of traumatic spinal cord injury and neurodegenerative diseases	2011	2014
7E12046	MSM	RuminOmics	2012	2015
ED2.1.00/03.0124	MSM	ExAM Experimental Animal Models	2012	2015
GBP503/12/G147	GAO	Centre for studies on toxicity of nanoparticles	2012	2018
GCP302/12/J059	GAO	Cellular and molecular mechanisms in tooth-bone complex formation	2012	2014
GPP506/12/P857	GAO	Where does a species start and end? Speciation in a ring studied in the era of phylogenomics with application to European spined loaches	2012	2014
LH12057	MSM	The signaling pathways synchronizing nuclear envelope break down, chromosome condensation a spindle formation during mammalian meiosis of oocytes	2012	2015
GA13-12291S	GAO	Retention of specific mRNAs in the nucleus of the fully grown mammalian oocyte	2013	2017
GA13-12580S	GAO	Which mechanisms affect the diversity of clones and their coexistence with sexual species? European loaches of the genus <i>Cobitis</i> as a model	2013	2017
GA13-37277S	GAO	Mechanisms and impact of polyploidisation in evolution of animals – lessons from the fish family <i>Botiidae</i>	2013	2016
GP13-24730P	GAO	The Role of Skp1-Cullin1-F-box Complex in Protein Ubiquitination and Degradation during Bovine Preimplantation Development	2013	2018
7AMB14PL031	MSM	The ways to unisexuality: mechanisms initiating parthenogenesis in fish	2014	2015
7F14308	MSM	Comparative study of Huntington's disease using biochemical, immunocytochemical and molecular genetic methods on the mouse, minipig and human tissues and cells	2014	2017
EE2.3.45.0037	MSM	Mendel's interactive school of genetics	2014	2015
GA14-31540S	GAO	Mechanism of limb development and molecular basis of disruptions in skeletal patterning	2014	2016
GB14-37368G	GAO	Centre of orofacial development and regeneration	2014	2018
GP14-29273P	GAO	Study of developmental processes determining the number of tooth generations	2014	2016
GA15-13265S	GAO	High resolution genomic analysis of introgression across a species barrier	2015	2019
GA15-22765S	GAO	Role of the regulatory factors acting at 3'end of mRNA in correct progression of mammalian oocyte meiotic maturation.	2015	2019
GJ15-19947Y	GAO	When a hallmark of meiosis is lost: studying the formation of clonal and hemiclinal genomes in vertebrate animals using comparative cytogenomics	2015	2017

QJ1510138	MZE	Innovation of reproductive biotechniques in farm animals	2015	2018
QJ1510338	MZE	Fermented dairy products and cheeses for the health nutrition of people, manufacturing technological processes and evaluation methods with the emphasis on the high microbiological safety and improved nutrition parameters	2015	2018
EF15_003/0000460	MSM	EXCELLENCE in Molecular Aspects of the early development of vertebrates	2016	2022
GA16-03248S	GA0	Genomic study of adaptive population shifts in response to climate change	2016	2018
GA16-05534S	GA0	Microenvironment of malignant melanoma as a factor of tumor aggressiveness	2016	2018
GA16-12431S	GA0	Structure and synergism of fibrolytic enzymes in the rumen	2016	2018
GA16-23773S	GA0	Phylogeography, selection and mutation rate at the whole-genome level: Inference from mtDNA sequences of the house mouse	2016	2018
LH15255	MSM	Genomic study of a climate-driven population replacement	2016	2017
LO1609	MSM	Models of the Serious Human Diseases: Traumatic Spinal Cord Injury, Huntington's Disease, Melanoma and Infertility	2016	2020
NV16-31806A	MZ0	New methods of in vivo monitoring and management of colonic anastomosis leak in experimental model	2016	2019
GA17-09807S	GA0	Why and how animals abandon sex? On the causal role of hybridization in triggering asexual reproduction	2017	2019
GA17-14886S	GA0	Molecular and cellular dynamics of tooth-bone interface in model species with acrodont, pleurodont and thecodont dentition	2017	2019
GA17-22604S	GA0	The lizard perspective on mammalian sex chromosomes	2017	2019
GA17-25320S	GA0	Genotypes and phenotypes associated with Y chromosome introgression in the European house mouse hybrid zone: comparison among transects	2017	2019
LTAUSA17097	MSM	Spindle dynamics and chromosome segregation during oocyte meiotic maturation	2017	2021
NV17-31852A	MZ0	The interplay between the gut microbiota and brain functions: implication for metabolome and metabolic syndrome in schizophrenia	2017	2020
EF16_027/0008502	MSM	International mobility fo IAPG researchers for transfer of biomedical innovations	2018	2019
GA18-09323S	GA0	Genome duplication in sturgeon evolution and impact on their biology	2018	2020
GA18-19395S	GA0	Non-coding RNAs matters: role in mammalian oocyte and embryo	2018	2020
NV18-04-00455	MZ0	The role of CD36 gene in pathogenesis of Alzheimer´s disease	2018	2021
GA18-04393S	GA0	Experimental transplantation of the retinal pigmented epithelial cells in a large animal model	2018	2020
GA18-04859S	GA0	Fate decisions in the dental placode: an investigation into the signalling factors that determine cell fate decisions in the early oral cavity	2018	2020
LTC18079	MSM	Proteomic characterization of cell membrane surface proteins, secretome and exosomes in human cell based Huntington's disease model.	2018	2021
LTC18081	MSM	Caspases as novel regulators in osteogenic cellular networks	2018	2020
NV18-07-00073	MZ0	c-Myb and its transcriptional program in physiological and pathological osteogenic processes	2018	2021

Publications

2018 Papers

Bálek, L., Buchtová, M., Kunová Bosáková, M., Vařecha, M., Foldynová-Trantírková, S., Gudernová, I., Veselá, I., Havlík, J., Neburková, J., Turner, S., Krzysciak, M. A., Zakrzewska, M., Klimaschewski, L., Claus, P., Trantírek, L., Cígler, P., Krejčí, P. Nanodiamonds as “artificial proteins”: Regulation of a cell signalling system using low nanomolar solutions of inorganic nanocrystals. *Biomaterials*. 2018, 176(1), 106–121. ISSN 0142–9612.

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Macholán, M. *Základy fylogenetické analýzy* Brno: Masarykova univerzita, 2014. 289 s. ISBN 978–80–210–6363–1.

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IAPG is engaged in a wide range of popularization activities. Perhaps the biggest event is The Open Days. All three locations (Liběchov, Prague, Brno) are ready for a rich program for visitors of all ages in selected days. For the youngest one, the play of A Curious Scientist is prepared, as well as the presentation of one of the scientific themes of the institute, games and competitions on knowledge of animal kingdom, demonstration of laboratory work, and an exploration of experimental animal breeding. For older ones are prepared excursions in laboratories with commentary of scientists. The events meet with great interest mainly from schools and with a very positive response. Our Institute also release our own promotional items (bookmarks with the most interesting discoveries of our workplace and leaflet for the general public). The Institute has also participated in the largest science festival, the Science Fair, which takes place every year at the Letňany Exhibition Center, and its exposition enjoyed the great interest of a wide range of visitors. In addition, the Institute's labs are attended by high school students within the framework of the Open Science project (Project Open Science is offering annual possibility for talented secondary school students to get involved in basic research in all locations of the IAPG. Some of them became successful MS or PhD students later on.

IAPG Popularization Activities



The advantage of these activities is in long lasting contact with the students and stimulating their interests) and they are preparing many disseminating lectures, whether at secondary schools or universities. At our Brno workplace, the popularization activities are connected with the Mendelianum project. This project Mendelianum – Attractive World of Genetics, creation of Centrum Mendelianum is a modern bases for popularization of science, education and research established on 50 year tradition in development and propagation of Mendel's heritage. Institute of Animal Physiology and Genetics is the major partner of the Moravian Museum, the Centrum activities run under auspices of the Academy of Sciences of the Czech Republic.

Employees of the Institute also regularly publish and comment on the results of their work in popularizing journals, participate in textbooks and scripts, and publish scholarly books for the public.

IAPG Collaboration with Application Sphere

Much of the Institute's research has been translated into solutions, methods and results that are a benefit to both general and academic society. A constant exchange of ideas and cooperation between the IAPG researchers and companies in Czech Republic and worldwide is one of the characteristics that make the IAPG research successful.

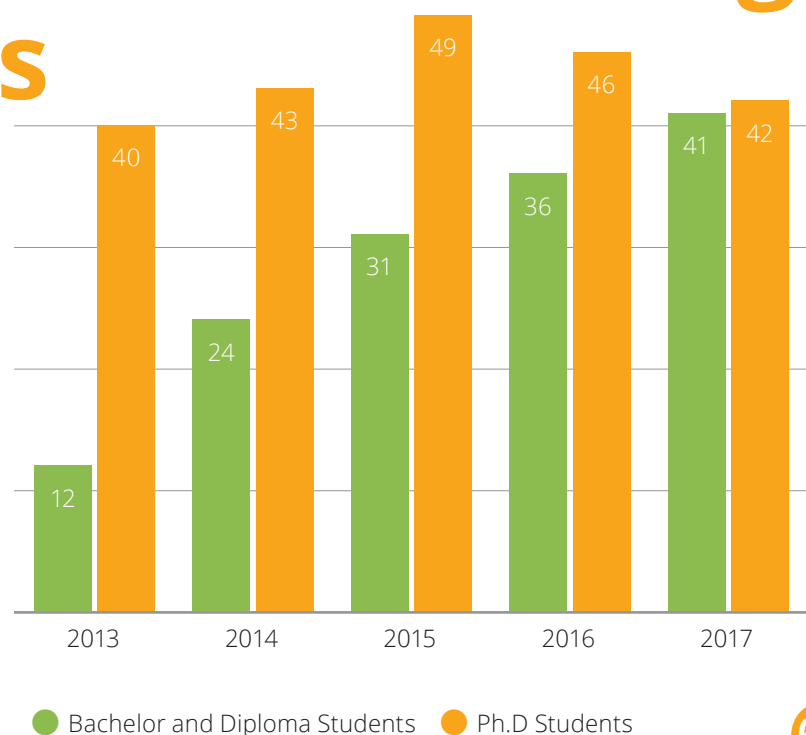
Application and commercialization of research mostly in the field of neurology and molecular biology was sped up by realization of the ExAM project in 2013 – 2015 and by building a new, competitive IAPG infrastructure perfect for partnering with private, commercial sector, applying for translational funding grants and facilitating the IAPG consultancy activity.

The IAPG's PIGMOD Centre (Pig Models of Diseases) has since extensively partnered with businesses worldwide, incl. top US companies and foundations (e.g. CHDI Foundation, Neuralstem Inc.), in the EU (e.g. Synovo GmbH, uniQure NV) as well as with Czech progressive companies (e.g. MediTox s.r.o.). Other forms of translational research consist of cooperation with hospitals and clinical centers in Czech Republic and EU (Motol Hospital, FNUSA-ICRC etc.) where the expertise of IAPG lies in providing analytical services, expert consultations, creating novel animal models, forming research concepts and coordinating research projects. Since 2013 the IAPG runs simultaneously 5 to 10 projects a year with different partners from applied sector. A yearly financing in the applied research field climbs up to 1 million EUR with half being from private companies and half from public sector translational projects.

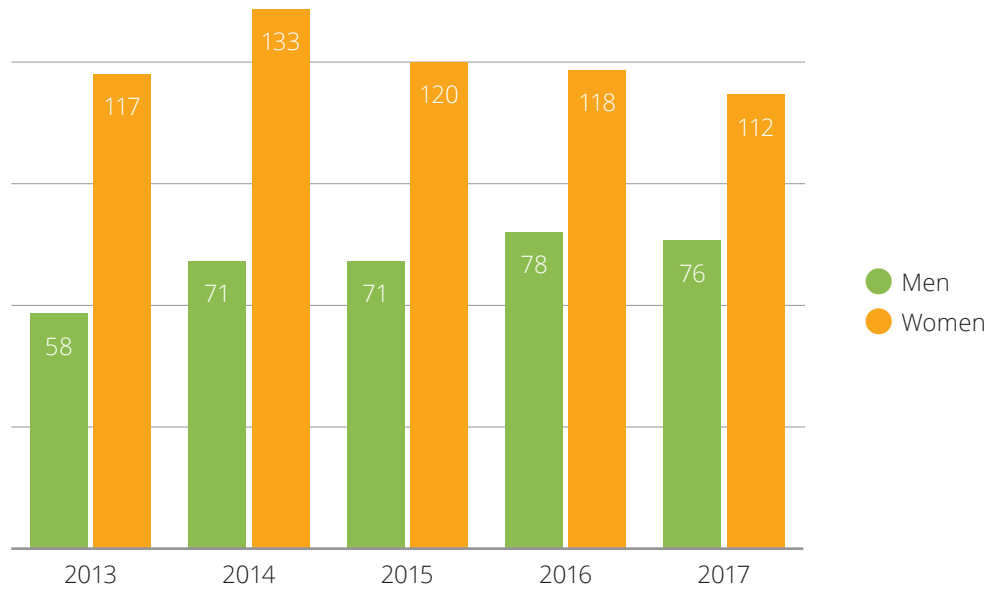


IAPG Education and Teaching Activities

Employees of IAPG are active in lecturing at 10 universities (the most important partners are Charles University in Prague, Masaryk University in Brno, University of Veterinary and Pharmaceutical Sciences in Brno, Czech University of Life Sciences in Prague and University of South Bohemia in České Budějovice) around the country and some of them also abroad. The level of collaboration is documented by many common publications and defended thesis and lectures presented at universities. There are always ongoing several grant projects. Many gradual students are also involved in research programs as you can see below.



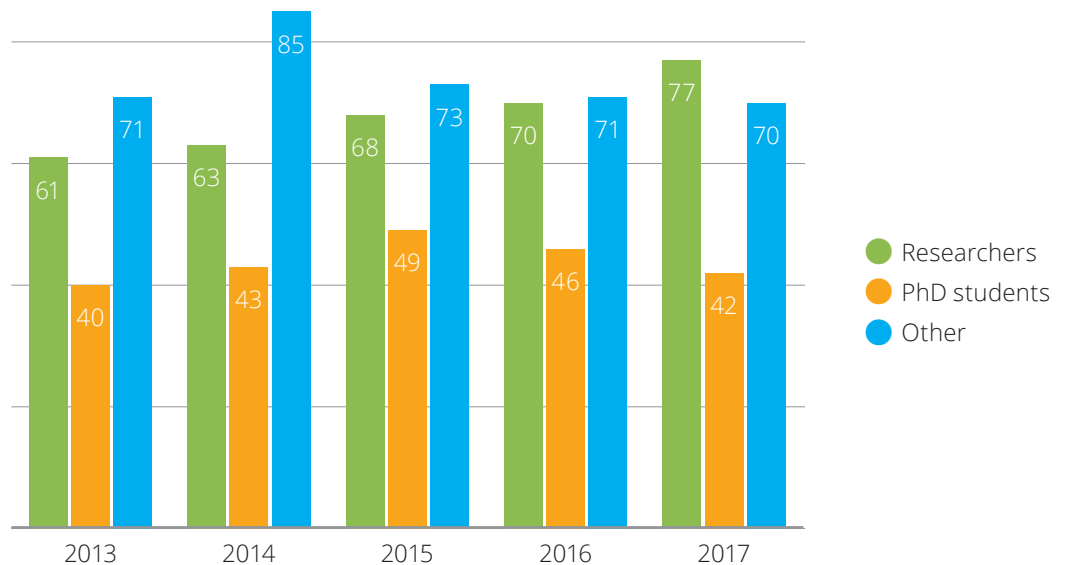
INSTITUTE EMPLOYEES, SIZE AND STRUCTURE



IAPG Staff and Budget

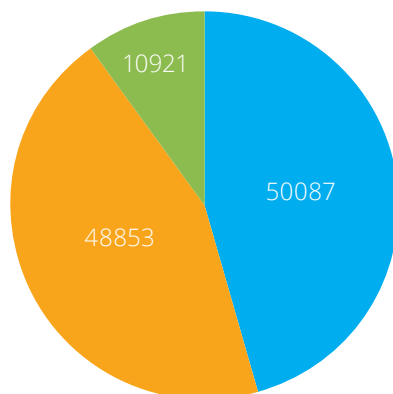
Number of employees covers both full time and part time positions. In a long time interval, the total counts of employees is slowly increasing but depends on actual funding structure. Increasing are primarily research positions. Institute budget in 2017 was covered by 58% from grant funding and contract research. The institutional funding decreased from 44.2% in 2013 to 41.7% in 2017.

INSTITUTE STAFF INVOLVED IN RESEARCH



TOTAL RESOURCES 2016

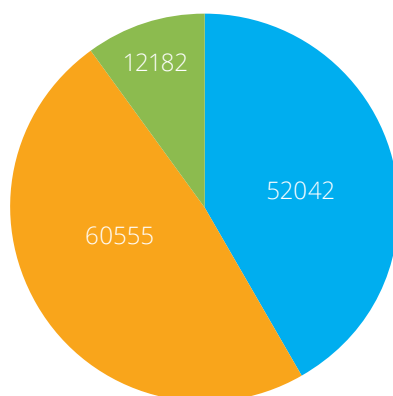
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- Contract research
- Subsidies from funds
- Institutional subsidies

TOTAL RESOURCES 2017

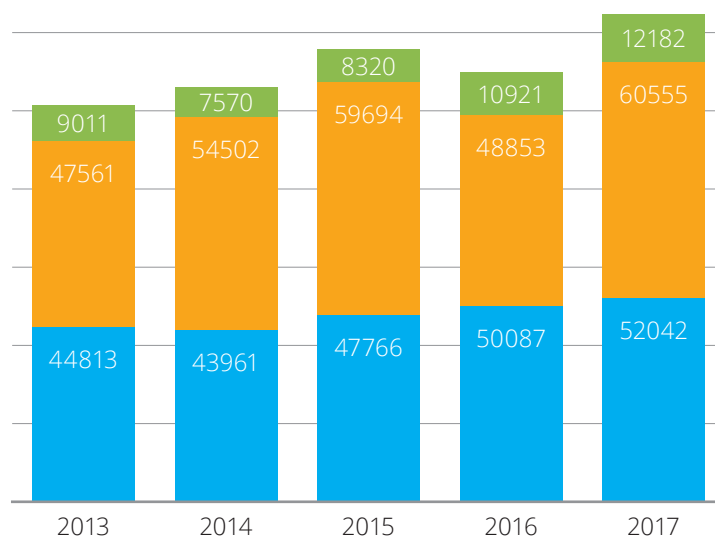
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- Contract research
- Subsidies from funds
- Institutional subsidies

TOTAL RESOURCES FOR THE MAIN ACTIVITY

(in thousands of CZK)



- Contract research
- Subsidies from funds
- Institutional subsidies

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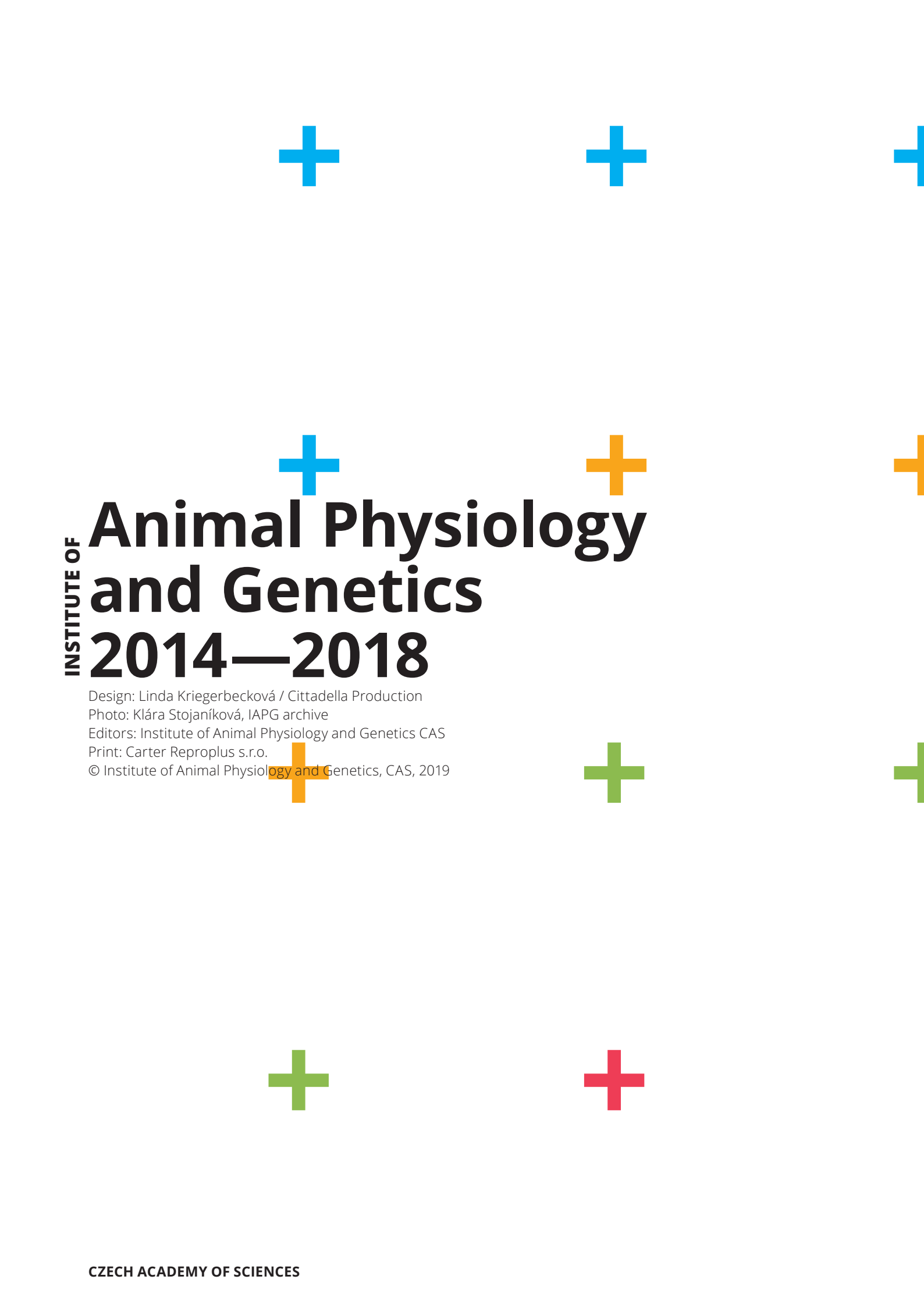
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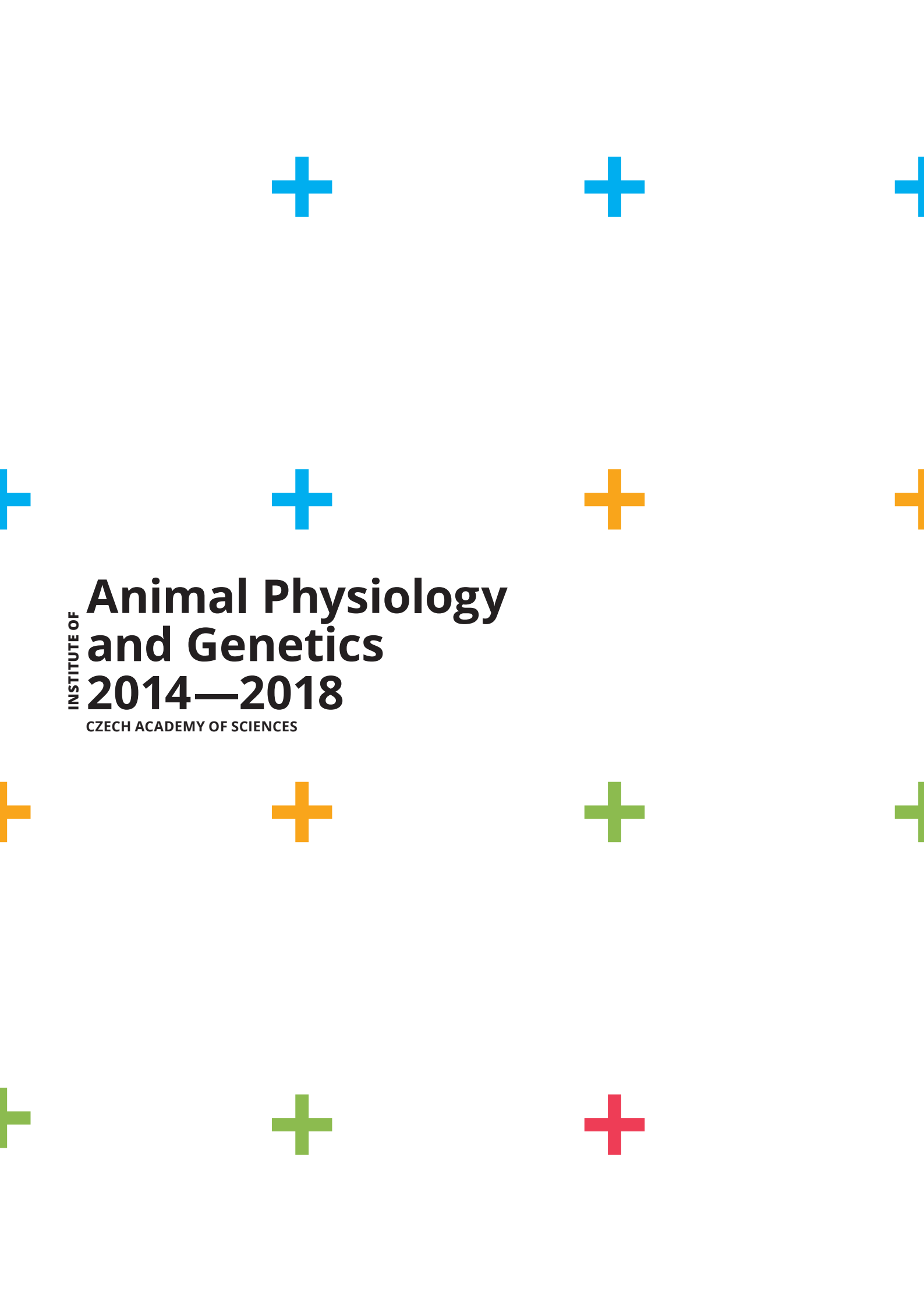
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