2024

70 YEARS ANNIVERSARY

MILESTONES IN IPHYS HISTORY 1954—2024

1954 **IPHYS founded** – three Departments: Neuromuscular Physiology (E. Gutmann), Developmental Physiology and Pathology (J. Křeček), and Excitability of Central Nervous System (Z. Servít)

1956 IPHYS journal Physiologia Bohemoslovaca (since 1991 Physiological Research) is published in English

1961 The Department of Physiology and Pathophysiology of Metabolism is added (O. Poupa)

1964—1965 IPHYS is moved to the new campus of biological institutes of the Czech Academy of Sciences in Prague - Krč

1980—1989 Four Sectors are established: Neurophysiology (T. Radil), Developmental Physiology (J. Jelínek), Biological and Experimental Models (P. Klír), and Cellular and Molecular Physiology (J. Houštěk)

1990 **IPHYS under democracy:**
The Scientific Council voted for the first time for the director of IPHYS
Twenty-one scientific departments are established
Beginning of the scientometric evaluation of research activities: IPHYS is one of the best institutes of the Czech Academy of Sciences

2001—2005 H. Illnerová (IPHYS) becomes the President of the Czech Academy of Sciences

2009 Opening of the new building (A2 wing) of IPHYS

2014 The first junior research group established

2016 Opening of OFF-campus laboratories in BIOCEV (European Scientific Centre of Excellence in Biotechnology and Biomedicine in Vestec)

2019 IPHYS is awarded the prestigious European HR Excellence in Research Award

2020 International Advisory Board of IPHYS is established

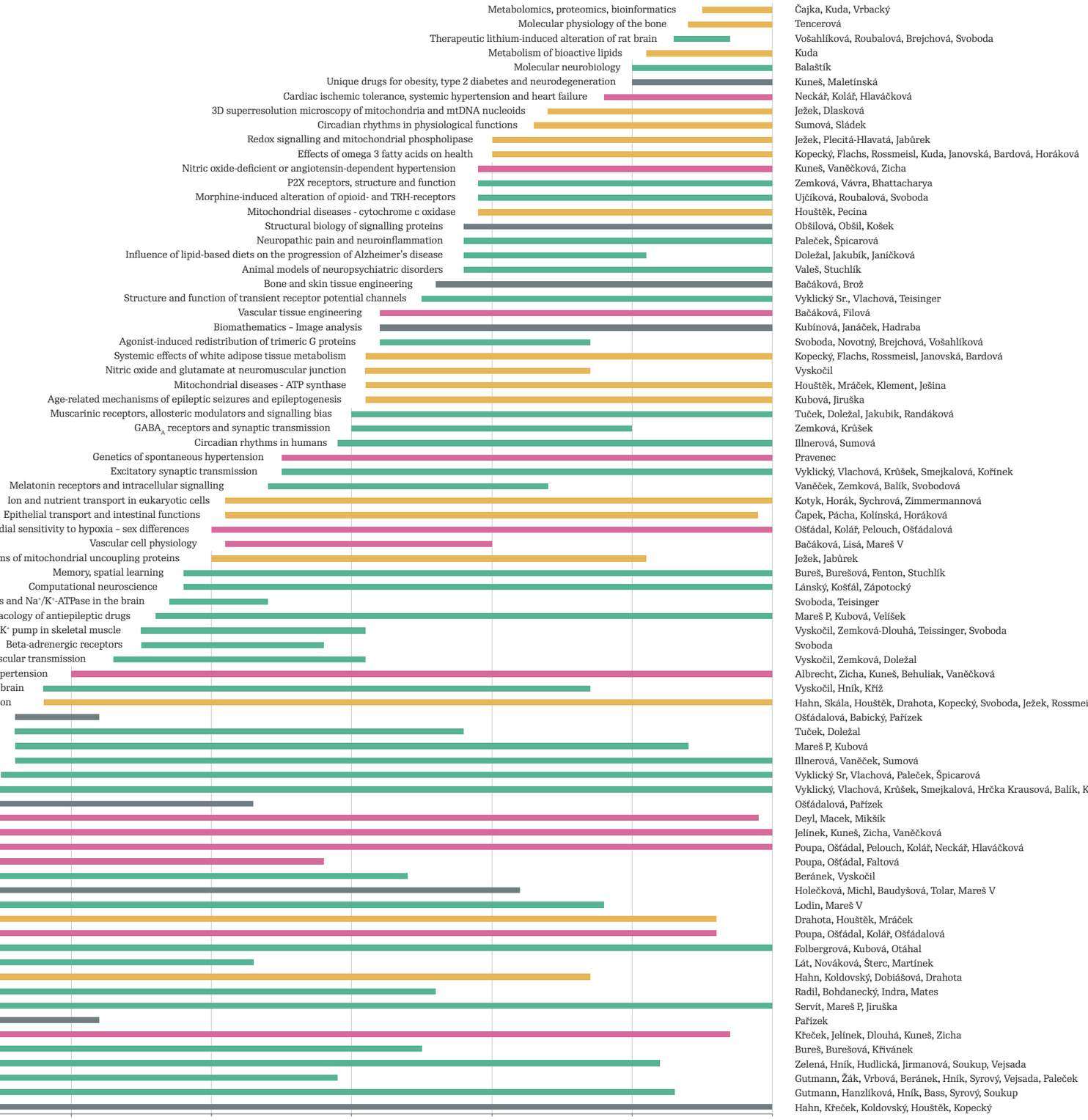
2021—2024 Reconstruction of Animal facility

2024 **Three research fields: Neuroscience, Cardiovascular Research, and Metabolic Research**
Twenty-one scientific laboratories and one junior research group
General aim: the characterization of basic biological mechanisms to improve the prevention, diagnosis and treatment of serious non-communicable diseases

70 YEARS OF SCIENCE AT IPHYS 1954–2024

FOR RELATED ARTICLES, SEE PAGE 89

- METABOLIC RESEARCH
- CARDIOVASCULAR RESEARCH
- NEUROSCIENCE
- INTERDISCIPLINARY RESEARCH



SCIENTISTS INVOLVED

Čajka, Kuda, Vrbacký
Tencerová
Vošahlíková, Roubalová, Brejchová, Svoboda
Kuda
Balaštík
Kuneš, Maletínská
Neckář, Kolář, Hlaváčková
Ježek, Dlasková
Sumová, Sládek
Ježek, Plecitá-Hlavatá, Jabůrek
Kopecký, Flachs, Rossmeisl, Kuda, Janovská, Bardová, Horáková
Kuneš, Vaněčková, Zicha
Zemková, Vávra, Bhattacharya
Ujčíková, Roubalová, Svoboda
Houštěk, Pecina
Obšilová, Obšil, Košek
Paleček, Špicarová
Doležal, Jakubík, Janíčková
Valeš, Stuchlík
Bačáková, Brož
Vyklický Sr., Vlachová, Teisinger
Bačáková, Filová
Kubínová, Janáček, Hadraba
Svoboda, Novotný, Brejchová, Vošahlíková
Kopecký, Flachs, Rossmeisl, Janovská, Bardová
Vyskočil
Houštěk, Mráček, Klement, Ješina
Kubová, Jiruška
Tuček, Doležal, Jakubik, Randáková
Zemková, Krůšek
Illnerová, Sumová
Pravenec
Vyklický, Vlachová, Krůšek, Smejkalová, Kořínek
Vaněček, Zemková, Balík, Svobodová
Kotyk, Horák, Sychrová, Zimmermannová
Čapek, Pácha, Kolínská, Horáková
Ošťádal, Kolář, Pelouch, Ošťádalová
Bačáková, Lisá, Mareš V
Ježek, Jabůrek
Bureš, Burešová, Fenton, Stuchlík
Lánský, Košťál, Zápotocký
Svoboda, Teisinger
Mareš P, Kubová, Velíšek
Vyskočil, Zemková-Dlouhá, Teissinger, Svoboda
Svoboda
Vyskočil, Zemková, Doležal
Albrecht, Zicha, Kuneš, Behuliak, Vaněčková
Vyskočil, Hník, Kříž
Hahn, Skála, Houštěk, Drahota, Kopecký, Svoboda, Ježek, Rossmeisl, Zouhar
Ošťádalová, Babický, Pařízek
Tuček, Doležal
Mareš P, Kubová
Illnerová, Vaněček, Sumová
Vyklický Sr, Vlachová, Paleček, Špicarová
Vyklický, Vlachová, Krůšek, Smejkalová, Hrčka Krausová, Balík, Kořínek
Ošťádalová, Pařízek
Deyl, Macek, Mikšík
Jelínek, Kuneš, Zicha, Vaněčková
Poupa, Ošťádal, Pelouch, Kolář, Neckář, Hlaváčková
Poupa, Ošťádal, Faltová
Beránek, Vyskočil
Holečková, Michl, Baudyšová, Tolar, Mareš V
Lodin, Mareš V
Drahota, Houštěk, Mráček
Poupa, Ošťádal, Kolář, Ošťádalová
Folbergrová, Kubová, Otáhal
Lát, Nováková, Šterc, Martínek
Hahn, Koldovský, Dobiášová, Drahota
Radil, Bohdanecký, Indra, Mates
Servít, Mareš P, Jiruška
Pařízek
Křeček, Jelínek, Dlouhá, Kuneš, Zicha
Bureš, Burešová, Křivánek
Zelená, Hník, Hudlická, Jirmanová, Soukup, Vejsada
Gutmann, Žák, Vrbová, Beránek, Hník, Syrový, Vejsada, Paleček
Gutmann, Hanzlíková, Hník, Bass, Syrový, Soukup
Hahn, Křeček, Koldovský, Houštěk, Kopecký


FYZIOLOGICKÝ ÚSTAV AV ČR, v.v.i.
MIKROBIOLOGICKÝ ÚSTAV AV ČR, v.v.i.

FOREWORD

WELCOME TO THE INSTITUTE OF PHYSIOLOGY OF THE CZECH ACADEMY OF SCIENCES

This year, we celebrate 70 years of the Institute of Physiology (IPHYS) of the Czech (former Czechoslovak) Academy of Sciences (CAS). True to its name, IPHYS has been systematically dedicated to research in the field of normal and pathological physiology, with a special focus on biomedical research. Three main, closely interconnected research directions have gradually crystallized, which IPHYS continues to pursue today: research in the fields of neuroscience, cardiovascular physiology, and metabolism.

Over the last seven decades, our society has grown considerably older and fatter, and obesity rates have tripled. Modern medicine is thus facing new challenges in the form of an increased onslaught of so-called lifestyle (also civilization) diseases. The cost of their treatment represents a major burden on healthcare systems worldwide. The main current goal of IPHYS is to characterize the causes of these non-communicable diseases associated with obesity and aging. We are characterizing the basic biological mechanisms in order to improve the prevention, diagnosis, and treatment of pathological conditions:

1. affecting the nervous system, such as Alzheimer's disease, epilepsy, and chronic pain;

2. linked to obesity, such as cardiovascular disease and diabetes; and

3. inherited diseases, especially those affecting mitochondrial energy metabolism.

Our research is also focused on developmental aspects, reflecting the notion that susceptibility to lifestyle diseases depends in part on various factors impacting pregnancy and birth.

IPHYS is well-equipped for biomedical research. The fundamental reconstruction of our animal facility was finished in the spring of 2024. IPHYS's instrumentation provides probably the best opportunities in the Czech Republic for the whole-body phenotyping of animal models of various diseases, including analyses of metabolism, body composition, blood pressure, cardiac functions, and animal behavior. Instruments for various imaging applications are available thanks to IPHYS's involvement in the CzechBioimaging infrastructure. High-throughput analytical methods are routinely performed in the service laboratories of Metabolomics (established in 2017) and Proteomics (established in 2020). Bioinformatics is being introduced to interpret all of these data, however the experience and knowledge of the researchers are the keys to understanding complex relationships.

We combine experiments on laboratory animals and cell models with clinical research. This is facilitated by IPHYS's participation in research consortia supported by the National Recovery Plan (2022–2025), i.e. in the National Institute for Metabolic and Cardiovascular Disease Research (CarDia; www.cardia.ikem.cz) and in the National Institute for Neurological Research (NPO-NEURO-D; www.ninr.cz). Thus, IPHYS collaborates with leading centers of clinical and academic research in our country, and also numerous partners in Europe and worldwide. Special partnerships with Czech universities provide IPHYS with the opportunity to serve as an important place for pre- and postgraduate education.

This brochure updates the information provided in the previous one, released in 2020. Of course, in contrast to the existing and continuously updated IPHYS website (www.fgu.cas.cz), the brochure can only mirror the current situation at the time of its release, i.e. the summer of 2024.

I am looking forward to continuing to serve as the Director of IPHYS to the end of my second term (2020 – 2025). I would like to take this opportunity to extend my appreciation to all of my colleagues, who are responsible for the friendly and enthusiastic atmosphere at IPHYS that helps to make it an excellent scientific institution. I believe that the future is bright for IPHYS.

Jan Kopecký
director of IPHYS

IPHYS

IPHYS IS THE LEADING RESEARCH INSTITUTION IN THE FIELD OF NORMAL AND PATHOLOGICAL PHYSIOLOGY.

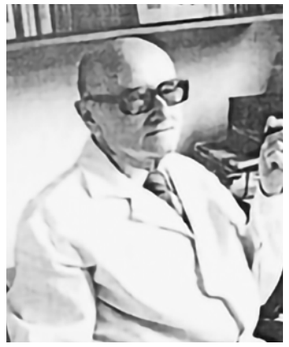
Its mission is to improve our fundamental knowledge on the physiological and pathological processes associated with the function of the nervous system, cardiovascular system, and specific areas of metabolism, and thus pave the way to novel prevention, diagnostic and therapeutic procedures for combating serious human diseases. All these activities emphasize the Institute's prominent role in biomedical research in the Czech Republic.

WHAT IS THERE TO KNOW ABOUT IPHYS?

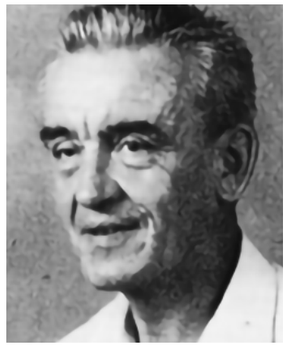
- IPHYS has a more than 70-year tradition (6–7)
- Research at IPHYS includes three main topics: neuroscience, cardiovascular research, and metabolic research (9–11)
- IPHYS is supervised by the director and the IPHYS Boards (12–14)
- IPHYS consists of 22 scientific laboratories and includes off-campus laboratories in BIOCEV within an excellent joint project of six institutes of the CAS and Charles University (15–60)
- Necessary services at IPHYS are provided by 10 service departments, including the Centre for Preclinical Testing (61–71)
- IPHYS publishes the peer-reviewed journal Physiological Research (69)
- A new facility for research animals was constructed at IPHYS (72–73)
- The European Commission awarded IPHYS the prestigious European HR Excellence in Research Award protecting also intellectual property of IPHYS (74)
- IPHYS has almost 410 employees with 60 principal investigators (75)
- Most of IPHYS research is conducted within the framework of national and international collaborations (76-78)
- IPHYS is a member of two European infrastructures Czech Bioimaging and EPTRI (79)
- More than 120 scientific articles are published per year by scientists of IPHYS (80–81)
- IPHYS employs world-renowned experts awarded major domestic and foreign prizes for their scientific work (82–83)
- Dozens of bachelor's, master's and PhD students are trained at IPHYS in collaboration with universities (84–85)
- Results obtained at IPHYS are actively disseminated to the scientific community as well as to the general public (86–87)
- More than 75 research topics have been studied at IPHYS since 1954 (89–107)

HISTORY OF IPHYS

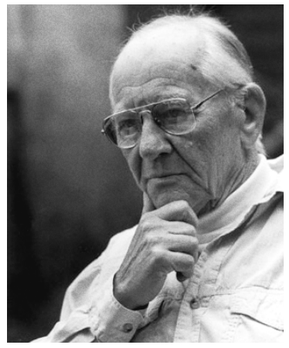
Zdeněk Servít



Arnošt Gutmann



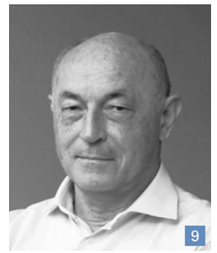
Jiří Křeček

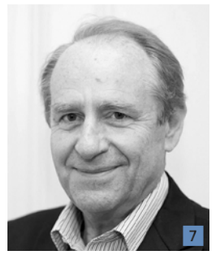


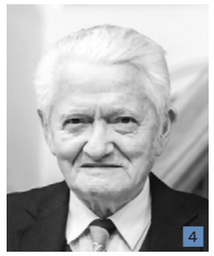
Otakar Poupa

The origin of the current IPHYS is traced back to 1950 when two outstanding personalities, **Prof. Zdeněk Servít** (1913–1986) and **Prof. Arnošt Gutmann** (1910–1977), met at the Department of Neurophysiology within the Central Biological Institutes. In 1952, the Czechoslovak Academy of Sciences (ČSAV) was founded. Servít´s laboratory (epileptology) and Gutmann´s laboratory (neuromuscular function) joined a group interested in critical periods of ontogenetic development headed by **Prof. Jiří Křeček** (1923–2014) to form a section of the new Biological Institute. On the basis of successful research and acceptance at home as well as abroad, IPHYS was officially founded on January 1, 1954 and consisted of these three laboratories. In 1956, a fourth group led by **Prof. Otakar Poupa** (1916–1999), who studied the adaptation of the organism to its environment, joined the Institute. The outstanding contribution of these scientists in the fields of neurophysiology, muscle regeneration, heart adaptation to hypoxia and late effects of early interventions was subsequently enriched by their students and follower scientists at IPHYS.

DIRECTORS OF THE INSTITUTE



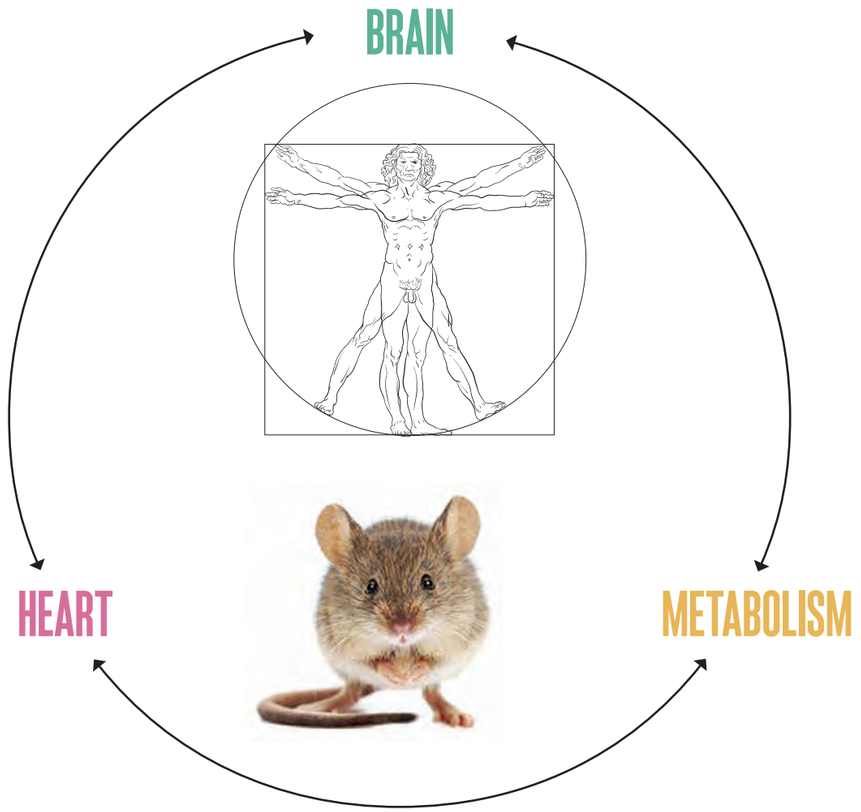




since 2015	9 MUDr. Jan KOPECKÝ, DrSc.
2010–2015	8 RNDr. Lucie KUBÍNOVÁ, CSc.
2003–2010	7 RNDr. Jaroslav KUNEŠ, DrSc.
1995–2003	6 Prof. MUDr. Pavel MAREŠ, DrSc.
1990–1995	5 Prof. MUDr. Bohuslav OŠŤÁDAL, DrSc.
1980–1989	4 RNDr. Zdeněk DRAHOTA, DrSc.
1970–1980	3 MUDr. Ladislav VYKLICKÝ, DrSc.
1970	2 Prof. MUDr. Jiří KŘEČEK, DrSc.
1954–1969	1 Prof. MUDr. Zdeněk SERVÍT, DrSc.

RESEARCH STRATEGY

THE OVERALL RESEARCH STRATEGY AT IPHYS COMBINES COMPLEMENTARY EFFORTS IN SEVERAL FIELDS. BOTH ANIMAL AND HUMAN STUDIES ARE PERFORMED.



MAIN RESEARCH FIELDS

NEUROSCIENCE

Neuroscience research covers studies aimed at understanding basic physiological and pathological processes related to human neurological and psychiatric diseases. Investigations at the system level study development and integrative functions of the central nervous system that include cognitive functions (memory, spatial orientation or learning), chronic and neuropathic pain, and epilepsy. At the cellular level, circadian rhythms (i.e. processes repeated rhythmically during a 24-hour period) and pathophysiological mechanisms of drug addictions and side effects are investigated. Studies at the molecular level are aimed at revealing the biochemical principles of neuron growth and guidance, signal transduction and transmission from one cell to another, structural and functional correlations of neurotransmitter receptor activation and their modulation by biological and pharmacological compounds. Aspects of neural signalling are studied *in vivo*, *in vitro* as well as theoretically using computer simulations and modelling.

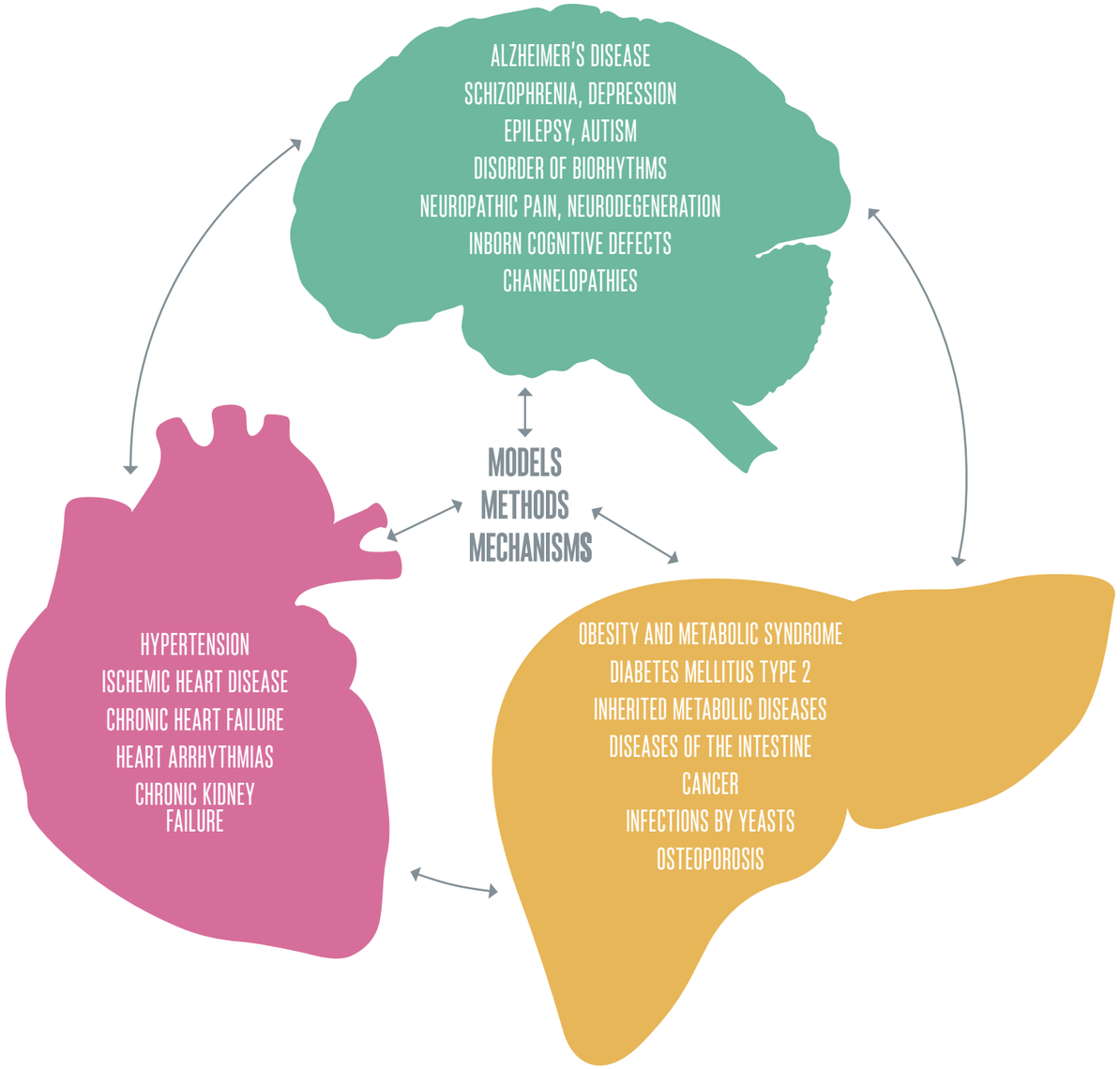
CARDIOVASCULAR RESEARCH

Research in the cardiovascular field is focused on the mechanisms of the development, therapy, and prevention of serious cardiovascular diseases, such as ischemic heart disease, hypertension, and chronic heart and kidney failure. Particular attention is paid to the development of cardiac adaptation to oxygen deprivation and to the mechanisms of cardiac protection against ischemic injury. Studies on the mechanisms of blood pressure regulation, the vascular contraction, and development of the conductive system represent a basis for new therapeutic approaches to hypertension and cardiac arrhythmias. The genetic approach deals with the modifications or defects of selected genes responsible for cardiovascular diseases. Work is also done on the development of new biomaterials that may be suitable for vascular and heart valve replacements, based on synthetic and biological scaffolds seeded with stem cells.

METABOLIC RESEARCH

Studies in this field cover specific aspects of metabolism from the cellular to whole-body level. The research is focused on characterisation of transport systems in cell membranes, specific signalling pathways affecting metabolism, the function of mitochondria and the impact of mitochondrial dysfunction on health, interactions between nutrition and the immune system that affect metabolism, circadian control of metabolism, genetic basis of obesity-related diseases as well as the ontogenic aspects and the role of ageing in metabolic health.

DISEASES IN FOCUS



IPHYS MANAGEMENT

Director
MUDr. Jan Kopecký, DrSc.

Deputy Director for Science
MUDr. Jiří Paleček, CSc.

Deputy Director for Administration
Ing. Petra Janečková

Chairman Board of IPHYS
RNDr. Ondřej Kuda, Ph.D.

BOARD OF INSTITUTE OF IPHYS

Chairman
RNDr. Ondřej Kuda, Ph.D.

Deputy Chairperson
Prof. PharmDr. Alena Sumová, DSc.

Internal Members
Mgr. Martin Balaštík, Ph.D.
Mgr. Jan Jakubík, Ph.D.
Prof. RNDr. František Kolář, CSc.
RNDr. Ivana Vaněčková, DSc.

External Members
Prof. RNDr. Jan Černý, Ph.D.
Charles University, Prague

Prof. Ing. Martin Fusek, CSc.
Institute of Organic Chemistry and Biochemistry CAS

Prof. MUDr. Pavel Martásek, DrSc.
BIOCEV

Secretary
Mgr. Adéla Bocková, Ph.D.

SUPERVISORY BOARD OF IPHYS

Chairman
RNDr. Zdeněk Havlas, DrSc.
Czech Academy of Sciences

Deputy Chairman
RNDr. Jaroslav Kuneš, DrSc.
IPHYS

Members
Mgr. Ing. Jindřich Hroch
attorney-at-law

Prof. MUDr. Zuzana Červinková, CSc.
Faculty of Medicine of Charles University, Hradec Králové

Prof. MUDr. Vojtěch Melenovský, CSc.
Institute for Clinical and Experimental Medicine, Prague

Secretary
Ing. Petra Janečková

INTERNATIONAL ADVISORY BOARD OF IPHYS

Chairman

Prof. Adam Szewczyk
Head of the Laboratory of Intracellular Ion Channels, Chair of the Scientific Council at Nencki Institute, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

Members

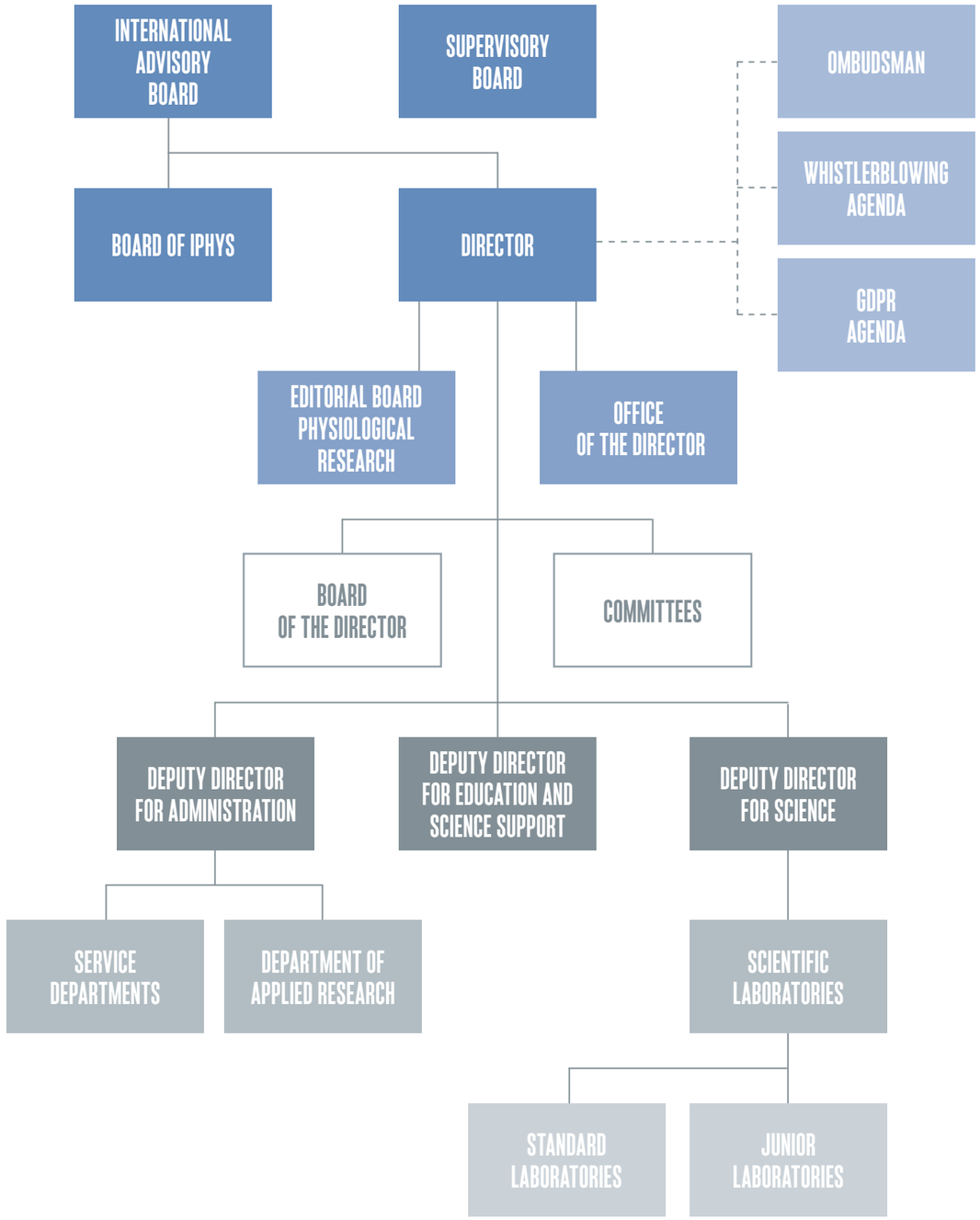
Prof. Bryndis Birnir, PhD.
Professor at the Department of Medical Cell Biology, University of Uppsala, Sweden

Prof. Dr. Matthias Blüher
Director of the Helmholtz Institute for Metabolic, Obesity and Vascular Research, Leipzig, Germany

Prof. Dr. med. Pontus Persson
Director of the Institute of Vegetative Physiology, Editor in Chief of Acta Physiologica, Berlin, Germany

Prof. Marianne Schultzberg, PhD.
Professor of clinical neuroscience, Karolinska Institutet, Sweden

ORGANIZATIONAL STRUCTURE



SCIENTIFIC LABORATORIES

- Laboratory of Adipose Tissue Biology (16)
- Laboratory of Bioenergetics (18)
- Laboratory of Biological Rhythms (20)
- Laboratory of Biomaterials and Tissue Engineering (22)
- Laboratory of Biomathematics (24)
- Laboratory of Cellular Neurophysiology (26)
- Laboratory of Computational Neuroscience (28)
- Laboratory of Developmental Cardiology (30)
- Laboratory of Developmental Epileptology (32)
- Laboratory of Experimental Hypertension (34)
- Laboratory of Genetics of Model Diseases (36)
- Laboratory of Membrane Transport (38)
- Laboratory of Metabolism of Bioactive Lipids (40)
- Laboratory of Mitochondrial Physiology (42)
- Laboratory of Molecular Neurobiology (44)
- Laboratory of Molecular Physiology of Bone (46)
- Laboratory of Neurochemistry (48)
- Laboratory of Neurophysiology of the Memory (50)
- Laboratory of Pain Research (52)
- Laboratory of Structural Biology of Signalling Proteins (54)
- Laboratory of Translational Metabolism (56)
- BIOCEV (58)
- Junior Research Group: Laboratory of Pancreatic Islet Research (60)

*KEEP SILENCE
IT IS NECESSARY FOR EXPERIMENTS

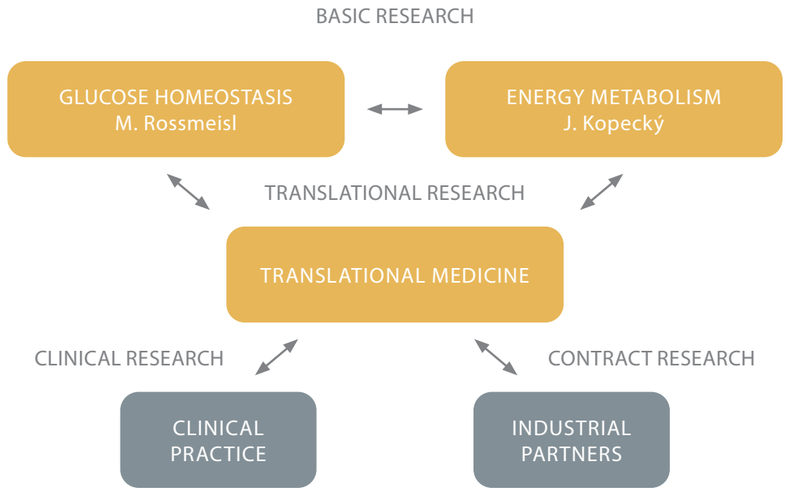
ADIPOSE TISSUE BIOLOGY

head **MUDr. Martin Rossmeisl, Ph.D.** 1 martin.rossmeisl@fgu.cas.cz
key researchers Kristina Bardová 2 Olga Horáková 3 Petra Janovská 4
Jan Kopecký 5 Petr Zouhar postdoc Gülnaz Köken 7
PhD students Eliška Haasová 8 Veronika Kleinová 9 Marko Mitrović 10
Sakina Poonawala 11 Isaiah Sabinari 12 Sara Stanić 13 students Anna Vávrová 14
technicians Jitka Ezrová 15 Karolína Seďová 16 Daniela Šálková 17 Karla Vagnerová 18

We study the physiological regulation of metabolism and its disturbances in obesity and related diseases (i.e. **METABOLIC SYNDROME**), focusing mainly on adipose tissue, the liver, skeletal muscle and intestine. In this context, we investigate the effects of drugs, experimental diets and natural substances such as n-3 polyunsaturated fatty acids of marine origin (**OMEGA-3S**), as well as the metabolic benefits of exercise. Our results emphasize the key role of **ADIPOSE TISSUE METABOLISM** in the development as well as treatment of obesity-related diseases. Our advanced methodological repertoire includes gene expression screening by RNA sequencing, gene transfer by viral vectors, metabolomics, proteomics, histological analysis, as well as the *in vivo* phenotyping of energy metabolism, body composition and insulin sensitivity in mice. By combining experiments in mice and cell models with clinical studies, we aim to apply new findings in clinical medicine.

CURRENT PROJECTS

- The role of adipose tissue metabolism in the development of obesity and cachexia and in the maintenance of metabolic health; the role of adipose tissue-derived lipokines in the metabolic effects of exercise
- Mechanisms involved in NAFLD progression and the role of omega-3s in the prevention or treatment of NAFLD
- Characterization of the effects of novel insulin analogs
- Mechanisms underlying tissue transcriptome changes during perinatal development in humans with a focus on preterm neonates
- The role of non-shivering thermogenesis in skeletal muscle in thermal and energy homeostasis



Basic research in the Laboratory is conducted by two Research units with complementary focus, which closely collaborate and are engaged in translational research carried out jointly with clinical centres as well as industrial partners from the Czech Republic and Norway.

SELECTED OUTPUTS

- The differential induction of lipid cycling in white fat and fatty acid release from the tissue (Flachs et al. (2017) Int J Obes 41:372-380) correlate with non-shivering thermogenesis in skeletal muscle (Janovska et al. (2023) Mol Metabolism 69:101683) and a genetically determined propensity to obesity in mice; the muscle phenotype could be imprinted early after birth (Buresova et al. (2020) Int J Obes 44:235-244).
- Omega-3s differentially modulate endocannabinoids in the adipose tissue of obese mice and diabetic patients (Rossmeisl et al. (2018) BBA - Mol Cell Biol Lipids 1863:712-725).
- Metformin inhibits intestinal glucose transport to acutely lower blood glucose (Horakova et al. (2019) Sci Rep 9:6156).
- Dysregulation of adipose tissue metabolism in cardiac patients with cachexia (Janovska et al. (2020) J Cachexia Sarcopenia Muscle 11:1614-1627).
- Exercise training induces PAHSA lipokines in adipose tissue of humans (Brezinova et al. (2020) BBA - Mol Cell Biol Lipids 1865:158576).

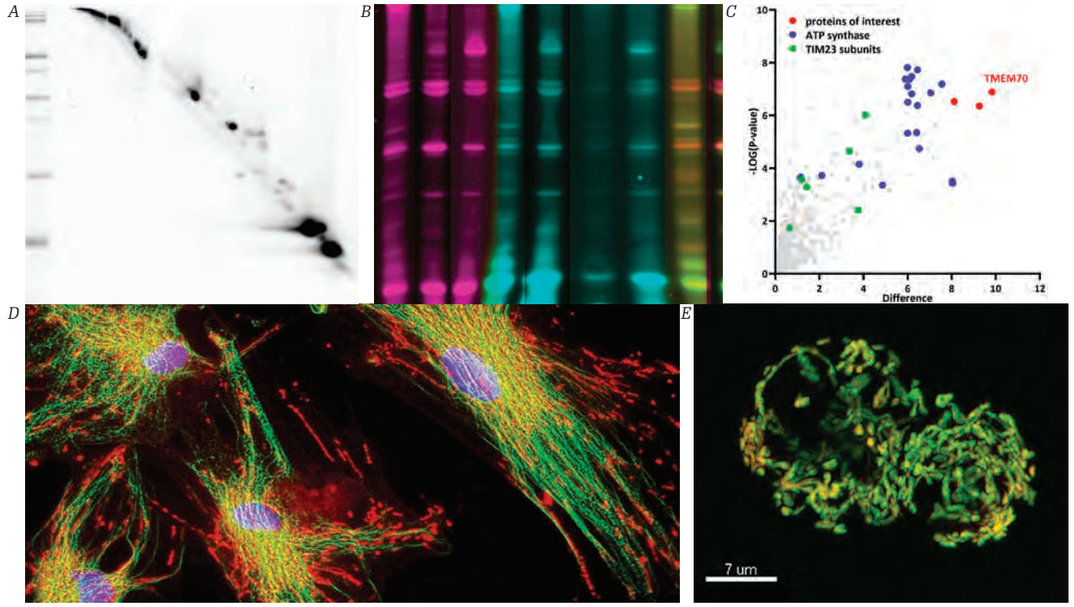
BIOENERGETICS

head **RNDr. Tomáš Mráček, Ph.D.** 1 tomas.mracek@fgu.cas.cz
key researchers Lukáš Alán, Zdeněk Drahota, Josef Houštěk 2 Vilma Kaplanová, Petr Pecina 3 Alena Pecinová 4 Kateřina Tauchmannová 5 Marek Vrbacký 6
PhD students Zuzana Korandová 7 Habiba Hayat, Abhishek Chattopadhyay 8 Michal Knězů 9 Aleksandra Markovic 10 Guillermo Puertas 11 Maria Jose Saucedo 12
students Barbora Kudrnovská 13 Soňa Koníčková 14 Pavel Sychra 15
technicians Vladimíra Brožková 16 Ivana Muricová

We study the physiology of **MITOCHONDRIA**, cell organelles responsible for most of the energy production at the molecular level. We have a long track record in mitochondrial diseases due to deficiencies in F1Fo ATP synthase. Our laboratory described the first patient with **ATP SYNTHASE** deficiency of nuclear origin back in 1999 and later discovered the disease-causing gene to be **TMEM70**. We use animal as well as cell-derived models to study biochemical changes associated with various mitochondrial disorders. Our research is focused mainly on (1) the assembly of **MITOCHONDRIAL RESPIRATORY CHAIN COMPLEXES** and supercomplexes and protein factors involved in this process; (2) human diseases caused by mutations in genes involved in mitochondrial energy provision – **MITOPATHIES**; (3) identifying new mitochondrial genes that play a causal role in **METABOLIC SYNDROME AND HEART FAILURE**; (4) interactions between mitochondrial and nuclear genomes; and (5) the role of **mtDNA** haplotypes in the development of complex metabolic phenotypes.

CURRENT PROJECTS

- Mitochondrial myopathies – the identification and validation of disease-causing genes
- Mitochondrial ATP synthase – the characterization of enzyme biogenesis, identification of new assembly factors
- Cytochrome c oxidase – tissue-specific isoforms of supernumerary subunits, their role in enzyme biogenesis, and the modulation of biochemical function
- Mitochondrial proteomics – evaluating changes in disease models
- New diagnostic approaches to mitochondrial diseases – the search for novel metabolomics markers as well as the development of protocols using lymphocytes as a frontline diagnostic tool for suspected patients



(A, B) *Analysis of subunit composition of ATP synthase.* ***(C)*** *Affinity enrichment of ATP5G interactors.* ***(D)*** *Mitochondrial reticulum (red) in fibroblasts from patient with mitochondrial disorder.* ***(E)*** *Co-localization of c15orf61 signal with mitochondria in HEK293 cells.*

SELECTED OUTPUTS

- Markovic et al.: Genetic Complementation of ATP synthase deficiency due to dysfunction of TMEM70 assembly factor in rat (2022) Biomedicines 10.(2):276.
- Cunatova et al.: Loss of COX4I1 leads to combined respiratory chain deficiency and impaired mitochondrial protein synthesis (2021) Cells 10.(2):369.
- Kovalciková J. et al.: TMEM70 facilitates biogenesis of mammalian ATP synthase by promoting subunit c incorporation into the rotor structure of the enzyme (2019) FASEB J 33(12):14103–14117.
- Melenovsky et al.: Myocardial iron content and mitochondrial function in human heart failure: a direct tissue analysis (2017) Eur J Heart Fail 19(4):522–530.
- Hartmannova et al.: Acadian variant of Fanconi syndrome is caused by mitochondrial respiratory chain complex I deficiency due to a non-coding mutation in complex I assembly factor NDUFAF6 (2016) Hum Mol Genet 25(18):4062–4079.

BIOLOGICAL RHYTHMS

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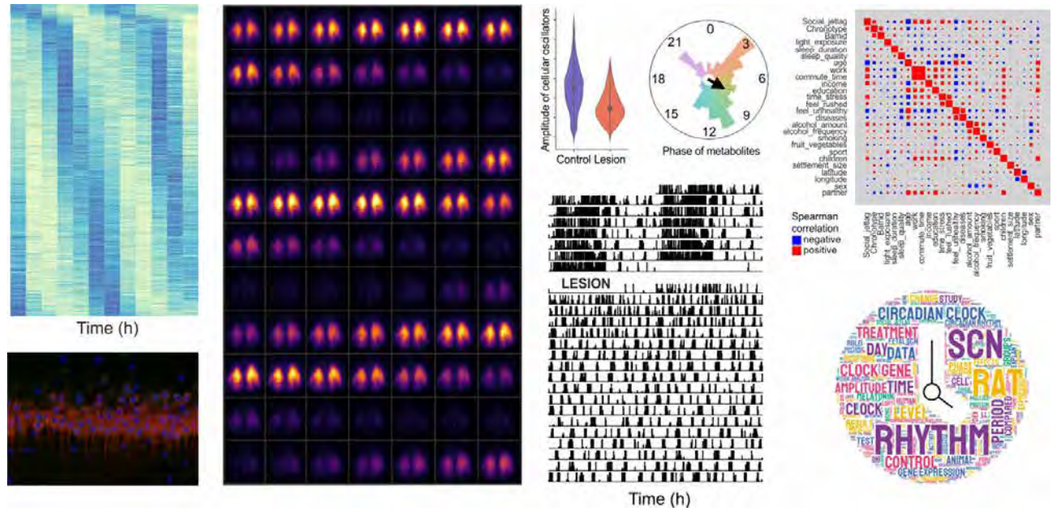
Our focus of interest is the endogenous time-keeping system, the **CIRCADIAN CLOCKS**, of mammals, including humans. The system anticipates regular changes in the environment and temporally regulates physiological processes, so that they take place at the proper time of day in synchrony with external time and relative to each other, resulting in tissue-specific **BIOLOGICAL RHYTHMS**. A failure of this temporal regulation has a negative impact on **HUMAN HEALTH**. Using *in vivo* and *in vitro* models and diverse approaches including animal behavior analysis, time-resolved transcriptomics or real-time monitoring of gene expression in cultured organotypic tissue explants, we study the **MOLECULAR MECHANISMS** of the circadian clocks, their development and means of regulation. We also investigate the consequences of circadian disruption on human health and collaborate on the development of novel chronopharmacological compounds.

CURRENT PROJECTS

- Ontogenesis of the circadian clock - investigating mechanisms of how the biological rhythms develop, with focus on the central clock in the suprachiasmatic nucleus of the hypothalamus (SCN)
- Entrainment of the circadian clock - exploring the mechanisms of how the clocks in the SCN, in the choroid plexus, and other peripheral tissues are synchronized with signals from the external environment and within our body
- Human circadian system - studying the association between the circadian system and health in the general population and in cohorts of patients suffering from disorders associated with disrupted sleep patterns



Multilevel circadian organization from the gene levels to studies of human populations. From left: rhythmically expressed genes in mouse choroid plexus; neurons in hippocampal region CA1 labeled with phosphorylated GSK3b; time-series of PER2 protein levels in suprachiasmatic nuclei from newborn mice visualizing oscillation over 3 days ex vivo; amplitude of PER2 rhythm in individual cells from mouse choroid plexus ex vivo; polar phase plot of rhythmic metabolites in rat plasma; actogram of locomotor activity of mouse before and after SCN lesion; correlation between components of social jetlag; word cloud of keywords from our recent publications.

SELECTED OUTPUTS

- Sládek M., Klusáček J., Hamplová D., Sumová A.: Population-representative study reveals cardiovascular and metabolic disease biomarkers associated with misaligned sleep schedules (2023) Sleep 46(6):zsad037 – The first study showing an association between social jetlag, chronotype and cardio-metabolic health in a representative Czech population.
- Liška K., Dočkal T., Houdek P., Sládek M., Lužná V., Semenovykh K., Drapšin M., Sumová A.: Lithium affects the circadian clock in the choroid plexus – A new role for an old mechanism (2023) Biomedicine & Pharmacotherapy 159:114292 – We showed that lithium affects the circadian clock in the choroid plexus independently of GSK3.
- Greiner P., Houdek P., Sládek M., Sumová A.: Early rhythmicity in the fetal suprachiasmatic nuclei in response to maternal signals detected by omics approach (2022) PLOS Biology 20(5):e3001637 – Using a unique approach, our results indicate the importance of a well-functioning maternal biological clock in providing a rhythmic environment during fetal brain development.
- Honzlová P., Novosadová Z., Houdek P., Sládek M., Sumová A.: Misaligned feeding schedule elicits divergent circadian reorganizations in endo- and exocrine pancreas clocks (2022) Cell Mol Life Sci 79(6):318 – The first evidence in rats and mice that whereas the clock in the endocrine pancreas shifts according to mealtime, the clock in the exocrine pancreas can be severely impaired by incorrect meal timing.
- Nováková M., Praško J., Látalová K., Sládek M., Sumová A.: The circadian system of patients with bipolar disorder differs in episodes of mania and depression (2015) Bipolar Disorders 17:303 - The first evidence for changes in the functional state of the circadian system during episodes of mania and depression.

BIOMATERIALS AND TISSUE ENGINEERING

head **Doc. MUDr. Lucie Bačáková, CSc.** 1 lucie.bacakova@fgu.cas.cz
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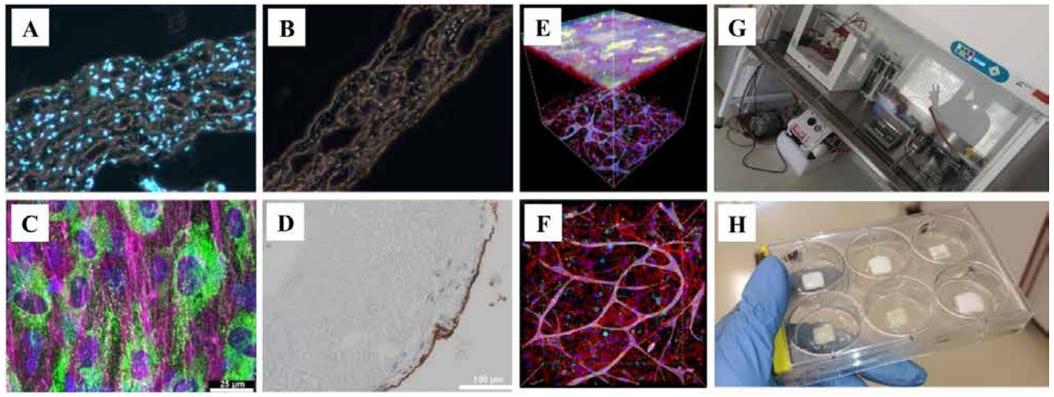
The Laboratory is subdivided into three research groups: **VASCULAR TISSUE ENGINEERING**, **SKIN TISSUE ENGINEERING** and **CONNECTIVE TISSUE ENGINEERING** (e.g. bone, cartilage). Within each group, the main tasks are (1) to improve currently-used tissue replacements by introducing cell and other biological components, (2) to construct completely new replacements on the basis of biomaterials and cells, and (3) to create **3D TISSUE MODELS** *in vitro* in order to replace laboratory animals in modern science according to the 3R principle. Our detached part of the laboratory at BIOCEV in Vestec near Prague, deals with the creation of tissue models based on **SPHEROIDS AND ORGANOIDS**, such as the *in vitro* model of glioblastoma. We use differentiated cells or **STEM CELLS** (derived from adipose tissue, bone marrow and Wharton jelly, or induced pluripotent stem cells) as the cell component of our constructs. The phenotypic maturation of cells is accelerated by mechanical stimulation in **DYNAMIC BIOREACTORS**. We are also developing the **3D BIOPRINTING** of various matrices together with cells.

CURRENT PROJECTS

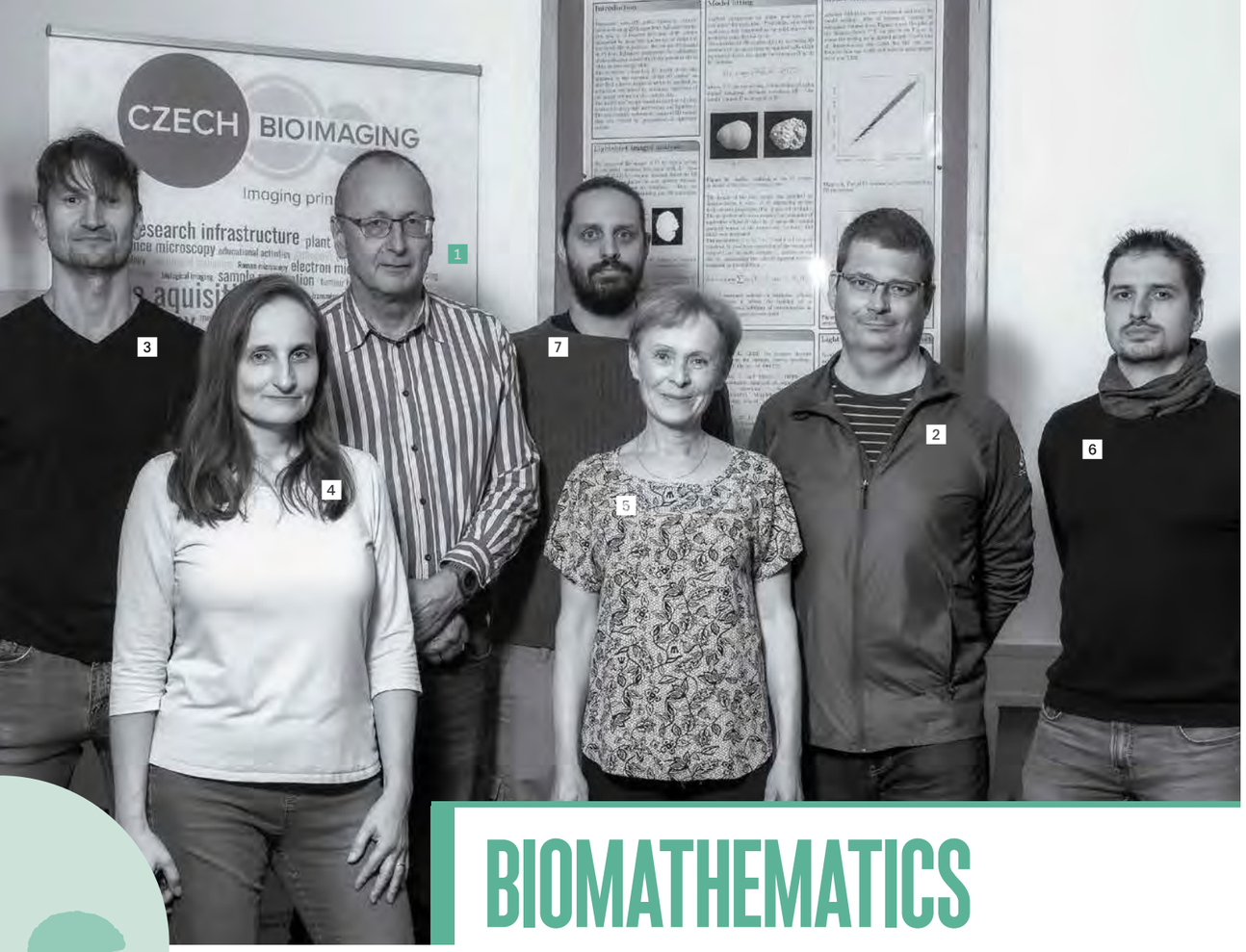
- "Praemium Academiae" – a large project focused on vascular, skin and bone tissue engineering including creating tissue models
- "CarDia" – a large project focused on vascular tissue engineering based on mainly on biological decellularized matrices
- "Center for Regenerative Medicine" – a large OP JAK project focused on vascular and skin tissue engineering and wound healing
- A novel tissue-engineered *in vitro* model for studying the pathogenesis and treatment of hypertrophic scars
- New functionalized plasmon-based sensors as tools for cell monitoring and advanced tissue engineering



Examples of vascular tissue engineering (A-D), skin tissue engineering (E, F) and connective tissue engineering (G, H). Porcine pericardium before (A) and after (B) decellularization, and after recellularization with adipose tissue-derived stem cells and endothelial cells (top view, C) and with endothelial cells stained in brown (cross-section, D). Vascularized Dermal-epidermal skin construct (E) with detail of capillary-like structures (F). 3D bioprinter in laminar flow box (G) and samples of 3D-bioprinted collagen matrix with fibroblasts.

SELECTED OUTPUTS

- We created a decellularized and electron beam-irradiated porcine pericardium matrix as a scaffold for human adipose-derived cells, differentiating vascular smooth muscle cells from adipocytes (Filova E. et al. Recellularized pericardium for cardiovascular replacements, utility model No. 36181, 2022)
- We created a dermal-epidermal skin construct as a potential skin replacement or skin model *in vitro* (Bacakova M. et al. (2019) Int J Nanomedicine 14:5033), further improved by introducing capillary-like structures based on endothelial cells and adipose tissue-derived stem cells (Tomšů J, PhD thesis "Interactions of Skin and Stem Cells with Polymer Nanofibers for Construction of Skin Substitutes")
- We participated in developing various novel bioactive coatings for metallic bone implants that modulate the adhesion, growth and osteogenic differentiation of human bone-derived cells, including stem cells (Brož et al. (2022) Mater Des 224:111373; Gabor et al. (2022) Mater Des 219:110811; Nemcakova et al. (2022) Sci Rep 12:5264; Vandrovcova et al. (2021) Coatings 11:210).



BIOMATHEMATICS

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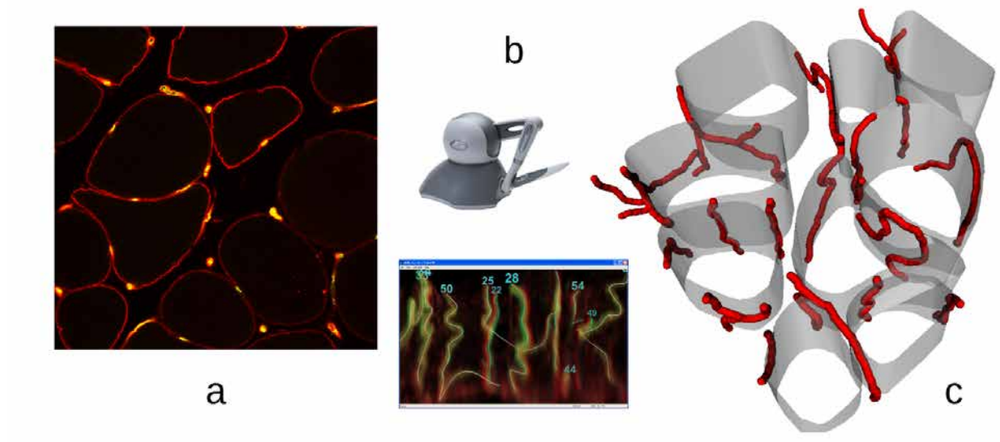
The Laboratory conducts research into 3D micro-anatomical aspects of physiological phenomena at the mesoscopic, microscopic, and ultrastructural level. We are engaged in a range of collaborative projects across the campus and beyond.

We measure quantitative geometric characteristics of various biological structures based on microscopic methods (**3D SHG, CLSM, CARS**) using original **STEREOLOGICAL METHODS**, image processing and virtual reality.

We are currently expanding our focus to include **LABEL-FREE IMAGING** and imaging methods that capture physiological events at a microscopic scale (**FLIM-FRET**, **PLIM**), and are moving towards the microscopic imaging of events *in vivo*, on 3D constructs and organoids under as close to physiological conditions as possible.

CURRENT PROJECTS

- Structural changes in the capillary network of muscles and in connective tissue due to diabetes
- The morphology of Langerhans islets isolated for therapeutic transplantations
- The correlative biomechanics of biomedical materials and tissue



Measurement of capillaries in skeletal muscle. Images from confocal microscope (a). Data are edited using desktop virtual reality with a haptic device (b). Model (c) is used for the calculation of length, directionality and tortuosity.

SELECTED OUTPUTS

- We visualized the structure and mechanical properties of tissue obtained from relapsed clubfoot during surgery. Label-free microscopy, AFM and image analysis were done at IPHYS. Vondráček et al. (2023) Microscopy and Microanalysis 29(1): Cover image of the Journal issue.
- Obese insulin-resistant mice increased capillarization selectively around small predominantly intermediate muscle fibres. We developed analytical methods and software and we also participated in the conception and design of the study. Umek et al. (2019) Histochem Cell Biol 152(5):323–331.
- Olejníčková V., Šaňková B., Sedmera D., Janáček J.: Trabecular architecture determines impulse propagation through the early embryonic mouse heart (2019) Front Physiol 9(8):1876.
- Janáček J., Jirák D.: Variance of the isotropic uniform systematic sampling (2019) Image Anal Stereol 38(3):261–267.

CELLULAR NEUROPHYSIOLOGY

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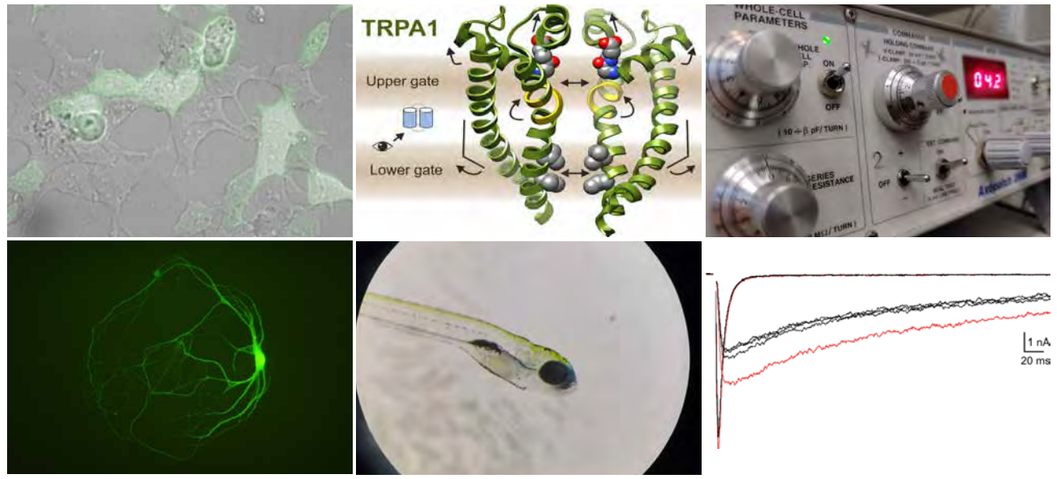
technicians Miloslava Kuldová 18

We study the functional and pharmacological properties of ion channels. We use advanced electrophysiology methods, primarily the **PATCH-CLAMP TECHNIQUE**, combined with analytical techniques, **MOLECULAR BIOLOGY**, **BIOCHEMISTRY**, **IMMUNOHISTOCHEMISTRY**, **MICROSCOPY AND MICROFLUOROMETRIC METHODS**. We focus on ionotropic glutamate receptors, specifically the **NMDA receptor** subtype, which plays an essential role in normal physiology, but under certain pathological conditions can participate in the development of serious **PSYCHIATRIC AND NEUROLOGICAL DISORDERS**. Through the detailed study of NMDA receptor structure, pharmacology, and trafficking, we aim to identify potential treatments for diseases associated with the dysfunction of the glutamate system. We also investigate the molecular and biophysical properties and the physiological significance of a specific subclass of **TRP ION CHANNELS** that are involved in the detection of noxious thermal, mechanical, and chemical stimuli.

CURRENT PROJECTS

- A study of structural, functional, and pharmacological consequences of mutations in genes encoding NMDA receptors associated with neuropsychiatric disorders
- A study of the molecular mechanisms of the positive and negative allosteric modulatory action of steroids at NMDA receptors and the influence of these compounds on synaptic transmission
- Investigation of the molecular basis of thermosensitive TRP channel regulation and the role of these channels in the mechanisms of acute and chronic pain



The study of structure, function, and pathophysiology of ionotropic glutamate receptors and TRP ion channels using molecular biology, patch-clamp electrophysiology, and behavioral assessment of mouse and zebrafish animal models.

SELECTED OUTPUTS

- In the field of NMDA receptors, we have studied (1) the conformational rearrangement of the NMDA receptor amino-terminal domain during receptor activation, (2) the palmitoylation of NMDA receptors, which controls receptor function and steroid sensitivity, (3) the potentiation of presynaptic glutamate release by pregnanolone and pregnanolone sulfate, (4) the modulation of NMDA receptors by novel pregnane-based steroids, which may compensate for the loss-of-function of mutated NMDA receptors found in patients with neuropsychiatric disorders, and (5) the multiple roles of plasma membrane cholesterol in glutamatergic synaptic transmission. (Vyklicky et al. (2021) Nat Comun 12:2697; Hrcka Krausova et al. (2020) J Neurosci 40(31):5922–5936; Hirschfeldova et al. (2021) J Pers Med 11:1250; Korinek et al. (2020) Sci Rep 10:12651; Hubalkova et al. (2021) J Neurosci 41:2119–2134; Holubova et al. (2021) Biomolecules 11:1026; Smejkalova et al. (2021) Br J Pharmacol 178:3888–3904; Štefková-Mazochová et al. (2022) Br J Pharmacol 179:65–83; Kysilov et al. (2022) Br J Pharmacol 179:3970–3990; Abramova et al. (2023) ACS Chem Neurosci 14:1870–1883).
- We have clarified the structural basis underlying TRPA1-channelopathy-associated pain syndrome and discovered that evolutionarily highly conserved N-terminal structural motifs critically, and each in a different way, contribute to the conformational stability of this channel. We have functionally and structurally characterized two regulatory sites through which TRPA1 interacts with annular and regulatory lipids. Moreover, we have identified Thr264 in the TRPV3 channel to be a key ERK phosphorylation site that mediates EGFR-induced sensitization signaling pathways involved in regulating skin homeostasis (Zimova et al. (2020) Front Phys 11:189; Nadezdhin et al. (2021) Nat Struct Mol Biol 28(7):564–572; Sinica et al. (2021) Physiol Res 70:363–381; Zimova et al. (2022) Biomed Pharmacother 152:113262; Ptakova et al. (2022) J Cell Physiol 237:3614–3626; Moparthi et al. (2022) Nat Commun 13:6113; Zhang et al. (2022) Nat Commun 13:7483).

COMPUTATIONAL NEUROSCIENCE

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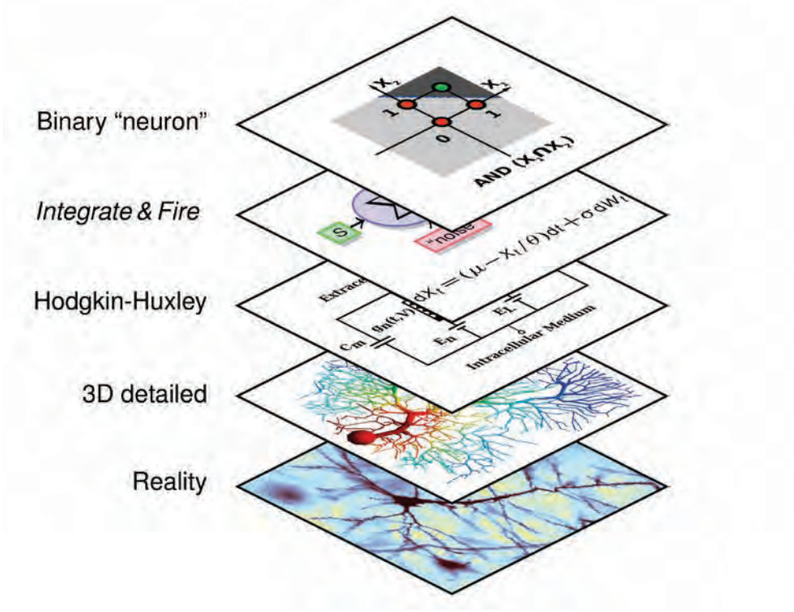
The Laboratory of Computational Neuroscience investigates the fundamental **MECHANISMS OF INFORMATION REPRESENTATION AND PROCESSING IN THE BRAIN**. **STOCHASTIC PROCESSES**, information theory, and statistical estimation theory methods are employed to analyse the **NEURONAL CODE**. Of particular interest is the **EFFICIENT CODING** hypothesis for **SENSORY NEURONS** and the role of **NOISE** and **ENERGETIC CONSTRAINTS** in the decoding process. The group proposes novel analytical and numerical modelling techniques to explore the properties and the function of **NEURAL ACTIVITY, CONTROL, AND DEVELOPMENT**. **BIOPHYSICS**, nonlinear dynamics, **CYBERNETICS**, and mathematical statistics methods provide the tools for both simulated and experimental data analysis. The group is also active in the organization of international conferences and workshops (biennial *Neural Coding* meetings, *OCNS* workshops).

CURRENT PROJECTS

- The analysis of stochastic neuronal models and estimation of key biophysical parameters under various stimulus encoding schemes
- The impact of different forms of noise together with metabolic energy consumption and decoding complexity on neuronal coding efficiency
- The biophysical modelling of neural connectivity and its dependence on the guided growth of axons during development
- Models and analysis of neural oscillations, both of physiological and pathophysiological origin



Models can range from detailed biophysical models, describing processes that take place in different parts of the neuron, through models neglecting the space structure of the neuron or the time course of action potentials, to binary neurons acting as logical units.

SELECTED OUTPUTS

- Barta, Kostal: The effect of inhibition on rate code efficiency indicators (2019) PLoS Comput Biol 15:e1007545.
- Levakova et al.: Moth olfactory receptor neurons adjust their encoding efficiency to temporal statistics of pheromone fluctuations (2018) PLoS Comput Biol 14:e1006586.
- Rajdl et al.: Entropy factor for randomness quantification in neuronal data (2017) Neural Networks 95:57–65.
- Smit et al.: Axon tension regulates fasciculation/defasciculation through the control of axon shaft zippering (2017) eLife 6:e19907.
- Kostal et al.: Performance breakdown in optimal stimulus decoding (2015) J Neural Eng 12:036012.
- Kostal et al.: Measures of statistical dispersion based on Shannon and Fisher information concepts (2013) Inform Sci 235:214–223.

DEVELOPMENTAL CARDIOLOGY

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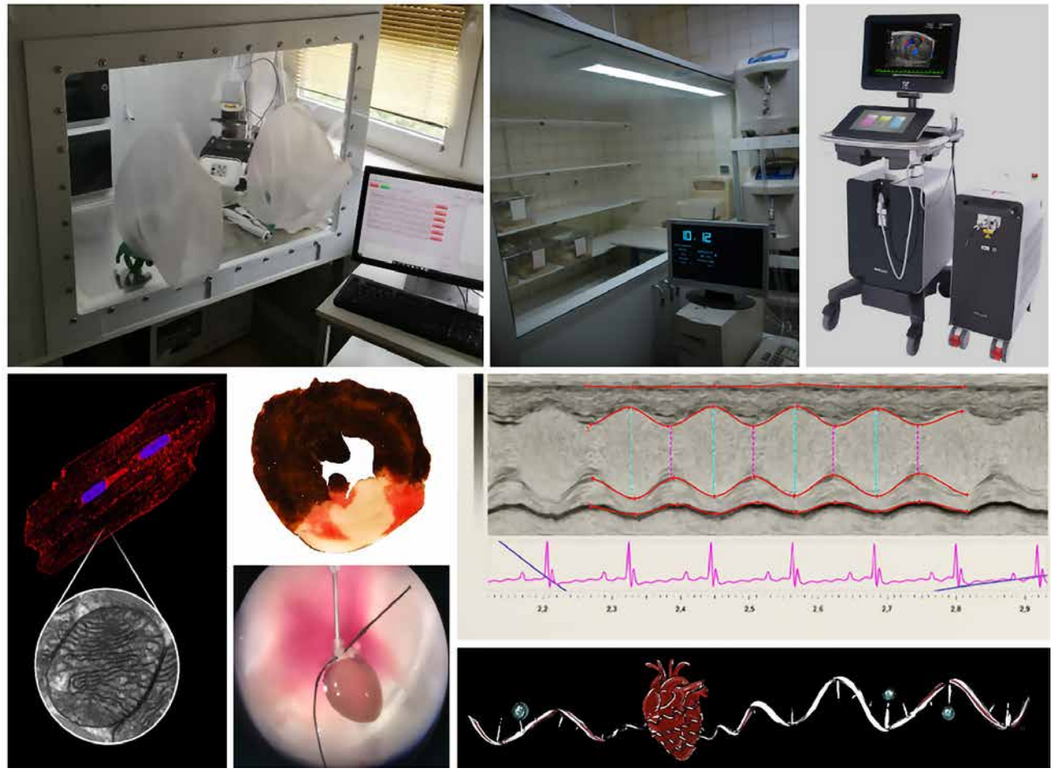
technicians Anna Jelínková Jokelová 15 Miloslava Marková, František Papoušek 16

ISCHEMIC HEART DISEASE is a leading cause of mortality globally. Our research delves into the tolerance of the heart to injuries stemming from acute **OXYGEN DEPRIVATION**, encompassing examinations from the molecular level to the entire organism using animal models. Our primary focus lies in investigating three fundamental aspects: i) understanding the mechanisms that support robust cardiac tolerance during **EARLY ONTOGENY**, ii) unveiling the enhanced cardiac tolerance achieved through adaptations to **CHRONIC HYPOXIA**, regular exercise training, and other unconventional interventions, and iii) exploring the modifications in cardiac tolerance that manifest in association with various **PATHOLOGICAL CONDITIONS**. Furthermore, our research efforts include an investigation into the pathogenetic mechanisms at play in the initiation and progression of cardiomyopathy and **HEART FAILURE**, spanning various causes. We pay particular attention to the influence of **METABOLIC RISK FACTORS** and comorbidities, aiming to pave the way for innovative **THERAPEUTIC** strategies.

CURRENT PROJECTS

- Molecular mechanisms of increased cardiac tolerance to oxygen deprivation.
- Role of hypoxia-inducible factor-1a in the pathophysiology of cardiovascular diseases.
- Epitranscriptomic regulations in heart development and disease.
- Pathogenetic mechanisms and novel experimental therapy of heart failure of various etiology.
- Development and maintenance of arrhythmogenic substrate in the failing heart.



Main experimental models and techniques used in the Laboratory of the Developmental Cardiology to study protective mechanisms against cardiac ischemia/reperfusion injury and heart failure, and the development of cardiac conduction system.

SELECTED OUTPUTS

- Alánová P., Alán L., Opletalová B., Buhuslavová R., Abaffy P., Matějková K., Holzerová K., Benák D., Kaludercic N., Menabo R., Di Lisa F., Ošťádal B., Kolář F., Pavlínková G.: HIF-1a limits myocardial infarction by promoting mitophagy in mouse hearts adapted to chronic hypoxia (2024) Acta Physiologica in press:e14202.
- Benák D., Holzerová K., Hrdlička J., Kolář F., Olsen M., Karelson M., Hlaváčková M.: Epitranscriptomic regulation in fasting hearts: implications for cardiac health (2024) RNA biology 21:1–14.
- Olejníčková V., Hamor P.U., Janaček J., Bartoš M., Zábrodská E., Saňková B., Kvasilová A., Kolesová H., Sedmera D.: Development of ventricular trabeculae affects electrical conduction in the early endothermic heart (2024) Developmental dynamics 253:78–90.
- Benák D., Kolář F., Zhang L., Devaux Y., Hlaváčková M.: RNA modification m(6)Am: the role in cardiac biology (2023) Epigenetics 18:2218771.
- Neckář J., Alánová P., Olejníčková V., Papoušek F., Hejnová L., Šilhavý J., Behuliak M., Bencze M., Hrdlička J., Vecka M., Jarkovská D., Švíglerová J., Mistrová E., Štengl M., Novotný J., Ošťádal B., Pravenec M., Kolář F.: Excess ischemic tachyarrhythmias trigger protection against myocardial infarction in hypertensive rats (2021) Clinical science 135:2143–2163.
- Ošťádal B., Ošťádal P.: Sex-based differences in cardiac ischaemic injury and protection: therapeutic implications (2014) British Journal of Pharmacology 171:541–554.

DEVELOPMENTAL EPILEPTOLOGY

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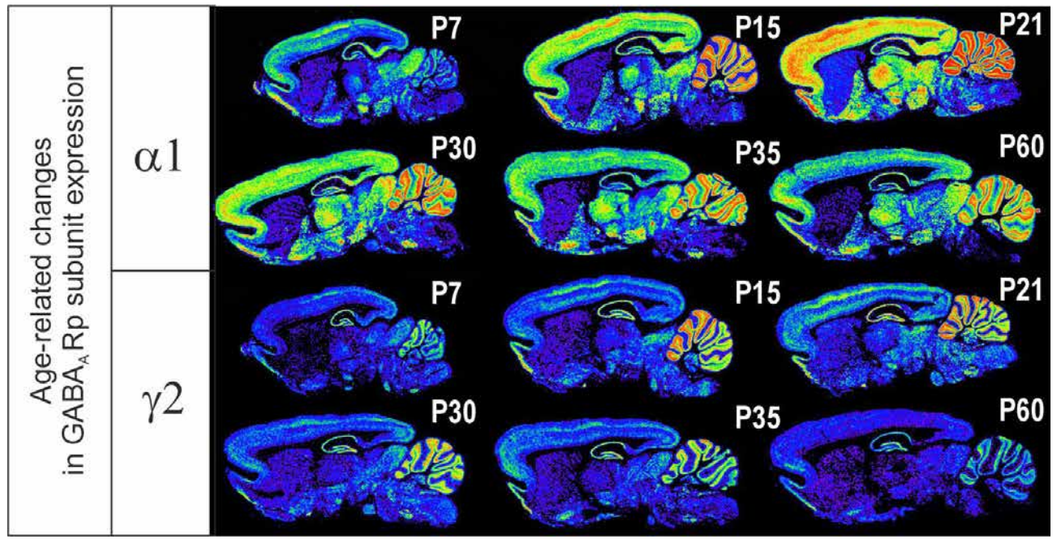
Our long-term research goals are (1) to better understand the **PATHOPHYSIOLOGY OF EPILEPTIC SEIZURE, EPILEPSY AND ITS COMORBIDITIES, PARTICULARLY IN THE DEVELOPING BRAIN**, (2) to develop new approaches to the treatment of epilepsy and its psychiatric comorbidities, and (3) to improve the safety of anti-seizure drugs for the developing brain. To elucidate the molecular, cellular and network mechanisms involved in epilepsy and to increase the translational potential of new observations, we make extensive use of various models of provoked seizures and chronic models of acquired epilepsy. In our research, we utilize modern electrophysiological, molecular, biochemical, pharmacological and behavioral techniques. Beyond basic research and close collaboration with clinical epilepsy centers, we work to a limited extent with the pharmaceutical industry to search for age-specific anti-seizure drugs and to ameliorate the potential adverse side effects of these drugs.

CURRENT PROJECTS

Age-specific molecular, cellular and structural mechanisms of ictogenesis, epileptogenesis and epilepsy-related comorbidities

- The molecular, cellular, structural and functional consequences of early-life seizures
- The long-term impact of early-life exposure to anti-seizure drugs on brain development and underlying mechanisms
- The developmental pharmacology of classical and potential anti-seizure drugs, age-related differences in efficacy and adverse effects



Changes in the expression of GABA$_A$ receptor α1 and γ2 subunit mRNA in developing rats, 7 to 60 days old.

SELECTED OUTPUTS

- The first experimental study on the prophylaxis of post-traumatic epilepsy (Servít (1960) Nature 188:669–670).
- A new extraction procedure that enables the measurement of precise levels of labile brain metabolites in small samples of brain tissue (Folbergrova et al. (1969) J Neurochem 16:191–203).
- Age-specific, flexion seizures induced with a systemic administration of NMDA as a model of human infantile spasms (Mareš et al. (1992) Dev Brain Res 65:185–189).
- Status epilepticus induces neuronal damage in the mediodorsal nucleus of the thalamus as early as at P12 in rats (Kubová et al. (2001) J Neurosci 21:3593–3599).
- Postictal potentiation precedes postictal refractoriness during early postnatal development (Mareš and Kubová (2015) Epilepsia 56:e10–14).
- Transition to seizures, which has been thought to be random, is a relatively complex process that is characterized by the slow and progressive loss of neuronal network resilience (Chang et al. (2018) Nat Neurosci 21:1742–1752).

EXPERIMENTAL HYPERTENSION

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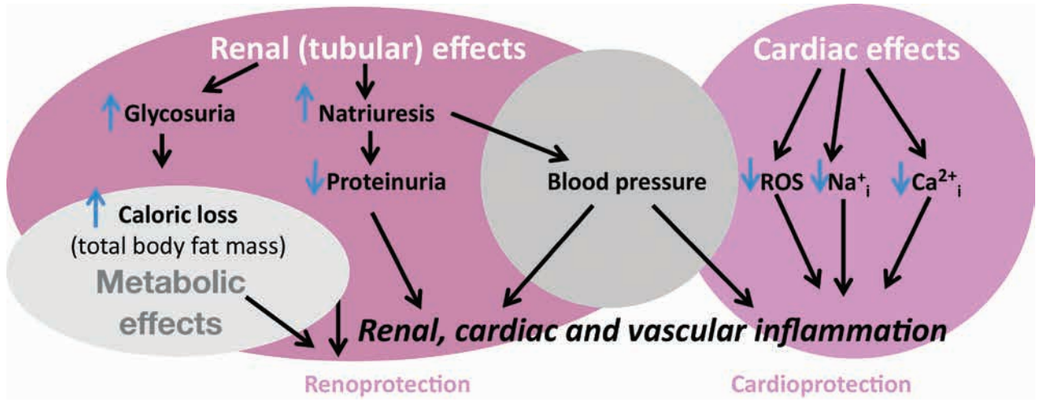
Our department studies the mechanisms of **BLOOD PRESSURE** regulation and **END-ORGAN DAMAGE** in **RATS** with different types of experimental hypertension, chronic kidney and heart disease with special attention given to the **ONTOGENETIC FACTORS** involved in these processes. Our research is focused on studying i) the mechanisms of beneficial effects of **EMPAGLIFLOZINS** on cardiorenal damage; ii) the central mechanisms participating in **BLOOD PRESSURE REGULATION** – with special attention given to the role of **CENTRAL ANGIOTENSIN II**, nitric oxide and reactive oxygen species; iii) changes in **SYMPATHETIC AND PARASYMPATHETIC TONE** in the **CONTROL OF THE BAROREFLEX**; iv) the role of **ENDOTHELIN** system in heart failure models; and v) metabolic and cardiovascular effects of new analogs of **NEUROPEPTIDES** regulating **FOOD INTAKE** in rats with a special focus on **NEUROINFLAMMATION** (in cooperation with the Institute of Organic Chemistry and Biochemistry CAS in Prague).

CURRENT PROJECTS

- The mechanism of therapeutic effects of gliflozins in heart failure
- The role of the endothelin system in the pathophysiology of chronic heart failure
- The effects of acetylcholinesterase inhibition on the cardiovascular system and cardiac ischemic tolerance in spontaneously hypertensive rats
- The possible role of prolactin-releasing peptide analogs in the treatment of obesity and hypertension with a special focus on neuroinflammation



New antidiabetics – gliflozins (inhibitors of sodium-glucose transporter 2) show many beneficial actions beyond their hypoglycemic effects. The underlying mechanisms of these additional cardiorenal protective effects are still not well understood, especially in hypertensive non-diabetic disease. Thus, we are interested in the mechanisms of beneficial effects empagliflozin on end-organ damage and metabolic parameters in different forms of experimental hypertension.

SELECTED OUTPUTS

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- Kala P., Vaňourková Z., Škaroupková P., Kompanowska-Jezierska E., Sadowski J., Walkowska A., Veselka J., Táborský M., Maxová H., Vaněčková I., Červenka L.: Endothelin type A receptor blockade increases renoprotection in congestive Heart failure combined with chronic kidney disease: Studies in 5/6 nephrectomized rats with aorto-caval fistula (2023) Biomed Pharmacother 158:114157.
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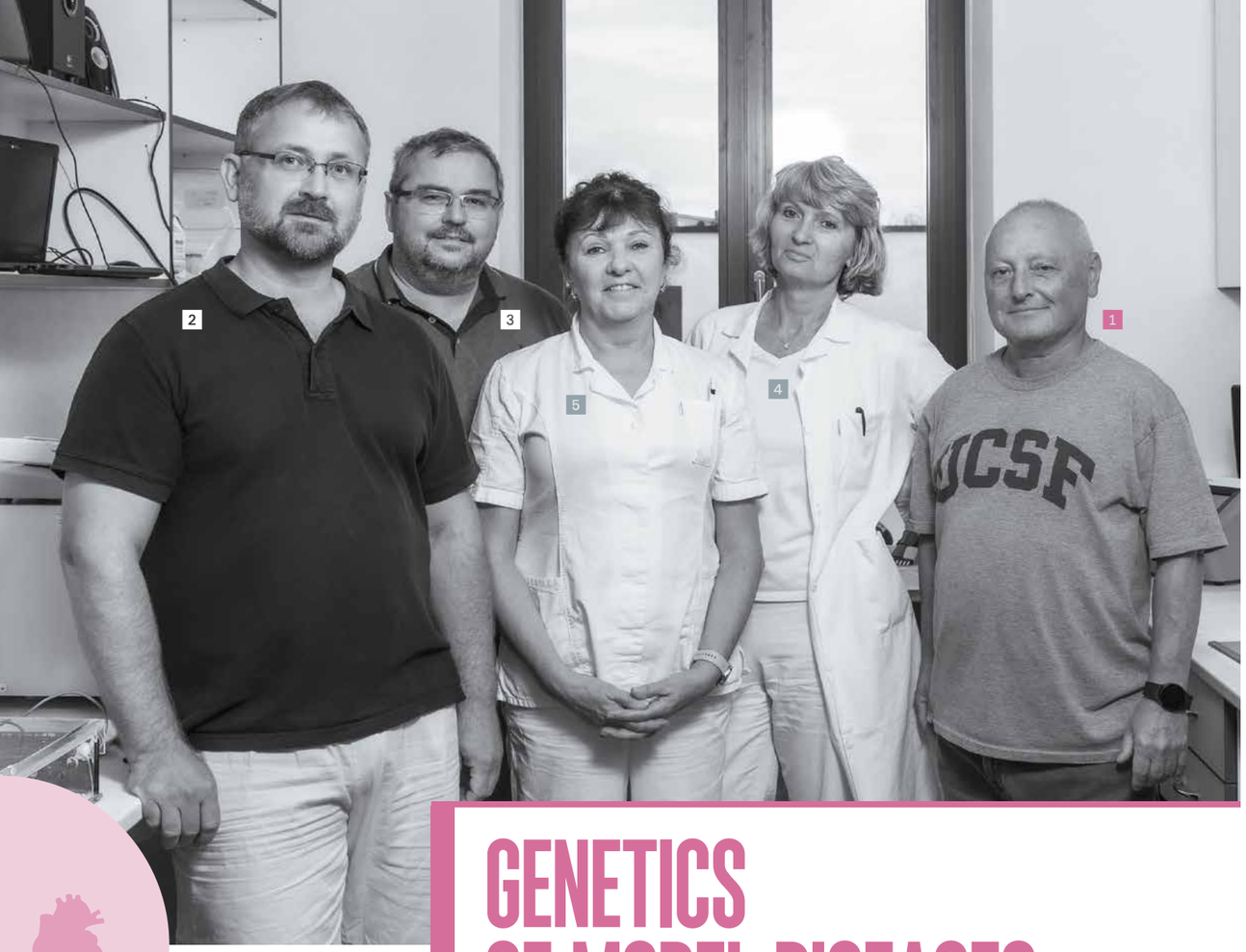

GENETICS OF MODEL DISEASES

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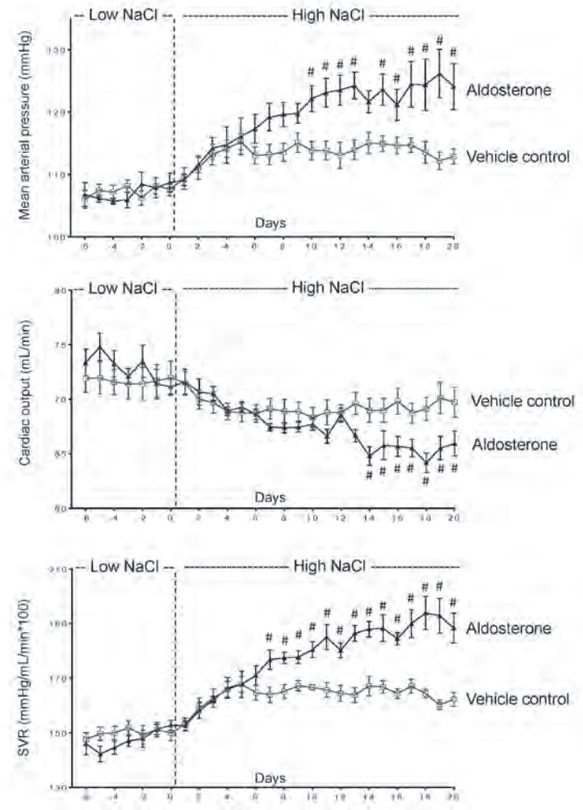
METABOLIC SYNDROME is a cluster of several risk factors for type 2 diabetes and cardiovascular disease, including obesity, hypertension, insulin resistance, and dyslipidemia. Genome-wide association studies in humans only identified a minor proportion of the total heritability of such complex traits so far. Studies in **ANIMAL MODELS OF HUMAN COMPLEX DISEASES** can provide a useful alternative. Experiments with rat models can control for both genetic background and environmental effects as well as enable the **GENETIC MANIPULATION** of experimental animals. The **SPONTANEOUSLY HYPERTENSIVE RAT (SHR)** is the most widely used animal model of essential hypertension and associated metabolic disturbances that are typical for metabolic syndrome. Although it cannot be expected that the individual predisposing genes themselves will be conserved between rats and humans, it is likely that the networks and pathways of genes leading to disease susceptibility will be conserved across species.

CURRENT PROJECTS

- Analysis of the hemodynamic mechanisms that initiate salt-sensitive hypertension in hyperaldosteronism
- Analysis of the molecular mechanisms underlying hemodynamic abnormalities that initiate the development of hypertension with increased salt intake
- Linkage and correlation analyses of intermediary phenotypes to reveal candidate genes underlying complex pathophysiological traits in the SHR strain using HXB/BXH recombinant inbred strains



Mean arterial pressure, cardiac output, and systemic vascular resistance (SVR) during the administration of a low-NaCl diet (0.26% NaCl) and a high-NaCl diet (4% NaCl) in control rats infused with the vehicle and in rats infused with aldosterone.

SELECTED OUTPUTS

- The development of a model system for genetic and correlation analyses of cardiovascular and metabolic disturbances in spontaneously hypertensive rats (SHRs), HXB/BXH recombinant inbred strains derived from crosses of SHRs with Brown Norway rats (Hübner et al.: Integrated transcriptional profiling and linkage analysis for identification of genes underlying disease (2005) Nat Genet 37:243–253; www.genenetwork.org).
- Identification of the first blood pressure regulatory QTL at the molecular level in SHRs as a deletion variant of the Cd36 gene (Pravenec et al. (2008) Nat Genet 40:952–954) as well as a number of other QTLs associated with metabolic and cardiac traits (reviewed by Pravenec et al. (2014) Physiol Res 63:Suppl 1, S1–S8).
- Identification of hemodynamic mechanisms of salt-dependent hypertension in primary aldosteronism (Kurtz et al.: Hypertension in primary aldosteronism is initiated by salt-induced increases in vascular resistance with reductions in cardiac output (2023) Hypertension 80:1077–1091).

MEMBRANE TRANSPORT

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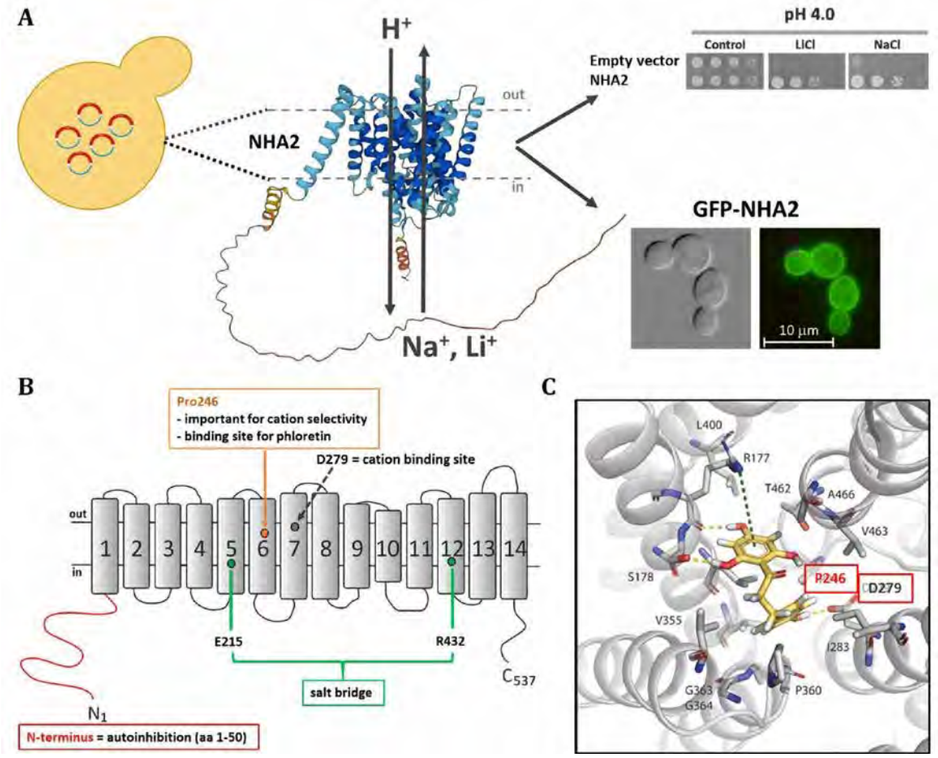
We study the proteins that transport compounds and signals across cell membranes. These proteins, called **TRANSPORTERS**, ensure the uptake of nutrients into cells, the efflux of waste compounds from cells and communication with the environment. We are not only interested in the molecular characterisation of transporters in terms of their **STRUCTURE/FUNCTION**, **SUBSTRATE SPECIFICITY AND TRANSPORT MECHANISM**, but also in their biogenesis and degradation, posttranslational regulation and their role in **EUKARYOTIC CELL PHYSIOLOGY**. We specialise in transporters related to the **INTRACELLULAR pH** and **CATION HOMEOSTASIS** of lower eukaryotes and in **TRANSPORTERS OF HIGHER EUKARYOTES RELATED TO HUMAN DISEASES**.

CURRENT PROJECTS

- The molecular characterization of cation transporters – the relationship between their protein structure, substrate specificity and affinity, transport capacity, biogenesis and organisation within the plasma membrane
- The characterization of non-transporting proteins involved in the maintenance of cation and pH homeostasis via their interaction with transporters
- Yeast as a tool to study transport processes in animal and plant cells
- Lipid composition of cell membranes, their contribution to transporter activity and their role as antifungal-drug targets



Structural and functional characterization of human Na^+/H^+ antiporter NHA2 in ***Saccharomyces cerevisiae****.* ***(A)*** *NHA2 was functionally expressed in the plasma membrane of the yeast S. cerevisiae and its activity improved the LiCl and NaCl tolerance of cells.* ***(B)*** *Several new features of NHA2 that are important for its transport activity were revealed.* ***(C)*** *The specific NHA2 inhibitor phloretin (in yellow) binds in the core of the protein close to the cation-binding site.*

SELECTED OUTPUTS

- The involvement of Trk1 and Trk2 potassium uptake systems in $Ca2^+$ signalling and stress survival has been described (Zimmermannova et al. (2021) FEMS Yeast Res 21:foab015; Duskova et al. (2021) Microbiology 167:001065).
- New mechanisms in the regulation of Nha1 and its role in yeast cell physiology have been elucidated (Albacar et al. (2021) J Fungi 7(12):1010; Papouskova et al. (2021) Mol Microbiol 15:41–57).
- Structural features contributing to the activity and affinity change of the Trk1 K^+ importers have been elucidated (Masaryk and Sychrova (2022) J Fungi 8:432; Masaryk et al. (2023) Comput Struct Biotech J 21:2705–2716; Papouskova et al. (2023) Yeast 40:63–83).
- Various types of potential antifungal drugs have been tested in conventional, pathogenic and non-conventional yeast (Csáky et al. (2020) Yeast 37(1):45–62; Vaitkienė et al. (2020) Front Microbiol 11:2077; Kodedová et al. (2023) Microbiol Res 26:127303).
- New structural features of the human NHA2 antiporter have been described (Velazquez et al. (2022) Protein Sci 31:e4460).

METABOLISM OF BIOACTIVE LIPIDS

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labmanager Martina Rombaldová 6 Jana Brejchová 7
students Monika Krakovková 8

The original **METABOLOMICS** laboratory became an independent Laboratory in 2019 within the Laboratory of Adipose Tissue Biology when Dr. Kuda was awarded the Lumina Quaeruntur 2018 praemium by the Academy Council of the Czech Academy of Sciences to support outstanding promising researchers in setting up new scientific teams. The Laboratory focuses on the analysis of **LIPID MEDIATORS** (eicosanoids, docosanoids, endocannabinoids), in particular for identifying the source of the production of various mediators and their effect on metabolism and immune cells (i.e. adipocytes vs. macrophages). Currently, the Laboratory is exploring new **ANTI-DIABETIC LIPIDS**, fatty acid esters of hydroxy fatty acids, and lipid-related metabolic **PATHWAYS** using **STABLE ISOTOPES**, spatial metabolomics, transcriptomics, and **LIPIDOMICS**. We combine biochemistry, analytical chemistry, and organic chemistry with animal physiology, molecular biology, and informatics. The Laboratory has a strong collaboration with the Laboratory of Adipose Tissue Biology and with the Laboratory of Metabolomics.

CURRENT PROJECTS

- The metabolism of branched fatty acid esters of hydroxy fatty acids (FAHFA), eicosanoids, docosanoids, and endocannabinoids
- Subcellular and spatial metabolomics in cancer
- Anti-inflammatory effects of novel omega-3 FAHFA in obesity
- The role of epicardial fat, subclinical inflammation, and novel lipid signalling molecules in the onset and development of heart failure
- Metabolic flux analysis, dynamic metabolomics, and lipidomics

(A) *Cell culture work.* ***(B)*** *Fixation of cells and staining of lipid droplets.* ***(C)*** *Solid phase extraction of lipid mediators.*

SELECTED OUTPUTS

- Vondrackova M., Kopczynski D., Hoffmann N., Kuda O.: LORA, Lipid Over-Representation Analysis based on structural information (2023) Anal Chem 95(34):12600–12604.
- Brejchova K., Paluchova V., Brezinova M., Cajka T., Balas L., Durand T., Krizova M., Stranak Z., Kuda O.: Triacylglycerols containing branched palmitic acid ester of hydroxystearic acid (PAHSA) are present in the breast milk and hydrolyzed by carboxyl ester lipase (2022) Food Chem 388:132983.
- Brejchova K., Radner F.P.W., Balas L., Paluchova V., Cajka T., Chodounska H., Kudova E., Schratter M., Schreiber R., Durand T., Zechner R., Kuda O.: Distinct roles of adipose triglyceride lipase and hormone-sensitive lipase in the catabolism of triacylglycerol estolides (2021) PNAS 118(2):e2020999118.
- Lopes M., Brejchova K., Riecan M., Novakova M., Rossmeisl M., Cajka T., Kuda O.: Metabolomics atlas of oral 13C-glucose tolerance test in mice (2021) Cell Rep 37(2):109833.
- Brejchova K., Balas L., Paluchova V., Brezinova M., Durand T., Kuda O.: Understanding FAHFAs: From structure to metabolic regulation (2020) Prog Lipid Res 79:101053.

MITOCHONDRIAL PHYSIOLOGY

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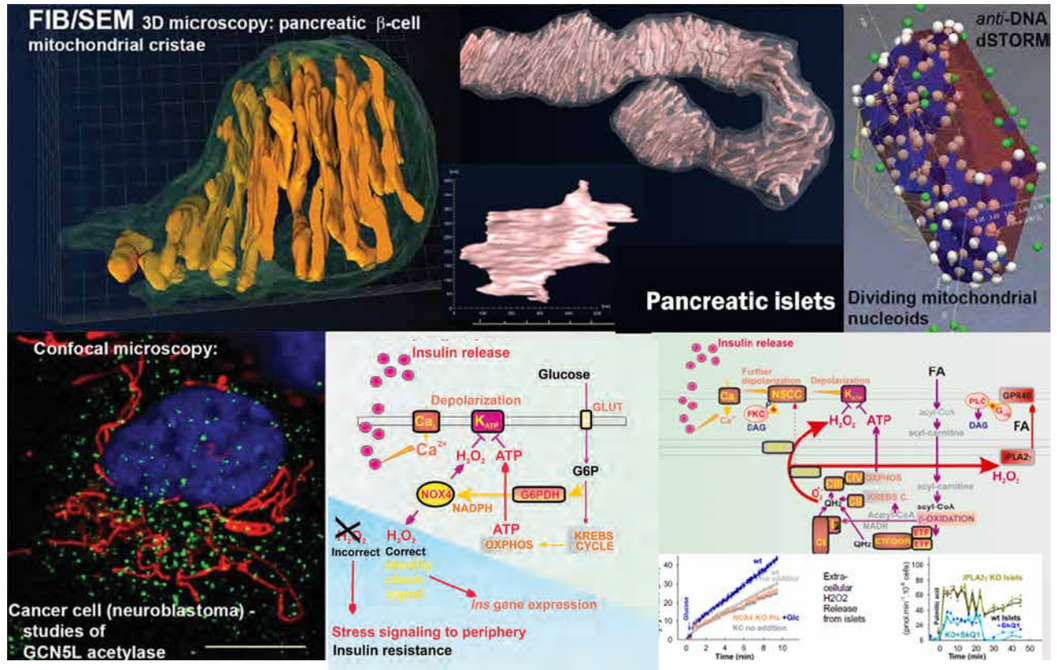
MITOCHONDRIA, being the main source of cellular energy, ATP, and an essential metabolic hub and source of redox signalling in physiological and pathophysiological processes, are studied in cell and GMO mice models, likewise the **PRODUCTION OF REACTIVE OXYGEN** species that essentially initiate redox signals, e.g. in **HYPOXIC ADAPTATION** or **INSULIN RELEASE STIMULATION**, but in excess negatively impact cell function. Prolonged **OXIDATIVE STRESS** leads to cell death, but chronic moderate oxidative stress accompanies **PATHOPHYSIOLOGICAL DISORDERS** including neurodegenerations, type 2 diabetes, and pulmonary hypertension. Mitochondria possess their own DNA (mtDNA) organized with accessory proteins within nucleoids, the biology of which is studied by 3D superresolution microscopy. “Nanoscopy” is being developed to study mitochondrial **CRISTAE** morphology in relation to their functions. Finally, **MITOCHONDRIAL SIGNALLING** in cancer cells and **CANCER-SPECIFIC METABOLISM** are studied as being essential for future **ANTICANCER DRUG DEVELOPMENT**.

CURRENT PROJECTS

- Reactive oxygen species, redox regulations, redox signalling, and endogenous antioxidant mechanisms
- Nucleoids of mitochondrial DNA in relation to diabetes, nucleoid division, and ultrastructure by 3D super-resolution microscopy
- Novel cancer-related metabolites and mitochondrial metabolism, oxidative stress, or hypoxia
- Mechanisms of insulin release in pancreatic β-cells
- Cristae morphology in relation to ATP-synthase oligomers and metabolic modes, including studies by FIB/SEM and 3D super-resolution fluorescence microscopy



FIB/SEM tomography of mitochondrial cristae (top left), 3D-superresolution microscopy of cristae (top middle), and mitochondrial DNA (top right), high resolution of cancer cell (bottom left and middle); discovered mechanism of insulin secretion stimulated fatty acids (bottom right).

SELECTED OUTPUTS

- Revisited the mechanism of insulin secretion in pancreatic β-cells: Plecitá-Hlavatá et al. Glucose-stimulated insulin secretion fundamentally requires H_2O_2 signaling by NADPH oxidase 4. (2020) Diabetes 69:1341–1354. The article introduces a revolutionary new concept of ATP plus redox signaling being required for insulin secretion in pancreatic β-cells stimulated by glucose (H_2O_2 signaling produced by the NADPH oxidase isoform 4, NOX4) or branched-chain keto acids and fatty acids (H_2O_2 signaling by mitochondria). This discovery will have a great impact on future translational research on antidiabetic drugs and nutritional guidance to prevent type 2 diabetes.
- Review: Ježek et al.: Contribution of mitochondria to insulin secretion by various secretagogues (2022) Antioxid Redox Signal 36:920–952.
- Clinical study of 2-hydroxyglutarate in breast cancer - Špačková et al.: Biochemical background in mitochondria affects 2HG production by IDH2 and ADHFE1 in breast carcinoma (2021) Cancers 13:1709.
- Mitochondrial phospholipase participates in cardiolipin remodeling - Průchová et al.: Antioxidant role and cardiolipin remodeling by redox-activated mitochondrial Ca^{2+}-independent phospholipase A2γ in the brain (2022) Antioxidants 11:198.
- Magnetic resonance imaging of pancreatic islets - Shapoval et al.: Poly(4-styrenesulfonic acid-co-maleic anhydride)-coated NaGdF4:Yb,Tb,Nd nanoparticles with luminescence and magnetic properties for imaging of pancreatic islets and β-cells (2022) ACS Appl Mater Interfaces 14:18233–18247.
- Multiple mtDNA copies in a single nucleoid - Pavluch et al. Possible frequent multiple mitochondrial DNA copies in a single nucleoid in HeLa cells (2023) Sci Rep 13:5788.
- Review: Ježek et al.: Mitochondrial cristae morphology reflecting metabolism, superoxide formation, redox homeostasis, and pathology (2023) Antioxid Redox Signal 39 (10-12):635-683.

MOLECULAR NEUROBIOLOGY

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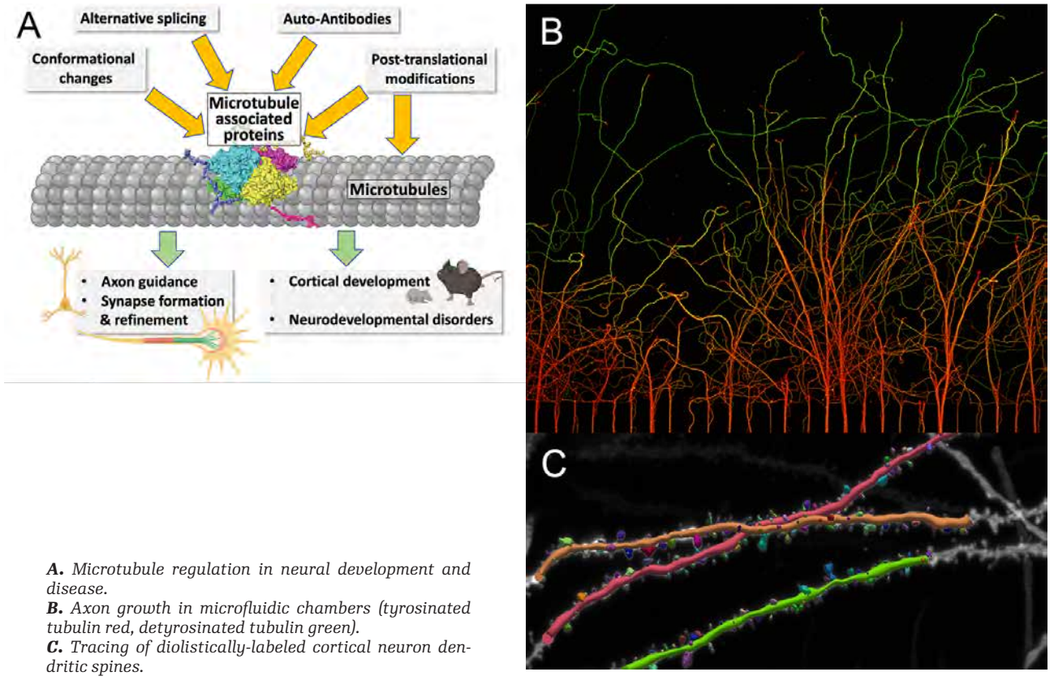
The Laboratory of Molecular Neurobiology studies the regulation of microtubules during **BRAIN DEVELOPMENT** and in **NEURODEVELOPMENTAL DISORDERS**. We focuse on **MICROTUBULE-ASSOCIATED PROTEINS** and their role in microtubule dynamics, axon guidance, synapse formation and refinement. The activity of microtubule-associated proteins is tightly regulated on multiple levels. We analyze how posttranslational modifications and conformational changes of microtubule-associated proteins control their function *in vitro* and in neurons, and what is their impact on brain development using mouse models. Finally, we test how deregulation of microtubule-associated proteins contributes to pathogenesis of neurodevelopmental disorders - in particular autism spectrum disorder, epilepsy, or schizophrenia.

CURRENT PROJECTS

- Analysis of the isoform-specific role of Collapsin response mediator protein 2 in microtubule polymerization, axon growth and brain development
- The TRAK protein family in axonal transport and neural development
- Human variants of microtubule-associated proteins and their role in the pathogenesis of epilepsy and spastic paraplegia



A. *Microtubule regulation in neural development and disease.*
B. *Axon growth in microfluidic chambers (tyrosinated tubulin red, detyrosinated tubulin green).*
C. *Tracing of diolistically-labeled cortical neuron dendritic spines.*

SELECTED OUTPUTS

- Ziak et al.: CRMP2 mediates Sema3F-dependent axon pruning and dendritic spine remodeling (2020) EMBO Rep 21(3):e48512.
- Maimon et al.: A CRMP4-dependent retrograde axon-to-soma death signal in amyotrophic lateral sclerosis (2021) EMBO J 40(17):e107586.
- Balaštík et al.: Prolyl isomerase Pin1 regulates axon guidance by stabilizing CRMP2A selectively in distal axons (2015) Cell Rep 13(4):812–828.

MOLECULAR PHYSIOLOGY OF BONE

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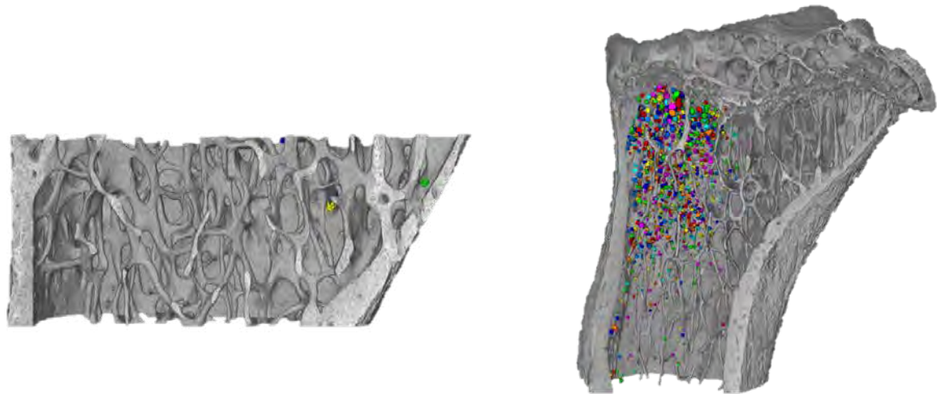
In obesity, the inability of adipose tissue to store excess calories leads to ectopic fat accumulation in the liver, muscles or cardiovascular system, and causes an impairment of glucose homeostasis. Recent studies have shown that bones are also affected by obesity, leading to enhanced adipocyte formation in bone marrow (**BMAT**). Higher **BMAT** volume is often associated with bone fragility fractures, an overlooked complication affecting the quality of life in patients with metabolic complications. However, there is limited information on the physiological role of **BMAT** in relation to bone and whole-body energy metabolism, and we focus on this topic. Our research projects employ murine and human cellular systems, mice biomodels, clinical studies and molecular, bioanalytical, and *in vivo* phenotyping techniques. The research is conducted as an international collaboration in Europe and the USA. The department was newly established in 2019, based on a 5-year "Start Up Research Program" financed by IPHYS.

CURRENT PROJECTS

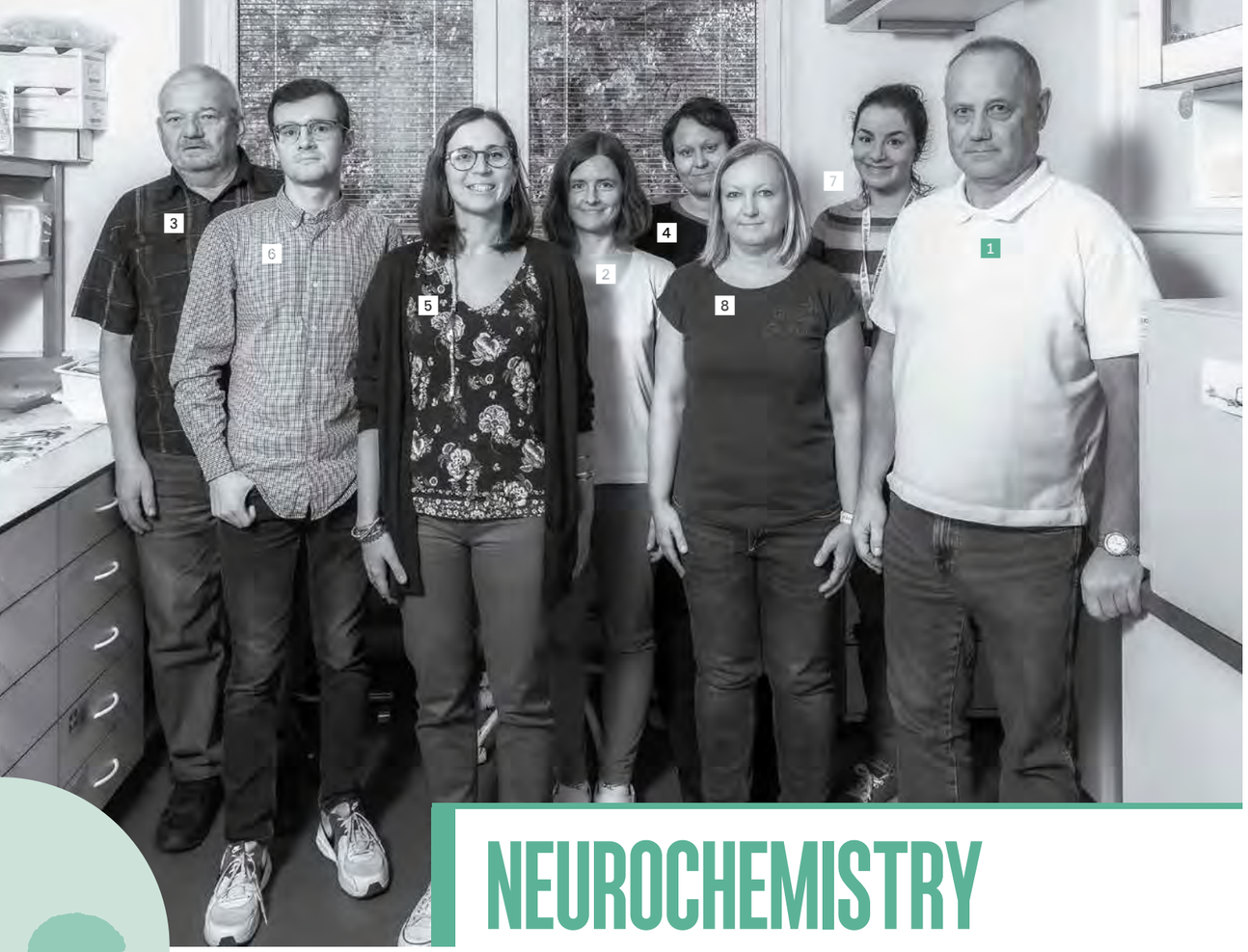
- Studying cellular and molecular changes in the bone marrow microenvironment in relation to bone and fat metabolism
- Studying the metabolic phenotype of BMAT and its contribution to bone homeostasis and whole-body energy metabolism using animal models and clinical settings



Representative images of Hexabrix-stained bone marrow adipocytes (BMAds) in the tibia of mice fed with a high-fat diet (HFD) (A) and HFD supplemented with omega-3 polyunsaturated fatty acids (HFD+F) (B).

SELECTED OUTPUTS

- Beňová A., Ferenčáková M., Bardová K., Funda J., Procházka J., Špoutil F., Čajka T., Džubanová M., Balcaen T., Kerckhofs G., Willekens W., van Lenthe G.H., Alquicer G., Pecinová A., Mráček T., Horáková O., Rossmeisl M., Kopecký J., Tencerová M.: Novel thiazolidinedione analog reduces a negative impact on bone and mesenchymal stem cell properties in obese mice compared to classical thiazolidinediones (2022) Mol Metabol 65:101598.
- Beňová A., Tencerová M.: Obesity-induced changes in bone marrow homeostasis (2020) Front Endocrinol 11:294.
- Tencerová M., Ferenčáková M., Kassem M.: Bone marrow adipose tissue: Role in bone remodeling and energy metabolism (2021) Best Pract Res Clin Endocrinol Metabol 35(4):101545.
- Beňová A., Ferenčáková M., Bardová K., Funda J., Procházka J., Špoutil F., Čajka T., Džubanova M., Balcaen T., Kerckhofs G., Willekens W., van Lenthe G.H., Charyyeva A., Alquicer G., Pecinová A., Mráček T., Horáková O., Coupeau R., Svarer Hansen M., Rossmeisl M., Kopecký J., Tencerova M.: Omega-3 PUFAs prevent bone impairment and bone marrow adiposity in mouse model of obesity (2023) Commun Biol 6(1):1043.



NEUROCHEMISTRY

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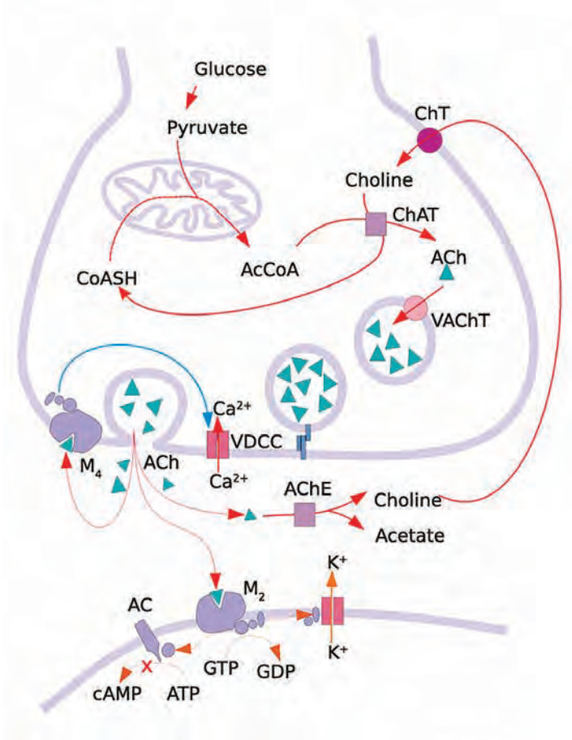
We study the physiology, biochemistry, and pharmacology of **CHOLINERGIC NEURONS** at the molecular level. In our studies we mainly employ cell lines, but also we use animal models. Our research is focused mainly on the following topics:

- The biochemical physiology and pharmacology of cholinergic neurons. The development and differentiation of cholinergic neurons. The synthesis, storage, and release of **ACETYLCHOLINE**. Presynaptic regulation of acetylcholine release.
- Cholinergic mechanisms in the pathogenesis of Alzheimer´s disease. The effects of β-amyloid on acetylcholine metabolism and muscarinic transmission.
- The molecular pharmacology of **MUSCARINIC RECEPTORS**. The allosteric modulation of receptor activation. The interaction of muscarinic receptors with G-proteins. The modelling of muscarinic receptor signal transduction.

CURRENT PROJECTS

- Effects of membrane cholesterol on the function of muscarinic receptor with the aim to delineate how membrane cholesterol binds to a muscarinic receptor and how it slows down their activation
- Signalling bias at muscarinic receptor with the aim to delineate why some muscarinic agonists activate individual subtypes to a different extent and exhibit signalling bias
- Cholinergic modulation of striatum-based behaviour with the aim to determine how the cholinergic activation of striatal GABAergic interneurons modulates striatal signalling and striatum-based behaviour



Upon Ca^{2+} entry via voltage-dependent calcium channels (VDCC), acetylcholine (ACh) is released to synapse. Postsynaptically ACh regulates cAMP synthesis and K^+ flow via M2 receptors. Presynaptically it inhibits its own release via M4 receptors. AC – adenylyl cyclase, AcCoA – acetyl coenzyme A, ChAT – choline acetyl transferase, ChT – choline transporter, VAChT – vesicular acetylcholine transporter.

SELECTED OUTPUTS

- Urushadze et al.: Timed Sequence Task: A new paradigm to study motor learning and flexibility in mice (2023) eNeuro 10:ENEURO.0145–23.
- Abbondanza et al.: Nicotinic acetylcholine receptors expressed by striatal interneurons inhibit striatal activity and control striatal-dependent behaviors (2022) J Neurosci 42:2786–2803.
- Randakova et al.: Fusion with promiscuous Gα16 subunit reveals signaling bias at muscarinic receptors (2021) Int J Mol Sci 22:10089.
- Randakova et al.: Novel M2-selective, Gi-biased agonists of muscarinic acetylcholine receptors (2020) Br J Pharmacol 177:2073–2089.
- Jakubik et al.: The operational model of allosteric modulation of pharmacological agonism (2020) Sci Rep 10:14421.
- Janickova et al.: Selective decrease of cholinergic signaling from pedunculopontine and laterodorsal tegmental nuclei has little impact on cognition but markedly increases susceptibility to stress (2019) FASEB J 33:7018–7036.
- Randakova et al.: Novel long-acting antagonists of muscarinic ACh receptors (2018) Br J Pharmacol 175:1731–1743.
- Randakova et al.: Role of membrane cholesterol in differential sensitivity of muscarinic receptor subtypes to persistently-bound xanomeline (2018) Neuropharmacol 133:129–144.

NEUROPHYSIOLOGY OF MEMORY

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PhD students Daniela Kunčická 10 Daniela Černotová 11 Karolína Hrůzová 12 Martina Janíková, Branislav Krajčovič, Anna Gunia 13 Sofiia Morarescu 14 Tereza Klausová 15 technicians Michaela Radostná 16 Jindřich Kalvoda, Vladimíra Marková 17 Barbara Stuchlíková

Our laboratory explores how we **LEARN**, **REMEMBER**, and **ACT**. We study **SPATIAL NAVIGATION**, which is analogous to remembering facts, events, and places. Conditions such as **ALZHEIMER'S**, **SCHIZOPHRENIA**, and other brain issues affect these areas. We don't fully understand these conditions, so current treatments only address symptoms. Lately, we have dived deeper into the science behind **LEARNING AND MEMORY** in both **HEALTHY** and **UNHEALTHY BRAINS**. To study behavior, we use cutting-edge tools such as special behavioral tests, light control of neuronal activity, and detailed brain scans.

CURRENT PROJECTS

- Understanding the hippocampus, an ancient part of human brain which is connected to a number of other parts, such as the Cornu Ammonis, dentate gyrus, and subicular complex. These parts work together in a large network.
- What is Obsessive-Compulsive Disorder (OCD)? OCD is a condition where people have unwanted and repeated thoughts, feelings, or behaviors. It is similar to having a song stuck in your head, but it is a thought or action that the affected individual cannnot stop repeating. We are studying it by looking at certain parts of the brain affected by a substance called quinpirole. Approximately 1-3% of people might experience OCD in their lifetime.
- Rats and their amazing sense of direction: It is commonly known that rats have a very good sense of direction. By watching how they navigate, we can learn a great deal about memory and decision-making.
- Studying how humans navigate: We are also curious about how humans find their way around. When in a new city without a map, how do we find our way. We are studying the tricks our brain uses to navigate and remember places.
- How drugs affect our brain: We are performing in-depth studies on how certain medications impact our thinking, analogous to how different fuels can improve or impair the performance of a vehicle.
- Using advanced techniques to see inside the brain: We utilise sophisticated tools to see which parts of the brain are active.

Selected neurobehavioral and molecular methods, setups, and outputs at the Laboratory of Neurophysiology of Memory.

SELECTED OUTPUTS

- Patrono E., Hrůzova K., Svoboda J., Stuchlík A.: The role of optogenetic stimulations of parvalbumin-positive interneurons in the prefrontal cortex and the ventral hippocampus on an acute MK-801 model of schizophrenia-like cognitive inflexibility (2023) Schizophr Res 252:198–205. This study discovered the role of GABAergic transmission in an animal model of psychosis. We are the first to use a complex cognitive task, the attentional set-shifting task. To our knowledge, no one has used a cognitive behavioral task in rats coupled with the optogenetic stimulation of PV+ interneurons to reverse cognitive impairments. Moreover, this work shows optogenetics to be a potential method of active exploration in models of schizophrenia. The entire study was conducted in our laboratory.
- Vojtěchová I., Macháček T., Krištofíková Z., Stuchlík A., Petrásek T.: Infectious origin of Alzheimer's disease: Amyloid beta as a component of brain antimicrobial immunity (2022) PLoS Pathogens 18(11):e1010929. The amyloid cascade hypothesis, focusing on pathological protein aggregation, did not reveal the underlying cause of Alzheimer's disease. This article reviews evidence from the current literature that amyloid beta, traditionally considered pathological, also acts as an antimicrobial peptide that protects the brain from pathogens. We discuss these new findings in terms of the AD infection hypothesis and offer suggestions for future research. The authors of this article are three members of the laboratory.
- Žiak J., Weissová R., Jeřábková K., Janíková M., Maimon R., Petrásek T., Pukajová B., Kleisnerová M., Wang M., Brill M.S., Kasparek P., Zhou X., Alvarez-Bolado G., Sedláček R., Misgeld T., Stuchlík A., Perlson E., Balaštík M.: CRMP2 mediates Sema3F-dependent axon pruning and dendritic spine remodeling (2020) EMBO Rep 21(3):e48512. The regulation of axon guidance and pruning of inappropriate synapses by class 3 semaphorins are critical for neural circuit development. This collaborative paper demonstrated that CRMP2 Sema3F-dependent synapse pruning and its dysfunction share histological and behavioral features with neurodevelopmental disorders. Our team were responsible for the behavioral results. The study was a broad collaboration of several laboratories from the Czech Republic and abroad, including two laboratories from IPHYS.

PAIN RESEARCH

head MUDr. Jiří Paleček, CSc. 1 jiri.palecek@fgu.cas.cz
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Hana Zemková 4 PhD students Jana Čiháková, Monica Pontearso 5
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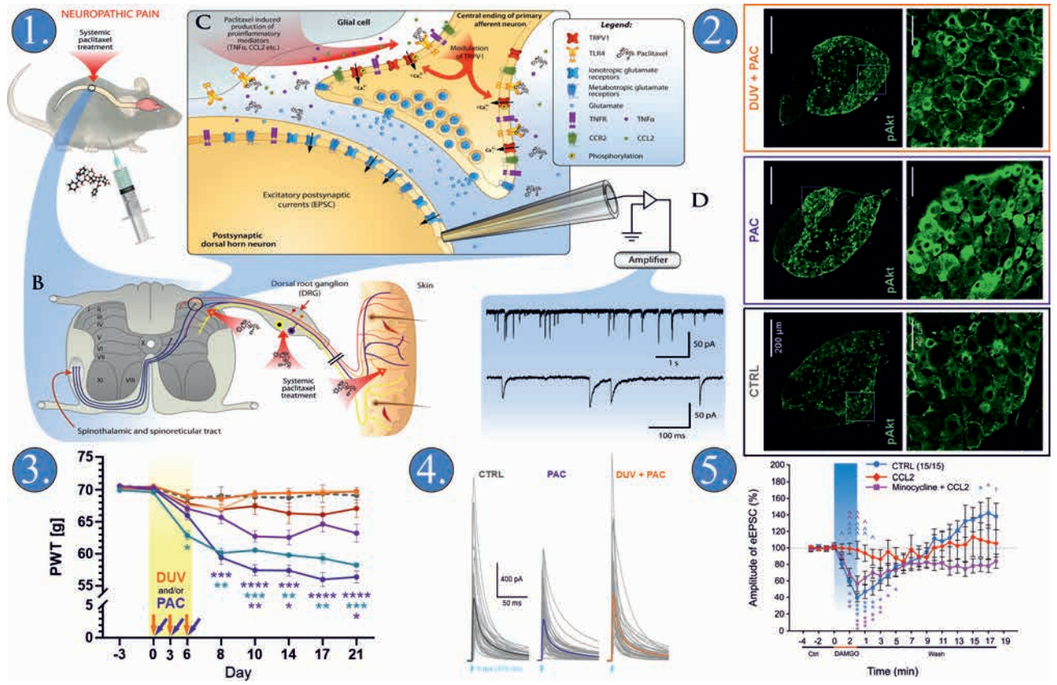
students Varsamia Vasiliki Manolopoulou 8 technicians Hana Janoušková 9
Kateřina Krämerová 10

The main research interest of the Laboratory is to study the **MECHANISMS OF PAIN** and to explore new possibilities for pain treatment, especially of chronic neuropathic states. Our experimental work is focused on the modulation of nociceptive information at the spinal cord level, which is the first relay center between the periphery and the higher brain areas. The goal is to study these modulatory mechanisms in order **TO IMPROVE THERAPY FOR NEUROPATHIC**, **INFLAMMATORY**, **AND CANCER-RELATED PAIN**. The focus is on the role of TRPV1, P2X and other receptors, neuroinflammation and glial cells in this process. In our research, we mainly use electrophysiological, optogenetic, immunohistochemical, and behavioral methods.

CURRENT PROJECTS

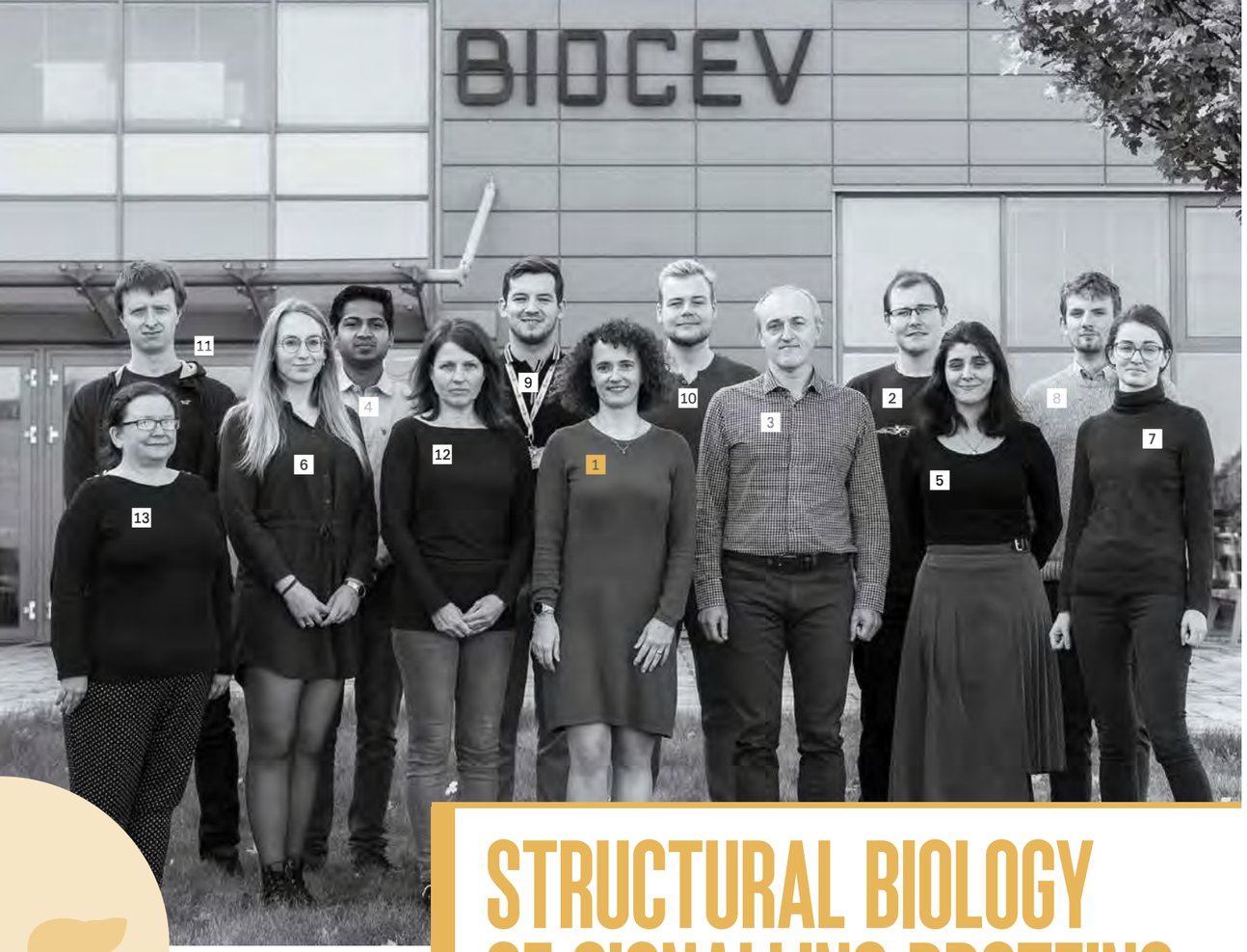
- Mechanisms of chemotherapy-induced and diabetic neuropathic pain
- The role of neuroinflammation in chronic pain conditions
- The modulation of spinal cord synaptic transmission by endocannabinoids and neurosteroids
- The interaction of opioid and TRPV1 receptors with cytokines in analgesia
- The physiology, pharmacology and molecular structure of purinergic P2X receptor-channels



*We studied chemotherapy-induced neuropathic pain using different approaches **(1)** and showed that the inhibition of PI3K by the specific FDA approved inhibitor Duvelisib prevented Paclitaxel increased PI3K expression in DRG neurons **(2)**, mechanical allodynia **(3)** and reduction of light-evoked inhibitory currents amplitude **(4)**. Experiments targeting neuroinflammation showed that CCL2 prevented the inhibitory/analgesic effects of the opioid agonist DAMGO on evoked currents in the spinal cord **(5)**.*

SELECTED OUTPUTS

- The inhibition of synaptic transmission by anandamide precursor 20:4-NAPE is mediated by TRPV1 receptors under inflammatory conditions (Špicarová et al. (2023) Front Mol Neurosci 16:1188503).
- Neurosteroids as positive and negative allosteric modulators of ligand-gated ion channels: P2X receptor perspective (Sivčev et al. (2023) Neuropharmacology 234:109542).
- The dual PI3Kγ/δ inhibitor duvelisib prevents development of neuropathic pain in model of Paclitaxel-induced peripheral neuropathy (Adámek et al. (2022) J Neurosci 42(9):1864–1881).
- The chemokine CCL2 prevents opioid-induced inhibition of nociceptive synaptic transmission in spinal cord dorsal horn (Heleš et al. (2021) J Neuroinflammation 18:279).
- Losartan attenuates neuroinflammation and neuropathic pain in paclitaxel-induced peripheral neuropathy (Kalynovska et al. (2020) J Cell Mol Med 24:7949–7958).
- Mechanical allodynia and enhanced responses to capsaicin are mediated by PI3K in a paclitaxel model of peripheral neuropathy (Adamek et al. (2019) Neuropharmacology 146:163–174).
- Peripheral inflammation affects the modulation of nociceptive synaptic transmission in the spinal cord induced by N-arachidonoylphosphatidylethanolamine (Nerandzic et al. (2018) British J Pharmacol 175:2322– 2336).
- The cancer chemotherapeutic Paclitaxel increases human and rodent sensory neuron responses to TRPV1 by activating TLR4 (Li et al. (2015) J Neurosci 35:13487–13500).



STRUCTURAL BIOLOGY OF SIGNALLING PROTEINS

head RNDr. Veronika Obšilová, Ph.D. 1 veronika.obsilova@fgu.cas.cz
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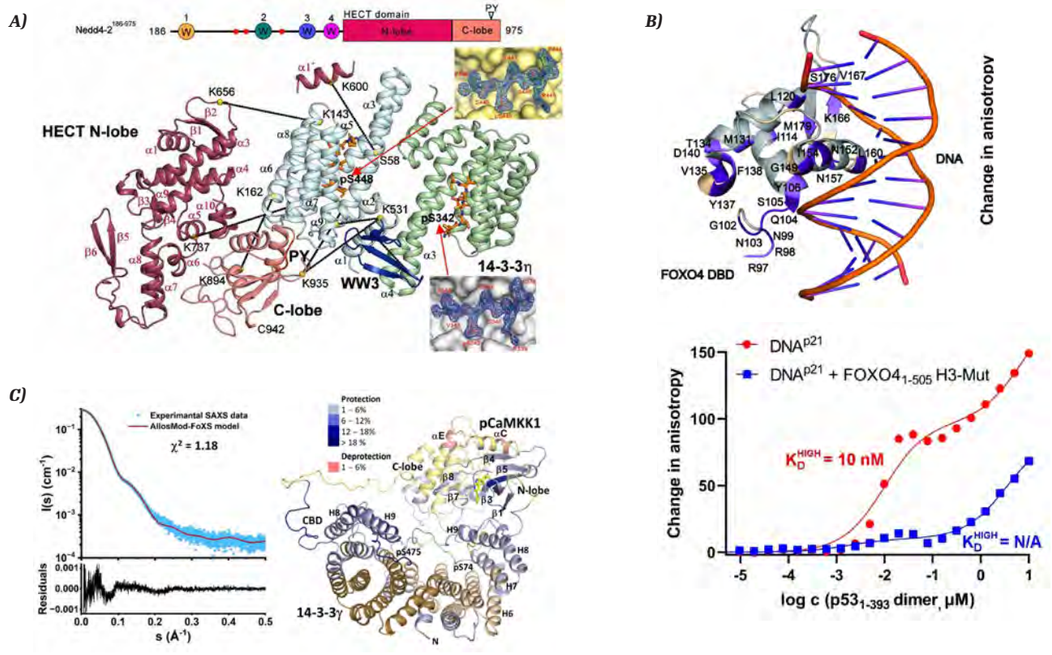
Maša Janošev 5 Karolína Honzejková 6 Klára Kohoutová 7 students Adam Brzezina 8
Matúš Fričeк 9 Martin Hýbl 10 Andrej Tekel 11 technicians Dana Kalábová 12
Gabriela Kočárová 13

Our group is focused on **STRUCTURAL BIOLOGY** (the relationship between the structure and function of certain groups of proteins), in particular we are interested in **14-3-3 PROTEINS AND THEIR COMPLEXES** with proteins involved in **APOPTOSIS**, **CANCER** and **CALCIUM-TRIGGERED SIGNALLING PATHWAYS**. 14-3-3 proteins specifically bind to phosphoserine- or phosphothreonine-containing motifs in a sequence-specific manner. Mechanistically, 14-3-3 proteins act as allosteric regulators and/or molecular scaffolds that constrain the conformation of the binding partner. Nonetheless, the underlying molecular mechanisms are only partially identified, mainly due to the lack of structural data. The methods we currently use include the expression of recombinant proteins and a range of biophysical methods to characterize **INTERMOLECULAR INTERACTIONS** and **PROTEIN STRUCTURE**, including cryo-EM, protein crystallography, NMR, SAXS and HDX-MS. All these methods enable us to better understand how the activity and function of protein-protein complexes is regulated.

CURRENT PROJECTS

- The structural biology of 14-3-3 proteins and their complexes
- Mechanistic insight into the regulation of apoptosis signal-regulating kinase 1 (ASK1)
- The role of calcium and 14-3-3 protein binding in the regulation of human ubiquitin ligase Nedd4-2
- The molecular mechanism of the regulation of cyclin-dependent kinase 16 (CDK 16) activity
- The molecular basis of the interaction between FOXO Forkhead transcription factors and tumor suppressor p53
- Biophysical characterization of protein-protein complexes involving protein phosphatase PPM1D (Wip1)



(A) *SAXS-based structural model of complex between Nedd4-2 and 14-3-3η protein. Black lines indicate intermolecular distance constraints assessed in chemical cross-linking experiments. The insets show the crystal structures of Nedd4-2 peptides containing the 14-3-3 binding motifs (PDB 6ZBT and 6ZC9).* ***(B)*** *Up, chemical shift perturbations obtained from ^{1}H-^{15}N HSQC spectra of ^{15}N-labeled FOXO4 in the presence of p53 mapped onto the crystal structure of the FOXO4 DBD:DNA complex. Down, fluorescence anisotropy measurements showing that the complex formation reduces the DNA-binding affinity of p53.* ***(C)*** *SAXS-based structural analysis of pCaMKK1: 14-3-3γ complex. Left, Experimental scattering curve of the complex superimposed with the calculated curve of the best-scoring CORAL AllosMod-FoXS model of the complex (shown in red). Right, ribbon representation of the best-scoring AllosMod-FoXS model of the complex.*

SELECTED OUTPUTS

- Our findings provided the first structural glimpse into 14-3-3-mediated Nedd4-2 regulation and highlight the potential of the Nedd4-2:14-3-3 complex as a pharmacological target for Nedd4-2-associated diseases such as hypertension, epilepsy, kidney disease and cancer (Pohl et al. (2021) Comm Biology 4:899).
- We characterized the interaction between the transcription factors p53 and FOXO4. We showed that the interaction between p53 transactivation domain and the FOXO4 Forkhead domain is essential for the overall stability of the p53:FOXO4 complex (Mandal et al. (2022) Protein Sci 31:e4287).
- We structurally characterized CaMKK1:14-3-3 and CaMKK2:14-3-3 complexes and provided the structural basis for 14-3-3-mediated CaMKK1 inhibition (Petrvalska et al. (2023) Protein Sci 32:e4805).

TRANSLATIONAL METABOLISM

head **Doc. Ing. Tomáš Čajka, Ph.D.** 1 tomas.cajka@fgu.cas.cz
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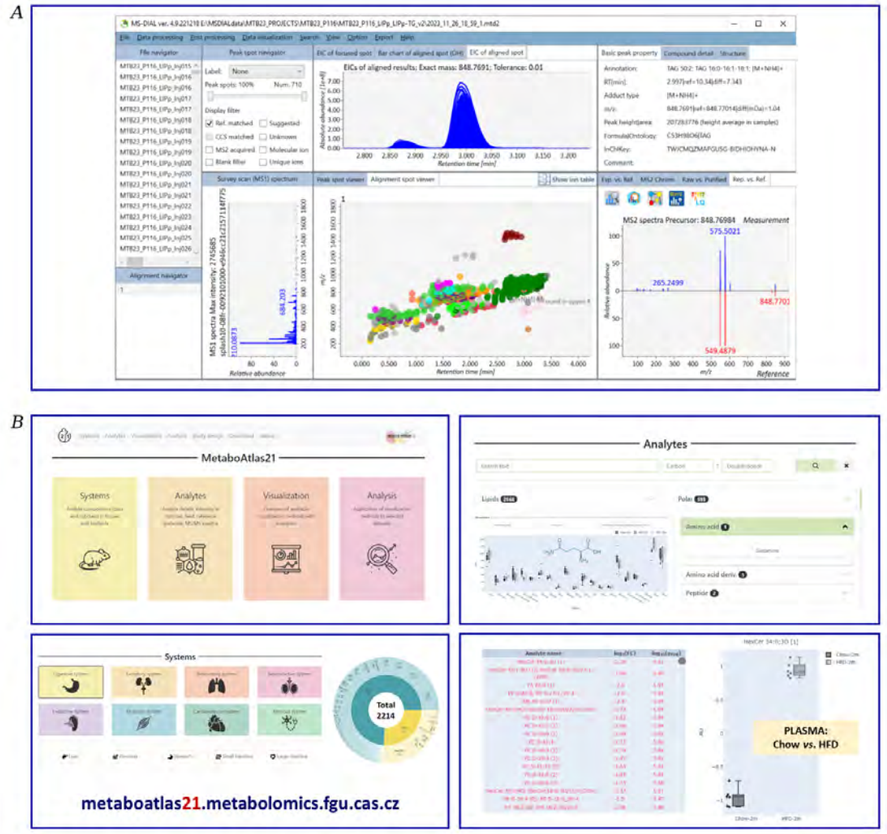
PhD students Stanislava Rakušanová 5
technicians Armenuhi Kirakosjanová

Our research involves applying mass spectrometry-based technologies to perform **METABOLOMIC, LIPIDOMIC AND PROTEOMIC ANALYSIS** of various biological samples. This work covers the development and use of both liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) methods for the in-depth characterization and quantification of polar metabolites – **METABOLOME**, simple and complex lipids – **LIPIDOME**, various exogenous compounds such as drugs – **EXPOSOME**, and proteins – **PROTEOME**. We also focus on improving data processing, automated data curation, statistical methods, and the visualization of omics data. We have successfully integrated LC-MS methods for the untargeted and targeted analysis of simple and complex lipids, polar metabolites, and exposome compounds (LIMeX) for a wide range of sample types and used them for studies focused on cardiovascular diseases, type 2 diabetes, lipogenesis, circadian rhythms, and drug adherence. We have also investigated the proteome related to clubfoot pathogenesis.

CURRENT PROJECTS

- Simple, fast, and robust protocols for metabolomics, lipidomics, and proteomics projects
- New separation methods (LC-MS, GC-MS) for physiological research
- Building LC-MS-based spectral libraries for reliable metabolite annotation
- Creating metabolomics and lipidomics atlases of biofluids and tissues
- Streamlining data processing, data curation, statistical analysis, and visualization of metabolomics and lipidomics data
- Metabolomics and proteomics for discovering new biomarkers of human health



(A) *Processing of complex lipids in biofluids and tissues using MS-DIAL software*
(B) *Visualization of interactive metabolomics/lipidomics atlas (web application) of 21 mouse tissues and biofluids in response to the metabolic challenge*

SELECTED OUTPUTS

- Rakušanová S., Fiehn O., Čajka T.: Toward building mass spectrometry-based metabolomics and lipidomics atlases for biological and clinical research (2023) Trends Anal Chem 158:116825.
- Rakušanová S., Čajka T.: Current analytical methods to monitor type 2 diabetes medication in biological samples (2023) Trend Anal Chem 158:116831.
- Čajka et al.: Optimization of mobile phase modifiers for fast LC-MS-based untargeted metabolomics and lipidomics (2023) Int J Mol Sci 24:1987
- Lopes et al.: Metabolomics atlas of oral 13C-glucose tolerance test in mice (2021) Cell Rep 37:109833
- Tsugawa et al.: A lipidome atlas in MS-DIAL 4 (2020) Nat Biotechnol 38:1159-1163.
- Eckhardt et al.: Novel contribution to clubfoot pathogenesis: The possible role of extracellular matrix proteins (2019) J Orthopaed Res 37:769-778.

OFF CAMPUS LABORATORY

BIOCEV

EUROPEAN SCIENTIFIC CENTRE OF EXCELLENCE IN BIOTECHNOLOGY AND BIOMEDICINE

IPHYS is a founding member and partner in BIOCEV. This is a joint project of six institutes of the CAS (Institute of Biotechnology, Institute of Molecular Genetics, IPHYS, Institute of Microbiology, Institute of Experimental Medicine, Institute of Macromolecular Chemistry) and two faculties of Charles University in Prague (Faculty of Science and First Faculty of Medicine). The goal of the project is to establish a European Centre of Excellence in biomedicine and biotechnology. The new building of the research centre was constructed in Vestec, in close vicinity of the IPHYS Krč campus, with financial support from the European Structural Funds. BIOCEV focuses on detailed study of cellular mechanisms at the molecular level, research and development of novel therapeutic strategies, early diagnostics, biologically active agents including chemotherapeutics, protein engineering, and other innovative technologies. Six IPHYS Laboratories participate in the BIOCEV project and have their laboratories at this centre since December of 2015.

RESEARCH PROGRAMMES:

The scientific scope of BIOCEV has been divided into five research programmes, each of them dealing with a number of separate research projects. Particular IPHYS projects in each programme are listed below. The programmes and projects have been designed to form a mutually integrated system of synergistic links inside BIOCEV:

1. Functional genomics
2. Cellular biology and virology
   - Mitochondrial structure and gene expression (Petr Ježek)
   - Structure and function of membrane receptors (Ladislav Vyklický, Jiří Paleček, Hana Zemková)
3. Structural biology and protein engineering
   - Structural biology of signalling proteins (Veronika Obšilová)
4. Biomaterials and tissue engineering
   - Bioartificial structures for replacement and regeneration of damaged tissue (Lucie Bačáková)
5. Development of diagnostic and therapeutic procedures

AVAILABLE CORE FACILITIES

The implementation of complex projects requires a high-quality methodological basis concentrated in core facilities. All are open to external users to provide them with the following research services:

- Czech Centre for Phenogenomics
- Imaging Methods
- Centre of Molecular Structure
- Gene Core – Quantitative and Digital PCR
- OMICS – Proteomics and Genomics
- Cryobank

CONTACT

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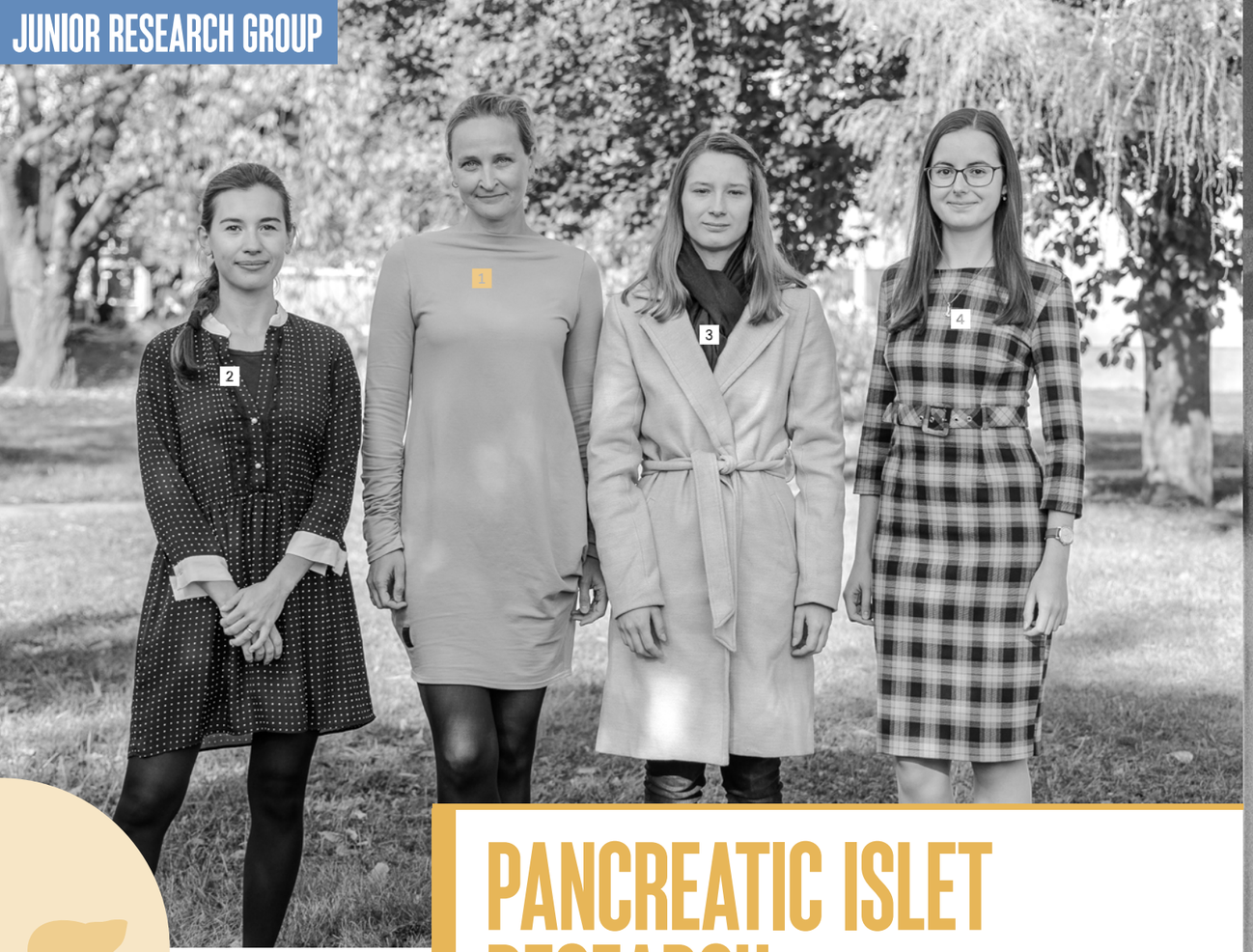

PANCREATIC ISLET RESEARCH

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PhD students Štěpánka Benáková 2 Monika Křivonosková 3
student Linda Stokičová 4

PANCREATIC β-CELLS constitute the majority of endocrine cells in the **ISLETS OF LANGERHANS**. They serve as glucose sensors and help maintain **GLUCOSE HOMEOSTASIS** in the body. Impairment of their function and quantity leads to the development of diabetes. Glucose homeostasis is regulated by **INSULIN**, which is secreted by β-cells. The main signaling pathways leading to the release of insulin granules have been described, but many details about the amplification of the pathways depending on the type of inducer are lacking. Our laboratory focuses on **REDOX SIGNALLING** as a key to regulating β-cell function. We study metabolites derived from glucose catabolism and redox signaling required for efficient insulin secretion. Its disruption and establishment of **OXIDATIVE STRESS** are the main triggers of the **DEVELOPMENT OF TYPE 2 DIABETES** in nutritional overload. In addition, β-cells are heterogeneous, and specific subpopulations are involved in the synchronized response of endocrine islet cells to glucose stimulation. We investigate the involvement of intracellular redox status in **β-CELL HETEROGENEITY**.

SERVICE DEPARTMENTS

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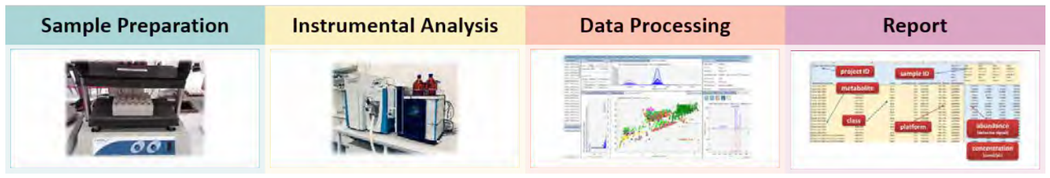
METABOLOMICS

head **Doc. Ing. Tomáš Čajka, Ph.D.** ■ tomas.cajka@fgu.cas.cz team members Jiří Hricko 1, Michaela Paučová 2, Tatyana Kobets, Michaela Nováková 3, Aleksandra Shumilova

The Department provides fee-based services for LC-MS and GC-MS-based metabolomics and lipidomics analysis of biofluids (e.g., plasma, serum, urine), tissue (e.g., liver, heart, adipose tissue), and cells, as well as bioinformatics analysis of generated data sets. The Laboratory is equipped with Vanquish UHPLC System/Q Exactive Plus, Vanquish UHPLC System/Orbitrap Exploris 480, Ultimate 3000 RSLC System/QTRAP 5500, Agilent 8890 GC/Pegasus BT2 instrumentation, and Agilent Bravo for automated liquid handling.
Platforms:
- LIMeX workflow (LIpids, Metabolites, and eXposome compounds) for the untargeted analysis of complex lipids, polar metabolites, and exposome compounds (food components and pharmaceutical drugs)
- Targeted analysis of specific low-abundant lipid mediators (eicosanoids, endocannabinoids, fatty acid esters of hydroxy fatty acids), metabolites labeled with stable isotopes (fluxomics), or pharmaceutical compounds for the ADME studies

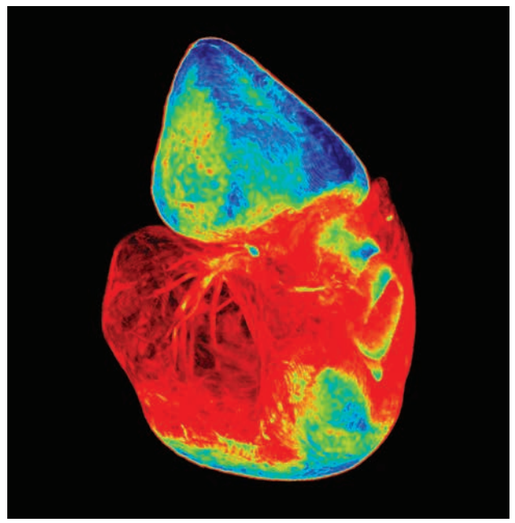


LIMeX workflow for combined untargeted and targeted analysis

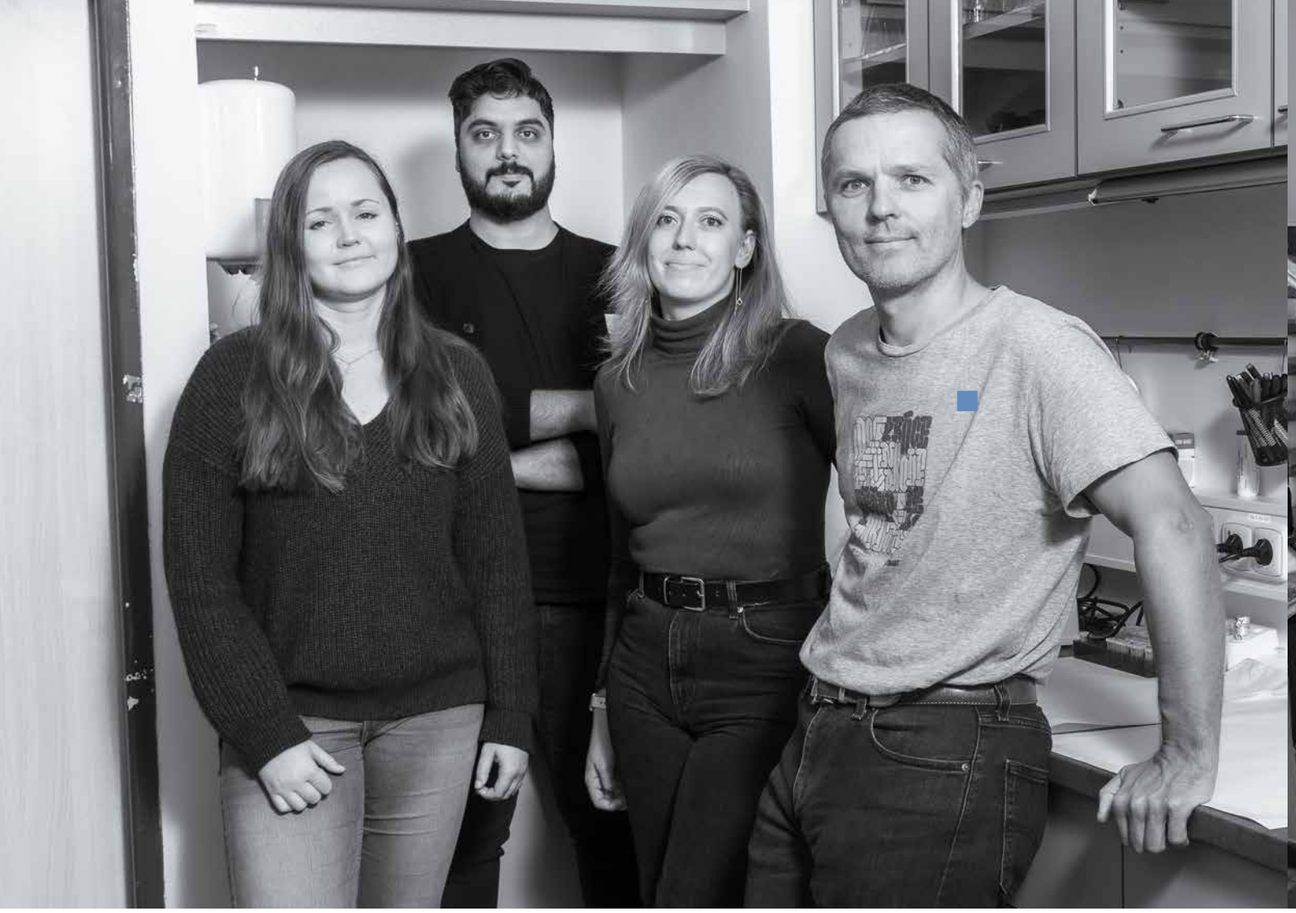
RADIOMETRY

head **Roman Liška** ■ roman.liska@fgu.cas.cz team member Karla Bohunová

The Department provides services dealing with all types of work with radioactive materials. In addition, with Computerized Tomography (CT) and Positron Emission Tomography (PET), we can also provide *in vivo* anatomical and molecular imaging of small laboratory animals (mice and rats) for the quantitative 3D tomographic imaging of biodistributed radiotracers, bones, and various soft tissues, using the μCT/PET apparatus Albira. Radioactivity measurements of all kinds of radionuclides in different samples are carried out for researchers of other Laboratories of IPHYS, as well as of other Institutes of the CAS in the campus and BIOCEV. We also provide storage space, advice, and services in the manipulation of radioactive materials and the ordering and purchasing of radioactive preparations.



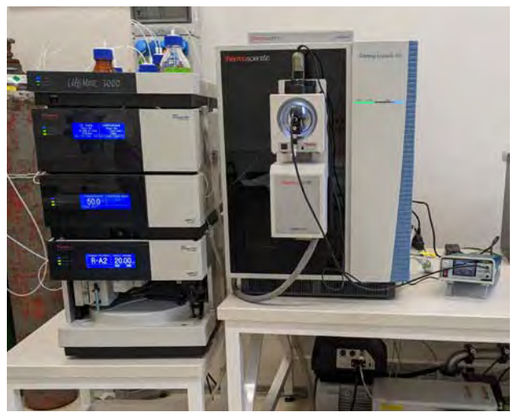
μCT scan of a shark heart using the contrast agent Lugol



PROTEOMICS SERVICE LABORATORY

head **RNDr. Marek Vrbacký, Ph.D.** ■ marek.vrbacky@fgu.cas.cz
team members (from the left) Elena Shcherbachenko, Rayyan Tariq Khan, Nadiia Prokopets

The proteomics service laboratory, also known as ProteoLab Krč (PLK), was jointly established by IPHYS and the Institute of Molecular Genetics of the CAS. It offers mass spectrometry-based bottom-up proteomic analyses to the research groups of both institutes, and also to other academic and non-academic subjects. The pay-per-sample service includes complete sample prep from various biological materials (e.g., cell lines, tissues, immunoprecipitation), untargeted or targeted LC-MS/MS of the resulting peptides and basic bioinformatic analysis. Prospective users should contact the lab to discuss the project, including the experimental design and statistical considerations. The laboratory is equipped with an Orbitrap Exploris 480 mass spectro-meter coupled to a nano UHPLC Ultimate 3000 liquid chromatograph.



ProteoLab KRC

ECONOMIC DEPARTMENT

head **Kateřina Uhrová** ■ katerina.uhrova@fgu.cas.cz
team members (bottom, from the left) Pavlína Hájková, Eva Hamalčíková, Lada Trčková, Lenka Nejedlá, Michaela Matějíčková, Michaela Trošková (above, from the left) Kamila Kohoutová, Dominika Šulcová, Gabriela Bartejsová, Běla Tobolová, Kateřina Rozsypalová, Jaroslava Králová, Lucie Němcová, Tereza Mádle, Dagmar Plzenská, Eva Syrová

The Economic Department is in charge of human resources, payroll and financial accounting, supply and the stocks, agenda of grants and operating programmes.

ANIMAL FACILITY

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team members (bottom, from the left) Kateřina Pavelková, Ilona Berková, Jana Lejčková, Hana Vančurová, Hana Ptáčková, Evelína Lavičková
(above, from the left) Yelizaveta Plisko, Jan Krämer, Nikola Danitová, Petr Havlena, Pavel Štrof, Jana Perná

The Department provides an enviroment for *in vivo* research. The used animal models are laboratory rats, laboratory mice and zebra fish. The animal facility is conventional and the rodents are housed in open cages.
Provided services:
Breeding of various common and unique strains of laboratory rats and mice. Housing of animals in experiments. All necessary and related services. All procedures correspond to requirements of Act No 246/1992 Coll., on the protection of animals against cruelty, and Decree No 419/2012 Coll., on the protection of experimental animals. The facility runs under a continuous veterinary supervision.

PROPERTY AND FACILITY DEPARTMENT

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team members (bottom, from the left) Irena Čechová, Agniezska Pelikán, Eva Půlová, Vladimíra Trůková, Jana Pechová
(above, from the left) Helena Reimerová, Pavel Šuba, Ivan Sluněčko

The Property and Facility Department provides all services related to the building maintenance and necessary health and safety rules. It also runs hostel rooms for IPHYS guests.

OFFICE OF THE DIRECTOR

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team members (from the left) Diana Moosová, Adéla Bocková, Petra Kubátová

The Office of the Director provides various administrative work of IPHYS. It organizes the events for the public and also the professional lectures. It ensures the popularization of the Institute to the media and the public. It records and manages the Institute´s intellectual property and coordinates activities of technology transfer.

INFORMATION TECHNOLOGY DEPARTMENT

head **Václav Pauločik** ■ vaclav.paulocik@fgu.cas.cz
team members (from the left) Tomáš Fišera, Nikola Jankov, Ondřej Švanda, Martin Kantor

Information Technology Department serves the whole campus with all services in the field of computer technology and traffic data network. It helps with the purchase, operation, and maintenance of hardware, data maintenance, and software upgrades.

LIBRARY

head **Mgr. Lucie Trajhanová** ■ lucie.trajhanova@fgu.cas.cz
team members (from the left) Zuzana Nováková, Blanka Liberová

The Library provides access to both traditional paper-based and electronic resources for the whole campus. It provides information services based on the latest information technologies, national and international interlibrary loans, access to printed sources, specialised databases, and on-line journals. The supply of approximately 80,000 books and journals ranks the Library as one of the largest libraries of the scientific institutes of the CAS.

PHYSIOLOGICAL RESEARCH JOURNAL

editor-in-chief **RNDr. Jaroslav Kuneš, DrSc.** 1 jaroslav.kunes@fgu.cas.cz
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team members Edita Balladová, Michal Růžička

Physiological Research is a scientific journal of IPHYS published bimonthly, containing articles on normal and pathological physiology, biochemistry, biophysics, pharmacology, and immunology. It was founded as Physiologia Bohemoslovaca in 1952. Since 1991, it has been published under the title Physiological Research. Its current impact factor is 2.103.

BIOLOGICAL CONTROLS

head Ing. Petr Mlejnek, Ph.D. ■ petr.mlejnek@fgu.cas.cz
team members (from the left) Renata Půtová, Lucie Heppnerová, Světlana Žufanová

We provide comprehensive preclinical and toxicological services in accordance with the principles of Good Laboratory Practice (GLP). We offer various biological and safety studies to our academic and business partners so as to fulfill their research and development goals, including studies under GLP regulations and in accordance with the OECD methods. We are an essential part of the newly established Centre for Preclinical Testing (CPT) within the CAS (www.prekliniky.cz). Our vision is to enable better prospects for the commercialization of potentially therapeutically effective medicinal products to both institutes within the CAS and to other customers from the academic sector and the pharmaceutical industry.

Provided services:
- Preclinical *in vivo* toxicity research testing for safety evaluation of pharmaceutical, biopharmaceutical, and veterinary products (MTD, DRF, pilot studies).
- General safety drug development studies on small laboratory animals (mice, rats, guinea pigs, rabbits), all routes of administration, non-GLP and GLP studies.
- Other customized safety tests and studies on rodents.
- Biodistribution studies in small laboratory animals after single/repeated administration (biological part).

PRECLINICAL TESTING OF POTENTIAL PHARMACEUTICALS

In the period 2017 - 2023, thanks to the involvement of the IPHYS in the AV21 Strategy and the financial support received, we were able to develop a programme of Preclinical testing of potential pharmaceuticals.
The programme reflected the need to use animal experiments as a key element in the development of new medicines, including tests and analyses carried out under GLP (GLP - Good Laboratory Practice) conditions. Laboratory animals are used exclusively for studies of potentially life-saving drugs and alternative methods are used where possible.

Tested items:
newly developed potential medicinal substances, human and veterinary medicinal products, food supplements, medical devices

Test systems:
mouse, rat, guinea pig, rabbit, (mini-pig in collaboration with Pigmod centre).

The Programme resulted in the establishment and construction of the Preclinical Testing Centre.

Participating institutes:
- Institute of Molecular Genetics CAS, Czech Centre for Phenogenomics (CCP)
- Institute of Biotechnology CAS
- Institute of Animal Physiology and Genetics CAS, Pigmod Centre

The Preclinical Testing Centre offers and provides a range of testing and analysis and relies on long-term collaboration between institutions. IPHYS holds the certificate "Decision of SÚKL (sukls124283/2016) on the authorization to conduct GLP toxicological studies. Studies and testing can be conducted under GLP or non-GLP regime within the collaborating institutions.

Portfolio of services offered:

Acute toxicity studies, MTD studies	GLP / non-GLP
Repeated substance treatment studies, DRF studies	GLP / non-GLP
PK and ADME (bio-distribution studies)	GLP / non-GLP

Study Proof of Concept (Pharmacology)

In vivo biocompatibility studies (for medical devices)

Toxicology tests - single or repeated administration of substances

Toxicokinetic testing - repeated, precisely timed blood draws

Pharmacological tests - testing the effects of substances

More information:
www.prekliniky.cz

CPT

DEVELOPMENT OF RESEARCH INFRASTRUCTURE

CONSTRUCTION AND TECHNOLOGICAL ADAPTATION OF THE ANIMAL FACILITY






A basic and necessary condition for research activities in the field of biomedicine is the possibility of working on laboratory animals. In the 1960s, a central animal facility was built in Building G to produce laboratory animals and allow experiments on animal models. In order to work with laboratory animals to current standards, Building G required major refurbishment and the installation of new washing technology for the breeding vessels, as well as technology for the distribution of clean and dirty litter. The challenging structural refurbishment itself began in January 2020 and, while sustaining operations in partial wings of the menagerie throughout the refurbishment, was successfully completed with a certificate of occupancy in December 2023. This provided IPHYS with modern facilities for the breeding and housing of laboratory animals. From 2024, its capacity will gradually be used for experiments on laboratory mice and rats, mostly unique models of serious diseases. Modern equipment will enable the characterization of the mechanisms of origin of these diseases and their whole-body manifestations.

HR EXCELLENCE IN RESEARCH AWARD

In 2019, the European Commission awarded IPHYS the prestigious European HR Excellence in Research Award, guaranteed by Euraxess and financially supported by Operational Programme "Research, Development, and Education". Hence IPHYS joined an exclusive group of research institutes and universities that have committed to improving their human resources strategy in accordance with the principles of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.

During the implementation phase of the program, IPHYS focused on two main objectives through the proposed action plan (available on the IPHYS website): (1) the introduction of a recruitment process in accordance with OTM-R, which brings transparency and objectivity to the recruitment process, thereby promoting fairness and increasing applicants' trust, and (2) the enhancement of career development opportunities for researchers, particularly at the postdoctoral stage. As part of the program, IPHYS encouraged employees to gain scientific experience abroad, providing them with better opportunities for independent advancement in research, including the potential to establish their own research groups. In 2024, the HR Award will be renewed based on an evaluation of HR processes at IPHYS and an on-site visit by the European Commission. IPHYS is now preparing a new action plan for the future.

INTELLECTUAL PROPERTY

Significant discoveries achieved at IPHYS are protected by patents and utility models. Also, IPHYS strived for the effective transfer of research results into practice. Currently, 10 granted patents or patent portfolios and 12 registered utility models are being managed. In recent years, scientific teams have preferred to protect technical solutions with utility models because of the faster and more affordable option to protect their results. Most often, IPHYS protects its results together with research partners. In addition to other partners from the Czech Academy of Sciences, there is a clear increase in joint utility models with technical universities. After the end of the program HR Excellence in Research, IPHYS aims to continue to maintain the intellectual property protection agenda at the same level using the processes set up during the program.

IPHYS – IOCB COLLABORATION

IPHYS co-owns the most significant patents or patent portfolios with the Institute of Organic Chemistry and Biochemistry of the CAS (IOCB). Four valid patent portfolios are currently co-registered by these two Institutes. The patent portfolio protecting the result of Lipidated peptides lowering blood glucose levels is one of the most successful research results of both Institutes. In 2017, the cooperating Institutes signed a research, collaboration, and license agreement with a leading global healthcare company, which is testing for a potential pharmaceutical product.

HR EXCELLENCE IN RESEARCH

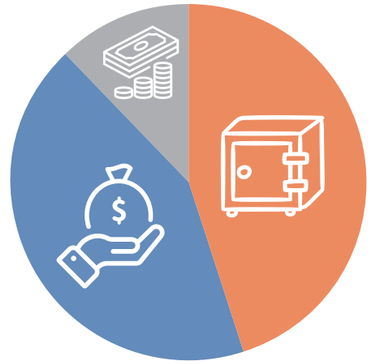
FUNDS AND EMPLOYEES

IPHYS IS SUCCESSFUL IN ATTRACTING RESEARCH FUNDING AT BOTH THE NATIONAL AND INTERNATIONAL LEVEL.

FINANCING BY THE TYPE OF RESOURCES

2023

Grants (43 %)
Institutional (45 %)
Own resources (12 %)



COST STRUCTURE

2023

Personal costs (57 %)
Other costs (43 %)

PROFESSIONAL CATEGORY STRUCTURE OF EMPLOYEES

2023

Scientific positions (199)
Non-scientific positions (122)
Student-doctorand (83)

INVESTMENT FUNDS

2023

Instrument costs (40 %)
Other investment costs (60 %)

NATIONAL COLLABORATIVE PROJECTS

MediAim
A TRANSLATIONAL RESEARCH PROJECT
2015—ongoing

Vision:
Development of new therapeutic agents and strategies to fight certain non-communicable and viral diseases.

Mission:
We aim to understand the essence of diseases and to seek out new strategies for treating cardiovascular, viral, neurodegenerative, and oncologic diseases as well as diabetes and obesity.

Participating organizations
Institute of Physiology CAS; Institute of Organic Chemistry and Biochemistry CAS; Institute for Clinical and Experimental Medicine

The MediAim consortium comprises three distinguished Prague-based research institutes specializing in preclinical and clinical research. Collaboration focuses on experimental, preclinical, translational, and clinical research on the nervous and cardiovascular systems with selected aspects of metabolic research.

The primary objectives are (1) the characterization of common mechanisms of pathogenesis associated with the occurrence of selected non-communicable diseases, (2) the improvement of strategies to prevent, diagnose, and treat these diseases, and (3) the treatment of selected viral diseases. The MediAim project comprises a unique strong link between experimental and clinical research in the Czech Republic as it bridges the gap between basic and translational medical research by facilitating and bolstering multidisciplinary collaboration. The project's added value lies in its embrace of full drug development, from initial synthesis to patented drug candidates. Among first real successes of the research teams involved belong studies focusing on roles of lipidized peptides in weight loss, mitigation of the manifestations of diabetes, and significant slowing of neurodegenerative processes, currently in the stage of preclinical studies on experimental models with very good therapeutic potential for type 2 diabetes using new drugs.

More information:
www.mediaim.cz

funded by the participating organizations

CarDia
NATIONAL INSTITUTE FOR METABOLIC AND CARDIOVASCULAR DISEASE RESEARCH
2022—2025

Vision:
To gain a deeper understanding of the causes of lifestyle diseases, to develop new drugs and to make modern technologies more involved in treatment.

Mission:
We focus on experimental, preclinical, translational and clinical research in lifestyle diseases - diabetes, obesity and cardiovascular disease (CVD).

Participating organizations:
Institute of Clinical and Experimental Medicine; Institute of Physiology CAS; Institute of Organic Chemistry and Biochemistry CAS; Charles University; Masaryk University

Originated from the MediAim project, this National Institute CarDia project is focused on non-communicable diseases, namely CVD, heart failure, type 2 diabetes mellitus and obesity, which are the most common causes of morbidity and mortality in developed countries worldwide. The prevalence of cardiovascular disease and related mortality is higher in the Czech Republic than in most developed EU countries. The cost of treating these complex multifactorial lifestyle diseases and their complications places an extreme financial burden on the entire healthcare system.
The combined efforts of the excellent and complementary participants of the CarDia project creates a comprehensive national research platform (institute) encompassing experimental, preclinical, translational and clinical research activities in the prevention and treatment of CVD, its most common risk factors such as obesity and diabetes, and related chronic complications. This will ultimately help to prevent and treat these diseases more effectively by translating the knowledge gained from experimental research into new treatments and interventions.

More information:
www.cardia.ikem.cz

"Program for the Support of Excellent Research in Priority Areas of Public Interest in Healthcare - EXCELES", funded by the EU through the Recovery and Resilience Instrument - Next Generation EU; reg. no. LX22NPO5104

EPIREC
EPILEPSY RESEARCH CENTRE PRAGUE
2019—ongoing

Vision:
Outstanding epilepsy research — paving the way to a seizure-free life.

Mission:
We aim to transform the lives of people with epilepsy through high-quality research rapidly translated into patient welfare.

Participating organizations:
Institute of Physiology CAS; Second Faculty of Medicine, Charles University, Prague; Motol University Hospital, Prague; Faculty of Electrical Engineering, Czech Technical University, Prague

Epilepsy has been intensely studied for decades, but we still do not understand its mechanisms. New drugs are continually being introduced into clinical practice, but their impact is minimal and the proportion of patients with severe pharmacoresistant epilepsy remains unchanged. Hence, new and effective therapies for epilepsy are urgently needed. In epilepsy, the implementation of disruptive research technologies such as gene therapy, molecular pharmacology, and artificial intelligence could significantly change disease outcomes by improving diagnosis, identifying new causes and discovering novel treatments. The ultimate goal of recently established multidisciplinary epilepsy research center, EpiReC, is to pave the way for the development of new strategies to cure most severe and intractable epilepsies in adults and children and to ensure a rapid laboratory-to-patient journey for new discoveries.

More information:
www.epirec.cz

Neur-IN
NATIONAL INSTITUTE FOR NEUROLOGICAL RESEARCH
2022—2025

Vision:
To support multidisciplinary research into neurological diseases in which neurodegeneration plays a significant role.

Mission:
We search the new discoveries about the brain and nervous system and to use them to reduce the burden of neurological diseases and improve the quality of life of the affected population.

Participating organizations
St. Anne's University Hospital, Brno; Masaryk University, Brno; Charles University, Prague; Palacký University, Olomouc; University of Ostrava, Ostrava; University of Technology, Brno; Czech Technical University, Prague; Institute of Physiology CAS, Prague; Institute of Experimental Medicine CAS, Prague; Institute of Biotechnology CAS, Prague; Institute of Scientific Instruments CAS, Brno

Neurological disorders are the most common cause of disability and the second most common cause of death. In connection with the aging of the population, there is also a worldwide increase in the incidence of neurodegenerative diseases. At the same time, the details of the causes and development of these diseases are often unknown and there is no preventive or causative therapy for them either. The health and economic impact of neurodegenerative diseases on our society will thus be likely increasing. Neur-IN responds to current needs and, through the integration of the efforts of top scientists, will contribute to mitigating the negative effects of neurodegeneration on society and the economy.
Over 250 preclinical and clinical researchers of eleven scientific research and clinical centres and universities are involved in Neur-IN participating in multidisciplinary research of neurodegeneration in a number of neurological diseases. In addition to the two notorious neurodegenerative diseases with a dramatically increasing prevalence of Alzheimer's and Parkinson's disease, Neur-IN also focusses on other neurological diseases in which neurodegeneration plays a significant role (for example, neurodevelopmental diseases, epilepsy, multiple sclerosis).

More information:
www.ninr.cz

"Program for the Support of Excellent Research in Priority Areas of Public Interest in Healthcare - EXCELES", funded by the EU through the Recovery and Resilience Instrument - Next Generation EU; reg. no LX22NPO5107

COLLABORATIONS

MOST OF IPHYS RESEARCH IS CONDUCTED IN THE FRAMEWORK OF DOMESTIC AND INTERNATIONAL COLLABORATION.

Among the principal Czech partners of IPHYS belong a number of institutes of the Czech Academy of Sciences, universities, hospitals, and other research institutions. Also, many research collaborations of individual IPHYS laboratories all around the world significantly increase the quality of research at IPHYS. The diagram shows only national and international partnerships based on formal agreements signed between 2019 – 2024.

GERMANY
Charité Universitätsmedizin Berlin

ITALY
University of Padua

JAPAN
National Institute of Informatics

POLAND
Nencki Institute of Experimental Biology

SLOVAKIA
Centre of Experimental Medicine, SAS

SPAIN
University of Málaga

UNITED KINGDOM
University of Central Lancashire of Preston

Medical Research Council

UKRAINE
Kharkiv National Medical University

USA
University of California

University of Arizona

University of Rochester Medical Center

IPHYS

ACADEMY OF SCIENCES
Biology Centre
Institute of Biotechnology
Institute of Physics
Institute of Microbiology
Institute of Experimental Botany
Institute of Experimental Medicine
Institute of Photonics and Electronics
J. Heyrovsky Institute of Physical Chemistry
Institute of Computer Science
Institute of Sociology
Institute of Molecular Genetics
Institute of Macromolecular Chemistry
Institute of Organic Chemistry and Biochemistry
Institute of Scientific Instruments
Institute of Rock Structure and Mechanics

HOSPITALS
University Hospital Hradec Králové
University Hospital Vinohrady
Motol University Hospital
Bulovka Hospital
General University Hospital in Prague
Institute of Clinical and Experimental Medicine
Institute of Endocrinology

UNIVERSITIES
Charles University
Masaryk University
Technical University of Liberec
Palacký University Olomouc
University of Chemistry and Technology
Food Research Institute Prague
Brno University of Technology
Jan Evangelista Purkyně University
Czech Technical University

OTHERS
IOCB Tech
Central European Institute of Technology
National Tissue Centre
National Institute of Mental Health

EUROPEAN PROJECTS

IPHYS PARTICIPATES IN TWO EUROPEAN INFRASTRUCTURES.

CZECH-BIOIMAGING

NATIONAL RESEARCH INFRASTRUCTURE FOR BIOLOGICAL AND MEDICAL IMAGING (MŠMT — LM2023050)

Ten partner institutions are involved in the project, providing open access to 16 leading imaging facilities in Prague, Vestec, Brno, České Budějovice and Olomouc. These core facilities cover all levels of biomedical imaging – from imaging of biomolecules and their interactions, structure and processes in cells and tissues to imaging of organs and whole organisms in both healthy and pathological conditions. The purpose of the project is to combine unique technological equipment for biomedical imaging accessible in the Czech Republic and to provide open access to a wide range of imaging technologies and expertise to national and international scientists from both the public and private sectors via a unified and coordinated logistic approach. The strength of the Czech-BioImaging is the unique combination of open access to top available equipment, extensive expertise in imaging, organisation of annual theoretical and practical courses and close cooperation with industry.

Scientific coordinator:
Ing. Daniel Hadraba, Ph.D.
(Laboratory of Biomathematics)

IPHYS Bioimaging facility provides service in the areas of image acquisition and image analysis. The facility operates nine high-end light microscopy and medical imaging systems. The facility excels in providing customised solutions to researches especially in label-free microscopy, correlative microscopy, multiphoton microscopy and data analysis. The facility currently works on its modernisation as being included in follow-up OP JAK infrastructure project: Modernisation of the VVI Czech-BioImaging (CZ.02.01.01/00/23_015/0008205).

More information:
www.czech-bioimaging.cz

CZECH BIOIMAGING
Imaging principles of life

EUROPEAN PEDIATRIC TRANSLATIONAL RESEARCH INFRASTRUCTURE AISBL (EPTRI AISBL)

PAN-EUROPEAN ORGANIZATION

Since developing human beings have very specific needs and there is a serious lack of medicines designed and developed specifically for children and the young in the EU and worldwide, the main aims of the EPTRI consortium are to build a research infrastructure dedicated to pediatric preclinical and translational research of new treatments for children. It focuses on developmental pharmacology, pediatric drug discovery, organ-on-a-chip, and other up-to-date fields of medicine dedicated to children. The work in EPTRI focuses on five domains: Human Development and Paediatric Medicine Discovery; Pediatric Biomarkers and Biosamples; Developmental Pharmacology; Paediatric Medicine Formulations and Medical Devices; Underpinning Medicine Development for Paediatric Clinical Studies.

Scientific coordinator:
Prof. RNDr. Aleš Stuchlík, DSc.
(Laboratory of Neurophysiology of Memory)

IPHYS Laboratories involved in EPTRI: Laboratory of the Neurophysiology of Memory, Laboratory of Developmental Epileptology. The project involves 26 partners from 19 EU and associated countries. IPHYS is included in EPTRI as a top basic and translational medicine center in the Czech Republic. EPTRI has obtained support from the President of the Czech Academy of Sciences, signed Memoranda of Understanding with top-tier institutes in the Czech Republic, got status of AISBL, and applies for various calls from the European Commission.

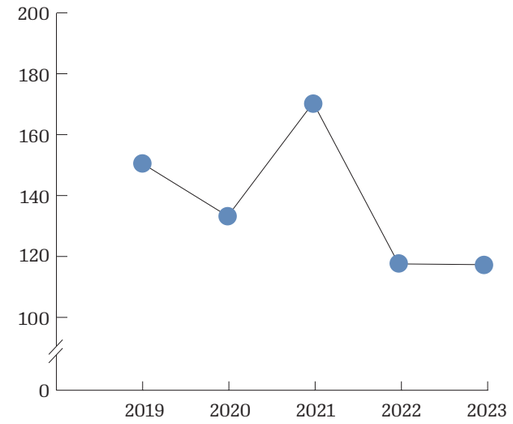
More information:
www.eptri.eu

ePTRI
European Paediatric Translational Research Infrastructure

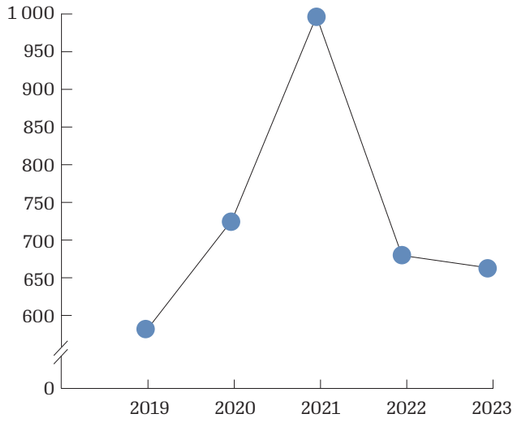
PUBLICATIONS 2019–2023

PUBLICATIONS IN IMPACT FACTOR (IF) JOURNALS IN ASEP DATABASE

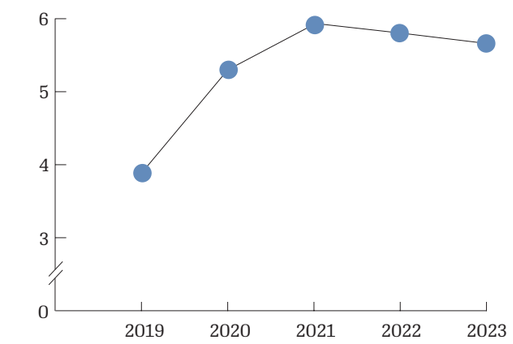
TOTAL NUMBER OF PUBLICATIONS



TOTAL IF



AVERAGE IF PER PUBLICATION



MOST CITED PAPERS – THE TOP TENS

DATA VALID TO 15TH APRIL 2024

Only the publications with the first or corresponding author with the affiliation to IPHYS are listed.

Publications with the highest number of citations over the history of IPHYS:

1. **Dobiášová M.**, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)) (2001) Clinical Biochemistry 34(7):583–588. No. of citations: 733
2. **Bačáková L.**, **Filová E.**, **Pařízek M.**, Ruml T., Švorčík V. Modulation of cell adhesion, proliferation and differentiation on materials designed for body implants (2011) Biotechnology Advances 29(6):739–767. No. of citations: 730
3. **Ježek P.**, **Hlavatá L.** Mitochondria in homeostasis of reactive oxygen species in cell, tissues, and organism (2005) International Journal of Biochemistry and Cell Biology 37(12):2478–2503. No. of citations: 578
4. **Vaněček J.** Cellular mechanisms of melatonin action (1998) Physiological Reviews 78(3): 687–721. No. of citations: 483
5. Hubner N., Wallace C. A., Zimdahl H., Petretto E., Schulz H., Maciver F., Mueller M., Hummel O., Monti J., **Zídek V.**, **Musilová A.**, **Křen V.**, Causton H., Game L., Born G., Schmidt S., Müller A., Cook S.A., Kurtz T. W., Whittaker J., **Pravenec M.**, Aitman T. J. Integrated transcriptional profiling and linkage analysis for identification of genes underlying disease (2005) Nature Genetics 37(3):243–253. No. of citations: 424
6. **Pařízek J.**, **Ošťádalová I.** Protective effect of small amounts of selenite in sublimate intoxication (1967) Experientia 23(2):142–143. No. of citations: 404
7. **Vaněček J.**, **Pavlík A.**, **Illnerová H.** Hypothalamic melatonin receptor sites revealed by autoradiography (1987) Brain Research 435(1–2):359–362. No. of citations: 394
8. **Jiruška P.**, de Curtis M., Jefferys J. G. R., Schevon C. A., Schiff S. J., Schindler K. Synchronization and desynchronization in epilepsy: controversies and hypotheses (2013) Journal of Physiology 591(4):787–797. No. of citations: 383
9. **Vyskočil F.**, **Bureš J.**, Kříž N. Potassium-selective microelectrodes used for measuring extracellular brain potassium during spreading depression and anoxic depolarization in rats (1972) Brain Research 39(1):255–259. No. of citations: 370
10. **Gutmann E.** Neurotrophic Relations (1976) Annual Review of Physiology 38:177–216. No. of citations: 314

Publications with the highest number of citations over the last 10 years:

1. **Bačáková L.**, **Zárubová J.**, **Travníčková M.**, **Musílková J.**, **Pajorová J.**, Slepička P., Kasálková-Slepičková N., Švorčík V., Kolská Z., Motarjemi H., Molitor M. Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells - a review (2018) Biotechnology Advances 36(4):1111–1126. No. of citations: 303
2. **Bačáková L.**, **Pajorová J.**, **Bačáková M.**, Skogberg A., Kallio P., Kolářová K., Švorčík V. Versatile application of nanocellulose: from industry to skin tissue engineering and wound healing (2019) Nanomaterials 9(2):164. No. of citations: 192
3. **Vyklický V.**, **Kořínek M.**, **Smejkalová T.**, **Balík A.**, **Krausová B.**, **Kaniaková M.**, **Lichnerová K.**, **Černý J.**, **Krůšek J.**, **Dittert I.**, **Horák M.**, **Vyklický ml. L.** Structure, function, and pharmacology of NMDA receptor channels (2014) Physiological Research 63(Suppl.1):S191–S203. No. of citations: 188
4. **Bačáková L.**, **Vandrovcová M.**, **Kopová I.**, Jirka I. Applications of zeolites in biotechnology and medicine – a review (2018) Biomaterials Science 6(5):974–986. No. of citations: 178
5. Masoodi M., **Kuda O.**, **Rossmeisl M.**, **Flachs P.**, **Kopecký J.** Lipid signalling in adipose tissue: Connecting inflammation & metabolism (2015) Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids 1851(4):503–518. No. of citations: 157
6. **Flachs P.**, **Rossmeisl M.**, **Kopecký J.** The effect of n-3 fatty acids on glucose homeostasis and insulin sensitivity (2014) Physiological Research 63(Suppl.1):S93–S118. No. of citations: 126
7. **Kuda O.**, **Březinová M.**, **Rombaldová M.**, Slavíková B., Pošta M., Beier P., **Janovská P.**, Veleba J., Kopecký Jr. J., Kudová E., Pelikánová T., **Kopecký J.** Docosahexaenoic Acid–Derived Fatty Acid Esters of Hydroxy Fatty Acids (FAHFAs) With Anti-inflammatory Properties (2016) Diabetes 65(9):2580–2590. No. of citations: 123
8. **Kopová I.**, Stráský J., Harcuba P., Landa M., Janeček M., **Bačáková L.** Newly developed Ti-Nb-Zr-Ta-Si-Fe biomedical beta titanium alloys with increased strength and enhanced biokompatibility (2016) Materials Science & Engineering C-Materials for Biological Applications 60(Mar 1):230–238. No. of citations: 122
9. **Kodedová M.**, **Sychrová H.** Changes in the sterol composition of the plasma membrane affect membrane potential, salt tolerance and the activity of multidrug resistance pumps in *Saccharomyces cerevisiae* (2015) PLoS ONE 10(9):e0139306. No. of citations: 116
10. **Jiruška P.**, Alvarado-Rojas C., Schevon C. A., Staba R., Stacey W., Wendling F., Avoli M. Update on the mechanisms and roles of high-frequency oscillations in seizures and epileptic disorders (2017) Epilepsia 58(8):1330–1339. No. of citations: 112

SELECTED AWARDS

THE WORLD-RENOWNED IPHYS EXPERTS REGULARLY GAIN RECOGNITION FOR THEIR SCIENTIFIC WORK AND RECEIVE MAJOR DOMESTIC AND FOREIGN AWARDS.


1


2


3


4


5

2023

RNDr. Ondřej Kuda, Ph.D. 1	Prize of the Minister of Education for outstanding results in research, experimental development and innovation

2022

Ing. Veronika Palůchová	Josef Hlávka Prize
Prof. MUDr. Přemysl Jiruška, Ph.D.	Award of the Minister of Health for Health Research and Development
Doc. MUDr. Lucie Bačáková, CSc. 2	Praemium Academiae award for outstanding scientific contribution
Ing. Michal Pravenec, DrSc. 3	G. J. Mendel Honorary Field Medal for merit in the biological sciences
Mgr. Dalibor Košek, Ph.D.	Otto Wichterle Prize for the scientific contribution in the field of life sciences
Prof. RNDr. František Vyskočil, DrSc.	Silver Medal of Charles University
MUDr. Jan Kopecký, DrSc.	Jan Evangelista Purkinje Honorary Field Medal for merit in the biomedical sciences

2021

RNDr. Petr Ježek, Ph.D.	Prize of Minister of Education for an exceptional research findings, experimental evolution and innovation in the field of natural sciences
Mgr. Michaela Tencerová, Ph.D.	3rd prize in the project L'Oréal-UNESCO For Women in Science
Prof. RNDr. Helena Illnerová, DrSc.	Silver Medal of the President of the Senate

2020

MUDr. Josef Zicha, DrSc.	Jan Evangelista Purkinje Honorary Field Medal for merit in the biomedical sciences
RNDr. Zdeněk Drahota, DrSc. 5	Jan Evangelista Purkinje Honorary Field Medal for merit in the biomedical sciences
Doc. PharmDr. Alena Sumová, DSc. 5	Vojtěch Náprstek Honorary Prize Medal for merit in the popularization of science

2019

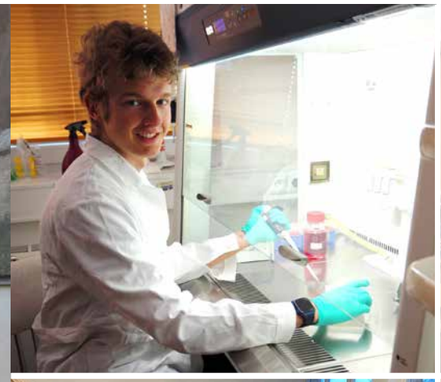
Prof. MUDr. Ladislav Vyklický, DrSc. 4	Prize of the Minister of Health for an exceptional result in research and development
Prof. RNDr. František Kolář, CSc.	Jan Evangelista Purkinje Honorary Field Medal for merit in the biomedical sciences
RNDr. Jaroslav Kuneš, DrSc.	G. J. Mendel Honorary Field Medal for merit in the biological sciences

STUDENTS AT IPHYS

IPHYS PROVIDES TRAINING FOR STUDENTS OF BACHELOR'S, MASTER'S AND DOCTORAL DEGREE PROGRAMMES IN COOPERATION WITH A NUMBER OF CZECH UNIVERSITIES AND INTERNATIONAL INSTITUTIONS.

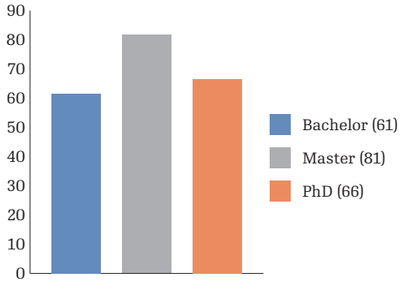
PhD PROGRAMME

Currently, around 80 PhD students are trained at IPHYS. PhD candidates enroll once per year in an open call with a deadline in March (the specific dates and deadlines are present at the IPHYS website). The candidates submit an online application form, in which they provide a detailed CV and research interests and choose up to three IPHYS research groups. The application is then evaluated by the principal investigators and the best candidates are selected to join the IPHYS PhD programme.



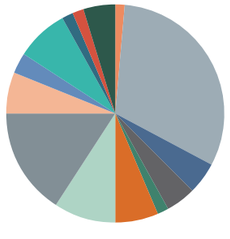
THESES DEFENDED

(2019–2023)



SCIENTIFIC FIELDS (PhD)

(Number of theses)
(2019–2023)



Analytical Chemistry (1)
Animal Physiology (21)
Biochemistry (3)
Developmental Biology (3)
Microbiology (1)
Molecular and Cell Biology, Genetics (4)
Physical Chemistry (6)
Biochemistry and Pathobiochemistry (11)
Human Physiology and Pathophysiology (4)
Medical Biophysics (2)
Neuroscience (5)
Biophysics and Chemical Physics (1)
Biomechanics (1)
Statistics and Mathematical Modelling (3)

PhD STUDENTS ACTIVITIES AND BENEFITS

- **research** in the fields of neuroscience, cardiovascular physiology, and metabolism
- **use of up to date** physiological, biochemical, and molecular biology **methods**
- employment with up to the full time salary and **benefits**
- participation in **regular events** organized for PhD students (seminars, physiological methods course, biannual conference of IPHYS PhD students)
- **advancement report** of the third year PhD students and the **internal PhD thesis** evaluation
- **English** language courses
- modern **campus** with on-site accommodation
- **sports** facilities

OUTREACH ACTIVITIES

IPHYS ORGANIZES NUMBER OF EVENTS DURING ALL THE YEAR.

ACTIVITIES FOR THE PROFESIONAL PUBLIC

Publicly accessible lectures of invited scientists from fields related to IPHYS research as well as those of IPHYS employees are organized weekly and include Bureš's lectures being delivered by first-class invited scientists.

ACTIVITIES FOR THE GENERAL PUBLIC

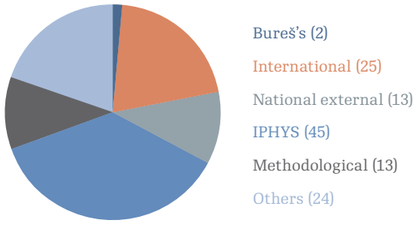
IPHYS research results are regularly presented at various science festivals organized by the Czech Academy of Sciences. In addition, several successful popular-science interactive programmes presenting the physiology of the human body and IPHYS research topics have been implemented recently.





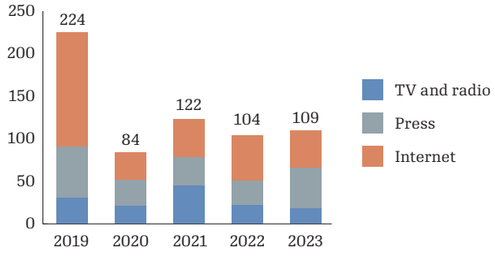

LECTURES FOR PROFESSIONAL PUBLIC

(2019–2023)



MEDIA COVERAGE OF IPHYS

(2019–2023)



BUREŠ'S LECTURE SERIES The lecture series was initiated in 2013 as part of the celebration of 60th anniversary of the establishment of IPHYS. The series is named in the honour of Jan Bureš (1926–2012), an outstanding neuroscientist (Laboratory of Neurophysiology of Memory), who worked at IPHYS from its foundation. Invited speakers were Michael Hastings (Great Britain) and Stefano Schiaffino (Italy) in 2023.

OPEN HOUSE DAY The Laboratories of IPHYS are opened to the public annually in November during the Week of the Czech Academy of Sciences.

PURKINJE CHAMBER OF PHYSIOLOGY An interactive exhibition, which is presented during Open House Day, explains biological clocks, the functioning of muscles, the significance of heartbeat frequency, and uncovers many other functions of the human body.

MEMORY PARK An interactive workshop with eleven unique psychological tests of memory and orientation skills, some of them developed at IPHYS (Laboratory of Neurophysiology of Memory) is offered to the public several times a year and online on IPHYS website.

WEEK OF THE BRAIN IPHYS researchers participate every year in the Week of the Brain – a unique cycle of lectures on the newest discoveries and trends in brain research and neuroscience, which is a part of the worldwide Brain Awareness Week.

THE HUMAN BODY IN HEALTH AND DISEASE Joint presentations of IPHYS's researchers and clinicians presenting collaboration between experts from basic research and clinical specialists, essential for the development of novel diagnostic and therapeutic procedures, are organized twice a year.

SCIENCE EXPO IPHYS participates in the annual Science Expo, a large festival of the Czech Academy of Sciences (45 000 visitors each year). Annualy updated exhibition of IPHYS entitled "Research of diseases from a molecule to the whole body" covers most of IPHYS's research.

OPEN SCIENCE The Czech Academy of Sciences offers student internships every year within the Open Science project, which allow high-school students to access scientific institutes and laboratories and motivate them to follow a career path in sciences. Students involved in the Open Science projects at IPHYS regularly achieve prestigious awards at the final Conference of Open-Science Students.

RESEARCH TOPICS STUDIED AT IPHYS (1954–2024)

*ARTICLES OF IPHYS SCIENTISTS CREATED/PUBLISHED ABROAD

CRITICAL PERIODS OF DEVELOPMENT, PERINATAL PROGRAMMING, LATE EFFECTS OF EARLY INTERVENTIONS (1954–2024)

Hahn, Křeček, Koldovský, Houštěk, Kopecký

Hahn P, Křeček J, Křečková J. The development of thermoregulation. I. The development of thermoregulatory mechanisms in young rats. *Physiol Bohemoslov* 1956;5:283–290.

Nováková V, Faltin J, Flandera V, Hahn P, Koldovský O. Effect of early and late weaning on learning in adult rats. *Nature* 1962;193:280.

Kraus M, Křeček J, Popp M. Development of corticosterone production by adrenal gland in normally and prematurely weaned rats. *Physiol Bohemoslov* 1967;16: 120–127.

Hahn P, Koldovsky O. Development of metabolic processes and their adaptation during postnatal life. In: *Physiology and Pathology of Adaptation Mechanisms*, ed. E. Bajusz, Pergamon Press, 1969, pp. 48–74.

Křeček J. The theory of critical developmental periods and post-natal development of endocrine functions. In: *The Biopsychology of Development*, eds E. Tobach et al., Academic Press, New York, 1971, pp. 233–248.

*Hahn P, Kirby L. Immediate and late effects of premature weaning and of feeding a high fat or high carbohydrate diet to weanling rats. *J Nutr* 1973;103: 690–696.

*Coates PM, Brown SA, Sonawane BR, Koldovsky O. Effect of early nutrition on serum cholesterol levels in adult rats challenged with high fat diet. *J Nutr* 1983;113:1046–1050.

*Hahn P. Effect of litter size on plasma cholesterol and insulin and some liver and adipose tissue enzymes in adult rodents. *J Nutr* 1984;114: 1231–1234.

*Koldovský O. Response of the gastrointestinal tract to premature weaning in experimental animals. *Pediatrics* 1985;75:199–206.

Houštěk J, Vízek K, Pavelka S, Kopecký J, Krejčová E, Heřmanská E, Čermáková S. Type II iodothyronine 5'-deiodinase and uncoupling protein in brown adipose tissue of human newborns. *J Clin Endocrinol Metab* 1993;77:382–387.

Pavelka S, Kopecký P, Bendlová B, Štolba P, Vítková I, Vobruba V, Plavka R, Houštěk J, Kopecký J. Tissue metabolism and plasma levels of thyroid hormones in critically ill very premature infants. *Pediatr Res* 1997;42:812–818.

Kus V, Prazak T, Brauner P, Hensler M, Kuda O, Flachs P, Janovska P, Medrikova D, Rossmeisl M, Jilkova Z, Stefl B, Pastalkova E, Drahota Z, Houstek J, Kopecky J. Induction of muscle thermogenesis by high-fat diet in mice: association with obesity-resistance. *Am J Physiol Endocrinol Metab* 2008;295:E356–E367.

MUSCLE PHYSIOLOGY (1954–1979)

Gutmann, Hanzlíková, Hník, Bass, Syrový

Hník P, Jirmanová I, Vyklický L, Zelená J. Fast and slow muscles of the chick after nerve cross-union. *J Physiol* 1967;193:309–325.

Syrový I, Gutmann E. Changes in speed of contraction and ATPase activity in striated muscle during old age. *Exp Gerontol* 1970;5:31–35.

Gutmann E, Hanzlíková V, Vyskočil F. Age changes in cross striated muscle of the rat. *J Physiol* 1971;216:331–343.

Gutmann E, Schiaffino S, Hanzliková V. Mechanism of compensatory hypertrophy in skeletal muscle of the rat. *Exp Neurol* 1971;31:451–464.

Carlson BM, Gutmann E. Development of contractile properties of minced muscle regenerates in the rat. *Exp Neurol* 1972;36:239–249.

Bass A, Gutmann E, Hanzlíková V. Biochemical and histochemical changes in energy supply enzyme pattern of muscles of the rat during old age. *Gerontologia* 1975;21:31–45.

Gutmann E, Carlson BM. Contractile and histochemical properties of regenerating cross-transplanted fast and slow muscles in the rat. *Pflügers Arch* 1975;353:227–239.

Syrový I, Gutmann E. Differentiation of myosin in soleus and extensor digitorum longus muscle in different animal species during development. *Pflügers Arch* 1977;369:85–89.

NEUROTROPHIC EFFECTS IN SKELETAL MUSCLE (1954–1993)

Gutmann, Žák, Vrbová, Beránek, Hník, Syrový, Vejsada, Paleček

Žák R, Gutmann E, Vrbová G. Quantitative changes of muscle proteins after stimulation of the muscle. *Experientia* 1957;13:80–81.

Beránek R, Hník P. Long-term effects of tenotomy on spinal monosynaptic response in the cat. *Science* 1959;130: 981.

Žák R, Gutmann E. Lack of correlation between synthesis of nucleic acids and proteins in denervated muscle. *Nature* 1960;185:766–767.

Gutmann E, Žák R. Nervous regulation of nucleic acid level in cross-striated muscle. Resynthesis of nucleic acids and proteins in normal and denervated muscle. *Physiol Bohemoslov* 1961;10:501–509.

Gutmann E, Sandow A. Caffeine-induced contracture and potentiation of contraction in normal and denervated rat muscle. *Life Sci* 1965;4:1149–1156.

Gutmann E, Melichna J, Syrový I. Contraction properties and ATPase activity in fast and slow muscle of the rat during denervation. *Exp Neurol* 1972;36:488–497.

Carlson BM, Gutmann E. Regneration in free grafts of normal and denervated muscles in the rat: morphology and histochemistry. *Anat Rec* 1975;183:47–62.

Carlson BM, Gutmann E. Regeneration in grafts of normal and denervated rat muscles. Contractile properties. *Pflügers Arch* 1975;353:215–225.

Gutmann E. Neurotrophic relations. *Annu Rev Physiol* 1976;38:177–216.

Vejsada R, Hník P, Navarrete R, Paleček J, Soukup T, Borecka U, Payne R. Motor functions in rat hindlimb muscles following neonatal sciatic nerve crush. *Neuroscience* 1991;40:267–275.

*Vejsada R, Sagot Y, Kato AC. Quantitative comparison of the transient rescue effects of neurotrophic factors on axotomized motoneurons in vivo. *Eur J Neurosci* 1995;7:1081–1015.
*Vejsada R, Tseng JL, Lindsay RM, Acheson A, Aebischer P, Kato AC. Synergistic but transient rescue effects of BDNF and GDNF on axotomized neonatal motoneurons. *Neuroscience* 1998;84:129–139.

MECHANORECEPTORS DEVELOPMENT, MORPHOLOGY AND FUNCTION (1954–2016)

Zelená, Hník, Hudlická, Jirmanová, Soukup, Vejsada

Zelená J. The morphogenetic influence of innervation on the ontogenetic development of muscle spindles. *J Embryol Exp Morphol* 1957;5:283–292.
Zelená J. Development, degeneration and regeneration of receptor organs. *Prog Brain Res* 1964;13:175–213.
Zelená J, Lubińska L, Gutmann E. Accumulation of organelles at the ends of interrupted axons. *Z Zellforsch Mikrosk Anat* 1968;91:200–219.
Hník P, Hudlická O, Kucera J, Payne R. Activation of muscle afferents by nonproprioceptive stimuli. *Am J Physiol* 1969;217:1451–1457.
Jirmanová I, Thesleff S. Ultrastructural study of experimental muscle degeneration and regeneration in the adult rat. *Z Zellforsch Mikrosk Anat* 1972;131:77–97.
Zelená J, Soukup T. Development of muscle spindles deprived of fusimotor innervation. *Z Zellforsch Mikrosk Anat* 1973;144:435–452.
Zelená J, Soukup T. The differentiation of intrafusal fibre types in rat muscle spindles after motor denervation. *Cell Tissue Res* 1974;153:115–136.
Zelená J. The development of Pacinian corpuscles. *J Neurocytol* 1978;7:71–91.
Hník P, Vejsada R, Goldspink DF, Kasicki S, Krekule I. Quantitative evaluation of electromyogram activity in rat extensor and flexor muscles immobilized at different lengths. *Exp Neurol* 1985;88:515–528.
Soukup T, Pedrosa F, Thornell LE. Influence of neonatal motor denervation on expression of myosin heavy chain isoforms in rat muscle spindles. *Histochemistry* 1990;94: 245–256.
Zelená J. *Nerves and Mechanoreceptors: the Role of Innervation in the Development and Maintenance of Mammalian Mechanoreceptors*. Chapman and Hall, London, 1994.
Soukup T, Zachařová G, Smerdu V. Fibre type composition of soleus and extensor digitorum longus muscles in normal female inbred Lewis rats. *Acta Histochem* 2002;104:399–405.

SPREADING DEPRESSION (1954–1999)

Bureš, Burešová, Křivánek

Bureš J, Burešová O. The use of Leao spreading depression in the study of interhemispheric transfer of memory traces. *J Comp Physiol Psychol* 1960;53: 558–563.
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Bureš J, Burešová O. Cortical spreading depression as a memory disturbing factor. *J Comp Physiol Psychol* 1963;56: 268–272.
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Gorelova NA, Bureš J. Spiral waves of spreading depression in the isolated chicken retina. *J Neurobiol* 1983;14:353–363.
Hernández-Cáceres J, Macias-González R, Brožek G, Bureš J. Systemic ketamine blocks cortical spreading depression but does not delay the onset of terminal anoxic depolarization in rats. *Brain Res* 1987;437:360–364.

WATER AND ELECTROLYTE METABOLISM, BODY FLUIDS, ION TRANSPORT (1954–2021)

Křeček, Jelínek, Dlouhá, Kuneš, Zicha

Čapek K, Jelínek J. The development of the control of water metabolism. I. The excretion of urine in young rats. *Physiol Bohemoslov* 1956;5:91–96.
Křeček J, Křečková J. The development of the regulation of water metabolism. III. The relation between water and milk intake in infant rats. *Physiol Bohemoslov* 1957;6: 26–34.
Jelínek J The development of the regulation of water metabolism .6. Changes in the volume of cellular and extracellular fluid in the body of the rat during development. *Physiol Bohemoslov* 1961;10:259-266.
Křeček J, Nováková V, Stibral K. Sex differences in the taste preference for a salt solution in the rat. *Physiol Behav* 1972;8:183–188.
Dlouhá H, Křeček J, Zicha J. Postnatal development and diabetes insipidus in Brattleboro rats. *Ann N Y Acad Sci* 1982;394:10–20.
Kuneš J, Štolba P, Pohlová I, Jelínek J, Zicha J. The importance of endogenous digoxin-like factors in rats with various forms of experimental hypertension. *Clin Exp Hypertens A* 1985;7:707–720.
Zicha J, Duhm J. Kinetics of Na^+ and K^+ transport in red blood cells of Dahl rats. Effects of age and salt. *Hypertension* 1990;15:612–627.
Zicha J, Negrin CD, Dobešová Z, Carr F, Vokurková M, McBride MW, Kuneš J, Dominiczak AF. Altered Na^+-K^+ pump activity and plasma lipids in salt-hypertensive Dahl rats: relationship to Atp1a1 gene. *Physiol Genomics* 2001;6:99–104.
Zicha J, Kuneš J, Devynck MA. Abnormalities of membrane function and lipid metabolism in hypertension. *Am J Hypertens* 1999;12:315–331.

TOXIC EFFECTS OF MERCURY AND CADMIUM (1956–1976)

Pařízek

Pařízek J, Záhoř Z. Effect of cadmium salts on testicular tissue. *Nature* 1956;177:1036.
Pařízek J. The destructive effect of cadmium ion on testicular tissue and its prevention by zinc. *J Endocrinol* 1957;15:56–63.
Pařízek J. Sterilization of the male by cadmium salts. *J Reprod Fertil* 1960;1: 294–309.
Pařízek J. Vascular changes at sites of oestrogen biosynthesis produced by parenteral injection of cadmium salts: the destruction of placenta by cadmium salts. *J Reprod Fertil* 1964;7:263–265.
Pařízek J. The peculiar toxicity of cadmium during pregnancy - an experimental "toxaemia of pregnancy" induced by cadmium salts. *J Reprod Fertil* 1965;9:111–112.

CLINICAL AND TRANSLATIONAL EPILEPTOLOGY (1958–2024)

Servít, Mareš P, Jiruška

Servit Z. Prophylactic treatment of post-traumatic audiogenic epilepsy. *Nature* 1960;188:669–670.
Servit Z, Machek J, Štercová A, Dudáš D, Krištof M, Červenková V. Reflex influences in the pathogenesis of epilepsy in the light of clinical statistics. *Epilepsia* 3: 315–322, 1962.
Hrbek A, Mareš P. Cortical evoked responses to visual stimulation in full-term and premature newborns. *Electroenceph Clin Neurophysiol* 1964;16:575–581.
Servít Z, Musil F. Prophylactic treatment of posttraumatic epilepsy: results of a long-term follow-up in Czechoslovakia. *Epilepsia* 1981;22:315–320.
Jiruska P, de Curtis M, Jefferys JG, Schevon CA, Schiff SJ, Schindler K. Synchronization and desynchronization in epilepsy: controversies and hypotheses. *J Physiol* 2013;591:787–797.
Janca R, Jezdik P, Cmejla R, Tomasek M, Worrell GA, Stead M, Wagenaar J, Jefferys JG, Krsek P, Komarek V, Jiruska P, Marusic P. Detection of interictal epileptiform discharges using signal envelope distribution modelling: application to epileptic and non-epileptic intracranial recordings. *Brain Topogr* 2015;28:172–183.
Jiruska P, Alvarado-Rojas C, Schevon CA, Staba R, Stacey W, Wendling F, Avoli M. Update on the mechanisms and roles of high-frequency oscillations in seizures and epileptic disorders. *Epilepsia* 2017;58:1330–1339.

HIGHER BRAIN FUNCTIONS (1958—2000)

Radil, Bohdanecký, Indra, Mates

Lánský P, Radil T. Statistical inference on spontaneous neuronal discharge patterns. I. Single neuron. *Biol Cybern* 1987;55:299–311.
Paus T, Babenko V, Radil T. Development of an ability to maintain verbally instructed central gaze fixation studied in 8- to 10-year-old children. *Int J Psychophysiol* 1990;10:53–61.
Franěk M, Mates J, Radil T, Beck K, Pöppel E. Finger tapping in musicians and nonmusicians. *Int J Psychophysiol* 1991;11:277–279.
Mates J, Radil T, Pöppel E. Cooperative tapping: time control under different feedback conditions. *Percept Psychophys* 1992;52:691–704.
Mates J, Müller U, Radil T, Pöppel E. Temporal integration in sensorimotor synchronization. *J Cogn Neurosci* 1994;6:332–340.
Radil T, Wysocki CJ. Spatiotemporal masking in pure olfaction. *Ann N Y Acad Sci* 1998;855:641–644.

LIPID METABOLISM — CHOLESTEROL TRANSPORT (1959—2011)

Hahn, Koldovský, Dobiášová

Drahota Z, P Hahn P, Kleinzeller A, Kostolánská A: Acetoacetate formation by liver slices from adult and infant rats. *Biochem J* 1964; 93:61–65.
Dobiasova M, Hahn P, Koldovsky O. Fatty acid composition in developing rats. Fatty acid composition of triglycerides and phospholipids in some organs of the rat during postnatal development. *Biochim Biophys Acta* 1964;84:538–549.
*Hahn P, Koldovsky O. Late effect of premature weaning on blood cholesterol levels in adult rats. *Nutr Rep Int* 1976;13: 87–91.
*Hahn P, Girard J, Assan R, Frohlich J, Kervran A. Control of blood cholesterol levels in suckling and weanling rats. *J Nutr* 1977;107:2062–2066.
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ONTOGENY OF ANIMAL BEHAVIOUR (1959—1987)

Lát, Nováková, Martínek

Nováková V, Faltin J, Flandera V, Hahn P, Koldovský O. Effect of early and late weaning on learning in adult rats. *Nature* 1962;193:280.
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Sandritter W, Nováková V, Pilny J, Kiefer G. Cytophotometrische Messungen des Nukleisäure und Proteingehaltes von Ganglienzellen der Ratte während der postnatalen Entwicklung und im Alter. *Z Zellforsch Mikrosk Anat* 1967;80:145–152.
Martínek Z, Lát J. Ontogenetic differences in spontaneous reactions of dogs to a new environment. *Physiol Bohemoslov* 1968;17:545–552.
Martínek Z, Lát J. Interindividual differences in habituation of spontaneous reactions of dogs to a new environment. *Physiol Bohemoslov* 1968;17:329–36.
Lát J, Gollová-Hémon E. Permanent effects of nutritional and endocrinological intervention in early ontogeny on the level of nonspecific excitability and on lability (emotionality). *Ann N Y Acad Sci* 1969;159:710–720.
Irmiš F, Radil-Weiss T, Lát J, Krekule I. Inter-individual differences in hippocampal theta activity during habituation. *Electroencephalogr Clin Neurophysiol* 1970;28:24–31.
Nováková V, Sandritter W, Schlueter G. DNA content of neurons in rat central nervous system. *Exp Cell Res* 1970;60:454–6.
Flandera V, Nováková V. The development of interspecies aggression of rats towards mice during lactation. *Physiol Behav* 1971;6:161–164.
Křeček J, Nováková V, Stibral K. Sex differences in the taste preference for a salt solution in the rat. *Physiol Behav* 1972;8:183–188.
Lát J. The analysis of habituation. *Acta Neurobiol Exp (Wars)* 1973;33:771–789.

EPILEPSY AND BRAIN METABOLISM (1960—2024)

Folbergrová, Kubová, Otáhal

Folbergrová J, Passonneau JV, Lowry OH, Schulz DW. Glycogen, ammonia and related metabolities in the brain during seizures evoked by methionine sulphoximine. *J Neurochem* 1969;16:191–203.
Folbergrová J, Zhao Q, Katsura K, Siesjö BK. N-tert-butyl-alpha-phenylnitrone improves recovery of brain energy state in rats following transient focal ischemia. *Proc Natl Acad Sci USA* 1995;92:5057–5061.
Folbergrová J, Haugvicová R, Mareš P. Behavioral and metabolic changes in immature rats during seizures induced by homocysteic acid: the protective effect of NMDA and non-NMDA receptor antagonists. *Exp Neurol* 2000;161:336–345.
Folbergrová J, Druga R, Otáhal J, Haugvicová R, Mareš P, Kubová H. Seizures induced in immature rats by homocysteic acid and the associated brain damage are prevented by group II metabotropic glutamate receptor agonist (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylate. *Exp Neurol* 2005;192:420–436.

Folbergrová J, Ješina P, Kubová H, Druga R, Otáhal J. Status epilepticus in immature rats is associated with oxidative stress and mitochondrial dysfunction. *Front Cell Neurosci* 2016;10:136.
Folbergrová J, Ješina P, Kubová H, Otáhal J. Effect of resveratrol on oxidative stress and mitochondrial dysfunction in immature brain during epileptogenesis. *Mol Neurobiol* 2018;55:7512–7522.
Daněk J, Danačíková Š, Kala D, Svoboda J, Kapoor S, Pošusta A, Folbergrová J, Tauchmannová K, Mráček T, Otáhal J. Sulforaphane ameliorates metabolic changes associated with status epilepticus in immature rats. *Front Cell Neurosci* 2022;16:855161.

CARDIAC DEVELOPMENT AND SENSITIVITY TO HYPOXIA (1963–2024)

Poupa, Ošťádal, Kolář, Ošťádalová

Rakušan K, Poupa O. Changes in the diffusion distance in the rat heart muscle during development. *Physiol Bohemoslov* 1963;12:220–227.
Poupa O, Ošťádal B. Experimental cardiomegalies and "cardiomegalies" in free-living animals. *Ann N Y Acad Sci* 1969;156:445–468.
Dušek J, Ošťádal B, Dušková M. Postnatal persistence of spongy myocardium with embryonic blood supply. *Arch Pathol* 1975;99:312–317.
Šamánek M, Bass A, Ošťádal B, Hučín B, Stejskalová M. Effect of hypoxaemia on enzymes supplying myocardial energy in children with congenital heart disease. *Int J Cardiol* 1989;25:265–269.
Ošťádalová I, Kolář F, Ošťádal B, Rohlíček V, Rohlíček J, Procházka J. Early postnatal development of contractile performance and responsiveness to Ca^{2+}, verapamil and ryanodine in the isolated rat heart. *J Mol Cell Cardiol* 1993;25:733–740.
Ošťádalová I, Ošťádal B, Kolář F, Parratt JR, Wilson S. Tolerance to ischaemia and ischaemic preconditioning in neonatal rat heart. *J Mol Cell Cardiol* 1998;30:857–865.
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Sedmera D, Thompson RP, Kolář F. Effect of increased pressure loading on heart growth in neonatal rats. *J Mol Cell Cardiol* 2003;35:301–309.
Škárka L, Bardová K, Brauner P, Flachs P, Jarkovská D, Kopecký J, Ošťádal B. Expression of mitochondrial uncoupling protein 3 and adenine nucleotide translocase 1 genes in developing rat heart: putative involvement in control of mitochondrial membrane potential. *J Mol Cell Cardiol* 2003;35:321–330.

MITOCHONDRIAL CALCIUM METABOLISM AND GLYCEROL-3-PHOSPHATE DEHYDROGENASE (1963–2020)

Drahota, Houštěk, Mráček

Drahota Z, Carafoli E, Rossi CS, Gamble RL, Lehninger AL. Steady state maintenance of accumulated Ca^{2+} in rat liver mitochondria. *J Biol Chem* 1965;240:12–20.
Drahota Z, Lehninger AL. Movements of H^+, K^+, and Na^+ during energy-dependent uptake and retention of Ca^{2+} in rat live mitochondria. *Biochem Biophys Res Commun* 1965;19:351–356.
Houštěk J, Cannon B, Lindberg O. Glycerol-3-phosphate shuttle and its function in intermediary metabolism of hamster brown adipose tissue. *Eur J Biochem* 1975;54:11–18.
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BONE AND SKIN TISSUE ENGINEERING (2000–2024)

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INFLUENCE OF LIPID-BASED DIETS ON THE PROGRESSION OF ALZHEIMER'S DISEASE (2002–2015)

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NEUROPATHIC PAIN AND NEUROINFLAMMATION (2002–2024)

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STRUCTURAL BIOLOGY OF SIGNAL PROTEINS (2002–2024)

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MORPHINE-INDUCED ALTERATION OF OPIOID- AND TRH-RECEPTORS IN RAT BRAIN (2003–2024)

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REDOX SIGNALLING AND MITOCHONDRIAL PHOSPHOLIPASE (2004–2024)

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3D SUPERRESOLUTION MICROSCOPY OF MITOCHONDRIA AND mtDNA NUCLEOIDS (2008–2024)

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UNIQUE DRUGS FOR OBESITY, TYPE 2 DIABETES AND NEURODEGENERATION (2014–2024)

Kuneš

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Kuda

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