# Laboratory of Metabolism and Bioenergetics

## [Page in Czech]

Welcome to the Laboratory of Metabolism and Bioenergetics!

Our laboratory focuses on mitochondrial function, cancer biology, and cardiovascular research.

#### Mitochondrial Research:

- Iron metabolism
- · Oxidative stress
- Transport of substances across the mitochondrial membrane
- Effects of drugs and environmental factors on mitochondrial function

#### **Cancer Biology:**

- Cultivation of organoids and 2D cell cultures from primary samples obtained from patients with pancreatic adenocarcinoma
- Personalized genotyping, metabotyping, and pharmacotyping of pancreatic tumors from patient biopsies
- · Investigation of tumor cell communication at the cellular level
- · Research on chemotherapeutic resistance

#### Cardiovascular Research:

- · Pathophysiology of atrial fibrillation
- Investigation of the molecular effects of new catheterization methods in arrhythmology
- · Gene transfection of cardiomyocytes

# **Laboratory Activities**

- Cell and tissue cultures (organoids)
- · Confocal and fluorescence microscopy
- Analysis of cellular respiration and metabolism
- · Flow cytometry
- Protein and gene expression analyses
- Electroporation of cell membranes
- · Fluoro/spectro/luminescence analyses
- Statistical analyses in accordance with the principles of open science (Open Science), including sharing experimental data and analytical scripts with a preference for Bayesian inference methods (R-Studio, Matlab)

#### Our team:

# The head of the lab:

prof. MUDr. Jan Trnka, Ph.D., M.Phil., M.Scjan.trnka@lf3.cuni.cz ORCID WebofScience

- $\cdot$  a graduate of general medicine at the 3rd Faculty of Medicine, Charles University, with postgraduate studies in biochemistry and the history and philosophy of science at the University of Cambridge, and medical education at Karolinska Institutet in Stockholm
- · head of the Laboratory of Metabolism and Bioenergetics since 2010 and the Institute of Biochemistry, Cell, and Molecular Biology since 2017
- · specializes in mitochondrial function and dysfunction, mitochondria-targeted drugs, tumor tissue metabolism, and Bayesian modeling

#### **Assistant Professors:**

Ing. Stanislava Martínková, Ph.D.Podnadpis Text

- a graduate of the doctoral program in Molecular and Cell Biology and Genetics at the Faculty of Science, University of South Bohemia in České Budějovice
- · specializes in research on pancreatic ductal adenocarcinoma
- · focuses on improving targeted therapy and studying chemotherapeutic resistance in pancreatic tumors
- works with primary 2D and 3D cell cultures, cell lines, performs gene transfection, cloning, confocal and fluorescence microscopy, and measures metabolism, cellular respiration, and protein expression
- · Has experience in molecular and cell biology, biochemistry, including developmental and cancer biology

Mgr. Ivana Fišerová, Ph.D.Podnadpis Text

- a graduate of Animal and Human Physiology at the Faculty of Science, Charles University, and a postgraduate degree in Human Pathophysiology at the 3rd Faculty of Medicine, Charles University
- · specializes in the pathophysiology of cardiovascular diseases
- · focuses on enhancing the safety and effectiveness of cardiac ablation for arrhythmogenic myocardial disorders
- works with cell cultures, performs irreversible electroporation and electrotransfection, operates fluorescence microscopy, measures metabolism and protein expression, and analyzes and visualizes data using Matlab

#### Researchers:

Bc. Jana VorelPodnadpis Text

- a graduate of the bachelor's program in Biochemistry and Biotechnology at the Faculty of Food and Biochemical Technology, University of Chemistry and Technology, currently pursuing a master's degree in Biochemistry
- · specializes in tumor biology metabolism
- · focuses on the influence of the cell cycle on cellular response to chemotherapeutic agents
- $\cdot$  works with cell cultures, pharmacotyping of cell lines and primary cultures, operates fluorescence microscopy and flow cytometry, and measures metabolism and protein expression

# Postgraduate students:

Mgr. Lucie Josefa LamačováPodnadpis Text

- · a graduate of the Organic Chemistry program at the Faculty of Science, Charles University
- · specializes in mitochondria-targeted compounds and iron metabolism
- focuses on studying deferiprone derivatives targeted to mitochondria and their impact on iron metabolism in cancer cells
- works with cell cultures, fluorescence microscopy, measures metabolism and protein expression, HPLC, LC-MS, analyzes and visualizes data using R, conducts Bayesian modeling, and engages in science communication

Mgr. Michal ZuzčákPodnadpis Text

- · a graduate of Molecular Biology at the Faculty of Science, Comenius University in Bratislava
- · specializes in the metabolism of pancreatic tumors
- focuses on the regulatory mechanism of the lactate transporter MCT1 and the influence of nutrients on its function in pancreatic tumors
- works with cell cultures, operates fluorescence microscopy and flow cytometry, and measures metabolism and protein expression

MUDr. Mário BoďoPodnadpis Text

- a graduate of general medicine from the 3rd Faculty of Medicine, Charles University, and a physician at the Internal Clinic of the FNKV and the 3rd Faculty of Medicine, Charles University.
- specializes in the pathophysiology of pancreatic ductal adenocarcinoma.
- focuses on researching the mechanisms of chemotherapeutic resistance in pancreatic ductal adenocarcinoma, particularly on the development of resistance at low concentrations of cytotoxic drugs.
- · works with cell cultures, operates fluorescence microscopy, measures metabolism, cellular respiration, and protein expression.

## **Undergraduate Students:**

Alice Kapáková David Kvapil Kateřina Šmejkalová Tomáš Wolf

#### Alumni:

Mgr. Anežka Kafková, Ph.D. Mgr. Zdeňka Syrová, Ph.D. Mgr. Jana Tůmová (Patková), Ph.D. (2009-2016) Moustafa Elkalaf, MBBCh, Ph.D. (2009-2019)

## **Current Projects:**

- Pharmacotyping, metabotyping, genotyping, and research on chemotherapeutic resistance in pancreatic ductal adenocarcinoma
- 3/2024-12/2028 Public competition of the ZEMĚ II Program Ministry of Agriculture QL24010123 Reproductive disorders in pigs exposure of farms to harmful substances. Co-investigator: Stanislava Martínková
- 2024/2026 GAUK 108624 Mechanisms of chemoresistance development in pancreatic adenocarcinoma at low concentrations of cytostatics. Principal Investigator: Mário Bodo
- UNCE 24/MED/015 Research on the influence of pathophysiological mechanisms in modern cardiovascular disease treatment
- Biophysical and safety aspects of pulsed field ablation (irreversible electroporation) of cardiomyocytes and surrounding tissue in vitro

# **Unique Instruments:**

- Seahorse XFp and XF24 real-time analysis of cellular respiration and anaerobic glycolysis
- TONAGENA electroporation system for electroporation and electrotransfection of adherent cell cultures

### **Collaborations:**

- · MRC Mitochondrial Biology Unit, University of Cambridge
- Internal Clinic of the 3rd Faculty of Medicine, Charles University, University Hospital Královské Vinohrady
- Cardiology Clinic of the 3rd Faculty of Medicine, Charles University, University Hospital Královské Vinohrady
- · Internal Clinic of the 3rd Faculty of Medicine, Charles University, Bulovka Hospital
- Institute of Histology and Embryology, Faculty of Medicine, Masaryk University

- · Faculty of Biomedical Engineering, Czech Technical University in Prague
- Vera Vávrová's Laboratory, Pediatric Clinic of the 2nd Faculty of Medicine, Charles University, and FN Motol
- Institute of Animal Production, Department of Reproductive Biology Regulation of Mammalian Oocyte Maturation
- Institute of Animal Physiology and Genetics, Czech Academy of Sciences, Laboratory of Biochemistry and Molecular Biology of Germ Cells
- · Tonagena Ltd.

#### **Recent Publications:**

Zloh, Miloslav, Patrik Kutilek, Jan Hejda, **Ivana Fiserova**, Jan Kubovciak, Masaaki Murakami, and Andrea Stofkova. 2024. "Visual Stimulation and Brain-Derived Neurotrophic Factor (BDNF) Have Protective Effects in Experimental Autoimmune Uveoretinitis." Life Sciences 355 (October). https://doi.org/10.1016/j.lfs.2024.122996

Acimovic I, Gabrielová V, **Martínková S**, Eid M, Vlažný J, Moravčík P, Hlavsa J, Moráň L, Cakmakci RC, Staňo P, Procházka V, Kala Z, **Trnka J**, Vaňhara P. (2024). Ex-vivo 3D cellular models of pancreatic ductal adenocarcinoma: from embryonic development to precision oncology. Pancreas. 2024 Jul 30. doi: 10.1097/MPA.0000000000002393. Epub ahead of print. PMID: 39074056.

**Fiserova, Ivana**, Ondrej Fiser, Marek Novak, **Jan Trnka, Antonia Gibalova, David Kvapil**, Barbora Bacova, Marek Hozman, Dalibor Herman, Klara Benesova, and Pavel Osmancik. 2024. "Significant Hemolysis Is Present during Irreversible Electroporation of Cardiomyocytes in Vitro." Heart Rhythm. doi: 10.1016/j.hrthm.2024.08.019.

Osmancik, Pavel, Barbora Bacova, Dalibor Herman, Marek Hozman, **Ivana Fiserova**, Sabri Hassouna, Vaclav Melenovsky, Jakub Karch, Jana Vesela, Klara Benesova, and Vivek Y. Reddy. 2024. "Periprocedural Intravascular Hemolysis During Atrial Fibrillation Ablation: A Comparison of Pulsed Field With Radiofrequency Ablation." JACC: Clinical Electrophysiology 10(7):1660–71. doi: 10.1016/j.jacep.2024.05.001.

**Lucie J. Lamačová**, and **Jan Trnka**. 2024. "Chelating Mitochondrial Iron and Copper: Recipes, Pitfalls and Promise." Mitochondrion. Elsevier B.V. <a href="https://doi.org/10.1016/j.mito.2024.101903">https://doi.org/10.1016/j.mito.2024.101903</a>.

Žalmanová T, Hošková K, Prokešová Š, Nevoral J, Ješeta M, Benc M, Yi YJ, Moravec J, Močáryová B, **Martínková S, Fontana J, Elkalaf M, Trnka J**, Žáková J, Petr J. (2023). The bisphenol S contamination level observed in human follicular fluid affects the development of porcine oocytes. Front Cell Dev Biol.Apr 6;11:1145182. doi: 10.3389/fcell.2023.1145182. PMID: 37091980; PMCID: PMC10115966.

**Anežka Kafková**, Lisa Tilokani, Filip Trčka, Veronika Šrámková, Marie Vancová, Tomáš Bílý, Jana Nebesářová, Julien Prudent, and **Jan Trnka**. 2023. "Selective and Reversible Disruption of Mitochondrial Inner Membrane Protein Complexes by Lipophilic Cations." Mitochondrion 68 (January):60–71. https://doi.org/10.1016/j.mito.2022.11.006.

**Fiserova I**, Trinh MD, Elkalaf M, Vacek L, Heide M, **Martinkova S**, Bechynska K, Kosek V, Hajslova J, Fiser O, Tousek P, Polak J. (2022). Isoprenaline modified the lipidomic profile and reduced ?-oxidation in HL-1 cardiomyocytes: In vitro model of takotsubo syndrome. Front Cardiovasc Med. Aug 22;9:917989. doi: 10.3389/fcvm.2022.917989. PMID: 36072861; PMCID: PMC9441769.

Michal Šíma, **Stanislava Martínková, Anežka Kafková**, Jan Pala, and **Jan Trnka**. 2022. "Cell-Tak Coating Interferes With DNA-Based Normalization of Metabolic Flux Data." Physiological Research 71 (4): 517–26. <a href="https://doi.org/10.33549/physiolres.934855">https://doi.org/10.33549/physiolres.934855</a>.

**Michal Zuzčák**, and **Jan Trnka**. 2022. "Cellular Metabolism in Pancreatic Cancer as a Tool for Prognosis and Treatment (Review)." International Journal of Oncology. Spandidos Publications. https://doi.org/10.3892/IJO.2022.5383.

**J. Fontana, S. Martínková**, J. Petr, T. Žalmanová, **J. Trnka**. Metabolic cooperation in the ovarian follicle. Physiol. Res. 69: 33-48, 2020; doi: 10.33549/physiolres.934233

Moráň Lukáš; Pivetta Tiziana; Masuri Sebastiano; Vašíčková Kateřina; Walter Franziska; Prehn Jochen; **Elkalaf Moustafa; Trnka Jan**; Havel Josef; Vaňhara Petr. Mixed copper(ii)-phenanthroline complexes induce cell death of ovarian cancer cells by evoking the unfolded protein response. Metallomics,11,9,1481-1489

Moráň, Lukáš, Tiziana Pivetta, Sebastiano Masuri, Kateřina Vašíčková, Franziska Walter, Jochen Prehn, **Moustafa Elkalaf, Jan Trnka**, Josef Havel, and Petr Vaňhara. 2019. "Mixed Copper(li)-Phenanthroline Complexes Induce Cell Death of Ovarian Cancer Cells by Evoking the Unfolded Protein Response." Metallomics 11 (9): 1481–89. https://doi.org/10.1039/c9mt00055k.