

Metabolism Reprogramming Lab

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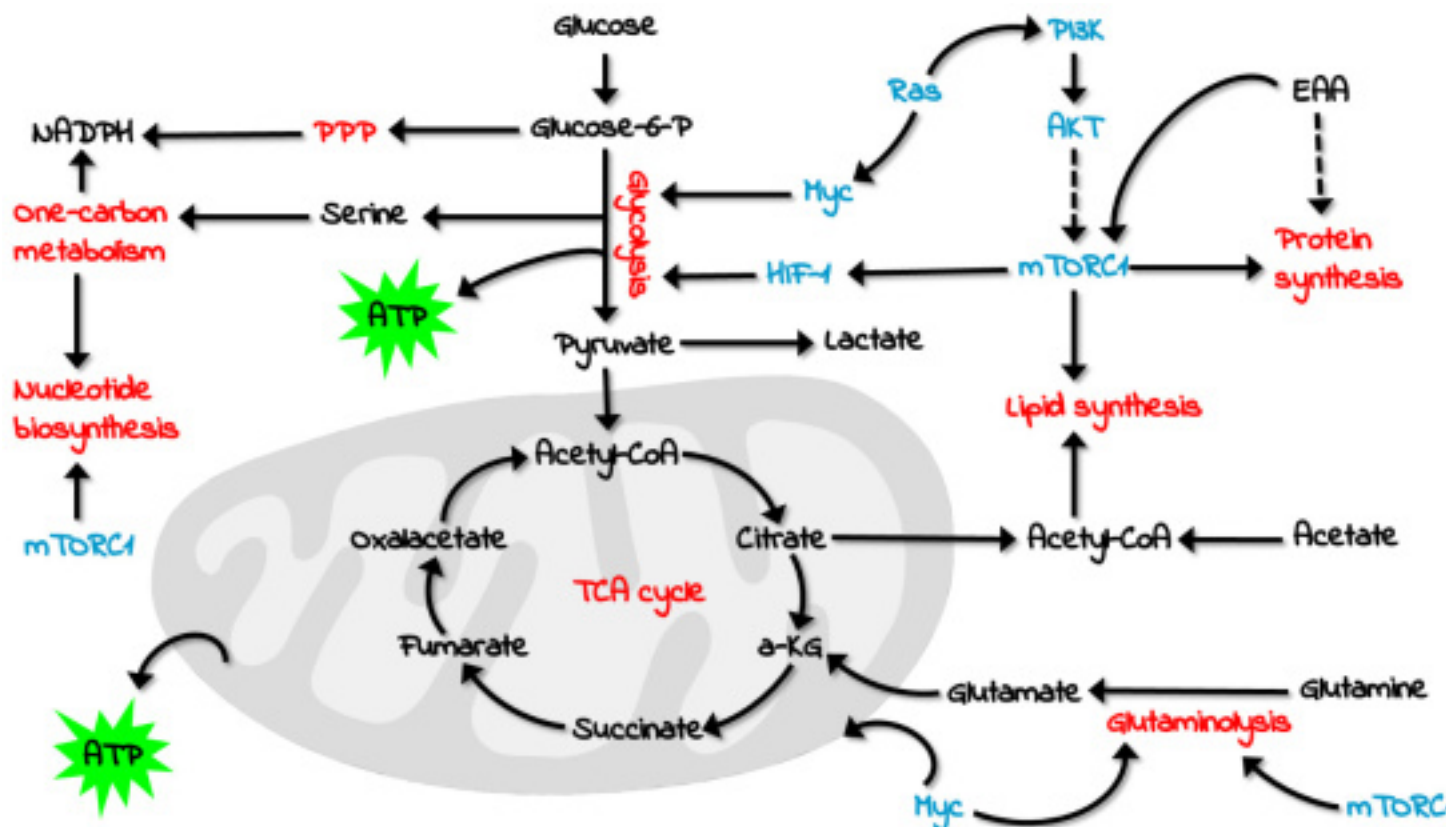


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Aims

We focus on interdisciplinary research of the metabolism of various cells, ranging from terminally differentiated ones to the cancer-transformed cells. We study the abilities of the cell to reprogram the cellular metabolism according to the availability of nutrients and their ability to employ various metabolic enzymes and their individual isoforms. The ability of the cancer cell to reprogram the energy metabolism represents one of key hallmarks of carcinogenesis (Hanahan D. & Weinberg R.A., Cell **144**: 646-674, 2011).



Our aim is to understand the molecular mechanisms of pathological changes in cellular metabolism and to uncover the weaknesses of the cancer metabolism, which could emerge as new targets of anti-cancer therapy. Pathological changes

in metabolism can be represented by both the causes and consequences of common civilization diseases or heritable diseases, including various types of diabetes.

Available positions

Potential bachelor, master and PhD students can choose from currently offered topics. We seek motivated and creative students, who are interested to explore scientifically attractive topics under the guidance of experienced lab workers in a friendly atmosphere. If interested, please send your motivation letter, brief C.V. (in case you worked previously in any lab, include also the recommendation, if possible) to the e-mail of [P. Heneberg](#).

- [We currently offer two Ph.D. positions](#).

We annually offer [SVA topics](#) to students of General Medicine at the Third Faculty of Science.

Newly opened course Precision Medicine

In the European ESF / ERDF project framework, we opened an undergraduate teaching laboratory, which contains state-of-the-art equipment that allows experiments in molecular biology. The annual summer block course for students of General Medicine from the Third Faculty of Medicine and others is organized in the laboratory, where it is possible to get in touch with modern techniques of **precision medicine**.

The course CPVL055 (Precision medicine: Practical course of biomedical research) covers a wide spectrum of approaches ranging from bioinformatics tools, DNA and RNA isolation and analysis, recombinant protein preparation, measurement of effects of DNA variations in clinically important enzymes, tissue culture, selected analytical methods, processing of obtained results, critical interpretation of a selected scientific publication related to the course topic, aiming to identify both reproducible approaches and errors within the examined publication. We present all tasks in a clinical context so that their usefulness in routine contact with patients is evident. The use of precision medicine becomes important primarily in clinical specializations that focus on the treatment of malignancies and hereditary diseases.

Current focus

We focus on the roles of hexokinases in cancer cell metabolism. Depending on the tissue context, human cells may express multiple isoforms of hexokinases. Cancer cells mostly upregulate the expression of hexokinase I or hexokinase II. To study the isoform-specific roles of hexokinases, we use genetic engineering techniques (CRISPR/Cas9, CRISPRi, Sleeping Beauty transposon system, lentiviruses) followed by the biochemical and molecular-biological methods. Using these approaches, we monitor changes at the level of metabolic pathways. We also extend our focus beyond metabolism towards the effects of hexokinases on intracellular signaling pathways that are associated with the development and progression of malignancies.

The laboratory has been approved for the use of genetically modified organisms of level II; the projects may include (optionally) work with laboratory animals or cells of patients and volunteers.

Selected publications

1. Heneberg, P.: Diabetes in stiff-person syndrome. *Trends Endocrinol Metab.* 2023; **34** (10): 640-651. doi: 10.1016/j.tem.2023.07.005.
2. Heneberg, P.: [A large portion of diabetes cases in sub-Saharan African populations with HIV represent drug-induced diabetes](#). *Diabetologia.* 2023; **66** (6): 1162-1164. doi: 10.1007/s00125-023-05904-9
3. Heneberg, P. (2022): [Lactic Acidosis in Patients with Solid Cancer](#). *Antioxid Redox Signal.* **37** (16-18): 1130-1152.
4. Šimčíková, D.; Gardáš, D.; Hložková, K.; Hruza, M.; Žáček, P.; Rob, L.; Heneberg, P. (2021): [Loss of hexokinase 1 sensitizes ovarian cancer to high-dose metformin](#). *Cancer Metab.* **9** (1): **41**.
5. Šimčíková, D.; Heneberg, P. (2019): [Identification of alkaline pH optimum of human glucokinase because of ATP-mediated bias correction in outcomes of enzyme assays](#). *Scientific Reports* **9** (1): 11422.
6. Šimčíková, D.; Heneberg, P. (2019): [Refinement of evolutionary medicine predictions based on clinical evidence for the manifestations of Mendelian diseases](#). *Scientific Reports* **9** (1): 18577.
7. Těšínský, M.; Šimčíková, D.; Heneberg, P. (2019): [First evidence of changes in enzyme kinetics and stability of the glucokinase affected by somatic cancer-associated variations](#). *Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics* **1867** (3): 213-218.
8. Heneberg, P. (2019): [Redox regulation of hexokinases](#). *Antioxidants & Redox Signaling* **30** (3): 415-442.
9. Heneberg, P. (2019): [Comment on Mulukutla et al. Autoantibodies to the IA-2 Extracellular Domain Refine the Definition of "A+" Subtypes of Ketosis-Prone Diabetes](#). *Diabetes Care* **42** (5): e81.
10. Heneberg, P.; Šimčíková, D.; Čecháková, M.; Rypáčková, B.; Kučera, P.; Anděl, M. (2019): [Autoantibodies against ZnT8 are rare in Central-European LADA patients and absent in MODY patients, including those positive for other autoantibodies](#). *Journal of Diabetes and its Complications* **33** (1): 46-52.
11. Heneberg, P.; Riegerová, K.; Říhová, A.; Šimčíková, D.; Kučera, P. (2018): [Updates on the surface antigens of basophils: CD16 on basophils of patients with respiratory or insect venom allergy and the rejection of CD203c and CD63 externalization decoupling by bisindolylmaleimides](#). *Clinical & Experimental Allergy* **49** (1): 54-67.

12. Šimčíková, D.; Kocková, L.; Vackářová, K.; Těšínský, M.; Heneberg, P. (2017): Evidence-based tailoring of bioinformatics approaches to optimize methods that predict the effects of nonsynonymous amino acid substitutions in glucokinase . Scientific Reports 7 (1): 9499.
13. Gandalovičová, A.; Rosel, D.; Fernandes, M.; Veselý, P.; Heneberg, P.; Čermák, V.; Petruželka, L.; Kumar, S.; Moreno, V.S.; Brábek, J. (2017): MIGRASTATICS, the anti-metastatic and anti-invasion drugs: the promise and challenges . Trends in Cancer 3 (6): 391-406.

People – the lab is led jointly by Petr Heneberg & Daniela Šimčíková

Petr Heneberg

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- Member of the Editorial Board of Diabetes Care (2018-2020), PLoS ONE (since 2015), and Anti-Cancer Agents in Medicinal Chemistry (since 2011)
- Principal investigator of projects GA ČR 15-03438Y (2015-2017), AZV 15-32432A (2015-2019), NU23-06-00045 (2023-2026), GA ČR P301/12/1686 (2012-2014), IGA MZ ČR NT13663-3 (2012-2014)

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- Principal investigator of projects GA UK 1428218 (2018-2020), EMBO Short-term Fellowship (2019).

Master students

Dominik Gardáš, Tomáš Pelikán, Vojtěch Charvát, and Robert Žak – our students present annually outcomes of their work at the Faculty Student Conference. For example, in 2021, our students achieved the first and second places for their poster presentations, namely Vojta for his poster entitled “Membrane transporter xCT/SLC7A11 is an important regulator of ovarian cancer cell proliferation” and Tomáš for his poster entitled „Expression of glutaminase 1 affects mTOR signaling in the TOV-21 ovarian cancer cell line“. Our students also present their results at international conferences; e.g., in 2021, Dominik presented at the Cold Spring Harbor Laboratory meeting Biology of Cancer: Microenvironment & Metastasis.

Cooperation

- prof. Roman Zchoval (Department of Urology 3FM CU and TUH) – metabolism of clear cell renal cell carcinoma
- prof. Lukáš Rob (Department of Gynecology and Obstetrics 3FM CU and UHKV), dr. Kateřina Hložková (UH Motol, Department of Paediatric Haematology and Oncology) – metabolism of ovarian and endometrial cancer
- dr. Miroslav Veith (Department of Ophthalmology 3FM CU and UHKV), dr. Jaroslava Dusová (Department of Ophthalmology, UH Hradec Králové), dr. Veronika Matušková (Department of Ophthalmology, UH Brno), dr. Jan Němčanský (Department of Ophthalmology, UH Ostrava) – new types of autoantibodies in patients with diabetic macular edema