



The Doctoral School of Exact and Natural Sciences MCB/JCET/Solaris invites applications for the position of a PhD student Offer no 2022-237

"Studies on the role of energy metabolism in the activity and function of blood platelets in murine models of hyperglycaemia and atherosclerosis"

Supervisor: dr hab. Patrycja Kaczara

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Project description:

Thrombosis, which is associated with various cardiovascular diseases, is one of the leading clinical concerns associated with high morbidity and mortality. Importantly, blood platelets in patients with metabolic diseases often exhibit hyperreactivity, leading to an increased risk of cardiovascular events related to thrombosis. Despite antithrombotic treatment, the risk of such events is not eliminated; furthermore, unwanted side effects, such as bleeding, may occur. Platelet aggregation is an energy-demanding process that can be supported by ATP provided by both glycolysis and mitochondrial respiration [1]. Most commonly used antiplatelet drugs are directed toward targets that do not affect energy metabolism, therefore current antiplatelet strategies may not provide optimal inhibition of platelet hyperreactivity. It is known that beyond ATP production, cellular metabolism controls the fate of cells. However, it is not yet clear how the imbalance between the cytosolic and mitochondrial energy metabolism processes affects the activity of blood platelets.

The central hypothesis of the project is that reprogramming platelet energy metabolism enhances the action of selected antiplatelet drugs in *in vivo* models of hyperglycaemia and atherosclerosis. The aim of the project is to explore the metabolic processes responsible for the development of platelet hyperreactivity and to investigate how combined *in vivo* treatment with selected antiplatelet drugs and metabolic inhibitors affects platelet energy metabolism and activity. Pharmacological modulation of metabolic pathways will be a tool for observing changes at the molecular, organellar, and cellular levels by analyzing metabolic fluxes, ROS and calcium signaling, mitochondrial quality control, and platelet function. The results of the project are expected to identify new metabolic targets for the development of innovative antiplatelet therapies that protect against or decrease thrombosis.

- [1] Kaczara et al., ATVB 2020; https://doi.org/10.1161/ATVBAHA.120.314284
- [2] Levoux et al., Cell Metabolism 2021; https://doi.org/10.1016/j.cmet.2020.12.006

To make the application process fast and easy, please follow the rules.

Send your <u>application documents</u> to <u>biomedical.phd@uj.edu.pl</u> and to the Project Manager - dr hab. Patrycja Kaczara: <u>patrycja.kaczara@uj.edu.pl</u>

Application submission deadline: 08.11.2022, noon