 

**Department of Gene Expression, Institute of Molecular Biology and Biotechnology, Faculty of Biology, Adam Mickiewicz University Adam Mickiewicz in Poznań**

**PhD student**

**About the project:**

**Polonez - bis UMO-2021/43/P/NZ4/03118 project " Multiomic level analyses in atypical diabetes patient derived iPSC and pancreatic cells- key to function"**

Diabetes is a metabolic disease characterized by abnormal glucose homeostasis. The glucose levels in blood serum are regulated by coordinated action of pancreatic hormones, with insulin being responsible for glucose uptake by cells in the periphery. The sole source of insulin in humans are pancreatic islet β-cells. Therefore, the insufficient β-cell number or function leads to hyperglycemia, which in turn might develop into diabetes. Diabetes is worldwide burden, affecting more than 400 million of people according to the International Diabetes Federation, and in Poland alone displays an upward trend with 2.8 million (2018). The insulin resistance in the periphery is an additional factor contributing to diabetes severeness, however, more evidence points to β-cells being the key factor in the disease. Multiple factors might affect β-cell number and health as highlighted by various studies over the years. The comprehensive quantitative multiomic analysis at various levels of organization (i.e., global transcriptome, proteome, and metabolome) has not yet been performed. In this proposal, we postulate a multiomic study of transcriptome, proteome, and metabolome to pinpoint the differential changes associated with human β-cell development (Aim 1), and disease (Aim 2). To achieve it, we propose to employ the human induced pluripotent stem cell (hiPSC) pancreatic differentiation model, enabling the recapitulation of the human β-cell development in vitro in stepwise manner, reflecting the key developmental events. Based on previous literature we hypothesize that various stages of development of human β-cells are associated with significant changes at different levels of organization of the cellular “-ome”. By performing the comprehensive multi-level omics investigations, we are expecting to reveal the differentially expressed genes (by RNA-seq), proteins with differential abundance (label-free quantitative proteomics) and differentially regulated metabolites (untargeted metabolomics) and finally the signaling cues behind the development of β-cells. Furthermore, to model human diabetes in vitro, we chose the ketosis prone (KPD) type of diabetes, and we will utilize the hiPSCs derived from a patient with KPD. We have previously performed genetic analysis coupled with preliminary multiomic investigations in β-cells derived from a KPD patient with an unusual clinical course and a potentially functional variant in the PDX1 gene and controls. During differentiation of this patient’s iPSCs through defined cellular stages of the pancreatic lineage, we were able to recapitulate the Leucine hypercatabolism common in KPD patients in pancreatic cells in vitro. In the second aim of the project, we propose to extend these findings, by combining the power of multi-level omics approach (on whole cells and isolated mitochondria), and following the treatment with a common diabetic drug, metformin with rigorous functional assessment in KPD patients’ cells. For comprehensive multiomics integration, in addition to selected bioinformatic platforms we will utilize fuzzy c‐means clustering, in which transcripts, proteins, and metabolites will be assigned clusters based on their abundance patterns and enriched gene ontology and KEGG pathways terms, to pinpoint differentially altered pathways and functional network modules suitable for subsequent functional validations.

With new lines of personalized medicine emerging, there is a growing demand to understand the specific disease mechanisms as well as to identify the prospective biomarkers to stratify patients and to monitor their treatment. The use of multiple omics technologies towards various forms of diabetes carries the potential to address such needs. This project will be performed in close collaboration with the host laboratory of Prof. Malgorzata Borowiak and her team at the Adam Mickiewicz University- Poznan, Poland. She is a world-leading expert in hiPSCs differentiation towards pancreatic β-cells as well as the β-cell biology and function, including diabetes molecular modeling. By combing the expertise of the host institution with the multiomics data integration expertise brought by the PI we propose to extend the available preliminary data and analyze the global changes at RNA, protein and metabolite level in control and patient developing pancreatic cells to build a dynamic map of changes in type 2 diabetes (T2D).

**Requirements:**

● Master's degree in biology or biotechnology

● preferred experience in cell culture, gene editing, molecular biology techniques

● advanced knowledge of the Office package, graphic programs and statistical software.

● excellent communication and writing skills in English

● conscientiousness, good organization of work, availability, mobility

● communication skills, ability to work in a team;

**Task description:**

● participation in research tasks in the Polonez - bis UMO-2021/43/P/NZ4/03118 project " Multiomic level analyses in atypical diabetes patient derived iPSC and pancreatic cells- key to function",

The Candidate for the offered position is expected to actively participate in the implementation of research tasks provided for in the project in cooperation with the Project Manager and other team members,

● designing an experiment, conducting experiments, data acquisition and analysis,

● preparation of figures and manuscripts, sharing data with colleagues,

● dissemination of partial research results (participation in national and international scientific conferences)

● participation in meetings of the research team, as well as in workshops, seminars, trainings and other events taking place as part of the project.

**Type of the NCN call:** Polonez – bis

Deadline for submission of tenders: 09.03.2023, 23:59

Form of submitting offers: email

**Conditions of employment:**

• Scholarship amount: PLN 5,000

• Employment period: 24 months or until the end of the project

• Place of work: Faculty of Biology, Adam Mickiewicz University in Poznań

• Date of settlement of the competition: to 13.03.2023

• Date of starting work: 15.03.2023

**Required documents:**

Persons interested in participating in the competition are asked to submit the following documents:

● CV containing detailed information on the Candidate's scientific achievements to date,

● reference letter of the scientific supervisor, supervisor or other independent researcher;

● scan of the master's degree diploma;

● a signed declaration of consent to the processing of personal data in the text "According to art. 6 section 1 lit. a of the general regulation on data protection of April 27, 2016 (Journal of Laws EU L 119/1 of May 4, 2016), I consent to the processing of personal data other than those indicated in art. 221 of the Labor Code (first name, given names and surname; parents' names; date of birth; place of residence; correspondence address; education; course of previous employment), contained in my job offer for the purposes of current recruitment"

The required documents should be sent to the e-mail address: maciej.lalowski@amu.edu.pl by 09.03.2023. All documents must be attached in PDF format. Incomplete applications, those that do not meet the formal requirements and submitted after the deadline will not be considered.

RODO information clause:

According to Art. 13 of the general regulation on the protection of personal data of April 27, 2016 (Journal of Laws EU L 119 of 04.05.2016), we inform that:

1. The administrator of your personal data is the University of Adam Mickiewicz in Poznań with its registered office at ul. Henryka Wieniawskiego 1, 61–712 Poznań.

2. The personal data administrator has appointed a Data Protection Officer supervising the correctness of personal data processing, who can be contacted via the e-mail address: iod@amu.edu.pl.

3. The purpose of processing your personal data is to carry out the recruitment process for the indicated position.

4. The legal basis for the processing of your personal data is Art. 6 para. 1 lit. a of the general regulation on the protection of personal data of April 27, 2016 and the Labor Code of June 26, 1974 (Journal of Laws of 1998, N21, item 94, as amended).

5. Your personal data will be stored for a period of 6 months from the end of the recruitment process.

6. Your personal data will not be made available to other entities, except for entities authorized under the law. Access to your data will be granted to persons authorized by the Administrator to process them as part of the performance of their official duties.

7. You have the right to access your data and, subject to the law, the right to rectify, delete, limit processing, the right to transfer data, the right to object to processing, the right to withdraw consent at any time.

8. You have the right to lodge a complaint with the supervisory body - the President of the Office for Personal Data Protection, ul. Stawki 2, 00 – 193 Warsaw.

9. Providing personal data is obligatory based on the law, in the remaining scope it is voluntary.

10. Your personal data will not be processed in an automated manner and will not be subject to profiling.

Consent clause for the processing of personal data

According to Art. 6 section 1 lit. a of the general regulation on data protection of April 27, 2016 (Journal of Laws EU L 119/1 of May 4, 2016), I consent to the processing of personal data other than those indicated in art. 221 of the Labor Code (first name, given names and surname; parents' names; date of birth; place of residence; correspondence address; education; previous employment history), contained in my job offer for the purposes of current recruitment.