



The International Institute of Molecular Mechanisms and Machines,

together with

Institute of Biochemistry and Biophysics of the Polish Academy of Sciences

announces the recruitment for the

PhD position

for the implementation of OPUS-22 project financed by the National Science Center entitled: *“Inhibiting the Mitochondrial Intermembrane Space Assembly pathway as a new approach to prevent metabolic reprogramming of therapy-resistant leukemia stem-cells”* (2021/43/B/NZ5/01684)

Project description:

AML is the most common form of acute leukemia in adults: it is responsible for 62% of all leukemia deaths and it has the fifth worst five-year survival by cancer type, after pancreatic, lung, liver and oesophageal cancers. Unfortunately, it is recognized that there is a population of leukemic stem cells (LSCs) which are more resistant to chemotherapy and can survive the consolidation phase leading to a recurrence of the disease.

APE1 is an essential enzyme in the DNA base excision repair (BER) pathway, which is responsible for repairing both nuclear and mitochondrial oxidative DNA lesions. APE1 is imported into mitochondria under oxidative stress conditions and the pathway responsible for the entrance of APE1 into the mitochondrial intermembrane space (IMS) is the Mitochondrial Intermembrane Space Assembly (MIA) pathway. Mia40 and ALR represent the central components of the MIA import machinery that uses a redox system to drive cysteine-enriched proteins into the mitochondrial compartment.

This project proposes to develop an innovative strategy to selectively target therapy-resistant LSCs by inhibiting the MIA pathway. To achieve this goal, we will use two parallel strategies to inhibit the MIA pathway: a Mia40 inhibitory peptide-based approach and a *in silico* drug screening approach for the development of small-molecule modulators.

This project will extend our understanding of the role of the MIA pathway in cancer cells' behavior and its role in the metabolic reprogramming of AML therapy-resistant cells, setting the basis for the development of alternative or adjuvant approaches for cancer treatment.

Description of tasks:

The successful candidate will be dealing with the screening and molecular modelling tasks including selected direct experimental testing. Special emphasis will be placed on data wrangling and molecular modelling skills. She/he will make use of computational techniques such as molecular docking, molecular mechanics and dynamics simulations. Finally she/he will be training and testing ML/DL models.

Requirements:

For this position a MSc degree is required with previous experience in bioinformatics and/or structural studies. Additional required skills:

1. Programming skills (preferably Python).
2. Knowledge of basic chemistry and/or computational chemistry will be a bonus.
3. Cheminformatics skills (rdkit, openbabel, Knime, etc) will be a bonus.
4. Basic knowledge of ML/DL frameworks (Tensorflow and/or PyTorch) will be a bonus.

Conditions of employment:

- Full-time employment for **36 months**; Participation in doctoral studies
- The anticipated fellowship: **5 000 PLN/month (net)**;
- Place of work: Institute of Biochemistry and Biophysics Polish Academy of Sciences (project consortium member)
- Participation in training activities of EU-funded project MITGEST

Date and form of submitting offers:

October 15th

Required documents:

- CV
- Motivation letter
- Copy of MSc degree diploma

To apply:

<https://forms.gle/vsiR6wscRvM6wazt8>