

"OPEN PHD POSITION"

[26/2023/IGC/PSD] Announcement concerning recruitment to the Poznań Doctoral School of the Institutes of the Polish Academy of Sciences (PDS IPAS) as part of a research project

The Director of the Institute of Human Genetics, Polish Academy of Sciences (IHG PAS), and leader of the current research project, Małgorzata Dawidowska, professor PhD gives notice of an open competition to be held for the position of PhD student-scholarship holder at the Poznan Doctoral School of Institutes PAS, Department of Molecular and Clinical Genetics IHG PAS

Number of vacancies: 1

- I. General information
- 1. Research group: Basic and Translational Hemato-oncology Research Group, Department of Molecular and Clinical Genetics
- 2. Discipline: Medical Science
- 3. Planned remuneration: scholarship to the value of 4300 PLN gross/per month (3800 PLN net /per month)
- 4. Period of involvement in research project: 44 months (extension possible)
- 5. Deadline for submission of documents: 08.10.2023 r.
- 6. Date of announcement: 04.09.2023 r.

The proposed study will be carried out within the OPUS-24 2022/47/B/NZ5/00663

PI – Małgorzata Dawidowska, professor PhD

Project title:

'Unraveling genes and mechanisms underlying relapse of T-cell acute lymphoblastic leukemia'

7. Description of research:

Acute lymphoblastic leukemia (ALL) is the most frequent cancer in children. ALL is treated by multi-drug chemotherapy, which cause serious side effects. Chemotherapy is ineffective in ~20% of children, which is related to drug resistance and relapse (disease recurrence). Relapsed ALL is very difficult to treat and often fatal. The majority of relapses occur in patients with T-ALL subtype (T-cell acute lymphoblastic leukemia). Genetic prognostic markers of the risk of relapse are still missing in T-ALL. Since ALL is the most frequent childhood cancer, it is of highest importance to expand the knowledge about the mechanisms of leukemia recurrence.

Accurate identification of patients at high-risk of relapse, successful relapse prevention and treatment are currently one of the most important challenges in pediatric oncology. There is an urgent need to identify reliable predictors of relapse and to develop novel therapeutic strategies to prevent the relapse. Yet, this requires an in depth understanding of the mechanisms of disease progression and recurrence.

We hypothesize that the mechanisms contributing to T-ALL relapse include: drug-resistance, cell stemness (related to biological plasticity, which enable the cells to 'escape' the anticancer effects of therapy), senescence-like phenotype induced by chemotherapy (related to increased survival potential after recovery

from the senescence-like state) clonal heterogeneity (meaning high diversity among leukemic cells, which make them prone to evolve towards relapse).

We aim to provide novel knowledge on the genes and biological processes, which drive the survival advantage of T-ALL cells and their evolution from diagnosis to relapse. We will use two state of the art methods: 1/ single-cell sequencing of the transcriptome (scRNA-seq) of T-ALL cells obtained from patients' samples at diagnosis and at relapse to investigate clonal heterogeneity and evolution, 2/ genome-wide dropout screen using CRISPR/Cas9 method to identify genes essential for leukemic cells to survive. We will select several genes and verify their importance for T-ALL cells – we will activate or inactivate the expression of these genes in T-ALL cell lines and investigate, how these changes impact the ability of leukemic cells to proliferate and survive. Finally, we will use bioinformatics approaches and publicly available data generated from T-ALL samples to verify, if the alterations of genes' expression observed in our study, are in fact related to the occurrence of T-ALL relapse in other cohorts.

The ultimate goal of the project is to unravel the mechanisms of T-ALL relapse and to pave the way towards precise identification of high risk patients, which will facilitate the determination of the best treatment options to prevent leukemia relapse and improve the survival of T-ALL patients.

Keywords:

T-cell acute lymphoblastic leukemia (T-ALL), relapse, bulk transcriptome sequencing (RNA-seq), single-cell RNA sequencing (scRNA-seq), genome-wide CRISPR/Cas9 screen, clonal evolution

Predicted tasks in the project:

- active participation in the realization of project goals and analysis of obtained results
- presenting at seminars and conferences, participation in writing scientific papers
- supervision of students

Opportunities:

- getting familiar with a wide range of molecular and cellular experimental techniques
- working with an engaged and enthusiastic research team
- participation in national and international trainings, conferences and workshops
- chance for an exciting scientific career

II. Requirements for candidates

- 1. master's degree in molecular biology, biotechnology, genetics or a related field
- 2. knowledge of molecular biology and cancer genetics
- 3. experience in molecular biology techniques: PCR, RT-qPCR, preferably also Western blot and flow cytometry
- 4. knowledge of the basics of genome editing based on CRISPR/Cas9
- 5. knowledge of the basics of transcriptome sequencing techniques (RNA-seq)
- 6. basic experience in cell line culture and cell transfection
- 7. experience in handling DNA and RNA, extraction of nucleic acids and QC
- 8. very good written and oral communication in English
- 8. high motivation and enthusiasm about working in science
- 9. good collaborative and team work skills

III. Required documents

- 1. CV, including research achievements.
- 2. Letter of motivation.
- 3. A copy of the diploma confirming completion of a Master's Studies Programme, or a certificate of their completion (in the case of diplomas issued by foreign institutions, the diploma referred to in article 326 para.2 point 2 or article 327 para. 2 of the Act of 20 July 2018 Law on Higher Education and Science (Journal of Laws of 2018, item 1668 as amended), giving the right to apply for a doctoral degree in the country in which the University of Higher Education issuing the diploma operates. If the candidate does not have the above-mentioned documents, s/he is obliged to provide them before being admitted to Poznań Doctoral School IPAS. More information about foreign diplomas is available at: https://nawa.gov.pl/en/recognition/recognition-for-academic-purposes/applying-for-admission-to-doctoral-studies.
- 4. Contact details of at least one current or previous supervisor or other researcher who has agreed to issue an opinion about the candidate. The opinion should not be included in the application.
- 5. Consent for the processing of candidate's personal data for the purposes of the recruitment process: http://bip.igcz.poznan.pl/wp-content/uploads/2018/10/Zgoda-rekrutacja-consent for the processing.pdf
- 6. Application for admission to the Poznań Doctoral School IPAS, together with a consent to the processing of personal data for the purposes of the recruitment procedure plus a statement on his/her familiarity with recruitment regulations for the Poznań Doctoral School (Application is available on: http://igcz.poznan.pl/en/phd-studies/poznan-doctoral-school-of-institutes-of-pas/recruitment-regulations-for-psd-ipan/)
- 7. Certificates or other documents indicating level of English language proficiency, if the candidate possesses any.

IV. Criteria for the evaluation of candidates

- Candidate's scientific and professional experience based on his/her participation in conferences, workshops, training courses and internships; participation in research and commercial projects; involvement in scientific societies and associations; international and professional mobility; experience in other sectors, including industry.
- 2. Knowledge in the field of molecular biology, in particular related to the subject of the project.
- 3. Candidate's scientific achievements, based on study grades, scientific and popular science publications, scholarships; prizes and awards resulting from research carried out; student activity or other achievements.
- 4. Communication skills in English.

V. Announcement of results

Up to 30 days after the deadline of documents submission.

VI. Additional conditions

 A condition of involvement in the project is the participation in The Poznań Doctoral School of Institutes of the Polish Academy of Sciences (after passing the recruitment procedure). Details of the studies are available on https://igcz.poznan.pl/en/phd-studies/poznan-doctoral-school-of-institutes-of-pas/. Fulfillment of requirements as set out in the Regulations for Granting Scholarships in Research Grants Financed by the National Research Center are available on (https://www.ncn.gov.pl/sites/default/files/pliki/uchwaly-rady/2019/uchwala25 2019zal1 ang.pdf).

VII. Additional information

Address to which documents should be submitted:

by e-mail to the Secretary for Scientific Purposes: **phdstudies@igcz.poznan.pl**. Please, include the number of the announcement: [26/2023/IGC/PSD] in the title of your e-mail.

Additional information is available from:

- Małgorzata Dawidowska: malgorzata.dawidowska@igcz.poznan.pl,
- Secretary for Scientific purposes: phdstudies@igcz.poznan.pl,

Application sent after the deadline will not be considered.

Once the recruitment process is finished, unsuccessful candidates will be informed about the scores they have obtained at each step of evaluation.

Refusal of admission to PDS IPAS takes place by way of an administrative decision. The candidate is entitled to submit a request for reconsideration of the decision to the director of the institute concerned.

Project Leader

Director of the Institute

Rapardo Dealha