

“OPEN PHD POSITION”

(20/2024/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 Deputy Director for Administration on behalf of the Director of the Institute of Human Genetics, Polish Academy of Sciences (IHG PAS),
and leader of the current research project, **Prof. Ewa Ziętkiewicz**, professor IHG
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,
Dept of **Molecular and Clinical Genetics IHG PAS**
Number of vacancies: **1**

I. General information

1. Department in which candidate will work: Dept 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)** before the mid-term evaluation
4. Period of involvement in research project: **48 months**
5. Deadline for submission of documents: **22.09.2024**
6. Date of announcement: **22.09.2024**

The proposed study will be carried out within the **OPUS 2023/49/B/NZ2/01356**

PI – Prof. dr hab. Ewa Ziętkiewicz

Project title: **“Amino acid substitutions as the molecular basis for primary ciliary dyskinesia (PCD)”**

7. Description of research:

Primary ciliary dyskinesia (PCD), with main symptoms of recurrent respiratory infections, male infertility and body symmetry disorders, belongs to a class of inherited diseases known as ciliopathies. In the case of PCD, the disease is related to the disruption of the function of motile cilia - projections extending from the surface of respiratory epithelium cells, as well as sperm and the embryonal node. PCD is a highly heterogeneous disease (over 50 genes published so far). It is caused by recessive mutations in genes encoding proteins that either form structural/functional elements of motile cilia or are necessary during their biogenesis.

PCD is most often caused by defects in the outer dynein arms (ODA), elements of the motile structure of the cilium responsible for generating their movement. To become functional components of the cilium, numerous ODA proteins are preassembled in the cytoplasm with the help of other proteins. Most pathogenic mutations in PCD patients result in the absence of full-length ciliary proteins. Missense mutations, resulting in amino acid (aa) substitutions, are less

common. The mechanisms by which such mutations disrupt ODA assembly, structure, and function in ciliated epithelial cells are poorly understood. DNAI1, a dynein intermediate chain protein, is part of ODA and one of two proteins that initiate the process of ODA initial assembly in the cytoplasm. DNAI1 is one of the eight PCD genes in which mutations are most frequently detected in Polish PCD patients. Among pathogenic DNAI1 variants, aa substitutions are more common than in most other PCD genes. Most of the pathogenic aa substitutions in DNAI1 resulting in lack of ODA occur in exons that encode the important WDR40 domain, known for its function in protein binding.

In the project, we will investigate how aa substitutions in the DNAI1 protein impair its structure, stability and/or protein-protein interactions important for proper initial assembly and functioning of ODA, ultimately leading to changes in structure and defects in ciliary motility. Project stages: 1. In silico prediction of the impact of aa DNAI1 substitutions detected in PCD patients on the structure and stability of the WDR domain. 2. Biophysical analyzes of isolated DNAI1 protein variants to verify in silico models. 3. Effect of aa substitution in DNAI1 on its binding with the known interactor, DNAI2. 4. Effect of amino acid substitution in DNAI1 on the functioning of respiratory epithelial cells. 5. The effect of DNAI1 amino acid substitution on its interactions with other proteins in epithelial cells. The PhD student will be involved in stages 3,4,5.

Keywords:

motile cilia, amino acid variants, WDR domains, protein interactions, respiratory epithelium cell cultures

Predicted tasks in the project:

- active participation in the implementation of the experimental tasks of the grant and the analysis of results using modern techniques (CRISPR, protein expression in mammalian cells, biophysical analyzes of the structure of molecular proteins)
- presenting at seminars and conferences, and participation in writing scientific publications
- supervision of students

Opportunities:

- training in challenging, competitive and advanced research using the latest technologies
- working with a team that is committed and enthusiastic about scientific work
- participation in national and international training and scientific internships
- possibility of rapid development of a scientific career

II. Requirements for candidates

1. Master degree in molecular biology, biotechnology, genetics, medicine or related field.
2. Background in molecular biology and genetics.
3. Experience in RNA, cell culture and molecular biology techniques (experience in CRISPR and protein expression is welcome), ability to search databases.
4. Very good written and oral communication skills in English.
5. Motivation and enthusiasm to work in science.
6. Good collaborative and team work skills.

III. Required documents

1. CV, including research achievements.
2. Cover letter.

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 supervisor or other researcher who has previously agreed to issue an opinion about the candidate. The opinion should not be included in the application.
5. 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-ipas/>)
6. Certificates or other documents indicating level of English language proficiency, if the candidate possesses any.

IV. Criteria for the evaluation of candidates

1. 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. Background in molecular biology.
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 45 days after the deadline of documents submission. Once the recruitment process is finished, unsuccessful candidates will be informed about the scores they have obtained at each step of evaluation.

VI. Additional conditions

1. A condition of involvement in the project is participation in the Institutes of PAS (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.

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: **(20/2024/IGC/PSD)** in the title of your e-mail.

Additional information is available from:

- Leader of the project: prof. Ewa Ziętkiewicz ewa.zietkiewicz@igcz.poznan.pl,
- Secretary for Scientific purposes: phdstudies@igcz.poznan.pl

Application sent after the deadline will not be considered.

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



Deputy Director for Administration

Z-C A DYREKTORA
ds. administracyjnych
Instytutu Genetyki Człowieka PAN

mgr Alicja Radaewska
