INSTITUTE
OF HUMAN GENETICS
POLISH ACADEMY OF SCIENCES

[6/AM/2019]- ANNOUNCEMENT OF THE COMPETITION FOR A POSITION OF A PhD STUDENT – A SCHOLARSHIP HOLDER IN THE DEPARTMENT OF MOLECULAR AND CLINICAL GENETICS

Director of the Institute of Human Genetics, Polish Academy of Sciences (IHG PAS), and the leader of the research project announce an open competition for the position of a PhD student- scholarship holder in the Department of Molecular and Clinical Genetics.

I. General information

1. Institution announcing the competition: Institute of Human Genetics PAS
2. City: Poznań
3. Position: PhD student – scholarship holder
4. Discipline: medical biology
5. Number of vacancies: 1
6. Planned remuneration: scholarship: 4 500 PLN per month
7. Deadline for documents submission: 15.08.2019
8. Address to which documents should be submitted: in person or via registered e-mail to Institute of Human Gentics PAS, ul. Strzeszyńska 32, 60-479 Poznań or by e-mail to: ewa.zietkiewicz@igcz.poznan.pl, with annotation: "OPUS-PhD"
9. Link: http://igcz.poznan.pl/en/
10. Keywords: primary ciliary dyskinesia, motile cilia, ciliopathy, mutations, transcriptome, large-scale genome deletions, aberrant splicing, transcript isoforms, cilia biogenesis; whole genome sequencing, RNAseq, air-liquid interface cultures, cilia imaging
11. Department in which the candidate would work: Department of Molecular and Clinical Genetics
12. A concise description of the scientific research:
    The study is carried out within the **OPUS 16 project**, led by **prof. Ewa Zietkiewicz**
    Project title: **„Unsolved issues in molecular basis of primary ciliary dyskinesia (PCD), a motile ciliopathy: identification of large genomic deletions and transcript isoforms"**

    Ciliopathies are a growing group of inherited diseases caused by dysfunction of primary or motile cilia, evolutionary conserved organelles present on the surface of many eukaryotic cells. During the recent years, intensive research efforts have been directed to understand genetics and molecular basis of ciliopathies, but so far, many areas remain unknown or unexplored. Primary ciliary dyskinesia (PCD), whose symptoms include recurrent airway infections, male infertility and *situs inversus,* is a flagship ciliopathy caused by a hereditary dysfunction of motile cilia. Genetically heterogeneous, PCD is caused by mutations in genes encoding proteins, which either form structural and functional elements of motile cilia, or are essential for cilia formation. Among hundreds of cilia-related genes (ciliome genes), over 40 have been found, mutations in which cause PCD (further referred to as PCD genes). In spite of a substantial progress achieved in elucidating molecular basis of PCD pathogenesis, mutations underlying the disease remain unknown in ~30% of patients. It is still not known, whether this is due to the presence of unknown pathogenic variants, lying outside the usually tested positions in known PCD genes, or to the presence of mutations in yet-unknown PCD genes. Application of modern sequencing techniques, such as whole exome sequencing (WES) technology, to the unsolved PCD cases is not always conclusive – only in some of these patients, biallelic mutations in relevant genes are found. In others, WES screening does not identify any pathogenic variants consistent with PCD. This can be due to the limitations of WES technology, which is not able to detect large genomic insertions/deletions (indels) or aberrant splicing events caused by mutations activating cryptic splice sites in introns. In such cases, other techniques have to be employed to explain the unknown genetic cause of the disease. Large genomic indels can be detected using copy-number sensitive techniques. Some pathogenic variants related to aberrant splicing cannot be identified by the genomic sequence analysis alone, and analysis of the ciliated cells transcriptome (e.g. by RNAseq) needs to be

employed. Proper interpretation of RNAseq findings requires comprehension of the role of ciliary gene transcripts isoforms at different stages of ciliated cells differentiation in healthy individuals. **The aim** of the current project is to extend the current knowledge on molecular causes of PCD. Based on the data from WES-based analysis performed in PCD patients, we will study in detail the genome and transcriptome of those PCD patients, in whom WES did not show conclusive results. **Our goals include**: identification of pathogenic variants resulting in structural changes of the genomic sequence, e.g. large-scale genomic deletions; identification of aberrant splicing events in PCD genes; elucidation of the relevance of different isoforms of PCD genes transcripts at different stages of motile cilia biogenesis.

Research project methodology. Whole genome sequencing will be performed in DNA from selected PCD WES-negative patients. For RNAseq, RNA isolated from the respiratory epithelial (RE) cells from WES-negative PCD patients and from healthy individuals will be used; the cells will be derived from the primary samples and/or differentiated in air-liquid interface (ALI) cultures. Downstream analysis of new mutations, candidate genes and transcripts indicated by the bioinformatic analysis of WGS or RNAseq data will include targeted genome screening, quantitative RT-PCR, cilia imaging in the relevant biological material, and functional analysis of the candidate genes in an animal model (RNAi in planaria).

Predicted tasks in the project:

1. Active participation in the realization of project goals.
2. Supervising master students.
3. Participation in writing scientific papers, presenting results during seminars and conferences.

II. Requirements for candidates

1. Master degree in molecular biology, biotechnology, genetics, medicine or related field.
2. Background in molecular biology.
3. Experience in RNA, DNA, cell culture and molecular biology techniques.
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. Copy of MSc diploma.
4. Minimum two recommendation letters from former supervisors/collaborators and their contact details.
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

IV. Criteria for the evaluation of candidates

1. Experience in laboratory work.
2. Background in molecular biology, especially topics relevant to the project.
3. Research achievements (scientific papers, participation in scientific conferences, activity in student research groups, awards).
4. Opinion about the candidate stated in recommendation letters.
5. Motivation for work in science.
6. Communication skills in English.

V. Announcement of results

Up to 30 days after the deadline of documents submission. Selected candidates will be invited for an interview.

VI. Additional conditions

1. Period of involvement in research project: 01.09.2019-31.08.2022
2. The condition of involvement in the project is participation in the International Doctoral School at IGC PAN (after passing the recruitment procedure; details of the studies are available on the website: http://igcz.poznan.pl/en/scientific-activity/phd-studies) and fulfillment of the requirements described in the Regulations for granting scholarships in research grants financed by National Research Center (https://www.ncn.gov.pl/sites/default/files/pliki/uchwaly-rady/2016/uchwala96_2016-zal1.pdf).

VII. Additional information: ewa.zietkiewicz@igcz.poznan.pl and Human Resources Unit, tel. 61 657 9222

Project Leader

DIRECTOR
Director of the Institute
Institute of Human Genetics
Polish Academy of Sciences

Prof. Michał Witt, MD PhD