Project 9.4 Genomics and Epigenomics of acute myelogenous leukemia (AML)

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WWW: https://bit.ly/3xkvFR7

Background:

Epigenomic changes play a prominent role in acute myelogenous leukemia (AML). Mutations in the methyltransferase DNMT3A and the dioxygenase TET2 are among the most frequent alterations in this type of malignancy. It has been proposed that defects in epigenomics entail DNA repair defects, which in turn lead to karyotype degradation. This contrasts with information from the Cancer Genome Atlas and the COSMIC database, which both identify AML as a typical M-type malignancy, i.e. a malignancy that is driven by mutations, rather than by copy-number variation. However, clinical observation suggests that a considerable fraction of AML patients have karyotype aberrations. In some cases, the chromosomal changes can be drastic and resemble the chromothripsis seen in other malignancies. Highly karyotype aberrant AMLs are poorly characterized. It is not clear whether the spectrum of exome mutations is similar in these leukemias and in M-type leukemias and what drives the karyotype degradation. It is also unclear whether changes in the epigenomic machinery and their possible effects on DNA signaling play a role in this process. We hope to clarify these issues, primarily by sequencing approaches, in collaboration with clinicians in Heidelberg and Dresden (Germany).

Aim:

The aim of the project is to obtain deep sequencing data for AML patients (bulk and single cell). We plan to compare the spectrum of mutations and copy number variation in highly aberrant and normal karyotype AMLs. We plan to test if the spectrum of mutations in the coding genome and tumor clonal histories are similar in the two types of AML. We want to learn if mutations in the epigenomic enzymes cause DNA repair phenotypes, which could ultimately lead to karyotype degradation.

Requirements:

- Master's degree in biology, biochemistry or a related field
- Eligibility for PhD studies in Poland
- Theoretical knowledge of genetics and epigenetics
- Practical experience with cellular fractionation by FACS
- Experience with preparation of libraries for DNA sequencing using Nanopore and Illumina technologies
- Experience with genotyping (high resolution melting analysis)
- Experience with or at least interest in bioinformatic analysis of deep sequencing data
- Written and spoken fluency in English
- Willingness to learn and take new challenges, ability to work independently, analytical thinking
- Good interpersonal skills and a collaborative attitude

Number of positions available: 1

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