Genetiska faktorer i leukemogenes - fokus på GATA2-brist/ Geneettiset tekijät leukememogeneesissä- fokuksessa GATA2-puutos/ Genetic factors in leukemogenesis - focus on GATA2 deficiency

Beräknad varaktighet för projektet

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Forskningshandledare och verksamhetsställe

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Huvudmål för studien

Acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and myelodysplastic syndrome (MDS) are clonal hematological malignancies resulting from multiple genetic alterations in hematopoietic stem cells. These hematopoietic neoplasms involve patients of all ages. Depending on the age and performance status of the patient and subtype of the disease, they still nowadays lead to death in 10-80% of cases despite the given anti-cancer therapy.

Hence, there is a great quest for advancing the use of genetic information in the hematologic clinics to advance the diagnostics and optimal outcome.

Targeted sequencing of somatic genetic alterations is routinely used in leukemia and MDS diagnostics. The methods are however also applicable to germline analyses aiming at recognizing disease predisposition, but still rarely utilized in clinical practice. Notably, the identified hereditary variants may not only increase the risk of malignancy, but also affect the clinical management of the disease (e.g. therapy, selection of an allogeneic donor for transplantation, supportive care or surveillance).

The object of this research proposal is to explore the genetic and cellular mechanisms and sequalae inherited and acquired genetic factors contribute to the development and clinical course of hematological malignancies - especially in the setting of GATA2 deficiency. Our goal is to (further) characterize the GATA2 mutation spectrum and reveal their effects on molecular level using digital transcriptional profiling of single (blood and bone marrow) cells to further understand the varying clinical features associated with the gene defects. We also specifically want to improve the diagnostics of GATA2 deficiency by developing methods aiming at detecting haploinsufficiency, meaning the situation when only one of the gene alleles is expressed due to a defect in regulation of GATA2.