University of Basel

DBM Basel
Department of Biomedicine

MASTER THESIS PROJECT

Functional characterization of RNA-binding proteins in acute myeloid leukemia

Childhood leukemia group,
University Children's Hospital,
Department of Biomedicine (DBM)

Scientific Background

Acute myeloid leukemia (AML) is an aggressive blood cancer that remains incurable for the majority of the patients. Chromosomal translocations leading to expression of fusion proteins like KMT2A-MLLT3 are among the most prevalent disease-driving genetic lesions. Even though compounds have been generated to selectively interfere with such fusion proteins, development of rapid resistance urges for novel strategies of therapeutic intervention. Increasing evidence suggests that the maintenance of KMT2A-MLLT3-driven AML is influenced by RNA-binding proteins (RBPs). RBPs regulate stability and translation efficiency of RNA molecules, some of them could thereby promote pro-leukemic transcription programs. Inactivation of certain RBPs could allow to selectively interfere with the AML-driving transcriptional machinery. In preliminary experiments we developed cellular models in which we can selectively control KMT2A-MLLT3 mRNA or protein levels. We used RNA-interaction capture assays to pulldown cellular as well as KMT2A-MLLT3 fusion mRNA-specific RBPs. We will now implement in silico data mining as well as extensive cellular experiments to identify and functionally validate

Your Contribution

You will genetically inactivate selected RBPs in mouse and human AML models using viral-based Crispr/Cas9 inactivation or by mir-shRNA knockdown. You will study cell growth, colony formation and differentiation of AML cells in vitro and in vivo. You will help to identify the genomic binding sites of selected RBPs by enhanced crosslinking and immunoprecipitation (eCLIP). You can obtain insights into bioinformatic data mining.

During your project you will:

- Establish/maintain mouse & human AML cell lines and primary cells
- Clone, prepare and transduce viral vectors for selective gene inactivation
- Explore AML differentiation by multi-color flow cytometry
- Help to setup and perform eCLIP experiments
- Learn how to compare AML-derived gene/protein expression signatures
- Characterize AML mouse models

Your Profile

You have a B.Sc. degree and some experience in basic molecular/cellular biology techniques. You are a highly-driven, curious, motivated and reliable person with good communication skills (fluent in English is mandatory) aiming to work in a friendly small team.

What do we offer

You can learn a wide range of state-of-the art technologies used in Cancer Research. You will be supervised by a highly talented and motivated PhD student and mentored by the PI. You enjoy all the support that allow you to prepare a Master thesis of high quality and impact.

We welcome you in our team starting from January 2025.

How to apply

Please send a motivation letter, CV and University degree records to:
Rathick Sivalingam, MSc/PhD student (r.sivalingam@unibas.ch) and/or Juerg Schwaller, Prof. (j.schwaller@unibas.ch).