University of Basel

DBM Basel
Department of Biomedicine

MASTER THESIS PROJECT

Characterization of the RNA-binding proteome in KMT2A-MLLT3-driven AML

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 transforming fusion proteins like KMT2A-MLLT3 are among the most prevalent disease-driving genetic lesions. Even though compounds have been generated selectively interfering with such fusion proteins, clinical studies show rapid resistance urging for novel strategies of therapeutic intervention. Increasing evidence suggests that maintenance of the transformed state of KMT2A-MLLT3-driven AML is influenced by RNA-binding proteins (RBPs) controlling stability and translational efficacy. In preliminary experiments we developed cellular models in which we can selectively control KMT2A-MLLT3 mRNA or protein levels. We used RNA-interaction capture (RIC) to pulldown cellular as well as KMT2-MLLT3 fusion mRNAspecific RBPs in these models. We will now implement in silico data mining and cellular experiments to functionally validate RBPs that are critical to maintain the transformed state of KMT2A-MLLT3+ AML.

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 in identifying the genomic binding sites of selected RBPs by enhanced crosslining and immunoprecipitation (eCLIP). You can obtain an insight into comparative bioinformatic data mining. In particular, you will learn:

- How to establish/maintain culture systems for mouse & human AML lines and primary cells
- How to clone, prepare and transduce viral vectors for selective gene inactivation
- How to explore AML differentiation by multi-color flow cytometry and sorting
- How to setup and perform eCLIP experiments
- How to compare AML-derived gene/protein expression signatures
- How to 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.

When Can You Start

Immediately or upon negotiation

How to Apply

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