Project 9.1. Elucidating the epigenetic contribution to cardiovascular lineage specification

Supervisor: Cecilia Winata

Institute: International Institute of Molecular and Cell Biology in Warsaw

Laboratory: Laboratory of Zebrafish Developmental Genomics

WWW: https://zdglab.iimcb.gov.pl/

Background:

One key question in the field of organogenesis relates to how the many types of cells required to make an organ are generated from a pool of progenitor cells with initially similar characteristics. Heart (cardiac) progenitor cells are located close to those that will also generate blood and blood vessels (hemoangiogenic). At very early stages of embryonic development, they express nkx2.5 in common. Subsequently, each type of cells expresses different sets of genes and adopts epigenetic states which signifies their identity. Despite the knowledge that nkx2.5-expressing progenitors could contribute to diverse cell lineage types, several key questions remain unanswered. First, it is unclear at which developmental stage the segregation between cardiac and hemoangiogenic fates begin to occur. Second, the exact pathway and intermediate stages which these progenitors go through during the process of lineage specification are still largely unknown. In addition, despite the knowledge that cardiac transcription factors including Nkx2.5 itself are known to interact with chromatin modifying factors and promote chromatin changes, it is still unknown to what extent epigenetics play a role in driving cell fate decisions at the individual cell level. By tracing the evolution of cellular heterogeneity over time, and at the same time assessing the dynamics of epigenetic landscape at the single cell level, we will elucidate the mechanism of cardiovascular lineage specification.

Aim:

The goal of this project is to elucidate the epigenetic contribution towards the lineage decision of nkx2.5-expressing progenitors into either cardiac or hemoangiogenic lineage. We hypothesize that distinct epigenetic states occur among subpopulations of nkx2.5-expressing progenitors according to their lineage diversification potential. We will profile open chromatin regions at single cell level and determine whether Nkx2.5 plays a role in establishing the epigenetic state by scATAC-seq method (Jia et al., 2018, Nat Commun 9, 4877).

Requirements:

- Master's degree in Biology, Biochemistry, or equivalent
- solid understanding of the principles of molecular biology and genetics
- previous laboratory experience in molecular biology and/or biochemistry techniques
- prior experience in flow cytometry, NGS, and/or working with animal models (mouse or zebrafish), as well as basic programming skills would be an advantage although not essential
- ability to communicate fluently in English and has a collaborative attitude