mgr inż. Eugeniusz Tralle

Cell lineage tracing in zebrafish heart development

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne

Promotor: dr hab. Cecilia L. Winata

Laboratorium Genomiki Rozwoju Danio Pręgowanego
Międzynarodowy Instytut Biologii Molekularnej i Komórkowej w Warszawie

Obrona rozprawy doktorskiej przed Radą Dyscypliny Nauk Medycznych
Warszawskiego Uniwersytetu Medycznego

Warszawa 2023 r.

Abstract

The vertebrate heart is one of the first formed organs during embryonic development. It begins during gastrulation with a formation of bilateral progenitor cell populations organized along the anteroposterior axis into the first and second heart fields. Recently, previously undescribed cardiac progenitor heterogeneity within these heart fields has been reported. I utilize the zebrafish, a potent model organism to study organogenesis, to investigate the questions of when and how this heterogeneity is established. In the first part of this thesis, I describe the current state of knowledge on heart development and its conservation across vertebrates, focusing on the recent reports of heterogeneity in the cells making up the heart. In the second chapter, I describe the first avenue of research I undertook while pursuing the answers to questions posed in this project. I investigate the putative enhancers proximal to the *isl1a*, a key cardiac transcription factor, with the aim of identifying an enhancer sequence capable of driving gene expression in a tissue-specific manner. In the third chapter, I describe a time course single-cell transcriptomic analysis on cells expressing *nkx2.5*, another key cardiac transcription factor, across the timeline of heart development in the zebrafish embryo. I coupled this experiment with a *nkx2.5/nkx2.7* loss of function approach in order to further investigate the role of *nkx2.5* in establishing the heterogeneity of cardiac progenitors. Finally, I establish in our lab a previously published single cell sequencing-compatible lineage tracing system based on CRISPR/Cas9 barcode editing. The results presented in this thesis are part of a larger, ongoing project with single cell data analysis ongoing. Nevertheless, it lays the foundation for future projects focusing on pursuing the questions uncovered by this work.