Project 9.2 Elucidating the contribution of non-coding genomic elements to heart development and disease (NCN/OPUS)

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Background:

Enhancers are a major type of non-coding *cis*-regulatory element in the genome which regulates the expression of their target genes. Through chromatin looping, they are brought into direct physical contact with their target gene promoters and thereby enhance transcription by interacting with the basal transcription machinery. Given its significant role in regulating gene expression, disruption in enhancer function is expected to have similar, or even more serious, consequences as disruption of its target protein-coding genes. The Assay of Transposase-Accessible Chromatin using sequencing (ATAC-seq) is a powerful method to identify active non-coding regulatory elements through profiling of open chromatin regions. At the single cell level, this technique (scATAC-seq) has been widely applied to identify cell-type-specific enhancers with high accuracy.

The zebrafish is a robust and valuable vertebrate model to study heart biology. Despite having only two chambers, the zebrafish heart shows a high degree of conservation to that of mammals in terms of evolutionary origins, physiological function, and developmental mechanism. Its established genetics renders the availability of tools for genetic modification and resources, including heart mutant lines and transgenic lines expressing fluorescent markers for various cardiovascular cell types. It is also a powerful system for *in vivo* functional analysis to elucidate the molecular mechanism of genetic factors, including enhancers. The project plans to employ an unbiased developmental epigenomics analysis in zebrafish to identify enhancers implicated in heart development at the single cell level.

Aim:

The project aims to elucidate the contribution of the noncoding regulatory elements to heart development. We hypothesize that mutations in these regulatory elements could affect heart development as much as mutations in protein coding genes. To test this hypothesis, we will first profile the open chromatin landscape of the developing zebrafish heart at the single cell level and identify putative enhancers specific to various cardiac cell types. We will then validate the activity of selected enhancers in vivo through enhancer activity assays and CRISPR/Cas9-mediated knockout.

Requirements:

- Master's degree in biology, biochemistry or related field,
- good knowledge of the principles of cell and molecular biology, genetics, and/or developmental biology,
- basic hands-on laboratory work experience in one of the fields: molecular biology, genomics, epigenetics, or genetic engineering,
- prior experience or knowledge in next generation sequencing, cell sorting, bioinformatics, and/or working with animal models will be an advantage,
- written and spoken fluency in English,
- willingness to learn and take new challenges, ability to work independently, analytical thinking,
- good interpersonal skills and a collaborative attitude

Number of positions available: 1

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