The role of the sarcomere protein, Titin, in heart development and function. Master thesis project

This project aims to characterize the consequences of mutations in genes identified in human patients with atrial fibrillation.
Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia, affecting more than 7 million people in the USA and Europe alone. The risk of developing AF increases with age.
Genome wide association studies have identified more than 100 loci in the human genome that are associated with AF6 Thus, common genetic variants play a role in the development of this multi-factorial disease (Roselli et al. Nature Genetics, June 2018)
Despite these advances, the knowledge of the underlying mechanisms of AF is still limited.
In a collaboration with the cardiology department at Rigshospitalet are we doing exome and genome sequencing of patients suffering from atrial fibrillation and other arrhythmias, to identify mutations in specific genes that might contribute to the development of cardiac arrhythmias.

Using this approach our group recently demonstrated that mutations in structural genes can predispose for the development of AF (Ahlberg et al. Nature Comm. Nov. 2018).
We have identified several other candidate genes, which we are now in the process of investigating. Among these are transcription factors, involved in cardiac development and function. Using the zebrafish as a model organism, we aim characterize the function of these genes. By using CRISPR/Cas9 modified zebrafish strains, carrying loss of function mutations in genes of interest, will you characterize the molecular and functional consequences of these mutations for heart function. The zebrafish is a small vertebrate model organism with a rapid external development and a high genetic conservation to humans.

We will teach you our state-of-the-art techniques and, to begin with, direct the research. We hope your enthusiasm will enable you to learn fast and quickly become more independent, thereby allowing you to take the research in a direction that interest you.
The project involves developmental biology, functional measurements of heart function and development, molecular biology (cloning, genome editing using CRISPR-Cas9), microscopy and zebrafish husbandry work.

The project is suitable for a Master thesis for students of the study courses human biology, biomedical engineering, molecular biomedicine, biochemistry. An animal experimental course is needed to participate in this project.

Place of project and contact information

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