Cardiac energetics and compartmentalization in heart failure with preserved ejection fraction

Summary

Heart muscle cells are densely packed with structures that divide the intracellular environment into compartments. This compartmentalization is necessary for adequate energy transfer and mitochondrial ATP generation in cardiomyocytes. Earlier studies have suggested that compartmentalization changes in heart failure, but a more detailed picture is missing. Within this project, you will be working with mice and doing experiments to study how the compartmentalization of cardiomyocytes changes in heart failure.

Research field:	Biomedicine and health technology
Supervisor:	Rikke Birkedal Nielsen
Availability:	This position is available.
Offered by:	School of Science Department of Cybernetics
Application deadline:	Applications are accepted between June 01, 2025 00:00 and June 30, 2025 23:59 (Europe/Zurich)

Description

The research

Heart muscles cells are packed with regularly arranged structures such as myofibrils, mitochondria and sarcoplasmic reticulum that compartmentalize the intracellular environment. Studies have suggested that this compartmentalization is necessary for adequate energy transfer within the cell. This, in turn, is crucial for adequate production of ATP to fuel the mechanical work of the cardiomyocytes.

Earlier studies suggested that the compartmentalization of cardiomyocytes changes in heart failure (HF). However, a more detailed picture is missing. This is a topic that deserves renewed attention, as it may lead to new therapeutic targets for HF treatment.

HF is generally divided into HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). HFrEF used to be the dominating form of HF, but as the population ages and the prevalence of obesity and metabolic diseases continues to rise, HFpEF is projected to become the dominant form.

In HFpEF, both metabolism and ultrastructure of the cardiomyocytes change. The metabolism of fatty acids, amino acids, ketones and glucose are reduced, leading to detrimental metabolic inflexibility. Ultrastructurally, the mitochondrial density decreases, and the mitochondria are swollen and fragmented. So far, it is unknown how this affects the energetic compartmentalization and energy transfer.

Within the project, you will assess experimentally how cardiomyocyte structure, compartmentalization, and metabolic regulation change in HFpEF. As we have an interdisciplinary laboratory, you will be working closely with others that use your experimental data for mathematical modeling.

Responsibilities and (foreseen) tasks

- Planning and monitoring how dietary changes lead to the development of HFpEF
- Assessing the severity of HFpEF
- Assessing how HFpEF affects isolated cardiomyocyte
  - Ultrastructure
  - Metabolism
  - Metabolic regulation
  - Compartmentalization
- Data analysis
- Writing academic papers
- Presenting the results in international meetings
- Supervision of junior students

- Participation in the courses given by laboratory staff members

Applicants should fulfil the following requirements:

- a master's degree in relevant field
- a clear interest in the topic of the position
- excellent spoken and written English (minimum C1 level)
- strong writing skills (English) that are compatible with doctoral-level requirements
- capacity to work both independently and as a part of an international team
- capacity and willingness to provide assistance in organizational tasks relevant to the project

The following experience is beneficial:

- Experience with laboratory animals (mice in particular)
- Experience with
  - Heart perfusion
  - Respirometry
  - Microscopy
- Working knowledge of SQL
- Working knowledge of statistical software for data analysis

We offer:

- Fully funded 4-year PhD position in one of the largest universities in Estonia
- The chance to do high-level interdisciplinary research in a supporting environment
- Great opportunities for self-development
- Opportunities for conference visits, research stays and networking with globally leading research centers in the field

About the department

The Laboratory of Systems Biology is a part of the Department of Cybernetics, School of Science, Tallinn University of Technology.

The main aim of the laboratory is to study regulation of intracellular processes and understand functional influences of intracellular interactions.

We use interdisciplinary approaches to tackle questions in cardiac physiology. For that, we have formed a team of researchers with backgrounds in biophysics, biology, and applied mathematics/physics. As a result, we are able to approach scientific questions on different scales, from organ to molecular level, using combinations of different experimental and theoretical techniques. When needed, we find new ways to characterize the data, develop new mathematical models, build new hardware, and program it to carry out novel experimental protocols.

(Additional information)

For further information, please contact Dr. Rikke Birkedal <rikke@sysbio.ioc.ee> or visit https://sysbio.ioc.ee.

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