

2023 Summer Research Fellowship Program Application

Project Description

1. **Project title:** Role of CXCR4 in cardiovascular diseases
2. **Principal Investigator:** Feng Dong, Associate Professor, RGE 234
3. **Abstract of project:**

Previously we found blunted stromal cell-derived factor-1 (SDF-1): CXCR4 axis in diabetes, and our preliminary results show an increase in chronic cardiac myocyte CXCR4 expression in diabetic murine hearts. Moreover, CXCR4 activation in diabetes produces a profound negative inotropic effect (which may seem counterintuitive, but we think is a key adaptation in the diabetic heart). Furthermore, our preliminary results also demonstrate a significantly increased mortality rate of diabetic (high fat, high sugar [HFHS]) mice null for CXCR4 in cardiac myocytes compared to HFHS diabetic wild-type mice. Recently, with our CXCR4 endothelial cell-specific knockout mice, we found that the deletion of CXCR4 in endothelial cells leads to aortic stenosis and left ventricular hypertrophy. This proposal leverages novel models of loss of CXCR4 function in different cells (cardiomyocytes and endothelial cells) to investigate the role of the SDF-1: CXCR4 pathway in cardiovascular diseases and define the mechanisms of how CXCR4 knockout could affect cardiac function in animals with/without diabetes.

4. **The significance of the overall research:**

Upon completion of these studies, we will have determined the importance of the SDF-1: CXCR4 axis in cardiovascular diseases. Novel physiology and treatment strategies will be developed based on a detailed understanding of the mechanisms involved in diabetes and cardiovascular diseases.

5. **The goals and objectives for the summer research project what aspect of the overall research will be the focus of the student's summer research experience? What is the specific research question being addressed by the summer research project?**

The goal of our proposed studies is to define the molecular mechanisms and physiology associated with the development of cardiovascular diseases. The focus of the student's summer research experience will be the scientific research procedures and principles on the cardiovascular complication of diabetes.

The specific research question being addressed by the summer research project are: Determine the role of CXCR4 in cardiac function using our cardiac/EC CXCR4 null mouse models.

6. **The research methods that will be used/learned by the student:**

The experiments will expose students to a variety of cellular, molecular, and biochemical techniques such as the culture of cells, western blot, q-PCR. The students will also be exposed to microscopic techniques and animal surgeries such as confocal microscopy, bone marrow transplantation, and echocardiography.

7. **The proposed methods of data analysis:**

Comparisons between 2 groups will be made with a 2-tailed Student t test. Comparisons among multiple groups will be made with 2-way ANOVA followed by the Tukey post hoc analysis.

8. A statement of how the anticipated findings from the summer research fellow contribute to the success of the overall research being investigated?

The summer research project is a part of an ongoing project in the lab. Our preliminary results show significant changes in SDF-1: CXCR4 axis in diet-induced diabetic mice. Anticipated findings from the summer research will answer an important question: how CXCR4 knockout could affect cardiac function in animals with/without diabetes?

Student Fellow Training/Mentoring Plan (limit of one-half page)

A. Plan for training/mentoring the summer research fellow – individual, group, lab meetings, journal clubs, seminars, etc.

After proper training, the variety of the experiments (cell biology, molecular biology and microscopy) ensures that each student will have unique and specific tasks relating to the overall completion of the project. The students will be taught troubleshooting methods and encouraged to design alternative strategies and hypotheses based on their findings. Students will present their results and updates on their project in formal lab meetings and informally to the PI. The meetings will focus on discussing the relevant literature, improving critical thinking, and oral presentation skills. The students will present their research at NEOMED (Cardiovascular group, IMS Department).

B. Description of resources available.

PI has lab space for students within the open laboratory of the department (4000 sq. ft.). In addition, PI has access to all core facilities, which includes an animal surgery room equipped with ventilators, surgical instruments, echocardiography systems as well as a station for processing and embedding tissue in paraffin; fully functional tissue culture facilities, dark rooms, FACS, RT-PCR, gel imaging and software for analyses. The laboratory is located in a modern complex that houses the Department of Integrative Medical Sciences and Pharmaceutical Science.

C. Site where the research will be conducted.

Most work will be done in RGE 200, and some work will be done in the room RGE 217, 218.