

## 2024 Summer Research Fellowship Program Application

### Project Description

1. **Project title:** Role of CXCR4 in aortic stenosis
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 it is a key adaptation in the diabetic heart). Furthermore, our preliminary results 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. This proposal leverages novel models of loss of CXCR4 function in endothelial cells to investigate the role of CXCR4 in aortic stenosis and define the mechanisms of how CXCR4 knockout could affect cardiac function.

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

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

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 aortic stenosis. The focus of the student's summer research experience will be the scientific research procedures and principles on aortic stenosis.

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

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

The experiments will expose students to various cellular, molecular, and biochemical techniques such as the culture of cells, western blot, and q-PCR. The students will also be exposed to microscopic techniques and animal surgeries such as confocal microscopy 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 that the deletion of CXCR4 in endothelial cells leads to aortic stenosis. Anticipated findings from the summer research will answer an important question: How could the CXCR4 knockout affect aortic stenosis and cardiac function?

**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 project updates in formal lab meetings and informally to the PI. The meetings will discuss 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 include an animal surgery room equipped with ventilators, surgical instruments, and 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 will be done in room RGE 217, 218.