2026 Summer Research Fellowship Program Application

Project Description

1. **Project title**: Molecular and Cellular Mechanisms Driving the Development of Aortic Stenosis
2. **Principal Investigator**: Feng Dong, Associate Professor, RGE 234
3. **Abstract of project**:
   Previously, we identified a blunted stromal cell–derived factor-1 (SDF-1)/CXCR4 signaling axis in diabetes, and our preliminary data indicate that chronic CXCR4 expression is increased in cardiac myocytes from diabetic mice. Although CXCR4 activation in the diabetic heart produces a pronounced negative inotropic effect, we believe this seemingly counterintuitive response represents a key adaptive mechanism. Importantly, our initial studies show that diabetic mice (high-fat, high-sugar diet) lacking CXCR4 specifically in cardiac myocytes exhibit markedly higher mortality than diet-matched wild-type controls. More recently, using our endothelial cell–specific CXCR4 knockout mice, we discovered that loss of CXCR4 in endothelial cells leads to the development of aortic stenosis. This proposal builds on these novel models of CXCR4 deficiency to investigate the role of CXCR4 in aortic valve stenosis and to define the mechanisms by which CXCR4 loss disrupts endothelial and cardiac function.
4. **The significance of the overall research:**
   Upon completion of these studies, we will define the critical contribution of the SDF-1/CXCR4 axis to the pathogenesis of aortic stenosis. This work will establish a mechanistic foundation for identifying novel physiological insights and developing new therapeutic strategies targeting the pathways that drive valve disease.
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 elucidate the molecular mechanisms and physiological processes that drive the development of aortic stenosis. The student's summer research experience will focus on learning and applying scientific principles and experimental approaches relevant to aortic stenosis research.

   The specific research question for the summer project is to determine how loss of CXCR4 affects cardiac function using our endothelial cell–specific CXCR4 knockout mouse models.
6. **The research methods that will be used/learned by the student:**
   The experiments will provide students with hands-on experience in a range of cellular, molecular, and biochemical techniques, including cell culture, Western blotting, and quantitative PCR. Students will also gain exposure to microscopy and in vivo methodologies, such as confocal imaging and echocardiography, as part of their training in interdisciplinary cardiovascular research.

7. **The proposed methods of data analysis:**
   Comparisons between two groups will be assessed using a two-tailed Student's t-test. For analyses involving multiple groups, we will use two-way ANOVA followed by Tukey's post hoc test.
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 part of an ongoing investigation in the lab. Our preliminary data indicate that deletion of CXCR4 in endothelial cells promotes the development of aortic stenosis. The anticipated outcomes of the summer project will address a key question: how does endothelial cell–specific CXCR4 loss influence aortic stenosis and overall 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 receiving appropriate training, students will engage in a variety of experiments spanning cell biology, molecular biology, and microscopy, with each student assigned unique tasks that contribute directly to the overall project. They will be trained in troubleshooting techniques and encouraged to develop alternative strategies and hypotheses based on their experimental findings. Students will regularly present their results and project updates both formally, during lab meetings, and informally to the PI. These meetings will include discussions of relevant literature to enhance critical thinking and oral presentation skills. At the conclusion of the program, students will present their research at the NEOMED Research Symposium.

B. Description of resources available.

The PI's laboratory is located within the department's 4,000 sq. ft. open laboratory space, providing students with a well-equipped and collaborative research environment. In addition, the PI has access to comprehensive core facilities, including an animal surgery suite with ventilators, surgical instruments, and echocardiography systems, as well as a station for tissue processing and paraffin embedding. The laboratory also includes fully equipped tissue culture facilities, dark rooms, FACS, RT-PCR, gel imaging, and analytical software. The lab is situated within a modern complex that houses the Departments of Integrative Medical Sciences and Pharmaceutical Sciences.

C. Site where the research will be conducted.

The majority of the work will be conducted in RGE 200, with additional experiments performed in RGE 217 and RGE 218.