Summer Student Research Program
Project Description

FACULTY SPONSOR’S NAME AND DEGREE: Melissa Rogers, Ph.D.
PHONE: (973) 972 - 2984
DEPARTMENT AND INTERNAL MAILING ADDRESS: Biochemistry/Mol Bio, MSB E627
E-MAIL: rogersmb@umdnj.edu
PROJECT TITLE (200 Characters max):

Conditional knockout of a BMP2 regulatory element conserved between mammals and fishes

HYPOTHESIS:
We hypothesize that deletion of “ultra-conserved sequence (UCS)” in the Bone morphogenetic protein 2 (BMP2) mRNA will disrupt the development of the heart and other organs.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

Bone morphogenetic protein 2 (BMP2) is an essential signal in neonatal development and adult physiology. Abnormal BMP2 levels cause birth defects, including lethal congenital malformations of the heart and other organs. Excessive BMP2 levels in the blood vasculature and coronary valves promote pathological calcification (e.g., atherosclerosis). We discovered a sequence within the regulatory part of the gene that has been largely unchanged since fishes and mammals diverged, the “ultra-conserved sequence” (UCS). The extraordinary conservation of this sequence supports a fundamental role in animal development and function. We discovered that one role is to turn off BMP2 synthesis in clinically relevant cell types (e.g., proepicardium, epicardium, heart valves, and vascular cells).

We have generated a transgenic mouse strain with a Bmp2 gene in which the UCS has been flanked by “loxP” sites. The site-specific recombinase, CRE, can delete any sequence flanked by loxP sites. By breeding the new Bmp2 allele mouse to CRE-synthesizing mouse strains, we can delete the BMP2 UCS in specific tissues and at chosen times. This will help us identify the mechanism by which the UCS influences embryogenesis. Our aim for this summer project is to test how UCS deletion influences heart morphology.

SPONSOR’S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:


IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS? Yes ☐ or No ☐
(IF YES, PLEASE SUPPLY THE GRANTING AGENCY’S NAME)

“BMP2 Gene Regulation in Calcific Aortic Valve Disease”
Multiple Principal Investigators: Melissa B. Rogers, Ph.D. and Douglas Mortlock, Ph.D, Vanderbilt University, equal distribution of effort and funds
Agency: National Heart, Lung, and Blood Institute
Type: Research Grant #1R01HL114751; Period: 07/01/2012 – 06/30/2016
The goal is to understand the transcriptional and post-transcriptional mechanisms that control BMP2 in the developing and adult aortic valves.

“BMP2 Repression and Embryogenesis and Adult Physiology”
Summer Student Research Program
Project Description

Principal Investigator: Melissa B. Rogers, Ph.D.
Agency: The Foundation of UMDNJ and Dean’s Biomedical Research Support Program
Type: Research Grant #PC53-12; Period: 04/01/2012-03/30/2013

This is a seed project to begin testing how a BMP2 regulatory sequence that is extremely conserved between mammals and fishes affects development and function in vivo.

THIS PROJECT IS:  ☐ Clinical   ☑ Laboratory   ☐ Behavioral   ☐ Other

THIS PROJECT IS CANCER-RELATED ☐
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD-RELATED ☑
Please explain Heart, Lung, Blood relevance

Congenital cardiovascular defects occur in a quarter of all infants who die from a birth defect. BMP2 is a critical signal whose concentration influences the carefully shaping of heart valves and the cardiac vasculature. The proposed study will greatly advance our understanding of how BMP2 regulates cell fate determination and tissue organization in the developing heart.

Vascular pathologies associated with atherosclerosis, coronary artery disease, post-angioplasty restenosis, diabetes, hypercholesterolemia, and chronic kidney disease are major causes of stroke, amputation, heart disease, and death. BMP2 is a critical protein whose concentration influences vascular cell behavior. In future studies, this new allele will be used to illuminate the signaling processes that regulate the behavior of vascular cells and potentially reveal novel approaches to preventing and treating these devastating pathologies.

THIS PROJECT EMPLOYS RADIOISOTOPES ☐

THIS PROJECT INVOLVES THE USE OF ANIMALS ☐
PENDING ☐  APPROVED ☑  IACUC PROTOCOL # 12336C0715

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS ☐
PENDING ☐  APPROVED ☑  IRB PROTOCOL # M

THIS PROJECT IS SUITABLE FOR:
UNDERGRADUATE STUDENTS ☐  ENTERING FRESHMAN ☐
SOPHOMORES ☐  ALL STUDENTS ☑

THIS PROJECT IS WORK-STUDY:  Yes ☑ or No ☐

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR
FOR INTERESTED VOLUNTEERS?:  Yes ☑ or No ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
Molecular and cellular techniques. Animal breeding and embryology. Relevance of growth factors to pathologies.