Cardiovascular & Muscle Disease Group

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Project #1
Blood Pressure Circadian Rhythm Disruption in Diabetes

Project #2
Mechanisms of Aortic Aneurysm

Experimental Approaches
- Disease models; Genetic mouse models
- Radiotelemetry measuring mouse blood pressure
- Physiology; Molecular Cell Biology; Pharmacology
Sarcomere level therapies for heart failure

Experiments performed on human cells collected from:
1) patients getting transplants at UK
2) patients getting mechanical pumps
3) organ donors

Animal studies investigating:
1) inherited cardiomyopathies
2) Frank-Starling relationship
3) myosin molecules as drug targets
Consider our lives: from neonates until mature adults
The heart grows proportionally to body size

How does the heart grow?

Can we harness mechanisms of heart growth to apply to develop novel, safe, effective treatments for patients with heart disease?

Techniques, models, & approaches:

- **In vivo** (neonates to adults): Echocardiography & ECG; genetically modified mice – including tissue-restricted, induced KO’s and GFP-fusion protein knock-in
- **In vitro**, live cell recordings, various modes of Ca^{2+} handling, electrophysiology; promoter reporter assays in cardiomyocytes, and cellular structural imaging modes

Andrea, Bryana & Brooke (not pictured: Mihir & Brandon)
Lab interests

• Congenital arrhythmias syndromes
• Ion channel structure & function
• Transcriptional & post-transcriptional regulation of ion channel expression
• Channel folding & transport (trafficking)
• Dogs, running, swimming, & long walks on the beach

Ion channel mutations

Class 1  
- disrupts synthesis
Class 2  
- disrupts trafficking
Class 3  
- disrupts gating
Class 4  
- disrupts permeation

Lab members: Allison Hall, Pierre Fwelo, Kaitlyn Samuels, & Don Burgess
Dr. Xiangan Li, PhD  
Professor, Department of Physiology  
Saha Cardiovascular Research Center;  
Director, HDL Receptor Laboratory

Dr. Li’s research focuses on the role of high density lipoprotein (HDL) and HDL receptor scavenger receptor BI (SR-BI) in sepsis. He is currently supported by two NIH fundings (R01GM121796; R01GM113832).

1. *Mechanisms of low HDL as a risk factor in sepsis* - Septic patients have low HDL levels, which is associated with a poor prognosis. Using ApoA-I knockout mice as a HDL-deficient animal model, we demonstrated that low HDL is a risk factor of sepsis. We currently develop synthetic HDL as a potential therapy for sepsis.

2. *Mechanisms of adrenal insufficiency as a risk factor in sepsis* – Adrenal insufficiency is common in septic patients. Using SR-BI null mice as an adrenal insufficiency model, we demonstrated that adrenal insufficiency is a risk factor of sepsis. We propose that precision medicine approach should be applied to septic patients, specifically, only using glucocorticoid therapy for septic individual with adrenal insufficiency but not without adrenal insufficiency. Our long term goal is to translate the mechanistic study into improving sepsis therapy.
McCarthy Lab

Focus: skeletal muscle hypertrophy

1. Role of stem cells in hypertrophy.

2. Regulation of ribosome biogenesis.

3. Ribosome specialization in muscle.

4. Role of microRNAs in muscle plasticity.