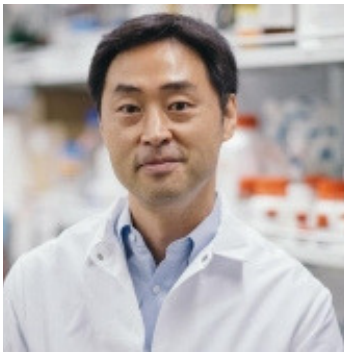
CHILDREN'S HEART RESEARCH AND OUTCOMES CENTER

Innovation of the Year Award
Hee Cheol Cho, PhD



Three researchers with the Petit Institute for Bioengineering and Bioscience at the Georgia Institute of Technology were recognized for innovative discoveries recently at Emory University's 12th annual Celebration of Technology and Innovation. Taking the top honor was Hee Cheol Cho, whose Messenger RNA-based Biopacemaker won the Innovation of the Year Award.

Millions of people experience arrhythmias (irregular heartbeats) due to heart disease, aging or congenital defects. The only medical intervention is implantation of an electronic cardiac pacemaker, which includes electrical wires fixed to the heart muscle and an electronic generator implanted under the chest skin, delivering electrical currents to stimulate the heart. Although they work well, the devices can get infected, cannot adjust the pacing rate on-demand, need battery changes, and are too big for pediatric patients.
Continued on page 4.

R21 Awarded
Erin Buckley, PhD

Dr. Buckley recently received an R21 award for her project "Objective biomarkers of cognitive outcome in repetitive concussion". Repetitive mild traumatic brain injury can have long lasting effects on a patient's cognitive, emotional, and physical well-being. Currently, it is difficult to assess injury severity, to determine when it is safe for a patient to resume the risk of injury, and to predict which patients will have the worst outcomes.

We will use an animal model of mild traumatic brain injury to investigate the utility of cerebral blood flow, oxygen metabolism, vascular reactivity, and resting state functional connectivity as potential predictors of adverse outcomes and as markers of cognitive outcome and of the brain's vulnerable window post-injury.

Continued on page 4.

Thank you Emerging Leaders - Children's Healthcare of Atlanta

It's official! The 2019 6th annual Scrubs Party will support the Children's Heart Research and Outcomes Center (HeRO),

Established in 2011, Emerging Leaders for Children's (ELC) is a leadership development board of accomplished business professionals, physicians and community volunteers in their 30s to early 40s. As ambassadors, advocates and fundraisers, members have a profound impact on Children's Healthcare of Atlanta. In 2018, ELC surpassed $1.25 million in cumulative net contributions to Children's through its annual Scrubs Party

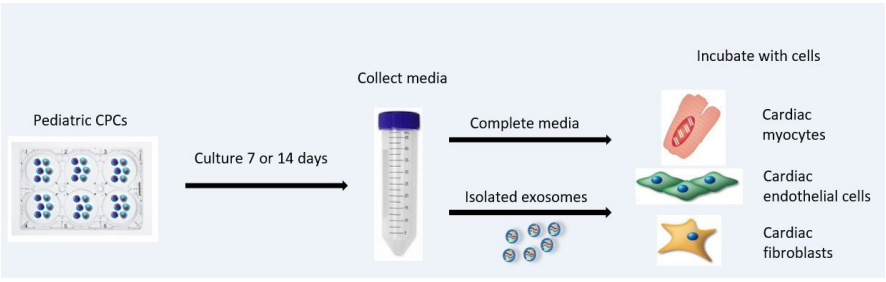
To learn more about the Scrubs Party, or purchase your ticket, click here.

Emerging Leaders for Children's

Pilot Grant
Josh Maxwell, PhD

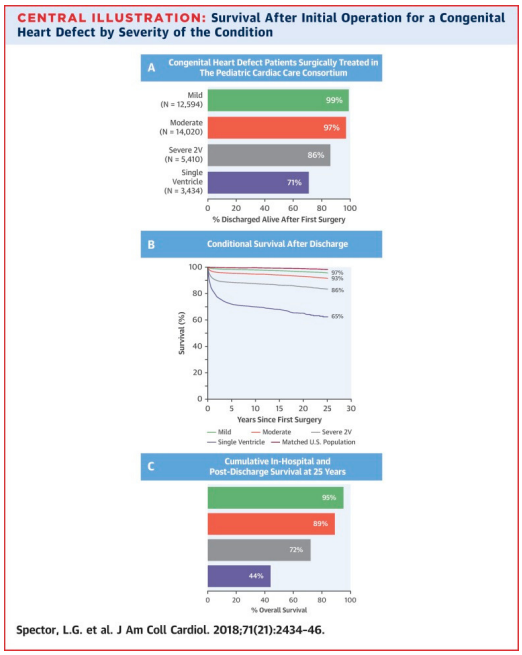
Dr. Josh Maxwell received a Pediatric Research Alliance Junior Faculty Focused (JFF) award for his project,"The Role of Paracrine Factors in Cardiac Progenitor Cell-mediated Cardiac Regeneration".

Stem cells such as cardiac progenitor cells (CPCs) have shown promise in restoring cardiac function in pediatric population for various cardiac pathologies including heart failure. However, it has yet to be determined whether stem cells mediate repair of the heart by direct differentiation of transferred cells or modulation of endogenous repair by the release of paracrine factors. Therefore, the project will examine the mechanism mediating the regenerative capacity of pediatric CPCs by characterizing the paracrine factors released by pediatric CPCs and determining their effect on cardiac cells in vitro.



Drs. Kochilas and Oster JACC Publication

The Journal of the American College of Cardiology recently published, "Public Health Approach to Decrease Mortality for Congenital Heart Defects: Dying too Soon". In this large U.S. cohort, long-term mortality after congenital heart surgery was elevated across all forms of CHD. Survival has improved over time, particularly for severe defects with significant changes in their management strategy, but still lags behind the general population. Click here to read the article.



Upcoming Visitors

Ronghu Wu, PhD
8/17/18

Mass spectrometry (MS) plays an increasingly important role in biomedical research as an extremely powerful technique used to characterize proteins and protein post-translational modifications (PTMs), measure corresponding abundance changes and investigate protein interactions. Our research interests are primarily directed towards developing novel MS-based proteomics methods and applying them to the biomedical studies.

Click here for seminar details or to RSVP

Mark Mercola, PhD
9/26/18

The Mercola laboratory is focused on developing new therapies for cardiovascular disease. Cardiovascular disease, including heart failure, remains a major cause of human mortality worldwide despite advances in clinical management. Our research combines in vitro disease models using cardiovascular cells generated from induced pluripotent stem cells (iPSCs) with high throughput screening to define disease mechanisms, identify drug targets and develop drug leads. Since iPSCs are derived from patient biopsies, these cells make it possible to visualize the effect of individual patient genetics on disease, and develop new and effective drugs. Seminar details will be announced shortly.

Lab Land
The Emory Health Sciences Research Blog

Quinn Eastman - Science Writer, Research Communications

Chunhui Xu, PhD

The term "stem cell" is increasingly stretchy. Orthopedic specialists have been using it when referring to bone marrow concentrate or platelet rich plasma, which are marketed as treatments for joint pain. At Lab Land, we have an interest in pluripotent stem cells, which can differentiate into many types of tissues.

For many applications, the stem cells are actually impurities that need to be removed, because pluripotent stem cells are capable of becoming teratomas, a type of tumor. For quality control, researchers want to figure out how to ensure that the stem-cell-derived cardiac muscle or neural progenitor or pancreas cells (or whatever) are as pure as possible.

Cardiologist and stem cell expert Chunhui Xu has been continuing a line of investigation on this topic. In a recent paper in ACS Chemical Biology, her team showed that "suicide-inducing molecules" can eliminate undifferentiated stem cells from a mixture of cells. This stem-cell-derived mixture was mostly cardiac muscle cells or their progenitors, which Xu's team wants to use for therapeutic purposes.

Other labs have used metabolic selection – depriving cells of glucose and giving them only lactate –as a selective method for eliminating stem cells from cardiac muscle cultures. This paper shows that the "selective suicide" method works for early-stage differentiation cultures, containing cardiac progenitors, while the metabolic method works only for late-stage cultures contains beating cardiomyocytes.

In the current paper, the researchers start out with a gene that converts a prodrug, 5-fluorocytosine, into a more toxic form, 5-fluorouracil. They can then selectively (by targeting the glycan SSEA-5) introduce this gene into the stem cells, not the differentiated cells. It works when there are leftover stem cells in a culture of differentiated cells, or when stem cells are spiked into differentiated cells. Xu had previously shown, in collaboration with Shuming Nie, how a spectroscopy technique can detect stray stem cells. This approach goes one step further in eliminating the stem cells, leaving a pure culture of cardiac muscle cells or cardiac progenitor cells. Click here to read more.

Vahid Serpooshan, PhD

New Emory/Georgia Tech BME faculty member Vahid Serpooshan has a recent paper published in ACS Nano making this point. He and his colleagues from Brigham and Women's Hospital and Stanford/McGill/UC Berkeley tested amniotic stem cells, derived from placental tissue. They found that female amniotic cells had significantly higher uptake of nanoparticles (quantum dots) than male cells.

The effect of cell sex on nanoparticle uptake was reversed in fibroblasts. The researchers also found out that female versus male amniotic stem cells exhibited different responses to reprogramming into induced pluripotent stem cells (iPSCs). "We believe this is a substantial discovery and a game changer in the field of nanomedicine, in taking safer and more effective and accurate steps towards successful clinical applications," says Serpooshan, who is part of the Department of Pediatrics and the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory.

Serpooshan's interests lie in the realm of pediatric cardiology. His K99 grant indicates that he is planning to develop techniques for recruiting and activating cardiomyoblasts, via "a bioengineered cardiac patch delivery of small molecules." Click here to read more.

Continued from page 1

Cho Innovation

Cho and his colleagues have envisioned hardware-free “biological pacemakers” that mimic the natural pacemaker in the heart and solve problems associated with device pacing. They have developed a gene therapy, successfully converting ordinary heart muscle into a biological pacemaker in vivo. Cho teamed up with Santangelo at Georgia Tech to deliver the gene as a messenger RNA, which sidesteps the problems associated with viral gene therapy vectors. They are anticipating a clinical trial in which the biological pacemakers will serve as adjuncts to electronic devices for patients with temporary pacing needs. If successful, the initial trial could open the door to a $5 billion (and growing) global pacemaker industry.

Submitted by: Holly Korschun

Buckley R21

This proposal will build upon our existing preclinical data to further explore the utility of blood flow, as well as several other promising biomarkers of cognitive outcome, including cerebral oxygen metabolism, cerebrovascular reactivity, and resting-state functional connectivity. Because of innate limitations of clinical experiments of mTBI, including patient/injury heterogeneity and time of assessment, we will perform initial testing of these biomarkers in a closed head mouse model of sports-related head injury that features blunt impact followed by rotational head acceleration. First, we will thoroughly quantify how blood flow, oxygen metabolism, vascular reactivity, and functional connectivity change with time before, during, and after repetitive closed head injury (Aim 1). We will quantify these parameters using three non-invasive optical modalities (frequency-domain near-infrared spectroscopy, diffuse correlation spectroscopy, and optical intrinsic signal imaging of functional connectivity) that are well-suited for longitudinal monitoring. From these data, we will identify several critical time points in order to investigate the prognostic ability of blood flow, oxygen metabolism, vascular reactivity, and functional connectivity to identify mice that will develop worse cognitive outcomes (Aim 2a).

Outcome will be quantified with a battery of tests for spatial learning and memory, anxiety, and depression. Finally, we will test whether cerebral blood flow and/or oxygen metabolism can be used as markers of the brain's vulnerable window following mTBI (Aim 2b). We will test whether mice whose blood flow and/or oxygen metabolism levels return to baseline prior to subsequent closed head injury have improved outcomes compared to those who do not return to baseline before subsequent closed head injury. Upon completion of the proposed aims, we will not only be poised to translate these biomarkers to well-controlled clinical experiments, but also to embark on future studies that delineate molecular mechanisms of blood flow, oxygen metabolism, vascular reactivity, and functional connectivity derangements in the context of novel therapies.

Stop by to learn more about the

Animal Physiology Core

HOSTED PERCS

Friday, Aug. 17th

10:00am - 10:45am

ECC 3rd floor breakroom

Click here to add to your calendar