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Pediatric Research Alliance

The Core Report

The spot for news from the cores of the Pediatric Research Alliance

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Fall 2018

Research Profile:

Bench to Bedside: Enabling Animal Models of Pediatric Cardiac Arrest

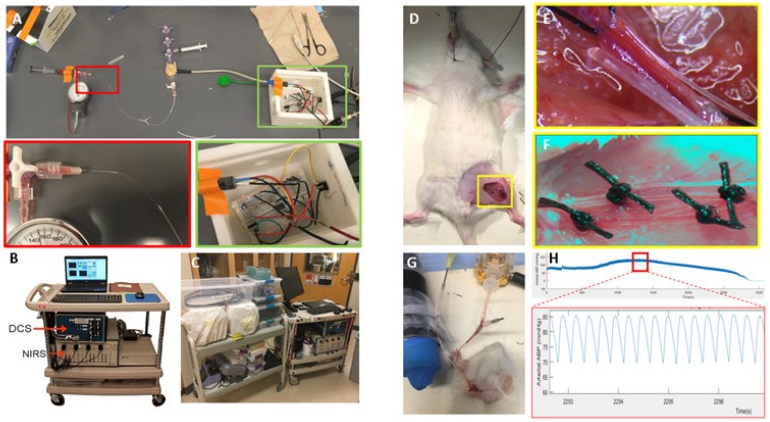
Cardiac arrest in children is a devastating event associated with <20% survival to discharge. Of survivors, many are faced with poor neurological outcomes due to the initial sustained lack of blood flow and oxygen to the brain, along with secondary injury that occurs in the hours to days post-arrest as the brain attempts to recover. Unfortunately, clinicians have limited tools available to monitor the brain post-arrest. At the Lab for Translational Diffuse Optical Spectroscopies, Erin Buckley, PhD and Kyle Cowdrick, MSE are developing non-invasive optical devices that enable real time, bedside quantification of brain vital signs, including brain blood flow, blood volume, and oxygen metabolism. The vision is that these tools could be used to guide patient care post-arrest in order to maximize brain health and ultimately improve outcomes in this devastating disorder.

Check out the Animal Physiology Core
www.pedsresearch.org

Challenge: Adapting a Model for Pediatrics

To complement ongoing clinical studies in the intensive care unit at CHOA, Dr. Buckley and Cowdrick needed a preclinical model to study pediatric cardiac arrest in order to test hypotheses generated from the clinical data. A literature search revealed a well-established rat model of asphyxia cardiac arrest developed by a lab in Pittsburgh. However, implementing this protocol here at Emory/CHOA entails unique technical challenges of placing catheters in blood vessels smaller than mechanical pencil led, and performing CPR on a rat. As engineers specializing in optics, these techniques fell far beyond our expertise.

Continued on page 2



Validation of Surgically Placed Arterial Line in P16-18 Rats
A) Benchtop setup depicting 2Fr catheter (red inset) attached to pressure transducer and custom signal amplifier (green inset) used to record real time ABP. B) Experimental portable cerebral vitals monitor. C) All equipment utilized in surgical development. D) P18 rat with E) PE10 and 1Fr catheter showing size comparisons with femoral artery and vein. F) Successful catheterization post-surgery utilizing 1Fr and 2Fr catheters. G) Post-arrest recovery in progress with H) longitudinal BP monitoring, data shown for pre-arrest/arrest.

INSIDE THIS ISSUE:

Staff Profile:

Scott Gillespie, MS, Biostats Core

Scott Gillespie, MS

Hello! My name is Scott Gillespie, and I'm a senior biostatistician in the Emory Pediatrics Biostatistics Core. I joined the core in early 2013, following the completion of my first Master's degree in Biostatistics and subsequent internship at the Rollins School of Public Health. In May of this year, I finished my second Master's degree focused in Public Health Informatics. Since joining the Department of Pediatrics, I have worked in many exciting and diverse research areas including infectious diseases, autism and developmental disabilities, and oncology. Moreover, our core has grown to service other clinical research areas including critical care medicine, cardiology, biomedical device and application development, surgery, and more. From these experiences, I have gained both expertise and a growing research interest in a number of statistical disciplines including multi-level and time-to-event regression modeling, observational data analysis, and machine learning. While I thoroughly enjoy the quantitative and technical challenges that come with being a biostatistician, the best part of my job is building strong professional relationships with our collaborators and effectively using statistics to answer their research questions, both numerically and intuitively.

Outside of work, I enjoy traveling, watching sports and socializing, riding my bicycle, and (newly) practicing Brazilian jiu jitsu. The latter two activities having helped me lose and maintain nearly 80 pounds lost over the last two years.

~submitted by Scott Gillespie, MS

Check out the Biostats Core
www.pedsresearch.org

Bench to Bedside continued

Solution: Team Science

We were fortunate to discover the services of the AP Core and immediately benefited from the expertise of Josh Maxwell, PhD and Ming Shen. Ming was instrumental to our success in accomplishing our surgical goals. From consulting on the technique itself to guiding post-surgical care, Ming provided over-and-beyond guidance for our team to not only develop the surgical technique needed, but also train our staff to perform the procedure as well. Through the AP Core, we were able to rapidly overcome technical barriers in this model and accelerate our study to do all of us do best: promoting scientific investigation through innovative strategies that we believe will ultimately enable us to positively impact pediatric patient care.

~submitted by Erin Buckley, PhD & Kyle Cowdrick, MSE

Clinical Processing Laboratory at the Center for Advanced Pediatrics:

New space with CTDC support for clinical research

The Emory University Clinical Processing Laboratory, located on the 5th floor of the Children's Healthcare of Atlanta Center for Advanced Pediatrics, provides a secure laboratory space for the processing of biological samples that are obtained as part of a clinical trial. The department of Pediatrics is excited to provide a space that will accommodate Emory University research teams in this brand new facility. Emory University clinical research coordinators will have access to all of the equipment necessary to process and store these bio-specimens, including calibrated centrifuges and pipettes. In order to accommodate the strict processing requirements of clinical studies, all centrifuges also have the ability to cool (refrigerate) to temperatures as low as 0°C. The laboratory also provides a monitored 4°C refrigerator, -20°C freezer, and -80°C freezer. A training course, that will cover the utilization of equipment and processing/storage of biological samples in Clinical Processing Laboratory, will be the prerequisite to access the space and use the equipment. This training will help to ensure that all individuals who use the space will understand the safety requirements of working in a laboratory, as required by the Emory University Environmental and Health Safety Office. Once completion of these training courses has been confirmed, keycard access to the Clinical Processing Laboratory will be granted. For more information, please contact Brad Hanberry at bradley.hanberry@emory.edu.

The Emory University Children's Clinical and Translational Discovery Core was established to collect and distribute pediatric and adult biological specimens for their future use in research at Emory University, Children's Healthcare of Atlanta, and collaborators outside of Emory University. The Biorepository is open to anyone who is willing to contribute biological samples. If you are interested in providing your own sample, we will draw 10-50 milliliters (2-10 teaspoons) of blood and may ask you to provide a urine and/or saliva sample. Each visit will take approximately 15 minutes to complete and all participants will be reimbursed in the form of a $20 gift card. For more information, please contact CCTDC@emory.edu.

~submitted by Brad Hanberry, PhD

Check out the CTDC Core www.pedsresearch.org

The new Clinical Processing Laboratory in the Center for Advanced Pediatrics.

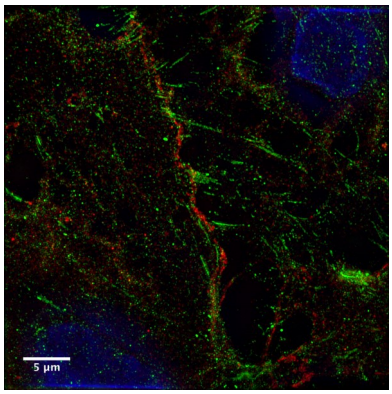
Research Profile:
ICI Peds Pilots

Earlier in 2018, the Integrated Cellular Imaging Core awarded pilots for child-health related research. Included below are images that have been collected thus far. Thanks to the individual labs for sharing these beautiful images.

Localization pattern of b1 integrin and talin at endothelial cell-cell junction

With guidance from the Emory ICI on the OMX super-resolution microscope, the Petrich lab was able to generate preliminary evidence suggesting a novel co-localization pattern in endothelial cells between VE-Cadherin (red channel), a protein vital for cell-cell adhesions, and the active form of β1 integrin (green channel), a protein which functions to anchor the cell to the underlying matrix at cell-matrix adhesions.

~submitted by Fadi Pulous (Petrich Lab)



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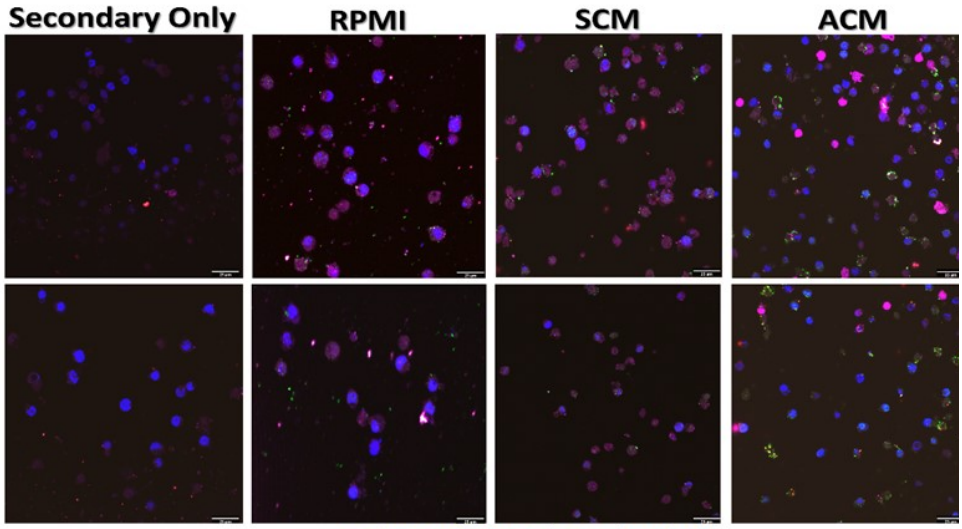


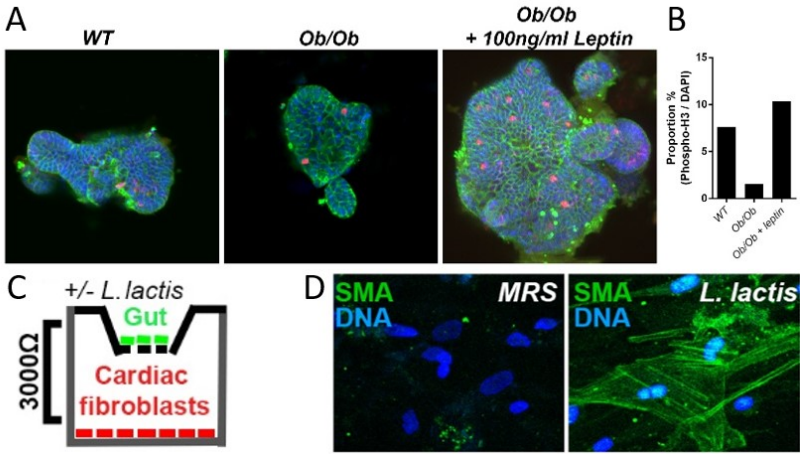
Adipocyte-secreted factors affect chronic inflammation in Acutelymphoblastic leukemia

Obesity leads to the accumulation of adipocytes which we found promotes chemoresistance in human B-leukemia cells through the upregulation of Galectin-9 and its receptor Tim-3. We recently found that adipocyte-secreted factors promote the co-localization of Galectin-9 and Tim-3, suggesting that the spatial distribution of this complex impacts chemoresistance.
Figure: Adipocyte-secreted factors induce the co-localization of Galectin-9 and Tim-3 on human B-leukemia cells (confocal microscopy).

~submitted by Curtis Henry, PhD

More pilots on the next page

ICI Peds Pilots continued

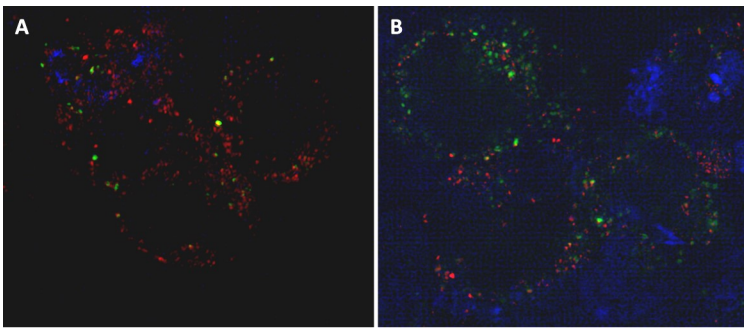


3-dimensional fibrotic scar reconstruction by immunofluorescent microscopy of whole-mounted mouse left ventricular tissue

(A) Mouse gastrointestinal enteroids were shot in 3D using confocal Z-stacks (videos not shown) to determine the number of phosphohistone H3 (proliferative marker, in red) positive cells, Beta catenin in green was labelled to show structure (B) quantification of 3 dimensional structures. (C) Human cardiac fibroblasts were grown on coverslips under transwells containing a layer of human gut cells. (D) the fibroblasts were labelled to with smooth muscle actin (a marker of differentiation to myofibroblasts) after treating the gut layer with probiotics.

This work is leading to optimization of protocols to work on how gut bacteria influence heart health and to 3 dimensionally look at tissues by fluorescence with the goal of better quantifying heart scar tissue after ischemic injury

~submitted by Crystal Naudin (Rheinallt Lab)



Imaging PD1 and Extracellular Vesicle Signaling in Cystic Fibrosis

PD1 expression in CF airway macrophages and neutrophils. Airway cells from bronchoalveolar lavage of CF patients were fixed, stained and imaged on the GE Delta Vision OMX Blaze microscope using SIM. Macrophages (A) and neutrophils (B) were assessed for colocalization of PD1 (green), lipid rafts signaling platforms (red) and intracellular mediator SHP2 (blue).

~submitted by Camilla Margaroli (Tirouvanziam Lab)

Please visit the ICI Core website for addition information about using the core

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Check out all cores at www.pedsresearch.org/research/cores

How to Acknowledge the Cores:

These cores are generously supported by Children's Healthcare of Atlanta and Emory University. When presenting or publishing work completed using the core, please include "Children's Healthcare of Atlanta and Emory University [core name]" in the acknowledgments.

This newsletter serves to highlight the activities of the cores supported by Emory University's Department of Pediatrics and Children's Healthcare of Atlanta. If you have a story idea for a future edition, please contact Karen Kennedy (kmurra5@emory.edu).