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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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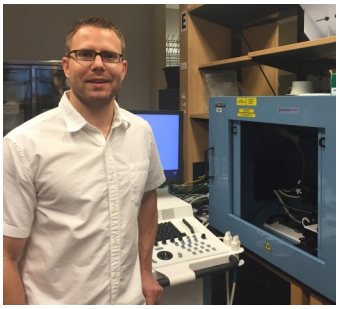
Fall 2016

# Meet the Animal Physiology Core Director: Joshua Maxwell, PhD

### Animal Physiology Core

As Director of the Animal Physiology Core, my role is to assist investigators in getting access to the core and utilizing all that we have to offer. We have a great team of administrators that handle much of the scheduling and budgeting details, which allows me to use my time to interact with investigators interested in using the core and develop strategies to get them the results they want. I've been in this position for about 3 months, and it's been a great experience working with investigators from various fields and learning about their projects.

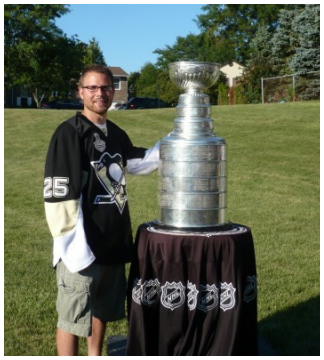


### The Maxwell Lab

My work prior to coming to Emory focused on the mechanisms of excitation-contraction coupling and calcium regulation in cardiac myocytes. I came to Emory a little over 2 years ago along with my wife. She was coming here for a residency in pathology, and I was fortunate enough to find a position in Dr. Michael E. Davis's laboratory working with cardiac stem cells. I was recently promoted to Instructor in the Department of Pediatrics and began my own research program. My main research interest is investigating ways to enhance cardiac stem cell therapies. Currently, we are studying calcium handling in cardiac progenitor cells as a mechanism of regulation of cardiogenic gene expression and a driver of cardiac differentiation. The long-term goal of our research is to develop novel stem cell-based therapies for pediatric heart failure.

### Life Outside the Lab

Outside of the lab, I play in an ice hockey league and enjoy outdoor activities in general. My wife and I spend time together hiking around Stone Mountain or walking the botanical gardens, and I like to garden around our house. I grew up outside of Pittsburgh, PA, so I am a huge Pittsburgh sports fan. I try to get home once or twice a year to see family and catch a football or hockey game.



~submitted by Joshua Maxwell, PhD

INSIDE THIS ISSUE:



Check out the Animal Physiology Core on www.pedsresearch.org

# Core Profile: CCTR Biorepository

## Biorepository Mission

The Center for Clinical and Translational Research (CCTR) has a new core that offers laboratory and technical assistance for collection, storage, and analysis of patient samples collected as part of a clinical study. These services are available to investigators who are conducting basic science, and epidemiologic, translational, and clinical research that is related to improving patient health. Our mission is to support and complement the research efforts of qualified investigators by providing laboratory research services and access to biological samples that represent a variety of diagnoses and healthy volunteers.

***"The use of the biorepository is open to investigators at Emory, Children's Healthcare of Atlanta and collaborators within and outside of Emory."***

## Using the Core

The use of the biorepository is open to investigators at Emory, Children's Healthcare of Atlanta (Children's), and collaborators within and outside of Emory. The CCTR Biorepository will process and store samples that are obtained as a part of an investigator initiated or industry funded clinical trial. The CCTR Biorepository is also able to ship and receive samples to/from external laboratories. In addition to the processing and long term storage of samples obtained through a clinical trial, the CCTR Biorepository is also pursuing prospective collection of samples that will be made available for research purposes. Biologic, genetic, demographic and clinical data will be collected in association with human specimens.

Samples that the CCTR Biorepository processes and stores include, but are not limited to: plasma, serum, peripheral blood mononuclear cells (PBMC), urine, stool, saliva, and biopsies. All collected biological specimens are tracked electronically via a secure Laboratory Information Management System (LIMS) and REDCap Clinical Data Collection Database. The biorepository stores samples in 4˚C, -80˚C, and -150˚C freezers. All storage locations are monitored by a Vaisala monitoring system to ensure specimen integrity. All freezers are also maintained by Southeast Scientific.

For more information please contact CCTRBiorepository@emory.edu

## Molecular & Clinical Trials Laboratory

The CCTR also provides assistance to investigators who are conducting basic science and translational and clinical research through the Molecular and Clinical Trials Laboratory (MCTL). The MCTL provides support and advice on the conduct of clinical trials throughout the entire research process, from initial study design and planning through the implementation and interpretation of molecular assays of drug targets and genomic correlates of disease. The MCTL is being established to provide technical support and conduct biologic assays in support of clinical trials, including protein and RNA and DNA analyses as well as cell culture assays.

The CCTR Biorepository and MCTL is also an Emory Green Labs Certified Lab. The Green Labs initiative is a voluntary program whose stated goal is to improve the sustainability of lab operations and practices throughout Emory University. The CCTR Biorepository is committed to the mission set forth by the Emory Sustainability Initiative by supporting healthy living and the reduction of the University's impact on the local environment.

The CCTR Biorepository and MCTL are located on the second floor of the Emory Health Sciences Research Building (E264). For more information please contact CCTRBiorepository@emory.edu.

~submitted by
Cynthia Wetmore, MD, PhD
Director, Center for Clinical and Translational Research
Bradley S. Hanberry, PhD
Director, Molecular Clinical Trials Laboratory and Biorepository

# Thiocyanate Project Using CF Discovery Core Services

## Thiocyanate & Cystic Fibrosis Lung

Thiocyanate (SCN) is a small (nominal mass of 58) pseudohalide anion and CFTR substrate. SCN effectively competes with chloride and other ions for neutrophil myeloperoxidase in vivo. This replaces strong, non-selective oxidants made during inflammation (such as hypochlorous acid) with the more selective hypothiocyanous acid (HOSCN). Interestingly, higher nasal SCN has been associated with better lung function in cystic fibrosis patients (1). We now know that redox metabolism of HOSCN is significantly different in humans and human lung pathogens, explaining how SCN may protect lung health (2). Indeed, SCN administration limits lung infection and lung inflammation in mice (3-4).

This knowledge supports the hypothesis that airway SCN is associated with better lung health outcomes in CF, such as fewer exacerbations or positive airway cultures. However, making this determination has been greatly hindered by the difficulty of routinely measuring airway SCN. The concentration of SCN in bronchoalveolar lavage (BAL) fluid can be relatively low (<1 μM), and requires invasive bronchoscopy. Exhaled breath condensate (EBC), a non-invasive airway sample, is even more dilute. This makes it practically impossible to measure EBC SCN with conventional methods, yet EBC sampling is convenient and practicable to clinicians and researchers.

Check out the CF Discovery Core on www.pedsresearch.org

## Discovering the CF Discovery Core

While I was researching gas chromatography-mass spectrometry (GC-MS)-based methods to detect SCN with greater sensitivity and selectivity than conventional methods, I attended a CF-AIR Workshop and became aware that the CF Discovery Core was banking plasma and EBC from CF patients and healthy donors. Afterward, I met with Arlene Stecenko, MD and her lab members to acquire matched healthy donor plasma and EBC. I then spent multiple months optimizing an improved GC-MS method for the highly sensitive detection of SCN using GC QExactive instrumentation in the lab of Dean P. Jones, PhD.

*"I attended a CF-AIR Workshop and became aware that the CF Discovery Core was banking plasma and EBC from CF patients and healthy donors."*

## Data & Collaboration

After the GC-MS method was well developed with a limit of detection at least two orders of magnitude lower than most published methods, I tested the donor EBC and plasma. As expected, EBC SCN is low in concentration (5-50 nM, or 3-4 orders of magnitude more dilute than plasma), but still detectable in this high resolution method. Intriguingly, EBC SCN did not correlate with plasma SCN in healthy donors (though more samples need to be analyzed to confirm this result). Currently, I am preparing the optimized method manuscript for submission. Additionally, I have analyzed SCN in early CF BAL fluid acquired in collaboration with Rabin Tirouvanizam, PhD, which will allow another means of assessing SCN in airway disease progression.

I am very grateful to the CF Discovery Core for their collaboration on this project, which has afforded me a unique opportunity to assess the importance of SCN in CF airway disease and provided the impetus to develop a cutting edge GC-MS method. I look forward to continued collaboration with the Discovery Core.

~submitted by Joshua D. Chandler, PhD
Postdoctoral Fellow (Dean P. Jones Lab)

References:
1.Lorentzen D et al. Free Radic Biol Med 2011:50
2.Chandler JD et al. J Biol Chem 2013:288
3.Chandler JD et al. Am J Respir Cell Mol Biol 2015:53
4.Chandler JD et al. Free Radic Res 2015:49

# Instrument Profile: Amnis ImageStream

## Unique Imaging & Flow Cytometry Mix

The Amnis ImageStream Mark II imaging flow cytometer combines the speed, sensitivity, and phenotyping abilities of flow cytometry with the detailed imagery and functional insights of microscopy. This unique combination enables a broad range of applications that would be impossible using either technique alone.

Our The Amnis ImageStream MKII is a bench-top imaging flow cytometer. It is equipped with 4 lasers (488 nm, 642 nm, 561nm and 405 nm) and is capable of analyzing up to 9 fluorochromes, side scatter, and bright field images.

## Using the ImageStream

We can utilize some of the same dyes and markers employed in microscopy and flow cytometry plus we can perform virtually any standard flow cytometry assay with the bonus of being able to visualize it as well, including features of cells such as co-localization, staining location, cell-cell location, spot counting and cell death analysis.

Check out the Flow Cytometry Core on www.pedsresearch.org

## ImageStream Use in Cancer and Microparticle Research

The ImageStream has varied applications including cancer and microparticle research. The links below show some of the different types of assays that can be performed:

http://www.accela.eu/files/products/9/oncology_cancer_research_pub_note_-_imagestream_-_april_2011.pdf

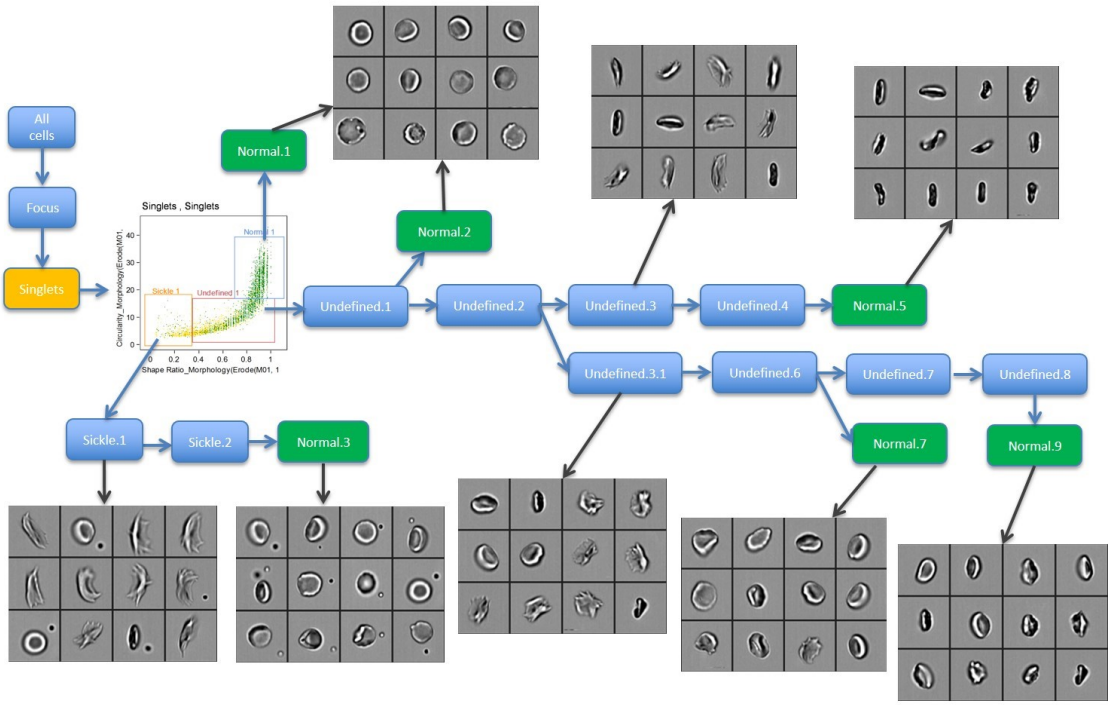
Cutting-Edge Analysis of Extracellular Microparticles using ImageStream Imaging Flow Cytometry:

http://www.nature.com/articles/srep05237

An example below shows the identification of Sickle Cells Utilizing the ImageStream in Human RBC's.

~submitted by the Pediatric Flow Cytometry Core

Automatic quantification of the percentage of human RBC sickle cells




% Sickle=(Singlets--Normal.1-Normal.3-Normal.2-normal.5-normal.7-normal.9)/Singlets*100

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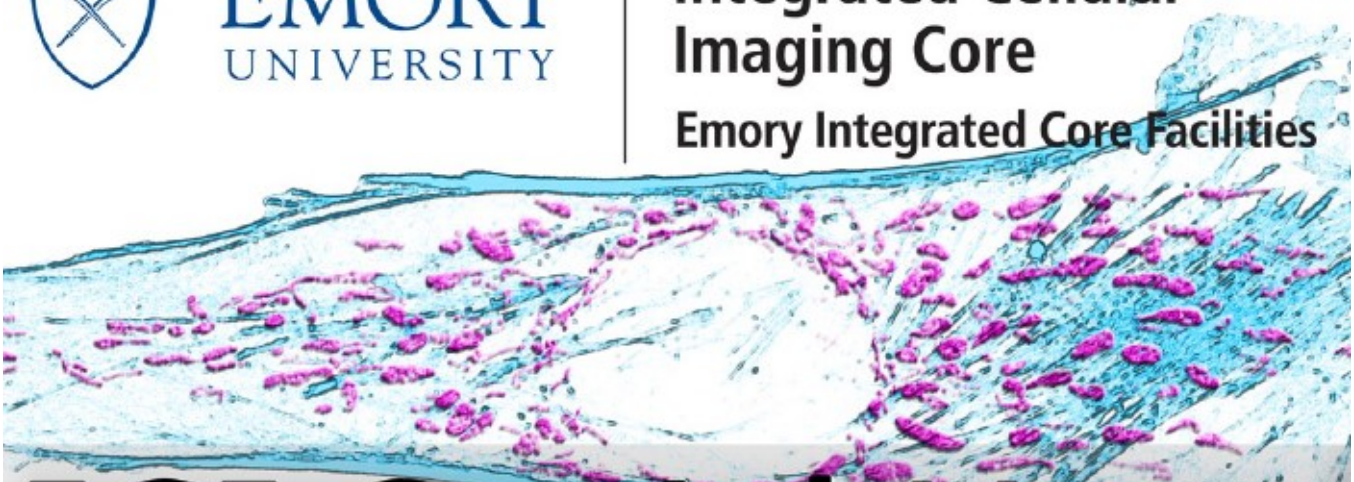
## Integrated Cellular Imaging Core

Emory Integrated Core Facilities



# ICI Social Hour

*Join the Integrated Cellular Imaging (ICI) team for a pizza and an informal presentation on the latest fluorescence imaging technology, including the new lattice light sheet.*

## September 7th
## Noon - 1 pm

## HSRB Lobby

## Please RSVP for pizza:

https://doodle.com/poll/pu8znxsaeavnve7w
or see pedsresearch.org/calendar for details

# Contact Information

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|---|---|---|
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| **Biorepository** | Cynthia Wetmore, MD, PhD | CCTRBiorepository@emory.edu |
| **Biostatistics Core** | Courtney McCracken, PhD | tinyurl.com/pedsbiostat |
| **Cardiovascular Imaging Core** | Ritu Sachdeva, MD | circ@choa.org |
| **CF Discovery Core** | Arlene Stecenko, MD | Julie Flores julie.flores@emory.edu |
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**Visit us at:**
**www.pedsresearch.org**

## 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).*