EMORY • Children's • GT
Pediatric Research Alliance

The Core Report

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

Volume 4, Issue 1
Spring 2019

New Partnership:
Pediatrics & Winship Advanced Flow Cytometry Core

2019 has brought exciting changes to the core: new instruments, new staff, a new partnership, and a new name! In addition to continued support from Emory University Department of Pediatrics and Children's Healthcare of Atlanta, we are excited to welcome the Winship Cancer Institute as a partner for the core. In light of the new partnership, we are now the **Pediatrics & Winship Advanced Flow Cytometry Core**.

Check out the Flow Core
www.pedsresearch.org

Instruments

In the past few months, the core added new instruments. A BD FACS Symphony arrived in December, and two Cytek Auroras arrived in February. Highly complex panels (up to 28 colors) can be run on all of these instruments. To learn more, visit the instrument information page of our website. One of the Cytek Auroras is located in our new location in Winship Building C, C-5027. To help support high content panel design and analysis we have invested in new staff so please discuss your projects with them as they develop.

Core Staff

For core staff, David Archer continues as core director, with Aaron Rae leading the lab as technical director. Jennifer Schmid joined the core in the fall, see her profile on page 3 to learn more about her unique role. Erich Williams started in March 2019.

Partnership with Winship

Our new partnership with Winship Cancer Institute allows for specific support of cancer-related projects. Just as child health-related projects receive a subsidized price, Winship members may also be eligible for a subsidy for cancer-related projects. A blended subsidy is available for those eligible for both subsidies. For specific details about subsidized pricing and to see if your project qualifies, contact Karen Kennedy.

~submitted by Pediatrics & Winship Advanced Flow Cytometry Core

First users being trained on the new BD FACS Symphony in January 2019

INSIDE THIS ISSUE:

Research Profile:

Henry Lab ICI pediatrics pilot: Adipocyte-secreted factors affect chronic inflammation in Acutelymphoblastic leukemia

Survival outcomes after chemotherapy treatment in obese patients with B-cell acute lymphoblastic leukemia (B-ALL) are 30% lower than those observed in lean patients. Despite the widely held belief that altered chemotherapy pharmacokinetics in obese patients account for survival differences, emerging data by our group and others suggest that adipose-rich microenvironments directly upregulate chemoresistance mechanisms in B-ALL cells.

Adipocytes accumulate systemically with weight gain and are capable of reshaping microenvironments through the chronic production of pro-inflammatory cytokines and chemokines. Therefore, we sought to determine how adipocyte-secreted factors altered the phenotype and chemosensitivity of human B-ALL cells. Exposing human B-ALL cells to adipocyte-conditioned media (ACM), but not unconditioned media (UCM) or stromal cell conditioned-media (SCM), promoted extensive cellular aggregation (data not shown). Unlike UCM and SCM exposure, pre-treating B-ALL cells with ACM abrogated chemotherapy-mediated cytotoxicity coinciding with an increase in surface

Continued on page 3

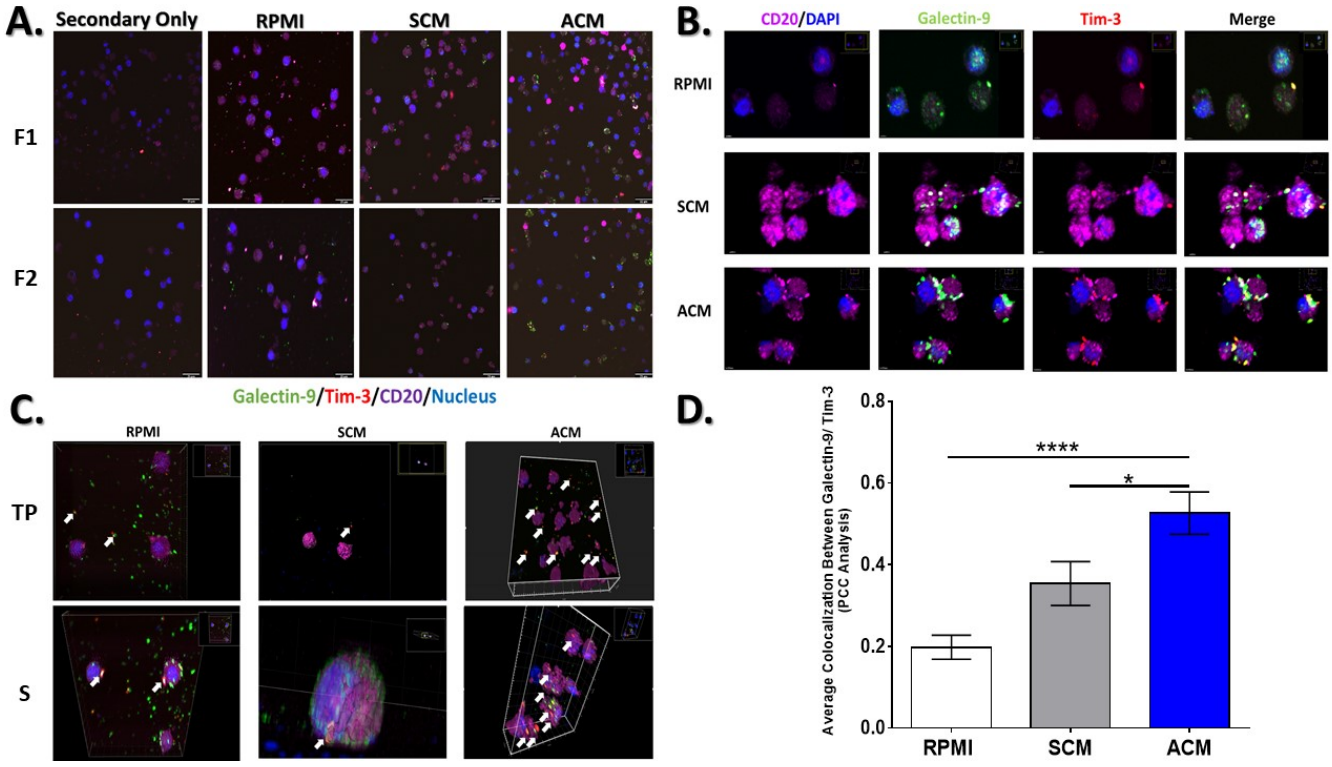


Figure 1: Adipocyte-secreted factors induce colocalization of Galectin-9 and Tim-3 on human B-leukemia cells. SEM cells (human B-ALL cell line) were cultured in RPMI, stromal cell-conditioned media (SCM), and adipocyte-conditioned media (ACM) for three days and confocal microscopy was performed to analyze Galectin-9 (green fluorescence) and Tim-3 (red fluorescence) distribution. The nucleus was stained with DAPI (blue) and CD20 (magenta) is a B-cell marker found on the cell membrane. The extent of colocalization between Gal-9 and Tim-3 (denoted by the white arrows) was determined using a Pearson's Correlation Coefficient analysis, and statistical significance was determine using a one-way ANOVA followed by a Tukey multiple comparison post-test with *p<0.05 and ****p<0.0001. In Figure 1A, F1= Field 1 and F2=Field 2. In Figure 1C, TP= top plane and S=Section.

Staff Profile:
Jennifer Schmid, CTDC & Flow Core

Howdy Pediatric Research Alliance! My name is Jennifer Schmid. I was hired this past October to join the Clinical Translational Discovery (CTDC) and Flow Cytometry Cores as their new junior Research Specialist. My role is to bridge the gap between the two growing Cores by providing a wider range of clinical trial support. In the CTDC, I assist Brad Hanberry with providing Emory's researchers with an extensive biorepository offering a wide range of healthy control samples. In addition to the biorepository, we coordinate with an array of clinical research both on and off campus. Apart from the CTDC, I assist in the Flow Core helping to establish and evaluate immunological assays. It is an exciting time to be apart of two Core labs and I look forward to continuing my education both on and off campus. Before joining Emory I graduated from Georgia Gwinnett College with a degree in biochemistry and chemistry. While in undergrad, my research was primarily based in microbiology and environmental ecology. Working with the Georgia Department of Natural Resources, I investigated biocontrol agents for the fungus, *Pseudogymnoascus desctrucans*. I also founded and presided over the small school's Biology Club. Aside from work, I enjoy applying my curious nature to my hobbies. I am an avid at home chef and I love to create and experiment with new techniques and recipes in the kitchen. I also enjoy collecting and preserving biological specimens, from taxidermy to skeletal articulation.

~submitted by Jennifer Schmid

Continued research profile from page 2

galectin-9 levels (data not shown).

Galectin-9 (Gal-9) is the ligand for T-cell immunoglobulin Mucin Receptor-3 (Tim-3), and has been shown to potentiate proliferative, survival, and self-renewal properties in myeloid leukemia cells. We therefore sought to determine the impact of ACM-induced Gal-9 surface expression on chemosensitivity and the spatial localization of the Gal-9/Tim-3 complex on human B-leukemia cells. We found that Gal-9 blocking antibodies dissociated the ACM-induced aggregation of B-ALL cells and abrogated chemoresistance (data not shown). Furthermore, we observed significant colocalization of the Gal-9/Tim-3 complex on human B-ALL cells exposed to ACM (Figures 1A, 1B, and 1D). Three dimensional analysis (Z-stacks) of human B-ALL cells revealed that ACM exposure also induced the internalization and secretion of the Gal-9/Tim-3 Complex (Figure 1C). These results provide important spatial information regarding how adipocyte-secreted factors promote Gal-9/Tim-3 mediated chemoresistance in human B-leukemia cells.

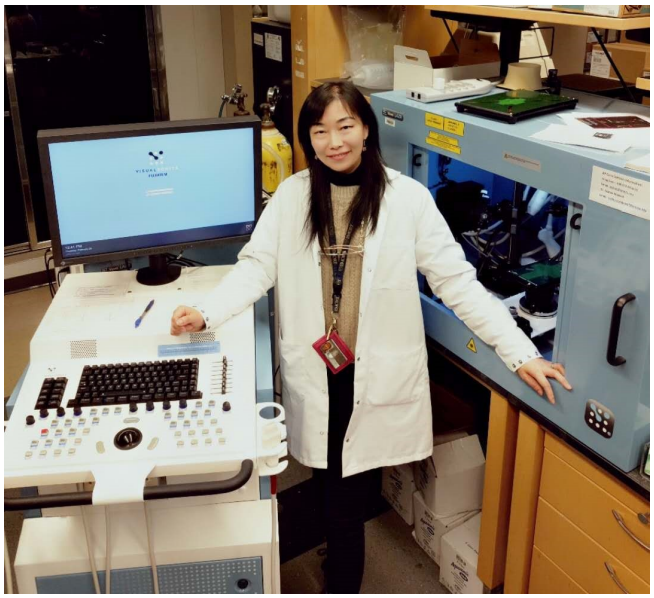
The imaging studies were supported by funding provided through the ICI pediatrics pilot grant, and Dr. April Reedy provided invaluable study design expertise.

~submitted by
Jamie G. Hamilton
& Curtis J. Henry, PhD

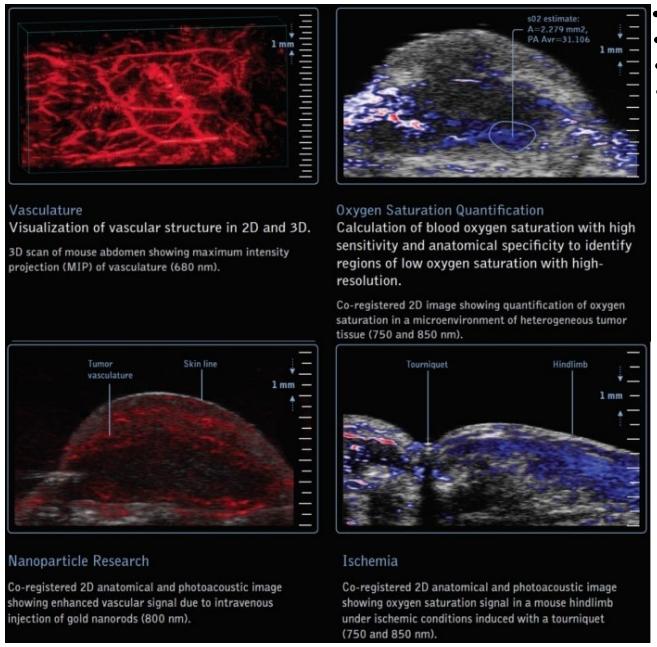
Instrument highlight-Animal Physiology Core:

Vevo LAZR System

The Vevo LAZR system is a photoacoustic imaging add on for the Vevo 2100 ultrasound system. Ultrasound imaging is a powerful tool in its own right, using high frequency sound waves to generate images of internal body structures such as organs, muscles, and blood vessels. Combining ultrasound imaging with photoacoustic imaging provides another level of capabilities beyond typical ultrasound. With photoacoustic (PA) imaging, pulsed laser light is emitted from a specialized transducer and is absorbed by chromophores. The chromophores undergo thermoelastic expansion and emit sound waves that can be detected by ultrasound transducers. This gives users the ability to simultaneously register high-resolution ultrasound and photoacoustic images for anatomical, functional, and molecular imaging. Ultrasound imaging provides a high-resolution frame-of-reference for identifying anatomy, while the photoacoustic imaging enables functional measurements such as blood and tissue oxygen saturation, blood flow, and the microdistribution of biomarkers. Nearly all vertebrates come pre-loaded with a natural photoacoustic agent, hemoglobin. This property of hemoglobin allows for acquisition of information on blood flow and tissue perfusion, oxygen saturation and hypoxia,



Core technician Ming Shen in the lab with the Vevo LAZR



Examples of data from the Vevo LAZR

and for visualization and quantification of volumes. The LAZR system can excite molecules over the range of wavelengths from ~680 – 970 nm with a resolution of ~45 microns. This makes the system ideal for applications such as labeled cell tracking in vivo, drug delivery and pharmacokinetic analysis, nanoparticle delivery and distribution, tumor microenvironment characterization, and hemodynamic and hypoxia measurements. The Vevo LAZR and 2100 Ultrasound system are located in Emory Children's Center room 260.

~submitted by Joshua Maxwell, PhD

Check out the Animal Physiology Core
www.pedsresearch.org

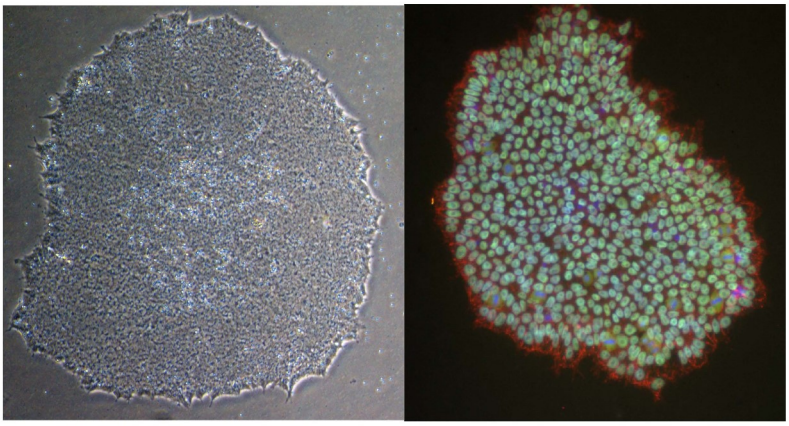
Local Core Highlight:
Emory Stem Cell Core

While not a Pediatrics-specific core, the Emory Stem Cell Core is a unique resource that can support child health-related research in powerful ways. Click the flyer below to learn more.

EMORY UNIVERSITY

Emory Stem Cell Core

Emory Integrated Core Facilities



Services Provided Include:

- Reprogramming and characterization of somatic cells to Induced Pluripotent Stem Cells (iPS)
- Biopsy Tissue Processing for Fibroblasts
- Whole Blood Processing for PBMCS and Erythroid Progenitors Cells
- Thawing and propagation of Fibroblasts
- Thawing and propagation of iPS or Human ESCs
- Karyotyping
- Training

Contact: Megan Merritt-Garza, Core Director, at ESCC@Emory.edu to discuss potential projects

http://www.cores.emory.edu/escc/

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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 (karen.kennedy@emory.edu).