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Research and Discovery

In the Emory Department of Pediatrics and Emory-Children's Center

Introducing our Newest Research Center: Center for Clinical Outcomes Research and Public Health (CORPH): Coming on line January 1, 2011

It started as an interest group facilitated by Stacy Heilman, and is now becoming one of the Children's Research Centers: a perfect example of how the pediatric research enterprise continues to evolve and strengthen. **Ann Mertens, PhD, MS,** has been named the Director for the Children's Center for Outcomes Research and Public Health, aka CORPH. Other members of the leadership team include:

- **Michele Marcus, PhD, MPH**, Epidemiology, SPH, Emory
- **Michael Schechter, MD, MPH**, Cystic Fibrosis, Pediatrics, Emory / CHOA
- **Paige Tolbert, PhD, MSPH**, Environmental Health, SPH, Emory
- **Karen Wasilewski-Masker, MD, MPH**, Hematology/Oncology, Pediatrics, Emory / CHOA

The mission of CORPH is to promote the development and conduct of high-quality epidemiologic and clinical research with a unique opportunity to become a leading clinical research enterprise within the US, because of the strong partners within the Atlanta area and through the large volume of patients seen at Children's Healthcare of Atlanta.

For the purposes of CORPH, clinical research is defined as patient-oriented research conducted with human subjects. This research encompasses epidemiologic and behavioral studies, outcomes research, and health services research. It includes research on the mechanisms of human disease as well as therapeutic interventions. It does not include in vitro studies using human tissues not linked to a living individual. The majority of the research will be the analytic studies, which include observational studies, such as case-control and cohort studies. Analytic studies also include experimental/Interventions such as behavioral interventions.

CORPH is organizing around **working groups** who share similar interests under the broader topics of ***Outcomes*** and ***Wellness***. These groups include:

Outcomes:

- Comparative Effectiveness:
- Transition of Care
- Quality Initiatives:
- Birth and Neonatal Outcomes:
- Neuro-developmental Outcomes:

Wellness:

- Environmental Health:
- Obesity / Nutrition:

Cores to be developed within CORPH include:

- Bioinformatics, including recruitment of a faculty member in clinical infomatics, and development of EPIC reporting tools for research.

Be on the lookout for the **research center pilot project RFAs** to be released in **December 2010**.

- Biostatistics, which will further develop the existing Biostatistics Core to include the expertise relevant to these areas of research.

Stay tuned for information on becoming a member or joining one of the working groups. Info to come in January!

Next Center to come on line in early 2011: Children's Clinical and Translational Research Center (CCTRC)

Complementary to CORPH but with its own distinct scope, this Center is planned to come on line early in 2011.

For the purposes of CCTRC, patient-oriented clinical research is research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) in which a researcher directly interacts with human subjects. It includes research on mechanisms of human disease, development of new technologies drugs and devices, and therapeutic interventions such as clinical trials or comparative effectiveness research.

Still in final stages of development by Kris Rogers, Director of Research at Children's, Carlton Dampier, MD, and Paul Spearman, MD, we expect this center to offer a home and resources to many clinical research investigators of the pediatric research enterprise who do not feel a strong affiliation with one of the existing centers. The CCTRC will provide support to expand clinical research with a focus on clinical trials that will directly impact the care of children within the local healthcare system. CCTRC will organize and help manage a centralized core of research coordinators, research nurses, and research managers to serve investigators' needs within each unit and clinical site in our system. This service should be particularly helpful to smaller programs or individual investigators with limited research staff or to allow other programs to rapidly expand recruitment or other activities for high priority or high volume studies.

CCTRC will include personnel who will serve a "navigator" function to provide trainees, entry-level faculty, and faculty with little experience in clinical or translational research with guidance on accessing institutional resources in protocol development, biostatistical/bioinformatics support, regulatory compliance, and support for investigational new drug (IND) and investigational device exemption (IDE) applications. Support will also be available to assist with feasibility and scientific review of clinical trial protocols, particularly for local investigator-initiated studies.

Stay tuned for more information as this Center comes into being in 2011!

Cores now available in the ECC building: Common Equipment and Specimen Processing

Common Equipment Core:

In an effort to ensure that all investigators have access to equipment necessary to conduct meaningful scientific research, DOP, in partnership with Children's, has established a common Equipment Core comprised of instruments that are central to a broad range of research endeavors. Most of these instruments have been generously donated by members of the DOP to Equipment Core for all to use in exchange for maintenance and support of the instrument.

While these instruments will be available to all researchers, they must be used according to the guidelines established for each. Many of these instruments are highly sensitive and require special training. Please check with the laboratory contact listed below to determine whether prior authorization and/or training are needed. Failure to obtain proper authorization or to follow the guidelines set forth for each instrument could result in termination of your privileges or in withdrawal of the instrument from the Equipment Core.

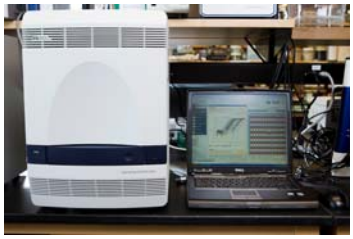
Current Equipment Core instruments include:

- A Beckman Coulter Avanti J-26 XP High Speed Centrifuge. This high speed centrifuge has 2 available rotors. The JLA16.250 has a maximum capacity of 6-250 ml bottles and a maximum speed of 16000 rpm. The JA25.50 has a maximum capacity of 8-50ml tubes and a maximum speed of 25000 rpm. You are responsible for providing your own centrifuge tubes and bottles and determining the true maximum speed for which they are rated. Login

required. **Specific authorization and training are required prior to using this instrument.** Please contact Jason Hammonds (jehammo@emory.edu, 678-358-9927) for more information.

-An Eppendorf 5810R Refrigerated Table Top Centrifuge. Two rotors are available for this centrifuge including a swinging bucket rotor with a maximum speed of 4000rpm, and a fixed angle rotor with a maximum speed of 12000rpm. Please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information on this instrument.

- **A BioRad iCycler Thermal Cycler.** This standard 96-well thermocycler is very user friendly and easy to program. The temperature gradient feature is useful for optimizing reaction conditions or performing PCR using multiple primers with differing annealing temperatures. Please contact Milton Brown (mbrow@emory.edu) or Katie Casper (kcasper@emory.edu) for more information on this instrument.



-**An ABI 7500 Real-time PCR system**. This is a popular real-time PCR instrument capable of supporting a broad range of dyes. It is useful for gene expression assays, pathogen detection, and SNP assays. Login required. If you are unfamiliar with this instrument, please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information.

- A Nanodrop ND-1000 Spectrophotometer. This spectrophotometer is capable of analyzing nucleic acid and protein samples over the 220 to 750nm range. The nanodrop requires only 1- 2ul of sample. It is 50 times more sensitive than traditional spectrophotometers and is capable of measuring 2-3700ng of double stranded DNA. Login required. Please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information on this instrument.

- A Bio-Tek Synergy 2 Plate Reader. This high performance plate reader is capable of measuring absorbance, fluorescence, and luminescence. Login required. If you are unfamiliar with this instrument, please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information.

- A Bio-Rad ChemDocTM XRS+ Imaging System with Image Lab Software. This is a gel and blot documentation system capable of supporting chemiluminscent, fluorescent, and colorimetric samples. Login Required. Please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information.

- A Li-Cor Odyssey Infrared Imaging System. This highly sensitive imaging system relies on fluorescently-labeled antibodies rather than enzymatic reactions and can be used for most protein analysis applications. One particularly useful feature of the Odyssey is its ability to detect 2 targets simultaneously. Login required. **Specific authorization and training are required prior to using this instrument.** Please contact Jason Hammonds (jehammo@emory.edu, 678-358-9927) for more information.

- A Perkin Elmer TopCount NXT Microplate Scintillation and Luminescence Reader. This scintillation/ luminescence counter is capable of analyzing up to 12 samples at a time in 24, 96, or 364 well microplate formats or in microcentrifuge tubes. It is capable of counting gamma, beta or luminescent samples. Login required. **Specific authorization and training are required prior to using this instrument.** Please contact Jason Hammonds ((jehammo@emory.edu, 678-358-9927) for more information.

A Bio-Rad Gene PulserXcell Electroporator. This modular electroporation device includes a CE (capacitance extender) module, a PC (pulse controller) module, and a shock pod cuvette chamber. Electroporation conditions including time, voltage, pulse interval, pulse time and wave form are easily modified. This instrument is recommended for both eukaryotic and prokaryotic transfections. Please contact Milton Brown (mbrow@emory.edu**)** or Katie Casper (kcasper@emory.edu) for more information on this instrument.

-An X-ray film developer. Located in Rm 405 ECC. Please contact Linda Campbell (lcampb3@emory.edu) for more information.

If you have any comments or suggestions for future additions to the Equipment Core, please contact Katie Casper at kcasper@emory.edu or 404 -727-3665.

Specimen Processing Core

A common specimen processing area is now available in Rm 260 of the ECC building for Department of Pediatrics affiliated researchers. This area provides a generous amount of bench space for the routine processing of specimens. As common space, this space that can be used on a temporary basis, meaning that investigators should not store any samples or

supplies in this space overnight - bring what you need, and take away the supplies at the end of use.

In addition to the 2 designated specimen processing benches (A & B) in the main laboratory, room 261D is fully equipped as a specimen processing/ culture prep room for work that requires processing under sterile or Biosafety level II conditions. Features of this area include:

-A 6-ft Baker SterilGard III Laminar Flow Biological Safety Cabinet (Class IIB3) for specimens requiring BSII conditions.

-2 Sanyo cell culture incubators currently maintained at 37°C, 5% CO_2. Incubator settings can be adjusted upon request for assays requiring specialized conditions.

-A Sorval Legend RT refrigerated centrifuge ideal for cell culture purposes and for processing clinical specimens. Adaptors for plates, 50ml and 15ml conical tubes, and select sizes of hematology tubes are available for this centrifuge.

-2 digital Precision water baths.

-A microscope for monitoring cultures.

-A Misonix XL-2000 ultrasonic processor horn useful for preparing cell lysates or shearing nucleic acids. This sonicator is equipped with a cup horn allows for sample preparation in sealed tubes away from the probe and is ideal for work that requires sterile conditions.

We encourage investigators to take advantage of these resources. Please note that all work performed in this area is to done in accordance to university biosafety guidelines. Please contact Milton Brown (mbrow05@emory.edu, 404-727-5709) for additional information or to schedule use of room 261D.

Children's IRB Recruiting New Members

Children's is looking for experienced clinical researchers to join the IRB. Must be able to attend one meeting per month (4th Thursday at 7am, Marcus Autism Center). Previous IRB member experience is not required. Member orientation and ongoing education are provided. Interested? Questions? Contact Sarah Marie Huban for more details. (SarahMarie.Huban@choa.org or 404-785-7477)

Pediatric Research Center Hours

As we head into the holiday season, please plan your patient visits keeping the following dates in mind.

The **PRC will be closed** on the following dates for the holidays

Christmas –**Thursday, 12/23 Friday, 12/24**
The PRC will reopen on Monday 12/27 at 8 am

New Years – **Thursday 12/30 Friday, 12/31**
The PRC will reopen on Monday, 1/3/2011 at 8 am

Additionally, we will not be scheduling any special weekend hours during the month of December.

November issue of NIH Office of Extramural Research's **Research Nexus**
Includes: Podcast on Summary Statements and resubmission advice, NIH Director 's Early Independence Award Program, & more

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Highlight on Research

Introducing our newest faculty member: Tracey Lamb, PhD

Dr. Tracey Lamb has joined the Children's Center for Vaccines and Immunology and DOP Division of ID from the School of Biological Sciences at University of Reading, located in the UK.

The major focus of the Lamb laboratory is to understand how malaria parasites trigger immune responses in the body. Using rodent models of malaria infection in mice, the major focus of the laboratory is on innate immune cells such as dendritic cells and macrophages; in particular the aim is to determine the factors that shape the response of innate immune cells responding to red blood cells parasitized by malaria parasites. The lab is currently investigating the cell signalling pathways activated by malaria-parasitized red blood cells with respect to the production of inflammatory cytokines in malaria infection; armed with this knowledge it may be possible to manipulate of these pathways chemotherapeutically to dampen inflammation.

Ongoing studies incorporate the influence of immune factors that adhere to malaria-parasitized red blood cells, principally antibodies and activated platelets. In a separate research project supported by the Royal Society, the Lamb lab has recently discovered that the Ephrin / Eph kinase family of molecules are upregulated in innate immune cells in malaria infection, and that these molecules drive inflammation, in turn enhancing pathology in mouse cerebral malaria. Now, by moving to Emory University the laboratory is in a position to expand this discovery by examining the role of these molecules in human malaria infection in collaboration with other scientists at Emory.

Research on Pediatric Cardiac Neurodevelopment: Shannon Hamrick, MD and Bill Mahle, MD

Long-term neurodevelopmental impairments are frequently seen in children with congenital heart disease. In 2008, CHOA and the Sibley Heart Center established the Pediatric Cardiac Neurodevelopmental Program, led by Drs. Bill Mahle and Shannon Hamrick, MD. The plan for this comprehensive program will include registries, basic and clinical research, and ultimately functional assessments and tailored interventions. Dr Mahle, Associate Professor of Pediatrics, Director of Research, Sibley Heart Center, came to Emory University in 2001 from Children's Hospital of Philadelphia. Dr Hamrick joined the Division of Neonatology in 2006, recruited from the University of California San Francisco. Dr Hamrick's research interest is brain injury in the surgical newborn.

Term infants with congenital heart disease (CHD) requiring neonatal surgery have an unusual susceptibility to white matter injury (WMI), a pattern of injury typically seen on magnetic resonance imaging (MRI) in preterm infants. The risk of WMI is almost exclusive to *newborns*, rather than older infants, undergoing cardiac surgery. Data from Dr Hamrick's work in San Francisco suggest delayed brain development in term newborns with CHD, an intriguing explanation for this susceptibility to WMI. Experimental models indicate that WMI occurs when specific cell populations in the developing brain are damaged by free radicals and inflammatory cytokines generated during ischemia and reperfusion, among other mechanisms. The long-term consequence of having WMI is unclear, although neurodevelopmental impairment is well established in children with CHD, and WMI in preterm infants is an established risk factor for poor outcome.

An ongoing study through the Sibley Heart Center, funded by the Thrasher Research Foundation, hypothesizes that term newborns with complex CHD requiring neonatal surgery have WMI due to neurotoxicity from the profound peri-operative inflammatory response. This prospective longitudinal study will characterize the systemic inflammatory response in a heterogeneous group of congenital lesions/surgeries, assess brain injury in the pre and post-operative period, determine whether inflammation is associated with injury, and asses neurodevelopment outcomes at 1 year (with intent to follow these children much longer). We hope that a description of the inflammatory response and its association with brain injury will impact which agents are chosen as neuroprotectants in future studies. Understanding the mechanism of WMI in this population will also influence our knowledge and treatment of *preterm* brain injury, and other high-risk surgical newborns.

Featured next month in Research Highlights: Global Health Organization of Pediatrics at Emory [GHOPE] Link to their inaugural newsletter here!
