

The Emory+Children's Cystic Fibrosis Center of Excellence

Volume 4, Issue 1

30 September 2014

Update from the Director



Nael A. McCarty, PhD
Center Director

We are happy to provide this update for you on behalf of the Emory+Children's Cystic Fibrosis Center of Excellence. It has been several months since the last update, so there is much to report!

The work to grow the best comprehensive CF program in the country continues at a rapid pace, including new efforts in all three domains: research, education, and clinical care. This report includes

descriptions of new faculty and staff hires (pages 2 and 3), new endeavors tying together our clinical programs (page 2), new activities in education and outreach (page 4), and new milestones in program growth (page 6).

Meanwhile, the work to develop new knowledge relevant to our patients also continues. You'll see on page 8 a list of 22 abstracts for posters/talks to be presented at the North American CF Conference – to be held in Atlanta next month. Exciting new findings are resulting from our team's research.

One major change, which took place last year, is the renaming of the Center for CF Research. The

leadership of the Emory+Children's Pediatric Research Center asked us to take on the activities of another one of the research centers that also started in 2010. This led to the merger of these two centers into the newly-named **Center for CF and Airways Disease Research (CF-AIR)**. In addition to the major focus on CF research, we also now include a research program focused on pediatric asthma. The new logo for CF-AIR is shown below.

We are proud of our growth, and look forward to achieving great things for our patients, our institutions, and our city. Thanks for your continued interest and support.



2014 Visitors To Date

- Eric Sorscher, MD, March 2014, University of Alabama, Birmingham, *Cystic Fibrosis Translational Research: Progress and Clinical Partnerships*
- Dexi Lui, PhD, April 2014, University of Georgia, *Hydrodynamic Gene Transfer for Gene Drug Discovery and Gene Therapy*
- Drew Dotson, June 2014, Atlanta, GA, *My Life with Cystic Fibrosis*
- Jennifer Guimbellot, MD/PhD, June 2014, University of North Carolina at Chapel Hill, *Challenges in the use of small molecule compounds for cystic fibrosis therapy*
- Hong Wei Chu, MD, September 2014, National Jewish Health, *SPLUNC1 in Inflammatory Lung Diseases*

Inside this issue:

- Clinical Team One CF@TLANTA 2
- Patient Highlight Research Team 3
- Hack for CF 4
- Great Strides 5
- Program Growth 6
- Pilot and Extramural Grants 7
- NACFC 2014 8
- Research Cores 9
- Research Workshop Contact Info 10

New Clinical Faculty: Alvin Jay Freeman, MD



A. Jay Freeman, MD

Clinical Team Changes

Lindsay Granger
CF Nurse Practitioner
Scottish Rite
Pediatric CF Program

Shavina Goedar, RN
Emory/Egleston
Pediatric CF Program

Our newest recruit to fighting CF in Atlanta is Alvin Jay Freeman, MD. Dr. Freeman became a pediatric CF gastrointestinal physician at the Egleston and Scottish Rite campuses on July 1, 2014, upon completion of his fellowship in Pediatric Gastroenterology, Hepatology and Nutrition at Emory University and Children's Healthcare of Atlanta. Dr. Freeman earned his medical degree from American University of the Caribbean and completed his pediatric internship and residency at the University of Mississippi Medical Center Blair E. Batson Children's Hospital. Dr. Freeman currently is the principal investigator on a three-year grant funded by the Cystic Fibrosis Foundation entitled, "Developing Innovative GastroEnterology Specialty Training (DIGEST) Program". This program is designed to support the role of GI providers in CF clinics.

Dr. Freeman's lifelong interest in medicine has been driven by his fascination with how the human body works, including his own. As an avid soccer player, while growing up he broke his ankle and had eight leg surgeries. These experiences sparked an interest in orthopedics until his residency at the University of Mississippi, where there was no pediatric pulmonologist. As a result, kids with cystic fibrosis often ended up on the GI service. Dr. Freeman realized that while CF kids lived due to pulmonary care, they often died due to CF-related GI issues. Dr. Freeman appreciated his ability to make big differences in these children's lives just by coaching them on small changes in their diets and addressing issues like acid suppression and constipation. The families were excited and receptive, and teens with CF had the highest

compliance rates compared to teens with other chronic diseases. The opportunities to improve patients' quality of life by addressing GI issues drew Dr. Freeman to Emory University, where he has been mentored by many faculty, including Drs. Stecenko, Romero, and Karpen. He is excited about beginning his new role as a faculty member in a collaborative, multidisciplinary atmosphere that provides a truly holistic approach to caring for CF patients.

While not at work, Dr. Freeman enjoys spending time with his wife, a corporate defense attorney, and their 16 month old son Blake. All three are anxiously awaiting the arrival of their newest family member in November. Dr. Freeman also regularly plays soccer at Silverbacks Park and tennis through the United States Tennis Association.

One CF@LANTA

In December 2013 the three CF campuses in Atlanta were one of eight sites in the US awarded a Leadership and Learning Collaborative Grant from the CF Foundation to participate in the ONE CF Initiative. The purpose of this initiative is to strengthen the continuum of CF care beginning from diagnosis through adulthood. To date, regular local and

web based meetings in conjunction with national meetings in Boston and Omaha have enhanced our abilities to both assess our current center approaches to care and utilize this knowledge to develop strategies to improve care. This grant has served as a catalyst to 1) improve relationships across all three campuses, 2) enhance program de-

velopment within and between the Scottish Rite, Egleston and Emory Adult Centers, 3) strengthen personal leadership skills, and 4) develop strategies to improve both quality and processes on all three campuses that can be implemented and improved upon for years to come. This grant will continue through March 2015.

Patient Highlight: Caroline Hilburn



Caroline Hilburn

My name is Caroline Hilburn and I am currently a Junior, Interior Design major, at Georgia Southern University. After graduation I aspire to work for an interior design firm to design medical facilities, such as hospitals. Aside from classes, and a ridiculous amount of homework, I stay busy by being on the leadership team of the Delta Phi Epsilon (DPhiE) sorority. I am the Vice President of Programming, and as such, one of my responsibilities includes overseeing our annual philanthropy events. One of Delta Phi Epsilon's national philanthropies is the Cystic Fibrosis Foundation. Through my position in DPhiE, I am able to educate my sisters and the local community about the causes and effects of CF, as well as share my passion for raising awareness

and funds to help find a cure for Cystic Fibrosis. Although balancing a full load of classes, a vice president position, and managing a chronic illness is not always easy, and sometimes I just want to give up, I remind myself why I am doing these things. I go to school so that I can get an education and eventually find a job; but I serve as the Vice President of Programming for DPhiE, not only for myself, but also for everyone who fights CF everyday.

New Research Faculty: Jessica A. Alvarez, PhD, RD

Jessica Alvarez, PhD, RD is excited to be a new member of the Center for Cystic Fibrosis and Airways Disease Research (CF-AIR). She is a registered dietitian with a PhD in Nutrition Sciences. Dr. Alvarez completed her dietetic internship and graduate training at the University of Alabama at Birmingham (UAB), including a clinical traineeship in the UAB Pediatric Pulmonary Center. It was here that she understood how vital proper nutrition is to the health and quality of life of individuals with CF. Dr. Alvarez joined Emory in 2011 as a postdoctoral fellow and played a critical role in the CF Foundation-funded clinical trial, "Vitamin D for Enhancing the Immune System in CF (DISC Study)," led by Dr. Vin Tangpricha. Dr. Alvarez is now a faculty member in the Emory School

of Medicine. She is the principal investigator in a National Institutes of Health career development grant entitled, "Integration of Nutritional Metabolomics with Bioenergetics in Cystic Fibrosis (BEAM-CF Study)." As medical therapies advance and individuals with CF enjoy longer lives, nutrition will continue to be a key contributor to the maintenance of health throughout adulthood. With the BEAM-CF study, Dr. Alvarez hopes to gain insight into nutrition-related pathways that can be modified to improve health in adults with CF. With Dr. Arlene Stecenko, Dr. Alvarez is also conducting studies in adult CF investigating body composition (body fat and muscle), as well as effects of high and low-glycemic index meals. Her ultimate goal is to use evidence-based nutrition

research to define optimal dietary guidelines for adults with CF. Dr. Alvarez has an excellent mentoring team of CF-AIR faculty, including Drs. Nael McCarty, Arlene Stecenko, Vin Tangpricha, Dean Jones, and Thomas Ziegler to guide her in her research and career goals. Outside of research, Dr. Alvarez enjoys training for half-marathons and reading fiction novels, but most of all she loves spending time with her husband and 2-yr old daughter.



Jessica Alvarez, PhD, RD

Hack for CF

Hack for CF: Cystic Fibrosis Hackathon was a first of its kind event for cystic fibrosis. On October 5 and 6, 2013, data scientists, designers and technologists collaborated with subject matter experts and stakeholders to work on real CF issues. Eight different teams worked on projects to benefit the CF community. The top three projects were:

Hack for CF



Cystic Fibrosis Hackathon

Atlanta, GA - October 5-6, 2013

1st Place: CF Digest – The overwhelming amount of online information related to CF can make valuable information difficult to find. To structure comments from forum.cysticfibrosis.com into an easy-to-digest format, this proof of concept project used state-of-the-art natural language processing tools to classify 180,000 forum posts based on product relevance and sentiment to create a user-friendly product recommendation website.

2nd Place: Track*D – This mobile-friendly website allows CF patients to easily track their medical and therapeutic compliance, moods, energy, and other disease management routines. Track*D stores patient histories to provide detailed charts and histories, and generates a weekly email summary of entries to help patients and caregivers maintain or improve compliance.

3rd Place: Awakening – “Awakening” is a game designed to motivate CF patients to engage in proactive self-care while providing valuable data to healthcare professionals and the CF community. Users create an avatar whose stats and activity points in the gamification platform directly correlate to the user’s compliance with their healthcare regimen. Awakening is available at <http://katercreations.com/awakening/>.

For details on other projects finished at Hack for CF, please visit <http://hackforcf.com>.

We would like to extend a special thank you to the sponsors who made the first Hack for CF possible:

Children’s Healthcare of Atlanta
Emory University School of Medicine
Porter Novelli
Microsoft
TriNet
CF@LANTA
Govathon
InvestAtlanta
IxDA Atlanta
Kwanza Hall: Atlanta City Council District 2
Data Science ATL
Hypepotamus
Georgia Tech School of Industrial Design
Atlanta Web Design Group
Georgia Tech Institute for People and Technology
My Inventor Club
CF Smackdown

Congratulations also to the founding team for a tremendously successful inaugural event!

Nael McCarty, PhD, Emory University
Ric Geyer, City of Atlanta
Terry Allen, Govathon, RHoK Atlanta, and ShootProof
Andrew Gardner, PhD, Momentics
Jeff Carter, Harvard Group International
Raj Bandyopadhyay, PhD, Pindrop Security
Michael Flanigan, Covello
Pierce Walker, Invest Atlanta
Seth Walker, MD, Emory Healthcare
Scott Henderson, Hypepotamus
Eloisa Klementich, PhD, Invest Atlanta
Shane Matthews, My Inventor Club

Great Strides

The Cystic Fibrosis Foundation (CFF), the world's leader in the search for a cure for cystic fibrosis, is a major funder of CF research across the world. CFF's largest national fundraising event is Great Strides, which consists of 600 walks nationwide. The Atlanta Great Strides walk, presented by Snellings Walters Insurance Agency, took place on May 17, 2014 and continues to be the largest cystic fibrosis walk in the country. This year, 120 teams of 3,000 walkers raised over \$1.66 million to finance drug discovery, research, and education.

The **CF@LANTA** Great Strides team was led by Dr. Nael McCarty in partnership with other program leaders. We would like to thank everyone

who donated to Great Strides for their contribution towards ending this devastating disease.

Missed this walk or interested in "adding tomorrows to the lives of people with CF" elsewhere in Georgia? Check out one of the [eight other Georgia cities](#) with Great Strides walks. Get involved by raising funds, forming a team, and/or volunteering at an event – you'll be glad you did!



Recent Accomplishments: Partnership with Celtaxsys

Celtaxsys, Inc., is an Atlanta-based biotech company with a unique immunomodulator program. The company has long-standing relationships with Dr. Tirouvanziam (one of our recruits to the Center and the Dept. of Pediatrics), with Georgia Tech, and with Atlanta's Advanced Technology Development Center, and is building relationships with Emory and especially with **CF@LANTA**. The team is moving their lead candidate drug into phase II trials later this year; this is a once daily, oral medicine designed to improve lung function in Cystic Fibrosis patients. The Celtaxsys team has a secondary goal of becoming an anchor biotech entity in the Atlanta

community. The leadership of our CF research program met recently with the leadership of Celtaxsys, and we are excited to be working together to benefit our patients. Last year, Celtaxsys closed down their internal research lab operation in a shift of the business model to one based more on collaboration with academic research labs. In the process of this shift, the company donated a large amount of equipment and supplies to the CF research team at Emory; the total value is on the order of \$250,000. This includes: an inverted microscope with environmental chamber, camera, and motorized stage; a cell culture hood; a benchtop centrifuge; a desktop flow cytometer system;

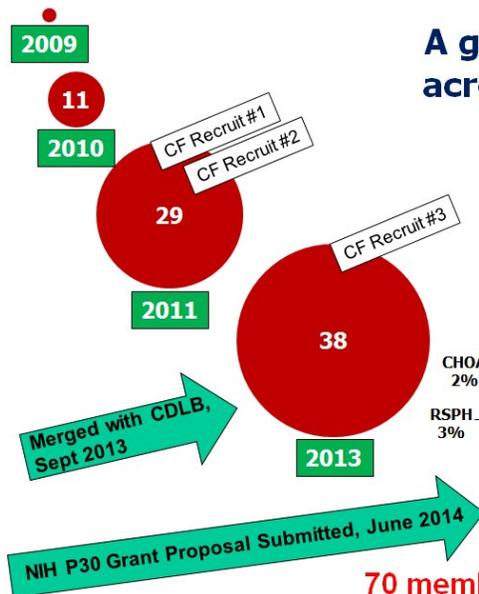
freezers; and an FPLC chromatography system. This extraordinary gift is greatly appreciated, and will allow us to focus our grant-writing and fundraising on the most important part of our research enterprise – the experiments themselves. We welcome this new relationship with Atlanta partners in the fight against CF, and look forward to working with Celtaxsys for years to come. Special thanks to the company's leadership team, including Greg Duncan (President and CEO), Bill Reddick (COO), Ralph Grosswald (VP, Operations), and Eric Springman, PhD (CSO).



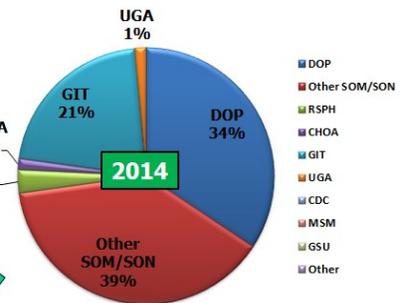
Milestones in Program Growth



In just a few short years there has been tremendous growth within the center!



A growing membership across our constituents and partnering institutions



70 members: 24 primary, 46 affiliate

NACFC 2014

We are excited to share that the **28th Annual North American Cystic Fibrosis Conference** will be held October 9-11, 2014 at the Georgia World Congress Center in Atlanta! This conference is designed for medical professionals in CF research and care, including physicians, research scientists, nurses, nutritionists and dietitians, social workers, physical and respiratory therapists, psychologists and psychiatrists, and research coordinators. Three days of more than 60 concurrent sessions will offer continuing medical education in the latest research and advances in CF and serve as a collaborative forum to advance research for the treatment and cure of CF. A special CF Advisory Board Track also is available for parents, partners, and caregivers of people with CF.

Members of **CF@LANTA** submitted 22 abstracts to the NACFC. Abstract titles and authors are as follows:

1. Inhaled Corticosteroid Use Is Associated With Chronic *Pseudomonas* Infection in Cystic Fibrosis. TCB Beaty, AM Fitzpatrick, K Kirchner, AA Stecenko
2. Increased prevalence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* infection in airways of CF-related diabetes patients. M Shah, B Helfman, AM Fitzpatrick, AA Stecenko and J Goldberg
3. Exocytosis of toxic primary granules by human neutrophils is associated with high surface TRPM2 expression and pinocytosis. S Ingersoll, O Forrest, J Bowen, M Brown, R Tirouvanziam
4. CTX-4430, a candidate LTA4H inhibitor, downregulates neutrophil transmigration through human bronchiolar epithelium in vitro. R Tirouvanziam, O Forrest, E Springman
5. Human resistin, a neutrophil-derived metabolic and inflammatory mediator, reaches strikingly high levels in cystic fibrosis airway fluid. O Forrest, D Chopyk, S Ingersoll, M Brown, C Conrad, V Tangpricha, R Tirouvanziam
6. Combined *in vivo* and *in vitro* analyses identify the caspase-1 / TRPM2 axis as a contributor to neutrophil-driven airway inflammation in cystic fibrosis. O Forrest, S Ingersoll, A Robertson, M Preininger, J Laval, M Brown, V Tangpricha, L O'Neill, M Cooper, R Tirouvanziam
7. Dynamic expression of T-cell suppressive molecules arginase-1 and programmed death ligand-1 by mature airway neutrophils in cystic fibrosis. S Ingersoll, O Forrest, J Laval, M Preininger, M Brown, V Tangpricha, R Tirouvanziam
8. Discovery-based, high-resolution plasma metabolomics following a vitamin D3 intervention in adult patients with cystic fibrosis. J Alvarez, E Smith, D Jones, R Grossmann, J Frediani, K Uppal, R Tirouvanziam, V Tangpricha, T Ziegler
9. Proteomic analyses of serum from CF patients with mild or severe disease reveal the differential expression of proteins that regulate the differentiation of cartilage, myeloid leukocytes, and intestinal epithelia. A Ziady, S Lin, SL Heltshe, T Kelley, M Muhlebach, F Accurso, JM Pilewski, JP Clancy, SD Sagel, E Joseloff
10. Validation of candidate serum protein and lipid markers of disease severity in CF. SD Sagel, B Wagner, A Ziady, T Kelley, M Muhlebach, F Accurso, J Pilewski, S Heltshe, JP Clancy, E Joseloff
11. A model of lung infection in CF^{-/-} mice reveals altered liver gene expression AJ Freeman, A Kusters, R Hunt, NA McCarty, SJ Karpen
12. Murine CFTR behavior differs from human CFTR in distinct aspects. G Cui, CZ Prince, NA McCarty
13. Feasibility of early detection of acute pulmonary exacerbations by exhaled breath condensate metabolomics. X Zang, M Monge, NA McCarty, AA Stecenko, FM Fernández
14. Modulation of neonatal alveolar macrophage in the CF lung-implications for impaired immune defense. TW Gauthier, XD Ping, LS Brown
15. Advanced glycation end products are elevated in cystic fibrosis related diabetes. WR Hunt, BR Helfman, NA McCarty, JM Hansen
16. Metabolic analysis of exhaled breath condensate in cystic fibrosis related diabetes. WR Hunt, VT Tran, AA Stecenko, NA McCarty, D Jones, JM Hansen
17. Positioning of the first extracellular loop of CFTR has significant effects on CFTR gating. D Infield, G Cui, C Kuang, NA McCarty
18. Identification of changes in lung microbial community composition that correlate with the appearance of acute pulmonary exacerbations. A Pena, JK Hatt, BR Helfman, NA McCarty, K Konstantinidis
19. Expression of $\Delta F508$ -CFTR by airway epithelial cells sensitizes tight junctions to glucose-induced stress. B. Schlingmann, S Molina, J Hansen, A Ziady, NA McCarty, M Koval
20. Chronic MRSA and *P. aeruginosa* co-infection and rate of lung function decline in cystic fibrosis. ML Maliniak, NA McCarty, AA Stecenko, WM McClellan
21. Hack for CF, the cystic fibrosis hackathon. NA McCarty, R Geyer, T Allen, A Gardner, J Carter, R Bandyopadhyay, M Flanigan, P Walker, S Walker, S Henderson, E Klementich, S Matthews, M Maliniak
22. Expression profiling reveals that NuLi and CuFi airway epithelial cell maturation requires extended time in culture. S Molina, B Stauffer, J Hansen, NA McCarty, M Koval

We are grateful to be part of the host city for this year's conference and can't wait to learn about the cutting edge research being conducted by our colleagues throughout the world. To learn more about this conference or to register, please visit www.nacfconference.org.

CF Discovery Core

The CF Discovery Core houses the Cystic Fibrosis Biospecimen Registry (CF-BR) which is a storage bank of several thousand biofluids collected from patients with cystic fibrosis at varying disease states. Patients are consented from both the adult and pediatric clinics at Emory+Children's and may donate samples at each outpatient clinic visit, at their annual visit only (which typically runs long and includes more lab tests), when hospitalized, or any combination of the above. We believe that these treasured samples may hold the keys that will allow our researchers to unlock the mysteries underlying the changes that occur in the

lungs of CF patients as the disease progresses.

The CF Discovery Core provides several services including: collection and processing of samples from Emory+Children's CF adult and pediatric clinics and their associated hospitals; storage and banking of these samples; and maintenance of a database of clinical information associated with each sample collected.

For more information about the CF Discovery Core, please visit www.pedsresearch.org/cores/detail/discovery-core

*Don't forget:
All abstracts,
publications, grant
proposals, and other
related documents
made possible through
the use of these cores
must cite
"Emory+Children's
Pediatric Research
Center [core name]" in
the acknowledgements
section of the
manuscript.*

CF Mouse Core

The Emory+Children's Pediatric Research CF Mouse Model Core provides murine models relevant to cystic fibrosis researchers. Multiple models are maintained and provided to researchers at a reasonable cost towards helping to address specific aspects of CF.

Currently available models:

1. The CFTR knockout mouse (B6.129P2-Cftrtm1Unc/J). This mouse is used as a homozygous negative knockout mouse, where there is no CFTR expression.
2. The gut corrected CFTR knockout mouse (Cftrtm1UncTg(FABPCFTR)1Jaw/J). This mouse is

a full CFTR knockout as listed above with the exception that a human CFTR gene has been inserted to be expressed in the gut epithelia on the FABP1 promoter.

3. Δ F508 CFTR mouse (B6.129S6-Cftrtm1Kth/J). The Δ F508 mutation constitutes the most predominate CFTR mutation in humans.

For more information about the CF Mouse Core, please visit www.pedsresearch.org/cores/detail/cf-mouse-model-core.

Biomarkers Core

The Pediatric Biomarkers Core facility provides the equipment and technical expertise to assay samples using methods that combine the features of gas-liquid chromatography and mass spectrometry. These core services are applicable to a wide variety of sample types and will allow small-molecule metabolite profile identification. The Core has an Agilent gas chromatography/mass spectrometer and a Waters High Performance Liquid Chromatography with fluorescence detector. The Biomarkers Core currently performs analysis of biomarkers of oxidative stress including reduced and oxidized glutathione, cysteine, cystine, isoprostanes,

hydroxynonenals, and malonyldialdehydes. This core also analyzes Fatty Acid Ethyl Esters (FAEE) from biological samples such as meconium, hair, placenta, blood, plasma as markers of alcohol use and exposure. The core is located in the Emory-Children's Center building.

For more information about the Biomarkers Core, please visit www.pedsresearch.org/cores/detail/biomarkers

CF-AIR Research Workshop 2014-2015

The CF-AIR Research Workshop meets weekly on Wednesdays at 4 pm in room 302 of the Emory-Children's Center. Each month follows a general pattern unless we have a special visitor or event.

1st week: Journal Club (contact Sarah Ingersoll to sign up)

2nd-4th week: Research Seminar (contact Danny Infield & Brandon Stauffer to sign up)

Upcoming:

October 1, 2014: Calvin Cotton, PhD, Case Western Reserve University
(HSRB Auditorium)

October 7, 2014 (Tuesday): NACFC Poster Warmup, 12:30-2 pm (HSRB Auditorium)

October 15, 2014: Steve Aller, PhD, University of Alabama, Birmingham
(HSRB Auditorium)

October 21, 2014 (Tuesday, 5:15 pm): Assem Ziady, PhD, Emory University (HSRB Auditorium)

Full scheduled updated on:

www.pedsresearch.org/centers/sub-pages/cf-air-seminars-workshops/

Staying in Touch

Clinics:

Emory Adult CF Clinic: 404-778-7929

Children's Healthcare of Atlanta
CF Care Center:

*NEW ADDRESS!

Children's at North Druid Hills
1605 Chantilly Drive NE
Atlanta, GA 30324
404-785-2000

Children's at Scottish Rite
Cystic Fibrosis Affiliate Program
5455 Meridian Mark Road, Suite 200
Atlanta GA 30342
404-785-2898

Website:

[www.pedsresearch.org/
centers/detail/CF-AIR](http://www.pedsresearch.org/centers/detail/CF-AIR)

If you are interested in supporting our research and outreach programs please visit: www.pedsresearch.org/centers/sub-pages/cf-air-donors-visitors/

Contact:

Nael McCarty, PhD: Program Director
namccar@emory.edu

Karen Kennedy, Program Coordinator
kmurra5@emory.edu