

# The Emory+Children's Cystic Fibrosis Center of Excellence

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## Update from the Director

Dear friends of *CF@LANTA*:

We are pleased to present you with the next edition of our e-newsletter, and hope that this finds you well. There is much exciting news to report, as you'll find in the following pages. This includes great progress in all facets of our comprehensive CF program (research, education, and clinical care), and the asthma research program that is also embodied in the Center for CF and Airways Disease Research (CF-AIR).

Two big stories to mention here: First, the successful recruitment of Dr. Eric Sorscher to our program, which was announced in a special newsletter in March (available [here](#)). Dr. Sorscher is recognized worldwide as a thought leader in the world of CF, and has led the CF research center at the University of Alabama at Birmingham for the past 21 years. Dr. Sorscher has held numerous national and international leadership roles in the CF scientific community and is widely respected. He is a prominent counselor to the national CF Foundation and the international CF research community, including serving as a consultant to several of the pharmaceutical companies involved in developing therapies for CF. He is Chair of the New Therapies Committee for the North American CF Conference supported by the CF Foundation, and Chair of the CF Folding Consortium, also supported by the Foundation.

Recruitment of Dr. Eric Sorscher to Atlanta will transform the landscape of CF research. The strong efforts in drug discovery at Emory will complement his efforts to develop new therapies for CF. Moreover, he will be a game-changer in elevating the research status and presence of the Atlanta CF research community, and will add great momentum to our ability to grow our program. Recruiting Dr. Sorscher to our Center is sending a loud message that we intend to be the home of the best comprehensive CF program in the country. More importantly, Dr. Sorscher's work is poised to bring life-changing therapies to children and adults suffering with CF and other diseases.

The second major news item: the large grant recently awarded to us by the CF Foundation to establish the Atlanta CF Research and Development Program (*CF@LANTA* RDP Program). This new grant will support infrastructure to facilitate the expansion of the funded CF research by Atlanta investigators. You'll recall that the February 2015 newsletter reported the submission of this proposal. Please see page 4 for further information.



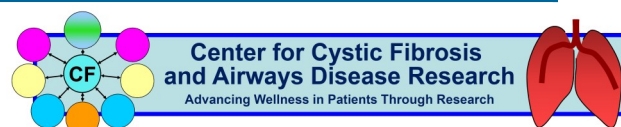
Nael A. McCarty, PhD  
Center Director

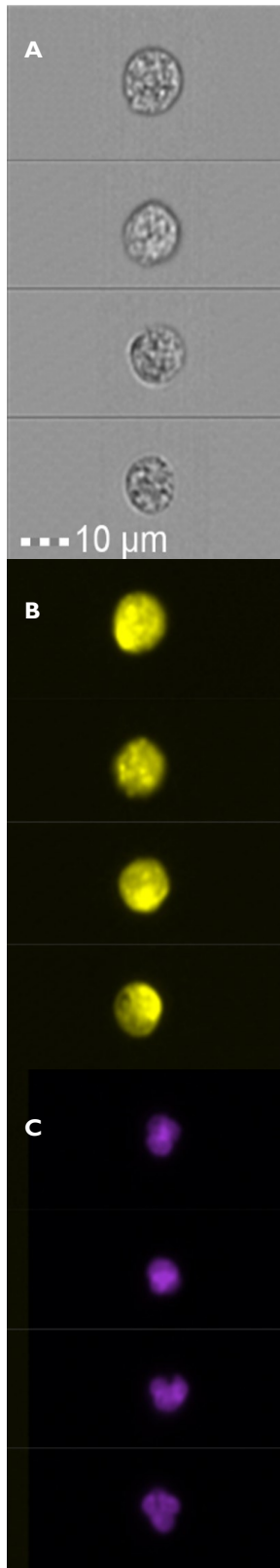
### Inside this issue:

Trainee Profiles: Sarah Fankhauser Haitham Shahrour	2
2015 Center Pilots	3
CFF RDP Award	4
Great Strides Team	5
Recent Publications	6
CF-AIR Brags	7

## Recent Visitors

- Eitan Kerem, MD, March 2015, Hadassah Hebrew University Medical Center, Israel, *Cystic Fibrosis: The story of a journey through phenotype, genotype and drug development*
- Sam Moskowitz, MD, March 2015, Massachusetts General Hospital, *Colistin resistance: threat to a last-line therapy for multidrug-resistant Gram-negative pathogens*
- Hong Wei Chu, MD, April 2015, National Jewish Health. *Translational Asthma Research*
- Jason Papin, PhD, April 2015, University of Virginia, *Metabolic network analysis of microbial pathogens*





Flow Cytometry Images from Ingersoll et al. (citation page 6). Image shows arginase I in neutrophils from CF blood samples

## Trainee Profile: Sarah Fankhauser, PhD

Sarah Fankhauser PhD, is excited to join the faculty at Oxford-Emory as an assistant professor in the biology department—a dream job for her. Dr. Fankhauser completed her PhD at Harvard University studying bacterial pathogenesis. She joined Emory in 2014 as a postdoctoral fellow in Joanna Goldberg’s lab and focused on studying virulence mechanisms in *Burkholderia cenocepacia*. Dr. Fankhauser is currently a FIRST (Fellowship in Research and Science Teaching) Fellow at Emory and has focused on using her own research to teach scientific concepts at the undergraduate level. One of Dr. Fankhauser’s goals at Oxford is to connect

Oxford students with the research community at Emory and prepare her students with the skills necessary to be excellent researchers. While at Oxford, Dr. Fankhauser plans to educate students about CF and stay connected to the CF-AIR community.

While not at work, Dr. Fankhauser spends time promoting science education in other ways. She has helped organize the Atlanta Science Festival for the last two years and also runs a science education non-profit (the *Journal of Emerging Investigators*). But her true joy is spending time with her husband and their 6 month old daughter. The three of them enjoy hiking

at Kennesaw Mountain, spending time with friends and family, and relaxing at the beach.



Sarah Fankhauser, PhD

## Fellow Profile: Haitham Shahrour, MD

Dr. Shahrour is currently a first year fellow in pediatric pulmonary medicine at Emory University. He earned his medical degree from Damascus University. He completed his pediatric residency at The Women and Children’s Hospital of Buffalo where he worked for several weeks at a multidisciplinary cystic fibrosis clinic. “This was my first real exposure to cystic fibrosis. I was fascinated by the wide variety of pathology, inspired by the physicians’ and ancillary staffs’ willingness to work together for the best

interest of the patients, and excited by the opportunity to also serve cystic fibrosis patients.

“I am very excited about my recently awarded Cystic Fibrosis Foundation grant. This grant will help me achieve my long long-term goals in developing excellence in patient care, as well as specifically, optimizing the care and quality of life in my cystic fibrosis patients. I plan to use the skills gained to continue this important research moving forward. “I like spending time with my wife and our 17 months

old daughter. I enjoy playing soccer, reading history books and watching political talk shows.”



Haitham Shahrour, MD

## CF-AIR Center Pilot Awards

For the 2015 call for CF-AIR Center pilots there was an emphasis on cystic fibrosis applications—even years our center pilots are for asthmas-focused applications. CF-AIR is excited to announce that we will be funding 2 applications. A third application to the CF-AIR center will be funded by the Center for Pediatric Nanomedicine, meaning 3 of our center pilot applications will be funded. We are very excited to be supporting great CF research through these pilots. Below are brief descriptions from the investigators of the 2 CF-AIR 2015 Center Pilots. Thanks to Dr. Michael Koval for overseeing the review process.

### Protease-activated drug delivery to live airway neutrophils: a disruptive approach to CF therapy

Rabin Tirouvanziam, PhD, Krishnendu Roy, PhD, Amit Gaggar, MD, PhD (UAB)

Our group discovered that neutrophils (aka PMNs, a type of white blood cells) are pathologically reprogrammed upon recruitment to cystic fibrosis (CF) airways, opening exciting avenues for molecular immunotherapy to halt PMN-driven CF small airway destruction, a currently intractable and fatal process. Here, we will combine recent multidisciplinary breakthroughs to advance toward the first nanoparticle-based targeted immunotherapy of these reprogrammed CF airway PMNs. Our aims are to: 1. Optimize protease-activated nanoparticle-inside microgels for targeted delivery to airway PMNs and minimal epithelial side effects *in vitro*; and 2. Demonstrate efficient protease-activated microgel-mediated delivery to airway PMNs and significant therapeutic effects *in vivo*. This study is significant for child health, as it ushers a new therapeutic approach to fatal airway disease in children with CF. The focus on the CF airway microenvironment as a peculiar cellular and molecular ecosystem that requires customized solutions to achieve therapeutic success is also very congruent with the "systems ecology" theme of our CF Center. Our proposal leverages complementary strengths and expertise of our groups at Emory (Tirouvanziam) and Georgia Tech (Roy), with help from a collaborator at UAB (Gaggar), ushering a new collaboration that this grant will help crystallize.



Rabin Tirouvanziam



Krishnendu Roy



Amit Gaggar

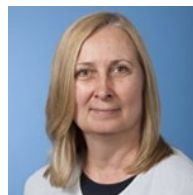
### Bacterial Burden and Diversity of the Airway Microbiome Prior to the Onset of CFRD

Joanna Goldberg, PhD, Arlene Stecenko, MD

Cystic fibrosis-related diabetes (CFRD) is one of the most important co-morbidities associated with cystic fibrosis (CF) and occurs in 20% of adolescents and 50% of adults. However, whether CFRD alters the community of bacteria present in the respiratory tract and if this correlates with a decline in lung function currently remains unknown. While certain studies have found a correlation with increased presence of predominant CF pathogens in hyperglycemic CF patients, others have failed to link the presence of a specific pathogen with the decline in lung function. In the current study, we propose to compare the airway microbiome of pre-diabetic patients to those with well-documented normal glucose tolerance (NGT). Prior studies have demonstrated that pre-diabetic patients already suffer from decreased lung function and this correlates with decreased glucose tolerance. Using this patient population will allow us to determine how hyperglycemia affects the microbiome, and control for secondary co-morbidities associated with long-standing diabetes. By focusing on a comparison between pre-diabetic CF patients and those with NGT, we will more readily be able to identify changes in the microbiome that precede the development of diabetes and thus potentially contribute to worse lung health outcomes. The specific aim of this proposal will begin to address this hypothesis through a small case-controlled study: Compare the bacterial community and its diversity, as well as the bacterial burden, in sputum samples obtained from 10 pairs of CF patients (matched for sex, age, CFTR genotype, FEV<sub>1</sub>, and body mass index (BMI)) that do or do not have pre-diabetes.



Joanna Goldberg



Arlene Stecenko

## Research Development Program Grant

As noted on the first page, the Emory+Children's CF Center of Excellence was recently awarded a Research Development Program (RDP) grant. Being recognized by the CF Foundation as a new RDP Center is a very large feather in our cap. It reflects years of effort to improve the quality of clinical care in our long-standing care program, the major advances we have made since 2007 in building a world-class research team and doing important science, and our establishment of innovative educational programs that will ensure that this progress continues. The CF Foundation has supported the RDP mechanism since the early 1980's, but our program never was in a position to compete successfully until now. We were invited to submit this proposal, in recognition of the enormous positive change that we have accomplished over the past several years. We are very grateful for that institutional support, and support from the local community, which has enabled us to establish and improve our program.

The RDP grant mechanism was started by the CF Foundation in 1981, with the first award given to the University of Alabama at Birmingham. An RDP grant is a marker of excellence, as the strongest CF research programs in the country (11, including ours) are currently receiving this support from the CFF. We have been working to build infrastructure funding for the CF program for many years and the RDP mechanism will enable us to leverage the investments that Children's and Emory already have made in the CF program.

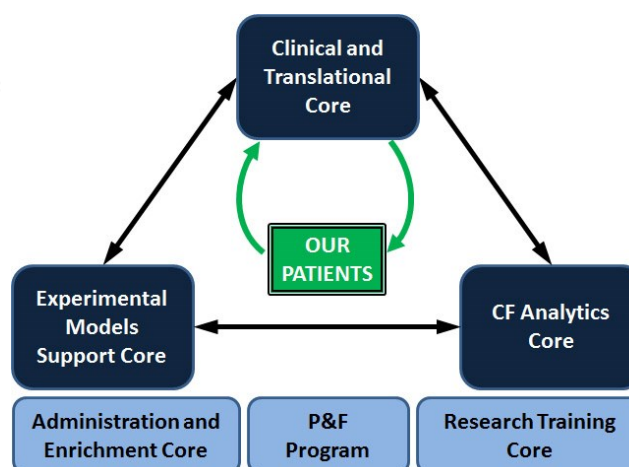
Respiratory disease in patients with CF is characterized by the triad of decreased mucociliary clearance, chronic airway infection, and neutrophil-dominated inflammation. People with CF die in early

adulthood because of progressive lung disease and ultimately respiratory failure. Our team's previous research has poised us to make the greatest impact on two disease foci critical to controlling disease progression in CF patients and were the focus of the RDP application: 1) acute pulmonary exacerbations (APEs) and 2) CF-related diabetes (CFRD).

The overarching goal of the **CF@LANTA** RDP Center is to

promote interdisciplinary research into the pathogenesis of CF and translate this new knowledge into therapeutic strategies for this life-shortening disease. Our strategy to reach this goal centers upon the ~660 CF patients cared for within our clinical program. Our team of CF scientists, physician-scientists, and engineers will use state-of-the-art approaches to: (1) study patients, patient-derived samples, and novel animal models of CF/CFRD to identify the changes in airway function with respect to inflammation and redox imbalance that accompany disease progression through APEs and the development of CFRD; and (2) use more traditional experimental tools to test mechanistic hypotheses in the context of patient data on disease progression. We will study the complex environment of the CF lung by considering each component as a member of a community, and applying the scientific principles of both systems biology and community ecology. The overall scientific theme for our program, therefore, is "The

Systems Ecology of the CF Lung." We will use a variety of approaches to characterize the changes in activities of each of the cell types that make up the community and in the signals by which they communicate to identify those changes that are associated with progressive lung disease and with progression from normal glucose tolerance to CFRD. We will apply systems biology approaches to understand how these components of the community interact.



This research will identify new therapeutic routes and lead to new understanding that will be translated back to the patient. This will be accomplished by the coordinated activities of three biomedical research Cores, and three support programs, as shown in the adjacent figure. We will roll out information to our investigators on how to make use of these Core services over the next couple of months. Meanwhile, you can learn more about the RDP Center grant here: <http://www.pedsresearch.org/centers/sub-pages/cf-air-cf-research-cflanta-core-center/>



## Great Strides

Every year, the CF Foundation’s Georgia Chapter hosts several events to raise funds for CF research, education, care, and patient and family support. The largest of those annual events is the “Great Strides Walk-a-Thon,” held this year on the Georgia Tech campus on May 16. According to Vicki Nix, of the GA Chapter, over 3,000 participants joined for this year’s walk – the most ever. Even better, those walkers raised \$1,800,750 (as of walk day) in support of the Foundation’s programs. This represents more than an 8% increase over the same point last year. It seems likely that this will be the fourth year in a row that the GA Chapter has broken the national record for amount raised via Great Strides. Congratulations to the GA Chapter, congratulations to all of the families, friends, and colleagues that raised these funds, and thanks to all of the members of the *CF@LANTA* team that came for the walk.



Photos from Nael McCarty

## Recent CF-AIR Publications

- Beveridge LA, Struthers AD, Khan F, Jorde R, Scragg R, Macdonald HM, Alvarez JA, Boxer RS, Dalbeni A, Gepner AD, Isbel NM, Larsen T, Nagpal J, Petchey WG, Stricker H, Strobel F, Tangpricha V, Toxqui L, Vaquero MP, Wamberg L, Zittermann A, Witham MD; D-PRESSURE Collaboration. Effect of Vitamin D Supplementation on Blood Pressure: A Systematic Review and Meta-analysis Incorporating Individual Patient Data. *JAMA Intern Med.* 2015 May 1;175(5):745-54. PubMed PMID: 25775274.
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- Hebbar KB, Cunningham C, McCracken C, Kamat P, Fortenberry JD. Simulation-based paediatric intensive care unit central venous line maintenance bundle training. *Intensive Crit Care Nurs.* 2015 Feb;31(1):44-50. PubMed PMID: 25468293.
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- Kamat PP, McCracken CE, Gillespie SE, Fortenberry JD, Stockwell JA, Cravero JP, Hebbar KB. Pediatric critical care physician-administered procedural sedation using propofol: a report from the Pediatric Sedation Research Consortium Database. *Pediatr Crit Care Med.* 2015 Jan;16(1):11-20. PubMed PMID: 25340297.
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## Center Brags

There is so much to brag about in the center, here are some recent highlights:

- Rabin Tirouvanziam, PhD (Emory Pediatrics) was a symposium chair and speaker at the 38th European Cystic Fibrosis Conference in Brussels, Belgium
- Osric Forrest (Tirouvanziam lab) will present an oral presentation at the 2015 Pediatric Research Conference on June 22 in Atlanta, GA
- A. Jay Freeman, MD (Emory Pediatrics, Children's Healthcare of Atlanta) contributed to the CFF guidelines on constipation, available through the CFF website
- Jessica Alvarez, PhD (Emory Medicine) was selected to participate in the Dannon Nutrition Leadership Institute which supports early stage nutritional scientists
- Arlene Stecenko, MD (Emory Pediatrics, Children's Healthcare of Atlanta) has been selected to be a member of the NIH study section Lung Cellular and Molecular Immunology (LCMI)
- Claudia Morris, MD (Emory Pediatrics, Children's Healthcare of Atlanta) and team have a contract with MAST for a Phase 3 randomized controlled trial at Grady
- Tim Beaty, MD (Emory Pediatrics, Children's Healthcare of Atlanta) will begin the Master of Science Clinical Research program this fall with a tuition scholarship
- Anne Fitzpatrick, PhD (Emory Pediatrics, Children's Healthcare of Atlanta) has earned the rank of associate professor with tenure as of September 1
- Nael McCarty, PhD (Emory Pediatrics) has earned the rank of full professor with tenure as of September 1

## Staying in Touch

### Clinics:

Children's Healthcare of Atlanta  
CF Care Center:  
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

Emory Adult CF Clinic: 404-778-7929

### 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/](http://www.pedsresearch.org/centers/sub-pages/cf-air-donors-visitors/)

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