

Cystic Fibrosis Center of Excellence

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Dear friends and colleagues,

We hope that this finds you well, and that you are able to enjoy some time of relaxation during the summer months.

We are pleased to provide you with the next edition of the e-newsletter from [CF@LANTA](#). In it, you will be able to read about the many activities underway in our comprehensive CF Center of Excellence.

There is a new dawn approaching for CF in Atlanta that will bring with it a new level of care, research and education for the CF community in our city and state. It is approaching with the endorsement and expertise of our great institutions, Emory University and Children's Healthcare of Atlanta, which will include greater information sharing and closer partnership between our two primary institutions. This is a long-time goal of our program that is now becoming a reality in an effort to ensure the success and effectiveness of our work to tackle this terrible disease.

Our intention is to be the Center that finds ways to turn this disease into a condition, one that no longer threatens the lives of our patients.

Why are we doing this? Why CF? Why now? The answer comes down to three things: increased momentum, strong existing institutional commitment, and lastly, because CF isn't waiting and neither can we.

The CF clinical program has been a joint operation for decades, with Emory faculty working with Children's staff at both the Egleston and Scottish Rite campuses - already a joint success. We have been successful in recruiting top-notch physicians, who are improving our ability to provide outstanding care for our patients.

We've done a great job of growing the basic and translational research program from ground zero, since the original Center for CF Research opened its virtual doors in 2010. We have been successful in recruiting top-notch investigators to the research program, including Dr. Eric Sorscher whose recruitment already reflected a joint effort between Emory, Children's, the Georgia Research Alliance, and local philanthropists.

These recruits have formed the nexus for initiating our novel educational programs, including the CF Scholars Program, and for strengthening our clinical fellowship program.

We have been successful in increasing our extramural research support from a variety of sources, including the National Institutes of Health, the CF Foundation, and the National Science Foundation.

We have been successful in obtaining extramural support for some of our research cores (although much more is needed), and efficient management of our Cores to provide services to our investigators at the lowest possible costs.

We also have been intentional in stretching across town to engage colleagues at Georgia Tech; indeed, one of the research cores within the [CF@LANTA](#) RDP Center is based there. We also have helped them recruit great scientists to their faculty - three in the College of Sciences and one in the College of Engineering.

Hence, we have shown that we can leverage institutional investment into both enhanced research activities and increased extramural grant support. In addition, we already have been actively engaging our community, through a number of friends that provide advice and encouragement.

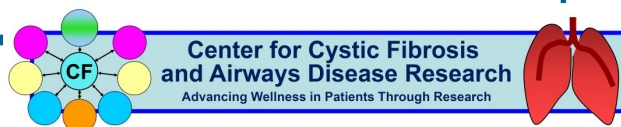
Sounds like a great story, right? The next chapter is coming.

These activities and efforts, undertaken by our physicians, scientists, staff, trainees, and many others, have positioned [CF@LANTA](#) well. Because of these past successes and our current momentum, we have been asked by leadership to dream. Not just to dream but to plan. Not just to plan but to pursue.

You will hear more about this next chapter very soon but please know that our efforts will require even more commitment, partnership and community involvement than ever before. The beneficiaries of this effort will be our patients, our three institutions, and our city.

Tomorrow is coming and bringing with it the warmth of a new and exciting sunrise. We look forward to updating you on our continued progress, and thank you for your support.

With best wishes,
 Nael A. McCarty, PhD, [CF@LANTA](#)
 Margaret Lesesne Adams, Emory Development
 Alicia Brady, Children's Development
 Steven Wagner, Emory Development
 Raymond Reynolds, Children's Development



CF Research Events in April 2016

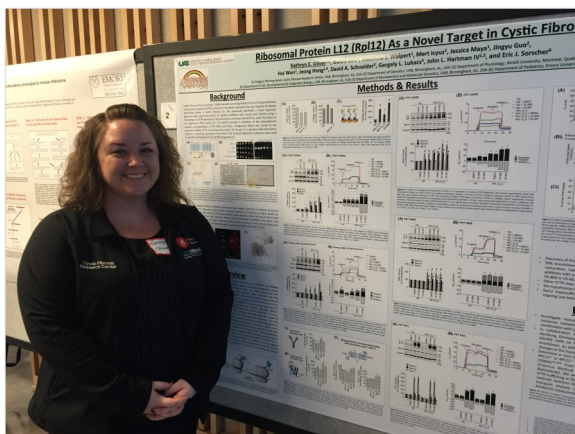
The Southeast Regional CF Research Symposium

CF@LANTA hosted a number of exciting scientific events in April 2016. The First Annual Southeast Regional CF Research Symposium took place on Monday, April 11, 2016. Held in HSRB, this was a joint conference including the **CF@LANTA** team and representatives of the CF group from the University of Alabama at Birmingham (UAB). About 70 people were in attendance ~50 from **CF@LANTA** and ~20 from UAB. Also some of our External Advisory Board (EAB) members and Drs. Bill Skach and Katherine Tuggle from the Cystic Fibrosis Foundation (CFF) national office were in attendance. The goals of this event included sharing information on our research activities, learning about our centers, and developing closer collaborations. Towards this end, an introduction to **CF@LANTA** was provided by Dr. Arlene Stecenko and to UAB was given by Dr. David Bedwell. The keynote speaker was Dr. Marcus Mall from the German Center for Lung Research who gave a talk entitled, “Early mucus obstruction and inflammation: pathogenesis and strategies for therapeutic intervention”. Alternating speakers from **CF@LANTA** and UAB followed this talk and spoke about “Inflammation” in the morning and “Drug Discovery” in the afternoon; both sessions included both basic and clinical research. In between these two sessions, lunch and a poster session was held. There were approximately 15 posters presented by trainees, equally split between those at **CF@LANTA** and UAB. In order to encourage interactions between our two institutions, faculty judges were from the opposite institutions. There was a \$500 prize each for the best poster/poster presentation given by a **CF@LANTA** and UAB trainee: Dr. Joshua Chandler from Dr. Dean Jones’ laboratory the Department of Medicine at Emory University and Kathryn Oliver from Dr. Eric Sorscher’s former laboratory in the Genetics, Genomics & Bioinformatics Program at UAB won these awards.

We feel that this event succeeded at bringing the **CF@LANTA** team closer together and also extending our interactions with the CF center at UAB and we intend to repeat this on a yearly basis. We hope to extend to other CF centers from states adjoining Georgia, as funding becomes available.

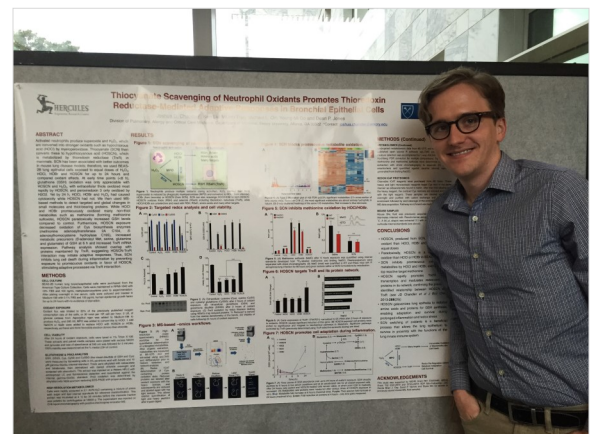
On Tuesday, April 12, 2016, we held our annual **CF@LANTA** RDP Research Retreat. This is a required annual event for our CFF-funded Research Development Program (RDP) and included over 30 members of our local team, most of the members of the EAB (Dr. Bruce Stanton, Dartmouth; Dr. Felix Ratjen, University of Toronto; Dr. John LiPuma, University of Michigan; and Dr. Bill Balch, Scripps), along with Dr. Tuggle representing the CFF. This was held on the grounds of the Atlanta Botanical Garden and provided us the opportunity to showcase our research program. There were reports on our mission and scientific cores. We also had research presentations from 11 **CF@LANTA** faculty members and the 2 trainees who are supported by the RDP. The final presentation was by Dr. Stanton, who shared his research on bacterial interactions with host cells. There was also free time to interact with colleagues and enjoy the gardens. The following day we received constructive feedback from the EAB and CFF with the goal of expanding and refining our research program to improve the lives of our patients.

~submitted by Joanna Goldberg, PhD



CF Research Symposium Poster Award Winners:
Left:
from UAB,
Kathryn Oliver

Right:
from Emory,
Joshua Chandler



CF Scholars Program Update

The CF Scholars program continues to evolve. This unique two-year program educates and mentors students and fellows with the goal of training the next CF Researchers. To encourage the interactions between Ph.D. and M.D., this program is now co-directed by Joanna B. Goldberg, Ph.D. and Tim Beaty, M.D. Also recent graduates of the program (Randy Hunt, MD, Sam Molina, Ph.D., and

Brandon Stauffer) have been enlisted to become part of the CF Scholars Education Committee. Together they will work to organize a new “meet the CF researcher” session. They will also organize times for PhD trainees to shadow physicians and for physicians to rotate in research labs. Finally, they will develop the next CF Basic Science sessions and CF Grand Rounds for the Fall semester.

Great Strides May 21, 2016

Record numbers of people participated in this year's Great Strides Walk-a-thon! This walk supports the Cystic Fibrosis Foundation and is locally put on by the Georgia Chapter. The Atlanta walk is the largest in the country to support the Cystic Fibrosis Foundation and this year raised a record-breaking \$2,030,918 (as of the day of the walk). Children's Healthcare of Atlanta served as a local sponsor again this year—even Hope and Will made an appearance! The [CF@LANTA](#) team was there in force and walking strong. Thanks to all who participated and supported the team.



New Faculty: Devon Greene, MD, MPH



Devon Greene, MD, MPH

Asthma is one of the most common chronic diseases of childhood, and it is a major cause of illness and hospitalization in Georgia. Dr. Greene joined our efforts to address asthma as a pediatric pulmonologist at the Egleston campus on August 1, 2015. Dr.

Greene earned his medical degree from the Medical College of Georgia in Augusta, and he completed his pediatric residency at T.C. Thompson's Children's Hospital in Chattanooga, TN. His first patient as a pediatric resident was a young girl who had been newly diagnosed with cystic fibrosis after being treated for nearly a decade as a bad asthmatic. The idea that two very distinct diseases with very different treatments stuck with Dr. Greene. It wasn't until this patient had seen a pulmonologist that the mystery of her uncontrolled disease could be teased out and revealed, and her life could be changed for the better.

Inspired by the story of this patient, among many others, Dr. Greene moved to Memphis for a fellowship in pediatric pulmonology at Le Bonheur Children's Hospital and St. Jude Children's Research

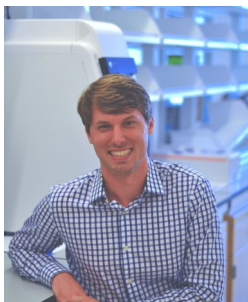
Hospital. While his research there focused on the pulmonary effects of sickle cell disease on sleep, he became increasingly involved in efforts to better understand and manage asthma. While there, he completed a Master's in Public Health, focusing on the identification of asthma control among asthmatics in a Tennessee county. After completing his formal training in 2013, he returned to Chattanooga to serve as an attending for 2 years.

While a great many individuals work to develop new, innovative therapies for asthma, Dr. Greene's focus is on implementing both new and established strategies in patients to improve the quality of their lives. This focus now brings Dr. Greene to Emory University. His efforts so far have focused on redesigning asthma care at the Egleston campus for those children at highest risk for asthma complications. He looks forward to working with the CF-AIR team to improve the quality of asthma care delivered in the region.

When not working on asthma or serving as a pediatric pulmonologist, Dr. Greene spends time with his wife and two children, Sophia and Woods. He would probably read, cook, and hike if his kids and pets allowed him to have time for hobbies.

~submitted by Devon Green

New Faculty: James Dahlman, PhD



James Dahlman, PhD

James Dahlman is an Assistant Professor in the Georgia Tech and Emory University BME Department who works at the interface of nanotechnology, genomics, and gene editing. He joined the Department in May 2016. He studied RNA design and gene editing as a post-doc with Feng Zhang at the Broad

Institute, and received his PhD from MIT and Harvard Medical School in 2014, where he studied RNA delivery with Robert Langer and Daniel Anderson.

James designs nanotechnology for targeted RNA delivery. He designed nanoparticles that deliver RNAs to the lung and heart; these nanoparticles have been used by over ten labs across the US, and

are under consideration for clinical trials. He has also developed targeted in vivo combination therapies; nanoparticles are designed to deliver multiple therapeutic RNAs at once, in order to manipulate several nodes on a single disease pathway.

More recently, James developed a method to quantify the targeting, biodistribution, and pharmacokinetics of hundreds of distinct nanoparticles at once directly in vivo. He will use this new technology to (a) deliver nucleic acids to new cell types, and (b) study how the chemical structure of nanoparticles affects their behavior in animals. As an example, James is using this technology to improve drug delivery to pulmonary epithelial cells, with the goal of developing CF gene therapies.

Continued on next page

James Dahلمان profile continued

Finally, James uses molecular biology to rationally design the genetic drugs he delivers. He recently reported 'dead' guide RNAs; these engineered RNAs can be used to simultaneously up- and down-regulate many genes in a single cell using a single Cas9 protein.

James has won the NSF, NDSEG, NIH OxCam, Whitaker Graduate, and LSRF Fellowships, the Weintraub Graduate Thesis Award, and was recently named a Bayer Young Investigator and Parkinson's Disease Foundation Stanley Fahn Junior Faculty Award winner. He has had significant help along the way. Besides having great scientific

advisors and colleagues, James has been fortunate to mentor great students, including two undergraduates that were finalists for the Rhodes Scholarship. More recently, he was lucky enough to recruit Kshitiz Singh, Ph.D, to his lab. Kshitiz has clinical and wet lab experience. He will help develop new CF gene therapies.



Kshitiz Singh, PhD

~submitted by James Dahلمان

Center Brags

- Recent CF-AIR visitors:
 - ◊ **Peter van der Sluijs, PhD**, March 8, *Mechanism of secretory lysosome exocytosis in hemopoietic cells*
 - ◊ **Beth Brown, PhD**, March 10, *Optimizing Exercise Prescription for Pulmonary Arterial Hypertension: Insight Gained from Acute and Chronic Exercise Studies in Rodent Models and in Patients*
 - ◊ **John LiPuma, MD**, April 13, *Things I was taught about infection in CF that are not true*
 - ◊ **Kambez Benam, DPhil**, May 25, *Microengineered Systems to Emulate Lung Pathophysiology*
 - ◊ **Luke Garratt, PhD**, May 26, *What is driving the formation of chronic airway inflammation in early cystic fibrosis – the epithelium or neutrophils?*
- **Eric Sorscher, Arlene Stecenko, and Joanna Goldberg** will be presenting talks at this year's NACFC
- **Jay Freeman** was asked to chair a workshop on "Gastroenterology and Hepatology" at this year's NACFC
- **Facundo Fernandez** was awarded the Georgia Tech CoS Faculty Mentor Award, supported by the College of Sciences ADVANCE Professorship
- Pediatric Clinics of the North America-invited review by **Jay Freeman**, "Gastrointestinal, Pancreatic and Hepatobiliary Manifestations of Cystic Fibrosis" accepted and awaiting print
- **Rabin Tirouvanziam** was awarded the CPN seed grant: *A disruptive approach to CF therapy: targeted RNAi delivery to reprogrammed airway neutrophils*
- **Sanjana Rao**, from the Tirouvanziam lab, graduated in May 2016 with an Honors Thesis on "Inflammasome-mediated IL1beta secretion in CF airway disease" that received the Highest Honors
- **Facundo Fernandez** was awarded the 13th Beynon Prize for best 2014-2015 paper in *Rap. Commun. Mass Spectrom.* Joint with T. Kauppila.
- **Eric Sorscher** was invited to be a guest professor at the University of Pittsburgh and National Jewish in Denver
- **Jay Freeman** was asked to conduct a "Meet the Professor" breakfast at this year's World Congress of Pediatric Gastroenterology, Hepatology and Nutrition entitled "GI Issues in CF Patients: Myths and Facts"
- **Osrice Forrest**, an IMP student in the Tirouvanziam lab, has received a Scholarly Inquiry and Research at Emory (SIRE) fellowship for 2016 and was selected to participate in the Technology Innovation: Generating Economic Results (TI:GER) program at the Sheller Business School in Georgia Tech
- **Haitham Shahrouf**, MD, Pulmonary Fellow in the PACS Division, has joined the Tirouvanziam lab to work on a project related to "Premature aging in CF"
- **Camilla Margaroli**, IMP student at Emory, joined the Tirouvanziam lab to work on a thesis dedicated to "Neutrophil plasticity in early airway disease in human CF infants"
- **James Dahلمان's** work with CRISPR-Cas9 was highlighted on <http://petitstitute.gatech.edu/dahلمان-crispr-cutting-edge>

Recent CF-AIR Publications

- Alvarez JA, Ziegler TR, Millson EC, Stecenko AA. Body composition and lung function in cystic fibrosis and their association with adiposity and normal-weight obesity. *Nutrition*. 2016 Apr;32(4):447-52. PubMed PMID: 26740256.
- Bakshi N, Morris CR. The role of the arginine metabolome in pain: implications for sickle cell disease. *J Pain Res*. 2016 Mar 30;9:167-75. Review. PubMed PMID: 27099528.
- Bedi B, Yuan Z, Joo M, Zughaier SM, Goldberg JB, Arbiser JL, Hart CM, Sadikot RT. Enhanced Clearance of *Pseudomonas aeruginosa* by PPAR γ . *Infect Immun*. 2016 Apr 18. pii: IAI.00164-16. PubMed PMID: 27091928.
- Dugan MC, McCracken CE, Hebbar KB. Does Simulation Improve Recognition and Management of Pediatric Septic Shock, and If One Simulation Is Good, Is More Simulation Better? *Pediatr Crit Care Med*. 2016 May 3. PubMed PMID: 27144833.
- Gernez Y, Waters J, Tirouvanziam R, Herzenberg L, Moss R. Basophil activation test determination of CD63 combined with CD203c is not superior to CD203c alone in identifying allergic bronchopulmonary aspergillosis in cystic fibrosis. *J Allergy Clin Immunol*. 2016 Apr 22. pii: S0091-6749(16)30098-7. PubMed PMID: 27215492.
- Gupta P, Richardson T, Hall M, Bertoch D, Hebbar KB, Fortenberry JD, Wetzel RC. Effect of Inhaled Nitric Oxide on Outcomes in Children With Acute Lung Injury: Propensity Matched Analysis From a Linked Database. *Crit Care Med*. 2016 May 9. PubMed PMID: 27163193.
- Hermes WA, Alvarez JA, Lee MJ, Chesdachai S, Lodin D, Horst R, Tangpricha V. A Prospective, Randomized, Double-Blind, Parallel-Group, Comparative Effectiveness Clinical Trial Comparing a Powder Vehicle Compound of Vitamin D With an Oil Vehicle Compound in Adults With Cystic Fibrosis. *JPEN J Parenter Enteral Nutr*. 2016 Feb 22. pii: 0148607116629673. PubMed PMID: 26903303.
- Johnson K, McEvoy CE, Naqvi S, Wendt C, Reilkoff RA, Kunisaki KM, Wetherbee EE, Nelson D, Tirouvanziam R, Niewoehner DE. High-dose oral N-acetylcysteine fails to improve respiratory health status in patients with chronic obstructive pulmonary disease and chronic bronchitis: a randomized, placebo-controlled trial. *Int J Chron Obstruct Pulmon Dis*. 2016 Apr 21;11:799-807. PubMed PMID: 27143871.
- Lazarus SG, Kelleman M, Adisa O, Zmitrovich AR, Hagbom R, Cohen S, McCracken CE, Morris CR. Are We Missing the Mark? Fever, Respiratory Symptoms, Chest Radiographs and Acute Chest Syndrome in Sickle Cell Disease. *Am J Hematol*. 2016 May 6. PubMed PMID: 27153121.
- Schadzek P, Schlingmann B, Schaarschmidt F, Lindner J, Koval M, Heisterkamp A, Ngezahayo A, Preller M. Data of the molecular dynamics simulations of mutations in the human connexin46 docking interface. *Data Brief*. 2016 Feb 13;7:93-9. PubMed PMID: 26958636.
- Singh AL, Klick JC, McCracken CE, Hebbar KB. Evaluating Hospice and Palliative Medicine Education in Pediatric Training Programs. *Am J Hosp Palliat Care*. 2016 Apr 26. pii: 1049909116643747. PubMed PMID: 27122617.
- Staubes BA, Metzger NL, Walker SD, Peasah SK. Evaluation of a Once-Daily Tobramycin Regimen to Achieve Target Concentrations in Adult Patients with Cystic Fibrosis. *Pharmacotherapy*. 2016 May 3. PubMed PMID: 27138730.
- Veit G, Oliver K, Apaja PM, Perdomo D, Bidaud-Meynard A, Lin ST, Guo J, Icyuz M, Sorscher EJ, Hartman Iv JL, Lukacs GL. Ribosomal Stalk Protein Silencing Partially Corrects the Δ F508-CFTR Functional Expression Defect. *PLoS Biol*. 2016 May 11;14(5):e1002462. PubMed PMID: 27168400.
- Veit G, Avramescu RG, Chiang AN, Houck SA, Cai Z, Peters KW, Hong JS, Pollard HB, Guggino WB, Balch WE, Skach WR, Cutting GR, Frizzell RA, Sheppard DN, Cyr DM, Sorscher EJ, Brodsky JL, Lukacs GL. From CFTR biology toward combinatorial pharmacotherapy: expanded classification of cystic fibrosis mutations. *Mol Biol Cell*. 2016 Feb 1;27(3):424-33. doi: 10.1091/mbc.E14-04-0935. PubMed PMID: 26823392.
- Wang W, Hong JS, Rab A, Sorscher EJ, Kirk KL. Robust Stimulation of W1282X-CFTR Channel Activity by a Combination of Allosteric Modulators. *PLoS One*. 2016 Mar 23;11(3):e0152232. PubMed PMID: 27007499.

If you have a publication you would like in the next newsletter, email Karen Kennedy, kmurra5@emory.edu.

Events for Researchers

These events will be taking a break for the summer months, check the websites below for the upcoming schedule.

Each month there are several opportunities for CF-AIR researchers to get together to discuss their work.

- **CF-AIR Faculty and Trainees Research (CF-TR):**
On the first Tuesday of the month, faculty chalk talks on either the overall work in their lab, or on a grant proposal planned for submission soon. On the third Tuesday of the month trainee chalk talks discussing planned manuscripts or fellowship proposals. Meet at noon in ECC 302
- **CF-AIR Workshop:**
A weekly Wednesday meeting for research-in-progress and journal club presentations. Meet at 4:30 pm in ECC 302
- **CF Scholars Meetings:**
A monthly program for CF Scholars, Friday afternoons, see website schedule

More information and current schedules can be found on
www.pedsresearch.org/research/centers/cf-air/seminars-workshops/
and

www.pedsresearch.org/research/centers/cf-air/cf-center-of-excellence/education-outreach/cf-scholars-program/

In our next book club, faculty and trainees will discuss the 2013 book by acclaimed biologist Sean Carroll, [*Brave Genius: A Scientist, a Philosopher, and Their Daring Adventures from the French Resistance to the Nobel Prize*](#). This book narrates how writer Albert Camus and biologist Jacques Monod joined the Resistance during WWII, became friends via twists of circumstance, and through their passionate determination and rare talent emerged as leading voices of literature and biology, each receiving the Nobel Prize in their respective fields. Contact Rabin Tirouvanziam (tirouvanziam@emory.edu) for more information. Details to come about meeting date in September!

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/research/centers/cf-air

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

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