The Emory+Children's Cystic Fibrosis Center of Excellence

Volume 6, Issue 1 February 2016

Dear friends, patients, families, and colleagues,

We are pleased to present you with the latest edition of our e-newsletter, and hope that this finds you well. There are many exciting things going on at the Center, which you can learn about in the following pages. One item to bring to your attention is a set of three important events that are scheduled to take place in April.

(1) The CF research program is endeavoring to host the first Southeast Regional CF Research Symposium. For this first year, we are collaborating with our colleagues at the University of Alabama – Birmingham (UAB), only. Other centers from states that border Georgia will be invited in future years, as funding for this program is established. The Symposium will feature presentations from researchers at both institutions, sharing their most exciting work in each of these themes: Inflammation, and Drug Discovery. A major goal of the Symposium is to encourage stronger ties between the Atlanta and Birmingham CF programs. A special emphasis will be placed upon identifying opportunities for joint clinical research trials testing new therapeutic approaches that target either inflammation or modulators of the function of CFTR, the protein defective in the disease. The Symposium will feature presentations from researchers at both institutions. We also have invited an international expert from Germany, Dr. Marcus Mall, to present his work as our Keynote Speaker. Three to four researchers will present their work in two sessions (morning and afternoon), each of which will be followed by a panel discussion that will encourage audience participation. A poster session is scheduled during lunch where invited trainees (students, fellows, postdocs) would be able to present their work to researchers from both institutions, thereby promoting collaboration, and would compete for awards for travel to the North American CF Conference next year.

The Symposium is open to the public, and will be held on the Emory campus. Registration information and a summary of the agenda are shown on page 2.

(2) The Annual Dr. Dan Caplan Family Science Dinner will be held immediately following the Symposium. This gathering, intended for families of people with CF, will feature brief talks from clinicians and scientists in the Emory+Children's CF Program, a brief talk from Dr. Marcus Mall about how CF care is advancing in Europe, and comments from two important members of the CF Foundation: Mr. Scot Rittenbaum, from the GA Chapter, and Dr. William Skach, from the national headquarters. The Family Science Dinner is named in honor of Dr. Dan Caplan, who we recognize as the Grandfather of CF in Atlanta. Its purpose is to update our patient families on advances in our clinical care, research, and education & outreach programs within the Emory+Children's CF Center of Excellence, and to serve as a forum for strengthening ties between the Center and the patients and families that we serve.

Parents and caregivers from Egleston (North Druid Hills), Scottish Rite, and Emory Adult CFF accredited programs are invited to attend this event. Researchers and clinical staff associated with these programs are also invited. Due to infection control risks to people with CF, we ask that no patients attend. Registration information and agenda are shown on page 2. Attendees who arrive early will be able to view the research posters presented at the earlier Symposium.

(3) The third event is the CF Research Retreat, open only to members of the core CF research team and their trainees and staff (by invitation only), with the important addition of the members of our External Advisory Board and representatives from the CF Foundation. Research Centers that are supported by the CF Foundation via a Research Development Program (RDP) grant, like ours, are required to sponsor a site visit each year so that the Center can receive guidance from the set of external advisors, including the research leadership at the CFF. We plan an all-day event, at the Atlanta Botanical Gardens, where we will show our progress to these important advisors, while also building our team identity and discussing how we can make our research more effective and efficient.

We look forward to reporting on the successes of these events in the next e-newsletter.

-Nael McCarty, PhD

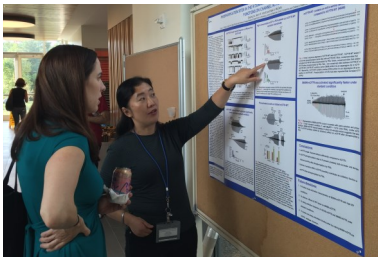
Inside this issue:

Center for Cystic Fibrosis and Airways Disease Research
Advancing Wellness in Patients Through Research

CF Research Events in April 2016

The Southeast Regional CF Research Symposium
co-sponsored by the CF Foundation
April 11, at the Health Science Research Building auditorium
8:00 a.m. – 6:00 p.m.
Welcome, Introduction to the Atlanta Center: Nael McCarty, PhD, Emory; Arlene Stecenko, MD, Emory
Morning Session: Focus on Inflammation
Keynote Speaker: Marcus Mall, MD, German Center for Lung Research
Speakers: Amit Gaggar, MD, PhD, UAB; Rabin Tirouvanziam, PhD, Emory
Discussion and Panel: Clinical Trials - Inflammation
Lunch and Poster Session/Contest
Introduction to the UAB Center: Dave Bedwell, PhD, UAB
Afternoon Session: Focus on Drug Discovery
Speakers: Eric Sorscher, MD, Emory; Nael McCarty, PhD, Emory; Dave Bedwell, PhD, UAB
Discussion and Panel: Clinical Trials - Drug Discovery
Closing Remarks, Poster Awards, Continued Poster Viewing with CF families

Parents and caregivers from Egleston (North Druid Hills), Scottish Rite, and Emory Adult CFF accredited programs are invited to attend this event. Researchers and clinical staff associated with these programs are also invited. Due to infection control risks to people with CF, we ask that no patients attend.
Register at: www.surveymonkey.com/r/CFResearchSymposium2016



The Second Annual Dr. Dan Caplan Family Science Dinner
April 11, at the Health Science Research Building auditorium
5:15 – 6:00 p.m.: Refreshments and Viewing of Poster Session with Scientists
6:00 – 6:55 p.m.: Buffet Dinner
7:00 – 8:00 pm: Scientific Program for CF Families
"Personalized Drug Development for CF"
- Eric Sorscher, MD, Emory
"Healthier and Happier CF People: Decreasing Depression and Anxiety in CF"
- Rachel Linnemann, MD, Emory
"Insight on the Causes of Pulmonary Flare Ups and How This Could Lead to Better Treatment"
- Arlene Stecenko, MD, Emory
"New Advances in European Approach to CF Care"
- Keynote: Marcus Mall, MD, German Center for Lung Research
CF Foundation - Scot Rittenbaum, Executive Director, GA Chapter
William Skach, MD, Vice President for Research Affairs

Parents and caregivers from Egleston (North Druid Hills), Scottish Rite, and Emory Adult CFF accredited programs are invited to attend this event. Researchers and clinical staff associated with these programs are also invited. Due to infection control risks to people with CF, we ask that no patients attend.
Register at: www.surveymonkey.com/r/CaplanFamilyDinnerRSVP

Annual CF Research Retreat
April 12, at the Atlanta Botanical Gardens
Attendees: Atlanta CF core team faculty, staff, and trainees. External Advisory Board Members, and CF Foundation Representatives
This event is by invitation only

New Faculty: Lokesh Guglani, MD

Dr. Guglani joined Emory University and Children's Healthcare of Atlanta in September 2015. He comes to Atlanta from Michigan where he had been working at Children's Hospital of Michigan for the past 4 years. His fellowship training in Pediatric Pulmonology was completed in 2011 at Children's Hospital of Pittsburgh. He is board-certified in Pediatrics and Pediatric Pulmonology. Dr. Guglani's current research interests include early CF lung disease, techniques to measure lung function and factors that affect sweat chloride concentrations. He will be working at the CF Center at Children's Healthcare of Atlanta and will participate in clinical and translational research projects. When not at work, Dr. Guglani enjoys running and bike riding, and spending time with and traveling with his family – his wife and two children aged 10 and 7 years.

Lokesh Guglani, MD

New Faculty: Sam Brown, PhD

Sam Brown is an evolutionary microbiologist and a new recruit to Atlanta, having moved from Edinburgh, UK to the Georgia Institute of Technology last August. Following a Ph.D. at the University of Cambridge, UK, and postdoctoral fellowships at the University of Montpellier, France, and the University of Texas at Austin, Texas, Dr. Brown leads a lab focused on developing novel treatments for microbial infections that are 'evolution proof', and so will continue to work without leading to the rapid evolution of drug resistance. "Working with the CF Clinic at Atlanta offers an incredible opportunity to learn about the real-world challenges of drug resistant microbes, and to work towards the development of more robust treatment strategies". Outside of the lab, Dr Brown is enjoying getting to know Atlanta and all these beautiful trees.

Sam Brown, PhD

Book Club

On January 29, trainees from the McCarty, Tirouvanziam, and Goldberg labs – forming a small "book club" – met to discuss the book we had read over the holidays: "Uncle Tungsten: Memories of a Chemical Boyhood," by Dr. Oliver Sacks. Conversation centered upon our own experiences falling in love with science, and what (personality traits, parental guidance, early experiences, etc.) drew us toward these careers. Aside from the trainees, also attending were Drs. Tirouvanziam and McCarty. Great conversation over snacks and theme-appropriate wine (see photo).

Research Development Program Grant Highlights: Cores

Clinical and Translational Research Core

The Clinical and Translational Research Core (CTRC), spearheaded by Dr. Stecenko, Chief of the Pediatric Pulmonology, Allergy/Immunology, CF, and Sleep (PACS) Division within the Department of Pediatrics at Emory University, is the centerpiece of the CF@LANTA RDP Center (Director: Nael McCarty), which earned four -year grant support from the CF Foundation in July 2015. The CTRC is focused upon the unique CF patient population cared for at our CF Center and serves two overarching goals: 1) Promote interdisciplinary human research in CF pathogenesis; and 2) Translate knowledge into preventative and personalized therapies.
Three guiding principles underlie the CTRC's operations.

First, the systematic collection and banking of biological samples and linking of these samples with clinical data, enabling translational research within optimized standard operating procedures and strict ethical guidelines. Second, the flexibility to conduct prospective sample collections tailored to the specific needs of investigators. Third, fostering creativity through stimulating new ideas and supporting established investigators as well as those new to CF research.

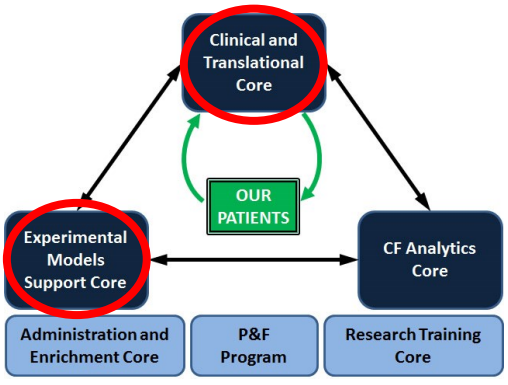
While an early emphasis is put on acute pulmonary exacerbations (APEs), the primary cause of increased disease severity, and CF-related diabetes (CFRD), a metabolic complication that doubles the risk of death, the CRTC will coordinate all needs related to human CF research within our CF@LANTA RDP Center.

Experimental Models Support Core

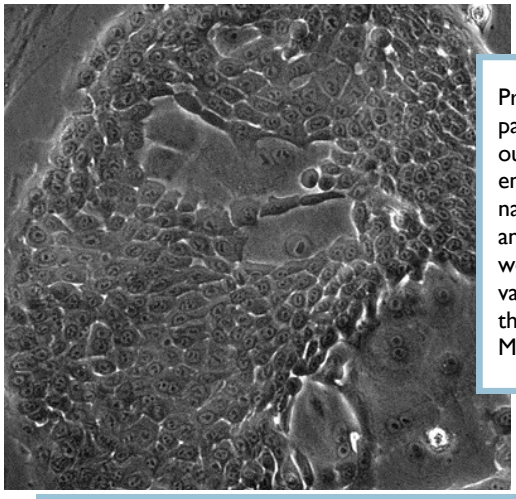
On December 16, 2015, Dr. Mike Koval (Professor of Medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine) presented a description of the Experimental Models Support Core within the CF@LANTA RDP Center.

Cultured cell lines, such as tumor-derived cells or other established cell lines, are good for use as a proxy until an investigator has easy access to primary airway epithelial cells. We have useful, relatively new cell lines ready for use and distribution: NuLi and CuFi cells. These were developed by the Zabner lab at Iowa (Zabner *et al.*, 2003, *AJP:Lung*, PMID: 12676769). NuLi-1 cells are homozygous for wildtype CFTR, while CuFi-5 cells are homozygous for F508del-CFTR. As described in a recent characterization of these cell lines from the Koval lab (Molina *et al.*, 2015, *AJP:Lung*, PMID: 26115671), it is important to use the NuLi-1 and CuFi-5 cells after about six weeks of growth at air-liquid interface, at which time their transepithelial resistance and expression of CFTR (and other genes) become stabilized. NuLi-1 and CuFi-5 cells, which at maturity exhibit a mixture of serous- and goblet-cell phenotypes, express similar abundance of CFTR as do primary airway epithelial cells, and therefore do not suffer the consequences of overexpression as are found in many cell lines used by the CF research community. Dr. Koval believes that these cell lines will serve as a valuable platform for many studies. Furthermore, the Core already has shown that NuLi-1 cells will form spheroids when grown in 3-D cultures. (images on page 5) This validates the use of this class of cells for testing efficacy of novel compounds that may repair the localization or function of mutant CFTR.

The Core also is establishing primary cell models derived from our patients. Primary airway epithelial cells are considered the gold standard by the CF research community, since they are directly isolated from patient airways and therefore more closely reflect the composition of cells within the airways than do immortalized cell lines (like NuLi and CuFi cells). By sampling the airways of a wide number of patients, we will be able to generate a whole panel of primary airway cell cultures expressing different disease-associated CFTR genotypes. We are fortunate that we have a wide array of CFTR genotypes embodied by our very large patient population. We have begun collecting airway cells from the nasal passages of some of our patients; these are collected by "nasal brushing," which is a quick and nearly painless procedure performed in the outpatient clinic setting. We hope that our patients will be excited about helping us to generate this library of primary airway cells, which will be distributed to local investigators to enable their CF-focused research. The CF Foundation considers the acquisition of cells such as these to be of fundamental importance to developing new therapeutics for CF patients.

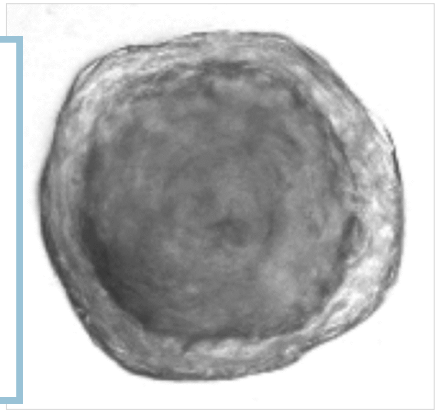


Learn more about the RDP grant using the QR code to the left or at www.pedsresearch.org/centers/sub-pages/cf-air-cf-research-cftlanta-core-center/



Primary airway epithelial cells grown from a nasal brushing taken from a patient homozygous for the F508del mutation. We are hoping to expand our ability to collect nasal epithelial cells from our patients, which is enormously important for our research programs. Fortunately, isolation of nasal epithelial cells can be done in the outpatient clinic, and is very fast and almost completely painless. We hope that our patients and families will work with the research team to help us build a pool of epithelial cells, with varying CFTR genotypes, to help propel research forward. Any patients that are interested in contributing to this effort should contact Dr. McCarty at namccar@emory.edu. Photo credit: Dr. Mike Koval.

Image shows NuLi-1 normal airway epithelial cells grown in 3-D culture to form "spheroids." These spheroids can be used to test new therapies under development, using a simple assay. We are building our capabilities to perform this assay – and therefore to test new potential CFTR modulators that have been identified in our labs – which will further require access to nasal epithelial cells from our patients. By collecting nasal cells from our patients and turning them into spheroids, we will be able to test potential therapeutics that may only work on specific CFTR genotypes for which there are no current therapies. Furthermore, we anticipate that this assay will enable us to test compounds on cells derived from each patient, to be able to gauge whether those drugs may work when given systemically in subsequent clinical trials. Photo credit: Dr. Sam Molina.



Center Brags

- Rabin Tirouvanziam, PhD was part of a team awarded patent: WO2012035369-A1, US9157912, Method for the diagnosis and/or prognosis of inflammatory states
- Eric Sorscher, MD and his lab received a philanthropic gift from Eva and Charles Lipman that will support Dr. Sorscher's work to develop drugs for CF patients with less common gene mutations
- Lou Ann Brown, PhD was appointed the Director of the Office of Postdoctoral Education at Emory University
- Rabin Tirouvanziam, PhD is part of a team recently awarded a DARPA THoR grant
- Claudia Morris, MD was named a 2015 Top Research Mentor by the Department of Pediatrics
- Rachel Linneman, MD was awarded a CF Foundation grant, "Implementation of the Depression and Anxiety Guidelines: Award for a Mental Health Coordinator," that will support a mental health nurse practitioner to support CF pediatric patients. Seth Walker, MD was awarded a matching grant to support this position for CF adult patients. This grant will help our centers implement the new CF mental health screening and treatment guidelines for our pediatric and adult CF patients and their families.
- Nael McCarty, PhD was appointed as the new Director of the Graduate Division of Biological and Biomedical Sciences (GDBBS) within the Laney Graduate School at Emory. The GDBBS includes eight interdisciplinary, interdepartmental graduate programs, which is where the lion's share of graduate education related to biomedical research is housed. This part-time appointment will take effect May 1, 2016. Recall from a prior newsletter that Dr. LouAnn Brown, Prof. of Pediatrics and member of the CF-AIR research center, recently became the Director of the Office of Postdoctoral Education at Emory. This combination of appointments will enhance our team's opportunities to grow training programs in CF, asthma, and other pulmonary diseases.
- On January 6, several members of the Center gathered for a (late) holiday lunch, potluck style. A contest was held with votes taken for the best entrée and the best dessert. Brandon Stauffer won for best entrée and Carmen Blount won for the best dessert.
- Two postdocs in the family, both in the lab of Dr. Mike Koval, tied the knot to create their own family. Dr. Barbara Schlingmann wed Dr. Sam Molina in January. We wish the couple the very best!

Recent CF-AIR Publications

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

- Ehrhardt A, Chung WJ, Pyle LC, Wang W, Nowotarski K, Mulvihill CM, Ramjeesingh M, Hong J, Velu SE, Lewis HA, Atwell S, Aller S, Bear CE, Lukacs GL, Kirk KL, Sorscher EJ. Channel Gating Regulation by the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) First Cytosolic Loop. J Biol Chem. 2015 Dec 1. pii: jbc.M115.704809. [Epub ahead of print] PubMed PMID: 26627831.
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- Hammer AM, Morris NL, Cannon AR, Shults JA, Curtis B, Casey CA, Sueblinvong V, Persidsky Y, Nixon K, Brown LA, Waldschmidt T, Mandrekar P, Kovacs EJ, Choudhry MA. Summary of the 2014 Alcohol and Immunology Research Interest Group (AIRIG) meeting. Alcohol. 2015 Dec;49(8):767-72. Epub 2015 Oct 8. PubMed PMID: 26520175; PubMed Central PMCID: PMC4691366.
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- Kavanaugh TE, Clark AY, Chan-Chan LH, Ramírez-Saldaña M, Vargas-Coronado RF, Cervantes-Uc JM, Hernández-Sánchez F, García AJ, Cauich-Rodríguez JV. Human mesenchymal stem cell behavior on segmented polyurethanes prepared with biologically active chain extenders. J Mater Sci Mater Med. 2016 Feb;27(2):38. Epub 2015 Dec 24. PubMed PMID: 26704555.
- Lee MJ, Alvarez JA, Smith EM, Killilea DW, Chmiel JF, Joseph PM, Grossmann RE, Gaggar A, Ziegler TR, Tangpricha V; Vitamin D for Enhancing the Immune System in Cystic Fibrosis Investigators. Changes in Mineral Micronutrient Status During and After Pulmonary Exacerbation in Adults With Cystic Fibrosis. Nutr Clin Pract. 2015 Dec;30(6):838-43. Epub 2015 Jun 15. PubMed PMID: 26078287; PubMed Central PMCID: PMC4701694.
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- Liu F, Koval M, Ranganathan S, Fanayan S, Hancock WS, Lundberg EK, Beavis RC, Lane L, Duek P, McQuade L, Kelleher NL, Baker MS. Systems Proteomics View of the Endogenous Human Claudin Protein Family. J Proteome Res. 2016 Jan 12. [Epub ahead of print] PubMed PMID: 26680015.
- Maliniak ML, Stecenko AA, McCarty NA. A longitudinal analysis of chronic MRSA and Pseudomonas aeruginosa co-infection in cystic fibrosis: A single-center study. J Cyst Fibros. 2015 Nov 20. pii: S1569-1993(15)00258-1. [Epub ahead of print] PubMed PMID: 26610860.
- Murray KE, Ressler KJ, Owens MJ. In vivo investigation of escitalopram's allosteric site on the serotonin transporter. Pharmacol Biochem Behav. 2016 Feb;141:50-7. PubMed PMID: 26621784; PubMed Central PMCID: PMC4724252.
- Owings JP, Kuiper EG, Prezioso SM, Meisner J, Varga JJ, Zelinskaya N, Dammer EB, Duong DM, Seyfried NT, Alberti S, Conn GL, Goldberg JB. Pseudomonas aeruginosa EftM is a Thermoregulated Methyltransferase. J Biol Chem. 2015 Dec 16. pii: jbc.M115.706853. [Epub ahead of print] PubMed PMID: 26677219.
- Ruth A, McCracken CE, Fortenberry JD, Hebbar KB. Extracorporeal therapies in pediatric severe sepsis: findings from the pediatric health-care information system. Crit Care. 2015 Nov 10;19:397. PubMed PMID: 26552921; PubMed Central PMCID: PMC4640405.
- Schadzek P, Schlingmann B, Schaarschmidt F, Lindner J, Koval M, Heisterkamp A, Preller M, Ngezahayo A. The cataract related mutation N188T in human connexin46 (hCx46) revealed a critical role for residue N188 in the docking process of gap junction channels. Biochim Biophys Acta. 2016 Jan;1858(1):57-66. Epub 2015 Oct 9. PubMed PMID: 26449341.
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- Varga JJ, Barbier M, Mulet X, Bielecki P, Bartell JA, Owings JP, Martinez-Ramos I, Hittle LE, Davis MR Jr, Damron FH, Liechti GW, Puchałka J, dos Santos VA, Ernst RK, Papin JA, Albertí S, Oliver A, Goldberg JB. Genotypic and phenotypic analyses of a Pseudomonas aeruginosa chronic bronchiectasis isolate reveal differences from cystic fibrosis and laboratory strains. BMC Genomics. 2015 Oct 30;16:883. PubMed PMID: 26519161; PubMed Central PMCID: PMC4628258.
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- Yeligar SM, Mehta AJ, Harris FL, Brown LA, Hart CM. PPARγ Regulates Chronic Alcohol-induced Alveolar Macrophage Dysfunction. Am J Respir Cell Mol Biol. 2015 Dec 17. [Epub ahead of print] PubMed PMID: 26677910.

Events for Researchers

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/centers/sub-pages/cf-air-seminars-workshops
and
www.pedsresearch.org/centers/detail/cf-air-cf-education-outreach-cf-scholars-program

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

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

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The Emory+Children's Cystic Fibrosis Center of Excellence

Center for Cystic Fibrosis and Airways Disease Research
Advancing Wellness in Patients Through Research