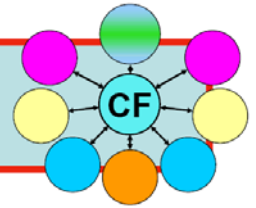


Center for Cystic Fibrosis Research

Advancing Wellness in CF Patients Through Research



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Inside this Issue

- 1 Update from the Director
Pilot Projects
- 2 Workshops
Recruitment
- 3 Presentations
Visitors
Publications
- 4 Funding
- 5 New Team Members
In Memoriam
- 6 CF Center of Excellence
- 7 Outreach Activities

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Update from the Director

This has been a very exciting time for the Center for CF Research. A lot has been happening and we have accomplished many things.

First off, the Center's activities and size have grown. We continue to do a great job of reaching out to collaborate with partners and increase the number of researchers in Atlanta that are studying CF.

In this newsletter, we are including a growing list of publications, grants awarded and the status of our committees and pilot projects.

Of particular note, we submitted our first progress report for the Center to Children's and Emory leadership, which has demonstrated the growth and potential further growth of the Center for CF Research.

We have had several presentations and hosted recent visitors to assist us in our growth. See more about these below.

This has also been a sad time for us in the CF community with the loss of **Dr. Lindy Wolfenden** on July 24, 2010 (*see memoriam below*). We will all miss Lindy's dedication and contributions to the CF community.

--Nael McCarty, PhD

Pilot Projects

Here is a scientific update on our pilot projects that were awarded in February:

Project #1: PIs: Stecenko and Gibson. "Genome-wide expression profiling in CFRD". The project is progressing nicely. The PIs have hired a Post-Doctoral Fellow, **Dr. Yue Luo**, who has developed the protocols for isolation of neutrophils from both peripheral blood and induced sputum. Dr. Luo is sampling from the four population groups outlined in phase I of the proposal (healthy controls, type 2 diabetics, CF patients, and CF-RD patients). With the help of the study coordinator hired by the Center, Ms. Amanda Castle (*see more info in New Staff Section below*), the team expects to enroll between 15 and 20 patients in each group by the end of the year and to have preliminary gene expression profiling results shortly thereafter.

Project #2: PIs: Hartzell and McCarty. "Colonic bicarbonate transport in cystic fibrosis". This project is also going well. In the several months that this pilot project has been funded, we have been testing the idea that bestrophins may be involved in bicarbonate secretion in the colon. Our previous studies suggested that bicarbonate secretion in distal colon was mediated by bestrophins. As an

initial descriptive test of this hypothesis and to understand bicarbonate secretion in the colon, we have started to systematically study bicarbonate secretion in the different segments of the gut. Bicarbonate secretion and short circuit current in the distal colon, the mid-colon, and proximal colon are different. We first measured basal secretory parameters, then substituted the luminal solution with a Cl free solution, then stimulated with carbachol to activate Ca-activated Cl channels including bestrophin and anoctamins, and then with forskolin to activate CFTR. Striking differences were observed in the secretory profiles of the different regions. Only the mid colon secreted bicarbonate at reasonable rates after agonist stimulation, which was a surprise because we expected the distal colon to exhibit the highest bicarbonate secretion, given the higher expression of bestrophin in distal colon. Because anoctamins, newly-identified calcium-activated chloride channels, also play a role in chloride secretion in colon and in airway, we are pursuing this new direction and looking at the roles of anoctamins in both colon and airway.

Project #3: PIs: Peng and McCarty. "Protein biomarker discovery in cystic fibrosis".

This project has gotten off to a slow start, primarily due to delays in getting the CF Biospecimen Registry up and running. However, the team already has provided some data that has been useful for larger NIH grant applications. In this proposal, we aim to identify potential protein biomarkers to differentiate the patients at different disease stages,

using a quantitative proteomics approach termed iTRAQ. We are now optimizing the quantitative method by testing the iTRAQ reagents and comparing the iTRAQ strategy to another similar method named TMT.

We are also developing computer software to analyze the experimental data. Once the samples are readily available, we will be able to analyze the patient specimens. This phase will begin very soon. These studies are highly relevant to the NIH Bioengineering Research Partnership proposal that the Center plans to submit soon. We anticipate having initial characterization of 25 samples, paired before and during *acute pulmonary exacerbation*, by the end of the first year.

Workshops

We have established two workshops, with strong attendance at each. The monthly CF Basic & Translational Research Workshop is attended by ~25 researchers, including several from Georgia Tech. This is so popular that we have outgrown the conference room in which we have been meeting! The CF Clinical Research Workshop also meets monthly, and is attended by ~10 investigators and staff active in CF clinical research. If you want to receive announcements regarding these workshops, please contact us at: namccar@emory.edu.

Recruitment

The recruitment of established investigators into the Center is a major goal. We have identified two areas in which we will focus our first

recruitment efforts: 1) airway innate immunity, and 2) systems biology of pulmonary disease. **Dr. Kenneth Brigham**, Professor of Medicine and Director of the Emory/GA Tech Predictive Health Initiative, has agreed to serve as Chair of the two search committees. The committees are composed as follows:

Airway innate immunity: Ken Brigham (Chair), **Nael McCarty**, **Arlene Stecenko**, **Susu Zughair** (Emory Med:ID), **Richard Compans** (Emory Micro/Immuno), **Bali Pulendran** (Emory Yerkes Vaccine Center)

Systems biology of pulmonary disease: **Ken Brigham** (Chair), **Nael McCarty**, **Arlene Stecenko**, **Dean Jones** (Emory Med:PULM), **Eberhard Voit** (GA Tech), **Mark Hay** (GA Tech), **Greg Gibson** (GA Tech).

We are also working with the Marketing department at Children's (**Mr. Brian Knowles** and **Ms. Danielle Goss**) to generate materials that can be sent to potential recruits, and to increase our web presence specifically with respect to recruitment.

We hope to have our first recruit arriving in late 2011.

Please help us identify superb candidates, and inform appropriate colleagues of the availability of these positions.

Presentations

The following are some of the CF-Related presentations that our team has made in the past year:

National Pre-doctoral Clinical Research Training Meeting. St. Louis, WA, May 2010. Glutamine supplementation and functional outcomes in adults with cystic fibrosis. **LM Mazer, G Hebbbar, L Wolfenden, A Stecenko, V Tangpricha, V Seublinvong, MS Schechter, TR Ziegler**

North American Cystic Fibrosis Conference, Bone Symposium, October 14, 2009, Minneapolis, MN. "Re-thinking the Vitamin D guidelines: What was right and what was wrong?" **V Tangpricha**

North American Cystic Fibrosis Conference, Endocrine & Bone, Joint Workshop. Co-Chair of workshop. October 15, 2009, Minneapolis, MN, **V Tangpricha**

Symposium on Coupling Gating to Permeation, North American Cystic Fibrosis Conference, Minneapolis, MN, November, 2009, "The Dynamic Nature of the CFTR Channel Pore," **N McCarty**

Family Education Day, Emory-Children's Cystic Fibrosis Center, May 1, 2010, "The Emory-Children's CF Center of Excellence," **N McCarty**

CF Education Day, Children's Healthcare of Atlanta at Scottish Rite, September 25, 2010. "Progress and Promise: Introducing the Emory-Children's CF Center of Excellence," **N McCarty**

Pediatric Grand Rounds, Children's Healthcare of Atlanta at Egleston, Atlanta, GA, Mar 10, 2010, Shifting the Bell Curve: The National Effort to Make Every Cystic Fibrosis Center Above Average, **M Schechter**

National Initiative for Children's Healthcare Quality National Forum, Atlanta, GA, March 9, 2010. Improving Care of Children with

Chronic Disease – Lessons from Cystic Fibrosis (Exploratorium moderator); National Efforts for Improving CF Care; Local Efforts for Improving CF Care at Children's Healthcare of Atlanta, **M Schechter**

33rd European Cystic Fibrosis Conference, Valencia, Spain, June 17, 2010. Introduction to The International Depression / Anxiety Epidemiological Study (symposium moderator), **M Schechter**

33rd European Cystic Fibrosis Conference, Valencia, Spain, June 16, 2010, What Makes Good CF Teams Work? **M Schechter**

Visitors to the Center for CF Research



Stephen Aller, Ph.D., University of Alabama at Birmingham, March 18, 2010, "Conformational

Dynamics in a Model ABC-Transporter: the P-glycoprotein."



Amit Gaggar, M.D., University of Alabama at Birmingham, May 13, 2010, "A Proteolytic System of

Pulmonary Inflammation: Novel Insights and Therapeutics"



Antoinette Moran, M.D., University of Minnesota, July 27, 2010, "Update on CF-related

Diabetes"

Dr. Moran is a well-known expert on CF-related diabetes, and spent part of her visit interacting with the members of the group (led by **Stecenko** and **McCarty**) that is building a proposal for an NIH Program Project Grant focused on that topic.



Bruce Stanton, Ph.D., Dartmouth University, September 9, 2010,

"Pseudomonas aeruginosa Regulation of CFTR Trafficking in Epithelial Cells: Hijacking the Host Ubiquitination Machinery"

Dr. Stanton is a basic researcher who is also the Director of the CF Foundation-sponsored Research Development Program Center at Dartmouth, one of 12 such centers in the country. Dr. Stanton comes highly recommended as the Center Director who has done the best job of establishing an effective CF research center. Because we plan to submit a proposal for a CFF center grant in the next few months, Dr. Stanton also spent part of his visit here advising us in this effort.

Publications

A. G. Ahmadi, Z. C. Peng, P. J. Hesketh, S. Nair, "A Wafer-Scale Process for Fabricating Arrays of Nanopore Devices", *Journal of Micro/Nanolithography, MEMS, and MOEMS* (in press).

Ahmadi, AG, S Nair, "Engineered Nanopores", in: *BioNanoFluidic MEMS* (Editor: P. J. Hesketh), Springer (2010).

Haack, K.K.V., M.R. Tougas, K.T. Jones, S. El-Dahr, H. Radhakrishna, and N.A.

McCarty. A novel assay for detecting GPCR heterodimerization: Transactivation of beta-2 adrenergic receptor by bradykinin receptor. *J. Biomol. Screen* 15: March 2010.

Cohen, S.P., K.K. Vincent, G. Halstead-Nussloch, K.F. Bernard, H. Hatt, J. Kubanek, and N.A. McCarty (2010) Identification of RL-TGR, a co-receptor involved in aversive chemical signaling. *Proc. Natl. Acad. Sci., U.S.A.* 107:12339-44.

Brown, MB, M Millard-Stafford, NA McCarty (2010) Decreased voluntary drinking during recovery from exercise-induced dehydration for CF athletes: implications of high sweat NaCl content on fluid and electrolyte balance. *Ped. Pulmonol. Supple.* (abstract, in press)

Mazer LM, TR Ziegler, MS Schechter. Early childhood nutrition as a predictor of adult clinical status in cystic fibrosis. Abstract accepted for poster *Ped. Pulmonol. Supple.* (abstract, in press)

Zughaier, SM, D Dhakal, V Tangpricha, NA McCarty (2010) Elevated NGAL levels contribute to dysfunctional innate immunity in cystic fibrosis. *Ped. Pulmonol. Supple.* (abstract, in press)

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Wang, W, J Wu, K Bernard, G Li, G Wang, MO Bevensee, KL Kirk (2010). ATP-independent CFTR channel gating and allosteric modulation by phosphorylation. *Proc Natl Acad Sci U S A.* 107:3888-93.

Fitzpatrick, AM, M Higgins, F Holguin, LAS Brown, WG Teague, National Institutes of Health/National Heart, Lung and Blood Institute's Severe Asthma Research Program (2010) The molecular phenotype of severe asthma in children. *J. Allergy Clin. Immunol.* 125: 851-857.

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Roby Greenwald, Michael Schechter and Michael Bergin, *Study of Air Pollution and Physical Activity Health*

Systems Institute Seed Grant Program, 2010-2011

Myung Choi, Michael Schechter, *Augmenting Cystic Fibrosis Management using Smart Device with Web2.0 Applications,* Health Systems Institute Seed Grant Program, 2010-2011

Nair, S, E Balog, A Chatterjee, P Hesketh, C Summers, *Integrated Nanosystem Combining Engineered Nanopore Devices with Hierarchical Model-Based Diagnosis Algorithms for Ultra-Rapid Biomolecule Analysis,* NSF (ECCS Division), 06/2008-05/2011, \$450,000

Tangpricha, Vin, *Analysis of vitamin D supplementation strategy in subjects with cystic fibrosis,* Mentor to PhD student Ruth Grossmann, Student Traineeship Grant, 04/01/2010-07/01/2010, \$1,500

New Team Members

Amanda Castle is a Senior Clinical Research Coordinator that joined our team in August. She is working on the CF Biospecimen Registry (part of the Discovery Core within the Center for CF Research) as well as two other CF protocols with **Dr. Stecenko**: "Prevention of Cystic Fibrosis Related Diabetes" and "Role of inflammation and oxidant stress in the development of CF diabetes." Ms. Castle has worked in clinical research for about 4 years working mostly on pain management trials for private practice. She served as the Research Administrator for her last practice and manager for the research department. Ms. Castle is certified through ACRP (Association of Clinical Research Professionals) and graduated from the University of Phoenix with Honors in 2007 with a BS in Health Administration. She lives in Carrollton and spends

most of her free time working on her home.

Barbara Kilbourne, RN, MPH started as our Center Program Coordinator in April. She comes to us with 20+ years of experience working at the Centers for Disease Control and Prevention, where she retired as a Captain (O6) in the US Public Health Service. Ms. Kilbourne also serves as program coordinator for the Center for Developmental Lung Biology and the Center for Endothelial Biology. Ms. Kilbourne lives in Dunwoody with her husband, Dr. Edwin Kilbourne, and their four children.

In Memoriam:



Dr. Lindy Wolfenden

Dr. Lindy Wolfenden was the Director of the Adult CF Program at Emory from January 2006 until she became ill with breast cancer in the spring of 2009. After several different courses of treatment for her disease, she died on July 24, 2010 at the age of 40. Lindy died at her home and as her husband Arjun said, "she was surrounded by loved ones and is now free of the suffering she endured with such grace and courage for the last year." The way Lindy died was exactly the way she lived, with grace and elegance, although one cannot forget her humor and strength.

Lindy had impeccable medical training at the Johns Hopkins Hospital in Baltimore, Maryland,

first as a resident in internal medicine and then as a fellow in pulmonary and critical care medicine. After completing her pulmonary fellowship in 2003, she joined the faculty in the Department of Medicine at Emory University. She initially was a pulmonologist at Emory Midtown with a focus on long term care of the technology dependent adult. However, she soon realized that she wanted more of a challenge that would utilize her leadership skills as well as her interest in outpatient pulmonary medicine.

The nascent Adult CF Program, which had begun under **Dr. Arlene Stecenko's** oversight in 2002, was able to convince Dr. Wolfenden that her skills were uniquely suited to lead the further development of that program. Lindy became a team member of the Adult CF Program in the fall of 2005 and then Director six months later. The Adult CF program flourished under Dr. Wolfenden. She brought her own brand of enthusiasm, rigor, and compassion to the program. Lindy was a caring and skilled CF physician, but her impact on CF care in Atlanta goes far beyond that. She attracted the attention and strong support of Emory University Hospital and Emory Healthcare, assembled a wonderful and enthusiastic multidisciplinary team, and rapidly turned the Emory program into one of the premier adult CF programs in the United States. She earned the respect of her staff and colleagues at Emory and the loyalty and appreciation of her patients.

Not only was Lindy a superb clinician and leader, she also honed

her skills as a clinical researcher in CF. She became a research collaborator of **Dr. Vin Tangpricha**, the Center’s CF Endocrinologist, in his clinical research program. The two formed an impressive team evaluating the importance of Vitamin D in CF health. In addition, Lindy was an outstanding teacher and mentor for pulmonary fellows, instilling in each of them a vision or memory of a passionate, caring physician who used science and knowledge to better the health of her patients.

Dr. Wolfenden’s death will not diminish the progress of the program – this would be her exact wish, and in fact, her demand. For example, **Dr. Viranuj Sueblinpong**, who was Associate Director, has now taken on the role of Interim Director of the Adult CF Program. In addition, a nationwide search for a physician to continue Dr. Wolfenden’s vision and growth of the Adult CF Program is well underway. Thus, there will be no change or interruption of care offered to adults with CF by The Emory Clinic. It is important to know that the current research activities of the program will continue and new research initiatives are being developed including: determining the role of Vitamin D in reversing CF-associated pathologies in bone turnover, diabetes, lung function, and immune response; delineating the molecular mechanisms for lung disease progression in CF diabetes; and developing a Biospecimen Registry (a repository) of CF patient airway fluid/sputum and blood samples in order to aid CF investigators to develop hypotheses on the basic biology of CF disease in

order to design better diagnostics and treatments. Education of tomorrow’s CF physicians and leaders will continue: the CF Program is delighted to announce that three pulmonary fellows (one from pediatric pulmonary and two from adult pulmonary) have chosen CF to be the focus for their pulmonary fellowship with the expectation that that focus will continue in their academic careers as faculty. Finally, the CF team has been chosen by the CF Foundation as one of six CF Centers nationwide to participate in a year-long program to enhance the diagnosis and care for CF patients with diabetes. Participation in this intensive program will translate to the type of improvement in care that Dr. Wolfenden was always challenging the team to strive towards.

We cannot overestimate how much Lindy will be missed. **Dr. David Guidot**, Lindy’s mentor and the Director of the Division of Pulmonary, Allergy, & Critical Care Medicine at Emory University said it best when he wrote four days before her death “This is the saddest message I have sent as Division Director. Our beloved colleague and friend Lindy Wolfenden is losing her courageous battle with cancer. Lindy is a wonderful mother, wife, friend, physician, and colleague, and the cruel reality of disease that we face every day is particularly painful when it strikes at one of our own. Lindy has always loved this Division, and her dedication to the Cystic Fibrosis Program has helped Emory gain full accreditation from the CF Foundation and made the adult program a vibrant place for great

care, scholarly teaching, and cutting-edge clinical research. Therefore, I can think of no greater legacy for Lindy within the Division and the CF Center than to create the Lindy Wolfenden Fellowship in Cystic Fibrosis.” Already, over 140 individuals have contributed to the fund that will support these fellowships. If you are interested in contributing, please contact Ms. Paige Martin at: 404.727.9346 or paige.martin@emory.edu.



Progress of the Comprehensive CF Center of Excellence

Mission Statement:

“to build a comprehensive program that will not only continue to provide the highest quality care but also will lead to new breakthroughs in CF research that will advance the quality and longevity of life for our patients.”

Committees for the Center of Excellence

All three of our committees/boards have met since the last newsletter. We are in the process of expanding the membership of each of these groups, to increase the range of representation.

The **Community Advisory Board** includes: an Emory Trustee, a Georgia Tech Trustee, senior representatives from Children’s, an adult CF patient, a CF parent, and representatives from the Atlanta biotech industry. This Board met on July 22, with great outcomes. The members of the CAB will serve as ambassadors for us, and provide important advice as we grow.

The **Internal Advisory Board**, which includes leaders at Emory, Children’s, and Georgia Tech, who have experience in putting together and/or directing very successful Centers, Divisions, or Departments, or who have access to internal resources that can be useful for us. The Board met on August 31.

The **Program Steering Committee**, which includes: CF physicians and scientists, other pulmonologists, and scientists relevant to our scientific theme. The Program Steering Committee is composed of people that will be making most of the decisions, generating plans and taking action for strengthening each of the components of the Center of Excellence. The Program Steering Committee takes advice from both the Community Advisory Board and the Internal Advisory Board. The Program Steering Committee met on August 26.

Braves’ Game Day

In an effort to get to know each other as we begin to work together

for the Center of Excellence, members of the Community Advisory Board plus a few other friends were invited to join us at Turner Field, as we watched the Braves take on Tampa Bay on June 16. Special thanks to an anonymous supporter of Children’s for allowing us to use their 755 Club Suite. The game was awesome, and those of us who stuck around to the end enjoyed a real treat.



(Pictured, left to right: Walt Strother, Paul Frilingos, Paige Martin, Dave McKenney)

Outreach Activities

Thanks to Bank of America in Alpharetta, GA!

We thank our first community partner, Bank of America in Alpharetta, GA, for their generous support of the Emory-Children’s Cystic Fibrosis Center of Excellence.

As we develop a center that will build the #1 Cystic Fibrosis program in the country and transform the medical approach to this deadly disease, Skip Guilliams and Walt Strother of Bank of America are launching a program that helps fund our mission. Skip and Walt, instructors for an investment strategy course offered through the Emory Center for Lifelong Learning, offer a personal and financial health workshop to companies in the

area. In appreciation for a company’s gift to the Emory-Children’s Cystic Fibrosis Center of Excellence – the full amount of which goes toward the Center – employees of the company benefit from a free one-hour “lunch ’n learn” workshop, which can be tailored to accommodate what the employer believes to be of most value to his/her employees.

According to Skip, First Vice President and Senior Financial Advisor of Merrill Lynch/Bank of America, “This is a real win-win for both parties, unique in that there is something in it for both the companies who participate *and* the CF patients cared for by Emory doctors. We are able to provide information that is helpful to employees of the companies that participate in our program *and* raise money for a wonderful cause.” In addition to the education and awareness the program makes possible, initial efforts have resulted in over \$5,000 to support the Emory-Children’s Cystic Fibrosis Center of Excellence.

Most recently, our community partner has developed a three-evening education course on financial planning for retirement. All tuition costs for “Passport to Retirement” are donated in full to The Emory-Children’s Cystic Fibrosis Center of Excellence. We are most grateful for Bank of America’s interest in supporting the Center and our patients with CF.

For information regarding upcoming courses in Dunwoody, Alpharetta and Gwinnett, call 678.886.2781.