CF FAMILY NEWSLETTER

Fall 2023

UNC HEALTH Children's

Kid First, CF Warrior Second

Zack Cashatt hasn't missed a beat since he was an infant. When asked how he would describe himself in three words he claims he is energetic, forward-thinking, and, as his wife chimed in, stubborn. These are all attributes that have served him well and allowed him to overcome and weather the obstacles CF has thrown at him over the years.

Zack was diagnosed with CF at 4 months old in 1986, before newborn screening was a thing. He was having trouble breathing and, he claims, "a country doctor saved me." He was sent to UNC to be tested for CF. Once diagnosed, he became one of Dr. Retsch-Bogart's first CF patients. Dr. Retsch-Bogart told his parents to treat him as a child first and then as a CF patient, and so they tried to make life as normal as possible for Zack. Dr. Retsch-Bogart made a huge impact on his CF journey, "I loved seeing him, telling him what I was doing athletically, physically. He always seemed happy to see what I was doing and he got to come to one of my football games senior year."

As a child, Zack knew something was "wrong", but it only drove him to push himself harder than most of his peers. In second grade he was set to do the Presidential exam in PE. Trying to be considerate of his CF, his PE teacher put him in the girls group. Zack was so angry that, to prove a point, he pushed himself to go way beyond what was planned, he got over 100 laps back and forth until he finally tripped and ran into the wall.

He played football in High School and college and then was diagnosed with CF-related diabetes at 27 years old. This dramatically changed him, from his diet to his fear of needles, and ultimately drove him to compete in the Ninja Warrior show in 2018. He had been watching the show while hospitalized with diabetes, came home, built his first obstacle and the rest is history.

Once Zack started Trikafta, his life changed again. At 6' and 170lbs, his doctors had rushed to get him onto the new drug and set his expectations low for the first several weeks. A week later, he stepped outside and took of running—he ran a full mile before he stopped. After gaining 40 lbs thanks to the new therapy, he realized his Ninja days were behind him, so he did what he does best and pivoted to the next best thing in his mind, the Highland Games.

Today Zack is a dairy farmer. He works 14 hour days and then spends time power lifting to keep himself in shape for the Highland games. He also manages to find time to love on his wife and 4 year old son.

Having a son was one hurdle Zack never anticipated. He hadn't realized he was infertile due to his CF. He and his wife, a CF carrier, didn't give up and finally welcomed their son via invitro fertilization.

When asked what advice he would give his younger self, he says he wouldn't change a thing and would encourage himself to just keep pushing as hard as you ever can. He says he would tell every kid with CF that same thing. As for parents, he says, "Push your kids! Dad never let me feel sorry for myself. My parents pushed me, encouraged me and let me be a kid."

A Distinguished Career: Farewell Dr. Leigh

Dr. Margaret Leigh is retiring this year after over 40 years caring for patients as a faculty member in the Dept of Pediatrics and the Pulmonary Division. She will be greatly missed, and we wish her well as she embraces retirement. Dr. Leigh greatly impacted many of those during her time at UNC, and we asked a few of those touched by her professionally to share their thoughts below.

Dr. Margaret Leigh (Magee) has significantly advanced the care of hundreds of children and their families impacted by cystic fibrosis through her compassion, astute skills as a physician and her exceptional dedication to providing cutting edge treatment. Dr. Leigh served as the CF Center Director for over thirty years, growing the team that served the children and families. Her vision to provide the best care possible to these children was met due to her consistent and unwavering focus on the child and family. She loved the families she cared for as if they were her own, attending celebrations and providing support during difficult times. She is a true hero, serving as an example for all of us.

Mentoring and training the next generation was a deep passion for Dr. Leigh. She trained many, many students, residents, fellows, and junior faculty. Dr. Leigh was known as the "wise one" who many approached for sage advice. She inspired all of us to be better clinicians, investigators and educators and reminded us not to forget why we practice medicine- to improve the care of children. I personally am honored to have worked so closely with Dr. Leigh for over two decades. I have learned so much from her and feel blessed to have had her as a mentor, sponsor, and close friend. Her impact, wisdom, empathy, and love for pediatrics will continue to serve as a guiding light for all of us.

Submitted by Stephanie Duggins Davis, MD
Edward C. Curnen, Jr. Distinguished Professor
Chair, Department of Pediatrics , UNC

Dr. Leigh was my first research supervisor and the most supportive and effective mentor of my career. Her dedication and unwavering support during my fellowship turned me into an expert on Primary Ciliary Dyskinesia (PCD), another chronic illness that has some similarities to CF. However, it was Dr. Leigh's ongoing support after my graduation that truly shaped my career. Through our collaborations over the past decade, she helped me become a world leader in PCD, and her sage approach to every aspect of this disease taught me how to continue the fantastic evolution for PCD that she orchestrated during her career. Her efforts have launched this rare respiratory disease to the forefront of pulmonary medicine worldwide, helping thousands of patients with PCD to live healthier lives.

No matter what dilemma may arise, Dr. Leigh always shows an amazing ability to digest the mundane details and somehow formulate the exact solution to the problem. Dr. Leigh always has the answer and everyone around the table looks to her for it. But Dr. Leigh never sits at the head of the table, for she is amazingly humble and will rarely claim credit for her influential thoughts or solutions. That is what is so special about her: her approach to everything is measured, balanced, unobtrusive, and inspiring. She has the ability to make others realize the correct approach without outwardly telling them how to do so, and this incredible capacity has trained generations of pediatricians, pulmonologists, and researchers to be leaders in their various fields. With Dr. Leigh's retirement, there will definitely be a void at the head of the table, and even though she would never take that place, it is where she belongs. Luckily for all of us, her decades of impeccable teaching and guidance have created some of the best minds in medicine. Thanks to Dr. Leigh, the future is truly bright for people with CF, PCD and all of the other respiratory diseases she has researched and trained others to care for during her distinguished career.

Submitted by Adam J. Shapiro, MD
Assoc. Professor of Pediatric Respiratory Medicine
Director - PCD Foundation Clinical and Research Center Network, Montreal Children's Hospital, McGill University Health Centre

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A Lectureship is being established in order to honor Dr. Leigh. If you would like to learn more and contribute to the Dr. Margaret Leigh Lectureship, you can do so here: https://unchf.org/margaretleigh.

Should the donations not reach the minimum required for a lectureship, the funds will be used in her honor within the UNC Children's Excellence Fund in support of the clinical, research and education efforts of UNC Children's.

Higher Education Scholarships for Cystic Fibrosis Patients

Did you know you could get help paying for college or school after high school? There are many scholarships available to people who have CF. The amount available varies from a couple hundred dollars up to tens of thousands of dollars. The deadlines are all different and each requires different information. It's never too early to start looking and thinking about what you might want to do after high school. If you need anything from your doctor, nurse, or social worker to complete the application, let us know as soon as possible so we can get everything back to you in time!

AbbVie CF Scholarship Program
https://www.abbviecfscholarship.com/
40 scholarships awarded for $3,000.00, 2 Thriving Student Scholarships awarded for $22,000.00

Boomer Esiason Foundation (BEF) Scholarship Program
https://www.esiason.org/cf-living/scholarships

The Bonnell Foundation Marge Carmona Education Scholarship Program
http://thebonnellfoundation.org/scholarship/
Awarded up to $2,500.00/per person, eligible to receive the scholarship twice

Elizabeth Nash Foundation Scholarship Program
http://www.elizabethnashfoundation.org/scholarships.html
Awarded $1,000.00 -$2,500.00

Susanna Delaurentis Charitable Foundation Scholarship Program
http://thesusannafoundation.org/scholarships/apply.php
Scholarship is $1,000

Mandy Wagner Foundation
http://www.mandywagnerfoundation.org/

Jennifer Leigh Soper Cystic Fibrosis Scholarship
https://www.bgcf.org/scholarships/
You will need to register on the BGCF Scholarship Portal in order to apply.

Wells Fargo Scholarship Program for People with Disabilities
https://scholarshipamerica.org/scholarship/wells-fargo-scholarship-program-for-people-with-disabilities/

Breathe for Bea Foundation Scholarship Program
www.breatheforbea.org/programs/scholarships

Dylan's Dream
https://www.dylansdream.org/apply-for-scholarship/

Submitted by Ellen Penta, LCSW

The Q.I. Corner: Screening for CF-Related Diabetes

Some people with Cystic Fibrosis develop a problem called Cystic Fibrosis-Related Diabetes (CFRD). This can happen when thick, sticky mucus causes the pancreas to not make as much insulin as it normally does. Finding and treating CFRD as early as possible is important to maintain good nutrition and keep your body healthy. In order to do this, the CF Foundation recommends that people with CF ages 10 and older be tested every year with an oral glucose tolerance test (OGTT). This test is the best way to diagnose CFRD and is done while fasting. If you are diagnosed with CFRD, we will ensure that you receive proper treatment in order to feel better and stay healthy.

Your CF team is working to make sure that everyone with CF at UNC receives the recommended screening for CFRD. For people who are due for screening, your care team will help you prepare for the OGTT before your visit and explain the results to you. If you have any questions about this screening, or any feedback about how we can make the experience better, please let us know!

Submitted by William Stoudemire, MD

RESEARCH

Many CF studies are ongoing at UNC! More information on clinical trials being done here at UNC and around the country can be found on the Clinical Trials page at www.cff.org or by searching www.clinicaltrials.gov. You can also contact one of your hard-working Pediatric CF Research Coordinators directly:
Rosie Lainez at Rhlainez@email.unc.edu OR Grace Morningstar at grace_morningstar@med.unc.edu.

CF Research Meeting 2023

The 2023 CF Foundation hosted their annual Research Meeting at the end of June in Big Sky, Montana. The Research Meeting brings together scientists from around the world to discuss a focused research topic, which for this year was "Addressing Challenges to Expand Genetic Therapies." Genetic therapies are a critical area of research since they are the best treatment strategy for those who are not eligible for CFTR modulators, such as Trikafta®, which represents a growing population of people with CF. However, these strategies face many challenges that will need to be overcome to cure CF.

The first day of the meeting was focused on premature termination codons (PTCs), also known as nonsense mutations since they create a nonsense code in the RNA that leads cells to stop making CFTR protein too early. Therapies called "read through agents" can allow cells to "read through" these nonsense mutations to create a full length CFTR protein, but initial clinical trials with these medications did not show promising results. One challenge is that cells tend to degrade RNA molecules containing nonsense mutations in a process known as nonsense mediated decay. We are now working on developing therapies to stop this decay, which could help read through agents work better. Other studies are attempting to create better read through agents using various genetic approaches. While promising, these strategies are still in early stages and will take some time to reach clinical trials.

The second day was focused on using gene editing strategies to correct or bypass the abnormal CFTR gene. Gene editing introduces permanent changes into the DNA, which is exciting since it offers the possibility of a real cure, but is also concerning if the DNA changes are not made correctly. Most gene editing strategies are based on a system called CRISPR-Cas9, which can edit specific sequences of DNA within living cells. However, CRISPR-Cas9 can generate random insertions and deletions ("indels") within the targeted gene or within other "off target" genes that are undesirable. Newer studies have combined CRISPR-Cas9 with other proteins to create more specific gene editing molecules that limit creation of indels. Another approach called CAST (CRISPR-associated transposons) can add large insertions of DNA, including a near full length normal CFTR that could effectively replace most CFTR mutations. While all of these strategies are effective in cell culture models, much more research is needed before they can be introduced into clinical trials in humans.

The last day of the meeting focused on the barriers to transferring genetic material into target cells. Many current approaches use viruses for the transfer, with adeno-associated virus (AAV) a common viral vector. Interestingly, at a European CF conference that took place shortly before the CFF Research meeting, the company 4DTM presented early results from 3 people with CF treated with a single dose of an AAV based gene transfer vector. While the study showed promising levels of CFTR after one dose, ongoing treatment may face challenges. Unfortunately, a person's immune system can attack AAV and other viruses, and that can limit the effectiveness of repeated treatments. We are learning more about these immune responses and how blocking specific components may allow for repeated dosing.

Another approach is to use lipid nanoparticles (LNPs) to coat the genetic material and help it transfer into the cell. LNPs generally do not induce immune responses, and the enormous variety of lipids offers the potential to fine-tune the system to target. Multiple studies are currently evaluating a large variety of LNPs to find the optimal one for CF gene therapy.

The meeting allowed for discussion of these and several other topics. It provided a unique opportunity for a group of highly productive scientists—including many who do not currently work on CF but do relevant research—to gather together for research seminars, shared meals, and social activities. These meetings helped stimulate new collaborations, which will help move this important area of research forward and expand treatment options for people living with CF.

Submitted by Charles Esther, MD.

Creating a Culture of Research in Your Family

Meet Julia Principe, a CF mom, whose child receives care at UNC.

Tell us about your family.

My husband, Ryan, and I have been married nine years, and we live in Columbia, South Carolina. Ryan works in health care finance, and I work part time as speech-language pathologist. We have two children- Coleman, a six-year-old boy, and Claire, a one-year-old girl. Coleman has cystic fibrosis.

Does anything stand out in your child's journey with CF?

What stands out to me about our journey is the rapid research developments and advancements in treatment and care for those living with CF that we have witnessed and gained access to since Coleman was diagnosed. It has been remarkable.

How did you become interested in and/or get involved in CF research?

We were lucky enough to be connected by a mutual friend for a long phone call with a CF specialist and researcher, Dr. Ronald Rubenstein, days after Coleman was diagnosed with CF. Dr. Rubenstein told us about a genetic modulator/triple combination drug being researched and encouraged us to stay hopeful about the treatment and care that Coleman would be able to access. Dr. Rubenstein also connected us to one of his colleagues, Dr. George Retsch-Bogart, at UNC who we have seen routinely for care since Coleman was three-months-old. We held tight to the possibility of this new medication and stayed abreast with research opportunities through Dr. Retsch-Bogart.

What influenced your decision to get involved in CF Research?

We value and trust the expertise of Dr. Retsch-Bogart. He has educated us along the way about clinical trials and CF research. The possible benefits for Coleman from the Trikafta clinical trial that we enrolled in were far more significant to us than any downsides. Research studies were already suggesting longer life expectancies and better quality of life for those with CF taking Trikafta.

How did your child feel about getting involved?

Coleman was four-years-old when we enrolled in the clinical trial at UNC, so he didn't have much to say about it other than "Can I take my monster trucks with us?" Dr. Jennifer Goralski did an exceptional job of explaining (on a child's level) to Coleman what the study was about, and why he was a part of it. Ryan and I would frequently remind Coleman on our visits why we chose for him to be a part of it and always try to mix in some fun while we are at UNC for research (museums, time at the parks, and special surprises). We have talked with him about how other children will have access to this life-changing drug because of his and others' participation.

Are there any parts of research that are hard? How do you navigate those?

The hardest part has been the routine lab work for Coleman. He is anxious before blood draws but has almost always tolerated them very well. We offer a treat after each lab draw, so he knows that something will be waiting for him each time. He would sometimes get irritable during the long days of testing when the protocol would take several hours in a small exam room. The frequent trial visit are inconvenient for us since we live about three and a half hours from UNC.

Have you seen any benefits of being involved in research/how is it going?

The trial has been great. Coleman's enzyme dosing was adjusted months after beginning the trial. He completed Kindergarten in-person this year, and he remains active with soccer, swimming, and running around with his friends. It's seems like to us that he is greatly benefiting from the trial.

Any thoughts or tips for parents considering getting involved in CF research?

My advice would be to connect yourself with a center that is involved with research and do your homework. Ask questions and then ask them again in a few months. Research is always changing and new opportunities will come.

Anything you'd like to add?

We are forever grateful to Dr. Retsch-Bogart and the entire UNC team for their knowledge, care, and expertise as well as Vertex and the CFF. They are the reason we were able to be involved in CF research.

If your school requires medical forms, please reach out to your CF nurse as soon as possible so these can be completed in time.

Help Us Make the Newsletter Better!

If you would like to submit an article or have an idea for the next CF Family Newsletter, please contact Kelly Moormann at kelly.moormann@unc.edu.

Join in on CF Parent Education Nights!

Don't miss an opportunity to join upcoming virtual workshops to help you navigate life as a parent of a child with Cystic Fibrosis! You can find out more, watch previous workshops, and sign up here:

www.cfparenteducation.com

Contact Us

Scheduling: 984-974-7337
(En Español: 919-966-6669)

Pulmonary Office:
919-966-1055 (8am-4:30pm)

CF Nurses:
919-966-1055 (9am-4pm)

Hospital Operator:
984-974-1000

Visit us on the web at:
www.uncchildrens.org/uncmc/unc-childrens/care-treatment/pulmonary-care/cf

UNC MyChart: https://myuncchart.org

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