Research We Fund

Contents

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Research We Fund

The Cystic Fibrosis Foundation supports a wide range of research that focuses not only on improving the quality of life for people with cystic fibrosis today, but also on accelerating innovative research and drug development to add tomorrows.

Over the past several decades, the Cystic Fibrosis Foundation's unwavering focus on CF research has resulted in at least 10 therapies to treat the disease. We have made incredible strides, including the approvals by the U.S. Food and Drug Administration (FDA) of tezacaftor/ivacaftor (Symdeko®), ivacaftor (Kalydeco®), lumacaftor/ivacaftor (Orkambi®), Cayston®, and tobramycin (TOBI®). We will continue to push the frontiers of science to find therapies that treat the underlying cause of this disease for 100 percent of people with CF, and we will not stop until we achieve this goal.

The Foundation supported over 60 multicenter trials in 2018 for a wide range of therapies and is continuing to build on this momentum by aggressively funding an innovative research agenda. In 2017, the Foundation spent $169 million on awards for laboratory research, preclinical drug development, clinical research, and high-quality, specialized care and training -- the largest amount ever. This funding includes more than $116 million to support laboratory research (also known as basic research) and clinical research. Knowing that time is of the essence, the Foundation is projected to spend even more on research in 2018.

We are committed to supporting and accelerating any potential treatment that we think may benefit people with CF. Because CF is a rare disease, the CF Foundation provides financial support to encourage companies to focus on CF and help advance therapies that would be unlikely to move beyond the lab and into clinical trials. In 2018, the Foundation interacted with more than 150 different companies in the biotech and pharmaceuticals industries. The Foundation is funding over 40 programs to help advance therapies for people with CF.

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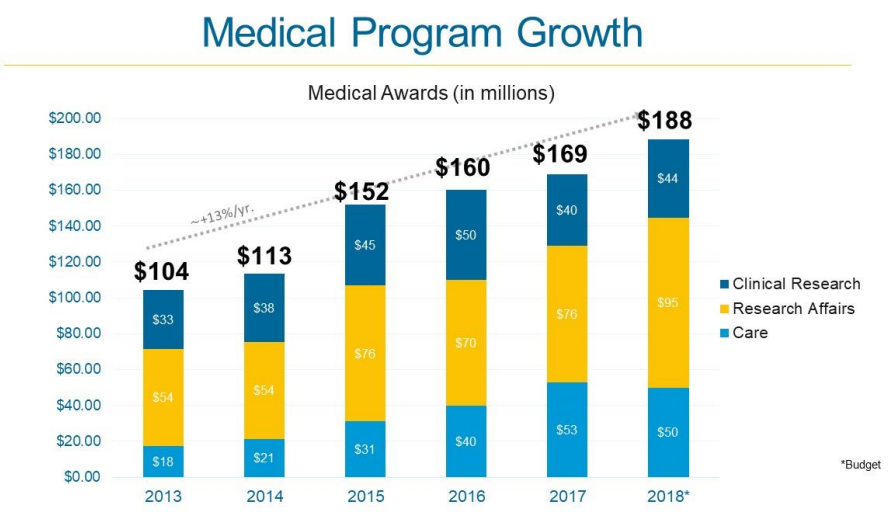
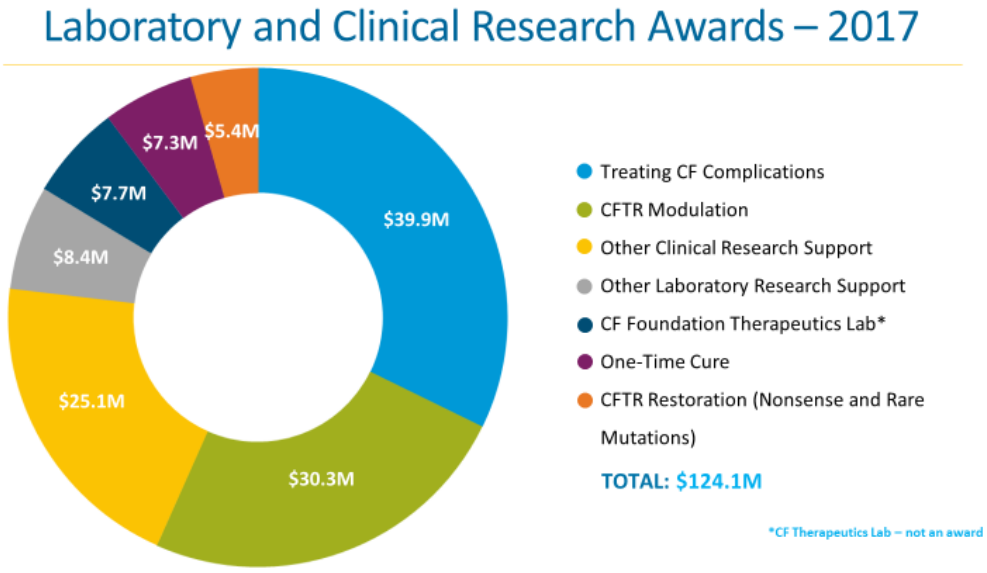


The Laboratory and Clinical Research Awards chart below includes $124 million that the Foundation distributed in awards (in the form of grants to academic institutions and therapeutic development contracts with industry) and support for its one-of-a-kind, CF-focused research lab, the Cystic Fibrosis Foundation Therapeutics (CFFT) Lab. Each category (such as "CFTR Modulation") includes both the funding for the basic (laboratory) research and clinical research being conducted in that area. "Other Laboratory Research Support" and "Other Clinical Research Support" refer to research that does not fall into the other categories listed.



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Laboratory and Clinical Research We Fund

To expedite the development of new therapies, the CF Foundation funded more than $124 million in laboratory and clinical research in 2017.

Laboratory Research

The Foundation funded $76.5 million in cutting-edge, innovative basic research (research conducted in the lab) in 2017. These funds highlight the critical role fundamental research plays in advancing new therapies by increasing our understanding of the disease and identifying new opportunities for developing treatments. The range of this laboratory research includes everything from gene editing to the structure and function of the CFTR protein. This CF Foundation-funded research is laying the groundwork for the next generation of treatments.

Much of the funding for laboratory research goes to academic institutions, including $6.36 million toward the Foundation's Research Development Program (RDP). This money helps pay for core lab facilities, pilot programs, and training at 11 pioneering academic centers. These centers have conducted innovative CF research that has resulted in some of the most significant advances in the field, including the identification of the first small-molecule CFTR modulators and the development of the original model of cystic fibrosis in a mouse.

The RDP also plays a critical role in fostering the next generation of CF scientists and clinicians. Many of today's top CF researchers began their careers at an RDP site. New researchers are critical to ensuring that the pace of development continues, and the Foundation is therefore investing heavily in training and career development.

To harness expertise, the Foundation has also recently facilitated several different research consortia, including the:

- Epithelial Stem Cell Consortium
- NTM Consortium
- Lung Transplant Consortium

Research consortia are accelerating advancements in these areas by bringing together the brightest minds in these specialized fields of study to resolve important questions and to overcome challenges. The Foundation previously funded consortia focused on solving problems related to CFTR folding, CFTR protein structure, mucociliary clearance, and the identification of inflammatory markers.

To accelerate the pace of research, the Foundation also invests in the development of tools, including cell lines, antibodies, and databases; the identification of biomarkers; and the creation of animal models that replicate various aspects of the disease. All these investments play a critical role in advancing new therapies for CF.

In 2018, the Foundation launched a project to sequence the entire genome of 5,000 people with CF. This whole genome sequencing project will enable researchers to identify genes that alter or modify the disease. This research could provide useful insight into how these modifying genes influence the progression of CF and explain why two individuals with the same CFTR

genes, lifestyle, and other characteristics have different manifestations of the disease and different responses to therapy. For this project, deoxyribonucleic acid (DNA) acquired from three long-term studies will be used and data will be made available as a tool for CF scientists to investigate new genetic questions.

Clinical Research

In 2017, the CF Foundation spent more than $40 million on clinical research. This funding helped to support the most robust drug development pipeline of potential new therapies for CF in the history of the Foundation. There are more than 25 drugs in development in the CF Foundation's Drug Development Pipeline.

In 2018, the Foundation enabled 64 multicenter clinical trials, more than doubling the number of trials from just six years ago. The breadth of trials has also increased, focusing not only on CFTR modulators, but also on a variety of treatments for complications of the disease, such as infections, excessive mucus, inflammation, and gastrointestinal (GI) issues.

These trials were made possible because of the largest CF clinical trials network in the world, the CF Foundation-supported Therapeutics Development Network (TDN). This coordinated network, which receives more than $20 million annually from the Foundation, allows trials to be performed more efficiently, accelerating the development of new therapies for people with CF. The TDN includes 89 Foundation-accredited care centers with specialized research teams able to perform clinical trials and is critical to ensuring advancements aren't delayed because of insufficient enrollment.

The Foundation also supports international clinical research initiatives in Canada, Australia, the United Kingdom, and other European countries in our ongoing effort to accelerate the delivery of new therapies to people with CF. More than 50 international research teams receive financial support to help conduct trials and ensure adequate enrollment.

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CFTR Modulation Research We Fund

In 2017, the CF Foundation spent more than $30 million on laboratory research and clinical trials for new and more effective drugs to restore the function of the defective CFTR protein.

For nearly 20 years, the Foundation has pursued a long-term strategy to develop effective CFTR modulator treatments that target the underlying defect in cystic fibrosis. Many different companies and academic investigators are testing an unprecedented number of new and potentially more effective CFTR modulators in clinical trials.

First-Generation Strategy

In early 2018, the CFTR modulator tezacaftor/ivacaftor (Symdeko®) was approved by the FDA, offering an alternative for people who cannot tolerate lumacaftor/ivacaftor (Orkambi®). Tezacaftor is also positioned to play a critical role in next-generation triple-combination therapies.

This first generation of FDA-approved CFTR modulators, which includes ivacaftor (Kalydeco®), lumacaftor/ivacaftor (Orkambi®), and tezacaftor/ivacaftor (Symdeko®), will eventually benefit more than 60 percent of people with CF. Ivacaftor was recently expanded to children ages 1-2 and lumacaftor/ivacaftor was expanded to children ages 2-5. Trials are already underway to determine the effectiveness and safety of these drugs in children as young as 6 months old. Obtaining access to these drugs early in life is an important step, as new research indicates that taking modulators before the disease has progressed could potentially preserve long-term lung and gastrointestinal (GI) function.

Next-Generation Strategy

Several companies are developing next-generation modulators that are either currently in clinical trials or will be entering clinical trials soon. Some of these next-generation modulators have the potential to be significantly more effective than current FDA-approved drugs and to benefit more people with CF than ever before. **This includes individuals with only one copy of the F508del mutation, regardless of their other mutation.**

Based on early-stage clinical trial results, two new CFTR modulator candidates were chosen by Vertex Pharmaceuticals for Phase 3 clinical trials. The candidates, VX-659 and VX-445, are being tested as part of two different triple-combination therapies. One of these next-generation modulators could be approved in late 2019 or early 2020. If approved, more than 90 percent of the CF population could have highly effective modulators for their specific mutations.

The Cystic Fibrosis Foundation is planning a study called PROMISE that will examine the short- and long-term clinical and research implications these triple combination therapies will have on people with CF. Researchers will investigate how the drugs affect the course of the disease, looking at lung function, mucus clearance, infections, gastrointestinal issues, and inflammation among other aspects of the disease.

Theratyping Initiative

Research is underway to categorize mutations based on how they respond to different modulators. By testing modulators on different CFTR mutations in the laboratory, scientists can identify treatments for people with mutations that are so rare as to make clinical trials impractical.

The Foundation is working with scientists, clinicians, and regulators to devise ways to use this technique, known as "theratyping," to identify mutations that respond to modulators already on the market. Theratype testing is underway at three Foundation-funded labs to investigate whether 650 rare CFTR mutations -- chosen because they produce the CFTR protein -- show improvement when exposed to a modulator therapy. If any of the tests display positive results, the Foundation plans to work with the drug company that developed the modulator, as the company will need to request that the FDA approve the medication for people with those mutations.

Theratyping has already proven successful. In early 2017, the FDA relied on a combination of theratyping results, clinical data, and the drug's established safety record to expand the use of ivacaftor to people ages 2 or older who have at least one of 23 CFTR mutations. However, it will take many years for the drugs to reach all the people who could potentially benefit.

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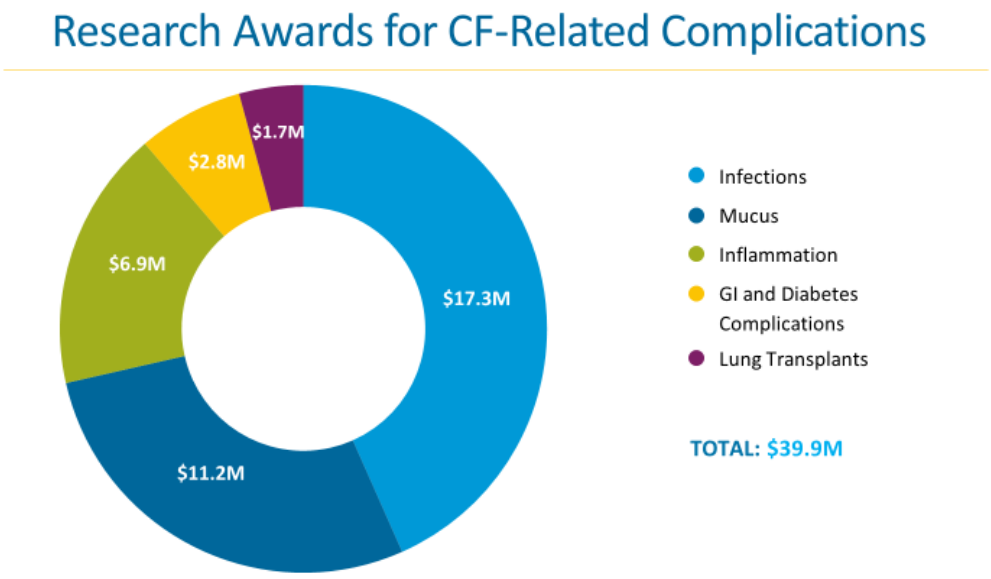
Research We Fund to Treat and Prevent CF Complications

The Cystic Fibrosis Foundation is actively pursuing and funding a broad portfolio of new treatments for complications of the disease to bring additional lifesaving therapies to the cystic fibrosis community as quickly as possible.

Overview

Even with the advancement of highly effective cystic fibrosis transmembrane conductance regulator (CFTR) modulators, there will be several generations of people with CF who have complications from the disease. We estimate that 20 years from now, a significant portion of our community will still require additional therapies to treat complications such as infections, inflammation, excessive mucus, and gastrointestinal (GI) issues. As such, improving treatments for complications of CF is critically important to the CF Foundation. I**n 2017, the CF Foundation spent more money in this area of research than any other.**

Approximately $40 million went to fund more than 200 different research projects related to complications. There are also more than 15 potential drugs in the pipeline to treat complications of CF, including anti-infectives, anti-inflammatories, mucociliary clearance therapies, and nutritional agents. The goal of these new treatments is to preserve lung function and maintain people's health until they can benefit from CFTR modulators as they are approved for more and more mutations.



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Infections

- The CF Foundation is investing in innovative and novel techniques to help tackle chronic, life-threatening infections.
- In 2018, the Foundation announced the **new $100 million Infection Research Initiative** to improve outcomes associated with infections.
- We funded more than 120 different projects in 2017 to improve our understanding of these infections and to develop new and more effective anti-infectives for people with CF.
- This includes funding for more than 10 industry antimicrobial programs, many of which are in either preclinical or early-stage clinical trials.
- It is the largest single area of funding of CF complications research.

During the 2018 North American CF Conference (NACFC), the Foundation launched the new Infection Research Initiative to improve outcomes associated with infections (bacterial, fungal, and viral) through enhanced detection, diagnosis, prevention, and treatment – areas of focus identified with input from the CF community. The Foundation has committed at least $100 million to the Initiative to further enhance the current robust portfolio of basic, clinical, and industry infection-related research programs. The funding will not result in reduced funding for other areas of CF research.

One project that is currently underway to develop better methods of detecting germs and diagnosing infections earlier is focused on nontuberculous mycobacteria (NTM).

NTM infections in CF are becoming increasingly common, and increasingly difficult to treat. It is, therefore, one of the Foundation's highest priority antimicrobial areas. Common NTM infections in people with CF include *Mycobacterium abscessus* (*M. abscessus*) and *Mycobacterium avium complex* (MAC). In 2017, the Foundation created the NTM Consortium to help standardize the diagnosis and treatments of NTM lung disease. The consortium is facilitating two large studies:

- The PREDICT study will focus on determining whether to treat NTM once it is detected.
- The PATIENCE study will follow those patients who are receiving treatment to see how well they do and whether the treatment should become standard.

The consortium of sites with expertise in NTM also forms a framework for future clinical trials for new therapies targeting NTM.

The CF Foundation is also funding the development of new therapies to bring the most effective and safest anti-infectives to people with CF as quickly as possible. One such project is focused on developing more effective treatments for NTM by leveraging advances made by the Bill and Melinda Gates Foundation during its efforts to accelerate the development of treatments for tuberculosis. In addition, researchers are exploring the possibility of repurposing existing therapies to bring new NTM drugs to the market.

In addition to NTM, there are many other concerning microorganisms prevalent in the CF community. They include fungi and the following bacteria: drug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*), *Burkholderia cepacia* (*B. cepacia*), *Achromobacter,* and methicillin-resistant *Staphylococcus aureus* (MRSA). Research is underway to improve our understanding of these CF microorganisms. Studying the microbial ecology of the airways as well as bacteria

and fungi in the environment will help researchers develop better strategies to prevent, manage, and treat infections.

Of particular concern to the community are drug-resistant organisms, bacteria that no longer respond to many of the available antibiotics. Because of this, the Foundation is focused on developing entirely new therapeutic agents with novel ways of fighting the infection.

The Foundation is currently working with more companies on the development of new treatments for infections than any other area of our research portfolio, including modulators. This includes funding for more than 13 industry antimicrobial programs, many of which are in early-stage clinical trials.

One innovative approach is using gallium, a metal that acts similarly to iron, to disrupt iron-dependent biological processes that are necessary for bacteria to survive. Promising laboratory research has shown that gallium can kill antibiotic-resistant strains of *P. aeruginosa* and other difficult-to-treat bacteria. As a result, a Phase 2 clinical trial was completed earlier this year to see if gallium(which has already been approved by the FDA for intravenous (IV) use) is safe and effective at controlling *P. aeruginosa* in people with CF. A second trial studying if gallium is effective in treating NTM will be starting in 2019.

Another unique approach is exploring the use of inhaled nitric oxide (NO), a natural antibiotic that is produced by the immune system. A clinical trial is underway to determine the effectiveness of this potential therapy on people with chronic bacterial infections as well as those with NTM infections.

Because approximately 25 percent of people with CF test positive for MRSA each year, the Foundation is supporting several studies exploring the best way to fight these bacteria. This includes providing funding for a Phase 3 clinical trial that started in late 2017 to test the use of inhaled vancomycin.

The CF Foundation is also focused on improving current treatments. In 2018, the CF Foundation awarded up to $3 million to Synspira to support the development of a novel molecule that could potentially make antibiotics more effective by breaking down biofilms, the protective layer that sometimes surrounds bacteria and increases their resistance to anti-infectives.

Additionally, the Foundation is funding a clinical trial that is looking at the safety and effectiveness of three different lengths of IV antibiotic treatment for pulmonary exacerbations. The STOP 2 trial complements an initial observational study, known as the STOP (Standardized Treatment of Pulmonary Exacerbations) trial, which sought to identify best practices for treating this common complication of CF. A third STOP trial is expected to begin in 2019 that will focus on children and oral antibiotics.

Common antibiotics, including aminoglycosides (such as tobramycin), can cause hearing loss. In an early phase study, researchers are testing a potential drug by Sound Pharmaceuticals called ebselen to prevent damage to the inner ear caused by antibiotics.

Bacteriophage (phage) therapy uses viruses that attack bacteria to treat bacterial infections. (Bacteriophage therapy has not been approved by the FDA for use in the United States.) The Foundation is funding three basic science studies to improve our understanding of the potential use of phage therapy to treat infections and its limitations, as well as supporting a group developing plans for early clinical trials of bacteriophage in CF.

Bacterial infections are not the only concern in the CF community. Many fungi, including *Aspergillus fumigatus*, cause complications for people with CF. The Foundation is supporting the development of an inhaled version of itraconazole to treat an allergic reaction to *Aspergillus* called allergic bronchopulmonary aspergillosis (ABPA). It is hoped that an inhaled version may cause fewer side effects and reduce drug-drug interactions.

With the progress of CFTR modulators, there are many questions about how these and other future treatments could impact infections. Scientists are studying how germs respond once individuals begin modulator therapies. The GOAL study, and a companion study based in Ireland, investigated how we might be able to eradicate certain infections with modulator therapy. Additional studies are planned to examine the effect of future modulators on infections in people with CF. The PROMISE study will look at how triple combination modulators affect infections in people with CF.

Mucus

Thick, sticky mucus is a major contributor to lung damage in people with CF. The Foundation is funding more than 35 projects to develop new and more effective treatments to improve the clearance of mucus from the lungs of people with CF.

Some promising potential therapies include agents that thin the mucus so it can be cleared away more easily. Another approach focuses on increasing the surface liquid in the lungs by inhibiting the epithelial sodium channel (ENaC), which is overactive in CF and contributes to the thickening of mucus by drying the airways. An important aspect of these approaches is that they could potentially help all people with CF, regardless of their CFTR mutations.

Inflammation

Inflammation is a natural part of the body's immune response to infection. However, people with CF have a much longer and more intense inflammatory response, which can be just as destructive to the lungs as the infection itself. Researchers believe that cells with a defective CFTR protein send out excessive signals that cause inflammation.

The CF Foundation is providing funding for around 40 projects to identify the causes of this excessive signaling and devise methods to block these signals. This includes support for four promising anti-inflammatories that could benefit everyone if approved.

Researchers involved in one of these clinical trials sponsored by Corbus announced promising results from an early-stage study. To advance the development of this novel anti-inflammatory drug, in early 2018 the Foundation awarded up to $25 million to help fund a Phase 2b trial, which is underway.

A recent Phase 2 trial by Celtaxsys testing a different anti-inflammatory agent demonstrated a reduction in pulmonary exacerbations for patients with forced expiratory volume (FEV_1) greater than 75 percent. Plans are currently underway for a follow up late-phase trial in 2019.

Complications in the Digestive System and CF-Related Diabetes

Although the lungs are usually the most seriously affected part of the body in CF, most people with this disease also experience complications in the digestive system. Getting adequate nutrition can be a problem for people with CF because a lack of fluid and bicarbonate in the pancreatic ducts can cause them to become blocked, preventing digestive enzymes from reaching the small intestine to digest food. This is important because data show that lung function and nutrition are closely linked. Other problems include abdominal pain, poor absorption of nutrients like vitamins, constipation, and liver disease.

The Foundation funded nearly 20 projects in 2017 related to GI complications and has helped organize a group of GI specialists who focus specifically on the treatment and research of GI issues in CF called the Developing Innovative Gastroenterology Specialty Training program, or DIGEST. This group of GI doctors is developing best practices and a better understanding of abdominal symptoms to lead to better treatments. DIGEST is also working on a study called GALAXY to gauge which GI symptoms affect people with CF the most so that researchers can prioritize them for further study.

In an innovative partnership with the National Institutes of Health (NIH), the Foundation is also investigating the best methods of screening for liver disease. Results from the recently completed PUSH study suggest that specialized ultrasound measurements can be utilized to identify individuals at risk of having progressive CF liver disease. This finding helps to set the stage for future trials aiming to intervene and prevent CF liver disease.

In addition, the Foundation supports clinical trials for glutathione, an antioxidant that is important to the normal functioning of the intestine and lungs. Glutathione levels have been shown to be lower in people with CF. Preliminary data suggest that oral glutathione may improve growth and decrease GI inflammation in children with CF.

CF-related diabetes (CFRD) is typically found in adults but also affects adolescents. This unique form of diabetes can accelerate lung complications if not properly controlled. The Foundation is funding research to better understand the underlying cause and genetics of CFRD, the best methods for delivering CFRD care, the potential benefit of CFTR modulators on preventing the development of CFRD, and the control of CFRD that does develop.

Lung Transplants

With more than 250 people with CF undergoing lung transplantation every year, the Foundation is dedicated to improving the lung transplant experience and to extending post-transplant survival. In order to accomplish this, we launched the Lung Transplant Initiative in 2016, committing more than $15 million over multiple years. (The $1.7 million in funding highlighted on the chart includes 2017 research funding only. It does not include money spent on other parts of the initiative.)

Through the Lung Transplant Initiative, the CF Foundation has created and funded a consortium of 10 academic transplant centers and laboratories dedicated to improving lung transplantation outcomes. The goals of the Cystic Fibrosis Lung Transplant Consortium are:

- To define and implement best practices
- Enhance quality improvement
- Conduct clinical trials to improve the delivery of lung transplant clinical care
- Improve our understanding of chronic rejection
- Develop new therapies for transplant recipients

At the forefront of the initiative is the development of clinical practice guidelines to improve and standardize the care received by people with CF for whom transplant is an option. To improve the lung transplant process, the initiative is working on three sets of guidelines for the CF and lung transplant communities -- referral guidelines, advanced lung disease guidelines, and post-transplant guidelines.

To improve post-transplant survival rates, the Foundation is also supporting research on the complications that often develop after transplant. We have funded nine basic science lung transplant studies as well as additional research specifically focused on improving our understanding of chronic lung allograft dysfunction (CLAD) and identifying paths toward developing therapies that might either prevent or treat CLAD.

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CFTR Restoration Research We Fund for Nonsense and Rare Mutations

The Cystic Fibrosis Foundation is aggressively pursuing and funding innovative research to ensure all people with cystic fibrosis, including those with nonsense and rare mutations, have an effective treatment that targets the underlying cause of their disease.

It is estimated that approximately 7 percent of people with CF will be unable to benefit solely from cystic fibrosis transmembrane conductance regulator (CFTR) modulators and will require different therapies to fix the underlying cause of their disease. The Foundation is funding research aimed at discovering new treatments for these individuals with nonsense and rare mutations that do not produce CFTR proteins.

In 2016, the CF Foundation launched the Nonsense and Rare Mutations Research and Therapeutics Initiative focused on funding research to address the needs of these individuals. The Foundation has committed $72 million to the initiative, which helps advance research by academic institutions and biotech and pharmaceutical companies focused exclusively on creating therapies to restore CFTR production and function.

Readthrough Screening Programs

In people with CF who have nonsense mutations (also known as “x” or “stop” mutations), CFTR protein production stops prematurely. This leads to a shorter, incomplete protein that usually doesn’t function. One unique strategy to develop new treatments for these mutations involves small-molecule compounds known as readthrough agents. These compounds would “read through,” or override, premature stop signals in the CFTR gene to make a full-length CFTR protein.

With funding from the Foundation, the nonprofit organization Southern Research, in collaboration with the University of Alabama at Birmingham, is using a novel and sophisticated screening process to identify readthrough compounds in its 750,000-compound chemical library. In addition, approximately half of the research being performed at the Cystic Fibrosis Foundation Therapeutics Lab is focused on therapies that could help provide new treatments for individuals with nonsense mutations.

In May 2018, the CF Foundation awarded up to $11 million to the biotech company Icagen to fund the largest high-throughput screen for readthrough agents the Foundation has conducted to date. As part of this contract, more than two million compounds will be screened to identify candidates that may be developed into drugs for people with nonsense mutations.

To further expedite the development of new treatments for individuals with nonsense mutations, the RARE cell-collection study was launched in early 2018. The study will collect cells from individuals with two stop mutations to enable the development of promising new therapies (readthrough agents as well as other compounds).

Transfer ribonucleic acid (tRNA) is a key component in the cell’s ability to translate DNA into a protein. A new company supported by the Foundation called ReCode is exploring the delivery of

a suppressor tRNA that will also allow readthrough of nonsense mutations to make a full-length CFTR protein.

RNA Therapy

Another innovative treatment that is part of the Foundation's strategy is ribonucleic acid (RNA) therapy. This treatment restores and stabilizes the messenger ribonucleic acid (mRNA) that is used in the cell as a template to create the CFTR protein. One of the benefits of this treatment is that it could potentially benefit everyone with CF regardless of their mutations.

For RNA therapy, we are pursuing two different approaches in parallel. The first approach would replace the defective mRNA by delivering normal mRNA to cells. The second approach is to repair the defective mRNA responsible for producing the CFTR protein. Both strategies would enable full-length, functional CFTR protein to be made.

The first mRNA therapy clinical trial began in mid-2018. This early-stage study by Translate Bio will test whether normal mRNA can be transmitted into the cell safely to make CFTR protein. A second company, Arcturus, is pursuing a similar approach in the laboratory with the goal of identifying a safe, effective delivery system for mRNA.

CF Foundation Therapeutics Lab

In 2016, the CF Foundation celebrated the expansion of a new, one-of-a-kind CF research facility to bridge the gap between discoveries made at academic institutions and the medications made by the pharmaceutical industry. Based in Lexington, Mass., the CF Foundation Therapeutics Lab identifies and tests potential groundbreaking therapies for CF, readying them for further development.

The CF Foundation Therapeutics Lab has screened its more than 200,000-compound library for potential new therapies -- including readthrough agents for nonsense mutations and new CFTR modulators -- to treat the underlying cause of CF. Currently, much of the work at the lab is concentrated on nonsense mutations, and the lab recently launched an initiative to create a cell culture bank with cells from people with CF who have rare mutations. This cell culture bank will aid in the development of nonsense-targeted therapies and may result in the extension of available therapies to people with rare mutations. The expanded facility also enables the lab to research gene editing and stem cell biology.

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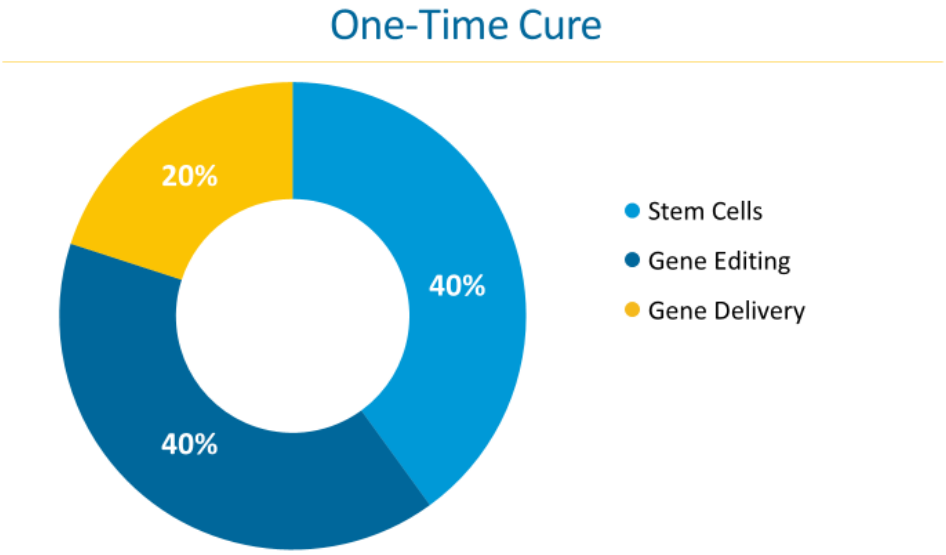
Research We Fund for a Cure

Our long-term goal is to create a cure that would benefit every person with cystic fibrosis regardless of their mutations.

The most promising options for a cure are either adding normal cystic fibrosis transmembrane conductance regulator (CFTR) genes to cells using gene therapy or repairing the defective CFTR genes using gene editing.

In 2017, the Foundation devoted more than $7.3 million to fund more than 30 groundbreaking gene editing, gene delivery, and stem cell research projects. Using the latest scientific discoveries in these areas of research, we are trying to tailor gene editing techniques for CF with the goal of one day curing the disease.

Although these technologies have progressed rapidly in the last few years, it will be many years before they reach patients.



Gene Editing and Gene Therapy

Gene editing and gene therapy are emerging technologies that could be used one day to correct the mutations in the CFTR genes that cause CF. Gene editing tools would repair the mutations in a patient's DNA, while gene therapy would introduce a healthy CFTR gene into the cells of people with CF. Editas Medicine Inc. has received funding from the Foundation to advance potential gene editing approaches that could be developed into therapies for CF. The company is using CRISPR/Cas9 technology -- a tool that uses an editing enzyme, allowing researchers to cut out and revise, or repair, DNA. Gene editing offers the potential to correct nearly every CFTR mutation.

Gene Delivery
Gene delivery refers to the process of transporting specifically engineered DNA molecules into cells, and it is an essential component of gene editing and gene therapy. The Foundation is providing funding to 4D Molecular Therapeutics and Talee Bio to expand preclinical work to develop and test their gene delivery vehicles, which would transport a healthy CFTR gene into the lung cells of people with CF. The Foundation is also investigating nonviral approaches (i.e., lipid nanoparticles) to package DNA or ribonucleic acid (RNA) for delivery to the lung and other tissue.

To advance gene editing for CF, the Foundation held a gene editing research conference in the summer of 2018. Scientific experts met to discuss barriers to gene delivery for cystic fibrosis and to identify tools or other resources needed to move the field forward toward eventual clinical application.

Stem Cell Research
In April 2018, the Foundation launched the Epithelial Stem Cell Consortium. The inaugural meeting brought together stem cell experts from across the country to focus on advancing our understanding of airway stem cells and how they may be targeted by gene therapy or other therapeutic approaches.

Additionally, the CF Foundation Therapeutics Lab has hired both gene editing and stem cell biologists to work together to explore and advance new treatments and to get us one step closer to our ultimate goal of a cure.

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