CYSTIC FIBROSIS FOUNDATION®

ACADEMIC RESEARCH HIGHLIGHTS

The CF Foundation is pursuing a wide range of research with the potential to cure cystic fibrosis and help all people with the disease lead long, fulfilling lives. In addition to working with companies to accelerate the next generation of transformative therapies for CF, the Foundation funds a wide range of academic research into CF treatment and care. Below is a sample of research we are funding to help address the complex needs of people with CF.

A NEW ERA IN CF: UNDERSTANDING THE IMPACT OF HIGHLY EFFECTIVE MODULATORS

We have seen dramatic improvements in lung function in people who are taking highly effective modulators, but we know that there is much more to learn about how modulators impact overall health. The **PROMISE** and **BEGIN** studies are measuring how treatment with elexacaftor + tezacaftor + ivacaftor (Trikafta®) affects the entire body, including effects on infections, inflammation, mucus clearance, gastrointestinal health, sinuses, blood sugar, growth, and liver function.

REDUCING TREATMENT BURDEN

People who are benefiting from highly effective modulators may wonder whether other therapies are still necessary. To help inform conversations between people with CF and care teams about treatment burden, the **SIMPLIFY** trial is testing whether people who are benefiting from Trikafta can safely stop taking either hypertonic saline or dornase alfa (Pulmozyme®) for several weeks. The **HERO 2** study will use real-world, patient-reported data to further explore questions around the use of established therapies and Trikafta.

Further reading: Restore CFTR Function

TREATMENTS FOR NONSENSE & RARE MUTATIONS

About 7 percent of people with CF have a combination of two nonsense or other rare mutations that will not respond to modulators. Through our **Path to a Cure**, we are exploring many scientific approaches that could benefit this population, including the **RARE** study to collect and grow cells from people with CF with nonsense and rare mutations. These cells are critical for lab research to identify potential treatment options. The cells from the RARE study will be made available to companies and CF scientists to advance research in this area.

Importantly, we know that people with CF of minority descent are more likely to have two mutations that do not qualify for current modulators. We are committed to research that acknowledges the diversity of the CF community and explores the unique needs and challenges faced by all individuals with CF.

Further reading: Exploring Treatments for Nonsense and Rare Mutations

GASTROINTESTINAL ISSUES & CF-RELATED DIABETES

The **GALAXY** trial, the largest-ever study of GI symptoms in CF, was designed to gauge which symptoms affect people with CF the most. Researchers are using these results to inform and prioritize future studies, including research to address adult malnutrition, constipation, small intestinal bacterial overgrowth, and the use of proton pump inhibitors in CF.

Another innovative study will evaluate the use of a "bionic pancreas" (iLET™) to treat cystic fibrosis-related diabetes (CFRD). If successful, this approach could simplify management of diabetes and improve glucose control.

LIVER DISEASE

Although upwards of 30 percent of people with CF have slightly elevated liver function levels, approximately 10 percent of people with CF develop more advanced CF-associated liver disease. The Cystic Fibrosis Liver Disease Network, a collaboration between the CF Foundation and the National Institute of Diabetes and Digestive and Kidney Diseases, is conducting the **PUSH** study, a study aimed at finding non-invasive measures to help understand who may be at risk of developing cirrhosis; the **ELASTIC** study, a study of a newer, noninvasive method to identify scarring in the liver; and a study using MRI as a tool to identify individuals with CF who have advanced liver disease.

Further reading: Gastrointestinal Issues and Cystic Fibrosis-Related Diabetes

SINUS DISEASE

More than half of adults with CF experience sinus disease. Although sinus surgery typically leads to improvements in sinus symptoms, further research is needed to understand the full impact of sinus surgery. A study to evaluate the effects of sinus surgery on pulmonary outcomes, sleep, smell, depression, and other Quality of Life (QOL) measures is under development.

Several other studies are looking at how sinus bacteria, sinus inflammation, and nasal airway cells change when Trikafta is started. These studies also include sinus-specific QOL measures, including changes in sense of smell.

INFECTIONS

Since the launch of the **Infection Research Initiative** in 2018, the Foundation has already committed more than $58 million for studies into infection. These studies are tackling a wide variety of infection-related issues, including research into difficult-to-treat bacteria, such as nontuberculous mycobacteria (NTM), *Burkholderia*, and multi-drug resistant *Pseudomonas*.

UNDERSTANDING FUNGI

There is a tremendous need to understand when to treat and how to treat people with CF who grow fungi in their lungs. We are bringing together international experts to discuss the state of the science in CF airway fungal infections, the lessons learned from previous or ongoing clinical trials, and the possible approaches to address fungal infections in people with CF, specifically *Aspergillus* and allergic bronchopulmonary aspergillosis (ABPA).

OPTIMIZING EXISTING TREATMENTS

Beyond funding the development of new treatments to address infections, we are also funding research to optimize existing therapies in CF. The **STOP 2** trial was designed to provide insight into the best length of IV antibiotic treatment for pulmonary exacerbations in adults with CF. The **STOP PEDS** trial will study the use of oral antibiotics for outpatient pulmonary exacerbations in children with CF.

The **PREDICT** and **PATIENCE** trials aim to create standard ways to diagnose and treat nontuberculous mycobacteria (NTM). The **TEACH** trial seeks to optimize treatment regimens by studying the effect of adding oral azithromycin to inhaled tobramycin in people infected with *Pseudomonas*.

Further reading: Infections

SEXUAL AND REPRODUCTIVE HEALTH

To address the unique and emerging needs of women with CF, the Foundation has formed a dedicated **research working group**. Researchers and women with CF will collaborate to identify gaps in knowledge around women's CF health issues and develop the infrastructure needed to move this research forward. One of the first studies led by this group, the **MAYFLOWERS** study, will focus on pregnancy in women with CF who are taking Trikafta. The study will look at a range of maternal and infant health outcomes to determine the overall impact of pregnancy in CF.

Other studies will look at the safety and effectiveness of contraceptives in CF, parenting experiences in people with CF, and whether an app can be used to assess CF symptoms throughout the menstrual cycle of a person with CF.

Further reading: Reproductive Health and Fertility

MENTAL AND BEHAVIORAL HEALTH

We are testing innovative ways to support people with CF in all aspects of the disease, including mental and emotional health. We are funding several research studies to evaluate behavioral therapy for stress management, anxiety, and depression in teens and adults with CF. Some of the interventions being tested include mindfulness therapy, acceptance and committment therapy, and cognitive behavioral therapy.

In June 2020, in collaboration with the Mental Health Advisory Committee, the CF Foundation deployed a Mental Health Prioritization Survey to the CF community and members of their care teams. Results of the survey will be used to develop research priorities and communicated to researchers in funding opportunities.

MANAGING THE BURDEN OF DAILY CARE

The average CF treatment regimen can take up to two hours or more per day. Financial, social, and psychological issues can make it even more difficult for people with CF to maintain their prescribed treatment plan. We're supporting the **Success with Therapies Research Consortium**, a group of researchers studying practical interventions to help people with CF manage their treatment regimen. Current studies are testing the effectiveness of a web-based nutrition tool, a medication planning mobile app, video-based telecoaching, and an in-clinic screening tool to identify individual and systemic barriers that prevent people with CF from adhering to their treatment.

Further reading: Emotional Wellness

ADVANCED LUNG DISEASE & TRANSPLANT

The Advanced Lung Disease (ALD) registry was launched in 2019 to allow CF care centers to capture specific data related to ALD, which will make it easier for researchers to study this very important topic. Additionally, the first ever ALD guidelines for CF were published in 2020.

PALLIATIVE CARE

We have funded two multicenter studies focusing on palliative care. Work on guidelines is underway, focusing on models of palliative care delivery and symptom management.

TRANSPLANT

We are funding the extension of the **Clinical Trials in Organ Transplantation** study to better understand chronic lung allograft dysfunction (CLAD), a post-transplant complication related to chronic organ rejection that is a primary obstacle to successful and lasting lung transplants. More than 800 samples have been collected through the study, and approximately 100 of those are from people with CF.

Further reading: Lung Transplantation

This document highlights selected research studies and is not meant to be comprehensive. To browse all multi-center CF clinical trials, visit the Clinical Trial Finder. To learn about CF drugs in development, check out the Drug Development Pipeline. To learn about the CF Foundation's research portfolio and funding, visit Research We Fund.