CFRI community
46 Years of Research, Education, Advocacy, & Support
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Many Faces of CF: Diversity and Inclusion are CFRI Values

By Siri Vaeth, MSW

Terry Wright was diagnosed with cystic fibrosis (CF) at the age of 54. While in his late thirties, after a lifetime of lung exacerbations, hospitalizations and surgeries, a physician told him, "If you weren't Black, I'd swear you have CF!" Despite these words, his doctor did not test him, and Terry remained undiagnosed for 17 more years. With greater awareness that CF impacts people of all races and ethnicities, Terry would likely have been diagnosed far earlier, saving him from decades of pain and suffering.

Cystic fibrosis impacts people of every race and ethnicity. According to the most recent published CF Foundation Patient Registry, 9.4% of individuals with CF identify as Hispanic (of any race); 4.7% are African American; 3.8% are clustered as "other race." Because those of European descent have the highest incidence rate, those who do not fit this profile may face delays in diagnosis and treatment. There are nearly 2,000 CFTR mutations, hundreds of which are associated with disease expression. Unfortunately, most state newborn screening tests will not detect cystic fibrosis in babies with rare mutations, which are more common in non-Caucasian CF patients.

Researchers at Stanford found that 40-50% of alleles present in South Asian and East Asian CF patients are not part of commonly used screening panels, and that 20-30% of patients had mutations in both alleles that are not part of these panels. Failure to detect CF through newborn screening usually leads to a delayed or incorrect diagnosis with negative impacts on health and longevity.

As was the case with Terry Wright, who founded the National Organization for African Americans with Cystic Fibrosis with his wife Michele, care providers may miss the signs of CF in individuals from underrepresented racial/ethnic groups and fail to order testing. CF is an isolating disease regardless of race; this is intensified for those from communities where CF is less common and therefore less understood.

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The Cystic Fibrosis Rapid Response to Phage Therapy

By Forest Rohwer, PhD

Near real-time microbiology approaches are enabling doctors to make better decisions about patient treatments. The San Diego research community has established a collaborative effort to generate and interpret metagenomics, metatranscriptomics, and metabolomics (i.e., -omics) data from cystic fibrosis (CF) sputum samples in approximately 1-2 days. This work is part of a greater background of a long-term sampling effort, where each patient serves as their own benchmarks for different disease states.

This approach allows us to more rapidly determine what has changed at any particular time in the patient's history. Using these "-omics" data we are identifying the underlying viral and microbial mechanisms that drive the cyclical nature – stable, exacerbation and recovery – of CF. This back-

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Marianela Fajardo remembers when her daughter Maria was first diagnosed with CF after months of inconclusive tests. "I was so distraught. I didn't know what cystic fibrosis was, and I didn't know anyone who had it." Soon after, Marianela stepped in to help families whose struggles were exacerbated by language barriers. "Imagine how hard this is," she says, "to learn about the disease when you don't speak English." These barriers exacerbate health disparities and worsen health outcomes.

CFRI recently launched its Faces of CF Diversity and Inclusion Program with the formation of a dynamic CF Diversity and Inclusion Advisory Committee to amplify the voices of all impacted groups and enhance CFRI's outreach, resources, and programs for our diverse community. The Diversity and Inclusion Advisory Committee, comprised of adults with CF and parents of children/adults with CF, provides vital leadership in ensuring CFRI's culture of inclusion is further enhanced to offer meaningful support to the community.

With advisory committee input and guidance, CFRI will expand its educational resources to increase accessibility and representation through enhanced content offerings in multiple languages. A series of webinars are in the works to address health disparities for those with CF from the African American, Latino, South Asian and East Asian communities. To achieve these goals, CFRI is working with our current organizational advocacy partners while developing new and impactful alliances with existing groups supporting diverse populations.

There is a vital need for focus and attention on the unique needs of all members of our cystic fibrosis community, as well as the development of resources and strategies to address them. CFRI is fully committed to reaching those in need of support and connection while expanding awareness of cystic fibrosis among members of all communities.

CFRI is grateful to the members of our Diversity and Inclusion Advisory Committee for sharing their time, perspectives and expertise:

Isa Stenzel Byrnes, LCSW, MPH
Marianela Fajardo
Jean Hanley, MD
Alicia Maciel, MBA
Haimlata Patel
Harini Seshadri
Michele Wright, PhD
Terry Wright

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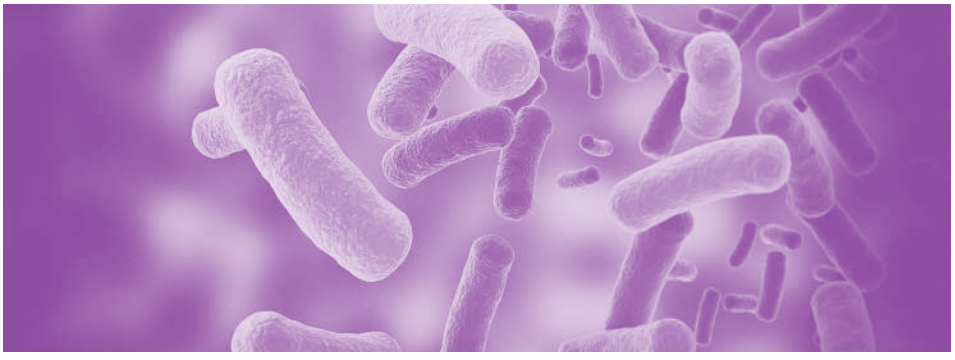
The Cystic Fibrosis Rapid Response to Phage Therapy *Continued from Cover*

background data is extremely useful for diagnosing what is unique about fatal and near-fatal exacerbations and points to possible treatment options. We are now using the DNA sequence data to build phage, which are viruses that kill bacteria, with the goal of performing phage therapy to stop severe exacerbations.

With the support of CFRI, we are developing phage and tailocins as a personalized treatment to kill multi-drug resistant pathogens affecting cystic fibrosis (CF) patients. Both the phage and tailocins are designed to kill *Stenotrophomonas* and *Achromobacter*. A tailocin identified in *Stenotrophomonas maltophilia* is used as a backbone to which tail fibers would be swapped to confer specific antibiotic activity against other *Stenotrophomonas* or *Achromobacter* strains.

We have aimed to clone the tail structural genes individually, and using this strategy, we successfully cloned 11 out of the 12 structural genes of *S. maltophilia* tailocin P28 into individual plasmids. To screen for additional tailocins, two *Achromobacter* spp. and two *Stenotrophomonas* spp. isolates from CF patients were sequenced, as well as 3 metagenomes from CF exacerbations. Expression of these tailocin proteins was accomplished.

Nineteen additional *Achromobacter* phages were included in our collection, and five new *Achromobacter* phages were isolated by our group and are referred to as the "San Diego collection." Fourteen *Achromobacter* phages were obtained from Dr. Christine Pourcel's group in France, this collection is referred as the "Côte d'Ivoire collection." 98% of the *Achromobacter* strains isolated at the San Diego CF clinic are susceptible to at least one those 30 phages. During this year, two patients in the San Diego CF clinic suffered multi-drug resistant *Achromobacter* infections. We screened our *Achromobacter* phages collection against their *Achromobacter* isolates and identified phages capable of killing these isolates.



Two *Achromophages* were identified and prepared for phage therapy for one patient and the FDA paperwork has been submitted. The second *Achromobacter*-infected patient has stabilized; we have isolated and prepped phages for this patient, but are holding off on treatment. Phages have also been isolated for a patient with a severe, acute exacerbation caused by an *E. coli* infection (the strain's genome has been sequenced). These phages are being prepped for phage therapy and the FDA paperwork was submitted in early 2021.

Most phage therapy is only performed under emergency conditions. Since CF exacerbations are usually not fatal, the emergency criteria do not apply, even though these disease flares substantially impact the patient's short- and long-term well-being. Therefore, these CFRI-sponsored studies are helping the FDA, doctors, and scientists understand how to navigate the complicated regulatory and scientific hurdles surrounding phage therapy in CF. The goal is to provide another tool to fight the chronic lung infections in a personalized fashion.