



## Research in Cystic Fibrosis

Headed by **Jay Kolls**, the Center for Translational Research in Infection and Inflammation is a dynamic, diverse group of Tulane researchers studying the basic biology and new therapeutic approaches of infection and inflammation.

One of the main areas of focus of this group is the interplay between infection and cystic fibrosis (CF). CF is a disease caused by mutations in an ion channel protein that causes, among other problems, excessive mucus buildup in the lungs.

The center is investigating the role of CD4+ TCells in the lungs of these patients, specifically the T-Helper (Th) cells that secrete IL17 and IL22. The center focuses mainly on extracellular pathogens, with limited attention on the intracellular tuberculosis bacteria.

The center utilizes a genetic mouse model of immunodeficiency infected with *Pneumocystis jirovecii* (*carinii*) pneumonia (PCP), which is an excellent model for human disease. These mouse models are paired with RNAseq data from human CF patient lung tissue. In CF, the microbial burden within the lung is many orders of magnitude higher than in patients without CF. This means that these patients are at risk for near-constant, chronic lung infection. The center is studying a variety of potential treatment options in an attempt to address this problem

# Center for Translational Research Infection & Inflammation



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## Immune-Derived Therapies for Bacterial Infection

In CF patients, there is a spectrum of lung function and susceptibility to infection despite identical or similar causative mutations. The center is investigating the possible reasons behind this with an eye toward clinical utility. It is possible that in patients with more improved lung function, better antibodies are produced. The center is working with patient samples in order to find strong antibodies that could be cloned and produced as a working biological.

In partnership with Genentech, the Lab is also exploring utilizing IL22 as an adjuvant to traditional treatments for chronic infection to improve patient response and bacterial clearance. IL22 activates the body's own innate defenses against bacteria. In theory, treatment with IL22 should prove effective against a wide variety of pathogens, including those that are resistant to multiple classes of antibiotics. Indeed, CF patients especially may benefit from IL22 treatment, as they have been found to express decoy molecules that serve as "bait" for endogenous IL22. This is studied through a chronic sinus infection murine model.

Lastly, they are studying the application of a fusion antibody-C-type-lectin protein as a novel, next-generation antifungal. All of these investigational approaches reflect the center's overall goal of leveraging the basic biology of infection and inflammation the developing next-generation anti-microbial treatments.

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