Division of
Pulmonary Medicine

Raouf Amin, MD
Professor and Director

Dan Benscoter, DO
Assistant Professor

John Brewington, MD
Instructor

Thomas Boat, MD
Professor

Ronald Bokulic, DO
Associate Professor

Lisa Burns, MD
Assistant Professor

Kelly Byars, PsyD
Professor

Barbara Chini, MD
Professor

JP Clancy, MD
Professor

Zackary Cleveland, PhD
Assistant Professor

Joseph Crisalli, MD
Assistant Professor

Daniel Grossoehme, DMin
Associate Professor

Theresa Guilbert, MD
Professor

Neepa Gurbani, DO
Assistant Professor

William Hardie, MD
Professor

Erik Hysinger, MD
Assistant Professor

Carolyn Kercsmar, MD
Professor

Elizabeth Kramer, MD
Instructor

Satish Madala, PhD
Assistant Professor

Karen McDowell, MD
Associate Professor

Gary McPhail, MD
Associate Professor

Anjaparavanda Naren, PhD
Professor

Hemant Sawnani, MD
Assistant Professor

Marc Schecter, MD
Associate Professor

Michael Seid, PhD
Professor

Narong Simakajornboon, MD
Professor

Christopher Siracusa, MD
Assistant Professor

Cherie Torres-Silva, MD
Assistant Professor

Christopher Towe, MD
Assistant Professor

Bruce Trapnell, MD
Professor

Robert Wood, PhD, MD
Professor

Jason Woods, PhD
Professor

Assem Ziady, PhD
Associate Professor

Holli Kunkel, MBA, MEd
Business Director

October 23rd, 2017

To the Editors of the Journal of Visualized Experiments:

We are excited to submit our manuscript "Generation of Human Nasal Epithelial Cell Spheroids for Individualized CFTR Study" for your review. All co-authors have seen and approved this submission. In this paper, we describe our novel method to form a non-invasively acquired human nasal epithelial cell-based three-dimensional model of CFTR function.

The introduction of modulator therapies to directly improve CFTR function marks an exciting new method of treatment in CF. These drugs are prescribed in a genotype-directed way that, while personalized, is imperfect. Represented genotypes only include those mutations that occur in a high enough frequency to facilitate large, randomized clinical trials, excluding many individuals. Additionally, as more modulators enter the market, the ability to individually choose the ideal therapy will become increasingly complex. These difficulties can be circumvented by individualized preclinical model systems, using patient-derived samples to quantify drug response. Individualized human cell-derived models of CFTR function are not novel; human bronchial cells and intestinal cells have both been used extensively for such models. Both remain invasive to acquire, however. As such, we generated the nasal cell-based model described within this manuscript. This three-dimensional "spheroid" model reliably quantifies CFTR function through a swelling-based assay.

This work represents is a significant step towards a non-invasive, personalized model of CFTR function to aid in clinical selection of modulator therapies on the individual level. We believe that this line of research will directly impact patient care in CF, and hope that sharing our method will continue to advance this work towards the clinic.

We appreciate your consideration, and look forward to hearing your comments. The authors have no conflicts of interest to declare; this work was funded in part by grants from the CF Foundation as indicated in the manuscript.

Sincerely,

John Brewington, MD
Pulmonary Medicine
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue / MLC 2021
Cincinnati, OH 45229
Phone: 513.636.6771
Fax: 513.636.4615