The genetic disorder cystic fibrosis is caused by reduced or absent cystic fibrosis transmembrane conductance regulator (CFTR) protein activity. While CTFR-focused therapies do exist, investigations into such therapies are inconsistent. CFTR–function-modulating therapies have shown significant clinical benefit, but studies regarding their molecular mechanism when used in combination have not been consistent with clinical results.

In a paper published Mar. 11 in the journal American Journal of Physiology – Lung Cellular and Molecular Physiology, Susan Birket, Pharm.D., PhD, instructor in the Division of Pulmonary, Allergy and Critical Care Medicine, UAB Department of Medicine, and her colleagues examined the mechanism of action of CFTR modulators, focusing on mucociliary clearance using Micro-Optical Coherence Tomography (µOCT) to evaluate epithelial function microanatomy. µOCT may better predict the success of therapeutics that target epithelial function since measurements of mucociliary transport and effective mucus viscosity can be readily acquired, and may dissociate with measures of ion transport alone.

Research revealed that primary human airway monolayers from patients with a G551D mutation responded to ivacaftor treatment with increased ion transport, airway surface liquid depth, ciliary beat frequency, and mucociliary transport rate, in addition to decreased mucus layer effective viscosity, a unique mechanism established by this project. Research also established a crucial link between in vitro data and clinical benefit, a finding not explained by ion transport studies alone.

Additionally, this research revealed established that F508del cells exhibit increased mucociliary transport and decreased mucus effective viscosity, but only when ivacaftor is added to the regimen. The project also displays that improvement in the functional microanatomy in vitro corresponds with lung function benefit observed in CTFR-function-modulating therapy clinical trials.