3D pulmospheres serve as a personalized and predictive multicellular model for assessment of antifibrotic drugs.

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Idiopathic pulmonary fibrosis, or IPF, is an interstitial lung disease in which lung tissue becomes progressively scarred over time. As tissue scarring worsens, the lungs are unable to properly move oxygen into the bloodstream. While IPF has no cure, there are therapy options available for patients with the illness. Unfortunately, there is no current clinical test to confirm if these treatments will be effective for a given patient. However, recent work by Veena Antony, M.D., professor in the UAB Division of Pulmonary, Allergy and Critical Care Medicine, and her colleagues may have taken the first steps to finding such a test.

“There is no cure for IPF, but there are two FDA-approved drugs that can help slow the rate of decline caused by the disease and improve quality of life,” said Antony, this project’s primary investigator. “Not all patients respond to both drugs, and some don’t respond to either. Having a reliable clinical test that can predict which drug works best for which patient is urgently needed.”

This reliable clinical test may be close to realization thanks to Antony’s work with pulmospheres. Pulmospheres, millimeter-sized spheroids composed of cells from individual patients, were shown to be effective in predicting IPF medication efficacy. This project’s research team grew pulmospheres from 20 IPF patients and nine control patients. These pulmospheres were then exposed to the two currently-used IPF medications, pirfenidone and nintedanib. In less than 24 hours, researchers were able to observe if the spheres responded favorably to one, both, or neither of the medications.

Of the 20 IPF subjects enrolled in this study, four patient pulmospheres responded only to pirfenidone, while three patient pulmospheres responded only to nintedanib. Eleven patient pulmospheres responded to both drugs and two patient pulmospheres did not respond to either drug. These initial findings were later confirmed through further study.

“Our results suggest that pulmospheres simulate the microenvironment in the lung and serve as a personalized and predictive model for assessing responsiveness to antifibrotic drugs in patients with IPF,” Antony said. “Lungs are three-dimensional organs and to truly understand the dynamics of IPF medications on the disease we require a 3D model, one that contains all the cell types found in a lung and that is able to function as a microcosm of the lung,” she continued.

This trial, the first to study pulmospheres in IPF treatment, is one Antony hopes will enhance further drug discovery and clinical testing.

“There are many potential therapeutic agents for IPF in the discovery pipeline now, and this technique might prove to be a very effective way to determining which are the most promising,” she said.