

Tulane is a leader in the fight against fibrosis

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Victor Thannickal, MD, (left) and Joseph Lasky, MD, of the Tulane School of Medicine, are united in their fight against pulmonary fibrosis, with a combination of research efforts that seek to create more effective diagnostic tools and find ways to treat and halt disease progression. (Photo by Cheryl Gerber)

Pulmonary fibrosis (PF) is a disease that gets little press, yet it dramatically impacts the lives of as many as a quarter million Americans.

PF has nonspecific symptoms that are easily dismissed – a dry, lingering cough, fatigue and shortness of breath on exertion. Marked by progressive damage that leads to permanent scarring of lung tissue, disability and eventually death, PF is

often underdiagnosed or misdiagnosed, in part because patients overlook symptoms as mere signs of “getting older.”

It is true that some forms of PF are associated with aging. Idiopathic pulmonary fibrosis (IPF) in particular occurs most frequently in people over age 50, who might overlook symptoms until the lung damage is advanced. PF often comes with a poor prognosis - many patients may live only three to five years after diagnosis.

Tulane University has been a leader in fighting PF for decades. Research conducted at the university’s School of Medicine leads to more effective new therapies and aligns patients with the clinical trials that test them, under the careful coordination of Joseph Lasky, MD, professor of medicine, pulmonary/critical care section chief and John W. Deming, MD, Endowed Chair in Internal Medicine; Sandy Ditta, senior research administrator; Jennifer Fitzgibbons, nurse practitioner; and Chris Glynn, research nurse. On the patient level, the Interstitial Lung Disease Center allows patients to receive the most recent advances in care and undergo pulmonary rehabilitation that improves their quality of life.

And now the PF program may position Tulane for recognition nationwide.

In 2021 pulmonologist and investigator Victor Thannickal, MD, joined the faculty of the School of Medicine from the University of Alabama – Birmingham, bringing with him an NIH grant to study the cellular and molecular mechanisms of lung repair and regeneration. Thannickal, professor of medicine and the Harry B. Greenberg Chair in the John W. Deming Department of Medicine, leads a multi-investigator translational program project that applies bench discoveries to patient treatment and is supported by the National Heart, Lung, and Blood Institute.

PINPOINTING THE CAUSE AND CORRECTION

Thannickal’s lab identified a molecule that is a primary driver of fibrosis. Now the researchers are partnering with a pharmaceutical firm to develop a drug that targets the fibrosis. The drug is in phase two clinical trials.

“Our group was one of the first to show that in this disease there is an accumulation of senescent cells in the lung. And those senescent cells drive this phenomenon of fibrosis. Now, there’s a similar theme in other diseases of aging, like Alzheimer’s, cardiovascular disease, and even in liver and kidney fibrosis, in that there’s an accumulation of senescent cells. There is growing interest in therapeutic development of so-called ‘senolytics’ to remove these senescent cells, similar to how

you get rid of cancer cells.”

“One paradigm that we have championed over the last few years is to induce apoptosis (meaning programmed cell death) of these scar-forming myofibroblasts that acquire senescent features in fibrotic tissues and organs. We are exploring a number of different strategies to directly kill these cells with targeted therapies.”

This robust background in research and clinical practice signals an exciting time for the PF program at Tulane. And with Tulane’s growing emphasis on innovation and biotechnology including both the School of Medicine’s own Business Development team and the opening of the Tulane Innovation Institute, it may take less time to get these therapies to market. Thannickal and his collaborators at Tulane are working with both groups to reach the goal of getting more effective therapies to patients, faster.

“That’s something that would be good for the biotech industry in this region,” he said. “PF may be an initial indication for eventual translation to a number of other more common age-related diseases.”

This work is particularly important because for years PF patients have been treated with anti-inflammatory drugs, which don’t work consistently across patient populations. In some patients, anti-inflammatory drugs may be more harmful than helpful to combat PF; *New England Journal of Medicine* published a study co-authored by Lasky, which showed that anti-inflammatory treatment may hasten death in patients with IPF.

LEADING PF RESEARCH AND CARE

For the last 30 years, Lasky has been researching PF at Tulane, with support from the National Heart Lung and Blood Institute, and treating patients from around the region. A longtime member of the Pulmonary Fibrosis Foundation, he was appointed as its chief medical officer in 2021.

The two roles inform each other. According to the foundation, more than 250,000 people in the United States live with PF, with more than 50,000 new diagnoses every year.

Over the years, Lasky’s lab has investigated mechanisms of PF, along with more effective diagnostic tools and ways to halt disease progression.

Part of Lasky's mission is to raise awareness of PF and increase participation in clinical trials. Nationally, less than 5% of PF patients are in clinical trials, and only 25% of patients are prescribed the latest therapies, whereas at Tulane, the vast majority are taking recommended and newer treatments.

"We want people afflicted with pulmonary fibrosis to get diagnosed earlier in their disease and get involved in clinical trials to receive the next generation of medications that are going to be more effective and have fewer side effects than the current ones that we have – that's something that we've been offering for over a decade at Tulane," Lasky said.

The university "is a regional referral resource for patients who want second opinions or improvements in their care for their fibrotic lung disease. What we're able to offer is a comprehensive center that aids in a more accurate diagnosis and all-inclusive management of interstitial lung disease through methods that are less hazardous for the patient," Lasky continued.

What causes the PF can be critical. The disease can be brought on by multiple factors including certain drugs or environmental exposures, as a consequence of autoimmune diseases, or by aging. On an X-ray, only subtle abnormalities may appear or may even be overlooked, whereas a high-resolution CAT scan of the chest is much more revealing and definitive.

Lasky said he sees approximately 400 patients a year and attempts to align them with clinical trials. "But that's only the tip of the iceberg regarding people afflicted with pulmonary fibrosis in the region," he added. Recent publications suggest that PF may occur in up to 1 in 200 patients over age 65.

TAKING A COMPREHENSIVE APPROACH

Other organs may also develop fibrosis independent of pulmonary fibrosis. "We're looking to repurpose current FDA-approved drugs for IPF – we have a program on that," Thannickal said. "And if we develop a novel agent, that could in the future be repurposed for other age-related diseases."

Tulane's extensive research capacity lends itself well to collaboration. Lasky, for example, received a two-year, \$500,000 grant to explore biomarker predictors of worsening pulmonary fibrosis, with input from Tony Hu, PhD, Weatherhead Presidential Chair in Biotechnology Innovation and director of the Center for Cellular and Molecular Diagnostics laboratory at the School of Medicine, and chemistry

Professor Janarthanan Jayawickramarajah, associate dean for research, faculty affairs and PhD programs at the School of Science and Engineering. Lasky has also worked with S. Michal Jazwinski, PhD, the John W. Deming, MD, Regents Chair in Aging and director of the Tulane Center for Aging, an interdisciplinary center that fosters and supports the development of research programs that address the problems of aging populations on all levels.

Other physician-scientists are advancing research as well, including Shigeki Saito, MD, and Qinyan Yin, PhD, assistant professors who are investigating novel molecular therapies to treat PF. In addition, Ramsy Abdelghani, MD, and David Becnel, MD, are interventional pulmonologists who employ the latest minimally invasive diagnostic techniques to help identify the specific cause of pulmonary fibrosis.

Thannickal said PF research has made significant progress over the last quarter - century, and Tulane's contributions and growth are reasons for hope as well. Drawing on the breadth of experience in the Department of Medicine and the Pulmonary Diseases, Critical Care and Environmental Medicine section, he hopes the PF program can eventually come together as a Center of Excellence dedicated to fibrotic and other advanced lung diseases.

"We have the opportunity to be the leaders in comprehensive care of patients with lung disease," Thannickal said.

"The future for advancing pulmonary research and patient care is extremely bright for Tulane."