An illustration of human lungs and the trachea. The lungs are depicted in a light brown color with a grid of small black dots. Several pieces of tan bandages are applied to the lungs, suggesting injury or treatment. The trachea is shown as a white, ribbed tube extending upwards from the lungs.

HOPING TO *Breathe* EASILY

BY TOMMY NEWTON

HUNDREDS OF THOUSANDS OF PEOPLE SUFFERING FROM INTERSTITIAL PULMONARY FIBROSIS, A DEVASTATING LUNG DISEASE, MAY BREATHE MORE EASILY ONE DAY THANKS TO RESEARCH UNDER WAY AT WESTERN KENTUCKY UNIVERSITY.

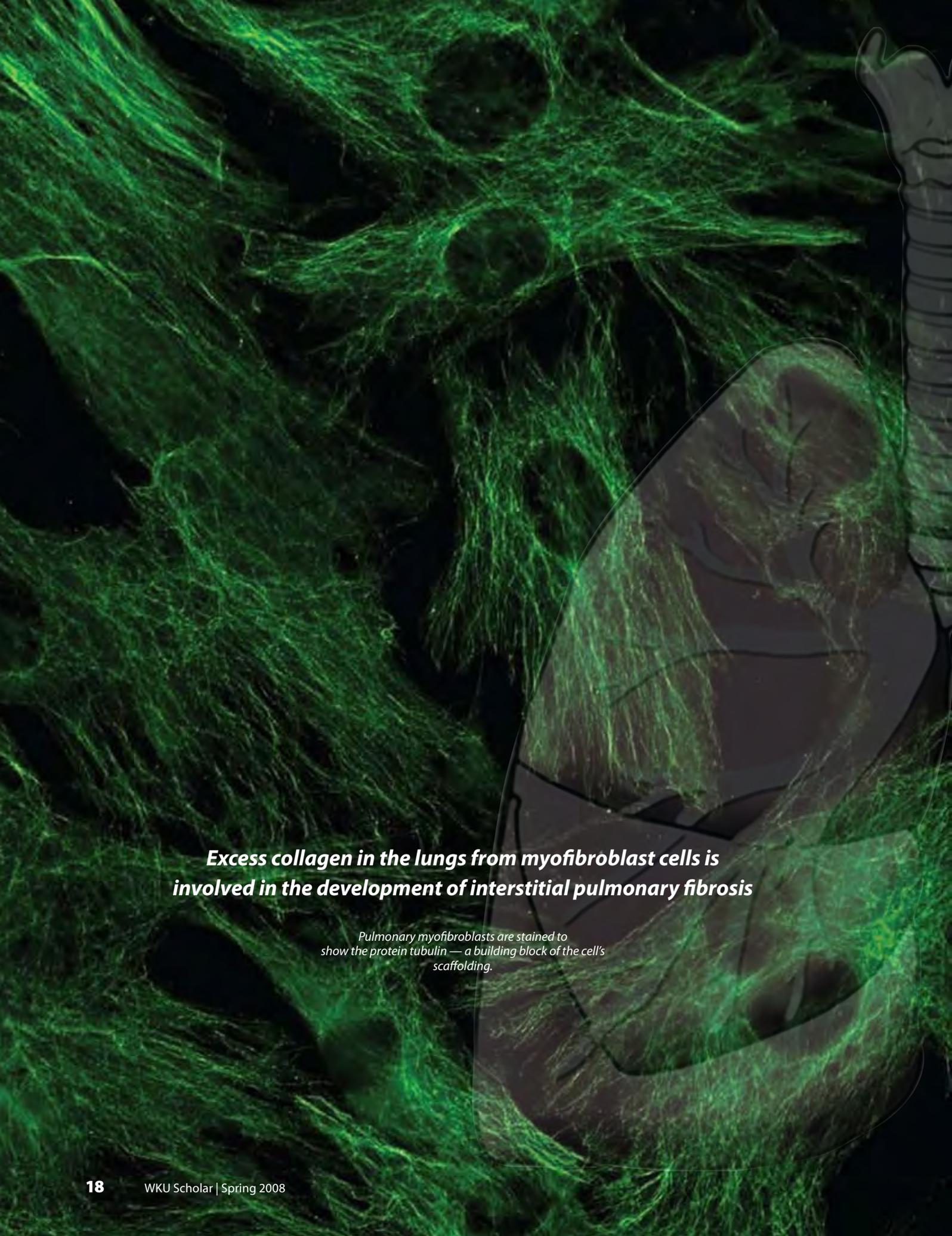
Dr. Nancy Rice, assistant professor of biology, and her students are using a three-year, \$204,000 grant from the National



Dr. Nancy Rice

Institutes of Health to study the role of nitric oxide in regulating the growth and proliferation of myofibroblast cells, that are involved in pulmonary fibrosis and other diseases.

“Myofibroblasts are kind of a Dr. Jekyll and Mr. Hyde type of cell,” explained Dr. Rice, who became intrigued by the cell during her post-doctoral work at the University of Colorado. “You need the cells for normal growth of organs and tissues and they’re also important

The image is a composite of two microscopic views of pulmonary myofibroblasts. The background is a large, dense field of green-stained tubulin filaments, appearing as a complex, interconnected network of fibers. Overlaid on the right side is a semi-transparent, dark grey silhouette of a human torso, showing the ribcage and spine. Within this silhouette, a smaller, more detailed view of a myofibroblast is shown, also stained with green tubulin, highlighting the internal cellular structure and the organization of the protein scaffolding.

Excess collagen in the lungs from myofibroblast cells is involved in the development of interstitial pulmonary fibrosis

Pulmonary myofibroblasts are stained to show the protein tubulin — a building block of the cell's scaffolding.

for wound healing.” When tissue is damaged, Rice said, these cells are recruited to help repair and remodel the tissue because they make and secrete collagen, which helps pull the wound together. On skin wounds, for example, you see the effect of myofibroblasts in scarring.

“Normally, after the wound is healed, the cells are triggered to die, but sometimes that doesn’t happen, which is the Mr. Hyde side,” said Dr. Rice, who graduated from WKU in 1993. “In that case, after the wound or injury is healed, the cells continue to make collagen so the tissue becomes stiff.” In the case of lung injuries, such as those caused by occupational and environmental exposure, the excess collagen in the lungs from myofibroblast cells is involved in the development of interstitial pulmonary fibrosis.

Dr. Rice also is interested in how the proliferation of these cells is implicated in lymphangioleiomyomatosis (LAM), a rare but devastating lung disease in young women characterized by the abnormal proliferation of “LAM cells” that share many common features with myofibroblasts. “We’re trying to build a basic understanding of the cells in order to apply our knowledge to two disease states — LAM and

“The nitric oxide pathway is an ideal place to begin because this signaling pathway is targeted by numerous pharmaceuticals that have already been evaluated and approved for use by the U.S. Food and Drug Administration. One of the most well-recognized of those is Viagra. The idea that a possible treatment is already FDA-approved is exciting because that eliminates years of clinical testing, saves millions of dollars and provides treatment for people faster.”

In the first year of the grant-funded project, Dr. Rice and her students worked on how much and when nitric oxide is made by myofibroblasts and how it induces cells to die. In the second and third years, they will move into animal modeling and testing.

“We believe this pathway is a good pathway to target,” she said. “I hope that after three years we can say conclusively whether it is or isn’t. But either way, I foresee this work as a continuing project in our lab because results and findings might take our work in different directions. These cells are intriguing and we’ve barely begun to understand them.”

“The nitric oxide pathway is an ideal place to begin because this signaling pathway is targeted by numerous pharmaceuticals that have already been evaluated and approved for use by the U.S. Food and Drug Administration. One of the most well-recognized of those is Viagra.”

pulmonary fibrosis,” she said. “We’re specifically interested in how nitric oxide mediates the growth and/or death of these cells.

Nitric oxide was first described as a signaling molecule in the early 1980s and understanding its physiological role led to the Nobel Prize in Physiology and Medicine in 1998. It has been implicated as a key mediator of myofibroblast activity in other tissues including the heart.

“Other people have shown that if the production of nitric oxide is blocked there is an accumulation of these cells, and that excess nitric oxide can cause cell death. We are hoping to build upon these studies within the context of lung and pulmonary disease.”

The nitric oxide pathway is leading Dr. Rice and her students on the road toward improved treatment options. About 100,000 people in the United States (most over fifty years of age) suffer from pulmonary fibrosis. “Since relatively few drugs are available for the treatment of pulmonary fibrosis, and their effectiveness is minimal at best, a thorough understanding of the mechanisms regulating myofibroblast activity and death is important in designing new, improved therapeutics,” she said.

Since returning to WKU in 2003, Dr. Rice has worked with about twenty undergraduate and graduate students on the myofibroblast study, as well as research on how the body stores and breaks down glycogen, and other projects. “The best way to understand science is to do science,” said Dr. Rice, who received her bachelor’s degree in recombinant genetics. “I was excited by the infrastructure WKU had in place to do research when I came back to interview for a job. I saw that I could have the best of both worlds here. I could have the interaction with undergraduates as well as do competitive, quality research.” ■

