New insights come from tracing cells that irreversibly scar lungs

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Idiopathic Pulmonary Fibrosis (IPF) is an incurable disease in which the delicate gas exchange region of the lung fills with scar tissue, which interferes with breathing. Now researchers at Duke University Medical Center have discovered that commonly held ideas about the origins of the scar-forming (fibrotic) cells were incorrect.

They found that small cells called pericytes move from blood vessels into fibrotic regions, and were in the lungs of both humans and mice.

They also found in mice that the epithelial cells, which make up the lacy sacs called alveoli, could divide and repair the damage in the gas-exchange location, but the cells were not the source of scarring accumulation.

Idiopathic pulmonary fibrosis affects about 100,000 people in the U.S. each year and leads to death within three years of diagnosis. The only treatment at this time is lung transplantation.

"We are the first to show that pericytes, a population of cells previously described to play a role in the development of fibrosis in other organs, are present in fibrotic lung tissue," said Christina Barkauskas, M.D., a pulmonary fellow in the Duke Division of Pulmonary, Allergery and Critical Care Medicine.

The study was published in this week's PNAS Plus issue online.

"We don't know yet whether the pericytes make the scar matrix itself or just release signals that stimulate the scarring process, so they are a potential target for new therapies," said Brigid Hogan, Ph.D., senior author and chair of the Duke Department of Cell Biology.

The researchers used genetic lineage tracing to study the origin of cells that gathered in fibrotic areas. They gave several different cell types an indelible fluorescent tag and then followed the cells over time.

The cells kept the tag even if they multiplied, migrated within the lung, or differentiated into another cell type.

Paul Noble, M.D., co-author and chief of the Pulmonary Division at Duke, said that identifying the source of the lethal expansion of the scarring (fibroblast) cells is a critical missing link in understanding disease progression.

Previous studies had suggested that the epithelial cells in the alveoli might have been a source of fibroblast accumulation after lung injury, he said.

"This study used the newest tracing approaches to conclusively demonstrate, however, that the alveolar epithelium isn't a significant source for fibroblast accumulation following lung injury in mice," Noble said. "The studies suggest that there may be several sources for the scar-forming cell accumulation in fibrosis, including pericytes, which hadn't been implicated in lung fibrosis until now."

Noble said that the study data provide new insights into the sources of scar-forming cells and would help to target the correct cell population that causes disease progression.

Now the researchers are focusing on what these cells may make that

could promote a healing process. "One idea is that perhaps in IPF these epithelial cells have lost the ability to repair damage to the lung, so that scarring continues inexorably and cannot be restrained – perhaps we could find a way to assist the repair process," Hogan said. "Promoting the healing process might be another therapeutic approach."

Provided by Duke University Medical Center