'Beneficial inflammation' may promote healing in pulmonary fibrosis

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Inflammation has long been considered an integral part of the biological process that leads to deadly scarring in idiopathic pulmonary fibrosis. New research at National Jewish Health, however, suggests that a little inflammation may also be crucial to the healing and repair processes in the lungs. Elizabeth Redente, PhD, assistant professor of cell biology at National Jewish Health, and her colleagues report in the April 2014 issue of the *American Journal of Respiratory Cell and Molecular Biology* that the pro-inflammatory cytokine TNF-α can speed recovery of injured lungs and accelerate the resolution of established fibrosis in a mouse model.

"The role of inflammation in the development of scarring has been hotly debated in recent years," said Dr. Redente. "Our findings show for the first time that TNF-α actually promotes inflammation during the resolution of established scarring. A little inflammation may actually be a good thing in the right place and time."

Idiopathic pulmonary fibrosis is a relentless, progressive scarring of the lungs for which there is no approved medical therapy. The disease has no known cause and patients generally die within three years of diagnosis. Approximately 40,000 Americans die of idiopathic pulmonary fibrosis every year.

Inflammation was long believed to be a precursor and cause of scarring in the lungs. However, anti-inflammatory treatments have shown no positive effect on the progress of the disease. In recent years, some

researchers have thought that inflammation may be part of the healing process as well as the scarring of the lungs.

Dr. Redente and her colleagues gave mice TNF-α after their lungs had been injured and developed scar tissue. While these mice do normally heal from the lung injury, the researchers found that the TNF-α accelerated the recovery process. It reduced levels of collagen, the main component of scar tissue, and improved the flexibility of lung tissue well before the natural healing process would have begun. The researchers also found that knockout mice lacking the gene for TNF-α failed to heal as wild type mice eventually do.

The researchers believe that TNF-α acts by inducing white blood cells known as macrophages to change from ones that promote fibrosis to ones that promote inflammation instead. TNF-α may also promote the death of some of the pro-fibrotic macrophages.

"Physicians would welcome any therapy that could just slow down or stop the scarring process in the lungs," said David Riches, PhD, professor and head of the program in cell biology at National Jewish Health, and senior author on the study. "Our findings suggest that TNF-α not only slows the fibrotic process, but actually reverses established scarring in the lungs."

The researchers are now investigating the role of TNF-α in various process that actually remove scar tissue including the removal of collagen-producing cells, the degradation and removal of collagen and restoration of healthy lung cells.

Provided by National Jewish Health

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