MedicalXpress

Researchers discover big role for microRNA in lethal lung fibrosis

April 29 2010

A small piece of RNA appears to play a big role in the development of idiopathic pulmonary fibrosis (IPF), according to lung disease researchers at the University of Pittsburgh School of Medicine. Their study, which is the first to examine microRNAs in the disease, is available online in the *American Journal of Respiratory and Critical Care Medicine*.

MicroRNAs are short strands of genetic material that are involved in regulating the expression, or activity, of genes, explained senior author Naftali Kaminski, M.D., associate professor of medicine, computational biology and pathology, and director of the Dorothy P. and Richard P. Simmons Center for Interstitial Lung Diseases at the University of Pittsburgh School of Medicine and University of Pittsburgh Medical Center. They are a new family of RNA molecules that are thought to be factors in embryonic development, multiple cancers and chronic heart failure.

"Our research now indicates that microRNA changes also contribute to IPF," Dr. Kaminski said. "We have identified an entirely new molecular mechanism for the disease, which gives us new ideas about how to treat it."

The researchers assessed microRNA profiles in samples of healthy lung tissue and samples of tissue affected by IPF, which is a chronic, progressive and usually lethal disease of lung scarring that affects more than 100,000 Americans and leads to 15,000 deaths annually.

"Ten percent of the microRNAs were different between IPF and control lungs," said Kusum Pandit, Ph.D., the study's lead author and a postdoctoral researcher in Dr. Kaminski's lab. "The changes were very impressive."

The researchers particularly noted a diminished amount of a microRNA called let-7d and examined it more closely. They found almost no expression of let-7d in the fibrotic, or scarred, areas of 40 IPF lung samples, whereas it was abundant in 20 healthy samples used for comparison. Further experimentation showed them that let-7d is inhibited by the cytokine TGF-beta, a signaling protein that promotes the development of fibrosis through several biological pathways.

In another experiment, the researchers made an antagonist that inhibits let-7d and administered it to several mice through their windpipes for a few days. When examined soon after, the lungs of the mice looked very much like what is seen in patients with early lung fibrosis.

"These results suggest that by increasing let-7d in the lung, we may be able to slow down or even prevent lung fibrosis," Dr. Kaminski said. "Our next challenge is to develop methods that will allow us to safely do that so we can test its therapeutic value."

Provided by University of Pittsburgh