

# Gene expression patterns predict rapid decline in idiopathic pulmonary fibrosis patients

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Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease typically characterized by the slow but progressive onset of shortness of breath or cough. Most patients live about five years after diagnosis. However, according to a new study being published today in the online journal PLoS ONE, a subset of patients with a specific genetic profile has a much more rapid progression to complete pulmonary failure and death without a lung transplant.

Based on observations in the clinic that some IPF patients display a more rapidly progressing disease course, researchers at the Simmons Center for Interstitial Lung Disease at the University of Pittsburgh School of Medicine, collaborating with pulmonary scientists in Mexico and California, used DNA microarray analysis to measure the gene expression patterns of 26 rapid progressors and 88 slow progressors. They identified 437 differentially expressed genes between the groups. Specifically, lungs of rapid progressors, who were predominantly males who smoked, overexpressed genes involved in the development of tissues and organs (morphogenesis), oxidative stress, cell migration and proliferation and genes from fibroblasts and smooth muscle cells.

According to Naftali Kaminski, M.D., director of the Simmons Center and director of the Lung Translational Genomics Center, division of pulmonary, allergy and critical care medicine, University of Pittsburgh School of Medicine, these findings offer strong evidence that rapid

progressors represent a distinct clinical phenotype compared with the usual slower progressing patients.

"We are only now starting to really understand IPF and to characterize it," Dr. Kaminski said. "Therefore, it is critical for patients with the disease to be seen in centers that are actively involved in IPF research, so we can help them better decide a course of action."

These findings also highlight the variability in the progression and outcome of IPF and may explain, in part, the difficulty in obtaining significant and reproducible results in studies of therapeutic interventions in patients with IPF, noted first author Moisés Selman, M.D., director of research at the National Institute of Respiratory Research in Mexico City. "This study suggests that physicians should pay more attention to the time of onset of symptoms in their patients," Dr. Selman said.

"Although preliminary, these results may allow investigators to identify biomarkers of disease progression and, more importantly, better evaluate the effectiveness of potential therapies," added Talmadge E. King Jr., M.D., chief of medicine at San Francisco General Hospital and an internationally renowned expert in research and management of pulmonary fibrosis.

Source: University of Pittsburgh Schools of the Health Sciences

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