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Test could predict which idiopathic pulmonary fibrosis patients will become severely ill

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A simple blood test could predict which patients with the lung-scarring disease known as idiopathic pulmonary fibrosis (IPF) are soon to get far worse, an indicator that could one day influence their treatment, according to researchers at the University of Pittsburgh School of Medicine. Their findings, published online last week in *PLoS One*, indicate that the body's immune cells attack healthy lung tissue, suggesting that IPF is in fact an immunologic disease.

In IPF, lung tissue gets progressively scarred, making it hard for patients to breathe, explained Steven R. Duncan, M.D., an associate professor in the Division of Pulmonary, Allergy and Critical Care Medicine at Pitt. The prognosis is grim; median survival is three years after diagnosis.

"If we knew who was in the gravest danger from this illness, we could direct them to lung transplantation or experimental therapy immediately," he said. "Also, we could possibly avoid prescribing grueling treatments for people whose disease is fairly stable."

Dr. Duncan and his colleagues may have found a way to test for that information. For their study, they collected blood samples from 89 IPF patients at various stages of disease severity, as well as 32 healthy individuals for comparison, and examined certain immune cells called CD4 T-cells. The cells, which typically respond to infectious threats, normally carry a surface protein called CD28.

The CD4 T-cells still bore their CD28 markers among patients whose disease was relatively stable. But, as a patient's disease got worse, the CD4 T-cells lost their CD28 protein markers and the cells were unusually "revved up," as Dr. Duncan put it. The greater the proportion of these distinctly abnormal cells in the blood, the greater the likelihood that the patient would quickly become gravely ill. In the study group, these patients were the ones who were most likely to require a lung transplant or to die within 12 months.

"We suspect that as these CD4 cells repeatedly multiply, subsequent generations become abnormal," Dr. Duncan said. "The altered cells send out signals that promote inflammatory processes, which perhaps could lead to the fibrosis of the lung tissue that characterizes IPF."

"What is remarkable about this result is that it suggests that we may be able to develop a screening test for patients with idiopathic pulmonary fibrosis, much like cholesterol levels in the case of atherosclerosis, that identifies the patients at greatest need for referral for life-saving lung transplantation," said Mark T. Gladwin, M.D., chief of the Division of Pulmonary, Allergy and Critical Care Medicine, Pitt School of Medicine. "In addition, it provides new insights into how the immune system is dysfunctional in this disease."

The findings also hint that a low-level, chronic infection or a chronic immune response to a normal protein (an auto-antigen) might be a triggering event for the abnormal immune response, and Dr. Duncan now is looking for genetic missteps that might lead to this quirky, autoimmune-like reaction.

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