

“Genetic susceptibility to IPF”

In the past three years, tremendous advances have been made in identifying genetic variants associated with pulmonary fibrosis. At ERS 2014, Dr. David Schwartz (University of Colorado Denver) presented several studies he and colleagues have authored, which suggest that pulmonary fibrosis, including IPF, has a significant genetic component.

MUC5B variant confers susceptibility to IPF

In 2011, Dr. Schwartz and colleagues identified a variant in a gel-forming mucin gene, *MUC5B*, which is strongly associated with IPF. The variant was found in more than half of subjects with a familial pulmonary fibrosis (at least 2 cases of pulmonary fibrosis in individuals who are 3rd degree relatives or closer), and in more than half the subjects with sporadic IPF (those with no family history of the disease). This variant alone is not sufficient for the development of IPF, as *MUC5B* variant is found in 20% of the general population. As Dr. Schwartz suggested that IPF, at least in some cases, may be a “two hit” disease: a genetic predisposition (e.g., *MUC5B* variant) combined with repetitive lung injury from environmental stressors (e.g. second hand smoking).

MUC5B variant is associated with improved survival in IPF patients

A 2013 study by Dr. Schwartz and colleagues showed that IPF patients with the *MUC5B* variant had significantly improved survival when compared to IPF patients who did not have the *MUC5B* variant. This result suggests that IPF may be considered a collection of fibrotic diseases with different underlying causes, including some with known genetic susceptibilities. Within this spectrum of IPF variants, *MUC5B*-associated IPF is less severe than some others.

Optimizing treatment and improving diagnosis

Dr. Schwartz’s group recently used a different approach to identify ten genetic variants associated with IPF, including three previously identified IPF susceptibility genes: *MUC5B*, *TERT* and *TERC*. As each genetic variant may promote fibrosis by a slightly different mechanism, future research may identify certain treatments that are most beneficial to patients with certain genetic variants.

Dr. Gerard Cox, the Director of Respiriology at St. Joseph’s Healthcare in Hamilton, took note of this important new information regarding genetics of IPF which suggests relatives of IPF patients may be at a heightened risk of developing the disease. “It certainly makes me more interested in patients’ relatives,” Dr. Cox observes. “Looking for early symptoms in first-degree relatives of patients may be a way of finding people with early disease.”