Genetic variation among patients with pulmonary fibrosis associated with improved survival

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Variation in the gene MUC5B among patients with idiopathic pulmonary fibrosis was associated with improved survival, according to a study published online by *JAMA*. The study is being released early online to coincide with its presentation at the American Thoracic Society international conference.

"Idiopathic pulmonary fibrosis (IPF) is a chronic progressive disease with a median [midpoint] survival of 3 years," according to background information in the article. The prognosis is variable; patients may remain stable for several years, slowly lose lung function, progress in an intermittent fashion, or experience precipitous acute exacerbations. "Current prediction models of mortality in IPF, which are based on clinical and physiological parameters, have modest value in predicting which patients will progress. In addition to the potential for improving prognostic models, identifying genetic and molecular features that are associated with IPF mortality may provide insight into the underlying mechanisms of disease and inform clinical trials."

Anna L. Peljto, Dr.P.H., of the University of Colorado Denver, and colleagues conducted a study to determine whether the variation (rs35705950) of the gene MUC5B, previously reported to be associated with the development of pulmonary fibrosis, is associated with survival among patients with IPF. The study included two independent cohorts of patients with IPF: the INSPIRE cohort, consisting of patients enrolled in

the interferon-γ1b trial (n=438; December 2003 - May 2009; 81 centers in 7 European countries, the United States, and Canada), and the Chicago cohort, consisting of IPF participants recruited from the Interstitial Lung Disease Clinic at the University of Chicago (n = 148; 2007-2010). The INSPIRE cohort was used to model the association of MUC5B genotype with survival. The Chicago cohort was used for replication of findings.

The median follow-up period was 1.6 years for INSPIRE and 2.1 years for Chicago. During follow-up, there were 73 deaths among the INSPIRE cohort patients and 64 deaths among the Chicago cohort patients. Analysis indicated that the unadjusted 2-year cumulative incidence of death was lower among patients carrying 1 or more copies of the IPF risk allele (an alternative form of a gene) (T) in both the INSPIRE cohort and the Chicago cohort.

According to the authors, "The addition of the MUC5B genotype to the survival models significantly improved the predictive accuracy of the model in both the INSPIRE cohort and the Chicago cohort."

"These findings suggest that the common polymorphism in the promoter of MUC5B (rs35705950), previously reported to be strongly associated with the development of familial interstitial pneumonia and idiopathic pulmonary fibrosis, is significantly associated with improved survival in IPF. These findings are consistent with a previous report of an association between the MUC5B variant and less severe pathological changes in familial interstitial pneumonia, as well as another report of slower decline in forced vital capacity for patients with IPF. This study is, to our knowledge, the first to demonstrate that a genetic variant is associated with survival in IPF."

"Further research is necessary to refine the risk estimates and to determine the clinical implications of these findings," the researchers

conclude.

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