Genetic risk factors for occupational fibrotic diseases

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There is a wide range of inter-individual variation in susceptibility to occupational/ environmental diseases. Although the underlying mechanisms remain largely unknown, genetic factors are important in determining disease susceptibility. Recent evidence suggests that common genetic variations in immune/inflammatory genes contribute to the pathogenesis of various lung diseases including pneumoconiosis. In light of this, functional variants in inflammatory/fibrogenic genes have been examined for evidence of association with silicosis and progressive massive fibrosis (PMF) in a large group of ex-coal miners. The study population consisted of underground coal miners participating in the National Coal Workers Autopsy Study (NCWAS). Single nucleotide polymorphisms (SNPs), which influence the regulation of interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha (TNFα), transforming growth factor beta-1 (TGFβ1), vascular endothelial growth factor (VEGF), intercellular cell adhesion molecule-1 (ICAM-1) and matrix metalloproteinase-2 (MMP-2) genes, were determined using 5'-nuclease real-time PCR and PCR-restriction fragment length polymorphism techniques from autopsy lung tissue DNA. The TNFα-308, -238 and interleukin-1 receptor antagonist (IL-1RA) +2018 variants were found to be associated with the development and severity of silicosis. Although there were no significant differences in the distribution of any individual SNP or haplotype between the PMF and control groups, the polygenotype of VEGF +405/ICAM +241/-IL6 -174 (C-A-G) conferred an increased risk for PMF. These findings suggest that genetic variations may influence individual susceptibility to dust-induced respiratory diseases. Such information can be used to help identify the most susceptible populations and apply relevant information to the risk assessment process, thereby helping to determining safe exposure levels for the most susceptible groups of workers.