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Single Nucleotide Polymorphisms (SNPs) Associated with Decline in Lung Function in Firefighters

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Firefighters are routinely exposed to respiratory toxicants, including smoke. While assiduous use of respiratory protection has resulted in improvements in pulmonary function compared with historical findings, there are still many firefighters who experience an accelerated rate of decline in lung function, defined as a decline in forced expiratory volume in one second (FEV1) exceeding 60 ml/yr, averaged over a minimum of 5 years. Understanding factors associated with increased loss of lung function should help determine the best means of prevention. Our study objectives were to assess the evidence for genetic involvement in the rate of lung function decline in a population of firefighters.

Pulmonary function data from 1988 to 2003 were retrieved from the Phoenix Fire Department's medical monitoring database. Information on date of birth, gender, race/ethnicity, history of smoking, and history of asthma was also collected. Rate of decline in FEV1 was calculated for each firefighter who had a minimum of 3 measures over 5 years of pulmonary function testing, by regressing the annual FEV1 values over age at testing. Blood or buccal cell samples were obtained from 451 firefighters. The samples were genotyped for 7 SNPs from genes thought to be involved in chronic obstructive pulmonary disease (COPD) or asthma, based on prior studies. Using the slope of FEV1 as the dependent variable, oneway analysis of variance was conducted to determine whether the mean slope differed by genotype. Stratified analyses were then used to evaluate whether differences in mean slope by genotype were consistent among ethnic/racial groups and between ever- and never-smokers. Lastly, multiple linear regression models were run to evaluate the relationship between slope and each SNP separately after adjusting for other variables related to decline in lung function and potential confounders. These included baseline FEV1, smoking, race/ethnicity, gender, age at last pulmonary function test, and number of years of follow-up.

The mean initial age of firefighters was 32 years. Sixty-six (17.6%) had an annual rate of decline in FEV1 of >60 ml/yr. All of the SNPs were in Hardy-Weinberg equilibrium. Two SNPs in the coding region for

Abstracts

Interleukin-1 β and IL-1 receptor antagonist (IL-1 β 3953 T/C, $p=0.015$; IL-1 RA 2018 C/T, $p=0.040$) and two SNPs in the promoter region of the gene for Tumor Necrosis Factor- α (TNF- α -238 A/G, $p=0.048$; TNF- α -308 G/A, $p=0.009$) were significantly associated with an increased rate of decline in FEV1 in multivariate analyses. Transforming Growth Factor- β (-509), IL-8 (-251), and IL-13 (1055) SNPs were also analyzed, but no association with decline in FEV1 was found. These results suggest that IL-1 β 3953, TNF- α -238 and -308, and IL-1RA 2018 variants may influence individual susceptibility for accelerated decline in lung function in firefighters.

Determining risk factors associated with decline in lung function is critical to the prevention of respiratory impairment including COPD. Firefighters are an ideal population to study because of routine annual surveillance of pulmonary function. Future studies in firefighters have been proposed to evaluate the interaction between exposure to products of combustion and genetic polymorphisms in relation to decline in lung function.

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