accurate diagnostic pathways in interstitial lung disease, as well as early referral for lung transplantation.

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Lung alert

Identification of novel targets for COPD research using genome-wide association techniques

Two recently published genome-wide association studies have highlighted the importance of large DNA databases in the identification of possible future targets for chronic obstructive pulmonary disease (COPD) therapy. The first study included over 7500 participants from the Framingham Heart Study. Four single nucleotide polymorphisms (SNPs) on chromosome 4 were found to be associated with a reduced FEV_1/FVC ratio. The associated SNPs corresponded to a non-gene transcript area near the hedgehog-interacting protein (HHIP) gene. HHIP is a regulatory component in some cell signalling pathways involved in fetal development. The group were unable to explain the regulatory effect of the association but felt that the region warrants further investigation. In the second study 1600 patients with COPD and smoking controls from Norway were compared. Two SNPs at the α-nicotinic acetylcholine receptor locus were found to be associated with lung function, and the association was confirmed by analysis in two other patient groups in the USA. The association with the HHIP area on chromosome 4 was replicated but did not reach genome-wide significance levels in this study.

Although COPD is thought to have a genetic predisposition, apart from α_1-antitrypsin there is little information about the specific genes which underlie the disease. Genome-wide association studies can be problematic due to the potential for false positive results as a consequence of the number and power of the statistical tests performed. This is exemplified by the fact that, although HHIP has a role in the development of cartilage, nerves and has altered expression in various cancers, it has not yet been demonstrated to have a role in any pulmonary disorders. These studies can therefore be seen as ''hypothesis generating''. The problem is in translating statistically significant associations in genome studies into credible models of pathogenesis which allow development of clinically meaningful disease-specific therapies. The identification of an association of obstructive lung disease with a gene involved in fetal development in two independent studies is of interest and provides a target for future analysis.

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