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Journal club

Genetic variants and risk of lung cancer in never smokers

This four-stage study systematically investigated common genetic variations associated with the risk of developing lung cancer in never smokers. Stage 1 involved a genome-wide association study at the Mayo Clinic. A total of 331 918 single nucleotide polymorphisms (SNPs) in 377 case–control matched pairs were analysed. The 44 most significant SNPs that might alter the risk of lung cancer in never smokers were selected. The MD Anderson Cancer Center and Harvard School of Public Health (n=735 and 335, respectively) tested these 44 most significant SNPs. The SNP rs2352028 (at 13q31.3) was the one most associated with lung cancer in never smokers. This finding was repeated in a replication cohort.

For all four studies the combined p value for the association between rs2352028 and lung cancer in never smokers was 5.94×10^{-6} (OR 1.46, 95% CI 1.26 to 1.70). 10% of lung cancer cases in never smokers could be attributed to genetic variation of SNP rs2352028. A gene expression profile analysis confirmed that the expression of the gene GPC5 was associated with genotypes of SNPs, with lower expression in high-risk alleles.

This study suggests that genetic variants affecting the expression of the GPC5 gene are responsible for increasing the risk of lung cancer in never smokers. However, it was concluded that the sample sizes used did not allow for enough power, and there was inconsistent adjustment for confounders such as second-hand smoke exposure across the different centres. GPC5 gene alterations have previously been shown to influence lung cancer development and merit further study.

► **Li Y**, Sheu CC, Ye Y, *et al*. Genetic variants and risk of lung cancer in never smokers: a genome-wide association study. *Lancet Oncol* 2010;**11**:321–30.

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