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Lung alert

Changes in the DENND1B gene increase the risk of childhood asthma

Previous studies have shown associations between asthma and single nucleotide polymorphisms (SNPs) on the 17q12 chromosome, but the risk associated with these SNPs is low.

This study used children of European ancestry as a 'discovery set'. Genome-wide association identified several SNPs in the 1q31.3 region associated with childhood onset asthma (typical OR 0.63; 95% CI 0.54 to 0.73). The earlier the onset of asthma, the higher the prevalence of risk alleles. These findings were replicated in a different group of European origin. The same locus was associated with asthma in an African-American cohort, but in these children the alleles associated with asthma were the opposite alleles to those in the European subjects. This may be related to modifying effects of other genes, or differences in linkage disequilibrium.

The SNPs with the strongest effect were within the intron of the DENND1B gene. This gene is expressed in dendritic cells and activated T cells and modulates the type 1/type 2 helper T cell response.

It seems likely that changes in the DENND1B gene alter the risk of childhood asthma. However, the risk attributable to this gene is low—the protective allele frequency of the strongest associated SNP was 15.2% in patients with asthma and 22.2% in controls. Single genes may confer an increased risk of certain asthma phenotypes, but their effect is modified by multiple other genetic and environmental factors.

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