A genome-wide association study identifies CDHR3 as a susceptibility locus for early childhood asthma with severe exacerbations.

Asthma exacerbations are among the most frequent causes of hospitalization during childhood, but the underlying mechanisms are poorly understood. We performed a genome-wide association study of a specific asthma phenotype characterized by recurrent, severe exacerbations occurring between 2 and 6 years of age in a total of 1,173 cases and 2,522 controls. Cases were identified from national health registries of hospitalization, and DNA was obtained from the Danish Neonatal Screening Biobank. We identified five loci with genome-wide significant association. Four of these, GSDMB, IL33, RAD50 and IL1RL1, were previously reported as asthma susceptibility loci, but the effect sizes for these loci in our cohort were considerably larger than in the previous genome-wide association studies of asthma. We also obtained strong evidence for a new susceptibility gene, CDHR3 (encoding cadherin-related family member 3), which is highly expressed in airway epithelium. These results demonstrate the strength of applying specific phenotyping in the search for asthma susceptibility genes.