

Large genome-wide association study is first to focus on both child and adult asthma

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Obstruction of the lumen of a bronchiole by mucoid exudate, goblet cell metaplasia, and epithelial basement membrane thickening in a person with asthma. Credit: Yale Rosen/Wikipedia/CC BY-SA 2.0

Asthma, a common respiratory disease that causes wheezing, coughing and shortness of breath, is the most prevalent chronic respiratory disease worldwide. A new study, published April 30, 2019 in *Lancet Respiratory Medicine*, is the first large investigation to examine the differences in



genetic risk factors for childhood-onset and adult-onset asthma.

This <u>genome-wide association study</u> (GWAS) found that childhoodonset asthma was associated with nearly three times as many genes as adult-onset asthma. Genes associated with adult onset asthma were a subset of those associated with childhood-onset asthma, nearly all with smaller effects on adult-onset asthma than on childhood-onset asthma.

The researchers also found that these childhood-onset genes were highly expressed in <u>epithelial cells</u> (skin). Both childhood-onset and adult-onset asthma genes were highly expressed in blood (immune) cells.

"This was the largest asthma-related GWAS yet attempted," said study co-author Carole Ober, Ph.D., professor and chair of the Department of Human Genetics at the University of Chicago, and her collaborator Hae Kyung Im, Ph.D., assistant professor in the Department of Medicine. "We found that the genes involved in adult-onset asthma are largely a subset of genes associated with childhood asthma. At later ages, however, the same genes tend to have smaller effects."

The authors concluded that different mechanisms cause the inception of asthma with onset in childhood compared to asthma with onset in adulthood. While both share an immunologic component, the origins of asthma in childhood involves defects in epithelial cell integrity similar to the defects that underlie other common childhood diseases, such as eczema and food allergies.

The researchers defined childhood-onset asthma as younger than 12 years of age. They defined adult-onset cases as those who developed the disease between the ages of 26 and 65.

The study used data from the UK Biobank, a large long-term study based in the United Kingdom that concentrates on the contributions of genetic



predisposition and environmental exposure to the development of disease.

The researchers focused on data from 37,846 British individuals who reported an asthma diagnosis, including 9,433 adults who developed asthma as children, 21,564 adults with adult-onset asthma, and an additional 6,849 young adults who developed asthma between the ages from 12 to 25. They also developed a control group of 318,237 people 38 years old or older who did not have asthma.

The GWAS of childhood and adult asthma revealed 61 independent asthma-related genes. Fifty-six of the 61 were significant in childhoodonset asthma and 19 were significant in adult-onset disease. Twentyeight of those loci had not been previously catalogued; 17 were significant for childhood onset only but only one was significant only for adult-onset asthma.

The authors add that both the "childhood-specific and shared loci were associated with development of asthma at younger ages and those alleles all had larger effects in childhood-onset compared to adult-onset <u>asthma</u> ."

More information: "Shared and distinct genetic risk factors for childhood-onset and adult-onset asthma: genome-wide and transcriptome-wide studies," *Lancet Respiratory Medicine* (2019). DOI: 10.1016/S2213-2600(19)30055-4

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