MedicalXpress

Study connects gene variant to response to asthma drugs

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A genetic variant may explain why some people with asthma do not respond well to inhaled corticosteroids, the most widely prescribed medicine for long-term asthma control. Researchers found that asthma patients who have two copies of a specific gene variant responded only one-third as well to steroid inhalers as those with two copies of the regular gene.

This genome-wide association study, funded by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health, analyzed data from over 1,000 people enrolled in five separate clinical trials that studied different steroid treatments for asthma.

The study was also funded by the National Human Genome Research Institute and the NIH Pharmacogenomics Research Network. The results will appear in the Sept. 26 online edition of the New England Journal of Medicine.

"This finding helps to explain the genetic basis for the long-standing observation that some people do not respond well to what is a common asthma treatment," said Susan Shurin, M.D., acting director of the NHLBI. "The study illustrates the importance of research examining the relationship between genetic makeup and response to therapy for asthma, and underscores the need for personalized treatment for those who have it."

Asthma is a complex inflammatory disease that affects over 22 million

people in the United States and roughly 300 million people worldwide. Many factors can influence how severely the disease affects people and how well they respond to treatments. Poor response to inhaled corticosteroids (ICS) often runs in families, suggesting that genetics plays a role in how people respond to asthma treatments.

The study first conducted a genome-wide scan of the DNA of children enrolled in the Childhood Asthma Management Program and of their parents. The genomic scan uncovered a variant in a gene called GLCCI1 that appeared to be associated with poor ICS response. Study researchers then verified this association in 935 additional people with asthma, both children and adults, enrolled in four independent ICS studies. Most of the participants in these studies were white; the results may not be applicable to persons of other ethnicities.

In this study, people carrying two copies of the GLCCI1 variant were more than twice as likely to respond poorly to ICS treatment as participants with two copies of the regular GLCCI1 gene. Those who responded poorly had an average of one-third the level of lung improvement following inhaler treatment as did people with two regular copies of the gene.

About 1 in 6 study participants had two copies of the GLCCI1 variant, which is thought to work in conjunction with other genetic and environmental factors to affect response to ICS.

More studies will be needed to understand how GLCCI1 operates in the lungs and to explore whether it contributes to response in patients of other ethnic groups.

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