

# Researchers identify genes associated with increased gout risk

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A team of researchers from the United States and the Netherlands has identified mutations in three genes that are associated with high levels of uric acid in the blood, which is a risk factor for gout. The team developed a genetic risk score composed of the number of uric acid-increasing mutations that each person carries (0 to 6), which was associated with up to a 40-fold increased risk for developing gout when comparing persons at lowest and highest risk. The findings are published in the October 4 issue of *The Lancet*.

More than 3 million adults in the United States have gout. Gout is a painful inflammation of the joints, which can occur with a build-up of uric acid in the blood (hyperuricaemia). Besides a genetic disposition, obesity, a diet high in meat and cheese, as well as alcohol consumption and certain medications can increase the risk for developing the disease.

The researchers conducted genome-wide association studies of more than 20,000 people enrolled in three large population-based studies investigating cardiovascular disease risk factors: the Framingham Heart Study based at Boston University Medical Center; the Rotterdam Study based at Erasmus Medical Centre in Rotterdam, the Netherlands; and the Atherosclerosis Risk in Communities (ARIC) study based at Johns Hopkins University. Of more than 500,000 genetic variations that were evaluated, the analysis identified two genes, ABCG2 and SLC17A3, as novel risk genes for gout and confirmed the association of a third gene, SLC2A9.

"This research gives us a better understanding of the underlying causes of gout, which could lead to better prevention and treatment. Our evidence supports that a common pathway, the handling of uric acid by the kidney, is important in uric acid build-up and therefore for the development of gout," said study author, Anna Köttgen, MD, MPH, an assistant scientist in the Johns Hopkins Bloomberg School of Public Health's Department of Epidemiology.

"Genetic risk scores like the one we developed for gout can help alert people at a very early age, well before uric acid levels rise, that they are susceptible to gout. The new insights are promising for drug development," said Josef Coresh, MD, PhD, MHS, professor in the Bloomberg School's departments of Epidemiology and Biostatistics. "An important unanswered question is whether we can use genetic risk information to motivate people to change their behavior. For gout, we know that moderate changes in diet and alcohol consumption can lower uric acid levels. In the future, we will need to test if identification of high-risk individuals can lead to behavior change."

Source: Johns Hopkins University Bloomberg School of Public Health

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