Gene variant linked to prognosis in inflammatory diseases

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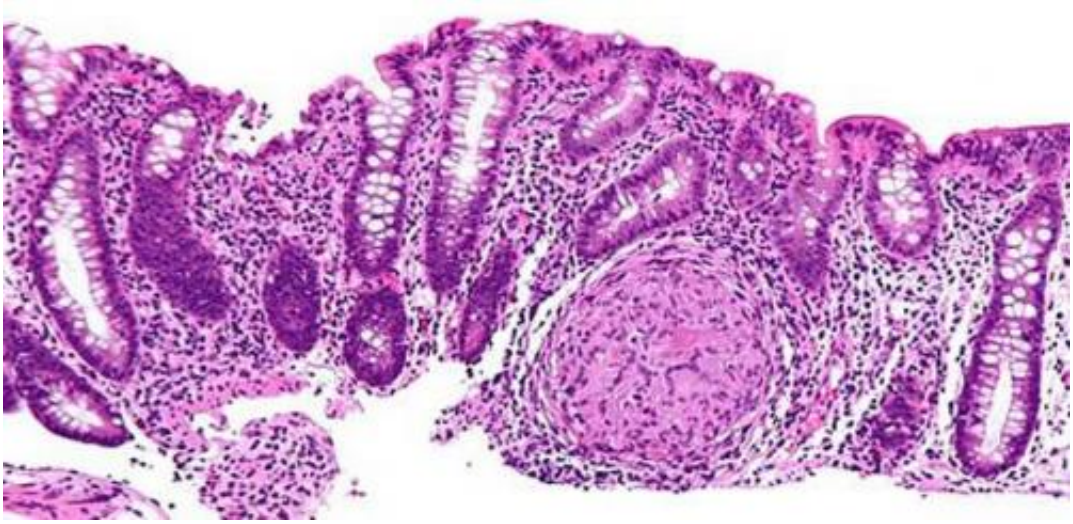

Credit: Nephron

(Medical Xpress)—Researchers have identified a gene that is linked to long term disease outcome in Crohn's disease, a common inflammatory bowel disorder, and rheumatoid arthritis. The findings reveal targets that could be exploited for new treatments.

The gene, which is involved in inflammation, is not associated with the overall risk of developing disease but patients with one particular variant experienced better clinical outcomes.

Genetic studies have contributed huge advances to our understanding of

susceptibility to complex diseases and the biological processes that drive the development of disease. However, understanding the factors that shape the course a disease takes once it has developed is equally important for ensuring patients have access to appropriate treatments.

The international team, led by researchers at the Cambridge Institute for Medical Research at the University of Cambridge, looked at existing data from genome-wide association studies in Crohn's disease to focus on prognosis rather than diagnosis. They identified a variant in the FOXO3A gene that is associated with the outcome of Crohn's disease, but which was not associated with its diagnosis.

By studying the effects of this particular gene variant on cells cultured in the lab, they found that it blocks the production of inflammatory chemicals, known as cytokines, that are known to be responsible for aggravating disease symptoms in Crohn's disease and other inflammatory diseases.

When the team looked at patients with another inflammatory disease, rheumatoid arthritis, they found that the same gene variant was linked with less joint damage over time, but not with susceptibility to developing the disease in the first place.

The study also looked at patients with malaria in Kenya and Vietnam, a disease where inflammatory cytokines have a positive rather than negative impact on disease outcome and are an important part of the immune response to the initial infection. The findings reveal that the same gene variant is linked with a greater susceptibility to severe malaria.

Professor Ken Smith from the Cambridge Institute for Medical Research and lead author of the study said: "Our findings have important implications for how we think about the biology of complex disease, and

in particular show that genetic variants might control pathways that drive the clinical outcome of disease without being associated with its diagnosis. These pathways, which may influence multiple diseases, may provide new targets for therapy to alter disease course."

The study is published online in the journal *Cell*.

Provided by University of Cambridge