

Genetic study sheds new light on auto-immune arthritis

Researchers are one step closer to understanding how an individual's genetic make-up predisposes them to Ankylosing Spondylitis (AS), a common auto-immune arthritis which causes pain and stiffness of the spine, and serious cases, progressive fusion of the vertebrae and other affected joints. The study is published recently in *Nature Genetics*.



The team of researchers from the Universities of Bristol, Queensland (Australia), Oxford, Texas and Toronto, used a technique called genome-wide association where millions of genetic markers are measured in thousands of people that have the disease and thousands of healthy individuals. Markers which are more frequent in individuals with the disease are more likely to be involved in the condition.

Using this approach the investigators found an additional seven genes likely to be involved in the condition, bringing the total number of genes known to predispose to AS to 13. Many of the new genes are already known to be involved in inflammatory and immune processes, providing researchers with further clues about how the disease arises. Two of the new genes are also known to predispose to other auto-immune conditions including Crohn's disease (a form of inflammatory bowel disease) and Celiac disease (an auto-immune intestinal disease).

Demonstrating an interaction between HLA-B27 and ERAP1

Researchers were also able to demonstrate an interaction between a genetic mutation called HLA-B27 and a mutation in a gene called ERAP1. Specifically, the ERAP1 mutation only predisposed to disease in those individuals who tested positive for the HLA-B27 mutation.

Dr David Evans from the University of Bristol said: "This finding is important in a number of ways. First of all it's one of the first convincing examples we have of one mutation influencing the effect of another mutation in the development of a relatively common disease. This is exciting because it implies that there may be other examples of this phenomenon in other common diseases that we don't know about yet.

"Second, the interaction itself tells us something very fundamental about how AS is caused. Prior to this study there were a number of competing theories about how the disease was caused. Our study suggests very strongly which one of these competing hypotheses is likely to be correct."

Finally, the researchers also identified a single genetic marker which could be used to assist in diagnosis of Ankylosing Spondylitis.

"AS is notoriously difficult to diagnose in its early stages which can lead to costly delays in its treatment," said Dr Evans. "Typically diagnosis consists of a combination of X-rays, patient symptoms and expensive immunological assays in the laboratory. This genetic marker could easily take the place of an expensive immunological assay. What would normally cost £40-£50 could be done easily for a fraction of the price."

Paper

'Interaction between ERAP1 and HLA-B27 in ankylosing spondylitis implicates peptide handling as the mechanism for HLA-B27 in disease susceptibility' by Evans et al in [<http://www.nature.com/ng/index.html>] *Nature Genetics*

About AS

Unlike most forms of arthritis, AS usually begins in young adulthood, and can therefore significantly impair a sufferer's ability to work, and usually involves life-long treatment. There is currently no cure for the condition although a recent group of drugs called TNF blockers show considerable promise in helping alleviate some of the symptoms.

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