SPONDYLOARTHROPATHIES

Novel genetic variants link ankylosing spondylitis and Crohn disease: evidence of a shared pathogenesis?

Results from a genome-wide association study published in *PLoS Genetics* demonstrate that several susceptibility genes for Crohn disease are also associated with ankylosing spondylitis (AS). “These associations were present even amongst ankylosing spondylitis cases lacking clinically evident Crohn disease,” points out Matthew Brown of the University of Queensland, Australia, and the corresponding author of the study.

AS and inflammatory bowel disease (IBD; Crohn disease and ulcerative colitis) often occur in the same families and individuals. Approximately 10% of patients with AS present with overt IBD, and 70% have subclinical inflammation in the terminal ileum.

As many more genetic associations have been found for Crohn disease than AS, the researchers genotyped 2,773 unrelated individuals of European ancestry with AS for 53 markers within

30 genetic loci previously linked to Crohn disease. The results were compared with archived genotype data for 2,215 population-matched controls. The known association of *IL23R* with AS was confirmed, and several new loci also correlated strongly with this disease. The most robust association involved a marker close to *KIF21B* on chromosome 1q32. Polymorphisms within and near *STAT3*, *IL12B*, *CDKAL1* and *LRRK2* or *MUC19*, as well as an intergenic region on chromosome 13q14, were also associated with AS. Exclusion of patients with overt IBD from the analysis did not weaken these associations.

Interestingly, the proteins encoded by *STAT3*, *IL12B* and *IL23R* are required for production of interleukin (IL)-17 by type 17 T helper cells, which highlights the involvement of these lymphocytes in the pathogenesis of both AS and Crohn disease.

“Given these findings, and the fact that blockade of IL-12 and IL-23 signaling with ustekinumab is effective in the treatment of Crohn disease, we have been encouraging companies with agents targeting this pathway to study the effect of those agents in ankylosing spondylitis,” says Brown. “Our findings indicate that shared genetic susceptibility is a common feature of epidemiologically related diseases,” he continues, “and support the use of strategies searching for pleiotropic genetic effects, such as the Immunochip program.”

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Original article Danoy, P. *et al.* Association of variants at 1q32 and *STAT3* with ankylosing spondylitis suggests genetic overlap with Crohn's disease. *PLoS Genet.* **6**, e1001195 (2010)

Further reading Elewaut, D. Linking Crohn's disease and ankylosing spondylitis: it's all about genes! *PLoS Genet.* **6**, e1001223 (2010)