SPONDYLOARTHROPATHIES

KIR status linked to susceptibility to ankylosing spondylitis

KIR3DL1 and *KIR3DS1*, which are thought to be two alleles of a gene in the killer cell immunoglobulin-like receptor (KIR) family, are implicated in the development of ankylosing spondylitis (AS), report Zvyagin and colleagues in their study published in *Cellular & Molecular Immunology*. "The observation that the inhibitory allele *KIR3DL1* and the activating allele *KIR3DS1* both contribute to the genetic risk of developing ankylosing spondylitis is the most significant finding of our work," says Dmitriy Chudakov, the study's corresponding author.

The KIR3DL1 and KIR3DS1 receptors are expressed on the surface of natural killer cells and a subpopulation of T lymphocytes, where they interact with HLA-B27, an MHC class I antigen strongly associated with AS and related diseases. The *HLA-B27* gene is found in >90% of patients with AS compared to 5–15% of individuals in the general population, but its presence accounts for only 16% of an individual's risk of developing the disease.

As *KIR3DS1* occurs more frequently and *KIR3DL1* less frequently in patients with AS than in healthy controls, the investigators expected that only the activating allele would influence disease risk. To test this hypothesis, they genotyped white Russian patients for functional (*KIR3DL1*F*) and nonfunctional (*KIR3DL1*004*) alleles of the inhibitory receptor, as well as *KIR3DS1*. The study included 83 *HLA-B27*-positive patients with AS and 107 *HLA-B27*-positive healthy controls.

> "...the presence of *KIR3DS1* has a stronger effect on disease risk than the absence of *KIR3DL1*F*"

Patients with AS had an increased frequency of the *KIR3DS1* allele, independent of the presence or absence of *KIR3DL1*F*. Thus, the presence of the activating allele seems to be crucial for disease initiation. By contrast, the homozygous *KIR3DL1*F* genotype had a low frequency in patients with AS and a high frequency in healthy controls, despite a similar frequency of *KIR3DL1*004* in both groups. These findings indicate that the inhibitory allele actively protects against disease development, although the presence of *KIR3DS1* has a stronger effect on disease risk than the absence of *KIR3DL1*F*.

"Understanding that *KIR3DL1* has a functional role in protection against ankylosing spondylitis is important for further deciphering the mechanisms of autoimmune diseases," concludes Chudakov. The researchers next plan to conduct functional studies of T lymphocytes carrying different KIR alleles and genome-wide association studies to identify other genes that contribute to the risk of AS.

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