What the Absence of ACPA Antibody Really Means in RA

A genetic study has found exactly how ACPA-positive and ACPA-negative rheumatoid arthritis differ, with implications for management.

Source: Rheumatology Network


While a positive test for anti-citrullinated-protein-autoantibody-positive antibody (ACPA+ status) is specific for ACPA+ rheumatoid arthritis (RA), it’s difficult to interpret the meaning of the absence of the antibody. Is it a false positive test? Is the diagnosis actually not RA at all?

An international team of genetic researchers has now clarified the situation, by identifying single nucleotide polymorphisms (SNPs) associated with ACPA negativity in the protein-binding groove of human leukocyte antigen (HLA). Using a custom immunochip array, the researchers screened 2,406 samples from patients with ACPA- RA and 13,930 controls to find molecular subtypes of HLA specific to ACPA- RA.

They found and molecularly defined three SNPs associated with ACPA- RA but not with ACPA positivity. This supports the idea that ACPA+ and ACPA- RA are genetically distinct and react to different autoantigens.

Individuals diagnosed with ACPA- RA may actually have other conditions that mimic RA and have atypical presentations. The researchers estimated that in each ACPA- RA cohort, 4-11 most likely had ankylosing spondylitis and some may have had Sjögren syndrome, making optimal treatment and long-term prognosis different than those for the initial diagnosis. In 15-37% of cases the serology was probably misleading, and the patients actually had ACPA+ RA despite a negative test.

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