A19 ANTI-CCP ANTIBODIES ARE A COLLECTION OF ACPA THAT ARE CROSS-REACTIVE TO MULTIPLE CITRULLINATED ANTIGENS

A Ioan-Facsinay,¹ H el-Bannoudi,¹ H U Scherer,¹ D van der Woude,¹ H A Ménard,² M Lora,² L A Trouw,¹ T W J Huizinga,¹ R E M Toes¹ ¹*Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands;* ²*Division of Rheumatology, McGill University Health Center, Montreal, Quebec, Canada*

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Objective Anti-citrullinated protein/peptide antibodies (ACPA/anti-CCP) are a hallmark of rheumatoid arthritis and are believed to play a role in disease pathogenesis. These antibodies are typically detected in ELISA with citrullinated peptides (eg, CCP2) or -proteins as antigens. The absolute concentration of anti-CCP antibodies in serum is unknown. Although antibodies to several citrullinated proteins can mainly be detected within anti-CCP-positive sera, it is currently unknown whether anti-CCP antibodies are in fact ACPA. Likewise, it is unknown to what extent antibody responses to different citrullinated proteins are cross-reactive.

Methods The authors established an affinity purification method in which citrullinated-antigen-specific antibodies were eluted from ELISA plates and then used for detection of citrullinated antigens in ELISA or Western Blot. For additional cross-reactivity studies, ELISA-based inhibition assays were performed with citrullinated or control peptides as inhibitors.

Results The authors estimated the concentration of anti-CCP IgG antibodies to be at least 30 µg/ml in patients with high anti-CCP antibody levels. Affinity-purified anti-CCP antibodies were able to recognise citrullinated-fibrinogen (cit-fib) and cit-MBP on Western Blot. Furthermore, antibodies specific for cit-fib and cit-MBP were cross-reactive. However, additional cross-reactivity studies indicated that non-overlapping antibody responses to citrullinated peptides can exist in patients.

Conclusions The authors show for the first time that anti-CCP antibodies recognise multiple citrullinated proteins and are thus ACPA. More importantly, our data indicate that different ACPA responses are cross-reactive, but the cross-reactivity is not complete, as distinct non-cross-reactive responses can also be detected in RA patients.