from IgM-BCR-triggering excludes naïve B cells as a source of ACPA and suggests that the ACPA produced originate from circulating plasmablasts.

3 ACPA PRODUCTION BY CIRCULATING B CELLS ISOLATED FROM PERIPHERAL BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS

Scherer H U, Kerkman P F, van der Voort E I H, Trouw L A, Huizinga T W J, Toes R E M *Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands*

10.1136/annrheumdis-2011-201234.3

Background and objectives Anticitrullinated protein antibodies (ACPA) show high specificity for rheumatoid arthritis (RA) and predict disease onset and severity. Several lines of research indicate that ACPA are pathogenetically involved in disease development and might contribute to joint destruction. So far, however, the nature (origin, characteristics, localisation) of ACPA producing B cells is unknown.
The authors developed an in vitro culture system for B cells isolated from peripheral blood of patients with RA in order to study the characteristics of ACPA-producing B cells.
Materials and Methods Peripheral blood mononuclear cells (PBMC) were obtained from patients with ACPA-positive RA, ACPA-negative RA and from healthy donors. CD19 expressing B cells isolated by magnetic bead-based positive selection were cultured in the presence of anti-IgM, IL-21 and BAFF on a layer of irradiated, CD40L transfected fibroblasts. After 6 days of culture, supernatants were assessed for the presence of ACPA-immunoglobulin G (IgG) and total IgG by ELISA. In a subgroup of patients, B cells were also cultured without BCR ligation.
Results After culture, ACPA were readily detected in up to 100% of culture wells. The degree of ACPA-production correlated with inflammatory disease activity and ACPA-titre. The ACPA reactivity detected was specific for citrullinated antigens, as no reactivity was detected against arginine containing control peptides. In addition, no ACPA production was found in B cell cultures of ACPA-negative patients and healthy controls. Of interest, IgM-BCR stimulation with anti-IgM enhanced ACPA production, but was generally dispensable, as ACPA could also be detected without BCR-triggering.
Conclusions Our results indicate the presence of circulating peripheral blood B cells capable of producing ACPA in patients with ACPA-positive RA. Independence of ACPA production