have also shown that approximately one third of the ACPA-positive RA-cases carry antibodies against the calcium-dependent thiol-enzyme which catalyses citrullination, namely peptidylarginine deiminase (PAD). These patients seem to suffer from a more severe form of RA. The presence of two distinct subsets of RA based on presence or absence of ACPA has been proposed. An increasing number of arginine-containing proteins have been implicated as substrates for PADs in RA. Of these potential targets, fibrinogen, fibrin, fibronectin and collagen are also substrates for transglutaminases (TGs), another family of calcium-dependent thiol-enzymes. TG type 2 is a major autoantigen in coeliac disease and has also been shown to aggravate collagen type II-induced arthritis in mice. Another TG is the thrombin-dependent plasma Factor XIII (FXIII), responsible for the covalent cross-linking of fibrin in the terminal step of blood coagulation. A cellular form of FXIII is found in platelets, monocytes, granulocytes, chondrocytes and osteoblasts. Our intention with this study was to investigate the potential role of cellular FXIII in the pathogenesis of RA.

Methods Recombinant cellular FXIII was treated in vitro with rabbit muscle PAD. Citrullinated and native FXIII were used as antigens in ELISAs. Sera from 51 blood donors and 67 RA-patients were tested. In order to measure TG-activity of native and citrullinated FXIII, agarose gel electrophoresis was combined with semiquantitative TG-activity staining.

Results IgA-antibodies against citrullinated cellular FXIII were present in 64% of all RA-patients compared with 5.9% among blood donors (OR 28.7 CI 95% 8.01 to 102). Only 7.5% of the RA-sera displayed IgA against native FXIII. Interestingly, the frequency of IgA against citrullinated FXIII was similar for CCP2-positive (65%) and CCP2-negative (62%) RA. A total of 84% of the RA-cases carried either IgA against citrullinated FXIII or IgG anti-CCP antibodies. Citrullination of cellular FXIII abolished TG-activity.

Conclusions Citrullinated human cellular FXIII is a novel autoantigen in RA. Citrullination is a general feature in RA. The novel autoantibody to citrullinated FXIII indicates common features between ACPA+ and ACPA- RA. The resulting malfunctions of cellular FXIII could have pathogenetic consequences and contribute to disease chronicity.

A9 CELLULAR FACTOR XIII AND PEPTIDYLARGININE DEIMINASE-CATALYSED CITRULLINATION IN RHEUMATOID ARTHRITIS

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Introduction Antibodies against citrullinated proteins (ACPA) have been reported in the order of 70% of all cases with rheumatoid arthritis (RA). The authors and other groups