

to more than 100 antigens can be analysed simultaneously using small volumes of sera, was employed. Four synthesised fibrinogen peptides (containing citrulline at the positions 573 (Fib 573), 591 (Fib 591) within the  $\alpha$ -chain and at the positions 72 (Fib 72) and 74 (Fib 74) within the  $\beta$ -chain, respectively) were immobilised onto a chemically modified glass slide in an arrayed fashion. After binding of antigens to the glass surface diluted serum from 936 RA patients (404 cyclic citrullinated peptide (CCP) positive and 532 CCP negative) and 461 healthy controls from the Epidemiological Investigations in Rheumatoid Arthritis (EIRA) case control cohort were applied into reactions sites on the glass slides, followed by fluorescent-labeled anti-human IgG antibody and scanning in a laser scanner. Cutoff values were determined as the 98th percentile of the healthy control responses.

**Results** The authors found that 31% (among them 87% are CCP positive) of patients were positive to Fib573 peptide. For the Fib2591 peptide, the corresponding figures were 10% (65%), for the Fib74 peptide 28% (68%) and for the Fib72 peptide 20% (68%).

**Conclusions** Here the authors show extensive autoantibody reactivity against fibrinogen epitopes that are citrullinated in vivo in RA synovial membranes. A substantial part of the ACPA peptide reactivities were found among anti-CCP2 negative RA patients. The results suggest the use of these citrullinated fibrinogen peptides as biomarkers in RA.

## 22 ACPA RESPONSE AGAINST FIBRINOGEN EPITOPES CITRULLINATED IN VIVO IN THE SYNOVIAL MEMBRANE IN RA PATIENTS DETECTED WITH AN AUTOANTIBODY MICROARRAY

E Ossipova,<sup>1</sup> M Hansson,<sup>1</sup> L Mathsson,<sup>2</sup> L Klareskog,<sup>1</sup> P-J Jakobsson,<sup>1</sup> J Rönnelid<sup>2</sup> <sup>1</sup>Department of Medicine, Unit of Rheumatology, Karolinska University Hospital, Stockholm, Sweden; <sup>2</sup>Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden

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**Background and objectives** Citrullination is a post-translational modification of proteins catalysed by specific peptidylarginine deiminases, which modify arginine residues to citrulline. Citrullinated proteins are frequently detected in various inflammatory states including rheumatoid arthritis, and a lot of attention has been drawn to the presence of auto-antibodies targeting proteins containing citrulline. Using high resolution mass spectrometry (MS) the authors have first identified citrullinated peptides corresponding to amino acids 559–575 of fibrinogen  $\alpha$ -chain and corresponding to amino acids 52–77 of the fibrinogen  $\beta$ -chain in synovial tissues from patient with rheumatoid arthritis (RA) (Hermansson *et al* Proteomics: Clinical Applications 2010). In this work the authors have also identified citrullinated peptide corresponding to amino acids 580–599 of fibrinogen  $\alpha$ -chain but decided do not include it to publication due to possible deamidation of asparagine or glutamine, which leads to the same mass shift as deamidation of arginine. In this follow-up study The authors test sera from RA patients for anticitrullinated protein antibodies (ACPA) response against MS identified citrullinated fibrinogen peptides.

**Material and methods** In this work a microarray assay based on Phadia's ImmunoCAP ISAC system, where reactivity