

## **A disease-modifying role for mucosal IgA antibodies to citrullinated antigens?**

Anna Svärd Läkare Kliniken för reumatologi, 791 82 Falun

Alf Kastbom Reumatologi/AIR, Institutionen för klinisk och experimentell medicin, Linköpings Universitet

Yngve Sommarin EuroDiagnostica AB, Malmö

Thomas Skogh Prof. Avdelningen för Reumatologi, Institutionen för Molekylär och Klinisk Medicin, Hälsouniversitetet i Linköping

### **Bakgrund**

The aim of this study was to investigate whether IgA antibodies to cyclic citrullinated peptides (CCP) can be detected in saliva of patients with rheumatoid arthritis (RA) and if it relates to clinical manifestations.

### **Metod**

Salivary samples were collected (by 'passive drooling') from 63 consecutive patients with established RA at the rheumatology outpatient clinic (Falun, Sweden), and from 20 healthy persons (hospital staff). The samples were centrifuged and kept frozen at -20°C until analysis. IgA-class anti-CCP antibodies in saliva were analysed by adaptation of a commercial ELISA (Immunoscan RA, Euro-Diagnostica AB) using polyclonal rabbit antihuman alpha-chain specific antibodies conjugated with horseradish peroxidase (DakoCytomation) as secondary antibody. To ensure specificity of the reaction, a corresponding ELISA was set up to analyse IgA antibodies to control antigen (cyclic arginine peptide, CAP), and anti-CCP/anti-CAP ratios were calculated. Also, inhibition studies were performed by preincubation of sera with soluble CCP or CAP. Clinical and laboratory data on disease activity, i.e. CRP, ESR, and DAS28 as well as radiological outcome were achieved retrospectively via the patients' medical records.

### **Resultat**

Background reactivity against CCP was found in virtually all patients and healthy subjects, whereas a positive anti-CCP/anti-CAP ratio ( $\geq 1.5$ ) was found in 14 out of 63 RA patients (22%) and in one healthy subject (5%). Salivary IgA-reactivity with CCP was dose-dependently inhibited by soluble CCP (but not with CAP) in sera with anti-CCP/anti-CAP ratios  $\geq 1.5$ . No IgG-reactivity to CCP was found in saliva, although all patients with salivary IgA anti-CCP tested IgG anti-CCP-positive in serum, strongly arguing against passive leakage of anti-CCP antibodies from blood to saliva. The patients testing positive for salivary IgA-CCP had lower average disease activity measures at presentation and fewer developed erosions within six years after presentation ( $p=0.043$ ).

### **Sammanfattning**

Salivary IgA-CCP were found in a subset of IgG anti-CCP positive RA patients. In contrast to their serum counterparts, salivary IgA antibodies may associate with a milder/less destructive disease course. This accords with the notion that secretory IgA antibodies exert anti-inflammatory actions, and that they may be associated with induction of systemic tolerance (oral tolerance). The possible disease-modifying role of mucosal immunity to citrullinated proteins needs further investigation!