Background Rheumatoid arthritis (RA) is a prototypic autoimmune disease characterised by a prominent humoral autoimmunity. Of particular relevance is the local production of autoantibodies such as rheumatoid factor and anti-citrullinated protein antibodies in the inflamed synovial tissue. The mechanisms underlying break of B cell tolerance and local autoantibody production remains poorly understood.

Objectives To identify cellular and molecular pathways implicated in RA-specific humoral autoimmunity.

Methods Synovial tissue samples were obtained by arthroscopy from untreated individuals with RA (n = 33) and inflammation matched SpA controls (n = 58). Gene expression profiling was performed on tissue samples of patients with established arthritis using 44K. Whole Genome Human microarrays (Agilent). Top differentially expressed genes were validated on three independent cohorts by Taqman based RT-qPCR and immunohistochemistry. Collagen-induced arthritis (CIA) and Experimental autoimmune encephalomyelitis (EAE) experiments were conducted using Bob1 knockout mice and their littermate controls.

Results Microarray screening for genes differentially expressed in the inflamed synovium, the key target of the disease process in RA, revealed a prominent and disease-specific B cell/plasma cell signature with the B cell-specific transcriptional co-activator Bob1 and its transcriptional target BCMA among the most upregulated genes. Validation by RT-qPCR on two independent cohorts representing early and established arthritis confirmed microarray data and demonstrated elevated expression of Bob1 and BCMA not only in established RA, but also at the early phase of the disease. Quantitative evaluation of immunohistochemical stainings of synovial tissue with monoclonal antibody for Bob1 revealed significant increase in Bob1 positive cells in RA synovium (p < 0.01). Next we determined whether lack of functional Bob1 modifies disease onset or severity in CIA. Interestingly, the results showed that Bob1−/− mice were fully resistant to CIA induction compared to their wild-type littermates. This remarkable protection from CIA is explained by decreased antigen-presentation/costimulatory capacity of B cells and by failure to produce pathogenic anti-collagen autoantibodies in the absence of Bob1.

Conclusions The specific increase in Bob1 expressing cells in RA synovitis and the resistance of Bob1-deficient mice to development of CIA indicate that Bob1/BCMA axis may contribute to humoral autoimmunity in RA. The relationship between an aberrant Bob1 expression and the break of peripheral tolerance in RA is currently under investigation.

6. Microbes and autoimmunity

**AB6.1 Antibody response against Porphyromonas gingivalis and matrix metalloproteinase-3 are associated with anti-citrullinated protein antibody in rheumatoid arthritis, but only matrix metalloproteinase-3 is a predictive factor of response to infliximab**

**Materials and Methods** Joint damage and severe periodontal disease were assessed in 101 RA patients included in this study. DA52, anti-citrullinated protein antibodies (ACPA), anti-P. gingivalis antibody, and MMP-3 were monitored before and at 6 months of infliximab therapy. ACPA, anti-P. gingivalis antibody, and MMP-3 were determined by ELISA.

**Results** At baseline, ACPA titers were associated with anti-P. gingivalis LPS-specific antibodies titers (P < 0.05). Anti-P. gingivalis antibodies were not significantly correlated with clinical, biological, or destruction parameters of RA disease. At 6 months of infliximab therapy, MMP-3 level decreased (from 119 ± 103 ng/ml to 62.44 ± 52 ng/ml; P = 0.0001), whereas P. gingivalis antibody levels remained at the same level. DA52 and immunization markers (CRP and ESR) also decreased significantly during infliximab therapy (P < 0.05) as ACPA levels (P < 0.001). Only high MMP-3 level at baseline was associated with infliximab efficacy (P < 0.01).

**Conclusions** MMP-3 level can be a useful marker of the efficacy of infliximab in RA patients. The treatment did not affect anti-P. gingivalis antibodies.