new identified citrullinated targets in the serum of RA patients in two distinct early RA cohorts (n = 393) and a cohort of non-RA patients (n = 236) as disease controls.

**Results** Bronchial lymphocyte infiltration and iBALT formation was observed in 55% of the ACPA+ RA patients but only 17% of ACPA- patients and 7% of healthy volunteers. Higher expression of CD3, HLA-DQ, HLA-DR and citrullinated targets was observed in bronchial biopsies of ACPA+ as compared to ACPA- RA patients. BAL fluids were enriched in both IgG and IgA ACPA as compared to aligned washes. Mass spectrometry identified 5 proteins in the synovium (in total 8 sites) and 4 in the lungs (in total 6 sites) containing citrullinated residues. Tumour vimentin derived citrullinated peptides were present in a majority of both synovial and lung biopsies with slightly higher citrullinated/unmodified peptides ratios in the smokers as compared to non-smokers.14.5% of the RA patients tested by ELISA showed antibody reactivity against the new identified citrullinated target compared to 3.4% in the disease controls.

**Conclusions** Signs of inflammation and local ACPA enrichment are present early in bronchial tissues of ACPA+ RA patients. Shared citrullinated targets in the lung and joints as well as systemic reactivity against these targets are present in RA patients. Our findings support the notion that early inflammatory events in the lungs may represent a critical initiating factor in the development of ACPA+ RA.

**A1.12 ENDODIGENOUS SLPI RELEASED BY RHEUMATOID SYNOVIAL FIBROBLASTS CONTROL BAFF-DEPENDENT B CELL ACTIVATION IN VITRO AND IN THE CIA AND RA/SCID-ARTHRITIS MODELS**

**Background and Aims** Secretory leukocyte protease inhibitor (SLPI) is a serine protease inhibitor with potent anti-microbial/immunoregulatory activities. Rheumatoid arthritis (RA) is characterised by synovial niches of autoreactive B cells. Auto-crine production of B cell survival factor BAFF by RA synovial fibroblasts (RAFs) supports ongoing B cell activation within the RA synovium. ACPAI+ RA patients. We investigated whether SLPI: (1) is produced by TLR3-ligands-treated RAF and regulates B cell activation; (2) exerts immunoregulatory effects in the RA synovium/SCID chimeric model and in collagen induced arthritis (CIA).

**Methods** mRNA and protein expression of SLPI in RA/SF/RAF (dual) stimulated with/without TLR2/TLR3/TLR4 ligands was assessed by QT-PCR and ELISA. RAF were treated with or without recombinant SLPI (rSLPI) to study: (1) BAFF expression; (2) AID expression and class-switching in co-culture with IgG+B cells; BAFF expression and antibody production were examined in rSLPI-treated RA/SCID mice. Severity of arthritis, anti-CII antibodies, and joint histopathology were studied in rSLPI-treated CIA mice.

**Results** Stimulation of RAF with TLR3 ligands led to a 15-fold induction of SLPI mRNA. SLPI protein was time-dependently released from TLR3-stimulated RAF, but not RAFA. SLPI restrained the production of BAFF, AID and IgG/GM in TLR3-treated RAF and co-cultures, respectively. SLPI reduced BAFF expression and IgG/GM production in RA/SCID mice while severity of arthritis, cartilage damage and anti-CII-IgG2a were reduced in SLPI-treated CIA.

**Conclusion** BAFF release high levels of SLPI constitutively and upon TLR3 stimulation. SLPI directly modulates BAFF and B cell activation in vitro/in vivo and reduces joint inflammation in CIA, highlighting a novel endogenous anti-inflammatory pathway with therapeutic potential in RA.