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Crosstalk in RA synovia—TLR3–BAFF axis sustains B-cell activation

A key facet of the crosstalk between stromal cells and B cells in rheumatoid arthritis (RA) has been characterized in cell studies; Michele Bombardieri *et al.* show that signaling by BAFF (also known as TNF ligand superfamily member 13B) and Toll-like receptor 3 (TLR3) enables autoreactive B-cell activation by RA synovial fibroblasts (RASf).

B cells—targets of several therapies in clinical use or development—are critically but enigmatically involved in RA pathology. Differentiation of synovial B cells to autoreactive plasma cells in RA is thought to occur *in situ*, in ectopic lymphoid structures (synovial niches). Activation-induced cytidine deaminase mediates the necessary immunoglobulin isotype switching; BAFF is also required. RASf are implicated in synovial niche functionality and promote B-cell survival and differentiation, but the mechanics of such interactions are unclear.

Now, Bombardieri and colleagues have shown that RASf produce large amounts of BAFF, and can rapidly induce sustained production of class-switched antibodies by co-cultured B cells. These effects were independent of direct cell–cell contact, and were augmented upon stimulation of TLR3. Inhibition of receptors for BAFF prevented the TLR3-mediated enhancement, and TLR3 ligands did not affect B cells directly.

TLR3 is known to mediate activation of RASf by necrosis-derived RNA. Understanding its role in synovial niche crosstalk will aid efforts to specifically target aberrant B-cell processes in RA.

Emma Leah

Original article Bombardieri, M. *et al.* A BAFF/APRIL-dependent TLR3-stimulated pathway enhances the capacity of rheumatoid synovial fibroblasts to induce AID expression and Ig class-switching in B cells. *Ann. Rheum. Dis.* doi:10.1136/ard.2011.150219