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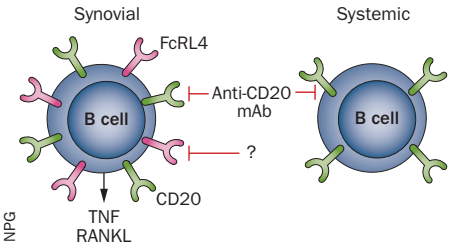
RHEUMATOID ARTHRITIS

Are FcRL4$^+$ B cells the next target for RA biologic therapy?

Researchers in Birmingham, UK, have discovered a functionally distinct subset of memory B cells in the synovium of patients with rheumatoid arthritis (RA). "FcRL4 is a surface protein unique to this subset," says the group leader of the study, Dagmar Scheel-Toellner. The data indicate that the Fc receptor-like 4 (FcRL4) positive B-cell subset, "which had not previously been associated with arthritis, has a pathogenic role by virtue of its proinflammatory cytokine production and antigen presenting capacity."

Previous work identified synovial B-cell-derived mediators of bone erosion and inflammation, such as TNF and RANKL (also known as TNF ligand superfamily member 11), cytokines shown to be reduced in the synovium of patients with RA after rituximab treatment. Current biologic therapies for RA can have adverse effects, possibly because they do not discriminate between pathogenic and protective B cells. FcRL4 is a transmembrane protein that is not systemically expressed by B cells in healthy individuals, it is predominantly tonsillar. Scheel-Toellner's latest study, published in *Annals of the Rheumatic Diseases*, hints that targeted therapies that deplete FcRL4$^+$ B cells in the synovium of patients with RA might treat the disease and be associated with a reduced risk of adverse side-effects.

Using flow cytometry to analyse synovial fluid, and immunohistochemistry for analysis of synovial B cells *in situ*, the researchers found that, compared with FcRL4$^-$ B cells, FcRL4$^+$ synovial B cells had higher expression of the chemokine receptors CCR1 and CCR5, co-stimulatory molecules CD80 and CD86, cytokines RANKL and TNF, and the target of rituximab, CD20, but lower expression of TGF-β, CD21 and BAFF (also known as TNF ligand superfamily member 13B). Synovial FcRL4 mRNA levels were higher in patients with RA ($n = 12$, 70% on DMARDs) than in patients undergoing arthroscopy for noninflammatory conditions ($n = 8$).



These data identify a marker of pathogenic B cells in RA synovium and might be the first step toward the next generation of biologic agents. "Ultimately," concludes Scheel-Toellner, "it will be important to determine whether therapeutic removal of this FcRL4$^+$ B-cell subset has clinical efficacy in RA."

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Original article Yeo, L. *et al.* Expression of FcRL4 defines a pro-inflammatory, RANKL-producing B cell subset in rheumatoid arthritis. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2013-204116