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RHEUMATOID ARTHRITIS

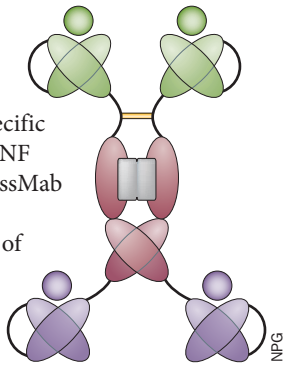
Anti-TNF and anti-IL-17 antibodies—better together!

Combined blockade of TNF and IL-17 could be a therapeutic approach for patients with rheumatoid arthritis (RA) who fail to respond, or who lose responsiveness, to single-cytokine inhibition, according to a paper now published in *Arthritis & Rheumatology*.

Georg Schett and colleagues from the University of Erlangen-Nuremberg, Germany, in collaboration with researchers at Roche, investigated the effects of combined inhibition of TNF and IL-17 in inflammatory arthritis. As Schett explains, "We were intrigued by reports on the role of IL-17 in nonresponders and access to cutting-edge protein engineering capabilities has allowed us to test the hypothesis that inhibiting both pathways simultaneously is of benefit."

Normal and RA fibroblast-like synoviocytes (FLSs) were stimulated *in vitro* with TNF or IL-17, both of which resulted in the production of proinflammatory cytokines. Combined stimulation with TNF and IL-17 resulted in additive increased production of IL-6 and IL-8, and synergistic increased production of granulocyte colony-stimulating factor.

To confirm these effects *in vivo,* the authors utilized the TNF transgenic inflammatory arthritis mouse model. Treatment with vehicle resulted in worsening of inflammatory disease, anti-IL-17 antibodies had no effect, low-dose anti-TNF antibodies had moderate effects, high-dose anti-TNF treatment had strong anti-inflammatory effects and, interestingly, a combination of anti-IL-17 and low-dose anti-TNF antibodies was as effective as high-dose anti-TNF treatment. "Combining a low dose of the antibodies against IL-17 and TNF acted synergistically to reduce inflammation and showed excellent protection from structural bone and cartilage damage, possibly by fostering intrinsic repair mechanisms in the joint," says Schett.



The researchers then generated bispecific antibodies against TNF and IL-17 using CrossMab technology (Roche) and tested the effect of these antibodies on RA FLSs. "The bispecific antibodies inhibited, as expected, the effect of TNF and IL-17 on proinflammatory cytokines and MMPs," continues Schett. He concludes, "Bispecific antibodies are a promising new modality to treat RA since they can offer the possibility to neutralize two pathways with a single therapeutic molecule."

Jenny Buckland

Original article Fischer, J. A. A. *et al.* Combined inhibition of TNFα and IL-17 as therapeutic opportunity for treatment in rheumatoid arthritis: development and characterization of a novel bispecific antibody. *Arthritis Rheumatol.* doi:10.1002/art.38896