RHEUMATOID ARTHRITIS

Spontaneous release of cytokines from synovial tissue is blocked by anti-TLR2

Targeting Toll-like receptor 2 (TLR2) in rheumatoid arthritis (RA) might be a new option for biologic therapy, according to tests of an anti-TLR2 antibody, OPN301, in cultured tissue from patients with the disease. Not only did OPN301 block the secretion of proinflammatory cytokines induced by a TLR2 agonist, but it also prevented the spontaneous release of such cytokines from synovial tissue, further supporting the involvement of TLR2 in RA pathogenesis.

To probe the effect of inducing or blocking TLR2, Ursula Fearon and colleagues chose to use *ex vivo* whole tissue synovial cultures from 13 patients with RA with an actively inflamed joint. “This model maintains the cell–cell contact and architecture of the synovial tissue,” says Fearon, adding that its spontaneous release of proinflammatory mediators mimics the environment of a joint in RA *in vivo* and thus is “ideal for preclinical proof-of-concept studies

to test new therapeutic targets.” With the use of immunohistochemistry, “we demonstrated that OPN301 can penetrate synovial tissue in culture and localizes to the lining layer and mononuclear infiltrates in perivascular regions,” continues Fearon.

Application of a TLR2 agonist induced angiogenesis and the secretion of IL-6 and IL-8 in the synovial tissue; these effects were blocked by OPN301. Furthermore, spontaneous cytokine release (of IL-8, tumor necrosis factor [TNF], interferon γ and IL-1 β) was significantly inhibited by OPN301. Categorizing these responses as low (<20% inhibition), moderate (21–49% inhibition) and good (>50% inhibition), the team compared them with the effect of adalimumab, an anti-TNF therapy. In ratings terms, 38% of OPN301 responses were low, 32% moderate and 30% good, which compare well to the 37%, 31% and 32% respective values for adalimumab.

Anti-TLR2 antibody OPN301 inhibits TLR2-agonist-induced angiogenesis in synovial tissue. Image courtesy of Ursula Fearon.

Biologic therapies such as anti-TNF agents have transformed RA therapeutics, but they are not effective in all patients. Besides supporting a role for TLR2 in RA pathogenesis, these data suggest that targeting TLR2 could be a valid alternative therapeutic option.

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