EXPERIMENTAL ARTHRITIS

A new co-therapeutic strategy for RA?

B cells have a crucial role in driving autoimmunity in rheumatoid arthritis (RA). Indeed, B-cell-depletion therapy involving the anti-CD20 antibody rituximab can be an effective therapeutic strategy for patients with RA. The improvement in clinical symptoms of these patients, however, is temporary and B cell populations eventually return, along with RA symptoms. Now, Pigott and Mandik-Nayak have published in *Arthritis & Rheumatism* that the addition of an inhibitor of indoleamine-2,3-dioxygenase (IDO)—an enzyme that drives the initial stages of the B-cell-mediated autoimmune response—to B-cell-depletion therapy could promote long-term clinical improvement in patients with RA.

The authors used immunoglobulin transgenic and arthritic transgenic mice to test the efficacy of the IDO inhibitor 1-methyltryptophan (1MT) *in vivo*. 1MT did not affect initial activation or survival of autoreactive B cells but did prevent their ability to differentiate into autoantibody-secreting cells. In arthritic

mice rituximab was effective in depleting the number of B cells and attenuating RA symptoms, but only for a limited period. Administration of 1MT prior to B-cell repopulation prevented the production of autoantibodies and inflammatory cytokines and flare in arthritis symptoms.

These findings indicate that IDO inhibitors and rituximab could be an effective co-therapeutic strategy for patients with RA by both eliminating pathogenic B cells and preventing new ones from being generated. Moreover, 1MT should not affect memory responses to pathogens acquired through vaccination. Indeed, 1MT is currently in early stage clinical trials as an anti-cancer therapeutic.

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Original article Pigott, E. & Mandik-Nayak, L. Addition of an indoleamine-2,3,-dioxygenase inhibitor to B cell depletion therapy blocks autoreactive B cell activation and recurrence of arthritis. *Arthritis Rheum.* doi 10.1002/art.34406.