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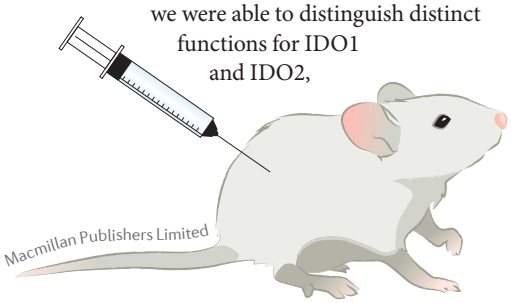
EXPERIMENTAL ARTHRITIS

Do you want to treat arthritis? IDO2!

> Treating mice with … autoimmune arthritis with this anti-IDO2 antibody reduced the severity of disease

Therapeutically targeting indoleamine 2,3-dioxygenase 2 (IDO2) using a specific monoclonal antibody alleviates experimental arthritis, according to new findings published in *Clinical Immunology*. "Treatment with anti-IDO2 antibody inhibits autoreactive T and B cell responses and alleviates joint inflammation in the KRN preclinical model of autoimmune arthritis, fully recapitulating genetic IDO2 deficiency," states Laura Mandik-Nayak, corresponding author of the study.

The indoleamine 2,3-dioxygenase enzymes (IDO1 and IDO2) catalyze the rate-limiting step in the catabolism of tryptophan. "Through a series of genetic knockout studies in mice, we were able to distinguish distinct functions for IDO1 and IDO2, identifying IDO2, and not the better studied IDO1, as a proinflammatory mediator of autoimmune disease," explains Lauren Merlo, lead author of the study. "However, small molecules that can be used to specifically target IDO2 *in vivo* have yet to be identified, so in the current study, we explored the use of a highly specific, monoclonal antibody therapy for IDO2," she continues.



Treating mice with the KRN model of autoimmune arthritis with this anti-IDO2 antibody reduced the severity of disease compared with mice treated with a control antibody, regardless of whether the antibody was administered before or after the onset of disease. Merlo and colleagues reported similar findings in mice with collagen-induced arthritis. Using the KRN model to track autoreactive lymphocytes, the researchers pinpointed some of the mechanistic effects of anti-IDO2 antibody administration, including reduced T cell numbers in all subsets except regulatory T cells, and a decrease in IL-21 levels in mice treated with the anti-IDO2 antibody as compared with those given a control antibody.

As an intracellular molecule, IDO2 would not traditionally be considered a candidate target for antibody therapy. "Mechanistic studies showed that anti-IDO2 is able to access its intracellular target to exert its anti-arthritic effect by internalization via the FcγRIIb receptor on B cells," explains Merlo. "This work validates IDO2 as a therapeutic target for rheumatoid arthritis and adds to a growing literature demonstrating antibody treatments that can target intracellular antigens to offer feasible and disease-selective approaches to treat disease," adds Mandik-Nayak.

Joanna Collison

ORIGINAL ARTICLE Merlo, L. M. F. *et al.* Therapeutic antibody targeting of indoleamine-2,3-dioxygenase (IDO2) inhibits autoimmune arthritis. *Clin. Immunol.* http://dx.doi.org/10.1016/j.clim.2017.01.016 (2017)

FURTHER READING Merlo, L. M. F. *et al.* IDO2 is a critical mediator of autoantibody production and inflammatory pathogenesis in a mouse model of autoimmune arthritis. *J. Immunol.* **192**, 2082–2090 (2014)