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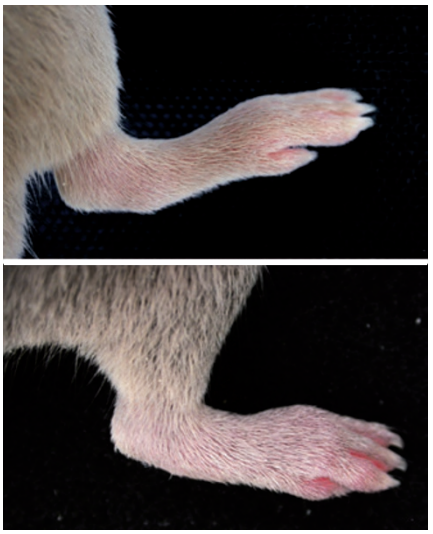
EXPERIMENTAL ARTHRITIS

APRIL suppresses CIA in mice

The TNF superfamily member a proliferation-inducing ligand (APRIL) "suppresses rather than promotes immune-mediated inflammatory diseases," write Michael Hahne and colleagues in *Annals of the Rheumatic Diseases*. This finding comes as a surprise, as elevated levels of APRIL have been previously detected in patients with inflammatory autoimmune diseases such as rheumatoid arthritis, and the agents belimumab (targeting BAFF, a cytokine closely related to APRIL) and atacicept (targeting both BAFF and APRIL) are in clinical trials in patients with autoimmune diseases. "APRIL's role in B-cell malignancies is established, but its role in autoimmunity is less clear and rather controversial," says Hahne.

The researchers induced collagen-induced arthritis (CIA) in APRIL transgenic (APRIL-Tg) mice backcrossed with DBA/1 mice and in littermate controls. Postmortem histological analyses of joint sections showed that overall incidence and severity of disease was lower in APRIL-Tg mice compared with controls. In addition, titres of anti-collagen type II (anti-CII) IgG antibodies were significantly lower in the former, as were numbers of mast cells in the joints. In a collagen antibody-induced model of arthritis, APRIL-Tg mice developed disease similarly to control mice following injection with a cocktail of anti-CII antibodies. These data suggest that APRIL negatively regulates anti-CII antibody production, but is not involved in the downstream effector mechanisms. In addition, T-cell-dependent humoral responses were reduced in APRIL-Tg mice and this reduction was associated with lower percentages of antigen-specific memory B cells in these mice. Furthermore, adenoviral delivery of APRIL into CII-immunized DBA/1 mice led to reduced severity of CIA compared with control mice.

Altogether, these findings indicate that "APRIL dampens CIA by controlling the generation of anti-collagen antibodies," comments Hahne. "Our findings suggest a therapeutic potential for APRIL agonists in inflammatory diseases," he concludes.



APRIL-Tg mice are less susceptible to CIA than littermate controls. Paws of APRIL-Tg mice (upper panel) display less swelling and redness than those of control mice (lower panel). Image courtesy of Michael Hahne.

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Original article Fernandez, L. *et al.* The TNF family member APRIL dampens collagen-induced arthritis. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2012-202382