IN BRIEF

INFLAMMATION

Linking malnutrition and intestinal inflammation

ACE2 (angiotensin-converting enzyme 2) is a key enzyme of the renin–angiotensin system, and studies in *Ace2*$^{-/-}$ mice now reveal a link between malnutrition and intestinal inflammation. Hashimoto *et al.* observed that *Ace2*$^{-/-}$ mice display more severe dextran sodium sulphate (DSS)-induced colitis than wild-type mice. ACE2 promotes the function of the amino acid transporter B^{0}AT1 (also known as SLC6A19), and *Ace2*$^{-/-}$ mice had low tryptophan levels in the serum. Similarly, wild-type mice on a protein-free or tryptophan-free diet developed severe DSS-induced colitis. This correlated with reduced expression of antimicrobial peptides in the small intestine, which affected the composition of the intestinal microbiota. The authors suggest that tryptophan reabsorption regulates the intestinal microbiome and gut homeostasis through the tryptophan derivative nicotinamide (also known as vitamin B3) and the activation of mTOR signalling.

ORIGINAL RESEARCH PAPER Hashimoto, T. *et al.* ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. *Nature* **487**, 477–481 (2012)

IMMUNOTHERAPY

JAK inhibitor effective in rheumatoid arthritis

Rheumatoid arthritis is an autoimmune disease characterized by chronic joint inflammation. Patients who do not respond to firstline therapies can be treated with anti-cytokine therapies, but these large biologics must be administered parenterally. Two studies describe promising results from Phase III clinical trials in which patients with rheumatoid arthritis were treated orally with tofacitinib (Pfizer), a small-molecule inhibitor of Janus kinases (JAKs). Inhibition of JAK1 and JAK3 by tofacitinib blocks signalling by multiple cytokines that are important for lymphocyte function, including interleukin-2 (IL-2), IL-4, IL-7, IL-9, IL-15 and IL-21. In both studies, patients treated with tofacitinib had improved clinical outcomes, and van Vollenhoven *et al.* found that tofacitinib was as effective as TNF blockade. On a cautionary note, the studies observed increased rates of infection and higher cholesterol levels in patients receiving tofacitinib. Both groups conclude that further trials are needed to evaluate the safety of this novel therapy.

ORIGINAL RESEARCH PAPERS Fleischmann, R. *et al.* Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. *N. Engl. J. Med.* **367**, 495–507 (2012) | van Vollenhoven, R. F. *et al.* Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. *N. Engl. J. Med.* **367**, 508–519 (2012)

CELL MIGRATION

Walking frames for dendritic cells

Dendritic cell (DC) migration to draining lymph nodes is crucial for adaptive immune responses and is driven by various chemokine receptors and adhesion molecules. This study identifies another molecular interaction involved in this process, showing that the expression of C-type lectin receptor 2 (CLEC2) by DCs promotes their migration along podoplanin (PDPN)-expressing stroma. PDPN is highly expressed by lymphatic endothelial cells and fibroblastic reticular cells; engagement of CLEC2 by PDPN led to cytoskeletal rearrangements in migrating DCs that allowed them to spread and migrate along these stromal surfaces. DCs that lacked CLEC2 expression had an impaired ability to migrate to draining lymph nodes and initiate adaptive T cell responses.

ORIGINAL RESEARCH PAPER Acton, S. E. *et al.* Podoplanin-rich stromal networks induce dendritic cell motility via activation of the C-type lectin receptor CLEC-2. *Immunity* 9 Aug 2012 (doi: 10.1016/j.immuni.2012.05.022)