cyclo-oxygenase 2 after 48 h of incubation, and also quickly induced phosphorylation of mitogen-activated protein kinases 1 and 3.

PAR-2 activation seems to make an important contribution to progression of osteoarthritic damage in cartilage. The authors conclude that PAR-2 could be a valuable therapeutic target, since reducing levels of PAR-2 in chondrocytes might provide analgesia as well as slow disease progression.

Original article Boileau C *et al.* (2007) Activation of proteinase-activated receptor 2 in human osteoarthritic cartilage upregulates catabolic and proinflammatory pathways capable of inducing cartilage degradation: a basic science study. *Arthritis Res Ther* **9:** R121

Why are glucosamine sulfate and chondroitin sulfate beneficial in osteoarthritis?

Osteoarthritis is extremely common, and its symptoms are universally known; however, mechanisms that describe how the complex interplay of inflammatory and other factors cause structural changes in the joint are not yet fully elucidated. While chondroitin sulfate and glucosamine sulfate both have well-documented, beneficial effects in patients with osteoarthritis, the exact molecular actions of these drugs are also unknown.

Tat *et al*. focused on human subchondral bone and the role of altered osteoblast metabolism in their study, which investigated whether these drugs affect proresorptive activity, or alter levels of osteoprotegerin and receptor activator of nuclear factor κB ligand (RANKL) in affected joints.

Their data showed that 200 μg/ml chondroitin sulfate, 50 μg/ml or 200 μg/ml glucosamine sulfate, or a combination of 200 μg/ml chondroitin sulfate and 200 μg/ml glucosamine sulfate affected neither basal levels nor vitamin-D_3-induced release of alkaline phosphatase or osteocalcin. However, both drugs upregulated osteoprotegerin expression in patients with osteoarthritis, irrespective of whether they were receiving vitamin D supplements. Chondroitin sulfate and the combination therapy reduced the expression of RANKL in patients not receiving vitamin D, but in those taking vitamin D, the effect failed to reach significance.

The authors conclude that, while the two drugs do not influence cell integrity or bone biomarkers, chondroitin sulfate either alone or together with glucosamine sulfate increases the expression ratio of osteoprotegerin: RANKL, suggesting they might help slow down the degeneration of subchondral bone in osteoarthritis.

Original article Tat SK *et al.* (2007) Chondroitin and glucosamine sulfate in combination decrease the pro-resorptive properties of human osteoarthritis subchondral bone osteoblasts: a basic science study. *Arthritis Res Ther* **9:** R117

Etanercept reduces cytokine production by T_H17 cells in patients with psoriasis

The newly recognized T-helper lymphocyte subset T_H17 has been implicated as a central component in psoriasis pathogenesis. Etanercept, a tumor necrosis factor (TNF) blocker, is an effective treatment for patients with this disease, but its specific effects on T_H17 activity are unclear. Zaba and colleagues studied the molecular and cellular effects of TNF blockade on the modulation of cytokine production by T_H17 and T_H1 cells in patients with psoriasis.

Etanercept 50 mg was administered to 20 patients twice weekly for 12 weeks. At the end of treatment, epidermal thinning and normalization of keratinocyte differentiation were seen in 16 patients; data from these patients were analyzed to study immunologic responses to etanercept treatment in psoriatic skin lesions.

Etanercept treatment significantly downregulated IL-17 and IL-22 (the main products of T_H17 cells) at weeks 1 and 2, respectively; by contrast, interferon-γ (the main product of T_H1 cells) levels were not significantly reduced until week 12. Dendritic cells (DCs) that secrete TNF-inducible nitric-oxide synthase are major pathogenic mediators of psoriasis; their products were also rapidly downregulated within the first 2 weeks, as were maturation markers of myeloid DCs.

The authors propose that etanercept causes early inhibition of cytokine production by inflammatory DCs, which reduces the activity of T_H17 cells; however, disease resolution seems to require the elimination of T_H1 cells, which occurs later in the treatment course.

Original article Zaba LC *et al.* (2007) Amelioration of epidermal hyperplasia by TNF inhibition is associated with reduced Th17 responses. *J Exp Med* **204:** 3183–3194