OSTEOARTHRITIS

Sclerostin inhibits Wnt signaling in OA chondrocytes and protects against inflammation-induced cartilage damage

Wnt- β -catenin signaling has an important role in bone and cartilage homeostasis in the adult skeleton, and has been implicated in the process of cartilage degradation in osteoarthritis (OA). Sclerostin (SOST) is a potent inhibitor of Wnt signaling and a regulator of bone metabolism. Little is known about changes in SOST expression or activity in the context of OA: decreased numbers of SOST-positive osteocytes are associated with increased cortical bone density in hip OA, and SOST has recently been shown to be expressed by chondrocytes in mineralized cartilage, indicating a potential role for this protein in global joint pathology in OA. Chan and colleagues performed a range of experiments to characterize the regulation of SOST in OA chondrocytes and its potential effects on cartilage loss.

The authors obtained osteochondral specimens from sheep that had undergone unilateral medial meniscectomy to induce OA 3 months earlier. Considerably

increased SOST immunostaining intensity and numbers of SOST-positive chondrocytes were observed in areas of cartilage degradation in post-meniscectomy specimens compared to specimens from sham-operated animals. Positive chondrocyte SOST staining was also observed in specimens obtained from mice with destabilized medial meniscus (DMM)-induced OA and in human specimens obtained from patients with late OA undergoing knee replacement.

Expression of SOST mRNA in chondrocytes was found to be significantly upregulated in response to stimulation with IL-1 α , but not tumor necrosis factor, in *ex vivo* cartilage culture of ovine osteochondral specimens. Interestingly, SOST seemed to inhibit Wnt- β -catenin signaling and expression of catabolic metalloproteinases, while at the same time also decreasing the mRNA levels of aggrecan, type II collagen and tissue inhibitors of metalloproteinases. SOST was also shown to inhibit IL-1 α -mediated

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aggrecanolytic. These findings indicate a regulatory role for SOST in OA pathogenesis, but seem to also suggest a dual effect in promoting subchondral bone loss while inhibiting cartilage degradation.

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Original article Chan, B.Y. *et al.* Increased chondrocyte sclerostin may protect against cartilage degradation in osteoarthritis. *Osteoarthritis Cartilage* doi:10.1016/j.joca.2011.04.014