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OSTEOARTHRITIS

UCMA links cartilage and bone in OA

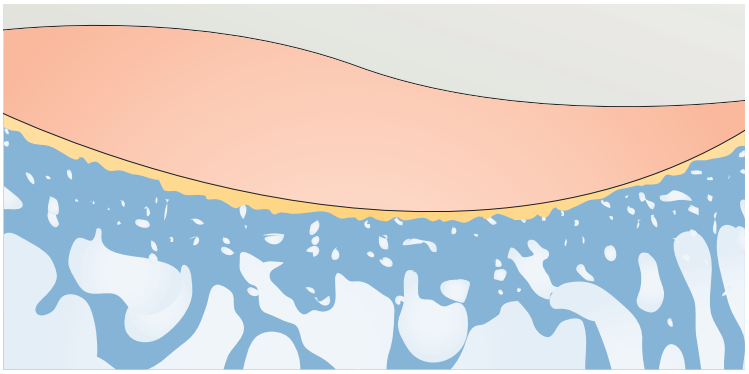
Changes in articular cartilage and subchondral bone are interconnected in osteoarthritis (OA), but the molecular mechanisms underlying bone–cartilage interactions are incompletely understood. New research shows that the chondrocyte-specific protein unique cartilage matrix-associated protein (UCMA, also known as upper zone of growth plate and cartilage matrix associated) not only stimulates subchondral bone turnover but also supports cartilage integrity, and could thus provide a link between cartilage and bone changes in OA.

"In order to establish the physiological role of UCMA, we generated a UCMA-deficient mouse strain," explains corresponding author Michael Stock. Previous work had established that these UMCA-deficient mice do not display any overt alterations in skeletal development; the current study investigated the relevance of UCMA to joint integrity under pathological conditions.

The researchers first demonstrated that UCMA expression is upregulated in human and mouse osteoarthritic cartilage. In a mouse model of OA induced by destabilization of the medial meniscus (DMM), cartilage damage, proteoglycan loss and chondrocyte cell death were exacerbated in UCMA-deficient mice compared with their wild-type littermates, suggesting UCMA might have chondroprotective effects. On the other hand, UCMA-deficient mice showed less pronounced osteophyte formation and subchondral bone sclerosis than wild-type mice following DMM surgery. Moreover, osteoblast and osteoclast numbers were lower in UCMA-deficient mice with experimental OA than their wild-type counterparts, indicating a role for UCMA in promoting bone turnover. Consistent with this notion, recombinant UCMA stimulated osteoclast differentiation *in vitro*, and co-culture with cartilage explants from wild-type mice (but not UCMA-deficient cartilage explants) promoted osteoclastogenic differentiation of bone marrow-derived cells.

"Together these data introduce UCMA as a cartilage-derived factor that stimulates bone remodelling during experimental OA," explains Stock. He notes that further investigations will explore the signalling pathways by which UCMA activates osteoclastogenesis, as well as the relevance of UCMA's aggrecanase-inhibiting properties in the context of novel therapies for OA and other joint diseases.

Sarah Onuora



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ORIGINAL ARTICLE Stock, M. *et al.* A dual role for UCMA in osteoarthritis - Inhibition of aggrecanases and promotion of bone turnover. *Arthritis Rheumatol.* http://dx.doi.org/10.1002/art.40042 (2017)

FURTHER READING Goldring, S. R. & Goldring, M. B. Changes in the osteochondral unit during osteoarthritis: structure, function and cartilage–bone crosstalk. *Nat. Rev. Rheumatol.* **12**, 632–644 (2016)