the cartilage matrix. Moreover, S100A8 and S100A9 were correlated with VDIPEN and NITEGE cartilage breakdown epitopes.
In addition, S100A8 and S100A9, but not the S100A8/A9 heterodimer, upregulated expression of MMP1, –3, –9 and –13 (3- to 6-fold) and cytokines interleukin (IL)-6, IL-8 and MCP-1 (3- to 24-fold) in human OA chondrocytes, on both mRNA and protein level. Furthermore, S100A8 and S100A9 downregulated mRNA expression of matrix molecules aggrecan and collagen type II (2- to 3-fold). Finally, the authors compared the effects of S100A8 and/or S100A9 on OA chondrocytes with those on non-OA chondrocytes. The catabolic effect of S100A8 and S100A9 on MMP1, MMP3 and aggrecan was significantly higher in OA chondrocytes compared to non-OA.
Conclusions S100A8 and S100A9 are found in and around human chondrocytes. S100A8 and S100A9, but not the heterodimeric S100A8/S100A9 complex, can skew human chondrocytes towards a catabolic phenotype promoting cartilage breakdown. This skewing seems to be specific for chondrocytes from OA patients.
S100A8 and/or S100A9 may prove crucial markers for measuring cartilage destruction.

A193 S100A8 AND S100A9 INDUCE A CATABOLIC SHIFT IN CHONDROCYTES FROM HUMAN OSTEOARTHRITIS PATIENTS

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Background and objective S100A8 and S100A9 are damage associated molecular patterns that are associated with inflammation and cartilage and bone erosion during human rheumatoid arthritis. They are produced in large amounts by monocytes and activated macrophages and can signal via Toll-like receptor 4. Recent studies in our lab show that S100A8 and S100A9 are also associated with cartilage degradation in experimental osteoarthritis (OA). In the present study, the authors investigated whether S100A8, S100A9 and/or S100A8/S100A9 complex could activate human chondrocytes and skew them towards a cartilage breakdown phenotype. Moreover, the authors wondered whether this catabolic shift was specific for chondrocytes from OA patients.
Methods S100A8 and S100A9 protein detection was performed in human cartilage from OA and non-OA donors using immunohistochemistry. In adjoining slides specific matrix metalloproteinase (MMP) and aggrecanases cartilage breakdown epitopes, VDIPEN and NITEGE, were detected with immunohistochemistry. Human chondrocytes from OA and non-OA donors were isolated and stimulated with recombinant S100A8, S100A9 and S100A8/A9 heterodimer. mRNA levels of MMP, cytokines and cartilage matrix molecules were determined with qPCR and protein levels using Luminex.
Results S100A8 and S100A9 proteins were abundantly present in and around chondrocytes derived from human cartilage as shown by immunolocalisation, suggesting that these small sized monomeric molecules (12 kD) are able to penetrate