MMP-3 IS A HIGHLY MECHANO-SENSITIVE GENE IN HUMAN SUBCHONDRAL OSTEOBLASTS

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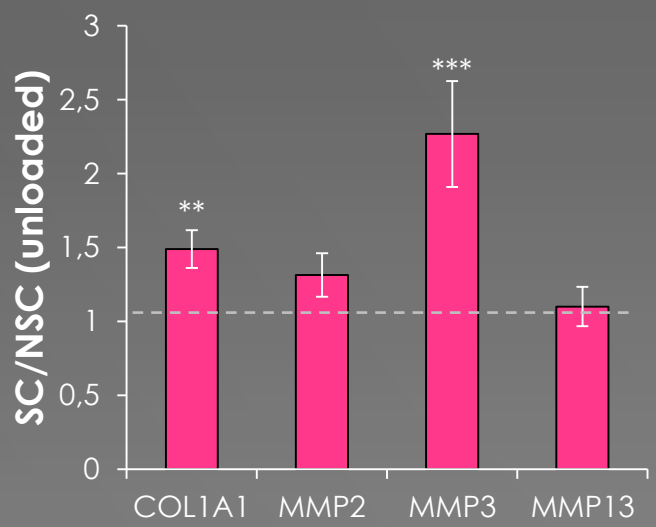
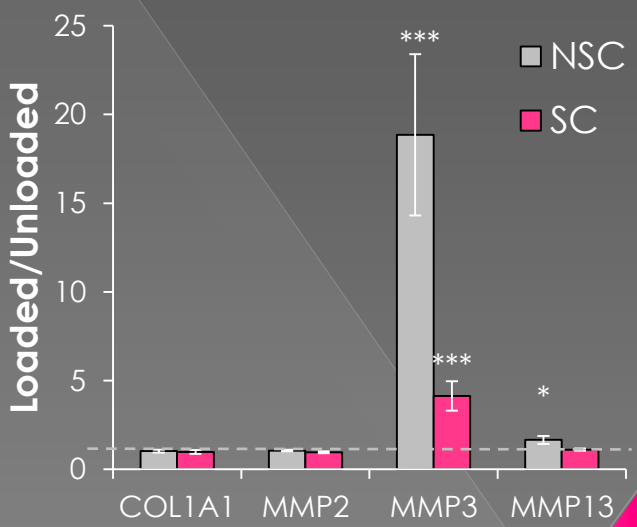
Purpose. Recent data showed that subchondral bone plays an important role in osteoarthritis (OA). Metabolic and morphologic modifications in this tissue contribute to the degradation of the overlaying cartilage. It was suggested that abnormal mechanical pressure applied to the articulation was responsible to these changes. Here, we evaluated the effects of compression on osteoblasts isolated from either nonsclerotic or sclerotic subchondral bone.

Methods. Osteoblasts were isolated from sclerotic (SC) or non-sclerotic (NSC) areas of human OA subchondral bone of 4 men. After 28 days, osteoblasts were surrounded by a newly synthesized matrix and formed a strong membrane. This osteoblasts-containing membrane was then placed onto a Biopress Flexercell plate and submitted to compression (1.67 MPa) for 2, 4 or 6 hours at the frequency of 1 Hz. The expression of COL1A1, MMP-2, MMP-3 and MMP-13 was evaluated by real time RT-PCR.

Results. Basal COL1A1 and MMP-3 mRNA levels were significantly higher in SC osteoblasts than in NSC (1.5-fold and 2.3-fold, $p<0.01$), while MMP-2 and MMP-13 expression was not different. Two to six hours of compression didn't significantly modify COL1A1 and MMP-2 gene expression in NSC or SC osteoblasts. MMP-3 expression was 19-fold increased after four hours of compression in NSC osteoblasts and 4-fold in SC osteoblasts. After four hours of compression, MMP-13 expression was 1.65-fold increased in NSC ($p<0.05$), but not significantly increased in SC osteoblasts. This stimulatory effect of compression on MMP-13 expression was not observed after 6h of compression.





Conclusions. By contrast with MMP-2, MMP-13 and type I collagen, MMP-3 is a highly mechano-sensitive gene in OA subchondral osteoblasts. These data indicate that mechanical stimuli through the synthesis of MMP-3 could be responsible for abnormal subchondral bone remodeling and subjacent cartilage matrix degradation in OA. This finding offer new perspective of research to explain the role play by mechanical stimuli in OA pathogenesis.

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