**Avocado/Soybean Unsaponifiables Prevent Osteoarthritic Subchondral Osteoblasts-Induced Cartilage Degradation.**

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**Introduction.** Previously, we have demonstrated that osteoblasts from the sclerotic subchondral bone express a particular phenotype characterized by an overproduction of IL-6, TGF-β1, ALP and OC but similar amount of IL-1β than non sclerotic osteoblasts.

**Aim of Study.** To determine the effects of avocado/soybean unsaponifiables (ASU) on osteoarthritic osteoblasts-induced chondrocyte metabolism dysregulation.

**Methods.** Human chondrocytes were isolated from OA cartilage and cultured in alginate beads for 4 days in the absence or in the presence of OA subchondral osteoblasts in monolayer (co-culture system). Before co-culture, OA osteoblasts were incubated or not with 10 µg/ml ASU for 72 hours. Aggrecan (AGG), type II collagen (COL2), matrix metalloproteases (MMP)-3 and -13 mRNA levels in chondrocytes were quantified by real time polymerase chain reaction. Aggrecan production was assayed by a specific enzyme amplified sensitivity immunoassay (EASIA).

**Results.** OA osteoblasts induced a significant inhibition of AGG production (-27%, p < 0.001) and AGG (-36%, p < 0.001) and COL2 (-78%, p < 0.001) gene expression but significantly increased MMP-3 and MMP-13 gene expression by chondrocytes in alginate beads (1.65 and 2 times, respectively, p < 0.001). Pre-treatment of OA osteoblasts with ASU fully prevented the inhibitory effects of OA osteoblasts on AGG production (p < 0.01), and increased by 2-fold the COL2 expression by chondrocytes (p < 0.001). The treatment of OA osteoblasts with ASU did not modify the expression of MMPs by chondrocytes.

**Conclusions.** These results demonstrate that OA subchondral osteoblasts could contribute to cartilage degradation by stimulating chondrocytes to produce more matrix metalloproteases and by inhibiting their production of AGG. ASU prevent osteoblasts-induced matrix molecules inhibition, suggesting a new mechanism of action for this drug.