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

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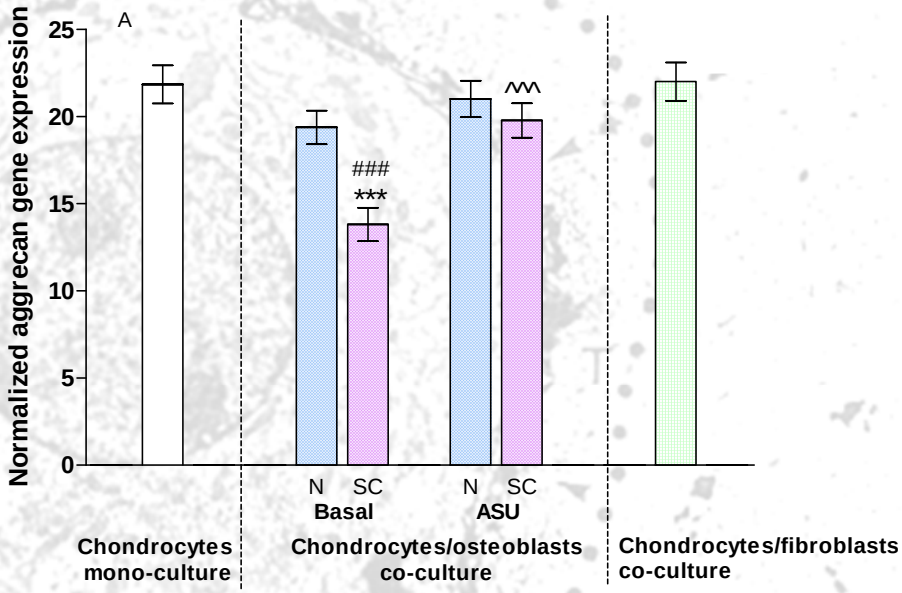
Introduction. Previously, we have demonstrated that osteoblasts from the sclerotic subchondral bone express a particular phentoype characterized by an overproduction of IL-6, TGF-β1, ALP and OC but similar amount of IL-1β than non sclerotic osteoblasts.

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.



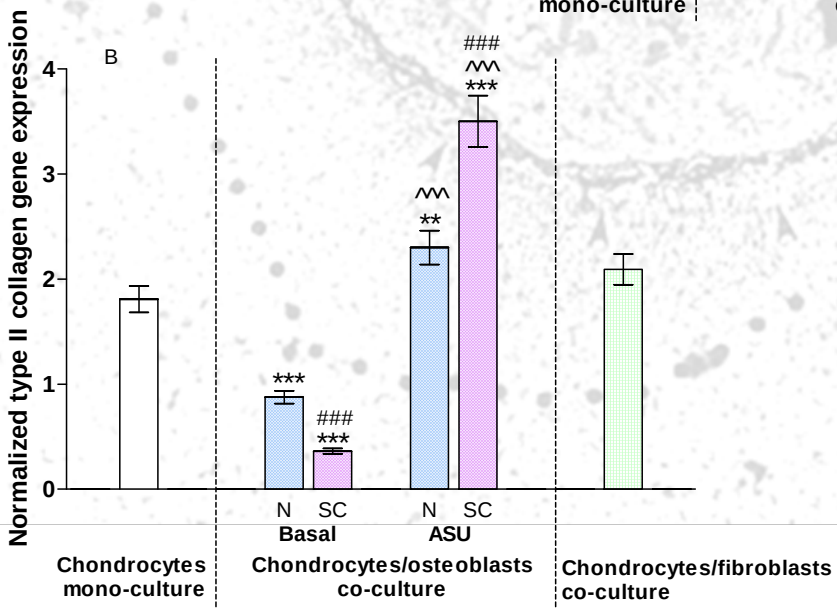


*Figure 1: GADPH-normalized AGG (A) and COL2 (B) gene expression by chondrocytes cultured 4 days with or without osteoblasts from non sclerotic (N) or sclerotic (SC) subchondral bone zones or normal skin fibroblasts. Osteoblasts were pre-treated or not with 10 µg/ml ASU during 72h before co-culture. Results are means of 3 co-culture experiments each realised in quadruplicate +/- SEM. ** p<0.01 and *** p<0.001 between co-culture and mono-culture experiments, ### p<0.001 between N and SC osteoblastes, ^^^ p<0.001 between basal and cytokine pre-treated osteoblasts.*

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.