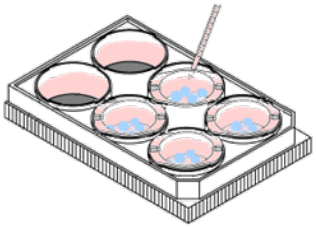
# Subchondral bone osteoblasts induce phenotypic changes in human osteoarthritic chondrocytes

Christelle Sanchez[1], Michelle A. Deberg[1], Nathalie Piccardi[2], Philippe Msika[2], Jean-Yves L. Reginster[1] and Yves E. Henrotin[1]

[1] Bone and Cartilage Research Unit, Liège, Belgium
[2] Laboratoires Expanscience, Epernon, France

***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.

***Objective.*** To determine the influence of osteoarthritic (OA) subchondral osteoblasts on the phenotype of human chondrocytes.



***Methods.*** Human chondrocytes were isolated from OA cartilage and cultured in alginate beads for 4 days in the absence or in the presence of human OA subchondral osteoblasts in monolayer. Sox-9, type I, II and X collagen (COL1, COL2, COL10), osteoblasts stimulating factor (OSF)-1, parathyroid hormone related peptide (PTHrP) and its receptor (PTHR), and bone alkaline phosphatase (ALP) mRNA levels in chondrocytes were quantified by real time polymerase chain reaction.

***Results***. In co-culture with subchondral osteoblasts from sclerotic or non sclerotic zones, chondrocytes expressed significantly less sox-9 and COL2 mRNA compared to chondrocytes cultured alone. The decrease of Sox-9 and COL2 gene expression was significantly more pronounced in the presence of sclerotic (SC) than in the presence of non sclerotic (N) subchondral osteoblasts (SC vs N $p < 0.001$). OSF-1 mRNA level in chondrocyte was increased by both N and SC osteoblasts, but to a larger extent by SC osteoblasts (SC vs N $p < 0.001$). PTHrP gene expression by chondrocytes was 17-fold increased by N osteoblasts but 4-fold inhibited by SC osteoblasts. SC, but not N osteoblasts, induced a significant decrease of PTH-R gene expression. In our experimental conditions, chondrocytes did not express COL1, COL10 or ALP, even after four days of co-culture with osteoblasts.

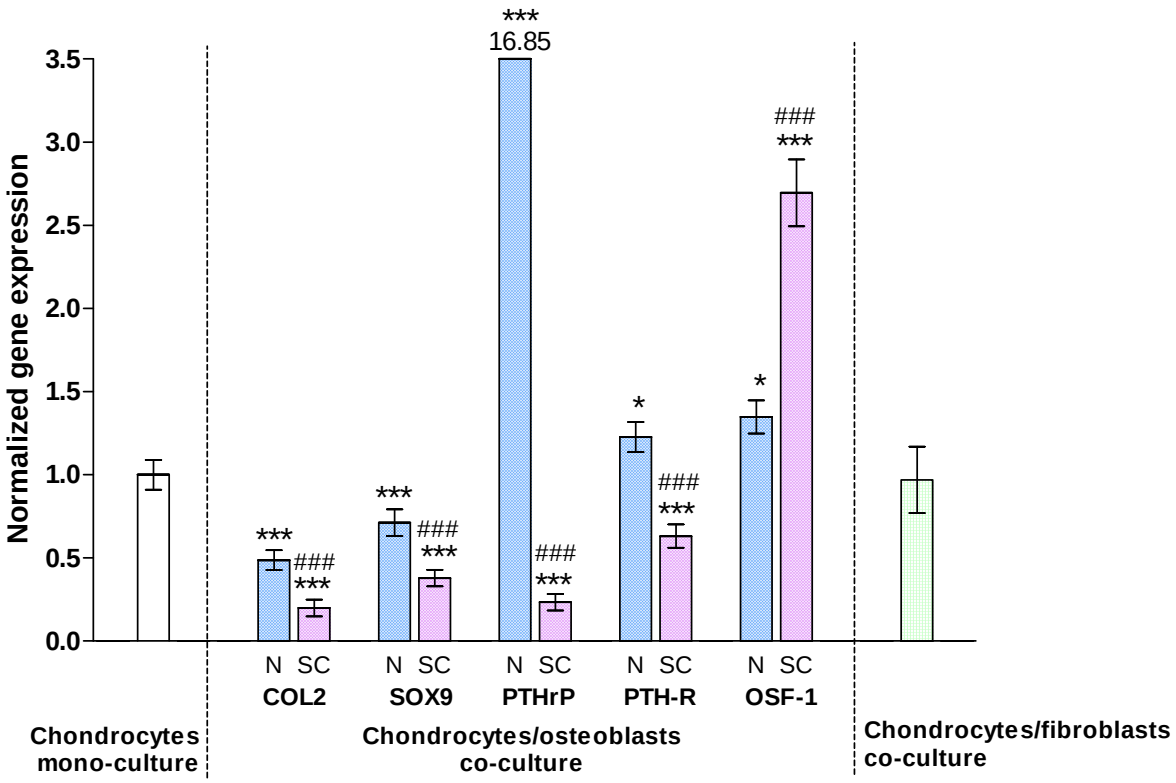



***Figure 1****: GADPH-normalized COL2, SOX9, PTHrP, PTH-R and OSF-1 gene expression by chondrocytes cultured 4 days with or without osteoblasts from non sclerotic (N) or sclerotic (SC) subchondral bone zones or normal skin fibroblasts. Results are means of 3 co-culture experiments each realised in quadruplicate +/- SEM. * $p<0.05$ and *** $p<0.001$ between co-culture and mono-culture experiments, ### $p<0.001$ between N and SC osteoblastes,.*

***Conclusions***. In co-culture with OA subchondral osteoblasts, chondrocytes initiate a dedifferentiation process, characterized by a decrease of sox-9 and COL2 gene expression, and initialize hypertrophic differentiation as indicated by an increase of OSF-1 expression and a decrease of PTHrP gene expression. These findings suggest that OA osteoblasts could initialize chondrocyte phenotype shift occurring in OA cartilage.