Association between CHONDROCYTE HYPERTROPHY and ANGIOGENESIS of cartilage in OSTEOARTHRITIS

PURPOSE
Chondrocyte hypertrophy is commonly observed in osteoarthritic (OA) cartilage, associated with matrix mineralization and vascularization. As hypertrophic differentiation of chondrocytes is an important feature of osteoarthritis, we developed a model of culture of hypertrophic chondrocytes in order to study the functional consequences of hypertrophic OA chondrocytes. The aim of this study was to investigate the link between hypertrophic differentiation of chondrocytes and angiogenesis in OA in order to demonstrate that OA hypertrophic chondrocytes expressed an angiogenic phenotype and that some specific factors could be implicated in both processes.

RESULTS
In alginate beads, OA chondrocytes cultivated 28 days in serum-supplemented medium but not in medium enriched with UG underwent a hypertrophic differentiation process. Indeed, culture of OA chondrocytes in FBS enriched medium was characterized by significant increased expression of hypertrophic markers (col10a1: p<0.05; runx2: p<0.01; MMP13: p<0.001) (Figure 1A) and activity of mineralization enzymes (PA: p<0.001; NTPPPH: p<0.001) (Figure 1B) with time of culture.

Functional angiogenesis assays showed that hypertrophic chondrocytes positively influenced migration (p<0.0001) (Figure 2A), invasion (p<0.001) (Figure 2B) and wound healing (p=0.0005) (Figure 2C and D) by endothelial cells.

Among the screened angiogenic factors expressed by OA chondrocytes, bone sialoprotein (BSP) expression (Figure 3A) and production (Figure 3B) (65 kDa) were highly upregulated in hypertrophic chondrocytes (p<0.05).

CONCLUSIONS
Our culture model allowed to mimic hypertrophic differentiation of chondrocytes and to investigate the relationship between this process and functional invasion and migration of endothelial cells, two functional steps in the process of angiogenesis. The results obtained in this study highlighted BSP as a specific factor that could be implicated in hypertrophic differentiation of chondrocytes and cartilage angiogenesis.