BCP crystals induce hypertrophic differentiation of chondrocytes by activating canonical WNT signaling

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Background
Calcification of cartilage is a common finding during osteoarthritis (OA) and is directly linked to the severity of cartilage degradation. We have found in a previous study that basic calcium phosphate (BCP) crystal calcification is present in murine and human OA cartilage. The observed cartilage changes resemble aspects of endochondral ossification. In this study we aim to investigate the effect of BCP crystals on articular cartilage matrix changes.

Methods
The tip-toe walking (ttw/ttw) mouse that carries a mutation in the cryap-1 gene encoding for NPP1 was used as a natural model of OA. Using von Kossa staining of tibia joint sections we assessed the calcification of articular cartilage and the severity of OA using the Mankin score over a time course from 8 to 22 weeks and compared the results to DMM induced OA. We analysed the influence of BCP crystals on chondrocyte phenotype using quantitative RT-PCR for the marker genes MMP13, PCNA and aggrecan. We compared these findings with data from ttw/ttw micromass cultures. The influence of BCP crystals on matrix composition in vitro was investigated in micro mass cultures with Safranin-O/ von Kossa staining and Alcian blue/ PAS staining pH 1 of wt articular cartilage w/o induction of OA using the DMM model.

Figure 1: Changes in articular cartilage matrix in tw/ttw mice

Figure 2: Matrix production is altered in tw/ttw articular cartilage

Figure 3: Canonical WNT signalling is activated by BCP crystals

Figure 4: Effects of BCP crystals on the chondrocyte phenotype

Figure 5: Ca2+ levels are in creased upon BCP stimulation

Conclusion
The calcification of articular cartilage seems to be associated with activation of canonical WNT signalling and subsequent hypertrophic differentiation of chondrocytes. Our data support the notion that OA is characterized by the re-initiation of developmental programmes associated with endochondral ossification.

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