focally in degenerated cartilage and differentially in FJ with active bone marrow infiltrates. TrkA was primarily found in all bone marrows and capsular tissues but not in cartilage. TrkA expression colocalized with osteocalcin in subchondral bone, indicating an association with new bone formation. SP strongly positive cells were found in the bone marrow, cartilage and synovial tissue of all FJ.

Abstract AB0100 – Figure 1

Conclusions: Here we define for the first time tissue compartments of the NGF axis in human FOA. The findings indicate that neurogenic inflammation is prevalent in different compartments of FOA. Based on these data NGFi might be efficient by targeting inflamed joint capsule or subchondral bone marrow as a source of pain. NGFi may thus have an impact on bone remodelling. Further studies are needed to more precisely examine this mechanism.

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AB0101

MESENCHYMAL STEM CELLS DERIVED FROM BONE MARROW, UMBILICAL CORD AND ADIPOSE TISSUE DO NOT HAVE THE SAME EFFECT ON HUMAN OSTEOARTHRITIC CARTILAGE

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Background: Osteoarthritis is a chronic debilitating disease characterised by degeneration of cartilage, synovitis and osteophytes formation.¹ This disease does not only affect aged people but it afflicts also young athletes where until today no medications has proven efficacy in stopping the progression of the disease and/or regenerate the loss of cartilage.² Recently cell therapy has attracted attention in many medical fields and especially in rheumatology and orthopaedic specialty. Stem cells due to their differentiation capacity, trophic and paracrine effects have been shown to serve as promising new modality in treating osteoarthritis.^{3,4}

Objectives: Our objective in this study is to investigate the effect and mechanism of action of the three sources of stem cells; bone marrow derived stem cells (B-MSC), adipose derived stem cells (A-MSC) and umbilical cord stem cells (U-MSC) on osteoarthritic chondrocytes.

Methods: Mesenchymal stem cells were isolated from bone marrow, adipose tissue and umbilical cord from 5 different donors respectively and cocultured with human osteoarthritic chondrocytes obtained from 5 patients undergoing total knee arthroplasty. The effect autophagy was determined using flow cytometry analysis. Quantitative polymerase chain reaction (qPCR) and ELISA were used to measure the changes in the major factors playing a role in OA such as (a disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5), Metalloproteinases (MMP-3, MMP13), tissue inhibitor of metalloproteinases (TIMP-1–2–3), Collagen, Cox-2, Il-6, the regulators of autophagy FOXO1, FOXO3, and LC3II and Beclin I in the tissues and cocultured media.

Results: In our study we found that the three stem cells sources increased significantly the proliferation of chondrocytes, and increased autophagy via increasing

Beclin 1 and LC3II, along with its regulators FOXO1, FOXO3 in human osteoarthritic chondrocytes with $p < 0.05$. Furthermore, the three sources of stem cells caused a dose dependent significant decrease in MMP-3, MMP-13, ADAMTS-5, IL-6, CCL20 and COX-2 with $p < 0.05$. Aggrecan, collagen, TIMPs were also significantly increased by the co-culture of A-MSC, B-MSC, U-MSC.

Conclusions: These results suggest that stem cells could be a promising therapeutic target for the treatment of osteoarthritis.

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AB0102

THE GINGER DERIVATIVE 6-SHOGAOL AS A TREATMENT IN OSTEOARTHRITIS. MODULATION OF CHONDROCYTE HYPERTROPHY AND MATRIX CALCIFICATION

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Background: Osteoarthritis (OA) is a complex joint disease characterised by a progressive loss of articular cartilage (AC), synovial inflammation and subchondral bone alterations. The latest theories of OA pathogenesis implicate the interplay between mechanical damage and chronic inflammation that has been associated to the activation of the innate immune system, intricately involved in the development of this low-grade inflammation. During the course of OA, Toll like receptor (TLR) activation has been related to the release of cytokines and inflammatory mediators, which further aggravate synovitis and AC damage.¹ In this scenario, hyaline chondrocytes seem to acquire a hypertrophic-like phenotype associated to AC degradation. 6-shogaol (6S), an effective anti-inflammatory Ginger derivative, is able to inhibit TLR4-mediated innate immune responses.²

Objectives: Our aim was to study the therapeutic benefit of 6-shogaol studying its anti-inflammatory effects in an OA mice model, and in the modulation of hypertrophic markers in chondrocyte cultures.

Methods: C57BL/6 male mice were randomly assigned to two groups: control (n=7) and OA (n=17). OA was induced by transection of the medial menisco-tibial ligament. Nine OA mice started receiving 6S (15 mg/kg/day; OA +6S) since surgery. After 8 weeks, animals were euthanized and joints were collected. Chondrogenic differentiation was induced *in vitro* in the pre-chondrogenic cell line ATDC5 in presence or absence of 5×10^{-6} M 6S. Gene expression of hypertrophic markers, as well as mineralization and proteoglycan synthesis were determined.

Results: Both synovial inflammation and AC damage were more severe in OA animals (Control: 0.1 ± 0.1 ; OA: 3.0 ± 0 ; $p < 0.005$, and Control: 0.5 ± 0.2 , OA: 5.4 ± 0.6 ; $p < 0.005$, respectively) with a significant reduction in OA+6S animals (2.4 ± 0.2 ; $p < 0.05$ and 2.6 ± 0.5 $p < 0.01$ vs. OA, respectively). Collagen X and MMP13 immunohistochemistry showed an increase in the AC of OA and OA-6S mice, while a significant reduction was found in 6S-treated mice (ColX: Control: 0.13 ± 0.03 , OA: 0.93 ± 0.1 ; OA-6S: 0.43 ± 0.1 ; $p < 0.05$ and MMP13: Control: 0.35 ± 0.1 , OA: 0.68 ± 0.1 , OA-6S: 0.28 ± 0.07 , $p < 0.05$). Similar results were found in the synovium and meniscus for these two markers. 6S was able to significantly inhibit the expression of Collagen X, Ihh and MMP13 in ITS-stimulated cells after 14 and 21 days of culture. Furthermore, 6S prevented the increase in mineralization and proteoglycan synthesis in ITS-stimulated ATDC5 cells after 14 days of culture ($p < 0.05$), as seen by Alizarin red and Alcian blue staining, respectively.

Conclusions: Our results showed that 6S significantly prevented cartilage degradation and synovial inflammation, in parallel to a reduction in the presence of hypertrophic markers in the cartilage of OA mice. *In vitro*, 6S inhibited the chondrogenic differentiation of ATDC5 cells. These results suggest that 6S could work as a good treatment in OA both inhibiting differentiation markers and reducing the severity of joint damage in an OA murine model.