over-expression of PGC-1 β promoted migration and invasion of RA-FLS (all $p < 0.05$, figure 1A–C). Down-regulation of PGC-1 β in RA-FLS significantly decreased the expression of MMP-3 and MMP-9 in the culture supernatant which was measured by Proteome Profiler human protease array (MMP-3: $p = 0.032$, MMP-9: $p = 0.037$). Further qRT-PCR and western blot analysis verified that both mRNA and protein expression of MMP-3 and MMP-9 in RA-FLS were significantly decreased compared with Lv-sh-GFP transfection group (all $p < 0.05$, figure 1D). Down-regulated PGC-1 β in RA-FLS significantly suppressed the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK in protein level, while over-expression of PGC-1 β promoted the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK (all $p < 0.05$, figure 1E).

Abstract AB0098 – Figure 1. Effects of PGC-1 β on the migration and invasion capacity as well as proteases expression, canonical and non-canonical NF- κ B signalling pathway activation in RA-FLS. **A–C** After down-regulation or over-expression of PGC-1 β , wound healing and transwell assay showed the capacity of horizontal migration (**A**), vertical migration (**B**) and invasion (**C**) of primary RA-FLS. **D** After down-regulation or overexpression of PGC-1 β , the expression of MMP-3 and MMP-9 was measured by qRT-PCR and western blot. **E** After down-regulation or overexpression of PGC-1 β , the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK was measured by Western blot. The data were representative as means $\pm$ SD from six different RA patients. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Conclusions: Our findings suggested that PGC-1 β facilitates the migration and invasion capacity and MMP-3/9 expression in RA-FLS through activation canonical and non-canonical NF- κ B signalling pathway.

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AB0099 ARTHROSCOPIC PECULIARITIES OF THE INFLAMMATORY PROCESS OF SYNOVIAL SHELL IN UROGENIC ARTHRITIS

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Background: In recent years there has been an increase in the incidence of reactive arthritis (ReA), associated with urogenital infection. Chronic synovitis of urogenital etiology is a nonspecific process, pathogenesis is very close to rheumatoid arthritis (RA), which complicates differential diagnosis. According to the literature, the inflammatory process in the synovial membrane (SM) supports the persistence of chlamydia, which reduces the effectiveness of standard anti-

inflammatory therapy of arthritis in patients with undifferentiated seronegative oligoarthritis, spondyloarthropathy, RA.

Objectives: Arthroscopic assessment of the level of the inflammatory process in the synovial membrane, depending on the duration of the disease and the activity of the pathological process in patients with urogenital arthritis.

Methods: The study involved 39 patients with RA of urogenital etiology complicated by synovitis of knee joint (KJ) were examined; 23 of them were women and 16 men; mean age was 35.5 ± 38.0 years. They received inpatient treatment at the Department of Traumatology and Orthopaedics of the 2nd TMA Clinic in 2014–2016 years. All these patients underwent diagnostic arthroscopy of KJ. Laboratory tests included enzyme-linked immunosorbent assay (ELISA) for TORCH infection, a polymerase reaction (PCR), determination of a rheumatic factor in synovial fluid and blood before and after treatment, arthroscopy of the joint.

Results: In arthroscopic examination in the acute phase (early period) of ReA, dull SM, vasodilation, and oedema are revealed, which is accompanied by an increase in the production of turbid synovial fluid (SF). On the surface of SM there are sections of fibrin filaments, expansion and hyperemia along the vessels. In the long-term (subacute phase) these violations partially disappear. The surface of the synovium can again become single-rowed, with moderate hyperemia of the vessels. The deposits of fibrin on the entire surface of SM can be significant. However, with reduced immunoreactivity of the organism, the reactive synovitis persists for a long time, and the chronic course of the pathological process leads to abundant deposits of fibrin masses and to the formation of villi in the form of large and flat petals. In some parts of the vascular vessels are pale, accompanied by disorganisation of the collagen frame of SM, which directly affects the cells of the articular cartilage.

Conclusions: Thus, reactive urogenital arthritis due to the persistence of an infectious agent is characterised by the polymorphism of the damage to the joint and cartilage of the joint. The arthroscopic changes revealed at various stages of the inflammatory process reflect the reactivity of the pathological process and determine the extent of the lesion. Arthroscopic examination of biopsy specimens of SM and cartilage allows to determine the dynamics of the disease, the degree of lesion, evaluate the effectiveness of the preventive and therapeutic measures being carried out, and also to determine the indications for joint synovectomy.

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AB0100 NEUROGENIC INFLAMMATION CHARACTERISED BY NERVE GROWTH FACTOR, TRKA AND SUBSTANCE P IS PREVALENT IN HUMAN FACET JOINT OSTEOARTHRITIS

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Background: Facet joint osteoarthritis (FOA) is a frequent cause of chronic low back pain and spinal stenosis. Neuron-derived molecules regulate pain sensation and inflammation. Nerve growth factor (NGF) is one of the most important mediators for this mechanism that is termed neurogenic inflammation.¹ Among many other effects, it regulates substance P (SP) expression as pivotal downstream peripheral pro-inflammatory molecule. Consequently, NGF inhibitors (NGFi) as a novel class of pain medication have shown significant efficacy in OA and to some extent also low back pain. However, it is unknown which tissue compartments in facet joints are involved in NGF signalling.

Objectives: To determine expression patterns of NGF, its high affinity transmembrane tyrosine kinase A (TrkA) receptor and SP in cartilage, subchondral bone marrow and capsular tissues of facet joints (FJ).

Methods: Dissected human FOA specimens of six donors were examined. OA severity was graded on HE-stained tissue sections. NGF, TrkA and SP expression was evaluated by immunohistochemistry with monoclonal antibodies. Similarly, new bone formation was assessed by staining for osteocalcin.

Results: FJ had low (n=2), high (n=2) and intermediate (n=2) inflammatory bone marrow infiltrates. NGF was strongly expressed in capsular tissue (figure, 40x),

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.