AB0105 EFFECTS OF CARRAGEENAN INDUCED SYNOVITIS ON JOINT DAMAGE AND PAIN IN A RAT MODEL OF KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis (OA) is associated with ongoing pain and joint damage that can be punctuated by acute flares of pain and inflammation. Acute synovitis in normal knees might resolve without long-term detriment to joint function.

Objectives: We hypothesised that osteoarthritis is associated with impaired resilience to acute inflammation.

Methods: We induced synovitis by intra-articular injection of carrageenan into rat knees with or without meniscal transection-induced OA, and measured synovitis, weightbearing asymmetry (an index of pain behaviour), and joint damage up to 35 days after OA induction (23 days after carrageenan-injection).

Results: Intra-articular injection of carrageenan was followed by weightbearing asymmetry for 1 week, synovitis, indicated by a transient increase in knee diameter for 2 days after injection, and a more sustained (through day 23) increase in synovial macrophages, endothelial cell proliferation and vascular density compared with naïve controls. Meniscal transection was followed by weightbearing asymmetry and histological evidence of OA through day 35. Carrageenan-injection in OA knees was followed for 2 days by increased weightbearing asymmetry compared either to OA knees, or to carrageenan-injected, SHAM-operated knees. OA structural damage and synovitis at day 35 were greater after carrageenan injection on day 12 compared to saline-injected, MNX-operated knees, and compared to carrageenan-injected, SHAM-operated knees. Carrageenan injection alone did not induce OA in SHAM-operated knees.

Conclusions: OA knees were more sensitive to pain behaviour, inflammation and structural damage following an episode of acute inflammatory pain flare than were non-arthritic knees. Preventing inflammatory flares may be particularly important in preventing symptoms and long term joint damage in OA.

Disclosure of Interest: None declared

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AB0106 FIBRIN-TRIGGERED CHONDROSYNOVIAL ADHESION AS A NOVEL MECHANISM OF CARTILAGE DAMAGE IN RHEUMATOID ARTHRITIS

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Background: Synovial pannus infiltration and inflammatory cytokines production are the main factors responsible for cartilage damage in rheumatoid arthritis (RA). The crosstalk between inflammation and coagulation further amplifies and maintains chronic inflammation. Although synovial extravascular fibrin deposits in synovial fluid and synovial membranes being hallmarks of RA, there are no reports on direct fibrin deposition is widespread in RA, little is known about fibrin deposition and its relation to cartilage damage in RA.

Objectives: To investigate if fibrin deposition occurs in murine and human RA cartilage, and its relationship with cartilage degradation. Moreover, to determine the possible mechanism by which fibrin could play a role in the pathogenesis of RA.

Methods: Full-thickness cartilage explants were obtained from RA patients undergoing total knee replacement. Immunohistochemistry was performed on paraffin sections to study fibrin deposition, while Safranin-O staining was used to investigate cartilage damage. An *in vitro* model of chondrosynovial adhesion was established using primary human RA synoviocytes seeded on human RA cartilage explants. Adherent synoviocytes to cartilage were evaluated on H and E-stained histological sections and fibrin immunohistochemistry was performed on adjacent sections. Antigen induced arthritis (AIA) was induced in wild-type (WT) and fibrinogen knock-out mice and paraffin sections of knee joints assessed for fibrin deposition, cartilage damage, and chondrosynovial adhesion.

Results: In human RA cartilage, the extent of fibrin deposits positively correlated with the degree of cartilage degradation (figure 1). In WT mice, fibrin deposition was preferentially found on damaged cartilage and on cartilage areas in direct contact with synovial membrane (i.e. chondrosynovial adhesions) (figure 2). In contrast, cartilage degradation and chondrosynovial adhesion were significantly lower in fibrin deficient mice (figure 2). Moreover, loss of superficial cartilage layers stained with fibrin was observed in regions of chondrosynovial adhesion (figure 3). Finally, in the *in vitro* model, synoviocytes were found to adhere to human OA cartilage, especially in severely damaged and fibrin-rich areas (figure 4).

Abstract AB0106 – Figure 1

Conclusions: Our results demonstrate that fibrin deposition on cartilage is highly associated with chondrosynovial adhesion and subsequent cartilage erosion in RA. We hypothesise that fibrin mediates chondrosynovial adhesion especially during joint resting periods (i.e. night-time), leading to mechanical stripping of superficial cartilage layers following motion.

Disclosure of Interest: None declared

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AB0107 INFLUENCE OF COBALT (II) + AND CHROMIUM (III)-IONS ON BONE FORMATION IN HUMAN OSTEOBLAST-LIKE CELLS IN-VITRO

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Background: Healthy bone is a result of the homeostasis between bone formation and resorption. The process of bone formation includes two major functions, which are the secretion of the organic matrix (mainly type I collagen) and the deposition of minerals into this matrix. This function of osteoblasts can be affected by numerous factors, as hormones, inflammation, mechanical load and other external stimuli.

In patients with artificial joint replacements, the release of particles or ions from arthroplasties may exert local effects on the periprosthetic tissue leading to prosthesis loosening.

Objectives: It was the aim of the study to analyse the effect of Co²⁺ and Cr³⁺ ions on the capability of osteoblast-like cells to form bone.

Methods: Two human osteoblast-like cell lines MG63 and SaOs-2 were used to study the influence of Co²⁺ and Cr³⁺ ions on matrix secretion and mineralization. Cells (3 × 10⁵) were seeded in 2 ml DMEM (10% FCS) onto 12 well plates and stimulated with CoCl₂ and CrCl₃ in concentrations between 50–250 µM for 24 hours. Total RNA was extracted and changes of expression levels of collagen1A1 were analysed by real-time PCR. Secretion of collagen1 was analysed by Sirius Red staining (0.1% in water-saturated picric acid). After extraction of dye with 0.1N NaOH the absorption was measured at 540 nm.

For mineralization the cells were cultured for up to 4 weeks in DMEM (10% FCS) supplemented with 0.2 mM ascorbic acid, 10 nM dexamethasone and 10 mM glycerophosphate and different concentrations of Co²⁺ and Cr³⁺. Calcium deposits were detected by 1% Alizarin Red S staining (pH 4.1), for quantification the dye was extracted using cetylpyridinium chloride, the absorption was determined at 562 nm.

Results: We observed that SaOs-2 cells, the more differentiated cells compared to MG63, exhibited a high potential for mineralization but secreted low amounts of collagen type 1. In contrast, MG63 cells produced high amounts of collagen1 and had a low potential for mineralization. When cultures were treated with Co²⁺ and