

intra-articular injection of monoiodoacetate (MIA), and the joint degeneration was assessed with the OARSI cartilage degeneration score in histological assessments of the joints of the rats.

Results: The MCP-1 itself enhanced the autocrine of MCP-1 in OA and normal human cartilage and the Expression of collagen I, V, IX, XI and Matrix metalloproteinases (MMP) increased after Stimulation of MCP-1. The MCP-1 also induced the apoptosis of normal and OA chondrocytes. The CCR-2 antagonist retarded the establishment of a monoiodoacetate (MIA)-induced animal model of OA in rats.

Conclusions: The results of this study prove that the MCP-1-CCR2 ligand-receptor axis plays an important role in the progress of the OA's pathology. Inhibition of the MCP-1-CCR2 ligand-receptor axis may retard the pathological progress of human OA. And, we speculate that lots of OA patients that etiology is unclear can gain some cues from the MCP-1-CCR2 ligand-receptor axis, according to our present study.

506 BONE GEOMETRY OF THE HIP IS ASSOCIATED WITH OBESITY AND EARLY STRUCTURAL DAMAGE – A 3.0T MRI STUDY OF COMMUNITY-BASED ADULTS

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Purpose: The mechanism by which obesity increases the risk of hip osteoarthritis (OA) is unclear. One mechanism may be by mediating abnormalities in bony geometry, which may in turn be associated with early structural abnormalities, such as cartilage defects and bone marrow lesions (BMLs).

Methods: 141 older adults with no diagnosed hip OA had weight and body mass index (BMI) measured between 1990 and 1994 and again in 2009-10. Acetabular depth and lateral centre edge angle (LCEA), both measures of acetabular over-coverage, as well as femoral head cartilage volume, cartilage defects and BMLs were assessed with 3.0T MRI performed in 2009-10.

Results: Current BMI, weight and weight gain were associated with increased acetabular depth and LCEA (all $p \leq 0.01$). For every one millimetre increase in acetabular depth, femoral head cartilage volume reduced by 59mm^3 (95% CI 98mm^3 to 20mm^3 , $p < 0.01$). Greater acetabular depth was associated with an increased risk of cartilage defects (OR 1.22, 95% CI 1.03–1.44, $p = 0.02$) and BMLs (OR 1.29, 95% CI 1.01–1.64, $p = 0.04$) in the central region of the femoral head. LCEA was not associated with hip structure.

Conclusions: Obesity is associated with acetabular over-coverage. Increased acetabular depth, but not the LCEA, is associated with reduced femoral head cartilage volume and an increased risk of cartilage defects and BMLs. Minimising any deepening of the acetabulum, for example through weight management, might help to reduce the incidence of hip OA.

507 THE BENEFICIAL ROLE OF PAI-1 IN BONE-CARTILAGE INTERACTION

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Purpose: In osteoarthritis (OA) subchondral bone changes are seen in addition to cartilage changes. In treatments targeted at bone, such as treatment with strontium ranelate (Reginster, 2013), or treatments with bone involvement such as osteotomy (Jung et al, 2014) or joint distraction (Intema et al, 2012) cartilage repair has been demonstrated. These studies support the hypothesis that a reset of bone can lead to cartilage repair. However, the exact biochemical interactions and how this contributes to repair and degradation processes is less well known. Plasminogen activator inhibitor (PAI)-1, inhibits plasmin which accounts for higher levels of MMPs in OA. It is expressed in subchondral bone and cartilage. The present study evaluates the role of plasminogen activator inhibitor 1 (PAI-1) in bone-cartilage interaction and its direct effects on osteoarthritic cartilage.

Methods: Osteoblast culture supernatant from healthy ($n=14$) and OA ($n=16$) donors was tested on both healthy and OA cartilage and proteoglycan (PG) synthesis was studied. Expression levels of mediators were assessed in the osteoblast culture supernatants by Luminex

analysis. Subsequently, OA cartilage ($n=11$ donors) was cultured in absence/presence of PAI-1 and PG synthesis changes were studied.

Results: PG synthesis of OA cartilage was increased (+34%, $p=0.036$) upon addition of healthy osteoblast supernatant. Importantly, a decrease was seen when OA osteoblast supernatant was added to healthy cartilage (-31% PG synthesis, $p=0.001$). PAI-1 was expressed at significant higher levels in healthy osteoblasts compared to OA osteoblasts (184ng/ml vs 91ng/ml, resp. $p=0.015$). Moreover, osteoblast PAI-1 levels were positively correlated with PG synthesis ($r=0.595$, $p=0.042$) influenced by the osteoblasts. Culturing OA cartilage in direct presence of PAI-1 (2000ng/ml) revealed 33% ($p=0.026$) increase of PG synthesis confirming the beneficial role of PAI-1 in the osteoblast cultures.

Conclusions: Healthy osteoblast derived mediators lead to PG synthesis increase in OA cartilage, while it has no effect on healthy cartilage. Moreover, OA osteoblast derived mediators lead to a decrease in PG synthesis in healthy cartilage, but not in OA cartilage. Higher PAI-1 levels in these osteoblasts cultures are clearly correlated with higher PG synthesis in cartilage, which hints at a role for PAI-1 in cartilage repair. Its direct effects on OA cartilage, increasing PG synthesis, further confirmed the relevance of PAI-1. This supports that targeting bone directly or involvement of bone might be feasible as treatment for OA.

508 INVOLVEMENT OF TGFβ1 IN THE INITIAL PHASE OF TMJ AND KNEE OSTEOARTHRITIS

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Purpose: The objective of this study was to elucidate OA progression in an animal model of Stickler syndrome by assessing the expression of an identified inflammatory marker associated with OA, viz., TGFβ1. The study provides potential mechanistic insight into disease progression based on the temporal expression of TGFβ1 in knee and temporomandibular joints (TMJ).

Methods: The study involved mice carrying the autosomal semi-dominant disproportionate micromelia (Dmm/+) mutation in the C-propeptide coding region of the Col2a1 gene. Specifically, six wild type control (+/+) and six heterozygous (Dmm/+) mice were evaluated for each joint. The mice were euthanized at three, six, and nine months of age, and their TMJs and knee joints were isolated, fixed, decalcified, embedded in paraffin, and sectioned at 6μm thickness. Three months of age coincides with the initial detection of histopathology in several murine models of OA. To determine OA status, selected tissues were stained with Safranin O to identify proteoglycans and counterstained with Fast Green. The extent of staining and onset of OA were quantified using Modified Mankin and OARSI scoring systems. Selected tissue sections of each genotype were also stained immunohistochemically for the presence of TGFβ1, the inflammatory mediator that has been identified to play a role in OA progression.

Results: The results revealed Mankin and OARSI scores consistent with OA-like changes. These changes were detectable as early as three months in Dmm/+ mice when compared with normal joint biology observed in control animals. Compared to basal expression in control TMJs and knee joints, staining for TGFβ1 demonstrated augmented expression in Dmm/+ mice as early as three months of age, with overexpression persisting in six-month-old mutant mice, but then disappearing at nine months of age. The present study demonstrated that TGFβ1 was overexpressed in TMJ and knee articular cartilage of three- and six-month-old Dmm/+ mice when compared with age-matched controls.

Conclusions: Early TGFβ1 expression levels suggested that this inflammatory mediator is involved in the earliest stages of TMJ OA. Further studies are underway that could shed light on TGFβ1 and the use of other inflammatory markers such as HtrA1 and SMADs as possible targets for therapeutic intervention.

509 ACTIVATION OF THE RENIN-ANGIOTENSIN SYSTEM INTRODUCES OSTEOARTHRITIS

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Purpose: In 2013, we reported that the local renin-angiotensin system (RAS) can modulate the hypertrophic differentiation of chondrocytes.