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Purpose: Increased levels of reactive oxygen species with aging may contribute to age-related diseases including OA. In this study, we tested the hypothesis that overexpression of the anti-oxidant enzyme catalase, targeted to mitochondria, would reduce OA severity in mice.

Methods: Mouse stifle (knee) joints were obtained from male transgenic mice (C57BL/6 background) that overexpress human catalase localized to the mitochondria (MCAT). MCAT (n=12) and male C57BL/6 wild-type controls (n=11) from 3 age groups were studied: young adult (10 months old), older adult (18-21 months), and very old adult (33 months old). Paraffin embedded stifle joints were serially sectioned in a coronal plane. Two representative midcoronal sections were selected for evaluation and stained with hematoxylin & eosin (H&E) and Safranin-O stains. Sections were scored by an observer, blinded to groups, for articular cartilage structure (ACS) changes (0-12), Safranin-O staining (0-12), size of osteophytes, % area of chondrocyte death and morphometric measures of articular cartilage and subchondral bone area and thickness. Separate and combined results for the medial and lateral tibial plates were analyzed by ANOVA.

Results: Examination of combined results for wild-type and MCAT mice revealed that the young adult mice had minimal to no OA lesions with significantly (p<0.001) lower ACS and Safr-O scores, less cell death, and better morphometric measures than the two older groups of mice which did not differ significantly from each other. In the young adult mice, there were no significant differences between MCAT and wild-type mice in any of the measures. Because the two older groups had similar OA severity scores, the results in these two groups were combined in order to increase the numbers for analysis of differences between MCAT and wild-type. The sum of the ACS scores (med+lat) was significantly (p=0.04) lower in the MCAT (11.8±1.5) vs wild-type mice (17.4±1.8) (Fig. 1) as were the Safr-O scores (5.6±1.7 for MCAT and 10.2±0.8 for wt). The remainder of the measures did not differ significantly between groups but the trend was for better scores in the MCAT mice.

Conclusions: Naturally occurring OA-like lesions appear with aging in male C57BL/6 mice becoming prevalent by 18-21 months of age. Overexpression of catalase targeted to the mitochondria did not prevent lesions from developing but did significantly reduce OA severity measured by articular cartilage structure changes and loss of Safranin-O staining. These results support a role for mitochondrial reactive oxygen species in age-related OA.
ml of pre-hydrogel solution (poly(ethylene glycol) dimethacrylate (10% w/v), photoinitiator (0.05% w/w) (Irgacure 2959) in phosphate buffered saline) was exposed to 365 nm light (2 mW/cm²) for 10 min solidifying the solution and encapsulating the cells in gels of 5mm diameter and height. Inorganic pyrophosphate (Pi) was added to the culture medium at 1mM. Control gels did not receive PPI. Hydrogel properties were characterized by compressive modulus, equilibrium swelling ratio (mass swollen gel/mass of dry gel), and mesh size in the presence and absence of PPI. Cell-laden constructs were cultured for 48 hours. Cell viability was assessed using the LIVE/DEAD membrane integrity assay after 48 hours. Cell proliferation was assessed by [3H]-thymidine incorporation and proteoglycan synthesis by 35SO4 incorporation. An n=3 was used for each condition. A student’s t-test was performed with a p-value <0.05 considered significant.

**Results:** The presence of PPI did not affect the macroscopic properties of the hydrogel (Table 1). From the equilibrium swelling ratio, which is a measure of the amount of water the hydrogel imbibles, the mesh size was determined to between 18-20 nm indicating that PPI can readily diffuse through the hydrogel.

| Table 1. Macroscopic Properties of PEG Hydrogels in the Presence of PPI |
|-----------------------------|-----------------------------|-----------------------------|
| Compressive Modulus (kPa)   | Equilibrium Swelling Ratio  | Mesh Size (nm)              |
| Control                     | 110±17                      | 12±2.2                      | 18±4.4                      |
| PPI                         | 110±6.0                     | 13±2.0                      | 20±4.1                      |

The effects of PPI on cell proliferation and matrix production is given in Table 2. PPI had no significant effect on cell proliferation. However, PPI dramatically inhibited proteoglycan synthesis by 72%. There was a 2.7-fold increase in proteoglycan loss into the culture medium in the presence of PPI, which suggests that proteoglycans are being degraded and which is mediated by PPI.

<table>
<thead>
<tr>
<th>Table 2. Chondrocyte Response to PPI</th>
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<tr>
<td>Cell Proliferation (cpm/construct)</td>
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<tr>
<td>Proteoglycan Synthesis (cpm/construct)</td>
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<tr>
<td>Percent Proteoglycan Loss (%/construct)</td>
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*Denotes statistical significance from control

**Conclusions:** High levels of exogenously delivered PPI to chondrocyte-laden hydrogels inhibited matrix synthesis and increased matrix loss into the culture medium, but did not affect cell proliferation. Our findings suggest a role for PPI in mediating matrix synthesis and degradation. PPI (at micromolar concentrations) and PPI-derived Pi (at millimolar concentrations) are known to be signaling molecules, and our results indicate that the elevated (micromolar) level of extracellular Pi in aging cartilage, by itself exerts functionally significant effects on chondrocyte matrix homeostasis.

**036**

DEVELOPMENT OF RADIOLOGICAL OSTEOARTHRITIS PATHOLOGY AT FOLLOW-UP IN PEOPLE WITH JOINT PAIN AT BASELINE

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**Purpose:** Many people present themselves with hip or knee pain at the general practitioners office each year. The cause of this pain is often thought to be osteoarthritis (OA), but not all these people have radiological signs of OA in the painful joint. It is not yet possible to determine in an early stage of the disease who will develop OA pathology in a later stage. In this study we aim to identify what the determinants are for developing OA pathology on x-ray at follow-up, in people with pain at baseline but no radiological OA (ROA) at baseline (Kellgren & Lawrence score [K&L] <2).

**Methods:** Data of participants of the Rotterdam study (a population-based cohort study), aged ≥55 years, was assessed on the presence of hip or knee pain. A total of 452 subjects with hip pain at baseline (mean age 68.5, 72.1% females) and 546 subjects with knee pain at baseline (mean age 70.0, 66.5% females) were included; all without ROA in the painful joint at baseline. Univariate and multivariate analyses (inclusion based on p < 0.1 in univariate analyses) were used to determine predictors for ROA at follow-up (mean 6.6 years). Tested baseline variables include: other joint complaints and medical consumption for these complaints, patient characteristics (age, sex, diabetes), OA related aspects (familial OA, herberdens’ nodes, OA in other joint (hip or knee) than the joint with complaints, morning stiffness, and lower limb disability) and for women only female-hormone related aspects (hormone use, age first last menstruation and years since menopause).

**Results:** Of the included subjects with hip or knee pain at baseline resp. 12.6% and 7.1% developed ROA at follow-up. Best predictor of hip ROA at follow-up in those with hip pain was ‘knee OA at baseline’ (K&L ≥2) in multivariate analysis of all subjects (OR = 4.362, p=0.016) as well as in univariat analysis in women only (OR=4.700, p=0.036). For the men ‘familial OA’ (OR=6.114, p=0.021) was the only significant determinant in univariat analysis. For predictors of knee ROA at follow-up in those with knee pain the multivariate analysis of all subjects resulted in a model including the determinants BMI (OR=1.305, p=0.016) and treatment of joint complaints in the 5 years preceding baseline (OR=0.103, p=0.044). In women the same variables remained significant in multivariate analysis with outcomes resp. OR=1.185, p=0.026 and OR=0.288, p=0.029. For the men no variable was significant (p<0.05) in univariat analysis. All outcomes are adjusted for age.

**Conclusions:** Determining who will develop ROA in a later stage, in people with joint pain but no radiographic OA, may help to discriminate between true OA diagnosis and other pathologies. It will also make it possible to identify subjects eligible for early prevention studies, and with this hopefully preventing deterioration into a severe OA in the future. In predicting development of hip ROA, having knee OA and familial OA seem to be the most important determinants. For development of knee ROA best predictors are a combination of high BMI and having had treatment for joint complaints in the five years preceding baseline.

**037**

A TOOL THAT IDENTIFIES NEUROPATHIC PAIN SYMPTOMS IN A COMMUNITY KNEE OA COHORT

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**Purpose:** Pain is the most common, disabling symptom for people with Osteoarthritis (OA). Improved understanding of pain mechanisms in OA, including the development of "clinically feasible" tools to identify individuals with central sensitization causing neuropathic pain (NP) is essential to the development of mechanism-based pain therapies. In adults with chronic symptomatic knee OA, this study assessed: 1. the proportion of participants with NP symptoms as measured by a NP questionnaire modified for use in OA, the modified painDETECT (mPD-Q); 2. convergent construct validity of the mPD-Q by co-administration of another NP questionnaire, the Self-completed Leeds Assessment of Neuropathic Symptoms...