intensity of chronic pain when awake and during sleep. These findings explain the excessive rate of syncope observed in the FM population during wakefulness, and the increased presence of CAP, PB and PLMs during sleep.
Disclosure of Interest: None declared
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WEDNESDAY, 14 JUNE 2017

Chondrocyte channels (role in mechanotransduction) or "channeling the chondrocyte"

OP0007 CCR2 INHIBITION ABROGATES IL-6–INDUCED ACTIVATION OF MATRIX METALLOPROTEINASES IN CARTILAGE

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Background: Interleukin 6 (IL-6) plays a crucial role in many rheumatic diseases, including osteoarthritis (OA) [1]. In cartilage, IL-6 activates chondrocyte catabolism by increasing the production of matrix-degrading enzymes, including matrix metalloproteinase 3 (MMP-3) and MMP-13, but it could have other roles.
Objectives: We aimed to identify new biological processes regulated by IL-6 in cartilage.
Methods: RNA-seq analysis (Illumina HiSeq platform) was used to determine biological pathways associated with IL-6/IL-6R (100 ng/ml) stimulation in mouse primary articular chondrocytes. Results were further validated by qPCR and western blot analysis. The effect of stimulation with CC chemokine ligand 2 (CCL2; 10 ng/ml), CCL7 and CCL8 (100 ng/ml) was investigated *in vitro* and *ex vivo* in mouse femoral head cartilage explants. The impact of targeted inhibition of CCL2 or CCL7 by siRNA or blockade of their common receptor CCR2 by a specific antagonist (RS-504393) was determined in IL-6–treated chondrocytes and/or cartilage explants.
Results: Transcriptomic analysis revealed overrepresentation of multiple functional clusters of genes in IL-6–stimulated chondrocytes, with strongly increased expression of signalling molecules and especially cytokines. Two of the 10 top genes upregulated by IL-6 were *Ccl7* (log2 fold change [FC] 2.33, adjusted p-value [p_{adj}] =3.35x10^{-62}) and *Ccl2* (log2 FC 1.85, p_{adj} =9.10x10^{-26}), which encode for CCR2 ligands. qPCR and western blot validations confirmed these results and revealed that IL-6 stimulation also increased the mRNA level of *Ccl8*, another CCR2 ligand not identified by RNA-seq analysis. CCL2 and CCL7 but not CCL8 activated extracellular signal-regulated kinase 1/2 and c-Jun N-terminal kinase signalling and increased MMP-3 and MMP-13 production and activation. CCR2 blockade but not the specific inhibition of CCL2 or CCL7 by siRNA, greatly abrogated the IL-6–induced catabolism *in vitro* and *ex vivo*.
Conclusions: We identified 2 chemokines, CCL2 and CCL7, as key targets of IL-6 in chondrocytes. Although their main role is to mediate monocyte/macrophage recruitment to the joint, their receptor, CCR2, is also strongly involved in IL-6–induced cartilage catabolism. These results suggest a novel mechanism by which CCL2/CCR2 and CCL7/CCR2 signalling could be involved in rheumatic diseases, especially OA [2].
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OP0008 DEFICIENT AUTOPHAGY INDUCES CHONDROCYTE DYSFUNCTION THROUGH LAMIN A/C ACCUMULATION IN AGING AND OSTEOARTHRITIS

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Background: Aging-related Osteoarthritis (OA) is characterized by insufficient extracellular matrix synthesis and articular cartilage degradation. Autophagy is essential to maintain chondrocyte homeostasis by regulating the intracellular macromolecule and organelle turnover (1). Previous findings indicated that autophagy is defective in Aging and OA articular cartilage (2,3). However, the specific target/-s that regulates this homeostatic mechanism and affect cartilage integrity are still unknown.
Objectives: The objective of study is to identify targets regulating autophagy in human chondrocytes.
Methods: We performed quantitative proteomic analysis of Atg5 knockdown primary uman chondrocytes using iTRAQ (isobaric tags for relative and absolute quantitation) labeling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software v 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for *Homo sapiens*. Human chondrocytes and human cartilage from healthy, aged and OA patients were employed to confirm the role of the identified target by Western Blot (WB), Inmunofluorescence (IF) and Inmunohistochemistry (IHC). Importanly, CRISPR/Cas9 genome editing technology was used for mechanism of action studies.
Results: 24 out of 487 proteins were significantly altered ($p<0.05$) in response to defective autophagy. Cytoskeleton organization, collagen catabolism, oxidative stress, and aging pathways were affected. Interestingly, Lamin A/C, a nuclear protein implicated in cell senescence, was found upregulated under defective autophagy. Increased Lamin A/C expression was found in human chondrocytes with reduced autophagy. Furthermore, aged and OA human cartilage showed increased Lamin A/C expression. Induction of chondrocyte senescence by genetic deletion of Zinc Metalloproteinase STE24 (Zmpste24) via CRISPR-Cas9, lead to Lamin A/C accumulation, accompanied by a reduction of LC3 and increased chondrocyte death and mitochondrial dysfunction, suggesting that deficient autophagy is correlated with senescence of human articular cartilage.
Conclusions: Lamin A/C, a nuclear protein contributing to structural integrity to the nucleus and matrix was identified as candidate target for regulating cartilage function under defective autophagy, such as aging and OA. These results support the hypothesis that autophagy is decreased with aging. Therefore, targeting Lamin A/C might be a promising strategy to find novel therapeutics for cartilage aging and OA.
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Wearable technologies in 21st century healthcare

OP0009-HPR THE EFFECT OF AN 8-WEEK WATER EXERCISE PROGRAM ON ANAEROBIC EXERCISE CAPACITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Anaerobic exercise capacity was reported to be lower in children with juvenile idiopathic arthritis (JIA) than healthy children. However, to our knowledge, there is no study focusing on improving anaerobic exercise capacity in JIA.
Objectives: To investigate the effect of an 8-week water exercise program, which was performed at the weekends, on anaerobic exercise capacity in children with JIA.
Methods: Forty-two children with JIA were divided into two groups as exercise and control. Prior to the study, anaerobic exercise capacity was measured performing a 30-second Wingate test. Deep water running was employed as the progressive water exercise program for the exercise group. Control group did not receive any additional treatment other than their usual care. Weekends were chosen for the exercise sessions considering the educational program of the children. Exercise intensity was set as moderate. Exercise intensity was determined with a wearable heart rate tracking system during the exercises. All children were reassessed regarding to anaerobic exercise capacity two months after the first assessment.
Results: All children completed the study without any adverse effects. Twenty-one children were in the exercise group, others were assessed as controls. No significant differences were determined between groups prior the study regarding to age, disease duration, height, weight, body-mass index, and anaerobic exercise capacity related parameters ($p<0.05$). While all anaerobic exercise capacity parameters improved in the exercise group, no improvement were seen in the control group. The in-group comparisons were shown at Table 1. The comparison of the changes between groups after 8 weeks were demonstrated at Table 2.