of primary MSC characteristics, these MSC lines are expected to be valuable tools for the research on Regenerative Medicine for OA as part of Tissue Engineering in vitro models.

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AB0103 A NOVEL PROTECTIVE ROLE OF GPNMB/OSTEOACTIVIN IN POST-TRAUMATIC OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a chronic joint disease causes irreversible damage to the articular cartilage resulting in loss of joint function and subchondral bone remodeling. There is no cure for OA and currently the available treatment like pain management, and joint replacement surgery is used to treat this disease. GPNMB/Osteoactivin is a type-I transmembrane protein plays a vital role in osteogenesis and bone remodeling.

Objectives: However, the function of GPNMB/Osteoactivin in chondrogenesis and cartilage repair is unknown. Hence, in this study, we examined the role of GPNMB/Osteoactivin using post-traumatic osteoarthritis model and ex vivo chondrocytes cell culture and assessing the effects of GPNMB/Osteoactivin as anti-inflammatory factor in chondrocytes.

Methods: We first examined the expression GPNMB/Osteoactivin in normal cartilage. Next, we assessed the effects of recombinant GPNMB/Osteoactivin on mouse primary chondrocytes proliferation/viability and extracellular matrix markers.

Results: We found that GPNMB/Osteoactivin treatment did not have any effect on cell proliferation/viability, however, there was an increased in Collagen Type II and aggrecan expression in a dose- and time-dependent manner. These data suggest that GPNMB/Osteoactivin plays a role in cartilage maintenance. Next we determined whether GPNMB/Osteoactivin contributes to the OA disease progression. Human osteoarthritic damaged and undamaged cartilage harvested following knee replacement were used to examine GPNMB/Osteoactivin expression and found that GPNMB/Osteoactivin mRNA was 6-7-fold increased in damaged compared to undamaged cartilage. Similar results were obtained from mouse primary chondrocytes treated with IL-1 β and showed a significant increase (4-fold) in GPNMB/Osteoactivin mRNA compared to untreated control. Next, we evaluated the effects of GPNMB/Osteoactivin deficiency on the OA progression using the DMM model. GPNMB/Osteoactivin mutant (DBA/2J) mice showed significant increased in OARS1 scores compared to WT mice.

Conclusion: Taken together, these data are the first to report a role for GPNMB/Osteoactivin in cartilage maintenance and protection against the progression of OA.

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AB0104 ARE POLLUTANTS A NEW RISK FACTOR FOR OSTEOARTHRITIS? RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

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Background: Prevalence of knee osteoarthritis (OA) has doubled since the mid-20th century. Interestingly, this increase cannot be explained solely by longer life expectancy and the obesity epidemics (1). Therefore, other environmental factors known to have increased in the recent years could be part of the explanation.

Objectives: We performed a systematic literature review (SLR) to summarize the existing knowledge about associations between OA and pollutants.

Methods: Pubmed database was used to identify studies reporting data on OA and pollutants in humans (examples of MeSH terms: "Polychlorinated Biphenyls (PCB)" or "Lead"). Abstracts from international congresses were reviewed for the past 2 years, combined with manual curation. Studies were classified in epidemiological clinical studies, pollutants assessments in ex vivo OA joint tissues, and in vitro effect on human chondrocyte.

Results: As of January 15, 2019, 193 potentially relevant articles were screened. Among them, 14 were selected. After manual curation, a total of 21 full text articles were analyzed. Ten articles reported epidemiological clinical studies. Four articles underlined the link between PCB and OA: in the 3 articles reporting association with past exposure to PCB, the most robust one showed that risk of OA was significantly increased, at least in men (OR 4.1 [95%CI: 1.8-11.2] for men and 1.3 [95%CI: 0.8-2.3] for women). In the 4th study, the highest serum concentration of PCB was associated with a higher risk of arthritis: maximal adjusted OR (aOR) was 3.2 [95%CI: 1.6-6.7], p<0.01. However, sensitivity analysis of OA patients did not find any significant association in this study. Two articles focused on serum levels of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS): aOR to have OA in the PFOA highest serum level quartile was 1.42 [95%CI: 1.26-1.59], p=0.00001 and 1.55 [95%CI: 0.99-2.43]. Data were conflicting for PFOS: aOR to have OA in the PFOS highest serum level quartile was 1.77 [95%CI: 1.05-2.96], p<0.05 and 0.76 [95%CI: 0.68-0.85], p=0.00001. Two articles showed an association between serum lead levels and knee OA in the general population. In Korea, the risk of radiographic OA was increased in the highest quartile of lead serum level compared to the lowest one (aOR 1.90 [95%CI: 1.09-3.32] for men and 1.81 [95%CI: 1.17-2.77] for women). In the United States, risk knee radiographic OA correlates with increased lead serum levels. In the last study, household air pollution induced by the cooking heat source was examined: compared to electricity, the risk of OA was increased with the use of liquids (kerosene/paraffin: aOR 1.73 [95%CI 1.33-2.25]) or solid (coal, wood: aOR 1.73 [1.32-2.27]), (agriculture/crop: aOR 2.0 [1.47-2.72]). Lead and zinc accumulation was reported in 7 articles: 4 of them analyzed the concentration in OA joint obtained during arthroplasty and showed highest concentration in cartilage versus bone. In another, lead serum levels were associated with biomarkers of joint tissue metabolism. Two studies with X-ray fluorescence on cadavers found a high accumulation of lead and zinc in the articular cartilage tidemark. Four studies assessed the in vitro effect of pollutants on human chondrocytes: the viability of chondrocytes was reduced in presence of PCB, gold, silver, fluoric acid and bisphenol A.

Conclusion: This SLR suggests a possible link between OA and pollutants but the designs of the studies, the populations investigated and the type of pollutants were still too heterogeneous and limited to conclude definitively that pollutants represent a new environmental risk factor for OA. However, this SLR highlights a critical need for novel epidemiological, clinical and basic research studies in order to identify other potential environmental factors in OA.

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AB0105 THE EFFECT OF TROMBOSIT RICH PLASMA APPLICATION ON DEGENERATED CARTILAGE: IN VITRO EXPERIMENTAL STUDY

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Background: Osteoarthritis is the most common problem among musculoskeletal system disorders. Platelet-rich plasma (PRP) has been suggested to be

beneficial in the treatment of degenerative musculoskeletal problems. The purpose of this study is to evaluate PRP treatment efficacy on degenerated cartilage.

Objectives: In this study, we aimed to determine the efficacy of platelet-rich plasma (PRP) on mechanically damaged chondrocyte cells by using different dose, different duration of exposure and different methods of activation of platelet.

Methods: Human source chondrocytes (CHON-001 ATTC CRL-2846) were used in the study. Chondrocyte cells were produced in appropriate medium and an experimental cartilage model was created. The platelet-rich plasma was produced from platelets obtained by apheresis in the laboratory, from blood of volunteer. The platelet-rich plasma was adjusted at five different doses as 4.8×10^6 , 2.4×10^6 , 1.2×10^6 , 6×10^5 , 3×10^5 . The first group of platelet rich plasma was left intact, the second group was detonated within seven minutes by applying ultrasound waves in water, the third group was activated with calcium chloride and the fourth group was determined as control group. Using a ten microliter pipette tip, a linear damage to the opposite side was created at the widest part of the well. Cell migration was monitored at 0-4-8-24 and 48 hours at $\times 10$ magnification by in vitro microscopy and wound healing was evaluated by photographing. Migration intervals were determined quantitatively using the program named Image J.

Results: When the rates of recovery were compared to the groups, no significant improvement was observed in the intact and detonated platelet groups at 4-8 and 24 hours compared to the control group. In the third group which was activated with calcium, no significant improvement was observed in all doses at 4 and 8 hours compared to the control group. However, at the 48th hours there was a significant improvement in the doses of 1.2×10^6 , 2.4×10^6 and 4.8×10^6 compared to the control group ($p < 0.0001$).

There were significant differences in intact and detonated platelets at 3×10^5 and 6×10^5 doses at 48th hours compared to control group ($p < 0.0001$). Significant improvement was observed in all groups at levels of 1.2×10^6 and above ($p < 0.0001$).

When evaluated in terms of activation, there was a significant improvement in the exploded and intact groups at the 48th hour, compared to the calcium-activated group at doses of 3×10^5 and 6×10^5 ($p < 0.01$).

Conclusion: Cartilage damage is the main pathology in the pathogenesis of osteoarthritis. All doses of PRP used in the study contributed to improvement. Meanwhile, the most critical parameter for platelet migration was timing and significant improvement was started after 48 hours.

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AB0106

CHANGES IN THE MIRNA PROFILE AND HYPOXIC BEHAVIOUR OF HUMAN CHONDROCYTES BY THERAPEUTIC NUCLEAR MAGNETIC RESONANCE THERAPY (NMRT)

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Background: Therapeutically applied nuclear magnetic resonance (NMRT) is discussed to participate in repair processes regarding cartilage and influences pain signaling. Studies concerning NMR therapy implemented within the treatment of patients with degenerative rheumatic diseases outlined pain reduction as the main clinical outcome (1). NMRT is also known to lead to improvements in pain from patients with knee OA due to a chondroprotective effect on the articular cartilage. In spite of this significant reduction in pain, the mechanism of action of NMRT at the cellular level remains to be elucidated.

Objectives: To substantiate the application of NMRT the aim of this work targets the underlying mechanisms at the cellular level. We investigated NMRT induced

changes of the miRNA profile of human healthy and OA chondrocytes and studied the respective miRNA targets. Based on the fact that articular cartilage functions as an avascular and hypoxic connective tissue we were further able to demonstrate that NMRT modulation seems to be more pronounced under hypoxic conditions.

Methods: Human primary chondrocytes and the chondrocyte cell line Tc28/2a were used for the experiments.

RNA was extracted using RNeasy Mini Kit and was used as input for the Thermo Fisher Ion Total RNA-Seq Kit v2. Sequencing was performed on Ion Proton sequencer using the Ion PI Hi-Q™ Sequencing 200 system. Signal processing and base calling was performed using Torrent Suite version 5.6. Hypoxic conditions were established and enabled cell growth in presence of 1-5% O₂. Expression of miRNAs and target proteins was studied by a standard PCR procedure as well as protein detection by western blot. HDAC activity was measured by HDAC-Glo II assay.

Results: Characterization of the miRNA profile showed a slight up regulation of miR-24-1-5p and miR-502-5p while miR-25-5p and miR-365a-5p was down regulated. For miR-365a-5p known to directly targeting HDAC and NFκB a decrease of HDAC activity by NMRT was detected. The miR-25-5p target COX2 was changed in expression by NMRT whereas no influence on CDK4 knowing to be controlled by miR-24-1-5p was detected. NMRT treatment of chondrocytes under hypoxic conditions (0-5 % O₂) changed the expression profile with respect to NOS, IGF2, PDGF and IGF1R and a change in the expression of Hif1/2 under the influence of IL1b was observed. The hypoxic conditions changed apoptotic behavior of the cells, NMRT showed no influence.

Conclusion: A closer look into the mechanism of the NMRT at the cellular level revealed a modulatory effect on miRNA, their regulatory units and chondrocytes under hypoxic conditions. The results underline our former results indicating that NMRT counteracts IL-1b induced changes which mean that pain reduction by NMRT might be due to NMRT holding against inflammatory mechanisms under OA.

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AB0107

S-ALLYL-L-CYSTEINE ATTENUATES INFLAMMATION RELATED OXIDATIVE STRESS PARAMETERS AND INCREASES ADHESION CAPACITY OF PRIMARY HUMAN OSTEOARTHRITIC ARTICULAR CHONDROCYTES

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Background: Osteoarthritis (OA) is characterized by progressive destruction of the articular cartilage, and chondrocytes, the only cells in articular cartilage, are in charge of maintaining the homeostasis of articular cartilage via modulating extracellular matrix anabolism and catabolism [1]. Due to the association of the degree of oxidative degeneration of chondrocytes and OA, preventing impaired redox signalling and oxidative death of chondrocyte are suggested as potential targets to relieve OA [2]. In this respect, some photochemicals have been shown to be potential agents for preventing or treating OA due to their antioxidant and anti-inflammatory properties [3].

Objectives: We studied the effects of an antioxidant S-allyl-cysteine (SAC), a major sulphur-containing amino acid compound of garlic [4], on the redox system, and its associations with the proliferation rate and index of human OA chondrocytes (OACs).

Methods: Chondrocytes were isolated from the joint cartilages of OA patients (grade 4, mean age = 66 years, BMI = 29.7 ± 4.4 kg/m²). The alterations in cell proliferation (MTT), adhesion profile (RTCA-iCELLigence System), reactive oxygen species generation (ROS), lipid hydroperoxide levels (LPO), HNE-protein adduct levels (HNE), AGE-protein adduct levels (AGE), 3-nitrotyrosine levels (3-NT),