or miR-140 expression level correlates with the disease progression of knee OA (Zhang et al.; Chao et al.). Under certain circumstances, miRNAs can be released into the body fluids and easily be detected in the blood samples. Therefore, miRNAs are hot candidates as biomarkers for early diagnosis or structural progression of OA.

Objectives: The aim of this study was to evaluate circulating miRNAs in patients with hand osteoarthritis (HOA) and healthy individuals. Simultaneously, we studied specific miRNAs in order to differentiate between erosive and non-erosive subsets of the disease.

Methods: Eight patients with HOA (erosive: n=4, 3 females, mean age=63.7±7 yrs; non-erosive: n=4, 3 females, mean age= 62.4±6 yrs) and 4 healthy controls (3 females, mean age=63.5±7 yrs) were included in this study. Firstly, Advance TaqMan low-density assay (TLDA) was performed for the purpose of miRNA high-throughput screening. Differently expressed miRNAs were further verified by real-time qPCR on the validation cohort in 31 patients with hand OA (19 females, mean age=66.2±7 yrs, erosive: n=9, non-erosive: n=10, healthy controls: n=12).

Results: TLDA profiling displayed 346 circulating miRNAs in plasma of patients with HOA and healthy controls. We demonstrated 40 differently expressed circulating miRNAs in patients with HOA compared with healthy controls. Using a real-time qPCR, we verified increased expression levels of 10 circulating miRNAs in patients with HOA compared with healthy controls, e.g. miR-191-5p (3.4 fold), miR-151a-3p (3.4 fold) or miR-222-3p (2.4 fold). We did not find any specific miRNA, which could distinct erosive from a non-erosive subset of the disease.

Conclusion: Extensive profiling of circulating miRNAs revealed several miRNAs that can be associated with HOA and can help to better understand OA pathogenesis.

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AB0039 AGRIN REPAIRS BONE AND CARTILAGE IN VIVO

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Background: Cartilage defects in the joints are reported in 61% of all arthroscopies^{1&2}. The size of the cartilage repair market is estimated to be \$2.195 million by 2025³. Cartilage defects can evolve into osteoarthritis, in which abnormal load results in cartilage breakdown, joint pain and reduced mobility. Osteoarthritis is the leading cause of permanent disability and absenteeism and affects up to 1/3 of the people over 60yrs. In western countries osteoarthritis costs 1.5-2% of the GDP⁴. Joint replacement with a prosthesis restores some degree of independence but in up to 20% of patients it does not meet expectations⁵ and has a limited life span. There is no pharmacological intervention that arrests or reverts the course of osteoarthritis, despite the desperate need.

We previously published that agrin plays an important role in cartilage homeostasis⁶. The addition of agrin to chondrocytes *in vivo* resulted in enhanced cartilage formation, suggesting a potential role for agrin in cartilage repair.

Objectives: Investigate the potential of agrin for use in cartilage repair.

Methods: Critical size osteochondral defects were generated in mice and sheep and injected intraarticularly with type I collagen gel containing agrin or vehicle. Animals were monitored for 8 weeks or 6 months respectively. MicroCT, histological analysis, qPCR, lineage tracking, reporter assays, chondrogenesis assay, immunohistochemistry were performed.

Results: A single intraarticular administration of agrin induced regeneration of critical-size osteochondral defects in mice, restoring the tissue architecture and bone-cartilage interface. Agrin stem cells to the site of injury and, through simultaneous activation of CREB and suppression of canonical WNT signalling, induced GDF5 expression and differentiation into stable articular chondrocytes, forming stable articular cartilage. In sheep, agrin treatment resulted in regeneration of bone and cartilage, which promoted increased ambulatory activity.

Conclusion: Agrin orchestrates repair morphogenesis at the joint surface by modulating multiple signalling pathways, supporting the therapeutic use of agrin for joint surface regeneration.

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AB0040 PYRUVATE DEHYDROGENASE KINASES AS A POTENTIAL TARGET IN THE TREATMENT OF OSTEOARTHRITIS TO UNLEASH THE METABOLIC FLOW?

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Background: While osteoarthritis (OA) is the most common joint disease worldwide, rheumatoid arthritis (RA) represents the most common type of autoimmune arthritis. In both diseases, fibroblast-like synoviocytes (FLS), which maintain the structural and dynamic integrity of the joint, have been identified as key drivers of cartilage degradation. FLS can be divided into two major populations. The destructive phenotype which is restricted to the THY1- FLS of the synovial lining promotes bone erosion, while THY1+ FLS of the sublining layer drives synovitis. The FLS phenotype is shaped by glucose metabolism, which promotes disease progression in patients with synovitis. However, profound knowledge about the contribution of FLS to pathogenic mechanisms in cartilage degradation is limited.

Objectives: Here, we present the phenotypic features of FLS obtained from patients with OA (OA-FLS) compared to bone marrow-derived mesenchymal stromal cells (MSC) on transcriptomic, proteomic and metabolic levels with the aims (i) to identify novel targets for the development of disease-modifying osteoarthritis drugs and (ii) to distinguish both cell types.

Methods: To this end, we comprehensively compared human bone marrow-derived MSC with OA-FLS isolated from human knee joint sections. MSC and OA-FLS were characterized in detail according to their multipotency, surface marker pattern, cell viability, proliferation rate, morphology and expression of fibroblast- and metabolic-related markers using flow cytometry, immunofluorescence and Seahorse™. More in-depth, selected gene and protein expression patterns were analyzed using qPCR and mass spectrometry.

Results: We observed a similar phenotype of OA-FLS and MSC with regard to the minimal criteria that define a MSC phenotype. In-depth comparison of