Conclusions: The results indicate a reduction of H₂S synthesis as a critical feature involved in hyperglucidic-mediated dysregulation of articular chondrocytes. The impairment of H₂S signalling could participate in the mechanisms underlying the predisposition to OA development in diabetic individuals and may open new opportunities for treating patients with a diabetes-related OA phenotype.

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SAT0060 PROTEOMIC ANALYSIS OF OSTEOBLASTS SECRETOME PROVIDES NEW INSIGHTS IN MECHANISMS UNDERLYING OSTEOARTHRITIS SUBCHONDRAL BONE SCLEROSIS

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Background: Osteoarthritis (OA) is characterised by cartilage degradation but also by other joint tissues modification like subchondral bone sclerosis

Objectives: In this study, we used a proteomic approach to compare secretome of osteoblasts isolated from sclerotic (SC) or non sclerotic (NSC) area of OA subchondral bone

Methods: Secretome was analysed using differential quantitative and relative label free analysis on nanoUPLC G2 HDMS system. mRNA of the more differentially secreted proteins were then quantified by RT-PCR and the most relevant proteins identified using western-blotting and immunoassays

Results: 175 proteins were identified in NSC osteoblasts secretome. Compared to NSC osteoblasts secretome, 13 proteins were significantly less secreted (Osteomodulin, CSF-1, IGFBP5, VCAM-1, IGF2, 78 kDa glucose-regulated

protein, versican, calumenin, IGFBP2, thrombospondin-4, periostin, reticulocalbin 1 and osteonectin), and 12 proteins significantly more secreted by SC osteoblasts (CHI3L1, fibulin-3, SERPINE2, IGFBP6, SH3BGRL3, SERPINE1, reticulocalbin3, alpha-2-HS-glycoprotein, TIMP-2, IGFBP3, TIMP-1, SERPINF1). Similar changes in periostin, osteomodulin, SERPINE1, IGFBP6, fibulin-3 and CHI3L1 mRNA levels were observed. Finally, osteomodulin and fibulin-3 specific sequences were quantified by western blot and immunoassays in serum and osteoblasts conditioned culture supernatants.

Conclusions: We highlighted some proteins differentially secreted by NSC and SC osteoblasts of OA subchondral bone sclerosis. These changes contribute to explain some features observed in OA subchondral bone, like the increase of bone remodelling or abnormalities in bone matrix mineralization. Among identified proteins, osteomodulin was found decreased and fibulin-3 increased in serum of OA patients. These findings suggest that osteomodulin and fibulin-3 fragments could be biomarkers to monitor early changes in subchondral bone metabolism in OA.

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SAT0061 TARGETING ACTIVATED SYNOVIAL FIBROBLASTS USING PHOTODYNAMIC THERAPY IN RHEUMATOID ARTHRITIS

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Background: Activated synovial fibroblasts (SF) play an important role in the pathogenesis of rheumatoid arthritis (RA). They contribute to the pro-inflammatory environment in the joint as well as to the degradation of cartilage. Depleting SF could ameliorate both the symptoms of joint inflammation and degradation in RA. SF are characterised by the expression of Fibroblast Activation Protein (FAP). Here, we investigated the potential of photodynamic therapy (PDT) targeting FAP to selectively induce cell death in these cells as well as in synovial tissue from RA patients. In PDT, a light-sensitive molecule is delivered to a target cell and activated with light of a specific wavelength. This causes cell death through the production of reactive oxygen species.

Methods: The anti-FAP antibody 28 H1 was conjugated with the photosensitizer IRDye700DX (28 H1–700DX). *In vitro* PDT assays were performed with 3 T3 fibroblasts stably transfected with FAP. 3T3-FAP cells were incubated with 28 H1–700DX or a control conjugate for 4 hours, and exposed to varying 690 nm light exposures. Subsequently, cell viability was measured using the CellTiter-Glo assay. For *ex vivo* evaluation of PDT efficiency, human RA synovial tissue obtained after joint replacement surgery was processed into standardised 6 mm biopsies and used for FAP-based PDT. The biopsies were incubated with 28 H1–700DX for 4 hours, subjected to 52 J/cm² light exposure and fixed in formalin after 1 hour. Tissue was then embedded in paraffin and stained for the presence of gH2AX and caspase 3 as indicators of DNA double-strand breaks and early apoptosis on sequential slides. The presence of FAP was also determined on subsequent slides.

Results: The effect of PDT was optimal at 13.7 J/cm² light exposure to 3T3-FAP cells incubated with 6.67 pM 28 H1–700DX, which dramatically reduced cell viability with 89.27%±2.48 compared to control ($p < 0.001$). No cell death was observed with the control 700DX-conjugate ($p = 0.16$).