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Publication date: 2019

Document Version
Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):
A proteomic investigation of synovial fluid in patients with knee osteoarthritis treated with intra-articular metallic gold micro particles

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Background and aims

Intraarticular gold may decrease osteoarthritis (OA) inflammation. Gold implant treatment correlate with clinically significant improvements in joint movement and pain management. Gold may decrease inflammation because of various mechanisms such as regulation of the NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells) pathway (Figure 1 - 4) (1-6).

Methods

A cohort of 30 patients, aged ≥18years, pain ≥ 3 months, synovial effusion on MRI, and Kellgren-Lawrence OA grade 3-4 were included. Metallic gold 20 mg, 72,000 pieces, 20-40 µm (Berlock-Micro-Implants, Human-GoldImplant) (7-9) were injected into the knee joint using the patient’s own synovial fluid as the carrier.

SF samples was investigated, before and 8 weeks after treatment in 17 patients. To determine protein concentration, a bicinchoninic acid (BCA) assay was used. Gel electrophoresis by SDS-PAGE was used to visualize the synovial prokine and relative quantitative changes between the treated and untreated samples. Mass spectrometry sample preparation was performed with filter aided sample preparation (FASP). The global proteome was investigated through LC-MS/MS in Orbitrap Q Exactive

Results

A distinctive protein band was visible in the treated patient columns at approximately 60 kDa in all of the patients (Figure 5). The MS analysis (Figure 6) revealed 23 of 164 proteins was significantly changed after treatment (Table 1). The expression of five proteins were down-regulated and 18 were upregulated. In the band 50 and 70 kDa we found a significant elevation of clusterin (P = 0.0022), vitamin D binding protein (DBP) (P = 0.026) and cartilage acidic protein1 (CAP1) (P = 0.045).

Conclusions

The elevated clusterin may be a sign of increased protection of cartilage and cells, which correlates with a regulation of the NF-kB pathway. DBP correlate with increased vitamin D level, but the overall effect is uncertain. CAP1 has been found to marker of mesenchymal stem cells undergoing chondrogenic differentiation. It is shown that gold microparticles induce differentiation of mesenchymal stem cells. This indicate gold particles induce chondrogenic differentiation of resident mesenchymal stem cells.

We hypothesize gold particles inhibit macrophage mediated inflammation, induce chondrogenic differentiation of resident mesenchymal stem cells and stimulate the release of cartilage protective protein. Not all regulated proteins were correlated with positive effects on OA and some inconclusive. Further studies need to investigate the mechanism and proteins involved in gold treatment of OA.