A72 H₂S STIMULATES CYTOKINE EXPRESSION IN FIBROBLAST-LIKE SYNOVIOCYTES VIA AN ERK-DEPENDENT BUT NF- κ B-INDEPENDENT PATHWAY

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Background and objectives Rheumatoid arthritis (RA) is an autoimmune disease characterised by inflammation of the synovial membrane, resulting in progressive joint destruction. Fibroblast-like synoviocytes (FLSs) play a crucial role in the joint inflammation and destructive processes.

An established treatment for patients with different forms of arthritis is sulphur bath therapy which belongs to the oldest forms of treatment for chronic inflammatory diseases and is still used today in many parts of the world. The fact that scientific reports about the potential beneficial effects of this kind of therapy are controversial and rare encouraged us to investigate the effects of an exogenous H₂S donor (NaHS) on FLSs isolated from synovial tissues of RA and OA patients.

Material and methods RA and OA-FLSs were isolated from synovial tissues obtained at joint replacement surgery and were cultivated under standard conditions. FLSs were utilised between the third and twelfth passage. Cells were incubated for 20–60 min with different concentrations of NaHS (0.06–1.0 mM) after which medium was changed and cells were further incubated for 12 h. After 1, 3, 6 and 12 h cell culture supernatants were collected and IL-6 levels were quantified by ELISA. Additionally, RNA levels were analysed by quantitative real time PCR. NF- κ B and MAPK activation (p38 MAPK and ERK1/2) were analysed by PathScan Sandwich ELISA Kits (Cell signaling) and Western blot experiments.

Results RA-FLSs constitutively expressed high levels of IL-6. In contrary, IL-6 expression of OA-FLSs was very low and not detectable. After incubation of cells for 20 min with high concentrations of H₂S (from 0.5 to 1.0 mM) IL-6 expression was dramatically upregulated in both cell types. H₂S concentrations below 0.5 mM had no stimulatory effects. Interestingly, when cells were incubated for 60 min with the same concentrations of H₂S stimulatory effects failed. Activation of IL-6 expression was accompanied by simultaneous phosphorylation of extra cellular signal regulated kinase (ERK1/2). However, activation of p38 MAPK and NF- κ Bp65 could not be observed.

Conclusion Data presented here shows that H₂S stimulated cytokine expression in RA and OA-FLSs via an ERK-dependent but NF- κ B-independent pathway. Our data seem of importance for studying (patho-) physiological functions of H₂S and for re-evaluating sulphur spa therapy as one of the oldest forms of therapy for rheumatic disorders.