Results Plasma concentrations of TGFb1 were significantly elevated in RA patients compared to OA patients (7.31 ± 1.10 ng/ml vs. 4.11 ± 0.35 ng/ml, mean $\pm$ SEM, $p < 0.05$), the other two isoforms did not show differences. Concentrations of TGFbs isolated from bone were strongly associated with each other with a predominance of TGFb1 >TGFb2 >TGFb3.

Although the concentrations of TGFb1 in bone were slightly elevated in the RA group compared to the OA group (0.49 ± 0.07 vs. 0.38 ± 0.04 ng/mg bone powder) no significant differences were found. No association was found for TGFb levels in peripheral blood and in the corresponding bone extracts. The highest concentrations of TGFb1 from bone were found in patients with reduced bone mineral density. A strong negative correlation was found between bone TGFb1 levels and T-score values ($r = -0.479$, $p = 0.002$).

Conclusion The finding of elevated TGFb1 concentrations in bone samples from patients with osteoporosis is in contrast to earlier findings, which suggest a protective effect of TGFb against matrix degradation. In this study the highest concentrations of extractable TGFb1 were found in RA patients with high bone loss. Thus it may be possible that more proinflammatory features of TGFb are important in bone metabolism, such as the stimulation of IL-6 as described for primary rat osteoblasts. The quantification of total TGFb in the bone matrix may not sufficiently describe the situation *in vivo*. Post translational processes like activation of the latent TGFb and its availability determine the biological effects of this regulatory cytokine.

THU0072 DISTRIBUTION OF SELECTIVE MATRIXINS, TIMP-1, CYTOKINES

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Background The most abundant joint disease is osteoarthritis. Recently it was classified as cartilagenous, synovial or osseous but the unique forms may be combined. The main feature of the disease is imbalance between synthetic and degradative processes within joint tissues. Executive part in degradative processes play matrix metalloproteinases, so called matrixins. *In situ*, they are induced by many stimuli, namely by cytokines and by interaction of different adhesive molecules with their ligands. Having been secreted into the extracellular space, they are activated by serine proteinases, or by other matrixins and inhibited by tissue inhibitors of matrix metalloproteinases, TIMPs.

Objectives

Methods In the sera of OA patients we found matrixins MMP-9, MMP-2 and MMP-3 and TIMP-1 together with cytokines IL-8 and TNF/alpha and adhesive molecules ICAM-1 and VCAM-1. To distinguish between the forms of osteoarthritis, we search for these molecules in all joint tissues that is in cartilage, synovium, granulation tissue, within subchondral bone, synovial fluid and blood serum. The joint tissues and fluids we obtain from surgery during total hip or knee replacement.

Results The joint tissues were derived from 22 patients. We obtained 10 samples of knee joints and 12 samples of hip joints. The patients were 17 female and 6 male, 67.5 ± 9.6 years old, age ranges 48–86 years. The metalloproteinase spectrum in the body fluids and extracts of joint tissues were evaluated by zymography. The concentration of metalloproteinases and TIMP-1 were assessed by ELISA (Biotrak, Amersham Pharmacia

Biotech), the concentration of adhesive immunoglobulins by Bender ELISA (MedSystems Diagnostics GmbH), and the concentration of IL-8 and TNF/alpha were determined on Immulite (DPC, USA).

We found that the most abundant matrixine within cartilage and synovium is either gelatinase A (MMP-2) or stromelysin-1 (MMP-3). On the other hand, within granulation tissue, blood sera and synovial fluid, the prevailing matrixine is gelatinase B or stromelysin-1. In cartilage, synovial fluid and blood serum TIMP-1 is abundant over sum of matrixins, whereas in synovium and granulation tissue the sum of matrixins is abundant over TIMP-1. There is about 2 to 10 times greater concentration of IL-8 in the cartilage than in other joint compartments.

We found significant correlation between levels of sICAM-1 and sVCAM-1, between TNF/alpha and MMP-3, TIMP-1, sICAM-1, sVCAM-1, and IL-8, and between IL-8 and sICAM-1 in all solid joint tissues. In the synovial fluid and blood serum the correlation was less pronounced.

Conclusion There is a great degradative potential within all compartments of osteoarthritic joint due to presence of matrixins, namely that of stromelysin-1. Within cartilage and synovial fluid the proteolytic potential is equilibrated by TIMP-1 whereas within synovium and granulation tissue is not. Synovium and granulation tissue are highly probably the propellers of degradative process in osteoarthritis.

Rheumatoid Arthritis – Aetiology and pathogenesis/Animal models

AB0022 LACTOFERRIN – A POTENT ANTI-INFLAMMATORY AGENT FOR TREATMENT OF ADJUVANT ARTHRITIS

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Background Lactoferrin is a multifunctional immunoregulatory protein, stored in specific granules of neutrophil granulocytes, from which it is released following cell activation. While the biochemical characterisation of lactoferrin as an iron-binding protein has been well described, its physiological role in inflammation remains undefined. Although lactoferrin was proven to exert certain antiinflammatory effects, there is a paucity of data concerning the possibility of administrating lactoferrin as an anti-inflammatory agent in rheumatoid arthritis.

Objectives To evaluate the anti-inflammatory properties of lactoferrin in treatment of adjuvant arthritis ? an adequate model of rheumatoid arthritis.

Methods Adjuvant arthritis was induced in Lewis rats by subplantar inoculation of a complete Freund's adjuvant. Human milk-derived lactoferrin was administered intravenously in the acute phase (8th day after adjuvant inoculation), and in the chronic phase of adjuvant arthritis (29–31 days).

Results The development of adjuvant arthritis in rats was characterised by hind paws swelling and hyperthermia, weight loss, increased white blood cell count and erythrocyte sedimentation rate, an increased level of serum elastase. In approximately 50% of rats a generalisation of inflammation with involvement of intact joints was observed. Treatment with low doses of lactoferrin (3–18 mg/kg) in the acute phase of adjuvant arthritis did not change the course of the disease, while higher doses of lactoferrin (30–60 mg/kg) caused a certain suppression of the inflammatory process, although it was not stable and lasted for only 2