disintegrin and metalloproteinase).¹ Some MDCs are involved in (patho-) physiological relevant processes such as remodelling of the extracellular matrix as well as shedding of membrane-bound cytokines (e.g. TNF- α).^{2,3} An implication of MDC15 in degenerative processes of the cartilage matrix is supported by a markedly strong up-regulated expression of this proteinase in the chondrocytes of arthritic cartilage.⁴

Objectives In the present study the expression of MDC15 in synovial membranes of patients with Rheumatoid Arthritis (RA) in comparison to osteoarthritic (OA) and normal specimens was analysed.

Methods Using *in situ* hybridization the expression of MDC15 mRNA was investigated in RA synovial tissues of synovectomy samples (n = 25), in OA tissues (n = 55) that was obtained at joint replacement surgery of hip or knee joints and normal synovial tissues (n = 8). On protein level the detection of MDC15 was performed by immunohistochemistry. A specific polyclonal antibody was generated in rabbits by immunisation with a synthetic cyclized peptide corresponding to the disintegrin domain. After affinity chromatographic purification specificity of the antibody was confirmed by Western blot analysis using COS-7 cells transfected with the full-length MDC15 cDNA.

Results By *in situ* hybridization as well as by immunohistochemistry highest expression of MDC15 could be detected in the synovial lining cells in all RA synovial tissues analysed. In comparison to the RA specimens, far lower levels of expression were observed in the synoviocytes of OA specimens that still exceeded the very low expression found in normal synovial tissues.

Conclusion The enhanced expression of MDC15 in the rheumatoid synovial lining layer suggests a potential role in the pathophysiology of cartilage destruction, since the membrane-bound proteinase might be of relevance in the activation of matrix metalloproteinases and/or also be involved in the direct proteolytic degradation of extracellular matrix molecules.

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THU0102 APO(A), A POTENTIAL LINK BETWEEN ATHEROSCLEROSIS AND ARTHRITIS

¹N Busso, ¹J Dudler, ¹R Salvi, ¹V Pédat, ²R Darioli, ³P Nicod, ¹A So, ³V Mooser. ¹Laboratory of Rheumatology; ²Medical Policlinic; ³Department of Medicine, CHUV, Lausanne, Switzerland

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Background Patients with rheumatic diseases have an excess in cardiovascular morbidity and mortality, suggesting the presence of common pathogenic abnormalities for both atherosclerosis and arthritis. One particularly atherogenic apolipoprotein, apo (a), an homologue of plasminogen, may be involved by competing with plasminogen for fibrin binding and by interfering with fibrinolysis.

Objectives To study the expression of apo (a) in arthritic joints.

Methods Human studies: synovial fluid and plasma from patients with osteoarthritis (OA, n = 8), rheumatoid arthritis (RA, n = 12) and other types of inflammatory arthritis (n = 12) and synovial tissues from OA and RA patients were collected.

Apo (a) was quantitated by ELISA and in tissues also by RNase protection. Moreover, immunohistochemical analyses of apo (a) and fibrin were performed on synovial tissues.

Animal studies: antigen-induced arthritis (AIA) was induced in genetically modified mice (LDL-receptor deficient (LDL-R $-/-$) mice expressing a human apoB-100 transgene (hApoB $+/+$) and a human apo (a) transgene (apo (a) $\pm$)). Joint inflammation was assessed by technetium scintigraphy and histology.

Results We detected the presence of apo (a) as a full-length glycoprotein in human arthritic joints. The amount of apo (a) in synovial fluid rose in proportion to plasma apo (a) levels and was higher in inflammatory arthritides than in osteoarthritis. In addition, apo (a) immunoreactive material, but not apo (a) transcripts, was detected in arthritic synovial tissues. This data indicated that synovial fluid apo (a) originates from the circulation and that diffusion through synovial tissue is facilitated in inflammatory types of arthritis. In synovial tissues, apo (a) colocalized with fibrin. These observations could be reproduced in a model of antigen-induced arthritis, using transgenic mice expressing human apo (a). In this particular mouse model, the presence of apo (a) did not change joint inflammation.

Conclusion Even if the presence of apo (a) did not change the severity of AIA, we speculate that when levels of apo (a) are sufficiently high to inhibit fibrinolysis in the joints, apo (a) may exacerbate in humans the severity of the disease.

THU0103 THERAPEUTICAL TARGETING OF ANTIGEN-INDUCED ARTHRITIS WITH LIPOSOMAL SECRETORY LEUKOCYTE PROTEASE INHIBITOR (ANTILEUKOPROTEINASE)

¹C Schneider, ²S Söder, ¹B Sehnert, ¹RE Voll, ¹JR Kalden, ¹H Burkhardt. ¹Department of Internal Medicine III, Institute for Clinical Immunology, Erlangen, Germany; ²Institute of Pathology, Cartilage Research Group, Erlangen, Germany

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Background Alternative therapeutic principles for rheumatoid arthritis (RA) are still in urgent need. Secretory leukocyte protease inhibitor (SLPI), or antileukoprotease (ALP), is a physiological serine protease inhibitor.¹ Its upregulation in macrophages leads to a reduced LPS response² most likely related to an inhibition of NF- κ B by interference with the proteolytic degradation of its cytosolic inhibitor I κ B β .³ However, the therapeutic use of this principle *in vivo* is hampered by difficulties to target the molecule into a cytosolic compartment. Phosphatidylserine containing liposomes can selectively be taken up by macrophages via Scavenger receptors⁴ thus representing a therapeutic strategy for targeting ALP to the cytosol.

Objectives In this preliminary study we applied a liposomal preparation of ALP in the murine antigen-induced arthritis (AIA) model to enhance intracellular accumulation in inflammatory cells to explore whether ALP can reduce inflammation.

Methods Liposomes were prepared by evaporation of a mixture of phosphatidylserine, phosphatidylcholine and cholesterol in chloroform/methanol and addition of ALP solution or PBS. Antigen-induced arthritis was induced in C57BL/6 mice by intraarticular injection of mBSA after prior immunisation with mBSA. Liposomal ALP was administered intraperitoneally (5 mg/kg/day) between days 1–4 after disease induction and compared with injections of PBS containing control liposomes or non-liposomal ALP. Arthritis was assessed by measuring knee joint diameter and evaluation of histological alterations in knee joint sections.

Results A marked amelioration of arthritis in mice treated with liposomal ALP was observed, already within 24 h after the first