secondary IFTC conjugated antibodies; and 2) in SDS-PAGE electrophoresis and blotting using the corresponding antibodies.

Results Fluorescence immunohistochemically shows specific extracellular expression of biglycan and decorin in chondrocytes cultured in standard [Na⁺] (154 nm) and western blotting intensities of these small proteoglycans varied with [Na⁺].

Conclusion This study demonstrates that biglycan and decorin are expressed in the human chondrocyte cell line C20A4. We are now searching if [Na⁺] variations is able to produce qualitative or quantitative alterations in the matrix synthesis as it have been found in osteoarthritis.

-Supported by FIS grant 99/0695-

AB0020 COMPARISON OF SYNOVIAL MMP-1 AND TIMP-1 LEVELS IN PATIENTS WITH VARIOUS INFLAMMATORY ARTHRITIDES

S Pay, H Erdem, M Serdar, A Dinc, I Simsek, M Turan. *Department of Internal Medicine Division of Rheumatology, Department of Hydroclimatology and Medical Ecology, and Department of Biochemistry, Gülhane School of Medicine, Ankara, Turkey*

10.1136/annrheumdis-2001.914

Background Some inflammatory arthritides like a rheumatoid arthritis cause erosion in bones and destruction in cartilage, but others such as Behçet's Disease (BD) and Familial Mediterranean Fever (FMF) do not.

Objectives The purpose of this study was to investigate synovial levels of matrix metalloproteinase ?1 (MMP-1) known to break collagen, and tissue inhibitor of metalloproteinase (TIMP-1), its natural antagonist, in patients with various inflammatory disorders.

Methods One hundred and nine patients with different inflammatory arthritides were enrolled in the study (20 BD, 20 FMF, 24 spondyloarthropathy (SPA), 26 rheumatoid arthritis (RA) and 19 osteoarthritis (OA)). All patients had at least one-sided knee arthritis from which synovial fluid samples were obtained. Patients with BD, FMF and SPA constituted three study groups. Patients with RA and OA were used as control groups. Synovial MMP-1 and TIMP-1 levels were measured by two-step sandwich ELISA.

Results The mean levels of synovial MMP-1 and TIMP-1 of the study and control groups presented in Table 1.

Abstract AB0020 Table 1

	BD	Study Groups FMF	SPA	Control RA	Groups OA	p*
MMP-1	0.305 ±	0.237 ± 0.253	0.190 ±	0.244 ±	0.126 ±	0.019
mcg/dl	0.217		0.224	0.230	0.113	
TIMP-1	6.040 ±	5.784 ± 3.378	6.080 ±	5.660 ±	8.574 ±	0.017
mcg/dl	2.490		3.960	2.931	2.702	

MMP-1 and TIMP-1 levels of the study and control groups (*Kruskal-Wallis test).

Conclusion Although FMF and BD are generally characterised by nonerosive arthritis, our results showed that synovial MMP-1 levels of patients with BD and FMF were not different from the patients with RA, which is a well-known erosive arthritis. We suggested two possible explanations for these unexpected data. First, BD and FMF generally cause short term arthritic attacks, remitting without permanent damage. Second, high synovial MMP-1 levels in BD and FMF may be resulted from extra

articular origin, because of their systemic nature. The comparison of synovial MMP-1 levels between RA and SPA was statistically significant. This may help to explain why SPA causes less prominent destruction in cartilages and erosion in bones than RA. Except OA, the difference between the groups with respect to the synovial TIMP-1 levels was statistically insignificant.

AB0021 TOPIRAMATE AS SUSPICIOUS CAUSE OF ARTHROPATHY- ANOTHER CASE REPORT

¹G Saviola, ¹L Abdi Ali, ²S Avanzi, ³M Castagna, ⁴D Idone. *¹Rheumatology Unit, Salvatore Maugeri Foundation IRCCS, Castel Goffredo, Mantua; ²Neuropsychology Unit; ³Rehabilitation Department; ⁴Department of Neurology, Pederzoli Hospital, Peschiera Del Garda, Verona, Italy*

10.1136/annrheumdis-2001.915

Background One year ago we described the case of a 23 year old female suffering from idiopathic generalised epilepsy treated with valproate and topiramate. The patient developed a poliartthritis that improved after topiramate was discontinued.¹

Objectives

Methods We present a 58 year old male suffering since 1996 from epileptic seizures and left hemiplegia secondary to subarachnoid haemorrhage; he had a history of hypertension, diabetes and cigarette smoke.

Results Since September 1999 the patient was treated with phenobarbital at the dose of 100 mg per day, since January 2000 topiramate was added at the dose of 100 mg per day. He was admitted in our department in July 2000 because of worsening of the motor performance: due to myalgias of the limbs, arthralgias to the left knee and hand, and a frozen left shoulder (it was impossible to obtain any passive movement of that joint). X-ray of the left shoulder showed Sudeck's atrophy; rheumatological blood tests were negative. We stopped topiramate and substituted it with gabapentin at the dose of 100 mg t.i.d.. 3 months after suspension of topiramate, continuing the treatment with gabapentin and phenobarbital, the patient showed a marked improvement in the range of motion of the left shoulder (passive abduction of 45°; because of hemiplegia, active movements were impossible); moreover arthralgias and myalgias at the limbs disappeared.

Conclusion Topiramate, a new anti-epileptic drug, seems to have a potential arthropathic role which should be better studied.

REFERENCE

- 1 Saviola G, Abdi Ali L, Avanzi S, Idone D. Poliartrite da Topiramato: caso clinico. *Reumatismo* 2000;**52**(3):627

THU0052 FIBROBLAST-LIKE SYNOVIOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS ARE MORE INVASIVE THAN FROM OSTEOARTHRITIS IN AN IN VITRO SYSTEM: CORRELATION WITH GROWTH CHARACTERISTICS AND EXPRESSION OF MMP-1, MMP-3 AND MMP-10

TC Tolboom¹, E Pieterman¹, WH Vd Laan², AL Huidekoper¹, RG Nelissen³, FC Breedveld¹, TW Huizinga¹. *¹Rheumatology; ²Gaubius Laboratory, TNO Prevention and Health, Leiden, The Netherlands; ³Orthopaedic Surgery*

10.1136/annrheumdis-2001.916

Background

Objectives Fibroblast-like synoviocytes (FLS) are involved in joint destruction. In this study the invasiveness in a transwell

system in vitro was correlated with origin of synoviocytes. Moreover the relation between invasive growth of FLS in the transwell system and growth characteristics and expression of MMP-1, -14, -17, -19, cathepsin K, TIMP-1 and -2 was determined.

Methods FLS were derived from 56 patients (30 rheumatoid arthritis (RA), 17 osteoarthritis (OA), 9 avascular necrosis (AVN) or fractures). Invasive growth of FLS through a collagen matrix was measured in a transwell system coated with matrigel. The number of cells grown through the matrix and the transwell membrane were counted. Growth rate was determined by counting of FLS after seven days of culturing. Expression of MMP's, cathepsin-K and TIMP's was investigated using RT-PCR and related to expression of a household gene, beta-actin.

Results FLS from RA invaded more easily in vitro than FLS from OA and AVN (median: RA: 4788 (cells grown through matrix and transwell membrane), OA: 1875; $p < 0.001$ and AVN: 1530; $p = 0.014$ respectively). The median rate of proliferation of RA FLS was 0.27 per day compared to OA 0.22 per day ($p = 0.012$) and AVN and fractures 0.25 per day (RA versus AVN: $p = 0.242$; OA versus AVN: $p = 0.553$), but there was no correlation between rate of proliferation and invasive growth in vitro. FLS that expressed MMP-1, MMP-3 or MMP-10 were significantly more invasive (median number of invasive cells: 3835, 4248, 4990, respectively) than cells that did not express MMP-1, MMP-3 or MMP-10 (1605, $p = 0.03$; 1970, $p = 0.004$; 2360, $p = 0.012$, respectively). Expression of the other MMP's, cathepsin-K and TIMP's did not show a significant relationship with invasive growth. Expression of MMP-9 showed a trend with higher expression in more invasive cells ($p = 0.066$). There was also a significant relationship between the expression of MMP-1 and MMP-9 and a diagnosis of RA (both $p = 0.013$).

Conclusion FLS of RA invade more easily in a matrigel matrix than OA FLS. This is not due to a greater rate of proliferation of RA FLS than OA FLS, although FLS from RA patients have a 25% higher rate of proliferation than FLS from OA patients. A significant relationship exists between the expression of MMP-1, MMP-3 and MMP-10 and invasive growth in a matrigel transwell system and this relationship was nearly significant for MMP-9. FLS of RA patients expressed significantly more often MMP-1 and MMP-9 than FLS from OA patients.

OP0025 GLUCOSAMINE SULFATE INHIBITS NITRIC OXIDE AND STROMELYSIN PRODUCTION IN CARTILAGE CULTURES AND REVERSES IL-1 INHIBITION OF OSTEOARTHRITIC ARTICULAR CARTILAGE SYNTHESIS

I Yaron, I Shirazi, R Judovich, M Yaron. *Department of Rheumatology, Ichilov Hospital, Tel Aviv, Israel*

10.1136/annrheumdis-2001.917

Background Glucosamine sulfate is used for the management of osteoarthritis of the knee.

The mechanism of its effects needs clarification.

Objectives To evaluate the effects of glucosamine sulfate on the production of nitric oxide (NO) and stromelysin (MMP3) and cartilage synthesis in human osteoarthritic cartilage in the presence of IL-1b or LPS.

Methods Cartilage was obtained in the operation theatre from patients undergoing total knee replacement for osteoarthritis, cut into small pieces and cultured in the presence or absence of IL-1b or LPS.

NO in culture media was measured with the Griess reagent, MMP-3 by ELISA and cartilage synthesis by ^{35}S incorporation.

Results IL-1b (1 ng/ml) and LPS (3 µg/ml) stimulated NO release in human osteoarthritic cartilage cultures about four fold. Glucosamine sulfate (1 µg/ml, 10 µg/ml, 100 µg/ml) inhibited stimulated NO production in a dose dependent manner, reaching statistical significance ($p < 0.05$) at 100 µg/ml glucosamine sulfate (60% and 38% inhibition respectively).

Glucosamine sulfate (100 µg/ml) significantly ($p < 0.05$) inhibited MMP-3 release in IL-1b and LPS stimulated cartilage cultures. IL-1b and LPS inhibited cartilage synthesis by 70% and 50% respectively ($p < 0.001$). Glucosamine sulfate reversed this inhibition in a dose dependent manner reaching statistical significance ($p < 0.05$) at 10 µg/ml glucosamine sulfate.

Conclusion Glucosamine sulfate may protect human osteoarthritic articular cartilage by inhibiting local NO and MMP-3 production and by reversing IL-1b inhibition of cartilage synthesis.

OP0026 IN VIVO INHIBITION OF ENDOGENOUS TGF-BETA ACTIVITY REDUCES OSTEOPHYTE SIZE AND CARTILAGE PROTEOGLYCAN CONTENT

A Scharstuhl, P Van der Kraan, E Vitters, H Van Beuningen, W Van der Berg. *Department of Rheumatology, University Medical Centre Nijmegen, Nijmegen, The Netherlands*

10.1136/annrheumdis-2001.918

Background Transforming Growth Factor-beta (TGF-beta) is considered to be a beneficial factor during cartilage repair. However, TGF-beta can also induce fibrosis and osteophytes. TGF-beta signalling starts with the binding of TGF-beta to the type II receptor, a constitutively active serine/threonine kinase. This complex then binds the type I receptor, which is subsequently phosphorylated by the type II receptor. This results in phosphorylation of downstream mediators by the type I receptor. Since the binding of TGF-beta to the extracellular domain of the type II receptor is one of high affinity, the soluble TGF-beta type II receptor, lacking cytoplasmic and membrane domains, was used as a TGF-beta antagonist.

Objectives The objective of this study was to determine the effect of inhibition of endogenous TGF-beta during an experimental model of cartilage damage.

Methods For the production of recombinant solRII, the methylotrophic yeast *Pichia pastoris* was used. Intra-articular injection of papaine was used as a model for experimental cartilage damage and osteophyte formation. The effect of systemic delivery of solRII on endogenous TGF-beta was investigated in this model. Therefore, Alzet osmotic pumps containing either 10 mg of solRII or pumps containing solvent were implanted i.p. in C57Bl/6 mice. One day later, a 1.2% papaine solution was injected in the right knee joint. Knees were dissected on day 7 and processed for routine histology.

Results Injection of papaine into murine knee joints resulted in the formation of osteophytes and a decrease in proteoglycan (PG) content of non-calcified articular cartilage. Blocking of endogenous TGF-beta via systemic administration of solRII resulted in a reduction of 75% in osteophyte size compared to controls. Moreover, cartilage PG content was significantly decreased in solRII treated animals compared to control animals.

Conclusion This study shows for the first time that inhibition of endogenous TGF-beta leads to a reduction in osteophyte size in the papaine model of cartilage damage and osteophyte formation. This finding implicates a direct role for TGF-beta in the