Bank, University and Hospital Centre of Coimbra, with approval by the Ethics Committee. Phosphorylated levels of JNK, p38, ERK1/2, PKA, Akt and PKC and the levels of LC3B-I and II were evaluated by Western Blot of total cell extracts from C28/I2 cells.

Results: Immunoreactivity for Y₁, Y₂ and Y₅ NPY receptors was observed in C28/I2 cells. In human cartilage, a positive signal was found for the Y₂ receptor in all samples while Y₅ receptor immunoreactivity was undetectable, regardless of disease state, gender and age of the donors. Y₁ receptor immunoreactivity was observed in male and female OA cartilage samples, as well as in those from non-OA females, but not in those from non-OA males. 50 nM NPY was sufficient to significantly increase the levels of phospho-JNK, -p38, -ERK1/2, -PKA, Akt and PKC with similar kinetics, but much slower than IL-1 β . A 6 hour stimulation with 50 or 100 nM NPY decreased LC3B-I and II levels in comparison with untreated cells. In the presence of chloroquine (ChQ), NPY increased LC3B-II levels relative to those found in cells treated with ChQ alone, indicating an increased delivery of LC3B-II to the lysosome consistent with autophagy activation by NPY.

Conclusions: This study shows that distinct NPY receptor subtypes are present and functional in C28/I2 cells and in human chondrocytes *in situ* in the articular cartilage, strongly suggesting that non-neuronal cells and tissues of the joints, namely chondrocytes, are relevant as NPY targets. The presence of each receptor subtype seems to be determined by gender and, in males, also by the disease state. The role of age is unclear as most cartilage donors were aged >55 years old. Future studies will be addressed at further elucidating the role of NPY and its receptors in modulating male and female chondrocyte functions, both in health, ageing and osteoarthritis.

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AB0097 INDIVIDUAL FUNCTIONS OF THE HISTONE-ACETYLTRANSFERASES CBP AND P300 IN RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: The close homologues cAMP-response element binding protein (CREB) binding protein (CBP) and p300 are writers of H3K27 histone acetylation marks found in active enhancers. In addition, their bromodomains are readers of acetylated lysine residues on histone tails and are subject of drug development for inflammatory and malignant diseases. CBP and p300 are widely accepted as redundant proteins and unique functions have not been investigated yet in depth.

Objectives: To analyse individual functions of CBP and p300 in rheumatoid arthritis synovial fibroblasts (SF).

Methods: SF were treated with the pan inhibitor I-CBP (1 μ M, 5 μ M), targeting the bromodomains of CBP and p300, in presence and absence of TNF- α (10 ng/ml) for 24 hour. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (5 nM) in SF. Knockdown was verified by Western blotting. 24 hour after transfection cells were stimulated with TNF- α (10 ng/ml) for 24 hour. The mRNA expression of potential target genes was measured by quantitative Real-time PCR, using RPLP0 as an endogenous control. The protein expression of HOXD10 after CBP and p300 silencing was verified by Western blotting.

Results: I-CBP dose-dependently reduced the TNF- α -induced expression of MMP1 (p<0,05), MMP3, IL6 and IL8 in SF (n=3). Antisense LNA gapmeRs targeting CBP reduced the protein expression of CBP by 68,7% ($\pm$ 12,9%, p<0,01, n=5) in unstimulated cells and by 89,7% ($\pm$ 12,9%) in presence of TNF- α . The protein expression of p300 was reduced by 55,3% ($\pm$ 29,8%, p<0,05, n=6) in unstimulated cells and by 62,7% ($\pm$ 27,9%) in presence of TNF- α after transfection of LNA gapmeRs targeting p300. Silencing of CBP in SF (n=7) reduced the TNF- α -induced expression of IL6 (p<0,05), IL8 (p<0,05), MMP3 (p<0,05), as well as the basal (p<0,001) and the TNF- α -induced expression of MMP1 (p<0,05). In contrast, silencing of p300 induced the basal expression of IL6 (p<0,05), IL8 (p<0,01),

MMP1 (p<0,05), and MMP3 (p<0,05), as well as the TNF- α -induced expression of IL6 (p=0,078), IL8 (p=0,078), MMP1 (p<0,05) and MMP3 (p=0,063). Silencing of CBP in hand SF (n=4) reduced the expression of hand-specific HOX genes including HOXD10 (0,53 $\pm$ 0,10 fold; p<0,01), HOXD11 (0,76 $\pm$ 0,19 fold; p=0,098) and HOXA13 (0,75 $\pm$ 0,17 fold; p=0,063), whereas HOXA9, HOXA10 and HOXA11 were not affected. Silencing of p300 reduced the expression of HOXD10 (0,65 $\pm$ 0,24 fold; p=0,061), HOXD11 (0,45 $\pm$ 0,10 fold; p<0,01), HOXA10 (0,70 $\pm$ 0,14 fold; p<0,05) and HOXA13 (0,55 $\pm$ 0,19 fold; p<0,05). The down regulation of HOXD10 after silencing of CBP and p300 in hand SF was confirmed on protein levels by Western blotting.

Abstract AB0097 – Table 1

	CBP gapmeR	CBP gapmeR +TNF	p300 gapmeR	p300 gapmeR +TNF
MMP1	0,46 $\pm$ 0,17	0,41 $\pm$ 0,75	25,86 $\pm$ 26,82	1,96 $\pm$ 1,35
MMP3	0,97 $\pm$ 0,31	0,64 $\pm$ 0,35	2,60 $\pm$ 1,62	3,05 $\pm$ 2,89
IL6	1,21 $\pm$ 0,43	0,29 $\pm$ 0,17	4,51 $\pm$ 3,32	1,90 $\pm$ 1,20
IL8	8,27 $\pm$ 9,70	0,52 $\pm$ 0,20	207,8 $\pm$ 96,17	4,75 $\pm$ 2,67

Conclusions: Our results unravel opposing functions of CBP and p300 in regulating the TNF- α -induced expression of inflammatory and matrix-degrading target genes in SF. In addition, CBP and p300 likely contribute to the maintenance of a joint-specific gene expression in SF by regulating the expression of hand-specific HOX genes.

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AB0098 PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR-1 β FACILITATES MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA ACTIVATION OF CANONICAL AND NON-CANONICAL NF-KB SIGNALLING PATHWAY

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Background: Fibroblast-like synovocytes (FLS) in rheumatoid arthritis (RA) manifest tumor-like properties including increased proliferation, prolonged survival, apoptosis resistance, adherence and invasiveness of adjacent tissues. Peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1) β is a transcriptional coactivator which plays important roles in regulating energy metabolism and cytokine signalling pathways. Our previous study showed that elevated PGC-1 β expressed in RA-FLS promoted their pro-inflammatory effect. However, the roles of PGC-1 β on regulating migration and invasion of RA-FLS remains to be identified.

Objectives: To investigate the role of PGC-1 β on regulating migration and invasion of RA-FLS and underlying mechanism.

Methods: Synovial tissues were obtained by closed needle biopsy from six patients with active RA and FLS were isolated and cultured. PGC-1 β in RA-FLS was down-regulated or over-expressed by lentivirus with same vectors marked Lv-sh-GFP or Lv-GFP as negative controls. Effects of PGC-1 β on migration and invasion capacity were detected by wound healing assays and transwell migration and invasion assays. The change of proteases in culture supernatants were detected by Proteome Profiler human protease array kit (R and D Systems, USA) and verified by qRT-PCR and western blot. The expression of key signalling molecules in canonical and non-canonical NF- κ B signalling pathway was detected by western blot.

Results: Down-regulation of PGC-1 β by Lv-sh-PGC-1 β transfection inhibited migration and invasion of RA-FLS compared with Lv-sh-GFP transfection group (wound healing: 1252 $\pm$ 214 vs. 764 $\pm$ 184 μ m, p<0.001; migration: 184 $\pm$ 74 vs. 642 $\pm$ 32 cells/field, p<0.001; invasion: 124 $\pm$ 47 vs. 445 $\pm$ 67 cells/field, p<0.001), while

over-expression of PGC-1 β promoted migration and invasion of RA-FLS (all $p < 0.05$, figure 1A–C). Down-regulation of PGC-1 β in RA-FLS significantly decreased the expression of MMP-3 and MMP-9 in the culture supernatant which was measured by Proteome Profiler human protease array (MMP-3: $p = 0.032$, MMP-9: $p = 0.037$). Further qRT-PCR and western blot analysis verified that both mRNA and protein expression of MMP-3 and MMP-9 in RA-FLS were significantly decreased compared with Lv-sh-GFP transfection group (all $p < 0.05$, figure 1D). Down-regulated PGC-1 β in RA-FLS significantly suppressed the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK in protein level, while over-expression of PGC-1 β promoted the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK (all $p < 0.05$, figure 1E).

Abstract AB0098 – Figure 1. Effects of PGC-1 β on the migration and invasion capacity as well as proteases expression, canonical and non-canonical NF- κ B signalling pathway activation in RA-FLS. **A–C** After down-regulation or over-expression of PGC-1 β , wound healing and transwell assay showed the capacity of horizontal migration (**A**), vertical migration (**B**) and invasion (**C**) of primary RA-FLS. **D** After down-regulation or overexpression of PGC-1 β , the expression of MMP-3 and MMP-9 was measured by qRT-PCR and western blot. **E** After down-regulation or overexpression of PGC-1 β , the expression of NF- κ B p65, NF- κ B p-p65, RelB and NIK was measured by western blot. The data were representative as means $\pm$ SD from six different RA patients. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Conclusions: Our findings suggested that PGC-1 β facilitates the migration and invasion capacity and MMP-3/9 expression in RA-FLS through activation canonical and non-canonical NF- κ B signalling pathway.

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AB0099 ARTHROSCOPIC PECULIARITIES OF THE INFLAMMATORY PROCESS OF SYNOVIAL SHELL IN UROGENIC ARTHRITIS

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Background: In recent years there has been an increase in the incidence of reactive arthritis (ReA), associated with urogenital infection. Chronic synovitis of urogenital etiology is a nonspecific process, pathogenesis is very close to rheumatoid arthritis (RA), which complicates differential diagnosis. According to the literature, the inflammatory process in the synovial membrane (SM) supports the persistence of chlamydia, which reduces the effectiveness of standard anti-

inflammatory therapy of arthritis in patients with undifferentiated seronegative oligoarthritis, spondyloarthropathy, RA.

Objectives: Arthroscopic assessment of the level of the inflammatory process in the synovial membrane, depending on the duration of the disease and the activity of the pathological process in patients with urogenital arthritis.

Methods: The study involved 39 patients with RA of urogenital etiology complicated by synovitis of knee joint (KJ) were examined; 23 of them were women and 16 men; mean age was 35.5 ± 38.0 years. They received inpatient treatment at the Department of Traumatology and Orthopaedics of the 2nd TMA Clinic in 2014–2016 years. All these patients underwent diagnostic arthroscopy of KJ. Laboratory tests included enzyme-linked immunosorbent assay (ELISA) for TORCH infection, a polymerase reaction (PCR), determination of a rheumatic factor in synovial fluid and blood before and after treatment, arthroscopy of the joint.

Results: In arthroscopic examination in the acute phase (early period) of ReA, dull SM, vasodilation, and oedema are revealed, which is accompanied by an increase in the production of turbid synovial fluid (SF). On the surface of SM there are sections of fibrin filaments, expansion and hyperemia along the vessels. In the long-term (subacute phase) these violations partially disappear. The surface of the synovium can again become single-rowed, with moderate hyperemia of the vessels. The deposits of fibrin on the entire surface of SM can be significant. However, with reduced immunoreactivity of the organism, the reactive synovitis persists for a long time, and the chronic course of the pathological process leads to abundant deposits of fibrin masses and to the formation of villi in the form of large and flat petals. In some parts of the vascular vessels are pale, accompanied by disorganisation of the collagen frame of SM, which directly affects the cells of the articular cartilage.

Conclusions: Thus, reactive urogenital arthritis due to the persistence of an infectious agent is characterised by the polymorphism of the damage to the joint and cartilage of the joint. The arthroscopic changes revealed at various stages of the inflammatory process reflect the reactivity of the pathological process and determine the extent of the lesion. Arthroscopic examination of biopsy specimens of SM and cartilage allows to determine the dynamics of the disease, the degree of lesion, evaluate the effectiveness of the preventive and therapeutic measures being carried out, and also to determine the indications for joint synovectomy.

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AB0100 NEUROGENIC INFLAMMATION CHARACTERISED BY NERVE GROWTH FACTOR, TRKA AND SUBSTANCE P IS PREVALENT IN HUMAN FACET JOINT OSTEOARTHRITIS

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Background: Facet joint osteoarthritis (FOA) is a frequent cause of chronic low back pain and spinal stenosis. Neuron-derived molecules regulate pain sensation and inflammation. Nerve growth factor (NGF) is one of the most important mediators for this mechanism that is termed neurogenic inflammation.¹ Among many other effects, it regulates substance P (SP) expression as pivotal downstream peripheral pro-inflammatory molecule. Consequently, NGF inhibitors (NGFi) as a novel class of pain medication have shown significant efficacy in OA and to some extent also low back pain. However, it is unknown which tissue compartments in facet joints are involved in NGF signalling.

Objectives: To determine expression patterns of NGF, its high affinity transmembrane tyrosine kinase A (TrkA) receptor and SP in cartilage, subchondral bone marrow and capsular tissues of facet joints (FJ).

Methods: Dissected human FOA specimens of six donors were examined. OA severity was graded on HE-stained tissue sections. NGF, TrkA and SP expression was evaluated by immunohistochemistry with monoclonal antibodies. Similarly, new bone formation was assessed by staining for osteocalcin.

Results: FJ had low (n=2), high (n=2) and intermediate (n=2) inflammatory bone marrow infiltrates. NGF was strongly expressed in capsular tissue (figure, 40x),