to IFN- γ production and subsequent induction of interferon-stimulated genes (ISGs).

Objectives: To explore the potential of TBK1 inhibitors to downregulate IFN- γ activation in SLE and SSc.

Methods: TBK1, IRF3, IRF7 and STAT1 were determined by qPCR in PAXgene samples and phosphorylated-TBK1 (pTBK1) was analysed by flowcytometry in plasmacytoid dendritic cells (pDCs) from IFN- γ positive (IFNpos) patients. Peripheral blood mononuclear cells (PBMCs) from SLE and SSc patients and TLR7-stimulated PBMCs from healthy controls (HCs) were cultured with the TBK1 inhibitors BX795 followed by analysis of ISGs.

Results: Increased expression of TBK1, IRF3, IRF7 and STAT1 in whole blood and pTBK1 in pDCs was observed in IFNpos pSS, SLE and SSc patients compared to HCs. Upon treatment with BX795, PBMCs from IFNpos pSS, SLE, SSc and TLR7-stimulated HCs downregulated the expression of the ISGs MxA, IFI44, IFI44L, IFIT1 and IFIT3. The TBK1 inhibitor inhibited the secretion of IFN- γ by TLR7-stimulated PBMCs from HCs.

Conclusions: TBK1 inhibition reduced expression of ISGs in PBMCs from IFNpos SLE and SSc patients indicating TBK1 as a potential treatment target.

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AB0039

IMMUNOSUPPRESSIVE EFFECT OF MESENCHYMAL STEM CELLS ON MONOCYTES DERIVED FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Mesenchymal stem cells (MSCs) are a heterogeneous population of fibroblast-like progenitor cells that may be isolated and expanded from bone marrow, umbilical cord and other tissues. Moreover, MSCs display the capacity to self-renew and differentiate into various mesodermal cell lineages. They also have drawn considerable attention for their regenerative and immunosuppressive effects in a range of autoimmune diseases, which raises the question for their potential use as therapeutic tool in rheumatoid arthritis.

Objectives: In line with aforementioned and taking in mind that monocytes playing pivotal role in orchestrating immunological tolerance, we aimed to study the immunosuppressive effects of adipose tissue derived mesenchymal stem cells (AT-MSC) on monocytes derived from patients with rheumatoid arthritis (RA).

Methods: We enrolled 12 patients matching the ACR/EULAR 2010 criteria for RA. AT-MSC were isolated and cultured according to well established protocols. ELISA was performed for testing the cytokines produced by AT-MSC (IL-1, IL-10, IL-4, IFN- γ , IL-6, IL-8, CCL-5, RANTES, IL-17). Peripheral blood mononuclear cells (PBMCs) isolated from RA patients' samples were cultured in AT-MSC conditioned media and in control media. Flow cytometry was used for detection of monocytes markers (CD14, CD80, CD86, HLA-DR).

Results: Our results revealed considerable increase in number of cells expressing the myeloid lineage surface marker CD14 ($p=0.026$) under the influence of AT-MSC medium. We further demonstrated decrease in percentage values of monocytes expressing HLA-DR ($p=0.004$) and CD80/86 surface molecules ($p=0.47$). Moreover, significant reduction in mean fluorescent intensity of HLA-DR surface expression ($p=0.016$) was also demonstrated.

Conclusions: Our study unambiguously points out that under the impact of AT-MSC media monocyte development into dendritic cells was hampered and was also skewed into direction of accumulation of monocytes displaying more tolerogenic phenotype characterised by down regulation of HLA-DR and B7 complex (CD80/86) surface expression. Furthermore, antigen presentation alongside with expression of the co-stimulatory B7 complex and cytokine ambience forms a three-way signalling pathway responsible for T helper activation and proliferation and consequent antibody production by plasma cells. Hence, effects exerted by AT-MSC conditioned media on monocyte lineage development should not be neglected in the context of developing novel therapeutic approaches and strategies for treatment of RA.

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AB0040

TOLL-LIKE RECEPTOR 9 INFLUENCES INFLAMMATORY ARTHRITIS AND OSTEOCLASTOGENESIS

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Background: Release and insufficient removal of endogenous nucleic acids may be involved in triggering autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 7 and 9, have been linked to pathogenic autoimmune processes, but their role in RA is less clear. Data obtained in rats with pristane-induced arthritis (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model¹.

Objectives: To gain more insight into the role of TLR9 in autoimmune arthritis, TLR9 inhibition with specific oligodeoxynucleotide sequences (ODN)² was investigated in rats with PIA. To further investigate TLR9 involvement, streptococcal cell wall (SCW) arthritis was induced in TLR9^{-/-} mice.

Methods: Arthritis was induced in mice with SCW lysates and in rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist, starting before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Levels of α -1-acid-glycoprotein (AGP), rheumatoid factor (RF) and IL-6 in sera were analysed. The role of TLR9 in osteoclast differentiation and activation was investigated *in vitro*.

Results: In PIA, the TLR9 antagonist reduced arthritis severity by ~50%, which was accompanied by a reduction of AGP, IL-6 and RF. TLR9 inhibition led to reduced inflammation, bone erosion and cartilage degradation. Moreover, the T cell-dependent chronic phase of SCW arthritis was significantly suppressed in TLR9^{-/-} mice. Remarkably, TLR7 and TLR9 mRNA levels strongly differed in the course of *in vitro* osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and stimulation with a TLR9 agonist (CpG) completely inhibited osteoclastogenesis.

Conclusions: Taken together, the results suggest a role for TLR9 in the T cell-dependent phases of PIA and SCW arthritis thus an important involvement of the DNA (CpG) recognising TLR9 in the initiation of autoimmune arthritis and during osteoclastogenesis. The precise role(s) of TLR9 in the different stages of arthritis needs to be further elucidated in future experiments.

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AB0041

HETEROGENEITY OF THE TYPE I INTERFERON SIGNATURE IN RHEUMATOID ARTHRITIS MAY ACCOUNT FOR DIFFERENCES IN ITS CLINICAL RELEVANCE

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Background: increased expression of interferon-responding genes (IRGs), the so-called IFN signature, has been reported in rheumatoid arthritis (RA) in peripheral blood and synovial tissue. However, some controversy exists concerning its clinical relevance, since longitudinal changes of the IFN signature have been reported upon different treatments and a physiological diversification of the type I IFN signature among different conditions has been recently described. Additionally, the relevance of the IFN signature in the very early stage of RA is unknown.

Objectives: to evaluate (i) whether quantitative and qualitative differences in the activation of the IFN signature can be found in RA patients depending on the clinical stage and (ii) if these differences may be linked to a clinical relevance of the IFN signature.

Methods: expression of IFI44, IFI44L, IFI6 and MX1 was determined in peripheral blood in 98 RA patients and 28 controls. RA patients were classified into groups according to their clinical stage and treatments received: very early RA (VERA, recruited at onset and not exposed to any treatment), bDMARD-naïve (patients on csDMARD treatment) and bDMARD (patients on biological treatment, all anti-TNF α agents). An additional group of 13 RA patients candidate for TNF α -blockade was also recruited and samples were taken before and after anti-TNF α treatment. The associations among IRGs were evaluated by network and principal component analyses.

Results: all IRGs was increased in RA, although differences were noted among them. The IFN score was increased in all RA groups (VERA, bDMARD-naïve and bDMARD), but differences in their degree of activation and in the relationships among IRGs were observed. VERA patients exhibited a lower activation of the IFN signature and a distinct picture of the structure of the IRG network (figure 1) compared to both their established disease-counterparts and the HC group. The IFN score correlated the accumulated DAS28 over one year ($r=0.593$, $p=0.025$) and it was found to be a predictor of a good clinical outcome (EULAR good clinical response) in VERA (AUC=0.917, $p=0.004$). However, no differences in the IFN score were observed between the bDMARD-naïve and bDMARD groups, but opposite associations with the clinical parameters were noted. Interestingly, the correlations among IRGs delineate different pictures between these two groups. The IFN score at baseline predicted poor clinical outcome upon TNF α -blockade. Although no absolute changes in the IFN score were found, TNF α -blockade shifted the associations among IRGs. These differences mirrored those found when comparing bDMARD-naïve and bDMARD groups.

Abstract AB0041 – Figure 1

Conclusions: a certain heterogeneity within the IFN signature can be recognised in RA, depending on the clinical stage. The structure of the IFN signature may be a potential explanation for the controversy in this field and may represent a limitation for its use as a clinical biomarker.

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AB0042

ESSENTIAL OIL EXTRACTED FROM CHAMAECYPARIS OBTUSA ATTENUATES THE SEVERITY OF COLLAGEN-INDUCED ARTHRITIS

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Background : *Chamaecyparis obtusa* (*C. obtusa*) is a tropical tree species found in Japan and the southern region of South Korea. Although the biological activities of essential oil extracted from *C. obtusa* (EOCO) are not yet fully understood, essential oil has been shown to have antibacterial activities and anti-inflammatory effects.

Objectives: We investigated the effect of essential oil extracted from *Chamaecyparis obtusa* on the development of collagen-induced arthritis (CIA), a well-characterised preclinical model of human RA.

Methods: DBA1/J mice were injected intraperitoneally with EOCO dissolved in dimethyl sulfoxide (DMSO) 3 times a week for 5 weeks after type II collagen (CII) immunisation. Arthritis severity was evaluated by clinical and histological parameters. Serum anti-CII antibody levels were assayed by ELISA. Interleukin-17 (IL-17) expressions in the joints were determined by immunohistochemistry. Effect of EOCO on Th17 cells and natural killer (NK) cells was analysed using flow cytometry.

Results: EOCO markedly reduced the clinical and histological severity of CIA. Serum anti-CII antibody levels and the expression of IL-17 in the joints were significantly lower in mice treated with EOCO than those treated with DMSO alone. EOCO inhibited the differentiation of Th17 cells in total splenocytes, not in isolated CD4⁺ T cells, from mice. EOCO increased the production of granzyme B and perforin in NK cells.

Conclusions: Our data demonstrate a protective effect of EOCO on the development of CIA through the inhibition of Th17 cell differentiation. This effect may be related with NK cell activity enhanced by EOCO.

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AB0043

THE ELASTICITY PROPERTIES OF PROBIOTIC BACTERIA WALL ASSOCIATED WITH BENEFICIAL MODULATORY ACTIVITY ON INNATE IMMUNITY OF THE HOST

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Background: Probiotics have tremendous potential to develop healthy diets and integrated approach for immunity-related diseases treatment and prevention;^{1,2} are effective actors in distant sites³ with strong potential for applications in rheumatology. The cell wall of probiotic bacteria plays an essential role in many aspects of modulating beneficial immune response;⁴ its elasticity properties associated with probiotic beneficial effects and can warrant to stratify strains on their modulatory activity on innate immunity to justify individualised and personalised approach for nutrition and prevention.

Objectives: The aim was to study the effect of lactic acid bacteria (LAB) and bifidobacteria strains on phagocytic system cells functional activity and immunoregulatory cytokines synthesis *in vitro* in regards to the bacteria surface properties as cell walls elasticity using atomic force microscopy (AFM).

Methods: We conducted experimental studies on BALB/c line mice 18–20 g weight using lyophilized strains of LAB – *Lactobacillus acidophilus* IMV B-7279, *L. casei* IMV B-7280, *L. delbrueckii* subsp. *bulgaricus* IMV B-7281 and bifidobacteria – *Bifidobacterium animalis* VKL, *B. animalis* VKB. We cultivated the macrophages received from the peritoneal cavity of mice by common method individually with the strains of LAB and bifidobacteria. We estimated the impact of LAB and bifidobacteria strains on the functional activity of peritoneal cavity macrophages using the conventional methods of study oxygen-dependent bactericidal activity, nitric oxide production, their effect on the immunoregulatory cytokines. We used AFM scanning to estimate bacteria cell walls elasticity.

Results: All strains demonstrated a stimulating effect on the functional activity of macrophages and ability to produce NO/NO₂ *in vitro*. Lactobacilli strains increased the production of IL-12 and IFN- γ *in vitro*. The AFM demonstrated different degree of the cell walls elasticity in various strains of LAB and bifidobacteria. Among lactobacilli the most elastic cell wall was found in *L. delbrueckii* subsp. *bulgaricus* IMV B-7281, and among bifidobacteria – in *B. animalis* VKL, which induced the considerable activation of the phagocytes. Probiotic strains survival in