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

Objectives: To explore the potential of TBK1 inhibitors to downregulate IFN-I 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-I 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-I 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.