Methods: Synovial fluid mononuclear cells (SFMCs), fibroblast like synovial cells (FLSs) and peripheral blood mononuclear cells (PBMCs) were obtained from a study population consisting of patients with active RA or peripheral SpA with at least one swollen joint (for obtaining synovial fluid) (n=14). SFMCs were cultured for 48 hours with and without addition of a MK2 inhibitor (Celnogene) at 1000 nM, 333 nM and 111 nM and supernatants were analysed by the Olink proseek multiplex interferon panel and commercially available ELISA assays. Because FLSs are only found in small amounts among SFMCs, autologous co-cultures of FLS and PBMCs and SFMCs were also used. SFMCs cultured for 21 days were used to study inflammatory macrophage differentiation and osteoclastogenesis.

Results: In SFMCs cultured for 48 hours, the MK2 inhibitor decreased the production of CXCL9 (p<0.001), CXCL10 (p<0.01), HGF (p<0.01), CXCL11 (p<0.01), TWEAK (p<0.05), and IL-12B (p<0.05) and increased the production of CXCL5 (p<0.0001), CXCL1 (p<0.001), TGFβ (p<0.01), MCP-3 (p<0.01), LAP (p<0.05) dose-dependently after Bonferroni correction (all corrected P values). At the highest concentration, the MK2 inhibitor also decreased MCP-1 production (p<0.05). In FLS-SFMC co-cultures, the MK2 inhibitor decreased MCP-1 production (p<0.05) but did not change the production of DKK1 and MMP3. In FLS-PBMC co-cultures, the MK2 inhibitor decreased the production of MCP-1 (p<0.05) but did not change DKK1 production. In SFMCs cultured for 21 days as a model of inflammatory macrophage differentiation and osteoclastogenesis, the MK2 inhibitor decreased the production of MCP-1 (p<0.05) and tartrate-resistant acid phosphatase (TRAP) (p<0.05) but did not change the production of IL-10.

Conclusions: This study reveals the effects of a MK2 inhibitor in ex vivo models of immune mediated inflammatory arthritis. The MK2 inhibitor changed the secretory profile of SFMCs and decreased inflammatory osteoclastogenesis. Taken together, this points to a role of this MK2 inhibitor in attenuating inflammatory and destructive arthritis.

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Abstract THU0096 – Figure 1. Modified from Wagner & Nebreda, Nature Review Cancer, 2009.

Conclusions: Our data suggest that apremilast was effective in preventing arthritis and bone erosion in CIA model, implicating a potential promise of therapy on rheumatoid arthritis.

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THU0097 PHOSPHODIESTERASES 4 (PDE4) INHIBITOR AMELIORATES EXPERIMENTAL ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory bone-destructive disorder with autoimmune features. Apremilast is a novel phosphodiesterase 4 (PDE4) inhibitor suppressing immune and inflammatory responses.

Objectives: We assessed the anti-inflammatory and bone protection effects of apremilast in collagen CII induced arthritis (CIA) model.

Methods: Apremilast was given starting from day 14 after immunisation, we investigated whether apremilast (5 mg/kg or 25 mg/kg) can ameliorate arthritis onset. Bone erosion was measured by histological and micro-computed tomographic analysis. Anti–mouse type II collagen (CII) antibody levels were measured by enzyme-linked immunosorbent assay. Human cartilage and rheumatoid arthritis (RA) synovial fibroblasts (RASFs) implantation in the severe combined immunodeficiency (SCID) mouse model of RA were used to study the role of apremilast in suppression of RASFs destroying cartilage in vivo.

Results: We found that apremilast therapy delayed arthritis onset and reduced arthritis scores in CIA model at a different dose, compared to CIA model and blank vector (figure 1A). Total serum IgG, IgG1, IgG2a, and IgG2b were all decreased in apremilast groups. Furthermore, apremilast can prevent CIA mice from bone erosion by CT analysis. High dose of apremilast (25 mg/kg) was superior to low dose (5 mg/kg) in treating CIA (figure 1B, C). Apremilast treatment can inhibit destroy and migratory ability of RASFs to cartilages. Compared to the model group, Apremilast treatment significantly reduced the invasion scores in both primary implant and contralateral implant.

Conclusions: Our data suggest that apremilast was effective in preventing arthritis and bone erosion in CIA model, implicating a potential promise of therapy on rheumatoid arthritis.

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THU0098 COMBINATION THERAPY OF RAPAMYCIN AND A GLUTAMINE ANTAGONIST FACILITATES THE EXPANSION OF MYELOID-DERIVED SUPPRESSOR CELLS AND AMELIORATES ARTHRITIS IN SKG MICE

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Background: Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature cells that increase in the pathological state such as tumour or inflammation and have the immunosuppressive ability. MDSCs have been