(RKIP), an endogenous inhibitor of the extracellular signal-regulated kinase (ERK) pathway, has been implicated as a suppressor of metastasis and NF- κ B pathway in cancers².

Objectives: The NF- κ B and ERK pathways are considered to be one of the most important pro-inflammatory signalling pathways in RA. Therefore, RKIP might be a potential therapeutic target for RA. However, whether and how RKIP regulates RA is not fully understood. The present study was performed to examine whether and how RKIP are differentially regulated in RA.

Methods: The expressions of RKIP were assessed in synovial tissue, fluid and fibroblast-like synoviocytes (FLS) from patients with RA and osteoarthritis (OA) by immunofluorescence staining and western blotting. RA- or OA-FLS were infected with either a recombinant adenoviral RKIP overexpressing vector (Ad-RKIP) or shRNA-expressing vector (Ad-shRKIP). Control cells infected with a GFP-targeted recombinant adenoviral vector (Ad-shGFP) (figure 1C). And then, we investigated the effects of RKIP on the migratory activity and invasion rates of FLS by transwell migration and invasion assay.

Results: Here, we show that RKIP expression is inversely correlated with RA. The levels of RKIP were significantly decreased in fibroblast-like synoviocytes (FLS), synovial fluid and synovium of RA patients compare to OA patients. And also find that migration and invasion of RKIP in RA were significantly increased by the inhibition of RKIP compare to OA-FLS. Knockdown of RKIP in RA or OA-FLS resulted in a dramatic increase of MMP3 and IL6. We also found osteoclastogenesis of RAW cells were increased by the knockdown of RKIP.

Conclusions: Our data identify a role of RKIP in RA and suggest that further studies on the potential involvement of RKIP will be beneficial in better understanding the pathology of and providing a new target for treatment for RA.

REFERENCES:

- [1] Ospelt C. Synovial fibroblasts in 2017. *RMD Open* 2017;3(2):e000471.
- [2] Yesilkalan AE, Rosner MR. Raf kinase inhibitory protein (RKIP) as a metastasis suppressor: regulation of signaling networks in cancer. *Crit Rev Oncog*. 2014;19:447–454.
- [3] Noh HS, Hah YS, Ha JH, Kang MY, Zada S, Rha SY, Kang SS, Kim HJ, Park J, Byun J, Hahm JR, Shin JK, Jeong S, Lee Y, Kim DR. Regulation of the epithelial to mesenchymal transition and metastasis by Raf kinase inhibitory protein-dependent Notch1 activity. *Oncotarget* 2016;7(4):4632–46.

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Spondyloarthritis – etiology, pathogenesis and animal models

AB0141 CERTOLIZUMAB PEGOL LIKE REDUCES INFLAMMATION AND BONE DAMAGE IN TMTNF TRANSGENIC MICE

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Background: Transmembrane (tm)TNF (TgA86) mice is a transgenic line that spontaneously develops peripheral arthritis and spondylitis at 4 weeks of age, mimicking human spondyloarthritis (SpA).

Objectives: The aim of this work is to understand the effect of TNF blockade in this SpA-like phenotype mouse strain, focusing on histological inflammation and bone damage.

Methods: (tm)TNF (TgA86) mice were treated with a certolizumab pegol like product mice equivalent (Ab501), 100 mg/kg twice a week intraperitoneal, or with vehicle (phosphate buffer saline), for 12 weeks, in a therapeutic (10 weeks of age) and preventive (4 weeks of age) experimental settings. A semi-quantitative score for the severity of histologic inflammation and bone damage, in the paws (infiltration, lining cells, erosions and global), and in the spine (inflammation, intervertebral disc destruction, cartilage damage, bone erosion and ectopic chondrocytes/chondrocyte) was applied to haematoxylin and eosin stained slides.

Results: 14 (tm)TNF (TgA86) mice (6M/8F) at 10 weeks of age (therapeutic group), and 15 (tm)TNF (TgA86) mice (10M/5F) at 4 weeks of age (preventive group), were treated with Ab501; and 30 (tm)TNF (TgA86) mice with the respective vehicles, for a period of 12 weeks. A statistically significant reduction of the inflammatory infiltrate ($p \leq 0.001$), lining cells layers ($p \leq 0.05$), erosions ($p \leq 0.05$) and global inflammatory score ($p \leq 0.05$) of the paws, was observed in the Ab501

treated group, when compared to the vehicle group, both in the 10 and 4 weeks of age treatment groups. In the spine, statistically significant reductions of the inflammation ($p \leq 0.001$), intervertebral disc destruction ($p \leq 0.05$), cartilage damage ($p \leq 0.001$), bone erosion ($p \leq 0.05$), and ectopic chondrocytes/chondrocyte scores ($p \leq 0.001$) was also depicted in Ab501 treated group in comparison with vehicle.

Conclusions: The certolizumab pegol like product mice equivalent reduced histologic inflammatory infiltrate in paws and spine of (tm)TNF (TgA86) mice. Bone damage, as defined by erosions in the paws and spine and ectopic chondrocytes/chondrocyte formation in the spine, also significantly improved in (tm)TNF (TgA86) mice.

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AB0142 A REGULATORY CCR10+ CD8+ T CELL POPULATION DIFFERENTIATES PSORIATIC ARTHRITIS FROM PSORIASIS LIMITED TO CUTANEOUS INVOLVEMENT

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Background: Few studies have compared the immune cell phenotype or function from patients with psoriatic arthritis (PsA) to patients with psoriasis limited to cutaneous involvement (Pso). Head-to-head comparisons of the immune cells in PsA and Pso can provide essential insights into the link between epithelial/cutaneous disease and rheumatic disease.

Objectives: Compare the immune cell phenotype and function from patients with PsA compared to Pso.

Methods: PBMCs were collected from 23 healthy controls, 21 patients with psoriasis in whom psoriatic arthritis was excluded by a rheumatologist (Pso), 23 patients with psoriatic arthritis (PsA) and 16 patients with ankylosing spondylitis. The Pso and PsA cohorts were free from immunomodulatory therapy and matched for demographics and skin severity. Extracellular and intracellular immunophenotyping using a highly standardised flow-cytometric approach detected over 110 different myeloid and lymphoid cell populations. Lesional and non-lesional skin biopsies and synovial fluid samples were collected from a subset of patients.

Results: The circulating immune cell composition showed a remarkable overlap in Pso and PsA, and only one specific cell population was different: CCR10 +CD8 +T cells, being enriched in PsA PBMCs as compared to Pso PBMCs. Further phenotypic and functional evaluation characterised them as effector memory, CXCR3-CCR6-, co-expressing the skin homing markers CCR4 and CLA, but lacking the gut homing marker $\alpha\beta 7$. Upon re-stimulation, CCR10 +CD8+T cells showed low IFN γ production, high IL-10 production and were enriched for FOXP3^{high}CD25+ phenotype. Their frequencies in PBMCs were unrelated to joint disease activity and were stable throughout joint disease fluctuations. Synovial fluid displayed low frequencies of CCR10 +CD8+T cells whereas skin contained the most abundant CCR10 +CD8+T cell frequencies. Lesional psoriasis skin displayed relatively fewer CCR10 +CD8+T cells compared to non-lesional skin.

Abstract AB0142 – Figure 1