1,000 cases of Psoriasis, 1,000 Crohn's disease (CD) and 1,001 healthy controls. Deletion genotyping was performed using TaqMan RealTime-PCR assays. The deletion genotype frequencies in controls did not deviate from Hardy-Weinberg Equilibrium ($p > .1$). We found an association between KRT77 deletion and CD risk ($p = 0.03$) and also a putative association with pustular psoriasis ($p < 0.05$). We also demonstrated that the KRT77 protein is expressed in the intestinal lumen and Peyer's Patches in addition to the known skin expression.

Conclusion: Given the strong association between SpA and subclinical gut inflammation and barrier defects in IBD these findings suggest that KRT77 heterozygous deletions with dysregulated gut permeability may play a role in IBD and the wider SpA phenotype.

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ANALYSIS OF BLOOD MONOCYTE TRANSCRIPTOMES AND BONE MARROW SAMPLES OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS REVEALS THEIR CHANGES RELATED TO ACTIVATION AND MYELOPOIESIS

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Background: Axial spondyloarthritis (axSpA) is characterized by inflammation within the axial skeleton. Previously, we observed preactivation of circulating monocytes of axSpA patients suggesting systemic immune activation apart from local skeletal inflammation.

Objectives: The aim of this study was to characterize systemic immune activation in axSpA by analyzing axSpA-specific monocyte transcriptomes and changes in myelopoiesis.

Methods: We performed transcriptomic analyses using GeneChip HG-U133 Plus2.0 arrays of CD14+ monocytes isolated from peripheral blood of 25 HLA-B27+ axSpA patients and 10 healthy controls (HC). 10 patients were classified as non-radiographic axSpA (nr-axSpA) and 15 patients as ankylosing spondylitis (AS). Robust Multichip Averaging Algorithm normalization and high performance chip data analysis were used to select differentially expressed transcripts that define 1) axSpA-gene-expression profile and 2) profile that discriminates nr-axSpA from AS patients. Functional analysis of significant IDs was performed with Gene ontology (GO) and reference transcriptomes that portrayed myelopoiesis in bone marrow and monocytes activation with TNF, LPS, IFN and G-CSF. Myelopoiesis in bone marrow was studied by immunohistology according to MPO and CD15 expression in sections from facet joints of AS patients and controls (CO) without skeletal disease (n=6/group).

Results: Comparison between axSpA and HC monocyte transcriptomes identified 957 differentially expressed transcripts that allowed separation of both groups by hierarchical clustering. GO analysis revealed associations of axSpA related transcripts with cell-cell adhesion, immune responses including Ras-signalling, Jak-STAT-signalling, innate immunity. Comparison of axSpA related transcripts with reference transcriptomes identified overlap with late myelopoiesis, pronounced mobilisation of monocytes from bone marrow into blood triggered by G-CSF and weak TNF/LPS activation.

Nr-axSpA and AS monocytes differed in 562 transcripts. GO analysis of these transcripts suggested alterations in mitochondrial activity, peptide transport and DNA repair. According to reference transcriptomes, profiles of nr-axSpA monocytes differed from those in AS by gene patterns of late myelopoiesis and G-CSF triggered mobilisation from bone marrow.

In histological analyses of bone marrow a significantly higher percentage of MPO+ cells indicative of left shifted granulopoiesis was found in AS vs. CO facet joints ($p < 0.01$).

Conclusion: AxSpA monocyte transcriptomes reflect weak immune activation by cytokine and/or LPS and premature release from bone marrow into blood. Bone marrow analysis shows a left shifted granulopoiesis in

AS – both of which may contribute to pathological immune response within the skeleton in axSpA.

REFERENCE:

- [1] Conrad K, Wu P, Sieper J, Syrbe U. In vivo pre-activation of monocytes in patients with axial spondyloarthritis. *Arthritis Res Ther.* 2015 Jul 16;17:179. Doi: 10.1186/s13075-015-0694-2. PubMed PMID: 26178906

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INNATE VERSUS ADAPTIVE IL-17A PRODUCING CELLS IN AXIAL SPONDYLOARTHRITIS

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Background: IL-17A-inhibition has been very successful in AxSpA but the cell populations targeted by this new therapeutic remain unknown. This question is relevant because the recent failure of anti-IL-23 in AxSpA demonstrated that IL-23-independent IL-17-producing cells may be of particular relevance for SpA pathogenesis. Some data from literature suggests the involvement of MAIT, $\gamma\delta$ T, and neutrophils as IL-17A producing cells in AxSpA (1–3). However, even though they may be responsible for IL-17A-mediated inflammation, it is still unclear which is the major IL-17A-producing cell population in this disease.

Objectives: To assess and compare gene expression profiles of neutrophils, MAIT, $\gamma\delta$, CD4+ and CD8+ T cells from AxSpA patients.

Fig. IL-17A expression in neutrophils, MAIT cells, $\gamma\delta$ T cells, CD4+ T cells and CD8+ T cells.

Methods: We recruited 5 healthy donors and 10 patients with a diagnosis of AxSpA according to the ASAS criteria. We compared the gene expression profiles of 5 sorted cell populations: 3 innate cell populations (neutrophils, MAIT and $\gamma\delta$ T cells) and 2 adaptive cell populations (CD4+T and CD8+T) after cell stimulation by PMA + A23187 (calcium ionophore) + β 1,3 glucan (extracted from *Aspergillus fumigatus* hyphae). Published data suggested that neutrophils stimulation by *Aspergillus fumigatus* induces IL-17A production by these cells(4). For each of these cell populations, cytokine production and the expression of a panel of 755 genes (Autoimmune discovery panel from Nanostring including 43 genes for which a polymorphism was associated with AS) were assessed. Patient and control groups were compared with a Mann-Whitney test and comparison of cell populations was performed by a multigroup comparison.

Results: There was no significant difference between patients and controls regarding gene expression profile of neutrophils, $\gamma\delta$ T, CD4+T and CD8+T. We observed that 34 genes were differentially expressed between patients and controls in MAIT cells ($p = 0.03$, $q = 0.1$). In particular, T cell activation genes (*TBX21*, *AHR*, *ZAP70*) and cell interaction genes (*ITAG6*, *CTNNB1*, *ICAM2*, *ITGB2*, *SELL*) were decreased in patients. Among AxSpA patients, MAIT cells were those significantly showing the highest level of IL-17A expression. *IL23R* and *RORC* were also more expressed by MAIT compared to others cell populations. IL-17A expression was very low in neutrophils but we observed that 18 out of the 43 AS associated genes were mainly expressed by neutrophils (p