allele and genotype frequencies polymorphisms were obtained by direct counting. In each group the Hardy-Weinberg equilibrium was evaluated using the ^{2} test. Associations were assessed using odds ratio (OR). Stata v.12.0 program was used to analyse data. The construction and analysis of haplotypes was performed using Haploview v.4.2

Results: In total 70 patients were HLA-B27 positive and 34 were HLA-B15 positive. 78 were women and 100 were men. Linkage disequilibrium map of the ERAP gene is depicted in figure 1. When analysed by ERAP2 haplotype it is observed that there is a statistically significant association with the combinations described in table 1. No associations were observed between ERAP1 haplotypes and HLA-B15 or B27

Conclusions: In the group of patients analysed, a statistically significant association was found between patients with SpA HLA-B15 positive and the haplotype TGT of ERAP2. Also HLA-B27 positive SpA patients were associated with haplotype TGC and CAT of ERAP2 with statistical significance

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THU0006 TRANS-ETHNIC META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IDENTIFIES GSDMA AND PRDM1 AS SUSCEPTIBILITY GENES TO SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis and composed of two subtypes, limited and diffuse cutaneous forms. Previous genetic studies including genome-wide association studies (GWAS) have identified 12 susceptibility loci satisfying genome-wide significance.

Objectives: To expand the list of susceptibility genes and deepen biological insights for SSc.

Methods: We performed trans-ethnic meta-analysis of GWAS in the Japanese and European populations, followed by a two-staged replication study comprising a total of 4,436 cases and 14,751 controls. Associations between significant single nuclear polymorphisms (SNPs) and neighboring genes were evaluated. Enrichment analysis of H3K4Me3, a representative histone mark for active promoter was conducted with an expanded list of SSc susceptibility genes.

Results: We identified two significant SNP in two loci, *GSDMA* and *PRDM1*, both of which are related with immune functions and associated with other autoimmune diseases ($p=1.4x10^{-10}$ and $6.6x10^{-10}$, respectively). *GSDMA* also showed a significant association with limited cutaneous SSc. We also replicated the associations of previously reported loci including a non-GWAS locus, *TNFAIP3*. *PRDM1* encodes BLIMP1, a transcription factor regulating T cell proliferation and plasma cell differentiation. The top SNP in *GSDMA* was a missense variant and correlated with gene expression of neighboring genes, and this could explain the association in this locus. We found different HLA association patterns between the two populations or two subtypes. Enrichment analysis suggested the importance of CD4 naïve primary T cell.

Conclusions: *GSDMA* and *PRDM1* are associated with SSc. These findings provide enhanced insight into the genetic and biological basis of SSc.

Disclosure of Interest: None declared

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THU0007 DEEP SEQUENCING TRANSCRIPTOME ANALYSIS OF THE EFFECT OF TRAUMEEL VERSUS DICLOFENAC THERAPEUTIC ACTION IN WOUND HEALING

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Background: Anti-inflammatory agents are used widely in treating numerous inflammatory conditions. The effect of Tr14, a multitargeted natural product, was compared to diclofenac, a non-selective cyclooxygenase inhibitor, on cutaneous wound repair in mice.

Objectives: To compare the effect of diclofenac with Tr14 on the transcriptome after cutaneous wounding in the mouse.

Methods: After abrasive wounding, the wounds were treated with topical Tr14 or diclofenac at clinically relevant doses. An additional group received subcutaneous Tr14 injections. The healing wounds were analyzed for RNA transcript profiling by RNAseq at specific times (12h, 24h, 36h, 72h, 96h, 120h, 196h) after injury. Differentially expressed genes (DEGs) were computed at each time point between diclofenac vs control or Tr14 vs control using EdgeR.

Results: Across time points, Tr14 treatment modulated a number of transcripts related to key wound repair pathways such as cellular differentiation, wound contraction, and cell mobility. Diclofenac, in contrast, changed gene expression mainly in two areas: Prominent effects were observed with regard to DNA chromatin regulation and ribosomal function, further effects were observed on the prostaglandin pathway and wound repair factors. In many of the key pathways modulated by Tr14, such as the defense response and cell motility, diclofenac tended to have an opposite effect on gene expression. At 12 hours post-injury, there were 521 transcripts significantly elevated and 1027 transcripts that were decreased by diclofenac treatment. By comparison, using a similar number of transcripts altered by Tr14 treatment, only 4 transcripts were increased in common, and 5 transcripts were decreased in common, suggesting that the therapies have different effects on the transcriptome.

Conclusions: The overall patterns of the Tr14 and diclofenac responses in the transcriptome during wound repair are very different. The Tr14 effect is most pronounced on the defense response, cell motility, and anti-apoptotic pathways. In contrast, diclofenac mainly affected histones and chromatin remodeling systems, as well as ribosomal systems that would be expected to alter the translational pattern of diclofenac-treated cells.

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THU0008 MAST CELLS SHOW A REPROGRAMMED TRANSCRIPTIONAL SIGNATURE FOLLOWING REPEATED IGG STIMULATIONS

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Background: Mast cell numbers are increased in the rheumatoid arthritis joint. We have previously shown that mast cells can be activated by IgG-ACPA leading to the production of proinflammatory cytokines. However, not much is known about the resulting function when mast cells would repeatedly engage IgG, a likely scenario given the long life span of mast cells (up to a year) and the perpetual presence of IgG-ACPA in the joints. We have recently shown that mast cells triggered repeatedly through their Ig Fc epsilon receptor undergo a reprogramming of their responses (*Suurmond et al. JACI, 2016* by expressing de-novo transcribed genes in the antigen presentation and pathogen defence response pathways.

Objectives: The aim of the current work was to determine whether mast cells show similar changes in their response mode following repeated interactions with IgG.

Methods: Human cord blood-derived mast cells were treated for 2 weeks with plate-bound IgG. The expression profile of naive or treated mast cells was measured through RNA sequencing, quantitative RT-PCR, flow cytometry. Protein secretion was measured with ELISA and Luminex assays. Metabolic changes were measured using HPLC mass-spectrometry.

Results: Similar to our previous work on Fc Epsilon receptor, we observe a dampening of the normal IgG responses with a set of novel genes upregulated. Interestingly, de-novo expressed genes consisted of *DHCR7* and *DHCR24*, key enzymes in the cholesterol pathway. Pathway analysis confirms an enrichment of genes in this pathway following repeated IgG triggering. Preliminary data on metabolic profiling reveals a decrease in phospholipid levels in repeatedly activated mast cells.

Conclusions: Our study provides evidence that mast cells are reprogrammed upon repeated IgG triggering. In contrast to repeated Fc Epsilon Receptor triggering, different pathways are affected, implying stimulus-specific effects. Our work has important implications for the understanding the role of mast cells in rheumatoid arthritis.