counts (p-SCMA staining) and of 23 serum inflammatory cytokines/chemokines (Mouse-Cytokine-23-plex, Bio-Rad Laboratories).

**Results:** 17-DMA decreased dermal thickening by 53±3% (p<0.001) (nintedanib by 45±2%, p<0.001), collagen content by 48±5% (p=0.004) (nintedanib by 50±4%, p=0.003), myofibroblast counts by 42±9% (p<0.001) (nintedanib by 44±7%, p<0.001), and levels of IL-1α, IL-6, IL-12(p40), CXCL1, MCP-1, MIP-1β, RANTES in (all in p<0.05) compared to vehicle-treated mice injected with bleomycin for 6w. Moreover, 17-DMA also induced regression of pre-established fibrosis to below the levels of vehicle-treated mice injected with bleomycin for 3w and NAC for 3w (dermal thickness by 14±3%, collagen content by 20±5%, myofibroblast counts by 13±9%; whereas in nintedanib by 10±3%, 21±4%, 17±7%, respectively; in all in p<0.05), and levels of IL-12(p40), CXCL1, MIP-1, MIP-1β, RANTES in (all in p<0.05). No significant weight loss, decrease in activity or changes in fur texture were observed upon 17-DMA treatment.

**Conclusion:** This is the first study on effects of Hsp90 inhibitor 17-DMA in the treatment of established dermal fibrosis. We demonstrate that 17-DMA effectively prevents the progression and induces regression of established bleomycin-induced dermal fibrosis, in an extent that is comparable to nintedanib in this study (which was recently FDA approved for slowing the rate of decline in lung function in adults with SSC-cI LD). 17-DMA was well tolerated without obvious clinical signs of toxicity. These data suggest that Hsp90 could be a novel potential target in the treatment of SSC dermal fibrosis.

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subtypes is jointly associated with RNA transcripts or FAIME scores with strong differences in relation to the geographical origin of samples; neutrophils emerged as the major determinant of gene expression in SSc-whole-blood samples.

**Conclusion:** We discovered a set of differentially expressed genes and pathways that could be validated in two independent sets of SSc patients highlighting a number of deregulated molecular processes that have relevance for the pathogenesis of autoimmunity and SSc.

**Figure:**

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**OP0139 FUNCTIONAL EVALUATION OF THE SJÖGREN’S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS DDIX-CXCR5 RISK INTERVAL**

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**Background:** Sjögren’s Syndrome (SS) and Systemic Lupus Erythematosus (SLE) are distinct chronic, complex autoimmune diseases with shared characteristics such as autoantibodies, heightened interferons, and polyarthritis. SS and SLE genome-wide association studies (GWAS) report strong associations with the DDIX-CXCR5 risk interval. DDIX suppresses interferon stimulated gene expression and CXCR5 regulates T cell functions implicated in autoimmunity.

**Objectives:** To identify functional variants that impact regulation in the DDIX-CXCR5 interval.

**Methods:** Fine-mapping was done using ImmunoChip data from 3785 SLE, 1916 SS cases and 6893 population controls of European ancestry that were imputed and tested for SNP-trait association. Bayesian statistics assigned posterior probabilities to SNPs and defined a credible set of risk variants. Bioinformatic analyses further prioritized variants with predicted functionality. Electrophoretic mobility shift assays (EMSA) and luciferase expression were used to validate predicted SNPs in EBV transformed B (EBV B) cells.

**Results:** While some differences were observed, the overall SS and SLE association signals were similar. SNP-SS rs9736016 near CXCR5 and SNP-SLE rs74609436 near DDIX were the most significant but did not show evidence of functionality. Bayesian statistics defined credible sets of variants in strong D’ in common between both SS and SLE. Bioinformatics analyses (Haploreg, RegulomeDB, ENCODE data, etc) further refined the credible set and identified 5 common SNPs with strong evidence of functionality in immune cell types: rs4938572, rs4960443, rs5749455, rs7117261 and rs4938573. EMSAs showed a significant increase in protein binding to the risk allele of rs5749455 (p=0.001), rs7117261 (p=0.001) and rs4938573 (p=0.003), but not the others, using nuclear lysates from EBV B cells. Luciferase vectors with a minimal promoter or no promoter were used to test for enhancer or promoter activity, respectively. To this end, the rs5749455 risk allele exhibited a significant increase in enhancer activity (p=0.001). In contrast, the rs7117261 risk allele decreased enhancer activity.