observed. The patients that showed an upregulation of CD40L had a moderate-severe clinical progression of ILD.

Conclusion In this study, we demonstrate the presence of His-tRNA-reactive CD4+ T cells in peripheral blood from anti-Jo-1 positive patients and a novel His-tRNA peptide, characterised by the expression of IFN-γ. This phenotype seemed to correlate to a moderate-severe clinical progression of ILD.

**02.10 X-LINKED MIRNAS ASSOCIATED WITH GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS**

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**Aim** The majority of auto-immune diseases predominate in females. Rheumatoid arthritis (RA) is one of these diseases for which female are three times more affected than men. Micro-RNAs have emerged as crucial regulators of the immune system, and have been reported abnormally expressed in RA. As protein-encoding genes, miRNA-encoding genes can be affected by nucleotide single polymorphisms (SNPs) that could affect their expression levels in disease. We aimed at quantifying the expression level of miRNAs located on the X chromosome and at identifying whether differences are associated with disease and/or sex.

**Materials and methods** A case–control study of 21 RA patients and 22 age- and sex-matched healthy controls was performed on peripheral blood mononuclear cells. Extraction of total RNA and DNA was performed and the expression level of 14 X-linked miRNAs quantified using real time quantitative polymerase chain reaction. Two FoxP3 polymorphisms were genotyped using the Sanger sequencing method. An analysis of expression quantitative trait loci (eQTL) was performed to detect transcriptional regulatory relationships between X-located miRNA expression levels and 2 single nucleotide polymorphisms in FOXP3 gene associated with RA susceptibility.

**Results** We showed that miR-221, miR-222, miR-532, miR-106a and miR-98 expression levels were significantly different between RA and controls only when stratifying according to the sex. Furthermore, the expression level of 4 miRNAs (miR-222, miR-532, miR-98, miR-92a) was significantly different between RA female and male. We performed an eQTL analysis and showed a significant gender effect of the FoxP3 promoter polymorphism rs3761548A/C on miR-221, miR-222, miR-532 expression levels, and of the FoxP3 polymorphism rs2232365A/G on miR-221 expression level in PBMC of RA patients.

**Conclusion** These data further support the involvement of the X chromosome in RA susceptibility. X-linked miRNAs, in the context of sex differences, might provide novel insight into new molecular mechanisms and potential therapeutic targets in RA for disease treatment and prevention.

**02.11 IL-38 IS NOT INVOLVED IN THE MODULATION OF IMQ-INDUCED SKIN INFLAMMATION**

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**Background** Psoriasis is a common chronic skin disorder caused by a dysregulated crosstalk between immune and resident cells (eg, keratinocytes). The identification of the pathogenic role of several cytokines in psoriasis led to the development of successful therapies. Recently, IL-36 cytokines, which belong to the IL-1 family, were shown to be involved in the pathogenesis of psoriasis. Mice deficient in IL-36 receptor (IL-36R) were protected from imiquimod (IMQ)-induced skin inflammation, whereas IL-36R antagonist (IL-36Ra) KO mice exhibited a more severe phenotype. The objective of our study was to examine the expression and function of IL-38, a newly discovered IL-1 family member with supposed IL-36 inhibitory properties, in the IMQ model of psoriasis.

**Materials and methods** IL-38 mRNA expression was determined in skin samples, at steady state or after IMQ application. IL-38 KO or IL-36Ra KO mice and their respective WT littermates were challenged with the topical application of IMQ on the left ear during 7 days. The severity of skin inflammation was assessed by daily measurement of ear thickness using a calliper, by semi-quantitative histologic scoring, and by measuring mRNA levels of inflammatory markers.

**Results** At the peak of IMQ-induced skin inflammation, IL-38 mRNA levels were lower than in normal skin, whereas IL-36Ra mRNA levels were increased in IMQ treated skin. The severity of skin inflammation, as assessed by ear thickness, histological changes (leukocyte infiltration and epidermis hyperplasia) and pro-inflammatory mediator transcript levels, was not significantly different in IL-38 KO and WT mice. After cessation of topical IMQ application, the resolution of skin inflammation was also not altered by IL-38 deficiency. As opposed to these findings, IL-36Ra deficient mice displayed more severe pathological changes as compared to WT mice.

**Conclusions** We showed that endogenous IL-38 is not involved in the development and the resolution of IMQ-induced skin inflammation. Our findings suggest that IL-38 does not exert IL-36 inhibitory activities in the skin.

**02.12 IL-38 OVEREXPRESSION INDUCES ANTI-INFLAMMATORY EFFECTS IN MICE ARTHRITIS MODELS AND IN HUMAN MACROPHAGES IN VITRO**

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**Background** IL-38 is a member of the IL-1 family that is highly overexpressed in many autoimmune/inflammatory diseases. IL-38 inhibits IL-1β, IL-6 and IL-18, mediates Th17 skewing, and has previously been shown to induce anti-inflammatory effects. Increased IL-38 levels have been observed in systemic rheumatic diseases such as rheumatoid arthritis (RA) and in psoriasis.

**Aim** We aimed to determine whether IL-38 overexpression in arthritic mouse models and in human macrophages generates anti-inflammatory effects.

**Materials and methods** Rheumatoid arthritis was induced in DBA/1, C57Bl/6 and C3H/HeJ mice by adjuvant and collagen-induced arthritis, respectively. IL-38 overexpression was induced by transgenic (TG) mice expressing IL-38 under the osteoclast-specific RUNX2 promoter. The role of IL-38 was investigated in collagen-induced arthritis (CIA) and in a Th17 cell-driven model of arthritis (TCRA). Human macrophages were stimulated with lipopolysaccharide (LPS) in the presence or absence of recombinant human IL-38.

**Results** Transgenic overexpression of IL-38 at the peak of CIA disease activity in C57Bl/6 mice protected against disease and induced anti-inflammatory gene expression. IL-38 overexpression reduced disease severity in Th17 cell-driven models of arthritis. Human macrophages stimulated with LPS in the presence of IL-38 showed decreased production of IL-1β, IL-6, TNF-α and IL-18, indicating a potent anti-inflammatory effect of IL-38 in human macrophages.

**Conclusions** These findings support the notion that IL-38 overexpression induces anti-inflammatory effects in arthritic mice and in human macrophages, providing a potential therapeutic target for the treatment of inflammatory diseases.