Conclusions: Committed pro-inflammatory IL-17A-producing CCR6+Th memory cells shift towards anti-inflammatory cells with functional regulatory capacities upon exposure to active vitamin D. This process can contribute to restoring the immunological balance and inhibiting synovial inflammation in RA.

Disclosure of Interest: None declared


**THU0049**

**DEVELOPMENT OF TFH-TH1 LIKE CELLS THROUGH EPIGENETIC MODIFICATION BY STATS FAMILY FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** Systemic lupus erythematosus (SLE) is a prototype of autoimmune disease characterised by chronic immune activation and multiple immunologic phenotypes(1). Among several types of immune cells, T follicular helper (Tfh) cells serve important roles in the development and progression of SLE(2).

**Objectives:** To assess the characteristics and mechanisms of differentiation of Tfh cells, we probe the phenotype of T helper cells in patients with SLE and underlying epigenetic modifications by cytokine-induced signal transducer and activators of transcription (STAT) family factors.

**Methods:** Naive CD4+ T cells and memory CD4+ T cells were isolated and stimulated by various cytokines and T cell receptor (TCR) in vitro. Expression of characteristic markers of Tfh-Th1-cell and phosphorylation of STATs were analysed by flow cytometry and qPCR. Histone modifications were evaluated by chromatin immunoprecipitation. Peripheral blood mononuclear cells from SLE patients and healthy controls were analysed by flow cytometry and productions of cytokines in serum were tested by cytometric bead array.

**Results:** Differentiation of CXCRe5/CXCR3+Bcl-6-T-bet(IL-21)IFN-y+ Tfh-Th1-like cells was induced by IL-12. Among STAT family, STAT1 and STAT4 were phosphorylated simultaneously by IL-12 independent of IFN-g, and STAT1 was found to be increased in patients with SLE.

**Conclusions:** Our findings suggest that IL-12-mediated co-activation of STAT1 and STAT4 alter histone modification, resulting in development of Tfh-Th1-like cells that are characteristically expanded in patients with SLE. These findings could be one of underlying pathogenesis of SLE and potentially helpful towards development of cell-specific treatment.

**REFERENCES:**

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**THU0051**

**TNF RECEPTOR 2 PLAYS AN IMMUNOREGULATORY AND ANTI-INFLAMMATORY ROLE IN ARTHRITIS**

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**Background:** Despite the overall success of TNFα inhibitors in rheumatoid arthritis (RA), up to half of patients are classified as either primary or secondary non-responders. One hypothesis put forward to explain resistance to anti-TNFα therapy is an ascendant effect of dysregulated regulatory T cells and increased Th17 responses following TNFα blockade. Previous studies have demonstrated that TNFR2 is critical for stabilisation and suppressive function of regulatory T cells. However, TNFR2 also activates pro-inflammatory signalling cascades and, to date, the net effect of TNFR2 on the pathogenesis of RA remains unclear.

**Objectives:** In this study we address this question by assessing the progression of collagen-induced arthritis (CIA) in mice deficient for TNFR1 or TNFR2.

**Methods:** C57Bl/6N.Q (H-2q) mice were immunised with bovine type II collagen emulsified in complete Freund’s adjuvant. The mice were monitored daily for arthritis and scored clinically from the day of onset of disease. Mice were culled on day 10 after arthritis onset and spleens, lymph nodes, serum and paws were collected for further analysis.

**Results:** As expected, TNFR1-/- mice were found to be largely resistant to arthritis both clinically and histologically (figure 1). In contrast, there was significantly enhanced disease activity at the clinical and histological levels in TNFR2-/- mice (figure 1) and this was accompanied by increased expression of the pro-inflammatory cytokines, TNFα and IL-6, reduced numbers of regulatory T cells, reduced FoxP3 expression and reduced expression of the immune inhibitory molecules, PD-1 and LAG3, in TNFR2-/- mice compared to WT mice.

**Conclusions:** This study has shown that TNFR2 signalling plays immunoregulatory and anti-inflammatory roles in CIA. First, it contributes to promotion of regulatory T cell generation and FoxP3 expression, and second, it limits the expression of pro-inflammatory cytokines. TNFR2 also regulates the expression immune inhibitory