in PBC group ($n=21$) (0.82 ± 0.76 vs 3.03 ± 4.23 , $p=0.028$). Immunofluorescence co-localization revealed that increased PD-1 positive cells in early PBC stage than late one, and less PD-L1 positive cells as well as PD-L1 and CK19 co-localised ones in PBC patients compared to HC. In the CTL and HiBEC co-culture system *in vitro*, the cytotoxicity of PD-1⁺ CD8⁺ T cells was weaker, with less proliferation and tendency of decreased production of IFN- γ and TGF- β compared to PD-1⁻ CD8⁺ T cells. Meanwhile, HiBEC apoptosis was relatively more in PD-1⁻ CD8⁺ T cells co-culture group. These effects could be antagonised by anti-PD-1 antibody and enhanced by PD-L1.

Abstract AB0036 – Figure 1

Conclusions: In PBC, the expression of Tbet is up-regulated in CD8⁺ T cells, which leads to the down-regulated expression of PD-1 on. Meanwhile, the expression of PD-L1 in HiBEC may be down-regulated. The silenced PD-1/PD-L1 pathway caused more CD8⁺ T cells proliferation, more related cytokines production and the enhanced CTL cytotoxic effects on HiBEC. PD-1/PD-L1 pathway functions as an important pathway in the immunological mechanism of PBC.

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AB0037

MIR-155 PROMOTES THE DIFFERENTIATION OF TH17 CELL BY TARGETING ETS-1 IN RHEUMATOID ARTHRITIS

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Background: MicroRNAs play important roles in arthritis. MiR-155 emerges as a central regulator of the immune response, but its function in autoimmune arthritis is poorly understood.

Objectives: To clarify the role of miR-155 in the balance of CD4⁺Th17 and Treg cell differentiations as well as how their mechanisms function in autoimmune arthritis.

Methods: CD4⁺ T cells were *in vitro* isolated from DBA1 mice. The transfections of miR-155 mimics and miR-155 inhibitors in CD4⁺ T cells were performed for

enhanced or knockdowns of miR-155 expression and RNA interference was applied to silence Ets-1 gene expression. In addition, we carried out *in vivo* experiments of enhanced miR-155 expression by lenti-virus mediated miR-155 (LV-miR-155) infection and silencing of miR-155 expression by lenti-virus-anti-miR-155 (LV-anti-miR-155) within our well-established type II collagen (CII)-induced arthritis (CIA) mice model. The ratios of IL-17⁺ TH17 cells were analysed using flow cytometry (FCM). The expressions of some key autoimmune-response of genes including ROR γ t, IFN- γ , Ets-1, IL-17, IL-23, and Stat3 were further determined by (Taqman) Quantitative Real-time PCR and Western blotting. Initially $n=6$ per group if not indicated further; totally 6 groups in parallel per experiment. * $p<0.05$, considered as significantly; ** $p<0.01$, considered as highly significantly.

Results: For the first time we showed that miR-155 may promote Th17 cell differentiation in RA pathogenesis. Firstly, we observed that miR-155 may significantly induce the expressions of some key autoimmune-response genes including ROR γ t, IFN- γ , IL-17, IL-23, and Stat3 but it significantly inhibited Ets-1 gene expression. 2ndly, miR-155 may in part modulates Th17 cell differentiation by targeting Ets-1 in that indeed the expression of miR-155 significantly co-related with disease index in CIA mice. Furthermore, the CIA mice with *in vivo* forced expression of miR-155 have significantly more Th17 cells (i.e. high ratio) and severe CIA disease index compared to their control CIA mice; strikingly, they also have a significantly higher expression of aforementioned autoimmune-response genes compared to their corresponding controls along with the response of Ets-1 exactly in a verse direction. Consistently, the CIA mice with *in vivo* knockdown of miR-155 expression resulted in significantly less Th17 cells and lesser severe CIA disease index compared to their control CIA mice. However, they have a significantly lower expression of above-mentioned autoimmune-response genes compared to their corresponding controls along with a response of Ets-1 in a verse direction (the data in part shown in Figure 1; sham=CIA treated with LV-nonspecific sequence).

Conclusions: For the first time our data show miR-155 has a critical role in Th17 differentiation and the RA pathogenesis via targeting the Ets-1. Although it warrants further investigations, miR-155 might be a promising therapeutic target for autoimmune diseases, esp. RA.

Abstract AB0037 – Figure 1

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Innate immunity in rheumatic diseases

AB0038

TBK1: A KEY REGULATOR AND POTENTIAL TREATMENT TARGET FOR INTERFERON POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS

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Background: Upregulation of type I interferons (IFN-I) is a hallmark of systemic autoimmune diseases like systemic lupus erythematosus (SLE) and systemic sclerosis (SSc). Three different receptor families are implicated in the induction of IFN-I production: Toll-like receptors (TLRs), RIG-like receptors (RLRs) and DNA-sensing receptors (DSRs). TANK-binding kinase (TBK1), is an important signalling hub downstream of RLRs and DSRs. TBK1 activates IRF3 and IRF7, leading