class III/IV LN. Using RNA-*in-situ* hybridization methods, we document infiltration of class III/IV nephrtis biopsy tissue with PDCs with IFN-signature positive cells surrounding them, supporting local production of type I IFNs.

Conclusions Our data support an association between type I IFN and class III/IV nephritis that is independent of overall SLEDAI and anti-dsDNA antibodies, suggesting that IFN is involved in renal pathogenesis. These data also suggest that IFN could predict renal disease activity or the future risk of developing LN, especially class III/IV LN in EA SLE patients.

TD-09 IL-34 PROMOTES MACROPHAGE-MEDIATED LUPUS NEPHRITIS IN MRL-*FAS*^{LPR} MICE

[1,2]Yukihiro Wada, [1,2]Hilda M Gonzalez-Sanchez, [3]Julia Weinmann-Menke, [2]Amrendra K Ajay, [1,2]Vicki R Kelley*. *[1]Laboratory of Autoimmune Disease; [2]Renal Division, Department of Medicine, Brigham and Women's Hospital, Boston, MA; [3]Department of Nephrology and Rheumatology, Johannes-Gutenberg University Mainz, Mainz, Germany*

10.1136/lupus-2018-lsm.128

Background Nephritis is the major cause of mortality and morbidity in patients with lupus. Macrophages (Mø) are central to kidney destruction in lupus-prone mice and patients. CSF-1, and the newly identified IL-34, mediate Mø survival and proliferation. However, IL-34 and CSF-1 differ during development and disease. While CSF-1 and IL-34 share the CSF-1 receptor (cFMS), expressed by Mø, IL-34 binds to a second receptor, Protein-Tyrosine Phosphatase ζ (PTPRZ) in inflamed kidneys. Intra-renal IL-34, cFMS, and PTPRZ are increased during the progression of lupus nephritis in MRL-*Fas*^{lpr} mice. Therefore, we hypothesized that IL-34 is a potential therapeutic target for lupus nephritis.

Methods and Results Using MRL-*Fas*^{lpr} IL-34 knockout (KO) mice, we found that the time-related magnitude of Mø-rich lupus nephritis and systemic illness (skin, salivary glands) were markedly suppressed in IL-34 KO MRL-*Fas*^{lpr} mice compared to wild-type (WT) or IL-34 heterzygous mice. IL-34 fostered intra-renal Mø accumulation via two mechanisms: 1) intra-renal Mø proliferation, and 2) monocyte proliferation in bone marrow that increases circulating monocytes, which are recruited into the kidney. cFMS is expressed on Mø and PTPRZ on tubular epithelial cells (TEC). We found IL-34 increased intra-renal Mø which in turn, released mediators that induced TEC apoptosis. Importantly, CSF-1 did not compensate for the absence of IL-34. These findings are translational as IL-34, *cFMS* and PTPRZ are upregulated on kidney TEC in patients with lupus nephritis compared with healthy controls and IL-34 levels are elevated and track with disease activity in the serum and urine in patients with lupus nephritis. We are currently detailing the distinct mechanistic contribution of each IL-34 receptor to the pathogenesis of lupus nephritis.

Conclusion Our findings suggest that IL-34 is a promising potential therapeutic target for patients with lupus nephritis.