vivo study. Toll-like receptor (TLR)-stimulated human PBMCs or murine bone marrow-derived dendritic cells were used for *in vitro* study.

Results Our study demonstrated that DZ2002 exerted a therapeutic effect on NZB/W F1 mice with established nephritis. The mechanism involves the modulation of T cell development in lupus by interfering with TLR-triggered APC function. Further study explored the regulatory mechanisms of SAHH on DC function in both innate and adaptive immune system, using the SAHH inhibitor with definite target and potent immunosuppressive activity.

Conclusions The present issue demostrated that the reversible SAHH inhibitor DZ2002 effectively ameliorates lupus syndrome in NZB/W F1 mice by regulating TLR signaling-mediated APC responses. This compound is prospective to become a novel drug for SLE treatment with Hcy as a potential biomarker in autoimmune disease.

108 IGURATIMOD INHIBITS HUMAN B CELL TERMINAL DIFFERENTIATION IN VITRO AND MAY BENEFIT PATIENTS WITH REFRACTORY LUPUS NEPHRITIS

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Background and Aims Iguratimod (IGT) is a small molecular immunomodulatory drug and has been approved for treating rheumatoid arthritis. In our previous work, IGT ameliorates lupus-like disease in MRL/*lpr* mice by inhibiting abnormal B cell differentiation. The aim of this study is to further investigate the effects of IGT on human B cells.

Methods We established a set of stimulations to induce naive human B cell into plasmablast (PB) *in vivo*. We also enrolled 7 patients with refractory lupus nephritis (LN) to assess the potential efficacy of IGT.

Results IGT significantly attenuates the generation of CD19+CD20-CD27hiCD38hi plasma cells upon both BCR-dependent and independent stimulations. IGT affects neither proliferation or apoptosis of B cell *in vitro*. In further investigation on B cell differentiation signalling pathwasys, we identifies that Blimp-1 and Xbp-1 can be remarkably impaired by IGT both in transcriptional and protein level; while Jak/STAT or NF-κB signalling are intact with IGT treatment. For explosive clinical study, seven patients with refractory LN were enrolled and administrated with IGT and steroids. ALL of these patients surprisingly show improved proteinuria after 8 week treatment. One patient quit the treatment because of anaemia.

Conclusions IGT has a unique effect to arrest B cell terminal differentiation, which provides strong evidence that this drug could be a new candidate drug to treat B cell related autoimmune diseases such as lupus.

109 LONG-TERM DATA ON SIROLIMUS TREATMENT IN LUPUS NEPHRITIS PATIENTS

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Background and aims Preliminary data suggested efficacy of sirolimus in treatment of lupus nephritis (LN), but its long-term efficacy and tolerability data is lacking.

Methods We reviewed Class III/IV/V LN patients who received prednisolone and sirolimus either as initial or maintenance treatment during Jan 2007 to Jan 2016.

Results Sixteen patients were included (duration of sirolimus treatment: 27.2±19.6 months). Ten patients received sirolimus due to intolerance to standard immunosuppressive treatments and six patients because of a history of malignancy. Five patients received sirolimus during active LN, and showed improvement in proteinuria (2.8±1.9 g/day and 0.1±0.1 g/day at baseline and 36 months, p=0.011 compared to baseline), anti-dsDNA (107.7±91.9 IU/mL and 37.0±55.4 IU/mL at baseline and 36 months, p=0.145) and C3 (54.8±26.1 mg/dL and 86.3±18.6 mg/dL at baseline and 36 months, p=0.084). Eleven patients received sirolimus during disease quiescence, and showed significant improvement in C3 (90.4±18.1 mg/dL and 117.7±25.1 mg/dL at baseline and 36 months, p=0.025) and stable renal function (58.5±25.2 ml/min and 56.7 ±29.0 mL/min at baseline and 36 months, p=0.199) and proteinuria (0.8±0.7 g/day and 0.7±0.7 g/day at baseline and 36 months, p=0.263). One patient, whose serum creatinine was 244 μmol/L when sirolimus was started, developed renal failure after 27 months. Renal flare occurred in one patient after 36 months. Sirolimus was discontinued in five patients including one with leucopenia. Four patients showed lipid profile deterioration which was adequately controlled with statin.

Conclusions Sirolimus can be an alternative treatment option for LN and the long-term results do not suggest excessive adverse effects.

110 SUCCESSFUL TREATMENT OF REFRACTORY LUPUS NEPHRITIS WITH SECUKINUMAB IN A PATIENT COMPLICATED WITH PSORIASIS VULGARIS

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Background and aims We report the case of a 62-year-old woman. Psoriasis Vulgaris (Psoriasis) was diagnosed in X-31 year and also SLE with nephritis (WHO IIIA) in X-11. She was treated with high-dose methylprednisolone and cyclosporine A (CsA) to achieve remission. Methylprednisolone was reduced to 4 mg/day.

Methods Because of renal dysfunction, although CsA was discontinued in May X, psoriasis, renal dysfunction and proteinuria became further worse, she was admitted to hospital in July X. She was diagnosed with SLE flare with class IV-G(A/C)+V lupus nephritis (INS/RPS) and associated psoriasis. The SLEDAI score was 16 and psoriasis area and severity index (PASI) score was 16. Although high-dose corticosteroid (1 mg/kg/day) and a concomitant first dose of IV cyclophosphamide (IVCY) were started, anasarca was still observed and S-Cr was increased from 1.98 to 2.85 mg/dL. Because proportion of activated Th17 cells were increased in peripheral blood(PD), and the infiltration of many lymphocytes and IL-17-positive cells in renal interstitium, secukinumab, an antibody against IL-17A, was administered.

Results Then, anasarca and nephrosis was improved and S-Cr was decreased to 1.20 mg/dL in proportion to the reduction in activated Th17 cells in PD.
Conclusions Although recent studies have begun to shed light on the role of IL-17 in the pathogenesis of SLE, there is no convincing evidence in actual patients. In this case, improvement of disease activity of SLE was correlated with the decrease of activated Th17. This is the first report that the IL-17-targeted therapy for SLE was shown to be effective in a patient skewing towards Th17-phenotype.

111 DEVELOPMENT OF ARTEMISININ ANALOGUEANALOG SM934 IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background and aims Besides their outstanding antimalarial activity, artemisinin and its derivatives also possess immunosuppressive activities and are clinical used to treat SLE. β-aminoarteether maleate (SM934), a water soluble artemisinin derivative, got the approval documents authorised by Chinese FDA for clinical trials. This study investigated the curative effects of SM934 on lupus-prone mice and explored its underlying therapeutic mechanisms.
Methods *In vivo*, SM934 was given orally to female NZB/W F1 and MRL/*lpr* mice; renal injury, peripheral lymphoid organ disease and serological changes were evaluated. Meanwhile, correlative pathological mechanisms were studied using different aged mice. Besides, the effects of SM934 on human PBMCs were also assessed.
Results We demonstrated that SM934 treatment could significantly improve SLE syndrome in lupus-prone animal models, including delayed the progression of glomerulonephritis; ameliorated proteinuria and renal lesion severity; increased the survival rate; decreased levels of BUN and serum anti–double-stranded DNA antibodies. Furthermore, clinical improvement was accompanied with decreased Th1-related anti- dsDNA IgG2a and IgG3 Abs, serum IL-17, and increased Th2-related anti-dsDNA IgG1 Ab, serum IL-10 and IL-4. Moreover, SM934 could significantly inhibit both of Th1 and Th17 responses, elevate Treg percentage and lower the percentage of $CD3^+$ $B220^+$ $CD4^-$ $CD8^-$ (double negative) T cells in MRL/*lpr* mice. We further elucidate that SM934 treatment restored the compartment of B cells in the spleen of MRL/*lpr* mice by increasing quiescent B cells, maintaining germinal centre B cells, decreasing activated B cells and reducing PCs.
Conclusions This work provides new evidence and clues for research about artemisinin compounds in the field of autoimmune diseases.

Other basic science

112 INCREASED NEUTROPHILS AND NEUTROPHIL SERINE PROTEASES IN THE SPLEENS OF ESTROGEN-TREATED C57BL/6 MICE AND IN SEVERAL STRAINS OF SPONTANEOUS LUPUS-PRONE MICE

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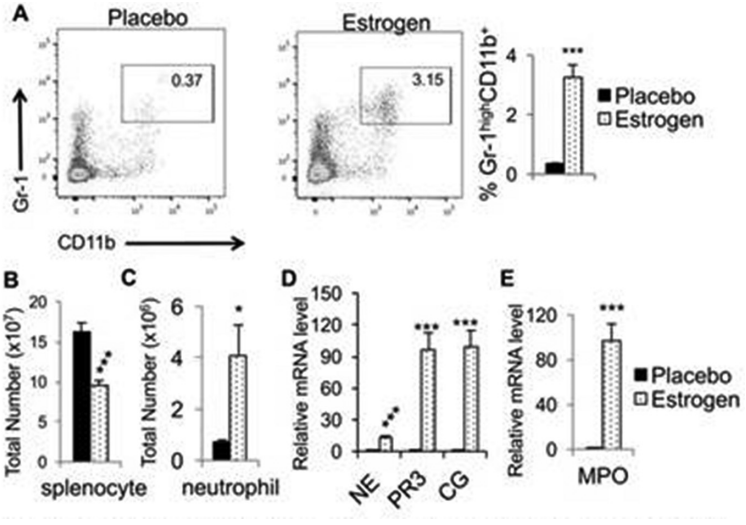
Background and aims Oestrogen, a natural immunomodulator, regulates the development and function of diverse immune cell types and has been implicated in lupus development.
Methods To determine the regulatory role of oestrogen on neutrophil development and function, we treated B6 mice with placebo- or oestrogen implants for 6–8 weeks, and then analysed splenic neutrophil serine proteases (NSPs, such as



Abstract 112 Figure 1 Estrogen treatment increasesneutrophil number, NSP and MPO expression in wild type B6 mice. (A) Flow cytometry analysis of splenic neutrophil percentage in placebo-and estrogen-treated B6 mice. (B)The total splenocytes count in placebo- and estrogen-treated mice. (C) The total CD11b*GR1* splenic neutrophilcounts in placebo- and estrogen-treated mice. (D and E) Real-time RT-PCR analysis the expressoin of NSPs (D), and MPO (E) *in* splenocytes from placebo- and estrogen- treated mice. The graphs show means±SEMs ($n \geq 4$). Unpaired students *t*tests (placebo vs estrogen) were performed.*, $p< 0.05$;**, $p< 0.01$; and ***, $p<0.001$.