the only autoantibody found in 474 patients (46.2%) and mucocutaneous involvements were the predominant features (84.5%).

Over a median of 2.5 years, damage accrual occurred in 20.8% patients and the risk was highest in cluster one (cluster 1 vs cluster 2: OR 1.34, P=0.008; cluster 1 vs cluster 3: OR 1.28, P=0.041). LLDAS-50 was most frequently achieved in cluster three (cluster 1: 49.6%, cluster 2: 48.7%, cluster 3: 59.1%) (figure 1). LLDAS-50 was associated with reduced risk of damage accrual across three clusters (cluster 1: OR 0.71, P=0.032; cluster 2: OR 0.63, P<0.001; cluster 3: OR 0.58, P<0.001).

Conclusions Three distinct subphenotypes were confirmed and associated with different risks of damage accrual. LLDAS-50 was an attainable target and associated with reduced risk of damage accrual across three clusters.

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Short oral presentation session 7: SLE etiology & pathogenesis 2

LSO-037 STING/TMEM173 MUTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: FROM ANIMAL MODEL TO INTRINSIC HUMAN GENETICS

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Background Abnormalities of type I interferon signaling and production can initiate lupus development. Disturbances of nucleic acid-sensing molecules triggered autoreactivity in lupus mouse models. Stimulator of interferon genes (STING) showed various effects in different lupus mouse models, which could be due to the diverse background of the lupus models and Sting-deficient mice. We aim to confirm the function of Sting/Tmem173 in pristane-induced lupus and identify the role of STING/TMEM173 variants in SLE susceptibility.

Methods Pristane-induced lupus model was introduced in the Sting-deficient mice (ENU-induced Goldenticket mutant mice). Autoantibody, histopathology, and immunophenotypes were analyzed after pristane injection for six months. Isolated DNA from 302 SLE patients and 173 healthy donors were tested for STING genotyping. We calculated the Odd Ratios of each STING variant and the inheritance patterns that significantly increased SLE susceptibility. Then, we analyzed the associations between STING genotypes and lupus phenotypes.

Results The absence of STING signaling in the Goldenticket mutant mice reduced the autoantibody production and severity of glomerulonephritis in pristane-induced lupus. The human STING mutation at p.R284S (gain-of-function) significantly increased the SLE risk in autosomal dominant pattern [OR = 64.0860 (95%CI = 22.8605–179.6555), p < 0.0001], while the mutation at p.R232H (loss of function) reduced the SLE risk in autosomal recessive pattern [OR = 0.2515 (95%CI = 0.1648–0.3836), p < 0.0001]. The combination of STING variants in a specific inheritance pattern increased the higher OR than a single variant. The patient who had p.R284S with p.R232H showed milder disease activity than those who had p.R284S alone at the time of diagnosis.

Conclusions The inhibition of STING rescued autoimmune phenotypes in pristane-induced lupus. Gain-of-function STING mutation increased SLE susceptibility and severity of the disease. These data suggested the critical function via STING-mediated signaling in SLE. Targeted at STING may provide a favorable outcome in SLE patients.

LSO-038 NLRP12 DEFICIENCY MICE PRESENT SEVERER LUPUS NEPHRITIS IN LUPUS PRONE MODEL AND PRISTANE-INDUCED LUPUS LIKE MODEL

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Background NLRP12 (NOD-like receptor family (NLR) pyrin domain containing 12) is an innate immune check-point in regulating type I IFNs expression. Since NLRP12 may participate in the pathogenesis of lupus, its role in lupus nephritis remained unknown.

Methods Wild type C57BL/6 and Nlrp12-/- mice in 12-week-old age were injected intra-peritoneally with a single dose of 500μl of pristane (2,6,10,14-tetramethylpentadecane, TMPD), and mice were sacrificed from 1st to 9th months after injection. Serum were collected for evaluation autoantibodies and renal functions. Kidneys sections were collected for immunoglobulin (IgG) evaluation and periodic-acid-Schiff (PAS) staining. Lupus prone mice with C57BL/6-Faslpr and C57BL/6-Faslpr-Nlrp12-/- mice were harvested and collected from 7th to 11th months.

Results Among animal models, both pristane induced mice and Faslpr mice revealed increasing autoantibodies production and severity of glomerulonephritis in Nlrp12-/- group in comparison with Nlrp12+/+ ones. Immunofluorescence staining for IgG revealed more profound deposition from 1st to 9th months after pristane injection group, with renal glomerulus damage from PAS staining. For Faslpr-Nlrp12-/- mice, more IgG deposition was noted. The CD43 staining revealed similar trend of both animal models. In serological evaluation, the dsDNA antibody in both animal model revealed significantly increased titer in Nlrp12-/- deficient ones (both group P < 0.01). Proteinuria analysis and serum creatinine all showed worsened presentation in Nlrp12-/- deficient mice.

Conclusions Animal models revealed Nlrp12 deficiency could exacerbate the lupus disease severity and progression of lupus nephritis in 2 different mouse models, both in histologic examinations and serological changes, reflecting the importance of Nlrp12 in controlling lupus pathogenesis.