recent *in vivo* pathogenesis studies in mice, have shown that intestinal colonization by RG strains isolated from Lupus patients in flare, but not RG strains from healthy adults, induce zonulin-dependent increases in intestinal permeability, RG translocation to mesenteric lymph nodes as well as serum IgG anti-RG antibody and anti-native DNA autoantibody responses.

Conclusions As many Lupus patients are known to suffer relapsing illness despite appropriate treatment, we speculate that gut blooms of pathogenic bacteria that impair gut barrier function and stoke systemic inflammation directly contribute to immunopathogenesis. We propose that future therapeutic interventions designed to promote a durable remission consider the potential necessity to target both the immunologic abnormalities of the disease, as well as re-establish stability within the gut microbiota community.

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512 THE RISING INCIDENCE, PREVALENCE AND MORTALITY GAP OF LUPUS NEPHRITIS: A POPULATION-BASED STUDY OVER FOUR DECADES

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Background There is paucity of population-based studies that investigate the epidemiology of lupus nephritis (LN) and its long-term outcomes.

Methods We used the Rochester Epidemiology Project (REP) a record-linkage system that includes all residents from Olmsted County, Minnesota since 1966 with additional counties since 2010. A cohort of LN patients between 1976 and 2018 in an eight-county region was identified based on (1) biopsy proven LN in the presence of a positive ANA or ds-DNA antibody, or (2) meeting ACR/EULAR 2019 criteria and having documented proteinuria (500 mg in 24hrs urine collection or protein/creatinine ratio > 0.5) that did not have a better

explanation than SLE. Age- and sex-specific incidence rates and point prevalence for four decades, adjusted to 2000 US total population, were reported. Standardized mortality ratio (SMR), survival rates, and time to end-stage renal disease (ESRD) were estimated using Kaplan-Meier methods. Poisson regression models were used to look at trends in relative survival over time.

Results There were 72 incident LN from 1976-2018. Mean age was 38.4 years (SD 16.24), 76% were female, and 69% non-Hispanic White. The overall LN incidence between 1976 and 2018 was estimated at 1 per 100,000 (95%CI 0.8-1.3). The incidence was highest in 30-39 age group. The overall incidence of LN increased from 0.7 to 1.3 with sex specific incidence in males quadrupling from 0.2 to 0.8 per 100,000 between 1976-1988 and 2000-2018 periods (table 1). LN prevalence increased from 16.8 per 100,000 in 1985 to 21.2 in 2015. LN had SMR of 6.33 (95%CI 3.81-9.89) compared to the general population. Survival was 50% at 20 years, and among survivors 40% had ESRD. There was a widening mortality gap with an increase in the SMR of 7% per year (1.07; 95%CI 1.03-1.10, p<0.001) or almost a doubling of the SMR every 10 years (1.90 per 10 years; 95%CI 1.33-2.70).

Conclusions The incidence and prevalence of LN has increased in the last 40 years. Long-term outcomes in patients with LN remain poor. Patients with LN had a mortality rate of more than 50% at 20 years and of those surviving, 40% had ESRD. The widening mortality gap we observed with near doubling of SMR each decade shows that the mortality reduction in LN patients is not keeping up with the mortality improvements of the general population despite changes in clinical practice over the decades.

513 RESPONSE GENE TO COMPLEMENT -32 FACILITATES LOCAL RECRUITMENT OF IL-17- PRODUCING CELLS IN IMMUNE COMPLEX MEDIATED GLOMERULONEPHRITIS THROUGH THE CCR6/CCL20 AXIS

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Background Response Gene to Complement (RGC)-32 is a cell cycle regulator induced by complement activation, growth factors and cytokines. RGC-32 mediates TGF- β dependent profibrotic pathways, while in immune cells promotes the

Abstract 512 Table 1 Age-adjusted incidence (1976-2018) and prevalence (1985,1995,2005,2015) rates of Lupus Nephritis (LN), 8-county region in Southeast Minnesota.†

	LN incidence rates/100,000 (95% CI) *					LN Prevalence rates/100,000 (95% CI) *				
	1976-1989	1990-1999	2000-2009	2010-2018	1976-2018	01/01/1985	01/01/1995	01/01/2005	01/01/2015	
Females	1.2 (0.4, 2.0)	1.3 (0.4, 2.2)	1.7 (0.7, 2.7)	1.7 (1.0, 2.4)	1.5 (1.1, 1.9)	25.9 (11.4, 40.5)	30.7 (16.7, 44.7)	36.5 (22.4, 50.7)	33.4 (24.7, 42.1)	
Males	0.2 (0.0, 0.6)	0.0 (0.0, 0.0)	0.6 (0.0, 1.2)	0.8 (0.4, 1.3)	0.5 (0.3, 0.8)	7.1 (0.0, 15.1)	6 (0.0, 13)	1.4 (0.0, 4.3)	8.6 (4.1, 13)	
Overall	0.7 (0.2, 1.2)	0.6 (0.2, 1.1)	1.2 (0.6, 1.8)	1.3 (0.9, 1.7)	1.0 (0.8, 1.3)	16.8 (8.3, 25.3)	18.5 (10.7, 26.4)	19.4 (12.1, 26.8)	21.2 (16.3, 26.2)	

*Rates for females and males were age-adjusted to the 2000 US Total population. Overall rates were age- and sex-adjusted to the 2000 US Total population.

†8-county region from Minnesota (Olmsted, Mower, Freeborn, Waseca, Steele, Dodge, Wabasha, Goodhue) Incidence rates were calculated using the number of incident cases as the numerator and population counts for residents from the Rochester Epidemiology Project (REP) census as the denominator. Incident and prevalent cases were from Olmsted County region between 1976 and 2010 and the 8 counties from 2010-2018.

differentiation of Th17 cells. In the nephrotoxic nephritis (NTN) mouse model of glomerulonephritis (GN), RGC-32 promotes organ damage through proinflammatory and profibrotic effects. To define the mechanisms underlying the role of RGC-32 in immune complex GN, we induced NTN in WT and RGC-32^{-/-} mice.

Methods Proteinuria, blood urea nitrogen and kidney histopathology were determined to assess kidney damage. Single cell suspension of infiltrating kidneys and spleens cells were analyzed by flow cytometry and PCR for expression of IL-17A, CCR6, CCL20, CXCL1, CXCL2 and CXCL5.

Results Induction of NTN in RGC-32^{-/-} mice resulted in decreased expression of IL-17A and CCR6 mRNA and decreased proportion of renal IL-17A⁺ CD4 T cells. The decrease in IL-17A⁺ CD4 cells was paralleled by decreased mRNA expression of CCL20 in both the renal tissue and infiltrating kidney cells of RGC-32^{-/-} mice. In vitro, CD4⁺ T cells from spleens of RGC-32^{-/-} mice cultured under Th17 conditions displayed decreased expression of CCL20 mRNA. These data suggest a role for RGC-32 in the positive feedback loop that enhances Th17 cell recruitment. The decrease in renal IL-17A⁺ cells was associated with decreased expression of IL-17 induced chemokines CXCL1, CXCL2 and CXCL5 and decreased local infiltration of neutrophils.

Conclusions These data suggest a role for RGC-32 in the positive feedback loop that enhances Th17 cell recruitment. The decrease in renal IL-17A⁺ cells was associated with decreased expression of IL-17 induced chemokines CXCL1, CXCL2 and CXCL5 and decreased local infiltration of neutrophils.

514 VOCLOSPORIN FOR LUPUS NEPHRITIS: INTERIM ANALYSIS OF THE AURORA 2 EXTENSION STUDY

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Background Voclosporin, a novel calcineurin inhibitor, has been tested successfully in two pivotal trials in adult patients

with lupus nephritis. The Phase 3 AURORA 1 study and the Phase 2 AURA-LV study showed that compared with mycophenolate mofetil (MMF) and low-dose steroids alone, the addition of voclosporin significantly increased the complete renal response rate at approximately one year of treatment. Patients that completed the AURORA 1 study were eligible to enroll in the AURORA 2 extension study. Here we report the first interim analysis of AURORA 2.

Methods AURORA 2 is a two-year, blinded, controlled extension study. Patients completing AURORA 1 continued the same randomized treatment in AURORA 2 of voclosporin (23.7 mg twice daily) or placebo, in combination with MMF (1 g twice daily) and low-dose steroids. The interim analysis evaluated urine protein creatinine ratio (UPCR) and estimated glomerular filtration rate (eGFR) in patients with up to two years of total treatment. In total, 116 patients in the voclosporin arm and 100 patients in the control arm enrolled in the extension study, of which 73 patients in the voclosporin arm and 51 patients in the control arm received two years of treatment at the time of this interim analysis.

Results Mean UPCR at pre-treatment AURORA 1 baseline was 3.9 mg/mg in the voclosporin arm (n=116) and 3.9 mg/mg in the control arm (n=100). The least square (LS) mean change in UPCR from pre-treatment AURORA 1 baseline to year two was -3.1 mg/mg for the voclosporin arm (n=73) and -2.1 mg/mg for control arm (n=51; figure 1). Mean corrected eGFR at pre-treatment AURORA 1 baseline was 79.6 mL/min/1.73 m² for the voclosporin arm (n=116) and 78.9 mL/min/1.73 m² for the control arm (n=100) and at year two, was 79.0 mL/min/1.73 m² for the voclosporin arm (n=73) and 82.9 mL/min/1.73 m² for the control arm (n=51). There was a small, expected, and early decrease in mean eGFR in the voclosporin arm in the first four weeks of treatment (in AURORA 1) after which eGFR remained stable throughout year one and year two. Additionally, there were no unexpected new adverse events observed in patients who continued with voclosporin treatment compared to control-treated patients.

Mixed effects model for repeated measures (MMRM) analysis of least squares mean change from pre-treatment

Abstract 514 Figure 1 UPCR change from baseline