relationship between intra-renal complement activation and kidney histology in LN, and whether complement activation products (CAPs) can serve as biomarkers to guide complement-directed therapies. In this investigation, urine CAPs levels were measured, and associations with kidney injury were determined.

Methods A cohort of 149 patients had urine and blood collected at the time of kidney biopsy for suspected LN. The CAPs C5a, C5b-9, and factor Ba were measured in the urine by ELISA. Biopsies were examined by routine histology, and the NIH activity and chronicity indexes (AI,CI) were calculated by two nephropathologists. CAPs levels were correlated with clinical and histologic data using the spearman correlation r.

Results The results are summarized in the table 1. The highest levels of CAPs were found in patients with proliferative or proliferative plus membranous LN, with lower levels in pure class II and V. All three urine CAPs correlated with AI, but the strongest correlation was between C5b-9 and AI. Only Ba and C5a correlated with CI, but this correlation was, at best, modest. All CAPs correlated with proteinuria, while only Ba and C5a correlated with serum creatinine.

Conclusion Urine C5b-9 was the best measure of histologic activity in LN. Given the size of the C5b-9 complex, it is unlikely to be filtered, even by glomeruli with a damaged glomerular permeability barrier. Urine C5b-9 therefore only reflects intra-renal complement activity. C5a and Ba associated modestly with active lesions, as well as kidney damage, likely accounting for their association with serum creatinine. We suggest levels of urine C5b-9 could be used to follow the success of anti-complement therapies in mitigating intra- renal complement activation in LN.

1102 **THE TRAJECTORY OF GLOMERULAR AND TUBULOINTERSTITIAL LESIONS AFTER TREATMENT OF LUPUS NEPHRITIS**

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Background Proliferative lupus nephritis (LN) is characterized histologically by glomerular and tubulointerstitial (TI) inflammation that presumably must resolve with treatment to achieve remission. Here we sought to document the trajectory of lesion resolution using serial kidney biopsies during LN treatment.

Methods A cohort of proliferative LN patients was prospectively followed during treatment with standard LN therapy. Patients had a diagnostic kidney biopsy (Bx1), a biopsy generally within the first year of treatment (Bx2), and a biopsy after at least 3 years of total immunosuppression (Bx3). The NIH activity and chronicity indices (AI, CI) were calculated at each biopsy.

Results The cohort (n=110) was followed for a median (range) of 109 (34, 202) months. Patients were treated with either MMF or cyclophosphamide initially. Overall, the patients did very well. Only 2 patients developed ESKD by last follow-up and only 9 patients had CKD (eGFR <60 ml/min/1.73m2), but this was pre-existing in 4 patients. AI followed an exponential decline after starting treatment. At the time of Bx2 (an average 9.7 months after Bx1), the percent of biopsies positive for cellular crescents (CC), fibrinoid necrosis (FN), and neutrophil infiltration NEU) fell precipitously, while the decline of endocapillary hypercellularity (EH) and hyaline deposits (HD) was more gradual. At Bx3 (an average of 42.6 months after Bx1) fewer than 5% of biopsies had residual CC, FN, NEU, or interstitial inflammation, but 25% still had EH and HD. By immunofluorescence microscopy over 90% of Bx1 biopsies had IgG and complement components C3 and C1q. At Bx3 only 30-40% of biopsies continued to show IF for complement, but IgG was still present in 66% of biopsies. The CI increased after Bx1. The rate of increase of all CI components was greatest from Bx1 to Bx2, slowed between Bx2 and Bx3, and actually declined for fibrous crescents.

Conclusion These data show that the most inflammatory lesions found in proliferative LN are rapidly responsive to immunosuppression, but EH and HD are more resistant. Complement deposition resolves quickly, but IgG is present in glomeruli for a long time. Despite rapid improvement in active inflammation, kidneys sustain chronic damage early in the disease course.

1103 **LUPUS CLINICAL FLARES IN PATIENTS WITH GUT PATHOBIONT BLOOMS SHARE A NOVEL PERIPHERAL BLOOD TRANSCRIPTOMIC IMMUNE ACTIVATION PROFILE**

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Background SLE is an inflammatory condition associated with hyperactivation of the immune system, with mounting evidence that imbalances in the gut microbiota communities are common. These imbalances can range from subtle patterns of dysbiosis to blooms in abundance of individual species that are concordant with clinical disease flares. Based on preliminary longitudinal surveys, almost half of Lupus nephritis (LN) flares were concurrent with transient expansions of a pathobiont, *Ruminococcus (blautia) gnavus*. As the transcriptomic patterns in the cells in our bloodstream can reflect disease activity, we sought to investigate gene expression patterns in groups of lupus patients, with comparisons to healthy controls (HC).

Methods From a well-characterized cohort, exploratory studies were performed on a selected group of 15 active female SLE patients, based in part on SLEDAI scores $\geq$ 4. Patients were grouped as without a history of renal involvement (i.e., non-renal) (N=7) or with LN in flare with Urine Protein creatinine ratio >0.5. Based on 16S rRNA fecal microbiota analyses, LN were subsetted as without bloom of individual species (N=4), or with a bloom (> 20-fold increased from HC, 3-9% abundance) of *R. gnavus* (N=4). In comparisons with 8 female HC, bulk RNA-seq was completed and after standard QC and filtering, 24,319 genes passed a minimum threshold of 4 reads in >50% samples and were used in downstream analysis.

Results Unsupervised clustering based on gene expression demonstrated significant separation between SLE samples and HC (figure 1). While there was no clear distinction between non-renal and renal (i.e., LN) groups, there were striking differences in the group of active LN without detectable gut