targets. Single-cell transcriptomics (scRNA-Seq) has advanced our understanding of LN pathogenesis, but tissue dissociation eliminates all spatial information and several rare cell types (such as podocytes) are under-represented using droplet-based scRNA-Seq protocols.

Methods Using the CosMx Spatial Molecular Imager (Nanostring), we performed spatial transcriptomics on 8 pediatric Class III/IV LN patients and 2 health controls. This platform generated 1000-plex gene expression data at single cell resolution using archived clinical biopsy tissue.

Results After data QC and cell segmentation, we identified a total of 447,892 cells, which were assigned to 33 reference cell types (figure 1A, B). Visualizing spatial relationships provided robust evidence of the accuracy of cell annotation, such as the colocalization of fenestrated glomerular endothelial cells, mesangial cells, and podocytes within glomeruli (figure 1C). Analysis of differential gene expression demonstrated that SLE induced broad transcriptional changes in resident glomerular cells, including markers of both injury response and initiation of tissue repair mechanisms. For example, glomerular endothelial cells downregulate expression of TEK (angiopoietin-1-binding TEK receptor tyrosine kinase), and the angiopoietin-1/TEK signal regulator DUSP1 (Dual Specificity Phosphatase 1), suggesting altered endothelial function and cross-talk with surrounding mesangial matrix. Upregulated genes in LN mesangial cells include: TAGLN, encoding transgrelin, a marker for proliferating mesangial cells; collagen molecules (COL3A1, COL1A2, COL4A1, COL6A); matrix metalloproteinases and inhibitors (MMP14, MMP19, TIMP1); and chemokines (CSF1, CXCL9). In parallel, we demonstrate that individual immune lineages traffic to specific regions in LN kidneys and that transcriptional signatures vary as a function of tissue location.

Conclusions Spatial transcriptomics is a powerful tool to uncover the heterogeneity of LN. The identification of new pathogenic mechanisms may inform the development of new targeted therapies.

Short oral presentation session 8: SLE biomarkers 2

LSO-043 URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) AS A MEDIATOR OF THE ASSOCIATION BETWEEN PARTICULATE MATTER EXPOSURE AND DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Neutrophil gelatinase-associated lipocalin (NGAL) is an acute-phase glycoprotein increased by inflammatory stimuli, oxidative stress, and tissue injury. Although NGAL is associated with global and renal disease activity in systemic lupus erythematosus (SLE), it is not known whether particulate matter (PM) affects NGAL levels and lupus activity in these patients. Thus, we investigated the mediating role of NGAL in the association between PM10 and PM2.5 exposure and lupus activity in a prospective, longitudinal cohort.

Methods The study enrolled 386 patients from three metropolitan regions in Korea. The daily average PM10 and PM2.5 concentrations were measured using portable air quality monitors and based on data from the National Ambient Air Monitoring System. Urinary NGAL (uNGAL) was measured at the time of enrollment and at 12 months, and disease activity was evaluated using the SLE Disease Activity Index 2000 (SLEDAI-2K) every 3 months for 1 year. Mixed Cox proportional hazard regression was performed to evaluate the associations of PM10 and PM2.5 with uNGAL and SLE disease activity.

Results Changes in PM10 and PM2.5 were associated with changes in uNGAL (β = 1.038, 95% confidence interval [CI]: 1.017–1.059, $p < 0.001$; β = 1.030, 95% CI: 1.001–1.045, $p = 0.013$, respectively), and with changes of SLEDAI-2K scores of > 8 over 1 year in SLE patients (β = 0.097, 95% CI: 0.048–0.146, $p < 0.001$; β = 0.100, 95% CI: 0.054–0.146, $p < 0.001$, respectively). In addition, changes in uNGAL were significantly associated with changes in SLEDAI-2K scores of > 8 (β = 1.000, 95% CI: 1.000–1.002, $p = 0.043$).

Conclusions The association between PM exposure and SLE disease activity may be partially explained by uNGAL levels.

LSO-044 SPHINGOLIPIDS ARE POTENTIAL DIAGNOSTIC BIOMARKERS FOR KOREAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Sphingolipids involved in regulating signal pathways in cell growth, differentiation, and apoptosis are increasingly recognized as playing an important role in the pathophysiology of chronic inflammatory diseases. This study aimed to evaluate the serum profile of sphingolipids in systemic lupus erythematosus (SLE) and to investigate the association between serum sphingolipids and disease activity.

Methods Levels of sphingolipids in plasma of women with SLE were assessed by liquid chromatography tandem mass spectrometry. The diagnostic value of plasma sphingolipids was analyzed using the area under the receiver operating characteristic curve (ROC). Pearson's correlation coefficient was used to analyze the relationship with disease activity markers.

Results Serum samples were collected from 38 women with SLE, including 11 lupus nephritis, and 30 controls. There were increases in concentration ceramide (Cer) and Cer to sphingosine-1-phosphate (S1P) ratio subspecies in patients with SLE, while the levels of sphingomyelins were decreased compared to the controls. The ratio of Cer16:0 to S1P showed a particularly strong increase in patients with lupus nephritis, with an area under the curve 0.739 (95% confidence interval, 0.581–0.898) to discriminate lupus nephritis in the control group. Furthermore, Cer16/S1P levels were correlated with disease duration, anti-double stranded DNA antibody, SLE disease activity index 2000, and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.