

biomarkers including neutrophil gelatinase – associated lipocalin (NGAL), monocyte chemoattractant protein-1 (MCP-1/CCL2), kidney injury molecule-1 (KIM-1), ceruloplasmin, adiponectin, and hemopexin) to monitor disease activity. It is critical to establish optimal sample handling conditions and storage prior to widespread clinical deployment and meaningful use in clinical trials. We have previously demonstrated the excellent short-term storage stability of NGAL and KIM-1; here we expand testing to include the other 4 RAIL biomarkers.

Methods Urine was collected from 10 patients enrolled in the SLE Clinical and Research Database (IRB 2008-0635). The urine was then aliquoted and tested under shipping conditions, including freeze/thaw, ambient and longer-term storage (figure 1). MCP-1, Ceruloplasmin, Adiponectin and Hemopexin were assayed by single-plex ELISA assay via commercially available kits. We performed Pearson Correlation Coefficient, Deming regression and Bland-Altman analysis.

Results There was no statistical difference in biomarker concentrations in any of the four biomarkers in any of the experimental conditions. Urinary MCP-1, Adiponectin, Hemopexin and Ceruloplasmin are stable following storage at -80°C for up to 3 months, and at 4° or 25°C up to 48 hours followed by -80°C . In addition, shipping on dry ice or with refrigeration leads to no significant loss of signal. The addition of 1 or 2 additional freeze thaw cycles also did not change mean biomarker levels.

Conclusions RAIL biomarkers are stable following short-term storage at clinically relevant conditions, including shipping on ice.

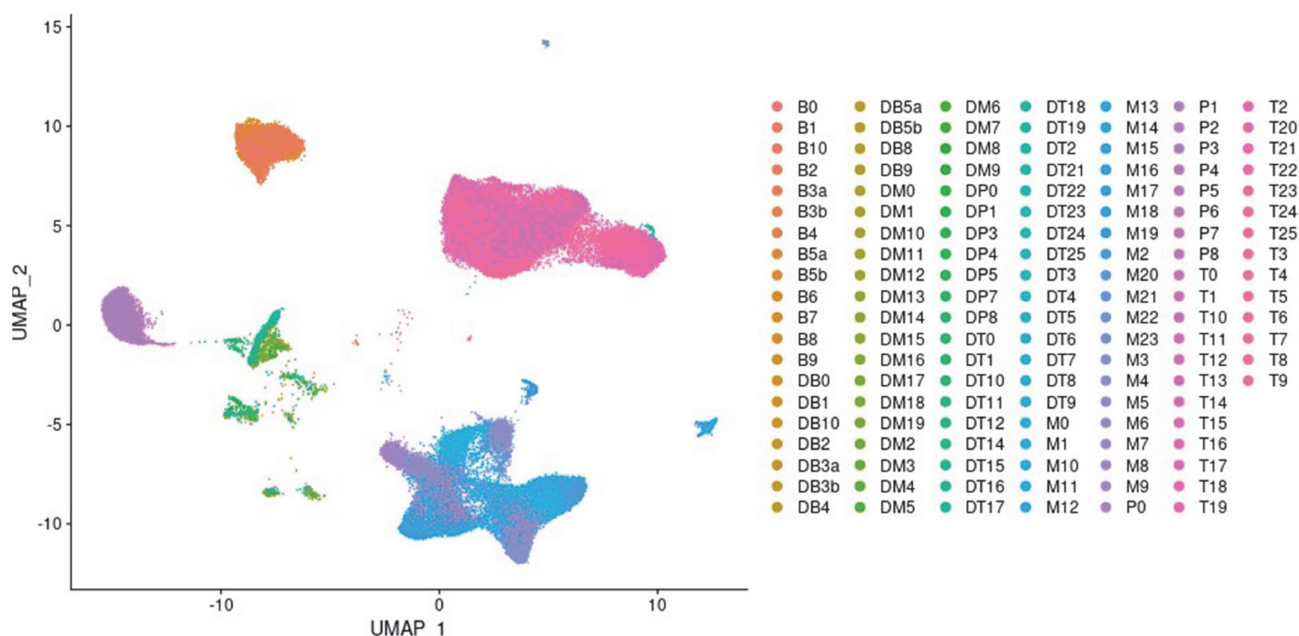
1107

IMMUNE CELL HETEROGENEITY IN LUPUS NEPHRITIS KIDNEYS AND ITS RELATION TO HISTOPATHOLOGICAL FEATURES: LESSONS FROM THE ACCELERATING MEDICINES PARTNERSHIP (AMP) IN SLE CONSORTIUM

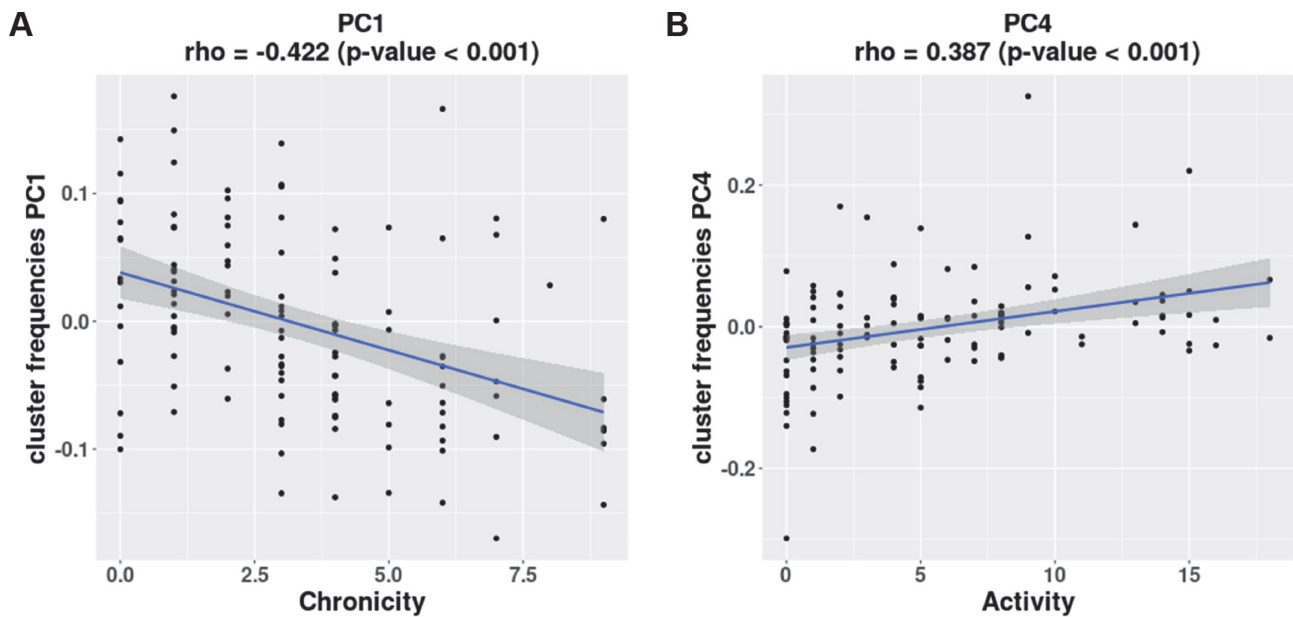
¹Arnon Arazi*, ²Jospeh Mears, ³Thomas M Eisenhaure, ²Qian Xiao, ³Paul J Hoover, ²Deepak A Rao, ⁴Celine C Berthier, ⁵Andrea Fava, ²Siddarth Gurajala, ³Michael Peters, ³Tony Jones, ²Saori Sakaue, ²William Apruzzese, ⁶Jennifer L Barnas, ⁵Derek Fine, ²James Lederer, ¹Richard Furie, ¹Anne Davidson, ⁷David A Hildeman, ⁷Steve Woodle, ⁸Judith A James, ⁸Joel M Guthridge, ⁹Maria Dall'Era, ⁹David Wofsy, ¹⁰Peter M Izmirly, ¹⁰H Michael Belmont, ¹⁰Robert Clancy, ¹¹Diane L Kamen, ¹²Chaim Putterman, ¹³Thomas Tuschl, ¹⁴Maureen A McMahon, ¹⁴Jennifer Grossman, ¹⁵Kenneth C Kalunian, ¹⁶Fernanda Payan-Schober, ¹⁷Mariko Ishimori, ¹⁷Michael Weisman, ⁴Matthias Kretzler, ⁴Jeffery Hodgjin, ²Michael B Brenner, ⁶Jennifer H Anolik, ⁵Michelle A Petri, ¹⁰Jill P Buyon, ²Soumya Raychaudhuri, ³Nir Hacohen, ¹Betty Diamond, the Accelerating Medicines Partnership (AMP) RA/SLE Network. ¹The Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY, USA; ²Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ³Broad Institute of MIT and Harvard, Cambridge, MA, USA; ⁴University of Michigan, Ann Arbor, MI, USA; ⁵Johns Hopkins University, Baltimore, MD, USA; ⁶University of Rochester Medical Center, Rochester, NY, USA; ⁷University of Cincinnati College of Medicine, Cincinnati, OH, USA; ⁸Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; ⁹University of California San Francisco, San Francisco, CA, USA; ¹⁰New York University School of Medicine, New York, NY, USA; ¹¹Medical University of South Carolina, Charleston, SC, USA; ¹²Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, USA; ¹³Rockefeller University, New York, NY, USA; ¹⁴University of California Los Angeles, Los Angeles, CA, USA; ¹⁵University of California San Diego School of Medicine, La Jolla, CA, USA; ¹⁶Texas Tech University Health Sciences Center, El Paso, TX, USA; ¹⁷Cedars-Sinai Medical Center, Los Angeles, CA, USA

10.1136/lupus-2022-lupus21century.72

Background Lupus nephritis (LN) is characterized by considerable variability in its clinical manifestations and histopathological findings. Understanding the cellular and molecular mechanisms underlying this heterogeneity is key for the development of personalized treatments for LN.



Abstract 1107 Figure 1 Single-cell RNA-sequencing was used to profile immune cells isolated from the kidneys of LN patients and healthy controls. Five main lineages of cells were identified, as shown in a Uniform Manifold Approximation and Projection (UMAP) plot: myeloid cells, T/NK cells, B cells, plasma cells and dividing cells. The cells of each lineage were further split into finer subsets of cells (color-coded).



Abstract 1107 Figure 2 PCA was used to characterize the variability in cell subset frequencies across LN patients. (A) The first PC, representing the balance between lymphoid cells and monocytes/macrophages, was found to be significantly correlated with the Chronicity index. (B) The fourth PC, representing the degree of macrophage differentiation, was found to be significantly correlated with the Activity index. Shown in each case are the Spearman correlation and its associated p-value.

Methods Droplet-based single-cell RNA-sequencing was applied to the analysis of dissociated kidney samples, collected from 155 LN patients with active kidney disease and 30 living donor controls as part of the Accelerating Medicines Partnership (AMP) in SLE consortium - a large-scale, multi-center study. 73,440 immune cells passing quality control were identified, spanning 134 cell subsets, representing various populations of tissue-resident and infiltrating leukocytes, as well as the activation states these cells assume as part of their disease-related activation and differentiation (figure 1). Principal component analysis (PCA) was used to characterize the variability in cell subset frequencies across the LN patients. Relationships between the resulting principal components (PCs) and the demographic, clinical and histopathological features of the patients were then assessed.

Results The main source of variability in immune cell subset frequencies, as represented by the first PC (PC1), reflected the balance between lymphocytes and monocytes/macrophages. Subsequent PCs represented the balance between B cells and T cells (PC2); the levels of cytotoxic T lymphocytes and NK cells, as compared to plasma cells (PC3); and the degree of macrophage differentiation to an alternatively activated phagocytic profile (PC4). PC1 was significantly correlated with the Chronicity index, such that patients with a higher percentage of lymphocytes compared to monocytes/macrophages had a higher Chronicity score ($\rho = -0.422$, $p\text{-value} < 0.001$; figure 2A). A high degree of macrophage differentiation, as represented by PC4, was associated with a high Activity score ($\rho = 0.387$, $p\text{-value} < 0.001$; figure 2B), and, in addition, with proliferative or mixed histology class, compared to pure membranous nephritis ($p\text{-value} = 0.001$, Kruskal–Wallis test). The ratio of B cells to T cells, as represented by PC2, demonstrated a positive correlation with the Activity index ($\rho = 0.311$, $p\text{-value} < 0.001$). We further identified a significant correlation of PC1 with age; specifically, older patients had a higher relative frequency of lymphocytes compared to

monocytes/macrophages ($\rho = -0.239$, $p\text{-value} = 0.003$). Our analysis indicated that these relations are not driven by demographic, clinical and technical sources of variation in our data, including race, ethnicity, the mixture of different nephritic classes, and the inclusion of both first and later biopsies.

Conclusion Our work identifies distinct leukocyte populations active in different LN patients and, possibly, different stages of disease, and points to potential therapeutic targets, that must be validated in mechanistic studies. This approach may pave the way to personalized treatment of LN.

1108

REPEAT KIDNEY BIOPSY FOR LUPUS NEPHRITIS AFTER INDUCTION: HISTOLOGIC AND CLINICAL RESPONSES IN CHILDHOOD-ONSET SLE

¹Scott E Wenderfer, ²Bianca Saenz, ³Maria M Pereira, ⁴M John Hicks. ¹Department of Pediatrics, Division of Pediatric Nephrology, University of British Columbia, B.C. Children's Hospital, Vancouver, BC, Canada; ²Department of Pediatrics, Pediatrics Residency Program, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA; ³Department of Pediatrics, Division of Rheumatology, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA; ⁴Department of Pathology and Immunology, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA

10.1136/lupus-2022-lupus21century.73

Background In children with proliferative lupus nephritis, response to induction treatment is based on clinical parameters. The added benefit of repeat kidney biopsy in defining therapy response remains unclear. Emerging adult data suggests a discordancy between clinical and histological outcomes. In children, we hypothesize that histologic reassessment after induction therapy correlates better with clinical remission.

Methods A single-center retrospective observational cohort study was conducted in childhood-onset proliferative lupus nephritis with a repeat biopsy after 5-9 months of induction therapy from 2007 to 2019. LN response was determined