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Molecular Signatures of Kidney Antibody–Secreting Cells in Lupus Patients With Active Nephritis Upon Immunosuppressive Therapy

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Abstract
Objective: This study was undertaken to characterize kidney and urine antibody-secreting cells (ASCs) from patients with active lupus nephritis, before and after induction therapy. Methods: We included patients with biopsy-proven active lupus nephritis and performed anti-CD138 staining of kidney biopsy samples to visualize ASCs. We performed single-cell gene expression profiling on sorted ASCs from fresh biopsy samples using multiplex reverse transcriptase–polymerase chain reaction. We used a gene set that allowed for the study of ASC maturation from plasmablasts to long-lived plasma cells. We quantified urine ASCs from untreated patients with lupus nephritis at diagnosis and after 6 months of prospective follow-up during induction therapy. Results: The number of kidney CD138+ ASCs in 46 untreated patients with lupus nephritis was correlated with a low estimated glomerular filtration rate and with tubulointerstitial damage. Most kidney ASCs from 3 untreated patients had a plasmablast molecular signature; in contrast, in 4 patients with refractory lupus nephritis, the kidney ASCs were mainly long-lived plasma cells, representing an ASC transcriptional profile similar to that in the bone marrow of 2 healthy donors. Some urine ASCs with a plasmablast signature were detected in patients with untreated active lupus nephritis. The presence of urine ASCs at 6 months was associated with treatment failure. Conclusion: Our results suggest potential for ASC-directed therapy in refractory lupus nephritis. © 2021, American College of Rheumatology

Index Keywords
CD14 antigen, CD16 antigen, CD27 antigen, CD3 antigen, complementary DNA, cyclophosphamide, kidney antibody, mycophenolate mofetil, rituximab, syndecan 1, immunosuppressive agent; adult, antibody secreting cell, Article, bone marrow, cell maturation, cell selection, controlled study, correlational study, estimated glomerular filtration rate, female, fetal bovine serum, fibrosing alveolitis, follow up, gene expression profiling, human, immunosuppressive treatment, inflammatory infiltrate, kidney biopsy, kidney interstitium, lupus erythematosus nephritis, major clinical study, male, multiplex reverse transcription polymerase chain reaction, plasma cell, plasmablast, prospective study, real time polymerase chain reaction, single cell analysis, systemic lupus erythematosus, treatment failure, urine sampling, clinical trial, cytology, genetics, immunoglobulin producing cell, induction chemotherapy, kidney, lupus erythematosus nephritis, metabolism, multicenter study, multiplex polymerase chain reaction, treatment outcome, urine; Antibody-Producing Cells, Follow-Up Studies, Gene Expression Profiling, Humans, Immunosuppressive Agents, Induction Chemotherapy, Kidney, Lupus Nephritis, Multiplex Polymerase Chain Reaction, Plasma Cells, Prospective Studies, Treatment Outcome, Urine

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