Supplementary Figure 1 SLE Healthy 1000 proteins **Z-score** 0 Count

Supplementary Figure 1. Overview of the urine biomarkers. Heatmap showing the relative concentration of the 1000 measure analytes (scaled by subject and analyte). Hierarchical clustering based on Ward's rule and Euclidean distance.

-4 0 4



Supplementary Figure 2. Principal component analysis of all urine analytes separates healthy subjects from lupus nephritis. PCA plot (n=37) of the first 2 principal components with % variance explained. Principal components are calculated independently in each analysis: PC1 in this figure does not correspond to PC in Figure 1.



Supplementary Figure 3. Treatment with prednisone is not associated with urinary PC1. Box plots illustrating PC1 values (n=30) based on any prednisone use (A) or by dose greater or lower than 20mg daily (B). No significant difference was detected (t test). The scatter plot (C) shows the absence of association between PC1 values and prednisone daily doses analyzed as a continuous variable (Pearson r=0.18, p=0.34).



Supplementary Figure 4. Principal component 2 detects collection site. (A-B) PCA (n=30) of the first 2 principal components of the urine proteome (% variance explained is indicated). PC2, but not PC1, was associated with the urine collection site. There was no biological pathway significantly enriched in PC2.

chemokine-mediated signaling pathway (GO:0070098)	
positive regulation of leukocyte chemotaxis (GO:0002690)	
lymphocyte chemotaxis (GO:0048247)	
positive regulation of GTPase activity (GO:0043547)	
monocyte chemotaxis (GO:0002548)	
cellular response to interferon–gamma (GO:0071346)	
response to interleukin–1 (GO:0070555)	
positive regulation of hydrolase activity (GO:0051345)	
neutrophil chemotaxis (GO:0030593)	
neutrophil migration (GO:1990266)	
inflammatory response (GO:0006954)	
response to tumor necrosis factor (GO:0034612)	
response to interferon–gamma (GO:0034341)	
granulocyte chemotaxis (GO:0071621)	
regulation of GTPase activity (GO:0043087)	
cellular response to interleukin–1 (GO:00/134/)	
positive regulation of peptidyl-tyrosine phosphorylation (GO:0050731)	
positive regulation of neutrophil migration (GO:1902624)	
cellular response to tumor necrosis factor (GO:00/1356)	
regulation of neutrophil chemotaxis (GO:0090022)	
regulation of leukocyte chemotaxis (GO:0002688)	
positive regulation of tyrosine phosphorylation of STAT protein (GO:0042531)	
eosinophil migration (GO:00/2677)	
eosinophil chemolaxis (GO.0048245)	
positive regulation of B cell promeration (GO:0030890)	
cytokine-mediated signaling pathway (GO:0019221)	
cellular divelent increanic eation homeostasis (GO:0000075)	
calcium ion homeostasis (GO:0072503)	
cellular calcium ion homeostasis (GO:0006874)	
regulation of B cell proliferation (GO:0030888)	
response to lipopolysaccharide (GO:0032496)	
regulation of tyrosine phosphorylation of STAT protein (GO:0042509)	
positive regulation of chemotaxis (GO:0050921)	
positive regulation of leukocyte migration (GO:0002687)	
regulation of peptidyl-tyrosine phosphorylation (GO:0050730)	
protein kinase B signaling (GO:0043491)	
cellular response to lipopolysaccharide (GO:0071222)	
cellular response to cytokine stimulus (GO:0071345)	
positive regulation of B cell activation (GO:0050871)	
positive regulation of JAK–STAT cascade (GO:0046427)	
positive regulation of lymphocyte proliferation (GO:0050671)	
cellular response to organic substance (GO:0071310)	
positive regulation of myeloid leukocyte differentiation (GO:0002763)	
response to molecule of bacterial origin (GO:0002237)	
negative regulation of smooth muscle cell proliferation (GO:0048662)	
positive regulation of MAPK cascade (GO:0043410)	
cellular response to organic cyclic compound (GO:00/140/)	
regulation of cellular component movement (GO:0051270)	
positive regulation of cell proliferation (GO:0008284)	
regulation of smooth muscle cell proliferation (GO:0048660)	
negative regulation of proteolysis (GO:0045861)	
response to lipid (GO:003093)	
positive regulation of extrinsic aportatic signaling pathway (CO:2001237)	
nositive regulation of cytokine production (GO:0001819)	
positive regulation of MAP kinase activity (GO:0043406)	
regulation of cell proliferation (GO:0042127)	
positive regulation of defense response (GO:0031349)	
positive regulation of intracellular signal transduction (GO 1902533)	
regulation of ERK1 and ERK2 cascade (GO:0070372)	
positive regulation of protein kinase B signaling (GO:0051897)	
positive regulation of cellular process (GO:0048522)	
negative	regulation of protein kinase activity (GO:0006469)
-3 -2 -1 0	1 2
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Supplementary Figure 5. Complete list of pathways enriched in the urine proteome PC1. 2018 Gene Ontology Biological Process pathways with a FDR <5% are ordered by their normalized enrichment score.



Normalized enrichment score

Supplementary Figure 6. Definition of a chemokine score. First, the genes coding for the proteins defining the leading edge of "Chemokine-mediated signaling pathway GO:0070098", the most enriched pathway in urine PC1 were identified. Then, a score for each cell was defined based on the sum of the normalized expression at the single cell level in the kidney. The same operation was repeated for "Cellular response to interferon-gamma (GO:0071346)".

Supplementary Figure 7



Supplementary Figure 7. Adjustment for glomerular (albumin) or tubular (B2M) dysfunction. Urine analyte concentrations were normalized for the concentration of albumin (A-D), beta-2 microglobulin (E-H), or both (I-M) in order to account for non-specific protein excretion through the glomerulus, tubule, or both, respectively. Panels A,B, E, F, I, and J show the PCA (n=30) of the first 2 principal components of the urine proteome (% variance explained is indicated). Panels C, G, and L showed the top and bottom 10 PC1 loading values of the measured urine protein. Panels D, H, and M the top 10 enriched pathways PC1 using Gene Ontology Biological Process indicating the biological significance of PC1.



Supplementary Figure 8. Distribution of cytokine positive cells among patients. Cells with positive cytokine unique molecular identifiers (UMIs) were quantified in the renal biopsy single cell transcriptomics. The bar plot summarizes the individual contribution from samples with at least 10 high quality cells. As detailed in table S1, cytokine positive cells were found in all patients.



Supplementary Figure 9. No expression of type 2 (Th2) immunity cytokines was detected in lupus nephritis kidney. Violin plots showing that there was abundant expression of the type 1 (Th1) immunity cytokine IFNG but none of the type 2 (Th2) immunity cytokines (IL4, IL5, and IL13) were detected in lupus nephritis kidney by single cell RNA sequencing.

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