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Supplemental Table 1: Groupings of individual morphologic descriptors

Individual Glomerular, Tubulointerstitial/Vascular, or Ultrastructural Descriptor	Global sclerosis/Obsolescent	Any Collapse	Any Deflation	Segmental obliteration	Hyalinosis	Any visceral epithelial cell (podocyte) abnormality	Mesangiopathic changes	IF/TA	Inflammation (Mononuclear WBCs only)	Arterial damage (presence vs. absence)	GBM abnormalities	Endothelial cell abnormalities
No/minimal changes												
Global sclerosis with hyalinosis	X											
Global sclerosis without hyalinosis	X											
Global deflation			X									
Global collapse		X										
Obsolescent	X											
Global mesangial sclerosis												
Segmental perihilar sclerosis				X								
Segmental extended perihilar sclerosis				X								
Segmental sclerosis away from vascular and tubular pole				X								
Segmental sclerosis cannot determine location				X								
Cellular tip lesion				X								
Sclerosing tip lesion				X								
Extended cellular tip lesion				X								
Extended sclerosing tip lesion				X								
Mid-glomerular sclerosis				X								
Cellular non-tip				X								
Segmental collapse		X										
Segmental deflation			X									
Periglomerular fibrosis												
Glomerular foam cells				X								
Hyalin droplets in epithelial cells						X						
Hyalinosis at the vascular pole					X							
Hyalinosis at the tubular pole					X							
Hyalinosis away from vascular and tubular pole					X							
Hyalinosis cannot determine location					X							
Adhesion				X								
Segmental epithelial cell hypertrophy						X						
Global epithelial cell hypertrophy						X						
Segmental epithelial cell hyperplasia						X						
Global epithelial cell hyperplasia						X						

Halo				X					
Segmental mesangial hypercellularity					X				
Global mesangial hypercellularity					X				
Marginating leukocytes									
Segmental increased mesangial matrix without hypercellularity					X				
Global increased mesangial matrix without hypercellularity					X				
Interstitial fibrosis						X			
Tubular atrophy						X			
Acute tubular injury									
Microcysts									
Interstitial edema									
Mononuclear WBC							X		
Eosinophils							x*		
Neutrophils							x*		
Interstitial foam cells									
Arteriosclerosis								X	
Arterial hyalinosis								X	
Foot process effacement									
Condensation of cytoskeleton									
Microvillous transformation									
Loss of primary processes									
Epithelial cell (podocyte) detachment									
Thickening of the GBM									X
Thinning of the GBM									X
GBM abnormal texture									X
Tubuloreticular inclusions									
Loss of Glomerular endothelial cell fenestration									X
Absence of Endothelium honeycombing-like appearance									X
Electron densities/hyaline material									
Mesangial electron dense deposits									

Supplemental Table 2: Other clinical characteristics of the study sample at the time of biopsy or NEPTUNE study enrollment, not included in analyses.

	Median (IQR) or % (N)
Family history of kidney disease,[a] % (N)	35% (77)
Obese at baseline study visit (BMI ≥30 kg/m^2 for adults or BMI >95th percentile for pediatric participants),[b] % (N)	40% (87)
Any edema present at enrollment study visit,[b] % (N)	43% (94)
On RAAS blocker before biopsy or at biopsy, % (N)	33% (73)
Serum albumin g/dL,[c] median (IQR)	3.3 (2.4 – 4.0)

BMI, body mass index; RAAS, Renin-angiotensin-aldosterone system
[a] Missing <1%; [b] Missing 1-5%; [c] Missing n=43

Supplemental Table 3: Descriptive table of individual pathology descriptors, by MCD vs. MCD-Like vs. FSGS

	MCD (n=39)		MCD-Like (n=61)		FSGS (n=124)	
Individual Glomerular Descriptors	**% (N) Patients with any**	**Median % Glomeruli among any**	**% (N) Patients with any**	**Median % Glomeruli among any**	**% (N) Patients with any**	**Median % Glomeruli among any**
No/minimal changes	100% (39)	100.0	100% (61)	98.1	100% (124)	76.0
Global sclerosis with hyalinosis	5% (2)	2.8	2% (1)	10.0	33% (41)	7.7
Global sclerosis without hyalinosis	13% (5)	6.9	23% (14)	9.3	58% (72)	14.3
Global deflation	5% (2)	11.9	8% (5)	2.3	40% (49)	6.1
Global collapse	0% (0)	--	2% (1)	1.9	19% (23)	6.7
Obsolescent	15% (6)	5.6	41% (25)	3.3	44% (54)	15.0
Global mesangial sclerosis	0% (0)	--	0% (0)	--	2% (2)	6.4
Segmental perihilar sclerosis	0% (0)	--	0% (0)	--	44% (54)	5.0
Segmental extended perihilar sclerosis	0% (0)	--	0% (0)	--	21% (26)	3.4
Segmental sclerosis away from vascular and tubular pole	0% (0)	--	0% (0)	--	24% (30)	3.6
Segmental sclerosis cannot determine location	3% (1)	6.5	0% (0)	--	73% (91)	9.5
Cellular tip lesion	3% (1)	3.2	0% (0)	--	12% (15)	4.3
Sclerosing tip lesion	0% (0)	--	0% (0)	--	10% (13)	4.3
Extended cellular tip lesion	0% (0)	--	0% (0)	--	1% (1)	2.6
Extended sclerosing tip lesion	0% (0)	--	0% (0)	--	3% (4)	4.1
Mid-glomerular sclerosis	0% (0)	--	2% (1)	2.4	3% (4)	4.1
Cellular non-tip	3% (1)	6.5	0% (0)	--	10% (12)	3.4
Segmental collapse	0% (0)	--	0% (0)	--	19% (23)	4.5
Segmental deflation	0% (0)	--	0% (0)	--	12% (15)	5.0
Periglomerular fibrosis	0% (0)	--	10% (6)	5.8	40% (49)	7.7
Glomerular foam cells	8% (3)	9.7	0% (0)	--	40% (49)	6.3
Hyalin droplets in epithelial cells	0% (0)	--	0% (0)	--	28% (35)	4.3
Hyalinosis at the vascular pole	3% (1)	3.8	0% (0)	--	35% (44)	4.8
Hyalinosis at the tubular pole	0% (0)	--	0% (0)	--	6% (8)	2.4
Hyalinosis away from vascular and tubular pole	0% (0)	--	0% (0)	--	14% (17)	3.7
Hyalinosis cannot determine location	3% (1)	3.2	0% (0)	--	41% (51)	4.8
Adhesion	0% (0)	--	11% (7)	3.6	65% (80)	6.7
Segmental epithelial cell hypertrophy	10% (4)	5.3	13% (8)	3.3	72% (89)	7.7
Global epithelial cell hypertrophy	5% (2)	5.4	7% (4)	2.3	31% (38)	7.2
Segmental epithelial cell hyperplasia	0% (0)	--	3% (2)	6.6	28% (35)	6.1
Global epithelial cell hyperplasia	0% (0)	--	0% (0)	--	16% (20)	4.3
Halo[1]	0% (0)	--	0% (0)	--	19% (23)	3.6
Segmental mesangial hypercellularity	8% (3)	25.0	15% (9)	14.3	28% (35)	8.1
Global mesangial hypercellularity	3% (1)	11.5	3% (2)	38.3	9% (11)	7.1
Marginating leukocytes	0% (0)	--	0% (0)	--	3% (4)	2.9
Segmental increased mesangial matrix without hypercellularity	3% (1)	4.0	2% (1)	2.4	5% (6)	3.9
Global increased mesangial matrix without hypercellularity	0% (0)	--	0% (0)	--	2% (3)	1.8
Individual Tubulointerstitial and Vascular Descriptors	**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**	
Interstitial fibrosis	1.0 (0.0 - 5.0)		1.0 (0.0 - 3.0)		16.0 (4.0 - 35.0)	
Tubular atrophy	0.0 (0.0 - 2.0)		1.0 (0.0 - 2.0)		13.0 (3.5 - 32.5)	
Acute tubular injury						
Absent	41% (16)		48% (29)		18% (22)	
Mild (1-25%)	36% (14)		44% (27)		55% (68)	
Moderate (26-50%)	21% (8)		7% (4)		21% (26)	
Severe (>50%)	3% (1)		2% (1)		6% (8)	

Microcysts	5% (2)	2% (1)	23% (29)
Interstitial edema	10% (4)	5% (3)	26% (32)
Mononuclear WBC	0.0 (0.0 - 3.0)	0.0 (0.0 - 0.0)	8.5 (1.0 - 29.0)
Eosinophils	3% (1)	0% (0)	5% (6)
Neutrophils	0% (0)	0% (0)	2% (3)
Interstitial foam cells	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Arteriosclerosis			
Absent (0%)	64% (23)	82% (50)	52% (63)
Mild (1-25%)	17% (6)	15% (9)	24% (29)
Moderate (26-50%)	14% (5)	2% (1)	13% (16)
Severe (>50%)	6% (2)	2% (1)	11% (13)
Arterial hyalinosis			
Absent (0%)	79% (31)	89% (54)	63% (78)
Mild (1-25%)	21% (8)	10% (6)	27% (33)
Moderate (26-50%)	0% (0)	2% (1)	10% (13)
Severe (>50%)	0% (0)	0% (0)	0% (0)
Electron Microscopy Descriptors	**% (N) or Median (IQR) amount**	**% (N) or Median (IQR) amount**	**% (N) or Median (IQR) amount**
Foot process effacement			
0-10%	0% (0)	23% (14)	3% (4)
11-25%	0% (0)	20% (12)	10% (12)
26-50%	0% (0)	18% (11)	16% (19)
51-75%	0% (0)	28% (17)	21% (26)
76-100%	100% (39)	11% (7)	50% (60)
Condensation of cytoskeleton			
Absent (0-5%)	31% (12)	68% (40)	39% (48)
Focal (6-50%)	46% (18)	25% (15)	50% (62)
Diffuse (>50%)	23% (9)	7% (4)	11% (14)
Microvillous transformation			
Absent (0-5%)	0% (0)	35% (21)	30% (37)
Focal (6-50%)	51% (20)	40% (24)	48% (60)
Diffuse (>50%)	49% (19)	25% (15)	22% (27)
Loss of primary processes	8% (3)	5% (3)	11% (14)
Epithelial cell (podocyte) detachment[1]	5% (2)	8% (5)	9% (11)
Thickening of the GBM	18% (7)	20% (12)	37% (46)
Thinning of the GBM	18% (7)	13% (8)	15% (18)
GBM abnormal texture	18% (7)	13% (8)	23% (28)
Tubuloreticular inclusions	3% (1)	0% (0)	2% (2)
Glomerular endothelial cell fenestration			
Present (0-5% loss)	21% (8)	62% (37)	28% (34)
Focal loss (6-50%)	62% (24)	35% (21)	43% (52)
Diffuse loss (>50%)	18% (7)	3% (2)	29% (35)
Absence of Endothelium honeycombing-like appearance	18% (7)	17% (10)	31% (37)
Electron densities/hyaline material	10% (4)	18% (11)	25% (30)
Mesangial electron dense deposits	3% (1)	2% (1)	4% (5)

[1]Halo on light microscopy and Epithelial cell detachment on electron microscopy represent the same structural change.

Supplemental Table 4: Descriptive table of grouped glomerular, tubulointerstitial, vascular and ultrastructural pathology descriptors, by MCD vs. MCD-Like vs. FSGS

	MCD (n=39)		MCD-Like (n=61)		FSGS (n=124)	
Grouped Glomerular Descriptors	**% (N) Patients with any**	**Median % Glomeruli among any**	**% (N) Patients with any**	**Median % Glomeruli among any**	**% (N) Patients with any**	**Median % Glomeruli among any**
Global sclerosis/Obsolescent	21% (8)	6.8	49% (30)	4.3	67% (83)	23.1
Any Collapse	0% (0)	--	2% (1)	1.9	30% (37)	5.3
Any Deflation	5% (2)	11.9	8% (5)	2.3	43% (53)	7.7
Segmental obliteration	8% (3)	9.7	13% (8)	3.4	91% (113)	11.8
Hyalinosis	5% (2)	3.5	0% (0)	--	59% (73)	6.1
Any visceral epithelial cell (podocyte) abnormality	13% (5)	6.9	16% (10)	2.7	83% (103)	8.6
Mesangiopathic changes	10% (4)	19.8	15% (9)	14.3	31% (38)	8.4
Grouped Tubulointerstitial and Vascular Descriptors	**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**	
IF/TA	0.5 (0.0 - 3.5)		1.0 (0.0 - 3.0)		14.8 (4.0 - 33.5)	
Inflammation	0.0 (0.0 - 3.0)		0.0 (0.0 - 0.0)		8.5 (1.0 - 29.0)	
Arterial damage	23% (9)		11% (7)		32% (40)	
Grouped Ultrastructural Descriptors	**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**		**% (N) or Median (IQR) amount**	
GBM abnormalities	38% (15)		36% (22)		55% (68)	
Endothelial cell abnormalities	79% (31)		49% (30)		75% (93)	

Supplemental Table 5. iAUC values from different machine learning algorithms. EN = elastic net model with given mixing parameter; EM = ultrastructural descriptors from electron microscopy; Dem/Clin = demographics and clinical characteristics.

			Ridge	EN 0.25	EN 0.50	EN 0.75	LASSO	Random Forest
Outcome: Disease Progression								
Individual Descriptors	+ EM	+ Dem/Clin	0.913	0.894	0.882	0.883	0.884	0.944
		- Dem/Clin	0.911	0.897	0.887	0.888	0.888	0.946
	- EM	+ Dem/Clin	0.907	0.894	0.877	0.877	0.875	0.941
		- Dem/Clin	0.864	0.854	0.850	0.848	0.846	0.909
Grouped Descriptors	+ EM	+ Dem/Clin	0.912	0.893	0.891	0.896	0.879	0.938
		- Dem/Clin	0.866	0.867	0.851	0.857	0.853	0.903
	- EM	+ Dem/Clin	0.910	0.908	0.894	0.897	0.917	0.934
		- Dem/Clin	0.858	0.856	0.859	0.853	0.843	0.900
Outcome: Complete Remission								
Individual Descriptors	+ EM	+ Dem/Clin	0.836	0.806	0.808	0.813	0.800	0.883
		- Dem/Clin	0.806	0.809	0.778	0.780	0.787	0.873
	- EM	+ Dem/Clin	0.814	0.782	0.782	0.785	0.783	0.879
		- Dem/Clin	0.774	0.755	0.797	0.769	0.765	0.872
Grouped Descriptors	+ EM	+ Dem/Clin	0.844	0.828	0.823	0.824	0.821	0.867
		- Dem/Clin	0.810	0.807	0.812	0.805	0.811	0.854
	- EM	+ Dem/Clin	0.783	0.774	0.768	0.767	0.766	0.862
		- Dem/Clin	0.749	0.749	0.746	0.742	0.738	0.848
Outcome: treatment response (complete proteinuria remission among participants treated with immunosuppression medication)								
Individual Descriptors	+ EM	+ Dem/Clin	0.804	0.620	0.597	0.500	0.619	0.856
		- Dem/Clin	0.824	0.500	0.500	0.500	0.681	0.854
	- EM	+ Dem/Clin	0.737	0.500	0.734	0.500	0.500	0.861
		- Dem/Clin	0.780	0.650	0.727	0.500	0.500	0.860
Grouped Descriptors	+ EM	+ Dem/Clin	0.775	0.500	0.619	0.617	0.500	0.840
		- Dem/Clin	0.749	0.739	0.701	0.704	0.500	0.811
	- EM	+ Dem/Clin	0.701	0.500	0.664	0.688	0.566	0.837
		- Dem/Clin	0.720	0.676	0.607	0.500	0.661	0.818

Supplemental Table 6: Unadjusted associations between top descriptors and disease progression.

A. Individual descriptors *(top 15 most important predictors)*	*Disease Progression (all participants)*		***B. Grouped descriptors*** *(top 15 most important predictors)*	*Disease Progression (all participants)*	
	HR (95% CI)	*P-value*		*HR (95% CI)*	*P-value*
(WSI) Obsolescent (per 10% increase)	1.56 (1.30, 1.86)	<.0001	(WSI) Global sclerosis/Obsolescent (>20% vs. 0-20%)	6.88 (3.37, 14.06)	<.0001
(WSI) Segmental sclerosis cannot determine location (per 10% increase)	1.44 (1.20, 1.73)	<.0001	(WSI) No/minimal changes (per 10% increase)	0.72 (0.64, 0.81)	<.0001
(WSI) No/minimal changes (per 10% increase)	0.72 (0.64, 0.81)	<.0001	(WSI) Interstitial Fibrosis/Tubular Atrophy (per 10% increase)	1.42 (1.25, 1.61)	<.0001
(WSI) Interstitial fibrosis (per 10% increase)	1.43 (1.26, 1.62)	<.0001	(WSI) Inflammation (per 10% increase)	1.47 (1.27, 1.70)	<.0001
(WSI) Mononuclear WBC (per 10% increase)	1.47 (1.27, 1.70)	<.0001	(WSI) Segmental obliteration (per 10% increase)	1.31 (1.14, 1.51)	0.0002
(WSI) Tubular atrophy (per 10% increase)	1.41 (1.24, 1.59)	<.0001	(WSI) Any Deflation (per 5% increase)	1.39 (1.19, 1.63)	<.0001
(WSI) Segmental sclerosis away from vascular and tubular pole (present vs. absent)	3.15 (1.48, 6.69)	0.0028	(WSI) Any visceral epithelial cell (podocyte) abnormality (>10% vs. 0-10%)	3.01 (1.48, 6.12)	0.0023
(WSI) Adhesion (>5% vs. 0-5%)	4.64 (2.25, 9.57)	<.0001	FSGS vs MCD	10.43 (2.49, 43.70)	0.0013
(WSI) Segmental deflation (present vs. absent)	4.12 (1.58, 10.74)	0.0038	(WSI) Interstitial foam cells (present vs. absent)	3.63 (1.67, 7.89)	0.0011
(WSI) Interstitial foam cells (present vs. absent)	3.63 (1.67, 7.89)	0.0011	(WSI) Periglomerular fibrosis (present vs. absent)	2.07 (1.00, 4.26)	0.0489
(WSI) Global deflation (per 5% increase)	1.35 (1.14, 1.60)	0.0004	(WSI) Any Collapse (present vs. absent)	2.06 (0.92, 4.61)	0.0780
(WSI) Periglomerular fibrosis (present vs. absent)	2.07 (1.00, 4.26)	0.0489	(WSI) Acute tubular injury (ref=Absent)		0.0027
(WSI) Global sclerosis with hyalinosis (present vs. absent)	2.22 (1.05, 4.72)	0.0377	Mild (1-25%)	5.96 (1.37, 25.97)	0.0174
FSGS vs. MCD	10.43 (2.49, 43.70)	0.0013	Moderate or severe (26-100%)	12.08 (2.72, 53.61)	0.0010
(EM) Endothelial cell honeycombing (absent vs. present)	2.93 (1.44, 5.95)	0.0030	UPCR at biopsy (ref=0 to 1.5 g/g)		0.0109
			>1.5 to 3 g/g	10.22 (2.24, 46.67)	0.0027
			>3 g/g	7.37 (1.72, 31.64)	0.0072
			eGFR at biopsy (per 10mL/min/1.73m^2 increase)	0.82 (0.74, 0.92)	0.0003
			(WSI) Hyalinosis (per 5% increase)	1.23 (1.05, 1.45)	0.0116

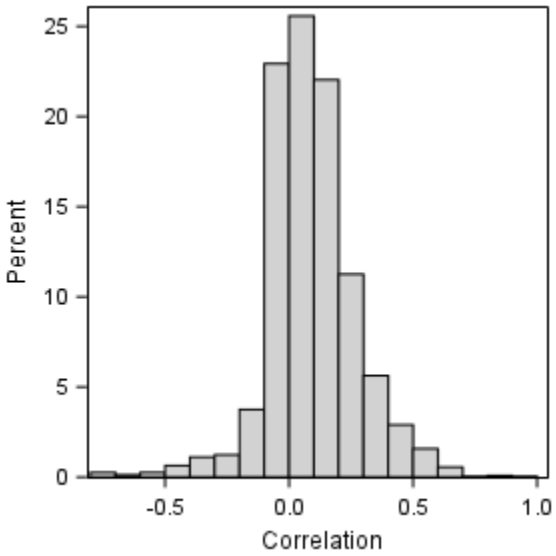
Supplemental Table 7: Unadjusted associations between top descriptors and complete proteinuria remission.

A. Individual descriptors *(top 15 most important predictors)*	*Remission (all participants)*		***B. Grouped descriptors*** *(top 15 most important predictors)*	*Remission (all participants)*	
	HR (95% CI)	*P-value*		*HR (95% CI)*	*P-value*
(WSI) Segmental sclerosis cannot determine location (present vs. absent)	0.28 (0.19, 0.43)	<.0001	(WSI) Segmental obliteration (per 10% increase)	0.71 (0.59, 0.86)	0.0004
FSGS vs MCD	0.35 (0.24, 0.51)	<.0001	FSGS vs MCD	0.35 (0.24, 0.51)	<.0001
(WSI) Hyalinosis cannot determine location (per 5% increase)	0.43 (0.28, 0.67)	0.0002	(EM) Endothelial cell abnormalities (present vs. absent)	0.41 (0.28, 0.60)	<.0001
(WSI) Obsolescent (per 10% increase)	0.58 (0.44, 0.77)	0.0002	(WSI) No/minimal changes (per 10% increase)	1.26 (1.15, 1.39)	<.0001
(WSI) Tubular atrophy (per 10% increase)	0.76 (0.66, 0.87)	0.0001	(WSI) Inflammation (per 10% increase)	0.70 (0.60, 0.83)	<.0001
(WSI) Mononuclear WBC (per 10% increase)	0.70 (0.60, 0.83)	<.0001	(WSI) Interstitial Fibrosis/Tubular Atrophy (per 10% increase)	0.76 (0.66, 0.87)	<.0001
(WSI) Adhesion (per 10% increase)	0.54 (0.37, 0.78)	0.0012	(WSI) Global sclerosis/Obsolescent (per 10% increase)	0.75 (0.65, 0.86)	<.0001
(WSI) No/minimal changes (per 10% increase)	1.26 (1.15, 1.39)	<.0001	(EM) Microvillous transformation (ref=absent [0-5%])		0.0015
(WSI) Interstitial fibrosis (per 10% increase)	0.76 (0.66, 0.87)	<.0001	Focal (6-50%)	1.30 (0.79, 2.14)	0.3023
(EM) Microvillous transformation (ref=absent [0-5%])		0.0015	Diffuse (>50%)	2.39 (1.41, 4.04)	0.0011
Focal (6-50%)	1.30 (0.79, 2.14)	0.3023	(WSI) Hyalinosis (per 5% increase)	0.58 (0.45, 0.76)	<.0001
Diffuse (>50%)	2.39 (1.41, 4.04)	0.0011	UPCR at biopsy (ref= >0.3 to 1.5 g/g)		0.0493
Age (ref= ≤18 years)		0.0543	>1.5 to 3 g/g	0.58 (0.32, 1.05)	0.0714
>18 to 45 years	0.59 (0.37, 0.95)	0.0285	>3 g/g	1.13 (0.73, 1.74)	0.5875
>45 years	0.69 (0.44, 1.08)	0.1023	Age (ref= ≤18 years)		0.0543
UPCR at biopsy (ref= >0.3 to 1.5 g/g)		0.0493	>18 to 45 years	0.59 (0.37, 0.95)	0.0285
>1.5 to 3 g/g	0.58 (0.32, 1.05)	0.0714	>45 years	0.69 (0.44, 1.08)	0.1023
>3 g/g	1.13 (0.73, 1.74)	0.5875	(WSI) Any visceral epithelial cell (podocyte) abnormality (>10% vs. 0-10%)	0.72 (0.45, 1.13)	0.1560
(WSI) Global deflation (per 5% increase)	0.71 (0.55, 0.90)	0.0053	(WSI) Periglomerular fibrosis (>5% vs. 0-5%)	0.44 (0.24, 0.79)	0.0066
(EM) Loss of endothelial cell fenestration (ref=present [0-5% loss])		0.0007	(WSI) Any Deflation (per 5% increase)	0.71 (0.56, 0.89)	0.0028
Focal loss (6-50%)	0.48 (0.32, 0.72)	0.0004	(EM) GBM abnormalities (present vs. absent)	0.63 (0.43, 0.91)	0.0145
Diffuse loss (>50%)	0.49 (0.29, 0.83)	0.0079			
(WSI) Segmental perihilar sclerosis (>5% vs. 0-5%)	0.33 (0.16, 0.69)	0.0028			

Supplemental Table 8. Unadjusted associations between top descriptors and treatment response (complete proteinuria remission among participants treated with immunosuppression medication [ISM]).

A. Individual descriptors	*Treatment Response (ISM participants)*		***B. Grouped descriptors***	*Treatment Response (ISM participants)*	
(top 10 most important predictors)	*HR (95% CI)*	*P-value*	*(top 10 most important predictors)*	*HR (95% CI)*	*P-value*
(WSI) Segmental sclerosis cannot determine location (present vs. absent)	0.50 (0.30, 0.82)	0.0062	(WSI) Segmental obliteration (per 10% increase)	0.89 (0.74, 1.07)	0.2252
Age (ref= ≤18 years)		0.2388	Age (ref= ≤18 years)		
>18 to 45 years	0.63 (0.32, 1.25)	0.1838	>18 to 45 years	0.63 (0.32, 1.25)	0.1838
>45 years	1.27 (0.69, 2.36)	0.4425	>45 years	1.27 (0.69, 2.36)	0.4425
(WSI) Tubular atrophy (per 10% increase)	0.86 (0.71, 1.04)	0.1174	(WSI) Interstitial Fibrosis/Tubular Atrophy (per 10% increase)	0.86 (0.71, 1.03)	0.1091
eGFR at biopsy (per 10mL/min/1.73m^2 increase)	1.01 (0.95, 1.07)	0.8493	(EM) Microvillous transformation (ref=absent [0-5%])		
(WSI) Mononuclear WBC (per 10% increase)	0.81 (0.65, 1.00)	0.0522	Focal (6-50%)	0.91 (0.47, 1.76)	0.7854
(EM) Microvillous transformation (ref=absent [0-5%])		0.0015	Diffuse (>50%)	1.66 (0.86, 3.23)	0.1326
Focal (6-50%)	0.91 (0.47, 1.76)	0.7854	(WSI) Inflammation (per 10% increase)	0.81 (0.65, 1.00)	0.0522
Diffuse (>50%)	1.66 (0.86, 3.23)	0.1326	(WSI) Acute tubular injury (ref=Absent)		
(WSI) Segmental extended perihilar sclerosis (present vs. absent)	0.35 (0.13, 0.95)	0.0400	Mild (1-25%)	0.91 (0.52, 1.58)	0.7286
(WSI) Interstitial fibrosis (per 10% increase)	0.86 (0.72, 1.03)	0.1026	Moderate or severe (26-100%)	1.90 (0.98, 3.71)	0.0593
(WSI) Acute tubular injury (ref=Absent)		0.0501	(WSI) Periglomerular fibrosis (present vs. absent)	0.62 (0.31, 1.26)	0.1852
Mild (1-25%)	0.91 (0.52, 1.58)	0.7286	(WSI) Interstitial foam cells (present vs. absent)	0.55 (0.24, 1.28)	0.1663
Moderate or severe (26-100%)	1.90 (0.98, 3.71)	0.0593	(WSI) Any Deflation (per 5% increase)	0.84 (0.62, 1.13)	0.2459
(WSI) Interstitial foam cells (present vs. absent)	0.55 (0.24, 1.28)	0.1663	(EM) GBM abnormalities (present vs. absent)	0.74 (0.46, 1.20)	0.2273

Supplemental Figure 1. Distribution of pairwise Spearman's correlation coefficients between predictors (using individual morphologic descriptors).



Only the following pairs of predictors had correlations ρ<-0.75 or ρ>0.75:

% glomeruli with no or minimal changes & % interstitial fibrosis (ρ=-0.753)

% glomeruli with no or minimal changes & % tubular atrophy (ρ=-0.766)

% interstitial fibrosis & % tubular atrophy (ρ=0.976)

% interstitial fibrosis & % mononuclear white blood cells (ρ=0.835)

% tubular atrophy & % mononuclear white blood cells (ρ=0.839)

Supplemental Figure 2. Predictor rankings from models of disease progression with and without demographics and clinical characteristics (Dem/Clin) and with and without ultrastructural descriptors from electron microscopy (EM). A) Models using only individual morphology descriptors. B) Models using grouped morphology descriptors. Rows are sorted by rankings from the model with Dem/Clin and ultrastructural descriptors from EM. Darker shadings correspond to higher ranks and lighter shadings correspond to lower ranks.

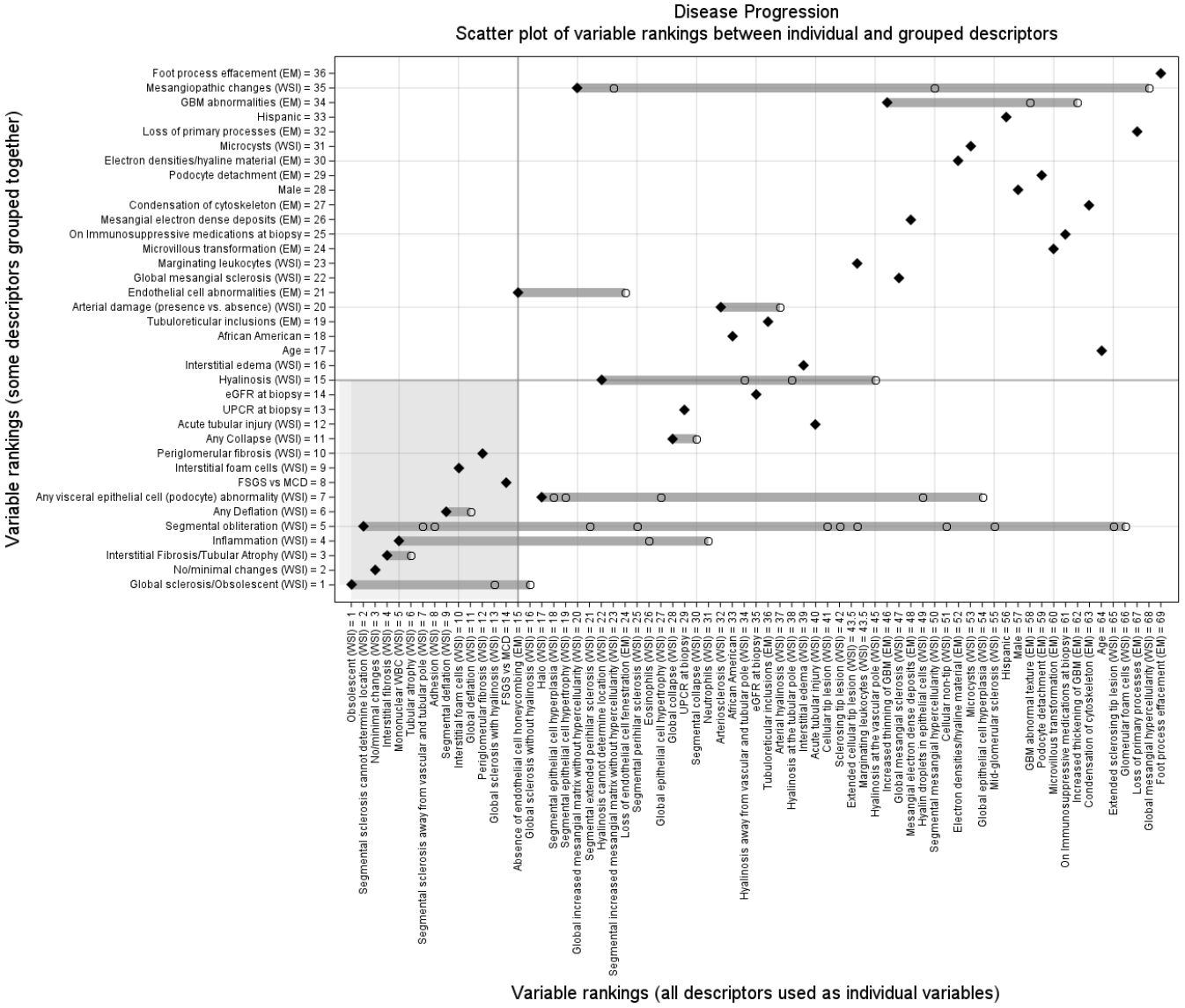
A. Individual morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Obsolescent	2	1	2	1
Segmental sclerosis cannot determine location	3	3	1	2
No/minimal changes	1	2	3	3
Interstitial fibrosis	4	5	4	4
Mononuclear WBC	5	4	5	5
Tubular atrophy	6	6	6	6
Segmental sclerosis away from vascular and tubular pole	9	9	8	7
Adhesion	7	7	7	8
Segmental deflation	8	8	9	9
Interstitial foam cells	10	10	11	10
Global deflation	11	13	10	11
Periglomerular fibrosis	14	12	12	12
Global sclerosis with hyalinosis	12	11	14	13
FSGS vs MCD		16		14
(EM) Absence of endothelial cell honeycombing			13	15
Global sclerosis without hyalinosis	13	14	15	16
Halo	16	15	16	17
Segmental epithelial cell hyperplasia	22	22	17	18
Segmental epithelial cell hypertrophy	15	19	18	19
Global increased mesangial matrix without hypercellularity	21	17	21	20
Segmental extended perihilar sclerosis	25	21	25	21
Hyalinosis cannot determine location	28	31	20	22
Segmental increased mesangial matrix without hypercellularity	19	18	24	23
(EM) Loss of endothelial cell fenestration			26	24
Segmental perihilar sclerosis	23	32	23	25
Eosinophils	20	20	22	26
Global epithelial cell hypertrophy	17	28	19	27
Global collapse	18	26	27	28
UPCR at biopsy		23		29
Segmental collapse	32	33	32	30
Neutrophils	29	30	30	31
Arteriosclerosis	27	24	28	32
African American		38		33
Hyalinosis away from vascular and tubular pole	30	29	29	34
eGFR at biopsy		56		35
(EM) Tubuloreticular inclusions			33	36
Arterial hyalinosis	35	37	41	37
Hyalinosis at the tubular pole	42	50	37	38
Interstitial edema	26	27	48	39
Acute tubular injury	24	25	31	40

Cellular tip lesion	37	39	38	41
Sclerosing tip lesion	33	35	34	42
Extended cellular tip lesion	38.5	40.5	39.5	43.5
Marginating leukocytes	38.5	40.5	39.5	43.5
Hyalinosis at the vascular pole	31	34	42	45
(EM) Increased thinning of GBM			45	46
Global mesangial sclerosis	41	42	43	47
(EM) Mesangial electron dense deposits			47	48
Hyalin droplets in epithelial cells	36	46	36	49
Segmental mesangial hypercellularity	34	44	35	50
Cellular non-tip	40	45	44	51
(EM) Electron densities/hyaline material			53	52
Microcysts	45	47	49	53
Global epithelial cell hyperplasia	47	51	54	54
Mid-glomerular sclerosis	43	48	50	55
Hispanic		52		56
Male		36		57
(EM) GBM abnormal texture			58	58
(EM) Podocyte detachment			52	59
(EM) Microvillous transformation			60	60
On Immunosuppressive medications at biopsy		43		61
(EM) Increased thickening of GBM			57	62
(EM) Condensation of cytoskeleton			46	63
Age		55		64
Extended sclerosing tip lesion	46	49	51	65
Glomerular foam cells	44	53	56	66
(EM) Loss of primary processes			55	67
Global mesangial hypercellularity	48	54	59	68
(EM) Foot process effacement			61	69

B. Grouped morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Global sclerosis/Obsolescent	1	1	1	1
No/minimal changes	2	2	2	2
Interstitial Fibrosis/Tubular Atrophy	4	4	3	3
Inflammation	3	3	4	4
Segmental obliteration	5	5	5	5
Any Deflation	7	6	7	6
Any visceral epithelial cell (podocyte) abnormality	6	8	6	7
FSGS vs MCD		12		8
Interstitial foam cells	9	9	8	9
Periglomerular fibrosis	11	11	10	10
Any Collapse	10	10	9	11
Acute tubular injury	8	7	11	12
UPCR at biopsy		14		13
eGFR at biopsy		23		14
Hyalinosis	13	15	12	15

Interstitial edema	12	13	14	16
Age		16		17
African American		20		18
(EM) Tubuloreticular inclusions			13	19
Arterial damage (presence vs. absence)	15	18	15	20
(EM) Endothelial cell abnormalities			21	21
Global mesangial sclerosis	17	21	17	22
Marginating leukocytes	16	19	16	23
(EM) Microvillous transformation			18	24
On Immunosuppressive medications at biopsy		17		25
(EM) Mesangial electron dense deposits			19	26
(EM) Condensation of cytoskeleton			20	27
Male		22		28
(EM) Podocyte detachment			23	29
(EM) Electron densities/hyaline material			26	30
Microcysts	18	24	22	31
(EM) Loss of primary processes			24	32
Hispanic		25		33
(EM) GBM abnormalities			27	34
Mesangiopathic changes	14	26	25	35
(EM) Foot process effacement			28	36

Supplemental Figure 3. Predictor rankings from models of <u>disease progression</u> using individual vs. grouped morphology descriptors. Both models included demographics and clinical characteristics and ultrastructural descriptors. Gray horizontal bands represent each grouped descriptor and its component individual descriptors. Solid diamonds represent the top ranked individual descriptor within a grouped descriptor, the individual descriptors not combined into grouped descriptors, and demographics and clinical characteristics. Open circles represent the individual descriptors within grouped descriptors that were not ranked first. The bottom left shaded region represents variables ranked in the top 15 from both models using individual vs. grouped descriptors.



Supplemental Figure 4. Predictor rankings from models of complete proteinuria remission with and without demographics and clinical characteristics (Dem/Clin) and with and without ultrastructural descriptors from electron microscopy (EM). A) Models using only individual morphology descriptors. B) Models using grouped morphology descriptors. Rows are sorted by rankings from the model with Dem/Clin and ultrastructural descriptors from EM. Darker shadings correspond to higher ranks and lighter shadings correspond to lower ranks.

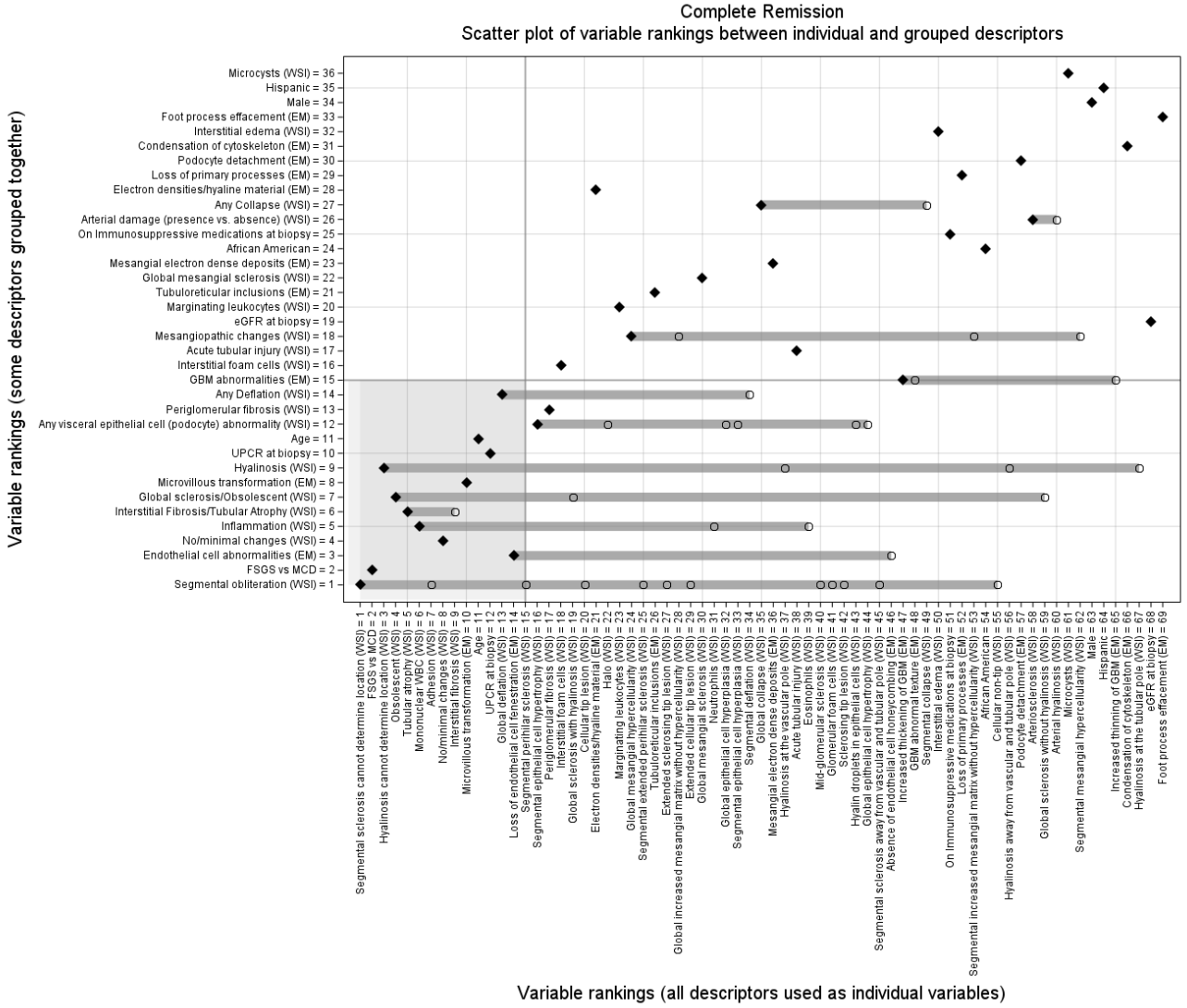
A. Individual morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Segmental sclerosis cannot determine location	1	1	1	1
FSGS vs MCD		2		2
Hyalinosis cannot determine location	2	4	2	3
Obsolescent	3	3	3	4
Tubular atrophy	7	6	8	5
Mononuclear WBC	8	8	5	6
Adhesion	4	5	6	7
No/minimal changes	5	7	4	8
Interstitial fibrosis	11	10	11	9
(EM) Microvillous transformation			10	10
Age		11		11
UPCR at biopsy		9		12
Global deflation	6	12	7	13
(EM) Loss of endothelial cell fenestration			9	14
Segmental perihilar sclerosis	9	14	12	15
Segmental epithelial cell hypertrophy	10	13	14	16
Periglomerular fibrosis	14	15	13	17
Interstitial foam cells	12	16	16	18
Global sclerosis with hyalinosis	47	17	58	19
Cellular tip lesion	17	18	20	20
(EM) Electron densities/hyaline material			15	21
Halo	15	19	17	22
Marginating leukocytes	20	22	25	23
Global mesangial hypercellularity	27	29	21	24
Segmental extended perihilar sclerosis	16	24	18	25
(EM) Tubuloreticular inclusions			29	26
Extended sclerosing tip lesion	21	23	28	27
Global increased mesangial matrix without hypercellularity	22	26	30	28
Extended cellular tip lesion	23	27	31	29
Global mesangial sclerosis	24	25	27	30
Neutrophils	25	28	32	31
Global epithelial cell hyperplasia	26	31	33	32
Segmental epithelial cell hyperplasia	29	33	39	33
Segmental deflation	32	21	36	34
Global collapse	28	30	26	35
(EM) Mesangial electron dense deposits			38	36
Hyalinosis at the vascular pole	42	38	24	37
Acute tubular injury	46	40	54	38
Eosinophils	30	34	37	39

Mid-glomerular sclerosis	31	39	35	40
Glomerular foam cells	18	20	22	41
Sclerosing tip lesion	37	44	44	42
Hyalin droplets in epithelial cells	39	41	45	43
Global epithelial cell hypertrophy	33	32	41	44
Segmental sclerosis away from vascular and tubular pole	38	35	43	45
(EM) Absence of endothelial cell honeycombing			19	46
(EM) Increased thickening of GBM			48	47
(EM) GBM abnormal texture			53	48
Segmental collapse	19	37	23	49
Interstitial edema	41	47	49	50
On Immunosuppressive medications at biopsy		42		51
(EM) Loss of primary processes			50	52
Segmental increased mesangial matrix without hypercellularity	34	46	42	53
African American		49		54
Cellular non-tip	35	36	46	55
Hyalinosis away from vascular and tubular pole	36	48	40	56
(EM) Podocyte detachment			47	57
Arteriosclerosis	13	45	34	58
Global sclerosis without hyalinosis	48	43	59	59
Arterial hyalinosis	43	50	52	60
Microcysts	44	53	57	61
Segmental mesangial hypercellularity	45	54	55	62
Male		51		63
Hispanic		55		64
(EM) Increased thinning of GBM			51	65
(EM) Condensation of cytoskeleton			60	66
Hyalinosis at the tubular pole	40	52	56	67
eGFR at biopsy		56		68
(EM) Foot process effacement			61	69

B. Grouped morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Segmental obliteration	1	1	1	1
FSGS vs MCD		2		2
(EM) Endothelial cell abnormalities			2	3
No/minimal changes	2	3	3	4
Inflammation	5	4	5	5
Interstitial Fibrosis/Tubular Atrophy	8	5	9	6
Global sclerosis/Obsolescent	6	7	8	7
(EM) Microvillous transformation			6	8
Hyalinosis	4	9	4	9
UPCR at biopsy		6		10
Age		8		11
Any visceral epithelial cell (podocyte) abnormality	9	10	7	12

Periglomerular fibrosis	7	11	11	13
Any Deflation	3	12	10	14
(EM) GBM abnormalities			15	15
Interstitial foam cells	10	13	12	16
Acute tubular injury	17	15	21	17
Mesangiopathic changes	14	14	13	18
eGFR at biopsy		17		19
Marginating leukocytes	11	16	16	20
(EM) Tubuloreticular inclusions			18	21
Global mesangial sclerosis	12	18	19	22
(EM) Mesangial electron dense deposits			20	23
African American		23		24
On Immunosuppressive medications at biopsy		19		25
Arterial damage (presence vs. absence)	15	20	23	26
Any Collapse	13	21	14	27
(EM) Electron densities/hyaline material			17	28
(EM) Loss of primary processes			24	29
(EM) Podocyte detachment			22	30
(EM) Condensation of cytoskeleton			27	31
Interstitial edema	16	24	25	32
(EM) Foot process effacement			28	33
Male		22		34
Hispanic		25		35
Microcysts	18	26	26	36

Supplemental Figure 5. Predictor rankings from models of <u>complete proteinuria remission</u> using individual vs. grouped morphology descriptors. Both models included demographics and clinical characteristics and ultrastructural descriptors. Gray horizontal bands represent each grouped descriptor and its component individual descriptors. Solid diamonds represent the top ranked individual descriptor within a grouped descriptor, the individual descriptors not combined into grouped descriptors, and demographics and clinical characteristics. Open circles represent the individual descriptors within grouped descriptors that were not ranked first. The bottom left shaded region represents variables ranked in the top 15 from both models using individual vs. grouped descriptors.



Supplemental Figure 6. Predictor rankings from models of <u>treatment response</u> (complete proteinuria remission only among patients treated with immunosuppression medication) with and without demographics and clinical characteristics (Dem/Clin) and with and without ultrastructural descriptors from electron microscopy (EM). A) Models using only individual morphology descriptors. B) Models using grouped morphology descriptors. Rows are sorted by rankings from the model with Dem/Clin and ultrastructural descriptors from EM. Darker shadings correspond to higher ranks and lighter shadings correspond to lower ranks.

A. Individual morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Segmental sclerosis cannot determine location	1	1	1	1
Age		3		2
Tubular atrophy	43	9	50	3
eGFR at biopsy		4		4
Mononuclear WBC	37	10	8	5
(EM) Microvillous transformation			3	6
Segmental extended perihilar sclerosis	2	5	2	7
Interstitial fibrosis	45	8	55	8
Acute tubular injury	3	2	11	9
Interstitial foam cells	4	7	4	10
Global deflation	7	11	5	11
Adhesion	5	6	6	12
(EM) Electron densities/hyaline material			24	13
Global mesangial hypercellularity	19	13	13	14
(EM) Podocyte detachment			10	15
Glomerular foam cells	8	14	12	16
African American		26		17
Extended sclerosing tip lesion	11	16	15	18
Global epithelial cell hyperplasia	20	24	25	19
Global mesangial sclerosis	14.5	20.5	19	23.5
Extended cellular tip lesion	14.5	20.5	19	23.5
Mid-glomerular sclerosis	14.5	20.5	19	23.5
Global increased mesangial matrix without hypercellularity	14.5	20.5	19	23.5
Marginating leukocytes	18	17	23	23.5
Eosinophils	14.5	20.5	19	23.5
Neutrophils	14.5	20.5	19	23.5
(EM) Tubuloreticular inclusions			19	23.5
(EM) Mesangial electron dense deposits			28	28
Hyalinosis at the tubular pole	10	15	14	29
Cellular non-tip	23	27	31	30
Segmental deflation	21	29	26	31
Global collapse	22	30	27	32
(EM) Loss of primary processes			29	33
Hyalin droplets in epithelial cells	24	28	34	34
(EM) Increased thinning of GBM			32	35
FSGS vs MCD		32		36
(EM) Increased thickening of GBM			39	37
(EM) Absence of endothelial cell honeycombing			7	38
Cellular tip lesion	25	31	35	39

Interstitial edema	31	41	41	40
Periglomerular fibrosis	27	43	9	41
Hyalinosis away from vascular and tubular pole	28	35	36	42
Microcysts	26	33	33	43
Sclerosing tip lesion	30	34	38	44
(EM) GBM abnormal texture			45	45
Obsolescent	9	36	30	46
(EM) Condensation of cytoskeleton			44	47
Global sclerosis without hyalinosis	42	46	48	48
Male		39		49
Segmental epithelial cell hypertrophy	38	25	52	50
Segmental epithelial cell hyperplasia	36	38	43	51
(EM) Loss of endothelial cell fenestration			57	52
Global epithelial cell hypertrophy	32	40	42	53
Hispanic		44		54
Segmental sclerosis away from vascular and tubular pole	35	37	46	55
Segmental collapse	29	42	37	56
Halo	33	45	47	57
(EM) Foot process effacement			56	58
Segmental increased mesangial matrix without hypercellularity	39	47	53	59
Hyalinosis cannot determine location	47	51	61	60
Global sclerosis with hyalinosis	40	48	49	61
UPCR at biopsy		50		62
Arteriosclerosis	41	52	54	63
Segmental perihilar sclerosis	34	49	51	64
Arterial hyalinosis	6	12	40	65
No/minimal changes	48	53	59	66
Segmental mesangial hypercellularity	46	54	60	67
Hyalinosis at the vascular pole	44	55	58	68

B. Grouped morphology descriptors and demographics/clinical characteristics	Glom, TI, and Vasc	+ Dem/Clin	+ EM	+ EM + Dem/Clin
Segmental obliteration	1	1	1	1
Age		3		2
Interstitial Fibrosis/Tubular Atrophy	15	5	23	3
(EM) Microvillous transformation			2	4
Inflammation	6	4	6	5
Acute tubular injury	2	2	5	6
Periglomerular fibrosis	5	8	3	7
Interstitial foam cells	3	6	7	8
Any Deflation	4	9	4	9
(EM) GBM abnormalities			18	10
eGFR at biopsy		7		11
FSGS vs MCD		10		12
Arterial damage (presence vs. absence)	10	14	15	13
(EM) Podocyte detachment			9	14

(EM) Loss of primary processes			14	15
Marginating leukocytes	7	11	12	16
Global mesangial sclerosis	8	12	10.5	17.5
(EM) Tubuloreticular inclusions			10.5	17.5
(EM) Mesangial electron dense deposits			13	19
African American		13		20
(EM) Endothelial cell abnormalities			8	21
(EM) Electron densities/hyaline material			16	22
Interstitial edema	9	15	17	23
Male		16		24
(EM) Condensation of cytoskeleton			20	25
Hispanic		18		26
Mesangiopathic changes	13	21	21	27
Microcysts	12	17	22	28
Any visceral epithelial cell (podocyte) abnormality	14	20	25	29
(EM) Foot process effacement			26	30
Any Collapse	11	19	19	31
Global sclerosis/Obsolescent	17	23	24	32
No/minimal changes	16	22	27	33
UPCR at biopsy		24		34
Hyalinosis	18	25	28	35

Supplemental Figure 7. Predictor rankings from models of <u>treatment response (complete proteinuria remission among participants treated with immunosuppression medication)</u> using individual vs. grouped morphology descriptors. Both models included demographics and clinical characteristics and ultrastructural descriptors. Gray horizontal bands represent each grouped descriptor and its component individual descriptors. Solid diamonds represent the top ranked individual descriptor within a grouped descriptor, the individual descriptors not combined into grouped descriptors, and demographics and clinical characteristics. Open circles represent the individual descriptors within grouped descriptors that were not ranked first. The bottom left shaded region represents variables ranked in the top 10 from both models using individual vs. grouped descriptors.