

Intrarenal synthesis of complement C3 localized to distinct vascular compartments in ANCA-associated renal vasculitis

Supplementary material

Samy Hakroush^{1,2}, Désirée Tampe³, Eva Baier³, Ingmar Alexander Kluge¹, Philipp Ströbel¹,
Björn Tampe³

¹*Institute of Pathology, University Medical Center Göttingen, Germany*

²*SYNLAB Pathology Hannover, SYNLAB Holding Germany, Augsburg, Germany*

³*Department of Nephrology and Rheumatology, University Medical Center Göttingen, Germany*

Corresponding author

Björn Tampe, MD

Department of Nephrology and Rheumatology

University Medical Center Göttingen

Germany

Email: bjoern.tampe@med.uni-goettingen.de

Supplementary Table 1. Clinical and laboratory parameters of the total cohort.

<i>Clinical data</i>		<i>Value</i>	
Female sex – no. (%)		16 (37.2)	
Age – years		62.1 ± 15	
ANCA subtype MPA/GPA – no. (%)		21/22 (48.8/51.2)	
AAV relapse – no. (%)		6 (14)	
BVAS – points		17.6 ± 4.3	
SAPS II – points		25.7 ± 9.7	
KRT – no. (%)		13 (30.2)	
<i>Laboratory data</i>		<i>Value</i>	<i>Reference range</i>
MPO-ANCA – IU/mL		35 ± 47	<3.5
PR3-ANCA – IU/mL		29 ± 44.6	<2
CRP – mg/L		78.9 ± 77.6	≤5
C3c – g/L		1.21 ± 0.31	0.82-1.93
C4 – g/L		0.26 ± 0.08	0.15-0.57
Serum creatinine – mg/dL		3.6 ± 2.6	0.7-1.2
eGFR – mL/min/1.73 m ²		33.8 ± 32.3	>60
Acanthocytes – no. (%)		5 (11.6)	Neg
Hematuria – no. (%)		42 (97.7)	Neg
uPCR – mg/g		1651 ± 2096	<300
uACR – mg/g		851.8 ± 1349	<30
α ₁ -microglobulin – mg/g		116.9 ± 117.5	<14
IgG – mg/g		118 ± 174.5	<9.6
<i>Histopathological data</i>		<i>Value</i>	
Crescentic class – no. (%)		14 (32.6)	
Focal class – no. (%)		21 (48.8)	
Mixed class – no. (%)		6 (14)	
Sclerotic class – no. (%)		2 (4.7)	
ARRS low risk – no. (%)		17 (32.6)	
ARRS medium risk – no. (%)		21 (48.8)	
ARRS high risk – no. (%)		5 (11.6)	
Normal glomeruli – no. (%) of total		49.8 ± 27.4	
Necrotic glomeruli – % of total		25.1 ± 27.3	
Crescentic glomeruli – % of total		35.1 ± 27.2	
Sclerotic glomeruli – % of total		15.6 ± 22.8	
Kidney fibrosis – %		26.3 ± 19.9	
<i>Extrarenal AAV manifestations</i>		<i>Value</i>	
Lung involvement – no. (%)		23 (53.5)	
Pulmonary hemorrhage – no. (%)		4 (9.3)	
Sinus involvement – no. (%)		6 (14)	
Joint involvement – no. (%)		10 (23.3)	
Ear involvement – no. (%)		3 (7)	
Eye involvement – no. (%)		3 (7)	
Nerve involvement – no. (%)		4 (9.3)	
Skin involvement – no. (%)		7 (16.3)	
<i>Co-medication</i>		<i>Value</i>	
NSAIDs – no. (%)		2 (4.7)	
Antibiotics – no. (%)		8 (18.6)	
PPIs – no. (%)		26 (60.5)	

Abbreviations: AAV, ANCA-associated vasculitis; *ah*, arteriolar hyalinosis; ARRS, ANCA renal risk score; BVAS, Birmingham Vasculitis Activity Score; CRP, C-reactive protein; *ct*, tubular atrophy; eGFR, estimated glomerular filtration rate (CKD-EPI); *g*, glomerulitis; *i*, interstitial inflammation; ICU, intensive care unit; IgG, immunoglobulin G; *i-IFTA*, inflammation in IFTA; KRT, kidney replacement therapy; MPO, myeloperoxidase; no., number; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton-pump inhibitors; PR3, proteinase 3; SAPS II, simplified acute physiology score; *t*, tubulitis; *ptc*, peritubular capillaritis; *ti*, total inflammation; *t-IFTA*, tubulitis in IFTA; uACR, urinary albumin-to-creatinine ratio; uPCR, urinary protein-to-creatinine ratio; *v*, intimal arteritis.

Supplementary Table 2. Frequency of C3 deposits in the total cohort.

<i>C3 deposits</i>	
Any C3 deposits – no. (%)	39 (90.7)
Glomerular tuft – no. (%)	37 (86.0)
Interlobular arteries – no. (%)	3 (7.0)
Peritubular capillaries – no. (%)	34 (79.1)
Venules – no. (%)	1 (2.3)

Abbreviations: ANCA, anti-neutrophil cytoplasmic antibodies; no., number.

Supplementary Table 3. Multiple linear regression analysis between intrarenal C3 deposits and co-medication.

	β	<i>p</i> value
<i>Any C3 deposits</i>		
NSAIDs	0.005	0.976
Antibiotics	0.148	0.422
PPIs	-0.075	0.652
<i>Glomerular tuft</i>		
NSAIDs	-0.013	0.939
Antibiotics	0.149	0.407
PPIs	0.186	0.253
<i>Interlobular arteries</i>		
NSAIDs	0.009	0.960
Antibiotics	-0.102	0.579
PPIs	-0.127	0.444
<i>Peritubular capillaries</i>		
NSAIDs	0.085	0.640
Antibiotics	0.054	0.769
PPIs	0.022	0.893
<i>Venules</i>		
NSAIDs	-0.011	0.950
Antibiotics	-0.110	0.550
PPIs	0.156	0.348

Abbreviations: NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton-pump inhibitors.

Supplementary Table 4. Included samples extracted from Nephroseq for tubulointerstitial C3 mRNA expression.

Sample name	Patient ID	Group	Tubulointerstitial log ₂ C3
H5Tub.HGU133A.Stanford373.Stanford373	Stanford373	Healthy	1.18608
H5Tub.HGU133A.Stanford374.Stanford374	Stanford374	Healthy	1.4522
H5Tub.HGU133A.Stanford375.Stanford375	Stanford375	Healthy	1.05834
H5Tub.HGU133A.Stanford378.Stanford378	Stanford378	Healthy	1.33897
H7Tub.HGU133Plus2.Stanford1164.Stanford1164	Stanford1164	Healthy	1.63881
H7Tub.HGU133Plus2.Stanford1165.Stanford1165	Stanford1165	Healthy	1.58544
H7Tub.HGU133Plus2.Stanford1166.Stanford1166	Stanford1166	Healthy	1.34654
H7Tub.HGU133Plus2.Stanford1168.Stanford1168	Stanford1168	Healthy	1.42545
H7Tub.HGU133Plus2.Stanford1169.Stanford1169	Stanford1169	Healthy	1.2802
H7Tub.HGU133Plus2.Stanford1170.Stanford1170	Stanford1170	Healthy	1.64367
H7Tub.HGU133Plus2.Stanford1171.Stanford1171	Stanford1171	Healthy	0.96254
H7Tub.HGU133Plus2.Stanford1172.Stanford1172	Stanford1172	Healthy	1.19831
H7Tub.HGU133Plus2.Stanford1173.Stanford1173	Stanford1173	Healthy	1.63517
H7Tub.HGU133Plus2.Stanford1174.Stanford1174	Stanford1174	Healthy	1.13815
H7Tub.HGU133Plus2.Stanford1175.Stanford1175	Stanford1175	Healthy	3.04019
H7Tub.HGU133Plus2.Stanford1177.Stanford1177	Stanford1177	Healthy	0.92792
H7Tub.HGU133Plus2.Stanford1178.Stanford1178	Stanford1178	Healthy	1.14101
H7Tub.HGU133Plus2.Stanford1179.Stanford1179	Stanford1179	Healthy	0.91488
H7Tub.HGU133Plus2.Stanford1180.Stanford1180	Stanford1180	Healthy	2.22042
H7Tub.HGU133Plus2.Stanford1182.Stanford1182	Stanford1182	Healthy	1.11715
H7Tub.HGU133Plus2.Stanford1183.Stanford1183	Stanford1183	Healthy	0.91563
H7Tub.HGU133Plus2.Stanford1184.Stanford1184	Stanford1184	Healthy	1.17409
H8Tub-HGU133Plus2-LD_Stanford1296-	Stanford1296	Healthy	3.57734
H8Tub-HGU133Plus2-LD_Stanford1298-	Stanford1298	Healthy	2.91503
H8Tub-HGU133Plus2-LD_Stanford1299-	Stanford1299	Healthy	3.69989
H8Tub-HGU133Plus2-LD_Stanford1301-	Stanford1301	Healthy	1.35007
H8Tub-HGU133Plus2-LD_Stanford1302-	Stanford1302	Healthy	2.02234
H8Tub-HGU133Plus2-LD_Stanford1303-	Stanford1303	Healthy	1.88202
H8Tub-HGU133Plus2-LD_Stanford1304-	Stanford1304	Healthy	1.70099
H8Tub-HGU133Plus2-LD_Stanford1305-	Stanford1305	Healthy	3.99738
H8Tub-HGU133Plus2-LD_Stanford1306-	Stanford1306	Healthy	2.23019
H7Tub.HGU133Plus2.RPGN1102.RPGN1102	RPGN1102	Renal vasculitis	4.2392
H7Tub.HGU133Plus2.RPGN1103.RPGN1103	RPGN1103	Renal vasculitis	4.45666
H7Tub.HGU133Plus2.RPGN1106.RPGN1106	RPGN1106	Renal vasculitis	4.46796
H7Tub.HGU133Plus2.RPGN1107.RPGN1107	RPGN1107	Renal vasculitis	2.9338
H7Tub.HGU133Plus2.RPGN1109.RPGN1109	RPGN1109	Renal vasculitis	3.9937
H7Tub.HGU133Plus2.RPGN1113.RPGN1113	RPGN1113	Renal vasculitis	4.32035
H7Tub.HGU133Plus2.RPGN1118.RPGN1118	RPGN1118	Renal vasculitis	3.63919
H7Tub.HGU133Plus2.RPGN1119.RPGN1119	RPGN1119	Renal vasculitis	4.57307
H7Tub.HGU133Plus2.RPGN1120.RPGN1120	RPGN1120	Renal vasculitis	5.03807
H7Tub.HGU133Plus2.RPGN1121.RPGN1121	RPGN1121	Renal vasculitis	3.09016
H7Tub.HGU133Plus2.RPGN1122.RPGN1122	RPGN1122	Renal vasculitis	3.5084
H7Tub.HGU133Plus2.RPGN1123.RPGN1123	RPGN1123	Renal vasculitis	4.95806
H7Tub.HGU133Plus2.RPGN1126.RPGN1126	RPGN1126	Renal vasculitis	4.82531
H7Tub.HGU133Plus2.RPGN1127.RPGN1127	RPGN1127	Renal vasculitis	1.56258
H7Tub.HGU133Plus2.RPGN1128.RPGN1128	RPGN1128	Renal vasculitis	3.44624
H7Tub.HGU133Plus2.RPGN1129.RPGN1129	RPGN1129	Renal vasculitis	4.78321
H7Tub.HGU133Plus2.RPGN1130.RPGN1130	RPGN1130	Renal vasculitis	3.72571
H7Tub.HGU133Plus2.RPGN1131.RPGN1131	RPGN1131	Renal vasculitis	4.59822
H7Tub.HGU133Plus2.RPGN1134.RPGN1134	RPGN1134	Renal vasculitis	5.20859
H7Tub.HGU133Plus2.RPGN1135.RPGN1135	RPGN1135	Renal vasculitis	3.0198
H7Tub.HGU133Plus2.RPGN1138.RPGN1138	RPGN1138	Renal vasculitis	4.7673
H5Tub.HGU133A.SLE301.SLE301	LN301	Lupus nephritis	1.99694
H5Tub.HGU133A.SLE302.SLE302	LN302	Lupus nephritis	2.16951
H5Tub.HGU133A.SLE304.SLE304	LN304	Lupus nephritis	1.31963
H5Tub.HGU133A.SLE305.SLE305	LN305	Lupus nephritis	1.30958

H5Tub.HGU133A.SLE306.SLE306	LN306	Lupus nephritis	2.08157
H5Tub.HGU133A.SLE307.SLE307	LN307	Lupus nephritis	1.61445
H5Tub.HGU133A.SLE308.SLE308	LN308	Lupus nephritis	5.69739
H5Tub.HGU133A.SLE309.SLE309	LN309	Lupus nephritis	2.1144
H5Tub.HGU133A.SLE310.SLE310	LN310	Lupus nephritis	2.92977
H5Tub.HGU133A.SLE311.SLE311	LN311	Lupus nephritis	2.11648
H5Tub.HGU133A.SLE312.SLE312	LN312	Lupus nephritis	3.73365
H5Tub.HGU133A.SLE313.SLE313	LN313	Lupus nephritis	1.74295
H5Tub.HGU133A.SLE314.SLE314	LN314	Lupus nephritis	3.44151
H5Tub.HGU133A.SLE318.SLE318	LN318	Lupus nephritis	1.91488
H5Tub.HGU133A.SLE319.SLE319	LN319	Lupus nephritis	2.09194
H5Tub.HGU133A.SLE323.SLE323	LN323	Lupus nephritis	1.04124
H5Tub.HGU133A.SLE329.SLE329	LN329	Lupus nephritis	2.3369
H5Tub.HGU133A.SLE336.SLE336	LN336	Lupus nephritis	2.97771
H5Tub.HGU133A.SLE338.SLE338	LN338	Lupus nephritis	3.42099
H5Tub.HGU133A.SLE340.SLE340	LN340	Lupus nephritis	2.65519
H5Tub.HGU133A.SLE342.SLE342	LN342	Lupus nephritis	4.8202
H5Tub.HGU133A.SLE343.SLE343	LN343	Lupus nephritis	3.57772
H5Tub.HGU133A.SLE346.SLE346	LN346	Lupus nephritis	1.19084
H5Tub.HGU133A.SLE348.SLE348	LN348	Lupus nephritis	0.62296
H5Tub.HGU133A.SLE349.SLE349	LN349	Lupus nephritis	0.97913
H5Tub.HGU133A.SLE352.SLE352	LN352	Lupus nephritis	4.16264
H5Tub.HGU133A.SLE357.SLE357	LN357	Lupus nephritis	2.57463
H5Tub.HGU133A.SLE358.SLE358	LN358	Lupus nephritis	1.0347
H5Tub.HGU133A.SLE359.SLE359	LN359	Lupus nephritis	3.51707
H5Tub.HGU133A.SLE360.SLE360	LN360	Lupus nephritis	5.0509
H5Tub.HGU133A.SLE361.SLE361	LN361	Lupus nephritis	1.17674
H5Tub.HGU133A.SLE362.SLE362	LN362	Lupus nephritis	3.80162

Supplementary Table 5. Included samples extracted from Nephroseq for glomerular C3 mRNA expression.

Sample name	Patient ID	Group	Glomerular log ₂ C3
H5Glom.HGU133A.Stanford478.Stanford478	Stanford478	Healthy	0.59695
H5Glom.HGU133A.Stanford479.Stanford479	Stanford479	Healthy	-0.13277
H5Glom.HGU133A.Stanford482.Stanford482	Stanford482	Healthy	0.2522
H7Glom.HGU133Plus2.Stanford974.Stanford974	Stanford974	Healthy	1.21446
H7Glom.HGU133Plus2.Stanford975.Stanford975	Stanford975	Healthy	1.23765
H7Glom.HGU133Plus2.Stanford976.Stanford976	Stanford976	Healthy	0.99962
H7Glom.HGU133Plus2.Stanford978.Stanford978	Stanford978	Healthy	0.5926
H7Glom.HGU133Plus2.Stanford979.Stanford979	Stanford979	Healthy	0.318
H7Glom.HGU133Plus2.Stanford980.Stanford980	Stanford980	Healthy	0.59036
H7Glom.HGU133Plus2.Stanford981.Stanford981	Stanford981	Healthy	-0.5319
H7Glom.HGU133Plus2.Stanford982.Stanford982	Stanford982	Healthy	0.72646
H7Glom.HGU133Plus2.Stanford983.Stanford983	Stanford983	Healthy	0.27873
H7Glom.HGU133Plus2.Stanford984.Stanford984	Stanford984	Healthy	0.6479
H7Glom.HGU133Plus2.Stanford985.Stanford985	Stanford985	Healthy	0.41799
H7Glom.HGU133Plus2.Stanford987.Stanford987	Stanford987	Healthy	0.08685
H7Glom.HGU133Plus2.Stanford988.Stanford988	Stanford988	Healthy	0.28446
H7Glom.HGU133Plus2.Stanford989.Stanford989	Stanford989	Healthy	1.7351
H7Glom.HGU133Plus2.Stanford990.Stanford990	Stanford990	Healthy	0.02396
H7Glom.HGU133Plus2.Stanford992.Stanford992	Stanford992	Healthy	-0.30769
H7Glom.HGU133Plus2.Stanford993.Stanford993	Stanford993	Healthy	-0.06812
H7Glom.HGU133Plus2.Stanford994.Stanford994	Stanford994	Healthy	0.44956
H7Glom.HGU133Plus2.RPGN902.RPGN902	RPGN902	Renal vasculitis	4.12747
H7Glom.HGU133Plus2.RPGN904.RPGN904	RPGN904	Renal vasculitis	3.3193
H7Glom.HGU133Plus2.RPGN906.RPGN906	RPGN906	Renal vasculitis	4.84192
H7Glom.HGU133Plus2.RPGN907.RPGN907	RPGN907	Renal vasculitis	2.13367
H7Glom.HGU133Plus2.RPGN908.RPGN908	RPGN908	Renal vasculitis	3.79695
H7Glom.HGU133Plus2.RPGN909.RPGN909	RPGN909	Renal vasculitis	2.33319
H7Glom.HGU133Plus2.RPGN911.RPGN911	RPGN911	Renal vasculitis	4.60739
H7Glom.HGU133Plus2.RPGN913.RPGN913	RPGN913	Renal vasculitis	3.98494
H7Glom.HGU133Plus2.RPGN924.RPGN924	RPGN924	Renal vasculitis	2.75692
H7Glom.HGU133Plus2.RPGN925.RPGN925	RPGN925	Renal vasculitis	4.92981
H7Glom.HGU133Plus2.RPGN926.RPGN926	RPGN926	Renal vasculitis	4.33436
H7Glom.HGU133Plus2.RPGN928.RPGN928	RPGN928	Renal vasculitis	2.59336
H7Glom.HGU133Plus2.RPGN929.RPGN929	RPGN929	Renal vasculitis	1.6781
H7Glom.HGU133Plus2.RPGN930.RPGN930	RPGN930	Renal vasculitis	4.17405
H7Glom.HGU133Plus2.RPGN934.RPGN934	RPGN934	Renal vasculitis	4.71123
H7Glom.HGU133Plus2.RPGN935.RPGN935	RPGN935	Renal vasculitis	1.74054
H7Glom.HGU133Plus2.RPGN936.RPGN936	RPGN936	Renal vasculitis	2.88882
H7Glom.HGU133Plus2.RPGN937.RPGN937	RPGN937	Renal vasculitis	1.30766
H7Glom.HGU133Plus2.RPGN938.RPGN938	RPGN938	Renal vasculitis	3.04163
H7Glom.HGU133Plus2.RPGN939.RPGN939	RPGN939	Renal vasculitis	3.83197
H7Glom.HGU133Plus2.RPGN942.RPGN942	RPGN942	Renal vasculitis	3.99187
H7Glom.HGU133Plus2.RPGN943.RPGN943	RPGN943	Renal vasculitis	3.74546
H7Glom.HGU133Plus2.RPGN946.RPGN946	RPGN946	Renal vasculitis	4.46189
H5Glom.HGU133A.SLE401.SLE401	LN401	Lupus nephritis	0.40711
H5Glom.HGU133A.SLE402.SLE402	LN402	Lupus nephritis	1.10319
H5Glom.HGU133A.SLE404.SLE404	LN404	Lupus nephritis	0.86213
H5Glom.HGU133A.SLE405.SLE405	LN405	Lupus nephritis	0.47511
H5Glom.HGU133A.SLE406.SLE406	LN406	Lupus nephritis	4.17154
H5Glom.HGU133A.SLE407.SLE407	LN407	Lupus nephritis	0.84931
H5Glom.HGU133A.SLE408.SLE408	LN408	Lupus nephritis	5.07462
H5Glom.HGU133A.SLE409.SLE409	LN409	Lupus nephritis	0.94287
H5Glom.HGU133A.SLE410.SLE410	LN410	Lupus nephritis	0.96251
H5Glom.HGU133A.SLE411.SLE411	LN411	Lupus nephritis	2.26289
H5Glom.HGU133A.SLE412.SLE412	LN412	Lupus nephritis	3.63777
H5Glom.HGU133A.SLE413.SLE413	LN413	Lupus nephritis	1.75773
H5Glom.HGU133A.SLE414.SLE414	LN414	Lupus nephritis	2.79467

H5Glom.HGU133A.SLE418.SLE418	LN418	Lupus nephritis	2.55946
H5Glom.HGU133A.SLE419.SLE419	LN419	Lupus nephritis	2.86429
H5Glom.HGU133A.SLE423.SLE423	LN423	Lupus nephritis	0.50021
H5Glom.HGU133A.SLE430.SLE430	LN430	Lupus nephritis	4.27862
H5Glom.HGU133A.SLE438.SLE438	LN438	Lupus nephritis	5.013
H5Glom.HGU133A.SLE440.SLE440	LN440	Lupus nephritis	2.67137
H5Glom.HGU133A.SLE442.SLE442	LN442	Lupus nephritis	4.26628
H5Glom.HGU133A.SLE444.SLE444	LN444	Lupus nephritis	4.31194
H5Glom.HGU133A.SLE445.SLE445	LN445	Lupus nephritis	3.02927
H5Glom.HGU133A.SLE448.SLE448	LN448	Lupus nephritis	1.49411
H5Glom.HGU133A.SLE450.SLE450	LN450	Lupus nephritis	1.44047
H5Glom.HGU133A.SLE451.SLE451	LN451	Lupus nephritis	-0.09065
H5Glom.HGU133A.SLE454.SLE454	LN454	Lupus nephritis	1.2343
H5Glom.HGU133A.SLE462.SLE462	LN462	Lupus nephritis	1.08277
H5Glom.HGU133A.SLE463.SLE463	LN463	Lupus nephritis	1.64144
H5Glom.HGU133A.SLE464.SLE464	LN464	Lupus nephritis	3.76997
H5Glom.HGU133A.SLE465.SLE465	LN465	Lupus nephritis	1.56929
H5Glom.HGU133A.SLE466.SLE466	LN466	Lupus nephritis	-0.04065
H5Glom.HGU133A.SLE467.SLE467	LN467	Lupus nephritis	1.65458

Supplementary Table 6. Top 20 pathways correlated with tubulointerstitial C3 mRNA expression.

Pathway	Entities found	Entities total	Entities ratio	Entities p	Entities FDR	Species
Interferon gamma signaling	118	250	0.017	1.11E-16	6.55E-15	Homo sapiens
ER-Phagosome pathway	83	173	0.011	1.11E-16	6.55E-15	Homo sapiens
Antigen Presentation: Folding, assembly and peptide loading of class I MHC	75	108	0.007	1.11E-16	6.55E-15	Homo sapiens
Endosomal/Vacuolar pathway	74	82	0.005	1.11E-16	6.55E-15	Homo sapiens
Class I MHC mediated antigen processing & presentation	86	479	0.032	1.11E-16	6.55E-15	Homo sapiens
Antigen processing-Cross presentation	84	195	0.013	1.11E-16	6.55E-15	Homo sapiens
Interferon Signaling	130	395	0.026	1.11E-16	6.55E-15	Homo sapiens
Interferon alpha/beta signaling	96	190	0.013	1.11E-16	6.55E-15	Homo sapiens
Adaptive Immune System	126	1,012	0.067	1.11E-16	6.55E-15	Homo sapiens
Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell	78	316	0.021	1.11E-16	6.55E-15	Homo sapiens
Immune System	227	2,691	0.178	1.11E-16	6.55E-15	Homo sapiens
Cytokine Signaling in Immune system	169	1,094	0.072	1.11E-16	6.55E-15	Homo sapiens
MHC class II antigen presentation	28	149	0.01	2.38E-14	1.33E-12	Homo sapiens
Phosphorylation of CD3 and TCR zeta chains	17	45	0.003	7.22E-14	3.61E-12	Homo sapiens
PD-1 signaling	17	45	0.003	7.22E-14	3.61E-12	Homo sapiens
Translocation of ZAP-70 to Immunological synapse	16	42	0.003	3.46E-13	1.56E-11	Homo sapiens
Generation of second messenger molecules	16	59	0.004	5.06E-11	2.18E-9	Homo sapiens
Downstream TCR signaling	21	124	0.008	2.75E-10	1.15E-8	Homo sapiens
TCR signaling	22	147	0.01	9.91E-10	3.96E-8	Homo sapiens
Costimulation by the CD28 family	17	99	0.007	1.13E-8	4.31E-7	Homo sapiens

Supplementary Table 7. Top 20 pathways correlated with glomerular C3 mRNA expression.

Pathway	Entities found	Entities total	Entities ratio	Entities p	Entities FDR	Species
Integrin cell surface interactions	4	86	0.006	1.66E-5	1.91E-3	Homo sapiens
Collagen chain trimerization	3	44	0.003	6.86E-5	3.91E-3	Homo sapiens
Chemokine receptors bind chemokines	3	57	0.004	1.47E-4	5.58E-3	Homo sapiens
Collagen degradation	3	69	0.005	2.57E-4	6.1E-3	Homo sapiens
Extracellular matrix organization	5	329	0.022	2.65E-4	6.1E-3	Homo sapiens
Collagen biosynthesis and modifying enzymes	3	76	0.005	3.4E-4	6.1E-3	Homo sapiens
ECM proteoglycans	3	79	0.005	3.81E-4	6.1E-3	Homo sapiens
Collagen formation	3	104	0.007	8.44E-4	1.04E-2	Homo sapiens
Rap1 signalling	2	24	0.002	8.63E-4	1.04E-2	Homo sapiens
Degradation of the extracellular matrix	3	148	0.01	2.31E-3	2.54E-2	Homo sapiens
NCAM1 interactions	2	44	0.003	2.84E-3	2.84E-2	Homo sapiens
NGF-stimulated transcription	2	56	0.004	4.54E-3	4.08E-2	Homo sapiens
Peptide ligand-binding receptors	3	203	0.013	5.58E-3	4.19E-2	Homo sapiens
Assembly of collagen fibrils and other multimeric structures	2	67	0.004	6.42E-3	4.19E-2	Homo sapiens
NCAM signaling for neurite out-growth	2	70	0.005	6.98E-3	4.19E-2	Homo sapiens
Signaling by PDGF	2	70	0.005	6.98E-3	4.19E-2	Homo sapiens
Nuclear Events (kinase and transcription factor activation)	2	80	0.005	9.02E-3	5.34E-2	Homo sapiens
Interleukin-10 signaling	2	86	0.006	1.04E-2	5.34E-2	Homo sapiens
Alternative complement activation	1	6	0	1.07E-2	5.34E-2	Homo sapiens
Activation of C3 and C5	1	7	0	1.24E-2	6.22E-2	Homo sapiens