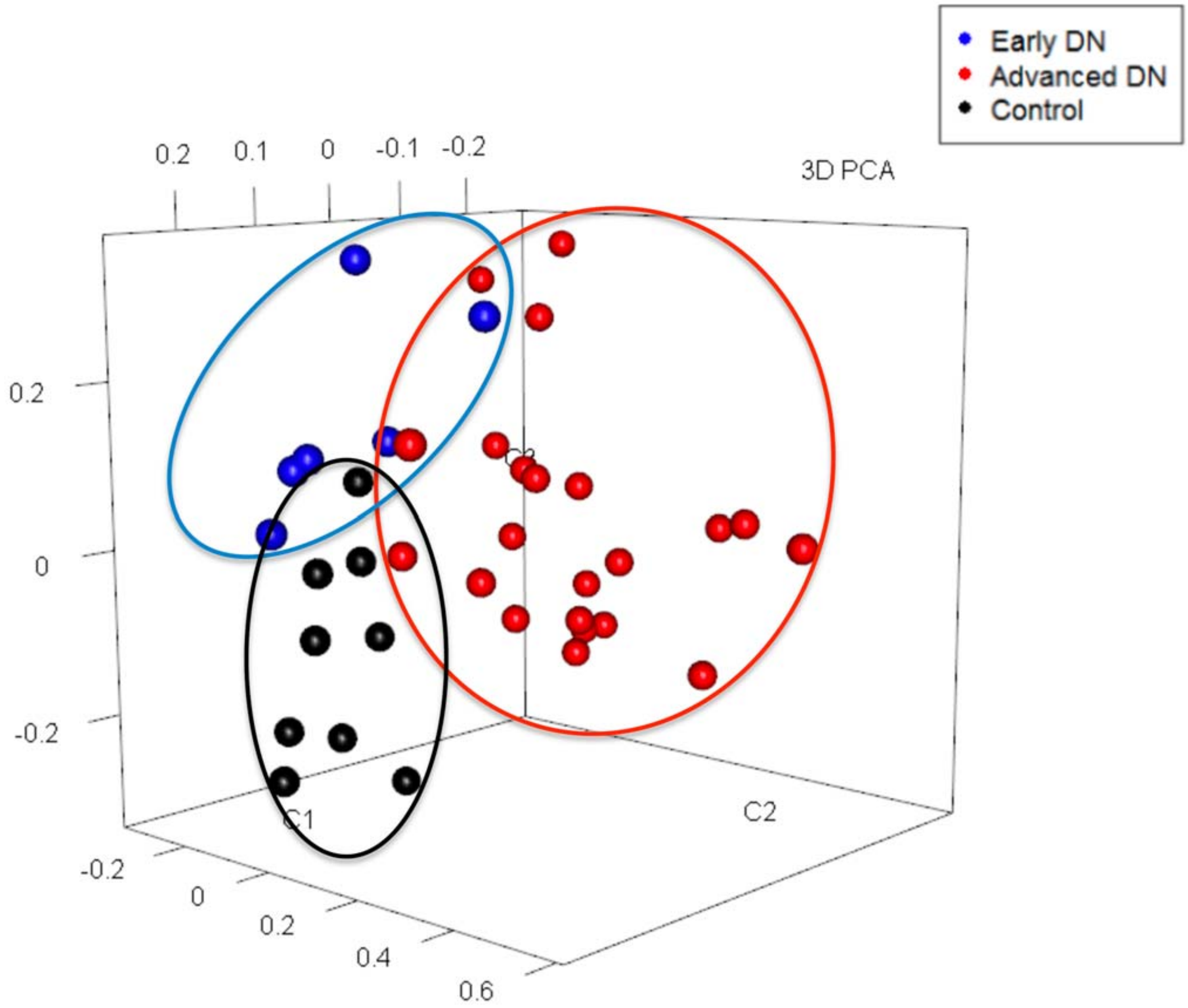
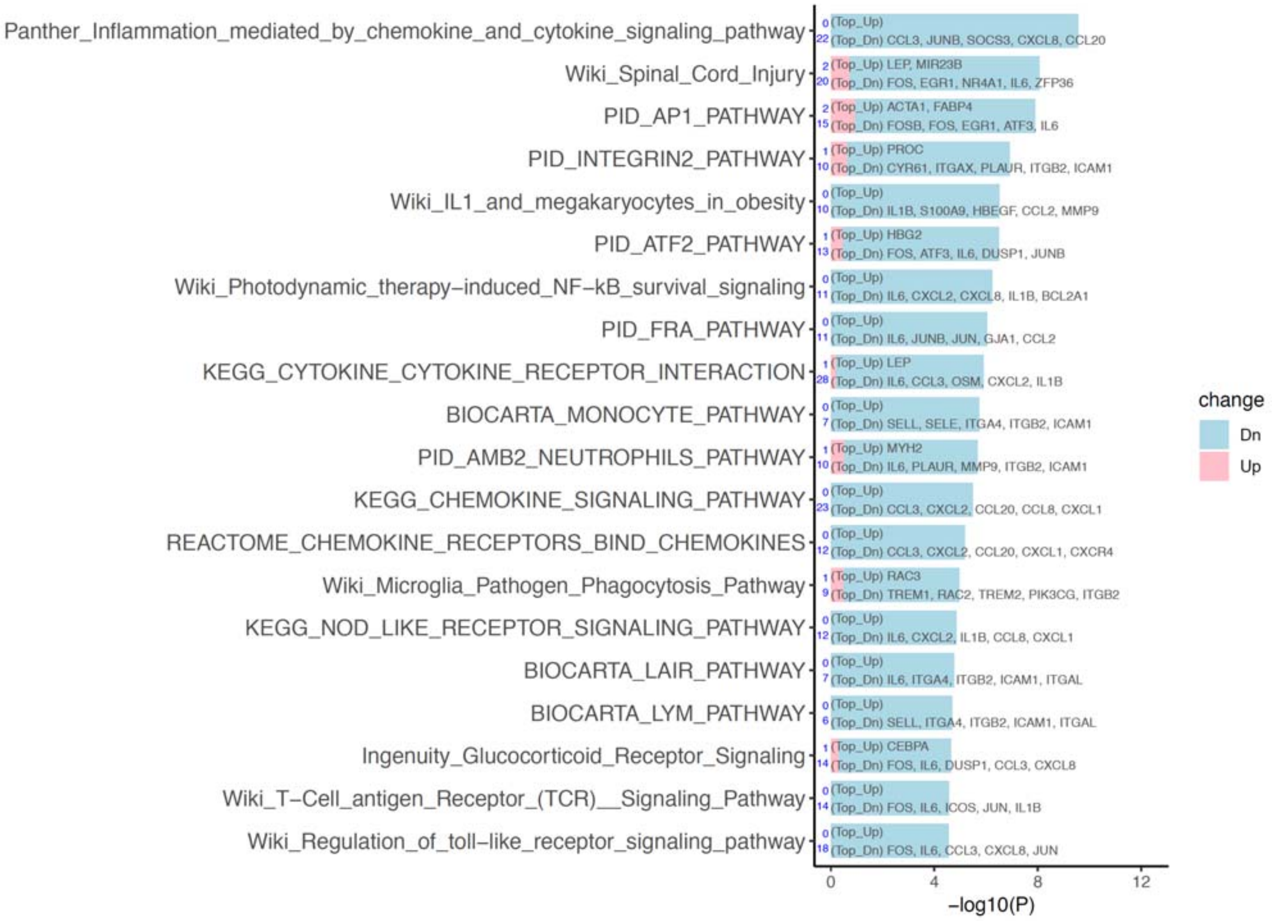
SUPPLEMENTARY DATA

Supplementary Figure 1. Principle component analysis of RNAseq data from control, early DN, and advanced DN samples.



Supplementary Figure 2. Top 20 enriched pathways for all DEGs between early DN vs. control. The number of upregulated and downregulated DEGs are indicated on the left of the bars in blue, and top 5 genes in each pathway are indicated.



Supplementary Figure 3. Top 20 enriched pathways for all DEGs between advanced DN vs. early DN. The number of upregulated and downregulated DEGs are indicated on the left of the bars in blue, and top 5 genes in each pathway are indicated.

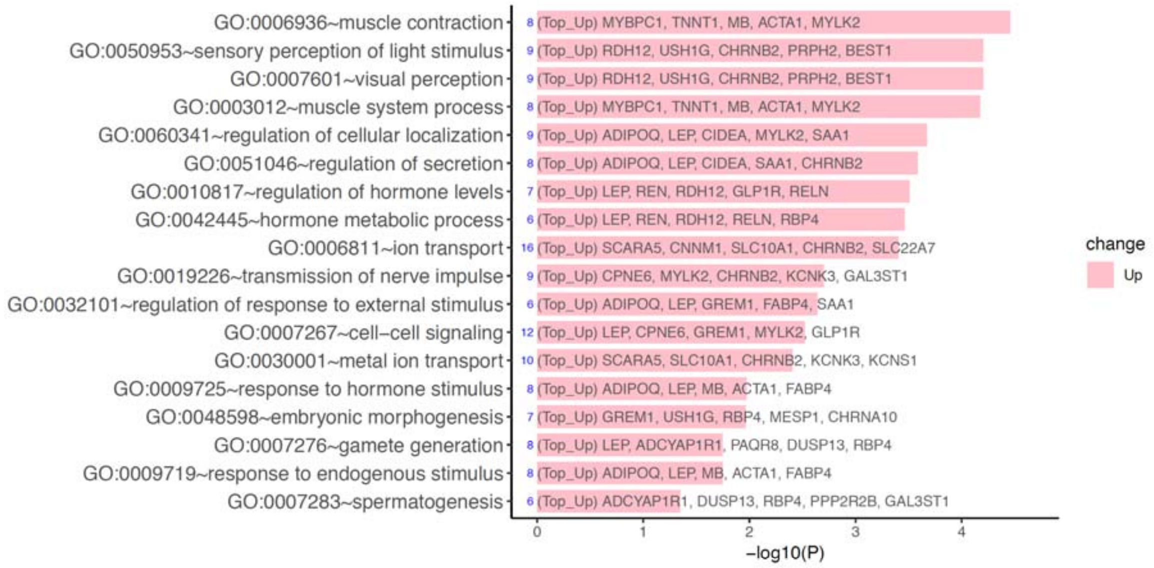
Supplementary Figure 4. Top 20 enriched pathways genes that correlated with eGFR in DN patients. The number of upregulated and downregulated genes are indicated on the left of the bars in blue, and top 5 genes in each pathway are indicated.

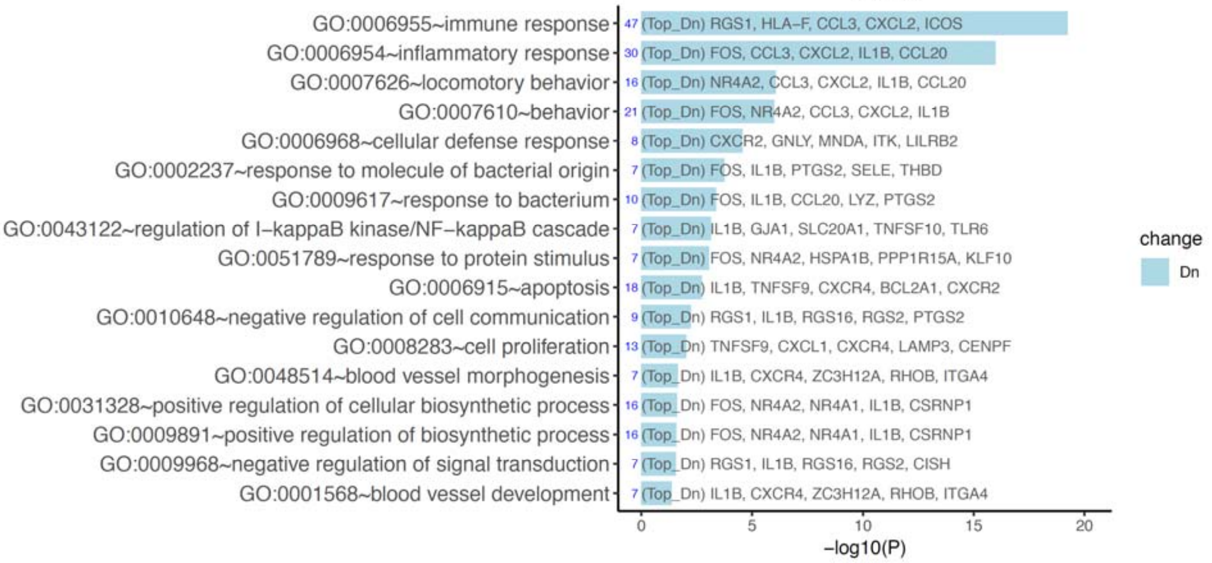
SUPPLEMENTARY DATA

Supplementary Figure 5. GO pathway analysis for differentially expressed genes for early DN vs. control with adjustment of estimated cell populations. The number of upregulated and downregulated genes are indicated on the left of the bars in blue, and top 5 genes in each pathway are indicated.

Early DN vs. control:

Gene expression change	Unadjusted Early DN vs. Ctrl. DEGs (#)	Adjusted Early DN vs. Ctrl. DEGs (#)	# overlapping DEGs	% overlapping DEGs
up	303	310	267	0.8612
down	445	405	383	0.9457



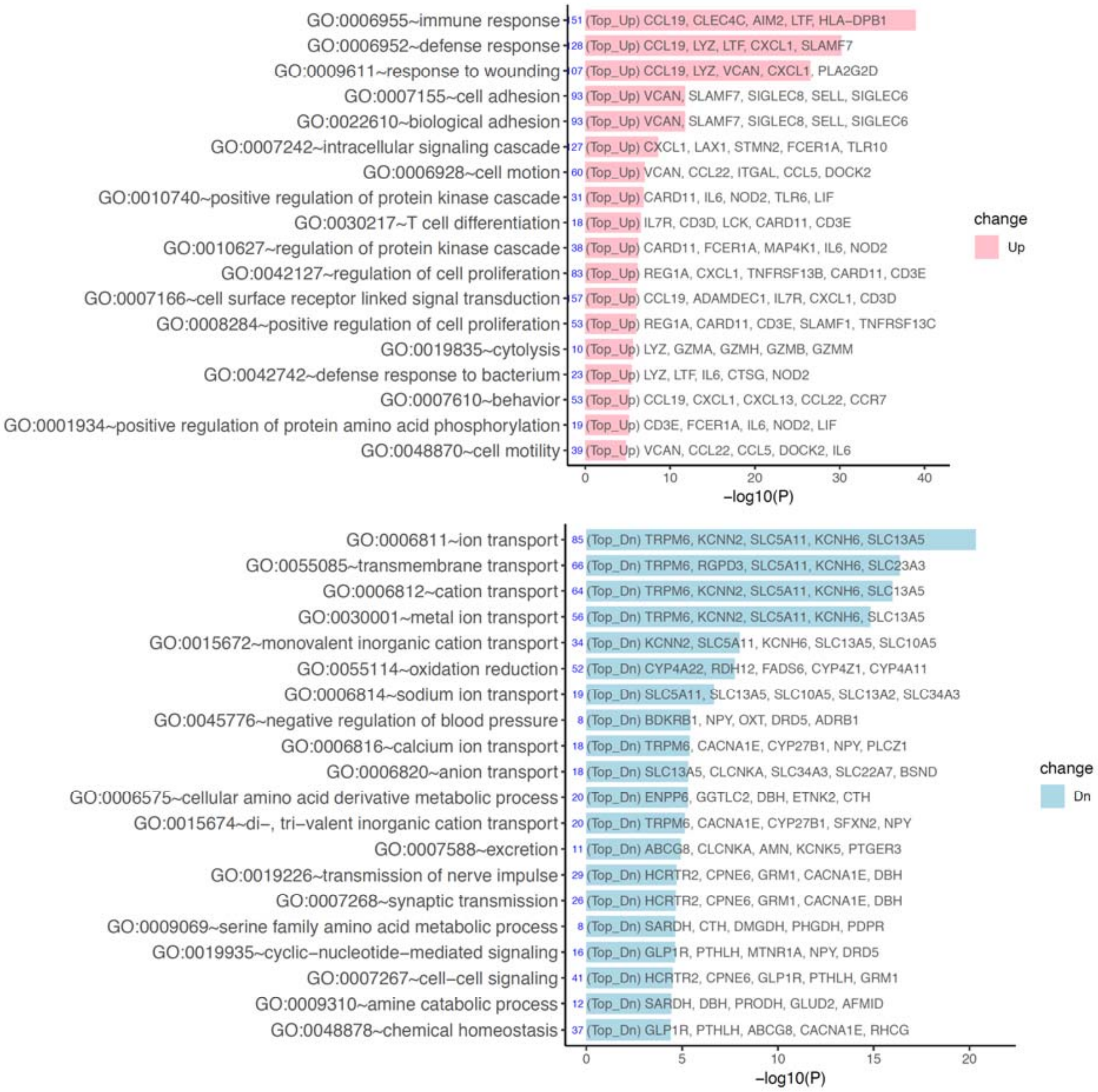


SUPPLEMENTARY DATA

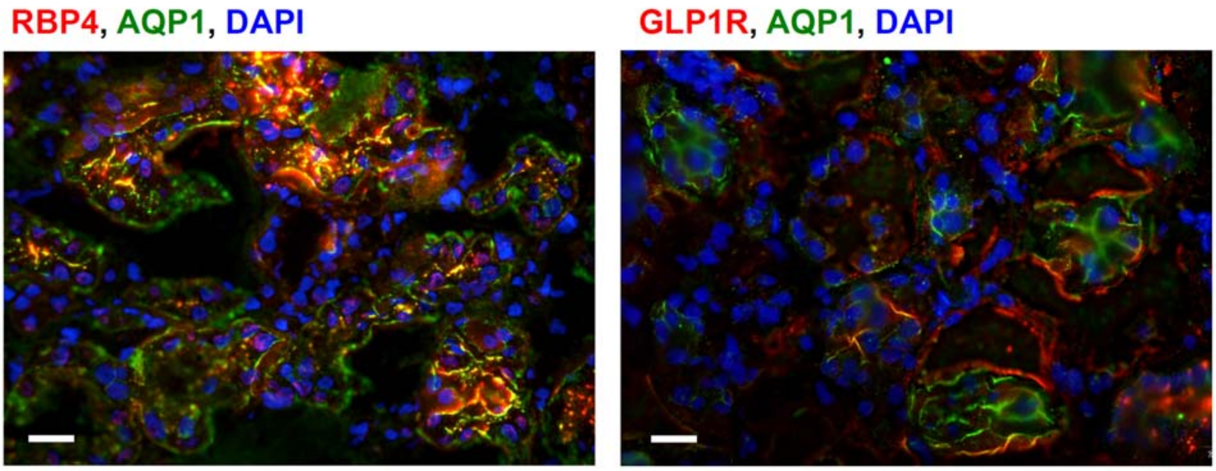
Supplementary Figure 6. GO pathway analysis for differentially expressed genes for advanced vs. early DN with adjustment of estimated cell populations. The number of upregulated and downregulated genes are indicated on the left of the bars in blue, and top 5 genes in each pathway are indicated.

Advanced vs. Early DN:

Gene expression change	Unadjusted Early DN vs. Ctrl. DEGs (#)	Adjusted Early DN vs. Ctrl. DEGs (#)	# overlapping DEGs	% overlapping DEGs
up	1903	1741	1714	0.9845
down	1783	1488	1421	0.9550

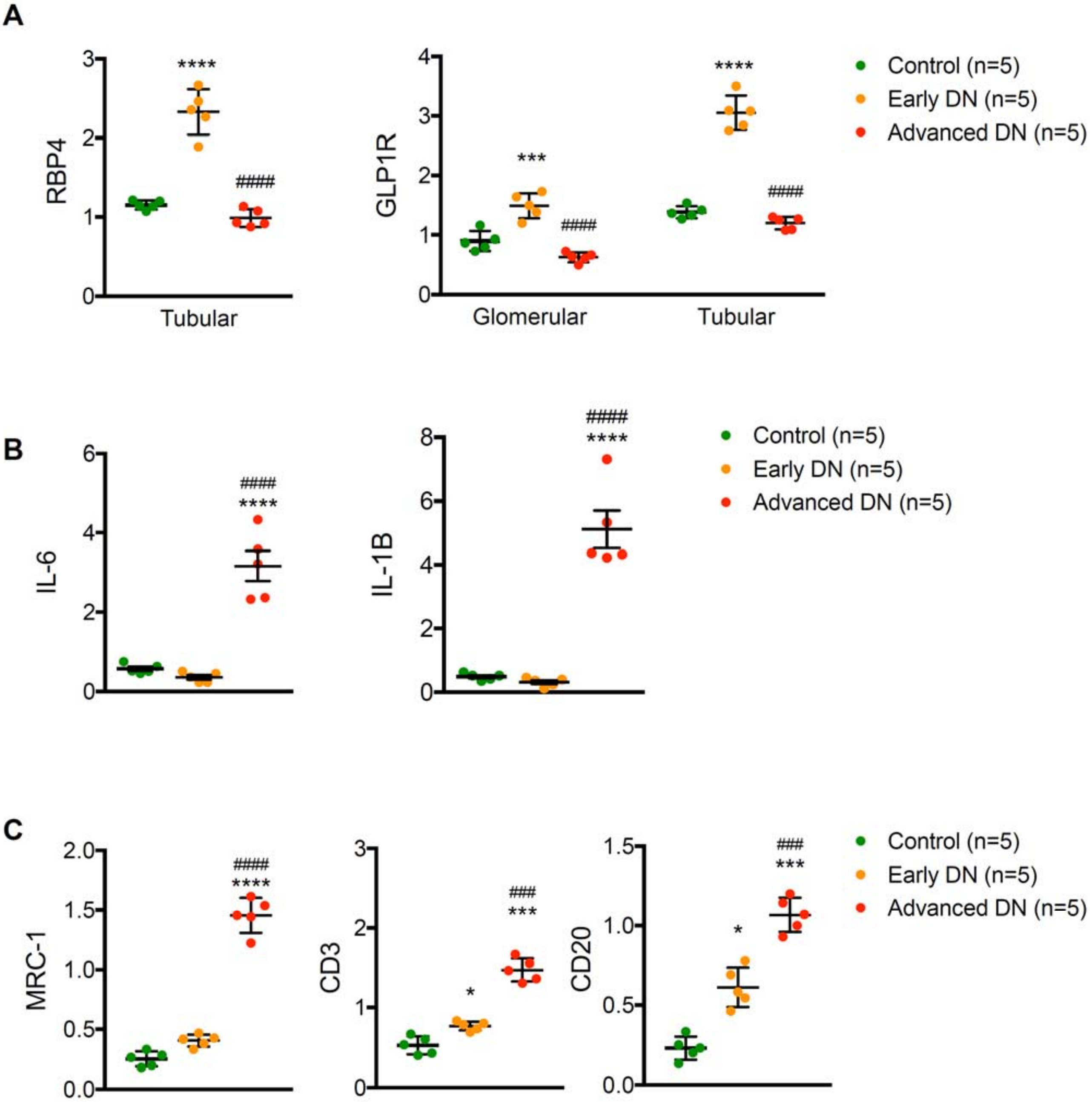


Supplementary Figure 7. Immunofluorescence staining of RBP4 and GLP1R in early DN kidneys. Both RBP4 and GLP1R were expressed in the proximal tubules of early DN patient kidneys, which co-localized with AQP1. Scale bar indicates 50 microns.



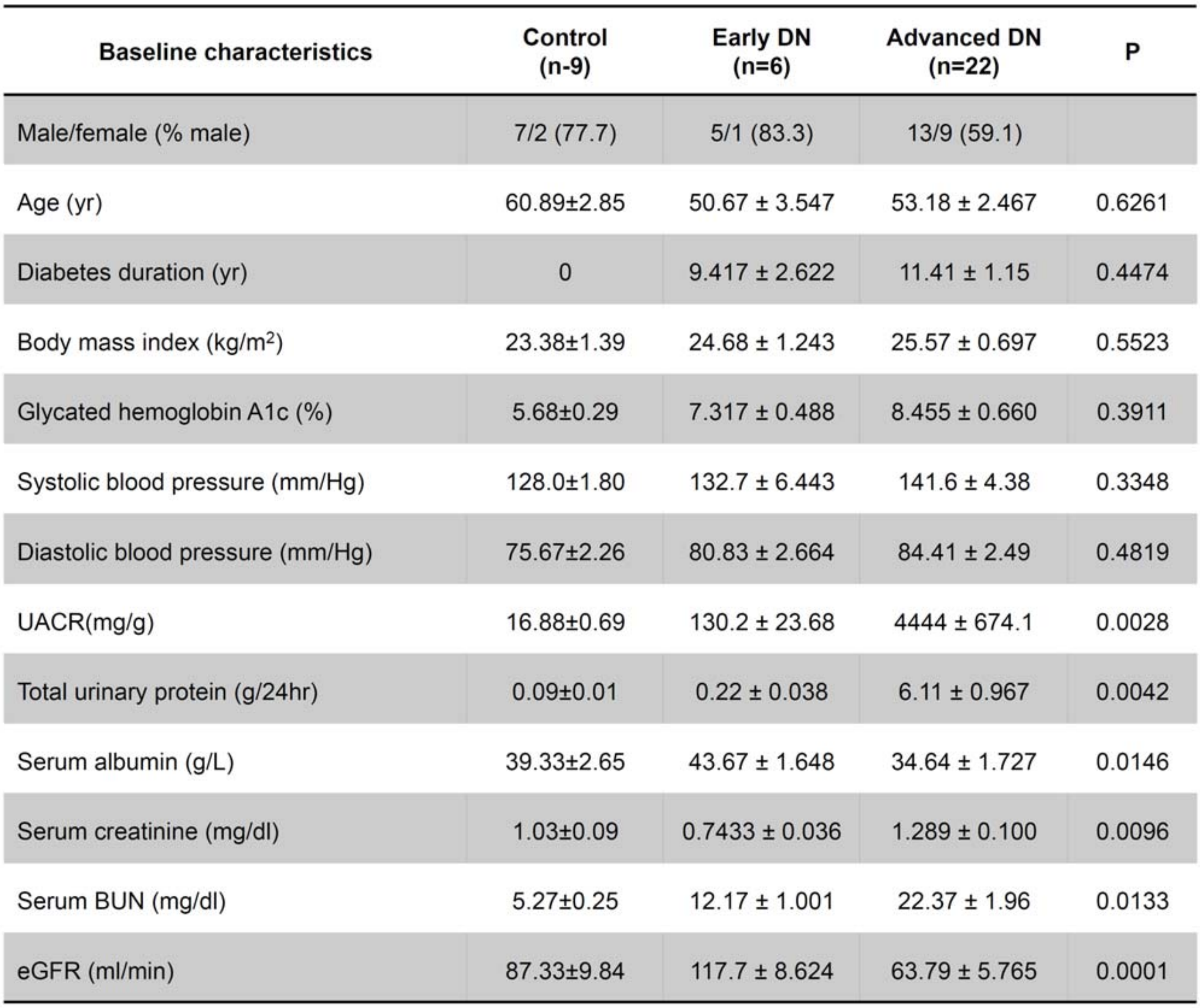
SUPPLEMENTARY DATA

Supplementary Figure 8. Semi-quantification of immunostaining in human kidneys (in Figure 8). Average scores of immunostaining. N=5 per group, *P<0.05, ***P<0.001, ****P<0.0001 vs. control; $^{\#\#\#}$P<0.001 and $^{\#\#\#\#}$P<0.0001 vs. Early DN.



SUPPLEMENTARY DATA

Supplementary Table 1. Demographic and clinical characteristics of kidney biopsy patients

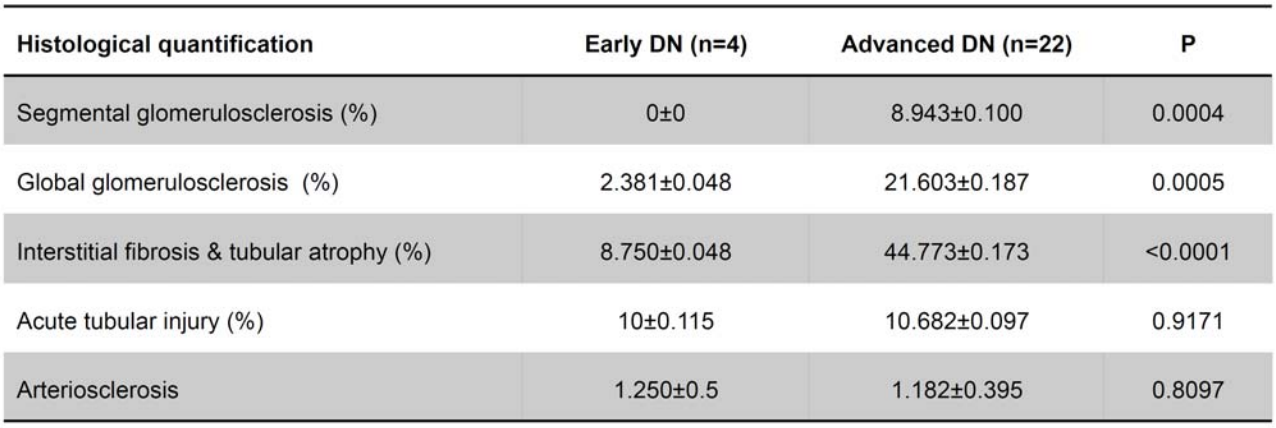


Baseline characteristics	Control (n-9)	Early DN (n=6)	Advanced DN (n=22)	P
Male/female (% male)	7/2 (77.7)	5/1 (83.3)	13/9 (59.1)	
Age (yr)	60.89±2.85	50.67 ± 3.547	53.18 ± 2.467	0.6261
Diabetes duration (yr)	0	9.417 ± 2.622	11.41 ± 1.15	0.4474
Body mass index (kg/m^2)	23.38±1.39	24.68 ± 1.243	25.57 ± 0.697	0.5523
Glycated hemoglobin A1c (%)	5.68±0.29	7.317 ± 0.488	8.455 ± 0.660	0.3911
Systolic blood pressure (mm/Hg)	128.0±1.80	132.7 ± 6.443	141.6 ± 4.38	0.3348
Diastolic blood pressure (mm/Hg)	75.67±2.26	80.83 ± 2.664	84.41 ± 2.49	0.4819
UACR(mg/g)	16.88±0.69	130.2 ± 23.68	4444 ± 674.1	0.0028
Total urinary protein (g/24hr)	0.09±0.01	0.22 ± 0.038	6.11 ± 0.967	0.0042
Serum albumin (g/L)	39.33±2.65	43.67 ± 1.648	34.64 ± 1.727	0.0146
Serum creatinine (mg/dl)	1.03±0.09	0.7433 ± 0.036	1.289 ± 0.100	0.0096
Serum BUN (mg/dl)	5.27±0.25	12.17 ± 1.001	22.37 ± 1.96	0.0133
eGFR (ml/min)	87.33±9.84	117.7 ± 8.624	63.79 ± 5.765	0.0001

Data are presented as n or means ± SD. eGFR was calculated using the Modification of Diet in Renal Disease formula. The two-sided unpaired t-test was used to determine the statistical significance between groups for age, diabetes duration, body mass index, glycated hemoglobin A1c, systolic blood pressure, diastolic blood pressure, Urinary albumin-to-creatinine ratio (UACR), total urinary protein, serum creatinine, serum BUN, and estimated glomerular filtration rate (eGFR).

SUPPLEMENTARY DATA

Supplementary Table 2. Renal pathologic characteristics of patients with early and advanced diabetic nephropathy

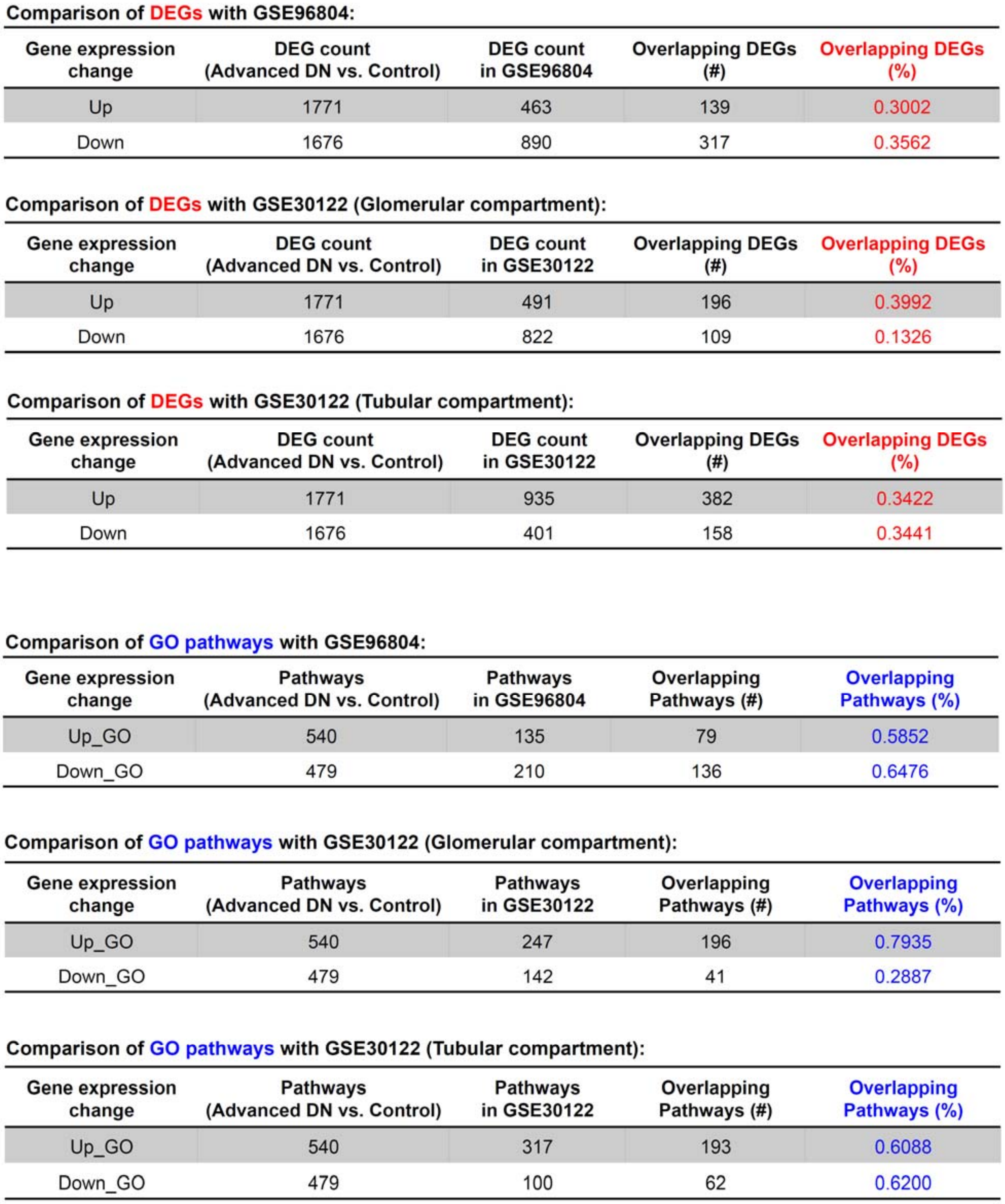


Histological quantification	Early DN (n=4)	Advanced DN (n=22)	P
Segmental glomerulosclerosis (%)	0±0	8.943±0.100	0.0004
Global glomerulosclerosis (%)	2.381±0.048	21.603±0.187	0.0005
Interstitial fibrosis & tubular atrophy (%)	8.750±0.048	44.773±0.173	<0.0001
Acute tubular injury (%)	10±0.115	10.682±0.097	0.9171
Arteriosclerosis	1.250±0.5	1.182±0.395	0.8097

Histological changes were scored according to the consensus classification of DN by the Renal Pathology Society (18). Data are presented as means ± SD for percentages observed for all except arteriosclerosis. Arteriosclerosis: 0 = no intimal thickening; 1 = intimal thickening less than the thickness of media; 2 = Intimal thickening greater than the thickness of media. The t-test was applied for statistical significance.

SUPPLEMENTARY DATA

Supplementary Table 3. Comparison with previously published RNA-seq datasets



Comparison of DEGs with GSE96804:

Gene expression change	DEG count (Advanced DN vs. Control)	DEG count in GSE96804	Overlapping DEGs (#)	Overlapping DEGs (%)
Up	1771	463	139	0.3002
Down	1676	890	317	0.3562

Comparison of DEGs with GSE30122 (Glomerular compartment):

Gene expression change	DEG count (Advanced DN vs. Control)	DEG count in GSE30122	Overlapping DEGs (#)	Overlapping DEGs (%)
Up	1771	491	196	0.3992
Down	1676	822	109	0.1326

Comparison of DEGs with GSE30122 (Tubular compartment):

Gene expression change	DEG count (Advanced DN vs. Control)	DEG count in GSE30122	Overlapping DEGs (#)	Overlapping DEGs (%)
Up	1771	935	382	0.3422
Down	1676	401	158	0.3441

Comparison of GO pathways with GSE96804:

Gene expression change	Pathways (Advanced DN vs. Control)	Pathways in GSE96804	Overlapping Pathways (#)	Overlapping Pathways (%)
Up_GO	540	135	79	0.5852
Down_GO	479	210	136	0.6476

Comparison of GO pathways with GSE30122 (Glomerular compartment):

Gene expression change	Pathways (Advanced DN vs. Control)	Pathways in GSE30122	Overlapping Pathways (#)	Overlapping Pathways (%)
Up_GO	540	247	196	0.7935
Down_GO	479	142	41	0.2887

Comparison of GO pathways with GSE30122 (Tubular compartment):

Gene expression change	Pathways (Advanced DN vs. Control)	Pathways in GSE30122	Overlapping Pathways (#)	Overlapping Pathways (%)
Up_GO	540	317	193	0.6088
Down_GO	479	100	62	0.6200