

**Supplemental Table 1. Gene ontology identities for top 20 groups in unit (hexagon) 1,1 in Fig. 4A and B**

GO biological process complete	Genome GO Term Frequency	Observed GO Term Frequency	Fold Enrichment	Adjusted p-value
small molecule metabolic process (GO:0044281)	1514 of 22262 genes	76 of 403 genes	2.77	2.68E-11
organic acid metabolic process (GO:0006082)	841 of 22262 genes	51 of 403 genes	3.35	1.45E-09
carboxylic acid metabolic process (GO:0019752)	750 of 22262 genes	43 of 403 genes	3.17	4.79E-07
monocarboxylic acid metabolic process (GO:0032787)	427 of 22262 genes	31 of 403 genes	4.01	9.08E-07
oxoacid metabolic process (GO:0043436)	791 of 22262 genes	43 of 403 genes	3	1.38E-06
lipid metabolic process (GO:0006629)	1012 of 22262 genes	47 of 403 genes	2.57	2.59E-05
small molecule biosynthetic process (GO:0044283)	476 of 22262 genes	28 of 403 genes	3.25	2.12E-04
nephron development (GO:0072006)	119 of 22262 genes	14 of 403 genes	6.5	2.19E-04
regulation of developmental process (GO:0050793)	2515 of 22262 genes	81 of 403 genes	1.78	6.82E-04
urate transport (GO:0015747)	12 of 22262 genes	6 of 403 genes	27.62	7.28E-04
fatty acid metabolic process (GO:0006631)	284 of 22262 genes	20 of 403 genes	3.89	7.85E-04
kidney development (GO:0001822)	248 of 22262 genes	18 of 403 genes	4.01	1.44E-03
cellular lipid metabolic process (GO:0044255)	758 of 22262 genes	35 of 403 genes	2.55	1.50E-03
metabolic process (GO:0008152)	8386 of 22262 genes	200 of 403 genes	1.32	1.58E-03
sodium-independent organic anion transport (GO:0043252)	40 of 22262 genes	8 of 403 genes	11.05	1.71E-03
metanephros development (GO:0001656)	78 of 22262 genes	10 of 403 genes	7.08	3.01E-03
anatomical structure morphogenesis (GO:0009653)	2104 of 22262 genes	68 of 403 genes	1.79	3.44E-03
renal system development (GO:0072001)	270 of 22262 genes	18 of 403 genes	3.68	3.53E-03
cardiovascular system development (GO:0072358)	549 of 22262 genes	27 of 403 genes	2.72	3.74E-03
kidney epithelium development (GO:0072073)	127 of 22262 genes	12 of 403 genes	2.3	4.97E-03

**Supplemental Table 2. Top 20 Developmental-associated DEGs down-regulated in glomeruli from *eNOS* *-/- db/db* vs. *eNOS* *+/+ db/+* untreated mice**

Gene ID	Symbol	Description	log <sub>2</sub> (FC)	FDR
320840	<i>Negr1</i>	Neuronal growth regulator 1	-3.25	0.00
57810	<i>Cdon</i>	Cell adhesion molecule-related/down-regulated by oncogenes	-3.14	0.02
16840	<i>Lect1</i>	Leukocyte cell-derived chemotaxin 1	-2.72	0.00
16840	<i>Lect1</i>	Leukocyte cell-derived chemotaxin 1	-2.37	0.00
20319	<i>Sfrp2</i>	Secreted frizzled-related protein 2	-2.29	0.00
20713	<i>Serpini1</i>	Neuroserpin	-2.19	0.00
18004	<i>Nek1</i>	Serine/threonine-protein kinase Nek1	-2.03	0.01
1E+08	<i>Hist1h4m</i>	Histone H4	-1.98	0.03
18127	<i>Nos3</i>	Nitric oxide synthase, endothelial	-1.92	0.04
19242	<i>Ptn</i>	Pleiotrophin	-1.91	0.00
235402	<i>Lingo1</i>	Leucine-rich repeat and immunoglobulin-like domain-containing nogo receptor-interacting protein 1	-1.74	0.00
18816	<i>Serpinf2</i>	Alpha-2-antiplasmin	-1.66	0.02
19242	<i>Ptn</i>	Pleiotrophin	-1.64	0.00
14560	<i>Gdf10</i>	Growth/differentiation factor 10	-1.62	0.00
237759	<i>Col23a1</i>	Collagen alpha-1(XXIII) chain	-1.62	0.00
18596	<i>Pdgfrb</i>	Platelet-derived growth factor receptor beta	-1.57	0.00
244058	<i>Rgma</i>	Repulsive guidance molecule A	-1.54	0.01
20349	<i>Sema3e</i>	Semaphorin-3E	-1.51	0.03
50791	<i>Magi2</i>	Membrane-associated guanylate kinase, WW and PDZ domain-containing protein 2	-1.47	0.02
73181	<i>Nfatc4</i>	Nuclear factor of activated T-cells, cytoplasmic 4	-1.47	0.00

log<sub>2</sub>(FC): log<sub>2</sub> fold-change, FDR: false-discovery rate

**Supplemental Table 3. Gene ontology identities for top 20 groups in unit (hexagon) 7,7 in Fig. 4A and B**

GO biological process complete	Genome GO Term Frequency	Observed GO Term Frequency	Fold Enrichment	Adjusted p-value
immune system process (GO:0002376)	2057 of 22262 genes	121 of 268 genes	4.89	6.02E-48
defense response (GO:0006952)	1284 of 22262 genes	97 of 268 genes	6.28	2.50E-45
regulation of immune system process (GO:0002682)	1339 of 22262 genes	91 of 268 genes	5.65	1.41E-38
inflammatory response (GO:0006954)	430 of 22262 genes	59 of 268 genes	11.4	1.90E-38
positive regulation of immune system process (GO:0002684)	927 of 22262 genes	74 of 268 genes	6.63	1.18E-34
leukocyte migration (GO:0050900)	190 of 22262 genes	40 of 268 genes	17.49	1.90E-31
immune response (GO:0006955)	1211 of 22262 genes	78 of 268 genes	5.35	6.99E-31
response to stress (GO:0006950)	2984 of 22262 genes	118 of 268 genes	3.28	1.30E-30
leukocyte chemotaxis (GO:0030595)	116 of 22262 genes	31 of 268 genes	22.2	1.06E-26
response to external stimulus (GO:0009605)	1785 of 22262 genes	87 of 268 genes	4.05	1.11E-26
regulation of response to external stimulus (GO:0032101)	704 of 22262 genes	57 of 268 genes	6.73	3.20E-26
positive regulation of response to stimulus (GO:0048584)	2060 of 22262 genes	92 of 268 genes	3.71	5.93E-26
regulation of response to stimulus (GO:0048583)	3589 of 22262 genes	119 of 268 genes	2.75	3.52E-24
response to chemical (GO:0042221)	3259 of 22262 genes	112 of 268 genes	2.85	1.51E-23
cell chemotaxis (GO:0060326)	172 of 22262 genes	32 of 268 genes	15.45	1.60E-23
response to stimulus (GO:0050896)	7941 of 22262 genes	182 of 268 genes	1.9	2.01E-23
chemotaxis (GO:0006935)	429 of 22262 genes	43 of 268 genes	8.33	1.46E-22
taxis (GO:0042330)	431 of 22262 genes	43 of 268 genes	8.29	1.63E-22
cellular response to chemical stimulus (GO:0070887)	2153 of 22262 genes	88 of 268 genes	3.4	4.04E-22
positive regulation of response to external stimulus (GO:0032103)	283 of 22262 genes	36 of 268 genes	10.57	9.38E-22

**Supplemental Table 4. Top 20 Inflammatory DEGs enriched in glomeruli from *eNOS* <sup>-/-</sup> *db/db* vs. *eNOS* <sup>+/+</sup> *db/+* untreated mice**

Gene ID	Symbol	Description	log <sub>2</sub> (FC)	FDR
16819	<i>Lcn2</i>	lipocalin 2	6.47	0.00
14825	<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 1	6.03	0.00
20568	<i>Slpi</i>	secretory leukocyte peptidase inhibitor	5.44	0.00
14293	<i>Frp1</i>	formyl peptide receptor 1	5.12	0.00
50778	<i>Rgs1</i>	regulator of G-protein signaling 1	4.87	0.02
20296	<i>Ccl2</i>	chemokine (C-C motif) ligand 2	4.71	0.00
56619	<i>Clec4e</i>	C-type lectin domain family 4, member e	4.56	0.00
20303	<i>Ccl4</i>	chemokine (C-C motif) ligand 4	4.47	0.00
12273	<i>C5ar1</i>	complement component 5a receptor 1	4.27	0.00
17381	<i>Mmp12</i>	matrix metalloproteinase 12	4.26	0.00
20202	<i>S100a9</i>	S100 calcium binding protein A9 (calgranulin B)	4.25	0.00
20201	<i>S100a8</i>	S100 calcium binding protein A8 (calgranulin A)	4.22	0.00
20288	<i>Msr1</i>	macrophage scavenger receptor 1	4.14	0.01
14289	<i>Fpr2</i>	formyl peptide receptor 2	4.07	0.00
12768	<i>Ccr1</i>	chemokine (C-C motif) receptor 1	3.6	0.00
12266	<i>C3</i>	complement component 3	3.5	0.00
216799	<i>Nlrp3</i>	NLR family, pyrin domain containing 3	3.49	0.04
56744	<i>Pf4</i>	platelet factor 4	3.44	0.00
17395	<i>Mmp9</i>	matrix metalloproteinase 9	3.36	0.00
21926	<i>Tnf</i>	tumor necrosis factor	3.24	0.04

log<sub>2</sub>(FC): log<sub>2</sub> fold-change, FDR: false-discovery rate

**Supplemental Table 5. Significant Biological Pathways Represented in SOM cluster identified in Fig. 4D.**

Ingenuity Canonical Pathways	-log(p-value)	Ratio
Granulocyte Adhesion and Diapedesis	3.35E+01	3.54E-01
Agranulocyte Adhesion and Diapedesis	2.61E+01	3.01E-01
Leukocyte Extravasation Signaling	1.92E+01	2.46E-01
IL-10 Signaling	1.58E+01	3.91E-01
<b>Hepatic Fibrosis / Hepatic Stellate Cell Activation</b>	<b>1.55E+01</b>	<b>2.35E-01</b>
Neuroinflammation Signaling Pathway	1.52E+01	1.86E-01
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	1.51E+01	1.85E-01
Acute Phase Response Signaling	1.49E+01	2.41E-01
LXR/RXR Activation	1.38E+01	2.73E-01
Atherosclerosis Signaling	1.31E+01	2.60E-01
Dendritic Cell Maturation	1.28E+01	2.11E-01
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	1.09E+01	1.96E-01
Graft-versus-Host Disease Signaling	9.36E+00	3.54E-01
TREM1 Signaling	9.24E+00	2.80E-01
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	9.18E+00	2.56E-01
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	9.00E+00	1.67E-01
Type I Diabetes Mellitus Signaling	8.68E+00	2.25E-01
IL-6 Signaling	8.64E+00	2.11E-01
Osteoarthritis Pathway	8.53E+00	1.70E-01
Phagosome Formation	8.41E+00	2.06E-01
Fc $\gamma$ 3 Receptor-mediated Phagocytosis in Macrophages and Monocytes	8.13E+00	2.37E-01
VDR/RXR Activation	8.10E+00	2.56E-01
Th1 and Th2 Activation Pathway	7.86E+00	1.73E-01
Axonal Guidance Signaling	7.52E+00	1.24E-01
Role of Hypercytokinemia/hyperchemokinememia in the Pathogenesis of Influenza	7.28E+00	3.26E-01
IL-8 Signaling	7.19E+00	1.62E-01
Hepatic Cholestasis	7.07E+00	1.75E-01
Toll-like Receptor Signaling	6.78E+00	2.37E-01
Colorectal Cancer Metastasis Signaling	6.73E+00	1.45E-01
IL-17A Signaling in Fibroblasts	6.61E+00	3.43E-01
Communication between Innate and Adaptive Immune Cells	6.56E+00	2.11E-01
Tec Kinase Signaling	6.50E+00	1.65E-01
LPS/IL-1 Mediated Inhibition of RXR Function	6.46E+00	1.49E-01
TNFR2 Signaling	6.45E+00	3.67E-01

T Helper Cell Differentiation	6.33E+00	2.33E-01
Th1 Pathway	6.29E+00	1.78E-01
Role of NFAT in Regulation of the Immune Response	6.20E+00	1.56E-01
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	6.17E+00	1.75E-01
iNOS Signaling	6.13E+00	2.89E-01
Th2 Pathway	5.98E+00	1.67E-01
NF- $\hat{\text{I}}^{\text{B}}$ Signaling	5.94E+00	1.55E-01
Natural Killer Cell Signaling	5.93E+00	1.80E-01
PPAR Signaling	5.91E+00	2.00E-01
B Cell Receptor Signaling	5.91E+00	1.51E-01
CD28 Signaling in T Helper Cells	5.89E+00	1.74E-01
G-Protein Coupled Receptor Signaling	5.56E+00	1.30E-01
PKC $\hat{\text{I}}$ , Signaling in T Lymphocytes	5.50E+00	1.57E-01
p38 MAPK Signaling	5.47E+00	1.75E-01
Complement System	5.41E+00	2.97E-01
Death Receptor Signaling	5.41E+00	1.94E-01
Renin-Angiotensin Signaling	5.35E+00	1.72E-01
Induction of Apoptosis by HIV1	5.24E+00	2.30E-01
Sertoli Cell-Sertoli Cell Junction Signaling	5.09E+00	1.46E-01
Crosstalk between Dendritic Cells and Natural Killer Cells	5.07E+00	1.91E-01
Glucocorticoid Receptor Signaling	5.06E+00	1.18E-01
Apoptosis Signaling	5.00E+00	1.89E-01
PI3K Signaling in B Lymphocytes	4.91E+00	1.62E-01
Adrenomedullin signaling pathway	4.87E+00	1.39E-01
TNFR1 Signaling	4.79E+00	2.40E-01
iCOS-iCOSL Signaling in T Helper Cells	4.75E+00	1.63E-01
Iron homeostasis signaling pathway	4.75E+00	1.58E-01
GP6 Signaling Pathway	4.70E+00	1.57E-01
IL-12 Signaling and Production in Macrophages	4.62E+00	1.51E-01
Role of IL-17A in Arthritis	4.59E+00	2.03E-01
Airway Pathology in Chronic Obstructive Pulmonary Disease	4.56E+00	6.25E-01
Molecular Mechanisms of Cancer	4.55E+00	1.09E-01
cAMP-mediated signaling	4.43E+00	1.27E-01
Xenobiotic Metabolism Signaling	4.34E+00	1.17E-01
Cholecystokinin/Gastrin-mediated Signaling	4.32E+00	1.68E-01
Pathogenesis of Multiple Sclerosis	4.23E+00	5.56E-01
Role of Tissue Factor in Cancer	4.18E+00	1.53E-01
Inflammasome pathway	4.14E+00	3.50E-01
Protein Kinase A Signaling	4.05E+00	1.05E-01
NF- $\hat{\text{I}}^{\text{B}}$ Activation by Viruses	4.01E+00	1.72E-01
Integrin Signaling	3.94E+00	1.23E-01

Glioma Invasiveness Signaling	3.89E+00	1.86E-01
ILK Signaling	3.89E+00	1.27E-01
B Cell Development	3.88E+00	2.50E-01
Aryl Hydrocarbon Receptor Signaling	3.88E+00	1.42E-01
HMGB1 Signaling	3.76E+00	1.43E-01
IL-1 Signaling	3.73E+00	1.63E-01
Role of IL-17F in Allergic Inflammatory Airway Diseases	3.70E+00	2.17E-01
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	3.70E+00	3.04E-01
Antigen Presentation Pathway	3.68E+00	2.37E-01
Inhibition of Matrix Metalloproteases	3.59E+00	2.31E-01
FXR/RXR Activation	3.59E+00	1.43E-01
Calcium-induced T Lymphocyte Apoptosis	3.54E+00	1.82E-01
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	3.48E+00	3.33E-01
STAT3 Pathway	3.47E+00	1.55E-01
GÎ±i Signaling	3.38E+00	1.42E-01
Gustation Pathway	3.37E+00	1.30E-01
CD40 Signaling	3.35E+00	1.65E-01
IL-4 Signaling	3.35E+00	1.57E-01
Endothelin-1 Signaling	3.33E+00	1.21E-01
Inhibition of Angiogenesis by TSP1	3.31E+00	2.35E-01
Role of IL-17A in Psoriasis	3.30E+00	3.85E-01
Macropinocytosis Signaling	3.24E+00	1.60E-01
Chemokine Signaling	3.24E+00	1.69E-01
Coagulation System	3.22E+00	2.29E-01
TWEAK Signaling	3.22E+00	2.29E-01
GÎ±12/13 Signaling	3.22E+00	1.33E-01
PI3K/AKT Signaling	3.18E+00	1.36E-01
MSP-RON Signaling Pathway	3.18E+00	1.67E-01
HGF Signaling	3.13E+00	1.39E-01
Germ Cell-Sertoli Cell Junction Signaling	3.11E+00	1.21E-01
CCR5 Signaling in Macrophages	3.06E+00	1.47E-01
Prostanoid Biosynthesis	2.99E+00	4.44E-01
Antioxidant Action of Vitamin C	2.96E+00	1.39E-01
PEDF Signaling	2.94E+00	1.49E-01
Eicosanoid Signaling	2.91E+00	1.64E-01
Phospholipase C Signaling	2.90E+00	1.07E-01
Autoimmune Thyroid Disease Signaling	2.89E+00	1.88E-01
fMLP Signaling in Neutrophils	2.82E+00	1.30E-01
Relaxin Signaling	2.82E+00	1.20E-01
Thyroid Cancer Signaling	2.81E+00	2.00E-01

Nur77 Signaling in T Lymphocytes	2.80E+00	1.69E-01
eNOS Signaling	2.76E+00	1.16E-01
GÎ±q Signaling	2.73E+00	1.18E-01
Caveolar-mediated Endocytosis Signaling	2.70E+00	1.55E-01
ERK/MAPK Signaling	2.67E+00	1.10E-01
Acute Myeloid Leukemia Signaling	2.67E+00	1.40E-01
IL-17A Signaling in Gastric Cells	2.65E+00	2.40E-01
Role of JAK family kinases in IL-6-type Cytokine Signaling	2.65E+00	2.40E-01
GNRH Signaling	2.60E+00	1.15E-01
Opioid Signaling Pathway	2.55E+00	1.03E-01
Fc Epsilon RI Signaling	2.54E+00	1.26E-01
Growth Hormone Signaling	2.54E+00	1.41E-01
IL-17 Signaling	2.54E+00	1.41E-01
Tight Junction Signaling	2.54E+00	1.14E-01
Breast Cancer Regulation by Stathmin1	2.53E+00	1.07E-01
Pancreatic Adenocarcinoma Signaling	2.51E+00	1.25E-01
p70S6K Signaling	2.50E+00	1.21E-01
LPS-stimulated MAPK Signaling	2.46E+00	1.38E-01
Virus Entry via Endocytic Pathways	2.45E+00	1.27E-01
CDK5 Signaling	2.43E+00	1.31E-01
p53 Signaling	2.41E+00	1.26E-01
Cell Cycle Control of Chromosomal Replication	2.41E+00	1.61E-01
Phagosome Maturation	2.38E+00	1.15E-01
Cell Cycle Regulation by BTG Family Proteins	2.38E+00	1.89E-01
IL-17A Signaling in Airway Cells	2.37E+00	1.41E-01
Nitric Oxide Signaling in the Cardiovascular System	2.34E+00	1.24E-01
Paxillin Signaling	2.34E+00	1.24E-01
Systemic Lupus Erythematosus Signaling	2.31E+00	1.01E-01
RhoGDI Signaling	2.27E+00	1.07E-01
Neuropathic Pain Signaling In Dorsal Horn Neurons	2.27E+00	1.22E-01
Reelin Signaling in Neurons	2.26E+00	1.30E-01
Erythropoietin Signaling	2.24E+00	1.36E-01
Cardiac Î²-adrenergic Signaling	2.22E+00	1.13E-01
Type II Diabetes Mellitus Signaling	2.20E+00	1.10E-01
IGF-1 Signaling	2.17E+00	1.23E-01
JAK/Stat Signaling	2.16E+00	1.33E-01
Prolactin Signaling	2.16E+00	1.33E-01
Clathrin-mediated Endocytosis Signaling	2.16E+00	1.01E-01
14-3-3-mediated Signaling	2.15E+00	1.15E-01
PTEN Signaling	2.14E+00	1.18E-01
Role of PKR in Interferon Induction and Antiviral Response	2.13E+00	1.71E-01



GM-CSF Signaling	2.11E+00	1.37E-01
Small Cell Lung Cancer Signaling	2.09E+00	1.29E-01
Superpathway of Citrulline Metabolism	2.08E+00	2.67E-01
Intrinsic Prothrombin Activation Pathway	2.07E+00	1.67E-01
Adipogenesis pathway	2.06E+00	1.12E-01
P2Y Purigenic Receptor Signaling Pathway	2.06E+00	1.12E-01
CD27 Signaling in Lymphocytes	2.03E+00	1.51E-01
MIF Regulation of Innate Immunity	2.01E+00	1.63E-01
RhoA Signaling	1.99E+00	1.13E-01
IL-15 Signaling	1.99E+00	1.32E-01
PXR/RXR Activation	1.98E+00	1.38E-01
Role of Cytokines in Mediating Communication between Immune Cells	1.98E+00	1.48E-01
Extrinsic Prothrombin Activation Pathway	1.97E+00	2.50E-01
Oncostatin M Signaling	1.96E+00	1.76E-01
Sphingosine-1-phosphate Signaling	1.96E+00	1.12E-01
Angiopoietin Signaling	1.92E+00	1.28E-01
Glioma Signaling	1.92E+00	1.14E-01
Corticotropin Releasing Hormone Signaling	1.92E+00	1.08E-01
RANK Signaling in Osteoclasts	1.91E+00	1.18E-01
Lymphotoxin $\hat{I}^2$ Receptor Signaling	1.90E+00	1.34E-01
Cdc42 Signaling	1.87E+00	1.02E-01
Agrin Interactions at Neuromuscular Junction	1.82E+00	1.30E-01
Remodeling of Epithelial Adherens Junctions	1.82E+00	1.30E-01
Ceramide Signaling	1.81E+00	1.18E-01
Ovarian Cancer Signaling	1.79E+00	1.04E-01
Neuroprotective Role of THOP1 in Alzheimer's Disease	1.77E+00	1.09E-01
Arsenate Detoxification I (Glutaredoxin)	1.75E+00	5.00E-01
$\hat{I}^{\pm}$ -tocopherol Degradation	1.75E+00	5.00E-01
Actin Cytoskeleton Signaling	1.74E+00	9.25E-02
Role of JAK1 and JAK3 in $\hat{I}^3c$ Cytokine Signaling	1.74E+00	1.27E-01
Primary Immunodeficiency Signaling	1.71E+00	1.43E-01
T Cell Receptor Signaling	1.70E+00	1.10E-01
GADD45 Signaling	1.70E+00	2.11E-01
Purine Nucleotides Degradation II (Aerobic)	1.70E+00	2.11E-01
April Mediated Signaling	1.68E+00	1.54E-01
Allograft Rejection Signaling	1.67E+00	1.18E-01
Thrombin Signaling	1.65E+00	9.31E-02
TR/RXR Activation	1.65E+00	1.12E-01
Amyotrophic Lateral Sclerosis Signaling	1.64E+00	1.08E-01
Amyloid Processing	1.63E+00	1.37E-01
Role of NFAT in Cardiac Hypertrophy	1.63E+00	9.13E-02

Activation of IRF by Cytosolic Pattern Recognition Receptors	1.61E+00	1.27E-01
NRF2-mediated Oxidative Stress Response	1.60E+00	9.33E-02
Cardiac Hypertrophy Signaling	1.59E+00	8.94E-02
B Cell Activating Factor Signaling	1.58E+00	1.46E-01
Bladder Cancer Signaling	1.58E+00	1.14E-01
HER-2 Signaling in Breast Cancer	1.58E+00	1.14E-01
IL-2 Signaling	1.57E+00	1.25E-01
GDNF Family Ligand-Receptor Interactions	1.57E+00	1.18E-01
Guanosine Nucleotides Degradation III	1.57E+00	2.50E-01
Citrulline-Nitric Oxide Cycle	1.55E+00	4.00E-01
Folate Polyglutamylation	1.55E+00	4.00E-01
Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate	1.55E+00	4.00E-01
Signaling by Rho Family GTPases	1.54E+00	8.73E-02
tRNA Splicing	1.53E+00	1.43E-01
VEGF Signaling	1.51E+00	1.07E-01
ERK5 Signaling	1.50E+00	1.21E-01
Thyroid Hormone Metabolism II (via Conjugation and/or Degradation)	1.49E+00	1.40E-01
OX40 Signaling Pathway	1.49E+00	1.10E-01
4-1BB Signaling in T Lymphocytes	1.49E+00	1.56E-01
G Protein Signaling Mediated by Tubby	1.49E+00	1.56E-01
Polyamine Regulation in Colon Cancer	1.48E+00	1.82E-01
Fc $\gamma$ RIIB Signaling in B Lymphocytes	1.47E+00	1.14E-01
HIF1 $\alpha$ Signaling	1.46E+00	1.02E-01
Wnt/ $\beta$ -catenin Signaling	1.46E+00	9.30E-02
Mouse Embryonic Stem Cell Pluripotency	1.43E+00	1.04E-01
UVA-Induced MAPK Signaling	1.43E+00	1.04E-01
Epithelial Adherens Junction Signaling	1.43E+00	9.59E-02
Ephrin Receptor Signaling	1.41E+00	9.14E-02
IL-9 Signaling	1.40E+00	1.33E-01
Glioblastoma Multiforme Signaling	1.39E+00	9.26E-02
Superpathway of Inositol Phosphate Compounds	1.34E+00	8.47E-02
MIF-mediated Glucocorticoid Regulation	1.34E+00	1.43E-01
Salvage Pathways of Pyrimidine Ribonucleotides	1.33E+00	1.03E-01
CXCR4 Signaling	1.33E+00	9.09E-02
Melatonin Signaling	1.31E+00	1.11E-01
Role of MAPK Signaling in the Pathogenesis of Influenza	1.31E+00	1.11E-01
PPAR $\alpha$ /RXR $\alpha$ Activation	1.31E+00	8.89E-02
Gap Junction Signaling	1.30E+00	8.72E-02
Interferon Signaling	1.30E+00	1.39E-01
Melanocyte Development and Pigmentation Signaling	1.30E+00	1.02E-01

**Supplemental Table 6. Inflammatory DEGs enriched in DRG from *db/db eNOS* *-/-* treated vs. untreated mice**

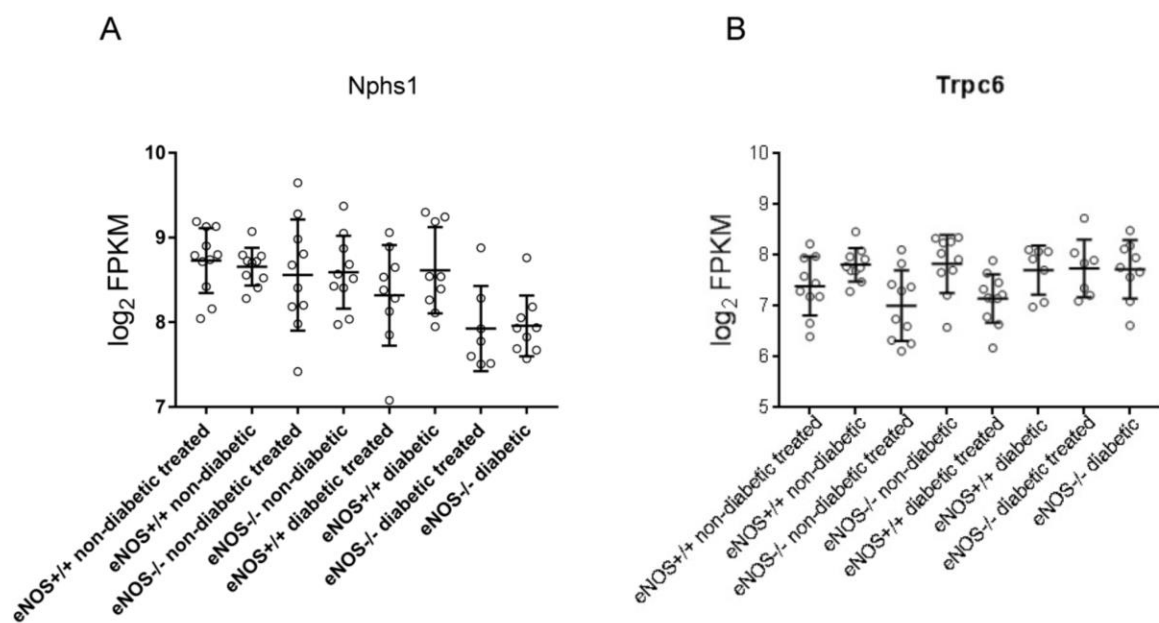
GeneID	Symbol	Description	FC	FDR
12628	Cfh	complement component factor h	2.16	0.01
12655	Chi3l3	chitinase-like 3	3.63	0.03
14268	Fn1	fibronectin 1	1.96	0.01
16010	Igfbp4	insulin-like growth factor binding protein 4	1.38	0.01
16414	Itgb2	integrin beta 2	6.99	0.04
17084	Ly86	lymphocyte antigen 86	1.54	0.01

FC: fold-change, FDR: false-discovery rate

**Supplemental Table 7. Top 20 significantly enriched canonical pathways of DEGs in DRG from *db/db* eNOS *-/-* treated vs. untreated mice using IPA\*.**

Ingenuity Canonical Pathways	P-value	Genes
Hepatic Fibrosis / Hepatic Stellate Cell Activation	6.46E-10	MYH4,COL1A1,IGFBP4,COL5A2,FN1,COL6A1,COL6A3,IGFBP5,STAT1,MMP9,COL3A1
ILK Signaling	2.04E-05	MYH4,ITGB2,FN1,FLNA,Actn3,MMP9,ACTA1
Atherosclerosis Signaling	2.09E-05	COL1A1,ITGB2,LYZ,S100A8,MMP9,COL3A1
Granulocyte Adhesion and Diapedesis	2.14E-04	MYH4,ITGB2,FN1,MMP8,MMP9,ACTA1
Leukocyte Extravasation Signaling	2.75E-04	ITGB2,MMP8,CYBB,Actn3,MMP9,ACTA1
Actin Cytoskeleton Signaling	4.37E-04	MYH4,FN1,FLNA,MYLPP,Actn3,ACTA1
Airway Pathology in Chronic Obstructive Pulmonary Disease	5.50E-04	MMP8,MMP9
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	1.35E-03	LYZ,HOXA10,CYBB,S100A8,STAT1
Role of IL-17A in Psoriasis	1.51E-03	S100A9,S100A8
Caveolar-mediated Endocytosis Signaling	4.07E-03	ITGB2,FLNA,ACTA1
Colorectal Cancer Metastasis Signaling	4.37E-03	MMP8,WNT2B,STAT1,MMP9,WNT5A
VDR/RXR Activation	5.25E-03	CAMP,HOXA10,IGFBP5
Intrinsic Prothrombin Activation Pathway	7.59E-03	COL1A1,COL3A1
Virus Entry via Endocytic Pathways	7.59E-03	ITGB2,FLNA,ACTA1
Calcium Signaling	8.71E-03	MYH4,TNNI2,TNNC2,ACTA1
Proline Degradation	8.91E-03	ALDH4A1
4-hydroxyproline Degradation I	8.91E-03	ALDH4A1
Clathrin-mediated Endocytosis Signaling	9.77E-03	ITGB2,LYZ,S100A8,ACTA1
Paxillin Signaling	1.07E-02	ITGB2,Actn3,ACTA1
Complement System	1.20E-02	ITGB2,CFH

\* IPA = Ingenuity Pathway Analysis



**Supplemental Figure 1.** Gene expression of two podocyte-specific genes Nphs1 (panel A) and Trpc6 (panel B) was determined in kidney glomeruli of all experimental groups and either stayed relatively stable across most (panel A) or all (panel B) of the groups.