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Supplemental Table 1. Disposition of all founders.

Transgene	Founder #	Sex	Age	Kidney expression	Comments
Tg-G2	18	F	129		Died in 1st pregnancy
	19	F	122		Died in 1st pregnancy
	20	F	279	-/+	No/low transgene expression, discontinued breeding
	7	M	275	++	Never mated successfully
	9	M	275	++	**Line established**
	10	M	201	-/+	No/low transgene expression, discontinued breeding
	23	M	356	++	Produced few transgenic pups, discontinued breeding
	24	M	356	++	**Line established**
Tg-G0	1	F	319	+++	Produced small litters, all pups died, discontinued breeding
	3	F	319	-/+	Never mated successfully
	4	F	319	-/+	No/low transgene expression, discontinued breeding
	10	F	282	-/+	Produced small litters with few transgenic pups, discontinued breeding
	11	F	319	+++	Never mated successfully
	12	F	359	++	Redundant expression pattern, discontinued breeding
	13	F	319	-/+	Produced few transgenic pups, discontinued breeding
	14	F	319	+	Produced small litters with few transgenic pups, discontinued breeding
	27	F	314	+++	**Line established**
	34	F	314	+	Produced small litters with few transgenic pups, discontinued breeding
	35	F	145		Died in 1st pregnancy
	38	F	277	++	**Line established**
	61	F	134		Died in 1st pregnancy
	68	F	210		Did not transmit transgene to offspring (chimera)
	20	M	319	-/+	No/low transgene expression, discontinued breeding
	22	M	282	++	Redundant expression pattern, discontinued breeding
	24	M	319	++	**Line established**
	25	M	158		Never mated successfully, died of unknown cause (no signs of seizure)
	45	M	314	+	Redundant expression pattern, discontinued breeding
	46	M	277	+	**Line established**
	47	M	314	+++	Redundant expression pattern, discontinued breeding
	48	M	314	+++	Redundant expression pattern, discontinued breeding
	50	M	314	+	Redundant expression pattern, discontinued breeding
	53	M	314	+	Redundant expression pattern, discontinued breeding
	55	M	314	+	Redundant expression pattern, discontinued breeding
	56	M	314	++	Never mated successfully
	58	M	314	+	Never mated successfully
	69	M	310	++	Produced small litters with few transgenic pups, discontinued breeding
	73	M	227		Did not transmit transgene to offspring (chimera)

Four additional founders (2 Tg-G0 and 2 Tg-G2) were sacrificed before breeding for preliminary technical evaluation and are not included here. Age is the age of death or terminal sacrifice. Expression data on semi-quantitative scale: -/+, +, ++, +++.

Supplemental Table 2: Semi-Quantitative Scoring of Glomerular Ultrastructural Changes.

Genotype	Sex	Age (days)	GBM[1]	Podocyte[2]	Total score	Mean Total score
wild type	F	215	1	1	2	
	F	175	0	1	1	
	F	202	1	1	2	
	M	210	1	1	2	1.75
Tg-G0	F	245	0	1	1	
	F	187	0	1	1	
	F	202	1	1	2	
	M	245	0	2	2	
	M	245	1	2	3	
	M	187	1	2	3	2
Tg-G2	F	203	0	1	1	
	F	219	0	0	0	
	F	215	1	2	3	
	M	219	0	1	1	
	M	210	1	1	2	
	M	210	1	1	2	1.5

Numbers in each category are the average of scores from two independent pathologists examining the same TEM images who were blinded to specimen identity.

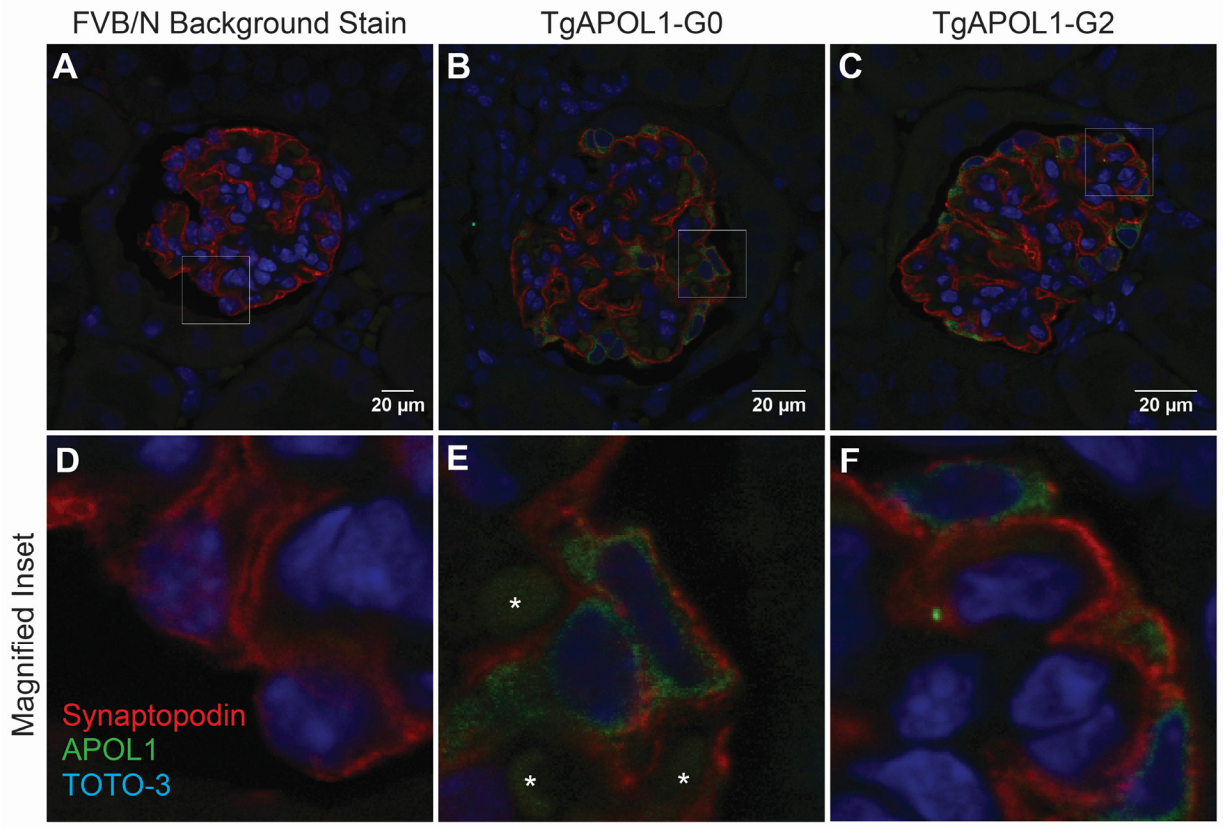
[1] GBM thickness irregularities (0=normal; 1=mildly/focally abnormal; 2=diffusely abnormal)

[2] Podocyte foot process effacement (0=0-10%; 1=11-25%; 2=26-50% 3=51-75%; 4=>75%)

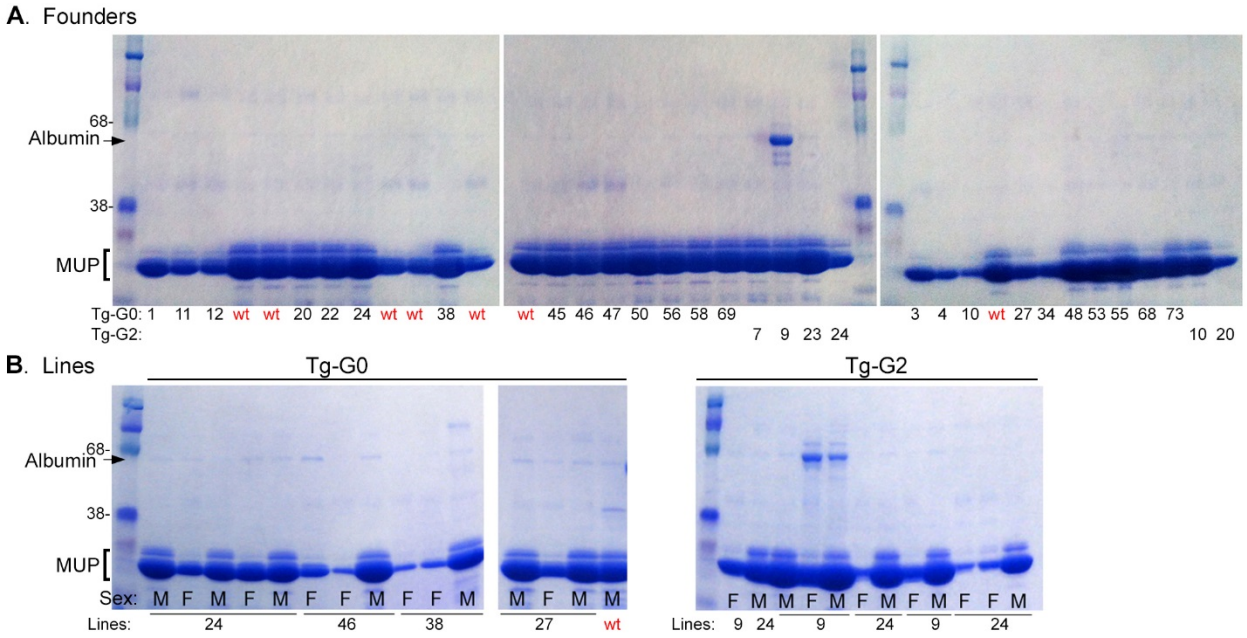
Supplemental Table 3: Standard serologic chemistries in pregnant mice (mean±SD).

Serum test	units	normal range	Wild-type pregnant (n=6)	Transgenic pregnant (n=9)	Transgenic pregnant with seizure (n=2)*
ALT(GPT)	U/L	10-77	41±12	81±69	44 (30-58)
Alkaline Phosphatase	U/L	15-96	41±7	36±11	57 (49-64)
Total Bilirubin	mg/dL	0-1.0	0.1±0.1	0.2±0.2	0.2 (0.1-0.3)
Cholesterol	mg/dL	50-250	112±17	133±86	127 (104-150)
Total Protein	g/dL	3.5-7.2	4.1±0.2	3.9±0.4	4.6 (4.4-4.7)
Albumin	g/dL	2.5-6.5	2.4±0.1	2.3±0.3	2.6 (2.3-2.9)
Globulin	g/dL	1.0-2.0	1.7±0.2	1.6±0.2	1.5 (1.2-1.8)
Urea Nitrogen	mg/dL	8-33	23±11	42±17	31 (30-31)
Creatinine	mg/dL	0.2-2.2	0.2±0.1	0.2±0.3	0.2 (0.1-0.2)
Glucose	mg/dL	62-175	222±19	210±21	104 (98-109)
Calcium	mg/dL	7.1-15.5	9.0±0.2	8.4±1.0	9.3 (9.1-9.4)
Sodium	mmol/L	140-160	147±4	143±5	156 (150-153)
Potassium	mmol/L	5.0-7.5	7.2±0.9	7.5±1.8	5.5 (4.9-6.1)
Chloride	mmol/L	88-115	113±4	109±3	113 (113-113)

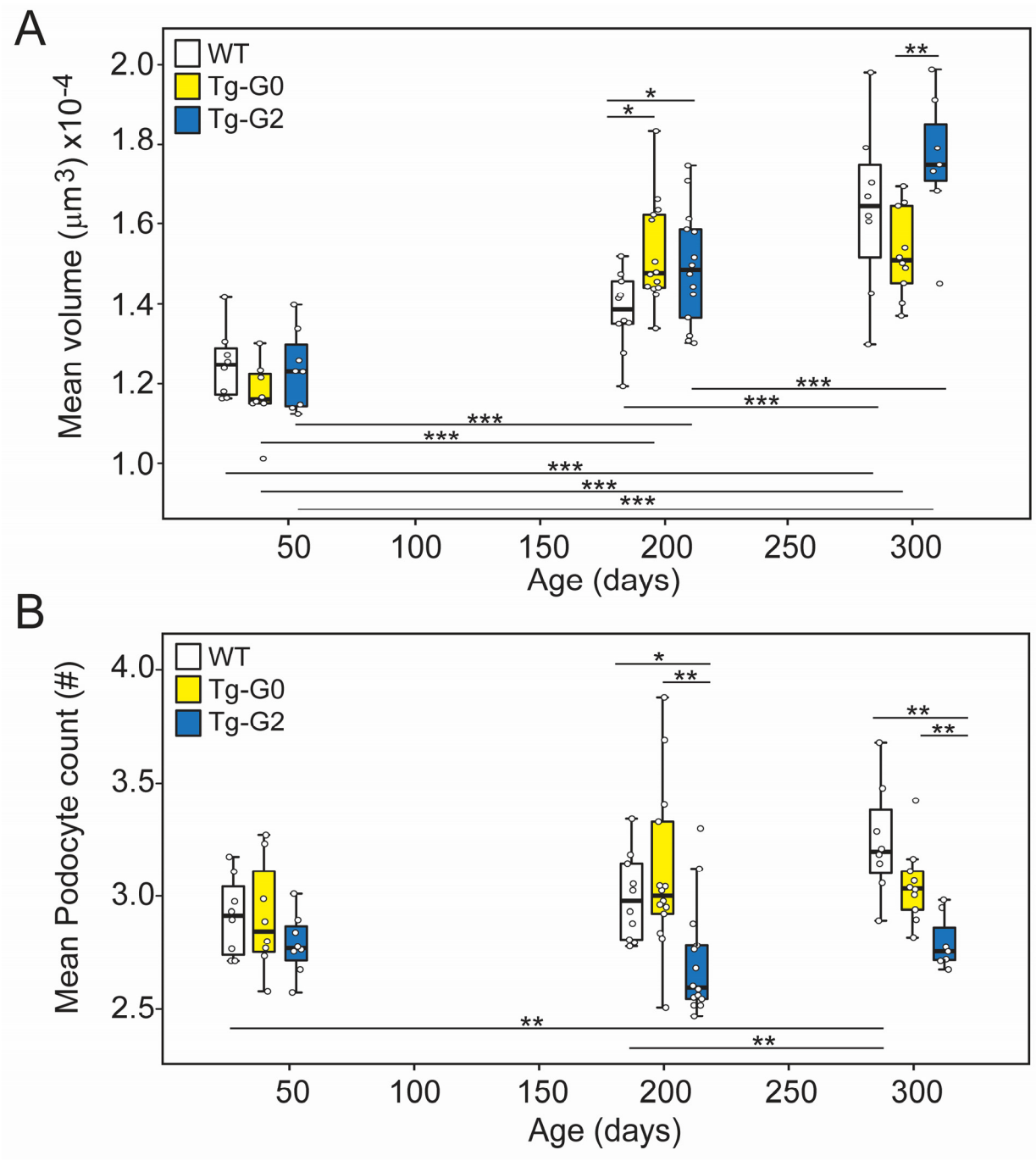
* mean (range)



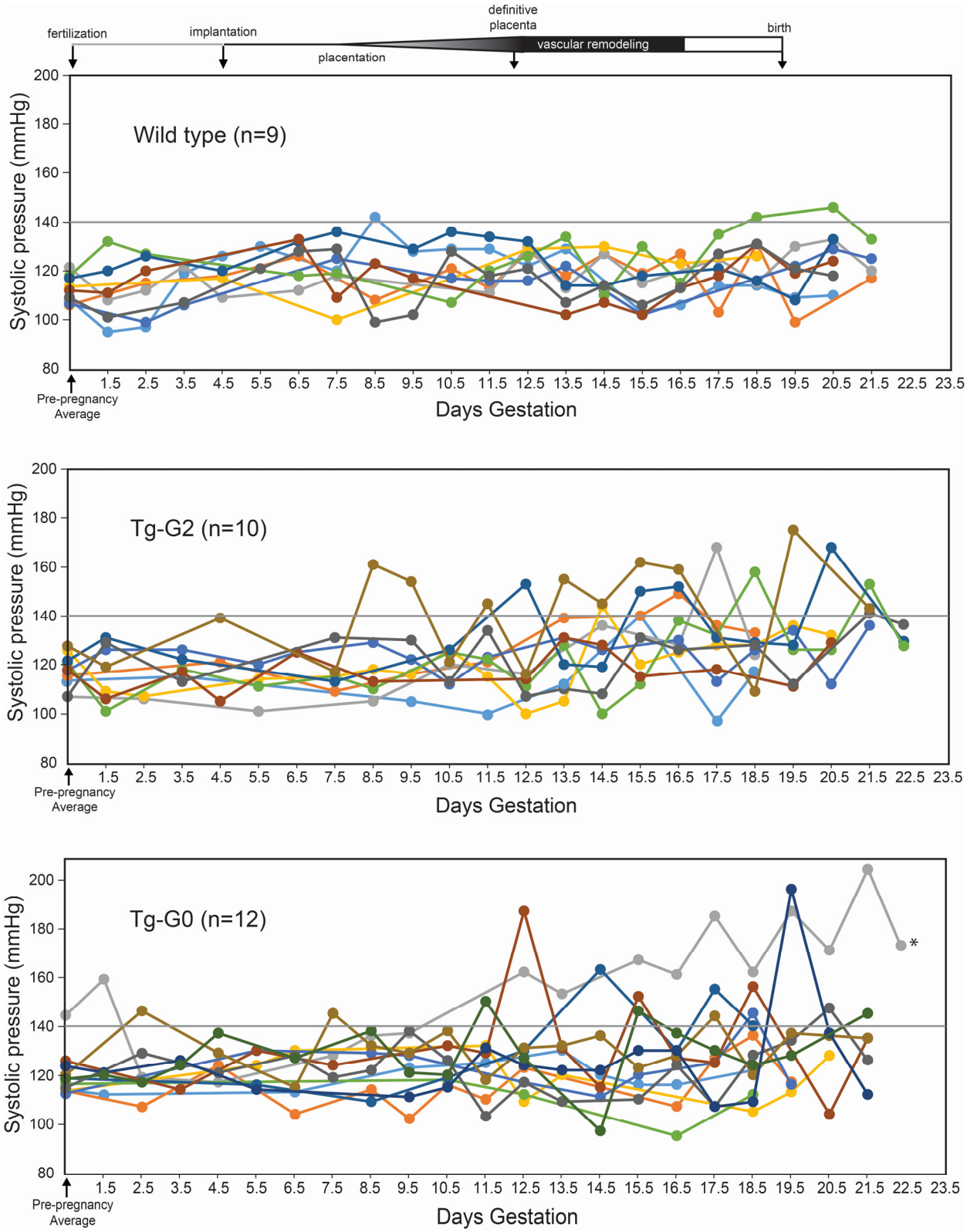
Supplemental Figure 1: APOL1 was present in glomerular cells that are positive for Synaptopodin. Immunofluorescent co-staining with APOL1 and Synaptopodin in a non-transgenic wild-type FVB/N (**A, D**), transgenic APOL1-G0 (**B, E**), and transgenic APOL1-G2 (**C, F**) mouse kidneys. White boxes in A-C are magnified insets shown in D-E and demonstrate APOL1 (green) and Synaptopodin (red) labeled the same cell and that the APOL1 staining is cytoplasmic. Nuclear stain was TOTO-3 (blue). Asterisks (*) indicate autofluorescence of red blood cells in capillary loops. There was no APOL1 staining in tubules.



Supplemental Figure 2: No proteinuria in founders and offspring of established lines. Coomassie-stained polyacrylamide gels of mouse urine noting the molecular weight of albumin (arrow) and the low molecular weight proteins common in mouse urine (MUP, major urinary proteins). **A**. Proteinuria of all surviving founders at terminal sacrifice (mean age of 302 days; see Supplemental Table 1 for exact age at sacrifice for each founder). **B**. Proteinuria in aged offspring from each of the six established transgenic lines (Tg-G0: lines 24, 27, 38, 46 and Tg-G2: lines 9, 24). Mean ages for the Tg-G0 and Tg-G2 mice shown on gel were 278 and 254 days respectively. Sample groupings designated by the line under the gel are littermates; founder number given below line, and sex (M, male; F, female) given above line. Wild-type (wt), non-transgenic mice in both A and B are age-matched.

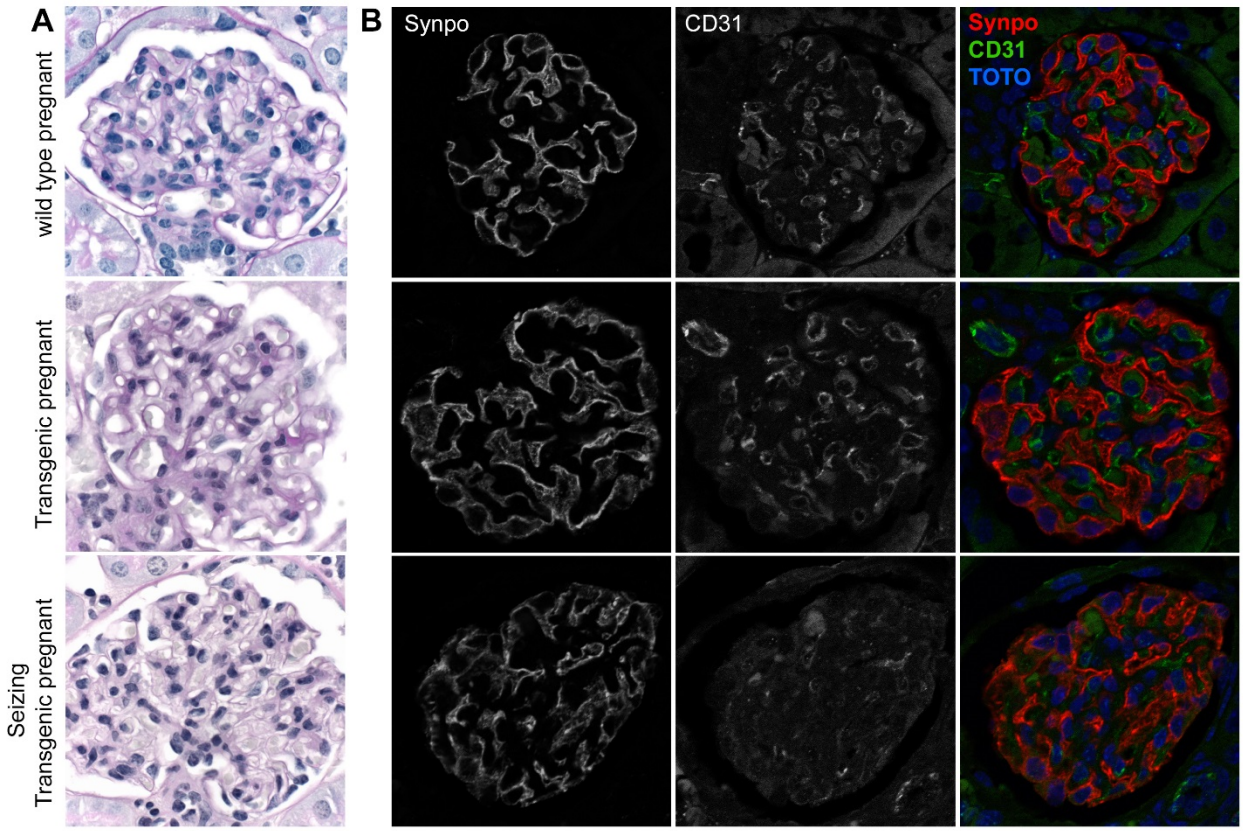


Supplemental Figure 3: Corrected podocyte number and glomerular tuft volumes used in Figure 4 podocyte density calculations. Mean glomerular tuft volume (**A**) and mean podocyte number (**B**) per glomerular tuft for each mouse, stratified by genotype. Approximately 100 glomeruli/mouse were counted; each circle represents one mouse. **P*<0.05, ***P*<0.01, ****P*<0.001 by ANOVA. Numbers in each group are the same as reported for Figure 4.

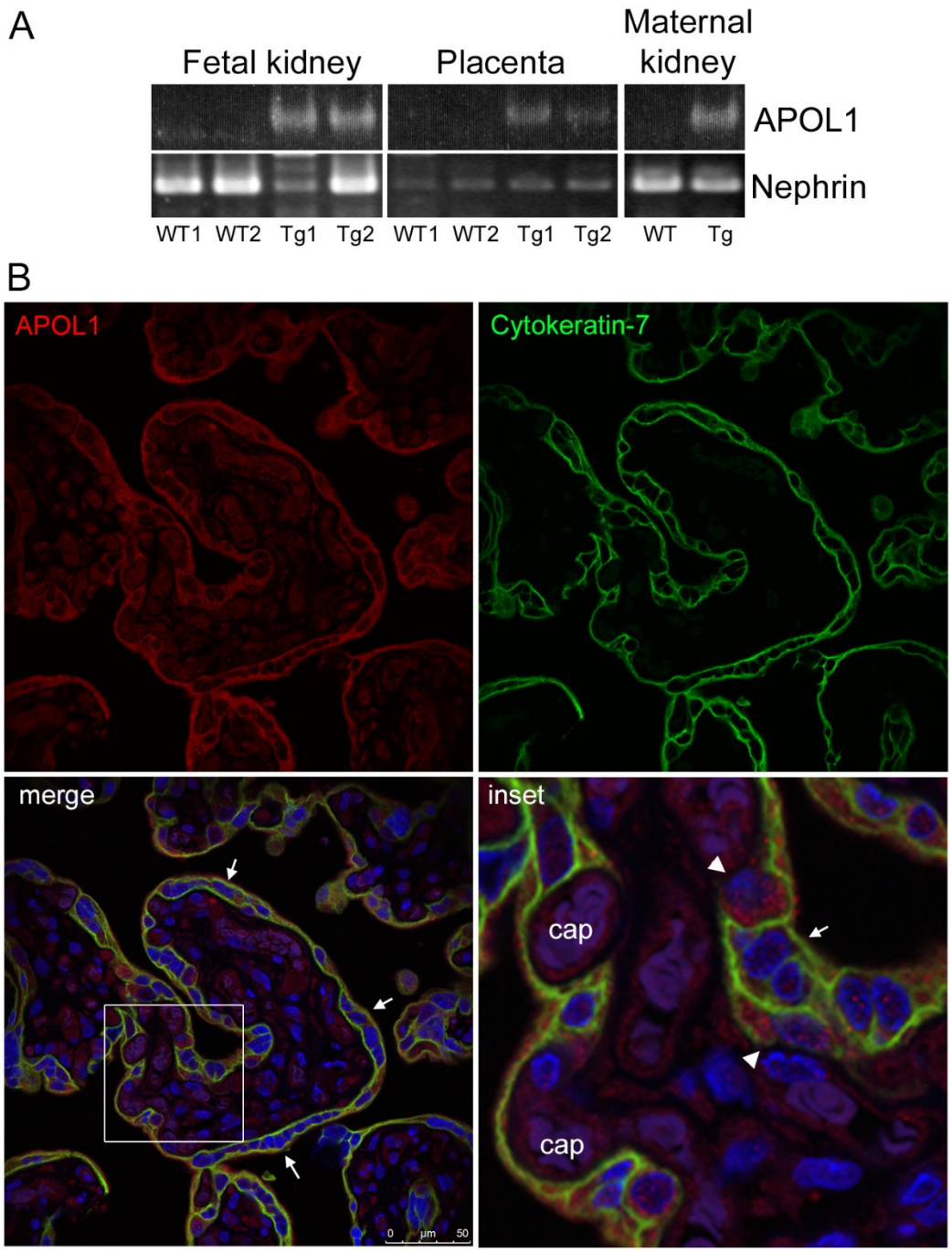


Supplemental Figure 4.

Supplemental Figure 4 legend. Tg-G0 and Tg-G2 mice had pregnancy-associated hypertension. Systolic blood pressures were recorded with tail cuff plethysmography; each line represents a single animal. **A**. Wild type, non-transgenic (n=9). **B**. Tg-G0 (n=12). **C**. Tg-G2 (n=10). Day 0.5 is the morning of the appearance of a postcoital vaginal plug. Time point zero is the pre-pregnancy average, the last pregnancy reading is on day 18.5, with full-term delivery on day 19, and postpartum blood pressure readings beginning on day 19.5 were recorded until pressures fell below 140mmHg. Asterisk (*) indicates a hypertensive female that became moribund and was euthanized. Some mice were sacrificed at day 18.5 to collect serum samples for sFlt-1 and APOL1 ELISAs and there are no postpartum readings for these animals. At top is a schematic for the time line of placental development, beginning at implantation at day 4 with placentation complete (definitive placenta) by day 12. Placentas grow in proportion to fetal growth from day 12 to term on day 19, although vascular remodeling takes place from day 12 to day 16.

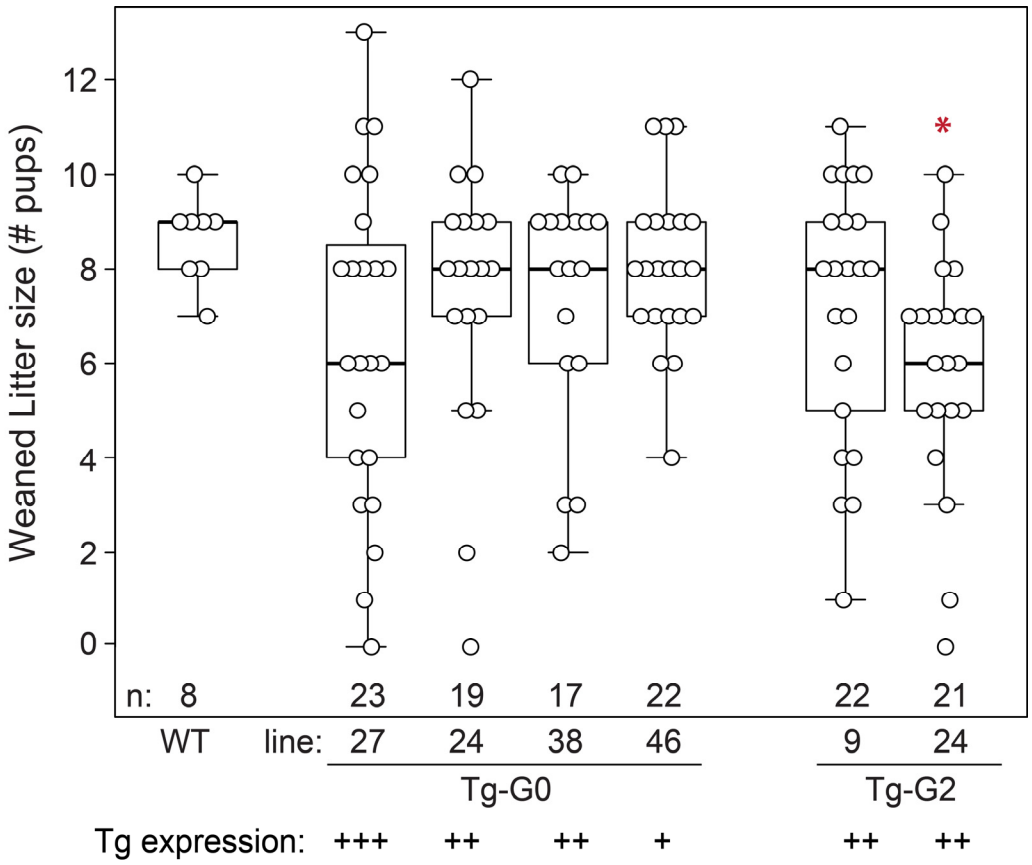


Supplemental Figure 5: Endothelial changes in glomeruli of seizing pregnant mice. **A**. Histology (PAS stain) of pregnant mouse kidneys. **B**. Immunostaining for Synaptopodin (Synpo) as a podocyte marker and CD31 as an endothelial marker (TOTO3 as a nuclear stain) showing diminished CD31 staining in the seizing transgenic pregnant glomeruli.



Supplemental Figure 6: APOL1 was expressed in transgenic mouse and human placentas. **A**. RT/PCR of total cellular RNA extracted from mouse fetal tissues using primers for murine Nephrin (endogenous Nephrin expression) and human APOL1 (expression originating from the transgene). Wild-type (WT) and transgenic (Tg) fetuses were dissected from their placentas, and fetal kidneys were removed. Two wild-type FVB/N pregnant and two Tg-G0 pregnant mice

were examined (days gestation: WT1 = e16.5; WT2 = e18.5; Tg1 = e14.5; Tg2 = e17.5). As a positive and negative control, maternal kidneys from one of the wild-type and Tg-G0 dams were similarly analyzed. **B**. Immunostaining for APOL1 (red) and Cytokeratin-7 (green, a marker for trophoblasts) in a term human placenta from an uncomplicated pregnancy. Nuclei were labeled with DAPI (blue). Merged image and inset show APOL1 expression in terminal villi syncytiotrophoblasts (arrows) and cytotrophoblasts (arrow heads) which co-label with Cytokeratin-7. Cap, Capillary loop.



Supplemental Figure 7: Weaned litter sizes were smaller for Tg-G2. Boxes are quartiles with a median line and 95th percentile whiskers; *P=0.004 compared to wild-type (WT) using t test (with Bonferroni correction for multiple testing, P=0.025). The reported average litter size for FVB/N is 8.8±0.4 pups. Number (n) of litters examined for each line are noted on the graph; line number and relative transgene (Tg) expression level for each line is given below graph.