

Supplementary Tables

Table S1. Baseline characteristics of Akita male mice with 5 graded *Tgfb1* expressions at age 40 weeks

	L/L Akita	L/+ Akita	WT Akita
Number of mice	10	11	11
Body weight (BW; g)	20.7 ± 0.9 [†]	25.0 ± 1.3	25.9 ± 1.5
Kidney weight (right; mg)	179 ± 13**	254 ± 13	254 ± 16
Kidney weight / BW (%)	8.50 ± 0.46*	10.24 ± 0.36	9.85 ± 0.46
Heart weight (mg)	108 ± 5**	123 ± 5	125 ± 4
Heart weight / BW (%)	4.50 ± 0.51	4.99 ± 0.20	4.95 ± 0.23
Plasma cholesterol (mmol/L)	1.82 ± 0.19	2.31 ± 0.21	2.77 ± 0.12
Plasma triglyceride (mmol/L)	1.17 ± 0.15	1.26 ± 0.14	1.51 ± 0.30

	H/+ Akita	H/H Akita
Number of mice	9	8
Body weight (BW; g)	24.4 ± 1.3	22.1 ± 1.0
Kidney weight (right; mg)	235 ± 16	279 ± 19
Kidney weight /BW (%)	9.65 ± 0.43	12.65 ± 0.69**
Heart weight (mg)	121 ± 3	100 ± 4*
Heart weight /BW (%)	5.03 ± 0.16	4.64 ± 0.26

Plasma total cholesterol (mmol/L)	2.34 ± 0.27	1.93 ± 0.39
Plasma triglyceride (mmol/L)	1.62 ± 0.12	1.56 ± 0.23

* $P < 0.05$, ** $P < 0.01$ vs. WT:A/+.

Table S2. Primers and probes for quantification of mRNA with real-time quantitative reverse transcription-PCR.

<u>Gene Symbol</u>		
<i>Tgfb1</i>	(Fwd primer)	5'-TGACGTCACTGGAGTTGTACGG-3'
	(Rev primer)	5'-GGTCATGTCATGGATGGATGGTGC-3'
	(Probe)	5'-FAM-TTCAGCGCTCACGTCTTGTGACAG-Tamra-3'
<i>Nphs1</i>	(Fwd primer)	5'-CAGCTGCTAGTCTGCGAGG-3'
	(Rev primer)	5'-ATCAATGACAGGAGGTCCCTG-3'
	(Probe)	5'-FAM-TCCAACCCAGCCTGGCCACTC-Tamra-3'
<i>Nphs2</i>	(Fwd primer)	5'-GTGAGGAGGGCACGGAAGT-3'
	(Rev primer)	5'-TAATCCAGAGGGCTTGATGC-3'
	(Probe)	5'-FAM-CCTCTGGTCGCTCGCTCTCCAGC-Tamra-3'
<i>Lrp2</i>	(Fwd primer)	5'-GAATCCGCCAAGACACTGAT-3'
	(Rev primer)	5'-ACAAGAGTCCCCTGGGCATA-3'
	(Probe)	5'-FAM-CCCTCGCTCAGCTGCTTCCCGTAA-Tamra-3'
<i>Cubn</i>	(Fwd primer)	5'-TTTGGACCGTTCTGTGGCAT-3'
	(Rev primer)	5'-GGAATCTTATGAAGACCCGA-3'
	(Probe)	5'-FAM-ACACTGTGGTAGCACCCTTCATGC-Tamra-3'

<i>Fcrlp</i>	(Fwd primer)	5'-ACGTGGAGATGAGCACCATT-3'
	(Rev primer)	5'-GCACAGAAGATCTGGCTGAT-3'
	(Probe)	5'-FAM-TGCCAGCCCCTCATGCTCCTCT-Tamra-3'
<i>Actb</i>	(Fwd primer)	5'-AAGAGCTATGAGCTGCCTGA-3'
	(Rev primer)	5'-ACGGATGTCAACGTCACACT-3'
	(Probe)	5'-FAM-CACTATTGGCAACGAGCGGTTCCG-Tamra-3'

Supplementary Figure Legends

Fig. S1. Heart rate of Akita mice having 5 graded expression levels of TGF β 1 at age 40 weeks.

Fig. S2. Urinary albumin excretion in non-diabetic mice having 5 graded expression levels of TGF β 1 at age 40 weeks. ** $P < 0.01$ vs. WT.

Fig. S3. Plasma urea nitrogen levels.

Fig. S4. Plasma creatinine levels.

Fig. S5. Creatinine clearance.

Fig. S6. Plasma aldosterone levels of Akita mice having 5 graded expression levels of TGF β 1 at age 40 weeks. ** $P < 0.01$ vs. WT:A/+.

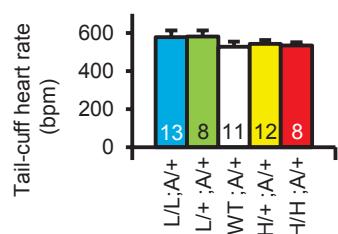
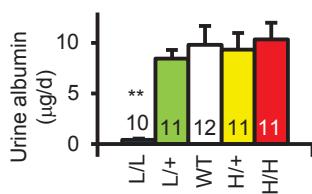
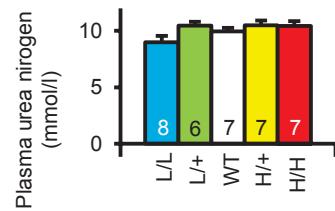
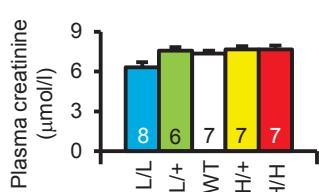
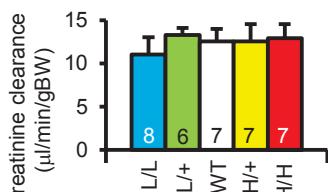
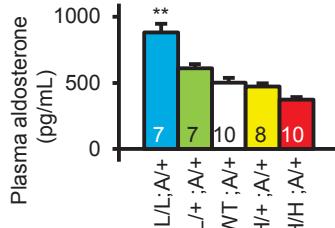
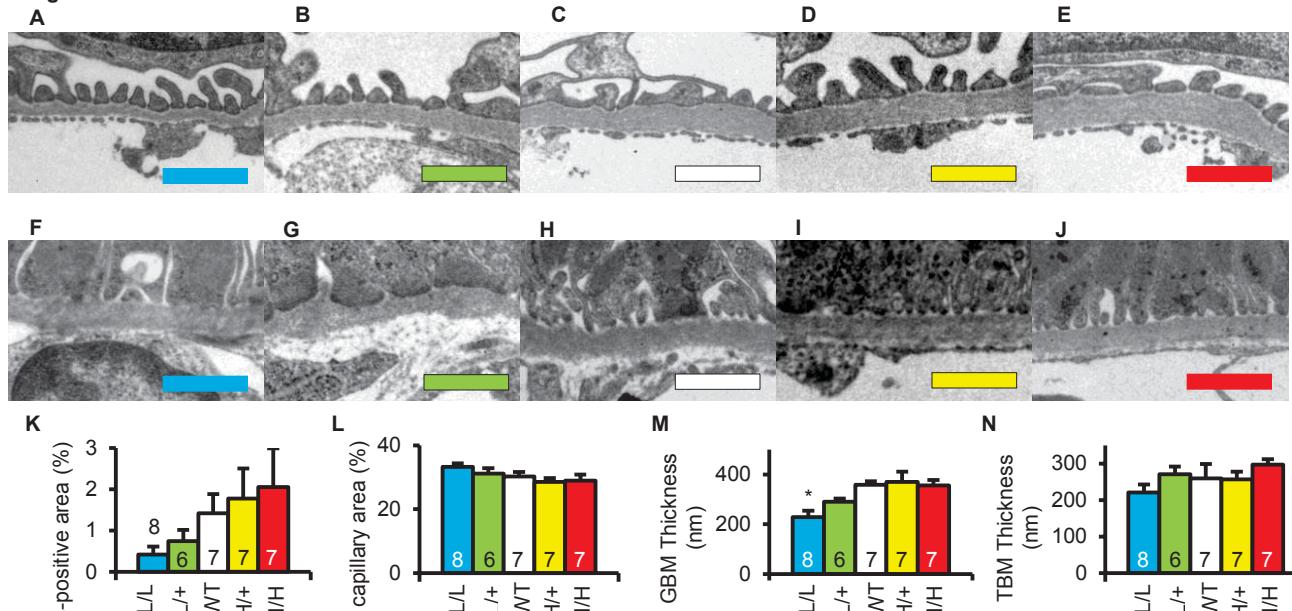
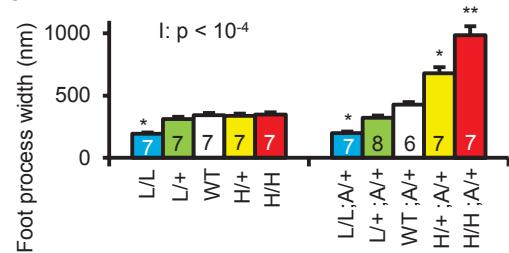
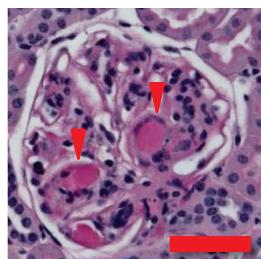
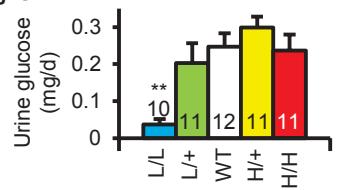
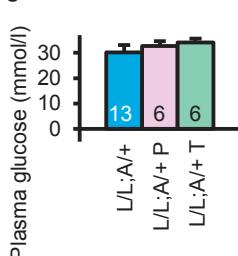
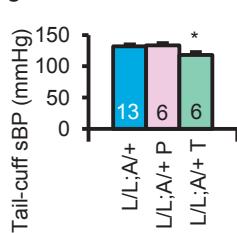
Fig. S7. Transmission electron microscopy in the kidney of mice having 5 graded expression levels of TGF β 1 at 40 weeks of age. Color-coded scale bar = 1 μ m. **A-E.** Glomerular basement membrane (GBM) in non-diabetic mice having 5 graded expression levels of TGF β 1. **A.** L/L. **B.** L/+ . **C.** WT. **D.** H/+ . **E.** H/H. **F-J.** Tubular basement membrane (TBM) of proximal tubules in non-diabetic mice having 5 graded expression levels of TGF β 1. **F.** L/L. **G.** L/+ . **H.** WT. **I.** H/+ . **J.** H/H. **K.** Fraction of PAS-positive mesangial material per total glomerular tuft cross-sectional area. **L.** Fraction of open capillary area per total glomerular tuft cross-sectional area. **M.** Thickness of GBM. **N.** Thickness of TBM in the proximal tubule. **O.** Width of foot processes of the podocyte. **I.** P value for the interaction of TGF β 1 and Akita genotype. Bars and images are color coded as indicated. * $P < 0.05$, ** $P < 0.01$ vs. WT or WT:A/+ . **P.** Nodular lesions (arrowheads) in the glomerulus in H/H:A/+ mouse; color-coded scale bar = 50 μ m; periodic acid-Schiff (PAS) staining with hematoxylin.

Fig. S8. Plasma glucose levels.

Fig. S9. Systolic blood pressure (sBP). * $P < 0.05$ vs. L/L:A/+.

Fig. S10. Transmission electron microscopy in the kidney of L/L:A/+ mice having tissue specific Cre recombinases at 40 weeks of age. Color-coded scale bar = 1 μ m. **A-B.** GBM. **C-D.** TBM. **A, C.** L/L:A/+ mice without Cre (L/L:A/+). **B, D.** L/L:A/+ mice with podocin promoter-driven Cre (L/L:A/+ N). **C, F.** L/L:A/+ mice with γ -glutamyl transferase (Ggt) 1 promoter-driven Cre (L/L:A/+ T).

Fig. S11. Urine glucose excretion in non-diabetic mice having 5 graded expression levels of TGF β 1. ** $P < 0.01$ vs. WT.

Fig. S1**Fig. S2****Fig. S3****Fig. S4****Fig. S5****Fig. S6****Fig. S7****O****P****Fig. S11****Fig. S8****Fig. S9****Fig. S10**