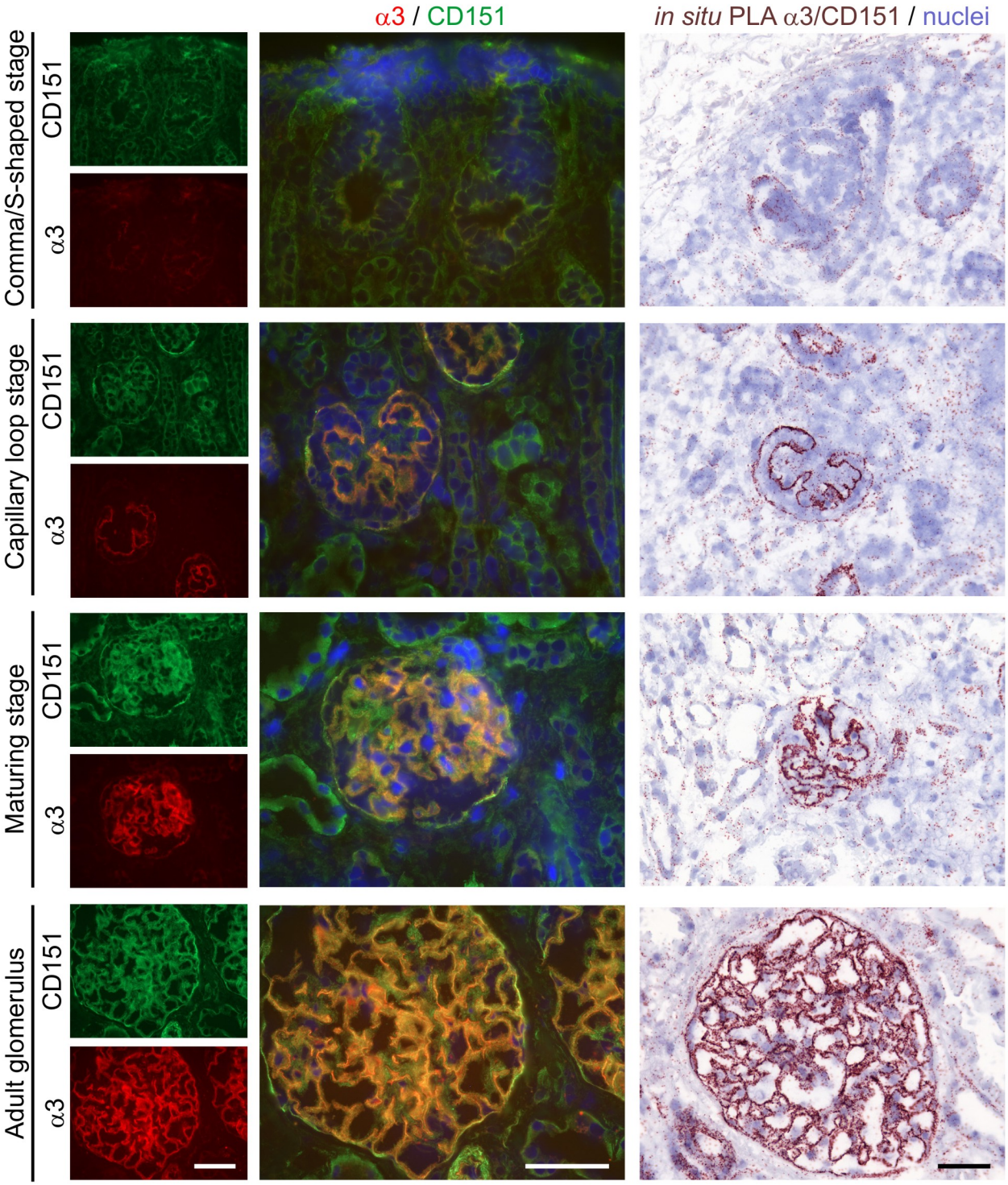
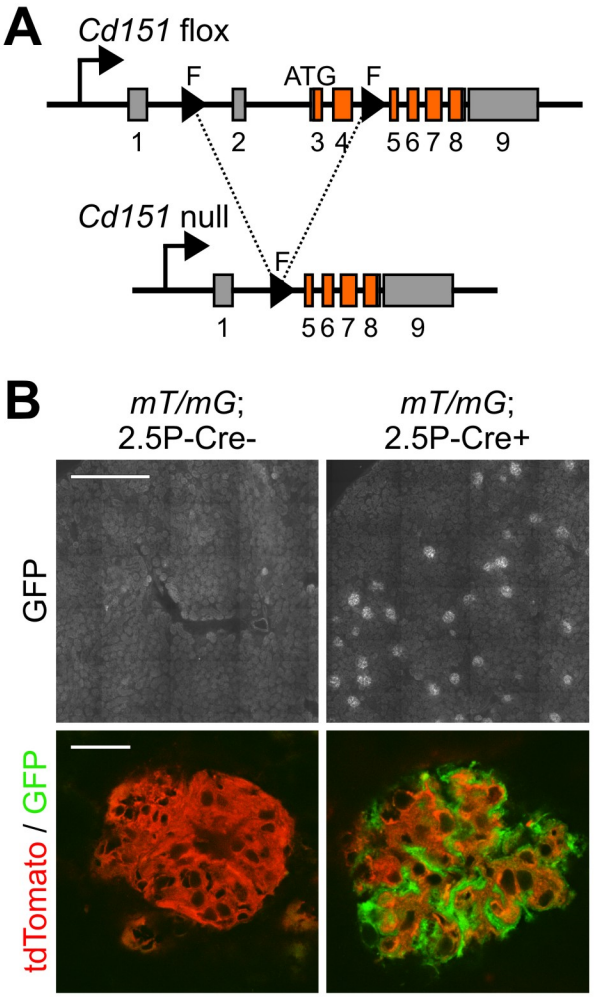


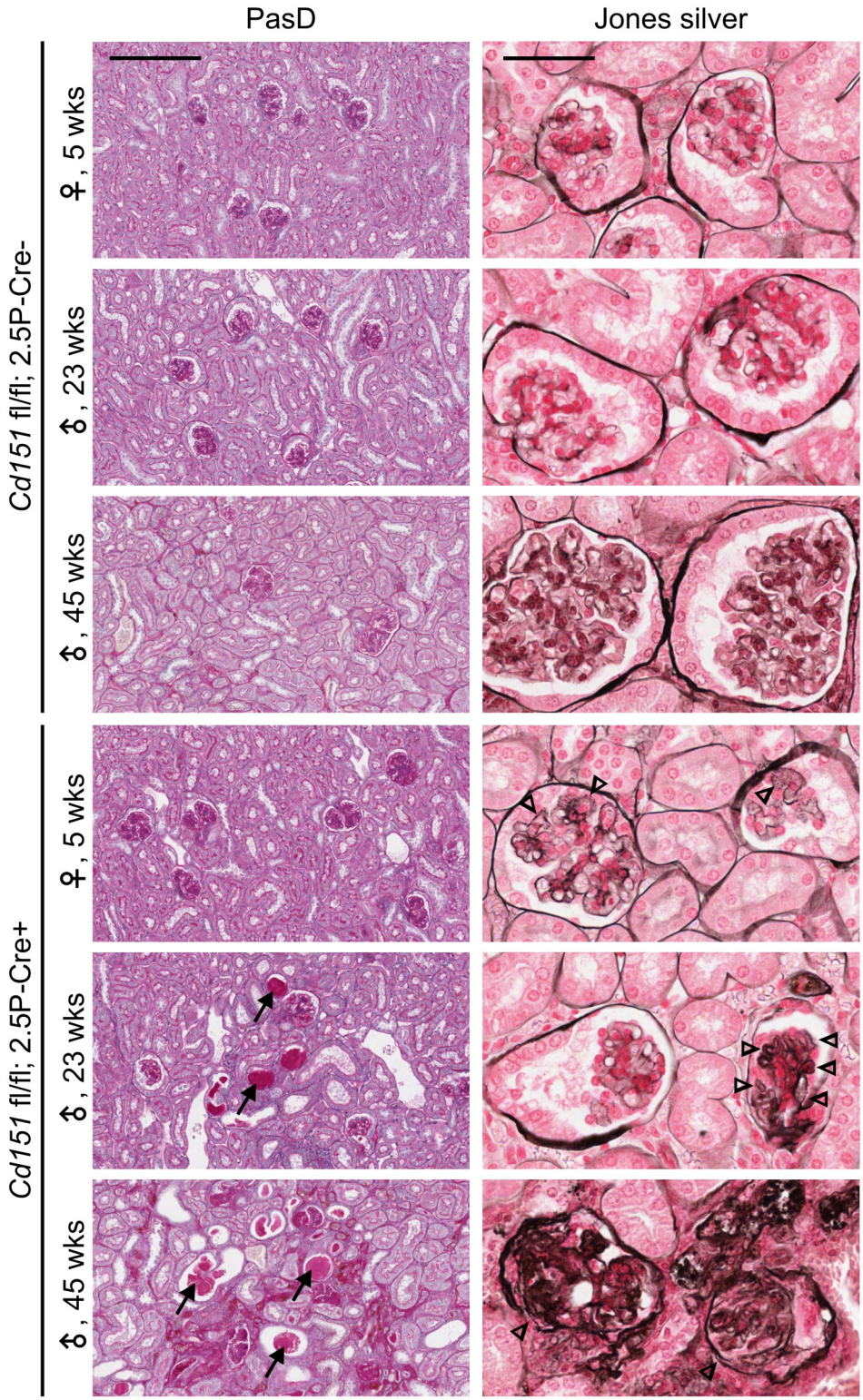
Supplemental Figure 1

Immunofluoresence and *in situ* PLA analysis of α3/CD151 in fetal and adult human kidney. Glomerular expression of CD151 and α3 increases in parallel after S-shape and capillary loop stage in the developing kidney. The presence of α3/CD151 complexes increases dramatically after S-shape stage. Scale bars: 50 μm.



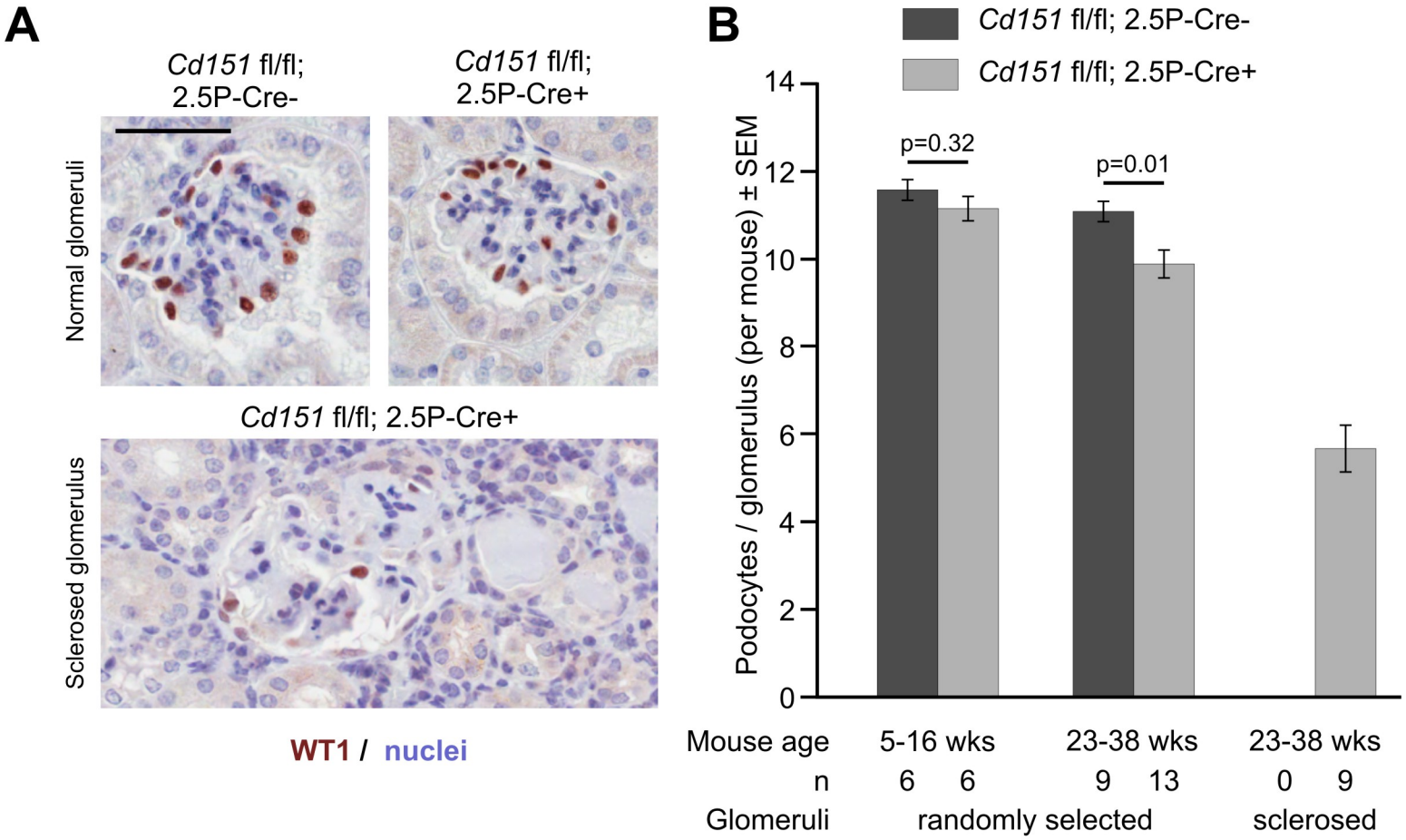
Supplemental Figure 2

Generation of podocyte specific *Cd151* knockout mice. (**A**) Schematic representation of the floxed *Cd151* allele before and after Cre mediated recombination. Numbered boxes represent the respective exons (gray: non-coding, orange: coding). (**B**) Cre mediated recombination in 2.5P-Cre^{+} mice occurs exclusively in podocytes as shown by immunofluorescent analysis of 5-wk old mT/mG; 2.5P-Cre^{+} reporter mice. Scale bars: 1 mm (B top row), 25 μm (B bottom row).



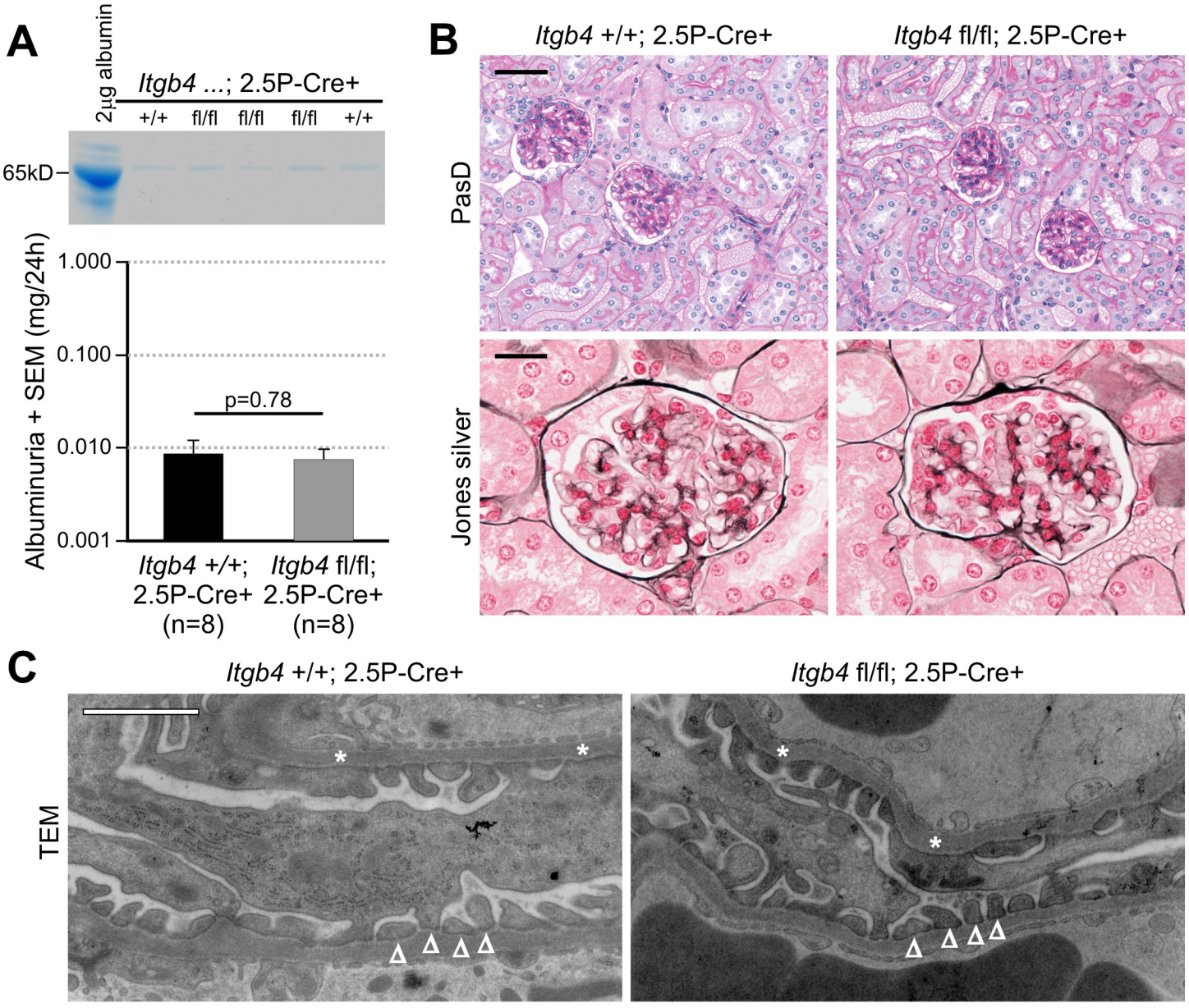
Supplemental Figure 3

Progressive abnormalities in podocyte specific *Cd151* knockout mice. Shown are PasD and Jones silver stainings of 5-, 23- and 45-wk old wild-type as well as podocyte-specific *Cd151* knockout mice. Kidneys of wild-type mice do not show any abnormalities. In contrast, *Cd151*$^{fl/fl}$; 2.5P-Cre^{+} mice develop first GBM irregularities at 5 weeks of age (∆). 18 weeks later GBM abnormalities are spread throughout entire glomeruli (∆) and proteinaceous casts occur frequently (arrows). At 45 weeks of age widespread glomerulosclerosis (∆), tubular dilation (*) and proteinaceous casts (arrows) are found in the entire kidney cortex. Scale bars: 200 μm (PasD), 50 μm (Jones).



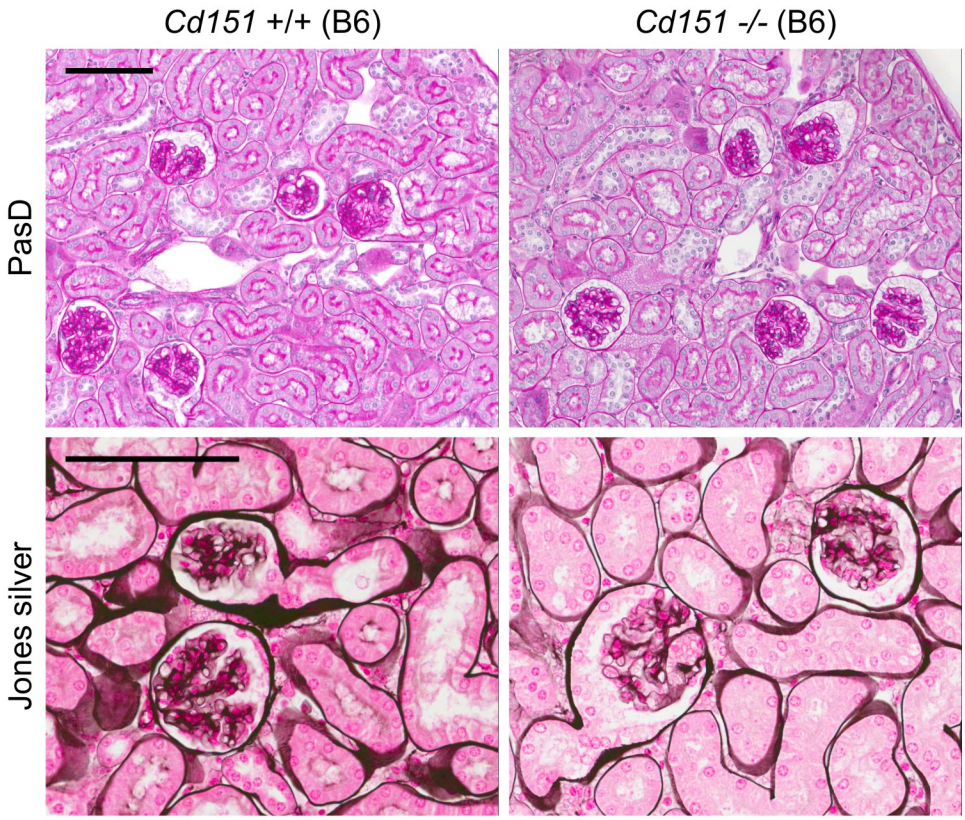
Supplemental Figure 4

Loss of *Cd151*-null podocytes due to glomerulosclerosis. (**A**) Representative micrographs of normal and sclerosed glomeruli stained for the podocyte marker WT1 (mouse age: 16 and 34 weeks respectively). (**B**) WT1-positive nuclei were counted in 40 randomly selected glomeruli of the indicated number of mice per group. No significant differences were observed when comparing the average number of podocytes per glomerulus of wild-type and podocyte-specific *Cd151* knockout mice at 5-16 weeks of age. However, at 23-38 weeks of age, podocyte-specific *Cd151* knockout mice had lost on average one podocyte per glomerulus. (Student's *t*-test, p=0.32 and 0.01 respectively). The loss of podocytes was mainly evident in sclerosed glomeruli which accounted for ~20% of all scored glomeruli per *Cd151*$^{fl/fl}$; 2.5P-Cre^{+} mouse. Scale bar: 50 μm.



Supplemental Figure 5

Podocyte- specific integrin β4 knockout mice do not develop renal abnormalities. (**A**) No significant albuminuria is detected in 16-wk old wild-type or podocyte specific-integrin β4 knockout mice (top: commassie blue stained protein gel of 1 μl urine/lane, bottom: ELISA for murine albumin present in 24h urine collections). (**B**) PasD stained kidney cortices and silver stained glomeruli of 23-wk old *Itgb4*$^{+/+}$; 2.5P-Cre^{+} and *Itgb4*$^{fl/fl}$; 2.5P-Cre^{+} mice show no signs of glomerulosclerosis, tubular dilation or proteinaceous casts. (**C**) Electron microscopy depicting regularly spaced podocyte foot processes (Δ) and an evenly thick glomerular basement membrane (*) in glomeruli of 23-wk old wild-type and podocyte-specific integrin β4 knockout mice. Scale bars: 50 μm (B top row), 20 μm (B bottom row), 1μm (C).



Supplemental Figure 6

Renal histology of old *Cd151*$^{-/-}$ mice on B6 background. No abnormalities in kidneys of a 40-wk old *Cd151*$^{-/-}$ (B6) mouse compared to a wild-type littermate. Proteinaceous casts are absent (PasD stain) and no GBM abnormalities are observed throughout glomeruli (Jones silver stain). Scale bar: 100μm.

Supplemental Table 1

Integrin cell surface levels in GEC lines as determined by FACS analysis
(mean fluorescent intensity ± SEM, n=3)

	GEC+	GEC-	GEC-re^{WT}	GEC-re^{QRD*}
Integrin α2	53.4 ± 10.1	47.1 ± 4.1	38.9 ± 8.4	46.8 ± 2.6
Integrin α3	41.0 ± 12.0	44.0 ± 20.2	46.0 ± 22.8	49.1± 22.5
Integrin α6	32.6 ± 14.1	24.7 ± 10.4	29.7 ± 12.2	34.4 ± 15.4
Integrin β1	191.2 ± 72.5	144.2 ± 30.5	125.9 ± 22.2	141.6 ± 25.2
Integrin β4	20.8 ± 7.2	19.0 ± 5.2	19.3 ± 6.0	20.6 ± 4.8

Supplemental Table 2

Albuminuria and cardiac parameters of wild-type B6 and FVB mice used in this study.

Group	**Albuminuria ± SEM (n)** (mg / 24 h)	**Dried heart weight ± SEM (n)** (mg / g BW)	**Systolic blood pressure ± SEM (n)** (mm Hg)	**Heart rate ± SEM (n)** (beats / min)
***Cd151*$^{+/+}$ (B6)**	0.031 ± 0.005 (4)	1.48 ± 0.06 (6)	77.7 ± 3.5 (6)	478 ± 11 (6)
***Cd151*$^{+/+}$ (FVB)**	0.008 ± 0.002 (6)	1.69 ± 0.15 (6)	82.2 ± 3.6 (6)	491 ± 8 (6)

Supplemental Table 3

Blood pressure measurements of untreated, enalapril- and verapamil-treated awake *Cd151*$^{-/-}$ (FVB) mice.

***Cd151*$^{-/-}$ (FVB) mice treated with**	**Systolic blood pressure ± SEM (n)** (mm Hg)	**Diastolic blood pressure ± SEM (n)** (mm Hg)	**Mean blood pressure ± SEM (n)** (mm Hg)
No drug	153.8 ± 7.0 (8)	120.5 ± 5.5 (8)	130.9 ± 6.3 (8)
20 mg/l enalapril	137.5 ± 4.3 (14)	105.8 ± 3.6 (14)	116.2 ± 3.7 (14)
(80) 20 mg/l verapamil	138.8 ± 2.2 (11)	106.6 ± 1.7 (11)	117.3 ± 1.7 (11)