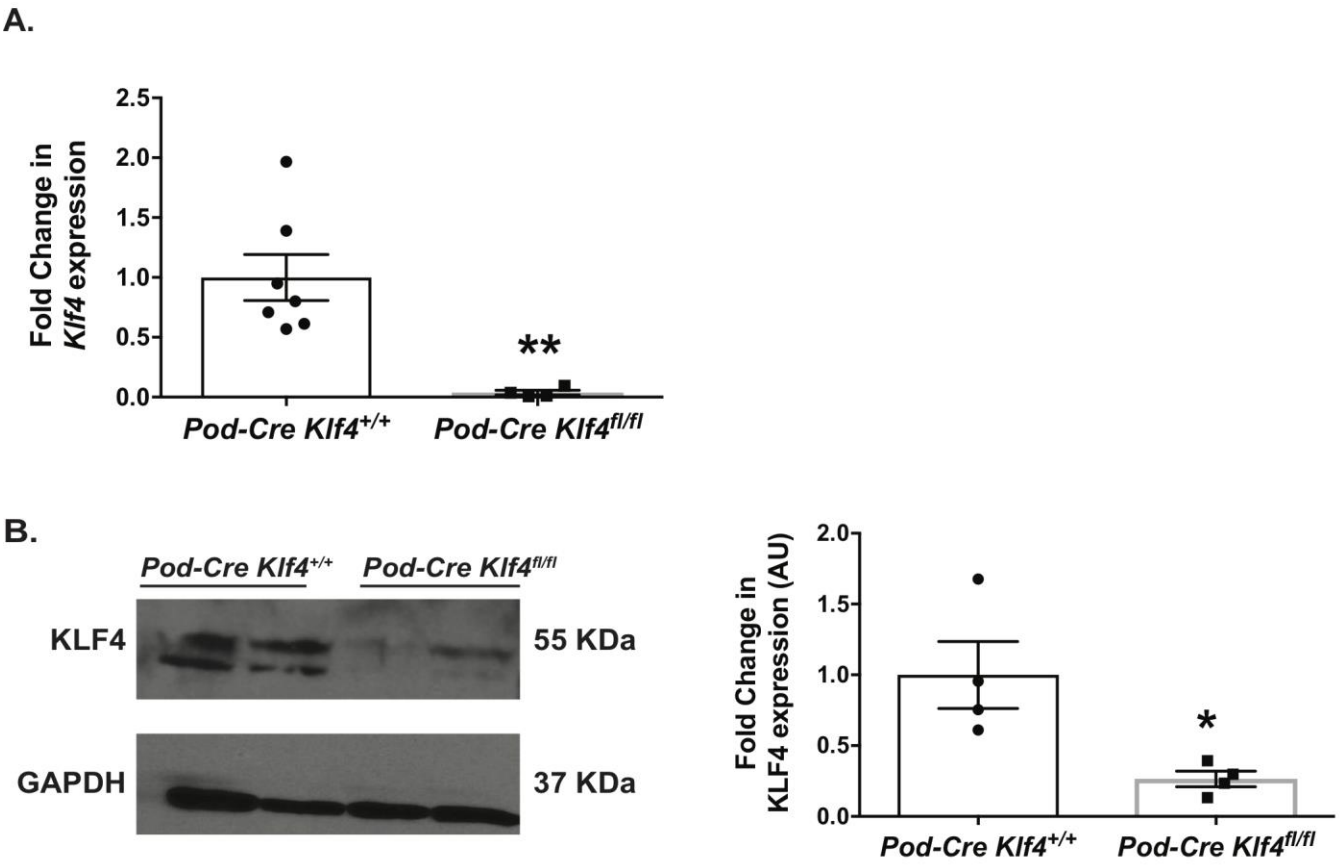
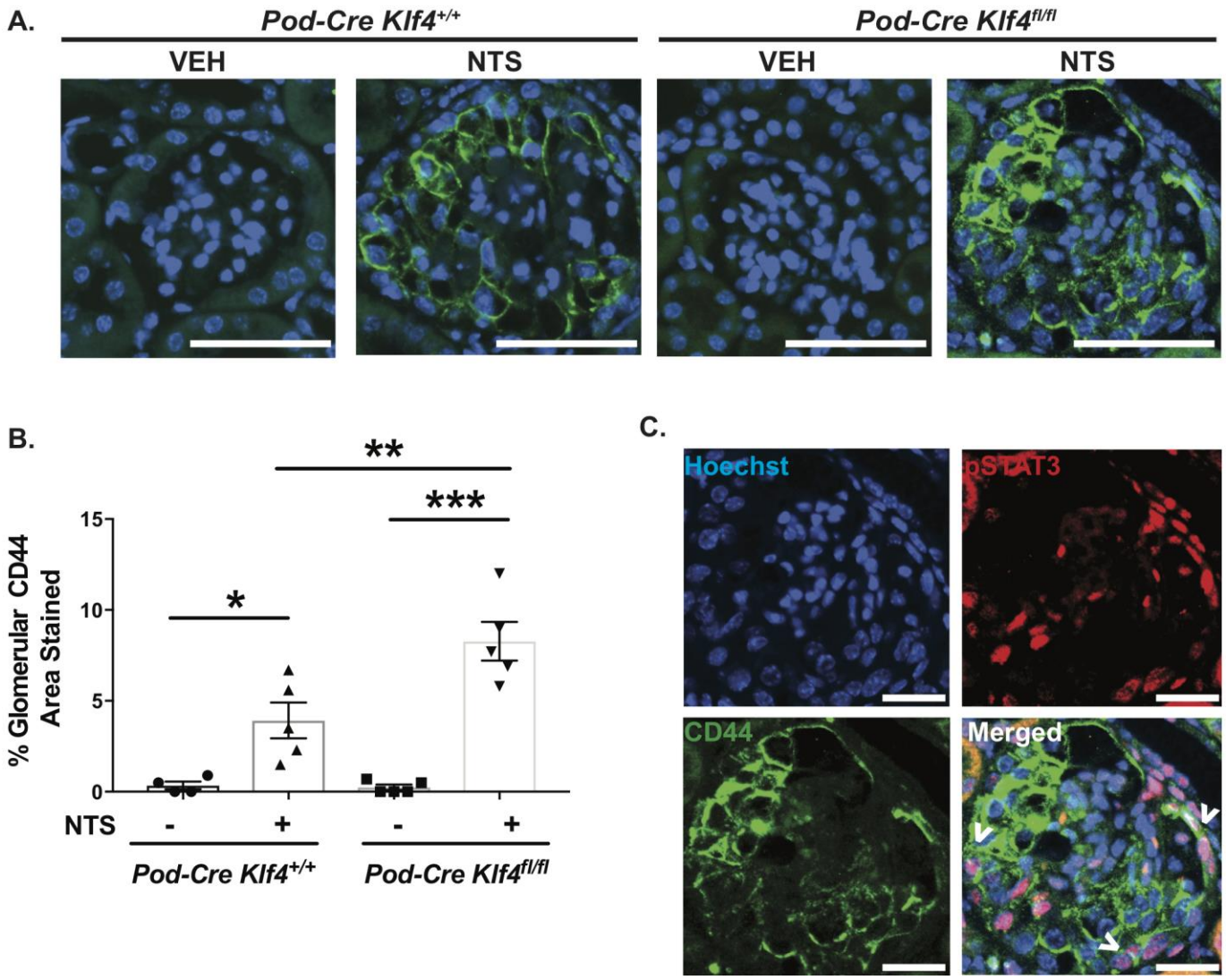
Supplemental Figure 1



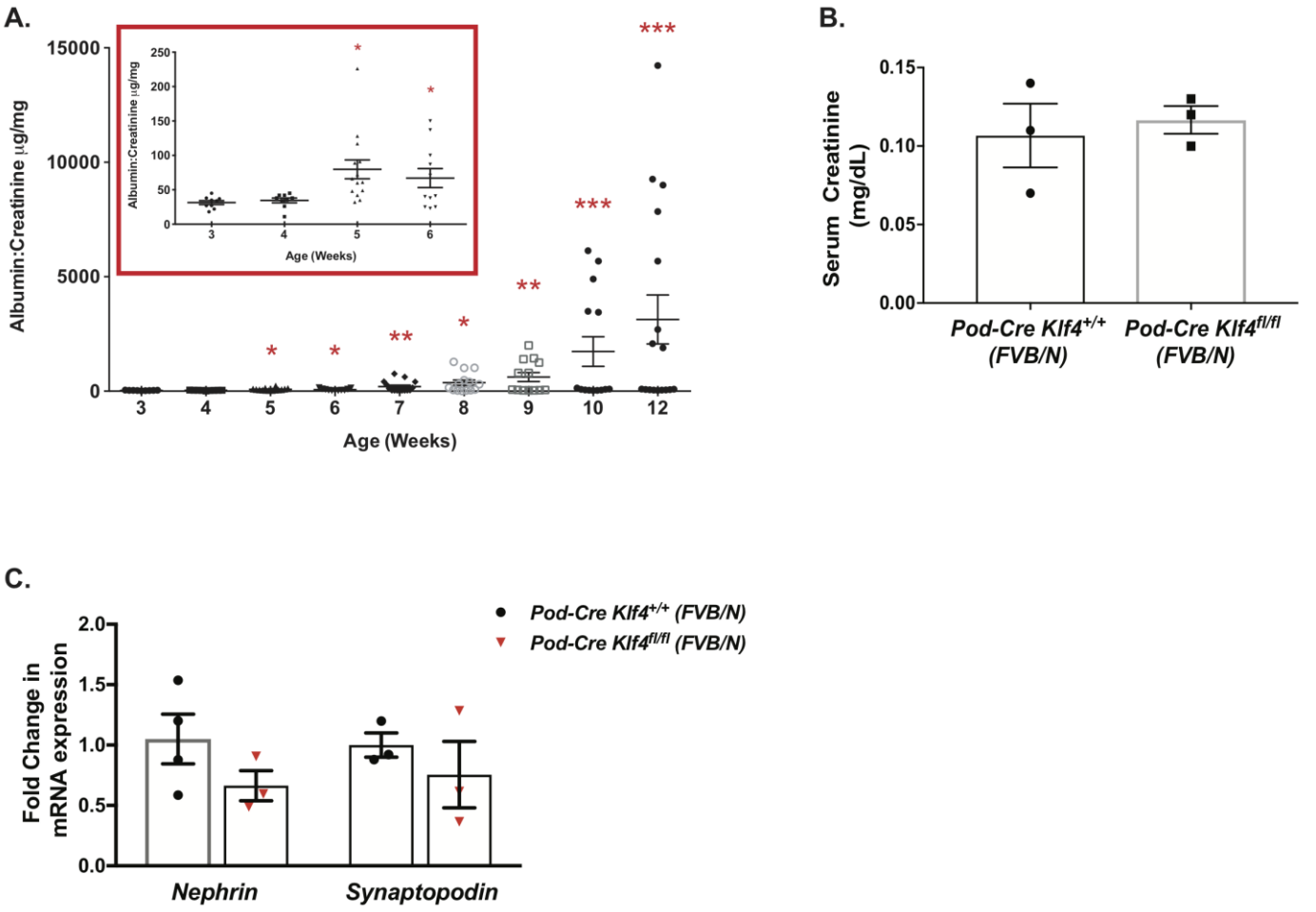
Supplemental Figure 1: Podocyte specific knockdown of *Klf4 in Podocin-Cre Klf4$^{flox/flox}$ mice was* confirmed. (A) Primary glomerular epithelial cells were isolated from 10-week old *Podocin-Cre Klf4$^{flox/flox}$* and *Podocin-Cre Klf4$^{+/+}$* mice and cultured at 37°C for 1 week. RNA was extracted and real-time PCR was performed for *Klf4* mRNA expression (n=4-7, **p<0.01, Mann-Whitney test). (B) Protein was also extracted and western blot analysis for KLF4 was performed. The representative blot of three independent experiments is shown in the left panel. The right panel shows the quantification of KLF4 expression by densitometry (n=4, *p<0.05, Mann-Whitney test).

Supplemental Figure 2



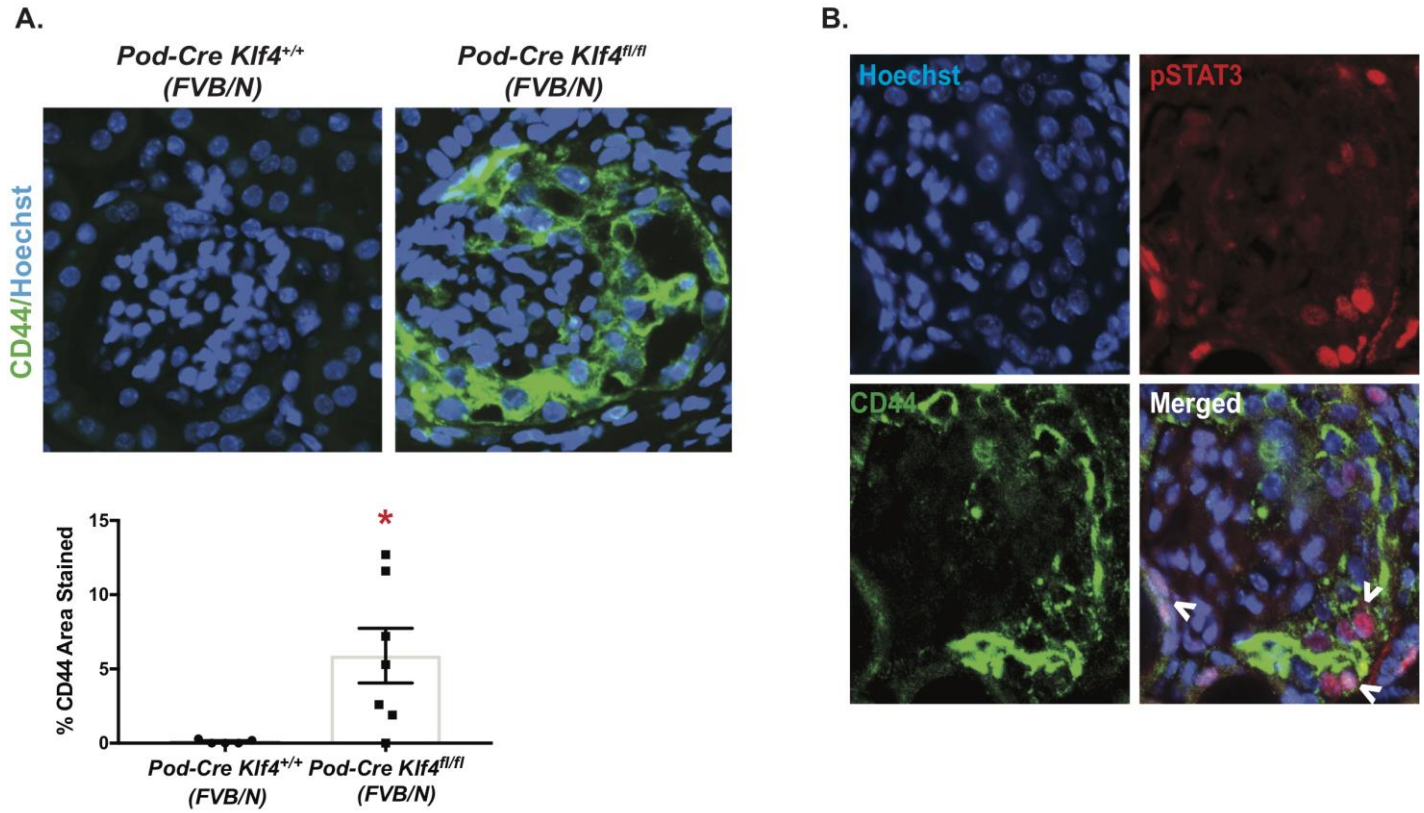
Supplemental Figure 2: Parietal Cell Activation in Nephrotoxic Serum Nephritis. *Podocin-Cre Klf4$^{flox/flox}$* and *Podocin-Cre Klf4$^{+/+}$* mice were treated with nephrotoxic serum (NTS) or VEH at 12 weeks of age. Mice were sacrificed after 7 days and renal cortex fixed for histology. (A) Immunostaining for CD44 performed in all 4 groups. The representative images from 4-5 mice in each group are shown. (B) The glomerular region was selected and percent glomerular CD44 area stained was measured. Magnification (X20); *P<0.05, **P<0.01, ***P<0.001 (n=4-5, Kruskal-Wallis test with Dunn's post-test). (C) Immunostaining for CD44 and pSTAT3 was performed in both NTS treated groups to evaluate cell specific STAT3 activation. Representative image from *Pod-Cre Klf4$^{flox/flox}$* mice is shown. Arrowheads demonstrate co-expression of nuclear pSTAT3 with CD44.

Supplemental Figure 3



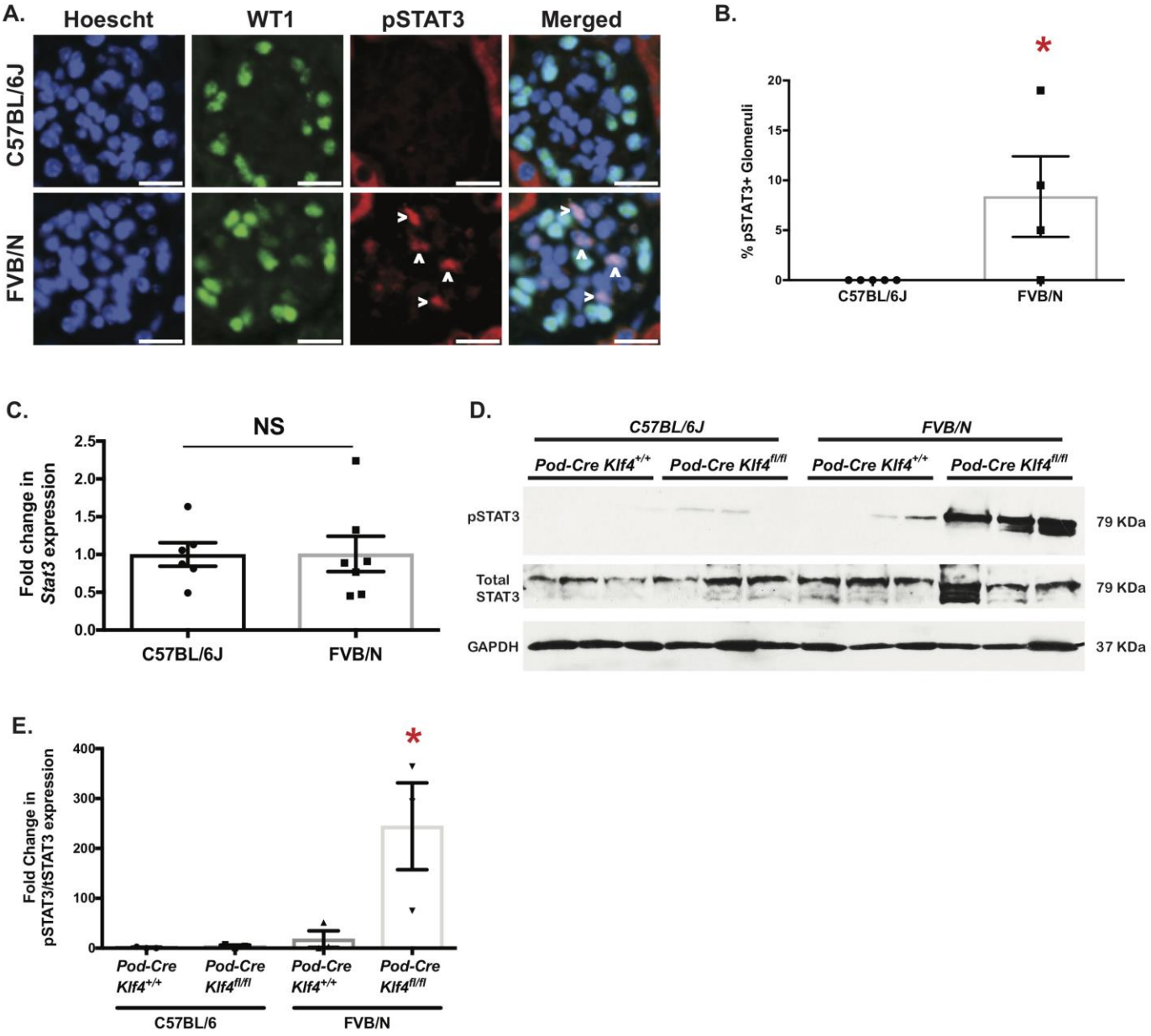
Supplemental Figure 3: Characterization of *Pod-Cre Klf4*$^{flox/flox}$ (FVB/N) mice at 3 to 12 weeks of age. (A) Urine was collected from *Pod-Cre Klf4*$^{flox/flox}$ (FVB/N) mice weekly, from 3 to 12 weeks of age. Inset shows the minor changes in albuminuria from 3 to 6 weeks of age (*P<0.05, **P<0.01, ***P<0.001 compare to 3 weeks of age, (n=10-16, Mann-Whitney test). Then, *Pod-Cre Klf4*$^{flox/flox}$ (FVB/N) and *Pod-Cre Klf4*$^{+/+}$ (FVB/N) were sacrificed at 6 weeks of age and serum was collected and RNA extracted from renal cortex for real-time PCR. (B) Serum Creatinine were measured at 6 weeks of age (n=3, Mann-Whitney test). **(C)** *Nephrin* and *Synaptopodin* mRNA expression from renal cortex is also shown (n=3-4, Mann-Whitney test).

Supplemental Figure 4



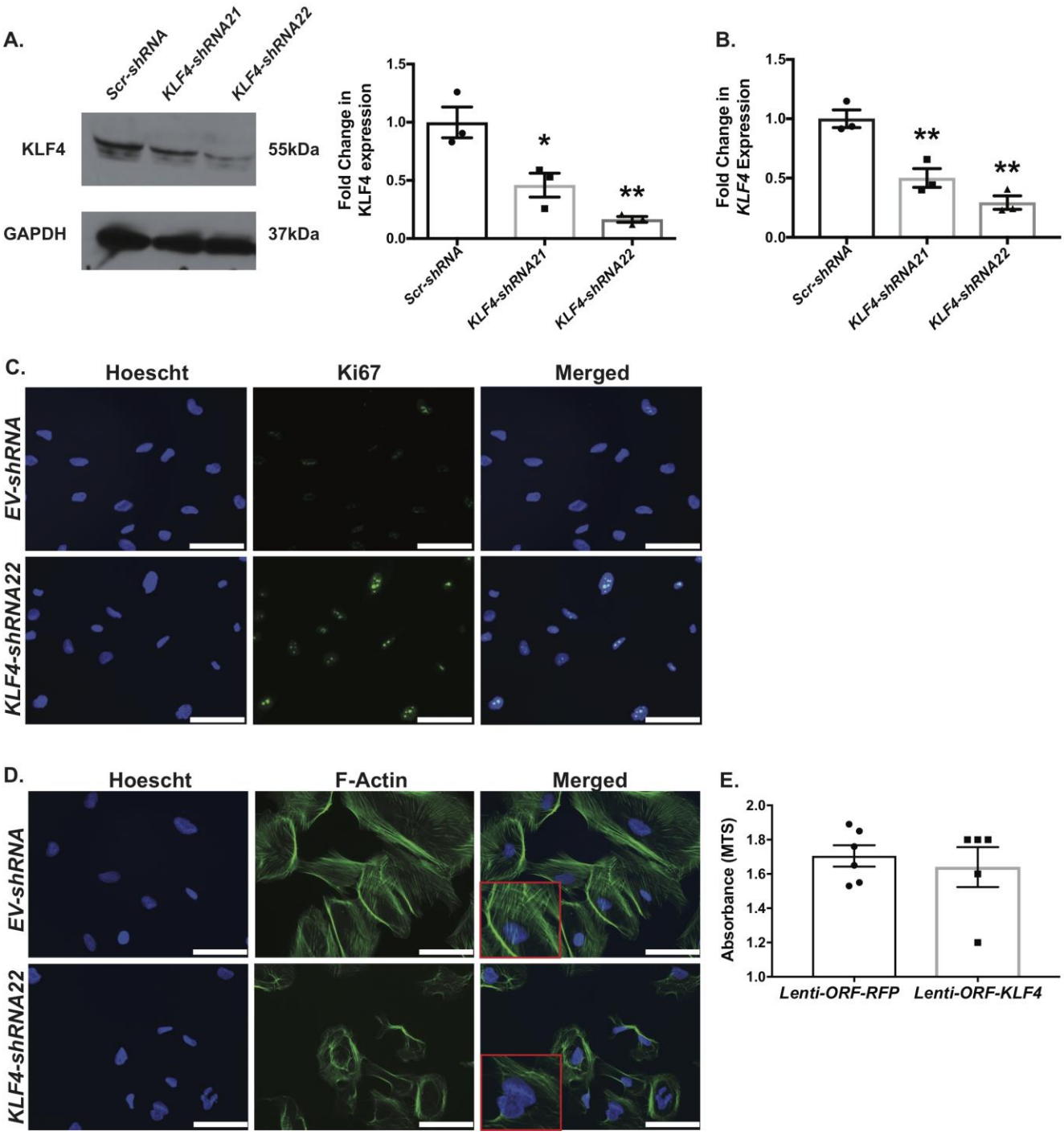
Supplemental Figure 4: Parietal Cell Activation in *Podocin-Cre Klf4$^{flox/flox}$* (FVB/N) Mice. (A) Immunostaining for CD44 was performed in *Podocin-Cre Klf4$^{+/+}$* and *Podocin-Cre Klf4$^{flox/flox}$* mice. The glomerular region was selected and percent CD44 area stained was measured. (Magnification (X20), n=5-7, *P<0.05, Mann-Whitney test). (B) Immunostaining for CD44 and pSTAT3 was performed to evaluate cell specific STAT3 activation in *Podocin-Cre Klf4$^{flox/flox}$* mice. Arrowheads demonstrate co-expression of nuclear pSTAT3 with CD44.

Supplemental Figure 5



Supplemental Figure 5: Wildtype FVB/N mice exhibit increased STAT3 activation as compared with wildtype C57BL/6J mice. FVB/N and C57BL/6J wildtype mice were sacrificed at 12 weeks and renal cortex fixed for immunostaining. (A) Representative images of immunostaining for phospho-STAT3 (pSTAT3) and WT1 in glomeruli are shown. Arrowheads indicate co-localization of pSTAT3 and WT1 (Magnification X20). (B) Percent of glomeruli with nuclear pSTAT3 staining was determined (n=4-5 in each group, 20 glomeruli per mouse) (*P<0.05, Mann-Whitney test). (C) *Stat3* mRNA expression from isolated glomerular fractions is also shown (n=7, Mann-Whitney test). (D) Western blot for pSTAT3, total-STAT3, and GAPDH was performed from total kidney cortex isolated from *Podocin-Cre Klf4*$^{+/+}$ and *Podocin-Cre Klf4*$^{flox/flox}$ FVB/N and C57BL/6J mice. Representative blots from three independent experiments are shown. (E) Quantification of pSTAT3 to total-STAT3 expression by densitometry is shown (n=3, *p<0.05, Mann-Whitney test).

Supplemental Figure 6



Supplemental Figure 6: shRNA-mediated *KLF4* knockdown podocytes exhibit increased cell-cycle entry. ShRNA-mediated *KLF4* knockdown was performed in human podocytes. (A) Protein was extracted and western blot analysis for KLF4 was performed. The representative blot from three independent experiments is shown. The right panel shows the quantification of KLF4 by densitometry (n=3, *P<0.05, **P<0.01, (Kruskal-Wallis test with Dunn's post-test). (B) RNA was extracted and real-time PCR was performed for *KLF4* mRNA expression (n=4, **p<0.01, (Kruskal-Wallis test with Dunn's post-test)). (C) Immunofluorescence was performed for Ki67 in *EV-shRNA* and *KLF4-shRNA22* podocytes on day 3 of differentiation. Representative images are shown. (X20) (D) To depict bi-nucleated podocytes and change in actin stress-fiber formation, immunofluorescence was performed for Hoechst and Phalloidin in *EV-shRNA* and *KLF4-shRNA22* podocytes on day 3 of differentiation (X20). Inset shows higher magnification (X60). (E) Immortalized mouse parietal epithelial cells were differentiated for 14 days and treated with the supernatant from *LentiORF-RFP* and *LentiORF-KLF4* podocytes respectively, cell proliferation was measured with MTS assay (n=5-6, Mann-Whitney test).

Supplementary Table 1: Primer Sequences for Real-Time PCR

Gene	Forward primer	Reverse primer
Mouse *Socs3*	ATGGTCACCCACAGCAAGTTT	TCCAGTAGAATCCGCTCTCCT
Mouse *Icam-1*	GTGATGCTCAGGTATCCATCCA	CACAGTTCTCAAAGCACAGCG
Mouse *Il-6*	CAAAGCCAGAGTCCTTCAGAG	GCCACTCCTTCTGTGACTCC
Mouse *Stat3*	CTACTGCGCTTCAGCGAGAGCAGC	GTCTTCAGGTACGGGGCAGCAC
Mouse *Nephrin*	GTGCCCTGAAGGACCCTACT	CCTGTGGATCCCTTTGACAT
Mouse *Synpo*	CTTTGGGGAAGAGGCCGATTG	GTTTTCGGTGAAGCTTGTGC
Mouse *Wt1*	GAGAGCCAGCCTACCATCC	GGGTCCTCGTGTTTGAAGGAA
Mouse *Klf4*	GAAGGTCGTGGCCCCGGAAA	TCAGTTCATCGGAGCGGGCG
Human *KLF4*	TTACGCGGGCTGCGGCAAAAC	GGCGGTGCCCCGTGTGTTTAC
Human *IL-6*	GGTACATCCTCGACGGCATCT	GTGCCTCTTTGCTGCTTTCAC
Human p57	AGATCAGCGCCTGAGAAGTC	GGGACCAGTGTACCTTCTCG