SUPPLEMENTARY DATA

Supplementary Table 1. Blood glucose, kidney and body weight measurements

Blood glucose	***Pod-Cre Klf6*$^{+/+}$**	***Pod-Cre Klf6*$^{+/+}$ + STZ**	***Pod-Cre Klf6*$^{fl/fl}$**	***Pod-Cre Klf6*$^{fl/fl}$ + STZ**
4 weeks (mg/dl)	119 ± 10	368 ± 40**	125 ± 3	386 ± 23**
6 weeks (mg/dl)	110 ± 15	413 ± 41**	114 ± 8	430 ± 44**
12 weeks (mg/dl)	96 ± 1	369 ± 48**	99 ± 3	401 ± 37**
Kidney Weight (g)	0.26 ± 0.02	0.21 ± 0.01	0.22 ± 0.02	0.32 ± 0.02#
Body Weight (g)	31.29 ± 0.91	27.31 ± 0.62	33.53 ± 1.33	29.67 ± 1.18

Values are mean ± SEM; n=12, blood glucose: **P<0.01 versus untreated mice; kidney weight: #P<0.01 versus all other groups; Kruskal-Wallis test.

Supplementary Table 2. Baseline Characteristics

Characteristics	**Controls, (N=12)**	**Early-stage DKD, (N=7)**	**Late-stage DKD, (N=17)**
Males/Females (n/n)	8/4	4/3	9/8
Age at time of bx (yrs)	64, 54-75	59, 42-69	62, 46-68
Average eGFR (ml/min/1.73m^2) (At time of biopsy)	87, 74-102	72, 70-77	26, 19-36**
HbA1c (%)	-	7.1, 6.6-8.3	6.6, 6.3-9.1
BMI (kg/m^2)	24, 21-38	32, 25-33	31, 29-35
Concurrent HTN, SBP>140/90 (%)	69%	86%**	94%**

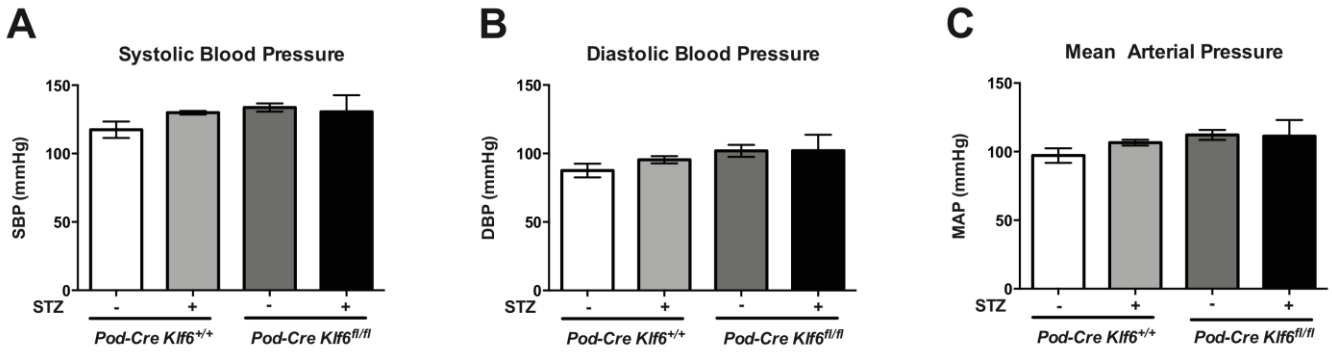
Median, interquartile range (25th to 75th percentile) shown for non-normal distribution of continuous variables (Kruskal–Wallis with Dunn post-test). Frequencies are shown for categorical variables (chi-squared test). —, not available; eGFR, estimated glomerular filtration rate (calculated using the Chronic Kidney Disease Epidemiology Collaboration equation); HbA1c, glycated hemoglobin; BMI, body mass index; SBP, systolic blood pressure; **p<0.01 as compared to control specimens.

SUPPLEMENTARY DATA

Supplementary Table 3. Primer Sequences for Real-Time PCR

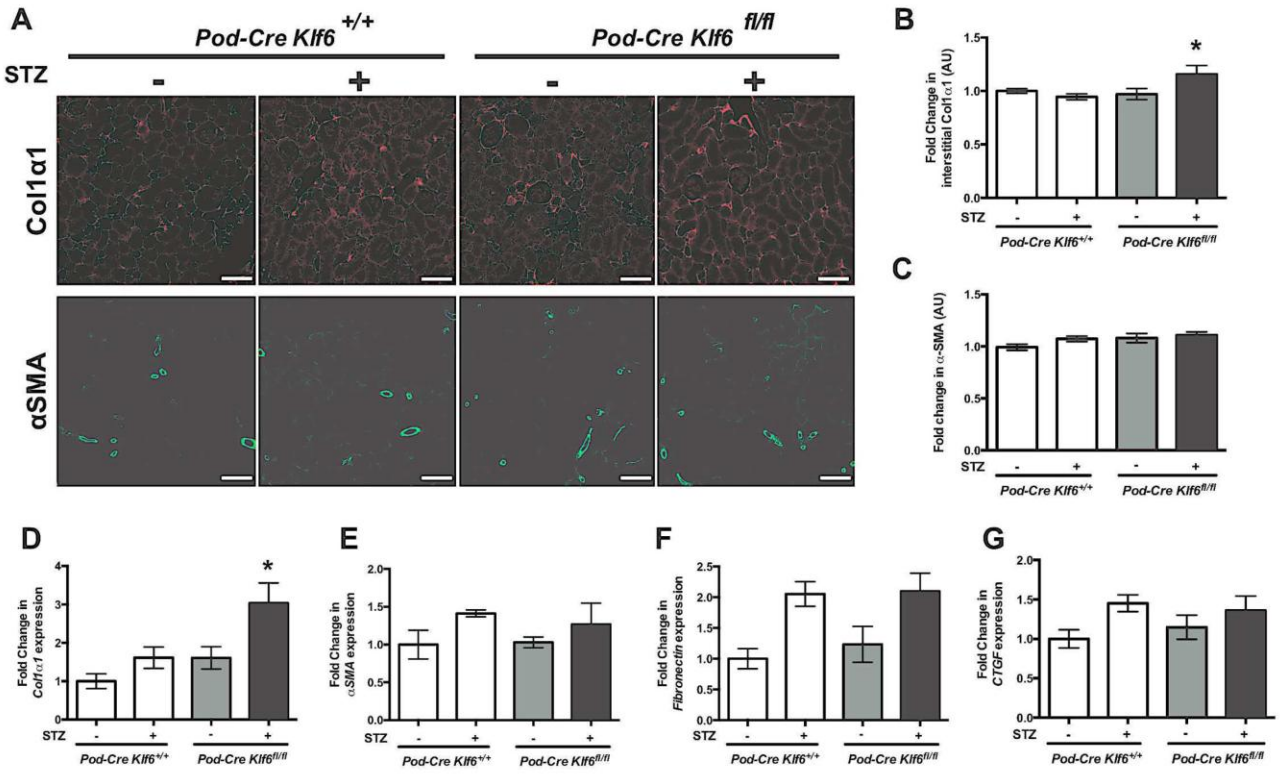
Gene	Forward primer	Reverse primer
Fibronectin	ATGGTACAGCTGATCCTGCC	GCCCTGGTTTGTACCTGCTA
Col1a1	GGGTCCCTCGACTCCTACAT	CCCGAGGTATGCTTGATCTG
α-Sma	GAGGCACCACTGAACCCTAA	CATCTCCAGAGTCCAGCACA
CTGF	CTGACCTGGAGGAAAACATTA	TTAGCCCTGTATGTCTTCACAC
Gapdh	GCCATCAACGACCCCTTCAT	ATGATGACCCGTTTGGCTCC
β-actin	GTTCCGATGCCCTGAGGCTCTT	CGTCACACTTCATGATGGAATTGA

Supplementary Figure 1. Mice show no significant changes in blood pressure. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were measured on conscious mice before being sacrificed. Measurements for **(A)** SBP, **(B)** DBP, and **(C)** MAP are shown (n = 6 per group).



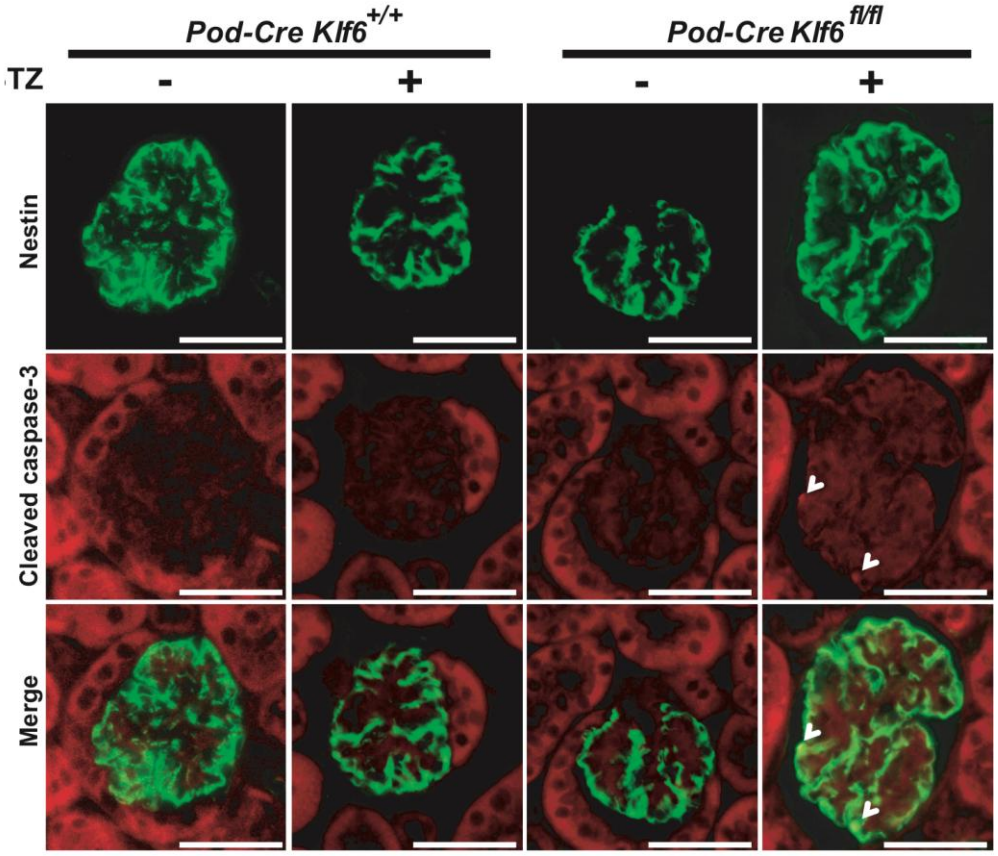
SUPPLEMENTARY DATA

Supplementary Figure 2. Measurement of interstitial fibrotic markers in *Podocin-Cre Klf6*$^{+/+}$ and *Podocin-Cre Klf6*$^{flox/flox}$ mice with and without diabetes. (A) Immunofluorescence staining for collagen 1α1 (Col1α1) alpha smooth muscle actin (α-SMA) was performed and representative images are shown. Quantification of changes by ImageJ is shown for **(B)** Col1α1 and **(C)** α-SMA expression. N=20 glomeruli per mouse, n=6 mice per group. Real-time PCR of mRNA extracted from renal cortex from all groups was performed for **(D)** *Col1α1*, **(E)** *α-SMA*, **(F)** *Fibronectin*, and **(G)** *CTGF* expression. n=6, *P<0.05, Kruskal-Wallis test with Dunn's post-test.



SUPPLEMENTARY DATA

Supplementary Figure 3. Diabetic *Podocin-Cre Klf6*$^{flox/flox}$ mice exhibit increased cleaved caspase-3 staining in podocytes. Immunofluorescence staining for nestin and cleaved caspase-3 staining was performed and representative images are shown (n=6 mice per group).



SUPPLEMENTARY DATA

Supplementary Figure 4. *KLF6* knockdown and overexpression human podocytes were treated under mannitol conditions. (A) Differentiated *EV-shRNA* and *KLF6-shRNA* human podocytes were initially treated under mannitol conditions for 7 days. Western blot for cleaved caspase-3 was performed and representative image of three independent experiments is shown. **(B)** Differentiated *lentiORF-KLF6* and *lentiORF-control* human podocytes were initially treated under mannitol conditions for 14 days. Western blot for cleaved caspase-3 was performed and representative image of three independent experiments is shown.