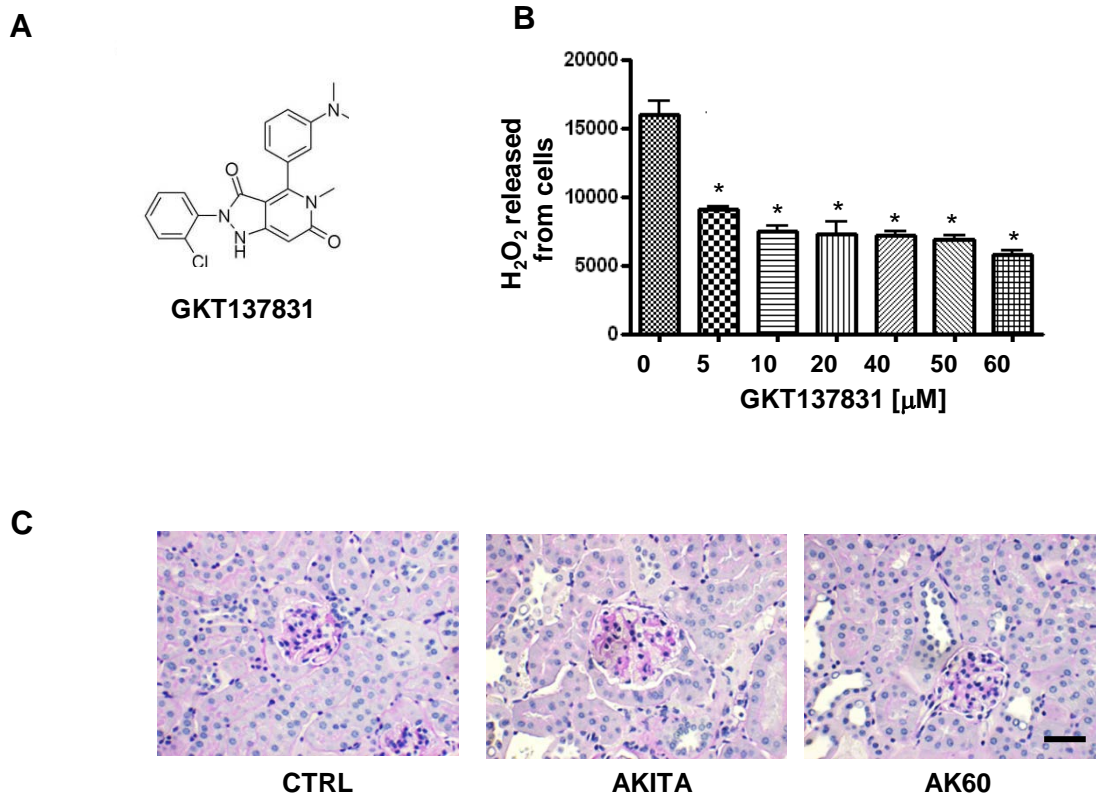


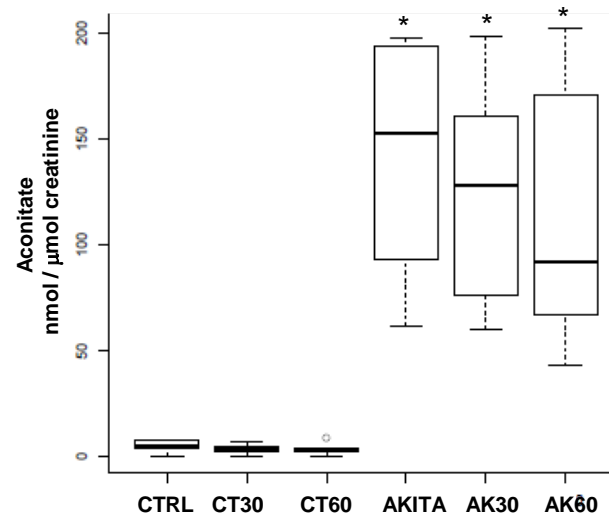
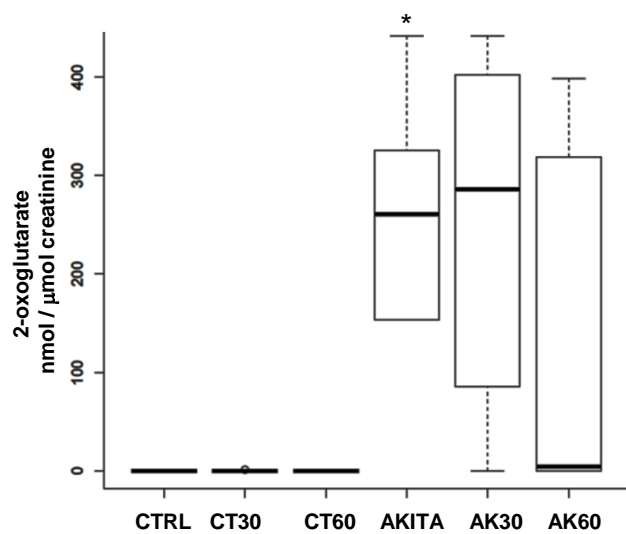
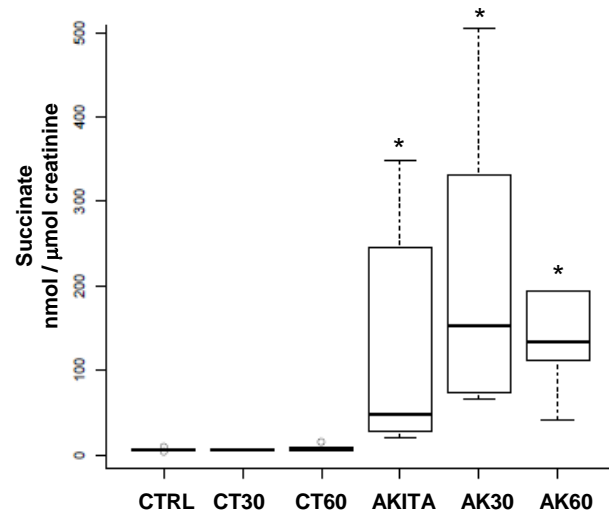
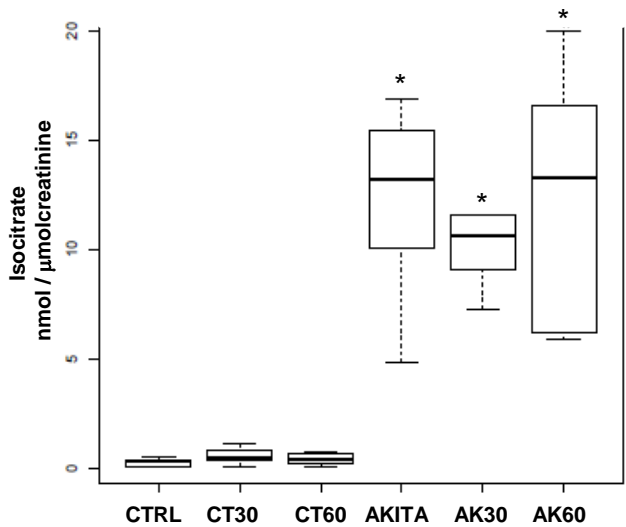
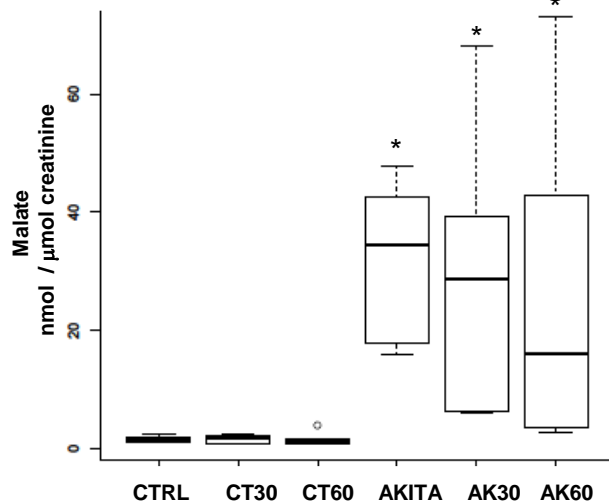
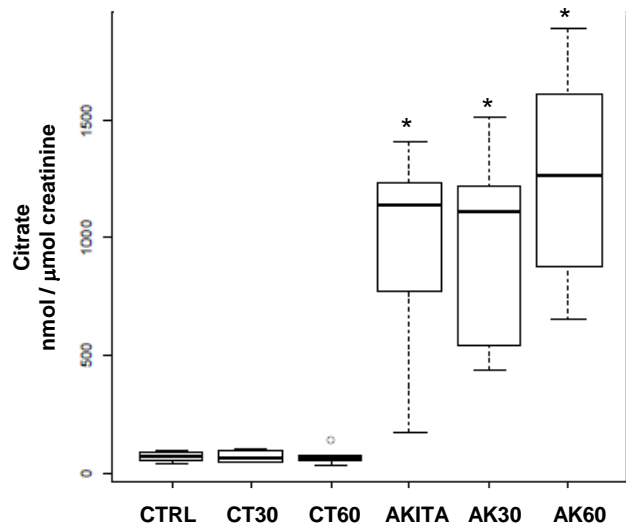
## Supplemental Figure 1.



## Supplemental Figure 1.

NOX4 inhibitor GKT137831 in rtTA-293 cells expressing NOX4 and F1 Akita diabetic mice. (A) Chemical structure of GKT137831. (B) Cellular  $\text{H}_2\text{O}_2$  levels in rtTA-293 cells stably expressing HA-NOX4 with the indicated concentration GKT137831 for 4h after 2  $\mu\text{g/ml}$  doxycycline for 24 h. (C) PAS staining of F1 control mice treated with vehicle (CTRL), F1 Akita mice treated with vehicle (AKITA) or 60mg/kg/day GKT137831 (AK60). Scale bar, 50  $\mu\text{m}$ .

## Supplemental Figure 2.



## Supplemental Figure 2.

Box-plots of metabolite analysis in F1 Akita diabetic urine after 16 weeks treatment with NOX4 inhibitor, GKT137831. TCA cycle intermediates such as citrate, malate, Isocitrate, succinate, 2-oxoglutarate and aconitate increased in the diabetic F1 Akita mice compared with the control mice, however they did not significantly reduce with the NOX1/4 inhibitor in a dose-dependent manner. F1 control mice treated with vehicle (CTRL), 30mg/kg/day (CT30), or 60mg/kg/day GKT137831 (CT60), F1 Akita diabetic mice treated with vehicle (AKITA), 30mg/kg/day (AK30), or 60mg/kg/day GKT137831 (AK60). Metabolite level is expressed as nmole metabolite/ $\mu$ mole creatinine.  $n=5-6$  per group,  $*P < 0.05$  vs. F1 controls, lines: median.

## Supplemental Table 1

Physiological characteristics of podocyte specific NOX4Tg mice after doxycycline treatment for 5 weeks.

Mice	Treatment Doxycycline	Number	Body Weight (g)	Blood Glucose (mg/dl)	Kidney /BW %
Control	5 weeks	7	27.73±7.70	157.2±0.5	0.82±0.09
NOX4 TG	5 weeks	8	29.88±6.62	194.8±31.6	0.88±0.05

## Supplemental Table 2

### Primers and Probes for real time q PCR

Primer Name	Forward	Reverse	Probe
Mouse Hif1 $\alpha$	CAT CTG ACC AAA ACT CAC CAT G	ATC CAC CTC TTT TGG CAA GCA	AG GAC AAG TCA CCA CAG GAC AGT ACA G Q
Mouse Fumarase	GAG AGC TGA TCT TGC CTG AA	ACA CTG AGT AGG GTT CAC CT	FCT GGC ATG ATG CTG CTC CCT GGC Q
Mouse PGC1 $\alpha$	TGA TAA ACT GAG CTA CCC TTG	ACA CTG AGT CTC GAC ACG G	FCA TTG TTC GAT GTG TCG CCT TCT TGC Q
Mouse TGF $\beta$ 1	TGC TTC AGC TCC ACA GAG AA	GTG GAT CCA CTT CCA ACC CA	FCC TTC CTA AAG TCA ATG TAC AGC TGC CG Q
Mouse 18S	AGA AAC GGC TAC CAC ATC CA	CTC GAA AGA GTC CTG TAT TGT	FAG GCA GCA GGC GCG CAA ATT AC Q
Mouse $\beta$ -Actin	CTG CCT GAC GGC CAG GTC	CAA GAA GGA AAGG CTG GAA AAG A	FCA CTA TTG GCAACG AGC GGT TCC G Q
Human Hif1 $\alpha$	CAT CTG ACC AAA ACT CAT CAT G	ATC CAC CTC TTT TGG CAA GCA	FAG GAC AAG TCA CCA CAG GAC AGT ACA G Q
Human Fumarase	GGA GAA TTG ATC TTG CCT GAA	ACACTG AGT AGG GTT CAC CT	FCC TGG CAT GAT ACT GCT TCC TGG TTC Q
Human TGF $\beta$ 1	TGC TTC AGC TCC ACG GAG AA	GTG GAT CCA CTT CCA GCC GA	FCC TTG CGG AAG TCA ATG TAC AGC TGC C Q
Human 18S	AGA AAC GGC TAC CAC ATC CA	CTC GAA AGA GTC CTG TAT TGT	FAG GCA GCA GGC GCG CAA ATT AC Q
Human $\beta$ -Actin	GGT CAT CAC CAT TGG CAA TG	TAG TTT CGT GGA TGC CAC AG	FCA GCC TTC CTT CCT GGG CAT GGA Q
Human CHOP	CTG GAA ATG AAG AGG AAG AAT C	TGG TTC TGG CTC CTC CTC A	FTC ACC ACT CTT GAC CCT GCT TCT CTG Q
Human GRP78	GCT TCT GAT AAT CAA CCA ACT G	TGT ACC CAG AAG ATG ATT GTC	FAG GTC TAT GAA GGT GAA AGA CCC CTG Q
Human $\alpha$ -SMA	ACC CAG CAC CAT GAA GAT CA	GGA TGG AGC CAC CGA TCC A	FTT GCC CCT CCG GAG CGC AAA TAC Q
Human Fibronectin	TGC ACA TGC TTT GGA GGC CA	AGT AGT GCC TTC GGG ACT G	FTG GCG CTG TGA CAA CTG CCG CAG AQ
Human Col 1A1	AAC AGC CGC TTA ACC TAC AG	TCA ATC ACT GTC TTG CCC CA	FTC GAT GGC TGC ACG AGT CAC ACC GQ