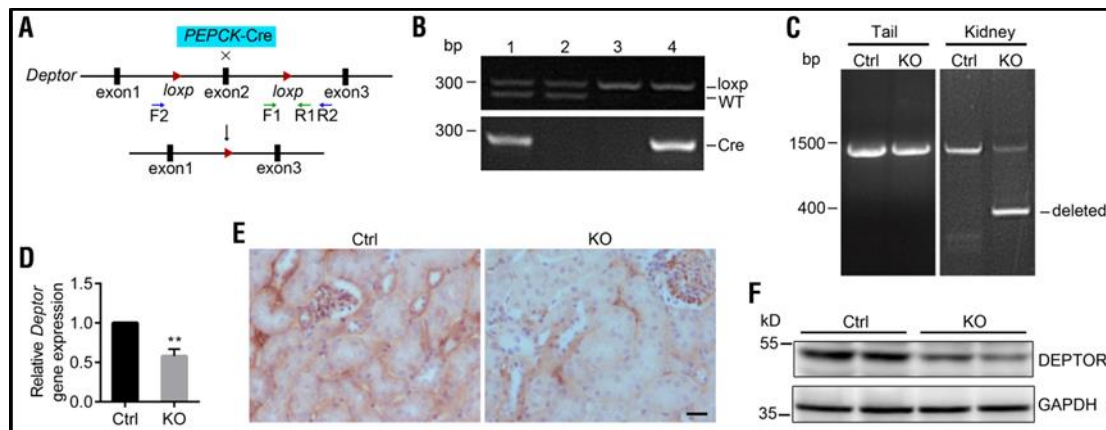
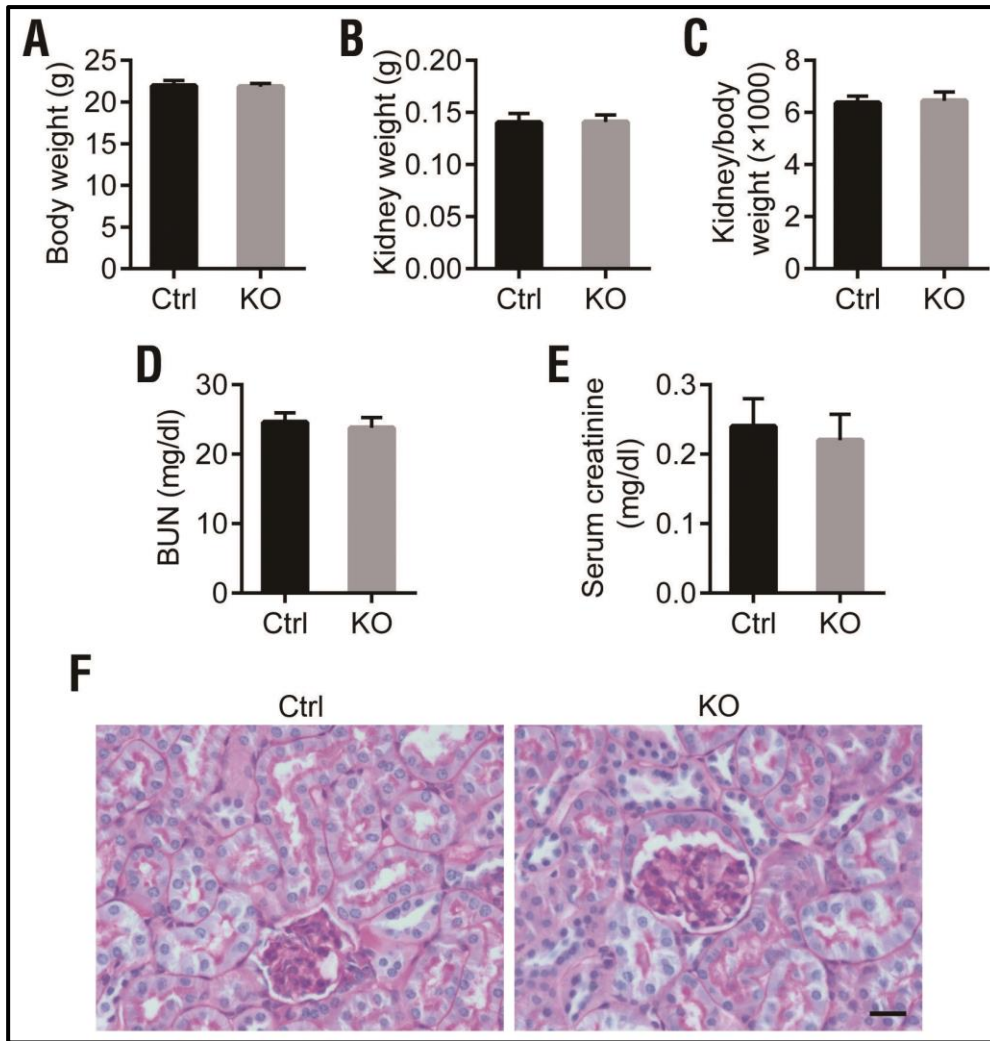


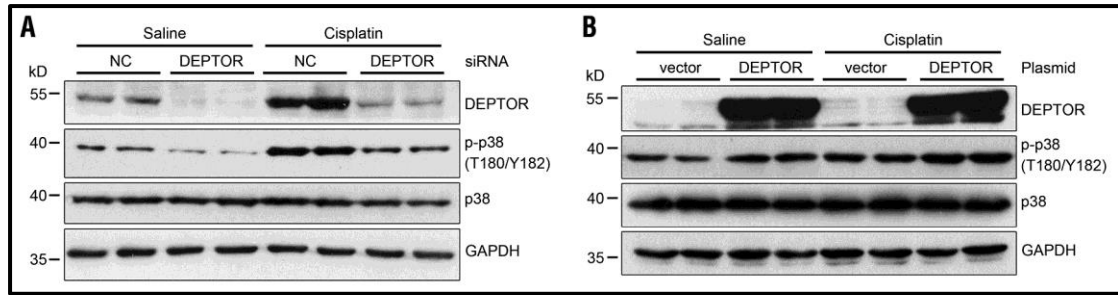
## Supplemental Materials



**Supplemental Figure 1. Generation of mice with *DEPTOR* specifically deleted in renal proximal tubules.** (A) Strategy for the production of *DEPTOR* cKO mice. *DEPTOR* flox mice were crossed with *PEPCK-Cre* mice to produce *DEPTOR* KO mice, in which the second exon of *DEPTOR* gene was deleted. F1/F2: forward primers for PCR identification, R1/R2: reverse primers for PCR identification. (B) Genotyping the F2 offspring by PCR with primers F1/R1 after mating the transgenic mice. M: DNA marker. (C) Identification of gene deletion in renal genomic DNA by PCR with primers F2/R2. Tail genomic DNA was used as the endogenous control. (D) qPCR analysis showed *DEPTOR* mRNA levels in the renal cortex of KO mice were obviously reduced compared with control mice. Data are expressed as mean values  $\pm$  SEM ( $n = 5$ ).  $**P < 0.01$ . (E) IHC staining showed *DEPTOR* expression was significantly reduced in renal proximal tubules of *DEPTOR* KO mice compared with control mice. Scale bar = 20  $\mu$ m. (F) Western blotting analysis showed *DEPTOR* expression in the renal cortex of KO mice was decreased.



**Supplemental Figure 2. Normal renal functions and histology in *DEPTOR* KO mice under physiological conditions.** No significant difference was observed in bodyweight (A), kidney weight (B), kidney/body weight ratio (C), BUN (D), or serum creatinine (E) between *DEPTOR* KO and control (Ctrl) mice. BUN and creatinine were measured with the IDEXX Catalyst Chemistry Analyzer. (F) Kidney histology of paired mice detected with PAS staining. Mice were 8-12 weeks old. Scale bar = 20  $\mu\text{m}$ . Bars indicate mean values  $\pm$  SEM.  $n = 8$ .



**Supplemental Figure 3. DEPTOR regulates p38 MAPK activity in HEK293 cells.**

(A) Immunoblotting showed that *DEPTOR* knockdown by siRNA inhibited p38 MAPK activity in HEK293 cells, with or without cisplatin treatment. In the cisplatin group, cells were incubated with 20  $\mu$ M cisplatin for 24 h, the same below. (B) Immunoblotting showed that *DEPTOR* overexpression enhanced p38 MAPK activity in HEK293 cells.

**Supplemental Table 1. Primers used for experiments**

Gene	Forward primers(5'-3')	Reverse primers(5'-3')
<i>DEPTOR</i> - <i>F1/R1</i>	GGAAGTGAAGACCTGTGAAGA TAAGAG	CAGTCTAGAAAAGCAGATAACC CAAGTA
<i>DEPTOR</i> - <i>F2/R2</i>	CGTCGAGAAGTTCCTATTCCGA AG	GTGTGCCATTGAAATTTGTTACC AT
<i>PEPCK</i> -Cre	GCATAACCAGTGAAACAGCATT GCTG	GGACATGTTCAGGGATCGCCAG GCG
<i>DEPTOR</i> - qPCR	AGCAGAGAGAGCTGGAACGC	CAGAGGCCTCCTTATGTTCA
<i>Mouse Kim1</i>	ATGCCCATCTTCTGCTTGTC	CCTTGTAGTTGTGGGTCTTCT
<i>Mouse NGAL</i>	TGGCCCTGAGTGTCATGTG	CTCTTGAGCTCATAGATGGTGC
<i>Mouse TNF<math>\alpha</math></i>	CCTGTAGCCACGTCGTAG	GGGAGTAGACAAGGTACAACCC
<i>Mouse Gapdh</i>	TGTGTCCGTCGTGGATCTGA	TTGCTGTTGAAAGTCGCAGGA
<i>Human TNF<math>\alpha</math></i>	CCTCTCTCTAATCAGCCCTCTG	GAGGACCTGGGAGTAGATGAG
<i>Human Gapdh</i>	ACAACCTTGGTATCGTGGAAGG	GCCATCACGCCACAGTTTC

**Supplemental Table 2. Antibodies used for experiments**

Antibody	Vendor	Catalog number	Application	Working dilution for WB or (IF/IHC)
Rabbit anti-DEPTOR	Cell Signaling Technology	11816	WB	1:2000
Mouse anti-DEPTOR	Santa Cruz Biotechnology	sc-398169	WB,IHC	1:2000 (1:100)
Rabbit anti-p-S6 (S235/236)	Cell Signaling Technology	4858	WB, IHC,IF	1:2000 (1:200)
Mouse anti-S6	Santa Cruz Biotechnology	sc-74459	WB	1:2000
Rabbit anti-p-Akt (S473)	Santa Cruz Biotechnology	sc-7985-R	WB	1:2000
Mouse anti-Akt	Cell Signaling Technology	2920	WB	1:2000
Rabbit anti-p-p38(T180/Y182)	Cell Signaling Technology	4511	WB	1:2000
Rabbit anti-p38	Cell Signaling Technology	8690	WB	1:2000
Rabbit anti-Ki67	Cell Signaling Technology	9129	IF	1:200
Rabbit anti-PARP	Cell Signaling Technology	9532	WB	1:500
Rabbit anti- GAPDH	Sungene	KM9002T	WB	1:5000
Rabbit anti-p-ERK1/2(T202/Y204)	Cell Signaling Technology	4370	WB	1:2000
Rabbit anti-ERK1/2	Cell Signaling Technology	4695	WB	1:2000
Rabbit anti-p-JNK(T183/Y185)	Cell Signaling Technology	4668	WB	1:2000
Rabbit anti-JNK	Cell Signaling Technology	8690	WB	1:2000
Rabbit anti-p53	Abclonal	A3185	WB	1:2000
Mouse anti-F4/80	Santa Cruz Biotechnology	sc-377009	IF	1:50

**Supplemental Table 3.** List of 46 genes with significant alteration in the mRNA level in the renal cortex of the *DEPTOR*-cKO mice vs that of the control mice under physiological condition by transcriptomic sequencing and screening assay.

Gene	log <sub>2</sub> (Fold change)	Description
Cyp2b10	-4.01	cytochrome P450, family 2, subfamily b, polypeptide 10
Ccl28	-3.68	chemokine (C-C motif) ligand 28
Rnf180	-3.41	ring finger protein 180
Rn7sk	-3.25	RNA, 7SK, nuclear
Rmrp	-3.02	RNA component of mitochondrial RNAase P
Hsd11b1	-2.81	hydroxysteroid 11-beta dehydrogenase 1
Ctxn3	-2.80	cortixin 3
Slco1a1	-2.73	solute carrier organic anion transporter family, member 1a1
Srd5a2	-2.61	steroid 5 alpha-reductase 2
Acsm3	-2.59	acyl-CoA synthetase medium-chain family member 3
Cyp4a12a	-2.56	cytochrome P450, family 4, subfamily a, polypeptide 12a
Rpph1	-2.48	ribonuclease P RNA component H1
Hapln1	-2.36	hyaluronan and proteoglycan link protein 1
Kif20b	-2.34	kinesin family member 20B
Eri2	-2.32	exoribonuclease 2
Pik3c2g	-2.29	phosphatidylinositol 3-kinase, C2 domain containing, gamma polypeptide
Mir6236	-2.25	microRNA 6236
Hprt	-2.17	hypoxanthine guanine phosphoribosyl transferase
Zpld1	-2.16	zona pellucida like domain containing 1
Mfsd2a	-1.97	major facilitator superfamily domain containing 2A
Odc1	-1.96	ornithine decarboxylase, structural 1
Frzb	-1.93	frizzled-related protein
Ces2b	-1.87	carboxyesterase 2B
Slc22a7	-1.80	solute carrier family 22 (organic anion transporter), member 7
Lipo1	-1.72	lipase, member O1
Nr4a1	-1.70	nuclear receptor subfamily 4, group A, member 1
Azgp1	-1.66	alpha-2-glycoprotein 1, zinc
Il34	-1.66	interleukin 34
Egr1	-1.63	early growth response 1
Cxcl12	-1.57	chemokine (C-X-C motif) ligand 12
Ttbk1	-1.55	tau tubulin kinase 1
Cd36	-1.54	CD36 antigen
Ces2c	-1.35	carboxylesterase 2C
Tnfsf10	-1.26	tumor necrosis factor (ligand) superfamily, member 10

B4galt5	-1.26	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 5
C1qtnf3	-1.20	C1q and tumor necrosis factor related protein 3
Scd1	1.35	stearoyl-Coenzyme A desaturase 1
ApoE	1.39	apolipoprotein E
Pdk4	1.49	pyruvate dehydrogenase kinase, isoenzyme 4
Cish	1.49	cytokine inducible SH2-containing protein
Tma7	1.88	translational machinery associated 7
B4galnt1	1.94	beta-1,4-N-acetyl-galactosaminyl transferase 1
Kynu	2.30	kynureninase (L-kynurenine hydrolase)
Cyp4a14	2.76	cytochrome P450, family 4, subfamily a, polypeptide 14
Prlr	3.14	prolactin receptor
Gpr112	3.70	adhesion G protein-coupled receptor G4

**Supplemental Figure 4.** Network for protein interactions among the 46 genes.

