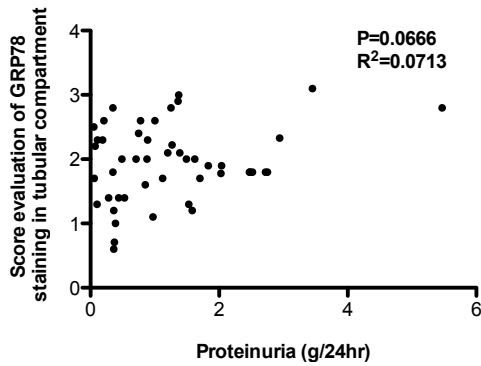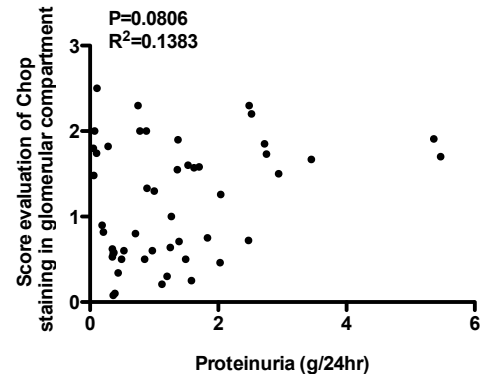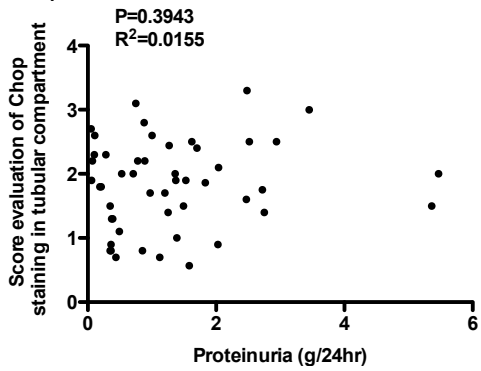**Supplementary Figure 1:** Renal function in patients with different stages of AKI. (A) Peak estimated glomerular filtration rate (eGFR) level in patients with AKI. (B) Peak serum creatinine (sCr) level in patients with AKI. (C) Nadir to Peak sCr level in patients with AKI.
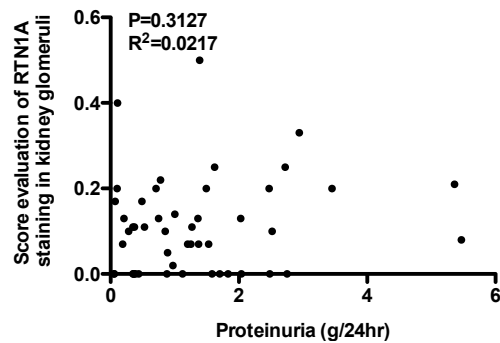
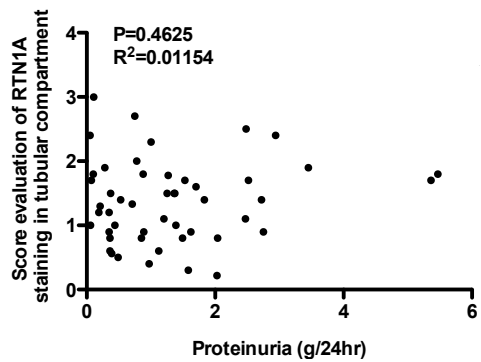**A** GRP78 expression

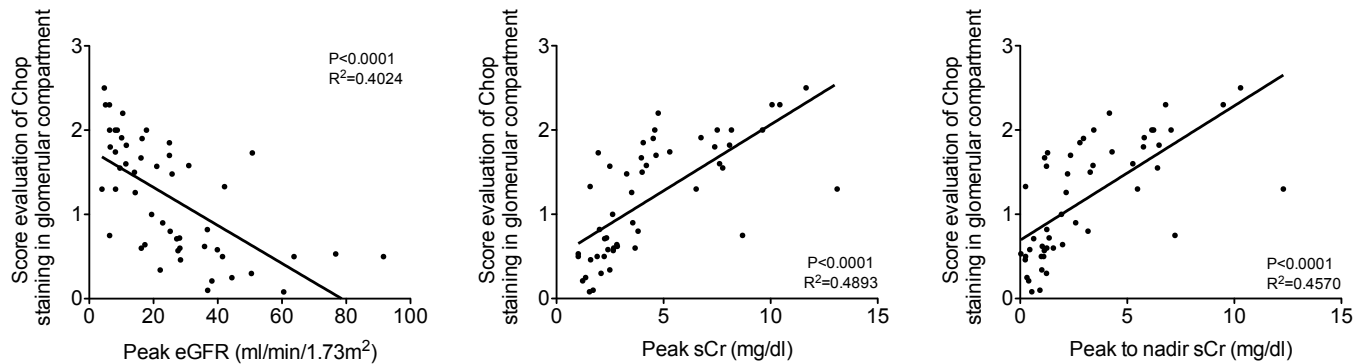**B** CHOP expression

C RTN1A expression

Supplementary Figure 2: No correlation was found between intensity of GRP78 (A), CHOP (B) and RTN1A (C) immunostaining in the tubular (left panels) or glomerular (right panels) compartment and proteinuria (g/24h) in patients with AKI. Pearson correlation analysis, P and R^2 values are indicated on the graph, n=51.

A Glomerular expression of p-PERK
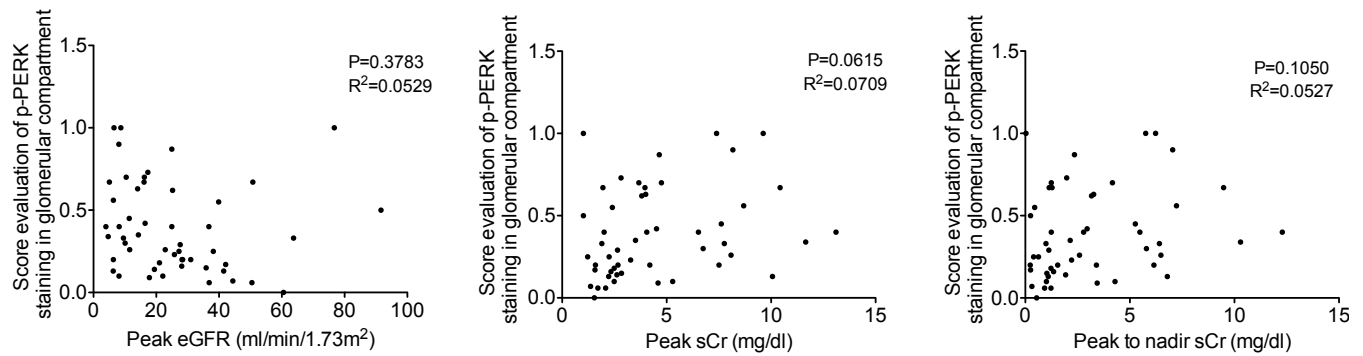
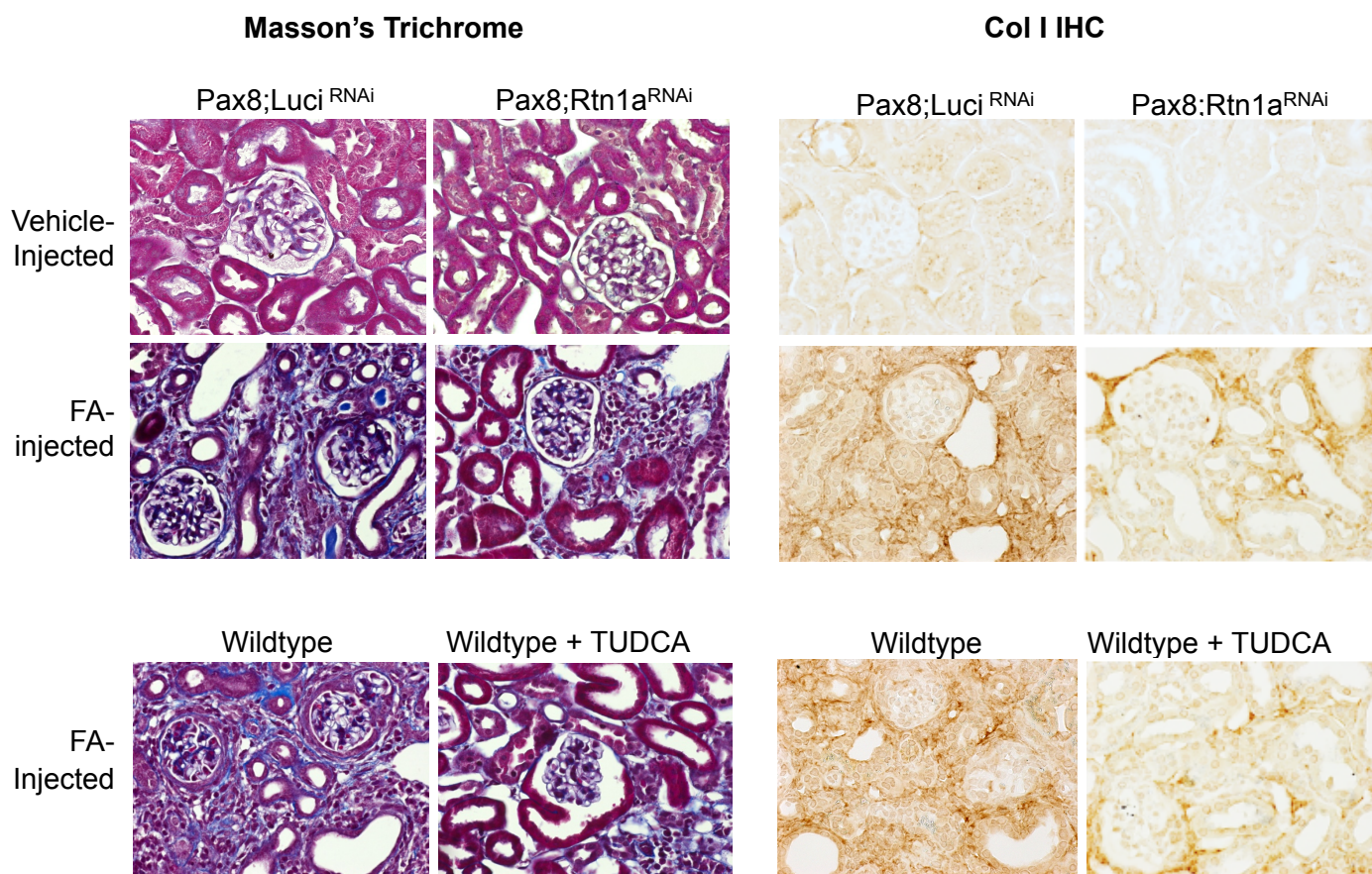**B** Glomerular expression of CHOP


C Glomerular expression of XBP-1s
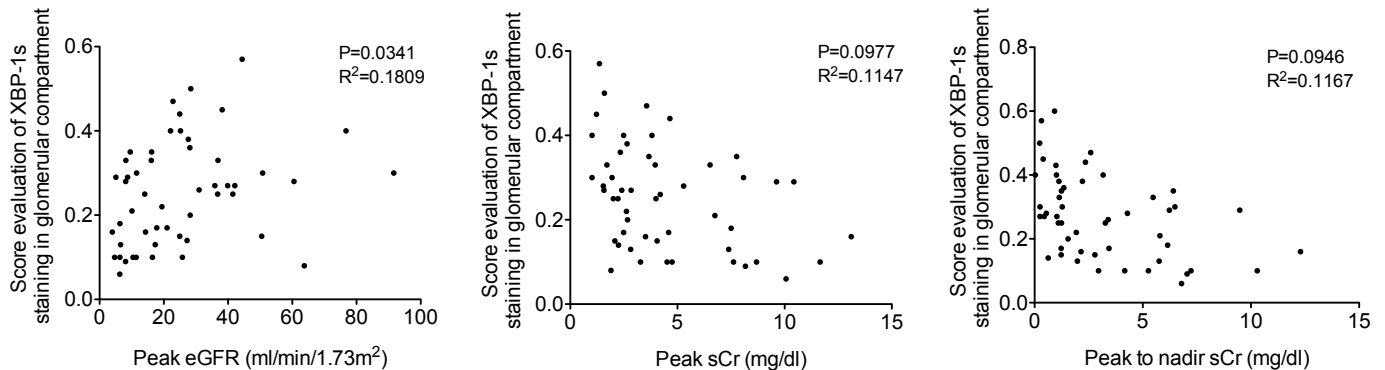
Supplementary Figure 3: Correlation between the intensity of p-PERK (A), CHOP (B) and XBP-1s (C) immunostaining in the glomerular compartment and renal function (peak eGFR, peak sCr, and peak to nadir sCr) was calculated in patients with AKI using Pearson analysis. P and R^2 are indicated on the graph, n=51.

Masson's Trichrome

Col I IHC

Pax8;Luci ^{RNAi}

Pax8;Rtn1a^{RNAi}

Pax8;Luci ^{RNAi}

Pax8:Rtn1a^{RNAi}

Vehicle-Injected

FA-injected

Wildtype

Wildtype + TUDCA

Wildtype

Wildtype + TUDCA

FA-Injected

Supplementary Figure 4: *Rtn1a* knockdown in renal tubular cells attenuated renal fibrosis in mice with FAN. Pax8;Rtn1a^{RNAi} and Pax8;Luci ^{RNAi} mice received either FA or vehicle injection after 3 weeks doxycycline (Dox) feeding, and Dox was withdrawn at day 7 after FA injection. Wildtype mice injected with FA were treated with TUDCA or vehicle starting at day 1 after FA injection and ended at day 7. Mice were sacrificed at either 3 days post-injection for assessing acute kidney injury or 4 weeks post-injection for renal fibrosis. Representative images of Masson's trichrome staining and Col I immunostaining of vehicle-injected and FA-injected mice are shown (n=5). Original magnification x400.
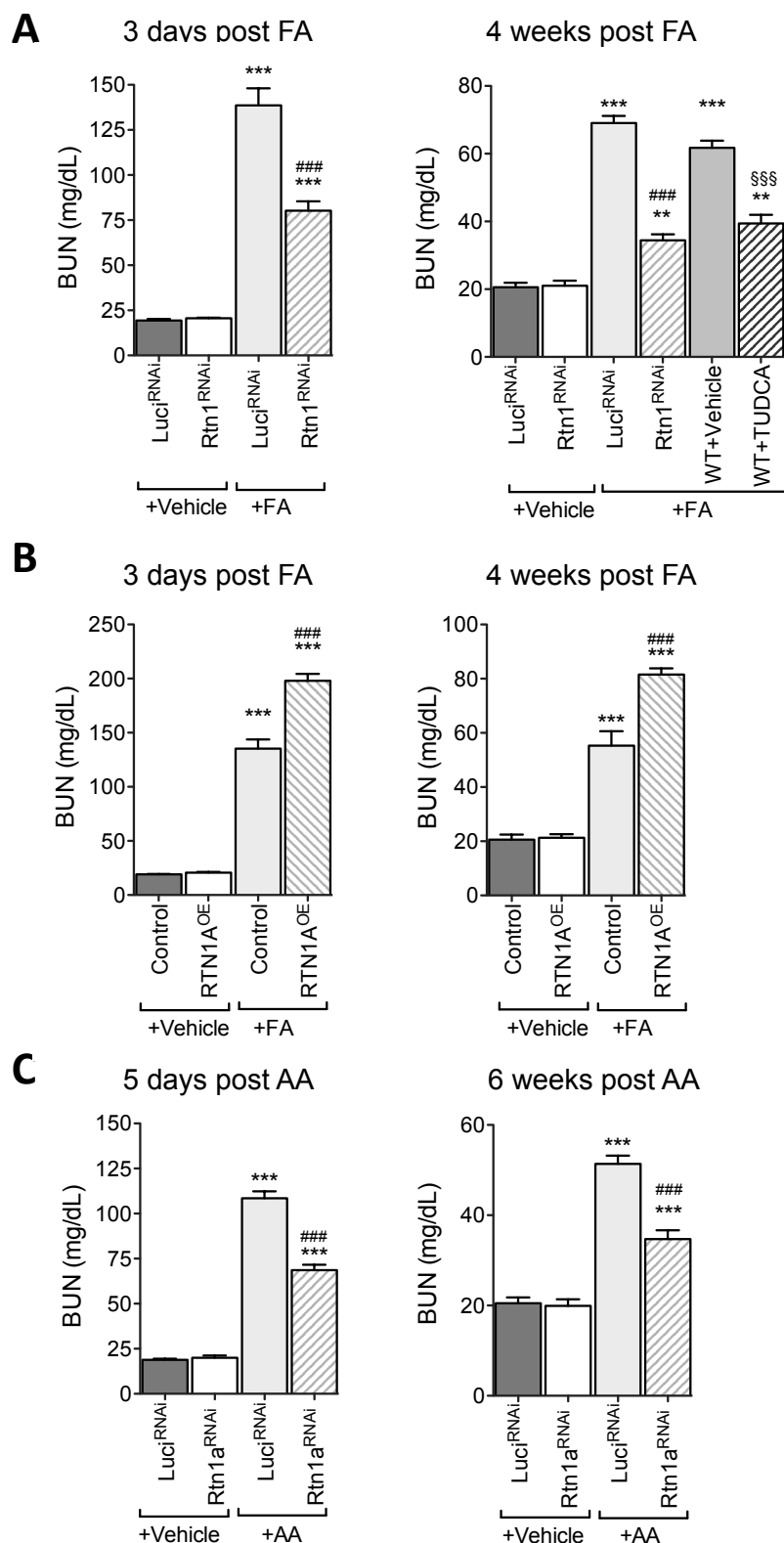
Supplementary Figure 5: Renal function was assessed by measuring BUN levels. (A) BUN levels in vehicle or FA-injected Pax8;Luci^{RNAi} and Pax8;Rtn1a^{RNAi} mice at 3 days or 4 weeks post injection. Vehicle or TUDCA-treated mice were also examined at 4 weeks post FA injection. **P<0.01 and ***P<0.001 compared to vehicle-treated control mice, ###P<0.001 compared to FA-treated Luci^{RNAi}, and §§§P<0.001 compared to vehicle-treated FA-injected wildtype mice   (n=5 in each group). (B) BUN levels in vehicle or FA-injected wildtype control and Pax8;RTN1A^{OE} mice. ***P<0.001 compared to vehicle-treated control mice, ###P<0.001 compared to FA-treated Pax8;RTN1A^{OE} mice (n=5 in each group). (C) BUN levels in vehicle or AA-injected Pax8;Luci^{RNAi} and Pax8;Rtn1a^{RNAi} mice at 5 days or 6 weeks post injection. and ***P<0.001 compared to vehicle-treated control mice, ###P<0.001 compared to AA-treated mice (n=5 in each group)

A
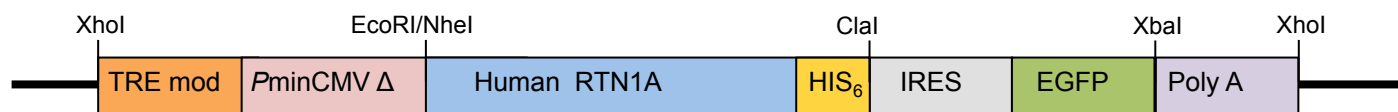
B
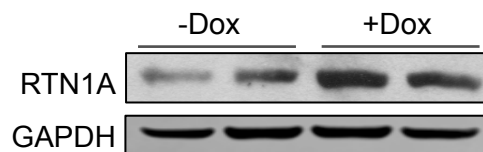
C
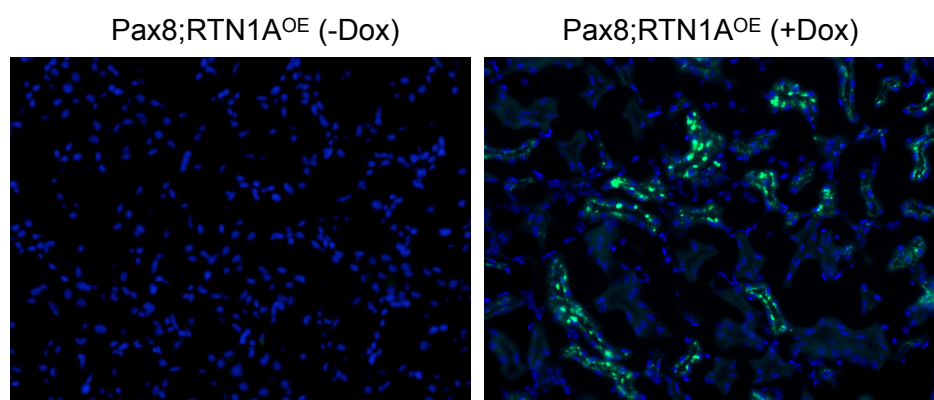
Supplementary Figure 6: Generation of tubular-specific RTN1A overexpression transgenic mice.
(A) Schematics of inducible expression vector of pTRE-Tight-hRTN1A-HIS$_6$-IRES-EGFP that was used to make the transgenic mouse line, which encodes a fusion protein of His$_6$-tagged human RTN1A under the transcriptional control of a tetracycline-responsive promoter element (TRE). IRES-containing bicistronic vector allows for simultaneous expression of EGFP. (B) Doxycycline-inducible expression of hRTN1A was confirmed in the Tet-ON U2OS cells before microinjection to generate the transgenic mice. (C) Dox-feeding of Pax8;RTN1A^{OE} mice led to an induction of hRTN1A overexpression, as detected by EGFP signals (~50-60% cells in the tubules) in their kidneys. Original magnification x200.

Masson's Trichrome   **Col I IHC**

WT control   Pax8;Rtn1a^{OE} WT control   Pax8;Rtn1a^{OE}

Vehicle-Injected

FA-injected
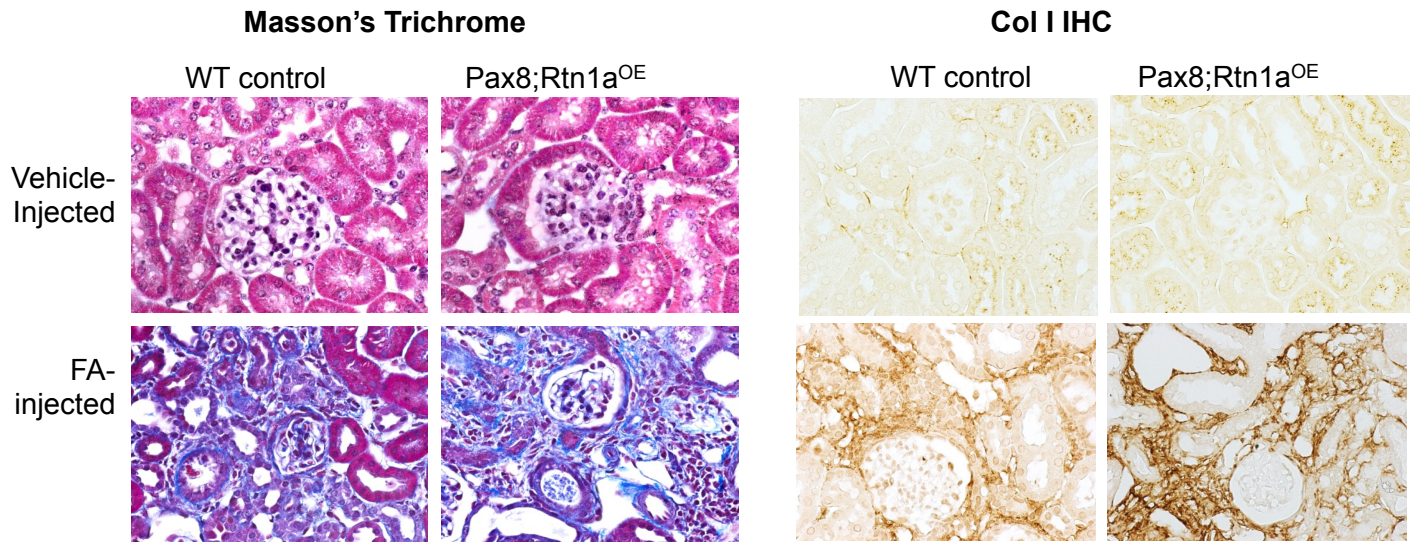
Supplementary Figure 7: *Rtn1a* overexpression in renal tubular cells exacerbated renal fibrosis in mice with FAN. Wildtype control and Pax8; Rtn1a^{OE} mice received either FA or vehicle injection after 3 weeks doxycycline (Dox) feeding and Dox was withdrawn at day 7 after FA injection. Mice were sacrificed at either 3 days post-injection for assessing acute kidney injury or 4 weeks post-injection for renal fibrosis. Representative images of Masson's trichrome staining and Col I immunostaining of vehicle-injected and FA-injected mice are shown (n=5). Original magnification x400.

Masson's Trichrome **Col I IHC**

Pax8; Luci RNAi Pax8; Rtn1aRNAi Pax8; Luci RNAi Pax8; Rtn1aRNAi

Vehicle-Injected

AA-injected
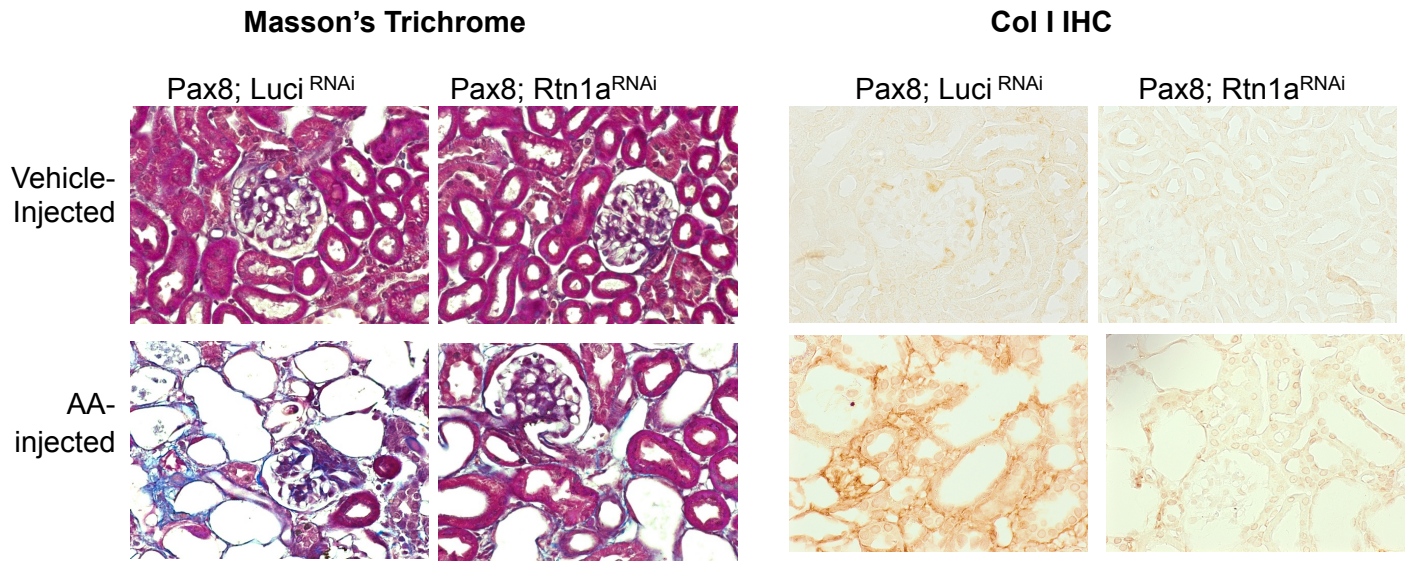
Supplementary Figure 8: *Rtn1a* knockdown in renal tubular cells attenuated renal fibrosis in mice with AAN. Pax8; Rtn1aRNAi and Pax8; Luci RNAi mice received either AA or vehicle injection after 3 weeks doxycycline (Dox) feeding and Dox was withdrawn at day 7 after AA injection. Mice were sacrificed at either 5 days post-injection for assessing acute kidney injury or 6 weeks post-injection for renal fibrosis. Representative images of Masson's trichrome staining and Col I immunostaining of vehicle-injected and AA-injected mice are shown (n=5). Original magnification x400.

Supplementary Table 1: Etiology and staging of the AKI patients

Classification	AKI (n=51)	
	AIN (n=42)	**ATN** (n=9)
Stage I	10	1
Stage II	12	1
Stage III - Non progressive	10	5
Stage III - Progressive	10	2

Supplementary Table 2: Clinical characteristics of patients at different AKI stages. Values are expressed as means ± SD or as percentages.

Characteristics	Stage I	Stage II	Stage III	P value
Patients (n)	11	13	27	
Age, years	48.00±11.84	47.69±12.12	58.08±15.95	0.048
Men, n(%)	3 (27.3)	7 (50.0)	14 (53.8)	0.996
SBP (mmHg)	129.5±25.32	137.1±16.63	144.3±21.05	0.146
DBP (mmHg)	81.82±15.07	83.64±17.32	84.81±11.37	0.837
Hgb (g/dl)	114.5±16.84	114.1±25.22	102.3±25.20	0.208
Baseline sCr (mg/dl)	1.23±0.48	1.21±0.38	1.41±0.79	0.558
Baseline eGFR (ml/min/1.73m^2)	71.35±24.47	72.39±34.74	73.96±36.48	0.977
Peak sCr (mg/dl)	1.80±0.81	2.82±1.43 *	6.49±2.87 *#	<0.0001
Peak eGFR (ml/min/1.73m2)	44.08±23.38	33.58±15.29 *	13.44±7.55 *#	<0.0001
Peak to nadir sCr (mg/dl)	0.60±0.44	1.53±1.32	5.20±2.68 *#	<0.0001
Albuminuria (g/24h)	0.82±0.57	1.10±0.90	2.17±2.89	0.145
Hospital stay (d)	10.73±3.90	13.57±5.33 *	26.56±19.92 *	0.0046
Renal outcome at discharge Non-progressing, n (%)	11 (100)	12 (92.86)	15 (55.56)	

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; Hgb, hemoglobin, sCr, serum creatinine; eGFR, estimated glomerular filtration rate; *P<0.05, compared to Stage I group; #P<0.05, compared to Stage II group.

Supplementary Table 3: Correlation of RTN1A expression with ER stress markers in kidney of AKI patients. Pearson correlation coefficient (r) between RTN1A expression in kidney and other ER stress markers such as CHOP, GRP78, p-PERK and XBP-1s is shown below.

	kidney expression of RTN1A in tubular compartment	
	r	P value
CHOP	0.8021	<0.0001
GRP78	0.4314	0.0016
p-PERK	0.3459	0.0129
XBP-1s	-0.6373	<0.0001

Supplementary Table 4: Quantitative PCR primer sequences used to detect the expression of genes in mouse kidneys.

Gene	Forward Primer (5'-3')	Reverse Primer (5'-3')
Rtn1a	ATGGAAACTGCATCCACA	AAAGTATGCAGAGTCCTC
CHOP	TTCACCTTGGAGACGGTG	CGCAGGGTCAAGAGTAGT
Gadd34	ACAGCCTGTGAAACATTGCG	ATGCCTCTGGGACTTC
Bim	TACCTCCCTACAGACAGAACC	GTCCCCATCAGCTGTCTTC
Col I	TGGACTTCCTGGTCCTCCTG	AGGCACGGAAACTCCAGC
Fn	TCTGGCTCCTTCACTGATGTC	TACCGTTGTAGGTGAACGGG
Mmp2	ATCTTTGCAGGAGACAAGTTC	TTCAGGTAATAAGCACCCTTG
α-SMA	CAGCGGGCATCCACGAA	GCCACCGATCCAGACAGA