

Loss of RTN3 phenocopies chronic kidney disease and results in activation of the IGF2-JAK2 pathway in proximal tubular epithelial cells

Running title: loss of RTN3 may lead to CKD

Liang-Liang Fan^{1,2,3#}; Ran Du^{1,2#}; Ji-Shi Liu^{1,4#}; Jie-Yuan Jin^{1,2}; Chen-Yu Wang^{1,2}; Yi Dong^{1,2}; Wan-Xia He⁵; Ri-Qiang Yan^{5*}; Rong Xiang^{1,2,3,4*}

¹ Department of Nephrology, The Third Xiangya Hospital of Central South University, Changsha, 410013, China;

² Department of Cell Biology, The School of Life Sciences, Central South University, Changsha 410013, China;

³ Hunan Key Laboratory of Animal Models for Human Diseases, School of Life Sciences, Central South University, Changsha, 410013, China;

⁴ Hunan Key Laboratory of Organ Fibrosis, The Third Xiangya Hospital of Central South University, Changsha, 410013, China.

⁵ Department of Neuroscience, University of Connecticut Health, Farmington, CT, 06032, USA;

These authors contributed equally to this study.

* Correspondence:

Ri-Qiang Yan, Ph.D

Email: riyan@uchc.edu

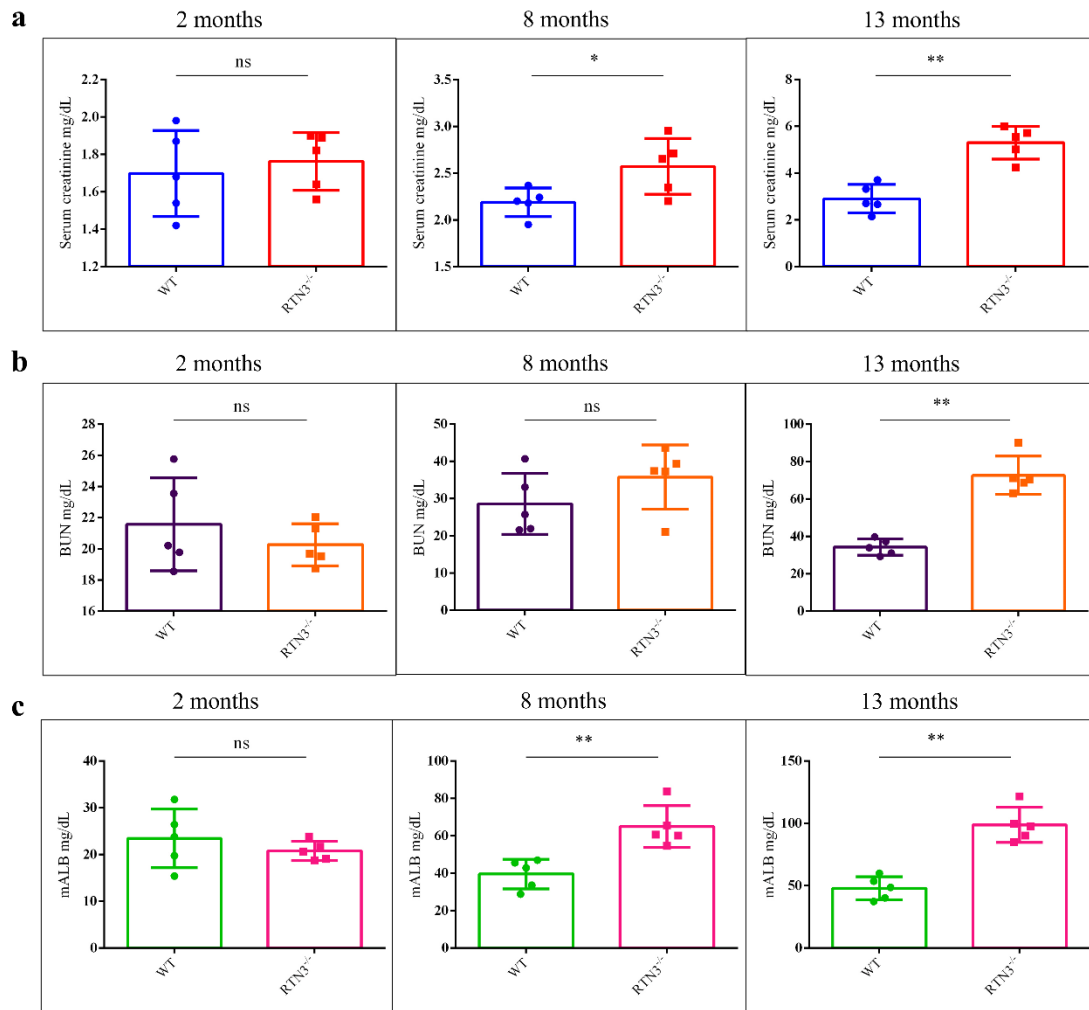
Department of Neuroscience, University of Connecticut Health, Farmington, CT, 06032, USA;

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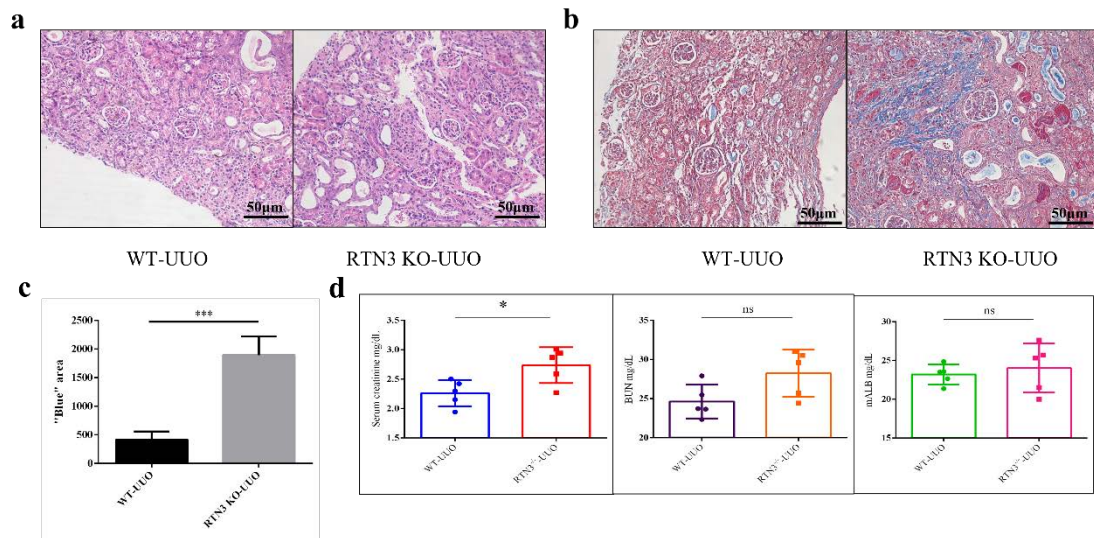
Rong Xiang, Ph.D.

Email: shirlesmile@csu.edu.cn

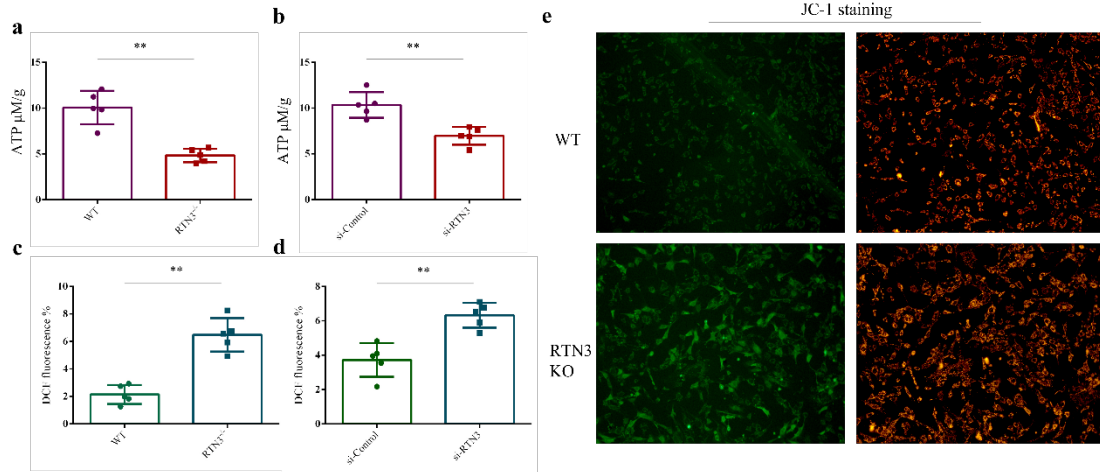
Department of Cell Biology, The School of Life Sciences, Central South University, Changsha 410013, China.



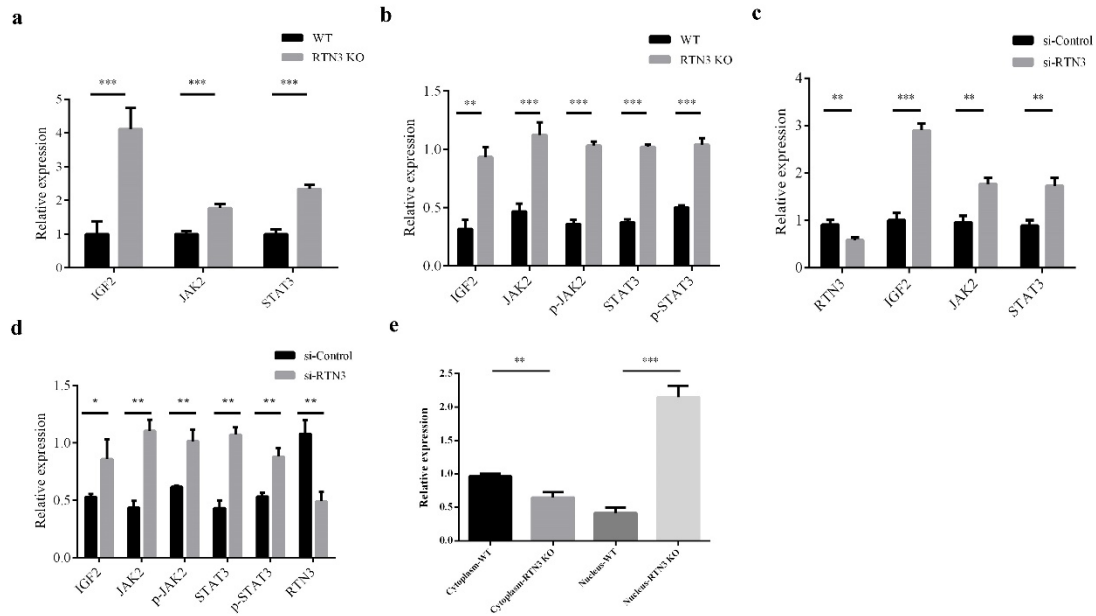
Supplementary Fig. 1. The levels of serum creatinine, blood urea nitrogen and mALB indicates RTN3-null mice are suffering from CKD. **(a)** Serum creatinine, **(b)** blood urea nitrogen and **(c)** urine mALB levels in WT (n=5) and RTN3-null mice (n=5) with different ages.



Supplementary Fig. 2. UUO models of RTN3-null mice show more severe CKD phenotypes. **(a)** H&E and **(b, c)** Masson staining exhibited the glomerular and tubular structures in WT-UUO (n=5) and RTN3-null-UUO mice (n=5) at 2 months. **(d)** Serum creatinine, blood urea nitrogen and urine mALB levels in WT-UUO (n=5) and RTN3-null-UUO mice (n=5) at 2 months.



Supplementary Fig. 3. RTN3-null mice kidney shows mitochondrial dysfunction. ATP levels in **(a)** WT and RTN3-null mice primary cultured renal tubular epithelial cells group, and **(b)** HEK293 cell with si-control and si-RTN3 group. ROS levels in **(c)** WT and RTN3-null mice primary cultured renal tubular epithelial cells group, and **(d)** HEK293 cell with si-control and si-RTN3 group. **(e)** JC-1 staining in WT and RTN3-null mice primary cultured renal tubular epithelial cells.



Supplementary Fig. 4. RTN3 can regulate the IGF2-JAK2-STAT3 pathway by interacting with GPBP1. **(a)** Real-time PCR analysis shows the mRNA levels of IGF2, JAK2 and STAT3 in WT and RTN3-null mice. **(b)** Statistical analysis of IGF2, JAK2, p-JAK2, STAT3 and p-STAT3 protein levels in WT and RTN3-null mice. **(c)** the mRNA levels of IGF2, JAK2 and STAT3 in HEK293 cell with si-Control and si-RTN3. **(d)** Statistical analysis of IGF2, JAK2, p-JAK2, STAT3, p-STAT3 and RTN3 protein levels in HEK293 cell with si-Control and si-RTN3. **(e)** Statistical analysis of the levels of GPBP1 in WT and RTN3-null mice primary cultured renal tubular epithelial cells cytoplasm and nucleus.