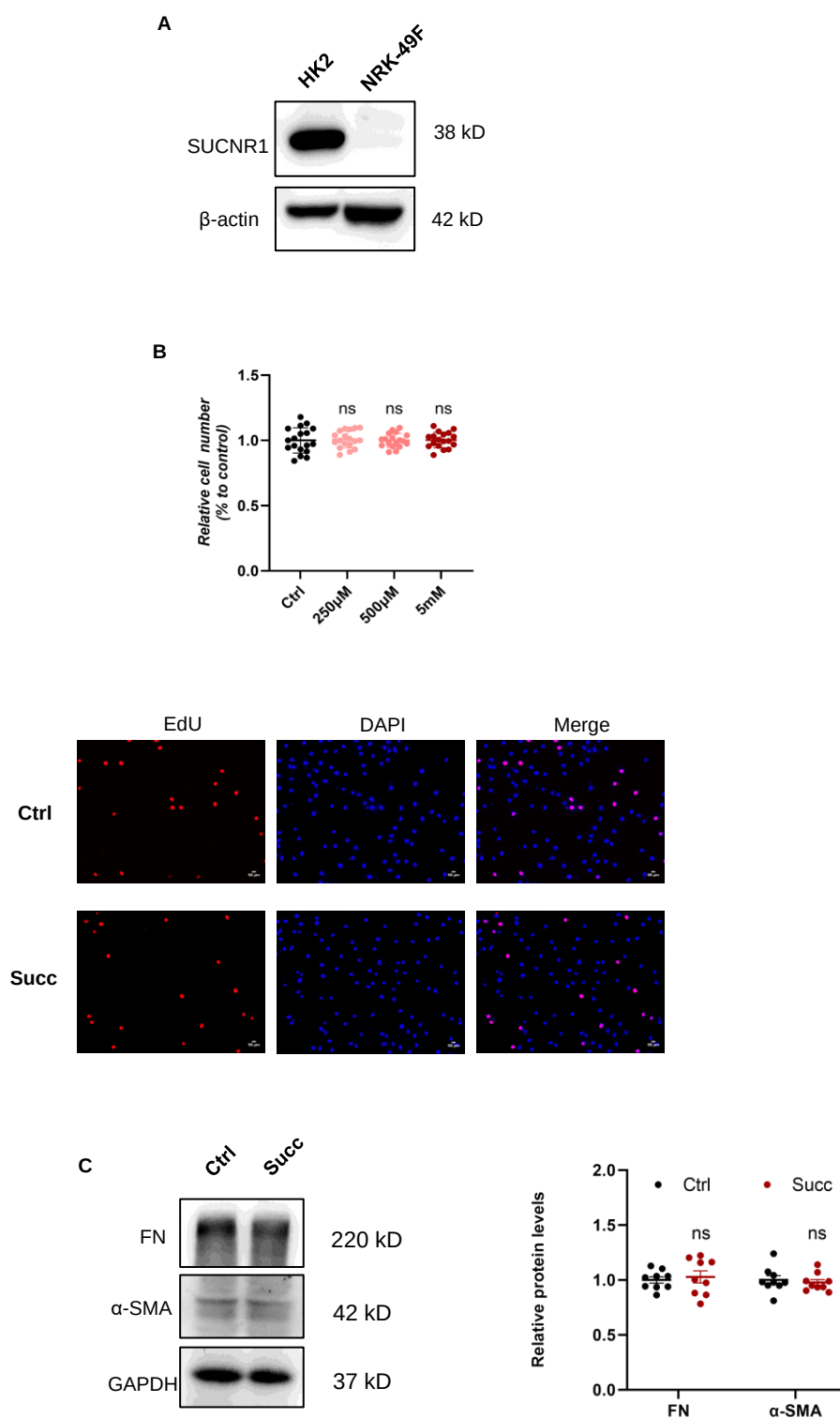


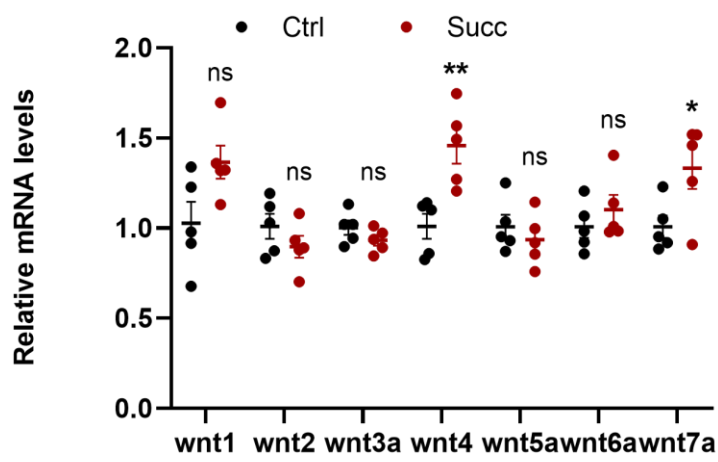


Supplementary figure 1 Succinate had no directive effects on NRK-49F

(A) Validation of SUCNR1 protein expression in NRK-49F by immunoblotting. HK2 was used for positive control. A range of 250μM and 5mM succinate was treated for NRK-49F for 48h.

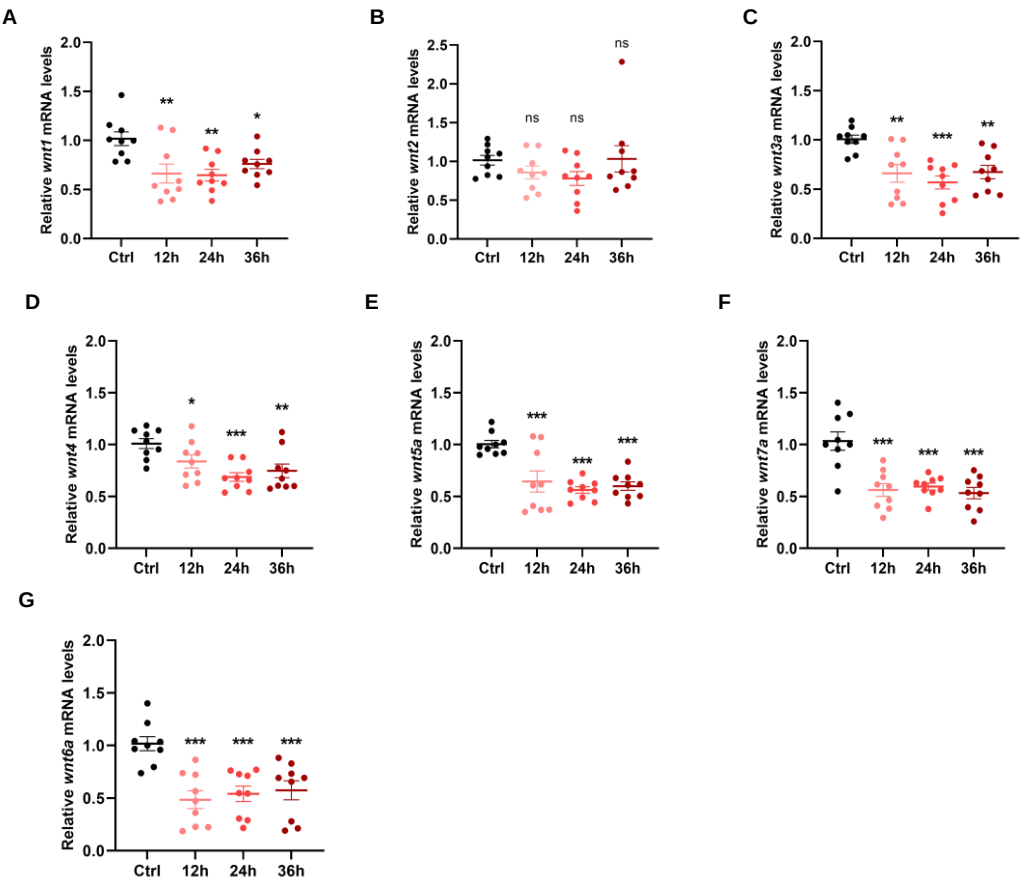
(B) The results of the CCK8 assay and EdU staining demonstrated that succinate had no effects on proliferation. ns>0.05, versus the control group, n=6 in CCK8 and n=3 in EdU staining, biologically repeated 3 times.

(C) Succinate could not trigger the elevation of fibronectin and α-SMA. ns>0.05, versus the control group, n=3, biologically repeated 3 times.



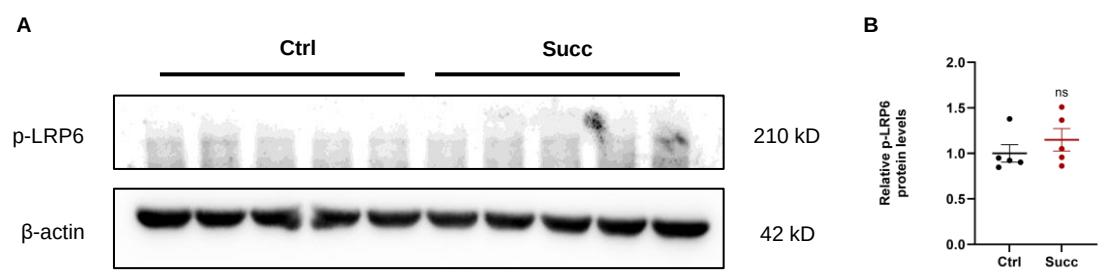
Supplementary figure 2 Succinate had no significant stimulatory effects on renal wnt3a and wnt5a

Succinate had no significant stimulatory effects on renal tissue WNTs ligands, including wnt3a and wnt5a. ns>0.05, versus the control group, n=5.



Supplementary figure 3 Succinate reduced mRNA levels of *wnt3a* and *wnt5a* in the macrophage

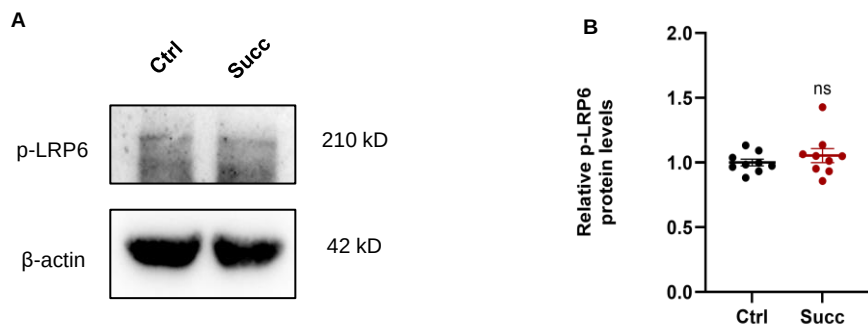
500 μ M succinate treated RAW 264.7 cells at different time points, succinate decreased mRNA levels of WNTs ligand including *wnts1*, *wnt3a*, *wnt4*, *wnt5a*, *wnt6a*, and *wnt7a*. ns>0.05, * P <0.05, ** P <0.01, *** P <0.001, versus the control group, n=3, biologically repeated 3 times.



Supplementary figure 4 Succinate had no significant stimulatory effect on renal tissue p-LRP6

The renal protein level of p-LRP6 was not altered by succinate.

ns>0.05, versus the control group, n=5.



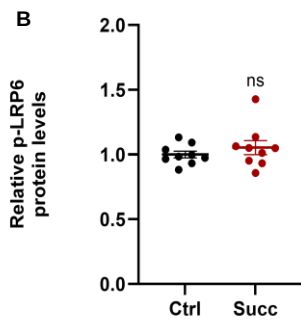
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98	0.00	0.00
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p-LRP6

210 kD

β-actin

42 kD

Relative p-LRP6
protein levels

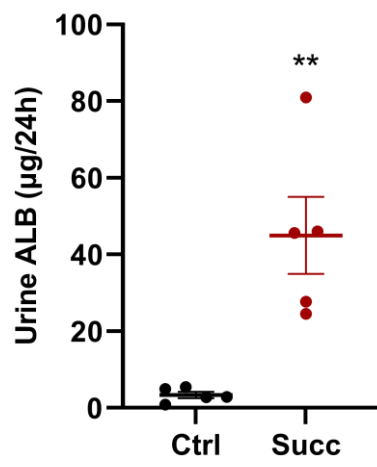
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Supplementary figure 5 Succinate had no significant stimulatory effect on renal tissue p-LRP6

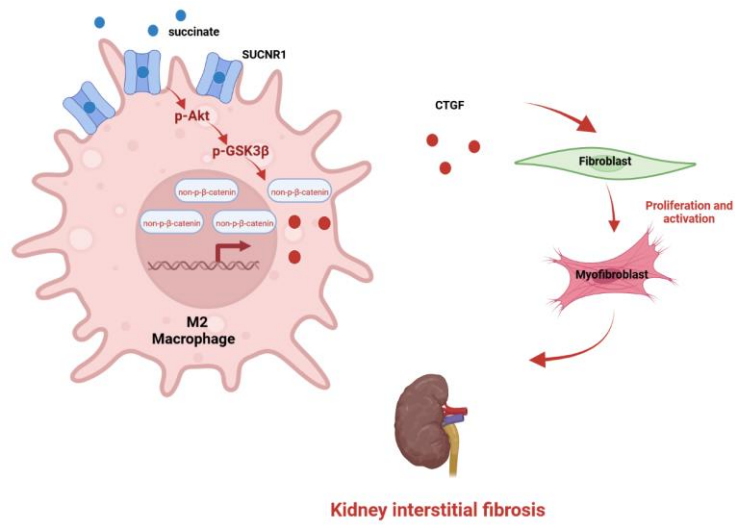
500 μ M succinate treated RAW 264.7 cells for 12h, and western blotting to detect the protein levels of p-LRP6.

Succinate had no significant stimulatory effect on macrophage p-LRP6 protein level. ns>0.05, versus the control group, n=3, biologically repeated 3 times.



Supplementary figure 6 Succinate caused mice proteinuria.

24h urine of C57/BL 6 male mice was collected after treatment by metabolic cage and analyzed for albumin excretion. Succinate significantly promoted urine albumin excretion. $**P < 0.01$, versus the control group, $n = 5$.



Supplementary figure 7 The working model of succinate induces renal fibrosis.

In Brief, we have shown that succinate-SUCNR1 of macrophages promoted M2 polarization and upregulation of CTGF via p-Akt/p-GSK3β/β-catenin signaling, which stimulated renal fibroblast proliferation and activation, resulting in kidney interstitial fibrosis.