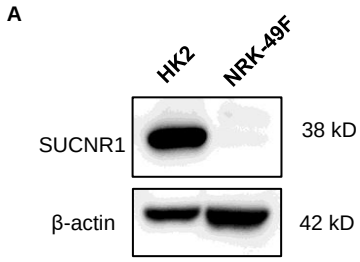
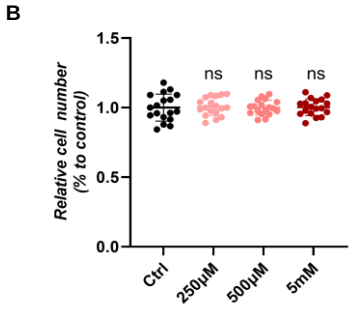
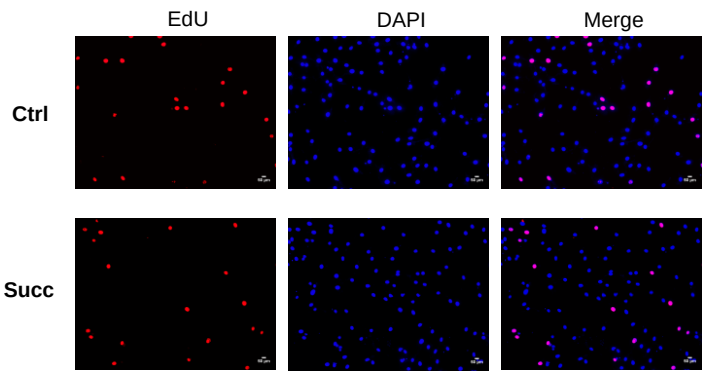
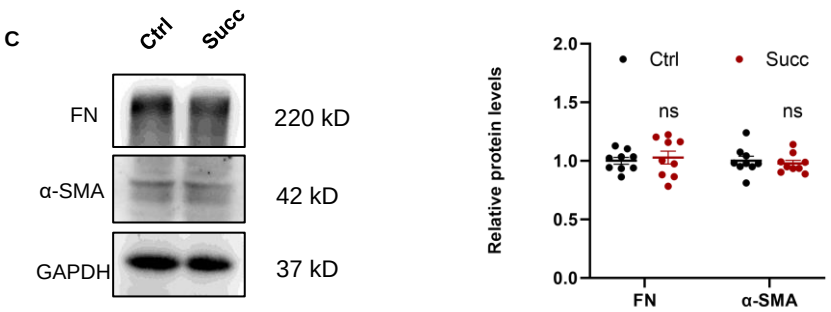






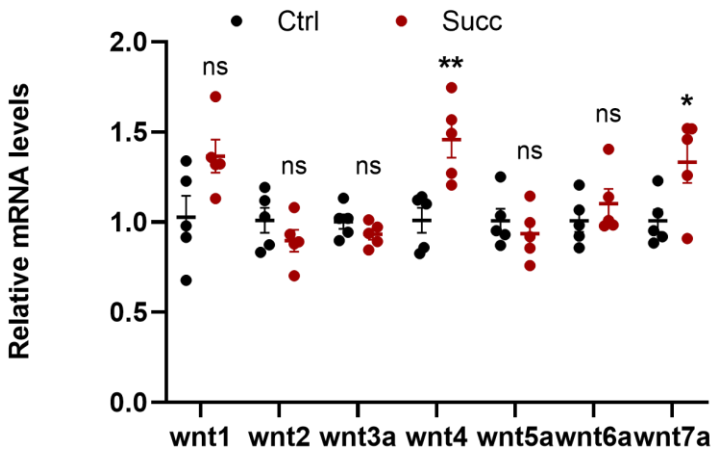


Supplementary figure 1 Succinate had no directive effects on NRK-49F

(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.

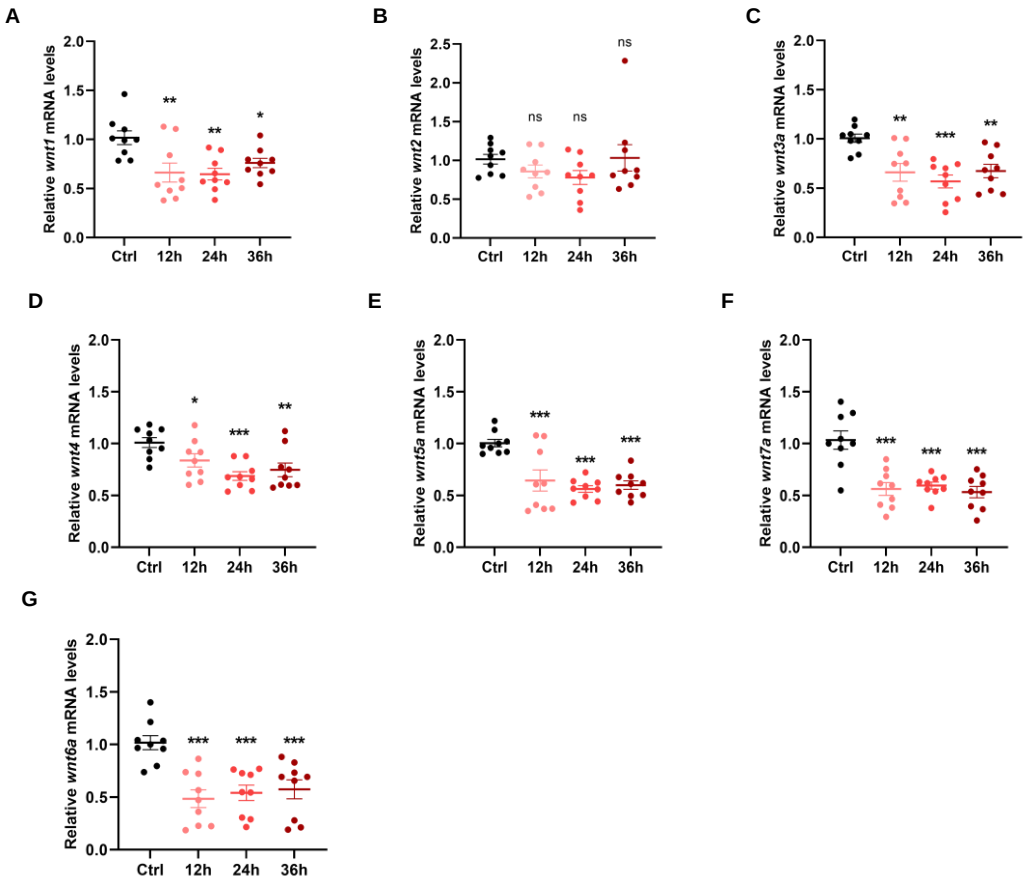
(B) The results of the CCK8 assay and EdU staining demonstrated that succinate had no effects on proliferation. ns>0.05, versus the control group, n=6 in CCK8 and n=3 in EdU staining, biologically repeated 3 times.

(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.



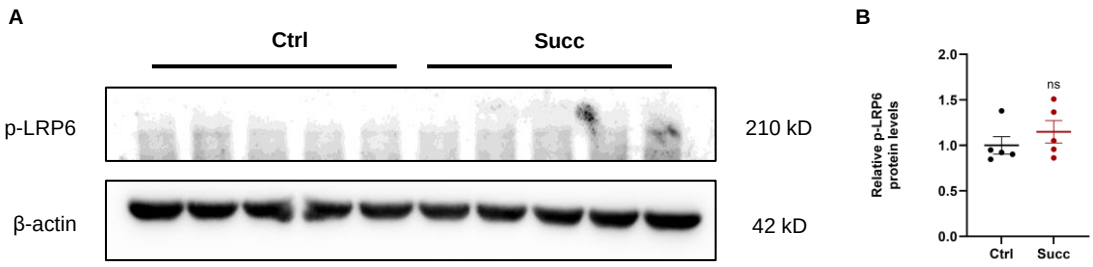
Supplementary figure 2 Succinate had no significant stimulatory effects on renal wnt3a and wnt5a

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

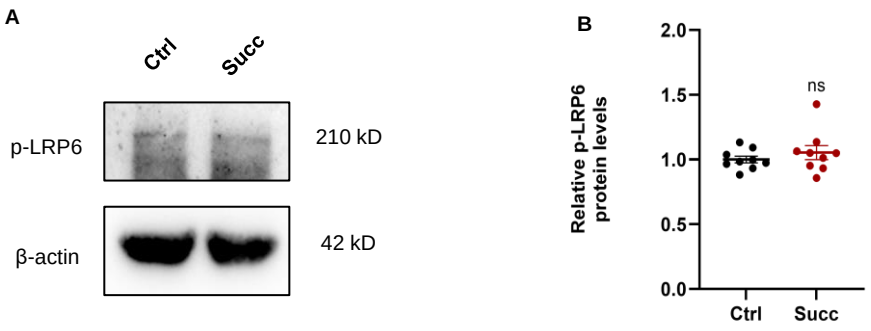
500 μM succinate treated RAW 264.7 cells at different time points, succinate decreased mRNA levels of WNTs ligand including wnts1, wnt3a, wnt4, wnt5a, wnt6a, and wnt7a. ns>0.05, *P<0.05, **P<0.01, **P<0.001, versus the control group, n=3, biologically repeated 3 times.



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.

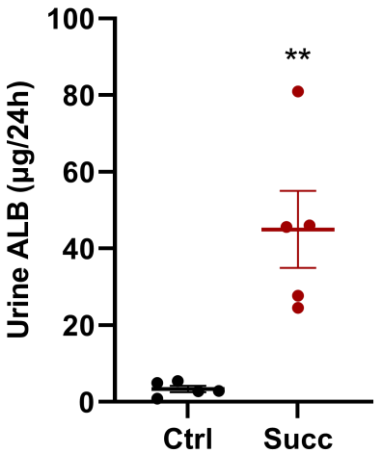
ns>0.05, versus the control group, n=5.



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

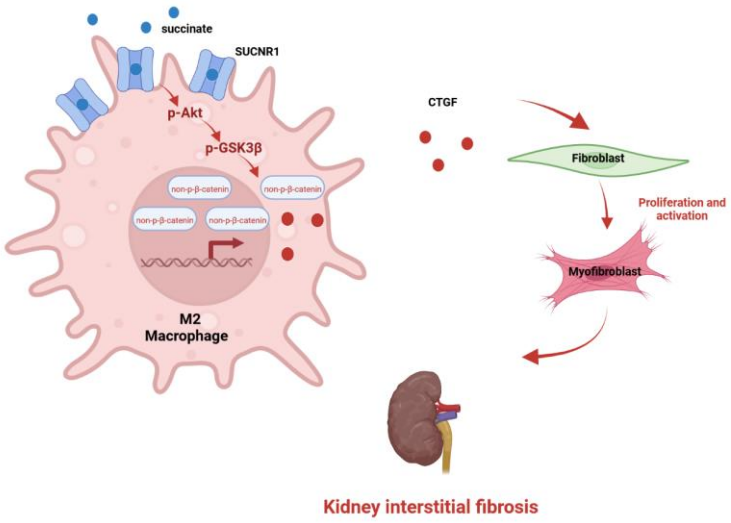
500 μM succinate treated RAW 264.7 cells for 12h, and western blotting to detect the protein levels of p-LRP6.

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.