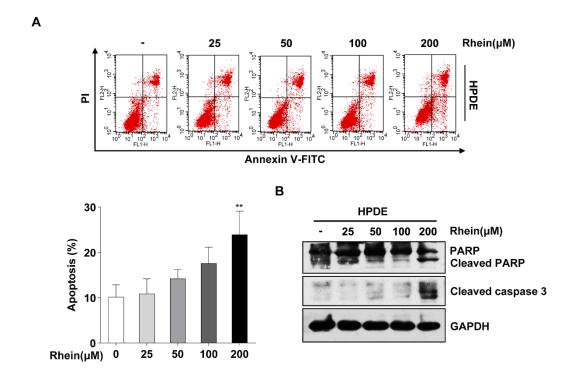
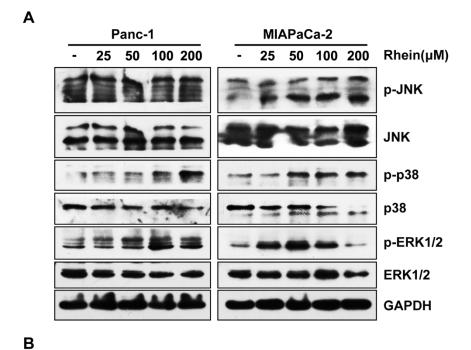
## **Supplementary Materials**

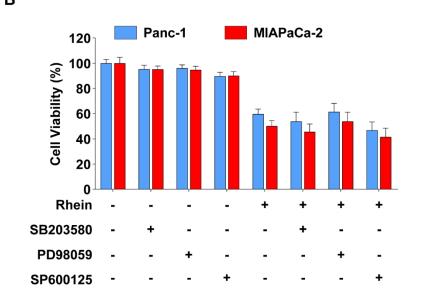
## **Antibodies and reagents**

SAPK/JNK (#9252), phospho-SAPK/JNK (Thr183/Tyr185) (#9255), p38 (#8690), phospho-p38 (Thr180/Tyr182) (#4511), ERK1/2 (#4695) and phospho-ERK1/2 (Thr202/Tyr204) (#8544) antibodies were purchased from Cell Signaling Technology (Beverly, MA, USA). SB203580 (HY-10256), PD98059 (HY-12028) and SP600125 (HY-12041) were purchased from MCE (Monmouth, NJ, USA).



**SUPPLEMENTARY FIGURE S1** Effects of Rhein on the apoptosis of HPDE cells. (A) Apoptosis rate of HPDE cells were determined by Annexin V/PI double staining after 0-200  $\mu$ M Rhein treatment for 24 h. Each bar represents means  $\pm$  SD from three independent experiments. \*\*p < 0.01. (B) Western blot analysis of PARP and cleaved-caspase-3 proteins levels in HPDE cells after 0-200  $\mu$ M Rhein treatment. GAPDH was used as loading control.





**SUPPLEMENTARY FIGURE S2** MAPKs signaling pathway was not relevant in Rhein-induced apoptosis. (A) Western blot analysis of MAPKs signaling proteins levels in Panc-1 and MIAPaCa-2 cells after 0-200  $\mu$ M Rhein treatment. (B) Panc-1 and MIAPaCa-2 cells were pretreated with SB203580 (25  $\mu$ M), PD98059 (25  $\mu$ M), or SP600125 (25  $\mu$ M) for 1 h followed by Rhein (100  $\mu$ M) treatment for 24 h. Cell viability was measured by CCK-8 assay. Each bar represents means  $\pm$  SD from three independent experiments.