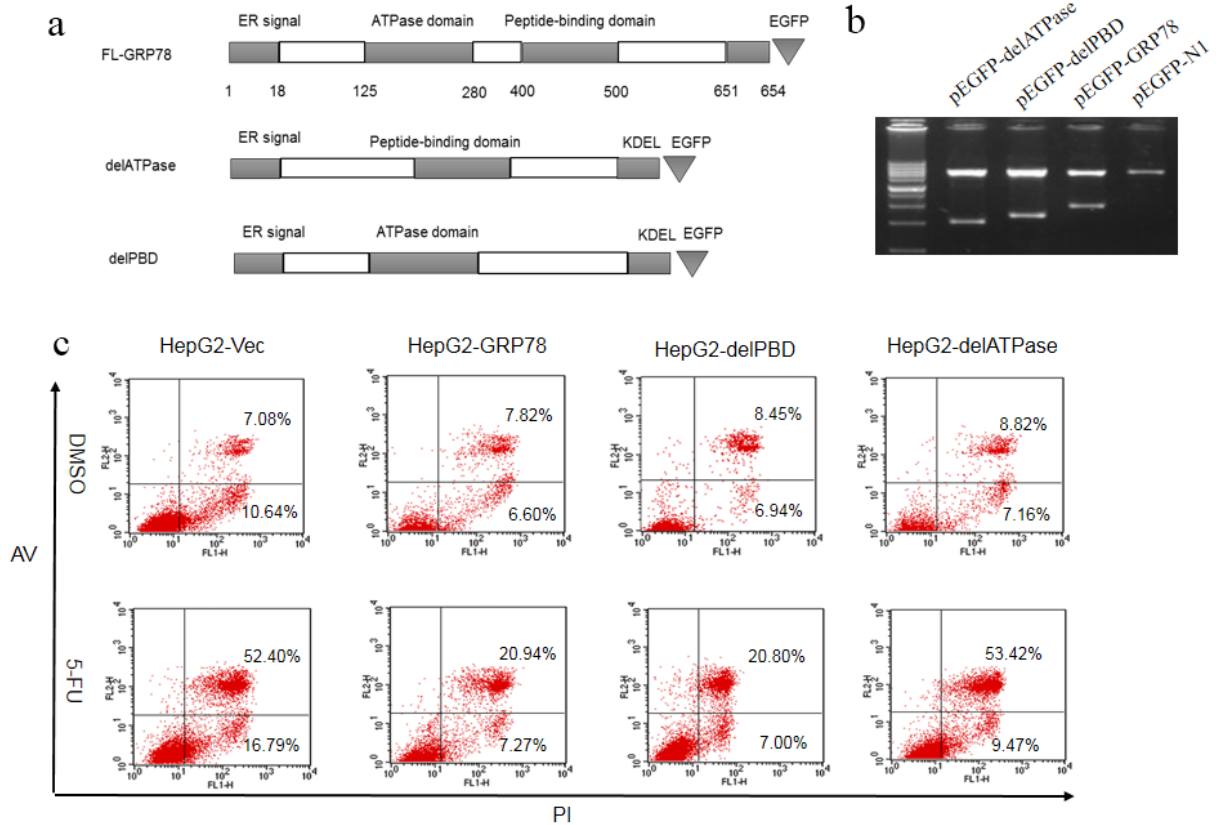
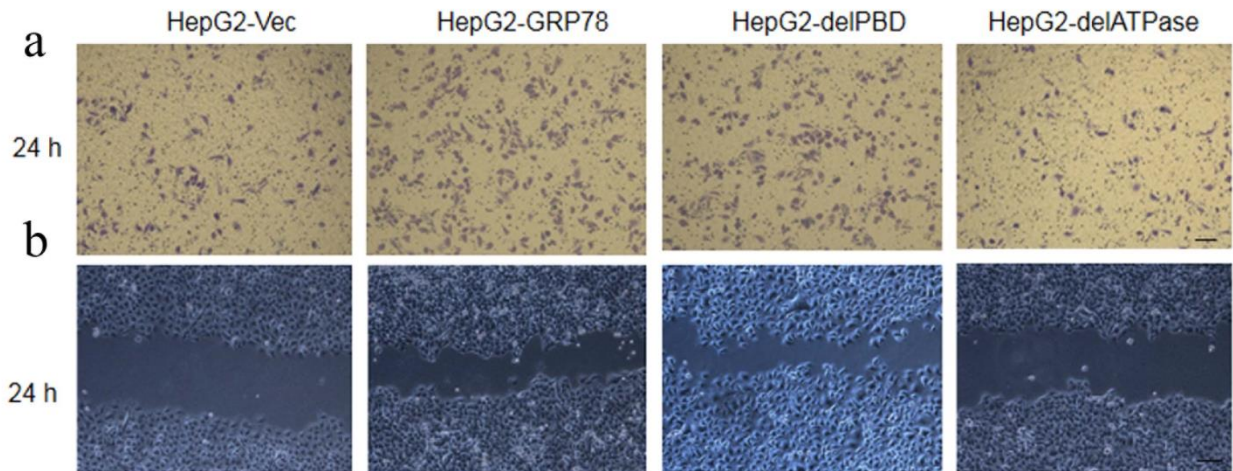


# GRP78 confers the resistance to 5-FU by activating the c-Src/LSF/TS Axis in hepatocellular carcinoma

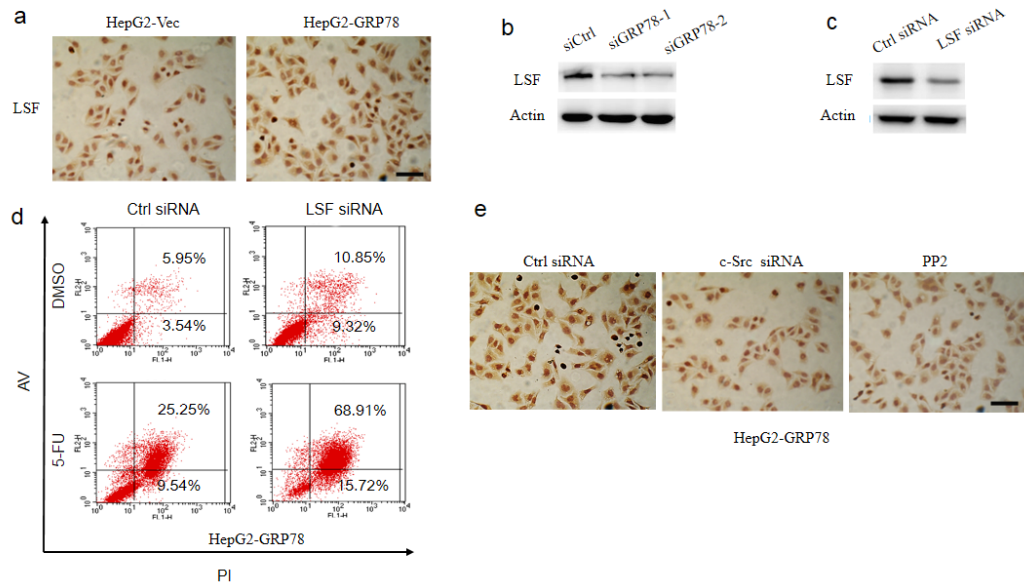
## Supplementary Material



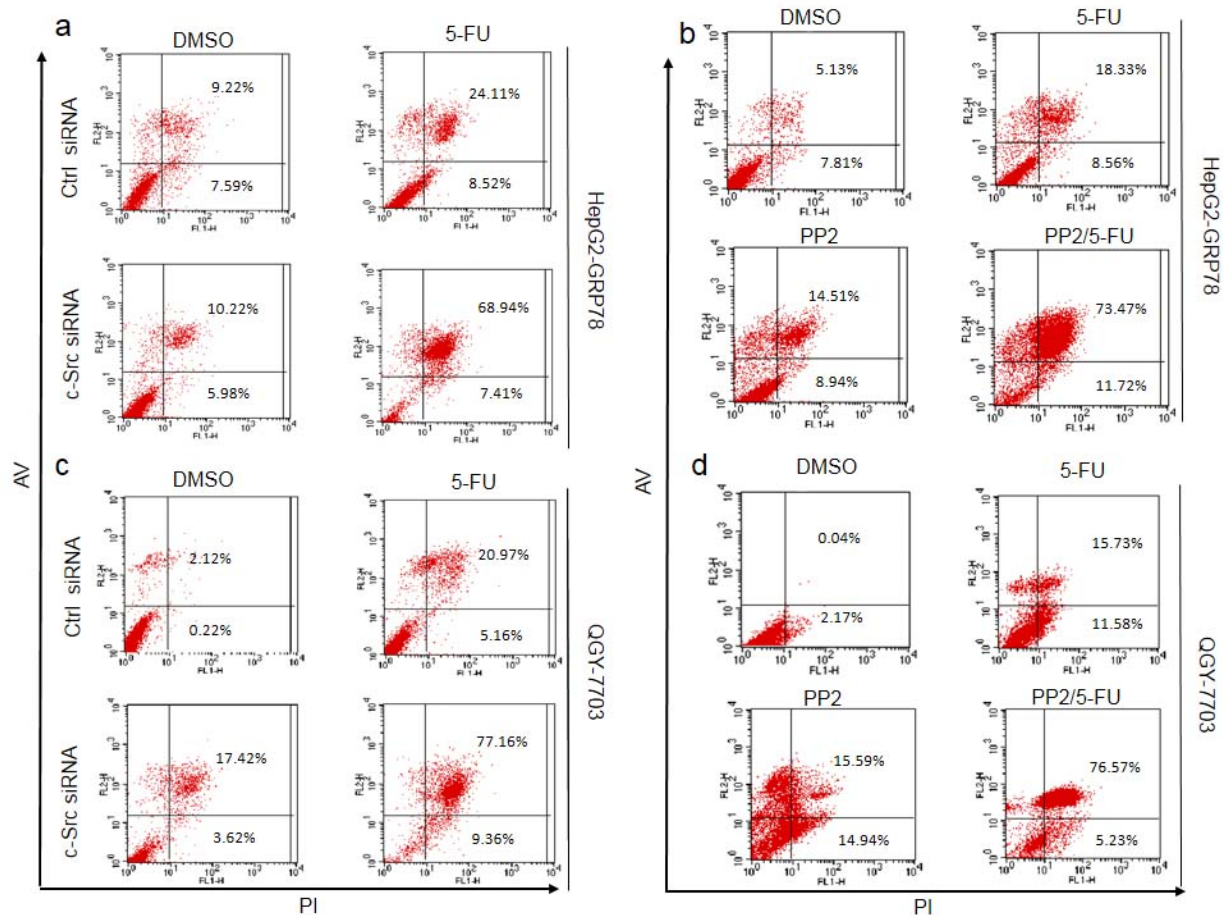
**Fig.S1:** (a) Schematic show of GRP78 and its ATPase or PBD domain deleted mutant. (b) Construction and identification of GRP78 and its ATPase and PBD deleted mutants. ATPase or PBD domain deleted mutants were constructed on the basis of pEGFP-N1-GRP78, verified by endonuclease cleavage using EcoRI and HindIII and separated by 1% agarose electrophoresis. (c) Flow cytometry analysis of the sensitivity to 5-FU in HepG2 cells transfected with EGFP-tagged GRP78, delPBD or delATPase. These experiments were repeated for three times.



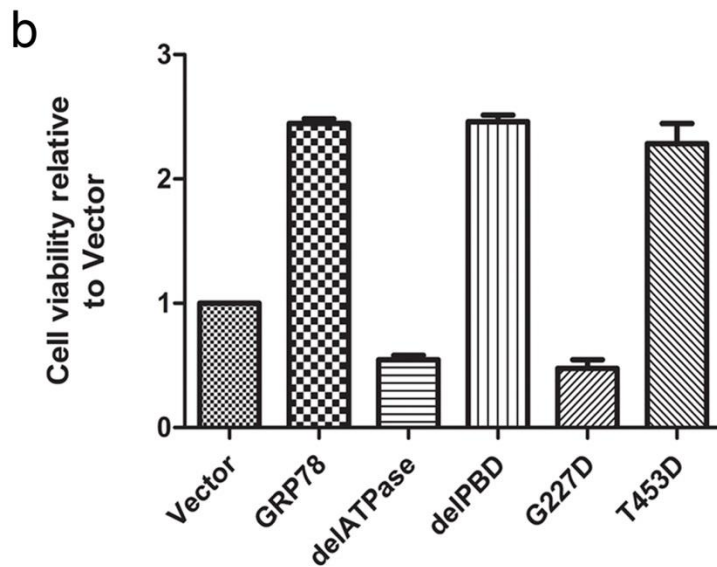
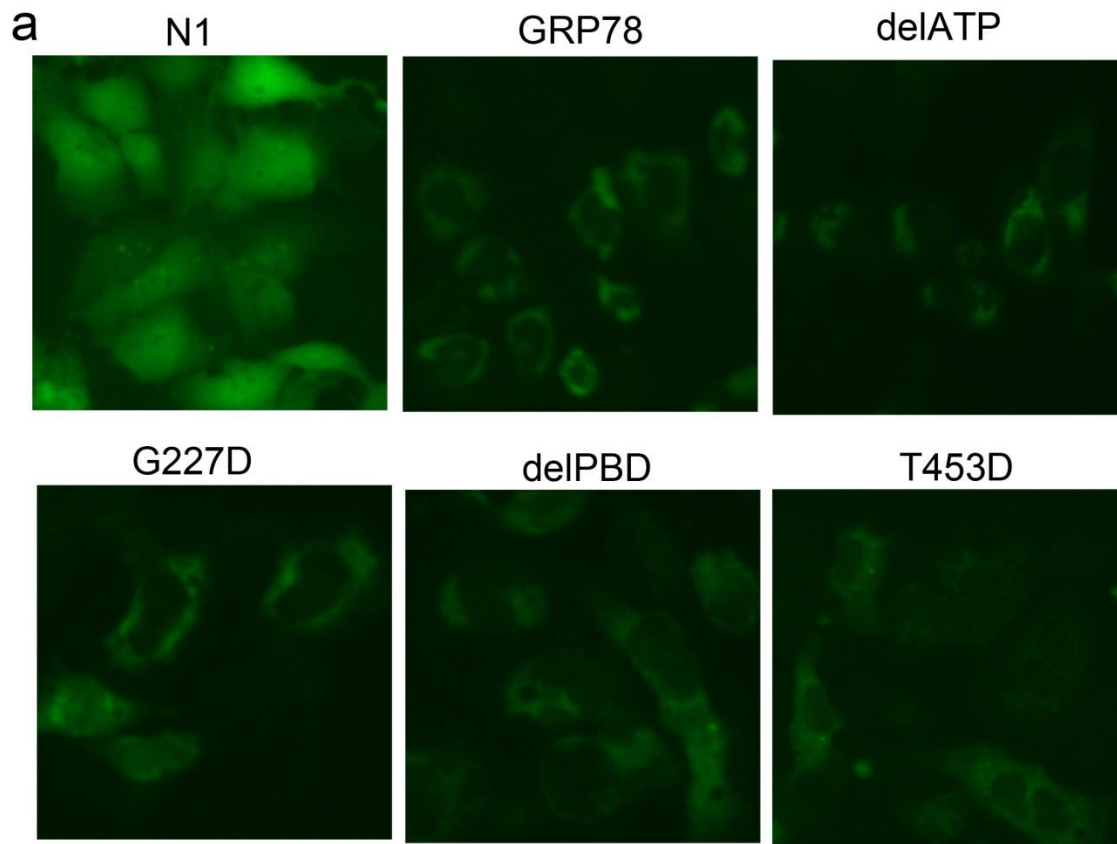
**Fig.S2: (a-b)** GRP78 promotes the invasion and migration of HepG2 cells through its ATPase domain. **(a)** Transwell analysis of the invasion of HepG2 cells transfected with EGFP tagged GRP78, delPBD or delATPase (Scale bar: 50  $\mu$ M). **(b)** Wound healing analysis of the migration of HepG2 cells overexpressing EGFP tagged GRP78, delPBD or delATPase (Scale bar: 50  $\mu$ M).



**Fig.S3:** (a) Immunocytochemical staining of LSF in HepG2-GRP78 or HepG2-Vec cells. (b) Western blot analysis of LSF in QGY-7703 cells transfected with siGRP78(Scale bar: 50  $\mu$ M). (c) Western blot analysis of LSF level in HepG2-GRP78 cells transfected with siRNA against LSF.(d) Flow cytometry analysis of apoptosis induced by 5-FU in HepG2-GRP78 cells transfected with siRNA against LSF.(e) Immunocytochemical staining of LSF in HepG2-GRP78 cells treated with siRNA against c-Src or PP2(Scale bar:50  $\mu$ M).



**Fig.S4:** (a) Flow cytometry analysis of apoptosis induced by 5-FU in HepG2-GRP78 cells transfected with siRNA against c-Src. (b) Flow cytometry analysis of apoptosis induced by 5-FU in HepG2-GRP78 cells treated with 5-FU, PP2 or 5-FU in combination of PP2. (c) Flow cytometry analysis of apoptosis induced by 5-FU in QGY-7703 cells transfected with siRNA against c-Src. (d) Flow cytometry analysis of apoptosis induced by 5-FU in QGY-7703 cells treated with 5-FU, PP2 or 5-FU in combination of PP2.



**Fig.S5:** (a) cellular localization of G227D, T473D, delATP and delPBD in hepG2 cells. (b). Cell viability analysis of hepG2 cells overexpressing G227D, T473D, delATP and delPBD.