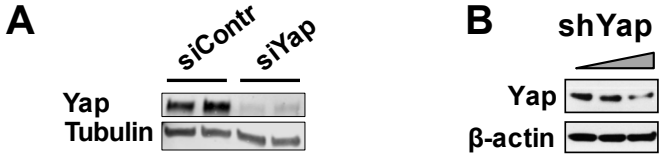
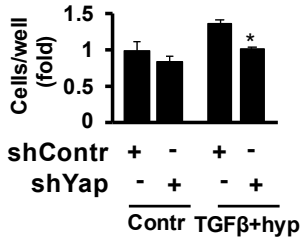
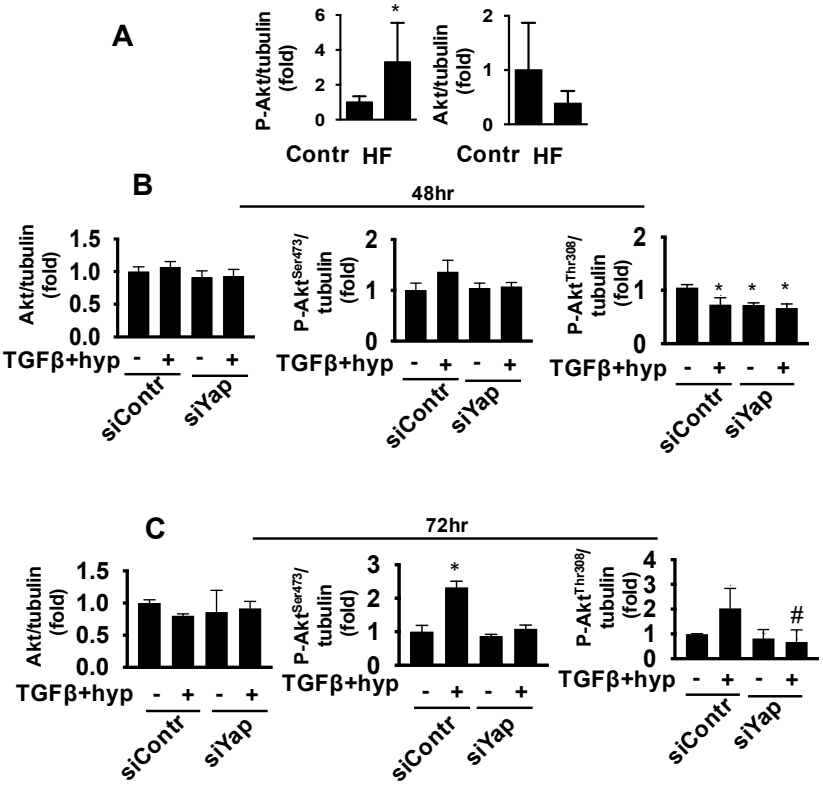
Supplemental Figures



Supplemental Figure S1. Efficient Yap downregulation. (**A**) Human adult cardiac fibroblasts were transfected with control (siContr) and Yap (siYap) siRNA, followed by immunoblot analysis to Yap protein level; n = 5. (**B**) Human adult cardiac fibroblasts were transduced with different doses of adenovirus expressing shRNA Yap (shYap) followed by immunoblot analysis to detect Yap; n = 2.

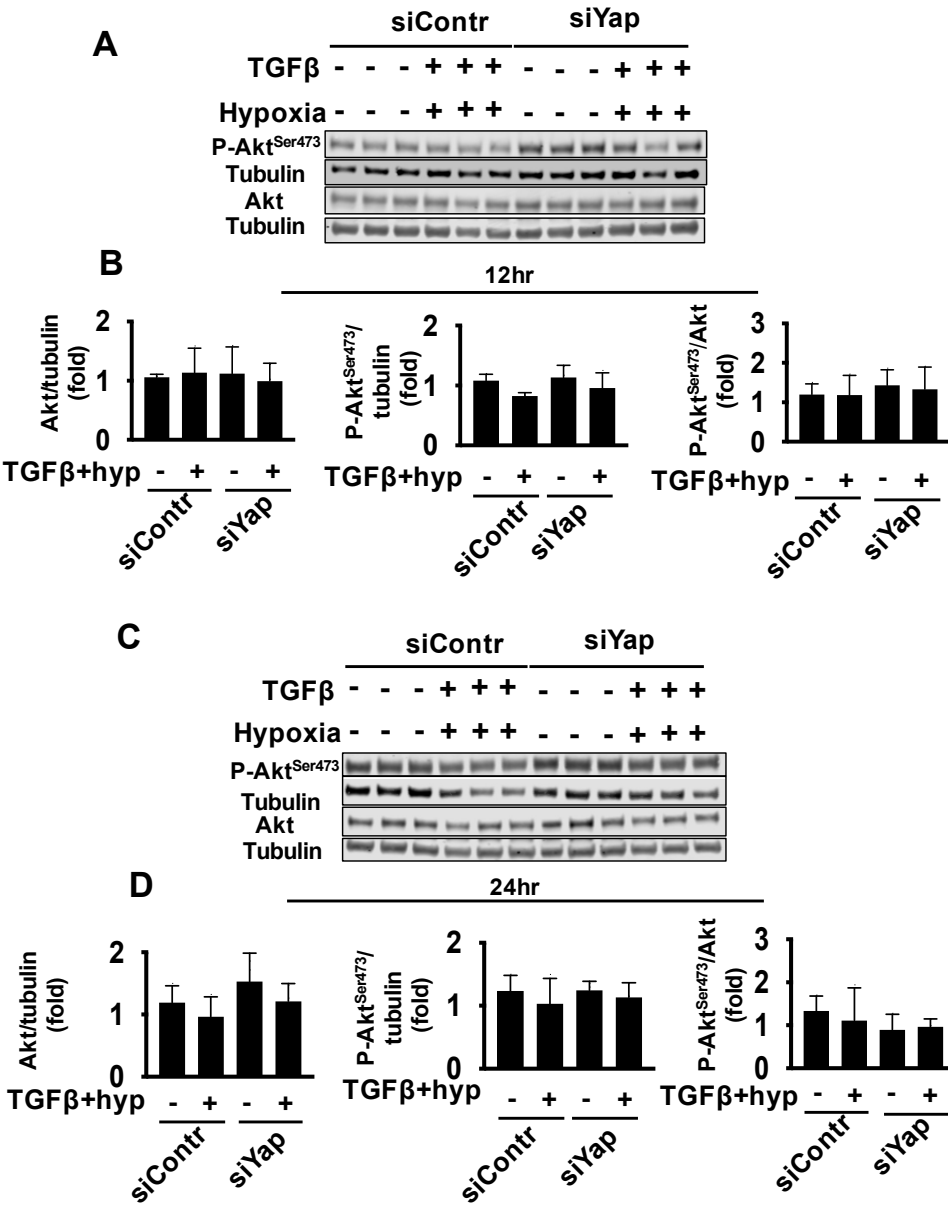


Supplemental Figure S2. Yap contributes to human adult cardiac fibroblast growth. Cardiac fibroblasts infected with adenovirus expressing shRNA Yap (shYap) or control adenovirus (shContr) and exposed to hypoxia (1% O2) and TGFβ (10 ng/mL) followed by cell count performed at day 5 of exposure. Data are mean ± S.E.M; * and # $p < 0.05$ vs. shContrl and shContrl+hypoxia/TGFβ, respectively, n = 3–4/condition.

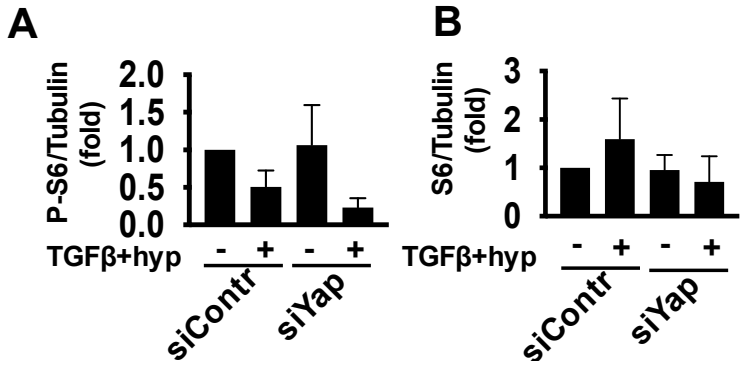


Supplemental Figure S3. Yap-dependent activation of Akt in HF and profibrotic conditions. (**A**) Detailed densitometry analysis of LV tissues from HF patients and control individuals from Figure 4A showing quantification of Akt and P-Akt normalized to

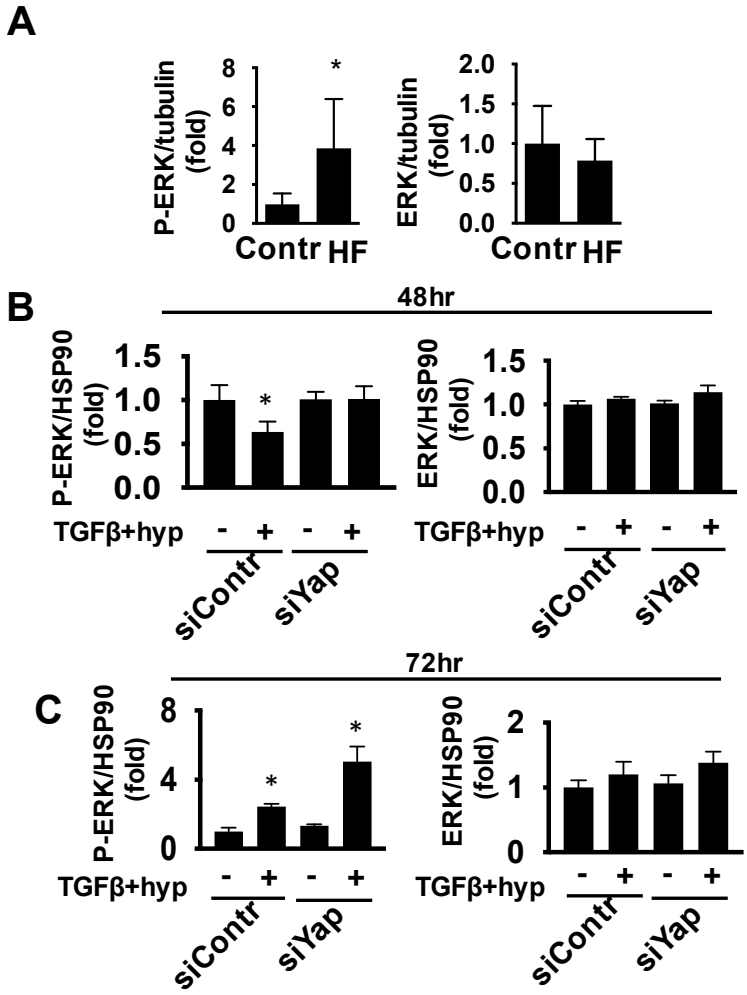
housekeeping control. Data represent mean ± S.E.M of fold changes from control; $n = 7$ subjects/group, $^{*}p < 0.05$ vs. control (**B**,**C**) Graphs representing fold change quantitative densitometry analysis normalized to corresponding loading control for total and phospho-Akt from Figures 4C–F of human cardiac fibroblasts transfected with siContr or siYap exposed to normoxia and vehicle (-) or hypoxia (1% O_2) and TGFβ (10 ng/mL) for stated durations. Data represent mean ± S.E.M. of fold changes from siContr control (-); $^{*}p < 0.05$ vs. siContr control (-),$^{\#}p < 0.05$ vs. siContr control exposed to hypoxia (1% O_2) and TGFβ (10 ng/mL); $n = 3$–4/condition.



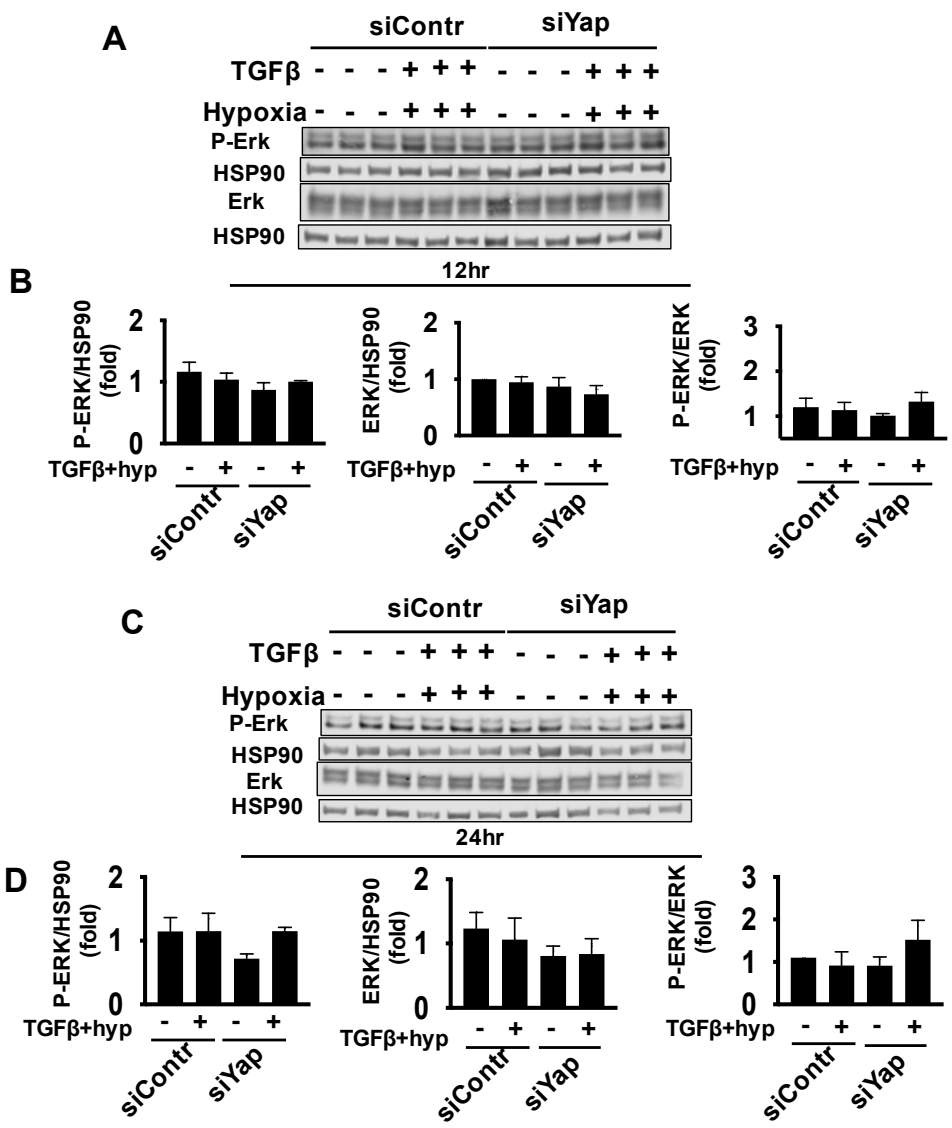
Supplemental Figure S4. Akt is not activated at early profibrotic stress timepoints. (**A**,**C**) Representative immunoblot for indicated proteins of human adult cardiac fibroblasts transfected with siYap or siContr and exposed to hypoxia/TGFβ. (**B**,**D**) Fold change immunoblot densitometry analyses of indicated proteins normalized to corresponding loading control. Data represent mean ± S.E.M of fold changes to siContr-infected vehicle-treated control group (-); $n = 3$/condition.



Supplemental Figure S5. Alleviation of mTOR signaling with profibrotic conditions does not alter with Yap silencing. (**A,B**) Fold change immunoblot densitometry analyses from Figure 5A of S6 and phospho-S6 (*p*-S6) normalized to corresponding loading control in human adult cardiac fibroblasts transfected with siYap or siContr and exposed to hypoxia/TGFβ. Data represent mean ± S.E.M of fold changes to siContr-infected vehicle-treated control group (-); *n* = 3–4/condition.



Supplemental Figure S6. Yap-independent elevation of ERK1/2 signaling under conditions of HF. (**A–C**) Quantitative densitometry analyses of indicated proteins in (A) LV tissues from HF patients and control individuals from Figure 6 A. Data represent mean ± S.E.M of fold changes from control; *n* = 7 subjects/group, **p* < 0.05 vs. control. (**B**,**C**) Human adult cardiac fibroblasts transfected with siYap or siContr and exposed to hypoxia/TGFβ for stated durations normalized to corresponding loading control from Figures 6C,E. Data represent mean ± S.E.M of fold changes from siContr-infected vehicle-treated control group (-); *n* = 3–4/condition, **p* < 0.05 vs. corresponding (-) control.



Supplemental Figure S7. Hypoxia/TGFβ does not activate Erk signaling at early timepoints. (**A**,**C**) Representative immunoblot for indicated proteins of human adult cardiac fibroblasts transfected with siYap or siContr and exposed to hypoxia/TGFβ. (**B**,**D**) Fold change immunoblot densitometry analyses of indicated proteins normalized to corresponding loading control. Data represent mean ± S.E.M of fold changes to siContr-infected vehicle-treated control group (-); *n* = 3/condition.