

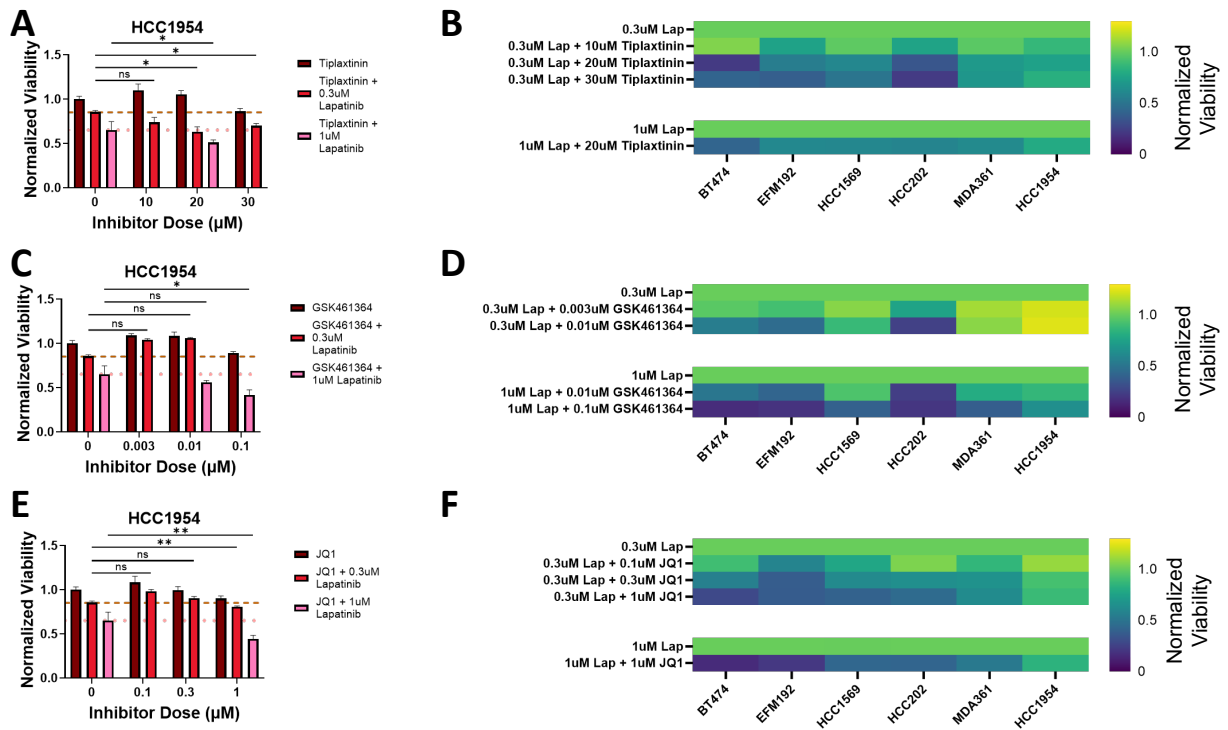


Figure S1: Fibroblast-insensitive HCC1954 cells are less responsive to combination therapies compared to fibroblast-protected cell lines.

(A) High doses of tiplaxtinin further reduces viability of HCC1954 cells treated with fibroblast-conditioned medium compared to lapatinib alone. Red and pink lines indicate viability in lapatinib-treated condition. Viability is normalized to untreated condition. (B) Response to tiplaxtinin (PAI1i) combination therapy for fibroblast-protected (BT474, EFM192, HCC1569, HCC202, MDA361) and fibroblast-insensitive (HCC1954) cells. Viability for combination therapies is normalized to lapatinib monotherapy. (C) HCC1954 response to GSK461364 (PLK1i) combination therapy is dose-dependent. (D) Viability of HER2+ breast cancer cell lines after treatment with GSK461364 combination therapy. Viability is normalized to lapatinib monotherapy. (E) Inhibition of PAI1 with JQ1 reduces HCC1954 viability compared to lapatinib alone. (F) Response of fibroblast-protected cell lines and fibroblast-insensitive HCC1954 cells to JQ1 combination therapy. *: $p < 0.05$, **: $p < 0.01$.

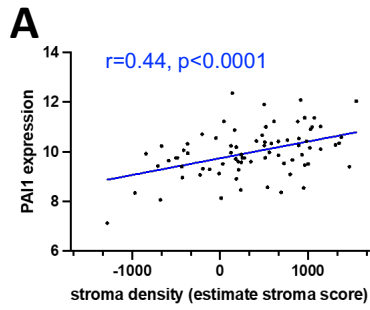


Fig. S2: PAI1 expression positively correlates with stroma score in independent dataset

(A) PAI1 expression in breast cancer patient data from The Cancer Genome Atlas (n=78) correlates with estimated stroma score. Pearson correlation coefficient $p<0.05$.