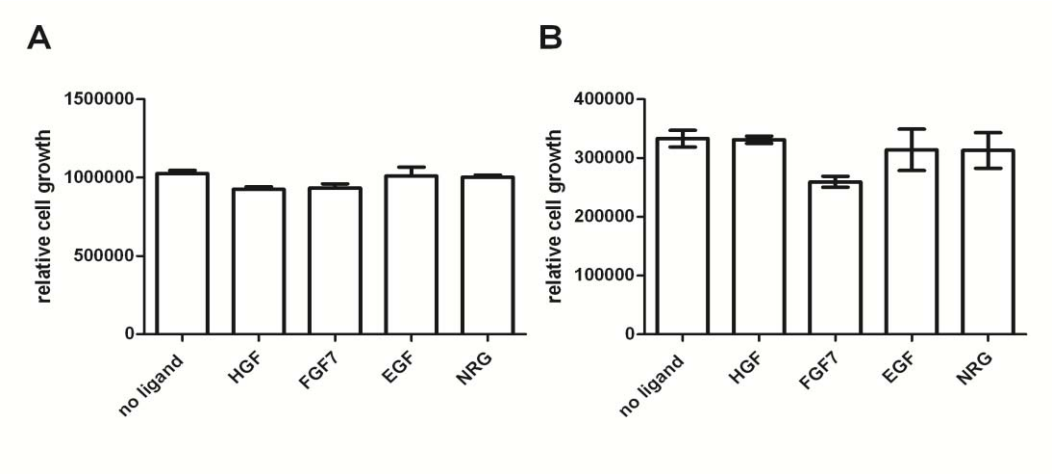

Figure S1. Validation of screening data using recombinant proteins in the absence of selective inhibitors. Relative cell growth measured after 96 h treatment of MKN45 and RT112 with recombinant proteins (250 ng/mL).

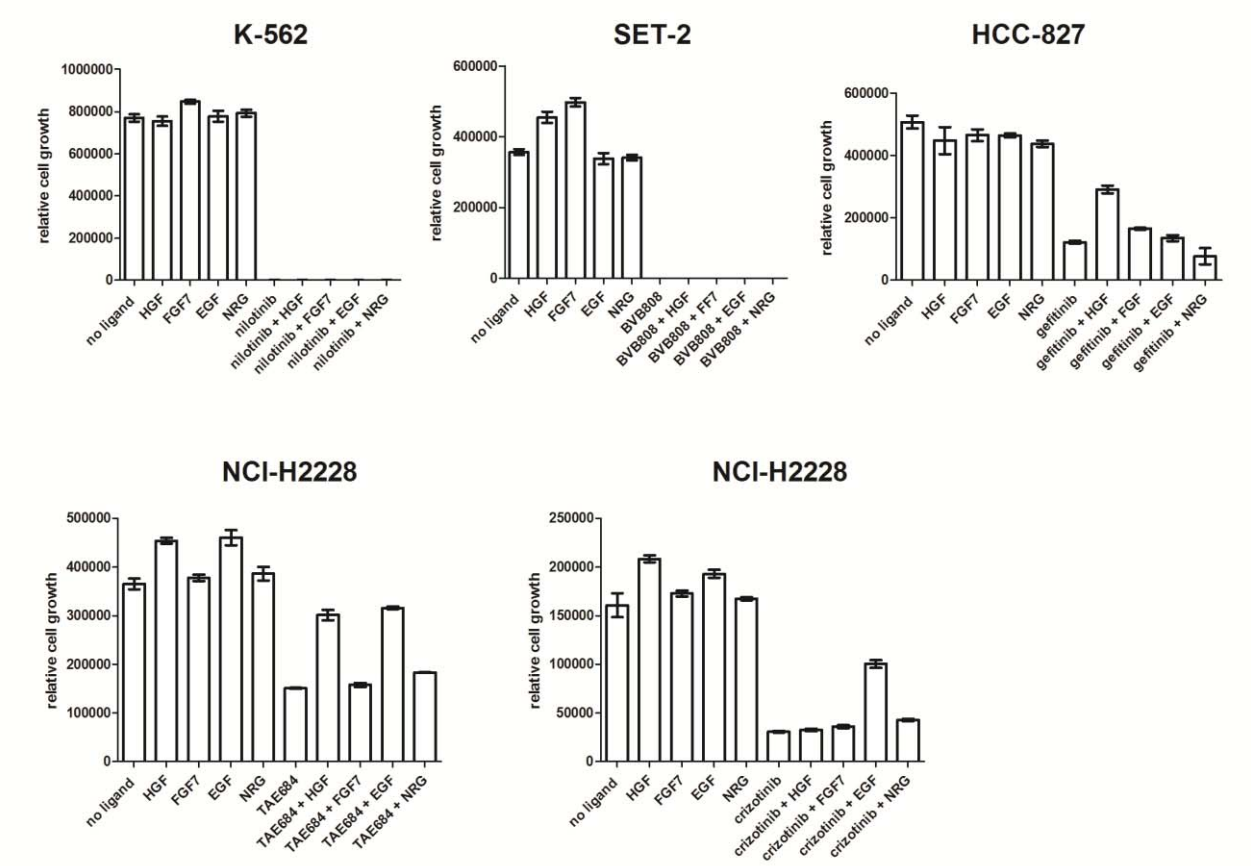

Figure S2. Treatment of RTK and non-RTK dependent cell lines with corresponding inhibitor in the presence or absence of recombinant ligands. All cell lines were treated for 96 h with their respective inhibitors and recombinant proteins were added at 250 ng/mL. K-562 cell line was treated with 0.03 μM nilotinib; SET-2 cell line was treated with 1 μM BVB808; HCC-827 cells were treated with 1 μM gefitinib; NCI-H2228 cells were treated with 0.5 μM TAE684 or 3 μM crizotinib. Relative cell growth was quantified using a CellTiter-Glo readout.

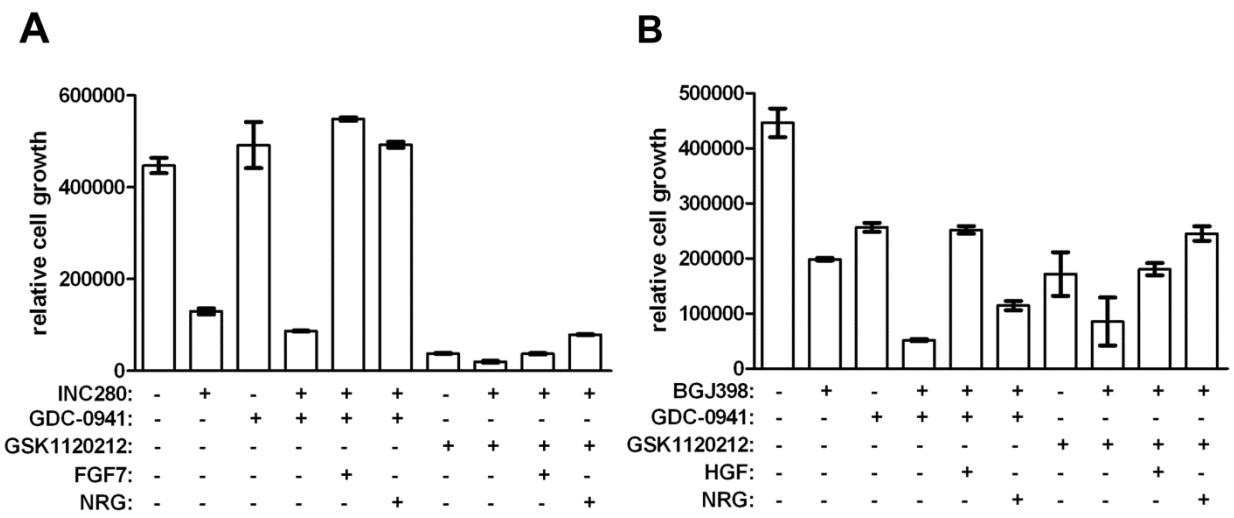

Figure S3. Comparison of MEK and PI3K pathway dependence in MKN45 and RT112 cell line rescue screens. (**A**) Rescue assay with in MKN45 cells and (**B**) RT112 cells with inhibitors as indicated. GDC-0941 and GSK1120212 tested at 1μM. INC280 and BGJ398 tested at 0.1 μM and 0.5 μM, respectively. rhFGF7 and rhNRG1 tested at 250 ng/mL.

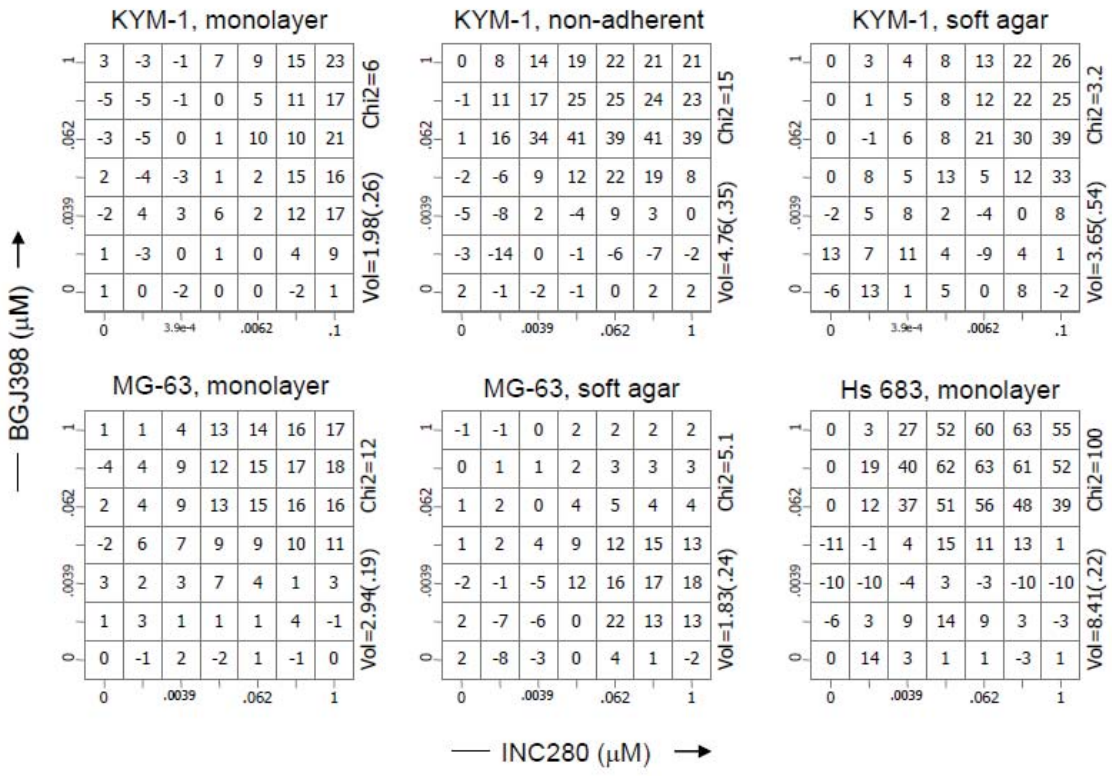

Figure S4. Additional (or reduced) effect level in percent relative to drug self combination based on the Loewe model. Compound concentrations are in micromolar. Layout is analogous to Figure 4B.

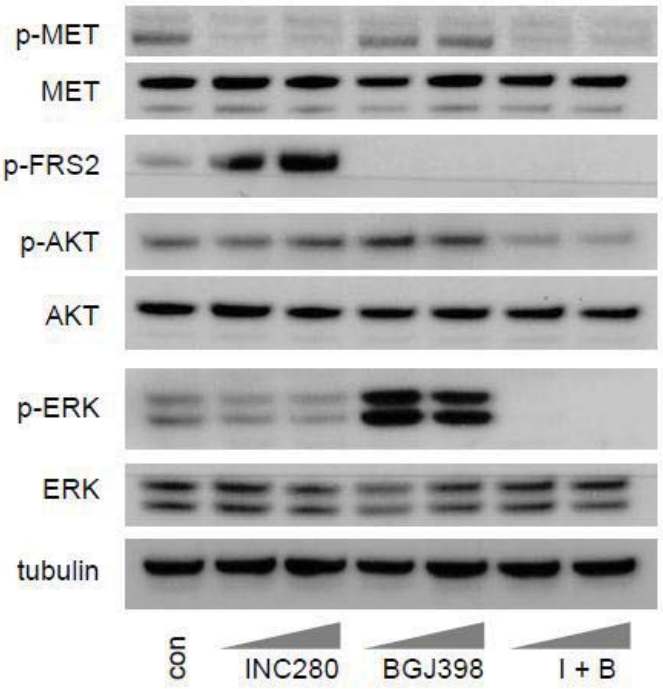

Figure S5. Protein phosphorylation in KYM-1 cells treated with RTK inhibitors on non-adherent plates. KYM-1 cells were grown on non-adherent cells, leading to cluster formation and tighter cell contacts than on adherent plates. Cells were treated for 2 hours with the indicated RTK inhibitors (0.1 or 1 μM, 0.1 + 0.1 μM or 1 + 1 μM in combination). The indicated (phospho-)proteins were visualized by Western blotting.