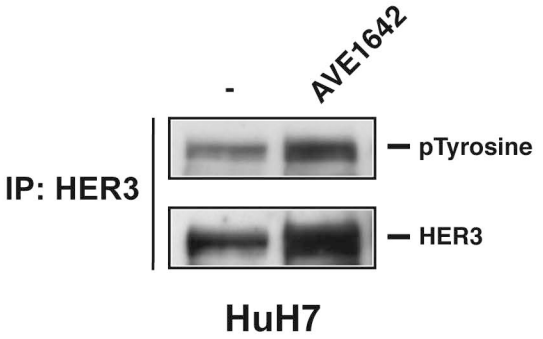
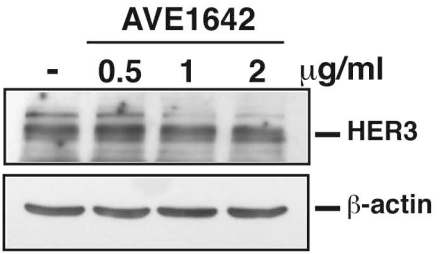
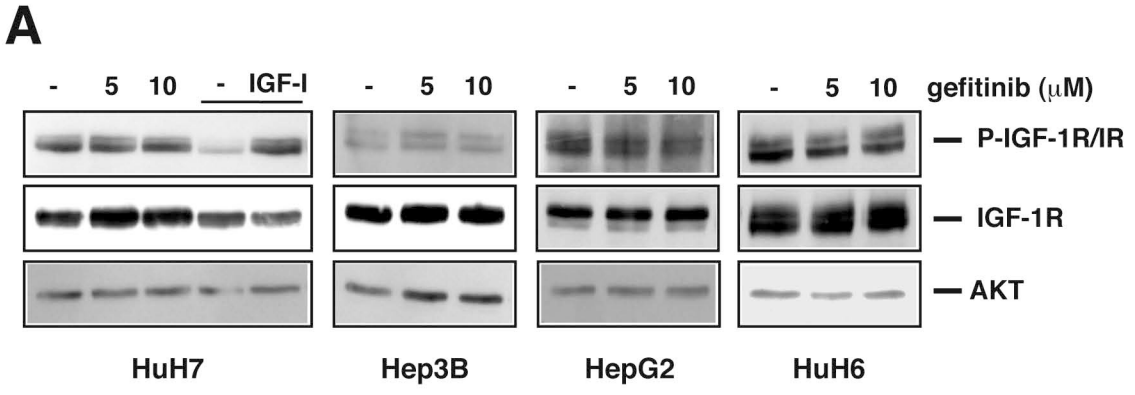
Supplementary Figure S1

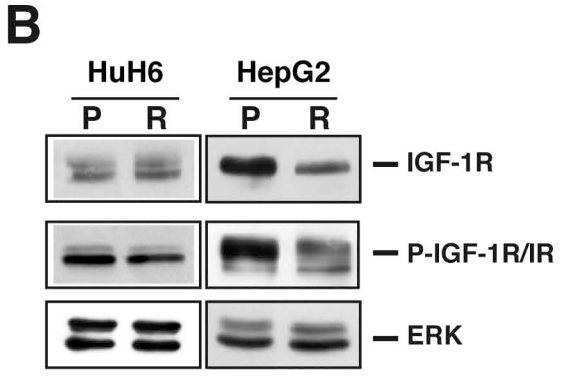


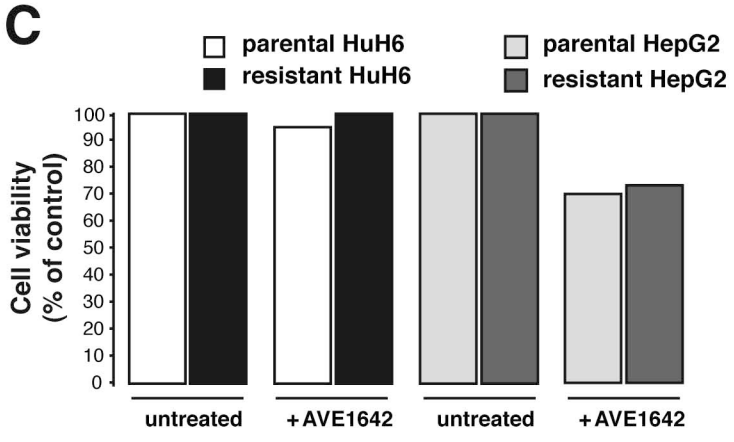
Supplementary Figure S2



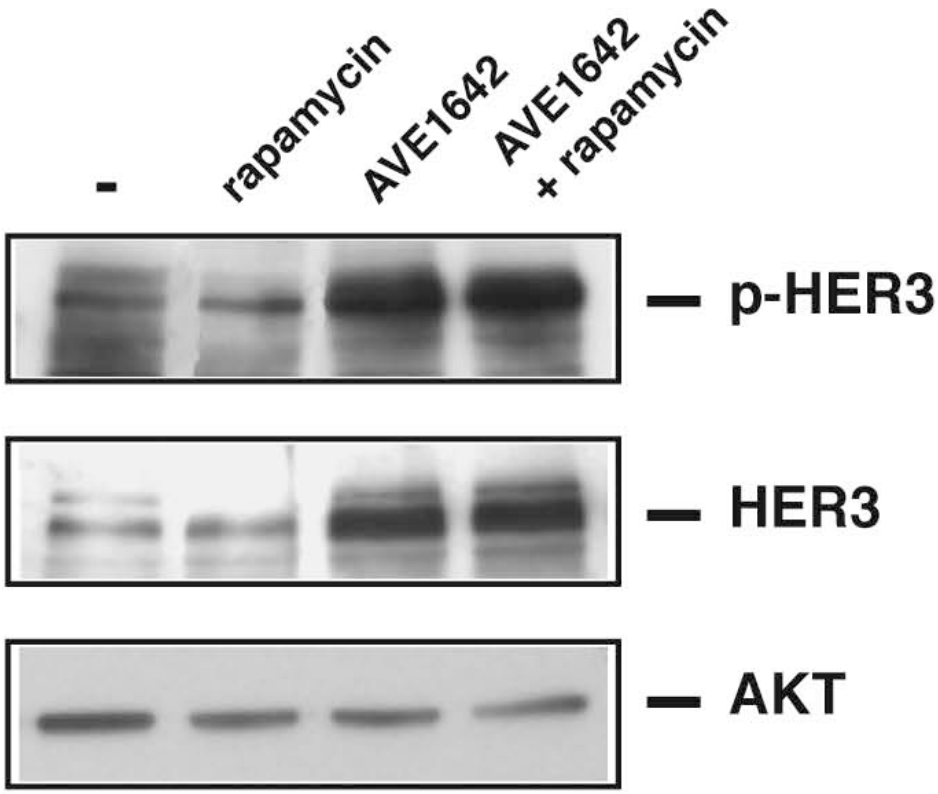
Supplementary Figure S3







Supplementary Figure S4



Legends to supplementary figures

Figure S1: Effect of AVE1642 on tyrosine phosphorylation and expression of HER3

HER3 was immunoprecipitated from whole-cell lysates obtained from HuH7 cells treated or not with AVE1642 (0.5 μg/ml) for 48 h and immunoblotted for phosphotyrosine and total contents. Blots are representative of two independent experiments.

Figure S2: Normal human hepatocytes were treated with increasing concentrations of AVE1642 (0-2 μg/ml) for 48 h and total expression levels of HER3 were assessed by Western blot analysis. Blots are representative of three independent experiments.

Figure S3: Effect of gefitinib on IGF-1R signalling in hepatoma cells

A, HCC cell lines were treated or not with gefitinib (5 and 10 μM) for 24 h (HuH6) or 48 h (HuH7, Hep3B and PLC/PRF5) before being analyzed by Western blot for phosphorylated and total levels of IGF-1R and AKT. As a positive control for IGF-1R activation, HuH7 cells were treated for 20 min with or without 10^{-8} M IGF-I. ***B***, gefitinib resistant pools of HuH6 and HepG2 cells (R) were compared to parental cells (P) for phosphorylated and total levels of IGF-1R and ERKs. ***C***, Parental and gefitinib resistant pools of HuH6 and HepG2 cells were incubated for 72 h with or without AVE1642 (0.5 μg/ml) and analyzed for cell viability in a MTT assay. Data are means of two experiments.

Figure S4: Effect of rapamycin on AVE1642 induction of HER3 phosphorylation and expression

HepG2 cells were pre-treated for 2 h with or without rapamycin (2 nM) and then incubated or not with AVE1642 (0.5 μg/ml, 48 h). Whole-cell extracts were analyzed by Western blotting

for phosphorylated and/or total HER3 levels. Blots are representative of two independent experiments.