Figure S1. Cellular localization of S1PR1 in A549 cells. A549 cells were treated with FTY720 or FTY720-P at the indicated concentrations. At 1 and 4 h after treatment, cells were fixed and stained with anti-S1PR1 antibody (green). Nuclei were stained using DAPI (blue). FTY720, Fingolimod; FTY720-P, FTY720 (S)-phosphate; S1PR1, sphingosine 1-phosphate receptor 1.

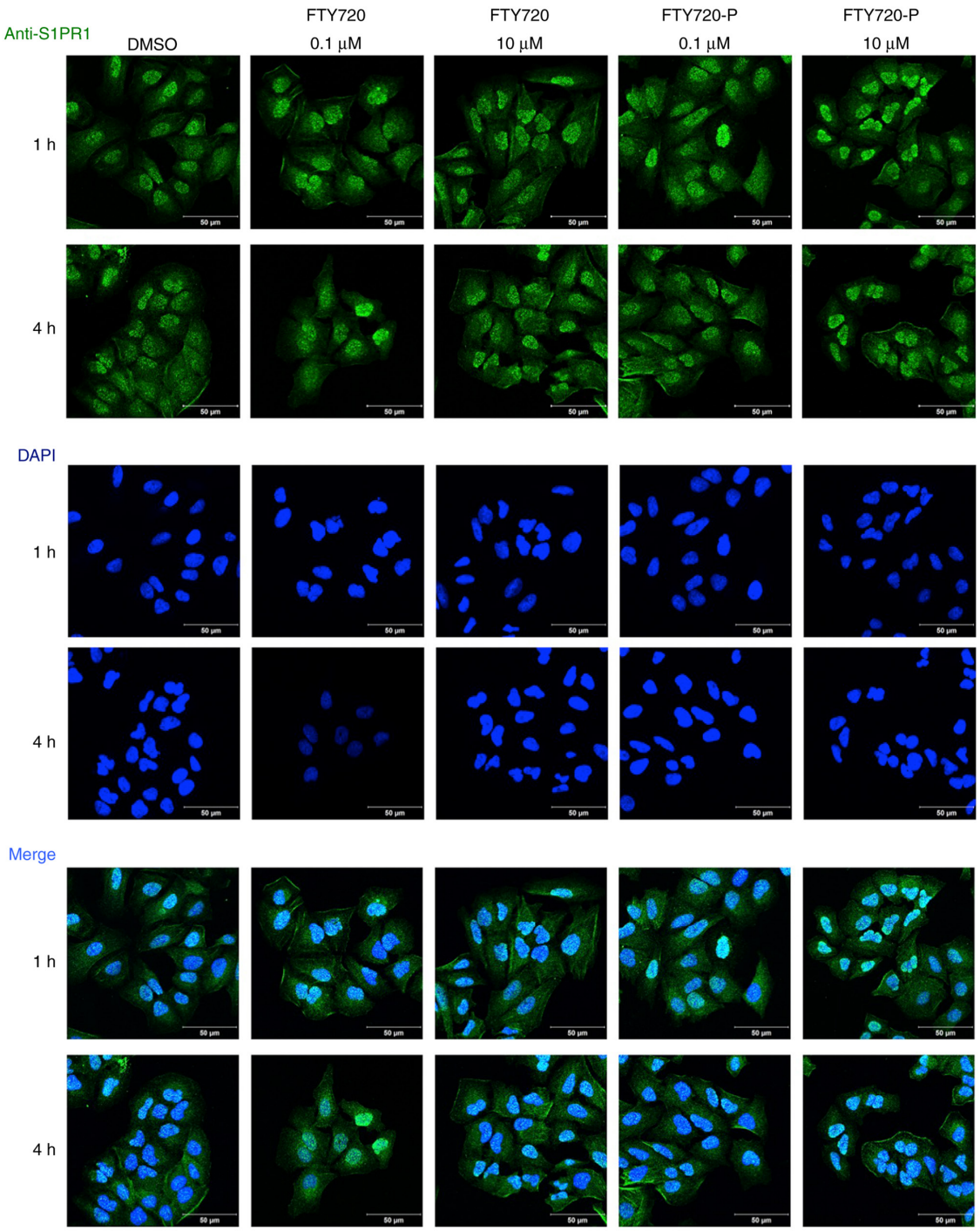

Figure S2. Cell growth inhibition in NSCLC cells. A549 cells were treated with azithromycin at the indicated concentrations combined with one of the following TKIs (10 μM); Sor, Gef, Erl, Lap or Ima. Cell viability was assessed 24 or 48 h after treatment. NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor; Sor, sorafenib; Gef, gefitinib; Erl, erlotinib; Lap, lapatinib; Ima, imatinib.

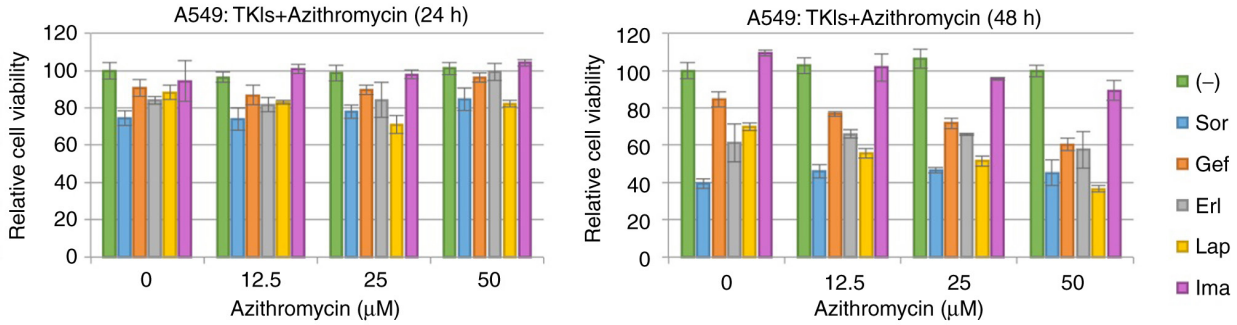

Figure S3. A549 cells or ATG5-KO A549 cells were treated with 10 nM BafA1 for 24 h. (A) Cellular proteins were separated by SDS-PAGE and then immunoblotted with anti-ATG5, anti-MAP1LC3B, anti-SQSTM1 and anti-GAPDH antibodies. (B) A549 cells or ATG5-KO A549 cells were treated with a combination of FTY720 (5 or 10 μM) and 10 μM TKIs (Sor, Gef or Lap). Cell viability was assessed 24 and 48 h after treatment. BafA1, bafilomycin A1; Sor, sorafenib; Gef, gefitinib; Lap, lapatinib; KO, knockout; ATG5, autophagy protein 5; MAP1LC3B, microtubule associated proteins 1A/1B light chain 3B; SQSTM1, sequestosome; FTY720, Fingolimod.

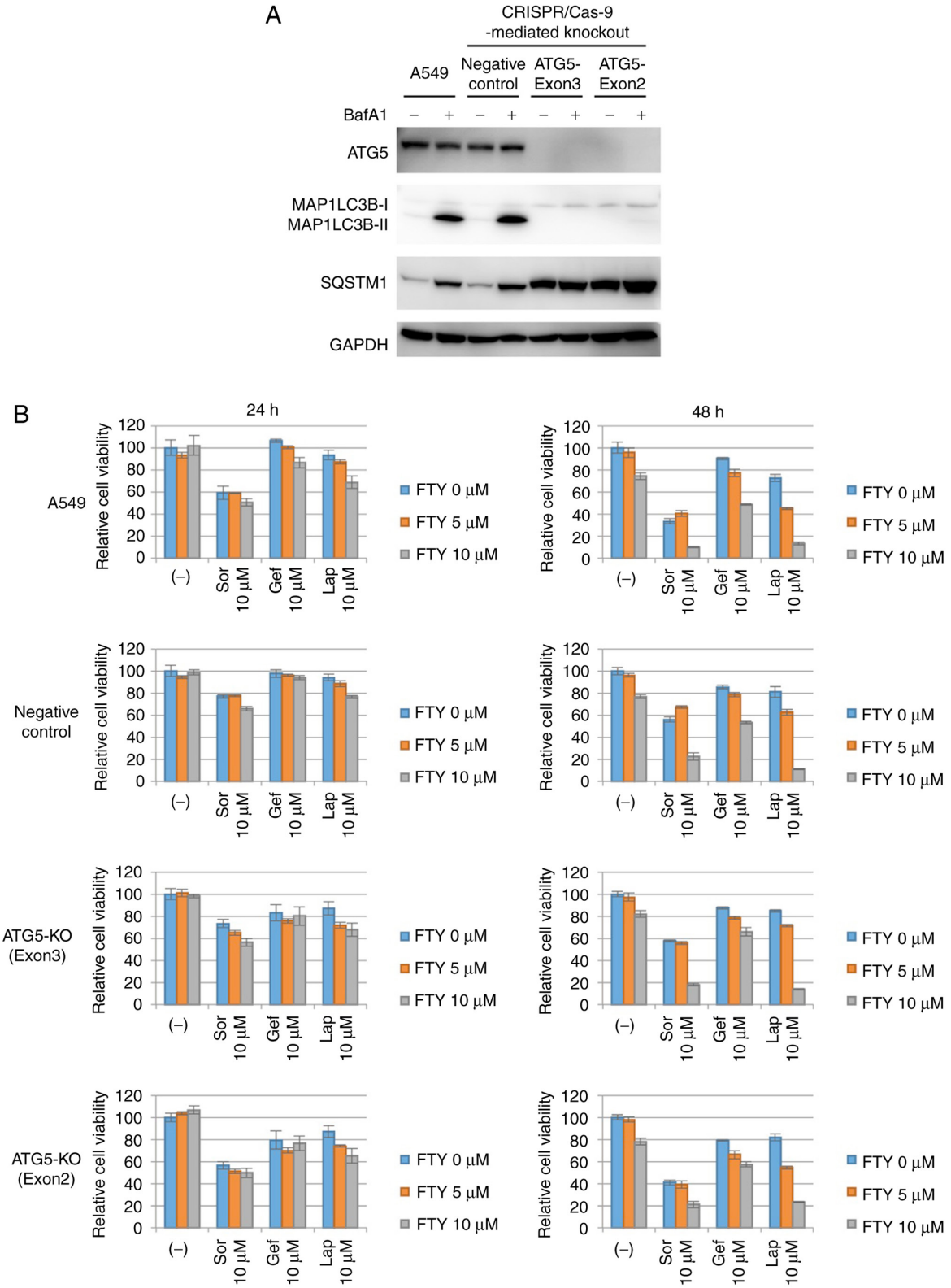

Figure S4. Comparison of morphological alterations. A549 cells were treated with Sor (10 μM) or Lap (10 μM) in the presence or absence of FTY720 (5 or 10 μM) for 24 or 48 h. Cells were stained with May-Grünwald-Giemsa and examined under a digital microscope. Sor, sorafenib; Lap, lapatinib; FTY720, Fingolimod; DMSO, dimethyl sulfoxide.

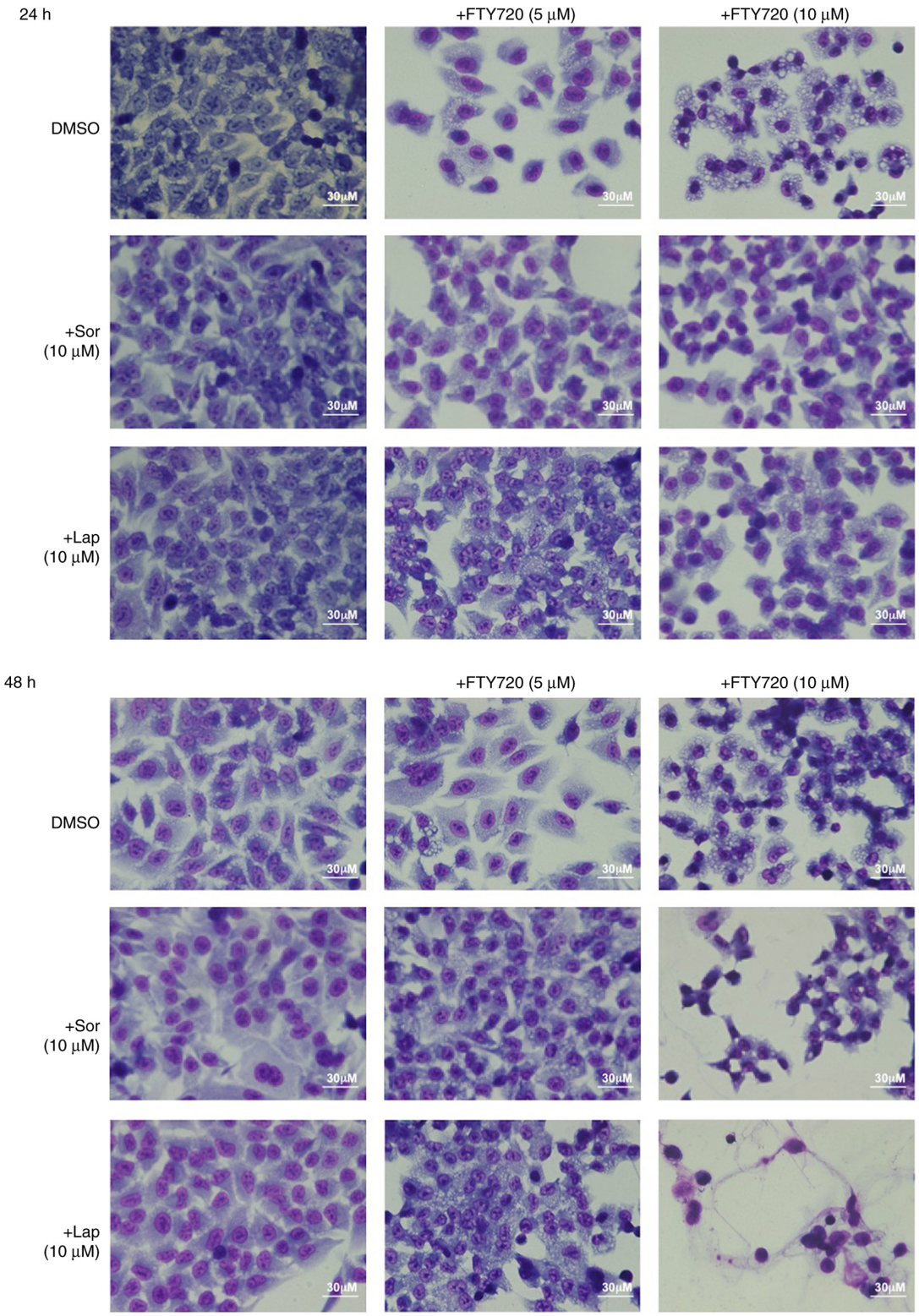

Figure S5. A549 cell viability. (A) Cells were treated with a combination of 10 μM FTY720 and 10 μM TKIs (Sor, Gef or Lap) in the absence or presence of Z-VAD (25 or 50 μM) or (B) Nec-1 (25 or 50 μM). At 24 and 48 h after treatment, cell viability was assessed. Z-VAD, Z-VAD-FMK; Nec-1, Necrostatin-1; Sor, sorafenib; Gef, gefitinib; Lap, lapatinib; FTY720, Fingolimod; TKI, tyrosine kinase inhibitor.

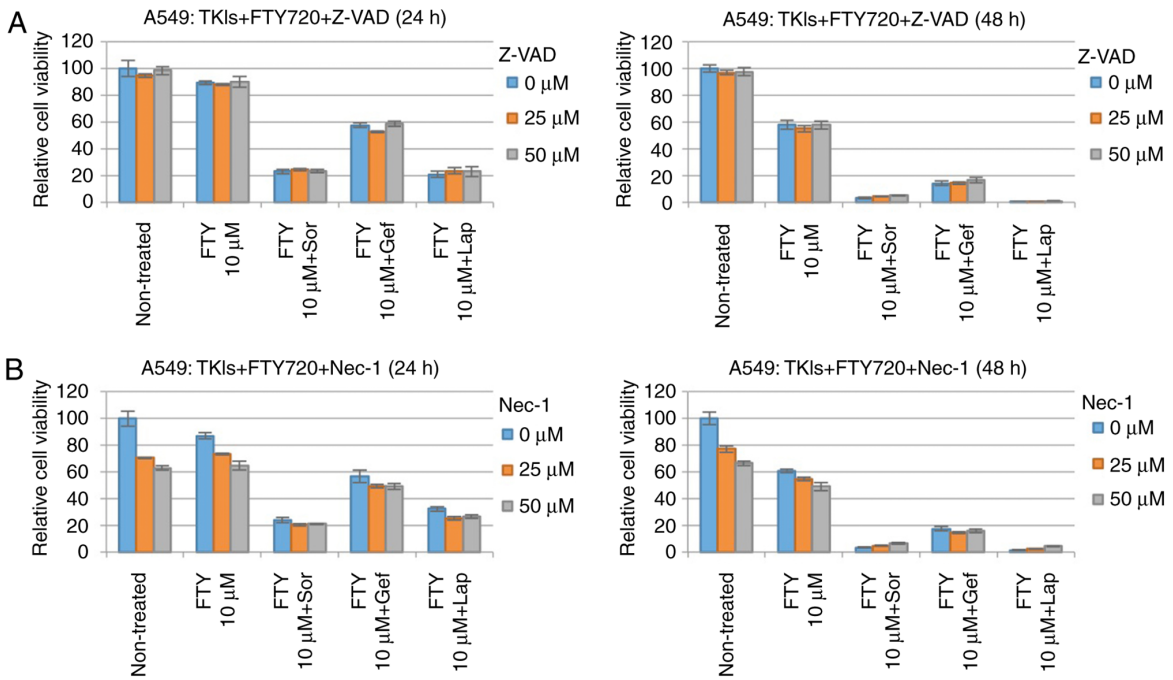

Figure S6. A549 cells were transfected with *RIPK1*-specific siRNA or NC siRNA. (A) Cellular proteins were separated by SDS-PAGE and immunoblotted with anti-RIPK1 and anti-GAPDH antibodies. (B) Time course of gene silencing of *RIPK1* and subsequent cell viability assay. (C) A549 cells, transfected *RIPK1*-specific siRNA or NC siRNA, were treated with a combination of FTY720 (5 or 10 μM) and 10 μM TKIs (Sor, Gef or Lap). Cell viability was assessed 24 and 48 h after treatment. RIPK1, receptor-interacting serine/threonine-protein kinase 1; siRNA, small interfering RNA; NC, negative control; Sor, sorafenib; Gef, gefitinib; Lap, lapatinib; FTY720, Fingolimod.

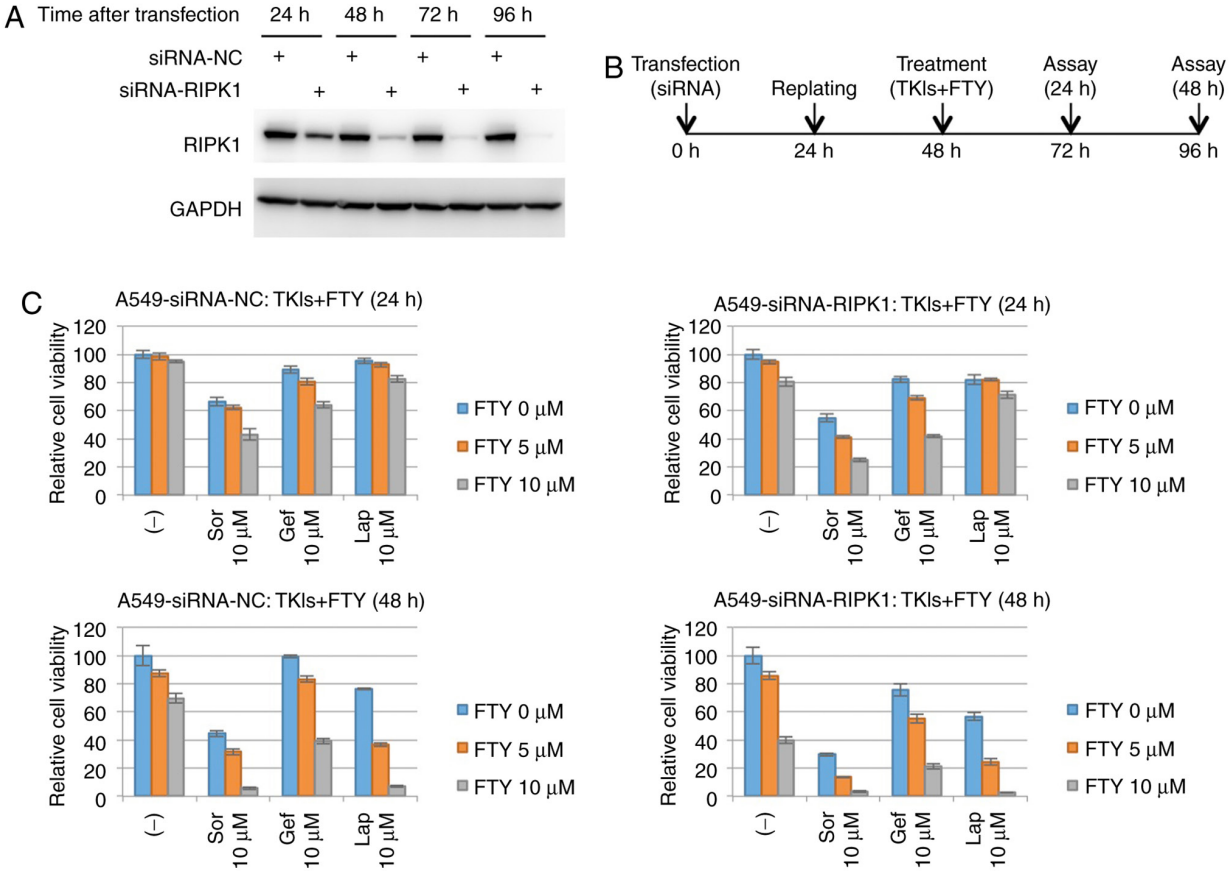

Figure S7. Non-small cell lung cancer cells (A549 or H226) were treated with FTY720 at the indicated concentrations in the absence or presence of increasing doses of Lapatinib. Cell viability was assessed 24 and 48 h after treatment. FTY720, Fingolimod.

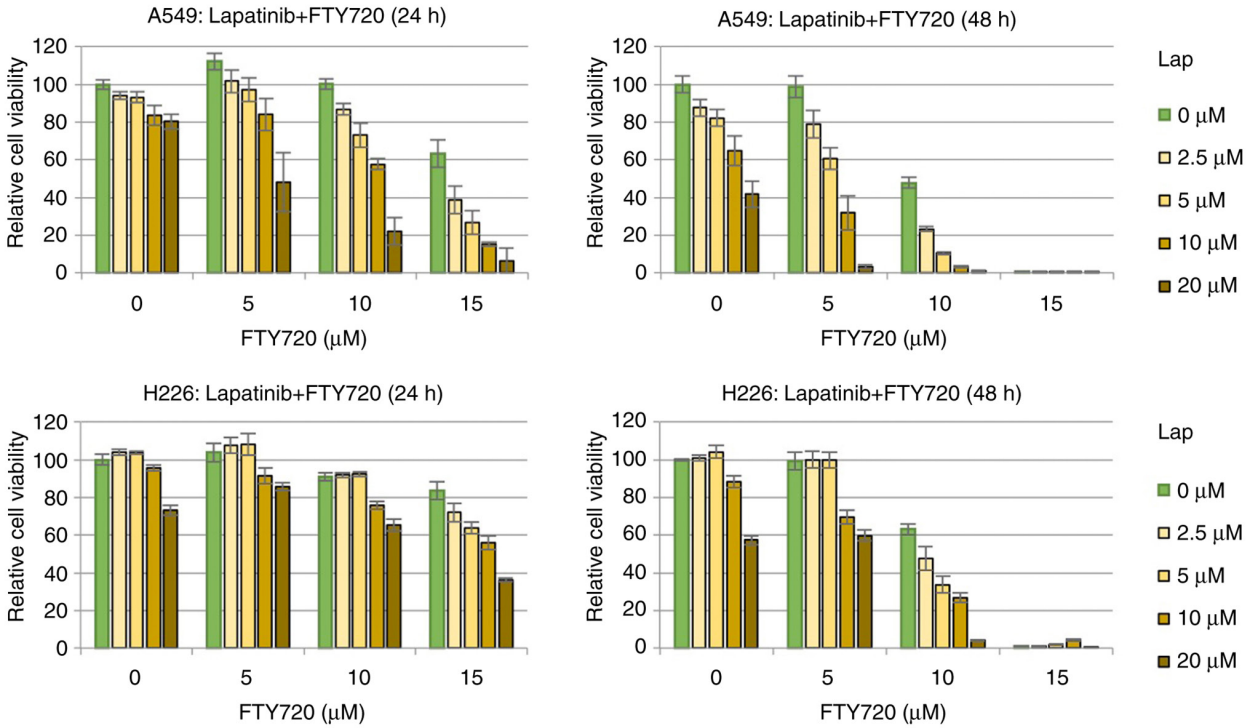

Figure S8. Cellular proteins prepared from A549, H596, H226 and BT474 (positive control) cells were separated by SDS-PAGE and immunoblotted with anti-EGFR, anti-p-EGFR, anti-ERBB2 and anti-p-ERBB2 antibodies. Immunoblotting using anti-ACTB and anti-GAPDH antibodies was performed as an internal control. Band intensities were determined by densitometry and the ratio of EGFR/GAPDH, p-EGFR/GAPDH, and p-EGFR/EGFR are shown in the graphs. The expression of ERBB2 and phosphorylated ERBB2 was not detected in A549, H596 or H226 cells. EGFR, p-, phosphorylated; EGFR, epidermal growth factor receptor; ERBB2, Erb-B2 receptor tyrosine kinase receptor.