SUPPORTING INFORMATION

Material and Methods

Materials. Sorafenib was obtained from Dr. Scott Wilhelm at Bayer HealthCare Pharmaceuticals, Montville, NJ. For *in vitro* use, sorafenib tosylate was dissolved in DMSO. For *in vivo* experiments, sorafenib was prepared as described previously.[1] Briefly, sorafenib was dissolved in Cremophor EL/ethanol (50:50; Sigma Cremophor EL, 95% ethyl alcohol); stock solutions were prepared fresh every 3 days. Final dosing solutions were prepared on the day of use by dilution of the stock solution with sterile H_2O to the final concentration. The Raf kinase inhibitor ZM336372 was purchased from Calbiochem (Gibbstown, NJ) (24). Recombinant human TRAIL was obtained from R&D Systems (Minneapolis, MN). EGFR-inhibitor AG 1478, ERK inhibitor II, Src-inhibitor AG 1879 and JAK inhibitor I were obtained from Calbiochem (San Diego, CA). Sodium-orthovanadate, hydrogen peroxide (H_2O_2) and catalase for the synthesis of sodium-pervanadate were from Sigma Chemical (St. Louis, MO); sodium pervanadate was generated as described previously by Imbert et al. (40). The following primary or secondary antibodies were used: polyclonal rabbit anti-Mcl-1 (#sc-819) anti-STAT3 (#sc-482), and anti-SOCS-1 (#sc-7005-R), polyclonal goat anti-β-actin (#sc-1615) from Santa Cruz Biotechnology (Santa Cruz, CA); monoclonal rabbit anti-Tyr^{705} phospho-STAT3 (#9145), anti-JAK1 (#3344), anti-JAK2 (#3229), anti-Tyr$^{1007/1008}$ phospho-JAK2 (#3776), and polyclonal rabbit anti-Tyr^{705} phospho-STAT3 (#9131), anti-SOCS-2 (#2779), anti-SOCS-3 (#2923), anti-SHP2 (#3752) and anti-Tyr^{580} phospho-SHP2 (#3703) from Cell Signaling Technology (Danvers, MA); rabbit polyclonal anti- Tyr$^{1022/1023}$ phospho-pJAK1

(#ab-5493) and anti-SHP1 (#ab-2020)from Abcam (Cambridge, MA); mouse monoclonal anti-human gp130 (Biosource, #AHT3001) and anti-human gp80 antibody (#AHR0061) from Biosource International (Camarillo, CA), and monoclonal mouse anti-phosphotyrosine (#05-1050) from Millipore (Temecula, CA), polyclonal goat anti-PTPRT (#AF3697) from R&D Systems (Minneapolis, MN). Primary antibodies were used at a concentration of 1:1,000. Horseradish peroxidase-conjugated anti-goat (Biosource International, #ACI 0404), -rabbit (Santa Cruz, #sc-2004), and –mouse (Invitrogen, #F21453) immunoglobulins were used at a dilution of 1:3,000.

Quantitation of IL-6 secretion. Levels of IL-6 in cell culture media were determined by an enzyme-linked immunosorbent assay using a commercially available kit (R&D Systems, Minneapolis, MN).

Statistical Analysis. All data represent at least 3 independent experiments using cells from a minimum of three separate isolations and are expressed as the means ± standard deviations. Differences between groups were compared using 2-tailed Student *t*-tests or chi-square tests.

Reference

1. Wilhelm SM, Carter C, Tang L, Wilkie D, McNabola A, Rong H, Chen C, et al. BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis. Cancer Res 2004;64:7099-7109.