Supplementary information:

Culture conditions. The human glioma cell lines U251 MG, A172, and U373 MG (from the American Type Culture Collection, Manassas, VA) were maintained in Dulbecco's modified Eagle's medium (DMEM)/F12 (1:1, vol/vol) supplemented with 10% fetal bovine serum (SAFC Biosciences, Lenexa, KS) and 1% antibiotic-antimycotic mixture containing penicillin 5,000 U/ml and streptomycin 5,000 U/ml. Neurospheroid cultures were established from acute cell dissociation in human glioblastoma (GBM) postsurgical specimens and maintained in DMEM/F12 supplemented with B27 (Invitrogen, Carlsbad, CA), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF; 20 ng/ml each; Sigma-Aldrich, St. Louis, MO) according to previously described procedures (Galli *et al.*, 2004; Singh *et al.*, 2004). We previously developed Tie2-overexpressing and vector-transfected U251 MG cells (U251.Tie2 and U251.vector, respectively), and we maintained these cells in growth medium containing G418 300 μg/ml (Lee *et al.*, 2006). Cells were incubated at 37ºC in a 5% CO_2 atmosphere.

Quantitative Real-Time PCR. We performed quantitative real-time PCR (qPCR) of ABC transporter mRNA levels using the SYBR green real-time PCR method with SYBR green PCR core reagents (ABI Systems; Foster City, CA) in the Chromo4 Real-Time PCR System (Bio-Rad; Hercules, CA). The sequences of the sense and antisense primers used were as follows: human ABCG2 , 5´-AGTTCCATGGCACTGGCCATA-3´ and 5´-TCAGGTAGGCAATTGTGAGG-3´; ABCC2, 5´-TCGCTGAAGTGAGAGTAGATT-3´and 5´-TCCTTGGCGAGCTGGATTACA-3´; human MDR1, 5´-CCCATCATTGCAATAGCAGG-3´ and 5´-TGTTCAAACTTCTGCTCCTGA-3´, human MRP1: 5´-ATGGGGAAGGTGAAGGTCGG-3´ and 5´-GACGGTGCCATGGAATTTGC-3´; and human GADPH: 5'-ATGGGGAAGGTGAAGGTCGG-3' and 5'-GACGGTGCCATGGAATTTGC-3'.

Each amplification cycle consisted of denaturation for 15 s at 95°C and annealing/extension for 1 min at 60°C. We conducted qPCR for 40 cycles, and we added one additional step, a melting curve, to distinguish the specific products from nonspecific products and primer dimers. We constructed the melting curve by increasing the temperature from 60°C to 95°C, with a temperature transition rate of 0.2°C/s. Each sample was tested in triplicate, and we analyzed the relative gene expression data using the comparative threshold cycle method (Alonso *et al.*, 2007).

Statistical comparisons were carried out using either the *t* test or one-way analysis of variance (ANOVA) followed by a Student-Newman-Keuls multiple range test.

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