**Supplementary Figure Legends**

**Supplementary Figure S1.** Effect of GSK3β RNA interference on the expression of GSK3β and the migration and invasion of glioblastoma cells. **A,** Western blotting analysis comparing the levels of expression of GSK3α and GSK3β between the cells treated with non-specific (NS) and GSK3β-specific (S) siRNA (10 nM each), respectively. **B,** Upper panels show the representative time course of glioblastoma cell (T98G and U251) migration in the wound healing assay for cells transfected with control or GSK3β-specific siRNA (10 nM each). The assay was performed by scratching confluent cells followed by serial observation of reference points at the indicated times under a phase-contrast microscope. In the lower panels, the widths of wounds was measured and expressed as a percentage of the initial gap at time zero. Values shown are the means ± SD of three separate points of observation. **C,** The effect of non-specific (NS) and GSK3β-specific (S) siRNA on invasion of glioblastoma cells. Invading cells through a matrigel-coated transwell chamber were scored for the same cells treated with the respective siRNA (NS, S). In each assay, the mean number of invading cells in 5 high-power microscopic fields was calculated with SDs. Representative photomicroscopic findings from the assay are shown below each column. **B, C,** \*: p < 0.05, statistically significant difference between cells treated with control (NS) and GSK3β-specific (S) siRNA.

**Supplementary Figure S2.** Effects of GSK3β inhibition on the subcellular localization of F-actin and Rac1 in T98G cells and on the lamellipodia formation in U251 and T98G cells. **A,** Cells were treated with either DMSO or 25 µM AR-A014418 (AR) for 24 hrs and then processed for immunofluorescence staining of F-actin (red fluorescence) and Rac1 (green fluorescence). Cell nuclei were counterstained with Hoechst 33342. Merged images are also shown. Scale bars in the left 6 panels indicate 100 µm and those in the right 6 panels indicate 10 µm. **B,** The effect of GSK3β inhibition on cell morphology and motility was reversible. T98G cells were treated with AR-A014418 (AR; 10 µM) for 24 hrs then washed by PBS and immediately replaced with medium containing DMSO alone (AR 10 µM → DMSO) and cultured for another 24 hrs. Cells were then processed for immunofluorescence staining of F-actin and Rac1. Cell nuclei were counterstained with Hoechst 33342. Merged images are also shown. The scale bar in each panel indicates 100 µm. **C,** Effect of non-specific (NS) and GSK3β-specific (S) siRNA on the incidence of lamellipodia-positive glioblastoma cells scored under phase-contrast and fluorescence (F-actin) microscopy, respectively. In each assay, the mean incidence (%) of lamellipodia-positive cells in 5 high-power microscopic fields was calculated with SDs. \*: p<0.05.

**Supplementary Figure S3.** Expression of mRNA of ECT2 and VaV3 **(A)** and various integrin subunits **(B)** measured by qRT-PCR in different glioblastoma cells (A172, U87, T98, U251) treated with either DMSO or 25 µM AR-A014418 for 24 hrs. The relative mRNA expression level of GEF and integrin genes (target mRNA:β-actin mRNA ratio) is shown. mRNA levels are expressed as a proportion of the mRNA level of A172 cells treated with DMSO, which was assigned a value of 1.

**Supplementary Figure S4.** Putative molecular pathway through which deregulated GSK3β promotes glioblastoma cell migration and invasion. This pathway was generated according to the results shown in Figures 2-5 and previous reports described in the text. The exact molecular pathway by which GSK3β mediates the activation of FAK (open arrow) remains to be determined.

**Supplementary Figure S5.** Effects of GSK3β inhibition on the formation of invadopodium-like microstructures and matrix degradation by U251 cells. **A,** U251 cells were treated with either DMSO (DM) or 25 μM AR-A014418 (AR) for 24 hrs. The mean number of invadopodium-like microstructures in randomly selected 5 cells was calculated with SDs and statistically compared between the same cells treated with the respective agents (DM and AR). \*: p < 0.05. **B,** The area of gelatin degradation (%) was measured by the Image J software and compared between the U251 cells treated with DMSO and 25 μM AR-A014418 (AR), respectively.

**Supplementary Figure S6.** Immunohistochemical and Western blotting examinations for the expression and level of glycogen synthase (GS; a substrate of GSK3β) phosphorylated at its serine 641 residue (pGSS641) in the brain tumors of rodents treated with DMSO or AR-A014418 (2 mg/kg body weight) for 2 weeks. **A,** Representative immunohistochemical findings of pGSS641 expression in the tumors. Scale bars, 50 m. **B,** Two mice (ID: 1 and 2) treated with DMSO and those (ID: 3 and 4) treated with AR-A014418 were examined for the levels of pGSS641, total GS and β-actin in the tumors by Western blotting. The value below each lane of the blot for pGSS641 shows the relative level of serine 641 phosphorylation quantified by densitometry and normalized to that of total GS. The reduced level of pGSS641 indicates an inhibitory effect of AR-A014418 on GSK3β activity in the tumor cells.