**Supplementary methods**

**Cell Cycle Analysis**

Cells with or without treatment of methionine depletion/statin addition were collected using Accutase® solution (Sigma, USA). The Cell Cycle Phase Determination Kit (Cayman Chemical, Ann Arbor, MI, USA) was used for cell cycle analysis. In brief, collected cells were rinsed twice with buffer, then fixed at −20°C overnight. Cells were washed twice with ice-cold phosphate buffered saline, and stained with propidium iodide/RNase staining buffer solution in the dark for 30 minutes at room temperature. Then, cells were analyzed with a flow cytometer (Guava® EasyCyte™ Mini, Luminex Japan, Tokyo, Japan). A histogram of the cell cycle distribution was generated from 5000 events per sample and data were analyzed using Guava® Cell Cycle software.

**Colony Formation Assay**

Cells were seeded into laminin-coated 12-well plates in triplicate at a density of 500 cells/well in 2 ml of medium with or without treatment medium. After 120 h, the cell colonies were stained for 15 min with a solution containing 0.5% crystal violet and 25% methanol, followed by three rinses with tap water to remove excess dye. The colony numbers were counted with an all-in-one fluorescence microscope (Model BZ-X810, Keyence, Osaka, Japan) and attached software Hybrid Cell Count (BZ-H4C, Keyence).

**Dye Exclusion Test**

Dye exclusion testing was performed to analyze cell viability. Fixed amounts of cells were seeded and cultured in medium with (control) or without methionine for 3 days. Harvested cells were suspended in phosphate buffered saline-containing trypan blue and then examined to determine the percentage of cells with blue clear cytoplasm (nonviable cells) versus total cells using a cell counter (LUNA, Logos Biosystems, Annandale, VA, USA). The relative rate against the control sample was calculated.

**Measurement of Cholesterol, S-adenosyl-methionine (SAM), and S-adenosylhomocysteine (SAH) in Tissue Using ELISA**

Measurement of cholesterol, SAM, and SAH used glioblastoma stem cells cultured with CELRENA medium or methionine-deprived CELRENA medium for 72 h and 10 ×106 cells/cell pellets were homogenized by sonication in ice-cold phosphate buffered saline followed by centrifugation at 10,000g for 15 min. Intracellular cholesterol, SAM, and SAH concentrations were measured using the Total Cholesterol Assay Kit (Colorimetric, Cell Biolabs, Inc., San Diego, CA, USA) and SAM and SAH ELISA Combo Kit (Cell Biolabs, Inc.) in accordance with the manufacturer's instructions under the indicated conditions. The standards were generated using the cholesterol standard and SAH/SAM-bovine serum albumin conjugate supplied in the kit.After the reaction was stopped, the OD450 and OD620 values were read using a SpectraMax iD3 Multi-Mode Microplate Reader (Molecular Devices, San Jose, CA, USA). SAH/SAM ratios were calculated as the ratio of SAM to average SAH using the intracellular concentration (µg/mL) to determine the relative methylation potential.

**RNA Extraction Including microRNA (miRNA), cDNA Synthesis, and quantitative PCR (qPCR) Analysis**

RNA from cultured tumor cells was extracted with the *mir*Vana miRNA Isolation Kit (Ambion, Thermo Fisher Scientific K.K., Tokyo, Japan) or RNeasy Plus Mini Kit (QIAGEN, Germantown, MD, USA). For cDNA synthesis, RNA was reverse transcribed from random hexamers using the SuperScriptTM VILO™ cDNA Synthesis Kit (Invitrogen, Life Technologies, Thermo Fisher Scientific, Waltham, MA, USA). Real-time qPCR was then performed in triplicate on the StepOne Plus or Quant3 (Applied Biosystems, Thermo Fisher Scientific) using SYBRTM Green Realtime PCR Master Mix (Applied Biosystems, Thermo Fisher Scientific) to determine the mRNA levels. PCR was performed using a 20 μl volume containing 2 µl cDNA, 300 µM of each primer, and 10 µl of 2 × PCR master mix under the following conditions: 95 °C for 10 min followed by 40 cycles of 95 °C for 15 s and annealing/extension at 60 °C for 1 min. The data were normalized to the amount of human 18S rRNA, and the values are represented as the mean ± SD of 2−ΔΔCt in a triplicate assay.

The primers used in this study were described in Supplementary Table S2.