METHODS

Cell culture.

3T3, Ras transformed 3T3, MDA-MB-231, 293T, M229, M249 cells are cultured at 37°C with 5% CO_2, in Dulbecco's modified Eagle's medium (DMEM, Corning) containing 25mM glucose and 4mM L-glutamine supplemented with 10% fetal bovine serum (FBS, Gemini Bio-Products), 100 units/mL of penicillin, and 100 µg/mL of streptomycin (Gemini Bio-Products). For low glutamine treatment, DMEM without glutamine (Invitrogen 11960) was supplemented with 10% dialyzed FBS (Gemini Bio-Products) and 0.1mM or 0.2mM L-glutamine (Corning, 25-005). For low glucose treatment, complete DMEM and DMEM without glucose (Invitrogen 11966) were mixed to make the medium with different glucose concentrations, supplemented with 10% dialyzed FBS. For the low essential amino acid treatment, DMEM Ham's F-12 with HEPES, NaHCO3, and without amino acids (US Biological D9811-01) was supplemented with 10% dialyzed FBS, non-essential amino acid solution (Sigma M7145) and 4mM L-glutamine. For the medium with 10% total amino acids, the DMEM without amino acids was supplemented with 10% dialyzed FBS and 10% of each amino acid in the normal complete DMEM. All the amino acids powder or crystal was purchased from Sigma. For the medium with low Ser, Arg, Asn, and Asp, the DMEM without amino acids was supplemented with 10% dialyzed FBS, 0.2mM Ser, 15µM Arg, 0.02mM Asn and 0.2mM Asp and other amino acids as in complete DMEM. For hypoxia culture, the cells were cultured in the hypoxia chamber with 2% O_2. No cell lines used in this study were found in the database of commonly misidentified cell lines that is maintained by ICLAC and NCBI Biosample.

Transfection and transduction .

To generate lenti viral particles, plasmids containing TRC lentiviral shRNA of human EZH2 (TRCN0000018365, TRCN0000040076) was purchased from Thermo Scientific. Viral particles of human KDM6B TRC lentiviral shRNA (TRCN0000236676) were purchased from Sigma. To generate lenti viral particles in a 6cm dish, 293T cells were co-transfected with 2.5μg pLKO.1 empty vector or shRNA vector, 1.25μg pMDL, 0.625μg pCMV-VSV-G and 0.625μg pRSV-Rev (4:2:1:1), viral supernatants were collected after 48h and 72h. Cells were infected with the virus for two to four times during 48h. Two days after infection, 2μg/ml puromycin was used to select infected cells. For cDNA and siRNA trasfection, M229 cells were transfected with cDNA or siRNA, cultured in the medium with 4mM or 0.1mM Gln, then whole cell lysates or histone were collected and analyzed by western blotting. Human EZH2 cDNA (#24230) was purchased from Addgene. HIF-1α siRNA (SMART pool L-004018-00-0005) was purchased from Dharmacon.

Animal models and xenografts.

All animal procedures were approved by the Institutional Animal Care and Use Committee at City of Hope Cancer Center in compliance with ethical regulations. In brief, 3 to 5 million cells were resuspended in 200μL DMEM without FBS or antibiotics, and tumours were established in female nude mice or NSG mice (nude mice were from Taconic Laboratories; NSG mice were from the animal core in City of Hope; cells were injected when the mice are around 7-week old) by subcutaneous injection. Tumour size was measured every 2-3 days as described [57]. For the glutaminase inhibitor treatment, the mice were treated with 968 (15mg/kg body weight) by intraperitoneal injection when the tumour volume was around 300mm^3. Three rounds of treatment were carried out within 6 days (one treatment every other day). For histone

methylation inhibitors (DZNep and EPZ005687) and PLX4032 treatment, when the tumour size was around 100mm^3, mice were treated with DZNep (1.5mg/kg body weight) or EPZ005687 (2.5mg/kg) by intraperitoneal injection, and PLX4032 (10mg/kg body weight) by oral gavage. Mice were continually treated for 2 to 4 weeks. After treatment, animals were euthanized, tumours were harvested and samples from core and peripheral regions were dissected for further analysis. The melanoma tumours from transgenic mice with *Braf*^{tm1Mmcm} /*Pten*^{tm1Hwu} mutations were purchased from Jackson Laboratory.

Immunohistochemistry.

Immunohistochemical staining was performed on 5μm thick sections prepared from formalin fixed, paraffin-embedded tissue. Tissue sections were deparaffinized in xylene followed by 100% ethanol. Samples were quenched in 3% hydrogen peroxide and pretreated to promote antigen retrieval by steam in citrate buffer (PH 6.0) solution. Slides were incubated in Protein Block (DAKO) for 5min followed by incubation with primary antibody (diluted in TBS with 1% BSA) for 30min at room temperature. Slides were rinsed 2 x 5min in TBS 0.025% Triton with gentle agitation. Slides were incubated with secondary antibody Rabbit Polymer (DAKO) for 30min at room temperature followed by rinsing 2 x 5min TBS 0.025% Triton with gentle agitation. After washing in DAKO buffer, slides were incubated with the chromogen diaminobenzidine tetrahydrochloride (DAB) (DAKO) for 8min, counterstained with hematoxylin, and mounted. The staining was performed with the following antibodies: H3K9me3 (Abcam, ab8898), H3K27me3 (Millipore, 17-622), HIF-1α (Cell Signaling Tech, 3716), cleaved caspase 3 (Cell Signaling Tech, 9661).

Histone extraction and western blotting.

Histones were extracted from tumour tissues and cells as previously described[12] with slight modification. Briefly, 3×10^6 cells or 20 mg of homogenized tissues (homogenized with Precellys 24 homogenizer (Bertin Technologies) and Precellys Ceramic kit (peQlab, #91-PCS-CK14)) were lysed in hypotonic lysis buffer (10mM HEPES, 10mM KCl, 1.5mM MgCl2, 0.5mM DTT) and homogenized on ice with protease inhibitors (Roche) for 1h. H_2SO_4 was added to a final concentration of 0.2N and incubated at 4°C overnight with rotation. Supernatant was collected after centrifugation and histones were precipitated with a final concentration of 30% (W/V) TCA for 1h on ice, washed with ice cold acetone and dissolved in water. For whole cell lysates, cells were lysed in RIPA buffer (1% sodium deoxycholate, 0.1% SDS, 1% Triton X-100, 10 mM Tris [pH 8.0], and 150 mM NaCl), and tumour tissues were homogenized in RIPA buffer. Protein concentration was determined by BCA protein assay kit (Thermo, #23225). Histones or proteins were separated by SDS-PAGE and transferred to PVDF membranes. After blocking in 5% non-fat milk in TBS with 0.1% Tween-20, membranes were probed with primary antibodies and horseradish-peroxidase-conjugated secondary antibodies. The signal was visualized by Western Lightning Plus-ECL (PerkinElmer). The antibodies used for western blotting can be found in Supplementary Table 2.

RNA extraction and quantitative real-time PCR.

Total RNA was extracted using Trizol (Invitrogen) according to the manufacturer's protocol. The qScript cDNA Synthesis Kit (Quanta Biosciences) was used for cDNA synthesis. Quantitative real-time PCR was performed on the iQ5 real-time PCR machine (Biorad) using

SYBR Green PCR Master Mix (Quanta Biosciences). Experimental results were normalized to rRNA ribosomal 18S. The primers used are listed in Supplementary Table 3.

Flow cytometry.

For cell viability, cells were seeded into 6-well plates. After different treatments, the medium in the wells and trypsinized cells were collected, spun down and washed with PBS. Cells were resuspended in propidium iodide (PI) solution in PBS and analyzed by flow cytometry. For the FACS analysis of CD271 and CD133 expression in melanoma cells, Alexa Flour® 647 conjugated CD271 or APC conjugated CD133 antibody was used to stain the cells. About 1 x 10^6 cells were trypsinized and resuspended in PBS, after incubation with IgG, antibodies were added to the cells. Cells were stained with the antibodies on ice for one hour. After washes with PBS, cells were resuspended in PBS and then analyzed by the CyAn ADP flow cytometer. For cell sorting, cells were trypsinized and washed with staining buffer (1×PBS, 2% serum), then cells were stained with Alexa Flour® 647 conjugated CD271 or APC conjugated CD133. After incubation at 4℃ for 30min, cells were washed with staining buffer and sorted by flow cytometry. CD271 negative and CD133 negative cells were collected and cultured in fresh medium. The antibodies used for flow cytometry can be found in Supplementary Table 2.

MTS assay.

Assay was carried out with the CellTiter 96® Aqueous Non-Radioactive Cell Proliferation Assay kit from Omega. Briefly, 2mg/ml 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) and 0.92mg/ml phenazine methosulfate (PMS) were mixed 20:1. Cells were seeded in 96-well plates and treated with different reagents. Then, the

MTS/PMS mixture was added to a 96-well plate to a final concentration of 20%. The plate was incubated in a cell culture incubator for 1 to 4 hours and absorbance was measured at 490nm.

Glutamine extraction and concentration measurement.

Glutamine was extracted from the tumour tissues as previously described[58, 59]. Briefly, 50-100mg of fresh tissue was homogenized in 70% ethanol by Precellys 24 homogenizer. After spinning down, the pellet was collected, evaporated to dryness and thoroughly extracted with distilled water (1μL water per mg of fresh tissue). The concentration of glutamine was then determined by the EnzyChrom Glutamine Assay Kit (BioAssay Systems) following the manufacturer's instructions.

3T3-L1 and human adipocyte derived stem cell differentiation, Oil-Red-O staining.

3T3-L1 cell differentiation was carried out in a 6-well plate. Confluent cells were stimulated with MDI induction medium (0.115mg/ml isobutylmethylxanthine, 1μg/ml insulin, 10μM dexamethasone (all from Sigma)) for two days; then the cells were maintained in the medium with 1μg/ml insulin for two more days followed by changing the medium to regular DMEM with 10% FBS before harvesting two days later. Human adipocyte derived stem cell differentiation was induced as previously described[60]. The differentiated cells were stained with 0.3% Oil-Red-O solution after 3.7% formaldehyde fixation. For quantification, isopropanol was added to the stained cells to dissolve Oil-Red-O, and absorbance was measured at 500nm.

3D staining.

Melanoma xenograft tumours were processed utilizing the Passive CLARITY Technique (PACT) methodology [18]. Briefly, the intact xenograft tumours were fixed in 4% paraformaldehyde at 4 °C overnight and then rinsed in PBS and placed in 4% acrylamide solution for two days at 4°C to generate hydrogel-hybrid tissues with 0.25% w/v VA-044 added. The acrylamide infused tissues were then polymerized after degassing and nitrogen backfilling the solutions by placing the tissues in a vial at 37°C for 4 hours until the bulk solution became viscous. The acrylamide-tissue hybrids were then cleared using 8% SDS for 5-7 days until clear. Tissues were then stained with primary antibody at room temperature at 1:100 dilution for two days, rinsed for one day in PBST (PBS + 0.05% Tween-20) and then placed in the fluorescent secondary antibody for two days. The tissues were rinsed for an additional day in PBS-T and then placed in RIMS-2 solution for one day. Tissues were imaged using a Zeiss 780 confocal microscope with a 5x or 10 x objectives. 3D maximal projection images were generated using IMARIS software. The antibodies used for the staining can be found in Supplementary Table 2.

Metabolite extraction and mass spectrometry.

Mice were euthanized by CO_2 asphyxiation followed by cervical dislocation. Tumours were harvested and placed on dry ice immediately. For most of the tumours, it took less than 5 minutes from sacrifice to isolation of the tumour. Tumours were then kept in liquid nitrogen for two weeks before the peripheral and core tissues were isolated on dry ice. Right after isolation, the peripheral and core tissues were soaked in pre-cooled 80% methanol (-80℃) in HPLC grade water (1mL 80% methanol per 100mg sample) in dry ice, then homogenized with Precellys 24 homogenizer and Precellys Ceramic kit. 150µl homogenate was mixed with ice cold 400µl 80% methanol. After centrifugation at 4°C, 500µl polar extracts was transferred to a new 1.5mL

centrifuge tube and dried with a speed vacuum. The dried metabolite pellets were stored at -80°C. Before mass spectrum analysis, the dried metabolite pellets were dissolved in mobile phase A (0.03% formic acid in water, 1µl mobile phase A per mg tumour tissue). Liquid chromatography–mass spectrometry (LC-MS) and data analysis was processed in the Centre for Metabolomics and Mass Spectrometry at The Scripps Research Institute (La Jolla, CA, USA) and Duke University (Durham NC, USA) [61]. For the cell culture sample preparation, medium were aspirated quickly from a 6-well plate and pre-cooled 80% methanol (-80℃) was added to cover the cells. The plate with cells was incubated at -80℃ for 15min, and then the cells were scraped into extraction solvent. After centrifugation, the supernatant was collected and dried with a speed vacuum. Samples were sent to Duke University for LC-MS analysis.

RNA sequencing.

mRNA deep sequencing was performed with Illumina Hiseq2500. Sequencing libraries were prepared with TruSeq RNA Sample Preparation Kit V2 (Illumina, San Diego) according to the manufacturer's protocol with minor modifications. Briefly, 500 ng of total RNA from each sample was used for polyadenylated RNA enrichment with oligo dT magnetic beads, and the poly (A) RNA was fragmented with divalent cations under elevated temperature. First-strand cDNA synthesis produced single-stranded DNA copies from the fragmented RNA by reverse transcription. After second-strand cDNA synthesis, the double-stranded DNA underwent end repair, and the 3′ ends were adenylated. Finally, universal adapters were ligated to the cDNA fragments, and 10 cycles of PCR was performed to produce the final sequencing library. Library templates were prepared for sequencing using the cBot cluster generation system (Illumina) with TruSeq SR Cluster V3 Kit. Sequencing was performed in single read mode of 40 cycles of read1

and 7 cycles of index read using Illumina HiSeq 2500 platform with TruSeq SBS V3 Kits. Real-time analysis (RTA) software was used to process the image analysis and base calling. Sequencing runs generated approximately 40 million single reads for each sample.

Chromatin immunoprecipitation (ChIP).

Cells were cultured in complete or 0.1mM glutamine for 4 days and then harvested for ChIP analysis. In brief, 10 million cells were cross-linked with 1% formaldehyde for 5 min and quenched with 125mM glycine for 5 min. After twice washing with PBS, cells were scraped and spun down in PBS. Cell pellets were resuspended in 0.5% SDS IP buffer and sonicated to generate 200-500bp DNA fragments. After centrifuge, 25µl magnetic beads and 1µg antibody were added into 100µl supernatant for each immunoprecipitation at 4°C overnight. The next day, samples were washed with low-salt and high-salt buffer, LiCl immune complex buffer and TE buffer. Samples were incubated at 65°C overnight to elute histone complexes. DNA was extracted by phenol/chloroform/isoamyl alcohol and precipitated by Glycogen and ethanol. DNA was then used for qPCR analysis. The qPCR primers are listed in Supplementary Table 2.

Statistics and reproducibility.

All western blot experiments were repeated at least three times with a representative gel being shown. For all other experiments, each was repeated independently at least two times with similar results. Results are shown as means; error bars represent the standard error of the mean (S.E.M.). The unpaired Student's t test was used to determine the statistical significance of differences between means (*P<.05, **P<.01, ***P<.001).

Data availability.

Data that support the findings of this study have been deposited in the Gene Expression Omnibus (GEO) under accession code GSE81817. Statistics source data for Fig. 1, Fig. 2, Fig. 4, Fig. 5, Fig.6, Fig 7, and Supplementary Fig. 2, Fig. 4 and Fig. 5 have been provided as Supplementary Table 4. All other data supporting the findings of this study are available from the corresponding author on request.

57. Hatzivassiliou, G. *et al.* ATP citrate lyase inhibition can suppress tumor cell growth. *Cancer cell* **8**, 311-321 (2005).

58. Reid, M.A. *et al.* The B55alpha subunit of PP2A drives a p53-dependent metabolic adaptation to glutamine deprivation. *Molecular cell* **50**, 200-211 (2013).

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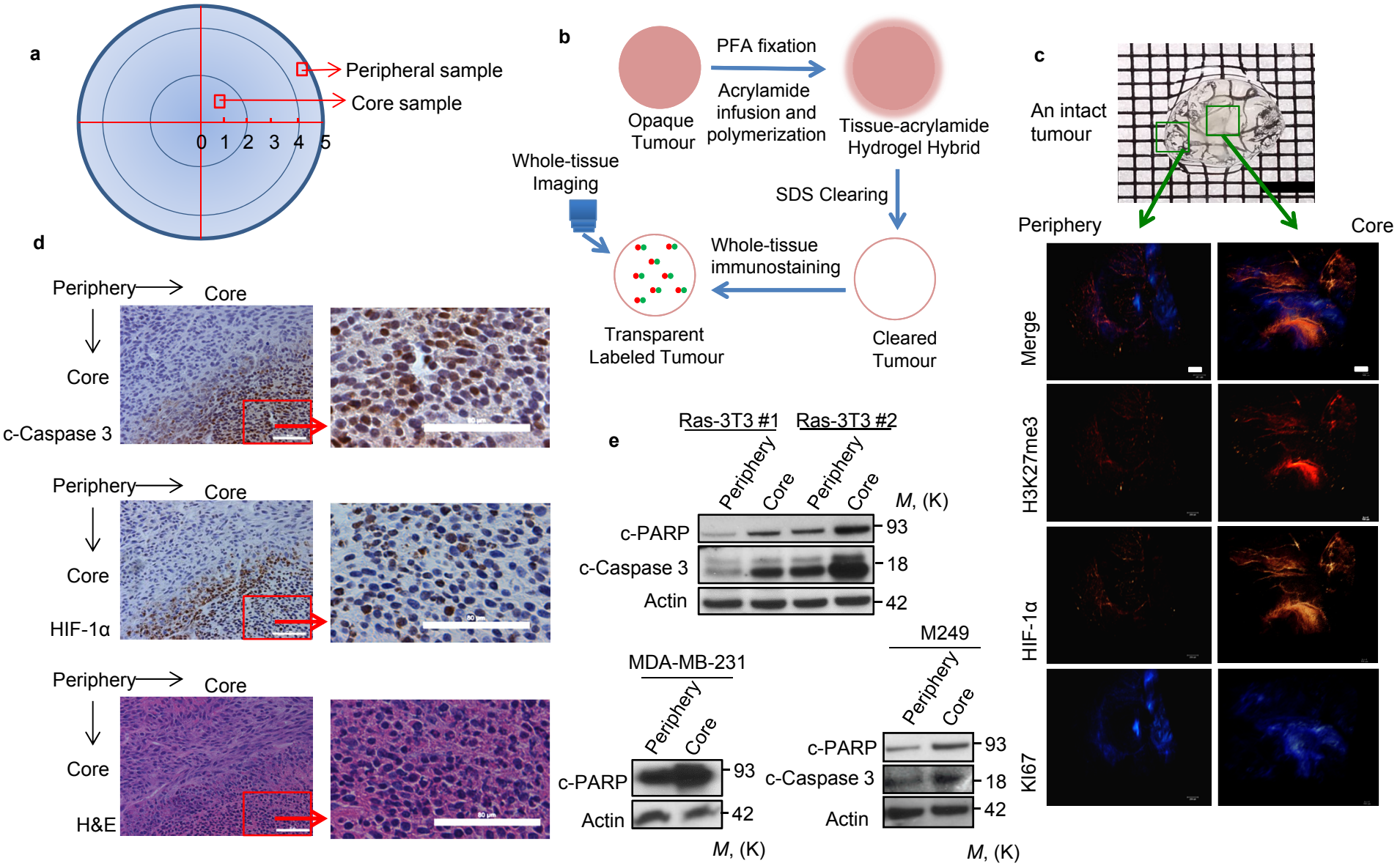
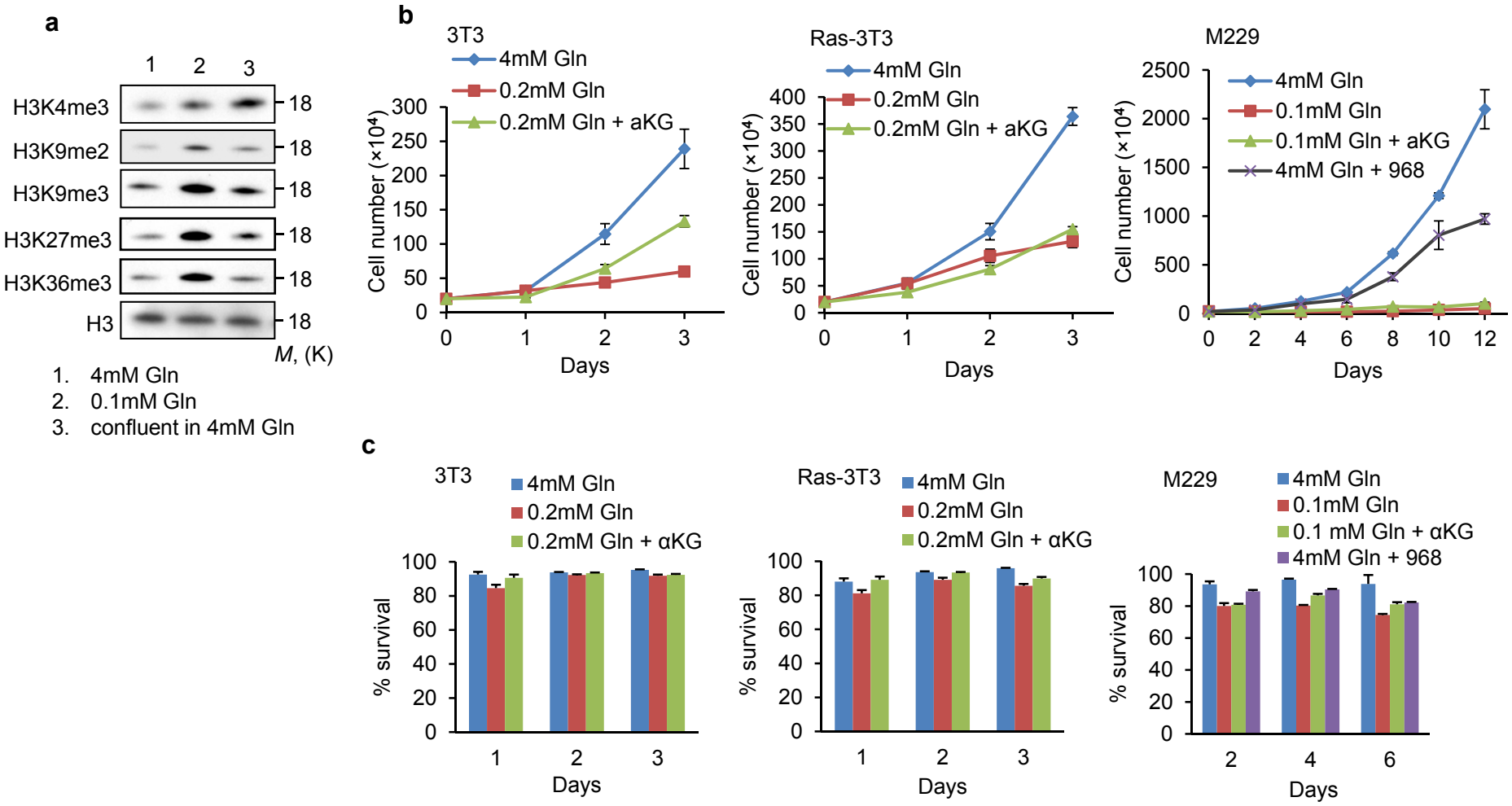
60. Yu, G. *et al.* Adipogenic differentiation of adipose-derived stem cells. *Methods in molecular biology* **702**, 193-200 (2011).

61. Liu, X., Ser, Z. & Locasale, J.W. Development and quantitative evaluation of a high-resolution metabolomics technology. *Analytical chemistry* **86**, 2175-2184 (2014).

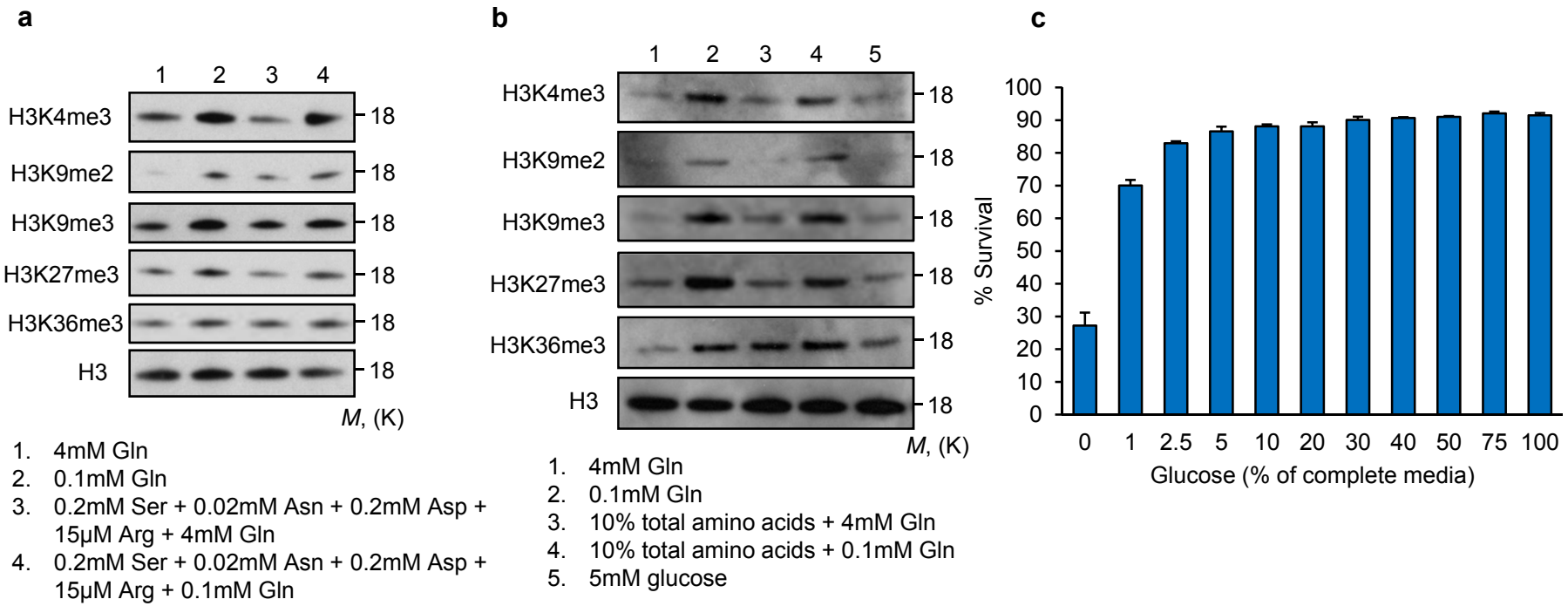
Supplementary Figure 1. Tumour core regions display heterogeneity.



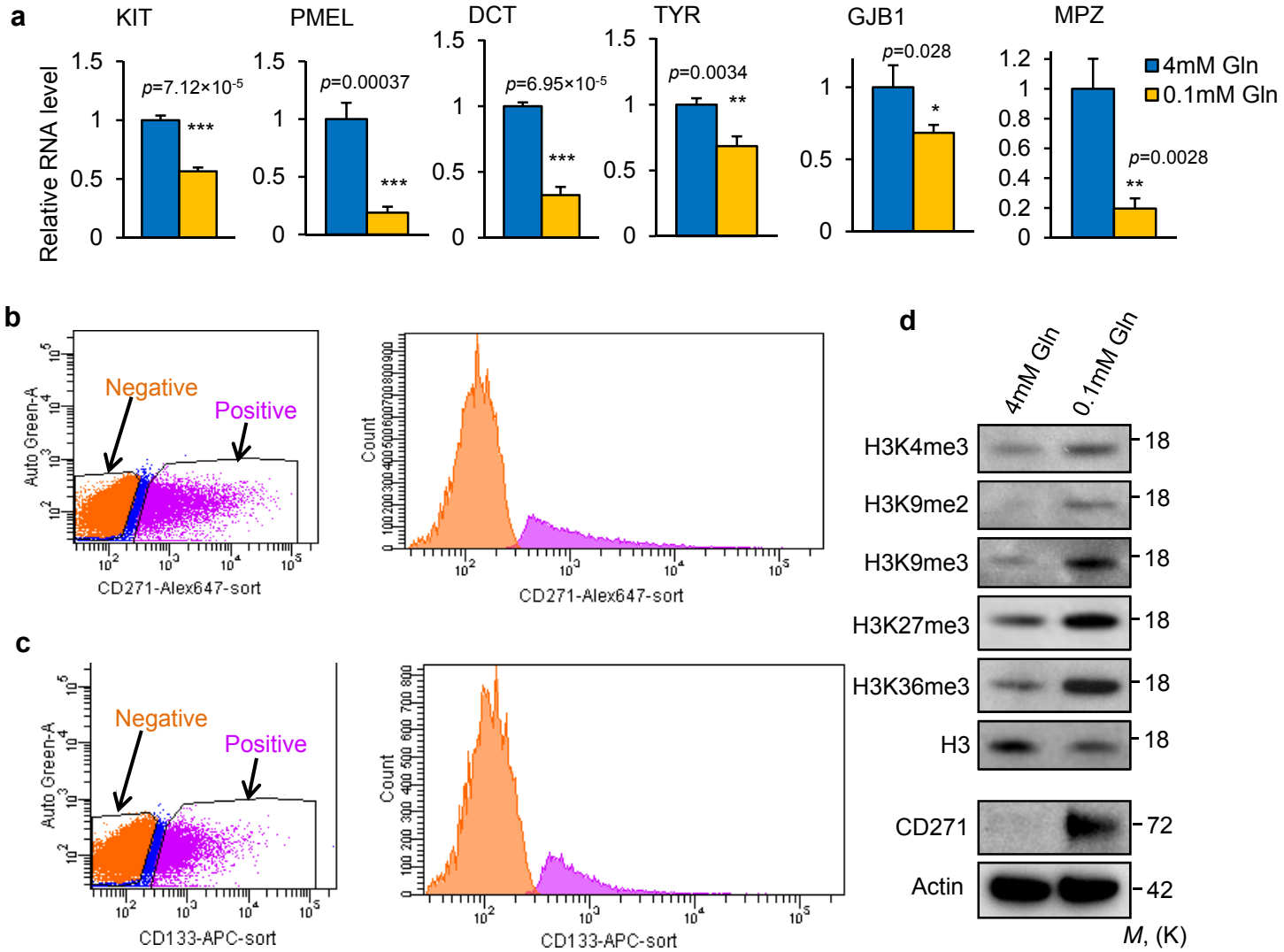
Supplementary Figure 2. Histone methylation induced by low glutamine levels is not due to low proliferation rate of cells.



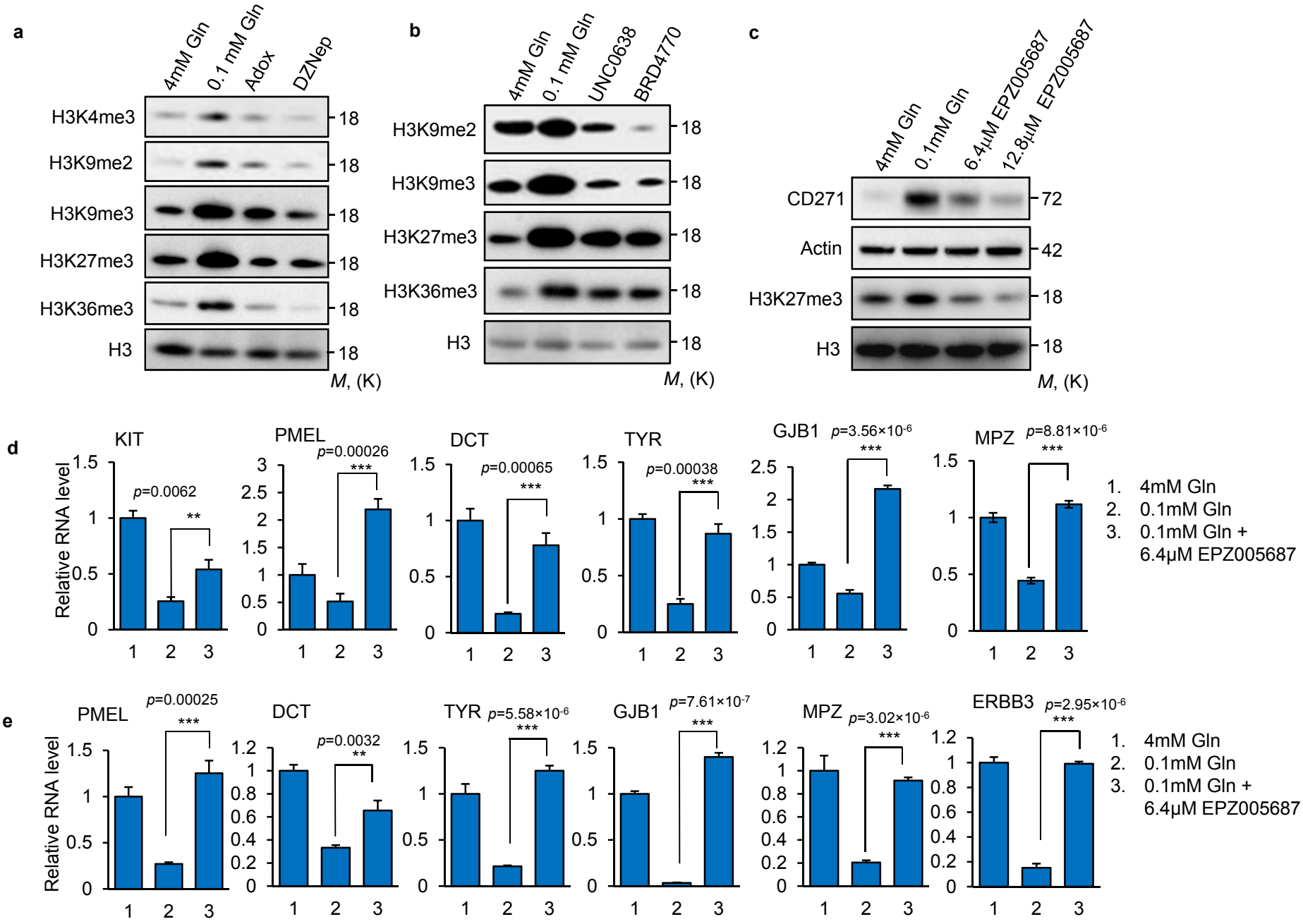
Supplementary Figure 3. Low glutamine is the major driver of histone methylation.



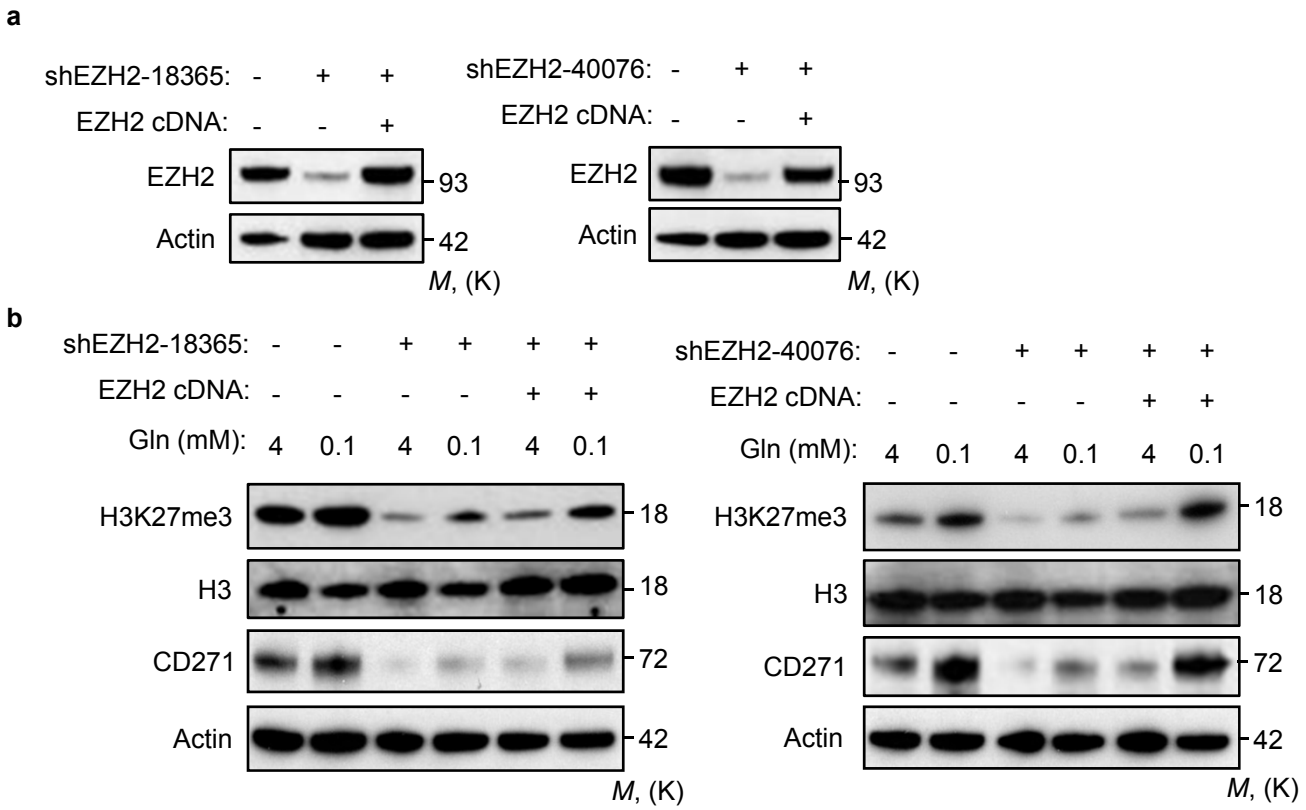
Supplementary Figure 4. Low glutamine suppresses differentiation genes and induces CD271.



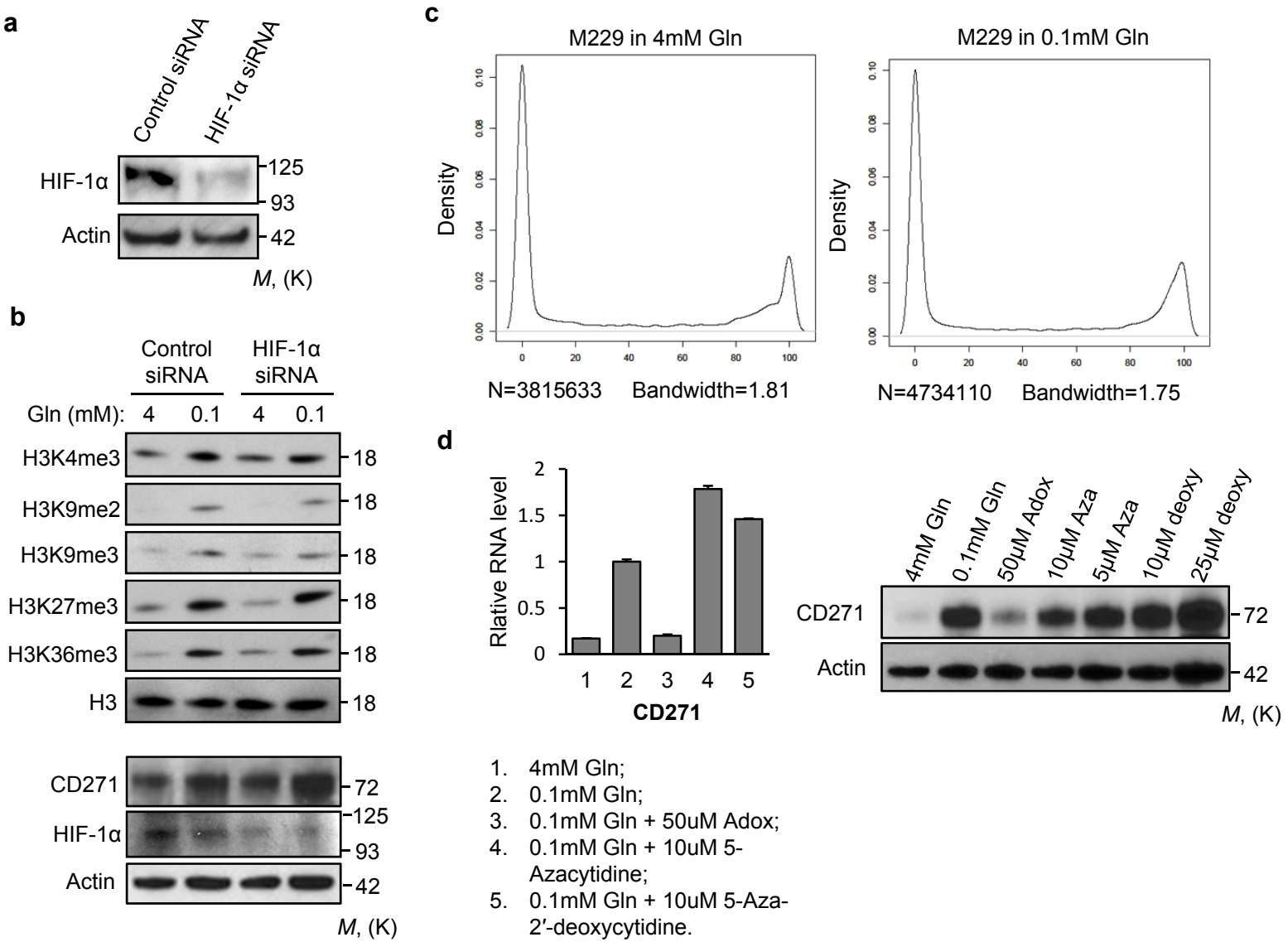
Supplementary Figure 5. Low glutamine-induced differential gene expression is reversed by H3K27me3 inhibitor.



Supplementary Figure 6. Ectopic EZH2 expression rescues the EZH2 shRNA effects.



Supplementary Figure 7. HIF-1α or DNA methylation is not involved in low glutamine-induced CD271 expression.



1. 4mM Gln;
2. 0.1mM Gln;
3. 0.1mM Gln + 50uM Adox;
4. 0.1mM Gln + 10uM 5-Azacytidine;
5. 0.1mM Gln + 10uM 5-Aza-2′-deoxycytidine.

Supplementary Figure Legends

Supplementary Figure 1 Tumour core regions display heterogeneity. (a) Schematic of tumour dissection. One unit equals 20% of the radius. (b) Schematic of CLARITY Technique procedure. (c) 3D imaging of M229 xenograft tumour depicting H3K27me3 (red), Hif1α (orange) and KI67 (blue) staining. Periphery and core of tumour are as indicated. Scale bar = 250 μm. (d) Immunohistochemistry staining in xenograft tumours. Whole tumours were sliced and stained with indicated antibodies (cleaved caspase 3, HIF-1α). H&E staining is also shown. Scale bar = 80 μm. (e) Tissues from periphery and core regions of xenograft tumours were lysed to collect whole cell lysate. Proteins were assessed by western blotting with specified antibodies. Unprocessed original scans of blots are shown in Supplementary Fig. 8.

Supplementary Figure 2 Histone methylation in low glutamine is not due to low proliferation rate of cells. **(a)** For lane 1 and 2, 50% confluent M229 cells were cultured in complete (4mM glutamine) or 0.1mM glutamine medium for 4 days. For lane 3, 100% confluent M229 cells were cultured in complete medium for 4 days. Cells were lysed for histone extraction and histone lysine methylation levels were assessed by western blotting. Total histone H3 was used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(b)** Cells were cultured under different conditions as indicated and cell number was determined by cell counting everyday (3T3 and Ras-3T3) or every other day (M229). Data represent mean ± S.E.M., n=3 independent experiments. **(c)** Cells were cultured under different conditions as indicated. After PI staining, cell survival was assessed by flow cytometry. Data represent mean ± S.E.M., n=3 independent experiments. Source data for **b** and **c** are shown in Supplementary Table 4.

Supplementary Figure 3 Low glutamine is the major driver of histone methylation. **(a,b)** M229 cells were cultured under different conditions for 4 days as indicated. After that, cells were lysed for histone extraction and histone lysine methylation levels were assessed by western blotting. Total histone H3 was used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(c)** M229 cell survival in low glucose medium. M229 cells were cultured in complete medium (25mM glucose) or medium with different glucose concentrations for 4 days. Medium was changed twice everyday. Cells were stained with PI and cell survival was measured by Flow cytometry. Data represent mean ± S.E.M., n=3 independent experiments.

Supplementary Figure 4 Low glutamine induces suppression of differentiation genes, which can be reversed by EPZ005687. **(a)** M249 cells were cultured in complete or 0.1mM glutamine medium for 12 days, then RNA was extracted and gene expression was assessed by qPCR. Data represent mean ± S.E.M. of three independent RNA extracts. $*P<.05$, $**P<.01$, $***P<.001$ by unpaired Student's *t*-test. Source data can be found in supplementary Table 4. **(b)** M229 cells were stained with Alexa647 conjugated CD271 antibody. Cells were then sorted by flow cytometry and CD271- cells were collected. **(c)** The CD271- cells were cultured for 2 days and then stained with APC conjugated CD133 antibody. The stained cells were sorted again and CD271-/CD133- cells were collected. **(d)** CD271-/CD133- cells were cultured in complete (4mM Gln) or 0.1mM Gln medium for 4 days, then cells were harvested for histone extraction or whole cell lysate collection. Histone lysine methylation and protein levels were assessed by western blotting. Total histone H3 and Actin were used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8.

Supplementary Figure 5 Low glutamine-induced differential gene expression is reversed by H3K27me3 inhibitor. **(a,b)** M229 cells were cultured in complete medium or 0.1mM glutamine medium with or without global histone methylation inhibitors **(a)** or H3K9 specific methylation inhibitors **(b)** for 4 days; histones were extracted and protein levels were assessed by western blotting. Total histone H3 was used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(c)** M229 cells were cultured in complete medium or 0.1mM glutamine medium with or without H3K27 methylation inhibitor EPZ005687 for 4 days, whole cell lysates were collected and protein levels were assessed by western blotting. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(d)** M229 and **(e)** M249 cells were cultured in complete medium or 0.1mM glutamine medium with or without H3K27 specific methylation inhibitor EPZ005687 for 4 days, then RNA was extracted and gene expression was assessed by qPCR. Data represent mean ± S.E.M. of three independent RNA extracts. $**P<.01$, $***P<.001$ by Student's *t*-test.

Supplementary Figure 6 Ectopic EZH2 expression rescues the EZH2 shRNA effects. **(a)** EZH2 was knocked down with two different shRNAs in M229 cells, then the cells were transiently transfected with EZH2 cDNA. Cells were harvested after 4 days and EZH2 protein was measured by western blotting. Actin was used as loading control. **(b)** EZH2 was knocked down with two different shRNAs in M229 cells, then the cells were transiently transfected with EZH2 cDNA in the medium with 4mM or 0.1mM Gln. Cells were harvested after 4 days, EZH2 protein and H3K27me3 were assayed by western blotting. Total H3 and Actin were used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8.

Supplementary Figure 7 Neither HIF-1α nor DNA methylation is involved in low glutamine-induced epigenetic modification. **(a)** M229 cells were transfected with HIF-1α siRNA in a 6-well plate at day 1. At day 6, cells were lysed to collect whole cell lysate and HIF-1α level was assessed by western blotting. Actin was used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(b)** M229 cells were transfected with HIF-1α siRNA in a 6-well plate at day 1. From day 2, cells were cultured in complete (4mM Gln) or 0.1mM Gln medium for 4 days. At day 6, cells were harvested for histone extraction or whole cell lysate collection. Histone lysine methylation and protein levels were assessed by western blotting. Total histone H3 and Actin were used as loading control. Unprocessed original scans of blots are shown in Supplementary Fig. 8. **(c)** M229 cells were cultured in complete or 0.1mM glutamine medium for 4 days, then DNA was extracted and used for whole genome DNA methylation sequencing. Methylation status of detected CpG sites (density) is shown. **(d)** M229 cells were cultured in complete medium, 0.1mM glutamine medium with or without histone methylation inhibitor Adox, DNA methylation inhibitors 5-Azacytidine and 5-Aza-2′-deoxycytidine. RNA and protein were harvested after 4 days for qPCR (left) and western blotting (right). PCR data represent mean ± S.E.M. of three independent experiments. Unprocessed original scans of blots are shown in Supplementary Fig. 8.

Supplementary Figure 8 Unprocessed blots of all figures. Black boxes indicate cropped portions that appear in the figures.

Supplementary Table 1 Amino acid concentrations in tumour periphery and core regions. M229 xenograft tumours were harvested and separated into periphery and core samples (n=8

tumours). Metabolites were extracted from each sample and used for LC-MS analysis. Core/periphery ratio of each amino acid was shown. p value was calculated by Student's *t*-test.

Supplementary Table 2 Sequences of primers used in the study.

Supplementary Table 3 Information on antibodies used in the study.

Supplementary Table 4 Statistic source data.