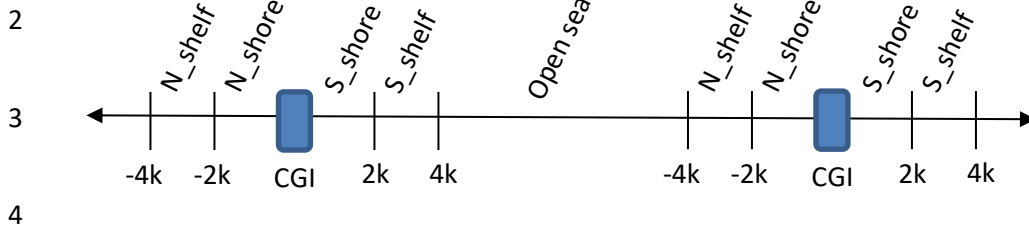


1 **Supplementary figure 1**



5 **Classification of the sites in the 450k bead array according to CGI.** The probes or sites were
6 grouped into four categories according to the distance from the closest CGI: i) “island” if a probe
7 is inside CGI, ii) “shore” if a probe is within 2000 bases, iii) “shelf” if a probe is between 2000
8 and 4000 bases, iv) “open sea” otherwise. Further categories were made by distinguishing 5’
9 and 3’ direction from the closest CGI denoted by ‘N_’ and ‘S_’ respectively such as ‘N_shore’
10 and ‘S_shore’.

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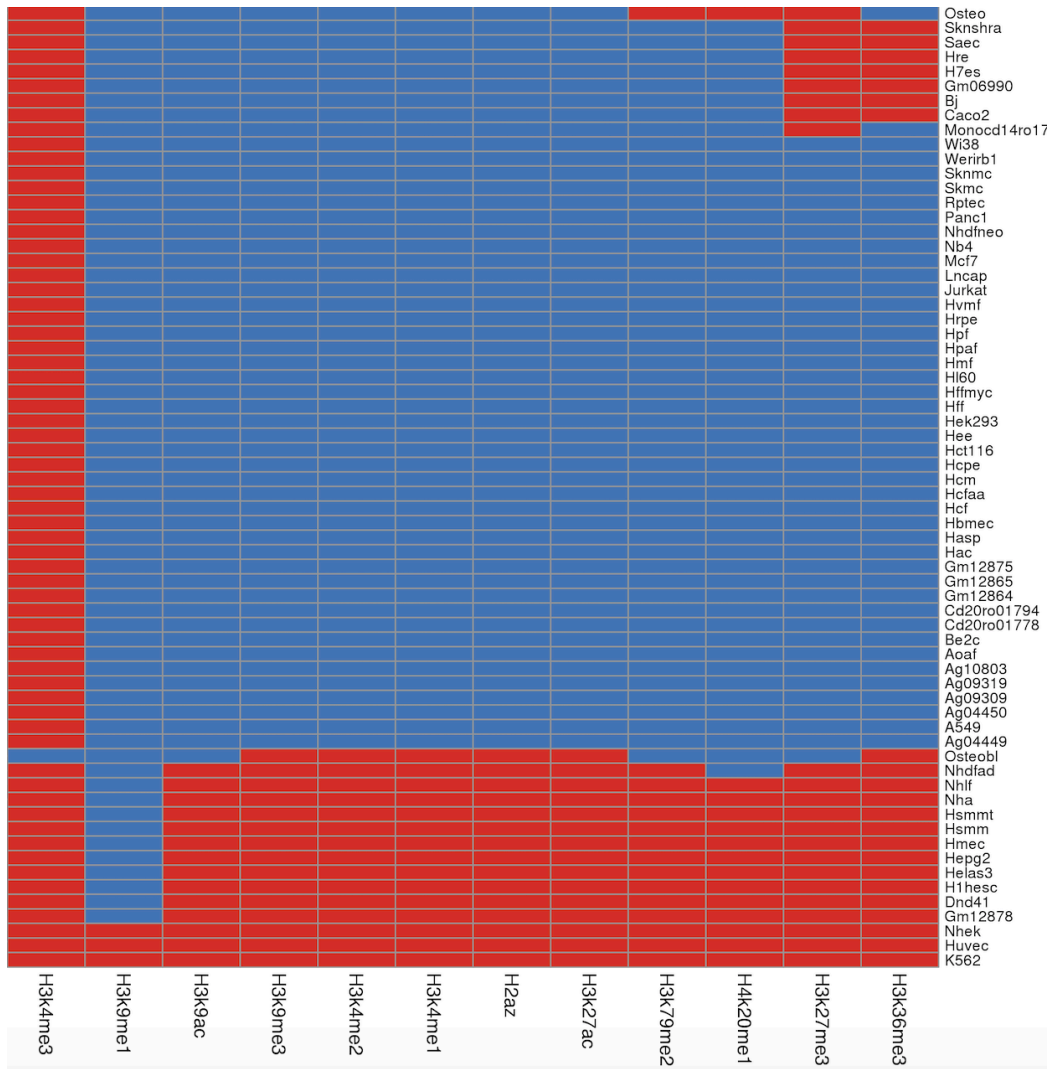
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20 **Supplementary figure 2**



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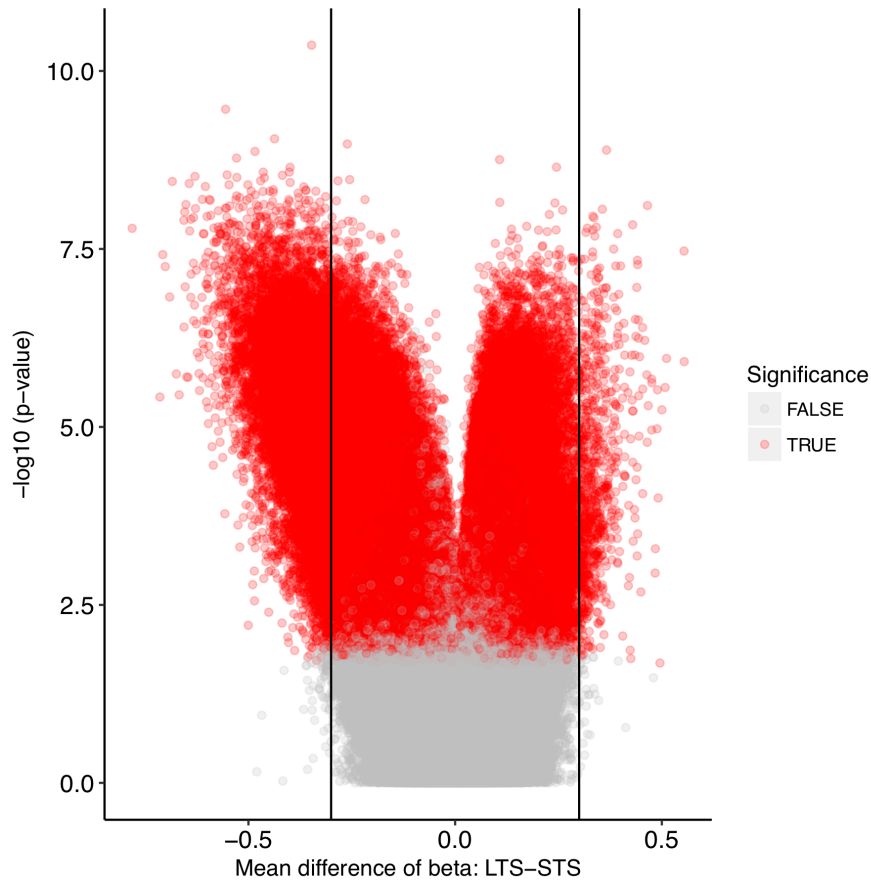
22 **The cells and histone marks obtained from ENCODE.** The red denotes the one used in the
 23 enrichment analyses while the blue indicates no data point available during this study.

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27 **Supplementary figure 3**



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29 **Volcano plot of differences between STS-GBM and LTS-GBM in DNA methylation level**

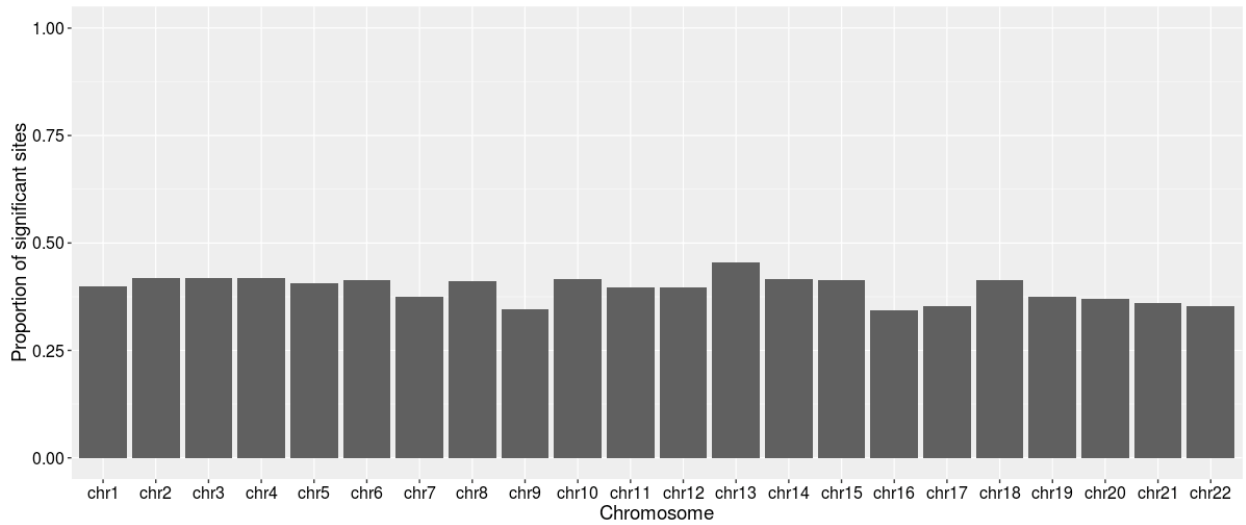
30 **(beta)**. Each dot is a single CpG site measured by a probe. X axis is mean difference of beta
31 values between STS-GBM and LTS-GBM groups. Y axis is statistical significance (p-value) in
32 negative log (base: 10) scale. Red dots indicate significant sites while green dots correspond to
33 sites without statistical significance, determined by the threshold of FDR of 0.01. Two vertical
34 lines denote mean differences of -0.3 and 0.3 respectively.

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38 **Supplementary figure 4**



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40 **Proportion of the number of significant sites according to chromosomes.** X axis is
41 autosomal chromosome and Y axis is proportion of the significant sites that identified in
42 discovery samples of LTS (n=17) and STS (n=12) in a given chromosome (number of significant
43 sites divided by total number of sites that were tested).

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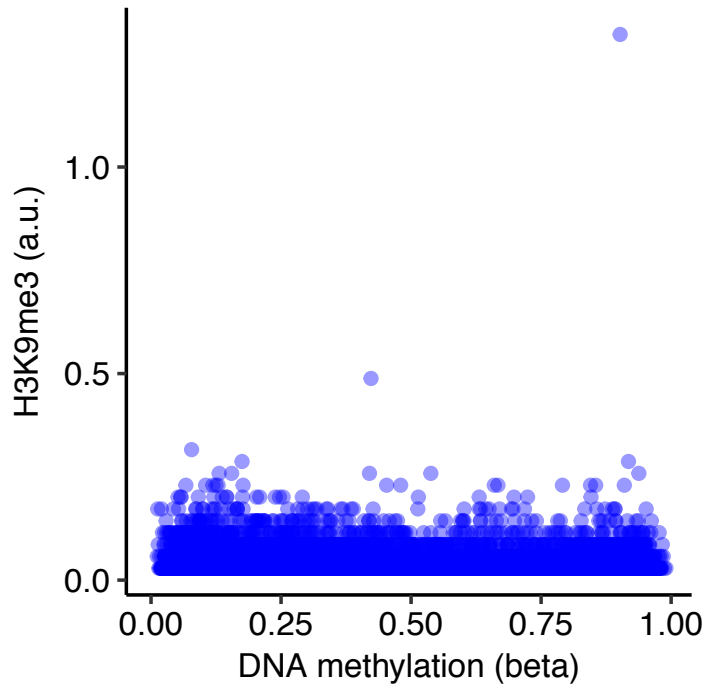
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54 **Supplementary figure 5**



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57 **The relation between the ChIP-seq signal of H3K9me3 and the DNA methylation level**
58 **(beta) for the hyper-methylated sites in U87 cell line.** Each dot denotes the hypomethylated
59 site.

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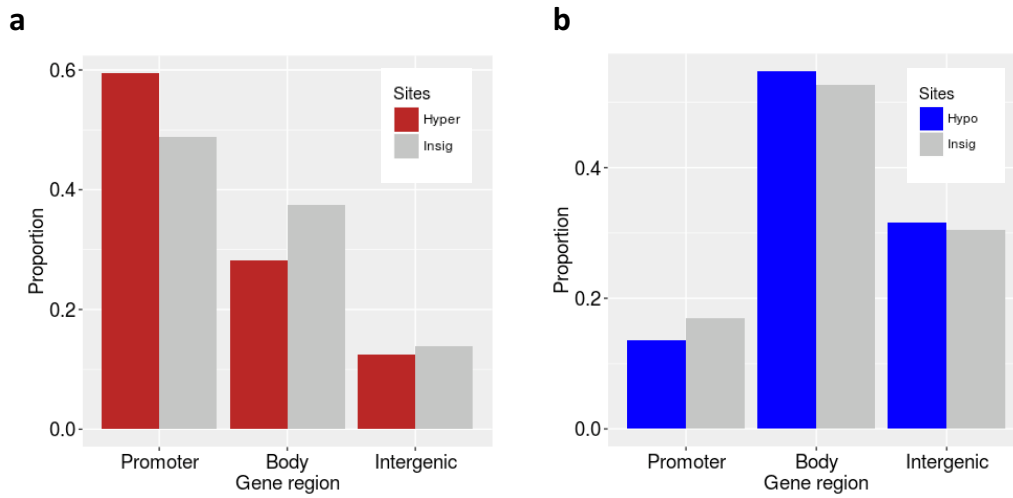
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70 **Supplementary figure 6**



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72 **Enrichment of significant differential sites in gene regions. (a)** Hypermethylated sites in
73 island **(b)** Hypomethylated sites in open sea. Promoter is enriched with the hypermethylated
74 site relative to gene body while gene body is enriched with the hypomethylated site relative to
75 promoter (p -values $< 10^{-15}$ from Fisher exact tests in both cases).

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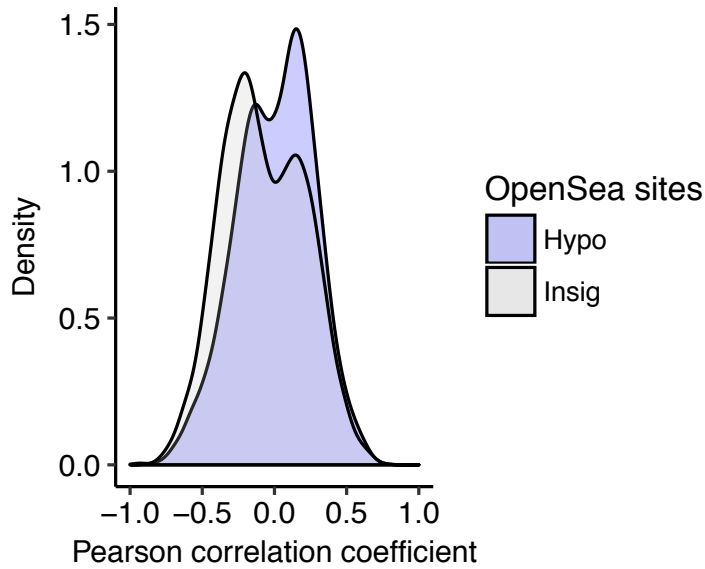
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89 **Supplementary figure 7**



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91 **Distribution of Pearson correlation coefficients between DNA methylation level (beta) and**
92 **gene expression measured by RNA-seq (FPKM) across GBM samples in TCGA.** The blue
93 describes the genes (# 3026) corresponding to the selected hypo-methylated sites while the
94 gray shows the genes (# 4717) matching to the insignificant sites associated with the open sea.

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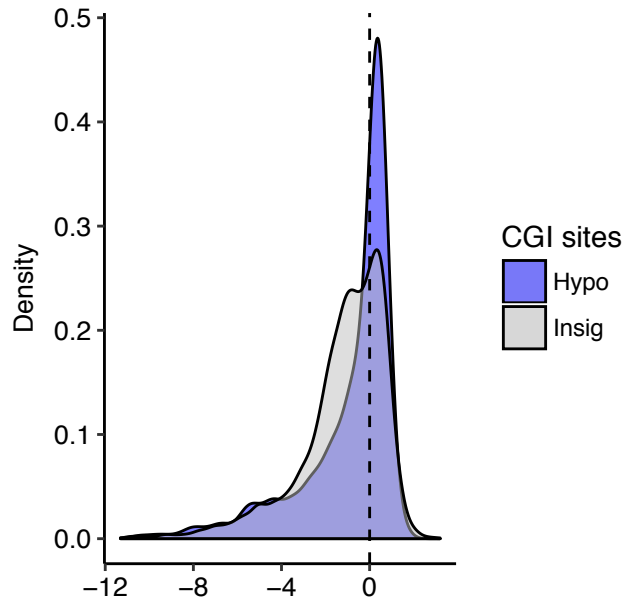
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107 **Supplementary figure 8**

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Z-score of DNA methylation value with mutation

110 **Distribution of Z-score of DNA methylation of the sample with somatic mutation.** A Z-
111 score, calculated by $(\text{beta-mean})/\text{standard deviation}$ represents the relative location of the
112 sample with mutation in terms of DNA methylation level. The hypo-methylated showed the
113 stronger shift to the right to the zero value of Z-score, meaning higher DNA methylation than
114 the other samples on average, compared to the insignificant sites.

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125 **Supplementary table 1**

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Cohort		Case No.	Gender	Age	Survival	Management protocol	IDH1 IHC	MGMT MSP	PFS	Final status
<i>Discovery cohort (SNU-LTS)</i>	LTS (>3 years)	SNUL TS-02	male	46 years	138 months	Resection-ACNU/CDDP-RT	negative	methylation	138 months	alive
		SNUL TS-07	female	30 years	104 months	Resection-ACNU/CDDP-RT	negative	N.A.	104 months	alive
		SNUL TS-10	female	48 years	95 months	Resection-ACNU/CDDP-RT	negative	N.A.	95 months	alive
		SNUL TS-18	male	50 years	59 months	Resection-ACNU/CDDP-RT	negative	N.A.	N.A.	dead
		SNUL TS-19	female	45 years	59 months	Resection-ACNU/CDDP-RT-TMZ	negative	methylation	20 months	dead
		SNUL TS-20	female	38 years	58 months	Resection-RT-TMZ	negative	unmethylation	58 months	alive
		SNUL TS-21	female	33 years	53 months	Resection-RT-TMZ	negative	N.A.	24 months	dead
		SNUL TS-22	female	28 years	49 months	Resection-CCRT/TMZ-TMZ	negative	methylation	41 months	dead
		SNUL TS-23	female	28 years	46 months	Resection-CCRT/TMZ	negative	unmethylation	46 months	alive
		SNUL TS-25	female	57 years	44 months	Biopsy-CCRT/TMZ-TMZ	negative	unmethylation	N.A.	dead
		SNUL TS-26	male	48 years	42 months	Resection-ACNU/CDDP-RT-TMZ	negative	unmethylation	N.A.	dead
		SNUL TS-27	male	81 years	42 months	Resection-CCRT/TMZ-TMZ	negative	methylation	N.A.	dead
SNUL TS-29	male	41 years	41 months	Resection-CCRT/TMZ-TMZ	negative	methylation	N.A.	dead		

		SNUL TS-30	male	57 years	41 months	Resection-CCRT/TMZ-TMZ	negative	unmethylation	26 months	dead
		SNUL TS-31	female	54 years	41 months	Resection-ACNU/CDDP-RT	negative	unmethylation	N.A.	dead
		SNUL TS-33	female	57 years	38 months	Resection-RT-TMZ	negative	N.A.	N.A.	dead
		SNUL TS-34	male	43 years	36 months	Resection-CCRT/TMZ-TMZ	negative	Unmethylated	27 months	dead
STS (<1 year)		SNUS TS-01	male	55 years	40 weeks	Resection-CCRT/TMZ-TMZ	negative	methylation	26 weeks	dead
		SNUS TS-02	male	45 years	54 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	26 weeks	dead
		SNUS TS-03	female	64 years	52 weeks	Resection-CCRT/TMZ-TMZ	negative	methylation	N.A.	dead
		SNUS TS-04	female	68 years	26 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	N.A.	dead
		SNUS TS-05	male	70 years	52 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	N.A.	dead
		SNUS TS-06	male	42 years	37 weeks	Resection-CCRT/TMZ-TMZ	negative	methylation	31 weeks	dead
		SNUS TS-07	male	63 years	50 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	38 weeks	dead
		SNUS TS-08	male	62 years	37 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	20 weeks	dead
		SNUS TS-09	female	60 years	45 weeks	Resection-CCRT/TMZ-TMZ	negative	unmethylation	15 weeks	dead
		SNUS TS-10	male	59 years	52 weeks	Resection-CCRT/TMZ-TMZ	negative	methylation	35 weeks	dead
		SNUS TS-11	male	39 years	47 weeks	Resection-CCRT/TMZ-TMZ	negative	methylation	40 weeks	dead

		SNUS TS-12	male	61 years	23 weeks	Resection- CCRT/TMZ- TMZ	negat ive	unmethyl ation	N.A.	dea d
<i>Valida tion cohort (AUS)</i>	LTS (>3 yea rs)	AUS- 01	male	56 yea rs	55 mont hs	Resection- CCRT/TMZ- TMZ/Bev	negat ive	unmethyl ation	38 mon ths	dea d
		AUS- 02	male	62 yea rs	86 mont hs	Resection- CCRT/TMZ- TMZ	negat ive	methylati on	N.A.	dea d
		AUS- 03	male	20 yea rs	76 mont hs	Resection- CCRT/Procarb azine	negat ive	methylati on	N.A.	dea d
		AUS- 04	fema le	36 yea rs	66 mont hs	Resection- TMZ/Procarba zine/Bev	negat ive	unmethyl ation	N.A.	dea d
		AUS- 05	male	61 yea rs	83 mont hs	Resection- CCRT/TMZ- TMZ/Procarba zine/Bev	negat ive	methylati on	N.A.	dea d
		AUS- 07	male	34 yea rs	135 mont hs	Resection- CCRT/TMZ- TMZ	positi ve	unmethyl ation	N.A.	dea d
		AUS- 08	male	64 yea rs	58 mont hs	Resection- CCRT/TMZ- TMZ	N.A.	unmethyl ation	45 mon ths	dea d
		AUS- 09	male	57 yea rs	48 mont hs	Resection- CCRT/TMZ- TMZ	N.A.	unmethyl ation	33 mon ths	dea d
		AUS- 10	fema le	54 yea rs	95 mont hs	Resection- CCRT/TMZ- TMZ	N.A.	unmethyl ation	16 mon ths	dea d
		AUS- 11	fema le	77 yea rs	76 mont hs	Resection- CCRT/TMZ- TMZ	N.A.	methylati on	N.A.	dea d
		<i>Valida tion cohort (TCG A patien t ID)</i>	LTS (>3 yea rs)	TCGA-06-0125, TCGA-76-4932, TCGA-14-1450						
STS (<1 yea r)	TCGA-14-1043, TCGA-14-0781, TCGA-32-1980, TCGA-14-1395, TCGA-06-6391, TCGA-81-5910, TCGA-19-5955, TCGA-12-5301, TCGA-76-4934, TCGA-76-6193, TCGA-06-5418, TCGA-76-4928, TCGA-12-5299, TCGA-76-6192, TCGA-74-6573, TCGA-06-5410, TCGA-76-4929, TCGA-06-5856, TCGA-06-5412, TCGA-76-4926, TCGA-19-1389, TCGA-76-4925, TCGA-28-5218, TCGA-06-6388, TCGA-06-6390, TCGA-28-6450, TCGA-19-5947, TCGA-06-0210,									

TCGA-19-5951, TCGA-06-5411, TCGA-76-6285, TCGA-26-5135, TCGA-76-4931, TCGA-06-0190, TCGA-28-5215, TCGA-28-5207, TCGA-06-5408, TCGA-06-0211, TCGA-14-0740
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128 **Sample information.** Cohort: class of patient sample group (LTS; long-term survivor, STS;
129 short-term survivor), Case No.: case-specific ID, Gender: male or female, Age: age at diagnosis
130 in years, Diagnosis: histological diagnosis, Survival: survival period between first operation and
131 death, IDH1 IHC: immunohistochemistry result of IDH1, MGMT MSP: MGMT methylation
132 specific PCR, PFS: progression free survival, Final status: survival status at the last follow-up.
133 For TCGA cohort, TCGA patient IDs are provided for reference. N.A. means “not available”.

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144 **Supplementary table 2 The list of 161,794 significant sites showing the DNA**
145 **methylation difference between LTS and STS.** This is provided as a separate file (additional
146 file 2) due to its size. The file includes the following information on the sites: 450K bead array ID
147 (“ProbeID”), Chromosome (“Chrom”), Coordinate (“Coord”), Gene name (“Gene”), CGI category
148 of a site (“CGI_group”), TSS category of a site (“Gene_group”), Average DNA methylation level
149 in discovery STS samples (“STS_Mean”), Average DNA methylation level in discovery LTS
150 samples (“LTS_Mean”). The genomic coordinate is based on UCSC hg19.

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163 **Supplementary table 3**

ID	Description	Number of genes (intersection/ total)	Significance (p-value, FDR)
GO:0002250	An immune response mediated by cells expressing specific receptors for antigen produced through a somatic diversification process, and allowing for an enhanced secondary response to subsequent exposures to the same antigen (immunological memory).	72 / 100	0, 0
GO:0050911	The series of events involved in the perception of smell in which an olfactory chemical stimulus is received and converted into a molecular signal.	135 / 302	0, 0
GO:0007031	A process that is carried out at the cellular level which results in the assembly, arrangement of constituent parts, or disassembly of a peroxisome. A peroxisome is a small, membrane-bounded	9 / 10	0.001, 0.051

	organelle that uses dioxygen (O2) to oxidize organic molecules.		
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164 **Gene Ontology (GO) results of the hypo-methylated sites.** No: number, ID: GO ID,
165 Description: GO Term description, Number of genes: “total” is the number of genes that are
166 mapped in the 450K bead array in the GO term, “intersection” means the number of genes that
167 have associations with the selected hyper-methylated sites, Significance: “p-value” was
168 obtained from permutation test, “FDR” is False Discovery Rate.

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