

Supplementary Files

**Global DNA methylation synergistically regulates the nuclear and mitochondrial genomes in glioblastoma cells.**

Xin Sun<sup>1,2</sup>, Jacqueline Johnson<sup>1</sup>, Justin C. St. John<sup>1,2</sup>

<sup>1</sup> Centre for Genetic Diseases, Hudson Institute of Medical Research, 27-31 Wright Street, Clayton VIC 3168, AUSTRALIA

<sup>2</sup> Department of Molecular and Translational Sciences, Monash University, 27-31 Wright Street, Clayton VIC 3168, AUSTRALIA

**Corresponding author:** Justin St. John, Voice: +61 3 8572 2678, Fax: +61 03 9594 7416;  
Email: [Justin.StJohn@hudson.org.au](mailto:Justin.StJohn@hudson.org.au)

**Supplementary Table 1: Primer pairs for long and real time PCR**

Human Gene	Forward primer (5'-3')	Product size	Annealing Tm ( °C)
β-globin-F	CAACTTCATCCACGTTCCACC	268	57
β-globin-R	GAAGAGCCAAGGACAGGTAC		
mtDNA-F	CGAAAGGACAAGAGAAATAAGG	152	53
mtDNA-R	CTGTAAAGTTTTAAGTTTTATGCG		
Long1-F (Set 1)	GACGGGCTCACATCACCCATAA	8382	63
Long1-R (Set 1)	GCGTACGGCCAGGGCTATTGGT		
Long2-F (Set 1)	GCCACAATAACCTCCTCGGACTCCT	8703	63
Long2-R (Set 1)	GGTGGCTGGCACGAAATTGACC		
Long1-F (Set 2)	TACACATGCAAGCATCCCCGTTCCA	7871	63
Long1-R (Set 2)	GGGCAATGAATGAAGCGAACAGATTTTCG		
Long2-F (Set 2)	CAGTGATTATAGGCTTTCGCTCTAAG	7985	63
Long2-R (Set 2)	TCTGTGTGAAAAGTGGCTGTGCAGA		
RNR1-F	TACACATGCAAGCATCCCCG	276	57.5
RNR1-R	GGGGAGGGGGTGATCTAAAA		
RNR2-F	GGGCATAACACAGCAAGACG	295	56.5
RNR2-R	AACATCGAGGTCGTAACCCT		
CO1-F	CTTCTCCTTACACCTAGCAG	143	55.5
CO1-R	GTAGGACTGCTGTGATTAGG		
ND4-F	CTGCCTACGACAAACAGAC	161	55.5
ND4-R	GGCAGAATAGTAATGAGGATG		
ND4L-F	GGATTAGACTGAACCGAATTG	176	54.5
ND4L-R	AGTAGGGAGGATATGAGGTG		
O <sub>L</sub> -F	CAGCTAAGCACCCCTAATCAAC	162	55.5
O <sub>L</sub> -R	TCTAAAGACAGGGGTAGGC		
ND5-F	AAACCCCATTAACGCCTGG	254	56.5
ND5-R	TGCGGTGTGTGATGCTAGG		
CO3-F	TCACCATTTCCGACGGCATC	109	57.5
CO3-R	TGGCGGATGAAGCAGATAGTG		
ND3-F	ACCACAACCTAACGGCTACAT	164	56.5
ND3-R	GGGCTCATGGTAGGGGTTAAA		
CYTB-F	ATGACCCCAATACGCAAACT	401	54.5
CYTB-R	GGGAGGACATAGCCTATGAA		
CO2-F	CTGCTTCCTAGTCCTGTATG	235	56.6
CO2-R	GTCGGTGTACTCGTAGGTTT		
ND6-F	CCGCACCAATAGGATCCTCCCGA	187	63.5
ND6-R	GCATGGGGGTCAGGGGTTGAG		
ATP6-F	CAGTGATTATAGGCTTTCGCTC	343	57.5
ATP6-R	GTGTTGTCGTGCAGGTAGAG		
ND2-F	ACCGTACAACCCTAACATAACC	166	57.5
ND2-R	GAGGAGGGTGGATGGAATTAAG		
ATP8-F	CACTATTCCTCATACCCCACTAA	140	56.5
ATP8-R	GGGCAATGAATGAAGCGAAC		
LSP-F	AGCCACTTTCCACACAGACATCATA	250	59
LSP-R	TAGGATGGGCGGGGTTGTA		
HSP-F	TCAATACAACCCCGCCCAT	257	57.5
HSP-R	TCGTGGTGATTAGAGGGTGAA		
O <sub>H</sub> -F	GAGCACCCCTATGTCGCAGTA	170	57
O <sub>H</sub> -R	TCTGTGTGAAAAGTGGCTGT		
POLG exon2-F	CAGACCTCCACGTCGAACAC	209	59.5
POLG exon2-R	GACAACCTGGACCAGCACTT		
TOP1MT intron10-F	AAGGACATGTCAGCCGTTGG	136	59.5
TOP1MT intron10-R	GACGACCTCTTCGACAGGC		
TOP1MT exon8-F	CCACCGGCACTCTGTTGTAG	197	59.5
TOP1MT exon8-R	ACCATTCCCCACCAACTAGC		

**Supplementary Table 2: Analytical parameters used for each of the bioinformatics analysis**

<b>Burrows-Wheeler Aligner (BWA; 0.7.16a)</b>	
index	-t 12 Homo_sapiens.GRCh38.dna.primary_assembly.fa
aln	-t 12
samse	
<b>Samtools (1.4)</b>	
view	
sort	
merge	
<b>MEDIPS (1.24.0)</b>	
extent	500
window size	100
shift	0
uniq	1
MEDIPS.couplingVector-pattern	CG
MEDIPS.couplingVector-RefObj	GBM[[1]]
MEDIPS.meth-diff.method	edgeR
MEDIPS.meth- MEDIPS	TRUE
MEDIPS.meth-minRowSum	100
MEDIPS.meth-p.adj	bonferroni
MEDIPS.selectSig-pvalue	0.05
MEDIPS.selectSig-agj	TRUE
<b>HTqPCR(1.28)</b>	
readCtData-na.value	40
normalizeCtData-norm	deltaCt
normalizeCtData-deltaCt.genes	OAZ1;HPRT1;ActB/18SrRNA
limmaCtData	
<b>STAR(2.5.3a)</b>	
genomeFastaFiles	Homo_sapiens.GRCh38.dna.primary_assembly.fa
sjdbGTFfile	gencode.v26.annotation.gtf
<b>Rsubread-FeatureCounts (1.26.0)</b>	
annot.inbuilt	hg38
edgeR for RNA seq	
calcNormFactors-method	TMM
estimateGLMCommonDisp	
estimateGLMTrendedDisp	
estimateGLMTagwiseDisp	
glmFit	
glmLRT	

**Supplementary Table 3. Taqman assays used in the Fluidigm qPCR arrays**

Gene name	Taqman assay number
18SrRNA	Hs99999901_s1
Actb	Hs99999903_m1
ADGRB1	Hs00181777_m1
AGAP3	Hs01553103_g1
AGPAT4	Hs01088853_m1
ASL	Hs00902699_m1
BCL2	Hs00608023_m1
BCL3	Hs00180403_m1
C10orf2	Hs00958168_g1
C2CD4C	Hs00985894_s1
C7orf57	Hs01102699_m1
CCDC71L	Hs00703139_s1
CLIP2	Hs00185593_m1
CLU	Hs00156548_m1
COL22A1	Hs01377218_m1
COL4A2	Hs01098873_m1
CYC1	Hs00357718_g1
CYP4F11	Hs01680107_m1
DNMT1	Hs00154749_m1
DNMT3A	Hs01027166_m1
DNMT3B	Hs00171876_m1
DNMT3L	Hs01081364_m1
EGFR	Hs01076090_m1
ELN	Hs00355783_m1
ESRRA	Hs01067166_g1
Esrrb	Hs01584024_m1
FAM20C	Hs00911619_m1
FAM222A	Hs00757936_m1
FAM49A	Hs01003627_m1
FBXO17	Hs00227695_m1
FCGBP	Hs00175398_m1
FNDC10	Hs00972832_s1
FZR1	Hs00393592_m1
GAS6	Hs01090305_m1
GTF2IRD1	Hs00249456_m1
HIF1a	Hs00153153_m1
HPRT1	Hs02800695_m1
HSD17B14	Hs00212233_m1
HSPG2	Hs01078536_m1
IDH1	Hs01855675_s1
IDH2	Hs00158033_m1
KIF17	Hs00325418_m1
KIF21B	Hs01118430_m1
LRRC4B	Hs00297475_s1
LTBP4	Hs00943217_m1
LYPLA1	Hs00911024_g1
MAN1C1	Hs01057229_m1
MASP2	Hs00373722_m1
MEIS3	Hs00908777_m1
MEST	Hs00853380_g1
MT-ATP6	Hs02596862_g1
MT-ATP6	Hs02596862_g1
MT-ATP8	Hs02596863_g1
MT-CO1	Hs02596864_g1
MT-CO2	Hs02596865_g1
MT-CO3	Hs02596866_g1
MT-CYB	Hs02596867_s1
MT-ND1	Hs02596873_s1

Gene name	Taqman assay number
MT-ND2	Hs02596874_g1
MT-ND3	Hs02596875_s1
MT-ND4	Hs02596876_g1
MT-ND4L	Hs02596877_g1
MT-ND5	Hs02596878_g1
MT-ND6	Hs02596879_g1
MTRNR1	Hs02596859_g1
MTRNR2	Hs02596860_s1
MTRNR2	Hs02596860_s1
MYC	Hs00153408_m1
MYT1	Hs01027966_m1
NACAD	Hs00322395_m1
NDUFAB1	Hs00192290_m1
NFE2L2	Hs00975961_g1
NKAIN4	Hs03806373_m1
NRF1	Hs01031046_m1
OAZ1	Hs00427923_m1
PALM3	Hs00908820_g1
PDGFA	Hs00234994_m1
PLEC	Hs00356986_g1
PLXNA4	Hs01039085_m1
POLG	Hs00160298_m1
POLG2	Hs00200546_m1
POLRMT	Hs04187596_g1
PPARGC1A	Hs01016719_m1
PRDM16	Hs00223161_m1
PRICKLE2	Hs00291033_s1
PRKAG2	Hs00211903_m1
PTPRS	Hs01548375_m1
RAB7B	Hs01088520_m1
SDHB	Hs00268117_m1
SDHC	Hs01698067_s1
SDHD	Hs00829723_g1
SEC61G	Hs00414142_m1
SHC2	Hs01044373_m1
SIRT1	Hs01009006_m1
SIRT3	Hs00953477_m1
SLCO4A1	Hs00249583_m1
SMARCD3	Hs00162003_m1
SNX10	Hs00203362_m1
SPPL2B	Hs01086493_m1
SSBP1	Hs00995376_g1
ST3GAL1	Hs00161688_m1
STAT3	Hs01047580_m1
TERT	Hs00972650_m1
TET1	Hs00286756_m1
TET2	Hs00325999_m1
TET3	Hs00379125_m1
TFAM	Hs00273372_s1
TFB1M	Hs00274971_m1
TFB2M	Hs00915025_m1
TLE3	Hs01032572_m1
TOP1MT	Hs01080056_m1
TP53	Hs01034249_m1
TSNARE1	Hs00417029_g1
TTYH1	Hs01012139_m1
WNK2	Hs00396601_m1

**Supplementary Table 4: DMRs overlapping with copy number gain regions**

CN gain-chr	CN gain-start	CN gain-end	Overlapping with VitC-DMR (Start-End)	Overlapping with 5Aza-DMR (Start-End)	Gene annotation
chr1	211088244	211213171			
chr1	219926421	220192189			
chr1	223872383	224349137	224012401-224012800; 224013301-224014100; 224014301-224014400	224012401-224013000; 224013301-224013900; 224014401-224014600	RefSeq: NR_136593.1 Status: Validated
chr1	225562969	226344033			
chr1	235871996	236467557	236097001-236097300		RefSeq: NR_136593.1 Status: Validated
chr1	240509953	240721167			
chr2	23830787	24168230			
chr2	24279904	24347049			
chr2	25745122	25923850			
chr2	31822420	32698792			
chr2	36938466	37061471			
chr2	38546335	38790197			
chr2	44102040	44280450			
chr2	47359069	47475052			
chr2	47475248	47478329			
chr2	47806619	48081697			
chr2	55217933	55756611			
chr2	61356413	61981762			
chr2	88374324	88473434			
chr2	128092312	128149383			
chr2	169775289	169886104			
chr2	171836010	172029793			
chr2	200954453	201120309			
chr2	202146246	203571593			
chr2	207636569	207680279			
chr2	227736331	227801294			
chr2	231671719	231767569			
chr3	27369211	27607977			
chr3	32627446	32758839			
chr3	47510474	48192618			
chr3	49195300	49415508			
chr3	49972414	50088975			
chr3	57659275	57987445			
chr3	93794694	93992813			
chr3	109246829	109451710			
chr3	121461715	121575559			
chr3	125446706	125586874			
chr3	136327166	136748776			
chr3	141928486	142383422			
chr3	153007487	153145543			
chr3	155707030	155906268			
chr3	177222323	177276348			
chr3	183596159	183831367			
chr3	185514495	185631566			
chr3	185793497	185916445			

chr3	195311174	195412448			
chr3	196397702	196534331			
chr3	196653381	196850362			
chr4	25732795	25758882			
chr4	39352717	40173338			
chr4	40471689	40801700			
chr4	48810828	48869071			
chr4	56732553	57039205			
chr4	70769273	71116641			
chr4	88138224	88262858			
chr4	108749303	108839687			
chr4	112521720	112697473			
chr4	127921622	128185413			
chr4	128712913	128778268			
chr4	139151702	139343727			
chr4	164745950	164910752			
chr4	188083155	188339073			
chr5	32297962	32409457			
chr5	45888519	46398991			
chr5	50144698	50405648			
chr5	56027372	56160869			
chr5	69077621	70328678			
chr5	80265268	80383186			
chr5	126561616	126796341			
chr5	134653706	134818494			
chr5	157005426	157095755			
chr5	160096285	160228116			
chr5	180401363	180451188			
chr6	10602105	10622676			
chr6	10762201	10794068	10786801-10787000;10787101-10787200	10786801-10787000;10787101-10787200	MAK
chr6	17299435	17688474			
chr6	18122311	18215201			
chr6	21572400	21701354			
chr6	30512251	30542286			
chr6	31070275	31074635			
chr6	31218147	31222799			
chr6	31586382	31590036			
chr6	32255921	32270672			
chr6	34590409	34823647			
chr6	42489126	42841567			
chr6	73203906	73640630			
chr6	87541110	87552228			
chr6	87584076	87800145			
chr6	88937618	89113196			
chr6	106646935	106691569			
chr6	106861004	107302026			
chr6	110697636	111057269			

chr6	134094530	134290122		
chr6	150898965	150927721		
chr6	154670203	154791629		
chr7	152474058	152553603		
chr7	152687630	152719713		
chr8	39968734	40003202		
chr8	42589865	42731214		
chr8	43548966	43976244		
chr8	45944781	46360719		
chr8	56000933	56084629		
chr8	66695906	67035970		
chr8	69867144	70008543		
chr8	73711496	74029019		
chr8	80150668	80454889		
chr8	94735791	94832007		
chr9	751662	902311		
chr9	6610145	6775089		
chr9	15360401	15417865		
chr9	15564504	15635380		
chr9	18988309	19331183		
chr9	26783678	27038539		
chr9	33807622	34365032		
chr9	36172516	36641994		
chr9	71803749	72152054		
chr9	76340497	76510161		
chr9	77167020	77231597		
chr9	83734515	83820030		
chr9	84345142	84421031		
chr9	86172815	86241971		
chr9	96263562	96844094		
chr9	104981387	105085205		
chr9	107432378	107544092		
chr9	111893087	112513884		
chr9	124849983	125364302		
chr9	129908240	130117264		
chr9	130538508	130623435		
chr10	11935705	12147092		
chr10	12212516	12320488		
chr10	13272317	13296478		
chr10	21373419	21636759		
chr10	30497226	30573492		
chr10	32152920	32195631		
chr10	34750153	34989940		
chr10	35216346	35261106		
chr10	36526302	36853269		
chr10	63089820	63416834		
chr10	67794325	68116947		

chr10	68157998	68197454		
chr10	68421227	69008370		
chr10	72374026	73528699		
chr10	74692645	74752987		
chr10	92112717	92793516		
chr11	3696967	3761630		
chr11	9224608	9585408		
chr11	18297908	18687715		
chr11	32497949	32570975		
chr11	33081598	33365070		
chr11	47335062	47335998		
chr11	47349863	47351432		
chr11	47614047	47962063		
chr11	55035600	55153102		
chr11	107756868	108142529		
chr12	676755	835156		
chr12	928247	1099344		
chr12	1200073	1282631		
chr12	7607454	7964524		
chr12	19229988	19571611		
chr12	31528597	31922673		
chr12	32011128	32082369		
chr12	37497617	38015281		
chr12	50163762	51302894		
chr12	56454563	56593167		
chr12	64455920	64626580		
chr12	95208795	95374695		
chr12	95536069	95694649		
chr12	96409093	96534052		
chr12	98437154	98612485		
chr12	101468859	101560180		
chr12	110115916	110645170		
chr12	111476554	111730027		
chr12	120834751	120980418		
chr12	121167560	121198618		
chr12	122249730	122773223		
chr13	19667630	19959928		
chr13	20860547	21006396		
chr13	28067988	28173463		
chr13	44641318	44695574		
chr13	44969959	45283991		
chr13	48013841	48057543		
chr13	48306330	48309352		
chr13	49448076	50008076		
chr13	72952170	73012708		
chr13	95287449	95387714		
chr14	18226020	18597531		



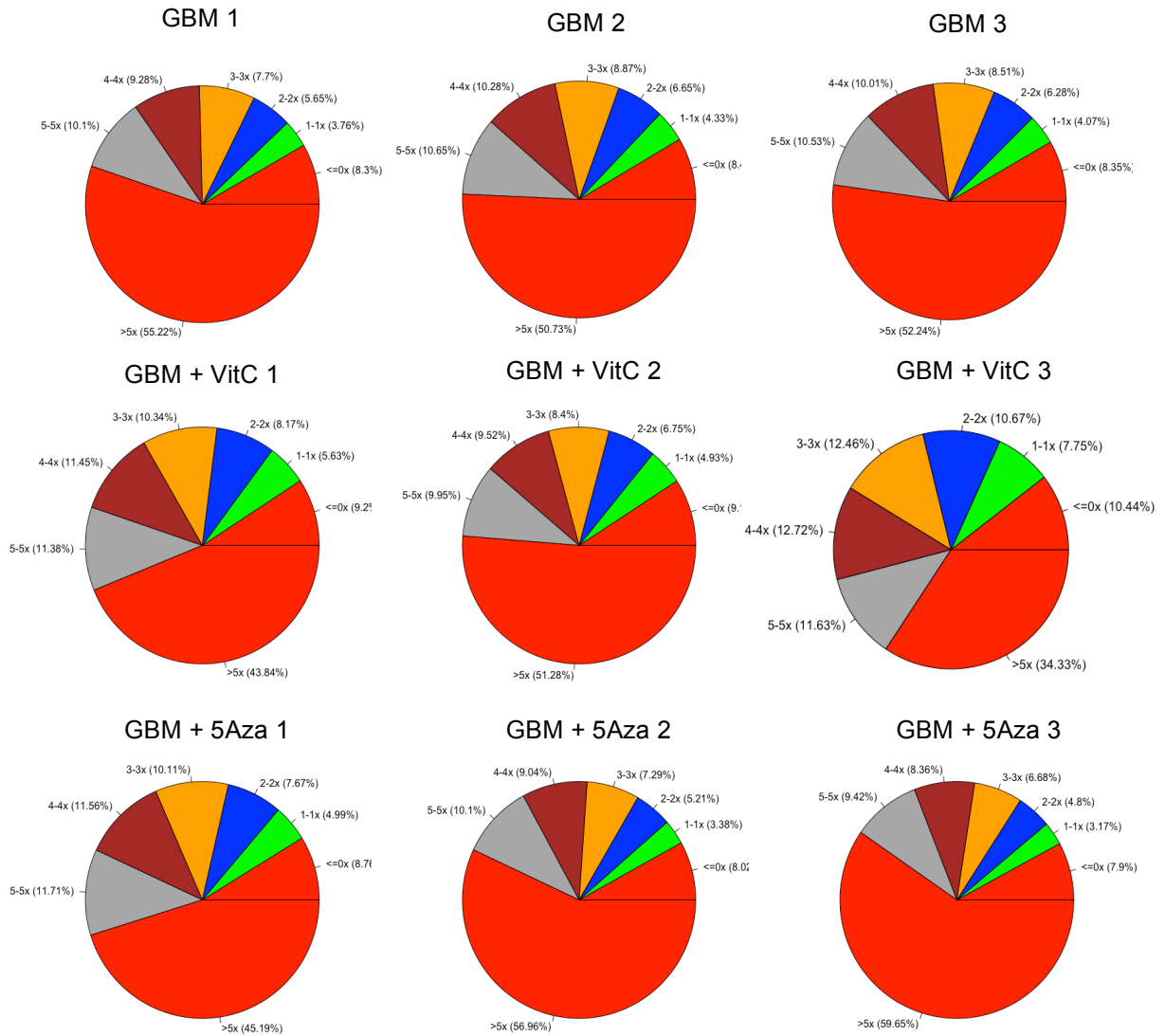
chr14	34414032	35392612		
chr14	49634985	49938786		
chr14	50126803	50298560		
chr14	63649056	63927604		
chr14	102536381	102607800		
chr15	22804033	23039644		
chr15	41030730	41413896		
chr15	44179266	44643219		
chr15	50258031	50737806		
chr15	64205413	64656404		
chr15	98562803	98588562		
chr16	9015048	9122794		
chr16	10264025	10492179		
chr16	18916138	19133410		
chr16	19438839	19616090		
chr16	35760404	36022890		
chr16	58675243	58832542		
chr16	68838934	69808567		
chr17	839486	934664		
chr17	1273696	1397225		
chr17	2488112	2670197		
chr17	2692871	2774484		
chr17	19837231	20050132		
chr17	26941116	27164482		
chr17	29299154	29492282		
chr17	37268235	37477828		
chr17	43063370	43092939		
chr17	43094516	43126420		
chr17	58631423	59375677		
chr17	59714615	59927560		
chr17	61598756	61693477		
chr17	61961298	62394188		
chr17	64544881	64696197		
chr18	20932565	21774317		
chr18	32028017	32147838		
chr18	57649601	57691915		
chr19	6533640	6643289		
chr19	6951095	7103959		
chr19	8134474	8208953		
chr19	11560254	11706482		
chr19	12597220	12649891		
chr19	14571552	14701255	14649801-14649900	ADGRE3
chr19	16680586	16817245	16754501-16754600	NWD1
chr19	20448323	21427482		
chr19	21689836	21838370		
chr19	23590034	23812918		
chr19	24049459	24435205	24179701-24179800	

chr19	27241251	27575884		
chr19	36432067	36632746		
chr19	53539770	53785562	53648201-53648600	
chr20	61563044	61634567		
chr20	63332435	63369826		
chr21	36112594	36192427		
chr22	17184683	17271460		
chr22	28696413	28786494		
chr22	31668448	31772794		
chr22	41003010	41174388		
chrX	32342021	32349467		
chrY	12733073	12846634		
chrY	13075160	13262055		
chrY	16701071	16989164		

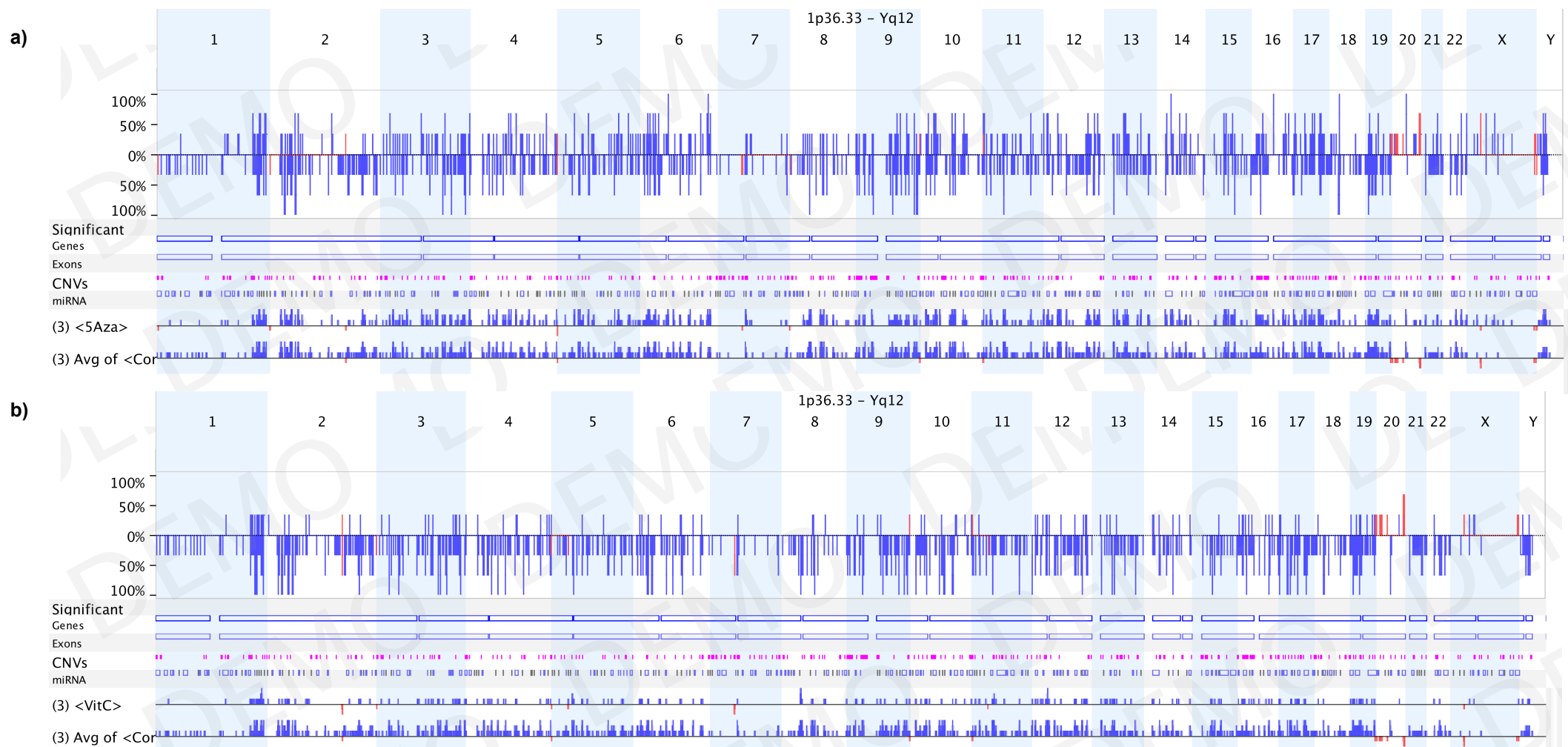
SupplementaryTable 5: Outputs from the Fluidigm qPCR array, as determined by the HTqPCR package

Gene	GBM+VitC vs. GBM-p.value	GBM+VitC vs. GBM-Mean of logFC	GBM+VitC vs. GBM-SEM of logFC	GBM+5Aza vs. GBM-p.value	GBM+5Aza vs. GBM-Mean of logFC	GBM+5Aza vs. GBM-SEM of logFC
ABHD17A	0.8490108	0.531815748	0.471267664	0.093669061	2.035206082	0.888290972
ABR	0.000779018	1.637500694	0.219994705	4.85E-05	2.177948773	0.371490866
ADGRB1	0.901807243	0.4540474	0.688531043	0.22862308	1.34541738	0.755178138
ANGPT2	0.6272323	0.567438859	0.275089159	0.009109337	-0.087223653	0.700368489
ARHGEF10	0.794460223	0.532310264	0.639460279	0.006046615	2.405845201	0.931744972
ARHGEF10L	0.174136941	1.160629147	0.794525951	0.000274234	3.450230016	0.925723315
ARHGEF7	0.444790778	0.116748582	0.685152105	0.067912114	1.624173397	0.791331168
ASIC3	0.872555138	0.484506505	0.73726712	0.005279999	2.430836802	0.769438041
B4GALNT3	0.188721827	1.06277943	0.717833631	0.000671238	2.967967263	0.910452133
BAHCC1	0.899497648	0.512426905	1.152050092	0.00179199	4.028273369	1.040520502
BMP7	0.172011155	0.810481803	0.450915782	0.001697444	1.978753202	0.720904415
CCDC88C	0.909230707	0.340595972	0.861606777	0.000592546	3.489416587	0.930328459
COL22A1	0.716688933	0.25197351	0.687462134	0.038996333	1.853451457	0.86072692
COL26A1	0.660491347	0.64674025	0.615210997	0.195662046	1.609787815	0.992982915
COL4A2	0.082828394	-0.266978376	0.337412828	0.692421062	0.742221011	0.732515011
COL8A2	0.153290071	-3.877288984	3.861033534	0.342694564	3.67197231	0.912532026
CROCCP2	0.560795708	0.628885328	0.674540634	0.010594962	1.985174326	0.769986149
CUX1	0.418386418	0.762785899	0.640724588	0.000265748	2.970052799	0.849109794
CYP4F11	0.088127715	2.854609297	0.101145164	0.036593216	3.584800989	0.089738439
DCC	0.121052958	-0.379223094	0.352091878	0.70821687	0.70555742	0.907759156
DGCR8	0.524954124	0.735930006	0.860358038	0.000671606	3.09782705	0.829034681
DMRTA2	0.671078557	0.734988459	0.770399736	0.02259973	2.826544555	1.280642807
DNAAF5	0.438932546	0.112988297	0.419509272	0.036320556	1.748867489	0.794028996
EGFR	0.00571896	1.466617051	0.339930905	5.09E-05	2.517367905	0.426870256
ELFN1	0.058460855	4.692104609	0.536038994	0.030896726	5.882679696	0.705224219
ELN	0.596834795	0.061281599	0.934233274	0.000457229	3.843044038	0.998020589
ENO2	0.039918341	1.16520356	0.325032835	0.526237815	1.104155215	0.755054982
ERICH3	0.783017539	0.263015918	0.834178296	0.00115282	3.018152102	0.608623099
EXD3	0.950460622	0.43934338	0.92006191	0.008645986	2.383839331	0.697640694
FAM20C	0.236367676	0.954935219	0.727710299	0.000452798	2.922464468	0.770603566
FAM234B	0.851388205	0.478811176	0.595640685	0.015070112	1.91844585	0.82672592
FAM49A	0.155342164	0.638597776	0.272015875	0.004948555	1.394296545	0.413237723
FZR1	0.429534978	0.749092528	0.477328788	0.005174275	2.285187686	0.903674987
GET4	0.516247405	0.629857459	0.551541197	0.030264064	1.692469056	0.729928408
GPR35	0.184704867	1.007091361	0.81966101	0.05956931	1.769290586	0.782553808
HIVEP3	0.022023753	1.639298763	0.718840156	0.000197309	3.298153169	0.892548001
HSD11B1L	0.372407775	0.126234137	0.461965533	0.074957102	1.479384972	0.683149226
IQCE	0.749193741	0.307979753	0.596453248	0.005612192	1.904330012	0.699370676
JRK	0.183310936	1.079186094	0.749824521	6.94E-05	3.598726556	0.928025804
KIF17	0.042888221	1.054665064	0.384972797	0.010331208	1.749389442	0.731742367
KREMEN1	0.150784988	1.142841279	0.802936154	9.02E-05	3.548327874	0.85345768
KRT7	0.153486987	-2.970079528	3.194383723	0.947768315	1.036736719	0.909057389
LINC01006	0.304569383	0.836487065	0.692540835	0.169730658	1.470145974	0.751196993
MEIS3	0.563825434	0.290231711	0.570791593	0.956106046	0.876685084	0.527024162

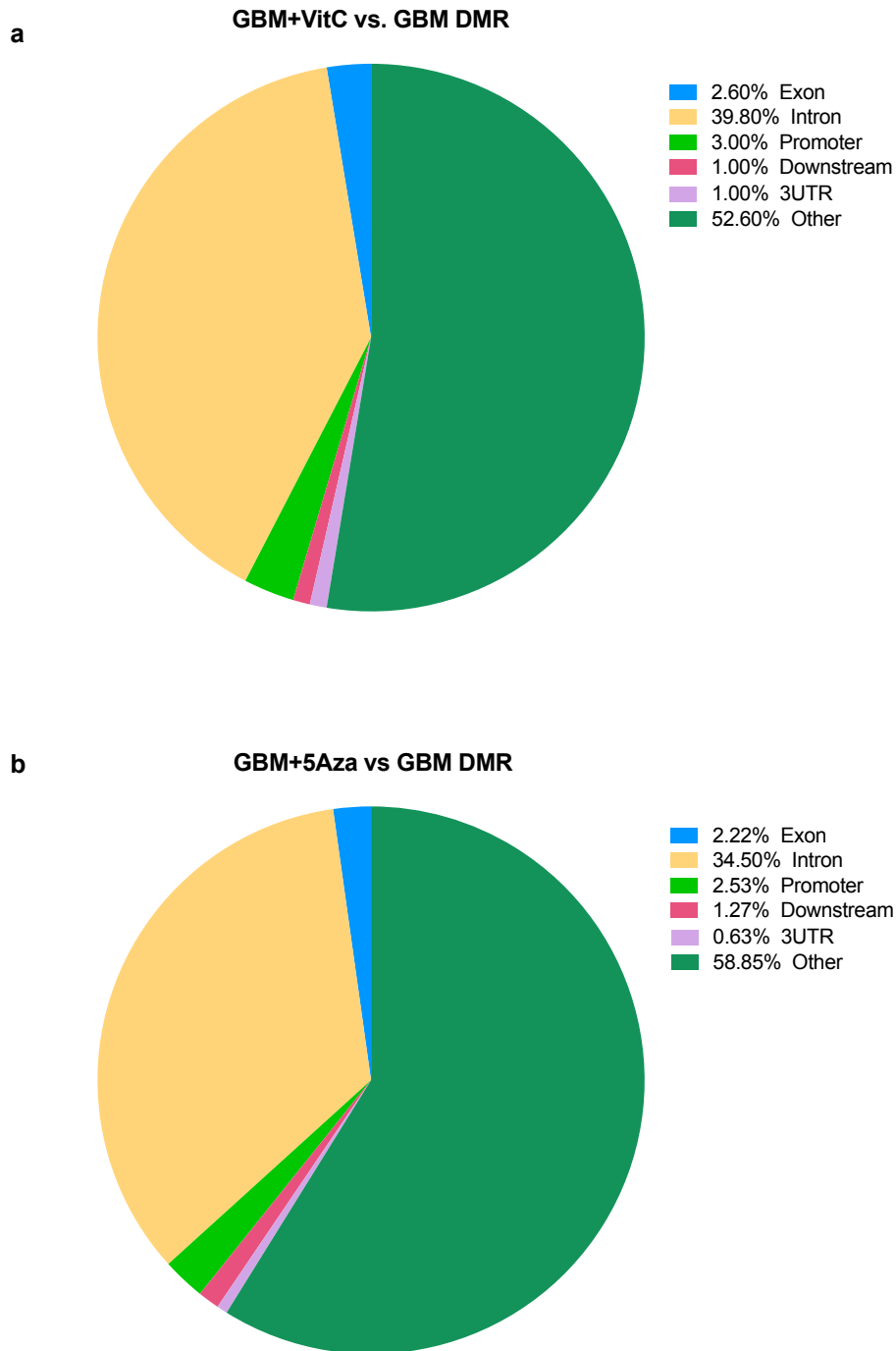
MTCL1	0.884138659	0.469029593	0.73036444	0.000140759	3.028597104	0.794233994
MUC12	0.122763335	5.824927242	3.580190106	0.006655766	11.43736147	2.881270576
MUC3A	0.655353067	-1.008341301	0.351205852	0.150456344	3.348173427	2.720679524
MYH7B	0.445250458	0.097644419	0.570342434	0.001873163	2.414622386	0.833969134
MYO7A	0.250117449	-0.040480267	0.541774236	0.001857696	2.332150526	0.816459006
MYRF	0.346945364	1.045647979	0.980357665	0.002034504	3.38496777	1.001549113
MYRFL	0.033506797	-5.397535906	3.393563686	0.573033184	2.303053497	0.770183617
NCAPG2	0.981581605	0.399490624	0.452877244	0.056127015	1.67059078	0.754820824
NDUFAF5	0.462794724	0.636094619	0.536227121	0.001808196	2.057395804	0.690379435
NFKBIB	0.810981403	0.33666836	0.445797632	0.073383711	1.461466479	0.692779129
NGEF	0.801052354	0.330759224	0.415671602	0.055146639	0.253319909	0.656874922
NKAIN4	0.778547483	-0.04463983	0.086030808	2.37E-06	1.11238846	0.133641299
NSUN6	0.403709282	0.174119076	0.396671019	0.023048073	1.58413776	0.632358839
NWD1	0.857355446	-0.372601495	3.623711857	0.248410402	6.030528405	3.126932966
OPRL1	0.084834048	1.225585995	0.733649909	0.000383764	2.953950872	0.809003863
P2RX5	0.183474667	0.089802362	0.371379764	0.623622491	1.001818772	0.599141145
PIP5K1C	0.629017123	0.642564811	0.804016979	0.00142785	2.783555429	0.82189893
PLEC	0.872214045	0.507208796	0.838106666	0.00092469	3.434203589	1.046629467
PLXNA4	0.000167548	2.292469529	0.317067072	0.002014605	1.731189525	0.406445124
POMT1	0.168035517	-0.028167793	0.460779463	0.765424874	0.9788782	0.685583749
PPP1R12C	0.000118611	1.386320935	0.156081694	1.43E-05	1.684477014	0.265178343
PRDM16	0.004437841	1.885771033	0.684583544	5.06E-06	4.051596416	0.816521399
PRKAR1B	0.07196897	0.876015598	0.486207345	4.51E-05	2.307608771	0.695967087
PRKCA	0.126022946	1.033887303	0.608802998	0.000344191	2.714153292	0.882939404
PRRT4	0.139283293	-0.47880361	0.835385891	0.420096376	1.357123279	0.989539503
PTPRN2	0.127327969	0.687940617	0.09231575	0.001251632	1.671138999	0.352194864
PTPRS	0.868916686	0.474686332	0.703179598	0.017645025	1.952494037	0.625356348
RFNG	0.599953728	0.584219477	0.565493026	0.001345222	2.208579384	0.7811225
SCNN1D	0.34004755	0.116942652	0.671369645	0.019633044	1.667745566	0.609978177
SDK1	0.347243942	0.840158146	0.658676427	0.000141135	3.220575872	0.912296081
SERINC2	0.015274435	-0.12683558	0.502223245	0.001161811	0.096546829	0.611766953
SH3RF3	0.13987869	0.848202747	0.494633341	1.24E-05	2.773435997	0.735752533
SHC2	2.02E-06	1.477460502	0.094607532	2.79E-06	1.439701646	0.167908811
SHC3	0.161511803	0.773608768	0.505351455	0.000978033	1.923219116	0.681860452
SLCO4A1	0.035094065	-0.257425132	0.358249729	0.643159226	0.753365369	0.71470039
SPPL2B	0.000430854	1.335409552	0.224466492	1.19E-05	1.884552985	0.242299864
ST3GAL3	0.463185087	0.669989037	0.536358768	0.001622079	2.252057487	0.847530649
TNS1	0.351653674	0.843156807	0.624777998	0.015812416	2.132530706	0.941698187
TOP1MT	0.195548665	0.815352568	0.517910783	5.76E-05	2.61525311	0.756431561
TSC2	0.278842802	0.807584718	0.679278961	0.000189351	2.691165774	0.759809656
TSNARE1	0.621189961	0.544640625	0.522681019	0.000783903	2.053011817	0.743674529
VSTM2A	0.021010852	0.643538211	0.194012205	0.672437995	0.108329681	0.132271922
WNK2	0.019155665	1.970983345	0.940689734	4.80E-05	4.343589222	0.846637115
ZNF358	0.539483405	0.255344064	0.51564775	0.11489287	1.297478229	0.610122424



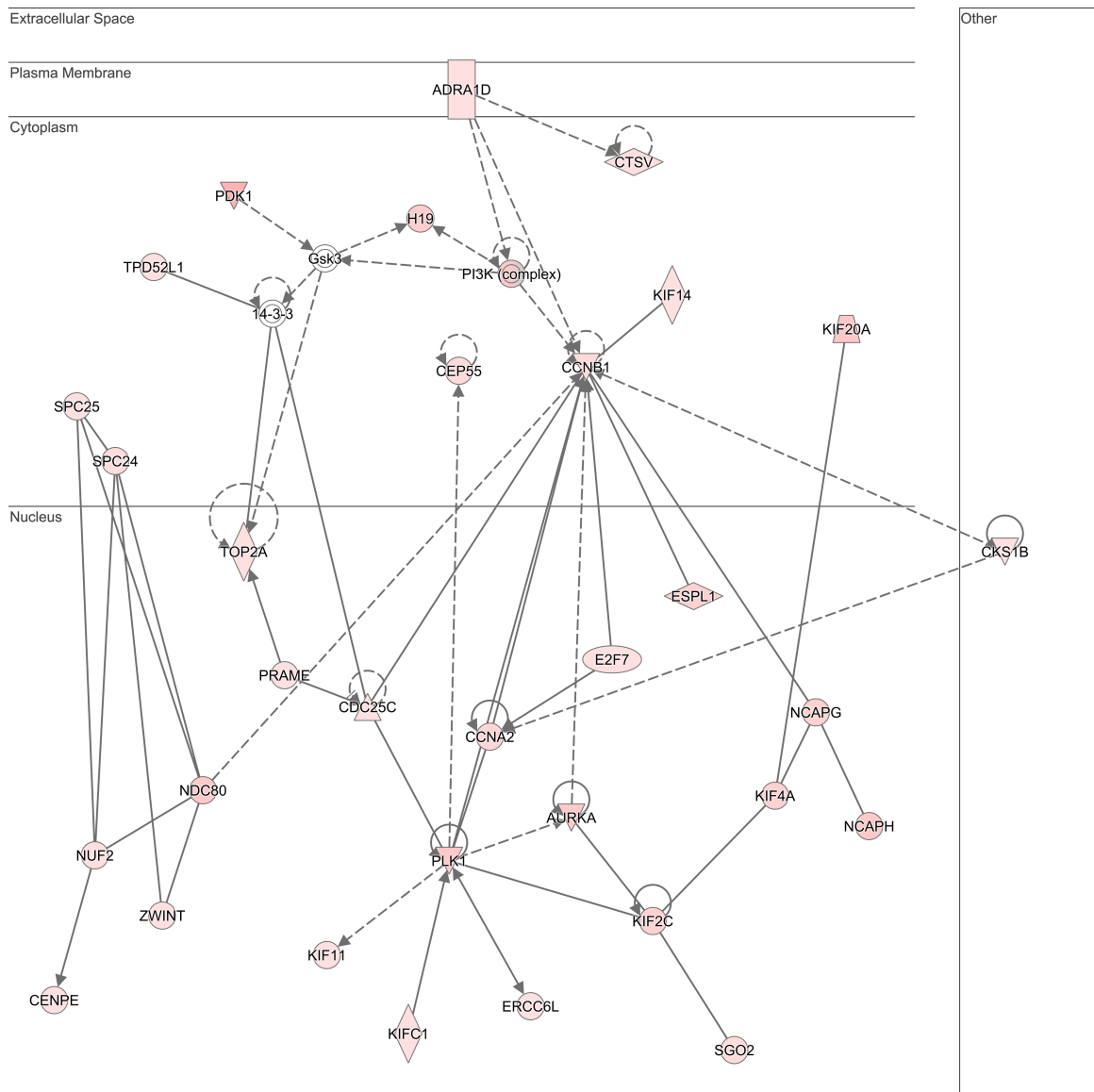
**Supplementary Figure 1. Coverage analysis of CpGs from the MeDIP-Seq data using the MEDIPS package.** The total number of CpG sites in the human genome was fractionised into pie charts according to the level of coverage. 7 fractions were used. <=0x in the upper red fraction: CpG sites that were not covered; 1-1x in the green fraction: CpG sites that were covered once; 2-2x in the blue fraction: CpG sites that were covered twice; 3-3x in the orange fraction: CpG sites covered three times; 4-4x in the brown fraction: CpG sites covered 4 times; 5-5x in the grey fraction: CpG sites covered 5 times; >5x in the lower red fraction: CpG sites covered more than 5 times. The first row is for the GBM cohort; the second row is for the GBM+VitC cohort; and the third row is for the GBM+5Aza cohort.



**Supplementary Figure 2. Whole genome CNV comparisons between the GBM, the GBM+VitC and the GBM+5Aza cohorts, as determined by Nexus Copy Number Module (9.0).** In comparisons between the: **a)** GBM+VitC and GBM cohorts; and **b)** GBM+5Aza and GBM cohorts, the upper panel shows copy number enrichment for each chromosome. Blue bars represent copy number gains, whereas red bars indicate copy number loss. Bars above 0% indicate CNVs identified in the treated cohorts, bars below 0% indicate CNVs in the GBM cohort. The panel 'Significant' indicates the significant CNVs between the two cohorts. The panels of 'Genes', 'Exons', 'CNVs', and 'miRNA' are genome annotations. The two panels at the bottom show the mean copy number value of the triplicates in each cohort.

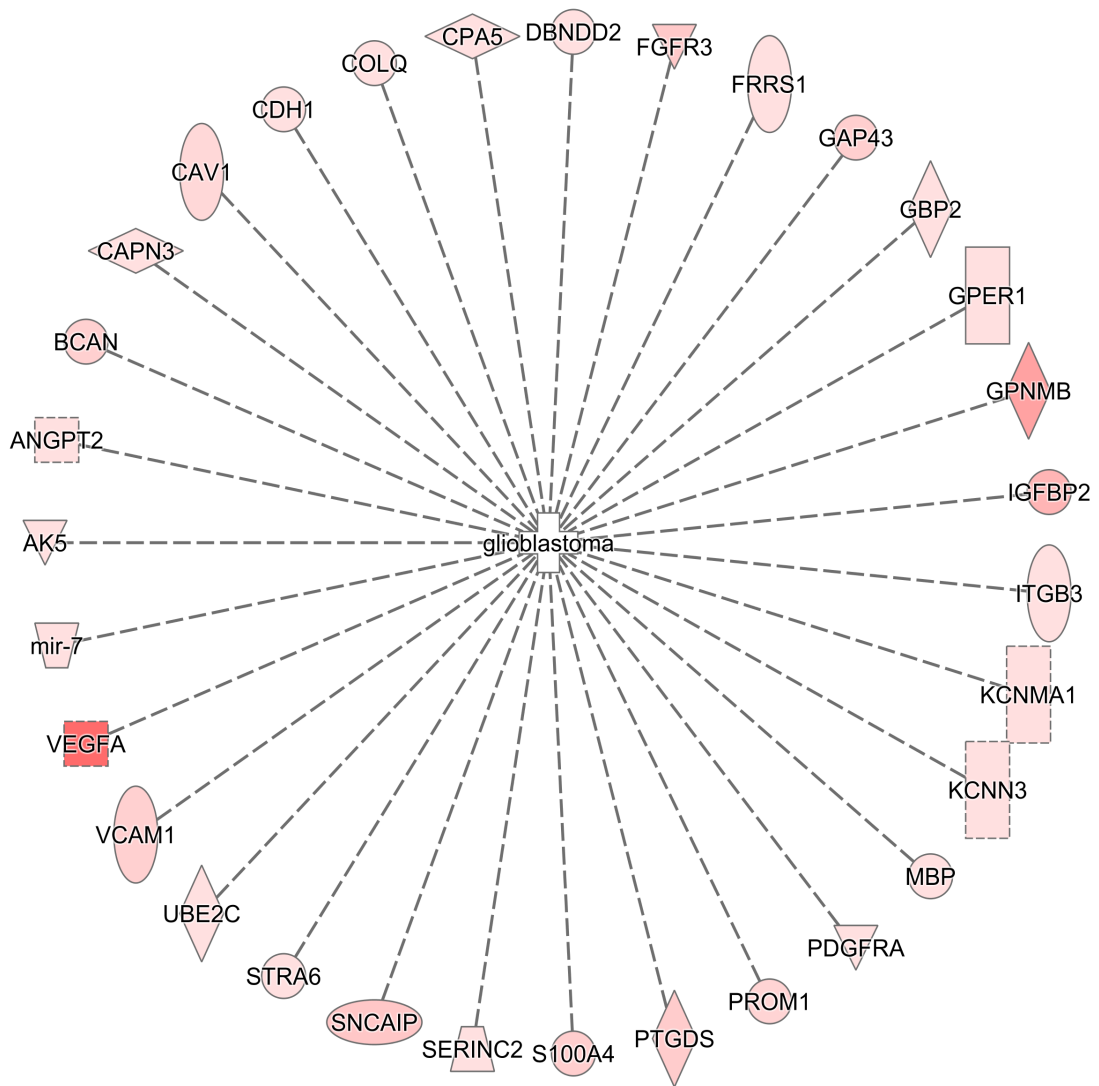


**Supplementary Figure 3. Annotations of the DMRs.** DMRs were sub-grouped into exon (blue), intron (yellow), promoter (green), downstream regions ( $\leq 3$ kb; pink), 3UTR (purple) and intragenic regions (dark green) based on their genomic locations. The percentages of each part were calculated based on the number of corresponding DMRs out of the total number of DMRs. The basal distribution for genomic elements, based on size, in the human genome is 1.5% for exons, 24% for introns and 75% for other intergenic regions (1).

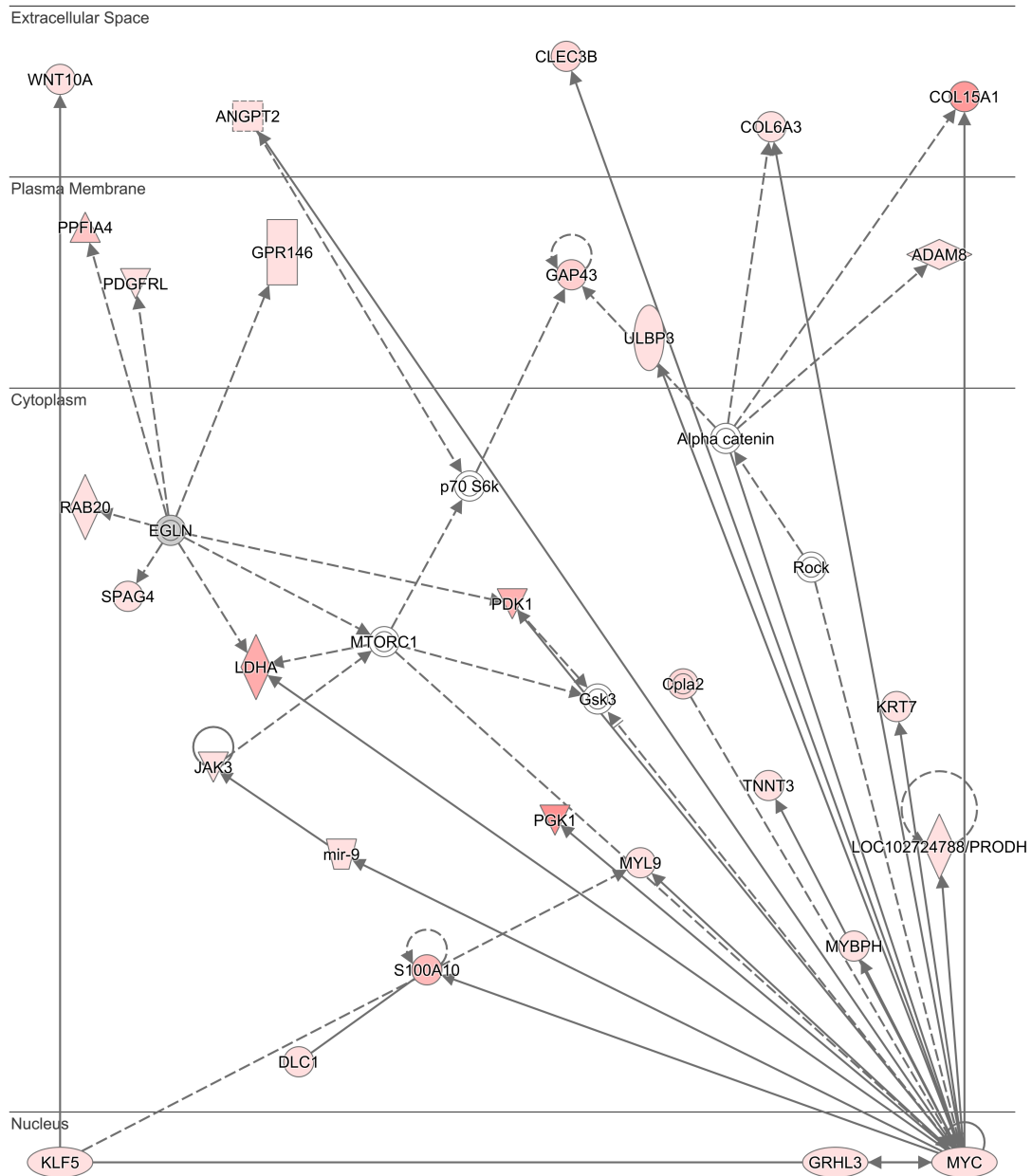


**Supplementary Figure 4. The top enriched network of differentially expressed genes induced by VitC.** A total of 32 molecules were identified to be associated with the functions of the cell cycle, cellular assembly and organization, and DNA replication, recombination, and repair. The network is presented in relation to its sub-cellular locations. The colour strength (from white to red) correlates with the fold-change in up-regulation of gene expression. Therefore, pink is indicative of up-regulation induced by VitC.

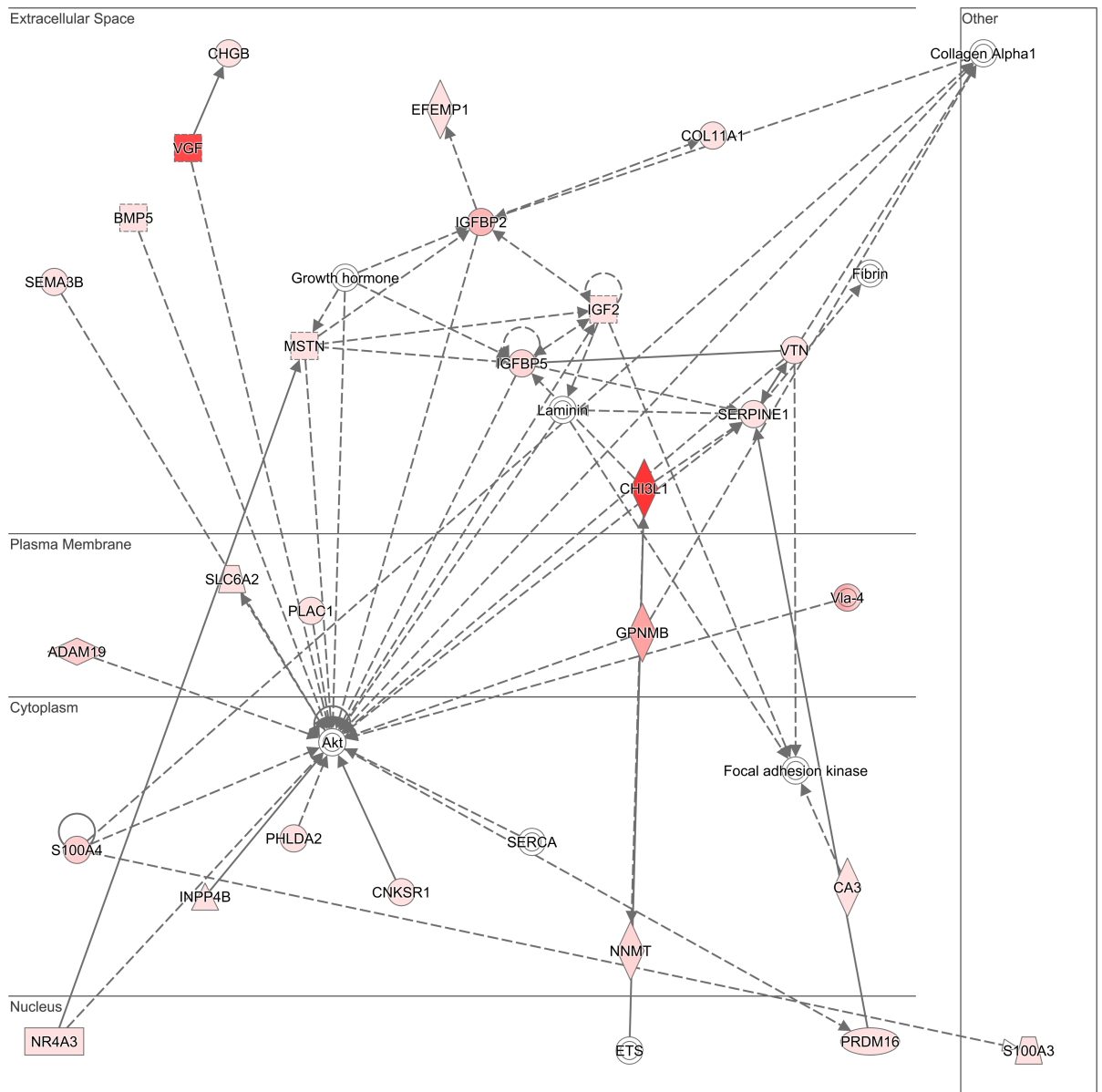




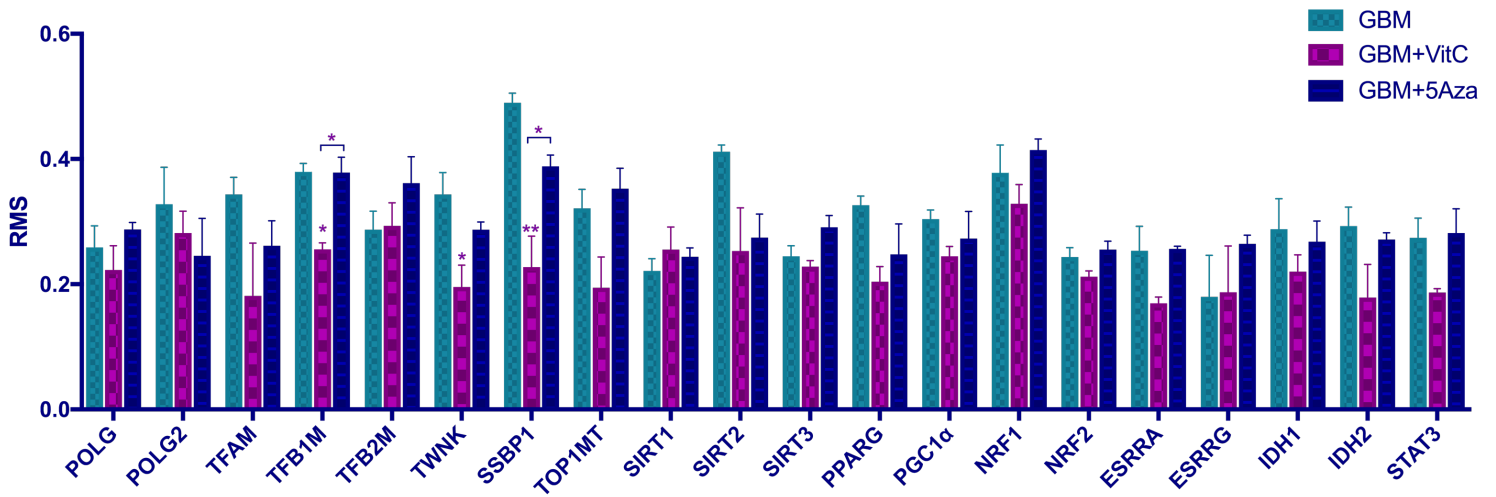
**Supplementary Figure 5. The glioblastoma disease pathway affected by VitC.** Genes associated with the disease pathway are presented as a circular display. The pathway figure was exported from IPA software. The colour strength (from white to red) correlates with the fold-change in up-regulation. Molecules in red indicate higher levels of increased gene expression whilst pink is more indicative of moderate up-regulation induced by VitC.



**Supplementary Figure 6. The top enriched network of differentially expressed genes induced by 5Aza.** The 28 molecules were identified to be associated with cell morphology, cellular function and maintenance, and carbohydrate metabolism. The network is presented in relation to its sub-cellular locations. The colour strength (from white to red) correlates with the fold-change in up-regulation of gene expression induced by 5Aza.



**Supplementary Figure 7. The second most enriched network of differentially expressed genes induced by 5Aza.** 26 molecules were identified to be associated with cancer, neurological disease, and organismal injury and abnormalities. The pathway figure was exported from IPA software. The network is presented in relation to its sub-cellular locations. Molecules in red indicate increased gene expression. The colour strength (from white to red) correlates with the fold-change in up-regulation of gene expression induced by 5Aza.



**Supplementary Figure 8.** DNA methylation levels over the CGIs located within the promoter regions of the mtDNA transcription and replication factors. DNA methylation levels expressed as RMS over the CGIs located in the promoter regions of the mtDNA transcription and replication factors are shown (n=3). Statistical analysis was performed using one-way ANOVA between the three cohorts. Bars represent the mean  $\pm$  SEM. \* and \*\* indicate *p* values of < 0.05 and 0.01, respectively. The GBM cohort is shown by the light blue bars; GBM+VitC cohort is shown by the purple bars, the GBM+5Aza cohort is represented by the dark blue bars.

## REFERENCE

1. Venter, J.C., Adams, M.D., Myers, E.W., Li, P.W., Mural, R.J., Sutton, G.G., Smith, H.O., Yandell, M., Evans, C.A., Holt, R.A. *et al.* (2001) The sequence of the human genome. *Science*, **291**, 1304-1351.