## **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: <u>Justin.StJohn@hudson.org.au</u>

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

Human Gene Forward primer (5'-3')		Product size A	nnealing Tm ( °C)
β-globin-F	β-globin-F CAACTTCATCCACGTTCACC		E7
β-globin-R	GAAGAGCCAAGGACAGGTAC	200	57
mtDNA-F	CGAAAGGACAAGAGAAATAAGG	150	F2
mtDNA-R	CTGTAAAGTTTTAAGTTTTATGCG		55
Long1-F (Set 1)	GACGGGCTCACATCACCCCATAA	0202	62
Long1-R (Set 1)	GCGTACGGCCAGGGCTATTGGT		03
Long2-F (Set 1)	GCCACAACTAACCTCCTCGGACTCCT	0700	<u></u>
Long2-R (Set 1)	GGTGGCTGGCACGAAATTGACC	8703	03
Long1-F (Set 2)	TACACATGCAAGCATCCCCGTTCCA	7071	62
Long1-R (Set 2)	GGGCAATGAATGAAGCGAACAGATTTTCG	/0/1	03
Long2-F (Set 2)	CAGTGATTATAGGCTTTCGCTCTAAG	7095	62
Long2-R (Set 2)	TCTGTGTGGAAAGTGGCTGTGCAGA	/965	03
RNR1-F	TACACATGCAAGCATCCCCG	070	F7 F
RNR1-R	GGGGAGGGGGTGATCTAAAA	276	57.5
RNR2-F	GGGCATAACACAGCAAGACG	205	
RNR2-R	AACATCGAGGTCGTAAACCCT	295	56.5
CO1-F	CTTCTCCTTACACCTAGCAG	140	
CO1-R	GTAGGACTGCTGTGATTAGG		55.5
ND4-F	CTGCCTACGACAAACAGAC	404	
ND4-R	GGCAGAATAGTAATGAGGATG		55.5
ND4L-F	ND4L-F GGATTAGACTGAACCGAATTG		
ND4L-R	AGTAGGGAGGATATGAGGTG	1/6	54.5
O <sub>L</sub> -F	CAGCTAAGCACCCTAATCAAC	100	
O <sub>L</sub> -R	TCTAAAGACAGGGGTTAGGC		00.0
ND5-F	AAACCCCATTAAACGCCTGG	054	
ND5-R	TGCGGTGTGTGATGCTAGG		56.5
CO3-F	TCACCATTTCCGACGGCATC	100	<b>F7 F</b>
CO3-R	CO3-R TGGCGGATGAAGCAGATAGTG		57.5
ND3-F	ACCACAACTCAACGGCTACAT	404	50 5
ND3-R	GGGCTCATGGTAGGGGTAAA		56.5
CYTB-F	ATGACCCCAATACGCAAAACT	404	545
CYTB-R	GGGAGGACATAGCCTATGAA		54.5
CO2-F	CTGCTTCCTAGTCCTGTATG	005	50.0
CO2-R	GTCGGTGTACTCGTAGGTTC	235	56.6
ND6-F	CCGCACCAATAGGATCCTCCCGA	407	
ND6-R	GCATGGGGGTCAGGGGTTGAG		63.5
ATP6-F	CAGTGATTATAGGCTTTCGCTC	0.10	
ATP6-R	GTGTTGTCGTGCAGGTAGAG	343	57.5
ND2-F	ACCGTACAACCCTAACATAACC		
ND2-R	GAGGAGGGTGGATGGAATTAAG	166	57.5
ATP8-F	CACTATTCCTCATCACCCAACTAA		
ATP8-R	GGGCAATGAATGAAGCGAAC	140	56.5
LSP-F	AGCCACTTTCCACAGAGACATCATA		
LSP-R	TAGGATGGGCGGGGGGGTTGTA	250	59
HSP-F	TCAATACAACCCCCGCCCAT		
HSP-R			57.5
O <sub>µ</sub> -F			
O <sub>µ</sub> -R	TCTGTGTGGAAAGTGGCTGT	170	57
POLG exon2-F			
POLG exon2-R	GACAACCTGGACCAGCACTT	209	59.5
TOP1MT intron10-F	AAGGACATGTCAGCCGTTGG		
TOP1MT intron10-R	GACGACCTCTTCGACAGGC	136 59.5	
TOP1MT exon8-F	CCACCGGCACTCTGTTGTAG		
TOP1MT exon8-R	ACCATTCCCCACCAACTAGC	197	59.5

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glmFit	estimateGLMTagwiseDisp	
gImLRT	glmFit	
	glmLRT	

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

# 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
ASI	Hs00902699 m1
BCI 2	Hs00608023 m1
BCL3	Hs00180403 m1
C10orf2	Hs00958168 g1
	He00085804 e1
CZOD4C	He01102600 m1
	He00702120 e1
	He00185502 m1
	HSU0156548_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
FBX017	Hs00227695 m1
FCGBP	Hs00175398 m1
ENDC10	Hs00972832 s1
F7R1	He00303502 m1
CAS6	He01000305 m1
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	HS00153153_111
	HS02800695_m1
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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 a1
MT-CO3	Hs02596866 a1
MT-CYB	Hs02596867 s1
	He02506873 e1
	1302330073_31

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 a1
PLXNA4	Hs01039085 m1
POLG	Hs00160298 m1
POLG2	Hs00200546 m1
POLRMT	Hs04187596 g1
PPARGC1A	Hs01016719 m1
PRDM16	Hs00223161 m1
PRICKI F2	Hs00291033_s1
PRKAG2	Hs00211903 m1
PTPRS	Hs01548375_m1
RAB7B	Hs01088520 m1
SDHB	Hs00268117 m1
SDHC	Hs01698067_s1
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SIRT3	Hs00953477 m1
	Hs00249583 m1
SMARCD3	Hs00162003_m1
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SPPI 2R	Hs01086403 m1
SSRP1	Hs00995376 a1
ST3GAL1	Hs00161688 m1
STATS	Hs01047580 m1
TEPT	He00072650 m1
	Hs00286756 m1
	He00325000 m1
	Hs00379125 m1
	Henno73372 e1
	He00274071 m1
	He00015025 m1
	He01022572 m1
	HSUU417U29_g1
	HSU1U12139_M1
WNK2	HS00396601_m1

Supplementary lable 4: Diviks overlapping with copy number dain
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Supplementa	rvTable 4: DMRs	overlapping with	n 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	RefSeg: 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			

ch319830702198634311986343431986343419863434198634341986343419863434198634341986343419863434198634341986343419863434198634341986343419863434198634341986343419863434198634341986343419863444198634441986344419863444198634441986344419863444198644419863444198634441986344419864441986444198644419864441986444198644419864441986444198644419864441986444198644441986444419864444198644441986444419864444198644441986444419864444198644441986444419864444198644441986444419864444 <th>chr3</th> <th>195311174</th> <th>195412448</th> <th></th> <th></th> <th></th>	chr3	195311174	195412448			
drd19663.00219668.002Index<IndexIndexIndexIndex </td <td>chr3</td> <td>196397702</td> <td>196534331</td> <td></td> <td></td> <td></td>	chr3	196397702	196534331			
nH4287327828758882875882Inc.Inc.cH4418470804090.170Inc.Inc.Inc.cH4418410824080.070Inc.Inc.Inc.cH44881082570.39205Inc.Inc.Inc.Inc.cH44872263570.39205Inc.Inc.Inc.Inc.Inc.cH4197249231083.9987Inc.	chr3	196653381	196850362			
m449393277401733840170384017030ch4445471894680170ch4445810234680071ch44557335557039205ch44707082737111641ch44108138248826258ch4411252172112807473ch44112521721281641ch441125217212817838ch441125172312877828ch441891517312877828ch441891517312877828ch451297192112877828ch461891517312877828ch47189151912877828ch47189151912877828ch48189151912877828ch47189151912877828ch4818915191893973ch4418915191893973ch4918915191893973ch4918915191893973ch41418915191893973ch41519905261893974ch415199052721990575	chr4	25732795	25758882			
ch4         44947089         4080170         Inc.         Inc.           ch4         4810028         48800071         Inc.         Inc.           ch4         59730505         57039005         Inc.         Inc.         Inc.           ch4         59730507         Inc.         Inc.         Inc.         Inc.           ch4         1024204         8826288         Inc.         Inc.         Inc.         Inc.           ch4         11252170         11280473         Inc.         In	chr4	39352717	40173338			
dr4448812824889071IndexIndexIndex647425357703205IndexIndexIndex6474770620737711641IndexIndexIndex64741084730310883987IndexIndexIndex647411221723112897473IndexIndexIndex647411221723112897473IndexIndexIndex64741122172312817828IndexIndexIndex64741129719213834377IndexIndexIndex64741892815518633973IndexIndexIndex64741892815518633973IndexIndexIndex647512877828IndexIndexIndexIndex64761892815518633973IndexIndexIndex64761892815518633973IndexIndexIndex64751892815518633973IndexIndexIndex6484498856449497IndexIndexIndex6491892815218633973IndexIndexIndex64965027372660988IndexIndexIndex649650273726609894IndexIndexIndex6491289586IndexIndexIndexIndex64912895875IndexIndexIndexIndex64912895876IndexIndexIndexIndex6491	chr4	40471689	40801700			
chr4         56732053         5730205         Inc.           chr4         70769237         71116641         Inc.         Inc.           chr4         10874930         8082288         Inc.         Inc.           chr4         112521720         11987473         Inc.         Inc.           chr4         112521720         11987473         Inc.         Inc.           chr4         112521720         11987473         Inc.         Inc.           chr4         112571203         12877628         Inc.         Inc.           chr4         18051702         13934577         Inc.         Inc.         Inc.           chr4         18061702         13934971         Inc.         Inc.         Inc.           chr5         32287962         32403471         Inc.         Inc.         Inc.           chr5         65014688         5040548         Inc.         Inc.         Inc.           chr5         5014688         5040548         Inc.         Inc.         Inc.           chr5         12805916         Inc.         Inc.         Inc.         Inc.           chr5         12805916         Inc.         Inc.         Inc.         Inc.	chr4	48810828	48869071			
hr44770'82737111641IndextIndextIndexthr4481832248822285IndextIndextIndextIndexthr44112621720112897473IndextIndextIndextIndextIndexthr441272192212819413IndextIndextIndextIndextIndextIndexthr441287129112817283IndextIndex	chr4	56732553	57039205			
bh4         88224         882248         Receiver of the second	chr4	70769273	71116641			
chr4         1074/303         1088/98/7         Interpretation         Interpretation           chr4         11252120         1128/123         1128/123         Interpretation         Interpretation           chr4         1128/1231         1287/828         Interpretation         Interpretation         Interpretation           chr4         139161720         139343721         Interpretation         Interpretation         Interpretation           chr4         16474500         16491072         169343721         Interpretation         Interpretation           chr4         16474500         16491072         33943721         Interpretation         Interpretation           chr5         3229762         3249457         Interpretation         Interpretation         Interpretation           chr5         5014498         5405648         Interpretation         Interpretation         Interpretation           chr5         5007727         7328678         Interpretation         Interpretation         Interpretation           chr5         6907781         7328678         Interpretation         Interpretation         Interpretation           chr5         1265616         12676641         Interpretation         Interpretation         Interpretation <t< td=""><td>chr4</td><td>88138224</td><td>88262858</td><td></td><td></td><td></td></t<>	chr4	88138224	88262858			
ohr         1128/120         1128/1213         128/1213 <th< td=""><td>chr4</td><td>108749303</td><td>108839687</td><td></td><td></td><td></td></th<>	chr4	108749303	108839687			
dhr4         1272(622         12819413         Image: Constant of the second o	chr4	112521720	112697473			
chr4         12877208         International strength         International strength           chr4         13915702         13939377         International strength         International strength           chr4         18030150         164910752         International strength         International strength           chr4         18080155         164901752         International strength         International strength           chr5         3229762         3340457         International strength         International strength           chr5         50144698         50405648         International strength         International strength           chr5         50014698         50405648         International strength         International strength           chr5         6907721         7032678         International strength         International strength           chr5         12661616         12769534         International strength         International strength           chr5         13463706         13481844         International strength         International strength           chr5         15705426         15705426         10072201         International strength         International strength           chr6         10602015         1062676         International strengt         Internatio	chr4	127921622	128185413			
chr4         13915702         139343727         Index (150)           chr4         164745050         16491752         Index (150)         Index (150)           chr5         13803073         Index (150)         Index (150)         Index (150)           chr5         13803073         Index (150)         Index (150)         Index (150)           chr5         14898891         46339901         Index (150)         Index (150)           chr5         5607372         5616089         Index (150)         Index (150)           chr5         6807762         70328678         Index (150)         Index (150)           chr5         13265676         126795341         Index (150)         Index (150)           chr5         13609285         180028116         Index (150)         Index (150)           chr5         13609285         180028110         Index (150)         Index (150)           chr5         136028116         Index (150)	chr4	128712913	128778268			
chr4         1644745950         164910752         Inclusion           chr4         18803156         18830373         Inclusion         Inclusion           chr5         3229782         32409457         Inclusion         Inclusion           chr5         3229782         32409457         Inclusion         Inclusion           chr5         50144698         50405648         Inclusion         Inclusion           chr5         50140698         5040564         Inclusion         Inclusion           chr5         5026526         803336         Inclusion         Inclusion           chr5         12656161         12679634         Inclusion         Inclusion           chr5         15000528         1502916         Inclusion         Inclusion           chr5         160005285         16022876         Inclusion         Inclusion           chr6         10762201         1078400107870010787101-1078700010787101-10787200         Inclusion         Incl	chr4	139151702	139343727			
ehr4         18833073         Image: state	chr4	164745950	164910752			
dnfs         32297962         32409457         Image: Constant of the state of the st	chr4	188083155	188339073			
chr5         46388619         46388991         46388991         46388619         463888519         463886519         463886519         463886519         463886519         463886519         463886519         463886519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         463888519         4638885188         4638885188         4638885188         4638885188         4638885188         4638885188         4638885188         4638885188         4638885188         4638885188         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         46388874         4638874         4638874         4638874         4638874         4638874         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         46388741         463888741         463888741 <td>chr5</td> <td>32297962</td> <td>32409457</td> <td></td> <td></td> <td></td>	chr5	32297962	32409457			
chris         50144698         50445648         chris         50144698         50407321         5616089           chris         56027321         5616089         chris         60077621         70328678         chris           chris         60077621         70328678         chris         60077621         70328678         chris           chris         12656166         126706341         chris         134683706         134818494         chris         chris         157005755         chris         157005755         chris         16002105         160228716         chris         160062105         10622876         chris         160062105         10622876         chris         chris         116062105         10622876         chris         chris         10786801-10787000;10787101-10787200         10786801-10787000;10787101-10787200         MAK           chris         118040138         118040138         11608474         chris         11798435         1768801-10787000;10787101-10787200         MAK           chris         118040138         118040138         118040138         11608247         chris         11602105         10622876         chris         10622076         chris         11602105         116794068         10786801-10787000;10787101-10787200         MAK         chr	chr5	45888519	46398991			
chris         56027372         56160869         Control         Control           chris         60077621         70328678         Control         Control           chris         80265268         80383186         Control         Control           chris         126561616         126796341         Control         Control           chris         13463706         13481494         Control         Control           chris         157005426         157095755         Control         Control           chris         160096285         16022816         Control         Control           chris         160041083         180451188         Control         Control           chris         10622015         10622676         Control         Control           chris         1076201         10784081-10787000;10787101-10787200         10786801-10787000;10787101-10787200         MAK           chris         12172403         17688474         Control         Control         Control           chris         131211         18215021         Control         Control         Control         Control           chris         31218147         3122279         Control         Control         Control         Control	chr5	50144698	50405648			
chr5         69077621         70328678         Control           chr5         80265268         80383186         Control         Control           chr5         126561616         126796341         Control         Control           chr5         134653706         134818494         Control         Control           chr5         15709575         Control         Control         Control           chr5         160096285         160228116         Control         Control           chr6         10602105         10622876         Control         Control           chr6         10762201         10786801-10787000;10787101-10787200         MAK           chr6         107299435         17688474         Control         Control           chr6         1072201         10786801-10787000;10787101-10787200         MAK         Control           chr6         117299435         17688474         Control         Control         Control           chr6         117299435         17688474         Control         Control         Control           chr6         18122311         18215201         Control         Control         Control           chr6         31070275         31074835         Control	chr5	56027372	56160869			
chr5         80285288         80383186         Chr6         1265616         126796341           chr5         134653706         134813494         Chr6         Chr6         134613494         Chr6           chr5         157005426         157095755         Chr6         Chr6         Chr6         Chr6         160026286         160228116         Chr6         Chr6         16022816         Chr6         Chr6         Chr6         10602105         10622676         Chr6         Chr6         10762201         10786801-10787000;10787101-10787200         MAK           chr6         10762201         10794088         10786801-10787000;10787101-10787200         MAK           chr6         1122311         18215201         Chr6         18122311         18215201         Chr6         Chr6         19174235         Chr6         Chr6         19174235         Chr6         Chr6         19174235         Chr6         Chr6         19174235         Chr6         Chr6         S1074035         Chr6	chr5	69077621	70328678			
chr5         126561616         126796341         Image: Chr5         Imag	chr5	80265268	80383186			
chr5         134653706         134818494         Image: chr5         Imag	chr5	126561616	126796341			
chr5         157005426         157095755         Iele           chr5         160096285         160228116         Iele         Iele           chr5         180401363         180451188         Iele         Iele           chr6         10602105         10622676         Iele         Iele           chr6         10752021         10794068         10786801-10787000;10787101-10787200         MAK           chr6         17299435         1768474         Iele         Iele           chr6         1812311         18215201         Iele         Iele           chr6         21572400         21701354         Iele         Iele           chr6         31070275         31074235         Iele         Iele           chr6         31070275         31074635         Iele         Iele           chr6         31218147         31222799         Iele         Iele           chr6         31285021         32270672         Iele         Iele         Iele           chr6         32255921         32270672         Iele         Iele         Iele           chr6         34590409         34823647         Iele         Iele         Iele           chr6         34590	chr5	134653706	134818494			
chr5         160096285         160228116         C           chr5         180401363         180451188         C         C           chr6         10602105         10622676         C         C           chr6         10762201         10794068         10786801-10787000;10787101-10787200         MAK           chr6         17299435         17688474         C         C           chr6         18122311         18215201         C         C           chr6         21572400         21701354         C         C           chr6         30512251         30542286         C         C           chr6         31070275         31074635         C         C           chr6         31218147         31222799         C         C         C           chr6         32255921         32270672         C         C         C           chr6         34590409         34823847         C         C         C           chr6         34590409         34823847         C         C         C           chr6         34590409         34823647         C         C         C           chr6         34590409         34823647 <td< td=""><td>chr5</td><td>157005426</td><td>157095755</td><td></td><td></td><td></td></td<>	chr5	157005426	157095755			
chr6       180401363       180451188	chr5	160096285	160228116			
chr6         10602105         10622676	chr5	180401363	180451188			
chr6         10762201         10784088         10786081-10787000;10787101-10787200         10786801-10787000;10787101-10787200         MAK           chr6         17299435         17688474              chr6         18122311         18215201              chr6         21572400         217701354              chr6         30512251         30542286               chr6         31070275         31074635                chr6         32255921         322270972                 chr6         34823647	chr6	10602105	10622676			
chr6       17299435       17688474	chr6	10762201	10794068	10786801-10787000;10787101-10787200	10786801-10787000;10787101-10787200	MAK
chr6       18122311       18215201       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       73020906       73640630	chr6	17299435	17688474			
chr6       215/2400       21701354	chr6	18122311	18215201			
chr6         30512251         30542286	chr6	21572400	21/01354			
Chr6         31070275         31074633	chr6	30512251	30542286			
Chr6         31286382         3159036         Chr6           chr6         32255921         32270672            chr6         34590409         34823647            chr6         42489126         42841567            chr6         73203906         73640630	chrG	310/02/5	31074035			
Chr6         31255921         32270672           chr6         34590409         34823647           chr6         42489126         42841567           chr6         73203906         73640630	chr6	31210147	31222799			
Chr6         34590409         3482647           chr6         42489126         42841567           chr6         73203906         73640630	chr6	31000002	31390030			
Chro         34389126         42489126         42841567           chr6         73203906         73640630	chr6	34500400	3/8236/7			
Chro 14-00120 1201001 Chro 73203906 73840630	chr6	42489126	42841567			
	chr6	73203906	73640630			
	chr6	87541110	87552228			
	chr6	87584076	87800145			
Chr6 88937618 89113196	chr6	88937618	89113196			
Chr6 106646335 106641569	chr6	106646935	106691569			
Chr6 106861004 107302026	chr6	106861004	107302026			
Chr6 110697636 111057269	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		
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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			120250
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	0.705555742	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 (<= 3kb; 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.

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