- **Supplementary Information**

Supplementary Materials and Methods

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1. Supplementary Materials and Methods

Establishment and preparation of cell cultures for DNA extraction, and mitochondrial and cell function assays

Biopsies originating from the main tumor mass were verified histologically as GBM and transferred to a sterile petri dish; rinsed with Hank’s Balanced Salt Solution and disaggregated to form a uniform cell suspension. This suspension was then transferred into a tissue culture flask containing Dulbecco's Modified Eagle Medium (DMEM) + 20% fetal bovine serum (FBS) for 7 days until cells attached. After establishment, all cell cultures were grown in DMEM + 10% FBS, with the exception of the control cell line which was grown in astrocyte growth medium + 10% human serum, in a humidified atmosphere at 37°C and 5% CO_2 and 25% O_2 until 80% confluent. The cells were then detached using trypsin, mixed with growth medium and centrifuged at 200 × g to either form a pellet for DNA extraction, or processing for mitochondrial and cell function assays.

Table S1A Details of cell lines derived from primary adult glioblastoma (unless otherwise indicated) screened for F18L and used in the mitochondrial and cellular functional studies*.

Cell line							Patient						
Sample ID	**Source**	**IDH1 (R132) status**	**IDH2 (R132) status**	**MGMT status**	**F18L**	**F18L screening method**	**Karnofsky Score**	**Ki67 (%)**	**Resection Chemotherapy Radiotherapy**	**Age at diagnosis**	**Time to death (months)**	**Ref**	**Genbank Accession No.**
SC1800**	Cerebral cortex, non-neoplastic astrocyte	Negative	Negative	Unmethylated	No	Total DNA + long PCR + mtDNA-seq	n/a	n/a	n/a	n/a	n/a	Lloyd et al. 2015	KJ735675.1
UP-029		Negative	Negative	Methylated	No	Total DNA + long PCR + mtDNA-seq	n.i.a	n.i.a	n.i.a	66	n.i.a	Lloyd et al. 2015	KJ735668.1
SNB-19***		Negative	Negative	Methylated	No	Total DNA + long PCR + mtDNA-seq	n.i.a	n.i.a	n.i.a	n.i.a	n.i.a	Lloyd et al. 2015	KJ735677.1
SEBTA-023		Negative	n.i.a	n.i.a****	Yes	Total DNA + long PCR + mtDNA-seq	n.i.a	30%	Stupp protocol	70	33.33	This study	MN150712
UP-007		Negative	Negative	Methylated	Yes	Total DNA + long PCR + mtDNA-seq	n.i.a	n.i.a	n.i.a	71	n.i.a	This study	MN150713

* Passages used for the functional studies: SC1800 (6), UP-029 (19-28), SNB-19 (n.i.a.), SEBTA-023 (11-20), and UP-007 (26)

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***DSMZ German Collection of Microorganisms and Cell Cultures

****Original tumour was methylated

n.i.a No information available

UP- and SEBTA- prefixes denote cell cultures were obtained in house from biopsies derived from Kings College Hospital (London, UK). All cells were confirmed to be mycoplasma-free and authenticated by short-term tandem repeat-PCR and capillary electrophoresis using an Applied Biosystems 3130xl Genetic Analyzer (profiles available on request).

Table S1B Details of TCGA glioblastoma patient and tissues used in the F18L survival studies.

PATIENT BARCODE	Subtype	sil_width	CORE_sample	GENDER	VITALSTATUS	KarnScore	AgeAtFirstDiagnosis	Survival (days)	MGMT_methylated	% Tumor Nuclei	% Necrosis	F18L
TCGA-02-0003	Proneural	0.21	CORE	MALE	DEAD	100.00	50.22	144.00	Unmethlyated	100.00	12.50	No
TCGA-02-0033	Mesenchymal	0.44	CORE	MALE	DEAD	100.00	54.95	86.00	Unmethlyated	100.00	15.00	No
TCGA-02-0047	Proneural	0.13	CORE	MALE	DEAD	90.00	78.74	448.00	Unmethlyated	92.50	5.00	Yes
TCGA-02-0055	Mesenchymal	0.42	CORE	FEMALE	DEAD	90.00	62.42	76.00	Unmethlyated	95.00	15.00	Yes
TCGA-06-0122	Mesenchymal	0.15	CORE	FEMALE	DEAD	70.00	84.80	181.00	Unmethlyated	100.00	20.00	No
TCGA-06-0124	Mesenchymal	0.26	CORE	MALE	DEAD	70.00	67.33	620.00	Methylated	100.00	10.00	Yes
TCGA-06-0125	Classical	0.23	CORE	FEMALE	DEAD	70.00	63.91	1448.00	Unmethlyated	100.00	5.00	No
TCGA-06-0126	Classical	0.10	CORE	MALE	DEAD	70.00	86.59	211.00	Unmethlyated	100.00	0.00	No
TCGA-06-0128	Proneural	0.15	CORE	MALE	DEAD	90.00	66.30	691.00	Unmethlyated	97.50	7.50	No
TCGA-06-0129	Proneural	0.27	CORE	MALE	DEAD	100.00	30.89	1024.00	Unmethlyated	97.50	0.00	No
TCGA-06-0130	Mesenchymal	0.39	CORE	MALE	DEAD	90.00	54.34	358.00	Unmethlyated	80.00	5.00	No
TCGA-06-0132	Neural	0.18	CORE	MALE	ALIVE	NA	49.62	295.00	Unmethlyated	97.50	2.50	No
TCGA-06-0137	Classical	0.22	CORE	FEMALE	DEAD	90.00	63.72	812.00	Unmethlyated	92.50	2.50	No
TCGA-06-0138	Neural	0.14	CORE	MALE	DEAD	90.00	43.08	737.00	Unmethlyated	97.50	2.50	No
TCGA-06-0139	Mesenchymal	0.41	CORE	MALE	DEAD	60.00	40.33	362.00	Unmethlyated	95.00	0.00	Yes
TCGA-06-0145	Classical	0.21	CORE	FEMALE	DEAD	NA	53.83	71.00	Methylated	100.00	5.00	No
TCGA-06-0152	Mesenchymal	0.05	CORE	MALE	DEAD	NA	68.03	373.00	Unmethlyated	97.00	36.50	Yes
TCGA-06-0154	Mesenchymal	0.21	CORE	MALE	DEAD	100.00	54.81	424.00	Unmethlyated	95.00	35.00	No
TCGA-06-0156	Proneural	0.15	CORE	MALE	DEAD	NA	57.39	148.00	Unmethlyated	97.50	5.00	No
TCGA-06-0157	Classical	-0.02	NO	FEMALE	DEAD	50.00	63.32	97.00	Unmethlyated	97.50	5.00	No
TCGA-06-0158	Classical	-0.03	NO	MALE	DEAD	80.00	73.53	161.00	Unmethlyated	97.50	2.50	Yes
TCGA-06-0166	Proneural	0.17	CORE	MALE	DEAD	NA	51.75	178.00	Unmethlyated	92.50	30.00	No
TCGA-06-0168	Mesenchymal	-0.04	NO	FEMALE	DEAD	100.00	59.62	598.00	Unmethlyated	92.50	30.00	No
TCGA-06-0171	Neural	0.12	CORE	MALE	DEAD	100.00	65.94	399.00	Unmethlyated	92.50	5.00	No
TCGA-06-0173	Neural	0.08	CORE	FEMALE	DEAD	NA	72.69	136.00	Methylated	95.00	17.50	Yes
TCGA-06-0174	Proneural	0.32	CORE	MALE	DEAD	80.00	54.28	98.00	Methylated	97.50	10.00	No
TCGA-06-0176	Mesenchymal	0.32	CORE	MALE	ALIVE	90.00	34.98	954.00	Unmethlyated	92.50	35.00	No
TCGA-06-0178	Neural	-0.06	NO	MALE	ALIVE	NA	39.03	1168.00	Unmethlyated	100.00	0.00	No
TCGA-06-0184	Mesenchymal	0.11	CORE	MALE	ALIVE	90.00	63.84	907.00	Unmethlyated	95.00	5.00	No
TCGA-06-0185	Neural	0.09	CORE	MALE	ALIVE	100.00	54.55	846.00	Methylated	100.00	5.00	No
TCGA-06-0187	Classical	0.07	CORE	MALE	ALIVE	70.00	69.32	414.00	Methylated	100.00	10.00	No

TCGA-06-0188	Neural	-0.10	NO	MALE	ALIVE	100.00	71.40	389.00	Unmethlyated	95.00	10.00	No
TCGA-06-0189	Mesenchymal	0.35	CORE	MALE	DEAD	NA	55.57	468.00	Unmethlyated	100.00	32.50	Yes
TCGA-06-0190	Mesenchymal	0.35	CORE	MALE	DEAD	80.00	62.52	317.00	Unmethlyated	100.00	40.00	No
TCGA-06-0195	Neural	0.09	CORE	MALE	DEAD	100.00	63.33	225.00	Methylated	90.00	0.00	No
TCGA-06-0210	Mesenchymal	0.21	CORE	FEMALE	DEAD	NA	72.83	225.00	Unmethlyated	92.50	10.00	Yes
TCGA-06-0211	Classical	0.15	CORE	MALE	DEAD	100.00	47.95	360.00	Unmethlyated	92.50	0.00	No
TCGA-06-0214	Neural	0.16	CORE	MALE	DEAD	40.00	66.22	457.00	Methylated	92.50	7.50	No
TCGA-06-0219	Neural	0.27	CORE	MALE	DEAD	40.00	67.07	15.00	Unmethlyated	100.00	12.50	No
TCGA-06-0221	Neural	0.05	CORE	MALE	DEAD	40.00	31.03	603.00	Methylated	90.00	5.00	Yes
TCGA-06-0237	Neural	0.20	CORE	FEMALE	DEAD	40.00	75.94	415.00	Unmethlyated	100.00	5.00	No
TCGA-06-0238	Proneural	0.11	CORE	MALE	DEAD	NA	46.65	405.00	Unmethlyated	100.00	5.00	No
TCGA-06-0241	Proneural	0.31	CORE	FEMALE	ALIVE	40.00	65.99	198.00	Methylated	100.00	7.50	No
TCGA-06-0644	Mesenchymal	0.34	CORE	MALE	ALIVE	80.00	71.86	122.00	Unmethlyated	95.00	20.00	No
TCGA-06-0645	Mesenchymal	0.32	CORE	FEMALE	ALIVE	NA	55.99	98.00	Methylated	97.50	15.00	No
TCGA-06-0646	Proneural	0.05	CORE	MALE	DEAD	90.00	60.98	175.00	Unmethlyated	95.00	7.50	No
TCGA-06-0648	Proneural	0.36	CORE	MALE	ALIVE	90.00	77.97	77.00	Methylated	100.00	10.00	No
TCGA-08-0386	Neural	0.02	CORE	MALE	DEAD	90.00	74.07	548.00	Methylated	97.50	7.50	No
TCGA-12-0615	Classical	-0.03	NO	FEMALE	DEAD	70.00	78.26	467.00	Unmethlyated	100.00	25.00	Yes
TCGA-12-0616	Proneural	0.22	CORE	FEMALE	DEAD	100.00	36.83	448.00	Unmethlyated	100.00	27.50	No
TCGA-12-0618	Proneural	0.32	CORE	MALE	DEAD	70.00	49.48	395.00	Unmethlyated	100.00	6.50	No
TCGA-12-0619	Mesenchymal	0.27	CORE	MALE	DEAD	90.00	60.01	1062.00	Methylated	100.00	7.50	No

The TCGA glioblastoma samples were originally classified into subtypes by Verhaak et al. 2010. From the original study that included 202 samples, only adult patients with primary GBM where we could also determine F18L status were included.

Table S2A Details of differences between F18L positive and negative cells analysed by ANOVA using a regression approach.

Test of SS Whole Model vs. SS Residual (Spreadsheet of adult cells only)										
	Multiple - R	**Multiple - R²**	**Adjusted - R²**	**SS - Model**	**df - Model**	**MS - Model**	**SS - Residual**	**df - Residual**	**MS - Residual**	**F**	**p**
CI activity/CS	0.51	0.26	0.24	10.84	1.00	10.84	30.79	34.00	0.91	11.98	0.001472
CII activity/CS	0.51	0.26	0.23	10.68	1.00	10.68	31.07	34.00	0.91	11.69	0.001652
CII+III activity/CS	0.69	0.47	0.45	19.91	1.00	19.91	22.44	34.00	0.66	30.17	0.000004
CIV activity/CS	0.46	0.21	0.19	5.89	1.00	5.89	22.08	34.00	0.65	9.07	0.004886

Table S2B Details of the discriminant function analysis.

Point	Given group	Classification	Jackknifed
3	UP007	UP007	UP007
4	UP007	UP029	UP029
5	UP007	UP007	UP007
6	UP029	UP029	UP029
7	UP029	UP029	UP029
8	UP029	UP029	UP029
9	Sebta 023	Sebta 023	Sebta 023
10	Sebta 023	Sebta 023	Sebta 023
11	Sebta 023	Sebta 023	Sebta 023
12	SNB19	SNB19	SNB19
13	SNB19	SNB19	SNB19
14	SNB19	SNB19	SNB19
15	UP007	UP007	UP007
16	UP007	UP007	UP007
17	UP007	UP007	UP007
18	UP029	UP029	UP029
19	UP029	UP007	UP007
20	UP029	UP007	UP007
21	Sebta 023	Sebta 023	Sebta 023
22	Sebta 023	Sebta 023	Sebta 023
23	Sebta 023	Sebta 023	Sebta 023
24	SNB19	SNB19	SNB19
25	SNB19	SNB19	UP007
26	SNB19	SNB19	SNB19
27	UP007	UP007	UP007
28	UP007	UP007	UP007
29	UP007	UP007	UP007
30	UP029	UP029	SNB19
31	UP029	UP029	UP029
32	UP029	UP029	UP029
33	Sebta 023	Sebta 023	Sebta 023

Green = correctly classified

Red = incorrectly classified

34	Sebta 023	Sebta 023	Sebta 023
35	Sebta 023	Sebta 023	Sebta 023
36	SNB19	SNB19	SNB19
37	SNB19	SNB19	SNB19
38	SNB19	SNB19	SNB19

Table S2C Details of PCA approach looking at correlations between individual MRC activities and CoQ10 levels.

	CI/CS activity	**CII/CS activity**	**CIV/CS activity**	**CII+III/CS activity**	**CoQ10/CS**
CI/CS activity	1	0.1924	0.0034	-0.3477	0.7763
	p= ---	p=.549	p=.992	p=.268	p=.003
CII/CS activity	0.1924	1	0.5799	0.5382	0.0552
	p=.549	p= ---	p=.048	p=.071	p=.865
CIV/CS activity	0.0034	0.5799	1	0.642	-0.1498
	p=.992	p=.048	p= ---	p=.024	p=.642
CII+III/CS activity:	-0.3477	0.5382	0.642	1	-0.5815
	p=.268	p=.071	p=.024	p= ---	p=.047
CoQ10/CS	0.7763	0.0552	-0.1498	-0.5815	1
	p=.003	p=.865	p=.642	p=.047	p= ---

Values are expressed as correlation coefficients (r values) and these are associated and presented with their relevant significances (p values). Significant correlations are highlighted in red.

Table S3 Details of the oxidative defence genes tested for a role in clomipramine sensitivity.

Gene	**Function in oxidative stress defense**	**Localisation**
Prx1	Thioredoxin peroxidase	Mito
Ahp1	Thioredoxin peroxidase	Cyto
Tsa1	Thioredoxin peroxidase	Cyto
Tsa2	Thioredoxin peroxidase	Cyto
Dot5	Thioredoxin peroxidase	nucleus
Ccp1	Cytochrome c peroxidase	MIS
Aim32	Thioredoxin like protein	mito
Gtt1	Glutathione peroxidase	ER
Grx1	Glutaredoxin	cyto/nucleus
Grx2	Glutaredoxin	cyto/mito
Fms1	Polyamine oxidase	cyto
Yhb1	Nitric oxide oxidoreductase	cyto/ mito
Mcr1	Cytochrome-b5 reductase	MIS
Cta1	Catalase	mito
Ctt1	Catalase	cyto
Sod1	Superoxide dismutase 1	cyto/mito
Sod2	Superoxide dismutase 2	mito