

Table S1. Single tandem repeat genotyping of GIN-28, GCE-28, GIN-31 and GCE-31 patient-derived primary lines isolated from the GBM 5ALA invasive edge (GIN) and contrast enhanced core (GCE). DNA was isolated from each sample and genetic characteristics determined by PCR-single-locus-technology, utilizing 21 independent PCR-systems. The GIN-28 line compared across two passages (p11 and p33), showed identical STR genotypes, with 20/21 DNA systems matching the STR genotype from primary invasive margin GBM tissue (T28.3) from which the cells were derived. GIN-31 p11 cells fully retain the genotype from primary invasive margin GBM tissue (T31.5) from which the cells were derived; GIN-31 p33 retains a matched STR genotype in 13/21 loci, with amplifications acquired in culture likely a result of the 22 passages between this sample and early passage. The GCE-28 line compared across two passages (p16 and p19), showed identical STR genotypes, with 20/21 DNA systems matching the STR genotype from primary invasive margin GBM tissue (T28.3) from which the cells were derived. The GCE-31 line compared across two passages (p7 and p16), showed identical STR genotypes, and fully retains the genotype from primary invasive margin GBM tissue (T31.5) from which the cells were derived. Collectively these results confirm that the cell lines utilized in this study have not been cross-contaminated with any other cell line and the primary lines derived from the GBM invasive margin and core regions, broadly retain the genotype of the tumor. Materials & Methods - Cell line authentication of the, GIN-28, GCE-28, GIN-31 and GCE-31 patient-derived primary lines were determined by PCR-single-locus-technology, utilizing 21 independent PCR-systems (Eurofins, Germany).

DNA-System	DNA-criteria T28.2 CL181019_025	DNA-criteria GIN-28 p11 CL18019_021	DNA-criteria GIN-28 p33 CL18019_022	DNA-criteria GCE-28 p16 CL18019_023	DNA-criteria GIN-28 p19 CL18019_024	DNA-criteria T31.5 CL18019_030	DNA-criteria GIN-31 p11 CL18019_026	DNA-criteria GIN-31 p31 CL18019_027	DNA-criteria GCE-31 p7 CL18019_028	DNA-criteria GCE-31 p16 CL18019_029
AM	X,Y	X,Y	X,Y	X,Y	X,Y	X,X	X,X	X,X	X,X	X,X
D3S1358	14,17	14,17	14,17	14,17	14,17	16,18	16,18	16,18	16,18	16,18
D1S1656	12,16	12,16	12,16	12,16	12,16	12,15	12,15	12,15	12,15	12,15
D6S1043	11,13	11,13	11,13	11,13	11,13	12,18	12,18	12,18	12,18	12,18
D13S317	11,12	11,12	11,12	11,12	11,12	13,13	11,13	11,13	11,13	11,13
Penta E	7,17	7,17	7,17	7,17	7,17	7,12	7,12	7,12	7,12	7,12
D16S539	9,12	9,12	9,12	9,12	9,12	10,11	10,11	10,11	10,11	10,11
D18S51	14,17	14,17	14,17	14,17	14,17	17,18	17,18	16,17,18	17,18	17,18
D2S1338	19,23	19,23	19,23	19,23	19,23	19,25	19,25	11,19,25	19,25	19,25
CSF1PO	11,13	11,13	11,13	11,13	11,13	11,12	11,12	11,12	11,12	11,12
Penta D	12,13,14	12,14	12,14	12,14	12,14	11,12	11,12	11,12	11,12	11,12
TH01	6,9,3	6,9,3	6,9,3	6,9,3	6,9,3	6,9	6,9	6,9	6,9	6,9
vWA	14,15	14,15	14,15	14,15	14,15	14,18	14,18	14,15,18,21	14,18	14,18
D21S11	27,33	27,33	27,33	27,33	27,33	29,29	29,29	29,29	29,29	29,29
D7S820	8,10	8,10	8,10	8,10	8,10	7,10	7,10	7,10	7,10	7,10
D5S818	11,12	11,12	11,12	11,12	11,12	11,12	11,12	11.1,12	11,12	11,12
TPOX	8,11	8,11	8,11	8,11	8,11	9,9	9,9	9,9	9,9	9,9
D8S1179	10,14	10,14	10,14	10,14	10,14	11,13	11,13	11,13,14.1	11,13	11,13
D12S391	20,21	20,21	20,21	20,21	20,21	23,23	17,23	16,17,22.3,23	17,23	17,23
D19S433	13,14	14,14	14,14	14,14	14,14	12,?	12,15	12,13.1,15	12,15	12,15
FGA	23,25	23,25	23,25	23,25	23,25	22,26	22,26	19.3,22,26	22,26	22,26

Table S2. Example of a reaction of interest: 'HMR_6436'. This reaction along with 'HMR_6453' are related to *ACSF2* (ENSG00000167107), a gene indirectly targeted by afuresertib. More information about the metabolites can be found at <https://metabolicatlas.org>.

Metabolite symbol	Metabolite name	Comment
m01096m[m]	5-carboxy-alpha-chromanol [Mitochondria]	Exclusively produced by 'HMR_6453'. Exclusively consumed by ' HMR_6436 '.
m01371m[m]	ATP [Mitochondria]	-
m01597m[m]	CoA [Mitochondria]	-
m02040m[m]	H2O [Mitochondria]	-
m02552m[m]	NAD+ [Mitochondria]	-
m02630m[m]	O2 [Mitochondria]	-
→		
m00766m[m]	3-carboxy-alpha-chromanol [Mitochondria]	Exclusively produced by ' HMR_6436 '. Exclusively consumed by 'HMR_6438' (transport to cytosol).
m01334m[m]	AMP [Mitochondria]	-
m02039m[m]	H+ [Mitochondria]	-
m02041m[m]	H2O2 [Mitochondria]	-
m02553m[m]	NADH [Mitochondria]	-
m02759m[m]	PPi [Mitochondria]	-
m02774m[m]	propanoyl-CoA [Mitochondria]	-