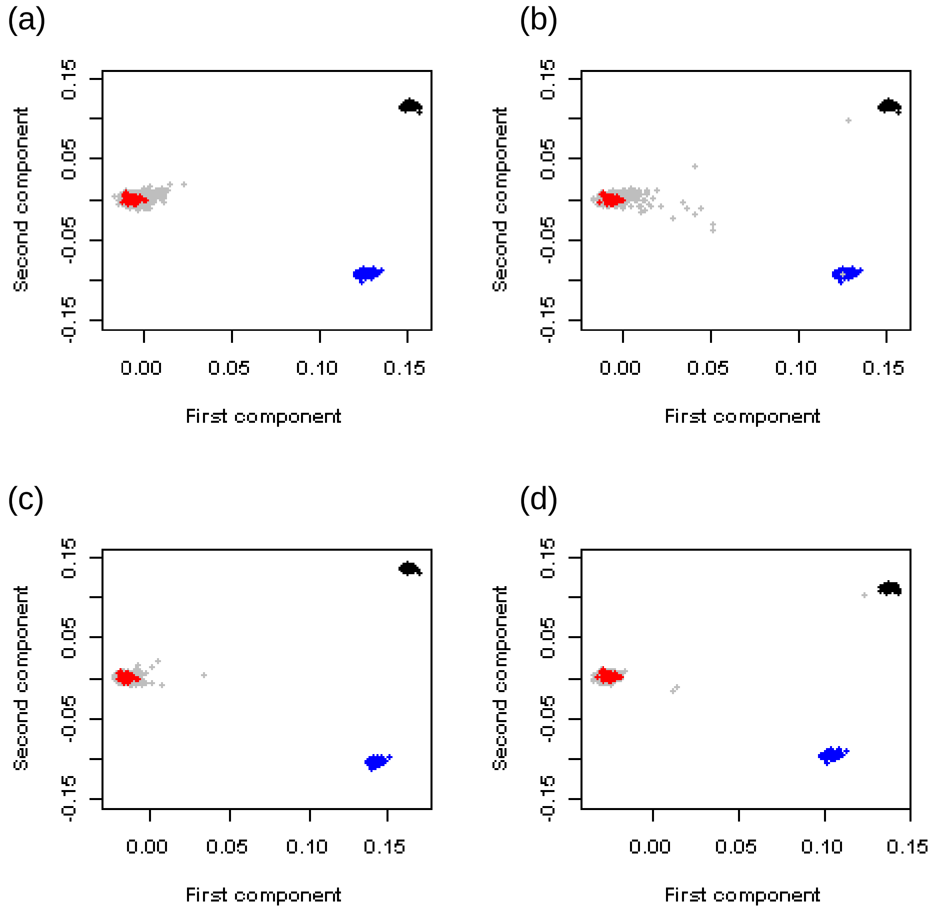
Genome-wide association study identifies five susceptibility loci for glioma

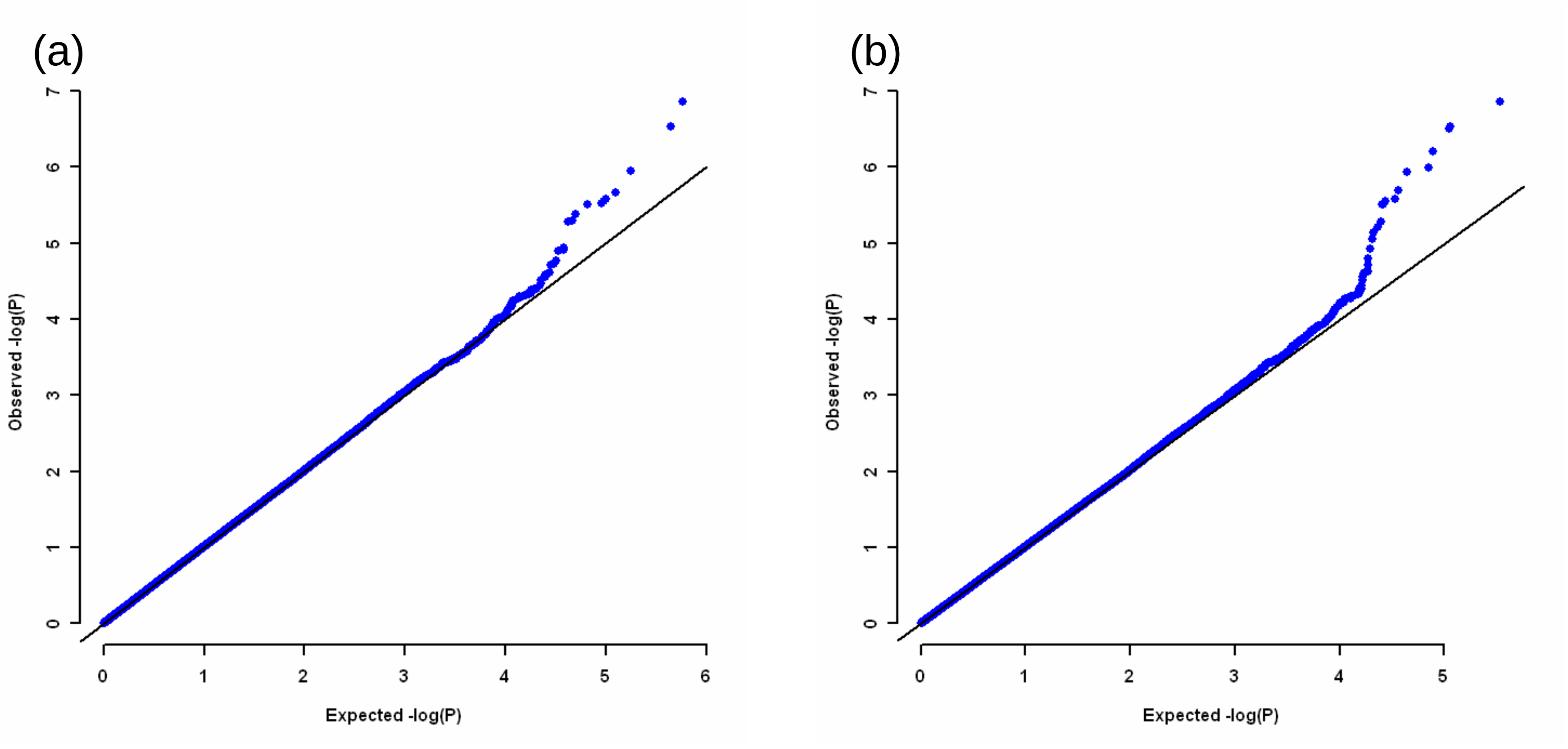
Sanjay Shete[1]*, Fay J Hosking[2]*, Lindsay B Robertson[2], Sara E Dobbins[2], Marc Sanson[3], Beatrice Malmer[4], Matthias Simon[5], Yannick Marie[3], Blandine Boisselier[3], Jean-Yves Delattre[3], Khe Hoang-Xuan[3], Soufiane El Hallani[3], Ahmed Idbaih[3], Diana Zelenika[6], Ulrika Andersson[4], Roger Henriksson[4], A Tommy Bergenheim[7], Maria Feychting[8], Stefan Lönn[9], Anders Ahlbom[7], Johannes Schramm[5], Michael Linnebank[10], Kari Hemminki[11], Rajiv Kumar[11], Sarah J Hepworth[12], Amy Price[2], Georgina Armstrong[1], Yanhong Liu[1], Xiangjun Gu[1], Robert Yu[1], Ching Lau[15], Minouk Schoemaker[14], Kenneth Muir[13], Anthony Swerdlow[14], Mark Lathrop[6,16], Melissa Bondy[1¥], Richard S Houlston[2¥]

1. Department of Epidemiology, University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA.
2. Section of Cancer Genetics, Institute of Cancer Research, Sutton, Surrey. UK.
3. Service de Neurologie Mazarin et INSERM U 711, Hôpital de la Salpêtrière 47, Bd de l'Hôpital 75 013 Paris. France.
4. Department of Radiation Sciences, Oncology, Umeå University, Sweden.
5. Neurochirurgische Universitätsklinik, Sigmund-Freud-Str. 25, 53105 Bonn, Germany.
6. Centre National de Génotypage, IG/CEA, 2 rue Gaston Crémieux CP 5721, 91057 Evry Cedex, France.
7. Department of Clinical Neuroscience, Umeå University, Sweden.
8. Institute of Environmental Medicine, Karolinska Institutet, Sweden.
9. Department of Medical Epidemiology and Biostatistics Karolinska Institutet, Sweden
10. Department of Neurology, University Hospital Zurich, Frauenklinikstrasse 26, CH-8091 Zurich, Switzerland.
11. Division of Molecular Genetic Epidemiology, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 580, D-69120 Heidelberg, Germany.
12. Centre for Epidemiology and Biostatistics, Faculty of Medicine and Health, University of Leeds, UK.
13. Division of Epidemiology and Public Health, University of Nottingham Medical School, Queen's Medical Centre, Nottingham, UK.
14. Section of Epidemiology, Institute of Cancer Research, Sutton, UK.
15. Texas Children's Cancer Center, Baylor College of Medicine, Houston, Texas 77030, USA.
16. Foundation Jean Dausett-CEPH, 27 Rue Julliette Dodu, 75010 Paris, France

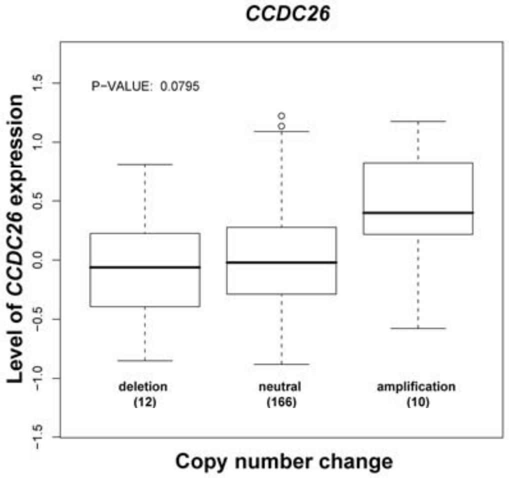
*equal status at this position
¥Corresponding authors

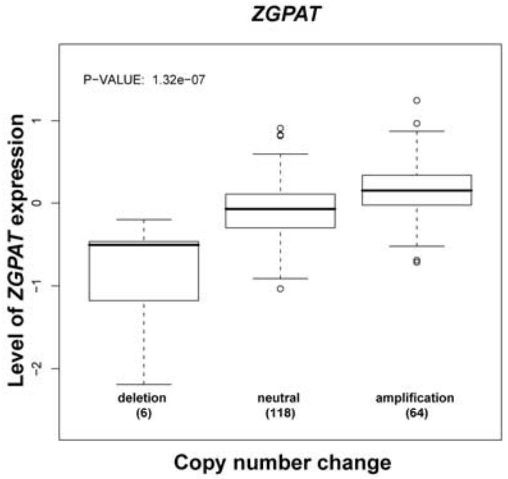


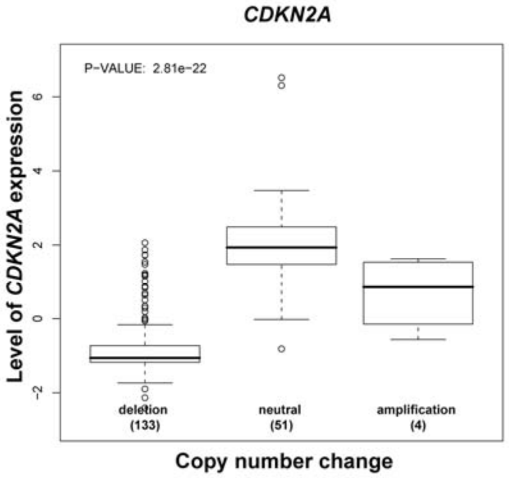
Supplementary Figure 1a: **Identification of individuals in the GWA scan of non-European ancestry.** The first two principal components of the analysis were plotted. HapMap CEU individuals are plotted in red; CHB+JPT are plotted in blue; YRI individuals are plotted in black; individuals in the GWA-UK and GWA-US are plotted in grey. GWA-US controls are plotted in (a), cases in (b); GWA-UK controls are plotted in (c) and cases in (d).

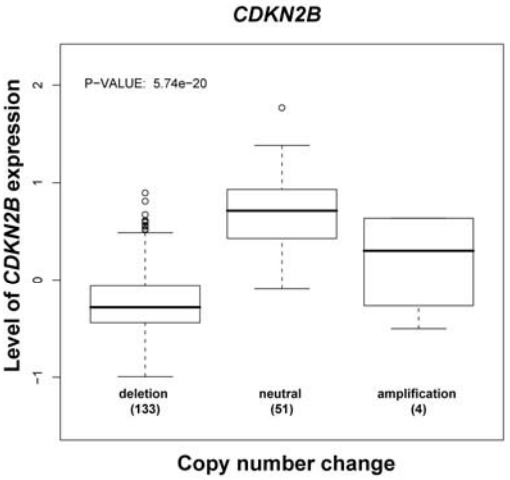


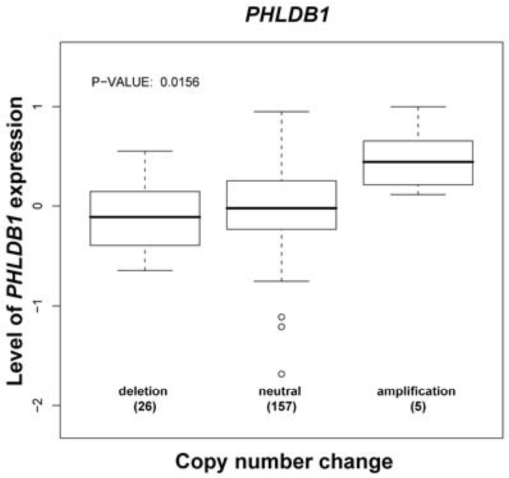
Supplementary Figure 1b: Quantile-quantile (Q-Q) plot of Cochran-Armitage test for trend for the two GWA studies. Results from UK-GWA are plotted in (a) and those from the US-GWA in (b). The black line represents the null hypothesis of no true association.

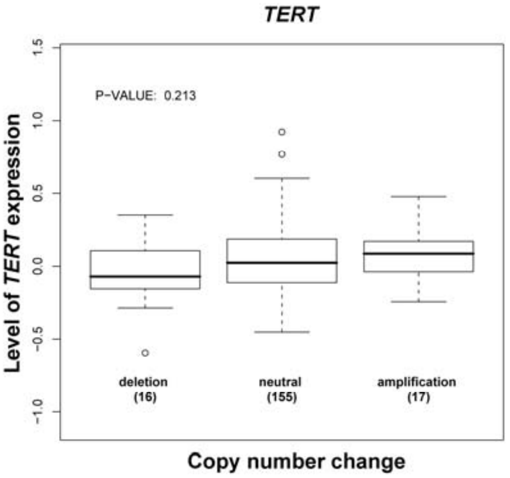

CCDC26
P−VALUE: 0.0795
Level of CCDC26 expression
1.5
1.0
0.5
0.0
−0.5
−1.0
−1.5
deletion
(12)
neutral
(166)
amplification
(10)
Copy number change

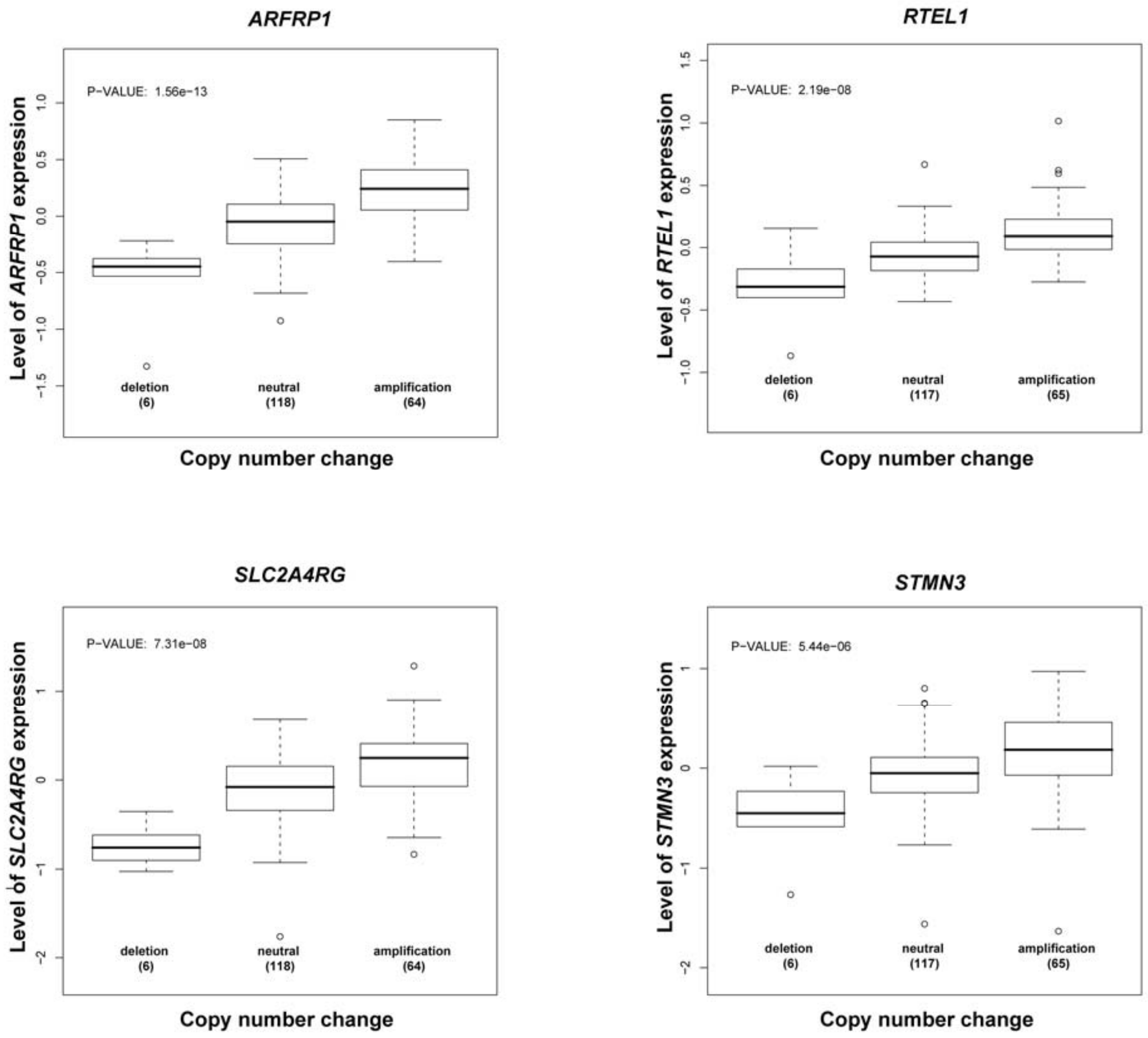

ZGPAT
P−VALUE: 1.32e−07
Level of ZGPAT expression
1
0
−1
−2
deletion
(6)
neutral
(118)
amplification
(64)
Copy number change


CDKN2A
P−VALUE: 2.81e−22
Level of CDKN2A expression
6
4
2
0
−2
deletion
(133)
neutral
(51)
amplification
(4)
Copy number change

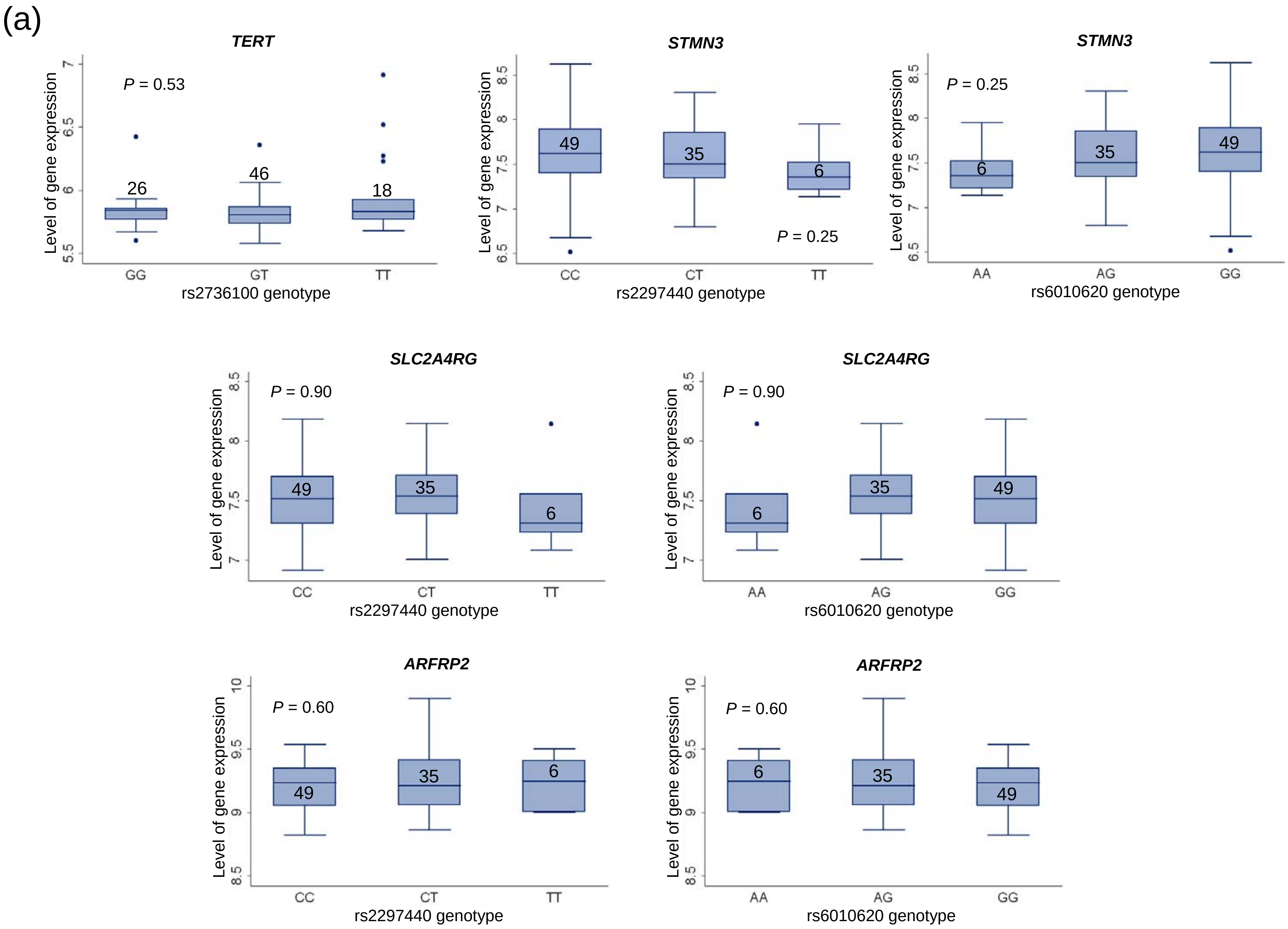

CDKN2B
P−VALUE: 5.74e−20
Level of CDKN2B expression
2
1
0
−1
deletion
(133)
neutral
(51)
amplification
(4)
Copy number change

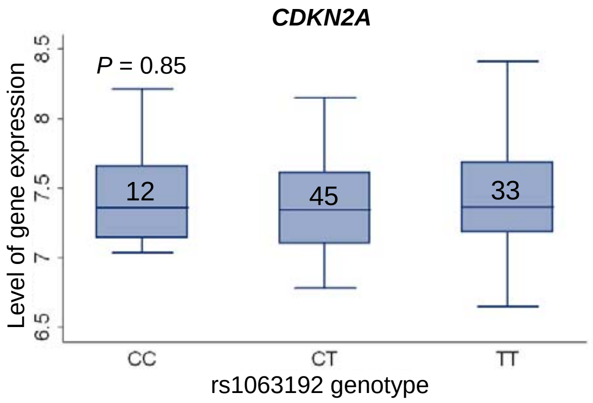

PHLDB1
P−VALUE: 0.0156
Level of PHLDB1 expression
1
0
−1
−2
deletion
(26)
neutral
(157)
amplification
(5)
Copy number change

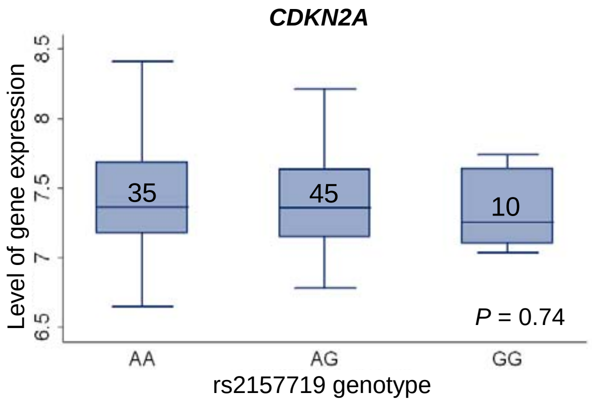

TERT
P−VALUE: 0.213
Level of TERT expression
1.5
1.0
0.5
0.0
−0.5
−1.0
deletion
(16)
neutral
(155)
amplification
(17)
Copy number change

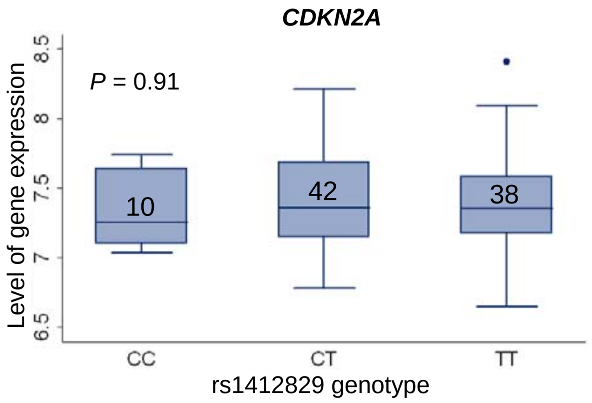


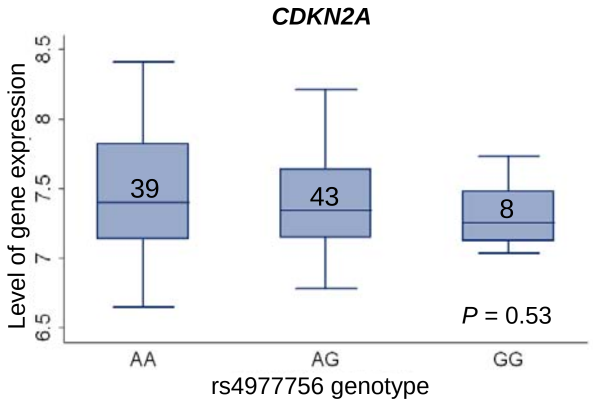
Supplementary Figure 2a: 5p15.33 (*TERT*), 8q24.21 (*CCDC26*), 9p21 (*CDKN2A, CDKN2B*), 11q23.3 (*PHLDB1*) and 20q13.33 (*RTEL1, ARFRP1, STMN3, SLC2A4RG, ZGPAT*) copy number variation (CNV) and mRNA expression in glioma. Plots show mRNA expression stratified by CNV status based on analysis of 188 glioblastoma multiforme (GBM) tumors. Expression data was derived from the MSKCC Cancer Genomics Data Portal (http://cbio.mskcc.org/cancergenomics-dataportal/). MSKCC expression data was generated by combining GBM expression data from the The Cancer Genome Atlas. The bioconductor module CGHcall was used to determine CNV status from Agilent human genome CGH microarray data taken from TCGA data portal. It should be noted that rates of amplification and deletion for a set of randomly selected probes are 9.9% and 13.4% respectively in the tumors. Differences in the distribution of expression by SNP genotype were compared using a Wilcoxon-type test.

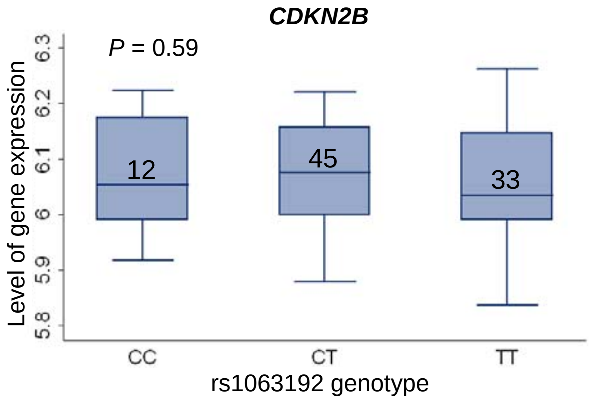

(a)
TERT
P = 0.53
26
46
18
GG
GT
TT
rs2736100 genotype
Level of gene expression
5.5
6
6.5
7
STMN3
49
35
6
P = 0.25
CC
CT
TT
rs2297440 genotype
Level of gene expression
6.5
7
7.5
8
8.5
STMN3
P = 0.25
6
35
49
AA
AG
GG
rs6010620 genotype
Level of gene expression
6.5
7
7.5
8
8.5
SLC2A4RG
P = 0.90
49
35
6
CC
CT
TT
rs2297440 genotype
Level of gene expression
7
7.5
8
8.5
SLC2A4RG
P = 0.90
6
35
49
AA
AG
GG
rs6010620 genotype
Level of gene expression
7
7.5
8
8.5
ARFRP2
P = 0.60
49
35
6
CC
CT
TT
rs2297440 genotype
Level of gene expression
8.5
9
9.5
10
ARFRP2
P = 0.60
6
35
49
AA
AG
GG
rs6010620 genotype
Level of gene expression
8.5
9
9.5
10

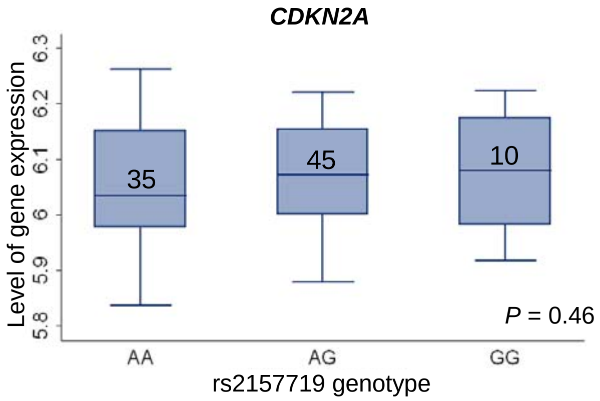

CDKN2A
P = 0.85
Level of gene expression
6.5
7
7.5
8
8.5
12
45
33
CC
CT
TT
rs1063192 genotype

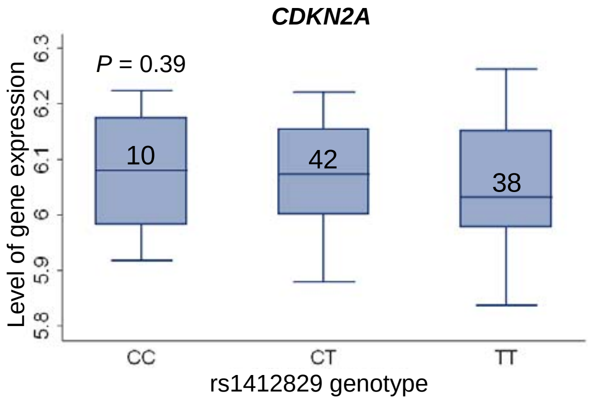

CDKN2A
Level of gene expression
6.5
7
7.5
8
8.5
35
45
10
P = 0.74
AA
AG
GG
rs2157719 genotype

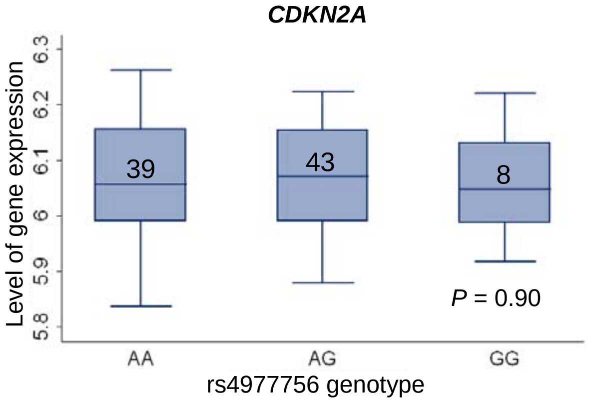

CDKN2A
P = 0.91
Level of gene expression
6.5
7
7.5
8
8.5
10
42
38
CC
CT
TT
rs1412829 genotype


CDKN2A
Level of gene expression
6.5
7
7.5
8
8.5
39
43
8
P = 0.53
AA
AG
GG
rs4977756 genotype

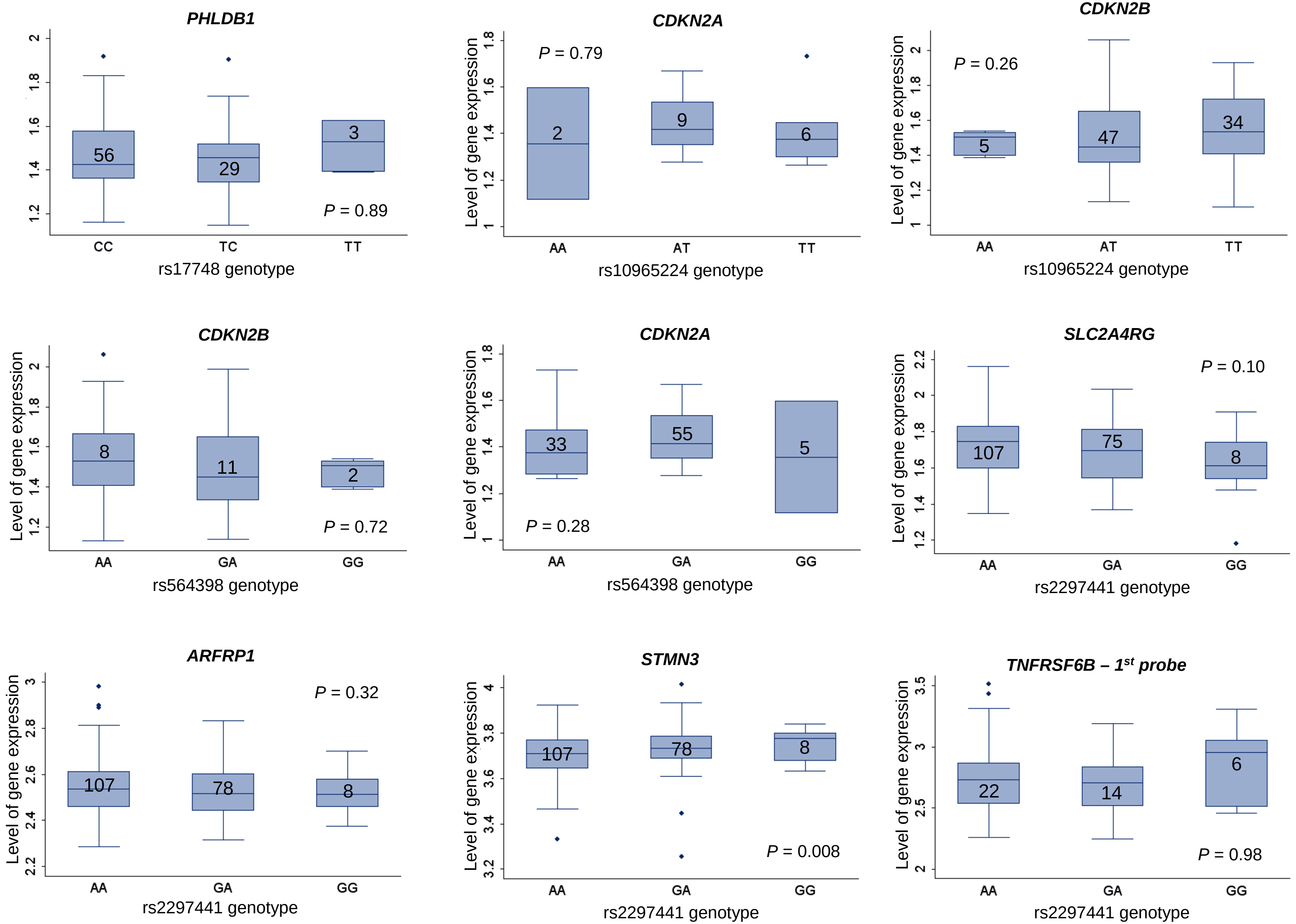

CDKN2B
P = 0.59
Level of gene expression
5.8
5.9
6
6.1
6.2
6.3
12
45
33
CC
CT
TT
rs1063192 genotype


CDKN2A
Level of gene expression
5.8
5.9
6
6.1
6.2
6.3
35
45
10
P = 0.46
AA
AG
GG
rs2157719 genotype

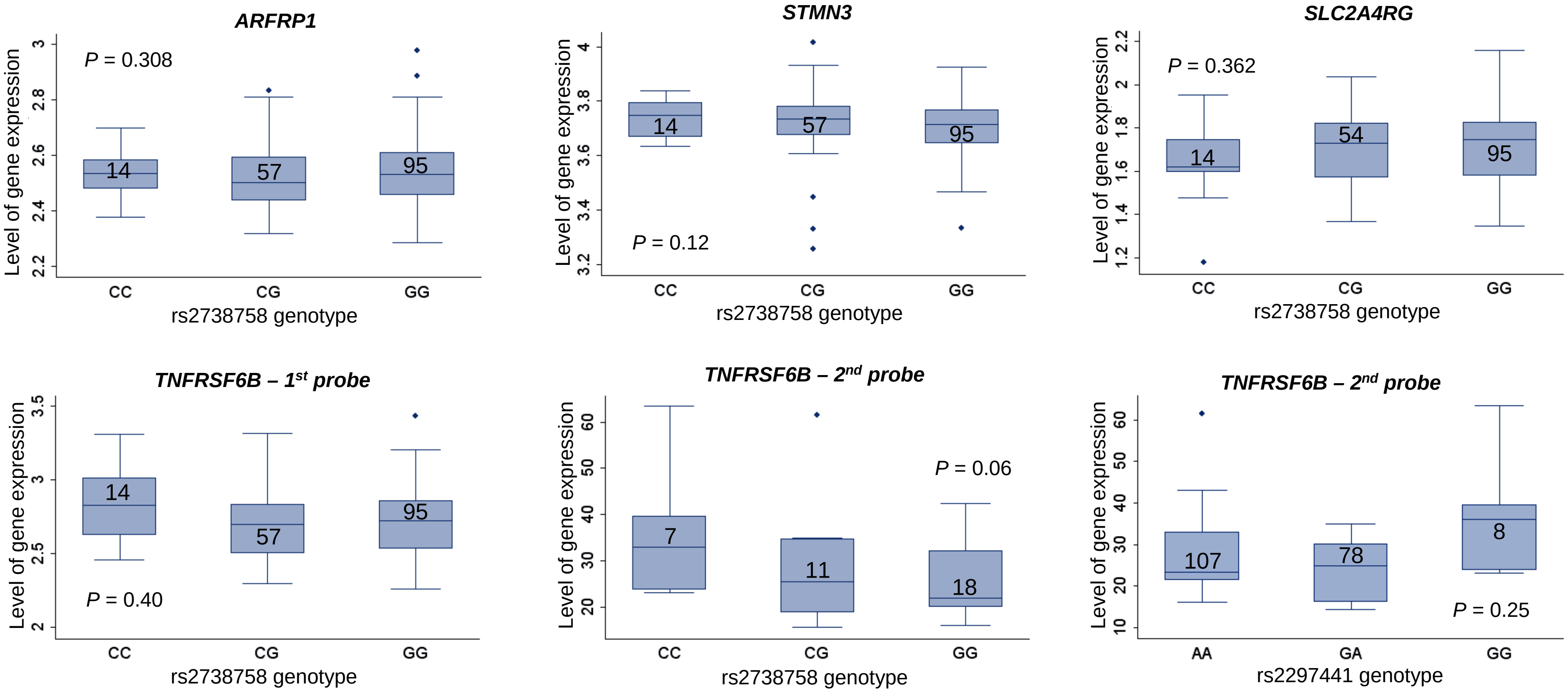

CDKN2A
P = 0.39
Level of gene expression
5.8
5.9
6
6.1
6.2
6.3
10
42
38
CC
CT
TT
rs1412829 genotype


CDKN2A
Level of gene expression
5.8
5.9
6
6.1
6.2
6.3
39
43
8
P = 0.90
AA
AG
GG
rs4977756 genotype

(b)



PHLDB1
1.2
1.4
1.6
1.8
2
56
29
3
P = 0.89
CC
TC
TT
rs17748 genotype
CDKN2A
Level of gene expression
1
1.2
1.4
1.6
1.8
P = 0.79
2
9
6
AA
AT
TT
rs10965224 genotype
CDKN2B
Level of gene expression
1
1.2
1.4
1.6
1.8
2
P = 0.26
5
47
34
AA
AT
TT
rs10965224 genotype
CDKN2B
Level of gene expression
1.2
1.4
1.6
1.8
2
8
11
2
P = 0.72
AA
GA
GG
rs564398 genotype
CDKN2A
Level of gene expression
1
1.2
1.4
1.6
1.8
33
55
5
P = 0.28
AA
GA
GG
rs564398 genotype
SLC2A4RG
Level of gene expression
1.2
1.4
1.6
1.8
2
2.2
P = 0.10
107
75
8
AA
GA
GG
rs2297441 genotype
ARFRP1
Level of gene expression
2.2
2.4
2.6
2.8
3
P = 0.32
107
78
8
AA
GA
GG
rs2297441 genotype
STMN3
Level of gene expression
3.2
3.4
3.6
3.8
4
107
78
8
P = 0.008
AA
GA
GG
rs2297441 genotype
TNFRSF6B – 1st probe
Level of gene expression
2
2.5
3
3.5
22
14
6
P = 0.98
AA
GA
GG
rs2297441 genotype



Supplementary Figure 2b: Relationship between (a) lymphocyte and (b) normal cortical mRNA expression levels of *PHLDB1* and rs17748 genotype, *CDKN2A/CDKN2B* and rs10965224/rs564398/rs1063192/rs2157719/rs1412829/rs49777656 genotype, *ARFRP1/STMN3/SLC2A4RG/TNFRSF6B* and rs2297441/rs2738758/rs2297440/rs6010620 genotype and *TERT* and rs2736100 genotype. Expression of *PHLDB1, CDKN2A, CDKN2B, ARFRP1, STMN3, SLC2A4RG* and *TNFRSF6B* in lymphocytes based on expression data from analysis of 90 Epstein-Barr virus–transformed lymphoblastoid cell lines using Sentrix Human-6 Expression BeadChip (Illumina, San Diego, USA)24,25. Expression of *PHLDB1, CDKN2A, CDKN2B, ARFRP1, STMN3, SLC2A4RG* and *TNFRSF6B* in normal human cortex based on expression data from analysis of 193 normal human brain samples using Affymetrix GeneChip Human Mapping 500K Arrays and Illumina HumanRefseq-8 Expression BeadChip platforms26. Expression and/or genotype information was not available for every sample and thus the total number of samples may be <193. Where SNPs genotyped in our study were not typed HAPMAP data was used to identify correlated SNPs in high LD (r2>0.8). The number of samples with each genotype is given for each plot. Combining the lowest frequency homozygote with the heterozygote and re-performing the statistical test produced no further significant results. Differences in the distribution of expression by SNP genotype were compared using a Wilcoxon-type test for trend.

SNP	Chr	Gene	Location (bp)	Ancestral allele frequency	Risk allele	GWA studies			Replication studies			Combined results			
						OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	P_{het}
rs2736100	5	*TERT*	1,339,516	0.51	G	1.20	1.1 - 1.33	$2.21x10^{-6}$	1.33	1.20 - 1.49	$2.87x10^{-13}$	1.27	1.19 - 1.37	$1.50x10^{-17}$	0.18
rs2853676	5	*TERT*	1,341,547	0.27	A	1.22	1.14 - 1.31	$5.30x10^{-6}$	1.30	1.21 - 1.38	$1.06x10^{-9}$	1.26	1.2 - 1.32	$4.21x10^{-14}$	0.67
rs10464870	8	*CCDC26*	130,547,005	0.21	C	1.24	1.15 - 1.34	$3.9x10^{-6}$	1.22	1.13 - 1.31	$1.77x10^{-5}$	1.23	1.17 - 1.3	$3.04x10^{-10}$	0.05
rs891835	8	*CCDC26*	130,560,934	0.22	**T**	1.24	1.15 - 1.33	$3.92x10^{-6}$	1.24	1.15 - 1.33	$4.43x10^{-6}$	1.24	1.17 - 1.3	$7.54x10^{-11}$	0.01
rs6470745	8	*CCDC26*	130,711,103	0.20	G	1.30	1.2 - 1.39	$5.79x10^{-6}$	1.31	1.22 - 1.41	$9.09x10^{-9}$	1.30	1.24 - 1.37	$2.77x10^{-15}$	0.01
rs16904140	8	*CCDC26*	130,734,825	0.21	A	1.25	1.16 - 1.35	$1.41x10^{-6}$	1.28	1.19 - 1.37	$1.14x10^{-7}$	1.27	1.2 - 1.33	$7.88x10^{-13}$	0.01
rs4295627	8	*CCDC26*	130,754,639	0.17	G	1.33	1.23 - 1.42	$1.47x10^{-8}$	1.39	1.3 - 1.49	$2.20x10^{-11}$	1.36	1.29 - 1.43	$2.34x10^{-18}$	0.01
rs1063192	9	*CDKN2A/B*	21,993,367	0.44	C	1.21	1.13 - 1.29	$1.44x10^{-6}$	1.21	1.14 - 1.29	$6.96x10^{-7}$	1.21	1.16 - 1.27	$4.61x10^{-12}$	0.81
rs2157719	9	*CDKN2A/B*	22,023,366	0.57	**G**	1.22	1.11 - 1.35	$6.80x10^{-7}$	1.22	1.11 - 1.33	$4.42x10^{-7}$	1.22	1.14 - 1.3	$1.41x10^{-12}$	0.68
rs1412829	9	*CDKN2A/B*	22,033,926	0.42	C	1.22	1.14 - 1.3	$7.23x10^{-7}$	1.23	1.15 - 1.3	$1.80x10^{-7}$	1.22	1.17 - 1.28	$6.23x10^{-13}$	0.67
rs4977756	9	*CDKN2A/B*	22,058,652	0.40	G	1.25	1.17 - 1.32	$2.39x10^{-9}$	1.24	1.16 - 1.31	$5.90x10^{-8}$	1.24	1.19 - 1.3	$7.24x10^{-15}$	0.94
rs498872	11	*PHLDB1*	117,982,577	0.31	T	1.26	1.17 - 1.34	$1.03x10^{-7}$	1.12	1.04 - 1.2	$4.56x10^{-3}$	1.18	1.13 - 1.24	$1.07x10^{-8}$	0.04
rs6010620	20	*RTEL1*	61,780,283	0.23	**G**	1.28	1.18 - 1.38	$8.38x10^{-7}$	1.28	1.18 - 1.38	$6.49x10^{-7}$	1.28	1.21 - 1.35	$2.52x10^{-12}$	0.38
rs2297440	20	*RTEL1*	61,782,743	0.22	**C**	1.28	1.18 - 1.38	$1.01x10^{-6}$	1.26	1.16 - 1.35	$4.44x10^{-6}$	1.27	1.2 - 1.34	$2.06x10^{-11}$	0.4
rs7124728	11		70,554,083	0.66	**C**	1.38	1.3 - 1.47	$2.28x10^{-13}$	1.05	0.97 - 1.13	0.02	1.18	1.13 - 1.24	$8.18x10^{-9}$	<0.01
rs7300686	12		127,113,162	0.49	C	1.29	1.22 - 1.37	$5.28x10^{-11}$	1.02*	0.91 - 1.12*	0.76*	1.17	1.11 - 1.23	$5.72x10^{-7}$	0.01
rs17748	11	*TREH,PHLDB1*	118,033,634	0.77	T	1.25	1.16 - 1.34	$2.36x10^{-6}$	1.13	1.04 - 1.21	$7.46x10^{-3}$	1.18	1.12 - 1.25	$2.14x10^{-7}$	0.06
rs9656979	8	*CCDC26*	130,733,589	0.57	C	1.20	1.12 - 1.28	$5.59x10^{-6}$	1.12^	1.01 - 1.23^	0.04^	1.17	1.11 - 1.24	$1.08x10^{-6}$	0.01
rs9369226	6		40,778,694	0.19	**A**	1.22	1.09 - 1.39	$9.17x10^{-5}$	1.14	1.02 - 1.26	0.01	1.18	1.09 - 1.28	$4.08x10^{-6}$	<0.01
rs171125	16		34,618,468	0.91	A	1.37	1.24 - 1.51	$2.48x10^{-6}$	1.11	0.99 - 1.24	0.09	1.23	1.14 - 1.32	$8.10x10^{-6}$	0.33
rs6931798	6		40,773,393	0.82	T	1.21	1.11 - 1.31	$1.25x10^{-5}$	1.10	1.0 - 1.2	0.05	1.15	1.09 - 1.22	$4.66x10^{-5}$	<0.01
rs6869535	5		40,633,375	0.82	**G**	1.29	1.18 - 1.4	$4.81x10^{-6}$	1.06	0.96 - 1.16	0.26	1.16	1.09 - 1.24	$7.73x10^{-5}$	0.28
rs2110922	2	*SLC8A1*	40,217,148	0.36	**T**	1.20	1.10 - 1.33	$9.33x10^{-6}$	1.04	0.96 - 1.14	0.30	1.12	1.05 - 1.19	$1.24x10^{-4}$	0.38
rs2072532	2	*SLC8A1*	40,219,805	0.52	**T**	1.19	1.11 - 1.27	$1.31x10^{-5}$	1.03	0.96 - 1.11	0.42	1.11	1.05 - 1.16	$3.02x10^{-4}$	<0.01
rs7257116	19	*MKNK2*	1,979,985	0.60	**C**	1.19	1.11 - 1.27	$4.12x10^{-5}$	1.03^	0.92 - 1.14^	0.62^	1.13	1.07 - 1.2	$2.80x10^{-4}$	<0.01
rs1509937	10		66,725,911	0.67	G	1.23	1.15 - 1.31	$8.22x10^{-7}$	0.99	0.91 - 1.07	0.84	1.10	1.04 - 1.16	$1.04x10^{-3}$	0.19
rs2206920	20		6,616,179	0.91	A	1.34	1.21 - 1.47	$1.18x10^{-5}$	1.01	0.88 - 1.14	0.90	1.16	1.07 - 1.25	$1.41x10^{-3}$	<0.01
rs12531711	7	*IRF5, TNP03*	128,404,702	0.89	G	1.36	1.23 - 1.48	$9.91x10^{-7}$	0.98	0.86 - 1.1	0.74	1.15	1.06 - 1.24	$1.41x10^{-3}$	<0.01
rs10488631	7	*IRF5, TNP03*	128,381,419	0.89	C	1.37	1.25 - 1.49	$4.94x10^{-7}$	0.97	0.85 - 1.09	0.59	1.15	1.06 - 1.23	$1.62x10^{-3}$	0.33
rs10924559	1		244,445,616	0.86	**G**	1.29	1.18 - 1.4	$7.47x10^{-6}$	1.00	0.9 - 1.11	0.93	1.13	1.05 - 1.21	$1.83x10^{-3}$	<0.01
rs1384847	4		53,370,591	0.91	**G**	1.40	1.25 - 1.56	$1.07x10^{-5}$	0.98	0.85 - 1.12	0.82	1.15	1.05 - 1.25	$5.62x10^{-3}$	<0.01
rs1941114	18	*CHST9*	22,868,217	0.15	G	1.35	1.16 - 1.59	$4.59x10^{-7}$	1.05	0.94 - 1.15	0.38	1.12	0.82 - 0.97	$5.64x10^{-3}$	<0.01

rs7325443	13	*ARHGEF7*	110,688,557	0.81	T	1.22	1.12 - 1.32	8.02×10^{-5}	0.97	0.88 - 1.07	0.56	1.08	1.01 - 1.15	0.02	<0.01
rs7325927	13		107,273,514	0.26	**T**	1.23	1.11 - 1.39	2.53×10^{-6}	0.88	0.81 - 0.95	4.76×10^{-3}	1.04	0.9 - 1.02	0.17	<0.01

* Only French data in replication studies
^ Only Swedish and German data in replication studies

SNP	**Chr**	**French case genotypes**						**French control genotypes**						**French results**		
														OR	**95% CI**	***P***
rs2736100	5	225	TT	686	TG	441	GG	383	TT	807	TG	371	GG	1.43	1.23 - 1.67	1.08×10^{-10}
rs2853676	5	164	AA	623	AG	574	GG	127	AA	622	AG	741	GG	1.29	1.18 - 1.4	7.71×10^{-6}
rs10464870	8	822	TT	460	TC	78	CC	1071	TT	452	TC	65	CC	1.29	1.17 - 1.42	6.04×10^{-5}
rs891835	8	820	TT	457	TG	85	GG	955	TT	442	TG	55	GG	1.26	1.14 - 1.39	2.93×10^{-3}
rs6470745	8	839	AA	455	AG	86	GG	1066	AA	479	AG	41	GG	1.36	1.24 - 1.49	1.84×10^{-6}
rs16904140	8	97	AA	466	AG	812	GG	44	AA	519	AG	1020	GG	1.33	1.2 - 1.45	7.63×10^{-6}
rs4295627	8	885	TT	418	TG	71	GG	1133	TT	421	TG	25	GG	1.46	1.32 - 1.59	5.13×10^{-8}
rs1063192	9	443	TT	649	TC	275	CC	573	TT	743	TC	250	CC	1.18	1.08 - 1.29	0.0014
rs2157719	9	458	AA	638	AG	271	GG	589	AA	735	AG	253	GG	1.16	1.04 - 1.32	0.0036
rs1412829	9	469	TT	643	TC	248	CC	607	TT	741	TC	228	CC	1.17	1.07 - 1.28	0.0026
rs4977756	9	474	AA	639	AG	239	GG	651	AA	723	AG	209	GG	1.24	1.14 - 1.35	4.35×10^{-5}
rs498872	11	184	TT	627	TC	562	CC	170	TT	668	TC	735	CC	1.20	1.09 - 1.31	8.05×10^{-4}
rs6010620	20	34	AA	386	AG	912	GG	59	AA	508	AG	978	GG	1.24	1.11 - 1.38	0.0017
rs2297440	20	32	TT	387	TC	910	CC	52	TT	478	TC	930	CC	1.23	1.09 - 1.36	0.0040
rs7124728	11	267	TT	661	TC	413	CC	319	TT	759	TC	470	CC	1.02	0.92 - 1.13	0.6669
rs7300686	12	340	TT	654	TC	365	CC	363	TT	739	TC	387	CC	1.00	0.9 - 1.1	0.7680
rs17748	11	112	TT	546	TC	717	CC	98	TT	554	TC	929	CC	1.24	1.13 - 1.36	2.14×10^{-4}
rs9369226	6	84	AA	484	AG	803	GG	65	AA	518	AG	962	GG	1.18	0.73 - 0.97	0.0105
rs171125	16	13	AA	271	AG	1089	GG	19	AA	301	AG	1221	GG	0.98	0.82 - 1.15	0.8216
rs6931798	6	63	TT	462	TC	811	CC	60	TT	494	TC	925	CC	1.08	0.95 - 1.21	0.2510
rs6869535	5	27	AA	371	AG	956	GG	34	AA	468	AG	1083	GG	1.10	0.96 - 1.24	0.1996
rs2110922	2	161	TT	661	TG	549	GG	185	TT	714	TG	628	GG	1.02	0.87 - 1.09	0.7742
rs2072532	2	371	TT	714	TC	286	CC	424	TT	804	TC	339	CC	1.02	0.91 - 1.12	0.7621
rs1509937	10	619	AA	595	AG	146	GG	735	AA	675	AG	166	GG	1.03	0.92 - 1.14	0.5901
rs2206920	20	12	AA	231	AG	1133	GG	16	AA	278	AG	1238	GG	0.91	0.73 - 1.08	0.2743
rs12531711	7	1110	AA	252	AG	15	GG	1273	AA	298	AG	14	GG	1.00	0.83 - 1.16	0.9552
rs10488631	7	1107	TT	255	TC	14	CC	1278	TT	294	TC	15	CC	1.01	0.84 - 1.18	0.9236
rs10924559	1	32	AA	341	AG	993	GG	34	AA	407	AG	1120	GG	0.97	0.83 - 1.17	0.6767

rs1384847	4	9	AA	172	AG	1190	GG	5	AA	211	AG	1331	GG	1.03	0.83 - 1.23	0.7500
rs1941114	18	27	AA	359	AG	977	GG	31	AA	384	AG	1169	GG	0.92	0.85 - 1.24	0.2420
rs7325443	13	53	TT	443	TC	884	CC	72	TT	489	TC	1023	CC	0.99	0.87 - 1.12	0.9317
rs7325927	13	96	TT	527	TC	751	CC	89	TT	611	TC	632	CC	0.83	0.75 - 0.94	0.0038

SNP	**Chr**	**German case genotypes**						**German control genotypes**						**German results**		
														OR	**95% CI**	***P***
rs2736100	5	91	TT	240	TG	160	GG	133	TT	269	TG	163	GG	1.19	1.02 - 3.49	0.0473
rs2853676	5	52	AA	217	AG	229	GG	45	AA	209	AG	311	GG	1.31	1.13 - 3.27	0.0041
rs10464870	8	276	TT	180	TC	42	CC	360	TT	182	TC	23	CC	1.41	1.21 - 3.37	$7.68\text{x}10^{-4}$
rs891835	8	258	TT	191	TG	52	GG	354	TT	195	TG	19	GG	1.60	1.4 - 3.56	$3.07\text{x}10^{-6}$
rs6470745	8	273	AA	196	AG	33	GG	392	AA	159	AG	17	GG	1.73	1.52 - 3.69	$4.33\text{x}10^{-7}$
rs16904140	8	39	AA	198	AG	263	GG	19	AA	173	AG	376	GG	1.67	1.46 - 3.63	$1.08\text{x}10^{-6}$
rs4295627	8	283	TT	185	TG	30	GG	414	TT	144	TG	13	GG	1.86	1.64 - 3.82	$3.17\text{x}10^{-8}$
rs1063192	9	136	TT	243	TC	112	CC	191	TT	279	TC	99	CC	1.26	1.08 - 3.22	0.0094
rs2157719	9	136	AA	253	AG	111	GG	198	AA	266	AG	101	GG	1.28	1.09 - 3.22	0.0052
rs1412829	9	147	TT	245	TC	111	CC	203	TT	272	TC	94	CC	1.27	1.1 - 3.23	0.0056
rs4977756	9	151	AA	240	AG	108	GG	211	AA	265	AG	90	GG	1.29	1.12 - 3.25	0.0034
rs498872	11	39	TT	214	TC	238	CC	55	TT	250	TC	264	CC	1.10	0.72 - 2.87	0.3381
rs6010620	20	16	AA	147	AG	336	GG	28	AA	177	AG	352	GG	1.21	0.99 - 3.17	0.0885
rs2297440	20	19	TT	147	TC	334	CC	28	TT	180	TC	358	CC	1.16	0.94 - 3.12	0.1814
rs7124728	11	100	TT	240	TC	161	CC	117	TT	281	TC	169	CC	1.06	0.89 - 3.02	0.4888
rs17748	11	16	TT	195	TC	292	CC	34	TT	215	TC	320	CC	0.87	0.67 - 2.83	0.1988
rs9656979	8	153	TT	235	TC	106	CC	194	TT	280	TC	89	CC	1.20	1.03 - 3.16	0.0349
rs9369226	6	15	AA	158	AG	321	GG	18	AA	168	AG	381	GG	1.08	0.71 - 2.89	0.5344
rs171125	16	7	AA	88	AG	401	GG	4	AA	96	AG	467	GG	1.13	0.85 - 3.09	0.3905
rs6931798	6	18	TT	160	TC	323	CC	16	TT	164	TC	390	CC	1.17	0.95 - 3.13	0.1553
rs6869535	5	18	AA	134	AG	326	GG	13	AA	191	AG	364	GG	1.09	0.87 - 3.05	0.4318
rs2110922	2	67	TT	254	TG	183	GG	77	TT	267	TG	222	GG	1.06	0.77 - 2.9	0.5281
rs2072532	2	153	TT	227	TC	112	CC	146	TT	274	TC	132	CC	1.12	0.95 - 3.08	0.1939
rs7257116	19	74	TT	246	TC	184	CC	87	TT	271	TC	211	CC	1.00	0.83 - 2.96	0.9938
rs1509937	10	214	AA	222	AG	66	GG	226	AA	258	AG	67	GG	0.99	0.81 - 2.95	0.8811
rs2206920	20	4	AA	85	AG	411	GG	3	AA	96	AG	467	GG	1.04	0.74 - 3	0.8151
rs12531711	7	410	AA	85	AG	6	GG	456	AA	96	AG	10	GG	0.93	0.66 - 2.89	0.6333
rs10488631	7	400	TT	79	TC	4	CC	460	TT	98	TC	10	CC	0.86	0.57 - 2.82	0.2982
rs10924559	1	10	AA	110	AG	372	GG	14	AA	136	AG	412	GG	0.89	0.67 - 3.08	0.3686

rs1384847	4	2	AA	89	AG	409	GG	6	AA	100	AG	462	GG	1.07	0.78 - 3.03	0.6854
rs1941114	18	12	AA	127	AG	361	GG	12	AA	160	AG	397	GG	1.09	0.68 - 2.88	0.4942
rs7325443	13	16	TT	139	TC	346	CC	27	TT	168	TC	376	CC	0.86	0.64 - 2.82	0.1657
rs7325927	13	24	TT	219	TC	261	CC	40	TT	227	TC	301	CC	0.97	0.63 - 2.99	0.7726

SNP	**Chr**	**Sweden case genotypes**						**Sweden control genotypes**						**Sweden results**		
														OR	**95% CI**	***P***
rs2736100	5	120	TT	326	TG	177	GG	212	TT	367	TG	185	GG	1.30	1.19 - 3.04	9.19x10^{-4}
rs2853676	5	51	AA	264	AG	324	GG	45	AA	269	AG	446	GG	1.30	1.13 - 3.26	0.0027
rs10464870	8	379	TT	210	TC	34	CC	448	TT	281	TC	34	CC	0.97	0.79 - 2.93	0.7249
rs891835	8	372	TT	226	TG	42	GG	426	TT	290	TG	42	GG	0.98	0.8 - 2.94	0.7822
rs6470745	8	386	AA	224	AG	31	GG	468	AA	258	AG	41	GG	1.01	0.83 - 2.97	0.9271
rs16904140	8	36	AA	225	AG	377	GG	52	AA	258	AG	458	GG	0.98	0.81 - 2.94	0.8586
rs4295627	8	393	TT	223	TG	27	GG	492	TT	247	TG	36	GG	1.06	0.88 - 3.02	0.5330
rs1063192	9	114	TT	331	TC	175	CC	199	TT	374	TC	191	CC	1.25	1.1 - 3.21	0.0041
rs2157719	9	129	AA	325	AG	187	GG	210	AA	380	AG	184	GG	1.28	1.12 - 3.23	0.0011
rs1412829	9	130	TT	333	TC	179	CC	218	TT	366	TC	176	CC	1.30	1.15 - 3.26	5.47x10^{-4}
rs4977756	9	150	AA	325	AG	157	GG	223	AA	379	AG	168	GG	1.18	1.03 - 3.14	0.0294
rs498872	11	78	TT	287	TC	278	CC	83	TT	323	TC	362	CC	1.12	0.97 - 3.08	0.1465
rs6010620	20	20	AA	195	AG	430	GG	54	AA	264	AG	456	GG	1.40	1.22 - 3.36	2.39x10^{-4}
rs2297440	20	20	TT	194	TC	430	CC	53	TT	263	TC	457	CC	1.40	1.22 - 3.36	3.09x10^{-4}
rs7124728	11	101	TT	305	TC	218	CC	138	TT	379	TC	248	CC	1.10	0.94 - 3.06	0.2428
rs17748	11	37	TT	245	TC	362	CC	47	TT	264	TC	455	CC	1.08	0.91 - 3.04	0.3889
rs9656979	8	182	TT	300	TC	152	CC	226	TT	381	TC	164	CC	1.07	0.92 - 3.03	0.3879
rs9369226	6	19	AA	188	AG	433	GG	24	AA	204	AG	538	GG	1.09	0.72 - 2.88	0.3990
rs171125	16	5	AA	123	AG	509	GG	6	AA	97	AG	663	GG	1.52	1.26 - 3.48	0.0020
rs6931798	6	21	TT	183	TC	438	CC	24	TT	200	TC	542	CC	1.10	0.9 - 3.06	0.3517
rs6869535	5	21	AA	202	AG	392	GG	28	AA	229	AG	476	GG	0.97	0.78 - 2.93	0.7948
rs2110922	2	93	TT	325	TG	223	GG	114	TT	352	TG	298	GG	1.09	0.77 - 2.88	0.2996
rs2072532	2	189	TT	301	TC	121	CC	242	TT	356	TC	158	CC	1.00	0.85 - 2.96	0.9963
rs7257116	19	81	TT	316	TC	237	CC	111	TT	379	TC	283	CC	1.05	0.9 - 3.01	0.5132
rs1509937	10	254	AA	300	AG	74	GG	312	AA	339	AG	120	GG	0.92	0.77 - 2.88	0.3090
rs2206920	20	7	AA	110	AG	528	GG	6	AA	108	AG	654	GG	1.25	0.99 - 3.21	0.0940
rs12531711	7	468	AA	164	AG	8	GG	558	AA	194	AG	12	GG	0.98	0.76 - 2.94	0.8740
rs10488631	7	465	TT	162	TC	8	CC	558	TT	202	TC	10	CC	0.97	0.75 - 2.93	0.7554
rs10924559	1	21	AA	189	AG	407	GG	25	AA	201	AG	530	GG	1.15	0.67 - 2.83	0.1506

rs1384847	4	8	AA	132	AG	500	GG	13	AA	131	AG	623	GG	0.88	0.64 - 2.84	0.2673
rs1941114	18	15	AA	174	AG	440	GG	13	AA	209	AG	543	GG	0.93	0.66 - 3.03	0.5292
rs7325443	13	27	TT	210	TC	408	CC	38	TT	237	TC	498	CC	1.01	0.83 - 2.97	0.8867
rs7325927	13	36	TT	240	TC	362	CC	65	TT	278	TC	431	CC	0.91	0.63 - 3.06	0.2558

SNP	**Chr**	**UK case genotypes**							**UK control genotypes**						**UK results**		
														OR	**95% CI**	***P***
rs2736100	5	115	TT	316	TG	200	GG	349	TT	676	TG	409	GG	1.20	1.03 - 3.2	0.0068
rs2853676	5	67	AA	263	AG	301	GG	113	AA	596	AG	724	GG	1.14	1 - 3.1	0.0718
rs10464870	8	355	TT	236	TC	40	CC	882	TT	484	TC	66	CC	1.22	1.06 - 3.18	0.0127
rs891835	8	344	TT	246	TG	41	GG	836	TT	496	TG	77	GG	1.17	1.02 - 3.13	0.0436
rs6470745	8	363	AA	231	AG	37	GG	921	AA	448	AG	64	GG	1.26	1.1 - 3.22	0.0037
rs16904140	8	46	AA	233	AG	352	GG	62	AA	474	AG	896	GG	1.31	1.16 - 3.27	$6.10x10^{-4}$
rs4295627	8	386	TT	216	TG	29	GG	976	TT	410	TG	48	GG	1.29	1.13 - 3.25	0.0023
rs1063192	9	165	TT	298	TC	168	CC	418	TT	689	TC	323	CC	1.15	1.02 - 3.11	0.0389
rs2157719	9	170	AA	295	AG	166	GG	431	AA	689	AG	311	GG	1.16	0.35 - 1.37	0.0245
rs1412829	9	178	TT	294	TC	158	CC	450	TT	686	TC	296	CC	1.16	1.03 - 3.12	0.0277
rs4977756	9	189	AA	604	AG	138	GG	501	AA	662	AG	270	GG	1.27	1.14 - 3.23	$1.71x10^{-4}$
rs498872	11	75	TT	288	TC	268	CC	119	TT	634	TC	681	CC	1.22	1.08 - 3.18	0.0055
rs6010620	20	26	AA	179	AG	426	GG	82	AA	533	AG	818	GG	1.43	1.26 - 3.39	$2.42x10^{-5}$
rs2297440	20	24	TT	175	TC	432	CC	79	TT	489	TC	818	CC	1.41	1.24 - 3.37	$6.68x10^{-5}$
rs7124728	11	45	TT	413	TC	173	CC	262	TT	688	TC	454	CC	1.17	1.02 - 3.13	0.0369
rs7300686	12	174	TT	238	TC	213	CC	360	TT	728	TC	320	CC	1.19	1.06 - 3.15	0.0092
rs17748	11	33	TT	252	TC	346	CC	61	TT	491	TC	882	CC	1.25	1.09 - 3.21	0.0060
rs9656979	8	180	TT	299	TC	152	CC	472	TT	687	TC	271	CC	1.21	1.08 - 3.17	0.0049
rs9369226	6	33	AA	196	AG	402	GG	48	AA	441	AG	944	GG	1.14	1.0 - 2.84	0.1319
rs171125	16	8	AA	129	AG	494	GG	1	AA	261	AG	1149	GG	1.28	1.06 - 3.24	0.0277
rs6931798	6	33	TT	195	TC	403	CC	47	TT	432	TC	925	CC	1.13	0.96 - 3.09	0.1480
rs6869535	5	17	AA	153	AG	461	GG	37	AA	430	AG	965	GG	1.23	1.05 - 3.19	0.0268
rs2110922	2	99	TT	331	TG	201	GG	195	TT	652	TG	573	GG	1.25	1.02 - 2.76	0.0014
rs2072532	2	203	TT	314	TC	114	CC	417	TT	687	TC	325	CC	1.16	1.02 - 3.12	0.0243
rs7257116	19	88	TT	285	TC	258	CC	221	TT	687	TC	524	CC	1.13	0.99 - 3.09	0.0797
rs1509937	10	232	AA	298	AG	101	GG	645	AA	653	AG	136	GG	1.39	1.25 - 3.35	$4.01x10^{-6}$
rs2206920	20	9	AA	136	AG	486	GG	9	AA	241	AG	1144	GG	1.37	1.15 - 3.33	0.0044
rs12531711	7	459	AA	157	AG	15	GG	1168	AA	249	AG	16	GG	1.59	1.39 - 3.55	$4.53x10^{-6}$
rs10488631	7	459	TT	157	TC	15	CC	1167	TT	246	TC	16	CC	1.60	1.4 - 3.56	$3.19x10^{-6}$

rs10924559	1	14	AA	161	AG	450	GG	21	AA	283	AG	1115	GG	1.37	1.10 - 2.69	0.0013
rs1384847	4	2	AA	75	AG	554	GG	11	AA	226	AG	1197	GG	1.42	1.16 - 3.38	0.0092
rs1941114	18	12	AA	133	AG	486	GG	30	AA	381	AG	1023	GG	1.28	1.07 - 2.74	0.0135
rs7325443	13	19	TT	209	TC	403	CC	40	TT	426	TC	967	CC	1.14	0.97 - 3.1	0.1357
rs7325927	13	56	TT	237	TC	336	CC	70	TT	527	TC	837	CC	1.27	1.06 - 2.75	0.0022

SNP	Chr	US case genotypes						US control genotypes						US results		
														OR	95% CI	*P*
rs2736100	5	230	TT	645	TG	372	GG	546	TT	1103	TG	584	GG	1.22	1.14-2.78	1.01×10^{-4}
rs2853676	5	109	AA	568	AG	570	GG	149	AA	894	AG	1191	GG	1.28	1.17-3.24	1.35×10^{-5}
rs10464870	8	683	TT	488	TC	76	CC	1370	TT	761	TC	101	CC	1.26	1.14-3.22	9.62×10^{-5}
rs891835	8	661	TT	498	TG	88	GG	1344	TT	773	TG	115	GG	1.28	1.16-3.24	2.16×10^{-6}
rs6470745	8	699	AA	469	AG	79	GG	1415	AA	730	AG	90	GG	1.32	1.2-3.28	4.20×10^{-6}
rs16904140	8	85	AA	476	AG	686	GG	110	AA	773	AG	1352	GG	1.22	1.11-3.18	5.29×10^{-4}
rs4295627	8	735	TT	451	TG	60	GG	1496	TT	667	TG	72	GG	1.35	1.22-3.31	1.68×10^{-6}
rs1063192	9	326	TT	602	TC	319	CC	700	TT	1092	TC	436	CC	1.25	1.15-3.21	7.62×10^{-6}
rs2157719	9	335	AA	601	AG	311	GG	726	AA	1078	AG	428	GG	1.25	1.17-2.78	6.15×10^{-6}
rs1412829	9	347	TT	596	TC	302	CC	749	TT	1072	TC	412	CC	1.25	1.16-3.21	5.59×10^{-6}
rs4977756	9	377	AA	594	AG	276	GG	782	AA	1083	AG	370	GG	1.23	1.13-3.19	3.46×10^{-5}
rs498872	11	156	TT	589	TC	502	CC	211	TT	954	TC	1070	CC	1.27	1.17-3.23	5.07×10^{-6}
rs6010620	20	46	AA	405	AG	796	GG	123	AA	785	AG	1327	GG	1.20	1.08-3.16	0.0025
rs2297440	20	45	TT	397	TC	804	CC	119	TT	777	TC	1330	CC	1.22	1.09-3.18	0.0016
rs7124728	11	76	TT	740	TC	431	CC	424	TT	1145	TC	663	CC	1.53	1.42 - 3.49	2.56×10^{-14}
rs7300686	12	307	TT	454	TC	466	CC	586	TT	1074	TC	508	CC	1.36	1.26 - 3.32	4.72×10^{-10}
rs17748	11	84	TT	487	TC	675	CC	119	TT	753	TC	1363	CC	1.25	1.14 - 3.21	1.23×10^{-4}
rs9656979	8	351	TT	630	TC	266	CC	742	TT	1098	TC	393	CC	1.20	1.1 - 3.16	3.65×10^{-4}
rs9369226	6	57	AA	428	AG	762	GG	73	AA	659	AG	1502	GG	1.27	1.14 - 2.75	1.73×10^{-4}
rs171125	16	19	AA	249	AG	978	GG	6	AA	359	AG	1838	GG	1.43	1.26 - 3.39	2.33×10^{-5}
rs6931798	6	56	TT	426	TC	765	CC	71	TT	656	TC	1500	CC	1.26	1.14 - 3.22	2.11×10^{-4}
rs6869535	5	28	AA	307	AG	912	GG	69	AA	682	AG	1483	GG	1.32	1.19 - 3.28	5.17×10^{-5}
rs2110922	2	188	TT	579	TG	478	GG	273	TT	980	TG	957	GG	1.17	1.06 - 2.81	0.0016
rs2072532	2	390	TT	606	TC	251	CC	572	TT	1128	TC	533	CC	1.21	1.11 - 3.17	1.71×10^{-4}
rs7257116	19	148	TT	581	TC	518	CC	339	TT	1095	TC	796	CC	1.22	1.12 - 3.18	1.36×10^{-4}
rs1509937	10	517	AA	552	AG	178	GG	997	AA	995	AG	243	GG	1.15	1.05 - 3.11	0.0062

rs2206920	20	18	AA	239	AG	990	GG	18	AA	342	AG	1850	GG	1.32	1.16 - 3.28	8.44x10^{-4}
rs12531711	7	966	AA	262	AG	19	GG	1807	AA	407	AG	20	GG	1.23	1.08 - 3.19	0.0089
rs10488631	7	965	TT	263	TC	19	CC	1810	TT	405	TC	20	CC	1.24	1.09 - 3.2	0.0063
rs10924559	1	29	AA	324	AG	872	GG	52	AA	460	AG	1699	GG	1.25	1.10 - 2.76	0.0014
rs1384847	4	0	AA	170	AG	1077	GG	28	AA	360	AG	1847	GG	1.40	1.21 - 3.36	3.85x10^{-4}
rs1941114	18	18	AA	268	AG	961	GG	60	AA	602	AG	1573	GG	1.39	1.20 - 2.68	8.90x10^{-4}
rs7325443	13	50	TT	427	TC	770	CC	73	TT	633	TC	1529	CC	1.27	1.15 - 3.23	1.54x10^{-4}
rs7325927	13	129	TT	456	TC	659	CC	147	TT	807	TC	1281	CC	1.22	1.07 - 2.78	3.27x10^{-4}

Supplementary Table 1: Genotypes for the 34 SNPs in cases and controls in each of the case-control series. Also shown are Odds ratios and associated 95% confidence intervals, for each of the SNPs genotyped.

rs2736100	rs2853676	Cases	Controls	OR	95% CI	*P*
TT	GG	678	1,414	1.00	Reference	
TT	GA	91	164	1.13	(0.86 - 1.49)	0.37
TT	AA	3	8	0.93	(0.24 - 3.53)	0.91
TG	GG	975	1,521	1.33	(1.18 - 1.5)	$5.36x10^{-6}$
TG	GA	1,158	1,569	1.53	(1.36 - 1.73)	$3.17x10^{-12}$
TG	AA	60	73	1.67	(1.17 - 2.39)	0.005
GG	GG	310	449	1.45	(1.22 - 1.72)	$2.67x10^{-5}$
GG	GA	654	842	1.64	(1.43 - 1.88)	$2.75x10^{-12}$
GG	AA	372	390	1.97	(1.66 - 2.33)	$7.77x10^{-15}$
	Per risk allele			1.08	(1.06-1.09)	1.19x10-^{19}
	P interaction					0.308

Haplotype*	Case frequency	Control frequency	*P*
TG	0.409	0.467	$4.23x10^{-17}$
GA	0.296	0.247	$5.1x10^{-16}$
GG	0.269	0.26	0.1439
TA	0.026	0.026	0.733

*Haplotype consists of rs2736100 and rs2853676

rs4295627	rs891835	Cases	Controls	OR	95% CI	*P*
TT	TT	3,349	2,044	1.00	Reference	
TT	TG	951	573	1.02	(0.90 - 1.15)	0.76
TT	GG	82	44	0.90	(0.62 - 1.30)	0.58
TG	TT	538	384	1.19	(1.03 - 1.38)	0.02
TG	TG	1,144	946	1.40	(1.25 - 1.54)	$4.66x10^{-10}$
TG	GG	141	145	1.73	(1.36 - 2.20)	$7.82x10^{-6}$
GG	TT	16	17	1.89	(0.95 - 3.78)	0.07
GG	TG	91	82	1.48	(1.09 - 2.01)	0.01
GG	GG	84	116	2.35	(1.76 - 3.14)	$7.04x10^{-9}$
	Per risk allele			1.08	(1.07-1.11)	$2.47x10^{-19}$
	P interaction					0.03

Haplotype$^{¥}$	Case frequency	Control frequency	*P*
TTATGT	0.424	0.462	$2.00x10^{-4}$
TTACGT	0.202	0.198	0.6561
CGGCAG	0.143	0.099	$7.46x10^{-12}$
CGATGT	0.087	0.094	0.2041
TTGCAG	0.062	0.059	0.6354
TGGCAG	0.02	0.02	0.9459
TTGCAT	0.016	0.02	0.1366
TTACAT	0.015	0.017	0.4222
CTATGT	0.011	0.011	0.9447

$^{¥}$Haplotype consists of rs10464870, rs891835, rs6470745, rs9656979, rs16904140 and rs4295627

Supplementary Table 2: Risk of glioma by combined genotypes for rs2736100-rs2853676 and rs4295627-rs891835.

SNP	**Comparison**	***P***	**Between study *P***
rs4295627	Glial vs GBM	2.52×10^{-9}	0.111
	Astrocytic vs GBM	5.12×10^{-5}	0.013
	Glial vs astrocytic	0.026	0.016
	Glial & astrocytic vs GBM	3.80×10^{-8}	0.014
rs498872	Glial vs GBM	0.009	0.748
	Astrocytic vs GBM	0.030	0.145
	Glial vs astrocytic	0.158	0.406
	Glial & astrocytic vs GBM	0.005	0.999
rs4977756	Glial vs GBM	0.230	9.60×10^{-5}
	Astrocytic vs GBM	0.0008	0.003
	Glial vs astrocytic	0.411	0.121
	Glial & astrocytic vs GBM	0.010	0.001
rs2736100	Glial vs GBM	3.30×10^{-4}	0.069
	Astrocytic vs GBM	1.91×10^{-4}	0.068
	Glial vs astrocytic	0.548	0.172
	Glial & astrocytic vs GBM	2.55×10^{-5}	0.047
rs6010620	Glial vs GBM	0.003	0.429
	Astrocytic vs GBM	0.138	0.126
	Glial vs astrocytic	0.070	0.003
	Glial & astrocytic vs GBM	0.016	0.043

Supplementary Table 3: Clinico-pathological association testing. Tumors of glial origin defined by ICD-O codes 93803, 94423, 94503, 94513, GBM by ICD-O codes 94401-13, and astrocytic tumors by ICD-O codes 94003-245.

		TERT	*CCDC26*					*CDKN2A/B*				*PHLDB1*	*RTEL1*	
		rs2853676	rs10464870	rs891835	rs6470745	rs16904140	rs4295627	rs1063192	rs2157719	rs1412829	rs4977756	rs498872	rs6010620	rs2297440
TERT	rs2736100	0.31 (10,731)	0.68 (10,800)	0.73 (10,667)	0.74 (10,850)	0.30 (10,836)	0.30 (10,846)	0.34 (10,774)	0.20 (10,825)	0.41 (10,810)	0.27 (10,811)	0.55 (10,825)	0.60 (10,763)	0.63 (10,623)
	rs2853676		0.26 (10,758)	0.78 (10,629)	0.38 (10,808)	0.41 (10.798)	0.41 (10,803)	0.74 (10,739)	0.85 (10,782)	0.97 (10,777)	0.40 (10,765)	0.20 (10,783)	0.66 (10,728)	0.56 (10,598)
CCDC26	rs10464870			0.62 (10,705)	5.57x10^{-5} (10,887)	3.92x10^{-12} (10,880)	0.02 (10,880)	0.86 (10,813)	0.80 (10,865)	0.55 (10,848)	0.73 (10,848)	0.18 (10,860)	0.94 (10,797)	0.86 (10,661)
	rs891835				1.56x10^{-4} (10,753)	1.45x10^{-4} (10.740)	0.03 (10,747)	0.77 (10,677)	0.71 (10,728)	0.53 (10,713)	0.67 (10,711)	0.24 (10,729)	0.33 (10,668)	0.22 (10,572)
	rs6470745					0.33 (10,926)	0.48 (10,933)	0.17 (10,861)	0.19 (10,911)	0.51 (10,900)	0.33 (10,898)	0.39 (10,912)	0.73 (10,846)	0.61 (10,711)
	rs16904140						0.26 (10,923)	0.41 (10,852)	0.49 (10,898)	0.96 (10,888)	0.50 (10,884)	0.41 (10,903)	0.89 (10,836)	0.78 (10,703)
	rs4295627							0.38 (10,859)	0.39 (10,911)	0.82 (10,896)	0.49 (10,894)	0.44 (10,909)	0.75 (10,846)	0.73 (10,708)
CDKN2A/B	rs1063192								0.60 (10,838)	0.58 (10,827)	0.76 (10,831)	0.73 (10,839)	0.87 (10,772)	0.97 (10,636)
	rs2157719									0.54 (10,874)	0.54 (10,874)	0.70 (10,889)	0.80 (10,823)	0.87 (10,687)
	rs1412829										0.59 (10,857)	0.44 (10,873)	0.60 (10,814)	0.65 (10,674)
	rs4977756											0.29 (10,869)	0.70 (10,808)	0.84 (10,670)
PHLDB1	rs498872												0.19 (10,820)	0.12 (10,690)
RTEL1	rs6010620													0.28 (10,632)

Supplementary Table 4: Pairwise analysis of all SNPs associated with glioma risk. For each row-column combination, numbers show the *P* value for inclusion of an interaction term between the two SNPs. Numbers in parentheses are the number of samples from which statistics are calculated.

Number of risk alleles	**Controls (%)**	**Cases (%)**	**OR (95% CI)**
0-1	153 (2.39)	39 (0.94)	0.5 (0.35 - 0.71)
2	454 (7.09)	170 (4.08)	0.73 (0.6 - 0.89)
3	1122 (17.51)	548 (13.14)	0.96 (0.84 - 1.09)
4	1885 (29.43)	964 (23.12)	1 (0.9 - 1.12)
5	1662 (25.94)	1137 (27.27)	1.34 (1.2 - 1.49)
6	810 (12.64)	833 (19.98)	2.01 (1.78 - 2.28)
7	270 (4.21)	356 (8.54)	2.58 (2.16 - 3.07)
8+	50 (0.78)	123 (2.95)	4.81 (3.43 - 6.74)
Total	6406 (100)	4170 (100)	1.31 (1.26 - 1.36) per allele $P_{\text{trend}} = 1.39 \times 10^{-74}$

Supplementary Table 5: Odds ratios corresponding to increasing numbers of risk alleles in rs4295627 (*CCDC26*), rs498872 (*PHLDB1*), rs497756 (*CDKN2A, CDKN2B*), rs2736100 (*TERT*) and rs6010620 (*RTEL1*). The median number of risk alleles, 4, is used as the reference group for the odds ratios.