

Supplementary Table 1: Linear mixed model on TwinsUK dataset RPM values showing β values for age, depression, smoking, alcohol and BMI. The nearest gene feature to a DMR is shown, DMRs occurring within a coding region are shown in bold.

Chr	start	Stop	X.Intercept.	age	depression	smoking	alcohol	BMI	pvalue	Gene	Description
chr2	55887751	55888250	-1.147	-0.003	0.932	0.356	0.242	0.017	1.50E-08	PNPT1	polyribonucleotide nucleotidyltransferase
chr6	139528751	139529250	-1.115	0.010	0.999	-0.252	-0.115	0.008	1.79E-08	HECA	headcase homolog (Drosophila)
chr6	18241001	18241500	-0.185	0.003	0.998	0.292	-0.022	-0.021	2.60E-08	DEK	DEK oncogene
chr2	53454751	53455250	-0.432	-0.003	-1.303	0.089	0.272	0.035	3.29E-08	LOC727915	uncharacterized LOC727915
chr15	87282501	87283000	0.018	0.005	-1.056	0.266	0.085	0.001	7.15E-08	AGBL1	ATP/GTP binding protein
chr18	7832001	7832500	1.162	-0.021	1.188	-0.580	-0.206	-0.004	7.42E-08	PTPRM	protein tyrosine phosphatase, type, M
chr6	135940501	135941000	-1.219	0.009	1.083	0.043	-0.055	0.006	8.19E-08	C6orf217	chromosome 6 open reading frame 217
chr4	38369501	38370000	-0.551	0.014	1.177	0.211	-0.228	-0.028	9.80E-08	TBC1D1	TBC1 (tre-2/USP6, BUB2, cdc16)
chr2	48168501	48169000	0.856	-0.005	-0.984	0.351	0.671	-0.025	1.09E-07	FBXO11	F-box protein 11 (FBXO11)
chr4	15620251	15620750	0.972	0.013	0.863	-0.137	-0.260	-0.066	2.02E-07	CC2D2A	coiled-coil and C2 domain
chr1	90696251	90696750	0.310	-0.001	1.226	0.179	-0.308	-0.026	2.15E-07	ZNF326	zinc finger protein 326
chr13	43750001	43750500	-1.050	0.012	1.250	-0.143	-0.028	-0.006	2.27E-07	ENOX1	ecto-NOX disulfide-thiol exchanger
chr2	12048001	12048500	0.012	0.018	-1.154	0.158	0.212	-0.025	2.66E-07	MIR4262	microRNA 4262
chr2	57364001	57364500	-0.240	0.005	-1.009	0.544	-0.089	0.008	2.79E-07	CCDC85A	coiled-coil domain containing 85A
chr8	130549751	130550250	-0.389	0.012	1.207	0.162	-0.061	-0.032	3.13E-07	GSDMC	gasdermin C
chr3	114618751	114619250	0.228	-0.004	1.073	-0.612	0.097	-0.009	3.43E-07	ZBTB20	zinc finger and BTB domain containing 20
chr1	58906001	58906500	0.445	-0.010	1.230	-0.057	0.084	-0.017	4.18E-07	OMA1	OMA1 homolog, zinc metallopeptidase
chr10	19516501	19517000	-0.051	0.005	0.986	-0.427	0.431	-0.029	4.32E-07	ARL5B	ADP-ribosylation factor-like 5B
chr3	62424751	62425250	-1.107	0.000	0.987	-0.539	-0.500	0.043	4.82E-07	CADPS1	Ca++-dependent secretion activator 1
chr1	24012751	24013250	-0.165	0.004	1.134	0.073	-0.239	-0.017	5.06E-07	RPL11	ribosomal protein L11 (RPL11)

Supplementary Table 2: Linear mixed model on RPM factoring β values for age, depression, smoking, alcohol, BMI and anti-depressant medication. The nearest gene feature to a DMR is shown, DMRs occurring within a coding region are shown in bold.

Chr	Start	Stop	age	depress	smoking	alcohol	BMI	Meds	p value	Gene	Description
chr2	55887751	55888250	-0.003	0.930	0.380	0.245	0.016	-0.376	1.547E-08	PNPT1	polyribonucleotide nucleotidyltransferase
chr6	139528751	139529250	0.010	0.997	-0.234	-0.112	0.007	-0.229	1.879E-08	HECA	headcase homolog (Drosophila)
chr6	18241001	18241500	0.003	1.003	0.262	-0.026	-0.020	0.332	2.364E-08	DEK	DEK oncogene
chr2	53454751	53455250	-0.003	-1.300	0.068	0.268	0.035	0.141	3.363E-08	ASB3	ankyrin repeat and SOCS box-containing 3
chr18	7832001	7832500	-0.020	1.194	-0.639	-0.212	-0.001	0.482	5.099E-08	PTPRM	protein tyrosine phosphatase, receptor
chr15	87282501	87283000	0.005	-1.060	0.303	0.086	-0.001	-0.391	6.207E-08	AGBL1	ATP/GTP binding protein-like 1
chr4	38369501	38370000	0.013	1.169	0.276	-0.229	-0.030	-0.606	7.348E-08	TBC1D1	TBC1 domain family
chr6	135940501	135941000	0.009	1.085	0.029	-0.057	0.006	0.151	7.699E-08	C6orf217	chromosome 6 open reading frame 217
chr2	48168501	48169000	-0.005	-0.985	0.358	0.673	-0.025	-0.078	1.080E-07	FBXO11	F-box protein 11 (FBXO11),
chr1	90696251	90696750	-0.001	1.223	0.197	-0.305	-0.027	-0.118	2.195E-07	ZNF326	zinc finger protein 326
chr13	43750001	43750500	0.012	1.250	-0.147	-0.029	-0.006	0.027	2.267E-07	ENOX1	Ecto-NOX disulfide-thiol exchanger 1 (ENOX1),
chr2	57364001	57364500	0.005	-1.011	0.564	-0.086	0.007	-0.225	2.585E-07	CCDC85A	coiled-coil domain containing 85A
chr2	12048001	12048500	0.019	-1.149	0.115	0.205	-0.023	0.329	2.654E-07	MIR4262	microRNA 4262 (MIR4262),
chr13	82560751	82561250	-0.013	-1.191	0.563	-0.001	0.020	-0.750	2.722E-07	SPRY2	sprouty homolog 2 (Drosophila)
chr8	130549751	130550250	0.011	1.200	0.212	-0.053	-0.034	-0.325	2.794E-07	GSDMC	gasdermin C
chr4	15620251	15620750	0.012	0.852	-0.073	-0.245	-0.066	-0.803	2.970E-07	FBXL5	F-box and leucine-rich repeat protein 5
chr3	114618751	114619250	-0.004	1.078	-0.656	0.081	-0.007	0.457	2.992E-07	ZBTB20	zinc finger and BTB domain containing 20
chr1	58906001	58906500	-0.010	1.222	0.000	0.093	-0.019	-0.366	3.617E-07	OMA1	OMA1 homolog, zinc metallopeptidase
chr4	112260501	112261000	0.007	-1.192	0.386	-0.050	-0.025	-0.411	4.226E-07	PITX2	paired-like homeodomain 2
chr3	62424751	62425250	0.000	0.985	-0.523	-0.497	0.042	-0.140	4.952E-07	CADPS1	Ca⁺⁺-dependent secretion activator

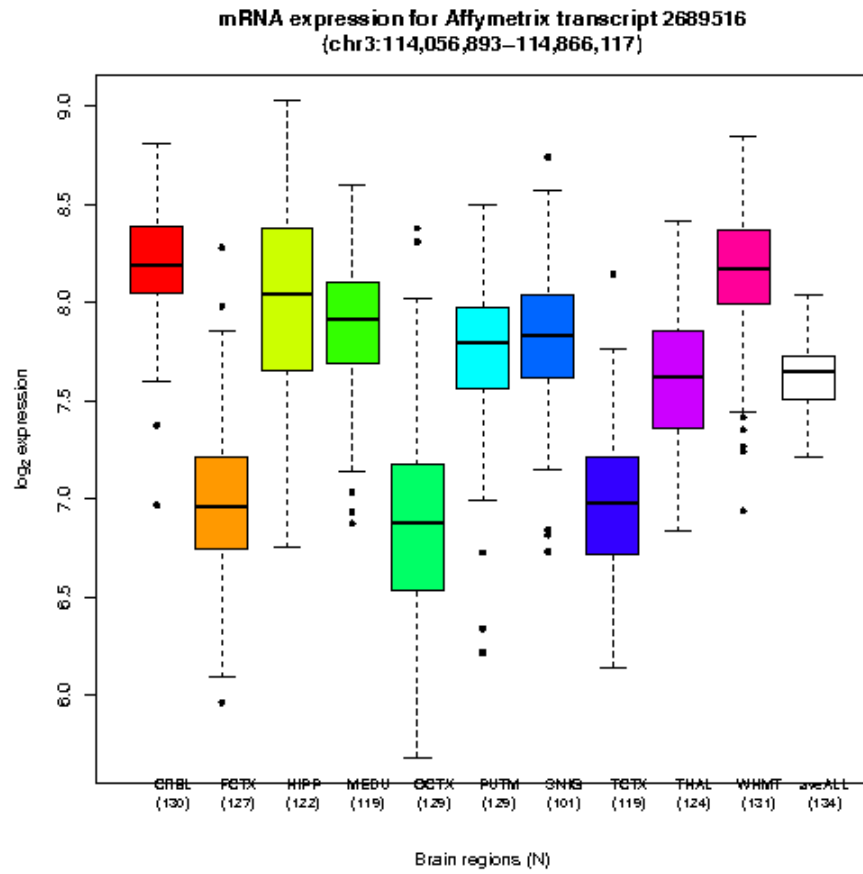
Supplementary Table 3: Linear mixed model on RPM factoring β values for age, depression, smoking, alcohol and BMI removing twin pairs taking anti-depressant medication. The nearest gene feature to a DMR is shown, DMRs occurring within a coding region are shown in bold.

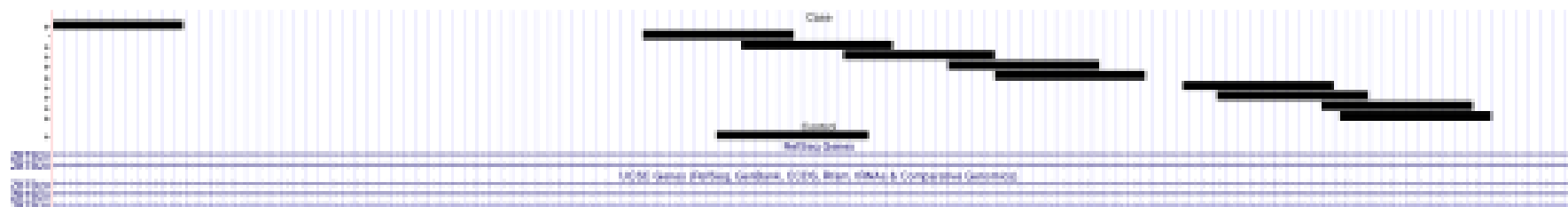
Chr	Start	Stop	age	depression	smoking	alcohol	BMI	p value	Gene	Description
chr4	78290251	78290750	-0.008	-1.510	0.302	-0.198	0.022	6.10E-10	CXCL13	chemokine (C-X-C motif) ligand 13
chr2	53454751	53455250	-0.013	-1.410	0.207	0.460	0.020	3.215E-09	ASB3	ankyrin repeat and SOCS box-containing 3
chr6	135940501	135941000	0.010	1.102	0.064	-0.325	0.008	7.234E-09	C6of217	chromosome 6 open reading frame 217
chr4	169263501	169264000	0.018	-1.111	0.339	0.212	0.032	2.962E-08	DDX60L	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like
chr12	39545251	39545750	0.013	-0.981	0.708	0.166	0.010	3.9165E-08	KIF21A	kinesin family member 21A (KIF21A)
chr8	135801001	135801500	0.009	1.368	-0.090	0.251	-0.022	5.521E-08	MIR30B	microRNA 30b (MIR30B)
chr4	5372501	5373000	-0.004	1.145	-0.805	0.105	0.031	7.6524E-08	STK32B	serine/threonine kinase 32B
chr2	57364001	57364500	0.005	-1.084	0.506	-0.124	0.010	8.6648E-08	CCDC85A	coiled-coil domain containing 85A
chr18	7832001	7832500	-0.022	1.245	-0.690	-0.079	-0.010	9.7331E-08	PTPRM	protein tyrosine phosphatase, receptor type, M
chr4	38369501	38370000	0.014	1.196	0.232	-0.340	-0.029	2.06855E-07	TBC1D1	TBC1 domain family, member 1 (TBC1D1)
chr15	54929501	54930000	0.004	1.255	0.269	0.353	-0.029	2.98876E-07	UNC13C	unc-13 homolog C (C. elegans)
chr12	5663001	5663500	-0.003	-1.121	0.114	0.618	0.006	3.36947E-07	ANO2	anoctamin 2
chr10	42449501	42450000	-0.005	1.280	0.022	-0.055	-0.045	3.6662E-07	LOC441666	zinc finger protein 91 pseudogene
chr1	121257001	121257500	-0.006	1.049	-0.106	0.134	-0.025	4.02892E-07	LOC647121	embigin homolog (mouse) pseudogene
chr1	182990501	182991000	-0.001	-1.302	-0.067	0.136	0.007	4.05204E-07	LAMC1	laminin, gamma 1 (formerly LAMB2)
chr18	11872501	11873000	-0.004	-0.918	0.334	0.136	-0.017	4.24429E-07	GNAL	guanine nucleotide binding protein (G protein)
chrX	74720751	74721250	-0.006	0.710	0.233	-0.681	-0.045	4.82299E-07	ZDHHC15	zinc finger, DHHC-type containing 15
chr3	78295751	78296250	-0.007	-1.232	0.464	0.058	0.006	5.17313E-07	ROBO1	roundabout, axon guidance receptor, homolog 1
chr1	155936001	155936500	0.023	0.911	-0.760	0.133	0.029	5.8406E-07	ARHGEF2	Rho/Rac guanine nucleotide exchange factor (GEF) 2
chr15	87282501	87283000	0.013	-1.014	0.423	0.127	0.016	6.14394E-07	ABGL1	ATP/GTP binding protein-like 1

Supplementary Table 4: Linear mixed model on Queensland dataset RPM values showing β values for age, depression, smoking, alcohol and BMI. The nearest gene feature to a DMR is shown, DMRs occurring within a coding region are shown in bold.

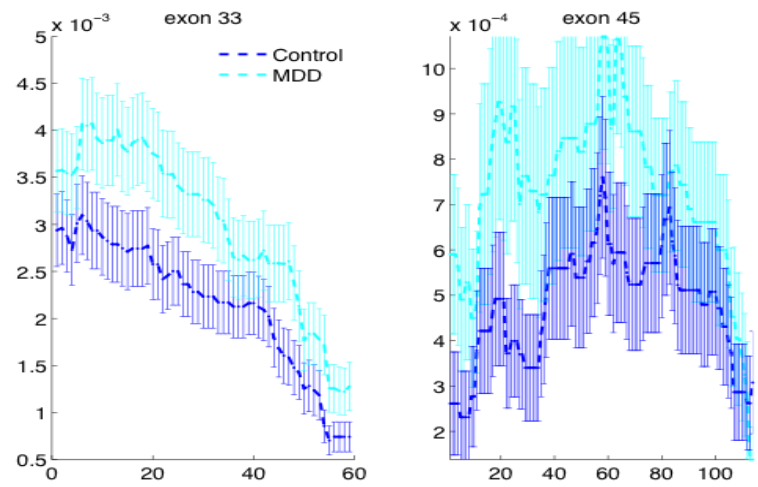
Chr	Start	Stop	depression	sex	age	alcohol	smoking	pvalue	Gene	Description
chr5	41245251	41245750	1.385	-0.209	-0.010	-0.488	0.445	6.08E-08	C6	complement component 6
chr3	134801751	134802250	-1.317	0.333	0.038	0.497	-0.098	8.86E-08	EPHB1	EPH receptor B1 (EPHB1), mRNA.
chr 4	151897751	151898250	1.358	-0.044	-0.030	-0.861	0.450	2.12E-07	LRBA	LPS-responsive vesicle trafficking
chr17	57718251	57718750	1.216	0.126	-0.002	-0.373	0.915	2.25E-07	CLTC	clathrin, heavy chain (Hc) (CLTC), mRNA.
chr3	150794001	150794500	-1.294	-0.158	-0.002	0.789	0.656	2.72E-07	CLRN1-AS1	CLRN1 antisense RNA 1 (non-protein coding)
chr6	41646751	41647250	-1.342	-0.013	0.017	0.393	0.246	3.17E-07	TFEB	transcription factor EB (TFEB), transcript variant 1,
chr9	71412501	71413000	-1.382	0.215	0.011	0.669	-0.740	3.30E-07	PIP5K1B	phosphatidylinositol-4-phosphate 5-kinase,
chr1	29137001	29137500	1.363	-0.154	-0.018	-0.143	0.230	3.54E-07	OPRD1	opioid receptor, delta 1 (OPRD1), mRNA.
chr6	163684001	163684500	1.376	0.125	0.007	-0.655	0.106	3.61E-07	PACRG	PARK2 co-regulated
chr3	136715501	136716000	1.251	-0.191	0.000	-1.020	0.614	3.82E-07	IL20RB	interleukin 20 receptor beta (IL20RB), mRNA.
chr6	96059251	96059750	1.346	0.332	0.002	-0.305	0.074	4.64E-07	MANEA	mannosidase, endo-alpha (MANEA), mRNA.
chr14	79080751	79081250	1.292	0.507	0.010	0.411	0.153	5.31E-07	NRXN3	neurexin 3 (NRXN3), transcript variant 1
chr4	169542751	169543250	1.171	0.495	-0.026	-0.202	0.451	6.43E-07	PALLD	palladin, cytoskeletal associated protein
chr14	90594001	90594500	-1.160	0.189	0.020	0.883	-0.633	6.69E-07	KCNK13	potassium channel, subfamily K,
chr1	164845751	164846250	1.352	-0.345	0.019	-0.044	-0.100	6.96E-07	PBX1	pre-B-cell leukemia homeobox 1
chr6	87788251	87788750	-1.254	-0.261	-0.011	0.276	0.474	7.02E-07	7SK	Rfam model RF00100
chr6	35890501	35891000	-1.228	0.341	-0.028	0.565	-0.404	7.46E-07	SRPK1	SRSF protein kinase 1
Chr4	5298251	5298750	0.846	0.329	-0.015	0.191	-0.349	7.76E-07	STK32B	serine/threonine kinase 32B (STK32B), mRNA.
chr6	51323001	51323500	-1.298	0.128	0.010	-0.300	0.168	7.86E-07	SNORD66	Rfam model RF00572
chr4	53457501	53458000	-1.307	-0.181	-0.019	0.025	0.450	8.29E-07	USP46	ubiquitin specific peptidase 46

Supplementary Figure 1: Averaged expression values of the ZBTB20 gene across ten brain regions





Supplementary Figure2. Example of discordant twin pair showing 10:1 ratio of case:control reads within the ZBTB20 DMR (chr3:114618751-114619251).



Supplementary Figure3. Average, per-base, normalized read counts in cases and controls for non-standard ZBTB20 exons 33 and 45 showing discordance for MDD. Positions are relative to the start of each exon. Error bars indicate the standard error.