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Table S1: Gene-Drug interaction mined from *The Drug-Gene interaction database*

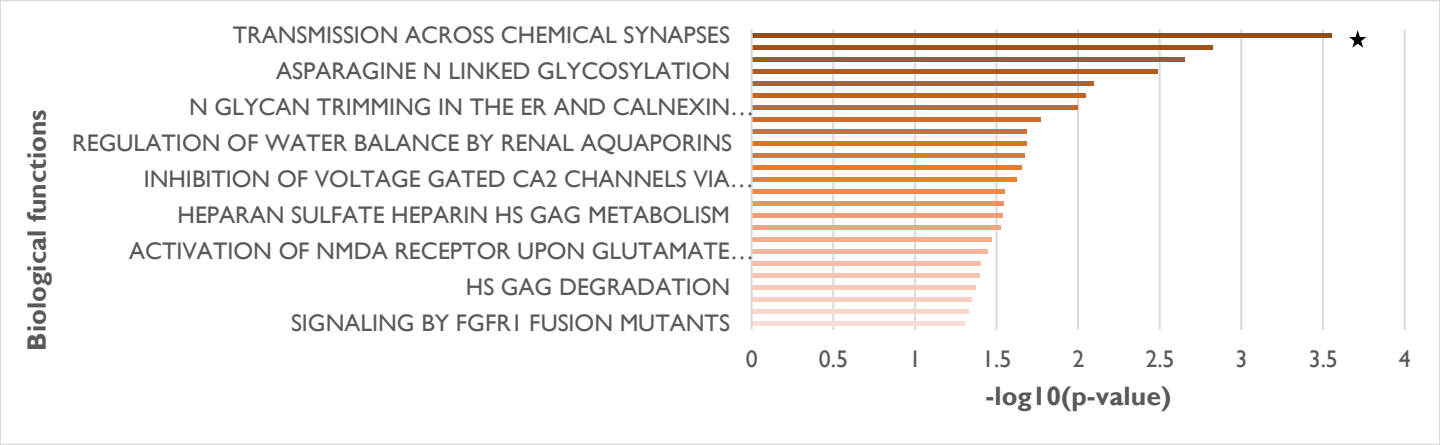
search_term	match_type	drug	interaction_types	sources	pmids
PTK6	Definite	VANDETANIB	inhibitor	ChemblInteractions|DrugBank	
PTK6	Definite	DYDROGESTERONE	inhibitor	GuideToPharmacologyInteractions	
PRKCI	Definite	CEP-2563	inhibitor	ChemblInteractions	
PRKCI	Definite	STAUROSPORINE	inhibitor	GuideToPharmacologyInteractions	
PRKCI	Definite	GSK-690693	inhibitor	ChemblInteractions	
PRKCI	Definite	(7S)-HYDROXYL-STAUROSPORINE	inhibitor	ChemblInteractions	
PRKCI	Definite	QUERCETIN	inhibitor	MyCancerGenome	
PRKCI	Definite	MIDOSTAURIN	inhibitor	ChemblInteractions	
PRKCI	Definite	SOTRASTAURIN	inhibitor	ChemblInteractions	
PRKCI	Definite	GF-109203		DrugBank	10592235
PRKCI	Definite	INGENOL MEBUTATE		TdgClinicalTrial	
NPY1R	Definite	CHEMBL422942	antagonist	TTD	
NPY1R	Definite	CHEMBL435278		DrugBank	
SRMS	Definite	TG100-801	inhibitor	ChemblInteractions	
SRMS	Definite	PIMOZIDE	inhibitor	GuideToPharmacologyInteractions	
SRMS	Definite	DASATINIB	inhibitor	ChemblInteractions	
SRMS	Definite	ENMD-981693	inhibitor	ChemblInteractions	
SRMS	Definite	ILORASERTIB	inhibitor	ChemblInteractions	
SRMS	Definite	XL-228	inhibitor	ChemblInteractions	
EPHX1	Definite	AR9281		TdgClinicalTrial	
EPHX1	Definite	DOCETAXEL		PharmGKB	
PARP1	Definite	NIACINAMIDE	binder	DrugBank|TTD	11752352
PARP1	Definite	OLAPARIB	inhibitor	MyCancerGenome|ClearityFoundationClinicalTrial|GuideToPharmacologyInteractions|ChemblInteractions|DrugBank|	25981132

				MyCancerGenomeClinicalTrial|TTD	
PARP1	Definite	RUCAPARIB	antagonist|inhibitor	TALC|MyCancerGenome|ClearityFoundationClinicalTrial|GuideToPharmacologyInteractions|ChemblInteractions|DrugBank	
PARP1	Definite	NIRAPARIB	inhibitor	TALC|MyCancerGenome|TdgClinicalTrial|ClearityFoundationClinicalTrial|GuideToPharmacologyInteractions|ChemblInteractions|TTD	
PARP1	Definite	HEPTANOATE	inhibitor	GuideToPharmacologyInteractions	
PARP1	Definite	TALAZOPARIB	inhibitor	TALC|ClearityFoundationClinicalTrial|GuideToPharmacologyInteractions|ChemblInteractions	
PARP1	Definite	VELIPARIB	inhibitor	TALC|MyCancerGenome|ClearityFoundationClinicalTrial|ChemblInteractions|DrugBank|CancerCommons|MyCancerGenomeClinicalTrial	10592235
PARP1	Definite	INOSINE	inhibitor	TTD	
PARP1	Definite	INIPARIB	inhibitor	TALC|MyCancerGenome|TdgClinicalTrial|TTD	
PARP1	Definite	TALAZOPARIB TOSYLATE	inhibitor	ChemblInteractions	
PARP1	Definite	RUCAPARIB CAMSYLATE	inhibitor	ChemblInteractions	
PARP1	Definite	CHEMBL123978		DrugBank	10592235|17139284|17016423
PARP1	Definite	CHEMBL134022		DrugBank	10592235
PARP1	Definite	CHEMBL452800		DrugBank	10592235
PARP1	Definite	CHEMBL123904		DrugBank	10592235
PARP1	Definite	CHEMBL125200		DrugBank	10592235|17139284|17016423

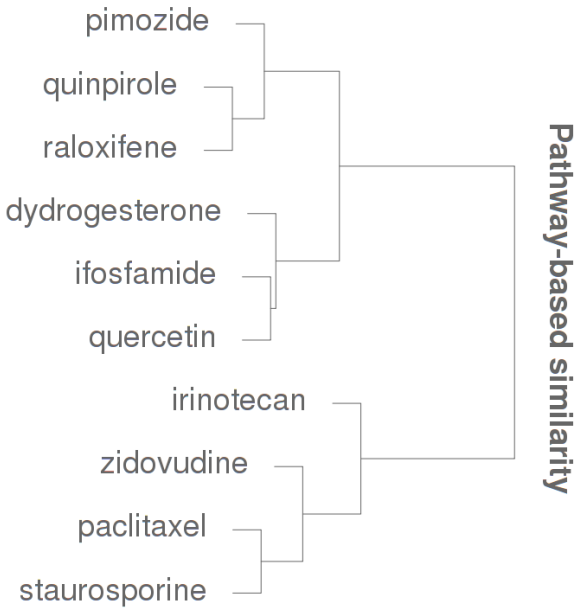
PARP1	Definite	CHEMBL401843		DrugBank	10592235|17139284|17016423
PARP1	Definite	CHEMBL338790		DrugBank	10592235
PARP1	Definite	CHEMBL361054		DrugBank	10592235
TERC	Definite	IFOSFAMIDE		NCI	10769656
TERC	Definite	CISPLATIN (CHEMBL2068237)		NCI	10769656
TERC	Definite	ZIDOVUDINE		NCI	11036953
SLK	Definite	DANUSERTIB	inhibitor	GuideToPharmacologyInteractions	
SLK	Definite	DASATINIB	inhibitor	TTD	
SLK	Definite	TOZASERTIB	inhibitor	TTD	
SLK	Definite	CHEMBL261720		DrugBank	10592235
PSME1	Definite	BORTEZOMIB	inhibitor	MyCancerGenome	
PSME1	Definite	CARFILZOMIB	inhibitor	MyCancerGenome	
SLC12A7	Definite	POTASSIUM CHLORIDE		DrugBank	16949074|16943364|17418819
ATM	Definite	CHEMBL1221601	inhibitor	GuideToPharmacologyInteractions	
ATM	Definite	KU-55933	inhibitor	GuideToPharmacologyInteractions	
ATM	Definite	SELUMETINIB		CIViC	27922010
ATM	Definite	VANDETANIB		CKB	27683183
ATM	Definite	BINIMETINIB		CKB	28514312
ATM	Definite	PACLITAXEL		CKB	26282658
ATM	Definite	VALPROIC ACID		CKB	20739657
ATM	Definite	TALAZOPARIB		ClearityFoundationBiomarkers|CKB	23881923
ATM	Definite	CHEMBL188678		CIViC	23761041
ATM	Definite	RUCAPARIB		ClearityFoundationBiomarkers	
ATM	Definite	BENDAMUSTINE		CKB	20739657
ATM	Definite	AZD-6738		CKB|CGI	26563132|26517239
ATM	Definite	TRAMETINIB		CIViC	27922010
ATM	Definite	VELIPARIB		ClearityFoundationBiomarkers|CKB	21300883|27638859
ATM	Definite	VX-970		CKB	28363999
ATM	Definite	NIRAPARIB		ClearityFoundationBiomarkers	
ATM	Definite	TEMOZOLOMIDE		CGI|CIViC	23960094

ATM	Definite	OLAPARIB		ClearityFoundationBiomarkers|OncoKB|CKB|CGI|CIViC	20739657|26510020|28363999|20124459|24841718|8|2014|26282658
ATM	Definite	CHEMBL1086377		CIViC	23761041
ATM	Definite	IRINOTECAN		CKB|CGI	27638859
ATM	Definite	AZD-6482		CKB	26563132
ATM	Definite	IBRUTINIB		CKB	26563132
ATM	Definite	FLUDARABINE		CKB	20739657
ATM	Definite	EVEROLIMUS		CKB	27683183
ATM	Definite	QUINPIROLE		CGI	
BCL2L2	Definite	NAVITOCLAX	inhibitor	TALC|TdgClinicalTrial|ChemblInteractions|DrugBank|TTD	
BCL2L2	Definite	CHEMBL376408	antagonist	GuideToPharmacologyInteractions	
BCL2L2	Definite	VENETOCLAX	antagonist	GuideToPharmacologyInteractions	
BCL2L2	Definite	OBATOCLAX MESYLATE	inhibitor	ChemblInteractions	
BCL2L2	Definite	CLADRIBINE		NCI	15813915
BCL2L2	Definite	BORTEZOMIB		NCI	15813915
DHRS4L2	Definite	MATAIRESINOL		DrugBank	10592235
TERT	Definite	ZIDOVUDINE	inhibitor	DrugBank	23303810
TERT	Definite	IMETELSTAT	inhibitor	TdgClinicalTrial|ChemblInteractions	
TERT	Definite	IMETELSTAT SODIUM	inhibitor	ChemblInteractions	
TERT	Definite	RALOXIFENE		NCI	15590986
TERT	Definite	ARSENIC TRIOXIDE		NCI	16285558
TERT	Definite	BEVACIZUMAB		NCI	15687494
TERT	Definite	OMACETAXINE MEPESUCCINATE		NCI	12744738

Fig S1. Drug Enrichment Set Analysis (DSEA). Analyzing enriched gene functions for drugs identified from drug-gene interaction



Mapped drugs on whom data was available in DSEA: dydrogesterone staurosporine quercetin pimozide ifosfamide zidovudine paclitaxel irinotecan quinpirole raloxifene



The bar graph on the top shows gene pathways that are nominally significant (p<0.05) and color of the bars correspond to the gradient of significance i.e. the lowest value p-value is shown from top to bottom. The FDR significant process is marked with a star. The x-axis shows -log10(p-value) of the processes from Reactome pathway database (y-axis). In the left box below the bar graphs are the 10 drugs on whom the data was available in the DSEA and were analyzed for gene function enrichment. The pathway similarity dendrogram on the right, groups drugs based on similarity of the drug-gene function sets.

Table S2: Tabular associations of DSEA shown in the above figure

Reactome Pathway Name	EScore	Pvalue	-log10(Pval)	FDR
TRANSMISSION ACROSS CHEMICAL SYNAPSES	-0.67	2.78E-04	3.555955	**0.018626**
AQUAPORIN MEDIATED TRANSPORT	-0.6	1.50E-03	2.823909	0.049803
CALNEXIN CALRETICULIN CYCLE	0.59	2.23E-03	2.651695	0.049803

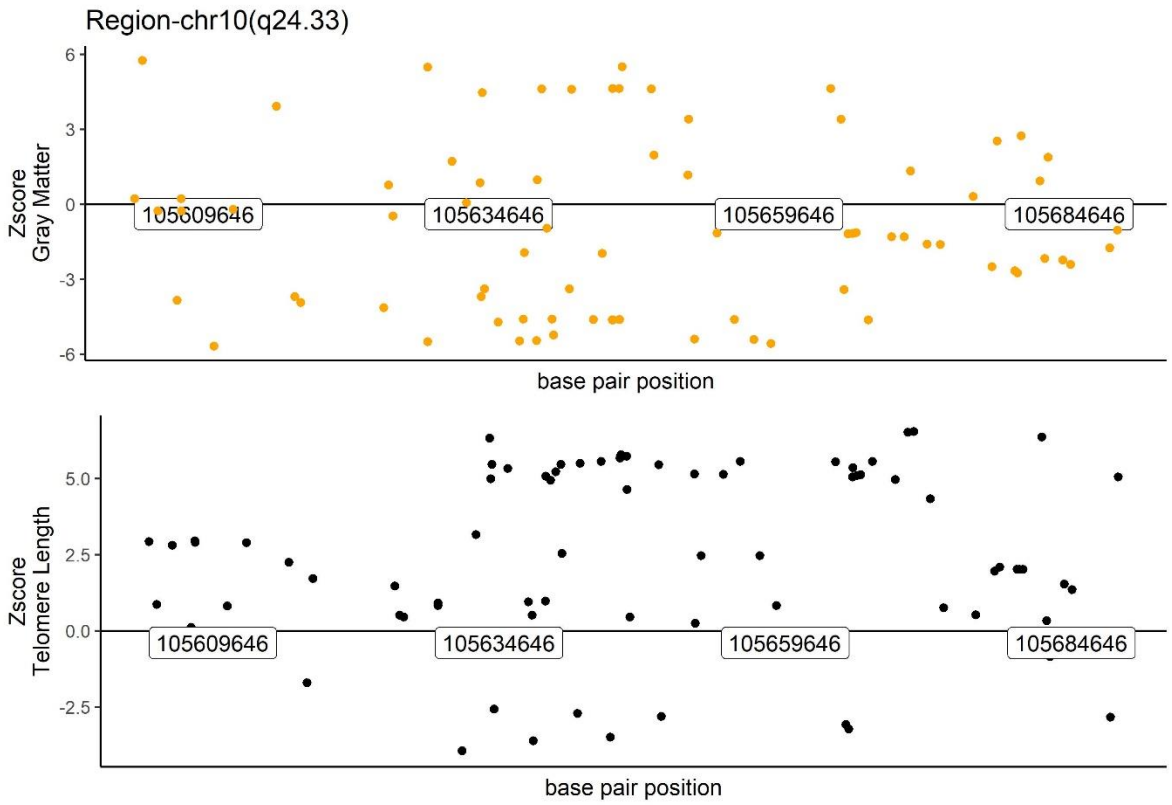
ASPARAGINE N LINKED GLYCOSYLATION	0.57	3.24E-03	2.489455	0.05427
MITOCHONDRIAL TRNA AMINOACYLATION	-0.53	8.02E-03	2.095826	0.095619
NEUROTRANSMITTER RECEPTOR BINDING AND DOWNSTREAM TRANSMISSION IN THE POSTSYNAPTIC CELL	-0.52	8.96E-03	2.047692	0.095619
N GLYCAN TRIMMING IN THE ER AND CALNEXIN CALRETICULIN CYCLE	0.52	9.99E-03	2.000435	0.095619
P38MAPK EVENTS	-0.49	1.69E-02	1.772113	0.117053
NEURONAL SYSTEM	-0.48	2.05E-02	1.688246	0.117053
REGULATION OF WATER BALANCE BY RENAL AQUAPORINS	-0.48	2.05E-02	1.688246	0.117053
POST TRANSLATIONAL PROTEIN MODIFICATION	0.48	2.11E-02	1.675718	0.117053
IL 7 SIGNALING	-0.48	2.20E-02	1.657577	0.117053
INHIBITION OF VOLTAGE GATED CA2 CHANNELS VIA GBETA GAMMA SUBUNITS	-0.47	2.36E-02	1.627088	0.117053
ACTIVATION OF THE PRE REPLICATIVE COMPLEX	-0.46	2.81E-02	1.551294	0.117053
IONOTROPIC ACTIVITY OF KAINATE RECEPTORS	-0.46	2.86E-02	1.543634	0.117053
HEPARAN SULFATE HEPARIN HS GAG METABOLISM	0.46	2.88E-02	1.540608	0.117053
COLLAGEN FORMATION	-0.46	2.97E-02	1.527244	0.117053
REGULATION OF INSULIN SECRETION BY GLUCAGON LIKE PEPTIDE1	-0.45	3.37E-02	1.47237	0.12
ACTIVATION OF NMDA RECEPTOR UPON GLUTAMATE BINDING AND POSTSYNAPTIC EVENTS	-0.45	3.57E-02	1.447332	0.12
DAG AND IP3 SIGNALING	-0.44	3.97E-02	1.401209	0.12
UNBLOCKING OF NMDA RECEPTOR GLUTAMATE BINDING AND ACTIVATION	-0.44	4.02E-02	1.395774	0.12
HS GAG DEGRADATION	0.44	4.24E-02	1.372634	0.12
E2F MEDIATED REGULATION OF DNA REPLICATION	-0.44	4.49E-02	1.347754	0.12
G BETA GAMMA SIGNALLING THROUGH PI3KGAMMA	-0.44	4.68E-02	1.329754	0.12
SIGNALING BY FGFR1 FUSION MUTANTS	-0.43	4.91E-02	1.308919	0.12
EXTRACELLULAR MATRIX ORGANIZATION	-0.43	5.13E-02	1.289883	0.12
PASSIVE TRANSPORT BY AQUAPORINS	-0.43	5.31E-02	1.274905	0.12
TRANSMEMBRANE TRANSPORT OF SMALL MOLECULES	-0.43	5.33E-02	1.273273	0.12
REPAIR SYNTHESIS FOR GAP FILLING BY DNA POL IN TC NER	-0.43	5.48E-02	1.261219	0.12
PYRUVATE METABOLISM AND CITRIC ACID TCA CYCLE	0.42	5.68E-02	1.245652	0.12
REGULATED PROTEOLYSIS OF P75NTR	0.42	5.90E-02	1.229148	0.12
PLATELET AGGREGATION PLUG FORMATION	-0.42	6.20E-02	1.207608	0.12
FANCONI ANEMIA PATHWAY	-0.42	6.29E-02	1.201349	0.12
RAP1 SIGNALLING	-0.41	7.31E-02	1.136083	0.12
METABOLISM OF NON CODING RNA	-0.41	7.32E-02	1.135489	0.12
ADVANCED GLYCOSYLATION ENDPRODUCT RECEPTOR SIGNALING	0.41	7.42E-02	1.129596	0.12
ACTIVATION OF RAC	-0.41	7.42E-02	1.129596	0.12
NITRIC OXIDE STIMULATES GUANYLATE CYCLASE	-0.41	7.62E-02	1.118045	0.12
INWARDLY RECTIFYING K CHANNELS	-0.4	7.97E-02	1.098542	0.12
SYNTHESIS OF PC	-0.4	8.38E-02	1.076756	0.12

G ALPHA S SIGNALLING EVENTS	-0.4	8.39E-02	1.076238	0.12
POST TRANSLATIONAL MODIFICATION SYNTHESIS OF GPI ANCHORED PROTEINS	0.4	8.49E-02	1.071092	0.12
TAK1 ACTIVATES NFKB BY PHOSPHORYLATION AND ACTIVATION OF IKKS COMPLEX	0.4	8.62E-02	1.064493	0.12
TRANSCRIPTIONAL REGULATION OF WHITE ADIPOCYTE DIFFERENTIATION	0.4	8.70E-02	1.060481	0.12
PACKAGING OF TELOMERE ENDS	0.4	8.91E-02	1.050122	0.12
GROWTH HORMONE RECEPTOR SIGNALING	-0.39	9.35E-02	1.029188	0.12
APOPTOSIS INDUCED DNA FRAGMENTATION	-0.39	9.46E-02	1.024109	0.12
GLUCAGON TYPE LIGAND RECEPTORS	-0.39	9.58E-02	1.018634	0.12
COSTIMULATION BY THE CD28 FAMILY	-0.39	9.71E-02	1.012781	0.12
CREB PHOSPHORYLATION THROUGH THE ACTIVATION OF CAMKII	-0.39	9.83E-02	1.007446	0.12
GENERIC TRANSCRIPTION PATHWAY	0.39	9.91E-02	1.003926	0.12
NUCLEAR EVENTS KINASE AND TRANSCRIPTION FACTOR ACTIVATION	0.39	9.92E-02	1.003488	0.12
INTRINSIC PATHWAY	-0.39	1.02E-01	0.9914	0.12
ACTIVATION OF KAINATE RECEPTORS UPON GLUTAMATE BINDING	-0.39	1.02E-01	0.9914	0.12
ADAPTIVE IMMUNE SYSTEM	0.39	1.03E-01	0.987163	0.12
RAS ACTIVATION UOPN CA2 INFUX THROUGH NMDA RECEPTOR	-0.39	1.05E-01	0.978811	0.12
HOST INTERACTIONS OF HIV FACTORS	-0.38	1.09E-01	0.962574	0.12
INTEGRATION OF PROVIRUS	-0.38	1.12E-01	0.950782	0.12
TRAFFICKING AND PROCESSING OF ENDOSOMAL TLR	0.38	1.12E-01	0.950782	0.12
SIGNALING BY ROBO RECEPTOR	-0.38	1.13E-01	0.946922	0.12
POST NMDA RECEPTOR ACTIVATION EVENTS	-0.38	1.16E-01	0.935542	0.12
CIRCADIAN CLOCK	0.38	1.17E-01	0.931814	0.12
NUCLEOTIDE LIKE PURINERGIC RECEPTORS	-0.38	1.17E-01	0.931814	0.12
ACTIVATION OF CHAPERONES BY ATF6 ALPHA	0.38	1.18E-01	0.928118	0.12
DOWNREGULATION OF TGF BETA RECEPTOR SIGNALING	-0.38	1.19E-01	0.924453	0.12
GAMMA CARBOXYLATION TRANSPORT AND AMINO TERMINAL CLEAVAGE OF PROTEINS	-0.38	1.20E-01	0.920819	0.12
RESOLUTION OF AP SITES VIA THE SINGLE NUCLEOTIDE REPLACEMENT PATHWAY	-0.38	1.20E-01	0.920819	0.12

Fig S2: Effect direction of SNPs in the shared causal region for LTL and brain volume measures

The regions which showed >90% probability of colocalization between LTL and brain volume measure have been shown here. The SNPs in each region exhibit different effect direction (Zscore) with respect to their phenotype. Therefore, their colocalization cannot be interpreted for direction of causality between the two phenotypes.

A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Zscore Gray Matter
6
3
0
-3
-6
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105634646
105659646
105684646
base pair position
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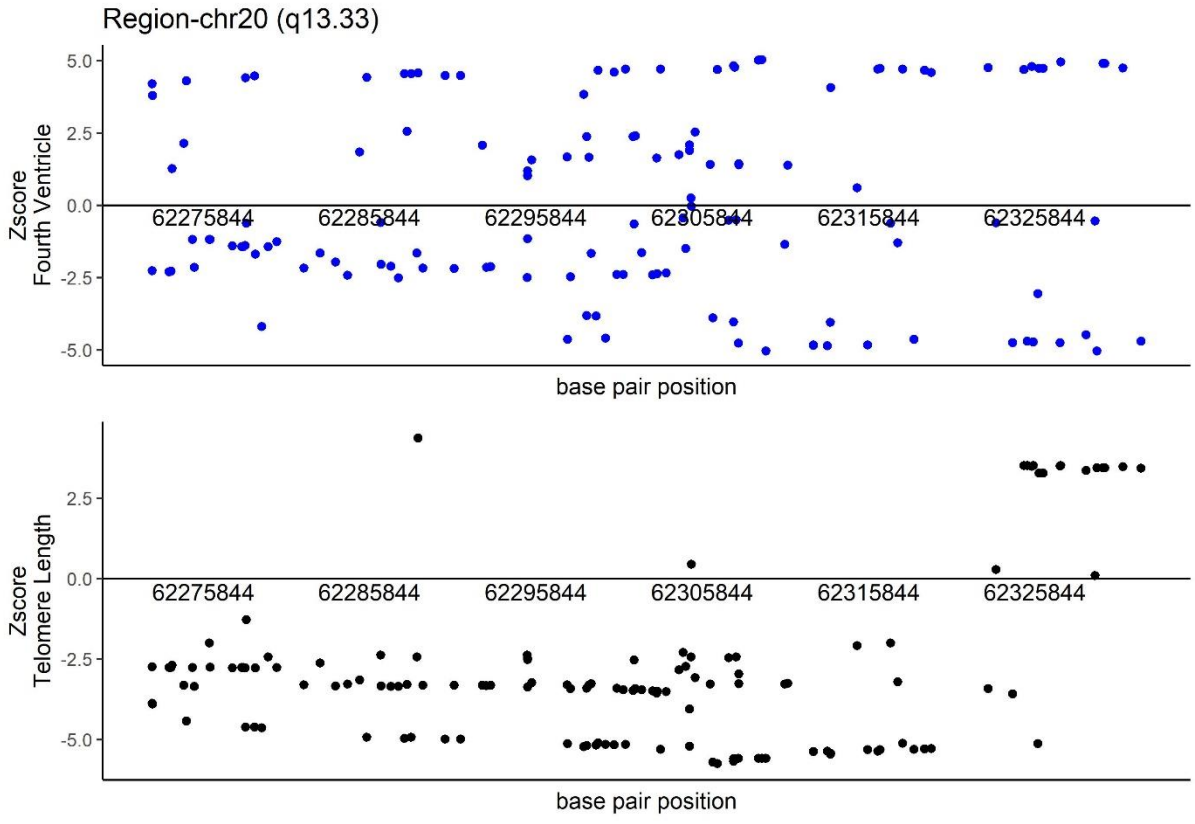
0.0
-2.5
105609646
105634646
105659646
105684646
base pair position

B


Region-chr20 (q13.33)
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-5.0
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62315844
62325844
base pair position
Zscore Telomere Length
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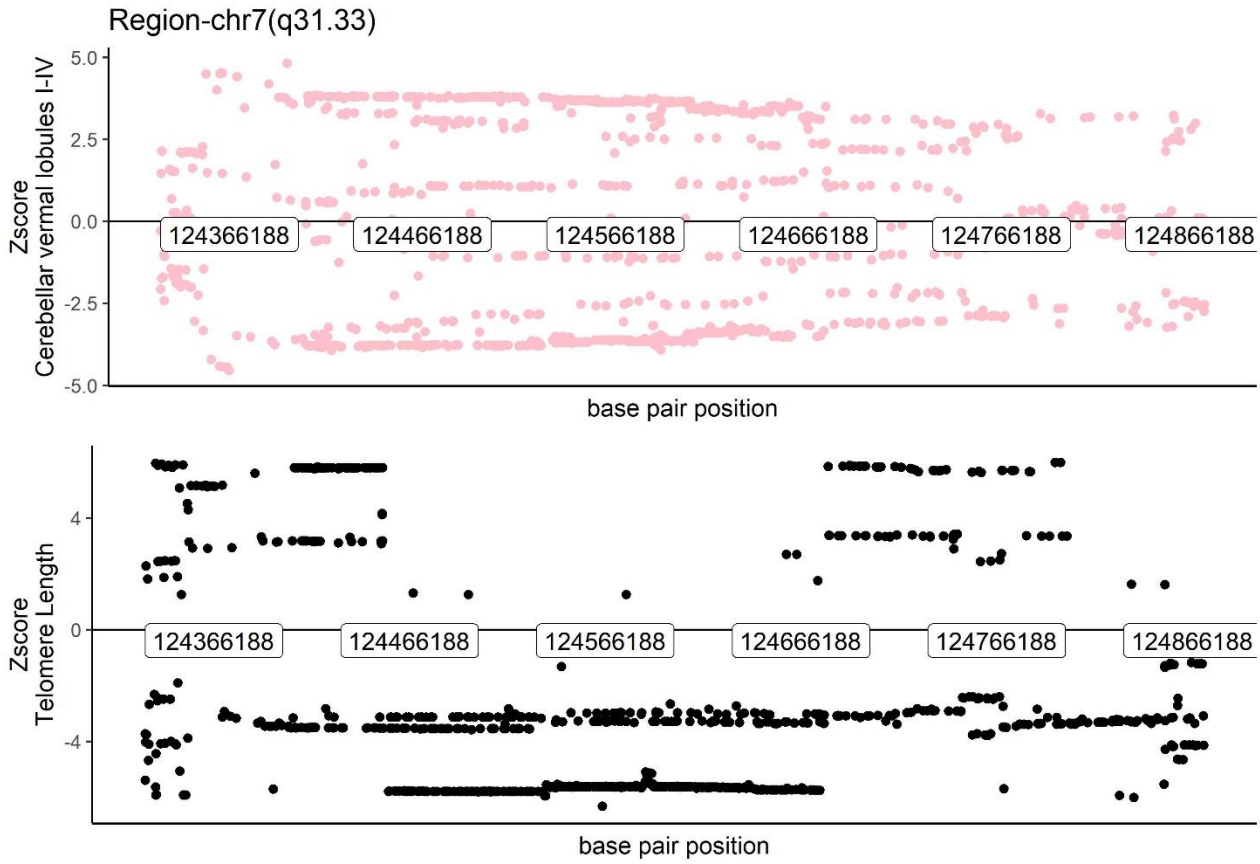
base pair position

C


Region-chr7(q31.33)
Zscore
Cerebellar vermal lobules I-IV
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2.5
0.0
-2.5
-5.0
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124466188
124566188
124666188
124766188
124866188
base pair position
Zscore
Telomere Length
4
0
-4
124366188
124466188
124566188
124666188
124766188
124866188
base pair position