

1 **Effects of MiR-137 Genetic Risk Score on Brain Volume and Cortical Measures in Patients with Schizophrenia and Controls**

Running title: Effect of MiR-137 PRS on sMRI Measures

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Abstract

Multiple genome-wide association studies of schizophrenia have implicated genetic variants within the gene encoding microRNA-137. As risk variants within or regulated by *MIR137* have been implicated in memory performance, we investigated the additive effects of schizophrenia-associated risk variants in genes empirically regulated by *MIR137* on brain regions associated with memory function. A polygenic risk score (PRS) was calculated (at a $p=0.05$ threshold), using this empirically regulated *MIR137* gene set, to investigate associations between this PRS and structural brain measures. These measures included total brain volume, cortical thickness, cortical surface area, and hippocampal volume, in a sample of 216 individuals consisting of healthy participants ($n= 171$) and patients with psychosis ($n=45$). We did not observe a significant association between *MIR137* PRS and these cortical thickness, surface area or hippocampal volume measures linked to memory function; a significant association between increasing PRS and decreasing total brain volume, independent of diagnosis status ($R^2 = 0.008$, Beta = -0.09 , $p = 0.029$), was observed. This did not survive correction for multiple testing. In conclusion, our study yielded only suggestive evidence that risk variants interacting with *MIR137* impacts on cortical structure.

Key words: polygene, GWAS, psychosis, total brain volume

Introduction

Genome-wide association studies (GWAS) of schizophrenia (SZ) have so far identified 108 regions of DNA encompassing ~350 genes. A strongly polygenic model of SZ, where the overall influence of many genes of small effect combine to increase an individual's predisposition to SZ has been robustly supported (Purcell et al., 2009). No one 'schizophrenia gene' of large effect has been identified, with the number of genes associated with the disorder increasing as GWAS sample size increases. This interplay of SZ risk genes is important to study, given the polygenic nature of the disorder. To characterise the phenotypic effects of multiple risk variants we and others have used polygenic risk scores calculated for gene sets based on either their involvement in a known biological pathway (Hargreaves et al., 2013), or based on evidence of their being regulated by target risk genes, e.g. *ZNF804A* (Nicodemus et al., 2014); *MIR137* (Cosgrove et al., 2017). In these studies, similar effects on cognitive function have been observed by studying either the risk variant individually or the gene network with which it interacts, although the network based analysis can sometimes explain a slightly higher percentage of variation (Cosgrove et al., 2017).

Genetic variants within the gene for microRNA 137 have been among the most significant findings in multiple GWAS (Ripke et al., 2013, The Schizophrenia Psychiatric GWAS Consortium, 2011, Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). In the 2011 PGC GWAS, the SNP rs1702294 was the strongest new finding; and in 2014, rs1625579 was the third most highly SZ-associated SNP, both sited in the region of *MIR137* ($r^2 = 0.99$ with rs1702294). Evidence also suggests that *MIR137* may not uniquely be associated with SZ (Hamshere et al., 2013). There is a strong genetic overlap between SZ and bipolar disorder (Cross-Disorder Group of the Psychiatric Genomics et al., 2013,

Moskvina et al., 2008), even leading to some questions about the diagnostic boundaries between these disorders (Lichtenstein et al., 2009). *In silico* and *in vitro* studies looking at the downstream effects of microRNA-137 have predicted or shown it to impact on the regulation of other genes linked to psychosis (Hill et al., 2014, Collins et al., 2014, Wright et al., 2013). In a study performed to characterise the regulatory effects of miR-137, under-expression of miR-137 led to a general upregulation of many genes, with the opposite shown in overexpression (Olde Loohuis et al., 2017). Risk alleles of four SZ-associated SNPs in the region of *MIR137* (rs1198588, rs1625579, rs2660304 and rs2802535) have been associated with downregulation of miR-137, specific to neuronal cells (Siegert et al., 2015).

MicroRNAs are responsible for the post-translational modification of RNA, altering the quantity of the gene products produced, which has implications for cell function (Yin et al., 2014). *MIR137* functions as a ‘fine-tuning’ agent for synaptic pruning and dendritic arborisation in neural cells and has been associated with, in addition to SZ, altered cognitive function (Kuswanto et al., 2015, Cummings et al., 2013, Green et al., 2013). Patients with SZ experience symptoms of cognitive dysfunction, which have been identified as being one of the largest obstacles to improving SZ patients’ functional outcome (Green et al., 2015). *MIR137* regulates processes that are potentially involved with cognitive dysfunction, in part by acting as a hippocampal gene network node, co-ordinating the expression of genes relating to nervous system function and development (Olde Loohuis et al., 2017). The risk alleles of each of the rs1702294 (C) and rs1625579 (T) SNPs have been linked to poorer scores on neuropsychological tests of memory performance (Cummings et al., 2013, Cosgrove et al., 2017). Furthermore, we previously observed an association between a *MIR137* PRS and memory scores, and between *MIR137* PRS and altered neural connectivity during performance of a fMRI working memory task (Cosgrove et al., 2017). There are conflicting

reports of the effect of the rs1625579 SNP on brain volume (Rose et al., 2014, Lett et al., 2013, Cousijn et al., 2014, Patel et al., 2015); however, to date, the effect of an empirically derived miR-137 regulated gene score on structural brain measures has not been established. Such investigations into potential associations between genetic pathways and brain-based correlates of cognitive phenotypes may assist in elucidating pathophysiological mechanisms that act as contributing factors to these cognitive deficits.

Given the link between *MIR137* and cognition, particularly memory function, the purpose of this study is to investigate the effects of a *MIR137* genetic risk score on measures of cortical thickness, cortical area, hippocampal volume and total brain volume in a sample of healthy participants and patients with psychosis. We hypothesise that participants carrying a higher *MIR137* polygenic risk burden, i.e. higher PRS, will show decreased cortical thickness, cortical area, hippocampal volume and total brain volume in comparison to those with a lower PRS.

Subjects and Methods

Participants

Participants were recruited in Dublin, patients through outpatient clinics (35 patients with SZ, 8 with schizoaffective disorder and 2 with bipolar disorder) and healthy participants through local media advertising. All participants were Irish, i.e. all four grandparents Irish. All participants were screened for MRI safety criteria, and provided written informed consent in accordance with the guidelines of the local ethics committee (St. James' Hospital). Healthy participants (n=171) age 18-65 were included if they had no history of psychiatric illness, head injury, or drug abuse. Healthy participant sampling at the Dublin site included individuals involved in the Trinity College Biobank project, described in (Rose et al., 2012). All patients (n=45) were chronic, but stable, medicated outpatients, with a confirmed a DSM-IV diagnosis. Demographic and other additional information is presented in **Table 1**.

Magnetic Resonance Imaging (MRI)

Structural MRI sequences were acquired on a Philips Intera Achieva 3T MR system, with whole-brain imaging consisting of a T1-weighted image (180 slices; duration 6 min) using a TFE gradient echo pulse sequence, with a slice thickness of 0.9 mm, and 230×230 FOV.

FreeSurfer MRI Processing

Structural MRI images were reconstructed into a three dimensional model of the cortical thickness measurements using FreeSurfer v5.3 which allows for cortical thickness and surface area measurements at numerous locations (vertices) across the surface (Dale et al.,

1999). Processed images were prepared for analysis using the ENIGMA protocol. Briefly, the automated -recon-all function was performed on each scan. Each image underwent motion correction, intensity normalisation, transformation to Talairach space and skull stripping. Mathematical outliers were detected by using R software as per the ENIGMA protocol. In addition to this, each output was visually inspected for T1 quality (artefacts, contrast, resolution, intensity) and to ensure adequate reconstruction. Manual edits to pial surfaces and white matter intensity were carried out where necessary by trained researchers (DC, JH).

Cortical reconstruction, parcellation and segmentation of T1 images were performed using the FreeSurfer 5.3 pipeline, available online. A full description of the FreeSurfer reconstruction process can be found by Dale et al. 1999 (Dale et al., 1999) and Fischl et al. 1999 (Fischl et al., 1999a). The MRI image is 3D rendered into a volume from the MRI into 256 coronal slices (1mm x 1mm x 1mm voxels) and undergoes automated transformation to the Talairach atlas (Talairach and Tournoux, 1988). Intensity normalization is then performed (Sled et al., 1998) to correct non-uniformity in the image due to radiofrequency field. The variation in white matter intensity is then used to estimate the bias field across the entire volume, and the effect of bias field removed by dividing the intensity at each voxel by the estimated bias field at that location. Following this, skull stripping (using a method combining watershed algorithms and deformable surface models) removes the non-brain tissue such as scalp, skull and neck tissue, extracting an initial brain volume (Ségonne et al., 2004). The grey/white matter boundary is estimated by classifying all white matter voxels in an MRI volume, and cerebral white matter segmentation is performed (Fischl and Dale, 2000), deforming this representation of the grey/white boundary outward to the pial surface (Fischl et al., 2001). The WM volume is tiled with a triangular tessellation on each hemisphere to generate an initial surface. The surface deformation follows intensity gradients between white and gray matter, placing the grey/white matter or cerebrospinal fluid borders

at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale and Sereno, 1993, Dale et al., 1999, Fischl and Dale, 2000). The average of the distance from the WM surface to the closest point on the pial surface and from that point back to the closest point on the WM surface gives us the thickness at each location of cortex (Fischl and Dale, 2000). The inflation of the cortical surface is performed so that activity occurring inside sulci may be easily visualized (Fischl et al., 1999b, Fischl et al., 1999a) and each location on the cortical surface is assigned a neuroanatomical label (34 gyral based regions) based on probabilistic information estimated from a manually labelled training set, and also scan-specific measured values (Fischl et al., 2004b, Desikan et al., 2006). Segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles) is performed (Fischl et al., 2002, Fischl et al., 2004a).

Using the ENIGMA protocol for the analysis of mean cortical thickness and surface area data within FreeSurfer ROIs, values for surface area and thickness were extracted. Following this, outliers were identified using R. MATLAB was used to plot cortical surface segmentations directly on each participant's scan and collate snapshots of these into a webpage for visual inspection (the internal surface QC method). The ENIGMA External QC method was performed to check cortical labels and anatomical boundaries. Furthermore, images underwent a thorough visual inspection of each image slice in the coronal, sagittal and axial planes using Freeview.

>>Table 1<<

The automatic segmentation tool Volbrain was used for estimation of hippocampal volume because it is the most accurate method to segment the hippocampus, according to the European Alzheimer's Disease Consortium harmonised hippocampus segmentation protocol, which compares results from software with results from expert manual tracing. This system was used for hippocampal reconstruction as it has been shown that other imaging segmentation software, including FreeSurfer, can overestimate subcortical structures (Manjón and Coupé, 2016). Further information on sMRI processing is available in **Appendix 1**.

VolBrain

The VolBrain pipeline is based on a library of manually labelled templates, constructed from publically available databases: 30 healthy adults, 10 patients with Alzheimer's disease, and 10 infant cases. The pipeline is a set of processing tasks that aims to improve image quality and intensity, and set images into a specific geometric space. Automatic pre-processing of T1-weighted images using the following steps is carried out: denoising and enhancement image quality, inhomogeneity correction, MNI space registration, fine inhomogeneity correction, intensity normalisation, non-local intracranial cavity extraction (white matter, gray matter, and cerebrospinal fluid), tissue classification, non-local hemisphere segmentation (splits brain into five: right and left cerebrum/cerebellum, and brainstem), and non-local subcortical structure segmentation. A more detailed description by Manjón and Coupé (2016) is available.

Genotyping

Genotyping was conducted on DNA samples that were extracted from whole blood or saliva. Samples were genotyped using either Affymetrix 6.0 chip (Santa Clara, CA, USA), as part of the WTCCC2 (Irish Schizophrenia Genomics Consortium and the Wellcome Trust Case Control Consortium, 2012), or Illumina HumanCoreExome chip Illumina (Cardiff sample; San Diego, CA) with full GWAS data available for all participants. Imputation was carried out on these data sets separately using 1000 Genomes Phase I integrated haplotypes (Dec 2013 release) and IMPUTE2 to give ~ 10 million SNPs genome-wide per sample.

Polygene Score

We constructed the *MIR137* PRS based on a set of 1991 genes affected by the up- and downregulation of *MIR137* in human neural progenitor cells (Hill et al., 2014). Of these, 1386 genes that were unambiguously mapped to autosomes were used to generate the PRS (**Supplementary Table 1**). First, the genetic coordinates (+/- 20kb) of these genes were identified (Kent et al., 2002), UCSC hg19 Feb 2009 release. SNPs within these regions were then extracted from our Irish GWAS samples (WTCCC2 and Cardiff; 208,040 and 194,123, respectively). PLINK v1.07 software (Purcell et al., 2007) was used to perform quality control on data from each sample (Affymetrix 6.0 and Illumina HumanCoreExome) separately: SNPs were excluded from further analysis if there was missing genotype data for >10%, Hardy-Weinberg equilibrium $< 1 \times 10^{-5}$, or MAF < 1%. Next, the lists of SNPs that passed QC for each sample were joined, providing a SNP list common to each sample (n=185,259 SNPs) regardless of genotyping platform used. This list of common SNPs was used in further analysis. LD clumping was performed separately in each sample using PLINK (-clump, $r = 0.25$, distance = 250kb) due to slightly differing LD, giving a list of 2,214 (Cardiff Illumina sample) and 2,235 (WTCCC2 Affymetrix sample) SNPs. Following this,

the PRS was generated for each sample using the LD clump results from the Affymetrix sample. The PRS did not significantly change based on which LD clump results were used: when the PRS was generated using the Illumina sample LD clump values, the results were highly correlated ($r=0.9$, $p<0.001$). The PRS risk threshold defined here was $p=0.05$. Previous studies have used multiple PRS thresholds to investigate associations, however, in prior work we have observed a threshold of $p=0.05$ to be the most informative (Cosgrove et al., 2017). Finally, each participant was given a PRS based number of risk alleles that they carried for each SNP, with alleles weighted by their effect size from the PGC2 GWAS (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014) (using the $-score$ function in PLINK). These effects sizes were taken from a meta-analysis of the PGC2 sample minus all Irish samples to make sure that the discovery and target samples used here were independent.

Statistical Analysis

Age, gender and intracranial volume were used as covariates in all analyses. Whole brain, vertex based analysis was carried out to estimate any effect of PRS on cortical thickness or cortical surface area of the left or right hemispheres. This was performed using the general linear model in QDEC (FreeSurfer), corrected for false discovery rate <0.05 . Analysis of *MIR137* PRS effect on total brain volume and hippocampal volume was performed in SPSS version 23 (IBM Corp, 2015), with moderation analyses carried out using the PROCESS macro for SPSS.

Results

Participant demographics, brain volume measures and *MIR137* PRS values are displayed in **table 1**. Reflecting the fact that healthy participants were recruited separately from patients rather than as a ‘control’ group, patients were on average older and mostly male. As expected, patients had a significantly higher *MIR137* PRS ($t_{(214)} = -3.16, p < 0.05$). The patient groups were also observed to show lower hippocampal volume ($t_{(214)} = 2.12, p < 0.05$) compared to healthy participants. Brain volume did not show statistically significant differences between cases and controls, although trend level differences for patients to show lower brain volumes were observed ($t_{(214)} = 1.82, p = 0.071$, **table 1**).

MIR137 PRS & Total Brain Volume

In the full sample of patients and controls, an effect of PRS on total brain volume was observed ($R^2 = 0.008$, Beta = -0.09, $p = 0.029$, **table 2**). After correcting for the four sets of analysis carried out however, this finding was no longer significant. As a *post hoc* analysis a moderation analysis was carried out using diagnosis (healthy participants vs. patients with psychosis) as the moderator to determine whether this trend level effect was influenced by diagnosis. After co-varying for the effects of age, gender and intracranial volume, no significant moderating effects of diagnosis on the relationship between *MIR137* PRS and brain volume ($p = 0.96$, $R^2 = 0.00$) were observed, suggesting that the relationship between *MIR137* and brain volume was comparable in both groups. An additional analysis was performed to investigate the effect of medication on this nominally significant finding. Most patients in our sample were medicated, with current medication dose in chlorpromazine equivalent (CPZE) available for 36 out of the 45 patients; healthy participants were not taking any antipsychotic medication. When the analysis was run again including CPZE as well as

age, gender and ICV, the strength of association observed between increasing *MIR137* PRS and lower brain volume decreased ($R^2 = 0.005$, Beta = -0.072, $p = 0.087$).

MIR137 PRS & Cortical Thickness and Surface Area

No effect of *MIR137* PRS was observed on either cortical thickness or surface area (corrected for false discovery rate <0.05).

MIR137 PRS & Hippocampal Volume

No effect of *MIR137* PRS on hippocampal volume, estimated from segmentation results from VolBrain was observed (**Table 2**).

>>Table 2<<

Discussion

In this study we sought to determine the effect of a SZ-associated, empirically derived, miR-137 regulated gene score on measures of cortical thickness and area, hippocampal volume, and total brain volume. Given the previous reported associations between *MIR137* PRS and cognitive performance, most notably with lower scores on neuropsychological measures of memory function, we hypothesised that a higher PRS would be associated with a decreased cortical thickness and surface area, decreased hippocampal volume and lower total brain volume. No significant association between either cortical thickness or surface area or hippocampal measures and *MIR137* PRS were observed. While association between PRS and total brain volume was nominally significant, when medication (CPZE) was included as an additional covariate in the analysis, this nominally significant association between increasing *MIR137* PRS and decreasing brain volume was no longer significant.

To the best of our knowledge, no study has examined the effect of a *MIR137* PRS score on cortical thickness, shape or volume. Previous imaging studies have investigated the effect of the SZ-associated *MIR137* SNP rs1625579 on brain structure, activation and connectivity and have provided mixed results: this might partly be expected based on the study samples (inclusion of healthy participants only, compared to those looking at patient populations), as well as different regions of interest studied, and the different fMRI tasks used, if any. The first study to investigate the effects of rs1625579 on brain structure by Lett et al. (2013) showed significantly increased ventricle volume in both SZ patients (n=92) and controls (n=121) homozygous for the risk (TT) allele, processed using tools from the FMRIB Software Library (FIRST). In addition, decreased hippocampal volume was observed, but only in patients homozygous for the risk (TT) allele (Lett et al., 2013). Two subsequent structural neuroimaging studies however did not replicate these findings. Cousijn et al. (2014) analysed a large sample of healthy participants (n=1300), also using FIRST. No effects of

rs1625579 genotype on total brain, grey matter, white matter, or hippocampal volumes were observed. Rose et al. (2014) Rose et al. (2014) also looked at the effect of the same *MIR137* rs1625579 risk variant in a voxel-based morphometry study (using SPM) of grey and white matter volume in patients with SZ (n=163) and healthy participants (n=150) and did not observe any significant effects. Similarly, no significant association between genotype and volume of any subcortical regions analysed (using FIRST) was identified in this study, including the hippocampus. The results of the present study are comparable to the results of the larger two of the three studies in terms of the lack of effect of rs1625579 on hippocampal volume. Furthermore, in one of these larger studies, an association between the rs1625579 risk allele and increased ventricle size was reported (Lett et al., 2013). As ventricle size and total brain volume are inversely correlated (Horga et al., 2011), this increased ventricular volume association may be comparable to the link between decreased total brain volume and PRS in the present study. A final structural MRI study reported by Patel et al. (2015) examined the effect of rs1625579 genotype on subcortical and callosal volumes and reported evidence of an association between the risk (G) allele and decreased corpus callosum volume in SZ patients only (n=362) compared to controls (n=490). We did not examine this measure in our sample, although potentially a decrease in corpus callosum volume may contribute to the decrease in overall brain volume reported here.

In this study, we selected only one threshold of polygene score for investigation to limit the multiple testing burden, but is possible that different score thresholds would yield different results. This was not the case in our previous analyses of the cognitive effects of the *MIR137* PRS however, where similar effects were observed across three thresholds analysed ($p=10^{-5}$, $p=0.05$, $p=0.5$), but most strongly at the $p=0.05$ threshold (Cosgrove et al., 2017), which was the threshold used in this study.

An endophenotypic approach was employed here, i.e. characterising the effects of SZ-associated variants on cortical metrics rather than disease or clinical symptoms (Gottesman and Gould, 2003). The selection of a robust sMRI phenotype to investigate genetic effects is one of the strengths of this study. Total cortical surface area and average cortical thickness are both highly heritable (Panizzon et al., 2009), as is total brain volume (Hulshoff Pol et al., 2002). As surface area and thickness are genetically uncorrelated metrics, these were both investigated (Winkler et al., 2010, Tandon et al., 2016). It has been suggested that cortical thickness is of greater aetiological interest than volume or surface area measures due to the proposed neurodevelopmental mechanisms thought to contribute to SZ and cognitive deficits (Geisler et al., 2015), although no association was observed here between either measure and the *MIR137* PRS. In a meta-analysis comparing cognitive and brain imaging phenotypes, results suggested that SZ variants have greater penetrance on measures of brain structure than other phenotypic measures, such as cognitive performance (Rose and Donohoe, 2013).

The lack of effect of the *MIR137* PRS on any specific cortical region or on the hippocampus and the small effect observed for total brain volume (although not significant after either multiple testing correction, or correction for medication effects) may imply a subtle effect of *MIR137* and its interacting network on more widespread neurological structure, as opposed to being specific to memory-related components. A role of *MIR137* in influencing brain microstructure has previously been established: it has an important role in regulation of target genes linked with neural stem cell proliferation and differentiation during neural development (Mahmoudi and Cairns, 2017). Its role beyond this in terms of how these molecular and cellular effects of *MIR137* itself and the whole *MIR137* network impact brain macrostructure is yet to be defined; however, multiple studies provide evidence that *MIR137* may exert some effect through influence of rs1625579 risk (T) genotype on functional connectivity and neural activation (Mothersill et al., 2013, Liu et al., 2014, Whalley et al., 2012, van Erp et al., 2014).

Due to the extensive regulation of other genes by miRNAs, the dysregulation of even one of these may confer a large polygenic effect. In addition to this, there is evidence that *MIR137* also regulates other genes that harbour SZ-associated variants such as *ZNF804A*, *TCF4*, *CACNA1C*, *CSMD1*, *C10orf26* (Kim et al., 2012, Wright et al., 2013, Guan et al., 2014, Kwon et al., 2013). These convergent pathways linked by *MIR137* may contribute to SZ: previous pathway analysis of miR-137 targets implicated several aspects of nervous system function and development associated with SZ, such as ephrin receptor signalling, axonal guidance signalling and long term potentiation (Wright et al., 2013).

In this study, our sample is comparable, in terms of sample size, with the other studies discussed that investigated the effects of rs1625579 on cortical structures and total brain or hippocampal volumes. Other studies reporting on effects of polygene scores on brain measures include a range of sample sizes. Neilson et al. (2016) reported an association between a SZ polygenic risk score on cortical thinning in patients based on a small sample of 46 patients and 33 controls. Studies such as this with smaller sample sizes report positive associations, however, the replicability of some findings in these smaller study sizes have been questioned (Button et al., 2013). Van der Auwera et al. (2015) observed no effect of a SZ PRS on various structural measures in a large sample of 1,470 healthy participants. Further studies are required to determine if the *MIR137* PRS effects on cortical and hippocampal measures reported here are truly non-significant or whether the uncorrected total brain volume finding may have underestimated an actual effect.

One limitation of this study is that most of our sample was made up of healthy participants. If a potential diagnosis-specific effect was to be identified, a larger patient group would likely be required. As this is the first study to characterise the effect of polygene score on brain structure measures, replication in a different sample is required to further support these findings, preferably in a larger patient population in order to determine whether or not there

are specific disease related consequences of carrying a higher burden of SZ-risk variants in this *MIR137* pathway. In addition, a potential limitation in all imaging studies is that different types of software are used to reconstruct T1 images that can estimate brain volumes differently based on the algorithms used, as well as different QC methodologies. No MDS components were included in the PRS analyses here as the Irish GWAS sample used in the study indicated that the sample was homogeneous. However, it may still be possible that some population stratification effects were present in this sample.

In conclusion, we have not shown evidence of any association between *MIR137* PRS and specific cortical correlates of memory. An association between increasing PRS and decreasing total brain volume however was identified. Further studies with larger sample sizes that include more SZ patients would help clarify the dissociable effects of this microRNA on measures of cognitive function compared to effects in controls. Additional investigations into this miRNA pathway may provide new lines of research to explore in terms of developing a biomarker or therapeutic strategy for SZ.

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Conflict of Interest

The authors declare no conflict of interest specific to this work.

Web Resources

UCSC: <http://genome.ucsc.edu>

ENIGMA: <http://enigma.usc.edu/>

FreeSurfer: <http://surfer.nmr.mgh.harvard.edu>

VolBrain: <http://volbrain.upv.es>

R: <https://www.r-project.org/>

Process: <http://processmacro.org>).

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Tables

Table 1. Participant demographics, brain volume measures and *MIR137* genetic risk score (PRS).

	Healthy Participants	Patients	t	df	p
n	171	45	-	-	-
Age	28.57 (10.06)	41.73 (9.77)	-7.85	214	<0.001
Female %	56.14	29.55	3.32	214	<0.05
Education Years	17.10 (3.16)	14.15 (3.95)	4.58	132	<0.001
<i>MIR137</i> PRS	-0.00201 (0.0003)	-0.00185 (0.0003)	-3.16	214	<0.05
<i>MIR137</i> PRS (standardised z score)	-0.11 (0.98)	0.41 (0.99)	-3.16	214	<0.05
Brain Volume (cm3)	11579.45 (1229.44)	11206.31 (1209.52)	1.82	214	0.071
Hippocampal Volume (cm3)	7.88 (0.85)	7.58 (0.87)	2.12	214	<0.05

Table 2. Effect of *MIR137* PRS (standardised z-score) on hippocampal and total brain volume (age, gender, ICV as covariates).

Measure	B	SE B	Beta	R ²	p
Hippocampal Volume (cm3)	0.032	0.044	0.037	0.001	0.472
Brain Volume (cm3)	-111.96	50.77	-0.091	0.008	0.029*

Supplementary File 1 - sMRI Processing and QC

FreeSurfer MRI Processing

Cortical reconstruction, parcellation and segmentation of T1 images were performed using the FreeSurfer 5.3 pipeline, available online (<http://surfer.nmr.mgh.harvard.edu/>). A full description of the FreeSurfer reconstruction process can be found by Dale et al. (1999) and Fischl et al. (1999a). The MRI image is 3D rendered into a volume from the MRI into 256 coronal slices (1mm x 1mm x 1mm voxels) and undergoes automated transformation to the Talairach atlas (Talairach and Tournoux, 1988). Intensity normalization is then performed (Sled et al., 1998) to correct non-uniformity in the image due to radiofrequency field. The variation in white matter intensity is then used to estimate the bias field across the entire volume, and the effect of bias field removed by dividing the intensity at each voxel by the estimated bias field at that location. Following this, skull stripping (using a method combining watershed algorithms and deformable surface models) removes the non-brain tissue such as scalp, skull and neck tissue, extracting an initial brain volume (Ségonne et al., 2004). The grey/white matter boundary is estimated by classifying all white matter voxels in an MRI volume, and cerebral white matter segmentation is performed (Fischl and Dale, 2000), deforming this representation of the grey/white boundary outward to the pial surface (Fischl et al., 2001). The WM volume is tiled with a triangular tessellation on each hemisphere to generate an initial surface. The surface deformation follows intensity gradients between white and gray matter, placing the grey/white matter or cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale and Sereno, 1993, Dale et al., 1999, Fischl and Dale, 2000). The average of the distance from the WM surface to the closest point on the pial surface and from that point back to the closest point on the WM surface gives us the thickness at each location of cortex (Fischl and Dale, 2000). The inflation of the cortical surface is performed so that activity

occurring inside sulci may be easily visualized (Fischl et al., 1999b, Fischl et al., 1999a) and each location on the cortical surface is assigned a neuroanatomical label (34 gyral based regions) based on probabilistic information estimated from a manually labelled training set, and also scan-specific measured values (Fischl et al., 2004b, Desikan et al., 2006). Segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles) is performed (Fischl et al., 2002, Fischl et al., 2004a).

Using the ENIGMA protocol for the analysis of mean cortical thickness and surface area data within FreeSurfer ROIs, values for surface area and thickness were extracted. Following this, outliers were identified using R (<https://www.r-project.org/>). This involves running an R script (<http://enigma.ini.usc.edu/wp-content/uploads/CORTEX/outliers.R>) to identify any images that have outlier values in any of the 73 cortical measures extracted from FreeSurfer. In this script, outliers are defined as any data points that are more than 1.5 times the interquartile range before quartile 1 or after quartile 3 (z scores equivalent to -2.68 or greater than 2.68). Observation of outlier values does not exclude these images from all further analysis automatically, but rather indicates that further inspection to verify image quality is required. Visual inspection is performed on any outlying regions, e.g. where the region may have been poorly segmented by the software. MATLAB was used to plot cortical surface segmentations directly on each participant's scan and collate snapshots of these into a webpage for visual inspection (the internal surface QC method). The ENIGMA External QC method was performed to check cortical labels and anatomical boundaries. Furthermore, images underwent a thorough visual inspection of each image slice in the coronal, sagittal and axial planes using Freeview. The ENIGMA Cortical Quality Control Protocol for QC of images was followed (<http://enigma.ini.usc.edu/protocols/imaging-protocols/>). While a number of outliers were identified in our sample, there were no more than two outliers/regions identified

for any one image. These were inspected visually and were not found to be visually abnormal; thus were kept in the analysis. One or two outlying regions are unlikely to bias a whole-hemisphere vertex based analysis. Based on this protocol, after QC, no scans met the criteria for exclusion.

VolBrain

The VolBrain pipeline is based on a library of manually labelled templates, constructed from publically available databases: 30 healthy adults, 10 patients with Alzheimer's disease, and 10 infant cases. The pipeline is a set of processing tasks that aims to improve image quality and intensity, and set images into a specific geometric space. Automatic pre-processing of T1-weighted images using the following steps is carried out: denoising and enhancement image quality, inhomogeneity correction, MNI space registration, fine inhomogeneity correction, intensity normalisation, non-local intracranial cavity extraction (WM, GM and CSF), tissue classification, non-local hemisphere segmentation (splits brain into five: right and left cerebrum/cerebellum, and brainstem), and non-local subcortical structure segmentation. A more detailed description by Manjón and Coupé (2016) is available.

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Chromosome	Start	Stop	Gene	1	38181626	38230844	EPHA10
1	1017178	1051756	C1orf159	1	40204497	40229606	PPIE
1	1152268	1167467	SDF4	1	41326708	41328038	CITED4
1	1477033	1510282	SSU72	1	41492851	41707835	SCMH1
1	2115879	2144179	C1orf86	1	41827308	41849283	FOXO6
1	6475272	6484744	HES2	1	43148040	43168044	YBX1
1	9789059	9884570	CLSTN1	1	44398972	44402932	ARTN
1	9789059	9884570	CLSTN1	1	44412458	44433714	IPO13
1	9982148	10003480	LZIC	1	44435633	44439063	DPH2
1	11734517	11751698	MAD2L2	1	46640729	46651654	TSPAN1
1	15479008	15546994	TMEM51	1	46769304	46782468	UQCRH
1	17345197	17380685	SDHB	1	47100691	47134119	ATPAF1
1	19197904	19229313	ALDH4A1	1	47799449	47844531	CMPK1
1	20439123	20446079	PLA2G2D	1	48761024	48937896	SPATA6
1	20808864	20812748	CAMK2N1	1	50906915	51425956	FAF1
1	21543720	21672054	ECE1	1	51434347	51440329	CDKN2C
1	22889984	22930107	EPHA8	1	52254844	52344629	NRD1
1	23037243	23241843	EPHB2	1	52497757	52499492	KTI12
1	23635933	23671163	HNRNPR	1	52870199	52884012	PRPF38A
1	23685921	23696377	ZNF436	1	54411979	54433861	LRRC42
1	24969574	24999792	SRRM1	1	58881032	59012489	OMA1
1	25548747	25559033	SYF2	1	59246443	59249805	JUN
1	25943939	26111278	MAN1C1	1	62146698	62191115	TM2D1
1	28099674	28150983	STX12	1	63249757	63330961	ATG4C
1	28526769	28559562	DNAJC8	1	64058927	64125936	PGM1
1	32372002	32404008	PTP4A2	1	65298886	65432613	JAK1
1	33116729	33151832	RBBP4	1	68150840	68154041	GADD45A
1	33473521	33502532	AK2	1	68894487	68915662	RPE65
1	36621731	36646470	MAP7D1	1	77333106	77533243	ST6GALNAC5
1	38022500	38032478	DNALI1	1	84963986	84972282	GNG5

1	89571795	89591862	GBP2	1	150547007	150552234	MCL1
1	90286553	90402011	LRR8D	1	151009009	151020096	BNIP1
1	90460658	90494121	ZNF326	1	151104141	151119166	SEMA6C
1	94352570	94375174	GCLM	1	152004962	152009531	S100A11
1	95448259	95538532	ALG14	1	153516075	153518302	S100A4
1	95448259	95538532	ALG14	1	153516075	153518302	S100A4
1	97187141	97280625	PTBP2	1	153954073	153958873	RAB13
1	97543279	98386635	DPYD	1	155023728	155035272	ADAM15
1	100174186	100232206	FRRS1	1	155158280	155162788	MUC1
1	101455159	101491385	DPH5	1	155216976	155225294	FAM189B
1	103342003	103574072	COL11A1	1	155278519	155290477	FDPS
1	108113762	108507565	VAV3	1	155629213	155658843	YY1AP1
1	109834967	109849683	MYBPHL	1	155657673	155708821	DAP3
1	109941633	109969128	PSMA5	1	155978819	155990778	SSR2
1	109941633	109969128	PSMA5	1	156002925	156023633	UBQLN4
1	110276534	110283680	GSTM3	1	156041784	156051809	MEX3A
1	111682229	111727744	CEPT1	1	156182759	156209888	PMF1
1	113252596	113257970	PPM1J	1	159997442	160001803	PIGM
1	114304434	114355090	RSBN1	1	160313043	160328762	NCSTN
1	114935379	115053801	TRIM33	1	161007398	161008907	TSTD1
1	117117000	117210397	IGSF3	1	161141080	161147778	B4GALT3
1	117452669	117532992	PTGFRN	1	161284146	161334561	SDHC
1	120254399	120286869	PHGDH	1	161511529	161520433	FCGR3A
1	145176359	145286290	NOTCH2NL	1	161511529	161520433	FCGR3A
1	145176359	145286290	NOTCH2NL	1	161719538	161726972	DUSP12
1	145524689	145543888	ITGA10	1	161952962	161994192	OLFML2B
1	148003011	148025885	NBPF14	1	162602208	162756429	DDR2
1	149874850	149889454	SV2A	1	165631429	165667920	ALDH9A1
1	150237779	150241629	APH1A	1	165693508	165738179	TMCO1
1	150266242	150281434	MRPS21	1	165796712	165880875	UCK2

1	168148151	168171372	TIPRL	1	229406789	229441661	RAB4A
1	169101238	169337206	NME7	1	230972845	231005355	C1orf198
1	171669276	171711399	VAMP4	1	231041967	231114638	TTC13
1	171810598	172387626	DNM3	1	233119835	233431479	PCNXL2
1	173793699	173827702	DARS2	1	233749730	233808278	KCNK1
1	175913947	176176406	RFWD2	1	236681494	236716301	LGALS8
1	179851157	179889232	TOR1AIP1	1	236712285	236767861	HEATR1
1	179851157	179889232	TOR1AIP1	1	242158772	242164650	MAP1LC3C
1	179851157	179889232	TOR1AIP1	1	243651515	244014401	AKT3
1	182613016	182653522	RGS8	1	246703843	246729585	TFB2M
1	192981476	193029257	UCHL5	1	246703843	246729585	TFB2M
1	193028532	193060927	TROVE2	1	247002380	247094746	AHCTF1
1	200374055	200379206	ZNF281	1	249144183	249153335	ZNF692
1	201434587	201438319	PHLDA3	2	279541	289022	FAM150B
1	201452638	201476407	CSRP1	2	1635639	1748311	PXDN
1	202847390	202858405	RABIF	2	3592655	3605977	RNASEH1
1	203096813	203136553	ADORA1	2	3622833	3628529	RPS7
1	204100170	204121327	ETNK2	2	7017776	7038390	RSAD2
1	205055250	205091170	RBBP5	2	10170756	10194983	KLF11
1	205350486	205391234	LEMD1	2	11319874	11484731	ROCK2
1	211499829	211548423	TRAF5	2	18735969	18741979	RDH14
1	212738656	212794139	ATF3	2	18735969	18741979	RDH14
1	212899475	212965159	NSL1	2	24714899	24993591	NCOA1
1	216676568	217311117	ESRRG	2	25962233	26101332	ASXL2
1	220701548	220837819	MARK1	2	26467596	26513353	HADHB
1	222791424	222841371	MIA3	2	26915561	26954086	KCNK3
1	224301769	224349769	FBXO28	2	27193505	27250107	MAPRE3
1	225997777	226033284	EPHX1	2	27587199	27593344	EIF2B4
1	226250388	226259723	H3F3A	2	27604046	27632570	PPM1G
1	226250388	226259723	H3F3A	2	28974594	29025826	PPP1CB

2	29204144	29275116	FAM179A	2	101008302	101034150	CHST10
2	29415620	30144497	ALK	2	101887661	101925198	RNF149
2	30454377	30482919	LBH	2	106361500	106510750	NCK2
2	32581715	32843986	BIRC6	2	112973419	113012684	ZC3H8
2	33808707	33824382	FAM98A	2	120517187	120742516	PTPN4
2	36583350	36778298	CRIM1	2	128056225	128100825	MAP3K2
2	38522007	38604452	ATL2	2	128603820	128615749	POLR2D
2	42275141	42285688	PKDCC	2	131594469	131804846	ARHGEF4
2	44395964	44471590	PPM1B	2	131805429	131851053	FAM168B
2	44395964	44471590	PPM1B	2	136289016	136482859	R3HDM1
2	46738966	46769571	ATP6V1E2	2	136871899	136875745	CXCR4
2	46808393	46844271	PIGF	2	149894961	150071796	LYPD6B
2	46844305	46852901	CRIP1	2	149894961	150071796	LYPD6B
2	53897097	54014166	ASB3	2	152657460	152685029	ARL5A
2	56093077	56151318	EFEMP1	2	175612300	175629220	CHRNA1
2	62423242	62451886	B3GNT2	2	175612300	175629220	CHRNA1
2	64119260	64246546	VPS54	2	175664022	175870691	CHN1
2	64319766	64371625	PELI1	2	176040966	176046510	ATP5G3
2	65215559	65251019	SLC1A4	2	178977129	178994403	RBM45
2	68694671	68839381	APLF	2	183697982	183731518	FRZB
2	74699065	74699962	MRPL53	2	190611366	190628040	OSGEPL1
2	75059762	75120501	HK2	2	198351288	198365018	HSPD1
2	86426458	86440933	MRPL35	2	198364701	198368207	HSPE1
2	86441096	86565226	REEP1	2	198591583	198651056	BOLL
2	96068419	96082377	FAHD2A	2	201980857	202037431	CFLAR
2	96778603	96782301	ADRA2B	2	201980857	202037431	CFLAR
2	96931864	96939937	CIAO1	2	202316372	202359521	STRADB
2	97426619	97477648	CNNM4	2	203745303	203776969	WDR12
2	97749300	97760623	FAHD2B	2	206547164	206662877	NRP2
2	99061301	99207516	INPP4A	2	209100931	209120498	IDH1

2	210288713	210598862	MAP2	3	33191517	33260727	SUSD5
2	217536808	217560292	IGFBP5	3	39448184	39454053	RPSA
2	219135095	219211536	PNKD	3	40498763	40503883	RPL14
2	220074468	220083732	ABCB6	3	42055274	42267402	TRAK1
2	220084082	220094407	ATG9A	3	42530771	42579085	VIPR1
2	220110172	220115079	STK16	3	42642127	42690253	NKTR
2	220403649	220408507	CHPF	3	43407798	43663580	ANO10
2	220408365	220415337	TMEM198	3	43732355	43764237	ABHD5
2	220492272	220506722	SLC4A3	3	44666491	44689983	ZNF197
2	227596013	227664565	IRS1	3	45123746	45187934	CDCP1
2	227596013	227664565	IRS1	3	46477476	46506618	LTF
2	228336833	228425958	AGFG1	3	47422363	47454951	PTPN23
2	230899670	230933735	SLC16A14	3	48509177	48542279	SHISA5
2	233412759	233415246	TIGD1	3	48725416	48754731	IP6K2
2	234160197	234204340	ATG16L1	3	48894336	48936446	SLC25A20
2	234263129	234380764	DGKD	3	49057888	49060948	NDUFAF3
2	238875567	238951443	UBE2F	3	49314557	49377556	USP4
2	241499451	241503451	DUSP28	3	49761708	49823993	IP6K1
2	242254703	242293462	SEPT2	3	50229023	50235149	GNAT1
3	4402809	4508986	SUMF1	3	50362321	50365688	TUSC2
3	5229339	5261670	EDEM1	3	50388245	50391520	CYB561D2
3	9691097	9744098	MTMR14	3	52002506	52008666	ABHD14B
3	9821628	9834715	TADA3	3	52728480	52740119	GLT8D1
3	12194548	12200871	TIMP4	3	57741928	57915617	SLMAP
3	15422762	15469074	METTL6	3	58223213	58280483	ABHD6
3	15491620	15563297	COLQ	3	58413337	58419599	PDHB
3	16357332	16555242	RFTN1	3	58477803	58488107	KCTD6
3	20202065	20227744	SGOL1	3	58549821	58613357	FAM107A
3	32023246	32033248	ZNF860	3	73431562	73674092	PDZRN3
3	32433143	32496353	CMTM7	3	88101080	88199036	CGGBP1

3	99979641	100044116	TBC1D23	3	165490672	165555280	BCHE
3	101399914	101405584	RPL24	3	169490599	169507524	MYNN
3	119147787	119182549	TMEM39A	3	170606184	170626446	EIF5A2
3	121488588	121553946	IQCB1	3	170780272	171178217	TNIK
3	121488588	121553946	IQCB1	3	180630076	180700561	FXR1
3	122130680	122134902	WDR5B	3	181429692	181432244	SOX2
3	122513881	122600006	DIRC2	3	183960097	183967333	ALG3
3	124449193	124468140	UMPS	3	190231820	190378876	IL1RAP
3	124449193	124468140	UMPS	3	194075956	194090492	LRRC15
3	124944493	125094218	ZNF148	3	196281004	196295647	WDR53
3	125725180	125820418	SLC41A3	3	196662253	196669484	NCBP2
3	127407885	127542113	MGLL	3	196769411	197026191	DLG1
3	128338793	128369739	RPN1	3	197476404	197511337	FYTTD1
3	128806392	128841013	RAB43	4	666205	668147	ATP5I
3	128886638	128902830	CNBP	4	669697	675842	MYL5
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3	131252393	131759172	CPNE4	4	1004692	1020706	FGFRL1
3	131252393	131759172	CPNE4	4	1283622	1333945	MAEA
3	133292414	133309138	CDV3	4	2043700	2045717	C4orf48
3	133292414	133309138	CDV3	4	6641798	6644492	MRFAP1
3	133543059	133614711	RAB6B	4	6641798	6644492	MRFAP1
3	134074167	134094341	AMOTL2	4	8951457	8952147	LOC650293
3	137906095	138017251	ARMC8	4	9400847	9405311	LOC100133128
3	139062841	139075908	MRPS22	4	9400847	9405311	LOC100133128
3	142025429	142166924	XRN1	4	17578907	17609610	LAP3
3	142536682	142608065	PCOLCE2	4	20702016	20730000	PACRGL
3	143690620	143711230	C3orf58	4	25378828	25420140	ANAPC4
3	151044076	151047357	P2RY13	4	39046288	39127873	KLHL5
3	157813780	157823972	SHOX2	4	48832579	48863854	OCIAD1
3	160801651	160823180	B3GALNT1	4	56294048	56413096	CLOCK

4	57276662	57327554	PAICS	4	169137422	169239978	DDX60
4	57514134	57547894	HOPX	4	169418195	169849628	PALLD
4	71570627	71674356	RUFY3	4	177241070	177253416	SPCS3
4	76831788	76862186	NAAA	4	184426200	184433442	ING2
4	76871044	76912135	SDAD1	4	189060578	189068669	TRIML1
4	76942249	76944709	CXCL10	4	189060578	189068669	TRIML1
4	77035792	77069688	NUP54	5	204855	218353	CCDC127
4	83274447	83295169	HNRNPD	5	7859252	7869170	FASTKD3
4	83550670	83720030	SCD5	5	10225599	10250165	FAM173B
4	83739794	83812439	SEC31A	5	16661996	16936405	MYO10
4	88928779	88998951	PKD2	5	31532353	31555185	C5orf22
4	89299818	89364269	HERC6	5	32227091	32313134	MTMR12
4	99391498	99579832	TSPAN5	5	32354436	32444864	ZFR
4	100737937	100791367	DAPP1	5	34915800	34925807	BRIX1
4	110736646	110745913	GAR1	5	37291715	37371248	NUP155
4	110736646	110745913	GAR1	5	40831410	40835407	RPL37
4	113434652	113437348	NEUROG2	5	52285136	52390629	ITGA2
4	114372168	114683689	CAMK2D	5	64885487	64920207	TRIM23
4	114372168	114683689	CAMK2D	5	67511564	67597669	PIK3R1
4	122745464	122791672	BBS7	5	69321058	69338955	SERF1B
4	122745464	122791672	BBS7	5	69321058	69338955	SERF1B
4	128982401	129144106	LARP1B	5	70883095	70954553	MCCC2
4	140374941	140397090	RAB33B	5	71515216	71616104	MRPS27
4	145567128	145662562	HHIP	5	72794230	72801468	BTF3
4	146540520	146581207	MMAA	5	76248660	76265319	CRHBP
4	150999406	151178629	DCLK2	5	78985639	79096069	CMYA5
4	151185791	151936899	LRBA	5	79922025	79950820	DHFR
4	154265781	154336267	MND1	5	79922025	79950820	DHFR
4	157997257	158093271	GLRB	5	79950447	80172654	MSH3
4	159587807	159593427	C4orf46	5	80597382	80608986	ZCCHC9

5	86687290	86708870	CCNH	5	147258254	147261776	SCGB3A2
5	95997721	96110407	CAST	5	148737550	148749241	PCYOX1L
5	102201507	102366829	PAM	5	149340280	149366983	SLC26A2
5	102594422	102614381	C5orf30	5	150040383	150058950	MYOZ3
5	110427850	110466220	WDR36	5	150480247	150537463	ANXA6
5	112212061	112258359	REEP5	5	150560593	150603674	CCDC69
5	114602865	114632478	CCDC112	5	151040637	151066635	SPARC
5	121398870	121414226	LOX	5	156512823	156536268	HAVCR2
5	121647435	121799814	SNCAIP	5	167719045	167899328	WWC1
5	122359058	122372445	PPIC	5	169780471	170163656	KCNIP1
5	125936587	125962964	PHAX	5	171288533	171433897	FBXW11
5	131528279	131563576	P4HA2	5	172261203	172379708	ERGIC1
5	132387642	132440729	HSPA4	5	172410743	172461920	ATP6V0E1
5	137273618	137387670	FAM13B	5	172410743	172461920	ATP6V0E1
5	137475435	137514378	BRD8	5	175810920	175815783	NOP16
5	138089055	138270743	CTNNA1	5	176732481	176741116	MXD3
5	138282389	138534085	SIL1	5	176784684	176799619	RGS14
5	138609421	138667386	MATR3	5	176883593	176900714	DBN1
5	138745872	138780191	DNAJC18	5	176910375	176924626	PDLIM7
5	140018992	140025009	TMCO6	5	177631488	177638204	HNRNPAB
5	140018992	140025009	TMCO6	5	177631488	177638204	HNRNPAB
5	140024928	140027390	NDUFA2	5	179124999	179158662	CANX
5	140743709	140892566	PCDHGA5	5	179224577	179233972	MGAT4B
5	140855549	140892566	PCDHGC3	5	180217521	180237959	MGAT1
5	140855549	140892566	PCDHGC3	5	180683353	180688181	TRIM52
5	141032948	141061820	ARAP3	6	485118	693161	EXOC2
5	145492569	145562314	LARS	6	3000047	3020017	NQO2
5	145826853	145891091	TCERG1	6	7281263	7313561	SSR1
5	146770351	146889639	DPYSL3	6	8073573	8102848	EEF1E1
5	147258254	147261776	SCGB3A2	6	10695160	10710035	PAK1IP1

6	12012704	12212290	HIVEP1	6	91223272	91297040	MAP3K7
6	13574486	13615410	SIRT5	6	100956305	101329263	ASCC3
6	13612511	13633109	NOL7	6	106632331	106773715	ATG5
6	13621710	13711816	RANBP9	6	108188940	108279502	SEC63
6	16299323	16761741	ATXN1	6	108881006	109005992	FOXO3
6	17600498	17611970	FAM8A1	6	110501604	110553443	CDC40
6	24705069	24721084	C6orf62	6	111981515	112194675	FYN
6	26104156	26104585	HIST1H4C	6	112429114	112575944	LAMA4
6	26124350	26139357	HIST1H2AC	6	116892563	116914458	RWDD1
6	31078980	31080352	C6orf15	6	118228669	118638859	SLC35F1
6	31830949	31846843	SLC44A4	6	129204266	129837731	LAMA2
6	32152490	32157983	PBX2	6	131160467	131384482	EPB41L2
6	32808474	32812732	PSMB8	6	132269296	132272538	CTGF
6	33244897	33246622	B3GALT4	6	132269296	132272538	CTGF
6	33267451	33282184	TAPBP	6	134490364	134639216	SGK1
6	33286315	33290813	DAXX	6	137518601	137541001	IFNGR1
6	34555045	34664645	C6orf106	6	149068043	149398146	UST
6	34857018	35085822	ANKS1A	6	149915989	149970174	KATNA1
6	36461646	36515276	STK38	6	150045437	150067708	NUP43
6	42931591	42947001	PEX6	6	153332006	153452409	RGS17
6	44213883	44221645	HSP90AB1	6	158653248	158932880	TULP4
6	71377454	71571738	SMAP1	6	158653248	158932880	TULP4
6	73951017	74019958	KHDC1	6	158653248	158932880	TULP4
6	74078258	74079535	OOEP	6	159057486	159065824	DYNLT1
6	74171434	74211199	MTO1	6	159057486	159065824	DYNLT1
6	74225453	74230775	EEF1A1	6	160100128	160114373	SOD2
6	83920088	84140958	ME1	6	160147692	160177371	WTAP
6	86317482	86353588	SYNCRIP	6	160147692	160177371	WTAP
6	87647004	87726417	HTR1E	6	170884640	170893800	PDCD2
6	87647004	87726417	HTR1E	7	1855408	2272603	MAD1L1

7	5566759	5570252	ACTB	7	80371834	80551715	SEMA3C
7	6414106	6443618	RAC1	7	89975321	90020789	GTPBP10
7	12726432	12730579	ARL4A	7	92190052	92219726	FAM133B
7	16639381	16685462	ANKMY2	7	94214516	94285541	SGCE
7	16793331	16824181	TSPAN13	7	95034154	95064656	PON2
7	20821874	20826528	SP8	7	97481409	97501874	ASNS
7	23221426	23240650	NUPL2	7	99055764	99063844	ATP5J2
7	23221426	23240650	NUPL2	7	99055764	99063844	ATP5J2
7	26191827	26226777	NFE2L3	7	99955606	99965474	PILRB
7	27778972	27869406	TAX1BP1	7	100171614	100183826	LRCH4
7	32524925	32534890	LSM5	7	100797665	100804577	AP1S1
7	37945514	37956545	SFRP4	7	101459164	101927270	CUX1
7	38217788	38270292	STARD3NL	7	102952901	102985340	DNAJC2
7	45139679	45151366	TBRG4	7	104754028	105039634	SRPK2
7	45951824	45960891	IGFBP3	7	107204382	107218988	DUS4L
7	45951824	45960891	IGFBP3	7	108110846	108168625	PNPLA8
7	55538283	55640220	VOPP1	7	120988885	121036442	FAM3C
7	55538283	55640220	VOPP1	7	127950409	127983982	RBM28
7	66093848	66113984	KCTD7	7	134127087	134143908	AKR1B1
7	66147131	66276471	RABGEF1	7	135046527	135194895	CNOT4
7	69063885	70257905	AUTS2	7	138145059	138270353	TRIM24
7	72716493	72722884	NSUN5	7	138728246	138794486	ZC3HAV1
7	73150404	73153210	ABHD11	7	138728246	138794486	ZC3HAV1
7	73703785	73820293	CLIP2	7	138728246	138794486	ZC3HAV1
7	73868100	74016951	GTF2IRD1	7	139723524	139764106	PARP12
7	74210463	74267892	GTF2IRD2	7	140033532	140104044	SLC37A3
7	75162599	75368310	HIP1	7	141251058	141354229	AGK
7	75508297	75518264	RHBDD2	7	143078318	143088224	ZYX
7	75508297	75518264	RHBDD2	7	150076386	150095739	ZNF775
7	75931855	75933634	HSPB1	7	150755279	150773634	SLC4A2

7	150773688	150777990	FASTK	8	86019303	86058335	LRRCC1
7	151253180	151574336	PRKAG2	8	90769315	90803312	RIPK2
7	156931635	157062086	UBE3C	8	92261488	92410398	SLC26A7
7	156931635	157062086	UBE3C	8	92967175	93115474	RUNX1T1
7	157129672	157210153	DNAJB6	8	97274147	97346794	PTDSS1
8	11700013	11725666	CTSB	8	98787789	98864850	LAPTM4B
8	12039593	12051644	FAM86B1	8	98881264	99048968	MATN2
8	13424332	13425817	C8orf48	8	100025279	100890467	VPS13B
8	21964363	21966952	NUDT18	8	100025279	100890467	VPS13B
8	23048950	23082700	TNFRSF10A	8	101269265	101348466	RNF19A
8	26239874	26270664	BNIP3L	8	117858153	117887125	RAD21
8	27491080	27534306	SCARA3	8	117858153	117887125	RAD21
8	27950564	28048690	ELP3	8	118811582	119124078	EXT1
8	28351702	28431805	FZD3	8	120428532	120436698	NOV
8	28747891	28922476	HMBOX1	8	124332070	124408725	ATAD2
8	28747891	28922476	HMBOX1	8	130851819	131028917	FAM49B
8	29190559	29208287	DUSP4	8	132916336	133025909	EFR3A
8	30890758	31031297	WRN	8	145699095	145701738	FOXH1
8	33405252	33424666	RNF122	8	146277803	146281436	C8orf33
8	37716445	37757035	RAB11FIP1	9	2015322	2193644	SMARCA2
8	37962463	37997618	ASH2L	9	3824108	4300056	GLIS3
8	38088841	38120371	DDHD2	9	6010999	6015660	RANBP6
8	38585684	38710566	TACC1	9	6413131	6507074	UHRF2
8	42995572	43057990	HGSNAT	9	19115739	19127624	PLIN2
8	61429449	61536223	RAB2A	9	19376233	19380292	RPS6
8	67955294	67974582	COPS5	9	21967731	21994510	CDKN2A
8	70584090	70747319	SLCO5A1	9	26903348	26947488	PLAA
8	74206817	74237540	RDH10	9	26903348	26947488	PLAA
8	74888357	74895038	TMEM70	9	27109127	27230192	TEK
8	82569131	82599049	IMPA1	9	27546523	27573884	C9orf72

9	32553504	32573202	NDUFB6	9	134165049	134184669	PPAPDC3
9	37485925	37503714	POLR1E	9	134165049	134184669	PPAPDC3
9	38392641	38398682	ALDH1B1	9	134452137	134615384	RAPGEF1
9	71714855	71870144	TJP2	9	134735477	134955294	MED27
9	71714855	71870144	TJP2	9	134735477	134955294	MED27
9	73143959	74061802	TRPM3	9	136228305	136244840	SURF4
9	86274858	86323188	UBQLN1	9	140083009	140084842	SSNA1
9	89559257	89562124	GAS1	9	140317827	140328878	NOXA1
9	96208756	96215894	FAM120AOS	9	140446289	140447027	MRPL41
9	99075699	99146012	SLC35D2	10	1034329	1063728	GTPBP4
9	100818939	100845385	NANS	10	1095403	1178257	WDR37
9	103064337	103115876	TEX10	10	5090938	5149898	AKR1C3
9	112137954	112260613	PTPN3	10	5903573	5931880	ANKRD16
9	112137954	112260613	PTPN3	10	7830073	7849784	ATP5C1
9	114122953	114247045	KIAA0368	10	13319776	13342153	PHYH
9	114311982	114362155	PTGR1	10	16632595	16859529	RSU1
9	116037894	116056099	PRPF4	10	23728178	23731330	OTUD1
9	117781834	117880556	TNC	10	27399020	27443369	YME1L1
9	123151127	123342468	CDK5RAP2	10	28966404	28971888	BAMBI
9	123151127	123342468	CDK5RAP2	10	33189226	33247313	ITGB1
9	123617909	123657188	PHF19	10	33466399	33623853	NRP1
9	125132789	125158002	PTGS1	10	35927157	35930382	FZD8
9	125329807	125330776	OR1L8	10	38383244	38412300	ZNF37A
9	130209933	130213731	RPL12	10	43084512	43134036	ZNF33B
9	130628739	130640042	AK1	10	44101835	44113372	ZNF485
9	130830459	130871557	SLC25A25	10	45471689	45474350	C10orf10
9	130922519	130926227	C9orf16	10	51592060	51623406	TIMM23
9	131071376	131084717	TRUB2	10	61410502	61469669	SLC16A9
9	131937811	131940560	IER5L	10	69556407	69597957	DNAJC12
9	133320074	133376681	ASS1	10	70100844	70167071	RUFY2

10	71029720	71161658	HK1	10	124739536	124749926	PSTK
10	71962566	71993687	PPA1	10	126085852	126107565	OAT
10	75757816	75879938	VCL	10	129705305	129884200	PTPRE
10	79793498	79816591	RPS24	10	133747937	133770074	PPP2R2D
10	80828731	81076305	ZMIZ1	11	494492	507303	RNH1
10	88809939	88854796	GLUD1	11	644205	695760	DEAF1
10	90973306	91011680	LIPA	11	790455	798289	SLC25A22
10	91152283	91166264	IFIT1	11	839701	842549	POLR2L
10	93169017	93274606	HECTD2	11	1968482	2007315	MRPL23
10	93666325	93669278	FGFBP3	11	2421703	2425128	TSSC4
10	95066166	95242210	MYOF	11	3876913	4114460	STIM1
10	97889452	97923537	ZNF518A	11	6642536	6685340	DCHS1
10	98277847	98346829	TM9SF3	11	8008847	8017738	EIF3F
10	102295621	102313701	HIF1AN	11	27062232	27149374	BBOX1
10	102737559	102747292	MRPL43	11	27515945	27528346	LIN7C
10	103544180	103578950	MGEA5	11	27515945	27528346	LIN7C
10	104162354	104179711	PSD	11	27676420	27743625	BDNF
10	105036899	105050128	INA	11	32914772	33001836	QSER1
10	105206523	105212182	CALHM2	11	33106110	33183057	CSTF3
10	105353764	105615215	SH3PXD2A	11	34073210	34124177	CAPRIN1
10	105726923	105789011	SLK	11	35160397	35253969	CD44
10	111765607	111895343	ADD3	11	35639715	35642441	FJX1
10	112631533	112659784	PDCD4	11	43702088	43878189	HSD17B12
10	113907951	113975173	GPAM	11	46765064	46867879	CKAP5
10	115938995	115992445	TDRD1	11	47586868	47595033	PTPMT1
10	116581483	116659606	FAM160B1	11	61066899	61100711	DDB1
10	119764407	119806317	RAB11FIP2	11	61066899	61100711	DDB1
10	121332957	121356561	TIAL1	11	62380193	62382612	ROM1
10	124690399	124713939	C10orf88	11	62475046	62476698	GNG3
10	124739536	124749926	PSTK	11	62480077	62494877	HNRNPUL2

11	62559577	62572984	NXF1	11	77589746	77705791	INTS4
11	62574312	62599583	STX5	11	85405244	85522217	SYTL2
11	63742059	63744035	COX8A	11	88026740	88070961	CTSC
11	63753305	63765912	OTUB1	11	89933577	89956552	CHORDC1
11	63997574	64001773	DNAJC4	11	93463348	93474723	TAF1D
11	64126605	64139707	RPS6KA4	11	94898657	94965725	SESN3
11	64532056	64546535	SF1	11	95566024	95657391	MTMR2
11	64879306	64883727	TM7SF2	11	102188161	102210154	BIRC3
11	65306010	65325878	LTBP3	11	102188161	102210154	BIRC3
11	65343489	65360141	EHBP1L1	11	102188161	102210154	BIRC3
11	65360306	65363487	KCNK7	11	107992238	108018915	ACAT1
11	65601285	65621598	SNX32	11	108028097	108093385	NPAT
11	65601285	65621598	SNX32	11	111652899	111742325	ALG9
11	66202530	66206330	MRPL11	11	111797848	111893394	DIXDC1
11	66247464	66277150	DPP3	11	114310088	114321021	REXO2
11	66288834	66313729	ZDHHC24	11	118967193	118973144	DPAGT1
11	66406068	66435876	RBM4	11	119225905	119252456	USP2
11	66406068	66435876	RBM4	11	120107329	120190673	POU2F3
11	67056742	67069975	ANKRD13D	11	120207244	120360665	ARHGEF12
11	67159403	67165903	RAD9A	11	121322892	121504491	SORL1
11	67374303	67380032	NDUFV1	11	122526378	122685207	UBASH3B
11	67922310	67981270	SUV420H1	11	122753216	122830450	C11orf63
11	68522068	68611898	CPT1A	11	125315621	125366226	FEZ1
11	68658724	68671323	MRPL21	11	125439278	125454595	EI24
11	71639748	71708663	RNF121	11	125616160	125619763	PATE1
11	71900582	71907387	FOLR1	11	125763360	125773165	PUS3
11	74971146	75062895	ARRB1	12	3186501	3395750	TSPAN9
11	75526192	75855302	UVRAG	12	4382881	4414542	CCND2
11	75526192	75855302	UVRAG	12	6643565	6647557	GAPDH
11	76060984	76091900	PRKRIR	12	6759684	6772331	ING4

12	6833130	6841061	COPS7A	12	64798133	64842484	XPOT
12	7245980	7261889	C1RL	12	65563331	65642161	LEMD3
12	7341739	7371190	PEX5	12	66516829	66524553	LLPH
12	7965090	8043812	SLC2A14	12	69979186	70010615	CCT2
12	8798520	8815453	MFAP5	12	72079858	72097860	TMEM19
12	12878831	12944420	APOLD1	12	72079858	72097860	TMEM19
12	12966260	12982935	DDX47	12	76745557	76953609	OSBPL8
12	22199088	22218628	CMAS	12	77415006	77459380	E2F7
12	25358160	25403890	KRAS	12	98987383	98995798	SLC25A3
12	28110997	28125684	PTHLH	12	100422213	100536662	UHRF1BP1L
12	29493559	29534163	ERGIC2	12	104382742	104457981	GLT8D2
12	32832114	32898604	DNM1L	12	104458216	104500322	HCFC2
12	39687010	39837212	KIF21A	12	106631639	106641733	CKAP4
12	45609750	45834207	ANO6	12	106976665	107156602	RFX4
12	49208195	49222746	CACNB3	12	110288728	110318313	GLTP
12	49315722	49319350	FKBP11	12	110436954	110477257	ANKRD13A
12	49396035	49413032	PRKAG1	12	112123837	112194931	ACAD10
12	52562760	52585818	KRT80	12	120779113	120807003	MSI1
12	53399922	53436013	EIF4B	12	120884221	120901576	GATC
12	53845866	53874966	PCBP2	12	121200293	121342175	SPPL3
12	53873436	53893464	MAP3K12	12	121458075	121477065	OASL
12	53901620	54020220	ATF7	12	122956126	122985563	ZCCHC8
12	54058924	54070532	ATP5G2	12	122989170	123011580	RSRC2
12	56078332	56109841	ITGA7	12	122989170	123011580	RSRC2
12	56137044	56146685	GDF11	12	123237351	123255973	DENR
12	56498083	56507714	PA2G4	12	123349855	123380732	VPS37B
12	57106191	57119346	NACA	12	123405478	123451076	ABCB9
12	58213690	58240767	CTDSP2	12	123640923	123717805	MPHOSPH9
12	59265917	59314339	LRIG3	12	123955889	124018285	RILPL1
12	64798133	64842484	XPOT	12	124196845	124246322	ATP6V0A2

12	124457679	124500006	ZNF664	13	113862487	113919412	CUL4A
12	125549905	125627899	AACS	13	114110114	114145044	DCUN1D2
12	129277719	129308561	SLC15A4	13	114238983	114295808	TFDP1
12	129277719	129308561	SLC15A4	13	115047039	115071312	UPF3A
12	130646984	130650305	FZD10	14	20811753	20826083	PARP2
12	132434445	132565031	EP400	14	21558185	21572883	ZNF219
12	133200324	133264070	POLE	14	24658333	24666308	TM9SF1
12	133613858	133639905	ZNF84	14	24658333	24666308	TM9SF1
13	20397601	20437796	ZMYM5	14	24658333	24666308	TM9SF1
13	20397601	20437796	ZMYM5	14	24701613	24708468	GMPR2
13	25820319	25861724	MTMR6	14	31091440	31205054	SCFD1
13	27131820	27263102	WASF3	14	35030595	35099386	SNX6
13	31032857	31191962	HMGB1	14	35179568	35184049	CFL2
13	32974840	33002510	N4BP2L1	14	35179568	35184049	CFL2
13	35516404	36246894	NBEA	14	35514093	35552609	FAM177A1
13	39917009	40177376	LHFP	14	36295504	36341189	BRMS1L
13	41506035	41635564	ELF1	14	39616995	39639654	TRAPPC6B
13	41765691	41768722	KBTBD7	14	45431396	45543654	FAM179B
13	43460504	43566427	EPSTI1	14	50087440	50090219	MGAT2
13	45006259	45150721	TSC22D1	14	50110250	50155118	POLE2
13	45513364	45563633	NUFIP1	14	53173874	53194736	PSMC6
13	45513364	45563633	NUFIP1	14	53196863	53241727	STYX
13	49882766	50018241	CAB39L	14	54941182	54955805	GMFB
13	50018409	50069159	SETDB2	14	55518342	55536932	MAPK1IP1L
13	52586503	52603804	ALG11	14	58470788	58618867	C14orf37
13	53226810	53262453	SUGT1	14	58711503	58738747	PSMA3
13	72012078	72441350	DACH1	14	58711503	58738747	PSMA3
13	72012078	72441350	DACH1	14	60611476	60633054	DHRS7
13	78469596	78549684	EDNRB	14	63671060	63760250	RHOJ
13	79188401	79233334	RNF219	14	65007166	65009975	HSPA2

14	65171112	65213643	PLEKHG3	14	105266913	105271069	ZBTB42
14	65472799	65569433	MAX	14	105452105	105466076	C14orf79
14	66974105	67648545	GPHN	14	105452105	105466076	C14orf79
14	67827014	67853253	EIF2S1	14	105714859	105717450	BTBD6
14	68143497	68162530	RDH11	14	105952872	105955148	CRIP1
14	73957624	73960125	C14orf169	15	22833375	22873911	TUBGCP5
14	74111558	74170451	DNAL1	15	22892647	23003623	CYFIP1
14	76044920	76114532	FLVCR2	15	23888676	23893013	MAGEL2
14	77248056	77292626	ANGEL1	15	25068774	25223750	SNRPN
14	91006912	91282843	TTC7B	15	35270522	35280517	ZNF770
14	92588278	92630563	CPSF2	15	40226311	40327817	EIF2AK4
14	93170132	93215067	LG MN	15	40226311	40327817	EIF2AK4
14	93403239	93582283	ITPK1	15	49030115	49104112	CEP152
14	93669217	93673479	C14orf142	15	51739901	51915050	DMXL2
14	93703876	93799405	BTBD7	15	52230202	52264015	LEO1
14	94594098	94595977	IFI27L2	15	60780463	61521522	RORA
14	94594098	94595977	IFI27L2	15	63413979	63434280	LACTB
14	96152734	96159000	TCL1B	15	63796690	63886859	USP3
14	100150735	100193658	CYP46A1	15	64364741	64386227	FAM96A
14	100204036	100408417	EML1	15	64457696	64665988	CSNK1G1
14	100204036	100408417	EML1	15	65255343	65282271	SPG21
14	101003464	101036151	BEGAIN	15	66994654	67074358	SMAD6
14	101193182	101201487	DLK1	15	72533502	72564905	PARP6
14	102430845	102517155	DYNC1H1	15	74833498	74890492	ARID3B
14	102547055	102606106	HSP90AA1	15	74898307	74922562	CLK3
14	102606169	102690030	WDR20	15	75661700	75748201	SIN3A
14	102973159	102976148	ANKRD9	15	75759442	75871645	PTPN9
14	103995489	104003430	TRMT61A	15	78463167	78527069	ACSBG1
14	103995489	104003430	TRMT61A	15	85212748	85259711	SEC11A
14	105190514	105213682	ADSSL1	15	89178884	89198901	ISG20

15	89441894	89456705	MFGES	16	29452581	29466305	BOLA2
15	90293078	90294560	MESPI	16	29973331	29984393	TMEM219
15	90773457	90809011	CIB1	16	30016815	30023444	DOC2A
15	91260559	91358706	BLM	16	30535302	30538841	ZNF768
15	91473390	91497343	UNC45A	16	30709005	30709830	LOC730183
15	92396918	92715685	SLCO3A1	16	30960385	30966279	ORA13
15	92396918	92715685	SLCO3A1	16	46918288	46965221	GPT2
15	93586616	93632463	RGMA	16	48278191	48387908	LONP2
16	126998	135870	MPG	16	56485404	56511427	OGFOD1
16	222826	223729	HBA2	16	56504281	56554028	BBS2
16	222826	223729	HBA2	16	56763997	56882657	NUP93
16	446732	450774	NME4	16	58497529	58547543	NDRG4
16	691829	698494	FAM195A	16	58497529	58547543	NDRG4
16	770561	772675	FAM173A	16	66541886	66584335	TK2
16	1877205	1890228	FAHD1	16	67423690	67427469	TPPP3
16	1877205	1890228	FAHD1	16	67596290	67673108	CTCF
16	2028898	2031724	NOXO1	16	67708416	67753293	GFOD2
16	2089796	2097951	NTHL1	16	67906906	67918437	EDC4
16	2205743	2228150	TRAF7	16	67977357	68002617	SLC12A4
16	2732475	2759051	KCTD5	16	69373395	69377034	NIP7
16	3333360	3351421	ZNF263	16	70488478	70514197	FUK
16	3355386	3372955	ZNF75A	16	70721322	70835094	VAC14
16	3451170	3459384	ZNF174	16	72127595	72146831	DHX38
16	4404523	4466982	CORO7	16	75622698	75657241	ADAT1
16	4404523	4466982	CORO7	16	78133290	79246587	WVOX
16	8889017	8891525	TMEM186	16	84087348	84150537	MBTPS1
16	11641558	11681342	LITAF	16	84087348	84150537	MBTPS1
16	19727758	19869107	IQCK	16	84155724	84178820	HSDL1
16	22357237	22385958	CDR2	16	89334009	89556989	ANKRD11
16	25123027	25189571	LCMT1	16	89574782	89624194	SPG7

16	89613304	89633257	RPL13	17	26684667	26689109	TMEM199
16	89613304	89633257	RPL13	17	27055802	27069804	NEK8
16	89753056	89762792	CDK10	17	30469453	30552766	RHOT1
16	89762745	89768151	SPATA2L	17	34623822	34625750	CCL3L1
16	90071259	90085957	DBNDD1	17	34623822	34625750	CCL3L1
17	1324627	1359581	CRK	17	34842451	34855174	ZNHIT3
17	1367460	1396021	MYO1C	17	34842451	34855174	ZNHIT3
17	2207224	2228573	SRR	17	34900717	34946298	GGNBP2
17	2240786	2284373	SGSM2	17	36452969	36479121	MRPL45
17	4046421	4061015	CYB5D2	17	36584700	36668648	ARHGAP23
17	4688560	4689749	VMO1	17	37006301	37010073	RPL23
17	4840405	4843482	SLC25A11	17	37356516	37361000	RPL19
17	4848925	4852401	PFN1	17	37408877	37558550	FBXL20
17	4853384	4860446	ENO3	17	37827355	37844330	PGAP3
17	6481625	6545086	KIAA0753	17	38060828	38074923	GSDMB
17	7323632	7324976	SPEM1	17	40128419	40169735	DNAJC7
17	7465289	7475307	SENP3	17	40276974	40307082	RAB5C
17	7476004	7482344	EIF4A1	17	40731506	40761465	FAM134C
17	7482785	7485449	CD68	17	40761338	40767276	TUBG1
17	7494528	7518235	FXR2	17	40925434	40931638	VPS25
17	7554234	7561109	ATP1B2	17	41166602	41174479	VAT1
17	7571700	7590888	TP53	17	41177238	41184078	RND2
17	8243138	8249384	ODF4	17	42422471	42430494	GRN
17	15848211	15879230	ADORA2B	17	42927635	42977013	EFTUD2
17	16284347	16286079	UBB	17	42977060	42983561	CCDC103
17	17397731	17399729	RASD1	17	43100686	43138493	DKAKD
17	18853969	18924024	SLC5A10	17	43299172	43324705	FMNL1
17	19314471	19320609	RNF112	17	44668015	44834850	NSF
17	19552044	19580928	ALDH3A2	17	45331188	45390097	ITGB3
17	20352688	20370868	LGALS9B	17	47074754	47133527	IGF2BP1

17	54869254	54911276	C17orf67	18	158463	213759	USP14
17	54869254	54911276	C17orf67	18	3411905	3458429	TGIF1
17	54965250	54991429	TRIM25	18	9708208	9862573	RAB31
17	55333911	55762070	MSI2	18	10454605	10488718	APCDD1
17	56422516	56429619	SUPT4H1	18	12308198	12326588	TUBB6
17	56597591	56618199	SEPT4	18	12785457	12884357	PTPN2
17	57187288	57232820	SKA2	18	21086128	21166601	NPC1
17	62494354	62503062	DDX5	18	28645918	28682408	DSC2
17	66031828	66042990	KPNA2	18	29078007	29128834	DSG2
17	71161140	71168114	SSTR2	18	32820974	32838417	ZNF397
17	71244568	71258039	CPSF4L	18	32820974	32838417	ZNF397
17	72199775	72206039	RPL38	18	33688474	33709377	SLC39A6
17	72427460	72447817	GPRC5C	18	43664090	43684219	ATP5A1
17	72427460	72447817	GPRC5C	18	44056915	44237016	LOXHD1
17	73163805	73179118	SUMO2	18	46567826	46987192	DYM
17	73496321	73511684	CASKIN2	18	47014831	47018955	RPL17
17	73663379	73704159	SAP30BP	18	51677951	51751178	MBD2
17	74466955	74497529	RHBDF2	18	51884264	51908424	C18orf54
17	74708894	74722901	JMJD6	18	54270033	54305940	TXNL1
17	75277472	75496698	SEPT9	18	55267868	55289197	NARS
17	76352838	76356180	SOCS3	18	59711437	59854309	PIGN
17	76670110	76778396	CYTH1	18	60790559	60987031	BCL2
17	76849039	76921492	TIMP2	18	65173799	65183987	DSEL
17	77018996	77045890	C1QTNF1	18	65173799	65183987	DSEL
17	78075319	78093700	GAA	18	71920507	71959271	CYB5A
17	78234623	78372606	RNF213	18	72265086	72777648	ZNF407
17	78440613	78450424	NPTX1	18	77866895	77898249	ADNP2
17	79213019	79215118	C17orf89	19	305555	344811	MIER2
17	79218779	79269253	SLC38A10	19	416563	461016	SHC2
17	79648204	79650974	ARL16	19	1026254	1039084	CNN2

19	1065902	1086647	HMHA1	19	17830283	17845344	MAP1S
19	1383506	1395608	NDUFS7	19	18723662	18731869	TMEM59L
19	1481407	1490906	PCSK4	19	18942724	18979059	UPF1
19	1815225	1848540	REXO1	19	19734444	19739059	LPAR2
19	2328609	2355120	SPPL2B	19	20278000	20311319	ZNF486
19	3359541	3469235	NFIC	19	20802725	20844422	ZNF626
19	5830617	5839784	FUT6	19	30302785	30315244	CCNE1
19	6661244	6670619	TNFSF14	19	33087887	33166122	ANKRD27
19	7599013	7626673	PNPLA6	19	33877835	34012819	PEPD
19	7953370	7966928	LRR8E	19	35759876	35770744	USF2
19	8023437	8070549	ELAVL1	19	35759876	35770744	USF2
19	9361700	9362759	OR7E24	19	36233408	36236429	U2AF1L4
19	9473676	9493313	ZNF177	19	36236458	36238076	PSENE1
19	9920923	9930121	FBXL12	19	36486070	36487240	SDHAF1
19	9964374	10047090	OLFM2	19	36705484	36729696	ZNF146
19	10070217	10121167	COL5A3	19	36936001	36980824	ZNF566
19	10828709	10944189	DNM2	19	37638320	37663663	ZNF585A
19	10828709	10944189	DNM2	19	38893755	38899748	FAM98C
19	10982233	11033473	CARM1	19	39327008	39342999	HNRNPL
19	12799710	12807669	FBXW9	19	39421328	39423680	MRPS12
19	13056608	13064477	RAD23A	19	40021610	40023514	EID2B
19	13207982	13213994	LYL1	19	40021610	40023514	EID2B
19	13885237	13889607	C19orf53	19	40029426	40030858	EID2
19	13906238	13943088	ZSWIM4	19	41099052	41135745	LTBP4
19	15270424	15311812	NOTCH3	19	41256705	41271317	SNRPA
19	16435631	16438365	KLF2	19	41725084	41767692	AXL
19	16940189	16991186	SIN3B	19	41931244	41934655	B3GNT8
19	17186571	17324124	MYO9B	19	42460813	42463550	RABAC1
19	17502218	17516478	BST2	19	42751697	42759329	ERF
19	17622258	17632117	PGLS	19	42788714	42799969	CIC

19	42801165	42806972	PAFAH1B3	20	5095579	5107288	PCNA
19	42891151	42894464	CNFN	20	5931278	5975872	MCM8
19	44150227	44174518	PLAUR	20	25176307	25207385	ENTPD6
19	44416756	44439431	ZNF45	20	25176307	25207385	ENTPD6
19	44529474	44537283	ZNF222	20	25275359	25371638	ABHD12
19	46213867	46234171	FBXO46	20	25275359	25371638	ABHD12
19	46969728	46974840	PNMAL1	20	30865423	30922834	KIF3B
19	47177553	47220404	PRKD2	20	30865423	30922834	KIF3B
19	49118564	49122695	RPL18	20	31407679	31438231	MAPRE1
19	49467639	49470156	FTL	20	32077908	32237857	CBFA2T2
19	49467639	49470156	FTL	20	32868051	32899628	AHCY
19	49471362	49496630	GYS1	20	33302558	33413453	NCOA6
19	50194343	50217008	CPT1C	20	33462746	33515789	ACSS2
19	50410062	50433008	NUP62	20	33516216	33543814	GSS
19	51009234	51014632	JOSD2	20	33866689	33872639	EIF6
19	51870332	51872518	CLDND2	20	34236827	34252898	RBM12
19	52020931	52035130	SIGLEC6	20	34256590	34287307	NFS1
19	52359036	52391249	ZNF577	20	34287212	34288922	ROMO1
19	52392468	52408325	ZNF649	20	34995424	35157060	DLGAP4
19	54369591	54379709	MYADM	20	35169867	35178246	MYL9
19	54494383	54515940	CACNG6	20	43124844	43150746	SERINC3
19	55385529	55401859	FCAR	20	43248140	43280396	ADA
19	57862625	57871286	ZNF304	20	43380425	43438999	RIMS4
19	58944161	58951609	ZNF132	20	43514220	43537193	YWHAB
20	388676	411630	RBCK1	20	43720930	43729773	KCNS1
20	1349601	1373836	FKBP1A	20	44420556	44440086	DNTTIP1
20	2082508	2129221	STK35	20	44978147	44993117	SLC35C2
20	2462443	2489798	ZNF343	20	46286130	46415380	SULF2
20	3208043	3222129	SLC4A11	20	46286130	46415380	SULF2
20	5095579	5107288	PCNA	20	48552894	48570442	RNF114

20	49551384	49575101	DPM1	22	21271694	21308057	CRKL
20	52824482	52836512	PFDN4	22	21369422	21382322	P2RX6
20	56884751	56942583	RAB22A	22	22113926	22221990	MAPK1
20	58511867	58515372	PPP1R3D	22	24108001	24110161	CHCHD10
20	60877092	60884226	ADRM1	22	24313534	24322039	DDT
20	61273775	61317157	SLCO4A1	22	25348656	25593435	KIAA1671
20	61472447	61493135	TCFL5	22	26921694	26986109	TPST2
20	61826761	61847558	YTHDF1	22	26921694	26986109	TPST2
20	61924518	61962305	COL20A1	22	29168642	29185303	CCDC117
20	62151406	62153544	PPDPF	22	29702965	29708798	GAS2L1
20	62588037	62601243	ZNF512B	22	31058019	31063894	DUSP18
20	62612397	62664473	PRPF6	22	31500743	31503571	SELM
20	62711431	62732016	OPRL1	22	35653425	35691820	HMGXB4
21	18965948	18985288	BTG3	22	36677303	36784127	MYH9
21	35790890	35884593	KCNE1	22	37865081	37882519	MFNG
21	37529060	37666592	DOPEY2	22	38302135	38338485	MICALL1
21	38123169	38362565	HLCS	22	38686677	38714109	CSNK1E
21	38123169	38362565	HLCS	22	38864047	38879472	KDEL3
21	38445534	38575428	TTC3	22	38864047	38879472	KDEL3
21	40556082	40685765	BRWD1	22	38879423	38903642	DDX17
21	44394623	44453708	PKNOX1	22	39101713	39129612	GTPBP1
21	45193526	45196276	CSTB	22	39257448	39268278	CBX6
21	45193526	45196276	CSTB	22	39436589	39451997	APOBEC3F
21	46934609	46983065	SLC19A1	22	39436589	39451997	APOBEC3F
21	46934609	46983065	SLC19A1	22	40806272	41032710	MKL1
21	47518013	47552783	COL6A2	22	42017230	42060072	XRCC6
22	18900186	18924086	PRODH	22	42069917	42085316	NHP2L1
22	20103441	20114900	RANBP1	22	42229063	42303332	SREBF2
22	20119344	20135550	ZDHHC8	22	42979707	43010988	POLDIP3
22	21271694	21308057	CRKL	22	43013826	43045425	CYB5R3

22	43013826	43045425	CYB5R3
22	43192510	43253428	ARFGAP3
22	46316226	46373028	WNT7B
22	46731278	46753257	TRMU
22	51017367	51021448	CHKB
22	51061162	51066621	ARSA
22	51113050	51171660	SHANK3