Supplementary Web Appendix

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ADDITIONAL METHODS

MR & PET Imaging acquisition. MR imaging was performed on a 3T GE Signa HDxt scanner (software version HD23.0_V03_1614.b). Sagittal volumetric gradient echo T1-weighted (T1w) MRIs (TR = 7.27 ms, TE = 2.7, inversion time = 450 ms, matrix = 224 x 512 x 512, voxel = 0.7 x 0.47 x 0.47 mm) were obtained pre-operatively and on post-operative day 0 or 1 following catheter implantation to confirm catheter placement prior to infusion initiation. For the first infusion, MRIs were collected ~8 hours, ~14 hours, ~24 hours, and ~48 hours after the start of infusion, and ~8 hours, ~14 hours, and ~24 hours after completion. For the remaining infusions, MRIs were collected immediately prior to and ~48 hours after the start of each infusion. ^{18}F-FDG PET imaging was performed on Patients 3, 4 and 5 using a Siemens Biograph 64_mCT (software version VG60A; matrix = 400 x 400 x 148, voxel = 1.0 x 1.0 x 1.5 mm) pre-operatively, ~48 hours after start of pulse 1, and ~24 hours after start of pulse 4.

MR & PET Imaging analysis. MRI data were processed with FMRIB Software Library (FSL version 6.0.0) (1) and Matlab (2020b, MathWorks) software. T1w and PET images from all scanning sessions were co-registered to the pre-implantation T1w scan using FSL-FLIRT (linear, 6 degrees of freedom). T1w images were intensity normalized using histogram matching to a healthy control subject. To calculate the spatial distribution of the infused gadolinium contrast, the pre-implantation T1w image was subtracted from all subsequent T1w images. The difference images were then thresholded and binarized to create a 3D mask of the infused volume at each time point and the mask volumes were then plotted as a function of time for each patient. To estimate the time to peak volume and maximum achieved volume, the time course for each patient's first infusion was fit to a three-parameter gamma function

$$y_{fit} = y_{max} * \left(\frac{t}{t_{max}}\right)^{b*t_{max}} * e^{b*(t_{max}-t)}$$

where y_{max} represents the peak volume, t_{max} represents the time of peak volume and b represents the shape of the function. To estimate backflow from the catheter, a mask was drawn around the infused volume located in the subdural CSF at the base of the catheter and the volume plotted as a function of time. All ^{18}F-FDG-metabolism images were intensity normalized to the patient's pre-infusion, contralesional hemisphere using histogram matching. Post-infusion ^{18}F-FDG-metabolism images were converted to percent signal change by dividing by the pre-infusion image. The maximum infusion mask was used to estimate the effect of TPT on ^{18}F-FDG metabolism.

Immunohistochemistry. Paraffin embedded tissue was serially sectioned into 5µM sections mounted on immunoblank slides. Immunoperoxidase was performed using Antibodies to Sox2 (Rabbit, abcam #ab92494), Ki67 (Rabbit, Cell Signaling #9129), CD68 (Mouse, abcam #ab955), Neun (Mouse IGg1, Millipore #MAB377) under a standard staining protocol with deparaffinization, antigen retrieval using 10mM sodium citrate buffer, Vectastain ABC Kit (PK4001 for rabbit, PK4002 for mouse) and Dako DAB+ liquid substrate (#K3468). After peroxidase staining, slides were immersed in dH_2O, counterstained with hematoxylin, dehydrated and coverslips were mounted using Permount mounting medium (Fisher Chemical #SP15-100).

Immunohistochemistry quantification. Stained slides were scanned and digitized using a Leica SCN400 automated image digitizing system. A total of 87 MRI-localized biopsies were quantified for each stain, including pre-CED n=37) and post-CED (n=50). For each SCN file, ImageJ was used to outline tissue area at 20x magnification. Semi-automated quantification of DAB-stained cells and nuclei was performed as follows. Images were split into blue channels for nuclei quantification and red channels for DAB quantification. Images were converted to 8-bit, normalized and thresholded using the local thresholding algorithm first described by Phansalkar et al.[15] The local threshold is determined using the following algorithm: t=mean*(1+p*exp(-q*mean) + k*((stdev/r)-1)) where mean and STD are calculated from a 3x3 square of pixels centered on the pixel of interest. Values of k, r are optimized based on multiple high-powered fields of masks ensuring accurate quantification on each image. Concordance between manual and semi-automated quantification was confirmed for each stain with r^2 value greater than 0.90 in images from each patient before application to all biopsies. Labeling indices were calculated from dividing DAB+ cells over total number of cells (nuclei). Labeling indices pre-CED and post-CED were compared statistically using an unpaired student's T-test, as there were an unequal number of samples between pre- and post-resection due to the nature of the study design.

RNA isolation, quantification and sequencing. Biopsies (n=86) were lysed using a 5mm stainless steel bead (QIAGEN, 69989). RNA was extracted from tissue lysate using the RNeasy Mini kit (QIAGEN, 74106). Only samples with RNA Integrity Number (RIN) greater than 6 were used for sequencing. Expression profiles were generated using the Illumina TruSeq v2 RNA-Seq kit with 80 million paired end base reads on a Novaseq 6000 sequencer. Alignment and mapping of RNA sequencing reads was done in partnership with the Columbia Sulzberger Genome Center. Transcripts were pseudo-aligned, mapped and quantified to counts using the Kallisto pipeline.[16]

RNAseq normalization, Differential gene expression analysis, and gene set enrichment analysis. All downstream RNA sequencing analysis was performed in the statistical programming language R (version 4.0.3). Raw transcript counts for each sample were normalized via the "DESeq2" package after filtering out genes that are not protein-coding. Differential gene expression analysis was also performed via DESeq2, comparing post-treatment biopsies (n=51) to pre-treatment biopsies (n=35), both on a patient-by patient level, as well as by pooling samples across all patients (2). Volcano plot and heatmap were generated based on normalized expression between pre-and post-CED biopsies, generated via "EnhancedVolcano" package(3). Gene Set Enrichment Analysis

(implemented via the GSEA desktop version 4.1.0) was performed using the 50 Cancer Hallmarks gene sets patient-by patient comparing pre-treatment and post-treatment MRI-localized biopsies. Fisher p-integration was performed on FDR-adjusted p-values across all patients for each pathway, and significant pathways ($p<0.05$) were visualized on a heatmap with normalized enrichment scores for each patient.

Glioma State Analysis. GSVA analysis(4) was performed on all MRI-localized biopsies (86 samples) using gene signatures for six distinct glioma cell states derived from single-nuclei RNA sequencing (snRNAseq) (5), as well as scRNAseq signatures derived from Neftel et al(6), and a heatmap was generated displaying the enrichment scores for each gene set for each biopsy, scaled across all samples. Each biopsy was annotated by the glioma cell state it was most enriched in (**Supplementary Table S4**), and Pearson's chi-squared test was performed to statistically quantify change in phenotype between conditions.

Measurement of TPT concentrations. TPT concentrations were measured in tissue samples using matrix-assisted laser desorption/ionization mass spectrometric imaging (MALDI MSI) methodology.

MALDI tissue preparation

The MALDI MSI tissue mimetic for drug quantification of TPT was adopted from Groseclose and Castellino (7) and has been further developed for several MALDI MSI studies (8, 9). Here, a tissue microarray (TMA) mold with 1.5 mm core diameter channels composed of 40% gelatin was used to create a concentration ladder of TPT. To account for the tissue matrix, human autopsy brain homogenates were spiked with varying concentrations of TPT ranging from 1 - 20 µM. The spiked homogenates were punched into the TMA channels and frozen at -80 °C. Brain specimens and TMA were sectioned at 10 µm thickness, and thaw mounted directly onto indium tin oxide (ITO) slides. Serial sections were used for MALDI MRM MSI and brightfield microscopy imaging (Zeiss Observer Z.1, Oberkochen, Germany) of hematoxylin and eosin (H&E) staining. To avoid TPT interconversion between the lactone and carboxylate forms, a low pH phosphate solution was sprayed first on the tissues using a TM-sprayer (HTX imaging, Carrboro, NC). Two coats of the phosphate buffer solution (pH 3) were sprayed at a flow rate (0.05 mL/min), spray nozzle velocity (1200 mm/min), nitrogen gas pressure (10 psi), spray nozzle temperature (80 °C), and track spacing (2 mm) were sprayed on the tissue samples. The MALDI matrix 2,5-dihydroxybenzoic acid (160 mg/mL) was dissolved in 70:30 methanol: 0.1% TFA with 1 % DMSO. The ITO slides with tissue and mimetic sections coated with phosphate solution were sprayed with the matrix using a TM sprayer with a two-pass cycle at a flow rate (0.18 mL/min), spray nozzle velocity (1200 mm/min), nitrogen gas pressure (10 psi), spray nozzle temperature (75 °C), and track spacing (2 mm).

MALDI mass spectrometry imaging

Matrix assisted laser desorption ionization (MALDI) MS imaging and quantitation of TPT from clinical specimens was performed using a timsTOF fleX mass spectrometer (Bruker Daltonics, Billerica, MA) operating in positive ion mode. A multiple reaction monitoring (MRM) method was applied to improve sensitivity and selectivity for quantitation. Using the ESI configuration on the dual-source instrument, a method for TPT was developed in which the ion transfer funnels, quadrupole, collision cell, and focus pre-TOF settings were optimized. Calibration of the mass range for each method was performed through the direct infusion of an Agilent tune mix solution (Agilent Technologies, Santa Clara, CA) and the MRM settings were optimized with direct infusions of TPT. The optimal collision energy of 20 eV for TPT was determined with an isolation width of 3 *m/z*. The mass range was selected to encompass both the precursor and product ions and was set to *m/z* 300-600 for TPT. For MALDI MSI quantitation, the transition of precursor to product was *m/z* 422.171→377.111 for TPT. A spatial resolution of 100 µm was implemented for MALDI MSI sequences. A 5,000 Hz laser repetition rate and 3,000 laser shots per pixel were used. The 12 biopsies and a triplicate of the TPT mimetic were imaged and data analysis and visualization were performed using the SCiLS Lab software (version 2020a premium, Bruker Daltonics, Billerica, MA) . The data was normalized using total ion current (TIC). Using the three technical sections of the TPT mimetic, the pixels of each concentration channels were averaged. The MALDI signal intensity was calibrated for quantitation of TPT using a linear regression of the averaged ion intensity from each mimetic concentration. Relative standard deviation (RSD) for each concentration was calculated (0 µM- 18.3%, 1 µM- 11.5%, 3 µM- 27.9%, 5 µM- 16.9%, 10 µM- 10.3%, and 20 µM- 12.1%,) and the limit of detection (LOD) and limit of quantification (LOQ) were based on signal-to-noise (S/N) ratio of > 3 and > 10 respectively.

Additional Safety Data Unrelated to CED

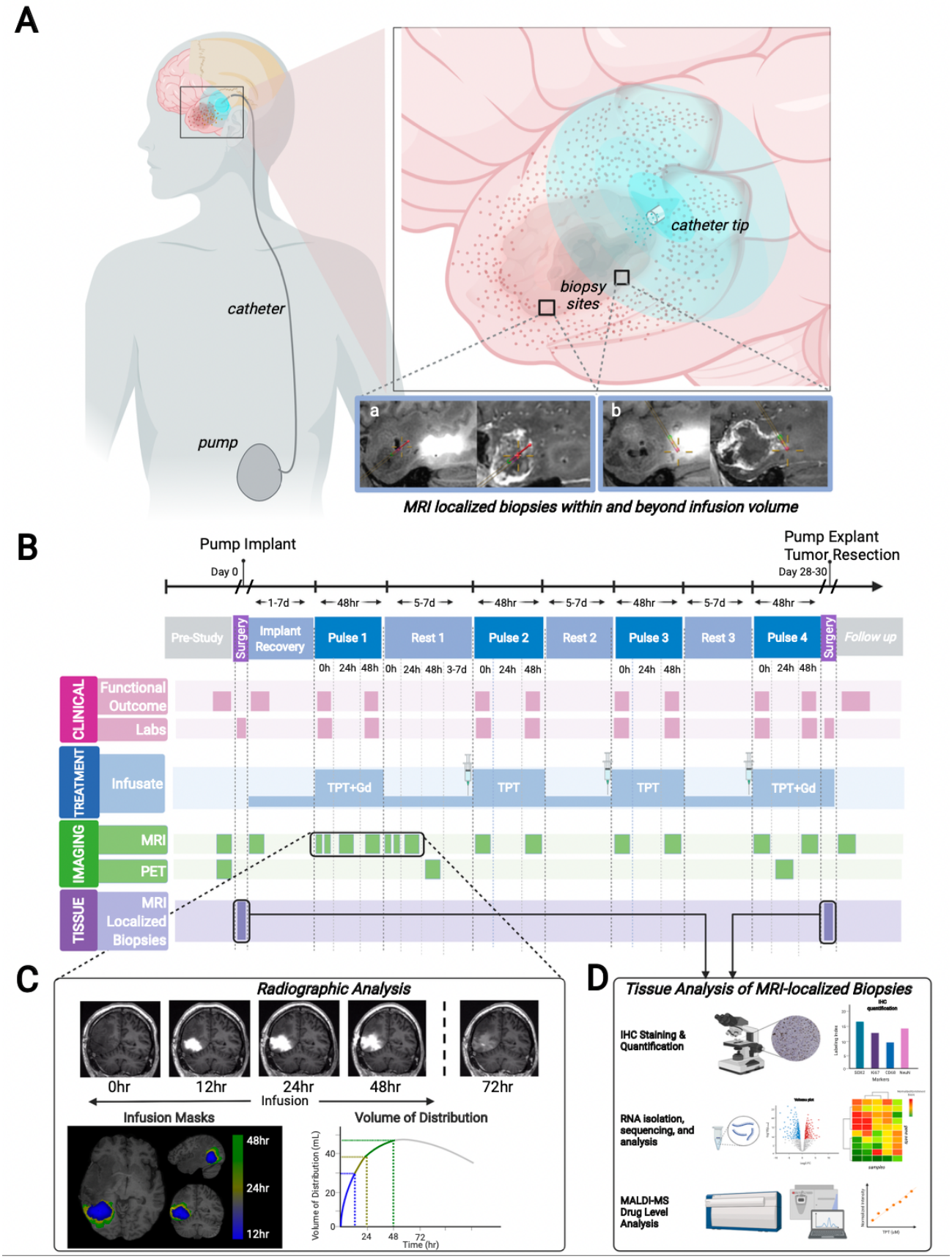
Patient 4 safely tolerated CED of TPT but suffered a stroke during surgical resection of the tumor; this adverse reaction is not directly related to the treatment delivery but affected the patient's postoperative Quality of Life (QoL) and performance outcomes. Patient 5 had arm and face weakness five days after completion of treatment due to a middle cerebral artery stroke which was attributed to a radiographically confirmed stenosis of the M2 branch from prior radiation therapy. SAEs and symptoms **prior** to and after enrollment in the trial are further summarized in Supplementary **Table 1**. Neither hematologic nor hepatic effects of the treatment were noted **(Supplementary Fig. S2**).

Patient 4 had a decrease in KPS to 40% due to the stroke during post-treatment tumor resection described above. Patient 5 maintained the baseline KPS of 80% despite the transient stroke after completion of treatment. No cognitive side effects were noted during or at the completion of the 4 treatment cycles **(Supplementary Table S1, Supplementary Fig. S1E).** A decrease in neurocognitive assessment score was noted in patient 3 after pulse 3 but recovered during pulse 4. These scores were not reflected in clinically significant cognitive deficits. A similar course was noted in patient 4 which was attributed to the overall declining health of the patient. Patient 4 had a very poor clinical course overall with only 5 months survival after CED and 13 months overall survival.

Additional molecular results

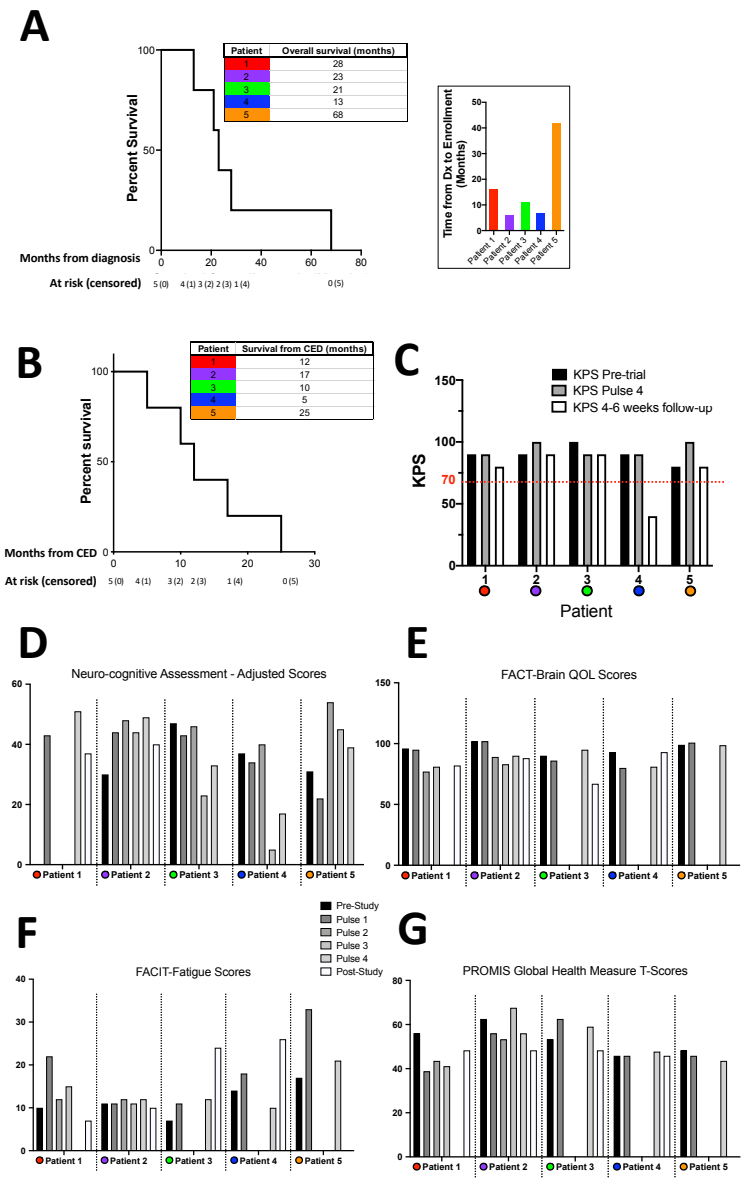
Chronic CED of TPT effectively targets proliferating tumor cells and shifts glioma phenotype. To understand the effects of TPT infusion on specific subpopulations of glioma cells, single-sample gene set en-richment analysis (GSVA) was performed on all 86 MRI-localized biopsies using gene signatures derived from snRNAseq for distinct glioma cell states, including proliferative states (gl_Pro1 and gl_Pro2), Proneural states (gl_PN1 and gl_PN2) and Mesenchymal states (gl_Mes1 and gl_Mes2) (Fig. 3J). In order to fully ascertain the spectrum of treatment effects, post-CED biopsies were further stratified by whether they were inside or outside the maximum volume of distribution, as described above. When comparing post-CED biopsies taken from within the treatment volume to the pre-CED biopsies, there was a significant shift in the enrichment scores for these glioma cell states, with a significant decrease in the samples showing highest enrichment for the proliferative or proneural signatures and a significant increase in the samples showing highest enrichment for mesenchymal signatures ($p<0.001$). Notably, the majority of post-CED samples from within the treatment volume showed the highest en-richment for the gl_Mes2 snRNAseq signature, and none showed highest enrichment for the proliferative signatures (gl_Pro1 and gl_Pro2). This analysis was repeated using glioma cell state gene sets derived by single-cell RNA sequencing (scRNAseq) as reported by Neftel et al, also demonstrating a significant enrichment ($p=0.01$) of mes-enchymal signature after treatment (Supplementary Figure 5A), Canonical mesenchymal genes were significantly upregulated post-CED within the treatment volume, and proliferation-associated and glioma progenitor genes were significantly negatively differentially expressed (Figure 3I, Supplemental Table S5). In contrast, comparing the pre-CED samples to the post-CED samples taken outside the treatment volume did not show a significant change in the distribution of enrichment scores for the glioma cell state signatures($p=0.07$). These results show that chronic CED of TPT causes a significant depletion of proliferating/proneural signatures and an increase in mesenchymal signatures selectively within the treatment volume.

Supplemental Figure S1



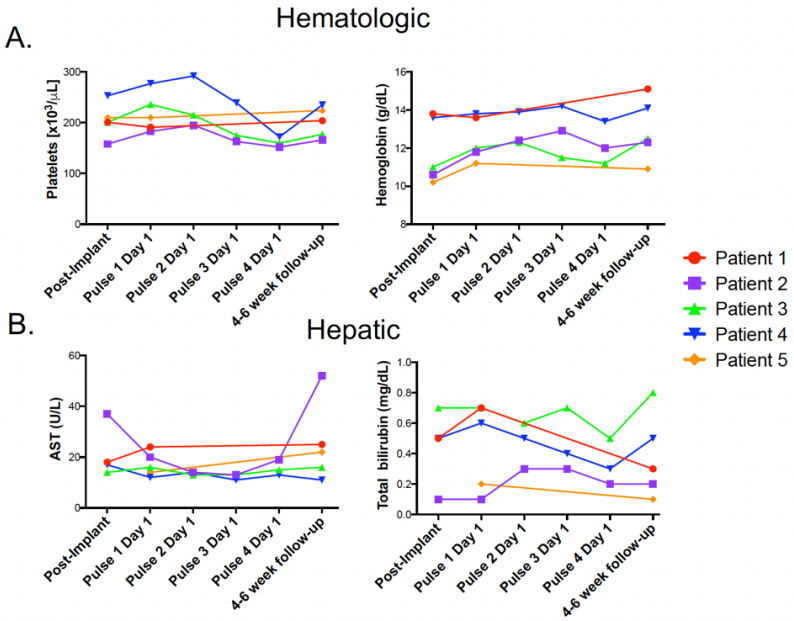
A: Overview of the implantable chronic CED pump-catheter system, as well as drug infusion and acquisition of MRI-localized biopsies. Clinical Trial Protocol is available as part of the Supplementary Material. A thin catheter was stereotactically placed midway between the tumor margin and the margin of the expected resection cavity, connected to silastic tubing that was tunneled subcutaneously and connected to a microinfusion pump implanted into the abdomen. MRI-localized biopsies were taken both at time of catheter implant and after treatment at explant. At explant, biopsies were taken both within and outside the volume of infused contrast. **B:** Schematic timeline describing the overall flow of the clinical trial. Patients enrolled in the trial underwent a baseline MRI and PET scan prior to undergoing stereotactically MRI-guided biopsies and implantation of the catheter with subcutaneous pump placement. TPT was delivered over 48 hours at 200 uL/mL in 4 cycles, with the pump refilled subcutaneously before cycles 2, 3 and 4 (syringe), and 5-7 days of rest between infusions. MRIs were performed at set time points throughout the four cycles. Functional outcome measurements, physical exams, and basic lab panels were collected and assessed throughout the duration of treatment. At the completion of the 4 cycles the pump was explanted, further MRI-localized biopsies were acquired, and the tumor was resected. **C:** Several MRIs were performed during the first pulse of TPT+Gd to characterize volume of distribution of the infusate, as well as to build radiographically-defined maximum infusion masks for further analyses. **D:** MRI localized biopsies collected before and after CED underwent tissue analysis, including immunohistochemical staining and quantification, as well as RNA isolation, sequencing and analysis. On a small subset of these biopsies, MALDI-MSI was performed to quantify concentration of TPT in the tissue after infusion.

Supplemental Figure S2



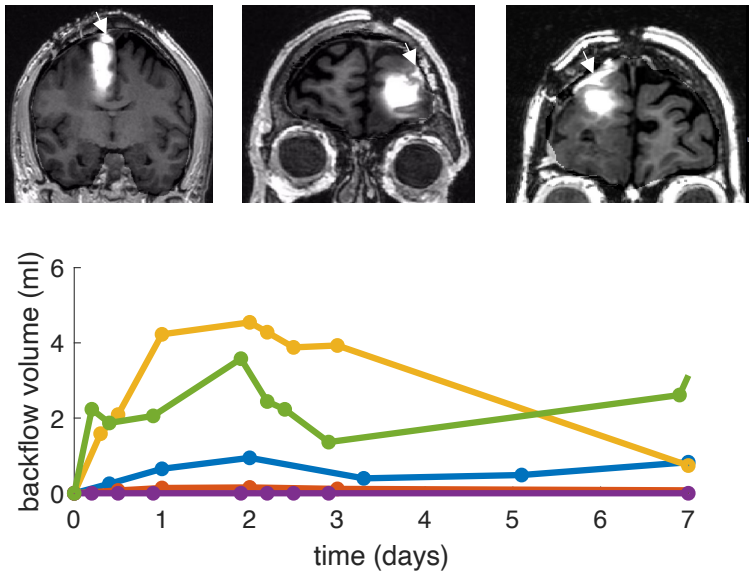
A: Kaplan Meier curve demonstrating overall survival from initial diagnosis, with accompanying bar graph depicting time from initial diagnosis to enrollment in the clinical trial /overall survival. **B:** Kaplan Meier curve demonstrating survival from initiation of CED TPT. **C:** Bar graphs showing KPS scores pre-trial, at the end of Pulse 4 and at 4-6 weeks follow-up. Red line marks a KPS of 70 considered to be the cutoff for significant changes in functional status. **D:** Bar graphs showing neurocognitive assessments throughout treatment. **E-G:** Bar graphs showcasing QoL assessment scores throughout treatment for all 5 patients.

Supplemental Figure S3



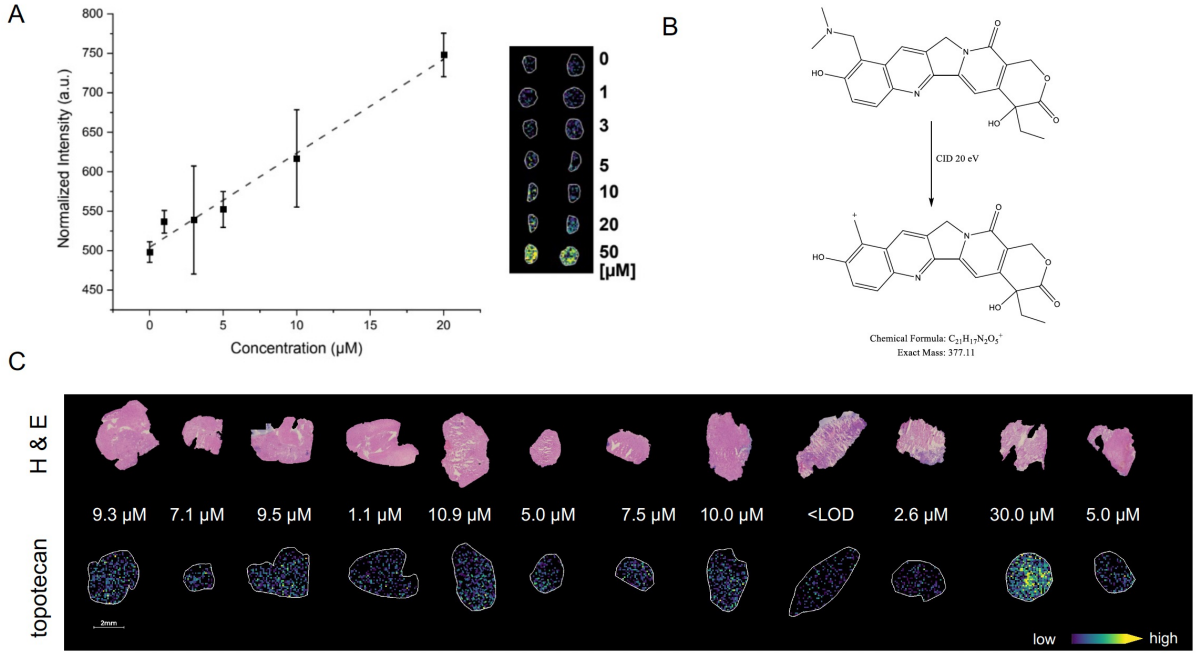
A-B: Laboratory values throughout the 4 pulses for platelets, hemoglobin, AST and total bilirubin to demonstrate systemic hematologic and hepatic safety.

Supplemental Figure S4



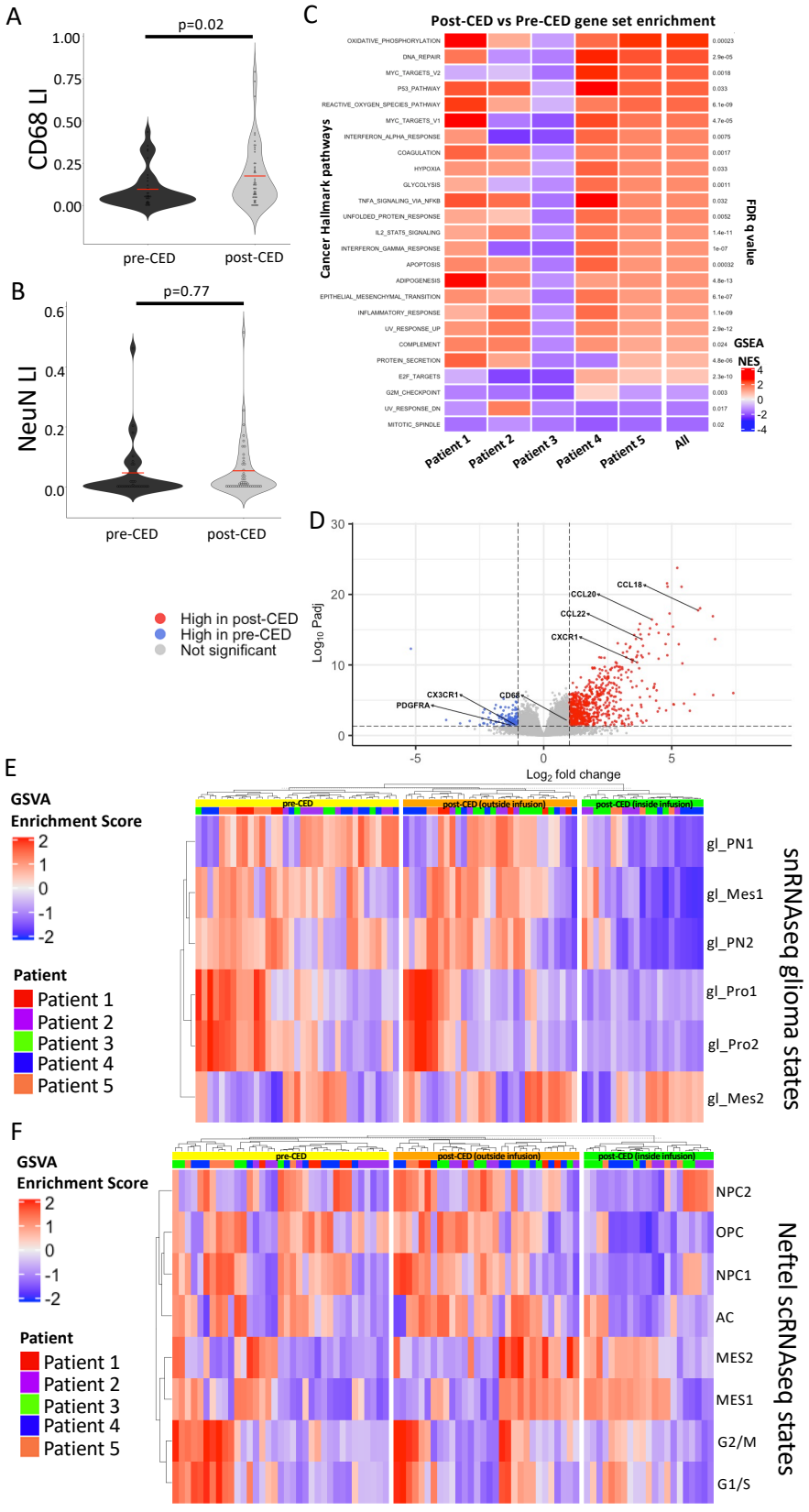
A small volume of contrast flowed back along the catheter to the brain surface (white arrows), with a time course similar to the volume infused into the brain. The maximum backflow volume was 8.8% (1.8 mL) of the volume infused into the brain suggesting that most of the drug was successfully delivered to the targeted tissue.

Supplemental Figure S5



A: Calibration curve for TPT MALDI MSI quantification with an $R^2 = 0.984$**. B:** The chemical structure of TPT precursor and product ion used for tissue quantification. **C:** H&E and TPT ion image of 12 post-CED biopsies, accompanied by estimates of average TPT concentration for each sample with detectable levels of TPT with maximum pixel values above the LOD (3.2 uM).

Supplemental Figure S6



A: Violin plot displaying quantification of CD68 by labeling index across all MRI-localized biopsies from all patients, comparing biopsies taken pre- and post-CED using a student's T-test (n=87)**. B**: Violin plot displaying quantification of NeuN by labeling index across all MRI-localized biopsies from all patients, comparing biopsies taken pre- and post-CED using a student's T-test (n=87)**. C**: Heatmap displaying patient-by-patient gene set enrichment analysis (GSEA) comparing MRI-localized biopsies before and after treatment for MSigDb "Cancer Hallmarks" ontologies. Red indicates a pathway is enriched post-CED, while blue indicates the pathway is enriched pre-CED. Significantly enriched gene sets across all patients via Fisher integration are displayed on the left of the heatmap, with the corresponding adjusted FDR q-value to the right. **D:** Volcano plot displaying differentially expressed genes between pre-CED and post-CED MRI-localized biopsies within volume of treatment across all 5 patients (n = 56). Cutoffs were log-2-fold-change > |1| and adjusted p-value < 0.05. Select significantly differentially expressed lineage-associated genes are marked. **E**: Heatmap displaying GSVA analysis of MRI-localized biopsies for six snRNAseq-derived glioma cell state signatures. GSVA scores for a given gene set are scaled across all samples. On the top of the heatmap, each biopsy is annotated by patient, as well as whether the biopsy was taken pre-CED or post-CED. The post-CED biopsies were further radiographically stratified by whether they were inside or outside the maximum volume of distribution. GSVA scores for a given gene set are scaled across all samples. On the top of the heatmap, each biopsy is annotated by patient, as well as whether the biopsy was taken pre-CED or post-CED. The post-CED biopsies were further radiographically stratified by whether they were inside or outside the maximum volume of distribution. **F:** Same analysis as E except with Neftel et al scRNAseq-derived glioma state signatures.

References for Supplementary Appendix

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Patient	Sex	Race	Initial Diagnosis
Patient 1	M	White	Anaplastic astrocytoma Grade 3
Patient 2	F	White	GBM Grade 4
Patient 3	M	White	GBM Grade 4
Patient 4	M	White	GBM Grade 4
Patient 5	F	White	GBM Grade 4

Patient	Tumor Location	Tumor Size	Date first resection
Patient 1	R, Frontal	1.6 x 1.5 x 1.9 cm	9/8/16
Patient 2	R, Temporal	4.0 x 2.8 cm	3/14/18
Patient 3	L, Frontal	2.3 x 2.2 cm	2/23/18
Patient 4	R, Temporal	2.0 x 1.6 cm	6/22/18
Patient 5	R, Frontal	3.5 x 2.6 cm	12/16/15

Patient	Age at diagnosis	Date of pump placement	Age at enrollment
Patient 1	2/2/00	1/22/18	34
Patient 2	2/26/00	9/17/18	58
Patient 3	2/29/00	1/24/19	61
Patient 4	2/25/00	2/14/19	56
Patient 5	2/17/00	7/8/19	51

Patient	Time Dx to enrollment (months)	ate of pump explant/resectic	Date of Death
Patient 1	16	2/22/18	2/2/19
Patient 2	6	10/12/18	3/4/20
Patient 3	11	2/20/19	12/16/19
Patient 4	7	3/11/19	7/23/19
Patient 5	42	7/31/19	8/20/21

Patient	Time from first CED to Death (months)	Overall survival (months)
Patient 1	12	28
Patient 2	17	23
Patient 3	10	21
Patient 4	5	13
Patient 5	25	68

Patient	Prior Treatments
Patient 1	• Concurrent RT/Temozolomide – 11/3/16 – 12/14/16 • Adjuvant Temozolomide – January 2017 – 11/11/17 (11 cycles completed)
Patient 2	• Concurrent RT/Temozolomide – 4/10/18 – 5/21/18 • Neratinib 240mg PO daily (INSIGhT R5763 Trial) – 6/19/18 – 8/14/18
Patient 3	• Concurrent RT/Temozolomide – 3/25/18 – 5/7/18 • Adjuvant Temozolomide (5 cycles) – 6/7/18 – 12/15/18 • Pembrolizumab (Keytruda) IV – 4/10/18 – 4/10/18 • Optune – 7/4/18 – 8/8/18
Patient 4	• (Atorvastatin, Pravastatin, Doxycycline, Mebendazole, Metformin) + Astragalus – 7/22/18 – 8/31/19 • Concurrent RT/Temozolomide – 7/23/18 – 8/31/18 • Optune – 9/10/18 – 2/7/19 • Adjuvant Temozolomide (4 cycles) – 10/1/18 – 12/28/18
Patient 5	• Concurrent RT/Temozolomide – 1/13/16 – 2/25/16 • Adjuvant Temozolomide – 4/5/16 – 9/18/16 • Opdivo – 1/26/16 – 1/30/18 • Optune – 4/8/16 – 6/10/19

	Primary tumor		Recurrent tumor		
			Stereotactic biopsy	Catheter explant/tumor resection	
Patient	IHC	Molecular pathology	IHC	IHC	Molecular pathology
Patient 1	Diffusely infiltrating glial neoplasm of variably increased cellularity. The tumor cells show prominent nuclear pleomorphism with some tumor cells having large and markedly atypical nuclei. Three mitotic figure is seen. Vascular proliferation and necrosis are not identified. The Ki67 proliferation index is increased, with up to 3.2% (32/1000) of cells staining positive. Glial fibrillary acidic protein (GFAP): diffusely positive Epidermal growth factor receptor (EGFR): strongly positive Phosphatase and tensin homolog	IDH1 wt, MGMT unmethylated, - EGFR Amplification, Chromosome 7 polysomy, - 1p/19q deletion	Varying amounts of hypercellularity in brain parenchyma with scattered cells showing nuclear atypia indicative of infiltrating glioma cells. No mitotic figures were seen but the Ki-67 proliferative index was elevated up to approximately 6%. Reactive changes and hyalinized vasculature were seen, consistent with treatment effect. Mutated isocitrate dehydrogenase-1 (IDH-1; R132H mutation): Negative Alpha thalassemia/mental retardation syndrome X-linked (ATRX): Labels a subset of nuclei Epidermal growth factor receptor (EGFR): Weakly stains a subset of cells Phosphatase and tensin homolog (PTEN): Negative	Variability in cellularity with glioma-infiltrated brain parenchyma and marked treatment effect that is causing necrosis, astrogliosis and microgliosis most prominent in the area adjacent to the catheter. The proliferation index varies across the specimen, and is highest in regions furthest from the catheter, in the most rostral portion of the specimen, where a KI67 labeling index of up to 19% is seen. The Ki-67 proliferation index is elevated up to 12.0% (120 labeled cells of 1000 total cells). Glial fibrillary acidic protein (GFAP): Diffusely positive; highlights reactive gliosis Sox-2: Highlights a	IDH1 wt, MGMT unmethylated, + TERT, - EGFR vIII, - 1p/19q deletion

Patient 2	Diffusely infiltrating hypercellular glial neoplasm with numerous mitotic figures, glomeruloid vasculature and occasionally pseudopalisading necrosis. Scattered microcalcifications are seen. The neoplastic cells are moderately pleomorphic with hyperchromatic nuclei. Ki-67 is variably increased with up to approximately 30-40% of tumor cells. Mutated isocitrate dehydrogenase-1 (IDH-1; R132H mutation): Negative Alpha thalassemia/mental retardation syndrome X-linked (ATRX): Preserved	IDH1 wt, MGMT unmethylated, + TERT, - EGFR vIII, - 1p/19q deletion	Diffusely infiltrating glioma in the setting of treatment effect. reactive astrocytosis (highlighted with immunostains for GFAP), patchy microgliosis (highlighted with immunostains for CD68) and a modest lymphocytic infiltrate (highlighted with immunostains for CD3). A subset of tumor cells show marked cellular atypia with large hyperchromatic nuclei. Gemistocytes, with abundant eosinophilic cytoplasm are also seen. No mitotic figures are seen. No glomeruloid-type vascular proliferation is identified, however reactive vascular changes, including thick hyalinized vessels, are noted. Necrosis is also seen. The Ki-67	[illegible] diffusely infiltrating glioma and reactive changes consistent with treatment effect. In some areas the recurrent glial neoplasm exhibits the histopathologic hallmarks ofglioblastoma, with marked nuclear atypia, pseudo-palisading necrosis, and microvascular proliferation. Many areas also show reactive changes associated with treatment effects, including fibrosis, vascular hyalinization, lymphocytic inflammation, and numerous macrophages. Neoplastic cells show fibrillary processes in some areas and have hyperchromatic pleomorphic nuclei. Mitotic figures are not	IDH1 wt, MGMT unmethylated, - TERT, - EGFR vIII, + EGFR amplification, - 1p/19q deletion

Patient 3	Diffusely infiltrating glial neoplasm with areas of high cellularity, glomeruloid vascular proliferation and necrosis. Numerous mitotic figures are identified. The tumor cells are atypical and have pleomorphic hyperchromatic nuclei. In areas, prominent perivascular lymphocytic infiltrates are noted. Ki67 proliferation index is variably increased, with up to approximately 30% of tumor cells. Mutated isocitrate dehydrogenase-1 (IDH-1; R132H mutation): negative p53: accumulated in rare scattered cells	IDH1 wt, MGMT methylated, + TERT, - EGFR vIII	Recurrent high grade glioma with variable mitotic activity, atypia, and increased cellularity. The Ki67 labeling index is increased, with up to 30-40% contralateral to prior tumor, and 5-10% ipsilateral to prior tumor. Treatment associated changes including astrogliosis, microgliosis, vascular hyalinization, and foamy macrophages are variably represented in the biopsies. No necrosis is seen. Glomeruloid-type vascular proliferation is not identified, however, hypertrophic reactive-type vasculature is evident. Mutated isocitrate dehydrogenase-1 (IDH-1; R132H mutation): Negative ATRX: Preserved P53: Positive in a subset	Diffusely infiltrating glial neoplasm, with areas of high cellularity and pleomorphism, amid many areas showing gliosis, numerous macrophages, necrosis, vascular hyalinization, and perivascular inflammation. The leptomeniges are edematous, fibrotic, and inflamed. Pseudo-palisading necrosis and glomeruloid vascular proliferation are not evident. The neoplastic cells show fibrillary processes in some areas and have hyperchromatic, pleomorphic nuclei. Occasional mitotic figures are seen. The Ki67 proliferation index is variably increased, with up to approximately 20%	IDH1 wt, MGMT methylated, + TERT, - EGFR vIII

Patient 4	surgery performed at (	IDH1 wt, MGMT unmethylated, + TERT, -EGFR vIII	A highly cellular, partially necrotic, primitive appearing neoplasm arranged in nests, cords, and sheets with deposition of myxoid matrix in the background. The neoplastic cells are highly atypical, with high nuclear to cytoplasmic ratios and a small amounts of eosinophilic cytoplasm. Only few cells show fibrillar processes. The nuclei are irregular, round to oval, hyperchromatic, with no conspicuous nucleoli, and show molding in \many areas. In some areas, the neoplastic cells show more noticeable cytoplasm with eccentric nuclei. In other areas, gemistocytic cells are noted. There are abundant mitotic figures. Multiple areas areas with apoptotic	Highly cellular, biphasic glial neoplasm arranged in nests, cords, and sheets in a background of rarefied white matter containing gemistocytes and inflammatory cells. Geographic necrosis, pseudopalisading necrosis and glomeruloid vascular proliferation are seen. The predominant population of neoplastic cells has high nuclear to cytoplasmic ratios and a small amount of eosinophilic cytoplasm. The nuclei are irregular, round to oval, hyperchromatic, with no conspicuous nucleoli, and may show molding. Frequent mitotes are noted. The Ki-67 proliferation index is variably increased, with labeling up to approximately 90% of	IDH1 wt, MGMT unmethylated, + TERT, -EGFR vIII

Patient 5	Diffusely infiltrating glial neoplasm with areas of high cellularity and frequent mitotic figures. A small focus of glomeruloid vascular proliferation and pseudopalisading necrosis . The neoplastic cells are atypical and highly pleomorphic, with angulated, hyperchromatic nuclei. Bizarre, occasionally multinucleated, giant cells are scattered throughout the specimens. The Ki67 proliferation index is variably increased, with up to 22.8% of cells staining positive. Glial fibrillary acidic protein (GFAP): strongly positive	IDH1 wt, MGMT methylated, + TERT, + EGFR vIII, no 1p/19q deletion	Diffusely infiltrating glial neoplasm with areas of increased cellularity, frequent mitotic figures, and robust microvascular proliferation. Frank necrosis is not seen. The tumor cells are atypical and highly pleomorphic. The Ki67 proliferation index is variably increased, with focally up to 40% of tumor cells staining positive. On parts C, D, E, and F, highly atypical tumor cells with similar morphology extensively involve brain parenchyma, which appear to be the infiltrating border of the tumor. Glial fibrillary acidic protein (GFAP): diffusely, strongly positive Mutated isocitrate dehydrogenase-1 (IDH-1; R132H mutation): negative	neoplasm with variably-increased cellularity. Treatment effects are evident where an acutely necrotic cavitating lesion involving cortex and white matter surrounded by many macrophages is present; however, scattered atypical cells are also still seen.There are regions of high cellularity in the adjacent tissue, with many atypical cells and microvascular proliferation. The tumor cells have hyperchromatic, pleomorphic nuclei and frequent mitotic figures are seen. Microvascular proliferation including glomeruloid forms is seen. No palisading necrosis is evident. A combined GFAP-SOX2	IDH1 wt, MGMT methylated, + TERT, - EGFR vIII, no 1p/19q deletion

Patient	Symptoms at enrollment	Symptoms end of trial
Patient 1	•Eczema – Grade 1 •Myalgia (left upper thigh) – Grade 1 •Seizure disorder – Grade 2 •Anxiety – Grade 2 •Insomnia – Grade 1	•Pain (incision site) – Grade 2 •Fatigue – Grade 1 •Photophobia – Grade 1 •Localized edema, abdomen – Grade 1 •Sinus tachycardia – Grade 2 and 1 •Thromboembolic event (LLE DVT) – Grade 2 •Thromboembolic event (RLE) – Grade 2 •Thromboembolic event (RUE) – Grade 2 •Thromboembolic event (LUE) – Grade 2 •Cough – Grade 1 •Upper respiratory infection – Grade 2 •Constipation – Grade 1 •Weight loss – Grade 1 •SIADH – Grade 1 •Seizure – Grade 1 •Supplementary motor area (SMA) syndrome – Grade 2 and 1 •Cerebral edema – Grade 2 •Cognitive disturbance – Grade 1 •Headache – Grade 1 •Hypokalemia – Grade 1 •Hypomagnesemia – Grade 1

Patient 2	•Fatigue – Grade 1 •Elevated intraocular pressure – Grade 1 •Ptosis (left eye) – Grade 1 •Tinnitus – Grade 1 •Alopecia – Grade 1 •Dry eye – Grade 2 •Blepharitis – Grade 1 •Left hemianopsia – Grade 1 •Pruritus – Grade 1 •Sinus bradycardia – Grade 1 •Flatulence – Grade 1 •Dyspepsia – Grade 2 •Constipation – Grade 2 •Arthritis – Grade 1 •Seizure disorder – Grade 2 •Headache – Grade 1 •Depression – Grade 2 •Anxiety – Grade 2 •Lymphocyte count decreased – Grade 2 •Platelets decreased – Grade 1	•Pain (incision site) – Grade 2 and 1 •Blurred vision – Grade 1 •Lip infection – Grade 2 •Constipation – Grade 2 •Hemorrhoids – Grade 2 and 1 •Cerebral edema – Grade 2 •Lymphocyte count decreased – Grade 3 and 2
Patient 3	•Fatigue – Grade 1 •Hearing impaired – Grade 2 •Thromboembolic event (Pulmonary embolism) – Grade 3 •Atrial fibrillation – Grade 2 •Hyperlipidemia – Grade 2 •Factor 5 Leiden mutation (heterozygous type) – Grade 2 •Back pain – Grade 2 •Osteoporosis – Grade 2	•Pain (incision site) – Grade 2 •Insomnia – Grade 2 •Sinus bradycardia – Grade 1 •Nausea – Grade 2 •Cerebral edema – Grade 2 •Headache – Grade 1

Patient 4	•Fatigue – Grade 1	•Fatigue – Grade 2 •Lethargy – Grade 2 •Pain (incision site) – Grade 2 •Insomnia – Grade 2 •Constipation – Grade 2 •Urinary retention – Grade 2 •Back pain – Grade 1 •Hyperglycemia – Grade 1 •Cerebral edema – Grade 2 •Left hemiplegia – Grade 3 •Dysphasia – Grade 2 and 1 •Dysarthria – Grade 2 •Stroke – Grade 3 •Anxiety – Grade 1 •Depression – Grade 2
Patient 5	•Insomnia – Grade 1 •Nausea – Grade 1 •Constipation – Grade 1 •Back Pain – Grade 1 •Hypothyroidism – Grade 2 •Restless leg syndrome •Headache – Grade 1 •Migraine – Grade 1 •Anxiety – Grade 1	•Pain (incision site) – Grade 2 •Fatigue – Grade 2 •Pain (bilateral knees) – Grade 2 •Cerebral edema – Grade 2 •Fronto-temporal fluid collection – Grade 1 •Stroke – Grade 2 •Seizure – Grade 2

Patient	Date of pump placement	Date of pump explant/resection	Concomitant medications
Patient 1	1/22/18	2/22/18	**AEDs:** •Carbamazepine ER 800 mg PO BID •Clobazam 20 mg PO qHS **Steroids:** •Dexamethasone 10/6/4/2 mg PO q6hr **Other:** •2%/3% hypertonic saline IV PRN •Enoxaparine 40 mg SQ qD
Patient 2	9/17/18	10/12/18	**AEDs:** •Levetiracetam 500 mg PO BID **Steroids:** •Dexamethasone 10/6/4 mg PO q6hr
Patient 3	1/24/19	2/20/19	**AEDs:** •Levetiracetam 500 mg PO BID **Steroids:** •Dexamethasone 10/6/4/2 mg PO q6hr
Patient 4	2/14/19	3/11/19	**AEDs:** •Levetiracetam 1500/1000 mg PO BID **Steroids:** •Dexamethasone 10/6 mg PO q6hr **Other:** •Lorazepam 1 mg IV PUSH
Patient 5	7/8/19	7/31/19	**AEDs:** •Levetiracetam 500 mg PO BID **Steroids:** •Dexamethasone 10/6/4/2 mg PO q6hr

	Serious Adverse Events
Patient 1	Nervous System Disorders Other: Supplementary motor area (SMA) syndrome, Grade 3 DLT – 1/26/18 – 1/28/18
Patient 2	No SAEs reported during trial
Patient 3	No SAEs reported during trial
Patient 4	Stroke, Grade 3 – 3/11/19 – 3/11/19 (intraoperative)
Patient 5	Stroke, Grade 2 – 8/14/19 – 9/3/19

	Karnofsky Performance Scores (KPS)			
	KPS Pre-Trial	KPS End infusion	KPS Post-Trial (4-6 wk follow-up)	Comments
Patient 1	90	90	80	Transient decrease in KPS during Pulse 2 secondary to transient SMA syndrome
Patient 2	90	100	90	
Patient 3	100	90	90	
Patient 4	90	90	40	Postoperative decrease in KPS secondary to intraoperative stroke
Patient 5	80	100	80	

	Neuro-Cognitive Assessments - Raw Scores					
	Pre-Study	Pulse 1	Pulse 4	1-4d Post-Infusion	1-2w Post-Infusion	4-6w Post-Infusion
Patient 1		43			51	37
Patient 2	29	43	47	43	48	39
Patient 3	44	40	43	20	30	
Patient 4	36	33	39	4	16	
Patient 5	31	22	54	45	39	

	Neuro-Cognitive Assessments - Adjusted Scores					
	Pre-Study	Pulse 1	Pulse 4	1-4d Post-Infusion	1-2w Post-Infusion	4-6w Post-Infusion
Patient 1		43			51	37
Patient 2	30	44	48	44	49	40
Patient 3	47	43	46	23	33	
Patient 4	37	34	40	5	17	
Patient 5	31	22	54	45	39	

	Percentiles					
	Pre-Study	Pulse 1	Pulse 4	1-4d Post-Infusion	1-2w Post-Infusion	4-6w Post-Infusion
Patient 1		67			87	43
Patient 2	16	69		69	82	58
Patient 3	78	43	76	4	27	
Patient 4	43	30	58	1	1	
Patient 5	19	3	92	72	50.3	

	FACT-Brain QOL Scores					
	Pre-Study	Pulse 1	Pulse 2	Pulse 3	Pulse 4	Post-Study
Patient 1	96	95	77	81		82
Patient 2	102	102	89	83	90	88
Patient 3	90	86			95	67
Patient 4	93	80			81	93
Patient 5	99	100.83			98.67	

FACT-Br score range 0-200

	FACIT-Fatigue scale					
	Pre-Study	Pulse 1	Pulse 2	Pulse 3	Pulse 4	Post-Study
Patient 1	10	22	12	15		7
Patient 2	11	11	12	11	12	10
Patient 3	7	11			12	24
Patient 4	14	18			10	26
Patient 5	17	33			21	

FACIT Fatigue scale 0-52

	PROMIS Global health measure (T-Score)					
	Pre-Study	Pulse 1	Pulse 2	Pulse 3	Pulse 4	Post-Study
Patient 1	56	38.8	43.5	41.1		48.3
Patient 2	62.5	56	53.3	67.6	56	48.3
Patient 3	53.3	62.5			59	48.3
Patient 4	45.8	45.8			47.7	45.8
Patient 5	48.3	45.8			43.5	

PROMIS Global health: Higher T-Score is healthier

Patient	Volume of distribution* (Vd	Volume of infusion* (Vi)	Vd/Vi*	Total volume of infusion
Patient 1	13.1 mL	5.4 mL	2.44	21.6 mL
Patient 2	35.9 mL	11.1 mL	3.23	38.4 mL
Patient 3	14.6 mL	7.2 mL	2.03	38.4 mL
Patient 4	26.6 mL	9.7 mL	2.73	38.4 mL
Patient 5	12.0 mL	9.6 mL	1.24	38.4 mL

(* = measured at the time of maximum volume of distribution)

Gene	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj
DKK1	746.5657276	5.215958324	0.468820988	11.12569286	9.40721E-29	1.73366E-24
WNK4	535.675532	4.816467155	0.454322863	10.60141926	2.93492E-26	2.70438E-22
NECTIN4	319.4882503	4.837993146	0.462467399	10.46126312	1.30109E-25	7.99263E-22
MCEMP1	196.1110339	5.382921395	0.516046368	10.43108086	1.78842E-25	8.23971E-22
HCAR3	161.9730513	6.109075777	0.628544004	9.719408244	2.49226E-22	9.18596E-19
CCL18	8767.073074	6.029873317	0.626056854	9.631510747	5.88577E-22	1.80781E-18
ANKRD1	483.1837736	4.914836792	0.516853739	9.509144312	1.92237E-21	5.06106E-18
RNASE7	91.88871869	6.605940165	0.702748969	9.400142097	5.44894E-21	1.25523E-17
CCL20	504.9079605	4.226323382	0.455661041	9.275147537	1.77373E-20	3.63202E-17
IGFBP6	5847.525994	3.758800792	0.412494897	9.112357074	8.06112E-20	1.48558E-16
GDF15	5104.918033	4.40737178	0.485072458	9.086007063	1.02743E-19	1.72132E-16
HCAR2	151.4654788	5.047967281	0.561376017	8.992132064	2.4248E-19	3.72389E-16
HBA1	76020.92924	4.152825857	0.465487559	8.921454028	4.60206E-19	6.52395E-16
CXCL1	477.6880951	3.704543842	0.417591959	8.871204918	7.23587E-19	9.52498E-16
C15orf48	697.9468837	4.487526544	0.513380911	8.741124665	2.30801E-18	2.83562E-15
HBA2	158638.8161	4.108053462	0.474089433	8.665144532	4.50941E-18	4.61688E-15
MMP7	1329.021406	4.869475807	0.56168038	8.669478197	4.34105E-18	4.61688E-15
TMMSF19	81.78149146	3.778182659	0.435578605	8.673939946	4.17421E-18	4.61688E-15
FXYD2	230.7816236	3.536696985	0.409548787	8.635593837	5.84227E-18	5.6667E-15
G0S2	1651.998321	3.601872054	0.42471032	8.480773569	2.23702E-17	2.0613E-14
CCL22	280.1877079	3.820516393	0.451396152	8.463777047	2.58854E-17	2.16838E-14
LCE1C	174.1032885	6.693593992	0.790370949	8.46892715	2.47664E-17	2.16838E-14
FDKR	4843.728136	2.892391272	0.348571707	8.297837187	1.06024E-16	8.49528E-14
TP53I3	4414.757994	3.205756368	0.387886378	8.264678908	1.40071E-16	1.07557E-13
CD70	401.1973522	4.760594062	0.57654432	8.25711727	1.49233E-16	1.10008E-13
CEACAM3	96.87577459	5.276709389	0.639925758	8.245814962	1.64038E-16	1.16272E-13
TFPI2	361.9941551	3.877695876	0.474000231	8.180789007	2.81991E-16	1.92475E-13
AQP9	1106.654714	3.385218821	0.415629688	8.144795515	3.79923E-16	2.50057E-13
IL1R2	170.5833996	3.357901493	0.41523341	8.086780614	6.12625E-16	3.89312E-13
KRT5	296.9766351	-5.188275979	0.644335967	-8.052128465	8.13664E-16	4.99834E-13
LRG1	257.7482472	3.251579459	0.40978952	7.934755042	2.10911E-15	1.25383E-12
KRT7	501.8556161	3.676853164	0.464137779	7.921900198	2.33908E-15	1.34709E-12
RRAD	2041.088539	3.096039335	0.392976517	7.878433448	3.31511E-15	1.85134E-12
S100A12	118.0813302	4.107454452	0.524097079	7.837201576	4.60698E-15	2.49712E-12
LAD1	80.49092625	4.828589171	0.621886116	7.764426716	8.20153E-15	4.31846E-12
PADI4	93.98103155	3.812085103	0.491495681	7.756090748	8.75874E-15	4.48374E-12
CLDN1	581.8876037	3.650159869	0.470899521	7.751462262	9.08403E-15	4.52459E-12
ACP5	5751.530347	3.618711267	0.471167208	7.680312223	1.58701E-14	7.6966E-12
CD52	1671.340291	3.221661732	0.419950701	7.671523636	1.69965E-14	8.03151E-12
PLIN2	6407.175298	2.175412047	0.283929328	7.661808172	1.83333E-14	8.24061E-12
SFN	3998.409197	3.861643534	0.503808675	7.66490083	1.78969E-14	8.24061E-12
GGHFR	1027.762208	2.245575037	0.293737332	7.64484046	2.09205E-14	9.1796E-12
SERTAD1	2222.54772	2.372249071	0.310720939	7.634661119	2.26415E-14	9.70373E-12
CCL23	73.12703956	4.486898264	0.590984629	7.592241901	3.14417E-14	1.31691E-11
SLAMF7	744.7685661	3.422807078	0.452739432	7.560214193	4.02406E-14	1.64799E-11
FCN1	404.5827848	3.48240168	0.461573139	7.544636776	4.5355E-14	1.81706E-11
S100P	67.53523437	3.45316154	0.463904753	7.443686482	9.79137E-14	3.83926E-11
LILRB5	1212.944492	2.812546865	0.37866254	7.427581478	1.10601E-13	4.2464E-11
CXCR1	84.74482919	3.648812592	0.491589615	7.422476961	1.1495E-13	4.32329E-11
RHOD	507.7557865	2.851258858	0.386112772	7.384523552	1.53E-13	5.63928E-11
LCE1E	64.34531981	5.416405249	0.734670982	7.37255912	1.67383E-13	6.04845E-11
DOK2	482.3134046	2.850600699	0.393047892	7.252553072	4.08988E-13	1.44947E-10
CFP	575.5028852	2.380592694	0.3301115	7.211480642	5.53467E-13	1.85452E-10
PMAIP1	491.4491538	2.928507964	0.405955961	7.213856298	5.43892E-13	1.85452E-10
CXCL3	264.0469778	2.981474391	0.413260548	7.214514923	5.41266E-13	1.85452E-10
MFAP5	381.3972013	2.774532803	0.385688567	7.193712852	6.30527E-13	2.075E-10
EVA1A	214.242523	3.063898782	0.426401933	7.18547113	6.69758E-13	2.16543E-10
NFKBIE	1579.559847	1.897801447	0.264915706	7.163793637	7.84745E-13	2.4512E-10
DHDH	133.5822234	1.974255793	0.275552291	7.164722842	7.79441E-13	2.4512E-10
C2CD4B	41.70516783	2.662145178	0.372334317	7.149878641	8.68547E-13	2.66774E-10
SPINT1	434.7616238	1.995874243	0.279774214	7.13387491	9.7582E-13	2.9481E-10
SELE	171.925076	3.729278624	0.523109971	7.129052845	1.01062E-12	3.00398E-10
COMTD1	810.7768498	1.915590164	0.269196922	7.115943793	1.1115E-12	3.25139E-10
LILRA5	280.9979821	3.07306272	0.433426392	7.090160577	1.33956E-12	3.85732E-10
APOBR	1801.254155	2.189328214	0.309127158	7.082290105	1.41791E-12	4.02011E-10
CLEC4E	746.5147551	2.988835334	0.422797951	7.069181214	1.55851E-12	4.35177E-10
TNFRSF10C	633.3626132	2.601458365	0.368158032	7.066145896	1.59296E-12	4.38159E-10
FAM83G	497.6251945	2.618549024	0.371742995	7.043976782	1.86829E-12	4.98997E-10
MMP8	84.36658376	3.309007812	0.469732775	7.044447378	1.86199E-12	4.98997E-10
SERINC2	1019.30458	2.28250899	0.324710542	7.029365209	2.07475E-12	5.46223E-10
TIMP1	72367.79365	2.920962446	0.417490905	6.996469655	2.62493E-12	6.81335E-10
IL1RL1	182.9103188	2.429698667	0.34746792	6.992584145	2.69869E-12	6.90751E-10
ALAS2	138.5786918	3.428464922	0.493465586	6.947728508	3.71214E-12	9.37139E-10
SLC52A1	296.0374861	3.217823705	0.464791788	6.923150942	4.41707E-12	1.10003E-09
B3GNT8	197.8743357	2.509942592	0.3646359	6.883421495	5.84318E-12	1.43579E-09
CDKN1A	14642.6047	2.200873737	0.320455136	6.867962121	6.51255E-12	1.57921E-09
KCNK15	127.2803018	3.027047969	0.445590052	6.793347287	1.09561E-11	2.62221E-09
EEF1AKMT4	140.1020534	2.134507223	0.316175019	6.751030592	1.46799E-11	3.4684E-09
GPX3	13044.79923	2.524616254	0.375573785	6.722024694	1.79217E-11	4.18074E-09
FOSL1	857.2842845	2.369291903	0.353101838	6.709939314	1.94705E-11	4.48528E-09
HIST1H2BJ	111.7100214	2.486521518	0.371480615	6.693543126	2.17831E-11	4.95605E-09
SIRPB1	698.4685452	2.187012318	0.327454513	6.678827835	2.40861E-11	5.4132E-09
SESN2	1909.792321	1.448703166	0.217380561	6.664363906	2.65814E-11	5.90203E-09
IFI30	23755.6933	2.519021016	0.378435765	6.656403145	2.8061E-11	6.08395E-09
CSF3	85.15688286	3.280096997	0.492687252	6.657564174	2.78403E-11	6.08395E-09
CD300E	257.7681785	2.765991199	0.415922949	6.650249055	2.92597E-11	6.27009E-09
IL1RN	721.104679	2.91236265	0.439063414	6.633125328	3.28653E-11	6.96177E-09
LAMC2	138.8642344	2.52389576	0.381059847	6.623357924	3.51129E-11	7.27075E-09
MYO1G	1417.944788	2.401910104	0.362556505	6.624926236	3.47422E-11	7.27075E-09
S100A3	581.9461275	2.478219222	0.377636466	6.562446804	5.29319E-11	1.08387E-08
STAP2	397.3148807	2.070929589	0.315916304	6.555310899	5.55261E-11	1.11227E-08
CCRL2	825.3985318	2.289840457	0.349251556	6.556421639	5.51143E-11	1.11227E-08
CCR7	220.5990017	3.032105575	0.463697855	6.538968299	6.19447E-11	1.2275E-08
TNFRSF9	157.1241927	2.270112451	0.347442195	6.533784572	6.41282E-11	1.25725E-08
BBC3	1091.513018	1.780087931	0.273752683	6.502540581	7.89747E-11	1.53203E-08
CAMP	60.1966797	3.838858398	0.592486617	6.479232254	9.21905E-11	1.76977E-08
LILRA3	66.90359898	3.40399386	0.527379852	6.454539068	1.08549E-10	2.06231E-08
S100A6	38182.49267	1.870697328	0.2920196	6.406067693	1.49321E-10	2.80799E-08
NFKB2	2347.577256	1.805492131	0.282144437	6.399176775	1.56217E-10	2.908E-08
CLDN4	149.3421853	2.562975247	0.400782477	6.394928405	1.60623E-10	2.96011E-08
CYSRT1	160.6288473	1.948397378	0.305258158	6.382785611	1.73895E-10	3.17299E-08
SPR	945.5792078	1.137258879	0.178728464	6.363054076	1.97781E-10	3.53874E-08
BNC1	58.09154065	2.634767826	0.414013818	6.36396108	1.96616E-10	3.53874E-08
AL049629.2	211.3034623	2.729247768	0.429450586	6.355207923	2.08145E-10	3.68837E-08
LILRA6	589.592039	2.3084299	0.363885532	6.343835343	2.24114E-10	3.93353E-08
PGLYRP1	20.29927718	4.333099175	0.687504045	6.302652625	2.92594E-10	5.087E-08
DDX1	61.55534497	2.761163583	0.438229465	6.30072554	2.96256E-10	5.10252E-08
HIST1H1C	1586.085693	1.759937513	0.279746918	6.291177486	3.15067E-10	5.37627E-08
HES2	75.07745966	2.509993224	0.400204638	6.27177445	3.56956E-10	6.03518E-08
HAS1	224.8789164	2.253416578	0.360974233	6.242596764	4.30365E-10	7.21018E-08
TNFRSF10A	222.2784732	2.05766301	0.330412484	6.227558302	4.7376E-10	7.8657E-08
SUCNR1	123.136629	2.845040601	0.456952682	6.226116435	4.78139E-10	7.86752E-08
BCL2A1	1134.591471	2.438116582	0.392846153	6.206288547	5.42505E-10	8.84764E-08
ACTL10	110.3745673	1.691770588	0.273529784	6.184959329	6.21185E-10	1.00419E-07
CXCL6	167.4240572	3.621554428	0.585983029	6.180305993	6.39775E-10	1.02525E-07

FGR	1745.699304	1.810715472	0.293904522	6.160896944	7.23341E-10	1.14918E-07
PRSS57	12.33719163	4.311095667	0.700741722	6.152189214	7.64206E-10	1.20372E-07
HTRA4	398.1972913	2.030387773	0.331639735	6.122269324	9.22519E-10	1.44077E-07
SERPINB2	47.45103551	2.94538212	0.481884182	6.112219963	9.82546E-10	1.52163E-07
AREG	201.8126181	3.46478229	0.567120595	6.109427735	9.9989E-10	1.52289E-07
MAP2K3	2158.23506	1.286550751	0.210566321	6.109955029	9.96592E-10	1.52289E-07
C11orf96	2670.338241	1.636625351	0.267966634	6.107571398	1.01159E-09	1.52807E-07
KRT18	130.6604169	2.232846804	0.365841557	6.103316487	1.0389E-09	1.55657E-07
CXCR2	208.9247896	2.166860115	0.355394823	6.097050309	1.08044E-09	1.60575E-07
CES1	873.3879639	2.689249309	0.442459626	6.077954122	1.21726E-09	1.78038E-07
NEURL3	174.4934217	2.056859994	0.338403728	6.078124513	1.21596E-09	1.78038E-07
S100A2	278.7278143	2.149836905	0.3540272	6.072519019	1.25919E-09	1.81294E-07
HKDC1	392.9498299	1.803023628	0.29689313	6.072971875	1.25564E-09	1.81294E-07
RAET1L	27.75020464	4.29516779	0.707580255	6.070219961	1.27735E-09	1.82483E-07
SEPHS2	3172.389004	0.869032443	0.143767675	6.04469984	1.49688E-09	2.12201E-07
IL4I1	991.8755059	2.294281521	0.379802318	6.040725435	1.53423E-09	2.15834E-07
ITLN1	15.67496337	4.044013911	0.671722692	6.020362212	1.74027E-09	2.42966E-07
S1PR4	162.2441547	2.401006345	0.399125269	6.015671098	1.79143E-09	2.48228E-07
HBB	86007.81609	2.837293424	0.471992427	6.011311327	1.84029E-09	2.53094E-07
PROCR	945.2700803	1.900758682	0.316365239	6.008114833	1.87693E-09	2.56222E-07
CITED1	1275.805935	2.201027208	0.370240053	5.944865198	2.76684E-09	3.74928E-07
OSCAR	1316.567763	1.800585322	0.302946072	5.943583656	2.78857E-09	3.75114E-07
LILRB3	990.286809	2.3573175	0.3968214	5.940499926	2.84154E-09	3.79469E-07
DGAT2	549.2116488	1.82619135	0.307850121	5.93207936	2.99122E-09	3.96584E-07
NPB	770.3105979	1.830751878	0.30873303	5.929886659	3.03144E-09	3.99046E-07
IL23A	125.9456127	2.59484402	0.437830101	5.926600325	3.0927E-09	4.01376E-07
DEFA1	23.05570689	4.411166217	0.744223903	5.927203093	3.08138E-09	4.01376E-07
TNFSF9	429.861207	1.793258049	0.302680765	5.924585423	3.13086E-09	4.03487E-07
ETV4	452.0022939	1.58743272	0.268068323	5.921746742	3.1854E-09	4.07665E-07
CCL14	39.79816023	2.356659252	0.399557269	5.8981764	3.67541E-09	4.67132E-07
CEACAM1	212.8878659	2.331565401	0.395444949	5.896055586	3.72294E-09	4.69931E-07
CXCL5	347.981597	2.34276828	0.398867832	5.873545296	4.26572E-09	5.34783E-07
GALR2	25.285045	2.840828674	0.484647378	5.861640453	4.58317E-09	5.70697E-07
RHCG	226.9021385	2.081509707	0.35544724	5.856030024	4.74063E-09	5.86342E-07
PTGES	308.9790242	1.868871872	0.319586585	5.847779484	4.98178E-09	6.12062E-07
SRGAP2	3525.122073	-0.693825748	0.118839739	-5.838331157	5.27263E-09	6.43505E-07
RETN	32.73890384	2.949244262	0.50589156	5.829795348	5.54954E-09	6.72845E-07
PALD1	2828.95151	-0.980759865	0.168280573	-5.828122922	5.60543E-09	6.75179E-07
CHMP4C	95.04227951	2.100421926	0.361473159	5.810727221	6.2202E-09	7.44365E-07
ABCB5	41.70399583	2.242436135	0.386288662	5.805078835	6.43357E-09	7.60028E-07
NR1H3	1249.653811	1.246876855	0.214790034	5.805096406	6.4329E-09	7.60028E-07
TAF7L	93.34500308	2.543404909	0.438474197	5.800580578	6.60857E-09	7.75728E-07
PIP5K1P1	446.0581872	2.291081189	0.395193467	5.797366051	6.73645E-09	7.85735E-07
DPP4	275.6182393	1.864330087	0.321709093	5.79508049	6.82884E-09	7.91501E-07
TRIAP1	1599.09702	1.354792338	0.234055955	5.788326722	7.1091E-09	8.18835E-07
MMGT1	1828.937655	0.346466976	0.059944612	5.779785121	7.47961E-09	8.5616E-07
KRT23	44.13058411	3.014403183	0.521953604	5.775232055	7.68471E-09	8.74207E-07
TMEM150B	155.7683648	2.095014381	0.363601771	5.761837662	8.3203E-09	9.40704E-07
C1orf68	17.5974416	7.404284899	1.286754607	5.754232283	8.70364E-09	9.72118E-07
S100A8	2696.46868	2.495932051	0.433734708	5.754513087	8.68919E-09	9.72118E-07
LYPLA2	2896.789662	1.144863568	0.199458153	5.739868495	9.47501E-09	1.0519E-06
RETREG3	2339.765227	0.601268245	0.10490994	5.731280013	9.96756E-09	1.09995E-06
ADAMDEC1	348.7531828	2.561597772	0.448603897	5.710154974	1.12873E-08	1.23818E-06
LSP1	3713.434998	1.900709669	0.333074977	5.706551976	1.15288E-08	1.25718E-06
AP5B1	952.7154269	1.088010307	0.190820446	5.701749119	1.18584E-08	1.27058E-06
MME	114.7661203	2.173821176	0.381234051	5.702064571	1.18365E-08	1.27058E-06
TMSB10	65205.27139	1.290752799	0.226303553	5.703634717	1.17279E-08	1.27058E-06
S100A9	6838.123038	2.328913019	0.408862285	5.696081789	1.22592E-08	1.30592E-06
KCNJ15	132.7040678	1.486869762	0.261240672	5.691570738	1.25876E-08	1.32558E-06
ST14	1967.854357	1.883857808	0.33094532	5.692353682	1.253E-08	1.32558E-06
ICAM3	545.6273448	1.484520782	0.260923436	5.68948809	1.27421E-08	1.33423E-06
GNPDA1	3549.909808	0.881702432	0.155033259	5.687182463	1.29152E-08	1.34472E-06
ISLR	1882.061538	1.446236503	0.254444844	5.683889997	1.31665E-08	1.36318E-06
NEU1	2988.218284	1.000189842	0.176045634	5.681423722	1.33578E-08	1.37526E-06
LCE1B	11.43038794	5.890092372	1.038899928	5.669547416	1.43175E-08	1.46588E-06
SLC4A1	116.4657114	2.112037807	0.372833706	5.664825296	1.47174E-08	1.49026E-06
CD244	114.354481	2.213705997	0.390746675	5.66532267	1.46748E-08	1.49026E-06
CTSL	14591.88991	1.476902803	0.260826666	5.662391906	1.49277E-08	1.5033E-06
TNIP2	1896.640523	1.173891211	0.207423503	5.659393436	1.51909E-08	1.52148E-06
PHF23	1793.856636	0.6143534	0.108588617	5.657622476	1.53484E-08	1.52895E-06
LIF	1000.880974	2.221449234	0.393172956	5.650056036	1.60396E-08	1.58921E-06
PTGIR	267.7698845	1.685291065	0.298522727	5.645436381	1.64763E-08	1.62375E-06
TSKU	931.8435566	1.225864435	0.217542428	5.635059085	1.74998E-08	1.70637E-06
TCN2	2905.428188	1.251928436	0.222160434	5.635244821	1.7481E-08	1.70637E-06
PBDC1	1117.850212	1.069863638	0.189925868	5.633059102	1.77041E-08	1.7172E-06
MRGPRX3	37.72330813	2.249106959	0.399362388	5.631744568	1.78396E-08	1.72129E-06
TSLP	137.7663863	2.079927635	0.369962827	5.621990867	1.88769E-08	1.77491E-06
APOBEC3C	2669.617614	1.645664499	0.292690619	5.622539262	1.88171E-08	1.77491E-06
NKX3-1	239.3599679	1.491982782	0.265351238	5.622671266	1.88027E-08	1.77491E-06
BATF	373.5098597	2.174082583	0.386596363	5.623649865	1.86964E-08	1.77491E-06
FSTL3	3883.951876	1.507025814	0.267934647	5.624602227	1.85936E-08	1.77491E-06
CST4	24.99587112	6.617505808	1.17936298 2	5.611084891	2.01062E-08	1.8809E-06
SLC25A19	1034.049417	1.160450299	0.20751959	5.592003627	2.24464E-08	2.08922E-06
CEBPZOS	2095.616151	0.43603017	0.078080957	5.584334347	2.34597E-08	2.17256E-06
TMEM92	26.13137947	2.153454753	0.386032474	5.578429009	2.427E-08	2.22524E-06
CCL26	53.19473979	2.650008825	0.475009575	5.578853486	2.42109E-08	2.22524E-06
HEBP2	1852.752266	0.806288401	0.144577267	5.576868478	2.44887E-08	2.23417E-06
FUCA1	4418.858917	1.658314753	0.297604698	5.572206224	2.51533E-08	2.2835E-06
SMIM4	856.2900556	1.152886954	0.207007969	5.569287784	2.55783E-08	2.3107E-06
GRN	28243.70039	1.537928426	0.276625853	5.559597592	2.70397E-08	2.43081E-06
FMNL3	3089.737026	-0.620590638	0.111705012	-5.555620332	2.76628E-08	2.47474E-06
MAPK13	1102.571589	1.331091754	0.239675928	5.553714812	2.79662E-08	2.47783E-06
LEP	25.38932301	2.618802652	0.471503587	5.554152135	2.78962E-08	2.47783E-06
MSC	298.3505176	2.172655442	0.391550977	5.548844393	2.87564E-08	2.53565E-06
NPM3	570.0584017	0.918804924	0.165636059	5.547131027	2.90395E-08	2.54842E-06
EPHA2	867.2905854	1.639906623	0.296076666	5.538790436	3.04568E-08	2.66013E-06
PODNL1	944.1748445	1.760902042	0.318149708	5.534822121	3.11544E-08	2.70823E-06
SPHK1	1750.448715	1.560026284	0.282148252	5.529101369	3.21875E-08	2.7849E-06
TNIP3	69.44186399	1.805431098	0.327047785	5.520389311	3.38249E-08	2.9129E-06
MMP3	37.07405556	2.804710637	0.509320609	5.506768408	3.65481E-08	3.11826E-06
DEFB1	14.26752686	4.144484913	0.752523822	5.507446795	3.64075E-08	3.11826E-06
PF4	38.37988134	2.747449047	0.499680997	5.498406107	3.8324E-08	3.23978E-06
PLA2G7	861.8866612	1.808222913	0.328847365	5.498669315	3.82668E-08	3.23978E-06
PDLIM4	3079.744039	1.279850519	0.233162322	5.489096654	4.03995E-08	3.39964E-06
PER3	1738.910214	-1.06493557	0.194145457	-5.485245879	4.12895E-08	3.45874E-06
TNFRSF6B	1210.139796	1.718523902	0.313670843	5.47874927	4.28343E-08	3.57191E-06
SIGLEC15	65.20401924	2.095368914	0.382555688	5.477291222	4.31886E-08	3.58524E-06
EFNB1	1814.793352	1.21882074	0.222626757	5.474727097	4.38186E-08	3.62123E-06
ANXA8	75.58214328	2.007578341	0.366968232	5.470714262	4.48225E-08	3.67127E-06
SHC1	6042.289695	1.400474917	0.255963406	5.471387251	4.46526E-08	3.67127E-06
PPP1R15A	5334.603528	1.228710023	0.224673271	5.468874942	4.52901E-08	3.69315E-06
KRT6B	13.95270233	3.759058529	0.689021737	5.45564578	4.87952E-08	3.96144E-06
ATG10 1	1852.530251	0.927043052	0.16995063	5.454778553	4.90339E-08	3.96336E-06
AGPAT2	1258.091364	1.170423144	0.214852339	5.447569947	5.10626E-08	4.09145E-06
CYP2S1	229.5237806	1.39143051	0.255402446	5.447992115	5.09416E-08	4.09145E-06
DEDD2	1869.968442	0.723472745	0.13298585	5.440223474	5.32138E-08	4.24535E-06

PLA2G2D	54.84895429	2.480547761	0.45610437	5.438552933	5.37151E-08	4.26687E-06
VPS18	3023.928733	0.833522258	0.153298934	5.43723454	5.41139E-08	4.28011E-06
AEN	1966.389437	1.208493315	0.222354398	5.434987242	5.48004E-08	4.29751E-06
UPP1	3042.662752	1.166111591	0.214528242	5.435701981	5.45811E-08	4.29751E-06
HPS6	859.7440363	0.856885794	0.157970247	5.424349286	5.8166E-08	4.54213E-06
ADAM8	1297.419267	1.73856675	0.321967336	5.399823379	6.67065E-08	5.18707E-06
MDK	9717.890695	1.6560212	0.306935429	5.395340664	6.83937E-08	5.29591E-06
SPATA2L	780.8878114	0.95164789	0.176444078	5.393481601	6.91054E-08	5.32863E-06
BAX	4797.750059	1.258299445	0.233695466	5.384355407	7.27047E-08	5.58281E-06
FPR2	200.3542912	2.503861304	0.466736004	5.364620009	8.11198E-08	6.20314E-06
MYO15B	4526.086965	-0.763247739	0.14235182	-5.361699912	8.24424E-08	6.25239E-06
VAMP5	3614.836939	1.476519822	0.275364539	5.36205507	8.22804E-08	6.25239E-06
NOP16	877.3877601	1.093851321	0.204154327	5.357962942	8.41655E-08	6.35691E-06
GFI1	29.86152294	-1.564569931	0.292394007	-5.350896021	8.75198E-08	6.55651E-06
TIMM22	1009.092804	0.702733915	0.131320986	5.351268965	8.73396E-08	6.55651E-06
HIST2H4B	476.6091529	1.109826673	0.207647919	5.344752212	9.05408E-08	6.75537E-06
KLK10	76.115255	1.620396168	0.303361371	5.341471672	9.2195E-08	6.85106E-06
SYTL1	441.7533115	1.939892623	0.363237116	5.340568292	9.26557E-08	6.85764E-06
RRAGD	2774.71421	0.489321948	0.091675897	5.337520123	9.42264E-08	6.946E-06
IFITM2	5901.852427	1.414787945	0.265110541	5.33659634	9.47076E-08	6.95365E-06
ETV7	354.8404993	1.999834688	0.374964004	5.333404446	9.63883E-08	7.02111E-06
PNP	2293.346074	1.27713278	0.239451845	5.333568341	9.63013E-08	7.02111E-06
TXN	6986.246274	1.00796215	0.1892612	5.325772804	1.00525E-07	7.29358E-06
CLCN1	20.70756121	2.142831755	0.403123468	5.315571837	1.06323E-07	7.68402E-06
HEXIM1	2998.377292	0.773720267	0.145836709	5.305387594	1.12434E-07	8.09392E-06
MMP25	324.2184162	2.202889707	0.41537361	5.303393505	1.1367E-07	8.15103E-06
NOP10	3475.077974	0.981005757	0.185159796	5.298157476	1.16977E-07	8.3557E-06
TMEM41A	1016.638415	0.40979862	0.077358494	5.297396585	1.17465E-07	8.35818E-06
ZBED6CL	288.5252996	1.907973902	0.36045101	5.293296039	1.20131E-07	8.51499E-06
AP1S1	4208.508133	0.877826733	0.165868569	5.292303038	1.20786E-07	8.52857E-06
EXOSC4	1625.033757	1.158688619	0.219107378	5.28822274	1.23511E-07	8.65466E-06
ADGRE3	27.72715108	3.001565208	0.567559484	5.288547359	1.23292E-07	8.65466E-06
FAM167B	156.4222381	1.677757629	0.317979699	5.276304217	1.31815E-07	9.2016E-06
PTGER2	78.39246997	2.20903574	0.419470524	5.266247842	1.3924E-07	9.68324E-06
ACOX1	2844.01443	0.398932949	0.075917944	5.254791271	1.48192E-07	1.02671E-05
ELL3	140.4280815	1.412854371	0.268963799	5.252953653	1.49679E-07	1.03312E-05
TREM1	780.9232343	2.479601468	0.472636505	5.246318134	1.55169E-07	1.06702E-05
ADTRP	190.3074501	1.956891069	0.373061174	5.245496468	1.55862E-07	1.0678E-05
CSTB	9431.424861	1.034625245	0.197704284	5.23319588	1.66604E-07	1.13716E-05
FURIN	4033.181479	0.876384383	0.167647461	5.22754342	1.71777E-07	1.15536E-05
GPR87	25.11433397	4.388707898	0.839478119	5.227900286	1.71446E-07	1.15536E-05
BST1	371.0602836	1.186343547	0.226919402	5.22803927	1.71317E-07	1.15536E-05
HSPB1	29697.67197	1.340761631	0.256443259	5.228297423	1.71078E-07	1.15536E-05
ORAI1	1045.0935	1.135391842	0.217729055	5.214700628	1.84114E-07	1.22936E-05
RAB42	661.5519624	1.574032552	0.301841912	5.214758095	1.84057E-07	1.22936E-05
SLC35E4	541.2193012	0.758213173	0.14548153	5.211748693	1.87069E-07	1.24458E-05
MS4A6E	36.73321986	2.718720502	0.5225687	5.202608772	1.9651E-07	1.30269E-05
ZNF189	1958.570392	-0.698371054	0.134312811	-5.199586327	1.99733E-07	1.31859E-05
FABP4	110.1638595	1.686669481	0.324420489	5.199022687	2.00339E-07	1.31859E-05
ZNF593	1344.473794	1.195997868	0.230121714	5.197240399	2.02269E-07	1.32655E-05
SRA1	3579.77238	0.989339372	0.190410762	5.195816452	2.03823E-07	1.33201E-05
DRAM1	1183.448979	1.416553625	0.273005502	5.18873655	2.11726E-07	1.37876E-05
SAC3D1	1214.476116	1.263209374	0.243753828	5.182316056	2.19147E-07	1.42207E-05
NLRP12	59.60296424	1.544551216	0.298184003	5.179859421	2.22053E-07	1.42586E-05
P2RY2	194.4035576	1.56555488	0.302208554	5.18037912	2.21435E-07	1.42586E-05
NME1	4787.477291	0.973896555	0.187973176	5.181040059	2.20652E-07	1.42586E-05
ORAI3	1534.632055	0.920387532	0.177712144	5.179091921	2.22969E-07	1.42677E-05
SCAND1	5080.172127	1.193297652	0.230700607	5.172494627	2.30989E-07	1.47298E-05
INTS5	912.5713638	0.71643266	0.138587074	5.169548943	2.3466E-07	1.49122E-05
ZNF622	2009.405319	0.783124544	0.15155127	5.167390164	2.37385E-07	1.49821E-05
CHMP7	2248.76411	0.525241105	0.101638841	5.167720334	2.36967E-07	1.49821E-05
RELB	1342.60651	1.389881151	0.269418048	5.158827198	2.48502E-07	1.56302E-05
MT2A	25365.03896	1.209124272	0.234490085	5.15639829	2.51745E-07	1.57268E-05
TPRA1	2116.814803	0.792947801	0.153773441	5.156597877	2.51477E-07	1.57268E-05
FKBP1A	10410.9148	0.64591364	0.125447472	5.148877311	2.6205E-07	1.63153E-05
AL160269.1	826.6116948	-1.088384527	0.211451401	-5.147208874	2.64391E-07	1.64056E-05
EIF6	4751.164186	0.96539504	0.187638691	5.14496788	2.67567E-07	1.65469E-05
PHLDB3	538.776384	1.076199074	0.209838386	5.128704494	2.91743E-07	1.79218E-05
SLC35F6	3078.802083	0.686079155	0.13375956	5.129197145	2.9098E-07	1.79218E-05
TNFRSF10D	492.6844271	1.402081432	0.273533082	5.125820334	2.96245E-07	1.81379E-05
TNFRSF14	4298.692781	1.173501208	0.229011091	5.124211254	2.98786E-07	1.82329E-05
DYRK3	532.4102436	1.446876113	0.282551295	5.120755559	3.04314E-07	1.85089E-05
C11orf86	15.79628455	2.828995193	0.552824985	5.117343227	3.09869E-07	1.87848E-05
PVR	1535.324962	1.020775508	0.199568144	5.114922102	3.1387E-07	1.8965E-05
FAM83H	881.6131003	1.053397064	0.205977086	5.114146836	3.15162E-07	1.89808E-05
PLAC8	167.5995969	1.76513639	0.345349764	5.111155624	3.20194E-07	1.91586E-05
GPAT3	115.4134386	1.64628527	0.32208461	5.111344102	3.19875E-07	1.91586E-05
IER3	2084.457678	1.887101856	0.36937659	5.108883201	3.24069E-07	1.93277E-05
YJIC	1088.666149	0.957303775	0.187577595	5.103508098	3.33414E-07	1.97572E-05
FOXS1	381.7522605	1.683911713	0.329925486	5.103915227	3.32697E-07	1.97572E-05
RSPH3	621.2758286	0.657900861	0.128977092	5.100912492	3.3802E-07	1.99659E-05
APOBEC3A	84.35135766	2.046951041	0.40145129	5.098877721	3.41673E-07	2.01172E-05
CSKMT	192.4876825	0.932171464	0.182948888	5.095256234	3.4827E-07	2.04403E-05
ACTRT3	72.96350715	1.066273009	0.209513493	5.089280864	3.59424E-07	2.1028E-05
POLR2L	6418.282856	1.144259938	0.224908205	5.087675373	3.62479E-07	2.11396E-05
TNNI2	108.8361922	1.561771487	0.307104613	5.085470625	3.66716E-07	2.12522E-05
HEXB	4737.146769	1.004618821	0.197534342	5.085793234	3.66093E-07	2.12522E-05
TEKT4	51.85599687	-1.058509793	0.208232128	-5.08331647	3.70901E-07	2.14274E-05
PPBP	46.20065594	2.40977916	0.47416628	5.082139458	3.73207E-07	2.14932E-05
CSTA	586.3550061	1.924957997	0.379154379	5.076976829	3.83488E-07	2.20165E-05
LRRC15	148.6946486	2.573745478	0.507724885	5.069173392	3.99547E-07	2.27261E-05
UTP3	1436.409135	0.585699144	0.115529137	5.069709312	3.98424E-07	2.27261E-05
S100A4	1920.545164	1.660627331	0.327552142	5.069810625	3.98212E-07	2.27261E-05
BLVRA	2137.487986	0.812821092	0.160412518	5.067067712	4.03991E-07	2.29081E-05
IL1A	113.8695513	1.689409221	0.333713715	5.062450677	4.13901E-07	2.33981E-05
ADM	2346.118392	1.610357914	0.318162653	5.061429742	4.16124E-07	2.34518E-05
MT1A	100.8114958	1.423148721	0.281284564	5.059462558	4.2044E-07	2.36228E-05
EMC3	4027.410001	0.620012796	0.122625004	5.056169411	4.27761E-07	2.39611E-05
MFSD5	1855.966322	0.768046095	0.152029707	5.05194747	4.37328E-07	2.44228E-05
GNPNAT1	984.4409676	0.437410643	0.086609736	5.050363434	4.4097E-07	2.45518E-05
ZNF165	75.09195286	1.141515618	0.226221337	5.04601216	4.51127E-07	2.50416E-05
TNNT3	26.05851917	1.984265002	0.393534682	5.042160428	4.60305E-07	2.53223E-05
INAFM1	2069.131541	1.11763885	0.221658415	5.04216747	4.60288E-07	2.53223E-05
PINX1	578.2703505	0.787288215	0.156107167	5.043254776	4.57679E-07	2.53223E-05
SDS	2121.309734	1.675557483	0.333232694	5.028190557	4.9513E-07	2.7157E-05
CMBL	1310.412585	0.880694737	0.175243001	5.025562985	5.01958E-07	2.73686E-05
SRSF8	2805.003433	0.425227334	0.084603374	5.026127397	5.00483E-07	2.73686E-05
PKD2L1	498.7156857	1.899130753	0.37802158	5.023868618	5.06409E-07	2.75298E-05
CLEC11A	1100.805473	0.864091193	0.172069507	5.021756661	5.1201E-07	2.77525E-05
ANPEP	399.0811631	1.367812366	0.272467587	5.020092048	5.16467E-07	2.79119E-05
RAB11FIP1	430.1509511	1.177976466	0.234743586	5.018141222	5.21738E-07	2.81144E-05
ASIP	115.3654677	1.760276824	0.350890399	5.016600137	5.25939E-07	2.82581E-05
KCTD11	1154.881511	1.007080115	0.200792331	5.015530773	5.28873E-07	2.83331E-05
MEPCE	3585.552786	0.646170656	0.128930204	5.01178649	5.3927E-07	2.87232E-05
LRRC61	418.4630543	1.343695274	0.268096636	5.011981102	5.38725E-07	2.87232E-05
TMEM253	59.17001424	1.31963897	0.263404848	5.009926658	5.44508E-07	2.89185E-05

TMED3	3378.479477	0.857872644	0.171266192	5.009001671	5.47131E-07	2.89744E-05
TTPAL	1077.572996	0.559117265	0.111732539	5.004068386	5.61328E-07	2.95563E-05
FAM207A	1047.150115	1.018617158	0.203555481	5.004125434	5.61162E-07	2.95563E-05
RHOB	26388.81989	-0.62719459	0.125373933	-5.002591658	5.65647E-07	2.96145E-05
AZGP1	2113.018909	1.624381729	0.324695618	5.002783037	5.65085E-07	2.96145E-05
MMP19	793.2385479	1.958559297	0.391566609	5.001854729	5.67814E-07	2.96437E-05
GPR150	103.6573029	1.793107451	0.358710124	4.998764543	5.76988E-07	2.98689E-05
HIST1H2BD	355.0257067	1.268767432	0.253792565	4.999230103	5.75597E-07	2.98689E-05
DUSP14	1031.103555	0.858462344	0.171718327	4.999247072	5.75546E-07	2.98689E-05
CATSPER1	36.96760371	1.683183992	0.336827477	4.997169492	5.81779E-07	3.00325E-05
LCE1F	5.977872937	5.477000679	1.09659975	4.994530301	5.89791E-07	3.02765E-05
ARPC5L	2406.931249	0.69965957	0.140072605	4.99497794	5.88425E-07	3.02765E-05
PERP	734.220125	1.358265049	0.27217815	4.990352982	6.02691E-07	3.08527E-05
TMEM127	4556.695302	0.517237923	0.103716631	4.987029713	6.13146E-07	3.1301E-05
GLA	1179.978346	0.879828047	0.17647638	4.985528633	6.17926E-07	3.14579E-05
IL2RG	738.9370385	1.722230356	0.345612379	4.983126937	6.25649E-07	3.17633E-05
STRA6	251.1455079	1.758932953	0.353516169	4.975537491	6.50668E-07	3.29428E-05
GEMIN7	624.6155721	0.767765226	0.154389507	4.972910667	6.59551E-07	3.3301E-05
BRAP	1317.550854	0.27352247	0.055032286	4.970218168	6.68776E-07	3.36745E-05
GALE	1106.507138	0.747079659	0.150341055	4.969232509	6.72184E-07	3.37539E-05
IERSL	2704.269292	1.202137708	0.24240408	4.959230499	7.0773E-07	3.54422E-05
OPA3	1253.997622	0.487982472	0.098415688	4.958380924	7.10831E-07	3.55011E-05
TEAD4	456.3804958	1.463951058	0.295325069	4.957083607	7.15592E-07	3.56423E-05
ST6GALL1	3340.276969	-0.853472132	0.172193575	-4.956469096	7.17858E-07	3.56588E-05
ZNF219	2411.217189	0.846888207	0.171118519	4.949132391	7.4545E-07	3.69298E-05
APOC3	4.255251318	5.067450981	1.024509148	4.946223261	7.56672E-07	3.73853E-05
RPP25	892.3090126	0.88406444	0.179177123	4.934025206	8.0552E-07	3.95865E-05
TRIP10	1416.949498	0.88617214	0.179604265	4.934026135	8.05517E-07	3.95865E-05
IL6	185.9930095	2.047646421	0.415171718	4.932046981	8.13723E-07	3.98833E-05
KRTAP2-3	6.858058477	5.083483602	1.03202202	4.925751102	8.40369E-07	4.108E-05
STARD10	2056.031134	1.160400579	0.235681485	4.923596681	8.49679E-07	4.14252E-05
CDC14B	1730.432944	-0.786373132	0.159795726	-4.921114928	8.60526E-07	4.18433E-05
SFMBT2	1486.268503	-0.789342537	0.160511162	-4.917680025	8.75759E-07	4.24005E-05
ASGR2	142.4292121	1.669038749	0.339408303	4.917495347	8.76585E-07	4.24005E-05
MAD2L1BP	914.9588457	0.679202945	0.138154353	4.916261624	8.82125E-07	4.25568E-05
KRT8	131.430647	1.122404132	0.228336358	4.91557342	8.8523E-07	4.2595E-05
CTU1	617.1923642	1.069079087	0.217515993	4.91494474	8.88075E-07	4.26207E-05
SFSWAP	3674.980605	-0.506535105	0.103082064	-4.913901454	8.92816E-07	4.27369E-05
ECI2	3262.693549	0.658359951	0.134082878	4.910097098	9.10313E-07	4.34616E-05
TMEM91	790.8952383	0.945217639	0.192524853	4.909587638	9.12681E-07	4.3462E-05
UBALD2	4860.796022	1.148626789	0.233989519	4.908881361	9.15974E-07	4.35064E-05
BLVRB	3245.637699	0.998469152	0.203426072	4.908265401	9.18855E-07	4.3531E-05
TNFSF4	234.842758	1.577928608	0.321591227	4.90662828	9.26554E-07	4.37832E-05
HDAC6	4322.774363	-0.355033447	0.072367958	-4.905948088	9.29771E-07	4.38229E-05
ANG	325.6073878	1.225153366	0.249846188	4.903630421	9.40814E-07	4.42303E-05
EVA1B	1205.948456	1.287781505	0.262686897	4.902343887	9.46999E-07	4.44077E-05
FAM76A	620.9292983	-0.389374909	0.079444645	-4.901210263	9.5248E-07	4.44386E-05
PRAMEF8	21.66949306	3.800886088	0.775439727	4.901588035	9.5065E-07	4.44386E-05
IMPDH2	5136.900719	0.766063455	0.156337634	4.900057894	9.58084E-07	4.45872E-05
POLR2H	2031.618814	0.775616054	0.158395078	4.89671815	9.74505E-07	4.52371E-05
RIN1	1750.918608	1.413300472	0.288875662	4.892417936	9.96047E-07	4.6121E-05
ADAMTSL4	966.1528855	1.547892963	0.316590405	4.889260504	1.01215E-06	4.66325E-05
ACD08397.2	413.5767876	2.345091602	0.479624109	4.889436449	1.01125E-06	4.66325E-05
S100A11	14389.0648	1.458157859	0.298313259	4.888008888	1.01861E-06	4.68128E-05
COL24A1	149.5913853	-1.868778259	0.382519649	-4.885443832	1.03196E-06	4.73085E-05
TSPO	5186.318325	1.072855747	0.219706802	4.883124869	1.04418E-06	4.76315E-05
RNF19B	1801.382453	0.722026124	0.147856893	4.883276707	1.04337E-06	4.76315E-05
LCP1	4802.484575	1.317994646	0.269983439	4.881761091	1.05143E-06	4.78438E-05
TMEM250	2101.010867	0.590018199	0.120896323	4.880365144	1.0589E-06	4.8065E-05
AP2S1	4987.406097	0.839130973	0.171981294	4.879199084	1.06518E-06	4.82312E-05
LAMB3	657.1593629	1.282920285	0.263057641	4.876955029	1.07736E-06	4.86634E-05
C6orf141	412.9032226	1.619326391	0.332454712	4.870817983	1.11137E-06	5.00769E-05
PLXDC1	1228.156142	-1.201744804	0.246790795	-4.869487949	1.11888E-06	5.02922E-05
HDHD3	1110.26534	0.711466748	0.146171386	4.867346263	1.13107E-06	5.07164E-05
KRT80	69.73532187	2.552075249	0.524583331	4.864956814	1.14482E-06	5.12084E-05
BAK1	1256.707889	0.907341778	0.186735722	4.858961998	1.18003E-06	5.24018E-05
ACOD1	12.46944576	3.445386701	0.709038885	4.859235188	1.1784E-06	5.24018E-05
SAT1	25631.38244	1.055472719	0.217186283	4.859757735	1.17529E-06	5.24018E-05
F11R	1866.998288	1.137907869	0.234372856	4.855117995	1.20315E-06	5.33002E-05
RPF2	1183.366095	0.545796618	0.112440477	4.854093747	1.20939E-06	5.34479E-05
MCHR1	543.9603383	1.681377145	0.346450045	4.853158972	1.2151E-06	5.3572E-05
MRE11	822.7685538	-0.408651923	0.084216695	-4.852386123	1.21985E-06	5.36529E-05
ANGPTL4	4599.999148	1.243905735	0.256520761	4.849142534	1.23996E-06	5.44078E-05
BTN3A1	1823.621023	-0.648998066	0.133902324	-4.846802101	1.25467E-06	5.49226E-05
RAB24	2540.704576	0.710505931	0.146698496	4.843307519	1.27695E-06	5.57654E-05
LRRK1	1827.000009	-0.582220754	0.120224386	-4.842784174	1.28032E-06	5.57803E-05
RHOC	13445.28691	0.923313196	0.190734933	4.84081853	1.29305E-06	5.62021E-05
PELO	984.4178382	0.675907747	0.139656766	4.839778011	1.29984E-06	5.63642E-05
CKAP4	3528.562225	0.928693324	0.192154995	4.833042848	1.34462E-06	5.81689E-05
TSPAN4	1551.930806	0.963712762	0.199492519	4.830821551	1.35971E-06	5.84104E-05
VDR	164.3684032	1.603931299	0.332009246	4.830983829	1.3586E-06	5.84104E-05
LY6K	36.72651817	1.667779087	0.345179707	4.831625531	1.35423E-06	5.84104E-05
RAP2B	2867.823183	0.913857798	0.189212796	4.829788551	1.36678E-06	5.85777E-05
VWCE	1088.119441	1.32692473	0.274950486	4.82604977	1.39268E-06	5.95491E-05
TSPAN17	2051.599309	0.581958509	0.120627051	4.824444491	1.40394E-06	5.98917E-05
CLDN14	22.29576181	2.030622265	0.420991695	4.823425945	1.41113E-06	6.00595E-05
APOBEC3H	112.1717371	1.74420378	0.361785665	4.821096989	1.42771E-06	6.0625E-05
DPP7	14610.82902	0.860707922	0.178655365	4.817699838	1.45223E-06	6.15243E-05
SDSL	1767.63339	1.320792751	0.274263044	4.815788268	1.4662E-06	6.19738E-05
PMPCA	2940.518291	0.49751538	0.103329625	4.814837775	1.4732E-06	6.2127E-05
ORMDL3	3268.540792	0.4740128	0.098532642	4.810718485	1.50389E-06	6.32766E-05
MSANTD3	1345.05813	0.801722074	0.166735939	4.808333929	1.52193E-06	6.389E-05
PSMD2	8881.620931	0.478192824	0.099485837	4.806642211	1.53486E-06	6.42863E-05
BDNF	98.95835307	1.669930244	0.347601364	4.804153312	1.55408E-06	6.49435E-05
MIOX	17.84404349	2.461685398	0.512954955	4.799028402	1.59437E-06	6.64766E-05
DBF4B	770.903073	-0.858165979	0.179190968	-4.789114036	1.67519E-06	6.96888E-05
BIRC3	5745.339151	0.926263774	0.193534197	4.786047053	1.70098E-06	7.06022E-05
SZT2	3289.459719	-0.411593288	0.086010896	-4.785362141	1.70679E-06	7.06842E-05
TWF2	3394.425934	0.746214986	0.156011118	4.783088519	1.72622E-06	7.13285E-05
NADK	4186.436865	0.577629504	0.120851079	4.779680157	1.75574E-06	7.23861E-05
PLEKHN1	23.21290803	2.205656409	0.46190062	4.775175254	1.79551E-06	7.38603E-05
ABRACL	743.9467146	1.02718624	0.215274197	4.771525124	1.82836E-06	7.50443E-05
TOM1	3564.531788	0.610561133	0.127976858	4.770871426	1.83431E-06	7.51209E-05
CES2	4325.840726	0.807315422	0.169289808	4.768836541	1.85293E-06	7.57154E-05
MRPS12	1494.342934	0.870786935	0.182633853	4.76793826	1.86121E-06	7.58854E-05
ITGA5	4052.214909	1.31252501	0.275736169	4.760075597	1.9352E-06	7.85548E-05
CIB1	4436.072101	0.867649458	0.182272685	4.760172686	1.93427E-06	7.85548E-05
DISC1	661.7319755	-0.805335807	0.169290892	-4.757112441	1.96382E-06	7.95411E-05
CALCA	17.51469241	2.75239878	0.579185533	4.752188417	2.01227E-06	8.13247E-05
LGALS3	8674.637661	1.046843493	0.220336491	4.751112667	2.023E-06	8.15797E-05
LRRC42	936.8067853	0.547655508	0.115403982	4.745551233	2.07939E-06	8.36706E-05
SLC46A2	28.45678506	2.180818057	0.460124808	4.739622857	2.14116E-06	8.59684E-05
PYGB	11120.4509	0.467782957	0.098772721	4.73595293	2.18028E-06	8.73487E-05
BYSL	705.9831399	0.973260088	0.205552686	4.734844906	2.19223E-06	8.76368E-05
APO03419.1	1627.304666	1.473044927	0.311337913	4.73133809	2.23045E-06	8.89717E-05
PDF	342.2230953	0.724587258	0.153346576	4.725160987	2.29933E-06	9.13241E-05

PTHLH	260.423577	1.338371673	0.283240258	4.725217006	2.2987E-06	9.13241E-05
FAM177B	37.49621356	-1.678235485	0.355494902	-4.720842628	2.3487E-06	9.30841E-05
BCL3	1487.536775	1.476453854	0.312908129	4.718489926	2.37602E-06	9.39649E-05
KRT75	120.3607713	2.486924985	0.527125019	4.717903527	2.38287E-06	9.40342E-05
CANT1	2703.417168	0.772515659	0.163774752	4.716939887	2.39418E-06	9.42787E-05
UACA	1502.492793	-0.646097925	0.137021505	-4.715303086	2.41351E-06	9.46353E-05
CLLU1OS	18.62554587	3.816464081	0.809352586	4.715453003	2.41174E-06	9.46353E-05
C1QTNF9	15.08707465	-1.499298709	0.318221712	-4.711490923	2.45911E-06	9.62186E-05
RSL1D1	4291.649239	0.505169522	0.107309474	4.707594781	2.50657E-06	9.78677E-05
EIF1AD	937.2418499	0.48747897	0.103588614	4.705912648	2.52733E-06	9.84696E-05
CSAD	1443.555339	-0.572060722	0.121740187	-4.699029443	2.61401E-06	0.000101632
CXCL13	5.203046847	-1.683347343	0.358303225	-4.698108264	2.62582E-06	0.000101878
MC1R	755.4610779	0.993849109	0.211681469	4.695021792	2.66578E-06	0.000103209
GSS	3101.334721	0.829253213	0.17674959	4.691683928	2.70966E-06	0.000104688
LYZ	7555.013776	1.924791208	0.410586345	4.687908483	2.76011E-06	0.000106192
PHPT1	8127.540225	0.942376555	0.20101904	4.687996488	2.75893E-06	0.000106192
SCIN	1560.287618	-1.366691038	0.291933297	-4.681518167	2.84758E-06	0.000108879
HNRNPDL	14043.36728	-0.297507682	0.063549499	-4.681511041	2.84768E-06	0.000108879
ABCD1	1715.667633	0.891622751	0.190427799	4.682208988	2.838E-06	0.000108879
TMEM159	383.9335432	0.883690119	0.188831286	4.679786596	2.87174E-06	0.000109572
IGF1	229.5684539	-1.103709264	0.235904564	-4.678626149	2.88803E-06	0.000109966
SLC52A2	1885.999128	0.793284467	0.169589454	4.677675679	2.90145E-06	0.000110249
HIST1H3H	40.32618123	2.095344194	0.448038398	4.676706732	2.91519E-06	0.000110543
LTA4H	3580.701466	0.662891871	0.14185482	4.673030291	2.96788E-06	0.00011231
FAM83F	80.62024613	1.396191213	0.298954533	4.670246003	3.00839E-06	0.000113378
MRPS18A	2285.813903	0.705899109	0.15113541	4.670640105	3.00263E-06	0.000113378
ATP6V1F	8318.084401	0.701209306	0.150321049	4.664744624	3.09001E-06	0.000115979
IL27RA	301.1495957	0.83801544	0.179637459	4.665037266	3.08561E-06	0.000115979
DUSP5	684.3568993	1.463316121	0.313760712	4.663796539	3.10428E-06	0.000116278
PGF	1007.836478	1.521508134	0.326514033	4.659855255	3.16432E-06	0.000118047
RCN1	6447.628863	1.007425871	0.216190465	4.659899651	3.16364E-06	0.000118047
RPS28	19819.20256	0.976991916	0.209701859	4.658956871	3.17816E-06	0.000118324
SHBBGRL3	12756.13946	0.921315441	0.197851629	4.656597694	3.21478E-06	0.000119446
TRAPPC5	3460.880433	0.926411814	0.199050136	4.654163182	3.25299E-06	0.000120622
CCDC107	1742.232544	0.902418007	0.194023539	4.651074871	3.30209E-06	0.000122197
SLC43A3	2136.647903	1.069823711	0.230151772	4.648340107	3.34617E-06	0.00012358
FUT11	842.4660242	0.34472225	0.07425189	4.642605716	3.44043E-06	0.000126302
AIFM2	839.900875	0.661598213	0.142495798	4.642931378	3.435E-06	0.000126302
MCOLN1	2740.281533	0.746031435	0.160665171	4.643392396	3.42735E-06	0.000126302
ALAS1	2183.373373	0.471371165	0.10154505	4.641990566	3.45069E-06	0.000126427
UVRAG	1266.64942	-0.645913767	0.139211001	-4.639818418	3.48715E-06	0.000127137
FAM210B	3240.161977	0.622716585	0.13422939	4.639197029	3.49765E-06	0.000127137
FAHD1	959.4894791	0.338997822	0.073066574	4.639574647	3.49127E-06	0.000127137
MGAT1	7308.824229	0.717140813	0.154551462	4.640142543	3.48169E-06	0.000127137
DELE1	3126.700431	-0.235374126	0.050746038	-4.638275956	3.51327E-06	0.000127279
SMPD2	513.3541793	0.614236273	0.13243124	4.638152382	3.51538E-06	0.000127279
SFXN2	392.1863136	-0.610148723	0.131568859	-4.637485839	3.52673E-06	0.000127379
ABHD14B	2250.270471	0.801829312	0.172913206	4.637177978	3.53198E-06	0.000127379
ARMC7	627.1803396	0.584536212	0.12609002	4.635864222	3.55449E-06	0.000127443
IER5	2631.595595	1.091813427	0.235497046	4.63620858	3.54858E-06	0.000127443
LAMTOR2	3013.625025	0.931834907	0.200976894	4.636527561	3.54311E-06	0.000127443
GNS	7463.181899	0.830481769	0.179234188	4.633500885	3.59533E-06	0.000128657
FCER2	27.90095272	2.409210582	0.520019455	4.632923938	3.60537E-06	0.000128766
PRR13	6677.772372	0.721879322	0.155883367	4.630893819	3.64091E-06	0.000129784
TIMM17A	2357.074357	0.556596501	0.120242467	4.628951095	3.67523E-06	0.000130754
IL17RC	1610.875749	0.560353216	0.121066118	4.628489188	3.68343E-06	0.000130794
PIM2	648.3550982	1.09238887	0.236178618	4.625265736	3.74118E-06	0.000132081
UQCC3	1205.508694	1.027552483	0.222153417	4.625418319	3.73843E-06	0.000132081
DHRS13	891.6809726	0.840464482	0.181686997	4.625892309	3.72989E-06	0.000132081
ZDHHC18	1611.124664	0.670295493	0.144954752	4.624170545	3.761E-06	0.000132527
CRABP2	348.2470467	1.362386335	0.294691813	4.623088508	3.78068E-06	0.000132966
RTL5	1391.139789	0.733743308	0.15880919	4.620282407	3.83218E-06	0.00013452
TACR2	60.96772258	1.033148956	0.223750398	4.617417287	3.88545E-06	0.000136131
NBPF12	1846.251632	-0.748162338	0.162136071	-4.614410181	3.94213E-06	0.00013766
RRP12	1435.096298	0.650847976	0.141049915	4.614309594	3.94404E-06	0.00013766
NAT16	156.7079496	1.482428845	0.321312022	4.613673758	3.95613E-06	0.000137821
NANS	1863.052332	0.802962584	0.174119121	4.611570404	3.99638E-06	0.000138699
CTSD	89805.60668	1.18901938	0.257816764	4.611877679	3.99048E-06	0.000138699
IVL	7.952133444	4.514111403	0.979114777	4.610400648	4.01894E-06	0.00013922
RTTN	765.8970012	-0.741234228	0.160899261	-4.606821808	4.0887E-06	0.000141106
BLOC1S4	656.2617125	0.731286603	0.158735323	4.606955722	4.08607E-06	0.000141106
ITIH1	32.17654584	2.049367307	0.445228388	4.602957414	4.16533E-06	0.000143482
TNFRSF18	108.9452429	1.441569704	0.313587607	4.59702383	4.28569E-06	0.000147352
HIST2H2AA3	939.7412975	2.161224666	0.470235711	4.596045379	4.30585E-06	0.00014777
TMEM251	875.7218029	0.699915889	0.152518256	4.589063011	4.4524E-06	0.000152515
XCL1	8.812174827	-1.911553662	0.416825968	-4.585975464	4.51872E-06	0.0001545
METRNL	2149.231716	1.16603054	0.254358693	4.584197713	4.55733E-06	0.000155531
PLEKHH1	2422.292033	0.712493893	0.155557166	4.580270364	4.64375E-06	0.000158188
CTSA	10837.46943	0.861967426	0.188286207	4.577963739	4.69524E-06	0.000159647
SECTM1	555.0111309	1.58398563	0.346075629	4.576992706	4.71708E-06	0.000160094
SRPRB	2452.241373	0.613758215	0.13417723	4.574235241	4.77963E-06	0.000161919
PRELID1	4412.4601	0.68429218	0.149785165	4.568491016	4.91248E-06	0.000166114
ANXA8L1	14.67058631	3.029530748	0.66323905	4.567781023	4.92915E-06	0.000166372
C17orf49	2836.524203	0.843340807	0.184783311	4.563944666	5.02013E-06	0.000168825
TLCD1	597.529117	1.26203702	0.276504385	4.564256799	5.01267E-06	0.000168825
PNPT1	1628.143004	-0.504107315	0.110604987	-4.557726832	5.17102E-06	0.000173582
LCN2	56.52549297	2.681341923	0.588602776	4.555435405	5.22772E-06	0.000175167
TFIP11	1980.47468	0.453066161	0.099480678	4.554313164	5.2557E-06	0.000175785
TRIB1	1630.935681	0.837751355	0.18400528	4.552865846	5.292E-06	0.000176678
PHAX	1669.03479	0.272266013	0.05983444	4.550322753	5.35637E-06	0.000178504
APOE	254438.7261	1.278296859	0.281111853	4.547289078	5.43413E-06	0.000180768
TPI1	26062.63512	0.624041731	0.137295858	4.545233478	5.48744E-06	0.000182213
TIAF1	983.5653033	-0.96906411	0.213380617	-4.541481433	5.58603E-06	0.000184159
ZNF581	757.4093019	0.719995017	0.158537373	4.541484469	5.58595E-06	0.000184159
PLD3	22910.89111	0.826529333	0.181992231	4.541563835	5.58385E-06	0.000184159
LMNA	12741.72414	0.957936846	0.210915986	4.541793451	5.57777E-06	0.000184159
SLC20A1	2976.984369	0.523634311	0.115345659	4.53969675	5.63352E-06	0.000185393
TMEM238	79.6894451	1.322796293	0.291475642	4.538273883	5.67166E-06	0.000185984
HMGCL	2236.260107	0.747397316	0.164681391	4.538444282	5.66708E-06	0.000185984
C19orf81	326.7578488	1.179243718	0.259968883	4.536095652	5.73052E-06	0.00018758
SLC2A3	2796.612455	1.131055301	0.249449121	4.53421242	5.78188E-06	0.000188926
ORM1	18.24453884	3.27410509	0.722584453	4.531103705	5.86763E-06	0.000191389
MMP12	43.3965937	2.943568941	0.649878045	4.529417427	5.91465E-06	0.000192582
KCNE1	82.53938757	1.247138345	0.275458155	4.527505626	5.9684E-06	0.000193989
LAMP3	147.9917927	1.692674278	0.374039438	4.52538985	6.02843E-06	0.000195595
TMEM8A	3216.89733	0.651584808	0.143999611	4.524906711	6.04222E-06	0.000195698
BMP4	149.0343191	1.195935264	0.264585876	4.520026851	6.18318E-06	0.000199912
TCTN3	1501.269109	0.550468817	0.121885338	4.516284115	6.29342E-06	0.00020312
BAG1	5371.933976	0.782311969	0.173289682	4.514475189	6.34738E-06	0.000204503
MOSPD1	442.3237868	0.605668288	0.13418127	4.513806486	6.36743E-06	0.000204791
GRPEL1	1557.827208	0.478404936	0.106013889	4.512662822	6.40188E-06	0.00020554
RNASEK	10772.99232	0.918468627	0.203582169	4.511537684	6.43593E-06	0.000206275
SLC4A5	227.6594076	-1.046174002	0.231995186	-4.509464265	6.49915E-06	0.000207741
TOR1AIP2	2782.143243	0.294435912	0.06529528	4.509298569	6.50423E-06	0.000207741
TMEM165	4816.887624	-0.707369742	0.156921281	-4.507799931	6.55033E-06	0.000208851
SUPV3L1	1300.142383	0.532722733	0.118280893	4.503878197	6.67245E-06	0.000212377

XCL2	7.364410798	-2.314858342	0.514244227	-4.501476579	6.7483E-06	0.000214421
MED18	592.9378045	0.597586353	0.132775167	4.500738847	6.77177E-06	0.000214797
MSANTD2	606.0812034	-0.54892741	0.121998672	-4.499453983	6.81282E-06	0.000215728
PPCDC	671.9630502	0.883638954	0.196416376	4.498804909	6.83365E-06	0.000216016
RANBP17	136.3095943	-1.054623541	0.234509928	-4.497138139	6.88742E-06	0.000217343
ZNF563	170.5551968	0.702892321	0.156329821	4.496213945	6.91741E-06	0.000217916
ANKRD33	18.35322591	2.759075554	0.613986063	4.493710394	6.99928E-06	0.000220119
IL11	135.3357258	1.857882608	0.413685174	4.491054371	7.08715E-06	0.000222503
SLC10A3	850.6850501	0.722444526	0.160962202	4.4882868	7.17982E-06	0.000223508
DUSP23	1540.39454	0.906276369	0.201917192	4.488356633	7.17747E-06	0.000223508
C8orf58	601.4646793	0.52586393	0.117158828	4.488470393	7.17364E-06	0.000223508
AJUBA	401.7185473	1.318370739	0.293721365	4.488508141	7.17237E-06	0.000223508
SLC16A6	390.9193821	1.069073498	0.238118744	4.48966545	7.13351E-06	0.000223508
OVCA2	1546.595992	0.76091805	0.169636093	4.485590508	7.27123E-06	0.000225972
MARK3	3802.279045	-0.291983369	0.065106699	-4.484690125	7.302E-06	0.000226546
VPS33A	1538.628955	0.28656753	0.063929167	4.482578846	7.37464E-06	0.000228415
DMTF1	3766.359057	-0.654703864	0.146109661	-4.480907426	7.43263E-06	0.000229826
WFDC2	307.3221674	0.964150086	0.215311899	4.477922916	7.53728E-06	0.000232671
SCART1	254.5163393	-1.211523018	0.270694858	-4.475604111	7.61956E-06	0.000234817
TP53INP2	38983.27437	-1.121942231	0.250729725	-4.47470769	7.65159E-06	0.000235411
DSP	382.2237508	1.443476677	0.322706836	4.473027883	7.71197E-06	0.000236086
TMD2	2276.244054	0.463997789	0.103728141	4.473210288	7.70539E-06	0.000236086
RARS	1725.063838	0.561203096	0.125446767	4.473635393	7.69008E-06	0.000236086
BIRC7	435.6748564	1.800079085	0.40261366	4.47098363	7.78607E-06	0.000236781
TNIP1	5508.394215	0.690746094	0.154486519	4.471238648	7.77679E-06	0.000236781
LAG3	2027.369868	0.804052059	0.179811328	4.471642967	7.76209E-06	0.000236781
CNFN	73.75362819	1.262368217	0.282280426	4.472035957	7.74784E-06	0.000236781
ST6GALNAC4	1010.886308	0.519730354	0.116303299	4.468749885	7.86781E-06	0.000238873
ZNRD1	691.2197732	0.767210406	0.171712661	4.467989722	7.89581E-06	0.000239329
PES1	4210.428442	0.806038154	0.180556548	4.464186767	8.03734E-06	0.000243219
NABP1	1541.933725	1.213486974	0.271873154	4.463430664	8.06577E-06	0.000243679
ARL14	6.748096691	3.303838884	0.74044512	4.461963209	8.12122E-06	0.000244952
MBOAT7	4398.216523	0.701454173	0.157600543	4.450836029	8.55366E-06	0.000257574
MRPS2	2058.104349	0.621205925	0.139664208	4.447853422	8.67327E-06	0.000260325
MICA	591.509264	1.064197371	0.239253971	4.447982055	8.66808E-06	0.000260325
FOLR3	27.53160425	2.104590957	0.473294003	4.446688405	8.72042E-06	0.000261315
CLP1	447.2972964	0.788252061	0.177343051	4.444786844	8.79791E-06	0.000262357
CD2BP2	5802.519375	0.529949722	0.119229011	4.444805137	8.79716E-06	0.000262357
ASGR1	282.5817138	0.983059941	0.221167748	4.444861242	8.79486E-06	0.000262357
LMAN2	6041.590005	0.738638416	0.166297563	4.44166712	8.92646E-06	0.00026576
TP53RK	1065.45709	0.534678406	0.120458557	4.438691763	9.05073E-06	0.000269026
SELP	41.65306654	2.250595608	0.507225931	4.437067328	9.11928E-06	0.000270627
AGTRAP	3072.39291	0.966168956	0.217774388	4.436559158	9.14082E-06	0.00027083
MRM3	609.0120951	0.622264505	0.140259528	4.435371116	9.19138E-06	0.000271891
TJAP1	4750.177198	-0.655264376	0.147794902	-4.43360608	9.26699E-06	0.00027325
LRPAP1	8389.806505	0.823784042	0.185802668	4.433650227	9.26509E-06	0.00027325
KLHDC8B	1358.70126	0.646585553	0.145893189	4.431910469	9.34018E-06	0.000274968
RPP25L	968.5280373	0.808487061	0.182463906	4.430942417	9.38221E-06	0.000275765
RBMX2	1108.560875	0.65271763	0.147380716	4.428785859	9.47651E-06	0.000278093
ICAM4	46.96977142	1.332768091	0.301125832	4.425950718	9.60184E-06	0.000281323
PIP	3.718161883	4.779430997	1.080371056	4.423879156	9.69443E-06	0.000283585
GGCT	1571.151501	0.592360203	0.133915496	4.423388051	9.7165E-06	0.00028378
ADCX1	835.281995	-0.516417906	0.116773074	-4.422405685	9.7608E-06	0.000284623
PUS3	420.0407076	0.505192311	0.114253734	4.42167001	9.7941E-06	0.000284693
KLHL34	31.89777445	1.251587958	0.283052486	4.421752221	9.79037E-06	0.000284693
MAN2A1	4106.624503	-0.972782122	0.220044061	-4.420851527	9.83127E-06	0.000285324
GTF3C6	3047.597648	0.698049742	0.157927445	4.420066084	9.86707E-06	0.000285912
MTFP1	498.9278195	0.957436079	0.216702484	4.418205367	9.95238E-06	0.000287932
CLEC4D	20.77242139	2.833229386	0.641556134	4.416183144	1.00459E-05	0.000290182
SLC16A3	3760.233784	1.169579872	0.264880987	4.415491974	1.00781E-05	0.000290655
WDR74	2019.706377	0.842844366	0.190901196	4.415081649	1.00972E-05	0.000290752
AGRP	20.54729371	1.559042648	0.353144967	4.414738408	1.01132E-05	0.000290759
LGALS1	23125.03687	1.095064411	0.248136478	4.413153681	1.01876E-05	0.00029244
NDUFAF8	3363.071649	0.895003434	0.202838633	4.412391365	1.02235E-05	0.000293016
RALGAPA2	1284.720715	-0.553455258	0.125501952	-4.409933461	1.03402E-05	0.000295056
NBPF11	917.7046495	-0.599998246	0.136057694	-4.40988103	1.03427E-05	0.000295056
SMCO3	4.69154191	3.121442214	0.707770744	4.410244756	1.03254E-05	0.000295056
ATOX1	5696.108213	1.113806505	0.252599919	4.409370004	1.03672E-05	0.000295296
PIM1	1565.145793	0.87395043	0.19833025	4.40654126	1.05034E-05	0.000297335
CLIC1	9900.04867	1.092580155	0.247943855	4.406562751	1.05024E-05	0.000297335
MRTO4	1852.7032	0.535045441	0.121418208	4.406632646	1.0499E-05	0.000297339
FAM32A	3738.95826	0.479943701	0.108913465	4.406651645	1.04981E-05	0.000297339
SPAG17	65.31951404	-1.569335026	0.356254421	-4.405096288	1.05737E-05	0.000297955
NHLH2	212.1941709	1.417804038	0.321838752	4.405324191	1.05626E-05	0.000297955
SMAGP	109.8242154	1.013231202	0.229989346	4.405557121	1.05512E-05	0.000297955
RDH14	813.9403872	0.369994193	0.084050493	4.402046653	1.07234E-05	0.000301714
ELOF1	3136.351593	0.671959691	0.152672766	4.401306856	1.07601E-05	0.000302283
C1QTNF12	77.06902822	1.24621926	0.283352874	4.398117597	1.09194E-05	0.000306293
APOA1	38.87327847	1.187329491	0.270042232	4.396828898	1.09844E-05	0.000307646
UBE2J2	2724.916524	0.548086064	0.12466539	4.396457309	1.10032E-05	0.000307706
CHKA	3522.81051	-0.515692626	0.117329739	-4.395242253	1.10649E-05	0.000308496
GPR157	175.6205586	1.010065171	0.229794455	4.395515867	1.1051E-05	0.000308496
SARS	9048.317982	0.553482685	0.125981105	4.393378546	1.11603E-05	0.000310215
COA7	975.615893	0.376343843	0.085661096	4.393404465	1.11589E-05	0.000310215
VEGFD	54.56974971	-0.99289075	0.226168803	-4.39004291	1.13328E-05	0.000314537
SLC35C1	1114.813098	0.631227139	0.143817692	4.389078499	1.13832E-05	0.00031546
PPP4C	3974.336544	0.702398266	0.160055714	4.388461042	1.14156E-05	0.000315882
CD40	612.0091649	1.139974775	0.259804498	4.387817719	1.14494E-05	0.000316342
NAB2	1527.696274	0.735712981	0.167786934	4.384804972	1.1609E-05	0.000320272
FDCSP	31.46801647	5.707928864	1.302100186	4.38363263	1.16717E-05	0.00032152
GOSR2	3131.979358	0.261104324	0.059610412	4.380179802	1.18581E-05	0.00032617
APEH	3651.064632	0.48863477	0.111577209	4.379342126	1.19038E-05	0.000326938
ARHGAP1	7386.843258	-0.470972956	0.10757915	-4.377920404	1.19817E-05	0.000328061
BMP2	395.9672184	1.028250567	0.234887878	4.377622952	1.19981E-05	0.000328061
GLMP	2819.053934	0.860482064	0.196543005	4.378085408	1.19726E-05	0.000328061
DDB2	2046.49149	0.913992376	0.208811947	4.377107667	1.20265E-05	0.000328349
NRBP2	10433.51211	-0.708234621	0.161855055	-4.375733715	1.21025E-05	0.000329935
KCNN4	311.0769509	1.355189512	0.309993495	4.371670806	1.23299E-05	0.00033564
AC098484.3	286.8031324	0.924489646	0.211573592	4.369589018	1.24481E-05	0.000338356
SPN	483.0325726	1.107848421	0.253730807	4.366235367	1.26406E-05	0.000343084
RPL36	18692.36023	0.898292733	0.205840198	4.364029685	1.27688E-05	0.000346054
RRS1	1051.757175	0.740740515	0.169771202	4.363169414	1.28192E-05	0.000346908
POLD4	3065.821897	0.965964053	0.221441176	4.362169987	1.28779E-05	0.000347986
HBM	23.48702769	2.525426799	0.579397766	4.358709931	1.30831E-05	0.000353015
BRF2	788.1001631	0.488090746	0.111991117	4.358298762	1.31077E-05	0.000353162
DNAH1	1392.268056	-0.823725095	0.18919568	-4.353826133	1.33782E-05	0.000359922
LAYN	3222.062777	1.123511643	0.258071602	4.353488086	1.33988E-05	0.000359952
WDR54	910.7131049	0.774299473	0.177939408	4.35147831	1.35223E-05	0.000362739
CCDC191	599.8038974	-0.607150548	0.139591984	-4.349465705	1.3647E-05	0.000365552
METTL7B	2891.219702	1.169461404	0.269055242	4.346547546	1.38297E-05	0.00036991
HRAS	3746.541318	0.892099692	0.205319289	4.344938538	1.39315E-05	0.000372091
RTL10	950.6771977	0.590516013	0.135919406	4.344604138	1.39527E-05	0.000372119
DECR2	1164.952814	0.707386706	0.162891124	4.342696454	1.40745E-05	0.000374824
NUPR1	9142.122162	1.130330913	0.260481876	4.339384103	1.42883E-05	0.000379968
PTRH2	1148.520762	0.61305562	0.141326785	4.337858679	1.43878E-05	0.000381514
BTG1	4769.06322	0.916107582	0.211183616	4.337967126	1.43807E-05	0.000381514

GUCY2D	19.78418529	1.576953216	0.363571831	4.337391073	1.44184E-05	0.000381777
MAB21L1	58.70829307	1.390003455	0.320634344	4.335167089	1.45649E-05	0.000385104
ADORA2A	376.7410974	1.202609945	0.2774529	4.334465224	1.46115E-05	0.000385781
VAMP8	3968.568765	1.367388928	0.315509487	4.333907488	1.46486E-05	0.000386207
NINJ1	7583.676144	0.868407315	0.200407377	4.333210319	1.46951E-05	0.000386879
S100A10	14607.80748	1.159496073	0.267654449	4.332063515	1.47718E-05	0.000388345
SLC25A3	11930.41903	0.3523714	0.081402119	4.328774298	1.49942E-05	0.000393628
ELMO1	4728.188891	-0.855482058	0.197738895	-4.326321619	1.5162E-05	0.000396904
MLEC	7592.689959	0.373366021	0.086294794	4.32663438	1.51405E-05	0.000396904
SF3B5	4649.463026	0.750320433	0.173478887	4.325139778	1.52435E-05	0.000398472
AICDA	14.99596187	1.068812133	0.247214635	4.323417724	1.5363E-05	0.000401028
ACD08763.3	81.12877922	4.454555237	1.03072334	4.321775848	1.54778E-05	0.000403453
RAB13	5152.07327	0.72773718	0.168432378	4.320648977	1.55571E-05	0.000404946
MLPH	178.689543	1.377238942	0.318870685	4.319114321	1.56657E-05	0.000407197
PDE8A	3483.843218	-0.837631912	0.193955869	-4.318672671	1.5697E-05	0.000407438
SRP68	3256.489653	0.369900718	0.085660508	4.318217683	1.57294E-05	0.000407704
ID1	3985.127307	1.03676262	0.240242185	4.315489478	1.5925E-05	0.000412193
ZNF708	1224.79428	-0.928932223	0.215303739	-4.314519702	1.5995E-05	0.000413425
GM2A	10745.35599	0.87162876	0.202116738	4.312501619	1.61418E-05	0.000416634
FAM110A	376.3399794	1.054780198	0.244741399	4.309774321	1.63421E-05	0.000421215
TXLNA	4297.281732	0.615282459	0.142793438	4.308898706	1.64069E-05	0.000421707
ADRM1	5843.651837	0.733139382	0.170143413	4.308949544	1.64032E-05	0.000421707
RAD51B	197.9324531	-0.766199875	0.177903864	-4.306819762	1.65618E-05	0.000424345
POLR1C	790.5529691	0.515229537	0.119637331	4.306595063	1.65787E-05	0.000424345
DDX41	3960.793537	0.476364926	0.110607126	4.306819496	1.65619E-05	0.000424345
FDX1	1045.457694	0.571121542	0.132652935	4.305381866	1.66698E-05	0.000426085
EMP3	5409.679941	1.212050631	0.281575813	4.304526785	1.67343E-05	0.000427142
NCLN	4022.06168	0.59590442	0.138453069	4.304017427	1.67728E-05	0.000427534
MUL1	2046.547497	0.488505383	0.113646332	4.298470317	1.71981E-05	0.000437767
CGB7	21.61560451	2.504362854	0.582745103	4.29752707	1.72714E-05	0.000439028
IMP3	2463.714774	0.485990037	0.113105531	4.296784003	1.73294E-05	0.000439894
TFAP2C	65.98976446	1.340932767	0.312174738	4.295455733	1.74335E-05	0.000441928
ANAPC13	2786.073853	0.430042708	0.100127665	4.294943931	1.74737E-05	0.00044234
PATL2	121.5782857	-0.997332533	0.232394286	-4.291553585	1.77427E-05	0.000447701
B9D2	277.4296148	0.670911418	0.156340133	4.291357598	1.77584E-05	0.000447701
HCC5	700.9370443	0.560451848	0.130591806	4.291631026	1.77365E-05	0.000447701
C5AR1	2103.191476	1.410984883	0.329101609	4.287383731	1.8079E-05	0.000455161
TRIML2	15.00711501	1.461840478	0.341098789	4.285680642	1.82181E-05	0.000457412
TYSND1	869.2378856	0.734295622	0.171327093	4.285928216	1.81978E-05	0.000457412
UGGT2	796.8918903	-0.475524946	0.110971076	-4.28512514	1.82636E-05	0.000457933
PDRG1	1401.772583	0.539056924	0.125846828	4.283436736	1.84028E-05	0.000460796
STXBP2	2045.635904	1.063842573	0.248429833	4.282265778	1.85E-05	0.000461348
CCDC51	797.5330093	0.773485298	0.180620367	4.282381386	1.84904E-05	0.000461348
TMUB1	2860.725842	0.750340459	0.175212422	4.282461529	1.84837E-05	0.000461348
ISG20	1180.422673	1.208960933	0.282702062	4.276448931	1.89898E-05	0.000472923
BCAP31	8891.951839	0.588551198	0.13767043	4.27507343	1.91074E-05	0.00047521
C16orf89	1837.57609	0.962295401	0.225193512	4.273193268	1.92693E-05	0.000478591
ARSA	5350.190841	0.854071278	0.199888004	4.272749051	1.93078E-05	0.0004789
MRPL17	1827.526237	0.72602979	0.169947236	4.272089435	1.9365E-05	0.000479674
PAN2	2629.673827	-0.60675278	0.142192698	-4.267116359	1.98016E-05	0.00048983
DNTTIP2	2233.375094	0.358522478	0.084025952	4.266806507	1.98291E-05	0.000489853
ATP6AP1	10254.46201	0.43375967	0.101700339	4.265075943	1.99834E-05	0.000493005
PSMG3	1699.655608	0.733223404	0.171929557	4.264673362	2.00195E-05	0.000493234
IFITM3	27511.47922	1.06369783	0.249591254	4.261759234	2.02824E-05	0.000499044
MICAL3	7026.844246	-0.660181788	0.154974214	-4.259946046	2.04476E-05	0.000502439
MRPL12	2798.780607	0.756274658	0.177573122	4.258947811	2.05391E-05	0.000504016
COASY	2932.370244	0.452044982	0.106174618	4.257561656	2.06669E-05	0.000505803
CLEC5A	732.8004918	1.50521916	0.353530581	4.257677385	2.06562E-05	0.000505803
RIMBP3C	207.4867623	1.985945369	0.466644263	4.255801532	2.08301E-05	0.000509123
GADD45GIP1	5202.188301	0.941017227	0.221184495	4.254444805	2.09568E-05	0.000510864
ICAM2	1128.207356	1.065953637	0.250536278	4.254687762	2.09341E-05	0.000510864
VPS52	3504.009167	-0.299159534	0.070370827	-4.251186872	2.12641E-05	0.000516513
PI4K2A	2389.708297	0.50391712	0.118546366	4.250801912	2.13006E-05	0.000516513
MYL12B	11373.70716	0.679428055	0.159824444	4.251089734	2.12733E-05	0.000516513
GNLY	399.3985676	1.46979921	0.34570802	4.251562371	2.12284E-05	0.000516513
H2AFJ	2532.801316	1.180370801	0.277817831	4.248722252	2.14993E-05	0.000519962
CARD16	771.8997144	1.266643037	0.298107523	4.248946908	2.14778E-05	0.000519962
RALGDS	13522.62907	-0.395491373	0.093114615	-4.247360887	2.16303E-05	0.000522445
APRT	2920.634918	0.770906253	0.181515206	4.247061562	2.16592E-05	0.000522458
SAT2	4941.9961	0.726724092	0.171252239	4.243588843	2.19973E-05	0.00052992
ARHGAP24	649.3635852	-0.93799139	0.221222775	-4.240030855	2.23489E-05	0.000537687
MARCO	781.1545798	2.154328112	0.508180573	4.239296476	2.24221E-05	0.000538745
CD63	44785.70511	0.903290083	0.21309766	4.238855003	2.24663E-05	0.000539103
CD86	704.4551079	1.594713566	0.376420042	4.2365267 18	2.27004E-05	0.000544012
TDP2	2213.441279	0.508920513	0.120151671	4.23565074	2.27891E-05	0.000545428
LSM10	1981.852804	0.522664	0.123426959	4.234601624	2.28957E-05	0.00054727
CDHR4	25.19468387	-2.370711474	0.559966077	-4.233669809	2.29908E-05	0.000548442
FAH	1655.765382	0.659623829	0.155809094	4.233538686	2.30043E-05	0.000548442
UBD	1791.920208	2.076805444	0.490810428	4.23138005	2.32262E-05	0.000553017
MRPL23	2416.389798	1.056380687	0.249715234	4.230341372	2.33337E-05	0.000554145
PPID	1346.122124	0.33837031	0.079982714	4.230542997	2.33128E-05	0.000554145
CD79A	37.23555489	1.583719565	0.374542572	4.228410028	2.35349E-05	0.000558203
BRK1	6741.896087	0.386545584	0.091422811	4.228108695	2.35664E-05	0.000558233
B3GALT6	2107.148721	0.629910411	0.14901914	4.227043655	2.36782E-05	0.000560161
FST	228.6620542	1.68734687	0.399484949	4.223805861	2.40211E-05	0.0005653 7
MRPS24	2721.845501	0.657499805	0.155662616	4.223877397	2.40135E-05	0.0005653 7
TMEM115	3166.319172	0.640913233	0.151735607	4.223881557	2.4013E-05	0.0005653 7
LYPD3	77.11453572	1.324007278	0.313407842	4.224550577	2.39418E-05	0.0005653 7
DDK5	25529.20168	-0.394834654	0.093510987	-4.222334363	2.41785E-05	0.000568349
GPAT4	5063.172034	0.450889656	0.106812523	4.221318272	2.42878E-05	0.0005701 9
FAAP20	4012.206519	0.791888609	0.187756157	4.217643885	2.46868E-05	0.000578821
PXK	4676.675517	-0.933600004	0.221387582	-4.21703872	2.47531E-05	0.000579526
ARPC4	9204.237324	0.567851889	0.134682557	4.216224425	2.48427E-05	0.000579526
SLC22A18AS	41.7956089	1.393310491	0.330445058	4.216466415	2.4816E-05	0.000579526
NDUFS5	8022.224836	0.719973548	0.170749861	4.216539579	2.4808E-05	0.000579526
PPAN	1469.912077	0.715874775	0.169888968	4.213780239	2.51132E-05	0.000585095
CRACR2B	574.6072469	1.036779127	0.246092309	4.212968417	2.52036E-05	0.000586462
HSPA4	5301.680584	0.260811126	0.061934538	4.211077299	2.54156E-05	0.000590648
DENND3	3189.488199	-0.61134414	0.145203956	-4.210244397	2.55095E-05	0.000592083
SOCS1	291.4549316	1.372631304	0.326153785	4.208540168	2.57026E-05	0.000595815
GNB2	12844.60019	0.629861212	0.149679918	4.208054232	2.57579E-05	0.000596347
SENP7	871.5866196	-0.799237453	0.190051145	-4.205380887	2.60643E-05	0.000602208
SLC39A2	16.86210572	1.645970089	0.39140597	4.205275892	2.60764E-05	0.000602208
ALG1	1451.334829	0.513677803	0.122185852	4.204069431	2.62158E-05	0.000604671
MOB3A	3321.124985	0.647251884	0.153999498	4.202947982	2.63461E-05	0.000606916
ITPA	2409.551913	0.640633435	0.152449363	4.202270328	2.64251E-05	0.000607976
SIGLEC5	191.129143	1.585497849	0.377412279	4.200970494	2.65773E-05	0.000610715
MCAT	789.5983148	0.652294544	0.155283458	4.200669867	2.66126E-05	0.000610765
MRPL27	2804.954547	0.811825215	0.193285768	4.200129289	2.66763E-05	0.000611464
RIPK2	899.0533077	0.710355798	0.16920074	4.198301966	2.68924E-05	0.000615652
TTC32	428.1296147	-0.484263462	0.115434222	-4.195146418	2.72695E-05	0.000623512
VAT1	9761.795526	0.712967097	0.169996885	4.194000961	2.74077E-05	0.000625119
RAB34	2518.171326	0.564018892	0.134477573	4.194148355	2.73899E-05	0.000625119
GPR3	247.8877747	1.131231934	0.26976725	4.193362739	2.74849E-05	0.000626108
VMO1	486.2437367	1.229957788	0.293359866	4.192658679	2.75704E-05	0.000627278
IRAK1	7208.95574	0.539533885	0.128711024	4.191823433	2.76721E-05	0.000628816

LPCAT3	1595.50377	0.615695263	0.146951118	4.189796385	2.79205E-05	0.000632899
DUSP3	5972.40664	0.501025434	0.119576903	4.189985044	2.78973E-05	0.000632899
BRMS1	2748.40185	0.848258004	0.202499161	4.188945769	2.80253E-05	0.000634495
C11orf98	2271.046499	0.823209424	0.196556809	4.188150116	2.81237E-05	0.000635942
RAB32	1245.294185	1.006342072	0.240365567	4.186714782	2.83021E-05	0.000639191
TACO1	1158.215378	0.553742719	0.1323098	4.185198071	2.84918E-05	0.0006419
RNF25	1777.596521	0.581188739	0.13886044 5	4.185416065	2.84644E-05	0.0006419
RRP9	1187.782584	0.710738311	0.169927774	4.182590617	2.88206E-05	0.000648516
POGZ	4353.800652	-0.572815519	0.136985158	-4.181588199	2.8948E-05	0.000650588
KDM4C	1022.951452	-0.596662433	0.14271323	-4.180848772	2.90423E-05	0.000651913
EIF4E2	2735.092133	0.282138092	0.067518254	4.178693529	2.93188E-05	0.00065732
MRPS16	2786.553516	0.416851467	0.099775146	4.177908878	2.94201E-05	0.000658754
IKBIP	862.3345479	1.035039756	0.247888673	4.175421743	2.97434E-05	0.000665221
C5AR2	349.137954	0.977614615	0.234164786	4.174900218	2.98117E-05	0.000665938
AATK	17624.14497	-0.959667751	0.229884783	-4.174559702	2.98563E-05	0.000666128
HMOX1	10602.26637	1.325827086	0.31771215	4.173044956	3.00556E-05	0.000669763
ZFYVE1	1552.458922	0.308000068	0.07384609	4.170837873	3.03482E-05	0.000675467
RRP36	1686.202603	0.497549262	0.119306509	4.170344669	3.04139E-05	0.000676114
NT5DC1	1951.239351	-0.69676471	0.167090797	-4.1699765 77	3.04631E-05	0.000676391
PGRMC2	2490.314406	0.32011407	0.076774536	4.169534399	3.05223E-05	0.000676885
GRWD1	1570.067388	0.567641885	0.13618203	4.168258365	3.06936E-05	0.00067987
SAR1A	4562.170557	0.346394772	0.083110767	4.167868786	3.07461E-05	0.000680216
AKR1D1	10.81417221	2.08785036	0.501121154	4.16635846	3.09504E-05	0.000683915
CEMIP	420.8273282	-1.043943605	0.250586358	-4.166003346	3.09986E-05	0.00068416
CDC26	867.980282	0.554872398	0.133251542	4.164097375	3.12587E-05	0.000689074
RPL36AL	6941.313163	0.765918541	0.183977632	4.163106856	3.13946E-05	0.000691245
FFAR2	42.35413393	1.507121698	0.36207881	4.162413419	3.14902E-05	0.00069252
RABSIF	3198.391631	0.642473701	0.154363284	4.16208885	3.1535E-05	0.000692679
MRPS10	1410.204535	0.337339791	0.081070123	4.161086476	3.16737E-05	0.000694899
FAM71F2	284.740648	-0.676627758	0.162643688	-4.160184606	3.1799E-05	0.000696815
PSMB3	5438.457519	0.794164399	0.190942941	4.159171299	3.19404E-05	0.000699086
CSF2RB	653.99511	1.326830897	0.319081683	4.158279732	3.20653E-05	0.000700987
CA3	720.6862354	-2.09410222	0.503702828	-4.157416043	3.21868E-05	0.000702808
GPSM2	2474.039669	-0.746883817	0.179692532	-4.156454406	3.23225E-05	0.000704936
TOR1A	2109.294614	0.50176909	0.120844125	4.152200941	3.29293E-05	0.000717321
MMP10	27.7697041	1.97495882	0.475678566	4.151876837	3.2976E-05	0.00071749
MRGBP	968.5611207	0.479076142	0.115398414	4.151496765	3.30308E-05	0.000717835
CREB3	3060.25086	0.471372508	0.113582955	4.150028558	3.32434E-05	0.000720756
PRKD2	1337.915654	0.631644601	0.152201913	4.150043775	3.32412E-05	0.000720756
SNAI1	294.9961408	0.971817506	0.234190407	4.149689637	3.32926E-05	0.000720975
HMGA1	5996.978265	0.968284973	0.233392846	4.148734594	3.34318E-05	0.000722292
APOC1	24459.16064	1.473520521	0.355161374	4.148876062	3.34112E-05	0.000722292
ALDH1B1	926.0903581	0.73759066	0.177816538	4.148043078	3.35329E-05	0.000722782
DDX54	3127.542722	0.591918575	0.142692024	4.148224666	3.35064E-05	0.000722782
PXDNL	48.19707377	-1.237626427	0.298606216	-4.144677369	3.40292E-05	0.000732623
LENG9	262.2203554	0.711790892	0.171821634	4.142615078	3.43368E-05	0.000738381
CXCL2	472.3709174	1.496718024	0.361543167	4.139804488	3.47602E-05	0.000746615
ZNF652	2648.626208	-0.657566916	0.158909106	-4.138006508	3.50336E-05	0.000750738
CITED4	1301.411748	1.158687501	0.279997955	4.138199866	3.50041E-05	0.000750738
DNMBP	704.689204	0.559563063	0.135238798	4.137592708	3.50969E-05	0.00075122
RPP30	905.1090165	0.325790439	0.078766058	4.136178055	3.53138E-05	0.000754987
SPNS1	2801.622407	0.584194961	0.141361002	4.132645868	3.58611E-05	0.000764912
ACP2	3262.958816	0.586489768	0.141912694	4.132750566	3.58448E-05	0.000764912
S100A16	7953.293671	0.941240537	0.227836879	4.131203609	3.60869E-05	0.000768838
PSMG4	742.8186359	0.602838519	0.145956533	4.130260603	3.62352E-05	0.000771107
ERGIC3	7563.737938	0.562456089	0.136217915	4.129090421	3.64201E-05	0.000774148
CD274	329.6678918	1.258581749	0.304936863	4.127351924	3.66965E-05	0.000779123
EI24	4993.232655	0.501034484	0.121427016	4.1262192	3.68776E-05	0.000782068
ZBTB47	6127.041602	-0.668142437	0.161944022	-4.125761658	3.6951E-05	0.000782724
PSAP	122041.2129	0.687347931	0.166654449	4.124389924	3.71719E-05	0.000783799
L3MBTL2	2183.199501	0.400530257	0.097111577	4.124433674	3.71648E-05	0.000783799
KRTAP3-1	7.471319944	3.634377111	0.881107811	4.124781401	3.71087E-05	0.000783799
SLAMF9	39.56248106	1.673814169	0.405782412	4.124905667	3.70887E-05	0.000783799
FCGR3B	243.446769	1.613489236	0.391317959	4.123217961	3.73616E-05	0.00078421
APOC4	44.20257675	1.945923914	0.471919534	4.123423114	3.73283E-05	0.00078421
LAMB2	9183.615791	0.724560601	0.175716855	4.123455314	3.73231E-05	0.00078421
UBA52	23734.88824	0.72408052	0.175589569	4.123710337	3.72818E-05	0.00078421
C12orf49	3029.073678	0.426845121	0.103540745	4.122484557	3.74808E-05	0.000785817
BSG	29470.94434	0.649583831	0.157596622	4.121813174	3.75902E-05	0.000787216
PSME2	4708.634753	0.902824972	0.219059604	4.121366772	3.76631E-05	0.000787848
UBAP1L	1116.564578	-0.794042773	0.19280729	-4.118323398	3.81639E-05	0.000795071
TOP1MT	744.6473727	0.705546057	0.17132306	4.118220026	3.8181E-05	0.000795071
RPS10-NUDT3	500.2517757	1.245431768	0.302411637	4.118332811	3.81623E-05	0.000795071
PSMD3	5764.383696	0.529574228	0.12857273	4.11886896	3.80737E-05	0.000795071
GAR1	661.6271628	0.675875805	0.164180439	4.116664617	3.84395E-05	0.000798648
THAP7	2125.451344	0.607894021	0.147665065	4.116708462	3.84322E-05	0.000798648
KEL	366.2882713	-1.086932776	0.264092412	-4.115728911	3.85958E-05	0.000800993
ACRBP	240.6112245	1.011936144	0.245945536	4.114472492	3.88066E-05	0.000804462
LONRF3	128.2949804	0.99391702	0.241708859	4.112042165	3.92175E-05	0.000812066
SCFD2	721.2085981	-0.78698471	0.191460179	-4.110435464	3.94914E-05	0.00081682
TSSC4	2477.218029	0.752137115	0.18303597	4.109231186	3.96979E-05	0.00082017
GPRC5A	671.8169098	1.348514709	0.328332858	4.107157345	4.00558E-05	0.000826639
YARS2	412.0450867	0.488881187	0.119082466	4.105400272	4.03615E-05	0.000831087
KIR3DL1	3.003331774	3.634312166	0.885248937	4.105412632	4.03594E-05	0.000831087
HBD	35.09208866	2.716026642	0.661677873	4.104756638	4.04741E-05	0.000832474
TLR4	2807.089847	0.83716307	0.203963346	4.104478025	4.05229E-05	0.000832549
MYEOV	17.57037029	1.737156484	0.423547658	4.101442783	4.10582E-05	0.000842608
PITX3	9.919636773	2.332150954	0.56874223	4.100541213	4.12185E-05	0.000844956
CFD	2888.023796	1.601110947	0.390551451	4.099615928	4.13836E-05	0.000847399
AURKAIP1	5696.341796	0.74931108	0.182822907	4.098562325	4.15724E-05	0.0008503
CCDC134	116.5785317	0.702333414	0.171415787	4.097250465	4.18086E-05	0.000852314
UNC119B	2475.751817	0.398888832	0.097353981	4.097303767	4.1799E-05	0.000852314
TMEM63B	3411.903993	0.60374593	0.147343063	4.097552446	4.17542E-05	0.000852314
ZNHIT2	723.796573	0.791948729	0.193317267	4.096626962	4.19214E-05	0.000853667
TMEM SF1	2347.011352	0.952468197	0.232530113	4.096106886	4.20156E-05	0.000854642
PSMD8	7379.428744	0.486120814	0.118719708	4.094693464	4.22727E-05	0.000858924
EPB42	9.927362598	2.428516128	0.593247438	4.093597328	4.24732E-05	0.000861098
TCHH	77.78309069	1.275380483	0.31153649	4.093839802	4.24288E-05	0.000861098
SYS1	2099.753244	0.402742764	0.098390974	4.093289718	4.25296E-05	0.000861294
P2RX1	124.5511275	1.369430697	0.334740125	4.091026423	4.29468E-05	0.000868789
NTMT1	1709.75864	0.587129865	0.143561188	4.089753464	4.31832E-05	0.000872613
ALOXE3	60.09102275	1.789612771	0.437656848	4.089077507	4.33092E-05	0.000873245
EXOSC6	2233.143127	0.365126252	0.089288292	4.089295973	4.32684E-05	0.000873245
FBXW5	6997.694072	0.536540123	0.131309692	4.086066427	4.38748E-05	0.000883682
SMIM12	2069.554798	0.570412211	0.139665106	4.084142601	4.42399E-05	0.000890062
OSBPL5	1237.650025	-0.340611818	0.083446105	-4.081818055	4.46848E-05	0.000898032
CHD1	3634.175548	0.56997656	0.139648119	4.081519785	4.47422E-05	0.000898206
MIEF1	2154.172098	0.323538624	0.079310985	4.079367117	4.51585E-05	0.000905577
EIF3B	7297.762564	0.621450891	0.152444796	4.076563506	4.57062E-05	0.000915564
ZDHHC7	2580.037902	0.412495498	0.101195025	4.076242866	4.57692E-05	0.000915832
STK11	4069.512215	0.570878563	0.14009128	4.075047099	4.6005E-05	0.000919552
KLHL30	54.32451226	1.547941165	0.379887993	4.074730426	4.60677E-05	0.000919806
DDX17	26132.84424	-0.532989027	0.130822328	-4.074144189	4.61839E-05	0.000920132
RPS19BP1	5537.374319	0.764980686	0.187761107	4.07422334	4.61682E-05	0.000920132
WDR46	1966.236603	0.590250229	0.144997527	4.070760656	4.68599E-05	0.000932593
PANX1	963.7765217	0.614367758	0.150947564	4.070074017	4.69982E-05	0.000934336

CERCAM	41925.12751	-1.031013631	0.253404181	-4.068652799	4.72857E-05	0.000938436
RPLP1	47338.13938	0.821441125	0.201900134	4.068551655	4.73063E-05	0.000938436
DSCAML1	1435.622365	-0.897227051	0.220562791	-4.067898524	4.7439E-05	0.000939048
KRTCAP2	4685.633606	0.784102536	0.192746193	4.068057187	4.74067E-05	0.000939048
KCNH8	1846.695775	-1.344686325	0.330632395	-4.067013236	4.76195E-05	0.000940601
TPST2	1618.816755	0.511980794	0.125882682	4.067126517	4.75964E-05	0.000940601
FPGS	2613.288841	0.57028292	0.140288193	4.065081371	4.80157E-05	0.000947411
WHRN	2767.817744	-0.694499439	0.170897929	-4.063825945	4.82748E-05	0.000951509
AGAP4	668.7855641	-0.670975762	0.165171477	-4.06229802	4.8592E-05	0.000956733
TMEM158	2106.209581	1.245441524	0.306666937	4.06121878	4.88172E-05	0.000960141
CECR2	1069.160038	-0.992721604	0.244461121	-4.060856792	4.8893E-05	0.000960606
RHBDD3	1860.998329	0.586219531	0.144394612	4.059843535	4.91056E-05	0.000963756
ZC3H12A	445.7249196	1.210149702	0.298167957	4.058617551	4.93641E-05	0.000967799
ZNF76	1905.047027	-0.245369963	0.060491213	-4.056290974	4.98581E-05	0.00097567
CEBPB	4168.408139	0.946846404	0.233430237	4.05622861	4.98714E-05	0.00097567
SH2D6	257.9364772	0.885625957	0.218380706	4.055422167	5.00438E-05	0.000978004
COPS8	3682.736632	0.248724871	0.061347969	4.054329322	5.02783E-05	0.000981546
ATP6V0C	18940.77178	0.65532241	0.161646616	4.054043485	5.03399E-05	0.000981707
SLU7	2832.395756	0.258164428	0.063688765	4.053531683	5.04502E-05	0.000982818
IFT80	2342.238394	-0.826827338	0.20406265	-4.051830839	5.08184E-05	0.000986683
PLXNB3	14055.30359	-0.78965783	0.194895611	-4.051696321	5.08476E-05	0.000986683
MAN2A2	10870.15281	-0.628056682	0.155019337	-4.051473142	5.08962E-05	0.000986683
THOC6	1023.788307	0.714834768	0.176442258	4.051380759	5.09163E-05	0.000986683
HIC1	433.1122903	0.937849093	0.231454378	4.051982519	5.07855E-05	0.000986683
TRPV6	301.9301748	-1.61639784	0.399081612	-4.050293957	5.11533E-05	0.000989197
RPS27L	4585.829893	0.898316496	0.221785229	4.050389198	5.11325E-05	0.000989197
C1QTNF3	614.4024612	-0.690473473	0.170534627	-4.048875503	5.14643E-05	0.000994167
ATP1B3	4229.00513	0.525397379	0.129851329	4.046145582	5.20679E-05	0.001004773
ETV3L	30.69218587	2.511084492	0.620721139	4.045430926	5.2227E-05	0.001005737
PTRH1	821.3057801	0.712324885	0.176076767	4.045535908	5.22036E-05	0.001005737
CD151	7103.243579	0.932005492	0.23043492	4.044549715	5.24238E-05	0.001008474
AP5Z1	3375.561113	0.535121877	0.132329131	4.043870557	5.2576E-05	0.001010346
TANC1	2295.255012	-0.760070149	0.187985062	-4.043247595	5.27159E-05	0.001010945
DNHD1	1121.294257	-0.806535259	0.199477288	-4.043243545	5.27168E-05	0.001010945
CD59	22984.48871	0.563023193	0.139301801	4.041750985	5.30536E-05	0.001016345
ZNF862	1782.480817	-0.397365711	0.098379744	-4.039100868	5.36565E-05	0.001026828
ZPR1	2239.286704	0.398711741	0.098721937	4.038734985	5.37402E-05	0.001027364
TXNDC11	1617.219705	0.393278859	0.097463498	4.03513999	5.45698E-05	0.001042141
PLEKHA7	932.7759273	-0.663731404	0.164548394	-4.033654718	5.4916E-05	0.001047668
CCT8	4429.609313	0.388224807	0.096406187	4.026969853	5.65003E-05	0.001075665
AC099850.2	53.44120268	1.699905262	0.422125912	4.027009988	5.64906E-05	0.001075665
TRIM62	1043.414107	-0.553969873	0.137583045	-4.026439973	5.66277E-05	0.001076978
BCL7C	3451.948238	0.833013323	0.206908769	4.025993319	5.67353E-05	0.001077912
ESPN	160.5297139	1.463653891	0.363665872	4.024721607	5.70428E-05	0.001082637
NDUFC2	5764.529405	0.475904733	0.118262782	4.02412936	5.71865E-05	0.001084249
HEXIM2	457.9702135	0.599510778	0.149002997	4.023481347	5.73441E-05	0.00108612
VASH1	6665.181411	-0.540456302	0.134338787	-4.023084562	5.74409E-05	0.001086835
NHLRC4	37.11987692	-0.978535924	0.243402453	-4.020238543	5.81392E-05	0.001098921
ZNF830	715.5541654	0.36393052	0.090602422	4.01678578	5.89973E-05	0.001113997
RABIF	963.1565847	0.330570224	0.082344767	4.014465463	5.95807E-05	0.001123861
C1orf127	78.73466865	1.416629798	0.352990308	4.013225766	5.98946E-05	0.001128627
ELOB	13485.26042	0.881031799	0.219554399	4.012817805	5.99982E-05	0.001129425
VAX1	236.1190824	1.238454826	0.308675117	4.012162817	6.0165E-05	0.001131409
MRPL37	2815.170227	0.531709017	0.132535498	4.011823443	6.02516E-05	0.001131882
MRPS6	1970.533537	0.483538048	0.120558542	4.010815326	6.05094E-05	0.001135568
ACP6	1505.953111	0.617202562	0.15389946	4.010427076	6.0609E-05	0.00113628
TMEM203	1811.459696	0.372489594	0.09289818	4.009654392	6.08077E-05	0.001138846
DSC2	571.3258336	0.808966446	0.201793759	4.008877436	6.10081E-05	0.001141439
P2RX4	1800.44092	0.728373732	0.181781996	4.006852969	6.15331E-05	0.001147767
PLAUR	2422.805416	1.246965765	0.311198064	4.006984331	6.14989E-05	0.001147767
PSMC1	4605.517444	0.456927177	0.114022974	4.007325557	6.14102E-05	0.001147767
PCGF1	650.1106214	0.486128084	0.121368892	4.0053763	6.19188E-05	0.001153794
CCDC9	1137.724407	0.468426014	0.116986414	4.00410609	6.22524E-05	0.001158838
SERPINB10	20.40257268	1.343125309	0.335488215	4.003494752	6.24136E-05	0.001160668
PHYH	1383.647989	0.513414305	0.128257645	4.002991845	6.25465E-05	0.001161964
STARD9	2110.689871	-0.865211386	0.216311835	-3.999833784	6.3387E-05	0.001173812
DAPK3	3933.580256	0.750714915	0.187729041	3.998927985	6.363E-05	0.001173812
MRPL55	2321.793077	0.663405925	0.165888982	3.999095761	6.3585E-05	0.001173812
SUGCT	204.109399	1.026433541	0.256652541	3.999311817	6.35269E-05	0.001173812
OAZ1	27148.3388	0.49748119	0.124383896	3.999562689	6.34596E-05	0.001173812
NUDT14	1641.243729	0.772360312	0.193093678	3.999925431	6.33624E-05	0.001173812
GPN2	1618.536478	0.29357353	0.073387948	4.000296202	6.32632E-05	0.001173812
MRPL14	1288.209225	0.64015368	0.160111562	3.998172716	6.38334E-05	0.00117521
ABCF3	2895.359558	0.326301641	0.081607994	3.998402921	6.37713E-05	0.00117521
S100PBP	1269.884164	-0.324228281	0.081109741	-3.997402502	6.40414E-05	0.00117682
L3MBTL1	986.4579886	-0.710248179	0.177695759	-3.996990046	6.4153E-05	0.00117682
FUT7	30.55040753	1.440030404	0.360286449	3.996904155	6.41763E-05	0.00117682
ZDHHC5	2652.503649	0.457073389	0.114351088	3.99710574	6.41217E-05	0.00117682
ZNF707	660.1738638	0.587474425	0.147018472	3.995922537	6.44428E-05	0.001177023
PIGV	795.4156874	0.447710459	0.11204177	3.995924555	6.44423E-05	0.001177023
RNF181	3958.490427	0.739626899	0.18508853	3.996070957	6.44024E-05	0.001177023
CRH	116.8564968	2.130275271	0.533045678	3.996421618	6.43072E-05	0.001177023
SH2D2A	129.9801239	1.273342167	0.318697673	3.995454862	6.45702E-05	0.001178182
HMCES	2031.046678	0.465066472	0.116410719	3.995048538	6.4681E-05	0.001179037
PPY	7.134727195	2.549087503	0.638252969	3.993851381	6.50086E-05	0.001183838
JPH2	565.7672026	-1.379116576	0.345429218	-3.992472277	6.5388E-05	0.001189571
ALDH3B1	1708.992561	0.844446068	0.211540014	3.991897562	6.55467E-05	0.001191282
SMIM29	4481.141205	0.601474596	0.150695744	3.991317731	6.57072E-05	0.001191848
EID2B	411.296352	0.612094854	0.153349669	3.991497726	6.56573E-05	0.001191848
TNFRSF12A	3632.263731	1.319198549	0.330544574	3.990985336	6.57993E-05	0.001192346
TTLL5	1288.140699	-0.527619048	0.132249934	-3.989560026	6.6196E-05	0.001196741
IL10RB	1487.157234	0.671171358	0.168238073	3.989414214	6.62367E-05	0.001196741
PHETA1	675.6872222	0.537512755	0.134733231	3.989459385	6.62241E-05	0.001196741
MAU2	3504.608046	-0.439411792	0.110179962	-3.988127991	6.65967E-05	0.001197377
GGN	180.0433728	0.990274102	0.24829675	3.988268475	6.65573E-05	0.001197377
DPM2	2962.098722	0.669641333	0.167901882	3.988289624	6.65514E-05	0.001197377
MMP24OS	5210.25278	0.719344508	0.18036392	3.988294923	6.65499E-05	0.001197377
PRG2	14.2920142	2.266517543	0.568261524	3.988511357	6.64892E-05	0.001197377
AHCY	4677.617451	0.511518071	0.128451812	3.982178725	6.82864E-05	0.001226559
HSDL1	1521.01266	0.287338969	0.072165411	3.981671618	6.84323E-05	0.001226788
MGAM	112.9874204	1.468509631	0.368806545	3.98178842	6.83987E-05	0.001226788
HERPUD1	4597.155749	-0.395701189	0.099407385	-3.980601515	6.87411E-05	0.001231127
M6PR	6304.024736	0.525591186	0.132070268	3.97963291	6.90218E-05	0.001234953
FMO1	12.30908521	-1.801499139	0.452905003	-3.977653434	6.95987E-05	0.00123687
TMEM102	184.7684035	0.926826932	0.23300809	3.977659879	6.95968E-05	0.00123687
STC2	673.0276788	1.711146911	0.43018774	3.977674746	6.95925E-05	0.00123687
RAE1	1503.933378	0.328380363	0.082548515	3.978028726	6.9489E-05	0.00123687
NDUFAF4	1142.543731	0.559619971	0.140663508	3.978430351	6.93717E-05	0.00123687
PSTPIP1	599.9222363	0.922613731	0.231903949	3.978430447	6.93717E-05	0.00123687
MYDGF	3783.616556	0.692571986	0.17405622	3.979013148	6.92019E-05	0.00123687
ACOT9	1208.455572	0.494653435	0.124425121	3.975510996	7.02283E-05	0.001246857
HSPB2	482.0115378	0.958744875	0.241300095	3.973246991	7.08995E-05	0.001257561
IL10	134.9785199	1.455800874	0.366741226	3.969558831	7.20058E-05	0.001275957
KLF7	1711.253792	-0.479531669	0.120834412	-3.968502532	7.23257E-05	0.001276715
GATA3	86.49052407	1.769031187	0.445757933	3.968591597	7.22987E-05	0.001276715
ORAI2	2814.887378	0.472541663	0.119066908	3.968706932	7.22637E-05	0.001276715

PSCA	44.84805439	1.232535124	0.310562472	3.968718807	7.22601E-05	0.001276715
AMIGO2	641.556643	0.933435224	0.235260908	3.967659705	7.25819E-05	0.001280011
ATP6V0D1	8919.173325	0.531431646	0.133963035	3.96700212	7.27823E-05	0.001281094
LBX2	67.61960212	1.393421152	0.351238444	3.967165823	7.27324E-05	0.001281094
CNTRL	912.3018296	-0.564919307	0.142502052	-3.964288922	7.36151E-05	0.001294515
PCNA	4318.577346	0.991174092	0.250055937	3.963809474	7.37631E-05	0.001295882
UROD	5471.585917	0.566422961	0.14292318	3.963128718	7.39739E-05	0.001298347
ZNF524	1194.197843	0.727620676	0.183681681	3.961313238	7.45387E-05	0.001307015
TMEM147	4218.104809	0.562065788	0.141940814	3.959860252	7.49936E-05	0.001313743
WDR59	2390.194819	-0.283186815	0.071539095	-3.958490297	7.5425E-05	0.001320004
ACTR8	985.4904183	0.277010622	0.069982733	3.958270973	7.54943E-05	0.001320004
EIF4EBP3	839.3035788	0.761903424	0.19250919	3.95775093	7.56588E-05	0.001321626
FOXL1	72.74697823	1.271245273	0.321231278	3.957414355	7.57654E-05	0.001322236
PF4V1	9.254141129	2.555359957	0.645840428	3.95664292	7.60104E-05	0.001325256
MIF	24456.18003	0.793319647	0.200515131	3.956407903	7.60852E-05	0.001325308
PRR4	283.1516058	-0.865228548	0.218756331	-3.955216044	7.64655E-05	0.001329912
SQOR	1723.192414	0.864792062	0.218650888	3.955127141	7.6494E-05	0.001329912
PROM2	159.0165983	-0.711146522	0.179860522	-3.953877784	7.68947E-05	0.00133562
PSEN2	1143.901582	0.572680838	0.144869063	3.95309271	7.71475E-05	0.001338749
SLC6A2	7.392239164	-1.66326597	0.420900944	-3.951680304	7.76044E-05	0.00134541
FTSJ1	1449.935176	0.334363833	0.084619394	3.951385323	7.77001E-05	0.001345804
DGUOK	2302.438745	0.534297885	0.135233203	3.950937153	7.78458E-05	0.001347061
CTTNBP2	1594.876371	-0.875849096	0.221718722	-3.950271255	7.80627E-05	0.001348282
CTXND2	8.142851828	2.954611307	0.747916365	3.950456821	7.80022E-05	0.001348282
VASP	2627.766797	0.78925694	0.199837862	3.94948651	7.8319E-05	0.001350179
CAMK1	2502.617046	0.750485484	0.190013646	3.949639939	7.82688E-05	0.001350179
TMEM52	58.96680357	1.384700063	0.350677633	3.948640954	7.85961E-05	0.00135369
PI15	69.13833544	-0.920293709	0.233098754	-3.948085059	7.87788E-05	0.001355569
MACF1	20723.4705	-0.599923994	0.152042857	-3.945755871	7.95486E-05	0.001367539
TMEM214	2823.524789	0.389529332	0.098732688	3.945292432	7.97026E-05	0.00136891
MTX1	1836.60708	0.560233877	0.1420754	3.943215197	8.03965E-05	0.001374421
BCKDK	3020.473666	0.45246618	0.114739201	3.943431508	8.03239E-05	0.001374421
HBEGF	2169.585551	0.884573022	0.224311305	3.9435062	8.02989E-05	0.001374421
NECTIN2	3141.014287	0.801646403	0.203277821	3.943599949	8.02675E-05	0.001374421
NME2	11120.90617	0.62404245	0.158235064	3.943768423	8.02111E-05	0.001374421
LRP10	10063.36884	0.727250101	0.18448473	3.942061229	8.07843E-05	0.001379773
MPG	2210.10711	0.582670114	0.14786775	3.94048138	8.13183E-05	0.001387606
CLPTM1L	3487.994241	0.414319227	0.105170734	3.939491633	8.16544E-05	0.001390767
SURF4	7892.046721	0.451489927	0.114601754	3.939642396	8.16032E-05	0.001390767
ZNF888	192.8625901	0.507535166	0.128859627	3.938667027	8.19355E-05	0.001391696
P2RY6	388.8868717	1.252533777	0.3180012	3.938770598	8.19002E-05	0.001391696
PPP1R3C	1520.389005	0.846933166	0.215021309	3.93883365	8.18787E-05	0.001391698
SLAIN1	12737.67208	-0.85681845	0.217589344	-3.937777626	8.22398E-05	0.001394926
CABYR	408.5491165	0.975963998	0.247867147	3.937447992	8.23528E-05	0.001394926
PTK6	24.65326571	0.832003481	0.211304338	3.937465225	8.23469E-05	0.001394926
NRBP1	4355.693913	0.377389032	0.095855851	3.937047421	8.24903E-05	0.001395972
METTL27	161.0972311	1.14331743	0.290427891	3.936665394	8.26217E-05	0.001396913
DHDDS	1672.747822	0.322667532	0.081969424	3.936437707	8.27001E-05	0.001396957
POC1B	1194.938416	-0.716247029	0.182052995	-3.934277644	8.34473E-05	0.001406999
TRIM25	2134.928983	0.628024371	0.15962586	3.934352312	8.34213E-05	0.001406999
CCS	2755.0273	0.78881133	0.200508404	3.934056201	8.35242E-05	0.001407009
NEK11	774.2785967	-0.769816912	0.195737117	-3.932912292	8.39229E-05	0.001412433
SURF2	1243.736134	0.764592007	0.19447527	3.931564194	8.4395E-05	0.001419083
ZNF280D	1040.057507	-0.623824173	0.158801258	-3.928332681	8.55368E-05	0.001435736
PSMD4	7584.56346	0.558986721	0.142296617	3.928320528	8.55412E-05	0.001435736
AMDHD2	3321.80336	0.731834867	0.186400727	3.926137396	8.63209E-05	0.001447504
MELTF	1438.973675	0.856208467	0.218162937	3.924628438	8.68637E-05	0.001455283
SDHAF2	1318.019068	0.537404058	0.136946462	3.924190877	8.70217E-05	0.001456606
VKORC1	3792.811899	0.724910714	0.184793205	3.922821258	8.75181E-05	0.001463585
FADS1	3348.639545	-0.60094314	0.153208387	-3.922390623	8.76747E-05	0.001464875
PPM1F	2559.620598	0.472123816	0.120379871	3.92194986	8.78353E-05	0.001466228
GAR5	4738.137199	0.521341074	0.132943821	3.921514141	8.79943E-05	0.001467554
B3GNT7	1167.136041	0.992682408	0.2532329	3.920037279	8.85353E-05	0.001475241
SLC3A2	10679.48757	0.531013525	0.135505815	3.918750828	8.90091E-05	0.001481798
CIB2	874.6609177	0.591541904	0.150971593	3.918233168	8.92004E-05	0.001483641
IP6K3	1082.076704	-0.88397301	0.225629608	-3.917805894	8.93586E-05	0.001484932
TAL1	434.5808793	-0.753408102	0.192324621	-3.917377296	8.95176E-05	0.001486234
UBE2Z	5302.953561	0.35062244	0.089544255	3.915632989	9.01673E-05	0.001495674
CEL	264.3029169	1.046383327	0.267299167	3.914652411	9.05345E-05	0.001499066
TAPBP	8873.685382	0.698816343	0.178512543	3.914662416	9.05308E-05	0.001499066
ZNF511-PRAP1	13.99067751	3.29810003	0.842699916	3.913730105	9.08812E-05	0.001502108
FGF5	40.1546547	1.417932965	0.362289358	3.913813457	9.08498E-05	0.001502108
CTSK	746.1835902	0.869539914	0.222191403	3.913472351	9.09783E-05	0.001502365
SUSD2	898.6236079	1.149233405	0.293748684	3.912301466	9.14207E-05	0.001508319
ARMC5	1667.437112	0.688539896	0.176007865	3.911983694	9.15411E-05	0.001508954
DRAXIN	934.6456117	1.131649567	0.289444735	3.909725868	9.24009E-05	0.001521766
PANK2	1634.243364	0.294251429	0.075265656	3.909504618	9.24856E-05	0.001521801
RBM19	1620.701967	-0.249155451	0.063739782	-3.908947369	9.26992E-05	0.001523954
GLE1	1536.655778	0.397754393	0.101762455	3.908655647	9.28111E-05	0.001524435
CYTL1	219.9912151	-0.756851855	0.193706303	-3.907213361	9.33667E-05	0.001530832
HLX	393.6142004	0.955047735	0.244423339	3.907350817	9.33136E-05	0.001530832
TMEM208	2024.396681	0.574598697	0.147262713	3.901861426	9.54558E-05	0.001563693
QSOX1	4387.126283	0.534827883	0.137131041	3.900122683	9.6144E-05	0.001565227
WNT4	115.5149636	1.006192295	0.257988691	3.900141097	9.61366E-05	0.001565227
SLAMF8	1047.192931	1.328906779	0.340702813	3.900486668	9.59995E-05	0.001565227
LILRB2	1150.9799	1.229915536	0.31530539	3.900712052	9.59102E-05	0.001565227
LRFN4	1986.711328	0.519589409	0.133197325	3.900899733	9.58358E-05	0.001565227
STK40	3791.774473	0.506651072	0.129879614	3.900928385	9.58245E-05	0.001565227
TENT5C	154.2083981	1.051403983	0.269496826	3.901359426	9.5654E-05	0.001565227
TNFAIP8	384.2060737	0.96064225	0.246348781	3.899521024	9.63832E-05	0.001566354
MUC12	97.03984622	1.243240929	0.318810341	3.899625477	9.63416E-05	0.001566354
APOBEC3F	236.5941881	0.932749872	0.239221061	3.899112685	9.65458E-05	0.001567615
DTX2	891.747994	0.692098612	0.177551664	3.898012538	9.69854E-05	0.001570601
CCL5	1057.178913	1.499373258	0.384633144	3.898190473	9.69142E-05	0.001570601
REEP2	7528.470617	0.834269102	0.214011504	3.898244186	9.68927E-05	0.001570601
TXNRD2	1503.955962	0.548296633	0.140737335	3.895886147	9.78403E-05	0.001583059
EDF1	15242.80289	0.834624764	0.214257898	3.895421231	9.80282E-05	0.001584704
STK3	644.8912313	-0.468233425	0.120244267	-3.894018705	9.8597E-05	0.001592502
USB1	2390.336812	0.461461714	0.118511823	3.893803187	9.86847E-05	0.001592523
GSPT1	5371.111022	0.360281858	0.092535875	3.89342898	9.88371E-05	0.001593587
MTFMT	462.4824504	0.417693215	0.107292833	3.893020648	9.90037E-05	0.001594877
PHLDB1	20372.98772	-0.657809065	0.169043409	-3.891361809	9.96832E-05	0.00160442
PPP1CA	5322.593187	0.539204863	0.138613781	3.889980198	0.000100252	0.001612174
SSR4	7338.255531	0.701488863	0.180391306	3.888706605	0.00010078	0.001619243
CA1	18.59316526	1.717290895	0.441715997	3.887771567	0.000101169	0.001624078
RAC2	1133.053924	1.128100683	0.290213494	3.887140699	0.000101432	0.001626884
RPUSD3	1338.206369	0.411951269	0.106012163	3.88588683	0.000101957	0.001633883
GBA	4872.840123	0.632790912	0.163010183	3.881910319	0.000103639	0.001659396
ELF2	1353.396632	-0.503850533	0.12983501	-3.880698518	0.000104157	0.001666239
GATA1	8.088917417	3.01968713	0.778219525	3.880251053	0.000104349	0.00166786
HLA-DQB2	25.46883152	-1.481056107	0.38183031	-3.878833263	0.000104959	0.001676159
ETHE1	1011.321102	0.617280921	0.159193272	3.877556591	0.000105511	0.001682057
FLOT2	4958.250229	0.453536553	0.116959734	3.877715307	0.000105442	0.001682057
ACAD11	1719.504282	-0.433892819	0.111919525	-3.876828636	0.000105827	0.001685638
STAT2	8652.51186	-0.533890809	0.137728819	-3.876391406	0.000106017	0.00168721
ITGA1	1047.014943	-0.794877591	0.205078531	-3.87596686	0.000106202	0.001688579

RILPL2	1357.076542	0.642780379	0.165845689	3.875773814	0.000106286	0.001688579
NUDT19	554.1002677	0.44171364	0.114006348	3.8744653	0.000106859	0.001696215
SLC50A1	902.0292301	0.630593555	0.16277513	3.874016411	0.000107056	0.001697882
TDRD6	135.0231321	-0.958404697	0.247515844	-3.872094335	0.000107904	0.001709859
CD300LB	56.6219522	1.456232192	0.37625997	3.870282009	0.00010871	0.001721141
ZNF354B	712.5443573	-0.742875341	0.191976116	-3.86962377	0.000109003	0.001722445
NAPRT	2013.196303	0.696837986	0.180086166	3.869469829	0.000109072	0.001722445
TRIM32	711.3803707	0.595500086	0.153893428	3.869561522	0.000109031	0.001722445
BMS1	1590.18473	0.294304237	0.076086405	3.868026598	0.00010972	0.001731185
TRIM41	5197.812295	-0.472310575	0.122121771	-3.867537866	0.00010994	0.001733174
CYP2D6	129.6512676	-0.916787569	0.237074447	-3.867087246	0.000110143	0.001734894
MRM1	405.0155081	0.580497912	0.150122218	3.866835441	0.000110257	0.001735202
PPFIA1	3431.795828	-0.477749728	0.123566271	-3.866344127	0.000110479	0.001736961
GLRX5	1883.740926	0.41425143	0.107147699	3.866171965	0.000110557	0.001736961
CLDN23	187.1267393	1.07439609	0.277931281	3.865689692	0.000110776	0.001738914
NDUFS6	4479.031664	0.823645933	0.213164364	3.863900683	0.000111591	0.001750216
TRIM35	1100.419379	0.355985134	0.092137785	3.863617242	0.00011172	0.001750759
VDAC2	5327.794026	0.389330142	0.100779804	3.863176204	0.000111922	0.001752434
CHD2	4639.630147	-0.46419907	0.120206792	-3.86167091	0.000112614	0.001761772
CCDC146	416.7916336	-0.907769096	0.235128936	-3.860728968	0.000113049	0.001767078
SPATA5L1	414.3481891	0.482798953	0.125091435	3.859568426	0.000113587	0.001773986
ATP2A3	437.8032129	0.980914577	0.254261535	3.857896069	0.000114367	0.001784652
ILDR1	23.18495724	1.202523048	0.311826783	3.85638153	0.000115078	0.001792704
CAPG	12691.54901	1.026594097	0.266201149	3.856460051	0.000115041	0.001792704
F5	291.9222083	1.31837956	0.342181244	3.85286916	0.000116742	0.00181709
SNIP1	779.7013584	0.290713174	0.075459965	3.852548495	0.000116895	0.001817936
UBA7	2448.391127	-0.538972021	0.139940697	-3.85143158	0.000117429	0.001824709
TMEM186	490.8399198	0.38629881	0.100342617	3.84979802	0.000118215	0.001835374
KLK4	44.00181989	1.378401533	0.358080191	3.849421357	0.000118397	0.001836651
FBXL15	1820.148267	0.791130976	0.205538454	3.849065518	0.000118569	0.001837774
CCIN	53.47667756	1.408651721	0.366078444	3.847950469	0.00011911	0.001844609
PLEKHH1	18712.99141	-1.093193853	0.284144425	-3.847317615	0.000119418	0.001846272
ICAM1	4350.662527	1.153599746	0.299843938	3.8473339	0.00011941	0.001846272
THBS3	1252.936914	0.501248918	0.130334305	3.845870958	0.000120125	0.001855644
EREG	50.76455787	1.372310138	0.35690684	3.845009351	0.000120548	0.00185908
PRS536	214.2507133	0.976672823	0.254001698	3.845142896	0.000120482	0.00185908
ARHGAP23	11443.2576	-0.63939676	0.166313939	-3.844516976	0.00012079	0.00186054
SAMM50	1928.426312	0.42653299	0.110949053	3.844404044	0.000120846	0.00186054
FOXI1	3.525799948	3.65648664	0.95152054	3.842782667	0.000121647	0.001871315
NSUN6	547.6872202	-0.438105486	0.114028728	-3.84206237	0.000122005	0.001873479
CCDC66	617.1686301	-0.432315752	0.112528134	-3.841845917	0.000122112	0.001873479
FDX2	2058.836163	0.78578806	0.204542758	3.841681169	0.000122194	0.001873479
RNPEP	2654.724603	0.604175819	0.157264793	3.841774169	0.000122148	0.001873479
C5orf46	16.19143421	2.46131179	0.640810497	3.840935502	0.000122566	0.001876059
ESRRA	1849.950249	0.502741341	0.130884506	3.841106609	0.000122481	0.001876059
TRPV5	66.22579534	-1.741953585	0.453664004	-3.839743883	0.000123163	0.001883546
ROMO1	3642.771214	0.8074037	0.210286005	3.839550331	0.00012326	0.001883546
ARGLU1	6042.736174	-0.420796698	0.109659214	-3.837312712	0.000124388	0.001896444
GAA	8883.07373	0.574135676	0.149621102	3.837264065	0.000124413	0.001896444
UNC45A	2641.012479	0.425622548	0.11091814	3.837267284	0.000124411	0.001896444
MRPS17	1381.394396	0.6574625	0.171349143	3.836975713	0.000124559	0.001897102
SNRPD3	2162.2365	0.361014309	0.09410178	3.836423811	0.000124839	0.001899795
SLC9A9	1674.743383	-0.885768655	0.230897715	-3.836194981	0.000124955	0.0019
CES3	324.1930266	0.852989107	0.222400217	3.835378934	0.000125371	0.001904748
OXTR	1715.74808	1.227320239	0.320025524	3.835069857	0.000125529	0.001905574
ZSCAN30	1224.722566	-0.563540997	0.146987965	-3.833926111	0.000126114	0.001912885
ZNF514	1091.652096	-0.47164763	0.123032444	-3.833522389	0.000126321	0.001914453
SNX21	2028.177656	0.434211957	0.113306571	3.832186894	0.000127009	0.001923297
IRGQ	2422.420921	0.466328915	0.121726625	3.830952473	0.000127648	0.001929801
PGAM1	15032.55945	0.420324898	0.109717362	3.830978905	0.000127634	0.001929801
AC240274.1	2611.703441	-0.476378202	0.124358007	-3.830699892	0.000127779	0.0019302
PAX8	148.8465161	1.011316809	0.26404714	3.830061577	0.000128111	0.001933629
HM13	6738.863124	0.623707322	0.16289019	3.829004822	0.000128662	0.001940361
SLC4A11	771.4833859	0.917306623	0.239620239	3.828168379	0.0001291	0.001945373
ZMAT1	1923.132408	-0.818797306	0.213903773	-3.827876873	0.000129253	0.001946087
LUC7L2	3484.762825	-0.359388174	0.093911776	-3.826870185	0.000129783	0.001952465
ASB6	2264.696883	0.342460428	0.089504428	3.826184183	0.000130145	0.00195472
DSC3	38.08107506	1.950245094	0.509701984	3.826245837	0.000130112	0.00195472
CREB5	2604.45952	-0.704970503	0.184290625	-3.825319393	0.000130603	0.001959997
DHRS4L2	1570.555205	0.830157363	0.217037097	3.824956078	0.000130795	0.001961292
GTPBP4	1616.562788	0.318858081	0.08338441	3.823953192	0.000131329	0.001961312
SPRED3	1034.034518	0.983345709	0.257144795	3.824093386	0.000131254	0.001961312
MPZL3	139.5086311	0.954345559	0.249550961	3.824251193	0.00013117	0.001961312
RGL4	17.57131809	1.710670867	0.447316411	3.824297129	0.000131146	0.001961312
LTB	163.68151	1.201158679	0.314064847	3.824556268	0.000131008	0.001961312
C9orf78	3463.872384	0.314226634	0.082178643	3.823701884	0.000131463	0.001961724
KCNK6	582.6665384	0.727675062	0.190337635	3.823075045	0.000131798	0.001965128
ARID5A	2456.152985	0.72656493	0.190060793	3.8228028	0.000131943	0.00196577
ENOX1	529.7816224	-0.598027043	0.156459052	-3.822259137	0.000132235	0.001968459
AP2M1	19731.08341	0.452366876	0.11837275	3.821545703	0.000132618	0.00197257
SRXN1	2298.709616	0.722678106	0.189246223	3.818718776	0.000134147	0.0019937
KIF19	1176.970295	-1.123089939	0.294152227	-3.818056898	0.000134507	0.001997444
SEC61A1	14203.15729	0.660897779	0.173198547	3.815839043	0.000135721	0.00201385
MYLPF	19.47563942	1.087047438	0.284904937	3.8154742	0.000135922	0.002015205
PTGES2	3333.833861	0.597274583	0.156570803	3.814725179	0.000136335	0.00201808
EIF5A	10389.33556	0.50222489	0.131650314	3.814840041	0.000136271	0.00201808
EDDM13	5.767617855	2.118968859	0.555547552	3.814198892	0.000136625	0.002020762
RBM4	3509.118873	0.428686014	0.112402182	3.813858472	0.000136814	0.002021926
TNS2	6531.265877	-0.506241623	0.132774319	-3.812797731	0.000137403	0.00202
NAIF1	414.9343251	0.336810172	0.088351338	3.812168323	0.000137753	0.002032546
VPS25	1865.348629	0.470548945	0.123490685	3.810400308	0.000138742	0.0020455
PREB	2816.595165	0.3328874	0.087368402	3.810157795	0.000138878	0.002045871
WDR70	926.4013291	-0.435251308	0.114268805	-3.809012514	0.000139523	0.00205322
C16orf91	623.3101559	0.541558365	0.142190606	3.808678913	0.000139711	0.00205322
CD28	169.429435	1.773352574	0.46558592	3.808862117	0.000139608	0.00205322
ADA	885.1450643	0.903772219	0.237317431	3.808284182	0.000139934	0.002054861
PKM	61661.25691	0.574411716	0.150876191	3.807172715	0.000140565	0.002062472
GPNMB	19043.70215	1.317217816	0.346050415	3.806433274	0.000140985	0.002065356
SNX33	1272.672567	0.383454922	0.100737758	3.806466714	0.000140966	0.002065356
SNF8	2932.062094	0.559977037	0.147137392	3.805810542	0.000141341	0.002068916
RPP40	244.1379584	0.581121011	0.152708002	3.805439153	0.000141553	0.002070378
NCF2	1374.453628	1.058687311	0.27828953	3.804265691	0.000142225	0.002078567
RWDD2B	858.6886989	0.418191426	0.109961497	3.803071425	0.000142913	0.002086962
SUSD3	158.6709956	-1.033531814	0.271877732	-3.801458133	0.000143847	0.002098937
DIP2A	2637.467985	-0.512780082	0.134928095	-3.800395172	0.000144466	0.002106294
PEX1	1176.520861	-0.507285055	0.133511892	-3.799549592	0.000144959	0.002111822
PRS535	265.328851	1.294730633	0.34078566	3.799252098	0.000145133	0.002112688
ZNF672	1990.831538	0.462611993	0.121788774	3.798478117	0.000145587	0.002117623
C12orf43	1126.988436	0.373361081	0.0983449	3.796445788	0.000146785	0.002133367
TIMM13	3295.218742	0.644468792	0.16981391	3.795147229	0.000147556	0.002142874
RBM34	1816.995333	0.413606449	0.108991828	3.794839043	0.000147739	0.002143848
GLRX	2291.547981	0.724601015	0.190961212	3.794493176	0.000147945	0.002145149
SGK1	10709.12312	-0.602775017	0.158903508	-3.7933399	0.000148634	0.002153447
CCDC137	1502.072851	0.551432663	0.145378458	3.793083722	0.000148788	0.002153978
PHB	6680.447952	0.549906997	0.145010494	3.792187598	0.000149326	0.00216007
CLUH	3700.235951	0.396566335	0.104613139	3.79078898	0.00015017	0.002165472

RPS19	31806.34748	0.778714593	0.205415311	3.790927702	0.000150086	0.002165472
GPAA1	7169.129205	0.493434435	0.130156968	3.791071965	0.000149998	0.002165472
MAFF	6518.981254	0.83317106	0.2197549	3.791365111	0.000149822	0.002165472
ANO9	164.385076	1.902714676	0.50202776	3.790058694	0.000150612	0.002170151
IQCN	368.1175273	-0.639540206	0.168851642	-3.787586547	0.000152118	0.002188992
L3MBTL4	504.8847335	-0.604559224	0.159618647	-3.787522534	0.000152157	0.002188992
CUTA	7696.369382	0.633687471	0.167321187	3.787251828	0.000152323	0.002189668
CEACAM4	72.88476386	1.63237236	0.431129875	3.786265933	0.000152928	0.002196657
RHBDD2	9967.054492	0.582845121	0.154065914	3.783089376	0.000154894	0.00222316
RASSF7	511.4505152	0.675918784	0.178702329	3.782372551	0.000155341	0.002226106
EIF4A1	18490.74319	0.540228672	0.142824025	3.782477584	0.000155275	0.002226106
NIPBL1	350.5303963	-0.521506062	0.137927103	-3.781026719	0.000156183	0.002234721
TRNP1	1156.445044	1.089939582	0.288265679	3.781024457	0.000156184	0.002234721
MYMX	13.19709909	2.077437559	0.549486968	3.780685764	0.000156397	0.002236028
METTL3	2011.644234	-0.368521605	0.097506214	-3.779467899	0.000157164	0.002244459
PAZG4	6698.800797	0.533490978	0.141158977	3.779362735	0.00015723	0.002244459
SLC26A7	38.79949136	-1.373082436	0.363397394	-3.778459777	0.000157801	0.002250867
ARHGDIA	22343.80432	0.563467642	0.149146703	3.777942335	0.000158129	0.002253804
TRPV1	719.9196934	-0.499975326	0.132358151	-3.777442651	0.000158447	0.002256584
IFNAR1	3594.276288	0.296204602	0.078420506	3.777132016	0.000158645	0.002257654
ZNF717	339.6627206	-0.441006307	0.116798359	-3.775791969	0.0001595	0.002266268
DNA2	169.7438071	-0.834898876	0.221125777	-3.775674139	0.000159575	0.002266268
PARVB	1746.127586	0.602211646	0.15950064	3.775606463	0.000159619	0.002266268
GJB5	149.7778524	2.0042076	0.530986049	3.774501428	0.000160328	0.002274584
TUSC2	3070.105045	0.523771472	0.138790226	3.773835431	0.000160757	0.002278914
SCNN1B	41.93589788	1.873402767	0.496804339	3.770906616	0.000162656	0.002304058
PTTG1	1094.886069	1.345545691	0.356851381	3.770605244	0.000162852	0.00230507
FAM107B	7282.683759	-0.762609241	0.20227216	-3.770213571	0.000163108	0.002306919
GPR108	3015.246583	0.452225741	0.119962743	3.769718258	0.000163432	0.002307959
KARS	4703.904734	0.423240984	0.112271264	3.76980689	0.000163374	0.002307959
RBM33	2980.58554	-0.439990768	0.116762853	-3.768242687	0.000164401	0.002316687
ZBTB37	1279.624	-0.690935131	0.183368612	-3.768011997	0.000164553	0.002316687
PSPN	254.1731804	0.607797251	0.161296412	3.768200694	0.000164428	0.002316687
EIF3M	4514.224736	0.367040844	0.097396395	3.768525965	0.000164214	0.002316687
OMA1	572.3784808	-0.344820792	0.09152361	-3.767561078	0.00016485	0.002319103
SDC4	5982.251749	0.707480877	0.18789177	3.765363837	0.000166307	0.002337808
IMMP2L	262.1904873	-0.641021351	0.170334407	-3.763311015	0.000167678	0.002355294
EMC6	1774.548908	0.539628123	0.143406647	3.76292267	0.000167939	0.00235716
FAM43A	728.6717601	0.926197348	0.246366273	3.759432398	0.000170299	0.002388467
DNPEP	1767.504957	0.396147264	0.105397999	3.758584287	0.000170877	0.002394754
NLRX1	963.6807026	0.529933734	0.141019178	3.757884162	0.000171356	0.002397815
ALG2	1415.251675	0.473683398	0.126047464	3.757976432	0.000171293	0.002397815
DCAF8	7048.945144	-0.308337949	0.0820648	-3.757249763	0.000171791	0.002400556
KLF5	133.3160044	1.235752671	0.328900946	3.757218358	0.000171813	0.002400556
SLC2A6	1044.728791	0.784351341	0.208778826	3.75685291	0.000172064	0.002402242
GZMA	105.7418325	-1.306193811	0.347786953	-3.755729764	0.000172837	0.002409391
PAQR7	1085.723357	0.590950627	0.157340256	3.755876866	0.000172736	0.002409391
GOLT1A	79.9875575	1.348721969	0.359252302	3.754247261	0.000173863	0.002421863
CR1	540.5434832	1.520360847	0.405020033	3.753791721	0.00017418	0.002424438
CDH26	111.1426476	-0.734981988	0.195876629	-3.752269928	0.000175241	0.002435899
ISY1	1191.121193	0.467291436	0.124536936	3.752231681	0.000175267	0.002435899
ZNF263	1789.736043	0.323615047	0.086250595	3.75203263	0.000175407	0.002435998
TTC17	2092.571851	-0.308139455	0.08213852	-3.751461019	0.000175807	0.002437885
MLF2	13442.50582	0.532686313	0.141988543	3.751614751	0.000175699	0.002437885
WWC3	1943.363041	-0.377604154	0.100673824	-3.750767952	0.000176294	0.002441152
EPB41L2	10517.99882	-0.693611358	0.184944692	-3.750371795	0.000176573	0.002441152
PDCD11	1261.559343	0.340065982	0.0906742	3.750416131	0.000176541	0.002441152
MZT2B	7383.857558	0.679766069	0.181248414	3.750466295	0.000176506	0.002441152
AC131160.1	107.2831289	-1.638125103	0.436846536	-3.749886898	0.000176914	0.002442476
VNN1	237.7373146	1.147038942	0.305888477	3.749859923	0.000176933	0.002442476
PNPLA1	14.21243563	1.53453427	0.409293167	3.749230121	0.000177378	0.002446784
PRAP1	26.96077838	2.05792164	0.548949155	3.74883834	0.000177656	0.002448776
ZFHX3	7985.164464	1.196222082	0.319291914	3.746484106	0.00017933	0.002470014
DYNC1LI1	1690.083499	0.245189782	0.06545421	3.745974201	0.000179695	0.002473189
RALGPS1	1424.190805	-0.75659697	0.202013608	-3.745277243	0.000180195	0.002478215
CRNKL1	1282.271278	0.2832676	0.075665732	3.743670924	0.000181351	0.00249228
SPG11	2468.786341	-0.424938723	0.113551752	-3.742247183	0.000182382	0.002504231
TRMT13	639.9900516	-0.575733862	0.15385344	-3.742092869	0.000182494	0.002504231
ZSWIM6	1559.572246	-0.66865547	0.17871511	-3.741460204	0.000182954	0.002508677
CALHM2	662.5763368	0.568462492	0.151946509	3.741201405	0.000183143	0.002509395
AMBRA1	1384.46019	-0.2716812	0.07262519	-3.740867327	0.000183386	0.002510867
MRPL52	2458.165723	0.717601763	0.191905757	3.739344631	0.000184501	0.002524248
TRMT5	787.6377527	0.330582999	0.088412709	3.739089116	0.000184688	0.00252494
RPL7L1	4871.330135	0.289027295	0.077303992	3.738840479	0.000184871	0.002525565
PISD	2393.723566	0.453333034	0.12125864	3.738562752	0.000185075	0.002526483
MAN1B1	4889.523228	0.416829013	0.111554129	3.736562843	0.000186553	0.002544769
NUDT22	1814.619432	0.587329953	0.157196295	3.736283702	0.00018676	0.002545709
RP9	769.4763521	0.675340584	0.18077422	3.735823532	0.000187102	0.002546603
SYCE1L	185.4277461	0.947444199	0.253605348	3.735899917	0.000187045	0.002546603
CCDC60	6.98623493	2.065743642	0.552995442	3.735552747	0.000187303	0.002547463
ITPR2	2176.739501	-0.758985147	0.203193124	-3.735289514	0.000187499	0.002548249
FBXO33	776.3441511	0.37044548	0.09920262	3.7342308	0.00018829	0.002557105
THG1L	425.7316676	0.405589666	0.108642179	3.733261527	0.000189016	0.00256508
ERP29	5158.354952	0.490030814	0.131268964	3.733028733	0.000189191	0.002565564
IFI44	1938.717056	-0.591670931	0.158588051	-3.730867023	0.000190822	0.002585777
PRR7	1308.232613	0.597613317	0.160210227	3.730182086	0.000191341	0.002590912
PSMB4	10534.93763	0.496292037	0.133069638	3.729566302	0.00019181	0.002595345
CCDC71L	1344.184649	1.111896322	0.298183013	3.728905654	0.000192313	0.002600249
WRAP53	567.3595789	0.465817559	0.124929272	3.728650232	0.000192508	0.002600977
EID2	884.4236428	0.455264312	0.122118107	3.728065593	0.000192955	0.002605107
KDM6B	1977.838328	0.789809393	0.21188063	3.727614901	0.0001933	0.002607858
IFNAR2	1388.191829	0.397292155	0.106602246	3.72686477	0.000193876	0.002613715
SCO1	1404.778544	0.245269592	0.06584285	3.725075576	0.000195257	0.002630399
IBA57	546.085515	0.344737876	0.092565084	3.724275537	0.000195877	0.002636826
TXN2	5158.662874	0.489078638	0.131330921	3.72401742	0.000196077	0.002637599
RRP1	2507.405715	0.627390806	0.168510762	3.723149788	0.000196753	0.002644753
ZNF296	166.6666212	0.743352044	0.19974169	3.721566812	0.00019799	0.002659451
ZEB2	14282.45164	-0.85214994	0.229029502	-3.720699433	0.000198672	0.002666659
PEAK1	2648.016281	-0.587905033	0.158030498	-3.720199831	0.000199065	0.002669995
DNAJA1	8113.211403	0.342391316	0.092053086	3.719498503	0.000199619	0.002675472
ATP5PD	5392.404145	0.46171445	0.124176913	3.718198819	0.000200648	0.002687317
MAP4K5	2821.624406	-0.590021136	0.158700545	-3.717826791	0.000200944	0.002689327
PSMG1	980.2876561	0.425451253	0.114558191	3.713844039	0.000204135	0.002730041
ADGRG3	79.72013904	1.495836623	0.402905468	3.712624276	0.000205121	0.002741247
POLDIP2	4661.088475	0.31013511	0.083554306	3.711778915	0.000205808	0.002748428
SHBYL1	1456.442117	-0.517436766	0.139452835	-3.710478649	0.000206868	0.002758586
PRICKLE3	273.3150523	0.769156497	0.207291669	3.710503661	0.000206847	0.002758586
ELOA	2477.729206	0.360003574	0.09703826	3.709913753	0.00020733	0.002760753
MET	849.0145243	0.640359327	0.172605336	3.709962517	0.00020729	0.002760753
PRMT5	2161.107817	0.437128039	0.117833661	3.709704286	0.000207501	0.002761043
EGLN2	5372.794921	0.432331641	0.116547009	3.709504379	0.000207665	0.00276123
MEI51	846.6138614	-0.73300248	0.19761633	-3.709220189	0.000207899	0.002762338
USF1	3272.237493	0.414917543	0.111884706	3.708438414	0.000208541	0.002768882
RAD51C	1015.092786	0.412692172	0.111309666	3.707604092	0.000209229	0.002776018
HEXA	6924.46406	0.632209181	0.170604395	3.705702791	0.000210805	0.002794915
SLC38A7	1637.331825	0.377906154	0.101989703	3.705336363	0.00021111	0.002794938

NATD1	951.8468211	0.604373611	0.163102367	3.70548644	0.000210985	0.002794938
RPP21	1499.116616	0.574484675	0.155073871	3.704587189	0.000211735	0.002801198
RPL28	35876.60989	0.790081952	0.213282497	3.704391889	0.000211898	0.002801346
TMEM111	1341.687156	0.485858864	0.131172116	3.703979759	0.000212243	0.002801884
NFE2	62.50510535	1.244381728	0.335954792	3.704015412	0.000212213	0.002801884
PKP4	17195.94948	-0.889386269	0.240203321	-3.702639353	0.000213368	0.002810694
EXOC3L4	21.9492871	1.566442894	0.423045471	3.702776651	0.000213253	0.002810694
POP4	1932.634	0.428170404	0.115630718	3.70291227	0.000213139	0.002810694
ZC3H11A	5484.007792	-0.398890896	0.107784242	-3.700827586	0.000214897	0.002828818
WDR34	2258.084629	0.794182652	0.214606961	3.700637891	0.000215058	0.002828913
ABTB2	938.5196701	-0.531157247	0.143562341	-3.6998369	0.000215738	0.002833811
CTU2	1201.848838	0.501009511	0.135411013	3.699917	0.00021567	0.002833811
SGSH	1710.39777	0.453375367	0.1226013	3.697965403	0.000217335	0.002852748
CENPBD1	721.3122676	0.345377601	0.093420389	3.69702593	0.00021814	0.002861284
CLN3	2081.657277	0.549567255	0.148669322	3.696574693	0.000218528	0.002864333
PSMD13	4850.78414	0.476712163	0.128967019	3.696388151	0.000218689	0.002864
PLSCR3	1563.971205	0.50156921	0.135700436	3.69615032	0.000218893	0.002865047
COX8A	7857.549882	0.537270059	0.145394101	3.695267244	0.000219656	0.002872983
BBIP1	1409.832973	-0.487549296	0.131962019	-3.694618346	0.000220217	0.002876727
MIA	17.41690508	1.529047199	0.413862709	3.694575926	0.000220254	0.002876727
MFAP1	1471.192837	0.276189293	0.074760264	3.694332744	0.000220465	0.002877442
MRPS11	2134.546358	0.463586109	0.125557747	3.692214292	0.00022231	0.00289947
PDE6B	2166.254844	-0.854170274	0.231378306	-3.691661017	0.000222794	0.002903731
APOL1	1390.659549	0.985581691	0.26703594	3.690820389	0.000223532	0.002911286
AKR1B10	34.39556915	1.569336495	0.425257521	3.690320377	0.000223972	0.002914955
CCDC174	834.2489373	0.292587029	0.079326558	3.688386793	0.00022568	0.002935119
UTP4	1426.713547	0.455699055	0.123582035	3.687421524	0.000226538	0.002944194
MAMDC2	72.66688034	-1.068703568	0.289861079	-3.686950903	0.000226957	0.002944683
LRIG2	1152.069095	-0.430185473	0.116681311	-3.68684127	0.000227055	0.002944683
MCRIP2	1822.189116	0.659051343	0.178744041	3.687123437	0.000226803	0.002944683
CHMP1A	4854.065385	0.38123614	0.10341439	3.686490243	0.000227368	0.002946672
PTK2	8603.829213	-0.618294228	0.167751788	-3.685768342	0.000228014	0.002952962
NDUFS8	5188.909138	0.702730464	0.190699372	3.685017197	0.000228687	0.002959604
ZDHHC11	1278.705257	-0.930752988	0.252647709	-3.683995357	0.000229606	0.002969415
SELENOM	6424.692196	0.943729105	0.256184333	3.683789301	0.000229792	0.002969734
P4HB	18353.02861	0.649702625	0.176388788	3.683355565	0.000230184	0.002972709
WNT8B	2.425229175	-2.150153782	0.58381959	-3.682907905	0.000230588	0.002975816
B4GALT7	1606.241765	0.484290778	0.131503111	3.682732478	0.000230747	0.002975816
LPIN3	643.6653241	0.751613302	0.204114474	3.68231262	0.000231128	0.002978639
OGFR	5572.171384	0.522288111	0.141865499	3.681572436	0.0002318	0.002985214
IMP4	3296.614119	0.335027841	0.091029908	3.680415001	0.000232855	0.002996703
UBL4A	2243.591254	0.321044985	0.087241571	3.679954193	0.000233276	0.003000028
LLGL1	8058.851543	-0.57946953	0.157475334	-3.679747912	0.000233465	0.003000362
INVS	486.6134206	-0.586622823	0.159477953	-3.678394499	0.000234707	0.003014162
GHDC	1920.220348	0.410135574	0.111514523	3.677866912	0.000235193	0.003014162
CLTB	6103.216672	0.676509607	0.183940005	3.677881861	0.000235179	0.003014162
TPS3I11	2216.58711	0.694679727	0.188880352	3.677882432	0.000235178	0.003014162
TBC1D9B	10721.4241	-0.307271934	0.083550906	-3.677661319	0.000235382	0.003014495
TRIM43B	4.732891805	2.93854287	0.799205724	3.676829109	0.000236151	0.003022242
CD96	51.82409591	-1.235437233	0.336168429	-3.675054308	0.000237799	0.003041218
RRP7A	3898.38173	0.652870664	0.177665505	3.674718197	0.000238112	0.003043112
ATF5	2090.279233	0.672180471	0.182973224	3.673654846	0.000239106	0.003053693
TAS2R20	19.24587465	-1.073913842	0.292412639	-3.672597213	0.000240098	0.003064239
MRPL36	1175.075728	0.487237929	0.132701143	3.671693543	0.000240949	0.003070844
CISD2	1843.54553	0.336760926	0.091717733	3.671710099	0.000240933	0.003070844
NAV1	4415.784129	-0.533930998	0.145432017	-3.671344229	0.000241278	0.003072497
EHMT1	2105.83476	-0.388406763	0.105798232	-3.671202793	0.000241412	0.003072497
MRPL28	3922.755265	0.66187382	0.18030787	3.670798283	0.000241794	0.003075241
STRN	3012.836235	-0.758259954	0.206608501	-3.670032695	0.000242519	0.003082339
MOB3C	1541.187631	0.57479051	0.156643243	3.669424221	0.000243097	0.003085428
POP7	1478.281637	0.481827664	0.13130503	3.669529377	0.000242997	0.003085428
C15orf39	798.359195	0.763166985	0.208091234	3.667463407	0.000244969	0.003107038
MED9	1285.15205	0.273838141	0.074674399	3.667095365	0.000245321	0.003109372
RFK	1282.514441	0.704291468	0.192072013	3.666809429	0.000245596	0.00311071
MRPL49	2547.139869	0.501259738	0.136738215	3.66583502	0.000246533	0.003118293
YIF1A	3037.268242	0.657496806	0.179357845	3.665838004	0.00024653	0.003118293
TICAM1	856.9039103	0.560136013	0.152833236	3.665014408	0.000247325	0.003126163
IL32	2649.123375	1.259569896	0.343714501	3.664581779	0.000247743	0.003127162
TGIM	1344.387856	1.281466902	0.349680816	3.66467602	0.000247652	0.003127162
TAS2R10	5.475866914	-1.575791358	0.430127808	-3.663542171	0.000248751	0.003137739
ATM	2874.68022	-0.684685968	0.186922708	-3.66293628	0.000249341	0.003143022
SSPO	544.1439247	-1.012669479	0.27652192	-3.662167106	0.000250091	0.003150321
PTMS	12975.78377	0.752449745	0.205506685	3.661436828	0.000250805	0.003157158
TUFT1	393.6727062	0.77595492	0.211994455	3.660260449	0.000251959	0.003169524
TUBA1C	5506.147513	0.929154328	0.253872878	3.659919628	0.000252294	0.003171578
WNT2	117.5996039	1.084319664	0.296373791	3.658621973	0.000253575	0.003185504
TMEM40	30.95455549	1.425847326	0.389813205	3.657770715	0.000254418	0.003193922
PAN3	1091.88403	-0.463810661	0.126832697	-3.656869819	0.000255314	0.003202982
TSTA3	1817.316784	0.550442572	0.150567127	3.65579514	0.000256386	0.003214244
CTSZ	16516.41616	1.005061088	0.274947194	3.655469526	0.000256712	0.003216139
CDC42EP3	834.998637	0.724302195	0.198155377	3.655223524	0.000256958	0.003217037
FAM53C	2543.494875	0.338259648	0.092562895	3.654376286	0.000257808	0.003225487
NPIPB5	7991.067504	-0.503465142	0.137783243	-3.654037526	0.000258149	0.003226228
ANKS1A	1684.745694	-0.529331702	0.144864851	-3.653969195	0.000258217	0.003226228
TBC1D7	758.6080448	0.413956253	0.113309749	3.653315403	0.000258876	0.003232266
AIDA	4657.448774	-0.375773086	0.102873582	-3.65276565	0.000259431	0.003237003
FKBP10	5301.680678	0.748360985	0.204942443	3.651566627	0.000260645	0.003245564
B3GAT3	5310.33363	0.574035542	0.157201053	3.651601112	0.00026061	0.003245564
PLK3	1633.650868	0.871272833	0.238589736	3.651761583	0.000260448	0.003245564
IMPDH1	2078.544788	0.536619307	0.146983767	3.650874625	0.000261349	0.003252125
SLC39A1	5170.553769	0.583531563	0.15993206	3.648621569	0.000263651	0.00327635
ENO1	55298.80668	0.589950288	0.161685058	3.648761948	0.000263507	0.00327635
TECTA	206.8854084	-0.617604481	0.169324732	-3.647455821	0.00026485	0.003289028
CHST2	3241.386746	0.640334065	0.175626875	3.645991349	0.000266363	0.003305591
SHBKBP1	3006.142052	-0.455542636	0.124979103	-3.644950439	0.000267443	0.003316765
CEP85	1001.190435	-0.643561128	0.176589951	-3.644381384	0.000268036	0.003321876
JMJD6	1319.601799	0.362339213	0.099437145	3.643902021	0.000268536	0.003325836
SAMD4A	4364.593826	-0.766495522	0.210437668	-3.64238745	0.000270121	0.003340981
MAP1LC3B	9397.961608	0.302881023	0.083151525	3.642519166	0.000269983	0.003340981
BOLA2B	1391.766169	0.82212404	0.225910528	3.639157709	0.000273531	0.00338089
NMRK2	6.480558424	-1.737105267	0.477473001	-3.6381225	0.000274633	0.003399223
DOCK10	4272.144518	-0.84662756	0.232782996	-3.636981976	0.000275851	0.003400443
MED10	1699.715236	0.377868704	0.103894603	3.637038821	0.00027579	0.003400443
SERTAD2	1429.941089	0.401993653	0.110525012	3.637128343	0.000275695	0.003400443
NEK3	1437.512013	-0.646953372	0.177923083	-3.636140742	0.000276753	0.003408106
ENOSF1	2320.222557	-0.736634579	0.202601163	-3.63588524	0.000277028	0.003408106
AHSP	18.41852794	1.831285445	0.503664898	3.635920334	0.00027699	0.003408106
KLF9	3476.537596	-0.510657062	0.140483968	-3.634984579	0.000277997	0.003416138
PLD5	266.2555427	-0.708207271	0.194833572	-3.634934492	0.000278051	0.003416138
FAAH2	35.17461137	-0.879390333	0.2419397	-3.63475004	0.00027825	0.003416305
SCRG1	8116.444579	0.642609042	0.176814566	3.634367108	0.000278664	0.003419105
SHSA5	10571.74556	0.559663618	0.154027781	3.633523873	0.000279577	0.003428022
CNIH4	1805.638342	0.397628521	0.109454159	3.632831549	0.000280328	0.00343495
EIF3I	5527.019533	0.377405705	0.103930386	3.631331703	0.000281963	0.003452682
TXNDC17	1758.197996	0.547931631	0.150944471	3.63002122	0.000283398	0.003467955
TMTC2	3207.289437	-0.815954787	0.224836994	-3.629094887	0.000284417	0.003476609

ALG3	1464.750545	0.596499199	0.164368533	3.629035232	0.000284482	0.003476609
MGAT4B	4102.260064	0.438962658	0.120989471	3.62810626	0.000285508	0.003486827
DNAJC30	1283.813211	0.473874443	0.130640541	3.627315376	0.000286383	0.003492892
BCL9L	1985.585596	0.582803038	0.160666258	3.627414024	0.000286274	0.003492892
SLX4IP	512.971148	-0.377188391	0.104038384	-3.625473368	0.000288433	0.003508598
COMMD5	1386.970438	0.45273165	0.124875185	3.625473319	0.000288433	0.003508598
EFHD2	5562.007774	0.711705073	0.196302413	3.625554371	0.000288342	0.003508598
ESYT1	3536.001408	0.399015046	0.110046251	3.625884944	0.000287974	0.003508598
MNAT1	674.8924104	-0.298898398	0.08249184	-3.623369284	0.00029079	0.003534942
BTNL3	12.31202265	1.730307945	0.477961722	3.620180997	0.000294397	0.00357172
RNF113A	751.7027284	0.456585055	0.126119101	3.62026886	0.000294297	0.00357172
ZNF526	401.7624565	0.341131957	0.094226705	3.620332005	0.000294225	0.00357172
TTC14	1898.386107	-0.502640623	0.138877975	-3.619296899	0.000295405	0.003579412
IL3RA	208.560015	0.945832472	0.261331391	3.619283813	0.000295419	0.003579412
SERF2	26409.12372	0.652816861	0.180382974	3.619060302	0.000295675	0.003580151
LRIG3	533.7080559	-0.79938462	0.220954083	-3.617876664	0.00029703	0.003594198
RAN	9122.021688	0.392124124	0.108392837	3.617620282	0.000297324	0.003595398
TRPV2	748.1086398	0.768640363	0.212705795	3.6136315	0.000301938	0.003648798
GAB2	6886.854996	-0.703654846	0.1947827	-3.612512029	0.000303245	0.003662191
HIST1H2BG	42.8467591	1.087854087	0.301156515	3.612254872	0.000303546	0.003663425
PLEKHO2	3782.471656	0.596880544	0.165280759	3.611312942	0.000304651	0.003674352
FHL2	542.5604638	1.039732262	0.28792991	3.611060278	0.000304948	0.003675528
SEMA4C	4176.806624	-0.472226873	0.130803114	-3.610211239	0.000305948	0.003685171
TLCD2	293.7433217	0.581254959	0.161012527	3.609998358	0.000306199	0.003685787
SLC49A3	504.4815783	0.81908157	0.226905992	3.609783779	0.000306452	0.0036864
SEC61B	2912.376956	0.517692857	0.143452259	3.608816353	0.000307597	0.003692971
CD80	65.35348212	1.56622296	0.433990453	3.608888048	0.000307512	0.003692971
NOB1	1387.735979	0.451001277	0.12496584	3.608996478	0.000307384	0.003692971
POLR2D	1717.233823	0.376086598	0.104219595	3.608597786	0.000307856	0.003693676
SHBTC1	1884.171223	-0.692590325	0.19198901	-3.607447756	0.000309224	0.003704774
KRT1	16.83604205	1.774297785	0.491861354	3.607312853	0.000309385	0.003704774
PWWP2B	745.6042871	0.628396332	0.174185185	3.607633633	0.000309002	0.003704774
CXCL14	7744.234545	1.067252272	0.295880183	3.60704209	0.000309707	0.003706233
PSRC1	4659.424658	-0.595051939	0.164978282	-3.606850135	0.000309937	0.003706568
RTF1	2912.966362	0.338908892	0.093977606	3.606272882	0.000310626	0.00371241
C10orf95	10.94855767	1.224935593	0.339721729	3.605702814	0.000311309	0.003718158
EPM2A	1139.388754	-0.55539164	0.154100873	-3.60407848	0.000313262	0.003739063
RBAK-RBAKDN	46.40534739	0.766935295	0.212812933	3.603800225	0.000313598	0.003740647
ATPAF2	913.3397017	0.355725341	0.098724273	3.603220664	0.000314298	0.003746576
GKN1	3.659845199	2.549188888	0.707575005	3.602711899	0.000314915	0.003751493
SHISA3	76.51215984	1.279545385	0.3552008	3.602315098	0.000315396	0.003754798
ARSI	284.5964244	0.647340527	0.179711162	3.602116418	0.000315637	0.003755244
EVI2A	8112.494728	-1.029391753	0.285809106	-3.601675843	0.000316172	0.003759188
MRPL2	1635.722783	0.47968774	0.133211258	3.600954965	0.00031705	0.003767198
P4HA2	1043.520078	0.698125413	0.193885932	3.600701735	0.000317359	0.003768439
USP54	6690.590728	-0.699983778	0.194411661	-3.600523627	0.000317577	0.003768594
TUBB8	9.94166473	-1.311432904	0.364322473	-3.599648662	0.000318647	0.003776433
NOCT	185.8977737	0.703833305	0.195526645	3.599679753	0.000318609	0.003776433
C5	385.4692824	-0.600136326	0.166754918	-3.5989123	0.000319551	0.003784707
LILRA2	1274.618709	0.955347868	0.265470172	3.598701359	0.00031981	0.003785345
SRRM1	4207.762292	-0.453488572	0.126100958	-3.596234147	0.000322857	0.003818957
DEFA1B	9.440697305	3.322768187	0.92431163	3.594857057	0.00032457	0.003836751
CCDC43	1273.092581	0.233401773	0.064931468	3.59458643	0.000324907	0.00383828
ITK	129.9039473	-0.698625712	0.194366063	-3.594381151	0.000325164	0.003838846
NCK2	2381.701621	-0.500097928	0.139176713	-3.593258658	0.000326568	0.003845898
FAM136A	1123.815274	0.449182945	0.1250078	3.593236745	0.000326596	0.003845898
PLBD1	838.8259508	1.004164671	0.279456648	3.593275299	0.000326547	0.003845898
HIST1H4H	361.402072	0.730252716	0.203221811	3.593377651	0.000326419	0.003845898
HIST2H2AA4	734.8320941	1.384998085	0.385495865	3.592770276	0.000327181	0.003850331
ANXA2	18032.5126	0.961805407	0.267764512	3.591982374	0.000328172	0.003859529
ARHGAP21	17727.76927	-0.712242952	0.198377295	-3.590345122	0.00033024	0.003878938
INPP5B	1142.211345	-0.272401403	0.075870582	-3.590342876	0.000330243	0.003878938
NR2F6	1589.692966	0.552698269	0.154003048	3.588878777	0.000332103	0.003898299
PIGH	1122.292313	0.245426327	0.06839379	3.588430006	0.000332675	0.003902529
C1orf167	36.56692503	0.912418103	0.254287916	3.588130017	0.000333058	0.003904535
SIK3	5926.103966	-0.603599125	0.16827769	-3.586923043	0.000334603	0.003920152
RPLP2	24398.98003	0.755799755	0.210732253	3.586540479	0.000335094	0.003923411
C21orf58	294.4517836	-0.724006224	0.202039356	-3.583491043	0.000339032	0.003967002
SCLT1	339.4054032	-0.50930307	0.142178435	-3.582139971	0.000340791	0.003983336
UQCRFS1	4384.252302	0.470012694	0.131211981	3.58208671	0.000340861	0.003983336
CCDC22	1212.267813	0.360246616	0.100583586	3.581564657	0.000341543	0.003988776
GPR142	6.400111831	-2.395286068	0.66898294	-3.580489016	0.000342952	0.004002697
BLOC1S2	3494.98629	0.621658537	0.173683562	3.579259479	0.000344569	0.004019029
SLF2	2845.821117	-0.593319768	0.165813571	-3.578234063	0.000345924	0.004032275
SENP6	2958.161007	-0.35016363	0.097870726	-3.577817856	0.000346475	0.004033596
DNLZ	987.2605118	0.849462285	0.237419942	3.577889359	0.00034638	0.004033596
SOX18	727.0589223	0.822960743	0.230053119	3.577264002	0.000347209	0.004039598
RNF220	7562.818566	-0.408832396	0.114295045	-3.576991416	0.000347572	0.004041266
ZDHHC16	1064.155013	0.345232769	0.096527638	3.57651739	0.000348202	0.004046039
ZNF738	431.4082832	-0.593579454	0.166073241	-3.574202866	0.000351296	0.004079002
TIMM50	3154.29074	0.398413646	0.111473532	3.574064962	0.000351482	0.004079002
TPCN1	4710.270104	-0.455693653	0.12750953	-3.573805696	0.00035183	0.004080476
ZNF83	3074.349407	-0.491434728	0.137530559	-3.573276592	0.000352542	0.004086162
PRPF31	3007.078175	0.488045954	0.136590667	3.573054919	0.000352841	0.004087053
AC093323.1	1276.922336	0.380761612	0.106587451	3.572293071	0.000353869	0.00409639
C14orf119	2189.558756	0.519251267	0.14540698	3.571020223	0.000355593	0.004111187
HTRA2	1612.497979	0.36702743	0.102775298	3.571163876	0.000355398	0.004111187
ANKRD44	933.45234	-0.631940169	0.177052373	-3.569227332	0.000358036	0.004136827
PUS1	971.5057605	0.511881795	0.143438055	3.56866103	0.00035881	0.00414318
HID1	4383.244949	-0.67071236	0.187967141	-3.56824259	0.000359384	0.004147202
SLC15A3	3730.430595	0.971944292	0.272414849	3.567882946	0.000359877	0.004150298
LMLN2	30.44426232	-1.361479305	0.381621389	-3.567617922	0.000360241	0.004151585
NMNAT1	543.3072788	0.294733093	0.082616755	3.567473605	0.00036044	0.004151585
SHPXD2A	6358.708646	-0.770290614	0.215995251	-3.566238659	0.000362142	0.004168587
PPP1R14B	2574.646441	0.691576201	0.193938055	3.565964411	0.000362521	0.004170344
SDF4	8642.616223	0.440014892	0.123426172	3.565004757	0.00036385	0.004183022
LSM7	2803.019276	0.666728339	0.187076952	3.563925612	0.00036535	0.004197647
MTSS1	3367.923082	-0.609738335	0.17110784	-3.563473976	0.000365979	0.00420226
CCDC180	654.1223422	-0.660356639	0.185355822	-3.562643095	0.00036714	0.004212962
IRF1	2078.303661	0.941333082	0.264246654	3.562327346	0.000367582	0.004215409
DAXX	2550.138336	0.44510276	0.124980964	3.561364427	0.000368933	0.00422827
KSR1	2182.888443	-0.403678862	0.113372932	-3.560628224	0.000369969	0.004237509
CDK7	645.4292791	0.316157898	0.08880904	3.559939657	0.00037094	0.004245996
ASTE1	442.3788019	-0.227043042	0.063783499	-3.559589025	0.000371436	0.00424903
C19orf53	4694.146752	0.552695776	0.155329064	3.558225125	0.000373369	0.0042685
TADA2B	1210.539961	0.2318312	0.065160986	3.557822175	0.000373942	0.004272401
COL4A5	4694.500414	-1.020278676	0.286823235	-3.557168846	0.000374873	0.004277733
PSMA4	4281.550125	0.468812058	0.13178908	3.557290504	0.0003747	0.004277733
RPL13	48959.00533	0.616788197	0.173490831	3.55516308	0.000377745	0.004302508
JPT1	3682.313751	0.651030228	0.183121266	3.555186348	0.000377711	0.004302508
NOC2L	4137.974922	0.542316924	0.152541686	3.555204725	0.000377685	0.004302508
MAT2A	18511.70269	-0.332356542	0.093491886	-3.554923927	0.000378088	0.004303763
SORCS2	1963.60492	-0.742024647	0.2087541	-3.554539269	0.000378642	0.004304801
RNF185	3049.936425	0.225357756	0.063400051	3.554535862	0.000378647	0.004304801
PTBP2	1679.308639	-0.575545984	0.161936621	-3.554143481	0.000379212	0.004308571
KIF1C	28429.85172	-0.727907543	0.204869193	-3.553035632	0.000380813	0.004324092

SRRD	1132.858782	0.230201114	0.064804498	3.552239879	0.000381966	0.00433452
ADGRG6	134.2172726	-0.813726736	0.229138453	-3.551244785	0.000383414	0.00434559
FKBP2	5238.562972	0.770521783	0.216968959	3.551299623	0.000383334	0.00434559
DCUN1D3	724.1051505	0.488720896	0.13768703	3.549505684	0.000385955	0.00437107
COPRS	3770.374629	0.434540258	0.122432764	3.549215456	0.000386381	0.00437384
GOLGA8N	1328.872529	-0.69047656	0.194555829	-3.548989332	0.000386713	0.00437491
SPATA6	1036.717946	-0.641169925	0.180726548	-3.547735142	0.000388559	0.00439309
CLEC10A	163.3526061	1.795292868	0.506210983	3.546530851	0.000390339	0.00440781
STAT5A	1851.603404	0.60033569	0.169272609	3.546561325	0.000390294	0.00440781
STAT6	2955.912935	0.548185628	0.154581975	3.546245471	0.000390762	0.00440989
UQCRC1	8298.373906	0.469398989	0.132397095	3.545387361	0.000392037	0.00441886
DNAJC5B	70.89824691	1.234319904	0.348134922	3.545521653	0.000391837	0.00441886
SHC4	745.6414083	-0.653890955	0.18444765	-3.54513117	0.000392418	0.00442045
FAM89B	2121.619336	0.510944323	0.144175797	3.543898021	0.000394258	0.0044384
MAP4	38215.00983	-0.561612445	0.158496243	-3.543380161	0.000395033	0.00444448
OTOS	1127.536771	1.291952524	0.36468453	3.542657877	0.000396116	0.00445395
CIAPIN1	1721.289306	0.418673623	0.118241654	3.540830218	0.00039887	0.00447945
RPL26L1	962.0532891	0.458924085	0.129605096	3.540941684	0.000398702	0.00447945
AUP1	7661.244799	0.469936817	0.132754198	3.539901707	0.000400276	0.00449250
TACR3	32.5571196	-1.381021967	0.390184435	-3.539408145	0.000401025	0.00449286
HSD3B7	1098.494328	0.712107545	0.201194504	3.539398597	0.00040104	0.00449286
C16orf95	190.5720851	0.515024542	0.145510995	3.539420114	0.000401007	0.00449286
ANKRD22	209.7143171	-1.14666181	0.324243027	-3.536427045	0.000405579	0.00453822
FEM1A	2515.670222	0.28660649	0.081044128	3.5364251	0.000405581	0.00453822
RACK1	28936.11293	0.54316602	0.153612752	3.535943554	0.000406322	0.00454374
PRR18	5705.500689	-1.155228505	0.326786715	-3.535114658	0.000407598	0.00455526
OSTM1	1787.329204	0.516502045	0.146124315	3.534675552	0.000408276	0.00456007
FFAR1	116.9251424	-1.176138253	0.33276881	-3.534400516	0.000408701	0.00456011
NUMA1	12891.35158	-0.306412194	0.086709381	-3.533783644	0.000409656	0.00456011
SPTY2D1	662.6143651	0.443141039	0.125403771	3.53371382	0.000409764	0.00456011
PDCD5	2972.681512	0.480770379	0.136040252	3.534030339	0.000409274	0.00456011
C19orf48	1867.572234	0.743688068	0.210436025	3.534033999	0.000409268	0.00456011
C12orf57	5521.930781	0.626978398	0.177408317	3.534098106	0.000409169	0.00456011
HSPA8	45352.66481	0.314358298	0.088971764	3.533236618	0.000410505	0.00456559
PLK2	1637.564149	1.051437326	0.297606098	3.53298314	0.000410899	0.00456722
KLRG2	9.324663939	1.816946966	0.514429945	3.531961898	0.000412489	0.00458213
PIDD1	3748.43581	0.737852787	0.208959956	3.531072658	0.000413878	0.00458926
GPATCH4	1846.050232	0.517554615	0.146568543	3.531143892	0.000413767	0.00458926
PARS2	298.3697744	0.375579618	0.106358779	3.531251679	0.000413598	0.00458926
TSEN34	1806.568773	0.447966139	0.126870635	3.530889054	0.000414165	0.00458969
TMEM222	4121.643507	0.476764467	0.13505222	3.530223093	0.000415209	0.00459849
FAM95C	829.998563	-1.120964251	0.31757937	-3.529713698	0.00041601	0.00460182
NAT14	2182.663383	0.601125	0.170302104	3.529756747	0.000415942	0.00460182
PHF21A	2114.859187	-0.298950004	0.084710958	-3.529059408	0.000417039	0.00461045
RPE65	380.4058103	-1.299843424	0.368359661	-3.528734446	0.000417552	0.00461058
RPL7	29047.62048	0.445446335	0.126230044	3.528845605	0.000417377	0.00461058
DENND2D	871.2376256	0.931178866	0.263940041	3.527993947	0.000418722	0.00461520
SIGLEC12	33.49371219	1.775447939	0.50323713	3.528054339	0.000418626	0.00461520
CD300C	292.7424853	0.928654867	0.263217937	3.528083521	0.00041858	0.00461520
PER2	867.9644941	-0.43332172	0.122834146	-3.527697588	0.000419191	0.00461761
PLPP6	544.3117252	0.329451479	0.093418645	3.526613741	0.00042091	0.00463378
GPRC5D	2.502498103	-1.638668254	0.464798893	-3.525542504	0.000422616	0.00464978
TTLL11	685.2085609	-0.712663273	0.202197114	-3.524596661	0.000424128	0.00466319
ACY1	1294.786579	0.508867582	0.144381566	3.524463663	0.000424341	0.00466319
FRYL	4962.492699	-0.762932941	0.216510761	-3.523764531	0.000425462	0.00466716
RNF187	9951.118297	0.479489888	0.136071653	3.523804365	0.000425398	0.00466716
COMMD4	3915.678008	0.622058143	0.176522246	3.523964576	0.000425141	0.00466716
SLC25A20	1165.933924	0.326965934	0.092799715	3.523350637	0.000426127	0.00467168
ATP6V0D2	83.55775825	1.432419844	0.406621083	3.522738745	0.000427112	0.00467969
PAPOLG	793.1221478	-0.510443907	0.144914655	-3.522376042	0.000427697	0.00468332
DAAM2	18516.96894	-0.978577685	0.27786053	-3.521830484	0.000428578	0.00468927
VPREB3	30.08322833	1.311201298	0.372317988	3.521724282	0.00042875	0.00468927
IL17RE	198.9392097	0.735248099	0.208903797	3.51955355	0.000432274	0.00472501
MRPL11	1368.79348	0.508875061	0.144614527	3.518837771	0.000433442	0.00473497
TRH	69.39346537	1.478919065	0.4203495	3.518308138	0.000434308	0.00474162
SPATA13	4318.501461	-0.680839799	0.193531509	-3.517979066	0.000434847	0.00474469
DUSP13	8.230228117	1.549602824	0.440524658	3.51763016	0.000435419	0.00474812
TSGA10	265.6504788	-0.539468225	0.153376749	-3.517275138	0.000436002	0.00474886
BAG5	2263.441173	0.192660639	0.054775329	3.517288583	0.00043598	0.00474886
ABCA8	3181.334092	-0.928091959	0.263927886	-3.516460395	0.000437342	0.00475871
TESK2	793.8561912	-0.777241191	0.221040929	-3.516277257	0.000437644	0.00475871
RAB3D	838.664551	0.354427614	0.100796918	3.516254483	0.000437681	0.00475871
PREX1	15999.14599	-0.561264412	0.159641006	-3.515791	0.000438446	0.00476422
LLGL2	599.2676676	-0.521968178	0.148503153	-3.514862584	0.000439982	0.00477527
SYF2	1964.92306	0.370683543	0.10545897	3.514955091	0.000439828	0.00477527
NUCB1	12423.54068	0.525890495	0.149654942	3.51402023	0.000441379	0.00478762
RBM39	7351.420654	-0.273618766	0.077894039	-3.512704836	0.00044357	0.00480855
SMURF1	1716.223225	-0.255316874	0.072726741	-3.510632697	0.000447042	0.00484334
ADGB	30.95936633	-0.929082037	0.26466739	-3.51037593	0.000447474	0.00484517
BUD23	3263.235884	0.437523736	0.124728835	3.507799439	0.00045183	0.00488947
HDAC3	2230.006663	0.348925028	0.099487489	3.5072252	0.000452806	0.00489428
DCTPP1	1163.376939	0.464454438	0.132424166	3.507323871	0.000452638	0.00489428
ELOVL3	15.81856901	1.528497782	0.435962815	3.506027871	0.000454848	0.00491059
QPCTL	428.158457	0.478327136	0.136428418	3.506066721	0.000454781	0.00491059
CDCP1	540.2140767	0.853508198	0.243482584	3.505417859	0.000455891	0.00491898
REXO4	1561.860361	0.43466719	0.124004789	3.505245185	0.000456187	0.00491929
APIP	1160.847084	-0.407252272	0.116193362	-3.50495298	0.000456688	0.00492181
SEMA6A	5697.138184	-0.652779075	0.186261838	-3.504631396	0.00045724	0.00492488
MAPKAPK3	2468.881097	0.495194485	0.141312445	3.504252474	0.000457891	0.00492901
RIC8A	4683.400047	0.328669128	0.093796229	3.504076143	0.000458194	0.00492940
RETSAT	4405.765756	0.566319171	0.161652421	3.503313874	0.000459508	0.00493488
CDA	136.2950266	0.836856125	0.23886823	3.50342163	0.000459322	0.00493488
HIST1H3D	7.324050728	2.087987901	0.595971995	3.503500026	0.000459187	0.00493488
TMEM260	890.6603461	-0.326101217	0.093088223	-3.503141507	0.000459805	0.00493520
DDX28	678.1995881	0.361610711	0.103237391	3.50271068	0.000460549	0.00494031
MRPS30	1274.229207	0.269386386	0.07691333	3.502466816	0.000460971	0.00494196
FABP5	5725.078096	0.703315104	0.20082427	3.502141963	0.000461534	0.00494511
LRRC66	83.06447661	-0.900793678	0.257254791	-3.501562307	0.000462539	0.00495300
RPL18	24765.68754	0.583481159	0.166674009	3.500732727	0.000463981	0.00496268
INO80C	689.3415044	0.420222633	0.120036749	3.500783178	0.000463893	0.00496268
EEF1AKMT1	463.3788145	0.432709516	0.123675739	3.4987421	0.000467458	0.00499697
CTNNA3	1934.860789	-1.498761765	0.428447427	-3.498122921	0.000468545	0.00500569
PSMD6	2772.185286	0.209026657	0.059763708	3.497551664	0.00046955	0.00501351
ARHGAP15	295.8606561	-0.794868869	0.227302336	-3.496967437	0.000470579	0.00502160
IFI44L	4055.135291	-0.885352788	0.253246444	-3.496012702	0.000472266	0.00503668
ZSCAN22	253.3531896	0.304772125	0.087222197	3.494203732	0.000475478	0.00506800
DHX35	594.2309762	-0.292762638	0.083808171	-3.493246954	0.000477185	0.00508032
SF3A3	3388.915892	0.374726403	0.107270475	3.493285573	0.000477116	0.00508032
UFSP1	103.071284	0.646693158	0.185160683	3.492605166	0.000478333	0.00508960
LCMT2	1809.326441	0.647731166	0.185535015	3.491153234	0.00048094	0.00511439
LSR	954.1800851	0.891949834	0.255504984	3.490929297	0.000481344	0.00511573
GTDC1	2131.744574	-0.630939361	0.180757671	-3.490526053	0.000482071	0.00512050
YBX3	4252.440418	0.752710835	0.215663099	3.490216161	0.00048263	0.00512349
ABCF2	2966.114949	0.371149368	0.106369902	3.489232954	0.000484409	0.00513646
IL20	5.44938544	3.215028814	0.921403623	3.489273034	0.000484336	0.00513646
MEMO1	942.4308783	-0.271209117	0.077731442	-3.48905295	0.000484735	0.00513696

ITGA3	3808.395936	0.945804372	0.27109928	3.48877493	0.00048524	0.005139356
SSR2	6183.509691	0.489486827	0.140352832	3.487545061	0.000487477	0.005160086
TOMM34	1727.257428	0.69797273	0.200146375	3.487311371	0.000487903	0.005161632
EMC9	756.5979144	0.539835768	0.154835619	3.486508935	0.000489369	0.005174172
TRIM27	2306.141817	0.268139314	0.076935292	3.485257626	0.000491663	0.00519545
YEATS4	744.8552476	-0.738276188	0.211857927	-3.484770185	0.00049256	0.005201941
ZDHHC12	1188.582417	0.656820711	0.188509916	3.484276721	0.000493469	0.005208557
HLA-DOB	84.65066256	-0.891756324	0.255966028	-3.483885469	0.000494191	0.005213191
TIMM8A	292.8052879	0.622495692	0.178692456	3.483614835	0.000494691	0.005215479
GRIN A	16414.36557	0.454648371	0.130560685	3.482276248	0.000497171	0.005232642
CAVIN 3	588.411681	0.847809152	0.243463958	3.482277854	0.000497168	0.005232642
FAM50A	6284.256279	0.723151347	0.20765134	3.482526755	0.000496706	0.005232642
ARHGEF35	38.44509888	1.621890929	0.465979124	3.480608566	0.000500276	0.005262321
ATP5F1D	7481.666727	0.781937754	0.224688447	3.480097726	0.000501231	0.005269358
COLQ	382.3467204	-0.525574661	0.151031903	-3.479891681	0.000501617	0.005270408
CREBZF	2716.797307	-0.509895583	0.146549299	-3.479345084	0.000502641	0.005276251
AL031777.3	20.55334183	1.437566682	0.413178252	3.479289323	0.000502745	0.005276251
ZNF333	969.2556438	-0.383839531	0.110338812	-3.478735404	0.000503786	0.005280945
PAQR6	31405.28844	-0.992161363	0.285231598	-3.47844126	0.000504339	0.005280945
SYCE3	80.27981304	1.207731989	0.347204201	3.47844866	0.000504325	0.005280945
TRMT10C	716.1582316	0.378290804	0.108738717	3.47889708	0.000503482	0.005280945
SIK1B	1156.451094	1.006136388	0.289320022	3.477589907	0.000505943	0.005294736
USP40	2581.489352	-0.343819872	0.098877115	-3.477244176	0.000506596	0.00529856
RARA	1842.495689	0.66457767	0.191162458	3.476507241	0.000507991	0.005310129
SLC35F2	530.2313881	0.600004995	0.172603271	3.476208719	0.000508556	0.00531303
ASPA	4475.639301	-0.873701641	0.251383687	-3.475570157	0.000509769	0.005322678
CORO2B	7045.466356	-0.504532753	0.145192714	-3.474917851	0.00051101	0.005326177
PHACTR3	3483.298788	-0.725194157	0.208710886	-3.47463503	0.000511549	0.005326177
HSD17B10	3598.52671	0.575155605	0.165523941	3.474757805	0.000511315	0.005326177
EBP	1023.220957	0.540032664	0.155414555	3.474788215	0.000511257	0.005326177
ING2	629.8895286	0.460169642	0.132414424	3.475222928	0.000510429	0.005326177
ZNF697	242.7410916	0.890282444	0.256234743	3.474479818	0.000511845	0.00532625
GCH1	256.7690422	0.877224591	0.252497865	3.474186176	0.000512405	0.005329074
DGCR6L	3320.553523	0.503610163	0.145088394	3.471057542	0.000518413	0.005385474
LINC01556	6.646071821	1.455190018	0.41922833	3.47111565	0.000518301	0.005385474
CYBA	9960.838628	1.000171248	0.288198839	3.47042081	0.000519644	0.005395217
IKZF4	786.0507544	-0.462058621	0.13318455	-3.469310969	0.000521795	0.00541293
ATP6V1G1	4124.589493	0.524435015	0.151167208	3.469237958	0.000521937	0.00541293
P2RY12	864.5026935	-1.319753585	0.380493571	-3.468530572	0.000523313	0.005424148
CSNK2B	6829.947386	0.505866574	0.145876363	3.467776152	0.000524784	0.00543634
ZNF546	282.2596453	-0.474811582	0.136936141	-3.467394195	0.000525531	0.005441013
ZP3	194.9400527	0.914014535	0.263618399	3.467187946	0.000525934	0.005442132
HAPLN3	307.2974497	0.811814098	0.23416745	3.466810172	0.000526674	0.005446728
DNM2	9185.712619	-0.382114167	0.110233206	-3.466416163	0.000527446	0.005451658
CPLANE2	172.0112278	0.499541443	0.144120212	3.466144238	0.00052798	0.005454116
SLC16A5	168.9371292	0.848135495	0.244718903	3.465753916	0.000528747	0.005458979
FNBP1	6922.513644	-0.564178219	0.162889724	-3.463559306	0.000533079	0.00549909
ETF1	4298.160272	0.270942184	0.078228225	3.463483737	0.000533229	0.00549909
TPD52L2	7180.117377	0.322793226	0.093210613	3.463052291	0.000534085	0.005504835
ENTPD6	4839.845411	0.381893117	0.110384816	3.459652615	0.000540873	0.005571684
PSMD9	2322.923271	0.4362735	0.126157494	3.458165548	0.000543867	0.0055994
DDX60	743.5741224	-0.614206001	0.177620269	-3.457972478	0.000544257	0.005600235
WWC1	2863.169669	-0.478923171	0.138504186	-3.45782452	0.000544556	0.005600235
GAST	11.02884014	1.612869321	0.466486111	3.457486266	0.00054524	0.005604143
GGT1	1497.861601	0.801435426	0.231850292	3.456693618	0.000546846	0.005617519
KRCC1	1219.952637	-0.442842101	0.128155658	-3.45550176	0.00054927	0.00563927
NRBF2	893.1360771	0.455110793	0.131723755	3.455039619	0.000550212	0.005642658
C6orf132	31.44689216	0.852333382	0.246690169	3.455076408	0.000550137	0.005642658
TEPP	35.68153135	0.959088244	0.277698509	3.453703256	0.000552945	0.005667537
MVB12B	8196.644598	-0.686880994	0.198927668	-3.452918332	0.000554557	0.005668731
SMPDL3B	29.85116124	1.279899295	0.370674004	3.452897375	0.0005546	0.005668731
CXCR5	11.69291588	1.941804593	0.562345441	3.453045855	0.000554295	0.005668731
TMEM263	1427.070554	0.402927994	0.116678773	3.45331017	0.000553752	0.005668731
ISCU	6551.978435	0.507258159	0.146886133	3.453410812	0.000553545	0.005668731
HDAC9	750.8568276	-0.56556122	0.163860906	-3.451471332	0.000557539	0.005689308
UBTD1	1356.738552	0.462023757	0.133861862	3.451496565	0.000557487	0.005689308
S100A13	6732.740125	0.743521997	0.215412929	3.451612679	0.000557247	0.005689308
GABPB2	938.990684	-0.395972756	0.11473471	-3.451202839	0.000558094	0.005691817
KTI12	458.2032295	0.453393278	0.131407391	3.450287494	0.00055999	0.005707994
STK31	74.15268905	-0.905801164	0.262567934	-3.449778305	0.000561047	0.005712533
AGPAT4	5315.99369	-0.66135589	0.191709894	-3.449774422	0.000561055	0.005712533
STAG3	385.0913136	-0.464657222	0.134705321	-3.44943481	0.000561761	0.005714868
DDA1	3441.81861	0.35970334	0.104281002	3.449365964	0.000561905	0.005714868
USP6	323.9639364	-0.586593519	0.170076439	-3.448999298	0.000562668	0.005719477
TMEM53	656.2434509	0.459495193	0.133249568	3.44838036	0.000563959	0.00572944
SLC25A39	6336.426897	0.487544221	0.141400013	3.447978624	0.000564799	0.005734808
HNRNPA2B1	23417.82647	-0.31539293	0.091476968	-3.447785132	0.000565203	0.005735757
RCOR3	1849.33662	-0.350007829	0.101525931	-3.447472244	0.000565859	0.005736542
TP53I13	2525.254501	0.597862507	0.173421619	3.447450851	0.000565903	0.005736542
FAN1	1786.272027	-0.39480153	0.114535011	-3.446994299	0.000566861	0.005743086
FCHSD2	2265.750712	-0.536551268	0.155692494	-3.446224381	0.000568478	0.00575631
SOAT1	2182.069544	0.671305699	0.194829484	3.44560631	0.00056978	0.005756838
MRPL4	3063.058331	0.522133128	0.15153325	3.445667048	0.000569652	0.005756838
MRPS7	2323.325033	0.337061101	0.097818497	3.445780825	0.000569412	0.005756838
PUM3	704.0321684	0.510742945	0.148212841	3.44601008	0.000568929	0.005756838
CD22	2894.927987	-0.869991972	0.252537975	-3.444994645	0.000571071	0.005766719
F8A1	2583.420365	0.58733627	0.170517894	3.44442602	0.000572273	0.005775697
RBM8A	5622.280086	0.319733527	0.092830994	3.444254049	0.000572637	0.005776209
YIPF2	1808.112459	0.430281067	0.124971818	3.443024779	0.000575247	0.005799354
PPP1R12B	2883.727014	-0.607262404	0.176405548	-3.442422337	0.000576529	0.005805934
STOML2	3006.548432	0.360304058	0.104662445	3.442534304	0.000576291	0.005805934
UCN	371.3883624	0.686037034	0.199315699	3.441961853	0.000577512	0.00581265
ATP10B	1596.040566	-0.894450577	0.25993105	-3.441107084	0.000579339	0.005827861
MARVELD1	1328.051488	0.871577607	0.25332604	3.440536971	0.000580561	0.005836967
AC012651.1	299.6441842	-0.934671794	0.271707389	-3.439994025	0.000581727	0.0058455
ATP6AP2	7438.256825	0.335472474	0.097531915	3.439617434	0.000582537	0.005850449
NTM	3790.951585	-0.894664416	0.260227343	-3.4380108	0.000586004	0.005882066
SEMA4D	11660.48705	-0.859358883	0.250025236	-3.437088577	0.000588003	0.005898602
ANO4	726.7198026	-0.799995883	0.232762931	-3.436955696	0.000588292	0.005898602
ITPKC	2150.405257	0.690470355	0.200930561	3.436363044	0.00058958	0.005908307
GNL2	1917.445894	0.444785798	0.129476376	3.435266036	0.000591972	0.005929054
NOP56	5916.812831	0.468827068	0.136528849	3.433904779	0.000594953	0.005955672
LSS	7324.049689	-0.447528485	0.13033869	-3.433581273	0.000595664	0.005959546
ADCK5	567.2406385	0.53592846	0.156196794	3.431110496	0.000601116	0.006010831
MAP4K4	27748.4543	-0.644873384	0.18798114	-3.430521717	0.000602422	0.006020624
NACC1	5980.255732	0.302113334	0.088071042	3.430336771	0.000602833	0.006021464
HS3ST2	808.9626989	1.220993265	0.356014925	3.429612582	0.000604444	0.006034286
WSB1	11701.93597	-0.542084132	0.158110609	-3.428512074	0.0006069	0.006052247
B3GNT2	655.5318817	0.627057596	0.182893984	3.428530458	0.000606858	0.006052247
LENG8	18420.29521	-0.392017304	0.114351081	-3.428190613	0.000607619	0.006056141
HAAO	448.5057524	0.935089015	0.272825642	3.427423491	0.000609338	0.006063439
LRTM1	111.0461498	0.876786685	0.255811139	3.427476566	0.000609219	0.006063439
IL7R	508.6229092	1.450681305	0.423233782	3.427612272	0.000608914	0.006063439
CLDND2	129.5681181	0.786308481	0.229435154	3.427149099	0.000609954	0.006066294
MAD2L2	2649.861304	0.611195741	0.178372974	3.426504174	0.000611404	0.006077439
MRPS23	2273.861927	0.320097414	0.093438767	3.425745273	0.000613115	0.006091158

NARF	2712.824343	0.403164145	0.117694149	3.425524112	0.000613614	0.006092835
CDC34	3873.894684	0.510815914	0.149154926	3.424733782	0.000615402	0.006107294
ABCF1	3553.900079	0.355834328	0.103913605	3.424328572	0.000616321	0.006109829
EIF1	34594.24351	0.351281581	0.102580707	3.424441033	0.000616066	0.006109829
RABGGTA	1569.510756	0.46220272	0.135014429	3.423357953	0.000618526	0.006128392
YKT6	7807.191647	0.40035306	0.116958104	3.423046772	0.000619234	0.006132116
PSMB10	3345.59749	0.72305598	0.211262556	3.422546779	0.000620374	0.00613681
MFSD3	1184.067475	0.566798846	0.165605459	3.422585515	0.000620286	0.00613681
NOL6	2572.773837	0.479796592	0.140207987	3.422034666	0.000621544	0.006141787
ARAF	2862.573861	0.441700406	0.129072548	3.422109597	0.000621373	0.006141787
CC2D2B	51.66942333	-0.858653131	0.250935257	-3.421811424	0.000622054	0.006143231
NOL7	2514.064833	0.239544788	0.070007959	3.421679317	0.000622357	0.006143231
DDRGK1	5648.701332	0.55025084	0.160836535	3.421180632	0.000623499	0.006151212
MACC1	101.90438	0.843106162	0.246488499	3.420468562	0.000625134	0.006164038
DAAM1	1515.577802	-0.482938333	0.141253213	-3.418954682	0.000628622	0.00619512
SLC22A15	1252.141973	-0.721239965	0.210978921	-3.418540408	0.00062958	0.006201242
PFKFB2	2617.423595	-0.50553863	0.147896082	-3.418201647	0.000630364	0.006202341
TRPC1	757.7952873	-0.515688854	0.150865554	-3.418201439	0.000630364	0.006202341
MYCN	244.8363937	-0.889800854	0.260347177	-3.41774728	0.000631417	0.006209384
C1orf216	2976.758585	0.477633441	0.139823218	3.415980884	0.000635527	0.006246469
NSL1	1743.770333	-0.409915333	0.120019327	-3.415411018	0.000636858	0.006256217
LRCH1	570.5676511	-0.512654897	0.150129793	-3.414744583	0.000638418	0.00625963
PRKD1	528.5824256	-0.647378344	0.189583892	-3.41473285	0.000638446	0.00625963
CLEC17A	34.86512667	-1.221382677	0.357685598	-3.414682286	0.000638564	0.00625963
SNRPB	4241.0719	0.610122277	0.178657284	3.41504283	0.00063772	0.00625963
SIGLEC7	550.7179709	1.032308566	0.302440656	3.413259909	0.000641907	0.00628905
BTN3A3	1467.258168	-0.434589038	0.12739035	-3.411475353	0.000646123	0.006323759
BLCAP	5322.42871	0.423399545	0.124110584	3.411470101	0.000646136	0.006323759
ZNF79	307.2046415	0.476084124	0.13959116	3.410560689	0.000648295	0.006341518
USP50	6.144826858	-1.408839639	0.413213725	-3.409469609	0.000650893	0.006363561
CDC42EP5	159.6930833	0.928846963	0.272474935	3.408926264	0.000652191	0.006372868
LAMTOR4	7422.308346	0.785773575	0.230562988	3.408064684	0.000654254	0.006389636
PNLIP	3.322693848	-3.809549431	1.117857582	-3.407902305	0.000654643	0.006390054
AGAP5	316.4779263	-0.47533446	0.139488893	-3.407686794	0.00065516	0.006391717
SNRPE	1683.585337	0.478241958	0.140450738	3.40505122	0.000661516	0.00645031
CLEC9A	44.0790602	-1.389573226	0.408171163	-3.404388536	0.000663124	0.006459311
SLC39A3	2524.569879	0.5847345	0.171759391	3.404381547	0.000663141	0.006459311
MRPL44	1313.168447	0.377785696	0.110993148	3.40368484	0.000664834	0.00646897
NUAK2	366.6527725	0.637927249	0.18741959	3.403738365	0.000664704	0.00646897
ZNF579	1583.351288	0.55103821	0.161911382	3.403332134	0.000665693	0.006473909
PINLYP	376.5564476	0.474574899	0.139454473	3.403081216	0.000666305	0.00647644
MEFV	82.9365512	0.993707055	0.2920215	3.402855796	0.000666855	0.006478368
CSMD2	724.3515576	-0.879405374	0.258472646	-3.402315052	0.000668176	0.006487781
TMED9	5703.072838	0.505274807	0.148541949	3.401563058	0.000670017	0.006502231
TUBB6	2920.450292	0.895163717	0.26319752	3.401109995	0.000671128	0.006506166
SPSB2	579.4353463	0.582193764	0.17117363	3.401188396	0.000670936	0.006506166
GP2	5.318112153	-1.147042288	0.337299972	-3.400659303	0.000672236	0.006513479
AZIN2	1647.078902	-0.615020841	0.180885331	-3.400059249	0.000673713	0.006524355
EFEMP2	3640.789222	0.529775423	0.15583311	3.399633248	0.000674763	0.006531096
BOP1	2429.690365	0.653343234	0.192194508	3.399385559	0.000675374	0.006533582
HIGD2A	3457.62074	0.460960982	0.135608798	3.39919671	0.000675841	0.006534665
TBL3	2247.017272	0.504598688	0.148467759	3.398708855	0.000677047	0.006542899
EVL	7303.889664	-0.399471318	0.117542591	-3.398524014	0.000677505	0.006543554
GTF2E2	749.2859152	0.307406125	0.090456274	3.398394735	0.000677825	0.006543554
FAM221A	725.5870334	-0.540334853	0.159019741	-3.397910546	0.000679026	0.006541618
NXF5	14.93544612	-1.452760903	0.427568659	-3.397725428	0.000679486	0.006541618
TARBP2	1276.852164	0.41269948	0.121463895	3.397713195	0.000679516	0.006541618
CD7	191.242937	1.131771368	0.333069998	3.397998546	0.000678808	0.006541618
ELMOD3	1152.184219	-0.238581892	0.070257061	-3.395842185	0.000684178	0.006587626
CHST7	809.0366998	0.532540945	0.156856802	3.395077152	0.000686093	0.006602612
C2D2DLF	583.470398	1.072810808	0.316097726	3.393921307	0.000688995	0.006627081
CHCHD6	1378.368309	0.614609791	0.181104374	3.393677234	0.000689609	0.006629529
STX16	5816.443946	-0.420900094	0.124043435	-3.393167037	0.000690895	0.006638427
HERC2	4566.224516	-0.450933608	0.132901839	-3.392982442	0.000691361	0.00663944
CEP162	410.9218704	-0.485880446	0.1432471	-3.391904245	0.000694087	0.006662151
DENND5A	10227.81841	-0.477315658	0.140731798	-3.391668858	0.000694683	0.006664404
C18orf21	737.2651201	0.419790033	0.123791486	3.391105853	0.000696112	0.006674636
TMEM185A	1059.634631	0.240041625	0.070795419	3.390637831	0.000697302	0.006682566
NCKAP5L	2164.712335	-0.2526992	0.074536602	-3.390269941	0.000698238	0.006686243
MYL5	1458.832564	0.641513883	0.189225852	3.390202115	0.000698411	0.006686243
DAOA	1.017396953	-1.515186863	0.446970624	-3.389902562	0.000699175	0.006688817
FRMD5	2033.05516	-0.677482915	0.199858556	-3.389811924	0.000699406	0.006688817
MRPL9	2118.292727	0.364637641	0.107610605	3.38849169	0.000702782	0.006717615
ABT1	1041.758771	0.433170952	0.127850646	3.388101386	0.000703782	0.006723694
ZXDC	1371.300131	-0.295409588	0.087245266	-3.385966969	0.000709279	0.006770305
WIPI2	5247.527483	0.257335083	0.076007862	3.38563769	0.000710131	0.006770305
CCDC32	1134.647538	0.349403381	0.1031975	3.385773696	0.000709779	0.006770305
TAF12	890.5054031	0.371670659	0.109771634	3.385853403	0.000709573	0.006770305
PNPO	2858.503056	0.428773866	0.126697813	3.384224674	0.000713796	0.006801727
AK9	435.4849208	-0.576220587	0.170296097	-3.383639426	0.000715319	0.006809669
TMEM60	712.754667	0.398412361	0.117747355	3.38362047	0.000715368	0.006809669
CPA4	186.7122348	1.318366971	0.389796097	3.382196436	0.000719087	0.006841538
EPS8L2	1968.938757	0.756349254	0.223653752	3.381786566	0.000720161	0.006844684
TUSC1	1179.474413	0.395381951	0.116910892	3.3819086	0.000719841	0.006844684
BCAS1	37561.41635	-0.892990709	0.264095337	-3.381319492	0.000721386	0.006849266
DIRAS3	504.6230786	0.824517408	0.243843669	3.381336133	0.000721342	0.006849266
MED14	1774.03917	-0.424069567	0.12543258	-3.380856604	0.000722602	0.006857281
PPRC1	1369.788102	0.361740542	0.107006159	3.380558145	0.000723388	0.0068612
ARRDC2	8304.893679	-0.637164897	0.188510106	-3.380003916	0.000724848	0.006868625
DUSP15	1468.070016	0.737474349	0.218189089	3.379978134	0.000724916	0.006868625
SNX29	1951.457807	-0.610419589	0.180612782	-3.379714221	0.000725612	0.006871691
GCC1	1052.919372	0.306881388	0.090809138	3.379410855	0.000726414	0.006875745
TARBP1	2221.161295	-0.559216756	0.165509612	-3.378756972	0.000728143	0.006888581
ZFPM1	1172.543424	0.645229459	0.191010482	3.377979333	0.000730206	0.006904546
NID2	506.2505958	-0.979074531	0.290016626	-3.375925532	0.000735678	0.006945602
CLDN7	142.7362776	0.935994026	0.277253664	3.375948268	0.000735617	0.006945602
RABAC1	5528.705127	0.610855152	0.180934488	3.376112314	0.000735179	0.006945602
TMEM26	114.7746667	1.108780514	0.328459316	3.375701223	0.000736278	0.006947707
PRDX5	13343.98996	0.594375285	0.176084338	3.375514783	0.000736777	0.006948859
TPM2	6115.784125	1.023826711	0.303414446	3.374350578	0.000739901	0.006974747
RCC1L	2225.358697	0.393787225	0.116743694	3.373092026	0.000743291	0.007003124
BBS2	5219.875556	-0.419116705	0.12429256	-3.372017633	0.000746197	0.007023319
GNA15	686.8454393	0.798336346	0.236743507	3.3721573	0.000745818	0.007023319
NFYB	2041.35221	-0.429303384	0.127336361	-3.371412391	0.000747838	0.007035176
CTSB	68766.11166	0.787648875	0.233644823	3.37113772	0.000748584	0.007038602
SUPT20H	1277.090242	-0.332778778	0.098750335	-3.369900244	0.000751954	0.00706668
ADAMTS18	442.6951678	-1.35042501	0.400758641	-3.369671594	0.000752578	0.007068941
TWISTNB	849.0319225	0.263103979	0.078088207	3.369317728	0.000753545	0.007074418
TRMT61A	2385.269784	0.530769027	0.157553544	3.368816802	0.000754916	0.007083678
FHIT	496.4218819	-0.867992694	0.257743397	-3.36766219	0.000758084	0.007095049
CCDC190	45.15919657	-1.186438811	0.352331477	-3.367393747	0.000758823	0.007095049
SPINK6	9.958638245	1.946240029	0.577960164	3.367429365	0.000758725	0.007095049
PLPP5	1328.583892	0.427714638	0.127014097	3.367458007	0.000758646	0.007095049
MUC2	12.97833003	2.221029998	0.659529677	3.367596752	0.000758264	0.007095049
TMEM150A	1196.796434	0.51428271	0.152710148	3.367704928	0.000757967	0.007095049
SNUPN	1035.006683	0.269736825	0.080089196	3.367955198	0.000757279	0.007095049

KRT74	4.062417561	-2.061914671	0.612517468	-3.366295297	0.000761851	0.007116144
CHPF	7143.216875	0.699908989	0.207915964	3.36630711	0.000761818	0.007116144
PSME3	3917.256454	0.275476461	0.081840382	3.366021202	0.000762608	0.007119611
ACVRL1	1383.508679	0.736692516	0.218898684	3.365449728	0.00076419	0.007130762
NOS1P	3730.444441	0.690613977	0.205247105	3.364792773	0.000766012	0.007144144
FXN	619.2683482	0.36758866	0.109251994	3.364594529	0.000766562	0.007145663
NPHP4	797.1791913	-0.599646223	0.178248377	-3.364104817	0.000767924	0.007154735
CTSE	1.505925928	2.142294091	0.637032101	3.36292957	0.0007712	0.007178008
ELMO3	165.4423269	0.656550479	0.195224148	3.363059775	0.000770837	0.007178006
EML1	1198.278977	-0.455474239	0.135451602	-3.362634553	0.000772025	0.007182053
PEF1	4263.938291	0.418923415	0.124596232	3.362247865	0.000773107	0.00718849
MRM2	1418.369734	0.331867258	0.098739754	3.361029829	0.000776524	0.007216625
FAM49B	3861.558167	-0.393836344	0.117208462	-3.360135758	0.000779042	0.007233864
DYNLT3	1842.141468	0.496526247	0.14777161	3.360092283	0.000779164	0.007233864
UBR2	1835.319487	-0.333669771	0.099313973	-3.359746498	0.00078014	0.007239109
CCDC127	1625.225053	0.207888478	0.061878683	3.359613817	0.000780515	0.007239109
AFMID	2861.404661	-0.614678694	0.183013231	-3.35865714	0.000783222	0.007253263
GPR132	284.0705355	0.928561166	0.276458836	3.358768273	0.000782907	0.007253263
SPINK1	73.54755948	1.671516408	0.497655234	3.358783939	0.000782863	0.007253263
KMO	185.6372578	0.996735284	0.296845465	3.357758167	0.000785773	0.007265935
GEMIN6	554.5341048	0.344694175	0.102652723	3.35786684	0.000785464	0.007265935
RPP38	539.7145404	0.399993162	0.119118115	3.35795409	0.000785217	0.007265939
POT1	925.0605625	-0.424755026	0.126531966	-3.356898957	0.000788219	0.0072849
DUSP4	534.5803737	1.007641749	0.300278602	3.355689489	0.000791674	0.007313163
CBR3	675.7420951	0.546406808	0.162852914	3.355216641	0.000793029	0.007318335
MAP2K2	8917.714974	0.542742211	0.161755918	3.355315935	0.000792744	0.007318335
MBNL1	3094.956682	-0.35357419	0.105390585	-3.354893501	0.000793955	0.007323226
MDH2	8212.339172	0.462747256	0.137950432	3.354445872	0.000795241	0.007331415
GPD1	3787.631301	-0.842177137	0.251088166	-3.35410923	0.000796209	0.00733667
IRF3	3102.585203	0.469631369	0.140048159	3.353356252	0.000798379	0.007352984
PLCG2	2832.143966	0.789277312	0.235399926	3.352920819	0.000799636	0.007360883
PSMB6	5305.912438	0.477898029	0.142557247	3.352323637	0.000801363	0.007373098
TIA1	2843.480052	-0.467192099	0.139432444	-3.350669951	0.000806163	0.007413564
NDUFA13	14383.03953	0.711213828	0.212269963	3.350515624	0.000806613	0.007413997
USP16	2329.591502	-0.322180929	0.096171442	-3.350068628	0.000807915	0.007420599
PMVK	3416.862079	0.595748256	0.177835676	3.349992924	0.000808136	0.007420599
CLBA1	898.3170222	0.488271925	0.145760367	3.349826399	0.000808622	0.007421364
SRGAP2C	1756.441866	-0.598835877	0.178776489	-3.349634402	0.000809183	0.007422813
RARRES2	2267.558617	0.803423488	0.239867962	3.349440591	0.000809749	0.007424312
PTPRK	2749.744138	-0.545855349	0.163029581	-3.34819817	0.000813388	0.007453969
FAM86C1	284.4024002	0.569217774	0.170014918	3.34804605	0.000813835	0.007454355
RPLP0	42340.76461	0.525633167	0.157023494	3.347481027	0.000815496	0.007465857
SRM	4193.756383	0.572597046	0.171139363	3.345793958	0.000820473	0.007507698
UBE2Q1	3899.248243	0.379607969	0.11349897	3.344593954	0.000824031	0.007532773
GPR143	293.6257831	0.832365646	0.248863753	3.344664043	0.000823823	0.007532773
CST3	126355.9074	0.727263502	0.217468854	3.344219129	0.000825145	0.007539218
DOCK9	4113.463964	-0.801392898	0.239676657	-3.343641843	0.000826864	0.007542216
TCHO1	2388.977755	-0.604709791	0.180858109	-3.343559182	0.000827111	0.007542216
TPBG	468.9770781	0.956260689	0.285988689	3.343701082	0.000826688	0.007542216
PILRA	1114.936942	0.707616966	0.211615446	3.343881461	0.00082615	0.007542216
KLHL3	823.7412581	-0.738731851	0.221003003	-3.342632644	0.000829877	0.007556225
CCT7	8559.353354	0.409687155	0.122559659	3.34275697	0.000829505	0.007556225
DNAJB1	9571.006133	0.572574649	0.171286876	3.342781789	0.000829431	0.007556225
AIFM1	1438.999813	0.368568684	0.110269407	3.342438264	0.000830458	0.007557785
MFSD14C	1216.517909	-0.391476544	0.117152728	-3.34159136	0.000832996	0.007572703
CLEC2D	430.6875814	-0.465008508	0.139162438	-3.34148022	0.00083333	0.007572703
TNFRSF1A	6328.585954	0.619028058	0.185244454	3.341682002	0.000832724	0.007572703
COG5	1253.77085	-0.501204239	0.150006629	-3.341213931	0.000834129	0.007576229
ATRIP	667.9475867	0.492725967	0.147494556	3.34063834	0.00083586	0.007588211
RPS6KC1	1735.445103	-0.451810255	0.135255756	-3.340414253	0.000836535	0.007590598
PARL	1749.547211	0.342663187	0.10259275	3.340033164	0.000837684	0.007597281
BCO2	320.9809529	-0.47824436	0.143195845	-3.33979215	0.000838411	0.007600137
ZBTB14	901.5359583	-0.394759976	0.118241598	-3.338587971	0.000842054	0.007627459
PPP1R35	1172.830848	0.509975747	0.152754936	3.338522217	0.000842253	0.007627459
ZNF117	1028.166034	-0.573234858	0.171734129	-3.337920428	0.000844079	0.007635782
MTG2	1756.94099	0.352584875	0.105633599	3.337809912	0.000844415	0.007635782
B4GALT1	2097.819935	0.730788069	0.218926379	3.338053978	0.000843674	0.007635782
ACADS	1874.195846	0.492362514	0.147543013	3.337077814	0.000846642	0.007652169
MXI1	4882.877939	-0.484892564	0.145319024	-3.336745252	0.000847656	0.007653855
RAB28	1142.91861	-0.319935694	0.095882598	-3.336744096	0.00084766	0.007653855
MDM4	1910.308982	-0.428309869	0.128408801	-3.33551801	0.000851406	0.007683922
CPLX4	2.768816155	-1.141298533	0.342213699	-3.335046308	0.000852852	0.007693201
EIF4G3	4357.24533	-0.449621195	0.134830701	-3.334709318	0.000853886	0.007694998
PDLIM7	3835.732546	0.828574218	0.248464247	3.3347824 75	0.000853661	0.007694998
NAV3	1435.153673	-0.725865315	0.217730517	-3.333778485	0.000856749	0.00771551
PLIN4	616.8585818	0.983296151	0.294956676	3.333696886	0.000857	0.007715511
PSMA5	3121.288413	0.414259946	0.124288967	3.333038764	0.00085903	0.007722468
PRDX4	3089.227019	0.659597507	0.197890398	3.333145587	0.0008587	0.007722468
SURF6	2858.556974	0.325375873	0.097613523	3.333307359	0.000858201	0.007722468
RCE1	639.5497933	0.435597678	0.130703547	3.332715061	0.00086003	0.007723922
RER1	6942.210066	0.329969153	0.09900708	3.332783409	0.000859818	0.007723922
PDLIM2	1499.813874	0.442449852	0.132775111	3.332325218	0.000861235	0.007730983
TMEM37	566.6711388	0.970214979	0.291186398	3.331937842	0.000862435	0.007737983
PLCH2	4378.672561	-0.740121355	0.222179639	-3.331184438	0.000864773	0.007751947
ADA2	5162.282349	0.803432056	0.241186499	3.331165135	0.000864833	0.007751947
TBCK	1062.797252	-0.502709265	0.150949809	-3.330307405	0.000867502	0.007772088
CEP44	555.7742739	-0.492293327	0.147860463	-3.329445319	0.000870191	0.0077924
TRIM11	1263.788589	0.408969034	0.122843085	3.329198657	0.000870963	0.007795517
EXOSC7	1046.248629	0.403912138	0.121330029	3.329036861	0.000871469	0.00779626
CD68	13029.57244	0.91754257	0.275711435	3.327909012	0.000875004	0.007824093
ARHGAP19	743.760063	-0.36583964	0.109956545	-3.327129275	0.000877457	0.007838414
CMTM2	44.6883593	1.043631204	0.313662446	3.327243088	0.000877098	0.007838414
CYHR1	5433.843194	0.42129823	0.126655796	3.326324127	0.000879995	0.007857284
POLK	1006.312547	-0.53398929	0.160559149	-3.32581041	0.000881619	0.007867967
HIPK2	39176.87102	-0.976641063	0.293743374	-3.324810527	0.000884786	0.007888597
DEFA3	19.64535967	4.007156859	1.205207078	3.32487	0.000884598	0.007888597
CCDC124	4995.852076	0.586572894	0.176445914	3.324377879	0.00088616	0.007897026
C6orf47	1417.035181	0.334415507	0.100647714	3.322633922	0.000891719	0.007942717
LRRCC1	1231.832831	-0.543674639	0.163651004	-3.322158891	0.000893238	0.007952408
CDKN2AIPNL	1106.022141	0.437509673	0.131706547	3.321852122	0.000894221	0.007957312
IFI35	2116.552719	0.826523144	0.248826404	3.321685849	0.000894754	0.007958213
CAPN1	5218.948929	0.527551112	0.158845053	3.321168029	0.000896416	0.007969147
SLC1A7	55.16422131	1.500723615	0.451886309	3.32102032	0.00089689	0.007969521
COL27A1	1261.499061	-0.551267481	0.166019002	-3.320508351	0.000898537	0.007980305
EIF2B4	2171.131637	0.304413122	0.091680842	3.320356951	0.000899024	0.007980788
TRAPPC3	3243.341604	0.442637406	0.133346925	3.319442172	0.000901975	0.008003127
DFFB	344.0224815	-0.434280636	0.130845465	-3.319034666	0.000903292	0.008010958
GPR34	1695.114709	-1.038064207	0.312834622	-3.318252309	0.000905826	0.008018017
KCTD10	3125.126385	0.293970158	0.088595463	3.318117513	0.000906263	0.008018017
NME1-NME2	742.0986341	0.968061237	0.29174439	3.318182867	0.000906051	0.008018017
TRADD	1421.657876	0.619989863	0.186829623	3.318477297	0.000905097	0.008018017
HLA-A	74912.31376	0.785470699	0.23669107	3.318548094	0.000904867	0.008018017
CDH1	330.7594042	-0.741786359	0.223568102	-3.317943618	0.000906828	0.008019161
KDELR1	6249.97917	0.442225647	0.1332886	3.317805479	0.000907276	0.008019279
ARHGAP6	343.8934964	-0.775858538	0.233881842	-3.317309845	0.000908888	0.008029666
SHROOM4	2102.041287	-0.603871755	0.182046483	-3.317129471	0.000909475	0.008031005

ATP6V0B	10887.14662	0.503554638	0.151844698	3.316247784	0.000912349	0.008052528
MANF	2237.14055	0.625177826	0.188559262	3.315550874	0.000914627	0.008064909
SNRPD2	5393.220031	0.538275831	0.162343206	3.315665894	0.000914251	0.008064909
CRADD	434.8434437	-0.401809404	0.121215323	-3.314840032	0.000916956	0.008073859
IL1B	659.0091199	1.268802315	0.382763215	3.314849141	0.000916926	0.008073859
TTC36	21.01405456	0.890822381	0.268728109	3.314957949	0.000916569	0.008073859
RPUSD2	518.3868016	0.38372077	0.115825497	3.31292141	0.000923269	0.008125563
SQSTM1	27474.3737	0.482131026	0.145557406	3.312308444	0.000925295	0.008139502
PHACTR4	1545.675156	-0.357577281	0.107980648	-3.31149411	0.000927992	0.008159334
MFHAS1	1258.877828	0.371900776	0.112317681	3.311150772	0.000929131	0.008165456
GAREM1	1158.480091	-0.496833672	0.150057083	-3.310964475	0.00092975	0.008166999
EIF2S1	2673.572355	0.257266827	0.077728094	3.309830622	0.000933524	0.008196247
POC5	412.9782494	-0.335252914	0.101333717	-3.308404395	0.000938292	0.008234184
SKAP1	30.93069619	-0.902013148	0.272682974	-3.307918844	0.00093992	0.008244547
ATP5F1B	18739.44826	0.328461432	0.099320227	3.307095046	0.000942689	0.008253119
DYNLRB1	10667.64196	0.558990453	0.169023093	3.3071839	0.00094239	0.008253119
C11orf68	3076.425989	0.455075795	0.137595846	3.307336718	0.000941876	0.008253119
CYB5R1	3290.031948	0.38386557	0.116064769	3.307339294	0.000941867	0.008253119
R3HDM4	2909.772004	0.410440926	0.124121104	3.306777909	0.000943757	0.008258545
TMEM205	5639.002384	0.582298042	0.17615334	3.30563157	0.000947626	0.008288467
TANC2	2378.33725	-0.586149337	0.177355753	-3.304935581	0.000949982	0.008303932
PDE6D	1531.081629	-0.359481623	0.108774183	-3.304843231	0.000950295	0.008303932
SH2D3A	69.87878862	0.868327035	0.262774106	3.304461951	0.000951589	0.008311295
ANLN	11224.75052	-0.945177009	0.286045653	-3.304287261	0.000952182	0.008312536
EPC1	1164.558606	-0.217367374	0.065795263	-3.303693387	0.000954201	0.00832622
RPL8	39511.36865	0.524279839	0.158713964	3.303300018	0.000955541	0.008330021
FBXL8	452.3260244	0.579977512	0.175570498	3.303388204	0.00095524	0.008330021
USP31	2034.266594	-0.390671531	0.118272655	-3.303143338	0.000956075	0.008330107
RPL35	23894.78179	0.652933657	0.197677063	3.303031968	0.000956455	0.008330107
EFS	3687.732756	-0.636430162	0.192718013	-3.302390634	0.000958645	0.008343856
ADAMTS14	1463.959748	-0.632557486	0.19155032	-3.302304513	0.000958939	0.008343856
HRCT1	223.1400801	1.246714821	0.377605	3.301637481	0.000961222	0.008359775
ANAPC10	387.5169251	-0.325417809	0.09857078	-3.301361822	0.000962167	0.008363483
HBS1L	2919.803074	-0.404284609	0.122464158	-3.301248421	0.000962556	0.008363483
RIOX1	483.8678876	0.570582303	0.172912242	3.29983751	0.000967408	0.008401681
TAX1BP3	5442.024969	0.596694899	0.180917015	3.29816905	0.000973175	0.008447785
STXBP3	2729.566307	-0.470885397	0.142783328	-3.29790181	0.000974102	0.008451848
ARL9	104.151156	0.751647114	0.227969534	3.297138445	0.000976753	0.008470865
GATAD1	2266.427167	-0.350083428	0.106204283	-3.296321181	0.0009796	0.008491552
DNASE2	3279.522674	0.57254227	0.173758281	3.29505027	0.000984041	0.008502057
RUNX3	684.523422	0.647752569	0.196582523	3.295066927	0.000983982	0.008502057
CDKN2B	834.7313449	0.844693163	0.256344635	3.295146637	0.000983703	0.008502057
KRTAP3-2	4.045460444	3.803037071	1.154042756	3.295403961	0.000982803	0.008502057
AKIP1	1300.84624	0.44331794	0.13452383	3.295460301	0.000982606	0.008502057
SGMS2	202.9642781	1.047794477	0.317929424	3.295682615	0.000981829	0.008502057
NOC4L	1407.21438	0.619924251	0.188098612	3.295740705	0.000981626	0.008502057
MFSD4B	149.5479517	0.475599311	0.144356203	3.294623313	0.000985537	0.008510993
FADD	1150.226835	0.44436917	0.134893072	3.294232708	0.000986908	0.008518838
KRT17	324.9229772	1.179160851	0.358040692	3.293371057	0.000989937	0.00854099
NCBP2	3634.197679	0.29703442	0.090206861	3.292814062	0.0009919	0.008553923
TMA7	8141.885724	0.465046623	0.141246561	3.292445629	0.000993201	0.008561132
AL159163.1	19.35641313	1.271417326	0.386186835	3.292233737	0.00099395	0.00856358
RPS24	26773.4814	0.542693428	0.164858542	3.291873264	0.000995225	0.008570557
ZNF532	6060.101899	-0.500135093	0.151967717	-3.291061436	0.000998101	0.008587304
TEN1	934.7344109	0.545457188	0.165733178	3.291176785	0.000997692	0.008587304
PSMC5	7362.843007	0.406380283	0.1234937	3.290695936	0.000999399	0.008594458
NEB	331.106234	-0.639172953	0.194270712	-3.290114841	0.001001465	0.008608208
TTYH2	12060.50896	-0.749040908	0.227677011	-3.289927717	0.001002131	0.008609919
TRIM21	1018.196884	0.726441802	0.220834886	3.289524658	0.001003568	0.008618242
GSDMD	2126.237915	0.630179001	0.191591967	3.289172353	0.001004825	0.008625018
TNFRSF4	149.9421832	1.075791783	0.327202479	3.287847286	0.001009566	0.00866168
NLE1	827.4363968	0.353083904	0.107404665	3.287416836	0.00101111	0.008670896
ZDHHC15	456.9338287	-0.541685197	0.164791369	-3.287096886	0.00101226	0.008676716
KRT36	18.07952678	1.516578431	0.461583253	3.285601069	0.00101765	0.008718864
C17orf58	603.176689	0.357287962	0.108776921	3.28459346	0.001021296	0.008746035
SFRP4	539.6167957	-0.885273028	0.269560047	-3.284140352	0.00102294	0.00875604
ZNF589	970.639648	0.322169657	0.098121565	3.283372585	0.00102573	0.008771776
MOCS3	381.3704763	0.297493293	0.090603959	3.283446965	0.001025459	0.008771776
ARHGAP22	2471.837363	-0.637394723	0.194163202	-3.282778179	0.001027895	0.008782142
RPL23A	14228.30647	0.533468134	0.162503903	3.282801974	0.001027808	0.008782142
RALB	2806.08316	0.362959022	0.11057184	3.282562918	0.00102868	0.008784777
C11orf52	89.17893304	0.932040648	0.284003894	3.281788267	0.00103151	0.008804865
FMNL2	13927.40999	-0.811270126	0.247245881	-3.281228072	0.001033561	0.008807259
N4BP2L2	3308.133457	-0.371221804	0.113141363	-3.281044119	0.001034236	0.008807259
GAS2	70.54085504	-0.759449112	0.231478629	-3.28086059	0.001034909	0.008807259
FZD7	1061.807488	0.819025068	0.249641977	3.280798671	0.001035136	0.008807259
SSR3	6175.111909	0.37784678	0.115160984	3.281031203	0.001034283	0.008807259
IGSF22	88.44048455	0.750254022	0.228659258	3.281100569	0.001034029	0.008807259
NAT9	1692.695656	0.344725273	0.105061484	3.281176496	0.00103375	0.008807259
FRS2	2038.559336	-0.728083445	0.221943987	-3.280482865	0.001036296	0.008808991
CCL8	158.7080499	1.599740008	0.487640886	3.280569891	0.001035976	0.008808991
MKRN3	245.9634696	-0.663562553	0.20234967	-3.279286563	0.001040699	0.008842343
CHMP1B	3213.125616	0.373206182	0.113827478	3.278700258	0.001042863	0.00885665
HIBCH	1116.453179	-0.313734125	0.095702747	-3.278214406	0.00104466	0.008867822
MVK	1111.27456	-0.422797356	0.128982245	-3.277950047	0.001045639	0.008867962
MROH6	325.8358639	0.538087614	0.164151306	3.277997761	0.001045462	0.008867962
DDOST	5563.398132	0.41142753	0.125524805	3.277659177	0.001046717	0.008873021
LGALS7B	11.87524524	3.064600761	0.935165068	3.277069328	0.001048906	0.00888749
TAGLN2	14095.97756	0.740845843	0.226083434	3.276869204	0.00104965	0.008889704
PIRS1	3.944372954	-2.888947015	0.881932458	-3.275700976	0.001054001	0.008918358
RSAD1	2216.571387	0.269745381	0.08234507	3.27579272	0.001053659	0.008918358
SLC30A1	1904.596797	0.557702584	0.17027459	3.275313031	0.00105545	0.008926516
NTAN1	1313.521757	0.365795443	0.111692187	3.275031609	0.001056502	0.008931319
CCL17	16.11717807	1.802985659	0.550578777	3.274709695	0.001057706	0.008937398
STK38	1503.764834	0.392236262	0.119815293	3.273674441	0.001061588	0.008966092
TSR3	4366.631324	0.566938143	0.173206048	3.273200614	0.00106337	0.008972913
INHBA	277.4041488	0.92113046	0.281409609	3.273272942	0.001063098	0.008972913
GPN1	1627.187521	0.36991135	0.113124646	3.269944812	0.001075685	0.009072674
CPED1	183.3965464	-0.866450465	0.265092013	-3.268489515	0.001081232	0.009115049
MOBP	59976.19528	-1.242906618	0.380284325	-3.268361428	0.001081721	0.009115049
PWP1	2059.319406	0.149676905	0.045797429	3.268238175	0.001082193	0.009115049
AC010463.1	3.518703315	2.779702835	0.850578505	3.268014437	0.001083048	0.00911809
ZNF408	879.4667814	0.503404943	0.154049613	3.267810494	0.001083829	0.009120496
TTC31	973.8519483	-0.263865952	0.080788228	-3.266143583	0.00109023	0.009166446
IL1RL2	37.52948124	1.221411129	0.373962877	3.26612935	0.001090284	0.009166446
ATP8B4	486.797	-0.836915924	0.256355806	-3.264665377	0.001095935	0.009204197
SYNDIG1	2406.198464	-0.693129243	0.212318176	-3.264577978	0.001096273	0.009204197
CLTA	10511.71287	0.492176492	0.150760364	3.264627922	0.00109608	0.009204197
AFDN	3084.745782	-0.443415435	0.135888921	-3.263072749	0.001102112	0.009246637
MARCH1	1405.835748	-0.716273221	0.219515792	-3.262969899	0.001102516	0.009246637
OSBPL3	1454.358399	-0.533321156	0.163450674	-3.262887476	0.001102833	0.009246637
GOLGA7	5441.490684	-0.437611274	0.134132699	-3.262524915	0.001104245	0.009254263
ETFB	6497.559281	0.705291317	0.216197705	3.262251641	0.00110531	0.009258979
RILP	705.1774701	0.572210084	0.175440466	3.261562727	0.001107999	0.009277291
TMEM117	368.8878924	-0.70992349	0.217705167	-3.260940009	0.001110435	0.009293466
CARF	599.4934424	-0.689049939	0.211323374	-3.260642333	0.001111602	0.009299004

NT5C3B	2450.531891	0.389039751	0.119321158	3.260442294	0.001112386	0.009301344
DPM3	1399.156573	0.645057141	0.197859656	3.260175185	0.001113434	0.009301668
EGR4	221.5274775	1.841872695	0.564956309	3.26020378	0.001113322	0.009301668
QRFP	7.468202824	1.733831379	0.531877404	3.259832746	0.001114779	0.009308685
SH3GL3	3461.441618	-0.931148676	0.285729086	-3.258851551	0.001118642	0.009333046
PAPPA2	123.0067086	-1.01722475	0.31215604	-3.258705966	0.001119216	0.009333046
PDLIM1	1746.534448	1.055417198	0.323873594	3.258731859	0.001119114	0.009333046
TBRG4	2328.67099	0.383414604	0.117670208	3.258382995	0.001120491	0.00933945
ATXN1	2440.104327	-0.521079444	0.159953349	-3.257696369	0.001123205	0.009353614
SLC34A3	9.308040772	1.721812833	0.52851757	3.25781569	0.001122733	0.009353614
FAM76B	566.500319	-0.415674727	0.127612658	-3.257315761	0.001124712	0.009359978
MED30	430.5408449	-0.429471712	0.131851136	-3.257246956	0.001124985	0.009359978
TRPV3	645.7934585	-0.66154519	0.203115206	-3.256994904	0.001125985	0.009364066
ARF5	6935.715886	0.38342864	0.117734814	3.256714189	0.001127099	0.009369102
UMPS	995.5499864	0.437235129	0.134277176	3.256213327	0.001129089	0.009381419
CDK6	1841.345392	-0.76257471	0.234209404	-3.255952573	0.001130126	0.009385803
PAM16	1045.587807	0.535577549	0.164528062	3.255235267	0.001132985	0.009405304
AC006254.1	322.4990954	-0.719246856	0.220964399	-3.255035019	0.001133784	0.0094077
FRG1	1518.408143	0.473538731	0.145493012	3.254718037	0.00113505	0.009413967
SLC25A13	1750.536996	-0.546958808	0.168069501	-3.254360881	0.001136478	0.009421572
PIK3C2B	2503.19283	-0.604781356	0.185875284	-3.253694315	0.001139148	0.009439459
FAD53	4373.924542	0.479666866	0.147472151	3.252592858	0.001143572	0.009471862
NKTR	4027.225472	-0.567946526	0.174622113	-3.252431874	0.00114422	0.009472971
TCF15	38.62623911	1.114212823	0.342626366	3.251976306	0.001146056	0.009483907
SLC25A11	4293.241789	0.342792523	0.105426784	3.251474713	0.00114808	0.009496393
WWC2	772.6698086	-0.644942148	0.198423036	-3.250339071	0.001152675	0.009530123
USP21	1464.325803	-0.269036195	0.082799073	-3.249265794	0.001157033	0.009559484
BTF3	11954.8748	0.405664807	0.124850321	3.249209172	0.001157263	0.009559484
HYDIN	538.2562847	-0.707276407	0.217712392	-3.248673175	0.001159446	0.009573222
COL5A3	6280.905317	-0.858533951	0.264321772	-3.248063696	0.001161933	0.009589456
FZD1	794.1077121	0.575197452	0.177111558	3.247656199	0.001163598	0.0095989
KCTD18	953.4232822	-0.363336986	0.11191976	-3.246406056	0.00116872	0.009635566
SPOP	2582.195014	-0.201596448	0.062100061	-3.246316421	0.001169088	0.009635566
ORMDL2	1148.213807	0.619486307	0.190836896	3.246155856	0.001169748	0.009636693
ACER3	2743.022764	-0.507077641	0.156224378	-3.245829156	0.001171091	0.009643447
APTX	1276.659034	0.283595836	0.087383753	3.245406913	0.001172829	0.009653446
POR	3260.391654	0.368003366	0.113398147	3.245232628	0.001173547	0.009655045
MANBAL	3128.692295	0.375211585	0.115634551	3.244805134	0.00117531	0.009665235
RRM2B	2679.600242	0.547959686	0.1689536	3.243255465	0.001181722	0.009700648
HSD17B14	2115.272866	0.610238049	0.188156007	3.24325574	0.001181721	0.009700648
SPATC1L	946.3970048	0.53970834	0.166406393	3.243314931	0.001181475	0.009700648
TCEA3	978.6822017	0.675486577	0.208256641	3.243529586	0.001180585	0.009700648
ARID1B	2337.662279	-0.49817055	0.153677177	-3.241669061	0.001188319	0.009749053
MIP	2098.408073	0.567019473	0.174920528	3.241583356	0.001188677	0.009749053
MZT2A	2349.438282	0.55470114	0.171180855	3.240439127	0.001193458	0.009779559
QPCT	372.3729692	0.884598628	0.272982493	3.240495826	0.00119322	0.009779559
ZNF787	1681.29111	0.422887802	0.130556898	3.239107294	0.001199045	0.009820974
C1QTNF9B	13.76514025	-1.233210514	0.380743348	-3.238954868	0.001199686	0.009821859
MAPK15	124.3366817	-1.488924448	0.459802868	-3.238179994	0.001202949	0.009844203
TREX1	1219.19768	0.615129799	0.190021997	3.237150484	0.001207297	0.009875402
NDUFA7	2522.712794	0.487013179	0.150452033	3.236999666	0.001207936	0.00987624
STX16-NPEPL1	324.175951	-0.882378093	0.272689503	-3.235834467	0.001212877	0.009911038
FLAD1	1654.524158	0.391863712	0.121104722	3.23574264	0.001213267	0.009911038
TRMT10A	218.8330904	-0.354631136	0.109612468	-3.235317515	0.001215075	0.00992141
PXN	5208.309762	0.473297205	0.146353654	3.233928181	0.001221002	0.009965384
ZNF638	4894.564354	-0.279888821	0.086564124	-3.233311985	0.001223639	0.009975029
RFFL	4009.802159	-0.5632023	0.174189549	-3.233272623	0.001223807	0.009975029
TENT5A	1119.859537	0.885113902	0.273745156	3.233350003	0.001223476	0.009975029
MEF2A	3746.471194	-0.433066884	0.133950814	-3.233029135	0.001224851	0.009979122
PRDM6	54.69496654	-0.864739611	0.267570245	-3.231822767	0.001230033	0.010005146
EEF1G	39757.00499	0.374931725	0.116013994	3.231780167	0.001230217	0.010005146
NBEAL2	1971.681056	0.533006083	0.16492026	3.231867178	0.001229842	0.010005146
ABCB6	1639.680828	0.416098327	0.128742316	3.232024548	0.001229165	0.010005146
SLCO1A2	8134.992369	-1.195960032	0.370086395	-3.23156984	0.001231122	0.010008096
NLRC3	92.45074932	-0.763967495	0.236433436	-3.231215977	0.001232648	0.010016077
ZBTB45	1054.740881	0.382510959	0.118429826	3.229853247	0.001238538	0.010059503
LYAR	496.56183	0.456884793	0.141477775	3.22937502	0.001240611	0.010071903
THAP9	292.6580665	-0.463940992	0.143692264	-3.228712376	0.001243489	0.010090822
HECW2	1068.444594	-0.657190814	0.2035639	-3.228425141	0.001244738	0.010096515
SLC29A1	2043.430112	0.497523926	0.154178382	3.226937014	0.00125123	0.010144706
TSEN15	2039.860717	-0.300458092	0.093128685	-3.226267965	0.001254159	0.010163981
ERF	4137.284741	-0.336420001	0.10428807	-3.225872345	0.001255894	0.010173566
C1orf131	477.5842141	-0.256448208	0.079520219	-3.224943443	0.001259976	0.010202148
CXCR6	42.80334655	-1.381269835	0.428351309	-3.224619149	0.001261404	0.010209225
MALSU1	1218.365421	0.40544624	0.125743257	3.224397463	0.001262381	0.010212648
DNAJC7	4769.640602	0.353893187	0.1097652	3.224092752	0.001263725	0.010219035
CCDC17	83.39898997	-0.727906081	0.225839737	-3.223108963	0.001268073	0.010249701
ECM1	1219.865258	0.752652329	0.233621994	3.221667266	0.00127447	0.010296894
ARFGAP1	7693.960365	0.442757222	0.137473571	3.220671583	0.001278906	0.01032368
FBL	3370.651965	0.599184452	0.186037108	3.220779226	0.001278426	0.01032368
ATG10	357.0349106	-0.394868402	0.122626149	-3.220099508	0.001281461	0.010339775
SNX19	4672.384335	-0.329297749	0.102270891	-3.21985803	0.001282541	0.010343959
C8orf76	617.6481359	0.348201505	0.108164893	3.219173028	0.001285609	0.010359635
NUDT8	275.6846828	0.727124306	0.225864526	3.219293968	0.001285067	0.010359635
SEC22A	719.9284606	0.252370891	0.078419128	3.218231303	0.001289838	0.010389168
CHEK2	274.0087474	0.688421699	0.213953141	3.217628375	0.001292552	0.010406481
VPS37D	436.3939489	0.530718673	0.164995004	3.216574201	0.00129731	0.010440228
KANTR	746.3597795	-0.545933532	0.169749724	-3.216108517	0.001299417	0.01044808
BCDIN3D	838.6534862	0.482713247	0.150088396	3.216192997	0.001299034	0.01044806
ZNF330	1258.511741	0.305941955	0.095144655	3.215545375	0.001301969	0.010464016
PHB2	6011.966099	0.298176008	0.092735134	3.215351015	0.001302851	0.010466654
TMEM80	762.7434474	-0.335845474	0.104478513	-3.214493244	0.00130675	0.010493287
CHST13	136.2917238	1.154749105	0.359252011	3.214314938	0.001307562	0.010495233
FRMD4A	2171.992696	-0.355014585	0.110460994	-3.213936193	0.001309288	0.010504511
CDBA	195.5878181	-0.810344396	0.252199119	-3.213113505	0.001313044	0.010520907
SOST	7.495894196	1.792495115	0.557850368	3.213218486	0.001312564	0.010520907
SH2D4A	276.84773	0.597120687	0.185828666	3.213286199	0.001312255	0.010520907
INPP4B	276.4866152	-0.610524105	0.190020218	-3.21294287	0.001313824	0.010522584
SRGAP2B	1338.289496	-0.662750822	0.206283677	-3.212812721	0.00131442	0.01052278
C7orf50	5685.17911	0.457207331	0.142336302	3.212162499	0.001317398	0.010542047
NPR2	1100.032648	0.482941568	0.150425238	3.210508925	0.001325002	0.010598287
GZMB	103.6374091	1.186808894	0.369743703	3.209815025	0.001328204	0.010619299
SCHIP1	3765.714459	-0.718157846	0.223771764	-3.209331828	0.001330439	0.010627937
ZGPAT	1899.086638	0.481221281	0.149942003	3.209382762	0.001330203	0.010627937
DOCK4	3141.73997	-0.748829798	0.233371199	-3.208749828	0.001333134	0.010644858
ERN1	615.2677298	0.594424336	0.185305748	3.207803015	0.001337531	0.010675338
FRK	377.748204	-0.605097917	0.188655917	-3.207415528	0.001339334	0.010685101
ATMIN	3813.877791	0.183240004	0.057137208	3.207017113	0.00134119	0.010695281
ZNF683	22.98451323	-1.27096542	0.396432963	-3.206007181	0.001345906	0.010728247
MTUS1	7983.176714	-0.679689341	0.212018064	-3.205808638	0.001346835	0.010729545
ZACN	8.161323945	1.552346359	0.484260915	3.205599109	0.001347816	0.010729545
RAB35	2294.401578	0.314356541	0.098062164	3.205686342	0.001347408	0.010729545
DGKA	1213.51782	0.614371723	0.191685553	3.205101866	0.001350147	0.010743462
RPS2	43460.00138	0.536384248	0.167391704	3.204365758	0.001353604	0.010766322
CD69	104.3343411	-1.268082499	0.395812911	-3.203742134	0.001356539	0.010785013
C6orf226	683.752581	0.584478623	0.182482784	3.202924729	0.001360395	0.010806347

ZNF584	546.6008718	0.357366077	0.111573936	3.20295303	0.001360262	0.010806347
BORCS6	728.2387595	0.500158796	0.156166774	3.202722225	0.001361352	0.010809289
CCDC73	1.369855751	-1.461721192	0.456632144	-3.201091319	0.001369081	0.010841353
IQCJ-SCHIP1	2466.861044	-0.648179254	0.202488859	-3.201061325	0.001369224	0.010841353
PPM1B	2811.103002	-0.368086711	0.11499111	-3.201001474	0.001369508	0.010841353
RRAS	1982.541064	0.654145862	0.20434299	3.201215083	0.001368493	0.010841353
RBM38	2028.000388	0.515614208	0.161059638	3.201386847	0.001367678	0.010841353
LMNB2	2241.477866	0.497970576	0.155537793	3.201604992	0.001366643	0.010841353
SIGLEC14	736.7281855	1.027948714	0.321069827	3.201635599	0.001366496	0.010841353
NDUFA6	1855.833969	0.531516823	0.16611818	3.199630668	0.001376038	0.010888366
PRIMPOL	408.1042917	-0.33680004	0.10527634	-3.199199751	0.001378096	0.010899974
DOCK3	2339.955661	-0.865224493	0.270475019	-3.198907228	0.001379496	0.010906359
FTL	389573.5673	0.800418685	0.250251868	3.198452393	0.001381673	0.010918894
ZFAND3	4584.727781	-0.453239972	0.141724615	-3.198032835	0.001383685	0.010930105
EXOC6B	2476.502099	-0.658516969	0.205976018	-3.197056501	0.001388377	0.010955232
RALGAPA1	2237.29493	-0.591314978	0.184959332	-3.19699996	0.001388649	0.010955232
NAPA	9143.049665	0.3899063	0.121952908	3.197187385	0.001387747	0.010955232
ZDHHC11B	2226.331264	-0.753003551	0.235618601	-3.195857833	0.001394158	0.010993982
NDUFA8	2783.541984	0.412132532	0.128968213	3.195613262	0.00139534	0.010998598
MCRIP1	7748.76375	0.5010936	0.156824227	3.195256309	0.001397067	0.011007503
SHBTC2	1498.684884	-0.837401143	0.262115974	-3.194773404	0.001399407	0.01101233
PDE4B	4144.977991	-0.485028171	0.151819916	-3.194759845	0.001399472	0.01101233
FXYD5	3842.619513	0.821324397	0.257071387	3.194927312	0.001398661	0.01101233
BIN3	1080.686195	0.335315758	0.104985016	3.19393921	0.001403457	0.011034259
BCL2L14	18.27212276	1.308430049	0.409658734	3.193951304	0.001403398	0.011034259
GMPPA	2092.603931	0.459992687	0.144076793	3.192691038	0.001409537	0.011077336
SIAH2	1217.847831	0.383567616	0.120149168	3.192428392	0.001410819	0.011082688
CFAP43	230.3758713	-0.845798297	0.264954909	-3.192234863	0.001411765	0.011085392
MFAP2	211.9629264	1.320101821	0.413747237	3.190599724	0.001419778	0.011143567
CHMP2A	8263.206878	0.603646471	0.189213032	3.190300716	0.001421248	0.01114561
NIFK	1566.858023	0.330045391	0.103449163	3.190411436	0.001420704	0.01114561
KCNK16	1.633386532	-1.880210999	0.589465579	-3.189687519	0.001424267	0.011164533
DPCD	795.4641011	0.4640304	0.145513201	3.188923044	0.001428039	0.01118934
EBNA1BP2	3143.154611	0.398221949	0.124898977	3.188352371	0.001430861	0.011206685
BATF3	347.577792	0.822245965	0.257985125	3.187183615	0.001436655	0.011247291
BMP2K	2999.306867	-0.537937733	0.168834228	-3.186188848	0.001441605	0.01126774
DCUN1D5	749.0533425	0.272150212	0.085422753	3.185921789	0.001442936	0.01126774
GJB3	38.49189157	1.628020289	0.510998316	3.185960184	0.001442745	0.01126774
TMPRSS5	2069.965116	0.762345901	0.239273558	3.186085053	0.001442122	0.01126774
WDR77	1838.121324	0.378462767	0.118779632	3.186259799	0.001441251	0.01126774
DDX50	1283.584238	0.24975814	0.078380354	3.18648907	0.001440109	0.01126774
NIP7	752.910011	0.360987407	0.113319307	3.18557727	0.001444655	0.011276387
PEX2	2045.541782	-0.406144684	0.127511291	-3.185166427	0.001446708	0.011287628
PTGDR	13.66033414	-1.20299875	0.377763929	-3.184525195	0.001449917	0.011307879
GADD45A	4392.468551	0.811045307	0.254698163	3.18433905	0.00145085	0.011310368
PLEKHG3	6975.809368	-0.627962197	0.197239652	-3.183752312	0.001453794	0.011328525
MYO1D	3585.160199	-0.778624211	0.244605177	-3.183187784	0.001456631	0.011345839
JAZF1	1085.394165	-0.510827309	0.160489007	-3.182942676	0.001457865	0.01135065
FAM170A	1.991151495	-1.75585485	0.551684952	-3.182712967	0.001459022	0.011354779
NMT2	712.511623	0.396939387	0.124722014	3.182592817	0.001459627	0.011354779
H2BFS	31.73915086	0.874749029	0.274905371	3.182000499	0.001462616	0.011373225
MYRF	24347.16299	-0.714670803	0.224637608	-3.18143881	0.001465455	0.011390498
DIS3L2	1157.210959	-0.44803608	0.14084902	-3.180966962	0.001467844	0.011404254
TLR10	100.7586675	-0.842050278	0.264776082	-3.18023543	0.001471554	0.011428267
SERPINB7	10.28241549	2.838273294	0.892634234	3.179659916	0.00147448	0.011446162
HESX1	64.68170156	-0.617064245	0.194081729	-3.179404094	0.001475782	0.011447992
CAMLG	2204.895977	0.277446213	0.087264538	3.179369537	0.001475958	0.011447992
CDC42BPA	4211.825174	-0.584867544	0.184002681	-3.178581639	0.001479975	0.011474323
REV1	1426.885062	-0.289748189	0.091194288	-3.177262486	0.001486724	0.011518685
CAPNS1	19488.91126	0.492191354	0.154918576	3.177097071	0.001487572	0.011518685
SSB	3699.566403	0.237169616	0.074674396	3.177198775	0.001487051	0.011518685
ANKRD36B	594.4518718	-0.557009103	0.175361099	-3.176355003	0.001491383	0.011543344
ERICH2	107.0245624	0.588020567	0.185153435	3.175855563	0.001493953	0.011558381
NCF4	1484.72845	0.881088899	0.277452522	3.175638456	0.001495072	0.01156218
ZNF394	798.6254224	0.351844292	0.110805024	3.175346028	0.001496579	0.011568984
RIPK3	369.7313201	0.831237317	0.26182133	3.174826578	0.001499261	0.011584854
ANKRD53	104.0027962	0.924998639	0.291373338	3.174616609	0.001500346	0.01158838
MBP	996824.2098	-1.07427992	0.338459746	-3.174025664	0.001503404	0.011607135
RYR1	1418.693355	-0.74140552	0.233652602	-3.173110478	0.001508151	0.011638911
MRPL57	2284.584928	0.339257666	0.106922574	3.172928355	0.001509098	0.011641335
PIM3	4047.251118	0.493507708	0.155569944	3.172256116	0.001512595	0.01166344
KLHL32	1974.766892	-0.866827103	0.273348076	-3.171147633	0.00151838	0.011703144
FBP1	775.571609	0.851221086	0.268486905	3.170438004	0.001522093	0.011726862
COQ8A	2895.560985	0.328611859	0.103673781	3.169671803	0.001526112	0.011752912
RNF146	2295.729345	-0.295191433	0.093142976	-3.169229143	0.001528438	0.011765911
RPUSD1	1427.259857	0.427768733	0.134986485	3.168974524	0.001529778	0.011771307
VPS8	2419.502965	-0.378430465	0.119438314	-3.168417686	0.001532711	0.011788956
MSH5	462.7834052	-0.466494278	0.147262938	-3.167764298	0.00153616	0.011806409
XAF1	2273.544916	-0.534348491	0.168685907	-3.167712709	0.001536433	0.011806409
CISD3	1532.380157	0.522923458	0.165083825	3.167623827	0.001536902	0.011806409
AC010422.3	591.5003064	1.188682563	0.375285908	3.167405272	0.001538058	0.011810364
RUNDC1	1020.866185	0.31265918	0.09874017	3.16648411	0.001542938	0.011837968
C19orf12	1678.977553	0.290846058	0.0918493	3.1665568	0.001542552	0.011837968
PRTFDC1	1499.147501	-0.527356247	0.166653462	-3.164388196	0.001554094	0.011918598
FAM181A	1089.937556	0.697158139	0.220356888	3.163768302	0.001557407	0.011939043
SLC35A3	816.6522449	-0.393344363	0.124367104	-3.162768537	0.001562765	0.011975136
ERP27	36.91700078	-0.781116699	0.24699119	-3.162528587	0.001564054	0.011980028
ADK	760.1182359	-0.505003956	0.159698189	-3.162239716	0.001565606	0.011986937
BCLAF3	618.2006781	-0.310348635	0.098164863	-3.161504275	0.001569565	0.012012258
ZBED3	2342.453371	-0.43153256	0.136538549	-3.160518138	0.001574888	0.012047991
RTRAF	4709.333419	0.383353527	0.121302014	3.160322838	0.001575944	0.012051068
POLR3H	3477.900904	0.30159673	0.095448349	3.159789914	0.001578829	0.012068124
TFCP2	1841.734636	-0.236787937	0.074945556	-3.159465994	0.001580585	0.012076538
PGAP2	986.7909444	-0.285760009	0.090472206	-3.158539212	0.00158562	0.012102148
RNF144A	2902.906513	-0.644654275	0.204100612	-3.158512209	0.001585767	0.012102148
C1orf226	471.6495314	-0.888732518	0.281418825	-3.158042168	0.001588326	0.012102148
TBC1D12	2489.54454	-0.790010323	0.25015908	-3.158031777	0.001588382	0.012102148
KDM6A	955.2112368	-0.645547913	0.204439354	-3.157649934	0.001590464	0.012102148
APLP2	21067.06696	0.428030863	0.135559096	3.157522263	0.001591161	0.012102148
PHLDA3	9244.346802	0.67797715	0.21471575	3.157556094	0.001590976	0.012102148
WDR89	439.7601647	0.216946548	0.068700224	3.15787248	0.001589251	0.012102148
ACADVL	19295.90746	0.441727605	0.13988092	3.157883189	0.001589192	0.012102148
SCAMP3	4036.905327	0.454676918	0.143980171	3.157913444	0.001589027	0.012102148
MRPS15	2286.045129	0.398315154	0.126131928	3.157924887	0.001588965	0.012102148
C12orf76	2761.11767	-0.491150804	0.155608599	-3.156321745	0.001597725	0.012147061
GOLGA1	1581.03259	-0.210689244	0.066764764	-3.155695165	0.001601161	0.012164386
BTNL8	17.85634763	1.215999209	0.38533844	3.15566547	0.001601324	0.012164386
WDR20	1083.112273	-0.299375108	0.09488143	-3.15525503	0.001603579	0.012176494
RPA4	4.839149587	1.772400036	0.561832092	3.154679236	0.001606747	0.012190503
SIRT7	1386.936332	0.372589483	0.118104397	3.154746931	0.001606374	0.012190503
CLMN	3678.374528	-0.659329144	0.209014033	-3.154473101	0.001607882	0.012194098
TAS2R14	103.469154	-0.783322829	0.248351306	-3.154091848	0.001609984	0.012201182
PTPRD	6179.431222	-0.839479368	0.266167566	-3.15395065	0.001610763	0.012201182
CENPC	703.08458	-0.418955012	0.132841492	-3.153796351	0.001611615	0.012201182
SLC10A7	252.3975987	-0.619039887	0.196294758	-3.153624136	0.001612566	0.012201182
PSMD12	1997.982529	0.249324023	0.079060532	3.15358393	0.001612788	0.012201182

SH3D21	919.5192773	0.726682773	0.2304093	3.153877786	0.001611165	0.012201182
PGPEP1	3382.305817	0.370779037	0.117600999	3.152856172	0.001616814	0.01222662
NR0B1	45.50259112	1.083470835	0.343742309	3.151985674	0.001621642	0.012258099
C4orf33	686.2669466	-0.338040422	0.107266703	-3.151401255	0.001624891	0.012272588
TMEM199	1479.249868	0.25176232	0.079886735	3.151490917	0.001624392	0.012272588
MBD5	778.9201245	-0.465615557	0.147766957	-3.151012682	0.001627054	0.012279861
OST4	6441.401982	0.477896394	0.151665526	3.150988933	0.001627187	0.012279861
POLR1D	2236.653463	0.386898431	0.1227984	3.150679749	0.00162891	0.012287835
PCYT1A	3553.956221	0.227873836	0.072330515	3.150452284	0.001630179	0.012292375
NUDT16	5519.381146	-0.34579642	0.109765126	-3.150330453	0.001630859	0.012292473
NDUFB11	4362.90193	0.526239906	0.167093343	3.149376842	0.001636191	0.012317547
CHCHD1	1089.110721	0.423966427	0.134616648	3.149435323	0.001635863	0.012317547
PQBP1	3291.555525	0.500791402	0.159002871	3.149574579	0.001635084	0.012317547
NCOR2	10700.60497	-0.286374328	0.090941899	-3.148981174	0.001638407	0.0123292
CXCL9	116.3334044	-1.143668604	0.363280832	-3.148166665	0.00164298	0.012358562
NFAM1	1169.67933	0.754553522	0.239703739	3.147858793	0.001644711	0.012366537
S100A14	44.42265163	0.989658813	0.314417658	3.147592977	0.001646207	0.012367695
ACOT2	1476.962317	0.387043711	0.122963215	3.147638201	0.001645953	0.012367695
EIF3K	8052.396155	0.519630252	0.165104796	3.147275342	0.001647997	0.012376094
BHLHE40	4089.582	0.575124212	0.182775927	3.146608093	0.001651762	0.012399316
RGS2	2318.072942	0.820007034	0.260666088	3.145814024	0.001656253	0.012427966
ACY3	109.2840044	-1.108338096	0.352356412	-3.145502846	0.001658016	0.012435054
ZSWIM1	405.0386819	0.307597291	0.097799856	3.145171217	0.001659897	0.012435054
SSU72	5487.289424	0.352556333	0.112091058	3.145267251	0.001659352	0.012435054
COL17A1	80.58245368	1.016168157	0.323068817	3.145361312	0.001658818	0.012435054
SNX31	46.38485854	-1.278055264	0.40650857	-3.143981103	0.001666662	0.012475668
TOMM22	3209.165059	0.35834903	0.113983755	3.143860536	0.001667349	0.012475668
GDPGP1	279.2221639	0.31549946	0.10035285	3.143901362	0.001667116	0.012475668
DNAL4	776.8939234	0.369231293	0.117450106	3.143728903	0.001668099	0.012476216
GRK6	1467.890153	0.373128501	0.118744748	3.142273723	0.001676412	0.012533308
MLLT10	938.535722	-0.443811023	0.141255763	-3.141896754	0.00167857	0.012544366
KIF13B	5840.970144	-0.59502988	0.189474109	-3.140428438	0.001687009	0.012602307
RRAGC	2400.85958	0.354596121	0.11292301	3.140158251	0.001688566	0.012608826
MARVELD2	155.8730842	0.626072794	0.1993858	3.140006929	0.001689438	0.012610231
ADPRHL2	2216.494315	0.383187415	0.12204923	3.139613542	0.001691708	0.012622063
ATP6AP1L	330.0124332	-0.404963641	0.129002865	-3.139183303	0.001694194	0.012630929
CADM1	5144.823235	-0.409569966	0.130470756	-3.139170642	0.001694268	0.012630929
LGMN	10233.08927	0.880928678	0.280663474	3.138736455	0.00169678	0.012639432
FAM110D	180.0059502	0.845232546	0.269286099	3.138790112	0.001696469	0.012639432
RNF215	1135.803862	0.354261191	0.112891379	3.138071241	0.001700635	0.012663034
F12	221.876038	0.932805649	0.297296875	3.137623455	0.001703235	0.012677271
SLC35E1	2180.486094	0.386531649	0.123198669	3.137466098	0.00170415	0.012678957
MRPL21	1401.115476	0.398953063	0.127171136	3.137135334	0.001706074	0.012688148
LRRC47	3494.390421	0.309048302	0.098518064	3.136970915	0.001707031	0.012690144
CACNA2D4	379.698103	0.7660442	0.244215424	3.136756016	0.001708282	0.012694328
MXD1	974.5949806	0.470805462	0.150126616	3.13605591	0.001712366	0.012719542
CHMP4B	8263.906795	0.339146914	0.108172413	3.135244037	0.001717112	0.012744526
VSIG10L	270.4790526	0.430940947	0.137447828	3.13530562	0.001716752	0.012744526
MSRB1	1481.725079	0.412791258	0.131669756	3.135049919	0.001718249	0.012747828
SERPINB6	10632.79924	0.56695711	0.180914678	3.133836984	0.001725367	0.012795487
MFSD10	3581.331518	0.397962963	0.127001595	3.133527278	0.001727189	0.012803845
TTI2	431.0356168	0.315658459	0.100756893	3.132872114	0.001731048	0.012827295
PITHD1	4939.460775	0.32525634	0.103839108	3.132310616	0.001734363	0.012846693
MYSM1	1531.113966	-0.609617241	0.194674088	-3.131476036	0.0017393	0.012878086
WDR55	1791.89782	0.229657769	0.073342568	3.13130253	0.001740328	0.012880523
NUB1	3219.00594	0.264191025	0.084385107	3.130777884	0.00174344	0.012888026
APOL2	5166.037402	0.608458887	0.194341473	3.130875144	0.001742862	0.012888026
JOSD2	3513.522549	0.781228391	0.249518175	3.130947841	0.001742431	0.012888026
ZNF682	305.7336144	-0.416499735	0.133043869	-3.130544358	0.001744826	0.012893106
AL358113.1	689.6026845	-0.635148199	0.202948045	-3.12960984	0.001750386	0.012929005
PPIB	15676.25529	0.607656241	0.194195931	3.129088425	0.001753495	0.012946781
FUT8	3065.559001	-0.652220257	0.208482449	-3.128418055	0.0017575	0.012971153
KLHL21	3995.446406	0.427767185	0.136770333	3.127631373	0.00176221	0.013000711
SWI5	1162.108967	0.555583366	0.177667901	3.127089148	0.001765464	0.013019501
SWT1	276.9821926	-0.393364862	0.125803957	-3.126808332	0.001767151	0.01302673
ATP6V0E1	7582.945586	0.506326969	0.161938317	3.12666563	0.001768009	0.013027843
FKTN	1067.500495	-0.425877752	0.136225691	-3.126266037	0.001770413	0.013036057
DENR	2023.102154	0.216923723	0.069387942	3.126245244	0.001770538	0.013036057
CDIPT	4136.135067	0.298746244	0.095575982	3.125746005	0.001773547	0.013052991
KEAP1	4828.29415	0.293960182	0.094063145	3.125136644	0.001777225	0.013074841
CDC42SE2	3177.479613	-0.424480949	0.135836583	-3.124938354	0.001778423	0.013076544
TRIR	9469.655107	0.486151645	0.155575319	3.124863559	0.001778875	0.013076544
ZNF37A	1282.199105	-0.320753637	0.102661051	-3.124394647	0.001781713	0.013092181
VPS28	7319.233477	0.45015741	0.144118753	3.123517237	0.001787034	0.013126048
EFHD1	11369.54363	-0.723046992	0.231540733	-3.122763683	0.001791615	0.013154019
FAM219A	6720.537884	-0.357943509	0.114627897	-3.122656166	0.00179227	0.013154019
CEP192	1347.258336	-0.497425418	0.159319112	-3.122195527	0.001795077	0.013169375
LACTB	950.2536374	0.576893999	0.184858261	3.120736918	0.001803991	0.013229508
TCIRG1	3151.816428	0.732096859	0.234602825	3.120579888	0.001804953	0.013231299
OXSM	344.5670468	0.303651637	0.097327233	3.119904146	0.001809099	0.013256416
AVIL	865.7670593	-1.081305499	0.346626861	-3.119508676	0.001811529	0.013268948
ZNF536	2414.980409	-0.810952811	0.259976556	-3.119330541	0.001812625	0.013271698
MKRN1	3873.992815	0.182991948	0.058669196	3.119046451	0.001814374	0.013279228
HSH2D	119.7997031	1.110015338	0.355928581	3.118646266	0.001816839	0.013291994
AC004832.3	100.4117044	1.270942175	0.407604446	3.118077314	0.00182035	0.013312396
EHD1	4444.192724	0.53509675	0.171631395	3.117709019	0.001822627	0.013323754
TAP1	5068.347805	0.705542604	0.226342246	3.11714943	0.00182609	0.01333845
TRIP6	5642.390338	0.630538517	0.202274279	3.117245155	0.001825497	0.01333845
SLC34A2	102.167713	1.296905128	0.416113224	3.116712117	0.001828801	0.013352998
SAR1B	3628.243426	-0.335821102	0.107815029	-3.114789322	0.001840763	0.013432341
LPAR1	11222.63987	-0.828603415	0.266047191	-3.114497886	0.001842583	0.013432341
PLTP	18343.81742	0.739109162	0.237303852	3.114610889	0.001841877	0.013432341
PSMD7	3990.551334	0.272732565	0.087564609	3.114643774	0.001841672	0.013432341
C5orf58	4.024090348	-1.845534917	0.592663396	-3.113968113	0.001845894	0.013451162
SPAG8	337.575142	-0.717248007	0.230351674	-3.113708682	0.001847518	0.013457672
C19orf25	2599.45176	0.483180928	0.155193906	3.113401419	0.001849443	0.01346637
CENPQ	328.2739009	-0.552091336	0.177341019	-3.113162082	0.001850943	0.013471236
SELENON	7161.72878	0.339155271	0.108945888	3.113061688	0.001851573	0.013471236
TYROBP	10586.54728	0.916818038	0.294518064	3.112943314	0.001852316	0.013471322
WDR27	612.4346955	-0.371306024	0.119291925	-3.11258306	0.001854578	0.013477138
MFSD13A	713.7621724	0.385242653	0.123769396	3.112584088	0.001854572	0.013477138
SPIDR	1477.522621	-0.522143352	0.167763354	-3.112380255	0.001855853	0.013481089
DST	29061.20717	-0.672878569	0.216223192	-3.111962981	0.001858478	0.013494835
PNISR	4966.239526	-0.419945206	0.135006789	-3.110548806	0.0018674	0.013541426
DOCK5	4808.132718	-0.749674579	0.241024699	-3.11036414	0.001868568	0.013541426
GGH	948.5838662	0.708341532	0.227733936	3.110390773	0.0018684	0.013541426
ATOH8	1184.656195	0.545743284	0.175449987	3.110534769	0.001867489	0.013541426
TRAPPC1	4629.772674	0.507447356	0.16312538	3.110781152	0.001865932	0.013541426
SPOCD1	6794.012079	1.241579397	0.399295292	3.109426584	0.001874509	0.013563141
NAA50	3019.260469	0.260512328	0.083780054	3.109479135	0.001874175	0.013563141
BMF	946.955567	0.79012426	0.254101248	3.109485946	0.001874132	0.013563141
ECI1	2148.768034	0.465853671	0.149804055	3.109753411	0.001872436	0.013563141
CASP4	1244.438016	0.771146202	0.248053921	3.108784574	0.001878586	0.013587311
BACH2	305.5183721	-0.468046456	0.150580591	-3.10827879	0.001881805	0.013600262
GFOD2	1123.060606	0.353173995	0.113628168	3.108155333	0.001882591	0.013600262
CSF2	3.414433297	2.675395405	0.860741929	3.108243385	0.00188203	0.013600262

CALML6	80.45619783	1.031837276	0.332090121	3.107100184	0.001889324	0.013643552
GSDMC	48.95106793	-0.944912023	0.304126906	-3.106966215	0.00189018	0.01364439
PRELID3A	608.1950409	-0.225540858	0.072595341	-3.106822757	0.001891097	0.013645668
ELMO2	4078.116032	-0.240471697	0.077413246	-3.106337871	0.001894201	0.013659844
CCDC102A	362.4333075	0.606282492	0.195179329	3.106284333	0.001894544	0.013659844
ZNF518A	1199.461647	-0.582764851	0.187619028	-3.106107399	0.001895679	0.013662675
LRWD1	1822.041189	0.41348892	0.133137104	3.105737668	0.00189805	0.01367442
MOGS	1912.649101	0.286982173	0.092429836	3.104865105	0.001903658	0.013709464
NAA25	1151.940372	-0.415477259	0.133829446	-3.104527979	0.001905829	0.013719736
NLRC5	1700.263392	-0.538429013	0.173482816	-3.103644638	0.001911528	0.013755387
LTB4R	749.3358282	0.586490904	0.189056906	3.10219244	0.00192093	0.013817653
STARD13	1200.378973	-0.419280559	0.135175348	-3.101753134	0.001923783	0.013827379
TNFRSF10B	2132.405044	0.605983326	0.195364072	3.101815594	0.001923377	0.013827379
FAM162A	2845.907111	0.376220272	0.121339804	3.100551168	0.001931608	0.013878211
SLC35B1	2172.427817	0.279361242	0.090107705	3.100303598	0.001933224	0.013884404
CSF1	5203.545718	0.581060476	0.187430112	3.10014474	0.001934261	0.013886441
CYSLTR1	194.0463032	-0.433473431	0.139849914	-3.099561653	0.001938072	0.013908386
ALG13	1323.120292	-0.289018731	0.093254327	-3.099252769	0.001940094	0.013917476
TOR3A	1846.369614	0.418891825	0.135179628	3.098779249	0.001943197	0.013934314
INTU	1152.003196	-0.561187056	0.181157522	-3.097785005	0.001949728	0.013975706
SUPT5H	8456.532991	0.237016418	0.076526885	3.097165376	0.001953808	0.013999508
GOT2	4862.327064	0.315611222	0.101919876	3.096660194	0.001957141	0.014017936
TLE4	2614.040557	-0.428881396	0.138534467	-3.09584615	0.001962522	0.014051014
LPAR5	868.9312352	-0.852770368	0.275496328	-3.095396492	0.0019655	0.014066871
NSUN5	1571.298756	0.460870385	0.148899156	3.09518466	0.001966904	0.014071457
BOLA2	557.9943308	0.512551588	0.165607316	3.094981548	0.001968251	0.014075633
NAV2	3132.252133	-0.553861825	0.178982607	-3.094500818	0.001971444	0.014090095
KIAA1755	3025.0725	-0.588707841	0.190246554	-3.094446813	0.001971803	0.014090095
CRIP2	9235.667235	0.497398265	0.160787057	3.093521793	0.00197796	0.014128616
IGFBP4	2825.959855	0.754255563	0.243840939	3.093227765	0.001979921	0.014137143
BCL2L12	349.9188529	0.558053953	0.180506919	3.091593144	0.001990855	0.014204208
CDC37	9245.151371	0.385531269	0.124700668	3.091653599	0.00199045	0.014204208
MBD3	8707.247316	0.459633674	0.148697879	3.091057354	0.001994451	0.014224357
PLA2G15	2324.82912	0.505760467	0.163631901	3.090842711	0.001995893	0.014229138
ENO3	399.7282164	0.611232671	0.197778667	3.090488378	0.001998276	0.014240616
GDF3	2.640373352	3.434553126	1.111377058	3.09035813	0.001999153	0.014241356
KANSL1L	463.2738575	-0.516894207	0.167294108	-3.089733482	0.002003362	0.014265825
PHF8	1301.643322	-0.380608405	0.123209323	-3.089120175	0.002007502	0.014289787
ERAL1	2716.158109	0.281841861	0.091261782	3.088279179	0.002013192	0.014324758
PACRGL	524.5375204	-0.317350668	0.10277903	-3.087698606	0.002017129	0.014347231
ALPK1	815.7226997	-0.570842669	0.184888374	-3.087499001	0.002018484	0.014351331
PTDSS1	2508.625558	0.330611769	0.10713933	3.08581144	0.002029975	0.014427463
DTNA	19581.01059	-0.671105488	0.217554301	-3.084772324	0.00203708	0.014466802
SCNM1	2046.246491	0.444771043	0.144178176	3.084870786	0.002036406	0.014466802
DERL3	152.5883672	-0.669693466	0.21711556	-3.084502396	0.00203893	0.014474359
RPS26	9587.393442	0.654098754	0.212068065	3.084381209	0.00203976	0.014474681
DIP2C	2813.773144	-0.545413205	0.176852092	-3.084007657	0.002042323	0.014483665
AARS1	1385.285719	0.411359661	0.133386505	3.08396761	0.002042598	0.014483665
CYFIP1	6132.008771	-0.417727654	0.135463369	-3.083694552	0.002044474	0.014491388
OTUD7A	1693.213981	-0.760452872	0.246626417	-3.083420181	0.00204636	0.01449918
CNN3	14818.96875	-0.434631567	0.140965039	-3.083257872	0.002047476	0.014501516
KCTD3	3691.316	-0.430125794	0.139538146	-3.082496121	0.002052724	0.014533097
DUSP11	672.6617216	0.437540824	0.141970857	3.081905922	0.002056798	0.01455635
RPL12	26726.95423	0.46996257	0.152506506	3.081590311	0.00205898	0.014566197
CCDC70	2.652360292	2.391595785	0.7761657	3.081295379	0.002061021	0.014575039
SDF2	2018.080146	0.335812959	0.10899163	3.081089415	0.002062447	0.014579531
APOL3	1109.029497	0.683825719	0.221969504	3.080719226	0.002065013	0.014592071
HLA-G	14.48197525	1.454831818	0.472278599	3.080452558	0.002066863	0.014599546
AASS	1155.956637	-0.653481949	0.212154245	-3.080220944	0.002068471	0.014602599
NEU3	795.1207931	0.382611327	0.12421792	3.080162072	0.00206888	0.014602599
WASF2	6823.786278	-0.310495848	0.100812392	-3.079937299	0.002070442	0.014608025
WDR45	2929.812238	0.26406563	0.08574443	3.079682618	0.002072213	0.014609339
BECN1	3403.248909	0.173922136	0.056474016	3.079684205	0.002072202	0.014609339
CLCN7	7976.615093	0.324698893	0.105436985	3.079554025	0.002073108	0.014610058
HSPB2-C11orf52	463.7333087	0.758166546	0.2462216	3.079204044	0.002075545	0.014621642
DLG1	5208.184432	-0.645567648	0.209715698	-3.078299117	0.002081858	0.014660515
BRAT1	3546.110029	0.399602411	0.12987301	3.076870326	0.002091863	0.01472534
UQCRQ	6767.951369	0.504756352	0.164058265	3.076689571	0.002093132	0.014728645
GIT2	2678.980455	-0.203759453	0.066231452	-3.076475693	0.002094634	0.01473359
SUPT3H	288.353308	-0.552423191	0.179570433	-3.076359414	0.002095451	0.014733714
DOCK1	4329.432213	-0.722505479	0.234903998	-3.075747884	0.002099753	0.014749793
SSBP2	1536.426746	-0.453734398	0.147520825	-3.075731156	0.002099871	0.014749793
LSG1	1572.457192	0.247038578	0.080319644	3.075693129	0.002100139	0.014749793
MAGOH	893.0399994	0.388047746	0.126177119	3.075420876	0.002102057	0.014757641
C1orf112	363.5242544	-0.341509709	0.111049714	-3.075286716	0.002103003	0.014758659
SLC18A1	33.72988846	1.274687809	0.414546715	3.074895449	0.002105764	0.014772408
UPB1	62.3660111	0.99761344	0.324637047	3.073011689	0.002119102	0.014860323
TMCC1	1632.613877	-0.300374667	0.097764127	-3.072442576	0.002123147	0.014877454
ZBTB48	1294.917245	0.433426477	0.141069108	3.072440806	0.002123159	0.014877454
CCDC88B	2423.68909	0.679769032	0.221295173	3.07177523	0.002127899	0.014904998
TYMP	7215.903825	0.973154332	0.316863899	3.071206079	0.002131959	0.014927767
NCF1	1279.369088	0.850993307	0.277102978	3.071036306	0.002133172	0.014930584
SLC13A3	1614.318645	-0.69143105	0.22516327	-3.070798584	0.002134871	0.014934534
CLNK	10.8716975	-0.872939545	0.284277476	-3.070730606	0.002135357	0.014934534
CISD1	1391.345855	0.404111837	0.131614952	3.07040979	0.002137653	0.014944916
CXorf65	12.07743161	1.425801602	0.464386283	3.070292242	0.002138494	0.01494513
CYB561	1502.964866	0.539213258	0.17564128	3.069968848	0.002140811	0.014955565
NEK5	109.8806024	-0.747548112	0.243516934	-3.069799297	0.002142027	0.014958472
RIOK1	716.3095671	0.314135534	0.102336336	3.069638281	0.002143182	0.014960869
CCDC155	8.571938048	-0.973198761	0.317072952	-3.06932129	0.002145457	0.014971083
SUPT4H1	3188.093836	0.274430865	0.089434123	3.068525241	0.002151182	0.015005346
TTC7A	2347.574762	-0.385071678	0.125497748	-3.068355293	0.002152405	0.015005554
HIP1	4976.011834	-0.469416343	0.152989312	-3.068295002	0.00215284	0.015005554
SOWAHD	146.0317688	0.888938361	0.28979025	3.067523357	0.002158406	0.015038663
SNRPF	1712.076189	0.491722546	0.160325199	3.067032194	0.002161956	0.015057703
UNKL	1244.230583	-0.278080389	0.090676744	-3.06672226	0.002164198	0.015057811
TNFAIP1	3403.931371	0.327437507	0.106772242	3.066691315	0.002164422	0.015057811
KLHL12	2137.65534	0.203535576	0.066367562	3.066793018	0.002163686	0.015057811
EIF2D	1738.497127	-0.195898483	0.063894687	-3.06595886	0.002169732	0.015083359
FATE1	18.34576011	1.956043948	0.637981975	3.065986227	0.002169533	0.015083359
RHOU	8572.37549	-0.599388046	0.195522954	-3.065563576	0.002172602	0.015089437
TCHP	1040.495002	-0.398061321	0.129867866	-3.065125591	0.002175786	0.015089437
DNTT	0.831781985	-2.071016209	0.675676484	-3.065100323	0.00217597	0.015089437
PROSER2	47.76619465	0.888571924	0.289904562	3.065049814	0.002176337	0.015089437
STX5	2239.290351	0.397574699	0.129706381	3.065189981	0.002175318	0.015089437
ODC1	4221.971788	0.687218578	0.224197523	3.065237155	0.002174975	0.015089437
VIPF3	5667.538412	0.35464955	0.115698842	3.065281768	0.00217465	0.015089437
ATP6V1B2	9958.11053	0.37865827	0.12355501	3.064693772	0.00217893	0.015096051
MKNK2	4140.431207	0.380688024	0.124213566	3.064786211	0.002178256	0.015096051
SMC6	926.3489606	-0.339106731	0.110661582	-3.064358235	0.002181375	0.015096284
ALDH8A1	175.6981083	-0.630360288	0.205707284	-3.064355699	0.002181394	0.015096284
PANK1	272.6260287	0.691278258	0.225587093	3.064351994	0.002181421	0.015096284
LIN37	664.9941784	0.402515092	0.131364838	3.064100696	0.002183254	0.015103299
TRAPPC4	2074.515966	0.302502393	0.098744958	3.063471785	0.002187848	0.015129402
GLO1	5194.594506	0.171348062	0.055936076	3.06328357	0.002189225	0.015133244
MCM3AP	4408.496256	-0.203441615	0.066418654	-3.063019243	0.00219116	0.015136875

RIPOR1	4281.103964	0.421082647	0.137474497	3.062987365	0.002191393	0.015136875
PIGC	1100.088127	0.308350987	0.100684623	3.062543001	0.002194649	0.015153688
AIG1	2401.249187	-0.391210921	0.127768116	-3.061882211	0.0021995	0.015181492
ZFP57	72.97727524	2.092588425	0.683488834	3.061627815	0.00220137	0.01518871
DIDO1	3020.066401	-0.226651245	0.074049255	-3.060817369	0.002207337	0.015210717
COLEC12	3063.152904	-0.688684554	0.225005435	-3.060746302	0.002207861	0.015210717
UPF3B	959.3815884	0.277050895	0.09051598	3.060795391	0.002207499	0.015210717
TGFBI	5434.0126	0.937909199	0.306413738	3.06092411	0.00220655	0.015210717
CYP2E1	227.8761925	-0.621099902	0.202936099	-3.060568842	0.00220917	0.015214046
NDE1	1501.498736	-0.559794524	0.182914843	-3.060410592	0.002210337	0.015214983
ADH5	4874.926639	0.268444123	0.087717473	3.060326687	0.002210957	0.015214983
ULBP1	173.5199087	0.991138548	0.323903398	3.059981943	0.002213503	0.015226821
OR6N1	2.215537318	3.871806389	1.265460362	3.059603052	0.002216305	0.015240407
NIT2	1617.800771	0.234570632	0.076692506	3.058586073	0.002223842	0.015286528
SIRT4	66.46553397	0.726328187	0.237629373	3.05655895	0.002238935	0.015384535
KAZN	4839.26419	-0.495914586	0.16225751	-3.056342885	0.002240549	0.015389888
TTLL4	2156.778999	-0.286251611	0.093666323	-3.056078252	0.002242527	0.015392005
FAM104A	1478.36874	0.243328721	0.079621196	3.056079721	0.002242516	0.015392005
HAL	20.25286073	1.333891502	0.436627105	3.054990142	0.002250679	0.015442207
F2RL2	164.6348018	1.086019582	0.355596237	3.054080638	0.002257514	0.015483336
ADSL	1588.530595	0.313685371	0.102716219	3.053903026	0.002258851	0.015486742
DUSP2	308.2729687	1.033888661	0.338560431	3.053778788	0.002259786	0.015487395
PTX3	1169.126879	1.275037005	0.417611634	3.053164474	0.002264418	0.015513367
DNTTIP1	1561.602798	0.379315215	0.124302147	3.051558023	0.00227657	0.015590827
PCSK5	1173.622955	0.789747264	0.258870008	3.05074841	0.002282718	0.015627119
C2orf81	383.0297968	0.522591961	0.171334074	3.050134455	0.002287389	0.015653286
UCHL3	842.9613707	0.36656956	0.120192896	3.049843812	0.002289604	0.015656814
RPS15	25790.07637	0.523704692	0.171710111	3.049935078	0.002288908	0.015656814
MRPL20	3981.06019	0.463056911	0.151839144	3.049654385	0.002291048	0.01566088
NR2C1	1104.481152	-0.27320377	0.089613027	-3.048705978	0.002298293	0.015692939
RHBDF1	989.0403598	0.537302226	0.176236064	3.048764335	0.002297847	0.015692939
CCNG1	2754.488997	0.408972396	0.134140441	3.048837424	0.002297288	0.015692939
LRRC37A2	482.9007954	-0.334866762	0.109851108	-3.048369461	0.002300869	0.015693283
OPALIN	7548.098503	-1.211928658	0.397579227	-3.04826957	0.002301634	0.015693283
NDUFC1	2297.963583	0.345197532	0.113244331	3.048254408	0.00230175	0.015693283
RPL18A	25404.22534	0.505410284	0.165794806	3.048408427	0.00230057	0.015693283
ZNF326	2015.338612	-0.383999477	0.125987457	-3.047918313	0.002304326	0.01569923
APOBEC3G	901.0403172	0.755713512	0.247943206	3.047929896	0.002304237	0.01569923
SHTN1	13010.85719	-0.735596744	0.24138682	-3.047377419	0.002308477	0.015718974
TTC13	911.3408453	-0.217112053	0.07124692	-3.047318458	0.002308929	0.015718974
PARP1	9268.790566	-0.314978675	0.103373512	-3.046995978	0.002311408	0.01572423
DNAJA2	3440.556402	0.19536227	0.064115863	3.047019289	0.002311229	0.01572423
PRDX6	13838.35862	0.398314371	0.130735632	3.046716215	0.00231356	0.015733063
FAR1	4134.350825	-0.474879685	0.155905767	-3.045940461	0.002319538	0.015767893
MFSD12	5489.067321	0.505337581	0.16591738	3.045718175	0.002321253	0.015773736
FAM193A	1979.077861	-0.262823007	0.086297903	-3.045531788	0.002322692	0.015777698
FAM214A	1504.825751	-0.415901179	0.136589063	-3.044908354	0.002327512	0.015804523
ATF3	1829.049271	0.746291066	0.245103534	3.044799292	0.002328356	0.015804523
EXOC8	823.8845056	0.234566967	0.0770572	3.044062957	0.002334063	0.015837425
ARHGEF1	6060.805583	-0.33155735	0.108933422	-3.043669657	0.002337116	0.015843998
INTS6L	562.9209748	-0.477653618	0.15693567	-3.043626852	0.002337449	0.015843998
OR6J1	59.16787885	-0.504292938	0.165689297	-3.043605981	0.002337611	0.015843998
PFN1	27447.02207	0.564428687	0.185471353	3.043212212	0.002340672	0.015858914
CAV2	1277.917545	0.580156477	0.190729108	3.041782569	0.002351817	0.015928569
XRN1	1145.969265	-0.469006226	0.154229064	-3.040971755	0.00235816	0.015954417
TUBGCP3	1171.121349	-0.318928839	0.104877591	-3.040962677	0.002358231	0.015954417
MDFI	619.0692418	1.004796311	0.330418243	3.040983156	0.00235807	0.015954417
CRISPLD1	1634.417838	-0.91568587	0.301142077	-3.040710479	0.002360207	0.015961926
RBMX	5716.26774	-0.312934203	0.102950233	-3.039664826	0.002368416	0.016011567
ST18	3669.931887	-0.910424494	0.299675089	-3.038038621	0.002381234	0.016092324
KCNK17	7.120014771	-1.372277889	0.451740139	-3.037759479	0.002383441	0.016094645
MMP21	9.173448117	-1.153915799	0.379868139	-3.037674609	0.002384112	0.016094645
UBASH3A	16.93218373	-1.283701531	0.422594998	-3.037663807	0.002384198	0.016094645
TIMM8B	2380.656785	0.523798429	0.172478961	3.036883033	0.002390382	0.016130483
PDCL3	982.8235763	0.35925845	0.118304936	3.036715634	0.00239171	0.016133535
LIPE	3124.867426	-0.739682685	0.243591191	-3.036574037	0.002392833	0.016135209
DIABLO	3032.519061	0.29366166	0.096743735	3.035459189	0.002401697	0.016183137
TPGS1	1421.419948	0.586779292	0.193307394	3.035472574	0.002401591	0.016183137
RGS1	4532.392013	-1.019990526	0.33604288	-3.035298706	0.002402976	0.016183688
C9	2.102375582	-1.32579492	0.43680941	-3.03517939	0.002403927	0.016183688
MIS18BP1	447.4216503	-0.530187047	0.174690485	-3.035008163	0.002405292	0.016183688
VSTM1	90.42947646	0.809637698	0.266764468	3.03502825	0.002405132	0.016183688
SRSF6	7396.998933	-0.23810174	0.078459723	-3.034700254	0.002407749	0.016191518
SP6	75.03618308	1.145554113	0.377492326	3.034642125	0.002408213	0.016191518
ADPRH	785.0305519	0.590283419	0.194539689	3.034257026	0.002411289	0.016206285
FEM1C	2204.016038	0.380171735	0.125298434	3.03412997	0.002412305	0.016207206
SCYL1	4706.902957	0.349561924	0.115238887	3.033367758	0.002418407	0.016242281
NSMCE1	2998.508285	0.533509358	0.17593341	3.032450506	0.002425769	0.016285789
ACAP1	354.4627388	0.747305729	0.246465521	3.03209035	0.002428665	0.016299296
RELT	1509.626113	0.415879547	0.137164349	3.031979878	0.002429554	0.016299327
GNG5	4611.598689	0.447097583	0.147478409	3.031613828	0.002432502	0.016313165
LANCL1	10518.20535	-0.586573399	0.193506916	-3.031278733	0.002435203	0.016313472
KRT15	26.29627428	1.133568141	0.373950964	3.0313283	0.002434804	0.016313472
CLCF1	625.9716613	1.12605108	0.37145796	3.03143613	0.002433934	0.016313472
NOG	149.8550795	0.749651321	0.247332977	3.030939633	0.00243794	0.01632587
FARP2	1663.762399	-0.318446812	0.105087718	-3.03029525	0.002443148	0.016342929
OGFOD2	1162.554431	0.338157906	0.111590029	3.030359504	0.002442628	0.016342929
BUD31	4475.700342	0.467513823	0.154270723	3.030476638	0.002441681	0.016342929
PROC	42.87077086	0.807913609	0.266625416	3.030144769	0.002444365	0.016345142
FRMD4B	2575.583304	-0.644700641	0.21278877	-3.029768158	0.002447415	0.0163596
AGTPBP1	2321.479384	-0.545039494	0.179926854	-3.029228167	0.002451794	0.016382929
RBM48	933.0531932	-0.251084992	0.082894323	-3.028976938	0.002453834	0.016390616
CCND3	3535.414804	0.313047229	0.103365138	3.028557154	0.002457246	0.016401516
UTP6	1609.990489	0.263916298	0.087140324	3.02863572	0.002456607	0.016401516
ACYP2	2490.128159	-0.560761505	0.185167929	-3.028394327	0.00245857	0.016401537
GADD45B	5735.635698	0.813032123	0.268474699	3.028337961	0.002459029	0.016401537
WDR83OS	4720.997765	0.438611828	0.144856588	3.027903944	0.002462563	0.016419169
FAM13C	1800.810954	-0.766061067	0.253044321	-3.027379016	0.002466844	0.016441763
FER	1010.465304	-0.551651158	0.182254605	-3.026816011	0.002471443	0.016466461
ZYX	12222.10898	0.555116626	0.18344339	3.026092279	0.002477367	0.016499961
CHCHD5	1245.563004	0.52219904	0.172584157	3.02576465	0.002480053	0.016511882
SLC26A2	1022.670234	0.654379108	0.216300241	3.025327685	0.002483639	0.016529787
HMGB1	14524.74222	-0.230791422	0.076305599	-3.024567329	0.00248989	0.016565412
G2E3	502.1899291	-0.445310086	0.147277759	-3.023607149	0.002497806	0.016606082
DMAP1	3439.143609	0.430030253	0.142222982	3.023634057	0.002497583	0.016606082
DHRS2	68.74080091	0.850887182	0.281448488	3.023243045	0.002500813	0.016620081
RAPGEF4	8284.100248	-1.238292323	0.409627822	-3.022969281	0.002503077	0.016629127
ZC3H6	902.3560069	-0.425146329	0.14064909	-3.022744972	0.002504932	0.01663546
ACD12314.1	668.2177382	0.697596472	0.230812743	3.022348174	0.002508219	0.016645287
GET4	3872.514164	0.398944109	0.131994074	3.022439547	0.002507462	0.016645287
EMG1	1506.023738	0.326209652	0.107939935	3.022140516	0.00250994	0.016650715
LRGUK	64.96727546	-1.091992624	0.361523309	-3.020531727	0.002523313	0.016727385
RASSF6	14.83706246	0.88250153	0.292161544	3.020594418	0.00252279	0.016727385
MPO	139.4860166	0.696386559	0.230570955	3.020270223	0.002525493	0.016729799
CDV3	6883.817963	0.290510906	0.096184123	3.020362374	0.002524724	0.016729799
SMS	3974.533364	0.390444181	0.129286223	3.01999836	0.002527761	0.016738807

MTA2	4949.737557	0.367406933	0.121680729	3.019434015	0.002532475	0.0167579
FMOD	602.0747145	0.78353126	0.259491179	3.019490923	0.002531999	0.0167579
ITPRIPL2	1573.634945	0.444742128	0.147313799	3.019012013	0.002536005	0.0167753
PLEKHM1	2934.397148	0.313598368	0.103888745	3.018598101	0.002539472	0.0167922
ZMAT2	4497.89423	0.265632931	0.088012046	3.018142879	0.00254329	0.0168114
SLC35B3	793.8371464	-0.335570218	0.111193193	-3.017902513	0.002545308	0.0168174
SRCIN1	11020.67602	-0.686669551	0.22754428	-3.017740336	0.00254667	0.0168217
ZNF705G	1.806498466	-1.606171311	0.532318078	-3.01731498	0.002550247	0.0168272
MFSD9	224.0546809	0.492762549	0.163306637	3.017406753	0.002549475	0.0168272
APEX2	1220.28198	0.457302385	0.15155453	3.017411527	0.002549434	0.0168272
ATP5MF	6959.173028	0.43914098	0.145581511	3.016461213	0.002557439	0.0168686
MDN1	3131.304032	-0.556380573	0.184476038	-3.016004564	0.002561294	0.0168831
KIAA0355	1710.125098	-0.357293348	0.118469732	-3.015904077	0.002562143	0.0168831
ADIPOR2	8963.726831	-0.492626295	0.163344379	-3.015875415	0.002562385	0.0168831
SLC35A2	1107.024459	0.314443854	0.104270425	3.015657154	0.00256423	0.0168832
POP5	1219.754255	0.346970443	0.11505596	3.015666839	0.002564148	0.0168832
ITB	5666.604097	0.362844818	0.12033355	3.015325469	0.002567036	0.0168896
HOMEZ	757.1722469	0.326977675	0.108435141	3.015421681	0.002566222	0.0168896
KLHDC1	297.3624128	-0.647781253	0.214862055	-3.014870421	0.002570891	0.0169089
DNMT3A	2041.186338	-0.303477839	0.100678112	-3.014337817	0.00257549	0.0169326
RPL29	21574.78833	0.469260482	0.155688123	3.01410586	0.002577379	0.0169335
SPATA20	4762.899396	0.370963879	0.123075357	3.014119865	0.00257726	0.0169335
ZRANB2	3138.018608	-0.321850686	0.106795761	-3.013702827	0.002580805	0.0169499
FCN3	31.75065345	1.211217798	0.401956048	3.013309049	0.002584156	0.0169659
OPF3	651.1824378	-0.53307391	0.176959118	-3.012412789	0.002591799	0.0170100
RNF145	3274.966126	0.335623204	0.111466555	3.010976749	0.002604088	0.0170846
STARD3	3617.879377	0.295024021	0.09799409	3.010630749	0.002607057	0.0170980
PI4K2B	494.0019104	0.467829271	0.155473738	3.009056554	0.002620603	0.0171746
SERTAD3	880.6414705	0.490368473	0.162963638	3.009066811	0.002620515	0.0171746
ZNF320	213.2710289	-0.744412354	0.24744268	-3.008423416	0.00262607	0.0172043
USP29	5.58127609	1.515244875	0.503693638	3.008266853	0.002627423	0.0172071
COBL	8407.21324	-0.72472119	0.240968883	-3.00753019	0.0026338	0.0172366
NOL9	1169.0101	0.300202305	0.099816249	3.007549463	0.002633633	0.0172366
SERPINB4	1.844187835	3.059495963	1.017457457	3.007001366	0.002638386	0.0172604
LRCH3	1822.078688	-0.332739874	0.110663635	-3.006767971	0.002640412	0.0172676
TMEM63A	10729.12179	-0.751704898	0.250017987	-3.006603279	0.002641843	0.0172708
ZCRB1	3085.860012	-0.359737253	0.119654895	-3.006456636	0.002643117	0.0172730
AMELX	0.987150437	2.409665374	0.801574752	3.006164263	0.00264566	0.0172774
PCBD1	1721.113943	0.357796066	0.119018488	3.006222578	0.002645153	0.0172774
ICE2	1355.260827	-0.301838593	0.100420281	-3.00575332	0.002649238	0.0172946
AAGAB	1744.863462	0.182353364	0.060673356	3.005493297	0.002651504	0.0173033
ZNF784	512.3295087	0.562985616	0.187371896	3.00464279	0.002658929	0.0173456
ALYREF	1977.932784	0.50367906	0.167641886	3.004494105	0.002660229	0.0173479
PTCD3	3033.437364	-0.234311607	0.078010116	-3.00360541	0.002668011	0.0173924
MYOM3	58.25683408	0.730565895	0.243238269	3.003498991	0.002668944	0.0173924
FOXO4	2786.607833	-0.653368814	0.217551684	-3.003280883	0.002670858	0.0173988
RASGRF1	2247.200457	-0.669886703	0.223132745	-3.002189128	0.002680456	0.0174551
ZNF224	1210.261814	-0.324184394	0.107994578	-3.001858046	0.002683373	0.0174679
VPS33B	968.3520249	0.260744752	0.086877991	3.001275102	0.002688516	0.0174952
ARF1	16076.4418	0.287001049	0.095630017	3.001160705	0.002689526	0.0174956
BNIPL	29.66680142	-0.510649876	0.170158591	-3.001023178	0.002690741	0.0174974
MAPRE2	8315.639674	-0.438982842	0.146306637	-3.000430134	0.002695986	0.0175191
ROM1	4508.182306	0.648061568	0.215988185	3.000449167	0.002695817	0.0175191
CFAP44	652.2418286	-0.595902022	0.198647923	-2.999789848	0.002701659	0.0175440
ALAD	9912.075443	-0.446971099	0.14900119	-2.999782063	0.002701728	0.0175440
OXT	6.073522576	1.529941862	0.510058403	2.999542507	0.002703854	0.0175517
PRS521	31.0486303	1.088415496	0.362932739	2.998945475	0.002709158	0.0175799
PHKG2	1881.062008	0.360177373	0.120150111	2.997728172	0.002720002	0.0176441
ZNF580	2968.03781	0.489271761	0.163299746	2.996157515	0.002734052	0.0177290
RNF13	7222.916186	-0.590099161	0.196987538	-2.995616716	0.002738905	0.0177542
DNAH10	145.0840433	-0.558164988	0.186392095	-2.994574351	0.002748281	0.0178087
NDUFA11	8364.504238	0.541811052	0.180985142	2.993676975	0.002756376	0.0178549
MS4A4E	151.4044121	-0.719624618	0.240412758	-2.993287973	0.002759892	0.0178598
DRAP1	7310.61085	0.536897438	0.179368079	2.993271939	0.002760037	0.0178598
CYP1B1	769.2724827	0.843572888	0.281812656	2.993381846	0.002759043	0.0178598
CASP1	1488.269879	0.825708105	0.275876712	2.993033008	0.002762199	0.0178675
TM2D1	1198.00883	-0.357506515	0.119480944	-2.992163454	0.002770079	0.0179122
MEX3B	197.8985245	0.800161479	0.267477153	2.991513364	0.002775984	0.0179440
DDX52	1064.57296	0.25680797	0.085854632	2.99119529	0.002778877	0.0179564
HS3ST5	357.8837925	-0.619885874	0.20724491	-2.991078884	0.002779937	0.0179570
VWA5B1	18.72457537	-0.970852481	0.324597075	-2.990946489	0.002781142	0.0179585
BBS9	685.0925903	-0.569620157	0.19047183	-2.990574289	0.002784534	0.0179741
POLR1E	853.5487991	0.405164625	0.135508503	2.989957211	0.002790165	0.0180041
KIAA0556	1536.599292	-0.401399475	0.13426931	-2.989510213	0.002794251	0.0180242
STX3	1389.222017	0.393509959	0.131646877	2.989132513	0.002797708	0.0180276
TOMM40L	1249.550092	0.292407188	0.097823266	2.989137442	0.002797663	0.0180276
CLN6	2026.969957	0.430934287	0.144156984	2.989340334	0.002795805	0.0180276
RFXANK	2552.178975	0.594226035	0.198828398	2.988637649	0.002802242	0.0180505
TBL2	1301.641016	0.30952361	0.103620944	2.987075769	0.002816599	0.0181303
LPCAT1	4288.18745	0.480075584	0.160714007	2.987142144	0.002815988	0.0181303
ACAD9	2048.480898	0.224620293	0.075203501	2.986832945	0.002818837	0.0181383
LPCAT2	1121.437384	-0.646321475	0.216447711	-2.986039776	0.002826159	0.0181759
RPS4X	27526.30767	0.406389587	0.136103812	2.985879545	0.00282764	0.0181759
BLK	11.58510309	1.239190983	0.415013902	2.985902348	0.002827429	0.0181759
ASCC3	1398.3652	-0.343471809	0.115057883	-2.98520884	0.002833848	0.0182095
RNASE1	38577.71394	0.828655918	0.277659474	2.984432352	0.00284105	0.0182494
ZNF599	342.9175899	-0.306654831	0.102756222	-2.984294514	0.00284233	0.0182513
EML3	4952.845086	0.442142035	0.148177792	2.983861677	0.002846354	0.0182707
PARD3B	628.7546224	-0.877710351	0.294259162	-2.982780028	0.002856432	0.0183291
EIF2S2	5454.723699	0.290575685	0.097425938	2.982528997	0.002858776	0.0183313
UQCR11	9531.697801	0.566707555	0.190008182	2.982542905	0.002858646	0.0183313
CMTM6	2347.964277	0.555766249	0.186349216	2.982391131	0.002860063	0.0183332
PIK3C3	2163.807419	-0.31367733	0.105213883	-2.981330221	0.002869991	0.0183882
OSBPL9	2583.234474	-0.328088985	0.110050373	-2.981261906	0.002870632	0.0183882
KIFC3	3361.818175	0.32039556	0.107483175	2.980890345	0.002874117	0.0184041
COPS6	5896.078135	0.364461018	0.122276126	2.980639217	0.002876475	0.0184128
BCAS3	1362.076219	-0.549273201	0.184297038	-2.980369148	0.002879012	0.0184226
XAB2	3850.406058	0.438212131	0.147046216	2.980097986	0.002881562	0.0184325
EIF3D	5400.033822	0.332453085	0.111562759	2.979964699	0.002882816	0.0184342
CMPK2	612.6102297	-0.576700791	0.1935379	-2.979782199	0.002884534	0.0184388
ADM5	108.4824063	0.833106993	0.279613125	2.979498879	0.002887203	0.0184494
POLR3G	292.8866089	-0.41480284	0.139235316	-2.97914962	0.002890496	0.0184641
RAPGEF6	1168.971602	-0.578582113	0.194230005	-2.978881728	0.002893024	0.0184674
SUPT16H	3998.228686	0.26700864	0.0896331	2.978906695	0.002892789	0.0184674
IFI27L2	4903.135971	0.652437202	0.219086774	2.977985337	0.002901499	0.0185153
IFIT1	3800.921085	-0.623403683	0.209388001	-2.977265556	0.00290832	0.0185343
TULP4	3312.381931	-0.553331469	0.185874438	-2.976909984	0.002911695	0.0185343
CD320	2180.200512	0.544798096	0.183013516	2.976818914	0.00291256	0.0185343
HK1	6725.946913	0.448035722	0.150498218	2.977016784	0.002910681	0.0185343
RALBP1	4735.606885	0.153695147	0.051626524	2.977057801	0.002910291	0.0185343
CTHRC1	533.7300381	1.079968027	0.362744063	2.977217652	0.002908774	0.0185343
RPL4	40770.12469	0.290085495	0.097429418	2.977391237	0.002907128	0.0185343
FUT2	23.44431424	0.756116777	0.2539408	2.977530859	0.002905804	0.0185343
TMBIM1	10910.51119	0.487604517	0.16385398	2.975847872	0.002921798	0.0185867
SMU1	3105.604979	0.150984551	0.050740149	2.975642623	0.002923754	0.0185927
HDAC4	1559.997572	-0.409036801	0.137533728	-2.974083577	0.00293865	0.0186746

ATF4	15758.43658	0.347863263	0.116961541	2.974167928	0.002937842	0.018674615
SYTL4	788.9957998	0.643754267	0.216486774	2.973642484	0.002942877	0.018695032
AFG3L2	2820.156754	0.202585698	0.068130265	2.97350519	0.002944194	0.018696953
OTX2	1.425652434	-2.356695479	0.792894294	-2.97226944	0.002956071	0.018765911
SNRPD1	2025.266466	0.346664648	0.116637725	2.972148571	0.002957235	0.018766836
JAKMIP3	1486.558967	-0.769552163	0.258969844	-2.971589857	0.002962622	0.018782377
GNAI1	3619.270584	-0.552434517	0.185906151	-2.971577404	0.002962742	0.018782377
REX1BD	4260.557804	0.54954696	0.184932144	2.971614071	0.002962388	0.018782377
C6orf89	6457.386225	0.158956131	0.053499648	2.971162195	0.002966751	0.018801322
LILRA4	760.7566231	1.186005653	0.399302319	2.970194758	0.00297611	0.018854153
CD40LG	9.060806542	-1.10370618	0.371627905	-2.969922782	0.002978746	0.018864369
SPATA12	38.46322376	0.909900915	0.306384707	2.96979873	0.002979949	0.018865505
MEP1B	3.51111873	-1.125972028	0.37922762	-2.969119253	0.002986547	0.018898762
PYM1	1072.04098	0.357093304	0.120272046	2.969046546	0.002987253	0.018898762
HIP1R	10995.38069	-0.517700653	0.174381328	-2.968784892	0.002989798	0.018901968
MMP14	6881.95115	0.775642414	0.261266075	2.968783506	0.002989812	0.018901968
UQCR10	5595.682243	0.434071516	0.146229195	2.968432639	0.002993227	0.018917072
ARL6IP4	9194.59843	0.509523718	0.17169336	2.967637873	0.003000977	0.018959547
CNP	82461.60252	-0.752101557	0.253474605	-2.96716729	0.003005574	0.018960427
TMEM177	483.976312	0.325208561	0.109604961	2.967097085	0.00300626	0.018960427
MRPL18	2273.835529	0.245455038	0.082720313	2.96728854	0.003004389	0.018960427
SERPINB8	1088.346047	0.597437306	0.201333349	2.96740361	0.003003264	0.018960427
SCX	230.2780004	0.666251326	0.224516007	2.96750033	0.00300232	0.018960427
SLC25A37	3015.480236	0.466135669	0.157107571	2.966984115	0.003007365	0.018960908
RNF216	2641.221395	-0.256771288	0.086562859	-2.966298585	0.003014077	0.018996728
RNASEH2C	2833.905978	0.453513721	0.152895933	2.966159482	0.003015441	0.018998823
SLTM	3780.884722	-0.283860725	0.095710995	-2.965811044	0.003018859	0.019004112
VXN	5416.47018	-0.625922359	0.211046748	-2.96579959	0.003018971	0.019004112
ZNF431	643.0437137	-0.439181319	0.148083973	-2.965758611	0.003019374	0.019004112
ZBTB9	542.7522853	0.325348175	0.10972709	2.965067053	0.00302617	0.019033884
ARL4C	3783.12597	0.615359779	0.207534191	2.965100713	0.003025839	0.019033884
CENPP	280.6029783	-0.478466972	0.161374786	-2.964942562	0.003027394	0.019035091
FGF16	3.38426829	1.985502868	0.669746513	2.964558725	0.003031174	0.019052354
XBP1	2908.178818	0.495938353	0.167302712	2.964317471	0.003033551	0.019060798
MAN1C1	4611.149982	-0.646166103	0.218010594	-2.963920656	0.003037466	0.019072388
POPDC2	185.6469121	0.619068736	0.208861002	2.964022623	0.00303646	0.019072388
SMCO4	483.442296	0.635830007	0.214556867	2.963456806	0.003042048	0.01909465
TOMM6	4224.203833	0.387856202	0.130943565	2.9620104	0.003056375	0.019178048
CACFD1	1661.244466	0.425406938	0.143631565	2.961792823	0.003058535	0.019185073
PLXNB2	10101.28372	0.419544125	0.1416588	2.961652393	0.00305993	0.019187293
NUDT6	379.1430769	-0.257745121	0.087040958	-2.961193483	0.003064494	0.019209371
ATP5F1E	16670.63913	0.545933009	0.184376725	2.960964882	0.003066769	0.019210567
ANKRD37	252.0196116	0.524984879	0.177301266	2.960976483	0.003066654	0.019210567
MRPS21	4011.157252	0.362510685	0.122445403	2.960590395	0.0030705	0.019227402
MAGEC3	51.56491689	-1.122226595	0.379152638	-2.959827999	0.003078108	0.019268499
RGCC	5747.754737	-0.56096442	0.189539251	-2.959621381	0.003080173	0.019274878
AOX1	167.8899242	0.874963513	0.295653243	2.959424716	0.00308214	0.019280637
GJC3	32.42809584	1.030480858	0.348260161	2.95893982	0.003086994	0.019304448
DNPH1	1678.265324	0.42250991	0.142812836	2.958486947	0.003091533	0.019326278
PPP1R7	3558.941565	0.390437936	0.131981635	2.958274742	0.003093663	0.019333031
LARP7	1947.958935	-0.195525735	0.066103208	-2.957885735	0.003097569	0.019345039
FYB1	1614.396382	-0.748079157	0.252911066	-2.957874362	0.003097684	0.019345039
PAIP2B	9710.61987	-1.042429679	0.352451565	-2.957653711	0.003099902	0.019352332
ADAM12	574.6995972	-0.879404309	0.29736561	-2.957316779	0.003103291	0.019357657
C21orf91	1560.008591	-0.734893474	0.248503083	-2.957281119	0.00310365	0.019357657
RFTN1	2067.001885	-0.485538739	0.16418902	-2.957193713	0.00310453	0.019357657
S100A5	4.059464902	1.685558425	0.569993951	2.957151427	0.003104956	0.019357657
MCF2L	5324.908519	-0.592683011	0.200466808	-2.956514434	0.003111377	0.019388793
SOD3	2231.41344	0.668360203	0.226068704	2.956447277	0.003112054	0.019388793
TCFL5	2012.977121	-0.603997777	0.204312723	-2.956241625	0.00311413	0.019395169
RPL10L	1.995005317	-3.26300717	1.104063118	-2.955453466	0.003122098	0.019438224
SERPINA11	0.929649168	-2.324792066	0.787297154	-2.952877519	0.003148269	0.019594542
TJP1	7638.473571	-0.491966776	0.166632213	-2.952410984	0.00315303	0.01961755
POLR3K	588.1318431	0.316150251	0.107097179	2.951994194	0.003157289	0.019637419
PRPF38B	2372.62838	-0.306346131	0.103790306	-2.95158713	0.003161453	0.019656688
ABCA9	375.2875706	-0.797103586	0.270125442	-2.950864537	0.003168859	0.019696086
COA5	2009.161384	-0.284578462	0.096445853	-2.950655236	0.003171007	0.019702791
RPF1	1321.308782	0.251713272	0.085315858	2.950369083	0.003173945	0.019714404
TWNK	419.8988874	0.45972286	0.155842792	2.949914166	0.003178622	0.019736802
VGLL4	3406.125724	0.260290445	0.088242525	2.94971665	0.003180655	0.019742771
GPATCH8	1013.032763	0.392289412	0.13299914	2.949563523	0.003182231	0.019745907
DBP	1334.845695	-0.588241882	0.19946579	-2.949086563	0.003187147	0.019763099
OTUD1	738.4417792	0.392060609	0.132941903	2.949112361	0.003186881	0.019763099
NAGLU	3217.883448	0.506327668	0.171711664	2.948708638	0.003191047	0.019780625
DPYD	1040.654264	-0.708410212	0.240262344	-2.948486224	0.003193344	0.019788208
SOC1	1809.752006	1.328990429	0.450869909	2.947613943	0.003202367	0.019837453
MRC1	942.1734803	0.967470253	0.328315301	2.946771747	0.003211101	0.019884875
CEP57L1	362.6311001	-0.289646654	0.0983002	-2.946552043	0.003213383	0.019892322
TRRAP	2590.162242	-0.462013909	0.156858127	-2.945425375	0.003225109	0.019958207
THOC5	1118.994678	0.351281986	0.119270777	2.945247728	0.003226962	0.019962967
PTGS2	286.2560754	1.071766784	0.363923062	2.94503673	0.003229163	0.019969882
ZNF605	855.9940009	-0.427347717	0.145121762	-2.944752805	0.003232128	0.019981511
NPHP3-ACAD11	282.4327645	-1.150153409	0.390790323	-2.943147105	0.0032494	0.020073952
ACD05324.3	8.018031781	-1.219980613	0.414519962	-2.943116679	0.003249259	0.020073952
MED15	4564.406296	0.265351861	0.090174937	2.942634275	0.003254326	0.020098518
LMF2	4868.351816	0.384324014	0.130613371	2.94245536	0.003256207	0.020103398
CCDC14	2008.845124	-0.514307994	0.17480555	-2.942171988	0.003259189	0.020115066
SRSF5	12235.29179	-0.23615754	0.080293161	-2.941191216	0.003269526	0.020172113
PMM1	2079.289528	0.329595137	0.112090429	2.940439592	0.003277469	0.020200828
TMEM99	303.0124004	0.337861683	0.114901058	2.940457525	0.003277279	0.020200828
POLR3C	1090.585023	0.245626173	0.083533118	2.940464556	0.003277205	0.020200828
ASAH2B	275.3470791	0.506350949	0.172232301	2.93993023	0.003282862	0.020227301
STARD8	753.0682436	-0.485029958	0.165007068	-2.939449585	0.003287958	0.020245162
CCR3	9.325171614	1.488615566	0.506425348	2.939457063	0.003287878	0.020245162
ARG1	13.68127868	1.554821748	0.529229176	2.937898776	0.003304449	0.02033991
CLTRN	50.28602422	0.845459015	0.287806779	2.937592423	0.003307716	0.020353219
MRPL47	1550.819034	0.30926035	0.10529851	2.936986938	0.003314181	0.020386193
CHPF2	2692.474559	0.420327486	0.143131639	2.936649702	0.003317786	0.020401564
SPTBN1	31653.16461	-0.491690994	0.167442541	-2.936475942	0.003319646	0.020405564
AC116366.3	1463.982285	-0.361002959	0.122941416	-2.936381983	0.003320651	0.020405564
PML	2940.332512	0.409457964	0.139461086	2.936001541	0.003324727	0.020423796
CCDC65	94.96609082	-0.735798394	0.250629047	-2.935806531	0.003326817	0.020429829
MPP1	3005.534361	0.445133132	0.151640905	2.935442332	0.003330725	0.020447013
DLEC1	318.5219844	-0.803492828	0.273779502	-2.934817334	0.003337441	0.020481418
STAG1	1265.634837	-0.42567643	0.145057948	-2.934526746	0.003340568	0.020493782
PTPDC1	1061.971153	-0.524610916	0.178793996	-2.934170574	0.003344404	0.020503638
RSPH10B	34.74954709	-0.71809319	0.244743221	-2.934067739	0.003345512	0.020503638
CFB	1537.445543	0.922350523	0.314355413	2.934100977	0.003345154	0.020503638
DHRS4	1105.597223	0.439531973	0.149850899	2.933128701	0.003355648	0.020558919
PIH1D1	2826.193345	0.393105068	0.134034357	2.932867932	0.003358467	0.020569356
ATF7	2380.25311	-0.327373706	0.111630552	-2.932653298	0.00336079	0.020569908
AL162231.1	585.0319908	0.577374372	0.19687633	2.932675405	0.00336055	0.020569908
ZNF768	2720.508289	0.314397802	0.107214298	2.932424196	0.00336327	0.020578256
CXCL12	1159.61935	-0.47109561	0.16066602	-2.932142159	0.003366326	0.020590118
C2orf92	428.3644448	-0.448853693	0.153101156	-2.931745942	0.003370624	0.020603309
DIP2B	5866.649823	-0.59254823	0.202115058	-2.931737178	0.003370719	0.020603309

CWC27	935.7151626	-0.374435902	0.127733937	-2.931373689	0.003374666	0.020616408
CDKL3	293.1302715	-0.270916005	0.092420725	-2.931333792	0.003375099	0.020616408
ZC3H7B	7238.355107	-0.300174448	0.102440886	-2.930221134	0.003387209	0.020676671
ALDOA	54794.48509	0.451579835	0.154108264	2.930276564	0.003386604	0.020676671
APBB2	3482.87884	-0.518588548	0.177028878	-2.929400858	0.003396161	0.020724456
CCNE2	700.3601696	-0.817072662	0.278934204	-2.929266648	0.003397628	0.020726544
GRID1	1581.639462	-0.650655938	0.222199597	-2.928249856	0.00340876	0.020784984
ZNF565	253.208683	-0.358129555	0.122304251	-2.928185678	0.003409464	0.020784984
NCAPD3	786.7974072	-0.361376895	0.123428074	-2.927833874	0.003413324	0.020798853
ERBIN	8865.630598	-0.553518239	0.189057794	-2.92777265	0.003413996	0.020798853
TLNRD1	1387.009258	0.46783479	0.159804214	2.927549776	0.003416444	0.020806887
COQ3	301.0140886	0.397986681	0.13597091	2.92699872	0.003422503	0.020836903
TUT4	1637.863293	-0.510552982	0.174462614	-2.926432034	0.003428744	0.020868007
MYO6	4231.603344	-0.47497533	0.162359133	-2.925461109	0.003439462	0.020908053
ATG4C	1452.226901	-0.500465119	0.171073861	-2.925432997	0.003439772	0.020908053
CDC37L1	967.3149541	0.252410111	0.086287573	2.925219715	0.003442131	0.020908053
DDX56	3205.676095	0.31942494	0.109193371	2.925314383	0.003441084	0.020908053
ZNF48	849.5741003	0.376274986	0.128622426	2.92542287	0.003439884	0.020908053
MCTS1	1150.962054	0.327038122	0.111780537	2.925716139	0.003436644	0.020908053
SPATC1	37.11319148	1.270003295	0.434174661	2.925097685	0.003443481	0.020909362
SMOX	6500.718713	0.469560549	0.16054394	2.924810168	0.003446664	0.020921796
FKBPL	381.969783	0.474741521	0.162424951	2.922836165	0.00346859	0.021047959
SPOCK3	5849.340907	-0.982378867	0.336345952	-2.920739378	0.003492018	0.021169211
CGB5	2.822452933	3.139226192	1.074798466	2.920757976	0.0034918	0.021169211
ZMYND19	956.8770593	0.367201043	0.125720725	2.920767784	0.0034917	0.021169211
PLB1	533.365418	-0.579047165	0.198289518	-2.920210661	0.003497948	0.02119122
STUB1	7210.053013	0.439319262	0.150437901	2.920269816	0.003497284	0.02119122
SHBG	46.69044786	0.631421941	0.216277951	2.919492898	0.003506014	0.021233102
RELA	3656.23026	0.349707155	0.119793687	2.919245286	0.0035088	0.021242995
ERCC1	4981.398418	0.339281983	0.116238397	2.918846022	0.003513297	0.021263236
MRPL38	3533.160734	0.417253878	0.142984484	2.918175924	0.003520856	0.021301991
HINT2	1896.491828	0.515546458	0.176719236	2.917319419	0.00353054	0.021353569
ATP11A	3245.853536	-0.555508552	0.190467327	-2.916555614	0.003539196	0.0213989
CPSF6	2730.46571	-0.437831228	0.150133223	-2.916284742	0.003542271	0.021410464
MT3	31406.93363	0.92070594	0.315728685	2.916130154	0.003544026	0.021414052
HIST1H2BK	347.902297	0.790392652	0.271055881	2.915976766	0.003545769	0.021417561
ZNF236	644.6532403	-0.565343642	0.193918073	-2.915373663	0.003552629	0.021451967
NID1	1144.25853	-0.735595897	0.25235427	-2.914933432	0.003557644	0.021475213
TPM3	11288.09945	0.222932499	0.076483858	2.91476537	0.00355956	0.021479744
JOSD1	2863.853294	0.227736508	0.078135048	2.9146524	0.003560849	0.021480487
UVSSA	2293.163522	-0.48713107	0.167151622	-2.914306571	0.003564796	0.021497262
RAB7B	515.6267799	0.677559228	0.232506343	2.914153742	0.003566542	0.021500754
VPS26A	2238.562909	0.276220799	0.094794319	2.913896114	0.003569487	0.021504436
ZNF598	2114.628565	0.358964541	0.123189796	2.913914576	0.003569276	0.021504436
PHYKPL	1973.668564	-0.296697082	0.101870544	-2.91249138	0.003585581	0.021587282
FITM2	819.3204913	0.266436033	0.091478403	2.912556662	0.003584832	0.021587282
XPO4	1000.407932	-0.363012405	0.124644256	-2.912387748	0.003586771	0.021587394
RAD54L2	1695.191927	-0.304443539	0.104538703	-2.912256695	0.003588276	0.021589403
POGK	4513.677953	-0.286873603	0.098512109	-2.912064383	0.003590486	0.02159565
MREG	408.1097377	0.574491857	0.197288139	2.911943215	0.003591879	0.02159698
LSM4	4028.503504	0.346825813	0.119121242	2.911536233	0.003596562	0.021618082
FREM1	312.7888719	-1.036211146	0.355978862	-2.910878304	0.003604144	0.021642477
NXF1	5054.512268	0.319660087	0.109813316	2.910941019	0.00360342	0.021642477
TMEM167B	2507.472847	0.167803037	0.057644975	2.910974211	0.003603038	0.021642477
RHOBTB1	935.4769765	-0.323385897	0.111106137	-2.910603371	0.003607316	0.021654472
AC090360.1	166.2909402	-0.513015621	0.176286118	-2.910130572	0.003612778	0.021680197
JMJD8	2719.842466	0.346858677	0.119255662	2.908530044	0.003631323	0.021784391
CHMP3	3936.421041	0.205904573	0.070802453	2.90815593	0.00363567	0.021803372
OFD1	1445.244479	-0.333228558	0.114590805	-2.907986886	0.003637636	0.021808065
PDE1C	2965.442706	-0.847859666	0.291595886	-2.907653044	0.003641521	0.021817163
PSTPIP2	349.9289119	0.876122232	0.301307669	2.907732929	0.003640591	0.021817163
UBE2S	3572.654022	0.611485731	0.210312796	2.907506068	0.003643233	0.021820324
YTHDC2	1394.529038	-0.403600648	0.138868319	-2.90635511	0.003656662	0.02188653
ATIC	2975.614757	0.274212524	0.094347722	2.906403219	0.0036561	0.02188653
EIF4EBP1	1535.729281	0.775958278	0.267015232	2.906044996	0.003660288	0.02190112
KMT2C	4125.104517	-0.589996899	0.203040043	-2.905815475	0.003662974	0.021902968
DOLK	1068.337067	0.382427681	0.1316046	2.905883838	0.003662174	0.021902968
AARD	37.62087249	0.898888299	0.309384474	2.905408561	0.00366774	0.021924353
DUOX2	51.96982878	-0.912178362	0.313974844	-2.90525938	0.003669489	0.021927694
EDA	188.9435893	-0.539777304	0.185807193	-2.905039873	0.003672063	0.021935965
TMEM161B	564.1062633	-0.379730638	0.130734383	-2.904596553	0.003677268	0.021959937
MTBP	190.5047957	-0.579347363	0.199555785	-2.903185005	0.003693884	0.022052018
CELA2A	4.798868554	-1.291839147	0.445094614	-2.902392222	0.003703246	0.022100749
TSNARE1	794.3980844	-0.328542602	0.113219999	-2.901807143	0.003710169	0.022127734
ADAD2	117.4432703	1.214773111	0.418617269	2.901870521	0.003709418	0.022127734
AL512506.3	37.50130906	-1.141942062	0.393731475	-2.90030677	0.003727976	0.022226746
IDO1	41.24360777	1.555846676	0.536525493	2.89985601	0.003733341	0.02224434
TIGAR	817.6498313	0.415041933	0.14312137	2.899929843	0.003732462	0.02224434
PIGL	545.484502	-0.293369691	0.101182951	-2.899398437	0.003738794	0.022250935
TPP2	1723.778331	-0.266140134	0.091795987	-2.899256726	0.003740485	0.022250935
LRRC8E	42.36311401	1.227872409	0.423512041	2.8992621	0.003740421	0.022250935
KLHDC7A	142.1899951	1.402420989	0.483679399	2.899484644	0.003737767	0.022250935
KLF11	515.0531644	0.486968034	0.167945804	2.899554623	0.003736932	0.022250935
SUCLG2	1347.359376	-0.442989405	0.152799659	-2.899151785	0.003741737	0.022251201
VPS4A	5632.749108	0.351779682	0.121355856	2.89874501	0.003746595	0.0222729
ANKS6	1798.830348	-0.296191763	0.102187577	-2.898510474	0.003749398	0.022282378
SCRN3	1176.358401	-0.400345367	0.138150641	-2.897890041	0.003756823	0.022319306
NOL4L	2107.18637	-0.317491781	0.109585823	-2.897197585	0.003765125	0.022361423
ELP5	1856.884232	0.251573683	0.086854337	2.896501113	0.003773493	0.022403899
PRR29	165.6902318	-1.003180602	0.346369533	-2.896272638	0.003776242	0.022412998
GPHN	1201.010659	-0.59989805	0.207138403	-2.896121829	0.003778057	0.022416552
OR8G5	1.202892247	3.055816315	1.055368358	2.89549738	0.003785582	0.022453971
ZNF585A	771.2096131	-0.260195104	0.089898514	-2.89432041	0.003799802	0.022531066
SHBP5L	2254.33156	0.309764437	0.107043587	2.893815921	0.003805912	0.022560037
SRSF11	6214.002925	-0.316307731	0.109316498	-2.893504056	0.003809694	0.022575191
ZNF362	1900.496288	-0.309973959	0.107150341	-2.892888229	0.003817171	0.022609195
TRMT112	4411.916406	0.382333863	0.132170669	2.892728512	0.003819113	0.022609195
PTCRA	116.6759447	1.012992716	0.350177753	2.892795752	0.003818295	0.022609195
C10orf143	178.3884152	-0.342038687	0.118254593	-2.892392418	0.003823201	0.02262613
ZNF334	830.3740089	-0.359330502	0.124237812	-2.892279711	0.003824573	0.022626983
PPP1R3E	1623.413943	-0.453345006	0.156749438	-2.892163517	0.003825988	0.022628085
RAB1B	10222.35132	0.321395819	0.111145604	2.891664689	0.003832067	0.022656773
SLCO3A1	3992.224	-0.604599147	0.209122571	-2.891123343	0.003838674	0.022679269
CERK	2566.931255	0.356596082	0.123344811	2.89105054	0.003839564	0.022679269
LIPH	24.5551406	0.941193663	0.325535727	2.891214656	0.003837559	0.022679269
KIF13A	2761.149662	-0.374062241	0.129393983	-2.890878165	0.00384167	0.02268099
NAA40	1279.604233	-0.299816872	0.103713245	-2.890825291	0.003842317	0.02268099
TIMD4	19.07505263	-0.91647843	0.317041901	-2.89071705	0.00384364	0.022681538
FITM1	28.42664398	0.713638191	0.24689475	2.890454638	0.00384685	0.022693216
RIPOR2	780.3093274	0.679067572	0.234967003	2.890055046	0.003851744	0.022714811
ZNF574	998.5904434	0.35676947	0.123478164	2.889332489	0.003860606	0.022759793
ECE1	5882.395535	0.447627365	0.154943831	2.888965393	0.003865116	0.022764533
ALKBH4	947.5654738	0.352718862	0.12208989	2.889009588	0.003864573	0.022764533
NKAP	1293.732814	0.219230002	0.075880629	2.889143197	0.003862931	0.022764533
IQCK	813.0641903	-0.399633378	0.138408148	-2.887354412	0.003884964	0.022874115
COX5A	5234.262706	0.37011541	0.128210209	2.886785802	0.003891991	0.022908176

UNC5C	1531.237582	-0.873805415	0.302714098	-2.886569937	0.003894662	0.022916578
TRIM45	466.1539831	-0.368835426	0.12785948	-2.884693622	0.003917947	0.023046235
FOXN3	2259.369504	-0.358400108	0.124255616	-2.884377532	0.003921883	0.023062022
PYCARD	1258.23211	0.791465214	0.274411159	2.884231153	0.003923706	0.023065385
IFRD2	1593.267928	0.39396631	0.136618441	2.88369789	0.003930356	0.023097109
FBXO31	2321.48739	0.335185248	0.116262629	2.883000769	0.003939065	0.023126163
ECSCR	883.497769	0.793323751	0.275164775	2.883086144	0.003937997	0.023126163
TMX4	3822.501932	0.310248067	0.107607196	2.883153534	0.003937155	0.023126163
LRRC59	3393.835289	0.347888265	0.120676963	2.882805923	0.003941502	0.023133102
GJC1	309.5337801	-0.547689056	0.190036483	-2.882020587	0.003951339	0.023183454
TMEM72	5.039614617	1.530119262	0.530943631	2.881886462	0.003953021	0.023185943
VPS13B	1428.78287	-0.65415139	0.227021357	-2.881453094	0.003958461	0.023203081
LGALSL	712.4711648	0.397850392	0.138069374	2.881525284	0.003957555	0.023203081
TCEAL9	2271.527762	0.329333852	0.114306691	2.881142371	0.003962366	0.023218584
ARMC2	225.6948932	-0.415501818	0.14423567	-2.880714726	0.003967746	0.023240016
ZDHHC24	1686.789368	0.42290419	0.146808539	2.88065118	0.003968546	0.023240016
FCGRT	11390.4869	0.643589863	0.223433819	2.880449643	0.003971084	0.023247492
EDEM1	1453.58051	0.445418524	0.154642838	2.8803049	0.003972908	0.023250782
PLG	28.05732059	-0.717222105	0.249030918	-2.880052444	0.00397609	0.023262021
CCDC82	2444.450443	-0.510965145	0.177431439	-2.879789217	0.003979411	0.023274062
LCMT1	1871.092253	0.362359835	0.125849841	2.879303093	0.003985551	0.023302576
FAM166B	32.20609626	-0.810727319	0.281614069	-2.878859436	0.003991162	0.0233279
THBS2	3340.957738	-0.457692792	0.159038888	-2.877867157	0.004003737	0.023394061
CTBP2	1778.154529	-0.268361231	0.093259462	-2.877576445	0.004007428	0.023408206
GATA2	227.5402575	0.68969562	0.239718201	2.877109948	0.004013357	0.023435413
ANO1	83.79005529	-0.952998948	0.331249164	-2.876985217	0.004014944	0.023437252
POLR2J	4528.940528	0.490431352	0.170483614	2.876706682	0.004018489	0.023450519
C10orf82	30.73394887	0.963743724	0.335037266	2.876526948	0.004020779	0.023456451
TLE3	2542.30965	0.439710969	0.152870827	2.876356313	0.004022953	0.02346171
AGO2	2576.975638	-0.422908862	0.147049424	-2.875964088	0.004027955	0.023483451
CASS4	193.0645489	-0.813812473	0.283002157	-2.875640527	0.004032086	0.0235001
MDGA1	1362.429756	0.47850922	0.166432544	2.875094073	0.004039071	0.023533369
PCP2	15.45725473	1.156229018	0.402192919	2.874811972	0.004042682	0.02354698
ADAM28	1245.193984	-0.756747842	0.263259689	-2.874529875	0.004046295	0.023560559
TRAF3IP2	1361.427074	0.464076843	0.16146263	2.874205901	0.004050448	0.023577292
TTC29	25.5577242	-1.125300098	0.391613351	-2.87349779	0.004059539	0.023598411
PDLIM3	1693.622654	-0.537472602	0.187049747	-2.873420624	0.004060531	0.023598411
GAPDH	196509.9123	0.474845978	0.165260095	2.873325093	0.004061759	0.023598411
SIRPD	14.50355674	1.194683515	0.41577909	2.873361227	0.004061295	0.023598411
PRDX1	27422.13463	0.444347797	0.154629179	2.873634851	0.004057778	0.023598411
PHOSPHO1	132.9568854	1.243350384	0.432648363	2.873812756	0.004055493	0.023598411
TMEM235	3202.388	-0.952616917	0.33155641	-2.873166948	0.004063793	0.023599373
ZNF839	744.7369027	-0.196010575	0.068229325	-2.872820067	0.004068258	0.023599373
C10orf90	1329.7562	-0.792375582	0.275818556	-2.872814625	0.004068328	0.023599373
TNFAIP6	315.9802838	0.766952464	0.266962025	2.872889744	0.00406736	0.023599373
KLF16	1813.212262	0.40132063	0.139688487	2.872968559	0.004066346	0.023599373
TMEM168	1241.855016	-0.271482412	0.09453988	-2.871617891	0.004083764	0.023680605
IFT172	1718.424304	-0.35843015	0.124822015	-2.871529912	0.004084901	0.023680605
EMD	2650.216344	0.288077373	0.100327006	2.871384128	0.004086786	0.0236848
CXCL8	1313.602517	1.288192648	0.448666952	2.871155634	0.004089741	0.023693757
CD38	1095.492924	-0.595918209	0.207563501	-2.871016377	0.004091543	0.023696748
ZNF668	751.4797203	0.353052474	0.122998842	2.870372334	0.004099887	0.023737613
GTF2IRD2B	1550.294473	-0.305994026	0.106630901	-2.869656193	0.004109183	0.023783963
CITED2	1824.331832	0.660813127	0.230296834	2.869397361	0.004112548	0.023795964
CLASP2	7951.41409	-0.576355996	0.200908332	-2.868751093	0.00412096	0.023837151
ENPEP	159.1882723	-0.894906759	0.311966427	-2.868599572	0.004122934	0.02383959
PRPF4	1171.751625	0.305207661	0.106398993	2.868520216	0.004123968	0.02383959
TRMT11	568.1791047	-0.412066599	0.143677741	-2.867991914	0.004130861	0.023871946
AKR1B1	7992.495997	0.404510418	0.141091502	2.867007658	0.00414373	0.023938808
FAM192A	5487.474139	-0.231772006	0.08084672	-2.866807793	0.004146347	0.023946424
RTCB	3542.809451	0.242429754	0.084597946	2.865669495	0.004161284	0.0240251
UPK3B	116.246639	0.637164173	0.222387975	2.865101738	0.004168753	0.024060741
FOSL2	3223.978279	0.681005338	0.237708229	2.864879108	0.004171685	0.024070124
PLAG1	162.6940674	-0.473239418	0.165209749	-2.864476349	0.004176993	0.024093212
NAIP	2137.803731	-0.572586679	0.199934298	-2.863874212	0.004184942	0.024128551
CCDC102B	314.3426466	-0.448396534	0.15657321	-2.86381389	0.004185739	0.024128551
CD1D	135.5370241	0.910479996	0.317986094	2.863269849	0.004192933	0.024147363
ZNF442	136.4725511	0.366714681	0.128071353	2.863362284	0.00419171	0.024147363
NDUFV2	4102.616488	0.367332572	0.12828535	2.863402337	0.00419118	0.024147363
BAMBI	1110.155445	0.459792315	0.160617594	2.862652239	0.004201114	0.024186915
CCL21	1.68652716	-1.953442676	0.682449818	-2.862397532	0.004204492	0.024198807
PPP1R3G	279.3445491	0.468572009	0.163726219	2.861924077	0.004210778	0.024219857
PPP1R18	3526.933968	0.55050295	0.192350437	2.861979204	0.004210045	0.024219857
HK3	802.2824974	0.919644745	0.321358833	2.861737884	0.004213252	0.024226527
NARS	6195.597667	0.162506603	0.056798827	2.861090849	0.004221861	0.024268455
DLL1	867.3440792	-0.621036727	0.217089802	-2.860736526	0.004226581	0.024288017
OCLN	619.9959528	-0.748284981	0.261593361	-2.860489194	0.00422988	0.024299393
SUPT6H	7076.02371	0.177336801	0.06199886	2.860323591	0.004232089	0.024304511
CLPP	2225.177717	0.396903698	0.138785754	2.85983025	0.004238678	0.024327188
PLOD1	6058.260821	0.51002091	0.178334331	2.859914343	0.004237554	0.024327188
MRPL33	2125.015885	0.444912057	0.155609141	2.859164014	0.004247591	0.024363167
IER3IP1	1104.12372	0.298414424	0.104368204	2.859246533	0.004246486	0.024363167
EAF1	1870.946075	0.393234718	0.137559888	2.858643768	0.004254563	0.024395562
ATP6V1D	4263.557743	0.283705079	0.099256489	2.858302589	0.00425914	0.024406622
SLAMF1	54.617279	1.367447792	0.478411563	2.858308405	0.004259062	0.024406622
TOGARAM2	356.5012764	-0.509464226	0.178285198	-2.85758005	0.004268849	0.024454655
PLK4	142.6272128	-0.881569164	0.30854073	-2.857221356	0.004273677	0.024473869
GANC	808.7585601	-0.290492784	0.101672808	-2.857133538	0.004274859	0.024473869
STAMBP	3433.92724	-0.304932266	0.106744652	-2.856651462	0.004281357	0.024503455
CAVIN4	101.9754387	-0.686254463	0.240254307	-2.856366955	0.004285196	0.024517811
GSTP1	14820.83775	0.831073804	0.290971359	2.856204837	0.004287384	0.024522721
MORC1	11.14795332	-1.336682115	0.468031222	-2.855967834	0.004290586	0.024533419
TIGD5	632.2315655	0.352606993	0.123474436	2.855708469	0.004294092	0.024545852
RBM22	3198.888852	0.242767335	0.085014538	2.855597871	0.004295588	0.024546789
MAP3K7	2333.417146	-0.233299052	0.081709172	-2.855237031	0.004300472	0.0245607
SESTD1	3232.273297	-0.512787457	0.17960735	-2.855047174	0.004303044	0.024574153
CTSH	6308.556466	0.655858916	0.229731348	2.854895168	0.004305104	0.024578301
SLC25A44	3039.026495	0.214263606	0.075069401	2.854206937	0.004314442	0.024616361
VARS	3238.548704	0.378271538	0.132527134	2.854295016	0.004313246	0.024616361
PAPSS2	581.7968361	0.637830579	0.223491019	2.853942779	0.004318031	0.024629214
PSMC3	6984.830775	0.379495866	0.132988426	2.853600694	0.004322683	0.024648118
RMC1	1106.399015	0.175837222	0.061622862	2.853441359	0.004324851	0.024652854
IMPG2	29.87661944	-0.785016835	0.275126752	-2.85329154	0.004326891	0.024656854
MOG	23533.43878	-0.87410639	0.306374004	-2.85306971	0.004329912	0.024666446
ADGRA2	844.4821045	-0.614186842	0.215296501	-2.852748836	0.004334286	0.024683734
PCCB	2287.915386	-0.258345241	0.090577262	-2.852208561	0.00434166	0.024718091
WDR24	1056.091225	0.319891401	0.112161931	2.852049687	0.004343831	0.024722811
ZNF205	1171.414068	0.431816258	0.151449619	2.851220504	0.004355176	0.024779725
NASP	6248.25572	-0.412499556	0.144692218	-2.850875897	0.004359898	0.02479894
SLURP2	23.62892039	1.719459844	0.6031763	2.850675406	0.004362648	0.024806924
ARF6	2944.87694	0.341261672	0.119723802	2.850407907	0.004366319	0.024820141
OR7G2	11.19622174	-0.809750529	0.284098583	-2.850244866	0.004368558	0.024825211
PHF2	2596.050107	-0.401148504	0.140763236	-2.849810189	0.004374533	0.024851499
ARHGEF7	4729.483494	-0.379987145	0.133351575	-2.849513724	0.004378612	0.024867008
PKN1	8480.59871	0.403145608	0.141502488	2.849035483	0.004385199	0.024896744
NPTX2	3217.679465	0.835670252	0.293339823	2.84881283	0.004388269	0.024898832

APMAP	5738.78196	0.232203061	0.081508701	2.848813157	0.004388264	0.024898832
FBN1	1778.913191	-0.53923651	0.189298076	-2.84861063	0.004391058	0.024903675
PLD1	1598.392223	-0.581079612	0.203991004	-2.848555082	0.004391825	0.024903675
CYTH1	6344.466069	-0.359577284	0.126265917	-2.847777875	0.004402564	0.024956891
F13A1	2114.671364	-1.154525914	0.405501238	-2.847157552	0.004411152	0.024997887
MICU2	1699.067995	-0.286881464	0.100791555	-2.84628474	0.004423262	0.025043411
RFNG	3010.759355	0.386458133	0.13577624	2.846286886	0.004423233	0.025043411
NIT1	1830.707738	0.250910873	0.088149614	2.846420552	0.004421376	0.025043411
MAML3	344.4720007	-0.488910319	0.171777758	-2.846179411	0.004424726	0.025044002
NTRK3	2316.093477	-0.640421378	0.225023914	-2.846014738	0.004427015	0.025049264
DCXR	3289.409675	0.551663293	0.193847392	2.845863889	0.004429112	0.02505344
EXO5	327.3634872	0.434512748	0.152688567	2.845745135	0.004430764	0.025055094
RBM5	6573.928041	-0.254361148	0.089407592	-2.844961378	0.004441681	0.025106196
CHTF8	1711.453146	0.274905202	0.096630857	2.844900799	0.004442526	0.025106196
DERA	1133.869783	-0.272952147	0.095948747	-2.844770315	0.004444346	0.025108782
ZFP69	229.1521687	-0.40956545	0.144032755	-2.843557706	0.004461293	0.025196803
TRAPPC13	977.1652837	-0.393810301	0.138523382	-2.842915728	0.004470289	0.025233125
PGD	5322.435633	0.261218339	0.091884354	2.842903354	0.004470462	0.025233125
MSRB2	1970.963339	0.521805081	0.183553163	2.842800821	0.004471901	0.025233515
ARMC6	1694.74402	0.305811437	0.1075817	2.842597172	0.004474759	0.025241913
GPRC5C	1181.734747	0.551809048	0.194131441	2.842450681	0.004476816	0.025245788
UBQLN4	3538.103712	0.281877297	0.099194238	2.841670072	0.004487791	0.025299938
NUDCD2	1502.595922	-0.280255636	0.098644835	-2.841057366	0.004496422	0.025340846
PICALM	9127.818554	-0.356331096	0.125445758	-2.840519292	0.004504015	0.025360952
FOLH1	4067.989415	-0.820692961	0.28892431	-2.840511968	0.004504118	0.025360952
TST	1937.797291	0.565202752	0.198975864	2.840559361	0.004503449	0.025360952
CRAT	3484.770497	0.338294998	0.1191076	2.840246962	0.004507862	0.025374279
CTSS	4964.919014	0.838492549	0.295253347	2.839908698	0.004512645	0.025393444
RNASE4	600.9948431	0.487104494	0.171545186	2.839511298	0.00451827	0.025409578
IL18R1	88.11439818	0.882091386	0.310646545	2.83953387	0.00451795	0.025409578
CFAP54	299.26584	-0.555834198	0.195763948	-2.839308272	0.004521146	0.025417996
SYAP1	2184.619057	0.209188488	0.073693968	2.838610708	0.00453104	0.025465853
RPUSD4	856.2496486	0.194121167	0.068393613	2.838293794	0.004535541	0.025483382
MFN1	1490.376653	-0.229857092	0.081013288	-2.837276423	0.00455002	0.02555694
GLI1	188.7154895	1.647877247	0.580927737	2.836630343	0.004559236	0.025600904
OSGEPL1	407.3323254	-0.429140782	0.15129935	-2.836369437	0.004562963	0.025614026
MAP7	5512.506895	-0.703911665	0.248190788	-2.836171607	0.004565791	0.025617303
SAS6	184.3501137	-0.444082028	0.156580053	-2.836134094	0.004566327	0.025617303
TMEM101	1292.284868	0.35061452	0.123628498	2.836033202	0.00456777	0.025617598
SLC28A3	18.28885013	1.084804293	0.382527963	2.835882337	0.004569928	0.025621905
CRBN	2492.576055	-0.400873588	0.141369464	-2.835644797	0.004573328	0.025633169
SMPDL3A	739.1062123	0.601185635	0.212031165	2.835364484	0.004577343	0.025647873
SLC44A1	17329.57355	-0.601432561	0.212148831	-2.834955808	0.004583203	0.025669347
RASA3	3444.583487	-0.395607344	0.139550997	-2.834858609	0.004584597	0.025669347
PPARD	2723.573956	-0.246141057	0.086828188	-2.834805859	0.004585354	0.025669347
TDRD9	154.5021949	0.725620237	0.255990305	2.834561401	0.004588864	0.025681194
AVPR1A	34.95902406	-1.085708029	0.383088336	-2.834093151	0.004595593	0.02570281
PTPRJ	2854.834394	-0.292550895	0.10322891	-2.83400159	0.00459691	0.02570281
CCDC106	2764.382052	0.446461329	0.157532104	2.834097416	0.004595532	0.02570281
CYREN	1301.805909	0.325760363	0.114977165	2.833261388	0.004607569	0.025754593
IL24	5.692574474	1.977915649	0.698135199	2.833141279	0.004609301	0.025756461
STIP1	4650.736658	0.273488471	0.096539711	2.832911628	0.004612614	0.025767158
ECH1	5332.321232	0.42296862	0.149322311	2.832588224	0.004617282	0.025785423
RFX4	2310.639376	-0.64590771	0.228105975	-2.831612409	0.004631395	0.025856401
CFAP69	237.449519	-0.515868242	0.182214257	-2.8311108	0.004638706	0.025882327
TOMM5	2111.276012	0.375671747	0.132694708	2.831098188	0.004638848	0.025882327
RUVBL2	3588.863056	0.414895771	0.146563322	2.830829469	0.004642747	0.025888405
CARD17	6.68235749	1.93268878	0.68271928	2.830868903	0.004642174	0.025888405
TIMM44	1937.649099	0.296532047	0.104767325	2.830386725	0.004649177	0.025908583
CD300A	1538.973905	0.730489927	0.258080824	2.830469598	0.004647973	0.025908583
POLL	1395.466321	0.307545285	0.108679421	2.82983918	0.004657141	0.025945117
NSRP1	1755.002506	-0.282480119	0.099846021	-2.829157513	0.004667072	0.025992588
LRRC8D	3160.121486	-0.442253403	0.156330765	-2.828959499	0.004669961	0.026000818
SIRPG	16.30059746	-1.077224782	0.380802926	-2.828824851	0.004671926	0.026003903
CFAP47	52.65090706	-1.076392288	0.380568788	-2.82837774	0.004678457	0.026016681
SLC35B4	2132.799052	0.205134378	0.072526245	2.828415805	0.0046779	0.026016681
FAM98C	1584.367632	0.392732241	0.138850345	2.828457076	0.004677297	0.026016681
ANAPC11	3357.318824	0.414853436	0.146700029	2.827902894	0.004685402	0.026047441
PYGM	1277.61471	-0.844952889	0.298921189	-2.826674454	0.004703412	0.026131798
HAS3	326.5288043	0.956557897	0.338401905	2.826691823	0.004703157	0.026131798
SRC	1910.416692	0.544799904	0.192765878	2.82622583	0.004710005	0.02616054
CFAP46	281.690908	-0.671975089	0.237782939	-2.826002113	0.004713295	0.026170931
TRIM13	1176.170918	0.222218554	0.078653505	2.825284819	0.00472386	0.026221694
BABAM1	4451.567281	0.311467624	0.110280447	2.824323182	0.004738058	0.026292588
UCP3	100.6384587	-0.510322457	0.180703365	-2.824089403	0.004741516	0.026303851
MEIOC	35.84519162	0.533108786	0.188809857	2.823521995	0.004749917	0.026334601
SLC39A7	4947.25152	0.381206807	0.135010064	2.823543636	0.004749596	0.026334601
PSG2	24.82511671	0.790827695	0.280095304	2.823423616	0.004751375	0.026334762
FUCA2	3224.298871	0.398358725	0.141099458	2.823247743	0.00475382	0.026341291
MYO19	1284.632404	-0.341307965	0.120913402	-2.822747185	0.00476141	0.02637452
RAD17	1178.708307	-0.201338993	0.071334197	-2.822475089	0.004765452	0.026388979
NKAIN2	2742.568274	-0.948711721	0.336178417	-2.822048276	0.004771799	0.026411054
NRIP2	579.9256297	-0.877735903	0.3110317	-2.822014293	0.004772305	0.026411054
COPA	8058.831245	-0.309735962	0.109768681	-2.821715255	0.004776757	0.026427755
VPS54	1018.464258	-0.297341781	0.105385382	-2.821470822	0.004780399	0.026439966
SEC61G	2438.16896	0.562118628	0.199255294	2.821097576	0.004785964	0.026462807
TIMM29	638.9487656	0.263885889	0.093557311	2.820580103	0.00479369	0.026497576
ZNF720	529.5431871	-0.272756959	0.096711024	-2.820329536	0.004797435	0.026510326
AGAP6	738.852907	-0.597183782	0.211813302	-2.819387533	0.004811539	0.026580291
SMTN	1917.779257	0.53777426	0.190761148	2.819097422	0.00481589	0.026588387
LMCD1	805.4191398	0.479662841	0.170145919	2.819126338	0.004815456	0.026588387
HSF1	3735.349641	0.30737522	0.109090623	2.817613581	0.0048382	0.02670356
ASCL2	190.5196553	0.840141066	0.298186299	2.817503918	0.004839852	0.026704683
ECH1	5770.355296	0.367251497	0.130381335	2.816749008	0.004851242	0.026759515
MRPL32	1553.651677	0.345277808	0.122620589	2.815822449	0.004865255	0.026828779
IMPA2	358.9498799	0.377049092	0.13395008	2.814847822	0.004880034	0.026902226
CEBPG	1890.588231	0.290121104	0.10308074	2.814503508	0.004885264	0.026923008
EDRF1	666.4136109	-0.316141846	0.112350446	-2.813890432	0.004894591	0.026966342
TAC4	40.05135198	-0.738139305	0.262347235	-2.813596663	0.004899065	0.0269734
KLF4	698.5228219	0.634355133	0.225466875	2.813518099	0.004900263	0.0269734
LASP1	6788.752895	0.293197525	0.104207893	2.813582691	0.004899278	0.0269734
FLYWCH2	1489.180506	0.382221137	0.135876122	2.813011809	0.004907985	0.027007839
RAPGEF5	9517.634766	-0.778874508	0.276904689	-2.812789166	0.004911384	0.027018477
WDFY3	4715.018099	-0.55981809	0.199064471	-2.812245132	0.004919699	0.027056145
REG1A	2.19282896	-2.2005167	0.782531473	-2.812048813	0.004922703	0.027058512
CDK19	3760.636138	-0.516743194	0.183761944	-2.812025081	0.004923066	0.027058512
SMCP	1.141444268	3.318163848	1.180137204	2.811676335	0.004928407	0.027079788
TSTD2	1201.923897	-0.304641966	0.108358139	-2.81143594	0.004932091	0.027091954
SURF1	2224.309428	0.379269306	0.134918683	2.811095525	0.004937312	0.027112554
FNDC4	2741.904599	0.429848454	0.152920616	2.810925469	0.004939923	0.027118807
THAP3	1059.700353	0.347254079	0.123542831	2.810799107	0.004941863	0.02712138
ZNF471	1264.129376	-0.487005299	0.173279625	-2.810516813	0.0049462	0.027129913
RAMP1	8986.730862	0.57462373	0.204455593	2.810506296	0.004946362	0.027129913
MYD88	1984.468892	0.616472408	0.219358363	2.810343765	0.004948861	0.027135543
POLR3GL	1660.712056	0.279680602	0.099536306	2.809835057	0.00495669	0.027170384
CD46	4206.8399	-0.512576573	0.18244872	-2.809428164	0.004962959	0.027195996

WNK1	20499.019	-0.611312931	0.217613123	-2.809173101	0.004966893	0.027195996
RAB11FIP4	8965.170222	-0.569876938	0.202864616	-2.809149024	0.004967265	0.027195996
SDF2L1	1006.785927	0.565681023	0.201364421	2.809240191	0.004965858	0.027195996
ARHGAP33	3963.988085	-0.471560752	0.167882968	-2.808865957	0.004971634	0.027211834
TAS2R50	1.388786099	-1.418822535	0.50515534	-2.80868561	0.00497442	0.027218997
COL5A2	1516.849973	-0.647891107	0.230698213	-2.808392392	0.004978952	0.027235709
ANKRD40	9960.502908	-0.556952667	0.198326757	-2.808257824	0.004981033	0.027239008
ZBBX	114.9912563	-0.717426159	0.255484683	-2.808098518	0.004983498	0.027240009
PI4KB	5072.926655	0.192468631	0.068543949	2.807959453	0.00498565	0.027240009
YIPF1	1464.46498	0.305142861	0.108670008	2.807976837	0.004985381	0.027240009
USP27X	281.4138564	0.470436863	0.16757524	2.807317254	0.004995602	0.027278205
C20orf27	2554.721716	0.436213241	0.155383372	2.807335394	0.00499532	0.027278205
CDHR3	236.7446131	-0.592448023	0.211056826	-2.807054549	0.004999677	0.027284292
LEO1	1001.278864	0.245705239	0.087528965	2.807130628	0.004998497	0.027284292
MAGI1	1715.617973	-0.511695442	0.182314743	-2.806659704	0.005005809	0.027309668
MLH1	1500.679281	-0.189760044	0.067616304	-2.806424366	0.005009467	0.027319081
YBEY	840.358305	0.524590238	0.186929194	2.806357991	0.005010499	0.027319081
IKZF2	432.7152746	-0.586403178	0.208977888	-2.806053704	0.005015233	0.027336804
ENPP2	15639.61306	-0.72969909	0.260056089	-2.805929651	0.005017164	0.027339244
GZMK	82.05552535	-1.056997783	0.376836768	-2.804922109	0.005032874	0.027416741
SLC25A35	533.0376483	-0.365244157	0.130222937	-2.804760552	0.005035397	0.02742238
MTOR	2761.468054	-0.25382724	0.090508518	-2.804456935	0.005040142	0.027440111
RANGRF	1137.305306	0.417929103	0.149040289	2.804135093	0.005045176	0.027459406
NME8	41.95822542	-0.993606601	0.354381045	-2.803780323	0.00505073	0.02747341
NRM	661.3952384	0.653880063	0.233212339	2.803797031	0.005050469	0.02747341
CYSLTR2	147.1339069	-0.826640111	0.294938854	-2.802750812	0.00506688	0.027553123
PUS7L	873.7473511	-0.336825776	0.120227328	-2.801574175	0.005085395	0.027645647
DNAIC5	7645.955334	0.278627203	0.099470576	2.801101722	0.005092846	0.02767799
PIBF1	338.4685012	-0.377872441	0.134906559	-2.800993831	0.005094549	0.027679083
SPATS2L	3816.763566	-0.337768013	0.120625125	-2.800146426	0.005107943	0.027743673
PPM1N	598.8876678	0.599668642	0.214171683	2.799943637	0.005111153	0.027744754
MUC3A	44.73586197	1.271128729	0.453969264	2.800032582	0.005109745	0.027744754
PPM1G	3986.728113	0.385899088	0.137852917	2.799353803	0.0051205	0.027787308
HYAL1	149.1443809	0.677395963	0.242033068	2.798774429	0.005129696	0.027812641
PPIC	514.9871524	0.565019079	0.201878085	2.798813347	0.005129078	0.027812641
MBD3L3	1.667392682	3.446189909	1.231297129	2.798828835	0.005128832	0.027812641
CLASRP	4327.908814	-0.348634898	0.124589724	-2.798263671	0.005137815	0.02783302
TMEM119	1415.209182	-0.79132081	0.28279102	-2.79825297	0.005137985	0.02783302
KLHL36	1749.494105	0.308832759	0.110360407	2.798401781	0.005135619	0.02783302
MKNK1	2491.206632	-0.298240204	0.106596299	-2.797847653	0.005144437	0.02785978
ARPC2	9701.450027	0.280242234	0.100171582	2.797622117	0.00514803	0.027871049
NKG7	187.9352394	0.898326905	0.321125581	2.797431773	0.005151065	0.027879286
SNX27	2839.544598	-0.231081163	0.082609571	-2.797268641	0.005153666	0.027885178
UCN2	74.57402704	1.193509201	0.426721479	2.796927876	0.005159105	0.027906411
SGMS1	1332.721488	-0.517480855	0.185032342	-2.796704878	0.005162667	0.027909294
SERPINA1	3667.677291	0.858455734	0.306950841	2.796720576	0.005162416	0.027909294
DUSP27	52.62689608	-0.800382503	0.286292285	-2.795683098	0.005179016	0.027986981
IFIT1B	7.016693227	1.631623807	0.583636383	2.795617022	0.005180074	0.027986981
PSMD1	4399.760121	0.220033751	0.078721403	2.79509439	0.005188456	0.028024051
GIN1	332.0910194	-0.332814339	0.119099805	-2.794415486	0.005199363	0.028059793
MXRA5	486.8930394	-0.936124666	0.335006017	-2.794351797	0.005200387	0.028059793
MON2	2343.195614	-0.38396835	0.137410012	-2.794325868	0.005200804	0.028059793
COL9A1	377.9130804	-1.066718893	0.381747687	-2.794303488	0.005201164	0.028059793
MYO1C	2372.276967	0.412383608	0.147601885	2.793891203	0.0052078	0.028079151
SELENOH	3962.141928	0.422420742	0.151190606	2.793961567	0.005206667	0.028079151
SRP14	12448.78164	0.248376425	0.088939338	2.792649815	0.005227825	0.02817888
MBTD1	745.7111431	-0.504924628	0.18081364	-2.792514048	0.00523002	0.028182466
PRPH	484.5682127	0.924814536	0.331188862	2.79240833	0.005231729	0.028183435
PNN	3839.470815	-0.297989695	0.106719585	-2.792268133	0.005233996	0.028183914
MRPL51	4363.154501	0.381869565	0.136762297	2.792213742	0.005234876	0.028183914
SLC9A1	1642.606672	0.436266316	0.156286393	2.791454247	0.005247178	0.028241891
FIBP	3995.227095	0.372660469	0.133507171	2.791314215	0.005249448	0.028245864
CPB1	82.02140989	-1.012929084	0.36290463	-2.791171569	0.005251763	0.028250068
FLVCR2	647.9236988	0.699026016	0.250549098	2.789976188	0.005271192	0.028346307
SF3B1	10921.2497	-0.303288384	0.108728452	-2.789411392	0.005280394	0.028387511
ANTXR1	3657.170641	-0.575286545	0.206294295	-2.788669198	0.005292509	0.028437673
CASP6	368.0051489	0.436623702	0.15657167	2.788650721	0.005292811	0.028437673
FRAT2	509.6833939	0.330036643	0.118362698	2.788350127	0.005297725	0.028447489
GSTK1	5166.133712	0.353029655	0.126607505	2.78837858	0.00529726	0.028447489
NDUFB2	6508.830602	0.464821051	0.166721151	2.788014885	0.005303211	0.028468648
BPIFB2	18.36671744	-1.453678667	0.521434493	-2.787845234	0.005305989	0.028475266
CHPT1	2890.44818	0.323800287	0.116183837	2.786965001	0.005320422	0.028544415
MRPL34	2111.232045	0.286551386	0.102822657	2.786850624	0.005322301	0.028546181
SEC61A2	1438.205992	-0.417636941	0.149871604	-2.786631544	0.0053259	0.028557174
DGAT1	1758.126351	0.358256925	0.128573905	2.786389089	0.005329885	0.028570232
ZFP28	710.9323057	-0.285606581	0.102512045	-2.786078278	0.005334999	0.028589326
NDUFB7	7684.455708	0.544217601	0.195360542	2.785708905	0.005341081	0.0286136
ZBTB20	4028.35527	-0.45776905	0.164336483	-2.785559495	0.005343543	0.028617696
ATXN2	2559.365341	-0.308093044	0.110614448	-2.785287581	0.005348027	0.028617696
LIX1L	1939.845614	0.214650201	0.077065774	2.785285745	0.005348057	0.028617696
TEX264	2829.051821	0.329471217	0.118288113	2.785328196	0.005347357	0.028617696
HSPA9	12161.80504	0.152732695	0.054853465	2.784376421	0.005363075	0.028689729
FBXL7	1616.587797	-0.622951313	0.223779408	-2.78377407	0.005373045	0.028730711
H3.Y	8.082132713	2.750699908	0.98823648	2.783442995	0.005378531	0.028730711
BIK	16.29559665	1.179970053	0.42391742	2.783490365	0.005377746	0.028730711
FAM229A	526.6344033	0.385464249	0.138480058	2.783536137	0.005376987	0.028730711
OGFOD3	1615.066411	0.293578045	0.105464865	2.783657342	0.005374979	0.028730711
LDHA	15103.70609	0.514284629	0.184775687	2.783291667	0.005381041	0.028735787
COL4A1	6778.483792	-0.937743636	0.336997422	-2.782643351	0.005391804	0.028784924
EFCAB6	122.7187138	-0.529684778	0.190370526	-2.782388584	0.005396039	0.02879919
HDX	162.4918173	-0.360655043	0.129639451	-2.781985263	0.005402749	0.028826655
TRIM6	168.8374581	0.810557863	0.291370882	2.781876686	0.005404557	0.028827955
EFCAB2	867.2144106	-0.368458937	0.132505863	-2.780699132	0.005424198	0.028898519
DBNDD2	38866.17019	-0.722700194	0.259923651	-2.780432602	0.005428653	0.028898519
NLRP2B	4.088731327	-1.147426492	0.412682129	-2.780412362	0.005428991	0.028898519
AC270107.1	13.52201388	-0.847943315	0.304979134	-2.780332231	0.005430331	0.028898519
AC270107.2	13.52201388	-0.847943315	0.304979134	-2.780332231	0.005430331	0.028898519
AC270107.6	13.52201388	-0.847943315	0.304979134	-2.780332231	0.005430331	0.028898519
AC270107.5	13.52201388	-0.847943315	0.304979134	-2.780332231	0.005430331	0.028898519
MYO1A	57.65385186	0.666648598	0.239746732	2.780636851	0.005425239	0.028898519
VSX2	14.28920488	-0.986470895	0.35485413	-2.77993353	0.005437003	0.02892171
KCNQ1	582.2973748	-0.68905663	0.247872417	-2.779884256	0.005437828	0.02892171
AGAP1	6194.397261	-0.608441414	0.219001598	-2.778251019	0.005465238	0.029059109
ATG4D	1303.69431	0.334849549	0.120541503	2.777877668	0.005471521	0.029084127
DNAIC2	991.217005	0.315251462	0.113496249	2.777637723	0.005475563	0.029097218
RDH5	546.1401786	0.590227383	0.212509858	2.777411781	0.005479371	0.029109061
KIRREL3	1561.073326	-0.74181742	0.267133224	-2.77695679	0.005487047	0.029141439
TENM4	1566.074586	-0.624935408	0.225201768	-2.77500223	0.005520133	0.029307842
NPC2	14376.04016	0.643133526	0.231774486	2.774824511	0.00552315	0.029307842
ST3GAL2	1281.897523	0.322362727	0.116171635	2.774883269	0.005522152	0.029307842
PDIA5	391.3494575	0.544910825	0.196503866	2.773028517	0.005553725	0.029461602
PYCR3	854.9859484	0.375936616	0.135659585	2.77117623	0.005585419	0.029621204
TENT2	1422.13854	-0.275442952	0.099416623	-2.770592515	0.00559544	0.029665813
TH5D1	543.4328981	0.631125571	0.227827951	2.770184986	0.005602446	0.029694418
OGN	91.92127786	-0.996770309	0.359882698	-2.769708895	0.005610641	0.029729301
CUX1	4628.827127	-0.334451403	0.120760208	-2.769549749	0.005613383	0.029735279

FRMPD3	666.0455875	-0.586245345	0.211699975	-2.76922728	0.005618942	0.02975107
RTEL1-TNFRSF6B	778.5534695	-0.554445797	0.20022672	-2.769089939	0.005621312	0.02975107
C2CD4A	28.16106603	0.997683678	0.36031654	2.768908903	0.005624436	0.02975107
PMFBP1	112.8703772	0.697632222	0.251948838	2.768943996	0.00562383	0.02975107
C4orf48	3683.178085	0.773943847	0.279490616	2.769122836	0.005620744	0.02975107
GSDMA	129.7222831	1.171577591	0.423145933	2.768731776	0.005627494	0.029758707
AUH	643.3184643	-0.369359323	0.133443848	-2.767900712	0.005641864	0.029826137
ACD74143.1	1455.71382	0.989799809	0.357615752	2.767774636	0.005644047	0.02982912
BCKDHB	1004.383078	-0.498443335	0.180104124	-2.767528715	0.005648307	0.02983769
C11orf54	950.3814667	-0.398479233	0.143995295	-2.76730731	0.005652145	0.02983769
EBPL	536.1043573	0.288077297	0.104098506	2.767352835	0.005651355	0.02983769
ABCA7	1362.292465	0.438448656	0.158428929	2.767478512	0.005649177	0.02983769
FAM133B	947.5497334	-0.216551464	0.078271643	-2.766665618	0.005663281	0.02988791
ST6GALNAC3	1093.838843	-0.682456814	0.246720913	-2.766108501	0.005672966	0.029930456
GATD3B	4844.936385	0.370290962	0.133879817	2.765846046	0.005677533	0.02994598
CRTC3	2822.453243	-0.317011621	0.114643066	-2.765205373	0.005688697	0.029996278
MBD4	1906.59038	0.221443093	0.080085239	2.765092504	0.005690666	0.029998077
PPM1H	1899.947206	-0.608089756	0.219965844	-2.764473543	0.005701473	0.030041952
CYB561D2	943.8076691	0.396761669	0.143528748	2.76433588	0.005703879	0.030041952
WDR83	857.4439805	0.384919271	0.139243916	2.764352528	0.005703588	0.030041952
ERCC6L2	643.3889055	-0.379053088	0.137127858	-2.764231082	0.005705712	0.03004301
CCDC12	1826.979633	0.46299643	0.167551508	2.763308042	0.005721874	0.030119512
NXT1	661.9847817	0.49782479	0.180173136	2.763035612	0.005726652	0.030127452
MRPL53	2022.417089	0.437291098	0.15826258	2.763073227	0.005725992	0.030127452
NTRK1	36.00610114	-0.674083795	0.244057831	-2.761983881	0.005745131	0.030212358
CASP3	1366.290913	0.367238571	0.132964447	2.761930575	0.00574607	0.030212358
HLA-C	51389.4643	0.604917131	0.219085957	2.761094961	0.005760792	0.03028113
LONP2	3755.933272	-0.232266908	0.084124206	-2.760999693	0.005762473	0.030281328
DEXI	2190.13354	0.269689132	0.097711689	2.760049831	0.005779255	0.030360856
RTKN	7969.353195	-0.505224127	0.183066368	-2.759786725	0.005783911	0.030376657
BAHCC1	2527.843834	-0.414778618	0.150305219	-2.759575617	0.005787649	0.030387631
HS3ST1	407.8314047	0.535585803	0.194154743	2.758551219	0.005805821	0.030474357
PLEKHA5	1191.264519	-0.434729583	0.157616015	-2.758156166	0.005812842	0.030502525
MRNIP	1707.160433	-0.220917628	0.080118826	-2.757374729	0.005826753	0.030560281
DRG1	1916.555853	0.27539911	0.099878125	2.757351626	0.005827165	0.030560281
OR4D1	13.57424717	0.886103913	0.321524963	2.755941266	0.00585235	0.030683632
SGCE	2293.448183	-0.310936829	0.112828499	-2.75583591	0.005854236	0.030684787
SCO2	979.3680114	0.593986577	0.215548396	2.755699365	0.00585668	0.03068887
PLCL1	2467.408844	-0.795910864	0.288848155	-2.755464592	0.005860885	0.030702173
PTGIR1	1191.688656	0.27849582	0.101093861	2.754824244	0.005872367	0.030753582
XRCC6	9736.136894	0.259245871	0.094112245	2.754645483	0.005875576	0.030761646
CTNND2	11050.45455	-0.708866172	0.257367636	-2.754294141	0.005881888	0.030785945
BZW2	1166.283319	0.502966459	0.182622106	2.754137877	0.005884697	0.030791903
CTAGE1	0.706601705	-2.498257866	0.907207168	-2.753789823	0.005890959	0.030808074
IGFBP3	3943.682552	0.965879156	0.350746635	2.753780249	0.005891131	0.030808074
BLOC1S3	755.9280022	0.270745496	0.09832692	2.753523601	0.005895752	0.030823493
POLR3E	1303.727536	-0.199434794	0.072436639	-2.753230922	0.005901026	0.030842045
PCLAF	127.7290221	-0.697470739	0.253336372	-2.753140952	0.005902648	0.030842045
RBMS3	389.2945508	-0.547133673	0.1987446	-2.752950563	0.005906081	0.03085124
MRPL15	1390.969286	0.231589038	0.084141268	2.752383502	0.005916319	0.030895961
GAB1	3158.357331	-0.549255041	0.199570127	-2.752190664	0.005919804	0.030905404
EVI5L	4503.382589	-0.395579349	0.143749689	-2.751862302	0.005925743	0.030927647
TRMT1	2822.933225	0.390327077	0.141849198	2.751704514	0.005928599	0.03093379
GPHB5	0.651585874	-1.569165712	0.570315011	-2.751401737	0.005934082	0.030953636
SEC14L5	4068.293959	-0.835349111	0.303647222	-2.751051389	0.005940432	0.030977993
RUFY2	2272.834379	-0.502046415	0.18250458	-2.750870179	0.005943719	0.030986366
AL034430.1	90.52865014	2.62010881	0.95251749	2.750719894	0.005946447	0.030991817
TBL1XR1	3276.26116	-0.25336357	0.09211509	-2.750511023	0.005950239	0.030994051
IGF2R	3949.048396	0.415056847	0.150898547	2.750568873	0.005949188	0.030994051
LYL1	1124.142591	0.724139399	0.263336105	2.749867507	0.005961937	0.031046208
PHKB	2619.765376	-0.354747206	0.129020272	-2.749546269	0.005967784	0.031059103
C6orf52	98.02877854	0.659050807	0.239687046	2.749630474	0.005966251	0.031059103
SDHAF1	1270.995475	0.453590357	0.164981848	2.749334935	0.005971633	0.031070364
PTPRM	1661.981095	-0.559669696	0.203593808	-2.748952448	0.005978606	0.031097863
UBE2M	5289.608408	0.369740994	0.134554352	2.747893247	0.005997953	0.031189698
CBFA2T2	1702.916904	-0.266302315	0.096930074	-2.747365235	0.006007619	0.03121966
UBE4B	2830.785259	-0.278414061	0.101340941	-2.747300909	0.006008798	0.03121966
CD79B	63.86911729	0.878646031	0.319814171	2.747364283	0.006007637	0.03121966
SERPINB1	3188.2312	0.513496035	0.186965396	2.746476286	0.006023924	0.031280613
SELL	890.415852	0.784405342	0.285598749	2.746529336	0.00602295	0.031280613
ZNF107	555.0527789	-0.583743755	0.212560895	-2.746242455	0.00602822	0.031294101
HSF5	4.046854278	-1.03071649	0.375350507	-2.746010649	0.006032481	0.031302973
ABCA2	62918.19697	-0.635780635	0.231532706	-2.745964686	0.006033326	0.031302973
RBM26	2225.169498	-0.247691364	0.090217984	-2.745476605	0.006042308	0.031326591
RECK	520.4260155	-0.334597888	0.121874038	-2.745440225	0.006042978	0.031326591
SLC25A1	3686.649475	0.389918753	0.142015901	2.745599253	0.006040049	0.031326591
CYP26C1	12.48258325	-0.926258719	0.337430199	-2.745038	0.006050389	0.031347377
RAET1G	20.65469495	0.848906145	0.309245776	2.745085663	0.00604951	0.031347377
ITFG2	1037.702649	-0.195737206	0.071333971	-2.743954998	0.006070386	0.031442142
SGCA	58.51299065	0.940124678	0.342684025	2.743415531	0.006080369	0.031485001
ZNF789	713.3764107	-0.344340332	0.125553914	-2.742569473	0.006096055	0.03155736
EIF3G	8316.310299	0.45130849	0.164588495	2.742041543	0.006105862	0.03159925
GYG1	2615.027548	0.288559651	0.105245967	2.741764444	0.006111015	0.031617035
MSANTD3-TMEFF1	972.9830558	-0.59822969	0.218200021	-2.74165734	0.006113008	0.031618472
TMEM62	938.7515405	-0.229527366	0.08373961	-2.740965319	0.006125897	0.031676252
OLAH	24.25997726	0.976266058	0.356198148	2.740794876	0.006129076	0.031683797
FTSJ3	2375.810176	0.306477618	0.111829039	2.740590656	0.006132886	0.031694604
L3HYPDH	810.1775983	-0.389993304	0.142311624	-2.740417784	0.006136113	0.031702391
HSD17B4	7281.313575	-0.366472911	0.133744269	-2.740101781	0.006142016	0.031708636
ZNF721	1120.58406	-0.396938936	0.144863834	-2.74008305	0.006142366	0.031708636
SPOCK2	14865.00319	0.576455438	0.210379302	2.740076765	0.006142484	0.031708636
MOB3B	2303.010174	-0.626173711	0.22853705	-2.739922085	0.006145375	0.031714675
ABHD18	493.0900114	-0.30755383	0.112265829	-2.739514185	0.006153006	0.031727405
MGAT2	1096.515729	0.453826292	0.165657558	2.739544751	0.006152434	0.031727405
HIST1H4E	100.9830452	0.768227476	0.280413671	2.73962205	0.006150987	0.031727405
CEP295	627.0215005	-0.359270066	0.131183154	-2.738690569	0.00616844	0.031798092
B4GALT3	1281.313368	0.296281456	0.108199893	2.738278626	0.006176173	0.03182905
LRRC63	223.244074	-0.931510922	0.340229097	-2.737893174	0.006183416	0.03185747
PREX2	1630.374959	-0.642736021	0.234764981	-2.737784905	0.006185452	0.031859052
PGAM5	1125.356521	0.314509526	0.114892871	2.737415501	0.006192403	0.031885942
TNNC2	73.800153	0.756379444	0.276346684	2.737067193	0.006198963	0.031901896
RPS5	17291.18655	0.443254032	0.161939823	2.73715275	0.006197351	0.031901896
EZH1	3688.724721	-0.26585128	0.097146967	-2.736588565	0.006207988	0.031939423
EMC10	11514.81029	0.361108229	0.132000725	2.735653381	0.006225657	0.032021385
DENND1C	732.9361524	0.645748821	0.236121999	2.734810067	0.006241628	0.032094578
IL4R	2027.788895	0.57916347	0.211855765	2.733763082	0.006261508	0.032187815
DTHD1	36.74511086	-1.141674545	0.417650366	-2.733565295	0.00626527	0.032198176
CFTR	44.94853151	-1.162144172	0.425267094	-2.732739467	0.006280999	0.032270013
RSRC1	892.7708336	-0.458807831	0.167956178	-2.731711548	0.006300628	0.032361836
DNAJC15	2849.742124	-0.358385609	0.131225877	-2.731058979	0.006313117	0.032416951
ELOVL5	6100.470743	-0.370516614	0.135673372	-2.730945711	0.006315287	0.032419062
PIEZO2	1907.96993	-0.859274601	0.314808882	-2.729511935	0.006342815	0.032544672
C14orf178	7.705526205	-0.786959923	0.28831785	-2.729487348	0.006343288	0.032544672
MRPL40	1946.900537	0.360572479	0.132145248	2.728607236	0.006360241	0.032622568
NDST1	9018.677847	-0.276705339	0.101413604	-2.728483443	0.006362628	0.032625731
PIFO	1179.178735	-0.554067734	0.203092733	-2.728151446	0.006369036	0.032640424

MED19	758.2384048	0.265937707	0.097476685	2.728218629	0.006367739	0.032640424
ANKRD42	530.162518	0.359855062	0.131912775	2.727977343	0.006372398	0.032648577
SERP1	5730.199418	0.230109428	0.084371274	2.727343286	0.006384658	0.032702295
GPR19	408.3471287	0.413153022	0.151495899	2.727156483	0.006388274	0.032711724
MMP2	2592.816373	-0.637420011	0.233784854	-2.726523985	0.00640053	0.032752088
NEO1	6003.405543	-0.433493099	0.158999341	-2.726382986	0.006403265	0.032752088
CAV1	3232.566516	0.701355859	0.257247265	2.726388014	0.006403168	0.032752088
PSMA1	3567.065679	0.23833554	0.087416024	2.726451394	0.006401938	0.032752088
SLC4A1AP	1942.072751	0.171822662	0.063029531	2.726065988	0.006409418	0.032774464
DHRS9	252.6353236	0.845622331	0.310247779	2.72563541	0.006417785	0.032808142
TGFA	1141.654358	-0.503887242	0.184890417	-2.725329142	0.006423741	0.032829487
UTP14A	756.3334839	0.252806832	0.092765835	2.725214858	0.006425965	0.032831749
IFT81	582.7687943	-0.470187112	0.172581087	-2.724441701	0.00644103	0.032899596
NDUFB10	4829.372148	0.46397151	0.170323566	2.724059398	0.006448491	0.032928578
FNBP4	2644.081345	-0.325681086	0.119561782	-2.723956451	0.006450501	0.032929719
CSF1R	7547.816806	-0.750764501	0.275651599	-2.723599299	0.00645748	0.032950338
ATAD2B	437.6409439	-0.452662463	0.166207977	-2.723470151	0.006460005	0.032950338
CX3CR1	2468.23739	-1.103187554	0.405069854	-2.72345015	0.006460396	0.032950338
RAD54L	139.3690344	-0.834615564	0.306462691	-2.723383917	0.006461692	0.032950338
ZNF215	35.88820064	0.727814601	0.267328655	2.722546154	0.00647809	0.033024862
RETREG2	7010.936899	0.219355041	0.080633724	2.720388334	0.006520529	0.033231977
TMMSF19-TCTEX1D2	6.85118056	1.715106038	0.630543842	2.720042483	0.006527353	0.033257558
PHLDA1	4063.767157	0.754215401	0.277301331	2.719840536	0.00653134	0.033268677
MZF1	1968.142478	-0.269203259	0.098987046	-2.719580702	0.006536474	0.033282107
CRYBG1	468.4391886	0.804509706	0.295827364	2.719524309	0.006537589	0.033282107
PDZK1	32.00037779	-0.661060378	0.243117206	-2.719101582	0.00654595	0.033305437
DCP1B	618.8504159	0.271311859	0.099783011	2.71901856	0.006547593	0.033305437
CERS5	2795.483542	0.24709147	0.090873902	2.719058662	0.0065468	0.033305437
CCDC69	869.4743653	0.521333093	0.191767123	2.718573883	0.006556401	0.033331839
EMC7	3500.372252	0.285015943	0.104837437	2.718646602	0.00655496	0.033331839
TRIM31	5.474834282	1.457202118	0.536075396	2.718278305	0.006562262	0.033352432
ABCA10	128.9996799	-0.427136359	0.157179272	-2.717510738	0.006577502	0.033420674
HAVCR1	8.554618212	-1.101426506	0.405392607	-2.716937821	0.006588898	0.033469352
RPS9	10733.4278	0.7018463	0.25840794	2.716039992	0.006606794	0.033551008
C20orf194	3340.858391	-0.425641169	0.15676234	-2.715200406	0.006623568	0.033626922
SNX12	2405.680461	0.135482879	0.049900961	2.715035456	0.006626868	0.03363441
ISLR2	740.1136034	0.987888859	0.363883808	2.714846983	0.00663064	0.03364429
KLHL4	1152.458747	-0.779822449	0.287255795	-2.714731829	0.006632946	0.033646726
CIITA	1797.779035	-0.607156516	0.223694022	-2.714227728	0.006643048	0.0336887
ZNF429	435.7698681	-0.498183819	0.18357215	-2.713831155	0.006651006	0.033719775
CDK13	2078.669613	-0.254360496	0.093748516	-2.713221564	0.006663254	0.033763295
CHMP6	1715.317313	0.412952743	0.152197722	2.713264929	0.006662382	0.033763295
RBM15	385.9633767	0.337602603	0.124433229	2.713122572	0.006665245	0.0337641
KDM8	320.132276	0.280637195	0.10345077	2.712760808	0.006672525	0.033791691
CXorf40B	1051.281492	0.238483214	0.087928358	2.712244594	0.006682926	0.033825774
PLEKHF1	1155.537484	0.46741581	0.17233499	2.712251355	0.00668279	0.033825774
DMC1	31.79534583	-0.619898479	0.228568888	-2.712085986	0.006686125	0.033832677
NIPAL1	34.44497662	0.858150948	0.316490889	2.711455455	0.006698854	0.03388778
ANKRD36	815.0738518	-0.625372927	0.230672901	-2.711081034	0.006706423	0.033892489
ENY2	2452.529304	0.265414562	0.097901182	2.711045546	0.006707141	0.033892489
MXRA7	8725.372198	0.259916167	0.095869947	2.711132897	0.006705375	0.033892489
KIF3B	4200.931436	0.239970418	0.088512262	2.711154518	0.006704937	0.033892489
NAT10	1902.552176	0.176792625	0.065221598	2.710645395	0.00671524	0.033914814
HDHD5	1469.464977	0.368985428	0.13612209	2.71069471	0.006714241	0.033914814
PPP1R10	3384.30026	-0.252414459	0.093130485	-2.710331202	0.006721605	0.033929855
PFKFB4	1228.612913	0.602659901	0.222357746	2.710316645	0.0067219	0.033929855
FA2H	5699.692607	-0.758430326	0.279850779	-2.710124046	0.006725805	0.033930977
PSMB2	4936.147795	0.245343629	0.090527772	2.710147641	0.006725326	0.033930977
PRODH	1645.979548	-0.737499379	0.272371202	-2.707699542	0.006775133	0.034170477
GPATCH8	2624.636317	-0.372038823	0.137429714	-2.707120697	0.006786958	0.034220751
CDKAL1	545.8103154	-0.428414196	0.15827441	-2.706781195	0.006793902	0.034238537
UBXN1	5817.584314	0.463070583	0.171084613	2.7066758	0.006796059	0.034238537
ABCB9	1338.070654	0.350829593	0.129616372	2.706676539	0.006796044	0.034238537
RYR3	2325.331395	-0.763857412	0.282240718	-2.706404015	0.006801624	0.034244959
CATIP	107.9265695	0.745648914	0.275519169	2.706341332	0.006802908	0.034244959
CCT5	5929.260676	0.349281168	0.129052736	2.706499517	0.006799668	0.034244959
PPP1R2	2002.115604	0.257542458	0.095170748	2.706109416	0.006807661	0.034259527
C19orf71	57.34532636	-0.750421398	0.277379289	-2.705398088	0.006822258	0.034297972
METTL15	404.0256726	-0.357083032	0.131993009	-2.70531776	0.006823908	0.034297972
POU2F1	1287.022251	-0.362528111	0.134005925	-2.705314032	0.006823985	0.034297972
RIC3	1053.287292	-0.464162599	0.171576306	-2.705283784	0.006824606	0.034297972
AGPAT1	6616.873439	0.242701327	0.089710771	2.705375562	0.006822721	0.034297972
CCDC63	5.668248432	1.624898598	0.600766641	2.70470843	0.006836437	0.0343387
C3orf52	52.07666448	1.038212553	0.383846359	2.704760719	0.006835361	0.0343387
MYL4	27.53471173	1.076646901	0.398106142	2.704421729	0.006842339	0.034358981
PPP1R1C	191.6880801	-0.715634648	0.264676309	-2.703810748	0.006854932	0.034412841
DPYSL5	8215.198246	-0.66663763	0.246583155	-2.703500289	0.006861339	0.034435625
TRIM28	10379.69797	0.435267926	0.161023541	2.703132255	0.006868941	0.034464392
NR6A1	201.4072307	-0.435660761	0.161213537	-2.702383249	0.006884436	0.034532734
ARC	3465.841963	0.835156797	0.309140279	2.701546363	0.006901786	0.034600927
PRPF19	5147.185656	0.297934888	0.110281223	2.701592155	0.006900835	0.034600927
ZNF596	398.2241236	-0.254010982	0.094050887	-2.70078241	0.006917658	0.034651427
CNOT11	1461.299393	0.276694925	0.102453054	2.700699626	0.00691938	0.034651427
MEI1	102.4097853	0.673411269	0.249345242	2.700718339	0.006918991	0.034651427
SOCS3	3333.421019	0.880000835	0.325809485	2.700967516	0.006913809	0.034651427
IDH3G	3570.096675	0.38124246	0.141193001	2.700151256	0.006930796	0.034699168
MATN2	3970.373778	-0.58321076	0.21602107	-2.699786457	0.0069384	0.034712467
FAM122C	383.1246644	-0.284466702	0.105367661	-2.699753413	0.006939089	0.034712467
XPNPEP3	691.765826	-0.254511889	0.094272296	-2.699752727	0.006939103	0.034712467
MAP3K13	1718.215151	-0.194851375	0.07217934	-2.699544998	0.006943437	0.03472472
ACD07040.2	48.16869115	0.721045955	0.267116481	2.699369026	0.006947109	0.034733663
FCER1A	132.0325563	1.322190381	0.489890644	2.698950056	0.006955861	0.034767988
ATP5IF1	5282.636366	0.341350005	0.126479966	2.698846442	0.006958027	0.034769384
ARPC1A	4700.856343	0.179820808	0.066638642	2.698446458	0.006966394	0.034801757
FEZ1	28766.40691	-0.521621627	0.193315453	-2.698292443	0.006969618	0.034808428
KRIT1	1210.645299	-0.373433575	0.138427239	-2.697688531	0.006982274	0.034862183
RPN2	9193.932815	0.363751954	0.134859649	2.697263086	0.006991201	0.034897304
RPL41	56119.90591	0.401872421	0.149014225	2.696872873	0.006999399	0.034928762
MTMR14	1907.462164	0.262255983	0.09724858	2.696758718	0.007001798	0.034931278
SKP2	560.4607428	-0.461134701	0.171009605	-2.696542702	0.007006341	0.034944483
GPBP1L1	3063.818483	-0.172289	0.063902373	-2.696128365	0.007015063	0.034978515
INTS2	737.5602341	-0.371748288	0.137887246	-2.696030979	0.007017114	0.034979279
KLRC1	13.50999922	-0.917676747	0.340409886	-2.695799346	0.007021995	0.034987128
ADAMTS13	810.5159856	-0.337926025	0.125353892	-2.695776086	0.007022486	0.034987128
SHKBP1	2924.240668	0.453277726	0.168155994	2.695578757	0.007026646	0.03498894
DERL1	2363.424648	0.214337321	0.079512914	2.695629058	0.007025586	0.03498894
PIWIL3	3.348115973	-1.111033469	0.412255926	-2.695009093	0.007038671	0.035039349
VPS35L	3413.469045	-0.211406301	0.078459935	-2.694449104	0.007050509	0.035083371
AQP1	28725.04209	-1.060086468	0.393439079	-2.694410709	0.007051322	0.035083371
SRPK3	864.8897149	-0.550982925	0.204500193	-2.694290484	0.007053866	0.035086557
C11orf94	11.09044093	1.127178509	0.418414449	2.693928251	0.007061536	0.035115233
LYPD1	1947.52445	0.585774129	0.217497645	2.693243542	0.007076056	0.035177943
G6PC3	5592.716791	0.39677449	0.147333537	2.693035801	0.007080467	0.035190377
CFL2	6854.174772	-0.518745029	0.192635494	-2.692883941	0.007083692	0.035196917
CCNT2	1593.595922	-0.347231029	0.128952657	-2.69270163	0.007087567	0.035203195
KIF6	646.0706196	-0.640949647	0.238042557	-2.692584286	0.007090061	0.035203195

TXNDC12	2809.188401	0.210716239	0.078258846	2.692554881	0.007090686	0.035203195
CARNS1	26349.72854	-0.822975442	0.305704183	-2.692064712	0.007101117	0.035245482
B3GAT1	14151.47912	-0.5015663	0.186351672	-2.691504155	0.007113061	0.035295263
PNKD	4658.67417	0.367767437	0.136673613	2.690844478	0.007127141	0.035355608
SP2	1435.340395	-0.278056716	0.10334095	-2.690673126	0.007130803	0.035364252
UBASH3B	644.8778825	0.577771113	0.214760677	2.690302154	0.007138735	0.035394067
SETD5	3573.724571	-0.398950996	0.148307239	-2.690030506	0.007144549	0.035413364
PPP2R2B	5190.0312	-0.581122435	0.216052154	-2.689732192	0.007150938	0.035429523
HSBP1L1	657.5529415	0.362577946	0.134802435	2.689698792	0.007151654	0.035429523
MITF	823.5461245	-0.497745526	0.185134211	-2.688565887	0.007175967	0.035540419
DGKD	2551.311114	-0.314803068	0.117116702	-2.687943425	0.007189358	0.03558761
TDG	865.9906139	0.400372863	0.1489483	2.687998877	0.007188164	0.03558761
USP30	1458.48204	-0.296244588	0.110220696	-2.68774014	0.007193736	0.035599719
TTLL9	563.5954102	-0.577850484	0.21501134	-2.687534922	0.007198157	0.035612039
C3orf33	289.1375646	0.3948014	0.146915049	2.687276777	0.007203723	0.03563001
DYNC1LI2	19880.18971	-0.433887011	0.161467081	-2.687154605	0.007206359	0.035633482
NME4	3766.559146	0.288671694	0.107432024	2.687017182	0.007209324	0.035638584
ZZEF1	3242.474069	-0.222727962	0.08291547	-2.686205137	0.00722687	0.03571574
CALCR	6.473377581	-1.322189765	0.492302537	-2.685726085	0.007237239	0.035757395
ARAP2	3651.835301	-0.504424314	0.187825334	-2.685603182	0.007239902	0.035760962
BIRC6	3144.943129	-0.502528695	0.187133097	-2.685407892	0.007244134	0.035772278
RBM23	2468.727226	0.17835496	0.066421055	2.685217196	0.007248269	0.035783108
RFTN2	2228.233143	-0.54899404	0.204494845	-2.68463511	0.007260903	0.035835881
POLI	1175.384427	-0.333665637	0.12431431	-2.684048491	0.007273656	0.03587493
SH2D1A	30.39027405	-0.922587415	0.343739164	-2.683975273	0.007275249	0.03587493
EEF2KMT	586.0631972	0.330937248	0.123308118	2.68382368	0.007278548	0.03587493
CPSF3	1662.555419	0.323593478	0.12057085	2.683845042	0.007278083	0.03587493
VDAC1	7596.946059	0.281553848	0.10490507	2.683891708	0.007277067	0.03587493
ZNF564	324.9902695	0.348083527	0.129715781	2.683432382	0.007287071	0.035907334
IL1R1	1202.252347	0.694097328	0.258715592	2.682858516	0.007299586	0.03595939
MSX1	1126.434771	0.594324334	0.221548738	2.682589572	0.007305459	0.0359787
LRP1B	883.8714631	-0.872725345	0.325346715	-2.682447076	0.007308571	0.035984415
MRPL22	1005.767481	0.279954138	0.104374413	2.682210425	0.007313744	0.036000264
C15orf62	25.13500086	0.925076199	0.344925738	2.681957583	0.007319274	0.036017864
AS3MT	440.9414918	0.364497309	0.135916925	2.681765427	0.007323479	0.036028937
MTRF1	331.7878898	-0.30475202	0.113660846	-2.681240115	0.007334986	0.036075918
P2RY13	822.2065407	-0.698588496	0.260584379	-2.680853314	0.00734347	0.036105331
TXNRD3	281.0089058	0.306177168	0.114211595	2.680788828	0.007344885	0.036105331
PWWP2A	857.946863	-0.286503858	0.106885245	-2.680480906	0.007351646	0.036106921
YPEL2	1582.105843	-0.422598577	0.15765859	-2.680466554	0.007351961	0.036106921
MTURN	100150.9795	-0.756297631	0.282156685	-2.680417197	0.007353045	0.036106921
TRABD	2342.737602	0.395993811	0.147728354	2.680553873	0.007350043	0.036106921
PSMA7	5946.356768	0.29857143	0.111401576	2.680136512	0.007359214	0.036127586
OGT	6463.249089	-0.424082179	0.158285822	-2.679217714	0.00737944	0.036213798
CCDC88A	8740.79373	-0.498189701	0.18597326	-2.678824363	0.007388114	0.036213798
PLP2	2771.901498	0.699845263	0.261252895	2.67880386	0.007388566	0.036213798
OR11G2	8.16703615	0.904728813	0.337715936	2.678963932	0.007385035	0.036213798
PUSL1	835.4580422	0.390864582	0.145895845	2.67906589	0.007382786	0.036213798
RTP4	552.5219042	0.664080701	0.24787218	2.679125589	0.00738147	0.036213798
RASSF4	10923.00696	-0.406448546	0.151739641	-2.678591723	0.007393248	0.036227112
GIMAP8	532.9355626	-0.424041134	0.158395624	-2.677101323	0.007426217	0.03637899
ARSG	390.4659147	0.336933681	0.125883496	2.676551673	0.007438409	0.036429032
INKA2	1469.122368	0.669773	0.250300646	2.675874033	0.007453465	0.036483376
SLC12A8	221.6985059	0.48867419	0.182622106	2.675876431	0.007453412	0.036483376
COMMD10	450.2652731	-0.547275901	0.204557745	-2.675410321	0.007463784	0.036497017
TMED1	1305.628456	0.37451647	0.1399856	2.675392816	0.007464174	0.036497017
XPNPEP1	2148.711191	0.187243626	0.069984359	2.675506774	0.007461637	0.036497017
PNRC1	3548.68137	0.330905082	0.123677075	2.675557142	0.007460515	0.036497017
TMIGD2	93.7876462	-0.742077758	0.277476114	-2.674384281	0.007486661	0.036590117
ZNF404	381.1955263	-0.523960316	0.195919831	-2.674360808	0.007487185	0.036590117
CMTM3	3431.873843	0.520928749	0.194839268	2.673633273	0.007503446	0.036659861
PPIAL4G	38.80697024	0.771803728	0.28869303	2.673440811	0.007507752	0.036671182
OVCH1	10.3399843	-0.846432555	0.316638166	-2.673185497	0.007513469	0.036689381
GARNL3	1065.555564	-0.513229207	0.192020768	-2.672779685	0.007522564	0.03672408
SH2B1	3949.878953	-0.20976288	0.078485401	-2.672635396	0.0075258	0.036730128
C2orf88	1105.667792	-0.462191148	0.172964109	-2.672179513	0.007536032	0.036760597
ZNF561	1607.885925	0.472119057	0.176679212	2.672182262	0.00753597	0.036760597
P2RX7	2787.169475	-0.501266902	0.187595905	-2.672056744	0.00753879	0.036764318
PPP1R16A	2795.945029	0.331429111	0.124062746	2.671463606	0.007552126	0.036819612
ARPC3	9248.765881	0.340174542	0.127347964	2.671220882	0.00755759	0.036836504
OTUB2	101.7130462	0.497285446	0.18623955	2.670138781	0.00758199	0.036945663
FAM222A	3113.216463	-0.605237962	0.226728491	-2.669439375	0.007597799	0.037012909
ULK2	2980.388099	-0.499454681	0.187108093	-2.669337671	0.0076001	0.037014335
ADGRV1	1914.29792	-0.78603533	0.294676952	-2.667447609	0.00764298	0.037203528
PDGFRA	4885.140752	-1.26493886	0.474213224	-2.667447459	0.007642984	0.037203528
AL354822.1	117.1688942	-0.706739228	0.264964689	-2.667295894	0.007646432	0.037210481
GNAO1	13841.99043	-0.578122676	0.216758777	-2.667124648	0.007650329	0.037219619
SETDB1	1577.1035	-0.201237607	0.075461371	-2.666763204	0.007658561	0.037249835
RSRC2	2557.053497	-0.18560961	0.069604762	-2.666622302	0.007661772	0.037252565
POSTN	289.2283722	-1.168599239	0.438242048	-2.666561195	0.007663165	0.037252565
SHD19	1390.388298	-0.522384566	0.195938872	-2.666058855	0.007674626	0.037298438
GID8	2517.552277	0.232674127	0.087289159	2.665555825	0.007686117	0.037344437
KATNAL2	378.3626881	-0.481952167	0.18086585	-2.664694128	0.007705838	0.037430385
TOM1L2	7402.827903	-0.328503605	0.123292624	-2.664422205	0.00771207	0.037450788
POLA1	675.6659269	-0.495813758	0.186098984	-2.664247528	0.007716076	0.037460371
MYH8	343.9559742	-0.48223723	0.181015203	-2.664070321	0.007720142	0.037465568
TRIM10	2.526238088	2.417248594	0.907367532	2.664023684	0.007721213	0.037465568
GPX4	20485.00103	0.424839044	0.159488811	2.663754534	0.007727393	0.037485686
ENOX2	623.7742012	-0.400692778	0.150432503	-2.663605079	0.007730826	0.037492473
AKR7A2	2918.522513	0.322407639	0.121045956	2.663514332	0.007732912	0.037492721
GALK2	668.1633442	-0.335935067	0.126141017	-2.663170758	0.007740812	0.037521154
PAPSS1	3775.753091	-0.333822888	0.125367544	-2.662753677	0.007750413	0.037557811
RPS6KA5	931.43606	-0.43658685	0.163970951	-2.662586561	0.007754262	0.037566588
PKN2	1422.980554	-0.372852837	0.140042753	-2.662421495	0.007758066	0.037575139
TNRC6A	3574.280978	-0.330866677	0.124284883	-2.662163478	0.007764016	0.037594076
SPDYE16	42.72365002	-0.622394962	0.233827351	-2.661771429	0.007773064	0.03762302
MIDIP1	8552.011546	-0.401997486	0.151040048	-2.661529114	0.007778661	0.03762302
TCTEX1D1	334.8476673	-0.726868141	0.273108544	-2.661462471	0.007780201	0.03762302
NOLC1	3503.709768	0.208205317	0.078224549	2.661636538	0.00777618	0.03762302
KIAA2013	4282.970208	0.325797466	0.122401307	2.661715582	0.007774354	0.03762302
UNC5CL	150.239677	-0.515316451	0.193654854	-2.661004573	0.0077909	0.037654463
TAF10	4949.145647	0.421690422	0.158469649	2.661016945	0.007790504	0.037654463
SETD3	3400.493174	-0.254249	0.095565802	-2.660460065	0.007803398	0.037695629
PLBD2	4776.687326	0.266667647	0.100231096	2.660528111	0.007801821	0.037695629
RAB11FIP5	2192.60026	0.493367895	0.185516515	2.659428439	0.007827336	0.037791451
ARL4A	1191.44367	0.427857052	0.160878109	2.659510707	0.007825424	0.037791451
RDH16	83.37483065	-0.454383516	0.170877316	-2.659121333	0.007834474	0.037806108
RGS12	3976.343252	0.297491982	0.111874913	2.659148272	0.007833848	0.037806108
GPR35	253.4075655	0.441020643	0.165858227	2.659021807	0.007836789	0.037807378
BCL7B	2881.676705	0.247138997	0.092953935	2.658725491	0.007843684	0.03783074
AGPAT5	2620.667617	0.290900341	0.109437686	2.658136813	0.007857399	0.037886971
ASB13	1231.960654	0.28827555	0.108464505	2.65778699	0.007865559	0.037916397
GSDME	2326.890821	0.365109854	0.137384643	2.657573983	0.007870531	0.037930445
ZNF594	473.008904	-0.405847108	0.152719698	-2.657464035	0.007873099	0.037932
ZNF506	909.6635207	-0.246953578	0.092949997	-2.65684332	0.007887609	0.037987184
PPIA	40907.22646	0.271679164	0.102261211	2.656717659	0.00789055	0.037987184

PDHA1	3443.591519	0.345496116	0.130044747	2.656747948	0.007889841	0.037987184
CCDC160	121.4044074	-0.558074431	0.210076614	-2.656528118	0.007894987	0.037998618
LTBP3	13828.71092	0.38548977	0.145149926	2.655804114	0.007911956	0.038070348
ZNF347	607.2516928	-0.310405773	0.116883324	-2.65568913	0.007914654	0.038070992
NME6	916.8091583	0.22575792	0.085011305	2.655622341	0.007916221	0.038070992
C18orf54	275.095145	-0.475676201	0.179133133	-2.655433936	0.007920645	0.038075391
FAIM	736.7770142	-0.246668168	0.092892777	-2.655407388	0.007921268	0.038075391
CLDND1	37127.15429	-0.674128422	0.253939965	-2.654676357	0.007938453	0.0381381
FBLIM1	487.9420391	0.64047214	0.241255544	2.654745795	0.007936819	0.0381381
KLHL35	327.3698551	0.700250081	0.263825091	2.654220939	0.007949176	0.038179662
GLCE	958.046733	-0.278176187	0.104819424	-2.653861059	0.007957659	0.038210445
GPR85	1131.355352	0.429623564	0.161959798	2.652655593	0.007986131	0.038337174
ACAP3	11493.62675	-0.397816805	0.14997867	-2.652489215	0.007990068	0.038346084
CCP110	3235.226802	-0.561154719	0.211619417	-2.651716589	0.008008373	0.038387031
ZNF571	471.4555307	-0.249248158	0.093995981	-2.651689533	0.008009015	0.038387031
FBXO39	18.41561929	0.857884533	0.323512841	2.651778926	0.008006895	0.038387031
NR2C2AP	756.8189818	0.426643711	0.160885224	2.651851427	0.008005176	0.038387031
MAN2B2	3561.242384	0.230034171	0.086742532	2.65191904	0.008003573	0.038387031
TDRD7	1506.593763	-0.260087562	0.098095811	-2.651362577	0.008016773	0.038414225
SPAG7	2968.266474	0.323671848	0.122093409	2.651018188	0.008024952	0.038443421
GTF2A2	1981.895092	0.269017784	0.101490861	2.650660187	0.008033462	0.038464192
VPS37B	3248.424878	0.357944621	0.135036269	2.650729506	0.008031814	0.038464192
NUSAP1	497.7701119	-0.912712328	0.344367505	-2.650402013	0.008039604	0.038474181
METTL26	3317.000804	0.442618637	0.167006409	2.650309289	0.008041811	0.038474181
DCAF13	1385.545082	0.344406604	0.12994955	2.650309939	0.008041796	0.038474181
LIN52	555.155843	-0.376687087	0.142171667	-2.649522893	0.008060551	0.038551643
PTPN7	331.9070082	0.796767942	0.30072907	2.649454351	0.008062186	0.038551643
LIAS	725.6246036	-0.2257166	0.085198118	-2.64931438	0.008065526	0.03855761
TXNL4B	926.6456858	0.245101715	0.092545982	2.648431734	0.008086618	0.038648413
ANKRD30BL	981.2733336	0.943359096	0.356255288	2.647986229	0.008097282	0.038689348
SHBGL1	4775.758505	0.347726097	0.131357602	2.647171469	0.008116818	0.038762593
CMTM7	789.4695467	0.572292277	0.216189066	2.647184188	0.008116513	0.038762593
CPQ	1875.79093	-0.428650693	0.161965862	-2.646549629	0.008131757	0.038814866
STK39	2761.104013	-0.507177355	0.191644201	-2.646452913	0.008134083	0.038814866
ACSF2	1103.108641	0.363415144	0.137317982	2.646522609	0.008132407	0.038814866
HINFP	981.1574787	0.207501994	0.078412237	2.646296069	0.008137856	0.038822817
HIVEP3	913.5307908	-0.240618923	0.09094297	-2.645822143	0.008149265	0.038867186
SBF2	1846.518328	-0.541010868	0.204496554	-2.645574497	0.008155233	0.038875526
LAMP1	19202.96004	0.391831873	0.148107391	2.645592964	0.008154788	0.038875526
METRN	18388.21	0.507059096	0.191677302	2.645378924	0.008159948	0.038877892
EIF2AK4	1904.215542	0.208395147	0.07877543	2.645433094	0.008158642	0.038877892
BST2	6115.990783	0.677066087	0.256037452	2.64440254	0.008183527	0.038980155
PDE1A	1174.056105	-0.957600573	0.362155415	-2.644170248	0.008189146	0.038996838
SYNJ2	6777.202316	-0.600061788	0.226992354	-2.643533037	0.008204576	0.039060224
EFTUD2	4003.853675	0.263421599	0.09965828	2.643248503	0.008211474	0.039072879
HSP90AA1	48261.9486	0.174838708	0.066143387	2.643328629	0.008209531	0.039072879
ZNF488	2223.734461	-0.674065768	0.255053413	-2.642841592	0.008221349	0.039109767
C10orf55	22.60031714	1.005130807	0.380493121	2.64165303	0.008250253	0.039237137
ARID1A	3800.24758	-0.335244055	0.126930709	-2.641157987	0.008262318	0.039284381
MIEN1	3469.054542	0.392210715	0.148536697	2.640497077	0.008278451	0.039350933
EPB41L4A	510.4410461	-0.3989132	0.151080391	-2.640403547	0.008280736	0.039351646
AGO3	1417.834076	-0.331021458	0.12537422	-2.640267338	0.008284065	0.039357318
TRIM59	926.2168113	-0.763584617	0.289266621	-2.639725988	0.008297308	0.039370327
CCL19	26.12030876	-1.306707562	0.495029367	-2.639656653	0.008299006	0.039370327
C9orf152	5.644719349	-0.738486667	0.279768848	-2.639631515	0.008299621	0.039370327
SNRPB2	2055.786104	0.28000648	0.106077809	2.639632947	0.008299586	0.039370327
YARS	3989.254394	0.250254437	0.094801009	2.63978664	0.008295824	0.039370327
IPPK	918.4048893	0.21661403	0.082052366	2.639948604	0.00829186	0.039370327
DNM3	2606.86423	-0.647801527	0.245438121	-2.639368016	0.008306076	0.039390806
ANKIB1	3902.599476	-0.490548305	0.185895873	-2.638833754	0.008319177	0.039435766
POLR2J3	2400.922978	-0.315220201	0.119455578	-2.638806885	0.008319836	0.039435766
ATP8A1	6804.927337	-0.735745958	0.278844998	-2.638548163	0.008326187	0.039455722
OR2M3	243.2938929	-0.371299586	0.140746085	-2.638081098	0.008337664	0.039489799
ARMH1	450.6559089	0.472847736	0.179234551	2.638150589	0.008335956	0.039489799
DUS4L	454.7522227	-0.298937689	0.113322589	-2.637935567	0.008341243	0.039496599
JADE3	545.3099328	-0.590009276	0.22367871	-2.637753391	0.008345725	0.039501504
TMEM233	131.8135985	0.902904169	0.342316183	2.637632143	0.008348709	0.039501504
JAML	689.5901454	0.98684209	0.374132253	2.637682481	0.00834747	0.039501504
RSU1	2120.591687	-0.411387406	0.155975965	-2.637505121	0.008351836	0.039506159
FANCF	511.6651404	0.341569408	0.129509335	2.637411487	0.008354142	0.039506928
EFNA4	149.1502	0.589559897	0.223553039	2.637226049	0.008358711	0.03951839
MMS22L	365.5941149	-0.428337095	0.162452971	-2.636683667	0.008372086	0.03956658
MFSD8	877.9218518	-0.288978518	0.10960164	-2.636625865	0.008373513	0.03956658
TAOK3	2628.464787	-0.287330819	0.10897978	-2.636551652	0.008375345	0.03956658
CHRNA6	33.59444242	0.984682682	0.373532387	2.636137362	0.008385578	0.039584481
MVP	9363.946101	0.58577066	0.222200934	2.636220507	0.008383523	0.039584481
WDR75	1554.281539	0.186621837	0.070790487	2.63625589	0.008382649	0.039584481
HPS1	3689.183471	0.312635676	0.118606065	2.635916439	0.008391039	0.039600118
SEPSECS	647.0767087	-0.320834171	0.121738804	-2.635430611	0.00840306	0.039646698
DCAF17	757.443018	-0.353692854	0.134234919	-2.634879628	0.008416713	0.039700946
BTAF1	1704.830051	-0.513396669	0.1948724	-2.63452736	0.008425451	0.039731996
POMP	4307.680816	0.382238698	0.145146639	2.633465718	0.008451837	0.039846227
P3H4	745.2862344	0.427723358	0.162430636	2.633267773	0.008456765	0.039859262
OR1L8	9.82344913	-0.906003088	0.344071888	-2.633179637	0.008458959	0.039859413
SERPING1	14361.51849	0.802976042	0.304989419	2.632799675	0.008468428	0.039883633
APOC4-APOC2	81.9335866	0.997524488	0.378876345	2.632849744	0.00846718	0.039883633
ANGEL2	1427.793731	-0.213766862	0.081230514	-2.631607888	0.008498188	0.040013568
PCCA	843.5204235	-0.363569134	0.138164202	-2.631427896	0.008502691	0.040024543
TMEM161A	1231.923809	0.361105446	0.137245754	2.631086469	0.008511238	0.040054546
MSH3	506.4769753	-0.306445	0.116481546	-2.630845931	0.008517264	0.040072672
SBF1	10875.19445	-0.303129859	0.115240521	-2.630410347	0.008528186	0.040112202
PCDHB14	436.9151528	-0.461701564	0.175532655	-2.630288724	0.008531238	0.040112202
TNFSF15	72.01410534	0.864874431	0.328818266	2.630250566	0.008532196	0.040112202
MTMR4	2685.88866	-0.350611265	0.133346229	-2.629330193	0.008555325	0.04021068
GCLC	3209.191617	-0.403743898	0.153570065	-2.629053382	0.008562292	0.04022291
ALKBH5	4826.602606	0.233172864	0.088690539	2.629061315	0.008562092	0.04022291
XKR3	5.686680006	1.764786378	0.671488364	2.628171197	0.00858453	0.040317101
NSMCE2	505.880434	-0.309900654	0.117983683	-2.626639948	0.008623252	0.040478329
INHBE	11.07561664	1.23578927	0.470481972	2.626645322	0.008623116	0.040478329
PEX5L	4359.413691	-0.720053327	0.274174329	-2.626260931	0.008632861	0.040509766
ZNF552	232.1292534	0.403763302	0.153744168	2.626202395	0.008634346	0.040509766
AKTIP	2699.106692	-0.32235273	0.122777321	-2.625507111	0.008652	0.040582263
GLIPR2	5472.5714	0.529609356	0.20177032	2.624812979	0.008669657	0.040644394
RITA1	1031.25228	0.301692209	0.114934784	2.624899092	0.008667465	0.040644394
SMARCAL1	1039.636987	0.21158332	0.080633095	2.624025774	0.008689721	0.040728094
FAF1	2089.060555	-0.41294093	0.157399806	-2.623516132	0.008702732	0.040769525
MPIG6B	22.53721057	1.029339192	0.392352485	2.62350624	0.008702985	0.040769525
ZNF100	432.2162714	-0.420516688	0.160332916	-2.622772025	0.008721761	0.040842471
SPX	1415.353141	-0.909959853	0.346966968	-2.622612344	0.008725849	0.040842471
ATF6	2281.854159	-0.244284608	0.093147656	-2.622552401	0.008727385	0.040842471
GRM3	3683.121025	-0.766067108	0.292133759	-2.622316267	0.008733434	0.040842471
CHCHD10	3329.944455	0.579910597	0.221146507	2.62229146	0.00873407	0.040842471
ZNF747	1053.119457	0.158562075	0.060463428	2.622445994	0.00873011	0.040842471
TUT1	1214.284547	0.273023852	0.104107258	2.622524636	0.008728096	0.040842471
UBN2	1224.789896	-0.353723514	0.134918307	-2.621760686	0.008747683	0.040895752
PRUNE2	9071.600396	-0.506373567	0.193164326	-2.621465243	0.008755269	0.040920835

RASSF1	1520.251331	0.326689246	0.124628431	2.621305932	0.008759362	0.040929584
ERMN	31930.48124	-0.856835971	0.326891066	-2.621166681	0.008762941	0.040935927
RAP1GDS1	4683.4061	-0.395050168	0.150720652	-2.621075223	0.008765292	0.040936534
NOP2	1281.86212	0.402377195	0.153525087	2.620921467	0.008769246	0.040944625
CEP290	1113.285437	-0.335391197	0.127973415	-2.620788049	0.008772678	0.040950276
TESK1	3205.206425	0.280780833	0.107145261	2.620562311	0.008778489	0.040967021
TUFM	9680.357667	0.303493455	0.115824738	2.620281816	0.008785713	0.040990355
GLRX2	709.4704542	0.231437032	0.088336345	2.619952542	0.0087942	0.04101957
FASTKD5	694.9688013	0.310613852	0.118582071	2.619399802	0.008808465	0.041075707
TMEM128	1355.918699	-0.296436488	0.113187526	-2.618985491	0.00881917	0.041094433
CUL7	1349.979495	0.326460446	0.124650663	2.619002878	0.00881872	0.041094433
PRSS23	4875.116313	0.711311428	0.271592222	2.61904197	0.00881771	0.041094433
EXOC3	4066.238602	0.213370507	0.081473882	2.618882297	0.008821838	0.041096479
TMEM179B	1938.192872	0.396380024	0.151388929	2.618289367	0.008837183	0.041157555
QKI	29917.147	-0.584580737	0.223291628	-2.618014576	0.008844303	0.041171918
MBOAT2	3349.287096	-0.324236661	0.123852113	-2.617934032	0.008846391	0.041171918
MAF1	4933.31523	0.282632756	0.107961149	2.617911711	0.008846969	0.041171918
PYROXD2	625.4701341	-0.314640348	0.12023736	-2.61682681	0.008875136	0.04128364
AC007325.4	938.1849736	0.5380641	0.205617976	2.616814496	0.008875456	0.04128364
PRMT3	875.419653	-0.363713217	0.139004073	-2.616565184	0.00888194	0.041303376
ATP5MC3	5397.565389	0.244825158	0.093586896	2.616019636	0.008896144	0.041358991
MAOB	18597.83469	-0.649658006	0.248357031	-2.615822886	0.008901272	0.041361961
SNAPC2	1137.956357	0.34515951	0.131949592	2.615843713	0.008900729	0.041361961
HDGF	8948.87866	0.254222028	0.097191353	2.615685671	0.008904849	0.041368154
SYT14	447.853473	-0.521603343	0.199437291	-2.615375191	0.008912949	0.041395347
JMJD7-PLA2G4B	1226.077663	-0.556776618	0.212909283	-2.615088498	0.008920434	0.041409238
OCIAD2	1521.172244	0.545935438	0.208757591	2.615164487	0.008918449	0.041409238
ZNRF2	622.5559555	-0.348206983	0.133159396	-2.614963683	0.008923694	0.041413942
UBE3B	2320.786873	-0.190340632	0.072802359	-2.614484413	0.008936224	0.041461649
CLEC16A	1641.812147	-0.192181409	0.073510869	-2.614326443	0.008940357	0.041470385
PTPN13	3588.882264	-0.516287167	0.197514118	-2.613925389	0.008950858	0.04147761
RENBP	2639.8268	0.515302769	0.197137691	2.613923129	0.008950917	0.04147761
DPEP2	696.7302388	0.779473026	0.298191956	2.613997493	0.008948969	0.04147761
AAMP	4738.204027	0.191188858	0.073137188	2.614112755	0.008945951	0.04147761
METTL25	167.9447013	-0.349815621	0.1338329	-2.613823805	0.00895352	0.041479239
TFPT	2576.863602	0.581088633	0.22238538	2.612980367	0.008975646	0.041550409
LRRTM1	442.3590967	0.929287599	0.355633085	2.613051595	0.008973775	0.041550409
MTRF1L	1685.23783	0.205406625	0.078606151	2.613111333	0.008972207	0.041550409
CRYL1	3928.91161	-0.393176641	0.150485228	-2.612725828	0.008982333	0.041570922
EHD4	1808.299831	0.387875968	0.148484631	2.612229734	0.008995378	0.041610399
PRPF18	481.7469023	0.226828099	0.086830688	2.612303374	0.008993441	0.041610399
TTLL7	5912.678217	-0.695484936	0.266262382	-2.612028517	0.009000675	0.04162445
CCDC141	54.36630995	-0.488482545	0.187035076	-2.611716232	0.0090089	0.041652035
FBH1	2402.849381	0.177322666	0.067903189	2.611404088	0.009017128	0.04167962
CREG1	7646.348344	0.474073768	0.181599582	2.610544373	0.009039824	0.041774053
BCL10	657.6438712	0.966185826	0.370159166	2.610190199	0.009049189	0.041806847
ZDHHC9	8274.007914	-0.429716215	0.164661057	-2.609701552	0.009062124	0.041856113
LIMCH1	7580.717159	-0.583565945	0.223690288	-2.60881219	0.009085709	0.041954532
WDR43	1148.562203	0.264341166	0.101338308	2.608501858	0.009093952	0.041982074
THBD	630.8239051	0.766357452	0.293832908	2.608140323	0.009103563	0.042015917
NRDE2	975.6024104	-0.189638582	0.072722296	-2.607708934	0.009115042	0.042016287
SHBRF2	77.4775943	0.825453367	0.316537662	2.607757198	0.009113757	0.042016287
PRAMEF2	2.020423039	3.169644466	1.215456709	2.607780634	0.009113134	0.042016287
MFGE8	5507.202023	0.541306875	0.207568573	2.607846015	0.009111393	0.042016287
SHMT2	2461.205002	0.445967723	0.171007339	2.607886462	0.009110317	0.042016287
CDK18	22979.86952	-0.562923976	0.215891726	-2.60743654	0.009122298	0.042039216
DHX8	1697.573386	0.199709796	0.076615527	2.606649131	0.0091433	0.042125468
CDB3	1332.045927	0.506063551	0.194166018	2.606344593	0.009151434	0.042152407
SLC25A48	350.7420902	-0.875861891	0.336065735	-2.60622194	0.009154712	0.042156969
CSNK2A2	2487.947623	0.1724749	0.066184992	2.605951815	0.009161935	0.042169156
RAD23A	6641.561321	0.272976481	0.104750564	2.605966696	0.009161537	0.042169156
NFKBIL1	1494.794094	0.400755711	0.153799733	2.605698347	0.009168717	0.042189834
SFTPD	128.2420309	0.77291283	0.296678822	2.605217403	0.009181598	0.04223856
KDR	959.2963236	-0.451275583	0.173233541	-2.605012752	0.009187084	0.04225325
SLC35A4	3713.859699	0.281224938	0.107959683	2.604907045	0.009189919	0.042255742
MYH7B	797.222621	-0.757394698	0.290771287	-2.60477816	0.009193376	0.042261096
MRPS5	2671.809697	0.280342685	0.107664058	2.603865116	0.009217903	0.042363274
NUDT18	667.8963759	0.488543437	0.187638438	2.603642641	0.009223888	0.042380211
VRK3	1736.894885	0.23700643	0.091033648	2.603503592	0.00922763	0.042386838
EXOSC1	887.503177	0.30009476	0.115286824	2.603027399	0.009240457	0.042435181
BICRA	1313.903853	-0.248271041	0.095393105	-2.602609903	0.009251716	0.0424763
PADI2	21132.6662	-0.588994021	0.226321992	-2.602460392	0.009255751	0.042484241
CCL24	1.312186354	2.40821082	0.925564028	2.60188463	0.009271304	0.042545033
OR56A1	20.86103066	-0.645603856	0.248187851	-2.601270986	0.009287906	0.042610608
CATSPERE	76.60265059	-0.480001752	0.184538635	-2.601090833	0.009292785	0.042622381
CMSS1	914.7700048	-0.383085933	0.147331775	-2.600158277	0.009318077	0.042717126
BAHD1	1509.209527	0.299172398	0.115056362	2.600224744	0.009316272	0.042717126
AC036214.3	9.766072198	-0.867362437	0.33360228	-2.599989539	0.00932266	0.042727507
DMKN	232.1761888	0.621013125	0.238886613	2.599614595	0.009332851	0.042742325
IL18RAP	60.57294661	1.018778864	0.39189501	2.599621936	0.009332652	0.042742325
GSX2	295.1223786	1.075614959	0.413748706	2.599681747	0.009331025	0.042742325
TTLL3	4115.282958	-0.287240772	0.110508886	-2.599254974	0.009342635	0.042765877
PRAMEF1	3.032403749	2.399536471	0.9231357	2.599332331	0.00934053	0.042765877
AKR1A1	4508.174288	0.361774351	0.13919065	2.599128261	0.009346085	0.042771043
CRHBP	383.754863	-0.650836886	0.250439196	-2.598782048	0.009355515	0.042792949
TINCR	231.6788078	0.649690729	0.249996133	2.598803115	0.009354941	0.042792949
COG7	1039.998656	-0.205063894	0.078942381	-2.597640083	0.009386682	0.042924856
PLXDC2	3874.343782	-0.63485024	0.244466063	-2.596884947	0.009407343	0.042987335
RNF7	2586.601206	0.332916363	0.128197334	2.596905497	0.00940678	0.042987335
COX19	866.4752547	0.215775963	0.083086186	2.59701368	0.009403818	0.042987335
NFATC2	609.4102219	-0.527147605	0.203020636	-2.596522288	0.00941728	0.043022074
MPDU1	2779.034151	0.340057495	0.130973013	2.596393624	0.009420807	0.043027523
B3GNT9	1236.22713	-0.410218474	0.1580169	-2.596041774	0.00943046	0.043060938
HECTD4	4216.90908	-0.464903428	0.179114045	-2.59557216	0.009443357	0.043109148
DLG2	4106.733128	-0.797326922	0.30720936	-2.595386163	0.00944847	0.043121805
CSDC2	1223.254618	0.649587937	0.25030205	2.595216209	0.009453143	0.043132453
MCFD2	5026.6563	0.283493025	0.109255964	2.59476018	0.009465694	0.043179025
AC005702.1	82.81889817	0.657007309	0.253219365	2.594617152	0.009469634	0.043186309
ANKAR	95.81887806	-0.403599445	0.15557552	-2.59423491	0.009480169	0.043218599
UTP11	1242.123802	0.239963215	0.092500242	2.594190124	0.009481404	0.043218599
GABRR3	7.551517931	-0.8011012	0.308929515	-2.593152031	0.009510072	0.043338555
ORBD4	5.295185747	-0.86860926	0.334988089	-2.592955652	0.009515504	0.043352589
MRRF	946.0334134	-0.206908743	0.079822029	-2.592125829	0.009538488	0.043446562
ANKRD11	6337.309223	-0.25576054	0.098677495	-2.591883194	0.009545217	0.043449573
DNAJB5	2307.179776	0.45896188	0.17707908	2.591846991	0.009546222	0.043449573
BORCS8	1378.149325	0.300219199	0.115827551	2.591949802	0.00954337	0.043449573
ARMH3	1343.584272	-0.18464973	0.071256419	-2.591341699	0.009560251	0.043502685
VGF	3337.181126	1.069919553	0.412906063	2.591193612	0.009564367	0.043510667
TNFAIP3	1313.873886	0.709694863	0.273912173	2.590957733	0.009570925	0.043529755
AC092718.8	134.6971023	-0.581096926	0.224303084	-2.590677375	0.009578724	0.043554481
TPRG1L	4825.611666	0.401627547	0.155045002	2.590393386	0.009586631	0.043579681
DCBLD1	570.1640484	0.400043691	0.154447451	2.590160528	0.009593119	0.043598417
BBX	3741.508765	-0.528935147	0.204232339	-2.589869702	0.009601227	0.043608628
KBTBD6	1017.520401	0.285855161	0.110379847	2.589740497	0.009604831	0.043608628
TXNDC5	3997.617201	0.370812231	0.143185006	2.589742053	0.009604787	0.043608628
CHST15	1671.449981	0.429312315	0.165766118	2.589867699	0.009601282	0.043608628

RAPGEF3	5351.633227	-0.586326088	0.226474956	-2.588922407	0.009627679	0.043701598
CLCA4	775.9799375	-0.843411306	0.325912722	-2.587844071	0.009657869	0.043821192
ATG16L2	2834.259769	0.481555539	0.186086017	2.587811524	0.009658781	0.043821192
HSPA2	13238.38744	-0.640153446	0.247397663	-2.587548475	0.009666159	0.043843872
AL157935.2	723.0385345	0.583783799	0.225638767	2.587249554	0.00967455	0.043871131
FCMR	199.397025	0.78089797	0.301838875	2.587135176	0.009677762	0.043874901
HIST1H4B	3.455783348	1.749004566	0.676095498	2.586919411	0.009683824	0.043891588
NELFB	3793.790691	0.250827016	0.096965449	2.586766924	0.00968811	0.043900216
MRPL54	2181.318619	0.500105683	0.193338671	2.58668212	0.009690495	0.043900227
TP63	14.47731218	-1.144817026	0.442707603	-2.585943899	0.009711274	0.043983549
MRPL10	1912.920052	0.192940367	0.074613919	2.585849527	0.009713933	0.043984783
AP1M1	3940.324089	0.206016076	0.079681153	2.585505697	0.009723627	0.044017862
NMI	752.2594162	0.518879043	0.20070559	2.585274499	0.00973015	0.044036574
SPAG4	250.0920474	0.703217968	0.272076297	2.584635176	0.009748208	0.044107472
EML6	527.1469889	-0.455583957	0.17628218	-2.584401649	0.009754812	0.044126518
LONP1	5950.310992	0.31865908	0.12331525	2.584101145	0.009763316	0.044143314
ZFYVE27	2282.9393	0.272924869	0.105614393	2.5841636	0.009761548	0.044143314
OTOA	205.8676337	0.840421974	0.3252587 6	2.583856538	0.009770243	0.044163797
PIGG	2265.000082	-0.191058303	0.073945888	-2.583758328	0.009773025	0.044165541
ALPL	1169.338063	0.458139914	0.177322043	2.583660257	0.009775804	0.044167265
EPST11	728.4175242	-0.529172272	0.204824552	-2.583539268	0.009779233	0.044171934
ENAM	3.363256387	1.027745783	0.397874548	2.583090044	0.009791976	0.044218659
NDUFA3	457.8198385	0.409741689	0.158641716	2.582811762	0.009799878	0.044243494
RPL38	17995.80175	0.47674165	0.184593513	2.58265657	0.009804286	0.044252558
PKD2	1978.074915	-0.341596962	0.132297292	-2.582040466	0.009821807	0.044320783
TBC1D10C	315.5367753	0.792048858	0.306783478	2.581784594	0.009829091	0.044342796
NOMO2	6833.890831	0.323050154	0.125140574	2.581498097	0.009837253	0.044347051
HINT1	8539.17998	0.320730369	0.124238678	2.581566178	0.009835313	0.044347051
YWHAB	15244.48045	0.224007215	0.086769695	2.58162961	0.009833506	0.044347051
ACR	31.68911541	-0.569217222	0.220515895	-2.581297925	0.00984296	0.044361923
ARV1	1152.380343	-0.246227978	0.095407717	-2.580797296	0.009857244	0.044415441
ZNF664	8826.788417	-0.37432366	0.14506126	-2.580452289	0.009867099	0.044448977
PPP1R32	320.759692	-0.529142492	0.205085208	-2.580110475	0.009876871	0.044452608
AC011511.4	1547.915895	0.706996361	0.274020396	2.580086629	0.009877553	0.044452608
SELENOS	2270.534349	0.294545274	0.114158073	2.580152829	0.00987566	0.044452608
CCL2	6010.622612	0.919420549	0.356321252	2.580313531	0.009871065	0.044452608
BX004987.1	49.17308302	-0.924982307	0.358521236	-2.57999308	0.009880229	0.044453796
CCDC86	1434.676073	0.385204998	0.149334252	2.579481892	0.009894865	0.044508777
ENOPH1	4449.890371	-0.298484715	0.115722642	-2.579311272	0.009899754	0.044519903
STK26	89.69883193	0.813385348	0.315386989	2.579007303	0.009908469	0.044537361
PARP10	4219.17666	0.488457993	0.189394994	2.579043843	0.009907421	0.044537361
RNF8	1142.831259	0.204443856	0.079275577	2.57890087	0.009911522	0.044540221
AOC1	10.77899487	1.376826301	0.533975366	2.578445354	0.0099246	0.044588115
CCDC7	118.2296334	-0.439086858	0.170314697	-2.578091406	0.009934771	0.044622829
GBP2	5594.070323	0.808605457	0.313655136	2.578008019	0.009937169	0.044622829
LRBA	841.5975627	-0.442617102	0.171735006	-2.577326042	0.009956798	0.044700083
DDF	3507.080943	0.393448887	0.152676465	2.577010723	0.009965886	0.044729983
ZGRF1	452.1358196	-0.669164304	0.259703565	-2.576646591	0.009976389	0.044756007
RPL23	21395.31913	0.375774788	0.145838997	2.576641334	0.009976541	0.044756007
PNPLA2	5042.058069	0.31696265	0.123018284	2.576549113	0.009979203	0.044757052
RGL1	3955.272232	-0.377333261	0.146484269	-2.575930259	0.009997081	0.044805069
ZMYND11	4774.190612	-0.395357888	0.153484983	-2.575873422	0.009998724	0.044805069
NDUFV3	2345.844208	0.266610487	0.103510965	2.575673866	0.010004496	0.044805069
EXTL3	3626.836802	0.253914275	0.098579178	2.575739419	0.0100026	0.044805069
CKS2	498.3435979	0.747021664	0.290017431	2.575781946	0.01000137	0.044805069
ZNF628	405.9210383	0.387973549	0.150620085	2.575842059	0.009999631	0.044805069
MMP13	1.350688395	-1.613903031	0.626793513	-2.574855988	0.010028183	0.04490024
TBC1D10A	1132.482337	0.351637155	0.136579796	2.574591303	0.010035859	0.044923696
ATXN7	833.7560491	-0.366298087	0.142318634	-2.573788668	0.010059169	0.045017104
RELN	263.7008736	-0.710381465	0.276055683	-2.573326718	0.010072607	0.045064004
TES	381.9030086	0.587263702	0.228217758	2.573260324	0.01007454	0.045064004
ZNF511	954.5730301	0.289977796	0.112739775	2.5720984	0.010108416	0.04520456
NUF2	133.1507225	-0.821416912	0.319580381	-2.570298309	0.010161098	0.045429128
NPW	95.22304737	1.03272553	0.401825619	2.570083844	0.01016739	0.045446238
KRTAP5-7	21.3801816	-0.916248098	0.356575971	-2.569573309	0.010182385	0.045482501
USP6NL	758.1154551	-0.289136366	0.112523883	-2.569555522	0.010182907	0.045482501
HYAL3	248.9779925	0.533991012	0.207801802	2.569713102	0.010178277	0.045482501
WBP1L	3306.838303	0.236522703	0.092058131	2.56927552	0.01019114	0.045497217
ARID3A	502.3746068	0.301730333	0.117435347	2.569331473	0.010189494	0.045497217
INPP5K	2128.877291	0.185063175	0.072044968	2.568717551	0.010207562	0.045559495
ZNF606	718.13333	-0.292345633	0.11382557	-2.568365211	0.010217944	0.045594792
TCF12	4370.988924	-0.591136764	0.230205661	-2.567863719	0.010232738	0.045649751
TCEAL7	2616.151997	-0.382835467	0.149129969	-2.567126316	0.010254525	0.045735876
INTS4	893.0986872	-0.230814163	0.089914897	-2.567029156	0.010257399	0.045735949
RAD52	540.3049449	-0.349659292	0.136217888	-2.566911713	0.010260873	0.045735949
CST2	4.04097599	1.926974247	0.750782079	2.566622593	0.010269432	0.045735949
PORCN	941.3306237	0.378790574	0.14758053	2.566670373	0.010268017	0.045735949
IPO4	1333.634571	0.436086128	0.169901968	2.566692625	0.010267358	0.045735949
HPX	79.45360144	0.627842774	0.244608375	2.566726403	0.010266358	0.045735949
SMYD5	1629.734597	0.211584589	0.082442919	2.566437379	0.010274918	0.045749325
DTL	178.2166904	-1.04651158	0.407793852	-2.56627601	0.010279699	0.04575956
CEP85L	453.1954419	-0.373538322	0.145565999	-2.566109708	0.010284629	0.045764169
VDAC3	4626.41051	0.245375082	0.095622778	2.566073563	0.010285701	0.045764169
PSMC4	4557.996338	0.27844808	0.108531921	2.565586945	0.01030014	0.045817351
UBXN11	1947.491376	0.336820145	0.131301052	2.565250919	0.010310122	0.045850683
TGFBRAP1	1631.576409	0.183742379	0.071640633	2.564778819	0.010324159	0.045902034
SEC13	4238.69953	0.271686707	0.105956671	2.564130268	0.010343472	0.045976806
BTNL9	562.3352281	-0.783864805	0.30575451	-2.563706438	0.010356109	0.046013728
MMP28	1326.583914	0.560081309	0.218467352	2.563684246	0.010356772	0.046013728
HIST2H4A	186.3437811	0.787460395	0.307171276	2.563587343	0.010359663	0.046015481
ZNF644	1565.948727	-0.325435525	0.126965715	-2.563176405	0.010371934	0.046058883
CYB561A3	2247.520962	0.472287192	0.184265334	2.563082174	0.010374749	0.046060287
NT5C2	3175.415814	-0.294839306	0.115052916	-2.562640877	0.010387944	0.046107758
RFX3	907.5337356	-0.510431428	0.199201135	-2.562392167	0.010395386	0.046129683
TMEM134	2193.832089	0.396215579	0.15463386	2.562282154	0.01039868	0.046133191
CNKSR3	876.7246468	-0.359791388	0.140447484	-2.561750329	0.010414616	0.046192768
RPGRIP1	47.22397317	-0.555225582	0.216759847	-2.561478009	0.010422784	0.046217874
INAFM2	1747.883232	0.316739167	0.12366786	2.561208428	0.010430876	0.046242629
ITGA2	1113.14035	-0.527262016	0.205875431	-2.561073035	0.010434942	0.046245093
MXRA8	2367.302218	0.573374998	0.223885158	2.561022817	0.01043645	0.046245093
TMEM171	68.84853394	-0.893230534	0.348877334	-2.560299704	0.010458193	0.046330298
MIEF2	744.633157	0.223243263	0.087221196	2.559507003	0.010482074	0.046424934
FAM149B1	1278.332443	-0.442468891	0.172880157	-2.559396633	0.010485403	0.046428519
EXOC2	1376.007072	-0.271646536	0.106149778	-2.559087176	0.010494742	0.046436399
SLCO4C1	15.31211109	1.196475423	0.467531875	2.559131232	0.010493412	0.046436399
SLC25A5	7068.318809	0.281204388	0.109880677	2.55917961	0.010491952	0.046436399
SYCP2L	56.60721327	-0.636847363	0.248928634	-2.558353182	0.010516922	0.046512521
GDNF	193.4409988	0.760697664	0.297348772	2.55826738	0.010519517	0.046512521
C12orf65	699.675377	0.187996926	0.073485076	2.558300764	0.010518507	0.046512521
C9orf85	468.363475	-0.223359314	0.087321104	-2.557907572	0.010530408	0.046538693
SPATA25	66.08431019	-0.782177476	0.305788327	-2.557904948	0.010530487	0.046538693
HCST	687.3664286	0.658997847	0.25774956	2.556737036	0.010565906	0.046684027
EIF4G1	11913.15944	0.238222763	0.093194844	2.556179646	0.010582847	0.046747671
HAMP	788.791507	0.818835376	0.320361611	2.55597221	0.010589158	0.046764338
PLCD3	5272.780291	0.30903006	0.120931208	2.555420271	0.010605966	0.046827345
RNF148	3.500784274	1.286251494	0.503456941	2.554839134	0.010623688	0.04689436

BCHE	738.8221824	-0.646434688	0.253051189	-2.554560955	0.010632181	0.04692061
ERCC2	1554.169293	0.302268682	0.118333314	2.55438364	0.010637598	0.046933275
ZSCAN20	164.1105437	0.319097497	0.124959576	2.553605795	0.010661388	0.047026981
ATXN7L1	307.661546	-0.340050138	0.133172158	-2.553462704	0.01066577	0.047035051
IKZF3	138.3408155	-0.516898771	0.202442593	-2.553310368	0.010670437	0.047035297
PKDREJ	10.91724202	-0.881479835	0.345232374	-2.553294248	0.01067093	0.047035297
ZNF428	4828.468122	0.429504466	0.168238517	2.552949675	0.010681493	0.047070598
TARSL2	2048.856783	-0.399297857	0.156439175	-2.552416014	0.01069787	0.047126679
HMGB3	1535.068684	0.46921681	0.183841849	2.552285085	0.010701891	0.047126679
POLR2E	7053.832363	0.25370028	0.099398941	2.552343901	0.010700084	0.047126679
SLC24A2	6300.75569	-0.764351036	0.299490297	-2.552172956	0.010705336	0.047130588
PRCD	826.5889792	-0.719659921	0.282013975	-2.551859072	0.010714985	0.047161&
FAM72B	102.8106716	-0.702849096	0.27565389	-2.549752143	0.010779953	0.047425101
MR1	1903.152688	0.494467544	0.193923295	2.549809932	0.010778166	0.047425101
PPWD1	1185.150912	-0.237261712	0.093060621	-2.549539325	0.010786535	0.047442731
PROX1	1305.278559	-0.527450936	0.206896557	-2.549346123	0.010792513	0.047457699
JARID2	1059.601617	-0.337938433	0.132584118	-2.548860589	0.010807549	0.047494828
ZCCHC24	13468.84578	-0.508292494	0.19942237	-2.548823853	0.010808688	0.047494828
TFE3	5646.589747	0.240477214	0.094343021	2.548966653	0.010804263	0.047494828
CNTNAP4	6833.374729	-0.787846948	0.309129246	-2.548600493	0.010815612	0.047502601
SAYSD1	734.7029682	0.219498765	0.086122416	2.548683335	0.010813044	0.047502601
LAMA2	857.5628813	-0.490266773	0.192393317	-2.548252614	0.010826404	0.047538672
TMEFF2	1719.673892	-0.606455883	0.238053303	-2.547563409	0.010847814	0.047611556
TIMM23B	463.894014	-0.277698706	0.109006101	-2.547551954	0.01084817	0.047611556
C11orf45	161.0629403	0.540138787	0.21209128	2.54672793	0.010873817	0.047712757
FLT3LG	455.4363043	0.476971331	0.187295097	2.546630103	0.010876866	0.047714773
UBL7	2925.070563	0.370206214	0.145376968	2.546525892	0.010880114	0.047717663
TUBA1B	57529.5509	-0.336117067	0.132051894	-2.545340745	0.010917115	0.047868549
ZNF891	330.7991844	-0.433043061	0.1701513	-2.545047032	0.010926302	0.047897436
IFT88	943.458087	-0.348419417	0.136907843	-2.544919331	0.010930299	0.047900466
GPR84	192.2010924	0.854117683	0.335624775	2.544858859	0.010932192	0.047900466
HIST1H1E	33.19657662	0.927133895	0.364380323	2.544412627	0.010946169	0.04795031
RIOK2	794.6965555	0.182776195	0.071842879	2.544110124	0.010955654	0.047969053
CASZ1	171.503567	0.526378969	0.206894566	2.544189434	0.010953166	0.047969053
TRIB3	734.3996186	0.761040766	0.299162642	2.543903082	0.01096215	0.047986094
GBF1	3078.577134	-0.209370744	0.082319032	-2.543406281	0.01097775	0.04801639
MAN2C1	6244.347214	-0.212488693	0.083546617	-2.543354845	0.010979367	0.04801639
PET117	496.7208311	0.266277729	0.104695635	2.543350832	0.010979493	0.04801639
WDR53	335.5497686	0.255457864	0.100438805	2.543417989	0.010977382	0.04801639
MEA1	4178.235828	0.286272067	0.112571408	2.543026432	0.010989692	0.048038194
CUEDC2	4033.020684	0.346330496	0.13618619	2.543066192	0.010988441	0.048038194
COPG2	1254.615982	-0.276009203	0.108539773	-2.542931463	0.010992679	0.048039858
ENAH	4627.0266	-0.318611315	0.125313562	-2.542512637	0.011005862	0.048086068
SLC39A13	3364.186997	0.323202821	0.127133277	2.542236215	0.011014571	0.048101309
HLA-B	50507.6501	0.618993017	0.243478031	2.542295148	0.011012714	0.048101309
SLCO2B1	9535.94382	-0.604002712	0.237601719	-2.542080562	0.011019477	0.048104442
CLCA2	160.9315789	0.98215057	0.386361952	2.542047848	0.011020509	0.048104442
ZNF274	1207.307079	-0.31958827	0.125754297	-2.541370571	0.011041882	0.048186323
RPIA	432.0823055	0.290818851	0.114439423	2.541247084	0.011045783	0.048191935
BAIAP2	3040.812129	0.448832415	0.176662508	2.540620632	0.011065591	0.048266931
NPHP3	1028.942282	-0.417409682	0.164338071	-2.539945117	0.011086987	0.04832594
UNC119	1434.736074	0.304243438	0.119779618	2.540026795	0.011084398	0.04832594
STEAP4	98.98409863	0.679660711	0.267576601	2.540060337	0.011083335	0.04832594
ZNF726	94.4113365	-0.543859825	0.214165909	-2.539432292	0.011103253	0.048369729
NCBP3	2524.746815	-0.292804955	0.115305677	-2.539380211	0.011104907	0.048369729
LOXL4	193.3568325	0.586877953	0.231108149	2.539408312	0.011104015	0.048369729
PLEKHO1	4034.795408	0.371353008	0.146246306	2.539230011	0.011109676	0.048379067
CYCS	5385.354834	0.281469717	0.110854049	2.539101804	0.011113748	0.048385367
KCNE4	410.1653167	-0.580918632	0.228801817	-2.538959872	0.011118257	0.048393568
CST6	12.09306582	1.097740228	0.432384285	2.538806929	0.011123119	0.048403295
RASA1	1471.549314	-0.377609768	0.148745426	-2.538631127	0.011128709	0.048406483
DCK	1147.919843	-0.480964262	0.189459041	-2.538618689	0.011129105	0.048406483
CCL7	70.91794352	1.656561424	0.65276908	2.537744934	0.011156927	0.048516045
VSTM2B	1591.115081	-0.762512472	0.300509529	-2.537398645	0.01116797	0.048552612
COPZ1	4731.905653	0.237088189	0.093444359	2.537212436	0.011173913	0.048566988
TBC1D5	3212.091064	-0.551599319	0.217444873	-2.536731776	0.011189265	0.048622249
SEC14L1	5820.021817	-0.283228268	0.111676433	-2.536150728	0.011207848	0.048691522
PPIAL4C	2.65844094	2.333861432	0.920269017	2.536064335	0.011210614	0.048692057
POLR3D	907.2755408	0.27447352	0.108238421	2.535823382	0.01121833	0.048702614
ENDOG	1068.269929	0.467468543	0.184340755	2.535893609	0.01121608	0.048702614
CRK	3313.622239	0.14032862	0.055343342	2.535600754	0.011225463	0.048722106
TMEM160	2413.586298	0.603095038	0.237882443	2.535265029	0.011236228	0.048757346
NR1D2	1617.907144	-0.345351201	0.136227283	-2.535110391	0.01124119	0.048764361
XKR7	198.1184936	1.095816173	0.432266147	2.535049714	0.011243137	0.048764361
DHRS7	4177.257679	0.327706752	0.129279824	2.534863843	0.011249104	0.048778762
FKBP11	614.6554217	0.39941358	0.157598841	2.534368767	0.011265011	0.048824763
RPL37A	35860.79789	0.411310907	0.162292342	2.534382727	0.011264562	0.048824763
LRRC1	962.46785	-0.42644644	0.168286163	-2.534055273	0.011275095	0.048848456
KRTAP5-5	1.729640401	-1.475491175	0.582269683	-2.534034003	0.011275779	0.048848456
RICTOR	1647.06186	-0.43853322	0.173076139	-2.533758971	0.011284632	0.04887532
RBM44	21.53274259	-0.691246314	0.272901866	-2.532948286	0.011310764	0.048976989
NUBPL	489.437832	-0.374564993	0.147883662	-2.53283553	0.011314403	0.048981237
TYW1	924.7712169	-0.331076378	0.130727997	-2.532559085	0.011323328	0.049008365
UBE2E1	4007.772581	-0.20382418	0.080486681	-2.532396368	0.011328585	0.049019604
AC007906.2	55.92873622	0.806426645	0.31846242	2.532250574	0.011333297	0.049028481
DYNC1I2	8781.446286	-0.336753038	0.133002943	-2.531921704	0.011343932	0.049059262
RGS11	4360.557025	-0.506612058	0.200094346	-2.531865929	0.011345736	0.049059262
SARNP	2229.757964	0.30077251	0.118804799	2.531652859	0.011352632	0.049077565
ANO8	2660.496978	-0.383305275	0.15141367	-2.531510372	0.011357246	0.049085995
TOR2A	707.4362556	0.276469979	0.10924882	2.530644991	0.011385302	0.049195716
PXDN	1889.414127	-0.585404592	0.23137552	-2.530105999	0.011402807	0.049254519
USP48	2743.263935	-0.220086007	0.086988405	-2.530061426	0.011404256	0.049254519
BCL2L2	5989.567599	-0.44876803	0.177406357	-2.529605127	0.011419096	0.049303953
NEK7	2965.735839	-0.62097534	0.245488947	-2.529545006	0.011421053	0.049303953
CALCB	28.19686596	0.954760369	0.377538062	2.528911561	0.011441685	0.049358338
LRRC25	852.6356517	0.691207031	0.273316503	2.528961931	0.011440044	0.049358338
CAPN10	1697.952066	0.273069801	0.107972797	2.529061107	0.011436811	0.049358338
LDB3	2687.892111	-0.754091187	0.29828072	-2.528125809	0.011467325	0.049457369
COIL	669.1703181	0.18503908	0.073195677	2.528005569	0.011471253	0.049462734
MEF2B	253.0720635	0.744002137	0.29439171	2.527252334	0.011495887	0.049557359
GALNT7	1567.08775	-0.433852276	0.171676461	-2.527150631	0.011499217	0.04956012
CCNF	309.8409567	0.670635925	0.26539967	2.526890578	0.011507735	0.049585239
APP	46288.27976	-0.396614073	0.156991149	-2.526346714	0.011525567	0.049650463
NSFL1C	5309.300949	0.23538677	0.09318092	2.526126256	0.011532803	0.049670021
UBL5	6977.063529	0.399165155	0.158037099	2.525768682	0.011544547	0.049708984
CXCL16	5546.629597	0.577715689	0.228834735	2.524597886	0.011583074	0.049863227
TOR1B	1171.308283	0.290197558	0.114955049	2.524443765	0.011588154	0.049873446
SAXO2	112.0180693	-0.533133409	0.211239928	-2.52382878	0.011608445	0.049937451
NIPA2	1822.271401	0.218691143	0.086648211	2.5238968	0.011606199	0.049937451
MAP1S	3690.319366	0.323216671	0.128072529	2.52370024	0.01161269	0.049944054
PI3	531.919295	1.656404959	0.656416543	2.523405265	0.011622437	0.04997431
USP53	1252.990848	-0.397081309	0.157370609	-2.523224065	0.011628428	0.049987771
PTAFR	1643.869441	0.609254819	0.241466285	2.523146528	0.011630993	0.049987771

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
HALLMARK_P53_PATHWAY	195	0.5515	2.9842005	0	0	0	2063	tags=42%, list=1
HALLMARK_OXIDATIVE_PHOSPHORYLATION	200	0.4791	2.6175818	0	0	0	2998	tags=42%, list=1
HALLMARK_TNFA_SIGNALING_VIA_NFKB	198	0.4707	2.5340328	0	0	0	3033	tags=39%, list=1
HALLMARK_MYC_TARGETS_V2	58	0.5291	2.272414	0	0	0	2058	tags=33%, list=1
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY	49	0.4948	2.1158695	0	0	0	3292	tags=43%, list=1
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HALLMARK_DNA_REPAIR	149	0.3662	1.889633	0	0.002303855	0.003	4395	tags=42%, list=2
HALLMARK_COAGULATION	138	0.363	1.8870662	0	0.002015873	0.003	3451	tags=36%, list=1
HALLMARK_HYPOXIA	197	0.3498	1.8562508	0	0.002559564	0.005	3627	tags=34%, list=1
HALLMARK_APOPTOSIS	159	0.3336	1.7487315	0	0.003331323	0.009	2772	tags=28%, list=1
HALLMARK_UV_RESPONSE_UP	156	0.3332	1.7478431	0	0.003028476	0.009	3926	tags=36%, list=2
HALLMARK_COMPLEMENT	199	0.315	1.7045422	0	0.004497797	0.014	2304	tags=28%, list=1
HALLMARK_IL2_STAT5_SIGNALING	199	0.3112	1.6965114	0	0.004749615	0.016	3181	tags=31%, list=1
HALLMARK_ADIPOGENESIS	199	0.3065	1.6222962	0	0.008268605	0.033	2826	tags=28%, list=1
HALLMARK_XENOBIOTIC_METABOLISM	198	0.2926	1.5997667	0	0.008300723	0.036	2527	tags=25%, list=1
HALLMARK_GLYCOLYSIS	197	0.2913	1.5712166	0	0.009666126	0.044	3292	tags=27%, list=1
HALLMARK_ESTROGEN_RESPONSE_LATE	198	0.2795	1.4800677	0	0.021792695	0.093	2994	tags=24%, list=1
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HALLMARK_FATTY_ACID_METABOLISM	156	0.2546	1.3096892	0.020408163	0.05987752	0.307	3336	tags=28%, list=1
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HALLMARK_APICAL_SURFACE	44	0.2861	1.1696348	0.1696113	0.15290487	0.681	3371	tags=27%, list=1
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HALLMARK_KRAS_SIGNALING_UP	199	0.2009	1.0790316	0.22689076	0.28989896	0.917	2128	tags=15%, list=1
HALLMARK_APICAL_JUNCTION	200	0.187	0.9974	0.52755904	0.49565935	0.985	2773	tags=19%, list=1
HALLMARK_PI3K_AKT_MTOR_SIGNALING	104	0.1902	0.9272463	0.6782178	0.6878964	0.998	654	tags=9%, list=3%
HALLMARK_PANCREAS_BETA_CELLS	40	0.1649	0.6593815	0.9640288	0.9910655	1	4680	tags=33%, list=2

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HALLMARK_G2M_CHECKPOINT	192	-0.2799	-1.2624408	0.068571426	0.30963138	0.976	9514	tags=63%, list=4
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snRNAseq	gl_Pro1	4	6	0
	gl_Pro2	5	0	0
	gl_PN1	11	5	1
	gl_PN2	6	5	4
	gl_Mes1	2	3	2
	gl_Mes2	7	11	14
scRNAseq	AC_Neftel	3	2	3
	G1/S_Neftel	3	1	2
	G2/M Neftel	7	5	0
	MES1_Neftel	1	4	9
	MES2_Neftel	5	8	2
	NPC1_Neftel	2	0	0
	NPC2_Neftel	5	4	5
	OPC_Neftel	9	6	0

COLUMBIA UNIVERSITY MEDICAL CENTER

Herbert Irving Comprehensive Cancer Center
Protocol

NCI·CC
A Cancer Center Designated by the National Cancer Institute

CUMC IRB#: AAAQ9520
Version Date: 04/03/2019

TITLE: CHRONIC CONVECTION ENHANCED DELIVERY OF TOPOTECAN FOR RECURRENT HIGH GRADE GLIOMAS

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Funding Source:	NIH/NCI National Institutes of Health 9000 Rockville Pike Bethesda, Maryland 20892 301-496-4000
Study Agent:	Topotecan
Other Agent:	Gadolinium
IND Status:	**IND #:** 131889 **IND Sponsor:** Jeffrey Bruce, MD

Affiliate Institutions:

Site Principal Investigator and Contact Information:	**Other Investigators at Site**
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Protocol Signature Page

I confirm that I have read this protocol, I understand it, and I will work according to this protocol and to the ethical principles stated in the latest version of the Declaration of Helsinki, the applicable ICH guidelines for good clinical practices, and the applicable federal, state, and local laws, rules, and regulations relating to the conduct of the protocol. I have read and understand the information in the Investigators' Brochure (or Manufacturer's Brochure) regarding the risks and potential benefits. I will promptly submit the protocol to the applicable IRB for review and approval. Once the protocol has been approved by the IRB, I understand that any modification made during the course of the study must first be approved by the IRB, prior to implementation except when such modification is made to remove an immediate hazard to the subject. I certify that I, and the study staff, have received the requisite training to conduct this research protocol. I agree to maintain adequate and accurate records in accordance with Columbia University and Herbert Irving Comprehensive Cancer Center policies, Federal, state and local laws and regulations. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

Instructions to Principal Investigator: Sign and Date this signature page and print your name. Return the original, completed and signed to the Clinical Protocol & Data Management Office. Retain a copy in the regulatory binder.

_____ _____
Signature of Principal Investigator Date

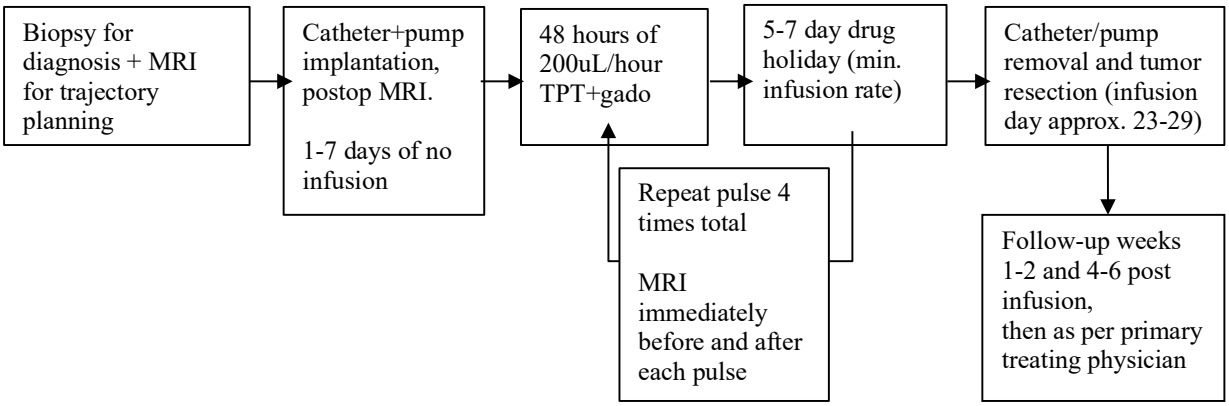
_____
Principal Investigator Name (Print)

_____
Name of Institution

Protocol Synopsis

Title	Chronic Convection Enhanced Delivery of Topotecan for Recurrent High Grade Gliomas
Short Title	Chronic TPT CED for Recurrent HGG
Protocol Number	AAAQ9520
Phase	Phase Ib
Methodology	Open label
Study Duration	5 years
Study Center(s)	Single center
Objectives	The aim of this study is to assess safety of chronic TPT CED in patients with recurrent high grade glioma (WHO grade III-IV), and to characterize the drug's intracerebral distribution using an innovative, non-invasive methodology.
Number of Subjects	5 Evaluable
Diagnosis and Main Inclusion Criteria	Patients with recurrent high grade glioma (WHO grade III-IV).
Study Product, Dose, Route, Regimen	~20 mL of 146 uM topotecan with 1:100 gadolinium by chronic pulsatile intracerebral convection enhanced delivery.
Duration of administration	Approximately 23-29 days
Reference therapy	Standard reference therapy: temozolomide, radiation
Statistical Methodology	Clinical toxicity (defined by a serious adverse event) is projected to be ≤ 5% at approximately 23-29 days. A clinical toxicity rate that exceeds 20% will be considered unacceptable for this procedure. We will use a truncated Sequential Probability Ratio Test (SPRT) to determine whether the rate of toxicity exceeds our target. We will use correlation analysis to determine the relationship between gadolinium signal intensity and distribution on MRI and the direct measurement of TPT levels. The power calculations are framed to assess our ability to detect these correlations. Since volume of distribution is determined by infusion rate once equilibrium is achieved (within the first 24-48 hours), we do not expect to see a difference in overall volume of distribution at the end of each pulse. We will verify the lack of change with a t-test analysis.

Protocol Schema:



Contents

1. INTRODUCTION

This document is a protocol for a human research study. This study is to be conducted according to U.S. and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations, and Columbia University Medical Center institutional research policies and procedures.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary goal of this study is to establish, for the first time, safety of prolonged intracerebral convection enhanced delivery of chemotherapy in patients with recurrent high grade glioma (WHO grade III-IV).

2.2 Secondary Objective

Secondary objectives will include determination of TPT distribution and radiographic tumor response with prolonged intracerebral CED.

3. BACKGROUND

Malignant gliomas are among the most pernicious of human tumors. They are locally invasive and universally recurrent, with recurrence usually occurring within two centimeters of the original resection cavity. Although numerous chemotherapeutic drugs demonstrate significant anti-tumor activity in preclinical studies, their efficacy in clinical trials has been dismal because systemic delivery fails to achieve therapeutic drug levels in tumor cells due to various factors including limited blood-brain barrier permeability and systemic toxicity. Convection-enhanced delivery (CED) is a method of regional drug delivery that circumvents this problem. We have shown in a phase 1 clinical trial that a potent topoisomerase inhibitor, topotecan (TPT), can be safely and effectively delivered by CED into patients with recurrent malignant gliomas[1]. Our current proposal will expand on these clinical results to address two current limitations to the clinical application of CED: 1) A reliable method for non-invasively monitoring drug distribution throughout the tumor and brain does not exist; and 2) Duration of CED therapy has been limited to short-term infusions secondary to the use of externalized infusion pumps. We hypothesize that extended chronic pulsatile local-regional delivery of TPT is safe, effective and feasible in patients with recurrent gliomas. To test this hypothesis, we will optimize the ability to chronically deliver TPT directly into the tumor and surrounding brain by CED through subcutaneously implanted pumps while innovating a methodology for monitoring the drug distribution through non-invasive imaging. This strategy will overcome the limitations of chemotherapy as currently used in the treatment of gliomas, and may be applicable to other CNS diseases currently limited by drug delivery barriers.

The aim of this study is to implement chronic pulsatile CED of TPT in patients with recurrent high

grade glioma (HGG) (WHO grade III-IV) and characterize the drug's distribution using an innovative, non-invasive methodology for measuring intracerebral distribution of TPT.

Hypothesis: TPT can be safely, effectively and chronically infused into recurrent HGG patients via intracerebral CED, and drug distribution can be accurately measured non-invasively. The chronic CED and non-invasive imaging methodology developed in our pig model[2] will require validation in recurrent HGG patients where a significantly more complex experimental environment exists. Patients with recurrent HGGs will undergo implantation of CED catheters and subcutaneously implanted pumps through which 4 cycles of TPT/gadolinium CED will be administered. These cycles will include 48 hours of active drug infusion followed by 5-7 days of drug holiday. Following the four cycles, catheters and pumps will be removed, and tumors will be resected. Tumoral and parenchymal distribution of gadolinium measured through MRI will be correlated with TPT levels measured by mass spectrophotometry of tissue samples obtained upon tumor resection. Cytotoxic response to TPT will be investigated by histological comparison of tissue samples taken at resection versus initial biopsy and by MRI.

At the conclusion of these studies, the expected outcome will be a novel, measurable strategy to treat recurrent HGG patients with chronically delivered high doses of TPT directly into their tumors, thereby avoid the limitations imposed by conventional systemic delivery. On a broader level, we will have demonstrated, for the first time in humans, the ability to chronically achieve a local-regional distribution of a drug directly into the brain parenchyma.

4. INVESTIGATIONAL AGENT

Topotecan (TPT)

Our choice of TPT for this study is based on a preponderance of animal and human data demonstrating its safety and efficacy with CED[2-5]. Because of the inherent advantage of CED over systemic delivery, many different drugs could be successfully substituted for TPT in this proposal. However, TPT is the ideal candidate because it has been validated in clinical trials[3], shown to be the most effective drug compared to over 20 other drugs in our rat glioma model[4, 6-8], and is easily measurable in tumor and brain tissue[4]. TPT, a camptothecin analog inhibitor of topoisomerase 1, is suitable for the treatment of malignant brain tumors as it is cytotoxic to proliferating glioma cells but remains relatively innocuous to normal brain where topoisomerase levels are low[4]. Although TPT had potent anti-neoplastic effects in preclinical models of glioma, it failed to show appreciable effects in glioma patients when delivered systemically[9]. However, CED of TPT proved to be safe and showed surprising efficacy in our recent phase 1 trial indicating that more effective therapy is possible when limitations to systemic delivery are overcome[3]. In this phase 1 study, TPT was administered through an externalized catheter and external micro infusion pump. As such, the treatment period was limited to four days to minimize hospital time and the risk of infection in this externalized system. However, a compelling rationale for pursuing chronic CED of TPT in clinical trials was provided by our rat glioma studies that demonstrated increased survival when TPT was delivered for longer periods of time[5]. Based on these studies, we hypothesized that prolonged CED of TPT would enhance its therapeutic effect in patients with malignant gliomas.

The infusate will consist of gadolinium plus TPT (146 uM) with the TPT dosage based on the results of our phase I clinical trial where a maximum tolerated dose of 218uM was established after 4 days of treatment[3]. Our choice of 146 uM is the next lower level tested in the phase I trial. Although no toxicity was seen at 218 uM, a lower dose is desirable to decrease the likelihood of toxicity during longer infusion durations.

Although we hope to gain information on the efficacy of this drug in treating malignant brain tumors, there may or may not be benefit from taking part in this study.

The tumors being studied are highly malignant and rapidly fatal. The major risks of this therapy are the direct effects of the topotecan and the infusion technique which may exacerbate increased intracranial pressure. These risks have been well-tolerated in preclinical animal and phase I human studies. The monitoring strategy outlined in the protocol is designed to minimize complications associated with these risks. There are no proven alternative therapies for patients with recurrent HGG who have failed radiation and temozolomide chemotherapy.

4.1 Preclinical Data

In the previous phase 1 study, TPT was administered through an externalized catheters and external microinfusion pumps, and the treatment period was limited to four days to minimize hospital time and the risk of infection in this externalized system. However, preclinical rat glioma studies have demonstrated increased survival when TPT was delivered for longer periods of time[5]. This finding provides a compelling rationale for pursuing chronic exposure to TPT CED in clinical trial. This finding likely relates to topotecan's mechanism of action, which is cell cycle dependent. Thus, when cells are exposed to topotecan at multiple time points, more cells will have likely passed through the appropriate phase of the cycle for topotecan to take action. We hypothesize that prolonged duration of TPT CED will enhance its therapeutic effect in malignant glioma patients. We have evaluated the feasibility of short term and prolonged TPT administration by CED in a large porcine animal model by using a subcutaneous implantable pump, the same pump that will be used for the current study. 136 uM TPT with gadodiamide (28.7 mg/mL) were first administered for either 3 day or 10 days using the Medtronic Synchromed-II pumps[2]. In another set of preclinical porcine experiments, similar infusions were administered for between 3-32 days (see study report). Pigs underwent MRI imaging at various time points throughout the treatment period. Areas of enhancement were analyzed and volumes of distribution (Vd) were calculated. CED of TPT/gadolinium was well tolerated for the 3 day, 10 day, and the 32 day infusions. No animals showed evidence of significant neurological deficit or systemic toxicity throughout either the short-term or long-term infusions. In the long-term infusions, maximum enhancement volume was typically reached by day three or four, with the largest gains in volume of distribution occurring within the first 48 hours of infusion (see study report). Furthermore, the volume of distribution reached a plateau at a medium volume of infusion of 14.25 mL during the 10-day course. During 32 day infusions, volume of distribution declined from max distribution as steady state was achieved. In these long-term infusions, anticipated local MRI signal change was seen at the catheter tip likely representing local tissue changes in response to infusion. Again, such radiographic changes were not associated with neurological deficit or evidence of toxicity.

The study investigators recognize that the tissue properties of normal pig brains are not

necessarily completely representative of human high grade glioma tissue. Due to tumor hypercellularity and peritumoral edema, it is possible that tumor tissue in these patients is less compliant than normal brain tissue. Such a decrease in compliance has the potential to affect the delivery of drugs via convection, as it will subject the catheter tip and infusion system to variable pressures. This difference in compliance may represent a distinct change from the type of tissue compliance that was encountered in preclinical porcine studies. Yet, this difference does not pose a problem for this study. In fact, one of the aims of this study is specifically to understand the nature of CED flow dynamics in the context of a variably complaint brain tumor. Given the fact that high grade gliomas are heterogeneous tumors with areas of variable cellularity, drugs delivered via CED are likely to flow down the path of least resistance out of the tumor and into peritumoral white matter tracts. Such tendency for CED to flow down white matter tracts is suggested by our preclinical porcine work described above, as these tracts represent the paths of least resistance to flow. In clinical application, drug will, thus, be able to reach diffusely infiltrative tumor cells in more normal, and likely more compliant white matter. These diffusely infiltrative cells are the ones that are typically left behind in brain tumor resection and account for tumor recurrence. As such, these cells are specifically the target of CED therapy. Since our protocol includes serial MRI throughout the infusion, the assessment of CED dynamics and likely proclivity of CED fluids to follow white matter tracts can thus be assessed.

4.2 Clinical Data to Date

We have previously performed a phase 1b, open label, nonrandomized, dose escalation study employing CED of TPT in patients with recurrent WHO grade III anaplastic astrocytoma or glioblastoma[1]. CED was performed for 100 hours using a Medfusion 2010 external syringe pump. This phase 1b study had the following enrollment and study results:

Total Enrollment	18
Total Completed Treatment	18
Patients Still Active on Treatment	0
Patients Completed Treatment Still in Long-term Follow-up	0
Completed Protocol Follow−up	17
Withdrew Consent Prior to Completing Follow-up	1
Termination associated with an adverse experience	0

Of the 18 adult patients studied, 1 remains alive at 347 weeks post-treatment, but has withdrawn consent and is no longer in follow-up, as of March 11, 2015. Survival ranged from 13 to 524 weeks with a median overall survival of 60 weeks. Progression-free survival ranged from 4 to 347 weeks with median progression-free survival of 23 weeks. The 6-month progression-free survival and 6-month overall survival were 44% and 75%, respectively. 6-month progression-free survival in the group of patients with GBM was 55%. One patient, due to his unrelated death not long after his treatment (see below), was not evaluable for treatment response, and was censored from future analyses. The serum concentrations of active and inactive forms of TPT were undetectable

(<0.5ng/mL) at all time points in all patients. At 1 week after infusion 1 patient had grade 1 leukopenia, and 1 patient had grade 2 thrombocytopenia, both of which resolved by week 2 with no adverse sequelae. There were two dose limiting toxicities (DLT) seen at the highest dose (0.133mg/mL), The first patient experienced a dose limiting toxicity (DLT) manifested by a right parietal syndrome with dysmetria and hemineglect. Treatment was terminated after 3.53 mg of infusion, and symptoms partially improved. This patient also suffered DVT, which was deemed unrelated to topotecan infusion. Another patient treated with the highest TPT concentration developed a transient DLT consisting of left upper extremity weakness, which resolved spontaneously. A patient with history of systemic chemotherapy, bone marrow transplant, and seizure disorder was readmitted 7 weeks after infusion with worsening of seizure disorder and severe metabolic disarray. This patient ultimately suffered cardiac arrest and died; autopsy was notable for aspergillus pneumonitis. This mortality was thus deemed unlikely to be related to the local topotecan therapy. In addition to the above severe events, seizure, headache, fatigue, or worsening hemiparesis each occurred in 5 patients (31%). GI symptoms or back/extremity pain were both seen in 4 patients (25%). 3 patients (19%) experienced either DVT, pneumonia, aphasia, memory impairment/confusion, or urinary symptoms. Right hand dyscoordination, poor wound healing, thrombocytopenia/leukopenia, dizziness, or anxiety/depression were each seen in 2 patients (13%). ICH (intratumoral hemorrhage >1 month following infusion), dry gangrene, upper extremity weakness, right parietal syndrome, tremor, rash, thrush, or sinusitis were each seen in individual patients (6%). The Average Karnofsky performance score before treatment was 84 and after treatment was 83. Except for the 2 patients experiencing DLTs, all patients remained ambulatory following infusion. No significant changes were seen in Cognitive Stability Index or the Physical or Mental Quality of Life assessments. Thus, all quality of life and neurocognitive testing verified the safety and tolerability of the treatment. Overall, this study suggested that TPT by CED has antitumor activity at concentrations that are non-toxic to the normal brain.

4.3 Other Agent(s)
Gadolinium (gado)

Prior work has established the utility of using diffusion-weighted MRI[10, 11], T2-weighted MRI[12] and dynamic-contrast enhanced MRI[13] among other modalities to determine the intraparenchymal volume of distribution (Vd) of drugs administered via CED. Intracerebral co-infusion of gadolinium with therapeutic compounds via CED is a delivery paradigm that offers real-time assessment of the volume of drug distribution. Additionally, co-infusion of gadolinium contrast is significantly less complex to implement than other direct imaging tracer-drug labeling strategies, such as liposomes or radio-labeled compounds. The technical and economic complexities of these other imaging approaches create significant limitations in human multi-center clinical trials involving numerous patients. Gadolinium is a widely available MRI contrast agent that is used routinely in clinical practice via IV administration, especially for imaging of intracranial tumors. In addition, to IV administration, there have been investigational of use of gadolinium in intraparenchymal convection enhanced delivery. The volume of distribution of gadolinium can be easily visualized and quantified on T1 weighted MRI, and several studies[10, 14-18], including both animal and human trials[2, 5, 17-22] have shown that intracerebral infusion of gadolinium compounds are safe and well tolerated. Pre-clinical animal studies have

demonstrated that gadolinium is safe in long-term chronic co-infusion up to 6 weeks[14, 15]. In our previous long-term CED in porcine models, gadolinium was utilized without toxicity issues [2], including in infusions of up to 32 days. Gadolinium has thus been employed in many previous CED studies with promising results, and can be safely used in this study.

The interactions between topotecan and gadolinium have been evaluated, and no concerning interactions have been identified. During our porcine trial, gadolinium was included in all infusions. Characteristic hyperintense T1 gadolinium signal was appreciated on all MRIs performed, suggesting that gadolinium's imaging properties are retained despite presence of topotecan. MTS assays were performed on human U87 glioma cell lines in which cytotoxic efficacy of 146uM topotecan both with and without 1:100 gadolinium were assessed. In comparison to nutrient rich media without drug, both the TPT-alone and TPT-gadolinium treated cells demonstrated a statistically significant reduction in glioma cell density ($p<0.01$ for both). However, no difference in cytotoxicity was seen when the TPT-alone and TPT-gadolinium treated cells were compared ($p = 0.48$; see study report). TPT, therefore, retains its anti-tumoral activity at 48 hours despite the presence of gadolinium.

Implanted pumps:

Synchromed II:

1) **PMA/510(k) number:** P860004
2) **Model Number:** Model 8637-20
3) **Indication for Use**
    a. **Approved:** "Chronic intraspinal (epidural and intrathecal) infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain, chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain, and chronic intrathecal infusion of Lioresal® Intrathecal (baclofen injection) for the management of severe spasticity; chronic intravascular infusion of floxuridine (FUDR) or methotrexate for the treatment of primary or metastatic cancer. Outside of US: Chronic infusion of drugs or fluids tested as compatible and listed in the product labeling."[23]
    b. **Proposed:** Chronic intracerebral infusion of topotecan-gadolinium for patients with recurrent high grade glioma.
4) **Administration routes/drugs**
    a. **Approved:**
        i. **Drugs:** Morphine sulfate, Baclofen, Ziconotide, Floxuridine, Methotrexate
        ii. **Routes:** Epidural, Intrathecal, Intravascular
    b. **Proposed:**
        i. **Drugs:** Topotecan, gadolinium
        ii. **Route:** Intracerebral (intratumoral)
5) **Critical Performance Attributes**
        i. **Approved:** Flow rates: 0.048mL/day-24mL/day

ii. **Proposed:** Flow rates: 0.048mL/day & 4.8mL/day

6) **Accessories (software programmer, catheters, tubing, etc.)**
   a. **Catheters:** Ascenda intrathecal catheter (models 8780, 8781), Intrathecal catheter (8731SC)
   b. **Progammers: Synchromed II Tablet Clinician Programmer,** N'Vision Clinician Programmer (model 8840), myPTM Personal Therapy Manager (model 8835)

Synchromed II infusion pumps (Medtronic), currently FDA-approved for the treatment of spasticity and chronic pain, will be implanted subcutaneously to facilitate chronic infusion. This application of the Synchromed pump to human CED represents an off label use of this device. While the primary goal of our study is to evaluate safety and tolerability of prolonged convection enhanced delivery of topotecan, such chronic pulsatile infusion is not feasible by using conventional externalized pumps. Firstly, prolonged four week infusions via externalized pumps would require inpatient hospitalization in an ICU setting for all days prior to tumor resection in addition to standard postoperative inpatient hospital stay. Such a prolonged hospitalization would predispose patients to multiple nosocomial and iatrogenic complications including, but not limited to, deep vein thrombosis, pulmonary embolism, ICU delirium, pneumonia, clostridium difficile infections, decubitus ulcers, and general deconditioning. Secondly, prolonged duration of externally implanted intracerebral catheters predisposes patients to ventriculitis. Such a relationship between time of catheter implantation and risk of infection has been demonstrated in previous trials evaluating ventriculitis in patient with external ventricular drains[24]. As a result of these limitations, this study will require an alternative route of CED. To this end, a fully internalized sterile infusion system would allow the extension of CED from days to weeks, and will ultimately provide the rationale and feasibility for prolonged CED in the outpatient setting. We have previously tested the safety and feasibility of implanted infusion systems for CED in a pig model[2]without any pump-related complications. In our long-term infusion trial in which pigs were infused for up to 32-day, there were never any issues relating to prolonged pump stalls or battery failures despite repeated MRIs. There were no issues relating to pump site infections, pump refill complications, or catheter disconnection at the pump site (see study report).

Notably, with respect to pump function, the tissue characteristics of high grade gliomas must be taken into account. High grade glioma tissue properties are distinct from those of normal human brain. Due to tumor hypercellularity and peritumoral edema, it is possible that tumor tissue in these patients is less compliant than normal brain tissue. Such a decrease in compliance has the potential to affect the delivery of drugs via convection, as it will subject the catheter tip and infusion system to variable pressures. This difference in compliance may represent a distinct change from the type of tissue compliance that was encountered in preclinical porcine studies. Yet, this difference does not pose a problem for this study. In fact, one of the aims of this study is specifically to understand the nature of CED flow dynamics in the context of a variably complaint brain tumor. Given the fact that high grade gliomas are heterogeneous tumors with areas of variable cellularity, drugs delivered via CED are likely to flow down the path of least resistance out of the tumor and into peritumoral white matter tracts. Such tendency for CED to flow down white matter tracts is suggested by our preclinical porcine work, as these tracts represent the paths of least resistance to flow. In clinical application, drug will, thus, be able to

reach diffusely infiltrative tumor cells in more normal, and likely more compliant white matter. These diffusely infiltrative cells are the ones that are typically left behind in brain tumor resection and account for tumor recurrence. As such, these cells are specifically the target of CED therapy. Since our protocol includes serial MRI throughout the infusion, the assessment of CED dynamics and likely proclivity of CED fluids to follow white matter tracts can thus be assessed.

It is possible that in cases of extreme brain non-compliance, there will be obstruction to drug delivery through the catheter. This situation is unlikely as even elevated intracerebral pressures are relatively low. But, if pressures did become high enough to occlude the infusion system, this event would serve as a fail-safe, preventing excess fluid from entering the noncompliant brain. Since patients will be monitored continuously throughout active infusions, any clinical sign of increase ICP will be acted on immediately by urgent discontinuation of drug infusion, use of steroids, hypertonics, mannitol, and possible surgical intervention if necessary.

5. STUDY DESIGN

5.1 General:

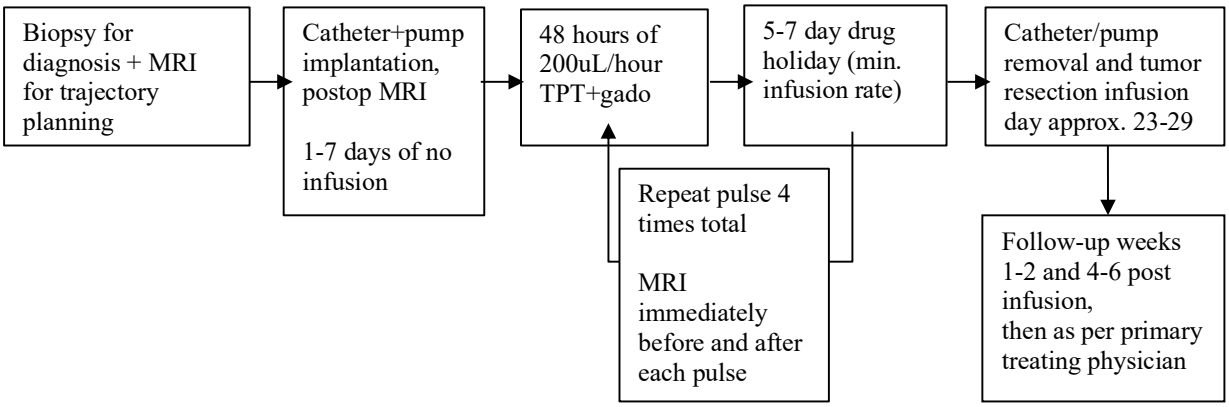
Allocation: Non-randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

5.2 Primary Study Endpoints:

The primary endpoint of this study is assessment of safety of chronic pulsatile intracerebral topotecan infusion. Safety will be assessed by evaluation of physical and neurologic examinations, laboratory studies, radiographic studies, and by adverse events. An adverse event is any new or worsening symptom or clinical finding which occurs during the study period (see section 10). Adverse events are to be recorded irrespective of causality, on the adverse events form. Each event will be described by its severity (mild, moderate, severe, life-threatening), duration, and relation to study medication (unrelated, unlikely, possible, probable, definite). Additional secondary endpoints that will be assessed are steady state volume of drug distribution as measured on volumetric MRI, correlation of intraparenchymal TPT concentration with contrast enhancement intensity on MRI, as well as time to tumor progression/recurrence, and time to death.

5.3 Design

This is a **phase Ib** open label non-randomized trial. See schema below. All times indicated are optimal but should be considered approximate.



For effective clinical translation, the correlations between drug distribution and non-invasive imaging established in a pig model must be validated in humans with GBM[2]. Although drug infusions into normal pig brain serve as a convenient model for establishing these correlations, they must be re-calibrated in the significantly more complex intracerebral environment of patients with HGG. A series of 5 patients with recurrent HGGs will be recruited for a study in which TPT and gado will be co-delivered by CED via an implanted pump-catheter system in a pulsatile fashion prior to surgical resection about four weeks later. The infusate consists of gadolinium (approx. 1:100) plus TPT (146 uM). Active infusion will be initiated on post-operative day 1-7 at the discretion of the attending neurosurgeon to allow time for expected and routine recovery from surgery. The patients will then undergo four 48-hour pulses of therapy interspersed by several day therapy holidays. Notably, gadolinium will only be included in the CED infusion during the first and fourth pulses of therapy; during the second and third pulses, topotecan will be infused alone.

In each pulse cycle, patients will receive 200uL/hr of 146uM topotecan for 48 hours (daily volume = 4.8 mL; total volume = 9.6 mL) followed by between five to seven days of therapy holiday during which the pumps will be set at the minimum programmable rate (2uL/hr; 5-7 day volume = 0.24-0.34mL). This cycle will be repeated two more times. After three complete cycles, patients will receive a fourth and final pulse at the same infusion rate (200uL/hr for 48 hours). After this fourth dose, patients will be taken to the OR for pump removal and tumor resection as described. As such, once infusions are initiated, they will be carried out over a total of approximately 23-29 days. Four 48-hour infusion pulses at 200uL/hr will be administered for a total volume infused of 38.4mL. When accounting for the near negligible volume delivered while the pump is placed at minimum performance rate (0.048mL/day for 15-28 days), a combined total volume of 39.12-39.41mL will be infused. Rationale for 48-hour pulsatile infusion is derived from preclinical porcine studies demonstrating that the largest relative gains in volume of distribution of infusate occur within the first 24-48 hours, which subsequently decline as infusions reach a steady state. Similarly, the total volume of infusion and dose concentration is based on our previous clinical trial in which 40mL of drug was infused and an MTD of 218uM TPT was defined. Additionally, the reason for including possible variability in the length of each infusion holiday (5-7 days) is that it will allow investigators to ensure that all surgical procedures, including pump removals, tumor

resections, pump refills, as well as infusion initiations occur during weekdays when all staff members and support personnel are available to provide appropriate safety monitoring.

Tumor and parenchymal distribution and concentration of TPT will be investigated by MRI using gado as a surrogate tracer as well as mass spectrophotometric measurement from the tumor samples obtained at the time of tumor resection. A preoperative MRI will be performed to optimize catheter trajectory selection to ensure optimal CED and tumor coverage. Patients will undergo stereotactic biopsies of the tumor. Intraoperative histopathologic assessment of localized tumor biopsies will be performed to verify the diagnosis and distinguish active tumor from radiation necrosis prior to catheter/pump placement and infusion. These specimens taken at the time of catheter placement will also be used for secondary more comprehensive diagnostic immunohistopathologic and/or molecular analysis as well as for comparison to post treatment specimens.
As secondary objectives, tumor response to TPT will be investigated by MRI and by comparing signs of cytotoxicity between tissue samples from resection and initial biopsy obtained at study initiation. MRIs will be obtained on postoperative day 0 or 1 following catheter implantation prior infusion initiation to confirm catheter placement. For the first infusion, MRIs will then be performed around 8 hours, 14 hours, 24hours and 48 hours after the infusion is started, and then around 8 hours, 14 hours and 24 hours after completion of first infusion. For the remaining three two-day pulses of chemotherapy, MRIs will be performed just before and at 48 hours after start of each infusion. Catheters will be removed upon termination of the final 48-hour infusion pulse at which time patients will undergo surgical resection of the tumor and removal of catheters.

At the time of tumor resection, MRI-directed stereotactic biopsies from different areas within the volume of gado distribution and outside the volume (in areas of non-eloquent brain tissue) will be used to collect specimens for TPT concentration measurements at strategic distances from the catheter tip. Tumor and peritumoral brain tissue removed as part of the surgical resection will be collected for TPT and gadolinium measurements, as well as histological and immunohistochemical analysis of treatment effects, including apoptosis, necrosis, reactive gliosis, inflammation, and edema. These studies will validate the noninvasive parameters established in the pig model.

Patients will remain in the hospital during each two-day infusion, after which discharge safety will be assessed by the PI. At each visit they will undergo a full neurological and physical examination.

The implanted pumps are designed to be refilled percutaneously and will be refilled prior to each new 48-hour pulse. MRIs will be obtained on postoperative day 0 or 1 following catheter implantation prior infusion initiation to confirm catheter placement. For the first infusion, MRIs will then be performed around 8 hours, 14 hours, 24hours and 48 hours after the infusion is started, and then around 8 hours, 14 hours and 24 hours after completion of first infusion. For the remaining three two-day pulses of chemotherapy, MRIs will be performed just before and at 48 hours after start of each infusion. To account for the potential presence of intraparenchymal gadolinium, which would obscure intravenously administered contrast, IV contrast-enhanced MRI (and corresponding perfusion data) will not be performed during the first and fourth 48-hour infusion pulses. Since gadolinium is removed into brain capillaries and undergoes rapid renal

excretion with a blood concentration half-life between 20-70 min[25], we do not expect significant retention of CED gadolinium within the brain parenchyma when IV contrast-enhanced MR imaging occurs during the second and third dose pulses.

The primary goal of the study is to establish, for the first time, the safety of long-term pulsatile topotecan convection enhanced delivery via an implanted system in high grade glioma patients. Secondary outcomes will include determination of the TPT distribution and radiographic tumor response with prolonged CED. After four cycles of infusion, patients will undergo surgical resection of the tumor. At the time of tumor resection, MRI-directed stereotactic biopsies from sites within the gadolinium volume and sites outside (as in the above short-term studies) will be collected for TPT concentration measurements. Tumor and peritumoral brain tissue removed as part of the surgical resection will be collected for histological analysis of treatment effects.

In these initial human studies with CED, it is critical that the patient population be as uniform as possible. Although it will be desirable to expand this treatment to all HGG patients in the future, the purpose of these studies is to generate sufficient monitoring and toxicity data to advance the delivery methodology. Therefore, the study cohort will be carefully selected to consist of patients with minimal tumor resection cavities whose tumors are small and spherical. This selected population represents a very small percentage of patients with recurrent malignant gliomas. We have shown through our previous phase 1 trial that we can recruit this select type of patient who is optimal for CED since our institution treats a high volume of HGG patients.

Patients will return as outpatients for follow-up evaluation at one-two and four-five weeks post infusion termination unless there is clinical or radiographic indication for more frequent monitoring. At these visits, patients will undergo a physical/neurologic examination, neuropsychological evaluations. During the four-five week visit, a brain MRI will be performed to determine tumor response. Further outpatient follow-up will be determined by the patient's primary treating physician in accordance with standard of care. Patients will be contacted every 3-6 months by phone until death in order to assess survival data**.**

5.4 Study Drug Dose

5.4.1 Starting Dose

Concentration
Pulses 1, 2, 3 and 4 will be prepared with 146uM topotecan. This will not be modified at any time.

Pulses 1 and 4 will be prepared with topotecan AND gadolinium at approximately 1:100 concentration ratio to topotecan. This concentration will not be modified at any time.

Rate
Active pulse rate: The starting rate will be approximately 200 microliters/hour. Active pulse rate may be modified per section 5.4.2.

Resting rate: The resting pulse rate to be used will be approximately 2 microliters/hour

Study Drug Administration Duration: The duration of each pulse will be approximately 48 hours. This may be modified per section 5.4.2.

Resting Phase Duration: The duration of each resting period will be 5-7 days. This may be modified per section 5.4.2.

5.4.2 Dose Modifications and Delays

If at any time the principal investigator determines that the dose must be modified for patient safety they may make the following modifications: decrease active pulse rate, decrease active pulse duration, increase or decrease resting duration between active pulses to less than 5 or greater than 7 days. Implementation, effective duration of any of the listed modifications remains at the discretion of the principal investigator. If an implemented dose modification is no longer deemed necessary and the principal investigator determines that it is in the patient's best interest to proceed with study therapy for maximal therapeutic benefit, the next scheduled pulse should be administered and may be re-increased in rate or duration as tolerated.
Increased variability in the length of each infusion holiday is meant to allow investigators to ensure that all surgical procedures, including pump removals, tumor resections, pump refills, as well as infusion initiations are not compromised by scheduling conflicts such as weekends, holidays, operative room availability when staff members and support personnel are available. Additional modifications to timing of doses and dose decreases may be performed at the discretion of the PI.

5.5 Dose Limiting Toxicities

Dose limiting toxicities will be defined as any new (or increased from baseline) treatment related (drug and/or device),neurological deficits as found on neurological examination which are grade 3 or higher. These deficits include but are not limited to changes in level of consciousness, new onset speech difficulties (aphasia, mutism, dysarthria), confusion, visual field deficits, focal weakness, seizures.
Furthermore, DLT will include severe myelotoxicity defined as grade 4 thrombocytopenia, anemia, or neutropenia lasting at least 1 week using the current active version of the NCI CTCAE, he/she will be removed from study. However, systemic effects are thought to be minimal due to the small amount of drug expected to enter the systemic circulation.

Notably, maximum tolerated doses were established in a separate phase I trial of CED with topotecan. Toxicity of topotecan was not seen at concentrations of ≤0.10mg/ml, which established the maximum tolerated dose (MTD). Neurologic dose limiting toxicities (DLTs) occurred in two patients at the highest administered dose (level V, 0.133 mg/ml), including a parietal lobe syndrome and left upper-extremity weakness. Similar total volumes of drug infusion will also be used as in the prior study. During the previous human trial, two catheters infusing at a rate of

200uL/hr were placed in each patient, and infusions were continued for 100 hours, for a total infusion volume of 40mL.

In this trial, four approximately 48-hour infusion pulses at approximately 200uL/hr will be administered through one catheter for a volume of approximately 38.4mL. When accounting for the near negligible volume delivered while the pump is placed at minimum performance rate (0.048mL/day for 15-28 days), a combined total of approximately 39.12-39.41mL will be infused. During the previous human trial, two catheters infusing at a rate of 200uL/hr were placed in each patient, and infusions were continued for 100 hours, for a total infusion volume of 40mL[1]. In this trial, a MTD of 218uM was defined. Thus, patients tolerated both a higher total dose and similar volume infused as in the currently proposed trial.

Early Stopping Rule guidelines:
In the event 2 DLT's occur (as defined above), study enrollment will immediately be halted. After re-evaluation and consultation with the HICCC DSMC board, the trial may re-initiate enrollment with adjusted treatment parameters after a consensus is agreed upon by the Sponsor-Investigator and the HICCC DSMC, and a subsequent modification is reviewed/approved by the local PRMC/IRB. If a consensus cannot be reached, no further enrollment will be permitted on the trial and closure procedures will be initiated.

5.6 Number of Patients

Five evaluable patients with recurrent HGG will be recruited for infusion of TPT and gadolinium by pulsatile CED over approximately 23-29 days, followed by surgical resection of the tumor.

Since recurrent glioma and radiation necrosis are difficult to distinguish on imaging, several patients meeting enrollment criteria may not meet treatment criteria. As such, initial enrollment numbers may have to exceed treatment numbers to ensure that 5 patients enter the treatment study. Based on rates of radiation necrosis, which are roughly 10% of reoperations[26], we will cap enrollment at 10 patients (barring any early stopping rule concerns as indicated in section 5.5 above). Enrollment will stop when 5 evaluable patients have been obtained (barring any early stopping rule implementation as outlined above). Thus, we will have an initial enrollment of 10 patients, and a maximum of 5 evaluable patients that undergo catheter implantation and complete topotecan infusion. Furthermore, if patients who have catheters placed and infusion initiated fail to complete the full course of infusion due to reasons unrelated to treatment related toxicity, they will be considered inevaluable for the primary endpoint (but evaluable for toxicity), as the primary study endpoint is assessment of infusion safety over a full four cycles of infusion lasting between approximately 23-29 days. If a patient's infusion is terminated early for reasons unrelated to treatment toxicity/DLTs, then a new subject will be recruited to replace him/her to ensure a total of 5 evaluable subjects at the completion of the study. If patients are removed from the study as a result of failure to follow up with pre-defined safety follow-up evaluations, they will also be considered inevaluable, as assessment of infusion safety will not be ascertainable in such patients. As above, such inevaluable patients will be replaced with newly recruited and enrolled evaluable patients.

6. SUBJECT SELECTION AND WITHDRAWAL

6.1 Inclusion Criteria/Eligibility Requirements

1. Patients must have suspected recurrent malignant glioma (WHO grade III-IV), including recurrent glioblastoma, anaplastic astrocytoma, anaplastic oligodendroglioma, anaplastic oligoastrocytoma, and anaplastic ependymoma. Stereotactic biopsies will be performed to confirm the presence of active tumor by frozen section prior to initiating the treatment.
2. Patients with tumors of the brain must have been previously treated with surgical resection, temozolomide chemotherapy, and external beam radiation. Other additional treatments are permitted without limitation.

Note: Patients with tumors that are unmethylated are not required to have been treated with temozolomide chemotherapy, as current SOC and clinical trial treatment for patients with unmethylated tumors may exclude temozolomide chemotherapy.

3. An MR scan must be obtained within 30 days of enrollment and must demonstrate an enhancing mass without significant mass effect. Tumors must be less than approximately 32 cc in total volume, as assessed by the PI based on pre-enrollment MRI. The lesion must be stereotactically accessible.
4. Patients must have demonstrated evidence of increasing contrast enhancement on MR or CT imaging while on stable or increasing dose of steroid.
5. Karnofsky performance score of greater than or equal to 70.
6. Men and women of childbearing potential must practice birth control. Women of child bearing potential must have a urine pregnancy test within 7 days of study entry. In accordance with topotecan administration guidelines, women must practice birth control for at least 1 month following chemotherapy infusion. Men must practice birth control for at least four months following termination of chemotherapy infusion.
7. Patients or appropriate legally authorized representatives must possess the ability to give Informed Consent.
8. Patients must be willing to and medically capable of undergoing the surgical operation.
9. Patients must be at least 18 years old.
10. Patients must have normal organ and marrow function as defined below 14 days or fewer from registration:

- Leukocytes: ≥3,000/mcL
- Absolute neutrophil count: ≥1,500/mcL
- Platelets: ≥100,000/mcL
- Total bilirubin: within normal institutional limits
- AST(SGOT)/ALT(SGPT): ≤2.5 × institutional upper limit of normal
- Creatinine: within normal institutional limits

OR

- Creatinine clearance: ≥60 mL/min/1.73 m^2 for patients with creatinine levels above institutional normal.

The effects of Topotecan on the developing human fetus are unknown. For this reason and because category D agents are known to be teratogenic, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior

to study entry and for at least one month following topotecan infusion. Should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately. Men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 4 months after completion of Topotecan administration as topotecan may damage spermatozoa resulting in possible genetic and fetal abnormalities. These recommendations regarding men and women of child bearing age are based on the package insert for systemic administration of topotecan.

6.2 Exclusion Criteria

1. Patients with diffuse subependymal or CSF disease.
2. Patients with tumors involving the cerebellum or both cerebral hemispheres.
3. Patients with an active infection requiring treatment or having an unexplained febrile illness.
4. Patients who are known HIV, Hepatitis B or Hepatitis C positive. HIV-positive patients on combination antiretroviral therapy are ineligible because of the potential for pharmacokinetic interactions with topotecan. In addition, these patients are at increased risk of lethal infections when treated with marrow-suppressive therapy. Appropriate studies will be undertaken in patients receiving combination antiretroviral therapy when indicated. HIV, Hepatitis B and Hepatitis C testing is not required for patients not known to have those infections.
5. Patients with systemic diseases which may be associated with unacceptable anesthetic/operative risk.
6. Patients who have previously received systemic topotecan for their tumor.
7. Patients who are not able to receive MRI or PET scans.
8. History of allergic reactions attributed to compounds of similar chemical or biologic composition to topotecan, other topoisomerase inhibitors or gadolinium compounds.
9. Patients who are currently receiving treatment with agents that are metabolized solely through cytochrome P450 (CYP) 3A4/5 (CYP3A4/5) and have a narrow therapeutic index or are strong CYP2C8 inhibitors; or are receiving treatment with agents that carry a risk for QT prolongation and are CYP3A substrates. Caution should be used in patients taking other CYP2C8 - or CYP3A4/5-interacting agents as they may increase the serum concentrations of topotecan. If previously on such agents, the patient must be off of it for at least two weeks prior to study treatment.
10. Patients with uncontrolled intercurrent illness including, but not limited to, ongoing active infection, systemic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limited compliance with study requirements.
11. Women of child-bearing potential must have a negative pregnancy test 7 or fewer days from registration.
12. Women must agree not to breast feed while on study.

6.3 Inclusion of Women and Minorities

Both men and women of all races and ethnic groups are eligible for this trial.

6.4 Subject Recruitment

Patients will be recruited from the Neurology and Neurosurgery practices/clinics at Columbia University Medical Center. All patients will be seen by an attending physician who is an

investigator on the trial.

6.5 Early Withdrawal of Subjects

6.5.1 When and How to Withdraw Subjects

- If the patient's initial stereotactic biopsy is not consistent with recurrent high grade glioma, he/she will be deemed inevaluable and removed from the study **and replaced**. He/she will not undergo catheter implantation or topotecan infusion.
- If the patient's final pathology analysis of initial stereotactic biopsies fails to validate intraoperative assessment of tumor recurrence, he/she will be deemed inevaluable , and will be removed from the study **and replaced**. He/she will not initiate topotecan infusion, and will undergo removal of catheter and pump as needed.
- If at any time the patient develops unacceptable toxicity, such as severe myelotoxicity defined as grade 4 thrombocytopenia, anemia, or neutropenia lasting at least 1 week using the current active version of the NCI CTCAE, he/she will be removed from study. However, systemic effects are thought to be minimal due to the small amount of drug expected to enter the systemic circulation.
- If the patient fails to comply with the defined treatment plan and follow-up evaluations, the patient may be removed from the study at the discretion of the treatment investigator.
- If the patient withdraws consent for continued participation, he/she will be removed from study.

6.5.2 Data Collection and Follow-up for Withdrawn Subjects

Even though subjects may be withdrawn prematurely from the study, it is imperative to collect at least survival data on such subjects throughout the protocol defined follow-up period for that subject (though careful thought should be given to the full data set that should be collected on such subjects to fully support the analysis). Such data is important to the integrity of the final study analysis since early withdrawal could be related to the safety profile of the study drug. If a subject withdraws consent to participate in the study, attempts will be made to obtain consent from the subject to record at least survival data up to the protocol-described end of subject follow-up period. It must be a high priority to try to obtain at least survival data on all subjects lost to follow-up and to note what methods should be used before one can state the subject is truly lost to follow-up (e.g. number of phone calls to subject, phone calls to next-of-kin if possible, certified letters, etc.). Subjects who have received study drug and are withdrawn because of unacceptable adverse events will be followed until resolution or stabilization of the adverse event. An exception to this continued follow-up includes patients whose initial biopsies are not consistent with recurrent high-grade glioma and are removed from the study prior to catheter implantation and treatment initiation due to being inevaluable. Since these patients will not have undergone any experimental treatment intervention, study follow-up will be unnecessary beyond appropriate safety monitoring. They will undergo standard postoperative follow-up with the operating surgeon. In all cases, survival information may be available from public records, and will be collectable, consistent with FDA guidelines.

7 REGISTRATION PROCEDURES

7.1 CUMC Research Participant Registration

Confirm eligibility as defined in the section entitled Criteria for Subject Eligibility.

Obtain informed consent, by following procedures defined in section entitled Informed Consent Procedures, along with applicable institutional policies and federal regulations.

Only Investigators/Research personnel properly trained and delegated to consent subjects for this protocol will participate in the consenting process. Furthermore, properly delegated/trained Physician Investigators (e.g., MD, MD PhD) are required to sign/verify a protocol specific Eligibility Checklist for each subject enrolled on the study, in addition to providing the relevant source documentation confirmation subject eligibility.

All participants must be centrally registered through the Central Registration Office within Herbert Irving Comprehensive Cancer Center at CUMC prior to initiation of study treatment.

Registration hours are available Monday through Friday from 9:00am – 5:00pm EST (excluding holidays and weekends). Same day patient registrations (and after hour registrations) will be accommodated on a case by case basis provided that the study team has expressed all time sensitive registration concerns/cases in a timely manner to the Central Registration Office.

CPDM Central Registration Procedures:

Within 48 hours of obtaining consent (excluding holidays and weekends), a completed/signed IRB approved informed consent HIPAA form, and demographics forms should be submitted to the CPDM Central Registration Office via an email to CPDMRegistration@columbia.edu or fax to 212.305.5292, with the subject line "AAAQ9520 Pending Subject Registration Request (PHI)". Upon receipt, applicable subject information as well as a "pending eligibility" status will be entered into HICCC's institutional database. This status will remain until further source documentation is made available to confirm overall patient eligibility. Required materials for all pending registration submissions are as follows:

- Completed/signed IRB approved/stamped Informed Consent Forms, including additional study ICFs (e.g., tissue, DNA, etc.), as applicable.
- The completed/signed IRB approved HIPAA Authorization form
- Completed/signed CPDM ICF checklist
- Completed/signed HICCC personal census form
- Completed/signed CPDM Demographics Note to File

In order to confirm eligibility status, Investigators/designees (e.g., study specific Clinical Research Coordinator/Research Nurse, etc.) must submit the following documentation to the Central

Registration Office via email or fax:

- The completed/signed study specific Eligibility Checklist (signed by a Physician level Investigator)

- Copies of source documentation necessary for each item to be verified on the CPDM specific Eligibility Checklist, including but not limited to:

  - Copy of required laboratory test and procedure reports (e.g., hematology, serum chemistry, pregnancy test when applicable, MRI reports, CT/bone scans, etc.)

  - Copy of pathology and surgical reports

  - Copy of clinic note(s) or other appropriate medical records capturing the consent process information, along with providing source documentation of any other items needed for screening/eligibility that are not captured in other source document forms (e.g., positive investigator statements of unique eligibility items not captured via other direct source documentation, concomitant medication lists, etc.)

  - Protocol deviation/waiver approvals (if applicable)

- **Please note**: subject line of email or fax should include the following: "AAAQ9520 Complete Subject Registration Request (PHI)".

Upon receipt of the above mentioned documentation, participant eligibility information will be verified by a qualified Central Registration Registrar. If any questions arise during the review process, queries in the form of emails will be addressed to the applicable study team personnel for clarification prior to enrollment. All applicable finalized registration/eligibility information will then be entered into HICCC's institutional CTMS database by the Central Registration Registrar. Upon completion, an official subject registration notification email will be sent to the PI/research team which will include eligibility/enrollment status, as well as subject ID information. Protocol therapy may not be initiated prior to receipt of this notification from the Central Registration Office.

All screen fail/ineligible subjects, as well as subject's who withdraw consent prior to enrollment/initiation of protocol therapy must be submitted to the Central Registration office in a manner analogous to the procedures noted above. Applicable source documentation will be required within the corresponding submissions.

8. TREATMENT PLAN

Note: A detailed chronological description of study procedures has been included. Please see Appendix B.

8.1 Agent Administration

Patients will have treatment administered on an inpatient or outpatient basis per investigator discretion. Patients will be hospitalized during each active infusion pulse lasting 48 hours, plus or minus 6 hours. Patients may be discharged from the hospital during the intervening 5-7 day infusion holidays at the discretion of the investigator. Reported adverse events and potential risks for Topotecan and Gadolinium are described in Section 10. Appropriate dose modifications for Topotecan and Gadolinium are described in Section 9.

Patients will receive 200uL/hr of 146uM topotecan for 48 hours, plus or minus 6 hours (daily volume = 4.8 mL; total volume = 9.6 mL) followed by between five to seven days of therapy holiday during which the pumps will be set at the minimum programmable rate (2uL/hr; 5-7 day volume = 0.24-0.336mL). This cycle will be repeated two more times. After three complete cycles, patients will receive a fourth and final pulse at the same infusion rate (200uL/hr for 48 hours, plus or minus 6 hours). After this fourth dose, patients will be taken to the OR for pump removal and tumor resection as described. Once infusions are initiated, they will be carried out over a total of approximately 23-29 days. Gadolinium will only be included in the CED infusion during the first and fourth pulses of therapy; during the second and third pulses, topotecan will be infused alone. Minor under or over infusions of 10% or less are not considered protocol violations. See section 5.4.2 for dose modifications.

Gadolinium is a widely available MRI contrast agent that is used routinely in clinical practice via IV administration, especially for imaging of intracranial tumors. Gadolinium has been utilized in multiple previous CED investigations with promising results [2, 5, 17-22], and, thus, can be safely used as an intraparenchymal CED co-infusate in this study. The interactions between topotecan and gadolinium have been evaluated via multiple assessments, and no concerning interactions have been identified. During our porcine trial, gadolinium was included in all infusions. Characteristic hyperintense T1 gadolinium signal was appreciated on all MRIs performed, suggesting that gadolinium's imaging properties are retained despite presence of topotecan. MTS assays were performed on human U87 glioma cell lines in which cytotoxic efficacy of 146uM topotecan both with and without 1:100 gadolinium were assessed. In comparison to nutrient rich media without drug, both the TPT-alone and TPT-gadolinium treated cells demonstrated a statistically significant reduction in glioma cell density ($p<0.01$ for both). However, no difference in cytotoxicity was seen when the TPT-alone and TPT-gadolinium treated cells were compared ($p = 0.48$; see study report). TPT, therefore, retains its anti-tumoral activity at 48 hours despite the presence of gadolinium.

8.1.3 Other Modalities or Procedures

Implanted pumps:

Medtronic Synchromed II:

1) **PMA/510(k) number:** P860004
2) **Model Number:** Model 8637-20
3) **Indication for Use**

   a. **Approved:** "Chronic intraspinal (epidural and intrathecal) infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain, chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain, and chronic intrathecal infusion of Lioresal® Intrathecal (baclofen injection) for the management of severe spasticity; chronic intravascular infusion of floxuridine (FUDR) or methotrexate for the treatment of primary or metastatic cancer. Outside of US: Chronic infusion of drugs or fluids tested as compatible and listed in the product labeling."[23]
   b. **Proposed:** Chronic intracerebral infusion of topotecan-gadolinium for patients with recurrent high grade glioma.

4) **Administration routes/drugs**
   a. **Approved:**
      i. **Drugs:** Morphine sulfate, Baclofen, Ziconotide, Floxuridine, Methotrexate
      ii. **Routes:** Epidural, Intrathecal, Intravascular
   b. **Proposed:**
      i. **Drugs:** Topotecan, gadolinium
      ii. **Route:** Intracerebral (intratumoral)
5) **Critical Performance Attributes**
      i. **Approved:** Flow rates: 0.048mL/day-24mL/day
      ii. **Proposed:** Flow rates: 0.048mL/day & 4.8mL/day
6) **Accessories (software programmer, catheters, tubing, etc.)**
   a. **Catheters:** Ascenda intrathecal catheter (models 8780, 8781)
   b. **Programmers: Synchromed II Tablet Clnician Programmer;** N'Vision Clinician Programmer (model 8840), myPTM Personal Therapy Manager (model 8835)

Synchromed II infusion pumps (Medtronic), currently FDA-approved for the treatment of spasticity and chronic pain, will be implanted subcutaneously to facilitate chronic infusion of intracerebral chemotherapy. This application represents an off label used of this device. Such an internalized infusion system will allow the extension of CED to approximately 23-29 days while avoiding complications associated with externalized catheters. Preclinical studies in pig models have demonstrated both safety and feasibility of prolonged intracerebral topotecan CED utilizing internalized Synchromed II infusion pumps (see section 4.1).

The Synchromed II infusion pump will be used well within its critical performance range to chronically deliver a fixed volume of fluid over time. The Medtronic pump will be placed under the subcutaneous fascia. This is consistent with the approved use of this product, as such no bio-incompatibility is expected. In these regards, the proposed use of this product for this study is not different from its approved use. The differences that arise are two.

One difference is a change in the drug that is being delivered. Topotecan-gadolinium will be used instead of the approved morphine sulfate, baclofen, ziconotide, floxuridine, and methotrexate. Notably, since the pump is compatible with methotrexate, there is a precedent for

its use with chemotherapeutics. The risk of using topotecan-gadolinium, which is not currently approved for use with this pump, is that drug-device incompatibility could occur leading to over/underdosing of medication or damage to the device. However, based on our preclinical studies in pigs in which the same pumps and drugs were used, no device interactions were noted. Pumps did not experience unexpected stalls or interruptions in infusions. Pumps continued to infuse without complication throughout the entirety of the intended infusions (up to 32 days). Topotecan was detectable in the target tissue by LCMS and gadolinium was detectable by MRI, suggesting that neither drug was altered by the device components with which it came into contact. The risk of drug incompatibility causing dosing errors will be mitigated by regular pump interrogations following pump implantation as well as prior to and following all MRI procedures and pump refills. During pump refills, remaining drug volumes will be aspirated, measured, and compared to the expected remaining volume based on infusion rates. While passing through the Medtronic pump, the study drug will come into contact with the following materials: titanium, silicone, and polyvinylidene fluoride. There is no expected interaction between study drug and titanium or silicone, as these products are used in several implanted ports through which topotecan has been infused in human trials[27]**.** Polyvinylidene fluoride is a plastic that is particularly nonreactive, and resistant to solvents, acids, and bases. As such, this material would not be expected to interact with study drug. Furthermore, as mentioned above, in our porcine experiments, topotecan was detectable in the target tissue by LCMS and gadolinium was detectable by MRI, suggesting that neither drug significantly interacted with materials within the Medtronic pump.

The second difference that arises in this experiment is the target infusion location. The pump is approved for use in the epidural, intrathecal, and intravascular spaces; however, our project will employ its use in the intracerebral space. The issue should not present significant new risks, as the pumps ability to infuse a fixed volume of fluid over time should not be changed by the intracerebral location of the infusion catheter. By nature of the fact that the pump is certified for intrathecal use, it is capable of delivering drug despite normal fluctuations in ICP. In fact, the fluctuations in ICP encountered in lumbar intrathecal location would be greater than those found intracranial, as intrathecal lumbar pressure can fluctuate widely with patient position (standing, recumbent). Since intracerebral placement, would subject the pump to usual intracranial ICP (with fewer fluctuations than lumbar placement) there should be no pressure related mechanical issues preventing stable infusion. The risk that arises due to intracranial location is that errors in dosing could result in cerebral damage. Again, this risk is mitigated by the fact that the pump will be used within its critical performance attribute range. The pump will be regularly interrogated and drug dosing will be regularly checked as described above. Regular cerebral imaging (MRIs) will be obtained, in which brain swelling and mass effect will be assessed. In the case of complication related to drug infusion causing cerebral edema/mass effect, the following measures (as described in the protocol) can be performed if indicated: the infusion can be stopped, steroids, mannitol, hypertonics can be administered, and decompressive craniotomy/craniectomy can be performed.

Pump programmers:
All pump settings will be programmed into the pump using the Synchromed II Tablet clinician

programmer . Prior to pump implantation and catheter connection, the pump will be filled with study drug and then programmed to deliver a priming bolus of 0.3mL so that the internal pump tubing is primed with study drug. As mentioned, the use of this priming bolus program will be used prior to pump implantation, as is recommended in the Medtronic manual.

Following the priming bolus, the pump will be implanted. Active infusion will then be initiated 1-7 days following pump implantation. At that time, the pump will be programmed to the "simple continuous" setting at an infusion rate of approximately 0.2ml/hr for 48 hours, plus or minus 6 hours. Upon completion of the intended 48 hours of infusion, the pump will then be set at the minimal programmable flow rate of 0.048ml/hr, for 5-7 days, plus or minus one day. This processes will be repeated for every subsequent pulse. After each reprogramming, the pump will be interrogated with the Synchromed II Tablet clinician programmer to ensure the correct settings are programmed.

Notably, the myPTM Personal Therapy Manager will not be utilized, as all interrogations and infusion adjustments will be performed by the study investigators. In order to ensure safety, patients will not have the ability to modify the infusion rates, as such the myPTM Personal Therapy Manager will have no role in this study.

Infusion Catheters:

Spetzler Lumbar Peritoneal Catheter

1) **PMA/510(k) number:** K811288
2) **Model Number:** Integra (NL97105S01)
3) **Indication for Use- approved and proposed**
    a. **Approved:** CSF drainage from lumbar subarachnoid space to the peritoneum (lumboperitoneal shunt)
    b. **Proposed:** Intracerebral/intratumoral infusion of topotecan
4) **Administration routes/drugs**
    a. **Approved:** Intrathecal; CSF drainage
    b. **Proposed:** Intracerebral; topotecan-gadolinium infusion
5) **Critical Performance Attributes**
    a. Length-105cm; Outer diameter-1.5mm; Inner diameter-0.7mm
    b. Should not be used for CSF drainage in presence of non-communicating hydrocephalus, known or suspected meningitis, ventriculitis, skin infection, bacteremia, septicemia, or peritonitis.

The catheter is made of a silicone elastomer and approved for lumbar subarachnoid placement for drainage of CSF into the peritoneum. In the proposed study, the catheter will be placed intra-parenchymal which represents a difference from it approved placement route. This application represents an off label used of this device. Both of these spaces (intra-parenchymal and lumbar subarachnoid) however, are intradural and thus within the neuroaxis. As such, there should be no

increased risk of infection/meningitis with the proposed placement. In terms of catheter contact with the brain parenchyma, no additional risk is perceived as the catheter is made of the same silicone elastomer as all Integra CSF shunting products, many of which are purposely designed to traverse brain parenchyma. Furthermore a larger diameter Integra lumbo-peritoneal catheter of the same type was used in our previous human trial for intraparenchymal/intratumoral placement and topotecan infusion without catheter-associated complications[1].

In its approved use, the lumbar catheter tubing passes though muscle, fascia, fat, and subcutaneous tissue, and is thereby compatible with all of these spaces. The catheter, in the proposed use, will be placed below the subcutaneous fascia and above muscle. Since the catheter normally passes through these spaces, no biological incompatibility is expected with the proposed use. Furthermore, during our porcine preclinical experiments in which these catheters were placed in the subcutaneous soft tissue, no abnormal tissue swelling or breakdown was seen along the catheter tract.

The main risk arises from the fact that the catheter is not designed for drug delivery. As such, there is a risk of drug incompatibility with the catheter material. As mentioned above, this catheter is made of the same silicone elastomer as other Integra CSF shunting products. Specifically, the Integra Pudenz proximal catheter (Integra, Plainsboro NJ, NL850-1504) is also made of silicone elastomer, and is designed for both CSF shunting as well as drug delivery. This silicone catheter is used in conjunction with Integra Ommaya drains (Integra, Plainsboro NJ, product number: NL8501213**)** to deliver various intrathecal chemotherapeutics, including topotecan in various clinical trials [28-32]. As such, there is no reasonable expectation of drug-material interaction using the proposed catheter. This expectation is supported by the fact that topotecan-gadolinium was infused through proposed lumbar catheters in our preclinical porcine trial. Following infusion through these catheters, topotecan was detectable in the target tissue by LCMS and gadolinium was detectable by MRI, suggesting that neither drug was altered by the catheter components with which it came into contact. Following infusions, visual inspection of the catheters revealed no breaks or discontinuities in the catheter materials.

Additionally, since the catheter is not designed specifically for drug delivery, there is the possibility that the catheter will be unable to deliver drug at the desired rate due to flow limitations. This risk is extremely unlikely. The lumbar catheter is designed to accommodate fluid flow at a rate similar to (and exceeding) that of CSF production, which is roughly 20mL/hr. As such, the catheter should be capable of accommodating continuous fluid flow at the far lower rate of 0.2mL/hr required in this study. Again, in preclinical porcine studies, topotecan-gadolinium was successfully delivered through this catheter without obstructions to flow as evidence by the presence of intracerebral gadolinium observed on MRI. To ensure appropriate drug delivery through the catheter, regular pump interrogations will be performed as described above. During pump refills, remaining drug volumes will be aspirated, measured, and compared to the expected remaining volume based on infusion rates. Serial MRIs will be performed to ensure successful delivery of drug to the target tissues.

The only modification that will be made to the catheters is that roughly 20mm of the proximal end of the closed tipped catheters will be cut off. This modification will remove the multiple

draining holes that are found along the length of the first 17mm the catheters. This modification will ensure that there is only one efflux point for the drug infusion from catheters. It will also allow connection of the lumbar catheter to both the intracerebral catheter and infusion pump, thereby creating a closed system with no additional/unintended points of drug efflux. This modification will increase safety, as it will ensure that drug is delivered directly to the desired target area at the tip of the catheter. This modification should pose no increased risk to the patient.

While the lumbar catheter proposed is not approved for use with the Medtronic pump, it has been used in combination with the Synchromed II pump in our preclinical animal experiments without issue. The outer diameter of the proposed catheter is 1.5mm and the inner diameter is 0.7mm. This catheter has been used during preclinical pig experiments. A secure connection between the catheter tubing and the Synchromed II port is able to be formed without slippage of the catheter. However, the main risk of using this catheter with the Synchromed pump would be a catheter-pump disconnection. This risk is mitigated by tying a 2-0 silk suture around the connection site and securing it with tight surgical knots. This technique has been used in the pig experiments and no instances of catheter-pump disconnections occurred. To further mitigate risk of catheter pump disconnection, an excess loop of catheter will be left in the shunt pocket to allow for additional slack on the catheter thereby preventing tension from being placed on the catheter-pump connection.

Note: The contraindication to use of the lumbar catheters in patients with large intracranial masses, tumors or hematomas does not pertain to this study. The contraindication is specifically in reference to lumbar CSF drainage, which, when performed in patients with such masses, can induce brainstem herniation. Since the catheter will not be used for CSF drainage in this study, the contraindication does not apply. Furthermore no metal or valve elements of the typical Spetzler shunt system will be used in this experiment. The only part of the system that will be used is the MRI-safe silastic catheter.

Biopsies, Catheter placement and MRI imaging Procedures:
A pre-biopsy MRI will be performed to optimize catheter trajectory selection to ensure optimal CED and tumor coverage. Patients will then undergo stereotactic biopsies of the tumor to verify the diagnosis and distinguish active tumor from radiation necrosis (also called pseudoprogression or treatment effect). The specimens taken at the time of catheter placement will also be used for comparison to post treatment specimens. If the initial biopsies are consistent with active tumor/ recurrent tumor on a frozen section performed at the time of biopsy, the patient will be considered pathologically evaluable, and catheter placement will proceed. If the initial biopsies are consistent with active tumor/ recurrent tumor on a frozen section performed at the time of biopsy, the patient will be considered pathologically evaluable, and catheter placement will proceed. However, if the final pathology analysis fails to validate intraoperative assessment of tumor recurrence, treatment may not be necessary, the patient will be deemed inevaluable , and will be removed from the study and replaced. The patient will not initiate topotecan infusion, and will undergo removal of catheter and pump as needed.

If frozen section pathology does not clearly demonstrate active tumor consistent with high grade

glioma, the patient will be considered unevaluable (and subsequently replaced), the procedure will be stopped, and the patient's incision will be closed in standard surgical fashion. We recognize that final pathology may yield a diagnosis of recurrent tumor not confirmed on frozen section; such patients will be planned to undergo resection as part of standard of care at the discretion of the treating investigator, but we would prefer to exclude some patients who may ultimately be proven to have recurrence to guard against the possibility of treating a patient who does not have recurrent active tumor.

All measurements and volumes below are to be considered approximate and minor differences in technique at the discretion of the surgeon are not considered protocol violations.

For the pathologically evaluable patients, a cranial incision and burr hole will be made through which as single catheter will be placed stereotactically into the geometric center of the tumor at a site chosen to maximize coverage of the tumor and adjacent infiltrated brain tissue based on spherical distribution. We will utilize a simple 1.5 mm outer diameter silastic Spetzler lumbar shunt catheter that is commercially available (Integra, Plainsboro, NJ; see above) for intracranial placement. Our experience testing different catheters is that they play a minor role in CED. That is, the design of the catheter does not significantly alter the more important aspect of CED, which is to maximize the volume of distribution. Our use of the standard shunt catheter is in keeping with our goal of a CED system that will be readily available to other investigators. All catheters will be trimmed in order to remove multiple drainage slits from the proximal and distal ends of the catheter. This will require 1.7cm of catheter to be removed from the distal end and 4cm of catheter be removed from the proximal end. This trimming will occur intraoperatively on the sterile surgical equipment stand. The catheter will be trimmed at 90 degrees to the length of the catheter using standard sterile surgical scissors. The excess catheter ends will be immediately removed from the surgical field, counted, and discarded. The proximal catheter will be placed without priming, as an inner stylet will be required to assist placement. The distal catheter and pump will be primed with study drug prior to implantation. Importantly, since the proximal catheter will not be primed, there will be an unavoidable amount of dead space in the catheter system. The maximal proximal catheter length will be 99.3 cm, taking into account the 1.7 cm and 4 cm of length that will be removed from the distal and proximal ends of the catheter, respectively. The inner diameter of the catheter is 0.07 cm. Thus, the maximal dead space volume is 0.38 mL. In certain patients, the length of the proximal catheter may have to be shorted based on the depth of the tumor. However, any changes to the length of the catheter will result in sub-milliliter differences in the volume of dead space. Such a small volume of maximal dead space and inter-patient variability in dead space is considered negligible for the purposes of this study. Given the fact that maximal infusion volumes in out porcine preclinical studies have reached an average volume of 11.30 mL, a dead space volume of up to 0.38 mL should not present a barrier to assessment of therapy distribution.

A second incision roughly the size of the infusion pump will be made in the either the chest or the subcostal region (midway between the rib bone and hip bone) ipsilateral to the intracranial catheter. Chest or subcostal placement will be decided by the operative surgeon based on the patient's body habitus. A subcutaneous pocket large enough to hold the infusion pump will be created using blunt dissection. Once the pocket is created, a second, 1.5mm outer diameter silastic Spetzler Integra

lumbar catheter (see above) will be tunneled rostrally within the subcutaneous tissue to the cranial incision using a shunt passer as is done in typical ventriculoperitoneal shunt placement. The proximal and distal tubing will be connected with a nylon straight connector, and the distal tubing will be connected to the infusion pump, which will be placed in the subcutaneous pocket that was created. All connection points will be reinforced with 2-0 silk suture ties. Of note, the pump will be implanted with the device face up in the subcutaneous soft tissue while the patient is supine (required to allow for pump refills). In this position, the refill port face of the pump will run parallel to the patient's skin. This face up position relative to the patient will be confirmed prior to closure of the surgical site. This positioning is important as it will prevent permanent pump stalls caused by 90° alignment of the implanted pump with the Z axis of 1.5 T and 3.0 T horizontal, closed-bore magnetic resonance imaging (MRI) scanners during MRI procedures. After pump position is confirmed, the proximal and distal incisions will then be closed in standard fashion after hemostasis is achieved and the wounds are copiously irrigated with antibiotic irrigation as per typical protocol. Closure of all wounds will provide a safe, closed, sterile system suitable for chronic treatment. CT and/or MRI will be performed to confirm intracerebral catheter placement. Following pump-catheter placement, the patient will be given 1-7 days to recover from surgery prior to initiation of active infusion.

There is potential for permanent stall if there is 90° alignment of an implanted pump with the Z axis of 1.5 T and 3.0 T horizontal, closed-bore magnetic resonance imaging (MRI) scanners. As recommended by the Medtronic manual, prior to all MRIs, pumps will be palpated by the investigator to ensure that their positioning has not shifted and to confirm that there is no possibility for a 90-degree alignment with the Z axis of the MRI. In accordance with Medtronic recommendations, pumps will be interrogated with the Synchromed II Tablet clinician programmer following MRIs. The investigator will ensure that the event log has recorded the following events: "Motor stall occurred" and "Motor stall recovery occurred." If these events are not logged, the pump will be re-interrogated after 20 minutes as is recommended. This procedure will be repeated until stall recovery is recorded. If motor stall recovery is not achieved after repeated attempts, a Medtronic representative will be contacted for further troubleshooting assistance.

Pumps will be refilled percutaneously with new infusate prior to the start of each new 48-hour pulse.

Quality of life and cognitive stability assessments will be administered throughout the infusion process and at designated follow-up intervals (see section 12).

After four cycles of infusion, patients will undergo craniotomy for surgical resection of the tumor. Surgery will proceed in standard fashion with the use of frameless stereotactic neuronavigation. At the time of tumor resection, MRI-directed stereotactic biopsies from sites within the gado volume and sites outside will be collected for TPT concentration measurements at strategic distances from the catheter tip. Tumor and peritumoral brain tissue removed as part of the surgical resection will be collected for histological analysis of treatment effects. During this procedure, the entire infusion system will be removed, including the intracranial catheter, tunneled distal catheter,

and infusion pump. The infusion pump will be removed by reopening the previous chest or subcostal incision, which will then be closed in standard surgical fashion after the pump is removed and hemostasis is achieved.

Throughout the course of the infusions there will be multiple checks in place in order to identify system failures. Firstly, patients will undergo serial MRIs. This procedure will provide direct visual evidence of continued drug delivery. If a decreasing volume of drug distribution is seen during an active infusion, or if an increasing volume of drug distribution is seen during a rest phase, the system will be further investigated via pump interrogation and possible residual drug aspiration. Following every MRI and refill procedure, the pump will be interrogated using the Synchromed II Tablet clinician programmer. The programmed infusion rate will be verified, and any stalls or incorrectly programmed rates will be noted. The programmer will also be used to check the residual volume of drug in the pump. This value is the result of a calculation based on the programmed rate and initial drug volume in the pump. This calculated volume will then be compared to the volume of residual drug aspirated from the pump during refill procedures. Any discrepancy between calculated residual volume and actual residual volume may signal an infusion malfunction. Such discrepancies will be recorded. By comparing data from pump interrogations, refills, and MRIs, both the integrity of the pump and catheter can be assessed. For instance, if infusion is not seen on MRI, and both pump interrogation and residual pump volume investigation are normal, a potential catheter disconnection may explain the MRI findings. In this situation, an X-ray or ultrasound of the catheter course can be obtained to assess the integrity of the tubing. If infusion is not seen on MRI, electronic pump interrogation is normal, but excess residual drug is aspirated during a refill, a block in the tubing may have occurred. Again, an X-ray or ultrasound can be obtained to assess the integrity of the tubing. Failures in the pump itself will be recognized by electronic interrogation.

Pump Refills:
Pumps will need to be refilled prior to each pulse of therapy. Pump refills will be performed at the bedside while the patient is inpatient. The pump will be refilled in standard fashion in accordance with Medtronic guidelines using a designated Medronic SynchroMed II refill kit. The pump template will be used to localize the refill port. If factors such as seroma or deep pump placement limit the ability to localize the refill port by palpation, X-ray will be utilized in accordance with Medtronic recommendations. Once the refill port is localized, the skin and soft tissue will be locally anesthetized with a local anesthetic injection. A 22-gauge non-coring needle contained within the kit will be used to puncture the skin/soft tissue and access the refill port. Placement within the refill reservoir will be confirmed by aspirating drug from within the pump. All residual drug within the pump will be aspirated prior to refilling the pump with new infusate solution. Care will be taken to ensure that no drug extravasates subcutaneously or comes in contact with the patient's skin.

8.2 General Concomitant Medication and Supportive Care Guidelines

No prophylactic or supportive care regimens are required for topotecan or gadolinium administration. Renal function should be tested prior to topotecan administration. Systemic side

effects of topotecan are expected to be limited due to the small amount of drug expected to enter the systemic circulation.

Standard supportive care at the discretion of the investigator is allowable. The case report form must capture the concurrent use of all other drugs, over-the-counter medications, or alternative therapies.

8.3 Duration of Therapy

In the absence of treatment delays due to adverse events, treatment may continue for entire planned duration of drug infusion (approximately 23-29 days) unless one of the following criteria applies:

- Intercurrent illness that prevents further administration of treatment
- Unacceptable adverse event(s), per the discretion of the principal investigator and primary attending physician
- Patient decides to withdraw from treatment.
- General or specific changes in the patient's condition render the patient unacceptable for further treatment in the judgment of the investigator

8.4 Duration of Follow Up

Patients will return as outpatients for follow-up evaluation at one-two and four-five weeks following termination of infusion, unless there is clinical or radiographic indication for more frequent monitoring. Following this assessment, further medical follow-up will be guided by their primary treating physician in accordance with standard of care. Patients will be contacted by phone every 3-6 months until death to assess for survival data. Patients removed from study for unacceptable adverse events will be followed until resolution or stabilization of the adverse event.

8.5 Criteria for Removal from Study

Patients will be removed from study when any of the criteria listed in Section 8.3 applies. The reason for study removal and the date the patient was removed will be documented in the Case Report Form.

9 DOSING DELAYS/DOSE MODIFICATIONS

Refer to section 5.4 for dose, dose modifications, dose delays and dose limiting toxicities.

10 ADVERSE EVENTS: LIST AND REPORTING REQUIREMENTS

10.1 Adverse events

Topotecan:

We have extensive experience with TPT by CED in human and animal studies with little toxicity except at concentrations of drug greater than planned for in this study [3-5]. In this planned clinical study of topotecan for HGG, the drug will be injected mostly into the tumor and a small amount of brain around the tumor. The brain at risk will mostly be the brain immediately beside the tumor which might result in increased swelling around the tumor after treatment that could cause a brief worsening of brain function. Possible risks associated with such chemotherapy-induced irritation could include seizures, paralysis, sensory loss, language difficulty, loss of intellectual function, and death**.** Any swelling and the associated clinical worsening should go away in one to two weeks and should be helped by steroids. Systemic effects are thought to be minimal due to the small amount of drug expected to enter the systemic circulation. Upon refilling of the Medtronic infusion pumps, there is small risk of topotecan extravasation into the subcutaneous tissue which could lead to mild local tissue reactions including erythema and bruising as well as severe local tissue injury. There is also risk of similar local tissue injury due to drug extravasation in the event that the infusion catheter becomes disconnected or damaged. Topotecan is considered an irritant chemotherapeutic. Therefore, local extravasation or direct skin contact can lead to tissue inflammation, redness, swelling. There is potential for topotecan to cause local tissue necrosis, however reports of such severe soft tissue reactions were not found in the literature. As topotecan is used as an IV chemotherapeutic, extravasation does likely occur in clinical practice. Case reports document instances of extravasation leading to local discomfort and soft tissue swelling that resolve with cooling the area[33]. Various clinical guidelines at chemotherapy infusion centers similarly recommend cold pack application and washing with soap and water ([34, 35]). As such, should topotecan be found to extravasate or come into contact with skin during this study, the area will be irrigated with soap and water, a cold pack will be applied to extravasated area for 30 min every four hours for 24 hours, and topical hydrocortisone cream 1% will be applied every 6 hours for 7 days. If a subcutaneous drug fluid pocket is present, the pocket can be aspirated to remove as much drug as possible. The risk of extravasation will be mitigated by proper refill technique protocol.

Gadolinium:

Both animal and human trials[2, 5, 17-22] have shown that intracerebral infusion of gadolinium compounds are safe and well tolerated. Pre-clinical animal studies have demonstrated that gadolinium is safe in long-term chronic co-infusion up to 6 weeks[14, 15]. In our previous long-term CED in porcine models, gadolinium was utilized without toxicity issues [2], including in infusions of up to 32 days. Gadolinium has thus been employed in many previous CED studies with promising results, and can be safely used in this study. IV administered gadolinium-based contrast agents have been identified as the cause of the rare disease nephrogenic systemic fibrosis (NSF), which presents as acute to subacute edema of the extremities as well as cutaneous plaques[36]. NSF can also be associated with extremity pain and muscle contractures, and can lead to severe disability and even death. However, development of NSF after gadolinium administration has been linked to renal impairment, with prevalence of 2-6% in patients with severe renal impairment[36] It is unlikely that gadolinium CED would contribute to NSF since it will be given extravascularly in a dilute solution (1:100 gadolinium). Nevertheless, patients in this study will be

screened for appropriate renal function (see Section 6.1), as they will receive both intraparenchymal gadolinium with CED and IV gadolinium for follow-up MRIs. As with any medication, there is risk of allergic reaction and possible anaphylaxis with administration of gadolinium. Patient's will be monitored for allergic reactions and treated appropriately if any evidence of allergy is identified. Patient's with known pre-existing contrast allergies will be excluded from participation in the study.

Of note, the interactions between topotecan and gadolinium have been evaluated, and no concerning interactions have been identified. During our porcine trial, gadolinium was included in all infusions. Characteristic hyperintense T1 gadolinium signal was appreciated on all MRIs performed, suggesting that gadolinium's imaging properties are retained despite presence of topotecan. MTS assays were also performed on human U87 glioma cell lines in which cytotoxic efficacy of 146uM topotecan both with and without 1:100 gadolinium were assessed. In comparison to nutrient rich media without drug, both the TPT-alone and TPT-gadolinium treated cells demonstrated a statistically significant reduction in glioma cell density ($p<0.01$ for both). However, no difference in cytotoxicity was seen when the TPT-alone and TPT-gadolinium treated cells were compared ($p = 0.48$; see study report). TPT, therefore, retains its anti-tumoral activity at 48 hours despite the presence of gadolinium.

Convection enhanced delivery

The primary risk of CED has been the effects of increased fluid volume in the brain surrounding the tumor. Complications related to cerebral edema from the direct effects of increased volume occur in approximately 10 to 20% of patients [37]. These complications can be manifest by focal neurological deficits referable to the region of the brain being infused or they can result in general lethargy and decreased cognitive function if the edema is more generalized. Cerebral edema is usually reversible by stopping the infusion and treating the patient with dexamethasone and/or mannitol and hypertonic saline.

Operation [Stereotactic surgery]

The risks of inserting the infusion catheter into the tumor depend on the tumor's size and location. Possible risks include bleeding, worsening of brain functions (such as moving, feeling and thinking functions), and infection. These risks are expected to happen with a frequency of less than 1-2%. The chance of infection after operations in patients with recurrent malignant brain tumors may be slightly higher than 1-2% due to previous radiation damage to the skin, and because of a higher risk of infection in patients with malignant brain tumors.

In the event that there is a device malfunction, it may be reasonable to attempt revision surgery. Revision may be attempted for identified pump/catheter disconnections, pump failures/permanent stalls, and catheter kinking, all of which would result in failure to deliver drug to the target tissue. The risks of such a revision surgical procedure would be similar to the risks of the initial surgery and include infection, bleeding, as a well as risks associated with general anesthesia. During reoperations there is risk of damage to the catheter-pump system, which could

result in a catheter disconnection. Such an event could result in extravasation of chemotherapy into the soft tissue. Topotecan is considered an irritant chemotherapeutic. Therefore, local extravasation or direct skin contact can lead to tissue inflammation, redness, swelling. There is potential for topotecan to cause local tissue necrosis, however reports of such severe soft tissue reactions were not found in the literature. If such extravasation were to occur, the area would be thoroughly irrigated with saline fluid prior to wound closure. The patient's wound would treated with cold packs for 30 min every four hours for 24 hours, and the tissue will be monitored for visible signs of inflammation.

Biopsy

Because a small amount of brain tissue is being removed, there is a chance that some small blood vessels may be damaged and that some bleeding may occur. This frequency is on the order of 1%. Risks of bleeding include loss of neurological function and death.

Surgical complications

The stereotactic catheter implantation procedure and the craniotomy for tumor resection carry a risk for loss of neurologic function, non-neurologic complications and death. These risks depend primarily on the preoperative condition of the patient, the size and location of the tumor and associated diseases. The potential risk for the patient will be determined and will be discussed in detail with the patient prior to the catheter implantation and infusion as well as prior to tumor resection.

Internal infusion pumps:

Implantation of infusion pumps carry a risk of local tissue injury, swelling, hematoma, and infection around the implantation site. These risks will be mitigated by ensuring hemostasis prior to incision closure, as well as use of appropriate antibiotic irrigation and perioperative IV antibiotics. There is a risk of pump malfunction resulting in insufficient or excess drug delivery. There is risk of pump malfunction following magnetic resonance imaging; as such, pumps will be electronically interrogated to ensure proper functioning following all MRIs and at every follow up interval while that pump is in place. There is risk of pump-catheter disconnection causing infusion of drug into the local subcutaneous space, which can lead to local tissue reactions including possible severe tissue injury. To avoid such complications all connection points will be repeatedly checked and secured prior to incision closure. Infusion pump sites will be routinely inspected at follow up intervals. There is risk of damage to the infusion pump and extravasation of drug into the subcutaneous space during pump refills, which will be avoided by following specific manufacturer instructions for pump refills (see 8.1). All of these risks will be discussed with the patient in detail prior to pump implantation.

The Synchromed II infusion pump will be used in an off label manner in this study. However, the pumps will be used well within their critical performance range to chronically deliver a fixed volume of fluid over time. The Medtronic pump will be placed under the subcutaneous fascia. This is consistent with the approved use of this product, as such no bio-incompatibility is expected. In these regards, the proposed use of this product for this study is not different from its

approved use, and thus do not pose additional risk. The differences that arise are two, which may add additional risk to those discussed above.

One difference is a change in the drug that is being delivered. Topotecan-gadolinium will be used instead of the approved morphine sulfate, baclofen, ziconotide, floxuridine, and methotrexate. Notably, since the pump is compatible with methotrexate, there is a precedent for its use with chemotherapeutics. The risk of using topotecan-gadolinium, which is not currently approved for use with this pump, is that drug-device incompatibility could occur leading to over/underdosing of medication or damage to the device. While passing through the Medtronic pump, the study drug will come into contact with the following materials: titanium, silicone, and polyvinylidene fluoride. There is no expected interaction between study drug and titanium or silicone, as these products are used in several implanted ports through which topotecan has been infused in human trials[27]**.** Polyvinylidene fluoride is a plastic that is particularly nonreactive, and resistant to solvents, acids, and bases. As such, this material would not be expected to interact with study drug. Additionally, based on our preclinical studies in pigs in which the same pumps and drugs were used, no device interactions were noted. Pumps did not experience unexpected stalls or interruptions in infusions. Pumps continued to infuse without complication throughout the entirety of the intended infusions (up to 32 days). Topotecan was detectable in the target tissue by LCMS and gadolinium was detectable by MRI, suggesting that neither drug was altered by the device components with which it came into contact. The risk of drug incompatibility causing dosing errors will be mitigated by regular pump interrogations following pump implantation as well as prior to and following all MRI procedures and pump refills. During pump refills, remaining drug volumes will be aspirated, measured, and compared to the expected remaining volume based on infusion rates.

The second difference that arises in this experiment is the target infusion location. The pump is approved for use in the epidural, intrathecal, and intravascular spaces; however, our project will employ its use in the intracerebral space. The issue should not present significant new risks, as the pumps ability to infuse a fixed volume of fluid over time should not be changed by the intracerebral location of the infusion catheter. By nature of the fact that the pump is certified for intrathecal use, it is capable of delivering drug despite normal fluctuations in ICP. In fact, the fluctuations in ICP encountered in lumbar intrathecal location would be greater than those found intracranial, as intrathecal lumbar pressure can fluctuate widely with patient position (standing, recumbent). Since intracerebral placement, would subject the pump to usual intracranial ICP (with fewer fluctuations than lumbar placement) there should be no pressure related mechanical issues preventing stable infusion. The risk that arises due to intracranial location is that errors in dosing could result in cerebral damage. Again, this risk is mitigated by the fact that the pump will be used within its critical performance attribute range. The pump will be regularly interrogated and drug dosing will be regularly checked as described above. Regular cerebral imaging (MRIs) will be obtained, in which brain swelling and mass effect will be assessed. In the case of complication related to drug infusion causing cerebral edema/mass effect, the following measures (as described in the protocol) can be performed if indicated: the infusion can be stopped, steroids, mannitol, hypertonics can be administered, and decompressive craniotomy/craniectomy can be performed.

Throughout the course of the infusions there will be multiple checks in place in order to identify system failures. Firstly, patients will undergo serial MRIs. This procedure will provide direct visual evidence of continued drug delivery. If a decreasing volume of drug distribution is seen during an active infusion, or if an increasing volume of drug distribution is seen during a rest phase, the system will be further investigated via pump interrogation and possible residual drug aspiration. Following every MRI and refill procedure, the pump will be interrogated using the Synchromed II Tablet clinician programmer. The programmed infusion rate will be verified, and any stalls or incorrectly programmed rates will be noted. The programmer will also be used to check the residual volume of drug in the pump. This value is the result of a calculation based on the programmed rate and initial drug volume in the pump. This calculated volume will then be compared to the volume of residual drug aspirated from the pump during refill procedures. Any discrepancy between calculated residual volume and actual residual volume may signal an infusion malfunction. Such discrepancies will be recorded. By comparing data from pump interrogations, refills, and MRIs, both the integrity of the pump and catheter can be assessed. For instance, if infusion is not seen on MRI, and both pump interrogation and residual pump volume investigation are normal, a potential catheter disconnection may explain the MRI findings. In this situation, an X-ray or ultrasound of the catheter course can be obtained to assess the integrity of the tubing. If infusion is not seen on MRI, electronic pump interrogation is normal, but excess residual drug is aspirated during a refill, a block in the tubing may have occurred. Again, an X-ray or ultrasound can be obtained to assess the integrity of the tubing. Failures in the pump itself will be recognized by electronic interrogation.

Pump Refills:

Upon refilling of the Medtronic infusion pumps, there is small risk of topotecan extravasation into the subcutaneous tissue ("pocket fill") which could lead to mild local tissue reactions including erythema and bruising as well as severe local tissue injury. Topotecan is considered an irritant chemotherapeutic. Therefore, local extravasation or direct skin contact can lead to tissue inflammation, redness, swelling. There is potential for topotecan to cause local tissue necrosis, however reports of such severe soft tissue reactions were not found in the literature. As topotecan is used as an IV chemotherapeutic, extravasation does likely occur in clinical practice. Case reports document instances of extravasation leading to local discomfort and soft tissue swelling that resolve with cooling the area[33]. Various clinical guidelines at chemotherapy infusion centers similarly recommend cold pack application and washing with soap and water ([34, 35]). As such, should topotecan be found to extravasate or come into contact with skin during this study, the area will be irrigated with soap and water, a cold pack will be applied to extravasated area for 30 min every four hours for 24 hours, and topical hydrocortisone cream 1% will be applied every 6 hours for 7 days. If a subcutaneous drug fluid pocket is present, the pocket can be aspirated to remove as much drug as possible. The risk of extravasation will be mitigated by proper refill technique protocol.

MRI with Internal Pumps:

Medtronic Synchromed II pump performance has been established for 1.5 and 3T horizontal closed bore MRIs, which are the only types of MRIs that will be used in this study in order to

mitigate risks to the patients. To further mitigate risks, all product catalogue recommendations for MRI use will be followed (see below).

In general, the main risk of MRI is extended pump stalls. During MRI, pump stalls are expected and should occur, but should be temporary in nature. However, pump stalls of 2-24 hours have been reported. Stalls should resolve 20 minutes after the patient is removed from the magnetic field. In accordance with Medtronic recommendations, pumps will be interrogated with the Synchromed II Tablet clinician programmer following MRIs. The investigator will ensure that the event log has recorded the following events: "Motor stall occurred" and "Motor stall recovery occurred." If these events are not logged, the pump will be re-interrogated after 20 minutes as is recommended. This procedure will be repeated until stall recovery is recorded. If motor stall recovery is not achieved after repeated attempts, a Medtronic representative will be contacted for further troubleshooting assistance.

There is potential for permanent stall if there is 90° alignment of an implanted pump with the Z axis of 1.5 T and 3.0 T horizontal, closed-bore magnetic resonance imaging (MRI) scanners. This positioning will be avoided by implanting the device face up in the subcutaneous soft tissue (required to allow for pump refills). In this position, a 90-degree alignment with the Z axis in a closed bore MRI is not possible. As recommended by the Medtronic manual, prior to all MRIs, pumps will be palpated by the investigator to ensure that their positioning has not shifted and to confirm that there is no possibility for a 90-degree alignment with the Z axis of the MRI.

In general, the risk of any pump stall is acceptable, as cessation in topotecan infusion would not present an increased risk to the patient.

Catheters:

The Integra Spetzler catheter utilized in this study will be used in an off label manner for convection enhanced delivery. The catheter is made of a silicone elastomer and approved for lumbar subarachnoid placement for drainage of CSF into the peritoneum. In the proposed study, the catheter will be placed intra-parenchymal which represents a difference from it approved placement route. Both of these spaces (intra-paenchymal and lumbar subarachnoid) however, are intradural and thus within the neuraxis. As such, there should be no increased risk of infection/meningitis with the proposed placement. In terms of catheter contact with the brain parenchyma, no additional risk is perceived as the catheter is made of the same silicone elastomer as all Integra CSF shunting products, many of which are purposely designed to traverse brain parenchyma. Furthermore a larger diameter Integra lumbo-peritoneal catheter of the same type was used in our previous human trial for intraparenchymal/intratumoral placement and topotecan infusion without catheter-associated complications[1].

In its approved use, the lumbar catheter tubing passes though muscle, fascia, fat, and subcutaneous tissue, and is thereby compatible with all of these spaces. The catheter, in the proposed use, will be placed below the subcutaneous fascia and above muscle. Since the catheter normally passes through these spaces, no biological incompatibility is expected with the proposed use. Furthermore, during our porcine preclinical experiments in which these catheters

were placed in the subcutaneous soft tissue, no abnormal tissue swelling or breakdown was seen along the catheter tract.

The main risk arises from the fact that the catheter is not designed for drug delivery. As such, there is a risk of drug incompatibility with the catheter material. As mentioned above, this catheter is made of the same silicone elastomer as other Integra CSF shunting products. Specifically, the Integra Pudenz proximal catheter (Integra, Plainsboro NJ, NL850-1504) is also made of silicone elastomer, and is designed for both CSF shunting as well as drug delivery. This silicone catheter is used in conjunction with Integra Ommaya drains (Integra, Plainsboro NJ, product number: NL8501213**)** to deliver various intrathecal chemotherapeutics, including topotecan in various clinical trials[28, 29]. As such, there is no reasonable expectation of drug-material interaction using the proposed catheter. This expectation is supported by the fact that topotecan-gadolinium was infused through these catheters in our preclinical porcine trial. Following infusion through these catheters, topotecan was detectable in the target tissue by LCMS and gadolinium was detectable by MRI, suggesting that neither drug was altered by the catheter components with which it came into contact. Following infusions, visual inspection of the catheters revealed no breaks or discontinuities in the catheter materials.

Additionally, since the catheter is not designed specifically for drug delivery, there is the possibility that the catheter will be unable to deliver drug at the desired rate due to flow limitations. This risk is extremely unlikely. The lumbar catheter is designed to accommodate fluid flow at a rate similar to (and exceeding) that of CSF production, which is roughly 20mL/hr. As such, the catheter should be capable of accommodating continuous fluid flow at the far lower rate of 0.2mL/hr required in this study. Again, in preclinical porcine studies, topotecan-gadolinium was successfully delivered through this catheter without obstructions to flow as evidence by the presence of intracerebral gadolinium observed on MRI. To ensure appropriate drug delivery through the catheter, regular pump interrogations will be performed as described above. During pump refills, remaining drug volumes will be aspirated, measured, and compared to the expected remaining volume based on infusion rates. Serial MRIs will be performed to ensure successful delivery of drug to the target tissues.

The only modification that will be made to the lumbar catheter is that roughly 2cm of the proximal end of the closed tipped catheter will be cut off. This modification will remove the multiple draining holes that are found along the length of the first 1.7cm of the catheter. This modification will allow connection of the lumbar catheter to both the intracerebral catheter and infusion pump, thereby creating a closed system with no additional/unintended points of drug efflux. This modification will increase safety, as it will ensure that drug is delivered directly to the desired target area at the tip of the proximal catheter. We do not feel that this modification will increase risk to the patient.

While the lumbar catheter proposed is not approved for use with the Medtronic pump, it has been used in combination with the Synchromed II pump in our preclinical animal experiments without issue. The outer diameter of the proposed catheter is 1.5mm and the inner diameter is 0.7mm. This catheter has been used during preclinical pig experiments. A secure connection between the catheter tubing and the Synchromed II port is able to be formed without slippage of the catheter.

However, the main risk of using this catheter with the synchromed pump would be a catheter-pump disconnection. This risk is mitigated by tying a 2-0 silk suture around the connection site and securing it with tight surgical knots. This technique has been used in the pig experiments and no instances of catheter-pump disconnections occurred. To further mitigate risk of catheter pump disconnection, an excess loop of catheter will be left in the shunt pocket to allow for additional slack on the catheter thereby preventing tension from being placed on the catheter-pump connection.

Anesthesia:

Patients undergoing general anesthesia will be subjected to associated risks including pneumothorax, pneumonia, airway injury, hypotension, myocardial infarction, stroke, hepatic and renal injury and death. These risks will be discussed with the patient prior to enrollment by the primary surgeon/investigator as well as immediately prior to surgery by the anesthesia team.

Infection:

The probability of postoperative wound infection is increased due to immune suppression by steroids, which occurs in patients with brain tumors. All patients will be treated perioperatively and during the infusion with appropriate antibiotics per the discretion of the neurosurgeon. For patients with external catheter infusions, there is increased risk of meningitis/encephalitis due to skin flora tracking down the catheter and into the brain. In order to prophylaxis against meningitis/encephalitis, patients will continue to receive appropriate antibiotics per the discretion of the neurosurgeon, preferably 1 gram of IV cefazolin every 12 hours, plus or minus one hour, until the catheter is removed. For patients who are allergic to penicillin/cephalosporins, IV vancomycin will be used (dosing based on individual patient weight and renal function) or another appropriate antibiotic.

Elevated intracranial pressure:

Intracranial pressure falls under the category of events not described adequately by CTCAE and can be therefore be recorded by the investigator by severity (mild, moderate, severe, life-threatening). All events are evaluated and recorded for duration, and relation to study medication infusion (unrelated, unlikely, possible, probable, definite).
Given that brain tumor patients often present with symptoms and signs of increased intracranial pressure (ICP), increased intracranial pressure is classified as a preexisting condition which will be recorded as an adverse event if the frequency, intensity, or if the character of the condition worsens during the study period. Patients demonstrating evidence of *mild increased intracranial pressure* from baseline may be *treated with high doses of dexamethasone* prior to, during, and following the drug treatment. Patients with signs of *moderate increased intracranial pressure* from baseline may be *treated with high doses of dexamethasone* plus intravenous hypertonic saline prior to, during, and following the drug treatment. Patients with signs of *severe to severe increased intracranial pressure* from baseline may be *treated with high doses of dexamethasone*, intravenous hypertonic saline and mannitol as needed to reduce ICP during toxin infusions.

Infusion may be stopped if patients demonstrate signs of severe to life-threatening increased intracranial pressure following adjunct administration of high dose dexamethasone, hypertonic saline and mannitol. Patient may resume infusion at standard rate of infusion upon resolution of event and return to baseline ICP score has been achieved based on clinical and radiologic parameters (neurologic examination, MRI scan, and normalization of laboratory values.) If symptoms fail to abate following discontinuation of the infusion, CT or MR scan may be performed to evaluate for hemorrhage/edema. If symptoms remain unmanageable by medications, craniotomy may be performed.

Except for the infusion of TPT and gadolinium into the tumor, and MRI imaging of the infusion process, all procedures and treatments participants will experience during the care of their brain tumor are non-investigational; the types of medical treatments, procedures, and tests they experience will be Standard of Care for patients with brain tumors.

Patient Evaluation Procedures:

The evaluation of patients before and after Topotecan treatment should entail little risk. Blood testing requires a simple venipuncture to remove blood samples with minimal risk of peripheral nerve damage or wound infection. Idiosyncratic and allergic reactions to gadolinium for MRI scans are possible, but occur rarely and are usually self-limited.

Radiation:

The risks involved in exposure to the amount of radiation delivered during head CTs are very low. Patients will be counseled to monitor and minimize their cumulative radiation exposure.

Unknown risks:

There may as yet be unknown risks associated with the drug treatment not determined by preclinical studies. Neurological deficits are possible secondary to direct brain toxicity. The nature of these deficits would be dependent on the location of the tumor and infusion volume.

10.2 Definitions

Adverse Event:

An adverse event (AE) is any untoward or unfavorable medical occurrence in a human subject, including abnormal sign, symptom or disease, temporally associated with the subject's participation in research, whether or not considered related to the subject's participation in the research. Abnormal results of a procedure are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

Serious Adverse Event:

Adverse events are classified as serious or non-serious. A serious adverse event is any AE that is:

- fatal
- life-threatening
- requires inpatient hospitalization/prolongation of existing hospitalization, unless:
    - routine treatment or monitoring of the studied indication, not associated with any deterioration in condition (procedures such as central line placements, paracentesis, pain control)
    - elective or pre-planned treatment for a pre-existing condition that is unrelated to the indication under study and has not worsened since the start of study drug
    - treatment on an emergency outpatient basis for an event not fulfilling any of the definitions of an SAE given above/below and not resulting in hospital administrations
    - social reasons and respite care in the absence of any deterioration in the patient's general condition
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious events should be regarded as non-serious adverse events.

Unanticipated Problem:

An unanticipated problem is any incident, experience or outcome involving risks to subjects or others in any human subjects research that meets all of the following criteria:

- Unexpected (in terms of nature, severity or frequency) given (a) the research procedures that are described in the IRB-approval protocol and informed consent document, and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in such research (e.g., there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involved in such research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic or social harm) than was previously known or recognized.

Adverse Event Reporting Period

The study period during which adverse events must be reported is normally defined as the period from the initiation of any study procedures (e.g., after the first dose of study treatment) to the end of the study treatment (e.g., last dose of study treatment) and/or follow-up. For this study, the study treatment follow-up is defined as 30 days following the last administration of study treatment, or 30 days following the decision to remove the subject from study treatment, whichever is earliest.

Baseline/Preexisting Condition
A baseline/preexisting condition is one that is present at the start of the study. A preexisting condition should be recorded as an adverse event if the frequency, intensity, or if the character of the condition worsens during the study period.

General Physical Examination Findings
At screening, any clinically significant abnormality should be recorded as a preexisting condition. At the end of the study, any new clinically significant findings/abnormalities that meet the definition of an adverse event must also be recorded and documented as an adverse event.

Post-study Adverse Event
All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study.

Abnormal Laboratory Values
A clinical laboratory abnormality should be documented as an adverse event if any one of the following conditions is met:

- The laboratory abnormality is not otherwise refuted by a repeat test to confirm the abnormality
- The abnormality suggests a disease and/or organ toxicity
- The abnormality is of a degree that requires active management (e.g., change of dose, discontinuation of the drug, more frequent follow-up assessments, further diagnostic investigation, etc.).

Hospitalization, Prolonged Hospitalization or Surgery
Any adverse event that results in hospitalization or prolonged hospitalization should be documented and reported as a serious adverse event unless specifically instructed otherwise in this protocol. Any condition responsible for surgery should be documented as an adverse event if the condition meets the criteria for an adverse event.
Neither the condition, hospitalization, prolonged hospitalization, nor surgery are reported as an adverse event in the following circumstances:

- Hospitalization or prolonged hospitalization for diagnostic or elective surgical procedures for a preexisting condition. Surgery should not be reported as an outcome of an adverse event if the purpose of the surgery was elective or diagnostic and the outcome was uneventful.
- Hospitalization or prolonged hospitalization required to allow efficacy measurement for the study.

- Hospitalization or prolonged hospitalization for therapy of the target disease of the study, unless it is a worsening or increase in frequency of hospital admissions as judged by the clinical investigator.
    - Prolonged stay at CUMC or NeuroICU at the Investigator's discretion unless it is for an adverse event that otherwise qualifies as an SAE.

10.3 Recording of Adverse Events

At each contact with the subject, the investigator must seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events should be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should be recorded in the source document, though should be grouped under one diagnosis.

All adverse events occurring during the study period must be recorded. The clinical course of each event should be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period must be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation should be recorded and reported immediately.

The investigator will make every effort to determine the relationship of each AE to: surgical procedure, CED, topotecan, and gadolinium. Causality should be assessed using the following categories: not related, unlikely, possible, probable, and definite.

10.4 Reporting of Serious Adverse Events
10.4.1 IRB Notification by Sponsor-Investigator

Reports of all events (including follow-up information) that meet the definition of an unanticipated and serious problem posing risk to subjects or others must be submitted to the IRB within 5 business days following the occurrence of the unanticipated problem or the principal investigator's acquiring knowledge of the unanticipated problem in accordance with IRB policy. Additionally, the sponsor-investigator will submit a summary of all Unanticipated problems that occurred since the beginning of the study at the time of continuing review. Unanticipated events that are not considered serious adverse events, will be reported at the time of continuing review. Copies of each report and documentation of IRB notification and receipt will be kept in the Regulatory binder.

10.4.3 FDA Notification by Sponsor-Investigator

The Columbia University Medical Center Sponsor-Investigator, as holder of the IND, will be responsible for all communication with the FDA. Columbia University Medical Center Principal Investigator will report to the FDA, regardless of the site of occurrence, any adverse event that is serious, unexpected and there is evidence to suggest a causal relationship between the drug and

the adverse event. These must be reported to the FDA and any affiliate sites as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting. The Sponsor-Investigator will also submit an IND annual report to the FDA in accordance with 21.CFR 312.33.

The Columbia University Medical Center Sponsor Investigator must report to the FDA and any affiliate site investigators as follows:

- Any unexpected fatal or life-threatening event must be reported as soon as possible, but no later than 7 calendar days after the sponsor investigator initial receipt of the information
- Any findings from epidemiological studies, pooled analysis of multiple studies, or clinical studies, whether or not conducted under an IND, and whether or not conducted by the sponsor-investigator, that suggest a significant risk in humans exposed to the drug must be reported as soon as possible but no later than 15 calendar days after the sponsor-investigator determines that the information qualifies for reporting
- Any findings from animal or in vitro testing whether or not conducted under an IND, and whether or not conducted by the sponsor-investigator, that suggest a significant risk in humans exposed to the drug must be reported as soon as possible but no later than 15 calendar days after the sponsor-investigator determines that the information qualifies for reporting
- Any clinically important increase in the rate of a serious suspected adverse reactions over that listed in the protocol or Investigator Brochure
- Expected SAEs and AEs will be included in the IND Annual Reports.

Follow-up information to a safety report should be submitted as soon as the relevant information is available. However, if the results of a sponsor's investigation show that an adverse drug experience not initially determined to be reportable are so reportable, the sponsor investigator must report such experience as soon as possible, but no later than 15 calendar days after the determination is made.

All other serious unexpected experiences associated with the use of the study treatment will be reported to FDA as soon as possible but in no event later than 15 calendar days after initial receipt of the information.

10.4.4 DSMC Reporting by the Sponsor Investigator

Serious adverse events not constituting unanticipated problems are to be reported to the HICCC DSMC. Reporting should occur within 24 hours of knowledge of the SAE occurring at our institution or affiliate sites.

10.4.5 Reporting to Drug Manufacturer by Sponsor-Investigator

The Sponsor-Investigator will any serious adverse events that meet the reporting criteria to the Institutional Review Board and DSMC as described above. Since drug stock is being purchased directly from commercial entities, there is no need for adverse event reporting directly to the drug manufacturer.

10.5 Reporting Process

Adverse events may be submitted on FDA Form 3500A, the HICCC DSMC Serious Adverse Event Reporting Form, or in a narrative format. If supplied as in a narrative format, the minimum information to be supplied is noted above at the beginning of section 10.

11 PHARMACEUTICAL INFORMATION

Study Drugs

11.1 Description

The infusate administered to the patient consists of 146uM Topotecan (TPT, Hycamtin, Novartis, GalaxoSmithKlein) and approximately 1:100 Gadolinium.

Due to variability of the molecular weight of topotecan depending on the manufacturer the pharmacist preparing the infusate will need to calculate the micrograms/hour rate for each pulse which must then be verified by an investigator prior to filling and programming the pump.

11.2 Treatment Regimen

In each pulse cycle, patients will receive 200uL/hr of 146uM topotecan for 48 hours (daily volume = 4.8 mL; total volume = 9.6 mL) followed by between five to seven days of therapy holiday during which the pumps will be set at the minimum programmable rate (2uL/hr; 5-7 day volume = 0.24-0.336mL). This cycle will be repeated two more times. After three complete cycles, patients will receive a fourth and final pulse at the same infusion rate (200uL/hr for 48 hours, plus or minus 6 hours). After this fourth dose, patients will be taken to the OR for pump removal and tumor resection as described. Once infusions are initiated, they will be carried out over a total of approximately 23-29 days. Four 48-hour infusion pulses at 200uL/hr will be administered for a total volume infused of 38.4 mL. When accounting for the near negligible volume delivered while the pump is placed at minimum performance rate (0.048mL/day for 15-21 days), a combined total volume of 39.12-39.41mL will be infused. Gadolinium will not be included in the CED infusion during the second and third infusion cycles; during this time TPT will be infused alone. The reason for including possible variability in the length of each infusion holiday (5-7 days) is that it will allow investigators to ensure that all surgical procedures, including pump removals, tumor resections, pump refills, as well as infusion initiations occur during weekdays when all staff members and support personnel are available to provide appropriate safety monitoring.

Volume or dose deviations of 10% or less are not considered protocol violations.

11.3 Method for Assigning Subjects to Treatment Groups

Not applicable.

11.4 Preparation and Administration of Study Drug

The topotecan and gadolinium will be purchased, stored, prepared and dispensed by the CUMC Research Pharmacy (contact number: 212.305.1965).

11.5 Subject Compliance Monitoring

Patients will be hospitalized for the initial catheter implantation, each 48-hour active drug infusion, and for final tumor resection. To avoid infection complications associated with prolonged hospitalization patients, if medically stable and per investigator discretion, the patient may elect to be discharged during each of the 5-7 day infusion holidays. Pumps will be re-filled percutaneously prior to each new 48-hour pulse of TPT (3 refills total). Re-filling the pump prior to Day 0 of a pulse due to pharmacy availability is allowed and will not affect drug stability. Patients will be monitored throughout the infusion process. Compliance is not expected to be an issue in this study.

11.6 Prior and Concomitant Therapy

No concomitant medicine or therapies for treatment of recurrent glioma are permitted while the patient is enrolled in this study.

11.7 Packaging

Topotecan will be purchased from commercial stock and packaged/labeled accordingly and in compliance with CUMC Research Pharmacy procedures.

11.8 Blinding of Study Drug

Since this is a phase Ib study, in which the primary goal is monitoring safety of therapy, there is no need for blinding.

11.9 Receiving, Storage, Dispensing and Return

11.9.1 Receipt of Drug Supplies

The topotecan will be purchased, stored, prepared and dispensed by the CUMC Research Pharmacy (contact number: 212.305.1965).

11.9.2 Storage

Topotecan should be kept in a secure place in the CUMC research Pharmacy under appropriate storage conditions according to manufacturer guidelines and USP requirements. Study drug will be handled in accordance with institutional policies for appropriate handling and disposal of antineoplastic agents.

11.9.3 Dispensing of Study Drug

Regular study drug reconciliation will be performed to document drug assigned, drug consumed, and drug remaining. This reconciliation will be logged on the drug reconciliation form, and signed and dated by the study team.

11.9.4 Return or Destruction of Study Drug

Unused drug vials will be returned to the pharmacy and destroyed on site. Excess topotecan will be destroyed in accordance with institutional polices for appropriate disposal of antineoplastic agents. At the completion of the study, there will be a final reconciliation of drug shipped, drug consumed, and drug remaining. This reconciliation will be logged on the drug reconciliation form, signed and dated. Any discrepancies noted will be investigated, resolved, and documented prior to return or destruction of the study drug.

11.10 Other Agent(s)

Product description: Gadolinium is a widely available, low cost MR contrast agent that is technically and economically feasible to use, and is routinely used intravenously in clinical practice.

Solution preparation (how the dose is to be prepared): The gadolinium will be used at a dilution of approximately 1:100.

Storage requirements: The original gadolinium solution will be stored in the Research Pharmacy at a temperature of 20-25^0 C. The 1:100 dilution will be prepared fresh prior to being loaded in the pump.

Stability: The original form as well as the final diluted gadolinium is stable.

Route of administration:
Gadolinium will be administered in conjunction with topotecan by convection enhanced delivery at approximately 200uL/hr during the first and fourth cycles of infusion.

12 STUDY CALENDAR

An enumerated list of chronological study procedures has been provided below. Please see Appendix A – Study Calendar.

MRI: Specific imagining acquisition instructions are provided in a separate imaging reference guide. MRI scans not performed for any reason will not be considered violations of the protocol. Additional imaging will be performed at the PI's discretion.

Pre-study (14 days or less before registration unless specified otherwise elsewhere in this document):

1. Patient recruited
2. Enrollment criteria verified
3. Informed consent signed
4. MRI with and without IV contrast (within 30 days of enrollment)
5. PET (Brain) – FDG-F18 (within 30 days of enrollment)
6. Pre-study information collected
    a. Medical history
    b. Physical exam
    c. Vital signs
    d. Height
    e. Weight
    f. Performance status (KPS)
    g. Neurocognitive assessment preformed
    h. Quality of life assessments performed
    i. Basic labs/preop testing collected and reviewed
        i. CBC with differential
        ii. Coagulation studies (INR/PT/PTT)
        iii. Serum chemistry (BMP and hepatic function panel)
        iv. EKG (as indicated by primary care physician/anesthesiology)
        v. Urine B-HCG for women of childbearing potential

Procedure:

1. MRI with and without IV contrast for intraoperative navigation
2. Stereotactic biopsy performed
    a. If intraoperative pathology consistent with glioma recurrence, proceed to 3
    b. If intraoperative pathology not clearly demonstrative of active tumor/recurrent high grade glioma, patient will be deemed inevaluable and removed from trial and replaced. Surgery will be stopped and no catheter will be implanted Remainder of care will be dictated by primary surgeon and neuro-oncologist.
3. Catheter placement
    a. Proximal catheter placed into tumor
    b. Medtronic Synchromed II pump (prefilled with study drug) implanted subcutaneously
    c. Infusion initiated (Tpt+gadolinium) at rest rate

Implant Recovery:

1. Patient spends approximately 1-7 days post operatively in Neuro ICU in accordance with standard postoperative care. More time in the ICU may be required, per the discretion of the neurosurgeon and Neuro ICU team.

2. Postoperative day 0 or 1: MRI with and without IV contrast performed to confirm catheter placement prior to infusion initiation
3. Patient transferred out of Neuro ICU once stable
4. Assessments performed at any time during implant recovery and prior to Pulse 1 Day 0:
   - **i.** Physical exam
   - **ii.** Vitals
   - **iii.** CBC with differential
   - **iv.** Serum chemistry (BMP and hepatic function panel)

   Adverse event evaluation and concomitant medication review

Infusion pulse #1:

1. Infusion day 0:
   a. Active Infusion initiated (Tpt+Gadolinium)
   b. MRI without IV contrast performed at 8 hours (plus or minus 2 hours) and 14 hours (plus or minus 2 hours) post infusion initiation
   c. Assessments performed at any time on infusion day 0:
      i. Physical exam
      ii. Vitals
      iii. Performance status
      iv. CBC with differential
      v. Coagulation panel: PT/PTT/INR
      vi. Serum chemistry (BMP and hepatic function panel)
      vii. Adverse event evaluation and concomitant medication review

2. Infusion day 1:
   a. MRI without IV contrast performed at 24 hours, plus or minus 6 hours, post infusion initiation
   b. Assessments performed at any time on infusion day 1
      i. Physical exam
      ii. Vital signs
      iii. CBC with differential
      iv. Coagulation panel: PT/PTT/INR
      v. Serum chemistry (BMP and hepatic function panel)
      vi. Adverse event evaluation and concomitant medication review

3. Infusion day 2:
   a. MRI without IV contrast performed at 48 hours, plus or minus 6 hours, post infusion initiation
   b. Infusion turned down to rest rate
   c. Assessments performed at any time on infusion day 2
      i. Physical exam
      ii. Vital signs
      iii. Performance status
      iv. Neurocognitive assessment

v. Quality of life assessment
vi. Adverse event evaluation and concomitant medication review

Rest phase #1: (lasting 5-7 days):

1. Infusion remains at rest rate
2. Rest day 0, post completion of pulse 1
    a. MRI without IV contrast performed at 8 hours (plus or minus 2 hours) and 14 hours (plus or minus 2 hours) post infusion completion, rest day 0
3. Rest day 1, post completion of pulse 1
    a. MRI without IV contrast performed at 24 hours, plus or minus 6 hours, post infusion completion, rest day 1
4. Rest day 2, post completion of pulse 1
    a. PET (Brain) FDG F18 @ 48 hours plus or minus 6 hours, post-infusion completion Patient evaluated for discharge and discharged home at the investigator's discretion. Patient may stay at home for remainder of rest phase.

Infusion pulse #2:

1. Patient admitted to CUMC
2. MRI with and without IV contrast performed prior to restarting infusion
3. Pump refilled (Topotecan only, no gadolinium), interrogated, and reprogrammed
4. Pump reprogrammed to active infusion rate
5. Infusion continues for 48 hours, plus or minus 6 hours, while patient remains inpatient
6. Assessments to be performed at any time on the days indicated on the study calendar.
    a. Physical exam
    b. Vital signs
    c. Performance status
    d. Adverse event evaluation and concomitant medication review
7. MRI with and without IV contrast performed at 48 hours, plus or minus 6 hours, post infusion initiation
8. Infusion turned down to rest rate after completion of MRI
9. Patient evaluated for discharge and discharged home at the investigator's discretion

Rest phase #2: (lasting 5-7 days)

1. Infusion remains at rest rate
2. Patient may remain home at this time

Infusion pulse #3:

1. Patient admitted to CUMC
2. MRI with and without IV contrast performed prior to restarting infusion
3. Pump refilled (Topotecan only, no gadolinium), interrogated, and reprogrammed
4. Pump reprogrammed to active infusion rate
5. Infusion continues for 48 hours, plus or minus 6 hours, while patient remains inpatient
6. Assessments to be performed at any time on the days indicated on the study calendar

   a. Physical exam
   b. Vital signs
   c. Performance status
   d. Adverse event evaluation and concomitant medication review
7. MRI with and without IV contrast performed at 48 hours, plus or minus 6 hours, post infusion initiation
8. Infusion turned down to rest rate
9. Patient evaluated for discharge and discharged home at the investigator's discretion

Rest phase #3: (lasting 5-7 days)

1. Infusion remains at rest rate
2. Patient may remain at home at this time

Infusion pulse #4:

1. Patient admitted to CUMC
2. MRI with and without IV contrast performed prior to restarting infusion
3. Pump refilled (Topotecan+Gadolinium), interrogated, and reprogrammed
4. Pump reprogrammed to active infusion rate
5. Infusion continues for 48 hours, plus or minus 6 hours, while patient remains inpatient
6. Assessments to be performed at any time on the days indicated on the study calendar with the exception of the neurocognitive and quality of life assessments which should be performed prior to pulse 4 infusion start.
   a. Physical exam
   b. Vital signs
   c. Performance status
   d. Neurocognitive assessment
   e. Quality of life assessment
   f. Adverse event evaluation and concomitant medication review
   g. Preop labs (CBC with differential, BMP, coagulation panel (PT, INR, PTT), and hepatic function panel) drawn once
7. PET (Brain) FDG-F18 - Infusion day 1 @ 24 hours +/- 12 hours post initiation of infusion
8. MRI without IV contrast performed at 48 hours, plus or minus 6 hours, post infusion initiation
9. Infusion turned off
10. Patient returns to OR
    a. Stereotactic biopsies performed
    b. Tumor resection
    c. Pump removal
11. Patient admitted to NeuroICU

Patient remains in NeuroICU for 24-48 hours postop for routine care, more time may be required in the ICU, per the discretion of the Neurosurgery and ICU teams.

Post-infusion/Post-operative day 1 or 2:

1. MRI with IV contrast performed post op day 1 for assessment of extent of resection
2. Assessments performed on post-infusion/post-operative day 1:
    a. Physical exam
    b. Vital signs
    c. Adverse event evaluation and concomitant medication review
    d. CBC with differential
    e. Coagulation panel: PT/PTT/INR
    f. Serum chemistry (BMP and hepatic function panel)

Post-infusion/Post-operative day 3:

1. Assessments performed on post-infusion/post-operative day 3:
    a. Neurocognitive assessment to be performed within 72 hours plus or minus 24 hours post-infusion/post-op window
    b. Quality of life assessment to be performed within 72 hours plus or minus 24 hours post-infusion/post-op window

Post-infusion week 1-2:

1. Follow up office visit
2. Assessments performed for this visit:
    a. Physical exam
    b. Vital signs
    c. Weight
    d. Performance status
    e. Neurocognitive assessment
    f. Quality of life assessment
    g. Adverse event evaluation and concomitant medication review
    h. CBC with differential
    i. Serum chemistry (BMP and hepatic function panel)

Post-infusion week 4-6:

1. Follow up office visit
2. Assessments performed for this visit:
    a. MRI with IV gadolinium contrast
    b. Physical exam
    c. Vital signs
    d. Weight
    e. Performance status
    f. Neurocognitive assessment
    g. Quality of life assessment
    h. Adverse event evaluation and concomitant medication review
    i. CBC with differential
    j. Serum chemistry (BMP and hepatic function panel)

Every 3-6 months thereafter:

1. Phone call for survival assessment
2. Remainder of care per primary clinical team

MEASUREMENT OF EFFECT

13.1 Antitumor Effect – Solid Tumors

For the purposes of this study, patients should be re-evaluated for response by MRI 4-6 weeks following cessation of drug infusion. Thereafter, patients will have usual physician follow-up, in which further MRIs will be performed based on their primary neurologist/neurosurgeon's recommendations In addition to a baseline MRI scan, confirmatory scans should also be obtained at the following timepoints: immediately following placement of the infusion catheter (surgery day), Pulse 1 Day 2, Pulse 4 Day 2, 1 day post resection, 4-6 weeks following drug termination, and then as recommended by the primary treating physician.Response and progression will be evaluated in this study using the international criteria proposed by the updated Response Assessment in Neuro-oncology (RANO) guidelines[38].

Measurement of response will be based upon the volume of contrast enhancing lesion in the treatment area. If the MRI remains unclear as to whether the increase in enhancement volume is due to tumor progression vs. inflammatory change, a biopsy may be performed to make a definitive diagnosis. In order to categorize a response as stable or responding, patients must be on stable or decreasing dose of steroids. Any response must last a minimum of 4 weeks.

13.2 Disease Parameters

Measurable disease: Measurable lesions are defined as those that can be accurately measured in at least one dimension on T1 weighted MRI of the brain with IV gadolinium enhancement. Furthermore, recurrent high grade gliomas will be confirmed with stereotactic biopsies and intraoperative pathology prior to implantation of the infusion catheter.

Target lesions: Target lesions will be well circumscribed, solitary enhancing lesions within the brain parenchyma. Ideal target lesions for convection enhanced delivery will not have cystic resection cavities or extensive associated central necrosis.

13.3 Methods for Evaluation of Measurable Disease

Measurable disease will be determined from a preoperative T1 weighted brain MRI with IV gadolinium obtained no greater than 48 hours prior to planned implantation of the catheter. Lesions will be measured using hospital radiology tools and viewers as part of the standard assessment performed by neuroradiologists. The number and maximum diameters of the lesions will be recorded.

Prior to implantation of the catheter, stereotactic biopsies will be performed to obtain a sample of enhancing tissue to document the presence of recurrent glioma with intraoperative pathology consult.

13.4 Response Criteria

RANO criteria will be used (Wen PY et al, citation 38), summarized here. Response requires confirmation by repeat imaging at least 4 weeks apart. Non-sustained responses will be characterized as stale disease.

Table 4. Summary of the Proposed RANO Response Criteria

Criterion	CR	PR	SD	PD
T1 gadolinium enhancing disease	None	≥ 50% ↓	< 50% ↓ but < 25% ↑	≥ 25% ↑*
T2/FLAIR	Stable or ↓	Stable or ↓	Stable or ↓	↑*
New lesion	None	None	None	Present*
Corticosteroids	None	Stable or ↓	Stable or ↓	NA†
Clinical status	Stable or ↑	Stable or ↑	Stable or ↑	↓*
Requirement for response	All	All	All	Any*

Abbreviations: RANO, Response Assessment in Neuro-Oncology; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; FLAIR, fluid-attenuated inversion recovery; NA, not applicable.
*Progression occurs when this criterion is present.
†Increase in corticosteroids alone will not be taken into account in determining progression in the absence of persistent clinical deterioration.

13.4.1 Evaluation of Best Overall Response

The best overall response is the best response recorded from the start of the treatment until disease progression/recurrence The patient's best response assignment will depend on the achievement of both measurement and confirmation criteria.

13.4 Duration of Response

Duration of overall response: The duration of overall response is measured from the time measurement criteria are met for CR or PR (whichever is first recorded) until the first date that recurrent or progressive disease is objectively documented (taking as reference for progressive disease the smallest measurements recorded since the treatment started).

The duration of overall CR is measured from the time measurement criteria are first met for CR until the first date that progressive disease is objectively documented.

Duration of stable disease: Stable disease is measured from the start of the treatment until the criteria for progression are met, taking as reference the smallest measurements recorded since the treatment started, including the baseline measurements.

13.5 Progression-Free Survival (PFS) and Overall Survival (OS)

PFS is defined as the duration of time from start of topotecan treatment to time of progression or death from any cause, whichever occurs first. Overall survival is defined as the duration of time from the start of topotecan treatment to death from any cause.

13.6 Other Response Parameters

Additionally, we attempt to use MRS to monitor response as possible. In our preliminary studies we have seen that maps of normalized choline (Cho), creatine (Cr), N-acetylaspartate (NAA), and lactate (Lac) distributions have correlated well with clinical and radiographic measures of tumor response. There is also considerable evidence in the brain tumor literature that changes in these metabolites, with reduction or elimination of the so-called tumor pattern of proton MRS (elevated Cho, reduced NAA and elevated Lac), correlates well with histologic and clinical response of tumor to therapy. The MRS metabolite maps will be used to assess baseline and immediate post-treatment as well as long term treatment response. These measures may be used to supplement the changes based on T1-weighted contrast enhancement.

13.7 Stopping Rules

The primary endpoint of this study is safety. As such, subjects will be withdrawn from the study as per the guidelines outlined in section 6.5. Should similar toxicities occur in more than one patient, early interruption of the study will be considered.

14 DATA REPORTING / REGULATORY REQUIREMENTS

Adverse event lists, guidelines, and instructions for AE reporting can be found in Section 10.0 (Adverse Events: List and Reporting Requirements).

14.1 Data Collection

The Herbert Irving Comprehensive Cancer Center has an electronic clinical trials and data management system (CTMS) that will be used for data collection. CRFs for the study will be built into the CTMS for data entry. The system has full auditing capabilities which is web-based and housed on a server in a fully HIPAA compliant server room with restricted access and video camera monitoring. All users must login with their own application username and password. Users off campus must first access the Virtual Private Network with their assigned campus username and password and then use their application credentials. Users are only able to see study information if they are indicated as study personnel in our electronic IRB system. Users are limited to access based on the role assigned in their corresponding protocol. Subject data is entered directly into the system, which (in the case of Columbia subjects) confirms the correct identity of patients via an interface with the electronic medical patient index. Staff with the appropriate IRB defined roles can run reports within the system for reporting purposes.

14.2 Data Reporting

Case Report Forms will be completed for each subject enrolled into the clinical study through the CTMS. It is the investigator's responsibility for ensuring that all clinical and laboratory data entered on the corresponding CRFs are complete, accurate and authentic.

14.3 Data and Safety Monitoring Committee

The NCI-approved Data Safety and Monitoring Committee (DSMC) of the Herbert Irving Comprehensive Cancer Center (HICCC) will monitor every subject who receives treatment on this protocol for toxicity. This protocol will adhere to the policies of the currently approved HICCC Data and Safety Monitoring Plan (DSMP), which is in accordance with NCI and CUMC-IRB policy and guidelines. The committee is chair is appointed by the HICCC Director. The committee consists of HICCC faculty and staff with expertise in oncology, research pharmacy, research nursing, and data management. The DSMC convenes twice a month to review patient safety and the conduct of the trial. The PI will submit data and safety monitoring reports to the DSMC at a frequency to be determined by the DSMC based on risk to the subjects.

At the time of renewal, the study team will submit the most recent DSMC approval letter for safety review to the CUMC IRB. Any modifications that are required by the DSMC to ensure patient safety will be submitted to the IRB. All protocol deviations, violations, and eligibility waivers will be submitted to and approved by the DSMC prior to being reported to the IRB. All study data reviewed and discussed during these meetings will be kept confidential.

14.4 Quality Control and Quality Assurance

Independent monitoring of the clinical study for protocol and GCP compliance will be conducted periodically by the CPDM Compliance Core on behalf of the HICCC DSMC. Additionally, the Compliance Oversight Committee of the IRB at Columbia University Medical Center may audit the study at any time per institutional policies and procedures. The investigator-sponsor and Columbia University Medical Center will permit direct access of the study monitors and appropriate regulatory authorities to the study data and to the corresponding source data and documents to verify the accuracy of this data.

A risk-based approach will be used by the Compliance Core to determine the frequency, number of subject charts, and data elements to be monitored. The Compliance Coordinator will review the study status and summarize enrollment, toxicities, SAEs/UPs, dose escalation, statistical endpoints (e.g., stopping rules), etc. for the full DSMC membership at the regularly scheduled meetings.

Internal On-site Monitoring:

- The study Monitoring Visit Log will be completed and signed by the monitor and the PI/CRNP/CRN and/or CRC and will be filed in the regulatory binder.

- The Compliance Coordinator will communicate with the site coordinator/Site Principle Investigator to schedule the monitoring visit and arrange for access to study materials and documentation.

- The assigned Compliance Coordinator will monitor IIT trials within 1 month after the first subject is enrolled and throughout the life of the study to ensure that the study is being conducted in accordance with the protocol, GCP, applicable federal and local regulations, and per all applicable SOPs. The Compliance Coordinator is responsible to notify the PI and CRNP/CRN/CRC of upcoming monitor visits and convey what information and documentation will be required for the visit(s). The Compliance Coordinator is responsible for verifying that informed consent is properly obtained, eligibility is met (via the central registration process), and all study procedures are conducted according to the study protocol. The Compliance Coordinator will also verify that the data reported in the CRF's accurately reflect source documents, that all toxicities have been reported to date, and that all SAE's/UPs/deviations/violations have been reported according to local IRB and HICCC DSMC requirements. The Compliance Coordinator will issue queries and ensure resolution in a timely and efficient manner. The Compliance Coordinator will also monitor for applicable regulatory compliance and research pharmacy compliance (if applicable) and communicate any deficiencies as appropriate.

14.5 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (e.g., that the subject is alive) at the end of their scheduled study period.

The subject binders will be maintained with in the CPDM offices, a secured floor within the Herbert Irving Pavilion and only the investigator and study staff will have access to the file.

14.6 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

14.7 Case Report Forms

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF will be recorded. All missing data will be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, "N/D" will be documented. If the item is not applicable to the individual case, "N/A" will be documented.

14.8 Records Retention

Records relating to a specific research activity, including research records collected by investigators, will be maintained for at least three years after completion of the research (45 CFR 46.115(b); 21 CFR 56.115(b); 21 CFR 312.62). This minimum retention period will apply whether or not any subjects were enrolled in the study.

Since this research is FDA regulated, records will be retained for at least two years after approval of the investigational agent by FDA; if it is not approved, records will be retained at least two years after the study is terminated and FDA is notified.

Clinical records, including consent forms that document clinical intervention or clinical diagnostic procedure research-related procedures, will be retained in medical records by the institution for at least seven years, per CUMC and NYP policy which is based on state law.

15 STATISTICAL CONSIDERATIONS

15.1 Study Design/Endpoints

Safety is the main study endpoint. Safety is defined as the dose at which all patients have had no greater than grade 2 adverse reactions possibly, probably, or definitely related to the topotecan. For the purposes of this study, necrosis of tumor and edema which result in neurologic symptoms will not be considered as a safety limitation, as long as symptoms can be adequately controlled by corticosteroids, mannitol, and craniotomy if necessary. Safety will be assessed by evaluation of physical and neurologic examinations, laboratory studies, radiographic studies, and by adverse events. An adverse event is any new or worsening symptom or clinical finding which occurs during the study period which is possibly, probably, or definitely related to study-specific treatment. Adverse events are to be recorded irrespective of causality, on the adverse events form. The current version of the CTCAE will be used. For events not described adequately by the CTCAE, the investigator may record events by severity (mild, moderate, severe, life-threatening). All events will be recoreded for duration, and relation to study medication (unrelated, unlikely, possible, probable, definite). Any specific therapy for the adverse event will be recorded. Any serious adverse experience associated with the use of this drug will be reported to Institutional IRB.

15.2 Size/Accrual Rate

Five evaluable patients will be accrued for this study. Since radiation necrosis (also called pseudoprogression or treatment effect) is difficult to distinguish from true tumor recurrence

intraoperatively on frozen section, it is likely that several patients meeting enrollment criteria will not have biopsy confirmed tumor at the time the initial study biopsy is taken. Such patients will not be considered evaluable and will not actively enter the treatment phase of the study. As such, anticipated enrollment in the study must be greater than 5 to ensure that 5 evaluable patients are ultimately identified and treated. Based on rates of radiation necrosis, which are roughly 10% of reoperations[26], we will initially cap enrollment at 10 patients, and enrollment will stop when 5 evaluable patients have been obtained. Thus we will have an initial enrollment of 10 patients total (barring any early stopping rule concerns as outlined in section 5.5), and a maximum of 5 evaluable patients that undergo catheter implantation and complete topotecan infusion. Furthermore, if patients who have catheters placed and infusion initiated fail to complete the full course of infusion for reasons unrelated to treatment toxicity/DLTs, they will be considered inevaluable for the primary endpoint (but evaluable for toxicity), as the primary study endpoint is assessment of infusion safety over a full 23. If a patient's infusion is terminated early for reasons unrelated to treatment toxicity/DLTs, then a new subject will be recruited to replace him/her to ensure a total of 5 evaluable subjects at the completion of the study. If patients are removed from the study as a result of failure to follow up with pre-defined safety follow-up evaluations, they will also be considered inevaluable, as assessment of infusion will not be ascertainable in such patients. As above, such inevaluable patients will be replaced with newly recruited and enrolled evaluable patients. Additional patients may be replaced or accrued at the discretion of the PI in discussion with the DSMC if there is further clarity required to assess safety.

Given our previous experience, we expect to enroll approximately 1-2 patients/month.

15.3 Stratification Factors

N/A

15.4 Analysis of Secondary Endpoints

Anti-tumor effect will be a secondary endpoint of this study and will be analyzed as described in section 13. Furthermore, quality of life will be assessed using 4 questionnaires. All patients enrolled in this study will be administered the following four (4) paper and pencil measures at baseline, prior to receiving their medical treatment, during the pulses and follow-up as indicated on the study calendar. These measures are widely used and well validated and assess the patient's quality of life, in addition to other pertinent symptoms such as fatigue, pain, sleep, mood, etc. All these measures utilize a 5-point Likert-type scale (0 = Not at all; 1 = A little bit; 2 = Somewhat; 3 = Quite a bit; and 4 = Very Much) and the recall period for each question is "during the past 7 days" and this time frame is well comprehended by patients. Each subject's scores on these measures will be compared with their subsequent scores at each follow-up period to closely examine the trajectory of their QoL and symptoms over time while being treated and monitored on this study. Copies of the measures are attached.

1. The FACT-Brain: comprised of the FACT-G + Brain Tumor specific concerns
2. The FACIT-Fatigue scale
3. PROMIS Global health measure

The FACIT Measurement System (Functional Assessment of Chronic Illness Therapy) is a collection of QOL questionnaires targeted to the management of chronic illness. The measurement system, under development since 1987, began with the creation of a generic CORE questionnaire called the Functional Assessment of Cancer Therapy-General (FACT-G). These paper and pencil questionnaires are designed to be brief yet focused to accurately measure the symptoms that cancer patients can experience. The FACT-G (now in Version 4) is a 27-item compilation of general questions divided into four primary QOL domains: Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being. It is considered appropriate for use with patients with any form of cancer, and has also been used and validated in other chronic illness conditions (e.g., HIV/AIDS and multiple sclerosis) and in the general population. The FACT-Br includes a list of 23 additional concerns that brain tumor patients often experience.

The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F Scale) is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function. It was developed in 1994-1995 to meet a growing demand for the precise evaluation of fatigue associated with anemia in cancer patients. Subsequent to its development, it has been employed in over 70 published studies including over 20,000 people. Since 1995, studied groups have included cancer patients receiving chemotherapy, cancer patients not receiving chemotherapy, long term cancer survivors, and several other clinical samples.

The PROMIS Global Health items assess health in general (i.e. overall health). The global health items include global ratings of the five primary PROMIS domains (physical function, fatigue, pain, emotional distress, social health) as well as perceptions of general health that cut across domains. Global items allow respondents to weigh together different aspects of health to arrive at a "bottom-line" indicator of their health. Similar global health items have been found predictive of future health care utilization and mortality. The PROMIS Global Health items include the most widely used single self-rated health item ("In general, would you say your health is . . ."). PROMIS Global Health items include specific ratings of physical health and mental health, as well as a rating of overall quality of life. The remaining items provide global ratings of physical function, fatigue, pain, emotional distress, and social health. There is no reporting period specified for these items; current status is inferred.

15.5 Reporting and Exclusions

15.5.1 Evaluation of toxicity

All patients will be evaluable for toxicity from the time of their first treatment with the study drug.

15.5.2 Evaluation of response

Response will be evaluated based on degree of tumor recurrence progression seen on follow up MRIs at 3-months post infusion and MRIs performed thereafter per their primary treating physician. All conclusions should be based on all eligible patients. Subanalyses may then be performed on the basis of a subset of patients, excluding those for whom major protocol deviations have been identified (e.g., early death due to other reasons, early discontinuation of treatment, major protocol violations, etc.).

15.5.3 Pathologically Evaluable

Patient's whose pre-study (via standard of care processes) biopsy material is reviewed as active tumor, consistent with HGG.

16 PROTECTION OF HUMAN SUBJECTS

This study is to be conducted in accordance with applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be obtained before commencement of this study.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject or legally acceptable surrogate, as outlined in the IRB approved protocol, and the investigator-designated research professional obtaining the consent.

17 PUBLICATION PLAN

Neither the complete nor any part of the results of the study carried out under this protocol, nor any of the information provided by the sponsor for the purposes of performing the study, will be published or passed on to any third party without the consent of the study sponsor. Any investigator involved with this study is obligated to provide the sponsor with complete test results and all data derived from the study.

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