Supplementary material for

Inhibition of integrated stress response protects against lipid-Induced senescence in hypothalamic neural stem cells in adamantinomatous craniopharyngioma

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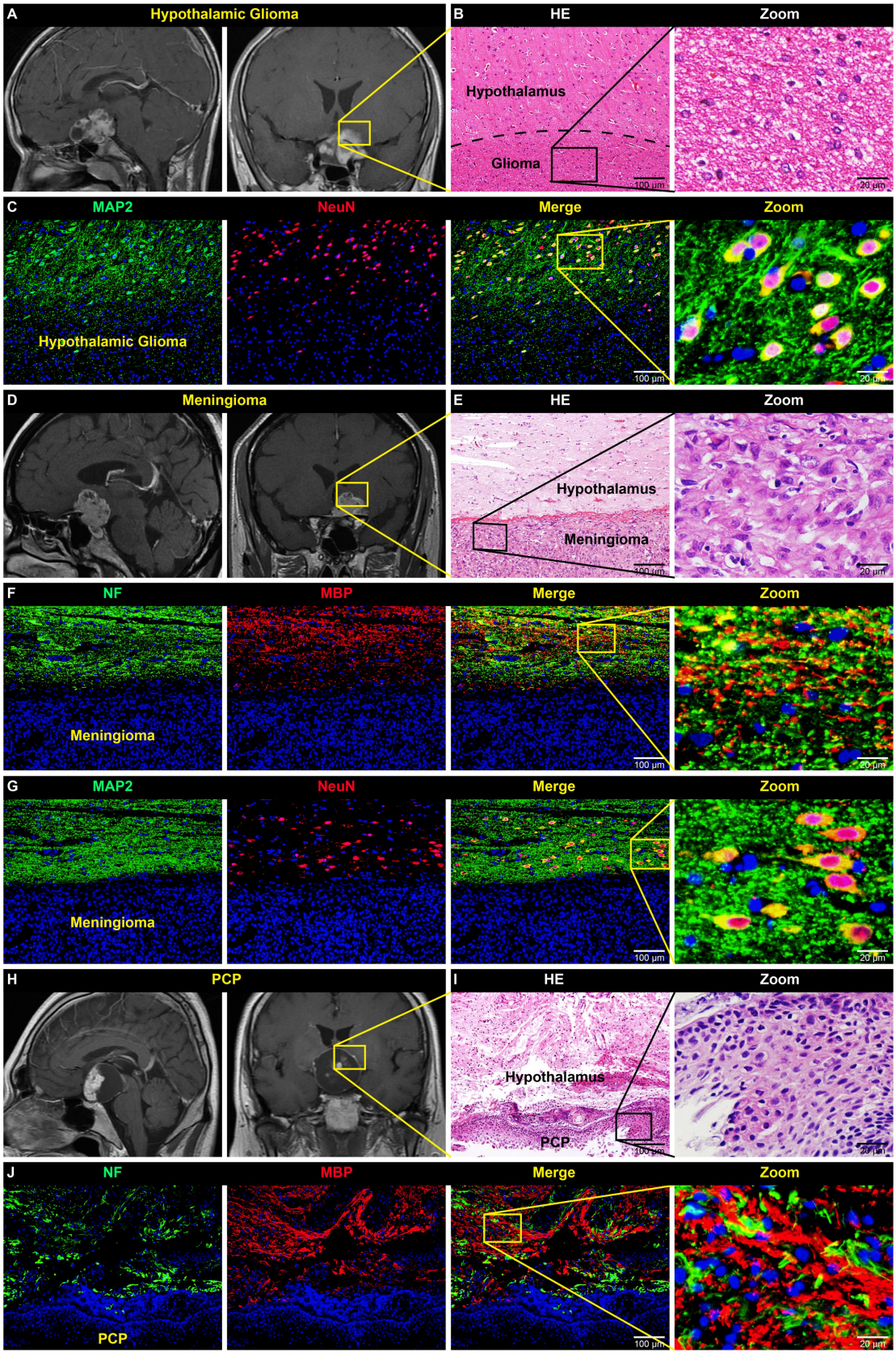
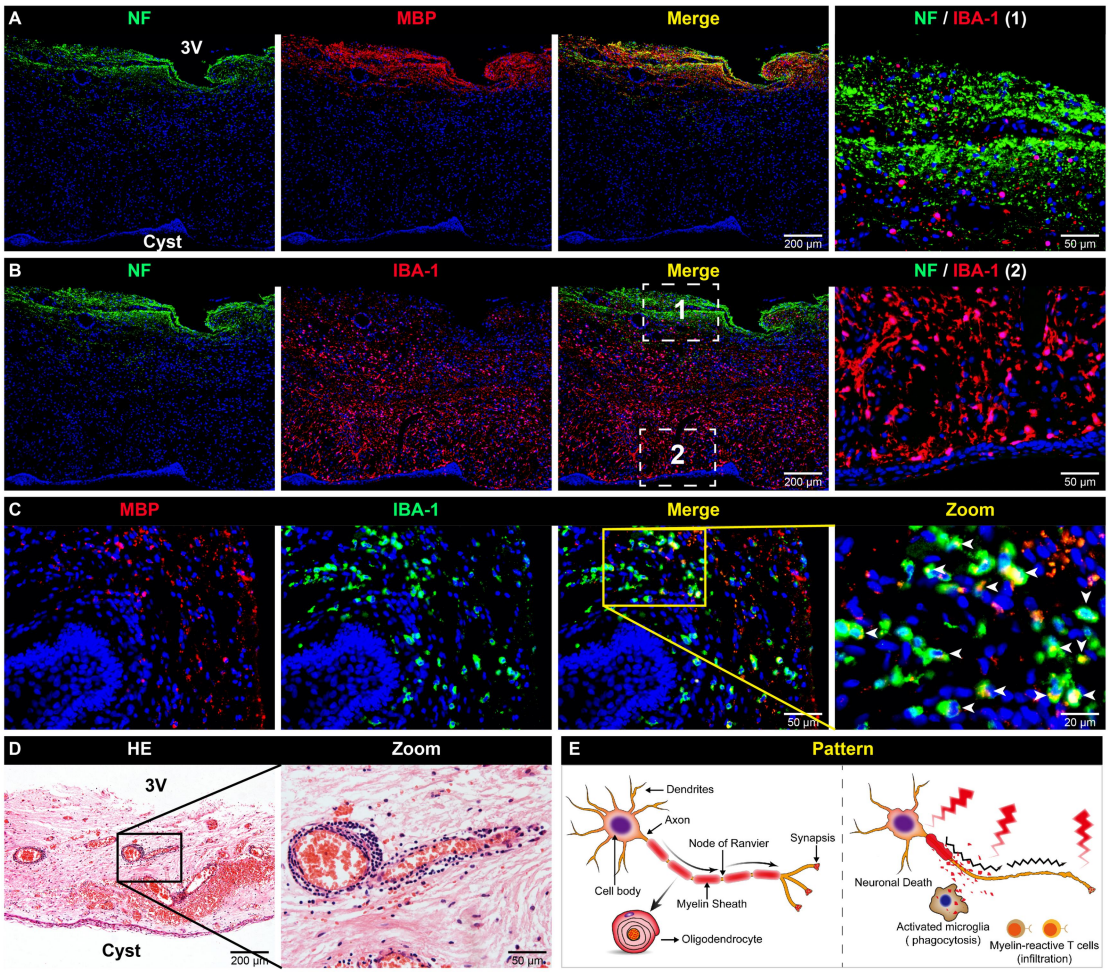
Overview on Supplementary material:

- Purification of $CD133^+$ NSCs
- Transmission Electron Microscopy (TEM)
- Gas Chromatography
- Sample Collection and RNA-seq Analysis Preparation
- Clustering and Sequencing
- Quality Control
- Reads Mapping To the Reference Genome
- Quantification of Gene Expression Levels
- Differential Expression Analysis
- Primary Cell Culture
- HtNSCs Characterization and Lipid Content Assays
- Immunocytochemistry (ICC)
- Western Blot
- RNA Extraction and Quantitative real-time PCR
- Animals Models
- Morris Water Maze (MWM)
- Mitochondria Fragmentation and Surface Area Assay
- Quantitative Analysis of Immunohistological Data
- Statistical Analysis

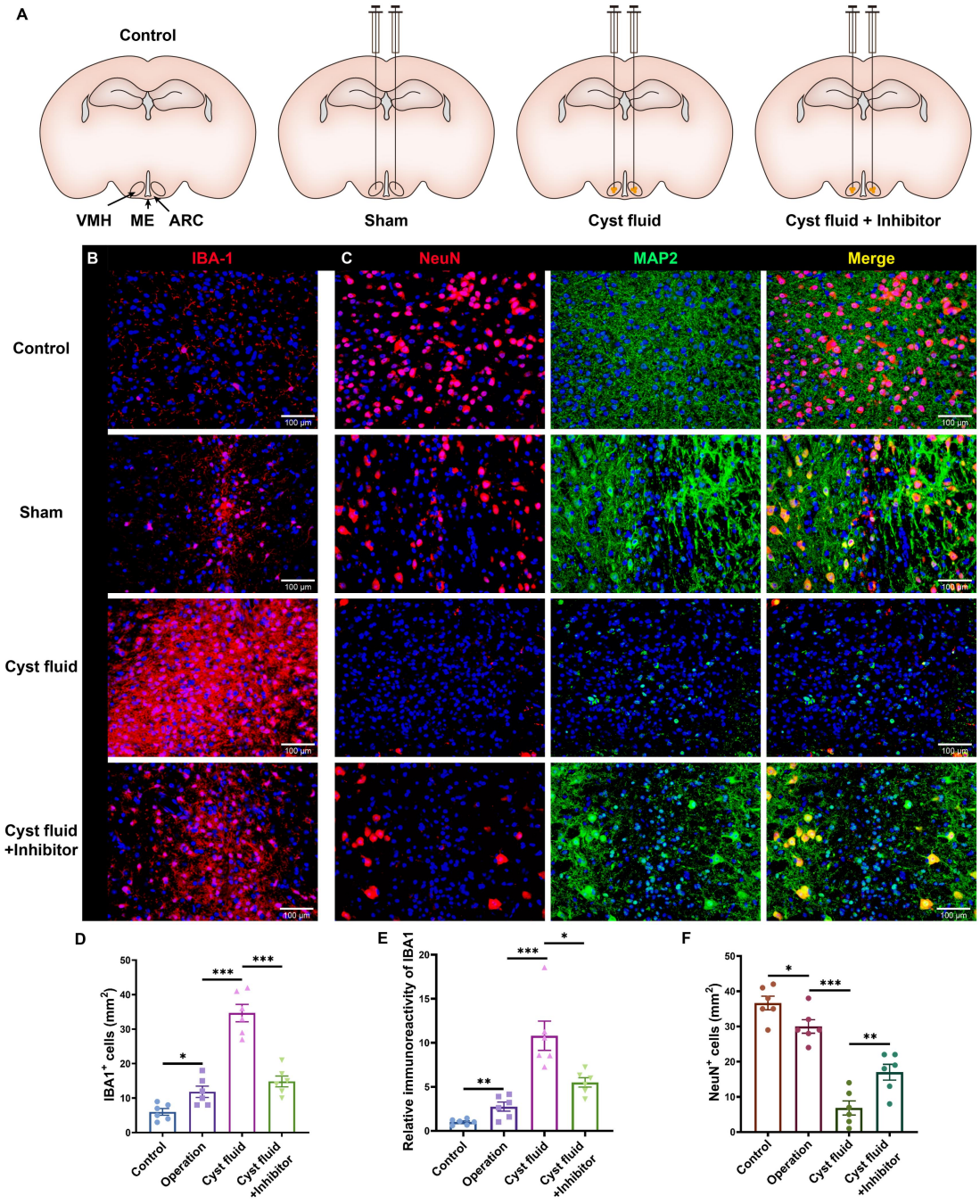
Supplementary Figures



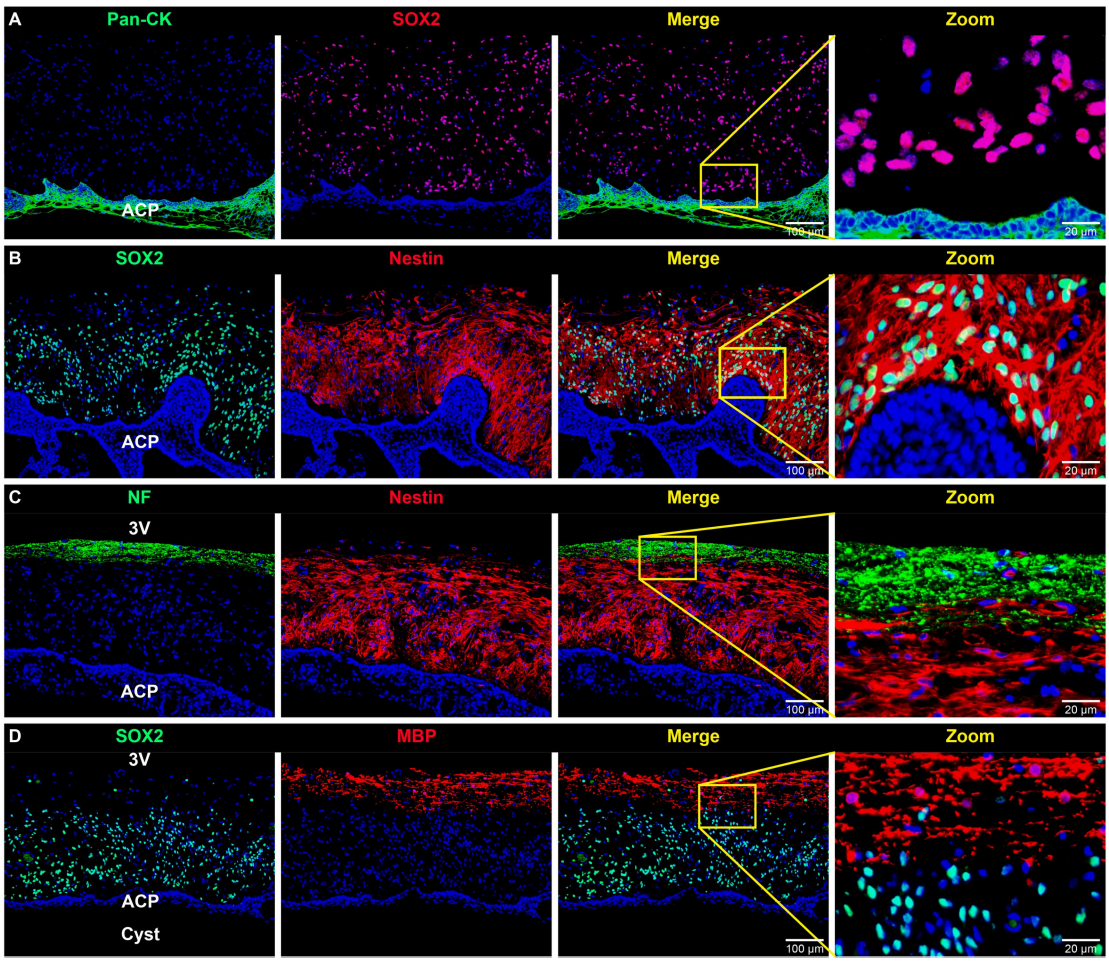
Supplementary Figure 1. No significant nerve damage of hypothalamus is found in glioma, meningioma, and papillary craniopharyngioma (PCP) of the sellar region. (A and **B)** Representative sagittal and coronal contrast-enhanced T1-weighted MR images (A) obtained before surgery and hematoxylin and eosin staining (H&E; B) obtained post-operation from a hypothalamic glioma patient. Boxed area is enlarged and presented on the right. **(C)** Immunofluorescence staining of nine hypothalamic glioma tissue samples, representative images of microtubule-associated protein 2 (MAP2) and NeuN co-staining. Boxed area is enlarged and presented on the right. **(D** and **E)** Representative sagittal and coronal contrast-enhanced T1-weighted MR images (D) obtained before surgery and H&E staining (E) obtained post-operation from a tuberculum sellae meningioma patient. Boxed area is enlarged and presented on the right. **(F)** Immunofluorescence staining of eight tuberculum sellae meningioma tissue samples, representative images of neurofilament (NF) and myelin basic protein (MBP) co-staining. Boxed area is enlarged and presented on the right. **(G)** Immunofluorescence staining of eight tuberculum sellae meningioma tissue samples, representative images of MAP2 and NeuN co-staining. Boxed area is enlarged and presented on the right. **(H** and **I)** Representative sagittal and coronal contrast-enhanced T1-weighted MR images (H) obtained before surgery and H&E staining (I) obtained post-operation from a PCP patient. Boxed area is enlarged and presented on the right. **(J)** Immunofluorescence staining of twelve PCP tissue samples, representative images of NF and MBP co-staining.



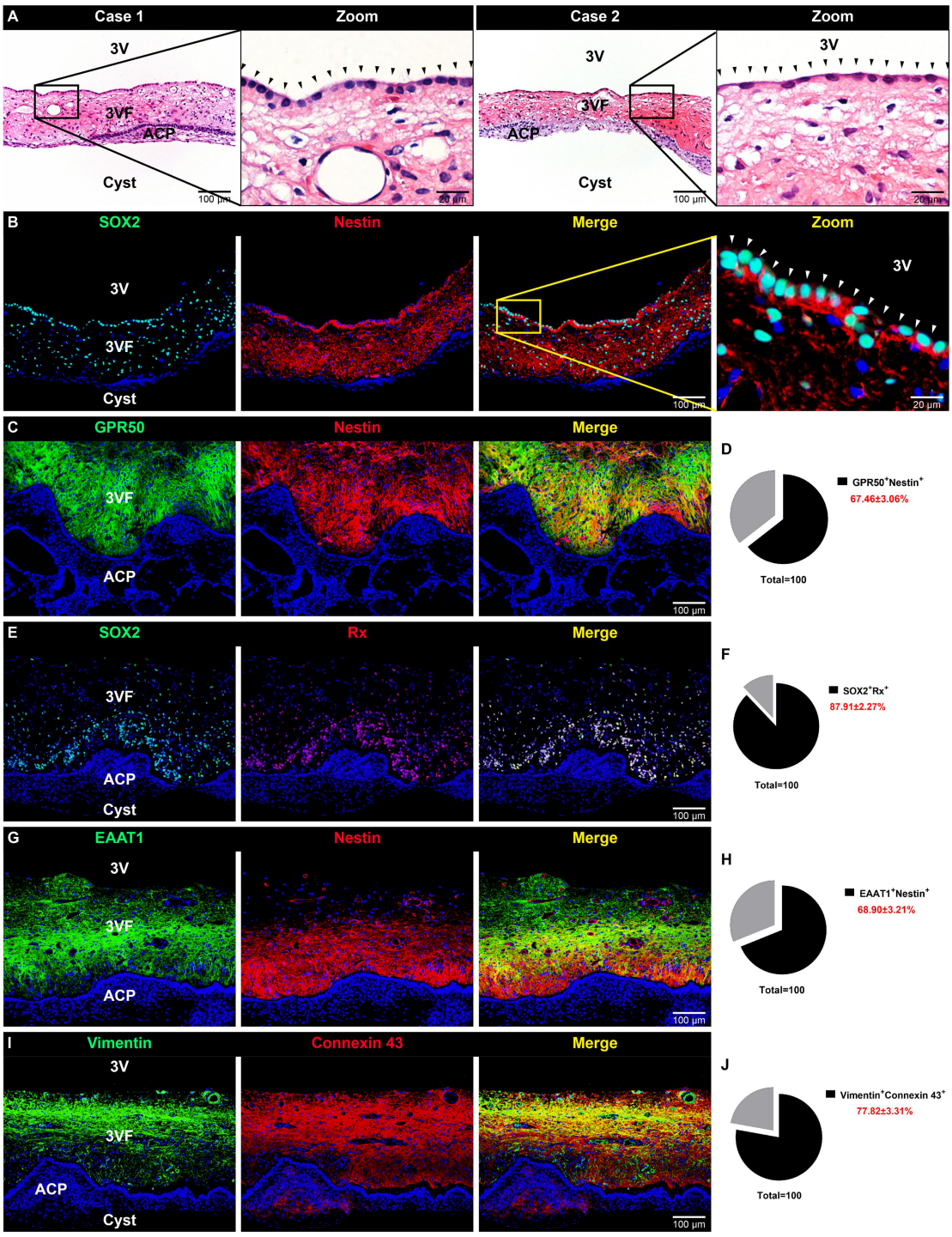
Supplementary Figure 2. Microglia infiltration is closely related to the nerve damage of third ventricle floor (3VF). (A) Representative dual immunofluorescence images of NF and MBP in ACP tissue samples. **(B)** Representative dual immunofluorescence images of NF and IBA-1 in ACP tissue samples. Boxed area is enlarged and presented in right panels. **(C)** Double immunofluorescence staining of ACP tissue samples, representative images of MBP and IBA-1 staining. White arrows represent the microglia that engulfs the myelin sheath. Boxed area is enlarged and presented on the right. **(D)** H&E staining of ACP tissue sections. representative images showing the lymphatic vascular sheath in the 3VF adjacent to ACP. Boxed area is enlarged and presented on the right. **(E)** Schematic diagram showing the structure of a neuron and the potential mechanism of neuronal damage may be that microglia and other immune cells engulf neuronal axons, leading to myelin disintegration and eventually neuronal death.


A
Control
VMH
ME
ARC
Sham
Cyst fluid
Cyst fluid + Inhibitor
B
IBA-1
C
NeuN
MAP2
Merge
Control
Sham
Cyst fluid
Cyst fluid +Inhibitor
100 μm
D
IBA1+ cells (mm2)
E
Relative immunoreactivity of IBA1
F
NeuN+ cells (mm2)
Control
Operation
Cyst fluid
Cyst fluid +Inhibitor

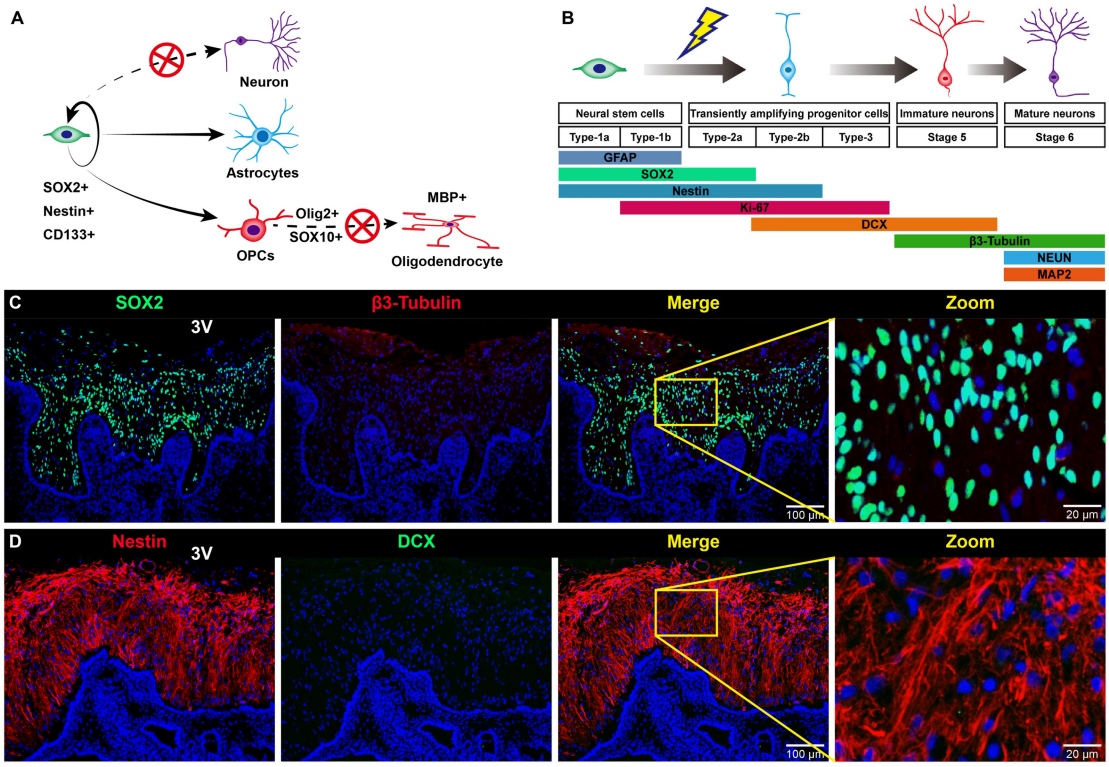
Supplementary Figure 3. Cystic fluid of ACP activates the microglia and causes hypothalamic damage in the mouse models. (A) Schematic diagram showing the procedure of animal experiment. **(B)** Activation of hypothalamic microglia induced by cystic fluid of ACP was confirmed by immunofluorescence staining of IBA-1, and inhibition of NF-κB signaling (BAY 11-7082) reduced the activation of microglia caused by cystic fluid of ACP. **(C)** Hypothalamic damage was verified by dual immunofluorescence staining of NeuN and MAP2, and NF-κB signaling inhibitor (BAY 11-7082) alleviated the hypothalamic damage caused by cystic fluid of ACP. **(D)** Quantification of the IBA-1$^+$ microglia in the hypothalamus of mice described in (B) (n = 6/group). **(E)** Quantification of the IBA-1 fluorescence intensity in the hypothalamus of mice described in (B) (n = 6/group). **(F)** Quantification of the NeuN$^+$ neurons in the hypothalamus of mice described in (C) (n = 6/group). Data are presented as the mean ± standard error of mean (SEM). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (D–F) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.



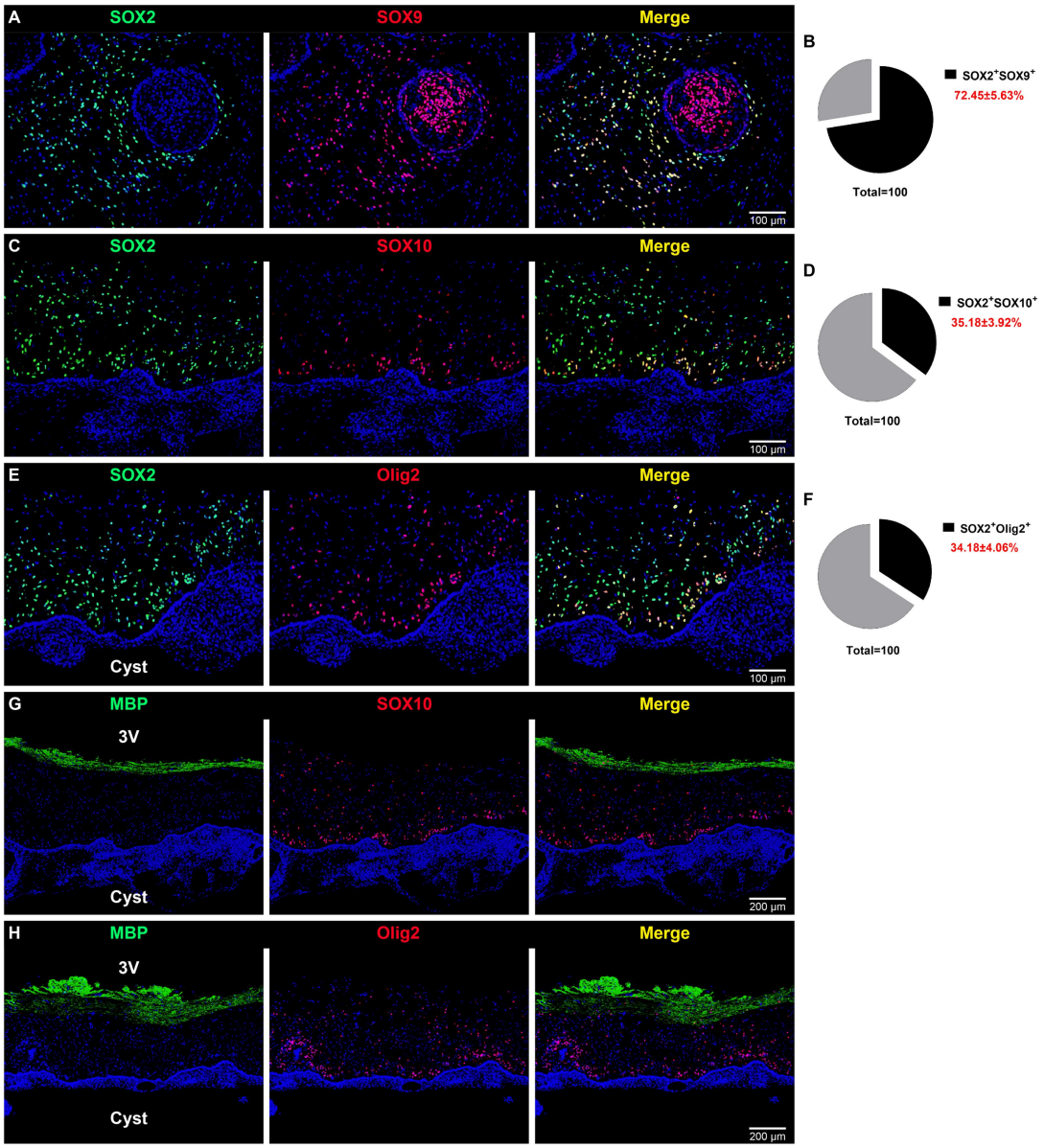
Supplementary Figure 4. Hypothalamic neural stem cells (htNSCs) are recruited to the damaged 3VF adjacent to ACP. (A) Immunofluorescence staining of ACP tissue samples, representative images of Pan-CK and SOX2 staining. Boxed area is enlarged and presented on the right. **(B)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and Nestin staining. Boxed area is enlarged and presented on the right. **(C)** Immunofluorescence staining of ACP tissue samples, representative images of NF and Nestin staining. Boxed area is enlarged and presented on the right. **(D)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and MBP staining. Boxed area is enlarged and presented on the right.


A
Case 1
Zoom
Case 2
Zoom
3V
3VF
ACP
Cyst
100 μm
20 μm
B
SOX2
Nestin
Merge
Zoom
C
GPR50
D
GPR50+Nestin+
67.46±3.06%
Total=100
E
SOX2
Rx
F
SOX2+Rx+
87.91±2.27%
G
EAAT1
H
EAAT1+Nestin+
68.90±3.21%
I
Vimentin
Connexin 43
J
Vimentin+Connexin 43+
77.82±3.31%

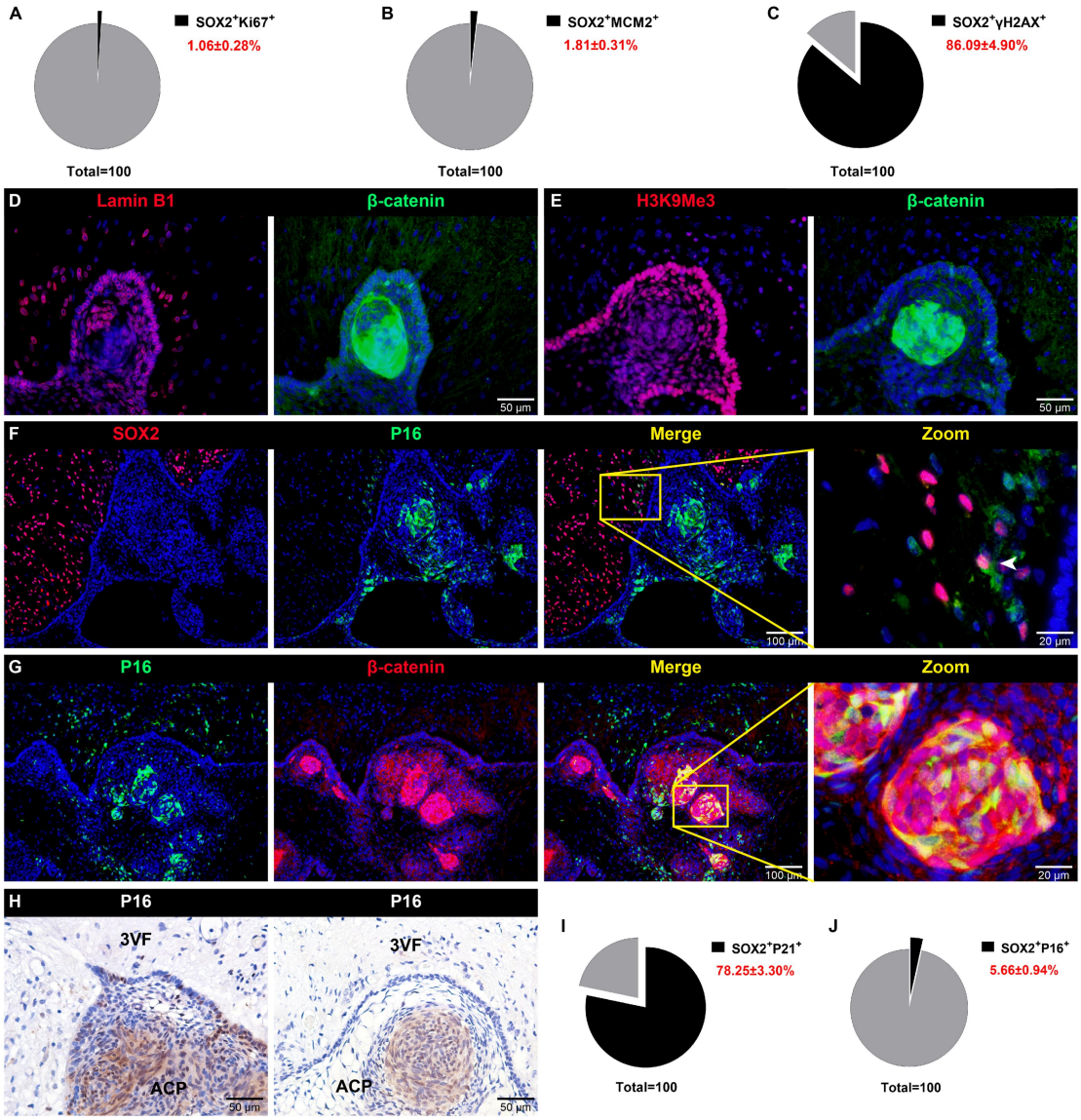
Supplementary Figure 5. Recruited htNSCs maybe derived from tanycytes. (A) H&E staining of two ACP tissue samples, representative images are shown. Black arrows indicate the ependymal layer of 3VF. Boxed area is enlarged and presented on the right. **(B)** Immunofluorescence staining of ACP tissue samples; representative images of SOX2 and Nestin staining. White arrows indicate the ependymal layer of 3VF. Boxed area is enlarged and presented on the right. **(C** and **D)** Immunofluorescence staining of ACP tissue samples, representative images of GPR50 and Nestin staining (C), and quantification of $Nestin^{+}GPR50^{+}$ cells in 3VF adjacent to ACP (D, n = 11). **(E** and **F)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and Rx staining (E), and quantification of $SOX2^{+}Rx^{+}$ cells in 3VF adjacent to ACP (F, n = 11). **(G** and **H)** Immunofluorescence staining of ACP tissue samples, representative images of EAAT1 and Nestin staining (G), and quantification of $EAAT1^{+}Nestin^{+}$ cells in 3VF adjacent to ACP (H, n = 11). **(I** and **J)** Immunofluorescence staining of ACP tissue samples, representative images of Vimentin and Connexin 43 staining (I), and quantification of $Vimentin^{+}Connexin\ 43^{+}$ cells in 3VF adjacent to ACP (J, n = 11). Data are presented as the mean ± SEM.



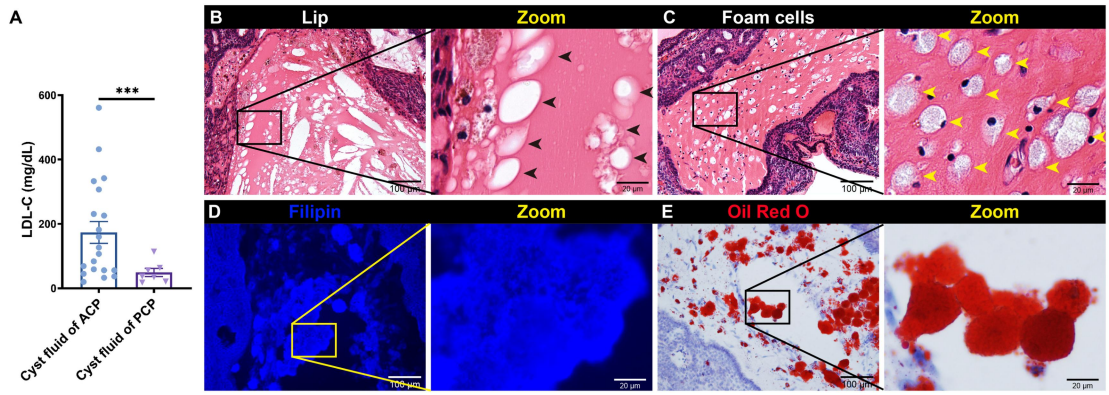
Supplementary Figure 6. Nearly no neuronal differentiation occur in the recruited htNSCs. (A) Schematic diagram showing the self-renewal and multi-directional differentiation ability of NSCs. **(B)** Schematic diagram showing stages of adult NSC neurogenesis and cell lineage-specific markers. **(C** and **D)** Double immunofluorescence staining of ACP tissue samples; representative images of (C) SOX2 and β3-Tubulin, and (D) Nestin and DCX staining. Boxed area is enlarged and presented on the right. DCX, doublecortin.


A
SOX2
SOX9
Merge
100 μm
B
SOX2+SOX9+
72.45±5.63%
Total=100
C
SOX2
SOX10
Merge
100 μm
D
SOX2+SOX10+
35.18±3.92%
Total=100
E
SOX2
Olig2
Merge
Cyst
100 μm
F
SOX2+Olig2+
34.18±4.06%
Total=100
G
MBP
SOX10
Merge
3V
Cyst
200 μm
H
MBP
Olig2
Merge
3V
Cyst
200 μm

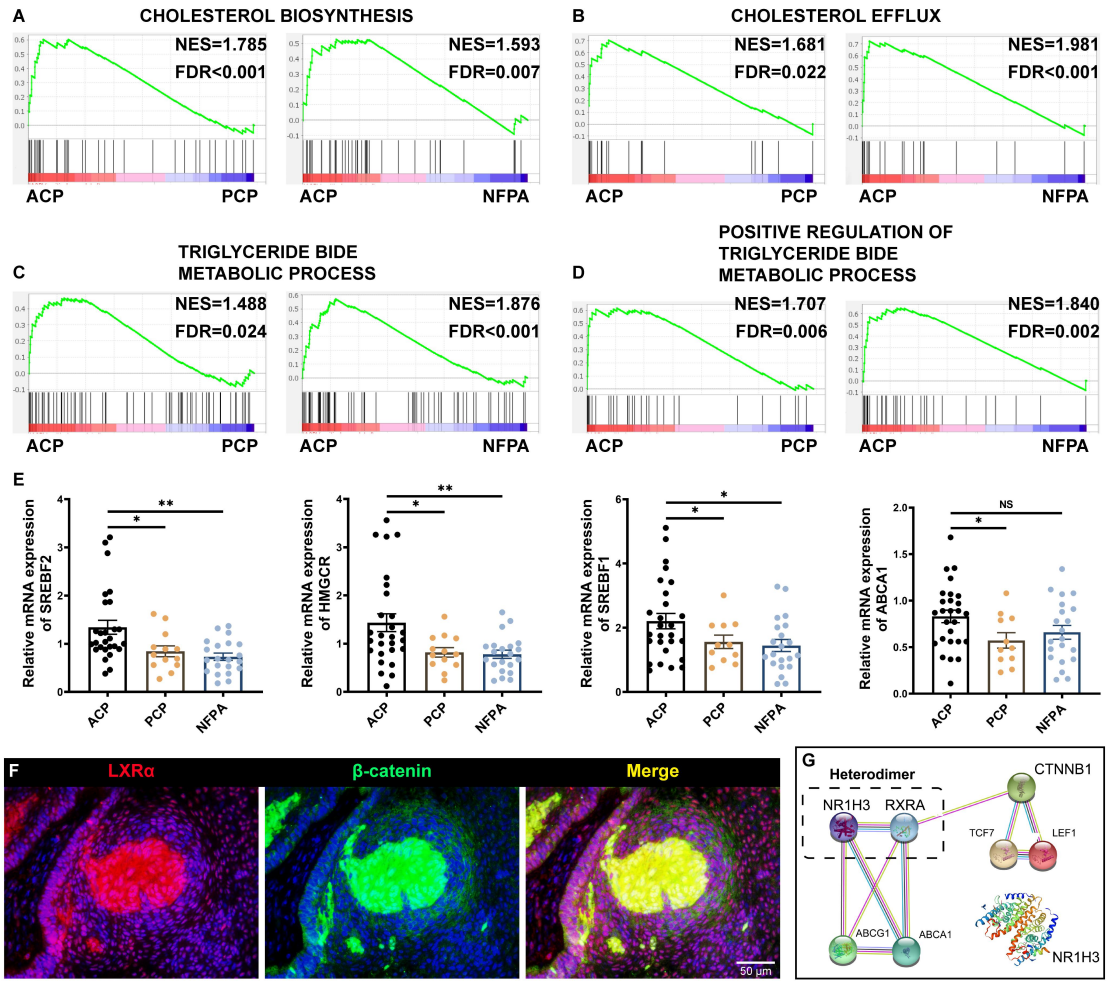
Supplementary Figure 7. Part of the recruited htNSCs expresses markers of oligodendrocyte precursors. (A and **B)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and SOX9 staining (A), and quantification of $SOX2^{+}SOX9^{+}$ cells (B, n = 11). **(C** and **D)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and SOX10 staining (C), and quantification of $SOX2^{+}SOX10^{+}$ cells (D, n = 11). **(E** and **F)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and Olig2 staining (E), and quantification of $SOX2^{+}Olig2^{+}$ cells (F, n = 11). **(G** and **H)** Immunofluorescence staining of ACP tissue samples, representative images showing the co-expression of MBP with different markers of oligodendrocyte precursors (SOX10, G; Olig2, H). Data are presented as the mean ± SEM.


A
SOX2+Ki67+
1.06±0.28%
Total=100
B
SOX2+MCM2+
1.81±0.31%
Total=100
C
SOX2+γH2AX+
86.09±4.90%
Total=100
D
Lamin B1
β-catenin
50 μm
E
H3K9Me3
β-catenin
50 μm
F
SOX2
P16
Merge
Zoom
100 μm
20 μm
G
P16
β-catenin
Merge
Zoom
100 μm
20 μm
H
P16
P16
3VF
ACP
50 μm
3VF
ACP
50 μm
I
SOX2+P21+
78.25±3.30%
Total=100
J
SOX2+P16+
5.66±0.94%
Total=100

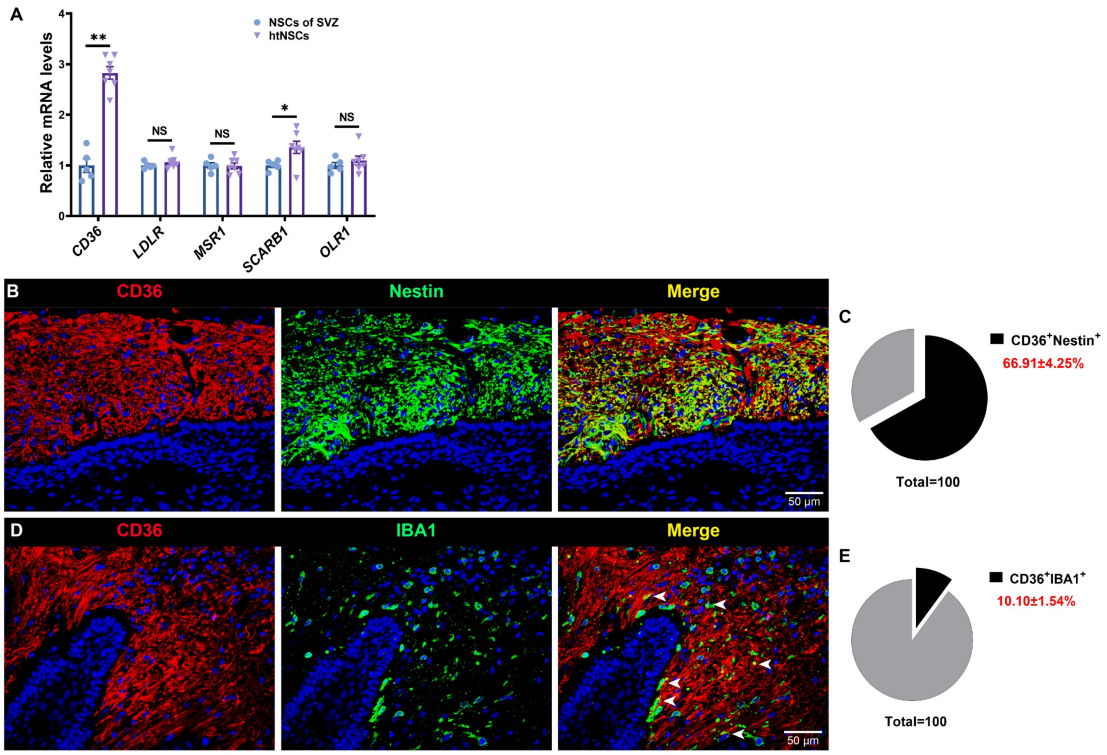
Supplementary Figure 8. Activated p16 senescence signaling pathway primarily occurs in ACP rather than htNSCs. (A–C) Quantification of double staining for SOX2 with Ki-67 (A, n = 16), MCM2 (B, n = 16) and γ-H2AX (C, n = 11). **(D)** Immunofluorescence staining of ACP tissue samples, representative images of Lamin B1 and β-catenin staining. **(E)** Immunofluorescence staining of ACP tissue samples, representative images of H3K9Me3 and β-catenin staining. **(F)** Immunofluorescence staining of ACP tissue samples, representative images of SOX2 and P16 staining. Boxed area is enlarged and presented on the right. **(G)** Immunofluorescence staining of ACP tissue samples; representative images of P16 and β-catenin staining. Boxed area is enlarged and presented on the right. **(H)** Immumohistochemical staining of ACP tissue samples; representative images of P16 staining. **(I** and **J)** Quantification of double staining for SOX2 with P21 (I, n = 16) and P16 (J, n = 16). Data are presented as the mean ± SEM.



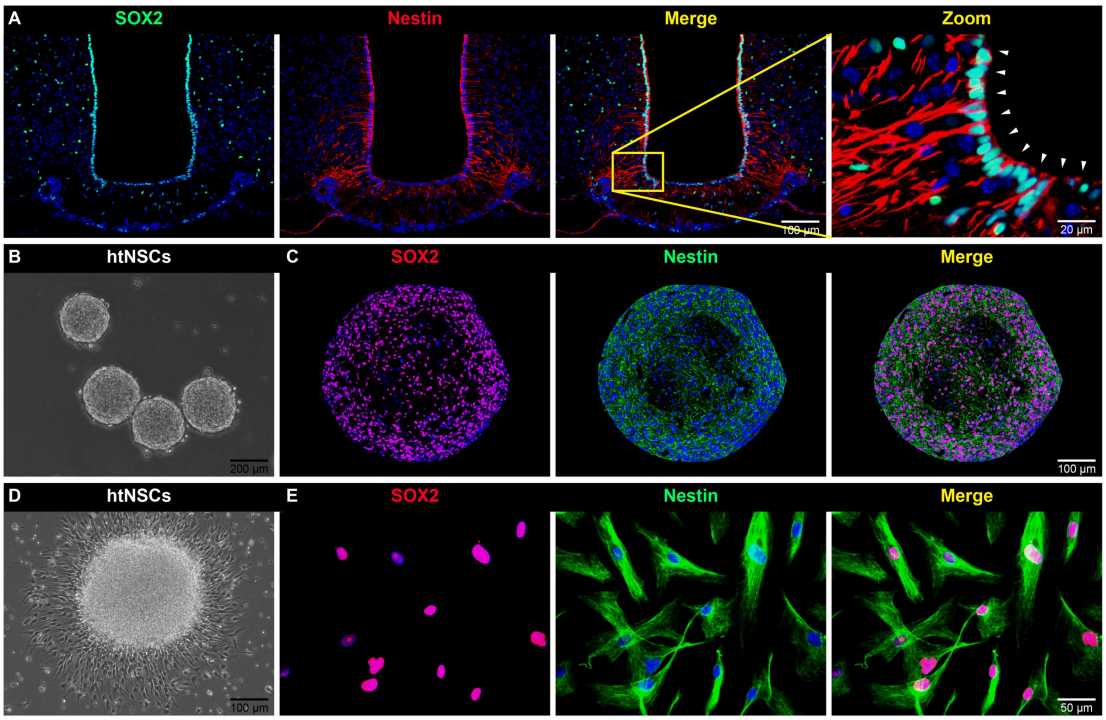
Supplementary Figure 9. ACP tissues and cystic fluid are rich in high concentration of lipids. (A) Quantification of low density lipoprotein-cholesterol (LDL-C) levels in the cystic fluid of ACP (n = 20) and PCP (n = 7). **(B** and **C)** H&E staining of ACP tissue sections; representative images showing fat vacuoles (black arrows; B) and foam cells (yellow arrows; C) in ACP tissue sections. Boxed area is enlarged and presented on the right. **(D)** Representative images of Filipin staining in ACP tissue samples. Boxed area is enlarged and presented on the right. **(E)** Representative images of Oil red O (ORO) staining showing the existence of lipid droplets (LDs) in ACP tissue samples. Boxed area is enlarged and presented on the right. Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (A) two-tailed Student's unpaired t-test.


A
CHOLESTEROL BIOSYNTHESIS
NES=1.785
FDR<0.001
ACP
PCP
NES=1.593
FDR=0.007
ACP
NFPA
B
CHOLESTEROL EFFLUX
NES=1.681
FDR=0.022
ACP
PCP
NES=1.981
FDR<0.001
ACP
NFPA
C
TRIGLYCERIDE BIDE METABOLIC PROCESS
NES=1.488
FDR=0.024
ACP
PCP
NES=1.876
FDR<0.001
ACP
NFPA
D
POSITIVE REGULATION OF TRIGLYCERIDE BIDE METABOLIC PROCESS
NES=1.707
FDR=0.006
ACP
PCP
NES=1.840
FDR=0.002
ACP
NFPA
E
Relative mRNA expression of SREBF2
Relative mRNA expression of HMGCR
Relative mRNA expression of SREBF1
Relative mRNA expression of ABCA1
NS
ACP
PCP
NFPA
F
LXRα
β-catenin
Merge
50 μm
G
Heterodimer
NR1H3
RXRA
CTNNB1
TCF7
LEF1
ABCG1
ABCA1
NR1H3

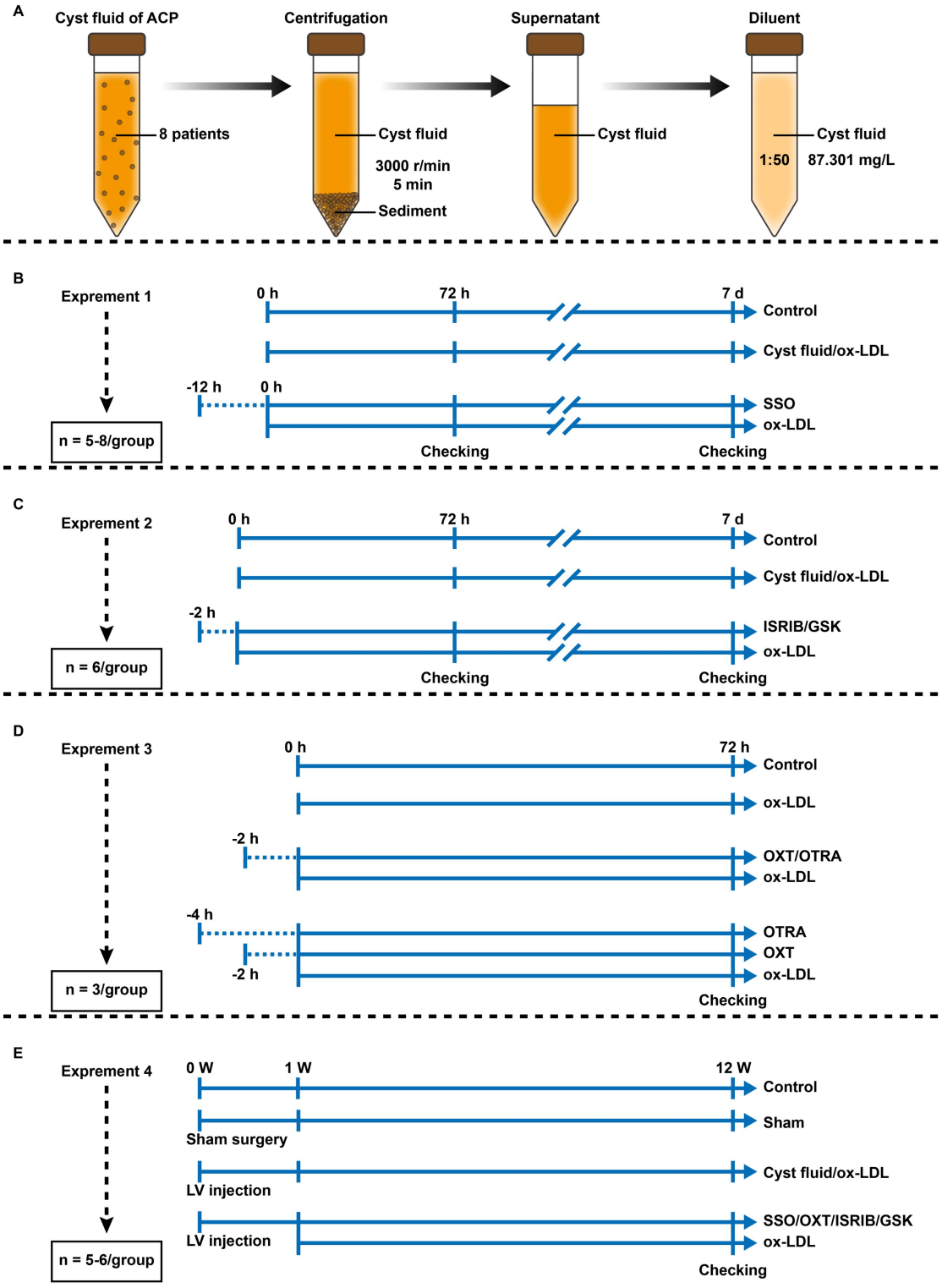
Supplementary Figure 10. ACP is in an aberrant metabolic state of high synthesis and high efflux of cholesterol. (A–D) Gene set enrichment analysis (GSEA) shows that, compared with PCP and nonfunctional pituitary adenoma (NFPA), the pathways related to cholesterol biosynthesis (A), cholesterol efflux (B), and triglyceride metabolic process (C and D) were significantly enriched in ACP. False discovery rate (FDR)<25 % and $p<0.05$ were considered significant. **(E)** qRT-PCR analysis was performed to examine the mRNA expression of cholesterol biosynthesis-related genes sterol regulatory element binding transcription factor 2 (*SREBF2*), 3-hydroxy-3-methylglutaryl coenzyme A reductase (*HMGCR*), sterol regulatory element binding transcription factor 1 (*SREBF1*), and cholesterol efflux-related gene ATP binding cassette subfamily A member 1 (*ABCA1*) in ACP (n = 27), PCP (n = 13) and NFPA (n = 21) samples. **(F)** Representative dual immunofluorescence images of LXRα and β-catenin in ACP tissue samples. **(G)** Protein interaction network analysis shows strong interaction between *CTNNB1* and complexus of *NR1H3* and *RXRA*. Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$, NS: not significant. Statistical analysis: (E) two-tailed Student's unpaired t-test. NES, normalized enrichment score.



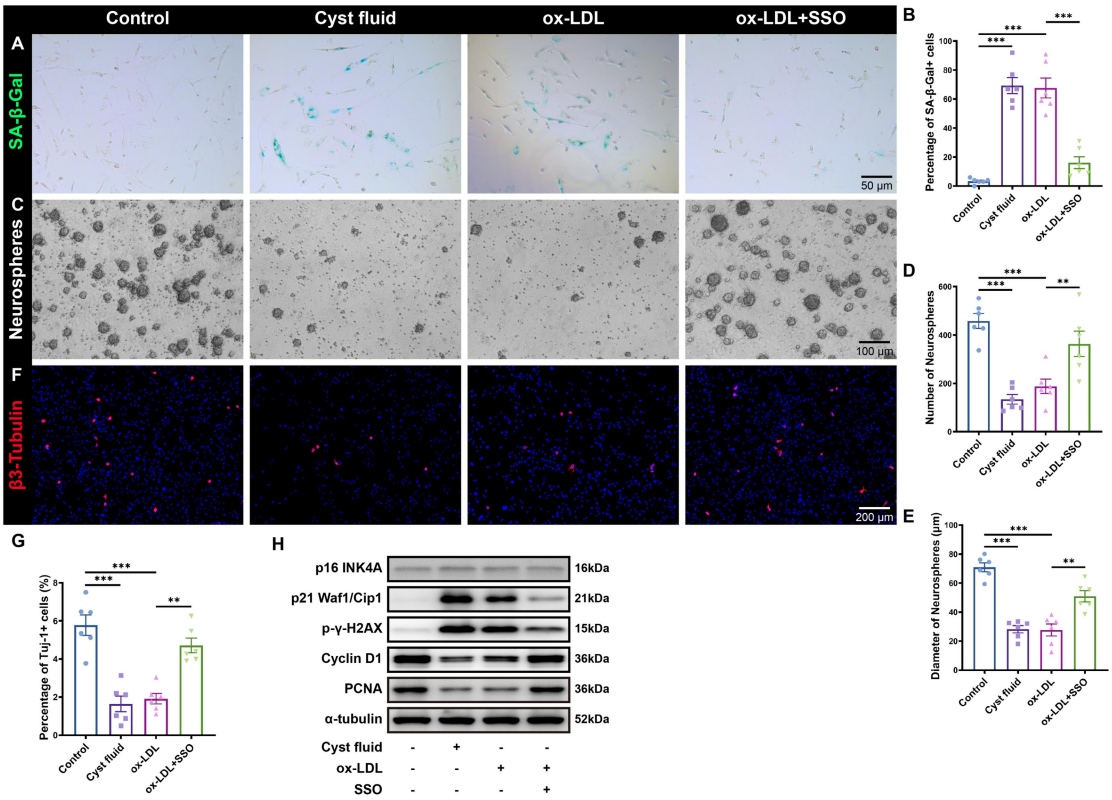
Supplementary Figure 11. Recruited htNSCs expresses high levels of scavenger receptor CD36. (A) qRT-PCR analysis of *CD36, LDLR, MSR1, SCARB1*, and *OLR1* expression in $CD133^{+}$ NSCs from the 3VF adjacent to ACP (n = 7) and SVZ of normal brain (NB; n = 5). **(B)** Immunofluorescence staining of ACP tissue samples, representative images of Nestin and CD36 staining. **(D)** Double immunofluorescence staining of ACP tissue samples, representative images of IBA-1 and CD36 staining. **(C** and **E)** Quantification of double staining for CD36 with Nestin (C, n = 11) and IBA-1 (E, n = 11). Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (A) two-tailed Student's unpaired t-test.



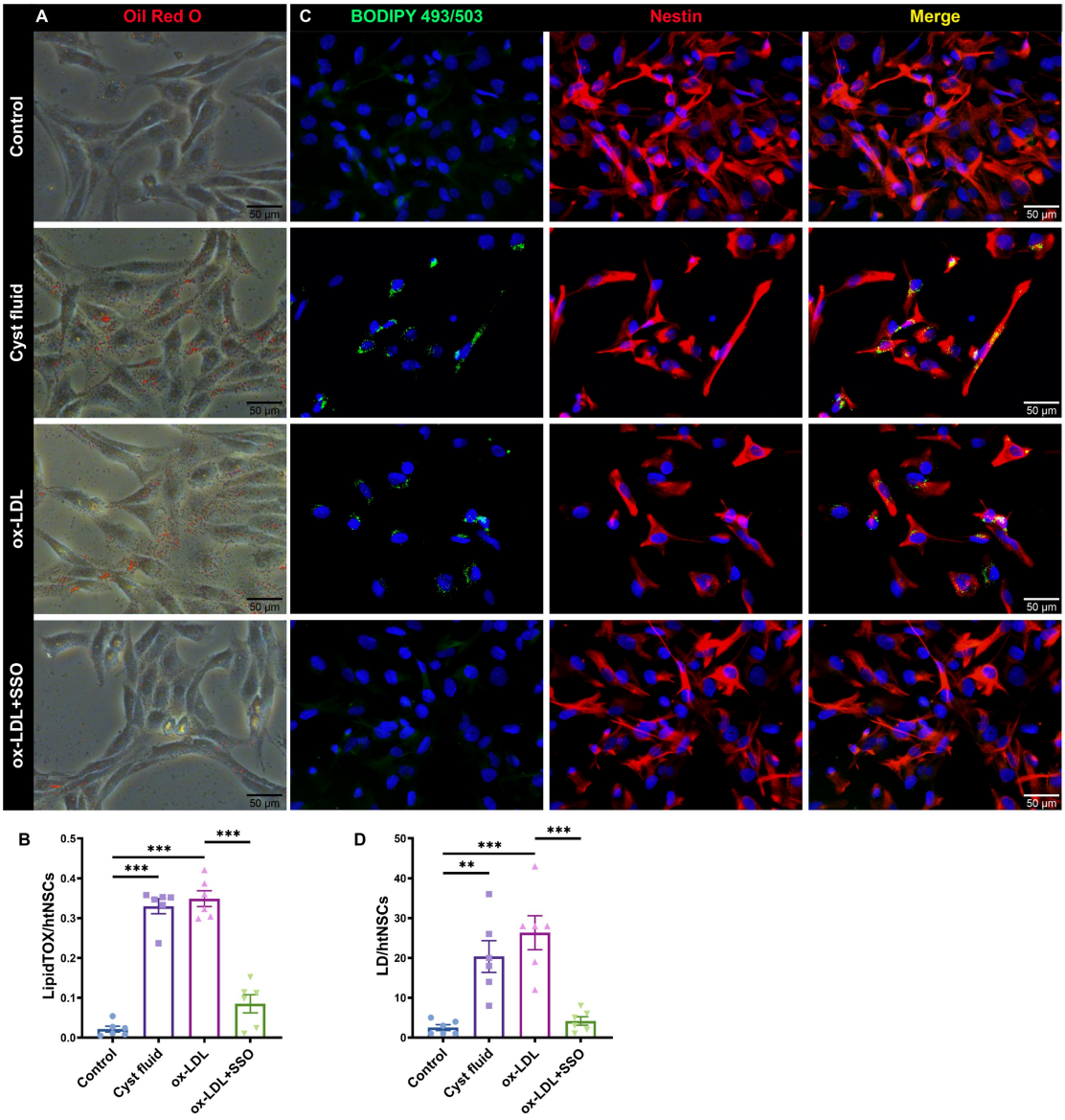
Supplementary Figure 12. Characterization of mouse htNSCs. (A) Double immunofluorescence staining of mouse median eminence (ME), representative image of SOX2 and Nestin staining. White arrows indicate the ependymal layer of 3VF. Boxed area is enlarged and presented on the right. **(B)** Representative reflection microscopy image of neurospheres generated from mouse htNSCs. **(C)** Double immunofluorescence staining of neurospheres generated from mouse htNSCs, representative images of SOX2 and Nestin staining. **(D)** Representative reflection microscopy image of adherent mouse htNSCs. **(E)** Double immunofluorescence staining of adherent mouse htNSCs, representative images of SOX2 and Nestin staining.


A
Cyst fluid of ACP
Centrifugation
Supernatant
Diluent
8 patients
Cyst fluid
3000 r/min
5 min
Sediment
Cyst fluid
Cyst fluid
1:50
87.301 mg/L
B
Exprement 1
n = 5-8/group
0 h
72 h
7 d
Control
Cyst fluid/ox-LDL
-12 h
0 h
SSO
ox-LDL
Checking
Checking
C
Exprement 2
n = 6/group
0 h
72 h
7 d
Control
Cyst fluid/ox-LDL
-2 h
ISRIB/GSK
ox-LDL
Checking
Checking
D
Exprement 3
n = 3/group
0 h
72 h
Control
ox-LDL
-2 h
OXT/OTRA
ox-LDL
-4 h
OTRA
-2 h
OXT
ox-LDL
Checking
E
Exprement 4
n = 5-6/group
0 W
1 W
12 W
Control
Sham
Sham surgery
Cyst fluid/ox-LDL
LV injection
SSO/OXT/ISRIB/GSK
LV injection
ox-LDL
Checking

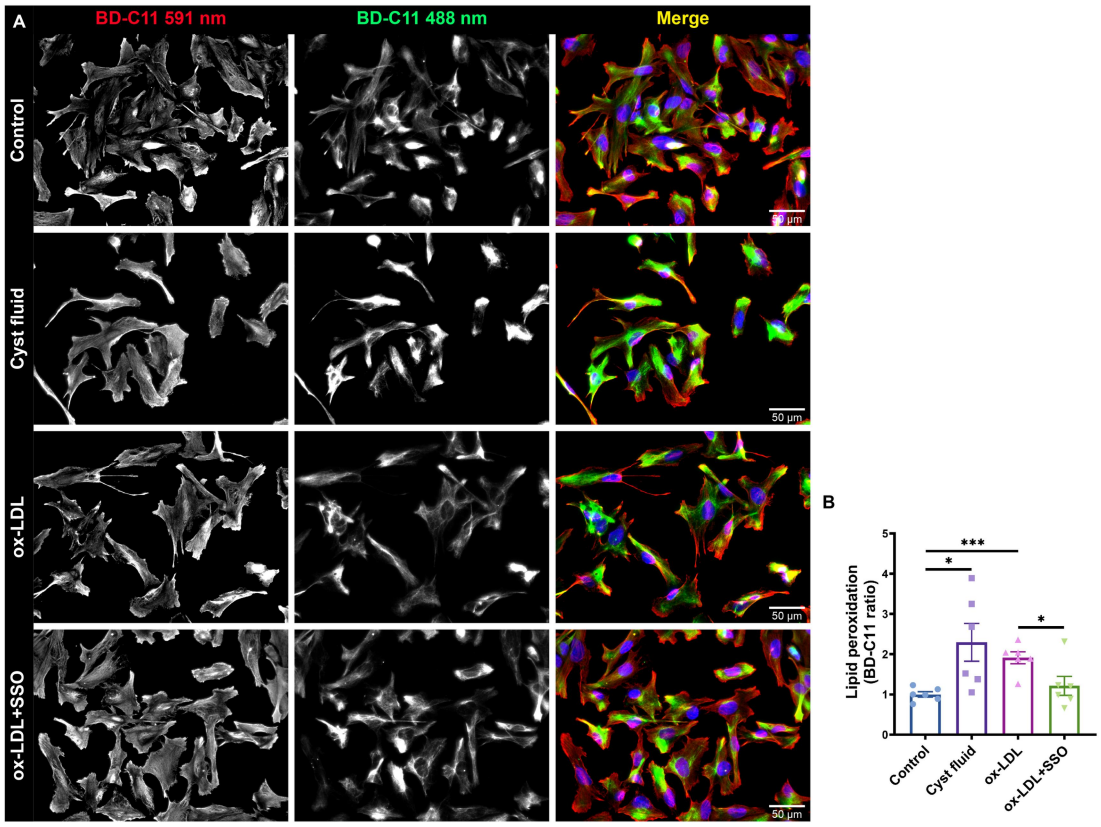
Supplementary Figure 13. Schematic diagrams of the cystic fluid purification, experimental design, and experimental timelines. (A) Schematic diagram of cystic fluid purification. **(B–D)** Experimental outlines of the *in vitro* experiments described in the article. **(E)** Experimental outlines of the *in vivo* experiments described in the article. (B) Related to Supplementary Figure 14–17; (C) related to Supplementary Figure 19F–19K, Supplementary Figure 20 and 21; (D) related to Supplementary Figure 22C and 22D; (E) related to Supplementary Figure 22E–22K, Supplementary Figure 24 and 25.


Control
Cyst fluid
ox-LDL
ox-LDL+SSO
A
SA-β-Gal
C
Neurospheres
F
β3-Tubulin
50 μm
100 μm
200 μm
B
Percentage of SA-β-Gal+ cells
D
Number of Neurospheres
E
Diameter of Neurospheres (μm)
G
Percentage of Tuj-1+ cells (%)
H
p16 INK4A
p21 Waf1/Cip1
p-γ-H2AX
Cyclin D1
PCNA
α-tubulin
16kDa
21kDa
15kDa
36kDa
36kDa
52kDa
Cyst fluid
ox-LDL
SSO

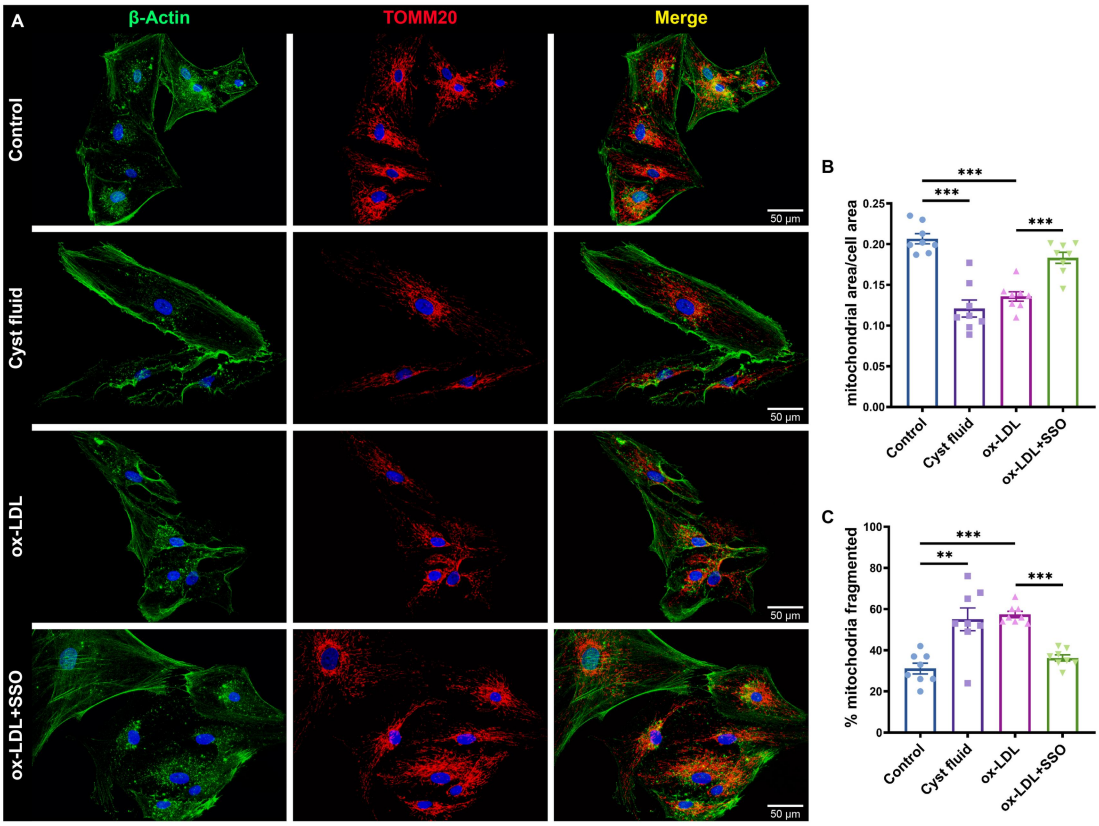
Supplementary Figure 14. SSO inhibits the senescence induced by ox-LDL in mouse htNSCs. (A) SA-β-gal staining of mouse htNSCs treated with cystic fluid or ox-LDL ± SSO; representative images, senescent cells are positive for SA-β-gal. **(B)** Quantification of senescent (SA-β-gal$^+$) cells shown in (A), data are presented as the percentage of SA-β-gal$^+$ cells, n = 6/group. **(C)** Neurospheres generated from mouse htNSCs treated with cystic fluid or ox-LDL ± SSO, representative reflection microscopy images are shown. **(D** and **E)** Quantification of neurospheres generated from mouse htNSCs described in (C); (D) number, and (E) diameter, n = 6/group. **(F)** Immunostaining of neurospheric cells for neuronal marker β3-Tubulin. Neurospheres were generated from the hypothalamus of young mice as described in the Methods section. Dissociated neurospheric cells (passages 5-10) were treated with cystic fluid or ox-LDL ± SSO and then differentiated for seven days. **(G)** Quantification of β3-Tubulin$^+$ cells described in (F); data are presented as the percentage of β3-Tubulin$^+$ cells, n = 6/group. **(H)** Protein expression of p16 INK4A, p21 Waf1/Cip1, p-γ-H2AX, Cyclin D1, and PCNA in htNSCs treated with cystic fluid or ox-LDL ± SSO was examined by Western blotting; a representative blot is shown (n = 3 blots in total). Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (B, D, E, and G) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.



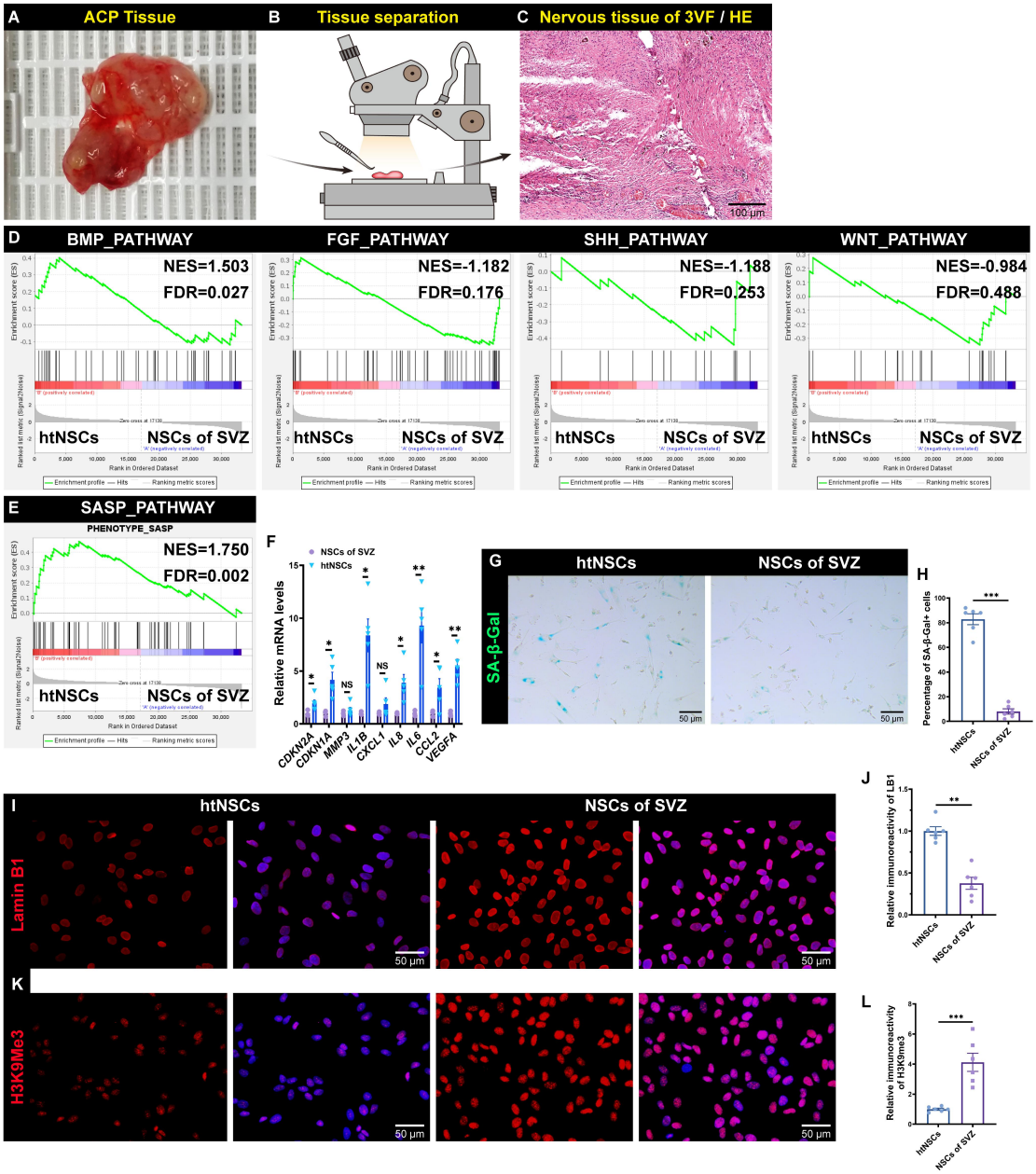
Supplementary Figure 15. LD aggregation induced by ox-LDL is inhibited by SSO in the cultured htNSCs. (A–D) Characterization of lipid deposition in mouse htNSCs treated with cystic fluid or ox-LDL ± SSO (n = 6/group); representative images and quantification of ORO staining (A, B), and immunofluorescence staining of Nestin and BODIPY 493/503 (C, D). Data are presented as the mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001, NS: not significant. Statistical analysis: (B and D) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.



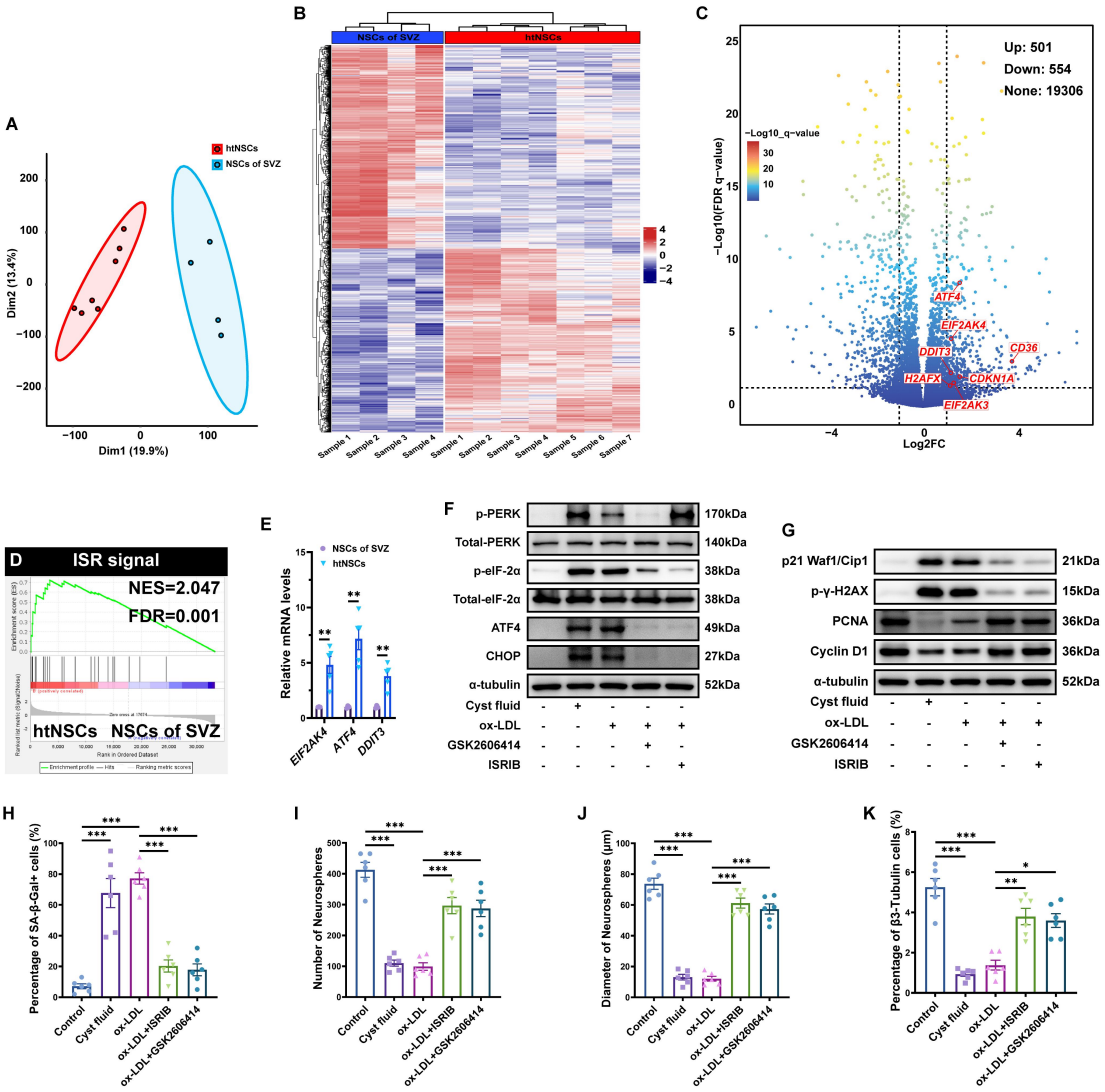
Supplementary Figure 16. SSO inhibits the lipid peroxidation induced by ox-LDL in the mouse htNSCs. (A) Mouse htNSCs were treated with cystic fluid or ox-LDL ± SSO and then labeled with BD-C11. Representative images show total (red, 591 nm) and peroxidated (green, 488 nm) lipids. **(B)** Quantification of peroxidated lipid ratio (green to red) for each group, n = 6/group. Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (B) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.



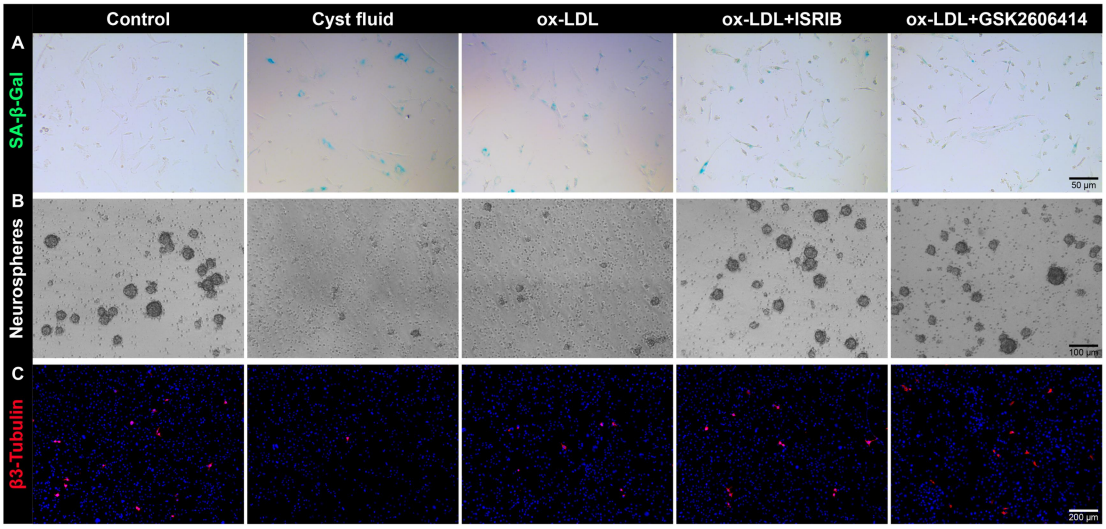
Supplementary Figure 17. SSO inhibits mitochondrial damage induced by ox-LDL in the mouse htNSCs. (A) Mitochondrial damage in mouse htNSCs treated with cystic fluid or ox-LDL ± SSO was assessed by immunofluorescence staining; β-actin, TOMM20; representative images are shown. **(B** and **C)** Quantification of images presented in (A); (B) mitochondrial area (%), and (C) mitochondrial fragments (%), n = 8/group. Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (B and C) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.


A ACP Tissue
B Tissue separation
C Nervous tissue of 3VF / HE
100 μm
D BMP_PATHWAY
NES=1.503
FDR=0.027
FGF_PATHWAY
NES=-1.182
FDR=0.176
SHH_PATHWAY
NES=-1.188
FDR=0.253
WNT_PATHWAY
NES=-0.984
FDR=0.488
htNSCs
NSCs of SVZ
E SASP_PATHWAY
PHENOTYPE_SASP
NES=1.750
FDR=0.002
F
NSCs of SVZ
htNSCs
Relative mRNA levels
CDKN2A
CDKN1A
MMP3
IL1B
CXCL1
IL8
IL6
CCL2
VEGFA
G
SA-β-Gal
50 μm
H
Percentage of SA-β-Gal+ cells
I
Lamin B1
J
Relative immunoreactivity of LB1
K
H3K9Me3
L
Relative immunoreactivity of H3K9me3

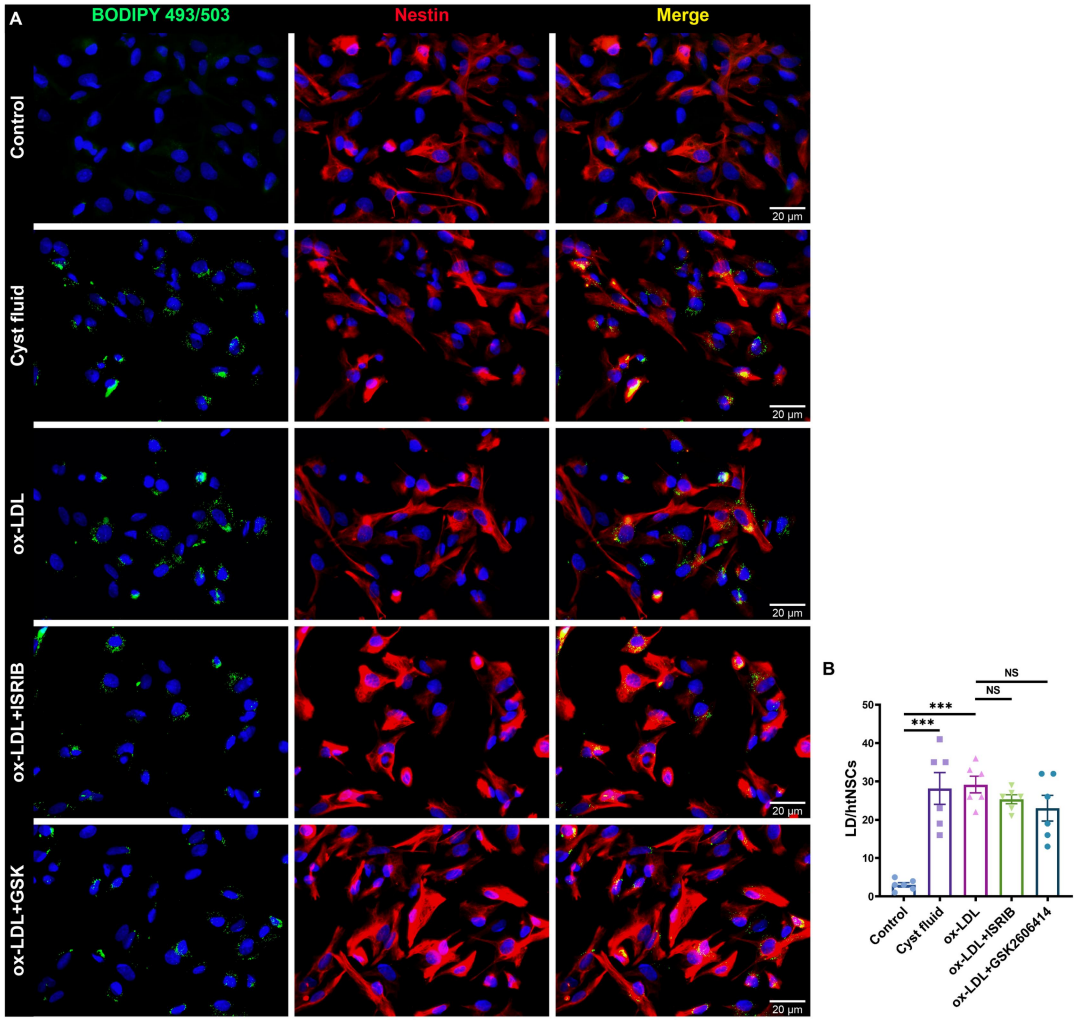
Supplementary Figure 18. Characterization of senescence characteristics in htNSCs acquired from the 3VF adjacent to ACP, removing the interference of β-catenin-accumulating clusters. (A–C) The hypothalamic tissue (A) adjacent to ACP were isolated under stereo microscopy (B) from fresh surgical ACP specimens obtained intraoperation, which were verified by H&E staining (C). **(D)** GSEA indicating strong enrichment for the BMP signaling pathway in htNSCs; however, FGF signaling pathway, SHH signaling pathway and WNT signaling pathway were not enriched in htNSCs. **(E)** GSEA indicating strong enrichment for the senescence-associated secretory phenotype (SASP) in htNSCs. **(F)** Relative mRNA expression levels of SASP target genes in htNSCs and NSCs of SVZ (htNSCs, n = 5; NSCs of SVZ, n = 3). **(G)** SA-β-gal staining of htNSCs and NSCs of SVZ; representative images are shown, senescent cells are positive for SA-β-gal. **(H)** Quantification of senescent (SA-β-gal$^+$) cells shown in (G), data are presented as the percentage of SA-β-gal$^+$ cells, n = 6/group. **(I)** Immunofluorescence staining of htNSCs and NSCs of SVZ, representative images of Lamin B1 staining. **(J)** Quantification of Lamin B1 fluorescence intensity in htNSCs and NSCs of SVZ described in (I) (n = 6/group). **(K)** Immunofluorescence staining of htNSCs and NSCs of SVZ, representative images of H3K9Me3 staining. **(L)** Quantification of H3K9Me3 fluorescence intensity in htNSCs and NSCs of SVZ described in (K) (n = 6/group). Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (F, H, J, and L) two-tailed Student's unpaired t-test.


A
htNSCs
NSCs of SVZ
Dim2 (13.4%)
Dim1 (19.9%)
B
NSCs of SVZ
htNSCs
C
Up: 501
Down: 554
None: 19306
−Log10_q−value
−Log10(FDR q−value)
Log2FC
ATF4
EIF2AK4
DDIT3
CD36
H2AFX
CDKN1A
EIF2AK3
D
ISR signal
NES=2.047
FDR=0.001
htNSCs
NSCs of SVZ
E
NSCs of SVZ
htNSCs
Relative mRNA levels
EIF2AK4
ATF4
DDIT3
F
p-PERK
Total-PERK
p-eIF-2α
Total-eIF-2α
ATF4
CHOP
α-tubulin
170kDa
140kDa
38kDa
38kDa
49kDa
27kDa
52kDa
Cyst fluid
ox-LDL
GSK2606414
ISRIB
G
p21 Waf1/Cip1
p-γ-H2AX
PCNA
Cyclin D1
α-tubulin
21kDa
15kDa
36kDa
36kDa
52kDa
Cyst fluid
ox-LDL
GSK2606414
ISRIB
H
Percentage of SA-β-Gal+ cells (%)
I
Number of Neurospheres
J
Diameter of Neurospheres (μm)
K
Percentage of β3-Tubulin cells (%)
Control
Cyst fluid
ox-LDL
ox-LDL+ISRIB
ox-LDL+GSK2606414

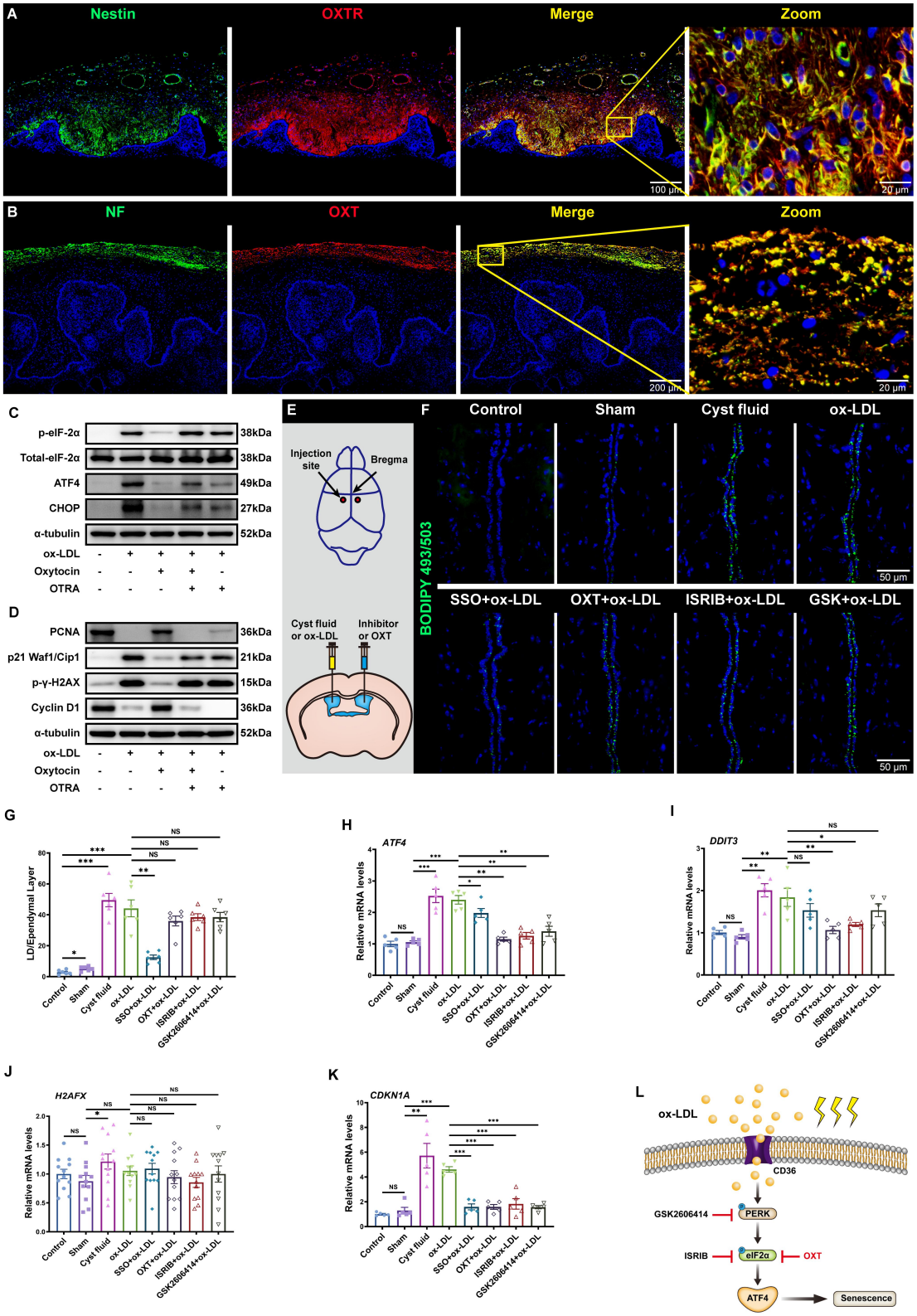
Supplementary Figure 19. Integrated stress response (ISR) signaling pathway is activated in lipotoxic htNSCs. (A) Principal component analysis (PCA) of NSCs from the 3VF adjacent to ACP and the SVZ of NB. **(B)** Gene expression profiling via RNA-sequencing shows differentially expressed genes (DEGs) between htNSCs and NSCs of SVZ based on hierarchization clustering using the following filter criteria: false discovery rate (FDR) < 0.05 and fold-change > 2. **(C)** A volcano plot of *p*-values as a function of weighted fold change showing the down-regulated and up-regulated DEGs of two groups as indicated. **(D)** Gene set enrichment analysis (GSEA) indicating strong enrichment for the ISR signaling pathway in htNSCs. **(E)** Relative mRNA expression levels of ISR signaling target genes in htNSCs and NSCs of SVZ (htNSCs, n = 5; NSCs of SVZ, n = 3). **(F** and **G)** Protein expression of phospho-PERK, total-PERK, phospho-eIF-2α, total-eIF-2α, ATF4 and CHOP (F), p21 Waf1/Cip1, p-γ-H2AX, Cyclin D1, and PCNA (G) in mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414 were evaluated using Western blotting. Representative blot is shown (n = 3 blots in total). **(H)** Quantification of senescent (SA-β-gal$^+$) cells in mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414. Data are presented as the percentage of SA-β-gal$^+$ cells (n = 6/group). **(I** and **J)** Quantification of neurospheres generated from mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414; (I) number, (J) diameter (n = 6/group). **(K)** Quantification of β3-Tubulin$^+$ cells in mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414. Data are presented as the percentage of β3-Tubulin$^+$ cells (n = 6/group). Data are presented as the mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001, NS: not significant. Statistical analysis: (E) two-tailed Student's unpaired t-test and (H–K) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test. NES, normalized enrichment score.



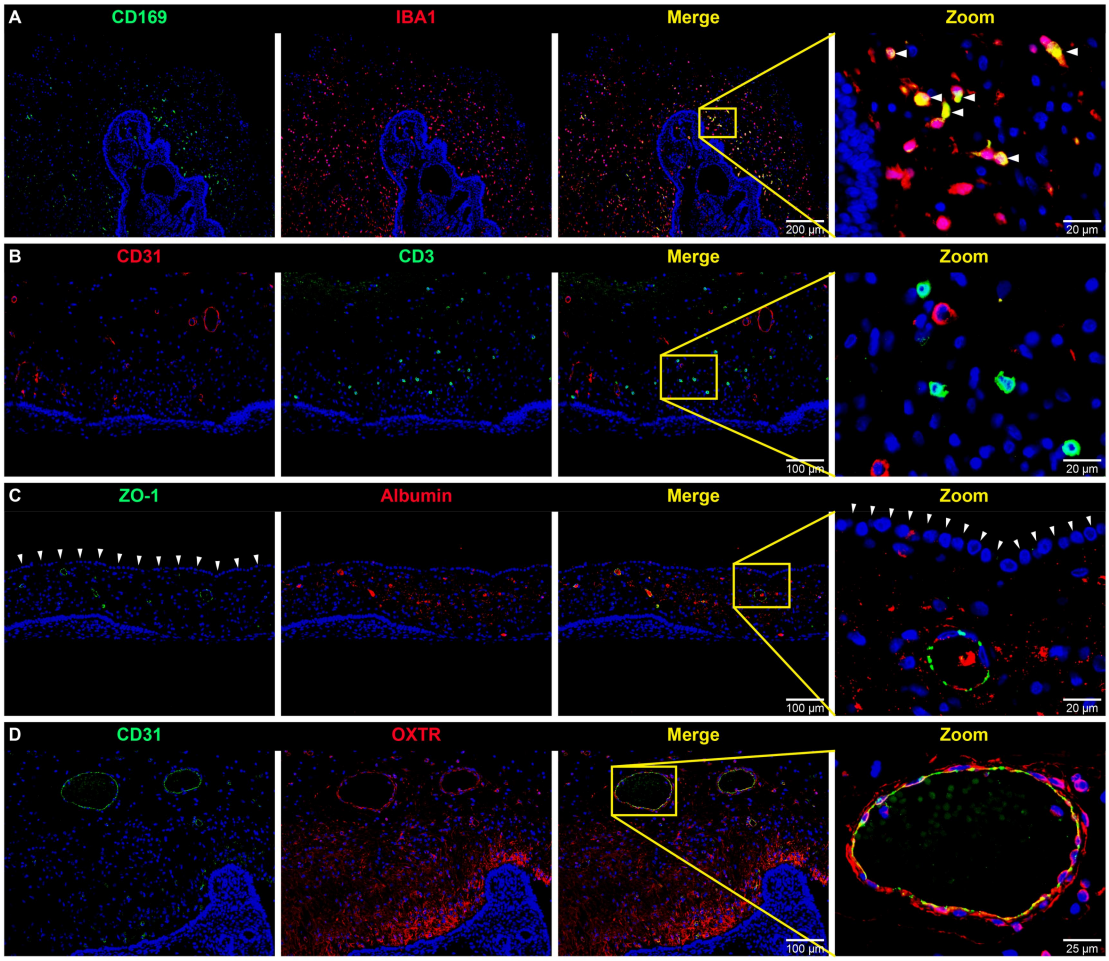
Supplementary Figure 20. The ISR inhibitors block the senescence of mouse htNSCs induced by ox-LDL. (A) SA-β-gal staining of mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414. Representative images showing senescent (SA-β-gal^{+}) cells. **(B)** Reflection microscopy of neurospheres generated from mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414. Representative images are shown. **(C)** Neurospheric cells (passages 5-10) treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414 were differentiated for seven days, fixed, and then immunostained for neuronal marker β3-Tubulin. Representative images are shown.



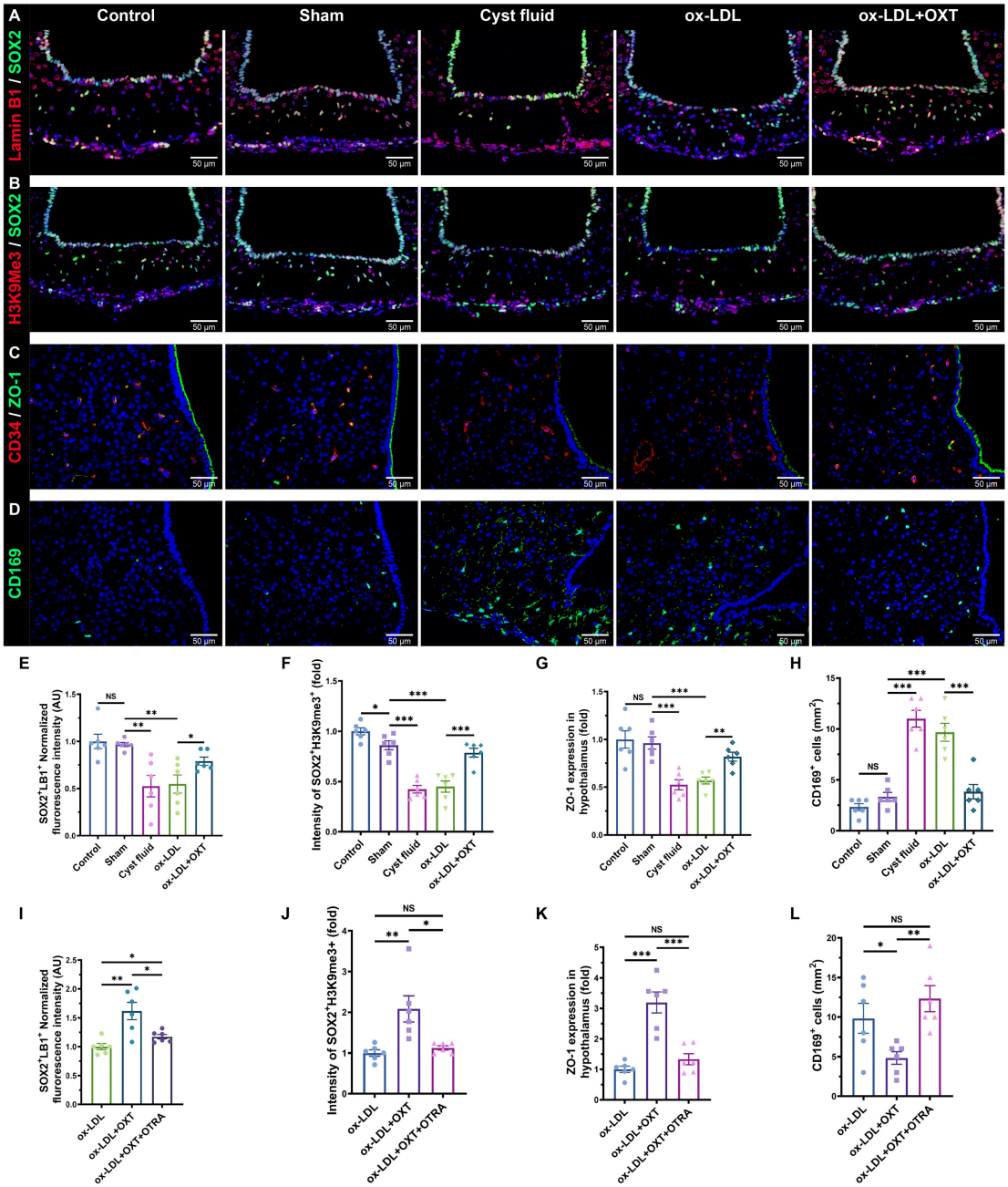
Supplementary Figure 21. The ISR inhibitors cannot block the accumulation of LDs in htNSCs induced by ox-LDL. (A and **B)** Mouse htNSCs treated with cystic fluid, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414 and lipid deposition was evaluated by immunofluorescence staining for Nestin and BODIPY 493/503. Representative images (A) and quantification (B) are shown (n = 6/group). Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (B) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.


A
Nestin
OXTR
Merge
Zoom
100 μm
20 μm
B
NF
OXT
Merge
Zoom
200 μm
20 μm
C
p-eIF-2α
Total-eIF-2α
ATF4
CHOP
α-tubulin
38kDa
38kDa
49kDa
27kDa
52kDa
ox-LDL
Oxytocin
OTRA
D
PCNA
p21 Waf1/Cip1
p-γ-H2AX
Cyclin D1
α-tubulin
36kDa
21kDa
15kDa
36kDa
52kDa
E
Injection site
Bregma
Cyst fluid or ox-LDL
Inhibitor or OXT
F
Control
Sham
Cyst fluid
ox-LDL
BODIPY 493/503
SSO+ox-LDL
OXT+ox-LDL
ISRIB+ox-LDL
GSK+ox-LDL
50 μm
G
LD/Ependymal Layer
H
ATF4
Relative mRNA levels
I
DDIT3
Relative mRNA levels
J
H2AFX
Relative mRNA levels
K
CDKN1A
Relative mRNA levels
L
ox-LDL
CD36
GSK2606414
PERK
ISRIB
eIF2α
OXT
ATF4
Senescence

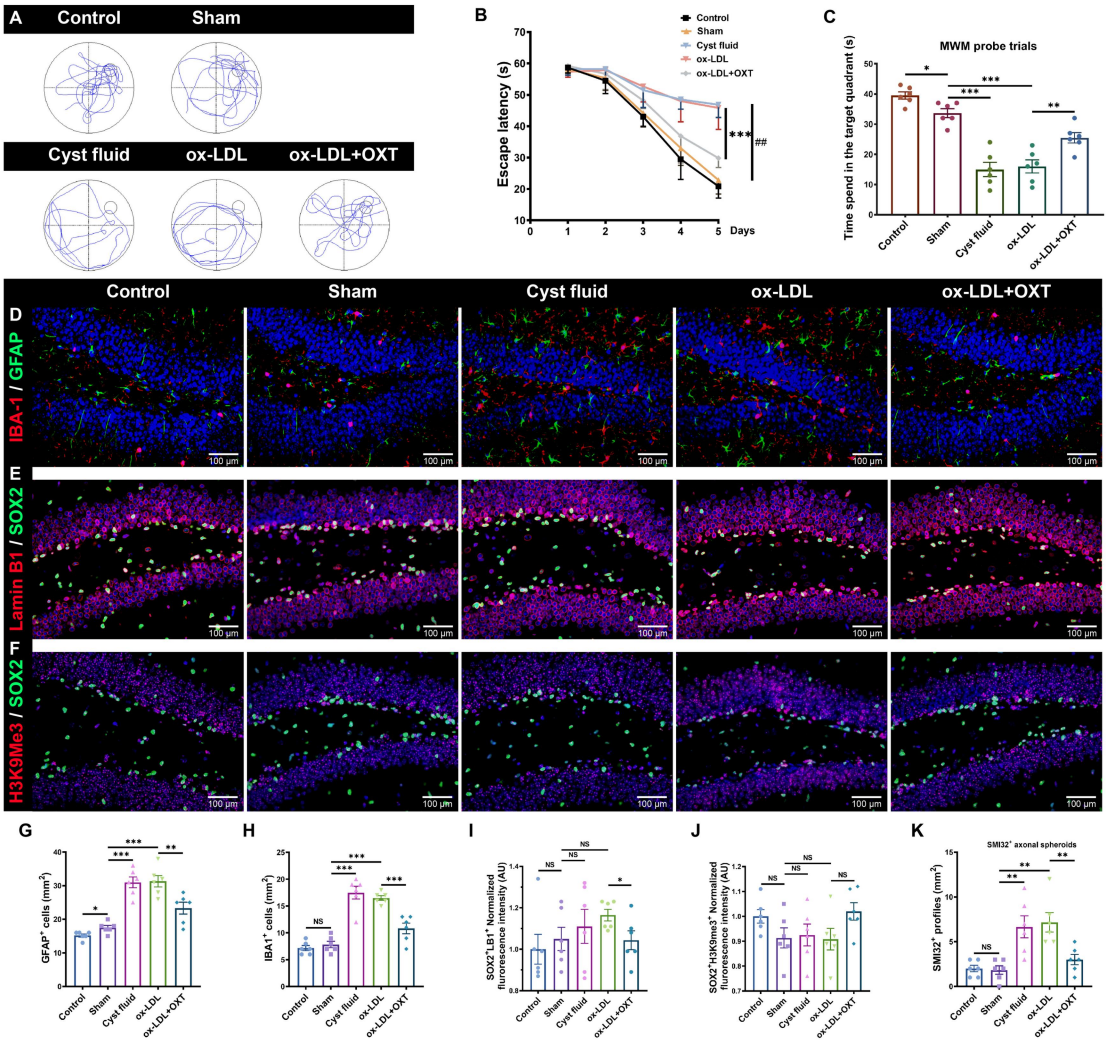
Supplementary Figure 22. Oxytocin (OXT) blocks ox-LDL induced senescence of htNSCs by inhibiting ISR signaling. (A and **B)** Immunofluorescence staining of different ACP tissue samples, representative images of Nestin and OXTR (A), NF and OXT (B) staining. Boxed area is enlarged and presented on the right. **(C** and **D)** Protein expression of phospho-eIF-2α, total-eIF-2α, ATF4 and CHOP (C), p21 Waf1/Cip1, p-γ-H2AX, Cyclin D1, and PCNA (D) in mouse htNSCs treated with ox-LDL ± OXT, ox-LDL + OXT + OTRA, or ox-LDL ± OTRA were evaluated by Western blotting. A representative blot is shown (n = 3 blots in total). **(E)** Schematic diagram showing the stereotaxic coordinates of LV localization injection. **(F** and **G)** Lipid deposition in the ependymal layer of 3V wall of mice treated with cystic fluid, ox-LDL ± SSO, ox-LDL ± OXT, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414 (GSK) was evaluated by immunofluorescence staining using BODIPY 493/503 (green). Representative images (F) and quantification (G) are shown (n = 6/group). **(H–K)** Relative mRNA expression levels of *ATF4* (H), *DDIT3* (I), *H2AFX* (J), and *CDKN1A* (K) in the arcuate nucleus (ARC) and median eminence (ME) tissues of mouse treated with cystic fluid, ox-LDL ± SSO, ox-LDL ± OXT, ox-LDL ± ISRIB, or ox-LDL ± GSK2606414 (H, I, and K, n = 5/group; J, n = 12/group). **(L)** Schematic diagram showing the targets of ISRIB, GSK2606414, and OXT in ISR signaling. Data are presented as the mean ± SEM. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, NS: not significant. Statistical analysis: (G–K) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.



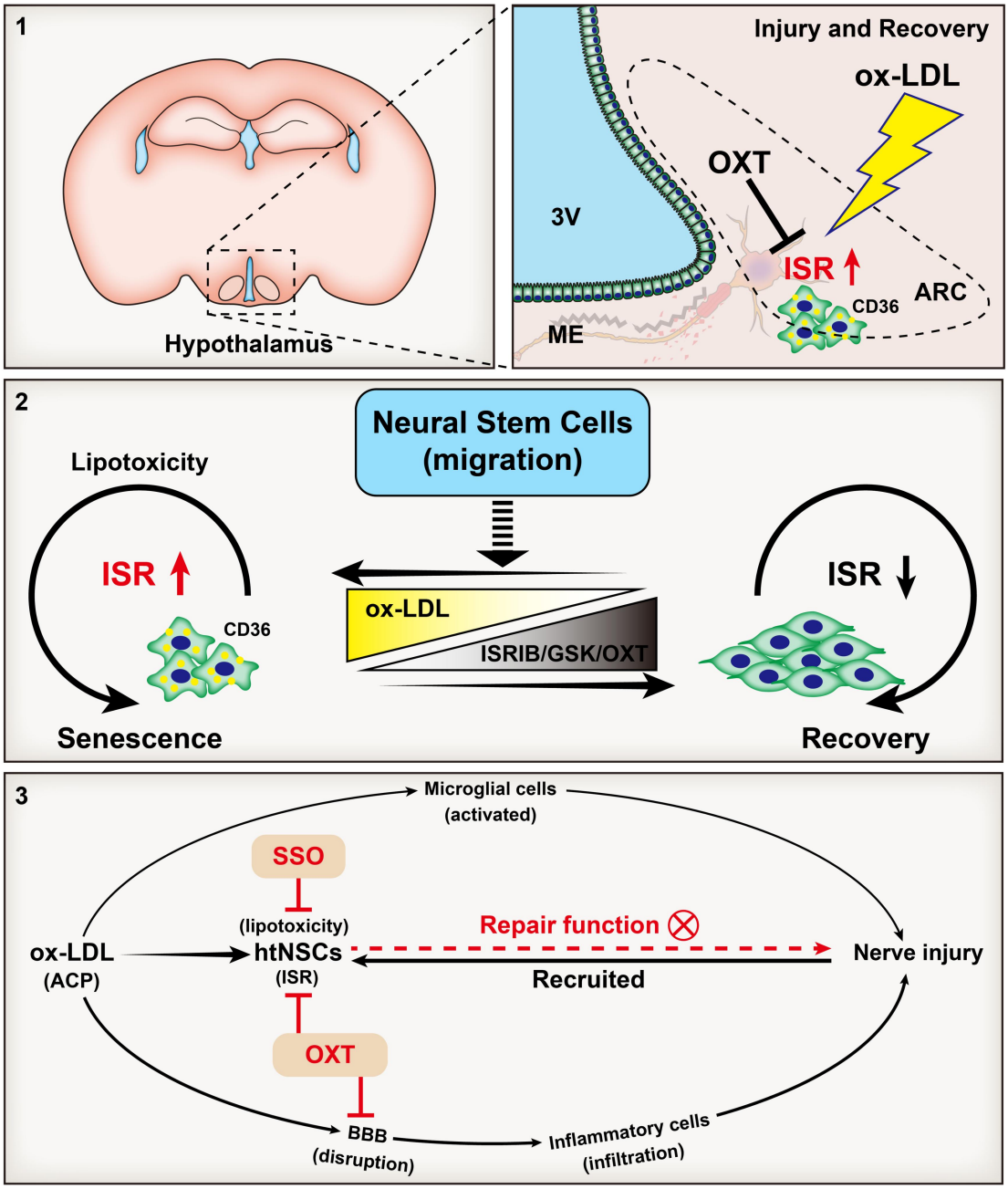
Supplementary Figure 23. Blood–brain barrier (BBB) is damaged in the 3VF adjacent to ACP. (A) Double immunofluorescence staining of ACP tissue samples. Representative images of CD169 and IBA1 staining. The white arrows indicate the IBA-1^{+}CD169^{+} cells. Boxed area is enlarged and presented on the right. **(B)** Immunofluorescence staining of ACP tissue samples. Representative images of CD31 and CD3 staining. Boxed area is enlarged and presented on the right. **(C)** Double immunofluorescence staining of ACP tissue samples. Representative images of ZO-1 and Albumin staining. The white arrows indicate the ependymal layer of 3VF. Boxed area is enlarged and presented on the right. **(D)** Double immunofluorescence staining of ACP tissue samples. Representative images of CD31 and OXTR staining. Boxed area is enlarged and presented on the right.


A
Control
Sham
Cyst fluid
ox-LDL
ox-LDL+OXT
Lamin B1 / SOX2
B
H3K9Me3 / SOX2
C
CD34 / ZO-1
D
CD169
50 μm
E
SOX2+LB1+ Normalized fluorescence intensity (AU)
F
Intensity of SOX2+H3K9me3+ (fold)
G
ZO-1 expression in hypothalamus (fold)
H
CD169+ cells (mm2)
Control
Sham
Cyst fluid
ox-LDL
ox-LDL+OXT
NS
I
J
K
L
ox-LDL
ox-LDL+OXT
ox-LDL+OXT+OTRA

Supplementary Figure 24. OXT blocks the ox-LDL–induced senescence of NSCs in the ME of mice. (A) Double immunofluorescence staining of the ME of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of Lamin B1 and SOX2 staining. **(B)** Double immunofluorescence staining of the ME of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of H3K9Me3 and SOX2 staining. **(C)** Double immunofluorescence staining of the ME of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of CD34 and ZO-1 staining. **(D)** Immunofluorescence staining of the ME of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of CD169 staining. **(E)** Quantification of Lamin B1 fluorescence intensity in $SOX2^+$ NSCs described in (A) (n = 6/group). **(F)** Quantification of H3K9Me3 fluorescence intensity in $SOX2^+$ NSCs described in (B) (n = 6/group). **(G)** Quantification of ZO-1 expression described in (C) (n = 6/group). **(H)** Quantification of $CD169^+$ cells described in (D) (n = 6/group). **(I** and **J)** Quantification of Lamin B1 (I) and H3K9Me3 (J) fluorescence intensity in the $SOX2^+$ NSCs of ME of mouse treated with ox-LDL ± OXT or ox-LDL + OXT + OTRA (n = 6/group). **(K)** Quantification of ZO-1 expression in the ME of mouse treated with ox-LDL ± OXT or ox-LDL + OXT + OTRA (n = 6/group). **(L)** Quantification of $CD169^+$ cells in the ME of mouse treated with ox-LDL ± OXT or ox-LDL + OXT + OTRA (n = 6/group). Data are presented as the mean ± SEM. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$, NS: not significant. Statistical analysis: (E–L) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.


A
Control
Sham
Cyst fluid
ox-LDL
ox-LDL+OXT
B
Control
Sham
Cyst fluid
ox-LDL
ox-LDL+OXT
Escape latency (s)
Days
***
##
C
MWM probe trials
Time spend in the target quadrant (s)
Control
Sham
Cyst fluid
ox-LDL
ox-LDL+OXT
D
IBA-1 / GFAP
E
Lamin B1 / SOX2
F
H3K9Me3 / SOX2
100 μm
G
GFAP+ cells (mm2)
H
IBA1+ cells (mm2)
I
SOX2+LB1+ Normalized fluorescence intensity (AU)
J
SOX2+H3K9me3+ Normalized fluorescence intensity (AU)
K
SMI32+ axonal spheroids
SMI32+ profiles (mm-2)
NS

Supplementary Figure 25. OXT blocks the ox-LDL-induced cognitive function descending of mouse models. (A) Representative swimming traces of mice treated with cystic fluid or ox-LDL ± OXT during the test phase. Small circles show the position of former escape platforms that were removed during the test phase. **(B)** Average latencies to find the escape platform during the training phase for the mice treated with cystic fluid or ox-LDL ± OXT (n = 6/group). **(C)** Average time spent in the target quadrant for the mice treated with cystic fluid or ox-LDL ± OXT during the test phase (n=6/group). **(D)** Double immunofluorescence staining of the hippocampus of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of IBA-1 and GFAP staining. **(E)** Double immunofluorescence staining of the hippocampus of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of Lamin B1 and SOX2 staining. **(F)** Double immunofluorescence staining of the hippocampus of mouse treated with cystic fluid or ox-LDL ± OXT. Representative images of H3K9Me3 and SOX2 staining. **(G)** Quantification of the $GFAP^+$ astrocytes described in (D) (n = 6/group). **(H)** Quantification of the IBA-1^+ microglia described in (D) (n = 6/group). **(I)** Quantification of Lamin B1 fluorescence intensity in $SOX2^+$ NSCs described in (E) (n = 6/group). **(J)** Quantification of H3K9Me3 fluorescence intensity in $SOX2^+$ NSCs described in (F) (n = 6/group). **(K)** Quantification of the SMI-32^+ axonal spheroids in the ME of mice treated with cystic fluid or ox-LDL ± OXT (n = 6/group). Data are presented as the mean ± SEM. $*p < 0.05$, $**p < 0.01$, $^{\#\#}p < 0.01$, $***p < 0.001$, NS: not significant. Statistical analysis: (B, C, G–K) one-way ANOVA followed by Fisher's LSD *post hoc* multiple comparison test.


1
Hypothalamus
Injury and Recovery
ox-LDL
OXT
3V
ISR
CD36
ARC
ME
2
Neural Stem Cells
(migration)
Lipotoxicity
ISR
CD36
ox-LDL
ISRIB/GSK/OXT
ISR
Senescence
Recovery
3
Microglial cells
(activated)
SSO
(lipotoxicity)
Repair function
ox-LDL
(ACP)
htNSCs
(ISR)
Recruited
Nerve injury
OXT
BBB
(disruption)
Inflammatory cells
(infiltration)

Graphical Abstract. Molecular mechanism by which OXT avoids the senescence of htNSCs induced by ox-LDL. On the one hand, the lipids from ACP resulting in not only the nerve damage by activating microglia, and BBB breakage in the hypothalamus including 3VF, but also the lipotoxicity, senescence and dysfunction of the recruited htNSCs by activating the ISR signaling. On the other hand, both SSO and OXT can prevent the senescence of htNSCs, among which, SSO prevents the senescence of htNSCs by restraining ox-LDL from entering the htNSCs, while OXT by targeting the ISR signaling thus blocking the htNSC senescence induced by ox-LDL. Except that, OXT can also repair the BBB and then decrease the inflammatory cells infiltration thereby improving the inflammatory microenvironment.

Supplementary Table 1. List of the antibodies used for immunofluorescence and immumohistochemical stainings.

Antibody	Dilution	Source	Identifier
Rabbit monoclonal anti-pan Cytokeratin (Pan-CK)	1:500	Abcam	Cat# ab234297; RRID: AB_2895302
Rabbit monoclonal anti-MAP2	1:400	Abcam	Cat# ab183830; RRID: AB_2895301
Rabbit monoclonal anti-NeuN	1:300	Abcam	Cat# ab177487; RRID: AB_2532109
Rabbit monoclonal anti-Myelin Basic Protein (MBP)	1:200	Abcam	Cat# ab218011; RRID: AB_2895537
Rabbit monoclonal anti-SOX2	1:300	Abcam	Cat# ab92494; RRID: AB_10585428
Rabbit monoclonal anti-Nestin	1:500	Abcam	Cat# ab176571; RRID: AB_2895536
Rabbit monoclonal anti-β3-Tubulin	1:250	Cell Signaling Technology	Cat# 5568; RRID: AB_10694505
Rabbit polyclonal anti-p-γ-H2AX	1:500	Abcam	Cat# ab2893; RRID: AB_303388
Rabbit monoclonal anti-p21 Wafl/Cip1	1:500	Abcam	Cat# ab188224; RRID: AB_2734729
Rabbit polyclonal anti-Ki-67	1:2000	Abcam	Cat# ab15580; RRID: AB_443209
Rabbit monoclonal anti-β-catenin	1:200	Abcam	Cat# ab32572; RRID: AB_725966
Rabbit monoclonal anti-CD36	1:300	Abcam	Cat# ab133625; RRID: AB_2716564
Rabbit monoclonal anti-TOMM20	1:400	Cell Signaling Technology	Cat# 42406; RRID: AB_2687663
Rabbit monoclonal anti-Oxytocin Receptor (OXTR)	1:200	Abcam	Cat# ab181077; RRID: AB_2895535
Rabbit monoclonal anti-Oxytocin (OXT)	1:1000	Abcam	Cat# ab212193; RRID: AB_2895534
Rabbit monoclonal anti-IBA1	1:300	Abcam	Cat# ab178847; RRID: AB_2832244
Rabbit polyclonal anti-CD31	1:150	Thermo Fischer Scientific	Cat# PA5-16301; RRID: AB_10981955
Rabbit monoclonal anti-CD34	1:300	Abcam	Cat# ab81289; RRID: AB_164033
Rabbit polyclonal anti-Albumin	1:150	Thermo Fischer Scientific	Cat# PA5-89332; RRID: AB_2805499
Rabbit monoclonal anti-POMC	1:200	Cell Signaling Technology	Cat# 23499; RRID: AB_2716565
Rabbit monoclonal anti-Cleaved caspase-3	1:100	Abcam	Cat# ab32042; RRID: AB_725947
Rabbit monoclonal anti-Lamin B1	1:800	Abcam	Cat# ab133741; RRID: AB_2616597
Rabbit monoclonal anti-H3K9Me3	1:600	Abcam	Cat# ab8898; RRID: AB_306848

Rabbit monoclonal anti-Rx	1:100	GeneTex	Cat# GTX77859; RRID: AB_424807
Rabbit monoclonal anti-Connexin 43	1:300	Abcam	Cat# ab11370; RRID: AB_297976
Rabbit monoclonal anti-SOX9	1:200	Abcam	Cat# ab185230; RRID: AB_2715497
Rabbit monoclonal anti-SOX10	1:200	Abcam	Cat# ab180862; RRID: AB_2721184
Rabbit monoclonal anti-Olig2	1:300	Abcam	Cat# ab109186; RRID: AB_10861310
Rabbit monoclonal anti-LXRα	1:100	Abcam	Cat# ab41902; RRID: AB_776094
Rabbit monoclonal anti-SMI-32	1:100	Abcam	Cat# ab73273; RRID: AB_1267590
Mouse monoclonal anti-GFAP	1:400	Sigma-Aldrich	Cat# SAB5201104; RRID: AB_2827276
Mouse monoclonal anti-NeuN	1:200	Millipore	Cat# MAB377; RRID: AB_2298772
Mouse monoclonal anti-MAP2	1:100	Santa Cruz	Cat# sc-74421; RRID:AB_1126215
Mouse monoclonal anti-Neurofilament (NF)	1:100	Abcam	Cat# ab134306; RRID: AB_2895532
Mouse monoclonal anti-pan Cytokeratin (pan-CK)	1:500	Abcam	Cat# ab7753; RRID: AB_306047
Rat monoclonal anti-SOX2	1:200	Thermo Fischer Scientific	Cat# 14-9811; RRID: AB_11219471
Mouse monoclonal anti-Doublecortin (DCX)	1:100	Santa Cruz	Cat# sc-271390; RRID: AB_10610966
Mouse monoclonal anti-p16 INK4a	1:50/1:200	Santa Cruz	Cat# sc-1661; RRID: AB_628067
Mouse monoclonal anti-Nestin	1:100	Thermo Fischer Scientific	Cat# MA1-110; RRID: AB_2536821
Mouse monoclonal anti-IBA1	1:200	Sigma-Aldrich	Cat# SAB2702364; RRID: AB_282025
Mouse monoclonal anti-CD169	1:400	Thermo Fischer Scientific	Cat# MA5-38471; RRID: AB_2895540
Rat monoclonal anti-CD3	1:100	Thermo Fischer Scientific	Cat# 14-0032; RRID: AB_467053
Mouse monoclonal anti-ZO-1	1:150	Thermo Fischer Scientific	Cat# 33-9100; RRID: AB_2533147
Goat polyclonal anti-CD31	1:100	R&D Systems	Cat# AF3628; RRID: AB_2161028
Mouse monoclonal anti-Vimentin (VIM)	1:800	Abcam	Cat# ab8978; RRID: AB_306907
Mouse monoclonal anti-GPR50	1:100	R&D Systems	Cat# MAB4645; RRID: AB_2112821
Mouse monoclonal anti-β-Actin	1:2000	Cell Signaling Technology	Cat# 3700; RRID: AB_2242334
Mouse monoclonal anti-Neuropeptide Y (NPY)	1:200	Abcam	Cat# ab112473; RRID: AB_10861167

Mouse monoclonal anti-MCM2	1:400	BD Biosciences	Cat# 610700; RRID: AB_2141952
Mouse monoclonal anti-EAAT1	1:100	R&D Systems	Cat# MAB6048; RRID: AB_2044669
Mouse monoclonal anti-MBP	1:250	Abcam	Cat# ab62631; RRID: AB_956157
Mouse monoclonal anti-β-catenin	1:500	Abcam	Cat# ab22656; RRID: AB_447227
Mouse monoclonal anti-GnRH	1:500	Santa Cruz	Cat# sc-271918; RRID: AB_10610657

Supplementary Table 2. List of the antibodies used for Western blot.

Antibody	Dilution	Source	Identifier
Rabbit polyclonal anti-p-γ-H2AX	1:1000	Abcam	Cat# ab2893; RRID: AB_303388
Rabbit monoclonal anti-p21 Wafl/Cip1	1:1000	Abcam	Cat# ab188224; RRID: AB_2734729
Rabbit polyclonal anti-p16 INK4a	1:500	Abcam	Cat# ab189034; RRID: AB_2737282
Rabbit monoclonal anti-Cyclin D1	1:1000	Cell Signaling Technology	Cat# 55506; RRID: AB_2827374
Mouse monoclonal anti-PCNA	1:1000	Abcam	Cat# ab29; RRID: AB_303394
Rabbit monoclonal anti-α-Tubulin	1:1000	Cell Signaling Technology	Cat# 2125; RRID: AB_2619646
Rabbit monoclonal anti-p-PERK	1:1000	Cell Signaling Technology	Cat# 3179; RRID: AB_2095853
Rabbit monoclonal anti-total-PERK	1:1000	Cell Signaling Technology	Cat# 3192; RRID: AB_2095847
Rabbit monoclonal anti-p-eIF2α	1:1000	Cell Signaling Technology	Cat# 3398; RRID: AB_2096481
Rabbit monoclonal anti-total-eIF2α	1:1000	Cell Signaling Technology	Cat# 5324; RRID: AB_10692650
Rabbit monoclonal anti-ATF4	1:1000	Cell Signaling Technology	Cat# 11815; RRID: AB_2616025
Mouse monoclonal anti-CHOP	1:1000	Cell Signaling Technology	Cat# 2895; RRID: AB_2089254

Supplementary Table 3. Secondary antibodies and conjugated fluorophores used in this study.

Antibody	Dilution	Source	Identifier

Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	1:1000	Thermo Fischer Scientific	Cat# A-11001; RRID: AB_2534069
Goat anti-Rat IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	1:1000	Thermo Fischer Scientific	Cat# A-11006; RRID: AB_2534074
Donkey anti-Goat IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	1:1000	Thermo Fischer Scientific	Cat# A-11055; RRID: AB_2534102
Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 594	1:1000	Thermo Fischer Scientific	Cat# A-11012; RRID: AB_2534079
HRP-conjugated goat anti-mouse IgG antibody	1:5000	Jackson ImmunoResearch	Cat # 115-035-003; RRID: AB_10015289
HRP-conjugated goat anti-rabbit IgG antibody	1:5000	Jackson ImmunoResearch	Cat# 111-035-003; RRID: AB_2313567

Supplementary Table 4. Primers for Quantitative real-time PCR used in this study.

Genes	Forward primer (5' to 3')	Reverse primer (5' to 3')
Homo Cd36	*CTTTGGCTTAATGAGACTGGGAC*	*GCAACAAACATCACCACACCA*
Homo Ldlr	*ACGGCGTCTCTTCCTATGACA*	*CCCTTGGTATCCGCAACAGA*
Homo Msr1	*GCAGTGGGATCACTTTCACAA*	*AGCTGTCATTGAGCGAGCATC*
Homo Scarb1	*ACTTCTGGCATTCCGATCAGT*	*ACGAAGCGATAGGTGGGGAT*
Homo Olr1	*GAAACCCTTGCTCGGAAGCTGA*	*CAGATCCAGTCTTGCGGACAAG*
Homo Eif2s1	*GAAGGCGTATCCGTTCTATCAAC*	*AGCAACATGACGAAGAATGCTAT*
Homo Atf4	*CTCCGGGACAGATTGGATGTT*	*GGCTGCTTATTAGTCTCCTGGAC*
Homo Ddit3	*GGAAACAGAGTGGTCATTCCC*	*CTGCTTGAGCCGTTCATTCTC*
Homo Cdkn2a	*ATGGAGCCTTCGGCTGACT*	*GTAACTATTCGGTGCGTTGGG*
Homo Cdkn1a	*TGTCCGTCAGAACCCATGC*	*AAAGTCGAAGTTCCATCGCTC*
Homo Mmp3	*CACTCACAGACCTGACTCGGTT*	*AAGCAGGATCACAGTTGGCTGG*

Homo Il1b	*CCACAGACCTTCCAGGAGAATG*	*GTGCAGTTCAGTGATCGTACAGG*
Homo Cxcl1	*AGCTTGCCTCAATCCTGCATCC*	*TCCTTCAGGAACAGCCACCAGT*
Homo Cxcl8	*GAGAGTGATTGAGAGTGGACCAC*	*CACAACCCTCTGCACCCAGTTT*
Homo Il-6	*AGACAGCCACTCACCTCTTCAG*	*TTCTGCCAGTGCCTCTTTGCTG*
Homo Ccl2	*GAGAGGCTGAGACTAACCCAGA*	*ATCACAGCTTCTTTGGGACACT*
Homo Vegfa	*TTGCCTTGCTGCTCTACCTCCA*	*GATGGCAGTAGCTGCGCTGATA*
Homo Srebf1	*CGGAACCATCTTGGCAACAGT*	*CGCTTCTCAATGGCGTTGT*
Homo Srebf2	*CCTGGGAGACATCGACGAGAT*	*TGAATGACCGTTGCACTGAAG*
Homo Hmgcr	*TGATTGACCTTTCCAGAGCAAG*	*CTAAAATTGCCATTCCACGAGC*
Homo Abca1	*ACCCACCCTATGAACAACATGA*	*GAGTCGGGTAACGGAAACAGG*
Homo Gapdh	*GTCTCCTCTGACTTCAACAGCG*	*ACCACCCTGTTGCTGTAGCCAA*
Mus Atf4	*AACCTCATGGGTTCTCCAGCGA*	*CTCCAACATCCAATCTGTCCCG*
Mus Ddit3	*GGAGGTCCTGTCCTCAGATGAA*	*GCTCCTCTGTCAGCCAAGCTAG*
Mus H2afx	*AACGACGAGGAGCTCAACAAGC*	*TGGCGCTGCTCTTCTTGGGCA*
Mus Cdkn1a	*TCGCTGTCTTGCACTCTGGTGT*	*CCAATCTGCGCTTGGAGTGATAG*
Mus Gapdh	*CATCACTGCCACCCAGAAGACTG*	*ATGCCAGTGAGCTTCCCGTTCAG*

Supplementary Table 5. Chemicals, peptides, recombinant proteins, and critical commercial assays used in this study.

Reagent	**Source**	**Identifier**
Chemicals, Peptides, and Recombinant Proteins		
Hematoxylin solution	ZSGB-BIO	Cat# ZLI-9610
Eosin solution	ZSGB-BIO	Cat# ZLI-9613
DAB Detection Kit	ZSGB-BIO	Cat# ZLI-9017
Oxidized low density lipoprotein (ox-LDL), human	Solarbio	Cat# IO1300

Sulfo-N-succinimidyl oleate (SSO)	MCE	Cat# HY-112847
ISRIB	Selleck	Cat# S0706
GSK2606414	Selleck	Cat# S7307
Oxytocin (OXT)	R&D Systems	Cat# 1910/1
OT receptor antagonist (OTRA; L-371257)	Tocris Bioscience	Cat# 2410/10
BAY 11-7082	Selleck	Cat# S2913
Oil Red O	Sigma-Aldrich	Cat# O0625
Filipin III	Sigma-Aldrich	Cat# SAE0087
RIPA lysis buffer	Beyotime	Cat# P0013B
Protease/phosphatase inhibitor cocktail	Coolaber	Cat# SL1088
Penicillin/Streptomycin	Thermo Fischer Scientific	Cat# 15140122
Sodium citrate buffer (pH 6.0)	Solarbio	Cat# C1010
Ethylenediaminetetraacetic acid (EDTA) (pH 8.0)	ZSGB-BIO	Cat# ZLI-9072
ReadyProbes™ 2.5% Normal Goat Serum (1X)	Thermo Fischer Scientific	Cat# R37624
SlowFade™ Gold (DAPI)	Thermo Fischer Scientific	Cat# S36938
BODIPY™ 493/503	Thermo Fisher Scientific	Cat# D3922
BODIPY™ 581/591 C11	Thermo Fisher Scientific	Cat# D3861
Papain Dissociation Enzyme	Worthington Biochemical	Cat# LS003119
Neurobasal™-A	Thermo Fischer Scientific	Cat# 10888022
TrypLE™ Express Enzyme	Thermo Fischer Scientific	Cat# 12605010
B-27™ Supplement (50X)	Thermo Fischer Scientific	Cat# 17504044
EGF	PeproTech	Cat# 100-15
bFGF	PeproTech	Cat# AF-100-18B-100
Poly-L-ornithine hydrochloride	Sigma-Aldrich	Cat# P2533
Fetal bovine serum (FBS)	Thermo Fischer Scientific	Cat# 10099141

Retinoic acid	Sigma-Aldrich	Cat# R2625
Bovine serum albumin (BSA)	Sigma-Aldrich	Cat# A1933
Phosphate buffer solution (PBS; 10X)	Solarbio	Cat# P1033
Triton X-100	Solarbio	Cat# P1080
Primary antibody dilution buffer	ZSGB-BIO	Cat# ZLI-902
Sucrose	Solarbio	Cat# S8271
Dimethyl Sulfoxide (DMSO)	MP Bio	Cat# 196055
4% paraformaldehyde (PFA)	Solarbio	Cat# P1110
Glutaraldehyde	Sigma-Aldrich	Cat# G6257
Sodium cacodylate	Sigma-Aldrich	Cat# C0250
Gelatin solution	Macklin	Cat# G885128
Osmium tetroxide	Electron Microscopy Sciences	Cat# EMS 19100
Uranyl acetate	Electron Microscopy Sciences	Cat# EMS 22400
Ethanol	VWR Chemicals	Cat# 20821.321
Epoxy resin	Macklin	Cat# R832312
Lead citrate	Macklin	Cat# L885990
HBSS	Thermo Fischer Scientific	Cat# C14175500BT
RNAiso Plus reagent	TaKaRa	Cat# 9108
TB Green® Premix Ex Taq™ II (Tli RNaseH Plus)	TaKaRa	Cat# RR820A
Isopropanol	Aladdin	Cat# I112011
Optimal Cutting Temperature (O.C.T.) Compound	Sakura	Cat# SAKURA 4583
Tri-decanoyl glycerol	Sigma-Aldrich	N/A
Cholesteryl myristate	Sigma-Aldrich	Cat# S455342
Tri-nonadecanoyl glycerol	Sigma-Aldrich	N/A
NaOH	Sigma-Aldrich	Cat# S5881

Boron trifluoride-methanol solution	Sigma-Aldrich	Cat# B1252
Critical Commercial Assays		
Senescence β-galactosidase staining Kit	Cell Signaling Technology	Cat# 9860
PrimeScript™ RT reagent Kit (Perfect Real Time)	TaKaRa	Cat# RR037A
BCA Protein Assay Kit	Solarbio	Cat# PC0020
Enhanced chemiluminescence (ECL) Plus blot kit	MERCK Millipore	Cat# WBULS0500
Bradford Assay	BioRad	Cat# 5000201
other		
Polyvinylidene fluoride (PVDF) transfer membrane Intracerebroventricular osmotic minipumps	MERCK Millipore RWD Life Science	Cat# IPVH00010 Cat# 1002W
Automatic stereotaxic apparatus	RWD Life Science	Cat# 71000-M
Indirect CD133 MicroBead Kit, human	Miltenyi Biotec	Cat# 130-091-895
MACS magnetic separation column (LS Columns)	Miltenyi Biotec	Cat# 130-042-401
LS Columns plus tubes	Miltenyi Biotec	Cat# 130-122-729
MACS® MultiStand	Miltenyi Biotec	Cat# 130-042-303
MidiMACS™ Separator and Starting Kits	Miltenyi Biotec	Cat# 130-042-302

Supplementary Table 6. Software used in this study.

Software	**Source**	**Identifier**
ImageJ	National Institutes of Health	https://imagej.nih.gov/ij/download.html
GraphPad Prism 8.0	GraphPad Software	https://www.graphpad.com/scientificsoftware/prism/
IBM SPSS Statistics 20.0	IBM Company	https://www.ibm.com/products/spss-statistics
RStudio v4.0.2	N/A	www.r-project.org
GSEA Desktop v4.1.0	Broad Institute, Massachusetts Institute of Technology	http://software.broadinstitute.org/gsea/index.jsp

Adobe Photoshop CC 19.0	Adobe	https://www.adobe.com/cn
Adobe Illustrator CC 19.0	Adobe	https://www.adobe.com/cn
Gatan Microscopy Suite software	Gatan	https://www.gatan.com/products/tem-anal

Supplementary Table 7. Gene list of DEGs between htNSCs and NSCs of SVZ.

No.	Gene ID	baseMean	log_2FoldChange	lfcSE	stat	*p* value	*p* adj	regulated
1	SELL	10.43853852	6.485363382	1.360213238	4.767901974	1.86E-06	4.12E-05	up
2	CPN2	10.41815117	6.483325275	1.254142021	5.169530376	2.35E-07	6.63E-06	up
3	F13A1	7.416015876	5.992785931	2.029600777	2.952691977	0.003150161	0.020571018	up
4	KCNG2	25.3649823	5.735872594	1.306362954	4.390718963	1.13E-05	0.000191693	up
5	TGM2	671.5248735	5.333306356	0.839386905	6.35381172	2.10E-10	1.28E-08	up
6	IL32	18.30733366	5.243060626	0.965507264	5.430368907	5.62E-08	1.92E-06	up
7	LRRC15	578.1009183	5.190315137	0.72218015	7.18700886	6.62E-13	6.61E-11	up
8	C11orf44	7.010209138	5.170507849	1.201228762	4.304349023	1.67E-05	0.000269779	up
9	CXCL8	4.165723509	5.160579849	1.200908549	4.297229669	1.73E-05	0.000276836	up
10	PLEK2	3.546360264	4.926637795	1.214243817	4.057371119	4.96E-05	0.000684538	up
11	IL7R	105.1641873	4.909530529	0.717716169	6.840490356	7.89E-12	6.43E-10	up
12	FLJ22447	3.469672971	4.894060663	1.252537138	3.907317808	9.33E-05	0.001162924	up
13	DUSP15	5.626397544	4.855472454	1.1548711	4.204341467	2.62E-05	0.000396386	up
14	AC003092.1	3.278588576	4.811427487	1.152433925	4.175013754	2.98E-05	0.000443489	up
15	MMP1	3.07932448	4.72468463	1.320540288	3.577842094	0.000346443	0.003470141	up
16	AC004817.3	4.650716942	4.569288579	1.255167674	3.640381023	0.000272235	0.002841094	up
17	AP000695.2	4.569923969	4.539438922	1.203310703	3.772457861	0.000161647	0.001832572	up

18	HLA-DMB	11.41941566	4.537166945	1.010244488	4.491157335	7.08E-06	0.000129089	up
19	AP000695.1	4.459740281	4.506128903	1.200724653	3.752841162	0.000174842	0.00195387	up
20	MLKL	2.610454147	4.489499841	1.175326885	3.819788264	0.000133566	0.001565655	up
21	C11orf91	2.507791571	4.433641001	1.222880471	3.625571842	0.000288323	0.002986032	up
22	KCTD4	10.30892525	4.41417702	0.927163144	4.760949623	1.93E-06	4.23E-05	up
23	SLC22A3	65.93500088	4.412362978	0.939066682	4.698668438	2.62E-06	5.51E-05	up
24	FOXL1	2.424425789	4.384372231	1.179469858	3.717239742	0.000201411	0.002202436	up
25	CGB8	3.91521577	4.322982787	1.257177547	3.438641421	0.000584641	0.005352463	up
26	C3orf80	3.208174869	4.014882866	1.279141832	3.138731583	0.001696808	0.012531269	up
27	AQP7P1	2.979255801	3.911226016	1.135338575	3.444986457	0.000571088	0.005246477	up
28	HLA-DPB1	7.309766373	3.895906463	1.031844682	3.775671406	0.000159577	0.001814155	up
29	MMP9	22.43064087	3.800524714	1.400784911	2.713139386	0.006664907	0.036947949	up
30	GREM1	216.1828895	3.782025899	0.506989149	7.459776811	8.67E-14	1.04E-11	up
31	LINGO3	2.746644368	3.781565402	1.192697079	3.170600036	0.001521244	0.011463382	up
32	TMEM92-AS1	6.656470875	3.766276274	1.000444429	3.764603176	0.000166814	0.001880673	up
33	CD36	11.02482297	3.753110647	0.931046968	4.031064786	5.55E-05	0.000748206	up
34	AC093627.3	10.9373774	3.725377881	0.870152235	4.281294389	1.86E-05	0.000295799	up
35	TNFRSF8	8.555317543	3.714001234	1.149608252	3.230666817	0.001235018	0.009708959	up
36	SMTNL2	4.360153091	3.713236962	1.219119758	3.045834454	0.002320356	0.016020603	up
37	CETP	2.590989019	3.712144793	1.186836671	3.127763813	0.001761417	0.01291473	up
38	CYP26C1	2.516706834	3.661408411	1.185266526	3.089101339	0.002007629	0.014307786	up
39	ABCA4	10.2355602	3.622069025	0.98987579	3.659114672	0.000253088	0.002679558	up
40	ADCY4	2.447120117	3.614478384	1.20105812	3.00941172	0.002617541	0.017676869	up
41	APCDD1L	9.897276559	3.60163194	1.059310538	3.399977449	0.000673914	0.00602616	up
42	PTGS2	11.49418893	3.544520444	0.712902139	4.971959331	6.63E-07	1.65E-05	up

43	KCNS3	3.817258822	3.522355116	1.16121178	3.033344286	0.002418595	0.016541825	up
44	PKP1	13.41276479	3.520339526	0.701076573	5.021333848	5.13E-07	1.33E-05	up
45	WNT9A	276.1023706	3.480443061	0.487700843	7.136430269	9.58E-13	9.16E-11	up
46	PAPPA2	20.35048032	3.475794569	0.535266947	6.493572205	8.38E-11	5.57E-09	up
47	AC137932.2	5.43528343	3.454437157	1.046218887	3.301830239	0.000960562	0.007995912	up
48	HLA-DRB5	3.435705653	3.366362279	1.166923115	2.884819261	0.003916384	0.024289218	up
49	MMP10	16.61348108	3.32723258	0.767755015	4.333716504	1.47E-05	0.00024113	up
50	AMIGO2	234.5056691	3.317204219	0.318484767	10.41558204	2.11E-25	1.86E-22	up
51	AC093627.1	13.11704893	3.307491784	0.713853171	4.633294237	3.60E-06	7.22E-05	up
52	GATA6	6.616604161	3.306203349	0.885616236	3.733223505	0.000189045	0.002094858	up
53	C3AR1	16.18206378	3.280070686	0.769203529	4.2642429	2.01E-05	0.000315265	up
54	ANPEP	596.4341966	3.270701151	0.626443525	5.221063068	1.78E-07	5.26E-06	up
55	VGLL2	37.3867824	3.245738708	0.81190366	3.997689463	6.40E-05	0.000843502	up
56	LBX2-AS1	3.174018073	3.234655713	1.160095016	2.788267916	0.00529907	0.030835772	up
57	OASL	6.156723688	3.207774607	0.85918575	3.733505363	0.000188833	0.002094135	up
58	NPS	18.21835044	3.197689686	0.722636283	4.425033398	9.64E-06	0.000167094	up
59	LINC01348	3.039163395	3.192934254	1.169231236	2.730797943	0.006318119	0.035411556	up
60	AC100797.1	3.068422843	3.190756861	1.177343213	2.710133143	0.00672562	0.037232289	up
61	AC254633.1	10.79564206	3.188464407	0.992823454	3.211511972	0.001320385	0.010233861	up
62	C10orf90	10.23017974	3.130366312	0.69384674	4.511610607	6.43E-06	0.000118764	up
63	HLA-DRB1	21.90191991	3.115823757	0.682647567	4.564322655	5.01E-06	9.58E-05	up
64	GJB2	190.2847276	3.081299942	0.746641944	4.126877636	3.68E-05	0.000532138	up
65	PDE6A	5.583085692	3.067413409	1.012706954	3.028924999	0.002454256	0.016757581	up
66	LY96	4.238068716	3.059315253	0.965312003	3.169250193	0.001528328	0.011503986	up
67	CYP1A1	43.56438763	3.036486653	0.455293495	6.669295051	2.57E-11	1.92E-09	up

68	CRYBB1	4.169146041	3.028773459	1.060491828	2.856008297	0.004290039	0.026051145	up
69	TBX6	6.74785922	2.988688438	0.797205308	3.748957025	0.000177572	0.001981114	up
70	SPOCD1	118.6735377	2.980587874	0.543974281	5.479280877	4.27E-08	1.51E-06	up
71	CHRNA1	15.91198577	2.974286766	0.591712264	5.026576173	4.99E-07	1.30E-05	up
72	PTPRN	95.02462815	2.915231138	0.349852713	8.332738403	7.90E-17	1.68E-14	up
73	SHISAL1	146.1992376	2.909530077	0.5093481	5.71226255	1.11E-08	4.62E-07	up
74	CYP1B1	1326.535778	2.906073279	0.41925497	6.931517777	4.16E-12	3.49E-10	up
75	GOLGA7B	7.664061287	2.88821184	0.795069827	3.6326518	0.000280523	0.002918619	up
76	P4HA3	54.99405136	2.856988288	0.347860675	8.213024622	2.16E-16	4.26E-14	up
77	CREG2	3.624882783	2.82740619	1.045056927	2.705504473	0.006820073	0.037581463	up
78	IFITM10	27.44902617	2.81912729	0.390002266	7.228489513	4.88E-13	5.02E-11	up
79	PCBP3	4.851245213	2.807982249	0.899337394	3.122278988	0.001794568	0.013110584	up
80	TEX29	9.477345509	2.799338397	0.732959241	3.819227918	0.00013387	0.00156651	up
81	COL10A1	34.08433517	2.798595062	0.794862321	3.520855105	0.000430158	0.004154857	up
82	TIE1	130.0285903	2.790407476	0.390614107	7.143642338	9.09E-13	8.73E-11	up
83	C6orf15	32.96579649	2.789306803	0.937074863	2.976610421	0.002914541	0.01926513	up
84	HTRA3	20.35149622	2.772459172	0.729386877	3.801081782	0.000144066	0.001661939	up
85	SLC16A3	459.9310738	2.764510407	0.45573961	6.065986681	1.31E-09	6.53E-08	up
86	DHRS2	3.467025804	2.748712804	1.01612827	2.705084472	0.006828702	0.037582098	up
87	SLC7A11-AS1	4.585584277	2.730398956	0.950561188	2.872407365	0.004073575	0.025094061	up
88	THBS1	8896.208708	2.722483348	0.199038817	13.67815281	1.37E-42	9.31E-39	up
89	IFNE	5.67458609	2.720865679	0.772821664	3.520690228	0.000430425	0.00415547	up
90	A4GALT	21.26254836	2.694377569	0.517264976	5.208892333	1.90E-07	5.53E-06	up
91	MSC	260.1568927	2.679908227	0.327281166	8.188397328	2.65E-16	5.09E-14	up
92	LUCAT1	139.6365841	2.661437433	0.35678517	7.459495672	8.69E-14	1.04E-11	up

93	TFCP2L1	62.50704347	2.641379339	0.724780216	3.644386644	0.00026803	0.002805842	up
94	LINC02081	6.467900696	2.630934132	0.853928181	3.080978225	0.002063217	0.014601727	up
95	PTPN22	7.226399884	2.57667202	0.707699996	3.64091004	0.000271676	0.002836716	up
96	AC069029.1	3.071914343	2.566148791	0.980543874	2.617066772	0.008868899	0.04620769	up
97	SLC7A11	531.7677467	2.558158657	0.235299768	10.87191323	1.57E-27	2.13E-24	up
98	SGK1	69.23421109	2.555961758	0.263124132	9.71390097	2.63E-22	1.49E-19	up
99	COL7A1	3594.521834	2.537851	0.512464977	4.952242815	7.34E-07	1.81E-05	up
100	CD274	131.8639472	2.507600553	0.252088604	9.947298339	2.59E-23	1.70E-20	up
101	CD74	638.6851149	2.5065036	0.692896851	3.617426745	0.000297547	0.00305977	up
102	PRR15	6.930870976	2.504411405	0.697602217	3.590027877	0.000330643	0.003341049	up
103	MYC	192.3073287	2.502155033	0.306376404	8.166931257	3.16E-16	5.96E-14	up
104	ITGB3	69.17028309	2.502076033	0.469463202	5.329653147	9.84E-08	3.11E-06	up
105	OPCML	55.73600929	2.473498816	0.672865317	3.67606823	0.000236856	0.002532893	up
106	TLR6	8.642503118	2.469802262	0.635124745	3.888688453	0.000100787	0.001236969	up
107	HLA-DPA1	28.73683084	2.449327751	0.63675272	3.846591738	0.000119772	0.001426131	up
108	CHAC1	47.87916617	2.424202482	0.703299519	3.446899104	0.00056706	0.005212603	up
109	KCNN2	22.31165885	2.407726351	0.516979306	4.657297345	3.20E-06	6.50E-05	up
110	IL1R1	104.7593336	2.407481243	0.65942756	3.650865372	0.000261358	0.00274588	up
111	RGS16	606.6298495	2.395331328	0.581667509	4.118042163	3.82E-05	0.000549438	up
112	MICAL2	503.8399218	2.395278355	0.459577079	5.211918666	1.87E-07	5.46E-06	up
113	AC100810.3	4.627396016	2.380667654	0.816769733	2.914735401	0.003559902	0.022531293	up
114	SYT7	32.96830219	2.379811494	0.487456566	4.882099578	1.05E-06	2.49E-05	up
115	BMP4	8.33165883	2.373418836	0.910537814	2.606612047	0.00914429	0.047255556	up
116	FILIP1L	714.809602	2.368334884	0.306640709	7.723484893	1.13E-14	1.66E-12	up
117	AL118505.1	3.639205638	2.362297849	0.873781241	2.703534636	0.00686063	0.037713089	up

118	AC008687.4	9.826940184	2.331915832	0.567303889	4.11052326	3.95E-05	0.000566041	up
119	WNT7B	953.4050449	2.330522418	0.449955801	5.179447432	2.23E-07	6.33E-06	up
120	PODNL1	47.20967257	2.317760693	0.691088407	3.353783206	0.000797148	0.006915521	up
121	DYSF	7.959108023	2.314230703	0.664524679	3.482535377	0.00049669	0.004675495	up
122	AC037198.1	15.1287254	2.309521658	0.584006226	3.954618216	7.67E-05	0.000987231	up
123	MFAP2	1733.829122	2.307961048	0.541008049	4.266038281	1.99E-05	0.000313327	up
124	ICAM1	62.53797695	2.302764824	0.718800573	3.203621296	0.001357109	0.010470666	up
125	ACKR3	20.47343368	2.28868861	0.647451907	3.534916781	0.000407904	0.003970041	up
126	MIR31HG	4.981658566	2.269394147	0.847598673	2.677439477	0.007418725	0.039918781	up
127	SLC14A1	11.92942636	2.268553535	0.510112732	4.447161173	8.70E-06	0.000152336	up
128	GCLM	1141.930924	2.257268272	0.435046738	5.188564987	2.12E-07	6.09E-06	up
129	AC068580.4	6.671442497	2.246736394	0.664702653	3.380062323	0.000724694	0.006409858	up
130	OLFML2B	558.9396881	2.24075018	0.528264637	4.241719057	2.22E-05	0.000343449	up
131	PCED1B	35.08019464	2.209956442	0.34784444	6.353289543	2.11E-10	1.28E-08	up
132	KIAA1755	6.439547052	2.194333362	0.789911712	2.777947624	0.005470344	0.031645752	up
133	KIT	11.90520416	2.19088133	0.696257926	3.146651908	0.001651514	0.012276921	up
134	ADM	25.73759686	2.171406057	0.38014385	5.71206415	1.12E-08	4.62E-07	up
135	HLA-DRA	276.4730452	2.16368359	0.622267153	3.477097544	0.000506873	0.004751588	up
136	PDCD6IPP2	6.414263218	2.158932221	0.654185126	3.300185428	0.00096621	0.008032927	up
137	COL13A1	83.80737219	2.158773016	0.637540245	3.386096849	0.000708944	0.006292415	up
138	FAM20C	7824.561246	2.135869157	0.387610643	5.510347035	3.58E-08	1.30E-06	up
139	SMIM11A	50.80561146	2.133304343	0.692657108	3.079885151	0.002070804	0.014650329	up
140	CCL2	156.6008269	2.131834931	0.353316701	6.03377911	1.60E-09	7.80E-08	up
141	SMIM32	142.7125081	2.103629293	0.522938814	4.022706361	5.75E-05	0.000773224	up
142	AC241585.2	4.560103464	2.102207218	0.761733524	2.75976723	0.005784256	0.033119582	up

143	ULBP1	42.6802973	2.100409949	0.448096472	4.687405685	2.77E-06	5.75E-05	up
144	TCAF2	39.27473247	2.096511276	0.380941192	5.503503742	3.72E-08	1.35E-06	up
145	PKIB	55.66832099	2.075342176	0.299027083	6.940315078	3.91E-12	3.31E-10	up
146	MOCOS	26.37502503	2.064459911	0.417557397	4.94413445	7.65E-07	1.88E-05	up
147	UCN2	25.28679769	2.064128438	0.430613156	4.793463478	1.64E-06	3.68E-05	up
148	KDR	134.3297229	2.063520276	0.691886481	2.982454974	0.002859467	0.019008034	up
149	ARHGEF38	4.435780238	2.04832497	0.754644684	2.714290598	0.006641788	0.036848348	up
150	CIITA	410.0965413	2.033118751	0.589280832	3.450169496	0.000560235	0.005159176	up
151	LAPTM5	15.19014875	2.004806081	0.446922144	4.485806106	7.26E-06	0.000131233	up
152	SIGLEC15	19.43138373	2.004153222	0.471632946	4.249391906	2.14E-05	0.000332653	up
153	AL390719.1	47.47967665	1.998026163	0.382902926	5.218101062	1.81E-07	5.32E-06	up
154	GPR160	10.84267679	1.995332505	0.594548439	3.356046998	0.000790651	0.00686794	up
155	HLA-DMA	85.54135275	1.986931347	0.582068815	3.41356777	0.000641182	0.005784275	up
156	MYLK2	11.30517481	1.977156199	0.553868998	3.569718118	0.000357366	0.003551613	up
157	OGN	18.70172454	1.973647839	0.68884939	2.865136947	0.004168289	0.025536522	up
158	PDGFB	49.44741666	1.966427521	0.4444474	4.424432503	9.67E-06	0.000167418	up
159	DSC2	7.775339419	1.962616047	0.561273352	3.496720517	0.000471015	0.004487757	up
160	MPP4	77.22912715	1.945808997	0.219336471	8.871342665	7.23E-19	2.20E-16	up
161	FOSL2	3698.51912	1.941012928	0.412800274	4.702063079	2.58E-06	5.43E-05	up
162	JAKMIP2-AS1	275.7782887	1.937317017	0.280803398	6.899193639	5.23E-12	4.35E-10	up
163	ITGA2	7.529661782	1.908895598	0.605841962	3.150814433	0.001628159	0.012112147	up
164	ADCY7	28.67955753	1.907972901	0.380629212	5.012681218	5.37E-07	1.38E-05	up
165	KIF26B	701.153606	1.903966447	0.516528324	3.686083337	0.000227732	0.002446885	up
166	SPHK1	111.3224078	1.903931976	0.354650323	5.36847664	7.94E-08	2.60E-06	up
167	PLEKHN1	15.89104101	1.897467028	0.521507355	3.638428128	0.000274307	0.002859789	up

168	FAP	228.0928443	1.894038099	0.227561047	8.323208758	8.56E-17	1.78E-14	up
169	FGD5	11.46889277	1.88451943	0.548656631	3.434788397	0.000593017	0.005416964	up
170	AL627309.7	8.062784916	1.882436019	0.564944444	3.332072805	0.000862017	0.007343736	up
171	HLA-DOA	34.99567221	1.881387769	0.606137952	3.103893694	0.001909919	0.013780251	up
172	GPR150	5.92231789	1.871592569	0.701646306	2.667430234	0.007643376	0.040900597	up
173	RCAN2	81.7464546	1.870977253	0.603284194	3.101319864	0.001926601	0.013876022	up
174	NKD2	7.207506641	1.865483701	0.669216341	2.787564478	0.005310588	0.030885145	up
175	TMEM255B	17.41131713	1.85975664	0.541024651	3.437471173	0.000587173	0.005373147	up
176	COL22A1	4258.081909	1.858157934	0.523639136	3.548546715	0.000387363	0.00380232	up
177	SLCO2A1	302.2364968	1.852057648	0.236462283	7.832359652	4.79E-15	7.68E-13	up
178	MFAP5	91.1295132	1.843149528	0.390904403	4.715090216	2.42E-06	5.15E-05	up
179	CLDN7	8.728981279	1.836699396	0.640612039	2.867100967	0.004142508	0.025421312	up
180	AC123595.1	9.809948032	1.835264098	0.551213353	3.329498619	0.000870025	0.007402665	up
181	GDNF	5.277323188	1.831540506	0.664727435	2.755325581	0.005863376	0.033487852	up
182	CNTN1	452.2140787	1.829657669	0.196122559	9.329154565	1.07E-20	4.53E-18	up
183	SLC7A5	5987.634005	1.823921895	0.270683896	6.73819876	1.60E-11	1.25E-09	up
184	SLC2A1	6271.56937	1.823361576	0.132355168	13.77627789	3.54E-43	7.21E-39	up
185	L1CAM	21.43587289	1.820644368	0.395937517	4.598312329	4.26E-06	8.35E-05	up
186	VDR	659.1215023	1.818717664	0.271397505	6.701305758	2.07E-11	1.56E-09	up
187	B4GALT1	3118.651107	1.816066369	0.22530513	8.060474991	7.60E-16	1.35E-13	up
188	FMN1	124.9428411	1.811695257	0.51643388	3.508087535	0.000451341	0.004322551	up
189	HMOX1	363.3530821	1.811377516	0.204413758	8.861328785	7.91E-19	2.37E-16	up
190	PLAUR	377.5089595	1.810558367	0.327907517	5.521551883	3.36E-08	1.23E-06	up
191	TFPI2	308.7292928	1.806599186	0.579785639	3.115977812	0.001833361	0.013330653	up
192	MESP2	6.432347879	1.80034125	0.621340186	2.897512974	0.003761342	0.02347783	up

193	NDRG1	303.052982	1.799717745	0.186624227	9.643537565	5.24E-22	2.81E-19	up
194	TNFAIP3	148.5840567	1.797311594	0.365668754	4.91513583	8.87E-07	2.15E-05	up
195	TPD52L1	61.07942122	1.794463625	0.391673054	4.581534539	4.62E-06	8.93E-05	up
196	GDF5	21.20710926	1.78656736	0.372907479	4.790913185	1.66E-06	3.71E-05	up
197	CPA4	26.78357393	1.785528502	0.50169687	3.558978756	0.0003723	0.003676233	up
198	DLG1	3679.197709	1.779816312	0.22682511	7.846645883	4.27E-15	7.02E-13	up
199	CFH	57.16153924	1.764413487	0.469177913	3.760649076	0.000169473	0.001906431	up
200	TGFA	245.8684248	1.763999398	0.298985667	5.899946363	3.64E-09	1.65E-07	up
201	GPRC5A	24.05035014	1.759078664	0.436118137	4.033491192	5.50E-05	0.0007415	up
202	CD40	26.36958938	1.7571413	0.382571407	4.59297602	4.37E-06	8.54E-05	up
203	ATP8B3	15.70901115	1.755972482	0.452533887	3.880311582	0.000104323	0.001274979	up
204	SLITRK6	29.86028653	1.750018523	0.285840256	6.122365504	9.22E-10	4.81E-08	up
205	CAPG	175.8932657	1.747503459	0.21605937	8.088070696	6.06E-16	1.08E-13	up
206	AC009229.3	12.30824847	1.745791902	0.488355216	3.574840291	0.000350442	0.00350115	up
207	FN1	1024.019977	1.739773809	0.500911762	3.473214129	0.000514265	0.004803187	up
208	CHST15	154.125922	1.734743246	0.513593805	3.377656093	0.000731064	0.006441023	up
209	C3orf52	44.13347036	1.727668839	0.248800167	6.944001941	3.81E-12	3.23E-10	up
210	NIPAL1	9.182825983	1.72669397	0.530472937	3.255008592	0.001133889	0.009087948	up
211	EMP2	1224.972796	1.725840667	0.489453618	3.526055591	0.000421798	0.004083803	up
212	SERPINA5	36.82014722	1.719350118	0.383068101	4.488366725	7.18E-06	0.000129896	up
213	FOXS1	18.48356082	1.716684949	0.553337422	3.102419756	0.001919456	0.013844151	up
214	MMP14	14791.68349	1.716673865	0.41619704	4.1246662	3.71E-05	0.000536514	up
215	SCN5A	7.281664183	1.712783947	0.624399684	2.743089068	0.006086417	0.034452473	up
216	LACC1	28.99295411	1.707975855	0.357289699	4.78036691	1.75E-06	3.89E-05	up
217	FXYD5	133.8865044	1.703984844	0.244114825	6.980259585	2.95E-12	2.56E-10	up

218	TCIM	345.4433571	1.700947645	0.42802539	3.973940992	7.07E-05	0.000917388	up
219	SERPINE1	1521.069313	1.698856517	0.274360803	6.192052581	5.94E-10	3.24E-08	up
220	SEL1L3	1006.675035	1.691035769	0.375288873	4.505957646	6.61E-06	0.000121311	up
221	NNMT	1474.274945	1.685780291	0.224406067	7.512186785	5.81E-14	7.26E-12	up
222	MIAT	3430.045989	1.684359342	0.530161543	3.177068132	0.001487721	0.011277544	up
223	RGS2	159.813435	1.671784295	0.376798348	4.436814292	9.13E-06	0.000158885	up
224	RNF128	36.16203296	1.670019251	0.430305551	3.881007922	0.000104024	0.001273627	up
225	EDN1	115.3127421	1.664761116	0.3529112	4.717223804	2.39E-06	5.10E-05	up
226	COL1A2	122.0167879	1.661008217	0.305463611	5.437663134	5.40E-08	1.85E-06	up
227	LIF	2787.667378	1.659211853	0.370284648	4.480909111	7.43E-06	0.000133924	up
228	MYO1D	16.68068747	1.658405161	0.406942746	4.075278841	4.60E-05	0.000640504	up
229	AL139220.2	13.14970355	1.656835565	0.587773734	2.818832262	0.00481987	0.028594805	up
230	MAP3K5	595.2740024	1.655937839	0.130121003	12.72613801	4.23E-37	1.23E-33	up
231	DIRC3	36.98657191	1.649010361	0.255573044	6.452207707	1.10E-10	7.13E-09	up
232	CRISPLD2	72.93411936	1.646141832	0.264504457	6.223493748	4.86E-10	2.73E-08	up
233	APOL3	9.960682773	1.637301036	0.545277171	3.002695003	0.002676005	0.018023861	up
234	MDGA1	350.570009	1.636841673	0.432216663	3.787086002	0.000152424	0.001741589	up
235	GALNT18	6.968438602	1.632716702	0.574824181	2.840375816	0.004506041	0.027184447	up
236	AC036214.1	9.851173871	1.632204897	0.464779473	3.511783527	0.00044511	0.004276967	up
237	SPSB1	146.1658404	1.631932496	0.231274752	7.056250122	1.71E-12	1.57E-10	up
238	INHBE	9.874816268	1.631124185	0.504856964	3.23086399	0.001234167	0.009706012	up
239	ADAM12	4132.243075	1.612042094	0.242276839	6.65371936	2.86E-11	2.10E-09	up
240	GFPT2	1331.996537	1.611332409	0.201498607	7.996742186	1.28E-15	2.22E-13	up
241	MET	522.6037761	1.611321412	0.228531409	7.050765668	1.78E-12	1.62E-10	up
242	AC092611.3	6.351270342	1.611282548	0.608923771	2.646115365	0.008142204	0.043150292	up

243	PLA2G4A	49.19973711	1.610853342	0.415904192	3.873135628	0.000107444	0.001305291	up
244	MTHFS	17.81996771	1.610733273	0.35361063	4.555104227	5.24E-06	9.94E-05	up
245	STC2	47.89068061	1.606609764	0.456200748	3.521716632	0.000428762	0.004143345	up
246	RHBDF2	133.6073892	1.602411154	0.205637949	7.792390277	6.58E-15	1.03E-12	up
247	IL11	135.3482205	1.600171621	0.263254696	6.078416253	1.21E-09	6.12E-08	up
248	ARRDC3	4740.587026	1.599290429	0.208726233	7.662143873	1.83E-14	2.47E-12	up
249	REPS2	16.86188254	1.593823102	0.408908654	3.897748522	9.71E-05	0.001201017	up
250	SKAP2	9.114414665	1.590723888	0.531874329	2.990788992	0.002782577	0.018606256	up
251	FAM83G	64.3145365	1.588295003	0.291769198	5.443669225	5.22E-08	1.80E-06	up
252	ZMIZ1-AS1	11.8689445	1.586614488	0.435672284	3.64176136	0.000270779	0.0028288	up
253	CDH6	118.6827624	1.585915015	0.296906599	5.341460977	9.22E-08	2.94E-06	up
254	DEPP1	47.94419911	1.585625522	0.382080022	4.149982807	3.33E-05	0.000486703	up
255	IL15RA	52.50297004	1.581840233	0.47713601	3.315281597	0.000915508	0.00770594	up
256	FSTL3	361.2092359	1.5774316	0.402510746	3.91898009	8.89E-05	0.001118339	up
257	PADI2	130.1056249	1.575834891	0.497001662	3.170683341	0.001520808	0.011463382	up
258	DSG2	45.27188172	1.557767231	0.30464298	5.113419096	3.16E-07	8.57E-06	up
259	MATN3	27.62316571	1.55363143	0.313599799	4.954185036	7.26E-07	1.80E-05	up
260	SLFN5	129.7344687	1.551150771	0.309860038	5.00597232	5.56E-07	1.41E-05	up
261	CDKN1A	13886.37949	1.550394623	0.472037548	3.284473085	0.001021733	0.008382542	up
262	AC007325.4	20.71022036	1.549920218	0.560807043	2.763731725	0.00571445	0.03281216	up
263	ATF4	8756.766697	1.548307179	0.234699175	6.596986033	4.20E-11	2.97E-09	up
264	PGM2L1	798.6672152	1.54802354	0.200458635	7.722408882	1.14E-14	1.66E-12	up
265	ZNF469	40.89534523	1.546585723	0.256227493	6.035986635	1.58E-09	7.73E-08	up
266	PDK4	41.08589963	1.54163093	0.355991004	4.330533396	1.49E-05	0.000243854	up
267	4-Mar	11.22319177	1.539110968	0.521221631	2.952891587	0.003148125	0.020568647	up

268	CSF1R	16.97159455	1.5338688	0.388683579	3.946317478	7.94E-05	0.001016912	up
269	PERP	161.45854	1.528281083	0.160544084	9.519385875	1.74E-21	7.88E-19	up
270	IGFBP3	2928.354984	1.525990684	0.198024103	7.706085588	1.30E-14	1.83E-12	up
271	NRP2	1666.52028	1.509711835	0.170994849	8.828990134	1.06E-18	3.03E-16	up
272	VCAN-AS1	21.98421676	1.506525882	0.482237151	3.124035298	0.001783891	0.013041937	up
273	C3orf67	18.28150913	1.501955209	0.331183164	4.535119446	5.76E-06	0.000107443	up
274	ITGA10	14.52221378	1.49661752	0.466863726	3.205683881	0.001347419	0.01041169	up
275	FAM129A	217.6721468	1.490821866	0.334841778	4.452317378	8.49E-06	0.000149622	up
276	AQP3	54.71162314	1.487592519	0.403327103	3.688302892	0.000225755	0.002432793	up
277	CAVIN2	83.1372098	1.477439557	0.41153097	3.5901054	0.000330544	0.003341049	up
278	TNFSF9	14.95970698	1.475540444	0.436716303	3.378716192	0.000728251	0.006419017	up
279	OSCAR	22.8037065	1.471985131	0.439080094	3.352429659	0.000801056	0.006942815	up
280	LHX6	11.10960313	1.47151696	0.474363714	3.102085837	0.001921622	0.013849965	up
281	FERMT1	393.2136986	1.469254866	0.237368659	6.189759303	6.03E-10	3.28E-08	up
282	GBP3	58.94666663	1.467625447	0.23743623	6.18113523	6.36E-10	3.45E-08	up
283	LMCD1	2242.757503	1.465674634	0.264421594	5.542946072	2.97E-08	1.10E-06	up
284	AC145676.1	24.06639808	1.463072678	0.388683155	3.764178244	0.000167098	0.001880749	up
285	COL24A1	68.38348187	1.460525757	0.439441676	3.323594087	0.000888654	0.007535982	up
286	PLPP2	11.49268261	1.456379196	0.500920014	2.907408676	0.003644367	0.022933896	up
287	TGFBI	7732.325635	1.454016182	0.238385029	6.099444187	1.06E-09	5.47E-08	up
288	PDP1	9863.783867	1.453173323	0.222045708	6.544478334	5.97E-11	4.08E-09	up
289	CPM	186.2119511	1.45025337	0.200553301	7.231261543	4.79E-13	5.00E-11	up
290	RUNDC3A-AS1	8.926480552	1.448372748	0.531544924	2.724836007	0.006433343	0.035926852	up
291	MGLL	32.15345335	1.445747789	0.370611013	3.900984423	9.58E-05	0.00118796	up
292	EPS8L1	28.28787219	1.44327121	0.346593489	4.164161351	3.12E-05	0.000461741	up

293	BCAR3	529.5699983	1.440727788	0.131318633	10.97123659	5.25E-28	7.64E-25	up
294	PLA2R1	14.55204934	1.439224293	0.403267362	3.568908446	0.000358472	0.00356041	up
295	VAV3	349.2177788	1.436314531	0.482091151	2.97934224	0.002888679	0.019164679	up
296	SPOCK1	1391.82144	1.436065977	0.23440147	6.126522924	8.98E-10	4.70E-08	up
297	GIPR	10.99885234	1.435708272	0.486922363	2.948536319	0.003192826	0.020769692	up
298	AC096921.2	6.671018495	1.430125857	0.536833159	2.664004324	0.007721657	0.041254437	up
299	TMEM92	8.761829361	1.429109769	0.458933717	3.113978592	0.001845829	0.013408106	up
300	TUBA4A	44.79004711	1.42806479	0.359295359	3.974626319	7.05E-05	0.000915334	up
301	TPST2	577.6910854	1.426691555	0.418096235	3.412352074	0.000644049	0.005801778	up
302	LCP1	16.2900393	1.42550199	0.407860238	3.495074679	0.000473929	0.00450288	up
303	TMEFF2	114.8928382	1.419919051	0.351432329	4.040376867	5.34E-05	0.000725017	up
304	HES7	25.66572348	1.418371096	0.385251914	3.681671766	0.00023171	0.00248569	up
305	SPON1	11.77212946	1.417707856	0.433091975	3.273456764	0.001062406	0.008628503	up
306	DOCK2	60.80967695	1.405856653	0.30837548	4.558911932	5.14E-06	9.80E-05	up
307	ELL2	1167.505786	1.405428571	0.125075916	11.2366043	2.70E-29	4.22E-26	up
308	LURAP1L	11.19657239	1.39739678	0.440494504	3.172336471	0.001512177	0.011420414	up
309	TMEM45A	142.1951581	1.395744429	0.212568793	6.566083432	5.17E-11	3.58E-09	up
310	ACSM3	14.22887966	1.394533453	0.380617251	3.663873484	0.00024843	0.002642776	up
311	FBXL21	26.29401572	1.393947909	0.422066406	3.302674391	0.000957675	0.007992619	up
312	GLI1	49.8171995	1.388002114	0.480727664	2.887294027	0.003885709	0.024135731	up
313	PROCR	45.65119077	1.382943707	0.27768145	4.980324418	6.35E-07	1.59E-05	up
314	SQOR	22.00780052	1.378121689	0.438708406	3.141315895	0.001681905	0.012448299	up
315	TUFT1	477.8530126	1.376754937	0.253635829	5.428077505	5.70E-08	1.94E-06	up
316	TIPARP	970.8667292	1.376105885	0.119282965	11.53648292	8.64E-31	1.76E-27	up
317	VEGFC	186.0069372	1.373586539	0.261822153	5.246257903	1.55E-07	4.64E-06	up

318	RFLNA	88.43244029	1.366967241	0.360106639	3.796006778	0.000147045	0.001690272	up
319	ADA	599.5929818	1.365978353	0.242852309	5.6247287	1.86E-08	7.21E-07	up
320	ST8SIA4	452.9620666	1.365143299	0.208007444	6.562954058	5.28E-11	3.63E-09	up
321	TRIM38	15.77705653	1.363645235	0.432878169	3.150182503	0.001631685	0.012133944	up
322	CYP27C1	40.98293017	1.35939399	0.22150011	6.13721588	8.40E-10	4.44E-08	up
323	ITGA2B	9.00938863	1.357647882	0.484103784	2.804456246	0.005040153	0.029625448	up
324	LINC01173	18.6405333	1.356844954	0.439207169	3.089305113	0.002006253	0.014307786	up
325	ENPP1	155.622443	1.356550198	0.2165951	6.263069652	3.77E-10	2.16E-08	up
326	GADD45B	333.0207924	1.350959166	0.225769303	5.983803603	2.18E-09	1.03E-07	up
327	ECM1	147.8989133	1.350907578	0.220233064	6.133990764	8.57E-10	4.52E-08	up
328	ATP13A2	2137.284698	1.350116703	0.213347499	6.328251843	2.48E-10	1.49E-08	up
329	KRT81	16.86436152	1.34870127	0.374023414	3.605927381	0.00031104	0.003176072	up
330	C13orf46	28.54304626	1.346184478	0.354934188	3.792772079	0.000148975	0.001706965	up
331	CASP4	15.75245002	1.341439819	0.406876512	3.296921248	0.000977509	0.008100554	up
332	IL4R	263.0950657	1.338022994	0.285405898	4.688140652	2.76E-06	5.74E-05	up
333	SLC12A8	104.4592067	1.33540983	0.417586636	3.19792281	0.001384213	0.010647513	up
334	DPP4	30.07590845	1.333702192	0.403192216	3.307856991	0.000940128	0.007870866	up
335	PDPN	5854.450211	1.329910905	0.356423196	3.731269234	0.000190517	0.002103648	up
336	ATP2A3	21.79225409	1.325890798	0.308877104	4.292615998	1.77E-05	0.000281988	up
337	SMN1	557.7961698	1.32566913	0.445543377	2.975398579	0.002926081	0.019329013	up
338	LINC00475	20.30222729	1.325033413	0.406666718	3.258278472	0.001120904	0.009006597	up
339	CDYL2	89.49954704	1.323772239	0.21134158	6.263662067	3.76E-10	2.16E-08	up
340	NID1	421.5418707	1.321085596	0.479973989	2.75241081	0.005915826	0.033725519	up
341	TESMIN	15.23761496	1.320012997	0.502588254	2.626430256	0.008628567	0.04519842	up
342	AC022613.1	24.03253376	1.319075251	0.41844256	3.152344855	0.001619649	0.012074187	up

343	SPINT2	9.143568334	1.311187081	0.501750158	2.613227045	0.00896917	0.046551431	up
344	FOXD1	137.8412714	1.309902916	0.243201071	5.386090252	7.20E-08	2.39E-06	up
345	AC124067.2	80.99476078	1.309243814	0.28793999	4.546932903	5.44E-06	0.000102527	up
346	ADAM19	6034.293505	1.30681451	0.137916289	9.475418133	2.66E-21	1.18E-18	up
347	WNT5B	111.4425377	1.302712262	0.290912538	4.478020346	7.53E-06	0.00013539	up
348	ANXA3	33.5878798	1.301294811	0.443795533	2.932194475	0.003365759	0.021632014	up
349	EIF2AK3	672.3704968	1.299451419	0.446814359	2.908257968	0.003634484	0.02290366	up
350	PSMB8-AS1	11.04833482	1.296646446	0.458416037	2.828536399	0.004676138	0.027945657	up
351	ADIRF-AS1	10.53355227	1.292749002	0.461155904	2.803279739	0.005058577	0.029664175	up
352	PRR5L	441.6105437	1.290186485	0.283703785	4.547653411	5.42E-06	0.000102366	up
353	IER3	1097.577456	1.289400209	0.280492142	4.596920964	4.29E-06	8.39E-05	up
354	ADAMTSL4	244.6206504	1.288275417	0.328472394	3.922020356	8.78E-05	0.001105684	up
355	SNAI1	382.1435807	1.286555639	0.416609823	3.088154833	0.002014035	0.014343396	up
356	RASL11A	16.06979531	1.286439873	0.374387428	3.436119313	0.000590111	0.005392841	up
357	CSMD2	161.3011194	1.285760617	0.475202916	2.705708601	0.006815883	0.037581463	up
358	CREB3L1	116.5974878	1.284261562	0.309781933	4.145695482	3.39E-05	0.000494833	up
359	MYLK	3560.617725	1.283405751	0.19448098	6.599132479	4.14E-11	2.93E-09	up
360	INKA1	27.01970119	1.281580475	0.268279395	4.777036544	1.78E-06	3.95E-05	up
361	GABRG3	22.47602066	1.275376149	0.43542343	2.929048049	0.003400019	0.021769742	up
362	RPS10P7	10.00233091	1.274652605	0.491516377	2.593306476	0.009505802	0.048740276	up
363	SRPX	3208.220628	1.270399383	0.208152322	6.103219841	1.04E-09	5.36E-08	up
364	RAC2	38.93250029	1.26885515	0.461812023	2.747557636	0.006004096	0.034090739	up
365	KIF21B	58.10560444	1.264360358	0.206200426	6.131705841	8.69E-10	4.56E-08	up
366	MLPH	67.08973138	1.262625173	0.233978422	5.396331693	6.80E-08	2.27E-06	up
367	CYP1B1-AS1	59.86507972	1.262128488	0.331400332	3.808470805	0.000139829	0.00162133	up

368	G0S2	53.86939889	1.258750274	0.253374511	4.967943573	6.77E-07	1.68E-05	up
369	GPAT3	691.7164313	1.25655343	0.259009754	4.85137495	1.23E-06	2.85E-05	up
370	CERKL	332.4068964	1.25587597	0.421688886	2.978205049	0.002899419	0.019217148	up
371	LSP1	65.7422431	1.252969695	0.224376016	5.584240763	2.35E-08	8.82E-07	up
372	NTM	555.2957448	1.252527971	0.317620151	3.94347766	8.03E-05	0.001025324	up
373	KLF9	1388.087635	1.247696228	0.289910765	4.303725074	1.68E-05	0.000270327	up
374	AL021392.1	32.34141036	1.246380771	0.377439403	3.302200989	0.000959293	0.007992619	up
375	IL18	28.69751598	1.243352193	0.36148145	3.439601657	0.000582571	0.00533591	up
376	PCOLCE2	49.06791653	1.242227358	0.410590998	3.025461742	0.002482538	0.016916653	up
377	SH2D6	12.6235607	1.233885772	0.457960736	2.694304721	0.007053565	0.038494429	up
378	RAB3IL1	25.46829142	1.233175867	0.391143238	3.152747506	0.001617416	0.012063083	up
379	STEAP1	77.23867398	1.231936826	0.170148986	7.240341851	4.48E-13	4.70E-11	up
380	PPP1R14A	24.42806037	1.23113683	0.374437794	3.287960907	0.001009159	0.008298658	up
381	NOX4	149.0875245	1.228131459	0.22690864	5.412449065	6.22E-08	2.10E-06	up
382	CD109	1319.730123	1.227281558	0.123104651	9.969416649	2.07E-23	1.41E-20	up
383	TFAP2C	193.0284342	1.226749883	0.203732954	6.021362084	1.73E-09	8.25E-08	up
384	ARL4C	2492.368058	1.222289614	0.280516115	4.357288407	1.32E-05	0.000220676	up
385	PARVB	28.39100372	1.217482315	0.271957055	4.476744731	7.58E-06	0.000135841	up
386	PSD4	33.78076342	1.216777086	0.340495937	3.573543626	0.000352183	0.003512849	up
387	BX255923.1	11.8186907	1.214361149	0.429033246	2.830459316	0.004648122	0.027798795	up
388	NUS1P1	59.43295862	1.210440733	0.302834732	3.997034038	6.41E-05	0.000844986	up
389	SSH1	2522.045732	1.210107225	0.187840676	6.442200111	1.18E-10	7.52E-09	up
390	PCK2	224.6383233	1.202305947	0.296655852	4.052864415	5.06E-05	0.000695109	up
391	AL139393.2	494.6592488	1.201979397	0.30533565	3.936583876	8.26E-05	0.001050457	up
392	MSC-AS1	227.4117142	1.200363138	0.276633865	4.339176405	1.43E-05	0.000236554	up

393	JUNB	1666.040149	1.198403437	0.282808647	4.237506347	2.26E-05	0.000349159	up
394	USP43	35.51214166	1.198222608	0.273002148	4.389059265	1.14E-05	0.00019284	up
395	NBL1	368.4535852	1.196979356	0.408815223	2.927922661	0.003412349	0.021832391	up
396	NTNG1	40.78098101	1.193584012	0.400954008	2.976860161	0.002912168	0.01926402	up
397	NRIP3	70.00038608	1.191964735	0.183267029	6.503978075	7.82E-11	5.22E-09	up
398	EIF2AK4	3967.432445	1.190804981	0.241970052	4.921290766	8.60E-07	2.09E-05	up
399	LYPD6B	13.97000561	1.188928282	0.421229198	2.822521058	0.004764769	0.028333957	up
400	VIPR1	21.21225579	1.1809272	0.323923957	3.645692682	0.000266673	0.002794503	up
401	ADGRG6	89.13281315	1.178393461	0.359179073	3.280796541	0.001035144	0.008447521	up
402	DDIT3	194.4589014	1.177657624	0.337877142	3.485461063	0.00049129	0.00463968	up
403	CAMK2N1	616.4209296	1.172893905	0.444394892	2.63930555	0.008307607	0.043867007	up
404	SIK1B	58.22690924	1.170974787	0.234101294	5.002000494	5.67E-07	1.44E-05	up
405	PICART1	16.93908903	1.170201712	0.359935248	3.251145084	0.001149412	0.009174118	up
406	LMO7	198.2974948	1.169607207	0.142520398	8.206595129	2.28E-16	4.41E-14	up
407	PROSER2	72.86715598	1.168050384	0.201325414	5.80180296	6.56E-09	2.81E-07	up
408	HLA-B	723.8851105	1.166841375	0.277784854	4.200521951	2.66E-05	0.000402236	up
409	TMEM154	33.53740995	1.165531884	0.376084364	3.099123487	0.001940941	0.013954626	up
410	L3MBTL4	14.68843286	1.164894618	0.362506352	3.213446083	0.001311524	0.010175172	up
411	ADAMTS6	123.3814142	1.164499909	0.224009317	5.198444086	2.01E-07	5.80E-06	up
412	HSPD1P11	57.78362092	1.157532594	0.35983883	3.21680846	0.001296251	0.0100852	up
413	THEMIS2	45.30093229	1.156776005	0.371805418	3.111240312	0.001863033	0.013499362	up
414	GAB3	17.60806234	1.151800307	0.444692181	2.590106948	0.009594612	0.049084395	up
415	H2AFX	6344.342117	1.149624126	0.420159217	2.736163053	0.006216022	0.034985284	up
416	HLA-H	18.54722681	1.148809357	0.380623154	3.018232982	0.002542534	0.017233197	up
417	HERC5	12.77298583	1.147266146	0.395539302	2.900511129	0.003725546	0.023318735	up

418	NET1	1245.258727	1.145271452	0.191733204	5.973255705	2.33E-09	1.09E-07	up
419	ITGA4	1685.021918	1.144371489	0.283256952	4.040047318	5.34E-05	0.0007254	up
420	TMCO4	34.37886127	1.141797789	0.336870225	3.389429239	0.000700383	0.006232734	up
421	SLC22A4	33.32033613	1.141647511	0.34616752	3.297962528	0.000973891	0.008077149	up
422	RNF152	43.18055979	1.136795335	0.214735948	5.293921891	1.20E-07	3.68E-06	up
423	TGFB2-AS1	30.52704183	1.135924287	0.321175553	3.536770705	0.000405051	0.00394794	up
424	SIPA1	392.6961014	1.133646665	0.157989664	7.175448305	7.21E-13	7.02E-11	up
425	VAT1L	1218.785336	1.133009042	0.185438203	6.109900898	9.97E-10	5.19E-08	up
426	SOCS2-AS1	96.29408659	1.131453266	0.392038341	2.88607809	0.003900754	0.024207023	up
427	PLIN2	449.0564246	1.130625892	0.174123313	6.493248232	8.40E-11	5.57E-09	up
428	LTBP2	871.9267854	1.129763659	0.25984649	4.347811897	1.38E-05	0.000229358	up
429	LINC01234	11.31052526	1.12861257	0.398522596	2.831991411	0.004625909	0.027694247	up
430	PALM2	64.82867902	1.127465865	0.239726586	4.703132368	2.56E-06	5.41E-05	up
431	AHNAK2	3225.411288	1.126546095	0.209528881	5.376567142	7.59E-08	2.51E-06	up
432	CADPS	149.278141	1.124959658	0.311011031	3.617105329	0.000297916	0.003062024	up
433	ACSL1	19.75962993	1.121247337	0.382218546	2.933524154	0.003351376	0.021559988	up
434	ADAM8	65.66261444	1.120736555	0.423759384	2.644747461	0.008175191	0.043268795	up
435	OSTF1	95.54762872	1.118762134	0.20732317	5.396223378	6.81E-08	2.27E-06	up
436	PORCN	456.3788764	1.11686614	0.140561472	7.945748755	1.93E-15	3.25E-13	up
437	NFKBIZ	173.7801741	1.115103927	0.249332147	4.472363236	7.74E-06	0.000137927	up
438	PMAIP1	713.4110593	1.110416041	0.212298493	5.230447129	1.69E-07	5.03E-06	up
439	MYOF	4884.413723	1.107817888	0.126076046	8.786902185	1.54E-18	4.23E-16	up
440	OLIG2	15.97567665	1.107494355	0.337509486	3.281372532	0.001033032	0.008440436	up
441	EVI2A	77.26098348	1.102447268	0.189734633	5.810469346	6.23E-09	2.68E-07	up
442	STEAP3	1765.585673	1.10198799	0.29556084	3.728464134	0.00019265	0.002123743	up

443	RHEBL1	15.98512902	1.101405391	0.379440687	2.902707665	0.003699518	0.023212907	up
444	SERINC5	105.4283501	1.100038178	0.195088942	5.638649571	1.71E-08	6.79E-07	up
445	AMPD3	16.22743634	1.099869902	0.369146349	2.979495541	0.002887234	0.019161336	up
446	ZFPM2	122.7937792	1.099761119	0.210837543	5.216154136	1.83E-07	5.36E-06	up
447	TES	779.4642206	1.095682939	0.123291098	8.886959018	6.28E-19	2.00E-16	up
448	PTPRH	41.64282789	1.094204836	0.417819988	2.618842726	0.008822861	0.046031932	up
449	SLC43A3	29.24229685	1.092743229	0.28782709	3.796526685	0.000146738	0.001688934	up
450	BMF	1104.159581	1.091037226	0.370612306	2.943877489	0.003241283	0.021004379	up
451	KREMEN2	17.53843705	1.090514345	0.304795148	3.57785992	0.000346419	0.003470141	up
452	PTHLH	188.2567674	1.090273248	0.193568755	5.632485723	1.78E-08	6.98E-07	up
453	PDZD7	47.94088233	1.089571674	0.28252534	3.856544948	0.000115001	0.001378184	up
454	ADAMTSL1	268.6486713	1.089367185	0.260816241	4.176761308	2.96E-05	0.000440419	up
455	MMP19	83.44065637	1.088417291	0.337210109	3.227712519	0.001247843	0.009798432	up
456	HMGA2	378.3523751	1.087758085	0.173225067	6.279449641	3.40E-10	1.96E-08	up
457	AC244153.1	12.02675158	1.084425012	0.414074219	2.618914589	0.008821003	0.046031932	up
458	HAPLN3	62.28519305	1.08404297	0.313968504	3.452712474	0.00055498	0.005117732	up
459	DRP2	17.42169021	1.083299234	0.314502295	3.44448753	0.000572143	0.005252211	up
460	SMAGP	138.4363423	1.083122276	0.17960423	6.030605589	1.63E-09	7.92E-08	up
461	SERPINB1	59.47734422	1.081474295	0.233671485	4.628182573	3.69E-06	7.36E-05	up
462	EFEMP1	119.6640544	1.080997495	0.334263866	3.233964551	0.001220846	0.009620243	up
463	SLC26A2	1307.568473	1.077433677	0.156685477	6.876410596	6.14E-12	5.06E-10	up
464	SMIM3	555.9673053	1.075697275	0.236413264	4.550071591	5.36E-06	0.000101291	up
465	IRAK2	78.15641252	1.072830493	0.223635412	4.797229935	1.61E-06	3.62E-05	up
466	VSIR	28.04698376	1.06885207	0.380422511	2.809644644	0.004959623	0.029236502	up
467	PFKFB3	10865.6473	1.067734601	0.350705325	3.044534898	0.002330404	0.016062747	up

468	SLC2A12	611.4175295	1.067541565	0.280514395	3.805656977	0.000141428	0.00163801	up
469	FAM83H	62.8753129	1.066308364	0.320224712	3.32987532	0.000868849	0.007395749	up
470	JAK3	24.99007297	1.062572431	0.40166069	2.645447906	0.008158285	0.043213017	up
471	TCF7	24.32502568	1.06224743	0.307596727	3.453376892	0.000553615	0.005107455	up
472	FAM72C	20.2350513	1.061323244	0.392272122	2.705579074	0.006818541	0.037581463	up
473	CMPK2	17.06224441	1.058522583	0.404805393	2.614892492	0.008925554	0.046407869	up
474	HERC6	34.20021844	1.058303258	0.276212135	3.83148719	0.000127371	0.00150255	up
475	RASSF5	45.53751528	1.057856123	0.344978886	3.066437297	0.002166262	0.015172779	up
476	PAPSS2	416.7917252	1.050059083	0.283020113	3.710192437	0.000207102	0.002256179	up
477	ERRFI1	6379.872927	1.049922314	0.151175254	6.945067303	3.78E-12	3.23E-10	up
478	SLC25A43	33.25711417	1.049131334	0.321645542	3.261762393	0.001107219	0.008935429	up
479	HOXB5	20.76342874	1.048242653	0.311144761	3.368986998	0.00075445	0.006612722	up
480	TYMP	27.10342093	1.047505954	0.347006196	3.01869524	0.002538658	0.017218391	up
481	SRC	240.3412834	1.047320287	0.118258066	8.85622706	8.28E-19	2.44E-16	up
482	P4HA2	412.7517326	1.044601947	0.114595373	9.115568259	7.83E-20	2.75E-17	up
483	ZC3H12A	178.9819572	1.038207953	0.208620675	4.976534336	6.47E-07	1.62E-05	up
484	EMB	75.05166183	1.034016261	0.251920034	4.104541605	4.05E-05	0.000578481	up
485	FHOD3	734.1528302	1.031470911	0.202527014	5.093004093	3.52E-07	9.44E-06	up
486	LLGL2	20.87139051	1.028339768	0.375469176	2.738812755	0.006166148	0.034764089	up
487	HLA-C	625.3154713	1.026973684	0.218543579	4.699171167	2.61E-06	5.50E-05	up
488	ITPRIP	460.9378532	1.025660324	0.132561583	7.737236551	1.02E-14	1.51E-12	up
489	IRF1	206.6704655	1.024200403	0.215961483	4.742514214	2.11E-06	4.58E-05	up
490	HIC1	1192.731912	1.023678984	0.15677776	6.529491064	6.60E-11	4.46E-09	up
491	RCN3	223.3086092	1.023639869	0.146802415	6.972908915	3.10E-12	2.69E-10	up
492	LAMC3	158.5581737	1.022374365	0.241824018	4.227761878	2.36E-05	0.000362698	up

493	SMAD7	324.9545208	1.022234873	0.253007909	4.040327737	5.34E-05	0.000725017	up
494	SH3TC1	129.2547693	1.021562566	0.237838071	4.295202028	1.75E-05	0.000279159	up
495	INSYN2B	300.8056051	1.01913107	0.173039648	5.889581258	3.87E-09	1.72E-07	up
496	STX3	62.051645	1.018855069	0.302700228	3.365888016	0.000762977	0.006675965	up
497	PGBD5	443.2667937	1.01870145	0.322881613	3.15503085	0.001604811	0.011977846	up
498	ALDH1L2	71.5197138	1.018313314	0.255627026	3.983590196	6.79E-05	0.000886558	up
499	QPCT	30.6892704	1.016665979	0.258611605	3.931246542	8.45E-05	0.001070049	up
500	BCL3	1282.975131	1.006816773	0.264113486	3.812061198	0.000137813	0.001600688	up
501	ACP6	722.624668	1.000650058	0.238159111	4.201603105	2.65E-05	0.000400617	up
502	NOL4	11.79745194	-1.000759675	0.357717779	-2.797623524	0.005148008	0.030085702	down
503	PROB1	83.0926845	-1.003797281	0.196335683	-5.112658409	3.18E-07	8.58E-06	down
504	CDH7	22.34709943	-1.005659502	0.301268305	-3.338085971	0.000843576	0.00722814	down
505	DMD	133.1086534	-1.007693208	0.308995713	-3.261188317	0.001109463	0.008946448	down
506	MAPK10	1111.289096	-1.008477428	0.145085111	-6.950936725	3.63E-12	3.12E-10	down
507	AC073050.1	14.71754908	-1.011149865	0.368712141	-2.742382887	0.00609952	0.034507452	down
508	OSR1	73.01379725	-1.011379799	0.221177542	-4.572705657	4.81E-06	9.25E-05	down
509	CAMKV	13.81538615	-1.012009056	0.348738468	-2.90191404	0.003708903	0.02325746	down
510	PLCE1	607.7983488	-1.014348346	0.206398536	-4.914513283	8.90E-07	2.15E-05	down
511	REEP2	977.1382286	-1.01565236	0.145421042	-6.984218679	2.86E-12	2.52E-10	down
512	MFSD2A	181.1171841	-1.016234636	0.302333499	-3.361303457	0.000775755	0.006761625	down
513	PTPRD	1623.764912	-1.018237411	0.098782582	-10.30786392	6.49E-25	5.08E-22	down
514	DDR1	8151.300509	-1.019140831	0.114871353	-8.872019055	7.18E-19	2.20E-16	down
515	FGD4	112.8577862	-1.020961735	0.278065406	-3.671660388	0.00024098	0.002571588	down
516	S1PR1	31.96362101	-1.024025419	0.363033328	-2.820747685	0.004791187	0.028441213	down
517	IRS2	2610.138545	-1.030585264	0.188347848	-5.471712429	4.46E-08	1.56E-06	down

518	AC009041.2	247.6060328	-1.036154761	0.234408261	-4.420299672	9.86E-06	0.000170217	down
519	TDRKH	163.8565468	-1.038393698	0.22286156	-4.659366558	3.17E-06	6.46E-05	down
520	SERPINI1	64.19254944	-1.038531174	0.29157655	-3.561778804	0.000368351	0.003640771	down
521	CDH10	47.78336163	-1.039487211	0.269744475	-3.853599637	0.000116394	0.0013916	down
522	DSCAM	23.22975771	-1.040259496	0.385594831	-2.697804565	0.00697984	0.038172584	down
523	MSI1	1259.859836	-1.043183603	0.099178986	-10.51819189	7.12E-26	6.91E-23	down
524	MMP15	791.6268759	-1.046085871	0.139108708	-7.519916515	5.48E-14	6.89E-12	down
525	LAG3	24.74192008	-1.046302213	0.255843113	-4.089624299	4.32E-05	0.000609662	down
526	SLC27A6	35.55088159	-1.048982497	0.246913112	-4.248387167	2.15E-05	0.00033364	down
527	SCN1A	427.2513689	-1.049671098	0.302504766	-3.469932434	0.000520589	0.00485113	down
528	SLC38A3	124.9636367	-1.053549869	0.191431677	-5.503529423	3.72E-08	1.35E-06	down
529	TCERG1L	572.889078	-1.056445486	0.183286631	-5.763898214	8.22E-09	3.48E-07	down
530	AC064875.1	46.48061331	-1.056774259	0.369502921	-2.859988917	0.004236558	0.025803338	down
531	CCDC85C	1306.185837	-1.057709012	0.191276864	-5.529727908	3.21E-08	1.17E-06	down
532	CUEDC1	568.6276009	-1.058005153	0.177727347	-5.952967686	2.63E-09	1.21E-07	down
533	ACKR1	76.4775659	-1.059539913	0.211799369	-5.002564069	5.66E-07	1.44E-05	down
534	PDE3A	494.3369079	-1.060746763	0.170890361	-6.207177248	5.39E-10	2.99E-08	down
535	CLDN20	14.29979721	-1.063525775	0.343782036	-3.093604852	0.001977407	0.014151837	down
536	GNAO1	47.59488748	-1.065559765	0.255112851	-4.176817282	2.96E-05	0.000440419	down
537	STON2	111.8007482	-1.067607134	0.295062477	-3.618240945	0.000296612	0.003051703	down
538	SCD	11388.4265	-1.073328436	0.291763328	-3.678764023	0.000234367	0.00250891	down
539	SLIT2	3018.773408	-1.075894247	0.29084673	-3.699179457	0.000216298	0.002345067	down
540	CDHR3	18.63804293	-1.079117146	0.332062975	-3.249736431	0.00115512	0.009198045	down
541	ATP1B1	104.7266035	-1.07947674	0.225200672	-4.793399285	1.64E-06	3.68E-05	down
542	HDAC9	196.9799886	-1.079491799	0.192787424	-5.599389098	2.15E-08	8.19E-07	down

543	WLS	4379.681042	-1.079582478	0.209365586	-5.156446664	2.52E-07	6.99E-06	down
544	NAB2	1448.713298	-1.07984565	0.198676826	-5.435186739	5.47E-08	1.88E-06	down
545	ARHGEF37	99.87038604	-1.080086399	0.205151891	-5.264813286	1.40E-07	4.24E-06	down
546	AC092675.1	22.5774845	-1.080737701	0.327282239	-3.30215811	0.00095944	0.007992619	down
547	INSM1	69.85336629	-1.08111093	0.359746081	-3.005205576	0.002654014	0.01788758	down
548	GVQW3	335.8091519	-1.081671448	0.153876056	-7.029498129	2.07E-12	1.86E-10	down
549	AL683813.1	46.28831904	-1.08224016	0.204303745	-5.297211566	1.18E-07	3.62E-06	down
550	AC004492.1	11.77150492	-1.082556583	0.368356309	-2.938884327	0.00329396	0.021264526	down
551	AC079416.1	8.358473284	-1.083410341	0.413761527	-2.618441468	0.008833244	0.046057283	down
552	ARHGEF4	32.84905358	-1.085257033	0.305966091	-3.546984664	0.000389667	0.003818102	down
553	MIR641	12.63893181	-1.088158534	0.364402278	-2.986146356	0.002825174	0.018810781	down
554	MAPK8IP1	678.872606	-1.090943821	0.122979708	-8.870925457	7.25E-19	2.20E-16	down
555	NOVA1	768.9154638	-1.091435711	0.1548791	-7.047017386	1.83E-12	1.66E-10	down
556	CDC42EP4	1069.840955	-1.096418796	0.270886767	-4.047517012	5.18E-05	0.000707777	down
557	CASC10	500.4916835	-1.09865807	0.236823817	-4.639136733	3.50E-06	7.03E-05	down
558	LYNX1	41.49885698	-1.101689748	0.327577109	-3.36314632	0.000770595	0.006731054	down
559	FBLN2	328.4966064	-1.101700543	0.328882193	-3.349833368	0.000808602	0.006991059	down
560	C6orf201	10.84375665	-1.102160732	0.400938414	-2.748952689	0.005978602	0.033983893	down
561	AL391807.1	91.00502225	-1.102489626	0.21764924	-5.065442103	4.07E-07	1.07E-05	down
562	TCF7L1	876.1151103	-1.103878248	0.140894459	-7.834788237	4.70E-15	7.59E-13	down
563	NRARP	92.42339566	-1.104569883	0.302759613	-3.648339591	0.000263941	0.002770152	down
564	SLC47A1	21.83609272	-1.105048628	0.401709938	-2.750862062	0.005943867	0.033833679	down
565	ST6GALNAC6	13.44914974	-1.107177183	0.345724996	-3.202479414	0.0013625	0.010508284	down
566	AC004696.1	12.48228923	-1.108321571	0.359219274	-3.085362201	0.002033044	0.014438371	down
567	GPRC5B	1604.596204	-1.109650029	0.135167887	-8.209420569	2.22E-16	4.35E-14	down

568	MBOAT1	201.5611088	-1.112160842	0.23871381	-4.65897152	3.18E-06	6.46E-05	down
569	SEMA3B	269.2874499	-1.113551828	0.293355706	-3.7959099	0.000147103	0.001690272	down
570	HIST1H2BD	38.79520114	-1.116567075	0.317980046	-3.511437552	0.00044569	0.004278499	down
571	SOX8	509.4543991	-1.121789684	0.310386676	-3.614168291	0.000301313	0.0030907	down
572	AC004540.2	44.92601188	-1.123963456	0.263008676	-4.273484325	1.92E-05	0.000304045	down
573	SLC25A34	18.92965393	-1.125320255	0.270651268	-4.157823686	3.21E-05	0.00047302	down
574	SLC25A18	369.2548655	-1.125740817	0.144777189	-7.775678095	7.50E-15	1.17E-12	down
575	AC024560.2	9.77605921	-1.125986102	0.384178306	-2.930894546	0.003379875	0.021695345	down
576	BEST1	15.73115143	-1.137786337	0.362395431	-3.139626605	0.001691633	0.01250212	down
577	PLCB4	486.3028606	-1.138834325	0.200879515	-5.669240719	1.43E-08	5.81E-07	down
578	AC010530.1	9.134044998	-1.140073501	0.426865113	-2.670805054	0.007566958	0.040585978	down
579	DHCR7	573.6126157	-1.140502687	0.309059645	-3.690234891	0.000224047	0.00241622	down
580	HIST1H2AC	136.4398441	-1.142234942	0.239624116	-4.766777917	1.87E-06	4.13E-05	down
581	TRIM9	1118.767567	-1.14284912	0.163646639	-6.983639441	2.88E-12	2.52E-10	down
582	AGFG2	191.220024	-1.143178368	0.211277201	-5.410798521	6.27E-08	2.11E-06	down
583	FDFT1	2324.334096	-1.145492741	0.374846445	-3.055898642	0.002243871	0.01563568	down
584	ADGRV1	296.2984728	-1.146892103	0.296707022	-3.865402627	0.000110906	0.001338565	down
585	AL109955.1	8.531177151	-1.14717301	0.40757421	-2.814635918	0.004883252	0.028878275	down
586	ARHGAP26	118.8393963	-1.148753366	0.208972273	-5.497156864	3.86E-08	1.39E-06	down
587	ARHGEF10L	409.6087372	-1.149008962	0.205678785	-5.586424301	2.32E-08	8.72E-07	down
588	C4B	99.95847001	-1.149141765	0.323869467	-3.548163328	0.000387928	0.003804718	down
589	ID3	7782.617611	-1.149334896	0.229869798	-4.999938681	5.73E-07	1.45E-05	down
590	NCALD	594.6794177	-1.162121787	0.211087409	-5.505405512	3.68E-08	1.34E-06	down
591	COL26A1	725.7511598	-1.162470392	0.213527464	-5.444125871	5.21E-08	1.80E-06	down
592	AC007666.1	12.72907354	-1.162571096	0.363643974	-3.197003603	0.001388632	0.010677468	down

593	FRRS1L	10.38769483	-1.163343871	0.418143153	-2.782166493	0.005399733	0.031314146	down
594	PTPRO	764.2891542	-1.164676919	0.391216796	-2.977062671	0.002910245	0.019257556	down
595	ADGRG1	1695.668274	-1.166030283	0.25001117	-4.663912749	3.10E-06	6.34E-05	down
596	SNTG1	28.5916329	-1.169107907	0.32248101	-3.625354267	0.000288566	0.002987028	down
597	MREG	347.1542995	-1.170976389	0.273726821	-4.277901534	1.89E-05	0.000299406	down
598	CNTN4	30.36799812	-1.179407858	0.229281554	-5.143928237	2.69E-07	7.43E-06	down
599	PPP1R14C	118.789902	-1.180469559	0.340762522	-3.464200093	0.000531811	0.004933977	down
600	AC006978.1	94.52706169	-1.18145037	0.184454643	-6.405099635	1.50E-10	9.41E-09	down
601	SPCS2P4	92.89913785	-1.182167562	0.360388453	-3.280259269	0.001037117	0.008456522	down
602	AC135050.5	11.96343905	-1.184269277	0.404496173	-2.927763861	0.003414092	0.021832391	down
603	LGR5	16.07670526	-1.185138676	0.364618592	-3.250351747	0.001152623	0.00919531	down
604	ADGRB3	204.28694	-1.1863152	0.208433743	-5.691569821	1.26E-08	5.13E-07	down
605	GAREM1	195.3986501	-1.1922866	0.247771206	-4.812046638	1.49E-06	3.40E-05	down
606	RND2	263.0634502	-1.193242905	0.192240973	-6.207016569	5.40E-10	2.99E-08	down
607	CPEB2	323.6240446	-1.195802683	0.172456478	-6.933938899	4.09E-12	3.44E-10	down
608	AC009242.1	8.589034992	-1.206731497	0.452251227	-2.668276891	0.00762414	0.040840597	down
609	LINC01422	8.326789784	-1.209994084	0.420079482	-2.880393205	0.003971795	0.024565527	down
610	TMEM47	753.6505777	-1.211974318	0.157250054	-7.707306202	1.29E-14	1.83E-12	down
611	IGSF5	6.47992264	-1.212426791	0.457176847	-2.651986424	0.008001976	0.042528904	down
612	PLCXD2	66.98027868	-1.212884689	0.231133048	-5.247560654	1.54E-07	4.61E-06	down
613	NTRK3	507.6121167	-1.214342448	0.313703803	-3.870984145	0.000108397	0.001315297	down
614	AC117489.1	7.725870648	-1.214833579	0.46208914	-2.629002662	0.008563569	0.044938874	down
615	EFCC1	27.90047344	-1.217557752	0.39411398	-3.089354385	0.00200592	0.014307786	down
616	POM121L9P	19.25685698	-1.218744358	0.359801793	-3.387265934	0.000705929	0.00627017	down
617	SNORA66	9.067785428	-1.219099169	0.397240033	-3.068923241	0.002148318	0.015067826	down

618	FLRT1	9.489743719	-1.220449846	0.426697102	-2.8602253	0.004233401	0.025791827	down
619	PCDH10	1444.358633	-1.220997968	0.200271977	-6.096699014	1.08E-09	5.55E-08	down
620	PRR36	119.7263812	-1.222727877	0.267963674	-4.563035947	5.04E-06	9.63E-05	down
621	MSMO1	810.2461616	-1.223600097	0.443495217	-2.758992767	0.005797982	0.03317019	down
622	AC093915.1	10.48002207	-1.224472985	0.382173713	-3.203969673	0.001355468	0.010461969	down
623	SYBU	461.2792189	-1.227538687	0.181484584	-6.763873051	1.34E-11	1.07E-09	down
624	LETM2	50.51603038	-1.227767674	0.201901892	-6.081011225	1.19E-09	6.03E-08	down
625	AL138921.2	7.365632461	-1.227997911	0.458484328	-2.678385796	0.007397795	0.039827212	down
626	RTN1	109.413695	-1.230052293	0.215366565	-5.711435727	1.12E-08	4.63E-07	down
627	AC008013.1	14.21578822	-1.231223735	0.385680777	-3.192338867	0.001411257	0.010814677	down
628	RALGPS1	50.23284495	-1.231897319	0.234449632	-5.254422055	1.48E-07	4.46E-06	down
629	FADS2	6424.554626	-1.240256986	0.276962425	-4.478069497	7.53E-06	0.00013539	down
630	PSPC1-AS2	8.518140183	-1.243161295	0.423586823	-2.934844113	0.003337153	0.021488859	down
631	SLITRK2	54.48947575	-1.24468504	0.304891942	-4.082380895	4.46E-05	0.000626813	down
632	MMEL1	9.152683541	-1.249264687	0.457144692	-2.732755534	0.006280693	0.035258117	down
633	NKAIN3	61.32008512	-1.254414096	0.212410366	-5.905616195	3.51E-09	1.59E-07	down
634	ITGB8	2430.627966	-1.259648591	0.199653935	-6.309159859	2.81E-10	1.67E-08	down
635	C6orf118	16.10477496	-1.260638167	0.425005432	-2.966169544	0.003015342	0.019817747	down
636	AL589987.1	13.20265028	-1.261293736	0.446939378	-2.822068939	0.004771492	0.028360813	down
637	TMEM158	1232.814635	-1.261533264	0.274242999	-4.600056406	4.22E-06	8.31E-05	down
638	P2RY1	103.4423729	-1.265540522	0.245262482	-5.159943378	2.47E-07	6.90E-06	down
639	CRB1	30.19459775	-1.268360845	0.325480634	-3.896885756	9.74E-05	0.001203839	down
640	CES3	40.39103341	-1.268799121	0.255390067	-4.968083286	6.76E-07	1.68E-05	down
641	HHIPL1	35.20224142	-1.271636892	0.373959621	-3.400465777	0.000672712	0.006018049	down
642	PCDHGC3	5543.183929	-1.275230743	0.226445423	-5.631514776	1.79E-08	6.98E-07	down

643	AC144831.1	12.89176906	-1.275556173	0.353023722	-3.613230767	0.000302405	0.00309878	down
644	AC020905.1	26.43222267	-1.279036732	0.312600499	-4.091601691	4.28E-05	0.000605745	down
645	MAP2	2693.251786	-1.280702019	0.214873229	-5.960267942	2.52E-09	1.17E-07	down
646	CXCL16	121.5109783	-1.287968545	0.208844855	-6.167106891	6.96E-10	3.72E-08	down
647	TAGLN3	167.6896213	-1.288482918	0.257986594	-4.994379345	5.90E-07	1.49E-05	down
648	PCDHGC4	107.512212	-1.289459543	0.277024577	-4.654675611	3.24E-06	6.58E-05	down
649	KCNA2	100.181191	-1.292032574	0.279451466	-4.623459633	3.77E-06	7.50E-05	down
650	MACROD2	69.27270661	-1.299928062	0.244701524	-5.312300633	1.08E-07	3.38E-06	down
651	ENC1	6744.686564	-1.301624436	0.20792237	-6.260146193	3.85E-10	2.20E-08	down
652	ZNRF2	347.075493	-1.313517986	0.187620418	-7.000933041	2.54E-12	2.25E-10	down
653	SLC13A3	32.23985776	-1.313641958	0.2449567	-5.362751687	8.20E-08	2.67E-06	down
654	SKIDA1	202.1546936	-1.314285379	0.231935273	-5.666604138	1.46E-08	5.87E-07	down
655	AL022315.1	8.258167654	-1.314425021	0.427946612	-3.071469631	0.002130078	0.014945046	down
656	C2orf70	8.904631119	-1.315124931	0.42535729	-3.091812367	0.001989386	0.01422257	down
657	KCNIP1	567.2756592	-1.316873403	0.258919891	-5.086026399	3.66E-07	9.76E-06	down
658	MT1F	16.57196004	-1.321105262	0.509656415	-2.592148793	0.009537851	0.048843105	down
659	NDRG2	141.3746887	-1.321209783	0.287910053	-4.588967178	4.45E-06	8.66E-05	down
660	AC092111.1	13.78841342	-1.322601622	0.349009559	-3.789585667	0.000150899	0.001727066	down
661	AC092958.1	13.10498585	-1.324331341	0.332150594	-3.987141276	6.69E-05	0.000875081	down
662	EPPK1	8.849566574	-1.325560096	0.502092146	-2.640073355	0.008288808	0.043790459	down
663	AC091181.1	6.11575833	-1.327028681	0.509743639	-2.603325631	0.009232422	0.047638454	down
664	THSD7A	190.4650547	-1.327089985	0.257349219	-5.156767103	2.51E-07	6.99E-06	down
665	FOS	245.0843318	-1.329469839	0.34084772	-3.90048037	9.60E-05	0.001189712	down
666	FAIM2	205.7640312	-1.330274592	0.17041876	-7.805916369	5.91E-15	9.40E-13	down
667	ITGB4	3054.561952	-1.341518031	0.271772743	-4.936175787	7.97E-07	1.94E-05	down

668	CTNND2	1694.581202	-1.34219163	0.227268656	-5.905748971	3.51E-09	1.59E-07	down
669	FAM124A	63.74701489	-1.343758746	0.294920943	-4.556335441	5.21E-06	9.90E-05	down
670	RAB7B	141.371978	-1.345786949	0.345382423	-3.896512564	9.76E-05	0.001204963	down
671	DIRAS2	166.5208478	-1.347240247	0.312511208	-4.31101417	1.63E-05	0.000262813	down
672	LSAMP	360.3071649	-1.347756906	0.187817785	-7.175874785	7.18E-13	7.02E-11	down
673	SLC26A7	31.58570133	-1.353566318	0.425294029	-3.182660053	0.001459288	0.011122001	down
674	SEMA5B	447.3175424	-1.354464793	0.269965742	-5.017172864	5.24E-07	1.35E-05	down
675	NKAIN3-IT1	263.8901041	-1.362988337	0.27996566	-4.868412563	1.12E-06	2.65E-05	down
676	NFIA	300.150639	-1.365988429	0.182757908	-7.47430546	7.76E-14	9.46E-12	down
677	FZD4	831.5987354	-1.371567144	0.199844394	-6.863175486	6.73E-12	5.53E-10	down
678	RNF112	39.40153138	-1.371903667	0.262304001	-5.230204883	1.69E-07	5.03E-06	down
679	DOK5	112.0286663	-1.382431588	0.533003462	-2.593663432	0.00949594	0.048720753	down
680	AC125613.1	49.622983	-1.383191308	0.180379722	-7.668219521	1.74E-14	2.38E-12	down
681	SLC5A4-AS1	12.6914524	-1.386507823	0.474559342	-2.921674281	0.003481554	0.022162616	down
682	PPL	154.7141912	-1.389009322	0.525213833	-2.644654872	0.008177428	0.043269387	down
683	AL078644.1	5.843108752	-1.39340121	0.536889666	-2.595321343	0.009450252	0.048516535	down
684	ABLIM2	19.42527388	-1.394348531	0.390324195	-3.572283118	0.000353883	0.003525148	down
685	ARHGEF6	2922.118495	-1.395691039	0.256637104	-5.438383683	5.38E-08	1.85E-06	down
686	KCNF1	28.79481016	-1.396010959	0.427933458	-3.262215032	0.001105453	0.00892825	down
687	ADCYAP1R1	527.5063189	-1.396237969	0.488215019	-2.859883278	0.00423797	0.025804216	down
688	MLC1	4275.192162	-1.398505366	0.200344962	-6.980486802	2.94E-12	2.56E-10	down
689	ILDR2	706.1293433	-1.399112696	0.487246581	-2.871467447	0.004085709	0.025147858	down
690	GRHL1	35.71605628	-1.402550837	0.393858493	-3.561052668	0.000369371	0.003649084	down
691	SEMA6A-AS1	67.50983533	-1.403645072	0.225927339	-6.212816375	5.20E-10	2.90E-08	down
692	C5AR1	16.0611184	-1.404389134	0.500581699	-2.805514336	0.005023635	0.029553951	down

693	KCNQ4	8.864783548	-1.406573755	0.463601083	-3.034017407	0.002413205	0.01652161	down
694	AC135977.1	9.172956904	-1.412076373	0.545418031	-2.58898	0.009626069	0.049220588	down
695	AP001528.2	29.35520811	-1.413362864	0.286277235	-4.937042456	7.93E-07	1.94E-05	down
696	FMN2	224.0637238	-1.414226833	0.166519898	-8.492839912	2.02E-17	4.61E-15	down
697	AC005154.4	5.707471053	-1.414238124	0.487780136	-2.899335214	0.003739549	0.023370457	down
698	NRG2	84.23299023	-1.414280963	0.171304042	-8.255969592	1.51E-16	3.07E-14	down
699	ANKRD55	9.475583339	-1.41722876	0.526730885	-2.690612607	0.007132096	0.03878966	down
700	AC006111.2	5.942847967	-1.422688245	0.500801375	-2.840823359	0.004499723	0.027154374	down
701	CNTFR	54.75812532	-1.426045969	0.41327367	-3.450609301	0.000559323	0.005153108	down
702	ZMYND15	5.036320839	-1.426191149	0.525284786	-2.715081777	0.006625941	0.03680054	down
703	SEMA6A	1587.434522	-1.427373883	0.184286389	-7.745411304	9.53E-15	1.46E-12	down
704	ZNF474	5.991937117	-1.42887508	0.53266675	-2.682493471	0.007307558	0.039508546	down
705	EPHB3	1723.141063	-1.431156031	0.197961047	-7.22948304	4.85E-13	5.01E-11	down
706	B3GAT1	582.3393006	-1.431430584	0.257945025	-5.549363017	2.87E-08	1.07E-06	down
707	GAREM2	564.6772712	-1.433105932	0.284257576	-5.041575153	4.62E-07	1.21E-05	down
708	ARC	115.9211679	-1.433192464	0.375608507	-3.815654967	0.000135822	0.001585579	down
709	CSRNP3	286.6836608	-1.433751051	0.196884167	-7.28220593	3.28E-13	3.58E-11	down
710	SREBF2	3543.049035	-1.434602326	0.357445001	-4.013491086	5.98E-05	0.000799306	down
711	PRDM8	68.2616109	-1.436124315	0.278248045	-5.161309625	2.45E-07	6.86E-06	down
712	SNORA5A	6.030807507	-1.443449122	0.536206998	-2.691962482	0.007103294	0.03871257	down
713	CLU	9831.745969	-1.445962642	0.151387248	-9.551416412	1.28E-21	6.20E-19	down
714	PCDH15	16.47840505	-1.449311678	0.536446926	-2.701686986	0.006898868	0.037831361	down
715	SLC5A3	2220.933259	-1.449864839	0.267440171	-5.421268001	5.92E-08	2.00E-06	down
716	BMP8A	7.033553107	-1.45924078	0.557124858	-2.619234737	0.008812728	0.046017767	down
717	FABP7	2712.729485	-1.462595328	0.274075939	-5.33646015	9.48E-08	3.01E-06	down

718	UBE2QL1	32.49796994	-1.463398082	0.353304211	-4.142034072	3.44E-05	0.000502441	down
719	HAS3	110.7603499	-1.463587353	0.225614285	-6.487121836	8.75E-11	5.75E-09	down
720	TMTC2	619.0261396	-1.465111563	0.28376773	-5.163066157	2.43E-07	6.80E-06	down
721	TPPP3	39.71046707	-1.466543047	0.314000728	-4.670508432	3.00E-06	6.18E-05	down
722	AL024508.2	5.14234298	-1.466933338	0.525537666	-2.791300095	0.005249677	0.030585298	down
723	AC068987.3	10.24798791	-1.469250303	0.45044133	-3.261801717	0.001107066	0.008935429	down
724	KCNJ6	201.8738526	-1.469988287	0.273042647	-5.383731453	7.30E-08	2.42E-06	down
725	LINC01715	5.560428477	-1.471810633	0.508489259	-2.894477332	0.003797903	0.023669761	down
726	FGFR1	5299.802531	-1.472025835	0.16408918	-8.970889076	2.94E-19	9.98E-17	down
727	RPS27P25	9.140532587	-1.479030679	0.399887398	-3.698617879	0.000216777	0.002347761	down
728	GUCY1B1	211.649697	-1.483156908	0.270550584	-5.481994845	4.21E-08	1.49E-06	down
729	LINC01748	9.101033517	-1.484770673	0.504401078	-2.943631048	0.003243865	0.021014421	down
730	SRGAP3	877.0969714	-1.486121429	0.138437379	-10.73497233	6.97E-27	8.35E-24	down
731	ABTB2	182.3183789	-1.489677786	0.24739236	-6.021518969	1.73E-09	8.25E-08	down
732	INKA2	28.62696158	-1.489779403	0.357579068	-4.166293658	3.10E-05	0.000458444	down
733	AC046134.1	4.711017177	-1.490204603	0.561200256	-2.655388318	0.007921716	0.042146344	down
734	TTBK1	41.43524537	-1.491660133	0.366330891	-4.071892839	4.66E-05	0.000649	down
735	NPIPA3	6.405053866	-1.499846011	0.475799457	-3.152265072	0.001620091	0.012074187	down
736	AC110619.1	18.90263879	-1.500293943	0.401977246	-3.732285742	0.00018975	0.002099729	down
737	CEND1	283.0464716	-1.50059423	0.297439778	-5.045035472	4.53E-07	1.19E-05	down
738	CACNA1C	62.68017101	-1.507382886	0.343609707	-4.386904258	1.15E-05	0.000194436	down
739	SOX6	296.7979275	-1.511245773	0.267364685	-5.652376161	1.58E-08	6.32E-07	down
740	CKB	7185.077283	-1.518087782	0.175176555	-8.666044276	4.47E-18	1.15E-15	down
741	BAIAP3	18.90308957	-1.521621383	0.541369961	-2.810686765	0.004943589	0.029167317	down
742	LRRN3	328.6265697	-1.529852868	0.418451813	-3.655983365	0.000256198	0.002702822	down

743	AC087623.1	40.61963078	-1.531422062	0.206943514	-7.400193582	1.36E-13	1.56E-11	down
744	PRKCB	258.1614233	-1.532641216	0.315475012	-4.858201621	1.18E-06	2.75E-05	down
745	FGD3	24.59058723	-1.533520734	0.364724569	-4.204599486	2.62E-05	0.000396386	down
746	UNC13D	30.96435033	-1.540119323	0.307269599	-5.012273671	5.38E-07	1.38E-05	down
747	FUT8-AS1	21.31597085	-1.541982363	0.368867917	-4.18031033	2.91E-05	0.000434575	down
748	FRMD3	20.97054774	-1.546779643	0.339567054	-4.555152291	5.23E-06	9.94E-05	down
749	AK5	128.501805	-1.550183303	0.369403048	-4.196455099	2.71E-05	0.000407709	down
750	LINC02044	6.534152868	-1.557458549	0.523243955	-2.976543797	0.002915174	0.01926513	down
751	PLEKHA7	554.5701562	-1.558028719	0.465901734	-3.344114443	0.000825457	0.007094608	down
752	NDST4	6.093221312	-1.563907378	0.531397609	-2.943007931	0.003250401	0.021045288	down
753	CSPG5	89.96361793	-1.574356784	0.308417104	-5.104635128	3.31E-07	8.93E-06	down
754	PLCE1-AS1	5.097318625	-1.57563974	0.60260037	-2.614734106	0.008929694	0.04641754	down
755	OGDHL	434.1521052	-1.581870971	0.224716894	-7.039394951	1.93E-12	1.75E-10	down
756	HIST2H2BE	137.2551089	-1.581941139	0.263379325	-6.006322394	1.90E-09	9.03E-08	down
757	OR7E14P	15.491524	-1.581992158	0.342198488	-4.623024975	3.78E-06	7.51E-05	down
758	NOS1AP	255.1804292	-1.583007699	0.245523631	-6.447475927	1.14E-10	7.30E-09	down
759	GLS2	4.193011998	-1.58827553	0.592247746	-2.681775559	0.007323257	0.039582916	down
760	AC009166.2	11.28657809	-1.58835037	0.427792621	-3.712898004	0.000204899	0.002234579	down
761	CHD5	28.4913424	-1.588944351	0.389308339	-4.081454701	4.48E-05	0.000628449	down
762	CEBPA	8.080970334	-1.592597296	0.604269336	-2.635575234	0.00839948	0.044283226	down
763	ST6GALNAC5	19.08095531	-1.603486079	0.396999859	-4.039009189	5.37E-05	0.000728132	down
764	ZBTB7C	25.68687652	-1.610026329	0.338461134	-4.756901657	1.97E-06	4.30E-05	down
765	PLEKHB1	588.6463199	-1.615654449	0.261054017	-6.188966045	6.06E-10	3.29E-08	down
766	DOCK10	376.072076	-1.621421084	0.212764269	-7.620739559	2.52E-14	3.36E-12	down
767	GPM6B	4913.007113	-1.62476385	0.182006543	-8.926952986	4.38E-19	1.44E-16	down

768	IDI1	555.7179595	-1.625004497	0.434776593	-3.737562055	0.000185813	0.002065144	down
769	ZNF467	12.19683563	-1.627356915	0.597514277	-2.723544824	0.006458545	0.036037938	down
770	PRSS35	7.739423074	-1.628291937	0.617644506	-2.636293082	0.00838173	0.044212541	down
771	LINC01342	6.551664326	-1.629350687	0.491039663	-3.31816513	0.000906109	0.007645787	down
772	C1QL1	385.3882907	-1.635259448	0.272888595	-5.99240672	2.07E-09	9.79E-08	down
773	COL11A1	1435.559658	-1.638232259	0.171988602	-9.525237344	1.65E-21	7.80E-19	down
774	MCF2L-AS1	9.270330853	-1.638969768	0.440749959	-3.718593125	0.000200335	0.002193206	down
775	NLGN3	260.5738351	-1.639182282	0.291883181	-5.61588468	1.96E-08	7.48E-07	down
776	PLEKHA6	192.8425199	-1.646660049	0.271634406	-6.062045211	1.34E-09	6.66E-08	down
777	NCKAP5	54.51018998	-1.653912252	0.377109419	-4.38576225	1.16E-05	0.000195297	down
778	HIST1H3E	43.58848702	-1.655845065	0.213440033	-7.757893587	8.64E-15	1.33E-12	down
779	PHYHIPL	25.07941688	-1.655995288	0.31414057	-5.271510415	1.35E-07	4.11E-06	down
780	AL139241.1	12.42418197	-1.662059766	0.437805273	-3.796344787	0.000146845	0.001689218	down
781	AC021739.5	8.631367051	-1.66502838	0.557838733	-2.984784456	0.002837782	0.01888238	down
782	PTGS1	9.896815763	-1.670669874	0.471394801	-3.544099067	0.000393957	0.003854571	down
783	AP001528.3	26.26883473	-1.674187622	0.345330363	-4.848075362	1.25E-06	2.89E-05	down
784	ATP1B2	770.5253661	-1.675915046	0.183456901	-9.135197648	6.53E-20	2.33E-17	down
785	AL136366.1	67.24689175	-1.677105973	0.199374433	-8.411840701	4.04E-17	9.03E-15	down
786	F3	935.0358689	-1.678672662	0.372494112	-4.506575026	6.59E-06	0.000121177	down
787	SYNE3	76.68350737	-1.678837234	0.458824293	-3.658998136	0.000253203	0.002679558	down
788	ESPN	23.88608777	-1.684096903	0.335684774	-5.016899875	5.25E-07	1.35E-05	down
789	FMOD	5.864685057	-1.684526377	0.574579551	-2.931754834	0.003370527	0.021648991	down
790	PI15	437.7900914	-1.686602428	0.301017935	-5.602996475	2.11E-08	8.03E-07	down
791	BLOC1S1-RDH5	37.02079482	-1.69420521	0.244637891	-6.925358948	4.35E-12	3.63E-10	down
792	ADAM33	12.53742155	-1.696080195	0.627002425	-2.705061619	0.006829172	0.037582098	down

793	TMEM130	17.12960334	-1.699294267	0.464036568	-3.661983523	0.00025027	0.002659575	down
794	TRIM47	311.5380979	-1.699757975	0.238925878	-7.114164411	1.13E-12	1.07E-10	down
795	HNRNPA1P41	5.17004695	-1.702173457	0.558307819	-3.0488082	0.002297511	0.01590062	down
796	SEMA6D	2454.645839	-1.711963652	0.231794314	-7.385701677	1.52E-13	1.72E-11	down
797	C1orf226	534.8984955	-1.713290645	0.198357217	-8.637400114	5.75E-18	1.46E-15	down
798	SPATA46	32.46597688	-1.713399692	0.331702639	-5.165468978	2.40E-07	6.73E-06	down
799	YBX2	4.162254179	-1.715382691	0.583619468	-2.939214307	0.003290455	0.021262122	down
800	LINC01508	46.42541977	-1.732244852	0.345826005	-5.009006919	5.47E-07	1.40E-05	down
801	SCRG1	25.2960518	-1.732584408	0.473744415	-3.65721337	0.000254972	0.002694078	down
802	TMPRSS5	84.39788602	-1.732938061	0.279052877	-6.210070582	5.30E-10	2.95E-08	down
803	ACAT2	348.6332901	-1.739618123	0.481500072	-3.612913527	0.000302776	0.003101014	down
804	APC2	1554.053442	-1.740166485	0.126975318	-13.70476173	9.51E-43	9.31E-39	down
805	COL4A6	483.9392178	-1.741605483	0.136417194	-12.76675936	2.51E-37	9.17E-34	down
806	MTTP	102.4954316	-1.758553499	0.24475912	-7.184833388	6.73E-13	6.65E-11	down
807	SLC15A3	12.75081662	-1.75895564	0.458089861	-3.839761126	0.000123154	0.001462123	down
808	ZFHX4-AS1	115.6406469	-1.7648261	0.242048975	-7.291194259	3.07E-13	3.38E-11	down
809	NAT8L	1154.330431	-1.776249639	0.192275702	-9.238034865	2.51E-20	9.83E-18	down
810	EDNRB	3003.527755	-1.784477691	0.429657272	-4.153258436	3.28E-05	0.000480822	down
811	KCNJ2-AS1	66.76403405	-1.788163313	0.399768713	-4.472994648	7.71E-06	0.000137641	down
812	SLIT3	361.234886	-1.791028408	0.438944354	-4.080308569	4.50E-05	0.000630686	down
813	THSD1	81.22399217	-1.791167086	0.329755212	-5.431808259	5.58E-08	1.91E-06	down
814	GRM1	5.101859611	-1.808278062	0.691829438	-2.613762817	0.008955118	0.046502208	down
815	SCG2	3407.703297	-1.809289155	0.237366874	-7.622332139	2.49E-14	3.34E-12	down
816	ADRA2C	13.16059625	-1.809813225	0.469930668	-3.851234549	0.000117524	0.00140264	down
817	VWA3B	5.701646445	-1.815468066	0.511336073	-3.55044004	0.000384588	0.003781067	down

818	DKFZp451B082	4.872306615	-1.817601732	0.643280563	-2.825519434	0.004720402	0.028152347	down
819	ERBB4	185.4806928	-1.819749376	0.253704474	-7.172712996	7.35E-13	7.13E-11	down
820	PRKG1	10.2005262	-1.841217275	0.422281505	-4.360165557	1.30E-05	0.000218333	down
821	AC131392.1	37.69303853	-1.841236982	0.504893872	-3.646780216	0.000265547	0.002785574	down
822	COL2A1	59.87606325	-1.847188298	0.402221566	-4.592464587	4.38E-06	8.55E-05	down
823	WWC1	724.2408582	-1.854011819	0.250912372	-7.3890809	1.48E-13	1.68E-11	down
824	ITGA7	4261.573141	-1.857743972	0.256372492	-7.246268729	4.28E-13	4.52E-11	down
825	RIMS4	356.7372723	-1.858740715	0.216836094	-8.572100166	1.02E-17	2.46E-15	down
826	AP000889.1	3.3231231	-1.861531348	0.714805884	-2.604247376	0.009207627	0.04752256	down
827	MIR4697HG	641.3521913	-1.862958127	0.20956339	-8.889711728	6.13E-19	1.98E-16	down
828	MYORG	326.3410495	-1.86679712	0.420390873	-4.440622386	8.97E-06	0.000156635	down
829	ZCCHC12	37.34674764	-1.877633948	0.342974547	-5.474557701	4.39E-08	1.55E-06	down
830	PDIA2	3.050730238	-1.879284887	0.716715832	-2.622078098	0.00873954	0.045697426	down
831	GRIA1	1159.25764	-1.879343188	0.203292761	-9.244516034	2.36E-20	9.62E-18	down
832	LINC02538	4.744483714	-1.885645304	0.620558138	-3.038627954	0.002376582	0.016331278	down
833	COL6A3	245.5328879	-1.901050504	0.634014394	-2.998434296	0.002713707	0.018235571	down
834	WSCD1	548.9715413	-1.901688981	0.386884475	-4.915392329	8.86E-07	2.15E-05	down
835	CX3CL1	369.6299315	-1.912238722	0.205256927	-9.316317626	1.20E-20	5.00E-18	down
836	SLC27A3	501.0495844	-1.9155494	0.280669092	-6.824938891	8.80E-12	7.08E-10	down
837	DCLK2	1539.287337	-1.915690611	0.273396448	-7.007006205	2.43E-12	2.16E-10	down
838	AC005740.4	4.888718195	-1.918372809	0.676089926	-2.837452141	0.004547516	0.02737082	down
839	ADGRB1	443.4763369	-1.923543916	0.289126271	-6.652954475	2.87E-11	2.10E-09	down
840	KCNJ2	494.1362714	-1.937344902	0.446207582	-4.34180184	1.41E-05	0.000234125	down
841	LINC02199	3.462049446	-1.937589321	0.710471273	-2.727188834	0.006387647	0.035730463	down
842	AL031686.1	4.352584829	-1.938267931	0.715051679	-2.710668316	0.006714776	0.037192479	down

843	ENHO	50.46794863	-1.949272906	0.350294654	-5.564666447	2.63E-08	9.79E-07	down
844	A2M	1174.392668	-1.951693021	0.376889292	-5.178425239	2.24E-07	6.35E-06	down
845	RMST	143.8167432	-1.955797154	0.198942843	-9.830950057	8.28E-23	5.27E-20	down
846	STX17-AS1	4.381274487	-1.958765365	0.60797911	-3.221764255	0.001274039	0.009950407	down
847	IFI44L	8.473967498	-1.973546359	0.518043683	-3.80961379	0.000139184	0.001614773	down
848	PCAT14	18.76981196	-1.974200344	0.605928673	-3.258139829	0.001121451	0.009007444	down
849	STOX1	15.00062652	-1.979682203	0.406817636	-4.866264459	1.14E-06	2.66E-05	down
850	BRINP1	5.230192431	-1.980438579	0.614160683	-3.224626116	0.001261373	0.009863865	down
851	SETBP1	637.0611258	-1.98134813	0.207420785	-9.552312385	1.27E-21	6.20E-19	down
852	IGSF9B	563.1842417	-1.985003078	0.191766432	-10.35114988	4.13E-25	3.51E-22	down
853	ASCL1	274.5747973	-1.985914581	0.489820026	-4.054376046	5.03E-05	0.000691563	down
854	TENT5B	73.37941193	-1.991102856	0.441581653	-4.509025329	6.51E-06	0.000119895	down
855	MAOB	36.56434365	-1.994799901	0.309174441	-6.452020728	1.10E-10	7.13E-09	down
856	PCDH7	192.0805156	-1.995419878	0.486709706	-4.099815256	4.13E-05	0.000587499	down
857	RDH5	55.99826946	-2.001813607	0.318589402	-6.283365335	3.31E-10	1.92E-08	down
858	MOB3B	47.27453108	-2.006131257	0.463626679	-4.327040159	1.51E-05	0.000247354	down
859	RNF157-AS1	47.68971005	-2.009565141	0.218575725	-9.193908175	3.79E-20	1.40E-17	down
860	AL445307.1	5.94827541	-2.013199903	0.507147155	-3.969656312	7.20E-05	0.000931666	down
861	EFL1P1	2.966327038	-2.013425064	0.70341647	-2.862351323	0.004205105	0.025673206	down
862	AC018659.2	6.86819177	-2.013937853	0.525617459	-3.831565748	0.00012733	0.00150255	down
863	ANGPTL1	32.92484966	-2.01737156	0.449744929	-4.485590453	7.27E-06	0.00013125	down
864	LRRN2	118.3659907	-2.023563056	0.223331999	-9.060784217	1.30E-19	4.47E-17	down
865	ID4	355.703654	-2.028146331	0.518658259	-3.910371226	9.22E-05	0.001153523	down
866	GDPD2	157.1667616	-2.029566401	0.264105602	-7.684677598	1.53E-14	2.12E-12	down
867	AC099792.1	18.64117114	-2.035878175	0.445414351	-4.570751191	4.86E-06	9.32E-05	down

868	HEPACAM	6.982622499	-2.047210861	0.761166055	-2.689571937	0.007154373	0.038876482	down
869	C11orf87	6.703437484	-2.062198829	0.752948966	-2.738829484	0.006165834	0.034764089	down
870	GAS1RR	3.024095741	-2.064778003	0.780458424	-2.645596407	0.008154705	0.043205293	down
871	KLF15	62.00107786	-2.079790324	0.406012094	-5.122483682	3.02E-07	8.22E-06	down
872	ELMO1	965.0590059	-2.081084948	0.513909804	-4.049514005	5.13E-05	0.000703237	down
873	EGR2	24.07962013	-2.088745311	0.634283294	-3.293079495	0.000990965	0.008188729	down
874	LHFPL3	17.34262865	-2.092176431	0.49069497	-4.263700584	2.01E-05	0.000315516	down
875	RIPOR3	40.77985383	-2.095243261	0.344410367	-6.083566187	1.18E-09	5.95E-08	down
876	C21orf62	45.13356087	-2.096925106	0.335908817	-6.242542621	4.31E-10	2.46E-08	down
877	PTPRZ1	3213.664892	-2.098424512	0.258655191	-8.112825815	4.95E-16	8.99E-14	down
878	LONRF2	1427.327824	-2.103865313	0.288715259	-7.28699036	3.17E-13	3.47E-11	down
879	BMPER	18.2724306	-2.107137408	0.399489268	-5.274578262	1.33E-07	4.04E-06	down
880	RHBDL3	513.9218827	-2.109741826	0.28625093	-7.370253168	1.70E-13	1.91E-11	down
881	AC021739.2	21.10641439	-2.112321559	0.536274311	-3.938882612	8.19E-05	0.001043049	down
882	AC007344.1	15.32371681	-2.115993069	0.516813543	-4.094306539	4.23E-05	0.000599968	down
883	AC120049.1	20.78017913	-2.119058232	0.388904704	-5.448785299	5.07E-08	1.76E-06	down
884	NRXN1	7.857755703	-2.129081645	0.49780463	-4.276942229	1.89E-05	0.000300464	down
885	PRIMA1	14.48425836	-2.130541424	0.434251901	-4.906233956	9.28E-07	2.23E-05	down
886	GPR158	46.60218833	-2.141016904	0.421281678	-5.082150534	3.73E-07	9.95E-06	down
887	HES6	1150.158237	-2.151582644	0.565780579	-3.802857018	0.000143037	0.00165288	down
888	RND1	38.12882901	-2.153702045	0.324573318	-6.63548703	3.23E-11	2.35E-09	down
889	APLNR	53.72991144	-2.156132786	0.413279135	-5.217134381	1.82E-07	5.34E-06	down
890	OPRD1	2.888744997	-2.156294857	0.826977404	-2.607441082	0.009122177	0.047177201	down
891	AC007448.4	2.915101088	-2.160243575	0.762251542	-2.834029786	0.004596505	0.027583093	down
892	SLCO1C1	16.08844011	-2.167262243	0.432428502	-5.011839486	5.39E-07	1.38E-05	down

893	RASGEF1B	6.849394454	-2.183575548	0.809320249	-2.69803647	0.00697498	0.038166505	down
894	VSTM4	99.20703389	-2.184735755	0.302196736	-7.229514737	4.85E-13	5.01E-11	down
895	EPHA7	35.84042105	-2.193101597	0.388747903	-5.641449337	1.69E-08	6.72E-07	down
896	ANKFN1	71.86562956	-2.195749804	0.388056114	-5.658330644	1.53E-08	6.13E-07	down
897	GATM	100.6052475	-2.202851944	0.211241111	-10.42814033	1.84E-25	1.71E-22	down
898	B3GAT2	15.75785133	-2.203368595	0.342709189	-6.429266169	1.28E-10	8.11E-09	down
899	WARS2-IT1	4.549128354	-2.208501716	0.644314192	-3.42767821	0.000608767	0.005531056	down
900	AC025154.2	21.24161179	-2.214210737	0.483999083	-4.574824242	4.77E-06	9.16E-05	down
901	COL9A3	480.5153392	-2.218414104	0.42172162	-5.26037556	1.44E-07	4.33E-06	down
902	GADD45G	287.9397762	-2.220743303	0.487977587	-4.550912501	5.34E-06	0.00010098	down
903	CITED1	7.668622721	-2.223123693	0.690560086	-3.219305225	0.001285016	0.010021661	down
904	LINC01750	58.63905355	-2.226939796	0.288571958	-7.717103945	1.19E-14	1.72E-12	down
905	FAM107A	3.961012746	-2.231210639	0.675603258	-3.302545707	0.000958115	0.007992619	down
906	AL359198.1	4.32652916	-2.232510615	0.697527674	-3.200605079	0.001371394	0.010564867	down
907	LPAR3	12.71552943	-2.236133111	0.547848153	-4.081665876	4.47E-05	0.000628311	down
908	AC107294.2	18.33117229	-2.237851579	0.434535698	-5.149983277	2.61E-07	7.22E-06	down
909	AL158064.1	19.09806601	-2.238925224	0.429813681	-5.209059934	1.90E-07	5.53E-06	down
910	FLVCR2	6.068525171	-2.271861395	0.675879901	-3.361338887	0.000775656	0.006761625	down
911	SLC1A2	246.4854446	-2.273267913	0.303090799	-7.500286772	6.37E-14	7.86E-12	down
912	ELAVL3	3.084891741	-2.282002668	0.706945279	-3.227976389	0.001246693	0.009793175	down
913	CLEC19A	7.18673733	-2.289557724	0.672113775	-3.406503198	0.000658008	0.005915098	down
914	NYAP1	16.0684352	-2.299106777	0.459733791	-5.000952338	5.70E-07	1.45E-05	down
915	SYT12	324.5578584	-2.302568707	0.308781275	-7.456957043	8.85E-14	1.05E-11	down
916	PTGDS	4.43595383	-2.307554244	0.692224118	-3.333536329	0.000857495	0.007311328	down
917	AL591686.2	6.604265278	-2.310612276	0.762993678	-3.028350488	0.002458927	0.016783847	down

918	SNRPGP10	37.38316043	-2.341623457	0.383615697	-6.104086651	1.03E-09	5.34E-08	down
919	AC091078.1	11.3185954	-2.343293654	0.451100466	-5.194615906	2.05E-07	5.92E-06	down
920	CTNNA3	34.7934774	-2.34957349	0.303462539	-7.742548702	9.74E-15	1.48E-12	down
921	AP003068.4	5.343884614	-2.35255556	0.586761972	-4.009386556	6.09E-05	0.00080908	down
922	TMEM163	5.423740584	-2.36533072	0.700814535	-3.375116529	0.000737844	0.006481126	down
923	CDH8	11.23283798	-2.373737477	0.567820158	-4.1804389	2.91E-05	0.000434575	down
924	ABAT	504.6277235	-2.381554291	0.225311028	-10.57007424	4.10E-26	4.32E-23	down
925	PDZRN4	2.89431635	-2.395684462	0.737433543	-3.248678453	0.001159425	0.009228711	down
926	AC046168.2	2.183783224	-2.406619411	0.928563717	-2.591765506	0.009548483	0.048885256	down
927	AL161910.1	21.10363566	-2.415380914	0.412047291	-5.861902181	4.58E-09	2.01E-07	down
928	ADGRA1	5.153628332	-2.415720298	0.750350933	-3.219453979	0.00128435	0.010021661	down
929	PLCH2	4.41894638	-2.430006574	0.930427064	-2.611710974	0.009009038	0.04668695	down
930	SLC6A11	946.0929929	-2.43562417	0.368360771	-6.612061758	3.79E-11	2.73E-09	down
931	FAM181B	39.33471872	-2.435706971	0.555882664	-4.381692631	1.18E-05	0.000198487	down
932	KCNB1	12.15638432	-2.436823622	0.683214303	-3.566704636	0.000361499	0.003585227	down
933	NCAN	532.7073494	-2.444379463	0.31886416	-7.665895921	1.78E-14	2.41E-12	down
934	UNC80	315.2866557	-2.444496078	0.241629199	-10.11672465	4.66E-24	3.38E-21	down
935	MGC32805	2.996977808	-2.450395609	0.755775649	-3.242226201	0.001185998	0.009388847	down
936	FGFR3	890.6624678	-2.451708277	0.445929135	-5.497977331	3.84E-08	1.39E-06	down
937	KLHDC8A	783.9268892	-2.454210791	0.281110464	-8.730414206	2.54E-18	6.89E-16	down
938	CYP4F24P	7.147621582	-2.457500267	0.542567088	-4.529394281	5.92E-06	0.000109792	down
939	MASP1	55.77752445	-2.458911573	0.670632913	-3.666553676	0.000245841	0.00262072	down
940	DCC	100.9669749	-2.467189784	0.366153707	-6.738125913	1.60E-11	1.25E-09	down
941	AC026620.1	4.551058562	-2.468884736	0.727935677	-3.391624857	0.000694795	0.006193836	down
942	DCX	229.7790282	-2.479830265	0.44106326	-5.622391365	1.88E-08	7.26E-07	down

943	AP000280.1	17.7304799	-2.485307119	0.5661037	-4.390197624	1.13E-05	0.000191993	down
944	LINC01176	12.52708441	-2.49217926	0.509816872	-4.888381298	1.02E-06	2.42E-05	down
945	KIAA1211L	67.37681054	-2.524471809	0.477379347	-5.288188155	1.24E-07	3.77E-06	down
946	FBN3	2.330580718	-2.535576639	0.956235085	-2.651624772	0.008010551	0.042552264	down
947	TMOD1	23.24589754	-2.53725377	0.439213796	-5.776808005	7.61E-09	3.24E-07	down
948	COL21A1	44.10889149	-2.537393583	0.850235436	-2.984342309	0.002841886	0.018903512	down
949	AC069120.1	13.32445098	-2.541585578	0.628241404	-4.045555675	5.22E-05	0.000711397	down
950	LIPG	1604.024716	-2.542155927	0.507416665	-5.00999692	5.44E-07	1.39E-05	down
951	AC025165.4	3.978929465	-2.5602923	0.759457491	-3.371212124	0.000748382	0.006568021	down
952	HMGCS1	1610.895841	-2.566369744	0.577598925	-4.443169186	8.86E-06	0.000154924	down
953	C2orf80	32.66918989	-2.570597005	0.362367704	-7.093891028	1.30E-12	1.21E-10	down
954	NPTX2	168.1773252	-2.576096912	0.602094865	-4.278556522	1.88E-05	0.000298759	down
955	CILP	3.208671104	-2.589974253	0.930989451	-2.781958755	0.005403191	0.031325275	down
956	AC245884.9	25.50198953	-2.61143495	0.395624562	-6.600790755	4.09E-11	2.92E-09	down
957	DHRS9	7.769951298	-2.619539486	0.555671026	-4.714191244	2.43E-06	5.16E-05	down
958	ROBO2	2.90595631	-2.646410048	0.839870113	-3.150975379	0.001627262	0.012112147	down
959	EGR3	31.94150817	-2.657286512	0.803216039	-3.308308576	0.000938613	0.007861417	down
960	KCND3	834.7867502	-2.659154983	0.274720853	-9.679479926	3.69E-22	2.03E-19	down
961	CADM2	14.34234904	-2.680016304	0.451116834	-5.940847478	2.84E-09	1.30E-07	down
962	SNCAIP	580.8020108	-2.684394802	0.220065386	-12.19816916	3.18E-34	8.09E-31	down
963	SPARCL1	490.588011	-2.698146458	0.235605829	-11.45195119	2.30E-30	4.26E-27	down
964	AC087289.5	5.972386279	-2.708961922	0.613020946	-4.419036478	9.91E-06	0.000170925	down
965	SORCS1	10.69628287	-2.718810173	0.565436199	-4.808341204	1.52E-06	3.45E-05	down
966	DNM3OS	6.457227329	-2.724903371	0.625246777	-4.35812462	1.31E-05	0.000220016	down
967	C1orf61	2249.434951	-2.732806604	0.377049812	-7.247866239	4.23E-13	4.50E-11	down

968	CRB2	694.1923181	-2.744907743	0.28734842	-9.55254162	1.27E-21	6.20E-19	down
969	RASSF10	8.734638507	-2.759749007	0.620344709	-4.448734658	8.64E-06	0.000151615	down
970	NPR1	23.62438543	-2.765930238	0.588710988	-4.698281997	2.62E-06	5.51E-05	down
971	MIR9-3HG	18.06710279	-2.768883248	0.726640951	-3.810524639	0.000138672	0.001609752	down
972	BCAN	272.2881934	-2.805271536	0.331950456	-8.45087417	2.89E-17	6.54E-15	down
973	AC107294.1	2.260249568	-2.808682557	0.920942666	-3.049790896	0.002290007	0.015870266	down
974	FGF1	87.93596188	-2.810159759	0.377916189	-7.435933781	1.04E-13	1.22E-11	down
975	ANOS1	118.4046558	-2.821661502	0.376068364	-7.503054679	6.23E-14	7.74E-12	down
976	AQP5	4.155161943	-2.832304294	0.865815854	-3.27125483	0.001070714	0.00868816	down
977	C4orf54	2.699388178	-2.856668999	1.033477925	-2.764131609	0.005707451	0.03280253	down
978	PCDH8	136.7430394	-2.857130005	0.551912704	-5.176778839	2.26E-07	6.39E-06	down
979	METTL7B	314.4906572	-2.865920757	0.320532694	-8.941118365	3.85E-19	1.29E-16	down
980	AC107294.3	7.072236169	-2.870656068	0.652769031	-4.397659709	1.09E-05	0.000186443	down
981	SUSD4	52.3124644	-2.873298124	0.689694624	-4.166043964	3.10E-05	0.000458612	down
982	RNA5SP61	2.362007989	-2.874534583	1.05917799	-2.713929681	0.006649028	0.036878468	down
983	AL359091.1	19.94051751	-2.937960258	0.547210476	-5.368976631	7.92E-08	2.60E-06	down
984	RGS4	127.102801	-2.959453114	0.70510778	-4.197164176	2.70E-05	0.000406832	down
985	KCNA4	7.388465519	-2.970735672	0.582644263	-5.09871265	3.42E-07	9.19E-06	down
986	PTX3	399.3305519	-2.977341154	0.457532382	-6.507388924	7.65E-11	5.12E-09	down
987	CP	506.2189679	-2.979262113	0.467947127	-6.366663975	1.93E-10	1.18E-08	down
988	WDR49	7.51120607	-2.98047816	0.574998016	-5.183458166	2.18E-07	6.22E-06	down
989	GRIK3	43.13058065	-2.984632034	0.350069699	-8.525822272	1.52E-17	3.55E-15	down
990	SEZ6L	28.82279977	-2.992704348	0.623586784	-4.799178599	1.59E-06	3.60E-05	down
991	LRRC4	48.35691763	-3.013163929	0.406648645	-7.409747859	1.27E-13	1.46E-11	down
992	CELF3	4.080732095	-3.013968155	0.777269531	-3.877635792	0.000105476	0.001284639	down

993	LINC01497	36.06906866	-3.034259785	0.829322072	-3.658723056	0.000253475	0.002681042	down
994	LINC01085	2.618563625	-3.055357279	0.979672917	-3.118752418	0.001816185	0.013249496	down
995	IGSF11	19.65079569	-3.066261718	0.565995812	-5.417463616	6.05E-08	2.04E-06	down
996	CCDC177	12.81365897	-3.093914473	0.48523956	-6.376055716	1.82E-10	1.12E-08	down
997	LINC00606	19.55338157	-3.135490046	0.41318084	-7.588662736	3.23E-14	4.25E-12	down
998	RFX4	251.1394024	-3.147241518	0.308531168	-10.20072474	1.97E-24	1.48E-21	down
999	STARD4	215.5280187	-3.158126673	0.740623738	-4.264144544	2.01E-05	0.000315265	down
1000	AC007036.1	2.814835488	-3.171258828	1.020454683	-3.107691973	0.001885545	0.013623697	down
1001	TTYH1	3432.069903	-3.173465627	0.418992227	-7.574044159	3.62E-14	4.66E-12	down
1002	AL137005.1	6.116546866	-3.176415802	0.730037432	-4.351031417	1.35E-05	0.00022669	down
1003	NWD1	19.61232266	-3.19243492	0.485622592	-6.573901162	4.90E-11	3.41E-09	down
1004	LINC02409	2.275379693	-3.208076636	1.053217595	-3.045977063	0.002319255	0.016018438	down
1005	HRK	79.91335979	-3.208434196	0.369947078	-8.672684252	4.22E-18	1.12E-15	down
1006	GFAP	31153.88037	-3.212371764	0.768062012	-4.182438023	2.88E-05	0.00043209	down
1007	SLIT1	25.36567099	-3.23066666	0.478159011	-6.756469255	1.41E-11	1.12E-09	down
1008	RYR2	2.940537913	-3.239782328	1.144633427	-2.830410376	0.004648833	0.027798795	down
1009	AC006305.1	5.827522336	-3.241881521	0.998471335	-3.246844859	0.00116692	0.009281115	down
1010	AC018647.1	5.929360839	-3.28669661	0.699656734	-4.69758447	2.63E-06	5.53E-05	down
1011	SLC15A2	78.91459474	-3.36979467	0.352591392	-9.557223312	1.21E-21	6.20E-19	down
1012	STUM	6.399106337	-3.423219413	0.668560532	-5.120283424	3.05E-07	8.30E-06	down
1013	SMOC1	29.61912639	-3.451775071	0.55639663	-6.203802978	5.51E-10	3.04E-08	down
1014	NTRK2	24.52935763	-3.462085768	0.549657011	-6.298629322	3.00E-10	1.76E-08	down
1015	SLC6A1	22.45746183	-3.479080336	0.459063945	-7.578639911	3.49E-14	4.55E-12	down
1016	ABCB11	299.4600409	-3.491468965	0.47063367	-7.418655288	1.18E-13	1.38E-11	down
1017	SSTR3	11.18092237	-3.541694321	0.682962589	-5.185780857	2.15E-07	6.15E-06	down

1018	GABRQ	315.4773753	-3.554377971	0.333129097	-10.66967132	1.41E-26	1.60E-23	down
1019	CNGA3	9.18757445	-3.577680062	0.545241448	-6.561643606	5.32E-11	3.65E-09	down
1020	HSD11B1	2.135236425	-3.578447638	1.069676938	-3.345353642	0.000821777	0.00706895	down
1021	ATP2B2	70.03403383	-3.607820041	0.452690909	-7.96972056	1.59E-15	2.70E-13	down
1022	CDH1	11.51796432	-3.627919826	0.695730384	-5.214548494	1.84E-07	5.40E-06	down
1023	CACNG5	285.9086196	-3.760972491	0.287308095	-13.0903812	3.74E-39	1.90E-35	down
1024	CMKLR1	2.430801005	-3.787289194	1.449788285	-2.612305005	0.008993398	0.046641952	down
1025	GALP	2.484170776	-3.814450487	1.264984333	-3.015413224	0.002566294	0.017382669	down
1026	AC008667.2	2.60073561	-3.892097182	0.999690388	-3.893302593	9.89E-05	0.001216373	down
1027	GABBR2	66.31636622	-3.893318832	0.710428279	-5.480241912	4.25E-08	1.50E-06	down
1028	CRABP1	39.79294284	-3.914669066	0.734573603	-5.329171987	9.87E-08	3.11E-06	down
1029	COL3A1	75.06042921	-3.936447018	1.012790033	-3.88673554	0.000101601	0.001245457	down
1030	GPR37L1	24.02881767	-3.956778696	0.530446323	-7.459338533	8.70E-14	1.04E-11	down
1031	MYCN	37.29312913	-4.126696169	0.956574877	-4.314033607	1.60E-05	0.000259453	down
1032	RPE65	44.06330872	-4.145287835	0.550333557	-7.532318871	4.98E-14	6.34E-12	down
1033	FAM69C	53.07103289	-4.199857873	0.741720005	-5.662322498	1.49E-08	6.00E-07	down
1034	FAM181A-AS1	14.78744802	-4.225465704	0.583025219	-7.247483583	4.25E-13	4.50E-11	down
1035	TMEM132E	96.55633374	-4.225993342	0.655879574	-6.443245847	1.17E-10	7.49E-09	down
1036	PLA2G3	5.875559121	-4.373382044	1.255954604	-3.48211793	0.000497465	0.004680627	down
1037	FOXJ1	37.58766101	-4.438156441	0.451678954	-9.825909305	8.71E-23	5.37E-20	down
1038	TNR	31.17826222	-4.596946656	1.214108154	-3.786274428	0.000152923	0.001746304	down
1039	NR4A3	110.8568331	-4.647099857	0.364159411	-12.76116918	2.70E-37	9.17E-34	down
1040	KCNJ10	109.8874696	-4.677150804	0.604568911	-7.736340257	1.02E-14	1.51E-12	down
1041	PCSK9	7.031248567	-4.679490659	1.225198023	-3.819374969	0.00013379	0.001566477	down
1042	AL354793.1	3.233276068	-4.698737827	1.071965587	-4.383291669	1.17E-05	0.000197199	down

1043	FGFBP3	999.7476471	-4.72223546	0.783490125	-6.027179295	1.67E-09	8.03E-08	down
1044	DBX2	3.69339694	-4.899937948	0.91833694	-5.335664651	9.52E-08	3.02E-06	down
1045	LRP2	548.7260998	-5.037284806	0.587877756	-8.56859229	1.05E-17	2.51E-15	down
1046	FAM181A	21.62935217	-5.056915084	0.572887441	-8.827065699	1.07E-18	3.04E-16	down
1047	RPS27P16	2.720974503	-5.352189166	1.02382128	-5.227659624	1.72E-07	5.10E-06	down
1048	KCNJ9	5.38053435	-5.465175648	1.112703934	-4.911617083	9.03E-07	2.18E-05	down
1049	ADRA2B	2.985516762	-5.487163939	1.369010606	-4.008123762	6.12E-05	0.000811828	down
1050	RALYL	18.11405213	-5.597051504	0.775301647	-7.219192069	5.23E-13	5.32E-11	down
1051	NKAIN4	4.701083272	-5.702130904	1.071559827	-5.321336952	1.03E-07	3.24E-06	down
1052	INHBB	17.42442787	-6.030800123	0.813487412	-7.413513761	1.23E-13	1.42E-11	down
1053	PCSK2	10.23502449	-6.415416433	1.103760801	-5.812324944	6.16E-09	2.65E-07	down
1054	AC009110.1	8.698248945	-6.602621069	0.856066418	-7.712743933	1.23E-14	1.77E-12	down
1055	HES5	34.1255024	-7.022552514	1.321261003	-5.315038059	1.07E-07	3.34E-06	down

MATERIALS AND METHODS

Patients and Clinical Samples: Adamantinomatous craniopharyngioma (ACP) tissue specimens (n=65) were collected after tumorectomy performed at the Nanfang Hospital between 2014 and 2019 using either the traditional transcranial approach (TCA) or endoscopic endonasal approach (EEA). Tissue samples were as follows: 17 papillary craniopharyngioma (PCP) samples, 21 nonfunctional pituitary adenoma (NFPA) samples, 9 hypothalamic glioma samples, 10 frontal glioma samples, 8 tuberculum sellae meningioma samples and 3 temporal lobe epilepsy excision brain tissue samples (used as controls). In addition, a total of 20 ACP cystic fluid samples, and 7 PCP cystic fluid samples were collected intraoperatively. All patients have signed informed consent to participate in the study according to the ethical protocols of the Ethics Committee of Nanfang Hospital, Southern Medical University.

Lipid detection in Cystic Fluids: Low Density Lipoprotein Cholesterol (LDL-C) was detected by an indirect method. First, we determined total cholesterol (TC) using the CHOD-PAP method, an enzymatic colorimetric assay. Briefly, samples were subjected to enzymatic hydrolysis and oxidation, and the formation of quinoneimine dye from hydrogen peroxide, 4-aminoantipyrine, and phenol in the presence of peroxidase was evaluated. To measure triglycerides (TGs), we used the GPO-PAP method. In this method, samples were hydrolyzed with lipases, and the formation of quinoneimine dye from hydrogen peroxide, 4-aminop-henazone, and 4-cholorophenol in the presence of peroxidase was determined. High density lipoprotein-cholesterol (HDL-C) was determined by HDL-C Immuno FS, a homogenous enzymatic colorimetric method. Briefly, antibodies against human lipoproteins were used to form antigen-antibody complexes with LDL (low density lipoproteins), VLDL (very low density lipoproteins), and Chylomicrons (CM), allowing HDL-C to be selectively determined by an enzymatic cholesterol measurement. Finally, LDL-C was estimated using Friedewald equation: [LDL-C] = [TC] - [HDL-C] - [TG/5]. The approximate value of LDL-C obtained was in mg/dl. To obtain LDL-C in mmol/l, the above

equation was modified by dividing TG by 2.2.

Histology and Immunofluorescence Staining: Formalin-fixed paraffin-embedded (FFPE) tumor sections and mouse brain sections (3 μm thickness) were prepared using a routine procedure. The sections were then stained with hematoxylin (ZSGB-BIO) and eosin (ZSGB-BIO) using a standard protocol. Immumohistochemical staining and immunofluorescence staining was performed using the established protocol as previously described[1]. Briefly, after deparaffinization and rehydration, antigen retrieval was performed by heating sections for 20 min in sodium citrate buffer (pH 6.0; Solarbio) or ethylenediaminetetraacetic acid (EDTA) (pH 8.0; ZSGB-BIO) in a microwave. Endogenous peroxidases were blocked by incubating the sections in 3% hydrogen peroxide for 10 min. Next, sections were blocked for 1 h in a blocking solution containing 10% goat serum (Thermo Fischer Scientific) in phosphate buffer solution (PBS; Solarbio), and then incubated with the primary antibodies overnight at 4℃. For immumohistochemical staining, the primary antibodies were detected using a Universal DAB Detection Kit (ZSGB-BIO), and the tissue sections were finally counterstained with hematoxylin (ZSGB-BIO) for 1 min. For immunofluorescence staining, the primary antibodies were detected using the corresponding fluorescent secondary antibodies. Nuclei were counterstained with 4′,6-diamidino-2-phenylindole (DAPI) (Thermo Fischer Scientific) for 5 min at room temperature (RT). The primary and fluorescent secondary antibodies that were used in this study are listed in Supplementary Table 1 and Supplementary Table 3.

BODIPY 493/503 Staining: BODIPY 493/503 staining was performed as previously described[2]. Briefly, mouse brain tissues and ACP tissue specimens were fixed in 4% paraformaldehyde (PFA; Solarbio) for 24 h, cryoprotected in 30% sucrose (Solarbio), and then sectioned (20 μm; sectioned coronally for mouse brain) using a freezing microtome (Leica). Sections were stored at -20℃. To stain lipid droplets, free-floating sections were washed twice in PBS (Solarbio) and incubated in PBS containing

BODIPY 493/503 (1:1000 dilution in dimethylsulfoxide (DMSO; MP Bio); Thermo Fisher Scientific). Nuclei were counterstained with DAPI (1:1000; Thermo Fischer Scientific) for 15 min at RT. Sections were mounted and embedded on microscope slides. Note that for successful lipid-droplet staining, antigen retrieval procedures and treatment with detergents must be avoided, and sections should be embedded while still wet.

Oil Red O Staining and Filipin Staining: ACP tissues were first fixed with 4% PFA (Solarbio), cryoprotected in 30% sucrose (Solarbio) and then embedded in tissue freezing medium (OCT; Sakura). The ACP tissues were sectioned (20 μm) and stored at -20℃. For oil red O (ORO) staining, the sections were immersed in ORO working solution (Sigma-Aldrich) for 20-30 min at RT, and then washed with 60% isopropanol (Aladdin) to remove unbound dye and counterstained with hematoxylin (ZSGB-BIO). Finally, images were captured by using a light microscope (Olympus; Japan). The cholesterol- binding compound filipin III (Sigma-Aldrich) was used to determine the cholesterol content. The ACP tissue slices were first fixed. Then, filipin staining (0.05 mg/mL filipin in a 1:4 solution of DMSO: PBS) was performed for 2 h at RT, and staining was examined using fluorescence microscopy (Olympus, Japan).

Purification of CD133$^+$ NSCs: Cells positive for CD133 surface marker were isolated from the 3VF adjacent to ACP and from the relatively normal SVZ far away from frontal glioma using the Indirect CD133 MicroBead Kit (Miltenyi Biotec) according to the manufacturer's instructions. To obtain the relatively normal NSCs of SVZ far away from frontal glioma, we first obtained relatively normal SVZ tissues according to the preoperative contrast-enhanced T1-weighted MRI sequence and the assistance of the surgeon during the operation and confirmed by the pathologist after the operation. The obtained SVZ tissues were subjected to Magnetic-Activated Cell Sorting (MACS) and then the sorted NSCs were used for subsequent experiments. To prepare single-cell suspensions, the tissues were incubated with 0.25% papain

(Worthington Biochemical) for 30 min at 37℃ and then gently triturated approximately 10 times using fire-polished tips. Next, cells were centrifuged, resuspended in PBS (Solarbio), incubated with CD133 (monoclonal antibody; MAb) conjugated to super paramagnetic microbeads (Indirect CD133 MicroBead Kit; Miltenyi Biotec), washed, and then separated using a MACS Column (Miltenyi Biotec) to obtain purified $CD133^+$ cells. These $CD133^+$ cells were used for further analysis.

Transmission Electron Microscopy (TEM): The NSCs were isolated from the 3VF adjacent to ACP and from the relatively normal SVZ far away from frontal glioma using the Indirect CD133 MicroBead Kit (Miltenyi Biotec). Next, the cells were fixed for 30 min in 2% glutaraldehyde (Sigma-Aldrich) and 4% PFA (Solarbio) in 0.1 M phosphate buffer solution (PBS; Solarbio) (pH 7.4), treated with 10% gelatin solution (Macklin) in sodium cacodylate buffer (Sigma-Aldrich), and incubated with 2% osmium tetroxide (Electron Microscopy Sciences) for 30 min at RT. Cell pellets were stained en-bloc with 1% uranyl acetate (Electron Microscopy Sciences) for 30 min, followed by dehydration in graded ethanol (VWR Chemicals) series 50%, 70%, 85%, 95%, 100%, 100%. Finally, the cells were embedded in the epoxy resin (Macklin). Sections (50 nm) were cut using a Leica EM UC7 ultramicrotome (Leica Microsystems), placed on grids, and stained with 2% uranyl acetate and Reynoid's lead citrate (Macklin). Grids were imaged with a JEM 1400 transmission electron microscope (JEOL) at 80 kV using the Gatan Microscopy Suite software (Gatan). Images were quantified using the ImageJ software (NIH) by an investigator blinded to experimental conditions.

Gas Chromatography: The $CD133^+$ cells were isolated from the 3VF adjacent to ACP and from the relatively normal SVZ far away from frontal glioma using the Indirect CD133 MicroBead Kit (Miltenyi Biotec). Cells were washed with PBS (Solarbio), placed on dry ice, and lipid extraction from frozen cell pellets was performed using

the standard Folch method. Cell pellet aliquot was lysed with NaOH (0.1M) and total cell protein was quantified using the Bradford assay. Triglycerides, cholesterol, and cholesteryl esters were directly analyzed by GC as previously described[3]. Briefly, lipids were separated using a GC-2010 gas chromatograph (Shimadzu) equipped with a programmed temperature vaporizer injector and a ZB-5HT capillary column (15 m × 0.32 mm × 0.1 μm; Phenomenex). Tri-decanoyl glycerol (Sigma- Aldrich), cholesteryl myristate (Sigma-Aldrich), and Tri-nonadecanoyl glycerol (Sigma-Aldrich) were used as standards for free, esterified cholesterol, and triglycerides, respectively. For fatty acid analysis, FOLCH-extracts were trans-esterified using the boron trifluoride-methanol solution (Sigma-Aldrich) at 80℃ for 2 h followed by extraction with hexane. Lipids were separated on a ZB-FFAP capillary column (15m × 0.32mm × 0.25μm; Phenomenex) using pentadecanoin (Sigma-Aldrich) as a standard. Chromatograms were analyzed using GC Solutions 2.3 (Shimadzu) and values were normalized to total cell protein.

Sample Collection and RNA-seq Analysis Preparation: Briefly, To test whether high content of lipids was originated from ACP cells, the ACP tissues (n=5), PCP tissues (n=4) and NFPA (n=3) tissues were prepared and sequenced. For NSCs senescence sequencing, $CD133^+$ NSCs from the 3VF adjacent to ACP (n=7) and from the relatively normal SVZ far away from frontal glioma (n=4) were prepared. A total amount of 1 μg RNA per sample was used as input material for RNA sample preparations. Sequencing libraries were generated using NEB Next® Ultra RNA Library Prep Kit for Illumina® (NEB, USA) following manufacturer's recommendations, and index codes were added to attribute sequences to each sample. Briefly, mRNA was purified from total RNA using poly-T oligo-attached magnetic beads. Fragmentation was carried out using divalent cations under elevated temperature in NEBNext First Strand Synthesis Reaction Buffer (5 ×). First-strand cDNA was synthesized using random hexamer primer and M-MuLV Reverse Transcriptase (RNase H^-). Second-strand cDNA synthesis was subsequently

performed using DNA polymerase I and RNase H. Remaining overhangs were converted into blunt ends using exonuclease/polymerase activity. After the adenylation of 3′ ends of DNA fragments, NEBNext Adaptor with hairpin loop structure was ligated to prepare for hybridization. To preferentially select cDNA fragments of 250~300 bp in length, the library fragments were purified with the AMPure XP system (Beckman Coulter, Beverly, USA). Next, 3 μL USER Enzyme (NEB, USA) was used with size-selected, adaptor-ligated cDNA at 37°C for 15 min followed by 5 min at 95°C before PCR. PCR was performed using Phusion High-Fidelity DNA polymerase, Universal PCR primers, and Index (X) Primer. Finally, PCR products were purified (AMPure XP system) and library quality was assessed on the Agilent Bioanalyzer 2100 system.

Clustering and Sequencing: The clustering of the index-coded samples was performed on a cBot Cluster Generation System using TruSeq PE Cluster Kit v3-cBot-HS (Illumina) according to the manufacturer's instructions. After cluster generation, the library preparations were sequenced on an Illumina Novaseq platform and 150 bp paired-end reads were generated.

Quality Control: First, raw data (raw reads) of fastq format were processed through in-house perl scripts. In this step, clean data (clean reads) were obtained by removing reads containing adapter, reads containing ploy-N, and low quality reads from raw data. At the same time, Q20, Q30, and GC content of the clean data was calculated. All downstream analyses were based on the clean data with high quality.

Reads Mapping To the Reference Genome: Reference genome and gene model annotation files were downloaded directly from the genome website. Index of the reference genome was built using Hisat2 v2.0.5, and paired-end clean reads were aligned to the reference genome using Hisat2 v2.0.5.

Quantification of Gene Expression Levels: Feature Counts v1.5.0-p3 was used to count the reads numbers mapped to each gene. Next, FPKM of each gene was calculated based on the length of the gene and reads count mapped to this gene.

Differential Expression Analysis: Differential expression analysis of two groups was performed using the DESeq2 R package (1.16.1). The *p*-values were adjusted using the Benjamini and Hochberg's approach for controlling the false discovery rate. Genes with an adjusted *p*-value <0.05 found by DESeq2 were assigned as differentially expressed. Next, we adopted GSEA for functional annotation.

Primary Cell Culture: Primary htNSCs were isolated using the established protocol as previously described[4-6]. Briefly, the hypothalamic tissues were dissected from newborn C57BL/6J mice, cut into small pieces (approximately 1 mm^3), digested with 0.25% papain (Worthington Biochemical) for 30 min at 37℃, and then gently triturated approximately 10 times using fire-polished tips. Next, cells were centrifuged, resuspended in growth medium containing Neurobasal-A (Thermo Fischer Scientific), 2% B27 without vitamin A (Thermo Fischer Scientific), 20 ng/mL EGF (PeproTech), 20 ng/mL bFGF (PeproTech), and 1% penicillin/streptomycin (Thermo Fischer Scientific), seeded in ultra-low adhesion 6-well plates (Corning) at a density of 1×10^5 cells per well, and then incubated in 5% CO_2 at 37℃. On day 7, the neurospheres were collected by centrifugation, dissociated into single cells by trypsinization using TrypLE™ express enzyme (Thermo Fischer Scientific), and then passaged and maintained in neurosphere culture until experimental use. To determine the neurosphere number, the neurospheres were cultured in 24-well plates and then counted under a microscope. To quantify the neurosphere size, the images were obtained using a microscope and the diameter of neurospheres was measured using the ImageJ software (NIH). For *in vitro* experiments, htNSCs were treated with cystic fluid (87.301 mg/L), ox-LDL (100 mg/L), SSO (0.2 mM), ISRIB (200 nM),

GSK2606414 (2 μM), OXT (1 μM), or OTRA (1 μM).

HtNSCs Characterization and Lipid Content Assays: The htNSCs differentiation and senescence assays were performed according to the established protocol as previously described[4, 5]. Briefly, for the htNSC differentiation assay, neurospheres were collected by centrifugation, dissociated into single cells by trypsinization using TrypLE™ express enzyme (Thermo Fischer Scientific), and then single cells were seeded on coverslips coated with Poly-L-ornithine (Sigma-Aldrich) and placed in 6-well plates (Corning). The cells were cultured in the differentiation medium containing Neurobasal-A (Thermo Fischer Scientific), 2% B27 supplement (Thermo Fischer Scientific), 0.5% fetal bovine serum (FBS; Thermo Fischer Scientific), 5 μM retinoic acid (Sigma-Aldrich), and 1% penicillin-streptomycin (Thermo Fischer Scientific). The differentiation medium was changed every two days, and neural differentiation was induced in about one week. For the cell senescence assay, the dissociated single cells were seeded in 6-well plates (Corning) coated with Poly-L-ornithine (Sigma-Aldrich). Cells were cultured for 72 h with different treatments and senescent cells were stained using a senescence β-galactosidase staining Kit (Cell Signaling Technology, #9860) according to the manufacturer's instructions. For the BODIPY 581/591 C11 lipid peroxidation assay, the dissociated single cells were seeded on coverslips coated with Poly-L-ornithine (Sigma-Aldrich) and placed in 6-well plates (Corning). After 24 h, htNSCs were incubated in HBSS (Thermo Fischer Scientific) containing different treatments for another 72 h. Next, htNSCs were incubated with 2 μM BODIPY 581/591 C11 for 1 h, washed with HBSS (Thermo Fischer Scientific), and then imaged live in HBSS using the Nikon spinning disk confocal microscope and Zeiss LSM 980. Images were taken using both green and red channels. Relative lipid peroxidation was determined as the ratio of green fluorescence intensity over red fluorescence intensity, with background subtracted, using the ImageJ software (NIH). For htNSC lipid staining, the dissociated single cells were seeded in 6-well plates (Corning) coated with Poly-L-ornithine (Sigma-Aldrich). Cells were cultured for 72 h

with different treatments, washed with PBS (Solarbio), dipped into 60% isopropanol three times, and then stained with 0.3% Oil Red O dye (Sigma-Aldrich) solution dissolved in 60% isopropanol for 10 min. Next, cells were washed with 75% isopropanol for 1 min and then covered with PBS (Solarbio). The deposition of lipid droplets in htNSCs was observed using the Olympus BX63 microscope (Japan). Images were obtained in a blinded manner and analyzed with the ImageJ software (NIH). To quantify lipid content, the ratio of ORO-positive area versus the total area was calculated.

Immunocytochemistry (ICC): The neurospheres were collected by centrifugation, dissociated into single cells by trypsinization using the TrypLE™ express enzyme (Thermo Fischer Scientific), and the cells were then seeded on coverslips coated with Poly-L-ornithine (Sigma-Aldrich) and placed in 6-well plates (Corning). After 24 h, htNSCs were fixed with 4% PFA (Solarbio) for 15 min at RT, permeabilized with 0.3% Triton X-100 solution (Solarbio) for 10 min, blocked with 10% goat serum (Thermo Fischer Scientific) for 1 h, and then incubated with primary antibodies at 4℃ overnight. Primary antibodies were detected using corresponding fluorescent secondary antibodies as described in Histology and Immunofluorescence Staining. Nuclei were counterstained with DAPI (Thermo Fischer Scientific).

Western Blot: Cells were lysed in the RIPA lysis buffer (Beyotime) containing protease/phosphatase inhibitor cocktail (Coolaber) according to the manufacturer's protocol. Lysates were sonicated for 10 min and then centrifugated at 4°C for 15 min at 12,000× g. Protein concentrations were determined using the BCA Protein Assay Kit (Solarbio) and the protein samples were heated at 100℃ for 5 min. Denatured protein samples (30 μg per lane) were separated using 10% sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and then transferred onto polyvinylidene fluoride (PVDF) membranes (MERCK Millipore). The PVDF membranes were blocked with 5% bovine serum albumin (BSA; Sigma-Aldrich) for 1

h at 25–28℃ and then probed with primary antibodies overnight at 4℃. Next, the membranes were incubated with horseradish peroxidase (HRP)-conjugated goat anti-mouse IgG or goat anti-rabbit IgG antibodies (Jackson ImmunoResearch) for 1 h at 25–28℃. The bands were visualized using the enhanced chemiluminescence (ECL) Plus blot kit (MERCK Millipore), scanned with a ChemiDoc XRS System, and analyzed using the ImageJ software (NIH). The primary and secondary antibodies that were used in Western blot are listed in Supplementary Table 2 and Supplementary Table 3.

RNA Extraction and Quantitative real-time PCR: Total RNA was extracted from cells or tissues using the RNAiso Plus reagent (TaKaRa) according to the manufacturer's instructions. First-strand cDNA was prepared by reverse transcription using PrimeScript™ RT reagent Kit (TaKaRa) and oligo (dT) primers and then stored at -20°C. The RT-PCR analysis was performed using the TB Green® Premix Ex Taq™ II (TaKaRa) and Applied Bio-systems 7500 Fast Real-Time PCR System (Applied Biosystems, Foster City, CA, USA). Each measurement was performed in triplicate, and the results were normalized to GAPDH (internal control). The relative expression of the target genes was determined by the $2^{-\triangle\triangle Ct}$ method. The specific primers used in this study are summarized in Supplementary Table 4.

Animals Models: Adult (6~8 weeks) and neonatal C57BL/6 mice were obtained from the Southern Medical University Animal Center (Guangzhou, China). Neonatal mice were used for the isolation of primary htNSCs, while adult mice were subjected to hypothalamic localization injection and lateral ventricular (LV) localization injection. In the first experiment, mice were divided into four groups: control group, sham group, cystic fluid group, cystic fluid + BAY 11-7082 (Selleck) group. The cystic fluid (1.747 mg/μL) and BAY 11-7082 (25 μg/μL) were delivered to bilateral ventromedial nucleus of the hypothalamus (VMH) by stereotactic microinjection (stereotaxic coordinate was as follows, AP: –1.58 mm from bregma, ML: ±0.3 mm,

DV: –5.5 mm below the surface of the skull). After stereotaxic microinjection, mice were continued to feed for another 8 weeks before being euthanized and their brain tissues were used for histological analysis. In the second experiment, mice were divided into 8 groups: control group, sham group, cystic fluid group, ox-LDL (Solarbio) group, ox-LDL + SSO (MCE) group, ox-LDL + OXT (R&D Systems) group, ox-LDL + ISRIB (Selleck) group, and ox-LDL + GSK2606414 (Selleck) group. The drugs or inhibitors were administered to adult mice *via* intracerebroventricular osmotic minipumps (RWD Life Science) as previously described[7]. Each minipump was positioned subcutaneously in the scapular region and attached to an infusion cannula targeting the left/right LV (stereotaxic coordinates for implantation of infusion cannula: AP: –0.34 mm from bregma, ML: ±1.0 mm, DV: –2.5 mm below the surface of the skull; (Paxinos and Franklin, 2001) via polyethylene tubing). When mice were given two drugs, they were administered from each side of the LV. The minipumps were filled with the vehicle (DMSO), cystic fluid (1.747 mg/μL), ox-LDL (2 mg/μL), SSO (4 μg/μL), ISRIB (0.4 μg/μL), GSK2606414 (2 μg/μL), or OXT (20 ng/μL). The drugs or inhibitors were injected at the rate of 0.25 μl/h for 3 months. To minimize the possibility of drug degradation inside the reservoirs, the osmotic minipumps filled with drugs were changed weekly. The body weight of the mice was measured zero, one, two, and three months after the LV localization injection. The mice were euthanized at week 12, and their brain tissues were used for histological analysis and qRT-PCR analysis. All animals were maintained on a 12-h light/dark cycle at 23°C with food and water available *ad libitum*. All animal studies were performed according to the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* and approved by the Experimental Animal Committee of the Nanfang Hospital, Southern Medical University.

Morris Water Maze (MWM): The Morris water maze (MWM) was used to evaluate the spatial learning and memory performance of mice at week 8 after the LV localization injection. according to the previously published methods[8]. The maze

consisted of a large circular pool (120 cm in diameter, 45 cm in height, filled to a depth of 30 cm with opaque water containing nontoxic, white chalk at 28 ± 1 °C) and divided into four equal-sized quadrants. Large visual cues surrounded the maze to make this a hippocampus-dependent task. A white platform (5 cm in diameter) was submerged and placed 1 cm below the water surface in the center of the target quadrant to provide an escape zone. All mice were given access to four training trials each day for five straight days in order to evaluate their capacity for spatial learning. Throughout the training session, the platform's position was held constant. The mice freely swam into the water along the four-quadrant pool wall in turn throughout the location navigation test. A maximum of 60 s were given to each mouse to locate the submerged white platform. The mice's discovery of the concealed platform was timed, and that information served as the escape latency time. The mouse is manually directed to the platform and given 30 s to rest if the mouse fails to find the platform within 60 s, and the escape latency time is then recorded as 60 s. The escape latency time to find the hidden platform of each mouse was recorded. On day 6, mice were put through a 60-s spatial probe experiment in which the platform was taken away to test their capacity for spatial memory. The numbers of crossing original platform’s location was assumed to be a measure of their spatial memory. The number of entries to platform location were recorded. A digital camera placed immediately above the water maze was used to record all behaviors of the mice took, and the data fed back to the computer was analyzed.

Mitochondria Fragmentation and Surface Area Assay: Mouse htNSCs were incubated with different treatments for 72 h, fixed with 4% PFA (Solarbio), stained for TOMM20 to label mitochondria, and then imaged using the Zeiss 980 LSM. Images of TOMM20-labelled cells were scored for mitochondrial fragmentation (“fragmented” or “non-fragmented”) by a blinded investigator. The standard deviation was calculated based on the binomial distribution, sqrt(np(1-p)) where n was the number of cells and p was the fraction of fragmented cells. For mitochondrial surface

area analysis, single confocal slices with the highest mitochondrial signal were used for quantification. Within ImageJ, a mask of the cell outline was made in such way that all pixels inside the htNSCs were equal to one and all pixels outside were null. Similarly, the mitochondria were thresholded in such way that all pixels inside the mitochondria were one and all pixels outside were null. The sum of all pixels was then measured for both images, essentially reporting the area occupied by either the total cell footprint or mitochondrial footprint. The ratio of the two was reported.

Quantitative Analysis of Immunohistological Data: To evaluate the damage of the hypothalamus adjacent to ACP, PCP, meningioma and hypothalamic glioma, the distance from tumor margin to the margin of NF and MBP positive expression was calculated. To assess the number of $SOX2^+$ NSCs per hypothalamus area, $SOX2^+$ NSCs from six randomly selected visual fields per patient were counted using the ImageJ software (NIH) and normalized to the corresponding hypothalamus area. To analyze the percentage of γ-$H2AX^+$ NSCs, the number of total $SOX2^+$ cells and γ-$H2AX^+SOX2^+$ cells was counted using the ImageJ software (NIH), and the percentage of γ-$H2AX^+$ NSCs was calculated. The percentage of $p21^+$ NSCs, $p16^+$ NSCs, Ki-67^+ NSCs, $MCM2^+$ NSCs, Lamin $B1^+$ NSCs, and $H3K9Me3^+$ NSCs was calculated as described above. Similarly, the percentage of $GPR50^+Nestin^+$ NSCs, $SOX2^+Rx^+$ NSCs, $EAAT1^+Nestin^+$ NSCs, $Vimentin^+Connexin\ 43^+$ NSCs, $SOX2^+SOX9^+$ NSCs, $SOX2^+SOX10^+$ NSCs, $SOX2^+Olig2^+$ NSCs, $CD36^+Nestin^+$ NSCs, and $CD36^+$IBA-1^+ microglia was also calculated as described above. To analyze the percentage of SA-β-gal^+ NSCs, the number of total cells and SA-β-gal^+ cells was counted using the ImageJ software (NIH), and the percentage of SA-β-gal^+ NSCs was calculated. To assess the percentage of β3-$Tubulin^+$ NSCs, the number of total $DAPI^+$ cells and β3-$Tubulin^+$ cells was counted using the ImageJ software (NIH), and the percentage of β3-$Tubulin^+$ NSCs was calculated. To quantify the number of $BODIPY^+$ LDs, $BODIPY^+$ LDs in every single cell per group was counted using the ImageJ software (NIH). To evaluate the expression of ZO-1 in the hypothalamus of

mouse brain in each group, the fluorescence intensity of ZO-1 in the ependymal layer was analyzed by using the ImageJ software (NIH), and the fold change of the fluorescence intensity of ZO-1 in each group compared to the control group was calculated. To assess the number of $CD169^+$ cells in hypothalamus area, $CD169^+$ cells from six randomly selected visual fields per animal were counted using the ImageJ software (NIH). The number of $POMC^+$ neurons, $GFAP^+$ astrocytes, IBA-1^+ microglia, and SMI-32^+ axonal spheroids was calculated in a similar manner. To analyze the expression of NPY in the hypothalamus of mouse brain in each group, the fluorescence intensity of NPY in the arcuate nucleus (ARC) was analyzed using the ImageJ software (NIH), and the fold change of the fluorescence intensity of NPY in each group compared to the control group was calculated. The expression of GnRH and IBA-1 was calculated in a similar manner.

Statistical Analysis: Data are presented as the mean ± SEM. Statistical analyses were performed using GraphPad Prism (version 8.0, GraphPad Software, San Diego, CA) and IBM SPSS (version 20.0, IBM, Chicago, IL, USA). Each group of data was subjected to Kolmogorov-Smirnov test or D'Agostino-Pearson omnibus test for normal distribution when applicable. *p*-values for normally distributed data were calculated using either the Student's t-test for two groups or one-way ANOVA with Fisher's LSD *post hoc* analysis when three or more groups were tested. Data that were not normally distributed were analyzed using the non-parametric Mann-Whitney U test or the uncorrected Dunn's test. Differences were considered statistically significant at $p < 0.05$. All statistical details regarding *p*-values and n values are specified in main and supplementary figure legends. Significance was defined as $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. Different groups of mice were allocated in a randomized manner and investigators were blinded to the allocation of different groups when performing surgeries and subsequent outcome evaluations. Exclusion criteria were based on animal well-being at the beginning of the study. No animals were excluded from the study. No power analysis was performed to determine the

sample size. The sample size for each study was based on previous animal studies in our lab.

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