**Supplementary table 3. The sequences of the siRNAs used for intracerebroventricular (i.c.v.) injection.**

| | | |
|---|---|---|
| *siSuv39h1*-1# | F | CCUGCACAAGUUUGCCUACAAdTdT |
| | R | UUGUAGGCAAACUUGUGCAGGdTdT |
| *siSuv39h1*-2# | F | CGAGUCCGUAUUGAAUGCAAAdTdT |
| | R | UUUGCAUUCAAUACGGACUCGdTdT |
| *siSuv39h1*-3# | F | GCCUUUGUACUCAGGAAAGAAdTdT |
| | R | UUCUUUCCUGAGUACAAAGGCdTdT |

**Supplementary table 4. The sequences of the siRNAs used for siRNA transfection *in vitro.***

| | | |
|---|---|---|
| siRNA-*Tfr1* | F | CCAGACCGUUAUGUUGUAGUAdTdT |
| | R | UACUACAACAUAACGGUCUGGdTdT |
| siRNA-*Suv39h1* | F | CGAGUCCGUAUUGAAUGCAAAdTdT |
| | R | UUUGCAUUCAAUACGGACUCGdTdT |

Supplementary table 5. Antibodies were used in immunofluorescence (IF) staining and Western blot (WB).

| | | | |
|---|---|---|---|
| anti-NeuN | 1:200 | ABN91 | Millipore |
| anti-GFAP | 1:500 | G3893 | Sigma |
| anti-Iba-1 | 1:500 | 019–19741 | Wako |
| anti-Olig2 | 1:300 | ab9610 | Millipore |
| anti-Histone H3 (tri methyl K9) | 1:400 (IF)<br>1:10000 (WB) | ab8898 | Abcam |
| anti-Suv39h1 | 1:200 | GTX112263 | GeneTex |
| anti-Suv39h1 | 1:200 | sc-23961 | Santa Cruz |
| Alexa Fluor 488 | 1:500 | A-11008 | Thermo |
| Alexa Fluor 594 | 1:500 | A-11042 | Thermo |
| Anti-xCT | 1:1000 | ab37185 | Abcam |
| Anti-glutathione peroxidase 4 | 1:1000 | ab125066 | Abcam |
| Anti-transferrin receptor | 1:1000 | ab84036 | Abcam |
| Anti-transferrin | 1:1000 | ab278498 | Abcam |
| Anti-ferritin | 1:1000 | ab75973 | Abcam |
| Anti-H3 | 1:10000 | ab1791 | Abcam |
| Anti-Histone H3 (di methyl K9) | 1:10000 | ab1220 | Abcam |
| Anti-Histone H3 (mono methyl K9) | 1:10000 | ab9045 | Abcam |
| Anti-Histone H3 (tri methyl K27) | 1:10000 | ab192985 | Abcam |
| Anti-Histone H3 | 1:10000 | ab24684 | Abcam |

| | | | |
|---|---|---|---|
| (di methyl K27) | | | |
| Anti-Histone H3 (tri methyl K4) | 1:10000 | ab8580 | Abcam |
| Anti-acetyl Lysine | 1:10000 | ab80178 | Abcam |
| Anti-HDAC1 | 1:10000 | ab7028 | Abcam |
| Anti-rabbit IgG, HRP-linked Antibody | 1:1000 | 7071S | CST |
| Anti-mouse IgG, HRP-linked Antibody | 1:1000 | 7076S | CST |

**Supplementary table 6. Primers were used in ChIP experiment and Real-time RT-PCR.**

| | | |
|---|---|---|
| *Tfr1*-#1 (ChIP) | F | GTGACTCCCTTGTCAG |
| | R | CCGTGACACTAGTAACC |
| *Tfr1*-#2 (ChIP) | F | GCTCTAGCGATTGGGTCTGTTTC |
| | R | GCCTCTTGCCTCCCAAGTACTAG |
| *Ptgs2* | F | TGAGCAACTATTCCAAACCAGC |
| | R | GCACGTAGTCTTCGATCACTATC |
| *Ftl1* | F | CCATCTGACCAACCTCCGC |
| | R | CGCTCAAAGAGATACTCGCC |
| *Fth1* | F | CAAGTGCGCCAGAACTACCA |
| | R | GCCACATCATCTCGGTCAAAA |
| *Tfr1* | F | GTTTCTGCCAGCCCCTTATTAT |
| | R | GCAAGGAAAGGATATGCAGCA |
| *Tfr2* | F | TTGGGGTCTACTTCGGAGAGT |
| | R | GACAGGAGCCTAAGTGCTCAG |
| *Slc7a11* | F | GCTCGTAATACGCCCTGGAG |
| | R | GGAAAATCTGGATCCGGGCA |
| *Gpx4* | F | CTGCTCTTCCAGAGGTCCTG |
| | R | GAGGTGTCCACCAGAGAAGC |
| *Suv39h1* | F | GCAGTGTGTGCTGTAAATCTTCT |
| | R | ATACCCACGCCACTTAACCAG |
| *Suv39h2* | F | CTGCCCAGGATAGCATTGTTC |
| | R | CAAGTCTCGGCTCCACATTTAC |
| *Setdb1* | F | CAACTTGCACAATCACGGAAAC |
| | R | CAAAGGTGACCGATATGTCTGG |
| *Kdm4a* | F | GACATAGTGAGTCAGGACTGTCT |
| | R | GGCCACAAACTTAGCCCCATA |
| *Kdm4b* | F | AGGGACTTCAACAGATATGTGGC |
| | R | GATGTCATCATACGTCTGCCG |

| | | |
|---|---|---|
| *Kdm4c* | F | TGGAGAGTCCCCTAAATCCCA |
| | R | CCTTGGCAAGACCTGCTCG |
| *Kdm4d* | F | CAGAGGCCATCAATTTTGCCA |
| | R | TTTCCACAGTTCATATCGCTCAG |
| *GAPDH* | F | TGTTCCTACCCCCAATGTGT |
| | R | TGTGAGGGAGATGCTCAGTG |

**Supplementary Material and methods**

**Animal perfusion and tissue collection**

Animals were anesthetized with chloral hydrate (0.5 g/kg, *i. p.*). For immunofluorescence, the mice were perfused with cold PBS (P1010, Solarbio, China), followed by 4% paraformaldehyde (PFA, P804536, MACKLIN, China). For extracting protein or testing MDA, the mice were perfused with cold PBS, and the ipsilateral striatum tissues were obtained.

**Immunofluorescence staining**

The brains were fixed in 4% PFA overnight at 4 °C and then dehydrated in 20% sucrose solutions (10021418, SCR, China) for 24 h and in 30% sucrose solutions for 48 h at 4 °C. The brain tissues were then embedded with OCT (4583, SAKURA, USA) and cut into 16 μm consecutive coronal sections. The frozen slices were washed with 0.01 M PBS three times for 5 min followed with incubation in 0.01 M citric acid buffer (pH 6.0) (10007118, SCR) at 95 °C for 10 min for antigen retrieval. The slices were then incubated in 1% Triton X-100 (T9284, Sigma) for 15 min at room temperature followed by washing with PBS three times. The slices were incubated in 0.3% $H_2O_2$ (10011208, SCR) for 10 min, and washed with PBS for three times. The slices were blocked in 5% goat serum (C0265, Beyotime, China) for 30 min, and then incubated overnight at 4 °C

with primary antibodies (listed in Supplementary table 5). The slices were washed with PBS and then incubated for 1 hour with secondary antibody (listed in Supplementary table 5) at room temperature in the dark. After washed with PBS, the sections were mounted in VECTASHIELD mounting medium containing DAPI (H-1200, VECTASHIELD, USA). All images were photographed under a fluorescence microscope (ECLIPSE Ci, Nikon) and analyzed with Image J software. Manders' colocalization coefficients were calculated using Image J software.

**Western blot**

Total proteins from cells or tissues were extracted with RIPA (C1053, Applygen, China) lysis buffer containing protease cocktail inhibitors (4693132001, Roche, USA), and protein concentration was determined with the BCA protein assay reagent (23228, Thermo Fisher Scientific, USA). The total protein at a concentration of 3 μg/μL was subjected to 12% SDS-PAGE electrophoresis and then transferred to a PVDF membrane (1620177, Millipore, USA). After incubating with specific primary and secondary antibodies, the Immobilon Wester chemilum HRP substrates (WBKLS0500, Millipore) were used to detect the blots using a chemiluminescence imager (Fusion SoloS. EDGE, VILBER, France). The antibodies and concentrations used in western blot were listed in Supplementary table 5.

**Real-time RT-PCR**

Total RNA from cells was extracted with TRIzol reagent (15596026, life technologies,

USA), and cDNA was synthesized with HiScript® III RT SuperMix for qPCR (+gDNA wiper) kit (R223-01, Vazyme, China) according to the manufacturer's instructions. PowerUp™SYBR™ Green Master Mix (A25742, Applied Biosystem, USA) was used for real-time PCR performed on the ABI 7500 Fast Real-Time Fluorescent Quantitative PCR system (Applied Biosystem, USA). The primers of mouse origin used in the Quantitative RT-PCR reaction are listed in Supplementary table 6.