# Supplementary Figure Caption

## Fig. S1

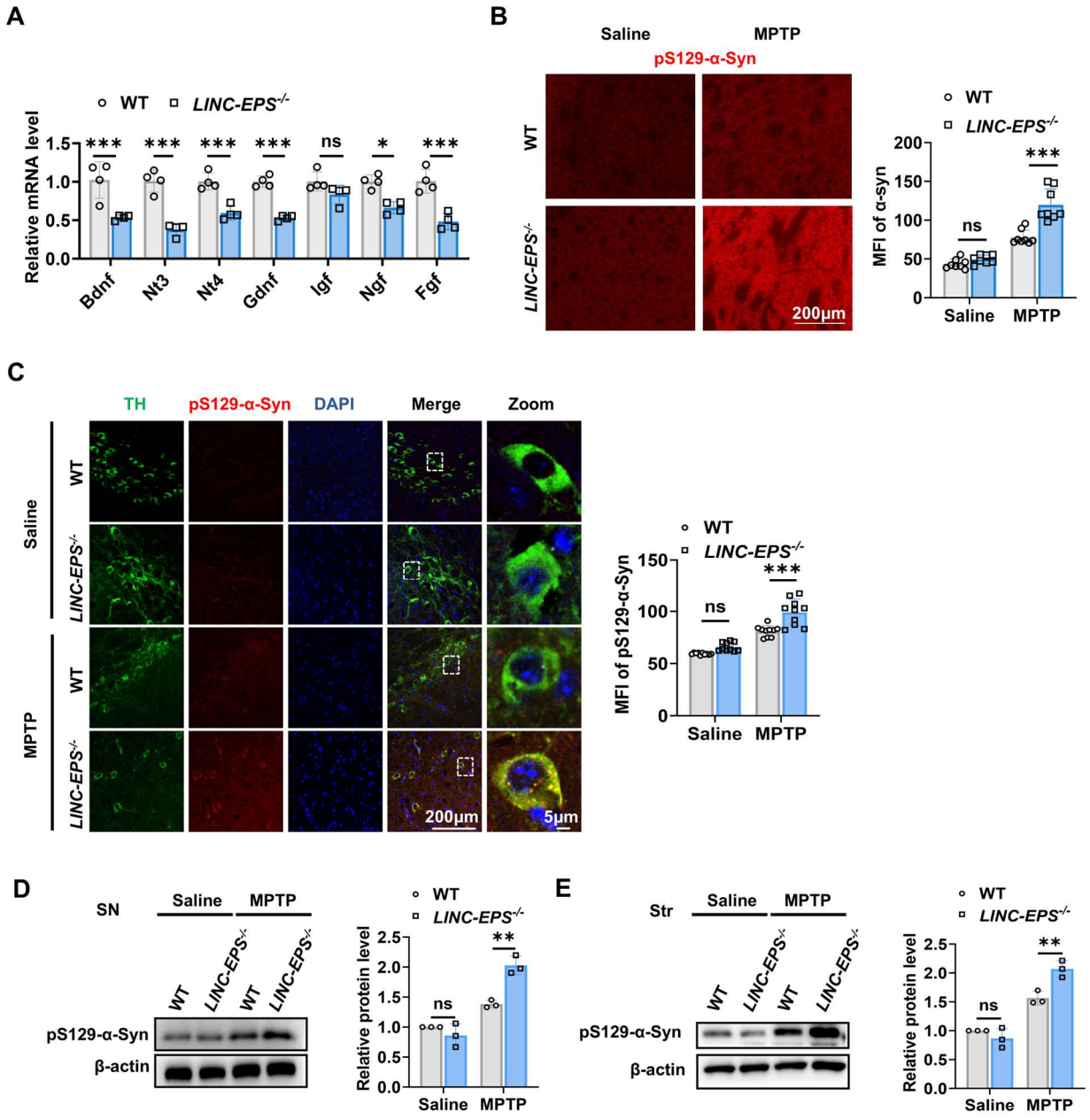


**Fig. S1 *LINC-EPS* Deficiency Exacerbates MPTP-Induced Neurochemical and Pathological Alterations**

**(A)** RT-qPCR analysis of neurotrophic factor mRNA levels (Bdnf, Nt3, Nt4, Gdnf, Igf, Ngf, Fgf) in midbrain tissue from the indicated groups (n = 4). **(B)** Representative immunofluorescence images of pS129-α-Syn (red) in the striatum and quantification of its mean fluorescence intensity (MFI) (n = 8).

Scale bar, 200 μm. **(C)** Representative co-immunofluorescence images for pS129-α-Syn (red), TH (green), and DAPI (blue) in the SNpc. Right panels show magnified views of the boxed areas. Far right: Quantification of pS129-α-Syn MFI within $TH^+$ neurons (n = 10). Scale bar, 200 μm. **(D, E)** Representative immunoblots and quantification of pS129-α-Syn protein levels in the SN **(D)** and striatum **(E)**. β-actin served as a loading control (n = 3). Data are presented as mean ± SEM. Statistical significance was determined by two-way ANOVA with Tukey's post-hoc test. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. ns, not significant.

**Fig. S2**

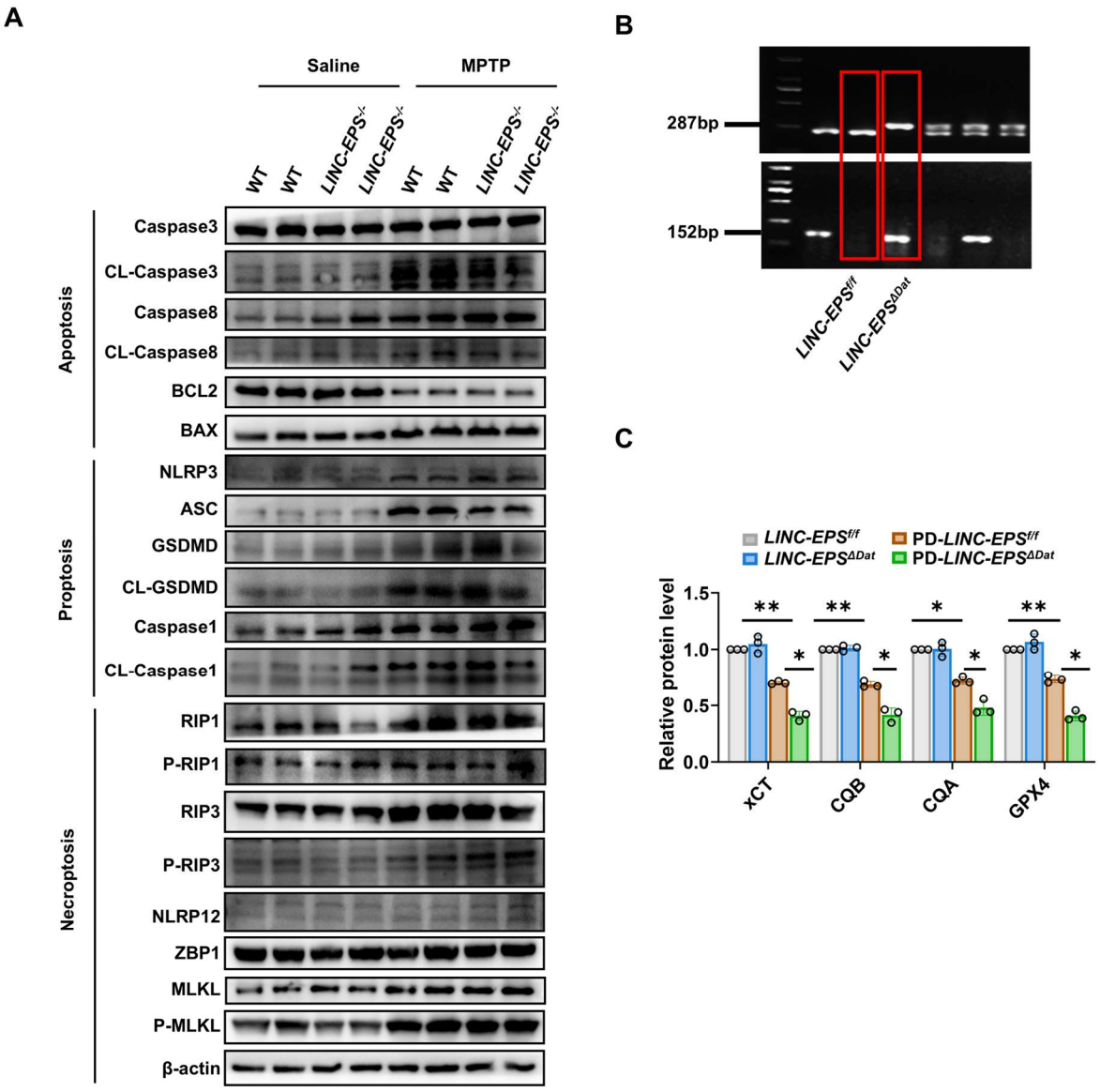


**Fig. S2 LINC-EPS Deficiency Does Not Activate Other Major Regulated Cell Death Pathways**

(A) Representative immunoblots of key protein markers for apoptosis (CL-Caspase-3), pyroptosis (CL- Caspase-1, GSDMD-N), and necroptosis (P-MLKL, P-RIP3) in primary neurons from WT and *LINC-EPS*$^{-/-}$ mice treated with or without $MPP^{+}$ (500 μM, 24 h). Due to limited primary neuron yield, two technical replicates from pooled neurons (six mice per pool). (B) Genotyping PCR validation of

dopamine neuron-specific LINC-EPS conditional knockout (*LINC-EPS*$^{\Delta Dat}$) mice. The 287 bp band represents the floxed allele (loxP sites flanking the target region), and the 152 bp band indicates the deleted allele after Cre-mediated excision of the intervening sequence. *LINC-EPS*$^{f/f}$ control mice showed only the 287 bp floxed allele, whereas *LINC-EPS*$^{\Delta Dat}$ mice displayed both the 287 bp band (from non-recombined cells) and the 152 bp band (from dopaminergic neurons with successful Cre-mediated deletion). **(C)** Quantification of relative protein levels for xCT, CQ10B, CQ10A and GPX4 from the immunoblots shown in Figure 3H (n = 3). Data are presented as mean ± SEM. Statistical significance was determined using two-way ANOVA followed by Tukey's post hoc test. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$; ns, not significant.

**Fig. S3**

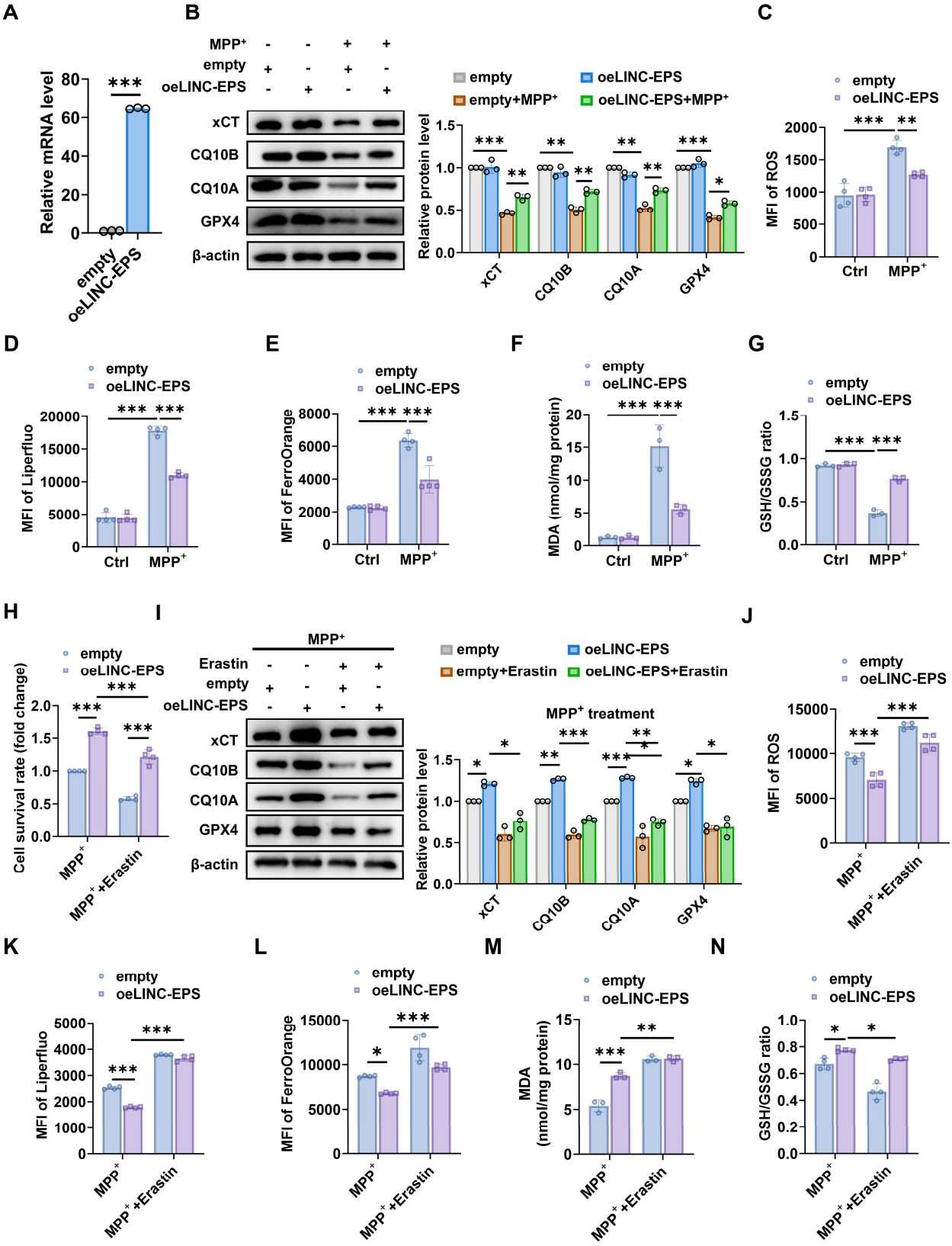
A
B
C
Relative mRNA level
empty
oeLINC-EPS
MPP+
xCT
CQ10B
CQ10A
GPX4
β-actin
Relative protein level
empty+MPP+
oeLINC-EPS+MPP+
MFI of ROS
Ctrl
D
E
F
G
MFI of Liperfluo
MFI of FerroOrange
MDA (nmol/mg protein)
GSH/GSSG ratio
H
I
J
Cell survival rate (fold change)
Erastin
empty+Erastin
oeLINC-EPS+Erastin
MPP+ treatment
MPP+ +Erastin
K
L
M
N

**Fig. S3 LINC-EPS overexpression protects SH-SY5Y cells from $MPP^+$- and Erastin-induced ferroptosis**

SH-SY5Y cells stably overexpressing LINC-EPS (oeLINC-EPS) or empty vector control were treated with $MPP^+$ (500 μM, 24 h) with or without erastin (10 μM, 24 h). **(A)** qRT-PCR validation of LINC-EPS overexpression (n = 3). **(B–G)** Effects of LINC-EPS overexpression on $MPP^+$-induced ferroptosis: **(B)** protein levels of xCT, CQ10B, CQ10A, and GPX4 (n = 3); **(C)** total ROS (n = 4); **(D)** lipid ROS (n = 4); **(E)** $Fe^{2+}$ levels (n = 4); **(F)** MDA content (n = 3); **(G)** GSH/GSSG ratio (n = 3). **(H–N)** Combined effects of LINC-EPS overexpression and erastin treatment: **(H)** cell viability (n = 4); **(I)** xCT, GPX4, CQ10A, and CQ10B protein levels (n = 3); **(J)** total ROS (n = 4); **(K)** lipid ROS (n = 4); **(L)** $Fe^{2+}$ levels (n = 4); **(M)** MDA content (n = 3); **(N)** GSH/GSSG ratio (n = 4). Data are mean ± SEM. Statistical analysis: two-tailed Student's t-test **(A)** or two-way ANOVA with Tukey's post-hoc test **(B–N)**. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. Detailed experimental procedures are described in Materials and Methods.

**Fig. S4**

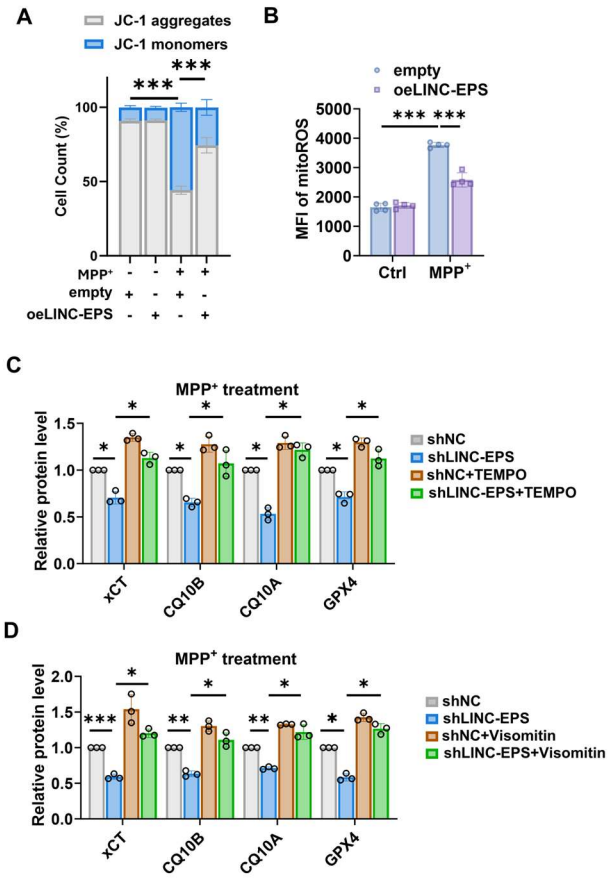


**Fig. S4 LINC-EPS Deficiency-Induced Ferroptotic Phenotypes are Rescued by mitoROS Scavengers**

**(A, B)** oeLINC-EPS or empty cells were treated with or without $MPP^+$ (500 μM, 24 h). **(A)** Flow cytometry analysis of MMP (n = 4). **(B)** Quantification of mitoROS levels (n = 4). **(C)** Quantification of relative protein levels from immunoblots shown in Figure 6G (n = 3). **(D)** Quantification of relative protein levels from immunoblots shown in Figure 6H (n = 3). Data are presented as mean ± SEM. Statistical significance was determined by two-way ANOVA with Tukey's post-hoc test. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

**Fig. S5**

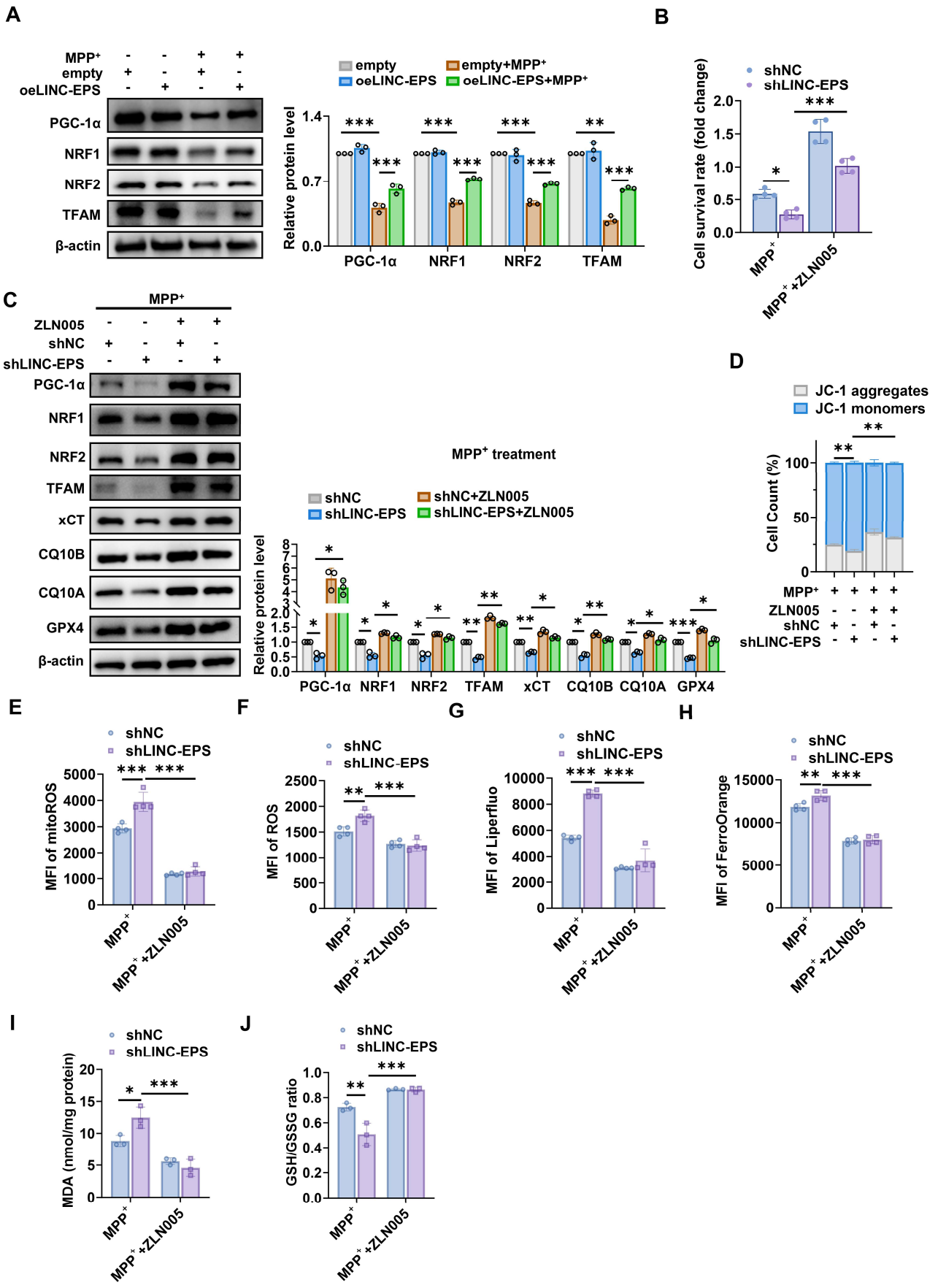
A
MPP+
empty
oeLINC-EPS
PGC-1α
NRF1
NRF2
TFAM
β-actin
empty
oeLINC-EPS
empty+MPP+
oeLINC-EPS+MPP+
Relative protein level
PGC-1α
NRF1
NRF2
TFAM
B
shNC
shLINC-EPS
Cell survival rate (fold change)
MPP+
MPP+ +ZLN005
C
MPP+
ZLN005
shNC
shLINC-EPS
PGC-1α
NRF1
NRF2
TFAM
xCT
CQ10B
CQ10A
GPX4
β-actin
MPP+ treatment
shNC
shLINC-EPS
shNC+ZLN005
shLINC-EPS+ZLN005
Relative protein level
PGC-1α
NRF1
NRF2
TFAM
xCT
CQ10B
CQ10A
GPX4
D
JC-1 aggregates
JC-1 monomers
Cell Count (%)
MPP+
ZLN005
shNC
shLINC-EPS
E
shNC
shLINC-EPS
MFI of mitoROS
MPP+
MPP+ +ZLN005
F
shNC
shLINC-EPS
MFI of ROS
MPP+
MPP+ +ZLN005
G
shNC
shLINC-EPS
MFI of Liperfluo
MPP+
MPP+ +ZLN005
H
shNC
shLINC-EPS
MFI of FerroOrange
MPP+
MPP+ +ZLN005
I
shNC
shLINC-EPS
MDA (nmol/mg protein)
MPP+
MPP+ +ZLN005
J
shNC
shLINC-EPS
GSH/GSSG ratio
MPP+
MPP+ +ZLN005

**Fig. S5 Pharmacological and Genetic Modulation of the LINC-EPS/PGC-1α Axis**

**(A)** PGC-1α axis protein expression in oeLINC-EPS or empty vector cells treated with or without $MPP^+$ (500 μM, 24 h) (n = 3). **(B–J)** shLINC-EPS cells were treated with $MPP^+$ (500 μM, 24 h) with or without the PGC-1α agonist ZLN005 (10 μM). **(B)** Cell viability (n = 4); **(C)** PGC-1α axis and ferroptosis defense protein levels (n = 3); **(D)** mitochondrial membrane potential (n = 4); **(E)** mitoROS levels (n = 4); **(F)** total ROS (n = 4); **(G)** lipid ROS (n = 4); **(H)** $Fe^{2+}$ levels (n = 4); **(I)** MDA content (n = 3); **(J)** GSH/GSSG ratio (n = 3). Data are mean ± SEM. Statistical analysis: two-way ANOVA with Tukey's post-hoc test. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. Detailed experimental procedures are described in Materials and Methods.

**Fig. S6**

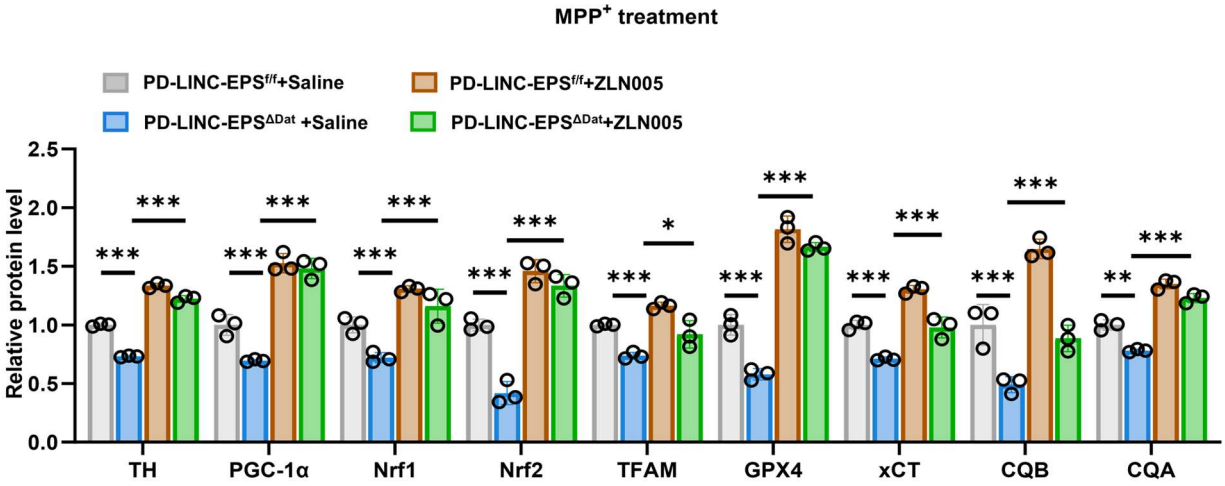


**Fig. S6 Quantification of Protein Expression Levels in the Midbrain**

Quantification of the immunoblot analysis shown in Figure 9I for TH, PGC-1α, NRF1, NRF2, TFAM, GPX4, xCT, CQ10B, and CQ10A. Protein levels were normalized to β-actin (n = 3). Data are presented as mean ± SEM. Statistical significance was determined by two-way ANOVA with Tukey's post-hoc test. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

# Supplementary Materials and Methods

## Immunohistochemistry and Imaging

Following terminal anesthesia with Avertin (30 µL/g, i.p.), animals were perfused transcardially with ice-cold saline and subsequently with 4% paraformaldehyde (PFA). Excised brains were post-fixed overnight in 4% PFA at 4°C, followed by cryoprotection in a 30% sucrose solution. Coronal sections (15–30 µm thickness) were then prepared using a Leica cryostat. For immunofluorescence staining, free-floating sections were first permeabilized with 0.3% Triton X-100 and then blocked in 5% BSA. Subsequently, sections were incubated with primary antibodies in the Supplementary Materials (Table S2) overnight at 4°C. After washing, sections were incubated with the appropriate Alexa Fluor-conjugated secondary antibodies and nuclei were counterstained with DAPI. Fluorescence signals were captured on a Zeiss LSM 880 confocal microscope, and subsequent image analysis was performed using Fiji software (ImageJ).

## Western Blot Analysis

For protein analysis, total lysates were extracted from cells or tissues using RIPA buffer supplemented with protease and phosphatase inhibitors. Protein concentration was quantified via a BCA assay. Equal protein quantities were resolved by SDS-PAGE and transferred to PVDF membranes (Millipore). The membranes were subsequently blocked with 5% non-fat milk in TBST and incubated overnight at 4°C with the indicated primary antibodies. Following incubation with HRP-conjugated secondary antibodies (see Supplementary Table 2 for details), immunoreactive bands were visualized using an ECL detection reagent and quantified by densitometry with ImageJ software.

## Flow Cytometry and Fluorescence Probes

Mitochondrial superoxide was detected using MitoSOX Red (MCE). General cellular ROS was measured with a Dihydroethidium (DHE) probe (KeyGEN BioTECH). Mitochondrial membrane potential was assessed using a JC-1 kit (Beyotime). Labile iron ($Fe^{2+}$) was detected with FerroOrange (Dojindo), and lipid peroxidation was visualized with Liperfluo (Dojindo). Cells were stained according to the manufacturers' protocols and analyzed on a CytoFLEX flow cytometer (Beckman Coulter). MDA levels and the ratio of GSH/GSSG were measured using commercial kits from Beyotime, following the manufacturer's instructions.

## RNA Isolation and Quantitative RT-PCR

Total RNA was isolated from cultured cells or tissue samples using TRIzol reagent (Invitrogen). Following the elimination of residual genomic DNA, complementary DNA (cDNA) was synthesized from 1 μg of total RNA utilizing the HiScript III RT SuperMix (Vazyme). The quantification of specific transcripts was subsequently performed by qPCR on a QuantStudio 5 system (Applied Biosystems) with SYBR Green Master Mix (Vazyme). Relative gene expression levels were determined using the $2^{-}\Delta\Delta Ct$ comparative threshold method, normalized to Actb (β-actin) as an endogenous reference gene. The specific primer sequences employed for amplification are provided in the Supplementary Materials (Table S5).

RNA Immunoprecipitation (RIP)

RNA immunoprecipitation (RIP) was conducted using the Magna RIP Kit (Millipore) in accordance with the manufacturer's guidelines. Cell lysates were subjected to immunoprecipitation with magnetic beads conjugated to either an anti-PGC-1α antibody (Proteintech, Cat# 66369-1-Ig) or a control IgG. Following stringent washing steps to remove non-specific binding, the co-precipitated RNA was isolated and subsequently quantified by RT-qPCR.

Chromatin Isolation by RNA Purification (ChIRP)

ChIRP was performed using the Magna ChIRP RNA Interactome Kit (Millipore). SH-SY5Y cells were cross-linked with 1% formaldehyde. Chromatin was sonicated to an average size of 200-500 bp. Biotinylated probes targeting LINC-EPS or LacZ (negative control) were hybridized with the chromatin lysate. The probe-chromatin complexes were captured with streptavidin magnetic beads. After washing and elution, the associated DNA was purified and analyzed by qPCR.

RNA Pull-down Assay

Biotinylated LINC-EPS and antisense control probes were transcribed *in vitro* (T7 RiboMAX, Promega). Probes were bound to streptavidin magnetic beads (Invitrogen) and incubated with SH-SY5Y cell lysates. After washing, bound proteins were eluted and analyzed by Western blotting.

## Lentivirus Production and Infection

Lentiviral vectors for LINC-EPS overexpression (pLV-LINC-EPS) and knockdown (sh-LINC-EPS; target sequence: GCCCCCTGCCCTGCCCACTG) were constructed by Tsingke Biotechnology (Beijing, China). Empty vector (empty) and non-targeting shRNA (shNC) served as controls. Lentivirus was produced by co-transfecting 293T cells with the transfer plasmid and packaging plasmids (psPAX2, pMD2.G) using Lipofectamine 8000 (Thermo Fisher). Viral supernatants were collected, filtered (0.45 μm), and used to infect SH-SY5Y cells in the presence of polybrene (8 μg/mL). Stable cell lines were selected using puromycin (2 μg/mL; Sigma-Aldrich).

## Dual-Luciferase Reporter Assay

The putative TBE was amplified from genomic DNA and inserted in either forward (TBE-F) or reverse (TBE-R) orientation downstream of a Ppargc1a promoter–luciferase cassette (2 kb upstream of the transcription start site, cloned into pGL3-basic; Promega). Control constructs included pGL3-

147 basic alone and pGL3 constructs containing TBE sequences without the Ppargc1a promoter. All
148 plasmids were verified by Sanger sequencing.

149 SH-SY5Y cells were transiently co-transfected with a firefly luciferase reporter construct (500
150 ng) and a pRL-TK Renilla luciferase normalization control vector (50 ng; Promega), utilizing
151 Lipofectamine 3000 (Invitrogen). Twenty-four hours post-transfection, cells were subjected to the
152 indicated treatments prior to lysis. The luminescence from both luciferases was quantified using the
153 Dual-Luciferase Reporter Assay System (Promega) with a GloMax 96 microplate luminometer. To
154 control for transfection efficiency, firefly luciferase activity was normalized to the corresponding
155 Renilla luciferase activity.

156

157

158 # Supplementary Table

159 **Table S1. The main reagents and kits**

| Product Name | Supplier | Catalog Number (if available) |
|---|---|---|
| Chemicals and Inhibitors | | |
| MPTP | Sigma-Aldrich (St. Louis, MO, USA) | M0896 |
| $MPP^+$ iodide | Sigma-Aldrich (St. Louis, MO, USA) | D048 |
| Ferrostatin-1 | MCE (Monmouth Junction, NJ, USA) | HY-100579 |
| Necrostatin-1 | MCE (Monmouth Junction, NJ, USA) | HY-15760 |
| Z-VAD-FMK | MCE (Monmouth Junction, NJ, USA) | HY-16658B |
| Mito-TEMPO | MCE (Monmouth Junction, NJ, USA) | HY-112879 |
| Visomitin (SkQ1) | MCE (Monmouth Junction, NJ, USA) | HY-112130 |
| Cell Culture and Transfection | | |
| DMEM, high glucose | Servicebio (Wuhan, China) | G4510 |
| Fetal Bovine Serum (FBS) | Gibco (Grand Island, NY, USA) | 10099141 |
| Penicillin-Streptomycin Solution | Beyotime (Shanghai, China) | C0222 |

| | | |
|---|---|---|
| Opti-MEM I Reduced Serum Medium | Gibco (Grand Island, NY, USA) | 31985070 |
| Molecular Biology Kits | | |
| AccuRT-SuperMix | Accurate Biology (Hunan, China) | AG11728 |
| RIPA Lysis Buffer | KeyGEN BioTECH (Jiangsu, China) | KGP702 |
| BCA Protein Assay Kit | Solarbio (Beijing, China) | PC0020 |
| SDS-PAGE Gel Preparation Kit | U-landy (Suzhou, China) | |
| Protein A/G Magnetic Beads | MCE (Monmouth Junction, NJ, USA) | HY-K0202 |
| Western Blotting Reagents | | |
| PVDF Membrane, 0.45 μm | Millipore (Billerica, MA, USA) | IPVH00010 |
| NcmColor Prestained Protein Ladder | NCM Biotech (Suzhou, China) | |
| Non-fat Dry Milk | Lanjieke Tech (China) | |
| Tris, Glycine, SDS, Tween-20 | Solarbio (Beijing, China) | |
| Fluorescent Probes and Assay Kits | | |
| MitoSOX™ Red Indicator | MCE (Monmouth Junction, NJ, USA) | HY-D0942 (from Invitrogen) |

| | | |
|---|---|---|
| DHE (ROS) Detection Kit | KeyGEN BioTECH (Jiangsu, China) | KGAF019 |
| FerroOrange | Dojindo (Kumamoto, Japan) | F374 |
| Liperfluo | Dojindo (Kumamoto, Japan) | L248 |
| Mitochondrial Membrane Potential Kit (JC-1) | Beyotime (Shanghai, China) | C2006 |
| MDA Assay Kit | Beyotime (Shanghai, China) | S0131S |
| GSH and GSSG Assay Kit | Beyotime (Shanghai, China) | S0053 |

**Table S2 The main antibodies**

| Antibody name | Manufacturer | Product Number | Dilution ratio （WB） | Dilution ratio （IF/IP） | Dilution ratio (IP/RIP/MERIP) |
|---|---|---|---|---|---|
| TH | Servicebio | GB11181-100 | 1:500 | 1:200 | |
| TH | Servicebio | GB12181-100 | 1:500 | 1:200 | |
| xCT | Servicebio | GB115276-100 | 1：500 | | |
| α-Syn | CST | 45083SF | 1:1000 | 1:200 | |
| p53 | CST | 9238 | 1:1000 | | |
| Bcl-2 | CST | 3948 | 1:1000 | | |
| β-Actin | CST | 3700S | 1:1000 | | |

| | | | | | |
|---|---|---|---|---|---|
| GPX4 | HUABIO | AB_3070665 | 1:10000 | 1:100 | |
| GPX4 | ABclonal | A13309 | 1:1000 | 1:100 | |
| CQ10B | UpingBio | YP-mAb-18654 | 1:1000 | | |
| CQ10A | UpingBio | YP-mAb-09554 | 1:1000 | | |
| FTL | Proteintech | 10727-1-AP | 1:1000 | | |
| FSP1 | Proteintech | 20886-1-AP | 1:1000 | | |
| Bax | CST | 2772 | 1:1000 | | |
| Gasdermin D | CST | 39754 | 1:1000 | | |
| GFAP | Abcam | ab7260 | 1:1000 | | |
| Iba1 | WAKO | 019-19741 | 1:1000 | | |
| ASC | CST | 67824 | 1:1000 | | |
| Phospho-RIP1 (Ser166) | CST | 31122 | 1:1000 | | |
| Phospho-RIP3 (Ser227) | CST | 91702 | 1:1000 | | |
| PGC-1α | Proteintech | 66369-1-Ig | 1:1000 | | 1:25 |
| ZBP1 | Proteintech | 13285-1-AP | 1:1000 | | |
| RIPK1 | CST | 3493 | 1:1000 | | |
| RIPK3 | CST | 15828 | 1:1000 | | |

| | | | |
|---|---|---|---|
| NLRP12 | Cusabio | CSB-PA015867GA01HU | 1:1000 |
| CL-Casp1 | CST | 89332 | 1:1000 |
| Casp1 | CST | 83383 | 1:1000 |
| CL-GSDMD | CST | 10137 | 1:1000 |
| CL-Casp3 | CST | 9664 | 1:1000 |
| Casp3 | CST | 14220 | 1:1000 |
| p-MLKL | CST | 37333 | 1:1000 |
| MLKL | CST | 26539 | 1:1000 |
| CL-Casp8 | CST | 8592 | 1:1000 |
| Casp8 | CST | 4790 | 1:1000 |
| NLRP3 | CST | 15101 | 1:1000 |
| HRP-conjugated Goat Anti-Rabbit IgG(H+L) | Proteintech | SA00001-2 | 1:10000 |
| HRP-conjugated Goat Anti-Mouse IgG(H+L) | Proteintech | SA00001-1 | 1:10000 |
| Multi-rAb™ | Proteintech | RGAR011 | 1:10000 |

| | | | |
|---|---|---|---|
| Polymer HRP-Goat Anti-Rabbit | | | |
| Multi-rAb™ CoraLite® Plus 488-Goat Anti-Rabbit | Proteintech | RGAR002 | 1:200 |
| Multi-rAb™ CoraLite® Plus 488-Goat Anti-Mouse | Proteintech | RGAM002 | 1:200 |
| Multi-rAb™ CoraLite® Plus 594-Goat Anti-Rabbit | Proteintech | RGAR004 | 1:200 |
| Multi-rAb™ CoraLite® Plus 594-Goat Anti-Mouse | Proteintech | RGAM004 | 1:200 |
| Multi-rAb™ CoraLite® Plus 647-Goat Anti-Rabbit | Proteintech | RGAR005 | 1:200 |

| | | | |
|---|---|---|---|
| Multi-rAb™ CoraLite® Plus 647-Goat Anti-Mouse | Proteintech | RGAM005 | 1:200 |

**Table S3: Human blood sample information**

**HD**

| Sample | Gender: 1 male and 2 females | Age |
|---|---|---|
| 1 | 2 | 39 |
| 2 | 2 | 87 |
| 3 | 2 | 53 |
| 4 | 1 | 38 |
| 5 | 1 | 38 |
| 6 | 1 | 72 |
| 7 | 1 | 59 |
| 8 | 2 | 50 |
| 9 | 2 | 75 |
| 10 | 2 | 70 |

| | | |
|---|---|---|
| 11 | 2 | 56 |
| 12 | 1 | 64 |
| 13 | 2 | 62 |
| 14 | 1 | 48 |
| 15 | 1 | 76 |
| 16 | 2 | 71 |
| 17 | 1 | 42 |
| 18 | 2 | 87 |
| 19 | 1 | 66 |
| 20 | 2 | 63 |
| 21 | 2 | 56 |
| 22 | 2 | 57 |
| 23 | 1 | 57 |
| 24 | 2 | 42 |
| 25 | 1 | 57 |
| 26 | 2 | 56 |
| 27 | 1 | 56 |
| 28 | 1 | 25 |

| | | | |
|---|---|---|---|
| 29 | 1 | | 56 |
| 30 | 1 | | 78 |

**PD**

| Sample | Course of the disease (years) | Gender: 1 male and 2 females | Age | UPDRS-III |
|---|---|---|---|---|
| 1 | 5 | 1 | 63 | 33 |
| 2 | 11 | 1 | 77 | 18 |
| 3 | 4.5 | 2 | 68 | 19 |
| 4 | 0.5 | 2 | 76 | 13 |
| 5 | 2 | 1 | 66 | 19 |
| 6 | 7 | 2 | 65 | 12 |
| 7 | 1 | 2 | 76 | 21 |
| 8 | 11 | 1 | 72 | 20 |
| 9 | 4 | 1 | 62 | 20 |
| 10 | 1.5 | 1 | 70 | 32 |
| 11 | 2 | 2 | 71 | 16 |
| 12 | 5 | 2 | 63 | 28 |
| 13 | 9 | 1 | 70 | 23 |
| 14 | 1 | 1 | 60 | 2 |
| 15 | 6 | 1 | 60 | 6 |
| 16 | 3 | 1 | 65 | 6 |
| 17 | 4 | 2 | 67 | 29 |
| 18 | 1 | 1 | 67 | 16 |
| 19 | 2 | 2 | 63 | 15 |
| 20 | 1.5 | 2 | 52 | 26 |

| | | | | |
|---|---|---|---|---|
| 21 | 1 | 1 | 78 | 8 |
| 22 | 10 | 2 | 77 | 28 |
| 23 | 3 | 1 | 60 | 12 |
| 24 | 1 | 1 | 61 | 8 |
| 25 | 2 | 1 | 53 | 13 |
| 26 | 2 | 2 | 62 | 13 |
| 27 | 1 | 1 | 75 | 10 |
| 28 | 6 | 2 | 74 | 12 |
| 29 | 10 | 1 | 80 | 26 |
| 30 | 11 | 1 | 82 | 29 |

**Table S4-1 Primer sequences for mouse tail identification**

| Primer name | Upstream sequence | Downstream sequence |
|---|---|---|
| LINC-EPS-1 | GCAGACAGGCGTGGACATTCATTCT | GCTTGTACTCGCCTCTTCTCTGCAA |
| LINC-EPS-2 | TCACTGAATACACAGGCTGCTGCAA | GCTTGTACTCGCCTCTTCTCTGCAA |

| Primer name | Upstream sequence | Downstream sequence |
|---|---|---|
| *LINC-EPS$^{f/f}$* | CCTTAACAAATGTGGTCGCATACC | CAACCCCAACCAGCAGATAAAG |
| *DAT$^{Cre}$* | TGGCTGTTGGTGTAAAGTGG | GGACAGGGACATGGTTGACT |

**Table S4-2 PCR Sample Loading System**

| Component | Volume |
|---|---|
| Forward Primer (10 μM) | 1 μL |
| Reverse Primer (10 μM) | 1 μL |
| DNA | 1.5 μL |
| 2×Taq PCR Master Mix | 12.5 μL |
| ddH2O | 9 μL |

**Table S4-3 PCR Program**

| Stage | temperature | time | cycle number |
|---|---|---|---|
| Stage 1 | 95℃ | 5 min | 1 |
| Stage 2 | 95℃ | 30 s | 35 |
| | 60℃ | 30 s | |
| | 72℃ | 45 s | |
| Stage 3 | Default Settings of the instrument | | 1 |

**Table S5 The primer sequences**

| Primer name | Upstream sequence | Downstream sequence |
|---|---|---|
| GAPDH | AAATCCCATCACCATCTTCCAG | AGGGGCCATCCACAGTCTTCT |
| m-LINC-EPS | GCGCACTTCTCTCATCTGTG | TCAGCTGTAGGATGGGAGGT |
| h-LINC-EPS | CGCATTAATGGGGGCATTCG | CTAAACCGTTTTCCCCGC |
| Bdnf | ATGGCGTTTCTCCGAAGCAT | TCCGCCCTATAAGCATCTTGA |
| Nt3 | CCGTGGCATCCAAGGTAACAA | GCAGTTCGGTGTCCATTGC |
| Nt4 | CTGTGTGCGATGCAGTCAGT | TGCAGCGGGTTTCAAAGAAGT |
| Gdnf | GGCAGTGCTTCCTAGAAGAGA | AAGACACAACCCCGGTTTTTG |
| Igf | GCTCTTCAGTTCGTGTGTGGA | GCCTCCTTAGATCACAGCTCC |
| Ngf | GGCAGACCCGCAACATTACT | CACCACCGACCTCGAAGTC |
| Fgf | CAGGCGGAGGCAGCTATAC | CCTGGTTCCCTGGATAGTACC |
| PGC-1α | GCTTTCTGGGTGGACTCAAGT | GAGGGCAATCCGTCTTCATCC |
| NRF1 | AGGAACACGGAGTGACCCAA | TATGCTCGGTGTAAGTAGCCA |
| NRF2 | TCAGCGACGGAAAGAGTATGA | CCACTGGTTTCTGACTGGATGT |
| TFAM | ATGGCGTTTCTCCGAAGCAT | TCCGCCCTATAAGCATCTTGA |
| MFN1 | TGGCTAAGAAGGCGATTACTGC | TCTCCGAGATAGCACCTCACC |
| MFN2 | CTCTCGATGCAACTCTATCGTC | TCCTGTACGTGTCTTCAAGGAA |

| | | |
|---|---|---|
| OPA1 | TGTGAGGTCTGCCAGTCTTTA | TGTCCTTAATTGGGGTCGTTG |
| DNM1L | CTGCCTCAAATCGTCGTAGTG | GAGGTCTCCGGGTGACAATTC |
| FIS1 | AGCGGGATTACGTCTTCTACC | CATGCCCACGAGTCCATCTTT |
| MFF | ACTGAAGGCATTAGTCAGCGA | TCCTGCTACAACAATCCTCTCC |
| PINK1 | CCCAAGCAACTAGCCCCTC | GGCAGCACATCAGGGTAGTC |
| Parkin | GTGTTTGTCAGGTTCAACTCCA | GAAAATCACACGCAACTGGTC |
| MT-ND1 | GGCTATATACAACTACGCAAAGGC | GGTAGATGTGGCGGGTTTTAGG |
| MT-ND3 | CCACAACTCAACGGCTACATAGAAA | GGGTAAAAGGAGGGCAATTTCTAGA |
| MT-ND6 | CAAACAATGTTCAACCAGTAACCACTAC | ATATACTACAGCGATGGCTATTGAGGA |
| NDUFA3 | GGGGCCTCGCTGTAATTCTG | GACGGGCACTGGGTAGTTG |
| MT-CYB | ATCACTCGAGACGTAAATTATGGCT | TGAACTAGGTCTGTCCCAATGTATG |
| ATP5F1A | GTATTGCCCGCGTACATGG | AGGACATACCCTTTAAGCCTGA |
| MT-ATP6 | TAGCCATACACAACACTAAAGGACGA | GGGCATTTTTAATCTTAGAGCGAAA |

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177 **Table S6 The English abbreviations and full names that appear in the article**

| Abbreviation | Full name |
|---|---|
| CHIRP | Chromatin Isolation by RNA Purification |
| Act-D | Actinomycin D |
| ChIP | Chromatin Immunoprecipitation |
| CHX | Cycloheximide |
| CCK-8 | Cell Counting Kit-8 |
| DAT | Dopamine Transporter |
| DAPI | 4’,6-diamidino-2-phenylindole |
| DA neurons | Dopaminergic neurons |
| DFO | Deferoxamine |
| $Fe^{2+}$ | Ferrous iron |
| FISH | Fluorescence *in situ* hybridization |
| GSEA | Gene Set Enrichment Analysis |
| GPX4 | Glutathione peroxidase 4 |
| GSH | Glutathione (reduced form) |

| | |
|---|---|
| GSSG | Glutathione disulfide (oxidized form) |
| IF | Immunofluorescence |
| IP | Immunoprecipitation |
| JC-1 | 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine iodide |
| KEGG | Kyoto Encyclopedia of Genes and Genomes |
| KO | Knockout |
| LINC-EPS | Long intergenic non-coding RNA-Enhancer of Polycomb-like protein |
| MDA | Malondialdehyde |
| MMP | Mitochondrial membrane potential |
| $MPP^+$ | 1-methyl-4-phenylpyridinium |
| MPTP | 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine |
| mitoROS | Mitochondrial reactive oxygen species |
| NRF1 | Nuclear respiratory factor 1 |
| NRF2 | Nuclear factor erythroid 2-related factor 2 |

| | |
|---|---|
| oeLINC-EPS | Overexpression of lncRNA-EPS |
| oeNC | Overexpression negative control |
| PD | Parkinson’s disease |
| PGC-1α | Peroxisome proliferator-activated receptor-gamma coactivator 1-alpha |
| qRT-PCR | Quantitative real-time polymerase chain reaction |
| RIP | RNA Immunoprecipitation |
| ROS | Reactive oxygen species |
| SEM | Standard error of the mean |
| shLINC-EPS | Short hairpin RNA targeting lncRNA-EPS |
| shNC | Non-targeting control short hairpin RNA |
| SNpc | Substantia nigra pars compacta |
| TBE | T-box element |
| TEAD | TEA domain family member |
| TEM | Transmission electron microscopy |

| | |
|---|---|
| TH | Tyrosine hydroxylase |
| TFAM | Mitochondrial transcription factor A |
| WT | Wild-type |
| xCT | Solute Carrier Family 7 Member 11 (SLC7A11) |
| FSP1 | Ferroptosis suppressor protein 1 (AIFM2) |
| FTL | Ferritin Light Polypeptide |
| ZLN005 | A specific agonist of PGC-1α |

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