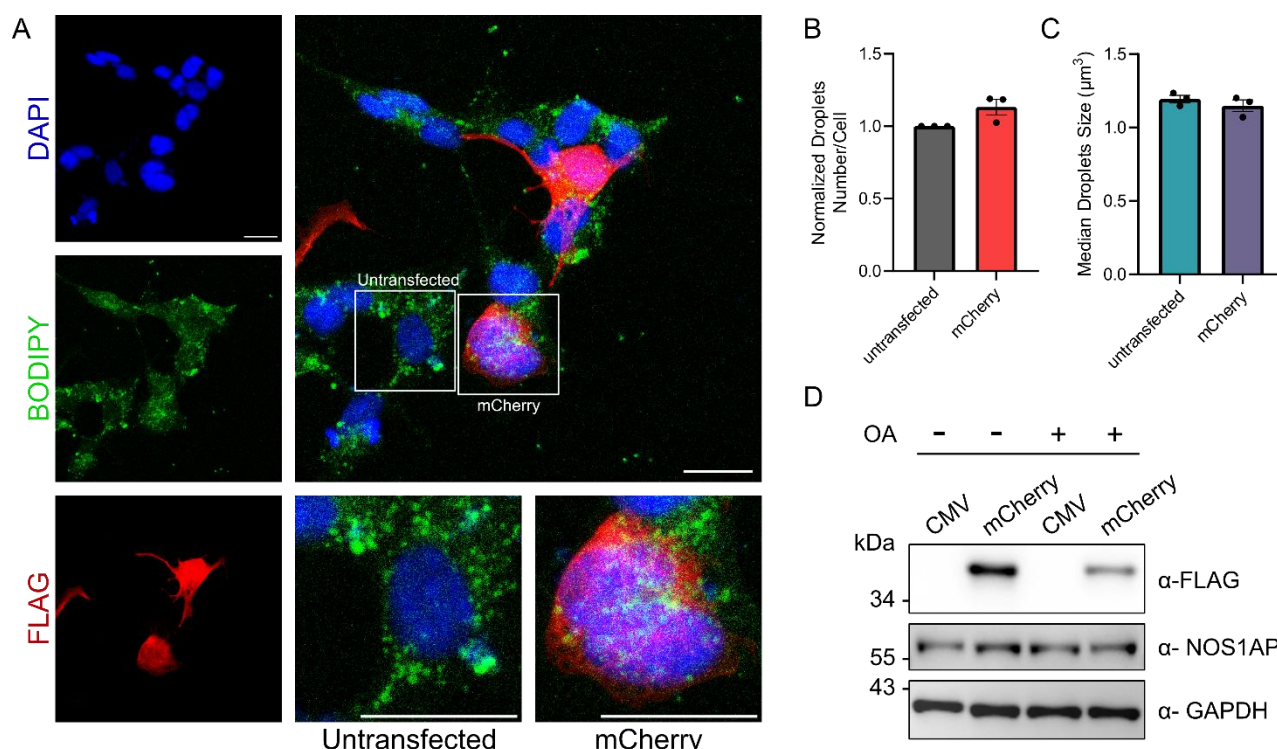
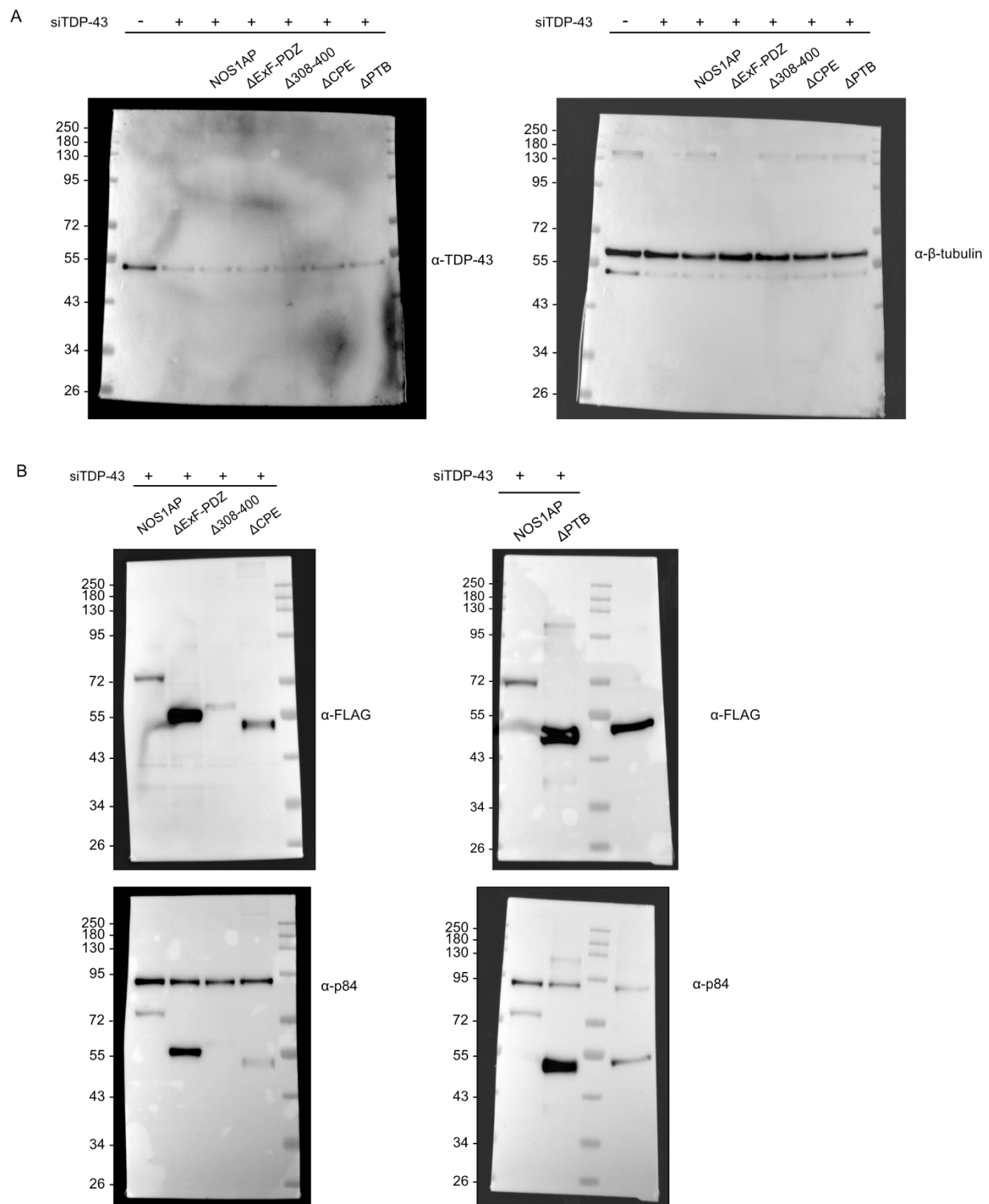
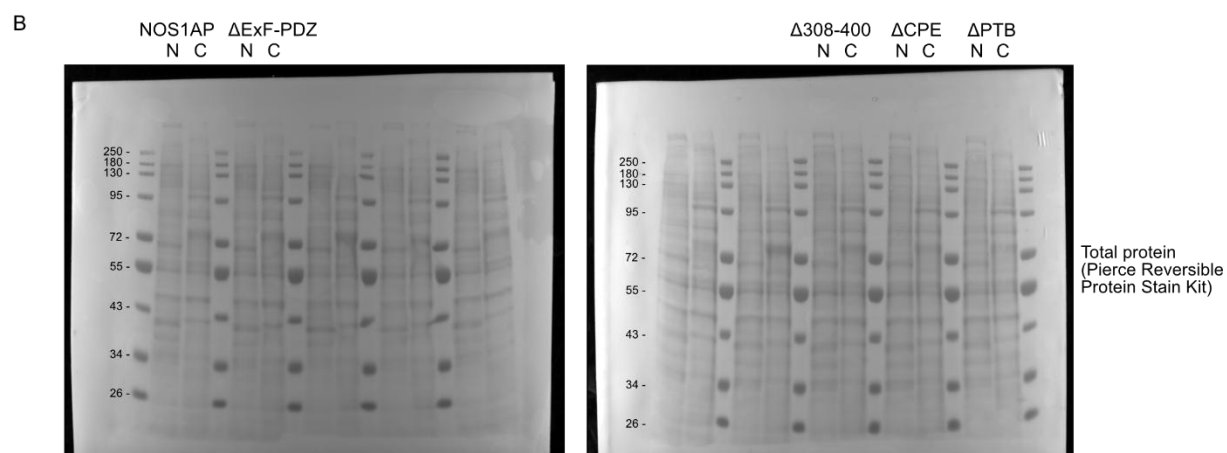
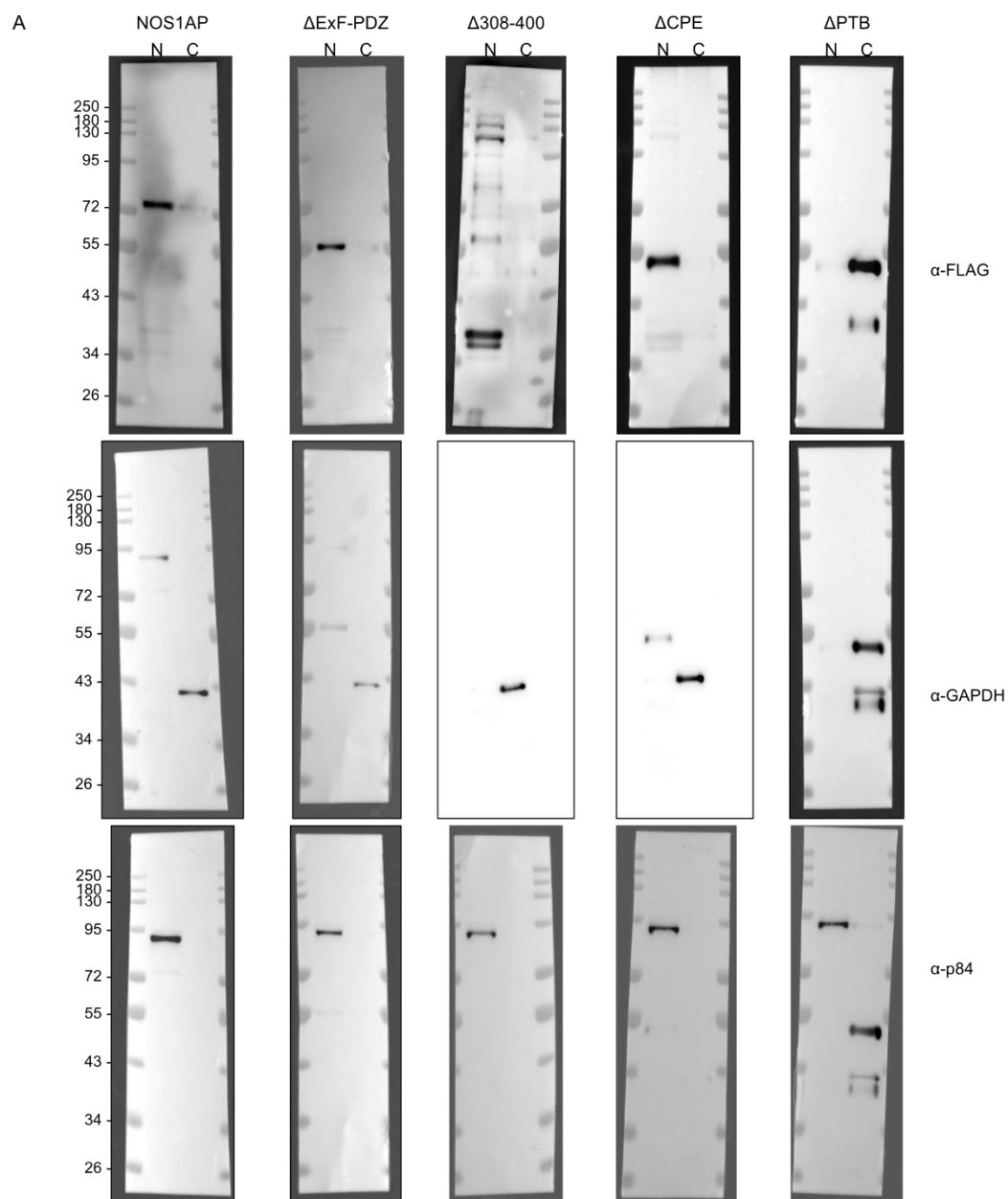




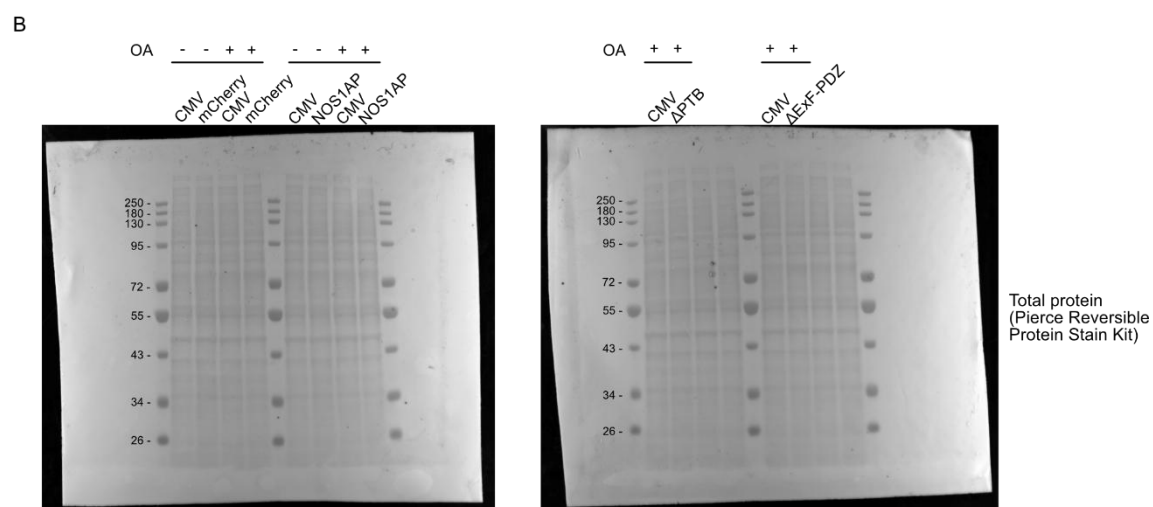
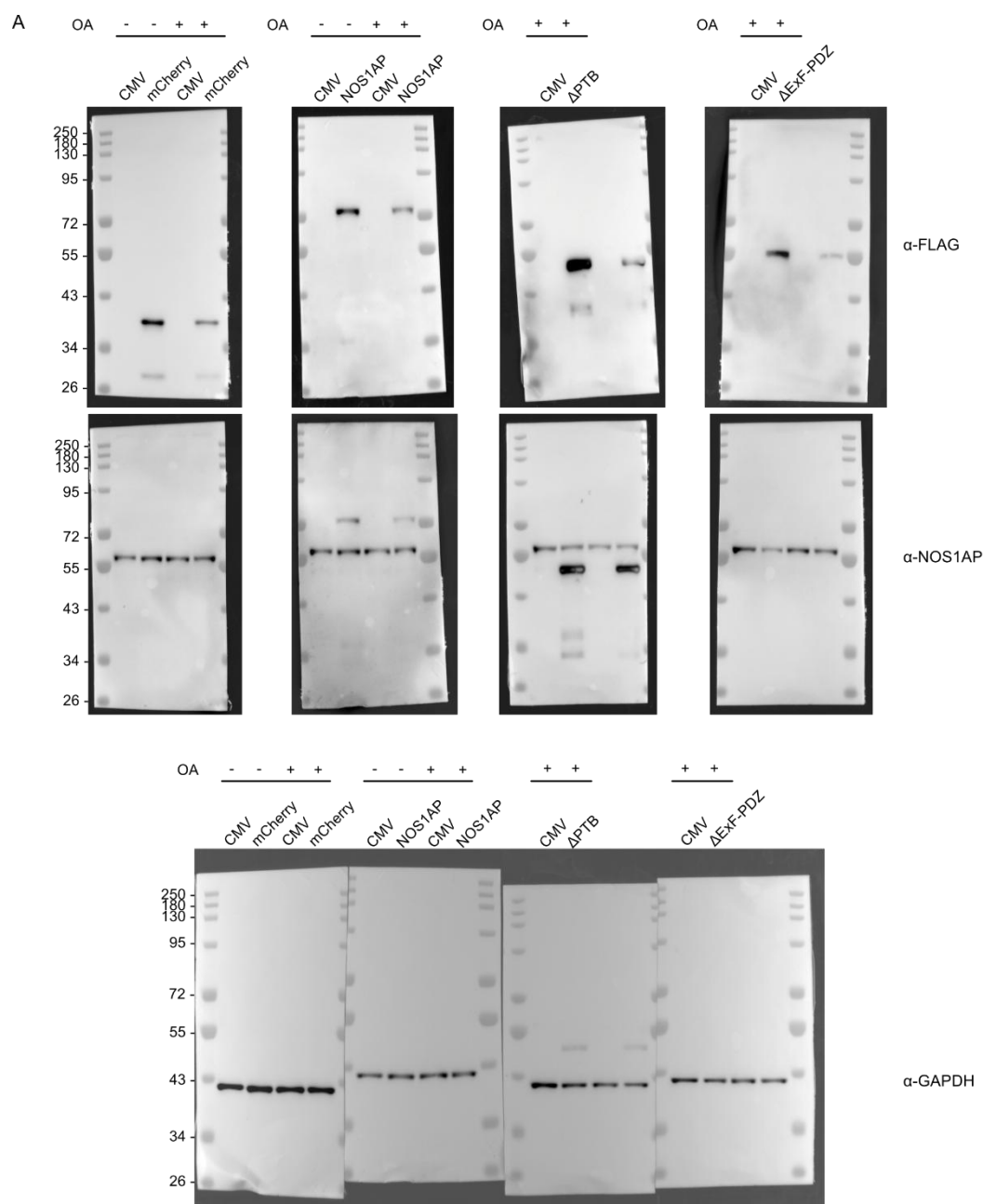
Supplementary Figure S1. Effect of mCherry overexpression on OA-induced lipid droplet accumulation. **A)** Immunofluorescence analysis of SH-SY5Y cells transfected with FLAG-tagged mCherry control plasmid and treated with 200 μM oleic acid (OA). Nuclei were stained with DAPI (blue), FLAG-tagged mCherry was detected using Alexa Fluor 594 (red), and lipid droplets (LDs) were stained with BODIPY 493/503 (green). Images were acquired using a Zeiss LSM 800 confocal microscope with a 63X objective. Scale bar, 20 μm . White boxes indicate the regions shown at higher magnification in the corresponding enlarged images. **B)** Quantification of the normalized number of LDs per cell in transfected compared with untransfected cells. Data are presented as normalized LD number per cell $\pm$ SEM from three independent experiments. Statistical significance was assessed using a one-sample t-test. **C)** Comparison of LD size between transfected and untransfected cells. Data are presented as median LD volume (μm^3) $\pm$ SEM from three independent experiments. Statistical significance was assessed using the Mann–Whitney test. **D)** Western blot analysis of cells transfected with FLAG-tagged mCherry and treated with OA. Cells transfected with the empty CMV vector were used as transfection control. GAPDH was used as a loading control.



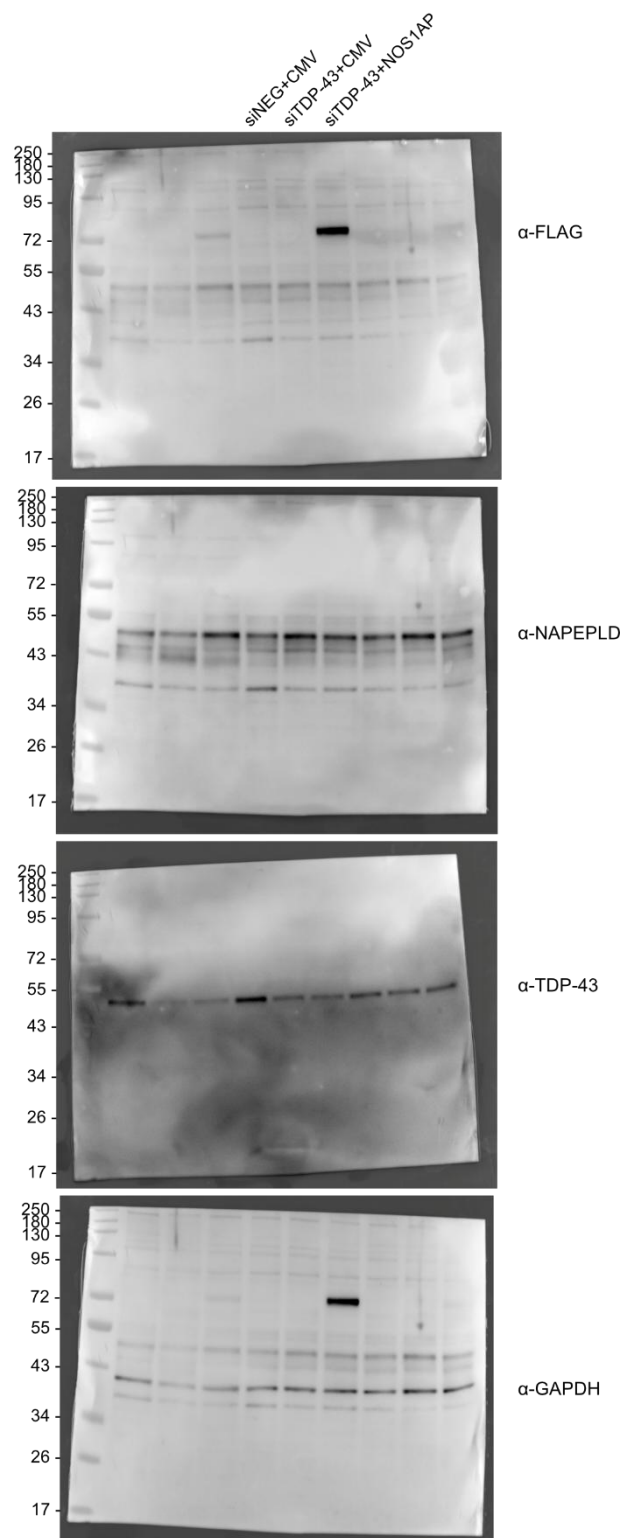
Supplementary Figure S2. Uncropped Western blot images corresponding to Fig. 1. A) Full-length blot of TDP-43 and β -tubulin corresponding to Fig. 1B. **B)** Full-length blots of FLAG and p84 corresponding to Fig. 1C.



Supplementary Figure S3. Uncropped Western blot images corresponding to Fig. 2B. A) Full-length blot of FLAG, p84, and GAPDH corresponding to Fig. 2B. **B)** Total protein staining (with Pierce Reversible Protein Stain Kit, Thermo; 24580) of full-length membranes reported on A.



Supplementary Figure S4. Uncropped Western blot images corresponding to Fig. 3E, 4D, 4H, and S1D. A) Full-length blot of FLAG, NOS1AP, and GAPDH corresponding to Fig. S1D, 3E, 4D, and 4H (from left to right). **B)** Total protein staining (with Pierce Reversible Protein Stain Kit, Thermo; 24580) of full-length membranes reported on A.



Supplementary Figure S5. Uncropped Western blot images corresponding to Fig. 5D. Full-length blot of FLAG, NAPEPLD, TDP-43, and GAPDH corresponding to Fig. 5D.

siRNA	Target	Sequence (5'-3')
siTDP-43	TARDBP	sense: GCAAAGCCAAGAUGAGCCU
		antisense: AGGCUCAUCUUGGCUUUGC
siLUC	Luciferase	sense: UAAGGCUAUGAAGAGAUAC
		antisense: GUAUCUCUUCAUAGCCUUA
siNEG (ON-TARGETplus Non-targeting siRNA #1)	Non-targeting control	target sequence: UGGUUUACAUGUCGACUAA

Supplementary Table 1. siRNA sequences.

Target	Type	Host/clonality	WB dilution	conjugate	supplier	Blocking buffer	Wash buffer
FLAG	primary	mouse/monoclonal (M2)	1:1000 in 2% non-fat dry milk/PBST 0.1%	-	Sigma-Aldrich (F1804)	4% non-fat dry milk/PBST 0.1%	PBST 0.1%
	secondary	goat/polyclonal	1:2000 in 2% non-fat dry milk/PBST 0.1%	HRP	Dako (P0447)		
TDP-43	primary	rabbit/polyclonal	1:1000 in Purity anti-rabbit HRP reagent (Vilber, PU4200500)	-	Proteintech (10782-2-AP)	PURITY Washing buffer 1X (Vilber; PU4000500)	PURITY Washing buffer 1X (Vilber; PU4000500)
GAPDH	primary	Mouse/monoclonal	1:1000 in Purity anti-mouse HRP reagent (Vilber, PU4200100)	-	Invitrogen (MA5-15738)	PURITY Washing buffer 1X (Vilber; PU4000500)	PURITY Washing buffer 1X (Vilber; PU4000500)
p84	primary	Mouse/monoclonal	1:1000 in 2% non-fat dry milk/PBST 0.1%	-	Invitrogen (MA1-23261)	4% non-fat dry milk/PBST 0.1%	PBST 0.1%
	secondary	goat/polyclonal	1:2000 in 2% non-fat dry milk/PBST 0.1%	HRP	Dako (P0447)		

NOS1AP	primary	rabbit/ monoclonal	1:1000 in Purity anti- rabbit HRP reagent	-	Abcam (ab19068 6)	PURITY Washing buffer 1X (Vilber; PU400050 0)	PURITY Washing buffer 1X (Vilber; PU400050 0)
NAPEPLD	primary	mouse/ monoclonal	1:1000 in 2% non-fat dry milk/ PBST 0.1%	-	Abcam (ab11925 9)	4% non-fat dry milk/ PBST 0.1%	PBST 0.1%
	secondary	goat/ polyclonal	1:2000 in 2% non-fat dry milk/ PBST 0.1%	HRP	Dako (P0447)		
β -tubulin	primary	mouse/ monoclonal	1:10000 in Purity anti- mouse HRP reagent (Vilber, PU420010 0)	-	In house	PURITY Washing buffer 1X (Vilber; PU400050 0)	PURITY Washing buffer 1X (Vilber; PU400050 0)

Supplementary Table 2. List of primary and secondary antibodies for western blot analysis.

Target gene	Forward sequence (5'-3')	Reverse sequence (5'-3')
<i>GAPDH</i>	GCAAATTCCATGGCACCCT	TCGCCCCACTTGATTTTGG
<i>GRIN1</i>	CTACCGCATACCCGTGCTG	GCATCATCTCAAACCACACGC
<i>GRIN2D</i>	GTGGGATAACCGGGATTACTCC	GAAGCGACCATAGCGGGAC
<i>DLG4</i>	TCGGTGACGACCCATCCAT	GCACGTCCACTTCATTTACAAAC
<i>B4GALT5</i>	GCAGGTGCTTCGGAGTGCTTAT	GGAAGGGAGTCTTTCAGGGCAG
<i>CD2AP</i>	GGCATGGGAATGTAGCAAGTC	CTTTACACTGACGCTTCTTGGTC
<i>EFR3A</i>	ATGCCTACCCGAGTATGCTG	CCTTTCTGCCAGGTAAGAACC
<i>GAPDH</i>	GCAAATTCCATGGCACCCT	TCGCCCCACTTGATTTTGG
<i>NAPEPLD</i>	GTGAATCCCGTGGCCAACATGG	CCAGCTTCCCTCACTCCAGC
<i>NOS1AP</i>	AGCCAAGAACATCAAGAAGAAG	TCACTTTCATCCATCCACTG
<i>PIBF1</i>	ACGATCAGCTCTTAGACAGGT	AGAAGTTGAACACGCTCACTTT
<i>PPARA</i>	CATCACGGACACGCTTTCACC	CACACGCGTGGACTCCGTAAT
<i>PRKAG2</i>	CACATTCCGGACCTGAGCTCCT	GTGCAGACATGGGGCTGGAG
<i>POLR2A</i>	GCACCACGTCCAATGACAT	GTGCGGCTGCTTCCATAA
<i>RNF213</i>	CTTCACTTCTGGGCTCAGGAGAC	TGAAGGTGCTGTCCAGCATGAG
<i>SCARB2</i>	AGCCAATACGTCAGACAATGC	TTGGTAAAAGTGTGGGAAAGACA
<i>SYNJ2</i>	ATGGACGATGGAGTGTCTATCT	CATGTGCCTGTCGAAAGCAG
<i>TARDBP</i>	ATCTGGTGTATGTTGTCAACTATCC	GAAGTTCTCAAAGGTACTAAAATACTC

Supplementary Table 3. List of qPCR primers.