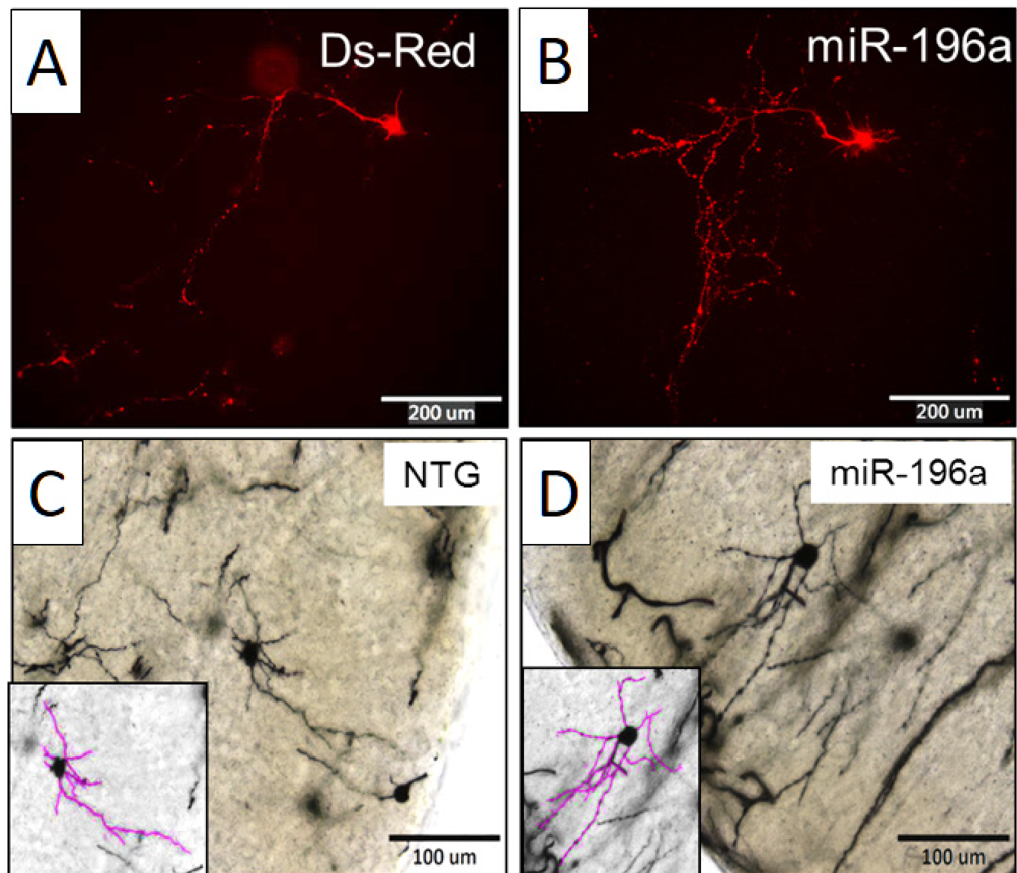
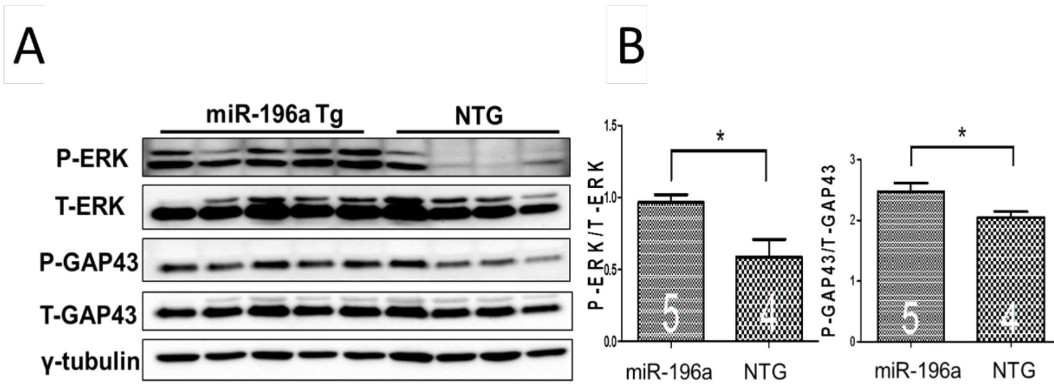
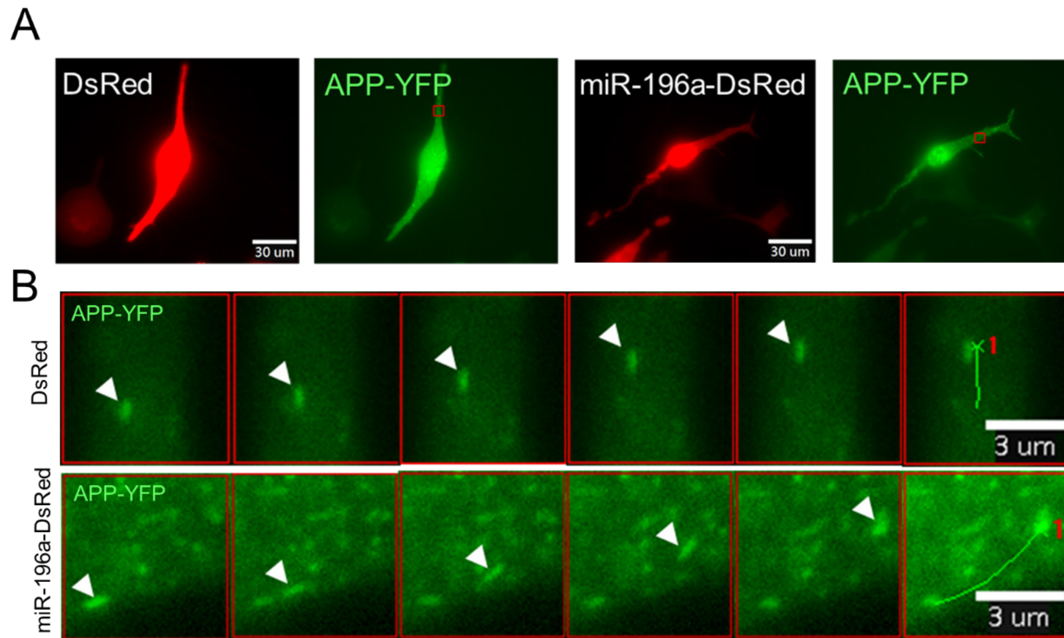


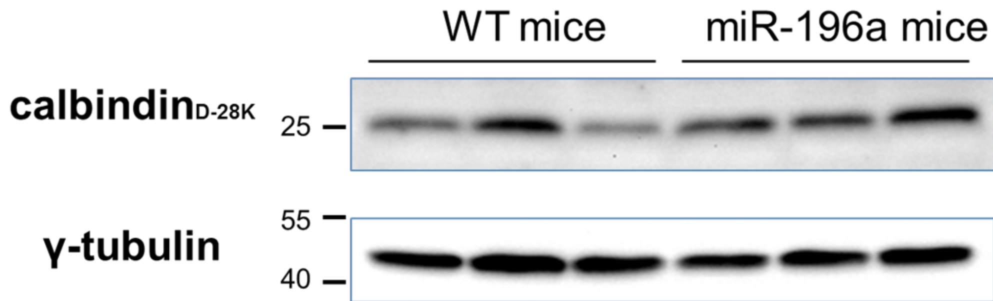
Supplementary Figure 1. miR-196a enhances neurite outgrowth in primary cortical neurons *in vitro* and transgenic mice *in vivo*. For the *in vitro* study, primary cortical neurons were transfected with *Ds-Red* or miR-196a-*DsRed*. For the *in vivo* study, the brains of non-transgenic (NTG) and miR-196a transgenic mice were subjected to Golgi staining. Representative images show neurite outgrowth in primary neurons transfected with Ds-Red **(A)** or miR-196a-DsRed **(B)**. Representative images of Golgi staining show neurite outgrowth in cortical neurons of NTG **(C)** and miR-196a transgenic **(D)** mice. Squares in the bottom left region show the cells examined using NeuronJ.

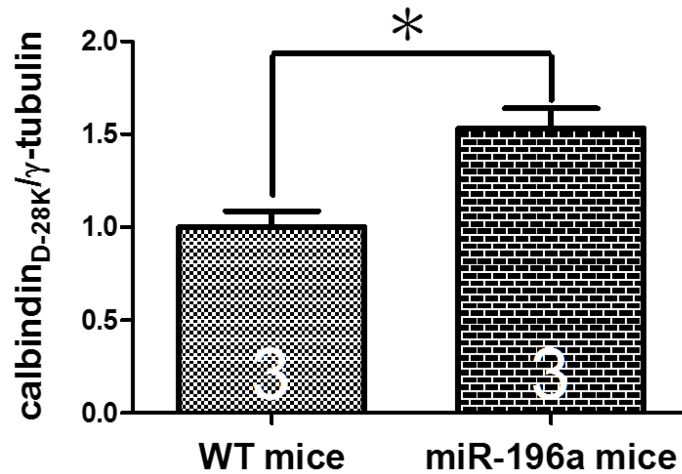


Supplementary Figure 2. miR-196a enhances ERK and GAP43 signaling in miR-196a transgenic mice. The brains of non-transgenic (NTG) and miR-196a transgenic mice were subjected to Western blotting to detect the expression profiling of ERK and GAP43. **(A)** Western blotting shows the expression of P-ERK, T-ERK, P-GAP43 and T-GAP43 in the brains of miR-196a transgenic and NTG mice. **(B)** Quantitation results from (A) show the increase of P-ERK/T-ERK and P-GAP43/T-GAP43 in the brains of miR-196a transgenic mice. γ-tubulin was used as an internal control. *indicates a significant difference with $P<0.05$.

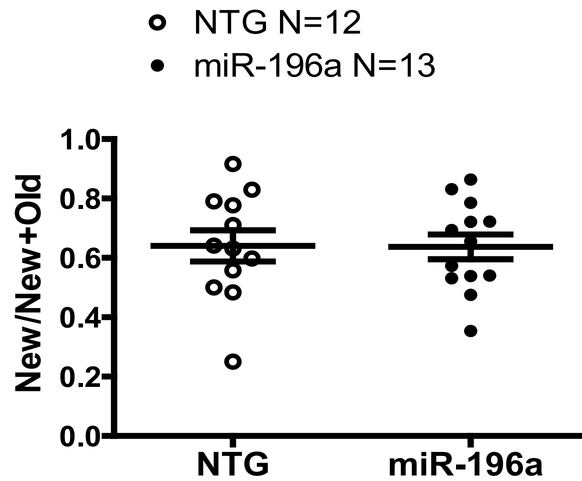


Supplementary Figure 3. miR-196a enhances the intracellular transport during anterograde transport. N2a cells cotransfected with Ds-Red & APP-YFP or miR-196a-Ds-Red & APP-YFP were used for APP-YFP fluorescent image recording every 0.44 seconds for 66 seconds. **(A)** Representative images show the cells coexpressing DsRed and APP-YFP, which were used for this study. The red squares indicate the area used for recording. **(B)** A series of six high magnification images show the movements of APP-YFP in DsRed (top panel) and miR-196a-DsRed (bottom panel) cells. Arrow heads indicate the movement of the traced APP-YFP particle, and green lines in the last images indicate the distance of APP-YFP movement.

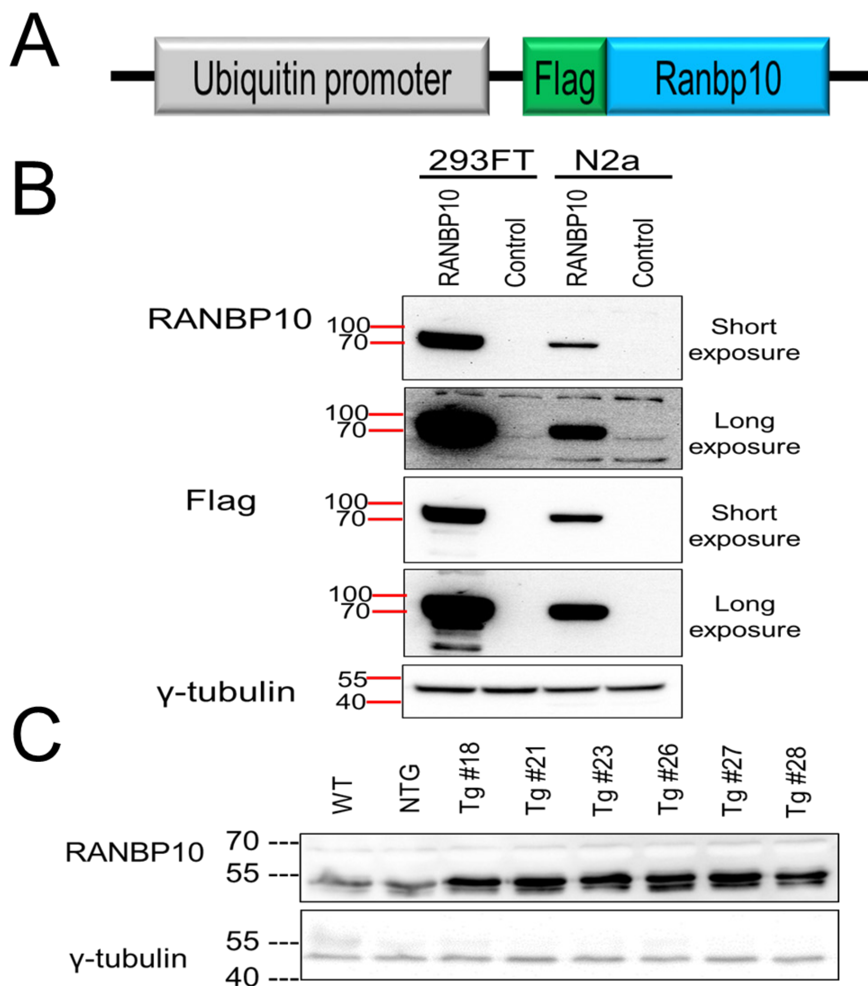




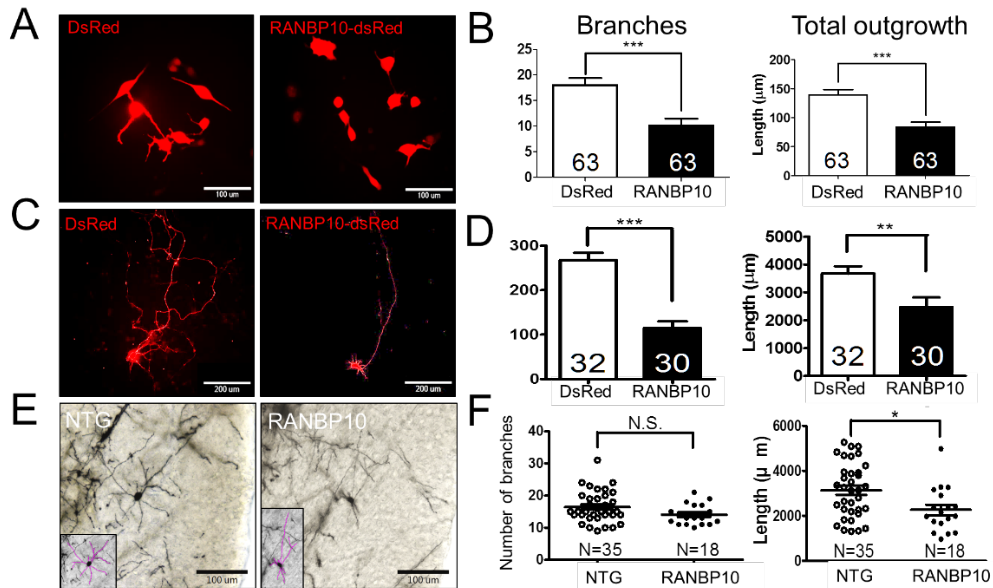
Supplementary Figure 4. miR-196a transgenic mice show higher expression levels of calbindin$_{D28K}$. Brain samples were subjected to Western blotting using c-Fos and calbindin$_{D28K}$ antibodies. **(A)** Western blotting shows the expression of calbindin$_{D28K}$ in the brains of WT and miR-196a transgenic mice. **(B)** Quantitation results from (A) show the significant increase in calbindin$_{D28K}$/γ-tubulin expression in miR-196a transgenic mice. γ-tubulin was used as an internal control. *indicates a significant difference with $P<0.05$. ***indicates a significant difference with $P<0.001$.



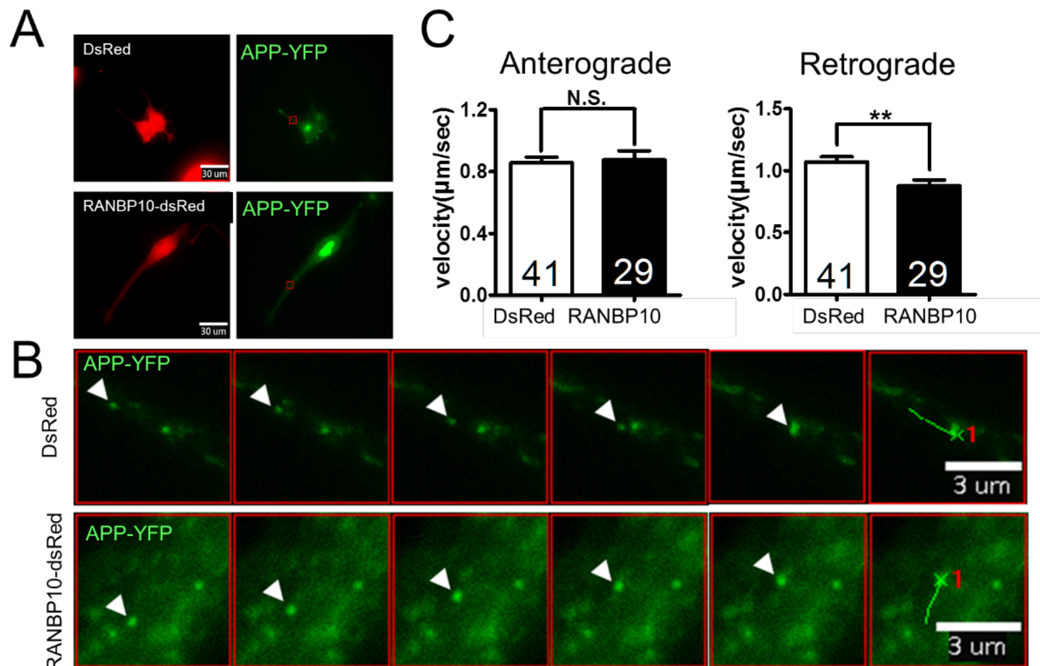
Supplementary Figure 5. miR-196a transgenic mice do not show better learning and memory in the novel object recognition test. Non-transgenic (NTG) and miR-196a transgenic mice were subjected to behavioral tests, and quantitation results of novel object recognition test do not show significant differences between the two groups.



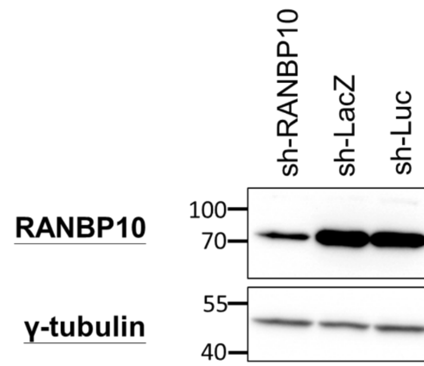
Supplementary Figure 6. Generation of RANBP10 transgenic mice. (A) The transgene construct shows that RANBP10 fused with Flag tag is under the control of an ubiquitin promoter. **(B)** The RANBP10 transgene was transfected into 293FT and N2a cells, and cells were collected for Western blotting using RANBP10 and Flag antibodies, showing the expression of exogenous RANBP10. γ-tubulin was used as an internal control. **(C)** Proteins extracted from mouse tails were subjected to Western blotting using a RANBP10 antibody. Different transgenic (Tg) mice show a higher expression of RANBP10. Wild-type and non-transgenic mice were used as control.



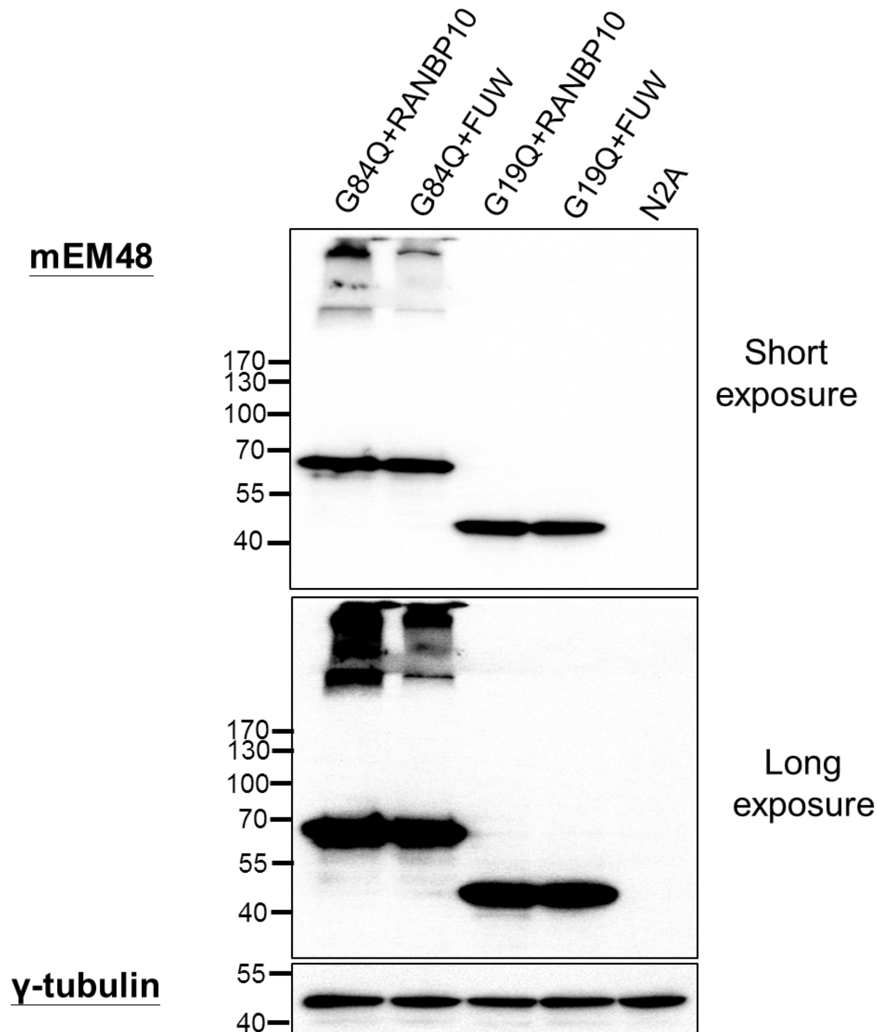
Supplementary Figure 7. RANBP10 exacerbates neurite outgrowth in N2a cells, primary cortical neurons and transgenic mice. For the *in vitro* study, N2a cells and primary cortical neurons were transfected with *Ds-Red* or RANBP10-*DsRed*, and the number of branches and total neurite length were determined by red fluorescence (A -D). For the *in vivo* study, the brains of non-transgenic (NTG) and RANBP10 transgenic mice were subjected to Golgi staining, and the number of branches and total neurite length were determined (E and F). **(A)** Representative images show neurite outgrowth in N2a cells transfected with Ds-Red(left) or RANBP10-DsRed(right). **(B)** Quantitation results show decreased branches (left) and total neurite length (right) after RANBP10 treatment. N2a cells from three batches were examined. The number of examined cells is indicated inside different bars. **(C)** Representative images show neurite outgrowth in primary neurons transfected with Ds-Red (left) or RANBP10-DsRed (right). **(D)** Quantitation results show decreased branches (left) and total neurite length (right) after RANBP10 treatment. Primary neurons from three batches were examined. The number of examined neurons is indicated inside different bars. **(E)** Representative images of Golgi staining show neurite outgrowth in cortical neurons of NTG (left) and RANBP10 transgenic (right) mice. Squares in the bottom left region show the cells examined using NeuronJ. **(F)** Quantitation results show the decreased total neurite length (right), but not branches (left), in the brains of RANBP10 transgenic mice. Two mice from each group were examined. The number of examined neurons are indicated. * indicates a significant difference with $P<0.05$; ** indicates a significant difference with $P <0.01$. *** indicates a significant difference with $P <0.001$.



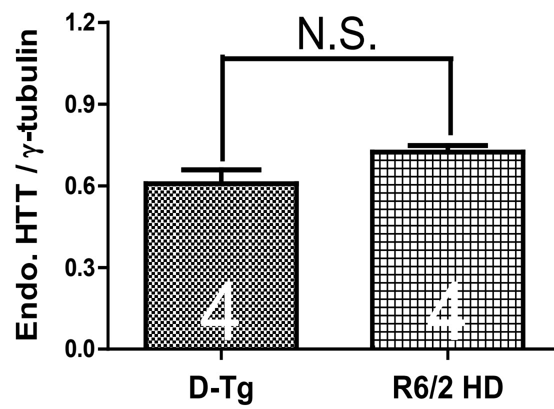
Supplementary Figure 8. RANBP10 exacerbates intracellular transport during retrograde transport. N2a cells cotransfected with Ds-Red & APP-YFP or RANBP10-Ds-Red & APP-YFP were used for APP-YFP fluorescent image recording every 0.44 seconds for 66 seconds. **(A)** Representative images show the cells coexpressing DsRed and APP-YFP, which were used for this study. The red squares indicate the area used for recording. **(B)** A series of six high magnification images show the movements of APP-YFP in DsRed (top panel) and RANBP10-DsRed (bottom panel) cells. Arrow heads indicate the movement of the traced APP-YFP particle, and the green lines in the last images indicate the distance of APP-YFP movement. **(C)** Quantitated results show the significantly slower velocity of APP-YFP movement during retrograde but not anterograde transport in RANBP10-Ds-Red cells. ** indicates a significant difference with P <0.01. N.S. indicates no significant difference.



Supplementary Figure 9. shRANBP10 knockdowns the expression of RANBP10 in 293FT cells. 293FT cells were cotransfected with RANBP10 and different shRNAs for 48 hours, and then subjected to Western blotting. shRANBP10 targeting on RANBP10 suppresses the expression of RANBP10. sh-lacZ and sh-luc were used as negative controls. γ-tubulin was used as an internal control.



Supplementary Figure 10. RANBP10 exacerbates pathological aggregates of G84Q, not G19Q, *in vitro*. Western blotting shows the expression of exogenous HTT using a mEM48 antibody after cotransfection of G84Q or G19Q with RANBP10 (overexpression) and FUW (empty vector control) in N2a cells. γ-tubulin was used as an internal control.



Supplementary Figure 11. Overexpression of RANBP10 does not affect the expression levels of endogenous mouse HTT in mouse brains of transgenic mice. Quantitation results of endogenous mouse HTT (MAB2166) from figure 4e show there is no significant difference between D-Tg and R6/2 transgenic mice. The number of examined mice is indicated inside different bars.

{MATRIX SCIENCE} **Mascot Search Results**

Protein View

Match to: **Ranbp10**

Matched peptides shown in **Bold Red**

1 MLTAHWLSKA NLVALLPAPS DTIAAPSKMA AATADPGAGN PQAGDSSGGD
51 SGGGLPSPGE QELSRRLQRL YPAVNQHETP LPRSWSPK**DK** **YNYIGLSQGN**
101 **LR**VHYKGHGK NHKDAASVRA THPIPAACGI YYFEVKIVSK **GRDGYMGIGL**
151 **SAQGVNMNR**L PGWDKHSYGY HGDDGHSFCS SGTGQPYGPT FTTGDVIGCC
201 VNLINGTCFY TKNGHSLGIA FTDLPANLYP TVGLQTPGEI VDANFGQQPF
251 LFDIEDYMRE WRAKVQGTVH GFPISARLGE WQAVLQNMVS SYLVHHGYCS
301 TATAFAR**MTE** **TPIQEEQASI** **KNR**QKIQKLV **LEGR**VGEAIE TTQRFYPGLL
351 EHNPNLLFML K**CRQFVEMVN** **GTDSEVRSLS** **SR**SPKSQDSY PGSPSLSPRH
401 GPSSSHIHNT GADSPSCSNG VASTKNKQNH SKYPAPSSSS SSSSSSSSSS
451 PSSVNYSESN STDSTKSQPH SSTSNQETSD SEMEMEAEHY PNGVLESVST
501 RIVNGAYK**HD** **DLQTDESSMD** **DGHPRRQLCG** **GNQAATERII** **LFGR**ELQALS
551 EQLGREYGKN LAHTEMLQDA FSLLAYSDPW SCPVGHQLDP IQREPVCAAL
601 NSAILESQNL PK**QPPLMLAL** **GQASECLRLM** **ARAGLGSCSF** **ARVDDYLH**

Supplementary Figure 12. The result of mass spectrometry shows the matches of protein sequence to RANBP10. 55kD band of RANBP10 was subjected to the analysis of mass spectrometry. The bold red shows the matched peptides to RANBP10.