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Supplementary Materials for

Tau and other proteins found in Alzheimer's disease spinal fluid are linked to retromer-mediated endosomal traffic in mice and humans

Sabrina Simoes, Jessica L. Neufeld, Gallen Triana-Baltzer, Setareh Moughadam, Emily I. Chen, Milankumar Kothiya, Yasir H. Qureshi, Vivek Patel, Lawrence S. Honig, Hartmuth Kolb, Scott A. Small*

*Corresponding author. Email: sas68@columbia.edu

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The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

(available at stm.sciencemag.org/cgi/content/full/12/571/eaba6334/DC1)

Supplemental Materials

Supplementary Figures

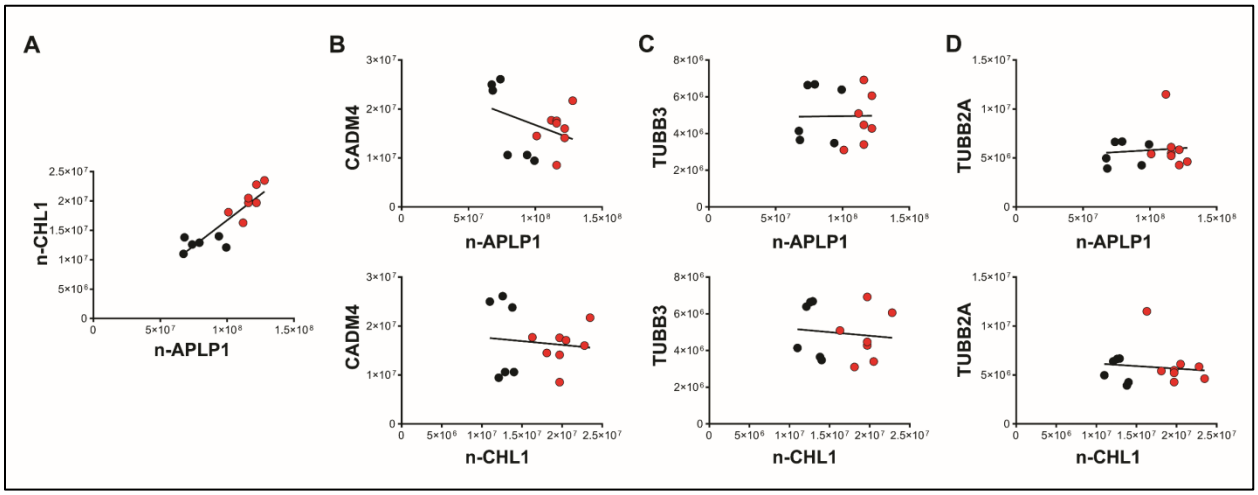

Fig. S1. n-APLP1 and n-CHL1 correlation analysis based on MS/MS peak intensity measurements. (A) Scatter plot showing relationship between n-APLP1 and n-CHL1 in the CSF of *Vps35* cKO mice (red circles) and controls (black circles) (n = 14, r = 0.89, P <0.0001, with a R^2 = 0.787). **(B)** Scatter plot showing relationship between CADM4 and n-APLP1 (n = 14, r = -0.377, P =0.184, with a R^2 = 0.142), or between CADM4 and n-CHL1 (n = 14, r = -0.111, P =0.706, with a R^2 = 0.012). **(C)** Scatter plot showing relationship between TUBB3 and n-APLP1 (n = 14, r = 0.013, P =0.967 with a R^2 = 0.00016), or between TUBB3 and n-CHL1 (n = 14, r = -0.108, P =0.7262, with a R^2 = 0.012). **(D)** Scatter plot showing relationship between TUBB2a and n-APLP1 (n = 14, r = 0.094, P =0.750 with a R^2 = 0.008), or between TUBB2a and n-CHL1 (n = 14, r = -0.117, P =0.689, with a R^2 = 0.014). Of note, all technical replicates were used for the analysis.

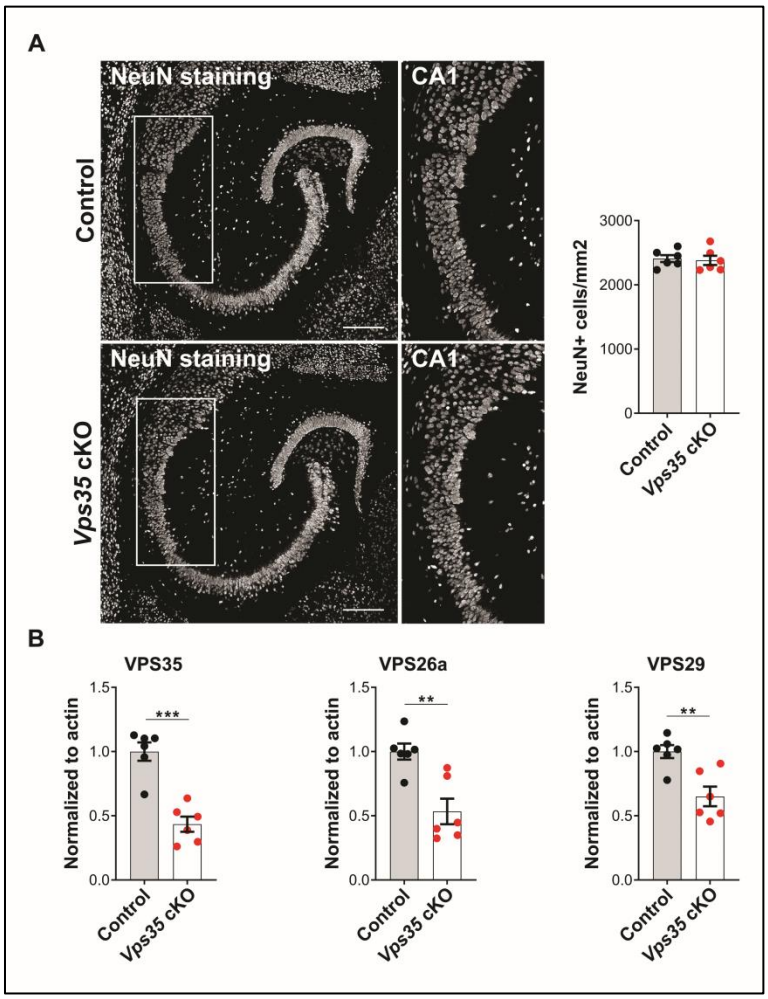

Fig. S2. NeuN immunostaining and quantification of retromer protein expression in 3-month-old *Vps35* cKOs and control littermates. (A) Representative NeuN staining showing neurons in the hippocampus of 3 month-old *Vps35* cKO mice compared to their control littermates (P = 0.6991, in a non-parametric Mann Whitney test. n = 6 animals/genotype). Hippocampal CA1 regions are shown at higher magnification. Scale bar, 200µm. **(B)** Quantification of western blot analysis shown in Figure 4D. Data are shown as means ± SEM. Two-tailed unpaired student T-test was used for the statistical analysis (*P < 0.05).

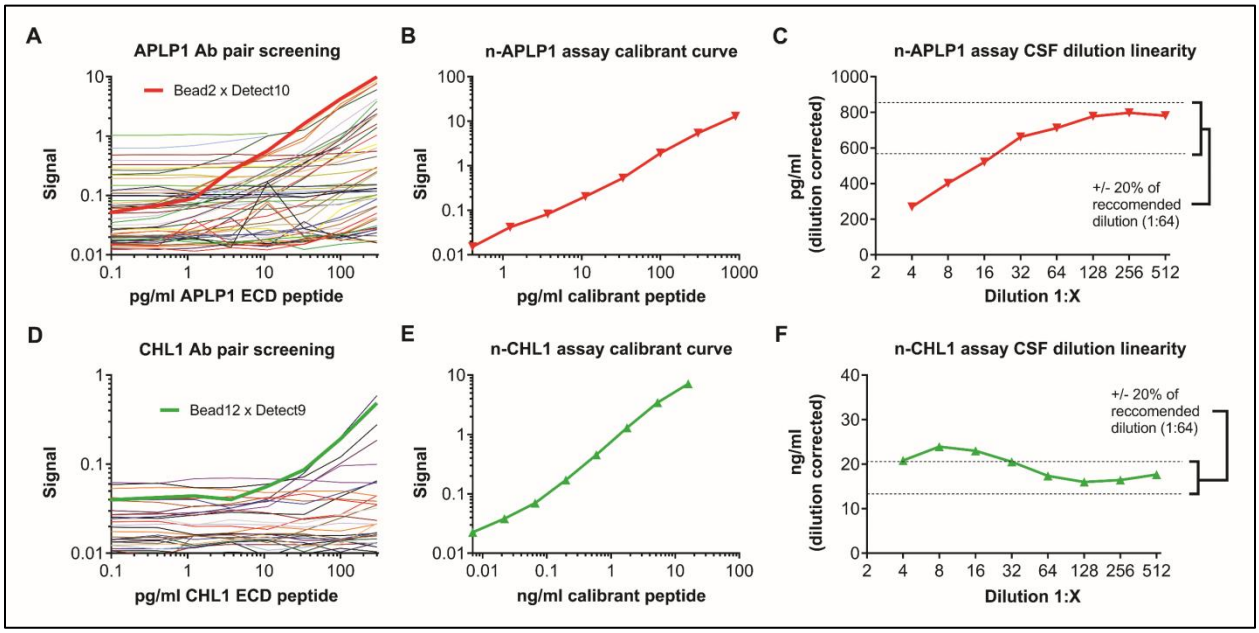

Fig. S3. Development and qualification of Simoa APLP1 and CHL1 assays. (upper panels): A panel of 8 commercial antibodies raised against human APLP1 were screened in all configurations against recombinant APLP1 protein on Simoa HD-1 platform **(A)**. The most sensitive assay (2x10 aka n-APLP1) was optimized; standard curve range **(B)** and dilution linearity with healthy control CSF **(C)** are shown. (**lower panels)**: A panel of 6 commercial antibodies raised against human CHL1 were screened in all configurations against recombinant CHL1 protein on Simoa HD-1 platform **(D)**. The most sensitive assay (12x9 aka n-CHL1) was optimized; standard curve range **(E)** and dilution linearity with healthy control CSF **(F)** are shown.

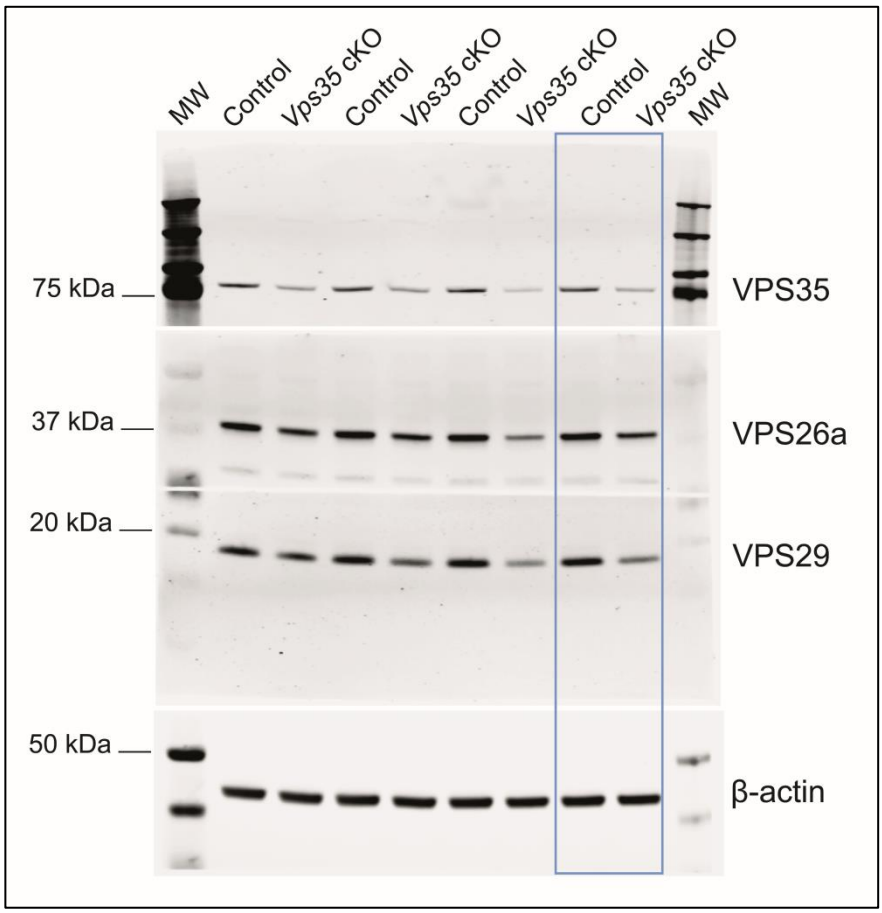

Fig. S4. Extended data of Western blots cropped in main Fig. 1. Blue rectangles indicate lanes cropped. MW, molecular weight.

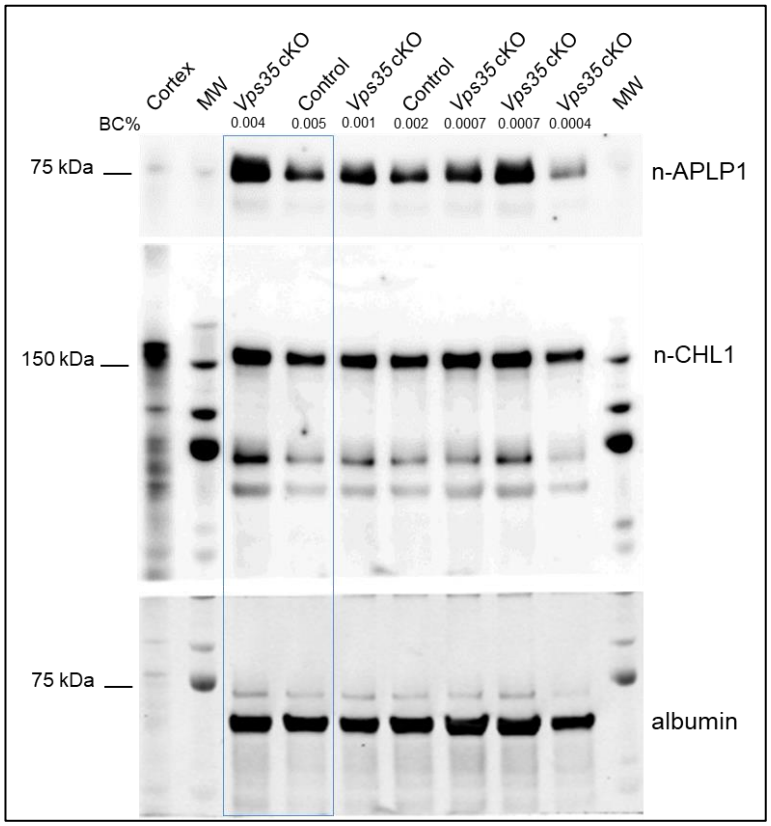

Fig. S5. Extended data of Western blots cropped in main Fig. 4A. Blue rectangles indicate lanes cropped. BC%, percentage of blood contamination; MW, molecular weight.

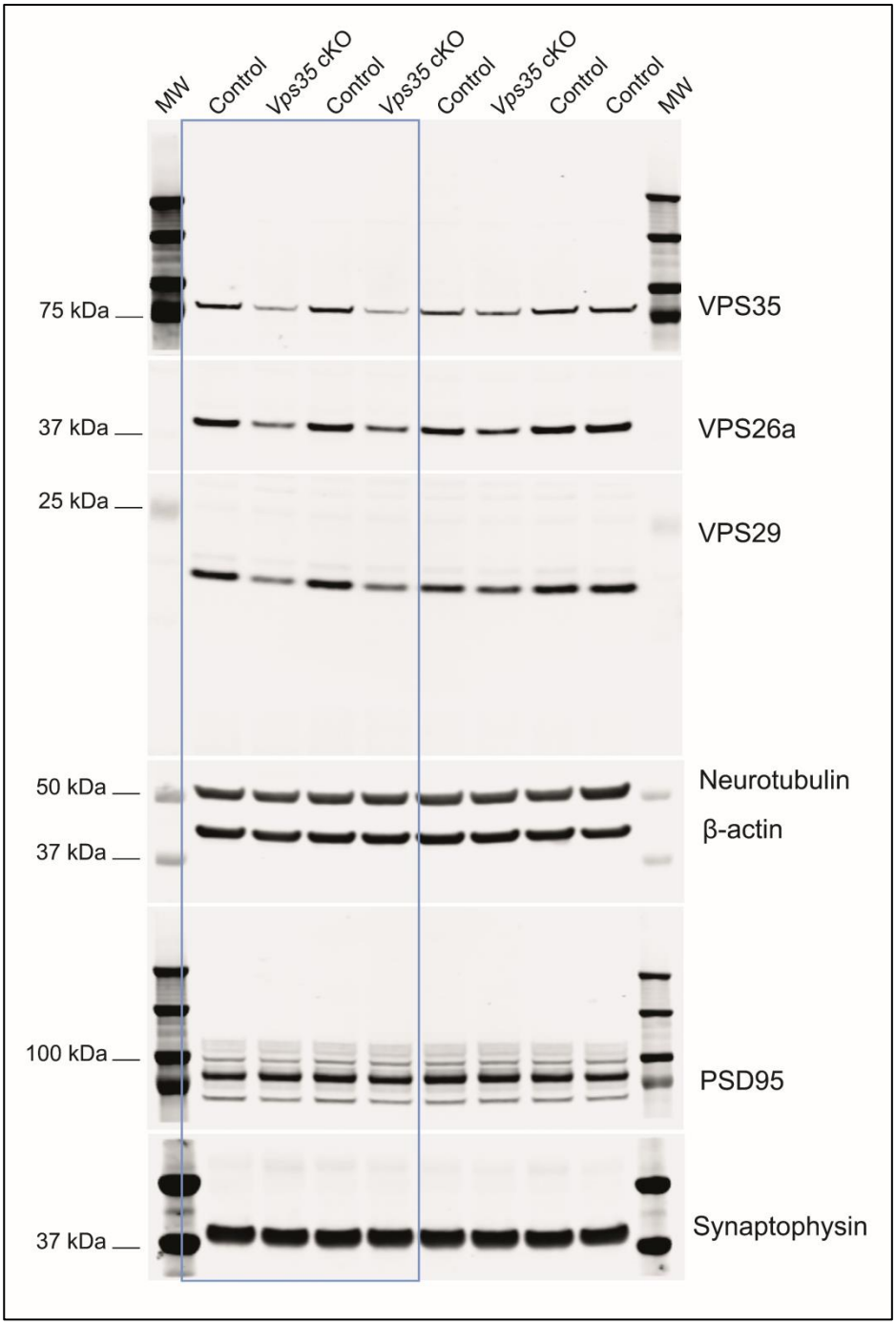

Fig. S6. Extended data of Western blots cropped in main Fig. 4D. Blue rectangles indicate lanes cropped. MW, molecular weight.

Data file S1. Completed list of proteins identified in murine CSF (provided as a separate Excel file).

Data file S2. List of peptides detected by MS/MS analysis (provided as a separate Excel file).

Data file S3. Individual-level data (provided as a separate Excel file).