Supplementary Figure Legends

Supplementary Figure 1. APP N-terminal, but not C-terminal fragments or full-length APP, localize to filamentous structures that stain for Rtn4, a marker of the tubular ER. (**a**) Dual labeling of CAD cells with antibodies to epitopes in the N- and C-terminal region of APP (APP_N and APP_C). Note that the distributions of APP_N and APP_C are largely distinct throughout the cell. Also note that APP_N shows a filamentary, while APP_C a discrete, punctate, distribution, both in the soma and neurites. In CAD cells with flat soma (lower images), APP_N shows a filamentary distribution, while APP_C concentrates at a compact region adjacent to the nucleus. Because the distributions of APP_N and APP_C are largely nonoverlaping, they likely reflect the presence of the APP fragments, sAPP and CTF, respectively, rather than full-length APP. (**b**) Extensive colocalization of APP_N with Rtn4 in the soma. (**c**) Similar, reticular distribution of APP_N and Rtn4 in growth cones of extending neurites. Right images show neurite terminals. Bars = 20 µm.

Supplementary Figure 2. Colocalization of APP N-terminal epitopes (APP_N) with neurofilaments (NFs). (**a**) Dual labeling of CAD cells with antibodies to APP_N and peripherin. Note that APP_N is absent in neurite regions devoid of NFs ("so-called "gaps"). The lower images show almost perfect colocalization of APP_N with the peripherin filaments. (**b**) Knocking down peripherin expression with siRNA reduces translocation of APP_N, but not APP_C in neurites. The bottom micrographs show that RNAi significantly reduces the peripherin levels in the neurites, and at their terminals, in transfected cells (see also [8]). Transfected cells are detected by the co-expression of

GFP. Arrows point to neurites of nontransfected cells. The phase contrast micrograph shows that the neurites of transfected and nontransfected cells are of similar caliber. Bars = 20 µm. (**c**) Silencing the expression of *prph* by transfection of CAD cells with peripherin siRNA diminishes the levels of peripherin protein (long arrow) by ~60% (immunoblot 2, probed with anti-peripherin antibody). The upper region of the blot was probed with an unrelated antibody, detecting two polypeptides (short arrows), to verify equal protein load (immunoblot 1). Molecular weight markers are given in kilodaltons.

Supplementary Figure 1

Supplementary Figure 2

a

APP$_N$

Peripherin

APP$_N$ Peripherin

b   Peripherin siRNA plus GFP

APP$_N$ APP$_C$

GFP   GFP

Peripherin   GFP

c (1)

(2)   - 85

- 38

+   -

Peripherin siRNA