Supplemental Figures

Supplemental Figure 1

**Serum-derived exosomes from AD patients are enriched with ceramide.** (A) Size distribution (Zetaview NTA analysis) of human serum exosomes. (B) Ceramide species profile using lipid mass spectrometry (LC-MS/MS) of AD patient serum-derived exosomes normalized to phosphate content. (C) Immunoblot for exosome markers CD63 and Flotillin-1 showing equal protein expression levels of GFAP in AD and healthy control individuals. (D) Structures of ceramide analogs S18 and B16.
Supplemental Figure 2

Serum derived exosomes from WT and 5xFAD mice are taken up by N2a cells. Representative fluorescence microscopy images of PKH67-labeled exosomes from wild type (A) and 5xFAD (B) mice showing their uptake by N2a cells and primary cultured neurons (C, wild type; D, 5xFAD exosomes).
**Supplemental Figure 3**

5xFAD exosomes retained complex formation between Aβ and ceramide after uptake into N2a cells. Either wild type (A) or 5xFAD (B, C, D) serum-derived exosomes were labeled with PKH67 dye and then used for incubation of N2a cells. PLA shows complex formation between Aβ and ceramide only with 5xFAD exosomes. C is similar to B at higher magnification. D is detail (frame) from C.
Interaction between Aβ and mitochondrial via VDAC1 in human brain. (A) Representative fluorescence image of human brain section showing colocalization of Aβ with mitochondrial Tom-20 around amyloid plaque (arrows). (B) PLA using antibodies against Aβ and mitochondrial VDAC1 showing complex formation in cells surrounding amyloid plaque.