Supplementary Figure S1

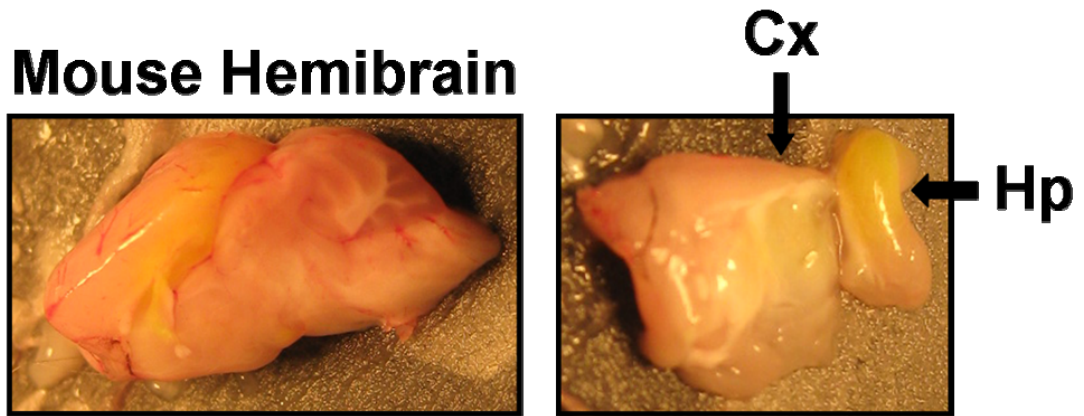

Fig. S1. Macroscopic GFP expression in adult mouse brain, 1 month after brain injection with 1.0 ul of AAV solution in the dorsal hippocampus. Left panel: intact mouse hemibrain viewed facing the midline of the brain with the cerebellum on the right side of the image. Right panel: mouse hemibrain with hippocampus dissected out and reflected away from the cortex. Cx – cortex; Hp – hippocampus.

Supplementary Figure S2

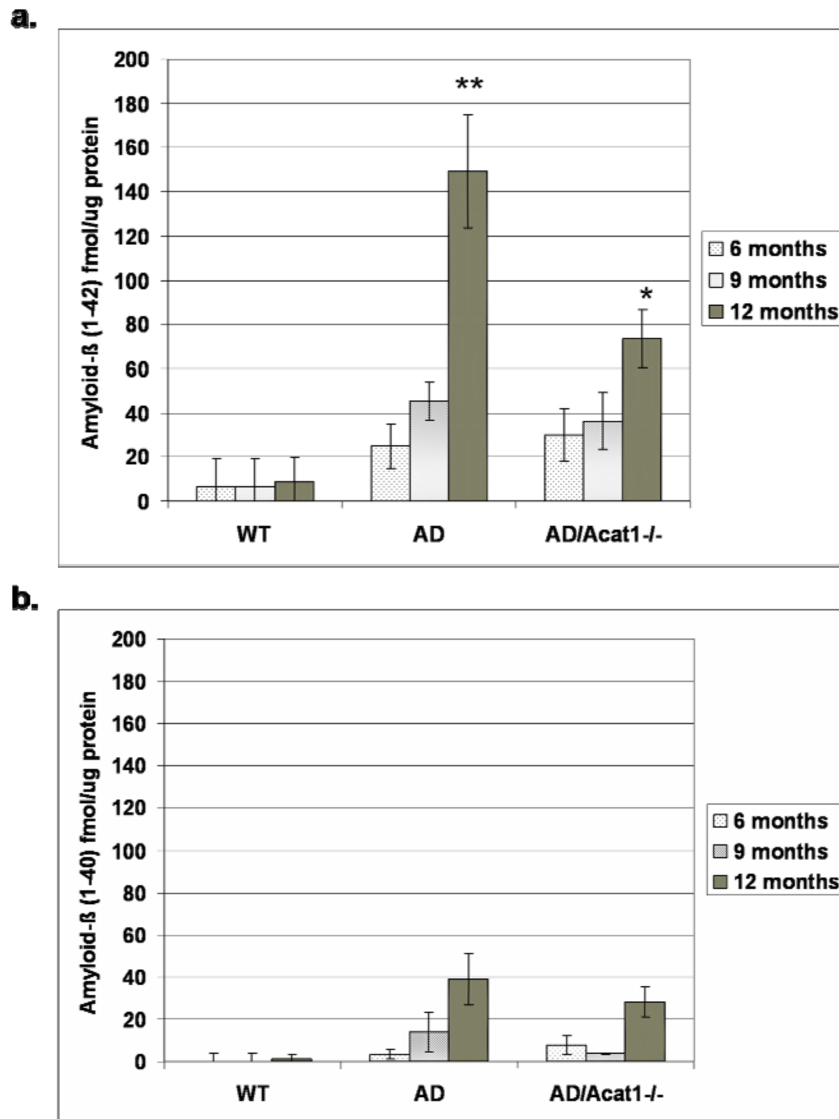

Fig. S2. Temporal characterization of Aß pathology in 3xTg-AD mice used in this study. Brain homogenates from AD or AD/*Acat1*$^{-/-}$ mice that were 6, 9, or 12 months of age were used for all of the experiments shown in this figure. (a) ELISA assay of Aß42 in formic acid extracts of mouse brain homogenates. The samples from each group (6 – 8 mice per group) were pooled and ELISA assay was performed twice in triplicate for each group's pooled sample. Error bars represent mean ± SEM. The difference between 9- and 12-month-old AD mice is statistically significant (**; $p<0.002$). The difference between 9- and 12-month-old AD/*Acat1*$^{-/-}$ mice is statistically significant (*; $p<0.02$). (b) Same as described in a, but ELISA assay is for Aß40. The difference between 9- and 12-month-old AD mice is trending toward statistical significance ($p=0.1$). The difference between 9- and 12-month-old AD/*Acat1*$^{-/-}$ mice is statistically significant ($p<0.05$)

Supplementary Figure S3

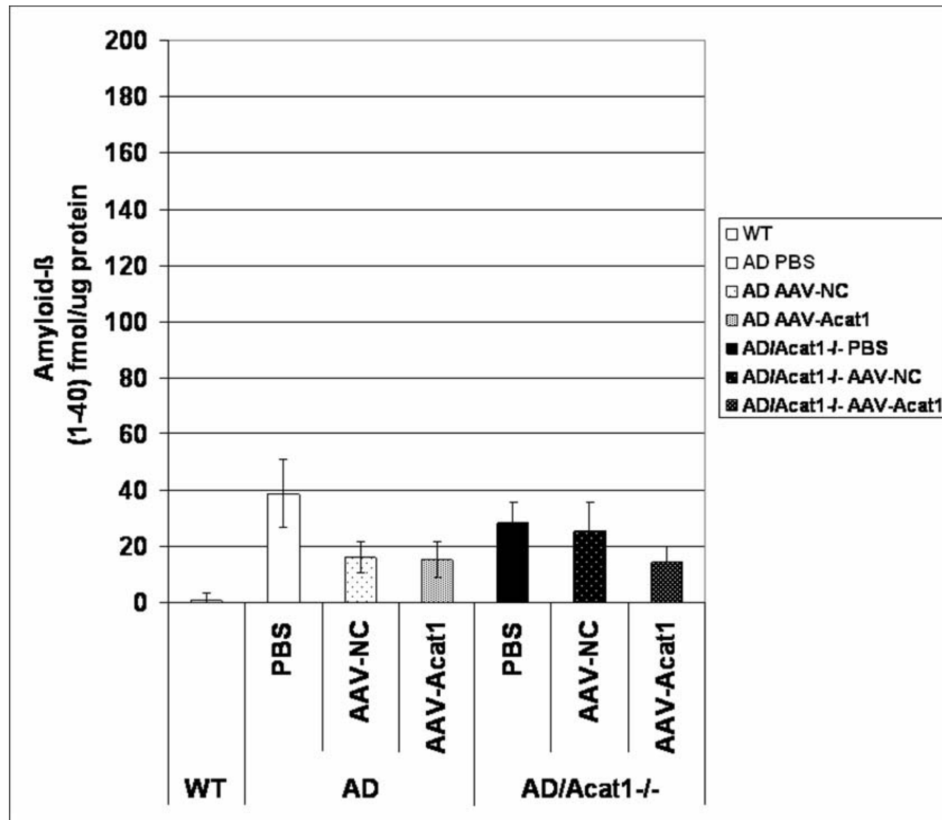

Fig. S3. Amyloid-ß (1-40) (Aß40) ELISA assay in brain homogenates from brain injected mice. Sample pools of mouse brain homogenates in sucrose buffer were subjected to formic acid extraction. The neutralized extracts were assayed for Aß40 by ELISA. Formic acid extraction followed by ELISA was performed N=3 separate times on different sample pools; each time the ELISA assay was run in duplicate or triplicate for each sample. Error bars represent mean ± SEM. ANOVA analysis showed that there was not a significant difference among the means.

Supplementary Table S1

Name of miRNA	Sequence	Incorporated into AAV?	AAV name
Negative Control	**5’-GAAATGTACTGCGCGTGGA GACGTTTTGGCCACTGACTGA CGTCTCCACGCAGTACATTT-3’**	**Yes**	**AAV-NC**
Soat1 #52	5’-TGCTGTGATGTGGTCCACTTC AAACAGTTTTGGCCACTGACTG ACTGTTTGAAGGACCACATCA-3’	No	-
Soat1 #53	5’-TGCTGATAAATAGTGGCTTCA GCTCCGTTTTGGCCACTGACTGA CGGAGCTGACCACTATTTAT-3’	No	-
Soat1 #54	**5’-TGCTGTCCAGTATCAGAATG AACCGGGTTTTGGCCACTGACT GACCCGGTTCACTGATACTGGA-3’**	**Yes**	**AAV-Acat1(54) *or* AAV-Acat1**
Soat1 #55	**5’-TGCTGTACAGTAGGAGTCCTT GGGTAGTTTTGGCCACTGACTG ACTACCCAAGCTCCTACTGTA-3’**	**Yes**	**AAV-Acat1(55) *or* AAV-Acat1**

Table S1. Sequences of artificial microRNAs. Sequence is as indicated with the targeting region underlined. Negative Control, Soat1 #54 and Soat1 #55 miRNAs were incorporated into AAV constructs from which viruses used in this study were produced. The names of the AAVs are indicated.

Supplementary Table S2

Gene	Primer Sequences
Iba1	5’-GGACAGACTGCCAGCCTAAG -3’ 5’-CAGCTCTAGGTGGGTCTTGG -3’
GFAP	5’-ATTGCTGGAGGGCGAAGAA-3’ 5’-CGGATCTGGAGGTTGGAGAA-3
TNFα	5’-TCTCATCAGTTCTATGGCCC-3’ 5’-GGGAGTAGACAAGGTACAAC-3’
iNOS	5’-AAGCTGCATGTGACATCGAC-3’ 5’-ATGTGTCTGCAGATGTGCTG-3’
Acat2	5’-TTTGCTCTATGCCTGCTTCA-3’ 5’-CCATGAAGAGAAAGGTCCACA-3’
HPRT (loading control)	5’-CCAGGTTATGACCTAGATTTGTTTT-3’ 5’- TTTCCAGTTAAAGTTGAGAGATCA-3’

Table S2. Primers used for Real Time PCR.