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Supplementary Materials for

Gene Transfer of Human *Apoe* Isoforms Results in Differential Modulation of Amyloid Deposition and Neurotoxicity in Mouse Brain

Eloise Hudry, Jonathan Dashkoff, Alysson D. Roe, Shuko Takeda, Robert M. Koffie, Tadafumi Hashimoto, Maria Scheel, Tara Spires-Jones, Michal Arbel-Ornath, Rebecca Betensky, Beverly L. Davidson, Bradley T. Hyman*

*Corresponding author. E-mail: bhyman@mgh.harvard.edu

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The PDF file includes:

Supplementary Materials:

Fig. S1.

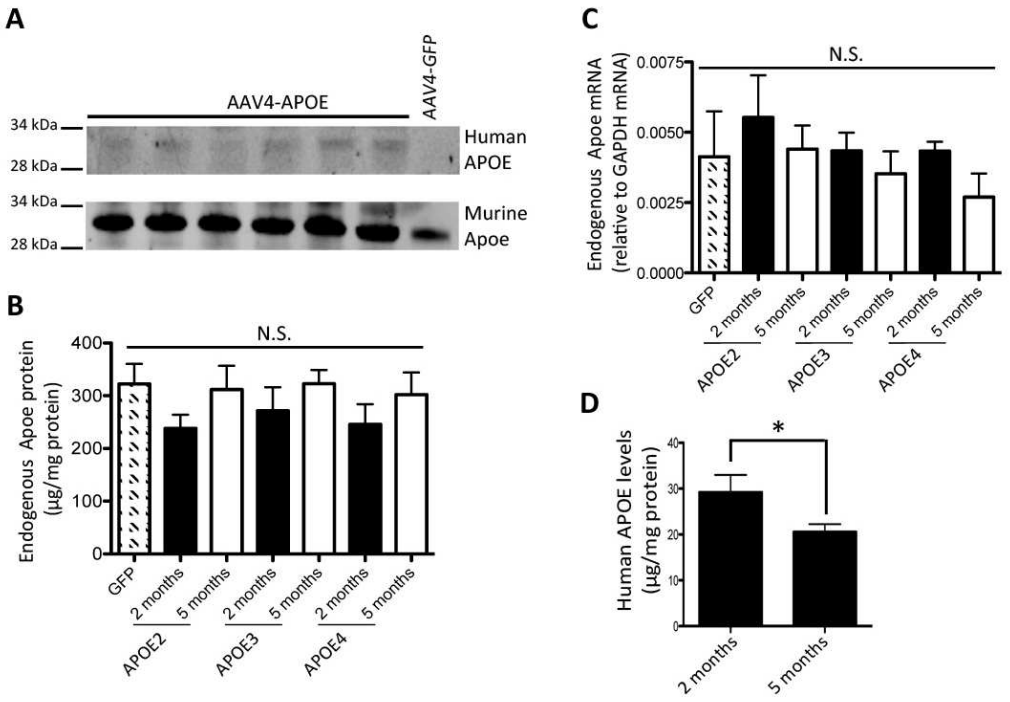

Fig. S1. Detection of human and endogenous murine APOE mRNA and protein after intracerebroventricular injection of AAV4-APOE in APP/PS1 mice. (**A**) Western blot analyses of human recombinant and endogenous ApoE proteins in AAV-APOE or AAV-GFP injected mice. (**B**) Box blot graphs representing the amounts of endogenous murine apoE protein in the brains of injected mice. (**C**) Box blot graphs representing the expression levels of endogenous murine *APOE* mRNA, normalized to the amount of GAPDH transcripts. (**D**) Comparison of the levels of ApoE protein 2 and 5 months after intracerebroventricular injection of AAV in APP/PS1 mice (samples from all ApoE injected mice were pooled together at 2 and 5 months, without discrimination for the APOE variant).
n= 4-6 animals per group (see Materials and Methods for details). *$p<0.05$

Fig. S2.

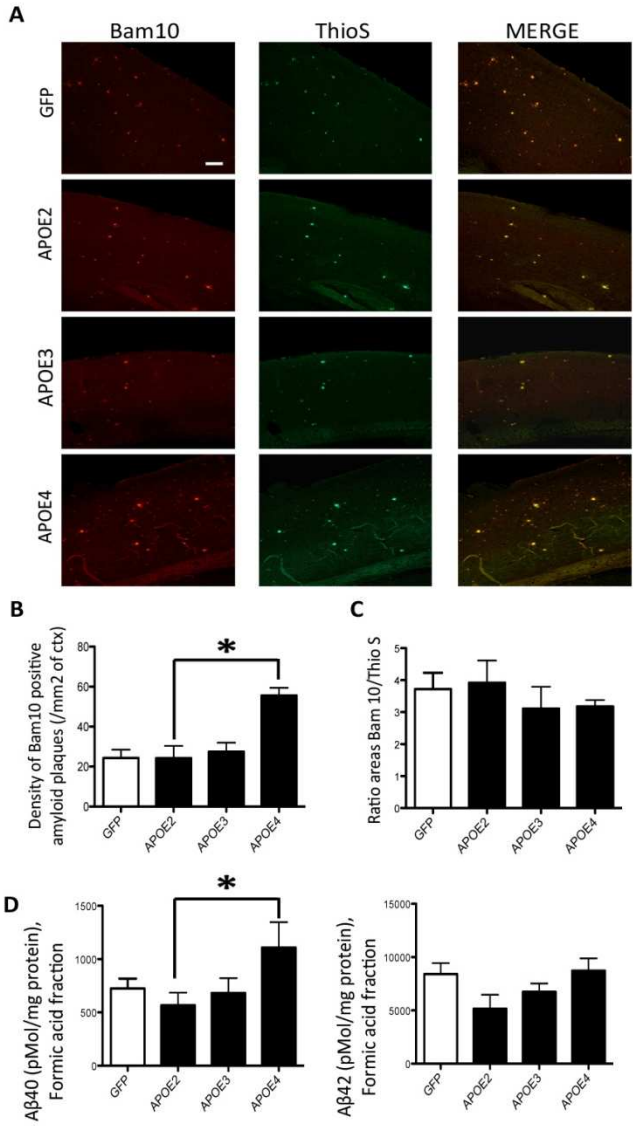

Fig. S2. Effects on Aβ pathology associated with each ApoE isoform after a short exposure (2 months). (**A**) Representative images of amyloid deposition in APP/PS1 mice 2 months after injection. Both immunostaining using the Bam10 antibody and ThioS were used to stain all amyloid deposits or dense-core plaques respectively. (**B**) Stereological analysis of the density of amyloid deposits in the cortex 2 months after injection of AAV-GFP, -APOE2, -APOE3 and APOE4. (**C**) Ratio between Bam10 and ThioS staining calculated for each mouse of each experimental group. (**D**) Determination of the concentrations of $A\beta_{40}$ (left panels) and $A\beta_{42}$ (right panels) peptides in the insoluble formic acid extracts after a short exposure with the different ApoE variants. Scale bar : 200µm. n= 4 AAV-GFP, n= 4 AAV-APOE2, n= 6 AAV-APOE3 and n= 5 AAV-APOE4 injected mice. *$p<0.05$

Fig. S3.

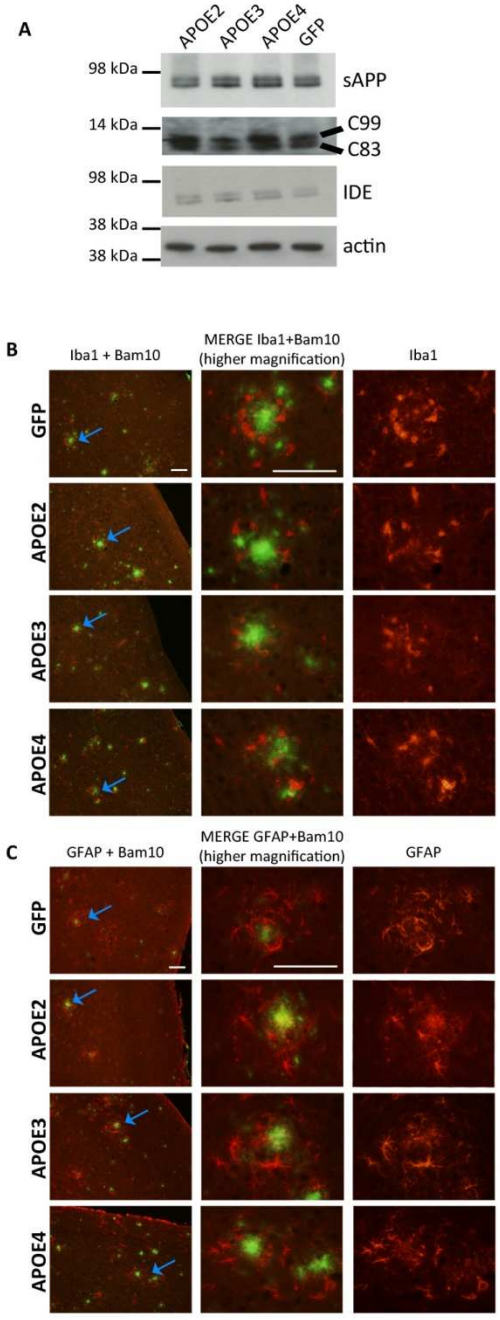

Fig. S3. No change in APP processing and glial cell recruitment around amyloid deposits upon expression of different ApoE isoforms. (**A**) Western blot analysis of sAPP, C99, C83 and IDE in the brain of injected mice. Representative images of Iba1 (microglia, **B**) and GFAP (astrocytes, **C**) positive cells around cortical amyloid deposits (labeled using the Bam10 antibody, indicated with blue arrows) after injection with AAV-GFP, -APOE2, -APOE3 and –APOE4. Bar scale: 100μm.

Fig. S4.

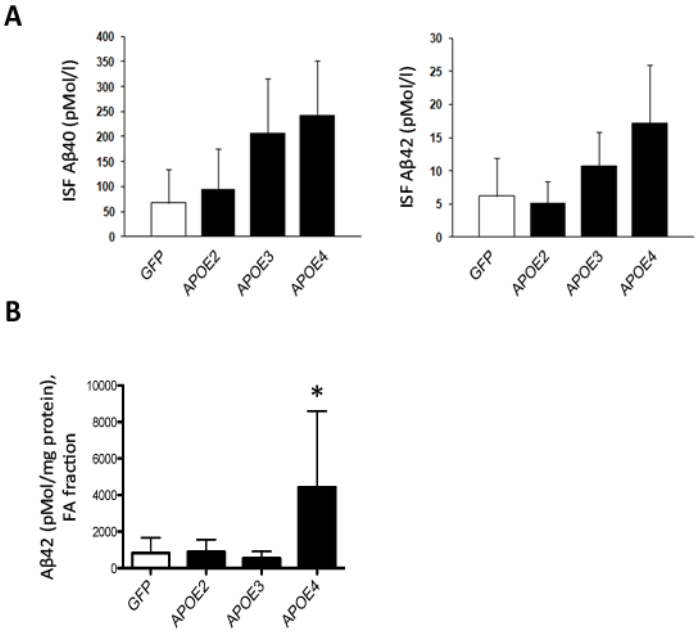

Fig. S4. Changes in soluble and insoluble Aβ species detected 3 months after injection in Tg2576 mice. (A) Quantification by ELISA of the ISF content in $A\beta_{40}$ and $A\beta_{42}$. (**B**) Concentrations of $A\ß_{42}$ in the formic acid fraction of Tg2576 mice after AAV4 injection.

n= 3 AAV-GFP, n= 3 AAV-APOE2, n= 5 AAV-APOE3 and n= 5 AAV-APOE4 injected mice. *$p<0.05$