Supplementary Material

Opposing effects of Apoe/Apoa1 double deletion on amyloid β pathology and cognitive performance in APP mice

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MATERIALS AND METHODS

Quantification of Atherosclerotic Lesions

The quantification of atherosclerotic lesions was performed as before (Lebherz *et al.*, 2007). Fixed aortas were stained with 0.5% Sudan IV, cut and pinned open for imaging. Total area of aortas covered by atherosclerotic lesions was quantified by color images utlilizing NIS Elements v3.0 (Nikon Inc. Melville, NY) .

Evans blue method

Disruption of BBB was quantified using an established Evans blue (EB) dye technique (Kakinuma *et al.*, 1998; Yanai *et al.*, 2000). Briefly, EB dye was injected intraperitoneally (50 µg/g body weight) and distribution of the dye confirmed by a visible change in the mouse skin color within 1 h post injection. Three hours after receiving injections, mice were anesthetized with avertin (100 mg/kg) and decapitated, with absorptive tissues used to soak up all exuding blood. The skull and the highly vascularized meninges were microsurgically opened, all traces of blood were absorbed and brain tissue collected. Evans blue leakage was quantified by placing brain tissues in a test tube containing formamide and incubating them for 72 h in the dark, then measuring optical density of collected formamide solution at 620nm by spectrophotometry

Supplementary Figure1: Evans blue leakage via BBB. Cerebellum and Cortex+hippocampus tissues from WT, Abca1^{ko}, DKO and E^{ko} mice were used to examine EB penetrability through BBB. N=4-8 per group. Analysis is by one-way ANOVA. NS = no significance

Supplementary Figure 2. Effects of *Abca1*, *Apoa1* and *Apoe* deletion on atherosclerosis: 12-month-old mice of various genotypes were examined for atherosclerotic plaques in aorta. **A**, representative pictures demonstrating atherosclerotic plaques in APP/WT, APP/Abca1^{ko} and APP/DKO mice are shown. **B**, Quantification of atherosclerosis in APP mice (on the left of the

graph) and non-APP mice (on the right). Used were male and female mice: APP/WT=10; APP/Abca1^{ko}=5; APP/DKO=16; APP/E^{ko}=16; APP/A^{ko}=4; WT=5; DKO=12; E^{ko}=7. Analysis is by one-way ANOVA ($p<0.001$) with Tukey's post-test (shown). *t*-test was used to determine difference between APP mice and there non-APP littermates. **, $p<0.01$ when DKO was compared to APP/DKO and $p<0.05$ when E^{ko} was compared to APP/DKO.

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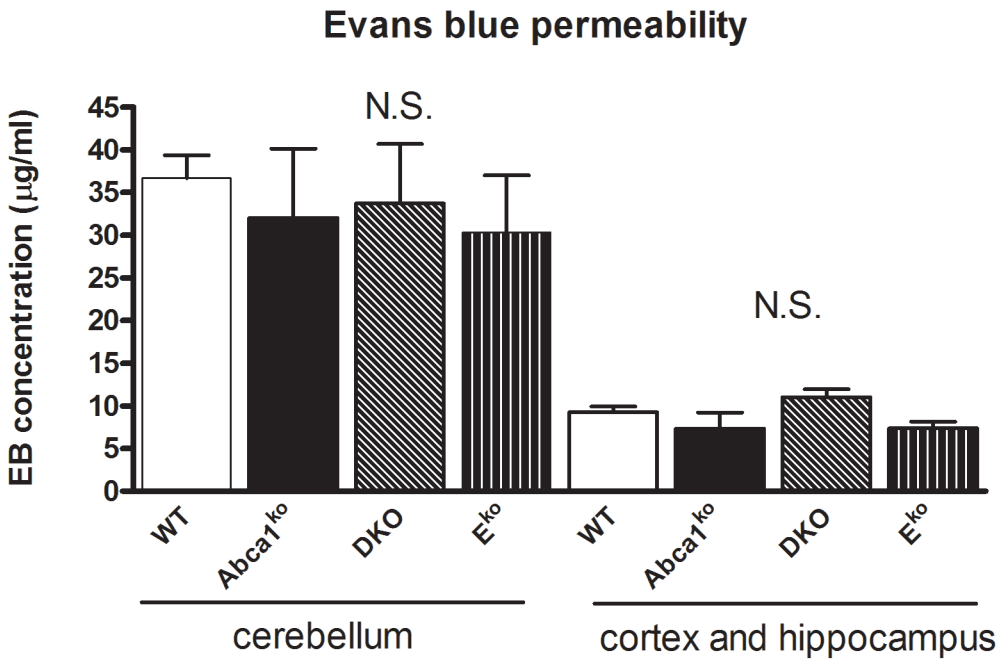

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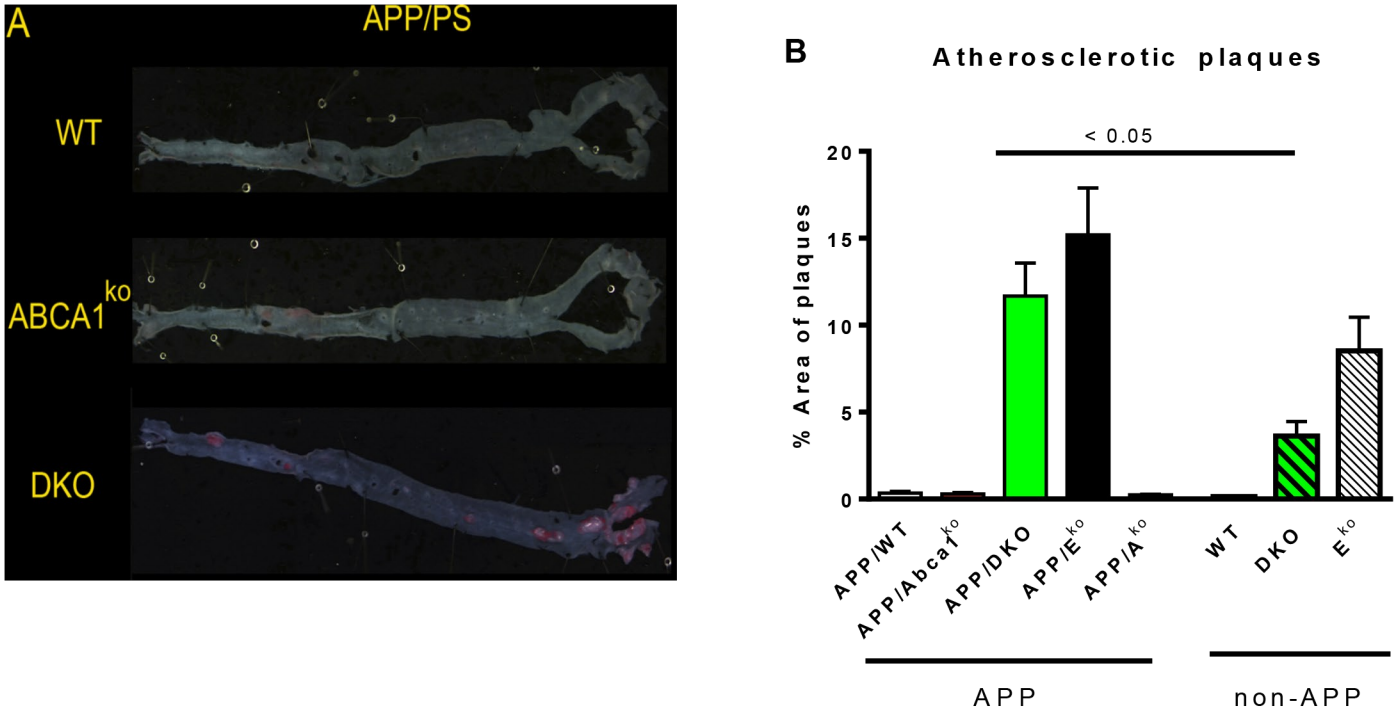

Supplementary Figure 2. Effects of *Abca1*, *Apoa1* and *Apoe* deletion on atherosclerosis: 12-month-old mice of various genotypes were examined for atherosclerotic plaques in aorta. **A**, representative pictures demonstrating atherosclerotic plaques in APP/WT, APP/Abca1^{ko} and APP/DKO mice are shown. **B**, Quantification of atherosclerosis in APP mice (on the left of the graph) and non-APP mice (on the right). Used were male and female mice: APP/WT=10; APP/Abca1^{ko}=5; APP/DKO=16; APP/E^{ko}=16; APP/A^{ko}=4; WT=5; DKO=12; E^{ko}=7. Analysis is by one-way ANOVA ($p<0.001$) with Tukey's post-test. Shown is post test for APP/DKO vs DKO mice.