SUPPLEMENTAL MATERIAL

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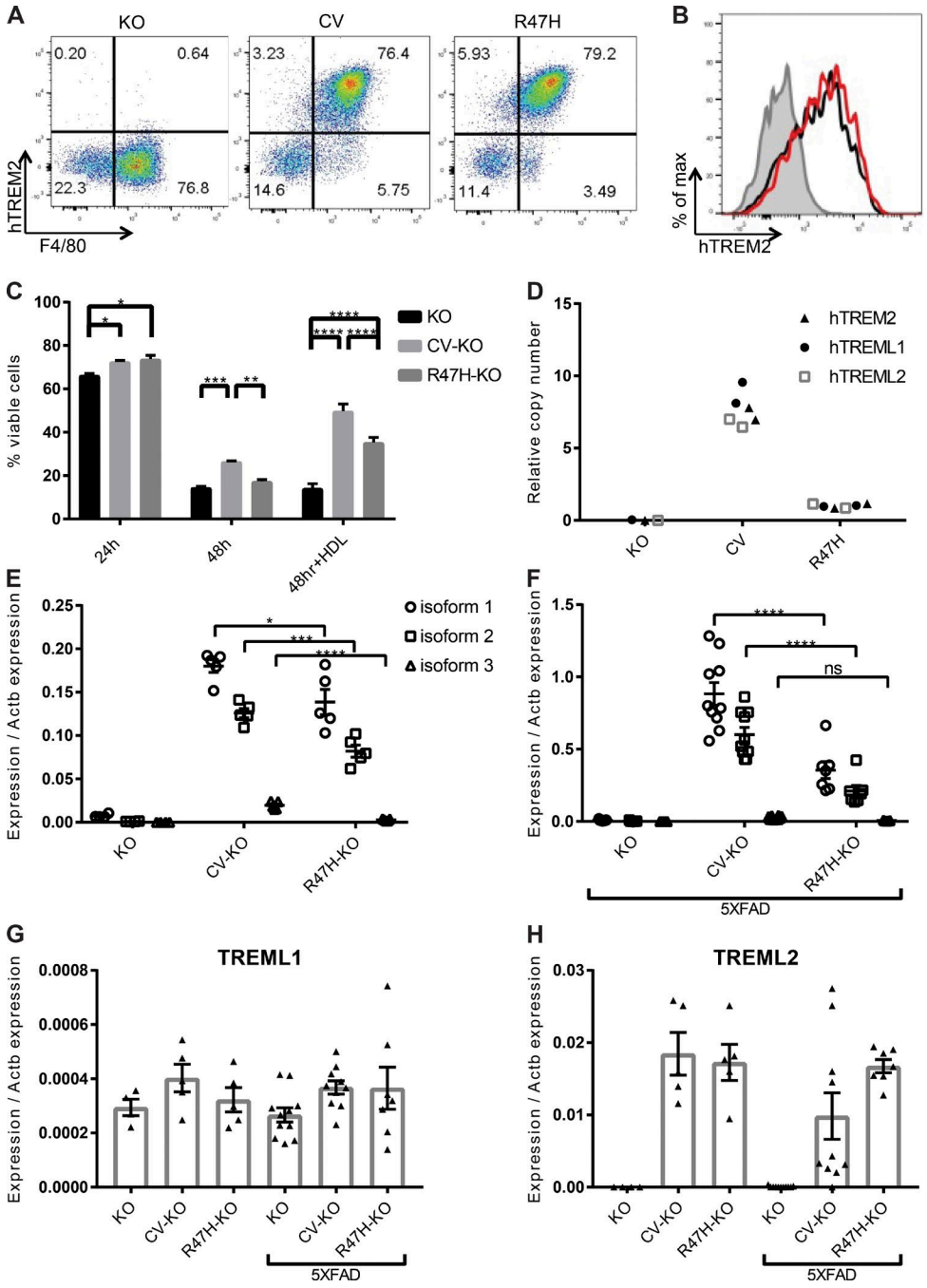

Figure S1. **Characterization of CV and R47H BAC transgenic mice. (A)** hTREM2 expression on thioglycollate-elicited peritoneal macrophages is restricted to F4/80 cells and has similar level between CV and R47H mice. **(B)** hTREM2 expression is similar on day 2 BMDMs from CV (red line) and R47H mice (black line). Isotype control is shown in gray. **(C)** Upon CSF1 starvation for 24 or 48 h, CV-KO BMDMs have higher viability than R47H-KO and KO BMDMs, and this effect is heightened in the presence of the TREM2 ligand human HDL. **(D)** Relative copy numbers of BAC insertions were determined by qPCR using primer pairs in hTREM2, hTREML1, and hTREML2 on genomic DNA isolated from the brains of one or two mice per genotype. CV mice appear to have a copy number six to eight times higher than R47H. **(E and F)** Expression of different hTREM2 mRNA isoforms in whole cortical tissue of non-5XFAD animals (E) or 5XFAD animals (F) by RT-qPCR. In the non-5XFAD background, CV-KO brains have slightly more RNA expression of isoforms 1 and 2. In the 5XFAD background, CV-KO-5XFAD brains also have higher expression of both isoforms 1 and 2 than R47H-KO-5XFAD. Isoform 3 is not very abundant and appears to be expressed preferentially in CV-KO brains; expression does not change between non-5XFAD and 5XFAD brains. **(G and H)** RT-qPCR on whole cortical tissue for TREML1 (G) and TREML2 (H). Very little TREML1 transcript is detected for either CV-KO or R47H-KO and is similar to background levels in KO. TREML2 is modestly expressed within the brain in both CV and R47H at comparable levels and does not appear to increase in 5XFAD mice. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$ by one-way ANOVA with Holm-Sidak multiple comparisons testing. Data are presented as mean ± SEM.

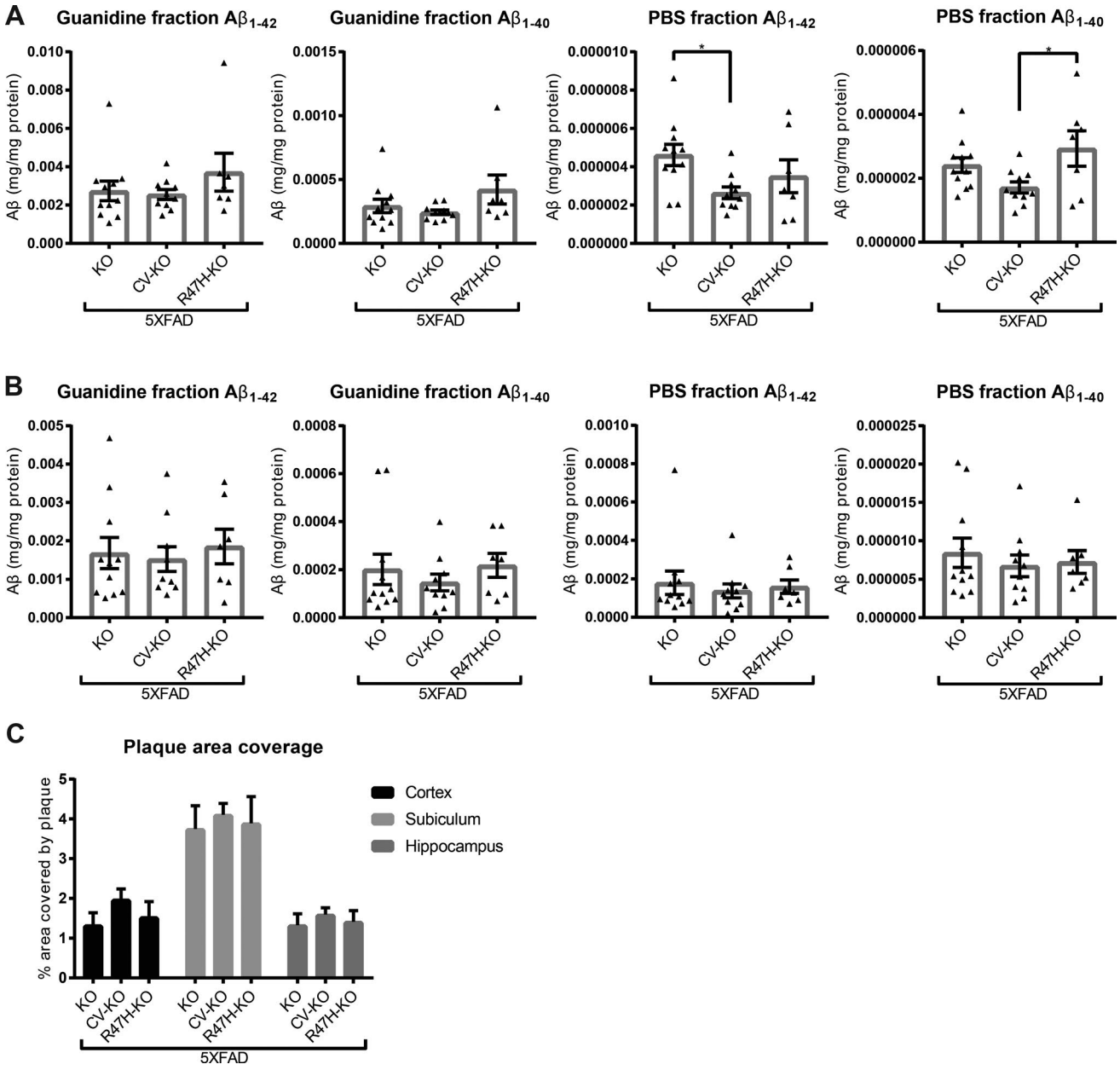

Figure S2. **Aβ levels show slight differences among KO-5XFAD, CV-KO-5XFAD, and R47H-KO-5XFAD brains. (A and B)** ELISA was performed on PBS-soluble and PBS-insoluble guanidine-soluble fractions of hippocampus (A) and cortex (B) for both $A\beta_{1-40}$ and $A\beta_{1-42}$. **(C)** Percent area coverage of cortex, subiculum, and hippocampus (excluding subiculum) by plaques was measured by staining with methoxy-X04, showing no difference between groups. *, $P < 0.05$ by one-way ANOVA with Holm-Sidak multiple comparisons testing. Data are presented as mean ± SEM.

Table S1, included as an Excel file, shows log2-transformed microarray values for activation genes shown in Fig. 3 B.