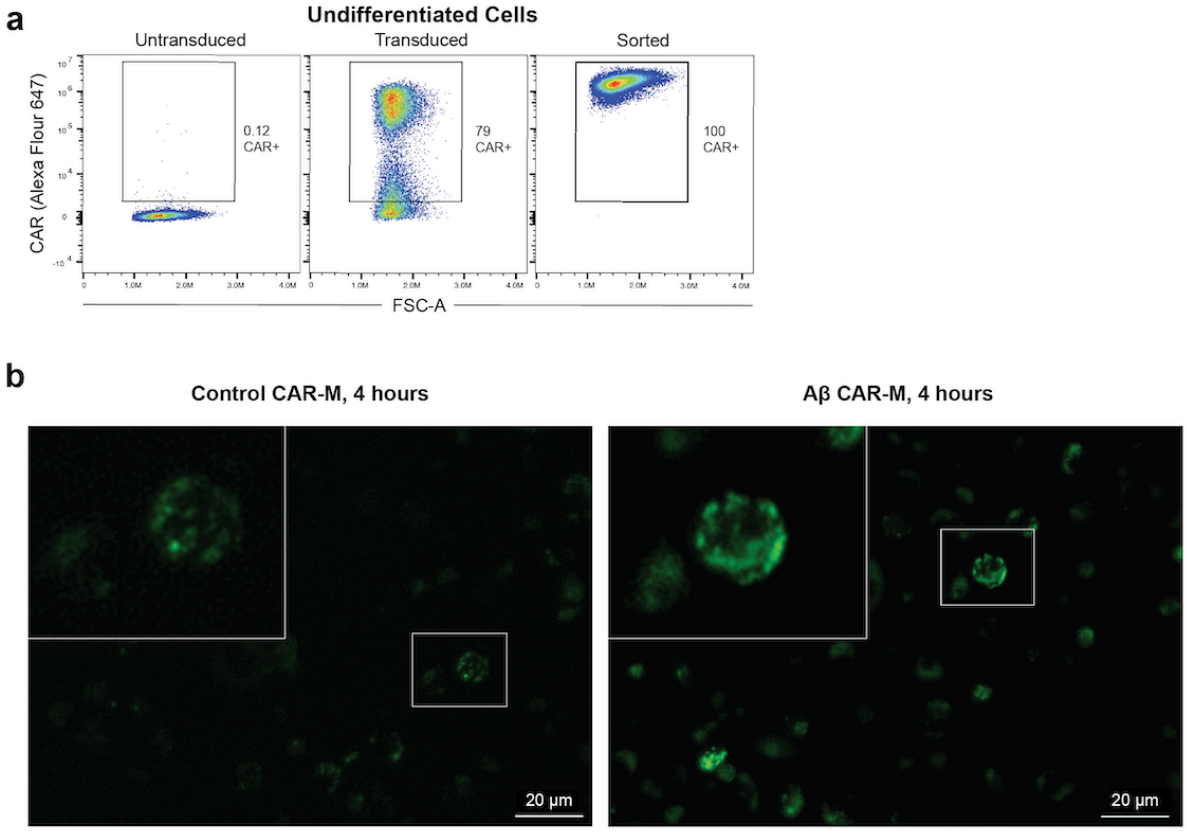
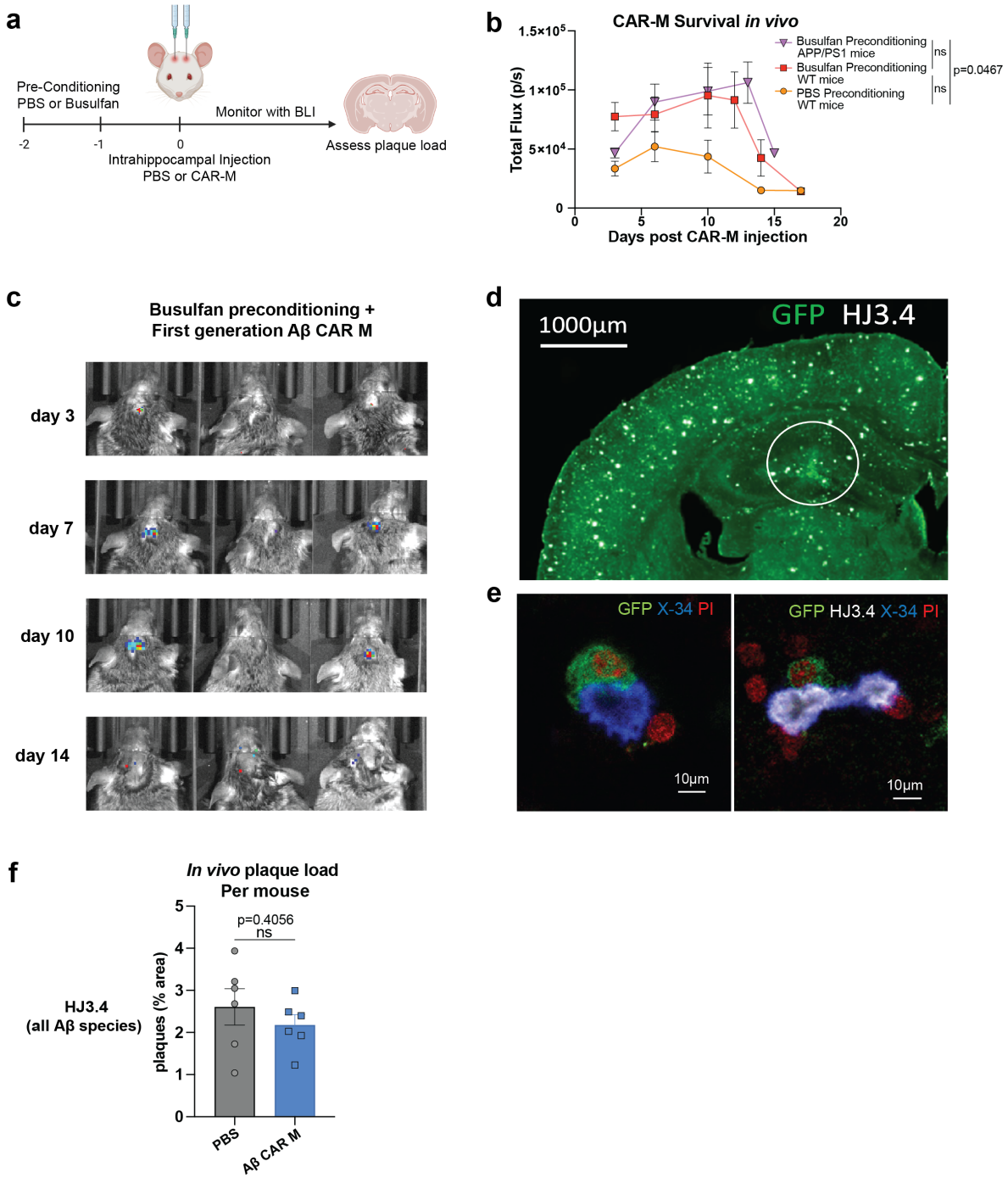
Supplemental Table 1

Antigen	Primary working concentration	Source	Secondary working concentration	Source
Iba1	1:1000	Rabbit anti-Iba1 (Wako Pure Chemical Industries, Ltd. cat# 019-19741)	1:800	Anti-rabbit Alexa488 (Thermo Fisher)
GFP	1:500	Goat anti-GFP (Rockland antibodies)	1:800	Anti-goat Alexa488 (Life Sciences)
Aβ (HJ3.4)	1:1000	Biotinylated antibody, gift from Dr. David M. Holtzman	1:800	Cy5 Streptavidin (Jackson ImmunoResearch Inc.)

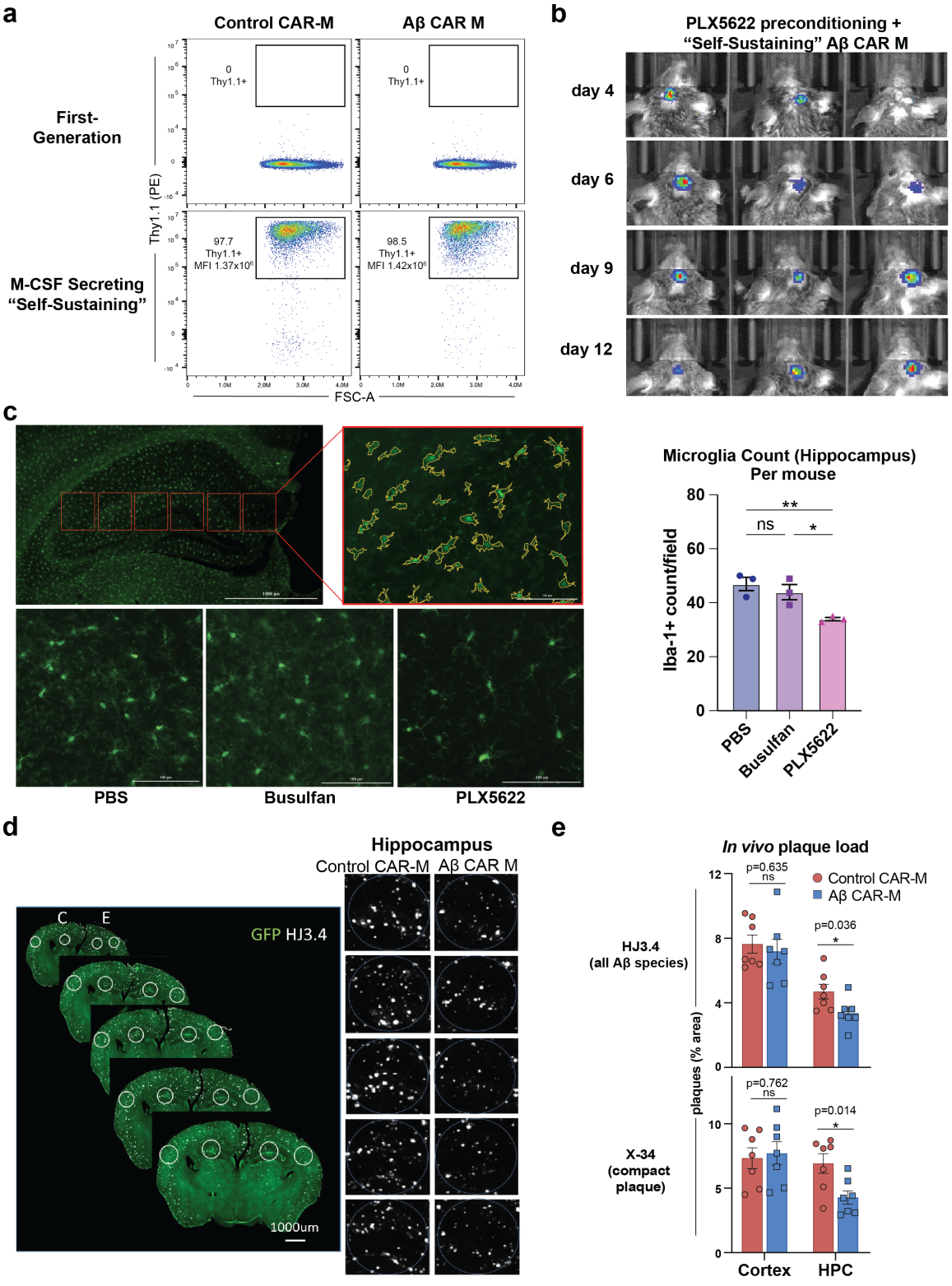


Supplemental Figure 1: Generation and validation of CAR HoxB8 cells.
a) Representative FACS plots showing surface expression of the Aβ CAR on untransduced, retrovirally transduced, and transduced and sorted HoxB8 cells used for downstream experiments. Numbers represent percentage of cells in the indicated gate. Representative of n>3 independent experiments. **b)** Representative images of control or Aβ CAR Ms co-cultured with AF488 tagged Aβ(1-42) for 4 hours.



Supplemental Figure 2: First generation Aβ CAR-Ms have limited expansion and survival and fail to reduce plaque load *in vivo* when administered with Busulfan preconditioning. **a)** Schematic of Busulfan pre-conditioning and intrahippocampal injection of Aβ CAR-Ms. **b)** Non-invasive bioluminescence imaging tracking CAR-M persistence after intrahippocampal injection. n=6-14 mice per group. Statistical significance calculated with one-way ANOVA with Tukey's multiple comparisons test. **c)** Representative bioluminescence images following Busulfan preconditioning and intrahippocampal injection of Aβ CAR-Ms. Days indicates days post-intrahippocampal injection. **d)** Representative immunofluorescence microscopy image

showing GFP+ CAR-Ms localized to the hippocampus 13 days after intrahippocampal injection. Circular region of interest indicates area in which plaque load was quantified. **e)** Representative immunofluorescence microscopy images of Aβ CAR-Ms binding to amyloid plaque *in vivo*. **f)** Assessment of plaque load after intrahippocampal injection of PBS or Aβ CAR-M in n=6 aged APP/PS1 mice. Mice were sacrificed on day 14 post intrahippocampal injection and brain tissue was sectioned and stained with HJ3.4 to assess plaque load. Data shown as mean ± s.e.m. Statistical significance was calculated with unpaired t-tests.



Supplemental Figure 3: Self-sustaining, M-CSF secreting Aβ CAR-Ms expand *in vivo* when administered with PLX5622 preconditioning and reduce plaque load in the locally in the hippocampus *in vivo*.

a) Representative FACS plots showing surface expression of Thy1.1 on control and Aβ CAR-Ms before and after retroviral transduction of HoxB8 cells with the M-CSF construct and sorting for Thy1.1+ cells. Gated on single, live, CAR+ cells. MFI, mean fluorescence intensity **b)** Representative bioluminescence images following PLX5622 preconditioning and intrahippocampal injection of self-sustaining Aβ CAR-Ms. Days indicates days post-intrahippocampal injection. **c)** (left upper) Representative image showing the six regions of interest (ROI) in which Iba-1 positive cells were quantified in each hippocampus and a higher power view of one ROI showing the cell masking used for quantification. (left lower) Representative images showing one ROI from mice treated with PBS for 2 days, 20 mg/kg Busulfan for 2 days, or 50 mg/kg PLX5622 for 4 days, twice a day. (right) quantification of Iba-1+ cells where each dot represents the average Iba-1+ cell count in all ROIs per mouse. Statistical significance was calculated with a one-way ANOVA with Tukey's multiple comparisons test. **d)** Representative images of brain sections from CAR-M treated aged APP/PS1 mice stained with HJ3.4. Images indicate circular regions of interest centered around GFP signal in the hippocampus representing the cell injection area in which plaque was quantified, highlighted in higher magnification on the right. Control regions of interest were quantified in the cortex to ensure uniform plaque load between mice. "C"= control CAR-M treated side, "E"= Aβ CAR-M treated side. **e)** Assessment of plaque load in the cortex and the hippocampus (HPC) after intrahippocampal injection of self-sustaining control or Aβ CAR-Ms in n=7 aged APP/PS1 mice. Mice were sacrificed on day 12 or 13 post intrahippocampal injection and brain tissue was sectioned and stained with HJ3.4 or X-34 to assess plaque load in the regions of interest shown in **d)**. Data shown as mean ± s.e.m. Statistical significance was calculated with unpaired t-tests. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001, ns, not significant.