SUPPLEMENTARY INFORMATION

[^{18}F]GE-180 PET detects reduced microglia activation after LM11A-31 therapy in a mouse model of Alzheimer's disease

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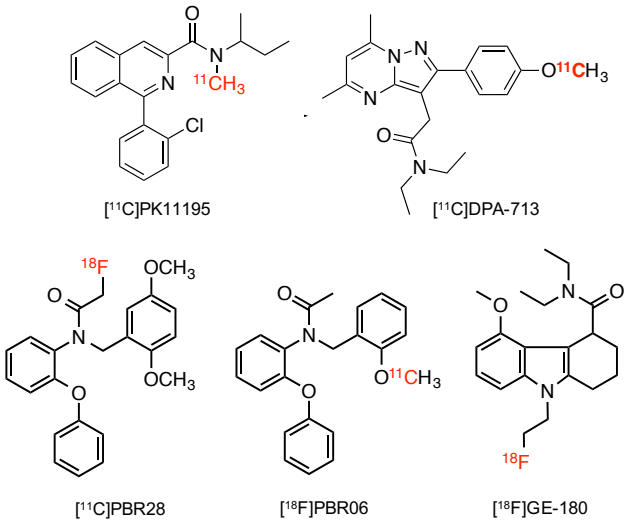
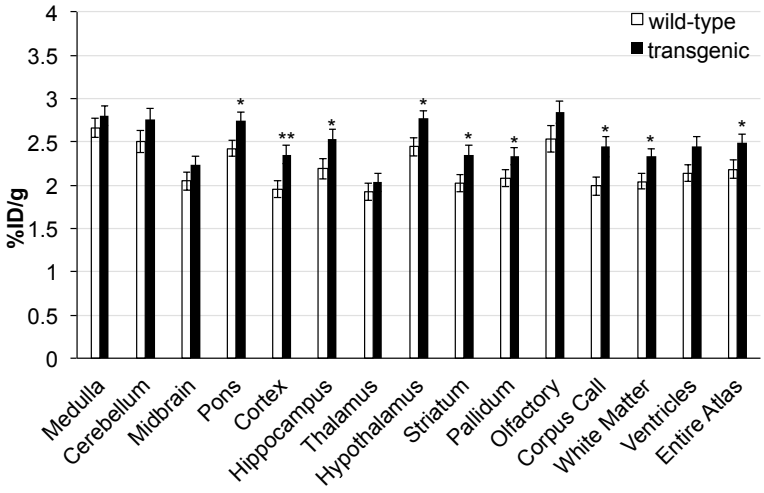
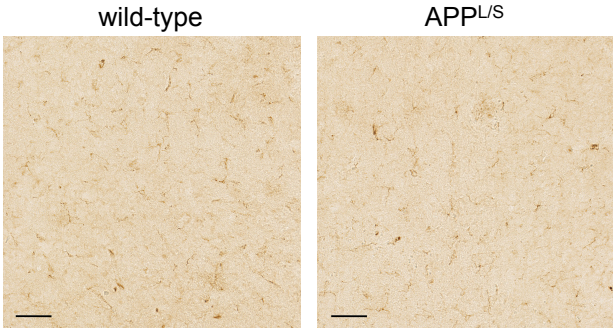
SUPPLEMENTARY FIGURES



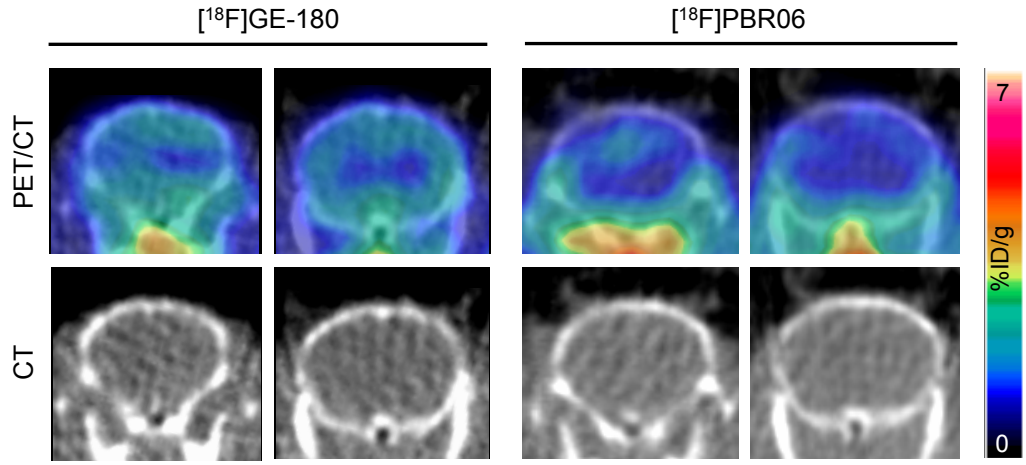
Supplementary Figure 1. Chemical structures of known TSPO radiotracers.



Supplementary Figure 2. [^{18}F]GE-180 uptake in 15 (automatically generated) brain regions of wild-type and transgenic APP$^{L/S}$ mice (8.5-10 months of age), as determined by fitting a 3D brain atlas to PET/CT images.



Supplementary Figure 3. TSPO staining in rostral thalamus. Representative 20x images from wild-type and APP$^{L/S}$ mouse (8.5-10 months old) shows negligible TSPO staining in rostral thalamus. Scale bar = 100 μm.

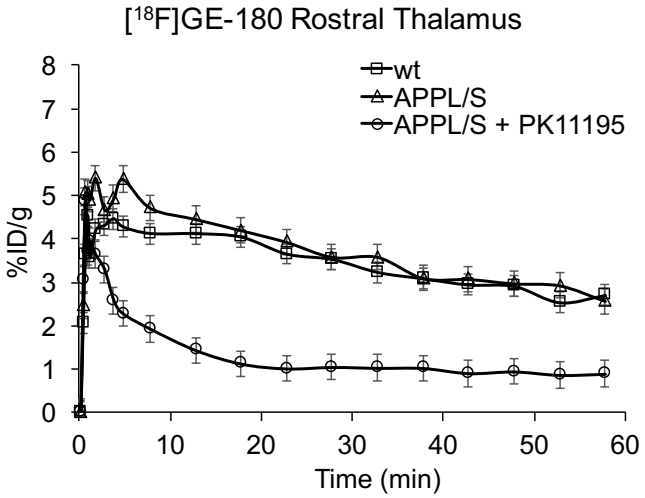


Supplementary Figure 4. Static PET/CT coronal brain images of [^{18}F]GE-180 and [^{18}F]PBR06 uptake in APP$^{L/S}$ mice aged 8.5-10 months (50-60 and 40-50 min after tracer injection, respectively). Two PET/CT images and their respective CT (only) images are shown for each tracer.

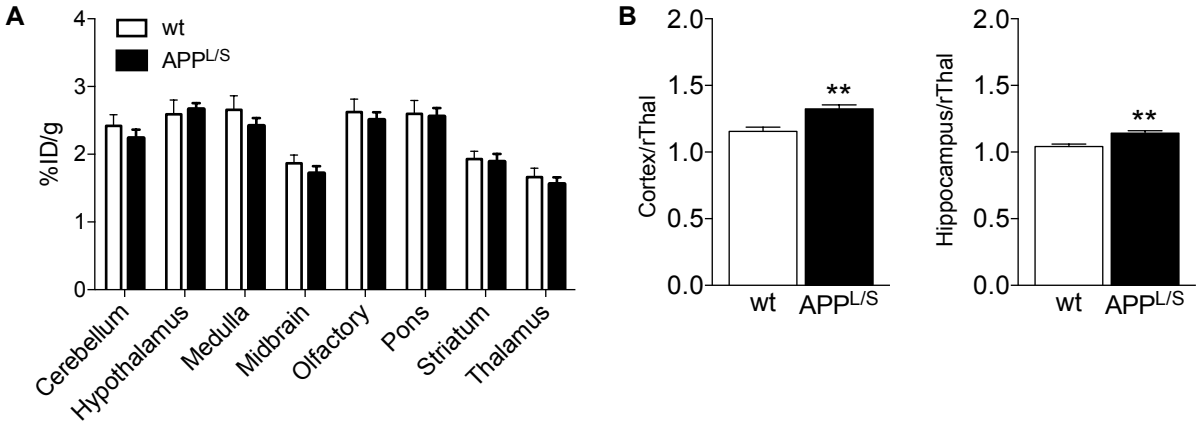
Supplemental Table 1. %ID/g and SUVR values using rostral thalamus as a reference region for [^{18}F]GE-180 PET studies of wild-type and APP$^{L/S}$ mice aged 8.5-10 months.

	Ctx **%ID/g**	*Ctx **SUVr***	HC **%ID/g**	*HC **SUVr***
APP$^{L/S}$				
Mean	2.52	*1.27*	2.39	*1.20*
SD	0.26	*0.05*	0.37	*0.08*
COV	10.40	*3.72*	15.55	*6.94*
wild-type				
Mean	1.89	*0.94*	1.88	*0.94*
SD	0.10	*0.10*	0.09	*0.11*
COV	5.06	*10.83*	4.65	*12.10*
Effect size	25%**	*26%***	21%*	*22%***

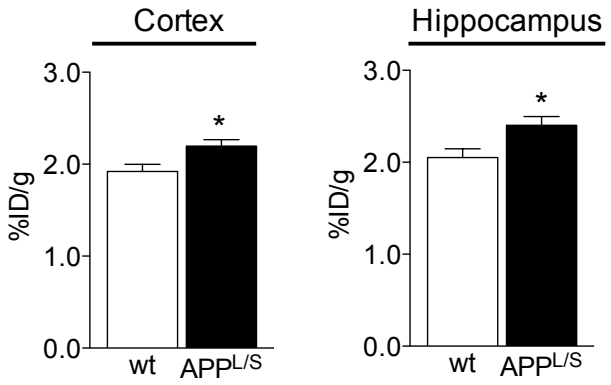
Abbreviations: SUVr, standardized uptake value ratio; SD, standard deviation; COV, coefficient of variance; Ctx, cortex; HC, hippocampus. *p<0.05, **p<0.01.



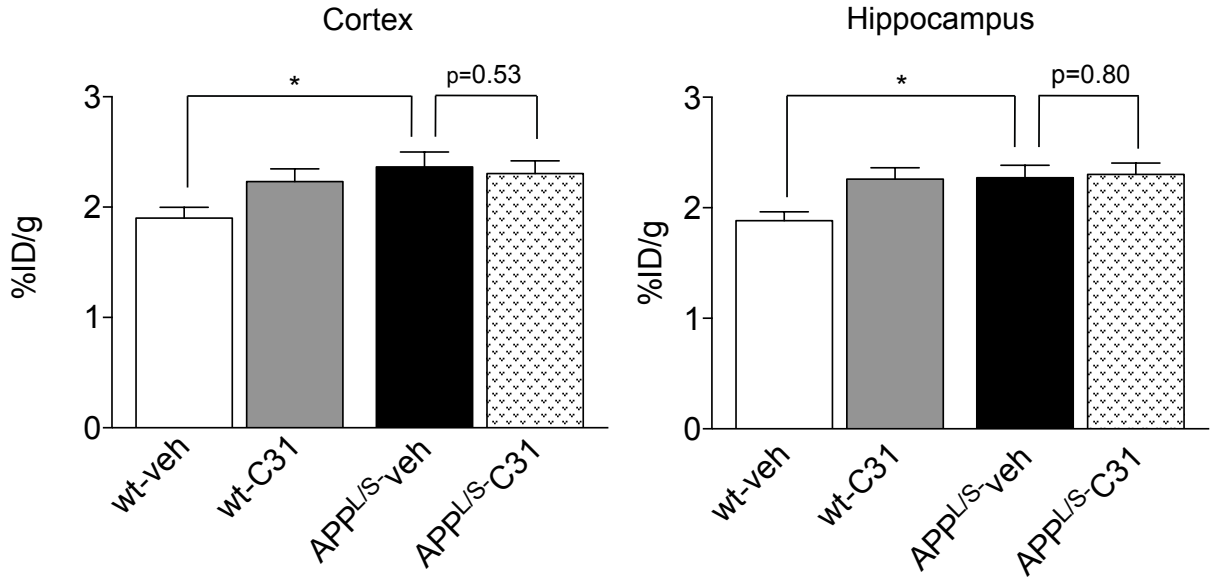
Supplemental Figure 5. Time activity curves show the kinetics of [^{18}F]GE-180 in rostral thalamus of 8.5-10 month old APP$^{L/S}$ (n = 6) and wild-type mice (n = 5), and in APP$^{L/S}$ mice pre-treated with PK11195 (1 mg/kg) (n = 4).



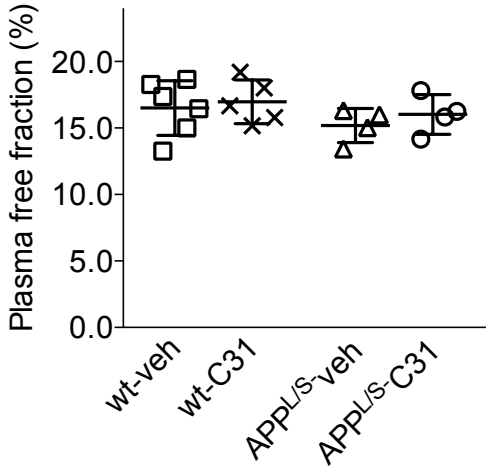
Supplementary Figure 6. Uptake of [^{18}F]PBR06 in different brain regions of age-matched APP$^{L/S}$ and wild-type mice. (A) [^{18}F]PBR06 uptake in cerebellum, hypothalamus, medulla, midbrain, olfactory, pons, striatum, and thalamus of wild-type (n = 6) and APP$^{L/S}$ mice (n = 7) aged 8.5-10 months. Uptake values are shown as percent injected dose per gram (% ID/g). (B) Uptake of [^{18}F]PBR06 in cortex and hippocampus normalized to uptake in the rostral thalamus (rThal). Standard error of mean (SEM) is shown. **p<0.01.



Supplementary Figure 7. Baseline PET imaging of 5.5-7 month old APP$^{L/S}$ and wild-type mice. Graphs depict uptake (%ID/g) of [^{18}F]GE-180 in cortex and hippocampus of APP$^{L/S}$ (n=17) versus wild-type (wt) mice (n=21) prior to the commencement of drug/vehicle treatment. *p-value <0.05.



Supplementary Figure 8. PET imaging of 8.5-10 month old APP$^{L/S}$ and wild-type mice 3 months post-treatment with C31 or vehicle. Graphs depict %ID/g of [^{18}F]GE-180 in cortex and hippocampus of APP$^{L/S}$-veh (n=9), wild-type-veh (n=10), APP$^{L/S}$-C31 (n=8), and wild-type-C31 (n=11). *p-value <0.05.



Supplementary Figure 9. Plasma free fraction (f_P) of [^{18}F]GE-180 after 3 months treatment with LM11A-31 (C31) or vehicle (veh).