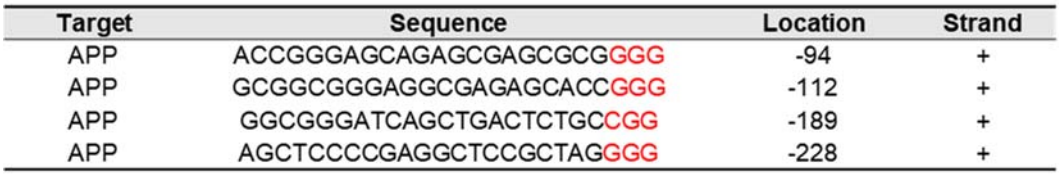
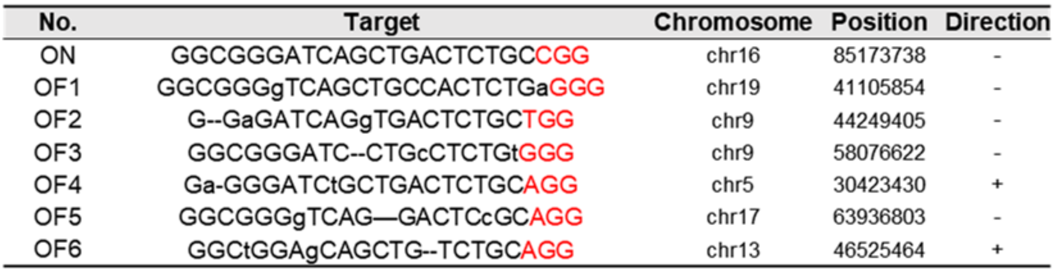
Supplementary Table S1. sgRNA sequences targeting *APP*.



Target	Sequence	Location	Strand
APP	ACCGGGAGCAGAGCGAGCGCGGGG	-94	+
APP	GCGGCGGGAGGCGAGAGCACCGGG	-112	+
APP	GGCGGGATCAGCTGACTCTGCCGG	-189	+
APP	AGCTCCCCGAGGCTCCGCTAGGGG	-228	+

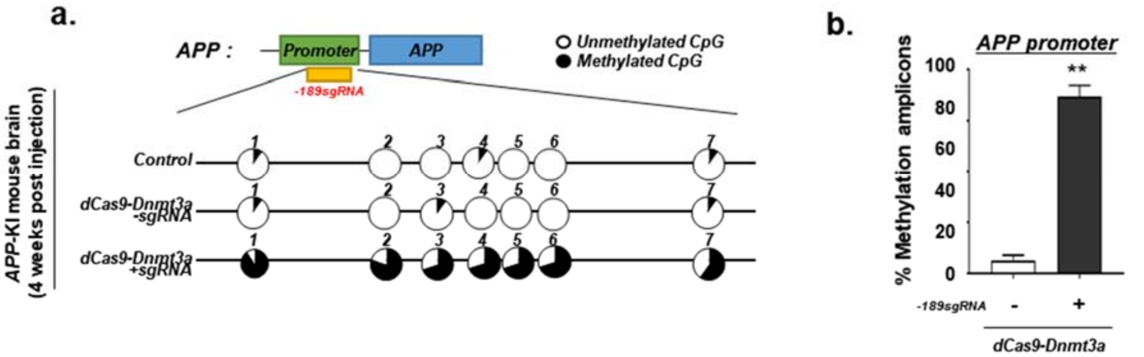
Protospacer adjacent motif sequences are underlined in red.

Supplementary Table S2. Predicted off-target sites for −189 sgRNA activity.



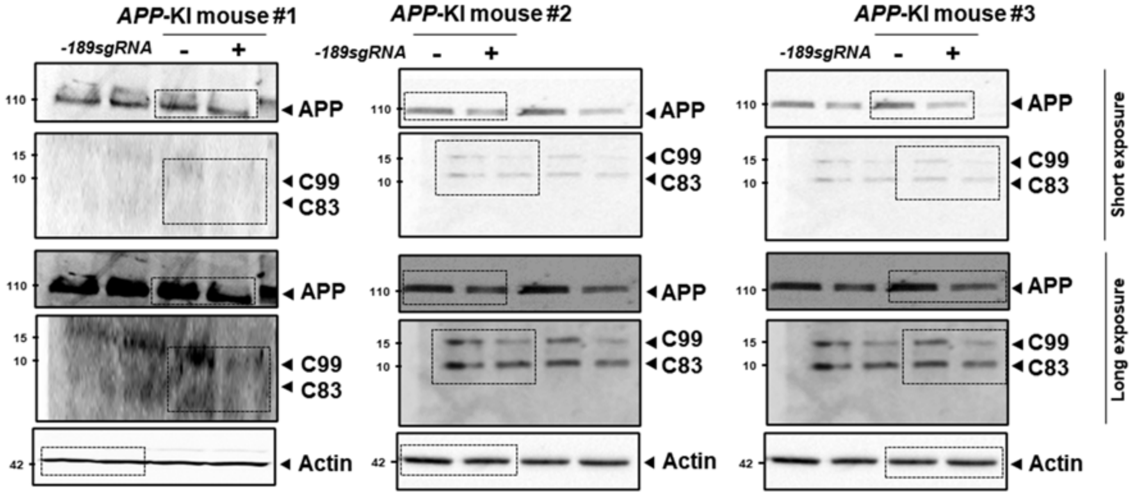
No.	Target	Chromosome	Position	Direction
ON	GGCGGGATCAGCTGACTCTGCCGG	chr16	85173738	-
OF1	GGCGGGgTCAGCTGCCACTCTGaGGG	chr19	41105854	-
OF2	G--GaGATCAGgTGACTCTGCTGG	chr9	44249405	-
OF3	GGCGGGATC--CTGcCTCTGtGGG	chr9	58076622	-
OF4	Ga-GGGATCtGCTGACTCTGCAGG	chr5	30423430	+
OF5	GGCGGGgTCAG—GACTCcGCAGG	chr17	63936803	-
OF6	GGCtGGAgCAGCTG--TCTGCAGG	chr13	46525464	+

Off-target sites were predicted as those having no more than two mismatches compared to the on-target sequence. ON, on-target; OF, off-target.



Supplementary Figure S1. Bisulfite sequencing analysis of the methylation status of the *APP* promoter in the hippocampus of *APP*-KI mice. (**a**) Bisulfite sequencing analysis of the promoter region of *APP* in the *APP*-KI mouse hippocampus transduced with −189 sgRNA and dCas9-Dnmt3a 4 weeks after injection. (**b**) Quantification of methylated amplicons. Data are expressed as mean ± SEM (*n* = 3). ***P* < 0.01, two-sided Student's *t*-test.

Figure 4b



Supplementary Figure S2. Full scans of the western blots shown in Fig. 4b. Blots for all three independent experiments are shown.