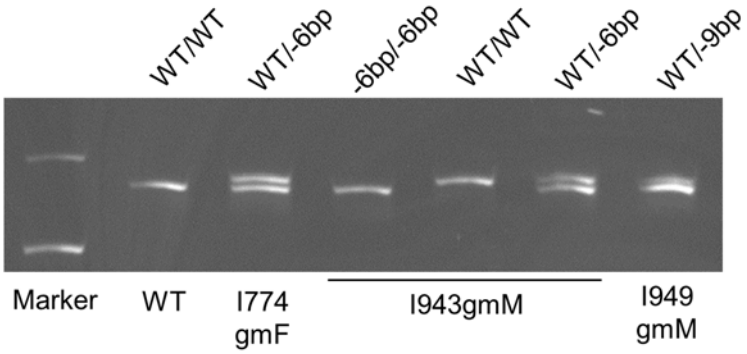
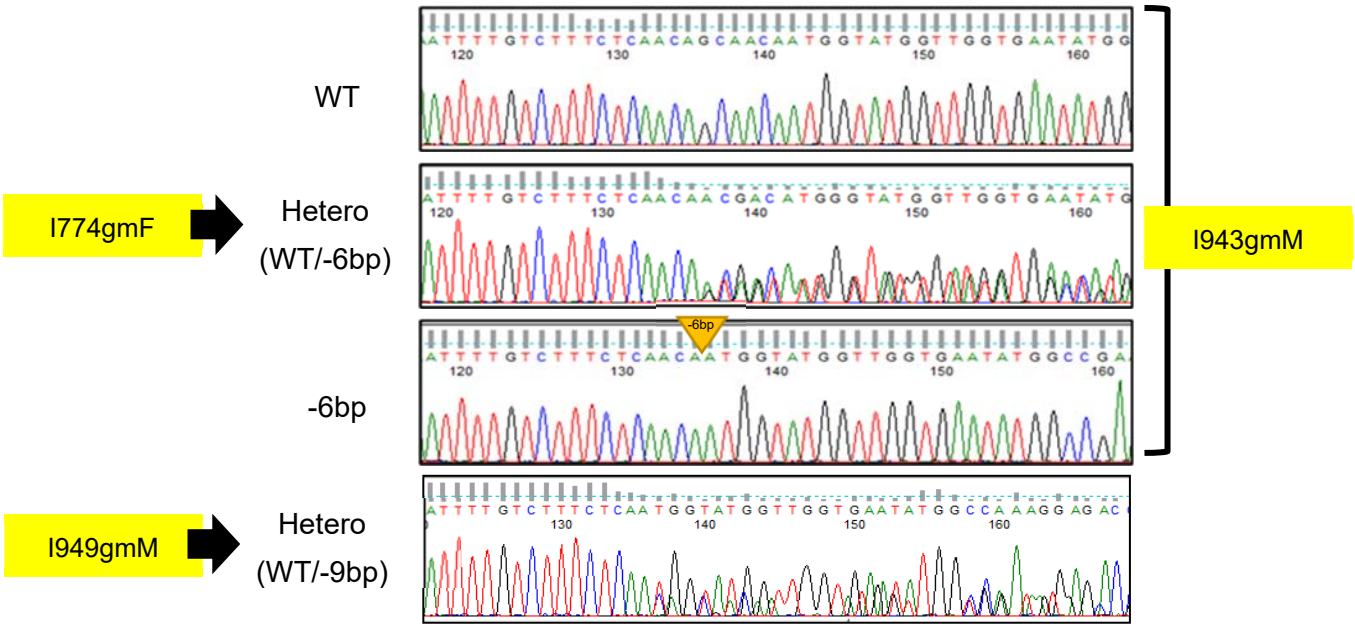
Supplementary Figure 1. The single-cell PCR analyses.

Cell sample No.	I774gmF	I943gmM	I949gmM
1	Hetero	-6bp	Hetero
2	Hetero	WT	Hetero
3	Hetero	Hetero	Hetero
4	Hetero	-6bp	Hetero
5	Hetero	-6bp	Hetero
6	Hetero	Hetero	Hetero
7	Hetero	WT	Hetero
8	Hetero	WT	Hetero
9	Hetero	WT	Hetero
10	Hetero	-6bp	Hetero
11		-6bp	
12		-6bp	
13		WT	
14		-6bp	
15		-6bp	
16		WT	
17		-6bp	
18		-6bp	
19		WT	
20		Hetero	
21		-6bp	
22		-6bp	
23		WT	
24		WT	





Fibroblasts obtained from *PSEN1*-ΔE9 marmosets were analyzed by single cell PCR. The results of sequence analyses and electrophoresis of PCR products indicated that each cell of I774gmF and I949gmM carried heterozygous mutations and that I943gmM was a mosaic individual containing a mixture of WT, homozygous and heterozygous 6bp deletion modification.

Supplementary Figure 2. The cDNA sequences of *PSEN1*.

>Wild type

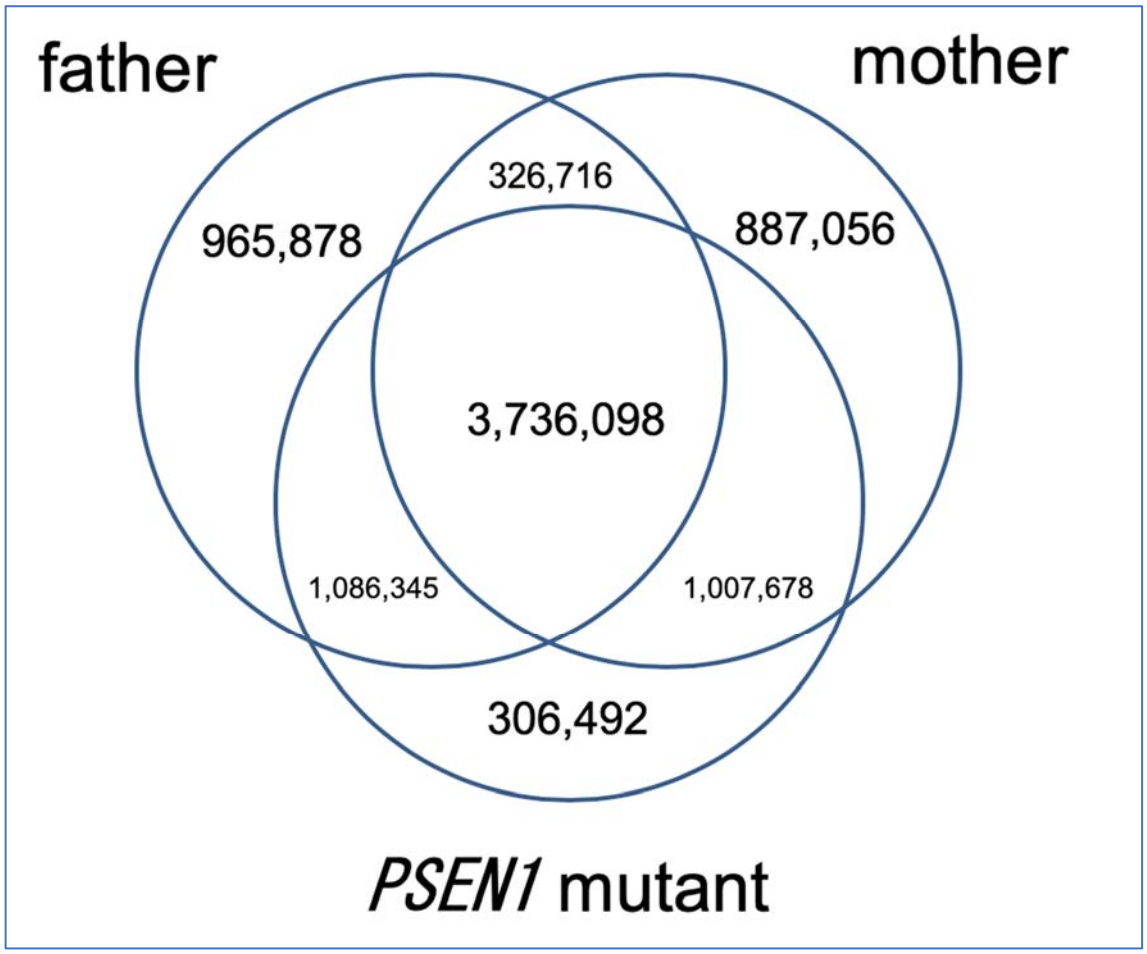
ATTTAGTGGCTGTTTTGTGTCCGAAAGGTCCACTTCGTATGCTGGTTGAAACAGC
TCAGGAGAGAAATGAAACGCTTTTTCCAGCTCTTATTTACTCCTCAACAATGGTA
TGGTTGGTGAATATGGCCGAAGGAGACCCTGAAGCTCAAAGGAGGGTATCCAAAA
ACTCCAAGTATAATGCAGAAA**GCACTGAAAGGGAGTCACAAGACACTGTTGCAGA**
GGATGATGGCGGCTTCAGTGAGGAATGGGAAGCCCAGAGGGACAGTCATCTAGGG
CCTCATCGCTCTACACCTGAGTCACGGGCTGCTGTCCAGGAACTTTCCAGCAGCA
TCCTTGCTGGTGAAGACCCAGAGGAAA

>ΔExon9

ATTTAGTGGCTGTTTTGTGTCCGAAAGGTCCACTTCGTATGCTGGTTGAAACAGC
TCAGGAGAGAAATGAAACGCTTTTTCCAGCTCTTATTTACTCC**TGCACTGAAAGG**
GAGTCACAAGACACTGTTGCAGAGGATGATGGCGGCTTCAGTGAGGAATGGGAAG
CCCAGAGGGACAGTCATCTAGGGCCTCATCGCTCTACACCTGAGTCACGGGCTGC
TGTCCAGGAACTTTCCAGCAGCATCCTTGCTGGTGAAGACCCAGAGGAAA

The cDNA sequences neighboring the exon 9 of wild-type and mutant *PSEN1* mRNAs are shown. Normal characters: exon 8, underlined characters: Exon 9, bold characters: Exon 10, and characters highlighted in yellow: codons that encode for the 290th amino acid in the *PSEN1* gene. Note that TCA and TGC encode for serine (S) and cysteine (C), respectively.

Supplementary Figure 3. Variants identified in trio whole genome sequencing.



Venn chart illustrating numbers and overlap of all the variants identified in whole genome sequencing of the *PSEN1*-ΔE9 marmoset (I774gmF) and those from her parents. Highly permissive parameter in variant calling by illumina DRAGEN pipeline (version 3.5.7) at a default setting was used, and no filtering was conducted. Of these, 306,492 variants were identified only in the *PSEN1*-ΔE9 marmoset (I774gmF). None of the 306,492 variants were present within the 10 off-target candidate sites.

Supplementary Table 1. Merits of using marmosets for AD research.

A. Characteristics advantageous as experimental non-human primates in general

1. Small body size: 350-500 g.
2. Relatively short gestation period (145 days) and effective reproduction (40 to 80 neonates per female) in primates.

B. Characteristics suitable for neuroscience

1. Genetic background and brain structure close to that of humans.
2. Human-like cognitive behaviors associated with prefrontal cortex[1].
3. Visual and auditory communications.
4. Established anatomical and imaging brain atlas[2-4].

C. Characteristics imperative for basic AD research

1. Aβ: identical to human Aβ sequence.
2. Aβ deposition with aging starting around 7 years or even earlier [5,6].
3. Phospho-tau (not NFTs) with aging starting from the medial temporal area[7].
4. Immune systems similar to those of humans[8].
5. Non-REM and probable REM cycles during sleep[9].
6. Relatively long life span particularly in captivity: maximum lifespan is 16.5 years[10].

D. Characteristics imperative for near-clinical research

1. Diabetes with aging[10].
2. Feasibility of repetitive collections of biofluid samples including cerebrospinal fluid and blood.
3. Application to functional MRI to define the default mode network[11,12] and to sensitive cognitive tests[13].
4. Drug metabolism similar to that of humans[14].

Supplementary Table 2. Summary of the off-target analysis.

Off target	Chromosome	Position	Reference	Spacer length	TAL1 Score	TAL2 Score	Average Score	Mutation
1	21	7990751-7990801	BLSI01000021.1	17	10.1	12.11	11.105	None
2	10	43948779-43948842	BLSI01000010.1	30	15.79	6.66	11.225	None
3	6	70230528-70230582	BLSI01000006.1	21	15.35	9.97	12.66	None
4	2	199375283-199375346	BLSI01000002.1	30	12.75	13.18	12.965	None
5	2	33516787-33516844	BLSI01000002.1	24	16.27	10.14	13.205	None
6	9	57942465-57942513	BLSI01000009.1	15	11.81	14.72	13.265	None
7	13	91441037-91441093	BLSI01000013.1	23	16.64	9.94	13.29	None
8	2	45917641-45917694	BLSI01000002.1	20	12.52	14.3	13.41	None
9	13	61953631-61953684	BLSI01000013.1	20	16.18	10.96	13.57	None
10	1	50319037-50319093	BLSI01000001.1	23	16.1	11.16	13.63	None

Supplementary Table 3. Statistics of the whole genome sequencing data.

Sample name	**father**	**mother**	***PSEN1*-ΔE9**
Average sequenced coverage over genome (times over genome)	57.41	62.19	42.07
Total input reads [read]	1,049,765,500	1,137,273,632	770,728,668
Mapped reads	1,043,044,330	1,130,059,433	765,829,950
Unmapped reads	6,721,170	7,214,199	4,898,718
Paired reads (itself & mate mapped)	1,039,914,838	1,126,580,296	763,452,884
Reads with MAPQ [40:inf)	982,059,798	1,064,082,451	714,555,792
Reads with MAPQ [30:40)	3,551,115	3,836,900	2,575,117
Reads with MAPQ [20:30)	5,595,307	6,015,031	4,192,941
Reads with MAPQ [10:20)	6,980,448	7,435,033	5,205,887
Reads with MAPQ [0:10)	44,857,662	48,690,018	39,300,213
Reads with MAPQ NA (Unmapped reads)	6,721,170	7,214,199	4,898,718
Q30 bases [bp]	145,168,078,063	156,463,755,481	106,214,269,234

Supplementary Table 4. Primers used in the present study.

Purpose	Category	Template	Primer Name	Sequence (5'-3')	Product size	Remarks
Genome analysis	1st PCR	Embryo Blastomere	Psen1_Ex9_up2	GCAGCCTCACACACTCTGAA	1223 bp	-
			cjPS_Int9_R2	TCTGTGTATTTCCTGGGCATT		
	2nd PCR	Tissue	Psen1_Ex9_up1	ACCCGCGACTCCCTATTATT	460 bp	289 bp + 171 bp
			Psen1_Ex9_dn1	TGCCTTGACTGTATTGTTGG		Surveyor assay[a]
cDNA analysis	1st PCR	Embryo Blastomere	Pn1_on_Ex7_up1	TACCTCCCTGAATGGACTGC	502 bp	415 bp
			Pn1_on_Ex11_dn2	TGGTTGTGTTCCAGTCTCCA		ΔExon9[b]
	2nd PCR	Tissue	Pn1_on_Ex8_up1	GGTCCACTTCGTATGCTGGT	402 bp	315 bp
			Pn1_on_Ex11_dn1	GGCTGTTGCTGAGGCTTTAC		ΔExon9[b]

[a]These fragment sizes indicate that the TALEN cleaved the center of the spacer sequence without insertions or deletions.

[b]PCR amplification product size with the exon9 (87 bp) deletion is included in the template.

Supplementary Table 5. Primers used for the off-target analysis.

Off-target	Primer Name	Sequence (5'-3')	Product size (bp)
1	OT-1_up1	TTATCTGCAGGACACGATGG	535
	OT-1_dn1	AGTTAGCAGGGTGTGGTGGT	
2	OT-2_up1	TTGAAAGGAAGGCTGGAAGA	492
	OT-2_dn1	TCAGGCTTTTCCTCTCCTCA	
3	OT-3_up1	AGCAAAGGGTGATGTGTTGA	550
	OT-3_dn1	TCCTCGGAATGTCTGAATCC	
4	OT-4_up1	GGGGAGAAAAGGGAACTTGA	696
	OT-4_dn1	GAGAGCAGCTGTGTGTGGAG	
5	OT-5_up1	GGATTTAGGGAGGGTGGGTA	670
	OT-5_dn1	TGGGAGACGATTAGGTCCTG	
6	OT-6_up2	AGTGGTCAATCTTGGCCTTGACAT	409
	OT-6_dn1r	AGATGGGCAGCTATGGTTTGCAAG	
7	OT-7_up1	TTTGCATAAAAGTGGCAAAA	659
	OT-7_dn1	CAATGATCCCTGGCAGACTT	
8	OT-8_up1	TGCAAATTGCTGCCTTCATA	536
	OT-8_dn1	TGAAGCCCCATAAAACAAGG	
9	OT-9_up1	TAGGACAATGACCCCAAACC	564
	OT-9_dn1	TTGGGGAGGCAATCATTTAG	
10	OT-10_up1	AGAAGTGAAAGTGGGGGATG	618
	OT-10_dn1	AGCCTAATTGCTGCCATTGT	

References

1 Miller, C. T. *et al.* Marmosets: A Neuroscientific Model of Human Social Behavior. *Neuron* **90**, 219-233, doi:10.1016/j.neuron.2016.03.018 (2016).

2 Hikishima, K. *et al.* Atlas of the developing brain of the marmoset monkey constructed using magnetic resonance histology. *Neuroscience* **230**, 102-113, doi:10.1016/j.neuroscience.2012.09.053 (2013).

3 Senoo, A., Tokuno, H. & Watson, C. Mini-atlas of the marmoset brain. *Neuroscience research* **93**, 128-135, doi:10.1016/j.neures.2014.12.014 (2015).

4 Hashikawa, T., Nakatomi, R. & Iriki, A. Current models of the marmoset brain. *Neuroscience research* **93**, 116-127, doi:10.1016/j.neures.2015.01.009 (2015).

5 Geula, C., Nagykery, N. & Wu, C. K. Amyloid-beta deposits in the cerebral cortex of the aged common marmoset (Callithrix jacchus): incidence and chemical composition. *Acta neuropathologica* **103**, 48-58, doi:10.1007/s004010100429 (2002).

6 Ridley, R. M., Baker, H. F., Windle, C. P. & Cummings, R. M. Very long term studies of the seeding of beta-amyloidosis in primates. *Journal of neural transmission (Vienna, Austria : 1996)* **113**, 1243-1251, doi:10.1007/s00702-005-0385-2 (2006).

7 Rodriguez-Callejas, J. D., Fuchs, E. & Perez-Cruz, C. Evidence of Tau Hyperphosphorylation and Dystrophic Microglia in the Common Marmoset. *Frontiers in aging neuroscience* **8**, 315, doi:10.3389/fnagi.2016.00315 (2016).

8 t Hart, B. A. & Massacesi, L. Clinical, pathological, and immunologic aspects of the multiple sclerosis model in common marmosets (Callithrix jacchus). *Journal of neuropathology and experimental neurology* **68**, 341-355, doi:10.1097/NEN.0b013e31819f1d24 (2009).

9 Crofts, H. S. *et al.* Investigation of the sleep electrocorticogram of the common marmoset (Callithrix jacchus) using radiotelemetry. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology* **112**, 2265-2273 (2001).

10 Tardif, S. D., Mansfield, K. G., Ratnam, R., Ross, C. N. & Ziegler, T. E. The marmoset as a model of aging and age-related diseases. *ILAR journal* **52**, 54-65 (2011).

11 Dennis, E. L. & Thompson, P. M. Functional brain connectivity using fMRI in aging and Alzheimer's disease. *Neuropsychol Rev* **24**, 49-62, doi:10.1007/s11065-014-9249-6 (2014).

12 Mohan, A. *et al.* The Significance of the Default Mode Network (DMN) in Neurological and Neuropsychiatric Disorders: A Review. *Yale J Biol Med* **89**, 49-57 (2016).

13 Kangas, B. D. & Bergman, J. Touchscreen technology in the study of cognition-related behavior. *Behav Pharmacol* **28**, 623-629, doi:10.1097/fbp.0000000000000356 (2017).

14 Aravalli, R. N. & Steer, C. J. Utility of Common Marmoset (Callithrix jacchus) Embryonic Stem Cells in Liver Disease Modeling, Tissue Engineering and Drug Metabolism. *Genes (Basel)* **11**, doi:10.3390/genes11070729 (2020).