

Supplementary Table 1

ID	Individual ID	Pedigree ID	Gene	Protein	cDNA	Exon	Region	Confirmed	ApoE
1	1	Sporadic	PSEN1	p.Leu85Pro	c.254T>C	4	TM-I	Performed	3*3
2	2	1	PSEN1	p.Val96Phe	c.286G>T	4	TM-I	Performed	NA
3	3	1	PSEN1	p.Val96Phe	c.286G>T	4	TM-I	Performed	NA
4	4	1	PSEN1	p.Val96Phe	c.286G>T	4	TM-I	Performed	NA
5	5	2	PSEN1	p.His163Arg	c.488A>G	6	HL-II	Performed	NA
6	6	3	PSEN1	p.His163Arg	NA	6	HL-II	Performed	NA
7	7	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Performed	3*3
8	8	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Performed	3*4
9	9	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Performed	3*4
10	10	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Not performed	NA
11	11	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Not performed	NA
12	12	4	PSEN1	p.Gly209Arg	c.625G>A	7	TM-IV	Not performed	NA
13	13	5	PSEN1	p.Ile213Thr	c.638T>C	7	TM-IV	Performed	NA
14	14	5	PSEN1	p.Ile213Thr	c.638T>C	7	TM-IV	Performed	NA
16	16	6	PSEN1	p.Met233Leu	NA	7	TM-V	Performed	NA
17	17	Sporadic	PSEN1	p.Phe237Ile	c.709A>T	7	TM-V	Performed	3*3
18	18	NA	PSEN1	p.Pro284Leu	NA	8	HL-VI(MA)	Performed	NA
19	19	7	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Performed	NA
20	20	7	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Performed	NA
21	21	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
22	22	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
23	23	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
24	24	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
25	25	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
26	26	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
27	27	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
28	28	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
29	29	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
30	30	8	PSEN1	p.(S290C:T291 S319del)	c.869 955del	8	HL-VI(MA)	Not performed	NA
31	31	9	PSEN1	p.Ala285Val	c.854C>T	8	HL-VI(MA)	Performed	NA
32	32	9	PSEN1	p.Ala285Val	c.854C>T	8	HL-VI(MA)	Not performed	NA
33	33	10	PSEN1	p.Ile143Thr	c.428C>T	5	TM-II	Performed	3*4
34	34	10	PSEN1	p.Ile143Thr	c.428C>T	5	TM-II	Performed	3*3
35	35	10	PSEN1	p.Ile143Thr	c.428C>T	5	TM-II	Not performed	NA
36	36	10	PSEN1	p.Ile143Thr	c.428C>T	5	TM-II	Not performed	NA
37	37	10	PSEN1	p.Ile143Thr	c.428C>T	5	TM-II	Not performed	NA
38	38	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Performed	3*3
39	39	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Performed	3*4
40	40	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Not performed	NA
41	41	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Not performed	NA
42	42	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Not performed	NA
43	43	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Not performed	NA
44	44	12	PSEN1	p.Leu250Val	c.748T>G	7	TM-VI	Not performed	NA
45	45	13	PSEN1	p.Leu282Phe	c.844C>T	8	HL-VI(MA)	Performed	3*4
46	46	13	PSEN1	p.Leu282Phe	c.844C>T	8	HL-VI(MA)	Not performed	NA
47	47	14	PSEN1	p.Tyr154Asn	c.460T>A	5	TM-II	Performed	3*3
48	48	14	PSEN1	p.Tyr154Asn	c.460T>A	5	TM-II	Not performed	NA
49	49	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	Performed	NA
50	50	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	Performed	NA
51	51	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
52	52	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
53	53	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
54	54	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
55	55	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
56	56	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
57	57	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
58	58	15	PSEN1	p.Ala260Val	c.779C>T	8	TM-VI	NA	NA
59	59	16	PSEN1	p.Ala285Val	c.854C>T	8	HL-VI(MA)	Performed	NA
60	60	16	PSEN1	p.Ala285Val	c.854C>T	8	HL-VI(MA)	Not performed	NA
61	61	16	PSEN1	p.Ala285Val	c.854C>T	8	HL-VI(MA)	Not performed	NA
62	62	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Performed	3*4
63	63	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Performed	3*4
64	64	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Not performed	NA
65	65	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Not performed	NA
66	66	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Not performed	NA
67	67	17	PSEN1	p.Leu173Phe	c.519G>C	6	TM-III	Not performed	NA
68	68	18	PSEN1	p.T440del	c.1318 1320delACC	12	TM-IX	Performed	3*3
69	69	18	PSEN1	p.T440del	c.1318 1320delACC	12	TM-IX	Not performed	NA
70	70	18	PSEN1	p.T440del	c.1318 1320delACC	12	TM-IX	Not performed	NA
71	71	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Not performed	NA
72	72	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Not performed	NA
73	73	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Not performed	NA
74	74	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Not performed	NA
75	75	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Not performed	NA
76	76	32	PSEN1	p.Gly266Ser	c.796G>A	8	HL-VIa	Performed	3*3
77	77	33	PSEN1	p.Ala431Val	c.1292C>T	12	HL-VIII	Performed	3*3
78	78	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
79	79	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
80	80	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
81	81	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
82	82	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
83	83	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Not performed	NA
84	84	34	PSEN1	p.Leu420Arg	c.1259T>C	12	TM-VIII	Performed	NA
85	85	35	PSEN1	p.Glu184Asp	c.552A>C	7	HL-III	Not performed	NA
86	86	35	PSEN1	p.Glu184Asp	c.552A>C	7	HL-III	Not performed	3*3
87	87	35	PSEN1	p.Glu184Asp	c.552A>C	7	HL-III	Not performed	NA
88	88	35	PSEN1	p.Glu184Asp	c.552A>C	7	HL-III	Performed	3*3
89	89	36	PSEN1	p.Gly217Asp	c.650G>A	7	HL-IV	Not performed	NA
90	90	36	PSEN1	p.Gly217Asp	c.650G>A	7	HL-IV	Performed	NA
91	91	36	PSEN1	p.Gly217Asp	c.650G>A	7	HL-IV	Not performed	NA
92	92	36	PSEN1	p.Gly217Asp	c.650G>A	7	HL-IV	Not performed	NA
93	93	36	PSEN1	p.Gly217Asp	c.650G>A	7	HL-IV	Not performed	NA
94	94	37	PSEN1	p.Glu280Ala	c.839A>C	8	HL-VI(MA)	Performed	3*3
95	95	37	PSEN1	p.Glu280Ala	c.839A>C	8	HL-VI(MA)	Not performed	3*3
96	96	Sporadic	PSEN1	p.Asn405Ser	c.1214A>G	11	HL-VII	Performed	3*4
97	97	38	PSEN1	p.Glu123Lys	c.367G>A	5	HL-I	Performed	2*3
98	98	38	PSEN1	p.Glu123Lys	c.367G>A	5	HL-I	Performed	3*3
99	99	38	PSEN1	p.Glu123Lys	c.367G>A	5	HL-I	Not performed	NA
100	100	38	PSEN1	p.Glu123Lys	c.367G>A	5	HL-I	Not performed	NA
101	101	39	PSEN1	p.His163Arg	c.488A>G	6	HL-II	Performed	3*3
102	102	39	PSEN1	p.His163Arg	c.488A>G	6	HL-II	Performed	3*3
103	103	39	PSEN1	p.His163Arg	c.488A>G	6	HL-II	Performed	NA
104	104	40	PSEN1	p.Arg269His	G>A	8	HL-VIa	Performed	3*4
105	105	41	PSEN1	p.Glu273Ala	A>C	8	HL-VIa	Performed	3*3
106	106	42	PSEN1	p.Gly384Ala	c.1151G>C	11	TM-VII	Performed	3*3
107	107	Sporadic	PSEN1	p.His163Arg	c.488A>G	6	HL-II	Performed	3*3

Supplementary Figure 1

(A) Gene search

Gene Search (Mutations)

http://alzdb.bri.niigata-u.ac.jp/jfad/gene_search_mutations.html / JFAD

Select a gene symbol:

APP
PSEN1
PSEN2
MAPT
GRN

(B) Phenotype search

Phenotype Search

http://alzdb.bri.niigata-u.ac.jp/jfad/phenotype_search.html / JFAD

Select a phenotype:

AD
AD with SP
bvFTD
Dementia
Depression followed by EOAD
DLB with SP
EOAD
EOAD with SP
FTD
FTLD
MCI
Perry syndrome
Pick's disease
PNFA
PNLD
PPA
PSP
SD

 Abbreviations are [here](#)

(C) List of mutation

Gene	# of Pedigrees	Mutation(Protein)	Mutation(DNA)	PMID	ICSID (Mainly Japanese)
APP	2	duplication		Kasuga K et al. (2009)	
APP	1	p.Lys510Asn	c.1530G>C		2010127819
APP	1	p.Lys510Asn	c.1530G>T or C		15320137
APP	1	p.Asp678Asn	c.2032G>A	Wakutani Y et al. (2004)	
APP	3	p.Glu693del	c.del2077-2079GAA	Tomiyama T et al. (2008)	
APP	7	p.Val717Ile	c.2149G>A	Matsumura Y et al. (1996) Yoshioka K et al. (1991) Naruse S et al. (1991) Yoshizawa T et al. (1993) Katsuya T et al. (1993) Imagawa M et al. (1992)	1993010101

(D) Detailed information on clinical features

ApoE	Familial or Sporadic	Age at Onset	Onset of Dementia	Initial Symptom	Psychiatric Symptom	Mood Disorder	Spastic Paraparesis	Parkinsonism or Rigidity	Epilepsy or Seizure	Age of Death
3*3	Familial	29	29	Ci			+			
	Familial									early 40s
	Familial	40	42	Sp			+	+		

Figure legend: Snapshot of “JFADdb”. Representative images of displays in databases such as “Gene Search” (A), “Phenotype Search” (B), “List of mutation” (C), and “Detailed information on clinical features” (D) for each patient are shown.

Supplementary Figure 2

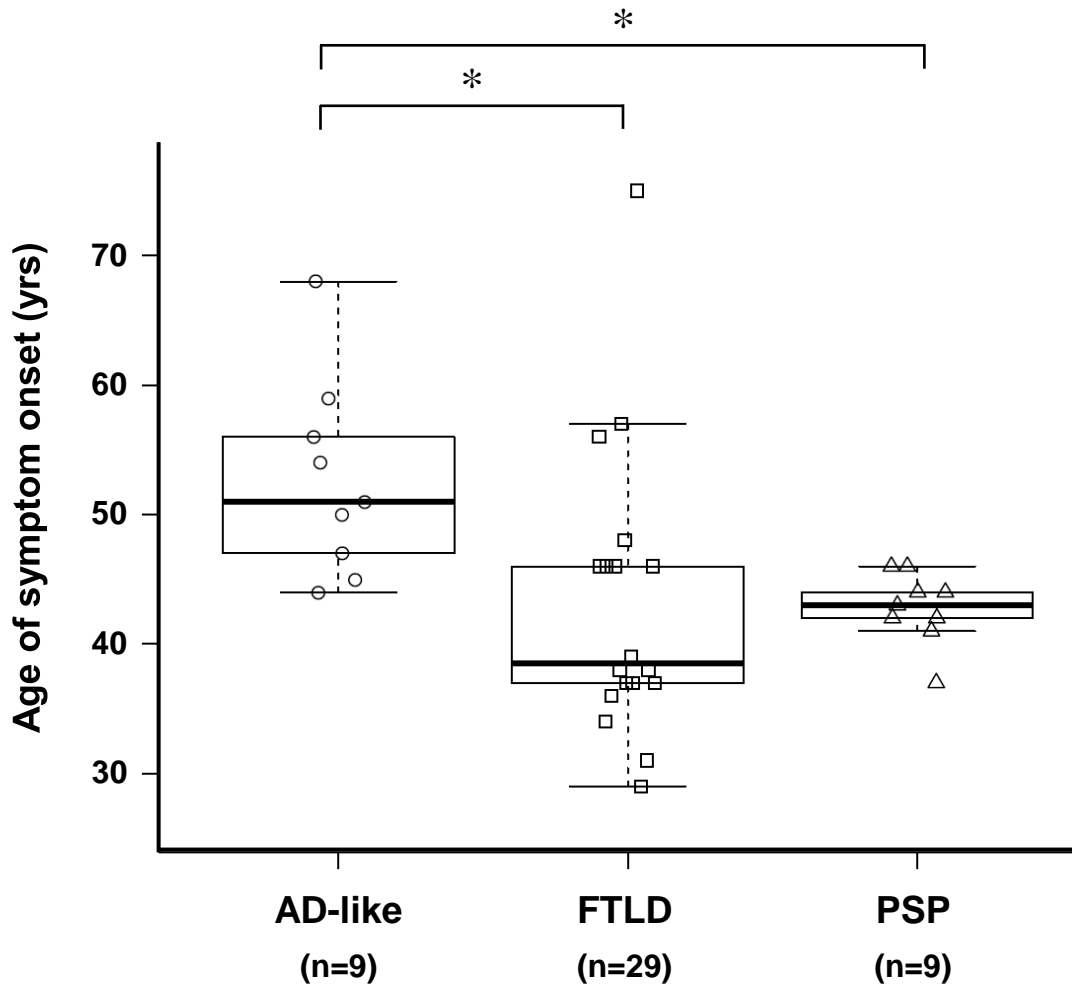


Figure legend: Ages at onset in three clinical phenotypes with *MAPT* mutations: FTLD, AD-like, and PSP phenotypes. The age at onset of patients with the FTLD (44 ± 10 years) or PSP phenotype (43 ± 3 years) was significantly younger than that with the AD-like phenotype (53 ± 8 years) (* $p < 0.05$, ANOVA with post-hoc Tukey's test). Results are shown as box-whistler plot.

Supplementary Figure 3

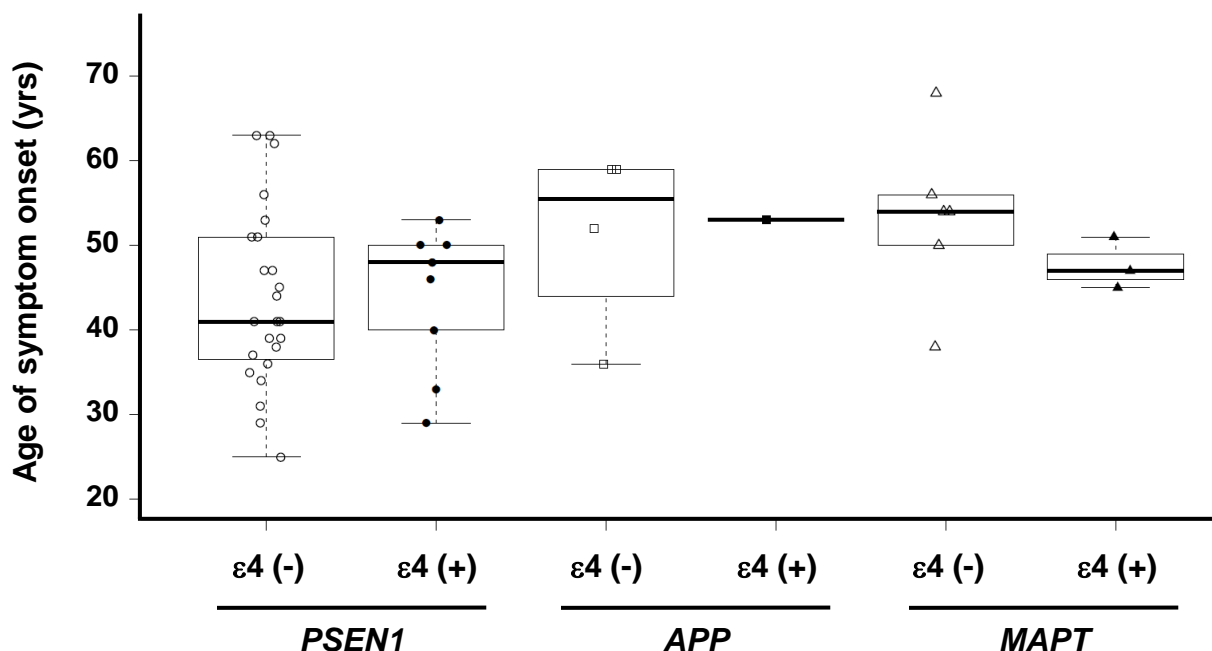


Figure legend: Effect of *APOE* $\epsilon 4$ on age at onset of Japanese FAD and FTDP-17. Forty-seven patients had additional information on their *APOE* genotypes. Each group of patients with gene mutations were stratified into *APOE* $\epsilon 4$ carriers and noncarriers. There was no significant difference in the age at onset between *APOE* $\epsilon 4$ carriers and noncarriers in familial dementia ($p=0.86$, Mann-Whitney *U*-test).

Supplementary Figure 4

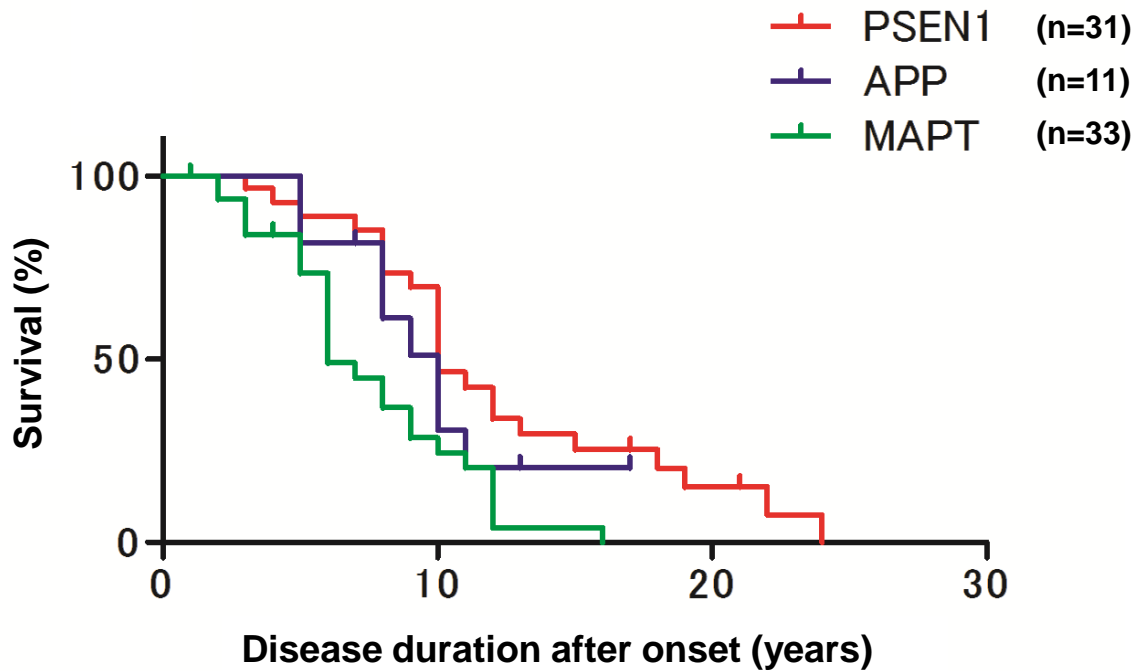


Figure legend: Survival of patients with *PSEN1* (n=31), *APP* (n=11), and *MAPT* mutations (n=33) examined by Kaplan-Meier analysis. The log-rank test revealed that patients with *MAPT* mutations showed a shorter survival than those with *PSEN1* or *APP* mutations ($p < 0.05$).