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Supplementary Data

The French Series of Autosomal Dominant Early Onset Alzheimer's Disease Cases: Mutation Spectrum and Cerebrospinal Fluid Biomarkers

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Supplementary Table 1
Primers used for PCR amplification of *PSEN1*, *PSEN2*, and *AβPP*

Gene	Exo	Primers	Sequence
PSEN1	2/3	PS1 ex2/3F	GGA TGA CCT GGT GAA ATC C
		PS1 ex2/3R	TCC TCC AGC AAT CAG CTG AA
	4	PS1 ex4F	TCA TAG TGA CGG GTC TGT TG
		PS1 ex4R	TCA ACT GCT CCT GAC CAT CA
	5	PS1 ex5F	GGT GAG TTG GGG AAA AGT GA
		PS1 ex5R	TGT TCC ACA GTG AGG AGG AA
	6	PS1 ex6F	TTT AAG GGT TGT GGG ACC TG
		PS1 ex6R	GCA AGG AGC AAC AGA AGA A
	7	PS1 ex7F	GGG AGC CAT CAC ATT ATT C
		PS1 ex7R	ATG GGA TGT ACA CGT TAC C
	8	PS1 ex8F	CAC CAG TTC ACC TGC CAT TT
		PS1 ex8R	AGT TCC AGG AAT GCT GTG CA
	9	PS1 ex9F	TGA ACA GTC TTA AGG CAG C
		PS1 ex9R	CTC AAA GGA GTC TAT GAC C
	10	PS1 ex10F	TGC TTT GTG GTT TAA GGG CC
		PS1 ex10R	TTC ATT TTA TTC TCA AAA AGG TTG
	11	PS1 ex11F	CAC ATA GAA TCT GGA ACT CC
		PS1 ex11R	AAA GCT CCT CAG ATA GCT GG
	12	PS1 ex12F	CCA GAT TGA ATG AAC GTC TG
		PS1 ex12R	GCC GGG AAT CTT GAC TTT GT
PSEN2	4	PS2 ex4F	TGT GTC CAA GTC TCC AGG TC
		PS2 ex4R	CAT CAG GGA ATG AAT GTC TGG
	5	PS2 ex5F	GGA AAG CAA CAT TCA AAC TTC
		PS2 ex5R	TGC AGG TAC AGT GAC CAA CAC
	6	PS2 ex6F	AAT GAG CTG GAG GAC AGG AAC
		PS2 ex6R	TCT AAA GGC GGC TGT TTC AC
	7	PS2 ex7F	AGA GCA TTC AGG CTT GGG TA
		PS2 ex7R	AGC TCG TGG TCA TCT TTC CCC
	8	PS2 ex8F	TGG GAC TGA ATG GTG GTA AAC
		PS2 ex8R	CAC CAG GAG TGT TCC AGA AA
	9	PS2 ex9F	TAC AGG GCA GGC TCT TCT TC
		PS2 ex9R	GCC CAG TCA ACT CTG AAA GC
	10	PS2 ex10F	GGT CCT GTG CAG GCT TTC T
		PS2 ex10R	GCT CCT GAA CTC ATG CCT CTC
	11	PS2 ex11F	ACC CCT TCT TGG AGC TTT GT
		PS2 ex11R	GAG ATG CCT CTG ATG GGA AA
	12	PS2 ex12F	TGG GCC TTC TGG GCC AGA GTT TCT CTT C
		PS2 ex12R	CCT AGG GAT CCT GAG ACC TG
	13	PS2 ex13F	TAT CCG ACT GGT CCT CGA AC
		PS2 ex13R	AAA CAG CTG GCA CCA AAG AG
AβPP	16	AβPP ex16F	CTT CTA ACT TCA GGC CTA G
		AβPP ex16R	GGT TAA TCC TAT AGG CAA GC
	17	AβPP ex17F	ATT TGA CCA ACC AGT TGG GC
		AβPP ex17R	CAT GGA AGC ACACTG ATT CG

Supplementary Table 2
Whole series of French ADEOAD families with PSEN1 mutations

Protein change	Nucleotide change◊	Exon	*APOE* (*index case*)	ID Fam ID Fam	PS (*n*)	AS (*n*)	Coseg	Pathogenicity nature	AOO range (years)	DD (years)
p.Ala79Val	c.236C>T	4	3-3	EXT 262	1	7	n/a	Definite	[60–62]	[4–10]
p.Val82Leu	c.244G>C	4	3-3	SAL 508	1	3	n/a	Definite	[53–55]	[8–12]
p.Phe105Ile	c.313T>A	4	3-3	ALZ 184	1	2	n/a	Definite	[58-59]	13
p.Leu113Pro	c.338T>C	4	2-3	SAL 513	3	6	Yes	Definite	[39–49]	[4–11]
p.Tyr115His	c.343C>T	5	3-4	ALZ 025	1	2	n/a	Definite	[33–35]	[6–13]
p.Tyr115His	c.343T>C	5	3-3	ALZ 076	1	3	n/a	Definite	[37–40]	[3-4]
p.Tyr115Cys	c.344A>G	5	2-3	EXT 238	1	2	n/a	Definite	[39-40]	3
p.Thr116Asn	c.347C>A	5	3-4	ALZ 157	1	2	n/a	Definite	[32–38]	15
p.Thr116Ile	c.347C>T	5	3-3	EXT 234	1	5	n/a	Definite	[38–44]	[3–5]
p.Pro117Ala	c.349C>G	5	3-3	MUL 706	1	3	n/a	Definite	[31–34]	[9-10]
p.Glu120Asp	c.360A>C	5	3-3	ALZ 043	1	4	n/a	Definite	[45–56]	[11–17]
p.Glu120Asp	c.360A>C	5	3-3	ALZ 057	4	8	Yes	Definite	[42–52]	[4–12]
p.Glu120Asp	c.360A>C	5	3-4	ALZ 231	3	4	Yes	Definite	[40–48]	[7-8]
p.Met139Lys	c.416T>A	5	3-3	ALZ 139	1	2	n/a	Definite	[37–50]	10
p.Met139Thr	c.416T>C	5	3-3	ALZ 248	1	4	n/a	Definite	[55–63]	[8–11]
p.Met139Thr	c.416T>C	5	3-3	ALZ 104	1	2	n/a	Definite	[42–55]	[9–15]
p.Met139Thr	c.416T>C	5	3-3	CAE 010	2	2	Yes	Definite	[48–50]	[5-6]
p.Ile143Asn	c.428T>A	5	3-3	ALZ 175	1	5	n/a	Definite	[50]	[13]
p.Ile143Thr	c.428T>C	5	3-3	EXT 139	1	2	n/a	Definite	[34]	[8–17]
p.Met146Leu	c.436A>C	5	3-3	EXT 208	2	2	Yes	Definite	[44-45]	[5]
p.Met146Leu	c.436A>C	5	3-3	ALZ 279	2	6	Yes	Definite	[39–41]	[9–12]
p.Met146Leu	c.436A>C	5	3-3	ALZ 249	1	5	n/a	Definite	[38–41]	[6–10]
p.Thr147Ile	c.440C>T	5	3-3	ALZ 047	2	4	Yes	Definite	[35–41]	[5–12]
p.Leu150Pro♮	c.449T>C	6	3-4	EXT 358	1	6	n/a	Probable	[54–65]	[5–10]
p.Leu153Val	c.457C>G	5	3-3	ALZ 180	1	3	n/a	Definite	[40–44]	[10–13]
p.Leu153Val	c.457C>G	5	3-3	ALZ 148	5	8	Yes	Definite	[30–40]	[5–11]
p.His163Arg	c.488A>G	6	2-3	SAL 001	2	3	Yes	Definite	[40–47]	[9]
p.His163Arg	c.488A>G	6	3-3	ALZ 430	3	6	Yes	Definite	[42–45]	[6–10]
p.His163Arg	c.488A>G	6	3-4	EXT 226	1	4	n/a	Definite	[36–44]	[8–12]
p.His163Arg	c.488A>G	6	3-4	ALZ 428	1	7	n/a	Definite	[31–40]	[6–9]
p.Trp165Cys	c.495G>C	6	3-3	ALZ 064	2	4	Yes	Definite	[37–47]	[2–11]
p.Leu173Trp	c.518T>G	6	2-4	ROU 118	2	3	n/a	Definite	[24–39]	[10]
p.Phe177Leu	c.529T>C	6	3-3	ALZ 156	1	4	n/a	Definite	[36–42]	[12]
p.Glu184Gly♮	c.551A>G	7	3-3	ALZ 013	2	8	Yes	Definite	[43–52]	[5–14]
p.Glu184Gly♮	c.551A>G	7	3-3	EXT 134	2	3	n/a	Definite	[51-52]	[7-8]
p.Gly206Ser	c.616G>A	7	3-3	EXT 103	2	15	n/a	Definite	[36–44]	[8–14]
p.Gly206Asp	c.617G>A	7	3-3	ALZ 219	3	4	Yes	Definite	[32–34]	[2–9]
p.Gly206Ala	c.617G>C	7	3-4	ALZ 243	1	3	n/a	Definite	[58–60]	[7]
p.Ile213Thr	c.638T>C	7	3-3	ALZ 059	1	3	n/a	Definite	[42–50]	[7–10]
p.His214Tyr	c.640C>T	7	3-3	ALZ 172	1	5	n/a	Definite	[37–46]	[6–15]
p.Gln222His	c.666G>C	7	2-3	ALZ 250	1	4	n/a	Definite	[44–47]	[5–10]
p.Gln223Arg	c.668A>G	7	3-3	EXT 141	1	2	n/a	Definite	[31–34]	5
p.Ser230Ile♮	c.689G>T	7	3-4	EXT 359	1	2	n/a	Possible	[50–58]	20
p.Met233Thr	c.698T>C	7	3-4	ALZ 202	1	6	n/a	Definite	[38–40]	[5–11]
p.Met233Thr	c.698T>C	7	3-4	EXT 059	1	2	n/a	Definite	[37–40]	5
p.Met233Thr	c.698T>C	7	3-3	ALZ 163	1	5	n/a	Definite	[36–45]	[2–7]
p.Met233Thr	c.698T>C	7	3-3	ALZ 079	4	12	Yes	Definite	[36–47]	[4–14]
p.Met233Ile♮	c.699G>A	7	3-3	SAL 613	2	2	Yes	Definite	[24–30]	11
p.Leu235Pro	c.704T>C	7	2-3	SAL 510	6	6	Yes	Definite	[29–36]	[3–6]
p.Ala260Val	c.779C>T	8	3-3	ALZ 512	1	6	n/a	Definite	[34–38]	[8]
p.Leu262Val♮	c.784T>G	8	3-3	EXT 140	3	8	Yes	Definite	[54–63]	[8]
p.Pro264Leu	c.791C>T	8	3-4	SAL 506	2	4	Yes	Definite	[46–52]	[4–14]
p.Pro264Leu	c.791C>T	8	3-3	ALZ 183	2	4	Yes	Definite	[47–51]	[11–13]
p.Pro264Leu	c.791C>T	8	3-4	SAL 511	11	11	Yes	Definite	[45–57]	[1–13]
p.Pro264Leu	c.791C>T	8	3-3	EXT 142	3	3	Yes	Definite	[47–55]	[6–19]
p.Pro264Leu	c.791C>T	8	3-4	SAL 1633	1	4	n/a	Definite	[45-58]	[5–7]
p.Pro264Leu	c.791C>T	8	3-3	EXT 143	1	5	n/a	Definite	[48–57]	[4–8]
p.Pro264Leu	c.791C>T	8	3-3	EXT 369	1	8	n/a	Definite	[47–55]	[7–10]
p.Glu273Gly♮	c.818A>G	8	3-3	SAL 294	1	4	n/a	Probable	[50–63]	[9]
p.Glu280Gly	c.839A>G	8	3-3	ALZ 150	1	3	n/a	Definite	[40–51]	[2–15]

Supplementary Table 2
(*Continued*)

Protein change	Nucleotide change◊	Exon	*APOE* (*index case*)	ID Fam ID Fam	PS (*n*)	AS (*n*)	Coseg	Pathogenicity nature	AOO range (years)	DD (years)
p.Leu286Val	c.856C>G	8	3-3	EXT 048	1	3	n/a	Definite	[41–45]	[7–10]
p.[S290C;T291_S319del]	c.869_955del	8	3-3	DF 149	1	4	n/a	Definite	[42–47]	[11–15]
p.Thr291Pro	c.871A>C	9	3-3	EXT 245	1	1	n/a	Definite	[33]	n/a
p.Arg377Trp♯	c.1129A>T	10	3-3	EXT 138	1	2	n/a	Probable	[50]	[8-9]
p.Phe386Ser	c.1157T>C	11	3-3	POI 060	4	4	Yes	Definite	[34–40]	[6–11]
p.Ser390Ile	c.1169G>T	11	3-3	ALZ 107	1	4	n/a	Definite	[39-40]	[6–10]
p.Val391Phe	c.1171G>T	11	3-3	ALZ 116	3	7	Yes	Definite	[54–55]	[5–10]
p.Val391Phe	c.1171G>T	11	3-3	ALZ 174	1	3	n/a	Definite	[31–40]	[10–16]
p.Val391Phe	c.1171G>T	11	3-3	EXT 035	1	2	n/a	Definite	[45–50]	3
p.Leu392Val	c.1174C>G	11	3-3	FAD R01	18	53	Yes	Definite	[34–62]	[2–24]
p.Cys410Tyr	c.1229G>A	11	3-3	EXT 074	1	4	n/a	Definite	[40–60]	[6–10]
p.Cys410Tyr	c.1229G>A	11	2-3	ROU 011	4	14	Yes	Definite	[40–60]	[3–15]
p.Leu418Phe	c.1254G>T	12	3-3	BRE 014	1	2	n/a	Definite	[31–35]	[5-6]
p.Leu424His	c.1271T>A	12	2-4	ALZ 161	1	2	n/a	Definite	[43–45]	11
Total & [range]				**74**	**149**	**380**	**25**		**[24–63]**	**[2–19]**

◊nucleotide change: according to RefSeq. NM_000021.3. ID Fam: family code; PS: patients sampled; coseg: cosegregation with the disease; AOO: Age of onset; AS: affected subjects in the same family; DD: disease duration; ♯(bold): mutation previously unreported. n/a: not applicable.

Supplementary Table 3
Whole series of French ADEOAD families with *PSEN2* mutations

Protein change	Nucleotide change◊	Exon	*APOE* (*index case*)	ID fam	PS (*n*)	AS (*n*)	coseg	Pathogenicity nature	AOO range (years)	DD (years)
p.Arg71Trp	c.211C>T	4	3-4	EXT 075	2	2	Yes	Definite	[63-64]	[6–9]
p.Arg71Trp	c.211C>T	4	3-4	EXT 179	1	3	n/a	Definite	[55-56]	[7–16]
p.Lys161Arg♯	c.482A>G	5	3-4	EXT 114	1	3	n/a	Possible	[61–69]	[7–16]
p.Met239Val	c.715A>G	7	3-4	ALZ 400	1	2	n/a	Definite	[47–55]	[7–13]
p.Met239Val	c.715A>G	7	3-4	TOU 035	1	5	n/a	Definite	[53–62]	[15]
p.Met239Val	c.715A>G	7	3-4	ALZ 434	1	5	n/a	Definite	[48–67]	[4–11]
p.Met239Val	c.715A>G	7	3-4	ROU 360	1	6	n/a	Definite	[49–57]	[10–19]
p.Met239Val	c.715A>G	7	3-4	EXT 062	1	2	n/a	Definite	[47–60]	[5–7]
Total & [range]				**8**	**9**	**28**	**1**		**[47–69]**	**[4–19]**

◊nucleotide change: according to RefSeq. NM_000447.2. ID Fam: family code; PS: patients sampled; coseg: cosegregation with the disease; AOO: Age of onset; AS: affected subjects in the same family; DD: disease duration; ♯(bold): mutation previously unreported; n/a: not applicable.

Supplementary Table 4
Whole series of French ADEOAD families with *AβPP* mutations

Protein change	Nucleotide change◊	Exon	*APOE* (*index case*)	ID fam	PS (*n*)	AS (*n*)	coseg	Pathogenicity nature	AOO range (years)	DD (years)
p.Thr714Ile	c.2141C>T	17	3-3	ALZ 191	1	1	n/a	Definite	35	13
p.Val715Met	c.2143G>A	17	3-3	ALZ 074	4	4	Yes	Definite	[40–52]	[13–18]
p.Val715Ala	c.2144T>C	17	3-3	EXT 147	1	10	n/a	Definite	[40–44]	[6–13]
p.Val717Ile	c.2149G>A	17	2–4	ALZ 166	1	4	n/a	Definite	[46–56]	[11–13]
p.Val717Ile	c.2149G>A	17	3-3	ALZ 196	1	2	n/a	Definite	[50–60]	14
p.Val717Ile	c.2149G>A	17	3-3	PRO 003	1	4	n/a	Definite	[51–55]	[10]
p.Val717Ile	c.2149G>A	17	3-3	ALZ 221	1	3	n/a	Definite	[40–54]	[8–10]
p.Val717Ile	c.2149G>A	17	3-3	ALZ 066	2	4	Yes	Definite	[53–61]	[8]
p.Val717Ile	c.2149G>A	17	3-3	EXT 076	1	5	n/a	Definite	[45–48]	[8–11]
p.Val717Ile	c.2149G>A	17	3-3	EXT 148	1	3	n/a	Definite	[47–55]	[5–10]
p.Val717Ile	c.2149G>A	17	3-3	ALZ 431	2	3	Yes	Definite	[49–52]	[5–7]
p.Val717Ile	c.2149G>A	17	3-3	FAD R03	2	5	Yes	Definite	[55–56]	[9–13]
p.Val717Ile	c.2149G>A	17	3-3	FAD R04	2	4	Yes	Definite	[48–58]	[10–12]
p.Val717Ile	c.2149G>A	17	3-3	JUB 001	1	9	n/a	Definite	[38–51]	[4–9]
p.Val717Ile	c.2149G>A	17	3-4	EXT 286	1	2	n/a	Definite	[53–60]	5
p.Leu723Pro	c.2168T>C	17	3-4	ALZ 523	1	7	n/a	Definite	[54–57]	[3-4]
Total & [range]				**16**	**23**	**70**	**5**		**[35–61]**	**[3–18]**

◊nucleotide change: according to RefSeq. NM_000484.3. ID Fam: family code; PS: patients sampled; coseg: cosegregation with the disease; AOO: Age of onset; AS: affected subjects in the same family; DD: disease duration; n/a: not applicable.

Supplementary Table 5
Whole series of French ADEOAD families with AβPP duplication

Duplication size (Mb)	*APOE (index case)*	ID fam	PS (n)	AS (n)	coseg	AOO range (years)	DD (years)
0.55	3-3	BES 262	7	13	Yes	[47–58]	[5–20]
0.58	3-4	ALZ 028	6	7	Yes	[45–48]	[5–15]
0.78	3-3	ROU 037	6	7	Yes	[48–59]	[3–12]
0.83♯	3-4	EXT 298	1	3	n/a	[50–53]	[6–10]
1.18♯	3-3	EXT 279	1	2	n/a	[50]	4
1.6♯	3-3	EXT 054	1	3	n/a	[41–55]	[10–13]
1.8	3-4	LIL 009	3	9	n/a	[46–57]	[3–9]
4	3-3	SAI 019	1	4	n/a	[43–62]	[4–13]
6♯	3-3	EXT 145	1	2	n/a	[48–52]	[0–6]
6.4	3-3	ALZ 229	1	5	n/a	[51–65]	[1–11]
9.7♯	2-3	EXT 144	2	4	Yes	[42–64]	n/a
14.2♯	3-3	EXT 187	1	3	n/a	[45–60]	[5–10]
14.7♯	3-3	ALZ 254	1	2	n/a	[52–55]	[6–10]
Total & [range]		**13**	**32**	**61**	**4**	**[41–65]**	**[0–15]**

ID Fam: family code; PS: patients sampled; coseg: cosegregation with the disease; AOO: Age of onset; AS: affected subjects in the same family; DD: disease duration; ♯(bold): mutation previously unreported; n/a: not applicable.

Supplementary Table 6
CSF biomarker levels in patients carrying mutations

Gene	Mutation or duplication size	ID fam	$A\beta_{42}$ pg/mL	Tau pg/mL	Phospho-Tau (pg/mL)	IATI	Phospho-Tau/ $A\beta_{42}$	CSF profile
			N > 500	*N < 350*	*N < 60*	*N > 0,8*	*N < 0,211*	
PSEN1	p.Ala79Val	EXT 262	602	1200	211	n/a	0,351	Fitted AD
	p.Leu113Pro	SAL 513	207	609	81	0,47	0,391	Fitted AD
	p.Thr116Ile	EXT 234	294	1174	127	0,18	0,433	Fitted AD
	p.Glu120Asp	ALZ 057	525	990	140	0,37	0,267	Fitted AD
	p.Met139Thr	ALZ 248	314	717	102	0,29	0,325	Fitted AD
	p.Met146Leu	ALZ 279	176	534	88	0,2	0,500	Fitted AD
	p.Leu150Pro	EXT 358	478	379	67	0,696	0,140	Fitted AD
	p.Leu153Val	ALZ 148	345	1025	177	0,24	0,513	Fitted AD
	p.His163Arg	ALZ 430	415	778	96	0,4	0,231	Fitted AD
	p.His163Arg	EXT 226	256	334	62	0,4	0,242	Fitted AD
	p.Trp165Cys	ALZ 061	350	996	131	0,25	0,375	Fitted AD
	p.Gln223Arg	EXT 141	187	708	105	0,17	0,562	Fitted AD
	p.Ser230Ile	EXT 359	275	589	123	0,294	0,447	Fitted AD
	p.Ala260Val	ALZ 512	364	546	98	0,41	0,283	Fitted AD
	p.Pro264Leu	EXT 369	242	1863	289	n/a	1,194	Fitted AD
	p.Leu286Val	EXT 048	346	650	131	0,34	0,379	Fitted AD
	p.Thr291Pro	EXT 245	854	474	94	1,07	0,110	Atypical
	p.Leu392Val	ROU 013	331	353	68	0,52	0,205	Fitted AD
	p.Leu392Val	ROU 013	347	433	73	0,46	0,210	Fitted AD
	p.Cys410Tyr	ROU 005	403	838	150	0,33	0,372	Fitted AD
	p.Cys410Tyr	ROU 005	244	333	71	0,39	0,291	Fitted AD
	p.Leu418Phe	ROU 1306	248	1768	236	n/a	0,952	Fitted AD
PSEN2	p.Arg62His	EXT 039	293	797	128	0,25	0,437	Fitted AD
	p.Arg71Trp	EXT 075	489	778	165	0,42	0,338	Fitted AD
	p.Arg71Trp	EXT 227	558	638	109	0,56	0,195	Atypical
	p.Arg71Trp	EXT 179	494	549	91	0,56	0,184	Fitted AD
	p.Met239Val	ALZ 434	259	176	62	0,58	0,239	Fitted AD
	p.Met239Val	ROU 360	222	214	49	0,45	0,221	Fitted AD
	p.Met239Val	ALZ 062	499	638	109	0,56	0,195	Fitted AD
AβPP	p.Val717Ile	ALZ 076	420	366	62	0,62	0,148	Fitted AD
	p.Val717Ile	ALZ 431	480	322	56	0,77	0,117	Atypical
	p.Val717Ile	ALZ 431	333	395	66	0,47	0,198	Fitted AD
	p.Val717Ile	EXT 286	723	651	60	0,71	0,083	Atypical
	p.Leu723Pro	ALZ 523	308	599	116	0,33	0,376	Fitted AD

Supplementary Table 6
(*Continued*)

Gene	Mutation or duplication size	ID fam	$A\beta_{42}$ pg/mL	Tau pg/mL	Phospho-Tau (pg/mL)	IATI	Phospho-Tau/$A\beta_{42}$	CSF profile
AβPP duplication	0,78 Mb	ROU 037	148	1096	117	0,1	0,794	Fitted AD
	1,18 Mb	EXT 279	325	370	61	0,48	0,184	Fitted AD
	1,6 Mb	EXT 054	343	247	78	0,65	0,227	Fitted AD
	1,8 Mb	ALZ 478	342	303	69	0,57	0,202	Atypical
	6 Mb	EXT 145	194	340	52	0,3	0,268	Fitted AD
	6,4 Mb	ALZ 229	222	477	67	0,28	0,302	Fitted AD
	9,7 Mb	EXT 144	449	561	86	0,5	0,192	Fitted AD
	14,2 Mb	EXT 187	227	831	108	0,19	0,476	Fitted AD
		Mean (±SD)	360,3 (±148,2)	658,1 (±371,1)	105,5 (±51,0)	0,42	0,337	
		First quartile	250	372	67	0,29	0,199	
		Last quartile	442	792	126	0,56	0,388	

ID Fam: family code; IATI: Innogenetics Amyloid Tau Index; n/a: not applicable; mean (±SD): mean value of CSF biomarkers and standard deviation; atypical: CSF samples without all AD criteria completely fulfilled; n/a: not applicable.

Supplementary Table 7
Whole series of 33 French ADEOAD families without known mutation

ID Fam	*APOE (index case)*	PS (*n*)	AS (*n*)	AOO range (years)	DD (years)	$A\beta_{42}$ (pg/mL)	Tau (pg/mL)	Phospho-Tau (pg/mL)	IATI	Phospho-Tau/$A\beta_{42}$	CSF profile
						N > 500	*N < 350*	*N < 60*	*N > 0,8*	*N < 0,211*	
EXT 094	3-4	1	4	[56–63]	[4–8]	287	466	90	0,36	0,314	Fitted AD
ALZ 198	3-4	1	2	[46–54]	3	205	324	49	0,33	0,239	Fitted AD
EXT 077	4-4	1	3	[46–55]	[5–22]	215	1050	109	0,15	0,507	Fitted AD
EXT 049	3-3	1	4	[60–65]	[7–13]	492	797	128	0,25	0,260	Fitted AD
ALZ 426	3-3	1	3	[55–60]	[15–23]	375	1140	175	0,24	0,467	Fitted AD
EXT 220	3-4	1	3	[62–65]	[9–15]	367	382	79	0,53	0,215	Fitted AD
EXT 050	3-4	1	3	[56–64]	[12–15]	372	768	111	0,32	0,298	Fitted AD
ROU 816	3-4	2	4	[60–66]	[4–10]	205	497	64	0,25	0,312	Fitted AD
ALZ 197	3-3	2	4	[48–65]	[10–15]	155	582	102	0,16	0,658	Fitted AD
EXT 017	3-4	1	2	[60–65]	8	305	1465	140	n/a	0,459	Fitted AD
EXT 247	3-4	1	3	[48–59]	5	250	645	71	0,24	0,284	Fitted AD
EXT 241	3-4	1	3	[53–58]	3	321	395	74	0,46	0,230	Fitted AD
EXT 272	3-4	1	3	[60–65]	[10–16]	362	536	85	0,41	0,235	Fitted AD
ROU 1280	3-4	1	2	[63–65]	[6-7]	332	736	102	0,30	0,307	Fitted AD
EXT 181	3-4	1	3	[60–64]	[10–20]	206	210	35	0,42	0,170	Atypical
EXT 231	3-3	1	2	[54–58]	13	274	263	41	0,50	0,150	Atypical
ROU 782	3-3	1	2	[56–58]	14	n/d	n/d	n/d	n/d	n/d	n/d
ROU 114	3-4	1	4	[57-58]	[11]	n/d	n/d	n/d	n/d	n/d	n/d
ROU 632	3-4	1	2	[61–63]	2	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 049	3-3	3	9	[60–72]	[6–20]	n/d	n/d	n/d	n/d	n/d	n/d
EXT 055	3-3	2	5	[53–58]	[5–20]	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 056	3-3	2	7	[59–74]	[8–11]	n/d	n/d	n/d	n/d	n/d	n/d
BOL 036	3-4	1	3	[52–61]	[7–12]	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 061	3-3	1	3	[44–59]	[1–15]	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 186	3-4	1	2	[53–55]	[9–15]	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 204	3-3	1	4	[46–55]	[8]	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 244	2-3	2	2	[46–65]	9	n/d	n/d	n/d	n/d	n/d	n/d
ALZ 497	3-3	1	2	[56–60]	13	n/d	n/d	n/d	n/d	n/d	n/d
ROU 728	3-3	1	2	[49–50]	8	n/d	n/d	n/d	n/d	n/d	n/d
ROU 603	3-3	1	2	[60–65]	14	n/d	n/d	n/d	n/d	n/d	n/d
SAI 015	3-4	1	3	[60–65]	[6–14]	n/d	n/d	n/d	n/d	n/d	n/d
ROU 099	3-4	1	3	[57–65]	[3–8]	n/d	n/d	n/d	n/d	n/d	n/d
STR 006	2–4	1	3	[59–65]	[9]	n/d	n/d	n/d	n/d	n/d	n/d
Total & [range]		**40**	**106**	**[44–74]**	**[1–23]**						

ID Fam: family code; PS: patients sampled; AOO: Age of onset; AS: affected subject in the same family; DD: disease duration; IATI: Innogenetics Amyloid Tau Index; atypical: CSF samples without all AD criteria completely fulfilled; n/a: not applicable; n/d: not done.

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