eTable 1. Descriptive Statistics for *ABCA7* pLOF mutation-carriers

Mutation Group			Carrier			Non-Carrier		
			All	AD	Controls	All	AD	Controls
p.E1679X	*N*		1	1	-	113	76	37
	Age, Mean ± SD		80	80	-	78.68 ± 8.26	77.32 ± 8.39	81.49 ± 7.32
	Female, *N*(%)		-	-	-	62 (54.9%)	40 (52.6%)	22 (59.5%)
	APOE, *N*(%)	ε2ε2	-	-	-	2 (1.8%)	-	2 (5.4%)
		ε2ε3	-	-	-	13 (11.5%)	7 (9.2%)	6 (16.2%)
		ε2ε4	-	-	-	4 (3.5%)	3 (3.9%)	1 (2.7%)
		ε3ε3	-	-	-	51 (45.1%)	31 (40.8%)	20 (54.1%)
		ε3ε4	-	-	-	38 (33.6%)	30 (39.5%)	8 (21.6%)
		ε4ε4	1 (100%)	1 (100%)	-	5 (4.4%)	5 (6.6%)	-
p.L1403fs	*N*		21	14	7	93	63	30
	Age, Mean ± SD		77.95 ± 10.33	73.43 ± 6.80	87.00 ± 10.60	79.02 ± 7.93	78.22 ± 8.44	80.7 ± 6.53
	Female, *N*(%)		11 (52.4%)	8 (57.1%)	3 (42.9%)	52 (55.9%)	32 (50.8%)	20 (66.7%)
	APOE, *N*(%)	ε2ε2	-	-	-	2 (2.2%)	-	2 (6.7%)
		ε2ε3	1 (4.8%)	-	1 (14.3%)	12 (12.9%)	7 (11.1%)	5 (16.7%)
		ε2ε4	1 (4.8%)	1 (7.1%)	-	3 (3.2%)	2 (3.2%)	1 (3.3%)
		ε3ε3	6 (28.6%)	1 (7.1%)	5 (71.4%)	45 (48.4%)	30 (47.6%)	15 (50%)
		ε3ε4	12 (57.1%)	11 (78.6%)	1 (14.3%)	26 (28.0%)	19 (30.2%)	7 (23.3%)
		ε4ε4	1 (4.8%)	1 (7.1%)	-	5 (5.4%)	5 (7.9%)	-
c.4416+2T>G	*N*		4	3	1	111	74	37
	Age, Mean ± SD		75.5 ± 9.33	71.67 ± 6.51	87	78.96 ± 8.33	77.58 ± 8.36	81.73 ± 7.65
	Female, *N*(%)		2 (50%)	2 (66.7%)	-	61 (55.0%)	38 (51.4%)	23 (62.2%)
	APOE, *N*(%)	ε2ε2	-	-	-	2 (1.8%)	-	2 (5.4%)
		ε2ε3	-	-	-	13 (11.7%)	7 (9.5%)	6 (16.2%)
		ε2ε4	-	-	-	4 (3.6%)	3 (4.1%)	1 (2.7%)
		ε3ε3	4 (100%)	3 (100%)	1 (100%)	48 (43.2%)	28 (37.8%)	20 (54.1%)
		ε3ε4	-	-	-	38 (34.2%)	30 (40.5%)	8 (21.6%)
		ε4ε4	-	-	-	6 (5.4%)	6 (8.1%)	-
c.5570+5G>C	*N*		60	40	20	56	38	18
	Age, Mean ± SD		78.2 ± 7.88	77.4 ± 8.33	79.8 ± 6.80	79.43 ± 8.81	77.18 ± 8.37	84.17 ± 7.96
	Female, *N*(%)		31 (51.7%)	18 (45%)	13 (65%)	33 (58.9%)	23 (60.5%)	10 (55.6%)
	APOE, *N*(%)	ε2ε2	2 (3.3%)	-	2 (10%)	-	-	-
		ε2ε3	7 (11.7%)	4 (10%)	3 (15%)	6 (10.7%)	3 (7.9%)	3 (16.7%)
		ε2ε4	1 (1.7%)	1 (2.5%)	-	3 (5.4%)	2 (5.3%)	1 (5.6%)
		ε3ε3	29 (48.3%)	19 (47.5%)	10 (50%)	23 (41.1%)	12 (31.6%)	11 (61.1%)
		ε3ε4	18 (30%)	13 (32.5%)	5 (25%)	21 (37.5%)	18 (47.4%)	3 (16.7%)
		ε4ε4	3 (5%)	3 (7.5%)	-	3 (5.4%)	3 (7.9%)	-

Mutation Group			Carrier			Non-Carrier		
			All	AD	Controls	All	AD	Controls
p.Trp1214X	*N*		3	2	1	113	76	37
	Age, Mean ± SD		77.33 ± 11.72	73 ± 12.73	86	78.83 ± 8.29	77.41 ± 8.25	81.76 ± 7.67
	Female, *N*(%)		2 (66.7%)	1 (50%)	1 (50%)	62 (54.9%)	40 (52.6%)	22 (59.5%)
	APOE, *N*(%)	ε2ε2	-	-	-	2 (1.8%)	-	2 (5.4%)
		ε2ε3	-	-	-	13 (11.5%)	7 (9.2%)	6 (16.2%)
		ε2ε4	-	-	-	4 (3.5%)	3 (3.9%)	1 (2.7%)
		ε3ε3	2 (66.7%)	2 (100%)	-	50 (44.2%)	29 (38.2%)	21 (56.8%)
		ε3ε4	1 (33.3%)	-	1 (100%)	38 (33.6%)	31 (40.8%)	7 (18.9%)
		ε4ε4	-	-	-	6 (5.3%)	6 (7.9%)	-
p.E709fs	*N*		27	18	9	83	54	29
	Age, Mean ± SD		81.37 ± 7.27	81.33 ± 8.06	81.44 ± 5.79	78.39 ± 8.49	76.44 ± 8.08	82 ± 8.16
	Female, *N*(%)		18 (66.7%)	12 (66.7%)	6 (66.7%)	43 (51.8%)	26 (48.1%)	17 (58.6%)
	APOE, *N*(%)	ε2ε2	-	-	-	2 (2.4%)	-	2 (6.9%)
		ε2ε3	5 (18.5%)	3 (16.7%)	2 (22.2%)	7 (8.4%)	3 (5.6%)	4 (13.8%)
		ε2ε4	2 (7.4%)	1 (5.6%)	1 (11.1%)	2 (2.4%)	2 (3.7%)	-
		ε3ε3	11 (40.7%)	6 (33.3%)	5 (55.6%)	40 (48.2%)	24 (44.4%)	16 (55.2%)
		ε3ε4	8 (29.6%)	7 (38.9%)	1 (11.1%)	27 (32.5%)	20 (37.0%)	7 (24.1%)
		ε4ε4	1 (3.7%)	1 (5.6%)	-	5 (6.0%)	5 (9.3%)	-
Collapsed	*N*		116	78	38	-	-	-
	Age, Mean ± SD		78.79 ± 8.33	77.29 ± 8.30	81.87 ± 7.60	-	-	-
	Female, *N*(%)		64 (55.2%)	41 (52.6%)	23 (60.5%)	-	-	-
	APOE, *N*(%)	ε2ε2	2 (1.7%)	-	2 (5.3%)	-	-	-
		ε2ε3	13 (11.2%)	7 (9.0%)	6 (15.8%)	-	-	-
		ε2ε4	4 (3.4%)	3 (3.8%)	1 (2.6%)	-	-	-
		ε3ε3	52 (44.8%)	31 (39.7%)	21 (66.3%)	-	-	-
		ε3ε4	39 (33.6%)	31 (39.7%)	8 (21.1%)	-	-	-
		ε4ε4	6 (5.2%)	6 (7.7%)	-	-	-	-

Abbreviations: *N* = number of participants; SD = standard deviation.

eTable 1. Demographics for the post-quality control participants included in the genetic association analyses who are carriers of at least one *ABCA7* pLOF mutation. Data is split by carrier and non-carrier for each individual mutation group and all groups collapsed.

eTable 2. Genetic associations with each *ABCA7* pLOF mutation and AD risk.

Mutation Group	AD			Control			OR	*p*
	Series	Carrier	Non-carrier	Series	Carrier	Non-carrier		
p.E1679X	All	1	2442				1.15	> 0.99
	Clinical	0*	1280	All	0*	2813	2.20	5.28E-01
	AUT	1	1162				2.42	4.99E-01
	JS	0*	734	JS	0*	858	1.17	> 0.99
	RS	0*	546	RS	0*	1955	3.58	3.89E-01
p.L1403fs	All	14	2473				2.30	7.96E-02
	Clinical	8	1302	All	7	2839	2.49	9.20E-02
	AUT	6	1171				2.08	2.21E-01
	JS	4	754	JS	1	863	4.58	1.92E-01
	RS	4	548	RS	6	1976	2.40	2.39E-01
c.4416+2T>G	All	3	2480				3.44	3.44E-01
	Clinical	2	1309	All	1	2844	4.35	2.36E-01
	AUT	1	1171				2.43	4.98E-01
	JS	2	757	JS	1	863	2.28	6.02E-01
	RS	0*	552	RS	0*	1981	3.59	3.89E-01
c.5570+5G>C	All	40	2423				2.31	**2.47E-03**
	Clinical	25	1268	All	20	2803	2.76	**9.66E-04**
	AUT	15	1155				1.82	9.22E-02
	JS	13	733	JS	5	843	2.99	**3.35E-02**
	RS	12	535	RS	15	1960	2.93	**7.93E-03**
p.Trp1214X	All	2	2452				2.30	6.00E-01
	Clinical	1	1285	All	1	2825	2.20	5.28E-01
	AUT	1	1167				2.42	4.99E-01
	JS	1	740	JS	0*	851	1.15	> 0.99
	RS	0*	545	RS	1	1974	3.62	3.86E-01
p.E709fs	All	18	2285				2.30	5.12E-02
	Clinical	6	1127	All	9	2632	1.56	4.05E-01
	AUT	12	1158				3.03	**1.50E-02**
	JS	3	585	JS	3	733	1.25	> 0.99
	RS	3	542	RS	6	1899	1.75	4.26E-01

Abbreviations: AD = Alzheimer's disease; Control = cognitively unimpaired controls; AUT = autopsy confirmed participants; JS = clinical participants from Mayo Clinic Jacksonville, FL; RS = clinical participants from Mayo Clinic Rochester, MN; OR = odds ratio; *p* = p-value.

eTable 2. Mutation frequencies and 2 sided Fisher's Exact analyses by odds showing AD association for each individual mutation group are displayed. *1 carrier count added for OR & Fisher's Exact analyses

eTable 3. Descriptive Statistics for subset of individuals with first degree relative information

Mutation Group		ALL	Cognitively Impaired	Cognitively Unimpaired
All	**Total *N***	63	52	11
	First Degree Relative, *n* (%)	24 (38.1%)	22 (42.3%)	2 (18.2%)
	Age of Onset, Mean ± SD (*n*)	78.98 ± 8.25 (20)	79.22 ± 8.21 (18)	76.75 ± 11.67 (2)
p.Trp1214X	**Total *N***	4	3	1
	First Degree Relative, *n* (%)	1 (25%)	1 (33.3%)	-
	Age of Onset, Mean ± SD (*n*)	70 (1)	70 (1)	-
p.E1679X	**Total *N***	1	1	-
	First Degree Relative, *n* (%)	1 (100%)	1 (100%)	-
	Age of Onset, Mean ± SD (*n*)	-	-	-
c.4416+2T>G	**Total *N***	3	3	-
	First Degree Relative, *n* (%)	2 (66.7%)	2 (66.7%)	-
	Age of Onset, Mean ± SD (*n*)	85 ± 0 (2)	85 ± 0 (2)	-
c.5570+5G>C	**Total *N***	34	27	7
	First Degree Relative, *n* (%)	10 (29.4%)	9 (33.3%)	1 (14.3%)
	Age of Onset, Mean ± SD (*n*)	81.83 ± 5.47 (9)	81.44 ± 5.72 (8)	85 (1)
p.E709fs	**Total *N***	11	9	2
	First Degree Relative, *n* (%)	4 (36.4%)	4 (44.4%)	-
	Age of Onset, Mean ± SD (*n*)	71.5 ± 14.91 (3)	71.5 ± 14.91 (3)	-
p.L1403fs	**Total *N***	10	9	1
	First Degree Relative, *n* (%)	6 (60%)	5 (55.6%)	1
	Age of Onset, Mean ± SD (*n*)	77.7 ± 7.17 (5)	80 ± 5.77 (4)	68.5 (1)

eTable 3. Descriptive statistics for the subset of 63 individuals with first degree relative information from the 100 carriers of *ABCA7* pLOF mutations who are included in the clinical chart review. Data is split by cognitively impaired and unimpaired participants, as well as by mutation type. Total *N* refers to the total number of individuals within each subgroup (ALL, Cognitively impaired/unimpaired) who had first degree relative information. *n* refers to the number of individuals with valid data for the tested variable (note: *n* may not add up to *N* due to missing first degree relative data). When an individual has more than one first degree relative, the mean onset age of relatives was used to calculate descriptive Mean Onset Age ± SD (*n*).

eTable 4. Mutation-specific clinical phenotypes for *ABCA7* pLOF mutation-carriers

Mutation Group			All	Cognitively Impaired	Cognitively Unimpaired
p.Trp1214X	***N* (%)**		4	3 (75%)	1 (25%)
	Female, *n* (%)		2 (50%)	1 (33.3%)	1 (100%)
	Age, Mean ± SD (Range)	**First Visit**	75.75 ± 11.18 (59 - 82)	74 ± 13 (59 - 82)	81
		Last Visit	79.5 ± 11.70 (62 - 86)	77.33 ± 13.32 (62 - 86)	86
	Duration of Follow Up, Mean ± SD (Range) [b]		4.00 ± 1.41 (2 - 5)	3.67 ± 1.53 (2 - 5)	5
	***APOE* ε4 Positive, *n* (%)**		1 (25%)	-	1 (100%)
	Depression, *n/N* (%) [c]		3/4 (75%)	2/3 (66.7%)	1/1 (100%)
	First Degree Relative, *n/N* (%) [d]		1/4 (25%)	1/3 (33.3%)	-
p.E1679X	***N* (%)**		1	1 (100%)	-
	Female, *n* (%)		-	-	-
	Age, Mean ± SD (Range)	**First Visit**	76	76	-
		Last Visit	78	78	-
	Duration of Follow Up, Mean ± SD (Range) [b]		2	2	-
	***APOE* ε4 Positive, *n* (%)**		1 (100%)	1 (100%)	-
	Depression, *n/N* (%) [c]		1/1 (100%)	1/1 (100%)	-
	First Degree Relative, *n/N* (%) [d]		1/1 (100%)	1/1 (100%)	-
c.4416+2T>G	***N* (%)**		4	3 (75%)	1 (25%)
	Female, *n* (%)		2 (50%)	2 (66.7%)	-
	Age, Mean ± SD (Range)	**First Visit**	78.75 ± 6.18 (72 - 87)	76 ± 3.46 (72 - 78)	87
		Last Visit	81.75 ± 6.18 (75 - 87)	80 ± 6.24 (75 - 87)	87
	Duration of Follow Up, Mean ± SD (Range) [b]		1.00 ± 1.41 (0 - 3)	1.33 ± 1.53 (0 - 3)	0
	***APOE* ε4 Positive, *n* (%)**		-	-	-
	Depression, *n/N* (%) [c]		2/4 (50%)	2/3 (66.7%)	-
	First Degree Relative, *n/N* (%) [d]		2/3 (66.7%)	2/3 (66.7%)	-
c.5570+5G>C	***N* (%)**		48	33 (68.8%)	15 (31.3%)
	Female, *n* (%)		29 (60.4%)	20 (60.6%)	9 (60%)
	Age, Mean ± SD (Range)	**First Visit**	76.81 ± 7.71 (57 - 92)	76.48 ± 8.52 (57 - 92)	77.53 ± 5.74 (62 - 86)
		Last Visit	81.04 ± 8.19 (62 - 94)	81.36 ± 8.87 (62 - 94)	80.33 ± 6.66 (62 - 93)
	Duration of Follow Up, Mean ± SD (Range) [b]		4.84 ± 4.37 (0 - 17)	5.19 ± 4.71 (0 - 17)	3.92 ± 3.34 (0 - 9)
	***APOE* ε4 Positive, *n* (%)**		16 (33.3%)	13 (39.4%)	3 (20%)
	Depression, *n/N* (%) [c]		16/45 (35.6%)	12/32 (37.5%)	4/13 (30.8%)
	First Degree Relative, *n/N* (%) [d]		10/34 (29.4%)	9/27 (33.3%)	1/7 (14.3%)

Mutation Group			All	Cognitively Impaired	Cognitively Unimpaired
p.E709fs	***N* (%)**		24	15 (62.5%)	9 (37.5%)
	Female, *n* (%)		18 (75%)	12 (80%)	6 (66.7%)
	Age, Mean ± SD (Range)	**First Visit**	76.63 ± 7.28 (59 - 86)	75.87 ± 7.91 (59 - 84)	77.89 ± 6.33 (67 - 86)
		Last Visit	81.57 ± 7.59 (67 - 96)[a]	82.29 ± 7.9 (67 - 96)[a]	80.44 ± 7.4 (67 - 90)
	Duration of Follow Up, Mean ± SD (Range) [b]		6.67 ± 6.53 (0 - 23)	8.17 ± 7.35 (0 - 23)	3.67 ± 3.14 (0 - 7)
	***APOE* ε4 Positive, *n* (%)**		6 (25%)	4 (26.7%)	2 (22.2%)
	Depression, *n/N* (%)[c]		8/20 (40%)	6/13 (46.2%)	2/7 (28.6%)
	First Degree Relative, *n/N* (%)[d]		4/11 (36.4%)	4/9 (44.4%)	-
p.L1403fs	***N* (%)**		19	12 (63.2%)	7 (36.8%)
	Female, *n* (%)		11 (57.9%)	8 (66.7%)	3 (42.9%)
	Age, Mean ± SD (Range)	**First Visit**	76.74 ± 9.65 (56 - 95)	73.25 ± 8.55 (56 - 90)	82.71 ± 8.92 (70 - 95)
		Last Visit	80.74 ± 11.58 (56 - 98)	77.08 ± 10.9 (56 - 96)	87 ± 10.6 (74 - 98)
	Duration of Follow Up, Mean ± SD (Range) [b]		4.41 ± 4.21 (0 - 15)	4.09 ± 5.03 (0 - 15)	5 ± 2.37 (3 - 8)
	***APOE* ε4 Positive, *n* (%)**		9 (47.4%)	8 (66.7%)	1 (14.3%)
	Depression, *n/N* (%)[c]		7/15 (46.7%)	6/11 (54.5%)	1/4 (25%)
	First Degree Relative, *n/N* (%)[d]		6/10 (60%)	5/9 (55.6%)	1/1 (100%)

eTable 4. Demographics for the 100 carriers of *ABCA7* pLOF mutations who are included in the clinical chart review. Data is split by cognitively impaired and unimpaired participants for each mutation type. [a.] Excludes one individual with missing data. [b.] Includes individuals with known follow up durations. [c.] *n* = number of individuals with history of depression, *N* = all individuals where depression history, whether present or absent, are available. [d.] *n* = number of individuals with a first degree relative who is cognitively impaired, *N* = all individuals where first degree relative history, whether present or absent, are available.