

Supporting Information for

Guam ALS-PDC is a distinct double prion disorder featuring both tau and A β prions

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This PDF file includes:

Figures S1 to S3
Tables S1 to S3

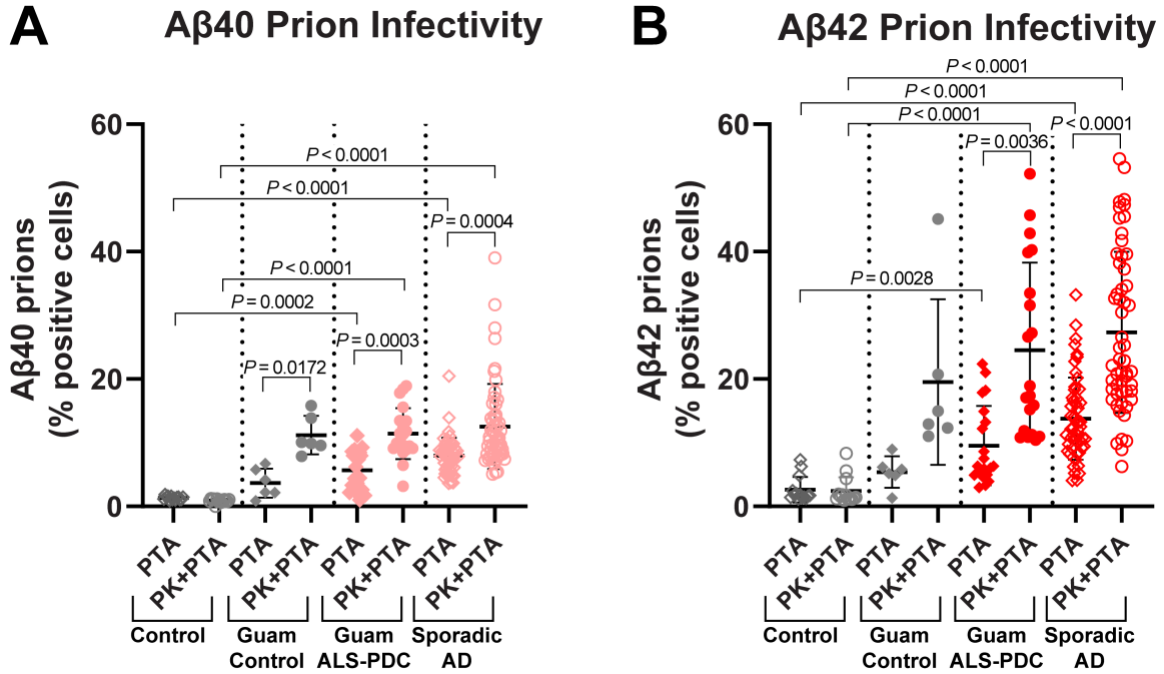


Fig. S1. Prion infectivity after limited digestion with proteinase K. Prion infectivity measurements using transfected HEK293T cells stably expressing the (A) YFP-Aβ40 (pink) and (B) YFP-Aβ42 (red) fusion proteins (see Methods). Brain-derived prions prepared by phosphotungstic acid (PTA) precipitation with (filled symbols) and without (open symbols) limited digestion by proteinase K (PK) were diluted [x0.015] prior to the lipofectamine-based transduction in recipient cell lines. Prion infectivity in the cells was quantified 2 and 3 d after the initial exposure to various prion preparations from sporadic AD (circles) or Guam ALS-PDC (triangles) donor brain extracts. Data shown are individual donor samples treated with and without PK as determined from four images per well in four wells per donor sample.

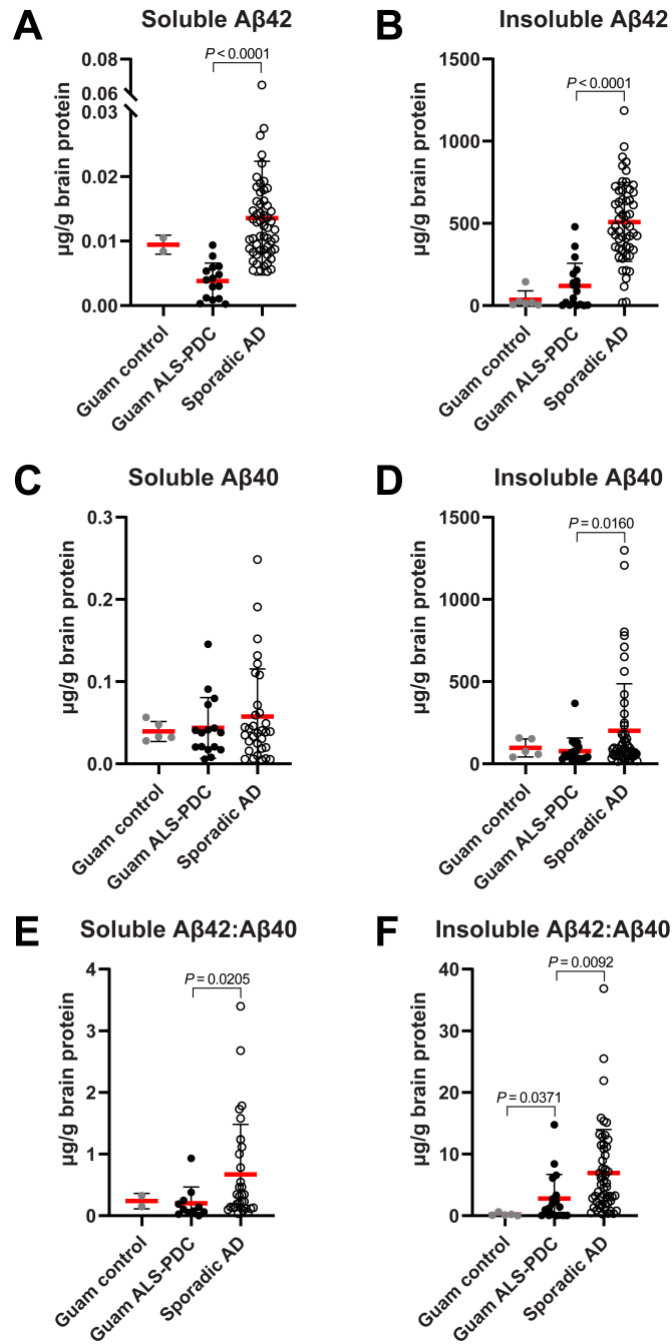


Fig. S2. Biochemical measurements of A β abundance in soluble and insoluble brain fractions. (A–F) ELISA was used to measure A β 42 and A β 40 proteins in soluble (PBS; clarified brain homogenate) and insoluble (formic acid solubilized) fractions prepared from frozen brain samples. (A and B) A β 42 in soluble and insoluble fractions. (C and D) A β 40 in soluble and insoluble fractions. (E and F) Ratio of A β 42 to A β 40 in soluble and insoluble fractions. The measurements were made in duplicate. Data shown are individual donors plotted with mean \pm SD.

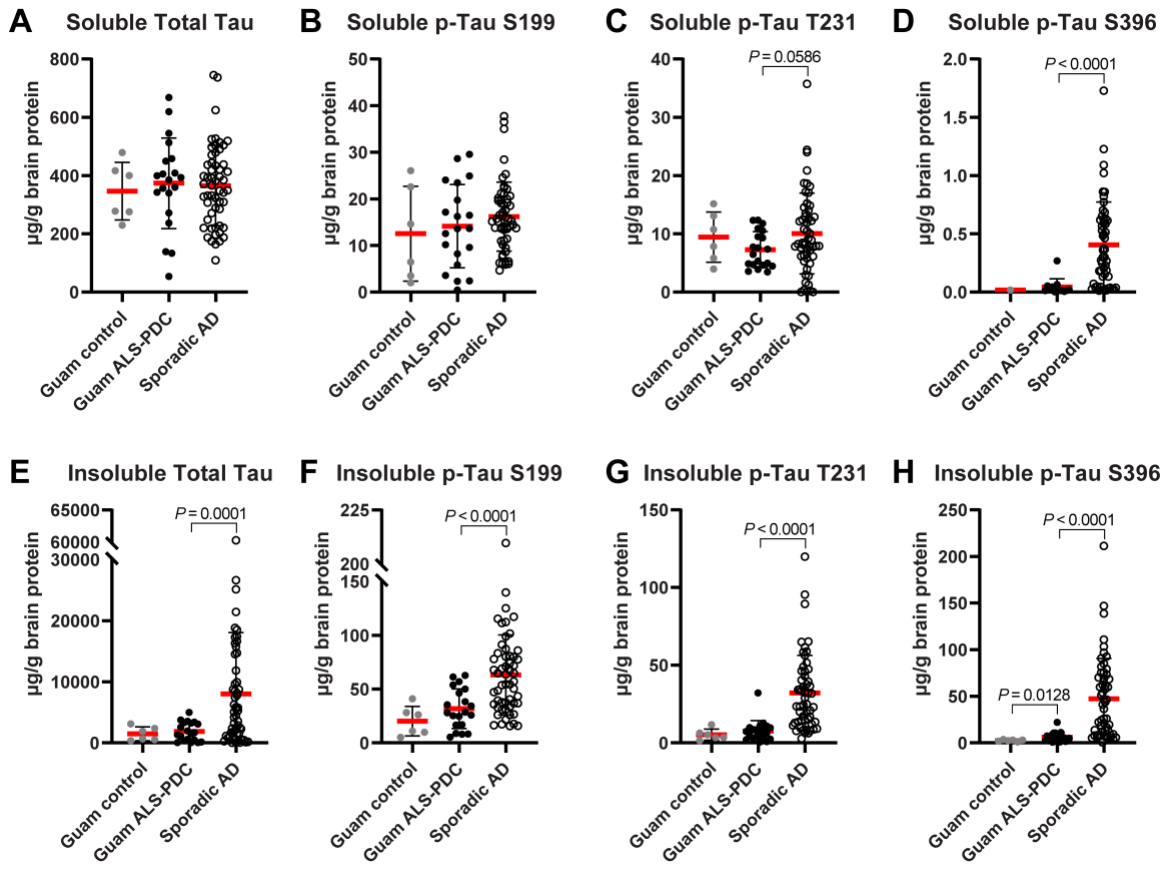


Fig. S3. Biochemical measurements of tau abundance in soluble and insoluble brain fractions. (A–H) ELISA was used to measure total tau, p-tau S199, p-tau T231, and p-tau S396 proteins in soluble (PBS; clarified brain homogenate) and insoluble (formic acid solubilized) fractions made from frozen brain samples. (A–D) Total tau, p-tau S199, p-tau T231, and p-tau S396 abundance in the soluble fraction. (E–H) Total tau, p-tau S199, p-tau T231, and p-tau S396 abundance in the insoluble fraction. The measurements were made in duplicate. Data shown are individual donors plotted with mean \pm SD.

Table S1. Source of postmortem human brain tissue samples from USUHS. Demographic and clinicopathological data for Guam ALS-PDC and control cases.

Cohort	Case P#	Sex	Age	Clinical Diagnosis/Cause of Death	Neuropathological Diagnosis	Comments
Guam ALS-PDC	98-005	F	79	PDC	PDC	Chamorro
Guam ALS-PDC	2000-10	F	65	PDC	PDC, recent cerebral + pons hemorrhage	Chamorro
Guam ALS-PDC	2002-04	M	73	PDC	PDC, Lewy body disease (lymbic)	Chamorro
Guam ALS-PDC	2003-04	F	89	PDC	-	Chamorro
Guam ALS-PDC	2004-003	M	83	PDC	-	Chamorro
Guam ALS-PDC	2004-004	M	81	PDC	-	Chamorro
Guam ALS-PDC	98-011	F	66	PDC	PDC	Chamorro
Guam ALS-PDC	2000-11	M	62	PDC	PDC	Chamorro
Guam ALS-PDC	2000-02	M	75	PDC + MID	PDC, MID, CVD	Chamorro
Guam ALS-PDC	2000-06	M	84	PDC	PDC, with added features of DCLB; widespread Lewy bodies	Chamorro
Guam ALS-PDC	98-18	M	72	PDC	Frontotemporal dementia + Parkinsonism	Filipino
Guam ALS-PDC	2000-13	M	67	PDC	PD, Lewy bodies in brain stem nuclei	Filipino
Guam ALS-PDC	99-001	F	73	PDC	PDC	Chamorro
Guam ALS-PDC	98-12	F	93	CVA, dementia - MID	MID, cerebral infarcts	Chamorro

Guam ALS-PDC	99-006	F	76	PDC	PDC (severe), possibly superimposed AD	Chamorro
Guam ALS-PDC	98-001	F	69	PDC	PDC	Chamorro
Guam ALS-PDC	2000-12	F	86	AD	AD	Chamorro
Guam ALS-PDC	98-006	F	86	AD	AD	Chamorro
Guam ALS-PDC	99-10	M	81	PDC	-	Chamorro
Guam ALS-PDC	99-007	F	74	PDC	PDC; CVD	Chamorro
Guam Control	2000-08	F	80	Control	SN degeneration without NFTs, rare NFT in brain	Chamorro
Guam Control	2002-08	M	78	Ca of colon, no neurologic dx	No significant pathology	Chamorro
Guam Control	2001-08	M	57	SP renal transplant; sepsis	No significant pathology	Filipino
Guam Control	2000-24	M	45	Ischemic heart dis. Control	-	Chamorro
Guam Control	97-006	M	71	Ca lung, control	No significant pathology	Chamorro
Guam Control	2003-08	F	80	COPD, ruptured aorta	No significant pathology	Chamorro
Control	Control 1	M	52	Hypertension, acute MI	No significant pathology	-
Control	Control 2	M	41	Cardiac arrest	No significant pathology	-
Control	Control 3	M	51	Cardiac arrest	No significant pathology	-
Control	Control 4	M	58	Acute MI	No significant pathology	-
Control	Control 5	M	35	Drowning	No significant pathology	-
Control	Control 6	M	27	Suicide (self-inflicted GSW)	No significant pathology	-
Control	Control 7	M	62	Cardiac arrest	No significant pathology	-

Control	Control 8	M	37	Drug overdose, accidental	No significant pathology	-
Control	Control 9	M	67	Suicide (hanging)	No significant pathology	-
Control	Control 10	M	42	Hypertension, cardiac arrest	No significant pathology	-
Control	Control 11	M	44	Motor vehicle accident	No significant pathology	-
Control	Control 12	M	70	Coronary atherosclerosis, MI	No significant pathology	-
Control	Control 13	M	66	Atherosclerosis, chronic alcoholism, renal failure	No significant pathology	-
Control	Control 14	M	35	Chronic alcohol abuse, suicide (hanging)	No significant pathology	-

Abbreviations: AD, Alzheimer's disease; ALS-PDC, amyotrophic lateral sclerosis-parkinsonism dementia complex; Ca, cancer; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; CVD, cerebrovascular disease; DCLB, diffuse large B-cell; DLBD, diffuse Lewy body disease; dis., disease; dx, diagnosis; GSW, gunshot wound; MI, myocardial infarction; MID, multi-infarct dementia; NFT, neurofibrillary tangles; PD, Parkinson's disease; SN, supranuclear; SP, senile plaque.

Table S2. Source of postmortem human brain tissue samples from UCSF. Demographic and clinicopathological data for sporadic AD cases.

Cohort	Case P#	Sex	Age	Clinical	Primary Neuropath Dx.	Comorbid	Thal Phase	Braak Stage	CERAD-NP Score	CERAD Diffuse Plaque Score	NIA-Reagan Criteria	ADNC Score	APOE Status
Sporadic AD	P2086	F	76	AD	AD	-	-	6	-	-	-	-	E3/E3
Sporadic AD	P2273	M	63	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2309.10	M	84	DLB	AD, LBD	-	-	5	Frequent	Frequent	High likelihood	Intermediate-High	E3/E4
Sporadic AD	P2312.10	M	59	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2314.10	F	54	AD	AD	-	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E4
Sporadic AD	P2315.10	M	69	AD	AD	-	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E3
Sporadic AD	P2330.11	M	70	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2344.11	M	58	AD	AD	-	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E4
Sporadic AD	P2349.11	M	77	AD, Vascular	AD	VBI	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E2/E3
Sporadic AD	P2352.11	F	93	AD, Vascular	AD	LBD, VBI	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E4
Sporadic AD	P2354.11	M	72	AD	AD	-	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E3
Sporadic AD	P2362.11	F	81	AD, Vascular	AD	-	-	6	Frequent	Moderate	High likelihood	Intermediate-High	E3/E4

Sporadic AD	P2367.11	M	65	AD	AD, LBD	-	-	6	Frequent	Frequent	High likelihood	Intermediate-High	E3/E3
Sporadic AD	P2371.11	M	72	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2376.11	M	80	AD	AD	-	4	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2382.11	M	64	AD, DLB, Vascular	AD	LBD, transitional limbic	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2402.12	F	81	AD, DLB, Vascular	AD	-	5	6	Frequent	Not assessed	High likelihood	High	E3/E3
Sporadic AD	P2405.12	M	72	AD, Vascular	AD, LBD	-	5	6	Frequent	Not assessed	High likelihood	High	E4/E4
Sporadic AD	P2474	F	87	MCI	AD, Braak IV	VBI	2	4	Frequent	Not assessed	Not conforming	Intermediate	E3/E3
Sporadic AD	P2485	M	83	AD	AD, LBD	-	5	6	Frequent	Moderate	High likelihood	High	E3/E3
Sporadic AD	P2497	M	64	AD	AD, LBD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2501	M	78	MCI	AD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2508	M	82	AD	AD	-	5	6	Frequent	Moderate	High likelihood	High	E3/E3
Sporadic AD	P2534	F	75	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2535	M	87	AD, Vascular	AD	-	5	6	Frequent	Moderate	High likelihood	High	-
Sporadic AD	P2565	M	64	AD, Vascular	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4

Sporadic AD	P2568	M	79	AD, DLB	AD	VBI	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2575	F	81	AD	AD	LBD, HS, TDP-U	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2585	M	72	MCI frontal/exec.	AD	-	4	6	Frequent	Moderate	High likelihood	High	E3/E4
Sporadic AD	P2589	F	86	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2604	M	81	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2611	M	77	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2612	M	82	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2631	M	64	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2638	M	63	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2645	M	83	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2684	F	66	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2698	M	81	MCI, mixed	AD	-	3	5	Frequent	Frequent	High likelihood	Intermediate	E3/E3
Sporadic AD	P2700	M	66	AD	AD, LBD	-	5	6	Frequent	Sparse	High likelihood	High	E4/E4
Sporadic AD	P2718	M	86	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4

Sporadic AD	P2746	M	69	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2752	M	62	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2753	F	94	AD	AD	-	5	4	Frequent	Frequent	Not conforming	Intermediate	E3/E3
Sporadic AD	P2794	F	83	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2799	F	61	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2803	M	82	AD, DLB	AD, LBD	VBI	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2804	F	64	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2813	M	87	AD, Vascular	AD	-	3	2	Moderate	Moderate	Not conforming	Low	E3/E3
Sporadic AD	P2817	M	62	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2818	F	80	AD, Vascular	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3
Sporadic AD	P2823	F	89	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E4/E4
Sporadic AD	P2824	M	89	MCI, mixed	AD	-	4	3	Moderate	Moderate	Intermediate likelihood	Intermediate	E3/E3
Sporadic AD	P2827	F	74	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2829	M	72	AD, PDD	AD, LBD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E3

Sporadic AD	P2837	F	97	Control	AD	-	4	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2838	F	62	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4
Sporadic AD	P2840	F	87	AD	AD	-	5	6	Frequent	Frequent	High likelihood	High	E3/E4

Abbreviations: AD, Alzheimer's disease; ADNC, Alzheimer's Disease Neuropathological Change; APOE, apolipoprotein E; CERAD-NP, Consortium to Establish a Registry for Alzheimer's Disease-Neuropsychological battery; DLB, dementia with Lewy bodies; Dx., diagnosis; exec., executive; HS, hippocampal sclerosis ; LBD, Lewy body disease; MCI, mild cognitive impairment; NIA, National Institute on Aging; PDD, Parkinson's disease with dementia; TDP-U, TAR DNA-binding protein-ubiquitin; VBI, vertebrobasilar insufficiency.

Table S3. Genome wide assessment of Guam ALS-PDC and control cases for neurodegenerative genetic risk variants. Summarized results of whole genome sequencing for Guam ALS-PDC and control cases.

Cohort	Case P#	Variants	Classification
Guam ALS-PDC	98-18	<i>CR1</i> , c.7310T>C (p. p.L2437P) <i>LRRK2</i> , c.632C>T (p.A211V) <i>ATP8B3</i> , c.732C>G (p.R244R) <i>EIF4G1</i> , c.27dupC <i>PDEBB</i> , c.2144C>T (p.T715M) <i>BTNL2</i> , c.83A>T (p.D28V) <i>KCNV2</i> , c.1344G>C (p.W448C)	VUS VUS VUS VUS VUS VUS VUS
Guam ALS-PDC	2002-04	<i>SPG11</i> , c.5449_5457del (p.E1817_E1819del) <i>TAF15</i> , c.511G>A (p.G171R) <i>APOE</i> , c.631G>A (p.A211T) <i>EPHA4</i> , c.1270C>G (p.P424A) <i>CHCHD10</i> , c.278C>T (p.P93L) <i>GAK</i> , c.3385G>A (p.A1129T)	VUS VUS VUS VUS VUS VUS
Guam ALS-PDC	2000-12	<i>SPG11</i> , c.2191G>A (p.D731N) <i>NEK1</i> , c.3157A>G (p.N1053D) <i>TMEM106B</i> , c.813G>C (p.Q271H) <i>TP53INP1</i> , c.706C>T (p.R236C)	VUS VUS VUS VUS
Guam ALS-PDC	98-011	<i>VPS13C</i> , c.8269G>A (p.V2757I) <i>COL12A1</i> , c.2473C>G (p.P825A)	VUS VUS
Guam ALS-PDC	2000-11	<i>ATP13A2</i> , c.745G>A (p.A249T) <i>PSEN2</i> , c.107A>G (p.Q36R) <i>PFN1</i> , c.369G>C (p.L123F) <i>GAK</i> , c.3385G>A (p.A1129T) <i>HSPA9</i> , c.1717C>T (p.R573W) <i>NME8</i> , c.967C>T (p.R323X)	VUS VUS VUS VUS VUS VUS

Guam ALS-PDC	99-007	<p><i>SLC24A4</i>, c.1049A>G (p.E350G) <i>SLC24A4</i>, c.1342C>T (p.R448C) <i>ABCA7</i>, c.3230A>G (p.Q1077R) <i>COL12A1</i>, c.2473C>G (p.P825A) <i>PON3</i>, c.608A>G (p.Y203C) <i>GLE1</i>, c.575A>G (p.E192G)</p>	<p>VUS VUS VUS VUS VUS VUS</p>
Guam ALS-PDC	2000-02	<i>UNC5C</i> , c.317T>C (p.I106T)	VUS
Guam ALS-PDC	99-10	<i>TH</i> , c.387G>T (p.E129D)	VUS
Guam ALS-PDC	98-006	<p><i>DAO</i>, c.680C>T (p.P227L) <i>PLCG2</i>, c.3109G>A (p.V1037I) <i>PFN1</i>, c.369G>C (p.L123F) <i>THSD7B</i>, c.376C>G (p.P126A) <i>COL12A1</i>, c.5615G>A (p.R1872H)</p>	<p>VUS VUS VUS VUS VUS</p>
Guam ALS-PDC	98-001	<p><i>HEXA</i>, c.1178G>A (p.R393Q) <i>CHMP2B</i>, c.56G>A (p.R19Q) <i>SCARB2</i>, c.1210A>G (p.M404V)</p>	<p>VUS VUS VUS</p>
Guam ALS-PDC	2000-13	<p><i>CTNNA3</i>, c.1303A>G (p.M435V) <i>RIN3</i>, c.1699G>A (p.V567M)</p>	<p>VUS VUS</p>
Guam ALS-PDC	2004-004	<p><i>ATXN2</i>, c.767T>C (p.V256A) <i>ANG</i>, c.261C>A (p.N87K) <i>SPG11</i>, c.5449_5457del (p.E1817_E1819del) <i>FUS</i>, c.1292C>T (p.P431L) <i>PFN1</i>, c.369G>C (p.L123F) <i>LCT</i>, c.4054G>A (p.A1352T) <i>THSD7B</i>, c.4171A>C (p.S1391R) <i>CHMP2B</i>, c.56G>A (p.R19Q)</p>	<p>VUS VUS VUS VUS VUS VUS VUS VUS</p>

		<i>TRRAP</i> , c.1513_1514insGC	VUS
Guam ALS-PDC	2003-04	<i>TBK1</i> , c.1343_1346del <i>CTNNA3</i> , c.1303A>G (p.M435V) <i>LRRK2</i> , c.632C>T (p.A211V) <i>RIN3</i> , c.691C>T (p.R231C) <i>UNC13A</i> , c.3886G>A (p.V1296I)	PATH VUS VUS VUS VUS
Guam ALS-PDC	98-005	<i>CTNNA3</i> , c.1303A>G (p.M435V) <i>LRRK1</i> , c.5251G>A (p.V1751I) <i>HEXA</i> , c.1178G>A (p.R393Q) <i>HSPA9</i> , c.1622G>A (p.R541H) <i>CSF1R</i> , c.2833_2835del (p.E945del) <i>COL12A1</i> , c.173C>T (p.T58M) <i>FLNC</i> , c.2845G>C (p.D949H)	VUS VUS VUS VUS VUS VUS VUS
Guam ALS-PDC	2000-10	<i>NEK1</i> , c.1666-2A>G <i>SORL1</i> , c.1786G>C (p.V596L) <i>SLC24A4</i> , c.1049A>G (p.E350G) <i>GIGYF2</i> , c.1381A>G (p.T461A) <i>COL19A1</i> , c.2188G>T (p.D730Y) <i>SND1</i> , c.2164C>G (p.P722A) <i>ALAD</i> , c.5C>T (p.P2L) <i>SETX</i> , c.64G>A (p.A22T)	LPATH VUS VUS VUS VUS VUS VUS VUS
Guam ALS-PDC	98-12	<i>DNAJC6</i> , c.2419C>A (p.P807T) <i>APOE</i> , c.631G>A (p.A211T) <i>GIGYF2</i> , c.3512A>G (p.H1171R) <i>SQSTM1</i> , c.1126G>A (p.G376R) <i>AK9</i> , c.2751+2insAAGAGG <i>COL12A1</i> , c.2473C>G (p.P825A) <i>FLNC</i> , c.1309C>T (p.R437C)	VUS VUS VUS VUS VUS VUS VUS

		<i>SETX</i> , c.64G>A (p.A22T)	VUS
Guam ALS-PDC	99-006	<i>PLCG2</i> , c.2173C>T (p.L725F) <i>STK36</i> , c.2616G>C (p.M872I) <i>GAK</i> , c.3385G>A (p.A1129T) <i>HSPA9</i> , c.1622G>A (p.R541H) <i>COL19A1</i> , c.2188G>T (p.D730Y) <i>NME8</i> , c.967C>T (p.R323X)	VUS VUS VUS VUS VUS VUS
Guam ALS-PDC	99-001	<i>TRPM2</i> , c.4174C>T (p.R1392W)	VUS
Guam ALS-PDC	2000-06	<i>SPG11</i> , c.5449_5457del (p.E1817_E1819del) <i>TAF15</i> , c.1422_1423ins25 (p.G485_Y486insGYGGDRGG) <i>ABCA7</i> , c.3418G>A (p.E1140K) <i>ABCA7</i> , c.3500C>T (p.T1167I)	VUS VUS VUS VUS
Guam ALS-PDC	2004-003	<i>SPG11</i> , c.23C>A (p.A8E) <i>VPS13C</i> , c.8269G>A (p.V2757I) <i>SNCAIP</i> , c.1021A>T (p.N341Y) <i>COL19A1</i> , c.2188G>T (p.D730Y) <i>COL12A1</i> , c.2473C>G (p.P825A)	VUS VUS VUS VUS VUS
Guam Control	2003-08	<i>PSEN2</i> , c.480C>A (p.Y160X) <i>MS4A4A</i> , c.467C>T (p.A156V) <i>EWSR1</i> , c.254C>T (p.A85V) <i>COL19A1</i> , c.971C>G (p.P324R) <i>COL12A1</i> , c.2473C>G (p.P825A) <i>TRRAP</i> , c.7256C>T (p.A2419V)	VUS VUS VUS VUS VUS VUS
Guam Control	2001-08	<i>TMEM230</i> , c.13G>A (p.A5T) <i>CHMP2B</i> , c.56G>A (p.R19Q)	VUS VUS
Guam Control	2000-08	<i>SLC24A4</i> , c.1049A>G (p.E350G)	VUS

		<p><i>SLC6A3</i>, c.1420C>T (p.L474F) <i>PON2</i>, c.598C>A (p.H200N) <i>SETX</i>, c.6353A>G (p.K2118R)</p>	<p>VUS VUS VUS</p>
Guam Control	2000-24	<p><i>SLC24A4</i>, c.1049A>G (p.E350G) <i>SLC24A4</i>, c.1342C>T (p.R448C) <i>THSD7B</i>, c.860A>G (p.H287R) <i>COL12A1</i>, c.4358A>G (p.N1453S) <i>COL12A1</i>, c.2473C>G (p.P825A)</p>	<p>VUS VUS VUS VUS VUS</p>
Guam Control	97-006	<p><i>ABCA7</i>, c.2237T>C (p.L746P) <i>CHMP2B</i>, c.56G>A (p.R19Q) <i>SCARB2</i>, c.1210A>G (p.M404V) <i>HSPA9</i>, c.1622G>A (p.R541H) <i>AK9</i>, c.3605T>C (p.I1202T) <i>COL12A1</i>, c.2473C>G (p.P825A)</p>	<p>VUS VUS VUS VUS VUS VUS</p>
Guam Control	2002-08	<p><i>CTNNA3</i>, c.1303A>G (p.M435V) <i>SLC24A4</i>, c.1049A>G (p.E350G) <i>LRRK1</i>, c.5251G>A (p.V1751I) <i>EIF4G1</i>, c.27dupC</p>	<p>VUS VUS VUS VUS</p>

Abbreviations: *PATH*, pathogenic; *LPATH*, likely pathogenic; *VUS*, variant of uncertain significance.