

Supplementary table S1. Mutations, found in the patient

Gene _Name	HGVS.c	HGVS.p	Zygosity	rs ID	p3_1000 G	p3_1000 G_EAS_ AF	gnomAD_ exomes_A F	gnomAD_ex omes_EAS_ AF	SIFT_ score	SIFT_ pred
ABC A13	c.1517C>T	p.Pro506Leu	HE T	rs1880738	0.40 655	0.6181	0.449307	0.575825	0.436	T
	c.4618T>C	p.Phe1540Leu	HE T	rs17712299	0.09 6446	0.1498	0.07085	0.179048	0	D
	c.6533C>A	p.Ala2178Glu	HO M	rs1880736	0.81 2899	0.9881	0.723538	0.989164	1	T
	c.6917A>C	p.Lys2306Thr	HE T	rs78334925	0.09 7244	0.1508	0.075345	0.186615	0.11	T
	c.8020C>T	p.Arg2674Trp	HO M	rs2222648	0.85 2236	0.9921	0.803456	0.991853	1	T
	c.11123A>T	p.Gln3708Leu	HE T	rs143050255	0.00 2995	0.0149	0.001078	0.014851	0.028	D
	c.12829A>G	p.Asn4277Asp	HE T	rs4917152	0.23 0831	0.2163	0.172627	0.239183	1	T
	c.12905A>G	p.Gln4302Arg	HE T	rs4917153	0.23 0631	0.2163	0.172591	0.239214	0.64	T
	c.13949A>G	p.Glu4650Gly	HE T	rs557105317	0.00 02	0.001	3.66E-05	0.000524	0.032	D
ABC A7	c.563A>G	p.Glu188Gly	HE T	rs3764645	0.39 9561	0.4355	0.497496	0.428977	0.647	T
	c.1388G>A	p.Arg463His	HE T	rs3752233	0.06 0703	0.1915	0.046649	0.176792	0.254	T
	c.2153A>C	p.Asn718Thr	HE T	rs3752239	0.05 9105	0.1855	0.047099	0.16968	0.239	T
	c.4046G>A	p.Arg1349Gln	HE T	rs3745842	0.39 0575	0.3482	0.427897	0.335604	0.546	T
	c.4580G>C	p.Gly1527Ala	HO M	rs3752246	0.82 5479	0.6478	0.840229	0.646508	0.877	T
	c.5057A>G	p.Gln1686Arg	HE T	rs4147918	0.05 651	0.1736	0.04749	0.1651	0.234	T.

	c.6133G>T	p.Ala2045Ser	HE T	rs4147934	0.60 5032	0.4325	0.71193	0.446435	0.962	T.
ACO X1	c.936C>G	p.Ile312Met	HO M	rs1135640	0.55 0719	0.7877	0.653791	0.800441	0.256	T
ADA M18	c.1883C>T	p.Thr628Ile	HE T	rs183758075	0.00 0599	0.003	0.000233	0.002922	0.286	T
ALS2	c.1102G>A	p.Val368Met	HO M	rs3219156	0.89 6565	1	0.912953	0.999826	0.191	T
ARA P2	c.4568G>A	p.Arg1523Gln	HO M	rs4833069	0.99 5208	1	0.992128	1	1	T
ATP1 3A2	c.3214G>A	p.Ala1072Thr	HO M	rs3170740	0.33 127	0.246	0.47141	0.295664	0.988	T
ATX N1	c.672_677delGCAGCA	p.Gln224_Gln225del	HE T	rs754954093	.	.	.	.	.	.
	c.647_648insTCA	p.Gln215_Gln216insHis	HE T	rs766029394	.	.	.	.	.	.
	c.642G>T	p.Gln214His	HE T	rs200111316	.	.	.	.	0.581	T
	c.639G>T	p.Gln213His	HE T	rs3817753	.	.	.	.	0.072	T
	c.633T>G	p.His211Gln	HE T	rs59310777	0.26 6374	0.3879	.	.	0.297	T
	c.627_629delTCA	p.His209del	HE T	rs751377396	.	.	.	.	.	.
	c.627T>G	p.His209Gln	HE T	rs11969612	.	.	.	.	0.065	T
ATX N2	c.2285A>T	p.Asn762Ile	HE T	rs191400641	0.00 1597	0.0079	0.00079	0.011027	0.077	T
	c.743G>A	p.Ser248Asn	HO M	rs7969300	0.17 9513	0.5228	0.076308	0.564288	0.136	T
	c.563_565delAGC	p.Gln188del	HO M	rs10560189;rs67658094	0.95 1078	1	.	.	.	.
BST1	c.434G>A	p.Arg145Gln	HE T	rs2302464	0.07 9074	0.2232	0.047079	0.208164	0.111	T

CAS S4	c.1978C>T	p.Pro660Ser	HO M	rs35031530	0.146765	0.2381	0.048838	0.254697	0.286	T
CD33	c.41C>T	p.Ala14Val	HE T	rs12459419	0.210663	0.1855	0.308116	0.184375	0.029	D
COL 4A1	c.4002A>C	p.Gln1334His	HE T	rs3742207	0.288339	0.2629	0.304165	0.251565	0.122	T
	c.19G>C	p.Val7Leu	HE T	rs9515185	0.424121	0.6161	0.435687	0.633385	0.575	T
CR1	c.5573C>T	p.Thr1858Met	HE T	rs3737002	0.248802	0.3264	0.282939	0.331399	0.019	D
	c.6178A>T	p.Thr2060Ser	HO M	rs4844609	0.995008	1	0.985426	1	0.804	T
	c.7255A>G	p.Thr2419Ala	HE T	rs2296160	0.828075	0.6885	0.819882	0.655775	0.987	T
CTSA	c.108_110delGCT	p.Leu37del	HE T	rs1457838268	0.649361	0.5784	.	.	.	.
DDX1	c.1620C>G	p.Phe540Leu	HE T	rs201143228	.	.	4.10E-05	0	0.267	T
DNMBP	c.4239T>G	p.Cys1413Trp	HE T	rs11190305	0.277157	0.244	0.344252	0.238694	0.181	T
	c.1143C>G	p.Ser381Arg	HE T	rs7077718	0.486821	0.2569	.	.	.	.
DSG2	c.1984G>A	p.Ala662Thr	HE T	rs1186896680	.	.	4.07E-06	0	0	D
	c.2318G>A	p.Arg773Lys	HE T	rs2278792	0.240016	0.4643	0.265563	0.466526	0.383	T
EPHA1	c.2698A>G	p.Met900Val	HO M	rs6967117	0.960264	1	0.940039	0.998493	1	T
	c.479T>C	p.Val160Ala	HO M	rs4725617	0.94349	0.9921	0.93221	0.991984	0.246	T
	c.71G>A	p.Arg24His	HE T	rs79587607	0.086062	0.3006	.	.	0.149	T
FBXO7	c.35T>G	p.Leu12Arg	HO M	rs8137714	0.154952	0.1567	0.190958	0.143187	0.258	T
	c.3G>A	p.Met1?	HO M	rs11107	0.48742	0.6915	.	.	.	.

FIG4	c.1090A>T	p.Met364Leu	HE T	rs2295837	0.10 004	0.1984	0.07893	0.207343	1	T
FND C1	c.1312A>G	p.Thr438Ala	HE T	rs509648	0.50 8586	0.7232	0.324572	0.751479	1	T
	c.1387G>C	p.Glu463Gln	HE T	rs420137	0.78 4545	0.621	0.866743	0.637705	1	T
	c.3007C>G	p.Gln1003Glu	HE T	rs370434	0.78 5743	0.626	0.867677	0.641117	1	T
	c.3540C>G	p.Asp1180Glu	HE T	rs420054	0.78 2348	0.626	0.850326	0.622257	1	T
	c.3782T>C	p.Leu1261Pro	HE T	rs3003174	0.78 6142	0.626	0.86882	0.641139	0.345	T
	c.3839A>G	p.Gln1280Arg	HE T	rs2501176	0.78 6142	0.626	0.869494	0.643025	1	T
	c.4436_4453delCCCG CCGCACGACCACC A	p.Thr1479_Thr1484del	HE T	rs141435210;rs384 2694	0.49 6406	0.4058	.	.	.	.
	c.4511C>A	p.Thr1504Lys	HE T	rs386360	0.78 4944	0.625	0.872142	0.644028	0.795	T
	c.4720A>G	p.Thr1574Ala	HE T	rs7763726	0.14 5567	0.3552	0.064727	0.318933	0.042	D
FOX F2	c.1139_1141dupGCG	p.Gly380dup	HO M	rs545470261;rs768 40944	0.15 2157	0.2867	.	.	.	.
	c.121_123dupGCC	p.Ala41dup	HE T	rs752348150	.	.	.	.	.	.
GAB 2	c.917_919dupGCG	p.Gly306dup	HO M	rs147426137;rs397 731476;rs5823052 2	0.39 2772	0.497	.	.	.	.
	c.404G>T	p.Gly135Val	HE T	rs76853537	0.01 1981	0.001	0.012685	0.002319	0.534	T
	c.1441C>A	p.Pro481Thr	HO M	rs2289912	0.08 3067	0.2302	0.054389	0.224298	0.133	T
GIG YF2	c.3692_3693insGC	p.Gln1232fs	HO M	rs371622656	.	.	.	.	.	.
	c.3693_3694insG	p.Gln1232fs	HO M	rs775324034	.	.	.	.	.	.

HIP1 R	c.1873C>T	p.Arg625Tr p	HE T	rs117866676	0.01 4177	0.0685	0.00527	0.066624	0.036	D
HTR A1	c.33_34insT	p.Leu12fs	HE T	rs541533723	.	.	.	.	.	.
	c.34_35insAT	p.Leu12fs	HE T	.	.	.	.	.	.	.
INPP 5D	c.3505C>T	p.His1169T yr	HO M	rs9247	0.24 0016	0.3482	0.218841	0.364107	0.119	T
LPA	c.5673A>G	p.Ile1891M et	HE T	rs3798220	0.05 1318	0.0883	0.055489	0.08888	0.116	T
	c.5036T>C	p.Met1679 Thr	HE T	rs1801693	0.64 8163	0.4494	0.642298	0.451334	1	T
	c.4114C>G	p.Leu1372 Val	HE T	rs7765781	0.41 4936	0.4107	0.355312	0.396864	0.967	T
	c.4072C>G	p.Leu1358 Val	HE T	rs7765803	0.40 9145	0.4107	0.353439	0.397132	1	T
LRR K2	c.149G>A	p.Arg50His	HO M	rs2256408	0.96 9249	1	0.993066	1	1	T
	c.3857A>G	p.Asn1286 Ser	HE T	rs777961379	.	.	2.44E-05	0	0.038	D
	c.4939T>A	p.Ser1647T hr	HO M	rs11564148	0.28 5942	0.3373	0.298352	0.33871	0.953	T
	c.7173C>G	p.His2391 Gln	HE T	rs199680004	.	.	6.93E-05	0.000986	0.43	T
	c.7190T>C	p.Met2397 Thr	HO M	rs3761863	0.55 1717	0.4603	0.618476	0.46794	0.466	T
MAP T	c.1321T>C	p.Tyr441Hi s	HO M	rs2258689	0.31 2899	0.628	0.281649	0.632031	0.978	T
NME 8	c.128G>A	p.Arg43Lys	HE T	rs2722372	0.24 5208	0.1815	0.228742	0.184027	1	T
	c.440C>T	p.Pro147Le u	HE T	rs143559107	0.00 0998	0.005	0.000285	0.003888	0.309	T
	c.622T>C	p.Cys208A rg	HO M	rs10250905	0.74 3411	0.5466	0.731553	0.560475	0.046	D
	c.1478T>C	p.Ile493Thr	HE T	rs56128139	0.15 7748	0.1359	0.27337	0.128381	0.032	D

NOT CH3	c.709G>A	p.Val237Met	HE T	rs2285981	0.000799	0.004	0.000195	0.002436	0.002	D
NOT CH4	c.1315G>C	p.Ala439Pro	HE T	rs200731043	0.0002	0.001	0.000756	0.010785	0.012	D
	c.349A>C	p.Lys117Gln	HO M	rs915894	0.398762	0.5109	0.351497	0.46229	0.399	T
	c.45_47delGCT	p.Leu16del	HO M	rs35795312	0.47524	0.4921	.	.	.	.
PDLIM5	c.41C>T	p.Ser14Phe	HO M	rs2452600	0.224641	0.378	0.265912	0.374971	0.024	D
	c.1120G>A	p.Ala374Thr	HO M	rs966845	0.993411	1	0.993729	1	0.709	T
	c.1562G>A	p.Ser521Asn	HO M	rs13107595	0.979633	1	0.989681	1	0.91	T
PSEN1	c.640C>A	p.His214Asn	HE T	.	.	.	.	.	0.001	D
PTK2B	c.2513A>C	p.Lys838Thr	HE T	rs751019	0.364617	0.3601	0.440573	0.343982	0.439	T
RIN3	c.331G>A	p.Glu111Lys	HE T	rs2274542	0.022364	0.0595	0.012089	0.077967	0.31	T
	c.2913_2915delCGG	p.Gly972del	HE T	rs570458246;rs68153141;rs71698059	.	.	.	.	.	.
SACS	c.10106T>C	p.Val3369Ala	HO M	rs17078605	0.258986	0.3145	0.286729	0.350505	0.014	D
SETX	c.7834A>G	p.Ser2612Gly	HE T	rs3739927	0.163538	0.3591	0.084295	0.387787	0.652	T
	c.7759A>G	p.Ile2587Val	HO M	rs1056899	0.538738	0.6835	0.38054	0.728828	1	T
	c.5563A>G	p.Thr1855Ala	HO M	rs2296871	0.443091	0.6379	0.263905	0.696578	0.83	T
	c.3455T>G	p.Phe1152Cys	HE T	rs3739922	0.089657	0.2371	0.064566	0.269655	0.003	D
	c.1979C>G	p.Ala660Gly	HO M	rs882709	0.213658	0.4117	0.115986	0.44578	0.008	D
SFRP4	c.958C>A	p.Pro320Thr	HE T	rs1802073	0.542732	0.5635	0.435974	0.550848	0.171	T

SIG MAR 1	c.5A>C	p.Gln2Pro	HE T	rs1800866	0.21 7252	0.3204	0.202067	0.314972	0.343	T
SLC2 4A4	c.1654A>C	p.Lys552Gln	HE T	rs45587635	0.06 7292	0.1796	0.059926	0.228744	0.184	T
SLC6 A5	c.304G>A	p.Gly102Ser	HO M	rs1443547	0.40 5751	0.3651	0.368835	0.393579	0.723	T
	c.371T>C	p.Phe124Ser	HO M	rs1443548	0.79 3131	0.75	0.771566	0.760212	0.44	T
	c.485C>G	p.Ala162Gly	HO M	rs1443549	0.99 361	1	0.998607	1	1	T
SMC 5	c.916G>A	p.Val306Ile	HO M	rs1180116	0.85 5032	0.8532	0.88404	0.855722	0.655	T
SOR L1	c.3220C>G	p.Gln1074Glu	HO M	rs1699107	0.98 4824	1	0.996113	1	0.168	T
	c.5899G>A	p.Val1967Ile	HO M	rs1792120	0.97 9433	1	0.996169	1	1	T
STK3 9	c.661G>A	p.Gly221Ser	HE T	rs200257510	0.00 02	0.001	9.83E-05	0.001113	0.07	T
SYT1 1	c.144G>C	p.Gln48His	HO M	rs822522	0.95 4673	1	0.990874	0.999942	0.866	T
TET1	c.485A>G	p.Asp162Gly	HO M	rs10823229	0.25 8586	0.3919	0.330584	0.383148	0.019	D
	c.3369A>G	p.Ile1123Met	HO M	rs3998860	0.69 3291	0.8502	0.777419	0.839626	0.157	T
TM2 D3	c.17T>G	p.Leu6Arg	HO M	rs2939587	0.99 3411	1	0.97935	1	0.311	T
TOM M40	c.934C>G	p.Leu312Val	HE T	rs1275991853	.	.	.	.	0.307	T
VEP H1	c.1564T>C	p.Ser522Pro	HE T	rs11918974	0.25 0599	0.3512	0.276265	0.392621	1	T
ZCW PW1	c.628G>C	p.Ala210Pro	HE T	rs768069661	.	.	8.13E-06	0.000116	0.003	D

Supplementary figures.

Supplementary figure S1. Structure predictions of PSEN1 mutations in His214 residue. (a) Normal PSEN1 (b) PSEN1 His214Asp (c) His214Arg (d) His214Tyr

Structure prediction of PSEN1 His214 other mutations. His214Asp seems to have similar effect like His214Asn, since it could also result in the loss of interaction between His214 and Trp215. His214Asp seems to have similar effect like His214Asn, since it could also result in the loss of interaction between His214 and Trp215. Due to its aromatic ring, Tyr214 may also interact with Trp215. The mutation may not significantly change the intramolecular interactions. However, histidine is a positively charged residue while tyrosine is a hydrophobic one, which may change the helix dynamics or result in putative abnormal intermolecular interactions.

Supplementary figure S1. Structure predictions of PSEN1 mutations in His214 residue. (a) Normal PSEN1 (b) PSEN1 His214Asp (c) His214Arg (d) His214Tyr

