

Supplementary Material

Progranulin Gene Mutation in Chinese Patients with Frontotemporal Dementia: A Case Report and Literature Review

Supplementary Table 1. List of genes known to be associated with AD, FTD, or other dementia-related neurodegenerative diseases.

Phenotype	Genes
AD	<i>APP, PSEN1, PSEN2</i>
Associated with or susceptible to AD	<i>APOE, A2M, ABCA7, ACE, APBB2, ATXN1, AKT1, AR, BIN1, BLMH, CASP3, CD2AP, CD33, CHCHD10, C9ORF72, CYP2C, CST3, CELF1, CLU, CRI, DNMT1, DSG2, EPHA1, ETS1, FERMT2, GSK3B, GRB2, HTR7, HFE, INPP5D, ITM2B, LRP1, MEF2C, MPO, MS4A4E, MPHOSPH1, MS4A6A, NME8, NOS3, NOTCH3, PICALM, PAXIP1, PLAU, PTK2B, SLC24A4, SORL1, TNF, TREM2, TYROBP, ZCWPW1, CSF1R, AARS2, HTRA1, COL4A1</i>
FTD	<i>BTNL2, C9orf72, CSF1R, CHCHD10, CHMP2B, CST3, CTSC, DCTN1, FUS, GRN, hnRNPA1, hnRNPA2B1, MAPT, OPTN, PRKAR1B, RAB38, SIGMAR1, SOD1, SQSTM1, TBK1, TARDBP, TMEM106B, TREM2, UBQLN2, VCP, CYLD, TIA1, CCNF, TUBA4A, ATXN2, ANXA11, PRNP, CHCHD2, EXT2, EWSR1, TAF15</i>
Other dementia-related diseases	<i>GBA, SNCA, SNCB, ATP13A2, EPM2A, ITM2B, NHLRC1, PRICKLE1, TRPM7, CFAP410, PSAP, EIF4G1, SCN8A, COQ2, TSC1, TSC2, PLA2G6, SLC9A6, LRRK2, PINK1, SERPIN1</i>

Supplementary Table 2. The list of primers used in this study.

Primer name	Purpose	Forward Sequences (5'-3')	Reverse Sequences (5'-3')	Annealing temperature (°C)	Product length
<i>GRN</i> (gDNA-PCR)	variant detection	CTTATCCCACCCCAGAGACATC	AGAAGTGTCCCTTCCCCACACTC	61.8	367 bp
<i>GRN</i> (cDNA-FL)	long-range PCR	AACTGAGGTAGGCGGGTCATCG	GGGATGGCAGCTTGTAATGTGG	65.9	2,081 bp
<i>GRN</i> (cDNA-exon 4-11)	shorter-range PCR	GGACTTCTCCACGTGCTGTG	TTCACGTTGCAGGTGTAGCC	62.1	1,071 bp
<i>GRN</i> (Exons 4-5)	qRT-PCR	GGACTTCTCCACGTGCTGTG	CAGCAGTGCACCCTGTCTTC	62.0	93 bp
<i>GRN</i> (Exons 10-11)	qRT-PCR	CAGAGACATCGGCTGTGACC	TTCACGTTGCAGGTGTAGCC	62.2	156 bp
<i>RPS17</i> (Internal control)	qRT-PCR	AAGCGCGTGTGCGAGGAGATCG	TCGCTTCATCAGATGCGTGACAT AACCTG	69.7	87 bp

PCR, polymerase chain reaction; qRT-PCR, quantitative reverse transcription PCR; FL, full length; gDNA, genomic DNA; cDNA, complementary DNA

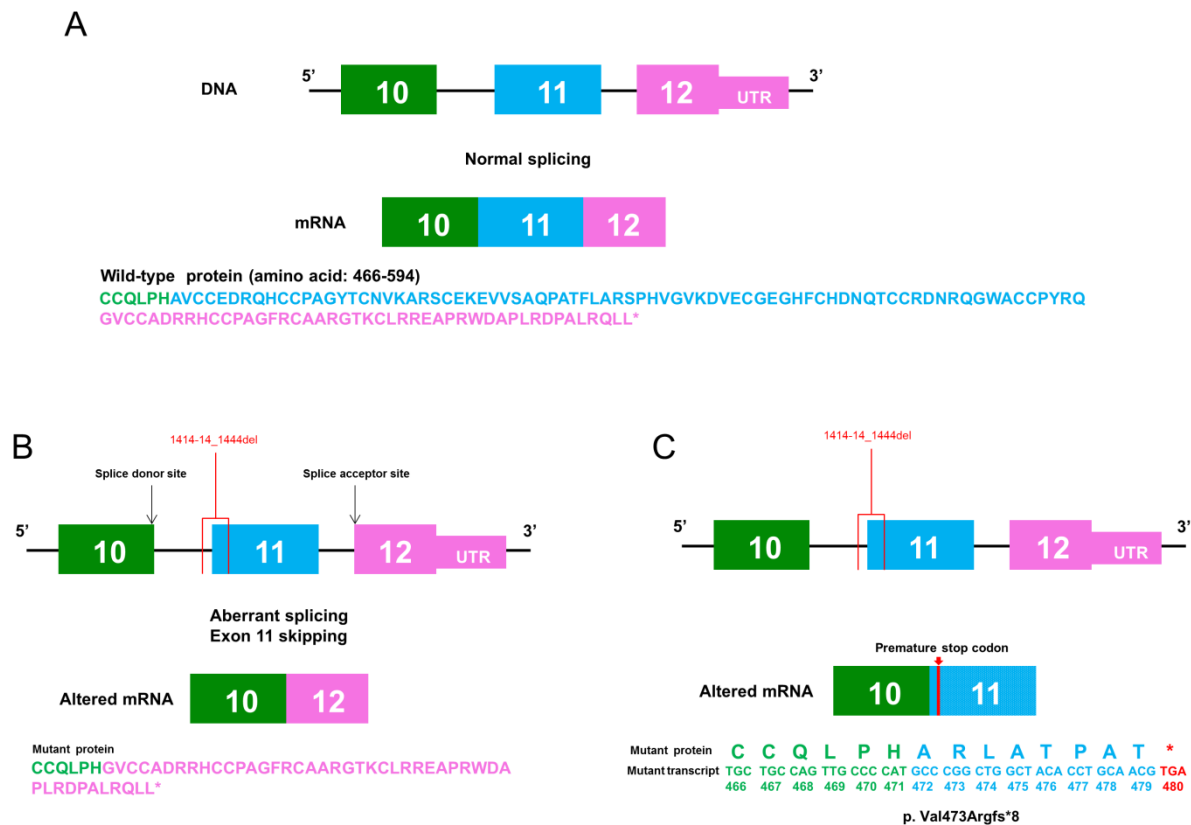
Supplementary Table 3. Frameshift mutations reported all around the world (GenBank accession number NM_002087.3)

<i>GRN</i> mutation	Phenotype	PMID
c.57_58insC	Frontotemporal lobar degeneration	29724592
c.62dupC	Frontotemporal dementia	16950801
c.63_64insC	Frontotemporal lobar degeneration	29724592
c.77delG	Progressive non-fluent aphasia	30057241
c.87_90dupCTGC	Frontotemporal dementia	16862116
c.87dupC	Frontotemporal lobar degeneration	29724592
c.88_89insC	Frontotemporal lobar degeneration	29724592
c.102delC	Frontotemporal dementia	16950801
c.117dupC	Frontotemporal lobar degeneration	29724592
c.139delG	Frontotemporal lobar degeneration	21482928
c.154delA	Frontotemporal dementia	16950801
c.156delA	Neurodegenerative disease	22348647
c.181delT	Frontotemporal dementia	19937047
c.232dupT	Dementia	30279455
c.234_235delAG	Frontotemporal dementia	16950801
c.243delC	Frontotemporal dementia	17228326
c.255delC	Frontotemporal dementia	18543312
c.295_308delTGCCCACGGGGCTT	Frontotemporal lobar degeneration	24081456
c.299delC	Frontotemporal dementia	20142524
c.314dupG	Cortico-basal syndrome	21863316
c.350delG	Frontotemporal dementia	18245784
c.361delG	Frontotemporal dementia	17436289
c.380_381delCT	Frontotemporal dementia	16862115
c.384_387delTAGT	Frontotemporal dementia	17436289
c.388_391delCAGT	Frontotemporal dementia	16862116
c.385dupA	Dementia	30279455

c.421_422delGT	Frontotemporal lobar degeneration	29724592
c.424dupA	Frontotemporal dementia	34561610
c.443_444delGG	Frontotemporal dementia	26401709
c.445_446delTG	Behavioral variant frontotemporal dementia	25261445
c.468_474delCTGCTGT	Frontotemporal dementia	17436289
c.481_482delAG	Frontotemporal dementia	28304311
c.512delG	Primary progressive aphasia	33980708
c.559delC	Frontotemporal lobar degeneration	29724592
c.559dupC	Frontotemporal dementia	31810826
c.560delT	Progressive aphasia	27439681
c.592_593delAG	Frontotemporal dementia	20142524
c.593_596delGGGC	Primary progressive aphasia	33612544
c.603dupC	Frontotemporal dementia	18234697
c.607delT	Frontotemporal dementia	20858962
c.619dupA	Frontotemporal lobar degeneration	29724592
c.675_676delCA	Frontotemporal dementia	16950801
c.759_760delTG	Frontotemporal dementia	16950801
c.759_760dupTG	Dementia	30279455
c.761_762insTG	Frontotemporal lobar degeneration	29724592
c.768_769dupCC	Alzheimer disease	22906081
c.775_778delAAGT	Progressive non-fluent aphasia	27082848
c.776dupA	Dementia	30279455
c.813_816delCACT	Frontotemporal dementia	18245784
c.833_834delCA	Frontotemporal lobar degeneration	20930271
c.834dupA	Frontotemporal lobar degeneration	29724592
c.848_854dupAATGTGA	Frontotemporal dementia	20142524
c.900_901dupGT	Frontotemporal dementia	18464284
c.907delG	Frontotemporal lobar degeneration	25317628

c.907dupG	Frontotemporal dementia	18543312
c.909delC	Frontotemporal dementia	17805587
c.910_911dupTG	Frontotemporal dementia	31914217
c.910_911insTG	Frontotemporal dementia	16950801
c.945_946delTG	Frontotemporal dementia	32843152
c.950_951delAC	Behavioral variant Frontotemporal dementia	27082848
c.975delG	Frontotemporal lobar degeneration	29724592
c.988_989delAC	Frontotemporal lobar degeneration	29724592
c.988_989dupAC	Frontotemporal dementia	26971930
c.998delG	Frontotemporal dementia	16950801
c.1014delG	Frontotemporal dementia	19101631
c.1012_1013delGGinsC	Frontotemporal lobar degeneration	22818528
c.1048dupG	Cortico-basal syndrome	19864668
c.1070delC	Frontotemporal dementia	17950702
c.1095_1096delCT	Frontotemporal dementia	17436289
c.1118_1119delCCinsG	Frontotemporal lobar degeneration	28915852
c.1144dupA	Frontotemporal dementia	17620546
c.1145delC	Frontotemporal dementia	16862116
c.1145_1146insA	Frontotemporal lobar degeneration	29724592
c.1160delG	Atypical Parkinson disease	24064467
c.1160dupG	Frontotemporal lobar degeneration	29724592
c.1165delT	Behavioral variant frontotemporal dementia	33737586
c.1196_1197delAC	Frontotemporal dementia	31810826
c.1231_1232delGT	Frontotemporal dementia	17228326
c.1231_1232dupGT	Frontotemporal dementia	17436289
c.1246dupT	Frontotemporal lobar degeneration	23463024
c.1256_1263dupGAAGCGAG	Alzheimer disease	23609919
c.1317delC	Frontotemporal lobar degeneration	31361008

c.1317_1318delCA	Frontotemporal dementia	20142524
c.1354delG	Frontotemporal lobar degeneration	21482928
c.1359dupG	Frontotemporal lobar degeneration	29724592
c.1395dupC	Frontotemporal dementia	16950801
c.1420_1421delTG	Frontotemporal lobar degeneration	21482928
c.1428_1431delGGAT	Frontotemporal dementia	23742080
c.1494_1498delAGTGG	Frontotemporal dementia	18245784
c.1535delC	Dementia, aphasic and cortico-basal syndrome	29264393
c.1538_1539delAC	Frontotemporal lobar degeneration	29724592



Supplementary Figure 1. Schematic drawing of splicing and transcription between exon 10 and exon 12 of *GRN*. A) Normal splicing and transcription between adjacent exons of *GRN* (wild type). B) Aberrant splicing and skipping of exon 11 due to the 45bp deletion in the important splicing site. C) The deletion at the beginning of exon 11 in *GRN* makes an early termination in amino acid production, which is expected to lead to a frameshift and a premature stop codon (p. Val473Argfs*8). *termination at the TGA stop codon generated.