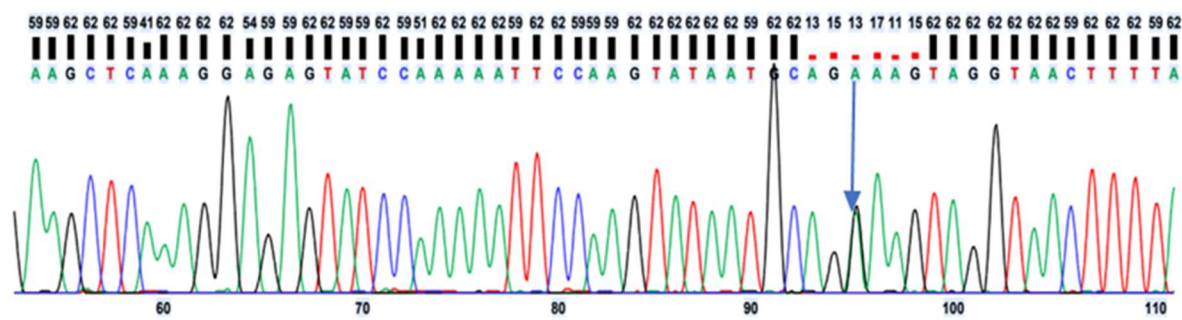


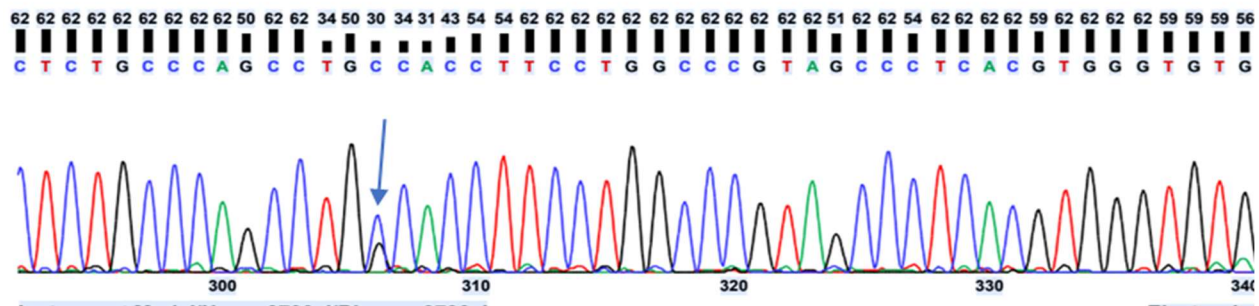
Supplement figure

Supplement figure S1. Sequencing data of the five variants, found the patient

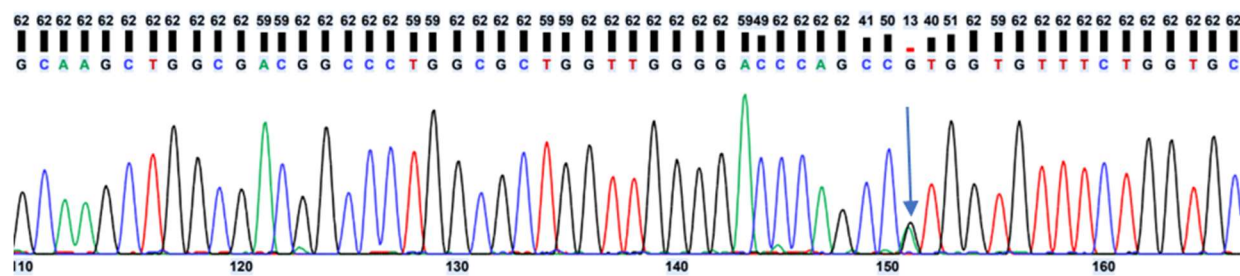
PSEN1 Glu318Gly



GRN Ala505Gly



ABCA7 Val1946Met



SORL1 Glu270Lys (3' sequencing). The patient also carried a silent variant H269H



**Supplement table S1. Supplement table S1.: Genes, included in our gene panel**

| Genes, used in the gene panel  |
|--|
| APP','PSEN1','PSEN2','S100A9','SACS','CR1','BIN1','TREM2','CLU','CTNNA3','DNMBP','SORL1','BACE1','PICALM','GAB2','LRP6','ADAM10','ABCA7',<br>'CD33','TOMM40','MS4A4A','MS4A6E','TM2D3','CD2AP','EPHA1','CASS4','PLD3','INPP5D','DSG2','CDH12','CDH18','MEF2C','NME8','PTK2B','SLC24<br>A4','RIN3','ZCWPW1','ACE','MTHFD1L','PINK1','PARK7','PARK9','ATP13A2','GBA','SNCA','PARK2','LRRK2','ACMSD','CD157','BST1','FBXO7','FGF2<br>0','GAK','GIGYF2','GPNMB','HIP1R','PTPRD','LAMP3','PLA2G6','STBD1','STK39','STX1B','SYT11','VPS35','TDP43','TARDBP','ATXN2','EWSR1','HNR<br>NPA2B1','PFN1','SETX','TMEM106B','CCNF','PPT1','TBK1','DCTN1','NEK1','CHMP2B','SQSTM1','SIGMAR1','VCP','FUS','GRN','MAPT','TAF15','ALS2'<br>,'UBQLN2','FIG4','OPTN','DAO','HNRNPA1','ANG','VAPB','SOD1','SPAST','CYP7B1','SPG11','CSF1R','NOTCH3','HTRA1','CTSA','PRNP','STX6','GAL3<br>ST1','PDIA4','BMERB1','LPA','FGF20','TET1','ACO1','POSTN','ABCA13','ADAM18','ARAP2','ATP13A3','C1orf51','CIART','DDX1','FAM105A','FGF20',' |

FNDC1','GBP4','GPR63','HACL1','MYOZ2','PDLIM5','PKP1','POLR1C','SFRP4','SLAIN2','SLC6A5','SMC5','TWF1','VEPH1','WDR64','ZNRB2','ATXN1'  
, 'NOTCH4','GLA','COL4A1','COL4A2','FOXC1','FOXF2','TREX1','PMF','ZCCHC14','WDR123','ICAL1','GCH1','S2B3','ACOX1'

**Supplement Table S2: Variants, found in the patient. The five variants of interest have been highlighted**

| Gene                | HGVS.p       | Zygosity | rs ID       | p3_1000G | p3_1000G EAS | gnomAD_exomes | gnomAD_exomes EAS | SIFT_score  | SIFT_pred |
|---------------------|--------------|----------|-------------|----------|--------------|---------------|-------------------|---|-----------|
| ABCA1 <sub>3</sub>  | p.Arg555His  | HET      | rs2361519   | 0.198083 | 0.1508       | 0.145723      | 0.169234          | 1   | T         |
| ABCA1 <sub>3</sub>  | p.Ile767Ser  | HET      | rs17712293  | 0.194489 | 0.2153       | 0.173606      | 0.224242          | 0.007   | D         |
| ABCA1 <sub>3</sub>  | p.Phe1540Leu | HET      | rs17712299  | 0.096446 | 0.1498       | 0.07085       | 0.179048          | 0   | D         |
| ABCA1 <sub>3</sub>  | p.Ala2178Glu | HOM      | rs1880736   | 0.812899 | 0.9881       | 0.723538      | 0.989164          | 1   | T         |
| ABCA1 <sub>3</sub>  | p.Lys2306Thr | HET      | rs78334925  | 0.097244 | 0.1508       | 0.075345      | 0.186615          | 0.11  | T         |
| ABCA1 <sub>3</sub>  | p.Arg2674Trp | HOM      | rs2222648   | 0.852236 | 0.9921       | 0.803456      | 0.991853          | 1   | T         |
| ABCA1 <sub>3</sub>  | p.Thr4550Ala | HET      | rs78734445  | 0.002596 | 0            | 0.004008      | 0                 | 0.112;0.084                                       | T         |
| ABCA7               | p.Arg1349Gln | HET      | rs3745842   | 0.390575 | 0.3482       | 0.427897      | 0.335604          | 0.546;0.546;.                                     | T;T;.     |
| ABCA7               | p.Arg1413Arg | HET      | rs881768    | 0.442093 | 0.3552       | .             | .                 | .   | .         |
| ABCA7               | p.Gly1527Ala | HET      | rs3752246   | 0.825479 | 0.6478       | 0.840229      | 0.646508          | 0.877;0.877;.                                     | T;T;.     |
| ABCA7               | p.Val1946Met | HET      | .           | .        | .            | .             | .                 | 0.031;0.031;.                                     | D;D;.     |
| ABCA7               | p.Ala2045Ser | HET      | rs4147934   | 0.605032 | 0.4325       | 0.71193       | 0.446435          | 0.962;0.962;.                                     | T;T;.     |
| ACOX1               | p.Ile312Met  | HET      | rs1135640   | 0.550719 | 0.7877       | 0.653791      | 0.800441          | 0.256;0.201                                       | T         |
| ALS2                | p.Val368Met  | HOM      | rs3219156   | 0.896565 | 1            | 0.912953      | 0.999826          | 0.191;0.172                                       | T         |
| ARAP2               | p.Arg1523Gln | HOM      | rs4833069   | 0.995208 | 1            | 0.992128      | 1                 | 1.0;.   | T;.       |
| ARAP2               | p.Pro89Leu   | HET      | rs35822395  | 0.005591 | 0            | 0.008379      | 0.000116          | 0.094   | T         |
| ATP13 <sub>A2</sub> | p.Pro1122Leu | HET      | rs15786     | 0.013179 | 0.001        | 0.04005       | 0                 | 0   | D         |
| ATP13 <sub>A2</sub> | p.Ala1072Thr | HET      | rs3170740   | 0.33127  | 0.246        | 0.47141       | 0.295664          | 0.988;1.0   | T         |
| ATP13 <sub>A2</sub> | p.Leu437Val  | HET      | rs149372969 | 0.000599 | 0            | 0.00106       | 0                 | 0.219;0.588;0.236;.;0.544                         | T;T;T;.;T |
| ATXN1               | p.Pro753Ser  | HET      | rs16885     | 0.122804 | 0.0069       | 0.195486      | 0.008407          | 0.015   | D         |
| ATXN1               | p.Gln225dup  | HOM      | rs769091061 | .        | .            | .             | .                 | .   | .         |
| ATXN2               | p.Pro425Leu  | HET      | .           | .        | .            | .             | .                 | 0.001;.;0.001;.;0.002;D;.;D;.;D;0.001;0.001;0.003 | D;D;D     |
| ATXN2               | p.Ser248Asn  | HET      | rs7969300   | 0.179513 | 0.5228       | 0.076308      | 0.564288          | .;0.136;0.128                                     | .;T;T     |
| CD33                | p.Arg69Gly   | HOM      | rs2455069   | 0.335064 | 0.1042       | 0.348885      | 0.080424          | 0.334;0.335                                       | T         |
| COL4A <sub>1</sub>  | p.Gln1334His | HET      | rs3742207   | 0.288339 | 0.2629       | 0.304165      | 0.251565          | 0.122   | T         |
| COL4A <sub>2</sub>  | p.Arg517Lys  | HOM      | rs7990383   | 0.509185 | 0.2232       | 0.523827      | 0.230619          | 1   | T         |
| CR1                 | p.His1658Arg | HET      | rs2274567   | 0.294329 | 0.3274       | 0.250551      | 0.291633          | 0.897;0.897;0.897;0.897;0.309                     | T         |

|        |                      |     |                                    |          |        |          |          |                               |         |
|--------|----------------------|-----|------------------------------------|----------|--------|----------|----------|-------------------------------|---------|
|        |                      |     |                                    |          |        |          |          |                               |         |
| CR1    | p.Thr2060Ser         | HOM | rs4844609                          | 0.995008 | 1      | 0.985426 | 1        | 0.804;0.804;0.804;0.804;1.0   | T       |
| CR1    | p.Ile2065Val         | HET | rs6691117                          | 0.493411 | 0.3433 | 0.321622 | 0.3062   | 1                             | T       |
| CR1    | p.Pro2277Arg         | HET | rs3811381                          | 0.26278  | 0.3224 | 0.241761 | 0.288787 | 0.446;0.446;0.446;0.446;0.394 | T       |
| CR1    | p.Thr2419Ala         | HOM | rs2296160                          | 0.828075 | 0.6885 | 0.819882 | 0.655775 | 0.987;0.987;0.987;0.987;1.0   | T       |
| CTSA   | p.Leu37del           | HOM | rs10582052,rs3080212,rs11468075    | 0.649361 | 0.5784 | .        | .        | .                             | .       |
| DSG2   | p.Arg773Lys          | HET | rs2278792                          | 0.240016 | 0.4643 | 0.265563 | 0.466526 | 0.383                         | T       |
| EPHA1  | p.Met900Val          | HOM | rs6967117                          | 0.960264 | 1      | 0.940039 | 0.998493 | 1                             | T       |
| EPHA1  | p.Arg492Gln          | HET | rs11768549                         | 0.00619  | 0      | 0.012483 | 0        | 0.599                         | T       |
| EPHA1  | p.Val160Ala          | HOM | rs4725617                          | 0.94349  | 0.9921 | 0.93221  | 0.991984 | 0.246                         | T       |
| FNDC1  | p.Ser36Pro           | HET | rs295332                           | 0.550919 | 0.628  | 0.540541 | 0        | 0.981                         | T       |
| FNDC1  | p.Thr438Ala          | HET | rs509648                           | 0.508586 | 0.7232 | 0.324572 | 0.751479 | 1                             | T       |
| FNDC1  | p.Glu463Gln          | HOM | rs420137                           | 0.784545 | 0.621  | 0.866743 | 0.637705 | 1                             | T       |
| FNDC1  | p.Gln1003Glu         | HOM | rs370434                           | 0.785743 | 0.626  | 0.867677 | 0.641117 | 1                             | T       |
| FNDC1  | p.Asp1180Glu         | HOM | rs420054                           | 0.782348 | 0.626  | 0.850326 | 0.622257 | 1                             | T       |
| FNDC1  | p.Leu1261Pro         | HOM | rs3003174                          | 0.786142 | 0.626  | 0.86882  | 0.641139 | 0.345                         | T       |
| FNDC1  | p.Gln1280Arg         | HOM | rs2501176                          | 0.786142 | 0.626  | 0.869494 | 0.643025 | 1                             | T       |
| FNDC1  | p.Thr1479_Thr1484del | HOM | rs141435210                        | 0.496406 | 0.4058 | .        | .        | .                             | .       |
| FNDC1  | p.Thr1504Lys         | HOM | rs369362288                        | 0.784944 | 0.625  | 0.872142 | 0.644028 | 0.795                         | T       |
| FOXC1  | p.Gly380dup          | HET | rs76840944                         | 0.152157 | 0.2867 | .        | .        | .                             | .       |
| FOXF2  | p.Gly306dup          | HOM | rs147426137,rs58230522,rs111257067 | 0.392772 | 0.497  | .        | .        | .                             | .       |
| GBP4   | p.Glu551Gly          | HOM | rs561042                           | 0.357428 | 0.3978 | 0.442432 | 0.399049 | 0.036                         | D       |
| GBP4   | p.Glu551Lys          | HOM | rs561037                           | 0.358826 | 0.3978 | 0.441993 | 0.398608 | 0.505                         | T       |
| GBP4   | p.Leu549Met          | HOM | rs608339                           | 0.359425 | 0.3988 | 0.43821  | 0.395317 | 1                             | T       |
| GBP4   | p.Glu546Lys          | HOM | rs1142890                          | 0.359026 | 0.3988 | 0.428369 | 0.38529  | 0.929                         | T       |
| GBP4   | p.Met545Ile          | HOM | rs1142889                          | 0.359026 | 0.3988 | 0.427021 | 0.384029 | 0.072                         | T       |
| GBP4   | p.Met545Leu          | HOM | rs1142888                          | 0.359026 | 0.3988 | 0.425834 | 0.382578 | 1                             | T       |
| GBP4   | p.Met542Ile          | HOM | rs1142886                          | 0.359625 | 0.3998 | 0.426034 | 0.381004 | 1                             | T       |
| GBP4   | p.Tyr541Asn          | HOM | rs655260                           | 0.359625 | 0.3998 | 0.430646 | 0.386015 | 1                             | T       |
| GRN    | p.Ala505Gly          | HET | rs780159686                        | .        | .      | 7.31E-05 | 0        | 0.257;.                       | T;.     |
| LAMP3  | p.Ile318Val          | HET | rs482912                           | 0.496406 | 0.4712 | 0.651055 | 0.506262 | 1                             | T       |
| LRP6   | p.Val1062Ile         | HET | rs2302685                          | 0.885583 | 0.9196 | 0.850649 | 0.9335   | 1                             | T       |
| LRRK2  | p.Arg50His           | HOM | rs2256408                          | 0.969249 | 1      | 0.993066 | 1        | 1                             | T       |
| LRRK2  | p.Met1646Thr         | HET | rs35303786                         | 0.004792 | 0      | 0.009376 | 5.81E-05 | 0.159                         | T       |
| LRRK2  | p.Met2397Thr         | HET | rs3761863                          | 0.551717 | 0.4603 | 0.618476 | 0.46794  | 0.466                         | T       |
| MAPT   | p.Tyr441His          | HET | rs2258689                          | 0.312899 | 0.628  | 0.281649 | 0.632031 | 0.978;0.933;0.978;.           | T;T;T;. |
| MS4A6E | p.Ile6Val            | HOM | rs2304935                          | 0.258187 | 0.254  | 0.325262 | 0.270819 | 1                             | T       |
| MS4A6E | p.Thr10Ala           | HOM | rs2304934                          | 0.258187 | 0.255  | 0.325243 | 0.27093  | 0.086                         | T       |
| MS4A6E | p.Val47Phe           | HOM | rs2304933                          | 0.257788 | 0.255  | 0.325162 | 0.270275 | 0.044                         | D       |
| NME8   | p.Cys208Arg          | HOM | rs10250905                         | 0.743411 | 0.5466 | 0.731553 | 0.560475 | 0.046                         | D       |
| NOTCH3 | p.Ala2223Val         | HOM | rs1044009                          | 0.629393 | 0.5724 | 0.715381 | 0.584804 | 0.175                         | T       |

|          |              |     |                                 |          |        |          |          |                                 |             |
|----------|--------------|-----|---------------------------------|----------|--------|----------|----------|---------------------------------|-------------|
|          |              |     |                                 |          |        |          |          |                                 |             |
| PARK2    | p.Val380Leu  | HET | rs1801582                       | 0.172125 | 0.0853 | 0.164749 | 0.076357 | 0.377;0.416;0.607;0.335;0.335;. | T;T;T;T;T;. |
| PARK2    | p.Ser167Asn  | HET | rs1801474                       | 0.117412 | 0.3393 | 0.069934 | 0.391814 | 0.219;0.229;0.155               | T           |
| PDLIM5   | p.Ser14Phe   | HET | rs2452600                       | 0.224641 | 0.378  | 0.265912 | 0.374971 | 0.024;.                         | D;.         |
| PDLIM5   | p.Ala374Thr  | HOM | rs966845                        | 0.993411 | 1      | 0.993729 | 1        | .;.;1.0;0.702;.;0.709           | .;.;T;T;.;T |
| PDLIM5   | p.Thr410Ala  | HET | rs7690296                       | 0.38758  | 0.3998 | 0.44145  | 0.399779 | .;.;1.0;1.0;.;0.433             | .;.;T;T;.;T |
| PDLIM5   | p.Ser521Asn  | HOM | rs13107595                      | 0.979633 | 1      | 0.989681 | 1        | .;.;0.74;0.571;.;0.91           | .;.;T;T;.;T |
| PSEN1    | p.Glu318Gly  | HET | rs17125721                      | 0.005591 | 0      | 0.014617 | 5.80E-05 | 0.135;0.132;0.135;0.004;0.224   | T;T;T;D;T   |
| PTK2B    | p.His447His  | HOM | rs7005936                       | 0.370208 | 0.1954 | .        | .        | .                               | .           |
| PTPRD    | p.Thr781Ala  | HET | rs72694737                      | 0.016973 | 0.001  | 0.022152 | 0.000759 | 1                               | T           |
| RIN3     | p.Thr425Met  | HET | rs3742717                       | 0.292532 | 0.4415 | 0.241143 | 0.467308 | 0.08;.                          | T;.         |
| RIN3     | p.Gly972del  | HOM | rs71721558,rs6153141,rs71698059 | .        | .      | .        | .        | .                               | .           |
| SETX     | p.Ile1386Val | HOM | rs543573                        | 0.55611  | 0.3621 | 0.736559 | 0.303514 | 0.872                           | T           |
| SETX     | p.Gly1252Arg | HOM | rs1183768                       | 0.55611  | 0.3621 | 0.736471 | 0.30334  | 0.133                           | T           |
| SETX     | p.Asp1192Glu | HOM | rs1185193                       | 0.640575 | 0.3681 | 0.769512 | 0.311333 | 0.377                           | T           |
| SFRP4    | p.Arg340Lys  | HET | rs1802074                       | 0.252995 | 0.2619 | 0.197331 | 0.243691 | 0.859                           | T           |
| SFRP4    | p.Pro320Thr  | HOM | rs1802073                       | 0.542732 | 0.5635 | 0.435974 | 0.550848 | 0.171                           | T           |
| SLC6A5   | p.Phe124Ser  | HOM | rs1443548                       | 0.793131 | 0.75   | 0.771566 | 0.760212 | 0.44                            | T           |
| SLC6A5   | p.Ala162Gly  | HOM | rs1443549                       | 0.99361  | 1      | 0.998607 | 1        | 1                               | T           |
| SMC5     | p.Val306Ile  | HOM | rs1180116                       | 0.855032 | 0.8532 | 0.88404  | 0.855722 | 0.655                           | T           |
| SORL1    | p.Glu270Lys  | HET | rs117260922                     | 0.007788 | 0      | 0.015071 | 0        | 0.008                           | D           |
| SORL1    | p.Gln1074Glu | HOM | rs1699107                       | 0.984824 | 1      | 0.996113 | 1        | 0.168;1.0                       | T           |
| SORL1    | p.Val1967Ile | HOM | rs1792120                       | 0.979433 | 1      | 0.996169 | 1        | 1                               | T           |
| SYT11    | p.Gln48His   | HOM | rs822522                        | 0.954673 | 1      | 0.990874 | 0.999942 | 0.866                           | T           |
| TET1     | p.Asp162Gly  | HET | rs10823229                      | 0.258586 | 0.3919 | 0.330584 | 0.383148 | 0.019                           | D           |
| TET1     | p.Cys832Tyr  | HET | rs74925160                      | 0.024161 | 0      | 0.005267 | 0        | 0                               | D           |
| TET1     | p.Ala985Ser  | HET | rs74412312                      | 0.024161 | 0      | 0.00526  | 0        | 0.013                           | D           |
| TET1     | p.Ile1123Met | HET | rs3998860                       | 0.693291 | 0.8502 | 0.777419 | 0.839626 | 0.157                           | T           |
| TM2D3    | p.Leu6Arg    | HOM | rs2939587                       | 0.993411 | 1      | 0.97935  | 1        | 0.311;0.318;0.466;0.404         | T           |
| TMEM106B | p.Thr185Ser  | HET | rs3173615                       | 0.595048 | 0.6508 | 0.489626 | 0.657474 | 0.214                           | T           |
| TOMM40   | p.Arg239Trp  | HET | rs142412517                     | 0.0002   | 0      | 0.0005   | 5.80E-05 | 0.011;0.011;.;0.011             | D;D;.;D     |
| VEPH1    | p.Ser522Pro  | HET | rs11918974                      | 0.250599 | 0.3512 | 0.276265 | 0.392621 | 1.0;0.992;0.992                 | T           |
| WDR64    | p.Asn521Asn  | HET | rs10802990                      | 0.590855 | 0.5149 | .        | .        | .                               | .           |
| ZCCHC14  | p.Val693Met  | HOM | rs3748400                       | 0.461462 | 0.3115 | 0.643568 | 0.307451 | 0                               | D           |