

# The Italian AICE-Genetics hemophilia A database: results and correlation with clinical phenotype

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Supplementary Table S1.

Location	Nucleotide	Protein	Occurrence	Effect	Reported/New	Clinical Phenotype
Exon 13			19	duplication	reported	moderate/mild
Exon 2	c.200dupA	p.Thr49AspfsX15	2	insertion	reported	severe
Exon 4	c.450_51 insT	p.Gly132TrpfsX10	1	insertion	new	severe
Exon 5	c.648_49 ins10bp	p.Lys198fsX6	1	insertion	new	severe
Exon 8	c.1073_74 insT	p.Asn339fsX	1	insertion	reported	severe
Exon 8	c.1189_1190insC	p.His378ProfsX3	1	insertion	new	severe
Exon 10	c.1464_1465 insCCAGAC	p.Ser470_Arg471insProAsp	1	insertion	new	moderate
Exon 10	c.1473_1474 insCCAGAC	p.Tyr473_Asn474insProAsp	1	insertion	new	moderate
Exon 14	c.2729_30 insC	p.Asp892ArgfsX8	1	insertion	new	severe
Exon 14	c.2777dupC	p.Ser908LysfsX7	1	insertion	new	severe
Exon 14	c.2945dupA	p.Val964CysfsX22	3	insertion	reported	severe/moderate
Exon 14	c.3637dupA	p.Ile1194AsnfsX26	6	insertion	reported	severe
Exon 14	c.3870dupA	p.Gly1272ArgfsX27	3	insertion	reported	severe
Exon 14	c.3911dupA	p.Gln1286AlafsX15	1	insertion	new	severe
Exon 14	c.3984dupA	p.Arg1310SerfsX2	1	insertion	new	severe
Exon 14	c.4329dupA	p.Asp1425ArgfsX18	3	insertion	reported	severe
Exon 14	c.4379dupA	p.Asn1442fsX	17	insertion	reported	severe/moderate
Exon 14	c.4774_75 insA	p.Thr1573AsnfsX20	1	insertion	new	severe
Exon 14	c.4788dupA	p.Glu1578ArgfsX15	1	insertion	new	severe
Exon 14	c.4825dupA	p.Thr1590AsnfsX3	2	insertion	reported	severe
Exon 14	c.4895_96 insT	p.Asn1614LysfsX1	1	insertion	reported	severe
Exon 14	c.4921_22 insT	p.Glu1623ArgfsX8	2	insertion	reported	severe/moderate
Exon 16	c.5501dupA	p.Thr1815AsnfsX12	3	insertion	new	severe
Exon 18	c.5961dupA	p.Glu1969ArgfsX4	1	insertion	reported	severe
Exon 22	c.6312_13 insG	p.Thr2086AspfsX20	1	insertion	new	severe
Exon 25	c.6894_95 insAAC	p.Val2280_Lys2281insAsn	1	insertion	new	severe
Exon 26	c.6966_67 insGACT	p.Arg2304AspfsX30	1	insertion	new	severe
Exon 1	c.172_188 del15bp	p.Tyr5_Val10del	1	small deletion	new	moderate
Exon 2	c.199_200 delAA	p.Lys48AspfsX14	1	small deletion	reported	severe
Exon 2	c.205_206 delCT	p.Leu50ValfsX13	3	small deletion	reported	severe
Exon 2	c.209_212 delTTGT	p.Phe51fsX	3	small deletion	reported	severe

Exon 2	c.224 delA	p.Asp56ValfsX17	1	small deletion	reported	severe
Exon 3	c.288_293 del GGCTGA	p.Gln77_Ala78del	1	small deletion	new	severe
Exon 3	c.347_353 delGTCTTCA	p.Ser97MetfsX42	1	small deletion	new	severe
Exon 4	c.427_428 delGA	p.Glu124ArgfsX2	1	small deletion	new	severe
Exon 4	c.486_87 delGA	p.Asn144TrpfsX6	1	small deletion	new	severe
Intron 4	c.602_-13+c.602_615del		1	small deletion	new	severe
Exon 5	c.654 delT	p.Phe199LeufsX17	1	small deletion	new	severe
Exon 5	c.665_670 +5del		1	small deletion	reported	severe
Exon 5	c.668_670 delAAG	p.Glu204del	1	small deletion	new	severe
Exon 6	c.677_9delGTT	p.S207fsX8	1	small deletion	new	severe
Exon 6	c.785 delC	p.Pro243GlnfsX2	1	small deletion	new	
Moderate						
Exon 7	c.919 delA	p.Ile288SerfsX3	1	small deletion	new	severe
Exon 7	c.957_59 delGAT	p.Leu300del	1	small deletion	reported	severe
Exon 7	c.958_60 delATG	p.Met301del	1	small deletion	reported	severe
Exon 9	c.1332 delA	p.Lys425SerfsX37	1	small deletion	reported	
Moderate						
Exon 11	c.1582_88 delTTCAAAT	p.Phe509_Tyr511lfsX5	1	small deletion	new	severe
Exon 11	c.1748 delA	p.Asn1564ThrfsX2	1	small deletion	new	severe
Exon 12	c.1845 delC	p.Asn597lfsX43	1	small deletion	new	severe
Exon 12	c.1874_75 delCA	p.Pro606ArgfsX16	1	small deletion	new	severe
Exon 13	c.2015_17 delTCT	p.Phe653del	1	small deletion	reported	severe
Exon 13	c.2058_2059 delAC	p.Leu669SerfsX40	1	small deletion	new	severe
Exon 13	c.2203_28 delAAACAC	p.Lys659_His660del	1	small deletion	new	severe
Exon 14	c.2202 delT	p.Gly716ValfsX15	1	small deletion	new	severe
Exon 14	c.2216 delA	p.Glu720GlyfsX11	1	small deletion	new	severe
Exon 14	c.2521_30 delCCTGGAGCAA	p.Pro822fsX	1	small deletion	new	severe
Exon 14	c.2534_37 delACAG	p.Asp826ValfsX7	1	small deletion	new	severe
Exon 14	c.2810 delA	p.Asp918ValfsX18	1	small deletion	new	severe
Exon 14	c.2842 delC	p.Thr930LeufsX7	1	small deletion	reported	severe
Exon 14	c.3060_3064 delCAAA	p.Lys1002LeufsX19	1	small deletion	reported	severe
Exon 14	c.3090 delAAGA	p.Lys1012LeufsX8	1	small deletion	reported	severe
Exon 14	c.3224 delC	p.Ala1056ValfsX3	1	small deletion	new	severe
Exon 14	c.3430 delA	p.Ser1125ValfsX4	1	small deletion	new	severe
Exon 14	c.3548_49 delAA	p.Lys1164ArgfsX13	1	small deletion	reported	severe
Exon 14	c.3618_3621 delACAC	p.Asn1188lfsX9	1	small deletion	reported	severe
Exon 14	c.3620_21 delAC giusta	p.His1188GlnfsX32	1	small deletion	reported	severe
Exon 14	c.3637 delA	p.Ile1194PhefsX4	15	small deletion	reported	
Severe/Moderate						
Exon 14	c.3652 delG	p.Glu1199LysfsX5	3	small deletion	new	severe
Exon 14	c.3835 delA	p.Arg1260GlnfsX28	2	small deletion	new	severe
Exon 14	c.3904 delCAAAC	p.Thr1283AlfsX14	1	small deletion	new	severe
Exon 14	c.4097 delT	p.Lys1347fsX	1	small deletion	new	severe
Exon 14	c.4121_24 del TAGA	p.Ile1355ThrfsX48	1	small deletion	reported	severe
Exon 14	c.4296_4300 delTTCTC	p.His1415SerfsX5	1	small deletion	reported	severe
Exon 14	c.4379 delA	p.Asn1441lfsX5	6	small deletion	reported	severe
Exon 14	c.4380 delT	p.Asn1441LysfsX5	1	small deletion	reported	mild
Exon 14	c.4388_91 delCTTT	p.Ser1444fsX	1	small deletion	new	severe
Exon 14	c.4477_80 delAAAG	p.Lys1474LeufsX74	1	small deletion	new	severe
Exon 14	c.4483 delG	p.Glu1476ArgfsX72	1	small deletion	new	severe
Exon 14	c.4687 delG	p.Val1154PhefsX4	1	small deletion	new	severe
Exon 14	c.5125 delA	p.Ser1690AlfsX23	1	small deletion	reported	severe
Exon 14	c.5213_16 delGAAA	p.Arg1719ThrfsX20	1	small deletion	reported	severe
Exon 16	c.5473_5478 delTTTGTC	p.Phe1806_Val1807del	1	small deletion	new	severe
Exon 16	c.5563 delG	p.Ala1836LeufsX16	1	small deletion	new	severe
Exon 17	c.5688_89 delCT	p.Leu1878ValfsX5	1	small deletion	new	
Moderate						
Exon 18	c.5961 delA	p.Glu1969ArgfsX41	4	small deletion	reported	
Severe/Moderate						
Exon 18	c.5973_76 del AATG	p.Ala1973HisfsX36	2	small deletion	reported	severe
Intron 22	c.6430_-21+c.6430_6439 del		1	small deletion	new	severe
Exon 24	c.6650 delA	p.Asn2198lfsX25	1	small deletion	new	severe
Exon 25	c.6875_76 delTC	p.Phe2274SerfsX90	1	small deletion	reported	severe
Exon 25	c.6881_82 delTT	p.Phe2275SerfsX90	1	small deletion	reported	severe
Exon 26	c.6916 delC	p.Gln2287LysfsX7	1	small deletion	reported	severe
Promoter Exon 6			1	large deletion	reported	severe
Exon 1			1	large deletion	reported	severe
Exons 2-6			1	large deletion	new	severe
Exons 2-25			2	large deletion	reported	severe
Exons 5-10			1	large deletion	new	severe
Exons 7-22			1	large deletion	reported	severe
Exons 14-22			1	large deletion	reported	severe
Exons 14-26			2	large deletion	new	severe
Exons 21-22			1	large deletion	reported	severe
Exon 26			1	large deletion	reported	severe

F8 gene			1	large deletion	reported	severe
Exon 1	c.3 G>C	p.Met-19Ile	1	missense	reported	severe
Exon 1	c.38 T>G	p.Leu-7Arg	2	missense	new	severe
Exon 1	c.63 A>G	p.Arg3Gly	1	missense	new	severe
Exon 1	c.102 C>G	p.Asp15Glu	1	missense	new	mild
Exon 1	c.103 T>C	p.Tyr16His	1	missense	reported	severe
Exon 1	c.104 A>G	p.Tyr16Cys	1	missense	new	severe
Exon 1	c.143 G>A	p.Arg29Lys	2	missense	reported	
Moderate						
Exon 2	c.201 A>G	p.Thr49Ala	1	missense	reported	severe
Exon 2	c.214 G>A	p.Glu53Lys	1	missense	reported	
Moderate						
Exon 2	c.214 G>C	p.Glu53Asp	1	missense	new	mild
Exon 2	c.223 G>T	p.Asp56Tyr	1	missense	reported	severe
Exon 2	c.265 G>A	p.Gly70Ser	1	missense/splicing	reported	severe
Exon 3	c.362G>T	p.Gly102Val	1	missense	reported	
Moderate						
Exon 3	c.275 G>A	p.Gly73Asp	1	missense	new	severe
Exon 3	c.276 C>T	p.Pro74Ser	1	missense	new	
Moderate						
Exon 3	c.293 A>T	p.Glu79Val	1	missense	reported	
Moderate						
Exon 3	c.308 T>A	p.Val84Glu	1	missense	new	severe
Exon 3	c.339 T>A	p.His94Gln	1	missense	new	severe
Exon 3	c.341 C>T	p.Pro95Leu	1	missense	new	
Moderate						
Exon 3	c.343 T>G	p.Val96Gly	1	missense	new	
Moderate						
Exon 3	c.350 T>C	p.Leu98Pro	1	missense	new	severe
Exon 3	c.353 A>G	p.His99Arg	1	missense	new	
Moderate						
Exon 3	c.362 G>C	p.Gly102Ala	1	missense	new	severe
Exon 3	c.392 A>G	p.Ile76Val	1	missense	new	mild
Exon 3	c.440 G>A	p.Ala92Thr	1	missense	reported	severe
Exon 4	c.403 G>T	p.Asp116Tyr	1	missense	reported	severe
Exon 4	c.446 C>T	p.Pro130Leu	1	missense	new	severe
Exon 4	c.518 T>G	p.Leu154Arg	1	missense	new	mild
Exon 4	c.523 A>G	p.Tyr156Cys	1	missense	new	
Moderate						
Exon 4	c.555 G>A	p.Asp167Lys	1	missense	new	
Moderate						
Exon 4	c.575 T>C	p.Ile173Thr	1	missense	new	
Moderate						
Exon 4	c.578 G>A	p.Gly174Glu	1	missense	new	severe
Exon 4	c.584 T>G	p.Leu176Arg	1	missense	new	severe
Exon 4	c.591 T>C	p.Cys179Gly	1	missense	reported	
Moderate						
Exon 5	c.642 T>G	p.Phe195Leu	1	missense	reported	mild
Exon 5	c.650 T>C	p.Lys198Pro	1	missense	new	severe
Exon 4	c.651 T>A	p.Val162Glu	1	missense	reported	mild
Exon 6	c.758 T>G	p.Val234Gly	1	missense	new	severe
Exon 6	c.761 A>G	p.Asn235Ser	1	missense	new	severe
Exon 6	c.761 A>T	p.Asn235Ile	2	missense	reported	severe
Exon 6	c.763 G>T	p.Gly236Cys	1	missense	new	severe
Exon 6	c.776 G>C	p.Arg240Thr	1	missense	new	mild
Exon 7	c.800 G>A	p.Cys248Tyr	1	missense	reported	
Moderate						
Exon 7	c.883T>C	p.Phe276Leu	1	missense	reported	
Moderate						
Exon 7	c.886 C>T	p.Leu277Phe	1	missense	new	severe
Exon 7	c.901 C>T	p.Arg282Cys	2	missense	reported	severe
Exon 7	c.902 G>A	p.Arg282His	2	missense	reported	
Severe/Moderate						
Exon 7	c.920 T>G	p.Ile288Ser	4	missense	reported	severe
Exon 7	c.938 T>G	p.Leu294Arg	1	missense	reported	severe
Exon 7	c.967 G>A	p.Gly304Arg	1	missense	new	severe
Exon 7	c.980 T>G	p.Leu308Arg	1	missense	new	severe
Exon 7	c.986 G>A	p.Cys310Tyr	1	missense	new	severe
Exon 8	c.1025 A>G	p.Tyr323Cys	1	missense	reported	
Moderate						
Exon 8	c.1030 A>C	p.Lys325Glu	1	missense	new	mild
Exon 8	c.1033 G>T	p.Val326Leu	2	missense	reported	
Moderate						
Exon 8	c.1171 C>T	p.Arg372Cys	3	missense	reported	
Moderate						

Exon 8	c.1171 C>G	p.Arg372Gly	1	missense	reported	
Moderate						
Exon 8	c.1172 G>A	p.Arg372His	1	missense	reported	
Moderate						
Exon 8	c.1173 T>C	p.Ser373Leu	3	missense	reported	
Moderate						
Exon 8	c.1202 G>C	p.Trp382Cys	1	missense	new	mild
Exon 9	c.1313 T>C	p.Ile419Tyr	1	missense	new	mild
Exon 9	c.1315 G>T	p.Gly420Cys	1	missense	new	severe
Exon 9	c.1316 G>C	p.Gly420Ala	1	missense	new	
Moderate						
Exon 9	c.1322 T>C	p.Tyr423Asn	1	missense	new	severe
Exon 9	c.1332 A>C	p.Lys425Asn	3	missense	reported	severe
Exon 9	c.1364 T>C	p.Phe436Ser	1	missense	new	severe
Exon 9	c.1372 C>T	p.Arg439Cys	3	missense	reported	mild
Exon 9	c.1396 G>A	p.Gly447Arg	2	missense	new	
Severe/Moderate						
Exon 9	c.1414 T>A	p.Leu453His	1	missense	new	
Moderate						
Exon 9	c.1424 G>A	p.Gly420Ser	1	missense	reported	
Moderate						
Exon 9	c.1430 G>T	p.Gly458Val	7	missense	reported	
Moderate						
Exon 10	c.1475 A>G	p.Tyr473Cys	2	missense	reported	mild
Exon 10	c.1492 G>A	p.Gly479Arg	3	missense	reported	
Moderate/Mild						
Exon 10	c.1537 G>A	p.Gly494Ser	1	missense	reported	severe
Exon 11	c.1630 G>A	p.Asp525Asn	1	missense	reported	mild
Exon 11	c.1636 C>T	p.Arg527Trp	4	missense	reported	mild
Exon 11	c.1640 G>A	p.Cys528Tyr	1	missense	reported	
Moderate						
Exon 11	c.1648 C>T	p.Arg531Cys	3	missense	reported	mild
Exon 11	c.1649 G>A	p.Arg531His	1	missense	reported	mild
Exon 11	c.1682 A>C	p.Asp542Ala	1	missense	reported	severe
Exon 11	c.1694 A>G	p.Lys510Glu	1	missense	reported	
Moderate						
Exon 11	c.1700 T>C	p.Ile548Thr	6	missense	reported	mild
Exon 12	c.1754 T>C	p.Ile566Thr	1	missense	reported	severe
Exon 12	c.1810 T>C	p.Trp585Arg	1	missense	new	severe
Exon 12	c.1813 T>C	p.Tyr586His	1	missense	reported	severe
Exon 12	c.1814 A>G	p.Tyr586Cys	1	missense	new	severe
Exon 12	c.1834 C>T	p.Arg593Cys	2	missense	reported	
Moderate/Mild						
Exon 12	c.1897 A>G	p.Met614Val	1	missense	new	mild
Exon 12	c.1909 G>T	p.Glu581Asp	1	missense	new	severe
Exon 13	c.1913 G>A	p.Gly619Asp	1	missense	new	severe
Exon 13	c.1945 T>C	p.Cys630Arg	1	missense	new	severe
Exon 13	c.1966 T>C	p.Trp637Arg	1	missense	new	severe
Exon 13	c.1966 T>G	p.Trp637Gly	1	missense	new	
Moderate						
Exon 13	c.1991 A>G	p.Gln645Arg	1	missense	new	
Moderate						
Exon 13	c.2029 T>G	p.Phe658Val	1	missense	new	
Moderate						
Exon 13	c.2043 G>T	p.Met662Ile	1	missense	reported	
Moderate						
Exon 13	c.2061 C>T	p.Pro672Ser	1	missense	new	severe
Exon 13	c.2081 G>A	p.Gly675Glu	2	missense	new	
Severe/Moderate						
Exon 13	c.2090 T>C	p.Val678Ala	1	missense	reported	mild
Exon 13	c.2102 T>C	p.Met682Thr	1	missense	new	mild
Exon 14	c.2149 C>T	p.Arg698Trp	1	missense	reported	mild
Exon 14	c.2158 G>A	p.Gly701Ser	1	missense	reported	severe
Exon 14	c.2161 A>G	p.Met702Val	1	missense	new	severe
Exon 14	c.2163 G>C	p.Met702Ile	1	missense	reported	severe
Exon 14	c.2167 G>A	p.Ala704Thr	8	missense	reported	
Severe/Moderate/Mild						
Exon 14	c.2225 A>G	p.Tyr723Cys	1	missense	reported	mild
Exon 14	c.4114 A>G	p.Thr1353Ala	1	missense	new	severe
Exon 14	c.5063 C>T	p.Ser1669Leu	1	missense	new	
Moderate						
Exon 14	c.5122 C>T	p.Arg1689Cys	4	missense	reported	
Severe/Moderate						
Exon 14	c.5140 A>T	p.Thr1695Ser	2	missense	reported	mild
Exon 14	c.5176 T>C	p.Trp1707Arg	1	missense	new	severe

Exon 15	c.5253A>T	p.Lys1732Asn	1	missense	new	severe
Exon 15	c.5275 G>A	p.Asp1740Asn	1	missense	new	mild
Exon 15	c.5302 C>T	p.Arg1749Cys	2	missense	reported	mild
Exon 15	c.5320 C>T	p.His1755Tyr	1	missense	reported	mild
Exon 15	c.5321 A>G	p.His1755Arg	1	missense	reported	severe
Exon 15	c.5323 T>G	p.Leu1756Val	1	missense	reported	
Moderate						
Exon 15	c.5330 T>C	p.Leu1758Pro	3	missense	reported	severe
Exon 15	c.5335 G>A	p.Gly1760Arg	1	missense	reported	severe
Exon 16	c.5387 A>G	p.Asn1777 Ser	1	missense	new	severe
Exon 16	c.5398 C>A	p.Arg1781Ser	1	missense	new	severe
Exon 16	c.5398 C>T	p.Arg1781Cys	2	missense	reported	
Moderate						
Exon 16	c.5399 G>A	p.Arg1781His	10	missense	reported	
Severe/Moderate/Mild						
Exon 16	c.5405 A>C	p.Tyr1783Arg	1	missense	new	severe
Exon 16	c.5405 A>G	p.Tyr1783Cys	1	missense	reported	
Moderate						
Exon 16	c.5411 T>C	p.Phe1785Ser	2	missense	reported	severe
Exon 16	c.5413 T>A	p.Tyr1786Asn	1	missense	new	severe
Exon 16	c.5419 A>G	p.Ser1788Gly	1	missense	new	mild
Exon 16	c.5422 C>T	p.Leu1789Phe	1	missense	reported	mild
Exon 16	c.5522 A>T	p.His1822Leu	1	missense	new	mild
Exon 16	c.5527 G>A	p.Ala1824Thr	1	missense	reported	mild
Exon 16	c.5533 A>C	p.Thr1826Pro	1	missense	reported	severe
Exon 16	c.5558 C>T	p.Ala1834Val	2	missense	reported	mild
Exon 16	c.5561 T>G	p.Trp1835Gly	1	missense	new	severe
Exon 17	c.5674 G>A	p.Val1873Ile	1	missense	new	
Moderate						
Exon 17	c.5715 G>A	p.Gly1850Asp	1	missense	reported	severe
Exon 17	c.5726 A>G	p.Tyr1890Cys	3	missense	reported	
Severe/Moderate						
Exon 17	c.5813 A>G	p.His1919Arg	2	missense	reported	mild
Exon 18	c.5824 G>A	p.Gly1923Asp	1	missense	new	severe
Exon 18	c.5837 A>T	p.Asp1927Val	1	missense	new	mild
Exon 18	c.5879 G>A	p.Arg1941Gln	2	missense	reported	
Severe/Mild						
Exon 18	c.5918 A>G	p.His 1954 Arg	1	missense	new	severe
Exon 18	c.5954 G>A	p.Arg1966Gln	2	missense	reported	mild
Exon 18	c.5981 T>C	p.Leu1975Pro	1	missense	reported	
Moderate						
Exon 18	c.5998 G>A	p.Gly1981Ser	2	missense	new	severe
Exon 19	c.6043 T>C	p.Trp1996Arg	3	missense	new	severe
Exon 19	c.6045 G>T	p.Trp1996Cys	1	missense	reported	severe
Exon 19	c.6046 T>C	p.Arg1997Trp	19	missense	reported	
Severe/Moderate/Mild						
Exon 19	c.6092 C>T	p.Thr2012Ile	1	missense	reported	mild
Exon 19	c.6104 T>G	p.Val2016Gly	1	missense	new	severe
Exon 20	c.6151 A>T	p.Ile2032Phe	1	missense	new	mild
Exon 20	c.6151 T>G	p.Ile2032Ser	1	missense	reported	severe
Exon 20	c.6172 G>C	p.Ala2039Pro	7	missense	reported	
Severe/Moderate						
Exon 21	c.6267 G>T	p.Trp2070Cys	2	missense	new	mild
Exon 21	c.6275 C>T	p.Ser2069Phe	1	missense	reported	severe
Exon 22	c.6320 G>A	p.Gly2088Asp	1	missense	new	severe
Exon 22	c.6371 A>G	p.Try2105Cys	6	missense	reported	mild
Exon 22	c.6374 G>C	p.Ser2106Thr	1	missense	new	severe
Exon 22	c.6531 C>A	p.Thr2122Asn	1	missense	reported	severe
Exon 23	c.6506 G>T	p.Arg2150Leu	1	missense	new	mild
Exon 23	c.6506 G>A	p.Arg2150His	13	missense	reported	
Severe/Moderate/Mild						
Exon 23	c.6532 C>T	p.Arg2159Cys	3	missense	reported	mild
Exon 23	c.6533 G>A	p.Arg2159His	1	missense	reported	
Moderate						
Exon 23	c.6545 G>A	p.Arg2163His	14	missense	reported	
Severe/Moderate						
Exon 23	c.6546T>C	p.Phe2127Ser	1	missense	new	mild
Exon 23	c.6560 G>A	p.Gly2168Asp	2	missense	new	severe
Exon 23	c.6563 G>A	p.Cys2169Tyr	1	missense	new	
Moderate						
Exon 24	c.6593 G>A	p.Gly2179Glu	1	missense	new	severe
Exon 24	c.6593 G>T	p.Gly2179Val	2	missense	reported	severe
Exon 24	c.6637 T>C	p.Ser2194Pro	1	missense	new	severe
Exon 24	c.6638 C>G	p.Ser2194Cys	3	missense	new	
Moderate						

Exon 24	c.6652 A>G	p.Met2199Val	1	missense	new	severe
Exon 24	c.6683 G>A	p.Arg2209Gln	5	missense	reported	severe
Exon 24	c.6685 C>T	p.Leu2210Phe	2	missense	reported	mild
Exon 25	c.6738 G>A	p.Glu2228Lys	1	missense	new	
Moderate						
Exon 25	c.6742 T>C	p.Trp2229Arg	1	missense	new	mild
Exon 25	c.6744 G>T	p.Trp2229Cys	1	missense	reported	
Moderate						
Exon 25	c.6746 T>C	p.Leu2230Pro	1	missense	new	severe
Exon 25	c.6751 T>C	p.Val2232Ala	3	missense	reported	mild
Exon 25	c.6769 A>G	p.Met2238Arg	1	missense	reported	mild
Exon 25	c.6776 T>C	p.Val2240Asp	1	missense	new	severe
Exon 25	c.6785 T>C	p.Val2243Ala	1	missense	new	
Moderate						
Exon 26	c.6956 C>G	p.Pro2300Arg	1	missense	new	severe
Exon 26	c.6956 C>T	p.Pro2300Leu	4	missense	reported	mild
Exon 26	c.6967 C>T	p.Arg2304Cys	7	missense	reported	
Severe/Moderate						
Exon 26	c.6977 G>A	p.Arg2307Gln	5	missense	reported	
Severe/Moderate/Mild						
Exon 26	c.6982 C>G	p.His2309Asp	1	missense	new	severe
Exon 26	c.6989 A>C	p.Gln2311Pro	1	missense	reported	severe
Exon 26	c.6994 T>C	p.Trp2313Arg	2	missense	reported	severe
Exon 26	c.6995 G>C	p.Trp2313Ser	1	missense	new	
Moderate						
Exon 26	c.7015 A>T	p.Arg2320Trp	1	missense	new	severe
Exon 26	c.7031 G>A	p.Gly2325Asp	1	missense	reported	severe
Exon 26	c.*1 T>C		1	missense	new	mild
Exon 1	c.43 C>T	p.Arg-5Stop	2	nonsense	reported	severe
Exon 1	c.207 G>A	p.Trp14Stop	1	nonsense	reported	severe
Exon 3	c.368 C>G	p.Ser104Stop	1	nonsense	new	severe
Exon 4	c.406 C>T	p.Gln117Stop	1	nonsense	reported	severe
Exon 4	c.436 A>T	p.Lys127Stop	1	nonsense	new	severe
Exon 6	c.686 C>G	p.Ser210Stop	2	nonsense	new	severe
Exon 6	c.709 C>T	p.Gln218Stop	1	nonsense	new	severe
Exon 6	c.741 G>A	p.Trp228Stop	1	nonsense	reported	severe
Exon 7	c.821 G>A	p.Trp255Stop	1	nonsense	reported	severe
Exon 8	c.1063 C>T	p.Arg336Stop	2	nonsense	reported	severe
Exon 9	c.1336 C>T	p.Arg427Stop	5	nonsense	reported	severe
Exon 10	c.1594 C>G	p.Tyr476Stop	1	nonsense	reported	
Moderate						
Exon 10	c.1629C>G	p.Ser488Stop	1	nonsense	reported	severe
Exon 11	c.1738 C>T	p.Gln561Stop	1	nonsense	new	severe
Exon 12	c.1804 C>T	p.Arg583Stop	5	nonsense	reported	
Severe/Moderate						
Exon 12	c.1811 G>A	p.Trp585Stop	1	nonsense	new	severe
Exon 12	c.1831 C>T	p.Gln592Stop	2	nonsense	reported	severe
Exon 13	c.1933 C>T	p.Gln626Stop	1	nonsense	reported	severe
Exon 13	c.2078 C>G	p.Ser674Stop	1	nonsense	new	severe
Exon 14	c.2372 G>A	p.Trp772Stop	2	nonsense	reported	severe
Exon 14	c.2440 C>T	p.Arg795Stop	3	nonsense	reported	severe
Exon 14	c.2742 T>G	p.Leu859Stop	1	nonsense	new	severe
Exon 14	c.3113 C>G	p.Ser1019Stop	1	nonsense	new	severe
Exon 14	c.3175 A>T	p.Lys1040Stop	1	nonsense	reported	severe
Exon 14	c.3381 G>A	p.Trp1108Stop	3	nonsense	reported	severe
Exon 14	c.3865 A>T	p.Lys1270Stop	1	nonsense	new	severe
Exon 14	c.3967 C>T	p.Gln1304Stop	1	nonsense	reported	
Moderate						
Exon 14	c.4067 C>A	p.Ser1337Stop	1	nonsense	new	severe
Exon 14	c.4077 G>A	p.Trp1340Stop	1	nonsense	new	severe
Exon 14	c.4156 C>T	p.Gln1367Stop	1	nonsense	new	severe
Exon 14	c.4363 C>T	p.Gln1436Stop	1	nonsense	new	severe
Exon 14	c.4483 G>T	p.Glu1476Stop	1	nonsense	new	severe
Exon 14	c.5143 C>T	p.Arg1696Stop	7	nonsense	reported	severe
Exon 14	c.5177 G>A	p.Trp1707Stop	2	nonsense	reported	
Severe/Moderate						
Exon 14	c.5184 T>A	p.Tyr1709Stop	1	nonsense	reported	severe
Exon 16	c.5508 G>A	p.Trp1817Stop	1	nonsense	reported	severe
Exon 16	c.5515C>T	p.Gln1820Stop	1	nonsense	new	severe
Exon 17	c.5662 A>T	p.Arg1869Stop	1	nonsense	new	severe
Exon 18	c.5878 C>T	p.Arg1941Stop	1	nonsense	reported	severe
Exon 18	c.5953 C>T	p.Arg1966Stop	5	nonsense	reported	
Severe/Moderate						
Exon 18	c.5985 C>A	p.Tyr1976Stop	1	nonsense	reported	severe
Exon 18	c.5992 G>A	p.Trp1942Stop	1	nonsense	reported	severe
Exon 21	c.6335 G>T	p.Gly2057Stop	1	nonsense	reported	severe

Exon 22	c.6310 A>T	p.Lys2085Stop	1	nonsense	new	severe
Exon 22	c.6403 C>T	p.Arg2116Stop	4	nonsense	reported	severe
Exon 23	c.6605 C>T	p.Arg2147Stop	1	nonsense	reported	severe
Exon 24	c.6682 C>T	p.Arg2209Stop	5	nonsense	reported	severe
Exon 25	c.6739 G>T	p.Glu2228Stop	2	nonsense	new	
Severe/Moderate						
Exon 26	c.6907 C>T	p.Gln2284Stop	1	nonsense	new	severe
Exon 1	c.-43 C>T		1	transcription	new	mild
Exon 1	c.-25 A>G		1	transcription	new	severe
Intron 2	c.144 -2 A>T		1	splicing	new	severe
Intron 2	c.144 -3 C>G		1	splicing	new	severe
Intron 3	c.388 +5 G>A		1	splicing	reported	severe
Intron 4	c.601 +5 G>T		1	splicing	new	mild
Intron 4	c.601 +5 G>A		1	splicing	reported	mild
Intron 4	c.602 -1 G>A		1	splicing	new	severe
Intron 5	c.670 +1 G>T		1	splicing	reported	severe
Intron 5	c.670 +6 A>G		1	splicing	new	mild
Intron 6	c.787 +1 G>A		1	splicing	reported	mild
Intron 6	c.787 +5 G>A		1	splicing	new	severe
Intron 6	c.788 -1 G>T		1	splicing	reported	severe
Intron 9	c.1443 +1 G>C		1	splicing	new	
Moderate						
Intron 9	c.1443 +1 G>T		1	splicing	new	Severe
Intron 10	c.1537 +1G>C		1	splicing	new	Severe
Intron 10	c.1538 -1 A>G		1	splicing	new	Severe
Intron 10	c.1538 -18 G>A		17	splicing	new	Moderate
Exon 11	c.1678 G>T		7	splicing	reported	Severe/Moderate
Intron 12	c.1903 +2 T>G		2	splicing	new	Severe
Intron 12	c.1903 +5 G>A		2	splicing	reported	Severe/Moderate
Intron 12	c.1904 -1G>A		1	splicing	new	Severe
Intron 12	c.1904 -2A>G		1	splicing	new	Severe
Intron 14	c.5219 +1 G>A		4	splicing	new	Severe
Intron 14	c.5219 +2 T>C		1	splicing	new	Severe
Intron 14	c.5219 +3 A>G		2	splicing	reported	Moderate
Intron 15	c.5220 -2 A>T		2	splicing	new	Severe
Intron 16	c.5373 +1 G>A		1	splicing	new	Severe
Intron 16	c.5373 +2 T>G		1	splicing	new	Moderate
Intron 19	c.6115 +4 A>G		1	splicing	new	Severe
Intron 19	c.6115 delGTG +1_+3		1	splicing	new	Severe
Intron 21	c.6187 -1 G>A		1	splicing	new	Severe
Intron 21	c.6188 +1 G>T		2	splicing	reported	Sever
Intron 25	c.6723 +1 G>T		1	splicing	reported	Severe
Exon 15	del 3bp inser22bp	p.Val1727delins22bp	1	insertion/small deletion	new	severe
Exon 24	c.6623_25 delAGA Gln2189p.Gln2189del + p.Thr2191del +c.6628 delA Thr2191		1	small deletions	new	severe

**Supplementary Table S2. F8 mutations occurring at a CpG site**

<i>Exon</i>	<i>Mutation</i>	<i>Type</i>	<i>Phenotype (number)</i>
1c.43C>T	p.Arg-5Stop	nonsense	severe(2)
7c.901C>T	p.Arg282Cys	missense	severe(1)
7c.902G>A	p.Arg282His	missense	severe(1)/moderate(2)
8c.1063C>T	p.Arg336Stop	nonsense	severe(2)
8c.1171C>T	p.Arg372Cys	missense	moderate(3)
8c.1172G>A	p.Arg372His	missense	moderate(1)
9c.1336C>T	p.Arg427Stop	nonsense	severe(5)
10c.1492 G>A	p.Gly479Arg	missense	moderate(2)/mild(1)
11c.1636C>T	p.Arg527Trp	missense	mild(3)
11c.1648C>T	p.Arg531Cys	missense	mild(3)
11c.1649G>A	p.Arg531His	missense	mild(1)
12c.1804C>T	p.Arg583Stop	nonsense	severe(3)/moderate(2)
12c.1834C>T	p.Arg593Cys	missense	moderate(1)/mild(1)
14c.2149C>T	p.Arg698Trp	missense	mild(1)
14c.2167G>A	p.Ala704Thr	missense	severe(1)/moderate(2)/mild(7)
14c.2440C>T	p.Arg795Stop	nonsense	severe(3)
14c.5122C>T	p.Arg1689Cys	missense	severe(1)/moderate(1)/mild(1)
14c.5123G>A	p.Arg1689His	missense	mild(1)
14c.5252C>T	p.Arg1696Stop	nonsense	severe(7)
15 c.5302C>T	p.Arg1749Cys	missense	mild(1)
16c.5398C>T	p.Arg1781Cys	missense	moderate(1)
16c.5399G>A	p.Arg1781His	missense	severe(2)/moderate(6)/mild(3)
18c.5878C>T	p.Arg1941Stop	nonsense	severe(1)
18c.5879G>A	p.Arg1941Gln	missense	severe(1)/mild(1)
18c.5953C>T	p.Arg1966Stop	nonsense	severe(4)/moderate(1)
18c.5954G>A	p.Arg1966Gln	missense	mild(1)
19c.6046C>T	p.Arg1997Trp	missense	severe(13)/moderate(5)/mild(1)
22c.6403C>T	p.Arg2116Stop	nonsense	severe(4)
23c.6496C>T	p.Arg2147Stop	nonsense	severe(1)
23c.6506G>A	p.Arg2150His	missense	severe(1)/moderate(7)/mild(5)
23c.6532C>T	p.Arg2159Cys	missense	mild(2)
23c.6533G>A	p.Arg2159His	missense	moderate(1)
23c.6544C>T	p.Arg2163Cys	missense	severe(2)
23c.6545G>A	p.Arg2163His	missense	severe(6)/moderate(5)
24c.6682C>T	p.Arg2209Stop	nonsense	severe(5)
24c.6683G>A	p.Arg2209Gln	missense	severe(5)
26c.6956C>T	p.Pro2300Leu	missense	mild(4)
26c.6967C>T	p.Arg2304Cys	missense	severe(5)/moderate(2)
26c.6977G>A	p.Arg2307Gln	missense	severe(1)/moderate(1)/mild(3)

**Supplementary Table S3. F8 mutations and clinical phenotype in patients with moderate and mild HA and inhibitors.**

<i>Location</i>	<i>Nucleotide</i>	<i>Protein</i>	<i>Effect</i>	<i>Clinical Phenotype</i>
Exon 2	c.214 G>A	p.Glu53Lys	missense	moderate
Exon 3	c.353 A>G	p.His99Arg	missense	moderate
Exon 9	c.1372 C>T	p.Arg439Cys	missense	mild
Exon 9	c.1430 G>T	p.Gly458Val	missense	mild
Intron 9	c.1443 +1 G>C		splicing	moderate
Exon 10	c.1594 C>G	p.Tyr476Stop	nonsense	moderate
Intron 10	c.1538 -18 G>A		splicing	mild
Intron 10	c.1538 -18 G>A		splicing	moderate
Exon 14	c.3967 C>T	p.Gln1304Stop	nonsense	moderate
Exon 16	c.5398 C>T	p.Arg1781Cys	missense	moderate
Exon 16	c.5399 G>A	p.Arg1781His	missense	moderate
Exon 16	IVS16 +2 t>g			moderate
Exon 17	c.5726 A>G	p.Tyr1890Cys	missense	moderate
Exon 22	c.6371 A>G	p.Tyr2105Cys	missense	mild
Exon 23	c.6506 G>A	p.Arg2150His	missense	mild
Exon 23	6506G>A	p.Arg2150His	missense	moderate
Exon 23	6506G>A	p.Arg2150His	missense	moderate