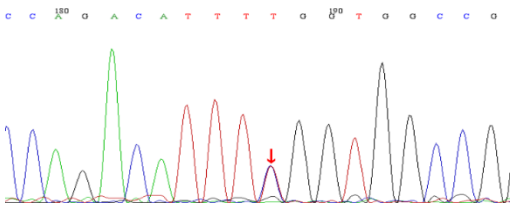
Supplementary material file 4: Validation of candidate mutations by PCR-Sanger sequencing and in silico function analysis on candidate mutations. Evolutionary conservation and structure of wild-type and mutant-type created by SWISS-MODEL.

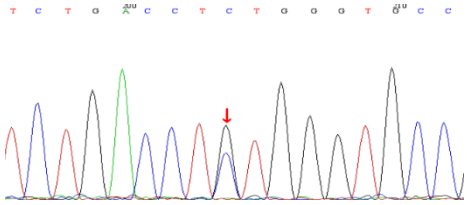
Autosomal Recessive（8/12）

NT41-III:2（F/1Y）

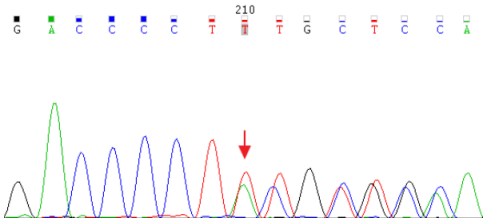
OTOF c.145C>T, p.R49W



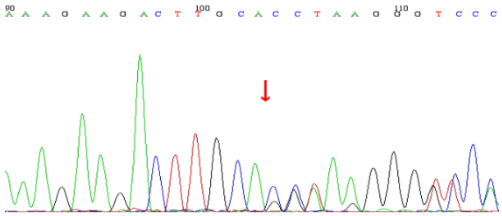
OTOF c.4961-3C>G



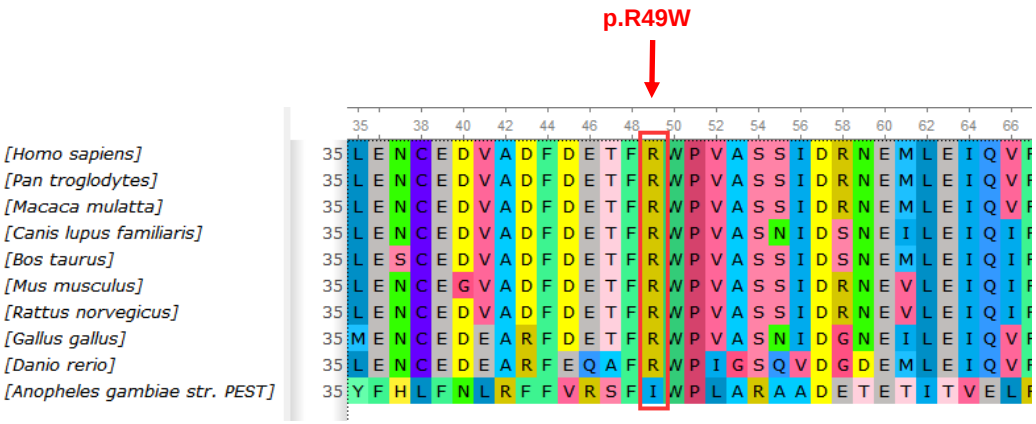
OTOF c.1364_1365AC>TT and c.1366_1367insC, p.Y455Ffs*21

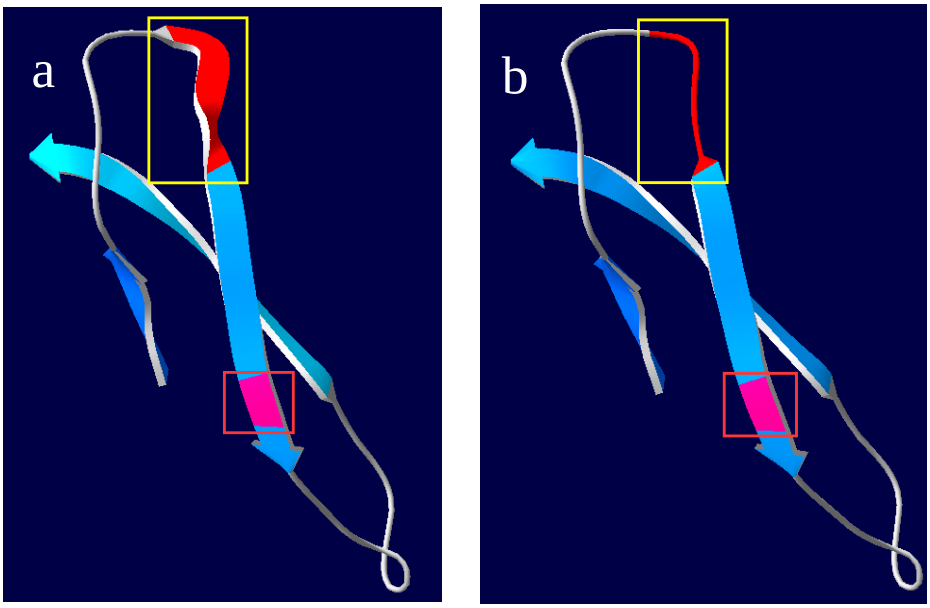


（The 5’ to 3’ strand sequence）



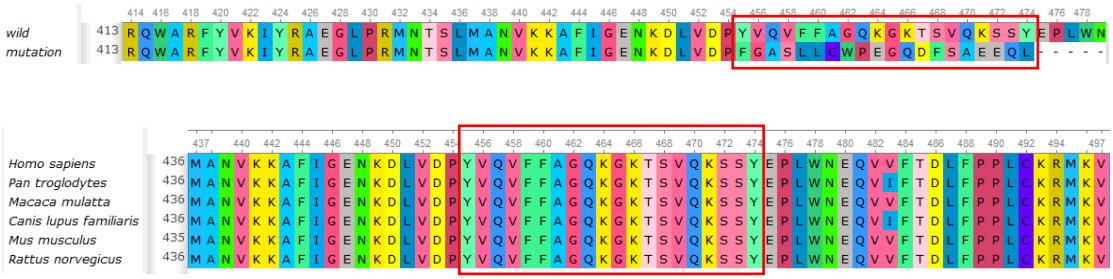
（The reverse sequence）





Wild（a），Mutation p.R49W（b）: A hydrogen bond between 34 and 36 was broken and two hydrogen bonds were formed among 41 and 43, 43 and 44 after the 49 Trp mutation.

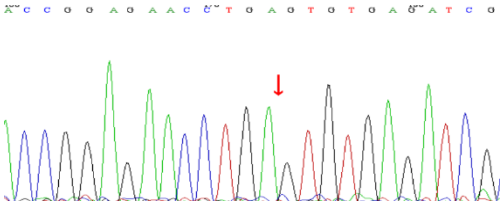
OTOF p.Y455Ffs*21

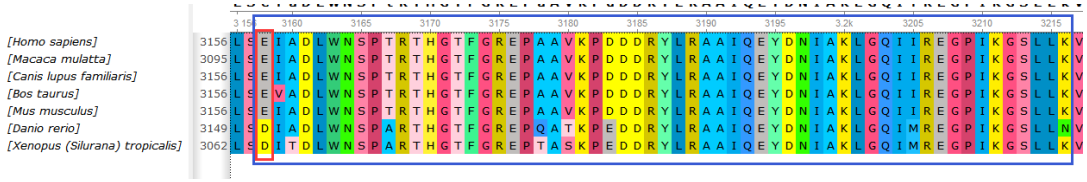


There is no protein structural homology-model for p.Y455Ffs*21.

NT44-II:1（M/11Months）

CDH23 c.9469_9470insGT, p.E3158Vfs*58

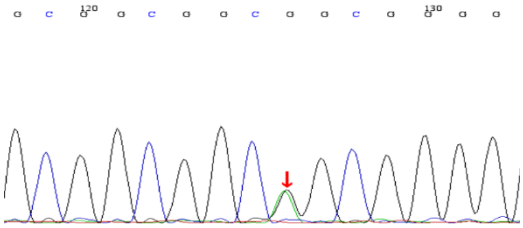




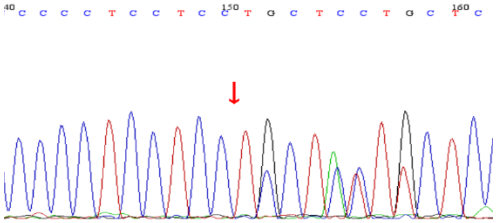
There is no protein structural homology-model for p.E3158Vfs*58.

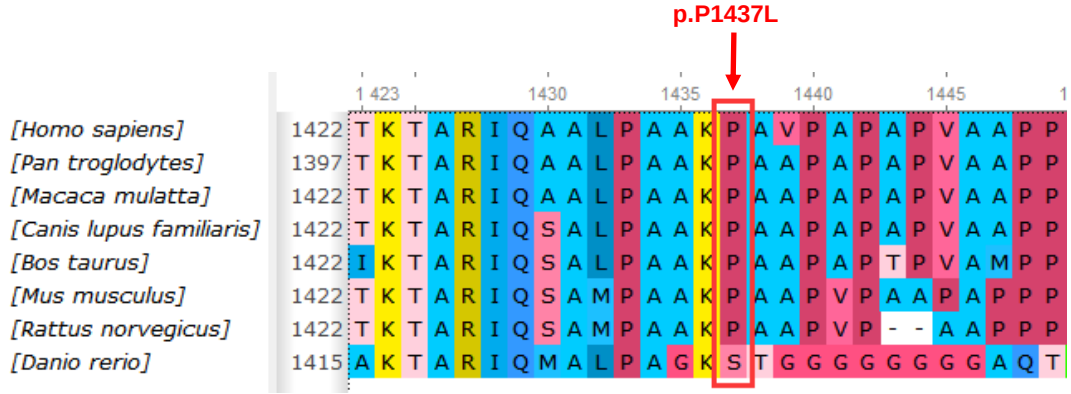
NT45-II:1（F/39Y）

PCDH15 c.4310C>T, p.P1437L



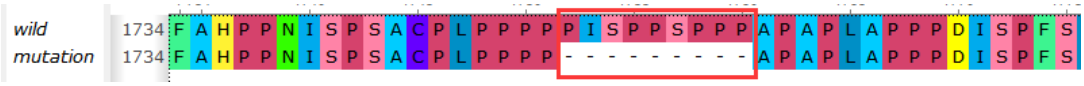
PCDH15 c.5254_5280del, p.1752_1760del





There is no protein structural homology-model for p.P1437L.

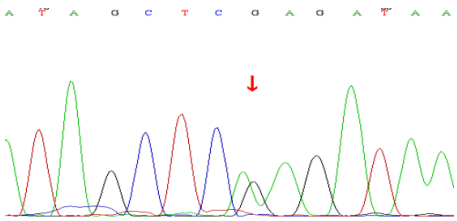
Mutation (p.1752_1760delPISPPSPPP)



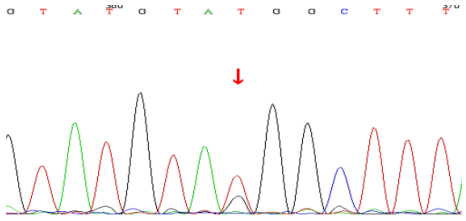
There is no protein structural homology-model for p.1752_1760delPISPPSPPP.

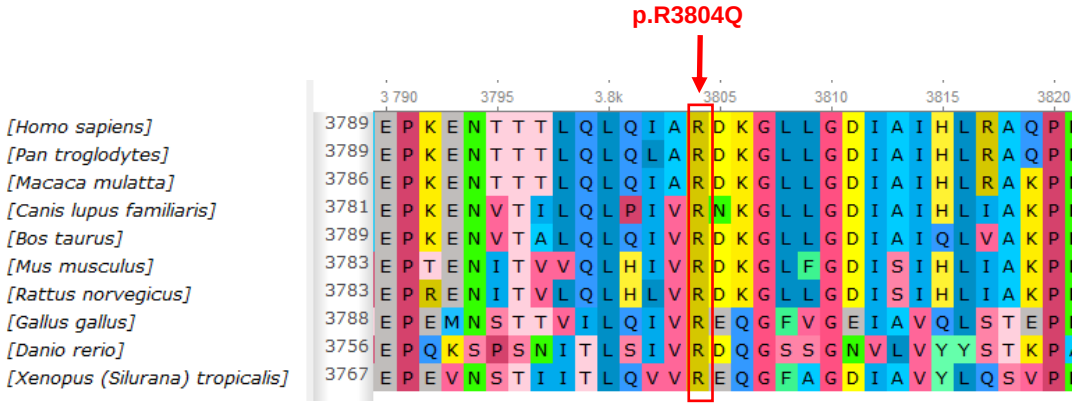
NT46-II:6（F/61Y）

ADGRV1 c.11411G>A, p.R3804Q



ADGRV1 c.13893+8T>G

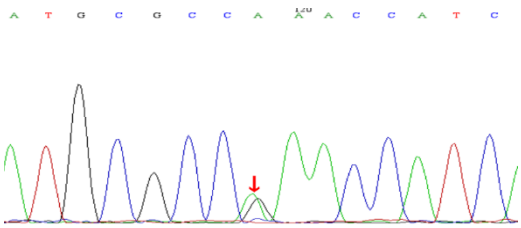




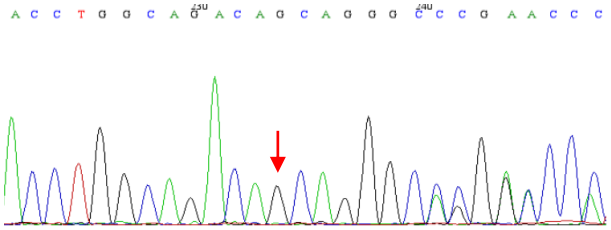
There is no protein structural homology-model for p.R3804Q.

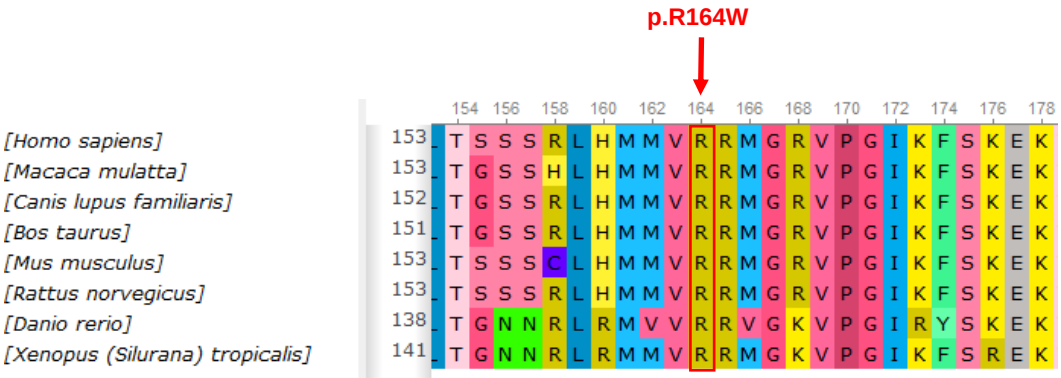
NT-47-II:1（M/2Y）

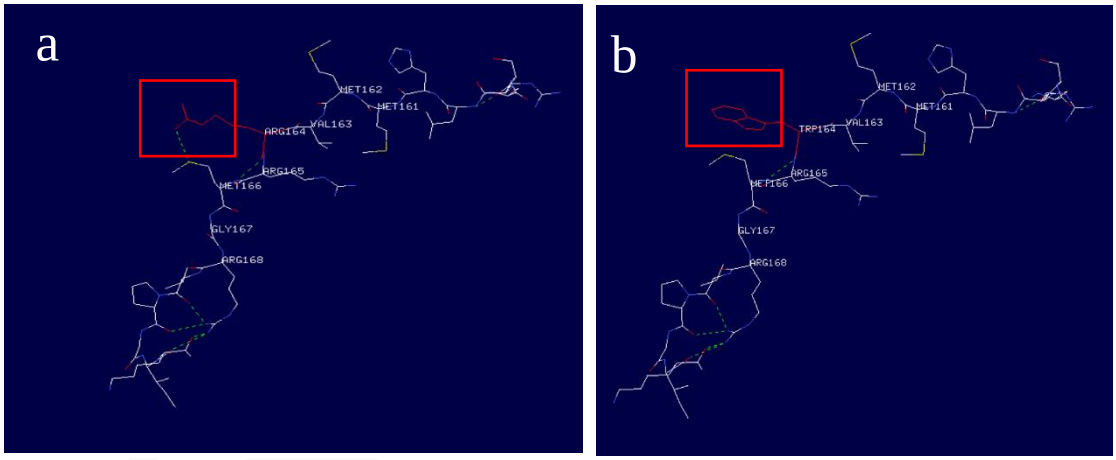
PDZD7 c.490C>T, p.R164W



PDZD7 c.1574_1597del, p.525_533del

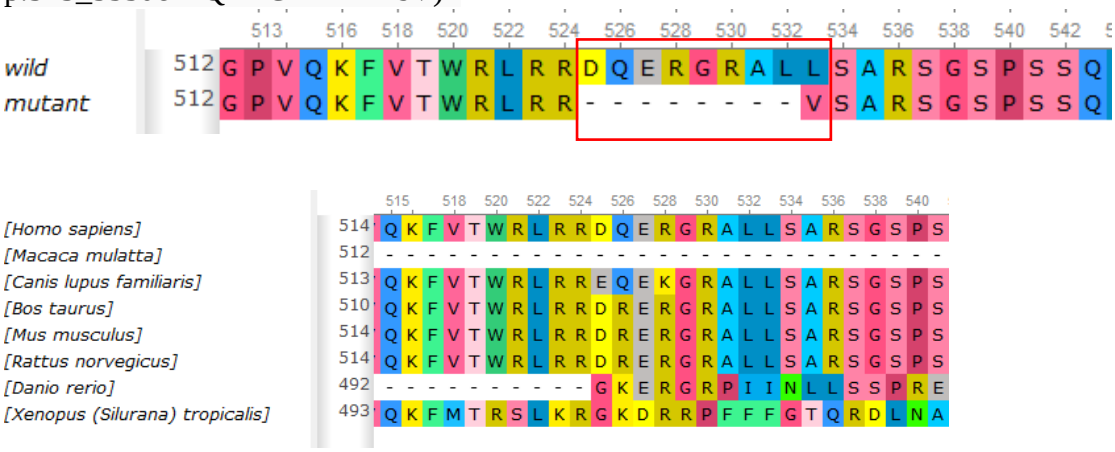






Wild（a），Mutation p.R164W（b）: A hydrogen bond between 164 and 166 were broken after the 164 Trp mutation.

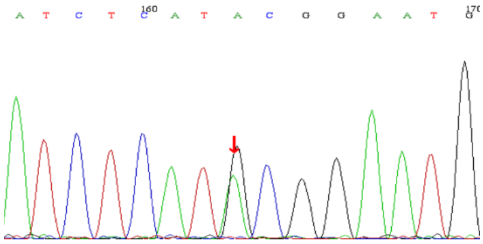
PDZD7(c.1574_1597delACCAGGAGAGGGGCCGGGCCCTGC, p.525_533delDQERGRALLinsV)



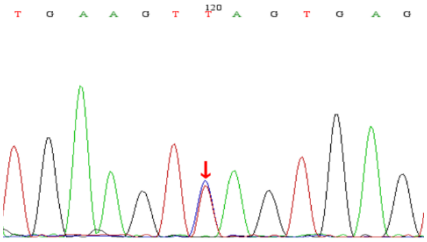
There is no protein structural homology-model for p.525_533delDQERGRALLinsV.

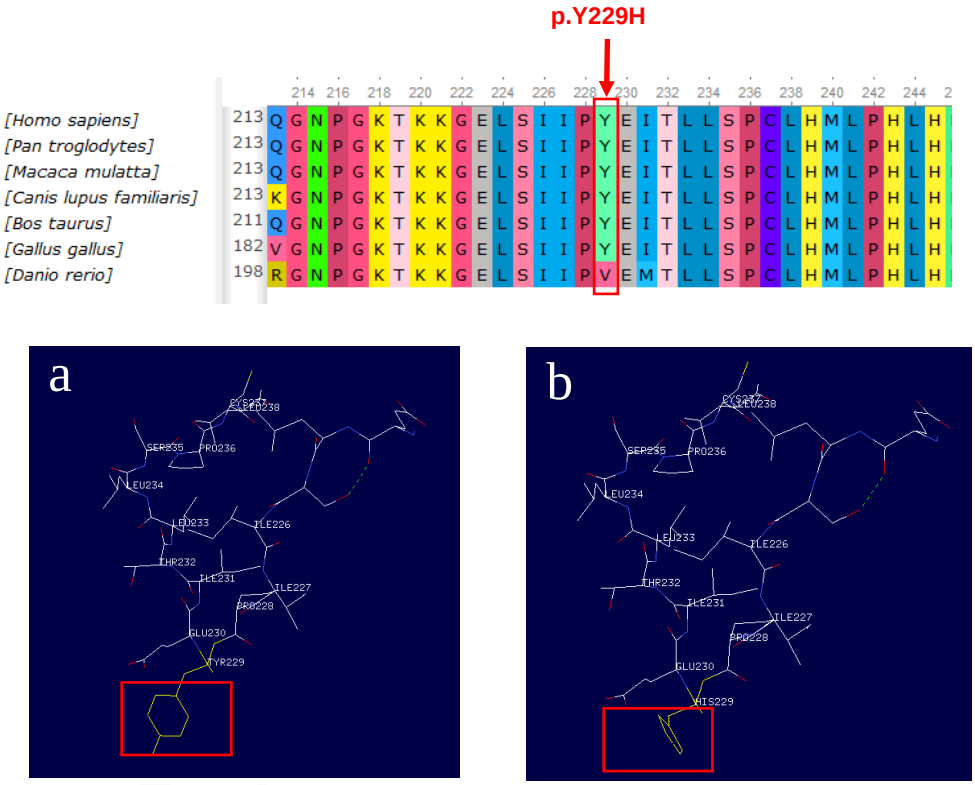
NT-48-II:5（F/47Y）

KARS c.685T>C, p.Y229H

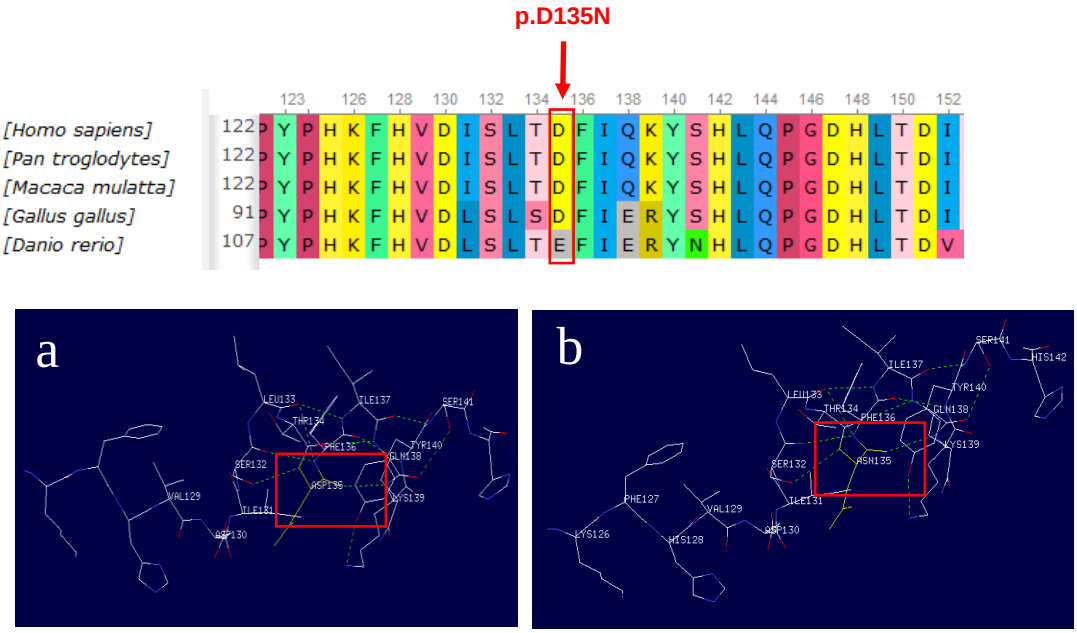


KARS c.403G>A, p.D135N





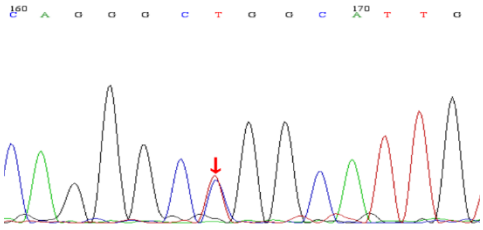
Wild（a），Mutation p.Y229H（b）: Nothing else changed expect the change p.Y229H.



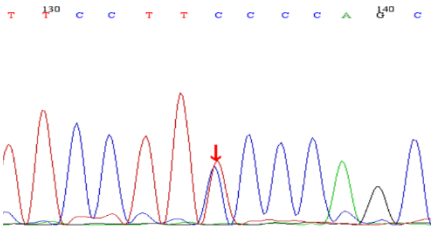
Wild（a），Mutation p.D135N（b）: Nothing else changed expect the change p.D135N.

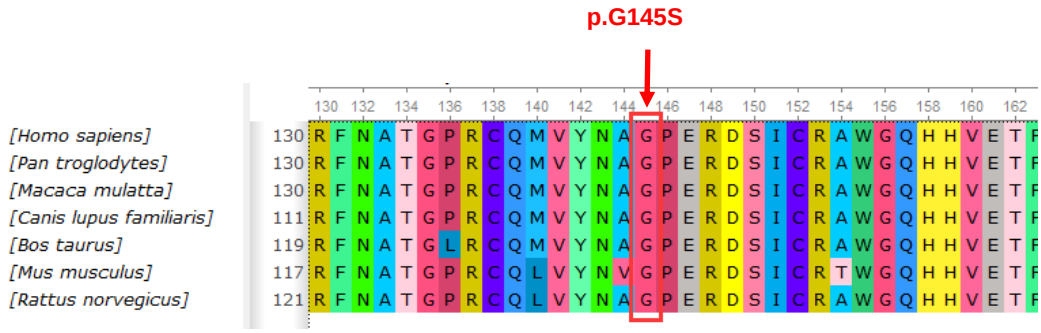
NT-51-II:1（F/30Y）

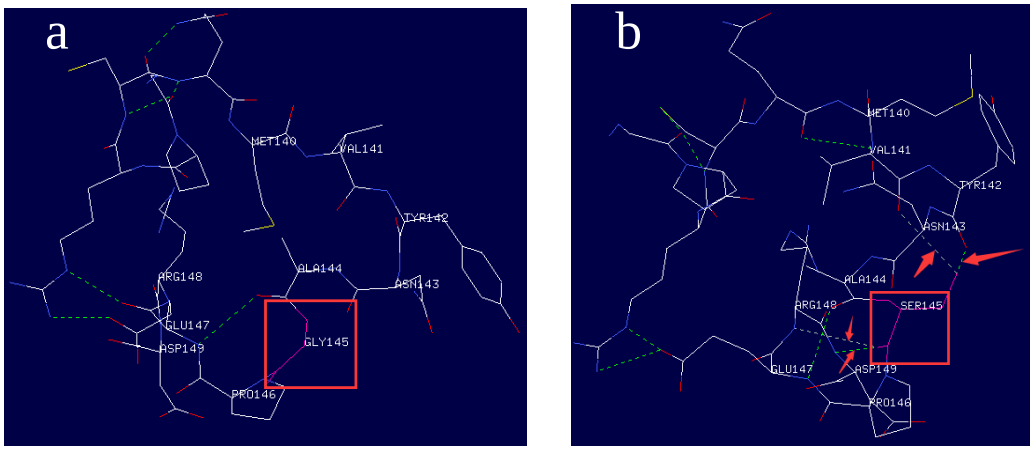
OTOG c.433G>A, p.G145S



OTOG c.2117-6C>T



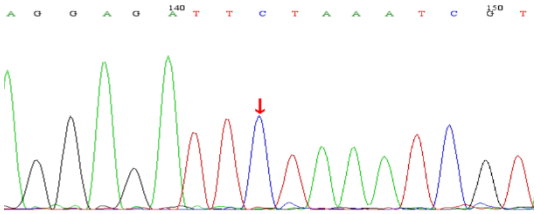


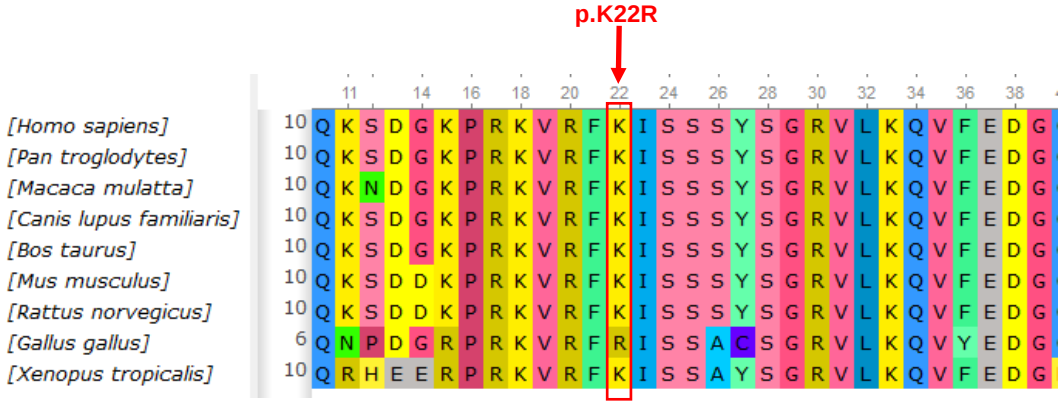


Wild（a），Mutation p.G145S（b）: Four hydrogen bonds were formed among 145 and 141, 142,148,149, respectively after the mutation.

NT-52-II:3（F/72Y）

GRXCR2 c.65A >G, p.K22R





There is no protein structural homology-model for p.K22R.