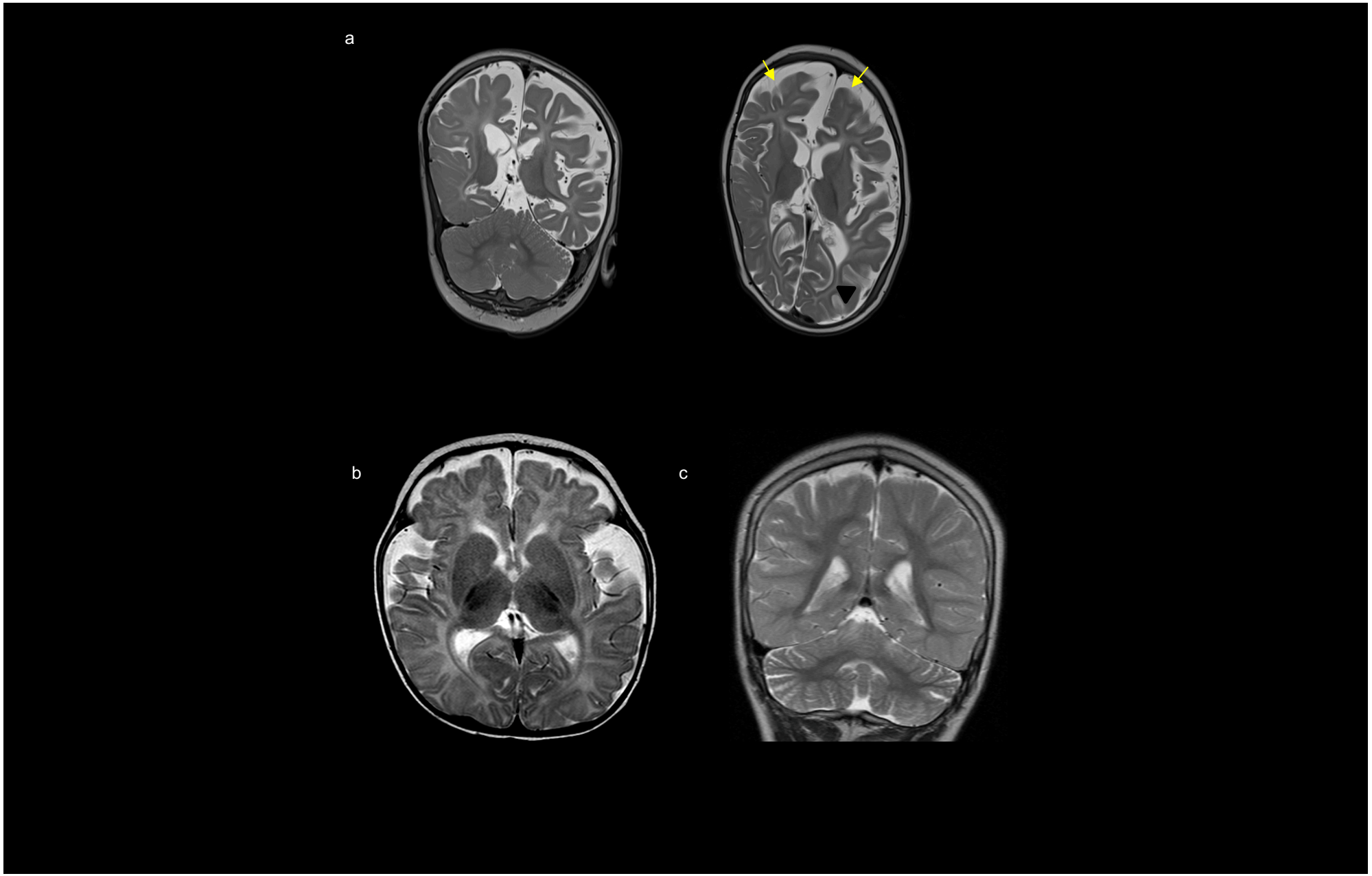


Figure e-1a: severely delayed myelination (black arrowheads), volume loss and frontal predominant atrophy(yellow arrows) with plagio/dolichocephaly at 10 months of age
Figure e-1b: MRI at 5 months of age reveals abnormally open operculum with lack of brain development
Figure e-1c: cerebellar atrophy at 8 years of age

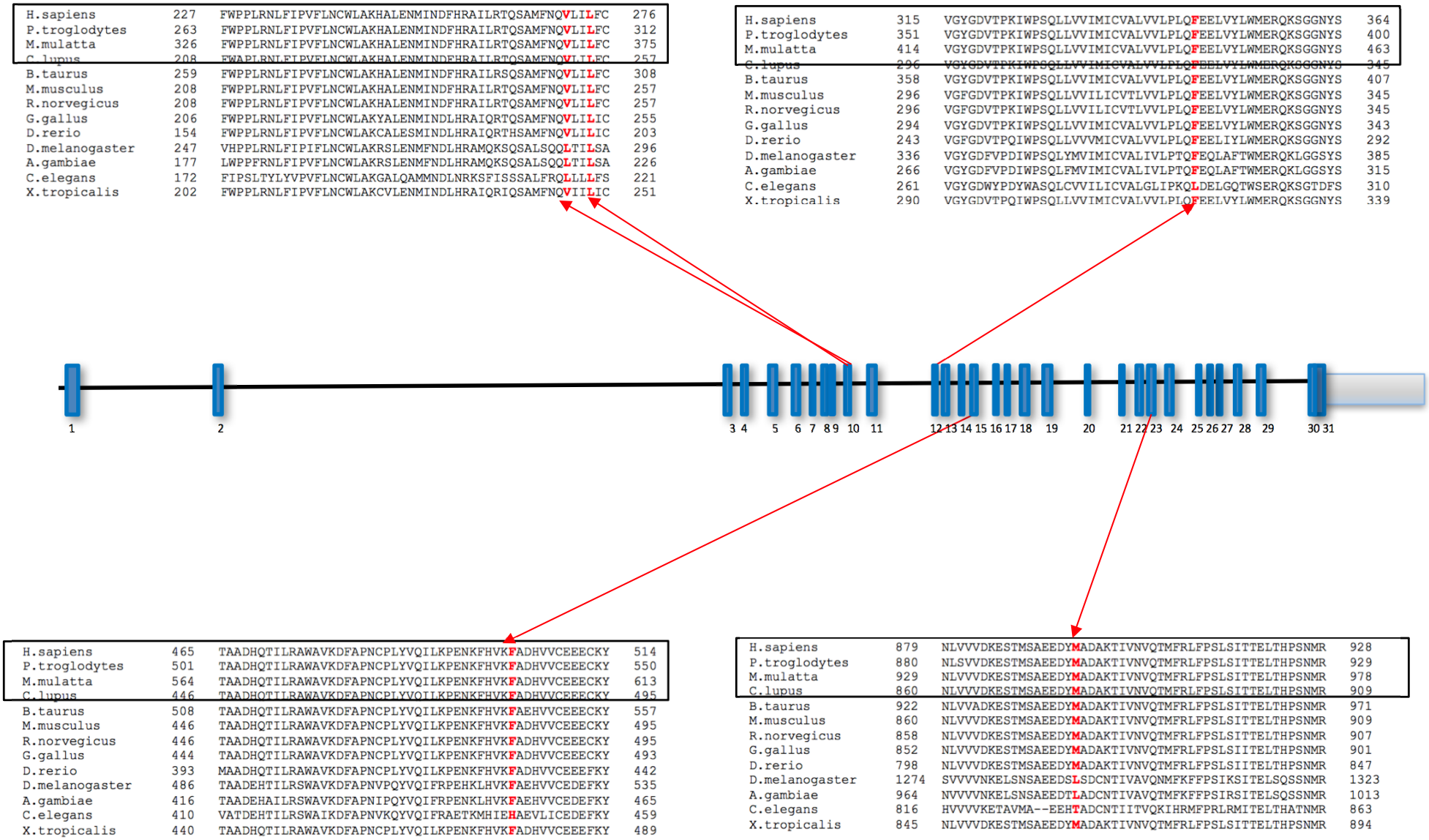


Figure e-2: Schematic drawing showing the 31 exons of *KCNT1* with multiple protein alignments showing residues where novel mutations occur (in red) to be highly conserved: F271 and L274, F346, F502. and M896.

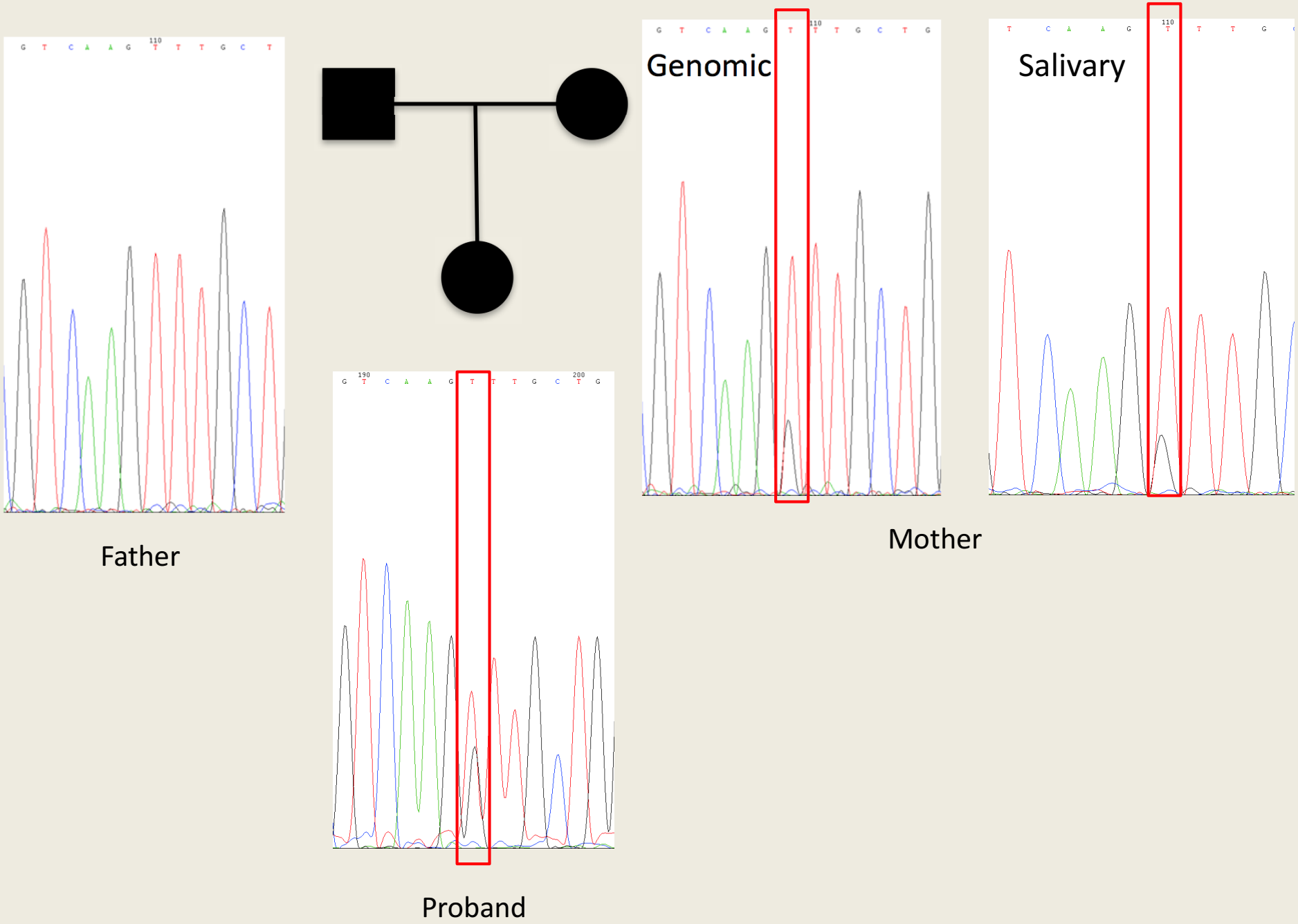
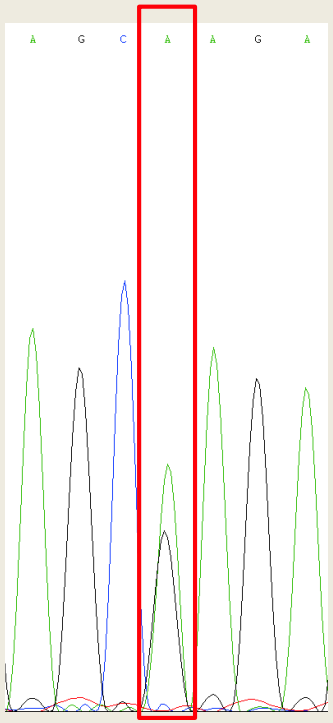
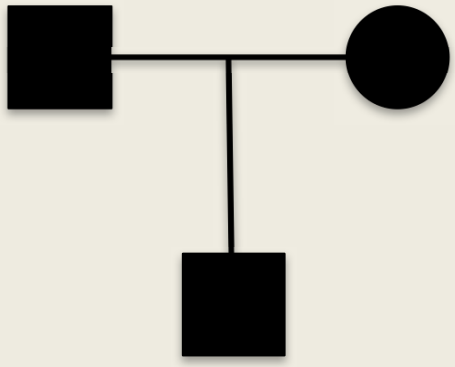
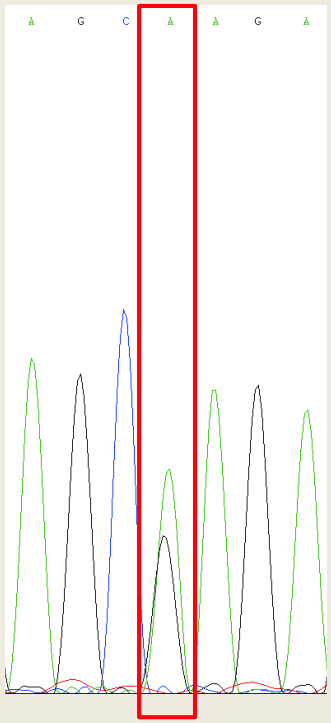


Figure e-3: maternal mosaicism for c.1504T>G, p.Phe502Val is revealed by a lower heterozygous peak which is also present in salivary DNA.

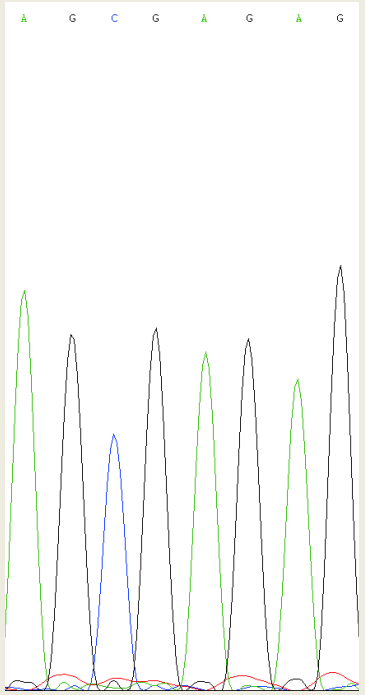


Father





Proband



Mother

Figure e-4: The mutation c.2849G>A p.Arg950Gln identified in Patient 7 appears to be paternally inherited.

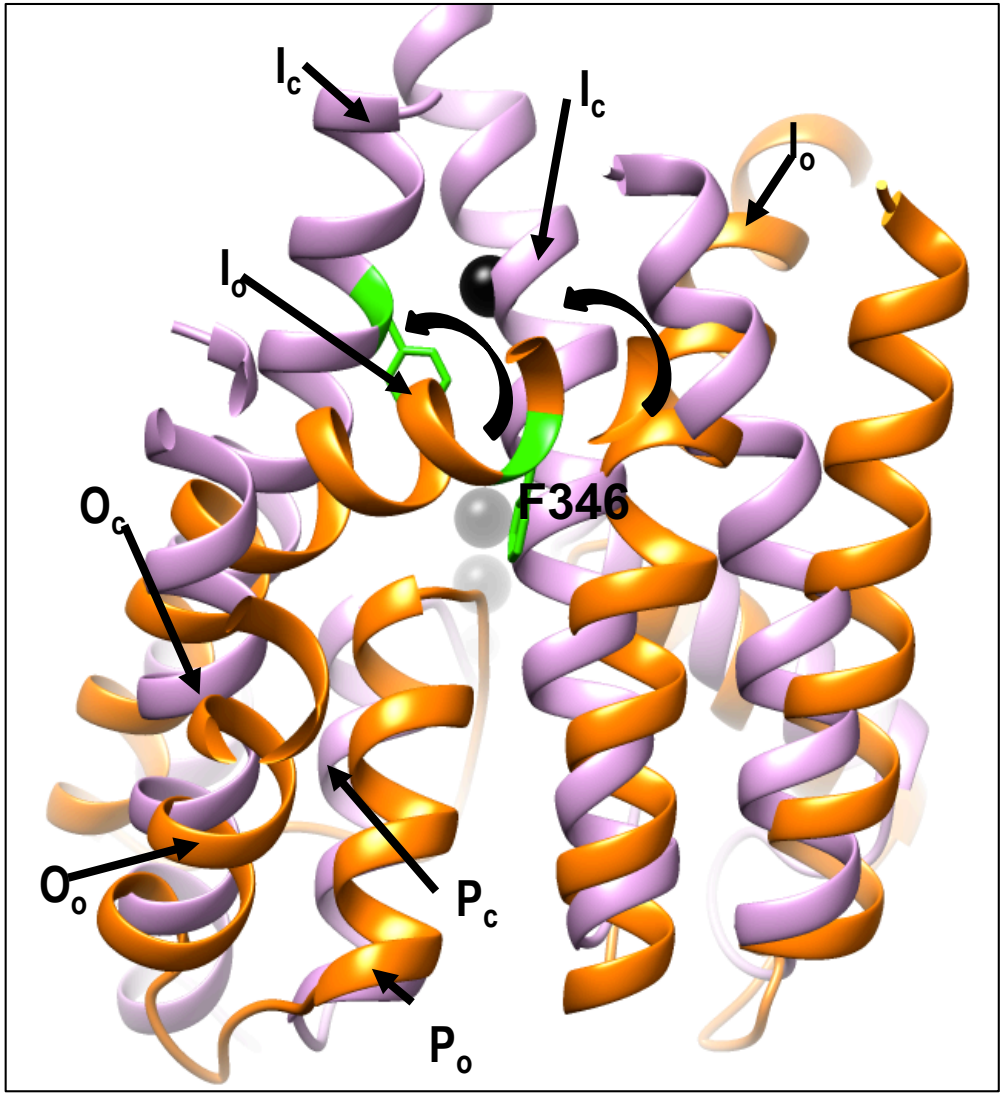


Figure e-5: Open-state (in orange) vs. closed state (in pink) model of the ion channel domain. F346, which is shown in green, is present at the dimeric interface between two inner helices (marked as I_o and I_c for inner helix in open and closed state respectively) (see Figure 1) in the open state but the two helices undergo conformational change in the closed state, as pointed out using black arrows. Potassium ions (shown as black spheres) are modelled into the tetrameric model using structure superposition with the K^+-bound open form (PDBID: 3LDC). The dimer of the open state is modeled based on the biological assembly of the open state of MthK from *Methanothermobacter thermautotrophicus* (PDBID: 3LDC). The dimer of the closed form of the ion channel domain is modeled using the closed form of potassium channel from *Streptomyces lividans* (PDBID: 2A9H). O_c and O_o correspond to outer helices in closed and open states and P_o and P_c represent the pore helices in closed and open state respectively.