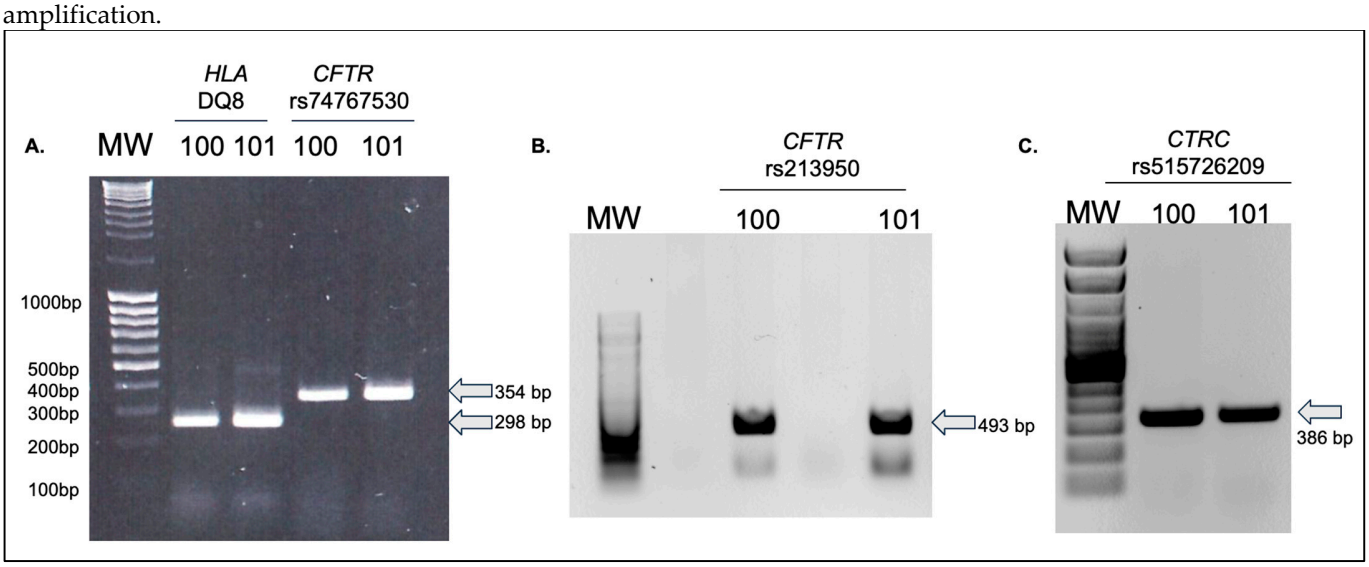
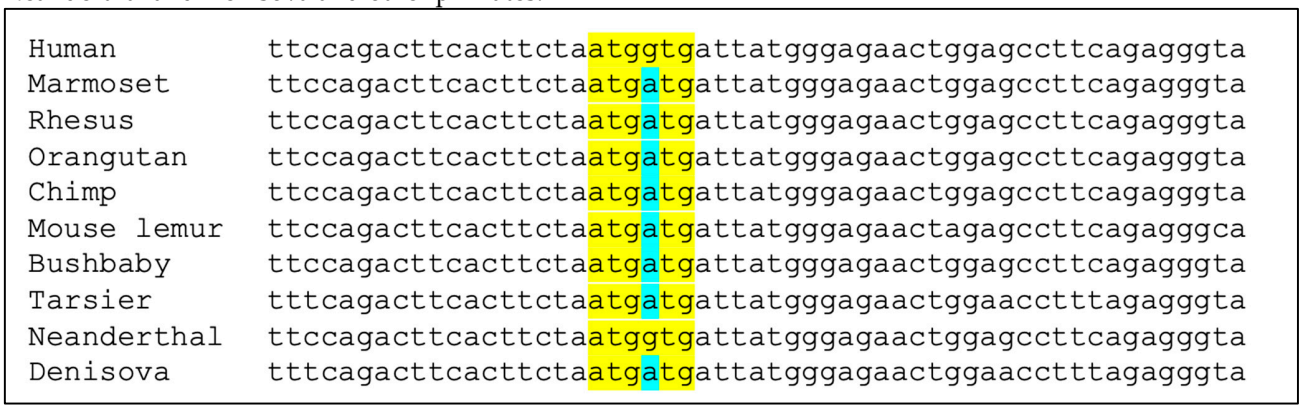
Supplemental Figure S1. PCR amplification of genomic DNA from sample 100 (proband) and 101 (son). **A.** *HLA-DQ8* and *CFTR* rs74767530 amplification. **B.** *CFTR*, rs213950 amplification **C.** *CTRC*, rs515726209 amplification.



Supplemental Figure S2. Phylogenetic comparison of the CTRC protein coding sequence from Humans, Neanderthal and Denisova and other primates.



Supplemental Table S1. Primers used for PCR amplification and sequencing of regions of interest.

Gene/variant	Forward Primer	Reverse Primer	Amplicon Size
CFTR/ rs74767530	5′-ACAGGCCTATACAGAGCCCA-3′	5′-AGCAGTGTTCAAATCTCACCCT-3′	493 bp
CFTR/ rs213950	5′-TGTGCATAGCAGAGTACCTGAA-3′	5′-TTGGCATGCTTTGATGACGC-3′	354 bp
CTRC/ rs515726209	5′-AGGTAAGCCTGTGTAGGGCT-3′	5′-AACTGAGTTACTGGGTGTGAGT-3′	333 bp
HLA-DQ8/ rs7454108	5′-GAGACCCCTTTGCAATCT-3′	5′-ATAATGGGAAACATCAGGCAGA-3′	495 bp

Supplemental Table S2. Effect of variants on protein stability according to I-Mutant 2.0. https://folding.biofold.org/cgi-bin/i-mutant2.0.cgi and MutPro 1.1 https://mupro.proteomics.ics.uci.edu/cgi-bin/predict.pl

I-Mutant 2.0 Stability Prediction			
Variant	**Delta delta G-Free Energy Change Value (kcal/mol)**	**Reliability Index (1-10 with 10 most reliable)**	**Stability**
CFTR rs213950 Val470Met	-1.53	7	Decreased
CTRC rs515726209 Ala73Thr	-1.00	7	Decreased
MuPro 1.0 Stability Prediction			
Variant	**Delta delta G-Free Energy Change Value (kcal/mol)**	**Confidence Score Smaller = more confident prediction**	**Stability**
CFTR rs213950 Val470Met	-1.07	-0.731	Decreased
CTRC rs515726209 Ala73Thr	-1.64	-0.998	Decreased