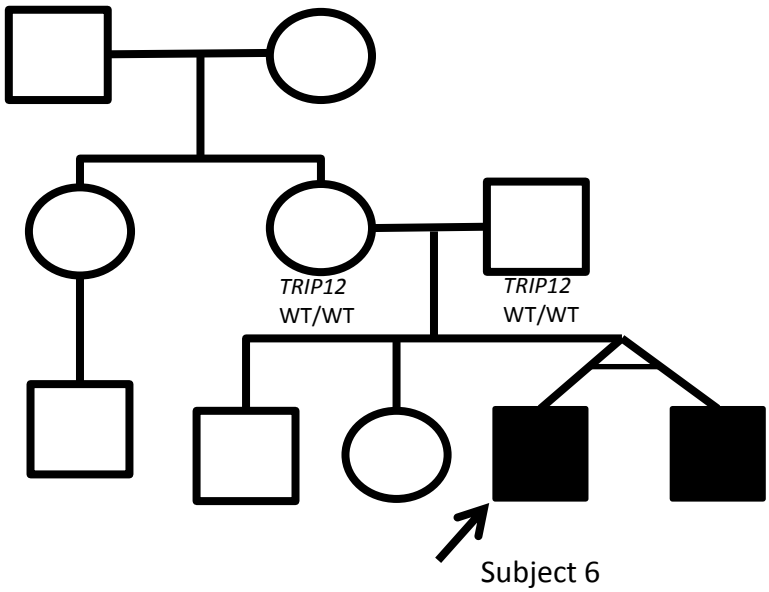
Supplementary Figure S1.

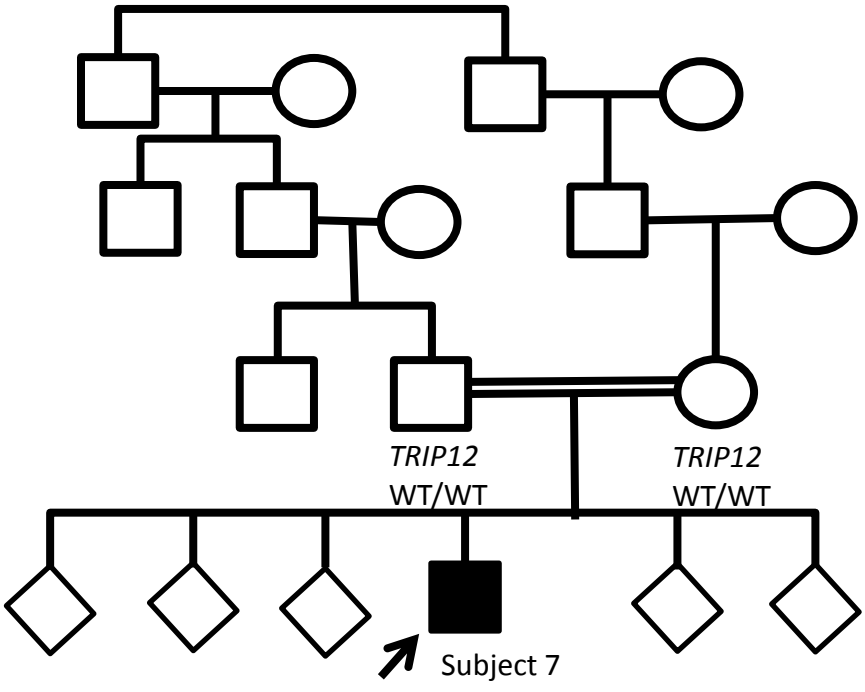
Family 6



Subject 6
4 years

TRIP12 c.3446_3447delCA
p.S1149*

Family 7

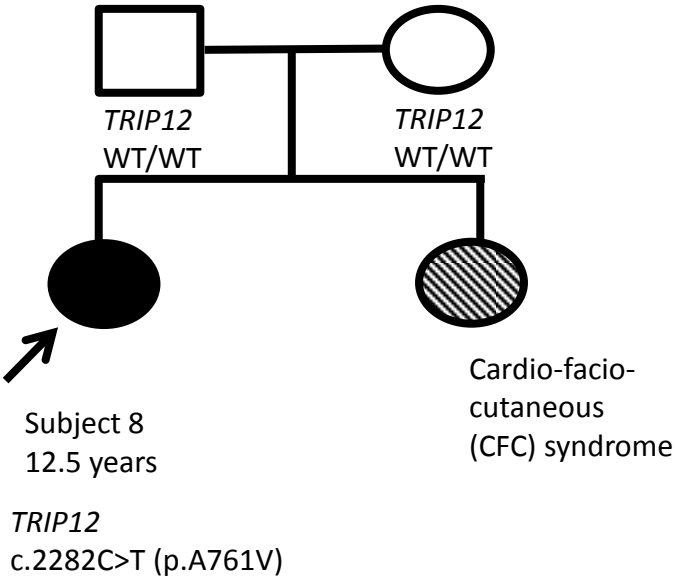


Subject 7
10 years

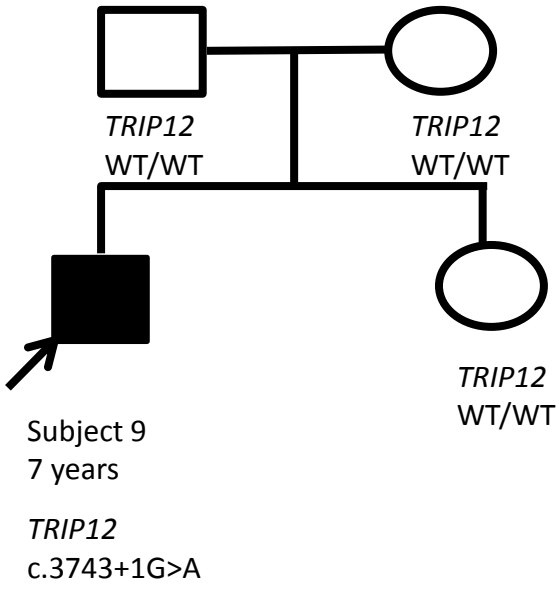
TRIP12 c.2979dupA
p.G994Rfs*5

Supplementary Figure S1.

Family 8

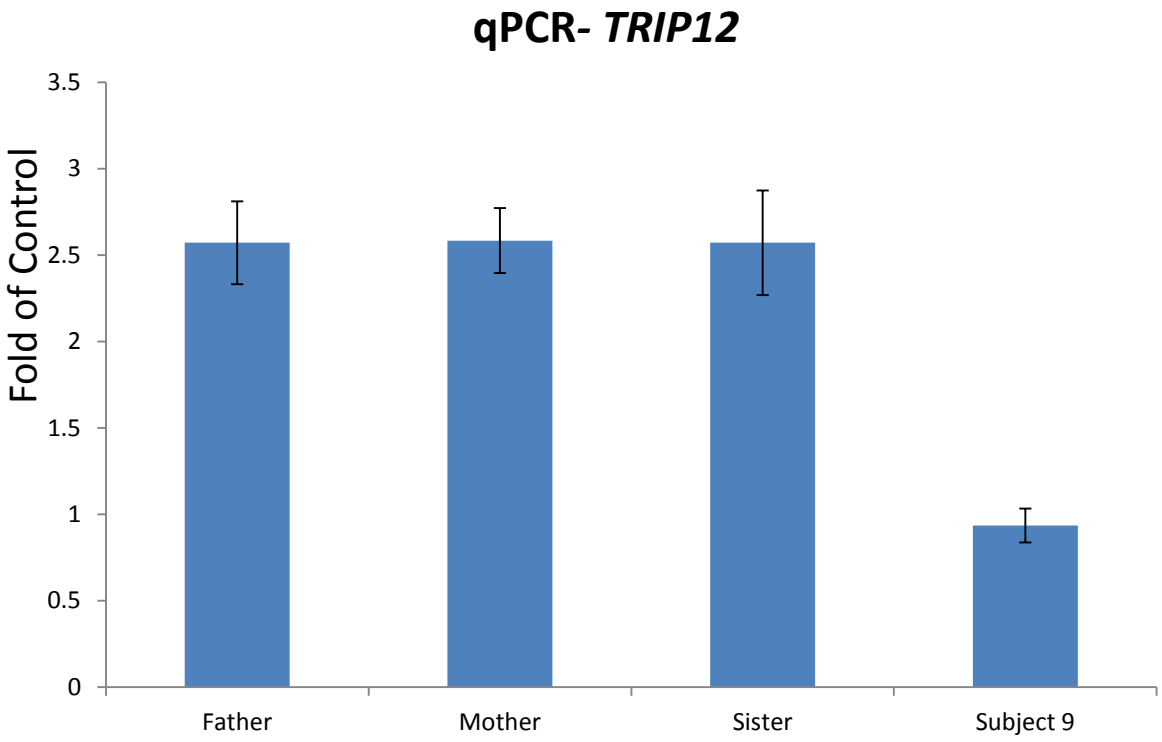


Family 9



Supplementary Figure S1. Pedigrees and genotypes of familes 6-9. The affected individuals are represented by filled symbols, and probands are indicated by arrows. Genotypes of the respective mutations are indicated on the bottom of each pedigree.

Supplementary Figure S2

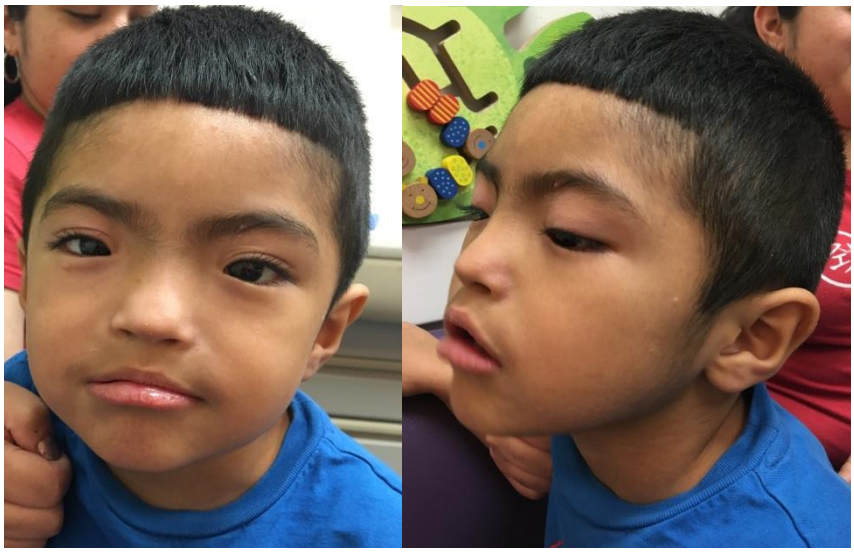


Supplementary Figure S2. Quantitative real-time PCR showed that *TRIP12* expression in the blood samples of subjects 9 was dramatically reduced comparing to the family member controls. Including father, mother and an unaffected sister. GAPDH was used as an internal control. The small number of patients available for analysis precludes statistical analysis to determine whether this difference is significant.

Supplementary Figure S3

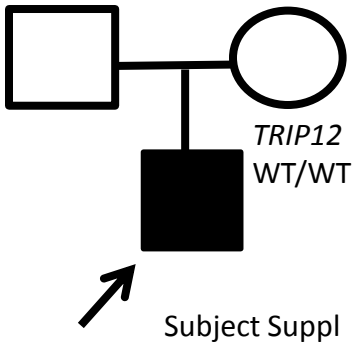
a

Subject #Suppl 1



b

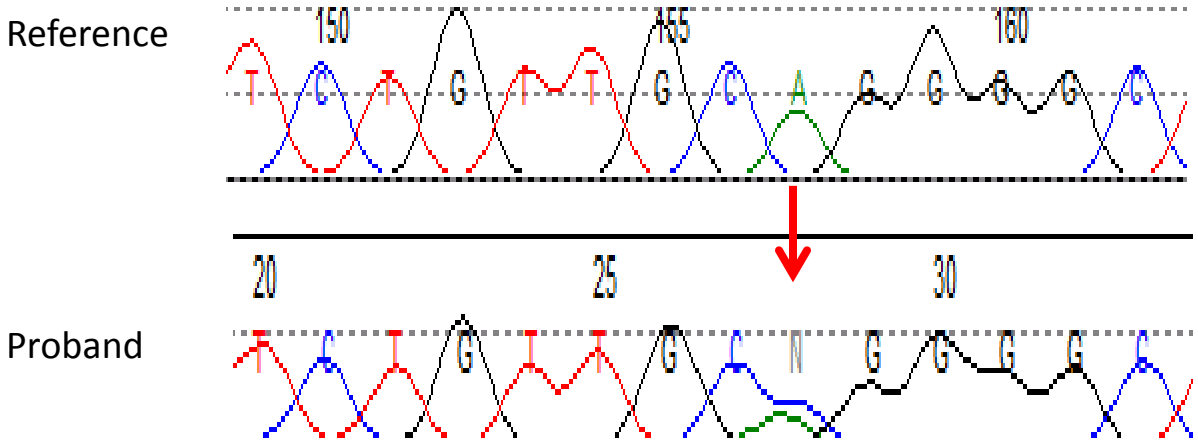
Family
#Suppl 1



Supplementary Figure S3. (a) Photographs of supplemental subject 1 are shown, (b) Pedigree and genotypes of family #Suppl. 1.

Supplementary Figure S4

a Subject suppl 1 (c.1145-2A>C)

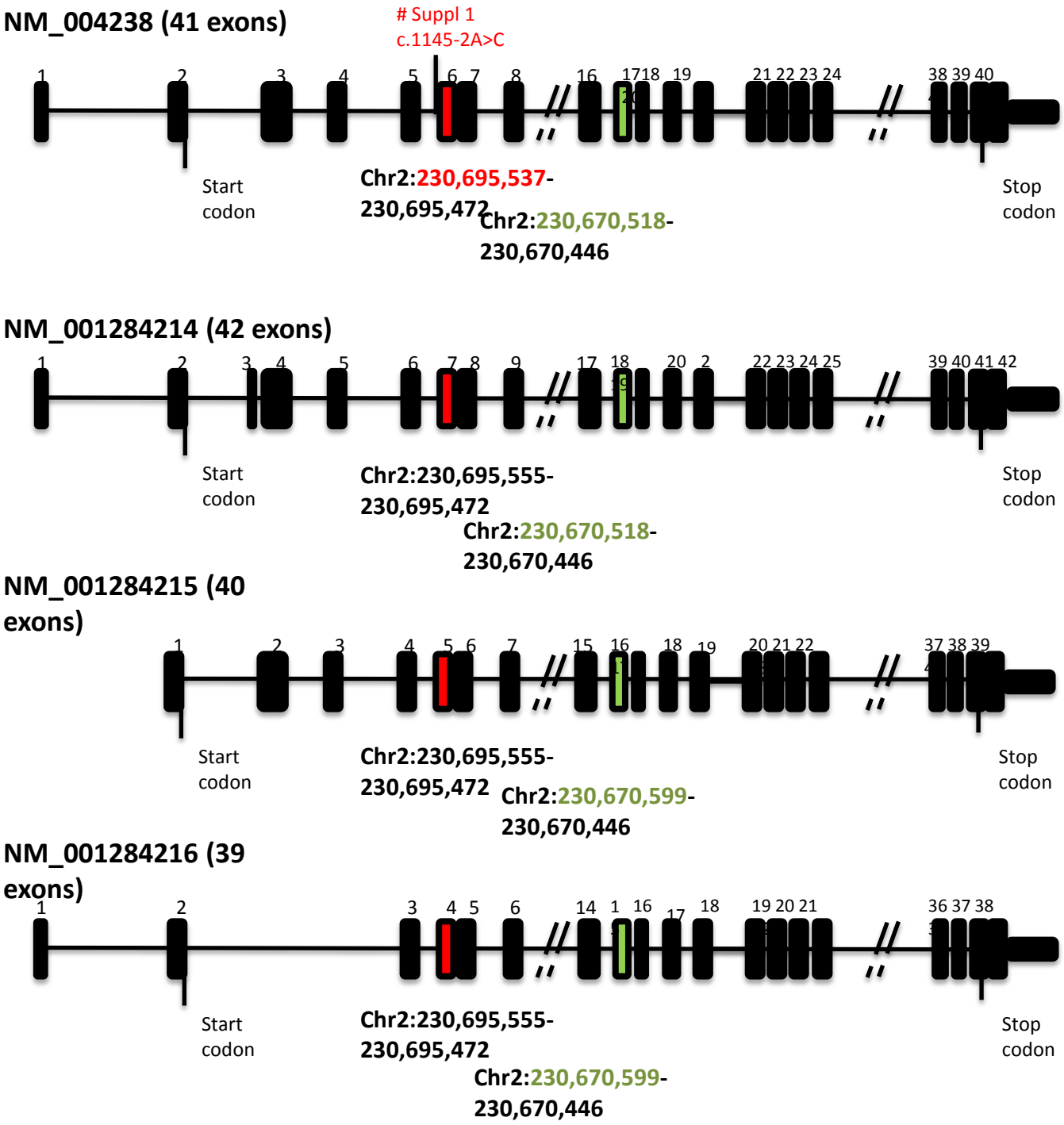


b Acceptor Sites prediction

	SSF [0-100]	MaxEnt [0-16]	NNSPLICE [0-1]	GeneSplicer [0-15]	HSF [0-100]
Threshold	*≥ 70*	*≥ 0*	*≥ 0.01*	*≥ 0*	*≥ 65*
c.1145-2A>C	**NA**	**3.32 ⇒ —**	**0.61 ⇒ —**	**3.32 ⇒ —**	**90.54 ⇒ —**

Supplementary Figure S4. (a) Chromatograms from the proband and reference hare been shown. (b) Results of in silico analysis of the *TRIP12* c.1145-2A>C variant found in subject #Suppl. 1 using four splicing prediction tools included in Alamut v2.7. The threshold used by each prediction tool indicates that above this threshold the positions are predicted to be true splice-sites. All four prediction tools suggested that the acceptor splice site was abolished at the variant position.

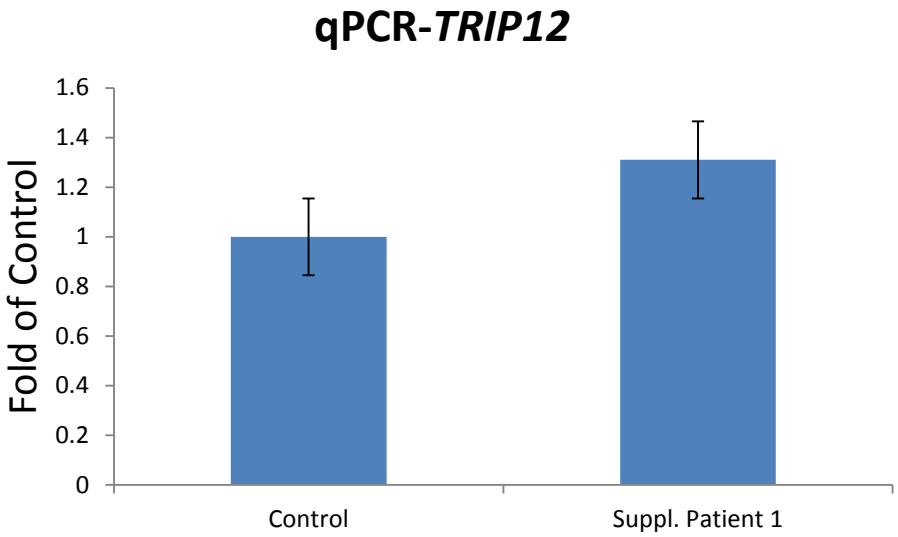
Supplementary Figure S5



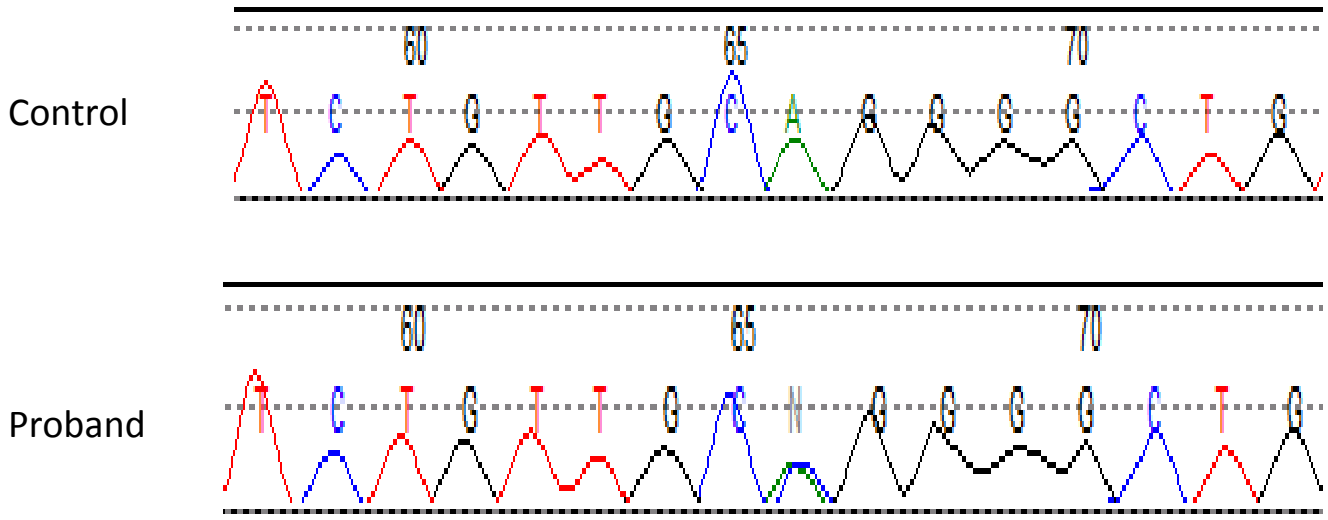
Supplementary Figure S5. Four *TRIP12* RefSeq isoforms: NM_004238, NM_001284214, NM_001284215, and NM_001284216. The exons highlighted in red and green mark two exons with alternative splicing sites which result in slightly different sizes of exons among different isoforms. Their respective genomic coordinate was indicated below each highlighted exon. The variant marked in red, found in #Suppl 1, results in loss of a consensus splice site only in isoform NM_004238, while this variant is exonic and synonymous in the other three isoforms.

Supplementary Figure S6

a



b



Supplementary Figure S6 (a) Quantitative real-time PCR showed that *TRIP12* expression in the blood samples of suppl. Patient 1 was similar to an unrelated control. GAPDH was used as an internal control. (b) RNA sequencing did not reveal a novel transcript caused by the splicing mutation in one of four isoforms of *TRIP12* gene. Chromatograms from the proband and an unrelated control have been shown.