Hypoplastic AI with Highly Variable Expressivity Caused by *ENAM* Mutations

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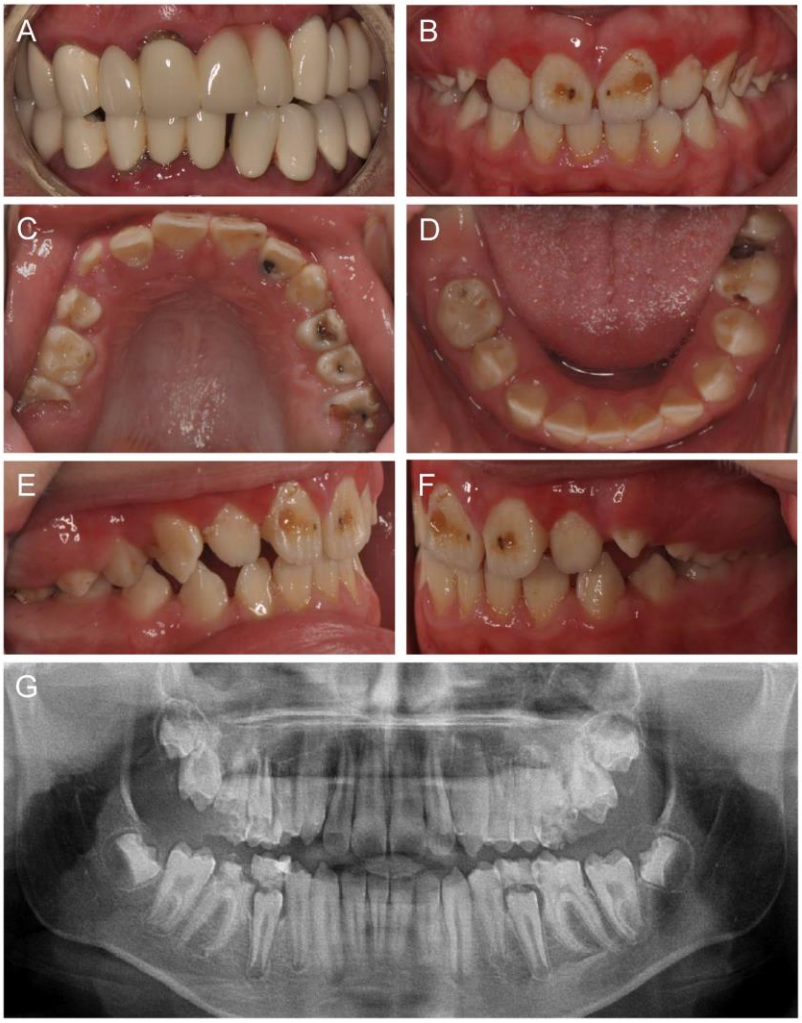
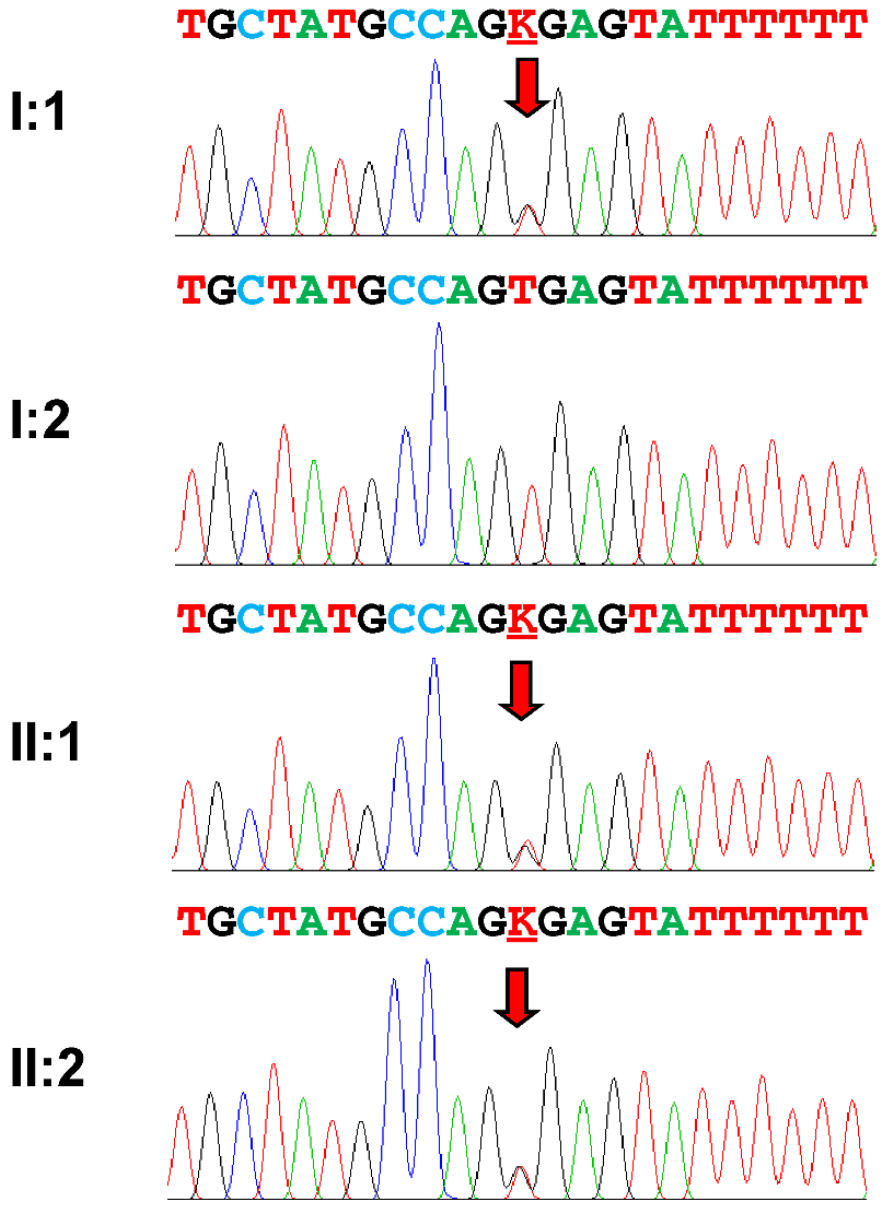
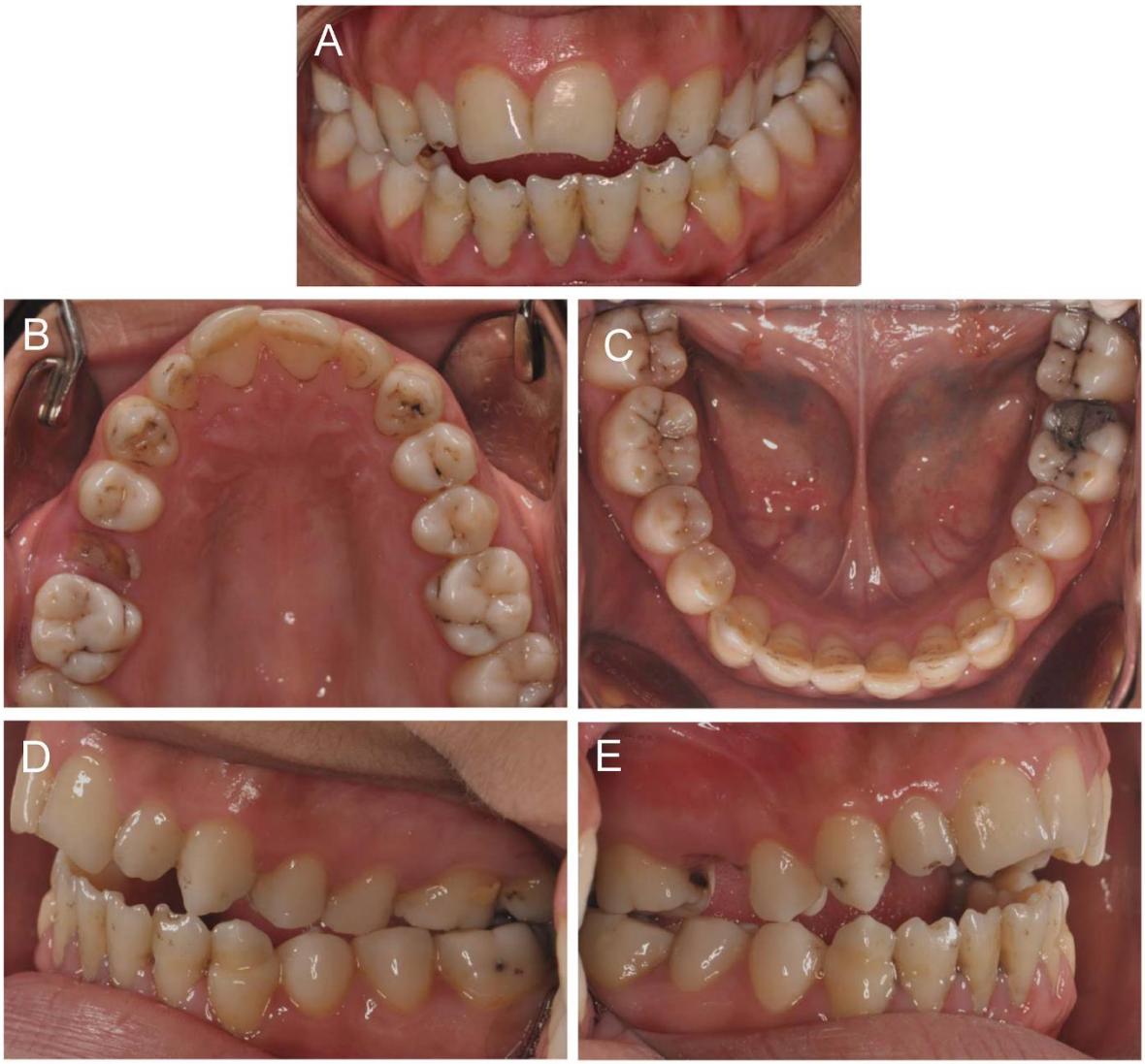
Appendix



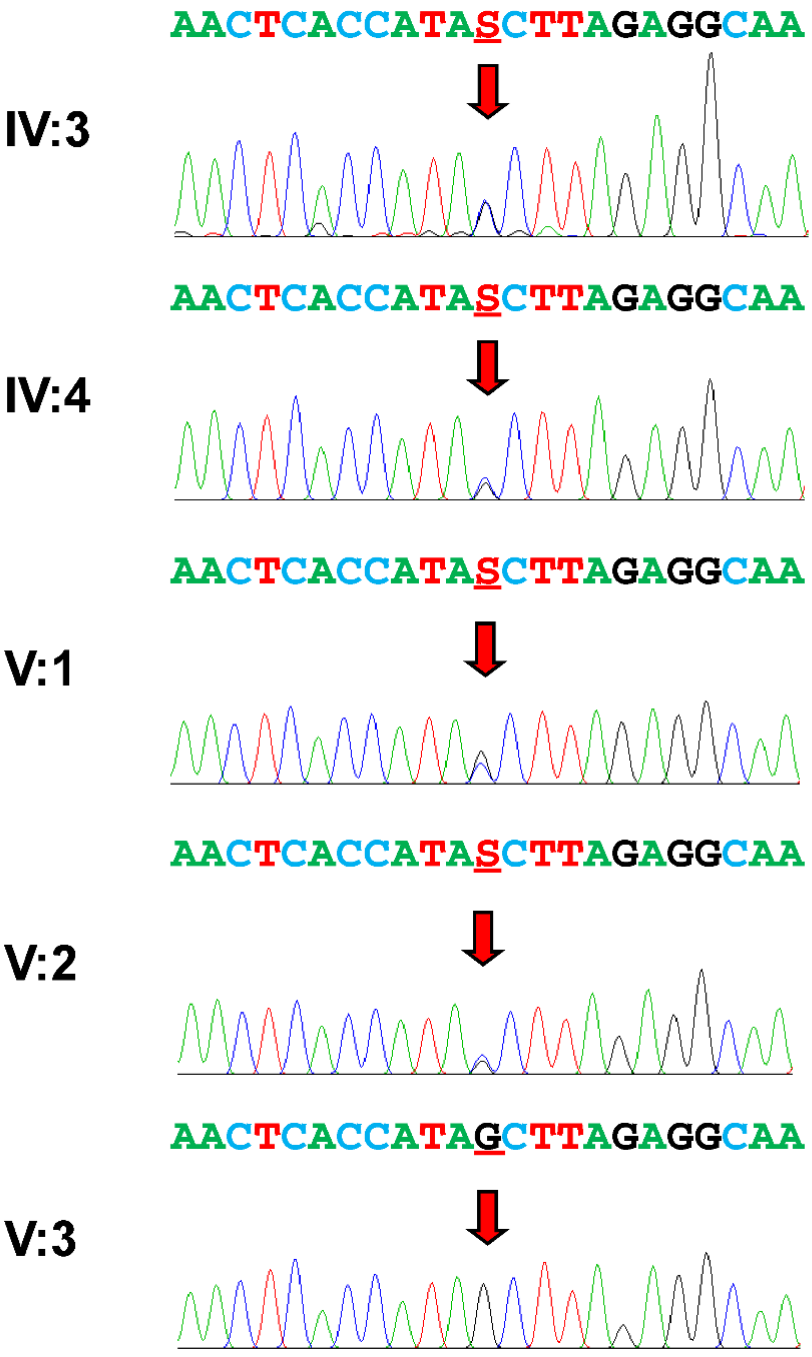
Appendix Figure 1. Clinical photos and panoramic radiograph from family 1. (**A**) Frontal clinical photo of the father (I:1). (**B-F**) Clinical photo of the affected brother of the proband (II:2) at age 11. Generalized hypoplastic enamel can be seen in all teeth. (**G**) Panoramic radiograph of the proband at age 11.



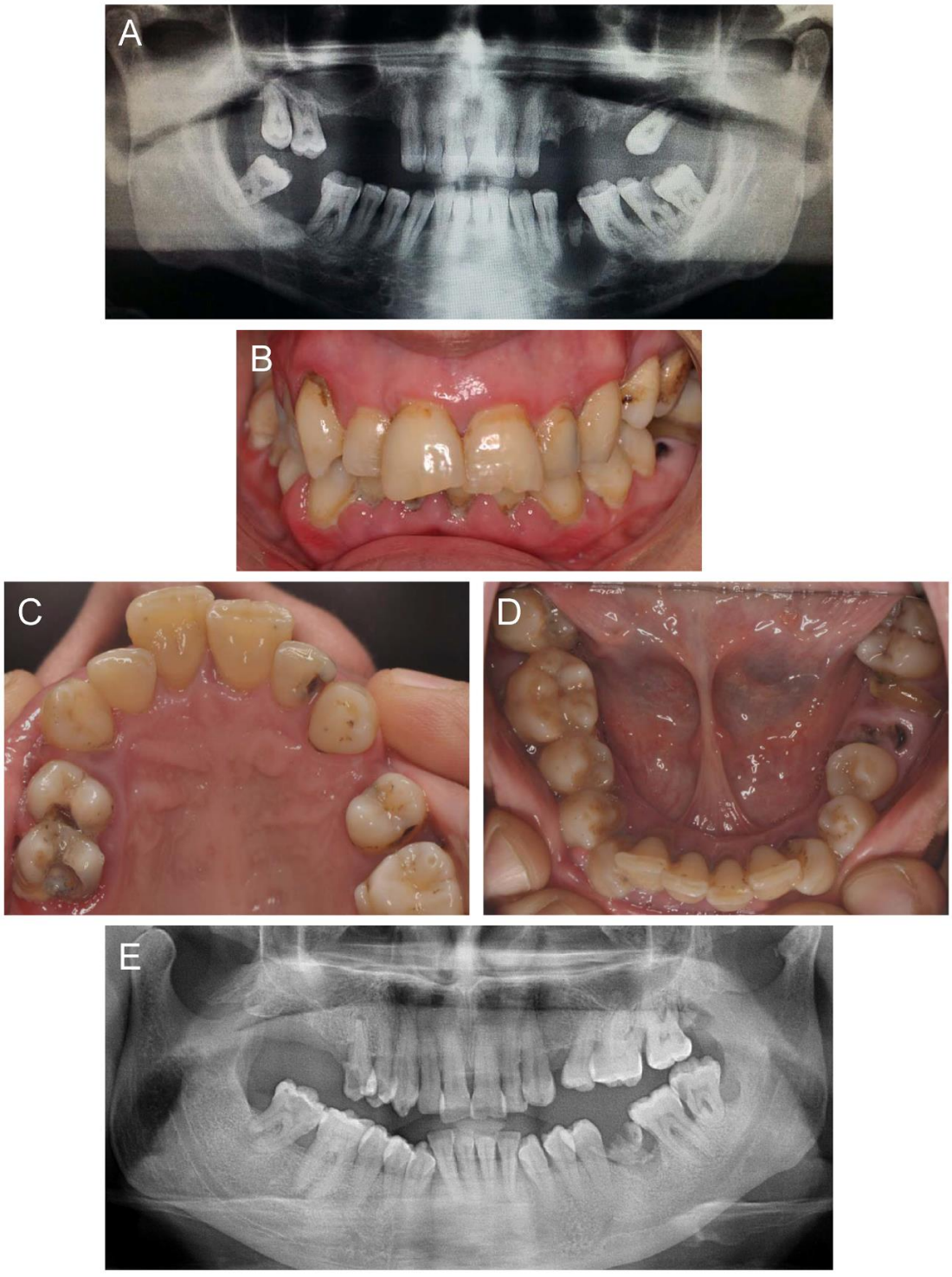
Appendix Figure 2. Mutational analysis of family 1. Sequencing chromatograms of all participating individuals. Nucleotide sequences are shown above the chromatograms. A red arrow indicates the mutation [*ENAM* (NM_031889); c.123+2T>G]. Mutant sequences are underlined with red line (K; T or G).



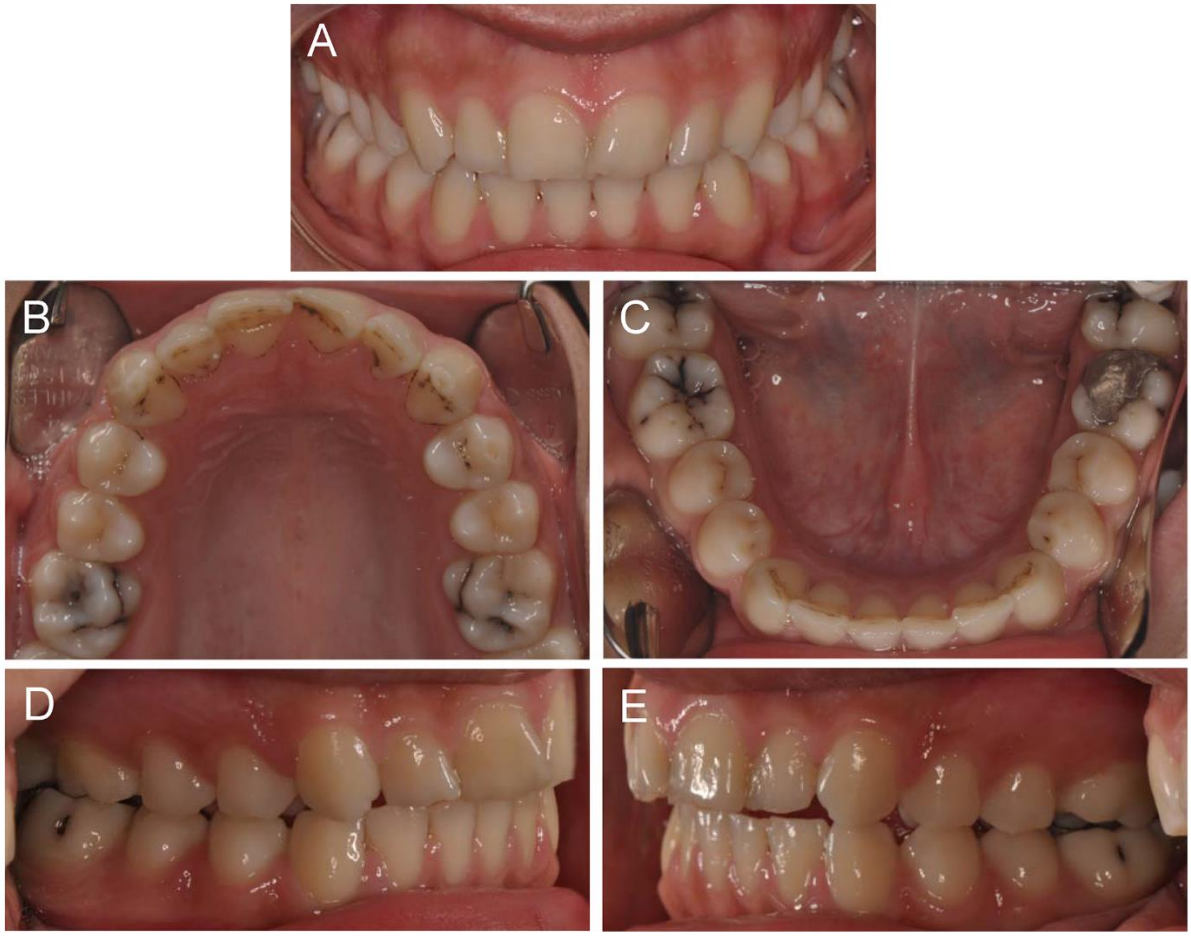
Appendix Figure 3. Clinical photos of the affected individual (V:1) in family 2 at age 22. (**A**) Frontal clinical photo. (**B**) Maxillary occlusal photo. (**C**) Mandibular occlusal photo. (**D**) Mirror image of right buccal photo. (**E**) Mirror image of left buccal photo.



Appendix Figure 4. Mutational analysis of family 2. Sequencing chromatograms of all participating individuals. Nucleotide sequences are shown above the chromatograms. A red arrow indicates the mutation [*ENAM* (NM_031889); c.1842C>G, p.(Tyr614*)]. Mutant sequences are underlined with red line (S; C or G).



Appendix Figure 5. Clinical photos of the parents of the proband in family 2. (**A**) Panoramic radiograph of the father of the proband (IV:3). (**B-D**) Clinical photos of the mother of the proband (IV:4). (**E**) Panoramic radiograph of the mother of the proband.



Appendix Figure 6. Clinical photos of the individual (V:2) in family 2 at age 19. (**A**) Frontal clinical photo. (**B**) Maxillary occlusal photo. (**C**) Mandibular occlusal photo. (**D**) Mirror image of left buccal photo. (**E**) Mirror image of right buccal photo.

Appendix Table 1. Statistics for exome sequencing.

Sample	Total reads	Mapping rate (%)	Median Target Coverage	Coverage of target region (%)	Fraction of target covered with at least	
					20X	10X
Family 1 II:1	110,797,272	99.8	102	96.9	91.8	93.9
Family 2 V:3	106,235,987	99.4	94	96.9	91.6	93.8

Appendix Table 2. Disease-causing mutations in *ENAM* gene.

Location	cDNA	Protein	Mode of inheritance	References
Exon 4	c.92T>G	p.Leu31Arg	AD	(Brookes et al. 2017)
Exon 4	c.107delA	p.Asn36Ilefs*22	AD	(Simmer et al. 2013)
Intron 4	c.123+1G>A	p.Val19-Pro41del	AD	(Prasad et al. 2016)
Intron 4	c.123+2T>G	p.Val19-Pro41del	AD	This report family 1
Exon 5	c.139delA	p.Met47Cysfs*11	AD	(Wang et al. 2015)
Exon 5	c.157A>T	p.Lys53*	AD	(Kim et al. 2006; Mardh et al. 2002)
Intron 6	c.211-2A>C	p.Met71-Gln157del	AD	(Kim et al. 2005)
Exon 7	c.358C>T	p.Gln120*	AD	(Seymen et al. 2014)
Exon 7	c.406_407insTCAAAA AAGCCGACCACAA	p.Lys136Ilefs*16	AD	(Wang et al. 2015)
Exon 7	c.454G>T	p.Glu152*	AD	(Seymen et al. 2014)
Intron 8	c.534+1G>A	p.Ala158-Gln178del	AD	(Rajpar et al. 2001; Song et al. 2012; Urzua et al. 2005)
Exon 9	c.536G>T	p.Arg179Met	AD	(Gutierrez et al. 2007)
Intron 9	c.588+1delG	p.Asn197Ilefs*81	AD	(Hart et al. 2003; Kida et al. 2002; Kim et al. 2005; Pavlic et al. 2007; Wright et al. 2011)
Exon 10	c.647C>T	p.Ser216Leu	AR/AD	(Chan et al. 2010)
Exon 10	c.737C>A	p.Ser246*	AD	(Ozdemir et al. 2005)
Exon 10	c.1020-1021insAGTCAGTACC AGTACTGTGTC	p.Val340-Met341insSerGlnT yrGlnTyrCysVal	AR/AD	(Ozdemir et al. 2005)
Exon 10	c.1259-1260insAG	p.Pro422Valfs*27	AR/AD	(Chan et al. 2010; Hart et al. 2003; Kang et al. 2009; Lindemeyer et al. 2010; Ozdemir et al. 2005; Pavlic et al. 2007; Wright et al. 2011)
Exon 10	c.1842C>G	p.Tyr614*	AR/AD	This report family 2
Exon 10	c.2991delT	p.Leu998Trpfs*65	AD	(Kang et al. 2009)

*Sequences based on the reference sequence for mRNA (NM_031889.2) and protein (NP_114095.2), where the A of the ATG translation initiation codon is nucleotide 1. These variants can be find in the LOVD database (http://dna2.leeds.ac.uk/LOVD/genes) and the ClinVar database at NCBI (https://www.ncbi.nlm.nih.gov/clinvar/).

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