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Novel *FAM20A* mutation causes autosomal recessive amelogenesis imperfecta

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ABSTRACT

Objective: To relate the peculiar phenotype of amelogenesis imperfecta in a large Bedouin family to the genotype determined by whole genome linkage analysis.
Design: Amelogenesis imperfecta (AI) is a broad group of inherited pathologies affecting enamel formation, characterized by variability in phenotypes, causing mutations and modes of inheritance. Autosomal recessive or compound heterozygous mutations in *FAM20A*, encoding sequence similarity 20, member A, have been shown to cause several AI phenotypes. Five members from a large consanguineous Bedouin family presented with hypoplastic amelogenesis imperfecta with unerupted and resorbed permanent molars. Following Soroka Medical Center IRB approval and informed consent, blood samples were obtained from six affected offspring, five obligatory carriers and two unaffected siblings. Whole genome linkage analysis was performed followed by Sanger sequencing of *FAM20A*.
Results: The sequencing unravelled a novel homozygous deletion mutation in exon 11 (c.1523delC), predicted to insert a premature stop codon (p.Thr508Lysfs*6).
Conclusions: We provide an interesting case of novel mutation in this rare disorder, in which the affected kindred is unique in the large number of family members sharing a similar phenotype.

1. Introduction

Amelogenesis imperfecta (AI) represents a broad spectrum of genetic diseases affecting enamel formation in both primary and permanent dentition. AI is the oldest hereditary disorder affecting enamel, observed in early hominids. It has been described in a *Homo erectus* child from Melka Kunture Ethiopia (Garba IV) dated to circa 1.5 MY.[1] AI has been classified into 14 different subtypes according to the clinical appearance of the enamel and the Mendelian mode of inheritance[2]; however, the molecular genetic basis for only some of the phenotypes has been defined. The prevalence of AI has been reported to be 1:14,000 in the USA,[2] 1:8000 in Israel,[3] 1:4000 in Sweden[4] and as high as 1:700 in the Vasterbotten country of Sweden.[5] The enamel abnormalities have been categorized into three major groups (hypocalcified, hypomaturation and hypoplastic), and the inheritance patterns reported include autosomal dominant or recessive as well as X-linked dominant or recessive heredity.[2] Distinctive clinical features may be observed in each

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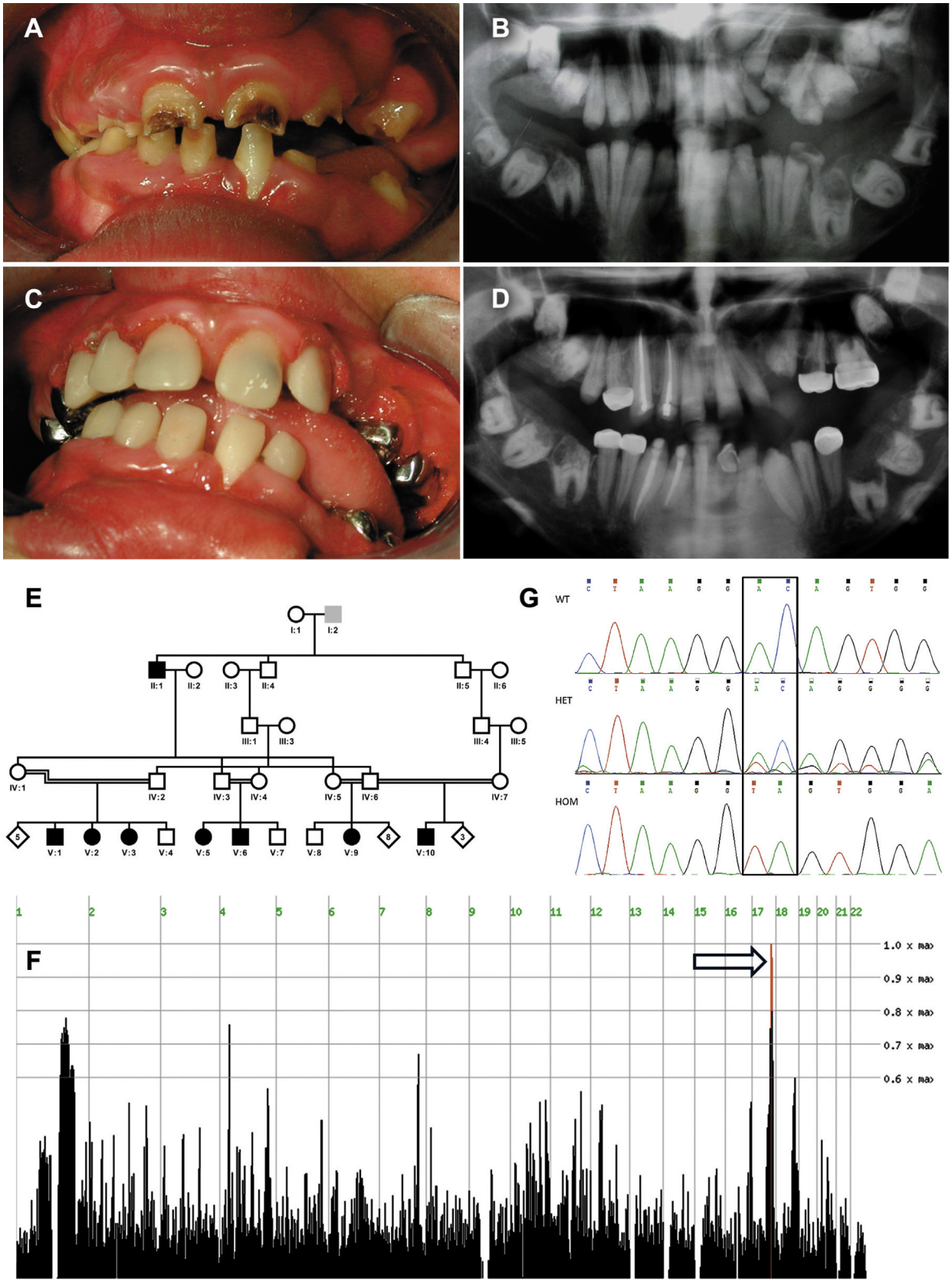

Fig. 1 – Clinical and molecular studies. (A) Affected individual – frontal view. Note the very thin enamel on the gingival half of the teeth crown and the exposed dentine on the occlusal half of the crowns. (B) Affected individual – panoramic view. Note the missing enamel on all teeth, the un-erupted permanent molars and upper left canine teeth and the absorption of the first molars crowns. (C) The end of stage 1 repair procedure. Note the composite restorations on anterior permanent teeth,