

Investigating the Role of the *PTH1R* gene in Individuals Affected with PFE

Heather M. Hendricks

Mutations in the *PTH1R* gene are associated with the non-syndromic dental disorder, primary failure of eruption (PFE), marked by clinical eruption failure of secondary teeth in the absence of mechanical obstruction. Clinical consequences include unsuccessful orthodontic extrusion, multiple extractions and/or surgical intervention to restore normal function. Studies in our laboratory revealed alterations in coding and non-coding regions that are associated with affected individuals.

Objective: The objective of this study was to test the hypothesis that PFE is a distinct clinical entity caused by mutations in the *PTH1R* gene.

Methods: Panoramic radiographs and intra-oral photos were analyzed to determine PFE classification including pattern of affected teeth, intra- versus supra-osseous eruption failure and uni- or bilateral affection etc. as described previously. Previously identified mutations and newly sequenced PCR products of *PTH1R* were analyzed for familial and sporadic cases of PFE.

Results: Out of 26 subjects clinically diagnosed with PFE, 15 harbored a genetic mutation in *PTH1R* and 8 exhibited a polymorphism/SNP in a non-coding region. Phenotypic analysis revealed that 100% of cases included an infraoccluded first molar in an affected quadrant, 88% also included infraoccluded premolars. Bilateral eruption failure was found in 65% of cases.

Conclusions: Our studies revealed that infraoccluded first molars in at least one quadrant are a consistent feature of PFE irrespective of an associated mutation in *PTH1R* and is therefore pathognomonic for PFE. Mutations in additional candidate genes likely explain the pathogenesis in individuals who did not have a mutation in *PTH1R*. Supported by NIH RR00046.