AAO Foundation Award Final Report

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Award Type	TELP Fellowship Award
Project Title	Identification of a gene locus for familial tooth agenesis in the human genome.
Project Year	1995
Institution	Harvard School of Dental Medicine
Summary/Abstract	Tooth agenesis, the failure of development of certain teeth is the most common anomaly of the human dentition. It may occur as part of a genetic syndrome or as an isolated sporadic or familial finding. The Human Genome Project has given fresh impetus to the experimental investigation of odontogenesis providing the art and science of locating defective dental genes. Genetic linkage analyses in a 28-member-family with autosomal dominant agenesis of second premolars and third molars identified a 10cM locus on chromosome 4p. In addition to establishing the first genetic locus for human tooth agenesis, sequences analyses were performed and demonstrated an Arg31Pro missense mutation in the homeodomain of MSX1 in all affected family members. The Arg31Pro mutation appears to specifically affect the permanent dentition, as suggested by the fact that a 3-year-old boy has full complement of primary teeth while he has an affected genotype. In addition, MSX1 is involved in dental patterning as the effects of this mutation at dental locations other than second premolars and third molars appear incomplete. Presumably either MSX1 is not critical there or other transcription factors have compensated for the defects at these positions.