Genes and Developmental Pathways Involved in Tooth Agenesis in Humans: A Systematic Review

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Objective: Tooth agenesis is a condition of the absence of teeth due to tooth developmental defects. There are three clinical categories of tooth agenesis; hypodontia (one to six missing teeth, excluding third molars), oligodontia (more than six missing teeth) or anodontia (complete absence of teeth). Tooth agenesis results from any defect at early stage of tooth development. Although tooth agenesis is one of the most common dental anomalies, it remains largely unknown what genes and pathways are involved.

Experimental Methods: We conducted a systematic review to determine the genes and variants which cause tooth agenesis. We collected and extracted publications including the information of genetic factors related to tooth agenesis through Scopus, PubMed, Embase, and Medline database search, with the search terms "tooth agenesis" or "hypodontia" or "oligodontia" or "anodontia" and "English". We then performed bioinformatic analyses using the genes and variants related to tooth agenesis, in order to identify common pathways and genes linked to their defects.

Results: We identified 4,481 articles using the search terms above. After the removal of duplicates, 4,236 articles were reviewed through Rayyan and 3,450 records were excluded as per the defined eligibility criteria. A total of 412 papers were further evaluated through full-text review. As a result, we found a total of 189 genes and variants related to tooth agenesis. Next, we performed bioinformatic analyses for these genes and variants in order to find genetic interactions and signatures. GO analysis highlighted odontogenesis, odontogenesis of dentin-containing tooth, and cranial skeletal system development.

Conclusion: Tooth development is regulated through complex genetic networks. The identified genes associated with tooth agenesis will be used to create a database, which will serve as a valuable tool for the genetic analysis and will provide opportunities to develop therapies to prevent tooth developmental defects.