



## Review Article

## Genetics and oral health

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## ABSTRACT

Genes represent hereditary blueprints of humans. Genetics plays a key role in the etiology of many body disorders. Appropriate knowledge regarding genetic diseases leads to a better understanding of the genetic basis of disorders thus facilitating early detection in high risk subjects. With advancements in molecular biology over the years, the scope of genetics has been expanded to the dental profession as well. The present article aims to discuss current applications of human genetics in the etiopathogenesis of various disorders affecting the oral cavity.

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## 1. Introduction

Genetics is the investigation of genes at all levels, from molecules to populaces.<sup>1</sup> In 1909, the British researcher William Bateson began the study of inheritance as genetics, and in mid 1950s, James Watson and Francis Crick discovered the sub-atomic structure of deoxyribonucleic acid (DNA). Genetics got outstanding support after culmination of the Human Genome Project in October 2004, which revealed that an individual contains 20,000 to 25,000 genes within nucleus of each somatic cell.<sup>2</sup> Gregor Johann Mendel is viewed as the “Father of Genetics”. Mendel demonstrated that the legacy of qualities adhere to specific laws, which were later named as Mendel’s laws of inheritance.

Genetic disorders are brought about by variations from the norm in genetic sequences and chromosome structure, which are actuated by single-base substitutions or missense mutations. Genetic information is stored in codon sequences

on the DNA, which are engendered from a parent to the offspring cells through DNA replication. At the same time the data is changed into mRNA and progressively into an amino acid sequence of a protein as per the hereditary code.<sup>2</sup>

Progress in genetics and molecular biology has resulted in the emergence of new concepts to explain the etiopathogenesis of many disorders affecting the oral cavity. The genetic basis of common dental pathologies has been talked about underneath:

## 1.1. Genetics and dental caries

Dental caries is a major health concern worldwide affecting a large fraction of the world population.<sup>3</sup> Multiple factors may predispose caries risk in an individual which include:

## 2. Environmental Factors:

1. Diet.
2. Oral hygiene.
3. Fluoride exposure.

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4. Level of colonization of cariogenic bacteria.

### 3. Host Factors

1. Salivary flow.
2. Salivary buffering capacity.

The Vipeholm study directed in the year 1954 gave proof of a person's protection from caries in spite of being on an exceptionally cariogenic diet.<sup>4</sup> This proposes vulnerability or protection from caries could be a consequence of at least one genotypic, phenotypic and environmental impact.

Various studies have been conducted in the past which correlate the genetic basis of dental caries. Goodman et al in the year 1959 established the role of inherited components influencing caries etiology while examining 38 like-sex monozygotic and dizygotic twin pairs and announced huge heritability for oral microorganisms, including Streptococci, salivary flow rate, salivary pH and salivary amylase activity.<sup>5</sup> Vieira et al detected a connection between low caries experience and loci 5q13.3, 14q11.2 and Xq27.1 in 46 Filipino families.<sup>6</sup> A protective locus for caries was identified on X-chromosome which may have implications for gender contrasts. According to the results of the study, high caries rate was observed linked to loci 13q31.1 and 14q24.3. The authors reported that 14q24.3 encodes a protein similar to the estrogen receptor which could signify the observed gender differences seen in the study. Furthermore, inherited disorders of tooth development, salivary stream and immune system additionally impact the incidence of dental caries.<sup>7</sup> Table 1 abridges few studies available in literature citing evidence for genetic contribution to dental caries through twin analysis.

This suggests a clear evidence of a genetic component controlling the development of caries at various aspects such as gender, salivary, immunological and surface heritability. Syndromes associated with craniofacial defects due to genetic mutation are listed in Table 2.

#### 3.1. Genetics and periodontitis

Periodontitis is viewed as a multifactorial infection wherein the ordinary harmony between microbial plaque and host reaction is disturbed. This interruption can happen through changes in the plaque composition, changes in the host reaction, or natural and behavioral impacts that can influence both plaque reaction and host reaction.<sup>8</sup> Almost fifty level of periodontitis susceptibility is ascribed to hereditary elements.<sup>9</sup> Roughly 38 disease related markers have been accounted for from candidate gene examinations. Of these, IL-1 gene varieties are the most commonly considered associations with extreme/progressive chronic periodontitis due to some extent to early reports of affiliation.<sup>10</sup>

Aggressive periodontitis affiliation contemplates has been appeared to have an intronic SNP in the glucosyl-

transferase gene GLT6D1, for which the related hazard allele demonstrated considerably decreased binding of transcription factor GATA3 in cell models.<sup>11</sup> Numerous SNPs right now been approved for aggressive periodontitis association, making ANRIL the best reproduced risk gene to date.<sup>12</sup> COX2 and IL10 genes additionally have been related with chance for aggressive periodontitis.

#### 3.2. Genetics and malocclusion

Dental occlusion mirrors the interaction between various components including tooth size, arch size and shape, the number and arrangement of teeth, size and connections of the jaws, and furthermore the impacts of soft tissues including lips, cheeks and tongue. Different investigations have been performed on formative phases of I and II molars, craniofacial complex, palatal stature & width and different parameters. The conclusion drawn from larger part of studies was that the dental advancement for most part is hereditarily decided and genetics assumes a significant job in malocclusion.<sup>13</sup>

#### 3.3. Genetics and oral cancer

Hereditary instability in oral cancer can be because of mutations in proto-oncogene (polymorphism in GST gene: GSTM1 and GSTT1 or CYP (cytochrome P450) or transformations in tumor suppressor gene (p16, 9p21, APC5q21–22 and p53). This may prompt loss of heterozygosity or inability to repair.<sup>14</sup> Directed treatments for the treatment of squamous cell carcinoma have been assessed in few clinical trials. These targets incorporate among others oncogenes, biomarkers related with epithelial–mesenchymal transition, gene amplifications, gene transformation, translocations and flagging pathways that manage cell development, cell motility and endurance.<sup>15</sup> Some of the more promising targets incorporate the epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF) and the intercellular signaling pathways MAPK/Erk and phosphatidylinositol-3' kinase (PI3)/Akt/mammalian target of rapamycin (mTOR).<sup>16,17</sup> The efficacies of current objective explicit operators are enormously improved and side effects are fundamentally diminished when utilized in combination with chemoradiation. This dual-targeting on approach has demonstrated to be fruitful for the treatment of human papillomavirus (HPV)- positive malignant growths of the head and neck.<sup>18</sup>

Another class of inhibitors that has gotten extensive consideration is the PI3-Akt/mTOR pathway inhibitors.<sup>19</sup> Transformations in PI3ck and PTEN oncogenes that actuate the mTOR pathway are a component of most human malignancies and have been appeared to assume a focal job in tumor progression and remedial obstruction.<sup>20</sup>

Cancer predisposition syndromes include Werner's syndrome, Bloom syndrome, Fanconi's anemia or disorders

**Table 1:** Evidence for genetic contribution to dental caries

Year	Author	Study Population	Control	Conclusion
1927	Bachrach & Young	MZ twins (130)	DZ twins (171)	Hereditary plays part in caries incidence
1930	Goldberg	MZ & DZ twins (42 pairs)	-	Hereditary affects caries by tooth form
1958	Horowitz et al	MZ twins (30)	DZ twins (9)	MZ have greater caries concordance
1959	Goodman et al	MZ twins (19)	DZ twins (19)	Intrapair variance of DZ > MZ
1963	Finn and Caldwell	MZ twins (35)	DZ twins (31)	Smooth surface caries have ↑ genetic link
1988	Boraas et al	MZ twins (64)	DZ twins (33)	Marked genetic component to caries

Source: Shuler CF. Inherited risks for susceptibility to dental caries. J Dent Educ 2001;65:1038-45. DZ=Dizygous; MZ=Monozygous

like Ataxia telangiectasia.

### 3.4. Other disorders

Hypodontia/Oligodontia: Hypodontia alludes to the condition wherein one to six teeth are missing and oligodontia alludes to the condition where in excess of six teeth are absent. Only four genes have been recognized to be related with non-syndromic hypodontia/oligodontia, which represent 5% of the complete cases. The identified genes are:<sup>21</sup>

1. MSX1 — hypodontia NS.
2. PAX9 — oligodontia NS.
3. AXIN2 — oligodontia associated with colorectal cancer.
4. EDA1 — oligodontia NS.

### 3.5. Ectodermal dysplasia

Ectodermal dysplasia is caused because of change in the EDA1 gene (Xq12-q13.1). It is an uncommon illness portrayed by hypoplasia or nonappearance of sweat glands, dry skin, inadequate hair, and articulated oligodontia.<sup>21</sup> Song et al. in 2009 distinguished three new transformations of the EDA gene (Ala259Glu, Arg289Cys, and Arg334His) in four male people (27%), from 15 examined people with non – syndromic oligodontia.<sup>22</sup>

### 3.6. Cleft lip and palate

Incidence of cleft lip/palate might be ascribed to chromosomal disorders or they might be of multifactorial inception. Out of which 70% are non – syndromic while of 30% rates are related with Syndromes; which can be autosomal dominant, autosomal recessive or X-linked. Kin of the influenced kid is at a danger of multiple times more than everyone.<sup>23</sup>

### 3.7. Future perspectives

Comprehension of the hereditary premise of different orofacial disorders can prompt the early intercession and counteraction of ailment onset. Different health promotional measures have been undertaken. Some of which include:

### 3.8. Genetic screening

Genetic screening shows the tests attempted on a populace wide premise to distinguish at-risk individuals. Hereditary testing implies measures for authoritative analysis; these are performed because of positive screening results, family ancestry, ethnicity, physical stigmata, or different reasons.<sup>24</sup>

### 3.9. Genetic counseling

Genetic counseling is a communication procedure between health-care expert and individual or families influenced by or in danger for a hereditary issue. The objectives of the procedure incorporate spreading consciousness of the clinical realities for the condition and understanding the commitment of heredity in the outflow of the condition, its hazard for recurrence. It likewise incorporates conversation of the choices accessible for managing issue and helping families in picking the choice which are most appropriate for them.<sup>24</sup>

Genomic advancements in dentistry ought to accentuate towards standards of crucial hereditary, genetic phrasing, hereditary transmission, populace hereditary qualities, subatomic science of the human genome and their applications towards the patient consideration.<sup>25</sup> Oral wellbeing experts ought to be situated towards the hereditary etiology and pathophysiology of lesions with the possibility to contribute for the new methodologies in diagnosing, forestalling and treating. Once high risk bunches are distinguished, there is a need to create awareness and teach those with respect to hereditary disorders. Progress in the field will require preparing of another age of the researchers with essential abilities, just as more noteworthy cooperation and

**Table 2:** Syndromes associated with craniofacial defects due to genetic mutation

Syndrome	Gene Mutations
Apert Syndrome	FGFR-2 gene Chromosome - 10q25-q26
Treacher – Collins Syndrome	TCOF – 1 gene Chromosome – 5q32-q33.1
Marfan Syndrome	FBN 1 gene Chromosome 15
Vander Woude Syndrome	IRF – 6 gene Chromosome – 1q32, 17p11
Crouzon Syndrome	FGFR-2, FGFR-3 gene
McCune – Albright Syndrome	GS alpha gene
Tricho-dento-osseous syndrome	Chromosome 17q21.3-q22
Turner’s Syndrome	45 (X0)
Patau Syndrome	Trisomy 13

Source: Gupta M, Jyoti B, Srivastava R, Pachauri A. Human genetics in oral medicine: A review. *J Indian Acad Oral Med Radiol* 2014;26:62-8.

interdisciplinary work.

#### 4. Conclusion

There is as yet a lack of information between hereditary disorders and its counteraction among everyone. The momentum worldview of malady treatment should be re-intended to represent the large number of hereditary data known to affect oral wellbeing. It is time for another change in our perspective on worldview of oral wellbeing and disease treatment. Dental health caregivers ought to know about the innovative and logical headways in the field of genetic testing and it is believed that use of standards of genetic medicine in the diagnosis and treatment of disorders will on a very basic level revolutionize the delivery of medicinal services.

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#### 6. Conflict of Interest

None.

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