Review Article

# GENETIC INFLUENCE AND MODULATION OF DENTAL CARIES: A REVIEW

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**Abstract**
In humans, dental caries is still the most common non-contagious infectious disease. The development of realistic ways to investigate genetic susceptibility to complex human disease aligns with the interest in understanding the factors underlying individual susceptibility to caries. As a result, the goal of this report is to compile information on the function of genetics and its impact on the dental systems, which results in the dissolution of dental hard tissues and the production of dental caries. Furthermore, details about gene expression and susceptibility are provided, allowing advanced genetic therapies to be used to treat and control dental caries.

**Conclusion**: Dental caries is the outcome of a complex interaction between a character's genetic structure and overlaying environmental circumstances, which is a combination of nature and nurture, similar to many other clinical and dental disorders. Engineering, molecular genetics, management, education, and research advancements have resulted in a surge of new approaches to caries treatment and prevention for patients.

## INTRODUCTION

The history of genetics is one of breathtaking discovery, from which patients and families have profited much, but progress in converting discoveries into disease treatment and prevention will be assessed in the future. The incidence of genetic illnesses, combined with their capacity severity and continual nature, imposes extremely good human, social and economic burdens on society.[1,2] Dental caries, a multi-factorial disorder starts with microbiological changes in the complicated biofilm and is stricken by the flow of saliva and its content, fluoride exposure, sugars in food consumption and by employing preventative measures (cleansing tooth).[3-8] The disorder could be seen in the portion crown and root of deciduous and succedaneous teeth, as well as on smooth and pitted surfaces.[9]

Although there may be clear proof about dental caries that it's a microbial infectious ailment, with plenty of other environmental factors playing a role, there is also compelling evidence that this disease's genesis has a genetic component.[10-14] It is difficult to isolate genetic contribution as there could be main symptoms directly related to the illness, as well as subsequent consequences resulting from an underlying genetically connected condition.[12]Dental caries, like many other dental and medical diseases, is the result of a complicated interaction between an individual's genetic form and overlying pediatric dentist encompass the potential to take and update family records, understand signs and symptoms of genetic sickness and include these facts within the differential prognosis, and prescribe and interpret the consequences of genetic checks.[17]

So the intention of this paper is to bring together the information on the role of genetics and its impact on the dental systems causing dissolution of the dental tough tissues and formation of dental caries. Also providing facts regarding the gene expression and susceptibility, accordingly rendering the remedy and control of the dental caries with advanced genetic interventions.

## ENAMEL FORMATION GENES ASSOCIATED WITH CARIES

One of the fundamental mechanism that would give an explanation is the developing enamel which is more prone to demineralization is a hereditary contributor to dental caries.[17] Slayton RL et al in 2005 and Patir et al in 2008 investigated that Tuftelin(TUFT1) as a genetic issue contributes susceptibility to dental caries, both by itself and/or in aggregate with environmental elements.[17,18]Enamelin (ENAM) which is involved in tooth mineralization and structural organization of the enamel and ameloblastin (AMBN) which is entailed in enamel matrix formation are analogous to dental caries.[19] Tannure et al. (2012) identified MMP20(matrix metalloproteinase 20), which destroys amelogenin, as a factor in increased caries risk.[20]

These researches indicate that the genes which are involved in enamel formation, with their alteration, there are possibilities of demineralization of tooth which can further lead to dental caries.

## INTERACTION OF S. MUTANS AND HUMAN GENES

Of all the oral streptococci, cariogenicity of streptococcus mutans is the most and is proven to be a major cause of caries globally. Meng et al. identified three genes, galactokinase2(GALK2), interlukin32(IL32) and CELF4 (elav like family member4), by streptococcus mutans interplay, those were possibly linked with a greater risk of caries in the deciduous dentition with plausible biological components GWAS (genome wide association study) published in 2019.[21]

## GENETIC STUDIES

The genome-wide and the candidate gene studies have both been used to investigate the genetics of complicated characteristics such as dental decay.

Candidate gene study - The majority of caries genetic research to date have attempted to solve the dilemma of identifying a genetic component that causes caries by examining genetic difference in individual genes. Based on factors that influence this disease, these genes can be classified into distinct categories. Genes which forms enamel, salivary-related genes, genes responding immune, genes related to taste and other potential gene categories have all been examined to date.[22]

GWAS (Genome-wide association studies)- Bigger panels of SNPs (single nucleotide polymorphisms) are commonly used in genome-wide association studies, with around 600,000 SNPs. A p value of $10^{-7}$ for a 600,000 SNP panel is an usual criterion for genome-wide statistical significance in such investigations, and p value between $10^{-5}$ and $10^{-7}$ is considered evocative.[23,24]

## GENETIC SCREENING

Screening is conventionally described as the assessment of asymptomatic humans in a defined populace to discover an unsuspected disease or hazard to enhance health outcome.[25] The introduction of latest technology has dramatically modified the present day exercise of screening and monitoring for genetic abnormalities in the foetus during pregnancy. Non-invasive cell-free foetal DNA-based screening and extended carrier screening panel for aneuploidy and single-gene diseases, and greater these days for sub-chromosomal deformities, are added into care of prenatal.[26] We can apply these principles/procedures for the screening of genetic abnormalities in the structure of dentine and/or enamel also the above mentioned procedures can help in screening of unfavorable genes causing dental caries or dental hard tissue destruction.

## GENETIC COUNSELLING

With the advancement of laboratory and clinical genetics expertise, interest in clinical genetics and genetically derived diseases has exploded in recent years.[27-30] In the broad and varied field of genomic treatment, genetic counselling plays a unique role.[31] The aims of counselling includes - To teach the family with whole and correct records about genetic problems, clarifying the family's options available treatment and prognosis and explaining options to reduce the hazard of genetic problems.[27]

## ROLE OF GENETICS IN CARIES PREVENTION

In order to comprehend the role of the dentition in the oral cavity, a number of genetically preventative approaches against dental caries have been introduced. The replication of enamel matrix genes, their chromosomal localisation, and their relation to human diseases of abnormal tooth evolution have all been accomplished by a number of researchers.[32-39] In 1981, Lehnar et al. looked at the distribution of HLA DR antigens and discovered that the DMFS index and HLA DRw6 had a strong connection and low dosage reactivity to antigens of S.mutans.[40]

In a rat experiment, Peter J et al in 2014 discovered a sort of microorganism naming Lactobacillus zeas, may be modified genetically for producing antibodies to make a connection with the surface of streptococcus mutans and assassinate their function.[41] Hillman in 2002 created a strain with deficient lactate dehydrogenase of s.mutans [BCS3-

L1] using recombinant DNA technology. The BCS3-L1 replacing therapy for caries prevention is a biofilm engineering example that enables for highly successful treatment and value effective enhancements of established preventative measures.[42] Some other preventive measures like genetically modified food and the gene alteration have been introduced in this field which can help an individual in the prevalence of dental caries.

## DISCUSSION

Despite more than a century of research into the pathophysiology of dental caries, it remains a major oral health issue in the majority of industrialised countries where 60–90% of school-aged children and the vast majority of adults are affected.[22] For decades, the importance of genetic factors in dental caries has been known, with heritability estimates ranging from 30% to 60%.[44,45] Mutations in the genes of enamel matrix, proteinaceous content material of tooth enamel, and distinct genes regulating their activity are known to cause inherited dental dysplasia and amelogenesisimperfecta, according to Shaffer et al. (2015).[45] Mao et al. in 2001 validated that tuftelin which in involved in enamel formation is extensively found in non-mineralizing tissues and is remarkably preserved throughout species.[46]Tannure et al. in 2012 concluded that the variation in matrix metalloproteinases (MMP20), which shape a multigene circle of relatives inside metalloproteinase magnificence of endopeptidades, which mediate the breakdown of almost all extracellular matrix components, are magnificent, may be related to caries revel particular among Caucasian subjects that show poor oral fitness.[20]

To far, numerous gene mapping initiatives have been conducted in order to identify particular genetic loci that contribute to caries risk.[47] According to Stooky in 2008, the physical flow of saliva aids in the removal of pathogens (bacteria, yeast and viruses) from mucosal surfaces and teeth, and it can also encourage germs to cluster together so that they can be ingested before becoming strongly attached.[48] Wendell et al. in 2010 stated that the combinations of cariogenic potential of meals (like sucrose), the rate of consumption, and the physical state of the food plan can affect the carious process alone or together.[49] In preventive part, Chen et al. in 1994 employed recombinant DNA to remove almost the complete open reading frame for lactic acid dehydrogenase.[50] Hillman et al. in 2007 concluded in their study that A2JM strain, constructed from BCS3-L1, was absolutely requiring exogenous d-alanine, but could infiltrate the oral cavity of rats in tiny quantities in the absence of dietary d-alanine.[51] Integration of other genetic and genomic data (like gene expression, metagenomics, evidence from multiple species and protein-protein interaction networks) could open up new pathways for understanding the aetiology of caries in future research.

## CONCLUSION

Caries stays the most usual non-contagious infectious disease in people. It, like many other clinical and dental illnesses, is the result of a complicated interaction between a character's genetic structure and overlaid environmental circumstances, which is a mixture of nature & nurture. Advances in engineering, molecular genetics, management, schooling and research have resulted in a slew of innovative approaches to caries treatment and prevention for patients.

In the future, clinicians may be able to explain to patients that certain types of caries are strongly linked to genetic risk, providing both the patient and the dentist with a framework as to why similar behavioural risks (such as dietary habits or tooth brushing frequency) have varying caries risk.

## REFERENCES


1. Turnpenny PD, Sian Ellard S. The history and impact of genetics in medicine: Emery's elements of medical genetics. 15th ed. Elsevier. China; 2017: 1.
2. Jameson JL, Kopp P. Principles of human genetics: Harrison's principles of internal medicine. 19th ed. McGraw-hill education. New York; 2015: 425.
3. Fejerskov O, Kidd EA. Clinical cariology and operative dentistry in the twenty-first century: Dental caries: the disease and its clinical management. 1st ed. Blackwell Munksgaard. Denmark; 2003: 3.

4. Marsh P, Martin MV. Plaque-mediated diseases – dental caries and periodontal diseases: Oral Microbiology. 5th ed. Elsevier. Oxford; 2009: 106
5. Pitts NB. Are we ready to move from operative to non-operative/preventive treatment of dental caries in clinical practice? Caries Res. 2004; 38(3): 294–304.
6. Featherstone JD. The science and practice of caries prevention. J Am Dent Assoc. 2000; 131: 887–99.
7. Satcher D, Nottingham JH. Revisiting oral health in America: a report of the surgeon general. Am J Public Health. 2017;107(1):32-33.
8. Kidd EA, Giedrys-Leeper E, Simons D. Take two dentists: a tale of root caries. Dent Update. 2000; 27: 222–30.
9. Vieira AR. Genetics and caries: prospects. Braz Oral Res. 2012; 26(1): 7-9.
10. Conry JP, Messer LB, Boraas JC, Aeppli DP, Bouchard TJ. Dental caries and treatment characteristics in human twins reared apart. Arch Oral Biol. 1993; 38: 937-943.
11. Liu H, Deng H, Cao CF, Ono H. Genetic analysis of dental traits in 82 pairs of female-female twins. Chin J Dent Res. 1998; 1(3): 12-16.
12. Shuler CF. Inherited risks for susceptibility to dental caries. J Dent Educ. 2001; 65: 1038-45.
13. Nariyama M, Shimizu K, Uematsu T, Maeda T. Identification of chromosomes associated with dental caries susceptibility using quantitative trait locus analysis in mice. Caries Res. 2004; 38: 79-84.
14. Pizanis VK. Technological advances in primary dental care: Harris O, Godoy FG, Nathe CN. Primary preventive dentistry. 8th ed. Pearson. England; 2014: 410.
15. Renuka P, Pushpanjali K, Sangeetha R. Review on "influence of host genes on dental caries". J Dnt Med Sci. 2013; 4(3): 86-92.
16. Johnson L, Genco RJ, Damsky C, Haden NK, Hart S, Hart TC et al. Genetics and its implications for clinical dental practice and education: report of panel 3 of the Macy study. J Dent Educ. 2008; 72(2): 86-94.
17. Patir A, Seymen F, Yildirim M, Deeley K, Cooper ME, Marazita ML et al. Enamel formation genes are associated with high caries experience in Turkish children. Caries Res. 2008; 42: 394–400.
18. Slayton RL, Cooper ME, Marazita ML: Tuftelin, mutans streptococci, and dental caries susceptibility. J Dent Res. 2005; 84(8): 711–714.
19. Shimizu T, Deeley K, Briseno RJ, Faraco IM, Poletta FA, Brancher JA et al. Fine-mapping of 5q12.1–13.3 unveils new genetic contributors to caries. Caries Res. 2013; 47: 273–283.
20. Tannure PN, Kuchler EC, Lips A, Costa MC, Luiz RR, Granjeiro JM et al. Genetic variation in MMP20 contributes to higher caries experience. J Dent. 2012 ; 40(5): 381-6.
21. Meng Y, Wu T, Billings R, Kedzierawski DT, Xiao J. Human genes influence the interaction between streptococcus mutans and host caries susceptibility: a genome-wide association study in children with primary dentition. Int J Oral Sci. 2019; 11(2): 19.
22. Vieira AR, Modesto A, Marazita ML. Caries: review of human genetics research. Caries Res. 2014; 48(5): 491-506.
23. Shaffer JR, Wang X, Feingold E, Lee M, Begum F, Weeks DE et al. Genome-wide association scan for childhood caries implicates novel genes. J Dent Res. 2011; 90(12): 1457–1462.
24. Wang X, Shaffer JR, Zeng Z, Begum F, Vieira AR, Noel J et al. Genome-wide association scan of dental caries in the permanent dentition. BMC Oral Health. 2012; 12:57.
25. Pos O, Budis J, Szemes T. Recent trends in prenatal genetic screening and testing. F1000Res. 2019; 8: 764.
26. Veyver IB. Recent advances in prenatal genetic screening and testing. F1000Res. 2016; 5: 2591.
27. Genetic counselling. Third report of the WHO expert committee on human genetics. World Health Organ Tech Rep Ser. 1969; 416: 1-23.
28. Day N, Holmes LB. The incidence of genetic disease in a university hospital population. Am J Hum Genet. 1973; 25: 237-46.
29. Carter CO. Changing patterns in the causes of death at the hospital for sick children. Great Ormond St J. 1956; 11: 65-8.
30. Roberts DF, Chavez J, Court SD. The genetic component in child mortality. Arch Dis Child. 1970; 45: 33-8.
31. Brothman AR, Newlin A, Phillips SE, Kinzie GQ, Leichtman LG. Prenatal detection of an inverted X

32. chromosome in a male. Clin Genet. 1993; 44(3): 139-41.
33. Aldred MJ, Crawford PJ, Roberts E, Thomas NS. Identification of a nonsense mutation in the amelogenin gene (AMELX) in a family with X-linked amelogenesisimperfecta (AIH1). Hum Genet. 1992; 90(4): 413-6.
34. George A, Gui J, Jenkins NA, Gilbert DJ, Copeland NG, Veis A. In situ localization and chromosomal mapping of the AG1 (Dmp1) gene. J HistochemCytochem. 1994 ; 42(12): 1527-31.
35. Lench NJ, Brook AH, Winter GB. SSCP detection of a nonsense mutation in exon 5 of the amelogenin gene (AMGX) causing X-linked amelogenesisimperfecta (AIH1). Hum Mol Genet. 1994 ; 3(5): 827-8.8081371.
36. Deutsch D, Palmon A, Dafni L, Catalano-Sherman J, Young MF, Fisher LW. The enamelin (tuftelin) gene. Int J Dev Biol. 1995 ;39(1): 135-43.
37. Lagerstrom-Fermer M, Nilsson M, Backman B, Salido E, Shapiro L, Pettersson U et al. Amelogenin signal peptide mutation: correlation between mutations in the amelogenin (AMGX) and manifestations of X-linked amelogenesisimperfecta. Genomics. 1995; 26: 159-62.
38. MacDougall M, DuPont BR, Simmons D, Reus B, Krebsbach P, Kärrman C et al. Ameloblastin gene (AMBN) maps within the critical region for autosomal dominant amelogenesisimperfecta at chromosome 4q21. Genomics. 1997 ;41(1):115-8.
39. Wright JT, Kula K, Hall K, Simmons JH, Hart TC. Analysis of the tricho-dento-osseous syndrome genotype and phenotype. Am J Med Genet. 1997;72:197-204.
40. Price JA, Bowden DW, Wright JT, Pettenati MJ, Hart TC. Identification of a mutation in DLX3 associated with tricho-dento-osseous (TCO) syndrome. Hum Molec Genet. 1998;7:563-9.
41. Lehner T, Lamb JR, Welsh KL, Batchelor RJ. Association between HLA-DR antigen and helper cell activity in the control of dental caries. Nature. 1981; 292: 770-2.
42. Peter J, Rupesh S, Mohan G, Sugumaran DK, Thayumanavan S, Venugopal N et al. Genetic aspects of dental caries- part ii. J of Evidence Based Med &Hlthcare. 2014; 1(11): 234-256.
43. Hillman JD. Genetically modified streptococcus mutans for the prevention of dental caries. Antonie van Leeuwenhoek. 2002; 82(1-4): 361–366.
44. Boraas JC, Messer LB, Till MJ. A genetic contribution to dental caries, occlusion and morphology as demonstrated by twins reared apart. J Dent Res. 1988; 67(9): 1150-5.
45. Wang XJ, Shaffer JR, Weyant RJ, Cuenco KT, DeSensi RS, Crout R et al. Genes and their effects on dental caries (tooth decay) may differ between primary and permanent dentitions. Caries Res. 2010; 44: 277–284.
46. Shaffer JR, Carlson JC, Stanley BO, Feingold E, Cooper M, Vanyukov MM et al. Effects of enamel matrix genes on dental caries are moderated by fluoride exposures. Hum Genet. 2015; 134(2): 159-67.
47. Mao Z, Shay B, Hekmati M, Fermon E, Taylor A, Dafni L et al. The human tuftelin gene: cloning and characterization. Gene. 2001; 279(2): 181-96.
48. Werneck R, Mira M, Trevilatto P. A critical review: an overview of genetic influence on dental caries. Oral Dis. 2010; 16: 613–623.
49. Stookey GK. The effect of saliva on dental caries. J Am Dent Assoc. 2008; 139: 11–17.
50. Wendell S, Wang X, Brown M, Cooper ME, DeSensi RS, Weyant RJ et al. Taste genes associated with dental caries. J Dent Res. 2010;89(11):1198-1202.
51. Hillman JD, Chen A, Duncan M, Lee SW. Evidence that L-lactate dehydrogenase deficiency is lethal in streptococcus mutans. Infect Immun. 1994; 62(1): 60-4.
52. Hillman JD, Mo J, McDonell E, Cvitkovitch D, Hillman CH. Modification of an effector strain for replacement therapy of dental caries to enable clinical safety trials. J Appl Microbiol. 2007; 102(5): 1209-19.

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