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Original Research Paper

Dentistry

GENE-OMICS IN DENTISTRY; A MAGICAL BLUEPRINT

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ABSTRACT Genetic disorders related to dentistry can be caused by a single gene or multiple genes causing changes in genes interacting with environmental influences. Oral diseases require a higher level understanding of genetic variability. Advances in the diagnosis and treatment of disease are driven by our growing skill in acquiring new data and analyzing it effectively. Genome is the complete set of genetic instructions carried in a single cell of an organism and provides a complete blueprint of cellular structures and activities throughout the life of each cell, for the initiation, construction, operation, maintenance, and repair of all living organisms. Human genomics is the study of the structure, function, and interactions of all genes in the human genome, which promises to improve the diagnosis, management, and prevention of disease. Two terminologies genetics and genomics; they are not the same but two different entities. Genetics is study of a single gene, while genomics is the study of the functions and interactions of all genes in the genome. The Human Genome Project is an international scientific research project launched in 1990 with the primary goal of determining the sequence of chemical base pairs that make up DNA and identifying the genes in the human genome. Inherited conditions or syndromes affecting any aspect of growth and development are caused by mutation, a random change in the genome. Genomics therefore helps in the intervention and treatment planning of several developmental abnormalities.This article provides an overview of the implications of genomics in oral health.

KEYWORDS : Genomics, Genetics, Human genome project, Dentistry

INTRODUCTION

Human experience depends on everything that can affect the state of the human brain. The genome is the entire genetic makeup of the nucleus of a human cell or the sum of the genes of all individual organisms. The genome is defined as the master blueprint for cellular structures and activities throughout the life of each cell; the genome contains the complete set of instructions for the initiation, construction, operation, maintenance, and repair of all living organisms.[3] Life is specified by genomes. The human genome is often referred to as a "magic wand", a tool that identifies the underlying cause of a disease (their genes), determines what diseases are in perspective, and prompts a range of effective treatments tailored to the individual patient.[4]

The human genome contains approximately 3.2 × 109 base pairs, distributed among 22 paired chromosomes, plus two X chromosomes in females and X and Y in males. The first human genomes were determined in 2001, the culmination of 10 years of pioneering work and dedication. Since then, advances in technology have made genomic sequencing cheaper and faster.[1]

Human genomics is the study of the structure, function, and interactions of all genes in the human genome, which promises to improve the diagnosis, treatment, and prevention of disease, while genetics is the study of a single gene.[3]

The study of genomics has significant health benefits by revealing the mechanisms of common complex diseases such as hypertension, diabetes and asthma. Some of the diseases for which genomics has not revealed etiopathogenesis are breast cancer, colorectal cancer, human immunodeficiency virus infection, tuberculosis, Parkinson's disease, and Alzheimer's disease.[16]

The contribution of genes and its evaluation in dentistry is abundant. From common oral disorders such as dental caries, periodontitis, missing or malformed teeth, to more advanced disorders such as orofacial anomalies, head and neck cancer, amelogenesis imperfecta, and oral genodermatosis, genetics play a vital role. A better understanding of genetic susceptibility, lifestyle, and risk factors for oral health allows the dentist to offer effective prevention and treatment strategies for oral disease.[12]

Human Genome Project

The Human Genome Project, it is an international research programme whose primary mission is to decode the chemical sequence of the complete human genome and to, identify all 50,000 to 100,000 genes contained in the genome, and provide research tools to analyze all of this genetic information. This diligent project is based on the fact that the isolation and assessment of the genetic material present in the DNA (Figure 1) that provides scientists with eloquent new approaches to understanding the etiopathogenesis of the diseases and generating new plan of action for their prevention and treatment.[5]

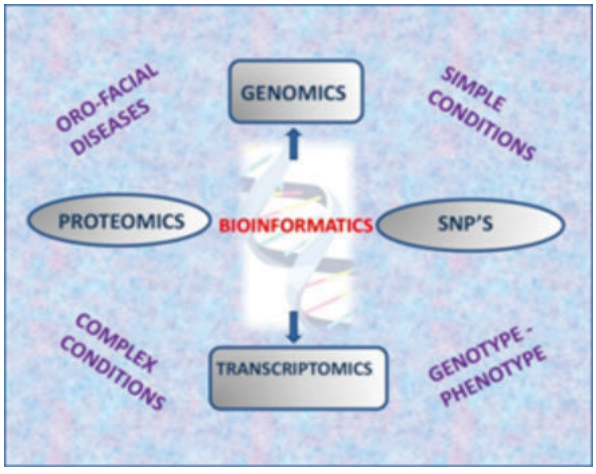
Figure 1: Double Helix DNA
Sources: www.googleimages .com/ DNA

The goal of the HGP is to identify all genes encoded in human DNA and sequence the entire 3 billions of base pairs of the human genomic code are nearing completion and providing even more enormous amounts of information. This explosion of information, coupled with the rapid development of molecular biology and computational technologies, is driving a number of related fields of study and research.Because the

major burden of oral disease in modern humans results from complex disorders involving multiple genes and environmental interactions, it will be necessary to understand genetic variability at an even greater level of detail than is necessary for simple inherited conditions. Finding multiple genes involved in complex conditions is difficult at best. The use of genomic locations where a single base in the DNA sequence is altered could provide a powerful tool for identifying genes associated with complex diseases. These single nucleotides polymorphisms (SNPs) are referred to as "chunks" and occur about every 1,000 bases along the genome.[5] Evaluating the vast amount of information generated by SNP studies to identify complex genes associated with disease has been daunting, but there have been successes (Crohn's disease, for example) . New technologies for genotyping and statistical analysis to separate disease-associated SNPs from normal genetic variation could make this approach useful for identifying genes associated with complex traits such as dental caries and periodontal disease.

HGP established the ELSI (Ethical, Legal and Social Issues) program as an integral part of the program financed part of the project to solve these problems. This program also addresses and solicits requests for proposals on how best to educate oral health professionals in these new fields of study and maintain optimal knowledge of translational technologies and health issues related to molecular biology.
Genomic research is rapidly increasing our understanding of the genetic basis of normal and abnormal growth, development, and disease. In the 21st century, the field of medicine has witnessed many new advances. With the completion of the HGP in 2003, a vast amount of new information was obtained on the sequencing of human DNA and the human genome.[18]

The achievements of genomics have inspired numerous omics disciplines such as proteomics, transcriptomics, metabolomics, epigenomics, glycomics, and pharmacogenomics, allowing us to understand the pathogenesis of diseases, leading to the identification of new diagnostic markers and therapeutic targets.[19] The study of genomics and other related fields helps in the diagnosis and treatment of simple and hereditary conditions that affect the craniofacial complex (Fig.:2).



Fig;2:Study of Genomics and other related disciplines that aids in the diagnosis and treatment of simple and hereditary conditions that affect craniofacial complex

CLINICAL IMPLICATIONS OF GENOMICS

In the near future, genomics and related technologies will be incorporated into all aspects of health care, including dentistry. Advances in genomics have led to a drastic paradigm shift in the field of oral medicine, which may include elucidation of disease etiopathogenesis, presymptomatic testing, and development of more robust disease nosology, diagnosis, prevention, and effective treatment. Genome-wide association studies (GWAS) also reveal a complete picture of the genome rather than smaller parts, allowing us to fully understand the cellular pathways and mechanisms of the disease process.[20]

The treatment of oral, dental, and craniofacial diseases has changed drastically because of these new genomic advances that are guiding researchers and clinicians to understand oral biology. Genomic and proteomic advances combined with the power of superfast computers are helping us understand oral, dental and craniofacial diseases. More accurate and faster diagnostic tests, new drugs and biologics, practice-based research, and culturally sensitive interventions provide new avenues to improve oral health.

The study of genomics has the greatest contribution to health by revealing the mechanisms of common complex diseases such as hypertension, diabetes and asthma. Some of the diseases for which genomics has not revealed etiopathogenesis are breast cancer, colorectal cancer, human immunodeficiency virus infection, tuberculosis, Parkinson's disease, and Alzheimer's disease[21]

Various diseases are caused by mutations; the most common mutation is loss of function. MODY1, MODY2 and MODY3 increase the risk of diabetes.[22]Genomic information can be applied at many important points during disease progression from a healthy state to a disease state. By assessing DNA in a healthy state, disease susceptibility and risk can be quantified.

Thus, there is a paradigm shift in health planning strategy from disease treatment to disease prevention.

Genomic information can be obtained through genetic screening with a family history of an oncogenic gene mutation, such as adenomatous polyposis coli, BRCA1 and BRCA2 genes (breast cancer). Genetic testing has also been used to identify patients at higher risk of developing colon cancer (DNA mutations, mismatch repair genes, MLH1 and MSH2) and multiple endocrine neoplasia type 2 (RET gene mutations)[24]

Implications Of Genomics In Oral Health Care

Head And Neck Cancer

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common malignancy in the world, with an annual global incidence of more than 600,000 cases per year and 350,000 deaths per year. In some parts of Asia, betel-quid chewing also plays a significant role in the development of malignancy. At the molecular level, these cancers often have p53 mutations and many show chromosomal instability. Human papilloma virus (HPV) has recently been shown to promote HNSCC and primarily cause oropharyngeal (subsite in the head and neck) cancer. Although most cases of HNSCC are triggered by carcinogens or viral infection, a small fraction of cases are familial. In non-syndromic families, initial follow-up studies demonstrated a genetic predisposition, with first-degree relatives having a 3.5-fold increased risk of HNSCC. It has been hypothesized that genetic differences in pathways such as DNA repair, carcinogen metabolism, and cell cycle control may increase the risk of carcinogenesis from tobacco or alcohol exposure. Subsequently, a genome-wide association study in upper aerodigestive malignancies confirmed the ADH SNP and also identified a SNP in HELQ (a DNA repair gene) as associated with malignancy risk. Cumulatively, these SNPs represented only 4%. family risk. In a pan-carcinogen analysis, the studies found that HNSCC had the 9th highest average mutational burden of the 30 tumor types studied, with patients having mutations ranging from

less than 1 mutation per Mb to more than 100 mutations per Mb. Other genes recurrently mutated in HNSCC are p53, CDKN2A, CASP8, FAT1, NOTCH1, HRAS, PIK3CA MLL2, FBXW7, TP53 and Tp63[27].

Dental Caries

More recent genome-wide association studies were performed for adult caries and early childhood caries and, similar to previous studies, reported no significant loci, but there were several suggestive, plausible ones (eg, NAMPT and BMP7 for adult caries). A recent consortial meta-analysis of childhood caries noted two significant genome-wide loci (ALLC, rs1594318 and NEDD9, rs7738851) as well as heterogeneity and low heritability (1%) in the measured trait when compared with the individual studies or previously publications.

Although not a traditional clinical definition, caries patterns and subtypes have been used with somewhat more striking results in the context of genome-wide association studies. For example, genome-wide significant signals were reported for LYZL2 (rs399593) and AJAP1 (rs3896439) for subtypes (ie, caries patterns) of adult caries and for KPNA4 (rs17236529) for pit and fissure lesions in caries. primary dentition. [26]

Periodontitis

The genome-wide association study of aggressive periodontitis reported by Schaefer et al marked the field's entry into the genomic era. In this study, researchers discovered and then replicated the association of rs1537415, located in the glycosyltransferase gene (GLT6D1), with aggressive periodontitis. Six genes showed genome-wide evidence of association with periodontitis, four of which were expressed with severe chronic periodontitis (NIN, $P = 1.6 \times 10$-7; ABHD12B, $P = 3.6 \times 10$-7; WHAMM, $P = 1.7 \times 10-6$; AP3B2, $P = 2.2 \times 10-6$) and two with high periodontal pathogen colonization (red complex-KCNK1, $P = 3.4 \times 10$-7; Porphyromonas gingivalis□DAB2IP, $P = 1.0 \times 10$-6). The top-ranked genes for moderate chronic periodontitis were HGD ($P = 1.4 \times 10$-5), ZNF675 ($P = 1.5 \times 10$-5), TNFRSF10C ($P = 2.0 \times 10$-5), and EMR1 ($P = 2.0 \times 10-5$).[26]

Oral Infections

The oral microbial ecosystem is essential for maintaining both oral and overall body health. An individual's microbiome is contributed by their genetic make-up, which would prevent the existence and action of some beneficial pathogenic species. Genetic makeup together with other factors such as poor oral hygiene, immunological disturbances can shift the ecological cycle in the oral microbiome for the activation and progression of diseases such as dental caries, periodontal disease and oral cancer. Newer omics, such as microbiomics and metagenomics, are helping to understand the microbiology and pathogenesis of oral diseases.[25]

Pain Perception

The interrelationship between a specific gene and a pain perception may be direct and informative – as in very rare condition like Mendelian inherited pain. Although very rare, both congenital insensitivity to pain (loss-of-function mutation) and pain amplification

(gain-of-function mutations) have been described. A study of certain individuals/families with extremely rare, altered pain conditions helped basic scientists uncover mutations in the sodium channel, Nav 1.7, which is preferentially expressed in dorsal root ganglion neurons,specifically nociceptive cells and the sympathetic ganglion cells. Other rare pain conditions affecting the genes encoding the Ca2+ channel, the Na+/K+ ATPase pump, among others, have also been described, including familial hemiplegic migraine (FHM) type 1 and FHM type 2, respectively.[28]

Perception Of Taste

Most of the evaluated studies analyzed the association of genetic variants with the bitter taste modality (n = 64), followed by articles on the effect of polymorphisms on sweet (n = 28) and fat preferences (n = 22). The number of studies investigating the association between umami, salty and sour taste perception and genetic polymorphisms was limited (n = 6, n = 6 and n = 4, respectively).

Genes associated with bitter taste are TAS2R38 TAS2R38 TAS2R38 TAS2R38 TAS2R38 . TAS2R38 rs713598, rs1726866, rs10246939 polymorphisms were associated with PTC (phenylthiourea) and PROP (6-n-propylthiouracil) phenotypes and with differences in perceived bitterness of bitter-tasting vegetables and berries, wine/alcohol and salithiouracil studies. The list of other polymorphisms with a possible explanatory mechanism, which were confirmed by individual studies, consists of genes involved in glucose metabolism, umami perception, metabolic processes, signal transduction and neurotransmission, regulation of energy homeostasis (SLC2A2, TAS1R1, ADIPOQ, ANKK1, DRD2, OPRM1, LEP , LEPR, NPY1, respectively) or clarify inconclusive findings related to genetic variants and individual sensitivity of the taste pathway.[29]

Syndromes Associated With Genetic Abnormalities

Many human genetic disorders result from unbalanced chromosomal abnormalities in which there is a net gain or loss of genetic material. Such imbalances often disrupt a large number of dose-sensitive developmentally important genes and lead to specific and complex phenotypes.

Some syndromes associated with chromosomal defect may be caused by addition, deletion or duplication of a single gene with various pleiotropic outcomes. Traditionally, chromosomal abnormalities were identified by visual inspection of chromosomes under a microscope. Microarrays have enabled the identification of many new syndromes through a genotype-first approach in which patients with the same or overlapping genomic alterations are identified and then phenotypes are described. Because many chromosomal alterations are large and involve numerous genes, identifying individuals with overlapping deletions and different clinical features may allow researchers to narrow down the area in which to search for candidate genes. For example, scientists have recently identified what is likely to be the causative gene for the 2q32q33 microdeletion syndrome features. Individuals with the syndrome have severe mental retardation, growth retardation, dysmorphic facial features, thin and sparse hair, difficulty eating, and cleft or high palate. Although deletions of different sizes have been reported, the smallest deleted region in all patients contains at least seven genes. One out of these seven genes, SATB2, is a DNA-binding protein which controls how genes are presented. Deletion of SATB2 is thought to cause cleft or high palate in individuals with 2q32q33 microdeletion syndrome. Recently, microarrays designed to interrogate known segmental duplication "hotspots" of the genome have identified several previously unrecognized genomic disorders. In this way, recurrent microdeletions of chromosome 10q22.3q23.3,90,91 15q24,13–15 16p11.2p12.2,16 17q21.31,10–12 and 17q23.1q23.292 were identified. In all cases, the majority of identified patients met the classic definition of a recurrent genomic disorder.[30]

Syndromes associated with genetic abnormalities according to Chromosomal disorders with oral manifestations are shown in Table 1.[31]

Table 1: Syndromes Associated With Various Chromosomal Disorders Along With Their Oral Manifestations

Abnormalities in number	Structural abnormalities	Abnormalities of sex chromosomes
9p Trisomy	13q Deletion syndrome	Female with multiple X chromosome

Down's syndrome	18q Deletion syndrome	Klinefelter syndrome
Edward's syndrome	Angelman syndrome	Turner syndrome
Mosaic 22 Trisomy	Cri-du-Chat syndrome	XYY syndrome
Pallister- Killian	Prader-Willi syndrome	
Patau syndrome	Velocardialfacial syndrome	
	William's syndrome	
	Wolf-Hirschhorn syndrome	

Genomics And Oral Genodermatoses

Oral genodermatoses (OG) are hereditary dermatological diseases with oral manifestations. The mucous membrane of the oral cavity, tongue, gums, palate, teeth and salivary glands are affected. A wide spectrum of diseases occurs in the oral cavity as a result of genetic mutations, including oral genodermatoses. Genodermatosis can be defined as "a skin phenotype caused by a single mutation, which may be a point mutation, deletion, or chromosomal aberration." The epidermis of the skin and the components of the oral cavity derive from a common embryological neural origin of the ectoderm. As a result, there are many skin diseases that manifest in the oral cavity and affect the oral mucosa and teeth. There should be clinical intimacy between the dentist and the dermatologist to manage such disorders.[32] Table 2 provides brief information regarding the various genes affected in the various Oral Genodermatoses. Genomics provides a clear picture of the genes that are abnormal or affected and helps in the early detection of several Oral Genodermatoses.

Table:2 Genes Affected In Various Oral Genodermatoses

Oral genodermatosis associated with pigmentations of oral cavity and the affected gene	Oral genodermatosis associated with premalignant and malignant lesions and the affected gene	Oral genodermatosis associated with jaw radiolucencies and the affected gene
Peutz jeghers syndrome (STK11 gene)	Dyskeratoses congenital (TERT, TERC, DKC1, or TINF2 gene).	Basal cell nevus syndrome (PTCH1gene)
Neurofibromatoses (NF1 gene)	Basal cell nevus syndrome (PTCH1)	Marfan syndrome (FBN1 gene)
Struge weber syndrome (GNAQ gene)	Gardners syndrome (APC gene)	Ehlers danlos syndrome (COL1A1, COL1A2, COL3A1, COL5A1, and COL5A2 genes)
	Cowden syndrome (PTEN gene)	

CONCLUSION

Advances in genomics and other omics, along with applied sciences, represent a powerful approach to understanding the molecular biology of a disease or abnormality. This evidence base study helps better diagnosis, treatment plan and valuable intervention of various abnormalities. The interrelationship between genetic makeup and environmental factors contributes to an individual's predisposition to many abnormalities. Knowledge of this interplay will help prevent the onset and progression of the disease by modifying the patient's behavior and lifestyle.[3] Therefore, it is recommended that future oral care and examination be an advanced step in dealing with multifaceted oral diseases. according to science, new schemas and upcoming knowledge from people from other fields are mandatory. Also, the unresolved, confusing, and changing structural and functional integrity of the human genome still requires effective prophylactic and curative therapies.

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