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Dental Medicine in the Era of the Genome

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ABSTRACT

Background: The mapping of the human genome and cracking the "code of life" have been huge and era-defining scientific achievements, comparable to walking on the moon. We have made exponential progress over the past century in our understanding of the biological, and more especially the molecular, causes of health and disease. Fundamental theoretical and scientific advancements in the study of heredity, the identification of the DNA molecule and genes, and the clarification of the fundamental tenet of biology characterise the early 20th century. Experimental and increasingly molecular research, including clinical and demographic applications, dominated the second half. The Human Genome Project's 2003 completion and ongoing technological advancements have democratised access to this knowledge and the capacity to produce data on health and disease associations; however, genomic and precision medicine have not yet been fully realised in terms of actually improving people's health.

The field of oral health has advanced significantly over the past century, greatly benefiting from genetic and genomic discoveries. It was discovered that tooth caries had a genetic component as early as the 1920s. Later advances were made in identifying the genetic underpinnings of uncommon illnesses such ectodermal dysplasias, orofacial clefts, and other craniofacial and dental deformities. More recently, genome-wide analyses have been carried out and published for a number of conditions and features, including periodontal disease, dental caries, tooth agenesis, head and neck malignancies, orofacial discomfort, temporomandibular disorders, and craniofacial morphometrics. The most recent frontier in the era of genomic medicine has been reached with gene therapies and CRISPR/Cas gene editing. There are a number of obstacles to overcome and chances to seize as genomics advances quickly. The increase of practitioner and public genomics literacy, the promotion of individual and population oral health, and the eradication of inequities are only a few of the important systematic initiatives required to fully fulfil the potential of genomics.

Keywords: Dentistry, Periodontal Disease, Genetics, Genomics, Precision Medicine

1. INTRODUCTION

There have been few human accomplishments of such scope and ambition as the exploration of the beginnings and limits of the observable cosmos, the identification of the fundamental components that comprise our planet, and the deciphering of the human genome.Like stepping foot on the moon, two of these historic and era-defining scientific achievements include deciphering the "code of life" and mapping the human genome.Although the

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foundations of heredity theories can be traced back to ancient philosophers like Hippocrates and Aristotle, Mendel's (1865) research on pea plants, which was carried out more than 2,000 years later, is regarded as the basis of the majority of modern work on biology and genetics. Our knowledge of the biological, genetic, and particularly molecular causes of health and disease has advanced at an extraordinary and exponential rate over the past century. This article outlines the accomplishments and significant contributions made in the field of oral and craniofacial health genomics over the last century and covers the developments and historical moments in the study of the human genome.

Heritability, chromosomes, and genes in the early part of the twenty-first century

Since Schwann's "cell theory" in the middle of the 19th century, it had been widely accepted that cells are the basic building blocks of life by the beginning of the 21st century. The terms genotype, phenotype, and gene were first coined and used in the early 20th century by Wilhelm Johannsen (2014), and separate research by Walter Sutton and Theodor Boveri reinforced the idea that chromosomes carry the genetic material. Hugo De Vries, Erich von Tschermak, and Carl Erich Correns, among other European scientists, conducted studies at about the same period that supported and revived Mendel's work on genetics and heredity, even while most of its mechanical components remained obscure.

The foundation for understanding the structure and function of the genome was gradually laid over the course of the following two decades.Jean Brachet proposed that DNA is present in the cell nucleus in 1933. Beadle and Tatum (1941) put forward the "one gene-one enzyme" theory seven years later, laying the groundwork for biology's core dogma. Oswald Avery (Avery et al. 1944) claimed that DNA is a "transforming principle." Erwin Chargaff stated in 1950 that while the balance of A-T and C-G ratios differs between species, the ratios of adenine to thymine and cytosine to guanine are equal. He then suggested that DNA "could very well serve as one of the agents, or possibly the agent, concerned with the transmission of inherited properties."

DNA and the "Code of Life" in the latter half of the twenty-first century

James Watson and Francis Crick published their foundational work on the double-helix structure of the DNA molecule in 1953 with the assistance of observations made by Rosalind Franklin and Maurice Wilkins (Fig. 1). A decade or so after that, Nirenberg and Matthaei(1961) reported that a synthetic triplet of DNA polynucleotide letters (a UUU codon) could control protein synthesis and generate a polyphenylalanine protein, which was the first step in deciphering the genetic code. After that, Nirenberg reported the amino acid nucleotide sequences that make up the "code of life" (Bernfield and Nirenberg 1965), for which he was given the 1968 Nobel Prize in Physiology and Medicine.Frederick Sanger, who invented DNA sequencing techniques and technologies in 1977 (Sanger et al. 1977), and Kary Mullis, who later invented the polymerase chain reaction, served as catalysts for further advancements (Saiki et al. 1988). Victor McKusick, a pioneer in the field, compiled a list of Mendelian features and disorders in the 1960s under the title Mendelian Inheritance in Man (McKusick 2016).

Today, the definitive, reference database of human genes and genetic traits is the Online Evolution of the Catalogue (OMIM). Meanwhile, genetic findings that had direct clinical application started to emerge. Lejeune et al. (1959) connected trisomy 21 to Down syndrome, while Gusella et al. (1983) mapped Huntington's disease to chromosome 4 and linked it to a particular trinucleotide repeat (Andrew et al. 1993)

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Three Decades of Genomics in the New Era

In an editorial written by Victor McKusick and Frank Ruddle (1987), which appeared in the inaugural volume of the journal Genomics, the term "genomics" made a daring premiere. The Human Genome Initiative, a $2.7 billion, 15-year project carried out by an unprecedented collaboration of various US-based and worldwide governmental and corporate entities, was one of the most ambitious projects ever began shortly after (Collins et al. 2003). 2001 saw the release of the first draught of the human genome, and 2003 saw the completion of the sequence (International Human Genome Sequencing Consortium 2004).As soon as this milestone was reached, there was a flurry of discussion among various stakeholders about how it related to health care and how it would alter how medicine was practised (i.e., "genomic medicine"; Strasser 2003; Green et al. 2011).

The whole human genome may now be sequenced (also known as whole genome sequencing) in a matter of days for less than $1,000 thanks to recent technical advancements.As a result, numerous studies have been conducted over the past ten years in an effort to uncover genomic markers (i.e., single markers, also known as single-nucleotide polymorphisms) linked to both uncommon and common diseases and features. As of September 1, 2016, there were more than 24,000 distinct single-nucleotide polymorphism-trait connections identified from genomewide association studies, which is an amazing number of associations between genomic areas and health variables (MacArthur et al. 2017). In contrast, the American College of Medical Genetics and Genomics states that only 59 genetic variants are deemed reportable (to research participants) (Kalia et al. 2017).

When it comes to common complex diseases with significant environmental or behavioural components, it is rare for the results of genome-wide association studies or whole genome sequencing to be immediately actionable. Nevertheless, these studies continue to produce insightful information and groundbreaking discoveries about the aetiology of a number of significant human diseases (Manolio et al. 2009). Furthermore, the US National Institutes of Health have launched a daring research strategy to address some of the ethical, legal, social, and diversity issues that have long been associated with genomics research (Sankar and Parker 2017). Finally, it is anticipated that the emergence of precision medicine (Collins and Varmus 2015) will enhance health by providing a more accurate accounting for individual variability, including but not limited to genetics.

Genomics and dental medicine advancements

Dental and Craniofacial Health Traits and Conditions: Genetic Insights

On the heritability of oral and craniofacial features, similar to other systemic illnesses and traits, there have been significant advances and early studies. As early as the 1920s, observations of a hereditary component of dental caries were made (Kappes 1928; Bunting 1934; Klein and Palmer 1940; Hunt et al. 1944). Carl Witkop, who later edited the book Genetics and Dental Health, provided an overview of dental hereditary diseases in a significant paper while working at the National Institute of Dental Research. These diseases included dentinogenesis imperfecta, dentin dysplasia, enamel hypoplasia, tooth agenesis, Ehlers-Danlos syndrome, ankyloglossia, and dental caries (Witkop 1958).

The genetic causes of rare disorders such ectodermal dysplasias, orofacial clefts, and other craniofacial and dental malformations have been uncovered as a result of several additional studies carried out over the past century. Slavkin presented a thorough and comprehensive assessment of genetics and genomics breakthroughs in relation to research on oral and

craniofacial health (2012). In a similar vein, Schaefer (2018) and Morelli et al. (2019) recently published thorough reviews on the genetics of periodontal disease and tooth morbidity. Vieira et al. (2014) provided an excellent review of human genomes research focused in dental caries (i.e., dental caries and tooth loss)

The era of genomics

In contrast to candidate-gene studies, genome-wide association studies have recently made it possible to examine significant portions of the human genome's variation. These studies have been conducted and reported for a number of oral and craniofacial diseases and traits, including periodontal disease (Schaefer et al. 2010; Divaris et al. 2013; Teumer et al. 2013), adult (Wang et al. 2012; Zeng et al. 2014; Morrison (Claes et al. 2018). Beyond the identification of novel genomic contributions to these conditions, data generated from this line of research and its aggregation within the context of large-scale collaborative consortia have allowed the application of novel methodological approaches for the investigation of causal effects (for example, Mendelian randomization; Shungin et al. 2015) and the study of oral systemic disease connections via derivation of genetic correlations (Shungin 2018).

The Future: Using Genome Editing and Molecular Therapies to Apply Genomics Knowledge

There will likely be an acceleration in the rate at which information about phenotype-genotype associations is made available. The dental profession and oral health community have a chance to pick up the pace of both their research and educational efforts. Oral health practitioners are in a good position since saliva is an accessible, simple-to-collect medium that enables genetic investigations and because routine dental checkups take place at regular intervals. The importance of potentially sampling or monitoring the oral microbiome via meta- (i.e., microbial) genomics is further increased by the realisation that the human microbiome is a key player for health (Cho and Blaser 2012), essentially functioning as an organ that is influenced by factors both innate and environmental. The dental and allied health education sectors ought to be at the forefront of genomics education for all of these reasons and more. Direct-to-consumer genetic and genomic testing services are currently available, which is imposing positive pressure on dentistry's professional and educational facets.

Importantly, the era of genomic medicine has advanced to the point that gene treatments and gene editing using CRISPR/Cas systems, which are regularly interspersed short palindromic repeats, are now possible (Cong et al. 2013; Allen et al. 2019). Some of the most active fields for genomics applications right now include personalised (or, rather, precision) cancer treatment, targeted pharmacotherapies, and prenatal screening and interventions. Beyond the acceleration of mechanistic, biological study, the possibilities for the oral and craniofacial area is considerable. Potential applications include the creation of precise molecular therapeutics, tissue engineering and restoration of craniofacial defects, as well as interventions relating to the microbiome and pharmacology. (Yu et al. 2018)

2. CONCLUSION

An implementation science approach is arguably required to realise the full potential of genomics and precision health care, despite the fact that improving individual and population health through the emerging genomics discoveries and knowledge base is both a significant

opportunity and subject to numerous challenges (National Academies of Sciences, Engineering, and Medicine 2016; Roberts et al. 2017). All levels of oral health education can make efforts in this regard while new findings are being made to increase the genomics literacy of present and future oral health professionals. In order to increase the diversity and representativeness of genomics outcomes as well as to identify gaps and possibilities in our translational programme, community involvement is another important direction of necessary activity. The sharing of genomes knowledge and the diversification of genomics research are becoming ethically more important.

Genomic information can and will be utilised to improve people's lives and keep them healthier, but it also carries with it the responsibility to minimise health disparities and do no harm.

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