Evolving concepts of heredity and genetics in orthodontics

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The field of genetics emerged from the study of heredity early in the 20th century. Since that time, genetics has progressed through a series of defined eras based on a number of major conceptual and technical advances. Orthodontics also progressed through a series of conceptual stages over the past 100 years based in part on the ongoing and often circular debate about the relative importance of heredity (nature) and the local environment (nurture) in the etiology and treatment of malocclusion and dentofacial deformities. During the past 20 years, significant advancements in understanding the genomic basis of craniofacial development and the gene variants associated with dentofacial deformities have resulted in a convergence of the principles and concepts in genetics and in orthodontics that will lead to significant advancement of orthodontic treatments. Fundamental concepts from genetics and applied translational research in orthodontics provide a foundation for a new emphasis on precision orthodontics, which will establish a modern genomic basis for major improvements in the treatment of malocclusion and dentofacial deformities as well as many other areas of concern to orthodontists through the assessment of gene variants on a patient-by-patient basis. (Am J Orthod Dentofacial Orthop 2015;148:922-38)

Heredity

I am the family face:
Flesh perishes, I live on,
Projecting trait and trace
Through time to times anon,
And leaping from place to place
Over oblivion.

The years-heired feature that can
In curve and voice and eye
Despise the human span
Of durance—that is I;
The eternal thing in man,
That heeds no call to die

Thomas Hardy (1840-1928)

Awareness that physical constitution and especially facial appearance are passed from one generation to the next, or are somehow inherited, is as old as humankind. Since the inception of orthodontics in the late 19th century, there has been debate regarding the roles of heredity and the environment, euphemistically referred to as nature and nurture, as causes of malocclusion and dentofacial deformities. Ideas regarding inheritance of malocclusion and dentofacial deformities during the early years of orthodontics were understandably naïve; even leaders in the study of heredity at that time lacked understanding of the principles of inheritance. Nevertheless, those early concepts established a foundation for opinions regarding the role of genetics in craniofacial growth as well as clinical treatment of malocclusion and dentofacial deformities for the past century or more.

The purpose of this article is to review the evolution of concepts in orthodontics in relation to discoveries and advances in genetics. Emphasis will be placed on discussions about heredity and genetics that have appeared primarily in the official journal of the American Association of Orthodontists. The rationale for that approach is threefold. First, consideration of the essential elements of genetics, even limited to orthodontics, is far too extensive to be covered adequately in this review. Comprehensive reviews of the basic principles of genetics that are important for modern orthodontists can be found in other recent articles.[1-4] Second, a major purpose of official journals associated with learned professions, such as

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orthodontics, is to give the community of professionals, in this case both practicing orthodontists and orthodontic researchers, the most timely and relevant information necessary to advance their specialty. Therefore, it is reasonable to assume that the content of the *AJO-DO* over its 100-year history provides a bellwether for contemporary thought and opinion in the orthodontic community for understanding genetics. Lastly, this article is part of the centennial celebration of the rich tradition of both scientific research and clinical advances provided by the American Association of Orthodontists through its official journal, and it is appropriate to celebrate the occasion by looking most closely at the *AJO-DO* to appreciate those contributions.

The field of genetics emerged from the broader study of heredity that was initiated by classically trained natural scientists beginning in the first part of the 20th century. At approximately the same time, pioneering dentists were developing mechanical devices for correction of irregularities of the occlusion and jaw deformities, marking the beginning of orthodontics. From the start, orthodontic pioneers understood at least intuitively that heredity was a factor to be considered in determining the physical constitution of progeny, including development of the face and jaws. Moreover, early orthodontic thought leaders such as Kingsley, Angle, and Case, among others, were aware of the major concepts of heredity espoused by the leading natural scientists of the late 19th century: Darwin, Weismann, and Mendel. Although it was not uncommon to see the terms "inheritance" and "heredity" in publications by early orthodontists, however, there was little real appreciation of their actual concepts and principles. Therefore, the orthodontic literature often contained opinions about the role of heredity in the development of overall constitution, dentofacial growth, and malocclusion that would now be considered archaic and in some instances fanciful. This is understandable, since genetics was immature, and the education of early dentists and orthodontists lacked the depth in biologic sciences that became the norm in dental schools decades later.[5,6]

Accepted concepts in genetics and orthodontics each progressed chronologically through a series of conceptual stages as they evolved. Most of those stages can be considered as definitive eras that arose from groundbreaking discoveries and advancements, such as the discovery of the structure of DNA and the completion of the human genome, leading in some cases to new paradigms in the biologic sciences.[7] Consideration of that progression provides a convenient framework for understanding the evolution of concepts from genetics in the field of orthodontics (Table).

BRIEF HISTORY OF GENETICS

Aristotle and Hippocrates, in the 4th century BC, are generally credited with the first scholarly efforts to provide an explanation of the mechanisms of heredity. Aristotle believed that physical traits are transmitted to progeny through instructions found in seminal fluid and menstrual blood. Hippocrates added that each physical trait is predetermined and contained in discrete particles derived separately from the various regions of the bodies of the progenitors.

Pre-Mendelian Era (19th Century)

Nearly 2400 years after Aristotle and Hippocrates, Charles Darwin (1809-1882) proposed that the inherited particles passed from parents to offspring ("gemmules") are "blended" together in the zygote through the process of pangenesis to produce a combination of discrete physical traits inherited separately from each progenitor. August Weismann (1834-1914), who is often called the father of genetics, added that the traits programmed by the units of heredity are predetermined and immutable; ie, they cannot be altered in development and form by environmental or other factors.

Classical Era (1900-1930)

The field of genetics began to emerge at the turn of the 20th century with the rediscovery of experiments on plant hybridization performed over 40 years earlier by Gregor Mendel. With Mendel's laws of inheritance as a foundation, quantitative methods were developed to study traits across generations of animals and plants, giving rise to the study of transmission genetics and quantitative population genetics. Research in structural genetics led to the discovery that genes located on chromosomes are the principal units of heredity. Finally, developmental genetics arose with recognition that genes produce phenotypic traits through their expression during the process of development. Thus began transformation of the study of heredity into the field of genetics as the study of the transmission, structure, and function of the genes.

DNA Era (1930-1970)

The DNA era of genetics was remarkable for groundbreaking discoveries that had wide-ranging impacts in all the biologic sciences. At the outset, the integration of Mendel's laws of inheritance with paleontology in the 1930s provided the basis for the synthetic theory of evolution. Also at that time, quantitative population geneticists developed approaches for analysis of the heritability of phenotypic traits.