While it was once assumed that genetic and environmental contributions to observed variation in many human physical and behavioral features were independent of each other, advances in the field of epigenetics have confirmed the dynamic nature of the interactions between the genome and the environment, which result in phenotypic variation.

Epigenetics can be defined broadly as any alteration in gene expression without changes in nucleotide sequencing. On this basis, the development of the dentition can be viewed as comprising a series of spatial and temporal interactions between epithelial and ectomesenchymal tissues, where minor perturbations in the process of odontogenesis may have significant effects on final phenotypic expression.

Describing dental phenotypes in greater detail (compared with traditional methods), together with application of modern approaches to large-scale genome scanning, now provides an opportunity to explore genetic, epigenetic and environmental influences on the human dentition in more detail than has been possible previously. This has led to a new era of dental phenomics, which involves either intensive (detailed descriptions of multiple features on a single tooth) or extensive (detailed descriptions of multiple features across multiple teeth) phenotyping of the dentition.

The development of new equipment for measuring teeth in two dimensions (2-D) and three dimensions (3-D), including laser scanners, has facilitated the development of dental phenomics. Recent studies have shown both 2-D and 3-D techniques display high levels of reliability, precision and accuracy, opening up a range of exciting possibilities for dental researchers to define new, and more biologically meaningful, phenotypes.

Figure 1 shows an example of 3-D imaging of the dental models of a pair of monozygotic (MZ) twins, demonstrating the high degree of detail and depth.
of dental features possible using 3-D laser technology.

The value of twin studies in dental phenomics

Our studies of Australian twins commenced in the School of Dentistry at the University of Adelaide in the early 1980s, and currently there are records of more than 1,200 pairs of twins across three main cohorts of participants.

The first cohort consists of around 300 pairs of teenage twins, for whom various records have been collected, including dental casts, facial photographs, finger and palm prints and information on laterality, including handedness.

The second cohort comprises around 300 pairs of twins who have been examined at three stages of dental development from approximately 4 to 14 years. These twins were examined in the primary and permanent dentition stages.

The most recent study of tooth emergence and oral health provides a third cohort of around 600 twin pairs, aged from birth to around 5 to 6 years.

Our broad aim in these studies has been to improve our understanding of similarities and dissimilarities and epigenetic factors contribute to variation in dental and facial features, and to oral health.

Inferences from our studies showing dental discordance between MZ co-twins in relation to tooth size, missing teeth, extra teeth and asymmetrical expression, not only highlight the importance of epigenetic influences on human dental development but are consistent with the concept that there is a group of genes that not only influence the size and shape of teeth but also the expression of missing or extra teeth, i.e., there are pleiotropic genetic effects operating on the human dentition, as well as spatial and/or temporal variations in local epigenetic events during odontogenesis, that lead to distinct phenotypic differences in the dentition, even in genetically identical twin pairs.

While the twin pair described in this article illustrates the value of identifying MZ co-twins as well as their similarities (i.e., the MZ co-twin model), there are other twin models available to researchers. These include the traditional or classical twin model (comparisons between MZ twin pairs and DZ twin pairs, which enable heritability estimates to be calculated); the twins-reared-apart model, the investigation of twins and other family members, the MZ half-sibling model, and the DZ opposite sex model.

Case study: MZ co-twins showing similarities, dissimilarities and asymmetry in the expression of various dental features

We have found many examples of MZ twin pairs who exhibit varying degrees of similarity and dissimilarity in the expression of various dental features.

This particular case study describes a pair of MZ co-twins selected from the second cohort for whom facial photographs, and study models of the primary and mixed dentition are available. Zygosity was determined by analysis of up to six highly variable genetic loci (FES, vWA1, FGA1, TH01, D21S11, FGA) on six different chromosomes, using DNA obtained from buccal cells.

This particular MZ co-twin pair has been selected to highlight how similarities, dissimilarities and asymmetry of dental features may all occur in a pair of genetically identical twins.

Similarities in the expression of Carabelli trait

Carabelli trait is evident on the lingual aspect of the mesio-lingual cusp for all primary and permanent maxillary primary first molars (Figure 2) for both Twin A and Twin B (arrowed). Qualitative comparison of the size and position of the feature suggests a high degree of similarity in the expression of the trait for both dentitions (primary and permanent), whereas making intra-twin and/or inter-twin comparisons.

Dissimilarities in the expression of fused primary maxillary incisor teeth

Study models of the lower primary dentition for Twins A and B are shown in Figure 3. Twin B exhibits fused lateral incisor and canine teeth (arrowed), while Twin A does not exhibit any fused teeth. The assumption that the teeth are fused (in contrast to being gminated) is based on the fact that there is one less tooth than expected in each quadrant.

Asymmetry (and mirror-imaging) in the expression of retained primary maxillary incisor teeth

One particularly interesting expression of asymmetry that can be observed in MZ twin pairs is the phenomenon of mirror imaging, where one twin mirrors the other for one or more features. An example of mirror imaging is shown in Figure 4, which presents a frontal view of the upper primary dentition of Twins A and B. The upper left lateral incisor of Twin B is worn and retained (with the upper right lateral incisor having been gminated), while Twin A exhibits a mirror image of this, i.e. the upper right lateral incisor is worn and retained (with the upper left lateral incisor missing) (arrowed).

There is evidence to suggest that many of these dental features discussed may be inter-related, for example, Carabelli trait and the size of teeth, but also the expression of number, size and shape of teeth. This case study highlights how MZ co-twins provide an extremely valuable research model, for example, just one pair of MZ co-twins displaying similarities, dissimilarities and asymmetry in their dentitions offers great opportunity to understand more deeply the underlying biological processes of tooth formation.

Use of high-precision 2-D and 3-D imaging equipment will not only enable us to quantify and describe dental variations, such as Carabelli trait, in more detail than has been possible previously, but to also define new phenotypes that we have not been able to measure previously, including small grooves and tubercles, as well as crown contours, areas and volumes.

How can dental phenomics enhance future understanding of biological processes related to dental development?

We plan to maximize the use of the longitudinal data and DNA we have collected, and continue to collect, by performing genome-wide association scans for putative genetic linkage peaks for a range of dental features, and then to test for association between a series of likely candidate genes and our phenotypes.

Identifying the key genes for dental development in humans would not only provide clinicians with a sounder scientific basis for monitoring individuals predisposed to developmental problems (e.g., missing teeth, malocclusions) but assist when counselling patients, especially where there is a familial history.

By developing the field of dental phenomics we hope to better understand how genetic, environmental and epigenetic factors interact to produce the extensive range of variation observed in the human dentition.

Authors’ contact information

Suzanna Mihailidis, BDS, BIC, PhD Craniofacial Biological Research Group Lecturer, School of Dentistry The University of Adelaide, South Australia 5005, Australia suzanna.mihailidis@adelaide.edu.au

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