have the same genotypes, may display different expressions of missing, tapering and microdont incisors. Presumably these MZ twin pairs have a genetic predisposition for hypodontia that places them near the threshold for agenesis, but minor variations in local epigenetic events during odontogenesis may lead to different phenotypic expression between co-twins. A similar explanation may also account for the discordant patterns of missing premolars or supernumerary teeth within MZ co-twins. Presumably, these MZ twin pairs have a genetic make-up that places them near to a threshold for either missing or extra teeth, but variations in local epigenetic events during odontogenesis, probably relating to the spatial arrangement of cells or temporal events, determine on which side of the threshold they fall.

Molenaar’s concept of developmental systems with emergent self-organizing properties is consistent with our current understanding of the molecular basis of tooth development. The various stages of odontogenesis, including initiation, regulation and differentiation, result from a series of epithelial-mesenchymal interactions between oral epithelial and ecto-mesenchymal tissues that are facilitated by the exchange of various signalling molecules. The work of Jernvall and colleagues in Helsinki has shown how the same genes are expressed and the same signalling molecules released in a reiterative fashion to produce each of the cusps of a molar tooth (Jernvall and Jung, 2000). In fact, these genes seem to be highly conserved in an evolutionary sense and once the process of odontogenesis has been initiated, it tends to proceed as a continuous self-organizing process as described by Molenaar and colleagues (Molenaar et al., 1995).

Our studies of intra-coronal dimensions of molar teeth in twins are also consistent with the concept of a dynamically developing crown pattern during odontogenesis, linked to the formation of signalling centres referred to as enamel knots (Townsend et al., 2005). We suggest that variations in dental crown form between species probably result from regulation of a relatively small number of highly conserved genes that control tooth formation in vertebrates, whereas variations observed within a species, for example in humans, probably result from alterations in the timing of interactions between cells during odontogenesis, as well as the positions of cells relative to each other.

Using our broad definition of epigenetics, both of these processes can be considered to be examples of epigenetic control. In the case of variation between species the control is likely to reside at the level of DNA, whereas in variation within a species the epigenetic influences are likely to occur at the local tissue level.

**Finding the genes for dental development**

Genome-wide association studies (GWAS) are currently being used to identify genes linked to various common diseases, including coronary heart disease, hypertension, diabetes and arthritis. We plan to use a similar approach to identify the key genes involved in dental development.

While the identification of key genes for dental development in humans will undoubtedly be a major step forward, there will still be much work to do. Merely identifying the genes will not necessarily mean that we will be able to explain fully how various dental anomalies arise in individuals. This is where further exploration of epigenetic factors will be essential. Already researchers are beginning to study epigenetic biomarkers in an attempt to explain the reasons for observed differences between MZ twin pairs (Wong et al., 2007). At this stage, the focus is on trying to determine the extent of differences in global genomic DNA methylation levels but it is likely that more specific analyses will be developed soon. Once these approaches aimed at the level of DNA are refined further, and our understanding of the nature of the epigenetic influences at a local tissue level improves, we should be able to provide a clearer picture of how genetic, epigenetic and environmental factors influence human dental development. With this knowledge, we will be in a better position to consider preventive and therapeutic approaches to many of the common developmental problems affecting the human dentition.