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INTRODUCTION

Craniofacial development: making faces

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Craniofacial development has traditionally been a field of research in which many divergent views are expressed and novel theories put forward to explain observed normal and abnormal phenomena. Decades of investigation have shown that craniofacial development is an intricate and complex series of events that require inductive and directive cell and molecular interactions to control the initiation, movement and differentiation of various embryonic cell populations across a spatial and temporal time continuum that results in the correct outgrowth, patterning and tissue integration required to make a face. This special issue of the *Journal of Anatomy* contains review articles written by speakers from the 'Craniofacial Development: Making Faces' symposium held as part of the Winter Meeting of the Anatomical Society at Oxford in January 2005. The volume covers wide-ranging aspects of craniofacial development from the evolution of the head, tissue patterning and morphogenesis to human syndromes and malformations. The thoughtful and insightful reviews illustrate many foci of current research in this area and highlight the challenges that lie ahead in fully understanding the mechanisms underlying the processes required to generate the vertebrate head.

Jim Hanken and J. B. Gross set the scene by examining the predominant role of neural crest cells during cranial development in amphibians. The data summarized by Hanken clearly show that neural crest cells possess some features that are highly conserved among many vertebrate classes, whereas others have a degree of evolutionary variability, an outcome that Hanken believes demonstrates the need for careful and accurate assessment of homology when looking at aspects of cranial development such as the formation of the skull. The articles by **Nicole Le Douarin** and **Jill Helms** and their respective colleagues (Creuzet et al. and Tapadia et al.) focus on tissue and molecular interactions that control development of the face, emphasizing the different mechanisms employed in the distinct regions of the face. Le Douarin highlights the role of the endoderm and Hox genes in patterning the facial structures whereas Helms highlights the role of neural crest cells. Helms and her colleagues also discuss the consequence of defective tissue interactions and the resulting human syndromes.

The patterning and evolution of the branchial arches is the basis of the next review in which **Anthony Graham** and his co-workers again illustrate the essential role of the endoderm and also discuss the evolution of the parathyroid gland. The evolutionary theme is continued by **Shigeru Kuratani** but with a focus on discussing how facial structures evolved. Kuratani postulates that the evolutionary acquisition of the jaw involves a transition from monorhiny to diplorhiny with a consequent heterotypic shift of tissue interactions and changes in the regulation of signalling molecule-encoding genes. The regional specification along the proximodistal axis of the branchial arches is addressed by **Michael Depew** and colleagues, who report findings from recent murine studies that re-enforce the idea of a *Dlx* code controlling proximodistal branchial arch identity and highlight the potential mechanisms through which *Dlx* genes may act.

Rich Schneider takes the evolution of avian beaks to illustrate some of the developmental mechanisms underlying tissue patterning. Schneider reviews recent experiments using transplants of quail and duck embryos that show that development of species-specific structures is promoted by specific patterning information from the ectomesenchyme combined with other cell and molecular events, plus a degree of plasticity of the developing structure. **Drew Noden and Paul Trainor** also explore tissue morphogenesis but focus on the progressive interactions between neural crest and mesoderm cells during craniofacial development and demonstrate again the substantial influence that neural crest cells have on the differentiation and morphogenesis of other tissues. Noden and Trainor review the cell and molecular interactions underlying the origins and initial morphogenesis of neural crest and mesoderm populations, but point out that in order to develop a real understanding of tissue morphogenesis

in the face, future work is needed to identify signals and interactions responsible for the subsequent promotion of integrated tissue assembly. Such knowledge may also give us insight into the basis of some craniofacial abnormalities.

The review by **Jo Price** and colleagues highlights the beauty of the deer antler as a potential model for structural regeneration in mammals. The evidence suggests that antler regeneration has a stem-cell basis, but unfortunately little is known about the molecular machinery underlying this process of re-growth. As the only example of whole organ regeneration in mammals, Price quite rightly emphasizes the need for the deer antler model, despite its limitations, to be exploited further.

Paul Sharpe's review discusses the role of *Barx1*, a homeobox gene, in patterning of the dentition and development of the stomach. Gene inactivation of *Barx1* affects both structures and the author postulates that co-evolution of molar teeth and the digestive system enabled changes in the diet associated with the origin of mammals.

The next set of reviews tackles the issue of normal vs. abnormal craniofacial development. **Andy Copp** looks at the process of cranial neurulation and highlights the differences in the cellular and molecular basis underlying various cranial neural tube defects. Copp shows for instance that defects such as exencephaly in mice are related to disturbances in one or more of a number of cellular based events during neural tube closure, whilst the basis of the condition craniorachischisis is probably related to a single event controlled by a single molecular cascade. The normal and abnormal growth of the mammalian skull vault is the focus of the review by **Gillian Morriss-Kay and Andrew Wilkie**. This paper integrates recent data from mouse and human studies looking at sutural growth and the authors show that mutations in a number of identified genes are responsible for the premature closure of cranial sutures leading to craniosynostosis. Experimental studies and clinical observations also suggest that interactions between neural crest and mesoderm-derived components of the skull are necessary for initiation of the sutural growth centres. **YiPing Chen** examines our understanding of the molecular basis of palatogenesis and reports differential expression of several genes along the anterior–posterior axis of the palate. This suggests that different mechanisms underlie the closure of anterior and posterior regions of the palate and may therefore help explain the aetiology of particular palatal abnormalities.

In the final paper of this special issue **Sven Kreiborg** and his co-workers (Krarup et al.) spotlight a new three-dimensional method for analysing mandibular growth and demonstrate that this technique gives us new insights into the understanding of various aspects of normal and abnormal jaw growth. For instance, this technique shows the translocation of the mandibular canals during growth and changes in tooth direction during the eruption process, both of which will aid in our understanding of certain craniofacial abnormalities.

In addition to thanking the speakers for their exciting contributions, we would like to express our gratitude to Professor Gillian Morriss-Kay, Editor-in-Chief of the journal, for her encouragement and help in putting together this special issue. Thanks must also go to Edward Fenton at the journal whose administrative and organizational skills made the rather daunting task of creating a symposium volume a great deal easier. Finally we thank Jonathan Bennett for his invaluable help in organizing the symposium meeting. We hope that you will agree that this collection of up-to-date review articles will be an invaluable and respected resource for anyone working in the field of craniofacial development, and act as stimulus of interest to those yet to be initiated into this fascinating world.