PREFACE

INTRODUCTION TO *CRANIOFACIAL DEVELOPMENT*

The development of the craniofacial complex lies at the core of what makes us human. The face houses our sensory organs and the cranium cradles the brain. Any aberrations in craniofacial development can therefore jeopardize fundamental processes that allow us to survive, thrive, and enjoy our world: our senses of sight, hearing, smell, and taste; our ability to eat, drink, and breathe; our intellectual capacity. Moreover, the uniquely individual face represents one of the most important and salient parts of the identity we present to our peers. For all of these reasons, craniofacial development has long been a source of fascination to scientists.

Beginning in the mid-twentieth century, it became clear that the unique challenges of understanding craniofacial biology are best suited to an interdisciplinary team approach, due in large part to luminaries of the field such as Hans Spemann, Hilde Mangold, and Samuel Pruzansky. The contributions to the present volume continue this tradition, building on scientific and technological advances in developmental biology, molecular genetics, and medicine to bring a multitude of perspectives to bear on issues pertaining to craniofacial development. The authors hail from the fields of developmental patterning, cell and molecular biology, stem cell biology, evolutionary biology, clinical genetics, and everything in between. As a result, this book provides a comprehensive overview of the current status of our understanding of craniofacial development.

This book is organized into three sections. The first section discusses aspects of craniofacial morphogenesis and regeneration on multiple scales, from cells to tissues to organs. Many of our unique organs are housed in the craniofacial region, yet the regulatory mechanisms of cell–cell interactions, tissue development, and organogenesis share common features with those that control the development of the rest of the body. The major families of growth factors (BMP/TGF-β, FGF, Wnt, and Hh) are all involved in the regulation of craniofacial development. The signaling specificity of these growth factors lies with the cells, which have unique transcription factors and other genetic and epigenetic regulators that collectively determine the outcome of growth factor signaling during craniofacial morphogenesis. The chapters in this section offer evolutionary and embryonic perspectives on the regulation of the facial

muscles, mandible, tongue, palate, temporomandibular joint, cranial sutures, tooth, and ear development. These studies provide an in-depth overview of cell fate determination and how continued tissue–tissue interactions control craniofacial development and regeneration.

The second section focuses on craniofacial patterning and signaling mechanisms. The principal goal of developmental biology is to understand how tissues are induced and patterned to generate different organs at the proper location and time. Evidence suggests that signals from the anterior visceral endoderm, anterior neural ridge, and mesoderm are required for the development of craniofacial structures. The formation of the vertebrate "New Head" depends upon the presence of cranial neural crest cells and additional sensory placodes. Multiple molecules have been identified as crucial regulators for tissue–tissue interactions during craniofacial development. Using fish, chick, mouse, and other animal models, the chapters in this section provide a summary of our current understanding of how early craniofacial patterning is established and how signaling networks control craniofacial morphogenesis.

The third section of the volume is centered around disease models, human genetics, genomics, and new approaches in dynamic imaging. Animal models have clearly played an important role in our understanding of normal and abnormal craniofacial development. Yet despite the vast amount of knowledge that we have gained from animal studies, shortcomings remain: for example, apparently only one third of mouse mutations associated with craniofacial defects have been linked to mutations of the orthologous human genes with similar dysmorphologies. It is not known what defects might arise from mutations of the other two thirds of these genes, as some of these mutations result in early embryonic lethality. It is of paramount importance that there are constant interactions between researchers involved in human and animal studies, as this will ensure a rapid translation of fundamental discoveries into treatment and prevention of craniofacial malformations in humans. Craniofacial malformations represent complex multifactorial diseases, amplified or attenuated by gene–gene interactions, gene–environmental interactions, environmental influences, and mechanical factors. The rapid technological advancement and decreased cost of sequencing the human genome will undoubtedly facilitate the discovery of genetic mutations involved in human craniofacial malformations. Furthermore, this new information will facilitate the design and implementation of precision medicine. Finally, the improved spatial and temporal resolution

of dynamic and live imaging will also elevate our study of craniofacial development to the next level of insight and excellence.

It has been an extremely rewarding experience working with so many talented and accomplished scientists and clinicians in putting together this book. I would like to express my tremendous gratitude to them for the time and effort they devoted to this project. It is my hope that our authors' diverse perspectives will provide a well-rounded view of the current state of affairs in craniofacial development and a springboard for further advances in the field.

YANG CHAI, DDS, PhD Professor
George and MaryLou Boone Chair in Craniofacial Biology
University of Southern California