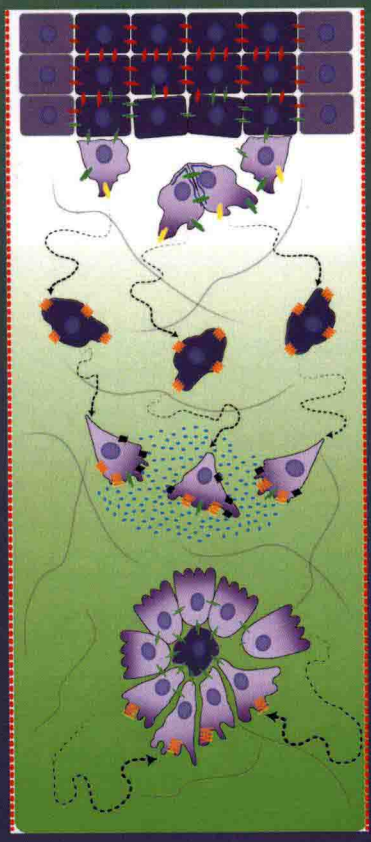
CELLULAR ADHESION IN DEVELOPMENT AND DISEASE



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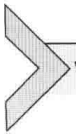

VOLUME ONE HUNDRED AND TWELVE

CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY

Cellular Adhesion in Development and Disease

Edited by

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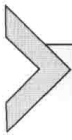

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Cellular Adhesion in Development and Disease

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"A meeting-ground for critical review and discussion of developmental processes"
A.A. Moscona and Alberto Monroy (Volume 1, 1966)

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PREFACE

Cell adhesion is a fundamental determinant of development in metazoan organisms. For over a century—from the early observations of HV Wilson, through the seminal studies of Townes and Holtfreter, and since—we have endeavored to understand how adhesion helps make multicellular organisms more than just the sum of their parts. We now know that physical interactions between cells and their environment (other cells and components of the extracellular matrix) influence critical parameters of development, including tissue cohesion, cellular patterning, differentiation, and population control. These diverse functional effects reflect the complex ways in which distinct adhesion systems interact with cellular processes such as signaling, the cytoskeleton, and membrane trafficking. In this volume, we aim to survey recent developments in understanding how the cellular and molecular mechanisms of adhesion determine the development of organisms and their constituent organs.

The early chapters in this volume endeavor to define some of the key processes that allow adhesion to influence development. Melanie White and Nicolas Plachta review how adhesion cooperates with the cytoskeleton to drive the earliest cellular events in the preimplantation mouse embryo: compaction, change in cell shape, polarity, and cell fate. François Fagotto then addresses one of the long-standing problems in developmental biology: understanding how boundaries are formed in the embryo. Building on the long-standing realization that boundaries reflect physical differences between populations of cells, Fagotto outlines how different cell–cell adhesion systems may cooperate with the cytoskeleton to segregate cell populations at boundaries.

We then have a series of chapters that focus on the mechanisms by which cadherin cell adhesion molecules influence animal development. Here, a major advance has come from the realization that cadherins cooperate with the contractile apparatus, that is, the actomyosin cytoskeleton. Accordingly, Rashmi Priya and Alpha Yap discuss the molecular and cellular mechanisms that allow cadherin adhesion systems to physically interact with, and also regulate, the actomyosin cytoskeleton. Katja Röper then addresses how cooperation between cell–cell adhesion and contractility determines morphogenesis in the early *Drosophila* embryo. In their chapter, Pierre McCrea, Meghan Maher, and Cara Gottardi broaden the discussion to review how

cadherins and their associated proteins signal to the nucleus, a paradigm that underlies canonical Wnt signaling and also impinges on other fundamental developmental pathways, such as the Hippo signaling pathway.

Of course, cadherins are not the only adhesion systems that influence development. Another large family of cell–cell adhesion molecules are the nectins and nectin-like proteins. Kenji Mandai, Yoshimi Takai, and their colleagues discuss the fundamental cell biology of nectins and review how these molecules affect the development of many organs in the body. Aidan Maartens and Nicholas Brown then outline developments in understanding how integrin cell–matrix adhesion molecules contribute to *Drosophila* development, including notable developments in how integrins influence cell fate, cell migration, and cell polarity.

The two subsequent chapters focus on developmental processes that integrate adhesion, signaling, and the cytoskeleton. Pierre Savagner discusses the concept of epithelial-to-mesenchymal transition, providing a historical and conceptual framework for this complex phenomenon, with its often controversial mechanistic underpinnings. Elias Barriga and Roberto Mayor then take the example of neural crest migration to consider how adhesive events generate collective patterns of cell migration.

Finally, we examine how cell adhesion influences the development of individual organs. Anne Lagendijk and Benjamin Hogan review how cell signaling and cell–cell adhesion cooperate during vascular development. Eliah Shamir and Andrew Ewald focus on how individual and collective cell migration are regulated by cell–cell adhesion to drive epithelial morphogenesis of the mammary gland. Kaelyn Sumigray and Terry Lechler review how multiple junctions (adherens, tight, and desmosomes) contribute to development of the epidermis as a fundamental biological barrier in the body. Lauren Friedman, Deanna Benson, and George Huntley consider the role that cadherins play in the nervous system, with a particular focus on understanding their role in synapse formation and the generation of synaptic networks, the bases of neural activity. And in the final chapter of this volume, Alexander Combes, Jamie Davies, and Melissa Little discuss how cell adhesion drives self-organization in the embryonic kidney, providing insights relevant to tissue engineering and regenerative medicine.

We hope that the contributions in this volume illustrate some of the different perspectives that are now being used to understand how cell adhesion contributes to development. A final perspective lies in the relationship between development and disease. Many of the cellular mechanisms and biological processes that we consider are also implicated in disease. Thus,

we also sought, where possible, to highlight how basic biology illuminates our understanding of disease and vice versa. We hope that these reviews will then be a useful guide to students of fundamental biology and pathology. And we will be well pleased if they prompt further research at the interface between these disciplines.

ALPHA S. YAP

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CHAPTER ONE

How Adhesion Forms the Early Mammalian Embryo

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Abstract

The early mouse embryo is an excellent system to study how a small group of initially rounded cells start to change shape and establish the first forms of adhesion-based cell–cell interactions in mammals *in vivo*. In addition to its critical role in the structural integrity of the embryo, we discuss here how adhesion is important to regulate cell polarity and cell fate. Recent evidence suggests that adherens junctions participate in signaling pathways by localizing key proteins to subcellular microdomains. E-cadherin has been identified as the main player required for the establishment of adhesion but other mechanisms involving additional proteins or physical forces acting in the embryo may also contribute. Application of new technologies that enable high-resolution quantitative imaging of adhesion protein dynamics and measurements of biomechanical forces will provide a greater understanding of how adhesion patterns the early mammalian embryo.

1. THE MOUSE PREIMPLANTATION EMBRYO AS A MODEL OF ADHESION IN MAMMALIAN DEVELOPMENT

Most research on adhesion has been performed on cells in tissue culture due to their availability and ease of manipulation. However, it is only

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