Preface

Cell–cell junctions emerged with the appearance of metazoan organisms. They serve many functions that are necessary for multicellular life, including adhesion, cell-to-cell communication, and the assembly of tissue barriers that separate the animal body from its environment and that segregate tissue compartments within the body. Conversely, dysfunction of cell–cell junctions is increasingly implicated in disease. The biology of cell–cell junctions must ultimately be understood as a hierarchy of processes that range from molecular mechanisms to the functioning of whole tissues, organs, and organisms. Since the first edition of this book was published, we have learned much more about the molecular apparatuses that constitute these junctions, the cellular processes with which they intersect, and the biological and pathobiological processes that they affect. In compiling this second edition of *Cell–Cell Junctions*, we have endeavored to build on the foundation of the first edition, to capture areas that have seen major advances or where new roles for cell–cell junctions have come to maturity.

The first section of this volume reviews advances in understanding how cell–cell junctions integrate physical connections between cells, cell signaling, and intracellular processes, such as the cytoskeleton and membrane traffic. An important development has come from realizing the important role that mechanical forces play in junctional biology. This is most evident for adherens junctions and desmosomes, which resist detachment forces and are thus inherently mechanical elements. The molecular mechanisms of adhesion are themselves regulated by mechanical force; this is best understood for adherens junctions (as discussed by Mège and Ishiyama) and increasingly evident for desmosomes (Hatzfeld et al.). Mechanical forces can also be detected to elicit cell signaling at junctions (mechanotransduction, Yap et al.). Cell–cell junctions intersect with diverse signaling pathways, including those found at the junctional cortex itself (such as the small GTPases discussed by Braga) or others that regulate transcription, notably the Hippo pathway (Karaman and Halder). Importantly, cell–cell junctions are dynamic structures that are regulated by cellular processes, such as membrane traffic (as discussed by Brüser and Bogden). Finally, assembly of cell–cell contacts by junctions allows a diverse range of other intercellular communication mechanisms to operate. This is discussed by Beamish et al., who highlight how signals first identified as guidance cues for neuronal migration have come to be appreciated for their broader role outside the nervous system.

The biological impact of these cellular mechanisms depends on the developmental and physiological context of the tissues in which they appear. This is considered in the second section of this volume. The more complex tissue environment requires functional collaboration and cross-talk between different junctions. To understand this, Garcia et al. compare and contrast the roles that different junctions play during epithelial homeostasis in the gastrointestinal tract and skin, while Rubsam et al. take an evolutionary perspective to understand how adherens junctions and desmosomes came to be utilized to mediate morphogenesis in complex tissues. The physical interactions mediated by cell–cell junctions influence fundamental drivers of tissue organization, such as movement and proliferation. Friedl and Mayor consider how cell–cell junctions influence the process of collective cell migration, and Chiasson-Mackenzie and McClatchey focus attention on the control of receptor tyrosine kinase signaling, a major mediator of cell proliferation. Two chapters in this section consider how the diverse developmental impact of cell–cell junctions is manifest during organ development. Symborska and Gerhardt review the role that cell–cell junctions play in coordinating the many steps of vascular development, and Krauss, Joseph, and Joel discuss how junctions regulate

muscle development. Finally, the roles of junctions in the physiology of hearing and neural network development are covered by Jaiganesh et al. and Jontes, respectively.

The third section of this volume then aims to consider how the biology of junctions may be perturbed in disease. Tight junctions seal the paracellular pathway that is essential for epithelia to form effective tissue barriers. Buckley and Turner review how the tight junction barrier is regulated and how that is perturbed by inflammation in the gastrointestinal tract. Endothelia constitute another form of tissue barrier and the role of cadherin dysfunction in vascular disease is discussed by Lampugnani, Dejana, and Giampietro. Bruner and Derksen review how cadherin dysfunction contributes to cancer. Finally, Delmar et al. consider how dysfunction of connexins, the constituent of gap junctions perturbs cell–cell communication in conditions that range from multisystem developmental disorders to degenerative diseases of the nervous system.

Altogether, we hope that these reviews give the reader a picture of recent developments in the field of cell–cell junctions. If, in tissues, no cell is an island, complete unto itself, then the diverse junctions that they form with one another are major reasons for this. And their impact is felt in many other contexts that we have been unable to include in this volume. Undoubtedly, this journey of understanding is not yet over.

Carien M. Niessen
Alpha S. Yap