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Cell-Cell Interactions

Methods and Protocols

Second Edition

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Preface

Cell–cell interactions, as well as interactions between cells and the extracellular matrix (ECM), are essential to the development and function of tissues and organs. While cell–cell interactions are generally dynamic, there are varying degrees of stability. Tight cell–cell junctions are stable, such as those in the heart, and play an essential role in the organization of the cells. Other interactions are transient in nature, such as interactions between cells of the immune system. Nevertheless, for the maintenance of proper form and function of all tissues and organs, cells must communicate with each other.

Cells can communicate with each other in multiple ways, including through chemical, mechanical, and electrical signals. Chemical signaling can occur through several different mechanisms. Autocrine signaling is when a cell secretes a chemical messenger that binds to autocrine receptors on the same cell, which in turn affects the way the cell functions. Paracrine signaling is a form of signaling in which the cell affects neighboring cells by secreting chemicals into the common intercellular space. In addition, cells can directly transfer ions or small molecules (miRNAs, small signaling proteins) from one cell to another through pores in the cell membrane called gap junctions. This is the quickest method of cell–cell communication and is found in tissues where fast, coordinated activity of cells is required, such as in the heart.

Cells can also respond to mechanical signals in the form of externally applied force or force generated by cell–cell or cell–ECM interactions. Many cell functions, such as motility, proliferation, differentiation, and survival, can be altered by changes in the stiffness of the substrate to which the cells are adhered or through the pull of other cells, even when chemical signals remain unchanged. Interestingly, mechanical deformation of cardiac fibroblasts can cause membrane depolarization leading to a concept of mechano-electrical transduction. Cell junctions, such as through connexins, are important for cellular communications in other organ systems and likely play similar roles in physical communication between fibroblasts and other cells within the myocardium. Indeed, it has been demonstrated through Cx43 that electrical coupling of myocytes and cardiac fibroblasts can occur. In addition, in vitro cell–cell interaction assays have shown that cardiac fibroblasts and myocytes communicate through the formation of tight cell–cell junctions. Moreover, ion channels also play an intriguing and important method of signaling because abnormalities in these channels can lead to tissue dysfunction. Clearly, it is a combination of the various signals (electrical, chemical, and mechanical) that allow for proper form and function of the tissue or organ.

While whole animal models provide insight into gene-specific mechanisms, these models are limited by the complexity of the whole organism. Therefore, the use of cell models to examine cell–cell interactions is critical for our understanding of how cells communicate and what genes or proteins are altered in disease states.

The aim of this volume of Methods in Molecular Biology: Cell–Cell Interactions is to provide a collection of protocols, incorporating in vivo and in vitro methods-based approaches. This book brings together many currently used assays in examining cell–cell interactions. It is my belief that this work will represent an important resource for researchers, which will be valuable not only to those already involved in the cell–cell interaction field but also to those who are new to the area. I hope that you will find cell–cell interactions instructive and useful in your studies.

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