

METHODS IN MOLECULAR BIOLOGY™

Series Editor
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Cell-Cell Interactions

Methods and Protocols

Second Edition

Edited by

Troy A. Baudino

*Texas A&M Health Science Center, Central Texas Veterans
Health Care System, Temple, TX, USA*

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Editor

Troy A. Baudino
Texas A&M Health Science Center
Central Texas Veterans Health Care System
Temple, TX, USA

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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.

Temple, TX, USA

Troy A. Baudino, Ph.D., F.A.H.A.

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Contributors

- KATHARINA AUSTEN • *Group of Molecular Mechanotransduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany*
- F. BARTSCH • *General, Visceral and Transplantation Surgery, Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany*
- TROY A. BAUDINO • *Texas A&M Health Science Center, Central Texas Veterans Health Care System, Temple, TX, USA*
- STEPHANIE L.K. BOWERS • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- LISANDRA E. DE CASTRO BRÁS • *San Antonio Cardiovascular Proteomics Center, The University of Texas Health Science Center, San Antonio, TX, USA; Barshop Institute for Longevity and Aging Studies, The University of Texas Health Science Center, San Antonio, TX, USA; Division of Geriatrics, Gerontology and Palliative Medicine, Department of Medicine, The University of Texas Health Science Center, San Antonio, TX, USA*
- JOSEPH BRESSLER • *Hugo Moser Laboratory at the Kennedy Krieger, Kennedy Krieger Institute, Baltimore, MD, USA; Department of Environmental Health Sciences, Center In Alternatives In Animal Testing, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA*
- CHRISTOPHER S. CHEN • *Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA*
- ANNA CHROSTEK-GRASHOFF • *Group of Molecular Mechanotransduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany*
- KATHERINE CLARK • *Department of Environmental Health Sciences, Center In Alternatives In Animal Testing, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA*
- DANIEL M. COHEN • *Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA*
- GEORGE E. DAVIS • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA; Department of Pathology and Anatomical Sciences, University of Missouri School of Medicine, Columbia, MO, USA*
- MATTHEW T. DAVIS • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- DAVID E. DOSTAL • *Division of Molecular Cardiology, Department of Medicine, Texas A&M Health Science Center, Cardiovascular Research Institute, Temple, TX, USA*
- TIMOTHY N. FEINSTEIN • *Department of Pharmacology and Chemical Biology, University of Pittsburgh, Pittsburgh, PA, USA*

- HAO FENG • *Texas A&M Health Science Center, College of Medicine, Cardiovascular Research Institute, Temple, TX, USA*
- DONALD M. FOSTER • *Central Texas Veterans Health Care System, Temple, TX, USA*
- ANDREA FREIKAMP • *Group of Molecular Mechanotransduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany*
- ERIC GABISON • *Univ Paris Diderot and Fondation A. de Rothschild, Paris, France*
- P. GASSMANN • *General, Visceral and Transplantation Surgery, Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany*
- FNU GERILECHAOGETU • *Texas A&M Health Science Center, College of Medicine, Cardiovascular Research Institute, Temple, TX, USA*
- SHANNON GLASER • *Central Texas Veterans Health Care System, Temple, TX, USA; Digestive Disease Research Center, Texas A&M Health Science Center, College of Medicine, Temple, TX, USA*
- HONEY B. GOLDEN • *Texas A&M Health Science Center, College of Medicine, Cardiovascular Research Institute, Temple, TX, USA*
- CARSTEN GRASHOFF • *Group of Molecular Mechanotransduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany*
- WEI-HUI GUO • *Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA, USA*
- J. HAIER • *Molecular Biology Lab, Department of General Surgery, University Hospital of Muenster, Muenster, Germany*
- KEVIN HAKALA • *Department of Biochemistry, San Antonio Cardiovascular Proteomics Center, The University of Texas Health Science Center, San Antonio, TX, USA*
- JUAN C. IBLA • *Department of Pediatrics, Genetics Medicine and Integrative Systems Biology, George Washington University, Washington, DC, USA*
- CLAUS JORGENSEN • *Division of Cancer Biology, The Institute of Cancer Research, London, UK*
- M.L. KANG • *Molecular Biology Lab, Department of General Surgery, University Hospital of Muenster, Muenster, Germany*
- FARAH KHAYATI • *Laboratoire de Pharmacologie and INSERM U940, Hôpital Saint-Louis, Paris, France*
- JOSEPH KHOURY • *Department of Cellular and Molecular Biology, Exogenesis Corporation, Billerica, MA, USA*
- DAE JOONG KIM • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- CARLEEN KLUGER • *Group of Molecular Mechanotransduction, Max-Planck-Institute of Biochemistry, Martinsried, Germany*
- WILLIAM T. LEE • *The Laboratory of Immunology, New York Department of Health, The Wadsworth Center, Albany, NY, USA*
- YAOJUN LI • *San Antonio Cardiovascular Proteomics Center, The University of Texas Health Science Center, San Antonio, TX, USA; Barshop Institute for Longevity and Aging Studies, The University of Texas Health Science Center, San Antonio, TX, USA; Division of Geriatrics, Gerontology and Palliative Medicine, Department of Medicine, The University of Texas Health Science Center, San Antonio, TX, USA*

- MERRY L. LINDSEY • *Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA*
- S.T. MEES • *Department of General and Visceral Surgery, University Hospital of Muenster, Muenster, Germany*
- SUZANNE MENASHI • *CNRS EAC 7149, Faculté des Sciences, Université Paris-Est Créteil, Créteil, France*
- CHUN-XIA MENG • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- KEITH MOORE • *Biomedical Engineering Program, University of South Carolina, Columbia, SC, USA*
- SAMIA MOURAH • *Laboratoire de Pharmacologie and INSERM U940, Hôpital Saint-Louis, Paris, France*
- DAMIR NIZAMUTDINOV • *Texas A&M Health Science Center, College of Medicine, Cardiovascular Research Institute, Temple, TX, USA*
- PIETER R. NORDEN • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- CLIONA O'DRISCOLL • *Hugo Moser Laboratory, Kennedy Krieger Institute, Baltimore, MD, USA; Department of Environmental Health Sciences, Center In Alternatives In Animal Testing, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA*
- ALEXEI POLIAKOV • *Division of Developmental Neurobiology, MRC National Institute of Medical Research, Mill Hill, London, UK*
- JAY D. POTTS • *Biomedical Engineering Program, University of South Carolina, Columbia, SC, USA; Department of Cell Biology and Anatomy, University of South Carolina School of Medicine, Columbia, SC, USA*
- ANDREW RAPE • *Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA, USA*
- ANNIE O. SMITH • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- KATHERINE R. SPEICHINGER • *Department of Medical Pharmacology and Physiology, University of Missouri School of Medicine and Dalton Cardiovascular Research Center, Columbia, MO, USA*
- AMBER N. STRATMAN • *Program in Genomics of Differentiation, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA*
- ADAM VANDERGRIF • *Biomedical Engineering Program, University of South Carolina, Columbia, SC, USA*
- YU-LI WANG • *Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA, USA*
- SUSAN T. WEINTRAUB • *Department of Biochemistry, San Antonio Cardiovascular Proteomics Center, The University of Texas Health Science Center, San Antonio, TX, USA*

- ANDRIY YABLUCHANSKIY • *San Antonio Cardiovascular Proteomics Center, The University of Texas Health Science Center, San Antonio, TX, USA; Barshop Institute for Longevity and Aging Studies, The University of Texas Health Science Center, San Antonio, TX, USA; Division of Geriatrics, Gerontology and Palliative Medicine, Department of Medicine, The University of Texas Health Science Center, San Antonio, TX, USA*
- MIKE T. YANG • *Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, USA*
- JIAN ZHANG • *Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA, USA*