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Cell Migration

*Developmental
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Edited by

Jun-Lin Guan



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Cell Migration

Developmental Methods and Protocols

Edited by

Jun-Lin Guan

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Preface

Cell migration plays an essential role in a variety of biological processes, including embryonic development, homeostasis, immune responses, wound healing, and cancer metastasis. Indeed, one of the defining features of life is the ability to move, which occurs at different levels from the macromolecular machines in a cell, to individual or populations of cells, and to the whole organism. The dramatic movements of layers of cells in gastrulation, a critical period of embryonic development of many animals, as well as the swimming of simple unicellular amoeba in search of nutrients, have fascinated biologists for years.

Cell migration is a complex process and has attracted the interest of researchers from diverse disciplines in biology. However, like many other areas of investigation, the recent exciting and explosive growth of cell migration studies are critically linked to the rapid advance of cell and molecular biology and its increasing influence on all the other fields of life sciences and biomedical research. Thanks to rapid progress at the cellular and molecular levels, unprecedented knowledge has been gathered regarding the components and interactions of the macromolecular machinery of cell movement, the signaling mechanisms and pathways involved in cellular responses to chemotactic and haptotactic stimulations, and the regulatory mechanisms that link the signaling pathways to the cell movement machinery.

A second major contributor to our modern understanding of, and research on, cell migration is the recent creation and success in using various model organisms in the study of cell migration. The power of genetics in these systems allowed for the discovery of novel molecules and signaling pathways that are important in the regulation of cell migration. The conservative nature of many of these molecules and pathways has also allowed researchers to move from one system to another when putting together the various puzzle pieces of the regulatory mechanisms, taking advantage of our knowledge in each of these different systems. Last but not least, the use of model organisms has also allowed scientists to study the intrinsically interesting biology of cell migration in the context of development and other biological processes *in vivo*.

A third emerging trend of modern cell migration research is the increasing use of more sophisticated imaging and other novel genetic approaches. However, it is important to note that many of the simple and classic cell migration assays developed in earlier times are still part of toolboxes of cell

migration researchers, and indeed they provide the basis from which the newer variations and novel approaches are developed. The combination of this long history with the recent expansion has ensured the development of a large number of methodologies and experimental protocols in the cell migration field that are derived from diverse biological disciplines, and sometimes as results of interdisciplinary efforts.

The aim of *Cell Migration: Developmental Methods and Protocols* is to bring together a wide range of novel and state-of-the-art methodologies as well as various classic methods in cell migration research in cultured cells, different model organisms, and as applied to specialized cells in normal development and in disease. Each chapter is presented in the user friendly format of the highly successful *Method in Molecular Biology* series by leading experts in their field who have contributed significantly to the development of the methods and/or applied the methods successfully in their research on various aspects of cell migration. This volume begins with an overview of the cell migration field that also discusses the methods presented. Part II (Chapters 2–8) describes various basic assays that apply to all cell migration studies in vitro. Part III (Chapters 9–12) includes cell migration assays for cancer cells, endothelial cells, and neurons both in vitro and in animal models. Part IV (Chapters 13–19) discusses cell migration assays in various model organisms. Part V (Chapters 20–24) combines chapters on biochemical methods to study the mechanisms of cell migration and several new approaches to the study of cell migration.

The overall goal of *Cell Migration: Developmental Methods and Protocols* is to provide comprehensive coverage on all relevant methods in one volume so that anyone who is interested in cell migration research can rely on it as a useful reference. It is intended for both beginning students and active researchers in the field. The primary target audience is cell and developmental biologists. However, it should also be very useful to geneticists, biochemists, and molecular biologists, as well as clinicians and others who are interested in looking at the mechanisms of cell migration or use of cell migration as biological assays in their studies of molecular mechanisms or disease processes.

The publication of *Cell Migration: Developmental Methods and Protocols* would not have been possible without outstanding contributions from all the authors. I am extremely grateful for their generosity in sharing with the readers their expertise and perspective on the various methods and protocols described. My heartfelt thanks also go to Cindy Westmiller, who has provided tremendous assistance in proofreading all the chapters and organizing the manuscripts. I would also like to acknowledge the series editor, Dr. John Walker, for his valuable input and guidance during the editing process.

We all share the hope that this book will find its place on the shelves on many laboratories and be used as a frequent reference by students and experienced researchers alike in the exciting field of cell migration studies.

Jun-Lin Guan

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I ---

INTRODUCTION

Cell Migration

An Overview

Donna J. Webb, Huaye Zhang, and Alan F. Horwitz

Summary

Cell migration is an essential process for normal development and homeostasis that can also contribute to important pathologies. Not surprisingly, there is considerable interest in understanding migration on a molecular level, but this is a difficult task. However, technologies are rapidly emerging to address the major intellectual challenges associated with migration. In this chapter, we outline the basics of cell migration with an emphasis on the diverse systems, methodologies, and techniques described in this book. From the contributions presented, it is apparent that the next few years should produce major advances in our understanding of cell migration.

Key Words: Cell migration; adhesion; signaling; protrusion; development.

1. Introduction

Cell migration is a complex process that is essential for embryonic development and homeostasis (1,2). In gastrulation, migration is particularly robust, where essentially all cells migrate as sheets to form the three layers, including endoderm, ectoderm, and mesoderm that comprise the resulting embryo. Cells within these layers migrate to target locations throughout the developing embryo, where they differentiate and form various tissues and organs. The migration of cells from epithelial layers to their targets is a general phenomenon that occurs throughout development. In the developing cerebellum, neuronal precursor cells migrate from the epithelium to their residences in distinct layers. One special form of migration during development is the extension of neurites. The tip of a developing neurite, the growth cone, shares many similarities with a migrating cell. The precise guidance and target recognition of

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