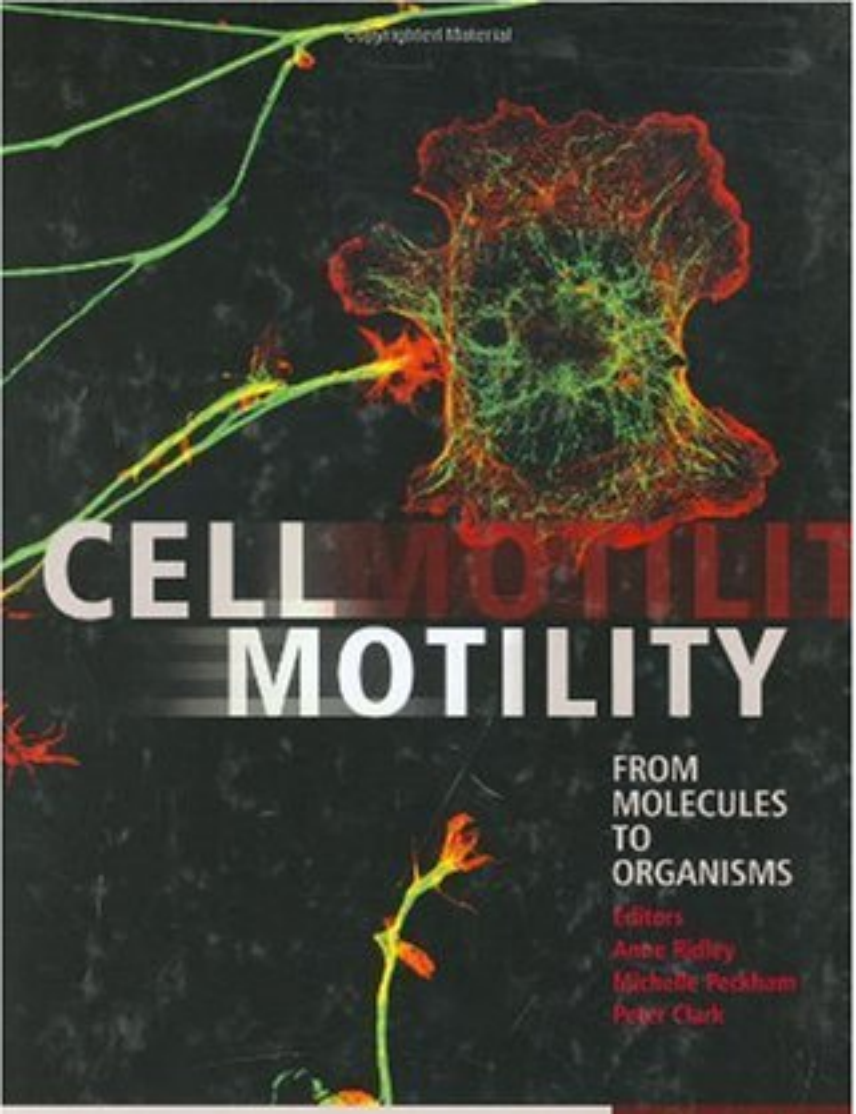

CELL MOTILITY

FROM MOLECULES TO ORGANISMS

Editors
Anne Ridley
Michelle Peckham
Peter Clark

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From molecules to organisms

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This book is dedicated to Joan Heaysman,
longtime collaborator of Michael Abercrombie,
to mark her reaching her seventieth year.

Contents

Preface

The study of cell motility encompasses a wide range of approaches and techniques. This book provides a series of reviews by experts on different aspects of cell motility, from those studying molecules *in vitro* to those studying whole organisms. The reviews were commissioned from speakers at the 5th Abercrombie Symposium on Cell Motility, held in Oxford, UK in September 2003. These symposia are held every five years to commemorate the work of Michael Abercrombie, who was one of the pioneers in studying cell behaviour. Many of the concepts on how cells move that we now take for granted were established through his careful analysis. He made numerous timelapse films of moving cells cultured *in vitro*, and established that they extended lamellipodia and that when they met each other normal cells stopped moving (contact inhibition), rather than crawling over each other. The Abercrombie Symposia have become a forum for presenting the latest results in Cell Motility research.

Several articles in this volume report the enormous progress that has been made in the last few years in establishing at a molecular level how cells extend lamellipodia. The biochemical basis for the actions of actin-regulatory proteins such as the Arp2/3 complex, cofilin, profilin and capping proteins has been intensively investigated, and is discussed by Tom Pollard. A major discovery of the last five years is that the WASp-related proteins are central players in signal transduction from the plasma membrane to the Arp2/3 complex, and the regulation and action of WASp proteins is the topic of articles by the groups of Laura Machesky, Robert Insall and Tadaomi Takenawa.

Severing of actin filaments as well as *de novo* nucleation is important for altering cell morphology, as described in the chapters by Daniel Louvard and John Condeelis. A new player in the actin dynamics field is dynamin, a GTPase first characterized for its role in vesicle fission; the involvement of dynamin in cell motility is introduced by Orth and colleagues.

Lamellipodium extension is required for cell migration, but the cell body needs to move to follow the extension. Several events are critical for this. First, cell adhesion to its surroundings is important for the cell to exert a traction

force. Meg Titus discusses the contribution of talin, which binds to transmembrane integrin receptors, and myosins with sequence homology to talin, in cell adhesion. Second, loss of cell adhesion by cell detachment selectively at the rear of the cell is essential for productive locomotion; Anna Huttenlocher reviews the role of the protease calpain in this process. Third, actin interaction with myosin is important for generating contractile forces and movement of actin filaments inside cells, and Soldati and Kistler discuss how class I myosins contribute to these processes.

Following the movement of and interaction between proteins within living cells is essential for understanding how they contribute to cell motility. Mark Holt and colleagues describe different microscopy techniques for tracing molecules in living cells. Delivery of new membrane components to the plasma membrane is often essential for initiating and/or maintaining membrane protrusion, for example during cell migration and phagocytosis. Pierre Chavier's group describe how the small GTPase ARF6 contributes to this process.

As well as the actin cytoskeleton, microtubules play a crucial role in cell migration in many cell types. This has been known for many years, but it is only recently that the molecular basis for the contribution and regulation of microtubules has been revealed. The Rho GTPases that are well known to regulate actin polymerization turn out to be central to microtubule dynamics as well, as reviewed here by Wittmann and Waterman-Storer. Recently it has become clear that microtubules are important for regulating the turnover of integrin-mediated adhesions to the substratum, as illustrated in the review by Alexander Bershadsky and colleagues.

One of the model systems that has been most informative for carrying out a genetic analysis of proteins important for cell migration is *Dictyostelium*, a slime mould that produces cAMP to attract other *Dictyostelium* cells under starvation conditions. The chapters by Rick Firtel's and Robert Insall's groups describe how *Dictyostelium* has been used to investigate how cells polarize and migrate towards a source of chemoattractant. This work has firmly established the crucial role of the generation of membrane phosphoinositides in cell polarization.

In vivo most cells do not move alone – they interact with other cells. The mechanisms whereby cells recognize and respond to other cells vary depending on the two types of cells involved. Epithelial cells meeting other epithelial cells form stable cell–cell adhesions, and Jason Ehrlich and colleagues describe how these adhesions form and mature. On the other hand, neuronal cells can be attracted or repulsed, depending on the stimulus. Kate Nobes' group describe how the transmembrane receptors ephrins and Ephs signal to the cytoskeleton to induce cell retraction, leading to loss of contact rather than stabilization of contact.

The last five years has seen an explosion of research monitoring the migration of cells in living organisms. For Michael Abercrombie this was not

possible, but it is now because of technical advances in microscopy and in genetic manipulation of cells. Three chapters demonstrate the power of tracking cells *in vivo* both in the context of normal development (groups of Ray Keller and Rick Horwitz) and in cancer cell migration (Condeelis' laboratory). Genetic manipulation in mice has been crucial for identifying proteins important for migration of cell populations during development, and this approach is described by Carmen Birchmeier.

We hope that this book will provide an overview of the field of cell motility research in the early 21st century and will serve as a reference for both novices and experts. We thank all the authors for contributing to this book, and Lene Harbott and Kate Nobes for providing the cover picture.

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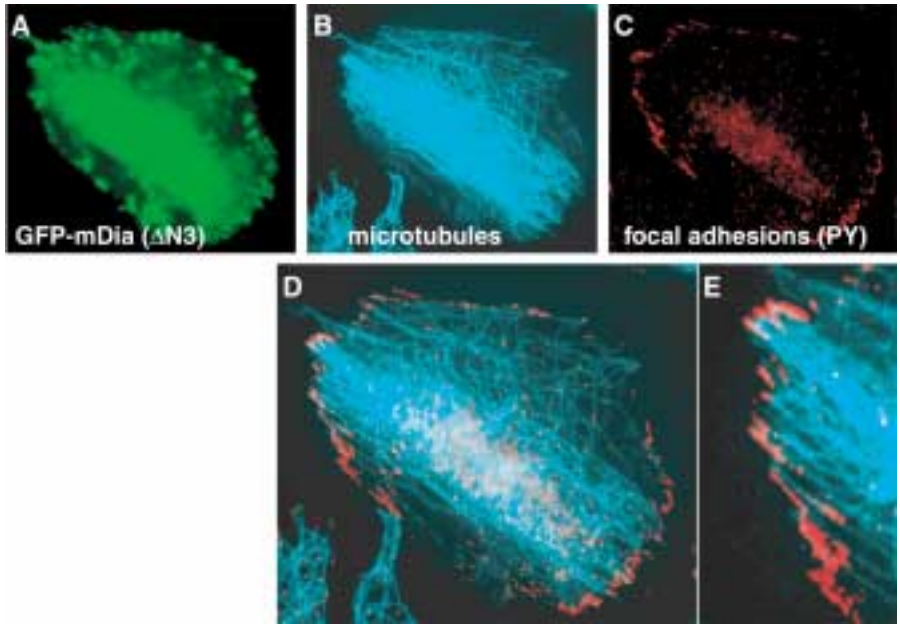

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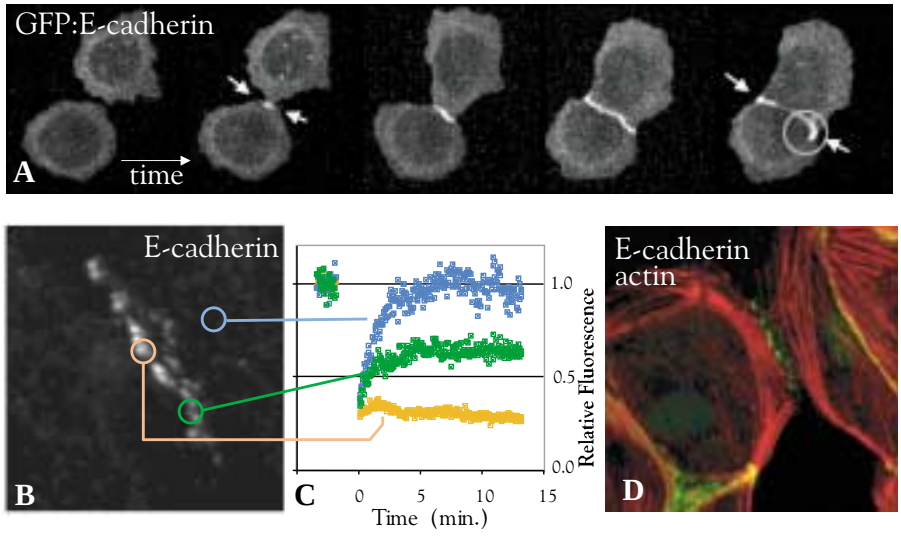

Figure 6.1

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