

Preface

In 1675, when Antonie van Leeuwenhoeks, the pioneer of microscopy, described the movements of bacteria in a letter sent to the Royal Society of London, the fascinating world of cell motility was born. However, at that time nobody could imagine how important – more than 325 years later – the molecular understanding of this process would be for medicine.

Cell migration is a fundamental process for unicellular but also multicellular organisms. It plays a key role in chemotaxis, development, infection, immunity, tissue regeneration and cancer. These processes were studied independently over a long period by zoologists, cell biologists and medical scientists – each discipline interpreting its subject as unique. Apart from advances in methods, such as the improvement of microscopic techniques and the introduction of GFP labeling, the largest impact in the field in recent years resulted from communication between the different disciplines and the ability of people to free themselves in their thinking.

This book will encourage students, young scientists and newcomers in cell migration research to keep an eye on motility factors, signaling pathways and molecules regulating cytoskeleton rearrangements, adhesion complexes and gene transcription in different organisms, and to look out for homologies or analogies in these systems.

Who would have expected that primordial germ cells use the same guiding molecules as lymphocytes? Jumping from Chapter 10 by Raz directly to Chapter 14 by Lipp you will be surprised by the evolutionary conservation of chemokine receptors. You might feel a similar “aha experience” when learning about the repulsive mechanism of roundabout/slit interaction during glial cell migration in the fly (Chapter 8 by Edenfeld and Klämbt) which is also used in vertebrates as a hindrance for trunc neural crest to enter the gut (Chapter 9 by Bronner-Fraser). Further examples are the signaling pathways repeatedly used in different systems. The JAK/Stat pathway involved in zebrafish gastrulation movement (Chapter 5 by Castanon and Heisenberg) also regulates border cell migration in the *Drosophila* egg chamber (Chapter 7 by MacDonald and

Montell). HGF/c-Met signaling driving pre-myoblast migration in limb development is often up-regulated in tumors with high invasive potential (Chapters 11 and 16). The most important motility factors and their signaling cascades, which were identified by extensive genetic screens and characterized by functional studies in different model organisms, are nowadays targets of tumor therapy, tissue regeneration and stem cell therapy. Thus, investigating cell migration in embryos has inspired the understanding of tumor invasion, regeneration and wound healing. However, there is also an impact from clinical studies on regulatory mechanisms of cell migration in the embryo. For many years now, the stimulatory effect of bioactive lipids on tumor cell dissemination has been known (Chapter 16), with their role in embryogenesis now coming to light.

Cell migration represents a complex program of cellular behavior including sensing, polarization, cytoskeletal reorganization, changes in adhesion and shape. As long as a cell migrates, these single behaviors underlie a continuous regulation and feedback control to direct and coordinate orientated cell movements. A perfect motility system has been evolved in unicellular organisms: sensor clustering and signaling used for orientation combined with a set of protein polymers, the cytoskeleton, allowing rapid changes of the cell shape in response to the environment. These basic principles of cell motility are best studied in single cells like fibroblasts or *Dictyostelium* and, as an introduction, these general aspects of cell migration are touched on in the first part of the book. The perfect motility system has been taken over, however, by multicellular organisms, a complex regulatory network was added to coordinate cell movements over short or long distances or to guide single cells or cohorts to their different destinations during embryogenesis. In the second part of the book, important examples are given on how cell migration drives morphogenetic movements and contributes to tissue differentiation in development. We learn that signaling cascades predominantly turn the adjusting knobs of the cellular motility system, the small GTPase, GEFs and GAPs. In the last part of the book cell migration is considered from the medical viewpoint. Previously mentioned molecular principles are re-addressed in a different context and we are surprised by the "tricks" of bacteria and invasive tumor cells in converting the cellular motility system for efficient dissemination of their own.

The journey through the molecular world of cell migration presented in this book was made possible because the authors invested much time to summarize and comment on important results from their research fields. I would like to thank them for their contributions. My gratitude is also extended to Andreas Sendtko from Wiley-VCH, who always kept me in a good mood when I saw the project sinking. I wish to thank Alexandra Schambony, Svetlana Kalinina and Ira Röder from my group for their support in preparing figures and manuscripts.

The roots of this book go back to the initiation of a priority program on Cell Migration funded over six years (1998–2004, SP1049) by the German Research Foundation (DFG). Annual group meetings and international conferences kept the discussions on cell migration in motion. Without the enthusiasm and commitment shown by Walter Birchmeier, Dietmar Vestweber, and Rudolf Tauber in bringing together the worldwide experts on cell migration at our meetings, such a cross-talk between cell and developmental biologist and medical scientist would never have evolved.

I would also like to mention and to thank Ingrid Ehse and Dorette Breitkreuz from the DFG, who constantly helped me in managing the priority program.

At the end of the priority program and with the “outcome” of this book, I hope to stimulate young scientists to draw their attention and research activities to the topic of cell migration, because we have just lifted the curtain in understanding this process. New tools developed in molecular biology and biophysics and fascinating new techniques of live microscopy are waiting in the wings to be used for more in-depth investigations.

Karlsruhe, October 2004

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