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Philipp Kaldis (Ed.)

# Cell Cycle Regulation

With 26 Figures, 1 in Color, and 9 Tables

PHILIPP KALDIS, PhD

National Cancer Institute, NCI-Frederick  
1050 Boyles Street  
Bldg. 560  
Frederick, MD 21702-1201  
USA

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## Preface

The cell cycle is tightly regulated on many different levels to ensure properly controlled proliferation. In the last 20 years, through the contributions of many laboratories, we have gained insight into many important aspects of the regulation of the cell cycle and its relation to cancer, which culminated in the 2001 Nobel Prize being awarded to Leland Hartwell, Tim Hunt, and Paul Nurse. In the investigations of cell cycle regulation, it has been essential to use different model systems from yeast to mouse, where the results from one system have led to advances in another system. Recently, studies have been done using more complex organisms like the mouse, which has taught us much about redundancy and flexibility in the regulation of the cell cycle. Some of the (even fundamental) results from yeast or mammalian cell lines had to be revised since they were not completely applicable to complex animal systems. It is a major challenge to keep an open mind when new results overthrow established dogmas, especially since some of the dogmas have never been backed by convincing experiments. This book will provide an updated view of some of the most exciting areas of cell cycle regulation.

The chapters of this book have been written by experts in the cell cycle field and cover topics ranging from yeast to mouse and from Rb to sterility. In the first chapter Moeller and Sheaff review recent results regarding G1 phase control, which might suggest that depending on the context or cell type, the G1 phase control could be different. The second chapter by Teer and Dutta deals with the regulation of DNA replication during the S phase. They discuss the origin of replication complex, MCMs, and how they are controlled by different factors. The next chapter, by Yang and Zou, reviews checkpoints and the response to DNA damage, followed by a chapter by Hoffmann, which deals with protein kinases that are involved in the regulation of the mitotic spindle checkpoint. The regulation of the centrosome cycle is discussed in the chapter by Mattison and Winey. In the sixth chapter Reed reviews the regulation of the cell cycle by ubiquitin-mediated degradation. The next chapter, by Dannenberg and Te Riele, deals with the Rb family and its control of the cell cycle using *in vivo* systems. Lili Yamasaki reviews the relations between cancer and the Rb/E2F pathway in the eighth chapter and Hiroaki Kiyokawa then discusses interactions of senescence and cell cycle control. Aleem and Kaldis follow with new concepts obtained by studying mouse models of cell cycle regulators. In

the eleventh chapter Bernard and Eilers review the functions of Myc in the control of cell growth and proliferation. The book concludes with a chapter by Rajesh and Pittman, who discuss the relations of cell cycle regulators and mammalian germ cells.

The future challenges in cell cycle research will be to integrate our knowledge coming from different systems, extend it to tumorigenesis in humans, and use all this information to design clinically relevant studies. This cannot happen in one step or overnight and will necessitate a lot of effort. It will continue to require broad-based basic research, along with the development of relevant animal models. These animal models need to recapitulate human diseases as closely as possible. Currently, many questions remain regarding animals being good models for human diseases. Nevertheless, more effort needs to be expended in developing better animal models before conclusions can be drawn. It is obvious that without appropriate animal models we will have to continue to test newly developed drugs in clinical trials without knowing the potential outcome. This is a time-consuming and risky procedure, which has been going on for too long a time. The future of cell cycle research is bright and the results of such studies will hopefully influence the battle against cancer.

This book could not have been completed without the outstanding contributions from the authors and I would like to thank them all for their valuable effort. In addition, I thank the members of the Kaldis lab as well as Michele Pagano for encouragement and support. I also acknowledge the support of Ursula Gramm, Sabine Schreck (Springer, Heidelberg), and Michael Reinfarth (Le-TeX GbR, Leipzig) for editorial managing and production of this book.

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Philipp Kaldis

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