

*Geoffrey M. Cooper*

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*A Molecular Approach*

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***Geoffrey M. Cooper***

Dana-Farber Cancer Institute  
Harvard Medical School



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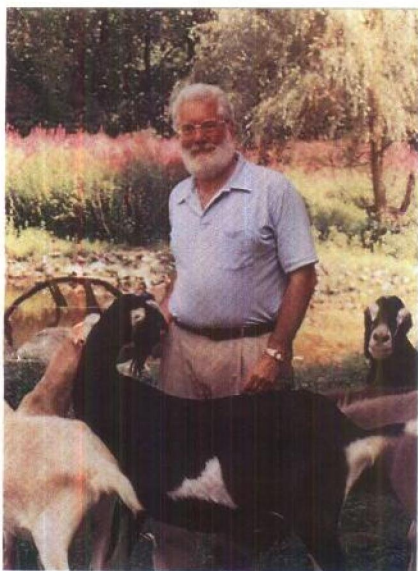
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## The Author

Geoffrey M. Cooper is Professor of Pathology at the Dana-Farber Cancer Institute and Harvard Medical School. He received his B.S. from the Massachusetts Institute of Technology in 1969, and his Ph.D. in Biochemistry from the University of Miami in 1973. He then pursued postdoctoral work with Howard Temin at the University of Wisconsin, where he developed gene transfer assays to characterize the proviral DNAs of Rous sarcoma virus and related retroviruses. After joining the faculty of Dana-Farber Cancer Institute and Harvard Medical School in 1975, he extended these studies to the identification of oncogenes in human tumors.

Dr. Cooper's current research is focused on understanding the roles of oncogene proteins in the signaling pathways that regulate cell proliferation, differentiation, and programmed cell death. He has published over 80 research papers in journals such as *Science*, *Nature*, and *Cell*, and received the U.S. Steel Award from the National Academy of Sciences in 1984 for "the identification and characterization of cellular oncogenes." In addition to training graduate students, medical students, and postdoctoral fellows, he has taught undergraduate courses in Harvard University's Biochemistry Department and served on the Board of Tutors in Biochemical Sciences. Dr. Cooper is the author of two textbooks on cancer, *Elements of Human Cancer* and *Oncogenes*, as well as *The Cancer Book*, written for the general public. He also edited, together with Rayla Greenberg Temin and Bill Sugden, the commemorative volume *The DNA Provirus: Howard Temin's Scientific Legacy*.



Dr. Cooper lives with his wife Ann and their family in Bedford, Massachusetts, where they enjoy a rural setting that provided a tranquil and diverse biological environment for writing *The Cell*.

# Preface

*The Cell* is a basic text for undergraduate or medical students who are taking a first course on cell and molecular biology. When I initially considered this project in 1991, I had just completed my advanced text *Oncogenes* and a general undergraduate text on cancer biology. While working on these books, I became aware of the need for a text that would provide undergraduate students with an accessible introduction to contemporary cell biology. To be sure, there were then and are now some outstanding cell biology texts—books that are accurate, detailed, and comprehensive. But there was also a need for another kind of book—a book that could be more easily approached and mastered by undergraduate students, while still conveying the excitement and challenges of research in this dynamic area of the biological sciences.

My goals from the beginning of this project were twofold. First, *The Cell* was designed to be an approachable and readable text that undergraduates could understand and master. At the same time, the book was planned to be intellectually gratifying and to convey not only the facts, but also a sense of the excitement of modern molecular and cellular biology.

To accomplish these goals, I felt the cohesiveness of a single-authored text was important. The book was then focused on the molecular biology of cells as a unifying theme, with specialized topics discussed throughout the book as examples of more general principles. Aspects of developmental biology, the immune system, the nervous system, and plant biology are thus discussed in their broader biological context in chapters covering areas such as gene expression, DNA rearrangements, the plasma membrane, cell signaling, and the cell cycle. This organization has helped keep *The Cell* to a manageable length, while still allowing coverage of some of the exciting areas at the frontiers of contemporary research.

Some of the most dramatic advances in recent years have come from understanding the molecular and cellular basis of human diseases, in some cases allowing the development of new strategies for prevention and treatment. Examples of such relationships between cell biology and medical practice are therefore discussed throughout the text, as well as being high-

lighted in the Molecular Medicine essays that are included as special features in each chapter. By illustrating the growing impact of molecular and cellular biology on human health, I hope these discussions will stimulate as well as inform the reader.

*The Cell* is necessarily an unfinished work, because the science upon which it is based is not a fixed, static set of facts. To the contrary, this book deals with one of the most rapidly progressing areas of biology. It is thus critical for students to recognize the experimental nature of cell and molecular biology, not only in order to understand the current status of our knowledge but also to appreciate and hopefully contribute to the advances that will continue to be made in coming years. Although it was impossible to fully discuss experimental details in a book of this length, I have taken two approaches to introduce the reader to the experimental foundations of contemporary cell biology. First, critical experiments are briefly discussed throughout the text to illustrate the kinds of contributions that have moved the field. Second, each chapter contains a Key Experiment essay that describes a seminal paper and its background in detail, with the intent of giving the reader a sense of "doing science. Together, I hope these approaches impart a flavor for the ways in which progress in this field has been and continues to be made.

Finally, I have considered it nearly as important to tell the reader what is not known as what is known. In so doing, I have tried to point out areas of controversy, gaps in our knowledge, and scientific frontiers awaiting exploration. I hope that this approach will convey not only the science, but also the challenges and excitement, of understanding the workings of the cell.

## ORGANIZATION AND FEATURES OF *The Cell*

*The Cell* has been designed to be an approachable and teachable text that can be covered in a single semester while allowing students to master the material in the entire book. It is assumed that most students will have had introductory biology and general chemistry courses, but will not have had previous courses in organic chemistry, biochemistry, or molecular biology. Several aspects of the organization and features of the book will help students to approach and understand its subject matter.

### **ORGANIZATION**

*The Cell* is divided into four parts, each of which is self-contained so that the order and emphasis of topics can be easily varied according to the needs of individual courses. In covering this vast subject matter, however, I developed an organizational overview of the book, as described below.

Part I of the book provides background chapters on the evolution of cells, methods for studying cells, the chemistry of cells, and the fundamentals of modern molecular biology. For those students who have a strong background from either a comprehensive introductory biology course or a previous course in molecular biology, various parts of these chapters can be skipped or used for review.

Part II focuses on the molecular biology of cells and contains chapters dealing with genome organization; DNA replication, repair, and recombination; transcription and RNA processing; and the synthesis, processing, and regulation of proteins. The order of chapters follows the flow of genetic information (DNA → RNA → protein) and provides a concise but up to date overview of these topics.

Part III contains the core block of chapters on cell structure and function, including chapters on the nucleus, cytoplasmic organelles, the cytoskeleton, and the cell surface. This part of the book starts with coverage of the nucleus, which puts the molecular biology of Part II within the context of the eukaryotic cell, and then works outward through cytoplasmic organelles and the cytoskeleton to the plasma membrane. These chap-



ters are relatively self-contained, however, and could be used in a different order should that be more appropriate for a particular course.

Finally, Part Four focuses on the exciting and fast-moving area of cell regulation, including coverage of topics such as cell signaling, the cell cycle, and programmed cell death. This part of the book concludes with a chapter on cancer, my own field of research, which synthesizes the consequences of defects in basic cell regulatory mechanisms.

## FEATURES

Several pedagogical features have been incorporated into *The Cell* in order to help students master and integrate its contents. These features are reviewed below as a guide to students studying from this book.

*Chapter organization.* Each chapter is divided into four or five major sections, which are further divided into a similar number of subsections. An outline listing the major sections at the beginning of each chapter provides a brief overview of its contents.

*Key terms and Glossary.* Key terms are identified as boldfaced words when they are introduced in each chapter. These key terms are reiterated in the chapter summary and defined in the glossary at the end of the book.

*Illustrations and micrographs.* An illustration program of full-color art and micrographs has been carefully developed to complement and visually reinforce the text.

*Key Experiment and Molecular Medicine essays.* Each chapter contains one Key Experiment and one Molecular Medicine feature. These essays are designed to provide the student with a sense of both the experimental basis of cell and molecular biology and its applications to modern medicine.

*Chapter summaries.* Chapter summaries are organized in outline form corresponding to the major sections and subsections of each chapter. This section-by-section format is coupled with a list of the key terms introduced in each section, providing a succinct but comprehensive review of the material.

*Questions and Answers.* Questions at the end of each chapter (with answers in the back of the book) are designed to further facilitate review by calling for students to understand and integrate the material presented in the chapter and to use this material to predict or interpret experimental results.

*References.* Comprehensive lists of references at the end of each chapter provide access to both reviews and selected papers from the primary literature. In order to help the student identify articles of interest, the references are organized according to chapter sections. Review articles and primary papers are distinguished by [R] and [P] designations, respectively.

## SUPPLEMENTS

In addition to these features of *The Cell* itself, two supplements are provided to facilitate study from the text and to help the reader keep up with the rapid progress in this area of science.

**CD-ROM.** Each copy of *The Cell* includes a CD-ROM designed to accompany the text. The disc contains minicourses that consist of an integrated series of text and figure entries reviewing selected topics covered in most chapters of *The Cell*. Many of the entries in these minicourses are illustrated by animations, which are particularly valuable in allowing the user to

appreciate the dynamic nature of cell behavior. In addition, the disc includes an extensive encyclopedia of cell and molecular biology, again with many animated entries. We think the CD-ROM will not only be useful for review and lecture organization, but will also provide students with a novel visual presentation of many key processes in cell biology.

**Newsletter.** This book deals with an active, rapidly moving area of science. To help keep *The Cell* current, we will provide updates in the form of newsletters published twice a year. Each newsletter will contain summaries of recent papers representing major advances, as well as new Molecular Medicine features when appropriate. These newsletter updates will be keyed to appropriate sections of *The Cell* and written so as to help the reader integrate and appreciate current advances in the context of the text. In addition to providing updated information, we believe these newsletters will further help convey the excitement of research in this field of science, where there are still so many key questions to be answered and so many beautiful experiments to be done.

# Acknowledgments

Any book, but especially one of this magnitude, represents the efforts of many people, and it is both a privilege and a pleasure for me to thank my colleagues, friends, and family for their contributions to *The Cell*.

At ASM Press, Patrick Fitzgerald deserves special thanks for helping to guide and develop this project from beginning to end. Working with Pat over the last five years has been both fun and enlightening, and Pat's ideas have contributed in many ways to the organization and features of this book.

A book dealing with a field as vast as cell biology is beyond the immediate expertise of any one individual, so I have relied heavily on the input of colleagues who are experts in their various fields of research. Seventy-one scientists (listed on the following pages) read and critiqued draft chapters of *The Cell*, giving generously of their time and expertise. I am deeply grateful for their efforts and advice. Among this group, Thomas Roberts (Florida State University) and Roger Sloboda (Dartmouth College) were particularly helpful in reading and providing general advice on almost the entire book from their viewpoints not only as scientists, but also as active and interested teachers. I am also grateful to Brian Storrie (Virginia Tech) for his help, perspectives, and advice during the early stages of development of this project. Finally, thanks are due to Yale Altman and Karen Jones of ASM Press for their efforts in obtaining and organizing the many reviews that were so critical to the development of the book.

The production of *The Cell* has been primarily undertaken by Andy Sinauer and his colleagues at Sinauer Associates. Andy and his team have been efficient, professional, and a pleasure to work with. Andy personally oversaw the entire project with attention to the smallest details, Dean Scudder provided valuable advice on a variety of issues, Carol Wigg deftly coordinated all the complex parts of editing and collating the text and artwork, Jane Potter did a wonderful job of obtaining the many micrographs included in the book, and Christopher Small put the many parts together to produce the completed volume. The artwork itself was done by John Woolsey and Patrick Lane of the J/B Woolsey studio. Illustrations are

a critical part of the book, and John and Patrick did a marvelous job of generating an outstanding art program based on my rough sketches. I am also grateful to Susan Schmidler for the attractive interior and cover design of *The Cell*.

Many authors acknowledge their families for their patience during the long hours of work required to write a book, and I am gratified to do so as well. However, my family also played a more active role in producing *The Cell*, with everyone contributing to its completion. My wife Ann, who is also a cell biologist, read and corrected multiple versions of the manuscript. The task of library research and compiling and copying the many papers I used as references was undertaken largely by Gwen and Ryan. At a later stage of production, Allison helped collate many chapters of the book during last minute dashes to meet production deadlines. And finally, the extensive glossary at the end of the book was drafted by Rachel, who brought a recent biology graduate's perspective to that undertaking.

# Reviewers

Gerald M. Adair  
M. D. Anderson Cancer Center  
University of Texas

Ibrahim Ades  
University of Maryland, College Park

Ronald Berezney  
State University of New York at Buffalo

Niels Bols  
University of Waterloo  
Ontario, Canada

Joan S. Brugge  
ARIAD Pharmaceuticals, Inc.  
Cambridge, MA

Brian Burke  
The University of Calgary  
Alberta, Canada

David A. Clayton  
Stanford University School of Medicine

Roger I. Davis  
Howard Hughes Medical Institute  
University of Massachusetts Medical  
Center

Michael Edidin  
Johns Hopkins University

Gary Felsenfeld  
National Institutes of Health  
Bethesda, MD

Michael Forman  
Purdue University

Errol C. Friedberg  
University of Texas Southwestern  
Medical Center

David Fromson  
California State University, Fullerton

Larry Gerace  
Scripps Research Institute  
La Jolla, CA

Reid Gilmore  
University of Massachusetts  
Medical Center

Dennis Goode  
University of Maryland

Michael M. Gottesman  
National Cancer Institute  
National Institutes of Health

Michael E. Greenberg  
Children's Hospital  
Harvard Medical School

Barry Gumbiner  
Memorial Sloan-Kettering Cancer Center

Alan Hall  
MRC Laboratory for Molecular Cell Biology  
University College London

Joyce L. Hamlin  
University of Virginia, Charlottesville

Ulla Hansen  
Dana-Farber Cancer Institute  
Harvard Medical School

F. Ulrich Hartl  
Howard Hughes Medical Institute  
Memorial Sloan-Kettering Cancer Center

Lawrence Hightower  
University of Connecticut, Storrs

Tony Hunter  
Salk Institute, La Jolla, CA

James N. Ihle  
St. Jude's Children's Research Hospital  
Memphis, TN

Judith A. Jaehning  
Indiana University, Bloomington

Haig H. Kazazian, Jr.  
University of Pennsylvania

Kenneth Keegstra  
MSU-DOE Plant Research Laboratory  
Michigan State University

Robert A. Koch  
California State University, Fullerton

Elaine Lai  
Brandeis University

Jerry B. Lingrel  
University of Cincinnati Medical Center

Elizabeth J. Luna  
Worcester Foundation for Experimental  
Biology  
Shrewsbury, MA

Carolyn Machamer  
Johns Hopkins University School of  
Medicine

Umadas Maitra  
Albert Einstein College of Medicine

Russell Malmberg  
University of Georgia, Athens

James Manley  
Columbia University

J. Richard McIntosh  
University of Colorado, Boulder

Donald Miles  
University of Missouri, Columbia

David A. Mullin  
Tulane University

Eva Neer  
Harvard Medical School

Carol S. Newlon  
UMDNJ/New Jersey Medical School

John Newport  
University of California, San Diego

Danton O'Day  
University of Toronto, Erindale Campus

Donata Oertel  
University of Wisconsin, Madison

Barbara Pearse  
MRC Laboratory of Molecular Biology  
Cambridge, UK

Hugh Pelham  
Medical Research Council  
Cambridge, UK

Jonathon Pines  
The Wellcome Cancer Research Centre  
Cambridge, UK

T. A. Rapoport  
Max-Delbrück-Centrum  
Berlin, Germany

Marilyn D. Resh  
Memorial Sloan-Kettering Cancer Center

Joel D. Richter  
Worcester Foundation for Biomedical  
Research  
Shrewsbury, MA

David A. Rintoul  
Kansas State University, Manhattan

Thomas M. Roberts  
Florida State University, Tallahassee

Alan Sachs  
University of California, Berkeley

Shelley Sazer  
Baylor College of Medicine

Gottfried Schatz  
University of Basel  
Switzerland

Randy Schekman  
University of California, Berkeley

Tom Shrader  
Albert Einstein College of Medicine

David Schlessinger  
Washington University, St. Louis

Kai Simons  
European Molecular Biology Laboratory  
Heidelberg, Germany

Roger Sloboda  
Dartmouth College

Timothy A. Springer  
Harvard Medical School

Joseph M. Steffen  
University of Louisville

Thomas P. Stossel  
Brigham and Women's Hospital  
Harvard Medical School

Suresh Subramani  
University of California, San Diego

John Taylor  
Wayne State University

Patricia Wadsworth  
University of Massachusetts, Amherst

Jonathan R. Warner  
Albert Einstein College of Medicine

Larry G. Williams  
Kansas State University, Manhattan

Fred Wilt  
University of California, Berkeley

Debra J. Wolgemuth  
Columbia University

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