Preface

Cell biology is a vast and rapidly progressing field in which discoveries are made at a staggering pace, continuously expanding our understanding of the molecular events that govern cell behavior in physiology as well as cell misbehavior in disease. Likewise, the tools and techniques through which such discoveries are made steadily advance, enabling experimental approaches with ever increasing sophistication. For college-level educators, this raises several pedagogical questions, including: *How can we best guide students toward an understanding of cell biology that aligns with the contemporary field? How do we avoid overwhelming students with never-ending details when many such details are necessary to understand* ***how*** *and* ***why*** *cells work instead of rotely memorizing* ***that*** *cells work? And how can we help students to integrate the product of science—knowledge—with the practice of science—experimentation and data interpretation?* Put another way, cell biology instructors face the challenge of cultivating both the foundational knowledge and analytical skills that students need for their entry into an increasingly complex field. From its First Edition to this Ninth, *The Cell: A Molecular Approach* has been designed to serve as a guide to meet that challenge.

Organization

The book is divided into four parts. **Part I: Fundamentals and Foundations** summarizes how cells evolved and describers basic model systems and techniques—microscopy and cell fractionation—used throughout cell research. The physical and chemical principles underlying cell structure and function are described, including chemical bonds, the laws of thermodynamics, the ubiquitous role of ATP as an energy source, and the major classes of molecules that make up cells. The key experiments that identified DNA as the hereditary material are reviewed, followed by discussion of discoveries through which the basic factors and steps of gene expression were elucidated. Part I concludes with analysis of essential tools—recombinant DNA and antibodies—that launched research into the molecular mechanisms described throughout Parts II, III, and IV.

Part II: The Flow of Genetic Information focuses on the molecular biology of cells and begins by dissecting the types of DNA sequences that make up genomes of diverse organisms and the mechanisms through which genomes are replicated and repaired when damaged. The molecular mechanisms of transcription and RNA processing are then discussed, followed by mechanisms of translation, protein processing, and protein regulation. Additional research tools and techniques that have been particularly critical to characterizing those mechanisms are integrated within the corresponding sections, and the last chapter in Part II introduces methodologies used for large-scale analyses.

Part III: Subcellular Structures and Functions includes chapters on the nucleus, cytoplasmic organelles, the cytoskeleton, the plasma membrane, and the extracellular matrix. 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 and the exterior of the cell. These chapters are relatively self-contained, however, and could be used in a different order should that be more appropriate for a particular course.

Finally, **Part IV: Cell Regulation** focuses on the exciting and fast-moving area of cell regulation, including coverage of topics such as cell signaling, the cell cycle, stem cells, and programmed cell death. This part of the book concludes with a chapter on cancer, which synthesizes the consequences of defects in basic cell regulatory mechanisms.

New to this Edition

This International Ninth Edition of *The Cell* is the result of a wholistic review of the previous edition. Not only has the content been updated to keep pace with key advances in the field but several additional changes have been incorporated, stemming from the following goals.

Expedite Discussion of the Flow of Genetic Information

A major change in this edition relates to its overall organization. The mechanisms that mediate the flow of genetic information arguably represent the most fundamental basis for cellular life, which is reflected by *The Cell*'s dedication of five chapters to this content: Genes and Genomes; Replication, Maintenance, and Repair of Genomic DNA; RNA Synthesis and Processing; Transcriptional Regulation and Epigenetics; and Protein Synthesis, Processing, and Regulation. For this International Ninth Edition, Parts I and II have been reorganized to place those five chapters earlier in the table of contents. To do so, the content covered in the Eighth Edition's Chapter 3, Bioenergetics and Metabolism, has been dispersed across several chapters. Given the centrality of the laws of thermodynamics in all cellular events (including the flow of genetic information) and the ubiquitous role of ATP as an energy source to drive those events, these concepts have been combined with discussion of molecules and membranes in Chapter 2, which is newly titled Physical Principles Underlying Cell Structure and Function. Discussion of glycolysis, oxidative phosphorylation, and photosynthesis have been moved to Chapter 12: Mitochondria, Chloroplasts, and Peroxisomes. Additionally, Chapter 5 in the Eighth Edition—Genomics, Proteomics, and Systems Biology—now follows discussion of Protein Synthesis, Processing, and Regulation. Not only does this revision move the chapters related to the flow of genetic information earlier in the book, it also allows students to develop a stronger foundational knowledge of the concepts therein before applying them in the context of methodologies for large-scale analysis discussed in Genomics, Proteomics, and Systems Biology.

Fill Gaps in Molecular Explanations

In 13 years of teaching Cell Biology, I have been continuously inspired by students' thirst for molecular explanations on **how** and **why** cellular events take place. From questions on how transcription by RNA polymerase II is terminated to why kinases exhibit substrate specificity to how importins pass through the selective barrier of the nuclear pore complex, students are seldom satisfied unless molecular explanations that go beyond rote memorization are provided. Indeed, the recognition that molecular explanations for all cellular events must exist, whether understood by the field or not, and the curiosity to seek out those explanations are essential characteristics of a cell biologist. Thus, an overarching goal while revising this International Ninth Edition was to fill in gaps where molecular explanations were less apparent or have changed since the Eighth Edition. Examples of where such details were added include

descriptions of transcription termination by RNA polymerase II in Chapter 6, factors that mediate epigenetic inheritance of DNA methylation in Chapter 7, the roles of recognition motifs in kinase–substrate specificity in Chapter 8, and the characteristics of importins that enable their passage through the nuclear pore complex in Chapter 10.

To supplement updates to the text, several new figures are included—for example, Figure 6.9, which illustrates the key factors and events that cause transcription termination by RNA polymerase II, and Figure 8.32, which provides an example of elements that mediate kinase–substrate specificity. Existing figures were revised to incorporate molecular explanations for the events they depict—for example, Figure 7.26 was revised to include factors responsible for epigenetic inheritance of DNA methylation patterns and Figure 10.10 illustrates how importins interact with and penetrate the subunits that make up the selective barrier within the nuclear pore complex.

Incorporate Recent Discoveries and Advances

A third goal in revising this edition was to incorporate key discoveries and concepts that have recently taken hold in the field. These include discussion of intrinsically disordered regions in protein structure in Chapter 2, their role in mediating liquid-liquid phase separation (LLPS) in Chapter 8, and the contributions of LLPS to formation of membraneless compartments (e.g., transcription hubs and the nucleolus in Chapter 10) and other molecular events (e.g., protein import into chloroplasts in Chapter 12). Updates on the ever-increasing list of noncoding RNAs (e.g., lncRNAs) expressed in eukaryotic organisms and their putative contributions to organismal complexity are added in the context of Chapter 4: Genes and Genomes and Chapter 9: Genomics, Proteomics, and Systems Biology and a more thorough analysis of the molecular machinery that mediates autophagy is provided in Chapter 11: Protein Processing and Sorting. Given the impact that CRISPR/Cas technology is having on research approaches, a new Key Experiment box in Chapter 3: Fundamentals of Molecular Biology describes the first demonstration by Jennifer Doudna and Emmanuelle Charpentier that bacterial CRISPR/Cas9 can be converted into an experimental tool for targeted genome modification. A new Molecular Medicine box is also added to Chapter 9, centered on the development of mRNA vaccines to combat the COVID-19 pandemic. The Molecular Medicine box on Alzheimer's Disease in Chapter 8: Protein Synthesis, Processing, and Regulation was also revised to include discussion of immunotherapy as an approach to treating the disease and the controversial approval of the first ever amyloid-β–directed immunotherapy (Aducanumab) by the US Food and Drug Administration in 2021.

Develop the Data Analysis Problems

A fourth goal of this edition was to re-envision the Data Analysis Problems that conclude each chapter to provide tools that help students integrate the product of science—knowledge—with the practice of science—experimentation and data interpretation. There are 16 new Data Analysis Problems; others have been significantly revised. Each of these new or updated Data Analysis Problems now include a brief background section to provide students a context within which to consider the experiments. While the Data Analysis Problems for Chapters 1–5 include data from a single experiment, those for Chapters 6–19 include data from multiple experiments, mimicking how research studies most often entail series of experiments that build on each other.

The top priority in selecting data for the Data Analysis Problems was that they relate to and reinforce concepts discussed in the corresponding chapter. For example, the new Data Analysis Problem for Chapter 10: The Nucleus investigates the nature of the selective barrier within the nuclear pore complex and how importins pass through that barrier. Opportunities to link content from the chapter to

disease also guided the selection of data. The Data Analysis Problem for Chapter 6: RNA Synthesis and Processing, for example, examines the potential contribution of TATA-binding protein to oncogenic transformation, the Data Analysis Problem for Chapter 13: The Cytoskeleton and Cell Movement examines the role of an actin-binding protein in metastasis, the Data Analysis Problem for Chapter 14: The Plasma Membrane evaluates whether receptor-mediated endocytosis may contribute to the spread of toxic tau proteins between neurons during Alzheimer's disease and other tauopathies, and the Data Analysis Problem for Chapter 18: Cell Renewal and Cell Death presents evidence that apoptosis induced through p53 and PUMA may contribute to neurodegeneration associated with amyotrophic lateral sclerosis and frontotemporal dementia.

Another priority in developing the Data Analysis Problems was to incorporate data from experimental techniques covered in the book and, in many cases, include multiple techniques to help students learn how different methods can complement each other to investigate an experimental question. For example, the new Data Analysis Problem for Chapter 7: Transcriptional Regulation and Epigenetics includes data from luciferase reporter assays, electrophoretic-mobility shift assays, and chromatin immunoprecipitation (all discussed in Chapter 7), whereas the Data Analysis Problem for Chapter 17: The Cell Cycle includes data from immunoblot, immunocytochemistry, and retroviral transduction (all discussed in Chapter 3: Fundamentals of Molecular Biology) as well as DNA content analysis by flow cytometry (discussed in Chapter 17). Whenever possible, data from recently published articles were selected, with many of the new Data Analysis Problems based on articles published since 2017.

To support students' understanding and analysis of the Data Analysis Problems, several figures from the Eighth Edition depicting research techniques have been revised to more thoroughly illustrate how they are conducted. Figures 3.18, 3.26, and 3.27 depict cDNA cloning, immunocytochemistry, and immunoblotting, respectively; Figure 7.5 depicts the use of reporter plasmids to identify *cis*-acting elements; and Figure 9.13 depicts yeast two-hybrid assays. Where appropriate, technique figures are cross-referenced to facilitate independent study of each Data Analysis Problem by students.

Another key resource added is interactive versions of each Data Analysis Problem (available online), which walk students through how each experiment was conducted to generate the data presented, using customized versions of the corresponding technique figures in the book. Overall, the goal is to provide a resource through which students can integrate and apply concepts from the book while simultaneously learning the intellectual process of scientific inquiry within the field of cell biology. Data Analysis Problems are available in Oxford Insight or via the enhanced e-book.

Features

Several pedagogical features are 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 three to 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. The major sections are numbered and self-contained to facilitate assignability.

Learning Objectives

Each of the major sections begins with Learning Objectives, which help to organize and focus students' attention on the material.

Summary and Questions

The major sections conclude with a review, including a section summary and questions (with answers in the back of the book). The questions span several levels of Bloom's taxonomy, ranging from knowledge and comprehension to analysis and synthesis.

Marginal Notes

Major points are summarized as marginal notes throughout the text, providing a running outline of the material.

Key Terms and Glossary

Key terms are identified as boldfaced words when they are introduced in each chapter 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 either two Key Experiment essays or one Key Experiment and one Molecular Medicine essay. These features 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. Additional questions are included in these essays, designed to focus attention on key aspects of the material. These essays are also a useful basis for student discussions, which can be accompanied with a review of the original paper upon which the experiments are based.

Data Analysis Problem

Each chapter concludes with Data Analysis Problem that present data from original research papers, together with questions that engage students in the analysis of experimental methods and results (with answers in the back of the book). Like the Key Experiment and Molecular Medicine essays, the Data Analysis Problem provide excellent material for discussions and opportunities for student participation in active learning.

FYIs

Each chapter contains sidebars that provide brief descriptive highlights of points of interest. The sidebars supplement the text and provide starting points for class discussion.

References

Two key references for each major section are included at the end of each chapter. Comprehensive lists of references are provided as an online supplement.

ACCESSIBLE COLOR CONTENT Every opportunity has been taken to ensure that the content herein is fully accessible to those who have difficulty perceiving color. Exceptions are cases where the colors provided are expressly required because of the purpose of the illustration.

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