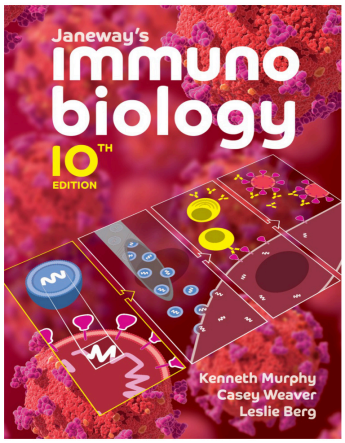


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Preface

Since early 2020, the field of immunology has moved to an unexpectedly prominent place in daily life. As SARS-CoV-2 spread around the globe, basic questions about how the immune system combats viruses moved into the forefront of public attention. Why were individual responses to the virus so variable? Why were outcomes in older patients so much more dire than in younger infected individuals? And, most important, how quickly would a vaccine be available, would it provide adequate protection, and for how long? While some questions have been answered, notably observing the most rapid vaccine development in human history, many other questions remain outstanding. Clearly, the need for continued research into basic mechanisms controlling human immunity is undeniable.

Though somewhat overshadowed during the COVID-19 pandemic, there has been a dramatic rise in the use of various other immunotherapies in the years since the last edition of *Janeway's Immunobiology*. Multiple methods for manipulating immune responses have significantly altered the practice of clinical medicine, benefiting patients who present with a diagnosis of cancer, autoimmune disease, or chronic inflammatory disorder. In large part, these clinical advances arose from decades of basic research aimed at uncovering the molecules and pathways that regulate immune cells at steady-state conditions or during infection, inflammation, or autoimmunity.

This Tenth Edition of *Janeway's Immunobiology* strives to carry on Charlie Janeway's legacy of providing a comprehensive, up-to-date textbook focused on the mechanisms underlying the responses to infection. In keeping with this mission, this edition's text and figures have been updated throughout. The immune response to SARS-CoV-2 and the multiple vaccine strategies utilized against this infection are introduced in Chapter 1 and further discussed in Chapters 12, 16, and Appendix I. Chapter 3 now includes a

detailed explanation of the mechanism by which mutations in innate sensors of infection can lead to autoimmunity. New developments in the identification of ligands for γδ T cells are highlighted in Chapter 4, and the new cryo-electron microscopy (cryo-EM) structure of the RAG-1:RAG-2 complex bound to DNA is described in Chapter 5. Recently discovered structural features of the peptide-loading machinery for antigen presentation to T cells are included in Chapter 6. The treatment of antigen receptor signaling in Chapter 7 now includes discussion of lymphocyte metabolism, a topic also revisited in the revised Chapters 9 and 11. Additionally, new information in Chapter 7 highlights the pathways targeted by checkpoint blockade immunotherapy and describes the signaling modules used to engineer chimeric antigen receptors (CARs) for cell-based therapies, a topic also elaborated in Chapter 16. The latest findings on T-cell localization and dynamics during priming interactions with dendritic cells are covered in Chapter 9, while Chapter 11 describes new insights into the development and functions of tissue-resident memory T cells. Chapter 12, which focuses on immunity at the barrier surfaces, has undergone a major overhaul and includes an expanded discussion of immune interactions with commensal microorganisms and a detailed discussion of the roles of diverse epithelial cell types in the intestine, respiratory tract, and the skin. Chapter 12 also includes a new section on respiratory virus infections, including influenza and SARS-CoV-2. Chapter 16 brings vaccines to the forefront and includes a detailed discussion of the new vaccine approaches used for SARS-CoV-2 and poliovirus vaccines. The Immunologist's Toolbox (Appendix I) has been updated with new sections on single-cell technologies such as single-cell RNA-seq and lineage-tracing approaches, antigen tetramers for identifying antigen-specific B cells, and parabiosis used to determine lymphocyte tissue residency. Also included in Appendix I is a new description of an analytic technique used to measure antibody responses to SARS-CoV-2 in infected or vaccinated individuals. End-of-chapter study questions have been reworked in the Tenth Edition, and an online learning platform for student self-assessment, InQuizitive, has been created.

We have benefited greatly from the major contribution of Gregory Barton, an expert in innate immune signaling, who has revised and updated Chapter 3. Many additional people deserve special thanks, including our thoughtful colleagues who reviewed the Ninth Edition and provided insights that helped direct revisions in this new edition. We benefited from the eagle-eyed accuracy reviewers who provided feedback on Tenth Edition chapters. All of these individuals are cited in the Acknowledgments section, and we express our gratitude for their efforts.

We have the good fortune to work with an outstanding editorial group at W. W. Norton. We thank Denise Schanck, our editorial advisor, who coordinated the entire project, guiding us gently but firmly back on track throughout the process. We thank Betsy Twitchell, our editor, who contributed her guidance, support, and wisdom. Sincere thanks also go to Judith Kromm, our developmental editor, and Christopher Curioli, our copyeditor, for their insights and attention to detail. As in all previous editions, Matt McClements has contributed his genius—and patience—reinterpreting the authors' sketches into elegant illustrations. Our editing, production, and permissions teams provided their expertise throughout; they are Maggie Stephens, David Bradley, Ben Reynolds, Stephanie Romeo, and Patricia Wong. Our media experts, Kate Brayton, Jasmine Ribeaux, Alexandra Malakhoff, and Kara Zaborowsky, created our excellent supplements package. The authors wish to thank their most important partners—Theresa, Cindy Lou, and Charles—colleagues in life who have supported this effort with their generosity of time, their own editorial insights, and their infinite patience.

We hope this Tenth Edition will continue to inspire students to appreciate immunology's beautiful subtlety—just as Charlie did. We encourage all readers to share with us their views on where we have come up short, so the next edition will further approach the asymptote. Happy reading and learning!

Kenneth Murphy

Casey Weaver

Leslie Berg

What's New in the Tenth Edition

New Coauthor

Janeway's Immunobiology is the premier text for immunology, giving students at all levels a current and authoritative understanding of immunology research. Leslie Berg joins Ken Murphy and Casey Weaver in comprehensively updating the textbook.

New Online Assessment in InQuizitive 

InQuizitive for *Janeway's Immunobiology* is an award-winning, adaptive learning tool that gives students personalized learning pathways as they work through the material. Through a variety of question types and answer-specific feedback, students learn the necessary vocabulary to succeed in the immunology course and practice applying that vocabulary to core concepts.

New Norton Teaching Tools Support Classroom Instruction

The Norton Teaching Tools site for *Janeway's Immunobiology* gives instructors ready access to primary literature suggestions for each chapter, active learning activities, lecture PowerPoint files, descriptions of all the animations and videos, and much more.

New Coverage of the COVID-19 Pandemic

COVID-19 coverage has been incorporated in Chapters 1, 12, 16, and Appendix I and is highlighted on the front cover with a new illustration of the novel mRNA vaccination strategy.

Highlights of New Research

Chapter 1:

- Brief introduction to coronavirus, which is then elaborated in later chapters.

Chapter 3:

- Latest research on the Toll-like receptors and cGAS–STING pathway.
- Discussion of mutations in RIG-I, MDA-5, and cGAS–STING pathways that lead to autoimmune disorders.
- Latest information on inflammasome activation and gasdermin pore formation in secretion of inflammatory cytokines.

Chapter 5:

- New cryo-EM structure of the RAG-1:RAG-2 tetrameric complex bound to recombination signal sequences in the DNA.
- Discussion of the latest research on the evolutionary origins of RAG-dependent V(D)J recombination.

Chapter 6:

- Newly discovered structural features of the peptide-loading machinery for TAP and the peptide-loading complex (PLC).

Chapter 7:

- Latest findings on the metabolic impact of antigen receptor stimulation.
- Up-to-date research on immune checkpoint therapy with CTLA-4 and PD-1 blockade.

- New section on chimeric antigen receptors for CAR T-cell cancer immunotherapy (CAR-T therapy).

Chapter 8:

- New discussion of development of ILCs and nonconventional T cells, including regulatory T cells, iNKT cells, and CD8αα intraepithelial lymphocytes.

Chapter 9:

- Addition of new information on dendritic-cell subsets.
- New section on metabolic control of T-cell activation and differentiation.
- Latest developments in spatiotemporal control of T-cell priming by dendritic cells.
- New insights into how IL-2 signaling regulates T-cell differentiation.

Chapter 11:

- New emphasis on the relationship between antibody isotypes and immune effector modules.
- Updates on T_{FH} cells and tissue-resident memory T cells.
- New research on T-cell metabolic reprograming in formation and maintenance of T-cell memory.

Chapter 12:

- Major revision that includes more than 25 new or revised illustrations.
- Detailed discussion of the emergence of the COVID-19 pandemic and basis for viral tropism for host cells.
- Major expansion of discussion of mucosal immunity in the intestines, lungs, and skin.
- Expanded consideration of the interplay of barrier tissues with the commensal microbiota.
- Enhanced treatment of specialized epithelial cell types in barrier tissues, including tuft cells, goblet cells, Paneth cells, enteroendocrine cells, and others.
- Extended treatment of intraepithelial lymphocytes (IELs).

- New section introducing the latest findings in neuroimmune regulation.

Chapter 13:

- Expanded treatment and new figures on HIV/AIDS, including the latest findings on CCR5- and CXCR4-tropic HIV variants and use of combination antiretroviral therapy (cART).
- Latest structural information on broadly neutralizing antibodies against HIV envelope protein.
- Expanded and updated coverage of immune evasion by pathogens, including targeting of complement and interferon pathways.
- New section on viral mechanisms promoting exhaustion of T cells and NK cells.
- Updated research on mechanisms used by viral pathogens to subvert host cytokine and chemokine responses.

Chapter 16:

- Vaccines are brought to the forefront, illustrating new vaccine approaches to COVID-19 and modern vaccine technologies for poliovirus eradication.
- New discussion of checkpoint blockade and CAR T-cell technology for cancer immunotherapy.

Appendix I:

- Multiplex bead assay for flow cytometric analysis of antibody responses and its use to measure serum antibodies to SARS-CoV-2.
- Description of antigen tetramers for identification of antigen-specific B cells.
- New description of parabiosis for analysis of lymphocyte tissue residency.
- New discussion of cell lineage tracing techniques.
- Description of techniques for single-cell molecular analyses.

Resources for Instructors and Students

Instructor Resources

Instructor resources for *Janeway's Immunobiology* are available at wwnorton.com

Art of *Janeway's Immunobiology,* Tenth Edition

All the images from the book are available in both labeled and unlabeled versions in PowerPoint and JPEG formats.

PowerPoint Lecture Slides

The section headings, concept headings, and figures from the text have been integrated into customizable PowerPoint presentations.

InQuizitive

InQuizitive is Norton's award-winning, easy-to-use adaptive learning tool that personalizes the learning experience for students, helping them to master—and retain—key learning objectives. The InQuizitive course for *Janeway's Immunobiology*, Tenth Edition, includes dynamic question types focused on vocabulary and critical thinking, with clickable glossary definitions throughout. Through a variety of question types, answer-specific feedback, and pedagogical elements that promote metacognition, students are motivated to keep working until they've mastered both the concepts and the tough terminology critical to success in the immunology course. As a result, students arrive better prepared for class, giving instructors more time for discussion and activities.