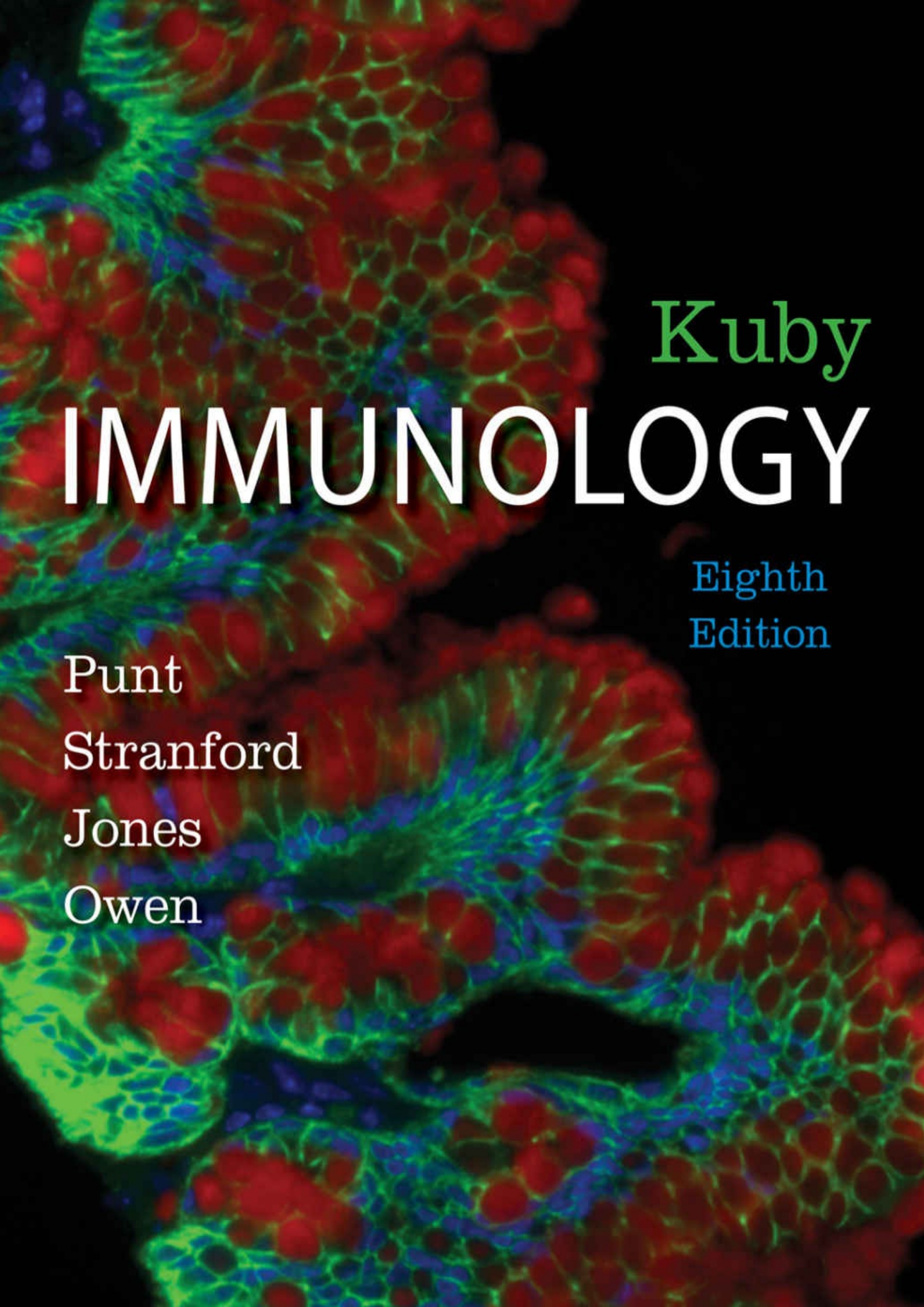
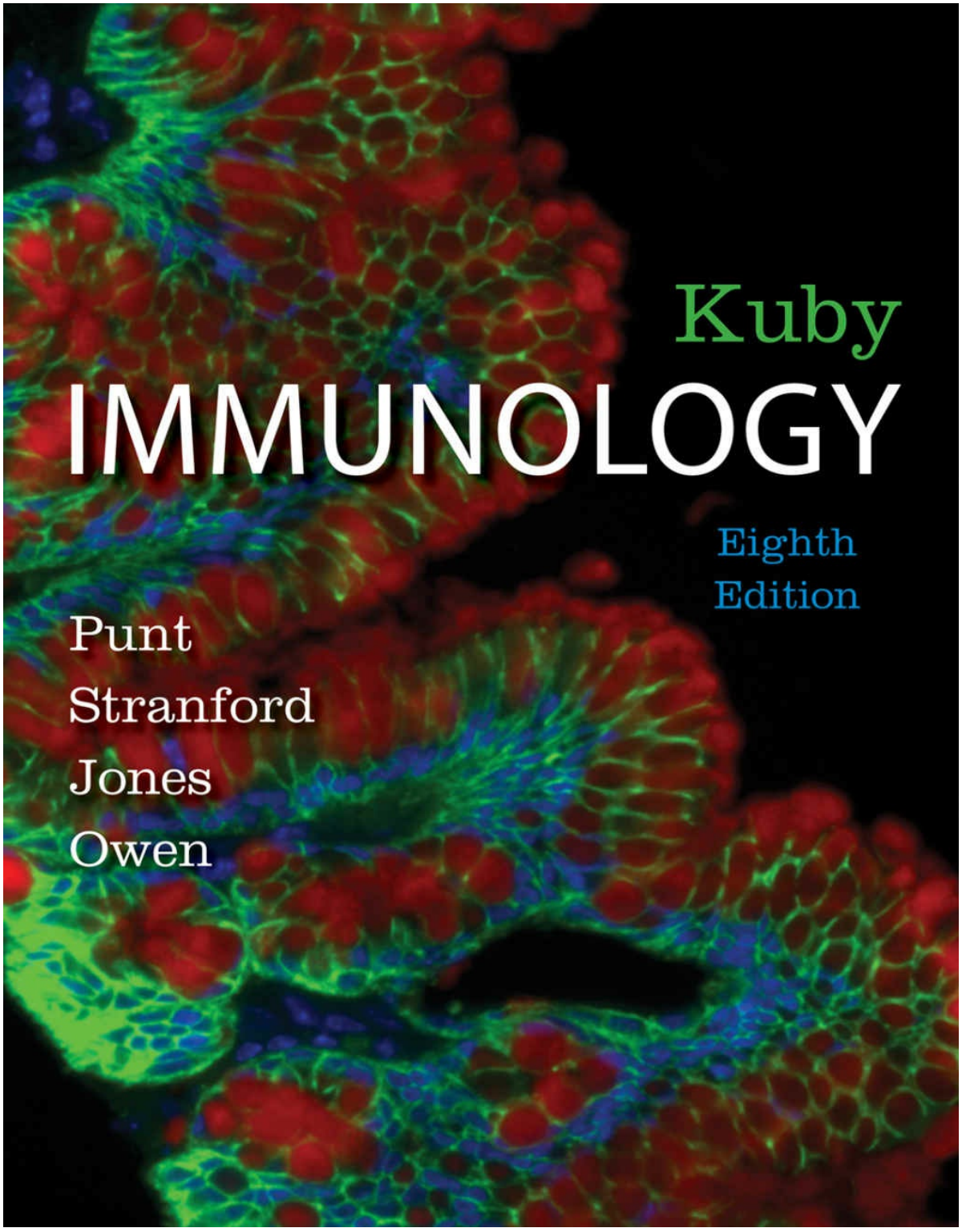
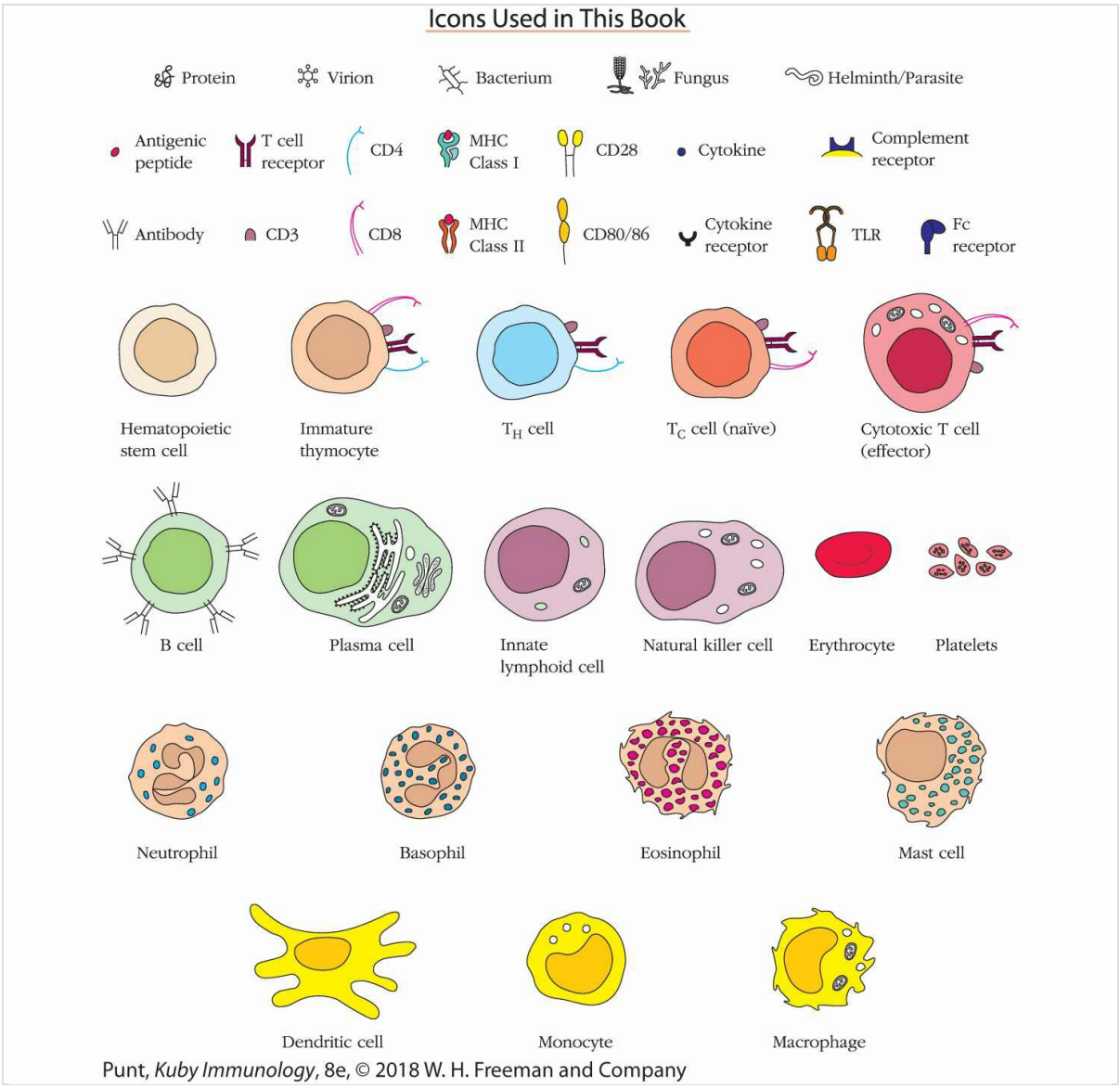

Kuby
IMMUNOLOGY
Eighth
Edition
Punt
Stranford
Jones
Owen


Kuby
IMMUNOLOGY
Eighth
Edition
Punt
Stranford
Jones
Owen

Kuby IMMUNOLOGY



Punt, *Kuby Immunology*, 8e, © 2018 W. H. Freeman and Company

Kuby IMMUNOLOGY

Eighth Edition

Jenni Punt
University of Pennsylvania

Sharon A. Stranford
Pomona College

Patricia P. Jones
Stanford University

Judith A. Owen
Haverford College

Vice President, STEM: Daryl Fox
Executive Editor: Lauren Schultz
Executive Marketing Manager: Will Moore
Marketing Assistant: Savannah DiMarco
Development Editor: Erica Champion
Development Editor: Erica Pantages Frost
Media Editor: Jennifer Compton
Assistant Editor: Kevin Davidson
Senior Content Project Manager: Liz Geller
Senior Media Project Manager: Jodi Isman
Permissions Manager: Jennifer MacMillan
Photo Researcher: Richard Fox
Director of Design, Content Management: Diana Blume
Designer: Blake Logan
Illustrations: Imagineering
Illustration Coordinator: Janice Donnola
Senior Workflow Project Supervisor: Susan Wein
Production Supervisor: Lawrence Guerra
Composition: Lumina Datamatics, Inc.
Printing and Binding: LSC Communications, Inc.

North American Edition
Cover Image: Courtesy of Audra Devoto and Xian-McKeon Laboratory

Library of Congress Control Number: 2018939693

ISBN-13 [mobi]:
978-1-319-26722-3

Printed in the United States of America

First printing

North American Edition
W. H. Freeman and Company
One New York Plaza
Suite 4500
New York, NY 10004-1562
www.macmillanlearning.com

To all the students, fellows, and colleagues who have made our careers in immunology a source of joy and excitement, and to our families and mentors who made these careers possible. We hope that future generations of immunology students will find this subject as fascinating and rewarding as we have. And in memory of Shannon Moloney, who had too little time to finish her own life goals but who will be remembered for how she helped us to meet our goals in this project.

About the Authors

All four authors are active scholars and teachers who have been/are recipients of research grants from the NIH and the NSF. They have all served in various capacities as grant proposal reviewers for the NSF, NIH, HHMI, and other funding bodies and, as well, have evaluated manuscripts submitted for publication in immunological journals. In addition, they are all active members of the American Association of Immunologists (AAI) and have served that national organization in a variety of ways.

Photo courtesy Jenni Punt

Jenni Punt received her A.B. from Bryn Mawr College, magna cum laude, with high honors in biology from Haverford College. She was a combined degree student at the University of Pennsylvania, graduating summa cum laude from the School of Veterinary Medicine (V.M.D.) with a Ph.D. in immunology. She pursued her interest in T-cell development as a Damon Runyon-Walter Winchell Physician-Scientist fellow with Dr. Alfred Singer at the National Institutes of Health and was appointed to the faculty of Haverford College in 1996. After 18 wonderful years there, working on T-cell and hematopoietic stem cell development, she accepted a position as associate dean for student research at Columbia University's College of Physicians and Surgeons. There she was the founding director of an M.D./M.Sc. dual degree program and co-ran a laboratory on hematopoiesis with her husband, Dr. Stephen Emerson. After being tempted back to the School of Veterinary Medicine at the University of Pennsylvania, she is now developing new educational programs as director of One Health Research Education. She has received multiple teaching awards over the course of her career and continues to find that students are her most inspirational colleagues.

Photo courtesy Sharon Stranford

Sharon Stranford received her Ph.D. in microbiology and immunology from Hahnemann University (now Drexel), where she studied multiple sclerosis. She then spent 3 years exploring transplant immunology as a postdoctoral fellow at Oxford University, followed by 3 years at the University of California, San Francisco, conducting human HIV/AIDS research. In 2001 she was hired as a Clare Boothe Luce Assistant Professor at Mount Holyoke College, a small liberal arts college for women in Massachusetts, where she served in the Department of Biological Sciences and the Program in Biochemistry for 12 years. Sharon is now a professor of biology at Pomona College in Claremont, California, where she investigates immunologic markers that influence susceptibility to immune deficiency. She also studies the science of teaching and learning; in particular, initiatives within STEM that foster a sense of inclusion and that welcome first-generation college students, like herself. Her teaching repertoire, past and present, includes cell biology, immunology, advanced laboratories in immunology, and seminars in infectious disease, as well as a team-taught course blending ethics and biology, entitled “Controversies in Public Health.”

Photo courtesy Rod Searcey

Pat Jones graduated from Oberlin College in Ohio with highest honors in biology and obtained her Ph.D. in biology with distinction from Johns Hopkins University. She was a postdoctoral fellow of the Arthritis Foundation for 2 years in the Department of Biochemistry and Biophysics at the University of California, San Francisco, Medical School, followed by 2 years as an NSF postdoctoral fellow in the Departments of Genetics and Medicine/Immunology at Stanford University School of Medicine. In 1978 she was appointed assistant professor of biology at Stanford and is now a full professor and currently holds the Dr. Nancy Chang Professorship in Humanities and Sciences. Pat has received several undergraduate teaching awards, was the founding director of the Ph.D. Program in Immunology, served as vice provost for faculty development and diversity, and in July 2011, she assumed the position of Director of Stanford Immunology, a position that coordinates immunology training activities across the university.

Photo courtesy Judith Owen

Judy Owen holds B.A. and M.A. (Hons) degrees in biochemistry from Cambridge University. She pursued her Ph.D. at the University of Pennsylvania with the late Dr. Norman Klinman and her postdoctoral fellowship with Dr. Peter Doherty in viral immunology. In 1981, she was appointed to the faculty of Haverford College, one of the first undergraduate colleges to offer a course in immunology. Judy teaches numerous laboratory and lecture courses in biochemistry and immunology; her teaching awards include the Excellence in Mentoring Award from the American Association of Immunologists. She is currently a participant in Haverford's First Year Writing Program and has been involved in curriculum development across the college. Judy served as director of the Marian E. Koshland Integrated Natural Sciences Center from 2013 to 2017 and currently holds the Elizabeth Ufford Green Professorship in Natural Sciences.

Together, Jenni Punt and Judy Owen developed and ran the first AAI introductory immunology course, which is now offered on an annual basis.

Brief Contents

Feature Boxes in *Kuby Immunology*, Eighth Edition

CLINICAL FOCUS

EVOLUTION

CLASSIC EXPERIMENT

ADVANCES

Contents

Preface

Like all of the previous authors of this book, we are dedicated to the concept that immunology is best taught and learned in an experimentally based manner, and we have retained that emphasis with this edition. It is our goal that students should complete an immunology course not only with a firm grasp of content, but also with a clear sense of how key discoveries were made, what interesting questions remain, and how they might best be answered. We believe that this approach ensures that students master fundamental immunological concepts, internalize a vision of immunology as an active and ongoing process, and develop the ability to contribute to new knowledge, themselves. Guided by this vision, this new edition has been extensively updated to reflect the recent advances in all aspects of our discipline.

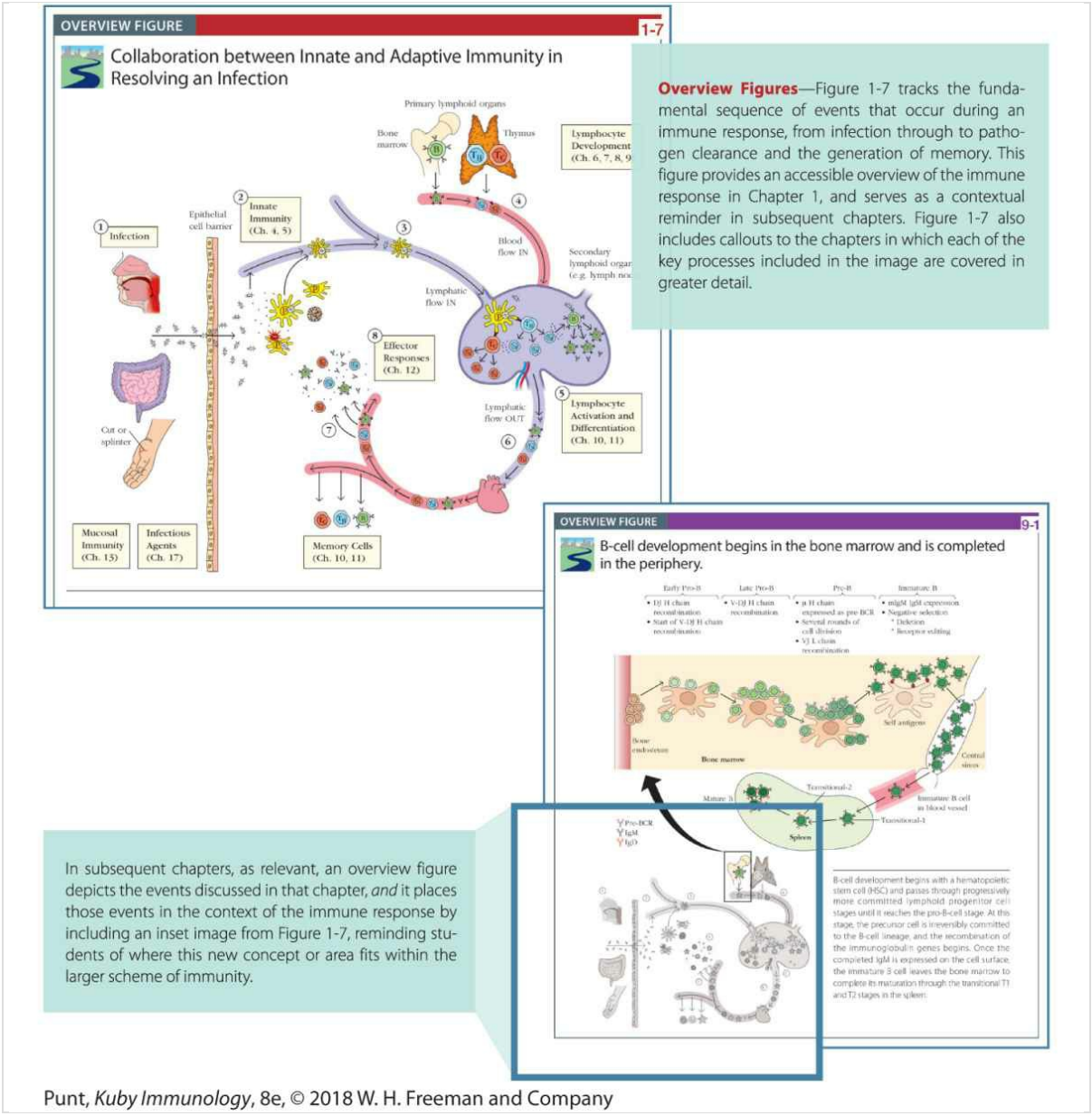
New Co-Author, Pat Jones

Photo courtesy Rod Searcey

The new edition of Kuby Immunology welcomes a new member to our author team, Patricia P. Jones, who had been a contributing author to the seventh edition. Dr. Jones is professor of biology at Stanford University and holds the Dr. Nancy Chang Professorship in Humanities and Sciences. Having earned her undergraduate degree in biology from Oberlin College and her Ph.D. in biology, with a focus on immunology, from Johns Hopkins University, Dr. Jones did postdoctoral training at both UCSF and Stanford University School of Medicine before joining the faculty at Stanford. She and her research group have made fundamental contributions to our understanding of the genetics, structure, and expression of MHC class II proteins and of mechanisms regulating adaptive and innate immune responses. Dr. Jones has served in various leadership positions at Stanford, including chairing the Department of Biology and the Faculty Senate, and serving as vice provost for faculty development and diversity. She was the founding director of the Ph.D. Program in Immunology and currently holds the position of Director of Stanford Immunology, which oversees all immunology training–related activities at Stanford. Dr. Jones has taught students at all levels, including teaching for many years the basic molecular and cellular immunology course for undergraduate and graduate students at Stanford. Her dedication to teaching and her enthusiasm for immunology shine through in her work.

Understanding the Big Picture

Two of the most challenging aspects of teaching immunology are the many important details (cell types, proteins, interactions, and terminology) and the interconnected or circular nature of the response. We find that students often fail to recognize how these pieces work together in an immune response that is dynamic. Our primary goal in the eighth edition is to bring this big picture to the forefront by providing a map or scaffold that both faculty and students can refer to in order to draw regular connections between concepts and individual players in the immune response.



Concepts and Context

Learning Objectives—Each chapter begins with a set of suggested learning objectives that highlight the main points of that chapter. Instructors may use these to frame their coursework, or students may use them to gauge their understanding of the concepts covered in that chapter. While this list is by no means comprehensive, we imagine it as a starting place and we encourage instructors to use or modify these suggestions by articulating their own learning objectives, with an eye toward generating their own desired learning outcomes.

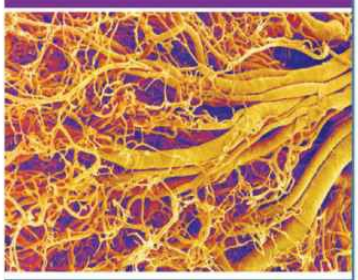
2

Cells, Organs, and Microenvironments of the Immune System

Learning Objectives

After reading this chapter, you should be able to:

1. Describe the types of blood cells that make up the immune system and outline the main events that occur during hematopoiesis, the process that gives rise to immune cells.
2. Identify the primary, secondary, and tertiary immune organs in vertebrates and describe their function.
3. Recognize and describe the microenvironments where immune cells mature and the immune response develops.
4. Identify several experimental approaches used to understand how blood cells and immune responses develop.



Scanning electron micrograph of blood vessels in a lymph node. *[Suzumu Nishinaga/Science Source.]*

Key Terms—Selected glossary terms from the chapter are listed on the first page as a preview of the important vocabulary.

Key Terms

- Hematopoiesis
- Hematopoietic stem cell (HSC)
- Myeloid lineage cells
- Lymphoid lineage cells
- Primary lymphoid organs
  - Bone marrow
  - Thymus
- Secondary lymphoid organs
  - Lymph nodes
  - Spleen
  - Barrier tissues (MALT and skin)
- Lymphatic system
- Tertiary lymphoid tissue
- T-cell zone
- B-cell follicle
- Germinal centers
- Fibroblastic reticular cell conduit (FRCC) system
- Follicular dendritic cells (FDCs)

Key Concepts:

- HSCs reside primarily in the bone marrow, where stromal cells regulate their quiescence, proliferation, and trafficking. Long-term HSCs reside in the perivascular niche, in association with cells that line the blood vessels.
- In the bone marrow, HSCs differentiate into progenitors, which can become myeloid or lymphoid cell lineages. B lymphocytes complete their maturation in the bone marrow, but progenitors that can differentiate into T lymphocytes exit and complete their maturation in the thymus.

Key Concepts—Each section in the text is followed by a bulleted summary list of Key Concepts. These encourage students to pause at the end of each section so they can reflect on and reinforce the content.

Conclusion—Chapters end with a conclusion section that reflects on the entire chapter, placing the specific topic in the larger context of the immune response. Both a summary and a preview, the conclusion relates the chapter's concepts to upcoming chapters, touching on how the events discussed influence other parts of the immune response and identifying weaknesses that might be exploited by pathogens.

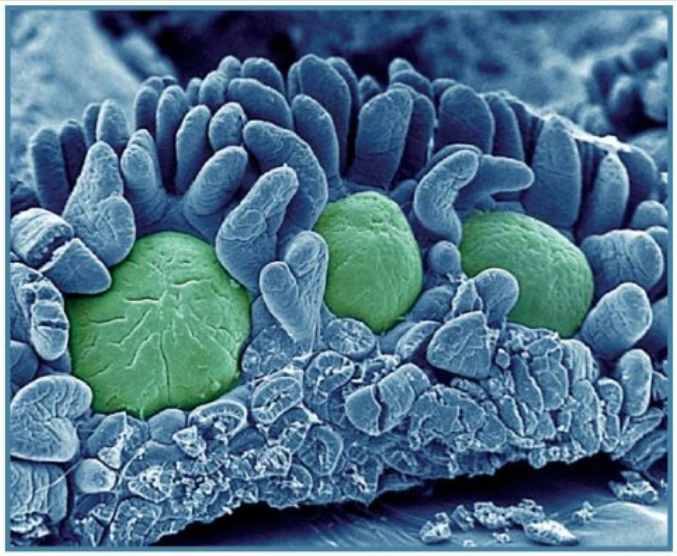
Punt, *Kuby Immunology*, 8e, © 2018 W. H. Freeman and Company

A Conceptual Approach to Signaling

Chapter 3 (Recognition and Response) now combines a description of the antigen receptors of innate and adaptive immunity with a brief introduction to cytokines, chemokines, and their respective receptors, formerly found in Chapter 4. Using a conceptual approach, Chapter 3 now foregrounds the major concepts required for understanding the processes of signal recognition and signal transduction throughout the immune system. We highlight the diverse roles of receptor diversity, multivalency, coreceptors, lipid rafts, and multiple signaling pathways in the regulation of immune responsiveness.

New Chapter—Barrier Immunity and the Microbiome

Research on the interaction between the microbiome and the immune response has flourished in recent years. Not only do our immune cells shape the diverse communities of microbes that live on our epithelial surfaces, but these communities have a powerful influence on the development and activity of a healthy immune system. The eighth edition of Kuby Immunology now includes a new chapter, **Barrier Immunity: The Immunology of Mucosa and Skin (Chapter 13)**, that reviews our new understanding of the interaction between microbes and immunity at epithelial surfaces, including mucosal tissues and skin.



SPL/Science Source

Advances in Immunology—Other Notable Updates

Immunology is a rapidly growing field, with new discoveries, advances in techniques, and previously unappreciated connections coming to light every day. In addition to a new chapter on barrier immunity, the eighth edition of Kuby Immunology has been thoroughly updated throughout, and now includes the following material and concepts.

- Natural killer (NK) cells are now recognized to be a subset of a larger group of innate lymphoid cells (ILCs) with characteristics similar to T_H cell subsets, but that originate in the myeloid lineage. ILCs are introduced in Chapter 2 and their roles in the innate and adaptive immune responses are discussed in Chapters 4 and 10, respectively.
- Exciting new immunotherapeutic approaches for treating a variety of conditions are described in Chapters 12, 15, 18, and 20.
- The role of the microbiome and its interactions with the immune system in health and disease is discussed in Chapters 1, 11, 13, 15, and 16.
- Insights gained from advanced imaging technology continue to be updated. For example, Chapter 6 describes immunofluorescence techniques that reveal changes in chromosomal organization accompanying V(D)J recombination.

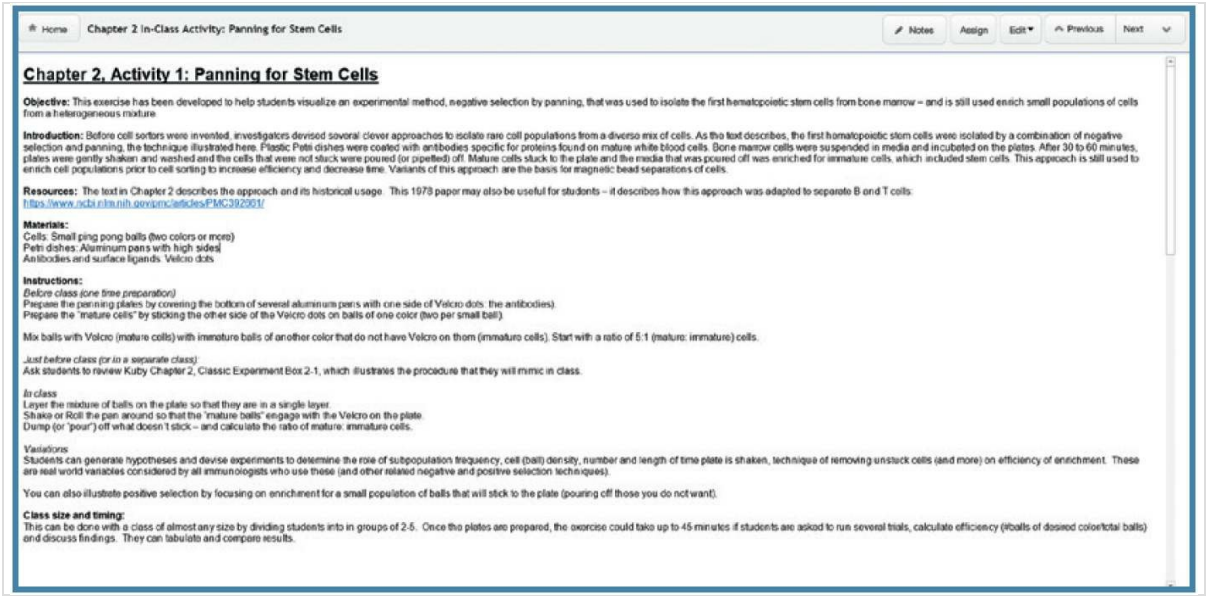
New boxes have been added on the following topics:

- **Classic Experiment Box 4-1:** Discovery of Invertebrate Toll and Vertebrate Toll-Like Receptors
- **Advances Box 5-2:** The role of complement in the development of the nervous system and vision
- **Evolution Box 6-3:** The evolution of V(D)J recombination and RAG genes
- **Clinical Focus Box 7-3:** MHC expression and Tasmanian devil facial tumor disease
- **Clinical Focus Box 10-2:** Checkpoint inhibitors and cancer therapy
- **Advances Box 10-4:** Jumping genes, T_{REG} cells and the evolution of immune tolerance during pregnancy
- **Advances Box 11-1:** Tracking the movements of B cells between the dark and light zones of the germinal center
- **Clinical Focus Box 12-1:** Therapeutic antibodies for the treatment of diseases
- **Advances Box 13-1:** Cells involved in barrier immunity
- **Clinical Focus Box 13-2:** Communication between the gut and the brain
- **Advances Box 13-3:** Germ-free animal model systems
- **Clinical Focus Box 17-1:** Zika virus and vaccine development
- **Advances Box 18-2:** Broadly neutralizing antibodies to HIV
- **Clinical Focus Box 19-2:** CAR-T cells as a potential cancer cure

LaunchPad for Kuby Immunology

The eighth edition of Kuby Immunology is fully supported in LaunchPad. We designed LaunchPad as a resource to help students achieve better results. Our goal was to increase their confidence by providing a place where they could read, study, practice, complete homework, and succeed. In addition, LaunchPad always provides instructors and students with superior service and support, based on Macmillan's legendary high-quality content. LaunchPad includes a suite of supplements that build on the text by engaging students inside and outside the classroom.

In-Class Activities—In many classrooms, student engagement is key to addressing misconceptions and reinforcing important concepts. The Kuby Immunology authors have provided instructions and materials for a variety of activities they use in their own classrooms to engage students. These tried-and-true activities range in length and complexity and can serve as a springboard for active learning in the classroom.


Home | Chapter 2 In-Class Activity: Panning for Stem Cells | Notes | Assign | Edit | Previous | Next

Chapter 2, Activity 1: Panning for Stem Cells

Objective: This exercise has been developed to help students visualize an experimental method, negative selection by panning, that was used to isolate the first hematopoietic stem cells from bone marrow – and is still used enrich small populations of cells from a heterogeneous mixture.

Introduction: Before cell sorters were invented, investigators devised several clever approaches to isolate rare cell populations from a diverse mix of cells. As the text describes, the first hematopoietic stem cells were isolated by a combination of negative selection and panning, the technique illustrated here. Plastic Petri dishes were coated with antibodies specific for proteins found on mature white blood cells. Bone marrow cells were suspended in media and incubated on the plates. After 30 to 60 minutes, plates were gently shaken and washed and the cells that were not stuck were poured (or pipetted) off. Mature cells stuck to the plate and the media that was poured off was enriched for immature cells, which included stem cells. This approach is still used to enrich cell populations prior to cell sorting to increase efficiency and decrease time. Variants of this approach are the basis for magnetic bead separations of cells.

Resources: The text in Chapter 2 describes the approach and its historical usage. This 1978 paper may also be useful for students – it describes how this approach was adapted to separate B and T cells:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC392061/

Materials:
Cells: Small ping pong balls (two colors or more)
Petri dishes: Aluminum pans with high sides
Antibodies and surface ligands: Velcro dots

Instructions:
Before class (one time preparation)
Prepare the panning plates by covering the bottom of several aluminum pans with one side of Velcro dots: the antibodies).
Prepare the "mature cells" by sticking the other side of the Velcro dots on balls of one color (two per small ball).

Mix balls with Velcro (mature cells) with immature balls of another color that do not have Velcro on them (immature cells). Start with a ratio of 5:1 (mature: immature) cells.

Just before class (or in a separate class)
Ask students to review Kuby Chapter 2, Classic Experiment Box 2-1, which illustrates the procedure that they will mimic in class.

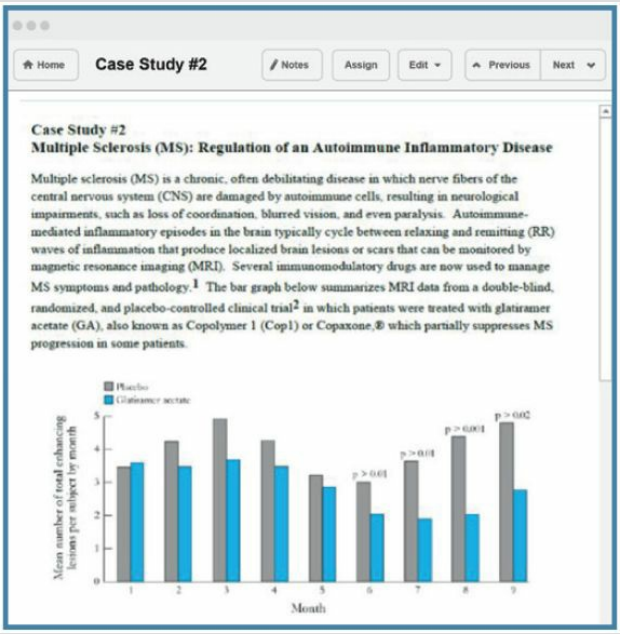
In class
Layer the mixture of balls on the plate so that they are in a single layer.
Shake or Roll the pan around so that the "mature balls" engage with the Velcro on the plate.
Dump (or "pour") off what doesn't stick – and calculate the ratio of mature: immature cells.

Variations
Students can generate hypotheses and devise experiments to determine the role of subpopulation frequency, cell (ball) density, number and length of time plate is shaken, technique of removing unstuck cells (and more) on efficiency of enrichment. These are real world variables considered by all immunologists who use these (and other related negative and positive selection techniques).

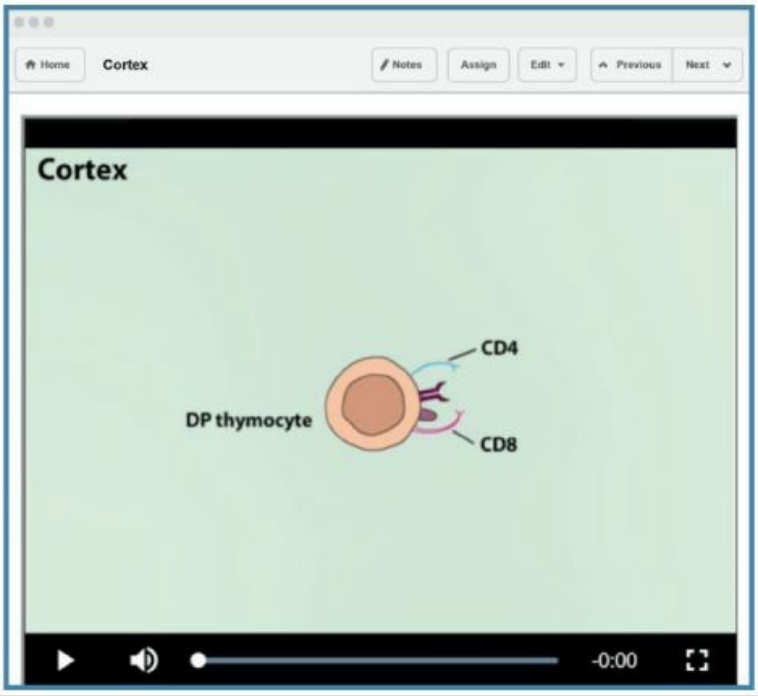
You can also illustrate positive selection by focusing on enrichment for a small population of balls that will stick to the plate (pouring off those you do not want).

Class size and timing:
This can be done with a class of almost any size by dividing students into in groups of 2-5. Once the plates are prepared, the exercise could take up to 45 minutes if students are asked to run several trials, calculate efficiency (#balls of desired color/total balls) and discuss findings. They can tabulate and compare results.

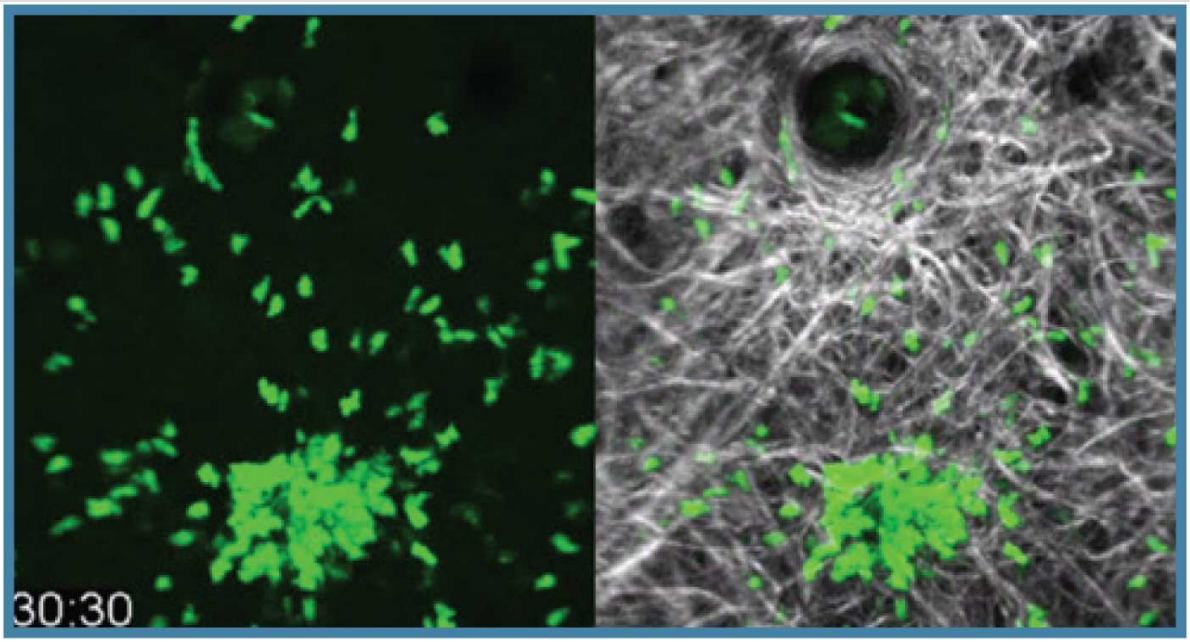
Case Studies—Interpreting experimental data is essential in understanding immunology. These case studies explore immune function, disease, and treatment through the application of primary research and data. Students are led through a series of experiments and challenged to interpret the data and draw conclusions. By integrating experimental techniques from immunology, molecular biology, and biochemistry, these case studies teach students to think critically and synthesize their knowledge of immunology and other branches of science.



Animations—Many of the most difficult topics in immunology are multistep events that are best visualized through animations. We have created a suite of 2D animations for the eighth edition that walk students through these difficult topics, showing each step of the process. Each animation is accompanied by assessments.

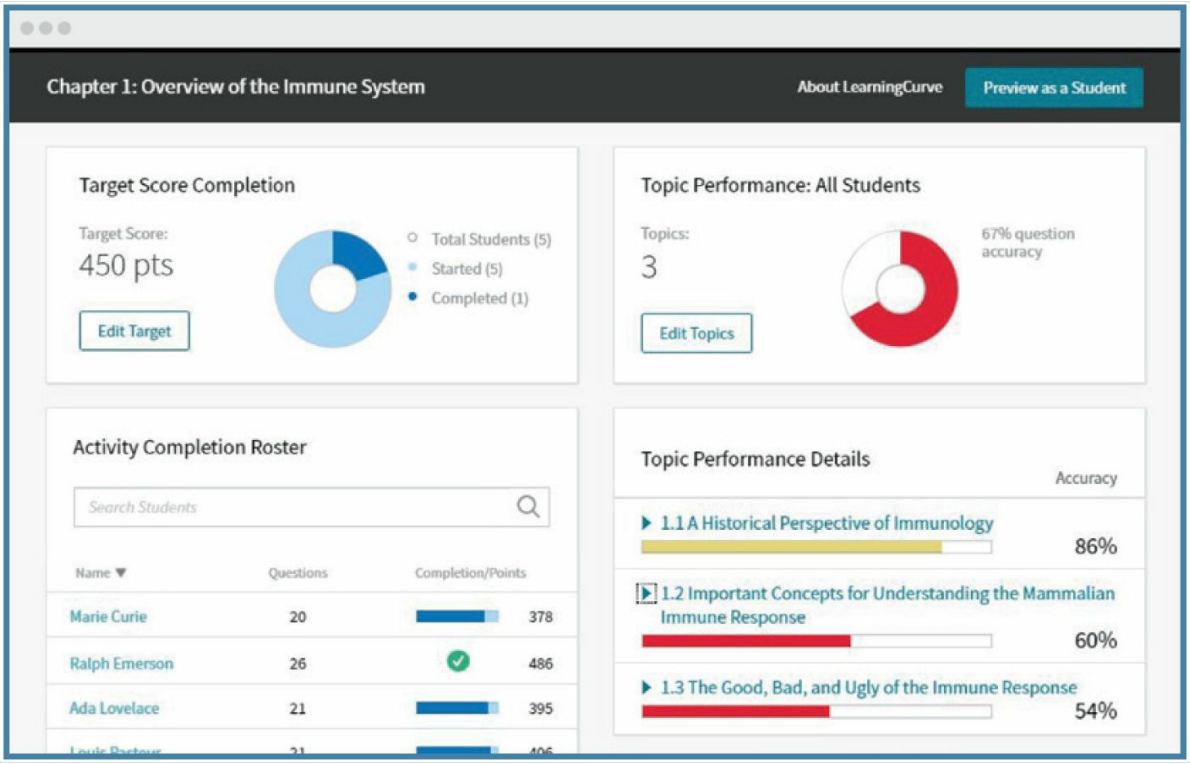


Videos—Dynamic imaging techniques allow immunologists to observe the immune system at work in vivo. These striking videos show a T cell crawling along a network of stromal cells, the change in behavior when a naïve B cell is activated, and the chemotactic response of neutrophils to a site of damage.



Lämmermann T., et al., "Neutrophil swarms require LTB4 and integrins at sites of cell death in vivo." *Nature* 2013, June 20; 498:371–75, Video 2.

Learning Curve—LearningCurve adaptive quizzing offers individualized question sets and feedback for each student based on his or her correct and incorrect responses. All the questions are tied back to the e-Book to encourage students to use the resources at hand.



e-Book—The Kuby Immunology, Eighth Edition, e-Book is available through Vital Source and LaunchPad. This fully enhanced e-Book includes embedded animations and videos, as well as web links to additional resources. e-Book access can be purchased through the Macmillan Student Store

and represents a significant cost savings versus a printed copy of the book.

Advanced Online Material—Feature boxes within the text describe clinical connections, classic experiments, technological advances, and evolutionary aspects of the immunology topics discussed. Boxes and other content that have been retired from the print text are available for instructor download at the catalog site.

Test Bank—The Kuby Immunology test bank has been expanded to include more higher-order questions in both multiple choice and short answer formats. Over 700 dynamic questions in PDF and editable Word formats are rated by level of difficulty and Bloom's taxonomy level, and tagged to specific sections of the text.

Optimized Art—Fully optimized JPEG files of every figure, photo, and table in the text are available, featuring enhanced color, higher resolution, and enlarged fonts. Images are also offered in PowerPoint format for each chapter.

Acknowledgments

We owe special thanks to individuals who offered insightful ideas, contributed detailed reviews that led to major improvements, and provided the support that made writing this text possible. These notable contributors include Dr. Stephen Emerson, Dr. Scott Owen, Dr. Alexander Stephan, and the many students—undergraduates and graduates—who provided invaluable perspectives on our chapters. We hope that the final product reflects the high quality of the input from these experts and colleagues and from all those listed below who provided critical analysis and guidance.

We are also grateful to the previous authors of Kuby Immunology, whose valiant efforts we now appreciate even more deeply. Their commitment to clarity, to providing the most current material in a fast-moving discipline, and to maintaining the experimental focus of the discussions set the standard that is the basis for the best of this text.

We also acknowledge that this book represents the work not only of its authors and editors, but also of all those whose scientific experiments, papers, and conversations provided us with ideas, inspiration, and information. We thank you and stress that all errors and inconsistencies of interpretation are ours alone.

We thank the following reviewers for their comments and suggestions about the manuscript during preparation of this eighth edition. Their expertise and insights have contributed greatly to the book.

Jorge N. Artaza, University of California, Los Angeles

Roberta Attanasio, Georgia State University

Avery August, Cornell University

Kenneth Balazovich, University of Michigan

Amorette Barber, Longwood University

Scott Barnum, University of Alabama at Birmingham

Carolyn A. Bergman, Georgian Court University

Ashok P. Bidwai, West Virginia University

Jay H. Bream, Johns Hopkins University

Walter J. Bruyninckx, Hanover College

Eric Buckles, Dillard University

Peter Burrows, University of Alabama at Birmingham

Stephen K. Chapes, Kansas State University

Janice Conway-Klaassen, University of Minnesota

Jason Cyster, University of California, San Francisco

Kelley Davis, Nova Southeastern University

Brian DeHaven, La Salle University

Joyce Doan, Bethel University

Erastus C. Dudley, Huntingdon College

Uthayashanker Ezekiel, Saint Louis University

Karen Golemboski, Bellarmine University

Sandra O. Gollnick, University at Buffalo, SUNY

Elizabeth A. Good, University of Illinois, Urbana-Champaign

Susan M. R. Gurney, Drexel University

Kirsten Hokeness, Bryant University

Judith Humphries, Lawrence University

Seth Jones, University of Kentucky

George Keller, Samford University

Kevin S. Kinney, DePauw University

Edward C. Kisailus, Canisius College

David Kittlesen, University of Virginia

Ashwini Kucknoor, Lamar University

Narendra Kumar, Texas A&M Health Science Center

Courtney Lappas, Lebanon Valley College

Melanie J. Lee-Brown, Guilford College

Vicky M. Lentz, SUNY Oneonta

Marlee B. Marsh, Columbia College

James McNew, Rice University

Daniel Meer, Cardinal Stritch University

JoAnn Meerschaert, St. Cloud State University

Pamela Monaco, Molloy College

Rajkumar Nathaniel, Nicholls State University

Samantha Terris Parks, Georgia State University

Rekha Patel, University of South Carolina

Sarah M. Richart, Azusa Pacific University

James E. Riggs, Rider University

Vanessa Rivera-Amill, Ponce Health Sciences University-School of Medicine

Ryan A. Shanks, University of North Georgia

Laurie P. Shornick, Saint Louis University

Paul K. Small, Eureka College

Jennifer Ripley Stueckle, West Virginia University

Gabor Szalai, West Virginia School of Osteopathic Medicine

Clara Toth, St. Thomas Aquinas College

Vishwanath Venketaraman, Western University of Health Sciences

Barbara Criscuolo Waldman, University of South Carolina

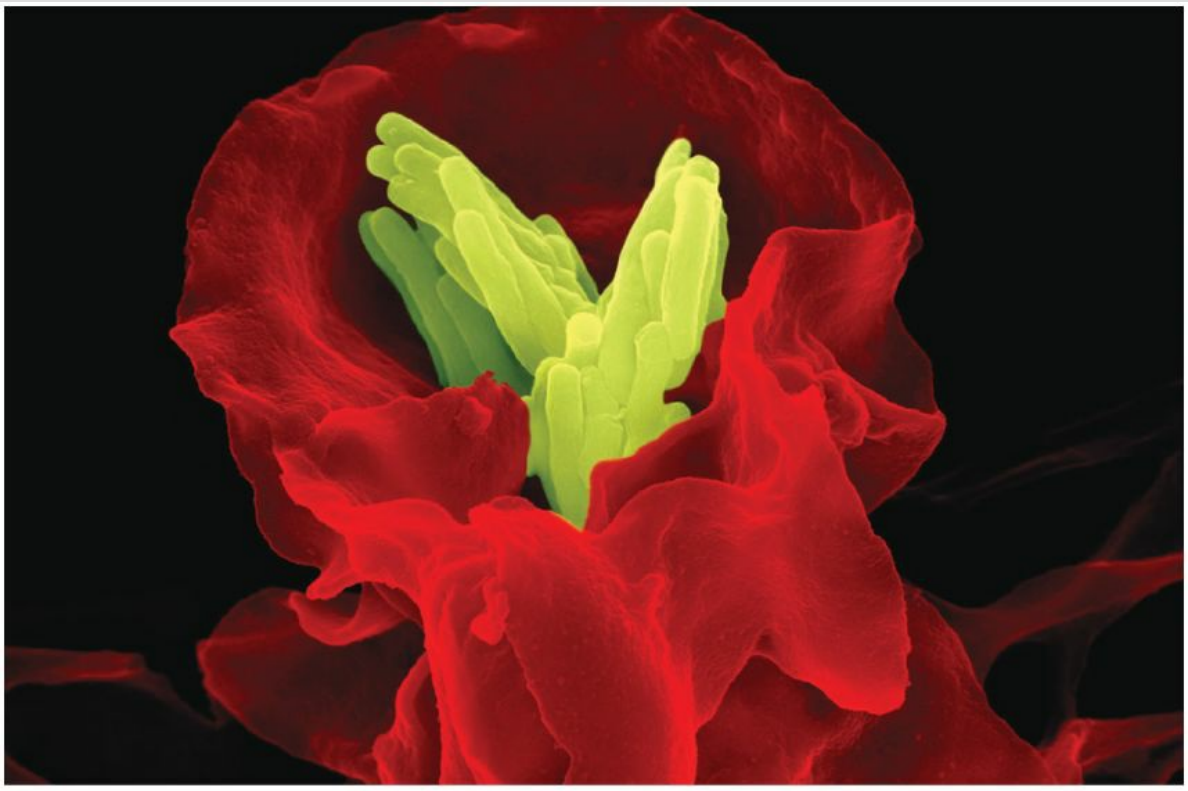
Denise G. Wingett, Boise State University

Laurence Wong, Burman University

Finally, we thank our experienced and talented colleagues at W. H. Freeman and Company. Particular thanks to the production team members Liz Geller, Susan Wein, Janice Donnola, Diana Blume, Jennifer MacMillan, Richard Fox, and Mark Mykytiuk and his team at Imagineering. Thanks are also due to the editorial, media, and marketing teams of Lauren Schultz, Kevin Davidson, Jennifer Compton, and Will Moore.

However, we are particularly grateful for the insights, diplomacy, energy, and quality of judgment of our heroic developmental editors, Erica Champion and Erica Frost. “Our” Ericas have guided us from the beginning with probing vision and keen eyes for narrative and clarity. They have exhibited endless patience for our complex schedules, perspectives, and needs as authors and professors. In short, these two extraordinarily talented team members have made this edition, and its ambitious aspirations, possible.

CHAPTER 1 Overview of the Immune System



Science Photo Library/Science Source.

A human macrophage (red) ingesting Mycobacterium tuberculosis (green), the bacterium that causes tuberculosis.