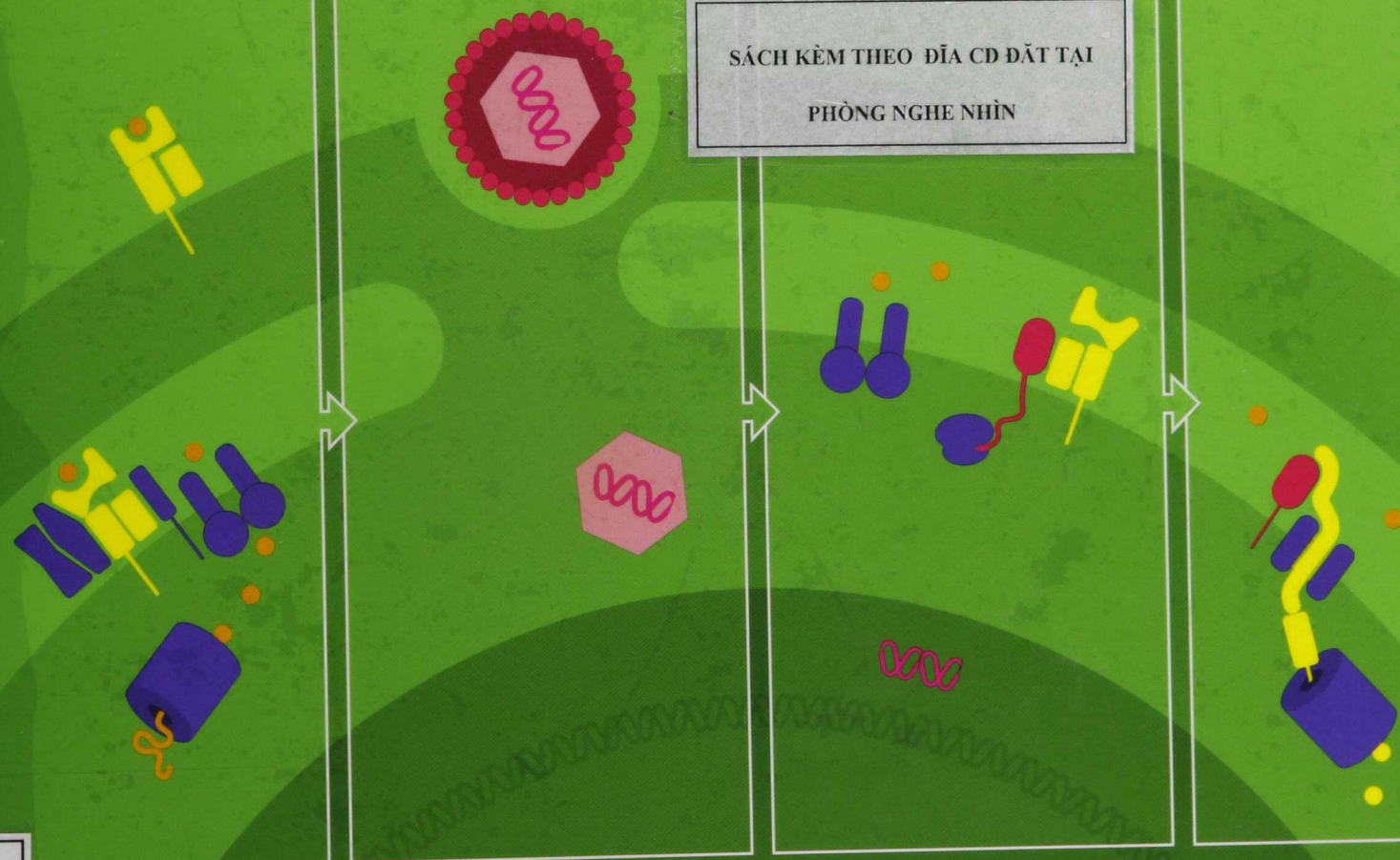


Janeway's

# Immuno biology

SEVENTH EDITION

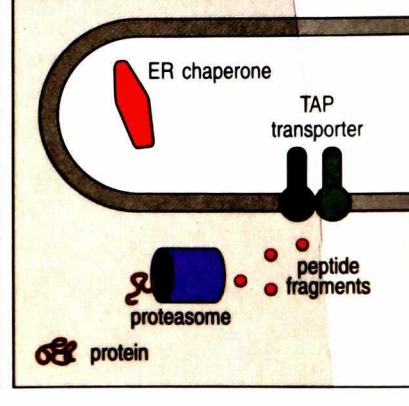
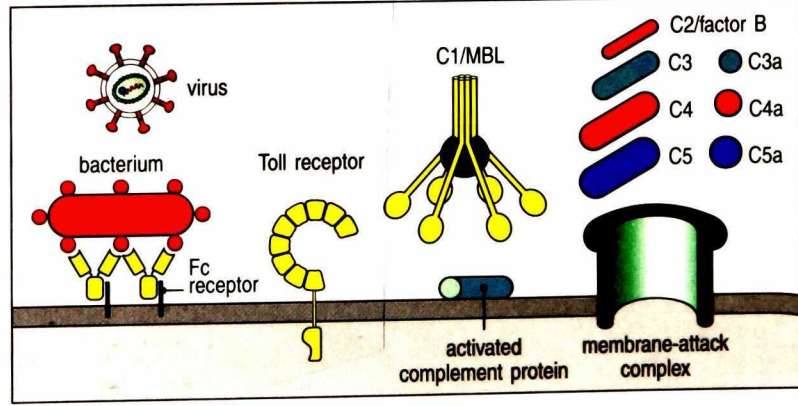
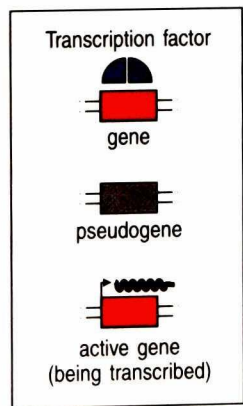
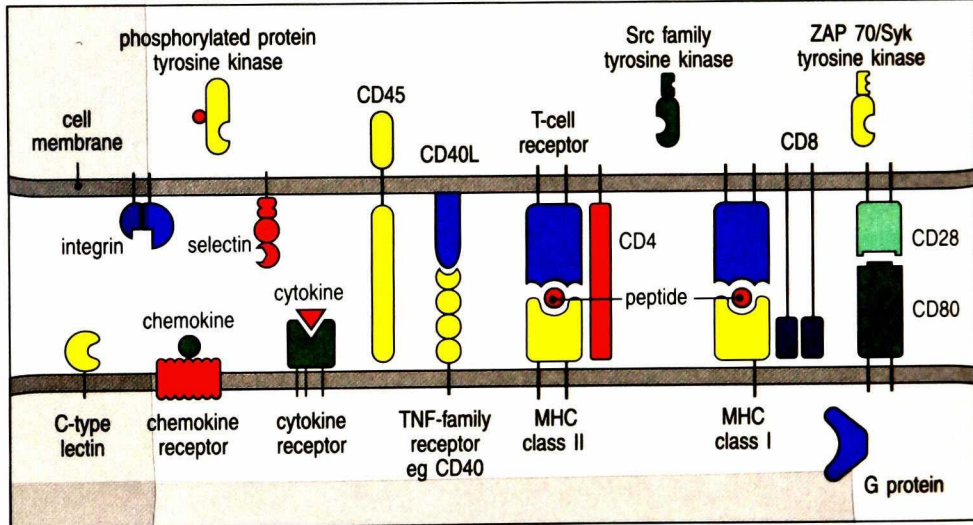
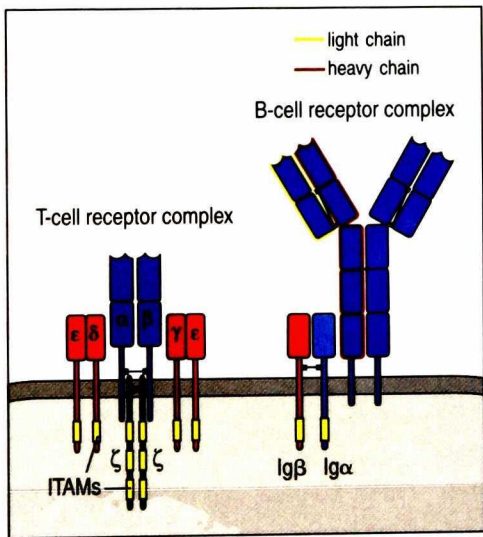
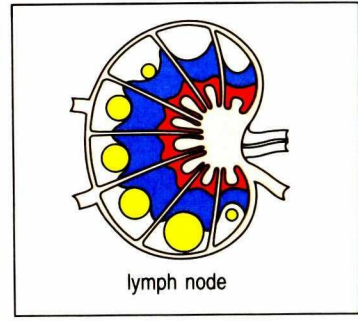
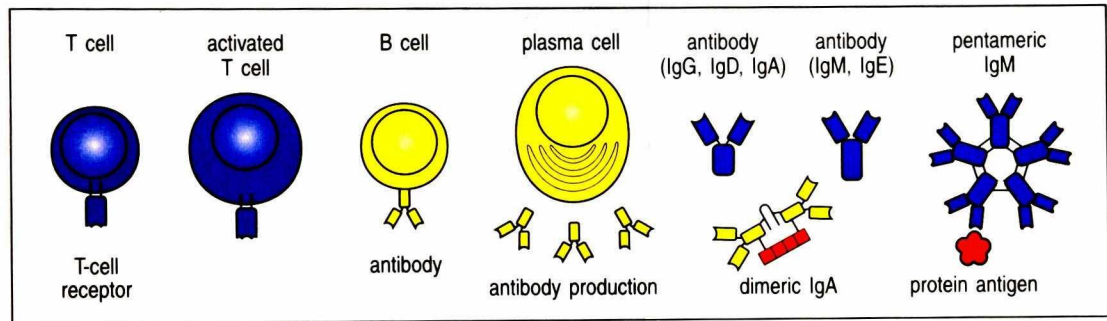
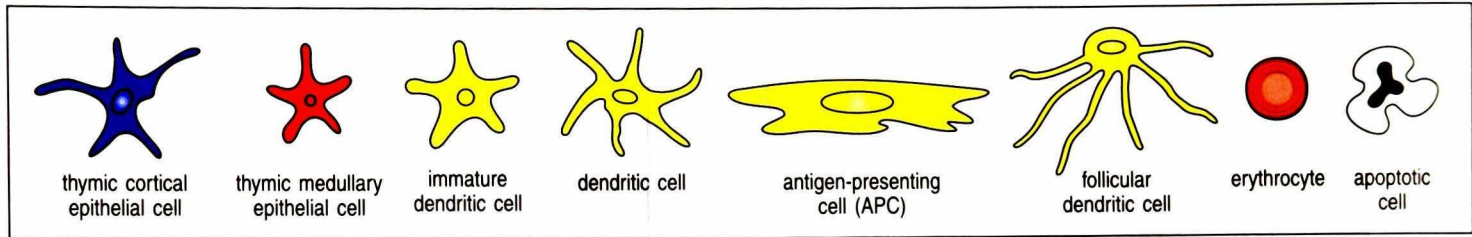
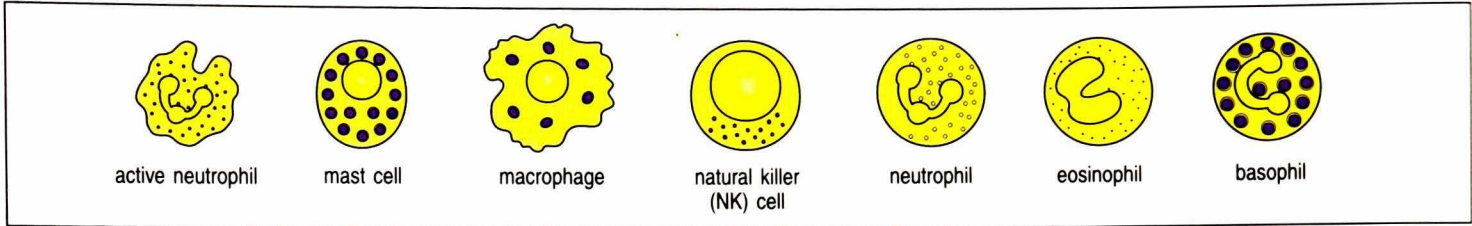
SÁCH KÈM THEO ĐĨA CD ĐẶT TẠI  
PHÒNG NGHE NHÌN



Kenneth Murphy • Paul Travers • Mark Walport

ÊN  
U

**Icons used throughout the book**



Janeway's  
**Immuno  
biology**

SEVENTH EDITION



Janeway's  
**Immuno  
biology**

SEVENTH EDITION

**Kenneth Murphy**

Washington University School of Medicine, St. Louis

**Paul Travers**

Anthony Nolan Research Institute, London

**Mark Walport**

The Wellcome Trust, London

With contributions by:

**Michael Ehrenstein**

University College London, Division of Medicine

**Claudia Mauri**

University College London, Division of Medicine

**Allan Mowat**

University of Glasgow

**Andrey Shaw**

Washington University School of Medicine, St. Louis



**GS** Garland Science  
Taylor & Francis Group  
NEW YORK AND LONDON

**Vice President:** Denise Schanck  
**Assistant Editor:** Sigrid Masson  
**Text Editor:** Eleanor Lawrence  
**Production Editor and Layout:** Georgina Lucas  
**Copy Editor:** Bruce Goatly  
**Illustration and Design:** Matthew McClements, Blink Studio, Ltd.  
**Permissions Coordinator:** Mary Dispenza  
**Indexer:** Merrall-Ross International Ltd.

***Immunobiology, Seventh Edition Interactive:***

**Storyboards by:** Kenneth Murphy, Paul Travers, and Peter Walter  
**Narrated by:** Julie Theriot  
**Animations, Interface Design, and Programming:** Matthew McClements, Blink Studio, Ltd.  
**Senior Media Editor:** Michael Morales

© 2008 by Garland Science, Taylor & Francis Group, LLC

This book contains information obtained from authentic and highly regarded sources. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

All rights reserved. No part of this book covered by the copyright hereon may be reproduced or used in any format in any form or by any means—graphic, electronic, or mechanical, including photocopying, recording, taping, or information storage and retrieval systems—without permission of the publisher.

10-digit ISBN 0-8153-4123-7  
0-8153-4290-X (International Student Edition)  
13-digit ISBN 978-0-8153-4123-9  
978-0-8153-4290-8 (International Student Edition)

**Library of Congress Cataloging-in-Publication Data**

Janeway, Charles.  
Janeway's immunobiology. -- 7th ed. / Kenneth Murphy, Paul Travers, Mark Walport.  
p. cm.  
Includes index.  
ISBN 0-8153-4123-7 (978-0-8153-4123-9)  
I. Murphy, Kenneth. II. Travers, Paul. III. Walport, Mark. IV. Title.  
QR181J37 2008  
616.07'9--dc22

2007002499

Published by Garland Science, Taylor & Francis Group, LLC, an informa business  
270 Madison Avenue, New York, NY 10016, US, and  
2 Park Square, Milton Park, Abingdon, OX14 4RN, UK

Printed in the United States of America  
15 14 13 12 11 10 9 8 7 6 5 4 3 2

**T&F** informa

Taylor & Francis Group, an informa business

Visit our web site at <http://www.garlandscience.com>

# Preface

This book is intended as an introductory text for use in immunology courses for medical students, advanced undergraduate biology students, graduate students, and scientists in other fields who want to know more about the immune system. It presents the field of immunology from a consistent viewpoint, that of the host's interaction with an environment containing many species of potentially harmful microbes. The justification for this approach is that the absence of one or more components of the immune system is virtually always made clear by an increased susceptibility to one or more specific infections. Thus, first and foremost, the immune system exists to protect the host from infection, and its evolutionary history must have been shaped largely by this challenge. Other aspects of immunology, such as allergy, autoimmunity, graft rejection, and immunity to tumors, are treated as variations on this basic protective function. In these cases the nature of the antigen is the major variable.

In this seventh edition, all chapters have been updated to incorporate new observations that extend our knowledge and understanding of the immune system. Examples include new work on NK receptors, the deeper understanding of the role of activation-induced cytidine deaminase (AID) in the generation of antibody diversity, viral immunoevasins, cross-presentation of antigen to T cells, dendritic cell and T-cell subsets, and new innate receptors that recognize pathogens, to name but a few. Our chapter on evolution includes fascinating new insights into alternative forms of adaptive immunity in both invertebrates and higher organisms. The clinical chapters contain new sections on celiac disease and its mechanism, Crohn's disease, and immunological approaches to cancer treatment. New discussion questions have been provided at the end of each chapter. These questions can be used for review, or as the basis for discussion in class or in informal study groups. The accompanying CD-ROM, *Janeway's Immunobiology 7 Interactive*, has been expanded and enhanced.

Following a comprehensive overview of the immune system in Chapter 1, innate immunity is treated in Chapter 2 as an important protective system in its own right and a necessary precursor to the adaptive immune response. The coverage of Toll receptors and other pathogen-sensing mechanisms has been updated to reflect the rapid progress in this field in the past three years and the description of the different families of activating and inhibitory NK receptors has been revised to reflect the growing understanding of these. The material on pathogens at the beginning of Chapter 10 in previous editions has been moved to Chapter 2 to provide a more complete introduction to infection earlier in the book. After the discussion of innate immunity, the emphasis shifts to adaptive immunity, because we know far more about this subject, thanks to the efforts of the vast majority of immunologists. The central theme of the subsequent text is clonal selection of lymphocytes.

As in the sixth edition, we consider the two lymphoid lineages, B lymphocytes and T lymphocytes, together for most of the book, because it seems to us that essentially common mechanisms work in both cell types. An example is the rearrangement of gene segments to generate the receptors by which lymphocytes recognize antigen (Chapter 4). Chapter 5, on recognition of antigen, has been updated to include the cross-presentation of antigen by MHC class I molecules, and the interference by viral immunoevasins in antigen presentation. Chapter 6, on signaling, has been revised to describe the T-cell signaling pathways in more detail, with an extended and updated discussion of co-stimulatory signaling. We have substantially reorganized Chapter 7 so that the development of B cells and T cells are considered in separate sections.

Chapters 8 and 9 elaborate the effector functions of T cells and B cells separately, since different mechanisms are involved. We have updated and extended the treatment of dendritic cells and included recent research findings on the  $T_H17$  and regulatory T-cell subsets (Chapter 8). We have taken the opportunity to refocus Chapter 10 on the dynamic nature of the immune response to infection, from innate immunity to the generation of immunological memory. We include recent advances in our understanding of the temporal changes in T-cell subsets during an immune response and of the nature of immunological memory. Because of its increasingly recognized role in immune defense, we have created a new chapter devoted entirely to mucosal immunity (Chapter 11).

The subsequent three chapters (Chapters 12-14) deal mainly with how diseases such as HIV/AIDS, autoimmunity, or allergy can be caused by inherited or acquired immunodeficiencies or by failure or malfunction of immunological mechanisms. As our understanding of the causes of disease grows, these chapters have been extended with descriptions of syndromes for which underlying gene defects have been newly identified. These chapters, which describe the failures of the immune system to maintain health, are followed by a chapter (Chapter 15) on how the immune response can be manipulated by vaccination and other means in attempts to combat not only infectious diseases, but also transplant rejections and cancer. These four chapters have been extensively revised and updated, especially in respect of the new generation of 'biological' therapeutics that are starting to enter medical practice.

The book ends with an updated chapter (Chapter 16) on the evolution of animal immune systems. The analysis of the genome sequences of both invertebrates and lower vertebrates has given us a new appreciation of the sophistication of invertebrate immune defenses and the discovery that our antibody and T-cell-based adaptive immune system is not the only way that adaptive immunity can be generated.

Diseases and immunological deficiencies are cross-referenced to the fifth edition of the clinical companion text *Case Studies in Immunology* by Raif Geha and Fred Rosen (ISBN: 9780815341451). This text presents major topics in immunology as background to a selection of real clinical cases that serve to reinforce and extend the basic science. There are five new cases in the fifth edition, bringing the total number to 47. A marginal icon in *Janeway's Immunobiology* provides the reader with a link to the relevant Case Study, where the science is applied in a clinical setting.

The seventh edition of *Janeway's Immunobiology* includes a CD-ROM with original immunological animations based on figures in the book and videos selected from visually compelling experiments. The animations have been revised and updated for this edition, and there are five new animations covering HIV Infection, DTH Response, Viral Evasins, Innate Recognition of Pathogens, and Pathogen Receptors. All the animations and videos are accompanied by a voice-over narration read by Julie Theriot, Stanford University School of Medicine. The CD-ROM also contains the figures and tables from



the book pre-loaded into PowerPoint® presentations. There is also a JPEG archive of all these images. Instructors who adopt *Janeway's Immunobiology* for their course will have access to Garland Science Classwire™. The Classwire course management system allows instructors to build websites for their courses easily. It also serves as an online archive for instructors' resources. After registering for Classwire, instructors will be able to download all of the figures from *Immunobiology*, which are available in JPEG and PowerPoint formats, and all of the videos and animations on the CD. Instructors may also download resources from other Garland Science textbooks. Please visit the Garland Science website at [www.garlandscience.com](http://www.garlandscience.com) or e-mail [science@garland.com](mailto:science@garland.com) for additional information on Classwire.

This edition has been retitled *Janeway's Immunobiology* in memory of Charles A. Janeway who originated this textbook and was its continual inspiration until his death in 2003. Andrey Shaw, Washington University School of Medicine, St. Louis, completely revised and updated Chapter 6 on signaling; Allan Mowat, University of Glasgow, did the same for Chapter 11 on mucosal immunity; and Claudia Mauri (Chapters 12 and 14) and Michael Ehrenstein (Chapters 13 and 15), University College London, revised and updated the clinical chapters. Appendix III, Cytokines and their Receptors, was updated and reorganized by Robert Schreiber, Washington University School of Medicine, St. Louis. Joost Oppenheim, National Cancer Institute, Washington, D.C., updated Appendix IV, Chemokines and their Receptors. We owe them all a great debt of gratitude for bringing their particular expertise to the book and for the care and effort they put into these revisions.

The editors, illustrators, and publishers are the essential glue that binds this book together. We have benefited from the editorial skills of Eleanor Lawrence, the book's developmental editor from its beginning, and from the creativity and artistic talent of Matt McClements, our illustrator since the second edition. Their 'institutional memory' sustains the overall coherence of this heavily updated edition. At Garland, Mike Morales has managed the creation of compelling animations that bring important concepts to life. None of these efforts would have borne fruit without the skillful (but patient) coordination of Sigrid Masson and the insightful suggestions and continuous support of our publisher, Denise Schanck. Kenneth Murphy would like to thank Theresa Murphy and Paul, Mike, Mark and Jason for their encouragement and support. Paul Travers would like to thank Rose Zamoyska for her infinite patience and support. Mark Walport would like to thank his wife, Julia, and children, Louise, Robert, Emily, and Fiona, for their unstinting support.

We would like to give great thanks to all those people who read parts or all of the chapters of the sixth edition, as well as drafts of the seventh edition, and advised us on how to improve them. They are listed by chapter on page ix. Every effort has been made to write a book that is error-free. Nonetheless, you may find them here and there, and it would be of great benefit if you took the trouble to communicate them to us.

Kenneth Murphy

Paul Travers

Mark Walport

PowerPoint is either a registered trademark or trademark of Microsoft Corporation in the United States and/or other countries.

Classwire is a trademark of Chalkfree, Inc.

# ***Immunobiology Interactive***

The *Immunobiology Interactive* CD-ROM contains the figures and tables from the book in PowerPoint® and JPEG formats. The videos and animations play in a self-contained interface and dynamically illustrate important concepts from the book. Videos are indicated with a (V).

## **Section I**

- 2.1 Innate Recognition of Pathogens
- 2.2 Phagocytosis
- 2.3 Pathogen Recognition Receptors
- 2.4 Complement System
- 2.5 Rolling Adhesion
- 2.6 Leukocyte Rolling (V)
- 2.7 Leukocyte Extravasation

## **Section II**

- 4.1 Somatic Recombination
- 5.1 MHC Class I Processing
- 5.2 Intracellular *Listeria* Infection (V)
- 5.3 MHC Class II Processing
- 5.4 Viral Evasins

## **Section III**

- 6.1 Lipid Rafts
- 6.2 TCR Signaling
- 6.3 Activated T Cell (V)
- 6.4 MAP Kinase
- 6.5 Cytokine Signaling
- 6.6 Chemokine Signaling
- 6.7 Induction of Apoptosis
- 6.8 Apoptosis (V)
- 7.1 T-Cell Development
- 7.2 Lymph Node Development

## **Section IV**

- 8.1 T-Cell Killing
- 8.2 Dendritic Cell Migration
- 8.3 TCR-APC Interaction
- 8.4 Immunological Synapse (V)
- 8.5 T-Cell Granule Release
- 10.1 The Immune Response
- 10.2 Chemotaxis (V)
- 10.3 Lymphocyte Trafficking
- 10.4 Lymphocyte Homing (V)
- 10.5 Germinal Centers

## **Section V**

- 11.1 Antigenic Drift
- 11.2 Antigenic Shift
- 12.1 HIV Infection
- 13.1 DTH Response