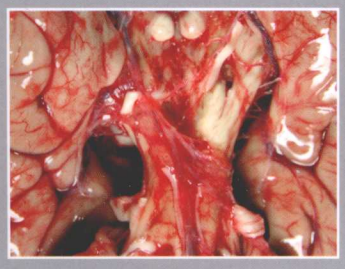
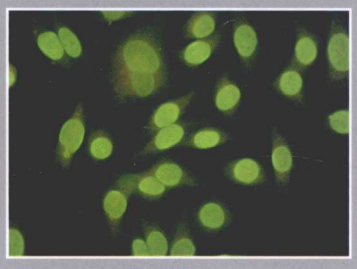
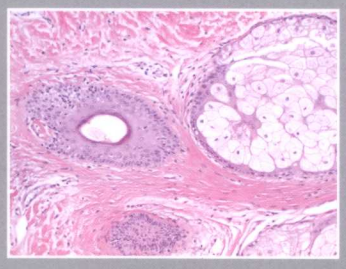
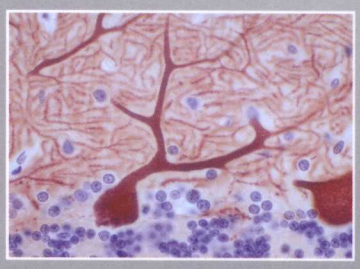
Study smart with Student Consult

KLATT
KUMAR

Robbins and Cotran REVIEW OF PATHOLOGY

FOURTH EDITION

ELSEVIER
SAUNDERS

Robbins and Cotran Review of Pathology

FOURTH EDITION

Edward C. Klatt, MD
Professor of Pathology
Department of Biomedical Sciences
Director, Biomedical Education Program
Mercer University School of Medicine
Savannah, Georgia

Vinay Kumar, MBBS, MD, FRCPath
Donald N. Pritzker Professor
Chair, Department of Pathology
Biologic Sciences Division and
Pritzker School of Medicine
The University of Chicago
Chicago, Illinois

ELSEVIER
SAUNDERS

ELSEVIER
SAUNDERS

1600 John F. Kennedy Blvd.
Ste. 1800
Philadelphia, PA 19103-2899

ROBBINS AND COTRAN REVIEW OF PATHOLOGY, FOURTH EDITION ISBN: 978-1-4557-5155-6

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

With respect to any drug or pharmaceutical products identified, readers are advised to check the most current information provided (i) on procedures featured or (ii) by the manufacturer of each product to be administered, to verify the recommended dose or formula, the method and duration of administration, and contraindications. It is the responsibility of practitioners, relying on their own experience and knowledge of their patients, to make diagnoses, to determine dosages and the best treatment for each individual patient, and to take all appropriate safety precautions.

To the fullest extent of the law, neither the publisher nor the authors, contributors, or editors assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Library of Congress Cataloging-in-Publication Data

Klatt, Edward C., 1951- , author.
Robbins and Cotran review of pathology / Edward C. Klatt, Vinay Kumar. -- Fourth edition.
p. ; cm.
Review of pathology
Complemented by: Robbins basic pathology / [edited by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. 9th ed. c2013; and Robbins and Cotran pathologic basis of disease / [edited by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. Ninth edition. [2015]
ISBN 978-1-4557-5155-6
I. Kumar, Vinay, 1944- , author. II. Robbins basic pathology. Complemented by (work): III. Robbins and Cotran pathologic basis of disease. Complemented by (work): IV. Title. V. Title: Review of pathology.
[DNLM: 1. Pathology--Examination Questions. QZ 18.2]
RB119
616.07076--dc23

2014031270

Executive Content Strategist: William R. Schmitt
Content Development Specialist: Laura Schmidt
Publishing Services Manager: Anne Altepeter
Project Manager: Louise King
Designer: Louis Forgione

Printed in Canada

Last digit is the print number: 9 8 7 6 5 4 3 2 1

NORMAL VALUES

BLOOD: PLASMA, SERUM	Reference Range
Alanine aminotransferase (ALT), serum	<30 U/L
Albumin	3.5-5.5 g/dL
Alkaline phosphatase, serum (adult)	30-130 U/L
Amylase, serum (adult)	30-110 U/L
Aspartate aminotransferase (AST), serum	<40 U/L
Bilirubin, serum (adult) total // direct	0.1-1.0 mg/dL // 0.0-0.3 mg/dL
Calcium, serum (Ca^{++})	8.4-10.2 mg/dL
Cholesterol, total // HDL	<200 mg/dL // >35 mg/dL
Creatinine, serum	0.5-1.2 mg/dL
D-dimer	<0.5 μg/mL
Electrolytes, serum	
Sodium (Na^+)	135-145 mEq/L
Potassium (K^+)	3.5-5.0 mEq/L
Chloride (Cl^-)	95-105 mEq/L
HCO_3	22-28 mEq/L
Anion gap	9-14 mEq/L
Gases, arterial blood (room air)	
pH	7.35-7.45
PCO_2	35-45 mm Hg
PO_2	80-100 mm Hg
HCO_3	22-28 mEq/L
Globulin	2.3-3.5 g/dL
Glucose, serum	70-110 mg/dL (fasting)
Haptoglobin	16-200 mg/dL
Hemoglobin A_{1c}	<6%
Iron, serum	50-160 μg/dL
Iron binding capacity, total (TIBC)	250-450 μg/dL
Lactate dehydrogenase (LDH), serum	45-90 U/L
Lipase, serum	16-63 U/L
Osmolality, serum	275-295 mOsmol/kg H_2O
Phosphorus (inorganic), serum	3.0-4.5 mg/dL
Proteins, serum, total	6.0-7.8 g/dL
Thyroid stimulating hormone (TSH)	0.5-5.0 μU/mL
Thyroxine (T4), serum	5-12 μg/dL
Triglycerides, serum	<150 mg/dL
Urea nitrogen, serum	7-20 mg/dL
Uric acid, serum	3.0-8.2 mg/dL
HEMATOLOGIC	
Erythrocyte (RBC) count	Male: 4.1-5.9 million/mm^3
	Female: 3.6-5.5 million/mm^3
Erythrocyte sedimentation rate (ESR)	Male: 0-15 mm/hr
	Female: 0-20 mm/hr
Hematocrit	Male: 41%-50%
	Female: 36%-46%
Hemoglobin, blood	Male: 13.5-16.5 g/dL
	Female: 12.0-15.0 g/dL
Leukocyte (WBC) count, total	4500-11,000/mm^3
Segmented neutrophils	54%-62%
Bands	3%-5%
Eosinophils	1%-3%
Basophils	0%-1%
Lymphocytes	25%-33%
Monocytes	3%-7%
Mean corpuscular hemoglobin (MCH)	26-34 pg/cell
Mean corpuscular volume (MCV)	80-100 μm^3
Partial thromboplastin time, activated (aPTT)	25-40 sec
Platelet count	150,000-400,000/mm^3
Prothrombin time (PT)	11-15 sec
BODY MASS INDEX (BMI)	Adult: 19-25 kg/m^2

Robbins and Cotran

Review of Pathology

To our students, for their constant challenge and stimulation

Preface

This book is designed to provide a comprehensive review of both general and organ-specific pathology through multiple choice questions with explanations of the answers. The source materials are the ninth editions of *Robbins and Cotran Pathologic Basis of Disease* (PBD9) and *Robbins Basic Pathology* (BP9), and in several chapters, *Robbins and Cotran Atlas of Pathology* (AP3). The questions in this review book follow the chapters and topics in these source materials to facilitate ongoing self-assessment as students work their way through a curriculum to gain and then apply their understanding of key concepts. This book is intended to be a useful resource for students in a variety of health science training programs.

In keeping with recommended question writing style for licensing examinations, we have included single best-answer questions, most with a clinical vignette, followed by a series of homogenous choices. This approach emphasizes an understanding of pathophysiologic mechanisms and manifestations of disease in a clinical context. We have incorporated relevant laboratory, radiologic, and physical diagnostic findings in the questions to emphasize clinicopathologic correlations. Although this adds to the extent of individual questions, the thoroughness reinforces learning, as a review should. Each answer includes a succinct explanation of why a particular choice is "correct" and the other choices are "incorrect." Each answer is referenced by page numbers to both *Robbins and Cotran Pathologic Basis of Disease* and *Robbins Basic Pathology* (both the current ninth edition and the previous eighth edition of each), and in several cases, to figures in the third edition of *Robbins and Cotran Atlas of Pathology*, to facilitate and encourage a more complete reading of topics targeted for further review. Pathology is a visually oriented discipline; hence full-color images accompany many of the questions. The illustrations are taken mainly from the Robbins textbooks, so students can reinforce their study of the figures in the texts with questions that utilize the same or similar images.

The revisions in this fourth edition reflect new topics and new understanding of disease processes reflected in the most recent editions of the Robbins textbooks. The questions are intentionally written to be fairly difficult, with the purpose of "pushing the envelope" of students' understanding of pathology. We are pushing it even further with a comprehensive final examination section that includes questions drawn from challenging topics covered in the entire book.

Mastery of this book will better prepare the student for further challenges. Many of the questions require the student to engage in a "multi-step" process: first, to interpret the information presented to arrive at a diagnosis, and then to solve a problem based on that diagnosis. This reinforces the clinical reasoning skills needed in delivery of health care. We must hasten to add that no review book is a substitute for textbooks and other course materials provided by individual instructors within the context of a curriculum. This book should be used in conjunction with thorough study of *Robbins and Cotran Pathologic Basis of Disease* and/or *Robbins Basic Pathology* and curricular materials. Finally, we hope that both students and their faculty will find this review book to be a useful adjunct to the learning of pathology.

Edward C. Klatt, MD
Vinay Kumar, MBBS, MD, FRCPath

To Our Students

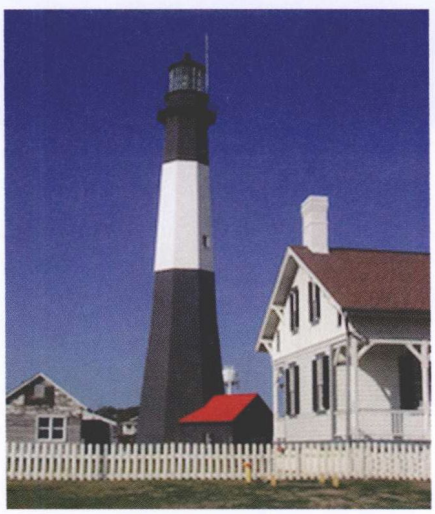
Although medical knowledge has increased exponentially over the past 100 years, the desire to learn and apply this knowledge to the service of others has not changed. The study and practice of the healing arts requires persistence more than brilliance. By continuing as a lifelong student, it is possible to become a better health practitioner with the passage of time. Use this book to find where you are on the pathway to excellence and be inspired to continue down that path. We provide a guide to light the way toward knowledge in pathology within the welcoming environment of this book.

Common mistakes made by students in answering questions result from failure to read and analyze information carefully by: (1) relying on a single finding as an exclusionary criterion, and (2) ignoring important diagnostic information. Medicine is mostly analogue, not digital, and the information you obtain is applicable across a continuum of probability. In selecting the best answer, remember these four key elements: (1) read the question thoroughly, (2) define the terms (use your vocabulary), (3) rank possible answers from common to uncommon, and (4) recognize key diagnostic information that differentiates the answers.

There are no magic formulas for academic achievement. The most important thing you can do is to spend some time each day in a learning process. Learning requires modification of synaptic interfaces at the dendritic level in the brain, and for learning to occur, there are a finite number of synaptic modifications that can be established per unit time, above which total comprehension is reduced. Increasing the rate or length of information delivery diminishes the efficiency of learning. Lack of break periods or engaging in "all nighters" presage onset of diminished performance, particularly when least desirable—during an examination. There is also decay of learning over time, with inevitable random loss of data elements. The key branch points in learning, where review with reinforcement can reduce data loss, occur at 20 to 40 minutes (transfer to intermediate memory) and at 24 to 48 hours (transfer to long-term memory) following initial learning.

Develop methods for filtering information from quality sources. We live in an age of information overload. Stay on task and avoid distractions. Identify the important data and underlying concepts. Develop a specific, personalized plan for approaching, reviewing, and preparing for assessments of your knowledge. Seek quality feedback, both positive to provide motivation for your commitment to further learning, as well as negative to focus on your rate of progress toward competency.

We hope, therefore, that this review will be useful not only in preparing for examinations but also for courses you take throughout your career. It is our sincere hope that this review book will make you a better health practitioner in your chosen career.

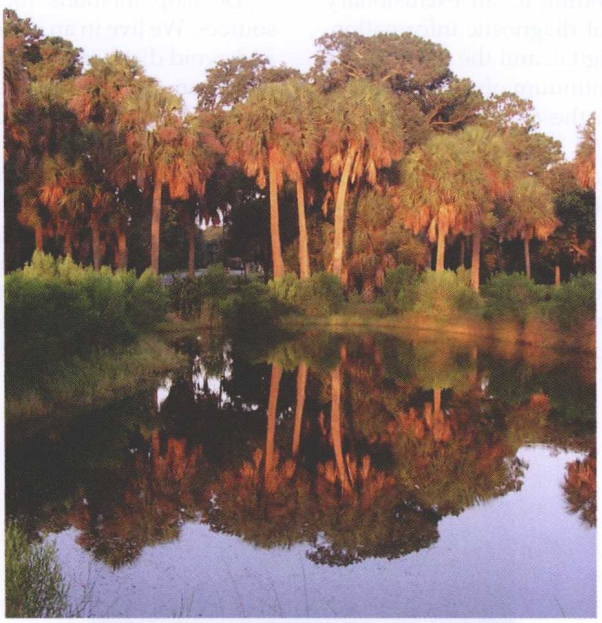


Acknowledgments

We are very grateful to Laura Schmidt, content development specialist, and William Schmitt, executive content strategist, at Elsevier, for their support of this project. Special thanks is due Louise King, project manager, for her understanding of the needs of the authors, for providing good advice, and for her willingness to accommodate multiple changes. Nhu Trinh at The University of Chicago is acknowledged for crucial secretarial support to one of us. We are grateful to our families and colleagues for graciously accepting this additional demand on our time.

The authors also are indebted to the pioneers in pathology education for the Robbins and Cotran series, starting with the founding author, Dr. Stanley Robbins, and continuing with Dr. Ramzi Cotran. These lead authors have set the standard of excellence that characterizes the series. There continue to be numerous contributing authors who have made the Robbins and Cotran series a valuable educational tool.

Edward C. Klatt
Vinay Kumar



Contents

UNIT I

General Pathology

UNIT 2

General Pathology

CHAPTER 1

The Cell as a Unit of Health and Disease

1 A study of peripheral blood smears shows that neutrophil nuclei of women have a Barr body, whereas those of men do not. The Barr body is an inactivated X chromosome. Which of the following forms of RNA is most likely to play a role in Barr body formation?

A lncRNA
C mRNA
B miRNA
D siRNA
E tRNA

2 In an experiment, a nuclear chromosomal gene is found to be actively transcribing messenger RNA (mRNA) that is transported into the cell cytoplasm. However, there is no observed protein product from translation of this mRNA. How is the silencing of this active gene's mRNA most likely to occur?

A Absence of tRNA
B Binding to miRNA
C Methylation of DNA
D Mutation of mRNA
E Upregulation of mtDNA

3 A proponent of Chilean Malbec, Syrah, and Merlot wines (all reds) touts their contribution to longevity, but this wine aficionado also controls his dietary caloric content so that his body mass index is <22. This lifestyle promotes increased insulin sensitivity and glucose utilization. He fully expects to live longer because he has read that caloric restriction prolongs life. In this man, which of the following intracellular substances will most likely mediate the effect of calorie restriction upon increased longevity?

A Caspase
B Glutathione
C Sirtuins
D Telomerase
E Ubiquitin

4 A 40-year-old woman has had chronic congestive heart failure for the past 3 years. In the past 2 months, she developed a cough productive of rust-colored sputum. A sputum cytology specimen now shows numerous hemosiderin-laden macrophages. Which of the following subcellular structures in these macrophages is most important for the accumulation of this pigment?

A Chromosome
B Endoplasmic reticulum
C Golgi apparatus
D Lysosome
E Ribosome

5 An experiment is conducted in which cells in tissue culture are subjected to high levels of ultraviolet radiant energy. Electron microscopy shows cellular damage in the form of increased cytosolic aggregates of denatured proteins. In situ hybridization reveals that protein components in these aggregates also are found in proteasomes. Which of the following substances most likely binds to the denatured proteins, targeting them for catabolism by cytosolic proteasomes?

A Adenosine monophosphate
B Calcium
C Caspase
D Granzyme B
E Hydrogen peroxide
F Ubiquitin

6 At the site of a surgical incision, endothelial cells elaborate vascular endothelial growth factor. There is sprouting with migration of endothelial cells into the wound to establish new capillaries. Which of the following intracellular proteins is most important in facilitating movement of endothelial cells?

A Actin
B Cytokeratin
C Desmin
D Lamin
E Myosin

7 In an experiment, release of epidermal growth factor into an area of denuded skin causes mitogenic stimulation of the skin epithelial cells. Which of the following proteins is most likely to be involved in transducing the mitogenic signal from the epidermal cell membrane to the nucleus?

A Cyclic AMP
B Cyclin D
C Cyclin-dependent kinase
D G proteins
E RAS proteins

8 Various soluble mediators are added to a cell culture containing epidermal cells to determine which of the mediators might be useful for promoting epidermal cell growth. When epidermal growth factor (EGF) is added, it binds to epidermal cell surface receptors, with subsequent transcription factor translocation and DNA transcription. This effect in the epidermal cells is most likely to be mediated through which of the following intracellular pathways?

A Calcium ion channel
B Cyclic AMP
C Cyclin-dependent kinase
D JAK/STAT system
E Mitogen-activated protein (MAP) kinase

9 An experiment involves factors controlling wound healing. Skin ulcerations are observed, and the factors involved in the healing process are analyzed. Which of the following factors is most likely to be effective in promoting angiogenesis?

A Basic fibroblast growth factor
B Endostatin
C Epidermal growth factor
D Interleukin-1
E Platelet-derived growth factor

10 In an experiment, surgical incisions are made in a study group of laboratory rats. Observations about the wounds are recorded over a 2-week period using various chemical mediators. Which of the following steps in the inflammatory-repair response is most likely affected by neutralization of transforming growth factor β (TGF-β)?

A Chemotaxis of lymphocytes
B Increase in vascular permeability
C Leukocyte extravasation
D Migration of epithelial cells
E Production of collagen

11 A 62-year-old man has had increasing knee pain with movement for the past 10 years. The knee joint surfaces are eroded and the joint space narrowed. There is loss of compressibility and lubrication of articular cartilaginous surfaces. Loss of which of the following extracellular matrix components has most likely occurred in this man?

A Elastin
B Fibronectin
C Hyaluronan
D Integrin
E Laminin

12 An experiment is conducted involving cellular aspects of wound healing. Components of the extracellular matrix are analyzed to determine their sites of production and their binding patterns to other tissue components. Which of the following molecules synthesized by fibroblasts can best bind to cellular integrins and extracellular collagen and attach epidermal basal cells to basement membrane?

A Dermatan sulfate
B Fibronectin
C Heparin
D Hyaluronic acid
E Procollagen

13 An experiment analyzes factors involved in the cell cycle during growth factor–induced cellular regeneration in a tissue culture. Cyclin B synthesis is induced; the cyclin B binds and activates cyclin-dependent kinase 1 (CDK1). The active kinase produced by this process is most likely to control progression in which of the following phases of the cell cycle?

A G0 to G1
B G1 to S
C S to G2
D G2 to M
E M to G1

14 In an experiment, the role of low-density lipoprotein (LDL) receptors in uptake of lipids in the liver is studied. A mouse model is created in which the LDL receptor gene is not expressed in the liver. For creating such a knockout mouse, which of the following cells would be most useful?

A Adult bone marrow mesenchymal progenitor cells
B Embryonic stem cells in culture
C Hematopoietic stem cells
D Hepatic oval cells
E Regenerating hepatocytes

15 Dermal fibroblasts are harvested from the skin biopsy specimen of an adult man. These fibroblasts are transduced with genes encoding for transcription factors including SOX2 and MYC. Under appropriate culture conditions these cells are then able to generate endodermal, mesodermal, and ectodermal cells. Into which of the following kinds of stem cell have these fibroblasts been transformed?

A Embryonic
B Lineage-committed
C Mesenchymal
D Pleuripotent

ANSWERS

1 A There are forms of noncoding RNA that play a role in gene expression. Long noncoding RNA (lncRNA) segments greater than 200 nucleotides in length can bind to chromatin to restrict access of RNA polymerase to coding segments. The X chromosome transcribes *XIST*, a lncRNA that binds to and represses X chromosome expression. However, not all genes on the "inactive" X chromosome are switched off. The RNA transcribed from nuclear DNA that directs protein synthesis through translation is mRNA. MicroRNAs (miRNAs) are noncoding RNA sequences that inhibit the translation of mRNAs. Gene-silencing RNAs (small interfering RNAs [siRNAs]) have the same function as miRNAs, but they are produced synthetically for experimental purposes. Transfer RNA (tRNA) participates in the translation of mRNA to proteins by linking to specific amino acids.

PBD9 5–6 BP9 217–218 PBD8 150–152 BP8 235–237

2 B MicroRNAs (miRNA) are encoded by about 5% of the human genome. miRNAs do not encode for proteins, but bind to and inactivate or cleave to mRNA, preventing translation of proteins by mRNA, effectively silencing gene expression without affecting the gene directly. There is abundant tRNA present in the cytoplasm that is not a rate-limiting step to translation. DNA methylation, particularly at CG dinucleotides, is a way of suppressing gene expression directly, as is seen with genomic imprinting. Mutations that occur in genes in DNA may result in reduced mRNA production or abnormal protein production, but mRNA itself is not mutated. Mitochondrial DNA (mtDNA) encodes for proteins mainly involved in oxidative phosphorylation metabolic pathways.

PBD9 4–5 BP9 217–218 BP8 137

3 C The one sure way to increase life span is calorie restriction. But why do without the things we like, only to do without them longer? Dietary excesses lead to increased morbidity with reduced quality of life, as well as mortality, from chronic diseases such as diabetes mellitus. The activity of sirtuins on histone acetylation and deacetylation may promote transcription of genes encoding for proteins that increase metabolic activity and inhibit effects of free radicals. Red wines have been shown to increase sirtuins, but don't drink too much! Moderation is the key. Glutathione promotes free radical breakdown, although chronic excessive alcohol consumption depletes hepatocyte glutathione. Caspases trigger apoptosis and cell death. Telomerases aid in promoting continued cell division, but cannot be altered by lifestyle, and turning them on is one feature of neoplasia. Ubiquitin is a peptide that is part of the ubiquitin-proteasome pathway of protein degradation seen with nutrient deficiencies, so when you eat less, be sure to eat a balanced diet.

PBD9 3–4, 68 BP9 26–27 PBD8 41, 444 BP8 28

4 D Heterophagocytosis by macrophages requires that endocytosed vacuoles fuse with lysosomes to degrade the engulfed material. With congestive heart failure, extravasation of RBCs into alveoli occurs, and pulmonary macrophages must phagocytose the RBCs, breaking down the hemoglobin and recycling the iron by hemosiderin formation. The other listed options are components that play a role in cell synthetic functions.

PBD9 10, 13 BP9 22–23 PBD8 52–53 BP8 12

5 F Heat-shock proteins provide for a variety of cellular "housekeeping" activities, including recycling and restoration of damaged proteins and removal of denatured proteins. Ubiquitin targets denatured proteins and facilitates their binding to proteasomes, which then break down the proteins to peptides. ADP increases when ATP is depleted, helping to drive anaerobic glycolysis. Cytosolic calcium levels may increase with cell injury that depletes ATP; the calcium activates phospholipases, endonucleases, and proteases, which damage the cell membranes, structural proteins, and mitochondria. Caspases are enzymes that facilitate apoptosis. Granzyme B is released from cytotoxic T lymphocytes and triggers apoptosis. Hydrogen peroxide is one of the activated oxygen species generated under conditions of cellular ischemia, producing nonspecific damage to cellular structures, particularly membranes.

PBD9 13–14 BP9 21–22 PBD8 37–38 BP8 22

6 A Actin is a microfilament involved with cell movement. The other possibilities listed in B to D are intermediate filaments, which are larger than actin but smaller than myosin (a thick filament interdigitating with actin, required for muscle movement). Cytokeratins form cytoskeletal elements of epithelial cells. Desmin forms the scaffold in muscle cells on which actin and myosin contract. Lamin is associated with the nuclear membrane.

PBD9 10–11 PBD8 50

7 E RAS proteins transduce signals from growth factor receptors, such as epidermal growth factor, that have intrinsic tyrosine kinase activity. G proteins perform a similar function for G protein–linked, seven-transmembrane receptors. Cyclic AMP is an effector in the G protein signaling pathway. Cyclins and cyclin-dependent kinases regulate the cell cycle in the nucleus.

PBD9 17 BP9 179 PBD8 90–92 BP8 64, 66

8 E The MAP kinase cascade is involved in signaling from activation via cell surface receptors for growth factors. This pathway is particularly important for signaling of EGF and fibroblast growth factor. Ligand binding, such as occurs with acetylcholine at a nerve-muscle junction, alters the conformation of ion channel receptors to allow flow of specific ions such as calcium into the cell, changing the electric potential across the cell membrane. Cyclic AMP is a second messenger that is typically activated via ligand binding to receptors with seven transmembrane segments that associate with GTP-hydrolyzing proteins; chemokine receptors