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DeVita, Hellman, and Rosenberg's

Cancer

Principles & Practice of Oncology

REVIEW

3rd edition

Ramaswamy Govindan

Wolters Kluwer Health | Lippincott Williams & Wilkins

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Cancer

Principles & Practice of Oncology

Review

3rd edition

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TO
MICHAEL C. PERRY
A GREAT PHYSICIAN, MENTOR, COLLEAGUE, AND ABOVE ALL—A FINE HUMAN BEING.

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PREFACE

The past decade has witnessed numerous advances in cancer therapy. Even since the publication of the previous edition of *Cancer: Principles and Practice of Oncology (PPO)*, or simply known as the "DeVita book," several new drugs have been approved for cancer therapy. Cancer Genome Sequencing projects are going ahead full steam. Molecular mechanisms that underline the course of several cancer types and responses to specific therapies are understood better than before. This companion review book, now in its third edition, is an attempt to cull out the key learning points from the massive tome of "the DeVita book" that captures all these advances in a timely manner. While these review books are often seen as "study-aids" for last minute cramming for the board examinations, we hope this book would serve to highlight key points from each chapter of *PPO*. Each chapter in the review book corresponds to one or more chapters in the main textbook just as they were in the first two editions. We hope you find this book useful and informative. Please do not hesitate to contact me with comments, criticisms, and suggestions. You can reach me by email at rgovinda@dom.wustl.edu.

Ramaswamy Govindan

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At the outset, I want to thank the contributors for their diligence, time, and patience. I thank my dear colleagues Dr. Saiama Waqar, Dr. Janakiraman Subramanian, and Dr. Daniel Morgensztern for their hard work, dedication, and commitment to make this project successful. As assistant editors, they worked tirelessly to procure and edit the chapters to keep our production schedule more or less on time. Special thanks to Dr. Waqar who took additional responsibilities. As always, Jonathan Pine from Wolters Kluwer supported this idea and shepherded this to a reality by keeping a constant pressure on all of us. Ryan Shaw from Wolters Kluwer kept the project moving along very well. Needless to say, these projects take a sizeable amount of time away from the family. I will always be grateful to my wife Prabha and my two very adorable children, Ashwin and Akshay.

Finally I want to say a few words about my long-term friend, mentor and guide Dr. Michael C Perry. Mike passed away a few months ago. Mike was a remarkable man—intelligent, thoughtful, hard-working, creative and yet humble and gentle. He knew how to guide individuals early in their career better than anyone I know. I learnt a lot from him even though we never worked at the same institution. I would miss him very much. It is my honor to dedicate this edition to Mike. The world will be a better place if only we had more individuals like Mike.

Ramaswamy Govindan

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CHAPTER 1 MOLECULAR BIOLOGY OF CANCER ■ PART 1

ROBERT A. KRATZKE

DIRECTIONS Each of the numbered items below is followed by lettered answers. Select the ONE lettered answer that is BEST in each case unless instructed otherwise.

QUESTIONS

Question 1.1. **Completion of the Human Genome Project has revealed that human cells have a repertoire of genes of which approximate number?**

A. 2500 genes
B. 25,000 genes
C. 250,000 genes
D. 2,500,000 genes

Question 1.2. **One of the reasons to use cancer cell culture experiments in preclinical studies of cancers is:**

A. Allows evaluation of cancer cell interaction with the tumor microenvironment.
B. Cell cultures are amenable to easily manipulated experimental techniques.
C. Adaptation of cancer cells to growth in culture corresponds exactly to cancer cell growth in vivo.
D. Allows evaluation of cancer cell interaction with the native immune system.

Question 1.3. **Which of the following is false with regard to genetic mutations in cancer?**

A. Gain-of-function mutations (oncogenes) are generally dominant at the cellular level.
B. Loss-of-functions mutations (tumor suppressor genes) are generally recessive at the cellular level.
C. One percent of the estimated total number of genes may contribute to some form of cancer.
D. Ninety percent of germ line mutations in familial cancer syndromes are in tumor suppressor genes.

Corresponding Chapters in *Cancer: Principles & Practice of Oncology*, Ninth Edition: 1 (The Cancer Genome), 2 (Mechanisms of Genomic Instability), 3 (Epigenetics of Cancer), 4 (Telomeres, Telomerase, and Cancer), and 5 (Cell Signaling Growth Factors and Their Receptors).

Question 1.4. **Which of the following proteins has inhibitory activity in the cell cycle?**

A. Cyclin D1
B. E2F
C. p16INK4a
D. Cyclin-dependent kinase 4

Question 1.5. **All of the following contribute to suppression of cancer progression, EXCEPT:**

A. Autophagy
B. Apoptosis
C. Senescence
D. Angiogenesis

Question 1.6. **Which of the following does successful invasion and metastasis NOT depend on?**

A. Senescence
B. Angiogenesis
C. Evasion of apoptosis
D. Self-sufficiency in growth signals

Question 1.7. **Which of the following best describes the term "protooncogene"?**

A. A normal cellular gene that has been transduced by a retrovirus that is then mutated following viral replication.
B. A homologue of a known oncogenic element identified in prehistoric specimens.
C. A transforming viral gene that can cause malignant transformation in fibroblasts in vitro.
D. The first oncogene discovered to be associated with human cancer.
E. A viral oncogene that, following infection, is the direct causative agent of human cancer.

Question 1.8. **The DNA damage checkpoints are located in which phase of the cell cycle?**

A. G1/S
B. S/G2
C. M
D. All of the above

Question 1.9. **Which of the following is a potential flaw in microarray studies?**

A. Inadequate controls
B. Biased estimation of prediction accuracy
C. Correlation between clusters and clinical outcome
D. All of the above

Question 1.10. **Which of the following about miRNAs is false?**

A. Are too small to be active inside a cell
B. Consist of RNA 19 to 24 nucleotides in length
C. Can be evaluated in array format as part of clinical studies
D. May downregulate gene expression and protein translation

Question 1.11. **The proteome is which of the following:**

A. The set of all expressed gene products at a given time
B. The proteins expressed preferentially in malignant cells
C. The set of all proteins potentially expressed by the genome
D. The set of protonated peptides subject to matrix-assisted laser desorption ionization-time of flight analysis

Question 1.12. **Information obtained for molecular profiling using gene arrays and proteomics includes the following, EXCEPT:**

A. Gene arrays can predict protein–protein interactions.
B. Protein levels and protein function do not correspond directly with gene transcript levels.
C. Polymerase chain reaction can be used to amplify biopsy material for use in gene arrays, whereas no signal amplification technology is standard in protein arrays.
D. Proteomics can be used to investigate posttranslationally modified proteins.

Question 1.13. **All is true about the peptidome, EXCEPT:**

A. Consists of fragments of larger proteins.
B. Included peptides must be less than 1000 daltons.
C. May be amplified in the circulation.
D. Many of the peptide fragments bind high-concentration blood proteins such as albumin.

Question 1.14. **Which of the following statements regarding microsatellite instability is correct?**

A. Hereditary nonpolyposis colon cancer syndrome (HNPCC) is associated with a 25% lifetime risk of developing colorectal cancer.
B. Approximately 10% of all cases of colorectal cancer are associated with HNPCC.
C. Microsatellite instability is associated with resistance to 5-fluorouracil chemotherapy.
D. None of the above.

Question 1.15. **Which of the following drugs is NOT a histone deacetylase inhibitor?**

A. Suberoylanilide hydroxamic acid (SAHA)
B. 5-Azacytidine
C. Depsipeptide
D. A and C

Question 1.16. **The presence of mutations in p53 has been associated with which of the following properties on cells:**

A. Loss of the G2 checkpoint following treatment with DNA-damaging agents
B. Enhanced capacity to undergo apoptosis following exposure to radiation
C. Increased capacity for DNA amplification
D. A and C

Question 1.17. **Which of the following is an example of gene amplification found in cancer?**

A. N-myc amplification in neuroblastoma
B. C-myc amplification in small cell lung cancer
C. Her2/neu amplification in breast cancer
D. All of the above

Question 1.18. **Which of the following is true regarding microsatellite instability in colon cancer?**

A. Approximately 15% of patients with hereditary nonpolyposis coli have mutations in MLH1 or MSH2.
B. There is potential resistance to 5-fluorouracil.
C. It has a less favorable prognosis.
D. Evidence is in favor of it occurring only late in sporadic colon cancer cases.

Question 1.19. **Which of the following is false about excision repair mechanisms?**

A. Reduced expression of ERCC1 in nonsmall cell lung cancer is associated with response to cisplatin.
B. There are two nucleotide excision repair pathways.
C. Base excision repair is involved in response to damage from chemicals and radiographs.
D. Numerous abnormalities in base excision repair machinery in multiple inherited cancers have been described.

Question 1.20. **ATR/CHK1 signaling is associated with all of the following, EXCEPT:**

A. Bone marrow failure
B. Predisposition to squamous cell carcinoma
C. Predisposition to acute leukemias
D. Decreased sensitivity to cisplatin

Question 1.21. **Which of the following syndromes are associated with abnormalities in the double-strand repair?**

A. Xeroderma pigmentosa
B. Fanconi anemia
C. Lynch syndrome
D. Bloom syndrome