the biology of
CANCER
SECOND EDITION
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11.12 Human cells are constructed to be highly resistant to immortalization and transformation.

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11.16 Inflammation-dependent tumor promotion operates through defined signaling pathways.

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11.18 Synopsis and prospects

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12.1 Tissues are organized to minimize the progressive accumulation of mutations.

12.2 Stem cells may or may not be targets of the mutagenesis that leads to cancer.

12.3 Apoptosis, drug pumps, and DNA replication mechanisms offer tissues a way to minimize the accumulation of mutant stem cells.

12.4 Cell genomes are threatened by errors made during DNA replication.

12.5 Cell genomes are under constant attack from endogenous biochemical processes.

12.6 Cell genomes are under occasional attack from exogenous mutagens and their metabolites.

12.7 Cells deploy a variety of defenses to protect DNA molecules from attack by mutagens.

12.8 Repair enzymes fix DNA that has been altered by mutagens.

12.9 Inherited defects in nucleotide-excision repair, base-excision repair, and mismatch repair lead to specific cancer susceptibility syndromes.

12.10 A variety of other DNA repair defects confer increased cancer susceptibility through poorly understood mechanisms.

12.11 The karyotype of cancer cells is often changed through alterations in chromosome structure.

12.12 The karyotype of cancer cells is often changed through alterations in chromosome number.

12.13 Synopsis and prospects

Chapter 13 Dialogue Replaces Monologue: Heterotypic Interactions and the Biology of Angiogenesis

13.1 Normal and neoplastic epithelial tissues are formed from interdependent cell types.

13.2 The cells forming cancer cell lines develop without heterotypic interactions and deviate from the behavior of cells within human tumors.

13.3 Tumors resemble wounded tissues that do not heal.

13.4 Experiments directly demonstrate that stromal cells are active contributors to tumorigenesis.

13.5 Macrophages and myeloid cells play important roles in activating the tumor-associated stroma.

13.6 Endothelial cells and the vessels that they form ensure tumors adequate access to the circulation.

13.7 Tripping the angiogenic switch is essential for tumor expansion.

13.8 The angiogenic switch initiates a highly complex process.

13.9 Angiogenesis is normally suppressed by physiologic inhibitors.

13.10 Anti-angiogenesis therapies can be employed to treat cancer.
15.1 The immune system functions to destroy foreign invaders and abnormal cells in the body's tissues.

15.2 The adaptive immune response leads to antibody production.

15.3 Another adaptive immune response leads to the formation of cytotoxic cells.

15.4 The innate immune response does not require prior sensitization.

15.5 The need to distinguish self from non-self results in immune tolerance.

15.6 Regulatory T cells are able to suppress major components of the adaptive immune response.

15.7 The immunosurveillance theory is born and then suffers major setbacks.

15.8 Use of genetically altered mice leads to a resurrection of the immunosurveillance theory.

15.9 The human immune system plays a critical role in warding off various types of human cancer.

15.10 Subtle differences between normal and neoplastic tissues may allow the immune system to distinguish between them.

15.11 Tumor transplantation antigens often prove potent immune responses.

15.12 Tumor-associated transplantation antigens may also evoke anti-tumor immunity.

15.13 Cancer cells can evade immune detection by suppressing cell-surface display of tumor antigens.

15.14 Cancer cells protect themselves from destruction by NK cells and macrophages.

15.15 Tumor cells launch counterattacks on immunocytes.

15.16 Cancer cells become intrinsically resistant to various forms of killing used by the immune system.

15.17 Cancer cells attract regulatory T cells to fend off attacks by other lymphocytes.

15.18 Passive immunization with monoclonal antibodies can be used to kill breast cancer cells.

15.19 Passive immunization with antibody can also be used to treat B-cell tumors.

15.20 Transfer of foreign immunocytes can lead to cures of certain hematopoietic malignancies.

15.21 Patients' immune systems can be mobilized to attack their tumors.

15.22 Synopsis and prospects.

16.1 The development and clinical use of effective therapies will depend on accurate diagnosis of disease.

16.2 Surgery, radiotherapy, and chemotherapy are the major pillars on which current cancer therapies rest.

16.3 Differentiation, apoptosis, and cell cycle checkpoints can be exploited to kill cancer cells.

16.4 Functional considerations dictate that only a subset of the defective proteins in cancer cells are attractive targets for drug development.

16.5 The biochemistry of proteins also determines whether they are attractive targets for intervention.

16.6 Pharmaceutical chemists can generate and explore the biochemical properties of a wide array of potential drugs.

16.7 Drug candidates must be tested on cell models as an initial measurement of their utility in whole organisms.

16.8 Studies of a drug's action in laboratory animals are an essential part of pre-clinical testing.

16.9 Promising candidate drugs are subjected to rigorous clinical tests in Phase I trials in humans.

16.10 Phase II and III trials provide credible indications of clinical efficacy.

16.11 Tumors often develop resistance to initially effective therapy.

16.12 Gleevec paved the way for the development of many other highly targeted compounds.

16.13 EGFR receptor antagonists may be useful for treating a wide variety of tumor types.

16.14 Proteasome inhibitors yield unexpected therapeutic benefit.

16.15 A sheep teratogen may be useful as a highly potent anti-cancer drug.

16.16 mTOR, a master regulator of cell physiology, represents an attractive target for anti-cancer therapy.

16.17 B-Raf discoveries have led to inroads into the melanoma problem.

16.18 Synopsis and prospects: challenges and opportunities on the road ahead.