

Contents

Preface	xi
About the Companion Website	xiii
1 Cancer Epidemiology	1
1.1 Cancer Incidence and Mortality	1
1.2 Childhood Cancer	4
1.3 Global Epidemiology	5
1.4 Cancer Survival Rates	8
1.5 Summary and Conclusions	12
Further Reading	12
2 Cancer Histopathology	13
2.1 Cancer Morphology, Phenotype, and Nomenclature	14
2.2 Apoptosis	16
2.3 Necrosis	22
2.4 Autophagy and Others	23
2.5 Summary and Conclusions	24
Further Reading	25
3 Carcinogenesis	27
3.1 Initiation	27
3.2 Promotion	29
3.3 Progression and Environmental Carcinogenesis	30
3.4 Cell Cycle	31
3.5 Summary and Conclusions	33
Further Reading	33
4 Molecular Biology of Cancer	35
4.1 Oncogenes: Disruptors and Instigators	36
4.2 Cellular Oncogenes	39
4.3 Viral Oncogenes	41

4.4	Altered Oncogenic Products	42
4.5	Biological Carcinogens.....	44
4.6	Tumor Suppressor Genes.....	46
4.7	Familial Cancers and Cancer Syndromes.....	50
4.8	Summary and Conclusions.....	52
	Further Reading	52
5	Cancer Metastasis	53
5.1	Detachment from the Primary Tumor	54
5.2	Migration of Cancer Cells from Primary Tumor	55
5.3	Intravasation of Tumor Cells into Vessels.....	57
5.4	Metastatic Transport.....	60
5.5	Extravasation	61
5.6	Growth of the Metastatic Tumor Mass.....	63
	5.6.1 Cancer Dormancy	63
	5.6.2 Extracellular Matrix of the Tumor Microenvironment ...	64
	5.6.3 Seed and Soil	65
5.7	Summary and Conclusions.....	66
	Further Reading	67
6	Health Professionals and Cancer Treatment.....	69
6.1	Pathology	69
6.2	Radiology	70
6.3	Biopsies.....	72
6.4	Surgical Treatment	73
6.5	Oncology Pharmacy	74
6.6	Oncology Nursing	75
6.7	Artificial Intelligence and Healthcare	75
6.8	Summary and Conclusions.....	75
	Further Reading	76
7	Principles of Cancer Chemotherapy.....	77
7.1	Staging, Treatment, and Monitoring.....	77
7.2	General Types of Chemotherapy.....	79

7.3	Biomarker Uses and Limitations	82
7.4	Pharmacogenetics, Pharmacogenomics, Pharmacokinetics, Pharmacodynamics, and Personalized Medicine.....	86
7.5	Summary and Conclusions.....	87
	Further Reading	88
8	Cytotoxic Compounds	89
8.1	Alkylating Agents	89
8.2	Intercalating Agents	94
8.3	Topoisomerase Blockers.....	104
8.4	Tubulin Disruptors	109
8.5	Summary and Conclusions.....	113
	Further Reading	113
9	Antimetabolites and Hormonal Blockers	115
9.1	Nucleic Acid Analogs.....	115
9.2	Folate Analogs	118
9.3	Amino Acid Blockers	120
9.4	Hormone Modulators.....	121
9.5	Estrogen Antagonists.....	124
9.6	Aromatase Inhibitors	127
9.7	Antiandrogens.....	127
9.8	Endocrine Therapy.....	128
9.9	Summary and Conclusions.....	129
	Further Reading	130
10	Cancer Research	131
10.1	Gel Electrophoresis Methods	131
10.2	Polymerase Chain Reaction	132
10.3	Molecular Cloning	133
10.4	Enzyme-Linked Immunosorbent Assay, Immunohistochemistry, and Immunofluorescence.....	134
10.5	Mass Spectroscopy and Proteomics	135
10.6	Genomics, Transcriptomics, and Metabolomics	136

10.7	Microarrays	137
10.8	Cell Culture and Exogenous Expression Strategies	138
10.9	Protein Expression and Targeting	141
10.9.1	Targeting RNA	143
10.9.2	Targeting the Genome	145
10.10	Animal Models	147
10.11	Delivery Systems	149
10.12	Resources	151
10.13	Summary and Conclusions	152
	Further Reading	153
11	Clinical Trials	155
11.1	Clinical Trial Design	158
11.2	Clinical Trials Governance and Quality Assurance	161
11.3	Clinical Trial Ethics	166
11.4	Clinical Trial Study Schema	168
11.5	Measurement of Clinical Endpoints, Response, and Outcomes	169
11.6	Local and National Organization of Clinical Trials	169
11.7	Summary and Conclusions	173
	Further Reading	174
12	Tumor Hypoxia	175
12.1	Effects of Hypoxia on Chemotherapy	177
12.2	Energy Reprogramming and the Warburg Effect	178
12.3	Hypoxia-Inducible Factor	181
12.4	Lactate Dehydrogenase and Carbonic Anhydrase	183
12.5	Hypoxic Vascularization and Imaging	185
12.6	Bioreductive Drugs	189
12.7	Summary and Conclusions	192
	Further Reading	192
13	Antiangiogenic and Antivascular Agents	193
13.1	History of Antiangiogenic Chemotherapy	193
13.2	Endogenous Integrin Blockers	195

13.3	Matrix Metalloproteinase Inhibitors	197
13.4	Synthetic Integrin Blockers	202
13.5	The Return of Thalidomide.....	204
13.6	Vascular Disrupting Agents	205
13.7	Antiangiogenic Antibodies	207
13.8	Summary and Conclusions.....	210
	Further Reading	210
14	Protein Kinase and Ras Blockers	211
14.1	Signal Transduction.....	211
14.2	Receptor Tyrosine Kinase Blockers.....	214
14.3	Nonreceptor Tyrosine Kinase Blockers.....	216
14.4	Receptor Serine/Threonine Kinase Blockers	220
14.5	Nonreceptor Serine/Threonine and Multiple Kinase Blockers... ..	223
14.6	Ras and PLC Blockers	226
14.7	Summary and Conclusions.....	228
	Further Reading	228
15	Modulating Global Gene and Protein Expression.....	231
15.1	Stress Protein Inhibitors	231
15.2	Proteasome Inhibitors	234
15.3	Ubiquitin Ligase Inhibitors.....	237
15.4	Histone Deacetylase Inhibitors	238
15.5	DNA Methylation Inhibitors.....	241
15.6	Summary and Conclusions.....	242
	Further Reading	243
16	Stem Cells – Telomerase, Wnt, Hedgehog, Notch, and Galectins	245
16.1	Telomerase Blockers.....	246
16.2	Wnt Blockers.....	250
16.3	Hedgehog Blockers	252
16.4	Notch Blockers.....	254
16.5	Galectin Blockers	257

16.6	Summary and Conclusions.....	258
	Further Reading	258
17	Immunotherapy and Oncolytic Viruses.....	261
17.1	Immunization.....	264
17.2	Immune Checkpoint Blockers.....	266
17.3	Chimeric Antigen Receptor T-Cells.....	268
17.4	Oncolytic Viruses.....	270
17.5	Summary and Conclusions.....	275
	Further Reading	275
18	Pharmaceutical Problems in Cancer Chemotherapy.....	277
18.1	Manifestation of Toxicity.....	277
18.2	Regimen-Related Toxicity.....	282
18.3	Secondary Malignancies	283
18.4	Drug Resistance	284
	18.4.1 Multiple Drug Resistance.....	284
	18.4.2 Enhanced DNA Repair.....	286
	18.4.3 Alteration of Drug Targets	287
18.5	Pharmaceutical Complications.....	287
	18.5.1 Extravasation.....	288
	18.5.2 Local and National Extravasation Guidelines.....	290
18.6	Phlebitis and Venous Irritation.....	290
18.7	Health and Safety.....	291
18.8	National Guidance on the Safe Administration of Intrathecal Chemotherapy.....	291
	Further Reading	292
	Index.....	295