
Contents

Part I General Principles

1 Principles of Molecular Cancer Treatment	3
References.....	5

Part II Molecular Basis of Anti-Cancer Drug Treatment

2 DNA Damaging Drugs	9
2.1 Alkylating Agents.....	9
2.1.1 Nitrogen Mustards	10
2.1.2 Nitrosoureas	23
2.1.3 Triazenes and Hydrazines	26
2.1.4 Ethylene Imines and Methylmelamines.....	30
2.1.5 Benzoquinone Containing Alkylating Agents.....	32
2.1.6 Alkyl Sulfonates	33
2.1.7 Illudins	35
2.1.8 Platinum Drugs.....	36
2.1.9 Others.....	43
2.2 Antibiotics.....	47
2.2.1 Cyclopropylpyrroloindole Antibiotics.....	47
2.2.2 Minor Groove DNA Binding Antibiotics.....	49
2.2.3 Aminoquinone Antibiotics.....	53
2.2.4 Polycyclic Aromatic Antibiotics	55
2.2.5 Eneidyne Antibiotics.....	66
2.2.6 Others	70
2.3 Topoisomerase Inhibitors	72
2.3.1 Topoisomerase 1 Inhibitors	72
2.3.2 Topoisomerase 2 Inhibitors.....	79
2.4 Anti-Metabolites.....	84
2.4.1 Anti-Folates.....	85
2.4.2 Anti-Pyrimidines.....	95
2.4.3 Anti-Purines	102
References.....	109
3 Drugs that Suppress Proliferation	113
3.1 Anti-Mitotic Agents.....	113
3.1.1 Taxanes	113
3.1.2 Epothilones.....	117
3.1.3 Other Microtubule Stabilizers	119
3.1.4 Alkaloids	121
3.1.5 Benzoylphenylureas	125

3.1.6	Other Microtubule Destabilizers.....	125
3.1.7	Anti-Mitotic Peptide Drugs	128
3.1.8	Kinesin Spindle Protein Inactivating Drugs.....	128
3.2	Differentiating Agents.....	132
3.2.1	Retinoids	132
3.2.2	Vitamin D	136
3.2.3	COX Inhibitors	137
3.2.4	HDAC Inhibitors	140
3.2.5	DNA Methyl Transferase Inhibitors	146
3.2.6	PPAR Activators.....	150
3.3	Inducers of Apoptosis.....	150
3.3.1	Modulators of Mitochondrial Function.....	151
3.3.2	BCL-2 Family Inhibitors.....	153
3.3.3	P53 Activators.....	154
3.3.4	Caspase Pathway Activators	156
3.3.5	Others.....	156
	References.....	161
4	Molecular Inhibitors of Growth Signals	163
4.1	Small Molecule Kinase Inhibitors	163
4.1.1	EGFR Family Inhibitors	165
4.1.2	ABL Inhibitors.....	172
4.1.3	RAS Pathway Inhibitors.....	179
4.1.4	Phosphoinositide 3-Kinase Pathway Inhibitors	186
4.1.5	FLT3 Inhibitors.....	191
4.1.6	Cell Cycle Kinase Inhibitors	195
4.1.7	Others	205
4.2	Inhibitors of Oncogene Functions.....	213
4.2.1	Farnesyl Transferase Inhibitors.....	213
4.2.2	Inhibitors of Protein Turnover	214
4.2.3	Others	225
4.3	Antibodies.....	228
4.3.1	EGFR Family Targets.....	231
4.3.2	Lymphocytic Surface Targets	234
4.3.3	Various Targets.....	236
4.3.4	Antibody Mimetics.....	241
	References.....	241
5	Anti-Metastasis Therapy	243
5.1	Integrin Inhibitors.....	243
5.1.1	Peptide Inhibitors.....	243
5.1.2	Antibodies	244
5.1.3	Others	245
5.2	CD44 Inhibitors.....	245
5.3	MMP Inhibitors	246
5.3.1	Hydroxamates	246
5.3.2	Thiol- or Sulfonamide- Based MMP Inhibitors.....	250
5.3.3	Tetracyclines	251
5.3.4	Pyrimidine-2,4,6-triones	251
5.3.5	Others.....	251
5.4	Chemokine Receptor Inhibitors	252
5.5	TGF- β Inhibitors.....	253
5.6	Bone Targeting Agents.....	255
5.6.1	Bisphosphonates.....	255

5.6.2	Antibodies.....	257
5.6.3	Others.....	258
5.7	Others.....	258
	References.....	259
6	Induction of Senescence.....	261
6.1	Telomerase Inhibitors	261
6.1.1	Non-Nucleoside Telomerase Inhibitors	261
6.1.2	Antisense Telomerase Inhibitors	261
6.1.3	G-quadruplex Ligands	262
	References.....	262
7	Combination Chemotherapy.....	263
7.1	Treatment of Hematologic Malignancies	263
7.1.1	Vincristine and Prednisone Based Regimens	263
7.1.2	Doxorubicin Based Regimens	266
7.1.3	Others	267
7.2	Treatment of Solid Tumors.....	269
7.2.1	Cyclophosphamide Based Regimens	269
7.2.2	Epirubicin Based Treatments	271
7.2.3	Platinum Based Chemotherapy	271
7.2.4	Others.....	272
7.3	Emerging Combination Chemotherapies	277
	References.....	278
Part III Emerging and Alternative Treatment Modalities		
8	Gene Therapy	283
8.1	Gene Silencing.....	283
8.1.1	Antisense	283
8.1.2	Ribozymes	287
8.1.3	RNA Interference	287
8.2	Suicide Genes	288
8.3	Oncolytic Viruses.....	288
8.3.1	Engineered Oncolytic Viruses	288
8.3.2	Immunostimulatory Oncolytic Viruses	289
8.3.3	Wild-Type Oncolytic Viruses.....	290
8.4	Gene Delivery.....	291
8.4.1	Viral Gene Delivery Systems.....	291
8.4.2	Non-Viral Gene Delivery Systems	293
8.5	Other Strategies	295
	References.....	295
9	Drugs with Diverse Modes of Action	297
	References.....	300
Part IV Molecular Targeting of Tumor-Host Interactions		
10	Hormone Therapy.....	303
10.1	Anti-estrogens	304
10.1.1	Selective Estrogen Receptor Modulators	304
10.1.2	Progesterone Derivatives	308
10.1.3	Aromatase and Sulfatase Inhibitors	310
10.1.4	Others	314
10.2	Anti-androgens	314
10.2.1	Steroidal Anti-androgens.....	315
10.2.2	Non-steroidal Anti-androgens	316

10.2.3 Dihydrotestosterone Reductase Inhibitors.....	318
10.2.4 Peptide Modulators.....	320
10.2.5 Others.....	324
10.3 Corticosteroids.....	324
References.....	332
11 Immunotherapy.....	333
11.1 Immunotoxins	333
11.2 Engineered Antibodies	336
11.3 Antigen Based Immunotherapy.....	339
11.4 Cytokine Based Immunotherapy.....	344
11.5 Immune Response Modifiers.....	347
11.6 Autologous Therapies	349
11.7 Other Regimens.....	350
References.....	351
12 Anti-Angiogenesis.....	353
12.1 VEGF Antagonists.....	353
12.1.1 VEGF Receptor Blockers	353
12.1.2 VEGF Inhibitors	360
12.2 FGF-2 Antagonists.....	361
12.3 Thalidomide Related Drugs	363
12.4 Integrin blockers.....	366
12.5 Endostatin and Angiostatin.....	366
12.6 Others.....	367
References.....	370
Part V Anti-Cancer Drug Pharmacokinetics	
13 Drug Delivery and Drug Transport.....	375
13.1 Targeting with Drug Conjugates	376
13.2 Radio-Targeting	377
13.3 Nano-Particles.....	380
13.4 Solubilizers.....	384
13.5 Various	385
References.....	387
14 Drug Metabolism	389
14.1 CYP450	389
14.2 Flavin Monooxygenases	391
14.3 GST	391
14.4 Others.....	392
References.....	393
15 Prodrug Activation.....	395
15.1 Photodynamic Therapy.....	395
15.2 Radio-Sensitization.....	400
References.....	406
16 Drug Resistance.....	407
16.1 Increased Efflux.....	409
16.1.1 ABC Transporters	410
16.2 Decreased Uptake.....	414
16.3 Anti-Apoptosis.....	415
16.4 Mutations in the Drug Target.....	417
16.5 Altered Repair of Drug Induced Damage.....	418
16.6 Other Mechanisms.....	420
References.....	420

Part VI Supportive Therapy

17 Protection from Adverse Effects	425
17.1 Anti-Emetics.....	425
17.2 Protection from Anemia	427
17.3 Immune Recovery.....	430
17.4 Cardiovascular Protection.....	431
17.5 Anti-Oxidants.....	434
17.6 Anti-Cachexia Drugs	436
17.7 Protection from Hepatotoxicity	436
17.8 Protection from Urinary Toxicity.....	437
17.9 Protection of the Gastrointestinal Tract.....	438
17.10 Treatment of Dermatologic Reactions to Chemotherapy.....	440
17.11 Electrolyte Balance.....	441
17.12 Reproductive Protection.....	442
17.13 Others.....	442
References.....	443
18 Pain Management	445
18.1 Non-Steroidal Drugs.....	445
18.2 Opioid Drugs	446
18.2.1 Weak Opioids.....	447
18.2.2 Strong Opioids.....	448
18.3 Others.....	449
References.....	450
19 Preventive Treatment	451
19.1 Vaccines.....	451
19.2 Chemoprevention	451
19.2.1 Nutrition	451
19.2.2 Nutrition Supplements.....	452
19.2.3 Others.....	453
References.....	453
Index	455

Molecular Therapies of Cancer

Weber, G.F.

2015, XV, 488 p. 120 illus., 86 illus. in color., Hardcover

ISBN: 978-3-319-13277-8