

Contents



| | |
|---|----------|
| Contributors | ix |
| Reviewers | xii |
| Acknowledgments | xiii |
| Introduction | xiv |
| Abbreviations | xvi |
| 1 Preclinical Drug Development: Translating Basic Research into Clinical Work | 1 |
| Introduction | 1 |
| In-vitro Evaluation of New Anti-cancer Agents | 2 |
| Studies in Animal Models | 4 |
| Companion Diagnostics Development | 6 |
| Summary | 7 |
| Further Reading | 8 |
| 2 Pharmacokinetics and Pharmacodynamics: Main Concepts and Clinical Applications | 9 |
| Introduction | 9 |
| Pharmacokinetics | 11 |
| Pharmacodynamics | 24 |
| Summary and Conclusions | 29 |
| Further Reading | 29 |

| | | |
|----------|---|-----|
| 3 | Alkylating Agents | 31 |
| | Introduction | 31 |
| | Clinical Pharmacokinetics | 34 |
| | Therapeutic Uses | 34 |
| | Toxicities | 35 |
| | Drug Resistance | 41 |
| | Further Reading | 43 |
| 4 | Platinum Agents | 44 |
| | Introduction | 44 |
| | Clinical Pharmacology | 45 |
| | Therapeutic Uses | 47 |
| | Toxicities | 50 |
| | Drug Resistance | 51 |
| | Further Reading | 52 |
| 5 | Antimetabolites | 53 |
| | Antifolates | 53 |
| | Pyrimidine Analogs | 58 |
| | Purine Analogs | 63 |
| | Further Reading | 68 |
| 6 | Topoisomerase-I and -II Inhibitors | 69 |
| | Topo-I Inhibitors | 69 |
| | Topo-II Inhibitors | 75 |
| | Further Reading | 90 |
| 7 | Tubulin-active Agents | 92 |
| | Introduction | 92 |
| | Vinca Alkaloids | 92 |
| | Taxanes and New Taxane Formulations | 93 |
| | Epothilones | 99 |
| | Further Reading | 102 |

| | | |
|-----------|---|-----|
| 8 | Miscellaneous | 103 |
| | Bleomycin, Mitomycin C, and Actinomycin | 103 |
| | L-Asparaginase, Anagrelide, and Arsenic Trioxide | 106 |
| | Hydroxyurea, Procarbazine, and Trabectedin | 110 |
| | Tretinoin and Bexarotene | 111 |
| | Further Reading | 116 |
| 9 | Hormonal Pathways Modulators of the Reproductive System | 117 |
| | Antiestrogens | 117 |
| | Aromatase Inhibitors (AIs) | 119 |
| | Gonadotropin-Releasing Hormone (GnRH) Analogs | 121 |
| | Gonadotropin-Releasing Hormone Antagonists | 123 |
| | Progestins | 124 |
| | Antiandrogens | 124 |
| | Further Reading | 128 |
| 10 | Growth Factor Receptor Targeting: Anti-HER and Anti-IGF-1R | 129 |
| | Introduction | 129 |
| | Anti-HER Agents | 129 |
| | Anti-IGF-1R Agents | 138 |
| | Further Reading | 140 |
| 11 | Tumor Vessel Targeting | 141 |
| | Angiogenesis | 141 |
| | Antiangiogenic Agents | 142 |
| | Vascular-targeting Agents (VTAs) | 148 |
| | Lenalidomide and Thalidomide | 149 |
| | Further Reading | 152 |
| 12 | Downstream Receptor Targeting: PI3K, mTOR, KRAS, BRAF, MEK | 153 |
| | PI3K-AKT-mTOR Signaling Pathway | 153 |
| | RAS-RAF-MEK-ERK Pathway | 158 |
| | Further Reading | 160 |

| | | |
|-----------|--|-----|
| 13 | Cancer-related Receptor Targeting: Bcr-Abl, KIT, MET | 161 |
| | Bcr-Abl | 161 |
| | KIT | 165 |
| | MET | 166 |
| | Further Reading | 169 |
| 14 | Epigenetic Therapy: DNA Methyltransferase Inhibitors and Histone Deacetylase Inhibitors | 170 |
| | Introduction | 170 |
| | DNA Methyltransferase Inhibitors | 171 |
| | Histone Deacetylase Inhibitors | 171 |
| | Further Reading | 175 |
| 15 | Proteasome Inhibitors | 176 |
| | The Ubiquitin Proteasome Pathway | 176 |
| | The Proteasome | 176 |
| | Perspectives | 179 |
| | Further Reading | 180 |
| 16 | Monoclonal Antibodies for Targeted Treatment of Lymphoproliferative Neoplasias | 181 |
| | Monoclonal Antibodies for Cancer Therapy | 181 |
| | Anti-CD20 Antibodies | 182 |
| | Anti-CD52 Antibodies | 187 |
| | Anti-TNF Receptor Superfamily Antibodies | 189 |
| | Further Reading | 192 |
| 17 | Immunomodulatory Drugs and Cytokines | 193 |
| | Interleukin-2 (IL-2) | 193 |
| | Interferon-alpha-2b/2a | 195 |
| | Ipilimumab | 198 |
| | Further Reading | 199 |
| | Index | 201 |