

## Index

### a

acute lymphoblastic leukemia (ALL) 28, 36  
 adenomatous polyposis coli protein (APC) 243  
 adenosine monophosphate-activated kinase (AMPK) 170  
 adrenocorticotrophic hormone (ACTH) 75  
 adult T cell leukemia/lymphoma (ATL) 225  
 AKT8 160  
 alpha-fetoprotein (AFP) 313  
 alvocidib 59  
 Alzheimer's disease 274  
 amino acids 170  
 angiogenesis 272  
 anti-cancer therapy  
 – “cytostatic and cytotoxic therapy” 10  
 – DNA alkylating drugs 13  
 – Drugs blocking synthesis of DNA and RNA 14  
 – DNA damage 12  
 – drug resistance 19, 20  
 – molecule-interfering drugs 18  
 – normal cell and tumor cell 10  
 – process-blocking drugs 14  
 – side effects and relapse 19  
 – therapeutic targets 11  
 anti-inflammatory drugs 233  
 apoptosis  
 – apoptotic initiation 80  
 – Bcl-2 protein family 92  
 – bone marrow 79  
 – caspases 82  
 – cIAP inhibitors 92  
 – conventional anti-cancer drugs 90  
 – execution phase 84  
 – external factors 79, 80

– extrinsic initiation 81  
 – internal factor 79, 80  
 – intrinsic initiation 83  
 – and necroptotic cells 75  
 – phagocytosis and degradation 85  
 – programmed cell death 79  
 – TNF pathway 81  
 – tumor cells 85  
 – TRAIL 92  
 autophagy 76, 86  
 axin coding genes 245

### b

base excision repair (BER) 57  
 B-cell lymphomas 222  
 B-cell malignancies 232  
 B-cell receptor signaling 213  
 BCR-ABL1 fusion gene  
 – allosteric inhibitors 132  
 – imatinib 129  
 – molecular diagnosis 125  
 – molecular weights, p185/p210 126  
 – nilotinib and dasatinib 132  
 – ponatinib 132  
 – structural aspects 126  
 – substrates and effects 128  
 – tyrosine kinase inhibitors 132  
 $\beta$ -catenin 245  
 bone marrow microenvironment 223  
 Bortezomib 232  
 BRaf  
 – ceramides 145  
 – gene mutations 147  
 – inhibitor 152  
 – Raf kinase inhibitor protein (RKIP) 146  
 breast cancer 269

**c**

- caspace recruiting domain (CARD) 84
- CDK inhibiting proteins (CDKIs) 54
- cell aging
  - animal model 72
  - cancer treatment 89
  - cell cycle 64
  - cellular senescence 64
  - chromosomal telomeres 67
  - non-replicative senescence 73
  - replicative senescence 65, 72
  - telomerase activity 70
- cell cycle
  - CDK inhibiting proteins 54
  - checkpoints 51
  - checkpoints and DNA integrity 55
  - cyclins 52
  - interphase 50
  - retinoblastoma-associated protein Rb 54
  - therapeutic target 58
  - tumor relevant proteins 57
- cell death
  - apoptosis 79
  - autophagy 76, 86
  - cancer treatment 89
  - cornification 74
  - necroptosis 76
  - necrotic cells 75
- cellular senescence 93
- cerebral autosomal dominant arteriopathy
  - with subcortical infarcts and leukoencephalopathy (CADASIL) 258, 272
- cetuximab 116
- cholangiocellular carcinoma (CCC) 270
- chromosome
  - analysis 120
  - chromosomal aberrations and tumorigenesis 121
  - Philadelphia chromosome 123
- chronic lymphocytic leukemia (CLL) 268
- chronic myeloid leukemia (CML) 34, 38
- chronic myelomonocytic leukemia (CMML) 269
- cisplatin 13
- clear cell renal cell carcinoma (CCRCC) 184, 187, 191
- clonal heterogeneity
  - childhood ALL 28
  - combinatorial therapies 36
  - cutaneous malignant melanoma 30
  - cytotoxic drugs 33
  - DNA replication 31
  - DNA sequencing technologies 30

- drug resistance 36
  - ETV6-RUNX1 fusion gene 28
  - gene expression mosaicism 25
  - genomic lesions 30
  - hereditary non-polyposis colorectal carcinomas 30
  - immunoglobulin (Ig) production 25
  - non-small cell lung cancer (NSCLC) 33
  - Philadelphia chromosome 28
  - plasma cells 25
  - serum protein electrophoresis 25
  - sporadic colorectal carcinomas 31
  - targeted drugs 34
  - targeted therapy 34
  - colitis-associated colorectal cancer (CAC) 229
  - cyclin D1 gene (*CCND1*) 52
  - cyclin-dependent kinases (CDKs) 52, 254
  - cyclins 52
  - cyclopamine 293
  - cyclophosphamide 13
- d**
- dabrafenib 153
  - dactinomycin 13
  - death associated protein kinase 1 (DAPK1) 89
  - death domain (DD) 210
  - diffuse large B-cell lymphoma (DLBCL) 177
  - dihydrofolate (DHF) 16
- e**
- EGF signaling pathway 33
  - epidermal growth factor receptor (EGFR)
    - biological effects 112
    - cytoplasmic sequences 110
    - family 103
    - mucin-1 (MUC-1) 113
    - and TGF $\beta$  114
  - epithelial-mesenchymal transition (EMT) 194, 290, 310
  - Erbitux 116
  - erlotinib 117
  - everolimus 178
- f**
- farnesyltransferase (FTase) reaction 150
  - fluorouracil (5-FU) 15
  - Fostamatinib 232
  - fumarate 189
- g**
- gefitinib 117
  - gene expression analyses 223
  - glutamine metabolism 198

**h**

- haploinsufficiency (HIS) 144
- hedgehog (Hh) signaling pathway
  - atypical protein kinase C-lambda/iota (aPKC $\lambda$ ) 288
  - basal cell carcinoma and medulloblastoma 285
  - ciliary trafficking inhibition 294
  - direct Smo inhibitors 295
  - Gli inhibition 294
  - Gli proteins 284
  - Gli transcription factors 283
  - inhibition, Hh ligands 293
  - KRAS oncogene 288
  - lipid-modified Hh 280
  - mTOR 290
  - N-terminal peptide 280
  - paracrine activation 291
  - pharmacological inhibition 292
  - PI3-Kinase-AKT (PI3K-AKT) pathway 289
  - primary cilium 280
  - Ptch-Smo regulation 283
  - Smo inhibition 285
  - Smoothened inhibitors 293
- Herceptin 116
- hereditary non-polyposis colorectal cancer (HNPCC) syndrome 309
- histone acetylases (HATs) 220
- Hodgkin's lymphoma 222
- homologous recombination (HR) 57
- HRAS 136
- human T-cell leukemia virus type I (HTLV-I) 225
- human vascular endothelial growth factor (VEGF) 115
- hypoxia inducible factor (HIF)
  - functional domains 185
  - glucose uptake and metabolism 195
  - HIF1 $\alpha$  and HIF2 $\alpha$  192
  - HIF1 $\alpha$  and Warburg effect 197
  - HIF1 $\alpha$ -dependent transactivation 202
  - HIF1 $\alpha$  stability 202
  - in human tumors 191
  - hypoxic conditions 189
  - mRNA expression 201
  - normoxic conditions 186
  - and oncogenic pathways 184
  - oxygen-independent regulation 189
  - protein translation 201
  - TCA cycle intermediates and tumor syndromes 200
  - tumor growth 193
  - VHL tumor suppressor gene 184

- Von Hippel-Lindau disease 191
- Warburg paradox 197

**i**

- ibrutinib 177
- imatinib 129, 254
  - mechanism 130
  - mutant KIT 130
  - resistance 130
  - tyrosine kinases 130
- immunoglobulin heavy chain locus (IGH) 223
- inhibitors of Wnt production (IWPs) 253
- Iressa 117

**j**

- Juvenile polyposis syndrome (JPS) 310

**k**

- lysyl oxidase (LOX) 194

**m**

- Marfan syndrome 300
- mechanistic target of rapamycin (mTOR) complex 1
  - AKT 170
  - amino acids 170
  - autophagy 171
  - energy status 170
  - glucose uptake and glycolysis 171
  - immunosuppressive drug FK-506 169
  - lipid synthesis 171
  - protein synthesis 171
  - receptor protein tyrosine kinases 172
  - Wnt pathways 170
- mechlorethamine 12
- medulloblastoma 285
- methotrexate (amethopterin) 15
- microsatellite instability (MSI) 147
- microtubules 16
- mitochondrial outer membrane permeabilization (MOMP) 83
- mitogen activated protein kinase (MAPK)
  - ERK 148
  - tumor therapy 149
  - tyrosine kinases 148
  - vemurafenib resistant tumors 155
- Morbus Recklinghausen* 143
- mouse mammary tumor virus (MMTV) 238, 269
- mucosa associated lymphoma tissue (MALT) 223
- multiple myelomas 223, 230
- mutation-mismatch-repair system 57

- myeloid cells 38
- myostatin (GDF 8) 315
- n**
- necroptosis 76
- necrosis 75
- neurofibromatosis type 1 (NF1) 143
- nevoid basal cell carcinoma syndrome (NBCCS) 286
- NF- $\kappa$ B pathway
  - adult T cell leukemia/lymphoma (ATL) 225
  - anti-inflammatory drugs 233
  - B-cell lymphomas 222
  - B-cell malignancies 232
  - B-cell receptor signaling 213
  - canonical pathway 214
  - carcinomas 233
  - CD40 ligand 215
  - cellular functions 206
  - cellular inhibitors of apoptosis (cIAP1 and cIAP2) 215
  - chronic inflammation and malignancy 215
  - DNA damage and reactive oxygen species (ROS) 207
  - genes and proteins 225
  - human carcinomas 227
  - I $\kappa$ B proteins 209
  - IKK $\alpha$  phosphorylates p100 215
  - inflammation and cancer 228
  - inflammatory response 206
  - intracellular pathogens 207
  - kinases (IKK) 209
  - multiple myeloma 223
  - mutantKRas 227
  - osteoclasts 230
  - perturbation 206
  - physiological role 221
  - p65/p50 heterodimer 208
  - protein A20 217
  - TNF receptor 1, 210
  - TRAF2 and TRAF3 215
  - transcriptional regulation 219
  - ubiquitinylation 217
- N-methyl-D-aspartate (NMDA) receptor 139
- non-Hodgkin's lymphoma 222
- non-small cell lung cancer (NSCLC) 33, 40
- non-steroidal anti-inflammatory drugs (NSAIDs) 254
- Notch intracellular (NIC) fragment 262
- Notch signaling
  - acute T cell leukemia (T-ALL) 266
  - angiogenesis 272
  - antibodies 274
  - breast cancer 269
  - cell fate decisions 258
  - cholangiocellular carcinoma (CCC) 270
  - chronic lymphocytic leukemia (CLL) 268
  - chronic myelomonocytic leukemia (CMML) 269
  - embryonic development and tissue homeostasis 258
  - $\gamma$ -secretase inhibitors (GSIs) 274
  - glycosylation 265
  - proteins and ligands 259
  - small cell lung cancer (SCLC) 272
  - squamous cell carcinomas (SCCs) 271
  - ubiquitinylation 264
- o**
- ommatidia 258
- p**
- paclitaxel 17
- pancreatic cancer 31
- panitumumab 116
- phagocytosis 85
- Philadelphia chromosome 28, 34, 122
- phosphatidylinositol-3-kinase (PI3K)
  - classes 161
  - GTPase binding domain (GBD) 162
  - pleckstrin homology (PH) 161
- phosphatase and tensin homologue (PTEN) 172
- phosphodiesterase  $\delta$  (PDE $\delta$ ) 151
- phospholipase C (PLC) 163
- phosphatidylserine (PS) 85
- PI3K-AKT-mTOR pathway
  - active site mTOR inhibitors 176
  - AKT inhibitors 176
  - anti-cancer drugs 176
  - biomass 160
  - hamartoma syndromes 174
  - isoform selective PI3K inhibitors 176
  - pan class I PI3K inhibitors 176
  - pan PI3K-mTOR inhibitors 176
  - rapamycin analogues (rapalogs) 160, 176
  - sporadic carcinomas 173
- platelet derived growth factor receptor (PDGFR) 4, 104
- Pleckstrin homology (PH) domain 8
- polycomb group (PcG) 225
- prostate specific antigen (PSA) 107
- protein kinase A (PKA) 4
- protein kinase B (PKB)
  - cell cycle 167

- cell growth 167
- cell survival 166
- protein kinase C (PKC)
  - activation and functions 165
  - DAG and phorbol esters 164
  - in cancer 175
- protein-protein interaction (PPIs) 4, 5–6
- pyruvate dehydrogenase kinase 196

**r**

- Raf kinase inhibitor protein (RKIP) 146
- rapalogs 160
- rapamycin 160
- Ras
  - CaaX box 137
  - direct targeting mutant 152
  - downstream signaling 144
  - farnesyl/geranylgeranyl and palmitoyl anchor 136
  - farnesyltransferase (FT) 137
  - genes encoding proteins 136
  - GRB2 activating phosphotyrosine proteins 138
  - GTPase reaction 139
  - guanine nucleotide exchange factors (GEFs) 138
  - KRas4B 137
  - mutation rates 136
  - neurofibromatosis type 1 (NF1) 143
  - posttranslational modification and membrane 150
  - Ras/Raf interaction surface 152
  - therapeutic target 150
- receptor protein tyrosine kinases (RTKs)
  - constitutive activation, in tumor cells 113
  - dimerization 102
  - EGF receptors 103, 109, 116
  - extracellular dimerization domain 100
  - growth factors and receptors 115
  - insulin receptor 107
  - phosphorylation 98
  - phosphotyrosine 98
  - platelet derived growth factor (PDGF) receptor 104, 109
  - proto-oncoproteins 98
  - PSA 107
  - signaling 108
  - substrate amino acid 101
  - tumor development 101
- repair mechanism 57
- replicative senescence 65
- roscovitine 59

**s**

- senescence-associated heterochromatin foci (SAHFs) 65
- shelterin 68
- signal transduction
  - anti-cancer drugs 10
  - cellular response 2
  - cytosolic calcium concentration 5
  - definition 2
  - GRB2 and SOS-1 4
  - interactome 5
  - protein concentration 5
  - protein kinase A (PKA) 4
  - protein – protein interaction (PPI) 4, 6
  - proto-oncogenes 8
  - tumor suppressor proteins 9
- small cell lung cancer (SCLC) 272
- squamous cell carcinomas (SCCs) 271
- stem cell factor (SCF) 102
- stem cells 37, 48, 307

**t**

- T-cell acute lymphoblastic leukemia (T-ALL) 266
- Temsirolimus 93
- TGF $\beta$  signaling pathway
  - ectodomains 303
  - inhibition 312
  - members 300
  - receptor kinase activity 313
  - R-Smads 304, 307
  - Smads 304
  - stem cell regulation 307
  - TGFR1 and TGFR2 303
  - transcriptional regulation 305
  - tumor cachexia 313
  - in tumor progression 310
  - tumor suppressors, in human cancer 309
- therapy-induced senescence (TIS) 94
- trastuzumab 116
- tricarboxylic acid (TCA) cycle 187
- tumor cell heterogeneity
  - clonal heterogeneity 24
  - epigenetics and phenotypic plasticity 40
  - genetics 24
  - microenvironment 42
  - tumor stem cells and cell hierarchies 37
- tumor cells
  - cell number 49
  - and normal cells in vitro 49
  - properties 48
  - and stem cells 48

**v**

vascular endothelial growth factor (VEGF)  
155  
Vectibix 116  
vemurafenib 153–155  
veratrum californicum 293  
vincristine (Oncovin) 17  
vismodegib 294  
von Hippel-Lindau (VHL) protein 187  
von Hippel-Lindau (VHL) disease 191, 192  
von Willebrand factor type C  
domain 261

**w**

Warburg effect 197  
Wnt pathway  
– anti-cancer drugs 253  
– anti Wnt drugs 250

– APC protein 243  
– autocrine and paracrine mechanisms 241  
– axin coding genes 245  
–  $\beta$ -catenin concentration 243, 245  
– biological effects, Wnt target genes 248  
– canonical pathway 238  
– extracellular proteins 239  
– history of 238  
– inhibitors of Wnt production (IWPs) 253  
– intracellular gene expression 243  
– lipid modification 241  
– phosphorylated  $\beta$ -catenin 240  
– therapeutic target 250  
– tumor suppressor proteins 242  
– Wnt targetome 247

**x**

xytarabine 15