

# Index

## A

accelerated fractionation, 4  
acetaldofosphamide, 218  
acrolein, 146, 179, 191, 213, 331, 332, 334  
acute lymphoblastic/lymphocytic leukemia  
(ALL), 36, 53, 162, 163, 169, 217, 324  
acute myeloblastic/myelogenous leukemia  
(AML), 35, 37, 41, 52, 55, 58, 162  
angiogenic growth factors, 241–242  
antibody-targeted therapy, 245–246  
apoptosis, 250–254  
chemokines in, 242  
cytokinetic resistance, 238–242  
hematopoietic growth factors in, 240–241  
leukemic/stromal cell interactions, 243  
multidrug resistance, 246–250  
remissions, 37, 238  
resistance mechanisms, 237–254  
stem cells, 243–244  
acute promyelocytic leukemia (APL), 237  
adaptive dosing, 324, 329, 334–335, 339  
Adriamycin. *see* doxorubicin  
AGT (O<sup>6</sup>-alkylguanine DNA  
alkyltransferase) protein, 132, 141, 148  
acrolein and, 191  
activity levels and resistance, 129, 143  
role of, 145–146  
aldehyde dehydrogenase  
insensitivity and, 161, 164–171  
medulloblastoma cells, 200, 203–204  
resistance role of, 129, 177, 179–180,  
212–213, 218–220  
aldoifosfamide, 179  
aldophosphamide, 212  
Alkeran. *see* melphalan  
O<sup>6</sup>-alkylguanine DNA alkyltransferase. *see*  
AGT  
ALL. *see* acute lymphoblastic/lymphocytic  
leukemia  
all-trans-retinoic acid (ATRA), 238  
AML. *see* acute myeloblastic/myelogenous  
leukemia  
Annamycin, 249  
antibodies, 245–246

aphidicolin, 147  
APL. *see* acute promyelocytic leukemia  
apoptosis, 264  
AML, 250–254  
CML, 229–230  
melphalan, 315  
modulation of, 254  
role of regulators, 251–254  
ATRA. *see* all-trans-retinoic acid  
Ara-C. *see* cytosine arabinoside  
Atlas arrays, 225–227

## B

B5 cells. *see* KBM-7/B5 tumor cells  
base excision repair (BER) pathway, 132  
base excision sequence scanning (BESS),  
356, 357  
Bcl-2 proteins, 94, 230, 243, 252–253, 254,  
276–277  
BCNU (1,3-bis(2-chlorethyl)-1-nitrosourea),  
5, 130, 132, 145, 191, 336  
cisplatin used with, 331, 336  
cyclophosphamide used with, 331, 336  
resistance, 129  
BEAM regimen, 310  
BER (base excision repair) pathway, 132  
BESS method, 356, 357  
bladder cancer, 13, 39, 73, 135  
bone marrow suppression, 148–149  
bone marrow transplantation (BMT). *see*  
hematopoietic stem cell transplantation  
(HSCT)  
brain cancer, 132, 144, 146, 148  
Brca1, 118  
Brca2, 118  
break-induced replication (BIR), 113, 116  
breast cancer, 1, 13, 35, 41, 59, 67, 349  
capecitabine treatment, 40  
cisplatin resistance, 267, 270  
cyclophosphamide treatment, 333  
doxorubicin sensitivity, 352  
5FU treatment, 10  
gemcitabine treatment, 39

- genes, 118  
 insensitivity, 167, 168  
 melphalan resistant, 134, 140, 143  
 melphalan treatment, 310  
 MDR1 expression, 53–56  
 risk of, 354, 362  
 breast cancer resistance protein (BCRP), 247  
 BSO. *see* buthionine sulfoximine  
 busulfan, 130  
   cyclophosphamide used with, 163,  
     326–329, 332  
   engraftment and, 327–328  
   melphalan used with, 317  
   pharmacokinetic characteristics of,  
     324–325  
   pharmacodynamics of, 326–329  
   relapse and, 326–327  
   resistance, 145, 218  
   toxicity and, 328–329  
 buthionine sulfoximine (BSO), 76–78, 186,  
 204, 272
- C**  
 capecitabine, 27, 35, 40–41, 363  
 carboplatin, 337–338  
   cisplatin used with, 264, 267  
   cyclophosphamide and thiotepa used  
     with, 332, 333–334, 337  
   melphalan used with, 309  
 carmustine. *see* BCNU  
   (1,3-bis(2-chlorethyl)-1-nitrosourea)  
 CCNU  
   (1-(2-chlorethyl)-3-cyclohexyl-1-nitrosou  
   rea), 5  
 CD33 antigen, 245, 246  
 CD45 antibody, 246  
 cell cycle checkpoints, 147, 222, 265  
 cervical cancer, 273, 276, 288, 295–297  
 CHART (continuous, hyperfractionated,  
 accelerated radiotherapy), 4  
 chemokines, 242  
 chlorambucil, 73, 74, 76  
 chloroethyl nitrosoureas. *see* BCNU and  
 CCNU  
 chloroquine, 20  
 chronic lymphocytic leukemia (CLL), 35,  
 38, 39, 139  
   cures, 162, 163  
   melphalan resistance, 134, 142–143  
 chronic myelogenous/myeloid leukemia  
 (CML), 134, 162, 212, 215, 229–231  
 busulfan/cyclophosphamide regimen for,  
 163, 326, 328  
 cyclophosphamide resistance, 294  
 cytarabine treatment for, 37  
*cib* transporter, 31, 34  
*cif* transporter, 31, 33–34  
 cisplatin, 6, 54, 75, 109, 130, 352  
   BCNU used with, 331, 336  
   biochemical mechanisms of resistance,  
     269–274  
   carboplatin used with, 264, 267  
   cyclophosphamide used with, 317, 331,  
     336  
   DNA repair, 129, 131, 273–274  
   DNA repair gene transcripts and, 141–142  
   drug accumulation, 269–271  
   electrochemotherapy and, 295  
   5FU used with, 141  
   GSH and, 271–273  
   HSCT use of, 338–339  
   measuring repair, 133–134  
   melphalan used with, 317  
   molecular resistance mechanisms,  
     275–277  
   penetration, 13  
   radiosensitivity with, 286, 288, 290–291  
   reactivation and, 138–139, 140  
   resistance, 75, 147, 218, 263–278  
   resistance markers, 288–289  
   resistance mechanisms, 213, 267–277  
   sensitivity, 59, 74, 99  
*cit* transporter, 31, 32–33  
 cladribine, 27, 35, 36, 39  
 CLL. *see* chronic lymphocytic leukemia  
 CML. *see* chronic myelogenous/myeloid  
 leukemia  
 CNT. *see* Concentrative Nucleoside  
 Transporter  
 CNT1 transporter, 31, 32–33  
 CNT2 transporter, 31, 33–34  
 CNT3 transporter, 31, 34  
 Cockayne's syndrome, 131, 274  
 colon cancer, 1, 53, 349  
   5FU treatment, 10  
   capecitabine treatment, 40  
   cisplatin resistance, 73, 74  
   melphalan treatment, 310  
 colorectal cancer, 55, 56, 58, 145, 362,  
 363–364  
 combined-modality therapy, 285–297  
   chemoresistance and radiation response,  
     290–294

- concomitant chemotherapy and subsequent radiation, 288–289  
 independent cell killing, 286–287  
 individualized molecular prescriptions, 295–297  
 neo-adjuvant chemotherapy and subsequent radiation, 289–290  
 reasons for, 286  
 Concentrative Nucleoside Transporter (CNT), 28  
 characterized processes, 31–32  
 transporters, 32–35  
 conformation sensitive gel electrophoresis (CSGE), 358  
 crosslinking. *see* interstrand crosslinks  
*csg* transporter, 31, 35  
*cs* transporter, 31, 35  
 cyclophosphamide, 5–6, 73, 109, 130, 148, 177, 211, 286  
 5FU used with, 361  
 aldehyde dehydrogenase and, 129  
 analogs, 183–184  
 BCNU used with, 331, 336  
 busulfan used with, 163, 326–329, 332  
 carboplatin used with, 332, 333–334, 337  
 cellular resistance mechanisms, 199–207  
 cisplatin used with, 317, 331, 336  
 CML resistance, 163, 211–231  
 DNA repair and, 131, 143, 188–191  
 GSH and, 185–188  
 insensitivity to, 161–171  
 measuring repair, 134–135  
 medulloblastoma resistance, 199–207  
 melphalan and, 311, 316, 317  
 metabolism, 179–184, 200  
 methotrexate used with, 361  
 pharmacodynamics of, 332–334  
 pharmacokinetics of, 329–332  
 radiosensitivity and, 294  
 resistance, 177–191, 199–207, 211–231  
 resistance mechanisms, 201  
 response, 332–333  
 stereochemistry, 182  
 thiotepa used with, 332, 333–334, 337  
 total body irradiation and, 334  
 toxicity and, 333–334  
 cyclosporine A (CsA), 55, 249–250  
 cyclosporins, 54, 80  
 Cytarabine. *see* cytosine arabinoside  
 cytochrome P450 (CYP) enzymes, 179, 335, 360, 361–363  
 cytokines, 238–242  
 Cytosar-U. *see* cytosine arabinoside  
 cytosine arabinoside, 27, 32, 35–38, 55, 98, 147, 218, 238, 240, 241, 249, 290  
 Cytosan. *see* cyclophosphamide
- D**  
 daunorubicin, 37, 238, 249  
 Daunoxome. *see* daunorubicin  
 differential display of mRNA, 228  
 DNA repair. *see* repair mechanisms  
 double-strand break repair, 109, 110, 289  
 doxorubicin, 75, 248, 290  
 penetration, 11, 13–17, 19, 20  
 resistance, 75  
 sensitivity, 59, 74, 218, 352  
 drug metabolism  
 cytochrome P450 enzymes and, 361–363  
 genomics and, 364–365  
 repetitive elements and, 363–364  
 drug penetration, 11–20, 313  
 anticancer drugs, 13–16  
 factors influencing, 16–20  
 methodology for studying, 11–12
- E**  
*E. coli*, 70, 110–111  
 ERCC1 protein, 120, 131, 140–144, 213, 225, 227, 274, 287  
*ei* transporter, 28, 29–31, 36  
 electrochemotherapy, 295  
 ENT. *see* Equilibrative Nucleoside Transporter (ENT)  
 ENT1 transporter, 28, 29  
 ENT2 transporter, 28, 29–31  
 ENT3 transporter, 31  
 epipodophyllotoxins, 247  
 Equilibrative Nucleoside Transporter (ENT), 28  
 characterized processes, 28–29  
 transporters, 29–31  
 esophageal cancer, 352  
*es* transporter, 28, 29, 36  
 ethacrynic acid, 79–80  
 etoposide, 54, 55, 147, 249  
 carboplatin used with, 337  
 penetration, 13  
 sensitivity, 59, 74, 218  
 total body irradiation and, 317  
 expressed sequence tags (ESTs), 29  
 extra-cellular matrix (ECM), 20

**F**

- Fanconi anemia (FA), 120–121
- Fas ligand (FasL), 251, 252
- 5FU (5-fluorouracil), 10, 40, 286, 288, 352
  - cisplatin used with, 141
  - cyclophosphamide used with, 361
  - methotrexate used with, 361
  - penetration, 11, 13
  - toxicity, 361
- 5' nuclease assay, 359
- FLT3 ligand (FL), 239–240
- fludarabine, 27, 35, 38–39, 147
- 4HC (4-hydroperoxycyclophosphamide), 134, 135, 143, 187, 201, 211
  - dosage, 217
  - sensitivity to, 161, 166, 169
- 4-hydroperoxyifosfamide, 161

**G**

- $\gamma$ -glutamylcysteine synthetase ( $\gamma$ -GCS), 57–58, 68, 69–71, 74–75, 186, 272
- $\gamma$ -radiation, 218
- gastric cancer, 59, 141, 144
- G-CSF. *see* granulocyte colony-stimulating factor
- gemcitabine, 13, 27, 32, 33, 35, 39–40
- gene expression profiling, 348–353
  - bioinformatic analysis, 350–351
  - DNA microarrays, 348–349
  - drug sensitivity analysis using, 351–352
  - tumor classification, 349
- gene-specific repair, 135
- genetic maps, 355–356
- genetic polymorphisms, 353–364
- gene transcripts, 348
- genotyping methodologies, 356–360
- Gilbert's syndrome, 364
- glutamine, 307, 313
- glutathione (GSH), 74–75, 220–221, 247, 306, 325
  - biosynthesis, 68–69
  - chemotherapy resistance and, 72–76, 212, 213
  - cisplatin, expression with, 271–273
  - cyclophosphamide and, 177, 185–188
  - ifosfamide and, 177, 185–188
  - insensitivity and, 163, 164
  - manipulation of system, 76–81
  - medulloblastoma cells, 204–205
  - melphalan binding, 310, 314
  - MRP1 expression and, 57

- glutathione-S-transferase (GST), 71–72, 73–74, 177, 220–221, 272, 306–307, 314, 325, 360
  - chemotherapy resistance and, 212, 213
  - medulloblastoma cells, 204–205
- glutathione synthetase, 68, 69–71
- granulocyte colony-stimulating factor (G-CSF), 238, 239, 240, 241
- GSH. *see* glutathione
- GST. *see* glutathione-S-transferase
- GS-X pump, 57, 72, 75–76, 80

**H**

- hairy cell leukemia, 39
- head and neck cancer, 3, 4, 5, 39
  - cisplatin treatment, 263, 270, 275
  - radiosensitivity, 287, 291
- heat shock protein 33 (Hsp33), 70
- hematopoietic growth factors, 238, 240–241
- hematopoietic stem cell transplantation (HSCT), 163, 323
  - busulfan for, 324, 326, 328
  - carboplatin for, 337–338
  - cyclophosphamide for, 329
  - ifosfamide for, 335
  - melphalan for, 305, 316
- hepatocellular carcinoma (HCC), 56, 79
- Hodgkin's lymphoma, 1, 37, 55, 291
- homologous recombination (HR), 113
- host-cell reactivation (HCR), 136–140
- HSCT. *see* hematopoietic stem cell transplantation
- human upstream binding factor (hUBF)
  - proteins, 266
- hydroxyurea, 147, 286, 288
- hypoxia, 287, 313

**I**

- IAPs (Inhibitors of Apoptosis Proteins), 253, 254
- idarubicin, 37, 238
- ifosfamide, 73, 177–191, 211, 335
  - analogs, 183–184
  - DNA repair, 188–191
  - GSH with, 185–188
  - insensitivity to, 161
  - metabolism, 179–184
  - stereochemistry, 182
- IM. *see* isophosphoramidate mustard
- infusional chemotherapy, 10
- interstrand crosslinks, 163, 200

- cisplatin, 109, 265, 266  
*E. coli*, 110–111  
 mediators of recombination, 113–119  
 processing in DNA, 119–122, 206–207  
 repair mechanisms, 109–123  
 repair of, 131, 206–207  
*S. cerevisiae*, 112–113  
 intrastrand adducts, 265, 266  
 irinotecan, 364  
 isophosphoramidate mustard, 179, 181,  
 183–184, 189–190, 218
- J**
- Janus kinase (JAK), 238–239  
 JNK (c-Jun NH<sub>2</sub> terminal kinase) pathway,  
 91–92  
 DNA repair, 96  
 proliferation differentiation, 95–96  
 signaling, 99–100
- K**
- KBM-7/B5 tumor cells, 215–216  
 aldehyde dehydrogenase activity, 218–220  
 apoptosis, 229–230  
 Atlas 7742-1:Human Cancer arrays, 225  
 Atlas 7850-1:Human 1.2 I arrays, 226–227  
 biological characteristics, 216  
 cell cycle checkpoints, 222  
 cross-resistance, 217–218  
 cytogenetics, 223–224  
 DNA repair, 221–222  
 genetic characterization, 223–229  
 GST activity, 220–221  
 stability, 216
- L**
- leptin (OB-R), 240  
 leucine, 306, 307, 309, 313  
 leukemia, 1, 10, 35, 75, 135. *see also*  
 specific types of leukemia  
 cisplatin resistance, 273  
 insensitivity, 161–171  
 melphalan treatment, 310  
 pediatric acute, 310  
 recurrence, 162, 294  
 secondary, 311  
 L-PAM. *see* melphalan  
 L-phenylalanine mustard. *see* melphalan  
 lung cancer, 54, 74, 133  
 melphalan treatment, 310  
 non-small cell (NSCLC), 4, 39, 54, 58,  
 59, 138, 269  
 predictor, 354  
 small cell, 54, 263, 291  
 lung resistance-related protein (LRP), 247,  
 270  
 lymphoma, 1, 10, 67, 310, 349. *see also*  
 Hodgkin's lymphoma; non-Hodgkin's  
 lymphoma
- M**
- M195 antibody, 245, 246  
 mafosfamide, 147, 161, 169, 211  
 MAPK (mitogen activated protein kinase)  
 pathway, 89–90, 239, 253  
 DNA repair, 96  
 proliferation differentiation, 93–94  
 signaling, 97–99  
 MassArray system, 359–360  
 Masscode system, 360  
 MDR1 gene, 51–56  
 AML and, 246–249  
 hematological neoplasm, expression in,  
 52–53  
 modulators, 249–250  
 role of, 52  
 solid tumor, expression in, 53–54  
 MDR2 gene, 51  
 MDR gene family, 49  
 biology, 51  
 regulation of expression, 51–52  
 relevance of MDR1, 52–56  
 mechlorethamine, 73, 74, 130, 139,  
 142–143, 147  
 medulloblastoma, 134, 143, 145, 229  
 cell lines, 201  
 cyclophosphamide therapy, 199  
 resistance, 202–206  
 melanoma, 139, 270, 295, 310  
 melphalan, 67, 77, 109, 130, 147, 218,  
 305–317  
 antitumor use, 310–311  
 apoptosis, 315  
 busulfan use with, 317  
 chemical structure, 305–306  
 DNA alkylation, 309–310  
 DNA repair and, 129, 134, 142–143  
 GSH binding, 73, 74, 310  
 high-dose strategies, 316–317  
 intravenous administration, 308–309  
 metabolism, 306–309  
 multi-agent treatment, 315–316

- oral administration, 307–308  
 pharmacodynamics, 309–310  
 resistance mechanisms, 213, 312–315  
 sensitivity, 74  
 toxicities, 311–312  
 melting curve analysis, 358  
 membrane transporters. *see* nucleoside transporters  
 metallothioneins, 273  
 methane sulfonic acid esters. *see* busulfan  
 methodologies, genotyping, 356–360  
 methotrexate, 324  
   cyclophosphamide and 5FU used with, 361  
   penetration, 11, 13, 16, 18–19  
 methylene tetrahydrofolate reductase (MTHFR), 361  
 mismatch repair (MMR), 109, 132, 145, 266, 274  
 mitogen activated protein kinase. *see* MAPK  
 mitomycin C, 59, 131  
 mitoxantrone, 13, 14, 15, 20, 55, 248, 249  
 MKK1/2, 89–90  
 MKK (MAPK kinase), 89, 91  
 MMR. *see* mismatch repair  
 MRE11, 117  
 MRP1, 56, 57, 58, 59, 76  
 MRP2, 56, 57, 58, 59  
 MRP3, 57, 58, 59  
 MRP4, 57  
 MRP5, 57, 58  
 MRP6, 57  
 multicellular layers, 11–12, 13, 16  
 multidrug resistance protein (MRP) gene family, 49, 56–59, 72, 247, 248  
   biology, 56–57  
   regulation of function, 57–59  
 multiple myeloma, 37, 52, 53, 55, 147, 310  
 myeloid leukemia, 94, 211–231. *see also*  
   acute myeloblastic/myelogenous leukemia (AML); chronic  
   myelogenous/myeloid leukemia (CML)  
 myeloma, *see* multiple myeloma
- N**
- N-acetyltransferases, 353–354, 360  
 NER. *see* nucleotide excision repair  
 neuroblastoma, 54  
 nifedipine, 59  
 nitrogen mustards. *see* cyclophosphamide;  
   mechlorethamine; melphalan  
 NOD/*scid* stem cell model, 243–244  
 non-Hodgkin's lymphoma, 37, 38, 39, 52, 55, 310  
 non-homologous end joining, 113, 115, 117, 118  
 non-small cell lung cancer (NSCLC), 4, 54, 58, 59, 138  
   cisplatin resistance, 269  
   gemcitabine treatment, 39  
   novobiocin, 147  
 NSCLC. *see* non-small cell lung cancer  
 nucleoside transporters, 27–28  
   cytotoxicity and, 35  
   measuring drug uptake, 41  
   mechanisms of drug resistance, 35–41  
   processes, 28–35  
   role of, 35–41  
 nucleotide excision repair (NER), 109, 110, 120, 130–131, 266, 274  
   melphalan, 314–315  
   plasmid probes for, 136–137  
   UV-irradiated virus for, 136–137
- O**
- oltipraz, 79  
 omeprazole, 20  
 oropharyngeal cancer, 6  
 osteosarcoma, 55–56  
 OTZ, 78–79  
 ovarian cancer, 53, 67, 138, 144, 148, 295  
   AGT and, 146  
   cisplatin resistance, 74, 133–134, 139, 141, 142, 147, 267, 269, 270, 272, 273, 275, 276, 290–291  
   cisplatin treatment, 263, 277  
   gemcitabine treatment, 39  
   gene-specific repair, 135  
   insensitivity, 166  
   melphalan resistance, 134, 143  
   melphalan treatment, 310  
   predictor, 354  
   PSC-833 treatment, 55  
 oxazaphosphorines. *see* cyclophosphamide;  
   4HC  
   (4-hydroperoxycyclophosphamide);  
   ifosfamide; mafosfamide  
 oxidative stress-response element (ORE), 70  
 Oxy R transcription factor, 70
- P**
- p53 gene, 58, 267, 275–276, 286  
 paclitaxel, 13, 287, 337

pediatric acute leukemia, 310  
 P-glycoprotein reversal agents, 54–56  
 P-gp (P-glycoproteins), 49, 51, 54, 247, 270, 286  
 phenylketocyclophosphamide (PKCP), 203  
 phosphoramidate mustard, 179, 183–184, 189–190, 200, 214, 217  
 polymerase, 314  
 polymerase chain reaction (PCR), 355  
 polymorphisms, 353–364  
 procarbazine, 145  
 proliferating cell nuclear antigen (PCNA), 131  
 prostate cancer, 58, 74, 349, 352  
 PSC-833, 55, 59, 248, 249  
 pyrosequencing, 356–358

## Q

quinidine, 249  
 quinine, 54

## R

RAD1 gene, 119  
 RAD3 gene, 112  
 RAD6 gene, 112  
 RAD10 gene, 119  
 RAD50 gene, 117  
 RAD51 gene  
   mammalian, 115, 116, 118, 225, 227  
   yeast, 113, 115, 116  
 RAD52 gene, 112, 116  
 RAD54 gene, 116–117  
 RAD55 gene, 113  
 RAD57 gene, 113  
 RAD59 gene, 116  
 radiation therapy. *see also*  
   combined-modality therapy  
   MAPK activity and, 97–98  
   radiosensitivity, 97, 286–294  
   repopulation and, 2, 3–5  
 Raf-1, 90, 97, 296  
 renal cancer, 53, 55, 310  
 repair mechanisms, 109–123, 221–222. *see also* interstrand crosslinks  
   AGT, 132, 145–146  
   bone marrow cytoprotection, 148–149  
   gene transcripts, 140–145  
   host-cell reactivation, 136–140  
   interstrand crosslink processing, 119–122, 206–207  
   inhibition, 147–148

  measurement of, 133–135  
   mismatch repair (MMR), 132, 145–146  
   pathways, 130–132  
   resistance and, 188–189  
 replication protein A (Rpa), 113, 131  
 repopulation, 2–11  
   chemotherapy and, 5–7  
   kinetic factors affecting cell response, 2–3  
   models, 7–11  
   radiation therapy and, 2, 3–5, 288  
 restriction fragment length polymorphisms (RFLPs), 354, 356, 357  
 RIP2, 90  
 Rpa (replication protein A), 113, 131  
 R-verapamil, 55

## S

*S. cerevisiae*, 112–113, 119, 121  
 SAENTA-fluorescein, 41  
 SAPK pathway. *see* JNK (c-Jun NH<sub>2</sub> terminal kinase) pathway  
 sarcoma, 5, 53, 54, 310  
 satellites, 354–355  
 sequestration of drugs, 19  
 short tandem repeats (STRs), 353  
 signal transduction pathways, 89–101. *see also* JNK (c-Jun NH<sub>2</sub> terminal kinase) pathway; MAPK (mitogen activated protein kinase) pathway  
 single nucleotide polymorphisms (SNPs), 353–354, 355  
   drug resistance and, 360–361  
   web resources, 356  
 single-strand annealing (SSA), 113, 116  
 SNPs. *see* single nucleotide polymorphisms  
 solid tumors, 1, 39, 53–54, 310  
 spheroids, 6  
 squamous cell carcinoma, 291  
 STAT (signal transducers and activators of transcription), 238–239  
 stem cells, 243–244  
 stem cell factor (SCF), 239  
 stomach cancer, 310  
 stress activated protein kinase pathway. *see* JNK (c-Jun NH<sub>2</sub> terminal kinase) pathway  
 stromal cells, 243  
 stromal-derived factor-1 (SDF-1), 242  
 STRs (short tandem repeats), 353  
 survivin, 253  
 synergism, 288

**T**

- Taxol. *see* paclitaxel  
TBI. *see* total body irradiation  
testicular cancer, 1, 10, 135  
    cisplatin resistance, 133, 270  
    cisplatin treatment, 139, 141–142, 263, 273  
    melphalan treatment, 310  
therapeutic drug monitoring (TDM), 324  
thiotepa, 317, 336–337  
    carboplatin used with, 332, 333–334, 337  
    cyclophosphamide used with, 332, 333–334, 337  
3-aminobenzamide, 147  
thymidylate synthase, 363–364  
tiapamil, 59  
tolerance resistance, 146–147  
topoisomerase, 247, 314  
total body irradiation (TBI), 163, 294, 317, 334  
TRAIL (TNF-related apoptosis inducing ligand), 251–252  
transcription-coupled repair, 135  
tumor doubling time ( $T_D$ ), 2  
tumor mean time ( $T_C$ ), 2  
tumor physiology, 1–21  
    drug penetration, 11–20  
    repopulation, 2–11

**U**

- uridine glucuronosyltransferase 1A1 (UGT1A1), 363–364

**V**

- valsopodar. *see* PSC-833  
variable number of tandem repeats (VNTRs), 353, 354  
vascular endothelial growth factor (VEGF), 241–242  
verapamil, 54, 59, 80, 248, 249  
vinblastine, 11, 13  
vinca alkaloids, 247, 290  
vincristine, 59  
VNTRs. *see* variable number of tandem repeats

**W**

- Waldenström's macroglobulinemia, 38

**X**

- xeroderma pigmentosum (XP), 131, 214, 274  
XPF protein, 131  
XRCC1 protein, 132, 225, 227  
XRCC2 protein, 115, 122, 131, 213  
XRCC3 protein, 115, 122, 131, 213