

Index

Bold entries also appear in the Glossary

- 3D tumour printing, 335–7
 α -tocopherol
 ROS scavenger, 122
 β -carotene, 39
 β -catenin, 174, 185, 198, 233
 β -particles, 50
 γ -rays, 50
- ABC transporter superfamily
 MDR1, P-gp, 300
- ABL1
 BCR–ABL1 in ALL and CML, 141
 inhibitor
 imatinib, 284
- Achong, Bert, 23
- acoustic cluster technology (ACT), 335
- acoustic neuroma**
 benign tumour, 172
 mobile phones, 60
- action potential**, 52
- acute lymphocytic leukaemia (**ALL**), 9,
 55, 142, 144, 146, 240, 244, 281,
 284, 289, 297, 317, 371
 childhood ALL
 ETV6–RUNX1 (TEL–AML1), 144
 leukaemic cells, 55
- acute myeloblastic leukaemia (**AML**), 6,
 78, 200, 282, 292, 297, 299,
 372
- acute promyelocytic leukaemia (**APL**)
 blast cells effect of retinoic acid,
 arsenic trioxide, 143
 combination therapy, 143, 282
 PML–RARA, 142
 childhood AML, 282
 IDH1/2 mutations, 288
 leukaemic cells, 55
 mutations, 82
- adenocarcinoma**, 66
 definition, 174
- adenovirus
 gene therapy, 288
 ornithine transcarbamylase, 313
- adherens junctions**, 212
- adjuvant**, 255, 295
- adoptive cell transfer**, 299
 autologous immunotherapy, 313
- Africa, 20–3
 AfrOx, 26
- African Americans, 8, 15
 triple-negative breast cancer, 16, 18,
 165, 214, 262, 267, 342
- age and cancer, 24–6
 age-related degenerative disease, 44
- age-standardised rates (ASRs)**, 2
- Alavi, Abass, 260
- alcohol
 association with major cancers, 36
- Alexandrov, Ludmil, 66
- Allison, James, 312
- allosteric**, 284
- α -particles, 50
- alternative splicing**
 EGFR (ERBB1), 136
 FGFR1, FGFR2, FGFR3, 139
 flower proteins, 118
 p53 (TP53), 154
 PML, 142
- alternative telomere lengthening, 185
- Alzheimer's disease, 83
- American Cancer Society, 11, 36, 65
- American Heart Association, 37
- American Indians, 15
- aneuploidy**, 85, 126, 128
- angiogenesis, 187–92
 regulators, 189–90
 angiostatin, endostatin, 189–90
 bevacizumab (Avastin), 293
 bevacizumab-bvzr (Zirabev), 294
 thalidomide, 295
- sphingosine 1-phosphate**, 245
- vascular damage
 ranibizumab, brolocizumab,
 pegaptanib, 294
- anoikis**, 218
- antibodies, 132
monoclonal antibodies, 285
 bevacizumab (Avastin), 190, 293
 ranibizumab (Lucentis), 294
 tocilizumab (Actemra), 304, 318
 antibody-directed enzyme pro-drug
 therapy (ADEPT), 285
 avelumab (anti-PD-1), 312
 cemiplimab (anti-PD-1), 312
cetuximab (EGFR), 305
 durvalumab (anti-PD-1), 312
 Herceptin (HER2), 285
 immunoliposomes, 285
 ipilimumab (anti-CTLA4), 312, 322,
 323
 nivolumab (anti-PD-1), 312
 pembrolizumab (anti-PD-1), 312
 pertuzumab (HER2), 285
 radioimmunotherapy, 285
 rituximab (CD20), 285
 trastuzumab (HER2), 305
- anti-oxidants, 39
- APC (adenomatous polyposis coli)
 APC/ β -catenin, 236
 colon cancer, 166
 germline mutations in colon cancer,
 83
 mutations, 236
 chromosome damage, 161
 circulating tumour cells, 323
- phosphorylation**, 231, 237
- apoptosis**, 46, 103, 124, 137, 154, 164,
 175, 178, 196, 204, 207, 212,
 218, 224, 226, 228, 230, 231,
 232, 233, 234, 236, 239, 242,

440 Index

- 248, 280, 284, 302, 305, 310, 312, 339
- DIABLO, 183
- extrinsic pathway, 235
- inhibition, 290–2
- intrinsic pathway, 181
- pro-apoptotic proteins
 BIM, PUMA, BID, BMF, BAD, BIK, NOXA, HRK, 181
- pro-survival proteins
 BCL-2, BCL-XL, MCL1, BCL-W, BOK and A1/BFL1 181
- survivin, 184
- apoptosome, 182
- aptamer**, 294
- ARAF, 130
- ARF
 DNA repair, 159
 E2F, 226
 MDM2, 226
 p53, RB1, 227
 signalling, 225
 transcription control by MYC, 231
 transgenic mice, 157
- Asian Americans, 15
- Asian Pacific Islanders, 15
- astrocytomas**, 155
- autoimmune diseases
 psoriasis, rheumatoid arthritis, Crohn's disease, 282
- autophagy**, 184
- autophagy addiction**, 235
- Babeş, Aurel, 253
- bacterial transfer, 46, 311
- Bacteroides thetaiotaomicron*, 40
- Barr, Yvonne, 23
- Barrett's oesophagus**, 45, 325
- basal-type breast cancers**, 213
- basement membrane**, 188
- basic helix–loop–helix**, 108
- BCL2
 antagonist
 venetoclax (ABT-199), 291
- apoptosis modulators, 290–2
- apoptosis versus survival, 231
- caspase, 233
- chromosomal translocation
non-Hodgkin's lymphoma, 13, 144
- miRNA-34, 164
- mitochondrial location
 BAX, 182–4
- MYC, 155
- p53, 165
- regulation
 NF- κ B, STAT3, 203
- BCR–ABL1
biomarker, 258
- chronic myeloid leukemia (CML), 141–2
- dasatinib, 284–5
- imatinib, 284
- mutations
 imatinib, 300
- nilotinib, 285
- oncogene addiction, 305
- signalling, 240
- BEAMing
 detection of PI3KCA mutations in breast cancer, 134
- Becquerel, Henri, 50
- Benaud, Richie, 3
- benign and malignant cancers, 171
- benign tumours**, 171–3
- benign–malignant boundary, 174
- birthmarks and moles, 173
- mutation patterns, 174
- warts, verrucas, HPV, 173
- Bhutan, 64
- biomarkers of cancer, 42, 73, 90, 165, 206, 216, 258, 269, 284, 296, 323, 325
- cancer antigen 125 (CA125), 257
- epididymus protein 4 (*WFCD2*), 258
- prostate-specific antigen (PSA)/kallikrein 3, 257
- Trefoil Factor 3 (TFF3), 325
- Bloom's syndrome**, 140
- body mass index (BMI), 44
- bone metastasis
 low-energy β -emitting radionuclides, 297
- radium-223, 297
- Booth, Tom, 264
- Börnert, Peter, 263
- Bradley, Allan, 153
- BRAF
 mutant inhibitor
 vemurafenib, 283
- mutations, 130–1
- PET imaging melanoma, 131
- brain cancer, 6
- glioblastoma multiforme**
 IDH1/2 mutations, 288
- BRCA1, BRCA2
 breast cancer, 6, 15, 17, 26, 82
- DNA repair, 159
- mutations, cancer risk, 160
- MYC amplification, 140
- synthetic lethality**
 olaparib, 293
- breast cancer, 2, 3, 13, 16, 36, 38, 44, 63, 66, 159, 165, 200, 209, 267, 283, 285, 286, 294, 302, 328, 346, 361–3
- BRCA1*, *BRCA2*, *PALB2*, *ATM* and *CHEK2* mutations, 160
- ductal carcinoma *in situ* (DCIS), 174
- microenvironment, 342–3
- somatic mutations**, 81
- triple negative, 81
- triple-negative breast cancer, 16, 18, 165, 214, 267, 342, 362
- X-ray imaging, 253
- Britton, Peter, 253
- Burkitt, Denis, 23
- Burkitt's lymphoma**, 23, 140
- Buscombe, John, 263
- cachexia, 221
- cadherin
 EMT, 210, 272
- intercellular junctions, 231
- signalling, 237
- VE-cadherin intercellular junctions, 197
- caffeine, 42
- Caldas, Carlos, 342
- California
 smoking control, 64
- California Environmental Protection Agency, 66
- calories**
 food calories, 43
- Campbell, Peter, 344
- cancer cells
 hallmarks of cancer, 176–8
- abnormal metabolism, 195
- angiogenesis, 187–9
- independent growth, 178–9
- resistance to cell death (apoptosis), 179–84
- resistance to inhibitory signals, 178–9
- unlimited replication, 184–7
- major signalling pathways, 230–2
- tumour phenotype, 246
- cancer detection and treatment prospects, 309–46. *See* epigenetics

- breath biopsy, 324–5
 analytical platforms, 325
- checkpoint inhibitors, 311–13
- CRISPR-Cas system, 317–19
 base editing, 317–19
 the future, 319–20
- Cytosponge, 325–6
 Barrett's oesophagus, oesophageal cancer, 325
- gene therapy, 313–18
- immunotherapy, 310–11
- liquid biopsy, 320–3
 Galleri test, 323
 leukapheresis, 323
- Pap test, 253
- cancer detection, diagnosis and radiotherapy, 251–74
 imaging tumours, 252–3
 mammography, 253–4
 screening, 253–4
 staging, diagnosis, grading and monitoring, 254–5
- cancer disparities, 13, 14, 16
- cancer incidence, 2–3
 Australia, 2, 3, 5, 8, 64
 Bhutan, 2
 breast cancer, 2
 colorectal (bowel) cancer, 2, 13
 Denmark, 2, 3, 60
 Europe, 2, 16–19
 global patterns, 8
 Ireland, 2, 3, 64
 lung cancer, 2, 6, 26
 Nepal, 2
 New Zealand, 2, 3, 8
 Niger, 2
 North America, 2
 prostate cancer, 2, 6
 Republic of Congo, 2
 The Gambia, 2
 USA, 2, 3, 5, 8, 10–16, 33, 37, 43, 53, 58, 61, 65, 217
- cancer mortality, 3–4
 breast cancer, 3
 Canada, 9
 Caribbean, 9
 Central America, 9
 China, 9, 19
 colorectal (bowel) cancer, 3
 Denmark, 18
 England, 6, 10, 27, 37
 Finland, 18
- global patterns, 8
 Hungary, 16
 India, 9
 Japan, 9
 liver cancer, 3
 lung cancer, 3
 Melanesia, 9
 Micronesia, 9
 Polynesia, 9
 prostate cancer, 9
 Russia, 16
 Scotland, 10
 South America, 9
 stomach cancer, 3
 UK, 9
 Ukraine, 17
 USA, 9, 13
 lung, prostate, bowel, pancreatic, liver, leukaemia, oesophageal, bladder, **non-Hodgkin's lymphoma**, kidney cancer, 11
 Wales, 27
- Cancer Research UK, 8, 9, 27, 33, 65, 354
- cancer survival rates**, 9
- Cancer Target Discovery and Development Network, 303
- cancer-associated fibroblasts**, 203
- CancerBACUP, 16
- Canon, Jude, 339
- carcinogen**, 40, 58
- carcinomas**, 174
- Caribbean and Central and South America, 20, 368
- caspases**, 233
 executioner caspases, 182
 apoptotic pathways, 182–3
- causes of cancer, 31–67, *See also*
 infection, radiation, radon, stress and tobacco
 alcohol, 35–9
 calcium, 41
 diet, 37–8
 European Prospective Investigation into Cancer and Nutrition (EPIC), 41
 fibre, 41–2
 The Polyp Prevention Trial, 31–67
 The Wheat Bran Fiber Trial, 31–67
 folate, 40–1
 food and drink, 35
 meat and vegetables, 39–40
- sugar, 43–4
 tea and coffee, 31–67
 The Nurses' Health Study, 38–9
- CD number**, 192
 CD4⁺, 342
 CD4⁺ T-cells, 205, 206
 CD40, 310
 CD44^{high}/CD24^{low}, 210, 213
 CD8⁺, 342
 cytotoxic T-cells, 205
 CD8⁺ T-cells, 192
- CDC25
 cell-cycle control, 103
- cell division cycle, 102
- cell growth
 positive and negative signals, 117, 147
- cell signalling
 basic principles, 246
- cellular barcoding**, 301
- cellular bookmarking, 216
- Centers for Disease Control and Prevention, 11, 65
- Central and South America, 8
- central dogma tagging (CD-tagging), 273
- cerebrovascular disease, 4
- cervical cancer, 6, 19, 26, 253, 294, 298, 365
 bevacizumab-bvzr, 294
 DNA viruses, 22, 229
- checkpoint proteins
 PD-1, CTLA4, 311
- chemotherapy, 276–307
 arsenic, 277
 Chinese herbal remedies, 277
 early development, 277–9
 efficacy, 306–7
 magic bullets, 276–7
 palliative chemotherapy, 277
 targets for anti-cancer drugs, 280–99
 angiogenesis, 293–5
 apoptosis, 290–2
 metabolism, 286–90
metastasis, 6, 296–7
 oncoproteins, 283–6
 proliferation, 280–3
synthetic lethality, 292–3
 tumour agnostic drugs, 299
 vaccines, 23, 298–9
 vascular targeting agents, 295–6
 timeline, 278
- Chernobyl Forum, 56

442 Index

- China, 19, 277, 315, 328
 smoking, 65
- cholesterol
 membrane component, 114, 240
- choriocarcinoma
methotrexate, 282
- chromosomal translocations
 ABL1/BCR, ABL1/ETV6, BCL2/IgH,
 CCND3/IgH, ERG/TLS,
 INK4A/TCRA, MYC/IgH,
 Igλ/Igκ, PDGFRB/TEL, RET/
 Protein kinase A, NTRK1/
 TPM3, PDGFB/COL1A1,
 144–7
- chromothripsis**, 84, 148–50
- chronic lymphocytic leukemia (CLL), 6
 leukaemic cells, 55
- chronic myeloid leukaemia (CML):
 leukaemic cells, 55
- Circos plots, 81
- circulating tumour cells, 218, 258, 320,
 323
 CancerSEEK, Galleri test, exome
 sequencing, exosomes, 323–4
 therapy response monitoring, 322–3
- circulating tumour DNA (ctDNA), 324
 liquid biopsy, 321
- Clevers, Hans, 47
- clinical trials**, 190
Clostridium botulinum, 40
- Cochrane Collaboration, 254
 mammography, 254
- COL1A1
 chromosomal translocation PDGFB,
 144
- Coley, William, 311
- colibactin, 47
 fingerprints, 47
- Collaborative Group study (2002), 36
- colorectal (bowel) cancer, 2, 3, 39, 45, 86,
 167, 200, 360
 alcohol, 36
 bacteria, 42
Escherichia coli, 47
Fusobacterium, 47
- cetuximab**, 286
 chemotherapy, 283
- China, 19
 diet, 42
 folic acid, 39
 incidence, 2
 malignant carcinoma, 160, 170
 polyps, 41
 red meat, 39
 screening, 258
- computed tomography (CT), 52, 252, 260
- contact inhibition**, 127
- Continuous Update Project, 37
- copy number**, 79
- COSMIC
 Catalogue of Somatic Mutations in
 Cancer, 300, 303, 343
- Coupland, R. E., 260
- CRISPR-Cas, 317–20
Francisella novicida, 319
- Crohn's disease, 83, 204
- Cuba, 8
- Curie, Marie, 50
 radium, 53
- Curie, Pierre, 50
- Currie, Alastair, 181
- cyclin-dependent kinase inhibitors (CDIs)
 CDKN2A (INK4A), CDKN2B
 (INK4B), 85
 cell-cycle arrest
 INK4, WAF1, KIP1, KIP2, 103
 senescence
 WAF1, KIP1, 229
 WAF1 and cell-cycle arrest, 154
 WAF1 transcription and MYC, 155
- cytochrome *c*, 182
- cytokine**, 95
- cytokine receptors, 111
- d'Amato, Robert, 294
- Dana-Farber Cancer Institute, 118
- de-differentiated**, 214
- deep sequencing**, 86
- Deerinck, Thomas, 180
- DeNardo, David, 205
- depth of coverage**, 86
- diarrhoea, 4
- differentiation**, 106
- DNA
 adducts, 40
 cost of sequencing, 78
 DNA methylation, 328
 HeliScope single-molecule sequencing,
 76
 ion torrent sequencing, 77–8
 mutation rates, 123
 nanopore sequencing, 76–7
**next-generation/second-generation
 sequencing**, 73, 75
 polymorphisms and cancer, 162–3
 pyrosequencing, 76
 repetitive DNA, 161–2
 Sanger dideoxy sequencing, 73
 sequencing,
 fluorescent resonant energy
 transfer, multiplex polony
 sequencing, 78
 single-molecule real-time sequencing,
 76
 third-generation sequencing, 76
 types of mutation, 128
- DNA and RNA viruses, 22, 23
- DNA repair, 159–62
 genes involved in, 159
- Doll, Richard, 39, 64
- Dominica, 8
- dormant tumours, 190–2
- double minutes**, 149
- Down's syndrome, 189
- Drosophila melanogaster*
 fitness fingerprint, 119
 Son of Sevenless, 104
- drug development, 302–4
- drug resistance, 299–302
- drugs
5-fluorouracil, 282
6-mercaptopurine, 282
6-thioguanine, 282
 abiraterone, 279
actinomycin D, 281
 alkylating agents
 altretamine, 279
 bendamustine, 279
 busulfan, 279
 carmustine, 279
chlorambucil, 279
cyclophosphamide, 279
 dacarbazine, 279
 lomustine, 279
 streptozocin, 279
 temozolomide, 279
 thiotepa, 279
- AMG 510, 339
- aminopterin**, 281
- bevacizumab (Avastin), 190
- bevacizumab-bvzr (Zirabev), 294
- bleomycin sulfate, 277
- bortezomib, 346
- camptothecin, 273, 281
- capecitabine, 282
- carboplatin, 279

- chlorambucil**, 281
 cilengitide, 295
 cisplatin, 279
 crizotinib, 303
cyclophosphamide, 281
 cytarabine (AraC), 300
 dacarbazine, 277
 doxorubicin, 281
 doxorubicin hydrochloride (Adriamycin), 277
 enasidenib, 288
 FOLFIRI
 cetuximab, 283
 irinotecan, 283
 FOLFOX
 fluorouracil, 283
 folinic acid, 283
 oxaliplatin, 283
 FTY720 (Fingolimod), 302
 gossypol, 290
 imatinib (Gleevec or Glivec), 258, 284
 imiquimod, 311
irinotecan, 281
 L-asparaginase, 289
 lenvatinib, 335
 leptomycin B, 291
methotrexate, 282
 dihydrofolate reductase (DHFR), 282
 metronidazole, 47
 nutlins, 291
 olaparib, 293
oxaliplatin, 279
 paclitaxel, 281
 pexidartinib, 311
prednisone, 305
 RG7112 and RG7388 (idasanutlin), 291
 RITA, 291
 salvarsan, 276
 simvastatin, 292
 sorafenib, 285
 tenovin-6, 291
 thalidomide, 294
 tirapazamine (SR-4233), 288
 trastuzumab, 132
 vemurafenib, 283
 venetoclax, 292
 vinblastine, 290
 vinblastine sulfate, 277
 dysbiosis, 48
 dyslipidaemia, 45
 E2F family
 RB1 binding, 152
 signalling, 225
 early response genes
 ornithine decarboxylase (ODC1), JUN, FOS, MYC, 107
 Earth BioGenome Project (EBP), 91
 e-cigarettes
 vapes, e-cigs, 64
 EGFR
 amplification in brain tumours, 146
 amplification in NSCL cancer, 138
 discovery, 278
 EGFR, ERBB2, ERBB3 and ERBB4 family, 136
 EGFR mutations
 lung carcinoma, glioblastoma, oesophageal cancer, 135–7
 ERBB2 (HER2) mutations
 breast, bladder and lung cancers, 137
 inhibitors trastuzumab, Herceptin, pertuzumab, 286
 ERBB3 (HER3) mutations
 breast, bowel and NSCL cancers, 137
 ERBB4 (HER4) mutations
 breast, lung and melanoma cancers, 137–8
 family ligands, 100, 137
 gefitinib resistance, 300
 inhibitors
 afatinib and dacomitinib, 285
 AZD9291, 285
 cetuximab, panitumumab, 286
 gefitinib, erlotinib, 285
 protein domain structure, 135
 receptor tyrosine kinase, 95
 receptor tyrosine kinase family, 98, 112, 125
 SRC, 99
 transphosphorylation, 111
 tumour biomarker, 258
 v-erbB protein domain structure, 135
 EGFR signalling network, 100
 Ehrlich, Paul, 276
 salvarsan, 276
 electromagnetic spectrum, 51
electron volts, 58
 Ellisman, Mark, 180
 endometrial cancer, 6
endothelial cells, 113
 von Willibrand factor, 191
endothelium, 179
 enzyme-linked receptors
 receptor guanylyl kinases, 97
 receptor serine/threonine kinases, 97
 receptor tyrosine kinases (RTKs), 96
 receptor-like tyrosine phosphatases, 97
 epidemiology, 1–28
 epidermal growth factor (EGF), 95, 98, 99, 100
 epigenetics, 327–8
 DNA, histone modification, 329–30
 epigenetic drugs, 329–30
 5-azacitidine, 330
 BET inhibitors, 330
 vorinostat, 330
 epiregulin
 EGFR family ligand, 100
epithelial-to-mesenchymal transition (EMT), 210
 Epstein, Anthony, 23
Erwinia chrysanthemi, 289
 Europe
 cancer patterns, 16–19
 total cancer deaths and breast cancer deaths in 39 European countries, 16–18
 European Union, 10, 10
 Evan, Gerard, 340
Ewing's sarcoma, 281
 exomeres, 296
 supermeres, 296
 exosomes, 216, 296
extracellular matrix, 177
 Farber, Sidney, 281
 fibroblast growth factor receptor (FGFR)
 family, 138–9
 Fitzgerald, Rebecca, 325
 flower proteins, 118
fluorescence in situ hybridization, 144
fluorescent labels, 119
 Folkman, Judah, 190
 free radicals, 39
 G-protein-coupled receptors (GPCRs)
 structure, 112
 Gallagher, Ferdia, 62
 gallbladder cancer, 9
 gallstones, 44
 Gelsinger, Jesse, 313
 gene deletion, 148–58
 gene-expression profiling, 271–3

444 Index

- genetic analysis of cancer, 72–91
 bioinformatics, 85–6
 exome sequencing, 86–7
 Genome Aggregation Database (gnomAD), 87–90
 genomic partitioning, 80–2
 human genome sequencing, 73–8
 Human Genome Project, 73
 impact of genomics on cancer, 90–1
 Pan-Cancer Project, 84–5
 whole-genome sequencing and cancer, 78–80
- genetic instability**, 167
- Gilman, Alfred, 279
- global trends, 24–8
- global variation in breast and lung cancers
 Australia/New Zealand, 8
 Eastern Africa, 8
 Japan, 8
 Northern Africa, 8
 South Africa, 8
 UK, 8
 USA, 8
 Western Africa, 8
- glycolysis, 193–5
 glucose transporters, 198
 glutaminolysis, fatty acid synthesis, 286
- glycosylphosphatidylinositol (GPI) anchor**, 237
- Goodman, Louis, 279
- G-protein-coupled receptors, 96
- granulocyte-macrophage colony-stimulating factor (GM-CSF)**, 299
- granzymes, 46
- Greaves, Mel, 146
- green fluorescent protein**, 218
- Green, Samuel, 64
- Guinness Book of Records, 118
- Haber, Fritz, 279
- haemoglobin, 95, 181
 modified, 287
- Haldane, J. B. S., 187
- half-life**, 52
- Hao Yan, 333
- haploinsufficient**, 234
- haplotypes**, 83
- Harvard School of Public Health, 45
- Hayes, Emily, 191
- He Jiankui
 HIV-resistant babies, 320
- heart disease, 4, 44
- hereditary cancers, 159
 breast cancer, 159–60
 colon cancer, 161
- Hesketh, Richard, 261
- HIFs
 hypoxia-inducible factors. *See* oxygen, hypoxia
- high tumour mutational burden
 immune checkpoint inhibitors, 284
- Hill, Austin Bradford, 64
- Hispanic Americans, 8, 15
- histones
 histone acetyltransferase, 116, 327
histone deacetylase, 198
 modifications, 329–30
- HIV**, 125
 AIDS, 4, 22, 24, 108
 human immunodeficiency virus
 lymphocyte transformation, 22
telomerase, 185
- Hodgkin's lymphoma**, 175, 259, 370
- Honjo, Tasuku, 311
- Hoshino, Ayuko, 217
- Hounsfield, Godfrey, 260
- House of Commons, 10
- HTLV**, 125
- Huggins, Charles, 279
- Human Genome Project, 343
- human genome sequences
 Yoruba, Nigeria, Han Chinese, 78
- Human Genome Sequencing Center in Houston, 78
- human immunodeficiency virus (HIV), 23, 185, 320, 125
- human T-cell lymphotropic virus (HTLV)
 HTLV-1 adult T-cell leukaemia, 23, 125
- Hungary, 5
- hypertension, 4, 45
- hypoxia**, 184, 187, 195
 cycling hypoxia, 193
 HIFs, 286
 hypoxia modifier
 atovaquone, 288
 hypoxia response elements (HREs), 288
 hypoxia/HIF-dependent replicative adenovirus, 288
 hypoxic cytotoxins
 tirapazamine (SR-4233), 288
- hypoxic radiosensitisers
 cisplatin, doxorubicin and docetaxel, 287
 tumour hypoxia
 hyperbaric oxygen, 287
- immune system**, 175
- immunoliposomes, 286
- immunotherapy, 284, 302, 311
 metastatic melanoma, 58
 radioimmunotherapy, 311
- India, 20
- infection, 49–50
Helicobacter pylori, 49
Mycobacterium tuberculosis, 50
- inflammation
 immune system, 200–2
- INK4A
 DNA repair, 159
 transgenic mice, 157
- innate lymphoid cells**, 46
- inositol 1,4,5-trisphosphate**, 101, 112, 131, 232
- insulin, 45–6
- integrin
 inhibitor
 cilengitide, 295
- metastasis**
 integrin $\alpha_4\beta_1$, 216
 receptor nanoparticle binding, 267
 signalling, 238
 structure, 96
- interferon- γ (IFN γ), 192
- interleukins
 IL-1 β , IL-23, 48
 interleukin-17, 48
 interleukin-2 (IL-2), 310
 interleukin-33, 46
- International Agency for Research on Cancer (IARC), 60
- International Human Cell Atlas, 343
- International Wheat Genome Sequencing Consortium (IWGSC), 91
- INTERPHONE Study Group, 60
- Ireland, 64
- ischaemic heart disease, 4
- isocitrate dehydrogenases
 mutant inhibitors
 enasidenib (AG-221), ivosidenib (AG-120), 288
- mutations
 IDH1, IDH2, 288–9

- J. Craig Venter Institute, 78
 JAK family
 cytokine signalling, 111
 Japan, 8
 Kaposi's sarcoma-associated herpesvirus,
 23, 125
karyotype, 81
 Keren, Leeat, 342
 Kerr, John, 181
 KIT
 gastrointestinal stromal tumour
 mutations, 138, 174, 284
 inhibitors
 sorafenib, sunitinib, SU10944, 305
oncogene addiction
 dasatinib, 305
 pexidartinib inhibitor, 311
 stem-cell factor receptor, 98
 Kortlever, Roderick, 341
 Lane, David, 154
 Latino Americans, 8, 15
 Lauterbur, Paul, 260
leucine zipper, 108
leucocytes, 175
leukaemia, 6, 175
 Lickint, Fritz, 64
 Li–Fraumeni syndrome
 p53 germline mutations, 154
 ligand-gated ion channels, 113
 Lilley, Kathryn, 270
 Lindskog, Gustaf, 279
 liver cancer, 3, 5, 9, 22, 36, 358
 adenoma, 39
 hepatitis, 298
 hepatocellular carcinoma (malignant
 hepatoma), 358
 liver cirrhosis, 36, 298
 Lowe, Scott, 269
low penetrance, 83
 lung cancer, 2–3, 19, 27, 32, 37, 40, 43,
 50, 65, 84, 138, 155, 199, 258,
 285, 354
 lung primary carcinoma, 62
mesothelioma, 67
non-small-cell lung carcinoma
 (NSCLC), 38
 radon, 61
small-cell lung cancer, 38
 smoking, 64
 the lung cancer microbiome, 47–8
 Staphylococcus, *Streptococcus*,
 Lactobacillus, 48
 Lyden, David, 216, 217
lymphocytes, 46, 175
 immune signature
 CD68^{high}/CD4^{high}/CD8^{low}, 205
lymphomas, 125, 175
 nitrogen mustard, 279
macrophages, 180, 203
 Madan, Esha, 119
 malaria, 4
malignant, 171
 malignant cancers
 primary and malignant tumours,
 207–8
 types of malignant cancers, 174–5
 uniqueness, 207
 mammography, 253–4
 Mansfield, Peter, 260
MAPK, 95
 central axis signalling, 230
 conserved MAPK pathways, 103
 hedgehog regulation, 241
 MAPK family, 105
 melanoma
 checkpoint inhibitors, 13, 312
 metastatic signatures, 214
 pathway inhibitor
 sorafenib, 285
 RAF-independent signalling, 130
 shRNA inhibitors, 305
 TGFβ1 regulation, 243
 yeast pathways, 247
mass spectrometry, 269
MALDI-TOF, 269
mast cells, 203
 matrix metalloproteinases (MMPs), 188,
 216, 243, 296
 Medawar, Peter, 187
meganucleases, 315
 Melanesia, Micronesia and Polynesia, 19
melanoma, 3, 33, 40, 137, 148, 174, 263, 283
 adoptive cell transfer, 299
 AKT survival pathway, 301
 BRAF mutation, mutational burden,
 66, 131
 chemotherapy resistance, 300
 CONEXIC, 82
 exosome proteome analysis, 324
 IL-2 (aldesleukin), interferon-α, 310
 interleukin-2 (IL-2), 313
 MAPK, PD-1 inhibitors, 312
 melanocytes, 58, 106, 173
metastasis, 214
 naevus, 172
 organ donor transfer, 191
 osteopontin, 241
 somatic mutations, 82, 84
 T-VEC, 315
 merlin (NF2)
 neurofibrosarcoma, 172
 MET (also known as hepatocyte
 growth factor receptor
 (HGFR)), 98
 metabolic syndrome, 45
 metabolomics, 271
metastasis, 62, 207, 212
 cachexia, 221
 EMT, 210
 how do cells become metastatic, 209
 metastasising metastases, 219
monocytes, 218
 seed and soil, 208
 Paget, Stephen, 208
 stromal cells, 202, 340
 targetting metastatic cells, 296
metastasis suppressor genes, 179
metastatic signatures, 214
 Mexico, 8
 microRNAs (miRNAs), 302, 163–6
 drug resistance, 301
 doxorubicin, tamoxifen, docetaxel,
 5-FU, cisplatin, 165
 oncogenes or tumour suppressors,
 302
microsatellites, 162
minisatellites, 162
mitogen, 107
 Mongolia, 5
 Montenegro, 5
 Morris, Peter, 260
 mutation signatures
 breast cancer, 341–2
 MammaPrint, Rotterdam signature, 272
 mutations
 causes, 32
 driver mutations, 33
 in cancer development, 32
 inherited mutations, 151, 160, 213
 number, 123
 passenger mutations, 33, 85, 95
 replicative mutations, 32, 39
 somatic and germline, 123

446 Index

- MYC
 cancer driver, 82
 cell cycle, 231
 cell proliferation, 108
 cellular protein concentrations, 140
 co-operation with RAS, 227
- MYCN, MYCL, 108, 340
- MAX
 omomyc, 340
- MAX and transcription, 108
- stromal reprogramming lung tumours
 CCL9, IL-23 340–1
- mycobiome, 48
Candida albicans, 48
Malassezia, 49
- myeloid cells, 140
- myofibroblasts, 203
- nano-oncology, 330–4
 DNA nanorobots, 333–4
 molecular origami, 334
 inert capsules, 335
 transarterial chemoembolisation
 (TACE), 335
- liposomes, 334–5
 LATTE, 335
- nanoparticles, 331–3
- nanotubes, graphene and nanocells,
 332–3
- National Center for Biotechnology
 Information (NCBI), 79
- natural killer cells, 46
- neoadjuvant, 206
- nerve growth factor (NGF), 105, 106
- neuregulins
 EGFR family ligands, 100, 137,
 299
- neuroblastoma, 140
- neurofibromin (NF1)
 neurofibrosarcoma, 172
- New York
 smoking control, 64
- NF- κ B, 200
- NM23, 214
- non-Hodgkin's lymphoma, 6, 22, 23, 27,
 125, 144, 175, 259, 370
- non-oncogene addiction
 DNA, VEGF, VEGFR, RAF1, KIT,
 PDGFRB, topoisomerase 1,
 DHFR, mitotic spindle,
 mTOR, Cd20, immune system,
 305
- olaparib, KU0058684, **5-fluorouracil**,
 bevacizumab (Avastin),
 sorafenib, sunitinib, SU10944,
 cisplatin, oxaplatin, **irinotecan**,
methotrexate, paclitaxel,
 vinblastine, vincristine,
 temsirolimus, rituximab,
prednisone, 282
- Nordling, Carl, 25
- NTRK1
 chromosome translocation, 144
 signalling, 299
- NTRK1, NTRK2 and NTRK3
 gene fusion, 299
- nucleotide excision repair**, 159
- O'Keefe, Stephen, 42
- obesity, 44
 gene associations, 45
 the obesity microbiome, 46
Bacteroidetes, 46
Firmicutes, 46
 USA levels, 45
- oesophageal cancer, 6, 19, 20, 45, 323,
 325, 363
 adenocarcinomas (OACs), 6
 mutations, 325
squamous-cell carcinomas (OSCCs), 6
- oestrogen, 44
 cancer growth, 36, 38, 44, 68
 hormone therapy, 38
 oestrogen receptors, 16, 38, 283
- Omomyc, 108, 339
 MYC inhibition in mouse lung
 tumours, 339
- oncogene addiction**, 227
 EGFR, ERBB2, BCR-ABL1, BRAF,
 PI3K, RAR, RXR, BRCA1, 305
 erlotinib, gefitinib, **cetuximab**,
 trastuzumab, imatinib,
 nilotinib, dasatinib, GDC-0879,
 PLX4720, BEZ235, **retinoic**
acid, 305
- oncogenes**, 106, 125
 first human oncogene, 125
 proto-oncogene to oncogene, 126
 abnormal *MYC*, 147
 BCR-ABL1, 141
 BRAF, 130, 131, 132
 chimeric protein
 ETV6-RUNX1 (TEL-AML1),
 144
- PML-RARA, 142
 EGFR family, 135
 MYC amplification, 139
 PI3K, 131
- oncogenes and tumour suppressor genes
 defined, 124
- ovarian cancer, 6, 44, 159, 254
 cancer antigen, 125, 258
 effect of contraceptives, 38
 liposome drug delivery, 334
 microRNA, 301
 screening, 258
- oxygen, 189
 aerobic glycolysis, 193
 effect on transcription
 HIFs, 195, 288
endothelial cells, 187
 prolyl hydroxylase (oxygenase), 196
 radiation sensitivity, 195
- p53 (TP53), 22, 47, 85, 153
 3D protein structure, 156
 apoptosis, 154, 181
 ATM and DNA damage, 159
 bortezomib, 315
 cancer, 155
 cell-cycle arrest, 103
 cell-cycle arrest, apoptosis and MYC,
 154
 colon cancer, 160
 CRISPR, 319
 dominant negative, 156
 gene therapy, 157
 glycolysis, 193, 198
 human papillomaviruses (HPVs), 22,
 229
 metabolism, 286
 microRNAs, 164
 modulators
 tenovin-6, RITA, leptomycin, 291
 MRI screening, 254
 mutation in benign tumours, 174
 mutation sites, 154
 mutations
 cigarette smoke, 66
 nutlins, 291
 PML-RARA, 142
 reactivation of p53 in mice, 269
 regulation by MDM2, 233
 regulation of p53 and RB1, 226
 RTK amplification, 146
 senescence, 227

- tumour cell phenotype, 225
 virotherapy
 Onyx-015, H101, 315
- pancreatic cancer, 6, 33, 38, 48, 80, 339, 340, 366
 extracellular vesicles, 216
 imaging, 259
 KRAS inhibition, 339
 mutations, 80
 obesity, 44
 pancreatic ductal adenocarcinoma (PDA), 48
 smoking, 64
 STAT3, 203
- Papanicolaou, George, 253
- PARP (poly(ADP-ribose) polymerase), 149, 293
 inhibitors
 niraparib, rucaparib, veliparib and talazoparib, 293
- Patched (PTCH)
 PTCH1, PTCH2
 Sonic hedgehog, 241
 structure, 96
- penicillin, 277
- perforin, 46
- persister cells**, 301
- personal versus impersonal medicine, 337–9
 targetting MYC, 339–41
 targetting RAS, 339
- Perutz, Max, 95
- Peto, Richard, 39, 67
- Pharmacologic Audit Trail, 345
- phosphatidylinositol 3-kinases (PI3Ks)**, 101, 131
 inhibitors, 132
 dual PI3K/mTOR inhibitor NVP-BEZ235, 287
 gefitinib, erlotinib, imatinib, sunitinib, rapamycin, temsirolimus, rapamycin, dasatinib, 284
- inositol phosphorylation, 132
- insulin signalling, 133
- mutations in breast cancer, 134
- PTEN, 131
- phosphatidylserine**, 180
- phosphoinositides**, 100
- phosphorylation**, 131
- Piwi-interacting RNAs
 subfamily
 Argonaute proteins, 163
- platelet-derived growth factor B
 chromosomal translocation
 dermatofibrosarcoma protuberans, 144
- platelet-derived growth factor receptor (PDGFR)
 breast cancer, 138
 domain structure, 135
oncogene addiction, 305
 PDGFRB chromosomal translocation
 in CML, 144
- polypectomy, 39
- potassium
 isotopes, 52
- progesterone
 hormone therapy, 38
- prostate cancer, 2, 13, 214, 248, 257, 268, 279, 293, 367
 diet, 38
 hormonal treatment
 abiraterone, 279
 mortality in US population groups, 15
 mouse models, 266
 national patterns, 16
 olaparib, 293
 PSA, 257
 replication errors, 33
 Sipuleucel-T, 298
 survival rates, 13
 USA 5-year survival rates, 306
- proteasome, 143
- protein imaging, 273
- proteomics, 166, 269
- PTEN
 dual phosphatase, 131
 Public Health England, 43
 Puerto Rico, 8
 Pykett, Ian, 260
- radiation, 50
 abnormal exposure
 α - and β -particles, 51
 γ -radiation, 50
 Chernobyl, 54
 Fukushima, 56
 Hiroshima and Nagasaki, 54
 radium girls, 53
 Becquerel, 50
 doses from medical radiation sources., 52
 high-frequency magnetic fields
 mobile phones, 60
 mobile phones Stewart report, 61
 ionising radiation, 51
 low-frequency magnetic fields, 59
 unethical human experimentation, 53
 vestibular schwannoma, 61
 X-rays, 52
- Radiation Effects Research Foundation, 54
- radiotherapy, 2, 255
 types of external radiation therapy, 256
- radon, 61
- RAF1**
 ERK activation, 130
 inhibitor
 sorafenib, 285
 lung tumours, 106
 MAKKK, 103
 RAS signalling, 103
 transient activation, 106
- RAS**
 human RAS genes
 NRAS, *HRAS*, *KRAS*, 126
 KRAS, 167, 258, 286, 306, 323
 inhibitors, 339
 KRAS mutations, 47, 305
 KRAS2, 161, 166
 Kras^{G12D}
 activation by Cre recombinase, 340
 point mutations, 129
 regulation by GTPase-activating proteins, 129
 superfamily
 RHO, RAC, CDC42, RAB, RAN, RAD/GEM, 104
- RB1**
 cancer signalling pathways, 152
 HPV, 229
- phosphorylation**
 palbociclib, 283
 promoter mutations, 147
 protein function, 152
 retinoblastoma protein
 cell-cycle progression, 103
 senescence, 227
 truncation, 324
 tumour suppressor, 151
- reactive oxygen species (ROS)**, 122, 187, 234, 288
 DNA damage, 51
- receptor tyrosine kinases**, 95
- RET**
 chromosomal translocations, 144
 domain structure, 98
 mouse melanocytes, 192

448 Index

- retinoblastoma**, 151
retrovirus, 125
 risk factors, 35
 case-control studies, 35
 cross-sectional studies, 35
 evaluation, 33
 observational and controlled studies, 35
 prospective and retrospective studies, 35
 relative risk or risk ratio (RR), 34
RNA editing, 80
 Röntgen, Wilhelm, 259
 Rosenberg, Steven, 313
- saccharin
 gut microbiota, 49
 Sanger, Fred, 73
sarcomas, 125, 175
 Sattely, Elizabeth, 40
 Saudi Arabia, 5
 selective oestrogen receptor modulators (SERMs)
 tamoxifen, raloxifen, toremifene, 117
senescence, 142, 155, 158, 184, *See*
 signalling in cancer cells:
 senescence
 Serbia, 5
 SH2 family signalling proteins
 domain structures, 101
 Sharpless, Barry, 331
 Shubin, Neil, 118
 signalling in cancer cells, 225
 ARF, MDM2, p53, INK4, RB1, 225
 BCR-ABL1, 240
 cadherin, 98, 210, 211, 212, 231, 236,
 237, 247, 272, 296
 death receptors, 235
 defence systems, 122
 DNA viruses, 6
 hedgehog and GLI, 212
 integrin, 238
 JAK-STAT, 111
 MYC and RAS, 227
 other pathways, 230, 235, 243
 PI3K 232, 233, 235, 305
 survival and apoptosis, 142, 155
 senescence, 184
 systems biology, 225, 246
transforming growth factor- β , 165, 179
 VEGF and Notch, 243
 WNT, 185, 212, 231
- signalling in normal cells, 94
 enzyme-coupled receptors, 95
 intracellular signalling, 96
 MAPK signalling, 95
 sustained versus transient activation,
 105
 receptor tyrosine kinases, 95, 247, 284,
 285
 talking to cells, 95
 single-nucleotide variants (SNVs), 79
 breast cancer risk
 TGFB1, FGFR2, TOX3, MAP3K1
 and LSP1, 163
 SNPs, 79
 single-photon emission computed
 tomography (SPECT), 259
single-cell sequencing, 146
single-nucleotide polymorphisms, 160
 Skin Cancer Foundation, 59
 sleep apnoea, 44
 Slovakia, 5
 small interfering RNA (siRNA), 163,
 287, 305
 smoking. *See* tobacco
 SRC
 constitutively activating mutation,
 135
 EGFR activation, 198
 FAK signalling, 234, 238, 239
 family, 284
 oncogene addiction, 305
 Rous sarcoma virus genome, 126
 Src homology domains (SH1, SH2, SH3),
 100
 tyrosine kinase, 112, 125
 Sri Lanka, 5
 STATs
 activation by cytokines, growth factors,
 112
 JAK-STAT signalling, 235
 receptor binding and dimerisation, 111
 STAT3
 colitis-associated cancer, 203
 NF- κ B cooperation, 203
 STAT5A colocalisation with ERBB4
 domains, 137
stem cells, 32, 33, 143, 146, 185, 212,
 213
 steroid hormones, 114
 testosterone, oestrogen, 114
 Stevens, Albert, 53
 stomach cancer, 3
- stress, 63
stroma, 202
 Subbarow, Yellapragada, 281
 superoxide dismutases, 122
 Swiss Medical Board, 254
synthetic lethality, 305
 olaparib, 293
 screens
 epigenetic-related synthetic lethal
 pairs, 293
- talimogene laherparepvec (T-VEC), 315
tandem duplication, 80
 targeted α -particle therapy, 337
telomeres, 85, 185
 testicular cancer, 13, 27, 84, 281, 282
**tetracycline-controlled transcriptional
 activation**, 339
 The Cancer Genome Atlas, 48
 The National Cancer Institute, 59
 The National Cancer Intelligence Centre
 Cancer Atlas, 10, 29
 The Pan-Cancer Analysis, 343
theranostics, 330
 neuroendocrine cancer diagnosis, 331
 therapeutic vaccines, 298
 Bacillus Calmette-Guérin (TheraCys),
 299
 Sipuleucel-T (Provenge), 298
 thyroid cancer, 6, 13, 56, 57, 220
 thyroid gland, 56, 57
tight junctions, 212
 tobacco, 6, 19, 20, 32, 35, 63–7, 79, 122,
 154
 betel quids, 64
 cancers associated with smoking, 64
 global smoking deaths, 63
 Russia, 17
 second-hand smoke
 blood cotinine, 65
 smoking and the genome, 66
 smoking restriction, 64
 third-hand smoke, 66
trans-activating, 152
transcription factors, 152
transcriptome, 206
transformation, 127
transforming growth factors (TGFs)
 miRNA
 TGF β , 165
 TGFA, 137
 TGFB1 (TGF β) signalling, 80

- TGFBI (TGFβ)
 negative growth signalling, 178
- transmembrane signalling
 receptors, 96
- Trau, Matt, 329
- tricarboxylic acid cycle (TCA cycle), 193, 286
- mutations
 aconitase, isocitrate dehydrogenase (IDH), succinate dehydrogenase, fumarate hydratase, 288
- tuberculosis, 4, 50, 301
- tumour cell microenvironment**, 136, 166, 202, 215, 340, 342
- breast cancer, 342–3
 multiplexed ion beam imaging by time-of-flight (MIBI-TOF), 342
- tumour imaging and molecular imaging, 259
- ¹³C-hyperpolarisation, 265
- human brain MRI, 264
- MRI (magnetic resonance imaging), 61, 252, 258, 260, 262
- optical imaging, 2
- PET (positron emission tomography)**, 200, 252
- smart contrast agents, 2
- SPIOs (superparamagnetic iron oxide nanoparticles), 267
- tumour necrosis factor receptor (TNFR)
 apoptosis, 235
 death ligands, 184
 structure, 96
- tumour necrosis factor-α (TNFα), 192
- tumour promoter**, 64
- tumour suppressor genes**. *See* p53 (TP53), **retinoblastoma** (RB1), ARF, BRCA1, BRCA2, NF1, Patched (PTCH), neurofibromin 1 (NF1), merlin (NF2)
- tumour vasculature, 170
 vascular mimicry, 192
- tumour-associated macrophages (TAMs), 204
- tumourigenic DNA viruses, 229
- type 2 diabetes, 38
- US Preventive Services Task Force, 254
- ubiquitin–proteasome pathway**, 196
- UK, 3, 9, 27, 64
 most common causes of cancer death, 6
 most common female cancers, 33
 survival rate trends, 14
- UK cancer hotspots, 10
- ultraviolet (UV) radiation
melanoma, 58
 wavelength, 51
- United Arab Emirates, 5
- University College London SUMMIT study
 lung cancer detection, 258
- University of Alabama at Birmingham, 62
- US Radium Corporation, 53
- US Surgeon General
 smoking and breast cancer report, 66
- USA, 3, 8, 64
 black–white cancer gap, 14
 most common causes of cancer death, 11
 trends and socioeconomic factors, 13–14
- USA states
 male and female incidence and mortality, 11
- vaccines, 23, 298. *See* chemotherapy:
 targets for anti-cancer drugs
 Cervarix, 298
 coronavirus, 331
 Engerix-B, 298
 Gardasil, 298
 HPV, HBV, 22, 23, 26, 173, 298
 Recombivax HB, 298
- vascular endothelial growth factor (VEGF)**, 188
- vascular endothelial growth factor receptor (VEGFR)
 domain structure, 98
 inhibitors
 lenvatinib, 335
 sorafenib, sunitinib, SU10944, 295
- viral vectors
retroviruses (including lentiviruses), adenoviruses, adeno-associated viruses, 314
- virotherapy**, 313
- vitamin C
 ROS scavenger, 122
- vitamins A, C and E (α-tocopherol), 39
- Vogelstein Bert, 32
- von Hagens, Gunther, 65
- von Hippel–Lindau (VHL)**, 196
 HIF1-α binding inhibition, 288
- Warburg, Otto
 pyruvate kinase isoforms, 197
 Warburg effect/aerobic glycolysis, 195
- wasting disease, 175
- Watson, James, 78
- WEE1
 cell-cycle control, 103
- Wellcome Trust Sanger Institute, 80
- Westminster Bridge, 10
- white Americans, 8, 14
- WHO Framework Convention on Tobacco Control, 17
- WNT signalling, 237
- Workman, Paul, 345
- World Health Organization (WHO), 5, 43, 45
 causes of cancer deaths, 35
- Wyllie, Andrew, 181
- X-rays, 52, 252, 259
 chest X-rays, 62
 external beam therapy, 255
 mammography, 253
- Yongjun Liu, 331
- zinc-finger nucleases**, 315