Author Index

A

Achinger-Kawecka, J, 41 Aguirre, AJ, 237 Alcantara Llaguno, SR, 31 Alderton, G, 299, 317, 323, 341 Allen, E, 21 Annunziato, S, 141

B

Barazas, M, 141 Berger, T, 85 Bergers, G, 21, 299 Bissell, MJ, 207 Boehm, JS, 237 Brugge, JS, 281, 301 Bruna, A, 227

С

Caldas, C, 227 Cho, H, 113 Cichowski, K, 304 Clark, SJ, 41, 306

D

Dang, CV, 73

E

Evan, G, 309

F

Faham, N, 177 Fearon, DT, 219 Feigin, ME, 231 Furita, S, 207

G

George, BM, 1 Gill, JG, 163 Graubert, A, 105 Griffith, M, 105 Griffith, OL, 105 Guo, JY, 73

Н

Haber, DA, 269, 311 Hahn, WC, 237 Hoffman, A, 105 Hong, AL, 237 Howard, TP, 237 Huang, CH, 257 Hundal, J, 105

J

Jonkers, J, 141

K

Kadoch, C, 53 Kaelin, WG, 113, 314 Kalluri, R, 275, 317 Kang, Y, 151 Kao, KS, 1 Kiberstis, P, 304, 326, 344 Kiwala, S, 105 Kvajo, M, 306, 320, 331

L

LeBleu, VS, 275 Letai, A, 131 Li, W, 151 Lockwood, WW, 247 Lowe, SW, 257, 320 Lozano, G, 37, 323 Lyden, D, 326

Μ

Maheswaran, S, 269 Mak, TW, 85 Manchado, E, 257 Mardis, ER, 105, 328 Marjon, KD, 1 McCracken, MN, 1 McKenna, E, 311, 338, 354, 360 McMichael, J, 105 Miller, CA, 105 Missiaen, R, 21 Miyamoto, DT, 269 Morrison, SJ, 163, 331 Muranen, T, 281

Ν

Neel, B, 334

0

Oudin, MJ, 189

Р

Palm, W, 67 Parada, LF, 31, 336 Pattabiraman, DR, 11 Piskounova, E, 163 Polyak, K, 123 Potter, DS, 131 Pulice, JL, 53

R

Raveh, T, 1 Rinne, M, 237 Roe, JS, 61 Rottenberg, S, 141 Rueda, OM, 227

S

Saunders, ME, 85 Sawyer, C, 291 Sever, R, 301, 309, 328, 334 Shaw, RJ, 93 Shiu, S, 123 Stratton, M, 338 Svensson, RU, 93

Т

Taberlay, PC, 41 Tasdemir, N, 257 Thompson, CB, 67 Ting, DT, 269 Toner, M, 269 Tschaharganeh, DF, 257 Tsherniak, A, 237 Tuveson, DA, 231, 341

U

Unni, AM, 247

V

Vakoc, CR, 61, 344 Varmus, H, 247, 347 Vazquez, F, 237 Vousden, K, 351

W

Walker, J, 105 Weaver, VM, 189, 354 Weinberg, RA, 11, 357 Weissman, IL, 1 Welm, AL, 177 White, E, 73, 360 Wilkinson, JE, 257 Witkowski, J, 314, 336, 347, 351, 357

Х

Xie, X, 31 Zheng, H, 151

Subject Index

A

ABT-737, 136 ACC. See Acetyl-CoA carboxylase Acetyl-CoA carboxylase (ACC) fatty acid metabolism regulation, 93, 96 - 97inhibitor development, 98-99 non-small cell lung cancer, fatty acid synthesis as metabolic liability, 99-100 therapeutic targeting, 96, 98-100 Acetyl-CoA synthetase short-chain family member 2 (ACSS2), therapeutic targeting, 94-95 ACLY. See ATP citrate lyase ACSS2. See Acetyl-CoA synthetase shortchain family member 2 Acute lymphoblastic leukemia (ALL), BH3 profiling and apoptosis priming, 137 Acute myeloid leukemia (AML) BRD4 effectors, 63-64 function and therapeutic targeting, 61 - 63IDH1 mutations, 88 ADAMTS1, bone metastasis promotion, 153 - 155AKT, 90, 93, 95, 197, 233 ALL. See Acute lymphoblastic leukemia AML. See Acute myeloid leukemia Anergy, therapeutic targeting, 86 Aneuploidy, therapeutic targeting, 90 Angiogenesis cell growth in vascularly compromised tumors, 69-70 innate immunity and antiangiogenic therapy, 22-24 metabolic endothelial cell adaptation, 23.25 metabolic tumor cell adaptations to antiangiogenic therapy, 25 - 27overview in cancer, 21-22 Antioxidants. See Reactive oxygen species APC, 320 APOBEC, 338-339 Apoptosis BH3 proteins BCL-2 targeting, 135-137 profiling, 134-135, 137 promotion, 132-133 intrinsic pathway, 131-133 priming, 133-134, 137-138 ARID1A, 54-57, 242-243 Atg7, 75-77 ATM, 88-89 ATP citrate lyase (ACLY), therapeutic targeting, 93, 95

Autophagy basal autophagy in tumors, 73 cancer metabolism promotion, 76–77, 383 macromolecule recycling, 75–76 prospects for study, 77 survival in starvation, 73–75 tumor dependence, 75, 360 tumorigenesis promotion, 75

В

BAF, 53-58 BCL-2 anti-apoptotic activity, 132 BH3 protein targeting, 135-137 BCR-ABL, 242, 247, 292, 329 Bergers, G, interview, 299-300 BH3 proteins. See Mimetics Bmal1, 79-80, 82 BMS-777607, 182 Bone metastasis epidemiology, 151 genes, 152-153 osteoclast microRNA studies, 157 progression mechanisms, 151-152 tumor-stroma interactions ADAMTS1 and MMP-1 promotion of metastasis, 153-155 therapeutic targeting Jagged1, 155-157 transforming growth factor-B, 155 - 157BRAF, 251, 285, 293-294, 360 BRCA1, oxidative stress in cancer, 89-90 BRD proteins BRD4 acute myeloid leukemia effectors, 63-64 function and therapeutic targeting, 61-63 hematopoietic lineage transcription factor cofactor, 63 therapeutic targeting, 285, 344-346 breast cancer inhibitors in triple-negative breast cancer, 125-126 proliferation role in estrogen receptor-positive cancers, 124-125 functional overview, 123-124 inhibitor resistance mechanisms, 126 - 128Breast cancer. See also Mammary tumor organoid BRD proteins inhibitors in triple-negative breast cancer, 125-126 proliferation role in estrogen receptor-positive cancers, 124-125

circulating tumor cell analysis of intratumoral heterogeneity, 271-272 classification, 227 epidemiology, 141 lineage switching and therapy resistance, 287-288 mouse models basal-like cancer BRCA mutations, 143 PARP inhibitor resistance mechanisms, 144-146 preclinical trials, 143-144 invasive lobular carcinoma, 142 - 144mammary tumor organoids, 147-148 nongermline models, 146-147 prospects, 148 xenograft collection and heterogeneity analysis, 227-230 BRG1, 53, 55, 58 Brugge, J, interview, 301-302

С

Cancer immunogenomics neoantigen prediction, 105-107 vaccine creation case reports, 107-110 Cancer stem cell (CSC) epithelial-to-mesenchymal transition and stemness, 12-13 glioblastoma multiforme in vivo model, 33 nestin-green fluorescent protein transgene characterization, 34 overview, 33 prospects for study, 34 therapeutic resistance, 34 leukemia, 1-2, 5-7CD47 innate immune invasion, 6-7 leukemic stem cell expression, 1-2 CDH1, 13-14, 16 CFI400945.90 Cichowski, K, interview, 304-305 Circulating tumor cells (CTCs) overview, 311-313 single-cell analysis intratumoral heterogeneity studies breast cancer, 271-272 pancreatic cancer, 271 prostate cancer, 270-271 microfluidic isolation, 269-270 overview, 269 prospects for study, 273 tumor evolution monitoring, 272-273 Clark, S, interview, 306-308 Clock, 79-80, 82 Coffin-Siris syndrome (CSS), 56-57

366

CpG islands, 306–307 CRISPR–Cas9 breast cancer mouse models, 146–147 large-scale cancer dependency functional genomics screens, 241–242 *CRKL*, 238 CSC. *See* Cancer stem cell CSS. *See* Coffin–Siris syndrome CTCF, 41, 43–44, 49 CTCs. *See* Circulating tumor cells CTLA4, 295 Cummings Lecture, 291–295 CYCLOPS, 243, 285–286 D2HG. *See* 2-Hydroxyglutarate

E

EGFR, lung cancer mutations, 249-251, 253 EMT. See Epithelial-to-mesenchymal transition Epithelial-to-mesenchymal transition (EMT) classification, 11 epithelial trait loss during malignancy, 13 - 15genes, 358-359 mesenchymal trait acquisition, 15 metastasis studies, 12 program redefining, 5 stemness role, 12-13 therapeutic targeting, 16-17 tumor progression, 11-12 ERK, 302-304 Evan, G, interview, 309-310 Exosome biogenesis, 275 double-stranded DNA functions, 277-278 identification, 277 mutation detection, 277 prospects for study, 278-279 drug delivery, 318 overview, 275-277 Extracellular matrix. See Mammary tumor organoid; Tumor microenvironment

F

FAK, 195-196, 198 FAM83 oncogenes, 211-212 FAS. See Fatty acid synthase Fatty acid synthase (FAS) elevation in tumors, 95 fatty acid synthesis overview, 93-95 metabolic tumor cell adaptations to antiangiogenic therapy, 26 Fibronectin, 195 FRS2, 238 Functional genomics, cancer challenges, 243 large-scale cancer dependency screens cancer dependency types, 242-243 CRISPR-Cas9, 241-242 RNA interference, 239-240 small molecule screens, 242 overview, 237-238 screens for alterations in cancer

SUBJECT INDEX

allele variants, 238–239 copy number alterations, 238

G

GATA3, 55 GBM. See Glioblastoma multiforme Gleevec, 292 Glioblastoma multiforme (GBM) cancer stem cells in vivo model, 33 nestin-green fluorescent protein transgene characterization, 34 overview, 33 prospects for study, 34 therapeutic resistance, 34 cancer vaccines, 107-110 cell memory, 32 lineages, 31 metabolic tumor cell adaptations to antiangiogenic therapy, 25 progenitor cells, 32-33 types in mouse models, 31-32 Glutamine, cancer cell uptake, 67-68 GSK3 β , 6

Н

Haber, D, interview, 311-313 Hematopoietic stem cell (HSC) characterization, 2-3 Hoxb5 expression in long-term stem cells, 4-5 leukemia mutations, 5 leukemic stem cell comparison, 5 - 7TLS cells, 2-3 transplantation, 1 HER2, 13 HGF, 159 HIF. See Hypoxia-inducible factor Hoxb5, hematopoietic stem cell expression, 4-5 HSC. See Hematopoietic stem cell HUGL2, 13 2-Hydroxyglutarate (D2HG), oncogenicity, 89, 314 Hypoxia-inducible factor (HIF) functional overview, 114 HIF2 in clear cell renal cell carcinoma carcinogenesis role, 115-116 therapeutic targeting, 116-118 regulation by VHL and oxygen, 115, 314 structure 114

I

IDH. See Isocitrate dehydrogenase
Innate immunity antiangiogenic therapy, 22–24 therapeutic targeting, 86
Isocitrate dehydrogenase (IDH), mutation effects on ATM and NOTCH, 88–89
2-hydroxyglutarate oncogenicity, 89 mouse models, 88 tumors, 87–88, 321 J

Jagged1, therapeutic targeting in bone metastasis, 155–157 JQ1, 124–128, 344–346

K

Kaelin, W, interview, 314–318 Kalluri, R, interview, 317–319 KEAP1, 164 c-Kit, hematopoietic stem cell expression, 3 *KRAS* lung cancer mutations, 249–251, 253 pancreatic cancer mutations, 232, 247 survival of tumors, 360–361

L

LAMA3, 213-214 Leukemia hematopoietic stem cell mutations, 5 leukemic stem cells, 1-2, 5-6lgl2, 13 LKB1, 195 Long-range epigenetic silencing (LRES), prostate cancer, 47-49 Lowe, S, interview, 320-322 LOXL2, 199 Lozano, G, interview, 323-325 LRES. See Long-range epigenetic silencing Lung cancer KRAS mutations, 249-251, 263 lineage switching and therapy resistance, 287 non-small cell lung cancer, fatty acid synthesis as metabolic liability, 99-100 Lyden, D, interview, 326-327

Μ

Macropinocytosis, regulation, 70 MAGE-A1, 105 Mammary tumor organoid human cells extracellular matrix-nucleus linkage, 213-215 formation on three-dimensional substrata, 208-210 morphogenesis assay and applications, 210-213 overview, 207 mouse models, 147-148 Mardis, E, interview, 328-330 Matrix metalloproteinases (MMPs) MMP-1 and promotion of bone metastasis, 153-155 MMP-9, 210 MCT cotransporters, 192 Mdm2, 37-38 MED1, 126 MET, 170, 182, 327 Microenvironment. See Tumor microenvironment

SUBJECT INDEX

MicroRNA, osteoclast microRNA in bone metastasis, 157 Mitochondrial outer membrane permeabilization (MOMP), 131-132, 135 MMPs. See Matrix metalloproteinases MOMP. See Mitochondrial outer membrane permeabilization Morrison, S, interview, 331-333 MSP, 179-180 MTAP, 243 mTORC1 cell growth effector, 71 lysosomal protein degradation regulation, 70 MYC, 310 circadian clock perturbation, 79-80 timing of metabolic therapies, 80-82

Ν

NADPH, regeneration, 168–170 Navitoclax, 136–137 ND-646, 99–100 Neel, B, interview, 334–335 NHE1, 192 NOTCH, 88–89 NRF2, 164–165, 167–168, 232–233, 284 Nrp1, 22, 47 Nutrient uptake, cancer cells glucose, 67–68 glutamine, 67–68 macropinocytosis regulation, 70 nutrient depletion survival, 68–69, 71 signal transduction, 67–68

0

Olaparib, 144–145 Oncogene mutations agonistic synthetic lethality, 252 general features, 247–248 genotype complexities, 248 lung cancer mutually exclusive oncogenes, 248–252 patterns and mutual exclusivity, 248 prospects for study, 253–254 Organoid. *See* Mammary tumor organoid OTX-015, 62 Oxidative stress. *See* Reactive oxygen species

Р

p53, 142, 320–321, 323–325, 352 DNA damage response, 38 Mdm2 alleles and physiological outcomes, 37–38 tumor suppressor pathway, 38–39 turnover, 37
Pancreatic cancer challenges and opportunities for study, 233–234 circulating tumor cell analysis of intratumoral heterogeneity, 271 KRAS mutations, 232 mouse models, 231–232

Nrf2 in progression, 232-233 organoid models, 231-232 tumor microenvironment, 233 Parada, L, interview, 336-337 PARP inhibitors, 143-144, 301 PATJ, 13 PAX8, 238 PBAF, 53-54 PD-L1, 300 PDGF, 164, 190, 194 PDGFRB, 258 PFKFB3, 23, 25 PGC-1a, 170 PHGDH, 168 PIK3CA, 238 PLXNA2, 49 PRMT5, 243 Prostate cancer circulating tumor cell analysis of intratumoral heterogeneity, 270-271 differential chromatin interactions, 44, 46 - 47long-range epigenetic silencing, 47-49 topologically associated domain disruptions, 41-45 PTEN, 90, 164 PTP1B, 334-335

R

Rac1, 196 RAD21, 41 RANKL. 151-152 Ras, 310 RCC. See Renal cell carcinoma Reactive oxygen species (ROS) antioxidants clinical trials in cancer prevention, 165-166 treatment, 165, 167 defenses, 164-165 cancer initiation and progression role, 167 handling in cancer cells, 87, 168-170 metastasis role, 167-168 serine limitation effects, 352 sources, 163-164 therapeutic targeting, 89-90 Receptor d'origine nantais (RON) cancer activation, 179-180 cell-autonomous versus non-cellautonomous functions in cancer progression, 181-182 history of study, 177 signaling downstream pathways in cancer progression, 180-181 ligand-dependent versus ligandindependent, 179 structure, 177-178 therapeutic targeting, 182-183 Renal cell carcinoma (RCC) clear cell carcinoma genetics, 113-114 HIF2 carcinogenesis role, 115-116 therapeutic targeting, 116-118 metabolic tumor cell adaptations to antiangiogenic therapy, 26

RNA interference drug target screens identification of targets, 258-260 therapeutic index establishment inducible and reversible transgenic mice, 263, 265 - 266liver regeneration studies, 262-264 overview, 262 validation in vitro, 260-261 in vivo, 261-262 large-scale cancer dependency screens, 239 - 240RNF213, 335 ROCK, 355 RON. See Receptor d'origine nantais ROS. See Reactive oxygen species

367

S

Sawyers, C, Dorcas Cummings Lecture, 291-295 SDF-1, 195 Single-cell analysis. See Circulating tumor cells SMAD4, 190 SMARCB1, 53-55 SOD. See Superoxide dismutase SREBPs. See Sterol regulatory elementbinding proteins Sterol regulatory element-binding proteins (SREBPs), 93 STK11, 250 Stratton, M, interview, 338-340 Superoxide dismutase (SOD), 164 SWI/SNF gain-of-function, 56 intellectual disability syndrome point mutations, 56-57 overview of mammalian complexes, 53 - 54promoter and enhancer state maintenance, 57-58 prospects for study, 58 sequencing studies in cancer, 54-55 tumor suppression, 55-56

Т

TAD. See Topologically associated domain Taverson, D, interview, 31-343 T-cell chimeric receptor T-cell therapy, 286-287 paucity in tumors CXCR3 impairment in colorectal tumor model, 221-222 chemokine mediation of T-cell accumulation, 220-221 inhibition by CXCR4, 222-223 immune escape, 219-220 overview, 219 prospects for study, 223-224 therapeutic targeting, 85-86 Tenascin C, 190-191 TET2, leukemia mutations, 5

368

TGF-β. See Transforming growth factor-β TME. See Tumor microenvironment Topologically associated domain (TAD), prostate cancer disruptions, 41 - 45Transforming growth factor- β (TGF- β), therapeutic targeting in bone metastasis, 155-157 TRAP, 154 TRIM33, 127 Tumor microenvironment (TME) bone metastasis ADAMTS1 and MMP-1 promotion, 153-155 niches beyond osteoclastogenesis, 157 - 159gradients chemokines and growth factors, 190 directional migration alignotaxis, 196 chemotaxis, 194-195 durotaxis, 196 galvanotaxis, 196-197 haptotaxis, 195-196 techniques for study, 193-194 electrical field alterations, 192-193 extracellular matrix changes, 190-191

SUBJECT INDEX

hypoxia establishment, 192 overview, 189-190 pH gradient inversion, 192, 197 prospects for study, 199-201 stiffness gradients, 191-192 therapeutic targeting for metastasis prevention disruption of gradient, 198-199 exploitation of gradient, 199 prediction of metastasis, 197 receptor and signaling blockade, 197-198 lineage switching and therapy resistance, 288 pancreatic cancer, 233 prospects for study, 284-285 therapeutic targeting, 86 TWIST, 126

V

Vaccines. *See* Cancer immunogenomics Vakoc, C, interview, 344–346 Varmus, H, interview, 347–350 Vascular endothelial growth factor (VEGF), 21–22, 27, 116, 159, 190, 288, 299–300, 314–315 VCAM-1, 159 VEGF. See Vascular endothelial growth factor Venetoclax, 137 VHL. See von Hippel–Lindau protein von Hippel–Lindau protein (VHL), 314 clear cell renal cell carcinoma genetics, 113–114 hypoxia-inducible factor regulation, 115 tumor suppression, 114 Vousden, K, interview, 351–353

W

Warburg effect, 87 Weaver, V, interview, 354–356 Weinberg, R, interview, 357–359 White, E, interview, 360–361

Y

YAP1, 238