Index

A
Abiraterone acetate, 441
AD. See Androstenedione
Adaptive immunity, escape by cancer cells, 438
Adenocarcinoma, prostate
  advanced or metastatic histopathology, 101
diagnostic criteria, 88–92
ductal adenocarcinoma, 97
histopathological features, 92–93
immunohistochemistry, 93–95
variants, 95–96
ADXS-PSA, 442
African Americans. See Race/ethnic disparities in prostate cancer
AKR1C3, 222
AKT, 192, 200
coclincial trial project targeting, 369–370
historical perspective in prostate cancer, 186–187
AMPK, therapeutic targeting, 384
Androgen receptor (AR)
  abnormalities in prostate cancer, 2–3
castration resistance mechanisms
gen expression amplification, 239
gen mutations, 239
overview, 238–239
splice variants, 239–240
coregulators, 225–226
DNA repair cross talk, 279–280, 288
history of study in prostate cancer, 184–186, 217
ligand-independent activation, 227–228
maturation and folding, 238
prostate development, 17–19, 25
signaling
  action, 226–227
cross talk, 222–228
modeling in mouse, 330
prereceptor modulation, 219–220
structure, 222–225, 236–237
therapeutic targeting
  chaperones, 241, 243
  combination strategies, 245–246
coregulators, 240–242
  genomic interplay with other receptors, 244–245
  non-ligand-binding domain targeting, 243–244
transcriptional activation, 222–225, 236–237
transcriptional maintenance of normal prostate identity, 147–148
Androgen-independent prostate cancer.
  See Castration-resistant prostate cancer
Androstenedione (AD), synthesis, 218–219
APC, 166, 169–170, 199, 399
AR. See Androgen receptor
ARN-509, 239
ASTX-727, 173
Atezolizumab, 441
ATM, 277, 281–282
  mouse models of prostate cancer, 330
mutations in prostate cancer, 65
ATRX, 164
AURKA, 268
AUY922, 245
Axl, 306

B
Basal cell carcinoma, prostate, 97–98
Base excision repair (BER), 276–277
BCL-2, 316
BCL-XL, 316
BER. See Base excision repair
β-catenin, prostate development, 20–22
Biomarkers, prostate cancer
  diagnosis and screening, 169–170, 398–399
disease burden and treatment response, 171
eyearly detection, 394–397
metabolomics for discovery, 384–385
overview, 168–169
prognosis, 399–401
prospects for study, 305
risk stratification and surveillance, 170–171
targeted therapeutics, 402–405
BMP. See Bone morphogenetic protein
Bone metastasis. See Metastasis, prostate cancer
Bone morphogenetic protein (BMP), prostate development role, 23–24
Bone scintigraphy, prostate cancer metastasis, 423–424
BRAF
  mouse models of prostate cancer, 339–340
BRCA1, 62–63, 65, 277–278, 281, 283, 288, 397
BRD4, 173
BRIP1, 277
BRN2, 257–258

C
CAE. See Cancer-associated fibroblast
Calcium intake, prostate cancer risk studies

© 2019 by Cold Spring Harbor Laboratory Press. All rights reserved.
Index


D

DDSP, See DNA damage secretory program Dehydroepiandrosterone (DHEA) prostate cancer synthesis, 220–221 synthesis, 218–219 Denosumab, 319 DHEA, See Dehydroepiandrosterone DHT, See Dihydrotestosterone Dihydrotestosterone (DHT) prostate cancer synthesis, 220–221 synthesis, 218–219 DKK, 316 DLL3, 268–269 DNA damage secretory program (DDSP), 302 DNA methylation, See Epigenetics, prostate cancer DNA methyltransferase, isoforms, 161

© 2019 by Cold Spring Harbor Laboratory Press. All rights reserved.
DNA repair
androgen receptor cross talk, 279–280, 288
coclinical trial project targeting, 369–370
defects in prostate cancer
advanced prostate cancer, 282–283
primary prostate cancer, 280–282
risk, 277–279
overview of DNA damage and repair, 276–277
therapeutic targeting
clinical trials, 285–287
kinases, 293
PARP, 283, 288
prospects, 288–289
Dutasteride, chemoprevention, 211–212

E
EMT. See Epithelial-to-mesenchymal transition
Enzalutamide, 239, 245
EPI-001, 243–244
EPI-506, 244
Epidemiology, prostate cancer. See also Race/ethnic disparities in prostate cancer
incidence, 33–34
mortality, 34–36
prospects for study, 4, 44
risk factors
calcium, dairy, and vitamin D studies, 42–43
coffee protection, 43
fish intake studies, 43
height, 39–40
lycopene and tomato product protection, 41–42
obesity, 39
overview, 36–37
physical activity protection, 40
smoking, 40–41
statin protection, 43, 44
total prostate cancer, 37–39
Epigenetics, prostate cancer
castration-resistant neuroendocrine prostate cancer, 260–261
clinical biomarkers for prostate cancer
diagnosis and screening, 169–170
disease burden and treatment response, 171
overview, 168–169
risk stratification and surveillance, 170–171
DNA methylation
detection, 172
overview, 161–164
prostate cancer, 166–167
driver mutations, 165–166
histone modification
overview, 164–165
prostate cancer, 167–168
metabolic rewiring, 381–383
mouse models of prostate cancer, 338
overview of machinery, 159–161
therapeutic targeting, 172–174
Epithelial-to-mesenchymal transition (EMT), 296, 300, 311
ERG, 188, 191–192, 201, 331, 398–399
Ethnicity. See Race/ethnic disparities in prostate cancer
ETS genes
fusions in prostate cancer precursor lesions, 113–114
historical perspective in prostate cancer, 188, 190–194
mouse models of prostate cancer, 326
ETVI
mouse models of prostate cancer, 331
transcriptional reprogramming of prostate cancer, 148, 188, 191–192
ETV4, transcriptional reprogramming of prostate cancer, 148, 188
Exercise. See Physical activity
Extracellular matrix. See Stroma, prostate cancer
EZH2, 164, 168, 173, 200, 260–261, 268, 338

F
FANCA, 282
FANCD2, 281
FAO. See Fatty acid oxidase
FASN. See Fatty acid synthase
Fatty acid oxidase (FAO), therapeutic targeting, 384
Fatty acid synthase (FASN)
prostate cancer alterations, 377
therapeutic targeting, 383
FGF. See Fibroblast growth factor
Fibroblast growth factor (FGF)
prostate development, 21–25
tumor microenvironment, 295
Finasteride, chemoprevention, 4, 210–211
Fish intake, prostate cancer risk studies, 43
FKBP51, 238
FKBP52, 238
FLI1, transcriptional reprogramming of prostate cancer, 148
FOXA1, 227
castration-resistant prostate cancer role, 152
mouse models of prostate cancer, 332
mutation in prostate cancer, 194
prostate cytodifferentiation, 26
FOXA2, 258
FRS2α, prostate development, 23

G
GAS6, 302
GATA2, 237
Genome-wide association study (GWAS), prostate cancer genetics, 52–62
Gleason grade, 99–100
GLUT1, prostate cancer alterations, 382
GSTP1, 120, 166, 169, 399
GWAS. See Genome-wide association study

H
HBP. See Hexosamine biosynthesis pathway
Height, prostate cancer risk studies, 39–40
**Index**

- **Hematopoietic stem cell (HSC),** prostate cancer stroma, 298
- **Hexosamine biosynthesis pathway (HBP),** prostate cancer alterations, 381
- **HGPIN.** See High-grade prostatic intraepithelial neoplasia
- **High-grade prostatic intraepithelial neoplasia (HGPIN) biopsy,** 111
  - chemoprevention studies, 116, 118–119
  - inflammation in development, 119
  - molecular pathways in development, 119–121
  - mouse models, 330–332
  - MYC role, 121–123
  - next-generation sequencing findings, 116
  - overview, 109–111
  - precursor of prostate cancer
    - molecular pathology evidence, 114–115
    - postinvasive intraepithelial carcinoma as cancer precursor comparison, 111–114
- **Histone modification.** See Epigenetics, prostate cancer
- **Histopathology, prostate cancer**
  - Adenocarcinoma
    - advanced or metastatic histopathology, 101
    - diagnostic criteria, 88–92
    - ductal adenocarcinoma, 97
    - histopathological features, 92–93
    - immunohistochemistry, 93–95
    - variants, 95–96
    - basal cell carcinoma, 97–98
    - grading, 99–101
    - intraductal carcinoma, 87–88
    - neuroendocrine carcinoma, 98
    - squamous carcinoma, 97
    - treatment response, 98–99
    - urothelial carcinoma, 97
  - Homologous recombination (HR), 277, 283, 288
  - **HOP,** 238
  - **HOX,** prostate development role, 19–20
  - **HOXB13**
    - castration-resistant prostate cancer role, 152
    - prostate cancer mutations, 52, 63–64, 227
  - **HR.** See Homologous recombination
  - **HSC.** See Hematopoietic stem cell
  - **HSP27,** 243
  - **HSP70,** 238, 243
  - **HSP90,** 238, 245

- **I**
  - **IDH1,** 174, 403
  - **IDH2,** 174
  - **IGF-1.** See Insulin-like growth factor-1
  - **IKBKB,** 193
  - **Imaging.** See specific techniques
  - **Immunocytogenetic cell death,** 444
  - **Immunotherapy.** See specific targets
  - **Inflammation**
    - chemoprevention targeting, 214
    - high-grade prostatic intraepithelial neoplasia role, 119
  - Insulin-like growth factor-1 (IGF-1), 315

- **Intraductal carcinoma, histopathology,** 87–88
  - **ITGB4,** 279

- **K**
  - **KDM6A,** prostate cancer mutations, 116
  - **KLF4,** 163
  - **KMT2C,** 165
  - **KMT2D,** prostate cancer mutations, 116
  - **KRAS,** mouse models of prostate cancer, 339–340

- **L**
  - Linkage analysis, prostate cancer mutations, 52
  - Low-density lipoprotein receptors, prostate cancer alterations, 378
  - **LRP5,** 316
  - **Lycopene** chemoprevention, 212–213
  - prostate cancer risk studies, 41–42
  - **Lynch syndrome, prostate cancer risk,** 63

- **M**
  - **MAGL.** See Monoacylglycerol lipase
  - **Magnetic resonance imaging (MRI),** prostate cancer diagnosis, 418
    - diffusion-weighted imaging, 415, 417
    - dynamic contrast-enhanced imaging, 417
    - endorectal coil, 417–418
    - guided biopsy
      - cognitive fusion prostate biopsy, 419–420
      - in-bore guided biopsy, 420
      - software-based fusion biopsy devices, 420
    - reporting systems, 418
    - T2-weighted imaging, 415
    - **3.0T MRI,** 417–418
    - treatment management
      - active surveillance, 421–422
      - staging, 422–423
      - ultrasound fusion biopsy, 420–421
  - Magnetic resonance spectroscopy imaging (MRSI), metabolic imaging, 385, 417
  - **Matrix metalloproteinases (MMPs),** tumor microenvironment, 295, 298
  - **MBD proteins,** 163, 165, 174
  - **MCL-1,** 316
  - **MECP2,** 163
  - **Metabolism, prostate cancer**
    - biomarker discovery, 384–385
    - cocrilical trial project targeting, 370–371
    - derangements
      - amino acid metabolism, 378
      - glucose metabolism, 376
      - hexosamine pathway, 381
      - lipid metabolism, 376–379
      - one-carbon metabolism, 378, 380–381
    - diet and systemic metabolism effects on metabolome, 381

© 2019 by Cold Spring Harbor Laboratory Press. All rights reserved.
imaging, 385–387
rewiring as integrator of genetic and epigenetic alterations, 381–383
therapeutic targeting, 383–384

Metastasis, prostate cancer
bone
experimental models, 317–318
management, 318
mechanisms, 314–316
epidemiology, 310
models, 311–312
mouse models, 338–340
residual disease and dormancy, 312–314
seed and soil hypothesis, 311
soft tissue, 316–317
steps, 310–311

MicroRNA, osteoclastogenesis role, 316
MLH1, 282
MMP7, genome-wide association study, 53
MMPs. See Matrix metalloproteinases
Monoacylglycerol lipase (MAGL), prostate cancer alterations, 377, 381

Mortality, prostate cancer, 1, 34–36
Mouse models, prostate cancer. See also Coclinical trial project
androgen receptor signaling modeling, 330
castration-resistant neuroendocrine prostate cancer, 262, 264–265
epigenetic regulators, 338
gene expression targeting in prostate, 329
gene targets, 326–327, 330
metastasis, 338–340
MYC activation, 332–333
overview, 325–326
premalignant and early-stage cancer, 330–332
prospects, 340–342
prostate comparison with humans, 328–329
PTEN loss of function, 333–337
TP53 defects, 337–338
WNT defects, 338
MRI. See Magnetic resonance imaging
MRSl. See Magnetic resonance spectroscopy imaging
MSH2, 63, 282, 404
MSH6, 404
MSMB, genome-wide association study, 54
mTOR
coclinical trial project targeting, 368–369
glutamine control of mTORC1 signaling, 378
MYC
castration-resistant neuroendocrine prostate cancer role, 257
castration-resistant prostate cancer role, 153
high-grade prostatic intraepithelial neoplasia and prostate cancer role, 117, 119, 121–123
historical perspective in prostate cancer, 186–187
metabolic rewiring, 382–383
mouse models of prostate cancer, 330, 332–333, 339
neuroendocrine prostate cancer role, 200
therapeutic targeting, 268
transcriptional reprogramming of prostate cancer, 149–150

N
NBS1, 64, 277
NER. See Nucleotide excision repair
Neuroendocrine prostate cancer, 98, 199–200
castration-resistant prostate cancer. See Castration-resistant neuroendocrine prostate cancer inducers, 256–257
neuroendocrine cells in prostate cancer, 256
Neuron specific enolase (NSE), 256
NHEJ. See Nonhomologous end joining
Nkx3.1
history of study in prostate cancer, 184
mouse models of prostate cancer, 326, 331, 340
prostate development, 21, 25
transcriptional maintenance of normal prostate identity, 146–147
Noggin, prostate development, 24
Nonhomologous end joining (NHEJ), 277
Nonsteroidal anti-inflammatory drugs (NSAIDs), chemoprevention, 213
NSAIDs. See Nonsteroidal anti-inflammatory drugs
NSD2, 338
NSE. See Neuron specific enolase
Nucleotide excision repair (NER), 277

O
Obesity, prostate cancer risk studies, 39
Oct1, 237
OGX-427, 243
Olaparib, 443
Organogenesis. See Prostate
Organoid
castration-resistant neuroendocrine prostate cancer, 265, 267
culture model of prostate cancer, 131–132, 355–357

P
p53. See TP53
p63
prostate development, 22
transcriptional maintenance of normal prostate identity, 147
P160, 226
PARP
inhibitors, 280, 282–283, 288, 341, 403, 443–444
prostate cancer studies, 279–280
Patient-derived explant (PDE)
generation, 354–355
overview, 354
proliferation index, 355

© 2019 by Cold Spring Harbor Laboratory Press. All rights reserved.
Index

Patient-derived xenograft (PDX)
- bone metastasis model, 317–318
- castration-resistant neuroendocrine prostate cancer, 265, 267
- disease stage-specific models, 352–354
- limitations, 354
- overview, 351–352
- tissue sources, 353
- transplant, 352–353

PCA3, early detection of prostate cancer, 397

PD-1
- immune escape in cancer, 438–440
- therapeutic targeting, 403, 405, 440–445

PDE. See Patient-derived explant

PD-L1
- expression in prostate cancer, 440
- immune escape in cancer, 438–440
- therapeutic targeting, 403, 405, 440–445

PDX. See Patient-derived xenograft

Pebrolizumab, 441–442

Pentose phosphate pathway, prostate cancer alterations, 376

PET. See Positron emission tomography

Physical activity, prostate cancer risk studies, 40

PIC. See Postinvasive intraepithelial carcinoma

Positron emission tomography (PET)
- metabolic imaging of prostate cancer, 385–387, 425–427
- prostate-specific membrane antigen, 427–430

Postinvasive intraepithelial carcinoma (PIC), prostate cancer precursor, 111–114

PP1ase, 238

PREX1, 279

Prostate
- Anatomy
  - human, 9–10
  - mouse, 12
- gene expression targeting in mouse, 329
- histology
  - human, 10–12
  - mouse, 12–14
- prostate epithelium, 131
- oncogenic transformation susceptibility, 1–2
- organogenesis
  - budding and branching morphogenesis, 22–25
  - cancer significance, 26–27
  - cytodifferentiation, 25–26, 133
  - initiation and identity, 17–22
  - overview, 16–17
- Prostate-specific antigen (PSA)
  - early detection of prostate cancer, 394–397
  - limitations as biomarker, 4
- Prostate-specific membrane antigen (PSMA), positron emission tomography, 427–430

Prostate stem cell
- adult progenitor cells
  - basal progenitor cells, 134
  - localization, 134
  - luminal progenitor cells, 134–135
- overview, 133

markers, 137
- prostate cancer cell origin identification, 135–136
- Prostatic intraepithelial neoplasia. See High-grade prostatic intraepithelial neoplasia
- PROSTVAC-V/E, 442

Protasphere, culture model of prostate cancer, 355–357

PSA. See Prostate-specific antigen

PSMA. See Prostate-specific membrane antigen

PTEN, 256
- castration-resistant neuroendocrine prostate cancer genomic alterations, 258
- diagnostic biomarker, 399
- historical perspective in prostate cancer, 186, 192, 194
- loss in prostate cancer precursor lesions, 113–114
- mouse models of prostate cancer, 330, 333–337
- prognostic biomarker, 399–401
- prostate cytodifferentiation, 26
- targeted therapeutics, 402–403

PTGS2, 169

R

Race/ethnic disparities in prostate cancer
- ancestral genome role, 75
- biomarker considerations, 78–79
- elimination, 80–81
- genetic studies, 75–78
- health care and health status, 79–80
- metrics, 71–74
- residential factors, 79
- risk factors, 79

RAD51B, genome-wide association study, 53

RAD51C, 279, 281–282

RAD54B, 279, 282

RANKL, 315–316

Ranolazine, 384

RARB, 169

RASSF1A, 166, 169–170

RB
- castration-resistant neuroendocrine prostate cancer genomic alterations, 258
- castration-resistant prostate cancer role, 152–153
- historical perspective in prostate cancer, 184
- mouse models of prostate cancer, 330, 338–339

REST, 256

Restriction fragment length polymorphism (RFLP),
  - historical perspective in prostate cancer, 183–184

RFLP. See Restriction fragment length polymorphism

ROCK2, 279

S

S-Adenosylmethionine (SAM), prostate cancer alterations, 380

SAM. See S-Adenosylmethionine

Sarcosine dehydrogenase (SARDH), prostate cancer alterations, 380–381

SARDH. See Sarcosine dehydrogenase

© 2019 by Cold Spring Harbor Laboratory Press. All rights reserved.
Selenium, chemoprevention, 212
Serotonin, neuroendocrine cells in prostate cancer, 256
Shh, prostate development, 25
Single nucleotide polymorphism (SNP), prostate cancer genetics, 52–62, 188
Single-photon emission computed tomography (SPECT), prostate cancer, 424
SMAD4, mouse models of prostate cancer, 340
Smoking, prostate cancer risk studies, 40–41
Snail2, 256
SNP. See Single nucleotide polymorphism
SOST, 316
SOX2, 265
Sox9, prostate development, 24–25
SOX11, 265
Soy, chemoprevention, 213
SPDEF, 260
SPECT. See Single-photon emission computed tomography
Spheroid, culture model of prostate cancer, 355–357
SPOP, 226
SPOP, mouse models of prostate cancer, 326, 331–332
prostate cancer mutations, 116, 194, 196, 198
Squamous carcinoma, prostate, 97
SRC1, 226
SRC2, 226
SRC3, 226
SREBP-2, prostate cancer alterations, 378
Statins
chemoprevention, 213–214
prostate cancer risk studies, 43, 44
Stem cell. See Cancer stem cell; Hematopoietic stem cell; Prostate stem cell
Stroma, prostate cancer
cell types
cancer-associated fibroblasts, 295–297
vascular cells, 297–298
drug delivery and efficacy barriers, 300
prospects for study, 303
protumorigenic damage responses, 302
tumor microenvironment, 294–295
tumor microenvironment protective niches, 301–302
T
Telomere, high-grade prostatic intraepithelial neoplasia findings, 120–121
Testosterone, synthesis, 218–219
TET, 163
Tfm, 19
TGF-β. See Transforming growth factor-β
TMPRSS2:ERG translocation, 3, 78–79, 98
androgen receptor signaling, 226–227
castration-resistant neuroendocrine prostate cancer genomic alterations, 258, 260
eyearly detection of prostate cancer, 397
heterogeneity of prostate cancer, 192–193
high-grade prostatic intraepithelial neoplasia, 113–116, 118–119
historical perspective in prostate cancer, 188, 190–193
mouse models of prostate cancer, 326, 331
transcriptional reprogramming of prostate cancer, 148–149
TNF-α. See Tumor necrosis factor-α
TOP2B, 193
Toremifene, chemoprevention, 213
TP53, 3, 152–153, 184, 194
castration-resistant neuroendocrine prostate cancer genomic alterations, 258
mouse models of prostate cancer, 330, 337–338
Transforming growth factor-β (TGF-β), 23–24, 315–316, 339
Transrectal ultrasound (TRUS), prostate cancer, 414–415
Trimetazidine, 384
TRUS. See Transrectal ultrasound
Tumor microenvironment. See also Stroma, prostate cancer
prospects for study, 303
prostate cancer, 294–295
protective niches, 301–302
protumorigenic damage responses, 302
Tumor necrosis factor-α (TNF-α), 315
TV-2640, 383
Twist1, 256
Tyro3, 306
U
Ultrasound. See Transrectal ultrasound
Urothelial carcinoma, prostate, 97
V
Vascular endothelial growth factor (VEGF), prostate cancer stroma, 297
VWF, 280
VCAM-1, 315
VEGF. See Vascular endothelial growth factor
Vimentin, 256
Vitamin D, prostate cancer risk studies, 42–43
Vitamin E, chemoprevention, 212
W
WNT
castration-resistant prostate cancer, 316
coclinical trial project targeting, 370
mouse models of prostate cancer, 338
prostate development, 20–22
X
Xenograft. See Patient-derived xenograft
XRCC2, 279
XRCC3, 279
Z
Zeb1, 256