

INDEX

A

- ABC transporters. *See* ATP-binding cassette (ABC) transporters
- Absolute lymphocyte count (ALC)84
- aCGH. *See* Array comparative genome hybridization (aCGH)
- Acral melanoma.....202
- ACT. *See* Adoptive cell transfer (ACT)
- Actin-related protein 2/3 complex,
subunit 2 (ARPC2).....263–264
- ADAM. *See* A disintegrin and metalloproteinase (ADAM)
- A disintegrin and metalloproteinase (ADAM)463
- Adjuvant therapy64–66
- biomarkers37–38
- high-dose interferon alpha 2b.....12–13
- in high-risk resected melanoma
- COMBI-AD58, 62
- dabrafenib58, 61
- EORTC 18071.....60, 61
- EORTC 18081.....57
- IFN- α 48–57
- ipilimumab.....61
- MAGE-A3 vaccine57, 60, 61
- RAF/MEK inhibitors.....61–62
- vemurafenib59, 61
- indications for.....46–47
- pegylated interferon alpha 2b12–13
- predictive and prognostic biomarkers
- autoimmunity, development of63–64
- MIA64
- MTAP protein expression.....64
- primary tumor ulceration.....63
- unresectable stage III and IV melanoma14
- Adoptive cell transfer (ACT)317
- Adverse events of special interest (AEOSI)83–84
- AEOSI. *See* Adverse events of special interest (AEOSI)
- AHH. *See* Ancestral HLA haplotypes (AHH)
- AJCC. *See* American Joint Committee
on Cancer (AJCC)
- Alanine transaminase (ALT)413
- ALC. *See* Absolute lymphocyte count (ALC)
- Alkaline phosphatase (AP).....88, 90, 413–415,
611, 612, 614
- AlphaImager™ 2200 documentation system.....530
- ALT. *See* Alanine transaminase (ALT)
- American Joint Committee on Cancer
(AJCC)177, 325, 398
- American Society of Clinical Oncology
(ASCO)389–390
- Amicon Ultra filter650
- Ancestral HLA haplotypes (AHH)355–357
- Antibody-beads coupling reactions510
- Antigen presenting machinery (APM).....355
- Anti-programmed cell death-1 (anti-PD1) therapy36
- Antitumor immunity and melanoma
- antigen recognition290–291
- immunogenic properties292
- immunologic tolerance292
- tumor surveillance hypothesis289–290
- AP. *See* Alkaline phosphatase (AP)
- APM. *See* Antigen presenting machinery (APM)
- AQUA. *See* Automated QUantitative Analysis (AQUA)
- ARPC2. *See* Actin-related protein 2/3 complex,
subunit 2 (ARPC2)
- Array comparative genome hybridization (aCGH)470
- on FFPE tissue samples (*see* Formalin-fixed paraffin-
embedded (FFPE))
- primary melanomas201
- ASCO. *See* American Society of Clinical Oncology
(ASCO)
- Aspartate transaminase (AST)413
- AST. *See* Aspartate transaminase (AST)
- ATP-binding cassette (ABC) transporters502
- Atypical melanocytic proliferation (AMP).....29
- Atypical Spitz tumors (ASTs)29, 203, 206, 207
- Automated QUantitative Analysis (AQUA)184, 231,
235, 238, 242–244, 252

B

- BACs. *See* Bacterial artificial chromosomes (BACs)
- Bacterial artificial chromosomes (BACs).....201
- B and T cell attenuator (BTLA).....370
- BAP-1 gene. *See* BRCA1-associated protein
(BAP-1) gene
- B7-H family members. *See* B7 homologues (B7-H)
family members
- B7 homologue 1 (B7-H1).....109, 316, 368–374, 377
- B7 homologue (B7-DC).....108, 316, 368–370

B7 homologues (B7-H) family members	
accessory signals.....	368
cell culture and treatment modalities.....	376
chemicals.....	375–376
clinical relevance.....	371–372
costimulatory and coinhibitory pathways	
characteristic of.....	368–370
tumor microenvironment.....	372–373
FACS	
intracellular staining.....	377
membrane staining.....	376–377
preparation of cells, flow cytometry.....	376
heterogeneous expression and function.....	370–371
immune checkpoints.....	375
immunoreagents.....	375
impaired antitumor immunity.....	373–374
intracellular levels.....	371, 378
materials and flow cytometers.....	376
molecular mechanisms.....	374–375
permeabilization.....	378
T cell receptor (TCR)-CD3.....	368
Biomarker	
adjuvant interferon.....	37–38
cell cycle proteins.....	186–187
cell lines and animal models.....	669
chemokines and receptors.....	185–186
classification of.....	178–179
clinical trials	
biomarker-guided therapy.....	675
biomarker-strategy design.....	674–676
herceptin therapy.....	675
MINDACT trial.....	676
phase I and II.....	673
phase III biomarker trial protocol.....	674, 675
T cell therapies.....	673
Cox model.....	668
C-reactive protein.....	183
diagnostically challenging lesions,	
FISH/CGH in.....	29–30
epigenetic biomarkers.....	190
galectin-3.....	188
histopathologic criteria.....	27
ICC.....	670, 671
identification methods	
2-dimensional gel electrophoresis.....	181
ELISA.....	180
immunohistochemistry.....	180
MALDI-TOF-MS.....	181
RT-PCR.....	180
tissue microarrays.....	180
for immunotherapy.....	36–37
integrins.....	188
intracellular adhesion molecules.....	188–189
lactate dehydrogenase.....	183
melanin-related metabolites	
L-DOPA/L-tyrosine.....	180–181
5-S-cysteinylDopa.....	189
metabolites.....	190
MIA.....	187
MMPs.....	185
molecular biomarkers, clinical	
applicability of.....	190–192
monitoring census.....	178
predicting recurrence/nodal metastasis	
tumor infiltrating lymphocytes.....	29
ulceration and mitosis.....	28–29
predictive marker.....	667, 668
primary cutaneous tumors.....	28
progression of disease and method	
of extraction.....	181, 182
purely prognostic marker.....	667–668
quantification.....	237–238
antigen retrieval.....	239–240
Aperio Scanscope™ CS brightfield platform,	
quantitative chromogenic IHC.....	240–242
primary anti-biomarker antibody selection and	
validation.....	238–239
QIF/AQUA®.....	242–244
REMARK criteria.....	191, 244
reproducibility study.....	670
S100β.....	183–184
stored, clinically annotated samples.....	671–673
stored patient samples.....	669–670
surrogate biomarkers.....	669
targeted therapy, metastatic disease	
BRAF mutation test.....	31–34
CKIT mutations.....	35
GNQA/GNA11 mutations.....	35–36
NRAS mutations.....	35
ultimate clinical context.....	668
unknown primary melanomas.....	30
VEGF.....	184
BRAF inhibitor (BRAFi).....	100–101, 163–164
cfDNA BRAF mutations.....	102–103
chemotherapy.....	104–105
HDAC inhibitors.....	106
ipilimumab.....	103–105
MEK1 mutations.....	166–167
clinical therapeutic implication.....	167
detection of.....	170, 172
PCR amplification and mutational	
analysis.....	167–169
mutant BRAF alterations.....	166
NRAS mutations	
clinical therapeutic implication.....	165–166
detection of.....	170, 171
PCR amplification and mutational analysis.....	167–169
quantitative PCR.....	167, 168

RTK	
clinical therapeutic implication.....	164–165
qPCR, detection of.....	169–170
tumor resistance	
ERK reactivation.....	19–21
extrinsic mechanisms of.....	19
BRAF ^{V600E} mutation	
allelic-specific PCR.....	125
BRAF-directed therapy.....	118–119
cDNA synthesis	
material.....	127
methods.....	130
mass spectrometry.....	125
materials required	
cell lines, tissue and peripheral blood	
acquisition.....	126
densitometry.....	128
PCRs and restriction digestions.....	127–128
total RNA isolation.....	127
melanoma tumor biopsies.....	121–123
PBLs.....	122–124
PBLs, isolation of	
materials.....	126
methods.....	129
PCR, locked oligonucleotides.....	125–126
polyacrylamide gel electrophoresis	
materials.....	128
methods.....	132–133
protocol	
schematic outline of.....	119–120
validation of.....	120, 121
RNA isolation, Trizol method.....	129–130
RT-PCR.....	124–125
18S RNA RT-PCR	
materials.....	127
methods.....	130
TspR1 digestion.....	120–122, 131
Xba1 digestion.....	132–133
BRCA1-associated protein (BAP-1) gene.....	36
BTLA. <i>See</i> B and T cell attenuator (BTLA)	
C	
Cancer immunotherapy monitoring. <i>See</i> Single cell network profiling (SCNP)	
Cancer initiating cells (CICs).....	524
Cancer testis antigens (CTAs).....	317
Cancer vaccine immunologic monitoring, ELISPOT assay. (<i>See</i> Enzyme-linked immunospot (ELISPOT) assay)	
Carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM-1).....	188, 189
CART. <i>See</i> Classification and Regression Tree (CART)	
CD20.....	502–503
CD34+/CD271+ subpopulation.....	504
CD34+/CD271-subpopulation.....	504
CDK. <i>See</i> Cyclin-dependent kinase (CDK)	
CDKN2A. <i>See</i> Cyclin-dependent kinase inhibitor 2A (CDKN2A)	
CD271/NGFR/p75 neurotrophin receptor.....	504
CD133/prominin-1.....	503–504
CEACAM-1. <i>See</i> Carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM-1)	
CGH. <i>See</i> Comparative genomic hybridization (CGH)	
Chemotherapy.....	3
BRAF inhibitors.....	104–105
ipilimumab.....	112–113
Chest radiograph (CXR).....	417
Chondroitin sulfate proteoglycan 4 (CSPG4)	
acral lentiginous melanoma.....	525
cell culture.....	526
cell lines.....	526
cellular and molecular heterogeneity.....	524, 534
cutaneous melanoma.....	525
HMW-MAA.....	523
IHC staining	
FFPE melanoma tissue sections.....	531–533
frozen melanoma tissue sections.....	531
score.....	533
section preparation, pelleted cells.....	530–531
monoclonal antibodies.....	528
patient lesions.....	525
RT-PCR	
first-strand cDNA synthesis.....	529–530
Gene Amp PCR system.....	530
solutions and reagents.....	526
total RNA extraction.....	528–529
trypsin.....	533
in vitro findings.....	524
Chromosomal copy number analysis	
CGH (<i>see</i> Comparative genomic hybridization (CGH))	
FISH (<i>see</i> Fluorescence in situ hybridization (FISH))	
in melanocytic tumors.....	199–200
CICs. <i>See</i> Cancer initiating cells (CICs)	
Circulating tumor cells (CTCs)	
acoustic wave detection and data acquisition	
materials.....	657
methods.....	659
antibody-coated magnetic bead.....	515
antibody sensitivity and specificity.....	515
assay features.....	514
detection apparatus	
materials.....	657
methods.....	656, 658
GAPDH (<i>see</i> Glycerinaldehyde-3-phosphate dehydrogenase (GAPDH))	
Kaplan–Meier survival curves.....	515, 516
mRNA biomarkers.....	514

Circulating tumor cells (CTCs) (<i>cont.</i>)	
PBL isolation	
materials	515
methods	518
PCR	
materials	517
methods	520
peripheral blood mononuclear cell layer isolation	
materials	657
methods	660–661
photoacoustics/laser-induced ultrasound	655
photoacoustic waveforms	656
reverse transcription	
materials	516–517
methods	519
RNA extraction	
materials	516
methods	518–519
RNA quantification	
materials	516
methods	519
RT-qPCR	514, 515
sample processing technique	661
samples and clearing system	661, 662
setup preparation and flow cell construction	661
Classification and Regression Tree (CART)	247
CLIA. <i>See</i> Clinical Laboratory Improvement Amendments (CLIA)	
Clinical Laboratory Improvement Amendments (CLIA)	238, 670
Clonogenicity	507, 510
CM. <i>See</i> Cutaneous melanoma (CM)	
Coamplification at lower denaturation temperature (COLD-PCR)	
amplicons and primers	630–631
fast-COLD-PCR	
DNA variant	631
heteroduplex formation	624, 625
methodological approach	624, 625
nested format	636
T _c amplicon	632
thermocycler	633
thermocycling protocol	628–329
full-COLD-PCR	
DNA variant	631
heteroduplex formation	625
interrogated amplicon	625
methodological approach	624, 625
nested approach	637
T _c amplicon	632
thermocycling program	626
thermocycling protocol	629
high resolution melting	635
ice-COLD-PCR	637
critical denaturation temperature	627
DNA variant	631
nested format	637
oligonucleotide	626
thermocycler	633
thermocycling protocol	628
T _m and T _c amplicon	631, 632
low-level mutations	624
MALDI-TOF genotyping	635
next-generation sequencing (NGS)	635
principle of	624, 625
pyrosequencing	635
reagents and equipment	626–627
Sanger sequencing	634–635
standard reagent conditions and concentrations	628
TaqMan genotyping	635
temperature-tolerant (TT)-COLD-PCR	637
critical denaturation temperature	628
cycling conditions	626
DNA variant	631
standard reagent conditions	628
temperature window	633
thermocycling protocol	628–629
T _m and T _c amplicon	631–633
COLD-PCR. <i>See</i> Coamplification at lower denaturation temperature (COLD-PCR)	
Collaborative Ocular Melanoma Study (COMS)	
abdominal ultrasound screening	417
cell type	409
chest radiographic imaging	417
degree of pigmentation	409
LFTs	414
tumor size	409
Combination therapy	
BRAF inhibitors	100–101
cfDNA BRAF mutations	102–103
chemotherapy	104–105
HDAC inhibitors	106
ipilimumab	103–105
immunotherapies	
AJCC/UICC-TNM staging	110
anti-CTLA-4 therapy	108
darleukine	109
immune contexture	110
MAGE-A3 antigen	110–111
oncolytic immunotherapy	109
PD-L1 and PD-L2 expression	108–109
Treg depletors	109
ipilimumab	
anti-PD-1	111–112
chemotherapy	112–113
and predictive markers	106–108
NRAS mutation	101–102
tumor gene profiling	
CDKN2A mutation	98–99
cDNA microarray analysis	99

in identical lesions	99–100
MC1R variant genotypes.....	99
tumor-infiltrating lymphocytes.....	100
Comparative genomic hybridization (CGH)	29–30, 200–201, 208
acral melanoma.....	202
array-based CGH.....	201
blue nevus and blue nevus-like melanoma.....	202–203
chronic sun exposure.....	201
congenital melanocytic nevi.....	204
intermittent sun damage.....	201
materials required	211
metastatic melanoma	204
mucosal melanoma	202
primary melanoma.....	209
Spitz nevus and spitzoid melanoma.....	203
uveal melanomas.....	203–204
COMS. <i>See</i> Collaborative Ocular Melanoma Study (COMS)	
Cox and Gamel-Boag models	401
Cox-Mantel method.....	355
C-reactive protein (CRP).....	183
CSPG4. <i>See</i> Chondroitin sulfate proteoglycan 4 (CSPG4)	
CTAs. <i>See</i> Cancer testis antigens (CTAs)	
CTCs. <i>See</i> Circulating tumor cells (CTCs)	
CTLs. <i>See</i> Cytotoxic T lymphocytes (CTLs)	
CTLA-4. <i>See</i> Cytotoxic T lymphocyte antigen-4 (CTLA-4)	
Cutaneous melanoma (CM)	
clinicopathological staging.....	481
epigenetics (<i>see</i> Epigenetics)	
intra-stage heterogeneity.....	481
mRNA/miRNA signatures.....	482
uveal melanoma (UM).....	397–398
Cutaneous squamous cell carcinomas (cuSCC).....	5
Cyclin-dependent kinase (CDK).....	385
Cyclin-dependent kinase inhibitor 2A (CDKN2A).....	483
Cytotoxic T lymphocyte antigen-4 (CTLA-4)	
absolute lymphocyte count/ALC.....	84, 92–94
activated T cell subpopulations	
materials	87
methods	90
AEOSI	83–84
antigen-specific humoral immune responses, ELISA	
materials	88
methods	90–91
CD4+ and CD8+ T cells	84–85
cell separation and cryopreservation	
materials	87
methods	89
clinical effects of.....	6–7
irAEs.....	83
myeloid-derived suppressor cell.....	86–87
materials	89
methods	92, 93
NY-ESO-1 cancer-testis antigen.....	85–86
peripheral blood collection	
materials	87
methods	89
tumor antigen-specific cellular responses	
intracellular cytokine staining.....	91–92
materials	88–89
tetramer staining.....	91, 92
in vitro stimulation	91
Cytotoxic T lymphocytes (CTLs)	288
D	
DAB. <i>See</i> 3,3'-Diaminobenzidine (DAB)	
Dako EnVision™+ System	528
Damage-associated molecular pattern molecules (DAMPs)	
ATP.....	545–546
cathelicidin	546
cellular injury.....	538
defensins	546
galectins.....	544–545
heat shock protein	545
HMGB1.....	538
carcinogenesis	542
functions and roles.....	541–542
highly conserved region	542
melanoma inhibitory activity.....	542
platinum-based chemotherapy.....	542–544
quercetin	544
hyaluronic acid.....	538
nucleolin.....	546
pathogen recognition receptors.....	538
RAGE	547
role of.....	546
soluble RAGE	548
S100B and proteins	539–541
TIM-3	548–549
toll-like receptors (TLR)	549
DAMPs. <i>See</i> Damage-associated molecular pattern molecules (DAMPs)	
2DE. <i>See</i> 2-Dimensional gel electrophoresis (2DE)	
Deparaffinize	270–271
3,3'-Diaminobenzidine (DAB)	282
3, 4-Dihydroxyphenylalanine (L-DOPA)	189–190
2-Dimensional gel electrophoresis (2DE)	181
L-DOPA. <i>See</i> 3, 4-Dihydroxyphenylalanine (L-DOPA)	
E	
ELISPOT assay. <i>See</i> Enzyme-linked immunospot (ELISPOT) assay	
Enzyme-linked immunospot (ELISPOT) assay.....	80–81, 180

Enzyme-linked immunospot (ELISPOT) assay (<i>cont.</i>)	
antigen-specific humoral immune responses	
materials	88
methods	90–91
clinical trial results	72
coating and incubation steps	72–73
coating plates	75
development of	71–72
ELISPOT plate, blocking of	76
IFN- γ development	78–80
materials	73–74
equipment	73
reagents	74–75
PBMC, thawing and adjusting	76
plating cells	77
reagents, preparation of	75–76
Epigenetics	
bisulfite DNA modification	
materials	489
methods	491
cells isolation	
materials	488
methods	490, 491
definition	482
DNA hypermethylation	483–484
DNA hypomethylation	484
DNA methylation	482–483
genomic DNA extraction	
materials	488–489
methods	489
LINE-1	
methylated and unmethylated standards	489–490, 492–493
qMSP analysis	490, 493–496
repetitive elements	484, 487–488
prognostic markers	
MGMT methylation	485
MINT31	485
PTEN methylation	484
TSLC1 methylation	484
whole-genome methylation profile	486
ERBB4. <i>See</i> Receptor tyrosine kinase ERBB4 mutation analysis (ERBB4)	
ESMO. <i>See</i> European Society of Medical Oncology (ESMO)	
European Society of Medical Oncology (ESMO)	178
ExoQuick precipitation	642
Extravascular migratory metastasis	337
F	
FACS. <i>See</i> Fluorescence-activated cell sorting (FACS)	
Familial atypical multiple mole and melanoma (FAMMM) syndrome	384
FAMMM syndrome. <i>See</i> Familial atypical multiple mole and melanoma (FAMMM) syndrome	
FDA-approved timeline, melanoma therapy	11, 12
FFPE. <i>See</i> Formalin-fixed paraffin-embedded (FFPE)	
FHWM. <i>See</i> Full width at half maximum (FHWM)	
Fibronectin 1 (FN1)	264–265
Fine needle aspiration (FNA)	682
Fine needle aspiration biopsy (FNAB)	
data analysis software	451
DNA based prognostic markers	
FISH	443
microsatellite analysis	444–446
MLPA	443–444
SNP arrays	446–448
DNA isolation kits	449
genomic DNA isolation	451
intraocular biopsy samples	455
microsatellite analysis	
materials	449–450
methods	452–453
prognostic markers of	442
SNP arrays	
materials	450–451
methods	453–455
UM samples (<i>see</i> Uveal melanoma (UM))	
First-strand cDNA synthesis	529–530
FISH. <i>See</i> Fluorescence in situ hybridization (FISH)	
Flow cytometry analysis	508–509
Fluorescence-activated cell sorting (FACS)	375, 507
intracellular staining	377
membrane staining	376–377
preparation of cells, flow cytometry	376
Fluorescence in situ hybridization (FISH)	29–30, 208
for FFPE (<i>see</i> Formalin-fixed paraffin-embedded (FFPE))	
materials required	209–211
primary melanoma	210
and prognosis	207
sensitivities and specificities	205–206
in spitzoid melanocytic neoplasms	206–207
FN1. <i>See</i> Fibronectin 1 (FN1)	
FNA. <i>See</i> Fine needle aspiration (FNA)	
FNAB. <i>See</i> Fine needle aspiration biopsy (FNAB)	
Formalin-fixed paraffin-embedded (FFPE)	
aCGH on	
array assembly and preparation	217, 218
array, cassette and scan	220
array for scanning	219–220
Bioprime Total FFPE DNA labeling	
module	215–216
Bioprime Total FFPE DNA purification	
module	216, 217
digestion and denaturation	213
fluorescent labeling	215–216
labeled genomic DNA, preparation of	218
microarray hybridization	219

microdissect tumor cells, slides213
 Nanodrop software217
 Phenol:Chloroform:Isoamyl alcohol.....214
 QIAmp DNA FFPE tissue kit214–215
 Qubit fluorometer.....215
FISH
 digestion and denaturation212
 post-hybridization wash212
 slide analysis212–213
 Vysis HYBrite instrument212
 IHC staining, D2-40 antibody282
 tissue blocks469
 Full width at half maximum (FWHM)555

G

Galectin-3 (gal-3).....188
 Gamma-glutamyl transferase (GGT).....413–414
 GAPDH. *See* Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)
 Gastrointestinal stromal tumor (GIST)141
 15-Gene expression profile (GEP)
 BAP1 mutations431
 biological insights429, 430
 chromosomal abnormalities428
 class 2 tumors430
 GIST Support Vector Machine learning algorithm432
 real-time PCR
 materials431
 methods435–436
 RNA preparation
 FFPE samples.....434–435
 needle biopsy samples432–433
 snap-frozen tumor samples434
 SDS software432
 support vector machine (SVM)436
 transition from chromosomal markers428–429
 tumor tissue preservation and RNA isolation431
 GenoMEL. *See* Melanoma Genetics Consortium (GenoMEL)
 Genome-Wide Association Studies (GWAS).....388
 Genotyping Console Software457
 GGT. *See* Gamma-glutamyl transferase (GGT)
 GIST. *See* Gastrointestinal stromal tumor (GIST)
 Glutamate receptor subunit epsilon-1 (GRIN2A)464
 Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)521
 GMCSF. *See* Granulocyte macrophage colony stimulating factor (GMCSF)
 GNA11. *See* G protein coupled receptor alpha subunit (GNA11)
 GNAQ. *See* G protein coupled receptor alpha subunit (GNAQ)
 GPCR. *See* G-protein-coupled receptors (GPCRs)
 GPR98. *See* G protein-coupled receptor 98 (GPR98)

G protein-coupled metabotropic glutamate receptor (GRM3)463–464
 G protein-coupled receptor 98 (GPR98)463
 G protein coupled receptor alpha subunit (GNA11)35–36
 G protein coupled receptor alpha subunit (GNAQ)35–36
 G-protein-coupled receptors (GPCRs).....463
 GP100 vaccine.....14
 Granulocyte macrophage colony stimulating factor (GMCSF).....312
 GRIN2A. *See* Glutamate receptor subunit epsilon-1 (GRIN2A)
 GRM3. *See* G protein-coupled metabotropic glutamate receptor (GRM3)
 GWAS. *See* Genome-Wide Association Studies (GWAS)

H

HDAC inhibitors. *See* Histone deacetylase (HDAC) inhibitors
 HD-IL2. *See* High-dose bolus interleukin-2 (HD-IL2)
 Heat shock proteins (HSPs)545
 Heparin648
 Herceptin therapy.....675
 High-dose bolus interleukin-2 (HD-IL2)14–16
 High mobility group box 1 protein (HMGB1)538
 carcinogenesis542
 functions and roles541–542
 highly conserved region542
 melanoma inhibitory activity542
 platinum-based chemotherapy.....542–544
 quercetin544
 High molecular weight-melanoma associated antigen (HMW-MAA)496, 523
 Histone deacetylase (HDAC) inhibitors106
 Histone demethylase jumonji ARID (JARID1B).....504
 HLA. *See* Human leukocyte antigen (HLA)
 HMGB1. *See* High mobility group box 1 protein (HMGB1)
 HMW-MAA. *See* High molecular weight-melanoma associated antigen (HMW-MAA)
 HSPs. *See* Heat shock proteins (HSPs)
 Human leukocyte antigen (HLA)
 amplifiable DNA, S14 PCR.....362–364
 ancestral haplotypes.....355–357
 blood and tissue sample collection358
 blood-derived DNA
 materials358
 methods361
 cancer patients357–358
 clinical correlations363–364
 conventional therapy.....357
 DNA extraction
 materials358
 methods359–361
 DNA samples364

Human leukocyte antigen (HLA) (<i>cont.</i>)	
equipment.....	359
FFPE-derived DNA	
materials	359
methods	361–363
immunological treatments	354
lung, head and neck tumors	354
MHC	354–355
molecular mechanisms.....	358
PCR product	364
SDS polyacrylamide gel electrophoresis	359
tumor-associated antigens	354
I	
ICAM-1. <i>See</i> Intracellular adhesion molecule-1 (ICAM-1)	
ICC. <i>See</i> Intraclass correlation coefficient (ICC)	
ICOS. <i>See</i> Inducible costimulator (ICOS)	
IDO. <i>See</i> Indoleamine-2,3-dioxygenase (IDO)	
IFN- γ . <i>See</i> Interferon gamma (IFN- γ)	
IHC. <i>See</i> Immunohistochemistry (IHC)	
Immune-related adverse events (irAEs)	83
Immunohistochemistry (IHC)	602, 603
biomarkers	180
diagnostic and prognostic markers	
ABC-HRP staining Kit.....	263
antibodies and dilutions	262–263
antigen retrieval, pressure cooking	271–273
ARPC2 immunostaining	263–264, 272
Avidin Biotin Blocking Kit.....	263
dehydration, graded alcohols	271
deparaffinize and rehydrate.....	270–271
FN1	264–265, 272
IHC scoring system	271–272
IHC staining	262
molecular diagnostic markers.....	259–260
molecular prognostic markers	260–261
multimarker diagnostic assay	260
multimarker prognostic assay.....	261
NCOA3	266–267, 272
RGS1.....	267–268, 272
SPP1.....	268–269, 272
WNT2.....	269–270, 272–273
FFPE melanoma tissue sections	531–533
frozen melanoma tissue sections.....	531
quantitative and spatial image analysis (<i>see</i> Quantitative and spatial image analysis)	
scoring	533
section preparation, pelleted cells.....	530–531
S-100 staining	282
Immunosorting	488
Immunotherapy	3–4
AJCC/UICC-TNM staging.....	110
anti-CTLA-4 therapy	108
biomarkers for.....	36–37
BRAF-inhibitors	21
darleukine	109
immune contexture	110
MAGE-A3 antigen.....	110–111
oncolytic immunotherapy.....	109
patient selection for	
CTLA-4	15, 16
HD IL-2.....	14–16
PD-L1 expression.....	16–17
PD-L1 and PD-L2 expression	108–109
Treg depletors.....	109
Indoleamine-2, 3-dioxygenase (IDO).....	312
Inducible costimulator (ICOS).....	85
Integrins	188
Interferon gamma (IFN- γ).....	78–80
Intracellular adhesion molecule-1 (ICAM-1)	188, 189
Intraclass correlation coefficient (ICC)	670, 671
Ipilimumab	
anti-PD-1.....	111–112
chemotherapy	112–113
FDA-approval timeline	11, 12
<i>vs.</i> GP100 vaccine	14
predictive markers.....	106–108
unresectable stage III and IV melanoma	14
irAEs. <i>See</i> Immune-related adverse events (irAEs)	
Italian Network for Tumor Biotherapy (NIBIT).....	112
J	
JARID1B. <i>See</i> Histone demethylase jumonji ARID (JARID1B)	
K	
Kaplan-Meier method.....	355, 356, 444
KIT. <i>See</i> Tyrosine-protein kinase KIT/CD117 (KIT)	
KIT inhibition, in melanoma	
agarose gel preparation, PCR products.....	156–157
dasatinib	147
DNA extraction, paraffin-embedded	
tissue	155–156, 158
expression, immunohistochemistry.....	140–141
GIST	141
imatinib, clinical trials of	144–146
KIT mutation sequencing.....	158
L576P mutation	141
materials required	153–154
mutational frequency	142–143
mutation sequencing.....	158
nilotinib.....	147–148
patient selection.....	148–151
primary resistance	152
secondary resistance.....	152–153
signaling	139–140
stock solution preparation.....	156
structure of.....	139
sunitinib.....	146–147

L

Lactate dehydrogenase (LDH).....183
LAG3. *See* Lymphocyte activation gene 3 (LAG3)
Largest tumor diameter (LTD)399–400
Laser capture microdissection (LCM).....488
LCM. *See* Laser capture microdissection (LCM)
LDH. *See* Lactate dehydrogenase (LDH)
LFTs. *See* Liver function tests (LFTs)
LI. *See* Lymphatic invasion (LI)
LINE-1. *See* Long interspersed nucleotide element-1 (LINE-1)
Liver function tests (LFTs)
 alkaline phosphatase (AP)413
 ALT413–414
 AST413–414
 COMS reports.....414
 GGT.....413–414
 hepatic metastases.....414, 416
 insensitive markers.....414
 LDH413–414
 metastatic disease.....412
 moureaux.....416
LOH. *See* loss of heterozygosity (LOH)
Long interspersed nucleotide element-1 (LINE-1)
 methylated and unmethylated standards
 materials489–490
 methods492–493
 qMSP analysis
 materials490
 methods493–496
 repetitive elements.....484, 487–488
Loss of heterozygosity (LOH)446
LTD. *See* Largest tumor diameter (LTD)
LVI. *See* Lymphovascular invasion (LVI)
Lymphangiogenesis.....276–277
Lymphatic invasion (LI)
 double staining, D2-40 and S-100 antibodies283–284
 D2-40 staining282–283
 frequency of.....277–279
 lymphovascular invasion
 and DFS/OS280–281
 and sentinel lymph status.....278–280
 materials required
 FFPE.....281–282
 IHC S-100 staining.....282
Lymphatic Vessel Endothelial Receptor 1 (LYVE-1)276, 277
Lymphocyte-activation gene 3 (LAG3)316
Lymphovascular invasion (LVI).....279, 280, 337
LYVE-1. *See* Lymphatic Vessel Endothelial Receptor 1 (LYVE-1)

M

MACS. *See* Magnetic-activated cell sorting (MACS)
MAGE. *See* Melanoma-associated antigen (MAGE) family

MAGE-A3. *See* Melanoma-Associated Antigen 3 (MAGE-A3)
Magnetic-activated cell sorting (MACS)81
Magnetic bead separation.....508
Magnetic Resonance Imaging (MRI).....419
Major histocompatibility complex (MHC)354–355
MALDI-TOF. *See* Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF)
MALDI-TOF-MS. *See* Matrix-assisted desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS)
Mass spectrometric (MS) analysis181
Matrix-assisted desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS).....181
Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF).....624
Matrix metalloproteinases (MMPs)185, 463
MC1R. *See* Melanocortin 1 receptor (MC1R)
MCAM. *See* Melanoma cell adhesion molecule (MCAM)
MDAs. *See* Melanoma differentiation antigens (MDAs)
MDSC. *See* Myeloid-derived suppressor cells (MDSC)
Mean diameter of the ten largest nucleoli (MLN).....405–406
Melanocortin 1 receptor (MC1R)383
Melanocytic tumor of uncertain malignant potential (MELTUMP).....29
Melanoma-Associated Antigen 3 (MAGE-A3)110–111, 514, 520
Melanoma-associated antigen (MAGE) family334
Melanoma cell adhesion molecule (MCAM).....189
Melanoma cell subpopulations
 antibody-beads coupling reactions.....510
 clonogenicity reagents.....507, 510
 enzymatic digestion media506
 FACS.....507
 flow cytometry analysis.....508–509
 isolation and purification505–506
 markers
 ABC transporters502
 CD20.....502–503
 CD271/NGFR/p75 neurotrophin receptor504
 CD133/prominin-1503–504
 JARID1B.....504
 Matrigel/subcutaneous tissues505
 xenografts505
 negative selection, magnetic beads.....508
 phenotypic and functional heterogeneity.....501
 preparation and sorting.....506–507
 Trypan Blue dye exclusion test509
 tumorigenic potential505, 510
 tumor tissue dissociation.....507–508
Melanoma differentiation antigens (MDAs).....317
Melanoma Genetics Consortium (GenoMEL)384, 390

Melanoma immune evasion mechanisms	
clonal anergy-induced tolerance	294–295
immune effector populations	294
melanoma differentiation antigen loss	292–293
NK cell-mediated destruction	293–294
reduced MHC class I expression	293
T cell exhaustion.....	297
Treg cell-mediated immune evasion.....	297–298
tumor-induced immune tolerance	296
tumor-mediated deletion	294
Melanoma immunotherapy. <i>See also</i> Immunotherapy	
ACT (<i>see</i> Adoptive cell transfer (ACT))	
CD25.....	314
classification	313
CTAs	317
CTLA-4 antibodies.....	315–316
IFN- α	314
MDAs	317
MHC class II expression	314
PD-1, PD-L1, and LAG3.....	316
TIL immunobiology.....	313
Treg cells.....	314
Melanoma inhibitory activity (MIA)	64, 187, 542
Melanoma susceptibility genes	
BAP1 locus.....	385–386
CDKN2A pathway	
chromosome 9p21	382
frequency of	385
GenoMEL.....	384
germline mutations.....	384
melanoma incidence areas.....	385
pancreatic cancer.....	384
p14ARF.....	382–383
penetrance of	383
p16INK4a.....	382, 383
population-based analysis	384
proteins coded.....	382
CDK4 pathway.....	385
cell proliferation.....	382
eumelanin	386
GWAS.....	388
management, familial melanoma	389–390
MC1R variants.....	387
melanin.....	382, 386
MITF	387
risk assessment.....	388–389
MELTUMP. <i>See</i> Melanocytic tumor of uncertain malignant potential (MELTUMP)	
Metastatic melanoma	
BRAFV600E mutation (<i>see</i> BRAF ^{V600E} mutation)	
HD IL-2	14–16
histopathological review and macrodissection	468, 469
incidence of.....	117
oncogenic mutations.....	463
treatment algorithm.....	18
WGS approach.....	464, 466
Methylated-in-tumor 31 loci (MINT31)	485
O ⁶ -Methylguanine DNA methyltransferase (MGMT)	
gene hypermethylation.....	483
Methylthioadenosine phosphorylase (MTAP)	64
MGMT gene hypermethylation. <i>See</i> O ⁶ -Methylguanine DNA methyltransferase (MGMT) gene hypermethylation	
MHC. <i>See</i> Major histocompatibility complex (MHC)	
MIA. <i>See</i> Melanoma inhibitory activity (MIA)	
Microphthalmia-associated transcription factor (MITF).....	187, 387
MicroRNAs (miRNAs)	
Agilent Bioanalyzer	650
ExoQuick precipitation	642, 648, 649
exosomes and shedding vesicles	642
integrity and quantity, exosomal RNA.....	643
isolation of exosomal RNA	
materials	643
methods	645–646
linear regression analysis, RT reactions.....	652
microvesicles	642, 643
patient samples	648
Pico RNA chip	650
platelet-poor plasma preparation	
materials	643
method	643, 644
qPCR.....	650, 651
materials	644
methods	647
quality and quantity, exosomal RNA	646
removal of clotting factors and isolation, exosomes	
materials	643
methods	644–645
reverse transcription synthesis,	
exosomal cDNA.....	646–647
RNase activity.....	642
Sanger miRBase database	647
target sequences	647
Microsatellite (MSI) analysis.....	444–446
MINDACT trial	676
MINT31. <i>See</i> Methylated-in-tumor 31 (MINT31)	
MITF. <i>See</i> Microphthalmia-associated transcription factor (MITF)	
MLN. <i>See</i> Mean diameter of the ten largest nucleoli (MLN)	
MLPA. <i>See</i> Multiplex ligation-dependent probe amplification (MLPA)	
MMPs. <i>See</i> Matrix metalloproteinases (MMPs)	
Molecular classification of melanoma.....	137–138
Molecular diagnostic markers.....	259–260
Molecular prognostic markers	260–261
Monoclonal antibodies (mAbs).....	528, 531–533
MRI. <i>See</i> Magnetic Resonance Imaging (MRI)	

MSI. *See* Microsatellite (MSI) analysis
 MTAP. *See* Methylthioadenosine phosphorylase (MTAP)
 Mucosal melanoma.....202
 Multimarker diagnostic assay260
 Multimarker expression index261
 Multimarker prognostic assay.....261
 Multimarker prognostic discriminators (MPDs).....192
 Multiparameter prognostic models.....233
 biomarker quantification (*see* Biomarker)
 computational methods244–245
 CART algorithm247
 Cox Proportional Hazards regression estimate245
 genetic algorithms.....246–247
 leave-one-out cross-validation249
 multivariable models.....248
 tenfold cross validation248–249
 discovery and validation cohorts.....235–236
 external validation
 multivariable Cox proportional hazards
 modeling.....249–250
 prediction error estimation250
 materials required
 antigen retrieval234
 Aperio ScanScope™ CS brightfield
 platform, quantitative chromogenic IHC234
 AQUA® technique, QIF.....235
 individual proteins, multivariable hazard
 ratios229–231
 tissue microarray construction (*see* Tissue microarrays
 (TMAs))
 Multiplex ligation-dependent probe amplification
 (MLPA).....443–444
 Multivariate Cox regression analysis261
 Myeloid-derived suppressor cells (MDSC) 86–87, 89, 92

N

National Comprehensive Cancer Network
 (NCCN) 119, 177
 NCCN. *See* National Comprehensive Cancer Network
 (NCCN)
 NCOA3. *See* Nuclear receptor coactivator 3 (NCOA3)
 Next-generation sequencing (NGS).....635
 NGS. *See* Next-generation sequencing (NGS)
 NMDA. *See* N-methyl-D-aspartate (NMDA) receptors
 N-methyl-D-aspartate receptors are a class of ionotropic
 glutamate receptors (NMDA)463
 Non-synonymous (NS) mutations.....462–463
 NRAS mutations
 biomarkers35
 in BRAF inhibitor-resistant melanomas
 clinical therapeutic implication.....165–166
 PCR amplification and mutational
 analysis.....167–169
 Sanger sequencing170, 171

combination therapy.....101–102
 tumor ERK-reactivation20
 Nuclear Algorithm241–242
 Nuclear receptor coactivator 3 (NCOA3).....266–267

O

OCT. *See* Optimal cutting temperature (OCT)
 Optimal cutting temperature (OCT) compound683
 Osteopontin (SSP1)268–269

P

Paired box homeotic gene transcription
 factor (PAX3).....514
 Pathogen-associated molecular pattern
 molecules (PAMPs)537
 Pathological staging
 age, sex, and anatomic location.....338
 Breslow's tumor thickness.....329–331
 Clark's levels of invasion328–329
 clinically apparent disease326
 definition325
 dermal mitotic rate331–333
 LVI337
 lymph node metastases338–339
 MAGE family334
 microscopic satellites336
 nodal metastases326
 nuclear morphometry337
 phase of tumor progression.....327–328
 primary tumors326
 prognostic models.....326, 327
 adjuvant therapy339
 AJCC classification.....343–344
 AJCC staging system.....340, 346–348
 Clark progression-based survival model340–343
 clinicopathologic database339
 Cox model339
 TNM system344–345
 prognostic variables326
 radial growth phase.....333
 regression, radial growth phase334–335
 staging325–327
 TIL response334
 ulceration336
 vertical growth phase333–334
 PAX3. *See* Paired box homeotic gene transcription factor
 (PAX3)
 PBMC. *See* Peripheral blood mononuclear cell (PBMC)
 PCNA. *See* Proliferating cell nuclear antigen (PCNA)
 PCR. *See* Polymerase chain reaction (PCR)
 PD-1. *See* Programmed death receptor 1 (PD-1)
 PD-L1. *See* Programmed cell death 1 ligand 1 (PD-L1);
 B7 homolog 1 (B7-H1)

PD-L2. <i>See</i> Programmed cell death 1 ligand 2 (PD-L2); B7 homolog (B7-DC)	¹⁸ F-FLT572–573
PD-1/PD-L1 blocking antibodies6–7	¹⁸ F-FP-RMSH-1572
Pelleted cells530–531	¹⁸ F-galacto-RGD.....572
Peripheral blood leukocytes (PBLs)514	hypoxia573
materials515	Positron emission tomography/computed tomography (PET/CT)418–419
methods518	PREX2. <i>See</i> Phosphatidylinositol-3,4,5-trisphosphate- dependent Rac exchange factor (PREX2)
Peripheral blood mononuclear cell (PBMC)663	Programmed cell death 1 ligand 1 (PD-L1).....316
PET/CT. <i>See</i> Positron emission tomography combined with computed tomography (PET/CT)	Programmed cell death 1 ligand 2 (PD-L2).....316
PHIP. <i>See</i> Pleckstrin homology domain-interacting protein (PHIP)	Programmed death receptor 1 (PD-1).....6–7
Phosphatidylinositol-3,4,5-trisphosphate-dependent Rac exchange factor (PREX2)465	Proliferating cell nuclear antigen (PCNA)337
Photoacoustic flowmetry. <i>See</i> Circulating tumor cells (CTCs)	Q
Pleckstrin homology domain-interacting protein (PHIP)99	QIAamp DNA Blood Mini Kit (Qiagen)497
Polymerase chain reaction (PCR)	QIF. <i>See</i> Quantitative immunofluorescence (QIF)
amplification and cleanup.....470	qMSP. <i>See</i> Quantitative methylation-specific PCR (qMSP) analysis
BRAF	Quantitative and spatial image analysis
amplification and mutational analysis.....167–169	antigen retrieval613–614
products purification and sequencing170, 172	application609–611
circulating tumor cells	deparaffinization and rehydration
materials517	materials610
methods520	methods613
Positive Pixel Count Algorithm242	image acquisition613
Positron emission tomography combined with computed tomography (PET/CT)	immunostaining.....614–615
biochemical and functional mechanisms554	multiplexed immunoenzyme labeling611–613
¹⁸ F-FDG	Nuance software615–616
advantages.....569–570	technology
biodistribution of558, 559	data management.....608–609
components, radiopharmaceutical.....556–557	digital imaging.....605
cutaneous malignant melanoma.....560	GemIdent software.....607–608, 617
cyclotron557	InForm software606–607, 617
glucose transporter-1557	MetaMorph software.....606
hexokinase-6.....557	spectral unmixing.....603–605
limitations and pitfalls570	Tissue Finding algorithm616
mannose triflate557	Vectra software615
oncological applications558, 559	Quantitative immunofluorescence (QIF)235, 244, 252
patient preparation.....565–569	Quantitative Immunofluorescence-based Automated Quantitative Analysis technology (QIF/AQUA)242–244
practical considerations.....561–564	Quantitative methylation-specific PCR (qMSP) analysis
standardized uptake value564–565	materials490
technical considerations.....569	methods493–496
uptake mechanisms.....557	Quantitative real-time polymerase chain reaction (RT-qPCR)514, 515
FHWM (<i>see</i> Full width at half maximum (FHWM))	Quercetin.....544
hardware and techniques573–575	R
metabolic foci555	RAGE. <i>See</i> Receptor for advanced glycation endproducts (RAGE)
partial volume effect555	RAR- β 2 gene. <i>See</i> Retinoic acid receptor β 2 (RAR- β 2) gene
radiopharmaceuticals	
angiogenesis.....572	
DNA synthesis proliferation agent572–573	
¹⁸ F-DOPA571	

Ras-association domain family 1 isoform A (RASSF1A) methylation.....	483
RASSF1A methylation. <i>See</i> Ras-association domain family 1 isoform A (RASSF1A) methylation	
Receptor for advanced glycation endproducts (RAGE).....	547
role of.....	546
soluble RAGE.....	548
Receptor tyrosine kinase (RTK)	
BRAFi-resistant melanoma	
clinical therapeutic implication.....	164–165
qPCR, detection of.....	169–170
tumor ERK-reactivation.....	20
Receptor tyrosine kinase ERBB4 mutation analysis (ERBB4)	
aCGH.....	470
BRAfV600 hotspot.....	478
capillary electrophoresis.....	476
equipment.....	469
formalin-fixed paraffin-embedded tissue blocks.....	469
genomic DNA isolation	
materials.....	470
methods.....	471–472
genomic landscape.....	461
GPCR family.....	463
GPR98.....	463
GRIN2A.....	464
GRM3.....	463–464
in vitro and in vivo testing.....	462–463
lapatinib treatment.....	468–469
NDMA receptor.....	464
PCR amplification	
materials.....	470
methods.....	472–475
PCR cleanup	
materials.....	470
methods.....	475
PREX2 dysregulation.....	465
Sanger sequencing.....	463, 478
materials.....	470
methods.....	476
sequence analysis.....	476
sequencing reaction.....	475, 477
somatic mutations	
clustering evolvement.....	466
EGFR/HER2.....	466–468
glutamate signal transduction.....	464
GPR98 and GRM3.....	463
GRIN2A.....	464
HER4.....	465
PREX2.....	465
recurrence patterns.....	466
tissue harvest.....	470–471
TRAPP gene.....	464
within tyrosine kinase family.....	465–466
ultraviolet irradiation.....	462
RECIST. <i>See</i> Response Evaluation Criteria in Solid Tumors (RECIST)	
Regulator of G-protein signaling 1 (RGS1).....	267–268
Regulatory T cells (Tregs).....	112, 310, 373
REMARK. <i>See</i> REporting recommendations for tumor MARKer prognostic studies (REMARK)	
REporting recommendations for tumor MARKer prognostic studies (REMARK).....	191, 244
Response Evaluation Criteria in Solid Tumors (RECIST).....	98
Retinoic acid receptor β 2 (RAR- β 2) gene.....	483
Reverse transcription-polymerase chain reaction (RT-PCR).....	180
electrophoresis.....	530
first-strand cDNA synthesis.....	529–530
Gene Amp PCR system.....	530
solutions and reagents.....	526
total RNA extraction.....	528–529
RGS1. <i>See</i> Regulator of G-protein signaling 1 (RGS1)	
Ring melanoma.....	403
RNAlater®.....	172
RTK. <i>See</i> Receptor tyrosine kinase (RTK)	
RT-PCR. <i>See</i> Reverse transcription-polymerase chain reaction (RT-PCR)	
S	
SAMPUS. <i>See</i> Superficial atypical melanocytic proliferation of uncertain significance (SAMPUS)	
Sanger sequencing.....	173, 463, 478
detection of	
MEK1 mutations.....	170, 172
NRAS mutations.....	170, 171
materials.....	470
methods.....	476
non-V600E mutations.....	34
Scale-invariant feature transform (SIFT) score.....	463
SCNP. <i>See</i> Single cell network profiling (SCNP)	
5-S-cysteinyldopa (5SCD).....	189
Secreted phosphoprotein 1 (SPP1).....	268–269
Secreted protein acidic and rich in cysteine (SPARC).....	113
Sentinel lymph node biopsy (SLNB).....	203, 304
Sequence Detection Systems (SDS) software.....	432
Sequence-specific primer (SSP).....	358
Ser722Phe hotspot.....	464
Serum glutamic oxaloacetic transaminase (SGOT).....	413
Serum glutamic pyruvate transaminase (SGPT).....	413
SGOT. <i>See</i> Serum glutamic oxaloacetic transaminase (SGOT)	
SGPT. <i>See</i> Serum glutamic pyruvate transaminase (SGPT)	
SIFT score. <i>See</i> Scale-invariant feature transform (SIFT) score	

- targeted therapy680–682
 - TMA. *See* Tissue microarrays (TMAs)685–687
 - TLR. *See* Toll like receptors (TLRs)
 - TMA. *See* Tissue microarrays (TMAs)
 - TNM. *See* Tumor-node-metastasis (TNM)
 - Toll like receptors (TLRs)549
 - Transient receptor potential cation channel, subfamily M, member 1 (TRPM1)186–187
 - Transient thermoelastic expansion655
 - Transport protein particle (TRAPP) gene464
 - TRAPP gene. *See* Transport protein particle (TRAPP) gene
 - Tregs. *See* Regulatory T cells (Tregs)
 - TRPM1. *See* Transient receptor potential cation channel, subfamily M, member 1 (TRPM1)
 - TSLC1. *See* Tumor Suppressor in Lung Cancer1 (TSLC1)
 - Tumor-draining lymph node (TDLN)601–602, 609
 - immune profile and nodal metastases610
 - T cell and B cell distributions611
 - Tumorigenic potential505, 510
 - Tumor-infiltrating lymphocyte (TIL)372–373
 - antitumor immunity and melanoma
 - antigen recognition290–291
 - immunogenic properties292
 - immunologic tolerance292
 - tumor surveillance hypothesis289–290
 - biomarkers29, 36
 - CTLs288
 - dermal lymphocyte infiltration288
 - harnessing (*see* Melanoma immunotherapy)
 - history and evolution
 - brisk and nonbrisk categories300
 - early, intermediate and late regression298
 - histologic examples298, 299
 - locoregional/distant metastases298
 - superficial dermal lymphocyte reaction298
 - immunoregulatory immune cell subsets289
 - in lymph nodes
 - CD4(+) and CD8(+) T cells310
 - cortex310
 - GM-CSF312
 - hematogenous and lymphatic spread307
 - IDO312
 - IFN therapy309
 - immunosuppression mechanism311–313
 - monocytes and DCs310–312
 - T cell antigen response309–310
 - TCR beta variables309
 - tryptophan312
 - veiled cell309–310
 - melanoma immune evasion mechanisms
 - clonal anergy-induced tolerance294–295
 - immune effector populations294
 - melanoma differentiation antigen loss292–293
 - NK cell-mediated destruction293–294
 - reduced MHC class I expression293
 - T cell exhaustion297
 - Treg cell-mediated immune evasion297–298
 - tumor-induced immune tolerance296
 - tumor-mediated deletion294
 - in melanoma prognosis
 - brisk TIL infiltrate304–305
 - mitotic rate303
 - SLN biopsy304, 305
 - staging limitations307
 - structured/synoptic pathology report307
 - TIL grade306–307
 - ulceration304
 - protumorigenic inflammatory processes287
 - quantification
 - absent, nonbrisk and brisk infiltrates300–302
 - grades302–303
 - Tumor-node-metastasis (TNM)344–345
 - Tumor Suppressor in Lung Cancer1 (TSLC1)484
 - Tyrosine phosphatases463, 464
 - Tyrosine-protein kinase KIT/CD117 (KIT)4, 13, 22, 137–158, 164, 680
- U**
- UICC. *See* Union Internationale Contra Cancer (UICC)
 - UM. *See* Uveal melanoma (UM)
 - Union Internationale Contra Cancer (UICC)325
 - Uveal melanoma (UM)203–204
 - clinical high-risk features
 - ciliary body involvement400–401
 - diffuse growth pattern402–403
 - extraocular extension401–402
 - LTD, largest399–400
 - older age399
 - optic nerve involvement403–404
 - ring melanoma403
 - tumor thickness400
 - cutaneous melanoma397–398
 - diagnosis of398
 - FNAB (*see* Fine needle aspiration biopsy (FNAB))
 - 15-GEP (*see* 15-Gene expression profile (GEP))
 - GNAQ and GNA11 mutations4
 - histologic features
 - cell type404–405
 - high mitotic rate406–407
 - inflammation410
 - microcirculation407–408
 - MLN405–406
 - pigmentation408–410
 - imaging
 - abdominal ultrasound417
 - chest radiography417
 - computed tomography (CT)418

Uveal melanoma (UM) (<i>cont.</i>)	
COMS trials.....	416–417
metastatic melanoma	416–417
MRI.....	419
PET/ CT.....	418–419
prognostic evaluation	419–420
immunohistochemical markers	
HMB-45	411
Ki-67	411–412
Melan-A.....	412
S100.....	411
LFTs	
alkaline phosphatase	413
ALT	413
COMS reports.....	414
GGT.....	413–414
hepatic metastases.....	414, 416
insensitive markers.....	414
lactate dehydrogenase (LDH).....	413
metastatic disease.....	412
PPV	415
primary intraocular malignancy, adults	397
risk factors	397
serum markers	416
uveal tissues, eye	397
V	
Vascular endothelial growth factor (VEGF).....	184, 276, 312
VEGF. <i>See</i> Vascular endothelial growth factor (VEGF)	
Vemurafenib	
FDA-approval timeline	11, 12
unresectable stage III and IV melanoma	14
Vertical growth phase (VGP)	186
VGP. <i>See</i> Vertical growth phase (VGP)	
Virchow, Rudolf	287
W	
WGS. <i>See</i> Whole-genome sequencing (WGS)	
Whole-genome methylation profile	486
Whole-genome sequencing (WGS).....	462
Wingless-type MMTV integration site family	
member 2 (WNT2)	269–270
WNT2. <i>See</i> Wingless-type MMTV integration site family member 2 (WNT2)	