

Index

- A**
- ABA. *See* Abscisic acid
 - ABCC2, 120
 - Abscisic acid (ABA), 136–138
 - Accelerated resistance to multiple drugs (ARMD), 245
 - Acetylcholinesterase (AChE), insecticide resistance, 89
 - AChE. *See* Acetylcholinesterase
 - Acidosis, pathogenesis in malaria, 188
 - ACT. *See* Artemisinin combination therapy
 - Adenylate cyclase, 144
 - AMA-1, 107, 286
 - Amodiaquine, 265
 - AnAPN1, 287
 - ApiAP2, 237
 - ApiAP2-G, 31–32
 - ARMD. *See* Accelerated resistance to multiple drugs
 - Artemisinin
 - overview, 264
 - resistance
 - elimination, 271, 273
 - mechanisms, 261, 263, 265, 270–272
 - Artemisinin combination therapy (ACT)
 - efficacy, 27–28
 - pregnancy, 206, 211
 - resistance, 255–257, 261, 273
 - Atg5, 123
 - Atg8, 123
 - Atovaquone, 269
 - ATSBs. *See* Attractive toxic sugar baits
 - Attractive toxic sugar baits (ATSBs), 75–76
 - Azithromycin, malaria treatment in pregnancy, 210–211
- B**
- Beclin-1, 123
- C**
- Calcium flux, merozoite egress from erythrocyte signaling, 136–138
 - Calpain-1, 137, 139
 - Carbonic anhydrase, 144
 - CD68, 107
 - CD81, 107, 117
 - Cerebral malaria (CM), pathogenesis, 188–189
 - Chemoprophylaxis with sporozoites (CPS), 284
 - Chloroquine (CQ)
 - early treatment, 284
 - malaria treatment in pregnancy, 206, 210, 211
 - overview, 265
 - CHM1, 286, 289, 291
 - Chondroitin sulfate A (CSA), 172, 198
 - Circumsporozoite protein (CSP), 101–104, 107, 114–116, 168–169, 176, 224, 282–283
 - CLAG3, 237
 - clag3.1*, 237
 - clag3.2*, 237
 - CM. *See* Cerebral malaria
 - COI. *See* Complexity of infection
 - Complexity of infection (COI), 221–222
 - CPS. *See* Chemoprophylaxis with sporozoites
 - CQ. *See* Chloroquine
 - CR1, 140
 - CRISPR/Cas9, mosquito control, 62
 - CSA. *See* Chondroitin sulfate A
 - CSP. *See* Circumsporozoite protein
 - Cytochrome P450s, insecticide resistance, 89–90
- D**
- DARC. *See* Duffy antigen receptor for chemokines
 - DBL. *See* Duffy-binding protein ligand
 - DBP. *See* Duffy-binding protein
 - DDOC2, 142
 - DDT. *See* Dichlorodiphenyltrichloroethane
 - Dichlorodiphenyltrichloroethane (DDT), 27, 69, 87–88, 92–93, 297–298
 - Dihydroartemisinin, malaria treatment in pregnancy, 210
 - Direct membrane feeding assay (DMFA), 34
 - DMFA. *See* Direct membrane feeding assay
 - Drug resistance
 - artemisinin resistance
 - elimination, 271, 273
 - mechanisms, 261, 263, 265, 270–272
 - drug characteristics, 264–269
 - drug efficacy assessment, 259–261
 - geographic distribution, 257–259
 - models, 302
 - molecular markers, 262–263
 - origins, 256–257
 - overview, 255–256
 - Plasmodium vivax*, 271
 - prospects for elimination, 271–274

Index

Duffy antigen receptor for chemokines (DARC), 140, 150–151, 154
Duffy-binding protein (DBP), 44
Duffy-binding protein ligand (DBL), 140, 150

E

Ecdysone, 57
Environmental determinants, malaria transmission
 human-made environment, 4–5
 interventions for control, 5–6
 natural environment, 3–4
 overview, 1–3, 17–19
 prospects for control, 6–9
EphA2, 117
Epigenetics, malaria
 antigenetic variation, 232, 235
 cytoadherence, 235–236
 environmental change adaptation, 238
 eradication studies
 malaria phenotype monitoring, 245
 therapeutic targeting of epigenetics, 245–247
 erythrocyte
 invasion, 236–237
 permeability after infection, 237
 overview, 231–232
 Plasmodium falciparum studies
 chromatin structure across life cycle, 239–241
 clonally variant gene expression regulation, 241, 243–244
 overview, 238–239
 responsive genes, 240–241
 var gene expression regulation, 243–244
 prospects for study, 247–248
 responsive genes, 233–234
 sexual conversion, 237–238
Erythrocyte-binding antigens, *Plasmodium falciparum*, 140–141, 150, 157–158
Erythrocyte membrane protein-1. *See* PfEMP1
EXP1, 120

F

Feeding assays. *See* Direct membrane feeding assay;
 Standard membrane feeding assay

G

Gametocyte
 density versus infectiousness, 34
 host factors in gametocytogenesis, 31
 immune response, 19–20
 production in human reservoirs, 14–16
 sequestration, 30–31
Genomics, malaria
 data abundance, 220

 intervention impact assessment, 223
 parasite tracking, 225–226
 prospects, 226–228
 toolkit
 deployment for eradication, 221–222
 development, 220–221
 transmission studies, 222–223
Global Malaria Eradication Program (GMEP), 27, 298
Glucose 6-phosphate dehydrogenase deficiency, 47
Glycophorins, *Plasmodium falciparum*, 140
GMEP. *See* Global Malaria Eradication Program

H

HEGs. *See* Homing endonuclease genes
HEP17, 169
Hepatocyte. *See* Liver infection
Histidine-rich protein 2 (HRP2), sensitivity of
 parasite detection, 14
Homing endonuclease genes (HEGs), 77–78
HP1, 243
HPX15, 59
HRP2. *See* Histidine-rich protein 2
HSP20, 106
Human reservoir
 demographics, 16–19
 gametocyte production, 14–16
 sensitivity of parasite detection tests, 13–14
20-Hydroxyecdysone, 57–59

I

Immune response, malaria
 asexual erythrocyte-stage responses
 effector mechanisms and assays, 170–171
 merozoite proteins, 171–172
 overview, 170
 parasite proteins on infected red cell surface, 172
 protective immune responses, 172–173
 T-cell responses, 173
 preerythrocytic antigens
 antibodies, 167–169
 T-cell responses, 169
 pregnancy
 antibodies
 parity-dependent acquisition, 199–200
 placental parasite antibodies and infection
 status/risk, 199, 201–202
 outcome effects of infection, 202–203
 prospects for study, 176–177
 sexual- and mosquito-stage parasites
 postfertilization antigens, 175
 prefertilization antigens, 174–175
 sexual-stage parasites
 characterization, 173–174
 host immune response, 175–176

Indoor residual spraying (IRS), 60, 62, 69–71, 87, 90, 93, 297–298

Insecticide resistance

- emergence and spread, 88–89
- management strategies, 93–94
- mechanisms
 - behavioral resistance, 90
 - metabolic resistance, 89–90
 - penetration reduction, 90
 - target site resistance, 89
- monitoring and limitations, 90–91
- prospects for study, 94–95
- vector control impact studies, 91–93

Insecticide-treated nets (ITNs), 69–71, 87, 90–92

Integrated vector management (IVM), 78–79

Interferons, immune response to liver stage infection, 123

Intermittent presumptive treatment (IPTp), pregnancy, 206–210

Intermittent screening and treatment in pregnancy (ISTp), 211

IPTp. *See* Intermittent presumptive treatment

IRS. *See* Indoor residual spraying

ISTp. *See* Intermittent screening and treatment in pregnancy

ITNs. *See* Insecticide-treated nets

IVM. *See* Integrated vector management

K

KARMA, 259

L

Larval source management (LSM), 71–73

LISP1, 120

LISP2, 120

Liver infection

- hepatocyte infection, 114–118
- hepatocyte infection, 114–118
 - parasite perturbations, 121–123
 - knockout mouse studies, 126–128
 - liver stage development, 118–120
 - models for study, 123–124
 - prospects for study, 125, 129
 - vaccination with attenuated preerythrocytic parasites, 125

LLINs. *See* Long-lasting insecticide-treated nets

Long-lasting insecticide-treated nets (LLINs), 60–62

LRIM9, 59

LSA1, 168

LSM. *See* Larval source management

Lumefantrine, 266

Lysine methyltransferase, therapeutic targeting, 247

M

MAEBL, 106

MAGs. *See* Male accessory glands

Male accessory glands (MAGs), 59–60

Mass drug administration (MDA), 223

Mating-induced stimulator of oogenesis (MISO), 59–60

MDA. *See* Mass drug administration

Mefloquine

- malaria treatment in pregnancy, 210
- overview, 266

Merozoite

- egress from erythrocyte
 - abscisic acid role, 136–137
 - apical organelle discharge in regulation, 139
 - calpain-1 role, 137, 139
 - signaling, 136–137
- immune response, 171–172
- invasion of erythrocytes
 - apical organelle discharge regulation, 140–144
 - signaling, 139–140
- prospects for study, 144

Merozoite surface protein 1 (MSP1), 171, 220, 286

MIC8, 142

MISO. *See* Mating-induced stimulator of oogenesis

Modeling, malaria

- geographic specificity, 303
- mosquito ecology, 301–302
- novel interventions, 301
- prediction and microstimulation models, 302–303
- prospects, 303–304
- resistance and evolutionary models, 302
- Ross–Macdonald model, 298
- spatial variation and movement, 300
- stochasticity, 300–301
- surveillance response, 198
- temporal dynamics, 298–300
- within-host dynamics, 301

Mosquito control

- CRISPR/Cas9, 62
- goals of vector control, 69
- host-mediated control
 - attractive toxic sugar baits, 75–76
 - endectocides, 73–74
 - genetic control, 76–78
 - integrated vector management, 78–79
 - push–pull strategies, 74
 - spatial repellents, 74–75
 - zooprophylaxis, 73
- indoor residual spraying, 60, 62, 69–71
- insecticide resistance. *See* Insecticide resistance
- insecticide-treated nets, 69–71
- larval source management, 71–73
- long-lasting insecticide-treated nets, 60–62

Index

- Mosquito control (*Continued*)
 mating behavior targeting, 62–63
 prospects, 63–64, 79
 sterile insect technique, 60–62
 World Health Organization core strategies, 70–73
MSP1. *See* Merozoite surface protein 1
MSPDBL2, 236
- N**
- NASBA. *See* Nucleic acid sequence-based amplification
Nucleic acid sequence-based amplification (NASBA),
 sensitivity of parasite detection, 14, 36
- O**
- Oocyte, resorption in mosquito, 58
- P**
- P36, 117
P52, 117
P53, 122
Parasitophorous vacuole membrane (PVM), 114,
 117–118, 120–123, 136, 283
Pathogenesis, malaria
 acidosis, 188
 cerebral malaria, 188–189
 overview, 183–184
 placental malaria, 188
 pregnancy, 198–199
 prospects for study, 189–190
 severe malaria
 anemia, 188
 Plasmodium knowlesi, 187–188
 Plasmodium vivax, 187
 syndromes, 189
 uncomplicated malaria
 overview, 184–185
 Plasmodium falciparum, 185–186
 Plasmodium knowlesi, 187
 Plasmodium malariae, 186–187
 Plasmodium ovale, 186
 Plasmodium vivax, 186
PCR. *See* Polymerase chain reaction
PCRMP3, 106
PCRMP4, 106
PE antigens. *See* Preerythrocytic antigens
Perforins, 136, 139
PfAMA1, 140–142, 171
PfAP2-G, 237–238
PfATP4, 263
PfCDPK1, 139, 141–142, 144
PfCDPK5, 139
PfCRT, 262
PfCYTB, 263
PfDHFR-TS, 262
PfEMP1, 32–33, 172–173, 185, 188, 190, 232,
 235–236, 243, 245, 286
PfHda2, 32
PfHPI1, 32
PfMDR1, 262
PfMRP1, 263
PfnHE, 263
PfPI3K, 270
PfPKA, 142
PfPPPK-DHPS, 262–263
PfrAP proteins, 141
PfrRH proteins, 140–142, 157, 171–172, 286
PfrON2, 140–141
PfrON4, 141
Pfs230, 174
Pfs25, 175–176, 287
PfSET2, 243–244
PfSPZ, 284
PfSub1, 136–138
Phospholipase C (PLC), 137, 141
Piperaquine
 malaria treatment in pregnancy, 210
 overview, 266–267
PknBXPb, 152
Plasmodial surface anion channel (PSAC), 237
Plasmodium brasilianum, diversity, 158
Plasmodium falciparum
 drug resistance geographic distribution,
 257–259
 epigenetics studies
 chromatin structure across life cycle,
 239–241
 clonally variant gene expression regulation, 241,
 243–244
 overview, 238–239
 responsive genes, 240–241
 var gene expression regulation, 243–244
 genotypes and complexity of infection,
 34–35
 invasion ligand diversity, 155, 157
 lethality of malaria, 28
 life cycle, 28–30, 135
 malaria pathogenesis, 185–186
 origins, 155
 Plasmodium falciparum tropism ligand targeting,
 157–158
 sex ratio, 35
 sexual conversion molecular mechanism,
 31–32
 sialic acid and host specificity, 157
 skin compartment localization, 35–36
Plasmodium knowlesi
 adaptation to human red blood cells,
 152–153
 diversity of strains, 152

- malaria pathogenesis, 187–188
 - zoonosis, 150–151, 159
 - Plasmodium* lactate dehydrogenase (pLDH), sensitivity of parasite detection, 14
 - Plasmodium malariae*
 - diversity, 158
 - malaria pathogenesis, 186–187
 - Plasmodium ovale*
 - diversity, 158
 - malaria pathogenesis, 186
 - Plasmodium rhodaini*, diversity, 158
 - Plasmodium vivax*
 - asymptomatic infection, 47–48
 - DARC status and infection, 154
 - diversity, 153
 - drug resistance, 271
 - drug resistance geographic distribution, 257–259
 - gametocyte biology, 46
 - genetic diversity, 47
 - geographic distribution, 45
 - life cycle, 44, 46
 - malaria pathogenesis, 186–187
 - origins, 153–154
 - population structure, 47
 - PvDBP–DARC interaction, 154
 - research techniques, 48–50
 - vaccine challenges, 154–155
 - PLC. *See* Phospholipase C
 - pLDH. *See* *Plasmodium* lactate dehydrogenase
 - Polymerase chain reaction (PCR)
 - drug efficacy assays, 261
 - sensitivity of parasite detection, 14, 36
 - PPO. *See* Prophenoloxidase
 - Preerythrocytic (PE) antigens, immune response
 - antibodies, 167–169
 - T-cell responses, 169
 - Pregnancy, malaria
 - diagnosis, 205–206
 - epidemiology, 196–198
 - host–parasite interactions, 195–196
 - immune response
 - antibodies
 - parity-dependent acquisition, 199–200
 - placental parasite antibodies and infection status/risk, 199, 201–202
 - pregnancy outcome effects, 202–203
 - pathogenesis, 198–199
 - placental malaria, 188
 - treatment
 - artemisinin combination therapy, 211
 - chloroquine–azithromycin, 210–211
 - dihydroartemisinin–piperaquine, 210
 - intermittent presumptive treatment, 206–210
 - intermittent screening and treatment in pregnancy, 211
 - mefloquine, 210
 - prospects, 212
 - vaccine development, 202–205
 - Primaquine, 28, 47, 267
 - Proguanil, 268–269
 - Prophenoloxidase (PPO), 59
 - PSAC. *See* Plasmodial surface anion channel
 - PUF2, 107
 - PvDBP, 154–155
 - PVM. *See* Parasitophorous vacuole membrane
 - PvRBP, 150
 - Pvs25, 175, 287
 - Pvs230, 175
 - Pyrimethamine, 268
- ## Q
- Quinine, 264–265
- ## R
- Rapid diagnostic test (RDT), sensitivity, 13–14
 - RDT. *See* Rapid diagnostic test
 - Release of insects with dominant lethality (RIDL), 77
 - Reservoir. *See* Human reservoir
 - Resistance. *See* Drug resistance; Insecticide resistance
 - RhopH proteins, 140
 - RIDL. *See* Release of insects with dominant lethality
 - RIFIN, 33, 172, 287
 - Ring-stage survival assay (RSA), 260
 - RNA polymerase II, 244
 - ROM4, 117
 - Ross–Macdonald model, 298
 - RSA. *See* Ring-stage survival assay
 - RTS,S, 20, 25, 102–104, 108–109, 168–169, 176, 224, 229, 285–291, 301–304
 - Ryanodine receptor (RyR), 141
 - RyR. *See* Ryanodine receptor
- ## S
- SEA-1. *See* Schizont egress antigen-1
 - SERAs. *See* Serine-repeat antigen proteins
 - Schizont egress antigen-1 (SEA-1), 286
 - Serine-repeat antigen proteins (SERAs), 137–138
 - Severe malaria anemia (SMA), 188
 - Sialic acid, host specificity role, 157
 - SIAP-1, 106
 - SIT. *See* Sterile insect technique
 - SMA. *See* Severe malaria anemia
 - SMFA. *See* Standard membrane feeding assay

Index

- SPECT, 107
- Sporogony, mosquito oogenesis relationship, 55–58
- Sporozoite
- circumsporozoite protein, 101–104, 107
 - hepatocyte
 - infection, 114–118
 - parasite perturbations, 121–123
 - invasion, 106–107
 - liver stage development, 118–120
 - motility mechanisms, 104–106
 - natural history, 100–101
 - prospects for study, 107–108
- Standard membrane feeding assay (SMFA), 34, 174–175, 288
- STARP, 169
- Sterile insect technique (SIT), 60–62, 69, 77
- STEVOR, 33, 172, 287
- Sulfadoxine, 267–268
- T**
- Target product profile (TPP), 301
- TEP1. *See* Thioester-containing protein 1
- TgCDPK1, 139, 141–142
- TgCDPK3, 139
- TgPKG, 139
- TgPLP1, 139
- Thioester-containing protein 1 (TEP1), 57
- Thrombospondin-related anonymous protein (TRAP), 104–107, 115–117, 140, 168
- TLR, 104–105
- TPP. *See* Target product profile
- Transmission, malaria
- blocking vaccines, 20–22
 - demographic factors, 16–19
 - environmental determinants. *See* Environmental determinants, malaria transmission
 - immune response effects, 19–20
 - intervention considerations, 20–21
 - stages
 - development, 28–30
 - sequestration, 32–33
- TRAP. *See* Thrombospondin-related anonymous protein
- TREP, 104
- Tropism
- molecular mediators, 150–152
 - PfRH5 as host restriction factor, 157
 - sialic acid and host specificity, 157
- TRPML1, 122
- U**
- UIS1, 107
- UIS3, 118, 120
- UIS4, 107, 118–120, 123
- V**
- Vaccination
- attenuated preerythrocytic parasites, 125
 - circumsporozoite protein, 168, 176
 - erythrocytic-stage targeting, 285–287
 - goals, 280, 282
 - intervention points, 281
 - mosquito-stage targeting, 287–288
 - Plasmodium vivax* challenges, 154–155
 - populations for vaccination, 290
 - pregnancy and vaccine development, 202–205
 - prospects, 290–291
 - target discovery, 288–289
 - transmission-blocking vaccines, 20–22, 144, 279–280, 285–290
 - vaccine to interrupt malaria transmission
 - exoerythrocytic cycle targeting, 282–285
 - overview, 279–280
- VAR2CSA, 172, 202–204, 286
- Vector control. *See* Mosquito control
- W**
- Worldwide Antimalarial Resistance Network (WWARN), 259
- WWARN. *See* WWARN
- Y**
- Yolk protein precursors (YPPs), 57–58
- YPPs. *See* Yolk protein precursors
- Z**
- ZIPCO, 120