Index

AARP 38, 73, 530, 530
ABO blood group antigens 468–9
ABRA (MSP-9) 35, 49–50
acetyl-CoA 225, 229, 256, 271
mitochondrial production 273
acylation, histone (and acetyltransferases – HATs) 154, 164–7, 170
inhibitors 164–7, 207
acquired/adaptive immunity (naturally) 431–3, 437, 497
HIV and 442
P. vivax 522
severe malaria and 496–7, 505
failure 505
uncomplicated malaria and 500, 502
ACT451840 (Actelion) 369
actin–myosin motor (and gliding motility) 10, 15, 16, 51, 54, 97, 293, 295, 338
acyl-CoA 130, 232, 249, 250
adaptive immunity see acquired/adaptive immunity
adenosine nucleotides see AMP; ATP
S-adenosylmethionine 242, 260
adenovirus-based vectors in vaccination 525
adenylyl cyclase (AC) 296, 297, 298
adherence/adhesion of host cells (cytoadherence) 446, 474, 554–8
candidate malaria-association genes relating to non-red blood cell products 480
P. vivax and 554–8
pregnancy malaria and 206
parasite (to host cells) 445, 446–8
during erythrocyte invasion 57–8
in placental malaria to chondroitin sulfate 533
as therapeutic target 429
adhesins 50, 54, 71, 341, 555–6
rhomboid proteases and 337, 338
vaccines and 529, 530
adjunctive therapies 429–30
adjuvants for vaccines 524, 526, 530, 531–2, 534, 535
adolescence, immunity acquired by 500
Affordable Medicines Facility for Malaria program 398
Africa
children 433
Kenya see Kenya
severe malaria 428, 433, 434–5, 507–10, 511
factors determining susceptibility to/risk of malaria autoimmune 507–10, 511
 genetic 465–6
sub-Saharan see sub-Saharan Africa
vaccine trials 524–5
African Region (WHO), epidemiology 410, 411, 414
age at peak incidence in endemic areas 432
susceptibility relating to 441
aggregation domain, conditional (CAD) 190
alanyl aminopeptidase (APN1) 94, 111, 333, 534
Alba, P. falciparum (PfAlba) 155–6, 159, 160–1, 163, 169
allopurinol 445
altitude affecting transmission 420
AMA-1 see apical membrane antigen 1
AMA-2 57
Americas (WHO region), epidemiology 410, 413
amino acids 240–50
δ-aminolevulinic acid (ALA) 247, 262
aminopeptidases
alanyl 333
dipeptidyl 25, 330, 331–2, 343
leucyl 334
methionyl 335
4-aminooquinoline 354, 368, 372
8-aminooquinoline 367, 371, 373, 397, 551
aminosugars metabolism 220, 225–7, 241, 246
amodiaquine
methylene blue with 372
resistance, time difference between date of introduction and first report of 384
sulfadoxine–pyrimethamine with, children 375
AMP (adenosine monophosphate) 252, 296
cyclic (cAMP) 296–8
development of parasite and 297–8
erthrocyte invasion and 74, 298
generation 297
anacardic acid 164–7, 207
anemia 428
epidemiology 432
P. vivax 551
animal models in therapeutics development 428–9
drugs 362, 365–6, 367
systemic lupus erythematosus and resistance to malaria 507, 510, 511
vaccines (immunization) 497, 501, 531, 532
Anopheles mosquito (vector of human malaria) 87, 102–5
breeding sites see breeding sites
parasite dynamics in 106–10
parasite influencing behavior 103
parasite transmission by 3, 103, 104, 105, 419
blocking interventions 110–14
historical perspectives 2
sporozoite injection 10
see also vectorial capacity
antibodies
  in immune response 437–8, 500–2, 505, 511
  memory see memory
monoclonal see monoclonal antibodies
anticoagulants 429
antigens
  red blood cell 468–79
  as targets of antibodies 437
  variation 132, 437
P. vivax 554
  see also vaccines
anti-inflammatory agents 429
anti-inflammatory response 435–7
antimalarial drugs see chemoprevention; drugs; drug resistance
antioxidants
  as defense mechanisms 221, 247, 260, 265, 268
  therapeutic 429
AP2‐O, P. falciparum (PfAP2‐O) 158, 159, 202
apex
  organelles 40, 50, 66, 74, 530
  reorientation 50–1
  see also thrombospondin‐related apical merozoite protein
ApiAP2 transcription factor 156, 157, 157–8, 158–60, 201–2
apical asparagine‐rich protein (AARP), P. falciparum 38, 73, 530, 531
apical membrane (merozoite) antigen 1 (AMA‐1; PfAMA‐1) 14, 15, 36, 41, 44, 45, 50–1, 52, 52–4, 53–4, 57, 65, 74, 75, 337, 338, 341, 502
rhoptry neck proteins interactions with 52–3
vaccine development 527, 530
apical membrane (merozoite) antigen 2 (AMA‐2) 57
apicidin 165, 167, 207, 208
apicomplexan parasites 39, 41
motility 54
apicoplast 16, 18, 20, 225, 236, 256, 262, 268, 273, 333–4
fatty acid synthesis 227–9, 235
in translation 210, 211
APN1 (alanyl aminopeptidase) 94, 111, 333, 534
apoptosis (programmed cell death) 25, 26, 27, 31
AQ‐13 372
aquaporins and aquaglyceroporins 314–15
arginine 244–5
  histone, methylation and methyltransferases, histone (PRMTs) 155, 166
  inhibition 168
  metabolism 243, 244–5
artemether
  lumefantrine with 355, 356
  sublingual (Artimist) 374
artemisinin 89, 111, 137, 355–6, 384, 388, 422
  alternative to/replace of 368
  combination therapies (ACT) 355–6, 384, 392–3
  cause of failures 392, 392–3
  naphthoquine 355, 374
history 353, 354
monotherapy prevention 399
proteome responses 211
resistance/failure 208, 355, 364, 368, 392–3, 396
  protection from development of 355
speed of action 365, 392
artemisone 373
Arterolane (OZ277/Rbx11160) 356, 368, 374
artesunate
  ferroquine with 372
pyronaridine with (Pyramax) 356, 373
artificial breeding sites (vector) 420
Artimist 374
AS01 vaccine adjuvant 376, 524, 527
AS02 vaccine adjuvant 524, 525, 526, 527
Ascaris lumbricoides 443
asexual reproduction (schizogony) 3, 18, 91
asparagine metabolism 244
aspartate, metabolism 244
aspartate aminotransferase (transaminase) 223, 245, 249, 254
aspartic proteases 325–9
association studies/analysis 133, 135
genome‐wide (GWAS) 133
asymptomatic malaria 466
children
  Kenya 446, 449
  Papua New Guinea 449
ovalocytosis and 474
P. falciparum 419
P. vivax 548, 549
A + T content 127
atovaquone 97, 269
  resistance, time difference between date of introduction
  and first report of 384
  transmission blockage by 113
ATP generation
  in glycolysis 221, 225
  mitochondrial 268, 269, 318–19
ATPases (parasite membranes)
  parasitophorous vacuole 312
  plasma membrane 314–16
Aurora kinases 168
autoimmune disease 507–11
autophagy, host cell 16, 19
azacitidine 169
azithromycin–chloroquine 373
B cells 502–3
  memory 502, 503, 532
bacteremia, invasive 442
base content, Plasmodium 127
basigin (BSG; CD147) 69, 70, 71, 481, 499, 529, 530
behavioral modification of mosquito influenced by parasite 103
benign tertian malaria 2, 438
Bignami, Amico 1, 2
biochemistry of P. falciparum see metabolism
biomass (parasite) 450
P. vivax 551, 554
vs P. falciparum 438
biota (diverse) influencing transmission 104–5
bisthiazolium compound 74 207, 212
BIX‐01294 166, 168
blasticidin S 181, 310
blood cell deficiencies in P vivax malaria 551
blood group antigens 468–74
blood meal factors influencing transmission 104–5
blood stage see erythrocyte
blood vessel, sporozoite injection into 10
bortezomib 339
brain
  endothelial receptors in 446
parasite sequestration 428, 435, 503
  see also cerebral malaria; neurological complications
breeding sites (vector) 419
artificial 420
bromodomains 155, 169, 170
Index 567

burden
of disease 409–10
P. vivax 547–9
of parasites in body see parasitemia
public health burden of drug resistance 384–5
Burkina Faso 422, 465, 532
Bxb integrase system 182–3
calcium ions (Ca2+) 292–6
calpains dependent on 332
life cycle and 292–4
merosome formation 26
protein kinases dependent on 294–5
signaling 292–6
erthrocyte invasion 74, 293, 294, 295
calpains 24, 332, 340
Cambodia, molecular surveillance guiding selection of therapeutic
efficacy sites in 395
Cameroon 440, 465
carbohydrate metabolism, P. falciparum 219–27
cardiolipin 233
cases of malaria 409
geographical distribution 411–13
routine case surveillance 415–17
by WHO region, number of, and proportion to
P. falciparum 409, 410
CD31 (PECAM‐1) 446, 447, 480
CD36 446, 447, 474, 480, 555
CD40LG 480
CD147 (basigin; BSG) 69, 70, 71, 481, 499, 529, 530
CDP‐choline (Kennedy) pathway 230
CDRI 97–78 (drug) 372
cell(s) (vertebrate host)
adherence/adhesion see adherence
cycle alterations 18
death 25, 26
programmed (apoptosis) 25, 26, 27, 31
invasion see invasion
protein export into 20–3
sporozoite transmigration through 3, 13–14
starvation conditions 16, 19
see also specific cell types
CelTOS (cell traversal protein for ookinetes and sporozoites)
94, 526
centromeres 154, 204, 205
ceramide 235, 236
cerebral malaria (CM) 428
adjunctive therapies 429
children 432
epidemiology 432
immune response 503, 505
inflammatory response and 436
non-immune adults 431
ovalocytosis and 474
parasite adhesion and 446, 448
systemic lupus erythematosus and 507, 508
challenge models (human volunteers)
new drugs 366
vaccines 532
chemokines, Duffy antigen for (DARC) 58, 59–60, 63, 468–70, 481, 528
chemoprevention (chemoprophylaxis/chemoprotection)
vaccines see vaccines
vulnerable populations 375–6
pregnancy 357, 375–6, 422
children
African see Africa
antimalarials 375
artemisinin-based combinations 356, 373
protection using 375
in endemic areas 427–30, 431–3
epidemiology 431–3
deaths 410
in utero exposure 440
as infectious reservoirs 104
P. vivax 548–9, 551
protection from/resistance to 432
antibodies conferring 437
severe malaria 432–3, 434–5, 450
see also adolescence; infants and toddlers
chimeric fusion proteins in vaccine development 532–3
chloroquine (CQ) 387
azithromycin combined with 373
digestive vacuole and 316
historical treatment 354
P. vivax see Plasmodium vivax
proteome responses 211
reversion of sensitivity 390
tafenoquine combined with 367
chloroquine resistance (CQR) 316–17, 354, 384, 387, 389, 390, 400, 543–4
mechanisms 387
microsatellite markers 389
P. vivax 384, 400, 552–4
time difference between date of introduction and first
report of 384
chloroquine-resistance transporter (CRT) 316, 317, 318
P. vivax 553
choline inhibitor compound T4 207, 212
chordonitin sulfate in placental malaria, adhesion to 533
chromatin
DNA-binding proteins and remodelling of 204
structure 150–6
trans-factors associated with 154–6
chromodomains 155, 169, 170
chromosome
core, chromatin compartmentalization 152
ends 554–5
structure 128–30
cipargamin (KAE609) 369, 372
circumsporozoite protein (CSP) 10, 11, 12, 14, 15, 21, 22, 98
vaccines 497–9, 524, 525
citric acid (TCA) cycle 219, 223, 245, 246, 256, 258, 269–73
cladogram, Plasmodium 126
clag (RhophH1) 38, 73–4
climatic factors affecting transmission 419–20
clinical spectrum of diseases 427–30
clinical trials (new treatments)
drugs 363
vaccines 354
see also specific phases
clonally variant gene expression 152–3, 203, 205
coenzyme A 256
coenzyme Q 261
cofactors 256–65
co-infections 442–4
combination therapy 359–60, 372, 374
artemisinin in 355–6
endoperoxides in 368
tafenoquine-chloroquine 367
comparative genomics 125, 127
  lineage-specific genes 130
complement system 436
  complement receptor-1 (CR1) 436, 471–3
complex I-V (mitochondria) 269
compliance issues 357, 366
complicated malaria
  see severe malaria
compound T4 207, 212
compound-1 185, 299
conditional knockdown of protein function 187–91
control measures incl. elimination and eradication 421–3
  drugs see chemoprevention; drugs
  elimination agenda 357, 367
  indoor residual spraying (IRS) 421–2, 423
  insecticide-treated nets 103, 375–6, 421
core particle of proteasome 339
cytoadherence
  see adherence
cytokines
  anti-inflammatory 436
  pro-inflammatory 434, 436, 444
cytomere 20
dAReC (Duffy antigen receptor for chemokines) 58, 59–60,
  63, 468–70, 481, 528
deadacetylation of histones 154, 165, 167–8
  inhibitors 165, 167–8, 207
deadenylolation, mRNA 162
deaths see mortalities
dectabine 169
demethylation and demethylases, histones 155, 166, 168
  inhibitors 166, 168
dendrimer 190
dendritic cells 497, 500, 508
dense granules 40, 293, 336
deoxy-o-xylulose-phosphate (DOXP) 236
deoxyribonucleotides 252, 254
destabilization domain (DD)
  DHFR–DD system and 190
  FKBP–DD system and 189, 291–2
development (parasite) 15–20
  cyclic AMP role 297–8
  cyclic GMP role 298
  intraerythrocytic see erythrocyte
  proteases in 340–43
  sexual see sexual development
  see also life cycle
diacylglycerols 229
diagnosis 422
  P. vivax malaria 550
digestive see food (digestive) vacuole
dihydroartemisinin–piperaquine (Eurartesim) 373
dihydrofolate 265
dihydrofolate reductase (DHFR) 181
  in conditional protein degradation 190
  in forward genetic screens 186
  inhibitors 190, 211, 369, 371
  mutations in gene for 386, 387, 394
dihydrofolate reductase-thymidylatesynthese (DHFR-TS) 181
dihydroorotate dehydrogenase (DHOdH) 254, 269
  as drug target 182, 370, 371
dihydropterotide synthase gene (dihps), mutations causing drug
  resistance 386, 387, 394
dipeptidyl-aminopeptidases (DPAPs) 25, 330, 331, 343
DNA (parasite)
  base content 127
  deletion of sequences (in studies of protein function) 187
  high-throughput sequencing 136, 138
  host susceptibility and 444–5
  methylation 138, 157, 165, 169
  transcription see transcription; transcriptomics
  transfection with see transfection
  see also nucleic acid-based tests of drug resistance; nucleotides
DNA-binding proteins 147–61
  chromatin remodelling and 204
DNA/RNA-binding proteins, nonspecific 160–1
  dolichol 226, 239–40, 241
  domain cassette of var (DCs) 448–9
  DC8 438, 449
  double crossover integration 185
  doxycycline, proteome responses 211
DPAPs (dipeptidyl-aminopeptidases) 25, 330, 331, 343
drug(s) 353–407
  adjunctive 429
discovey and development 353–82
  advances in 21st century 265–7
    in broader concept of eradication 370–5
    elimination agenda 357, 367
    future medicines and targets for 256–7
    global pipeline of new agents 368–70
    identifying new compounds 360–2
    partnerships in 357
    speed and duration of action 360, 361, 365
    eradication using 359, 370–6
  genome-wide association studies of responses to
    135, 395–6
  half-lives 359, 368, 369, 376, 386, 391
  historical treatments 254–5
  mass administration (MDA) 422
  microarray studies of responses to 137
  national policies 399
  process 359–65
  prophylactic see chemoprevention
  proteomics and responses to 211–12
  sensitivity
    in vitro testing 393
    reversion of 390
  targets for 256–7
  gene regulation as 164–9
  membrane transport proteins as 307–24, 394
  mutations causing resistance 387, 394
  population genomics in identifcation of 136
therapeutic efficacy studies, outcomes 391
transcription in response to 207
transfection studies of 182
determining efficacy 113–14
drug resistance (and treatment failure) 364–5, 383–407, 422
causes 386–90
current state of affairs 383–4
detection 390–7
management 397–9
prevention strategies 398–9
public health burden 384–5
slowing of and protection from the development and emergence of 353, 364–5
transcription and 208
see also specific drugs
DSM1 182, 370
DSM265 370
Duffy antigen (receptor for chemokines - DARC) 58, 59–60, 63, 468–70, 481, 528
Duffy binding–like (DBL) family 37, 58–63, 528–9
vaccine development and 528–9
Duffy binding proteins (DBP) 59–60, 469
E‐selectin 446, 447
E64 (inhibitor of cysteine proteases) 24, 341, 342
Eastern Mediterranean Region, epidemiology 410, 411
EBAs see erythrocyte‐binding antigens
EBL‐1 (erythrocyte‐binding ligand 1) 63
EBV (Epstein–Barr virus) 510–11
edema, reducing 429
egress, parasite 23–6, 43, 49, 74, 332, 337, 340–1
electron flow/transport in mitochondria 254, 268–9, 318
electroporation 179–80
elimination see control measures
emergence of resistance see evolution and emergence of resistance
EMP1, P. falciparum (erythrocyte membrane protein 1) 131, 152, 437–8, 448, 449, 450, 471, 476, 500, 502, 505, 522, 533, 554, 555
endemicity 415–17
children living in areas of 427–30, 431–3
classification of levels of 417, 418
P. falciparum in Africa 414
P. vivax 548, 549, 550, 553
resistance/immunity in areas of 501, 502, 504, 507, 508, 509–10, 522
endoperoxides, next generation 368
endoplasmic reticulum (ER) 18, 20, 21
calcium and 292
plasmepsins in 329
endothelium
binding to receptors on (infected red blood cells/erythrocytes/reticulocytes) 554, 555, 557
in brain 446
sinusoidal 10, 11, 12, 13
endpoint assessment of drug resistance 396–7
energy metabolism 219, 225, 259
enoyl‐ACP reductase 229
entomological inoculation rate (EIR) 417, 418
environmental factors affecting transmission 419–20
epidemiology 409–26, 431–3
children see children
complement receptor-1 and 472
drug resistance affecting 385
P. vivax 438, 547–9
P. knowlesi 439
epigenetics (and epigenomics) 138, 150–7, 203–4, 204
outside stimuli and 207
see also DNA, methylation
episodes 184, 185, 190
epitope tags 191
Epstein–Barr virus (EBV) 510–11
eradication see control measures
erthrocyte‐binding antigens (EBAs), P. falciparum 37, 60–2
EBAs 37, 60, 62–3
EBV 37, 41, 58, 59, 60–2, 63, 67, 72
vaccine development and 529
EBV 37, 63, 72
erythrocyte‐binding ligand 1 (EBL‐1) 63
erythrocyte membrane protein 1, P. falciparum (PIEMP1) 131, 152, 437–8, 448, 449, 450, 471, 476, 500, 502, 505, 522, 533, 554, 555
erythrocyte stage/blood stage (infected red blood cells; IEs; RBCs) 3, 4, 24, 450
adhesion of parasites and 446–7
African children with severe malaria 434
endochondral ossification 435
endothelial receptors for infected erythrocytes see endothelium
signaling see signaling
surface proteins of infected erythrocytes see sequestration
placenta 433–4
in severe malaria 505
in uncomplicated malaria 500–3
membrane, as therapeutic target 308–11
merozoite invasion 33–86, 292, 293, 295, 296, 298, 299, 300, 340–1
molecular basis 33–86
redundancy and ligand‐receptor interactions mediating parasite adhesion during 57–8
steps 41–57
P. vivax 544, 545, 548–9
placenta 433–4
sequestration of infected erythrocytes see sequestration
signaling see signaling
surface proteins of infected erythrocytes 448–9, 450
transcriptional profiling 198–200
vaccines targeting 522–3, 526–33
Eurartesim (dihydroartemisinin‐piperazine) 373
Europe, their system for drugs used outside Europe 363
European Region (WHO), epidemiology 410, 411
endogenous malarial pigment 432
endosomal pathway 294
endosome 295
enol‐ACP decarboxylase 228
environmental factors affecting transmission 419–20
epidemiology 409–26, 431–3
children see children
complement receptor-1 and 472
FAD (flavin adenine dinucleotide) 257–8, 268
falcilysin 334
hemoglobin degradation and 341, 374

Index

GNF156 (KAf156) 369, 371
Golgi, Camillo 1
Grassi, Giovanni Battista 1, 2, 9, 87
green fluorescent protein 190
growth inhibition screens/assays (GIA) high-throughput in vitro 307
vaccines 527, 531, 532, 533
growth perturbations as tool for gene annotation 207–8

Guanosine monophosphate see GMP
Guanylyl cyclase (GC) 296, 297, 298
gut, parasite sequestration 435

GYPs (glycophorins) 58, 60–3, 67, 473

half-lives of drugs 359, 368, 376, 386, 391
halofantrine resistance, time difference between date of introduction and first report of 384
HaloTag 191
heart, parasite sequestration 435
heavy chain variable regions 501
helminth co-infections 443

Hemoglobin C 475–6
plasmodins in 329
hemoglobin E 476–7
hemoglobin S (sickle hemoglobin) 439, 475, 476, 504
hemoglobin C and (HbSC) 475
heterozygosity (HbAS; sickle cell trait) 439, 442, 475, 476, 504–5

hemoglobinopathies 439, 474–8

hemozoin 276, 444
hepatocytes (invasion by sporozoites) 10–16, 17, 21, 24, 26, 340, 367, 498, 499, 522–3, 533
proteases and 340
in vaccine development 523–4
heredity, see entries under genetic
herpes virus infection 510–11

HSP101 312

Human(s)
challenge models (volunteers) see challenge models
epidemiological factors relating to 421
see also host
human immunodeficiency virus (HIV) infection 353–4, 442–3
humidity affecting transmission 420
hydroxamates 165, 167
hyperendemicity 417, 418
hypnose (dormant liver) stage, drugs targeting P. ovale 357
P. vivax 357, 367, 384, 397
hypooendemicity 417, 418
hypoxanphine 252, 253, 445
ICAM-1 (intercellular adhesion molecule 1) 446, 480, 555
ICP see inhibitor of cysteine proteases
illnesses in malaria 427–30
P. vivax severe disease 550–2
IMC1a 16
imidazolopiperazine 369, 371

immune response (mosquito) 96, 103–5
immune response (vertebrate host) 105–6, 431–2, 433–9
acquired see acquired/adaptive immunity
candidate malaria-associated genes involved 480
children in endemic areas 431–2
innate see innate (natural) immune response
life cycle of parasite and 523
malaria in absence of 431
mild/uncomplicated 495–6, 497–503
protective 432, 434, 437–8, 521–2
P. vivax 438, 548, 549
pregnant women 433, 435, 533
severe malaria see severe malaria

severe/complicated malaria see severe malaria
immunization see vaccines
immunopathogenesis 433–9
in utero exposure 440

incidence
children in endemic areas 432
trends in 411
incubation period 415
India, drug resistance 389, 390
monitoring 399–400
indoor residual spraying (IRS) 421–2, 423
infants and toddlers
African, in endemic areas 433
intermittent preventive treatment for (IPTi) 375, 422
infections
coop‐infecting organisms 442–4
cycle see life cycle
risk of see risk of transmission/infection
within‐host diversity of 396
inflammatory response 435–7
infection, see entries under genetic
inhibitor of cysteine proteases (ICP) 11, 21, 24
E64 as 24, 341, 342
P. berghei (PbICP) 11, 12, 14–15, 24, 25
innate (natural) immune response
mosquito 103, 105
vertebrate host 436
in merosome formation 26–7
in severe malaria 505–6
inositol phosphate metabolism 234
insecticide
indoor residual spraying (IRS) 421–2, 423
nets treated with 103, 375–6, 421
integration systems 184–6
Bxb 182–3
intercellular adhesion molecule 1 (ICAM‐1) 446, 480, 555
interferon‐γ (IFN‐γ) 434, 436, 480
interleukin (IL) genes 480
intermittent preventive treatment
infants (IPTi) 375, 422
pregnant women 357, 375–6
interventions (treatment and therapy)
adjunctive 422, 429–30
at gene regulation level 164–9
pharmacological see drugs
transmission‐blocking see transmission
vaccines see vaccines
invaded (mosquito midgut) 93–5, 340
invasion (vertebrate host cell) 340–1
erythrocyte by merozoite see erythrocyte stage
in liver by sporozoite 14–15
proteases and 340–1
ion channels 307
as therapeutic target 308–11
iron 441–2
chelation 429, 441–2
status 441–2
supplementation 441, 442–3
isoisoprenoid metabolism 249, 250
isoprenoid 236
ISPA‐28 310
junction (tight) 51–7
formation 51–7
molecular composition 57
moving (MJ) 51, 52, 54, 65
KAE609 369, 372
KAF156 369, 371
Kennedy pathway 230
Kenya 442, 446, 466
children 436, 437, 440, 441, 449
adolescent 441
placental malaria 442–3
keto‐acids 249, 250
β‐ketocacyl‐ACP synthase 229
α‐ketoglutarate 245, 247, 258
killing rates of antimalarials 365
knob‐associated histidine‐rich protein (KAHRP) 184–5
knockdown of protein function, conditional 187–91
knockin mutations 185–6
knockout, gene
in double crossover integration 185
in single crossover integration 184–5
Knops antigens 471–2, 472–3
Koch, Robert 547–8
 Krebs (citric acid/TCA) cycle 219, 223, 245, 246, 256, 258, 269–73
laboratory culture of Plasmodium 4–5
Laveran, Alphonse 1, 446
Laverania group of P. falciparum 131–2
LC3 15, 20
lethality see mortalities
leucine metabolism 249, 250
leucyl aminopeptidase 334–5
leupeptin 310, 340
life cycle (parasite) 3–4, 87–102, 413–15, 499–500
antimalarial activities in 112
calcium homeostasis and 292–4
historical perspectives 2
immune system targets in 523
phosphoinositides and 296
transcriptional profiling 198–201
vaccine targets in see vaccines
see also development and specific stages
ligands (parasite) in invasion
identification 73–4
interactions with receptors 57–8
light chain variable regions 501
lineage‐specific gene families 130–2
linkage mapping 133, 135
lipid metabolism, P. falciparum 227–40
LISP2 21–2
live attenuated vaccines 534–5
liver stage see exoerythrocytic stage; hepatocytes; hypnozoite stage
long‐chain fatty acid CoA synthetase 229
luciferases 191–2
combined with other drugs 355, 356
lung, parasite sequestration 435
see also respiratory distress
lysine, metabolism 249, 251
lysine methylation and methyltransferases, histone (HKMT)
155, 166, 168
inhibition 166, 168
lysosome, digestive vacuole resembling a 316
macrogametes 4, 89, 93
Malaria Box 362
Malaria Parasite Metabolic Pathways 219
malate 223, 245, 254, 271, 273
malignant tertian malaria 2
mannose 239
mannose‐binding protein 2 gene (MBL2) 480
Marchiafava, Ettore 1
mass drug administration (MDA) 422
Maurer's cleft proteins 185, 211, 449
MBL2 480
mdr1 see multidrug‐resistant transporter
Medicines for Malaria Venture (MMV) 307, 356, 359, 362, 369, 370, 401
malaria 2
malate 223, 245, 254, 271, 273
mefloquine 387–8
historical treatment 354
resistance 387–8
mechanisms 387–8
time difference between date of introduction and first report of 384
meiosis 93
membrane
cell see plasma membrane
transporters see transport proteins
membrane-feeding assay (MFA) 113, 369, 533–4, 534
memory (antibody) 502, 503, 505
B cells 502, 503, 532
merosome 23–4, 522
innate immune responses and 26
merozoite(s) 3, 10, 20, 23–4, 33–86
as antibody targets 501
in vaccine development 522, 523, 526–8, 530–2
erthrocyte invasion by see erythrocyte
innate immune responses and 26
structure 39–41
merozoite-specific TRAP homologue (MTRAP) 36, 55–6
merozoite surface proteins (MSPs) 35–6, 41–50, 299, 531–2
GPI anchoring 41–2, 45, 47, 48, 49, 50, 51, 240
MSP-1 35, 42–6, 189, 337, 341, 502
vaccine development 526–7, 529, 531, 533
MSP-2 35, 47
vaccine development 531–2
MSP-3 35, 46–7
vaccine development 532, 533
MSP-4 35, 48
MSP-5 35, 48
MSP-6 35, 42–6
MSP-7 35, 42–6
MSP-8 35, 48–9
vaccine development 533
MSP-9 (ABRA) 35, 49–50
MSP-10 35, 50
MSP-DBLs 36, 46
mesoendemicity 417, 418
metabolism of P. falciparum 219–90
amino acid 240–50
carbohydrate 219–27
cofactors 256–65
lipid 227–40
metabolomics 5
metalloproteases/metallopeptidases 326–7, 333–5
methionine metabolism 231, 238, 242, 243, 244
methionyl aminopeptidase 335
3-methyl-chloroquine 354
methylation
DNA 138, 157, 165, 169
histone 155, 157, 170, 203
inhibitors 166, 168, 169
methylene blue with amodiaquine 372
ME-TRAP (multiple epitope string with thrombospondin-related adhesion protein) 526
microarray analysis 137–8
microgametes 4, 92, 294
micronemes 40, 41
proteins 36, 37
in vaccine development 530
microRNAs and sickle hemoglobin 505
microsatellite markers of drug resistance 389
midgut
gamete release 500
immunizing against components of 534
invasion (mosquito by parasite) 93–5, 340
mild malaria see uncomplicated/mild malaria
minority variants of drug resistance 396
mitochondria 18, 20, 25, 268–73, 318–19
electron flow/transport 254, 268–9, 318
glycine cleavage system 247, 248
inner membrane 318–19
TCA cycle 219, 223, 245, 246, 256, 258, 269–73
in translation 210, 211
MMV (Medicines for Malaria Venture) 307, 356, 359, 362, 369, 370, 401
MMV390048 370, 371
molecular biology
doF drug resistance 386–7, 394
merozoite invasion of erythrocyte 33–86
severe P. vivax malaria 552–8
molecular force-of-blood-stage infection (molFOB) 548
molecular genetics see genetics; mutations
molecular studies, advent of 5
molecular surveillance guiding selection of therapeutic efficacy sites in Cambodia 395
monitoring of surveillance resistance 399–400
in vivo 390–3
molecular, guiding selection of therapeutic efficacy sites in Cambodia 395
transmission intensity 418
see also routine case surveillance
monoclonal antibodies 526
to AMA-1 53
to PIRH5 70
Montanide ISA51 534
Montanide ISA720 526, 529, 532
mortalities (deaths; lethality) 409–10
adjunctive therapies impacting on 429
P. vivax 551
reduction 411
Mosquirix (RTS,S) 375, 376, 497–9, 524–5, 535
mosquito (vector) 102–5
anopheline see Anopheles
see also vectorial capacity
motility, parasite (and its motor) 54, 55, 295, 338
gliding (and actin–myosin/glideosome motor) 10, 15, 16, 51, 54, 97, 293, 295, 338
mouse models in therapeutics development 428–9
drugs 362, 366, 367
immunization/vaccines 497, 531, 532
systemic lupus erythematosus and resistance to malaria 507, 510, 511
moving junction (MJ) 51, 52, 54, 65
MSPs see merozoite surface proteins
MTRAP (merozoite-specific TRAP homologue) 36, 55–6
multidrug-resistant transporter (PIMdr1/P-glycoprotein homologue 1) 211, 317–18, 386–7, 389, 390, 394, 395
chloroquine and 387, 553
copy number 553
copy number in P. vivax 553
copy number in P. falciparum malaria 317
and clinical outcomes 387, 388
multiple epitope string with thrombospondin-related adhesion protein (ME-TRAP) 526
Index

mutagenesis, transposon-mediated 138, 186
mutations
  human, affecting susceptibility 368, 470, 473, 474, 475, 476
detection 394
Myb1, P. falciparum (PfMyb1) 158, 159, 202
MYST (PfMyst) 154, 155, 165, 170
N-glycosylation 60, 225–6
NAD see nicotinamide adenine dinucleotide; nicotinamide adenine
dinucleotide dehydrogenase
NADP(H) see nicotinamide adenine dinucleotide phosphate
naphthoquine 368
artemisinin with 355, 374
next generation methods see high-throughput
next generation endoperoxides 368
nicotinamide 165, 167, 257
nicotinamide adenine dinucleotide (NAD) 154, 247, 257
nicotinamide adenine dinucleotide dehydrogenase (NADH
dehydrogenase) 258, 269
nicotinamide adenine dinucleotide phosphate (NADP(H)) 257
nicotinate 257
nitric oxide (NO) 244
adjunctive therapy 429, 430
nitric oxide (NO) synthase, inducible (NOS2) 442
gene (NOS2A) 480
NK cells 436, 501
NOD1/2 480
non-immune adults 431
NOS see nitric oxide synthase
NPC-1161-B 371
nucleic acid-based tests of drug resistance 394
endpoint 396–7
point-of-care 396
see also DNA; RNA
nucleolus, organization 156
nucleosome 150–1, 152, 154, 163
nucleotides
  base content 127
  cyclic see AMP; GMP
  metabolism 252–5
  purines 243, 252–4
  pyrimidines 220, 239, 244, 254–5
  nucleus (parasite) 156–7
  replication in liver stage 18
  nutrient channel as drug target 308–11
O blood group 469
O-glycosylation 226–7
oocyst
  formation 95–102
  sporozoite formation in 99
ookinete 4, 16, 93–5, 97, 102, 104, 107, 160, 295
  transmission-blocking interventions and 111, 112, 113, 534
  organelles 18–20
  merozoite 39, 40
  apical organelles 40, 50, 66, 74, 530
ornithine 242, 244, 245
orotate 254
orthologues 128, 169, 314
ApiAP2 160
DNA methyltransferase 157
EBA 62
falcipains 330
histone demethylases 155
long-chain fatty acid CoA synthetase 229
membrane transporters 314, 315
serine repeat antigen 332
ovalocytosis 374
Southwest Asian 439, 474
oxaloacetate 223, 245, 254, 273
oxidant stress 480
G6PD deficiency and 478
oxidation–reduction (redox) metabolism 246, 265–8
3-oxoacyl-ACP reductase 229
OZ277 (Arterolane/ RbX11160) 356, 368, 374
OZ439 356, 368, 372
P-glycoprotein homologue 1 see multidrug-resistant transporter
P47 protein 93
PA1003/SAR116242 371
PA21A092 370, 371
PAC (puramycin-N-acetyl-transferase) gene 181
P . vivax vs P . falciparum 438
PECAM-1 (CD31) 446, 447, 480
pediatrics see children
pentose phosphate pathway 221–3
Pexel motif 21, 206, 296, 312, 313, 329
Pl (genes and proteins prefixed with), see specific genes/proteins
e.g. Alba; AMA-1
pharmacokinetic and pharmacodynamic modeling 365–6
phase I trials
drugs 363, 364, 366, 369, 370, 371, 372
vaccines 529, 532, 534
phase II trials
drugs 363, 364, 368, 371, 372
vaccines 524–5
phase III trials
drugs 363, 364, 368, 373, 374
vaccines 376, 525
PHD domains 155, 169, 170
phenylalanine metabolism 249, 251
phosphatidylcholine 230, 232, 235, 243, 248
phosphatidylethanolamine 230, 241, 248
phosphatidylglycerol 233
phosphatidylinositol (PI) 233, 241, 295, 296
phosphatidylserine 220, 241, 248
phosphodiesterase, cyclic nucleotide 296, 297
phosphoenolpyruvate (PEP) 221, 223, 225, 271
phosphoinositide(s) (IPs) 295–6
life cycle and metabolism 233, 234, 295–6
polyphosphorylated (PIP) 274, 295, 296
signaling and trafficking 295–6
phosphoinositide-specific phospholipase C 292
phospholipase C (PLC) 74, 236, 292, 294, 295
phosphoinositide-specific 293
phospholipids 229, 230, 233, m 235
phosphorylation (protein) 291–2
histone (and histone kinases) 155, 166, 170
as drug target 168
physical factors affecting transmission 104
piggyBac transposon 186–7
piperazine
dihydroartemisinin (Eurartesim) with 373
fosmidomycin with 372
Rbx11160/OZ277 with (Synriam) 356, 368, 374
resistance, time difference between date of introduction and first report of 384
placental malaria 430, 433, 440, 533
adhesion to chondroitin sulfate 533
epidemiology 433
HIV and 442, 443
iron status and 441
susceptibility to infection (offspring) in 440
see also pregnancy malaria
plasma cells, long-lived antibody-secreting (LLPCs) 502–3
plasma membrane (cell membrane)
erthrocyte 308–11
proteins, as susceptibility factors 473–4
parasite 314–16
plasmepsins 328–9, 341–2
plasmids
gene function studies using 184–7
transfection using 179–84
plasmodial surface anion channel (PSAC) as drug target 308–11
Plasmodium (malaria parasite – non-species specific references)
burden see parasitemia
cladogram 126
clearance time and rate 392
development see development
dynamics in mosquito 106–10
egress 23–6, 43, 49, 74, 332, 337, 340–1
export element (Pexel motif) 21, 206, 296, 312, 313, 329
genome see genome
host cell see cell
killing rates (reduction ratio) with antimalarials 365
laboratory culture of 4–5
life cycle see life cycle
membrane transport proteins, as therapeutic targets 307–24
mixed infections (of two different species) 443–4
mosquito behavior influenced by 103
mosquito midgut and see midgut
naming/discovery 1
proteases see proteases
sequestration see sequestration
signaling see signaling
transcription factors 157–8
transmission biology 88–102
vaccine development efforts primarily focusing on 524
virulence 444–9
Plasmodium berghei
inhibitor of cysteine proteases (PbICP) 11, 12, 14–15, 24, 25
in vaccine development 531
Plasmodium falciparum
apical asparagine-rich protein (PIAAP) 38, 73, 530, 531
apical membrane antigen 1 see apical membrane (merozoite) antigen 1
biochemistry see metabolism
burden see parasitemia
cerebral malaria see cerebral malaria
epidemiology 409–26
resistance 385
erthrocyte-binding antigens see erythrocyte-binding antigens
global areas at risk for P. falciparum transmission 412, 414
laboratory culture of 4–5
Laverania group 131–2
merozoite invasion 33–75
erythrocyte stage 199
naming/discovery 1
resistance
chloroquine 384, 386, 387, 389, 390
emergence 386
epidemiology 385
mechanisms 386–8
molecular markers 394
reticulocyte binding-like homologous proteins see reticulocyte binding-like homologous proteins
thrombospordin-related apical merozoite protein (PTTRAMP) 56, 530, 530
Plasmodium knowlesi 438–9
Duffy binding proteins (PkdBP) 59–60, 469
severe disease 438–9
Plasmodium malariae
naming/discovery 1
quartan malaria 1, 2
Plasmodium ovale, drugs targeting hypnozoite stage (dormant in liver) 357
Plasmodium vivax 547–64
benign tertian malaria 2, 438
chloroquine
resistance 384, 400, 552–4
therapeutic efficacy studies 391
drug interventions
chloroquine, see subentry above
new models for 366–7
relapse prevention 366–7
resistance to, see subentry below
targeting dormant liver (hypnozoite) stages 357, 367, 384, 397
Plasmodium vivax (cont’d)
drug resistance 384, 400, 550–8
  emergence 386
  epidemiology 385
  molecular markers 394
Duffy binding proteins (PvDBP) 59–60, 469
  epidemiology 438, 547–9
  immunity/resistance to
    natural 522, 548, 549
  vaccines conferring 469–70, 528–9, 534
merozoite invasion 33, 39, 40, 50, 52, 58–9, 60, 63, 64
  erythrocyte stage 199
  naming/discovery 1
relapse
  see relapse
erythrocyte stage 199
severe disease 438, 550–8
  immunity to malaria in 433, 435, 533
  in utero exposure 440
  pathogenesis 430, 433, 434–5
  immune system and 433–4
  prevention 357, 375–6, 422
  transcriptomic studies 206
  see also placental malaria
pre-mRNA, alternative splicing 161–2
  prenylated proteins 237–9
  presenilin-like protease 330
prevention of malaria
drugs see chemoprevention; control
  intermittent see intermittent preventive treatment
  vaccines see vaccines
primaquine
  G6PD deficiency and 366, 551
  with P. vivax 366
programmed cell death (apoptosis) 25, 26, 27, 31
proguanil
  historical treatment 354
  resistance, time difference between date of introduction and first report of 384
pro-inflammatory response 435–7
  cytokines 434, 436, 444
proline metabolism 242
  polymers 244
  promoters 202–3
prophylaxis of malaria see chemoprevention
proplasmepsins 274
proteases (and proteolysis) 24, 25, 325–52
  cysteine see cysteine proteases
  in parasite development 340–43
  in post-translation processing 209
  rhomboid 41, 66, 336, 337–8, 342
  translation 210–11
proteasome 327, 338, 339
  protection from malaria see chemoprevention; control; host protein(s)
  biosynthesis 244, 246
  see also amino acids; translation
  conditional knockdown of function 187–91
  DNA-binding see DNA-binding proteins
  export into host cells 20–3
  GPI anchoring of see glycosylphosphatidylinositols
  localization tags 190–1
  membrane of erythrocytes affecting susceptibility 473–4
  of Plasmodium, transport see transport proteins
  P. falciparum erythrocyte invasion-related 35–8
  phosphorylation see phosphorylation
  prenylated 237–9
  reporters 190
  surface see surface proteins
  trafficking, conditional blockage 190
  protein kinase(s), calcium-dependent 294–5
  protein kinase A 74, 298
  protein kinase CK2 155
  protein kinase G (PKG) 74, 298–300
  inhibitor 186, 299
  proteolysis see proteases
  proteomics 5, 197, 208–9
  combined transcriptomics and 197
  drug responses and 231–2
PTEX complex 309, 312
  public health burden of drug resistance 384–5
  puramycin-N-acetyl-transferase (PAC) gene 181
  purine metabolism 243, 252–4
  putrescine 242
  Pyramax (pyronaridine-artesunate) 356, 373
  pyrazole 370, 371
  pyridoxal phosphate (vitB6) metabolism 220, 259–60
  pyrimidine metabolism 220, 239, 244, 254–5
  pyronaridine-artesunate (Pyramax) 356, 373
  pyruvate metabolism 220, 223–5, 246
quartan malaria 1, 2
quinine
  historical use 354
  resistance, time difference between date of introduction and first report of 384
rainfall affecting transmission 420
rapid diagnostic tests 422
Rbx11160 (Arterolane/OZ277) 356, 368, 374
receptors in invasion
  ligand–receptor interactions 57–8
for *P. falciparum* invasion–related proteins 35–8
red blood cell see erythrocyte stage
redox metabolism 246, 265–8
relapse (relapsing stage/relapsing fever)
  *P. vivax* 397, 548–9, 550–1
  prevention 366–7
  resistance in 397
research
  current agenda 88
  laboratory culture of *Plasmodium* as milestone in 4–5
  molecular genetics 170–95
  technologies (present–day) in, advent of 5–6
resistance
  of host to malaria see host of malaria to drugs
respiratory distress
  African children 428
  *P. knowlesi* 439
  *P. vivax* 438, 551
reticulocyte binding proteins, *P. vivax* (PvRBPs) 63–4, 65, 529
reticulocyte binding–like homologous (PIRH) proteins 37, 64–71, 529–31
  RH1 37, 65–6, 67, 69, 529, 530, 531
  RH2 66–8
  RH2a 37, 64, 66, 67, 529
  RH2b 37, 66, 67, 72
  RH4 37, 66, 68, 72, 529, 530, 531
  RH5 37, 68–71, 499–500, 501, 529, 530–1
  in vaccine development 529–31
reticulocyte binding–like family (RBL family) 68–72
  Duffy binding–like (DBL) family and 72
reverse genetics 138, 184
RH see reticulocyte binding–like homologous proteins
Rh5–Ripr membrane anchoring protein (RRMAP; cysteine–rich protective antigen; CyRPA; RRMAP) 37, 61, 70, 71, 73, 531
RNA
  messenger (mRNA) transcripts
    deadenylation 162
    global analysis 136–7
    stability, as gene regulation checkpoint 162
    translational regulation 162–4, 209–12
  micro– (miRNA), sickle hemoglobin (HbS) and 505
  non-coding (ncRNA) transcripts 205
  long 137, 162, 205
  microarray studies 137–8
    short 137, 162, 205
  pre-messenger, alternative splicing 161–2
  see also DNA/RNA-binding proteins, nonspecific; nucleic acid–based tests of drug resistance
  RNA polymerase II and III 156, 201
Roll Back Malaria Partnership 411, 421, 423
RON see rhoptry neck proteins
  rosetting, parasite 448
  *P. vivax* 557
Ross–MacDonald formula 87, 107, 110
routine case surveillance 415–17
RRMAP (cysteine–rich protective antigen; CyRPA; RRMAP) 37, 61, 70, 71, 73, 531
RTS,S (Mosquirix) 375, 376, 497–9, 524–5, 535
salivary glands (mosquito)
  immunizing against components of 534
  sporozoites 2, 98–9, 107, 110, 113, 201
  salmonellosis, non-typhi 442
SAR97276 372
SAR116242/PA1103 371
schistosomiasis 443
schizogony (asexual reproduction) 3, 18, 91
schizont–infected cell agglutination var (*SICAvar*) 130, 132, 449
schizonticides 89, 112, 367, 386
SCID (severe combined immunodeficiency) mouse model
  drugs 362, 366, 367
  vaccines 531, 532
  screening for new drugs 360–2
  seasonality affecting transmission 420
  seizure prophylaxis 429, 430
  selectins 446, 447
  selenocysteine 249–50, 252
  semaphorin-7A 56
sequestration (infected erythrocytes) 428, 434, 435, 446, 505, 522–3
  antibodies blocking 500, 501
  brain 428, 435, 503
  gut 435
  heart 435
  lung 435
  *P. vivax* 438, 554, 557
  serine, metabolism 247
  serine/arginine–rich (SR) proteins 161–2
  serine-decarboxylase phosphoethanolamine methyltransferase (SDPM) pathway 230
  serine proteases 327, 335–8
  serine repeat antigen (SERA) proteases 25, 332, 337, 340
  SET domain–containing enzymes 155, 166, 177
  severe combined immunodeficiency mouse model see SCID
  severe malaria (SM) and complicated malaria 428–64, 496–7
  adjunctive therapies 429–30
  children 432–3, 434–5, 450
  definition 551
  immunity/resistance to/protection from 434–5, 450, 495–6, 503–6
  blood group O antigen and 495
  *P. knowlesi* 438–9
  *P. vivax* 438, 550–8
  pathogenesis 428–64
  sequence of events in progression from mild malaria to 503–6
  sexual development 88–91
  transcriptional profiling 200–1
shedases see subtilisin/subtilisin-like proteases
shikimate metabolism 220, 262–3
SICAvar genes (schizont-infected cell agglutination var) 130, 132, 449
sickle hemoglobin see hemoglobin S
signaling (signal transduction) 291–305
  blood stage 293, 295–6, 296, 298, 299, 300
  erythrocyte invasion 74–5, 293, 294, 295
single crossover integration 184–5
single nucleotide polymorphisms (SNPs) 135–6
hemoglobin S 475
Plasmodium 135–6
  drug resistance and 394
sinusoidal endothelium 10, 11, 12, 13
SIP2, P. falciparum (PfSIP2) 159, 161, 204
skin, sporozoite movement to liver from 10–14
Sl (Swain–Langley) blood group system 471, 472–3
SLE see systemic lupus erythematosus
Sle-1 472
SLC4A1 474
socioeconomic status 421
solute carrier 4A1 gene (SLC4A1) 474
solute exchange, parasitophorous vacuole membrane 313
Southeast Asia (WHO region), epidemiology 410, 413
Southeast Asian ovalocytosis 439, 474
spermidine 242
spermine 242
sphingomyelin 235–6
spiroindolone 368, 369, 372
splitting of pre-mRNA, alternative 161–2
sporoblast 97
sporozoite 3, 10–26, 97–8
  formation 97
  of hepatocytes see hepatocytes
  invasion 14–15
  journey from skin to liver 10–14
  in salivary glands 2, 98–9, 107, 110, 113, 201
  transformation to trophozoite 16–17
  in vaccine development 497, 522–6, 534–5
Sri Lanka 466, 549
SSR-97193 (ferroquine) 368, 372
starvation conditions, host cell 16, 19
STEVOR 89, 91, 131, 132, 206, 449, 554
sub-Saharan Africa
  burden in 413
  helminth infection 443
subtelomeric regions 128, 130, 131, 151, 160, 204, 206
  chromatin compartmentalization 152
  P. vivax 554, 555
subtilisin/subtilisin-like proteases (sheddases) 25, 40, 327, 336–7, 340
  SUB1 40, 43, 54, 299, 327, 333, 336–7
  SUB2 43, 44, 45, 327, 336, 377, 341
  SUB3 336
succinate dehydrogenase 258, 269, 271
succinyl-CoA 262, 271
sulfadoxine–pyrimethamine 384, 387, 390, 391, 398
  children 375
  pregnancy 376
  resistance/failure 355, 376, 386, 387, 389, 394, 398
  India 400
  mechanisms 387
  time difference between date of introduction and first report of 384
sulfamethoxazole–trimethoprim 374
sulfonamides and sulfones 354
surface, erythrocyte, merozoite attachment to 41–50
surface proteins
  gamete, as vaccine targets 534
  infected erythrocytes 448–9, 450
  merozoite see merozoite surface proteins
  ookinetes, as vaccine targets 534
surveillance see monitoring
susceptibility factors see host
Swain–Langley (Sl) blood group system 471, 472–3
Syntiam (piperazine with Rbx11160/OZ277) 356, 368, 374
syndey 128–30
systemic lupus erythematosus (SLE) 507–11
T cells 497, 500, 503, 505
  vaccine development 524, 525, 526, 533
tafenoquine 373
  chloroquine combined with 357
target candidate profiles (TCPs) in combination medicines 359–60
TCA (citric acid/tricarboxylic acid) cycle 219, 223, 245, 246, 256, 258, 269–73
technologies (present-day) in research
  advent of 5–6
  merozoite invasion 34
telomere 138, 154, 156
  see also subtelomeric regions
tetrahydrofolate 264, 265
Thailand 354, 368, 388, 466
P. vivax 555, 557
thalassemias 477–8
  α-thalassemia 439, 477, 478
  β-thalassemia 477
The Gambia 136, 430, 433, 437, 466, 502, 506
therapy see interventions
thiamine (vitamin B1) 258–9
thioredoxin (Trx) system 268
thrombospondin domain-containing proteins 36
thrombospondin-like region 524
thrombospondin-related anonymous/adhesive protein (TRAP) 10, 54–5, 57, 338
  vaccine development 526
thrombospondin-related apical merozoite protein, P. falciparum
  (PITRAMP) 56, 530
thrombospondin repeat (TSR) domain 11, 15, 56
tight junction see junction
time trends 411
TLRs see Toll-like receptors
TNF-α 434, 436, 445, 480
Toll-like receptors (TLRs) 480, 499
  TLR-7 507–8
  TLR-9 444, 499
TRAMP, P. falciparum (PITRAMP; P. falciparum thrombospondin-related apical merozoite protein) 56, 530
trans-factors associated with histone modifications and chromatin structure 154–6
transcript(s)
  conditional degradation 189
  global analysis 136–8
intraerythrocytic development, direct sequencing of expressed transcripts, erythrocyte 199
transcription
basal machinery 201–2
drug resistance and 208
outside stimuli affecting 207
profiling
in vitro versus in vivo profiles 205–6
troughout life cycle 198–200
promoters 202–3
regulation 189–92, 201–5
systems for studying 187–9
RNA polymerase II and III-mediated 156, 201
start sites (TSS) 149, 150, 157
var 449
variation 205–8
transcription-associated factors/proteins (TAFs/TAPs) 157, 202
transcription factors 157–61, 201–2
transcriptomics 5, 197–217
combined proteomics and 197
transfection (genetic transformation) 138, 179–82
methods 179–80
stable 181–2
transient 180
transformation
 genetic see transfection
sporozoite to trophozoite 16–17
transgenic studies 184–5, 192
chloroquine resistance 553
cytoadherence 557
vaccines 534
translation, regulation 162–4, 209–12
translocations, chromosomal 128
transmembrane domain (TMD) of rhomboid proteases 337, 338
transmigration of sporozoite through cells 3, 13–14
transmission 87–123, 413–19
biology 87–123
blocking interventions 110–14
vaccines 111, 533–4
chain of 413–15
factors affecting 419–21
historical perspectives 2, 87–8
intensity
age at peak incidence related to 432
contributing to resistance 389–90
monitoring 418
measuring/assessing 417–18
risk for see risk of transmission
transport proteins
drug, mutations causing drug resistance 386–7, 389
as therapeutic targets 307–24
transposons 186–7
transposon-mediated mutagenesis 138, 186
TRAP see thrombospondin-related anonymous/adhesive protein
TRAP homologue, merozoite-specific (MTRAP) 36, 55–6
travelers, non-immune 431
treatment see interventions
trends (over time) 411
triaclyglycerols 229
tricarboxylic acid (TCA) cycle 219, 223, 245, 246, 256, 258, 269–73
trimetoprim 190
sulfamethoxazole with 374
trophozoite, sporozoite transformation to 16–17
TSR (thrombospondin repeat) domain 11, 15, 56
tumor necrosis factor-α (TNF-α) 434, 436, 445, 480
twin studies of genetic risk factors 466
tyrosine metabolism 249, 251
ubiquinone biosynthesis 260–1
ubiquitin 339
UMP (uridine 5’-monophosphate) 254
uncomplicated/mild malaria, resistance/immunity to 495–6, 497–503
sequence of events in progression to severe malaria from 503–6
uridine 5’-monophosphate (UMP) 254
uridine 5’-triposphate (UTP) 254
uroporphyrinogen III decarboxylase and synthase 262
UTP (uridine 5’-triposphate) 254
vaccines (immunization) 376, 521–45
development 375, 376, 521–45
life cycle points of intervention with 522–34
blood stage 522–3, 526–33
exoerythrocytic/pre-erythrocytic 524–6
transmission 111, 533–4
live attenuated 534–5
P. vivax 469–70, 521
PRH5 (reticulocyte binding-like homologous protein-5) and 69
population genomics in identification of targets for 136
RTS,S (Mosquirix) 375, 376, 497–9, 524–5, 535
severe malaria 451
valine metabolism 249, 250
var 59, 131, 132, 150, 152, 154, 155, 156, 157, 160–1, 203, 204, 205, 448–9, 533, 544
antibodies to 500, 533
domain cassettes see domain cassettes
schizont-infected cell agglutination (SICAvar) 130, 132, 449
variable regions of heavy and light chains 501
variantome 205
vascular cell adhesion molecule 1 (VCAM-1) 445, 446, 447
VCAM-1 (vascular cell adhesion molecule 1) 445, 446, 447
vectorial capacity 417
see also Anopheles; mosquito
dir and VIR (P. vivax) 132, 554–5, 555–7
viral vectors in vaccination 525
virulence 443–9
vitamin B1 (thiamine) 258–9
vitamin B2 (riboflavin) 257–8
vitamin B3 see nicotinamide; nicotinate
vitamin B6 (pyridoxal phosphate) metabolism 220, 259–60
vitamin B9 (folate) metabolism 243, 264–5, 266
volume expansion 429, 430
volunteers in human challenge models see challenge models
vulnerable populations, chemoprevention see chemoprevention

Western Pacific Region, epidemiology 410, 411, 413
WHO see World Health Organization
within-host diversity of infections 396
World Health Organization (WHO)
Global Malaria Eradication Programme 88, 411, 423
goals for incidence reduction 411
number of malaria cases and proportion to P. falciparum cases by WHO region 409, 410
number and proportion of deaths in young children by WHO region 410
World Wide Antimalarial Resistance Network (WWARN) 400
worldwide aspects see global aspects/dimensions
xanthine oxidoreductase (XO) and its inhibitors 445
zygote 93