

Stress Response in Microbiology

Edited by

Jose M. Requena

Centro de Biología Molecular ‘Severo Ochoa’ (CSIC-UAM)
Madrid
Spain



Caister Academic Press

Copyright © 2012

Caister Academic Press
Norfolk, UK

www.caister.com

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

ISBN: 978-1-908230-04-1

Description or mention of instrumentation, software, or other products in this book does not imply endorsement by the author or publisher. The author and publisher do not assume responsibility for the validity of any products or procedures mentioned or described in this book or for the consequences of their use.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the publisher. No claim to original U.S. Government works.

Cover design adapted from Figure 13.3

Printed and bound in Great Britain

Contents

Contributors	v
Preface	ix
1 Cell Wall Stress-sensing Regulatory Systems in Gram-negative Bacteria Juan A. Ayala, Felipe Cava and Miguel A. de Pedro	1
2 Stress Responses in <i>Streptococcus</i> Jacqueline Abrançhes and José A. Lemos	19
3 Oxidative and Nitrosative Stress Responses in Pathogenic <i>Neisseria</i> Isabel Delany and Kate L. Seib	41
4 Stress Response in <i>Listeria monocytogenes</i> Ewa Wałecka and Jacek Bania	91
5 Mechanisms Involved in Low-temperature Adaptation in <i>Bacillus cereus</i> Julien Brillard and Véronique Broussolle	125
6 Stress Responses in <i>Salmonella</i> Suzanne Humphrey, Tom J. Humphrey and Mark A. Jepson	147
7 Stress Response in the Pathogenic <i>Yersinia</i> Species N. Kaye Horstman and Andrew J. Darwin	177
8 Adaptations to Environmental Changes: Stress Response Mechanisms among <i>Vibrio</i> Species W. Brian Whitaker and E. Fidelma Boyd	201
9 Stress Responses in <i>Mycobacterium</i> Richard W. Stokes	229
10 Stress Response in Mycoplasmas Melissa L. Madsen and F. Chris Minion	247
11 Stress Responses in Yeast Eulàlia de Nadal and Francesc Posas	257

12	Stress Response in the Human Malaria Parasite <i>Plasmodium falciparum</i>	287
	Sylke Müller and Christian Doerig	
13	<i>Toxoplasma gondii</i> : Without Stress There is No Life	305
	Maria J. Figueras, Sergio O. Angel, Verónica M. Cáceres and María L. Alomar	
14	The Stressful Life of Pathogenic <i>Leishmania</i> Species	323
	Jose M. Requena	
15	The Stress Response of <i>Trypanosoma cruzi</i>	347
	Turán P. Ürményi, Deivid C. Rodrigues, Rosane Silva and Edson Rondinelli	
16	Stress Response in the Infective Stage of <i>Trypanosoma brucei</i>	377
	Marcelo A. Comini, Andrea Medeiros and Bruno Manta	
17	Stress Response in <i>Entamoeba histolytica</i>	405
	Alfonso Olivos-García, Emma Saavedra, Erika Rubí Luis-García, Mario Nequiz and Ruy Pérez-Tamayo	
	Index	429

Preface

Every living organism must cope with environmental changes that may represent stress situations, including elevated temperature, chemical stress or oxidative injury. Cells respond to stress stimuli through coordinated changes in gene expression, leading to the synthesis of specialized molecules that counteract the deleterious environmental insults. Bacteria and eukaryotic microorganisms are very useful for studying the stress response and its regulation as they have developed systems to constantly monitor the changing environment. One group of organisms that is subjected to dramatic environmental challenges throughout their life cycle, including large changes in temperature, availability of nutrients and exposure to host immune defenses, is the pathogenic microorganisms. For pathogenic bacteria and parasites that are transmitted from the environment (or by invertebrate vectors) to mammalian hosts, sudden changes in pH, osmotic pressure and temperature occur. Additionally, inside the body, invading microorganisms soon encounter the innate and adaptive defenses. The pathogens, as a group, have evolved a variety of mechanisms to circumvent the otherwise lethal effects of these defenses. On the other hand, pathogenic microorganisms have integrated the stress response into their life cycles, in which stress signalling pathways and the self-same stress proteins play specific functions in the differentiation programme.

Stress Response in Microbiology comprises 17 excellent chapters, each one dedicated to a particular microorganism or group of microorganisms; most of the selected organisms represent important health threats for humans. With its coverage of a broad range of model organisms,

the book gives a complete overview of the stress response in both prokaryotic and eukaryotic microorganisms, providing detailed information for researchers, as well as for teachers and students in the fields of microbiology and parasitology. The chapter authors, among the best in their respective fields, have done an excellent job of synthesizing data from numerous studies and making the book a well-referenced work. Thus, we hope that this work will serve as an informative resource for researchers and students at all levels.

The first chapter provides a complete description of the cell envelope stress responses and the stress-sensing regulatory systems, mainly in Gram-negative bacteria. Chapter 2 gives an overview on the stress responses in several pathogenic species of the genus *Streptococcus*; acid, oxidative and nutritional stresses are presented here in depth. Chapter 3 is devoted to oxidative and nitrosative defenses in pathogenic *Neisseria* species. In addition, the authors have included detailed information about biologically relevant oxidants and the chemical reactions involving oxidants in biological systems that are of considerable basic scientific interest. The relationship between stress response and virulence in the food-borne pathogen *Listeria monocytogenes* is the main focus of Chapter 4. Chapter 5 focuses on current knowledge and research activity about low-temperature adaptation of the spore former and human pathogen *Bacillus cereus*. Chapter 6 gives a complete overview of the main stress response mechanisms employed by *Salmonella* for survival in nutrient-limited conditions and during osmotic and acid stress exposure. In the next chapter, devoted to *Yersinia*, the authors

review the responses of this pathogen to heat and cold shocks, encounter with macrophages and macrophage-like conditions. Also, the extracytoplasmic stress responses are covered in detail in Chapter 7. Chapter 8 describes how the stress response systems are vitally important for the vibrios to successfully establish in the host. Chapter 9 describes the function of the major stress proteins within mycobacteria, paying special attention to the interaction between the bacterial heat shock proteins and the host's cell-mediated immune response. Chapter 10 focuses on the types of stresses that mycoplasmas encounter *in vivo*, such as heat shock, oxidative stress, osmolarity shifts, hormone exposure, iron deprivation and biofilm formation. In Chapter 11, the authors describe the different mechanisms used by model yeasts *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*, as well as the pathogenic fungus *Candida albicans*, to sense and transduce stress signals to stress-activated protein kinases pathways in response to osmotic, heat and oxidative stresses. Among eukaryotic microorganisms, one group that is subjected to dramatic environmental changes throughout their complex life cycle are the parasitic protozoa, which are the focus of the remaining chapters. Chapter 12 summarizes the current knowledge about the responses of the malaria parasite *Plasmodium falciparum* to a variety of stresses: drug treatments, changes in temperature and elevation of oxidative stress. Chapter 13 summarizes the recent findings on

the *Toxoplasma gondii* stress responses and the implication of these processes in the biology and pathogenesis of this parasite. The focus of Chapter 14 is the stress response in *Leishmania*, containing a comprehensive view on the implications of the stress response in parasite survival, in cytodifferentiation and in apoptotic processes. Chapter 15 reviews the components of the *Trypanosoma cruzi* stress response with emphasis on its relevance to the parasite biology and to Chagas' disease transmission, pathogenesis and treatment. In Chapter 16, the authors have compiled the most significant molecular and biological aspects related to the mechanisms and components of the stress response of *T. brucei* to adapt and survive in the bloodstream of mammals. The final chapter, devoted to *Entamoeba histolytica*, gives special emphasis to the oxidative and nitrosative stresses experienced by this protozoan parasite.

The acknowledgements list must start with our authors, who have generously expended time and effort in preparing and revising their chapters. Publication of a book requires the effort of many people besides the authors, and I wish to express special appreciation to the editorial and production staffs. In particular, I would like to thank Hugh Griffin for his guidance and support, and Emma Needs, who worked extremely hard coordinating production. Finally, without the comprehension and support of our families, this work could not be achieved. In particular, I would like to dedicate this book to my daughter Carmen.

Jose M. Requena

INDEX

A

A2 329, 331
 Acid stress 24–26, 102, 204–205, 382
 Acid tolerance response 25, 102, 150t, 153–154, 164, 203–207, 216, 219–220
Acidocalcisome 347, 349, 350, 351f, 366
AckA 3, 4f, 250
Acr 231
 ACT *see* Artemisinin combination therapy
ActA 93, 112
Actinomycin D 363
AdhC 65
 Adjuvant arthritis 233
 ADI *see* Arginine deamination system
Aeromonas hydrophila 8, 9f
 African trypanosomiasis *see* Sleeping sickness
 Agmatine deminase system 25, 105
AhpC 26, 29, 49t, 62, 150t, 159
 AI-2 31
 Alanine 9, 138, 336
 Alarmone ppGpp 5, 5f, 30–31, 101, 131
 Amastigote 324, 329, 331, 333, 337, 348
 American trypanosomiasis *see* Chagas' disease
 D-amino acids 12–14
 γ-Aminobutyrate 103
 Amoebe 406, 409f, 414
 Amoebal cysts 405
 Amoebiasis 405
 Amoebic colitis 405
 Amphotericin B 324, 332
 Anguibactin 222
AniA 62
Anopheles 287
 Antifolates 290–291
 Antigenic variation 385–387
 Antimonials 331, 332, 336, 391
 Antimycin A 336
ApiAP2 296
 Apicomplexa 305
 Apolipoprotein L1 387
 Apoptosis 63–64, 230–231, 262, 332, 335, 336–337, 378, 391–393, 413–414, 421
 Apurinic/apyrimidinic (AP) endonuclease 364
 Aquaglyceroporins 382

Aquaporin 351f, 366

Arginine deamination system 105–106
 Arginine kinase 353t, 361, 363
 Arsenicals 336, 391
 Arsenite 308, 311, 338, 367
 Artemisinin 291–292
 Artemisinin combination therapy 291–292
 Ascorbate peroxidase (APX) 335, 352t
Atf1 271
 Atg complex 383
 Atg8 conjugation system 363
AtpB 103, 250
 ATR *see* Acid tolerance response
 Autoimmunity 233, 239
 Autophagy 230, 336, 351f, 352t, 362, 363, 382, 383–384, 388
 Azurin 48t, 61

B

Babesia 313
Bacillus cereus 125
 sporulation 137–138
 taxonomy 126–127
Bacillus subtilis 12, 19, 28, 30, 31, 46, 74, 75, 108, 109, 110, 111f, 125, 126, 128, 129, 130, 131, 132, 133, 134f, 135, 136, 137, 138, 139, 413
Bacteroides fragilis 414
 BaeSR regulon 5–6, 187
BAG1 309
 Base excision repair (BER) pathway 363, 365
 BCCT transporters 215–216
 Benznidazole 350, 351, 368
 Betaine 99f, 100–101, 111–112, 183, 215, 366
BetL 100–101
BfrAB 59
Bifidobacterium longum 249
 Bile stress 91, 93, 113, 208
 Biofilms 3, 4, 6, 11, 20, 22, 23, 27, 30, 31, 32, 47t, 53, 55, 58, 63, 65, 71, 95, 101, 133, 161t, 162, 186–187, 252, 253f
BiP *see* GRP78
BlaR regulon 8–9
 Bloodstream form 379, 386, 390
 Bloodstream trypomastigote 348, 349, 351f, 358, 367

BlrAB 8, 9f
 BolA 10–12
Borrelia burgdorferi 251
 Bradyzoite 306, 309, 310f, 312
 Bsh 112
 BsrV 12

C

Cadaverine 205, 217, 220, 361
cadBA 205–206, 217
cadC 205, 217
 E-cadherin 92, 94f
 Calcineurin 328
 Calcyclin binding protein 310f, 315
 Calpain-related protein SKCRP14.1 332
Candida albicans 257, 258t, 264–265, 267–268, 271, 273
 Candidiasis 273
 CAP 128, 155
 Carbon catabolite repression 29–30
 Carbon-centred radical 43t
 Carnitine 99f, 100–101, 111–112, 215
 Catalase 41, 44t, 47t, 50f, 53, 54, 61, 67, 106, 107f, 108, 109, 151, 159, 164, 181, 221
 CcpA 29–30
 CCR see Carbon catabolite repression
 CD14 237
 CD43 237
 Cdc2 267
 Cdc4 266
 Cdc5 267
 Cdc25 267
 Cdc28 265
 Cdc42 260
 Cell cycle regulation 265, 266f, 267
 Cell envelope 1–2
 Cell envelope stress systems 2
 BaeSR 5–6, 187
 CpxAR 2–3, 4f, 157
 Rcs 7
 sigma E 3–5, 5f
 VR 7
 Cell volume 152, 336, 366
 Chagas' disease 347, 349–350
 Chaperokines 328
 Chaperonin 95, 181, 229, 231, 233, 235, 236, 238, 358–359, 417
 Chloramines 43t
 Chloroquine 289–290
 Cholera toxin 202
 Chromatin remodelling 271–272, 292, 295, 380
 CIRCE see Controlling inverted repeat of chaperone expression
 Clb2 267
 Clb5 266
 Cln1–2 266
 Clp ATPases 23, 96–97, 132, 155, 359
 ClpP 22, 132
 CodY 30, 31
 Cold shock proteins 128–129, 155–156
 Cold-shock response 1, 128, 130, 131, 132, 133, 136, 140f, 150t, 155–156, 181, 183, 185, 382

Common antigen 232, 236
 Compatible solutes 99–101, 147, 152, 165, 215–216
 Controlling inverted repeat of chaperone expression 22, 96, 248, 249
 Cpn10 236
 Cpn60 232–233
 Cpn60.1 234–235, 237
 Cpn60.2 234–235, 237
 CpxAR regulon 2–3, 4f, 15, 157, 187–188
 CreBC regulon 8
 CRISPRs 6
Crithidia fasciculata 389, 391
 Crm1 263
 Cruzipain 356
 α -Crystallin-like chaperone 232, 309
 CshA 131–132
 CSP see Cold shock proteins
 CspA 183
 CtsR 22–23, 97, 98f
 Cutaneous leishmaniasis 323
 Cyanide 336
 Cycloguanil 290
 Cycloheximide 362, 393
 Cypl 251
 Cytochrome c 49t, 64, 332, 337, 393
 Cytochrome c peroxidase 53
 Cytochrome P450 353t, 367, 390

D

Danger model 233–234
 Daunorubicin 365
 DC-SIGN 238
 DegP 4, 185, 187
 DegS 210
 DesKR 133–134
Desulfovibrio 407
 DHFR see Dihydrofolate reductase
 DHFR-TS 290–291
 DHPS see Dihydropteroate synthase
 Dihydrofolate reductase 290
 Dihydropteroate synthase 290
 Dihydroxyacetone 383
 Dimorphic yeast 257
 Dipicolinic acid 137
 Disulfides 55, 57, 65, 66, 109, 406, 407
 DNA damage 160, 363–364. See also Oxidative stress
 DNA gyrase 130
 DNA repair 24, 48t, 50f, 59–60, 68, 137, 159, 165, 250, 351f, 352t, 363–365
 DnaJ 95, 231, 235
 DnaJ1 236, 248
 DnaJ2 236, 248–249
 DnaJ3 248
 DnaK 22, 95, 155, 231, 235
 DnaN 251
 DnrN 64
 DOZI 295
 DPA see Dipicolinic acid
 Drug resistance 187, 288, 291, 292, 327t, 338, 361, 367, 368, 391
 DsbABCD 57

E

- Ectoine 215
eEF1b *see* Eukaryotic elongation factor 1B
EhNifS 412
eIF2 α *see* Eukaryotic translation initiation factor 2 α
eIF2 kinases 353–354, 362
Encystation 411, 417, 418
Endodiogeny 305
Endolimax nana 406
Endonuclease G (EndoG) 336–337, 392
Endoplasmic reticulum stress 337, 381, 386, 393
Entamoeba coli 406
Entamoeba dispar 406, 415, 419
Entamoeba hartmanni 406
Entamoeba histolytica 405
 life cycle 405–406
 pathogenesis 405, 418
Entamoeba invadens 411
Enterobacter aerogenes 236
Enterotoxins 126
Environmental stress response 269, 308
Epimastigote 348, 361
ER stress *see* Endoplasmic reticulum stress
Escherichia coli 1, 2, 3, 6, 7, 8, 10, 11, 13, 15, 22, 24, 42, 45,
 46, 52, 54, 59, 66, 67, 68, 70, 71, 72, 108, 131, 132, 136,
 150, 151, 154, 157, 160, 161t, 182, 183, 185, 187, 188,
 191, 193, 202, 204, 206, 210, 220, 231, 236, 365, 412,
 413, 414, 415, 416
Espundia 323
ESRs *see* Extracytoplasmic stress responses
EstD 65
Eukaryotic elongation factor 1B 335, 391
Eukaryotic translation initiation factor 2 α 287, 295–296,
 297, 310f, 311, 339, 353–354, 362
ExbB 213
ExbD 213
Extrachromosomal DNA amplification 337
Extracytoplasmic stress responses 156–158, 185–186.
 See also Cell envelope stress systems

F

- F0F1-ATPase 103–104, 190–191
FabM 26
FapR 136
Fe-S clusters *see* Iron-sulfur clusters
Fenton reaction 24, 27, 43t, 44t, 58, 59, 61, 73, 107, 408,
 410
Ferrodoxin 408, 409f, 415
Ferrichrome receptor 212
Fexinidazole 390
Filamentous growth 161–162
Flagellar pocket 347, 366, 381, 385
Flavodiiron protein 415
FNR 70
FtsA 161
FtsZ 160, 251
Fungal virulence 273
Fur 73–74, 211
Furanosyl borate diester *see* AI-2

G

- GABA *see* γ -Aminobutyrate
GAD *see* Glutamate decarboxylase system
Gametocytes 288, 290, 295
Gametogenesis 306
GAPDH 264
GAS *see* *S. pyogenes*
GBS *see* *S. agalactiae*
Gbu 100
Geldanamycin 311, 330, 332, 358
Genotoxic stress 351f, 363–364, 365
Giardia 405
Giardia intestinalis 415
Glucose-6-phosphate dehydrogenase 352t, 361
Glutamate 54, 100, 104, 152, 363, 410
Glutamate decarboxylase system 103–104
 γ -Glutamylcysteine synthetase 294
Glutaredoxin 55, 384
Glutathione 54, 406, 413
Glutathione oxidoreductase 54
Glutathione peroxidase 28, 289, 352t
Glutathione reductase 294, 406
Glutathione-S-transferase 390, 391
Glutathionylation 407, 416
Glycerol 253
Glycerol-3-phosphate oxidase 383
Glycine-betaine 129, 152, 153, 215, 216f
Glycolysis 250, 312, 383, 408, 411
Glycosome 347, 360, 377, 378f, 383, 384
Glyoxalase system 332
Gpx3 263
GroEL 22, 95, 154, 231–233, 234, 236, 248–249
GroES 154, 231–233, 234, 248–249
Group A *Streptococcus* *see* *S. pyogenes*
Group B *Streptococcus* *see* *S. agalactiae*
GRP78 327, 356, 381
GRP94 358
GRP170 327
GSH *see* Glutathione

H

- Haber-Weiss reaction 44t, 58, 409
Haem receptors 212
Heat-shock proteins 154, 155, 185, 229, 231, 248–249,
 289, 293, 305, 308, 310f, 312, 326, 327t, 335, 350, 369,
 380, 417–418
Heat-shock response 150t, 154–155, 181, 182–183,
 326–327, 335
Heat-shock stress 94, 248, 262, 292, 350, 354–355,
 380–381, 417–418
HF-I 151
High osmolarity glycerol pathway 259, 260, 261f, 262,
 268, 273
Hip 310f, 311
HOG *see* High osmolarity glycerol pathway
Hog1 260, 262, 266, 270f, 272
HOP 311
Hormone exposure 251
Hot1 269
HrcA 22, 96, 105, 248–249
Hrk1 260

Hsf1 transcription factor 263

Hsl1–Hsl7 267

Hsp10 232–233, 312, 352t, 358, 417

Hsp16 232, 359

Hsp20 231, 309, 313

Hsp21 309

Hsp28 309

Hsp29 309

Hsp30 309, 310f

Hsp40 235, 310f, 311, 314–315, 327, 352t, 355, 357, 381, 417

Hsp60 183, 231, 236, 312, 327t, 352t, 355, 358, 381, 417.
See also GroEL

Hsp65 232–234

Hsp70 231, 235–236, 309, 310f, 311, 314, 326, 332, 335, 352t, 355, 356–357, 381, 411, 417, 418

Hsp70.4 327, 356

Hsp70.a 356

Hsp70.b 327

Hsp70.c 327

Hsp75 358

Hsp83 see Hsp90

Hsp90 293, 308, 310f, 311, 326, 330, 332, 352t, 355, 357–358, 381, 417

Hsp100 308, 329, 330, 355, 381, 417

Hsp101 417, 418

Hsp104 352t, 359

Hsp110 327, 381

HSPs see Heat shock proteins

HspX 232

HtrA 21, 24, 33, 97–98, 150t, 156–157, 181, 185

Hydrogen peroxide 26, 42, 43t, 44t, 49t, 50f, 106, 107, 109, 110, 158, 164, 204, 221, 235, 250, 253, 258, 271, 333, 360, 361, 364, 365, 388, 406, 407, 414

Hydroxyl radical 21, 26, 27, 42, 43t, 44t, 50f, 61, 73, 106, 107f, 249, 333, 388, 406

Hyperoxia 294

Hypochlorous acid 43t, 388

Hypoxia 66, 406, 408, 419, 420, 421

I

IFN γ see Interferon- γ

IL-1 230, 234, 235, 237

IL-6 234, 235, 237, 387

IL-8 234, 237

IL-10 235, 236, 237

IL-12 237, 314, 360

Inducible nitric oxide synthase 333, 360, 388

Inner membrane complex (IMC) 309, 313

iNOS see Inducible nitric oxide synthase

Interferon- γ 231, 232, 235, 237, 306, 307, 314, 333, 387

Internalins 92, 94f

Intestinal abscesses 405

Iodamoeba bütschlii 406

IrgA 212

Iron

acquisition 212, 411

deprivation 251–252, 384

homeostasis 27, 59

limitation and scavenging 210–211, 218–219

Iron–sulfur clusters 44t, 51t, 61, 70, 71, 72, 74, 383, 385, 408, 410, 411, 412, 413, 415, 416

Iron sulfur flavoproteins 409f, 415

IscR 71–72

J

J-domain 314, 315, 357

K

Kala-azar 324

KatA 53–54, 221

kDNA see Kinetoplast DNA

Kinetochores 315

Kinetoplast 323, 347

Kinetoplast DNA 323, 364, 365

L

Lactacytin 411

Lactobacillus lactis 413

Laz see Azurin

Leishmania 323, 358, 377, 391

life cycle 324–325

pathogenesis 323–324

Leishmania aethiopica 323

Leishmania amazonensis 323

Leishmania braziliensis 323

Leishmania chagasi 308, 324, 334, 335

Leishmania donovani 308, 324, 330, 332, 334

Leishmania guyanensis 323

Leishmania infantum 324, 330, 334

Leishmania major 323, 328, 335

Leishmania mexicana 323

Leishmania tropica 323

Leishmaniasis 323

LexA 68, 160

Lipid peroxidation 43t, 44t, 107, 352, 361, 408–410

Lipophosphoglycan 333

Lipoproteins 250

Listeria monocytogenes 91

Listeriolysin O 93–94, 94f

Listeriosis 91–92

Liver abscess 405, 406, 418

LLO see Listeriolysin O

Low-temperature adaptation 126

LPG see Lipophosphoglycan

Lutzomyia 324

LuxS 31

Lysine decarboxylase operon see cadBA

M

Mak1–3 263

Malaria 287, 298

Malolactic fermentation 25

Manganese 58

MAPK see Mitogen-activated protein kinase

MAPKK 259

MAPKKK 259

Melarsoprol 390, 391

Membrane fluidity 129–130

Menadione 335

Merozoites 287

MerR 69

META1 329

Metacaspases 392

- Metacyclic trypomastigote 348, 351f, 353t, 354, 355, 359, 360, 361, 362, 378, 383, 387
 Metacyclics 324
 Metacyclogenesis 351, 361, 362
 Metal homeostasis 58, 73, 367
 Metallothionein 351f, 352t, 367, 391
Methanosarcina thermophila 415
 Methionine sulfoxide reductase 47t, 50f, 56–57, 59, 69, 352t, 361, 408, 413
 Methotrexate 331, 338
 N-Methylglucamine antimonate 324
 Metronidazole 414, 418
 Miltefosine 324, 332
 Minixerion 337
 Mismatch repair (MMR) pathway 363, 365
 Mitochondrion 273, 294, 309, 312, 313, 316, 323, 334, 336, 337, 347, 354, 356, 357, 358, 360, 365, 377, 378f, 381, 383, 384, 417
 Mitogen-activated protein kinase 258, 259f, 261, 262, 263, 264, 265, 267, 270, 273, 274, 296, 328, 339, 353, 354
 Mitosomes 412, 415, 417
 Mu 266
 MnSOD 220
 MntABC 58
 Molecular chaperones 95–96
 NG-monomethyl-l-arginine (L-NMMA) 333
 Moonlighting chaperones 236
 Mpkl 263
 Mprl 264
 mRNA
 biogenesis 268
 export 272–273
 stability 272–273, 295
 Msb2 260
 Msc4 264
 MseR 69
 Msn2,4 269
 MsrA 249
 MTP70 327
 MtsR 27
 Mucocutaneous leishmaniasis 335. *See also* *Espundia*
 Multidrug resistance transporter MDR2 289, 367
Mycobacterium 229
Mycobacterium tuberculosis 229–230, 288
Mycoplasma felis 250
Mycoplasma genitalium 248, 250
Mycoplasma hyopneumoniae 248, 250, 252, 253f
Mycoplasma hyorhinis 251
Mycoplasma mycoides 252
Mycoplasma pneumoniae 252
Mycoplasma pulmonis 252
 Mycoplasmas 247
- N**
- NADH dehydrogenases 312
 NADPH oxidase 333, 360, 388
 Nagana disease 379
 Nape 48t, 60
 NCDAAs *see* Non-canonical D-amino acids 12–14
Neisseria 41
Neisseria gonorrhoeae 41–42, 46
Neisseria meningitidis 41–42, 46
 Neurotoxin 236
 NEExo 48t, 60
 NGO0554 61
 NGO1686 61
 Nicotinamide adenine dinucleotides 408
Nifurtimox 350, 351, 362, 367, 368, 390
 Nitric oxide 23, 41, 42, 43t, 49t, 50f, 162, 232, 250, 314, 336, 360, 405, 406, 416–417, 421
 Nitroreductases 390
 Nitrosative stress 41, 47t, 51t, 63, 64, 66, 72, 73, 406, 412, 415–416
 Nitrosothiol 43t
 Nitrosylation 73, 416
NMB1436-8 61
NmlR 69
 NO *see* Nitric oxide
 Non-canonical D-amino acids 12–14
 Non-coding small RNAs 75
 Noradrenaline 251
 NorB 62–64
NsrR 72
 Nutritional stress 29–31, 350, 351f, 362, 382–383
- O**
- Ohr 249
OmpR/EnvZ 185, 202–203
OmpU 203, 222
Oocyst 288, 306, 309
Ookinete 288
OpuC 100–101
Opy2 261
 Organic hydroperoxide reductase 249
OSH *see* *Ovothiol A*
Osmosensor 260
Osmostress *see* Osmotic stress
 Osmotic stress 99–102, 150t, 152, 214–215, 250, 260, 261f, 266f, 332–334, 336, 350, 365–366, 382
Ovothiol A 332
 Oxidative burst 21, 45, 159, 335, 349, 351f, 359, 360, 420
 Oxidative phosphorylation 312
 Oxidative stress 26–29, 41–45, 106, 150t, 158, 249–250, 258, 261f, 263, 289, 293–295, 335, 350, 351f, 359–362, 406,
 DNA damage 59–60, 159
 defences 46, 50f, 54, 58, 388
 sources 45–46, 258
OxyR 66–68, 407
- P**
- p23 311–312, 358
 p38 kinase 260, 296, 328, 353
 P-bodies 273, 351f, 352t, 362
Panstrongylus 348
Pap1 264, 271
 Paraquat 27, 28, 49t, 52, 335
 Parasite differentiation 311, 312, 326, 327t, 328, 329–331, 336, 351f, 355, 358, 362, 378f, 382, 383, 387, 393
 Paromomycin 324
Pbs2 260
 PCD *see* Apoptosis
Pcr1 271

- Pentamidine 324
 Pentavalent antimony (SbV) 324
 Pentose phosphate pathway 133, 360, 361
 Periodontal bone breakdown 236
 Peroxidase 53
 Peroxide stress 27, 73, 204, 263, 264
 Peroxiredoxins 54, 109, 251, 294, 333, 334f, 389, 407, 412
 Peroxynitrite 42, 43t, 44t, 45, 49t, 62, 64, 160, 333, 360, 388, 406, 421
 PerR 27, 74, 109–110
 PezAT system 9–10
 PfCK1 296
 PfCK2 296
 PfeIK1 295
 PfeIK2 295
 PFEMP1 288
 Pfmap-1 296
 Pfmap-2 296
 PFOR *see* Pyruvate:ferredoxin oxidoreductase
 PfPK4 296
 Phage shock protein system 189
 Phage shock response 157
 Phagolysosome 324
 Phase variation 220
Phlebotomus 324
 PhoPQ 184
 Phosphatidylinositol 3-kinase (PI3K) 366
 Phosphatidylserine 337
 Phospholipases C 93, 94f, 112
 Phosphorelay system 7, 158, 186, 260, 261f, 263
 pJM1 222
 PKA *see* Protein kinase A
 PKC *see* Protein kinase C
Plasmodium berghei 294, 296
Plasmodium falciparum 287, 311
 genome 288
 life cycle 287–288
Plasmodium yoelii 311
 PLCs *see* Phospholipases C
 Poly(ADP-ribose) polymerase 352t, 364
 Polyamines 220, 336, 351f, 352t, 361
 Polyphosphate 58, 351f, 352t, 366, 382
 Polyphosphate kinase 48t, 59, 366
 PotA 253
 Ppa 48t, 59
 ppGpp *see* Alarmone ppGpp
 Ppk 48t, 59
 PrfA 94, 112
 PriA 48t, 60
 Procyclin 382
 Procyclic 337, 378f, 379, 380, 381, 382, 383, 384, 389, 393
 Programmed cell death (PCD) *see* Apoptosis
 Proguanil 290
 Proline metabolism 362
 Prokaryotic two component systems 31–33, 133–135
 OmpR/EnvZ 185
 PhoPQ 184
 websites 14–15
 Promastigote 324
 Proteasome 410–411, 417
 Protein carbonylation 289, 410
 Protein disulfide isomerase (PDI) 407
 Protein folding 132
 Protein kinase A 262, 269
 Protein kinase C 263
 Protein oxidation 24, 57, 289, 407, 410, 419
 Proteolytic stress 378f, 382
 ProU transporter 150t, 152, 183, 215–216
 Prr1 264
 PRXs *see* Peroxiredoxins
 PSP *see* Phage shock protein system
 PspA 189
 PspB 189, 192
 PspC 189, 192
 PspF 189
 Ptc1–3 262
 Pteridine reductase 335
 Ptp2–3 262
 Pyp1 264
 Pyridine nucleotide transhydrogenase 408
 Pyrimethamine 290
 Pyruvate dehydrogenase complex 312
 Pyruvate:ferredoxin oxidoreductase 407, 409f, 411, 414
- Q**
- Quercetin 309
 - Quorum-sensing systems 31
- R**
- Rad24 268f
 - RAD51 365
 - Radicicol 330
 - Rapamycin 328, 383
 - Rck1–2 267, 273
 - Rcs regulon 7, 15, 158, 186–187
 - Reactive nitrogen intermediates 231, 234, 314. *See also* Reactive nitrogen species
 - Reactive nitrogen species 50f, 61–62, 333, 359, 388, 408, 416
 - Reactive oxygen intermediates 230, 234. *See also* Reactive oxygen species
 - Reactive oxygen species 26, 50f, 106–107, 258, 289, 333, 337, 350, 359, 388, 406, 408
 - RecA 159
 - RecABCD 48t, 159
 - RecJOQ 48t
 - RecN 48t, 50f, 51t, 59–60, 68
 - Redox potential 211, 350, 409, 411, 413, 418, 419
 - Redox signalling 56, 406, 410
 - Regulatory volume decrease (RVD) 365
 - RelA 30, 101
 - Repair of DNA damage 59–60
 - ResDE 135
 - Reservosome 347, 351f, 362
 - RH strain 308
 - Rheumatoid arthritis 235
 - Rhodnius* 348
 - RNA editing 348
 - RNA helicases 130–132
 - RNI *see* Reactive nitrogen intermediates

- RNS *see* Reactive nitrogen species
 ROI *see* Reactive oxygen intermediates
 ROS *see* Reactive oxygen species
RpoE 24, 50f, 69, 156, 181, 188, 210. *See also* Sigma E regulon
RpoH 164, 188
RpoS 11, 13, 150–152, 162, 204. *See also* Sigma S factor
Rsb proteins 110, 111f, 135
RseA 156
Rubrerythrin 409f, 415
RuvACG 48t
- S**
- Saccharomyces cerevisiae* 257, 258t, 259, 265, 269–270, 363, 407, 411
SAG1 307
Salmonella enterica 147
 cell invasion 148–149
 pathology 147–148
SAPKs *see* Stress-activated protein kinases
Sarcoendoplasmatic reticulum calcium ATPase6 292
Schizosaccharomyces pombe 257, 258t, 263, 267, 271
Sco 55–56
Sec63 315
Secretins 191
Sestrin 407
Sho1 260, 265
sHsps *see* Small heat shock proteins
Sic1 266
Siderophores 212
Sigma B factor 110–112, 135–136
Sigma E regulon 3–5, 5f, 15, 69, 156. *See also* *RpoE*
Sigma S factor 150–151. *See also* *RpoS*
Signalling pathways 2, 31, 178, 237, 257, 259, 260, 262, 263, 264, 265, 269, 270, 274, 295, 296, 297, 326, 328, 339, 351, 353, 354, 364, 382, 386, 406, 416
Signature-tagged mutagenesis 181
Singlet oxygen 43t
Sis1 315, 357
Sgt1 315
Skn7 263, 270
Sko1 269
Sleeping sickness 379
Slender form 378f, 379, 383
Sln1 260, 263
Small heat shock proteins 309, 313, 327t, 352t, 359. *See also* α -Crystallin-like chaperone
Smp1 269
SOD *see* Superoxide dismutase
SodB 52
SodC 52–53
Sodium stibogluconate 324
Sol1 268
SOS response 150t, 159–160
Spermidine 253
Sporozoites 287, 313
Sporulation 137–139, 306, 307, 309, 313
Spx 28–29
Src1 267
Ssk1 260
Ssk2 260
Ssk22 260
Staphylococcus aureus 12, 22, 135, 413
Ste11 260
Ste20 260
Ste50 261
STI1 328, 352t, 358
Streptococcus 19
Streptococcus agalactiae 21, 23–24, 29
Streptococcus mutans 20, 23, 24–25
Streptococcus pneumoniae 21, 23, 28
Streptococcus pyogenes 20–21, 27–28
Stress-activated protein kinases 258, 259, 296
Stress adaptation responses 265
Stress granules *see* P-bodies
Stress-sensing regulatory systems 8
Stress sensor 270, 351
Stress signalling 2, 257, 258, 259, 263–264, 271, 351
Stumpy form 378f, 379, 382, 383, 393
Sty1/Spc1 MAPK 263, 264, 267, 271
Sulfenic acids 67, 109, 406, 407
Sulfinic acids 109, 406, 407, 410
Sulfonic acids 406, 407, 410
Sulphiredoxin 407
Sulphonamides 290
Superoxide 21, 26, 27, 42, 43t, 45, 46, 50f, 58, 65, 70, 75, 106, 107, 108, 150t, 158, 159, 220, 250, 258, 294, 333, 335, 336, 360, 388, 406, 408, 414, 421
Superoxide dismutase 28, 46–53, 108, 159, 252, 289, 294, 332, 334f, 335, 352t, 360, 389, 413
SulA 160, 162
Swe1 266
- T**
- T3SS* *see* Type III secretion system
Tachyzoite 306, 309, 310f, 312
TcJ1–4 357
TCP 202
TCS *see* Prokaryotic two-component systems
TGF β 235
Thenoyltrifluoroacetone 336
Thermotolerance 97, 113, 126, 164, 328, 354, 355, 359
Thioredoxin 26, 55, 56, 57, 61, 106, 109, 289, 359, 407, 409f, 412, 413
Thioredoxin peroxidase 264
Thioredoxin reductase 65, 294, 413
Thiyl radical 43t, 407, 413, 416
Thymidylate synthase 290
TlpA 49t, 55
TLR2/MyD88 314
TLR4 *see* Toll-like receptor 4
TNF α 230, 234, 235, 236, 237, 314, 333, 360, 387
Toll-like receptor 4 314
TonB 213
Topoisomerase I 251
TOR kinase 328, 382, 384
Toxin-antitoxin (TA) systems 9–10, 15
Toxin coregulated pilus *see* TCP
Toxoplasma gondii 296, 305
 life cycle 306, 307f
Toxoplasmosis 305–306
ToxRS 202–203, 208f

TPX *see* Tryparedoxin peroxidase

Tpx1 264

Transcriptional control 269–271

Transcriptional machinery 270

Transferrin 251, 384

Transferrin receptor 384–385

Translational regulation 151, 272, 291

Translesion synthesis (TLS) pathway 364, 365

TRAP-1 *see* Hsp75

Triatoma 348

Trichomonas vaginalis 63, 415

N,N,N-Trimethylglycine *see* Glycine-betaine

tRNA cleavage 352t, 362, 363

Trophozoite 405, 411, 417

TrxB 65

Trypanolytic factor (TLF) 387

Trypanosoma brucei 337, 358, 377

evolution 377

life cycle 378–379

pathogenesis 379

Trypanosoma brucei gambiense 379, 387

Trypanosoma brucei rhodesiense 379, 387

Trypanosoma congolense 379

Trypanosoma cruzi 347, 377, 390, 391

genome 347–348

life cycle 348–349

pathogenesis *see* Chagas' disease

Trypanosoma equiperdum 378

Trypanosoma evansi 379

Trypanosoma vivax 379

Trypanothione 332, 334f, 336, 350, 353t, 360, 388, 389, 391, 413

Trypanothione reductase 332, 334f, 353t, 360, 388

Trypanothione synthetase 360, 389

Trypanothione S-transferase 332, 336

Tryparedoxin 334f, 360, 389, 353t, 360

Tryparedoxin peroxidase 332, 333, 334f, 335, 336, 353t, 361

Trypomastigote 348, 361, 378

TS *see* Thymidylate synthase

TsaA 159

Tuberculosis 229–230

Tunicamycin 337, 356, 381

Two-component sensors 264

Two-component systems *see* Prokaryotic two component systems

TXNPx *see* Tryparedoxin peroxidase

Type III secretion system 148

U

Unfolded protein response 339, 380, 386, 416

Ureaplasma urealyticum 250

UspA 231

UvrA 24

UvrABD 48t

V

Variant surface glycoprotein 383, 385, 386–387

VctA 212

Vesicle release *see* VR

Viable but non-culturable phenomenon 220–221

Vibrio 201

Vibrio anguillarum 222

Vibrio cholerae 201–202

Vibrio fischeri 221

Vibrio parahaemolyticus 214

Vibrio splendidus 222

Vibrio vulnificus 219

Vibriobactin 212

Vibrioferrin 212, 218–219

Visceral leishmaniasis 324

Vitamin C 409

ViuA 212

VR regulon 7

VSG *see* Variant surface glycoprotein

VtrA 217

W

Win1 MAPKKKs 264

Wis4/Wak1 264

WR99210 290–291

X

Xenobiotics 332, 353t, 367, 390

Y

Yap1 263, 270

YDJ1 357

Yeast 257, 411

Yersinia 177, 179f

infection of macrophages 184

Yersinia enterocolitica 179–180

Yersinia pestis 178

Yersinia pseudotuberculosis 179–180

Ypd1 260

YscC 191

Z

Z-ring 160–161

Zeocin 365

ZipA 161

Zur 41, 47t, 50f, 51t, 73, 75, 109