

Contents

Preface XIX

List of Contributors XXI

Part I Intercellular Communication 1

Introduction 3

Claudia Anetzberger and Kirsten Jung

1 Cell–Cell Communication and Biofilm Formation in Gram-Positive Bacteria 7

Christine Heilmann and Friedrich Götz

1.1 Introduction 7

1.2 Staphylococcal Infections and Biofilms 8

1.3 Molecular Basis of Biofilm Formation in Staphylococci 8

1.3.1 Attachment to Abiotic Surfaces 8

1.3.2 Attachment to Biotic Surfaces 10

1.3.3 Accumulation Process 11

1.3.3.1 Polysaccharide-Associated Biofilm Accumulation 11

1.3.3.2 Extracellular DNA 12

1.3.3.3 Protein-Associated Biofilm Accumulation 12

1.3.4 Biofilm Escape Factors 12

1.4 QS in Staphylococcal Biofilms 13

1.4.1 agr QS Locus 13

1.4.2 luxS/AI-2 System 17

References 17

2 Cell–Cell Communication in Biofilms of Gram-Negative Bacteria 23

Claudio Aguilar, Aurelien Carlier, Kathrin Riedel, and Leo Eberl

2.1 Introduction 23

2.2 QS in Gram-Negative Bacteria 23

2.3	QS and Biofilm Formation	24
2.3.1	When in the Biofilm Cycle does QS Play a Role?	27
2.4	QS-Regulated Factors Involved in Biofilm Formation	29
2.4.1	EPSs	29
2.4.2	Biosurfactants	30
2.4.3	DNA Release	31
2.4.4	Physiology: Dissimilatory Nitrate Reduction in <i>P. aeruginosa</i>	32
2.5	QS as a Target for the Eradication of Biofilms	32
2.6	Interspecies Signaling in Mixed Biofilms	34
2.7	Conclusions	34
	References	35
3	Cell Interactions Guide the Swarming and Fruiting Body Development of Myxobacteria	41
	<i>Dale Kaiser</i>	
3.1	Introduction	41
3.2	Motility of Myxobacteria	41
3.3	Pilus Engine	42
3.4	Slime Secretion Engine	43
3.5	Swarming of Myxobacteria	44
3.6	Regulating Reversals	45
3.7	Fruiting Body Development	46
3.8	C-Signal and Fruiting Body Morphogenesis	48
3.9	Managing the Reversal Frequency	48
3.10	C-Signal Control of Gene Expression	49
	References	51
4	Communication Between Rhizobia and Plants	57
	<i>Michael Göttfert</i>	
4.1	Introduction	57
4.2	Nodulation (<i>nod</i>) Genes are Induced by Flavonoids and are Under Positive and Negative Regulation	59
4.3	Activation of the <i>nod</i> Genes Results in the Synthesis and Export of Lipo-Chito-Oligosaccharide Signal Molecules	61
4.4	Rhizobia use Secreted Proteins as Effector Molecules	64
4.5	Microarray Studies Help in Elucidating the Flavonoid Stimulons	65
4.6	<i>nod</i> Genes as Accessory Components of the Rhizobial Core Genome	66
4.7	Conclusions and Outlook	66
	References	67

5	Communication Between Pathogens and Eukaryotic Cells	75
	<i>Jürgen Heesemann</i>	
5.1	Introduction	75
5.2	Long-Distance Communication	77
5.2.1	Language of Pathogen-Associated Molecular Patterns	77
5.2.1.1	TLRs	78
5.2.1.2	Cytosolic PAMP Receptors	80
5.2.1.3	PAMPs as Chemoattractants	81
5.2.2	Language of Hormones	83
5.2.3	Extracellular Bacterial Toxins in Pathogen–Host Cell Communication	86
5.2.3.1	Superantigens	86
5.2.3.2	Cholera Toxin	86
5.2.3.3	Bordetella Modulins	87
5.2.3.4	Helicobacter	87
5.2.3.5	VacA	87
5.2.3.6	<i>Clostridium difficile</i> Toxins	87
5.3	Short-Distance Communication	88
5.3.1	Bacterial Adhesins and Host Cell Receptors	88
5.4	Conclusions	91
	References	91
6	Identification of Bacterial Autoinducers – Methods Chapter	95
	<i>Agnes Fekete, Michael Rothballer, Anton Hartmann, and Philippe Schmitt-Kopplin</i>	
6.1	Introduction	95
6.2	Biosensors	98
6.2.1	Biosensor Construction	98
6.2.2	AI Screening with Biosensors	98
6.3	Sample Preparation Prior to Analysis	99
6.3.1	Liquid–Liquid Extraction	99
6.3.2	Principles of Liquid Chromatography	99
6.3.2.1	SPE	100
6.3.2.2	TLC	101
6.3.2.3	(Semi)Preparative Liquid Chromatography	101
6.4	Techniques for the Structural Analysis of AIs	102
6.4.1	Mass Spectrometry	102
6.4.2	NMR Spectroscopy	103
6.5	Techniques for the Quantification of AIs	103
6.5.1	Principles of the Analysis Methods	103
6.5.2	Quantification Methods of the Known AIs	104
6.5.2.1	Analysis of AHL-Based QS Signals	105
6.5.2.2	Analysis of HAQ-Based QS Signals	106
6.6	Conclusions and Future Perspectives	107
	References	107

Part II Transmembrane Signaling 113**Introduction 115***Reinhard Krämer*

- 7 Outer Membrane Signaling in Gram-Negative Bacteria 117**
Volkmar Braun
- 7.1 Introduction 117
- 7.2 A Sophisticated Mechanism: A Signaling Cascade Across the Outer Membrane in Transcriptional Regulation of the Ferric Citrate Transport Genes 117
- 7.3 Transfer of the Signal Across the Cytoplasmic Membrane 121
- 7.4 Signal Transfer into the Cytoplasm 121
- 7.5 FecI is an ECF Sigma Factor 122
- 7.6 Mechanism of Ferric Citrate Transcription Regulation 123
- 7.7 Transcription Regulation of the Fec Type in *Pseudomonas putida* 123
- 7.8 Transcription Regulation of the Fec Type in *Pseudomonas aeruginosa* 124
- 7.9 Transcriptional Regulation of the Fec Type in *Bordetella* 126
- 7.10 ECF Signaling in *Serratia marcescens* 127
- 7.11 ECF Signaling in *Ralstonia solanacearum* 127
- 7.12 Signaling in Outer Membrane Transport 127
- 7.13 Assumed Outer Membrane Signaling 128
- 7.14 Conclusions 128
References 130
- 8 Stimulus Perception and Signaling in Histidine Kinases 135**
Ralf Heermann and Kirsten Jung
- 8.1 Introduction 135
- 8.2 Histidine Kinase Family 135
- 8.2.1 Basic Structure of Histidine Kinases 136
- 8.2.2 Specifics of Histidine Kinases in Comparison to Serine/Threonine/Tyrosine Kinases 138
- 8.3 Stimulus Perception and Signaling by Histidine Kinases 139
- 8.3.1 Chemical Stimuli 139
- 8.3.2 Physical Stimuli 145
- 8.4 Accessory Proteins of Histidine Kinases 148
- 8.5 Conclusions and Outlook 151
References 152
- 9 Chemotaxis and Receptor Localization 163**
Victor Sourjik
- 9.1 Introduction 163
- 9.2 Architecture of the Sensory Complex 165
- 9.2.1 Structure and Function of Chemoreceptors 165

9.2.2	Protein Interactions in the Ternary Complex	166
9.3	Clustering of Sensory Complexes	167
9.3.1	Chemoreceptor Clusters	167
9.3.2	Cluster Assembly and Positioning	168
9.3.3	Cluster Positioning	168
9.3.4	Cluster Stability	169
9.4	Role of Clustering in Signal Processing	170
9.4.1	Role of Protein Localization	170
9.4.2	Signal Amplification	170
9.4.3	Allosteric Models and the Role of the Methylation System in High Sensitivity	170
9.4.4	Signal Integration	172
9.4.5	Adaptational Assistance Neighborhoods	173
9.5	Conclusions and Outlook	173
	References	173
10	Photoreception and Signal Transduction	177
	<i>Sonja Brandt and Nicole Frankenberg-Dinkel</i>	
10.1	Introduction	177
10.2	Bacterial Blue-Light Photoreceptors	178
10.2.1	Microbial Rhodopsins	178
10.2.2	Cryptochromes	181
10.2.3	Photoactive Yellow Proteins (Xanthopsins)	183
10.2.4	BLUF Domain Proteins	183
10.2.5	Phototropin-Like Microbial Photoreceptors	184
10.3	Red-Light Sensing – Phytochromes	185
10.3.1	Principle of Phytochrome Action	185
10.3.2	Domain Organization of Phytochromes	186
10.3.3	Cyanobacterial Phytochromes and Phytochrome-Like Proteins	187
10.3.4	Phytochromes in other Phototrophic Bacteria	188
10.3.5	Phytochromes in Heterotrophic Bacteria	189
10.4	Conclusions	190
	References	190
11	Transmembrane Signaling	197
	<i>Melinda D. Baker and Matthew B. Neiditch</i>	
11.1	Introduction	197
11.2	Transmembrane Receptor Domain Architecture	198
11.2.1	Transmembrane Histidine Kinase Domain Architecture	198
11.2.2	Chemoreceptor Domain Architecture	201
11.3	Structural Analysis of Transmembrane Signaling	201
11.3.1	CitA Transmembrane Signaling	202
11.3.2	LuxPQ Transmembrane Signaling	203
11.3.3	Chemotaxis Receptor Transmembrane Signaling	204

11.3.4	HAMP Linker Domain Structure	205
11.4	Conclusions	206
	References	207
12	Sensory Transport Proteins	211
	<i>Reinhard Krämer</i>	
12.1	Introduction	211
12.2	Sensing of Transport Activity	212
12.2.1	<i>Escherichia coli</i> Maltose System and the Global Regulator Mlc	213
12.2.2	<i>E. coli</i> Uhp System	215
12.2.3	Dicarboxylic Acid Uptake in <i>E. coli</i> and Rhizobia	216
12.2.4	LysP/CadC System in <i>E. coli</i>	218
12.2.5	Ammonium Signaling	218
12.2.6	Further Transport Systems with Substrate Sensing Function	219
12.3	Stress Sensing by Transport Proteins	219
12.3.1	Mechanosensitive Channels	220
12.3.2	Osmosensory Uptake Systems	221
12.4	Conclusions and Perspective	223
	References	224
13	Regulated Intramembrane Proteolysis in Bacterial Transmembrane Signaling	229
	<i>Thomas Wiegert</i>	
13.1	Introduction	229
13.2	Bacterial I-CLiPs	231
13.3	Regulation of ECF Sigma Factors by RIP	233
13.3.1	Regulation of the <i>E. coli</i> σ^E -Dependent Envelope Stress Response	233
13.3.2	σ^E Homologous Systems in Gram-Negative Pathogenic Bacteria	234
13.3.3	Regulation of the <i>Bacillus subtilis</i> σ^W Regulon	235
13.3.4	Possible Role of RIP in Regulation of other ECF Sigma Factors	236
13.4	Regulation of ToxR-Like Transcriptional Regulators via RIP	236
13.5	Involvement of RIP in Regulation of Bacterial Cell Division and Differentiation	237
13.5.1	Involvement of RIP in Timing of Cell Division in <i>B. subtilis</i>	237
13.5.2	Activation of the Alternative Sporulation Sigma Factor σ^K of <i>B. subtilis</i>	237
13.5.3	Regulation of the Cell Polarity Determinant PodJ of <i>Caulobacter crescentus</i>	238
13.6	Involvement of RIP in Cell–Cell Communication	239
13.6.1	Production of Peptide Sex Pheromones in <i>Enterococcus faecalis</i>	239
13.6.2	Rhomboid-Mediated QS in <i>Providencia stuartii</i>	240
13.7	Conclusions	240
	References	240

14	Protein Chemical and Electron Paramagnetic Resonance Spectroscopic Approaches to Monitor Membrane Protein Structure and Dynamics – <i>Methods Chapter</i>	247
	<i>Daniel Hilger and Heinrich Jung</i>	
14.1	Introduction	247
14.2	Cysteine Chemistry	248
14.2.1	General Considerations	248
14.2.2	Applications of Cysteine Chemistry	250
14.2.2.1	Cysteine Accessibility Analyses	250
14.2.2.2	Proximity Relationships in Proteins by Cysteine Cross-Linking	252
14.3	Site-Directed Spin Labeling and EPR Spectroscopy	253
14.3.1	Why EPR Spectroscopy?	253
14.3.2	Site-Directed Spin Labeling of Proteins	253
14.3.3	Information on Protein Structure and Dynamics Based on Spin Label Dynamics	255
14.3.3.1	Example	256
14.3.4	Information on Protein Structure and Dynamics Based on Spin Label Accessibility	256
14.3.4.1	Example	257
14.3.5	Polarity and Proticity in the Spin Label Microenvironment	257
14.3.5.1	Example	258
14.3.6	Intra- and Intermolecular Distances by Double Spin Labeling and Interspin Distance Measurements	258
14.3.6.1	Example	258
14.4	Conclusions	259
	References	260
	Part III Intracellular Signaling	265
	Introduction	267
	<i>Kirsten Jung, Michael Y. Galperin, and Reinhard Krämer</i>	
15	Protein Domains Involved in Intracellular Signal Transduction	269
	<i>Michael Y. Galperin</i>	
15.1	Introduction	269
15.2	Computational Analysis of Signaling Domains	270
15.3	Intracellular Sensory Domains	271
15.3.1	PAS Domain	272
15.3.2	GAF Domain	273
15.3.3	BLUF Domain	273
15.3.4	GCS Domain	274
15.3.5	HNOB Domain	274
15.3.6	Hr Domain	274
15.3.7	KdpD Domain	275
15.3.8	PHY Domain	275

15.4	Intracellular Signal-Transducing and Output Domains	276
15.4.1	Two-Component Signal Transduction	276
15.4.2	Chemotaxis	276
15.4.3	Sugar: PTS	279
15.4.4	c-di-GMP-Mediated Signaling	279
15.4.5	Serine/threonine Protein Phosphorylation Signaling System	279
15.5	Diversity of Intracellular Signaling Pathways	280
	References	280

16 Sensing of Oxygen by Bacteria 289

Gottfried Uden, Martin Müllner, and Florian Reinhart

16.1	Introduction	289
16.2	O ₂ as a Signal	290
16.3	Direct O ₂ Sensors	291
16.3.1	Heme B-Containing Sensors	291
16.3.1.1	FixL	291
16.3.1.2	Dos	294
16.3.1.3	HemAT	294
16.3.2	[4Fe-4S] ²⁺ -Containing Sensors	294
16.3.2.1	FNR _{Ec}	294
16.3.2.2	FNR _{Bs}	296
16.3.2.3	NreB	296
16.3.2.4	WhiB3	296
16.3.2.5	[4Fe-4S] ²⁺ as a Universal Cofactor for O ₂ Sensing	296
16.3.3	FAD-Containing Sensors	297
16.3.3.1	NifL	297
16.4	Indirect O ₂ Sensors	298
16.4.1	Electron Transport-Linked Sensors	298
16.4.1.1	ArcB/ArcA	298
16.4.1.2	Aer	300
16.4.1.3	PrrB/PrrA and RegB/RegA	300
16.4.1.4	ResE/ResD and SrrA/SrrB	300
16.4.2	NADH-Linked Systems	301
16.4.2.1	Rex	301
	References	301

17 Microbial Sensor Systems for Dihydrogen, Nitric Oxide, and Carbon Monoxide 307

Rainer Cramm and Bärbel Friedrich

17.1	Introduction	307
17.2	Sensing of Molecular Hydrogen	309
17.2.1	Environmental Signals that Direct Hydrogenase Control	310
17.2.2	Hydrogen-Activating Proteins in Nature	310
17.2.3	What Makes the H ₂ Signaling Hydrogenase Different from the Energy-Providing Hydrogenase?	311

17.2.4	H ₂ Signaling Cascade	312
17.2.5	H ₂ Sensor Complex in Action	314
17.2.6	Concluding Remarks and Perspectives	315
17.3	Sensing of Nitric Oxide and Carbon Monoxide	315
17.3.1	Primary Sensors for NO	316
17.3.1.1	NorR-Type NO-Sensing Regulators	317
17.3.1.2	NsrR-Type NO Sensing Regulators	318
17.3.1.3	NO-Sensing Regulators Containing CAP Domains	318
17.3.2	Primary Sensors for CO	319
17.3.2.1	CooA – A CO Sensor of Anaerobic Carboxidotrophs	320
17.3.2.2	RcoM – A CO Sensor of Aerobic Carboxidotrophs	321
17.3.3	Hypothetical or Secondary Sensors Systems for NO and/or CO	321
17.3.3.1	Eukaryotic-Style NO Sensing in Prokaryotes	321
17.3.3.2	NO Sensing by Fur, SoxR, and OxyR	322
17.3.3.3	Detecting Multiple Diatomic Gases: Sensors Responding to O ₂ , CO, and NO	323
	References	324
18	Signal Transduction by Trigger Enzymes: Bifunctional Enzymes and Transporters Controlling Gene Expression	329
	<i>Fabian M. Commichau and Jörg Stülke</i>	
18.1	Introduction	329
18.2	Trigger Enzymes Active as DNA-Binding Transcription Factors	332
18.3	Trigger Enzymes Involved in Post-Transcriptional Regulation via Protein–RNA Interaction	333
18.4	Trigger Enzymes Controlling Gene Expression by Signal-Dependent Phosphorylation of Transcription Regulators	334
18.5	Trigger Enzymes Controlling the Activity of Transcription Factors by Protein–Protein Interactions	335
18.6	Evolution of Trigger Enzymes: From Enzymes via Trigger Enzymes to Regulators	338
	References	339
19	Regulation of Carbohydrate Utilization by Phosphotransferase System-Mediated Protein Phosphorylation	343
	<i>Boris Görke and Birte Reichenbach</i>	
19.1	Introduction	343
19.2	Unique Features of the Bacterial PTS	344
19.3	Phosphorylation of the IIA ^{Glc} Subunit of the Glucose Transporter Triggers Global CCR in Enteric Bacteria	345
19.4	A Second Key Mechanism of CCR: Phosphorylation of IIA ^{Glc} Controls Inducer Exclusion in Enteric Bacteria	347
19.5	Phosphorylation of Ser46 of HPr Triggers CCR in Low-GC Gram-Positive Bacteria	348

- 19.6 Phosphorylation of HPr by the Bifunctional Kinase/Phosphorylase Links CCR to the Metabolic State of the Cell in Gram-Positive Bacteria 349
- 19.7 HPr Controls Inducer Exclusion in Low-GC Gram-Positive Bacteria 349
- 19.8 Control of Transcription Regulators by EII 350
- 19.9 Catabolite Control of PRD-Containing Regulators by HPr(His~P)-Mediated Phosphorylation 351
- 19.10 PTS-Dependent Regulation of Chemotaxis 352
- 19.11 Regulatory Functions of Paralogous PTSs 352
References 353
- 20 cAMP Signaling in Prokaryotes 357**
Knut Jahreis
- 20.1 Introduction 357
- 20.2 CCR – A Short Historical Account 357
- 20.3 Regulation of Intracellular cAMP Levels: PTS as a Sensor and Signal Transduction System that Modulates AC Activity 358
- 20.4 Another Extension of the Simple Model: Catabolite Repression by Non-PTS Substrates: The PEP: Pyruvate Ratio is a Key Node in Carbon and Energy Metabolism 362
- 20.5 cAMP Excretion and Phosphodiesterase Activity 363
- 20.6 Function of the cAMP–CRP Complex 364
- 20.6.1 Transcriptional Regulation of the *crp* Gene 364
- 20.6.2 Properties of CRP 364
- 20.6.3 cAMP–CRP Complex-Dependent Promoter Activation and Repression 365
- 20.7 cAMP–CRP Modulon and the CFU “Carbohydrate Catabolism/Quest for Food” 366
- 20.8 Interactions with Other Regulatory Systems 367
- 20.8.1 Inducer Exclusion by Unphosphorylated EIIA^{Glc} 367
- 20.8.2 Interactions with Other Signaling Systems to Keep the Metabolic Balance: “Anticatabolite Repression” or Glucose Induction by Mlc 368
- 20.9 Mathematical and Computer-Assisted Modeling of Catabolite Repression 369
- 20.10 Conclusions 370
References 370
- 21 c-di-GMP Signaling 377**
Christina Pesavento and Regine Hengge
- 21.1 Introduction 377
- 21.2 Protein Domains Involved in c-di-GMP Signaling 377
- 21.2.1 Making and Breaking of c-di-GMP 377
- 21.2.2 Composite GGDEF, EAL, and HD-GYP Proteins 379

21.2.3	Recruitment of GGDEF and EAL Domains for c-di-GMP-Unrelated Functions	379
21.2.4	Regulation of DGC and PDE Activity and Expression	380
21.2.5	c-di-GMP-Binding Effectors	380
21.3	Signaling Specificity	381
21.4	c-di-GMP Signaling in <i>E. coli</i>	382
21.5	c-di-GMP signaling in <i>V. cholerae</i>	385
21.6	c-di-GMP Signaling in <i>C. crescentus</i>	387
21.7	Conclusions and Outlook	388
	References	389
22	ppGpp Signaling	395
	<i>Rolf Wagner</i>	
22.1	Introduction	395
22.2	Induction of the Effector (p)ppGpp Through Synthesis and Degradation	396
22.3	ppGpp – A <i>Bona Fide</i> Global Regulator	398
22.3.1	Transcriptional Profiling in Different Bacterial Strains	398
22.3.2	Lack of (p)ppGpp Signaling in Obligate Intracellular Bacterial Pathogens and Archaea	399
22.3.3	ppGpp in Plants	399
22.3.4	(p)ppGpp as a Mediator of Bacterial Social Behavior and Cell–Cell Signaling Mechanisms	400
22.3.5	(p)ppGpp Signaling in Virulence and Pathogen–Host Interaction	400
22.3.6	(p)ppGpp as a Regulator for Toxin–Antitoxin Systems in Bacterial Programmed Cell Death	401
22.3.7	Persistor Cells and Enhanced Mutation Frequency	401
22.4	Effects on Macromolecular Synthesis	402
22.4.1	Role of ppGpp as an Inhibitor of Replication	402
22.4.2	Inhibition of Translation: Effect on Initiation Factor 2	403
22.5	Regulation of Transcription: RNA Polymerase is the Target	403
22.5.1	Role of RNA Polymerase ω Subunit	404
22.5.2	Promoter-Specific Effects of (p)ppGpp	404
22.5.3	Rate-Limiting Step in ppGpp-Dependent Transcription Initiation	405
22.5.4	Different Mechanism of rRNA Regulation Between <i>E. coli</i> and <i>B. subtilis</i>	406
22.5.5	Involvement of Coregulators: RNA Polymerase Secondary Channel-Binding Proteins	406
22.5.6	Positive Stringent Control	407
22.5.7	Passive Regulation by Sigma Factor Competition – Direct Versus Indirect Effects	407
	References	408

23	Sensory RNAs	415
	<i>Franz Narberhaus</i>	
23.1	Introduction	415
23.2	RNA as a Regulatory Molecule	415
23.3	Riboswitches	416
23.4	RNA Thermometers	420
23.5	Conclusions	422
	References	423
24	Signal Transduction by Serine/Threonine Protein Kinases in Bacteria	427
	<i>Michael Bott</i>	
24.1	Introduction	427
24.2	Discovery and Distribution of STPKs in Prokaryotes	427
24.3	Serine/Threonine Phosphorylation versus Histidine/Aspartate Phosphorylation	428
24.4	Domain Architecture of STPKs	428
24.5	Structural Studies on STPKs	429
24.6	Signal Transduction by STPKs	432
24.7	Control of Gene Expression by PknB via the Activity of Sigma Factors	434
24.8	Control of Gene Expression by PknH via the Transcriptional Regulator EmbR	435
24.8.1	Discovery of EmbR in Mycobacteria and its Phosphorylation by PknH	435
24.8.2	Structure of EmbR	435
24.8.3	Effects of EmbR Phosphorylation by PknH	435
24.8.4	Model of Signal Transduction by PknH and EmbR	436
24.9	Direct Control of Enzyme Activities by STPKs	436
24.10	Indirect Control of Enzyme Activity by PknG and its Target Protein OdhI/GarA	438
24.10.1	Distribution of PknG	438
24.10.2	Structure of PknG	438
24.10.3	Evidence for a Role of PknG in the Pathogenicity of Mycobacteria	439
24.10.4	Studies on PknG and its Target Protein OdhI in <i>C. glutamicum</i>	439
24.10.5	Inhibition of 2-Oxoglutarate Dehydrogenase by Corynebacterial OdhI	440
24.10.6	Identification of the OdhI Homolog GarA in Mycobacteria	440
24.10.7	Identification of GarA as a Substrate of Mycobacterial PknB	440
24.10.8	Identification of GarA as Substrate of Mycobacterial PknG	441
24.10.9	Functions of GarA in Mycobacteria	441
24.10.10	Putative Mechanism of GarA/OdhI Function	442
24.10.11	Model of Signal Transduction by PknG and OdhI/GarA	443
24.11	Conclusions and Outlook	443
	References	444

25	Regulatory Proteolysis and Signal Transduction in Bacteria	449
	<i>Kürşad Turgay</i>	
25.1	Introduction	449
25.2	Hsp100/Clp and other AAA+ Protease Systems in Bacteria	450
25.3	Substrate Recognition and Adaptor Proteins	452
25.3.1	Substrate Recognition	452
25.3.2	Adaptor Proteins	452
25.4	Examples of Regulatory Proteolysis in <i>B. subtilis</i>	454
25.4.1	Competence Development and the Proteolytic Switch	454
25.4.2	Heat Shock Adaptation	455
25.5	Conclusions	456
	References	457
26	Intracellular Signaling and Gene Target Analysis – <i>Methods Chapter</i>	463
	<i>Jörn Kalinowski</i>	
26.1	Introduction	463
26.2	Genome-Wide Expression Analysis	463
26.3	Finding Unknown Target Genes	465
26.3.1	Systematic Evolution of Ligands by Exponential Enrichment (SELEX)	465
26.3.2	Chromatin Immunoprecipitation (ChIP)	467
26.4	Analyzing Known Targets	468
26.4.1	DNA Affinity Chromatography (DAC)	469
26.4.2	Electrophoretic Mobility Shift Assay (EMSA)	469
26.5	Conclusions and Outlook	471
	References	472
	Index	473

