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Nota di contenuto	Part I:Biochemistry/Structural Biology – Enzymes -- Chapter 1: Cyclic Dinucleotide Signaling In Mycobacteria -- Chapter 2: Structure and regulation of EAL domain proteins -- Chapter 3: Insights into the molecular basis of biofilm dispersal from crystal structures of di-domain containing proteins -- Chapter 4: Structure and function of HD-GYP phosphodiesterases -- Chapter 5: A unified catalytic mechanism for c-di-NMP hydrolysis by DHH/DHHA1 phosphodiesterases -- Chapter 6: Enzymatic degradation of linear dinucleotide intermediates of cyclic dinucleotides -- Part II: Biochemistry/Structural Biology – Receptors -- Chapter 7: Detection of cyclic dinucleotide binding proteins -- Chapter 8: Non-canonical c-di-GMP binding modes -- Part III:Biochemistry/Structural Biology – Sensing -- Chapter 9: Sensory domains that control cyclic di-GMP-modulating proteins: a critical frontier in bacterial signal transduction -- Part IV:Cyclic di-AMP biochemistry and physiology -- Chapter 10: Metabolic regulation by cyclic di-AMP signaling -- Chapter 11:

Osmoregulation via cyclic-di-AMP signaling -- Part V: Population diversity -- Chapter 12: Measuring individual cell c-di-GMP: Identifying population diversity and c-di-GMP heterogeneity.-Part VI: Cyclic di-GMP and exopolysaccharide regulation -- Chapter 13: Activation of bacterial cellulose biosynthesis by cyclic-di-GMP -- Chapter 14: The Regulation of Alginate Biosynthesis via C-di-GMP Signaling -- Part VII: Environmental bacteria -- Chapter 15: Cyclic di-GMP Signaling in *Bacillus subtilis* -- Chapter 16: C-di-GMP signaling systems in the Gram-positive *Bacillus cereus* group -- Chapter 17: Cyclic-di-AMP in *Bacillus subtilis* biofilm formation.-Chapter 18: Regulation by c-di-GMP in *Myxococcus xanthus* -- Chapter 19: Light-regulated nucleotide second messenger signaling in cyanobacteria -- Chapter 20: C-di-GMP-dependent regulation of antibiotic biosynthesis in *Lysobacter* -- Chapter 21: Cyclic di-GMP signaling in extreme acidophilic bacteria -- Part VIII: Pathogens -- Chapter 22: Signals modulating cyclic di-GMP pathways in *Vibrio cholera* -- Chapter 23: Cyclic di-GMP regulation of gene expression -- Chapter 24: Cyclic di-GMP signaling in *Salmonella enterica* serovar Typhimurium -- Chapter 25: Cyclic di-GMP signaling in the phytopathogen *Xanthomonas campestris* pv. *Campestris* -- Chapter 26: Cyclic di-AMP in *Mycobacterium tuberculosis* -- Chapter 27: Cyclic di-AMP signaling in *Streptococcus pneumoniae* -- Part IX: Gram-negative bacteria -- Chapter 28: Regulation of cyclic-di-GMP signaling in *Pseudomonas aeruginosa* -- Chapter 29: Unconventional Cyclic di-GMP Signaling in *Escherichia coli* -- Chapter 30: Cyclic di-GMP in *Burkholderia* spp -- Chapter 31: Cyclic di-GMP and the regulation of biofilm dispersion -- Part X: Cyclic di-GMP signaling in eukaryotes -- Chapter 32: Cyclic-di-GMP activates adenylate cyclase A and protein kinase A to induce stalk formation in *Dictyostelium* -- Part XI: Interference Strategies -- Chapter 33: Targeting cyclic di-nucleotide signaling with small molecules -- Part XII: Novel cyclic di-nucleotides -- Chapter 34: Cyclic di-GMP signaling gone astray: cGAMP signaling via Hypr GGDEF and HD-GYP enzymes -- Chapter 35: Microbial cyclic GMP-AMP signaling pathways.-Part XIII: Honorary cyclic nucleotides -- Chapter 36: 2',3'-cyclic mononucleotide metabolism and possible roles in bacterial physiology -- Part XIV: Horizontal gene transfer -- Chapter 37: Horizontal transfer of c-di-GMP associated genes. Theoretical underpinnings and future perspectives.-Part XV: Conclusion -- Chapter 38: Conclusion. .

## Sommario/riassunto

This book explores the broad and diverse biological and physiological impacts of established and newly discovered cyclic di-nucleotide second messenger signaling systems, while also providing descriptions of the intriguing biochemical characteristics of multiple turnover enzymes and receptors. The respective chapters discuss the commonalities and diversity of cyclic di-GMP, cyclic di-AMP and recently discovered cyclic GMP-AMP signaling systems in manifold Gram-negative and Gram-positive bacteria. The global human pathogens *Mycobacterium tuberculosis*, *Vibrio cholerae*, *Salmonella typhimurium*, *Escherichia coli* and *Streptococcus pneumoniae*, the facultative human pathogen *Pseudomonas aeruginosa*, global plant pathogens as exemplified by *Xanthomonas campestris* and *Burkholderia* spp., and the omnipresent probiotic *Lactobacilli*, as well as environmentally important photoautotrophic cyanobacteria, the multicellular *Myxococcus xanthus*, and chemolithotrophic *Acidithiobacillus* are among the representatives of the microbial kingdom that are described. In turn, the various aspects of bacterial physiology affected by these signaling systems— e.g. biofilm formation and dispersal, the cell cycle, motility, virulence, production of antimicrobials, fundamental metabolism and osmohomeostasis – are

discussed in detail in the context of different microorganisms. Dedicated chapters focus on the population diversity of cyclic dinucleotide signaling systems, their tendency to be horizontally transferred, the cyclic di-GMP signaling system in the social amoeba *Dictyostelium*, honorary cyclic (di)nucleotides, and the development of strategies for interfering with cyclic dinucleotide signaling in order to manipulate microbial behavior. Taken together, the chapters provide an authoritative source of information for a broad readership: beginners and advanced researchers from various disciplines; individuals seeking a broad overview of cyclic di-nucleotide signaling; and those who want to learn more about specific aspects. Also featuring reviews with a forward-looking perspective, the book offers a valuable source of inspiration for future research directions.

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