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The novel and significant roles played by cyclic-di-GMP in controlling a wide variety of bacterial physiology

The discovery of c-di-GMP second messenger is one of the most important breakthroughs in the microbial world in the past two decades. This molecule is present in most bacteria, regulating a plethora variety of important bacterial activities such as biofilm formation, biogenesis and function of flagella and pili, cell differentiation, and biosynthesis of natural product and secretion of pathogenic factors, through binding to an unprecedented array of effectors. There are usually tens or even hundreds of enzymes that make or break c-di-GMP in every bacterial genome. These enzymes usually carry extra domains to activate their activities for responding to environmental changes. Many c-di-GMP biosynthesis (diguanylate synthetase) or degradation (phosphodiesterase) enzymes have been elucidated. However, only a few c-di-GMP receptors have been characterized to date. To get a better understanding of how c-di-GMP carries out its diverse functions, it is of crucial importance to decipher the possible c-di-GMP binding motifs. Several c-di-GMP receptors have been found but most of them usually exhibit narrow phylogenetic distribution. Recently, MshE, an ATPase associated with the mannose-sensitive hemagglutinin type IV pilus formation in *Vibrio cholerae*, was shown to bind c-di-GMP well by a DRACALA methodology but no canonical binding motif was found in binding c-di-GMP. We have solved the crystal structure of the MshEN/c-di-GMP complex, which revealed an entirely new c-di-GMP binding mode. It is fused with many other domains such as ATPase, glycosyltransferase, CheA, CheX, REC, cNMP-binding, HD-GYP and guanylate cyclase, which have been found to play various important roles in bacterial physiology. MshEN is thus a new c-di-GMP binding protein that may serve as a good target for developing novel drugs against bacteria without causing drug resistance.

Biography

Shan-Ho Chou is currently a Chair Professor of the Institute of Biochemistry, National Chung Hsing University, Taiwan. He has received his Bachelor's degree in Chemistry from the National Taiwan Normal University, a Master's degree in Biochemistry from the National Taiwan University and a PhD in Chemistry from the University of Washington in Seattle, WA. He has been studying the structural biology of cyclic-di-nucleotide related issues in the plant pathogen *X. campestris* by NMR and X-ray crystallography and has solved several unique c-di-GMP-protein complex structures. He is currently combining X-ray, NMR, and single-particle cryo-EM techniques to study multi-domain protein complexes associated with c-di-GMP and c-di-AMP signaling. He is an author of more than 100 research papers, reviews and book chapters.

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