Universität Basel

Research Project

Molecular mechanisms of c-di-GMP signaling

Third-party funded project

Project title Molecular mechanisms of c-di-GMP signaling
Principal Investigator(s) Schirmer, Tilman ;
Project Members Dubey, Badri Nath ; Dias Teixeira, Raphael ; Fadel, Firas ;
Organisation / Research unit
Departement Biozentrum / Structural Biology (Schirmer)
Department
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Our general aim is to contribute to the understanding, on the molecular level, of the mechanisms by which proteins perform their biological action. For this we are combining X-ray structure analysis, functional and biophysical characterization, and site-directed mutagenesis. Here, we propose to continue our research on components of the bacterial signaling pathways that utilize cyclic di-GMP. Via this second messenger a large variety of cell surface associated traits and cell differentiation programs are regulated in response to internal and external stimuli. We want to determine the structures and ligand binding properties of novel c-di-GMP binding proteins (receptors) of C. crescentus and P. aeruginosa. The structures will reveal any changes induced by ligand binding that are crucial for down-stream signalling. We will strive to identify binding partners that interact with the receptors in a c-di-GMP dependent way. Structure/function investigations will be performed on PdeL from E. coli, a c-di-GMP specific phosphodiesterases with a DNA binding domain. These studies will unravel the intricate coupling between enzymatic and transcriptional activity of this signal node on the molecular level. Most recently, it has been discovered that the action of a central histidine kinase (CckA from C. crescentus) can be reverted to phosphatase activity by c-di-GMP binding. In this way, oscillating c-di-GMP levels during the cell cycle are synchronized with transcriptional activity. We propose to reveal the molecular determinants and the mechanism of this central signal node by structure-function analyses. In addition, we want to understand how also the receiver domain protein DivK can drive CckA into the phosphatase mode. Our general aim is to contribute to the understanding, on the molecular level, of the mechanisms by which proteins perform their biological action. For this we are combining X-ray structure analysis, functional and biophysical characterization, and site-directed mutagenesis. Here, we propose to continue our research on components of the bacterial signaling pathways that utilize cyclic di-GMP (c-di-GMP). Via this second messenger, a large variety of cell surface associated traits and cell differentiation programs are regulated in response to internal and external stimuli.

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Quite unexpectedly, also some bacterial histidine kinases are regulated by c-di-GMP. We are studying CckA from *C. crescentus* that can be reverted to phosphatase activity by c-di-GMP binding. In this way,

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Add publication

Published results

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