Crystal structure of the PilZ-FimX$_{EAL}$-c-di-GMP heterodimer complex and its involvement with Type IV pilus biogenesis.

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Type IV pilus (T4P) is a very thin filamentous located in the outer surfaces of many bacteria and it has been described to be important for different biological important processes such as biofilm formation, pathogenicity, natural transformation, autoagglutination, signal transduction, and motility. In recent years has emerged the idea that c-di-GMP is a bacteria second messenger that controls complex physiological processes in bacteria including motility, biofilm formation, virulence and cell division. At the central of this regulatory mechanisms exist enzymes with GGDEF domain that synthesis c-di-GMP, enzymes with EAL or HD-GYP domains, that degraded c-di-GMP molecules and protein receptors such as PilZ domains, and degenerated EAL domains. We are interested to study the signal transduction pathway mediated by c-di-GMP molecule in T4P biogenesis. PilB is a ATPase associated with the bacterial inner membrane involved in the polymerization of pilin subunit to build the T4P filamentous. This process is regulated in part by FimX, a multidomain protein with a C-terminal degenerated EAL domain, and by a non-canonical PilZ protein. EAL and PilZ domains often appear within multi-domain proteins involved in signal transduction and probably exert their functions via protein-protein interactions. We determined the crystal structure of the complex made up of PilZ, the FimX EAL domain and c-di-GMP. Although PilZ is unable to bind c-di-GMP, in the PilZ-FimX$_{EAL}$-c-di-GMP complex PilZ is closed to c-di-GMP EAL binding site making one contact with c-di-GMP molecule. The structure of the PilZ-FimX$_{EAL}$-c-di-GMP complex presents new insights into the molecular recognition mechanisms in c-di-GMP–mediated signaling pathways and is an important step to understand the T4P biogenesis regulation. The further steps will be study of the interactions between this heterodimer with the ATPase PilB.