MS5-P22 Crystal Structure of the cytoplasmic portion of histidine kinase SrrB from *Staphylococcus aureus*

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Staphylococcus aureus is a major cause of nosocomial infections today. *S. aureus* infection is considered to be the reason for the increasing number of antibiotic-resistant strains. Furthermore, *S. aureus* can produce slime layer or multilayered biofilm embedded with the glycocalyx on the surface of various biomaterials. *S. aureus* can persist in clinical settings and increase resistance to antimicrobial agents through biofilm formation. SrrB is a histidine kinase which responds to environmental stimuli by regulating its cognate response regulator SrrA. Under low-oxygen growth conditions, the staphylococcal regulator SrrAB induces *ica* locus transcription and polysaccharide intercellular adhesion (PIA) production, known as a major component of biofilm.

Here, we report the crystal structure of cytoplasmic portion of SrrB (SrrBc) from *S. aureus* in a dimeric form at 1.78 Å resolution. The overall structure of SrrBc forms a unique homodimer which is mediated by two pairs of long dimerization α-helices. To the rear of dimerization helices is the ATP binding domain of SrrB which consists of three parallel α-helices, one short anti-parallel β-sheet, one core mixed type β-sheet and a disordered ATP-lid region. Moreover, one disulfide bond (Cys469 and Cys506) is located within the core β-sheet to stable the structure. We propose that the redox state of this disulfide bond in the ATP binding domain of SrrB might play a key role to mediate the interaction between SrrB and SrrA, thus alter the target gene of SrrAB in transcription level in *S. aureus*.

Keywords: biofilm, multiple antibiotic resistant, two-component system

MS5-P23 Insight into recognition between aminoacyl carrier protein and its binding partner

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Acyl carrier-protein (ACP) is one of the most promiscuous protein in terms of protein-protein interactions within the cell. Common to both, primary and secondary cell metabolic pathways, ACP acts as a central acceptor of various intermediate products of fatty acid, polyketide and nonribosomal peptide synthesis pathways. Thus, it's quite puzzling how ACP selects correct protein partner among many possible upstream and downstream binding partners. To address this question we choose recently described protein-protein complex formed between aminoacyl carrier protein from *Bradyrhizobium japonicum* (Bj CP) and Bj Gly:CP ligase 1. We performed molecular dynamics simulations, MM-GBSA binding free energy calculations, alanine scanning mutagenesis, and multiple sequence alignment to get deeper insight into relevant protein-protein interactions between three forms of the aminoacyl carrier protein and their partner protein Bj Gly:CP ligase 1 (Figure 1). Our result are in line with experimental findings and indicate that correct protein-protein communication is regulated through specific non-polar contribution of the interacting amino acid residues placed at the interface between aminoacyl carrier protein and partner Bj Gly:CP ligase 1. *In silico* alanine scanning mutagenesis along with multiple sequence alignment aided in classifying interacting residues as universally required for aminoacyl carrier protein binding and those that determine the selectivity.

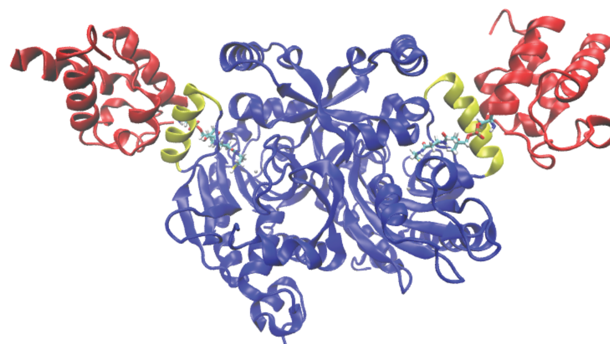

Figure 1. Bj CP - Bj Gly:CP ligase 1 2:1 complex given in the cartoon representation. Both Bj CPs are given in red, while Bj Gly:CP ligase 1 is shown in blue with CP-binding helices given in yellow.

Keywords: molecular recognition; molecular dynamics simulations; protein-protein interactions; acyl carrier proteins