

Structural studies for the interaction of receiver domain of sensor histidine kinase PA1611 and histidine-containing phosphotransfer protein in two-component regulatory system of *Pseudomonas aeruginosa*

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Abstract

Two-component regulatory system (TCS) is the signal transduction system widely occurring in prokaryotes and helps the organisms adapt the changing environment. In *P. aeruginosa*, an important opportunistic pathogen causing numerous acute and chronic infections, the hybrid TCS is responsible for regulating the swarming ability and biofilm formation. It consists of hybrid sensor histidine kinase (HK), histidine-containing phosphotransfer protein (Hpt), and response regulator (RR). After receiving environmental stimulus, the phosphoryl group from ATP hydrolysis, catalyzed by HK histidine kinase-like ATPase domain (HATPase), binds to HK histidine kinase phosphoacceptor domain (HisKA) and is subsequently received by the conserved Asp residue of HK receiver domain (REC). The phosphoryl group is then transferred to Hpt and further received by RR to regulate the gene expression.

We have determined the crystal structures of HK PA1611 REC and HptB, respectively. To further reveal the mechanism of signal transduction between REC and Hpt, the crystal structure of HK PA1611 REC/HptB complex will be characterized with synchrotron X-ray diffraction at high resolution, together with small angle X-ray scattering as a complimentary method, in this proposal project. The complex structure will make the hybrid TCS of *P. aeruginosa* be further understood and potentially lead to the discovery of new treatment, such as novel molecules which can interfere the interaction between HptB and corresponding REC domains, for *P. aeruginosa* infection.

Keywords - *P. aeruginosa*, Two-component regulatory system, sensor histidine kinase, histidine-containing phosphotransfer protein