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SUMMARY of
2021 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		Structures of Hpt and the C-terminal receiver domain of *P. aeruginosa*
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Summary

In aiding the adaptation of the cells to environmental condition changes, two-component regulatory systems (TCS) are widely distributed in prokaryotes, whereas a few are identified in lower eukaryotic organisms and plants. For *Pseudomonas aeruginosa* (*P. aeruginosa*), the histidine-containing phosphotransfer (Hpt)-mediated hybrid TCS serves as a basic stimulus-response coupling mechanism to reduce the environmental harm and ensure survival by activating the downstream response, including antibiotic susceptibility, swarming activity and biofilm formation. The Hpt-mediated multistep phosphorelay plays a central role in the infection process of *P. aeruginosa*. HptB in *P. aeruginosa* is closely related to biofilm formation, which could increase the ability of drug resistance and protect the cell from pinocytosis by the host. After the sensor protein, PA1611, is autophosphorylated, the phosphoryl group would be transferred to HptB and subsequently to the downstream response regulator protein PA3346. It is necessary to determine the structures of HptB and its interacting partner for elucidating this pathway.

The preliminary crystals were examined at BL44XU of SPring-8 at the earlier stage and before COVID-19. These crystals diffracted poorly with low resolution. We progressively improved the crystal quality and collected useful data at the beamlines of NSRRC in Taiwan. Because of COVID-19 situation, we could not go to SPring-8 for more experiment to improve resolution. We acknowledged the BL44XU beamline for early crystal testing. We determined the crystal structures of HptB and the C-terminal receiver domain of HK PA1611 for the complex study using data from NSRRC beamlines. The structural details allow us to model the complex of HptB/PA1611REC, which further clarifies the mechanism of HptB-mediated signal transduction pathway of *P. aeruginosa* and potentially lead to the discovery of new treatment for *P. aeruginosa* infection.