Poster Presentation

MS101.P08

Inward-facing conformation of the bacterial heme transporter

<u>H. Sugimoto</u>¹, Y. Naoe¹, N. Nakamura^{1,2}, A. Doi¹, Y. Shiro^{1,2} ¹*RIKEN SPring-8 Center, Hyogo, Japan,* ²*Hyogo University, Department of Life Science, Hyogo, Japan*

Iron is an essential element for almost all organisms, since iron serves as a catalytic center for redox reactions in many enzymes. Bacterial pathogens need to acquire iron from tissues of host to survive. Heme transport by ATP-binding cassette (ABC) transporter plays a key role in pathological processes. In gram-negative bacteria, the heme or heme protein binds to specific outer membrane receptors on the bacterial surface. The heme is then transported into the cell via ABC transporters. Here, we present the crystal structure of the heme transporter complex BhuUV-T from Burkholderia cenocepacia at 3.5 Å resolution in nucleotide-free state. The permeation pathway created by transmembrane helices of two BhuU subunit exhibits an inward-facing conformation. Comparison with the outward-facing conformation previously reported for the heme transporter HmuUV from Yersinia pestis and homologous vitamin B12 transporter BtuCD-F from E. coli indicates the structural mechanism involving the translational shift of nucleotide binding subunit and repositioning of the helices of permease subunits for substrate translocation. Structure of interface between BhuUV and periplasmic heme-binding protein BhuT suggests that the acidic residues of BhuU at the periplasmic interface may have an important role in releasing the heme from BhuT. We also determined the BhuT in apo and two types of holo form, providing the structural basis for transient and ambiguous heme recognition.

Keywords: ABC transporter, heme, pathogenic bacteria