Poster Presentation

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X-ray crystallographic analysis of a MATE multidrug transporter from V. cholerae

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MATE (Multidrug And Toxic compound Extrusion) family transporters are highly conserved from Bacteria to Eukarya including human, and export a broad range of xenobiotics using either a proton or a sodium ion gradient across the membrane. Especially in bacterial pathogens, MATE transporters contribute to their multiple drug resistance (MDR). To understand how MATE transporters export various substrates such as drugs and thus how pathogens acquire MDR, structural analyses are essential. The crystal structures of several MATE transporters from pathogens have been reported. However, because of the limited resolution and the lack of drug-MATE transporters complex structures, the recognition mechanism of various substrates and the coupling mechanism of the cation influx and the drug efflux have been poorly understood. Although the high-resolution structures of MATE transporters from non-pathogenic archaeal P. furiosus (PfMATE) have been reported, PfMATE shares low sequence identity with MATE transporters from pathogens such as V. cholerae. Therefore, further findings of the structural mechanism of MDR caused by MATE transporters from pathogens have been needed. To understand the substrate recognition and transport mechanism of MATE transporters from pathogens, we determined the crystal structures of one of MATE transporters from V. cholerae (VcMATE) at 2.5-2.7 Å resolutions using in meso crystallization method. The high-resolution structures of VcMATE show two distinct conformations, as observed in the structures of PfMATE, and reveal the large movement of transmembrane helix 1 and the putative substrate-binding site. The structures suggest that the bending of transmembrane helix 1 and the sequential collapse of the putative substrate-binding site induce the release of the bound substrate. This conformational change during the substrate transport may be a common mechanism among MATE transporters from pathogens to non-pathogens.

Keywords: multiple drug resistance, transporter