

## Cryo-EM Driven Paradigm Shift of ABC Transporter Mechanism

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Present in all kingdoms of life, ATP-binding cassette (ABC) transporters harness the energy of ATP binding and hydrolysis to translocate a multitude of chemically diverse substrates across cellular membranes. Despite decades of studies and many available structures, the molecular mechanisms of most ABC transporters are still poorly defined. The ongoing revolution of cryo-EM has enabled novel approaches for obtaining deep insights into these highly dynamic membrane protein machines. Through our cryo-EM studies of several ABC transporters that perform different functions, we have uncovered how distinct tasks of substrate translocation are accomplished by the unique actions of these transporters. Importantly, our own research experience in the past decade is an excellent demonstration of how single-particle cryo-EM methodology and the mechanistic study of ABC transporters stimulate each other's development, thus emphasizing the extremely versatile nature and yet-to-be-realized potential of cryo-EM in biological research. (<https://liao.bio.sustech.edu.cn/>)

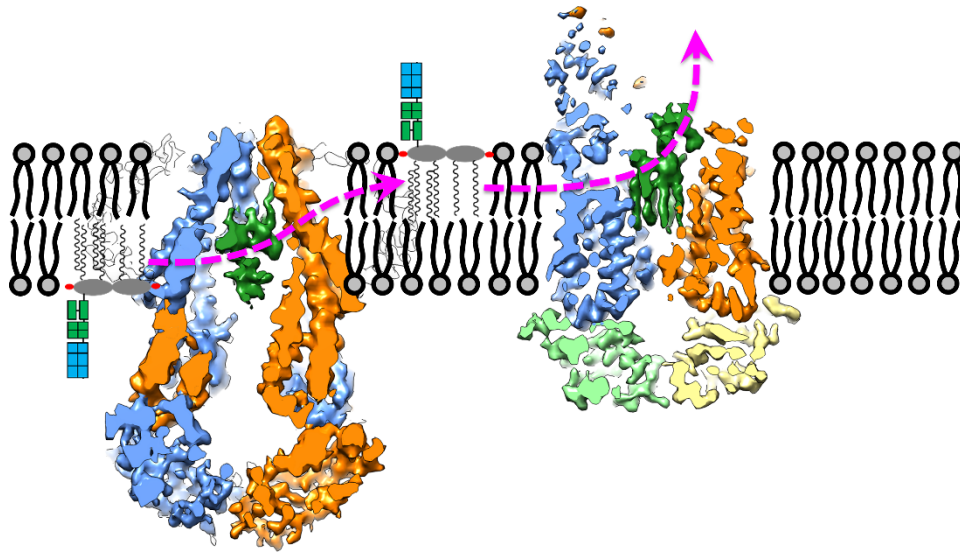


Figure 1. Cryo-EM reveals how lipopolysaccharide is flipped by MsbA(1, 2) (left) and extracted by LptB<sub>2</sub>FGC(3, 4) (right), two ABC transporters in *Escherichia coli*.

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