A single-molecule approach to reveal the molecular mechanism behind bacterial membrane permeability

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Abstract

The bacterial cell envelope evolved to have a sophisticated barrier playing a critical role in the permeation process. In the membrane, channel proteins form a barrel-like structure of one nanometer in diameter and permit the transport of small molecules such as ions and hydrophilic compounds via passive diffusion. The transport of large or hydrophobic compounds is assisted by energy-dependent active transporters. Furthermore, in recent years, it has been observed that bulky molecules traverse across the membrane without extra energy input. It is surprising how the permeation of much larger molecules through narrow pores is possible. A transmembrane pore might not only act as a molecular sieve but also allow for a more flexible interaction with the permeants. However, in depth understanding of translocation mechanisms especially with bulky molecules and hydrophobic polymers remains a challenge. Therefore, to reveal the translocation mechanism at the molecular level, I studied their translocation dynamics using a technique called single-channel recording. This approach enabled me to follow trajectories of a single substrate across the cell membrane and identify translocation events with transient intermediates, which were extremely difficult to approach other techniques. The molecular nature in these translocation mechanisms can be revealed in this way.

The bacterial cell surface is a remarkable example for observing dynamic interactions from both sides: transporting molecules and membrane channels. Antimicrobial reagents penetrate the cell envelope to reach to targets in the cytoplasm by exploiting membrane channels. The key factors for this translocation to happen are the dynamic interactions within the membrane channel during the translocation process. To reveal the molecular details of such translocation events, it is required to employ a single-molecule approach and detect hidden conformational states, which are masked by averaging out unsynchronized populations in ensemble assays. By observing one molecule at a time the rate constants can be directly obtained from kinetic studies. Also, the total energy cost for these translocation events with natural polymer as well as synthetic chemical compounds could be estimated.

This fundamental study will be helpful to gain a deeper understanding in the controlled permeation in the bacterial cellular membrane. It will also provide insights into the underlying mechanism of bacterial resistance to antibiotics.

Keywords: *nanotechnology, membrane, protein, transport*

Biography

I majored in Chemistry. To better understand diseases on a molecular level, I did my master in 'molecular medicine master program' in Goettingen, Germany. During doctoral program in MPI-BPC, I did research on 'dynamics of membrane protein targeting into the cell membrane' using biochemical and biophysical assays. Currently, I am investigating on 'how protein translocates through a transmembrane pore' using single-molecule method.