Simultaneous recording of conformational changes and ionic currents of single-molecular ion channels reveals the relationship between membrane potentials and motions of the channels

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【Outline of survey】

In cell membranes or microorganisms, membrane proteins are always affected by membrane potentials and its oscillations in their activities. How do they move and function in these physiological conditions? To answer this fundamental question I plan to develop a new measurement system using ion channels as a testing molecule. Ion channels are signal transduction molecules which transduce various stimuli, such as chemical substances in the body and membrane potentials, to electrical signals or ionic stream that runs across the membrane. In this transduction process, it had been predicted there were conformational changes for the openings and closings of their ion permeation pathway (gating). Our research group recently succeeded in recording these conformational changes in a single molecule as movies, which revealed that an ion channel twisted around the axis of the pathway upon gating. In this study, I will develop new measuring devices which enable simultaneous recording of the conformational changes and ionic currents through the channels by integrating the existing method for recording currents and our method for detecting motions.

【Expected results】

The results of this research will elucidate the mechanism of signal transduction in cells by revealing the relationship between the “function” and “motion” of channels. The simultaneous measurement of a single molecule, not averaged image of many molecules, will allow a detailed analysis of the transduction mechanism that is an essential part of biological processes. Furthermore, the developed measuring devices can be adapted to all the other membrane proteins including important targets of drugs. Thus, the results would contribute to the understanding of the mechanism of drug action and designing of a new drug by examining not only the “functions” and “structures” but “motions” of their target.

【References by the principal investigator】

・Shimizu, H., *et.al.* (2008) Global twisting motion of KcsA potassium channel upon gating. Cell 132, 67-78.

【Term of project】 FY2008－2012	【Budget allocation】 **70,600,000 yen** (direct cost)
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