

Molecular studies on force generation of recombinant dynein based on its structure and dynamics

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【Outline of survey】

Dynein is a microtubule-based motor essential for cellular processes such as intracellular transport, chromosomal segregation and locomotion by cilia and flagella. This motor protein is composed of huge heavy chain(s) with molecular mass of more than 500kDa and other accessory proteins. Dynein is a member of the AAA family that includes helicases and molecular chaperones, and has a ring-like structure characteristic of the AAA proteins. The other motor proteins associated with cytoskeletons (myosin and kinesin) are members of the G-protein family and have molecular structures different from that of dynein. Based on structural studies and single-molecule manipulations, molecular mechanism of energy transduction by myosin and kinesin is now well understood. However, because of the lack of a good expression system of active dynein molecules, the molecular mechanism of dynein function is only poorly understood. We have recently succeeded to construct a *Dictyostelium* system to express dynein fragments that maintain full motor activities including motility along a microtubule. Based on this powerful expression system, we are going to reveal how dynein works at the molecular level. For this goal, we will use structural-biological approaches such as X-ray crystallography and cryoEM, biochemical approaches to reveal structure-function relationship, and biophysical approaches of single-molecule manipulations and measurements.

【Expected results】

As far as myosin and kinesin are concerned, we now know structural details of their motor functions. Once we know how dynein works at the molecular level, we can compare the molecular mechanisms of two different types of motor proteins, and understand how nature's energy transducers are designed in general. Moreover, since dynein is a member of the AAA family, which includes DNA-based motors such as helicases, our understanding of dynein mechanism will have an impact on other fields of unconventional motor proteins such as helicases and chaperones.

【References by the principal researcher】

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【Term of project】 FY 2005 - 2009

【Budget allocation】 82,500,000 yen

【Homepage address】 <http://bio.c.u-tokyo.ac.jp/pnf/sutoh/> (no English version)