Microsc. Microanal. 8 (Suppl. 2), 2002
DOI 10.1017.S1431927602100316

Cryo-EM and X-ray crystallographic studies on the monomeric kinesin motor KIF1A

Masahide Kikkawa*,**, Elena P. Sablin***, Yasushi Okada**, Hiroaki Yajima**, Robert J.Fletterick*** & Nobutaka Hirokawa**

* University of Texas, Southwestern Medical Center, Dept. Cell Biology, Dallas, TX, 75390-9039 (current address)
** University of Tokyo, Dept. Cell Biology and Anatomy, Graduate School of Medicine, 7-3-1 Hongo Bunkyo-ku, Tokyo 113-0033, Japan
*** Department of Biochemistry/Biophysics, University of California, San Francisco, CA 94143-0448

Kinesin motors are specialized enzymes that use hydrolysis of ATP to generate force and movement along their cellular tracks, the microtubules. Although numerous biochemical and biophysical studies have accumulated much data that link microtubule assisted ATP hydrolysis to kinesin motion, the structural view of kinesin movement has remained unclear.

This study of the monomeric kinesin motor KIF1A combines X-ray crystallography and cryo-electron microscopy, and allows analysis of force-generating conformational changes at atomic resolution.

By using X-ray crystallography, the motor is revealed in its two functionally critical states: complexed with ADP and with a non-hydrolysable analog of ATP [FIG 3]. The conformational change observed between the ADP-bound and the ATP-like structures of the KIF1A catalytic core is modular, extends to all kinesins and is similar to the conformational change used by myosin motors and G proteins.

In order to understand the interaction between the motor and the microtubule, the structures of KIF1A-microtubule complex were studied by high resolution cryo-EM and helical image analysis [FIG 1,2]. Docking of the ADP-bound and ATP-like crystallographic models of KIF1A into the corresponding cryo-electron microscopy maps revealed detailed picture of the interaction between the motor and microtubule and suggests a rationale for the plus-end directional bias motion associated with the kinesin catalytic core [FIG 3].

References

[1] Kikkawa, M., et al. *Nature*, 411 (2001) 439-445
[2] Kikkawa, M., et. al *Cell*, 100 (2000) 241-252
[3] This research was supported by a Center of Excellence Grant-in-aid from the Ministry of Education, Science, Sports, and Culture of Japan

https://doi.org/10.1017/S1431927602100316 Published online by Cambridge University Press