Interactions between Dynein and Microtubules

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Dynein motors move various cargos along microtubules within the cytoplasm and power the beating of cilia and flagella. We studied interactions between dynein and microtubules by calculating distances between atoms on their interface. The cryo-electron microscopy study on the dynein-microtubule complex revealed how the dynein molecule bound to the microtubules not only for high-affinity form but also for low-affinity one (their PDB IDs are 3J1T and 3J1U, respectively). In the PDB data of 3J1T and 3J1U, chain A is dynein and chains B and C are tubulins forming a coiled coil stalk. We assume that chains B and C are α-and β-tubulins and then we refer to them as tubulin B and tubulin C, respectively. The analysis showed that, while the interactions between atoms on their interface in low- and high-affinity forms were not so much different between dynein and tubulin B, they are significantly different between dynein and tubulin C; the interactions are weaker in low-affinity form than high-affinity one. This fact suggests that the interaction between the stalk and the microtubule binding domain serves an important role in the dynein mechanism.

Mizuno et al. [1] and Carter et al. [2] revealed the scheme of interactions between dynein and microtubules by cryo-electron microscopy study. They showed that the spoke of dynein played an important role for binding to microtubules [1]. Redwine et al. [3] showed that a salt bridge was formed between ^{420}Glu of β-tubulin (tubulin C in our definition) and the microtubules binding site of dynein by molecular dynamical-simulation (see Figure 3 in ref [3]). The stalk, which emerges from AAA4 (the fourth nucleotide-binding AAA+ domain in the ring), extends as one α helix of an antiparallel coiled coil (termed CC1), forms the small and globular microtubule binding domain (MTBD), and then returns as the partner helix of the coiled coil (CC2) [2]. They also determined single-molecule velocity (nm/s) and ATPase measurements k_{mt} (Pi/s/dynein) for different lengths of stalk, i.e., native, minus-length (−7) and plus-length (+7) stalks from the native one as shown below [2]. A review by Kikkawa [4] is also helpful to understand the structure of the dynein.

	Native	(−7)	(+7)
Velocity (nm/s)	69±22	8±4	42±14
ATPase k_{mt} (k_{basal}) (Pi/s/dynein)	20±4 (6±2)	21±2 (13±2)	21±5 (6±2)

In order to investigate interactions between dynein and microtubule we calculated distances between dynein and tubulin B, and dynein and tubulin C, of high- and low-affinity forms. We searched the atom pairs on their interface for those separated by less than 3.5 Å. The results are shown in Figures (A)–(D) below. Figures (A) and (B) are interface between dynein and tubulin B in high- and low-affinity forms, respectively, and Figures (C) and (D) are interface between dynein and

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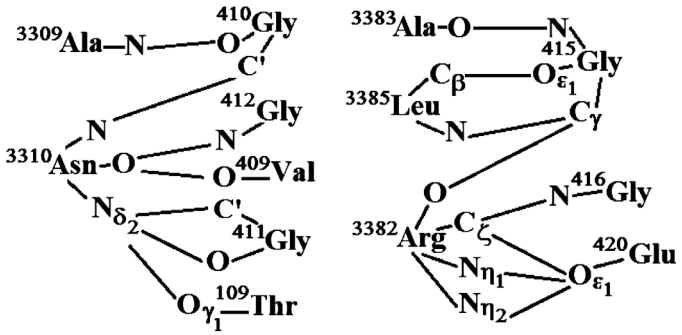
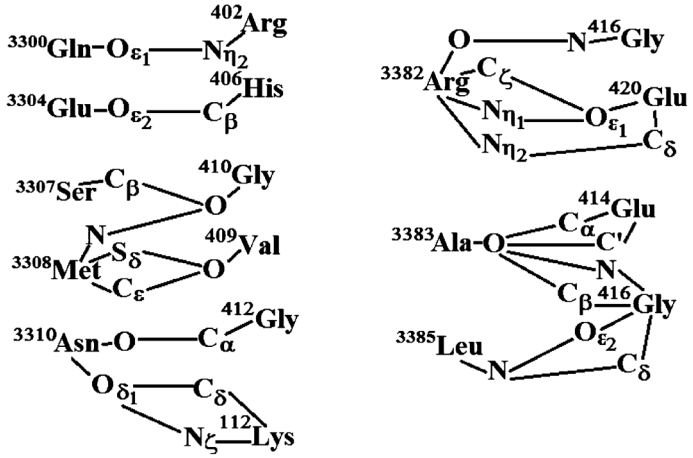
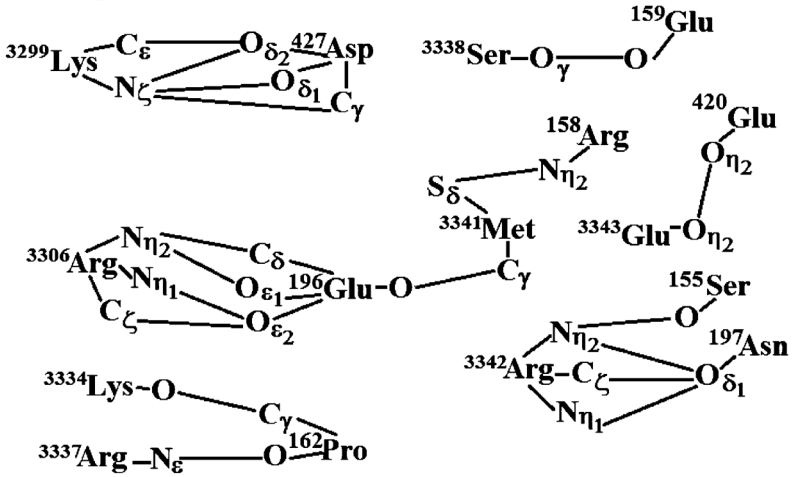
(A) High Affinity Case with Tubulin B (3J1T, chain B)



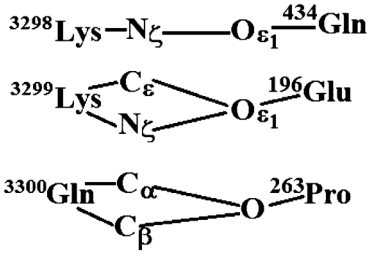
(B) Low Affinity Case with Tubulin B (3J1U, chain B)



(C) High Affinity Case with Tubulin C (3J1T, chain C)



(D) Low Affinity Case with Tubulin C (3J1U, chain C)



tubulin C in high- and low-affinity forms, respectively. In these figures the atom pairs separated by the distance of less than 3.5 Å are indicated by lines.

In dynein and tubulin B interface (Figs (A) and (B)), there are two clusters of atom-atom interaction networks for high-affinity form, while six clusters of them are found for low-affinity form. The number of interactions is slightly larger for low-affinity form than high-affinity one, but the difference is relatively small. On the contrast, the difference between high- and low-affinity forms is remarkable for dynein and tubulin C (Figs. (C) and (D)). It indicates that the strong contact occurred in tubulin C in the high-affinity form than the low-affinity one. Presumably, these features make it possible for dynein to move against microtubules. This is a very preliminary result, but this kind of network analysis by atomic distance examinations may be helpful to understand the dynein and microtubule system.

References

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