BIOMATERIALS

Forces in Biomolecular Systems SFB 863

A single-molecule view on kinesin motor-protein cooperation in intraflagellar transport in living C. elegans

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Abstract:

Intraflagellar transport (IFT) is an essential intracellular transport mechanism in cilia, the hair-like, microtubule-based protrusions of eukaryotic cells with sensory or motile functions. In the chemosensory cilia of the nematode C. elegans, IFT is driven by the cooperative action of IFT-dynein (responsible for transport from cilium tip to base) and two kinesin motor proteins, Kinesin-II and OSM-3, (responsible for transport in the opposite direction). Our goal was to understand why two kinesins are needed for IFT and what their respective roles are. To achieve this, we generated mutant nematodes expressing fluorescent versions of the motor proteins at endogenous levels and subjected them to in vivo fluorescence microscopy with single-molecule resolution. Images obtained were analyzed using automated kymograph and single-particle tracking analysis, providing unprecedented, quantitative insight in the role of the kinesins in IFT. We find that the two kinesins fulfill distinct roles in line with their distinct motility properties. Kinesin-II is the slower and less processive motor. In IFT its key role is to load of IFT trains - to initiate the transport of multiple, coupled motor proteins connected to cargo and to effectively traverse the transition zone, the semi-permeable protein barrier between cilium and rest of the cell. After successful crossing of the transition zone, Kinesin-II leaves the trains and the other, faster and more processive kinesin, OSM-3 binds and drives the longer-distance transport to the cilium tip. Our results provide insight in how cells use a combination of motor proteins to drive intracellular transport and demonstrate the power of single-molecule fluorescence microscopy to unravel complex processes in the cells of living, multicellular organisms.

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