

Motor cooperation in bi-directional early endosome motility

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Martin Schuster

Abstract

In mammalian cells and fungi, early endosomes form a dynamic compartment that undergoes bi-directional motility along microtubules. Previous work has shown that in the model system *Ustilago maydis* early endosome motility involves the opposing motor proteins dynein and kinesin-3. Here I performed a detailed analysis of the role of the motors in early endosome motility, using quantitative live cell imaging of kinesin-3, dynein and the endosomal GTPase Rab5a. In the first part of my work, I analysed the role of dynein at MT plus-ends, where the motor forms a strong accumulation that was thought to be involved in capturing early endosomes. I could demonstrate that ~55 dynein motors build up the dynein accumulation. In collaboration with Ms. Congping Lin and Prof. Peter Ashwin (Institute for Mathematics, Exeter), I found theoretical evidence that ~25 dynein motors concentrate and leave the plus-ends stochastically. In addition, dynein motors are captured by an interaction of dynactin and the plus-end binding protein EB1. Together both mechanisms increase the number of motors, which ensures that EEs will be loaded onto dynein before they reach the end of their track. In a second project, I provide evidence that loading of dynein is not restricted to the plus-ends. Instead, dynein leaves the plus-ends and is able to bind to kinesin-3 delivered early endosomes, which changes their transport direction from anterograde to retrograde. Kinesin-3 remains bound to these retrograde EEs. When dynein leaves the organelle, it switches back to anterograde motility. Interestingly, a single dynein wins over three to five kinesin-3 motors. I discuss these findings in the light of current motor cooperation concepts. In a third part, I demonstrated that kinesin-3 has an unexpected role in long-range retrograde endosome motility. In contrast, dynein is only responsible for the distal 10-20 μm . This is possible because most of the hyphal cells contain a symmetric and bi-polar MT array. This MT organization is reminiscent of that in dendrites. Kinesin-3-based retrograde motility is required to mix the organelles and might support long-range communication between both cell poles.

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