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MOLECULAR MOTORS

A new motor for traffic

A molecular motor that regulates the transport of early endosomes towards the plus end of microtubules has now been identified by Zerial and colleagues, and is described in *Cell*. The concerted activity of the GTPase Rab5 and its effector VPS34, a phosphatidylinositol 3-kinase, has previously been shown to be required for microtubule-mediated endosome motility *in vitro*. So, Zerial and co-workers searched genome databases for a motor with the potential to bind to phosphatidylinositol-3-phosphate (PtdIns3P).

They identified the kinesin KIF16B, which contains a PtdIns3P-binding Phox (PX)-homology domain, and used an *in vitro* assay to show that it is a plus-end-directed motor. Interestingly, the microtubule gliding velocities of KIF16B in this assay were in the same range as those for the long-distance movement of early endosomes *in vivo*.

As the PX domain of KIF16B also bound to lipids other than PtdIns3P in binding experiments *in vitro*, the authors verified the specific early endosomal localization of KIF16B *in vivo*. They also showed that inhibiting PtdIns3P production using pharmacological inhibitors led to the detachment of KIF16B from early endosomes. They could not detect a direct Rab5–KIF16B interaction *in vitro*, but found that a dominant-negative Rab5 mutant induced the release of KIF16B from early endosomes *in vivo*. This indicates that KIF16B recruitment to

early endosomes is dependent on Rab5–VPS34-mediated PtdIns3P production, and they showed that purified KIF16B can move PtdIns3P-containing liposomes, but not liposomes lacking this lipid, along microtubules *in vitro*.

Next, using an assay that specifically reconstitutes plus-end-directed movement in a cell-free system, Zerial and colleagues verified the involvement of KIF16B in the Rab5- and PtdIns3P-dependent motility of early endosomes. Disrupting or stimulating Rab5 activity decreased or increased motility, respectively, and inhibiting VPS34 using specific antibodies blocked early endosome motility. Motility was also dependent on KIF16B activity — movement was inhibited by dominant-negative KIF16B mutants or anti-KIF16B antibodies, and stimulated by recombinant KIF16B.

In the final part of this study, the authors used gain- and loss-of-function studies to show that KIF16B regulates the spatial distribution of early endosomes *in vivo* — KIF16B overexpression relocalized early endosomes to the cell periphery, whereas KIF16B mutants induced early endosome clustering in the perinuclear region. They further showed that the ablation of KIF16B disrupted the ability of early endosomes to recycle transferrin, and that KIF16B ablation accelerated the degradation of the epidermal growth factor receptor, whereas its overexpression prevented this

degradation. These data therefore indicate that “...KIF16B, by regulating the plus end motility of early endosomes, modulates the intracellular localization of early endosomes and the balance between receptor recycling and degradation”, which might have important implications for signalling.

Rachel Smallridge

References and links

ORIGINAL RESEARCH PAPER Hoepfner, S. *et al.* Modulation of receptor recycling and degradation by the endosomal kinesin KIF16B. *Cell* **121**, 437–450 (2005)

WEB SITE

Marino Zerial's laboratory: <http://www.mpi-cbg.de/research/groups/zerial/zerial.html>