

RESEARCH HIGHLIGHTS

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CELL BIOLOGY OF THE NEURON

Motoring activity

Filamentous actin (F-actin) is the main cytoskeletal component of the postsynaptic terminal and is important for maintaining synaptic integrity and function. Depolymerization of F-actin can disrupt the signalling of activated neurotransmitter receptors, but the molecular mechanism that is involved remains elusive. A new study shows that myosin VI might be the missing link between F-actin and neurotransmitter receptors, and could be crucial for synaptic vesicle endocytosis in neurons.

Myosins are motor proteins that move along polymerized actin filaments, thereby transporting macromolecules, vesicles and organelles. There are many myosin isoforms, and most of them move towards the fast-growing (plus) end of F-actin. However, Myosin VI is an exception. It moves towards the slow-growing (minus) end of F-actin, which is orientated towards the cell centre, and could be a mediator of synaptic vesicle endocytosis.

Reporting in the *Journal of Cell Biology*, Osterweil and colleagues show that myosin VI is expressed at high levels throughout the brain, including many layers of the cortex, hippocampus and cerebellum. In the neuron, myosin VI is present at synapses and is highly enriched at the postsynaptic density (PSD), where it colocalizes with postsynaptic density protein 95 (PSD-95). In myosin VI-deficient mice, there are fewer synapses in the hippocampus and the dendritic spines are shorter. These

differences are also observed in myosin VI-deficient hippocampal neurons in culture, which indicates that the effects on synaptic maturation might be due to the lack of myosin VI expression.

These observations prompted the authors to study the role of myosin VI in synaptic activity. Interestingly, myosin VI exists as a complex with AMPA (α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid)-type glutamate receptors and proteins that are involved in endocytosis, such as adaptor protein 2 and synapse-associated protein 97 (SNAP97). In myosin VI-deficient hippocampal neurons, a significant deficit was seen in AMPA receptor internalization after stimulation with either AMPA or insulin. The authors conclude that

myosin VI might regulate neurotransmission by mediating synaptic vesicle endocytosis.

The unique properties of myosin VI and its localization at the PSD have significant implications for synaptic function. It would be interesting to investigate whether other myosin proteins — those that move towards the fast-growing end of F-actin — might also be important in presynaptic exocytosis.

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References and links

ORIGINAL RESEARCH PAPER Osterweil, E. *et al.* A role for myosin VI in postsynaptic structure and glutamate receptor endocytosis. *J. Cell Biol.* **168**, 329–338 (2005)

FURTHER READING Buss, F. *et al.* Myosin VI: cellular functions and motor properties. *Annu. Rev. Cell Dev. Biol.* **20**, 649–676 (2004)

WEB SITE

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