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NEURON–GLIA INTERACTIONS

Kif1b motors mRNA

A new role for the kinesin motor protein Kif1b has been revealed. It seems that this multiple sclerosis-associated protein is essential for the delivery of specific mRNA molecules to the myelinating processes of oligodendrocytes, and for the correct outgrowth of myelinated axons.

Despite indications from cell culture studies that microtubules and associated motor molecules have roles in the transport of specific mRNA molecules — including the mRNA of myelin basic protein (Mbp) — to the distal processes of oligodendrocytes, the importance of this transport as well as its specific molecular requirements *in vivo* had remained unclear. Using positional cloning, the authors identified *kif1b* as the gene that is disrupted by a zebrafish mutation (st43) that impairs the localization of *mbp* mRNA in the CNS and the outgrowth of peripheral nerves.

The authors used antisense technology to block the activity of two mRNA isoforms encoded by *kif1b* (*kif1bα* and *kif1bβ*), confirming this finding. Targeting a *kif1bβ*-specific region, but not a *kif1bα*-specific region, disrupted *mbp* mRNA localization in oligodendrocytes in the CNS and peripheral nerve outgrowth, suggesting that it is the *kif1bβ* isoform that is important for transporting *mbp* mRNA. Axon outgrowth was also truncated in the mutants, and chimaera and transplantation analyses showed that *kif1b* is required autonomously in neurons for the normal development of some of the longest axons in the PNS and CNS.

Interestingly, transmission electron microscopy showed a significant reduction in the number of myelinated axons and in the amount of myelin surrounding axons in *kif1b*^{st43}-mutant zebrafish. These ultrastructural analyses further revealed that mutants produced ectopic myelin-like membranes in processes that did not ensheath axons and which were even observed to occasionally surround neuronal cell bodies. Production of these aberrant membranes was never observed in wild-type animals and coincided with the ectopic expression of myelin proteins (such as Mbp and 36k (also known as Flj13639)) in the cell bodies of the oligodendrocytes.

These findings suggest that Kif1b is involved in the restriction of specific mRNA molecules to appropriate regions of oligodendrocytes. This function seems to be key for the myelination of axons. Further work will be required to determine how localization of this mRNA contributes to these processes. The possibility that Kif1b-dependant disruption of oligodendrocytes or neurons could contribute to multiple sclerosis is an important step forward in the field.

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ORIGINAL RESEARCH PAPER Lyons, D. A. *et al.* Kif1b is essential for mRNA localization in oligodendrocytes and development of myelinated axons. *Nature Genet.* 7 Jun 2009 (doi:10.1038/ng.376)