When myosin heads go walking

Muscle myosin II has two identical "heads" that really act more like hands, gripping and displacing actin to generate the force that makes a muscle contract. On page 481, Kad et al. show that only one of the two heads actually generates motion, but the second maximizes the length of the displacement.

Previous work showed that each step of a wild-type double-headed myosin displaces actin twice as far, with twice as much force, as a single-headed construct. In the new work, Kad and colleagues generated heterodimeric myosin with one wild-type head and one mutant head that can bind to actin weakly but cannot displace it. Optical trapping experiments show that this motor takes the same size steps as the wild type, so although maximal actin displacement requires two myosin heads, only one needs to be fully functional.

There are at least two explanations for this result. The weak actin-binding activity of the mutant could help to align the wild-type head to the long axis of the actin filament, much as the front wheel of a bicycle keeps the power-generating rear wheel pointing forward. Alternatively, the mutant head could function more like a bicycle frame, stabilizing the wild-type head in a maximally active conformation. The authors are now generating mutations that completely abolish actin binding activity to distinguish between these possibilities.

More subtle mutations in muscle myosin can cause human genetic disorders such as familial hypertrophic cardiomyopathy. In this disease, decreased cardiac muscle strength is linked to a point mutation in one allele, which leads to the production of heterodimeric myosin complexes with one wild-type and one moderately defective head. The authors hope to use their system to determine why this heterodimer is less efficient than wild-type homodimers.

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Schwann cells don caps, touch nodes

In vertebrates, axons are covered with an insulating myelin sheath, punctuated by gaps called nodes of Ranvier where voltage-gated sodium channels cluster. The nodes are essential for propagating action potentials along the axon, but little is known about how they develop. Gatto et al. (page 489) imaged live cell cultures to watch Schwann cells myelinate explanted dorsal root ganglia and discovered a novel growth cone–like structure on the Schwann cells that appears to mediate node formation.

Previous studies have produced a controversy, since the development of nodes seems to require direct contact between Schwann cells and axons in some in vitro systems, but not in others. The authors used a new approach to transfect cultured Schwann cells with fluorescently labeled proteins and watch myelination using time-lapse videography. The Schwann cells initially migrate along axons and resemble aggressively motile fibroblasts, but as the culture matures they assume the bipolar shape characteristic of myelinating cells. Induction of myelination causes the Schwann cell microvillar components to reorganize into structures called caps at the cells’ tips.

Schwann cell caps are highly dynamic, and their protein composition and behavior are reminiscent of axonal growth cones. Cap formation requires activation of the Rho pathway, and uncoupling cap formation from myelination interferes with node formation. Efficient node development appears to require a direct interaction between the Schwann cell caps and axons. This coordination may ensure that axons are not completely myelinated.

The results bolster the idea that cell–cell contact is necessary for node formation, and the new methods provide an excellent approximation of in vivo myelination. Nonetheless, Gatto et al. concede that the issue will not be settled until node formation is characterized more fully. The authors are now transfecting cultured Schwann cells with dominant–negative forms of proteins found in the cap to see which components are required for node development.

Phosphorylated ERM proteins (red) localize to Schwann cell tips.