Actin-based organelle movements are driven by the related multifunctional myosin motors of class V in animals and fungi and class XI in plants. The versatility of these motors depends critically on their C-terminal globular tail domain that allows them to bind to a broad variety of cargo molecules. Regulation of this motor–cargo attachment is frequently employed to modulate organelle movement. While the overall structure of the cargo-binding globular tail appears to be conserved between myosin V and XI, it has become apparent that the motor–cargo interactions differ widely even within a single organism and involve protein complexes with different architecture and completely unrelated protein domains. At the same time, indirect evidence suggests that adaptor or receptor dimerization could facilitate efficient myosin capture. Comparison of myosin V and XI across the large evolutionary distance between animals and plants will likely reveal more fundamental insights into these important motors.

Key words: globular tail, myosin V, myosin XI, myosin–cargo interaction, organelle movement

Myosins comprise a large superfamily of motor proteins in eukaryotes, which convert chemical energy from ATP hydrolysis into physical force for movement along cytoskeletal actin filaments (1). Based on phylogenetic analysis of the conserved motor domain, myosins can be grouped into at least 24 classes (2–4). While the N-terminal motor domain of all myosins known so far carries out similar actin-based movements, it is their C-terminal tail domain that distinguishes them most strongly and confers a wide variety of functions to these motors. Among the most important of these functions is intracellular organelle transport, which is driven by class V myosins in animals and fungi and by class XI myosins in plants (5,6).

Class V and XI myosins share a number of features that invite comparisons across an evolutionary divide, which dates back to the earliest eukaryotes (3). In particular, the protein domain organization is identical in myosin V and XI (Figure 1). Both types of myosins consist of an N-terminal motor domain followed by six copies of calmodulin-binding IQ motifs and a C-terminal tail region, which contains a coiled-coil domain of variable length for dimerization and a globular domain for cargo binding (7,8). The identical domain organization is reflected in a very similar appearance of purified myosin V and XI proteins under the electron microscope (7,9). While the region with highest sequence similarity between these myosin classes is clearly the motor domain, there is also significant conservation in the so-called dilute domain (Pfam ID PF01843; named for the myosin V dilute mutant in mouse) within the globular tail, which is regarded as the signature element of myosin V and XI.

The salient features of this protein organization for the mechanical performance of these myosins are the relatively long neck and the dimerization that, when combined with a long dwell time on the actin filament, enable these myosins to take processive steps of approximately 35 nm. This allows the myosin to move on the same side of the actin cable, while pulling large cargo through the cytoplasm (10). Cargoes for myosin V in animal cells are motile organelles such as melanosomes, synaptic or endosomal vesicles (Table 1), while in plant cells, most membranous organelles have been shown to be propelled by myosin XI during cytoplasmic streaming (Table 1). In addition to membrane-bound organelles, messenger RNA (mRNA)- protein complexes are also ubiquitous cargoes that can be translocated by myosin V/XI in animals, fungi and plants (11–14). The long catalog of organelles and macromolecular complexes that are driven by myosin V/XI (Table 1) raises the questions of how a particular myosin can serve such a diverse set of cargoes and how differential movement of these cargoes is regulated. This is particularly evident in fungi and mammals that only possess two and three myosin V isoforms, respectively (4). Even in flowering plants whose genomes encode from 10 to 13 myosin XI isoforms (4), a number of isoforms have been shown to bind to several types of organelles (15–17). At the same time, a given organelle can recruit several isoforms of myosin XI (16,17). This functional redundancy of myosin XI explains the mild phenotypes observed for several myosin XI knockout mutants (15,18,19), in contrast to the severe phenotypes of myosin V mutants (20). This review will highlight recent progress in our understanding of myosin V/XI–cargo
reassociate in vivo and in vitro, and their tight association appears to be necessary for cargo binding in myosin V (22) but not in myosin XI (17). It is not clear whether this apparent discrepancy between myosin V and XI is caused by structural differences between two globular tails or whether it simply results from different experimental approaches. In particular, lack of cargo binding in myosin V (i.e. Myo2p) globular tail subdomains was deduced from the absence of dominant negative effects on organelle inheritance (22), whereas for myosin XI (i.e. MYA1 and others), cargo binding of yellow fluorescent protein-tagged globular tail subdomains was detected directly under the microscope (17). It is possible that some organelle binding of Myo2p globular tail subdomains may still occur without producing a dominant negative effect because the latter requires the saturation of all organelle-binding sites by nonfunctional myosins. It should also be noted that to date, no dominant negative effect of overexpressed tail constructs has been found for any myosin XI isoform (17,23). It is not known whether this reflects a functional difference between myosin V and XI or is an indirect result from the considerable functional redundancy of myosin XI isoforms in plants. Interestingly, the two subdomains of myosin V/XI globular tails each contain at least one organelle-binding site (17,21). The specific residues for vacuole binding and secretory vesicle binding in Myo2p are simultaneously exposed on the opposite surface of the globular tail (21), suggesting that the globular tail of myosin could be accessed by different types of organelles without major structural changes. However, there is mounting evidence for allosteric interactions between the two spatially distant binding sites (22,24,25), suggesting that intramolecular rearrangements of myosin globular tails can influence organelle binding (see Regulation of Myosin–Cargo Interaction).

**Myosin V–Organelle Interaction Models**

A number of interacting partners of myosin V globular tails on organelles have been identified (Table 1). No myosin XI-binding proteins have been described so far, but a recent study with the globular tail domain from the green alga Chara demonstrated that this myosin can bind directly to acidic phospholipids in the membrane (26). Here, we only focus on three recently deciphered myosin V–organelle interaction models and attempt to infer common features from these and other well-studied examples (13,27,28) (Figure 3).

**Myosin Va–melanophilin–Rab27 complex on melanosomes**

Myosin Va moves melanosomes along the actin network in the periphery of mammalian melanocytes (29). The assembly of the force-generating complex on melanosome occurs by the sequential recruitment of an adaptor protein, melanophilin and then myosin Va by Rab27a, a Rab GTPase on the melanosome surface (29,30). Melanophilin...
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#### Table 1: Functional repertoire of myosin V/Xi

<table>
<thead>
<tr>
<th>Motor</th>
<th>Organelle/particle</th>
<th>Receptor/adaptor</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myosin Va</td>
<td>Melanosomes</td>
<td>Rab27a/melanophilin</td>
<td>(29)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>Synaptic vesicles</td>
<td>Synaptobrevin</td>
<td>(44)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>Centrosome</td>
<td>Unknown</td>
<td>(57)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>Thyroxine-dependent vesicles</td>
<td>Unknown</td>
<td>(58)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>Chromaffin vesicles</td>
<td>Unknown</td>
<td>(59)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>MHC class II molecules</td>
<td>Unknown</td>
<td>(60)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>mRNA/protein complexes</td>
<td>TLS, Staufen&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(11, 12)</td>
</tr>
<tr>
<td>Myosin Va</td>
<td>Transferrin receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;11a/FIP2&lt;/sub&gt; or Hrs/BERP</td>
<td>(28, 38)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>Polymeric immunoglobulinA receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;11a/FIP2&lt;/sub&gt;</td>
<td>(28)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>M4 muscarinic acetylcholine receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;11a&lt;/sub&gt;</td>
<td>(61)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>Chemokine receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;11a/FIP2&lt;/sub&gt;</td>
<td>(62)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>Glutamate receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;11a&lt;/sub&gt;</td>
<td>(63)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>Aquaporin-2 recycling vesicles</td>
<td>Rab&lt;sub&gt;11a/FIP2&lt;/sub&gt;</td>
<td>(64)</td>
</tr>
<tr>
<td>Myosin Vb</td>
<td>Non-clathrin-dependent recycling vesicles</td>
<td>Rab&lt;sub&gt;8a&lt;/sub&gt;</td>
<td>(65)</td>
</tr>
<tr>
<td>Myosin Vc</td>
<td>Transferrin receptor recycling vesicles</td>
<td>Rab&lt;sub&gt;8b&lt;/sub&gt;/</td>
<td>(66)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Secretory vesicles</td>
<td>Vac8p/Vac17p</td>
<td>(24, 42)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Vacuoles</td>
<td>Unknown</td>
<td>(27)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Late Golgi</td>
<td>Unknown</td>
<td>(41)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Peroxisomes</td>
<td>Inp&lt;sub&gt;2p&lt;/sub&gt;/</td>
<td>(41)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Mitochondria</td>
<td>Mmr&lt;sub&gt;1p&lt;/sub&gt;</td>
<td>(43)</td>
</tr>
<tr>
<td>Myo2p</td>
<td>Mitotic spindle</td>
<td>Bim&lt;sub&gt;1p/Kar9p&lt;/sub&gt;</td>
<td>(68)</td>
</tr>
<tr>
<td>Myo4p</td>
<td>Cortical ER</td>
<td>She&lt;sub&gt;3p&lt;/sub&gt;/</td>
<td>(69)</td>
</tr>
<tr>
<td>Myo4p</td>
<td>mRNA/protein complexes</td>
<td>She&lt;sub&gt;2p/She3p&lt;/sub&gt;</td>
<td>(13)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>ER</td>
<td>Unknown</td>
<td>(70)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Chloroplasts</td>
<td>Unknown</td>
<td>(70)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Golgi stacks</td>
<td>Unknown</td>
<td>(71)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Peroxisomes</td>
<td>Unknown</td>
<td>(72)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Mitochondria</td>
<td>Unknown</td>
<td>(73)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Vacuoles</td>
<td>Unknown</td>
<td>(74)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>Pre-vacuolar/endosomal vesicles</td>
<td>Unknown</td>
<td>(75)</td>
</tr>
<tr>
<td>Myosin XI</td>
<td>mRNA/protein complexes</td>
<td>Unknown</td>
<td>(14)</td>
</tr>
</tbody>
</table>

ER, endoplasmic reticulum.

<sup>a</sup>Myosin Va, Vb and Vc are myosin V isoforms in mammals; Myo2p and Myo4p are myosin V isoforms in budding yeast (Saccharomyces cerevisiae); plant myosin XI isoforms responsible for specific organelle movement have not been identified.

<sup>b</sup>Myosin Va-mediated transport of mRNA/protein complexes could be divided into translocated in liposarcoma (TLS)-type and Staufen-type.

<sup>c</sup>An endash indicates that the corresponding component has not been identified.

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is composed of three domains, with the N-terminal part binding to activated (GTP-bound) Rab27a, the C-terminal part interacting with actin or EB1 (end-binding protein 1 on microtubules) and the central domain being responsible for myosin Va association (31). The myosin Va globular tail-binding site on melanophilin has been mapped to residues 176-201. This part of the protein is normally unstructured and therefore does not conform to any conventional protein–protein interaction domain (32). Interestingly, the in vivo interaction between myosin and melanophilin involves additional regions from both molecules where the residues 320-406 on melanophilin can bind to a melanocyte-specific exon F within the coiled-coil region of myosin Va tail (33, 34). This second interaction increases the affinity between these two proteins but by itself is insufficient for melanosome binding (35), suggesting that this dual binding is required for a more stable bond between motor and organelle during the movement through the viscous cytoplasm. Furthermore, a predicted coiled-coil region within the C-terminus of melanophilin was found to be absolutely required for myosin Va recruitment to melanosomes, although it did not show any interaction with myosin Va by itself (31).

**Myosin Vb-BERP-actinin-4-Hrs complex on early endosomes**

The globular tail of myosin V can interact with the C-terminal region of the ring-finger protein BERP (36) and its homolog NARF (37). The complex of myosin Vb and BERP was recently found to bind to early endosomes through actinin-4 and Hrs (38). The intact complex facilitates rapid return of receptors from the early endosome to the plasma membrane since disruption of any component of this complex slows down the recycling rate of transferrin receptors (38). The assembly of Hrs-actinin-4-BERP–myosin Vb complex on the early endosome is initiated by the attachment of Hrs to the endosome membrane, presumably through an interaction between its FYVE motif.
The membrane lipid phosphatidylinositol-3-phosphate (39). The two intervening adaptor proteins (actinin-4 and BERP) and myosin Vb are then assembled in a linear fashion. While the interaction of BERP with myosin Vb involves the C-terminal 124 residues of BERP which probably is part of a b-propeller structure (36), the N-terminal domain of BERP containing a coiled-coil region is responsible not only for self-dimerization but also for binding to actinin-4 (36,38).

**Myo2p–Inp2p complex on peroxisomes**

Peroxisome inheritance in budding yeast is dependent on the myosin-driven delivery of about half of these organelles into the emerging bud (40). Recently, the receptor for Myo2p on the peroxisome was discovered to be the integral membrane protein Inp2p, which contains a predicted transmembrane domain as well as two short coiled-coil regions (41). Interestingly, the short fragment between the two coiled-coil regions (residues 504–618) was able to interact directly with the globular tail of Myo2p in yeast two-hybrid assays, while the entire predicted cytoplasmic portion of Inp2p demonstrated enhanced affinity to Myo2p, suggesting that more than one region within Inp2p may be implicated in the interaction with Myo2p globular tail (41). It is not yet known whether Inp2p forms a dimer in the peroxisome membrane or whether the Myo2p–Inp2p complex involves any other proteins.

**Summary of myosin V–cargo interactions – common patterns or lack thereof**

The growing number of proteins known to attach the tail of myosin V to the organelles (Table 1) introduces the possibility of looking for commonalities in these interactions that...
could guide a broad search for other unknown myosin V/II anchors on organelles. On a superficial level, most myosin V–membrane interactions involve one or more adaptor proteins that act as a bridge between the myosin globular tail and the myosin receptor sitting on the membrane (28,29,38,42,43). However, in some cases, myosin V proteins do interact directly with membrane receptors, e.g. Myo2p–Inp2p on peroxisomes (41), MyoVa–synaptobrevin on synaptic vesicles (44) and MyoVb–Rab11a on recycling vesicles (28). In addition, the individual components in different myosin-anchoring complexes are usually not related to one another. Thus, it is not possible to draw any generalized conclusions regarding the architecture of myosin-anchoring complexes on organelles.

A more detailed analysis of the adaptor protein domains involved in myosin binding also does not reveal a simple common theme. In fact, most of these domains are not related to any characterized protein–protein interaction modules and also do not show any sequence similarity among each other that could suggest a common fold. The recent revelation that the myosin globular tail-binding region of melanophilin is actually unfolded (32) may make the search for such a common motif moot. Instead, it is tempting to speculate that all myosin V/II anchors would have intrinsically unstructured regions to bind to the globular tail of myosin. Several prediction algorithms indeed indicate short disordered regions in all known adaptors (unpublished data). These regions could form the basis of targeted experiments to test their ability to interact with their cognate myosin globular tails.

However, it is well established that the globular tails of myosin V/II contain at least two separate binding sites (17, 21). This implies that at least these two interactions have evolved independently of each other and could therefore involve very different proteins or mechanisms. The fact that very little of the globular tail surface was found conserved between myosin V and XI (17) furthermore suggests that the cargo interactions of these two types of myosins were not conserved and instead have evolved independently after the last common ancestor of animals and fungi on the one hand and plants on the other. If these speculations are correct, we are left with the conclusion that the globular tail of myosin V/II has an unusually high propensity of interacting with a wide variety of different proteins. Structural analysis of several myosin–adaptor complexes will likely be necessary to resolve this question.

While the direct interaction between myosin V and its various adaptors does not seem to follow a particular pattern, it is striking that all of these myosin adaptors/receptors contain coiled-coil domains, albeit usually outside the myosin-binding sites (13,28,29,38,41–44). For some of the adaptors/receptors like BERP and Rab11-FIP2, it is further known that their coiled-coil regions mediate dimerization (36,45). The common picture that seems to emerge from these observations is that the binding of myosin to its cargo may be facilitated if the adaptors/receptors on the organelle surface are dimerized. This would expose dual binding sites that thus could accommodate both globular tails of a myosin V/II dimer. In support of this contention, the coiled-coil domain of melanophilin was found indispensable for myosin Va binding (31). A possible reason for this postulated dimerization requirement could be the need to increase the affinity between the motor and its cargo. The interaction between melanophilin and myosin Va is relatively weak (Kd ≈ 0.5 μM) (32), and the combination of two of these binding sites could increase the strength with which the motor can pull its cargo. It will be interesting to see whether this postulate can be confirmed by direct experimental evidence in the future.

Regulation of Myosin–Cargo Interaction

Intracellular organelle and particle transport is tightly regulated, as the examples from organelle inheritance in budding yeast (27,41) and organelle positioning in animals (29) and plants (46) have demonstrated. On a general level, the regulation could target myosin directly, either by reversible inactivation of the motor activity or by irreversible degradation of myosin proteins (reviewed in 20). However, it is difficult to envision how this kind of interference could lead to specific movement patterns of different organelles using the same type of motor. Alternatively, the movement of different organelles could be regulated very specifically by modulating the association of myosin with different cargoes spatially and/or temporally. This form of regulation could be operating at several points in the system.

Alternatively spliced myosin transcripts

Alternative splicing is found in mammalian myosin Va that expresses different exons in the proximal tail domain (coiled-coil region) in different tissues. These exons serve as part of the cargo-binding sites and thus specify cargo docking. For example, the brain-expressed myosin Va isoform contains exon B that is necessary for binding to DLC2, a potential adaptor for post-synaptic vesicle association (47). A melanocyte-specific myosin Va isoform lacks exon B but contains exons D and F that binds to melanophilin for melanosome association (29), while a third isoform containing only exon D associates with vesicles near the Golgi in melanocytes (48). Myosin Vb may also use the alternatively spliced exon F for the Rab11a-mediated association with plasma membrane recycling vesicles (28). Intriguingly, some plant myosin XIs have also been found to be expressed with several different splice variants in the tail domain; however, the corresponding function has not yet been addressed (49).

Synthesis and turnover of specific lipids in organelle membranes

Some myosin-capturing complexes on the organelle surface appear to be dependent on specific membrane lipids.
For instance, the myosin Vb–BERP–actinin-4–Hrs complex on the early endosomes may attach to a phosphatidylinositol-3-phosphate-rich domain through the FYVE motif of Hrs (39), while the myosin Vb–Rab11a–FIP2 complex may associate with a phosphatidylinositol-3,4,5-trisphosphate domain on the membrane through the C2A motif of Rab11–FIP2 (50). Additionally, the Myo2p–Vac17p–Vac8p complex on the vacuole binds specifically to an ergosterol and sphingolipid-rich membrane domain after the palmitylation of Vac8p (51). In the case of Chara myosin XI, a direct interaction between the globular tail domain and negatively charged phospholipids (phosphatidylserine and phosphatidylinositol) could be detected (26). This may be a general property for all myosin XI but not for myosin V because the patch of basic residues that is believed to be responsible for lipid binding in Chara myosin (26) is highly conserved in flowering plants myosin XI but not in myosin V (unpublished data). Thus, transient accumulation of particular lipid components at a specific region of the membrane could promote the local recruitment of myosin V(XI), while the turnover of this lipid could likely cause the release of the myosin from the organelle, although direct evidence for this concept is still lacking.

**Turnover or conformational change of adaptors/receptors**

The interaction of myosin with an organelle can be regulated by spatiotemporal control of adaptor abundance through protein synthesis and degradation or by controlling the affinity of the adaptor protein for myosin through conformational changes. For example, the mRNA levels of myosin adaptors/receptors (e.g. Vac17p, Mmr1p and Inp2p) fluctuate during the cell cycle of budding yeast in a pattern that parallels the dynamics of their target organelles (52). Proteolytic degradation of the adaptor protein in the myosin-capturing complex may be one of the most effective mechanisms to deposit the moving organelle at the proper location. Two myosin V adaptors, Vac17p and melanophilin, were found to possess PEST sequences for rapid protein degradation and removal of the PEST sequence from them resulted in their stabilization and the subsequent mistargeting of the organelles (42,53). Another myosin V adaptor, Rab11–FIP2, which has no PEST sequence, was also highly susceptible to proteolysis even in the presence of protease inhibitors (54).

Conformational change of the adaptor protein is another possible way of regulating myosin–adaptor association and dissociation. For instance, Myo2p was found to interact much more efficiently with the isolated binding domain from Vac17p than with full-length Vac17p (24). Furthermore, a mutation outside the Myo2p-binding site of Vac17p can increase the affinity between Vac17p and Myo2p (24). Myosin Va was shown to interact more efficiently with Rab27a-associated melanophilin than with melanophilin alone (33). These findings suggest that regions outside the myosin-binding site of the adaptor proteins may negatively regulate the interaction between adaptor and myosin, probably by self-inhibition (24). It seems that the initial association of adaptor proteins with membrane receptors can somehow trigger a conformational change of the adaptor to favor its subsequent interaction with myosin. If this is the case, then it is also conceivable that other allosteric changes or phosphorylation could prevent myosin–adaptor binding, although no examples for this negative regulation are currently known.

**Intramolecular allostery of myosin**

In addition to regulation of the adaptor protein, there is growing evidence for an allosteric regulation of the cargo-binding sites of myosin. For example, removal of the secretory vesicle-binding site from the second subdomain of Myo2p globular tail increased the affinity between Vac17p and the first subdomain of Myo2p globular tail (24). This communication between the two globular tail subdomains was also suggested by the requirement for their tight association for full functionality (22). A likely explanation for this behavior is that initial binding to cargo molecules induces conformational changes in the local binding site of myosin globular tail that propagate to other binding site(s) and thereby reduces the ability of myosin to bind other cargo. In support of this, one point mutation outside of vacuole-binding site of Myo2p constitutively impairs its interaction with vacuoles and multiple other cargoes but does not affect secretory vesicle binding, thus mimicking the situation after binding to secretory vesicles (25). In the case of an unloaded globular tail, this communication may result in the dynamic alternation of binding states that gives different cargoes equal opportunities to attach (17).

It is not clear how the conformational changes are translated across the entire globular tail when myosin is loaded and how the dynamics of the globular tail are generated when myosin is unloaded, but recent results from myosin XI have suggested that the loop region between the two globular tail subdomains may be crucial. In particular, the two separate globular tail subdomains of several Arabidopsis myosin XIIs were able to bind to different organelles, but the reconstituted globular tail detected by bimolecular fluorescence complementation between co-overexpressed subdomains only localized to a single type of organelle (17). Apparently, the loss of the connecting loop between the two globular tail subdomains prevented the reconstituted globular tail from adopting all possible conformations and instead locked it in a rigid conformation that favored the binding of a single type of organelle. Interestingly, the deciphered structure of the Myo2p globular tail is based on crystals of the reassembled globular tail after proteolytic cleavage at the connecting loop because it was not possible to grow crystals for the full-length Myo2p globular tail (21). Further experiments will be necessary to test whether the predicted conformational dynamics of myosin V(XI) globular tails can be confirmed.

Finally, calcium-dependent phosphorylation at the globular tail of myosin Va was found to cause the detachment of
the motor from melanosomes (55) without weakening the interaction between myosin and melanophilin (33,34). This regulatory mechanism may be related to a larger scale allosteric regulation within myosin V where the motor domain of myosin folds back to compete with the organelle adaptor for binding to the globular tail (34,56). However, the biochemical mechanism underlying this regulation is still open to further investigation.

Perspectives

The past few years have seen major advances in our understanding of myosin–cargo interactions. Identification of several myosin-binding partners as well as elucidation of the structure of the myosin cargo-binding domain have revealed important molecular mechanisms underlying organelle movements. By comparing advances in different experimental systems, it is now possible to draw tentative conclusions regarding broadly applicable rules for motor–cargo interactions that may help direct future research. One of the most striking revelations is that the globular tail of myosin V/XI is able to interact with a wide range of adaptor/receptor proteins that do not seem to conform to a uniform template. Thus, it is possible that future elucidation of other myosin V/XI-organelle interactions will reveal novel types of myosin-binding mechanisms. However, it appears that dimerization of the adaptor protein may be a general requirement for cargo binding. Another conclusion emerging from the data is that several individual interactions between a myosin dimer and the receptor complex on the organelle appear to be necessary to ensure full function. This prediction should be tested rigorously both by biochemical determination of affinities and by biophysical force measurements with modified binding partners. Finally, a dynamic allosteric nature of the globular tail domain and its role in cargo selection have been suggested but still awaits further confirmation. While most progress in the past was limited to myosin V in animals and yeast, it has become apparent that myosin XI can provide important reference points against which the generality of findings from myosin V can be tested. It can be expected that the coming years will see a dramatic increase in our knowledge on plant myosin XI and that the resulting cross-fertilization between myosin V and XI research will bring new fundamental insights for myosin–cargo interactions.

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