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Moving Mitochondria: Establishing Distribution of an Essential Organelle

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Abstract

Mitochondria form a dynamic network responsible for energy production, calcium homeostasis and cell signaling. Appropriate distribution of the mitochondrial network contributes to organelle function and is essential for cell survival. Highly polarized cells, including neurons and budding yeast, are particularly sensitive to defects in mitochondrial movement and have emerged as model systems for studying mechanisms that regulate organelle distribution. Mitochondria in multicellular eukaryotes move along microtubule tracks. Actin, the primary cytoskeletal component used for transport in yeast, has more subtle functions in other organisms. Kinesin, dynein and myosin isoforms drive motor-based movement along cytoskeletal tracks. Milton and syntabulin have recently been identified as potential organelle-specific adaptor molecules for microtubule-based motors. Miro, a conserved GTPase, may function with Milton to regulate transport. In yeast, Mmr1p and Ypt11p, a Rab GTPase, are implicated in myosin V-based mitochondrial movement. These potential adaptors could regulate motor activity and therefore determine individual organelle movements. Anchoring of stationary mitochondria also contributes to organelle retention at specific sites in the cell. Together, movement and anchoring ultimately determine mitochondrial distribution throughout the cell.

Keywords

axonal transport; dynein; kinesin; mitochondria; myosin; organelle movement

Mitochondria are essential organelles that influence metabolism, cell growth and survival. In most cell types, mitochondria form a branched tubular network that is well distributed throughout the cell. Defects in mitochondrial distribution manifest potently in highly polarized cell types. For example, in neurons, mitochondria are likely required at the synapse to maintain local ATP levels (1,2). In budding yeast, transport of mitochondria into the emerging daughter cell (bud) is essential during cell division (3). In this review, we highlight recent work that illuminates the molecular mechanisms required to establish mitochondrial distribution.

Mitochondrial Movements *In vivo*

Time-lapse microscopy of fluorescently labeled organelles reveals that some mitochondria remain stationary, while others change positions within the cell (2–6). Mitochondria also fuse and divide, processes that are reviewed elsewhere (7–9). The mobile mitochondrial subpopulation can move in different directions (Figure 1). Directed long-range transport

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occurs both away from the nucleus (anterograde) as well as toward the center of the cell and nucleus (retrograde) in multicellular eukaryotes. In budding yeast, inheritance of mitochondria by the emerging bud requires anterograde movement (i.e. toward the bud tip), while retrograde movement (i.e. toward the base of the mother cell) promotes retention in the mother cell (10). Consequently, inheritance of mitochondria by buds is often used as an assay for mitochondrial transport in yeast.

Long neuronal processes are robust models for characterizing motility properties such as direction, duration and persistence of movement (Figure 1A). However, observations of run length, average velocity, pausing and persistence of direction vary, likely because of the use of different tissue and experimental conditions (4,11–16). Recent elegant studies in the Saxton laboratory (5) established an assay for tracking individual mitochondria in fly larval motor neurons. Intact nerve bundles are used immediately after dissection from a developing organism, allowing observation of *in vivo* mitochondrial movements without extended culturing (5), which changes mitochondrial behaviors. Although both motor and sensory neurons are present in this preparation, only motor neuron mitochondria are green fluorescent protein-labeled. Anterograde and retrograde movement can be distinguished because of the innate polarity of the motor neuron axons. Mitochondria in these nerves move, pause and often move again. Anterograde movement velocities averaged 0.26 μm/second, while retrograde velocities were slightly higher – approximately 0.45 μm/second. Notably, moving mitochondria that permanently change direction are never observed, suggesting that individual organelles are imprinted and somehow know in which direction they are moving. Directional changes are likely to occur *in vivo* in response to neuron stimulation and synapse formation.

In addition to individual organelle imprinting, the immediate cellular environment influences mitochondrial movement. Nitric oxide, local ADP concentration, neuronal age, synaptic activity and cellular zinc and calcium levels are all reported to affect mitochondrial distribution. For a more thorough treatment of how the cellular environment influences mitochondrial movement, we direct readers to Chang and Reynolds (17) and references therein.

Cytoskeletal Contributions to Mitochondrial Movement

Mitochondrial movement and distribution depend on both actin microfilaments and microtubules (Figure 1). In neurons, pollen tubes, filamentous fungi and fission yeast, mitochondrial movement is sensitive to disruption of microtubules (11,16,18–20). In addition, fission yeast mitochondria colocalize with microtubules in fluorescence microscopy studies (21), and three-dimensional tomo-graphic reconstructions reveal close associations between mitochondria and microtubules (22).

In budding yeast, cytoplasmic microtubules are sparse, and pharmacological (23) and genetic (24) disruption studies suggest that mitochondrial movement into buds does not rely on microtubules. In yeast, actin filaments cluster into cortical patches and bundle to form actin cables, the primary tracks for polarized growth (Figure 1B). Budding yeast mitochondria colocalize with and move along actin cables *in vivo* and display actin-based motor activity *in vitro* (3,25). These mitochondrial dynamics are halted by disruption of the actin cytoskeleton through pharmacological treatments (26), deletion of actin-binding proteins (27) or alteration of the myosin-binding site on the actin monomer (28,29). Thus, budding yeast primarily utilize the actin cytoskeleton to establish mitochondrial distribution throughout the cell.

Experiments that address actin-based transport in multicellular organisms are more difficult to interpret, partly because multicellular organisms from which neurons can be isolated are

not amenable to genetic disruption of cytoskeletal components. When microtubules are disturbed by drug treatment, mitochondrial flux in chick neurons shifts toward retrograde transport, suggesting that actin contributes to retrograde movement (11). In addition, pollen tube mitochondria display fast, irregular actin-based movement (30), and actin-dependent anchoring of mitochondria occurs at active neuronal growth cones (15,31). Finally, both actin and microtubules are important for directed mitochondrial movements in algal cells (6). These studies suggest that actin plays a significant role in establishing mitochondrial distribution in a variety of cell types. However, because pharmacological approaches have been used to disrupt the cytoskeleton in these studies, it is difficult to distinguish between primary and secondary effects on mitochondrial movement. Identification and analysis of the molecules that bridge interactions between mitochondria and the actin or microtubule cytoskeleton will help validate the conclusions drawn from these drug studies.

Motor-Based Mitochondrial Movement

Mitochondria primarily move by the action of molecular motors along cytoskeletal elements (Figure 2 and Table 1). Like other organelles, mitochondria associate with specific motor isoforms through organelle-specific adaptors, and their movement is sensitive to disruption of these motors and adaptor proteins. In multicellular eukaryotes, mitochondria utilize microtubule motors, including the plus-end-directed kinesins and minus-end-directed dyneins. In neurons, the minus ends of microtubules are generally oriented toward the microtubule-organizing center in the cell body. Thus, plus-end-directed movement represents anterograde movement down the axon to the peripheral regions of the cell, while minus-end-directed movement promotes retrograde movement toward the cell body (Figure 1). Kinesins are typical motor proteins in that they convert the energy of ATP hydrolysis into work; in this case, the movement of organelles. Specific kinesin isoforms, including a kinesin-1 (Kif1B) and a kinesin-3 (Kif5B) in mammals (32,33), a 105-kDa kinesin-like protein in plants (34) and a kinesin-3 (Nkin2) in filamentous fungi (35), associate with mitochondria. Alteration of kinesin function impairs anterograde movement, as predicted for a plus-end-directed motor. Surprisingly, in multiple systems, aberrant kinesin function leads to disruption of retrograde movement as well (5,35), suggesting that dynein function is also impaired. The possibility that bidirectional transport of organelles is controlled by coordinated regulation of opposing motors is discussed in detail elsewhere (5,36).

The minus-end-directed dynein motor is essential for returning organelles, including mitochondria, along microtubule tracks to the cell body. In HeLa cells, disruption of dynein function causes defects in mitochondrial movement (37). In flies, dynein hypomorphs bypass early pleiotropic defects and allow analysis of neurons of the third instar larvae. Mitochondria in these neurons exhibit decreased retrograde movement because of longer pausing and shorter run duration (5).

In budding yeast, where mitochondrial movement is actin based, the myosin V ortholog, Myo2p, is implicated in mitochondrial transport and inheritance. Myo2p mutations alter inheritance of multiple organelle types, including mitochondria (38). Moreover, mutation of residues in the Myo2p tail domain has been used to map binding surfaces for individual cargo adaptors (39). One mutant *myo2* allele specifically impairs mitochondrial inheritance. It also prevents Myo2p association with Mmr1p, a peripheral mitochondrial outer membrane protein required for efficient inheritance (40), suggesting that the effect of this *myo2* mutation on yeast mitochondrial movement is direct. At least one study argues against Myo2p motor-mediated mitochondrial movement in yeast (37). This argument is based on the observation that a mutant Myo2p isoform, an IQ repeat deletion, which decreases the motor's step size, does not decrease the rate of mitochondrial movement. However, the rate of secretory vesicle movement by the *myo2* IQ deletion mutant [(~0.3 μm/second), (41)] is

remarkably similar to that of mitochondria in wild-type cells [(~0.175 μm/second), (38)]. Because mitochondria normally move at about the minimal rate of cargo movement determined for the IQ deletion mutant, this mutant cannot be used to rule out Myo2p as a mitochondrial motor in yeast. If, as suggested by others (40,42), Myo2p does move mitochondria in yeast, this study (38) establishes that the rate of movement is not limited by motor step size.

Even though the cytoskeleton is utilized in different ways in diverse organisms, motor-based movement of mitochondria is a reoccurring theme. Because these motors often bind and transport multiple cargoes, organelle-specific adaptor proteins are essential to establish specificity and allow motor-cargo associations to occur (Figure 2).

Mitochondrial Adaptors for Motors

Mitochondrial motor adaptors for kinesins in higher organisms have been identified in genetic and biochemical screens. These screens often reveal components important for anterograde mitochondrial transport, in part because synaptic mitochondria contribute to neurotrans-mission. Similar screens have identified Myo2p adaptors for yeast mitochondria (40,42).

Milton, a kinesin-associated protein containing predicted coiled-coils with no identifiable yeast ortholog, is required for synaptic accumulation of mitochondria in flies (43,44). Milton also associates with the cytoplasmic face of the outer mitochondrial membrane. Milton mutants are lethal, although genetic strategies that generate homozygosity only in the eye reveal specific defects in mitochondrial transport down axons (43). Immunoprecipitation assays demonstrate that Milton associates with kinesin heavy chain in the absence of a light chain, raising the possibility that Milton functions as an organelle-specific light chain (45–47). Two additional polarized mitochondrial movement events are defective in the absence of Milton – mitochondrial elongation during spermatogenesis (48) and nurse cell dumping to generate the Balbiani body during fly oocyte development, a process that reflects microtubule minus-end-directed movement (49). Moreover, fly oocytes generated from follicles expressing certain *milton* alleles contain abnormally high numbers of mitochondria, suggesting that Milton could regulate either motor activity or selection of mitochondria for movement (49).

Miro, a mitochondrial Rho GTPase that is conserved from yeast to humans, associates with Milton (46,50), suggesting that Miro is present in a motor adaptor complex. Fly *miro* mutants phenocopy *milt* mutants (51), consistent with the idea that these two proteins function together. In both flies and mammalian fibroblasts, Miro and Milton are found in a complex (46,50), suggesting that Miro, Milton and kinesin function together to facilitate anterograde mitochondrial transport. Miro proteins are tail-anchored in the outer mitochondrial membrane and contain two switch-family GTPases that flank calcium-binding motifs (52,53). Studies in tissue culture cells have established that overexpression of Miro causes accumulation of mitochondria at the microtubule-organizing center (52). Among the potential kinesin adaptor complex members identified to date, Miro is unique in that there is an obvious budding yeast homolog, Gem1p, which is required for maintenance of normal mitochondrial morphology. Yeast mutants lacking Miro function contain globular mitochondria that are not inherited efficiently (53).

Several observations suggest that Miro and Milton mutant and overexpression phenotypes are because of direct disturbances of mitochondrial movement. How mutation of Miro or Milton affects the dynamics of mitochondrial transport is unclear. The accumulation of mitochondria in the neuronal cell body observed in fly mutants could be because of either defects in anterograde (i.e. kinesin-based) movement or upregulation of retrograde

movement. Given the apparent links between kinesin- and dynein-based movements in fly neurons, one attractive possibility is that Miro and Milton somehow determine which motor is active. Recent genetic studies reveal that yeast Miro functions independently of the known Myo2p adaptors, Mmr1p and Ypt11p, to promote efficient mitochondrial inheritance [(discussed below, (54)]. Because Miro is important for mitochondrial distribution in organisms that primarily utilize different cytoskeletal components for this process, Miro may have a conserved function with divergent outputs.

In budding yeast, Mmr1p and Ypt11p may function as Myo2p adaptors. Mmr1p has no obvious homologs in other organisms, although two fungi, *Ashbya* and *Candida*, have apparent orthologs (unpublished observations). As expected for an organelle-specific adaptor, Mmr1p localizes to mitochondria and is polarized such that more is present on bud mitochondria (i.e. organelles that have been moving) than on mother cell mitochondria (40). Mmr1p transcript levels increase at the S–G2 cell cycle transition (55), coincident with new bud growth and therefore at a time when polarized mitochondrial movement should be enhanced. The other myosin-associated protein that promotes mitochondrial inheritance is Ypt11p (42). Ypt11p is one of the several Rab GTPases that interact with a motor directly or indirectly to facilitate organelle transport (56). Ypt11p localizes to the endoplasmic reticulum (ER) and has been reported to increase the quantity of peripheral ER present in the bud (54,57), raising the possibility that ER and mitochondrial inheritance are coupled. However, at least one mutant with defects in ER inheritance does not exhibit defects in mitochondrial inheritance (58). A more recent study indicates that mitochondrial inheritance is not a prerequisite for ER inheritance (54), arguing against a permanent physical link between the two organelles. A role for Ypt11p in immobilizing mitochondria at the bud tip has also been proposed (38). It is possible that Ypt11p facilitates mitochondrial inheritance indirectly by transporting ER into the bud and thereby providing a docking site for mitochondria. Determining whether links between organelles exert direct effects on transport will be challenging, in part because ER and mitochondrial calcium dynamics are coupled (59), and calcium levels can affect mitochondrial distribution (see below).

Several other proteins whose roles in organelle distribution are not well characterized may also function as mitochondrial motor adaptors or regulators (Table 1). Syntabulin, which partially localizes as a peripheral outer mitochondrial membrane protein, is found in a complex with the kinesin Kif5B and promotes anterograde movement of mitochondria as well as other organelles (60). The relationship between Milton/Miro and syntabulin has not yet been addressed. Kinesin-binding protein (KBP), appears to facilitate anterograde mitochondrial transport through association with Kif1Bα (61). Finally, APLIP1, a kinesin-associated protein, does not affect anterograde mitochondrial movement but instead promotes dynein-dependent retrograde mitochondrial movement (62).

In all cases, these motor adaptor proteins may regulate motor recruitment or activity. Additional proteins likely function in these complexes because the biochemical approaches and genetic screens in model organisms are not yet saturated (43,51). It will be important to test whether the proposed adaptors bind directly to the tails of the relevant motor proteins, as predicted. In addition, it has not been shown in any case that the putative adapter proteins are required for motor association with mitochondria.

Evidence for Non-Motor-Based Mitochondrial Movement

In yeast, where mitochondrial movement depends primarily on actin, Pon and colleagues reported mitochondrial association of several subunits of the actin nucleator Arp2/3. This led to the proposal that mitochondria in yeast move by induced polymerization of actin, similar to the actin comet tail-based movement of the intracellular pathogen *Listeria* (10,63).

Perturbing actin dynamics by stabilizing actin cables led to decreases in mitochondrial motility, consistent with the idea that actin polymerization is required for mitochondrial movement in yeast (63). For several reasons, it is unlikely that this is the sole mechanism of actin-based mitochondrial transport in yeast. First, mitochondria appear to move along existing actin cables *in vivo* (25). Second, phalloidin-stabilized actin filaments slide along immobilized mitochondria *in vitro* at rates similar to that of mitochondrial movement *in vivo*, despite the fact that this drug blocks Arp2/3-driven actin dynamics (3). Third, all components of the outer membrane `mitochore complex', which are proposed to facilitate mitochondrial-actin associations (10), are now known to be essential for import of outer membrane β-barrel proteins (64,65). Thus, mitochore components could simply be required to import other proteins required for mitochondrial movement. Finally, mitochondrial inheritance depends partly on the Myo2p motor and its associated proteins, Mmr1p and Ypt11p [see above, (40,42)], consistent with the idea that at least some actin-based mitochondrial transport is Myo2p driven.

Mitochondrial movement induced by polymerization of cytoskeletal elements may be a common strategy used by fungi. Mitochondrial movements in fission yeast correlate with microtubule dynamics (21). When microtubule dynamics are closely monitored with time-lapse microscopy, microtubule extension is mirrored by lengthening or moving mitochondria. During microtubule shortening, mitochondria also shorten. Mitochondria are never observed moving along an existing microtubule, and mitochondria that are not associated with microtubules remain stationary (21).

Other Processes Affecting Mitochondrial Distribution

Additional factors can also affect mitochondrial distribution in cells. The shape and connectivity of mitochondria are likely to impinge upon the ability of relevant motors to attach to and/or move the organelle, although it remains unclear in many systems whether altered morphology is the result of defects in movement or vice versa. However, in the absence of both yeast Myo2p adaptor proteins, Mmr1p and Ypt11p, most mitochondria are tubular, although inheritance is severely compromised. This observation suggests that efficient mitochondrial movement is not required to generate mitochondrial tubules (54). In mammalian cells, overexpression of outer membrane proteins leads to collapse of mitochondria around the microtubule-organizing center. Although this phenotype has been used to suggest that the protein being overexpressed plays a direct role in mitochondrial movement, it is equally plausible that this perinuclear mitochondrial clustering results because protein overexpression indirectly alters mitochondrial shape or connectivity.

Actively anchoring mitochondria at sites where they are needed helps to maintain proper organelle distribution. In budding yeast, mitochondria are immobilized at the bud tip and at the base of the mother cell (10). Organelle anchoring is also a cytoskeleton-based process; actin-dependent anchoring occurs at neuronal growth cones (31). Stationary organelles are evenly distributed in neuronal processes, implying that individual mitochondria are anchored at sites within the axon. Interestingly, anchored mitochondria do not always remain stationary while docked with cytoskeletal elements. Time-lapse analysis of `non-moving' mitochondria in distal portions of axons reveals transport of those docked mitochondria at rates up to an average of 43 μm/h (0.012 μm/second), about 20-fold slower than the kinesin-based movement. These docked mitochondria maintain their relative positions, suggesting that motor proteins are not involved. Instead, the authors of the study propose that tension within the axon contributes to low-velocity axonal transport of docked mitochondria (66).

Regulation of Mitochondrial Movement

Mitochondria move in precise ways along cytoskeletal tracks, often displaying a preference for movement in a particular direction. During certain biological responses, mitochondria and other organelles move to establish a new population distribution, thus demonstrating that active regulation of these movements is occurring. For example, mitochondria move into and become stationary at active growth cones of stimulated cultured neurons. When the growth cone activity is lower, mitochondria switch to retrograde movement (11). In developing fly larval neurons, mitochondria display an anterograde bias during a period of development in which the larvae increase in size dramatically. Thus, as the axons elongate, mitochondria are actively recruited into them (5). Another dramatic example of regulated mitochondrial movement occurs in the developing fly oocyte. During nurse cell cytoplasmic dumping, mitochondria move in a minus-end-directed fashion from the nurse cells into the oocyte. Mutation of *milton* shifts the balance such that either too few or too many mitochondria are transferred into the oocyte (49).

Our knowledge of the mechanisms regulating mitochondrial movement remains piecemeal. It has been suggested that in the neuronal cell body, mitochondrial fission generates healthy mitochondria of the correct size that are selectively moved down axons toward the synapses. Dysfunctional mitochondria are moved toward the cell body to undergo repair by fusion with healthy mitochondria or degradation by mitophagy (1,2,17,67). Evidence for this model comes from studies in which neuronal mitochondrial populations are labeled with potential-dependent fluorescent dyes (4,68). Mitochondria moving in an anterograde fashion toward the axon terminal have higher membrane potential than those moving retrograde, suggesting that old or damaged mitochondria are returned to the cell body. An alternative interpretation of these data is that retrograde-directed mitochondria actively downregulate respiration. If sick mitochondria are actively returned to the cell body for repair, mitochondrial fusion, a process that requires apposition of two adjacent mitochondria, must be coupled with transport. Moreover, organelle size is likely to affect the ability of mitochondria to move efficiently. Thus, co-ordination between mitochondrial transport, fusion and division likely exists, even though molecular evidence for such pathways is lacking.

Mitochondrial distribution may also be regulated by intracellular calcium levels. Increased cytosolic calcium in cardiac myocytes reduces mitochondrial motility (69). However, in a different study, changes in mitochondrial movement are not detected when calcium transients are induced in cortical neurons (14). Underlying differences in the way mitochondrial distribution is regulated in these two cell types may be responsible for these disparate observations.

Molecular regulation of mitochondrial movement is likely achieved by altering motor recruitment, motor activity and/or organelle anchoring. Motor recruitment is unlikely to be the only mechanism of regulation because mitochondria isolated from neurons retain the ability to move bidirectionally, suggesting that both anterograde and retrograde motors can remain bound simultaneously (70). Achieving the desired balance between opposing motor activity may be regulated by factors that bind both motors, as suggested previously (36). In support of this idea, the dynactin complex can be found associated with dynein but has strong affects on kinesin-based transport. When dynactin activity is inhibited, mitochondria move faster in both directions, and anterograde-directed mitochondria pause less often. Thus, inhibition of dynactin increases overall mitochondrial motility (5). Furthermore, the adaptor protein APLIP1 is associated with kinesin but in the case of mitochondria promotes only retrograde (i.e. dynein driven) and not anterograde movements. By contrast, disruption of APLIP1 activity reduces both anterograde and retrograde synaptic vesicle movement (62). Thus, APLIP1 may co-ordinate activities of anterograde and retrograde motors.

It seems likely that motor adapter proteins regulate mitochondrial movement and, in multicellular organisms, may even determine which opposing motor is active. In yeast, where only one motor is proposed to mediate mitochondrial movement, overexpression of the Myo2p adaptors, Mmr1p and Ypt11p, causes gain of function phenotypes, wherein mitochondria accumulate in the bud (40,42). Thus, transcriptional and posttranslational control of adaptor protein abundance can affect motility, perhaps by promoting motor activity or recruitment. Moreover, the Mmr1p and Ypt11p adaptors preferentially associate with bud organelles, although whether this localization is caused by or is a consequence of movement remains unclear.

Concluding Remarks

The model emerging from multiple systems is that overall mitochondrial distribution is established by motor-based movement along cytoskeletal elements as well as anchoring at sites where their function is required. Clues from pharmacological and descriptive studies suggest that the processes required for establishing mitochondrial distribution are exquisitely regulated. Co-ordination between motors that normally operate in opposite directions and differential recruitment of adaptor proteins are likely contributors for regulation of mitochondrial movement. Mitochondrial distribution during development, while essential at least for the viability of neurons and other polarized cells, remains a remarkably undeveloped field. In the future, it will be important to understand when and where during development organisms are sensitive to mitochondrial distribution defects and why these defects tend to primarily affect neurons.

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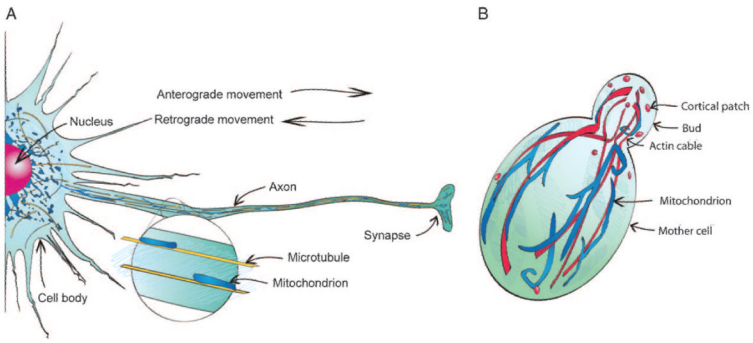

Figure 1. Mitochondria move directionally in polarized cells

A) In neurons, anterograde transport carries mitochondria (blue) away from the cell body and nucleus (pink) along microtubules (yellow) toward the synapse. Retrograde movement returns mitochondria from distal sites within the axon to the cell body. B) In budding yeast, mitochondria (blue) are moved anterograde along actin cables (red) into the daughter cell. Inheritance of mitochondria by the bud is required for cell viability. Retrograde movement toward the pole of the mother cell may contribute to retention of mitochondria in the mother cell.

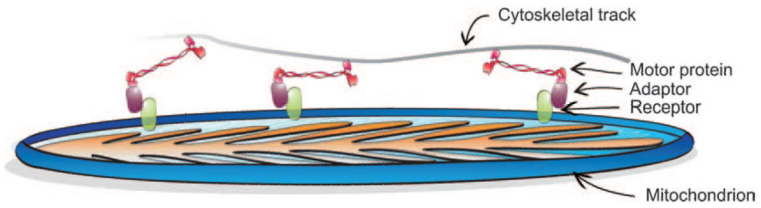

Figure 2. Molecular motor adaptor complexes mediate mitochondrial movement

Motor proteins (red) facilitate mitochondrial (blue) movement along cytoskeletal tracks (gray) such as actin filaments or microtubules. Organelle-specific interactions are established by adaptor proteins (purple) that complex with the motor. Adaptors likely require integral outer mitochondrial membrane proteins to serve as receptors (green), allowing localization of the motor adaptor complex to the organelle.

Table 1

Mitochondrial motor adaptor complex components

Potential adaptor	Possible receptor[a]	Associated motor[a]	Cytoskeletal track	Organism(s)	References
Milton[b]	Miro	Kinesin-1	Microtubules	Flies and mammals	(44,46,47,50)
Syntabulin	Unknown	Kif5B (a kinesin)	Microtubules	Mammals	(60)
APLIP1	Unknown	Kinesin-1	Microtubules	Flies	(62)
KBP	Unknown	Kif1Bα (a kinesin)	Microtubules	Mammals	(61)
Mmr1p	Unknown	Myo2p (a myosin V)	Actin cables	Budding yeast	(40)

[a]Directness of interactions between adaptor, receptor and motor protein has not been tested.

[b]Homologs named GRIF1 or OIP106 in mammals.