Structural and biomechanical basis of mitochondrial movement in eukaryotic cells

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Abstract: Mitochondria serve as energy-producing organelles in eukaryotic cells. In addition to providing the energy supply for cells, the mitochondria are also involved in other processes, such as proliferation, differentiation, information transfer, and apoptosis, and play an important role in regulation of cell growth and the cell cycle. In order to achieve these functions, the mitochondria need to move to the corresponding location. Therefore, mitochondrial movement has a crucial role in normal physiologic activity, and any mitochondrial movement disorder will cause irreparable damage to the organism. For example, recent studies have shown that abnormal movement of the mitochondria is likely to be the reason for Charcot–Marie–Tooth disease, amyotrophic lateral sclerosis, Alzheimer’s disease, Huntington’s disease, Parkinson’s disease, and schizophrenia. So, in the cell, especially in the particular polarized cell, the appropriate distribution of mitochondria is crucial to the function and survival of the cell. Mitochondrial movement is mainly associated with the cytoskeleton and related proteins. However, those components play different roles according to cell type. In this paper, we summarize the structural basis of mitochondrial movement, including microtubules, actin filaments, motor proteins, and adaptin, and review studies of the biomechanical mechanisms of mitochondrial movement in different types of cells.

Keywords: mitochondrial movement, microtubules, actin filaments, motor proteins, adaptin

Introduction

The movement of mitochondria, which serves to distribute mitochondrial functions in a dynamic and nonuniform fashion, has attracted particular interest in recent years following the discovery of functional connections between microtubules, motor proteins, and the mitochondria, and their influence in neurodegenerative disease.1 Mitochondrial movements are able to be directed by the various components of the cytoskeleton, including actin filaments, microtubules, intermediate filaments, and other proteins.2 Many studies have shown that both actin filaments and microtubules play a part in mitochondrial movement, although the contribution of each cytoskeletal element changes considerably depending on specific organisms and cells. In most animal cells and some algae, mitochondrial movements are associated with microtubules and motor proteins.3–6 Studies in insect cells7 and neuronal axons8 have revealed that actin filaments can also serve as tracks for mitochondrial transport.

In higher plants, it has been shown that the mitochondria are closely associated with actin filaments, and mitochondrial movement is mainly dependent on intact actin filaments.9–11 In addition, in microorganisms, particularly in yeast, mitochondrial movement depends on actin cables instead of microtubules. Actin cables are composed
of bundles of short actin filaments, and these undergo continuous turnover in yeast. Qualitatively similar actin dynamics have also been reported in plant cells, where single actin filaments are more dynamic than actin cables. Motor proteins and adaptor proteins are essential in the antegrade or retrograde movement of mitochondria. Here we review our current understanding of the regulatory mechanisms that govern mitochondrial movement to supply some theoretical foundation for treatment of neurodegenerative diseases and to offer an explanation for the mechanisms controlling organellar inheritance. In most studies of mitochondrial movement in animals and microorganisms, budding yeast and nerve cells are the research subjects, respectively, and studies on mitochondrial movement of plants mainly concentrate on pollen cells and root hair cells. As the representatives of mitochondrial movement patterns in microorganisms, animals, and plants, respectively, these materials are typical for most eukaryotic cells’ basic mechanisms for mitochondrial movement. In this paper, the structural and biomechanical basis of mitochondrial movements of budding yeast, neuronal axons, and higher plants are individually summarized.

**Budding yeast**

Budding yeast, *Saccharomyces cerevisiae*, is an anaerobe. If there is sufficient oxygen, facultative anaerobes get energy from mitochondrial aerobic respiration; if not, they can obtain energy by fermentation or anaerobic respiration. *S. cerevisiae* can tolerate mitochondrial mutations that would be lethal in other organisms. Therefore, budding yeast has been used widely to study the mechanisms of organellar inheritance. As a result, much of what we know regarding mitochondrial movement has come from using budding yeast as a model system. In budding yeast, cytoplasm microtubules are sparse, mitochondrial movement is not dependent on microtubules, and forces for movement are generated by Arp2/3 complex-stimulated actin polymerization. Mitochondria would stop moving if they were treated by drugs that destroy the actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers. Photographic images of actin cytoskeleton, remove actin-binding protein, or change the myosin binding sites on actin monomers.

Mitochondrial transport from mother to daughter buds during asymmetric cell division in budding yeast ensures that the healthiest organelles are inherited by the new generation. This inheritance is critical and is mediated by type V myosin motor Myo2, which transports mitochondrial membranes along actin cables into the bud. Two additional proteins, Ypt11 and Mmr1, interact with the cargo-binding domain on the Myo2 tail and participate in mitochondrial inheritance. A recent study using live cell microscopy revealed that Num1 is required for attachment of mitochondria to the cell cortex and retention in mother cells, and that expression of chimeric plasma membrane tethers rescued mitochondrial fission defects in Δnum1 and Δmdm36 mutants.

The pattern of mitochondrial distribution is closely linked to the cell cycle, and is demonstrated by time-lapse imaging of mitochondria in the cell cycle of budding yeast. Mitochondria are equally distributed between the daughter and mother cell prior to cell–cell separation. With improved spatial and temporal resolution of 4D imaging (time lapse imaging combined with 3D reconstruction), it was discovered that mitochondria undergo motility events that are more rapid and distributive than previously thought. It was also found that mitochondria undergo rapid, bi-directional movement in budding yeast. Budding is an important process in yeast cells, which produces more cells. Before budding, the mitochondria are arranged along the mother-daughter axis and converge to the future budding site. Mitochondrial movement into the bud occurs as soon as the bud emerges, while mitochondria in the mother cell also show retrograde movement to ensure a balanced distribution of mitochondria in the mother cell and daughter cells. Therefore, this balance is related to three states of mitochondrial movement, ie, antegrade movement, retrograde movement, and reservations at the ends.

**Retrograde movement of mitochondria in budding yeast**

Observation reveals that actin cables in yeast are in a state of constant movement, which is elongated in yeast budding. Using Abp140p-GFP to study actin cable dynamics, it was found that elongating actin cables move in a retrograde direction from the bud towards the mother cell at a rate of 0.3 µm per second. Actin cable elongation occurs by insertion of newly polymerized proteins into the end of the actin cable at the actin cable assembly site. The main proteins involved are F-actin, resident actin cable proteins, tropomyosin proteins (Tpm1/2p), and actin bundling proteins (Abp140p and Sac6p). These insertions happen during elongation of the actin cables (see Figure 1). Thus, the velocity of retrograde mitochondrial movement is similar to that of the associated retrograde actin cable flow. Mitochondria move with the retrograde flow of actin cables. Actin cable elongation occurs by insertion of newly polymerized F-actin and resident actin cable proteins, ie, tropomyosin proteins (Tpm1/2p) and actin bundling proteins (Abp140p and Sac6p), into the end of the actin cable at the actin cable assembly site. This insertion results in movement...
of the mitochondria along the elongating actin cable in the retrograde direction, ie, towards the mother cell.

**Antegrade mitochondrial movement**

During the budding process, mitochondria move in an antegrade manner to reach the daughter cells. This process requires not only the guidance of actin cables but also several mediator proteins. According to the model of antegrade mitochondrial movement, the mitochore complex (Mmm1p, Mdm10p, and Mdm12p) mediates cyclic binding of mitochondria to actin cables. At the same time, the Arp2/3 complex, which is recruited by the PUF protein, Jsn1p, stimulates actin polymerization for generation of antegrade force. This complex works at the interface between the organelle and its cytoskeletal track. The forces produced by this process are enough to overcome the opposing force of retrograde actin cable flow, and allow for mitochondrial movement toward the bud end (see Figure 2).

When mitochondria associated with the mitochore have not recruited the Arp2/3 complex with the help of Jsn1p, they have to move back to the mother end with retrograde flow of the actin cable. However, if they have recruited the Arp2/3 complex, which can supply energy by promoting actin polymerization, the mitochondria can move in an antegrade fashion to the daughter end.

The mitochore complex participates in the connection between mitochondria and actins by recruiting Arp2/3. A defect in Mmm1p, Mdm10p, or Mdm12p will result in genetic deletion of mitochondria, variation in mitochondrial morphology, and defective B-barrel proteins in the outer membrane of the mitochondria. If there is a defect in Mdm10p, the mitochondria form a ball-like structure, which hinders the movement of mitochondria toward the bud cell. However, mutation of Mdm10p would not affect nuclear inheritance or disturb cell activity and function.

The Arp2/3 complex produces the power needed for antegrade movement of the mitochondria. Photographic images of living cells demonstrate that recruitment and activation of Arp2/3 is needed for antegrade mitochondrial movement. The Arp2/3 complex can join with F-actin, which is associated with formation of the actin network on the mitochondrial surface. The mitochondrion combines with the actin cable with the help of the mitochore. Jsn1p recruits the Arp2/3 complex to provide power for antegrade movement. The mitochondrion can then be transported to the bud instead of back to the mother cell as happens with retrograde flow. Peripheral mitochondrial proteins, such as Jsn1p, can connect the purified Arp2/3 subunit, and are necessary for antegrade mitochondrial movement. Therefore, Jsn1p is likely to be the receptor protein for the Arp2/3 complex.

**Mitochondrial retention at the tips**

During division of budding yeast cells, the mitochondria first need to move from the mother cell to the bud; however, mitochondrial retention in the mother cell prevents all of the mitochondria being transported to the bud tips.
Theoretically, retrograde flow of actin cables would bring the mitochondria back to the mother cells. Thus, it is necessary for mitochondria to be anchored at the tips.

Some studies support a role for type V myosin and its binding partner, Rab-like G-protein (Ypt11p), in anchorage of mitochondria in the bud tips. There are two forms of type V myosin in budding yeast, ie, Myo2p and Myo4p. Type V myosin can act as a motor that directs active transport of cargo along actin cables in yeast. In the mutant form, by changing Myo2 or Ypt11, there are some defects of mitochondrial retention in the bud tips. However, deletion of Ypt11 or Myo2 has no effect on antegrade mitochondrial movement or colocalization of the mitochondria with actin cables. Thus, it is possible that Myo2p and Ypt11p drive transport of retention factors to the site of the bud tips (see Figure 3). Antegrade movement is powered by Myo2 bound to the mitochondria via an as yet unknown receptor protein (X). The black square in Figure 3 denotes hypothetical mitochondrial cortex anchors.

Motor-dependent mechanism of mitochondrial movement

There is another possible pathway for mitochondrial movement, whereby the mitochondria rely on connection to actin cables by a type of motor instead of the mitochondria. For example, Myo2p could participate in the transportation of some organelles, and peripherins, such as Mmr1p and Ypt11p, can combine with Myo2p. Their overexpression can drive the mitochondria to move toward the bud tips. There is some evidence that Myo2p can move along the actin cables as a mitochondrial motor protein, with Mmr1p or Ypt11p acting as its adaptor proteins.

Figure 3 Model of mitochondrial retention.

Nerve cells

Neurons are particularly susceptible to disturbance of mitochondrial motility and distribution due to their highly extended structures and specialized function. Regulation of mitochondrial motility plays a vital role in neuronal health and death. Experimental evidence points to the importance of mitochondrial movement defects as contributors to major neurodegenerative diseases, such as Parkinson’s disease. Recent research shows that two Parkinson’s disease proteins, Ser/Thr kinase (PINK1) and ubiquitin ligase (Parkin), participate in this regulation by arresting mitochondrial movement. This study provides important clues as to the mechanisms of Parkinson’s disease, and strengthens the relationship between mitochondrial movement and brain damage. As more mitochondrial movement-related protein is analyzed, we will understand these mechanisms better and be able to provide useful information for the treatment of neurodegenerative disease.

The neuron is a highly differentiated cell consisting of three distinct functional domains, ie, a cell body, a long axon, and a dendrite. The distribution of mitochondria in nerve cells is aligned with the level of cellular energy and the demand of metabolism. The extreme length of the axonal processes requires that aerobic adenosine triphosphate (ATP) production and Ca\(^{2+}\) homeostasis are nonuniformly organized in the cytoplasm. As a result, mitochondrial movement along axons is essential for neuronal homeostasis. Furthermore, mitochondrial starts, stops, and redistributions can be regulated by physiologic events and intracellular signals. Mitochondria undergo rapid but intermittent transport in both the antegrade and retrograde directions in axons.

Mitochondria with a high potential have been shown to move toward and accumulate in the growth cone, while mitochondria with a low potential are transported towards the cell body, which increases the possibility of antegrade movement of mitochondria to the sites of action of neurons, and retrograde movement to the cell body for decomposition and recycling.

Role of cytoskeleton in mitochondrial movement

The cytoskeleton not only provides structural support for neurons but also supplies the conditions for transport and retention of organelles. Eukaryotic cells contain three main kinds of cytoskeletal filaments, ie, actin filaments, intermediate filaments, and microtubules. Actin filaments and microtubules have both plus and minus ends and are polarized, whereas the intermediate filaments do not have plus and minus ends.
Microtubules are formed by polymerization of a dimer of two globular proteins, ie, alpha and beta tubulin. Many proteins bind to microtubules, including motor proteins such as kinesin, dynein, and katanin, as well as other proteins important for regulating microtubule dynamics. The directions of microtubule distribution are not the same in all parts of the neuron. Microtubules always run longitudinally and act as rails for transport in both axons and dendrites. In the axon, microtubules are polarized and arranged in parallel, with the positive terminal pointing towards the synapse. However, in dendrites, microtubules are arranged in parallel and antiparallel directions. This structure and arrangement of microtubules is very important for the combination between motor proteins and mitochondrial movement. Generally, kinesin mediates mitochondrial movement along the axon in an anterograde direction, and dynein would be involved in the relevant retrograde processing.

Actin filaments are helical polymers composed of actin monomers, the two ends of which grow at different rates. As the thinnest filaments of the cytoskeleton, actin filaments are composed of linear polymers of actin subunits, and generate force by elongation at one end of the filament coupled with shrinkage at the other, causing net movement of the intervening strand. In nerve cells, actin filaments distribute to the parts with fewer microtubules (such as the presynaptic terminal and dendritic spines), and are very important for the mitochondria during short distance transportation. In neurons, actin fibers can also form a reticulate structure which directly influences myosin activity. There are some mitochondrial movement-related motor proteins along the actin filaments. Indirect evidence suggests that the myosin I, II, V, VI family could be the motor proteins enabling the mitochondria to move along the actin filament, although the specific mechanism involved has not yet been identified.

The intermediate filaments, averaging 10 nm in diameter, are more stable (strongly bound) than actin filaments, and are heterogeneous constituents of the cytoskeleton. Like actin filaments, they function in the maintenance of cell shape by bearing tension. (Microtubules, by contrast, resist compression. It may be useful to think of micro- and intermediate filaments as cables, and of microtubules as cellular support beams.) These filaments provide potential binding sites for the mitochondria and other proteins. There is some evidence for an interaction between the intermediate filaments and mitochondria. For example, it has been proved that vimentin intermediate filaments join the mitochondrial binding with the N-end and inhibit mitochondrial movement. Being an intermediate filament protein, desmin can affect distribution of mitochondria in the striated muscle cell, but inhibits mitochondrial recruitment of kinesin in the cardiac muscle cell.

**Motor proteins involved in mitochondrial movement**

Motor proteins can transport membranous organelles and macromolecules fundamental for cellular function along microtubules, and the transporting roles of these proteins have been studied extensively in axons and dendrites. Recent findings have revealed that the specific interaction between cargoes and motors is mediated in many cases via adaptor proteins. Cargoes could be sorted into precise destinations by these motors, such as axons or dendrites. Long distance transport of mitochondria toward the axon is along microtubules, and depends on motor proteins powered by ATP from mitochondrial ATP synthase. Kinesin mediates anterograde mitochondrial movement along both the axon and dendrite, and dynein would be involved in the retrograde transportation.

Six members of the kinesin family (ie, kinesin-1, 2, 3, 4, 13, and 14) have been implicated in axonal organelle transport, with two of them particularly involved in mitochondrial movement. The widely expressed “conventional” kinesins of the kinesin-1 family are associated with the mitochondria as well as other axonal organelles, such as vesicles containing ApoER2, JNK scaffolding proteins, and amyloid precursor protein. The founding member of this superfamily, kinesin-1, was isolated as a heterotetrameric fast axonal organelle transport motor consisting of two identical motor subunits (KFCs; kinesin heavy chains) and two "light chains" (kinesin light chain) via microtubule affinity purification from neuronal cell extracts. The heavy chains of kinesin-1, also known as KIF5, can function as a motor and form homodimers or heterodimers among themselves through the coiled-coil region in the stalk domains. Each KIF5 heavy chain contains an N-terminal motor domain that binds directly to microtubules, whereas its C-terminal domain mediates the association of KIF5 with kinesin light chains or direct interaction with intracellular cargo vesicles. Therefore, attachment of kinesin-1 can transport directly through the specific cargo-binding region at the C-terminal domain, or indirectly via the light chains, indicating two distinct forms of motor-cargo coupling (see Figure 4). Biochemical and genetic evidence demonstrates that recruitment of kinesin heavy chain KIF5 and mitochondrial movement are independent of kinesin light chains, which inhibit KIF5 binding to Milton.
The kinesin heavy chain includes the heads, tails, and necks that connect the heads to the tails. The head is the signature of kinesin and its amino acid sequence is well conserved among various kinesins. Each head has two separate binding sites, ie, one for the microtubule and the other for ATP. ATP binding and hydrolysis as well as ADP release change the conformation of the microtubule-binding domains and the orientation of the neck linker with respect to the head, resulting in the motion of kinesin.

Dyneins can be divided into two groups, ie, cytoplasmic dyneins and axonemal dyneins, which are also called ciliary or flagellar dyneins. Cytoplasmic dynein, which has a molecular mass of about 1.5 mDa, contains approximately 12 polypeptide subunits: two identical “heavy chains,” 520 kDa in mass, which contain ATPase activity and are thus responsible for generating movement along the microtubule; two 74 kDa intermediate chains which are believed to anchor the dynein to its cargo; and four 53–59 kDa intermediate chains and several light chains which are less well understood (see Figure 5) at this moment. Axonemal dynein causes sliding of microtubules in the axonemes of cilia and flagella, and is found only in cells that have those structures. Axonemal dynein comes in multiple forms that contain either one, two, or three nonidentical heavy chains, depending on the organism and location in the cilium. Each heavy chain has a globular motor domain with a doughnut-shaped structure believed to resemble that of other proteins, a coiled coil “stalk” that binds to the microtubule, and an extended tail that attaches to a neighboring microtubule of the same axoneme. Cytoplasmic dynein is essential for axonal transport of mitochondria in neurons. In Drosophila, cytoplasmic dynein is the primary motor for mediating mitochondrial retrograde transport. Studies of single dynein-dynactin motor complexes revealed that the complex could move bidirectionally, although the overall bias in direction is towards the microtubule minus ends.

The two giant heads of dynein are made up of part of a heavy chain. The rest of the heavy chain and the intermediate light chain form the stem to bind heavy chain head and light chain tail. The light chain can associate with the cargo. Unlike kinesin, the heavy chain head does not connect with the microtubule directly; instead, it moves on the microtubule through a segment of stalk.

Neurons have multiple compartments that are devoid of microtubules where transport of organelles is still seen to occur. These areas are rich in other cytoskeletal polymers, such as actin filaments. Transported organelles have been shown to associate with multiple motor proteins including myosins, which suggests that nonmicrotubule-based transport may be a myosin-driven process. While the microtubule-based motor proteins, kinesin and dynein, quickly transport cargoes and organelles through lengthy axons, myosins drive short-distance trafficking along actin filaments at presynaptic terminals and growth cones. Most myosin molecules are composed of a head, neck, and tail domain. The head domain binds filamentous actin and uses ATP hydrolysis...
to generate force and “walk” along the filament towards the barbed (+) end (with the exception of myosin VI, which moves towards the pointed (−) end). The neck domain acts as a linker and as a lever arm for transducing force generated by the catalytic motor domain. The neck domain can also serve as a binding site for myosin light chains, which are distinct proteins forming part of a macromolecular complex and generally having regulatory functions. The tail domain generally mediates interaction with cargo molecules and/or other myosin subunits. In some cases, the tail domain may play a role in regulating motor activity. Although myosins I, II, V, and VI were reported to be involved in the transport of organelles and vesicles in neurons, with the exception of myosin V, little is known about the location and function of other unconventional myosins and their roles in axonal mitochondrial transport. Myosin V is a good candidate for driving actin-based mitochondrial movement, although it remains to be determined whether myosin V is attached to the axonal mitochondria and how much or to what degree synapse-directed transport of mitochondria is required for myosin V. A study reveals that a novel unconventional myosin, Myo19, is a mitochondria-associated motor that may play a role in either the transport or tethering of this organelle.

Adaptors essential for mitochondrial movement

Regarding neuronal mitochondria, the specificity of anterograde transport is achieved by direct interaction between KIF5s and the mitochondrial membrane or by indirect coupling via an adaptor that binds KIF5s and the mitochondria through lipid-binding or transmembrane domains. Several mitochondrial motor-adaptor complexes and receptors have been identified.

Syntabulin was first identified in our laboratory and serves as another KIF5 motor adaptor that links KIF5 to syntaxin-containing vesicles. Syntabulin plays a critical role in mitochondrial trafficking in neurons. It is a peripheral membrane-associated protein that targets to mitochondria through its carboxyl-terminal tail. Syntabulin is a peripheral membrane-associated protein, relatively enriched in the mitochondrial fraction, and associated with mitochondria via its sequence. Immunocytochemical and time-lapse imaging studies in live neurons demonstrated that syntabulin colocalized and comigrated with mitochondria within axonal processes. Syntabulin serves as a KIF5 adaptor and mediates anterograde transport of mitochondria along neuronal processes.

Milton, a mitochondrial motor adaptor, provides a link between kinesin motors and mitochondria through an interaction with Miro, a calcium-sensing member of the Rho-GTPase family present in the outer mitochondrial membrane. The N-terminal of Milton is responsible for recruiting kinesin heavy chain to the mitochondria. Mutation of Milton will lead to loss of mitochondria in the synaptic terminal and axon. Milton links with kinesin heavy chain, Milton mediates Milton and the mitochondrion, while PINK1 localizes on the mitochondrial outer membrane by interacting with Milton and Syntabulin (see Figure 6). Both Milton and syntabulin are important adaptins between the mitochondria and motor proteins, but work via different mechanisms, including the association with kinesin, the combination with mitochondria, the reaction to calcium signaling, and regulation of protein phosphorylation.

Higher plant cells

Strategic control of mitochondrial movements and cellular distribution is essential for correct plant cell function and survival. Despite being a vital process, mitochondrial movement in plant cells is a poorly documented phenomenon. Picea wilsonii pollen tubes and Arabidopsis root hairs have been used to investigate the role of actin filaments and microtubules in mitochondrial movement. Mitochondria can move rapidly along actin filaments over long distances in higher plants. In angiosperms, pollen tubes show a strong cytoplasmic streaming of organelles, which move along actin filaments, as shown by earlier studies with cytoskeleton inhibitors. Although less well supported, it is evident that microtubules also participate in regulation of mitochondrial movement.
mitochondrial movement in higher plants. In nonvascular plants, such as the alga Chara, both microtubules and actin filaments are involved in the transport and immobilization of mitochondria. Mitochondria from tobacco pollen tubes move slowly along microtubules but more rapidly along actin filaments, and these mitochondria are associated with a specific microtubule-dependent motor. A 170 kDa myosin is bound to mitochondria and Golgi vesicles, while a 90 kDa kinesin is associated with mitochondria but not with vesicles. Research also suggests that kinesin and myosin cooperate for the positioning of mitochondria in the pollen tube. The research on Arabidopsis root hairs showed that: myosin and actin turnover cooperates in driving linear mitochondrial movements; the transition of mitochondria from immobility to movement involves de novo actin polymerization and depolymerization; and microtubule dynamics have profound effects on mitochondrial velocity, trajectory, and positioning by directing the arrangement of actin filaments.

Thus, these data can be combined to generate a testable model which will expand our insights into the molecular control of mitochondrial movement in plant cells.

Conclusion
Cells precisely regulate mitochondrial movement in order to balance energy needs and avoid cell death. Mitochondrial movement and retention is a very important and complex process, involving many molecular motors and adaptor proteins.

In budding yeast cells, there are three states of movement of the mitochondria, i.e., retrograde movement, antegrade movement, and reservations at the ends. In retrograde movement, the mitochondria move with the retrograde flow of actin cables via the forces generated by actin polymerization. In antegrade movement, mitochondria move toward the bud end via the forces produced by Arp2/3 complex-stimulated actin polymerization. Arp2/3 is recruited by Jsm1p, and the mitochondria complex participates in cyclic binding of the mitochondria to actin cables. In mitochondrial retention, Ypt1p supports a role in anchorage of mitochondria to the bud tips. Myo2 is also essential in mitochondrial retention.

In nerve cells, mitochondria move mostly along microtubules. Actin filaments are very important for mitochondrial movement during short-distance transportation. The intermediate filaments can supply potential binding sites for the mitochondria and other proteins. A lot of motor proteins also participate in mitochondrial movement. Kinesin mediates antegrade mitochondrial movement along the axon, and dynein would be involved in the retrograde movement. Adaptors such as syntabulin and Milton also play a critical role in mitochondrial movement in neurons.

In plant cells, there is some evidence to suggest that mitochondrial movement at low speeds in pollen tubes is driven by myosin, while high-speed and variable-speed movements are powered by both actin filament dynamics and myosin, with kinesin and myosin cooperating in positioning of the mitochondria.

These discoveries continue to advance our field, but more importantly, provide new directions that expand our conceptualization of a more global cellular role for this fascinating organelle. The future of mitochondrial research is bright, and the contributions made in this area will provide a touchstone for future work.

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Mitochondrial movement in eukaryotic cells


