Minireview

Membrane traffic motors

Viki Allan*

School of Biological Sciences, University of Manchester, 2.205 Stopford Building, Oxford Road, Manchester M13 9PT, UK

Received 25 April 1995

Abstract There is a wealth of data suggesting that microtubules and associated motor proteins play important roles in orchestrating membrane traffic within higher eukaryotes, with myosins and actin filaments fulfilling similar functions in organisms such as fungi, algae and plants. In addition, evidence is accumulating that both cytoskeletal systems can co-operate within one cell. Recent studies have highlighted how individual motor proteins can act at multiple steps in the membrane-traffic pathways, and in contrast, how more than one motor type may be involved in each transport step and in generating organelle morphology.

Key words: Kinesin; Cytoplasmic dynein; Myosin; Endocytosis; Exocytosis

1. Introduction

It is ten years since the discovery of the microtubule motor protein kinesin. A great deal is now known about its biochemical and mechanochemical properties, and there has been an explosion in the number of related kinesin-like proteins (KLPs) identified by various means [1]. Kinesin and most KLPs move towards the rapidly-growing plus ends of microtubules (with some notable exceptions) and, since most microtubules are nucleated by the microtubule-organising centre (MTOC) which is located next to the nucleus, plus-end-directed movement will carry components from the cell centre to the periphery.

Cytoplasmic dynein, discovered shortly after kinesin [2], is a minus-end-directed motor related to ciliary and flagellar dyneins. So far, in contrast to the kinesin family, no 'cytoplasmic dynein-like' proteins have been identified.

The third group of players in membrane motility are the myosins, of which there are at least 10 groups [3], only a few of which are likely to be motors for membrane traffic.

Many studies have investigated the role of the cytoskeleton in exocytosis and endocytosis in non-neuronal cells. The consensus is that while the total amount of a protein arriving at its destination may not be affected, for instance, by depolymerising microtubules, the rate at which it is delivered is significantly reduced. These results, coupled with the fact that many transport steps can be reconstituted in cell-free extracts, show that membrane targeting and fusion events do not require the cytoskeleton, and that diffusion alone can bring membrane structures together. Further work has shown, however, that the cytoskeleton acts to organise membrane organelles within the cell, and to direct traffic between them: features which were not investigated in previous cruder experiments. This review will consider the evidence for more subtle roles of the microtubule and actin-based motor proteins in membrane traffic.

2. The exocytic pathway: organelle structure and position

2.1. Endoplasmic reticulum

Each membranous organelle in the cell has its own characteristic structure and distribution that is actively and dynamically maintained. The endoplasmic reticulum (ER) in higher eukaryotes, for example, is a network of membrane tubules and lamellae that extends by a microtubule-dependent mechanism [4] from the nuclear membrane out to the cell periphery (Fig. 1a). The movement of ER membrane tubules towards the cell periphery is driven by kinesin, since anti-sense oligonucleotide suppression of kinesin heavy chain expression in astrocytes results in collapse of the ER network back to the perinuclear area [5]. Recently, an integral ER membrane protein, kinectin, has been identified as a receptor for kinesin in the ER [6–9]. A monoclonal antibody to kinectin inhibits the plus-end-directed movement of microsomes in chick embryo fibroblast extracts in vitro [7], and it will be interesting to see whether ER network formation in these extracts [10] is also inhibited.

Kinesin is not the only motor capable of driving ER network formation, however. Cell-free extracts from *Xenopus laevis* eggs support active ER network formation in vitro, but surprisingly, the ER tubule movement is powered by cytoplasmic dynein [11,12]. In addition, the ER in sea urchin eggs and early embryos is clustered in the cell centre even though it possesses kinesin, and this distribution is not affected by microinjection of an antibody which inhibits kinesin motor activity [13]. This difference in direction of ER movement between eggs and fibroblasts may be due to egg-specific requirements, such as the need for pro-nuclear migration, or may simply result from such a huge cell needing to organise its ER differently to that of a small cell. It will be interesting to establish whether the direction of ER movement is developmentally regulated.

It is also worth noting that minus-end-directed ER movement could have gone unobserved in the studies of living fibroblasts. Indeed, the fact that an antibody to kinectin also inhibited minus-end-directed movement of microsomes in vitro by 50% [7] suggests that kinesin and cytoplasmic dynein, or perhaps a minus-end-directed KLP, may have a close functional relationship in the ER.

ER movement in plants and algae occurs along actin filaments rather than microtubules (e.g. [14,15]), although the particular myosins involved have not yet been identified conclusively. It is possible that the split between microtubule- and actin-based ER movement depends on whether cells undergo

*Corresponding author. Tel. (44) (161) 275-5646.
Fax: (44) (161) 275-5082.

SSDI 0014-5793(95)00615-X

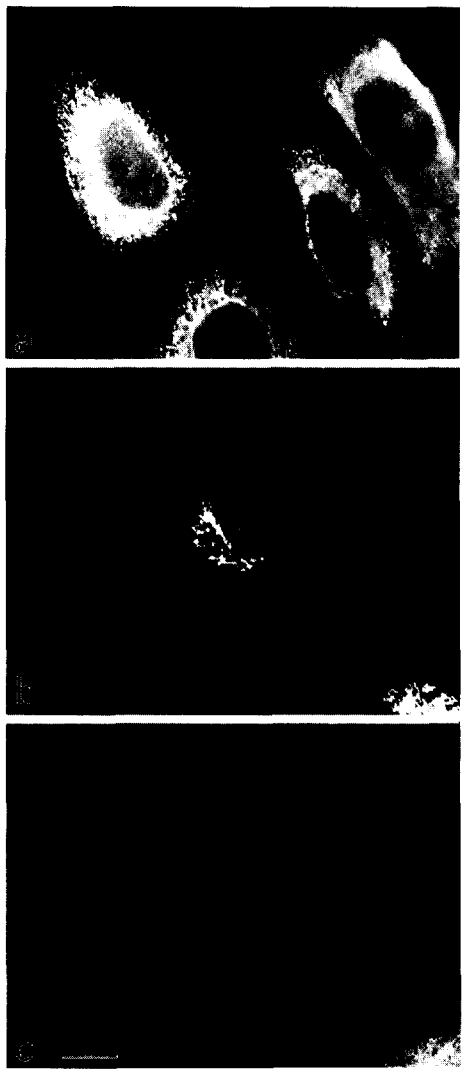

Fig. 1. Distribution of ER (a), the Golgi apparatus (b) and microtubules (c). *Xenopus* XTC cells were fixed and labelled with antibodies which recognise a) protein disulfide isomerase (1D3; kindly provided by Dr S. Fuller, EMBL); or double-labelled with anti-β-COP (E5A3) and a polyclonal anti-tubulin (both kindly provided by Dr T. Kreis, University of Geneva). Scale bar = 10 μm.

cytoplasmic streaming. However, the recent observation that moving ER tubules in squid axonal extracts can switch from microtubules to actin filaments [16] suggests that we should re-investigate the role of both motile systems in all species. Clearly, ER motility is more complicated than first thought, and it is quite possible that the selection and regulation of particular motor proteins plays a part in the formation of ER subdomains.

2.2. The Golgi apparatus

In contrast to the ER, the Golgi apparatus in most higher eukaryotic cells is clustered around the MTOC in the perinuclear region (Fig. 1b and c). When microtubules are depolymerised, the Golgi apparatus becomes fragmented and scattered throughout the cytoplasm. Elements of the scattered Golgi apparatus have been visualised moving back towards the cell centre on newly-polymerised microtubules [17], presumably using a minus-end-directed motor such as cytoplasmic dynein. Data from an assay for Golgi reclustering in semi-intact cells also support the involvement of cytoplasmic dynein [18].

The Golgi apparatus, whilst maintaining the same overall position in the cell, is also continually moving. Motile *trans*-Golgi tubules in astrocytes have been observed extending from one region of the Golgi apparatus to another [19], generating the rather extended Golgi apparatus found in these cells. Strikingly, the inhibition of kinesin function using an anti-sense approach results in a much more compact perinuclear Golgi apparatus [5], which suggests that Golgi apparatus morphology is the result of both cytoplasmic dynein and kinesin activities.

3. The exocytic pathway: traffic between organelles

3.1. ER-Golgi traffic

It is clear from the distribution of the ER and Golgi apparatus (Fig. 1) that a vesicle budding from a peripheral site in the ER must travel a considerable distance towards the minus ends of microtubules before reaching the Golgi apparatus, and would require a plus-end-directed motor for the return pathway (Fig. 2). This latter transport step is visualised dramatically when cells are treated with the drug Brefeldin A (BFA), which results in the formation of Golgi-derived tubules that then move along microtubules towards their plus ends and fuse with the ER [20]. Microinjection of antibodies which inhibit kinesin prevented the formation of these BFA-induced tubules [21]. Inhibiting kinesin function using antibodies or anti-sense suppression did not prevent the redistribution of Golgi enzymes to the ER, however [5,21], presumably because targeting and fusion events are unaffected. Interestingly, kinesin was found on all membranes cycling between ER and Golgi, and at steady state, was predominantly localised to peripheral structures containing material just released from the ER. As these elements would be expected to move towards the minus ends to reach

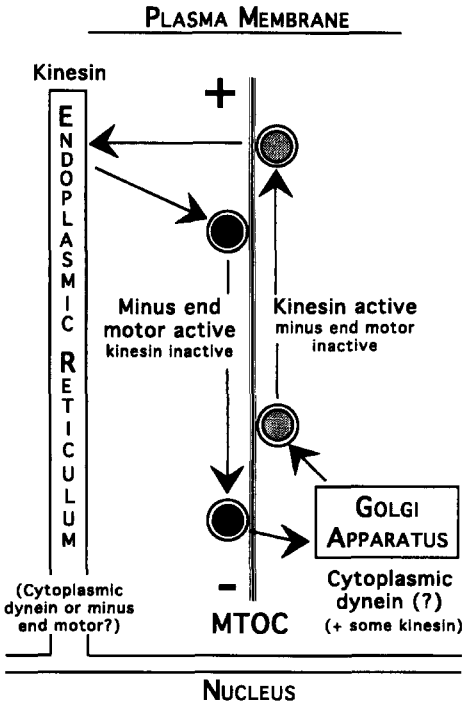

Fig. 2. Microtubule-based movement in the early exocytic pathway.

Table 1
Motors and membrane traffic in non-neuronal cells

Organelle/transport step	Motor	Approach	Cell/species	Ref.
ER morphology	KHC	anti-sense	Rat astrocytes	[5]
	CD	in vitro; inh	*Xenopus* egg extracts	[12]
Golgi morphology/position	KHC	anti-sense	Rat astrocytes	[5]
	CD	semi-intact; mAb, inh	CHOs (hamster)	[18]
Golgi – ER transport	KHC	MIJ of mAb	NRKs (rat)	[21]
Golgi – PM transport				
Lytic granules	KHC	in vitro; mAb, inh	Mouse T-cells + CEF cytosol	[45]
Transport vesicles	KHC	MIJ of mAb	Sea Urchin eggs + 3T3s (mouse)	[56]
	Myo2p + Smy1p	genetics; IF	*S. cerevisiae*	[28,29]
TGN-endosomes	KHC	anti-sense + BFA	Rat astrocytes	[5]
Endosome/lysosome morphology	KHC	MIJ of mAb, pAb	Mouse macrophages	[36]
plus position	KHC	anti-sense	Rat astrocytes	[5]
	CD	IF localisation	NRKs (rat)	[35]
Early–Late endosome transport	KHC/CD	in vitro; mAb, inh	MDCKs (dog)	[41]
	CD	in vitro; mAb, inh	BHKs (hamster)	[40]
	CD	in vitro; inh	Rat hepatocytes	[44]
Contractile vacuole function	Myosin IC	syringe-loaded mAb	*Acanthamoeba*	[57]

Abbreviations: BFA, Brefeldin A; BHK, baby hamster kidney; CD, cytoplasmic dynein; CEF, chick embryo fibroblast; CHO, Chinese hamster ovary; IF, immunofluorescence; inh, inhibitors; KHC, kinesin heavy chain; MDCK, Madin Darby canine kidney; MIJ, microinjection; mAb, pAb, mono- and poly-clonal antibodies; NRK, normal rat kidney; TGN, *trans*-Golgi network.

the Golgi apparatus, this implies that the activity of membrane-bound kinesin must be regulated, as must the minus-end-directed motor (probably cytoplasmic dynein).

These results pose a question: how can one motor protein drive multiple transport steps? How does kinesin know if it is in the ER, a vesicle en route for the Golgi, or a returning vesicle? Are there regulatory components associated with each class of membrane structure that define the direction to be moved by determining which motors are active? The question becomes even more complicated when one considers the full range of membranes that kinesin (and cytoplasmic dynein) are thought to move (see Table 1). It is possible that different isoforms of these complex proteins perform the various functions, and indeed, the anti-kinesin antibody that inhibits Golgi-ER movement does recognise a specific isoform [21]. Perhaps closely-related KLPs are involved in some steps.

Another interesting question is whether the motors themselves are actively sorted into particular membrane domains. This may well be the case, since kinesin is concentrated in regions of the intermediate compartment [21], and domains containing active motors and concentrated secretory products have been identified in ER and Golgi-derived membrane networks in vitro [22]. These results also raise the possibility that information about the contents of a membrane structure could be passed to the motor protein and its regulators on the cytoplasmic membrane face [22], perhaps via kinectin and associated lumenal proteins [7]. If we are to understand fully how motor proteins participate in membrane traffic it is clear that the trafficking of the motors and their receptors must be investigated.

3.2. The Golgi apparatus and beyond

As might be expected for a protein originally isolated from squid giant axons as a putative membrane motor, many studies have shown that kinesin is involved in fast axonal transport [1]. Similarly, there is evidence that kinesin transports both regulated and constitutive secretory vesicles (see Table 1 and [1]), and also BFA-induced TGN-derived tubules [5]. What has become clear is that there are a number of KLPs which are also involved in transporting various types of membrane vesicles and organelles from the neuronal cell body to the nerve terminal (Table 2). How many of these motor proteins are used in non-neuronal cells remains to be determined, but at least one (KIF4/XKLP1) may have a role in transporting vesicles during mitosis [23,24]. Some of these motors may transport specialised membrane cargoes such as mitochondria [25] or vesicles containing components for delivery to ciliary and flagellar membrane domains (see Table 2; [26,27]). We must now consider the possibility that some plus-end-directed movement in the membrane traffic pathways involves KLPs rather than kinesin itself.

Other classes of motor proteins may also act in post-Golgi traffic. For example, an intriguing collaboration has been observed in *Saccharomyces cerevisiae* between a kinesin-like protein, Smy1p, and a myosin V, Myo2p, in the polarised transport of secretory vesicles [28,29]. *SMY1* was identified as a suppressor of a temperature sensitive allele of *MYO2*, and both Myo2p and Smy1p co-localize [29], although the nature of their interaction is unknown. However, as squid axonal vesicles are able to move along actin filaments as well as microtubules [16], and both myosin I and cytoplasmic dynein are found in a Golgi-derived vesicle fraction [30], it seems highly likely that the movement of post-Golgi secretory vesicles will involve both the actin and microtubule cytoskeletons. It remains to be established whether other unconventional myosins that move unidentified particles within various cell types (e.g. [31,32]) participate in membrane traffic.

Table 2
Kinesin-like proteins in neuronal membrane traffic, and their homologues

Protein	Motor domain	Com-plex	Molecular mass (kDa)	Membranes (or other structures)	Motility shown?	Non-neuronal?	Develop-mentally regulated?	Species	Ref.
(A) Kinesin	N	dim	130 (+Light chains)	vesicles	+	yes		Various	[1]
nKinesin	N	?	133	Membranes	?	no	?	Human	[68]
(B) Unc 104	N		180	Synaptic vesicles?	?	?	?	*C. elegans*	[58,59]
KIF1A	N	mon	192	Synaptic vesicles	?	no	?	Mouse	[60,69]
KIF1B	N	mon	130	Mitochondria	+	yes	yes	Mouse	[25]
(C) KIF2	M	dim	80.9	100–200 nm vesicles (not synaptic or KHC/KIF3-containing vesicles)	+	yes (minor)	yes	Mouse	[61]
MCAK	M	?	90	Mitotic centromeres	?	yes	?	CHOs (Hamster)	[62]
(D) KIF3A	N	?	80/85 (+a 95k non-KLP)	Vesicles (not synaptic)	+	testis (others minor)	no	Mouse	[63]
KRP85/95	N	Tri	85/95 (+a 115k non-KLP)	?	+	yes	?	Sea urchin	[64]
Osm3	N	?	?	(Vesicles?; sensory cilia formation)	?	no	?	*C. elegans*	[26]
XKLP3	?	?	?	?	?	yes	yes	*Xenopus laevis*	[65]
KLP68D	N	?	85	?	+	early embryos	?	*Drosophila*	[66]
KHP1(FLA10)	N	?	87	Axonemes + ?	?		cell cycle	*Chlamydomonas*	[27]
(E) KIF4	N	dim.	140	vesicles in spindle and nerve terminals	+	All at birth; adult spleen	yes	Mouse	[23]
XKLP1	N	?	150	Chromosomes, midbody. Vesicles?	?	yes	yes	*Xenopus laevis*	[24]
Chromokinesin	N	?	approx. 125	Midbody, chromosome arms	?	proliferating cells	yes	Chicken	[67]

Motor domains are found at the N-terminus (N) or the middle (M) of the protein. Native motor structure is given where known: mon, monomeric; dim, dimeric; tri, trimeric. For reference, cytoplasmic dynein consists of the following polypeptides: $2 \times > 500$ kDa (motor domain); 3×74 kDa; 4×53–59 kDa.

4. The endocytic pathway

4.1. Structure and position of endocytic compartments

Higher eukaryotic endocytic structures are highly motile and can move along microtubules both towards, and away from, the cell centre [33], which suggests that they possess both plus- and minus-end-directed motors. Indeed, both kinesin and cytoplasmic dynein have been localised to endosomes and lysosomes by immunofluorescence [34,35], and plus-end-directed movement of late endosomes has been shown to be inhibited by anti-sense suppression of kinesin [5]. In addition, antibodies to kinesin abolish the extension of tubular lysosomes in macrophages [36]. In neurons, however, minus-end-directed movement predominates, as endocytic organelles travel large distances from the nerve terminal back to the cell body using cytoplasmic dynein [37,38]. Microtubules are also implicated in maintaining vacuolar structure in the budding yeast *S. cerevisiae* [39].

4.2. Traffic within the endocytic compartment

As is the case for ER-Golgi traffic, microtubules facilitate, but are not absolutely required, for traffic between endocytic compartments and for transcytosis. Transport between early and late endosomes in vitro is stimulated by cytoplasmic dynein [40] or both cytoplasmic dynein and kinesin ([41]; Table 1). Kinesin also drives the formation of endosomal tubules in the presence of BFA [5], and the recycling of transferrin receptors from the tubular compartment surrounding the MTOC out to the leading edge of motile fibroblasts would also require a plus-end-directed motor [42]. The rate of movement of multivesicular bodies in living cells [43] seems too slow to be due to kinesin or cytoplasmic dynein, so it may be that myosins or KLPs participate in the endocytic pathway. It has also been suggested that microtubule motors, and cytoplasmic dynein in particular, may facilitate the sorting of ligand from receptors in the endosome [44].

5. Regulation and co-ordination of membrane movement

The need for microtubule-based membrane movement is easily understood in neurons because of the distances that must be covered. In non-neuronal cells, while microtubule- and actin-based motility is not an absolute requirement for membrane traffic, it is clearly needed to establish and maintain organelle position as well as to facilitate transport between organelles. One attractive theory is that such a system provides the flexibility required for cell movements and reorganisation. The ability to use kinesin to direct traffic to particular areas of the plasma membrane is particularly important for cytotoxic

T-cell action [45]. In addition, cell movement may require delivery of membrane material from the Golgi apparatus [46] and the recycling compartments [42] to the leading edge. Inhibition of this process either by microinjection of antibodies to kinesin/KLPs [47] or by disrupting membrane traffic with BFA [48] results in loss of cell polarity, loss of leading edge dynamics and reduction in cell migration.

So it seems that the microtubule network in higher eukaryotes may provide a means of collecting material from throughout the cell (from the ER and the plasma membrane) for delivery to sorting organelles in the centre of the cell which then process the material and send it on to particular spatial destinations. The actin-based motors may provide the shorter range movements needed for final targeting in higher eukaryotes. This co-ordinated traffic network would clearly require close regulation at every stage to generate the spatial and organelle-specific control of motility, but so far our understanding of how this occurs is limited. Kinesin, kinectin and some associated proteins may all become phosphorylated under conditions where vesicle movement is also stimulated [49 and references therein; 50]. Cytoplasmic dynein-driven ER movement in *Xenopus* egg extracts is either inhibited [11] or stimulated [12] by phosphorylation, depending on the cell cycle status of the extracts. This data, together with the differing effects of phosphorylation on cytoplasmic dynein membrane association [51,52], suggests that there are multiple regulatory pathways. It remains to be determined how the dynactin complex [53] – a regulator of cytoplasmic dynein activity – fits into this scheme. It is possible that different control mechanisms exist for separate transport steps, and that there may also be variation between species.

Profound changes in organelle structure and position occur during mitosis, so another function of membrane motility may be to reorganise organelles following division. This would require an additional temporal layer of regulation on top of that described above. Indeed, the ER and most vesicles in *Xenopus* egg extracts are motile in interphase, but not in metaphase [11], although some vesicles may remain motile [24]. ER movement in vitro is stimulated greatly by the inhibition of protein phosphatase 1 [12], suggesting that there may be specific conditions under which ER motility needs to be increased. In fact, observation of ER movement in living cells revealed that only a small proportion of cells had highly motile ER [54]. Perhaps the re-establishment of the interphase ER network in early G1 could be just such a condition. It is also possible that control of motor activity is required for generating the changes in ER morphology that occur when secretory activity increases [55]. It will be interesting to see whether other membrane motors are similarly regulated during the cell cycle and according to secretory status.

6. Conclusions

It is clear that motor proteins are intimately involved in many aspects of the membrane traffic pathways. The complexity of their roles is now being appreciated: one motor may act at numerous steps within the pathways, and several different motors may be needed to co-ordinate movements of whole organelles and of transport vesicles. Understanding how these functions are regulated in parallel with traffic through the endocytic and exocytic pathways is a stimulating challenge for the future.

Acknowledgements: Space constraints have dictated that many original references have been omitted, for which I apologise. I would like to thank Neil Bulleid, Douglas Drummond and Pete Brown for their comments on the manuscript and Douglas Drummond for database searching. V.A. is a Lister Institute Fellow.

References

[1] Bloom, G.S. and Endow, S.A. (1994) Protein Profile 1, 1059–1116.
[2] Walker, R.A. and Sheetz, M.P. (1993) Annu. Rev. Biochem. 62, 429–451.
[3] Cheney, R.E., Riley, M.A. and Mooseker, M.S. (1993) Cell Motil. Cytoskel. 24, 215–223.
[4] Lee, C., Ferguson, M. and Chen, L.B. (1989) J. Cell Biol. 109, 2045–2055.
[5] Feiguin, F., Ferreira, A., Kosik, K.S. and Caceres, A. (1994) J. Cell Biol. 127, 1021–1039.
[6] Toyoshima, I., Yu, H., Steuer, E.R. and Sheetz, M.P. (1992) J. Cell Biol. 118, 1121–1131.
[7] Kumar, J., Yu, H. and Sheetz, M.P. (1995) Science 267, 1834–1837.
[8] Yu, H., Nicchitta, C.V., Kumar, J., Becker, M., Toyoshima, I. and Sheetz, M.P. (1995) Mol. Biol. Cell 6, 171–183.
[9] Fütterer, A., Kruppa, G., Krämer, B., Lemke, H. and Krönke, M. (1995) Mol. Biol. Cell 6, 161–170.
[10] Dabora, S.L. and Sheetz, M.P. (1988) Cell 54, 27–35.
[11] Allan, V.J. and Vale, R.D. (1991) J. Cell Biol. 113, 347–359.
[12] Allan, V. (1995) J. Cell Biol. 128, 879–891.
[13] Wright, B.D., Terasaki, M. and Scholey, J.M. (1993) J. Cell Biol. 123, 681–689.
[14] Kachar, B. and Reese, T.S. (1988) J. Cell Biol. 106, 1545–1552.
[15] Allen, N.S. and Brown, D.T. (1988) Cell Motil. Cytoskel. 10, 153–163.
[16] Kuznetsov, S.A., Langford, G.M. and Weiss, D.G. (1992) Nature 356, 722–725.
[17] Ho, W.C., Allan, V.J., van Meer, G., Berger, E.G. and Kreis, T.E. (1989) Eur. J. Cell Biol. 48, 250–263.
[18] Corthésy-Theulaz, I., Pauloin, A. and Pfeffer, S.R. (1992) J. Cell Biol. 118, 1333–1345.
[19] Cooper, M.S., Cornell-Bell, A.H., Chernjavsky, A., Dani, J.W. and Smith, S.J. (1990) Cell 61, 135–145.
[20] Lippincott-Schwarz, J., Donaldson, J.G., Schweizer, A., Berger, E.G., Hauri, H.-P., Yuan, L.C. and Klausner, R.D. (1990) Cell 60, 821–836.
[21] Lippincott-Schwarz, J., Cole, N.B., Marotta, A., Conrad, P.A. and Bloom, G.S. (1995) J. Cell Biol. 128, 293–306.
[22] Allan, V. and Vale, R. (1994) J. Cell Sci. 107, 1885–1897.
[23] Sekine, Y., Okada, Y., Noda, Y., Kondo, S., Aizawa, H., Takemura, R. and Hirokawa, N. (1994) J. Cell Biol. 127, 187–201.
[24] Vernos, I., Raats, J., Hirano, T., Heasman, J., Karsenti, E. and Wylie, C. (1995) Cell 81, 117–127.
[25] Nangaku, M., Sato-Yoshitake, R., Okada, Y., Noda, Y., Takemura, R., Yamazaki, H. and Hirokawa, N. (1994) Cell 79, 1209–1220.
[26] Shakir, M.A., Fukushige, T., Yasuda, H., Miwa, J. and Siddiqui, S.S. (1993) Mol. Neurosci. 4, 891–894.
[27] Walther, Z., Vashishtha, M. and Hall, J.L. (1994) J. Cell Biol. 126, 175–188.
[28] Lillie, S.H. and Brown, S.S. (1992) Nature 356, 358–361.
[29] Lillie, S.H. and Brown, S.S. (1994) J. Cell Biol. 125, 825–842.
[30] Fath, K.R., Trimbur, G.M. and Burgess, D.R. (1994) J. Cell Biol. 126, 661–675.
[31] Mermall, V., McNally, J.G. and Miller, K.G. (1994) Nature 369, 560–562.
[32] D'Andrea, L., Danon, M.A., Sgourdas, G.P. and Bonder, E.M. (1994) J. Cell Sci. 107, 2081–2094.
[33] Heuser, J. (1989) J. Cell Biol. 108, 855–864.
[34] Henson, J.H., Nesbitt, D., Wright, B.D. and Scholey, J.M. (1992) J. Cell Sci. 103, 309–320.
[35] Lin, S.X.H. and Collins, C.A. (1992) J. Cell Sci. 101, 125–137.
[36] Hollenbeck, P.J. and Swanson, J.A. (1990) Nature 346, 864–866.
[37] Hirokawa, N, Sato-Yoshitake, R., Yoshida, T. and Kawashima, T. (1990) J. Cell Biol. 111, 1027–1037.

[38] Schnapp, B.J. and Reese, T.S. (1989) Proc. Natl. Acad. Sci. USA 86, 1548–1552.
[39] Guthrie, B.A. and Wickner, W. (1988) J. Cell Biol. 107, 115–120.
[40] Aniento, F., Emans, N., Griffiths, G. and Gruenberg, J. (1993) J. Cell Biol. 123, 1373–1387.
[41] Bomsel, M., Parton, R., Kuznetsov, S.A., Schroer, T.A. and Gruenberg, J. (1990) Cell 62, 719–731.
[42] Hopkins, C.R., Gibson, A., Shipman, M., Strickland, D.K. and Trowbridge, I.S. (1994) J. Cell Biol. 125, 1265–1274.
[43] Hopkins, C.R., Gibson, A., Shipman, M. and Miller, K. (1990) Nature 346, 335–339.
[44] Goltz, J.S., Wolkoff, A.W., Novikoff, P.M., Stockert, R.J. and Satir, P. (1992) Proc. Natl. Acad. Sci. USA 89, 7026–7030.
[45] Burkhardt, J.K., McIlvain, J.M., Sheetz, M.P. and Argon, Y. (1993) J. Cell Sci. 104, 151–162.
[46] Bergmann, J.E., Kupfer, A. and Singer, S.J. (1983) Proc. Natl. Acad. Sci. USA 80, 1367–1371.
[47] Rodionov, V.I., Gyoeva, F.K., Tanaka, E., Bershadsky, A.D., Vasiliev, J.M. and Gelfand, V.I. (1993) J. Cell Biol. 123, 1811–1820.
[48] Bershadsky, A.D. and Futerman, A.H. (1994) Proc. Natl. Acad. Sci. USA 91, 5686–5689.
[49] Haimo, L. (1995) Trends Cell Biol. 5, 165–168.
[50] Lee, K.-D. and Hollenbeck, P.J. (1995) J. Biol. Chem. 270, 5600–5605.
[51] Lin, S.X.H., Ferro, K.L. and Collins, C.A. (1994) J. Cell Biol. 127, 1009–1019.
[52] Dillman, J.F. and Pfister, K.K. (1994) J. Cell Biol. 127, 1671–1681.
[53] Schroer, T.A. (1994) J. Cell Biol. 127, 1–4.
[54] Lee, C. and Chen, L.B. (1988) Cell 54, 37–46.
[55] Rajasekaran, A.K., Morimoto, T., Hanzel, D.K., Rodriguez-Boulan, E. and Kreibich, G. (1993) J. Cell Sci. 105, 333–345.
[56] Steinhardt, R.A., Bi, G. and Alderton, J.M. (1994) Science 263, 390–393.
[57] Doberstein, S.K., Baines, I.C., Wiegand, G., Korn, E.D. and Pollard, T.D. (1993) Nature 365, 841–843.
[58] Hall, D.H. and Hedgecock, E.M. (1991) Cell 65, 837–847.
[58] Otsuka, A.J., Jeyaprakash, A., García-Añoveros, J., Tang, L.Z., Fisk, G., Hartshorne, T., Franco, R. and Born, T. (1991) Neuron 6, 113–122.
[60] Aizawa, H., Sekine, Y., Takemura, R., Zhang, Z., Nangaku, M. and Hirokawa, N. (1992) J. Cell Biol. 119, 1287–1296.
[61] Noda, Y., Sato-Yoshitake, R., Kondo, S., Nangaku, M. and Hirokawa, N. (1995) J. Cell Biol. 129, 157–167.
[62] Wordeman, L. and Mitchison, T.J. (1995) J. Cell Biol. 128, 95–105.
[63] Kondo, S., Sato-Yoshitake, R., Noda, Y., Aizawa, H., Nakata, T., Matsura, Y. and Hirokawa, N. (1994) J. Cell Biol. 125, 1095–1107.
[64] Cole, D.G., Chinn, S.W., Wedaman, K.P., Hall, K., Vuong, T. and Scholey, J.M. (1993) Nature 366, 168–270.
[65] Vernos, I., Heasman, J. and Wylie, C. (1993) Dev. Biol. 157, 232–239.
[66] Pesavento, P.A., Stewart, R.J. and Goldstein, L.S.B. (1994) J. Cell Biol. 127, 1041–1048.
[67] Wang, S.-Z. and Adler, R. (1995) J. Cell Biol. 128, 761–768.
[68] Niclas, J., Navone, F., Hom-Booher, N. and Vale, R.D. (1994) Neuron 12, 1059–1072.
[69] Okada, Y., Yamazake, M., Sekine-Alzawa, Y. and Hirokawa, N. (1995) Cell 81, 769–780.