Cell. Mol. Life Sci. 64 (2007) 171–180
1420-682X/07/020171-10
DOI 10.1007/s00018-006-6286-1

Cellular and Molecular Life Sciences

Review

Directional mRNA transport in eukaryotes: lessons from yeast

M. Müller, A. Heuck and D. Niessing*

Gene Center of the Ludwig-Maximilians-University Munich and GSF – Institute of Molecular Immunology, Feodor-Lynen-Strasse 25, 81377 Munich (Germany), Fax: +49 89 2180 9976962, e-mail: niessing@lmb.uni-muenchen.de

Received 20 June 2006; received after revision 18 September 2006; accepted 18 October 2006
Online First 29 November 2006

Abstract. In eukaryotes, developmental processes and cell differentiation, as well as basic cellular functions require the propagation of information in an asymmetric manner. Localization of mRNA is a key mechanism to establish asymmetric cell fate. The first part of this review provides an overview of our current knowledge of motor protein-dependent mRNA transport in eukaryotes. The second part provides a more detailed description of the most comprehensively studied mRNA translocation complex to date: the *ASH1* messenger ribonucleoprotein particle (mRNP) from *Saccharomyces cerevisiae*. During budding of yeast, the *ASH1* mRNP transports cell fate determinants exclusively into the daughter cell. The core factors of the *ASH1* mRNP have been identified, their interactions have been studied in detail, and the three-dimensional structure of its mRNA-binding protein, She2p, has been determined. Because no other mRNP has been studied in such detail, the *ASH1* mRNP could serve as a model for asymmetric segregation of cell fate determinants in higher eukaryotes.

Keywords. mRNP, mRNA localization, myosin, She2p, She3p, Myo4p, *ASH1* mRNA, endoplasmic reticulum.

Introduction

For cellular asymmetry, cell fate determinants are directionally transported as part of large protein- and mRNA-containing complexes along microtubule or actin filaments. In the last 10 years, it became increasingly clear that directional transport and localized expression of mRNA serves as a particularly powerful tool to expand the temporal and spatial control of cellular gene expression [1–4]. Such asymmetric mRNA localization is required for cellular communication in plants [5], budding of yeast [4, 6, 7], polarity of somatic and germline cells [3], establishment of body axes in metazoans [4, 8], and synaptic plasticity [9, 10].

For motor protein-dependent, asymmetric localization of mRNA cargo, the transcripts are usually incorporated into large, translationally silent messenger-ribonucleoprotein particles (mRNP), which shuttle along the cytoskeleton [4]. After anchoring, mRNA translation is activated, resulting in spatially restricted protein expression. Translation of asymmetrically localized mRNAs is, for instance, a central mechanism to regulate local gene expression during oogenesis and embryogenesis [4, 8, 11]. During these early developmental stages, the zygotic transcription machinery is not yet fully activated and translation of maternally deposited mRNA is the only source for protein expression.

Directional mRNA transport requires an intact cytoskeleton and the formation of motor protein-containing complexes [12]. As part of such transport complexes, dedicated RNA-binding proteins bind to specific sequence regions, termed zip code elements, in the cargo mRNA and interact with additional proteins to form a functional mRNP. Such mRNPs are usually large particles, at least several million daltons in size, containing a great variety of different proteins, including even ribosomal subunits [13–19].

Three major classes of motor proteins provide locomotion for tethered mRNAs: dyneins and kinesins move cargo along microtubule fibers, whereas myosin motor

* Corresponding author.

proteins shuttle along actin filaments [12, 20]. The motile activities of different motor proteins vary considerably in speed and processivity and show different directionality [20]. For intermediate filaments, no associated motor proteins have been identified thus far [12].

Dynein-dependent mRNA transport

The protein complex that mediates cytoplasmic dynein motor function moves cargo along microtubules towards their minus end [21, 22]. The central core factor of this large dynein holo-enzyme is the dynein heavy chain [23]. It contains a microtubule-binding motor domain, a coiled-coil region for dimerization, and interaction motifs for the binding of dynein light chains [21, 22]. Dynein assembles into large multiprotein complexes with different cargo-specific factors and can transport a great variety of different cargoes [12, 21, 22].

To establish body axes during *Drosophila* oogenesis, dynein activity has to localize *gurken* mRNA and maintain *bicoid* mRNA localization at defined sites of the oocyte [24, 25]. *bicoid* mRNA localization has been shown to require several additional transport core factors, including Bicaudal D (BicD), Egalitarian (Egl), Exuperantia, Staufen, Swallow, and Ypsilon Schachtel [24, 26–33]. Disrupted *gurken* and *bicoid* mRNA localization results in impaired anterior-posterior and dorsal-ventral body axis formation [34].

In *Drosophila* embryos, dynein together with the transport-core factors BicD and Egl forms a multiprotein complex to facilitate the translocation of *even skipped* (*eve*), *wingless* (*wg*), *fushi tarazu* (*ftz*), and *runt* (*run*) mRNA into embryonic subdomains [30, 35, 36]. Localization of these mRNAs is required for the establishment of embryonic and larval segmentation [4]. Additional experiments will be necessary to identify the minimal set of core factors and their interactions for the localization of specific mRNAs.

In *Drosophila* embryonic neuroblasts, a dynein-dependent transport complex, which also contains BicD and Egl, is required for the localization of *inscuteable* mRNA [37]. Asymmetric localization of *inscuteable* mRNA regulates the expression of the cytoskeleton adapter protein Inscuteable and, thus, impacts apico-basal polarity and spindle elongation.

In mammalian cells, the BicD homologs BicD1 and BicD2 participate in dynein-dependent transport of COPI-independent Golgi-endoplasmic reticulum (ER) [38, 39]. BicD2 is also found in mouse oocytes [40], resembling the expression of BicD in *Drosophila* oocytes.

The use of identical core factors for various cargoes in different developmental stages and tissues suggests the existence of a universal dynein core complex. In addition, the expression of BicD in mouse and in *Drosophila* oocytes points towards a potential conservation of developmental functions. On the other hand, no mammalian homolog for Egl has been identified to date, indicating that pronounced differences exist between dynein-dependent transport complexes in different species. It remains to be shown whether additional conserved core factors can be identified and how similar the combinations of core factors are in different organisms.

Kinesin-dependent mRNA transport

The second type of microtubule-associated motor protein is plus-end directed kinesin [12]. The so-called conventional Kinesin I [41] has an N-terminal motor domain, a long coiled-coil dimerization domain, and a globular tail domain [12]. Kinesin I forms a homodimer and is required for transport of *oskar* (*osk*) mRNA in *Drosophila* oocytes [42]. In *Drosophila* embryos, *oskar* mRNA is translocated by a combination of Kinesin I and dynein motor protein functions to the posterior pole, where it is essential to define properly the posterior pole region [43, 44]. In *Xenopus laevis*, Kinesin I as well as unconventional, heterotrimeric Kinesin II [45] is required for the localization of *Vg1* mRNA to the vegetal pole of the oocyte [46, 47]. Vg1 protein, as a member of the transforming growth factor-β superfamily [48], has been implicated in mesoderm and endoderm specification [49–51]. Again, some essential proteins of the mRNA transport complexes have been identified, but their molecular interactions and the identities of other core factors remain elusive [52].

In vertebrate neurons, long-distance transport of mRNAs into their distal regions is mediated by kinesin-containing mRNPs, whereas local transport at the growth cones of immature neurons seems to be myosin dependent [10, 12, 20, 53]. Directional neuronal transport of mRNAs is required for proper synapse activity, axonal and dendritic growth [10, 12, 53], and affects learning and memory in mice [54]. Comprehensive analyses of neuronal mRNPs have identified a relatively large number of proteins as mRNP components [13, 14, 17–19,55]. Most likely these proteins represent a heterologous combination of factors from different mRNPs that have overlapping, but non-identical protein compositions. To distinguish core factors of neuronal mRNPs from loosely associated proteins, Nobutaka Hirokawa and colleagues performed Kinesin I-tethered mRNP purifications from mouse brain tissue under different buffer conditions [14]. Under stringent purification conditions, only four factors of the transport complex, i.e. Staufen, Pur-α, Pur-β, and hnRNP-U, remained associated with Kinesin I, suggesting that these proteins are neuronal mRNP core factors. This study paved the way for a more detailed, molecular understanding of neuronal mRNP formation and function in vertebrates.

Myosin-dependent mRNA transport

Because of its abundance in muscle tissue, myosin was the first motor protein to be discovered. In 1942, Szent-Györgyi and colleagues isolated myosin together with actin filaments and observed contraction of acto-myosin threads [56]. Beside muscular myosin, i.e. myosin type II, several non-muscular, so-called unconventional myosins with distinct functions have since been identified and classified into 36 types [57–62]. All myosin motor proteins contain an N-terminal motor domain and many have additional regions that are required for dimerization, efficient translocation, and/or cargo binding [12, 61, 62].
Like kinesins and dyneins, myosin motor proteins transport specific mRNAs. For *Drosophila* embryonic neuroblast differentiation, a myosin-dependent, *prospero* mRNA-containing complex translocates to the basal cortex of the neuroblast. *prospero* mRNA is recognized by the RNA-binding protein Staufen, which interacts with the adaptor protein Miranda [63–68]. Miranda itself is required for asymmetric localization of *prospero* mRNA, the transcription factor Prospero, Staufen, and Brain tumor, a translational repressor [69]. Miranda co-purifies with Zipper (myosin type II) and Jaguar (myosin type VI), two myosins with different motile directionalities [69–72]. Mutations in each individual myosin lead to distinct mislocalization of the Miranda complex, suggesting that myosin II and VI are both required for its localization by a different mechanism [70, 72; C. Petritsch, personal communication]. Additional factors may have to join the complex to form a functional mRNP [73].
In vertebrates, *β-actin* mRNA is likely to be transported by myosin type V to the leading edge of fibroblasts, where its protein product is required for the formation and protrusion of lamellipodia [74]. For specific incorporation of *β-actin* mRNA into the transport complex, the so-called zip code binding protein 1 (ZBP1) has to bind to specific zip code elements within the *β-actin* mRNA. After recruitment into myosin-containing particles, the *β-actin* mRNA moves along actin filaments toward the leading edge of fibroblasts [75–79]. In neurites, *β-actin* mRNA is transported to growth cones in the cellular periphery [80, 81]. It is likely that long-distance transport in neurites is mediated by a kinesin-dependent transport mechanism [80, 82].

The *ASH1* mRNA-translocation complex in yeast

For none of the mRNA-transport complexes described above have all core factors been identified and most of the underlying molecular interactions are not well understood. In contrast, for the *ASH1* mRNA-translocation complex of *Saccharomyces cerevisiae*, the essential components are known [83] and have been characterized comprehensively with genetic and biochemical approaches [3, 4, 7, 52, 84]. To date, translocation of *ASH1* mRNA is the only well-understood directional transport event that biases cell fate decisions.

ASH1 mRNP: the biological function

Upon germination, haploid spores of *S. cerevisiae* initiate an asymmetric cell division, resulting in one larger mother cell and one smaller daughter cell [7]. The mother cell undergoes genomic recombination at the *MAT* gene locus, resulting in an allelic switch from a to α, or vice versa [7]. This recombination event is inhibited in the daughter cell by the action of the transcriptional repressor Ash1p [7, 85, 86]. Exclusive expression of Ash1p in the daughter cell is achieved by active transport and localization of the *ASH1* mRNA to the tip of the daughter cell, followed by its translation after cytokinesis [83, 85–88].

Components of the *ASH1* mRNP

With the help of genetic screening, the core components of the *ASH1* mRNA-transport complex have been identified (Fig. 1) [83]. The motor protein Myo4p is a type V unconventional myosin that conveys *ASH1* mRNA translocation along actin filaments [83, 85, 87–91]. The RNA-binding protein, She2p, interacts with *ASH1* mRNA through four independent zip code elements and is connected to Myo4p via the adapter protein She3p [90, 92–97].
She2p is localized in the nucleus and in the cytoplasm. Upon inhibition of nuclear mRNA export, She2p accumulates exclusively in the nucleus [98], suggesting that She2p shuttles into the cytoplasm in co-complex with mRNA. In the cytoplasm, the She2p:*ASH1* RNA co-complex interacts with the adapter protein She3p, which itself is bound to Myo4p (Fig. 1) [90, 92–94, 99]. Together, these proteins assemble into a larger mRNP and move along actin filaments toward the tip of the daughter cell. This translocation process was visualized by live imaging with MS2-GFP-tethered *ASH1* mRNA [89, 100], a technique that is now also applied to mammalian cells [101]. The live imaging analyses showed that *ASH1* mRNPs move with an average velocity of about 300 nm per minute toward the bud tip. The Pumilio family protein Puf6p, which is not deemed to be part of the core translocation machinery, associates with the *ASH1* mRNP complex and might repress translation of *ASH1* mRNA during translocation [102]. In addition to these factors, the RNA-binding KH domain protein 1 (Khd1p) interacts with *ASH1* mRNA [103]. Although its exact role has not been determined, Khd1p appears to play a role in the translational control and anchoring of *ASH1* mRNA in the daughter cell [103]. After cytokinesis, translation of *ASH1* mRNA

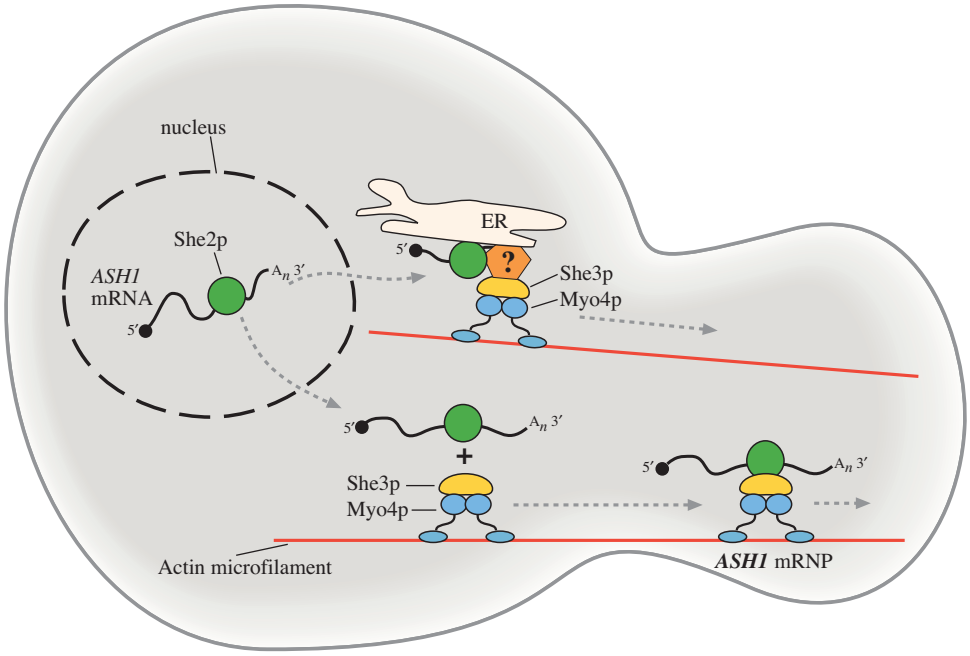

Figure 1. Schematic drawing of Myo4p-dependent transport in budding yeast. The prospective mother cell is shown on the left, the daughter cell buds out on the right. After transcription, *ASH1* mRNA is recognized in the nucleus by the RNA-binding protein She2p. *ASH1* mRNA and She2p shuttle as co-complex out of the nucleus and form a cytoplasmic transport complex, consisting of at least *ASH1* mRNA, She2p, the adapter protein She3p, and the myosin type V motor protein Myo4p. In addition to mRNA transport, the Myo4p:She3p co-complex is required for translocation of cortical ER. For further details, see text.

is activated and Ash1p is expressed exclusively in the daughter cell.

Interaction between motor and adapter protein

In its C-terminal half, Myo4p contains a coiled-coil dimerization domain and a globular tail region [61, 104]. In two hybrid and *in vitro* binding assays, the C-terminal half of Myo4p interacts with the N-terminal half of She3p [89, 90, 92, 93, 98]. *In vivo*, Myo4p and She3p form a stable co-complex in the cytoplasm (Fig. 1) [99]. Recent structural studies with the yeast paralog Myo2p showed that a domain within the tail region adopts a novel type of protein fold [105]. This domain is specific for myosin type V motor proteins [61] and is required for the interaction of Myo2p with its various adapter proteins [106–116]. Despite this information, the exact role of this domain for cargo transport is still not entirely clear and will have to be characterized further.

The cargo-binding protein She2p

Recently, the three-dimensional structure of She2p has been determined by X-ray crystallography [117]. The crystal structure of She2p, which has homologs only in yeast, reveals an almost exclusively α-helical protein that is unrelated to any previously described nucleic acid-binding protein. In the crystal lattice, She2p forms a stable dimer (Fig. 2a). Analytical equilibrium ultracentrifugation experiments confirmed that She2p is dimeric also in solution [117]. Each She2p monomer consists of a bundle of five α helices arranged like a pentacle around its hydrophobic core. Point mutations disrupting the integrity of the hydrophobic core of She2p also disrupt mRNA transport *in vivo* [117, 118: see supplementary table S1]. In addition to the helical bundle, each monomer contains a small helix that protrudes at right angles from the middle of the bundle into the solvent.

The basic helical hairpin motif of She2p

The recently described novel RNA-binding motif of She2p has been termed basic helical hairpin motif [117]. This motif consists of positively charged amino acids located on two adjacent anti-parallel α helices (Fig. 2b). The basic helical hairpin motif provides a positively charged surface patch on She2p for RNA binding [117]. Mutations in the motif result in loss of mRNA binding *in vitro* and defective mRNA transport *in vivo* [117, 118].

Interestingly, the two basic helical hairpin motifs of the She2p homodimer are located on surface regions at opposite sites of the dimer (Fig. 2a). Because each of the

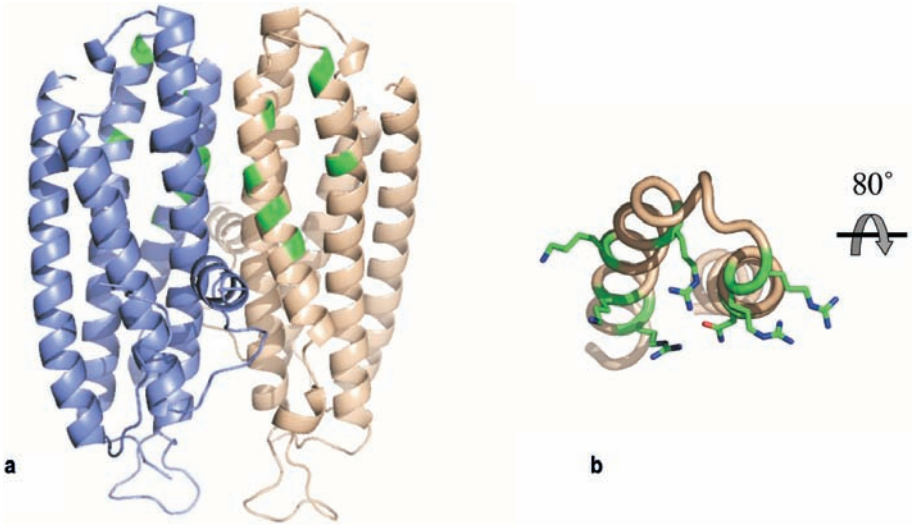

Figure 2. Model from the She2p crystal structure at 1.95 Å resolution. (*a*) She2p forms a stable homodimer via non-crystallographic symmetry. Each monomer consists of five α helices ordered like a pentacle around a hydrophobic core. Amino acids of the basic helical hairpin RNA-binding motif are highlighted in green. For the gray She2p monomer, the basic helical hairpin motif faces toward the viewer, for the blue monomer, the motif is located in the background. (*b*) View of the basic helical hairpin motif of the gray monomer, rotated 80° around the horizontal axis, with the top of She2p turned toward the reader. Amino acids of the basic helical hairpin motif required for RNA binding are highlighted in green with their side chains shown.

two basic helical hairpin motifs of the homodimer is located on a different monomer, the possibility was raised that each monomer can bind independently to zip code elements and that dimerization may not be required for RNA binding [117]. To test this possibility, mutant versions of She2p were generated to produce monomeric proteins. Monomeric She2p was unable to bind mRNA, demonstrating the requirement of She2p dimerization for proper function [117]. A possible explanation for the need of She2p dimerization is that additional surface regions from both subunits are required for efficient RNA binding by She2p. The small protruding helices, for example, are highly conserved in all She2p homologs and could provide additional RNA interactions (Fig. 2a).

Cargo for Myo4p-dependent transport

In addition to *ASH1* mRNA, She2p binds to at least 23 other RNAs, of which 18 are clearly localized in a She2p-dependent manner [119, 120]. It is not yet known whether these RNAs are transported as part of distinct, cargo-specific RNPs or in large RNP complexes that contain different RNAs. Several of these translocated RNAs contain more than one zip code element to which She2p binds. Attempts to find common features for all of these zip code elements have failed so far, but for several well-defined zip code elements a stem-loop structure is necessary for binding [93, 95–97]. Thus far, only for one single zip code element in the *ASH1* mRNA, i.e. the E3 element, binding has been quantified (Kd = 210 nM) [117].

In a recent study, Chartrand and colleagues used a three-hybrid assay to identify sequence motifs in a subset of zip code elements that are required for She2p binding [121]. The predicted consensus motif consists of a CGA base triplet located in a loop and a single cytosine in a second loop. Both loops are separated by a four to five-base pair stem. This study was followed by a publication from DeRisi and colleagues, who also used a three-hybrid assay to demonstrate that this defined base triplet may not be sufficient and the cytosine is not absolutely required for binding [122]. It seems obvious that further functional and structural studies with recombinant She2p and different RNA zip code elements are necessary to understand She2p binding to specific mRNAs.

Although common features of She2p-dependent zip code elements have been found in some but not all RNAs, it is clear that all zip code elements must have some common sequence and/or structural features to allow for specific She2p binding. Interestingly, it has been noted that several of the She2p-dependent mRNAs might also have a functional relationship. Almost half of the 24 She2p-dependent mRNAs encode membrane-associated proteins [119]. The relatively high number of mRNAs with a related function indicates that these mRNAs might be co-regulated by She2p to coordinate a certain cellular pathway.

It was recently suggested that posttranscriptional regulation of genes with related function by an RNA-binding protein constitutes a functional posttranscriptional operon [123]. Such posttranscriptional operons have since been described in yeast, *Drosophila*, and mouse [124–126].

For *ASH1* mRNP transport, She2p, She3p, and Myo4p could act as transacting regulators of a posttranscriptional She2p-dependent operon involved in membrane-related functions.

Beside mRNAs that encode membrane-associated proteins, membranes themselves are bound and transported by the Myo4p-containing complex [127, 128]. For the inheritance of cortical ER, Myo4p and She3p, but not She2p are required [127]. ER inheritance can be inhibited by blocking actin polymerization with latrunculin A, suggesting active Myo4p-dependent transport of ER along actin filaments [127]. Based on our current knowledge of the *ASH1* mRNP, it is reasonable to speculate that Myo4p-bound She3p provides the anchor to an unknown factor X that tethers cortical ER to She3p:Myo4p (see Fig. 1).

A recent study by Jansen and colleagues addressed the question whether mRNA and ER transport occur as part of one large particle or if both cargoes exclusively associate with distinct, co-existing transport complexes [128]. The study not only confirmed the previously described co-fractionation of Myo4p with ER in sucrose gradient fractionation experiments [127, 128], but also found that the RNA-binding protein She2p fractionates with ER [128]. Surprisingly, co-fractionation of She2p with ER is independent of Myo4p and She3p, suggesting a novel, not understood interaction of She2p with ER. The observed She2p:ER interaction could either be direct, occur via binding of She2p to an ER-associated protein, or be facilitated through an RNA-mediated interaction. In summary, the results show that ER and mRNA can be cargo of the same transport particle. On the other hand, these findings still allow for the possibility that distinct ER and mRNA transport complexes can form and translocate cargo independently. Future experiments will be required to identify how the different molecular interactions lead to the formation of certain transport particles. It should be noted that co-migration of mRNA with ER has also been described for invertebrates [129, 130] and vertebrates [131–135].

Assembly of the *ASH1* mRNP

Molecular details of *ASH1* mRNP assembly are mainly unknown. Although it seems clear that She2p and *ASH1* mRNA form an initial co-complex in the nucleus (Fig. 1), it remains to be seen which other proteins bind to the nuclear She2p:RNA co-complex to promote *ASH1* mRNP maturation and to achieve its nuclear export. The candidate protein Loc1p, for example, is strictly nuclear and binds to *ASH1* mRNA [136]. Because Loc1p also interacts with unrelated stem-loop structures [136], the specificity of Loc1p binding to *ASH1* mRNA remains to be demonstrated. In addition, the exact role of Loc1p in the nuclear processing of *ASH1* mRNP and the nuclear export of mature *ASH1* mRNP is mainly unknown.

In the cytoplasm, Myo4p and She3p form a co-complex and only after nuclear export of She2p:*ASH1* mRNA the minimal transport complex can assemble [90, 93, 98, 99]. Jansen and colleagues showed in co-precipitation experiments with yeast cell extracts that the absence of *ASH1* mRNA leads to decreased She2p interaction with the She3p:Myo4p co-complex [93], suggesting that a mature transport complex favorably assembles in the presence of its mRNA cargo. She2p binds to at least 23 additional RNAs, and their modes of interaction are not well understood. Therefore, it is not entirely surprising that in two-hybrid experiments, Long and colleagues still found an interaction between She3p and mutant versions of She2p that are deficient for *ASH1* mRNA binding [118].

When sequences of She2p yeast homologues were aligned and plotted onto the three-dimensional structure of She2p, sequence conservation was observed almost exclusively in the upper half of the protein [117]. Within this upper half of She2p are the basic helical hairpin motif and a hydrophobic, highly conserved region on top of the dimer. Mutations in the upper, uncharged surface region result in reduced RNA binding and loss of mRNA localization *in vivo* [117, 118]. Together, these observations led to the prediction that the *ASH1* mRNP might assemble on the upper half of the She2p dimer [117]. She2p association with ER might also be mediated by this surface region.

The example of yeast *ASH1* mRNA demonstrates the need for multidisciplinary approaches to understand molecular interactions that result in the assembly of a functional transport complex. Although myosin-dependent transport of mRNA has also been observed in vertebrate fibroblasts and neurons, most of the core factors that assemble the mRNP have not been identified to date. By sequence comparison alone, there is no pronounced homology between yeast She2p or She3p and metazoan genes. On the other hand, type V myosins are conserved from yeast to vertebrates. It is likely that the characterization of *ASH1* mRNP will yield a general understanding of principles of mRNP assembly, transport, and translational activation after anchoring. The specific mRNP core factors, however, may be different in metazoans.

Kinesin motor proteins show limited homology to myosins and are thought to have a common ancestor [137]. Kinesin-dependent mRNPs, however, are definitely more complex in their composition than the *ASH1* mRNP from yeast [4, 12]. Therefore, it will take much longer to understand molecular details of kinesin-dependent mRNP assembly and transport in vertebrates. Myosin-dependent *ASH1* mRNP transport in yeast may help by providing general principles of mRNP function that can be tested for kinesin-dependent mRNP transport.

Although dynein-dependent transport of mRNA plays a central role in many essential cellular events, it is likely

to be the most challenging type of transport particles to understand. To date, not even the composition of the dynein motor protein holoenzyme has been sufficiently characterized [12].

For all the differences between mRNPs described above, there seem to be general principles as well. For the mRNA transport complexes studied thus far, a common theme is the translational silencing during mRNA transport and the translational activation after mRNA anchoring. Recently, Singer and colleagues reported that translation of localized neuronal *β-actin* mRNA is controlled by phosphorylation of its RNA-binding protein [138]. A similar mechanism might also regulate the translation of mRNAs that are She2p dependently localized in yeast. Unraveling the interplay between core factors of the *ASH1* mRNP during assembly, translational silencing, transport, anchoring, and translational activation at the target site will help us to understand how core factors interact to choreograph the controlled transport of mRNAs. When comparing *ASH1* mRNP transport with other mRNA translocation events, it seems likely that yeast is, once again, a convincing model system to study the general principles of a basic cellular function.

Acknowledgements. The authors are grateful to C. Petritsch and R.-P. Jansen for fruitful discussions on mRNA localization and for critically reading this manuscript.

1 Farina, K. L. and Singer, R. H. (2002) The nuclear connection in RNA transport and localization. Trends Cell Biol. 12, 466–472.
2 Kloc, M., Zearfoss, N. R. and Etkin, L. D. (2002) Mechanisms of subcellular mRNA localization. Cell 108, 533–544.
3 Lopez de Heredia, M. and Jansen, R. P. (2004) mRNA localization and the cytoskeleton. Curr. Opin. Cell Biol. 16, 80–85.
4 St Johnston, D. (2005) Moving messages: the intracellular localization of mRNAs. Nat. Rev. Mol. Cell Biol. 6, 363–375.
5 Ding, B., Itaya, A. and Qi, Y. (2003) Symplasmic protein and RNA traffic: regulatory points and regulatory factors. Curr. Opin. Plant Biol. 6, 596–602.
6 Darzacq, X., Powrie, E., Gu, W., Singer, R. H. and Zenklusen, D. (2003) RNA asymmetric distribution and daughter/mother differentiation in yeast. Curr. Opin. Microbiol. 6, 614–620.
7 Chartrand, P., Singer, R. H. and Long, R. M. (2001) RNP localization and transport in yeast. Annu. Rev. Cell. Dev. Biol. 17, 297–310.
8 Mohr, E. and Richter, D. (2001) Messenger RNA on the move: implications for cell polarity. Int. J. Biochem. Cell Biol. 33, 669–679.
9 Steward, O. and Worley, P. (2001) Localization of mRNAs at synaptic sites on dendrites. Results Probl. Cell Differ. 34, 1–26.
10 Sotelo-Silveira, J. R., Calliari, A., Kun, A., Koenig, E. and Sotelo, J. R. (2006) RNA trafficking in axons. Traffic 7, 508–515.
11 Huynh, J. R. and St Johnston, D. (2004) The origin of asymmetry: early polarisation of the *Drosophila* germline cyst and oocyte. Curr. Biol. 14, R438–R449.
12 Vale, R. D. (2003) The molecular motor toolbox for intracellular transport. Cell 112, 467–480.
13 Barbarese, E., Koppel, D. E., Deutscher, M. P., Smith, C. L., Ainger, K., Morgan, F. and Carson, J. H. (1995) Protein translation components are colocalized in granules in oligodendrocytes. J. Cell Sci. 108, 2781–2790.
14 Kanai, Y., Dohmae, N. and Hirokawa, N. (2004) Kinesin transports RNA: isolation and characterization of an RNA-transporting granule. Neuron 43, 513–525.
15 Wilsch-Brauninger, M., Schwarz, H. and Nüsslein-Volhard, C. (1997) A sponge-like structure involved in the association and transport of maternal products during *Drosophila* oogenesis. J. Cell Biol. 139, 817–829.
16 Krichevsky, A. M. and Kosik, K. S. (2001) Neuronal RNA granules: a link between RNA localization and stimulation-dependent translation. Neuron 32, 683–696.
17 Angenstein, F., Evans, A. M., Ling, S. C., Settlage, R. E., Ficarro, S., Carrero-Martinez, F. A., Shabanowitz, J., Hunt, D. F. and Greenough, W. T. (2005) Proteomic characterization of messenger ribonucleoprotein complexes bound to nontranslated or translated poly(A) mRNAs in the rat cerebral cortex. J. Biol. Chem. 280, 6496–6503.
18 Elvira, G., Wasiak, S., Blandford, V., Tong, X. K., Serrano, A., Fan, X., del Rayo Sanchez-Carbente, M., Servant, F., Bell, A. W., Boismenu, D., Lacaille, J. C., McPherson, P. S., Des-Groseillers, L. and Sossin, W. S. (2006) Characterization of an RNA granule from developing brain. Mol. Cell Proteom. 5, 635–651.
19 Villace, P., Marion, R. M. and Ortin, J. (2004) The composition of Staufen-containing RNA granules from human cells indicates their role in the regulated transport and translation of messenger RNAs. Nucleic Acids Res. 32, 2411–2420.
20 Mallik, R. and Gross, S. P. (2004) Molecular motors: strategies to get along. Curr. Biol. 14, R971–R982.
21 Oiwa, K. and Sakakibara, H. (2005) Recent progress in dynein structure and mechanism. Curr. Opin. Cell Biol. 17, 98–103.
22 King, S. M. (2000) The dynein microtubule motor. Biochim. Biophys. Acta 1496, 60–75.
23 Samso, M., Radermacher, M., Frank, J. and Koonce, M. P. (1998) Structural characterization of a dynein motor domain. J. Mol. Biol. 276, 927–937.
24 Navarro, C., Puthalakath, H., Adams, J. M., Strasser, A. and Lehmann, R. (2004) Egalitarian binds dynein light chain to establish oocyte polarity and maintain oocyte fate. Nat. Cell Biol. 6, 381–383.
25 Weil, T. T., Forrest, K. M. and Gavis, E. R. (2006) Localization of bicoid mRNA in late oocytes is maintained by continual active transport. Dev. Cell 11, 251–262.
26 Berleth, T., Burri, M., Thoma, G., Bopp, D., Richstein, S., Frigerio, G., Noll, M. and Nüsslein-Volhard, C. (1988) The role of localization of *bicoid* RNA in organizing the anterior pattern of the *Drosophila* embryo. EMBO J. 7, 1749–1756.
27 Wilhelm, J. E., Mansfield, J., Hom-Booher, N., Wang, S., Turck, C. W., Hazelrigg, T. and Vale, R. D. (2000) Isolation of a ribonucleoprotein complex involved in mRNA localization in *Drosophila* oocytes. J. Cell Biol. 148, 427–440.
28 Cha, B. J., Koppetsch, B. S. and Theurkauf, W. E. (2001) *In vivo* analysis of *Drosophila bicoid* mRNA localization reveals a novel microtubule-dependent axis specification pathway. Cell 106, 35–46.
29 Wang, S. and Hazelrigg, T. (1994) Implications for *bcd* mRNA localization from spatial distribution of exu protein in *Drosophila* oogenesis. Nature 369, 400–403.
30 Bullock, S. L. and Ish-Horowicz, D. (2001) Conserved signals and machinery for RNA transport in *Drosophila* oogenesis and embryogenesis. Nature 414, 611–616.
31 Ferrandon, D., Koch, I., Westhof, E. and Nüsslein-Volhard, C. (1997) RNA-RNA interaction is required for the formation of specific *bicoid* mRNA 3′ UTR-STAUFEN ribonucleoprotein particles. EMBO J. 16, 1751–1758.
32 Ferrandon, D., Elphick, L., Nüsslein-Volhard, C. and St Johnston, D. (1994) Staufen protein associates with the 3′UTR of

bicoid mRNA to form particles that move in a microtubule-dependent manner. Cell 79, 1221–1232.
33 Suter, B. and Steward, R. (1991) Requirement for phosphorylation and localization of the Bicaudal-D protein in *Drosophila* oocyte differentiation. Cell 67, 917–926.
34 St Johnston, D. (1995) The intracellular localization of messenger RNAs. Cell 81, 161–170.
35 Wilkie, G. S. and Davis, I. (2001) *Drosophila* wingless and pair-rule transcripts localize apically by dynein-mediated transport of RNA particles. Cell 105, 209–219.
36 Simmonds, A. J., dosSantos, G., Livne-Bar, I. and Krause, H. M. (2001) Apical localization of *wingless* transcripts is required for wingless signaling. Cell 105, 197–207.
37 Hughes, J. R., Bullock, S. L. and Ish-Horowicz, D. (2004) Inscuteable mRNA localization is dynein-dependent and regulates apicobasal polarity and spindle length in *Drosophila* neuroblasts. Curr. Biol. 14, 1950–1956.
38 Hoogenraad, C. C., Akhmanova, A., Howell, S. A., Dortland, B. R., De Zeeuw, C. I., Willemsen, R., Visser, P., Grosveld, F. and Galjart, N. (2001) Mammalian Golgi-associated Bicaudal-D2 functions in the dynein-dynactin pathway by interacting with these complexes. EMBO J. 20, 4041–4054.
39 Matanis, T., Akhmanova, A., Wulf, P., Del Nery, E., Weide, T., Stepanova, T., Galjart, N., Grosveld, F., Goud, B., De Zeeuw, C. I., Barnekow, A. and Hoogenraad, C. C. (2002) Bicaudal-D regulates COPI-independent Golgi-ER transport by recruiting the dynein-dynactin motor complex. Nat. Cell Biol. 4, 986–992.
40 Herrera, L., Ottolenghi, C., Garcia-Ortiz, J. E., Pellegrini, M., Manini, F., Ko, M. S., Nagaraja, R., Forabosco, A. and Schlessinger, D. (2005) Mouse ovary developmental RNA and protein markers from gene expression profiling. Dev. Biol. 279, 271–290.
41 Vale, R. D., Reese, T. S. and Sheetz, M. P. (1985) Identification of a novel force-generating protein, kinesin, involved in microtubule-based motility. Cell 42, 39–50.
42 Brendza, R. P., Serbus, L. R., Duffy, J. B. and Saxton, W. M. (2000) A function for kinesin I in the posterior transport of oskar mRNA and Staufen protein. Science 289, 2120–2122.
43 Glotzer, J. B., Saffrich, R., Glotzer, M. and Ephrussi, A. (1997) Cytoplasmic flows localize injected oskar RNA in *Drosophila* oocytes. Curr. Biol. 7, 326–337.
44 Serbus, L. R., Cha, B. J., Theurkauf, W. E. and Saxton, W. M. (2005) Dynein and the actin cytoskeleton control kinesin-driven cytoplasmic streaming in *Drosophila* oocytes. Development 132, 3743–3752.
45 Cole, D. G., Chinn, S. W., Wedaman, K. P., Hall, K., Vuong, T. and Scholey, J. M. (1993) Novel heterotrimeric kinesin-related protein purified from sea urchin eggs. Nature 366, 268–270.
46 Yoon, Y. J. and Mowry, K. L. (2004) *Xenopus* Staufen is a component of a ribonucleoprotein complex containing *Vg1* RNA and kinesin. Development 131, 3035–3045.
47 Betley, J. N., Heinrich, B., Vernos, I., Sardet, C., Prodon, F. and Deshler, J. O. (2004) Kinesin II mediates *Vg1* mRNA transport in *Xenopus* oocytes. Curr. Biol. 14, 219–224.
48 Weeks, D. L. and Melton, D. A. (1987) A maternal mRNA localized to the vegetal hemisphere in *Xenopus* eggs codes for a growth factor related to TGF-beta. Cell 51, 861–867.
49 Joseph, E. M. and Melton, D. A. (1998) Mutant Vg1 ligands disrupt endoderm and mesoderm formation in *Xenopus* embryos. Development 125, 2677–2685.
50 Thomsen, G. H. and Melton, D. A. (1993) Processed Vg1 protein is an axial mesoderm inducer in *Xenopus*. Cell 74, 433–441.
51 Dale, L., Matthews, G. and Colman, A. (1993) Secretion and mesoderm-inducing activity of the TGF-beta-related domain of *Xenopus* Vg1. EMBO J. 12, 4471–4480.
52 Tekotte, H. and Davis, I. (2002) Intracellular mRNA localization: motors move messages. Trends Genet. 18, 636–642.
53 Anderson, P. and Kedersha, N. (2006) RNA granules. J. Cell Biol. 172, 803–808.
54 Wong, R. W., Setou, M., Teng, J., Takei, Y. and Hirokawa, N. (2002) Overexpression of motor protein KIF17 enhances spatial and working memory in transgenic mice. Proc. Natl. Acad. Sci. USA 99, 14500–14505.
55 Ohashi, S., Koike, K., Omori, A., Ichinose, S., Ohara, S., Kobayashi, S., Sato, T. A. and Anzai, K. (2002) Identification of mRNA/protein (mRNP) complexes containing Pur-alpha, mStaufen, fragile X protein, and myosin Va and their association with rough endoplasmic reticulum equipped with a kinesin motor. J. Biol. Chem. 277, 37804–37810.
56 Szent-Györgyi, A. G. (2004) The early history of the biochemistry of muscle contraction. J. Gen. Physiol. 123, 631–641.
57 Thompson, R. F. and Langford, G. M. (2002) Myosin superfamily evolutionary history. Anat. Rec. 268, 276–289.
58 Furusawa, T., Ikawa, S., Yanai, N. and Obinata, M. (2000) Isolation of a novel PDZ-containing myosin from hematopoietic supportive bone marrow stromal cell lines. Biochem. Biophys. Res. Commun. 270, 67–75.
59 Hodge, T. and Cope, M. J. (2000) A myosin family tree. J. Cell Sci. 113, 3353–3354.
60 Goodson, H. V. and Spudich, J. A. (1993) Molecular evolution of the myosin family: relationships derived from comparisons of amino acid sequences. Proc. Natl. Acad. Sci. USA 90, 659–663.
61 Richards, T. A. and Cavalier-Smith, T. (2005) Myosin domain evolution and the primary divergence of eukaryotes. Nature 436, 1113–1118.
62 Foth, B. J., Goedecke, M. C. and Soldati, D. (2006) New insights into myosin evolution and classification. Proc. Natl. Acad. Sci. USA 103, 3681–3686.
63 Li, P., Yang, X., Wasser, M., Cai, Y. and Chia, W. (1997) Inscuteable and Staufen mediate asymmetric localization and segregation of *prospero* RNA during *Drosophila* neuroblast cell divisions. Cell 90, 437–447.
64 Broadus, J., Fuerstenberg, S. and Doe, C. Q. (1998) Staufen-dependent localization of *prospero* mRNA contributes to neuroblast daughter-cell fate. Nature 391, 792–795.
65 Schuldt, A. J., Adams, J. H., Davidson, C. M., Micklem, D. R., Haseloff, J., St Johnston, D. and Brand, A. H. (1998) Miranda mediates asymmetric protein and RNA localization in the developing nervous system. Genes Dev. 12, 1847–1857.
66 Shen, C. P., Knoblich, J. A., Chan, Y. M., Jiang, M. M., Jan, L. Y. and Jan, Y. N. (1998) Miranda as a multidomain adapter linking apically localized Inscuteable and basally localized Staufen and Prospero during asymmetric cell division in *Drosophila.* Genes Dev. 12, 1837–1846.
67 Matsuzaki, F., Ohshiro, T., Ikeshima-Kataoka, H. and Izumi, H. (1998) Miranda localizes Staufen and Prospero asymmetrically in mitotic neuroblasts and epithelial cells in early *Drosophila* embryogenesis. Development 125, 4089–4098.
68 Betschinger, J., Mechtler, K. and Knoblich, J. A. (2003) The Par complex directs asymmetric cell division by phosphorylating the cytoskeletal protein Lgl. Nature 422, 326–330.
69 Lee, C. Y., Wilkinson, B. D., Siegrist, S. E., Wharton, R. P. and Doe, C. Q. (2006) Brat is a Miranda cargo protein that promotes neuronal differentiation and inhibits neuroblast self-renewal. Dev. Cell 10, 441–449.
70 Petritsch, C., Tavosanis, G., Turck, C. W., Jan, L. Y. and Jan, Y. N. (2003) The *Drosophila* myosin VI Jaguar is required for basal protein targeting and correct spindle orientation in mitotic neuroblasts. Dev. Cell 4, 273–281.
71 Betschinger, J., Mechtler, K. and Knoblich, J. A. (2006) Asymmetric segregation of the tumor suppressor brat regulates self-renewal in *Drosophila* neural stem cells. Cell 124, 1241–1253.
72 Barros, C. S., Phelps, C. B. and Brand, A. H. (2003) *Drosophila* nonmuscle myosin II promotes the asymmetric segregation

of cell fate determinants by cortical exclusion rather than active transport. Dev. Cell 5, 829–840.
73 Slack, C., Somers, W. G., Sousa-Nunes, R., Chia, W. and Overton, P. M. (2006) A mosaic genetic screen for novel mutations affecting *Drosophila* neuroblast divisions. BMC Genet. 7, 33.
74 Lawrence, J. B. and Singer, R. H. (1986) Intracellular localization of messenger RNAs for cytoskeletal proteins. Cell 45, 407–415.
75 Condeelis, J. and Singer, R. H. (2005) How and why does *beta-actin* mRNA target? Biol. Cell 97, 97–110.
76 Kislauskis, E. H., Li, Z., Singer, R. H. and Taneja, K. L. (1993) Isoform-specific 3′-untranslated sequences sort alpha-cardiac and beta-cytoplasmic actin messenger RNAs to different cytoplasmic compartments. J. Cell Biol. 123, 165–172.
77 Ross, A. F., Oleynikov, Y., Kislauskis, E. H., Taneja, K. L. and Singer, R. H. (1997) Characterization of a *beta-actin* mRNA zipcode-binding protein. Mol. Cell Biol. 17, 2158–2165.
78 Farina, K. L., Hüttelmaier, S., Musunuru, K., Darnell, R. and Singer, R. H. (2003) Two ZBP1 KH domains facilitate beta-actin mRNA localization, granule formation, and cytoskeletal attachment. J. Cell Biol. 160, 77–87.
79 Latham, V. M., Yu, E. H., Tullio, A. N., Adelstein, R. S. and Singer, R. H. (2001) A Rho-dependent signaling pathway operating through myosin localizes *beta-actin* mRNA in fibroblasts. Curr. Biol. 11, 1010–1016.
80 Zhang, H. L., Eom, T., Oleynikov, Y., Shenoy, S. M., Liebelt, D. A., Dictenberg, J. B., Singer, R. H. and Bassell, G. J. (2001) Neurotrophin-induced transport of a *beta-actin* mRNP complex increases beta-actin levels and stimulates growth cone motility. Neuron 31, 261–275.
81 Bassell, G. J., Zhang, H., Byrd, A. L., Femino, A. M., Singer, R. H., Taneja, K. L., Lifshitz, L. M., Herman, I. M. and Kosik, K. S. (1998) Sorting of *beta-actin* mRNA and protein to neurites and growth cones in culture. J. Neurosci. 18, 251–265.
82 Shav-Tal, Y. and Singer, R. H. (2005) RNA localization. J. Cell Sci. 118, 4077–4081.
83 Jansen, R. P., Dowzer, C., Michaelis, C., Galova, M. and Nasmyth, K. (1996) Mother cell-specific HO expression in budding yeast depends on the unconventional myosin myo4p and other cytoplasmic proteins. Cell 84, 687–697.
84 Gonsalvez, G. B., Urbinati, C. R. and Long, R. M. (2005) RNA localization in yeast: moving towards a mechanism. Biol. Cell. 97, 75–86.
85 Bobola, N., Jansen, R. P., Shin, T. H. and Nasmyth, K. (1996) Asymmetric accumulation of Ash1p in postanaphase nuclei depends on a myosin and restricts yeast mating-type switching to mother cells. Cell 84, 699–709.
86 Sil, A. and Herskowitz, I. (1996) Identification of asymmetrically localized determinant, Ash1p, required for lineage-specific transcription of the yeast *HO* gene. Cell 84, 711–722.
87 Long, R. M., Singer, R. H., Meng, X., Gonzalez, I., Nasmyth, K. and Jansen, R. P. (1997) Mating type switching in yeast controlled by asymmetric localization of *ASH1* mRNA. Science 277, 383–387.
88 Takizawa, P. A., Sil, A., Swedlow, J. R., Herskowitz, I. and Vale, R. D. (1997) Actin-dependent localization of an RNA encoding a cell-fate determinant in yeast. Nature 389, 90–93.
89 Bertrand, E., Chartrand, P., Schaefer, M., Shenoy, S. M., Singer, R. H. and Long, R. M. (1998) Localization of *ASH1* mRNA particles in living yeast. Mol. Cell 2, 437–445.
90 Münchow, S., Sauter, C. and Jansen, R. P. (1999) Association of the class V myosin Myo4p with a localised messenger RNA in budding yeast depends on She proteins. J. Cell Sci. 112, 1511–1518.
91 Reck-Peterson, S. L., Tyska, M. J., Novick, P. J. and Mooseker, M. S. (2001) The yeast class V myosins, Myo2p and Myo4p, are nonprocessive actin-based motors. J. Cell. Biol. 153, 1121–1126.
92 Takizawa, P. A. and Vale, R. D. (2000) The myosin motor, Myo4p, binds *ASH1* mRNA via the adapter protein, She3p. Proc. Natl. Acad. Sci. USA 97, 5273–5278.
93 Böhl, F., Kruse, C., Frank, A., Ferring, D. and Jansen, R. P. (2000) She2p, a novel RNA-binding protein tethers *ASH1* mRNA to the Myo4p myosin motor via She3p. EMBO J. 19, 5514–5524.
94 Long, R. M., Gu, W., Lorimer, E., Singer, R. H. and Chartrand, P. (2000) She2p is a novel RNA-binding protein that recruits the Myo4p-She3p complex to *ASH1* mRNA. EMBO J. 19, 6592–6601.
95 Chartrand, P., Meng, X. H., Singer, R. H. and Long, R. M. (1999) Structural elements required for the localization of *ASH1* mRNA and of a green fluorescent protein reporter particle *in vivo*. Curr. Biol. 9, 333–336.
96 Gonzalez, I., Buonomo, S. B., Nasmyth, K. and von Ahsen, U. (1999) *ASH1* mRNA localization in yeast involves multiple secondary structural elements and Ash1 protein translation. Curr. Biol. 9, 337–340.
97 Chartrand, P., Meng, X. H., Hüttelmaier, S., Donato, D. and Singer, R. H. (2002) Asymmetric sorting of ash1p in yeast results from inhibition of translation by localization elements in the mRNA. Mol. Cell 10, 1319–1330.
98 Kruse, C., Jaedicke, A., Beaudouin, J., Böhl, F., Ferring, D., Güttler, T., Ellenberg, J. and Jansen, R. P. (2002) Ribonucleoprotein-dependent localization of the yeast class V myosin Myo4p. J. Cell Biol. 159, 971–982.
99 Gonsalvez, G. B., Little, J. L. and Long, R. M. (2004) *ASH1* mRNA anchoring requires reorganization of the Myo4p/She3p/She2p transport complex. J. Biol. Chem 279, 46286–46294.
100 Beach, D. L., Salmon, E. D. and Bloom, K. (1999) Localization and anchoring of mRNA in budding yeast. Curr. Biol. 9, 569–578.
101 Singer, R. H., Lawrence, D. S., Ovryn, B. and Condeelis, J. (2005) Imaging of gene expression in living cells and tissues. J. Biomed. Opt. 10, 051406.
102 Gu, W., Deng, Y., Zenklusen, D. and Singer, R. H. (2004) A new yeast PUF family protein, Puf6p, represses *ASH1* mRNA translation and is required for its localization. Genes Dev. 18, 1452–1465.
103 Irie, K., Tadauchi, T., Takizawa, P. A., Vale, R. D., Matsumoto, K. and Herskowitz, I. (2002) The Khd1 protein, which has three KH RNA-binding motifs, is required for proper localization of *ASH1* mRNA in yeast. EMBO J. 21, 1158–1167.
104 Haarer, B. K., Petzold, A., Lillie, S. H. and Brown, S. S. (1994) Identification of MYO4, a second class V myosin gene in yeast. J. Cell Sci. 107, 1055–1064.
105 Pashkova, N., Jin, Y., Ramaswamy, S. and Weisman, L. S. (2006) Structural basis for myosin V discrimination between distinct cargoes. EMBO J. 25, 693–700.
106 Itoh, T., Toh, E. A. and Matsui, Y. (2004) Mmr1p is a mitochondrial factor for Myo2p-dependent inheritance of mitochondria in the budding yeast. EMBO J. 23, 2520–2530.
107 Govindan, B., Bowser, R. and Novick, P. (1995) The role of Myo2, a yeast class V myosin, in vesicular transport. J. Cell Biol. 128, 1055–1068.
108 Hill, K. L., Catlett, N. L. and Weisman, L. S. (1996) Actin and myosin function in directed vacuole movement during cell division in *Saccharomyces cerevisiae*. J. Cell Biol. 135, 1535–1549.
109 Catlett, N. L. and Weisman, L. S. (1998) The terminal tail region of a yeast myosin-V mediates its attachment to vacuole membranes and sites of polarized growth. Proc. Natl. Acad. Sci. USA 95, 14799–14804.
110 Schott, D., Ho, J., Pruyne, D. and Bretscher, A. (1999) The COOH-terminal domain of Myo2p, a yeast myosin V, has a direct role in secretory vesicle targeting. J. Cell Biol. 147, 791–808.

111 Beach, D. L., Thibodeaux, J., Maddox, P., Yeh, E. and Bloom, K. (2000) The role of the proteins Kar9 and Myo2 in orienting the mitotic spindle of budding yeast. Curr. Biol. 10, 1497–1506.
112 Yin, H., Pruyne, D., Huffaker, T. C. and Bretscher, A. (2000) Myosin V orientates the mitotic spindle in yeast. Nature 406, 1013–1015.
113 Hoepfner, D., van den Berg, M., Philippsen, P., Tabak, H. F. and Hettema, E. H. (2001) A role for Vps1p, actin, and the Myo2p motor in peroxisome abundance and inheritance in *Saccharomyces cerevisiae*. J. Cell Biol. 155, 979–990.
114 Rossanese, O. W., Reinke, C. A., Bevis, B. J., Hammond, A. T., Sears, I. B., O'Connor, J. and Glick, B. S. (2001) A role for actin, Cdc1p, and Myo2p in the inheritance of late Golgi elements in *Saccharomyces cerevisiae*. J. Cell Biol. 153, 47–62.
115 Boldogh, I. R., Fehrenbacher, K. L., Yang, H. C. and Pon, L. A. (2005) Mitochondrial movement and inheritance in budding yeast. Gene 354, 28–36.
116 Fagarasanu, A., Fagarasanu, M., Eitzen, G. A., Aitchison, J. D. and Rachubinski, R. A. (2006) The peroxisomal membrane protein Inp2p is the peroxisome-specific receptor for the myosin V motor Myo2p of *Saccharomyces cerevisiae.* Dev. Cell 10, 587–600.
117 Niessing, D., Hüttelmaier, S., Zenklusen, D., Singer, R. H. and Burley, S. K. (2004) She2p is a novel RNA-binding protein with a basic helical hairpin motif. Cell 119, 491–502.
118 Gonsalvez, G. B., Lehmann, K. A., Ho, D. K., Stanitsa, E. S., Williamson, J. R. and Long, R. M. (2003) RNA-protein interactions promote asymmetric sorting of the *ASH1* mRNA ribonucleoprotein complex. RNA 9, 1383–1399.
119 Shepard, K. A., Gerber, A. P., Jambhekar, A., Takizawa, P. A., Brown, P. O., Herschlag, D., DeRisi, J. L. and Vale, R. D. (2003) Widespread cytoplasmic mRNA transport in yeast: identification of 22 bud-localized transcripts using DNA microarray analysis. Proc. Natl. Acad. Sci. USA 100, 11429–11434.
120 Takizawa, P. A., DeRisi, J. L., Wilhelm, J. E. and Vale, R. D. (2000) Plasma membrane compartmentalization in yeast by messenger RNA transport and a septin diffusion barrier. Science 290, 341–344.
121 Olivier, C., Poirier, G., Gendron, P., Boisgontier, A., Major, F. and Chartrand, P. (2005) Identification of a conserved RNA motif essential for She2p recognition and mRNA localization to the yeast bud. Mol. Cell Biol. 25, 4752–4766.
122 Jambhekar, A., McDermott, K., Sorber, K., Shepard, K. A., Vale, R. D., Takizawa, P. A. and DeRisi, J. L. (2005) Unbiased selection of localization elements reveals cis-acting determinants of mRNA bud localization in *Saccharomyces cerevisiae*. Proc. Natl. Acad. Sci. USA 102, 18005–18010.
123 Keene, J. D. and Tenenbaum, S. A. (2002) Eukaryotic mRNPs may represent posttranscriptional operons. Mol. Cell 9, 1161–1167.
124 Gerber, A. P., Luschnig, S., Krasnow, M. A., Brown, P. O. and Herschlag, D. (2006) Genome-wide identification of mRNAs associated with the translational regulator PUMILIO in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA 103, 4487–4492.
125 Gerber, A. P., Herschlag, D. and Brown, P. O. (2004) Extensive association of functionally and cytotopically related mRNAs with Puf family RNA-binding proteins in yeast. PLoS Biol. 2, 342–354.
126 Ule, J., Jensen, K. B., Ruggiu, M., Mele, A., Ule, A. and Darnell, R. B. (2003) CLIP identifies Nova-regulated RNA networks in the brain. Science 302, 1212–1215.
127 Estrada, P., Kim, J., Coleman, J., Walker, L., Dunn, B., Takizawa, P., Novick, P. and Ferro-Novick, S. (2003) Myo4p and She3p are required for cortical ER inheritance in *Saccharomyces cerevisiae*. J. Cell Biol. 163, 1255–1266.
128 Schmid, M., Jaedicke, A., Du, T.-D. and Jansen, R.-P. (2006) Coordination of endoplasmic reticulum and mRNA localization to the yeast bud. Curr. Biol. 16, 1538–1543.
129 Wilhelm, J. E., Buszczak, M. and Sayles, S. (2005) Efficient protein trafficking requires trailer hitch, a component of a ribonucleoprotein complex localized to the ER in *Drosophila.* Dev. Cell 9, 675–685.
130 Squirrell, J. M., Eggers, Z. T., Luedke, N., Saari, B., Grimson, A., Lyons, G. E., Anderson, P. and White, J. G. (2006) CAR-1, a protein that localizes with the mRNA decapping component DCAP-1, is required for cytokinesis and ER organization in *Caenorhabditis elegans* embryos. Mol. Biol. Cell 17, 336–344.
131 Lerner, R. S., Seiser, R. M., Zheng, T., Lager, P. J., Reedy, M. C., Keene, J. D. and Nicchitta, C. V. (2003) Partitioning and translation of mRNAs encoding soluble proteins on membrane-bound ribosomes. RNA 9, 1123–1137.
132 Alarcon, V. B. and Elinson, R. P. (2001) RNA anchoring in the vegetal cortex of the *Xenopus* oocyte. J. Cell Sci. 114, 1731–1741.
133 Wickham, L., Duchaine, T., Luo, M., Nabi, I. R. and DesGroseillers, L. (1999) Mammalian staufen is a double-stranded-RNA- and tubulin-binding protein which localizes to the rough endoplasmic reticulum. Mol. Cell Biol. 19, 2220–2230.
134 Gautrey, H., McConnell, J., Hall, J. and Hesketh, J. (2005) Polarised distribution of the RNA-binding protein Staufen in differentiated intestinal epithelial cells. FEBS. Lett. 579, 2226–2230.
135 Allison, R., Czaplinski, K., Git, A., Adegbenro, E., Stennard, F., Houliston, E. and Standart, N. (2004) Two distinct Staufen isoforms in *Xenopus* are vegetally localized during oogenesis. RNA 10, 1751–1763.
136 Long, R. M., Gu, W., Meng, X., Gonsalvez, G., Singer, R. H. and Chartrand, P. (2001) An exclusively nuclear RNA-binding protein affects asymmetric localization of *ASH1* mRNA and Ash1p in yeast. J. Cell Biol. 153, 307–318.
137 Kull, F. J., Vale, R. D. and Fletterick, R. J. (1998) The case for a common ancestor: kinesin and myosin motor proteins and G proteins. J. Muscle Res. Cell Motil. 19, 877–886.
138 Hüttelmaier, S., Zenklusen, D., Lederer, M., Dictenberg, J., Lorenz, M., Meng, X., Bassell, G. J., Condeelis, J. and Singer, R. H. (2005) Spatial regulation of beta-actin translation by Src-dependent phosphorylation of ZBP1. Nature 438, 512–555.