RNA localization

Yaron Shav-Tal and Robert H. Singer*

Department of Anatomy and Structural Biology and Cell Biology, Albert Einstein College of Medicine, Bronx, NY 10461, USA

*Author for correspondence (e-mail: rhsinger@aecom.yu.edu)

Journal of Cell Science 118, 4077-4081
Published by The Company of Biologists 2005
doi:10.1242/jcs.02543

Messenger RNA (mRNA) molecules are transcribed in the nucleus and then undergo export into the cytoplasm, where they are translated to produce proteins. Some mRNA transcripts do not immediately undergo translation but, instead, are directed to specific areas for local translation or distribution. This produces an asymmetric distribution of cytoplasmic proteins, providing localized activities in polarized cells or developing embryos. Studies of the localization process in various eukaryotic systems have unearthed numerous nuclear RNA-binding proteins (RBPs) involved. We present here some representative examples from different organisms.

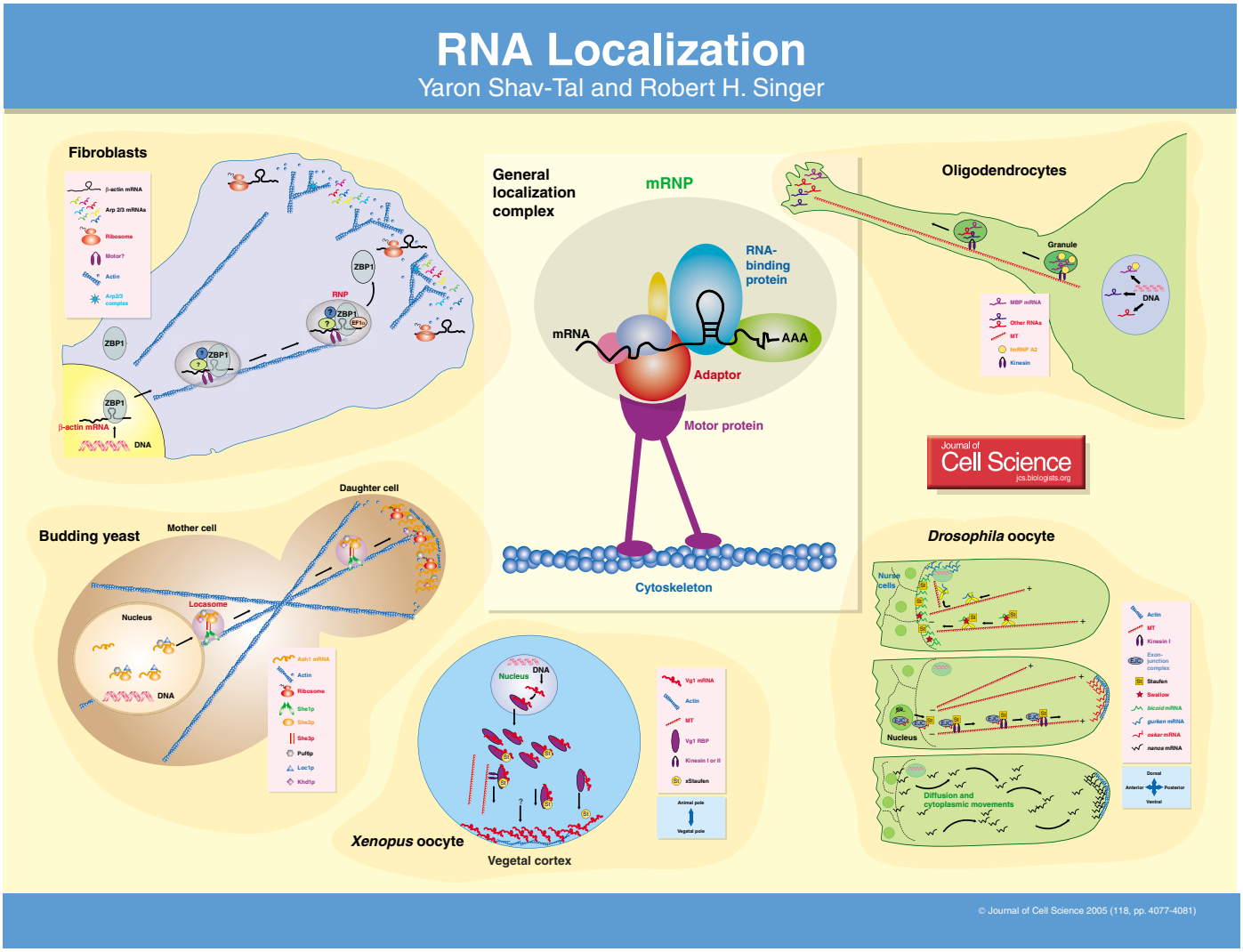
General features of mRNA localization systems

mRNA transcripts are coated by a variety of RBPs. Some of these are essential for mRNA localization and can be detected even when the mRNA is still nuclear. In many cases, specific sequence elements, 'zipcodes', in the untranslated region (UTR) form a secondary structure that serves as a docking site for the RBPs and thus promotes the localization process. Localizing mRNAs are shuttled to specific areas of the cell or the organism along cytoskeletal elements such as microtubules or actin filaments. They seem to be actively translocated by motor proteins of the myosin, kinesin and dynein families. Although our knowledge of the components of the mRNP complexes is growing, the list we give here is by no means comprehensive and merely a general impression of the multitude of interactions necessary for the localization process.

Mammalian cells

mRNA localization in fibroblasts

β-actin mRNA localization has been identified in several mammalian systems (Lawrence and Singer, 1986). In migrating fibroblasts, β-actin mRNA is



(See poster insert)

localized to the leading edge of the cells (Lawrence and Singer, 1986). This correlates with the elevated levels of β-actin protein required in lamellipodia, which depend on the rapid polymerization of actin for cell movement (Condeelis and Singer, 2005). Zipcode sequences (Kislauskis and Singer, 1992) immediately downstream of the stop codon (Kislauskis et al., 1993) recruit the zipcode-binding protein ZBP1 by interacting with its KH domains (Ross et al., 1997; Farina et al., 2003). ZBP1 and β-actin mRNA associate in the nucleus (Oleynikov and Singer, 2003) and travel in cytoplasmic granules to the leading edge. ZBP2, a predominantly nuclear protein, also binds the zipcode and affects localization (Gu et al., 2002). Translation is thought to be inhibited, perhaps by ZBP1, until the mRNA reaches the lamellipodia. β-actin-containing granules are transported on actin filaments (Sundell and Singer, 1991) and might anchor at specific sites through interactions with EF1α (Liu et al., 2002). The responsible motor is unidentified, although inhibition of myosin activity does disrupt the process (Latham et al., 2001).

The formation of the branched actin cytoskeleton at the protruding edge of migrating fibroblasts requires the Arp2/3 complex (Machesky et al., 1994). This seven-subunit complex (Machesky et al., 1997; Mullins et al., 1997; Welch et al., 1997), caps the slow-growing ends of actin filaments, while stabilizing the fast-growing polymerizing ends. The seven mRNAs that encode Arp2/3 subunits are all localized to the leading edge of fibroblasts, which supports the idea that localized translation of functionally-related mRNAs is coupled to the assembly of complexes (Mingle et al., 2005).

mRNA localization in the neuronal system

mRNA localization mechanisms also allow local translation in the extremities (dendrites and axons) of cells from the neuronal system (Job and Eberwine, 2001). The mRNAs typically travel from the cell body in granules that contain several copies of the mRNA or several types of mRNA. Myelin basic protein (MBP) mRNAs, for example, are targeted to the myelin membranes of oligodendrocyte cell processes (Ainger et al., 1993). They probably associate with microtubules through a kinesin motor (Carson et al., 1997) and are bound by the RNA-binding protein hnRNP A2 (Hoek et al., 1998). Other examples are localization of CamKIIα mRNA by kinesin in hippocampal dendrites (Kanai et al., 2004; Rook et al., 2000) and translocation of tau mRNA on microtubules in axons, in which a relative of ZBP1, IMP-1, is involved (Atlas et al., 2004). β-actin mRNA is localized to neuronal growth cones and hippocampal dendrites through similar association with ZBP1 (Bassell et al., 1998; Eom et al., 2003). Long-distance translocation occurs along microtubules (Zhang et al., 2001), using an unidentified motor protein, probably kinesin (our unpublished data). Since the distance between dendrites or axons and the cell nucleus can be extremely large, this localization mechanism allows rapid translational responses that are independent of the ongoing transcription in the nucleus.

Budding yeast

Actin-based translocation of localized mRNAs also occurs in yeast (Darzacq et al., 2003; Gonsalvez et al., 2005). In budding yeast, many RNAs translocate from the mother cell into the budding daughter cell and concentrate at the bud tip (Shepard et al., 2003). One of the best studied examples is *ASH1* mRNA (Long et al., 1997; Takizawa et al., 1997). Ash1p is a nuclear DNA-binding protein required for control of mating-type switching, and its asymmetric distribution causes the repression of *HO* endonuclease expression only in the daughter cell (Bobola et al., 1996; Sil and Herskowitz, 1996). *ASH1* RNA is moved along actin filaments by a type V myosin, She1p/Myo4p, as part of an RNP complex termed the locasome (Beach et al., 1999; Bertrand et al., 1998). She2p is an RBP that binds to the *ASH1* mRNA zipcode sequences in the nucleus, accompanies the mRNA in the cytoplasm (Bohl et al., 2000; Long et al., 2000; Niessing et al., 2004) and bridges the connection to the motor via She3p (Takizawa and Vale, 2000). Once at the bud tip, *ASH1* mRNA might be anchored to cortical actin. The Puf6p protein interacts directly with the *ASH1* mRNA and represses its translation during translocation to the daughter cell (Gu et al., 2004). Because Puf6p is nuclear, it might associate with *ASH1* mRNA in the nucleus. Khd1p is a component of the locasome and localizes with *ASH1* mRNA at the bud tip and also inhibits translation (Irie et al., 2002). Loc1p is another nuclear protein that associates with *ASH1* mRNA and might be important for mRNP assembly (Long et al., 2001).

Xenopus

Several mRNAs are localized to the different poles of *Xenopus* oocytes (Kloc and Etkin, 2005). The unequal distribution of specific mRNAs results in the development of unique daughter cells, providing a means by which germ cell lineages are defined and the primary axis for development is established. Vg1 protein is a member of the transforming growth factor β (TGFβ) superfamily and has roles in mesoderm and endoderm development. Vg1 mRNA is localized to a tight region in the vegetal cortex of frog oocytes during oogenesis (Melton, 1987). It harbors a zipcode (Mowry and Melton, 1992) that interacts with the protein Vg1-RBP/Vera (Deshler et al., 1998; Havin et al., 1998; Schwartz et al., 1992) through its KH domains (Git and Standart, 2002) and mediates association with microtubules (Elisha et al., 1995). *Xenopus* Vg1-RBP/Vera is highly related to mammalian ZBP1, and both are part of a family of closely related RBPs involved in RNA regulation (Yisraeli, 2005). Movement of Vg1 mRNA along microtubules (Yisraeli et al., 1990) could involve kinesin motors and the Staufen RBP (see below) (Allison et al., 2004; Betley et al., 2004; Yoon and Mowry, 2004). Interestingly, during these stages of *Xenopus* development most of the microtubules have their plus ends pointed towards the nucleus (Pfeiffer and Gard, 1999), and therefore it remains unclear how mRNAs localize in the opposite direction (Kloc and Etkin, 2005). Other transport mechanisms might exist – for instance, the association of Vg1 mRNA with ER-membrane vesicles (Deshler et al., 1997).

Several other proteins have also been implicated as being part of the zipcode-binding localization complex: VgRBP60/PTB/hnRNP I (Cote et al., 1999); Prrp (Zhao et al., 2001); xStau (Yoon and Mowry, 2004); VgRBP71 (Kroll et al., 2002); 40LoVe (Czaplinski et al., 2005). Some of these, like ZBP2, are predominantly nuclear, which suggests a nuclear connection for cytoplasmic localization (Farina and Singer, 2002; Kress et al., 2004).

Drosophila

Localization of *nanos*, *oskar*, *bicoid* and *gurken* mRNAs during oogenesis

Localized translation is controlled spatially and temporally in specified areas in *Drosophila* oocytes and embryos. In the oocyte, *nanos* mRNA is localized to the posterior during development, and Nanos protein is required for the formation of the anterior-posterior body axis (Gavis and Lehmann, 1992; Tautz, 1988). Most *nanos* mRNA does not localize and is translationally repressed (Bergsten and Gavis, 1999) or degraded (Bashirullah et al., 1999). Posterior-localized *nanos* mRNA, however, is stable and translated. The localization of *nanos* mRNA occurs late in oogenesis when the nurse cells release their cytoplasmic contents and the mRNA moves into the oocyte. In contrast to other systems, *nanos* mRNA seems to move by diffusion, enhanced by microtubule-dependent cytoplasmic streaming, to the posterior region, where it is anchored to the actin cytoskeleton (Forrest and Gavis, 2003). *nanos* mRNA contains several regions in its 3′ UTR that are required for its localization (Dahanukar and Wharton, 1996; Gavis et al., 1996). One stem-loop element is bound by the Smaug protein (Smg), which acts in translational repression of Nanos (Crucs et al., 2000; Dahanukar et al., 1999; Smibert et al., 1996).

The localization of *nanos* mRNA requires the Oskar protein (Ephrussi et al., 1991). *oskar* mRNA is also localized to the posterior of the embryo and is one of the first molecules to be recruited – probably by a kinesin-I-based mechanism (Brendza et al., 2000). Although *oskar* mRNA has a 3′ UTR that is required for its localization (Kim-Ha et al., 1993), protein components of the exon-junction-complex (EJC) accompany the mRNA from the nucleus to its destination (Hachet and Ephrussi, 2001; Mohr et al., 2001), and the splicing reaction itself may be necessary for *oskar* mRNA localization (Hachet and Ephrussi, 2004). Several other trans-acting factors required have been identified. Staufen, for example, is an RBP that colocalizes with *oskar* mRNA at the posterior pole and is required for its localization and translation (Micklem et al., 2000; Rongo et al., 1995; St Johnston et al., 1991).

Staufen is necessary for the localization of another *Drosophila* mRNA, *bicoid*, to the anterior pole during late stages of oogenesis (St Johnston et al., 1991), interacting with stem-loop structures in the 3′ UTR of this mRNA (Ferrandon et al., 1994). Bicoid is a transcription factor that diffuses from the anterior pole to form a gradient throughout the embryo. During earlier stages of oogenesis, *bicoid* localization depends on the Exuperantia protein (St Johnston et al., 1989) and then on Swallow protein for anterior anchoring (Stephenson et al., 1988). *bicoid* mRNA is transcribed in the oocyte nurse cells and then translocates into the oocyte, where it moves along microtubules (Cha et al., 2001), connecting through Swallow to a dynein motor (Duncan and Warrior, 2002; Januschke et al., 2002; Schnorrer et al., 2000).

Dynein also moves *gurken* mRNA along microtubules to the anterior; there it changes direction moving towards the oocyte nucleus, where it localizes (MacDougall et al., 2003). The localization of Gurken, the *Drosophila* homologue of transforming growth factor α (TGFα), is important for the establishment of both the antero-posterior and the dorso-ventral axes.

Localization in the embryo

Later stages of *Drosophila* development also require RNA localization events, which occur after the setting of anterior-posterior protein gradients in the oocyte. In the blastoderm embryo, gap genes are located in broad segments along the anterior-posterior axis, yielding local mRNA expression and protein translation. The differences in concentrations of gap gene products such as Krüppel, Hunchback and Giant give rise to embryo segmentation in conjunction with localized expression of pair-rule genes. The pair-rule genes *ftz*, *hairy* and *runt* are expressed in a segmental seven-stripe pattern in the syncytial embryo (Davis and Ish-Horowicz, 1991). When transcribed, these transcripts diffuse into the cytoplasm in all directions and later localize to their correct positions in RNA particles, moving on microtubules by dynein motors (Wilkie and Davis, 2001). Two other proteins, Bicaudal-D (BicD) and Egalitarian (Egl), are important for dynein-mediated transport of localized mRNAs both in the oocyte and the embryo (Bullock and Ish-Horowicz, 2001). Egl binds to dynein light chain and to BicD and might bridge the connection between the motor and RNA cargo (Mach and Lehmann, 1997; Navarro et al., 2004).

Outlook

The list of mRNAs known to be localized now stands at well over 100. In neurons alone, the number is probably even higher. Many questions remain: what are the complex motor systems that transport mRNAs and how do they ‘choose’ their respective cargos and cytoskeletal tracks, do mRNAs commit to localization in the nucleus, which proteins cooperate in the assembly of localization granules, which mRNAs are co-transported in the same granules and how is the translation of these mRNAs regulated? The combination of molecular and protein strategies in conjunction with live-cell imaging techniques should bring us closer to understanding the different mechanisms of mRNA localization and how they evolved in various species. For instance, following single, localizing mRNAs indicates that events involving RNA diffusion, assembly of motor complexes and interaction with cytoskeletal filaments are all probabilistic. Having a zipcode increases the probability of each of those events that lead to localization (Fusco et al., 2003). Further analysis of these factors at the molecular level will be an important next step in decoding the localization process.

References

Ainger, K., Avossa, D., Morgan, F., Hill, S. J., Barry, C., Barbarese, E. and Carson, J. H. (1993). Transport and localization of exogenous myelin basic protein mRNA microinjected into oligodendrocytes. *J. Cell Biol.* **123**, 431-441.

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.

Atlas, R., Behar, L., Elliott, E. and Ginzburg, I. (2004). The insulin-like growth factor mRNA binding-protein IMP-1 and the Ras-regulatory protein G3BP associate with tau mRNA and HuD protein in differentiated P19 neuronal cells. *J. Neurochem.* **89**, 613-626.

Bashirullah, A., Halsell, S. R., Cooperstock, R. L., Kloc, M., Karaiskakis, A., Fisher, W. W., Fu, W., Hamilton, J. K., Etkin, L. D. and Lipshitz, H. D. (1999). Joint action of two RNA degradation pathways controls the timing of maternal transcript elimination at the midblastula transition in Drosophila melanogaster. *EMBO J.* **18**, 2610-2620.

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.

Beach, D. L., Salmon, E. D. and Bloom, K. (1999). Localization and anchoring of mRNA in budding yeast. *Curr. Biol.* **9**, 569-578.

Bergsten, S. E. and Gavis, E. R. (1999). Role for mRNA localization in translational activation but not spatial restriction of nanos RNA. *Development* **126**, 659-669.

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.

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.

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.

Bohl, 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.

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.

Bullock, S. L. and Ish-Horowicz, D. (2001). Conserved signals and machinery for RNA transport in Drosophila oogenesis and embryogenesis. *Nature* **414**, 611-616.

Carson, J. H., Worboys, K., Ainger, K. and Barbarese, E. (1997). Translocation of myelin basic protein mRNA in oligodendrocytes requires microtubules and kinesin. *Cell Motil. Cytoskel.* **38**, 318-328.

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.

Condeelis, J. and Singer, R. H. (2005). How and why does beta-actin mRNA target? *Biol. Cell* **97**, 97-110.

Cote, C. A., Gautreau, D., Denegre, J. M., Kress, T. L., Terry, N. A. and Mowry, K. L. (1999). A Xenopus protein related to hnRNP I has a role in cytoplasmic RNA localization. *Mol. Cell* **4**, 431-437.

Crucs, S., Chatterjee, S. and Gavis, E. R. (2000). Overlapping but distinct RNA elements control repression and activation of nanos translation. *Mol. Cell* **5**, 457-467.

Czaplinski, K., Kocher, T., Schelder, M., Segref, A., Wilm, M. and Mattaj, I. W. (2005). Identification of 40LoVe, a Xenopus hnRNP D family protein involved in localizing a TGF-beta-related mRNA during oogenesis. *Dev. Cell* **8**, 505-515.

Dahanukar, A. and Wharton, R. P. (1996). The Nanos gradient in Drosophila embryos is generated by translational regulation. *Genes Dev.* **10**, 2610-2620.

Dahanukar, A., Walker, J. A. and Wharton, R. P. (1999). Smaug, a novel RNA-binding protein that operates a translational switch in Drosophila. *Mol. Cell* **4**, 209-218.

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.

Davis, I. and Ish-Horowicz, D. (1991). Apical localization of pair-rule transcripts requires 3′ sequences and limits protein diffusion in the Drosophila blastoderm embryo. *Cell* **67**, 927-940.

Deshler, J. O., Highett, M. I. and Schnapp, B. J. (1997). Localization of Xenopus Vg1 mRNA by Vera protein and the endoplasmic reticulum. *Science* **276**, 1128-1131.

Deshler, J. O., Highett, M. I., Abramson, T. and Schnapp, B. J. (1998). A highly conserved RNA-binding protein for cytoplasmic mRNA localization in vertebrates. *Curr. Biol.* **8**, 489-496.

Duncan, J. E. and Warrior, R. (2002). The cytoplasmic dynein and kinesin motors have interdependent roles in patterning the Drosophila oocyte. *Curr. Biol.* **12**, 1982-1991.

Elisha, Z., Havin, L., Ringel, I. and Yisraeli, J. K. (1995). Vg1 RNA binding protein mediates the association of Vg1 RNA with microtubules in Xenopus oocytes. *EMBO J.* **14**, 5109-5114.

Eom, T., Antar, L. N., Singer, R. H. and Bassell, G. J. (2003). Localization of a beta-actin messenger ribonucleoprotein complex with zipcode-binding protein modulates the density of dendritic filopodia and filopodial synapses. *J. Neurosci.* **23**, 10433-10444.

Ephrussi, A., Dickinson, L. K. and Lehmann, R. (1991). Oskar organizes the germ plasm and directs localization of the posterior determinant nanos. *Cell* **66**, 37-50.

Farina, K. L. and Singer, R. H. (2002). The nuclear connection in RNA transport and localization. *Trends Cell Biol.* **12**, 466-472.

Farina, K. L., Huttelmaier, 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.

Ferrandon, D., Elphick, L., Nusslein-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.

Forrest, K. M. and Gavis, E. R. (2003). Live imaging of endogenous RNA reveals a diffusion and entrapment mechanism for nanos mRNA localization in Drosophila. *Curr. Biol.* **13**, 1159-1168.

Fusco, D., Accornero, N., Lavoie, B., Shenoy, S. M., Blanchard, J. M., Singer, R. H. and Bertrand, E. (2003). Single mRNA Molecules demonstrate probabilistic movement in living mammalian cells. *Curr. Biol.* **13**, 161-167.

Gavis, E. R. and Lehmann, R. (1992). Localization of nanos RNA controls embryonic polarity. *Cell* **71**, 301-313.

Gavis, E. R., Curtis, D. and Lehmann, R. (1996). Identification of cis-acting sequences that control nanos RNA localization. *Dev. Biol.* **176**, 36-50.

Git, A. and Standart, N. (2002). The KH domains of Xenopus Vg1RBP mediate RNA binding and self-association. *RNA* **8**, 1319-1333.

Gonsalvez, G. B., Urbinati, C. R. and Long, R. M. (2005). RNA localization in yeast: moving towards a mechanism. *Biol. Cell* **97**, 75-86.

Gu, W., Pan, F., Zhang, H., Bassell, G. J. and Singer, R. H. (2002). A predominantly nuclear protein affecting cytoplasmic localization of beta-actin mRNA in fibroblasts and neurons. *J. Cell Biol.* **156**, 41-51.

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.

Hachet, O. and Ephrussi, A. (2001). Drosophila Y14 shuttles to the posterior of the oocyte and is required for oskar mRNA transport. *Curr. Biol.* **11**, 1666-1674.

Hachet, O. and Ephrussi, A. (2004). Splicing of oskar RNA in the nucleus is coupled to its cytoplasmic localization. *Nature* **428**, 959-963.

Havin, L., Git, A., Elisha, Z., Oberman, F., Yaniv, K., Schwartz, S. P., Standart, N. and Yisraeli, J. K. (1998). RNA-binding protein conserved in both microtubule- and microfilament-based RNA localization. *Genes Dev.* **12**, 1593-1598.

Hoek, K. S., Kidd, G. J., Carson, J. H. and Smith, R. (1998). hnRNP A2 selectively binds the cytoplasmic transport sequence of myelin basic protein mRNA. *Biochemistry* **37**, 7021-7029.

Huang, Y. S. and Richter, J. D. (2004). Regulation of local mRNA translation. *Curr. Opin. Cell Biol.* **16**, 308-313.

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.

Januschke, J., Gervais, L., Dass, S., Kaltschmidt, J. A., Lopez-Schier, H., St Johnston, D., Brand, A. H., Roth, S. and Guichet, A. (2002). Polar transport in the Drosophila oocyte requires Dynein and Kinesin I cooperation. *Curr. Biol.* **12**, 1971-1981.

Job, C. and Eberwine, J. (2001). Localization and translation of mRNA in dendrites and axons. *Nat. Rev. Neurosci.* **2**, 889-898.

Kanai, Y., Dohmae, N. and Hirokawa, N. (2004). Kinesin transports RNA: isolation and characterization of an RNA-transporting granule. *Neuron* **43**, 513-525.

Kim-Ha, J., Webster, P. J., Smith, J. L. and Macdonald, P. M. (1993). Multiple RNA regulatory elements mediate distinct steps in localization of oskar mRNA. *Development* **119**, 169-178.

Kislauskis, E. H. and Singer, R. H. (1992).

Determinants of mRNA localization. *Curr. Opin. Cell Biol.* **4**, 975-978.
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.
Kloc, M. and Etkin, L. D. (2005). RNA localization mechanisms in oocytes. *J. Cell Sci.* **118**, 269-282.
Kress, T. L., Yoon, Y. J. and Mowry, K. L. (2004). Nuclear RNP complex assembly initiates cytoplasmic RNA localization. *J. Cell Biol.* **165**, 203-211.
Kroll, T. T., Zhao, W. M., Jiang, C. and Huber, P. W. (2002). A homolog of FBP2/KSRP binds to localized mRNAs in Xenopus oocytes. *Development* **129**, 5609-5619.
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.
Lawrence, J. B. and Singer, R. H. (1986). Intracellular localization of messenger RNAs for cytoskeletal proteins. *Cell* **45**, 407-415.
Liu, G., Grant, W. M., Persky, D., Latham, V. M., Jr, Singer, R. H. and Condeelis, J. (2002). Interactions of elongation factor 1alpha with F-actin and beta-actin mRNA: implications for anchoring mRNA in cell protrusions. *Mol. Biol. Cell* **13**, 579-592.
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.
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.
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.
MacDougall, N., Clark, A., MacDougall, E. and Davis, I. (2003). Drosophila gurken (TGFalpha) mRNA localizes as particles that move within the oocyte in two dynein-dependent steps. *Dev. Cell* **4**, 307-319.
Mach, J. M. and Lehmann, R. (1997). An Egalitarian-BicaudalD complex is essential for oocyte specification and axis determination in Drosophila. *Genes Dev.* **11**, 423-435.
Machesky, L. M., Atkinson, S. J., Ampe, C., Vandekerckhove, J. and Pollard, T. D. (1994). Purification of a cortical complex containing two unconventional actins from Acanthamoeba by affinity chromatography on profilin-agarose. *J. Cell Biol.* **127**, 107-115.
Machesky, L. M., Reeves, E., Wientjes, F., Mattheyse, F. J., Grogan, A., Totty, N. F., Burlingame, A. L., Hsuan, J. J. and Segal, A. W. (1997). Mammalian actin-related protein 2/3 complex localizes to regions of lamellipodial protrusion and is composed of evolutionarily conserved proteins. *Biochem. J.* **328**, 105-112.
Melton, D. A. (1987). Translocation of a localized maternal mRNA to the vegetal pole of Xenopus oocytes. *Nature* **328**, 80-82.
Micklem, D. R., Adams, J., Grunert, S. and St Johnston, D. (2000). Distinct roles of two conserved Staufen domains in oskar mRNA localization and translation. *EMBO J.* **19**, 1366-1377.
Mingle, L. A., Okuhama, N. N., Shi, J., Singer, R. H., Condeelis, J. and Liu, G. (2005). Localization of all seven messenger RNAs for the actin-polymerization nucleator Arp2/3 complex in the protrusions of fibroblasts. *J. Cell Sci.* **118**, 2425-2433.
Mohr, S. E., Dillon, S. T. and Boswell, R. E. (2001). The RNA-binding protein Tsunagi interacts with Mago Nashi to establish polarity and localize oskar mRNA during Drosophila oogenesis. *Genes Dev.* **15**, 2886-2899.
Mowry, K. L. and Melton, D. A. (1992). Vegetal messenger RNA localization directed by a 340-nt RNA sequence element in Xenopus oocytes. *Science* **255**, 991-994.
Mullins, R. D., Stafford, W. F. and Pollard, T. D. (1997). Structure, subunit topology, and actin-binding activity of the Arp2/3 complex from Acanthamoeba. *J. Cell Biol.* **136**, 331-343.
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**, 427-335.
Niessing, D., Huttelmaier, 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.
Oleynikov, Y. and Singer, R. H. (2003). Real-time visualization of ZBP1 association with beta-actin mRNA during transcription and localization. *Curr. Biol.* **13**, 199-207.
Pfeiffer, D. C. and Gard, D. L. (1999). Microtubules in Xenopus oocytes are oriented with their minus-ends towards the cortex. *Cell Motil. Cytoskeleton* **44**, 34-43.
Rongo, C., Gavis, E. R. and Lehmann, R. (1995). Localization of oskar RNA regulates oskar translation and requires Oskar protein. *Development* **121**, 2737-2746.
Rook, M. S., Lu, M. and Kosik, K. S. (2000). CaMKIIalpha 3′ untranslated region-directed mRNA translocation in living neurons: visualization by GFP linkage. *J. Neurosci.* **20**, 6385-6893.
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.
Schnorrer, F., Bohmann, K. and Nusslein-Volhard, C. (2000). The molecular motor dynein is involved in targeting swallow and bicoid RNA to the anterior pole of Drosophila oocytes. *Nat. Cell Biol.* **2**, 185-190.
Schwartz, S. P., Aisenthal, L., Elisha, Z., Oberman, F. and Yisraeli, J. K. (1992). A 69-kDa RNA-binding protein from Xenopus oocytes recognizes a common motif in two vegetally localized maternal mRNAs. *Proc. Natl. Acad. Sci. USA* **89**, 11895-11899.
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.
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.
Smibert, C. A., Wilson, J. E., Kerr, K. and Macdonald, P. M. (1996). smaug protein represses translation of unlocalized nanos mRNA in the Drosophila embryo. *Genes Dev.* **10**, 2600-2609.
St Johnston, D., Driever, W., Berleth, T., Richstein, S. and Nusslein-Volhard, C. (1989). Multiple steps in the localization of bicoid RNA to the anterior pole of the Drosophila oocyte. *Development* **107**, 13-19.
St Johnston, D., Beuchle, D. and Nusslein-Volhard, C. (1991). Staufen, a gene required to localize maternal RNAs in the Drosophila egg. *Cell* **66**, 51-63.
Stephenson, E. C., Chao, Y. C. and Fackenthal, J. D. (1988). Molecular analysis of the swallow gene of Drosophila melanogaster. *Genes Dev.* **2**, 1655-1665.
Sundell, C. L. and Singer, R. H. (1991). Requirement of microfilaments in sorting of actin messenger RNA. *Science* **253**, 1275-1277.
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.
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.
Tautz, D. (1988). Regulation of the Drosophila segmentation gene hunchback by two maternal morphogenetic centres. *Nature* **332**, 281-284.
Welch, M. D., Iwamatsu, A. and Mitchison, T. J. (1997). Actin polymerization is induced by Arp2/3 protein complex at the surface of Listeria monocytogenes. *Nature* **385**, 265-269.
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.
Yisraeli, J. K. (2005). VICKZ proteins: a multi-talented family of regulatory RNA-binding proteins. *Biol. Cell* **97**, 87-96.
Yisraeli, J. K., Sokol, S. and Melton, D. A. (1990). A two-step model for the localization of maternal mRNA in Xenopus oocytes: involvement of microtubules and microfilaments in the translocation and anchoring of Vg1 mRNA. *Development* **108**, 289-298.
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.
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.
Zhao, W. M., Jiang, C., Kroll, T. T. and Huber, P. W. (2001). A proline-rich protein binds to the localization element of Xenopus Vg1 mRNA and to ligands involved in actin polymerization. *EMBO J.* **20**, 2315-2325.

Cell Science at a Glance on the Web
Electronic copies of the poster insert are available in the online version of this article at jcs.biologists.org. The JPEG images can be downloaded for printing or used as slides.

Journal of Cell Science