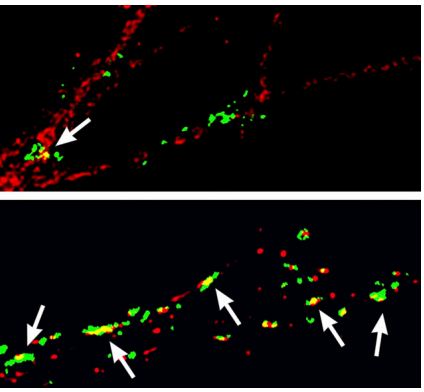
In This Issue



LSm1 protein (red) delivers mRNA to synapses (green) after glutamate receptor stimulation (bottom).

mRNP transport starts in the nucleus

A family of proteins involved in RNA degradation plays an unexpected role in transporting mRNAs out of the nucleus and directing them to neuronal dendrites for translation, report di Penta et al.

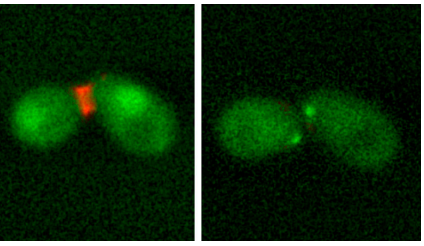
mRNAs encoding synaptic proteins are targeted to dendrites in the form of messenger ribonucleoprotein (mRNP) complexes. mRNA expression is silenced until the stimulation of synapses activates their translation into proteins that change synaptic strength, allowing neurons to record long-term memories and learning. But little is known about how and when mRNPs destined for dendrites are assembled.

Proteins involved in mRNA degradation would be last on a list of possible candidates for transporting mRNPs to synapses. But di Penta et al. had been studying one such degradation protein called LSm1 and found that in neurons the protein localized to dendrites—far away from the cell body where LSm proteins promote mRNA decay. The researchers' surprise and interest grew when they discovered that LSm1 was associated with mRNAs that localize to dendrites, and that these transcripts were not being degraded.

But, according to author Tilmann Achsel, the team was only convinced that LSm1 was involved in dendritic transport when they found that LSm1-mRNP complexes contained a cap-binding protein, indicating an intact 5′ end of the mRNA. This factor turned out to be the nuclear mRNA cap-binding protein CBP80, indicating that the LSm1-containing mRNP complexes had been assembled in the nucleus. The team showed that after nuclear export and transport to dendrites, the complexes delivered their mRNAs directly to the synapses for translation after synaptic stimulation.

Achsel says that the decision to transport mRNPs to dendrites is made in the nucleus when the complex is first assembled. Intriguingly, the LSm1-mRNP complex also localizes to the axons of spinal cord motor neurons and additionally contains a protein called SMN that is linked to spinal muscular atrophy. Achsel and colleagues are now interested in how this mRNP is involved in axonal development, and whether compromising its function results in disease.

di Penta, A., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200807033.



Fus2p (green) localizes to the nucleus (left) until after cell division, when it moves to the mating cell tips (right).

Cell cycle keeps Fus2p in check before yeast mate

Ydenberg and Rose show that yeast cells use both pheromone signaling and the cell cycle to ensure that a protein important for mating only operates at the right time and place.

When haploid yeast cells sense pheromones from an opposite mating type, they differentiate by inducing expression of mating-specific genes, arresting in the G1 phase of the cell cycle, and sending out protrusions called "shmoos" toward the source of the pheromone. One induced protein, Fus2p, initially localizes to the nucleus but moves to the shmoo tip after cell cycle arrest to mediate mating-cell fusion. Fus2p's expression and localization depends on the pheromone-activated MAP kinase Fus3p. But how Fus3p targets Fus2p to the shmoo tip, and why this only occurs after G1 arrest was unknown.

Ydenberg and Rose found that Fus3p directly phosphorylated Fus2p to promote its localization to the cytoplasm, but Fus2p always remained nuclear until after cell division. The cell cycle–regulated, cyclin-dependent kinase Cdc28p modulates the yeast response to pheromones, so the authors reasoned that it might control Fus2p's whereabouts by counteracting Fus3p. Indeed, they found that Cdc28p opposes Fus3p in two different ways, depending on which stage of the cell cycle the yeast are at.

In late G1 and S phase, it was already known that Cdc28p prevented the activation of Fus3p by pheromones. Later in the cell cycle, at G2/M phase, pheromone signaling and Fus3p were fully active but Cdc28p still prevented Fus2p from exiting the nucleus by an unknown mechanism. Only after cell division and G1 arrest was Cdc28p activity low enough for Fus3p to promote Fus2p's redistribution to the cytoplasm and shmoo tip.

Why do yeast regulate Fus2p's localization using both pheromone and cell cycle–regulated pathways? Ydenberg and Rose think that it may be vital for Fus2p to remain sequestered in the nucleus until after cell division so that it can't interfere with cytokinesis: Fus2p is likely to be an activator of Rho GTPases, so localizing it to the wrong place at the wrong time might have disastrous consequences for the cell. Differentiating cells in higher eukaryotes face similar problems as they turn on genes not normally expressed during the mitotic cycle. To safely differentiate, the authors suspect that other eukaryotes have evolved similar solutions to those used by mating yeast.

Ydenberg, C.A., and M.D. Rose. 2009. *J. Cell Biol.* doi:10.1083/jcb.200809066.

Text by Ben Short
bshort@rockefeller.edu

Mitotic spindle ties the Golgi ribbon

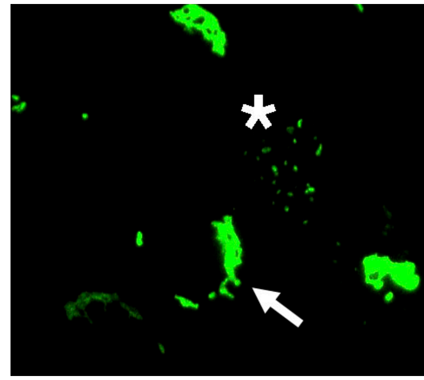
It seems that the mitotic spindle is important for segregating more than just a cell's chromosomes. Wei and Seemann reveal how a dividing cell uses the spindle to ensure that both of its daughter cells inherit a fully functional Golgi apparatus.

In mammalian cells, individual Golgi stacks assemble together into a single continuous ribbon. This is important for cell polarity and migration because the entire ribbon can be oriented to direct membrane traffic to a specific site within the cell. At the beginning of mitosis, the Golgi fragments into small tubules and vesicles that cluster around the spindle poles. The fragments then separate into the daughter cells before reforming the ribbon, but it wasn't known whether the spindle machinery was actually required for their partition.

Wei and Seemann took a difficult but direct approach to investigating this question: they made cells without mitotic spindles. Using a nifty series of manipulations, the authors were able to make cells divide so that one daughter received none of the spindle and therefore ended up with no DNA, no centrosomes, and no microtubules. Surprisingly, these unfortunate cells did contain small, scattered Golgi stacks capable of secreting protein, but the stacks weren't organized into a larger ribbon structure. The ribbon could be reassembled in these cells, however, if they were provided with a protein extract prepared from purified Golgi and some tubulin to make microtubules. Alternatively, allowing cells to inherit just a little bit of the mitotic spindle also enabled them to form a Golgi ribbon.

The researchers think that while Golgi stacks are inherited independently of the spindle, certain Golgi proteins essential for building the ribbon are segregated using the mitotic machinery, ensuring that both daughters can form a Golgi ribbon and polarize their membrane transport. The next challenge is to identify what these "ribbon determinants" are. The team already knows that the Golgi extract used in their experiments was enriched in trans-Golgi proteins, so one approach, says author Joachim Seemann, will be to add individual candidates back into their system to see whether ribbon formation can be rescued.

Wei, J.-H., and J. Seemann. 2009. *J. Cell Biol.* doi:10.1083/jcb.200809090.



The mitotic spindle allows daughter cells to form a Golgi ribbon (arrow) rather than a Golgi that is scattered throughout the cell (asterisk).

Fibroblasts invade at a Snail's pace

A transcription factor known to drive the formation of fibroblasts during development also promotes their ability to invade and remodel surrounding tissues, report Rowe et al.

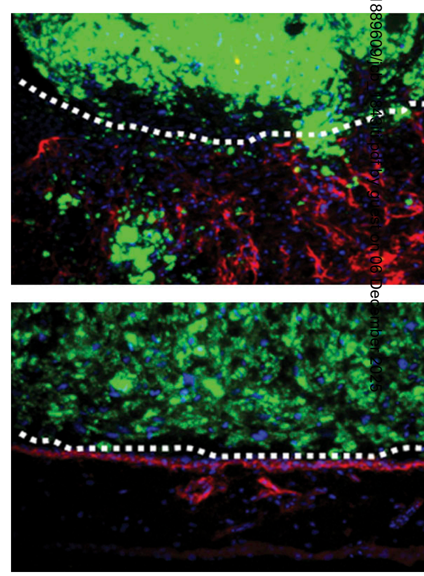
The conversion of epithelial cells into fibroblast-like mesenchymal cells is a critical event in both normal development and cancer. The transcription factor Snail1 induces this conversion (known as epithelial–mesenchymal transition, or EMT) by repressing the expression of epithelial-specific genes. Little was known about Snail1's role after EMT, although the transcription factor is up-regulated in mesenchymal tissue surrounding tumors and wounds.

Because Snail1 expression is thought to be required for maintenance of the mesenchymal phenotype in cancer, Rowe et al. were surprised to see that normal fibroblasts retained many mesenchymal characteristics when Snail1 was removed. The authors did find, however, that many genes important for cell motility, such as actin-binding proteins and matrix metalloproteinases, were expressed at lower levels in fibroblasts lacking Snail1.

Cells invade tissues by sending out actin-rich protrusions called invadopodia that contain proteolytic enzymes that degrade the surrounding extracellular matrix (ECM). Fibroblasts without Snail1 formed fewer invadopodia and were less able to degrade the ECM. Rowe et al. transplanted the Snail1-deficient fibroblasts into chick embryos and found that they were completely unable to penetrate the basement membrane and the complex mix of ECM proteins beneath. Moreover, unlike wild-type fibroblasts, Snail1-deficient cells didn't stimulate the ingrowth of new blood vessels—another key function of fibroblasts during wound healing and tissue remodeling.

The team thinks that in addition to its role in EMT, Snail1 also acts as a master regulator of fibroblast function. In cancer cells, says author Grant Rowe, sustained Snail1 expression may not only cause a loss of epithelial markers but also promote tumor aggression by stimulating tissue invasion and angiogenesis.

Rowe, R.G., et al. 2009. *J. Cell Biol.* doi:10.1083/jcb.200810113.



Wild-type fibroblasts (top panel, green) can invade the extracellular matrix (red), whereas fibroblasts lacking Snail1 cannot (bottom panel).