In This Issue

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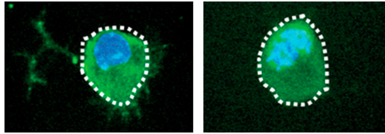
EGF takes dual control of mRNA



KOR mRNA (green) is largely confined to the nucleus (blue) in neurons lacking the EGF-regulated RNA-binding protein Grb7 (right).

EGF coordinates the nuclear and cytoplasmic activities of an RNA-binding protein to ensure a specific mRNA is translated at the right time and place in neurons, say Tsai et al.

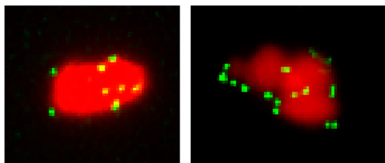
mRNAs localize to specific regions within neurons, where they can be translated to quickly generate large amounts of a protein in the place where it is needed. Due to the large size of neurons, this is much more efficient than translating all mRNAs in a single place and then shipping out each protein to its site of action. But the movement and translation of these mRNAs must be tightly regulated, potentially by extracellular signals such as growth factors.

Tsai et al. discovered that EGF boosts expression of the κ-opioid receptor (KOR) by stimulating both the nuclear export and translation of KOR mRNA. The key to this dual control was an RNA-binding protein called Grb7. EGF prods a phosphatase called SHP-2 to dephosphorylate Grb7 in the nucleus, prompting it to bind KOR mRNA and recruit a protein complex involved in nuclear export. But EGF also stimulated focal adhesion kinase to rephosphorylate Grb7 in the cytoplasm, causing it to release the mRNA for translation into KOR protein.

Senior author Li-Na Wei is now investigating what happens in between nuclear exit and translation. mRNA is transported from the cell body to the axons, a process that is also likely to be regulated, perhaps by signals other than EGF. The researchers are also interested to discover the signals that regulate the localization and translation of other mRNAs.

Tsai, N.-P., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200910083.

A SOLO performance in meiotic cohesion



In the absence of SOLO (right), sister chromatid centromeres (green) separate prematurely and appear as distinct dots in meiotic nuclei (red).

Yan et al. describe how a *Drosophila* protein works with the cohesin complex to hold sister chromatids together during meiosis, ensuring their faithful segregation into sperm.

Just as in mitosis, the cohesin complex keeps sister chromatids together until they separate in the second of meiosis' two divisions. In addition, sister chromatid cohesion helps homologous chromosomes pair up and divide in the first meiotic division. But the function of cohesins in *Drosophila* meiosis is largely unknown because mutations in the proteins are lethal, and flies lack a homologue of the meiosis-specific cohesin Rec8.

Yan et al. investigated a previously uncharacterized protein called SOLO (sisters on the loose), and found that it colocalized with the cohesin subunit SMC1 on meiotic centromeres in spermatocytes. SMC1 was mislocalized in the absence of SOLO, resulting in a loss of cohesion between the centromeres of sister chromatids. This caused chromosomes to missegregate in both rounds of meiotic division.

Although SOLO has no homology to cohesin proteins, it may be an integral component of the complex in flies, says senior author Bruce McKee. Alternatively, it may be a closely associated accessory protein. The team now plans to take a biochemical approach to studying how SOLO stabilizes the cohesin complex on meiotic centromeres. The researchers are also studying the function of SOLO in *Drosophila* oocytes, where cohesins are thought to have an additional role in joining homologous chromosomes together to facilitate meiotic recombination.

Yan, R., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200904040.

Identifying the prime suspects in vesicle release

Neurotransmitters are secreted rapidly after stimulation because synaptic vesicles wait at the presynapse with their membrane fusion machinery already part-assembled, say Walter et al.

Synaptic vesicles dock at the plasma membrane and become "primed" for quick release in response to increased calcium levels. The release stage is controlled by SNARE proteins in both the vesicle and presynaptic membranes, which assemble into a complex that promotes membrane fusion. Whether the vesicle SNARE synaptobrevin only binds its target membrane partners at the fusion step or whether it binds earlier during vesicle priming is unclear.

Walter et al. mutated synaptobrevin's SNARE-interaction domain and measured the protein's ability to support vesicle priming and fusion in neuroendocrine cells. Mutations at the N-terminal end that destabilized synaptobrevin's interaction with its SNARE partners lowered the number of primed vesicles. But the vesicles that remained were still secreted as quickly as they were in cells expressing wild-type synaptobrevin. In contrast, mutations in the C-terminal end of synaptobrevin's binding motif slowed the speed with which vesicles were released.

The researchers think that the interaction domains of synaptobrevin and the other SNARE proteins come together at their N termini to prime vesicles for release and pause in this intermediate state before calcium causes them to zip their C termini into a fully assembled SNARE complex driving membrane fusion. Once they are primed, synaptic vesicles might be committed to release, so senior author Jakob Sørensen now wants to investigate how the priming step is regulated.

Walter, A.M., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200907018.

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