In This Issue

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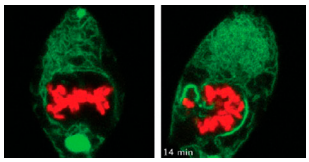
SUN proteins melt the nuclear envelope



Compared with a control cell (left), the nuclear envelope (green) remains associated with mitotic chromosomes (red) in a cell lacking SUN1 and SUN2 (right).

Turgay et al. reveal that SUN proteins help disassemble the nuclear envelope at the start of mitosis and promote assembly of the mitotic spindle during metaphase.

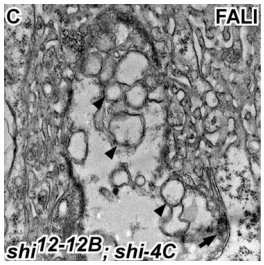
Early in mitosis, the microtubule-based motor protein dynein binds to the nuclear envelope to promote its breakdown and dispersal. Several proteins recruit dynein to nuclear pores during prophase, but, because nuclear pore complexes start to disassemble at the end of this phase, additional proteins may be required to recruit dynein to the nuclear envelope/ER network as cells progress into prometaphase. Inner nuclear membrane SUN proteins, in partnership with outer nuclear membrane KASH proteins, tether dynein to the nuclear envelope to support nuclear migration in interphase cells, but whether they assist membrane remodeling during mitotic entry was unknown.

Turgay et al. found that HeLa cells lacking both SUN1 and SUN2 recruited less dynein to the nuclear envelope during prophase. Accordingly, the cells formed fewer prophase nuclear envelope invaginations, a sign that dynein-dependent membrane remodeling was reduced. The SUN-deficient cells also took longer to clear their nuclear membranes away from chromosomes during prometaphase, indicating that SUN proteins are required to recruit dynein throughout early mitosis, presumably in conjunction with KASH family proteins.

After nuclear envelope breakdown, SUN1 and SUN2 disperse into the ER that surrounds the mitotic spindle. Surprisingly, SUN-deficient cells formed misoriented and disorganized spindles with fragmented centrosomes. Senior author Ulrike Kutay now wants to investigate how long SUN–KASH complexes persist during mitosis and how SUN proteins promote the organization of mitotic spindles.

Turgay, Y., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201310116.

Dynamin loss bulks up endocytosis



Membrane cisternae (arrowheads) accumulate in a synaptic bouton when dynamin is photoinactivated.

Kasprowicz et al. reveal that, in addition to its role in vesicle fission, dynamin helps recruit clathrin to the plasma membrane during the earliest stages of synaptic vesicle formation.

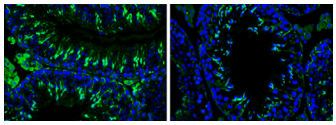
Neurons replenish their supply of synaptic vesicles by forming new vesicles from the presynaptic membrane, mostly via clathrin-mediated endocytosis. The dynamin GTPase helps separate internalizing vesicles from the plasma membrane. Accordingly, fly neurons expressing a temperature-sensitive dynamin mutant are unable to reform synaptic vesicles and accumulate deeply invaginated pits at restrictive temperatures. But temperature-sensitive dynamin might still be partially functional under these conditions, so Kasprowicz et al. completely inhibited the protein by photoinactivation.

Synaptic vesicle recycling was disrupted in fly neurons after dynamin photoinactivation, but, instead of accumulating deeply invaginated pits, the neurons accumulated large membrane cisternae that filled the cytoplasm of their presynaptic boutons. Similar cisternae accumulate in neurons upon clathrin inactivation, probably because the assembly of clathrin lattices on the presynaptic membrane prevents the membrane from being internalized via nonspecific, bulk endocytosis.

Using superresolution microscopy, Kasprowicz et al. found that neither clathrin nor its membrane adaptor α-adaptin was recruited to the presynaptic membrane when dynamin was photoinactivated or depleted by RNAi. Temperature-sensitive dynamin retained this ability to recruit clathrin, thereby inhibiting bulk membrane recycling and allowing clathrin-mediated endocytosis to proceed up to the vesicle fission step. Senior author Patrik Verstreken now wants to investigate how dynamin promotes assembly of the clathrin lattice.

Kasprowicz, J., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201310090.

p73 helps developing sperm stick to the right path



Compared with control testis (left), the junctions (green) that connect Sertoli cells to apical spermatids are disorganized in testis lacking TAp73 (right).

The transcription factor p73 promotes spermiogenesis by regulating the adhesions between developing sperm and their support cells, Holembowski et al. reveal.

The p53 family of transcription factors has an ancient and well-conserved function in protecting the germline. Mammalian p63, for example, promotes the death of male and female gametes that have sustained DNA damage, and female mice lacking p73 are infertile due to defects in oocyte development. Male mice lacking p73 are also infertile, but the reason for this is unknown. Holembowski et al. therefore studied the testes of p73-deficient rodents.

Sperm develop in the multilayered epithelia of seminiferous tubules. Basal stem cells give rise to precursors that undergo meiosis and differentiate as they move toward the apical lumen. This process is enabled and organized by somatic Sertoli cells, which span the seminiferous epithelium and tightly envelop maturing germ cells at each stage of their development in "nursing pouches," guiding their differentiation and movement toward the luminal surface, where they release mature spermatozoa. Developing spermatids lacking all forms of p73, or a specific isoform called TAp73, detached from the epithelium prematurely and underwent apoptosis. The p73-deficient germ cells showed altered expression levels of many proteins that regulate spermatids' adhesion to Sertoli cells, including integrins, proteases, and protease inhibitors.

Sertoli cells don't express p73, but they were also affected by the loss of germ cell adhesion in p73-null testes, losing their characteristic morphology as well as the inter-Sertoli cell adhesions that form the blood–testis barrier, which protects developing spermatids from circulating immune cells and toxins. Senior author Ute Moll now wants to investigate whether mutations in p73 can cause human infertility.

Holembowski, L., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201306066.