In This Issue

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Mitotic cells' shocking response to stress

Elsing et al. reveal how some vulnerable mitotic cells protect themselves from stress.

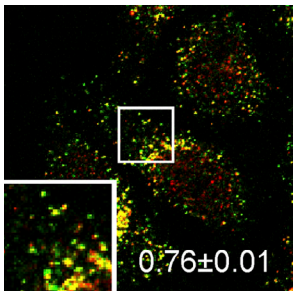
One way that cells cope with stress is by making heat-shock proteins such as Hsp70 that shield other proteins from damage. The transcription factor HSF1 serves as the main activator for heat-shock protein genes. During interphase, another transcription factor, HSF2, collaborates with HSF1 to switch on expression of heat-shock genes. During mitosis, however, cells become more susceptible to stress because they curtail this induction of heat-shock genes.

To their surprise, Elsing et al. found that HSF2 turns against its partner during mitosis. The researchers determined that stressed mitotic cells could still produce Hsp70 but only if HSF2 is absent. The team also discovered that the interaction between the two transcription factors changes. HSF2 obstructs HSF1's access to chromatin during mitosis, possibly because HSF2 binds tightly to the promoter for the Hsp70 gene. HSF2's actions also affect survival during stress. Compared with control cells, mitotic cells with low levels of HSF2 were more likely to live through a period of high temperatures and less likely to show defects in chromosome separation.

HSF2 therefore appears to increase mitotic cells' vulnerability. But Elsing et al. found that several cell lines, including the HeLa tumor cell line, adapt by turning down HSF2 expression during mitosis, allowing them to produce Hsp70 and endure hardship. It's still unclear why only some cell lines respond in this way, as researchers had thought that cells uniformly shut down gene transcription during mitosis. However, Elsing et al.'s results show that mitotic cells keep tight control on production of some proteins, such as Hsp70, in order to ensure their survival during mitosis.

Elsing, A.N., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201402002.

Sec12 heads for the exits



Sec12 (green) gathers at the protein exit sites (red) in the ER.

By collecting at specific sites in the ER the protein Sec12 permits collagen to depart from the organelle, Saito et al. show. The discovery brings researchers closer to explaining the mystery of how cells secrete large cargoes.

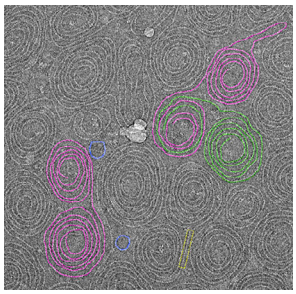
Cells that make collagen face a challenge. The COPII-coated vesicles that typically transport secretory proteins from the ER are 60–90 nm across, but collagen molecules are up to 400 nm long. Yet studies indicate that collagen secretion requires the molecular machinery that creates COPII vesicles. Researchers suspect that certain proteins modify this machinery so that it can handle larger cargo, but they aren't sure which proteins do the job.

Saito et al. searched for proteins in mammalian cells that bind to cTAGE5, a collagen receptor in the ER membrane. They identified Sec12, which activates the on–off switch for the COPII machinery, Sar1. The researchers found that cTAGE5 concentrates Sec12 at the spots where collagen leaves the ER. Moreover, if cTAGE5 doesn't guide Sec12 to these locations, cells can't secrete collagen VII, but they can secrete other proteins.

Although researchers knew that Sec12 localized to the ER, this study reveals that the protein accumulates at collagen exit sites and is essential for the protein's release. How collagen leaves the ER remains unclear, but Sec12 might stimulate the process by activating large amounts of Sar1 at the exit sites.

Saito, K., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201312062.

ESCRT-III gets the bends



The Vps32 subunits in the ESCRT-III complex naturally assemble into spirals.

Shen et al. reveal how a key portion of the membrane-snipping ESCRT-III complex gets in shape.

The ESCRT-III complex cuts membranes during processes such as cell division and viral budding. The complex contains several subunits, the most abundant of which is Vps32 (known as CHMP4 in mammals). How the different subunits coalesce to produce a full-fledged ESCRT-III complex remains unclear. Researchers have found that Vps32 subunits often polymerize into a flat spiral that could be the foundation on which the rest of the complex assembles.

Shen et al. used cryo-EM and other techniques to probe the architecture of the Vps32 coils. The team found that they form spontaneously when Vps32 proteins link up. The subunits, which line up end to end rather than side by side, are well suited to adopt a bowed conformation. Two of the helices in the Vps32 structure have a hinge in the middle. When the team mutated this hinge, the proteins could no longer form spirals. The researchers calculated that the most energetically favorable curvature for the subunits was 9°, and they found that the proteins in the center of the spirals bend at almost exactly that angle.

In contrast, Shen et al. discovered that the junctions between Vps32 subunits are stiff, suggesting that bending there doesn't contribute to the spiral shape. The bulky carboxyl terminus of Vps32 prevents other Vps32 proteins from sidling up to the filaments, and the authors found that a downstream ESCRT-III component, the Vps4 ATPase, helps tighten the spiral in a way that doesn't require ATP hydrolysis.

The results suggest that the Vps32 spirals might function like a coiled spring, storing energy that can be used to cut membranes.

Shen, Q.-T., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201403108.