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Nuclear envelope starts with a clean sheet

After mitosis, nuclear membranes form directly from ER cisternae before nuclear pore complex reassembly.

At the start of mitosis, the nuclear envelope breaks down and merges with the endoplasmic reticulum (ER). At the same time, the nuclear pore complexes that mediate transport across the inner and outer membranes of the envelope also disassemble. Transmembrane pore proteins move into the ER, while soluble components disperse into the cytoplasm. Lu et al. use rapid, live-cell 3D imaging to establish the sequence of events as the nuclear envelope and pores are rebuilt after mitosis (1).

The nuclear envelope has been proposed to reassemble through the fusion of ER tubules around the chromosomes (2, 3). In 2009, however, Tomas Kirchhausen and his postdoc Lei Lu from Harvard Medical School in Boston found that the ER mainly exists as large, sheet-like cisternae during mitosis (4). "This suggested to us that these cisternae provide the membrane for nuclear envelope reformation," says Lu, who is now starting his own laboratory at Nanyang Technological University in Singapore.

Lu and Kirchhausen therefore reexamined nuclear envelope reassembly in live HeLa cells expressing fluorescent markers of the ER and chromatin (1). The researchers found that, during anaphase, ER sheets first contacted the rims of the disk-shaped chromosome masses moving to opposite spindle poles before expanding to fully enclose the daughter cell nuclei. In collaboration with Mark Ladinsky from Caltech in Pasadena, Lu and Kirchhausen used high-resolution electron tomography to confirm that the ER membranes enveloping the chromosomes were cisternal, rather than tubular, in shape.

Lu et al. think that ER cisternae might initially target the rim of chromosome masses in HeLa cells because the mitotic spindle blocks the ER from contacting the outer and inner faces of the chromatin disks. "We don't think there's any special signal," explains Kirchhausen. "[The rim] is simply where you have topological access."

Focal Point

(Left to right) Lei Lu, Mark Ladinsky, and Tomas Kirchhausen describe the sequence of events by which the nuclear envelope and nuclear pore complexes reassemble after mitosis. In contrast to previous models, Lu et al. find that the nuclear envelope forms directly from mitotic ER cisternae. A 3D model constructed by electron tomography (far right) shows an ER sheet (green) contacting the surface of mitotic chromosomes (blue) and splitting into the inner and outer membranes of the nascent nuclear envelope. The researchers also demonstrate that nuclear pore complexes only form after nuclear envelope reassembly, rather than preassembling on chromatin in the absence of nuclear membranes.

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> "It unifies what happens in interphase [with] what happens in mitosis."

In support of this, the researchers found that depolymerizing spindle microtubules with nocodazole increased the rate of nuclear membrane reassembly, whereas stabilizing the spindle with taxol delayed envelope reformation. Because the dynamics of spindle disassembly vary in different cell types, nuclear envelope formation may differ in cell lines other than HeLa—Lu et al. saw cisternae initiate envelope assembly all over the anaphase chromosome masses of BSC1 cells, for example.

The researchers then turned their attention to the assembly of nuclear pores after mitosis. During interphase, nuclear pore components form new pore complexes by inserting themselves into the nuclear envelope. The same mechanism might apply to postmitotic pore assembly, but some groups have proposed an alternative pathway in which pore proteins form "prepore" complexes on the surface of the chromosome masses in early anaphase before nuclear envelope reformation (5, 6).

By imaging live cells expressing fluorescent markers of the ER and nuclear pores, Lu et al. found that pore complexes only reassembled in regions of the chromosome masses already covered by nuclear envelope. Moreover, by calibrating and quantifying the fluorescence of their nuclear pore marker, the researchers determined that the small amount of pore protein to accumulate on chromosomes before nuclear envelope formation corresponded to single protein units rather than higher-order prepore structures.

Nuclear pores are therefore always assembled within a preexisting nuclear envelope. "It unifies what happens in interphase, what happens in mitosis, and what happens in yeast [which undergo closed mitoses]," says Kirchhausen. "Of course there will be differences but, topologically, you don't have to postulate different models."

Lu and Kirchhausen now want to investigate the details of how nuclear pores reassemble after mitosis. "We want to generate a clearer molecular picture of how nuclear pore complexes make the hole in the intact nuclear membranes," Lu says.

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