In This Issue

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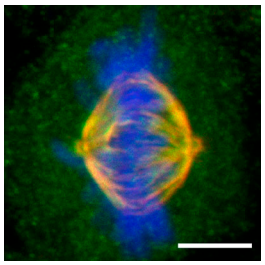
Adducin-1 moonlights at the mitotic spindle



Adducin-1 (green) turns the mitotic spindle yellow in this mitotic cell.

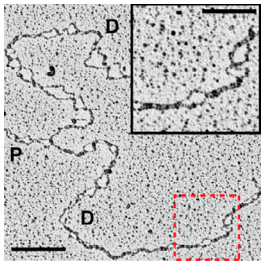
An actin-binding protein helps shape the mitotic spindle, Chan et al. report. Researchers long thought that actin and microtubules performed different tasks during mitosis. They believed that microtubules formed the mitotic spindle that pulls chromosomes apart, whereas actin joined with myosin to produce the contractile furrow that separates the mother and daughter cells. But recent studies have revealed that the roles of the two cytoskeletons converge. For instance, actin helps situate the mitotic spindle, and microtubules help localize the cleavage furrow.

Chan et al. discovered a surprising new example of this functional overlap when they tracked the protein adducin-1. During most of the cell cycle, adducin-1's C-terminal tail domain fastens onto actin at the cell membrane and helps brace the cortical cytoskeleton and cell–cell junctions. But Chan et al. found that during mitosis adducin-1 attaches to the spindle with its N-terminal head domain.

Adducin-1 relocates to the mitotic spindle when CDK1 phosphorylates two serines in the protein. However, it doesn't hitch to the spindle directly. Adducin-1 couples to the microtubule-binding motor myosin-X. Chan et al. determined that this connection was crucial for the formation of the mitotic spindle. In cells lacking adducin-1, the spindles were distorted and often displayed multiple poles. How adducin-1 shapes the spindle—and whether actin is involved in that process—remains unclear.

Chan, P.-C., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201306083.

Histone shortages hold back replication forks



In a cell low on histones, nucleosomes haven't reformed behind a replication fork (inset).

Much as an automobile assembly line slows if engines are in short supply, DNA replication slackens if the cell is low on new histones, Mejlvang et al. reveal.

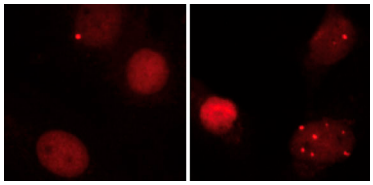
To replicate their DNA, cells require ample amounts of nucleotides. But whether the availability of fresh histones, which package DNA into nucleosomes, also controls the rate of DNA copying is unclear. Yeast can complete S phase without new histones, researchers have found. However, studies that blocked protein synthesis in mammalian cells showed that DNA duplication falters, suggesting that a scarcity of histones can impede replication.

Mejlvang et al. addressed the issue in mammalian cells by blocking two regulatory factors that are essential for synthesizing all six of the canonical histones. The resulting histone shortage slowed the advance of replication forks but didn't prevent the firing of new replication origins. Cells disassemble chromatin during DNA copying, and the first step in restoring it is the formation of nucleosomes behind the replication fork. Mejlvang et al. found that nucleosomes didn't reform properly when histones were in short supply. The researchers also showed that blocking nucleosome construction delays replication fork progression and prevents the departure of PCNA, an enzyme that coordinates multiple functions at replication forks, including DNA synthesis and nucleosome assembly.

Nucleotide shortages trigger DNA damage checkpoints. But to the researchers' surprise, histone scarcity didn't initially trip these checkpoints, indicating that cells can wait for supplies of histones to build up without jeopardizing genome integrity. The next challenge is resolving how cells sense that nucleosome assembly is incomplete.

Mejlvang, J., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201305017.

Thyroid hormones speed cellular aging



Cells treated with T3 (right) show more sites of DNA damage (red dots) than do control cells (left).

Stimulating one variety of thyroid hormone receptor spurs cellular senescence, Zambrano et al. report. The finding might explain how thyroid hormones accelerate aging and protect against cancer.

Thyroid hormones fire up metabolism by binding to either of two receptors, thyroid hormone receptor α (THRA) or thyroid hormone receptor β (THRB) and can induce opposing impacts on health. On the one hand, people with hyperthyroidism accumulate liver damage and have shortened life spans. On the other hand, thyroid hormone receptor blocks cancer growth and metastasis.

Zambrano et al. discovered a possible explanation for this contradiction. They found that one thyroid hormone, T3, spurs cultured cells to senesce. T3 only triggered this effect through THRB, not THRA. Senescence didn't require p53 but did require the DNA repair protein ATM.

T3 turned up mitochondrial activity, increasing production of noxious reactive oxygen species (ROS). This surge of ROS resulted in increased numbers of DNA double-strand breaks, thereby precipitating cellular senescence. Zambrano et al. also checked for the effect in young mice dosed with thyroid hormones for two weeks. Genetically altered mice lacking THRB showed little senescence, whereas wild-type animals carried a significant number of senescent cells in their livers.

Because senescent cells lose the ability to divide, the results suggest how activation of THRB can be both beneficial and detrimental. Although triggering senescence prevents damaged cells from becoming cancerous, it also might contribute to aging by curtailing the replacement of worn-out cells.

Zambrano, A., et al. 2014. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201305084.