In This Issue

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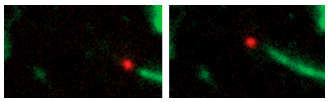
Virus takes the actin express



A baculovirus (red) zooms along at the tip of a polymerizing actin filament (green).

Viruses typically hitchhike around the cytoplasm on microtubules. Ohkawa et al. reveal that one type of virus can travel within the cell using actin filaments.

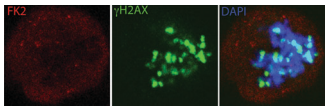
Once baculoviruses break into a cell, they need a lift to the nucleus so their genetic material can be copied. However, these viruses don't require microtubules for the journey. Ohkawa et al. investigated whether the baculovirus *Autographa californica* multiple nucleopolyhedrovirus (AcMNPV) relies on actin instead.

The researchers observed tagged viruses scooting through the cell at the tips of elongating actin filaments. A viral protein called P78/83 triggers actin polymerization by activating the Arp2/3 complex. Unable to steer, a virus keeps going until it runs into the nucleus. Actin polymerization continues even after the collision, driving the virus into the nuclear membrane hard enough to make a dent. However, the researchers don't think that the virus forces its way through the membrane. When they blocked transport through nuclear pores, the number of viral particles in the nucleus plunged 78%, suggesting that the virus enters via these passageways.

The vaccinia virus uses actin to cruise across the cell surface, but AcMNPV is the first virus shown to travel aboard actin within the cell. Actin also helps the virus make a move that might sustain an infection. Clusters of AcMNPV particles invade a cell and then break up after entry. Some of the viral particles head for the nucleus. Once the viral takeover of the cell is well under way, some viruses return to the plasma membrane and exit. The team showed that actin transports these viruses to the membrane. Even if the host spurs the cell to undergo apoptosis, these escapees survive to infect again.

Ohkawa, T., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201001162.

Mitosis first, DNA repair later



The lack of red in the merged image (right) shows that this mitotic cell is not ubiquitylating the sites of DNA breaks (green).

Mitotic cells are procrastinators—at least when it comes to making repairs. As Giunta et al. report, the cells label broken DNA, waiting until after mitosis to fix it.

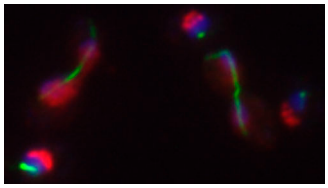
Triggered by radiation and certain chemicals, double-strand breaks (DSBs) are the most dangerous type of chromosome damage. They can lead to genomic instability that promotes cancer. A DSB triggers a complex series of molecular responses that eventually mends the DNA. But what if the DNA fractures during mitosis? Researchers have found that if the damage occurs early enough—up to the middle of prophase—a cell can slow or even halt mitosis to make repairs. After that, however, mitosis is unstoppable.

Giunta et al. discovered that cells don't ignore these late breaks. Instead, they fire up the DNA damage response, allowing early events such as the phosphorylation of the H2AX histone, which labels the site of the break. The process then ceases. Later events in the cascade, including the arrival of ubiquitin-adding proteins such as BRCA1, don't occur during mitosis.

Cells fix the breaks during the following interphase, the researchers found. The work suggests that during mitosis cells mark the sites of damage rather than actually patching up the DNA. But this step is crucial. If mitotic cells can't perform the early stages of DSB repair, they are more likely to die from radiation exposure, Giunta et al. showed. Why don't cells simply finish the job during mitosis? The answer isn't clear. The DNA might be too tightly condensed for repair proteins to gain access to the breaks, or these proteins might be inactive.

Giunta, S., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200911156.

Ins and outs of Cdc14



This image of cells at different stages of the cell cycle shows the changing location of Cdc14 (red). Microtubules are shown in green and DNA in blue.

The enzyme Cdc14, which helps shut down the mitotic machinery, cycles in and out of the nucleolus. Manzoni et al. reveal how cells control the enzyme's oscillations so that it is available at the crucial time.

Cdc14 strips phosphates from proteins activated by cyclins and cyclin-dependent kinases (Cdks). Cells free Cdc14 from the nucleolus late in mitosis. Two interacting pathways orchestrate the process. The FEAR pathway spurs Cdc14's release at the beginning of anaphase. The MEN pathway ensures that the release continues, enabling Cdc14 to spread to the cytoplasm. Previous studies have shown that three kinases in these pathways are key: the polo-like kinase Cdc5, a cyclin–Cdk combo (Clb–Cdk), and Dbf2.

Manzoni et al. teased out the effects of each kinase in yeast cells and found what they call a two-hit mechanism. The first hit is Cdc5, which is essential for Cdc14 release. The second hit is either Dbf2 or the cyclin–Cdk combo. The results suggest that the cyclin in the pair can be Clb2 or Clb5.

The researchers hypothesize that Cdc5 teams up with cyclin–Cdk complexes to unleash Cdc14. The cyclins start breaking down around the beginning of anaphase, so Dbf2, part of the MEN pathway, steps in to maintain Cdc14 levels. Later in mitosis Cdc5 starts to degrade, and Cdc14 returns to confinement. Manzoni et al. found that nondegradable cyclins triggered oscillations in which Cdc14 continually shuttled in and out of the nucleolus. They suggest that there are benefits to linking control of Cdc14 to the cyclin–Cdk complexes that drive the cell cycle. That could allow cells to manage Cdc14's oscillations so that its levels rise and fall only once during each cycle.

Manzoni, R., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201002026.