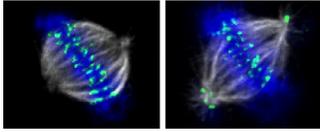


## TRAMM makes an unscheduled stop during mitosis



**Chromosomes (blue) line up across the middle of a control cell (left), but some chromosomes remain at the spindle poles in a cell lacking TRAMM (right). The mitotic spindle is labeled white, centromeres green.**

surprised to discover that cells lacking the TRAPP component TRAMM (also known as TrappC12) showed mitotic defects. Mitotic chromosomes remained bunched at the spindle poles instead of lining up along the cellular midsection.

Although TRAMM remains in the cytoplasm during interphase, the researchers found small amounts of it clinging to chromosomes during metaphase. In cells lacking TRAMM, the outer kinetochores

A membrane trafficking protein moonlights during mitosis, helping to direct the motor protein CENP-E to the kinetochores, Milev et al. show.

The TRAPP protein complex controls membrane trafficking events such as tethering of vesicles to the Golgi apparatus. Milev et al. were

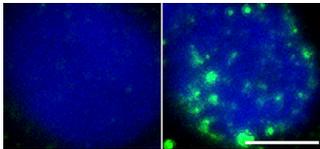
were missing several proteins. The kinetochore levels of CENP-E, which helps strengthen the attachments between chromosomes and microtubules, showed the largest decline in these cells.

To confirm that TRAMM helps attract CENP-E to the kinetochores, the researchers broke the microtubule–chromosome attachments with nocodazole. This treatment usually spurs some kinetochore components, whose levels drop after microtubule attachment, to return to the structures. Yet little CENP-E came back to the kinetochores in cells lacking TRAMM.

Milev et al. determined that TRAMM is phosphorylated early in mitosis and dephosphorylated before interphase begins, suggesting that its phosphorylation status determines which job it performs. Membrane trafficking shuts down during mitosis, so TRAMM is free to pursue its alternative role. How the protein recruits CENP-E to the kinetochores is unclear. Its interaction with CENP-E appears to be short-lived, but it could team up with other proteins.

Milev, M.P., et al. 2015. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201501090>.

## Mitotic proteins take on editorial duties



**R-loops (green), where DNA and RNA intertwine, are rare in a control cell (left) but prevalent in a cell deficient in BuGZ (right).**

age accumulates and p53 often gets switched on, triggering apoptosis. Researchers have assumed that the interruption in mitosis leads to DNA damage, which activates p53. However, whether taxol-induced tumor regression in vivo is due to mitotic arrest remains unclear. Some proteins that control mitosis also have nonmitotic roles, so cancer drugs could spur cell death by disrupting these alternative functions.

Two mitotic proteins help control RNA splicing during interphase, Wan et al. show. The findings may offer an alternative explanation for how some drugs kill cancer cells.

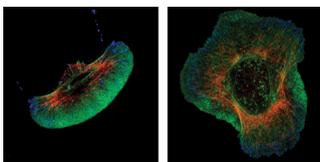
Cancer drugs such as taxol halt mitosis. If cells remain in this paused state, DNA dam-

Wan et al. focused on two proteins, BuGZ and Bub3, that work together to ensure that chromosomes line up properly during mitosis. BuGZ helps deliver Bub3 to the kinetochores, where Bub3 joins the spindle assembly checkpoint that stops mitosis if chromosomes aren't correctly connected to the spindle. Depleting BuGZ turned on p53 and caused cancer cells to commit suicide.

However, the researchers found BuGZ also bound to several proteins involved in RNA splicing. This process was perturbed when the researchers depleted BuGZ or Bub3 from control or cancer cells, causing DNA and RNA to intertwine and form so-called R-loops that promote DNA injury. If the researchers added an enzyme that removes R-loops, they could reduce the amounts of p53 activation and DNA damage in cells lacking BuGZ or Bub3. The study suggests that targeting the nonmitotic functions of mitotic proteins might offer a new way to turn on p53 and kill cancer cells.

Wan, Y., et al. 2015. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201409073>.

## MLCK stops cells from going full frontal



**A two-day-old keratocyte (left) shows a single protrusion, whereas a four-day-old keratocyte (right) sports several protrusions. Cells were stained for F-actin (green), myosin (red), and phospho-tyrosine (blue).**

gated the polarization of zebrafish keratocytes, a type of skin cell. Researchers often study migration mechanisms in keratocytes of other fish species, but zebrafish offer several advantages, including a sequenced genome and techniques for gene knockdown.

Cells from two-day-old embryos were fan shaped, with one large protrusion at the front end. But Lou et al. noticed that cells

Myosin light chain kinase (MLCK) controls the number of protrusions extended by crawling cells, Lou et al. report.

Migrating cells polarize to form a protrusive front end. Previous studies have found that Rho GTPases and membrane tension prevent other parts of the cell from forming protrusions. Lou et al. investi-

from four-day-old embryos often sported multiple protrusions. The difference affected the cells' movement. Keratocytes from two-day-old embryos crawled swiftly, but cells from four-day-old embryos rotated in place like pinwheels.

The researchers found that the activity of MLCK increased in keratocytes from four-day-old embryos. When the researchers inhibited MLCK, these cells extended only a single protrusion. Keratocytes from four-day-old embryos tended to have smaller protrusions than cells from younger embryos. Lou et al. determined that MLCK shrinks these protrusions and shortens their lifetime, thus allowing the cells to generate more of them. MLCK works by inducing myosin to gather in the extensions, causing them to retract. The team found that Rho kinase (ROCK), another molecule that regulates the number of protrusions, played a complementary role, mainly affecting myosin accumulation at the cell's rear end.

Lou, S.S., et al. 2015. *J. Cell Biol.* <http://dx.doi.org/10.1083/jcb.201409001>.