TRAMMM makes an unscheduled stop during mitosis

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

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

Miley 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.

Mitotic proteins take on editorial duties

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 damage 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.

MLCK stops cells from going full frontal

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. investigated 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 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.