In This Issue

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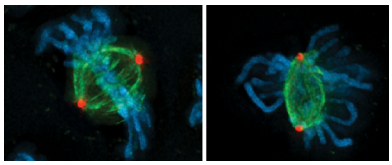
Shining new light on the function of Aurora A



Chromosomes (blue) line up neatly on the mitotic spindle (green) of a control cell (left) but are jumbled in a cell lacking Aurora A (right).

Aurora A isn't exactly a mystery protein, but researchers have struggled to determine its function. Hégarat et al. discovered that the kinase helps line up mitotic chromosomes and spurs disassembly of microtubules during anaphase, in collaboration with its cousin Aurora B.

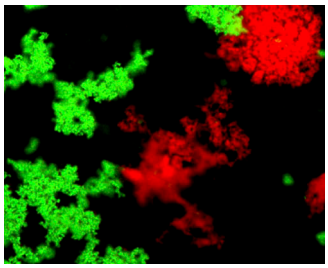
Studies on various cell types have furnished contradictory answers about what Aurora A does. Some work suggests that it's necessary to fashion a bipolar spindle. Other research indicates that absence of the protein stalls the cell in G2, leads to incorrectly aligned chromosomes, or prevents division. To try to nail down the protein's function, Hégarat et al. deleted the Aurora A gene from cells shortly before mitosis.

Although most of the Aurora A–lacking cells constructed a bipolar spindle, their chromosomes often didn't line up properly. The cells could complete mitosis, but the daughter cells frequently had missing or extra chromosomes, indicating that Aurora A helps to attach kinetochores to opposite spindle poles before chromosome separation. Given Aurora A's location on the centrosome, how it contributes to chromosome alignment isn't clear.

The scientists also followed cells that lacked Aurora A and Aurora B activity. Early in anaphase, spindle microtubules begin to break down, helping to tug the chromosomes apart. But in the doubly deficient cells, the microtubules didn't depolymerize, and chromosomes failed to separate. This result suggests that Aurora A and Aurora B team up to spur microtubule breakdown.

Hégarat, N., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201105058.

Protocadherins bring cells together



Beads carrying Protocadherin-19 and N-cadherin (green) don't mix with beads sporting only N-cadherin (red).

Emond et al. reveal a new mechanism that enables cells to stick to each other.

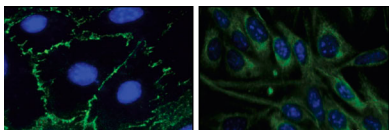
Cadherins make cells clingy, allowing them to adhere to their neighbors. This attachment occurs when cadherins on one cell interlock with matching molecules on an adjacent cell. However, the importance of one class of cadherins, the protocadherins, for cell–cell binding is unclear. The molecules are only slightly sticky, and some studies have dismissed their role in intercellular adhesion. The researchers previously discovered that one of these proteins, Protocadherin-19 (Pcdh19), teams up with the "classical" adhesion protein N-cadherin to guide cell movements during zebrafish development.

Emond et al. now suggest that the two molecules form a fastener that helps latch cells together. Beads carrying the extracellular sections of either Pcdh19 or a nonadhesive mutant of N-cadherin weren't sticky, but beads glommed onto each other if they carried segments of both molecules. The researchers obtained similar results when they transfected a cell line that doesn't normally make either protein with Pcdh19, nonadhesive N-cadherin, or both. Cells that carried only Pcdh19 clung weakly, whereas cells sporting the mutant N-cadherin remained unattached. But cells expressing both proteins formed clumps.

Further experiments on mutant versions of both proteins suggested that Pcdh19 is the main adhesion molecule, whereas N-cadherin augments Pcdh19's stickiness, possibly by distorting the molecule to expose the adhesion site.

Emond, M.R., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201108115.

Cdc6 licenses tumor growth



Unlike control cells (left), cells that overexpress Cdc6 (right) lose E-cadherin (green) from the plasma membrane.

A protein that permits cells to replicate their DNA also shuts down a tumor suppressor gene, Sideridou et al. report.

The cell adhesion molecule E-cadherin is a cancer fighter that is mutated in many tumors. In previous work, the researchers uncovered a possible link between E-cadherin and Cdc6, a protein that belongs to a complex that licenses DNA replication. Cells typically produce Cdc6 only for a brief period of time, destroying it to prevent their DNA from duplicating more than once per cell cycle. The researchers found that abnormal overproduction of Cdc6 led to a phenomenon called epithelial to mesenchymal transition (EMT). Cells that jettison E-cadherin often undergo EMT, a process that takes place during embryogenesis but that cancer cells also use to spur metastasis.

In the new study, Sideridou et al. found that Cdc6 attaches to the promoter of the E-cadherin gene and turns off its expression. Cdc6 binding triggered the promoter's conversion into heterochromatin, expelling the H2A.Z histone that prevents gene silencing and ejecting CTCF, a chromosomal insulator that allows gene expression. This chromatin remodeling was accompanied by activation of nearby replication origins, sites where DNA duplication begins. Thus, this work indicates that Cdc6 overproduction may aid cancer cells in two ways: by shuttering an antitumor gene and by sparking DNA replication. An unanswered question is what other genes Cdc6 overexpression influences in tumor cells.

Sideridou, M., et al. 2011. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201108121.