A budding role for a cellular dynamo

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Actin, a globular protein found in all eukaryotic cells, is a workhorse that varies remarkably little from baker's yeast to the human body. Part of the cytoskeleton, actin assembles into networks of filaments that give the cell structural plasticity while driving many essential functions, from cell motility and division, to vesicle and organelle transport within the cell. In a groundbreaking new study in the current issue of *Developmental Cell*, Brandeis researchers raise the curtain on how this actin maintains just the right filament length to keep the cell healthy and happily dividing.

Using baker's yeast as the model organism, Brandeis researchers Melissa Chesarone, Christopher Gould, and James Moseley, all in the lab of biologist Bruce Goode, set out to discover how the length of actin fibers is controlled. By answering this question, the scientists sought to advance understanding of asymmetrical cell division, a process that not only allows yeast to divide, but also ensures the proper renewal of human stem cells and plays a crucial role in early stages of embryonic development.

In yeast cells, as in all other cells, actin fibers serve as internal "railways" or tracks that give the cell directionality and provide the wherewithal for transporting various molecular and membrane-bound cargoes from one end of the cell to the other. Molecular machines called formins produce many of the actin fibers, but in the absence of a displacement factor to put a brake on the process, formins will essentially stop at nothing, producing excessively long actin filaments at ridiculously fast rates, and wreaking cellular havoc, says Goode. In humans, genetic defects in formins are associated with conditions such as infertility and deafness.

"We wanted to know how you turn the formins off. What disrupts the interaction of the formin with the actin filament, thus terminating actin assembly and regulating its length?" Goode explained.

The researchers discovered that a protein called Bud14 is a potent inhibitor, directly binding to the formin and displacing it, thereby producing actin filaments of normal length, a prerequisite for proper actin cable architecture and cargo transport.

"In all animal, plant, and human cells, life depends on rapidly producing actin filaments of defined lengths, and we now have an important clue as to how this is regulated," said Goode. "We're now homing in on the precise mechanism by which Bud14 works and extending this analysis to mammalian cells. Once again, yeast has provided the ideal system in which to pioneer a basic problem that applies to most other species."

Source: Brandeis University