

Johns Hopkins Researchers Reshape Basic Understanding of Cell Division

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Potentially big implications for cancer control

By tracking the flow of information in a cell preparing to split, Johns Hopkins scientists have identified a protein mechanism that coordinates and regulates the dynamics of shape change necessary for division of a single cell into two daughter cells.

The protein, called 14-3-3, sits at an intersection where it integrates converging signals from within the cell and cues cell shape change and, ultimately, the splitting that allows for normal and abnormal cell growth, such as in tumors.

In a report published Nov. 9 in [Current Biology](#), the Hopkins team links 14-3-3 directly to myosin II, a complex of motor proteins that monitors and smoothes out the shape changes to ensure accurate division.

“The discovery of this role for 14-3-3 has immediate and important medical implications because cell division already is one of the major targets of anticancer drugs,” says [Douglas Robinson, Ph.D.](#), an associate professor of cell biology at the Johns Hopkins School of Medicine. “This protein provides a new opportunity for tweaking the cell division system.”

The new findings grew out of studies of the so-called mitotic spindle in the one-celled amoeba *Dictyostelium*. The spindle’s job is to separate all the genetic material into two identical sets, one for each daughter cell, and coordinate cell division activities at the cell’s outer membrane.

Using a painstaking chemical-genetic approach, the scientists altered the cells so that they grew only half as well as normal. They then used tools of genetic engineering to try to make the cells grow normally again.

Specifically, they used a chemical that makes the spindles fall apart, and then they searched for genes “turned on” in response to this catastrophe. Out popped 14-3-3. When they increased production of 14-3-3, they found that the chemical lost its damaging effect.

Next, they blocked 14-3-3 and noticed traits in these cells reminiscent of what happens when myosin II muscle-moving machinery is disturbed, suggesting that 14-3-3 plays a critical role in cell shape dynamics and cell division.

The amoeba has only one form of the 14-3-3 protein compared to humans, whose seven forms interact with hundreds of proteins to regulate many cellular processes. Some 14-3-3s in humans are thought to be tumor suppressors because their function is lost in tumor cells; other 14-3-3s in humans are over-productive in certain types of cancers, suggesting that they may be biomarkers for disease progression.

Ironically, division failure may put a cell on the pathway of tumor development because it results in a cell having twice as many parts and chromosomes during the next cell cycle. Such chromosomal instability may put it at risk of losing genetic material such as tumor suppressors.

Tumor cells often have alterations in their mechanical properties, Robinson says, adding that those alterations are thought to contribute to how cells can metastasize, invade and pass through different cell layers to migrate to new locations in the body.

Says Robinson: “Having studied myosin II for 13 years, it still surprised us that 14-3-3 coordinates myosin II in the critical processes of cell shape change and division.”

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