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Worms Point to a Link Between Cellular Glue and Cancer Growth

Scientists have discovered that a protein that helps make cells sticks together also keeps them from dividing excessively, a hallmark of cancer progression. The discovery could lead to new ways to control cancer.

The findings, arising from a collaboration between Aaron Putzke, assistant professor of biology at Hope College in Holland, Mich., and Joel H. Rothman, a biology professor and chair of the Department of Molecular, Cellular and Developmental Biology at UC Santa Barbara, were described in a paper published in the Proceedings of the National Academy of Sciences, a widely cited interdisciplinary scientific journal.

"When we develop from an egg, cells divide many times, generating the vast number of cells present in an adult," Rothman said. "It is not only critical for cells to know when to divide, but when to stop dividing."

Putzke added: "Without this brake on division, cells would keep dividing and we might end up with arms that reach the ground or ears that flap in the wind. Or, even more seriously, with cancer."

It is equally important, according to Rothman, for cells to stick to each other so that they can work together in communities, rather than as free agents with no regard for the others around them.

Cancer cells do not stick together properly, allowing them to break free from the community and spread the disease.

Working with a tiny roundworm known as *C. elegans*, a major experimental model animal in biomedical science, the scientists discovered that a protein called Fer, which acts with other proteins to glue cells together, also prevents them from dividing excessively. When Fer is removed from cells, the researchers found that they keep proliferating. Their experiments may mimic what happens in certain human cancers.

"Other studies have shown that Fer protein levels are altered in cancers such as prostate cancer and myeloid leukemia," said Putzke. The Fer protein was well known for its role in sticking cells together, and the obvious conclusion was that the role in cancer progression was related to its function in cellular glue. But Putzke noted that altered Fer levels might actually be associated with tumors for a very different reason. "Our results suggest that Fer may act in cancer not by changing cell adhesion but by allowing cells to divide unchecked."

The research showed that the Fer protein normally acts by constraining a cell signaling system known as the Wnt (pronounced "wint") that causes cells to multiply.

When the Fer protein is absent, the Wnt signal becomes overzealous, overriding the normal brakes on cell division and causing cells to multiply when they shouldn't.

"Cell stickiness and the brake on multiplication of cells are coordinated during normal human development and both are affected in cancer," said Rothman, adding that the results are a reminder that obvious conclusions are not always the correct ones. "A complex set of events goes wrong in cancer cells. It may well be that Fer is an important player in cancer because it acts both in cell adhesion and in stopping cells from dividing."

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