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Discovery at UCSB May Lead to New Drugs to Treat Cancer, Control Fertility, Enhance Organ Regeneration

A recent discovery in cellular biology may allow scientists to enhance organ regeneration by stem cells, prevent the progression of cancer, and control fertility.

The discovery was made in the laboratory of Joel H. Rothman, professor of molecular, cellular and developmental biology at the University of California, Santa Barbara. It was described in a paper published in the May issue of the journal Developmental Cell, the most widely cited journal in developmental biology. In addition to Rothman, the authors of the paper are: Kenji Kontani (first author) who has moved on to the University of Tokyo, Japan, and Ivan P.G. Moskowitz (second author) now at Harvard University.

Rothman explained that cell fusion is analogous to the melding of soap bubbles, and the process is involved in creating many of our organs, including muscles, bones, and placentas. "When a cell fuses with others, it loses its individuality," said Rothman. "But it can also adopt a new career, either productive, as when stem cells regenerate organs, or sinister, as in cancer metastasis."

Fusion is the process that allows a sperm to fertilize an egg; it also allows a cancer cell to join with a normal cell.

The discovery by Rothman and his co-authors reveals that the inappropriate joining of cells by fusion is naturally prevented by a familiar protein, called vacuolar ATPase, acting in an entirely unanticipated context. The discovery suggests new avenues for pharmaceutical companies to develop drugs to enhance organ regeneration by stem cells, prevent cancer progression, and control fertility.

The protein, vacuolar ATPase, was already known to make certain compartments inside a cell become more acidic, an essential function in cell biology. Now it is understood that the protein also works on the surface of the cell to prevent cell fusion.

"The protein is in an unexpected place, doing an unexpected job," said Rothman. "This finding might make it possible to develop new methods, and new drugs, for controlling cell fusion."

Rothman studies the nematode worm C. elegans as a model organism. His research group looks at genetic mutations to see what effect they cause. From that information they can determine which genes are involved in certain biological processes. The mutation they found in this discovery is one that causes a large number of cells to fuse with each other. Normally these cells would not fuse.

He describes his approach in working with worm mutations as similar to figuring out how a machine, such as a car, is put together. "It's as if we reach in and remove a part of the car and then try to drive it, to see if it still works," said Rothman. "We pull out the radio and the car still works fine. But when we take off a wheel, the car doesn't move straight at all. We take out the brakes and everything is fine until you have to stop."

A few years ago a protein that allows for cell fusion, called EFF-1, was discovered by other laboratories using similar strategies, explained Rothman. The new discovery makes known a protein that prevents cell fusion from happening inappropriately.

"It's as if we now have a yin and yang of cell fusion," he said.

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