'Votes' of sub-cellular variables control cell fate

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Members of a population of identical cells often "choose" different fates, even though they exist in identical conditions.

The difference may rest with the "hidden variables" within the cells, said researchers from Baylor College of Medicine in a report that appears in the current issue of the journal *Cell*.

That finding, tested in bacterial cells of Escherichia coli infected with viruses called bacteriophage lambda, challenges the commonly held belief that the differences in fate rest with random chemical events that occur as the cells move among one another in their environment.

"One theme that recurs is that these cellular decisions are always noisy," said Dr. Ido Golding, assistant professor of biochemistry and molecular biology at BCM. "Sometimes cells choose fate A and sometimes fate B. The decision is never sharp - all one way or the other. "

The standard story as to why "noise" exists in cell fate decisions is the randomness of the environment inside the cell. Molecules bump into other molecules, and the resulting chemical reaction helps determine a cell's fate.

"There's merit to that hypothesis," said Golding. "You can also hypothesize that maybe it's not the whole story. Maybe we are missing an important parameter or a 'hidden variable.'"

Those "hidden variables" might make the cell fate decisions more understandable, he said.

The viruses (bacteriophage lambda) and the bacterial cells he used are common "models" in biology, often used to prove a principle before moving on to more complicated systems.

Suppose that two of these viruses infect the same cell. The cell has two possible fates. In one, the virus kills the cell, which explodes, releasing hundreds of new viruses. In the second, the cell survives with the virus' genome integrating itself into the cell's genome. The cell divides but lives under a shadow. At any point, the virus can switch to its "kill" mode.

What Golding and his colleagues found was that each virus independently makes a decision between cell life and cell death. With two viruses, that means there are four possible combinations of decisions. However, the cell continues to live only if both viruses choose that way. All other combinations result in the cell's death. The voting mechanism remains the same, no matter how many viruses invade the cell.

"Obviously, this is a simple system," said Golding.

"Is this framework useful for thinking about how decisions are made in higher systems," said Golding. "People know that copy number variation matters. You might have 10 copies of a gene and a higher concentration of the associated protein. Does each copy make its own decision about cell fate?"

More information: Cell: www.cell.com

Provided by Baylor College of Medicine