Protein clumps as memory: Yeast cells are able to form a memory through an aggregate

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Yeast has a somewhat complicated love life: on the one hand, a mother cell can produce genetically identical daughter cells through mitosis (cell division); on the other hand, yeast cells, who exist in two different mating types, are able to fuse with cells of the other mating type, thereby combining two different sets of genes. Two yeast cells with a single chromosome set each become a so-called yeast zygote with two sets of chromosomes.

To enable two fusion-inclined yeast cells to approach each other, each mating type releases a certain pheromone. If they thereby detect each other, they cease cell division and form a special extension towards each other in a kind of courtship. If these meet, the cells can fuse and form the zygote. If the partners miss, however, they both carry on producing offspring asexually.

Unexpected memory

ETH-Zurich researchers Fabrice Caudron and Yves Barral, a professor of biochemistry, have now discovered a previously unknown mechanism that enables yeast cells to memorise "bad experiences" during reproduction. If a mating attempt proves fruitless, the unsuccessful cell develops a molecular memory where the protein Whi3 is transformed and thus deactivated. Once transformed, the modified Whi3 "contaminates" other proteins of the same type. They attach themselves to each other and form aggregates, which the yeast cell can only break

apart with great difficulty. The Whi3 aggregates have the effect that future "lovers" have to release a much larger amount of the messenger substance for the cell to respond to it. If the amount is too low, the cell continues to reproduce solely through cell division.

"Nobody expected to find such a memory in a single-celled organism," explains Yves Barral, stressing the singularity of the discovery. Interestingly, there is a connection between memory and aging. As the cell grows older, the memories accumulate in a cell in the form of these aggregates. "Finding a suitable sexual partner becomes increasingly more difficult with time," says the ETH Zurich professor. After all, the aggregation process is extremely difficult to reverse. Only very rarely is the memory lost when the cell manages to dismantle the aggregates. The daughter cells that a mother cell pinches off do not inherit the memory and the aggregates remain in the mother. As a result, the offspring are not predisposed as the daughter cell is young. How the mother cell retains the protein aggregates is an important mechanism, which Barral and Caudron are currently researching.

Memory conserves energy

Research still needs to be conducted into why yeast cells store these (and other) substances. "A memory could thus be useful for the yeast to prevent further unproductive yet energy-intensive mating attempts," says Caudron, who has been researching this phenomenon for the last six years. The yeast faces a dilemma: if it only forms clones, the population will be genetically homogenous and, for instance, could die out in the event of a sudden change in the environmental conditions. While sexual reproduction leads to a genetically variable population, however, the cells have to expend far more energy.

"Cheating" yeasts are then a problem: if another cell or even a foreign organism produces the pheromone without offering a mating

opportunity, a naïve cell would wait in vain for its supposed partner without dividing in the meantime, which rules it out as a competitor for nutrients – much to its own detriment. Consequently, it is only worth responding to pheromones if successful reproduction is guaranteed. A yeast cell only stands a chance of this if the pheromone is present at high concentrations and indicates the immediate proximity of a partner.

From bacteria to multicellular organisms

With their work, the ETH Zurich scientists demonstrate a form of non-hereditary memory in a single-celled organism for the first time. The system of protein aggregates, however, appears to be universal and relatively old in the history of evolution. Barral also knows of bacteria that grow "old" like yeast cells. They, too, could have a similar memory mechanism, he suspects. Also, one such mechanism has been detected in the fruitfly, *Drosophila*. Males perform a courtship dance to win the affection of a female. If she has already been fertilised, she does not show any interest and the male memorises this experience in nerve endings, the synapses, with the aid of protein aggregates.

For Barral and Caudron, this is an indication that memory processes are very similar in single and multicellular organisms. "Who would have thought that a single-celled organism like yeast could help us to understand how we memorise our experiences?" says Barral.

More information: Caudron F & Barral Y. A Super-Assembly of Whi3 Encodes Memory of Deceptive Encounters by Single Cells during Yeast Courtship, Cell (2013) online publication 5th December 2013. dx.doi.org/10.1016/j.cell.2013.10.046

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