Biologists discover how yeast cells reverse aging

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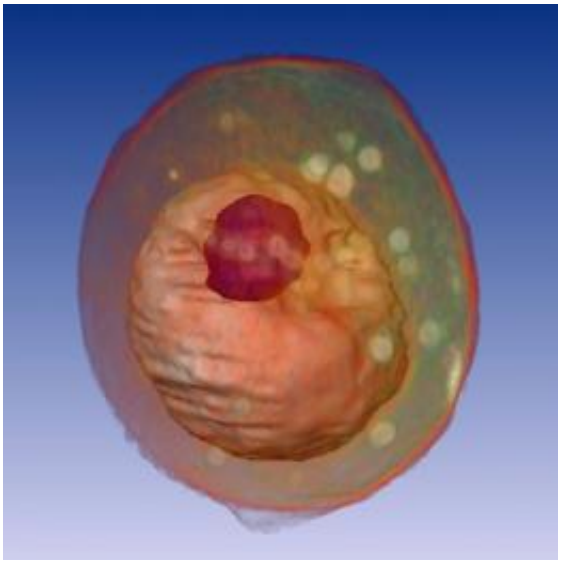

A whole yeast (Saccharomyces cerevisiae) cell viewed by X-ray microscopy. Inside, the nucleus and a large vacuole (red) are visible. Image: NIH

Human cells have a finite lifespan: They can only divide a certain number of times before they die. However, that lifespan is reset when reproductive cells are formed, which is why the children of a 20-year-old man have the same life expectancy as those of an 80-year-old man.

How that resetting occurs in human cells is not known, but MIT biologists have now found a gene that appears to control this process in yeast. Furthermore, by turning on that gene in aged yeast cells, they were

able to double their usual lifespan.

If the human cell lifespan is controlled in a similar way, it could offer a new approach to rejuvenating human cells or creating pluripotent stem cells, says Angelika Amon, professor of biology and senior author of a paper describing the work in the June 24 issue of the journal *Science*.

“If we can identify which genes reverse aging, we can start engineering ways to express them in normal cells,” says Amon, who is also a member of the David H. Koch Institute for Integrative Cancer Research. Lead author of the paper is Koch Institute postdoc Elçin Ünal.

Rejuvenation

Scientists already knew that aged yeast cells look different from younger cells. (Yeast have a normal lifespan of about 30 cell divisions.) Those age-related changes include accumulation of extra pieces of DNA, clumping of cellular proteins and abnormal structures of the nucleolus (a cluster of proteins and nucleic acids found in the cell nucleus that produce all other proteins in the cell).

However, they weren’t sure which of these physical markers were actually important to the aging process. “Nobody really knows what aging is,” Amon says. “We know all these things happen, but we don’t know what will eventually kill a cell or make it sick.”

When yeast cells reproduce, they undergo a special type of cell division called meiosis, which produces spores. The MIT team found that the signs of cellular aging disappear at the very end of meiosis. “There’s a true rejuvenation going on,” Amon says.

The researchers discovered that a gene called NDT80 is activated at the same time that the rejuvenation occurs. When they turned on this gene in

aged cells that were not reproducing, the cells lived twice as long as normal.

“It took an old cell and made it young again,” Amon says.

In aged cells with activated NDT80, the nucleolar damage was the only age-related change that disappeared. That suggests that nucleolar changes are the primary force behind the aging process, Amon says.

The next challenge, says Daniel Gottschling, a member of the Fred Hutchinson Cancer Research Center in Seattle, will be to figure out the cellular mechanisms driving those changes. “Something is going on that we don’t know about,” says Gottschling, who was not involved in this research. “It opens up some new biology, in terms of how lifespan is being reset.”

The protein produced by the NDT80 gene is a transcription factor, meaning that it activates other genes. The MIT researchers are now looking for the genes targeted by NDT80, which likely carry out the rejuvenation process.

Amon and her colleagues are also planning to study NDT80’s effects in the worm C. elegans, and may also investigate the effects of the analogous gene in mice, p63. Humans also have the p63 gene, a close relative of the cancer-protective gene p53 found in the cells that make sperm and eggs.

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