

'Housekeeping' proteins may set aging limit

[Aging cells may seal their fate by keeping worn-out proteins when they sprout offspring](#)

By Tina Hesman Saey

Web edition : Sunday, July 25th, 2010

Getting old means never letting go, a new study suggests.

Yeast, and possibly human cells, age at least in part because they hold on to broken-down proteins responsible for pumping out harmful chemicals and bringing in nutrients, researchers report in the August *Nature Cell Biology*. The finding could indicate that aging results both from a buildup of toxic substances, as researchers have previously suggested, and from a lack of essential nutrients.

Cells can replicate themselves only a finite number of times. For yeast cells that number is 20 to 30. But no one knows what sets the limit.

The new study suggests that a family of proteins known as multidrug resistance transporters is involved in determining how many times a cell can divide, and ultimately, how long an organism will live.

The discovery was serendipitous, says Rong Li, a cell biologist at the Stowers Institute for Medical Research in Kansas City, Mo. She and her colleagues study how cells divvy up proteins and other resources unequally when they divide. This unequal sharing of resources might seem unfair, but is actually necessary for cells to do their jobs. For instance, stem cells that make muscle, skin or other tissues divide to form two cells. One of the progeny is another stem cell. The other goes on to become muscle. In order for the two cells to follow their different destinies, they need to inherit different sets of proteins and other cellular resources.

Li studies the asymmetrical sharing process in yeast, which divide by budding. As a daughter cell buds off its mother, lots of new proteins are made and packed into the growing baby cell.

The researchers were looking for proteins that help resources move into the bud. Instead, the team discovered that mother yeast save some multidrug resistant proteins as heirlooms for themselves and give their daughters a new set.

Multidrug resistance transporters are proteins in a cell's membrane that pump toxic substances — such as drugs or harmful by-products of metabolism — out of the cell. The proteins got their name because their pumping action keeps cells from succumbing to drugs. But the

transporters do more than keep killer chemicals out of a cell. They also bring metal ions and other nutrients into cells.

All of a yeast cell's supply of the proteins is made just before a new cell separates from its mother, the researchers found. Mother cells keep the old proteins they were born with, and daughter cells get the fresh batch.

Over time, the mother cell's old proteins no longer pump as well, making it harder to take out cellular garbage. "At the same time they can't take the vitamin pills they need to survive," Li says. Giving yeast more of some transporter proteins increased the cell's life-span, the team showed.

Humans and other animals also carry the proteins, which some studies have linked to aging, says Brian Kennedy, a molecular biologist at the Buck Institute for Age Research in Novato, Calif. "The question is what are they getting rid of and why is that relevant to aging? We don't know that yet."

Boosting levels of the transporter proteins to fend off aging might not be such a great idea, Li says. The proteins may help protect against cancer by limiting the ability of cells with damaged DNA to divide. Cancer cells are notoriously chock-full of multidrug resistance transporters.