Scientists turn on fountain of youth in yeast

November 22 2011

(PhysOrg.com) -- Collaborations between Johns Hopkins and National Taiwan University researchers have successfully manipulated the life span of common, single-celled yeast organisms by figuring out how to remove and restore protein functions related to yeast aging.

A chemical variation of a “fuel-gauge” enzyme that senses energy in yeast acts like a life span clock: It is present in young organisms and progressively diminished as yeast cells age.

In a report in the September 16 edition of *Cell*, the scientists describe their identification of a new level of regulation of this age-related protein variant, showing that when they remove it, the organism’s life span is cut short and when they restore it, life span is dramatically extended.

In the case of yeast, the discovery reveals molecular components of an aging pathway that appears related to one that regulates longevity and lifespan in humans, according to Jef Boeke, Ph.D., professor of molecular biology, genetics and oncology, and director of the HiT Center and Technology Center for Networks and Pathways, Johns Hopkins University School of Medicine.

“This control of longevity is independent of the type described previously in yeast which had to do with calorie restriction,” Boeke says. “We believe that for the first time, we have a biochemical route to youth and aging that has nothing to do with diet.” The chemical variation, known as acetylation because it adds an acetyl group to an existing

molecule, is a kind of “decoration” that goes on and off a protein — in this case, the protein Sip2 — much like an ornament can be put on and taken off a Christmas tree, Boeke says. Acetylation can profoundly change protein function in order to help an organism or system adapt quickly to its environment. Until now, acetylation had not been directly implicated in the aging pathway, so this is an all-new role and potential target for prevention or treatment strategies, the researchers say.

The team showed that acetylation of the protein Sip2 affected longevity defined in terms of how many times a yeast cell can divide, or “replicative life span.” The normal replicative lifespan in natural yeast is 25. In the yeast genetically modified by researchers to restore the chemical modification, life span extended to 38, an increase of about 50 percent.

The researchers were able to manipulate the yeast life span by mutating certain chemical residues to mimic the acetylated and deacetylated forms of the protein Sip2. They worked with live yeast in a dish, measuring and comparing the life spans of natural and genetically altered types by removing buds from the yeast every 90 minutes. The average lifespan in normal yeast is about 25 generations, which meant the researchers removed 25 newly budded cells from the mother yeast cell. As yeast cells age, each new generation takes longer to develop, so each round of the experiment lasted two to four weeks.

“We performed anti-aging therapy on yeast,” says the study’s first author, Jin-Ying Lu, M.D., Ph.D., of National Taiwan University. “When we give back this protein acetylation, we rescued the life span shortening in old cells. Our next task is to prove that this phenomenon also happens in mammalian cells.”

Provided by Johns Hopkins University