Glucose to glycerol conversion in long-lived yeast provides anti-aging effects

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Cell biologists have found a more filling substitute for caloric restriction in extending the life span of simple organisms. In a study published May 8 in the open-access journal *PLoS Genetics*, researchers from the University of Southern California Andrus Gerontology Center show that yeast cells maintained on a glycerol diet live twice as long as normal -- as long as yeast cells on a severe caloric-restriction diet. They are also more resistant to cell damage.

Many studies have shown that caloric restriction can extend the life span of a variety of laboratory animals. Caloric restriction is also known to cause major improvements in a number of markers for cardiovascular diseases in humans. This study is the first to propose that "dietary substitution" can replace "dietary restriction" in a living species.

"If you add glycerol, or restrict caloric intake, you obtain the same effect," said senior author Valter Longo. "It's as good as calorie restriction, yet cells can take it up and utilize it to generate energy or for the synthesis of cellular components."

Longo and colleagues Min Wei and Paola Fabrizio introduced a glycerol diet after discovering that genetically engineered long-lived yeast cells that survive up to 5-fold longer than normal have increased levels of the genes that produce glycerol. In fact, they convert virtually all the glucose and ethanol into glycerol. Notably, these cells have a reduced activity in the TOR1/SCH9 pathway, which is also believed to extend life span in organisms ranging from worms to mice.

When the researchers blocked the genes that produce glycerol, the cells lost most of their life span advantage. However, Longo and colleagues believe that the "glucose to glycerol" switch represents only a component of the protective systems required for the extended survival. The current study indicates that glycerol biosynthesis is an important process in the metabolic switch that allows this simple organism to activate its protective systems and live longer.

"This is a fundamental observation in a very simple system," Longo said, "that at least introduces the possibility that you don't have to be calorie-restricted to achieve some of the remarkable protective effects of the hypocaloric diet observed in many organisms, including humans. It may be sufficient to substitute the carbon source and possibly other macronutrients with nutrients that do not promote the "pro-aging" changes induced by sugars."

More information: Wei M, Fabrizio P, Madia F, Hu J, Ge H, et al. (2009) Tor1/Sch9-Regulated Carbon Source Substitution Is as Effective as Calorie Restriction in Life Span Extension. *PLoS Genet* 5(5): e1000467. doi:10.1371/journal.pgen.1000467, www.plosgenetics.org/article/i … journal.pgen.1000467

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