MedicalXpress

Key protein may explain the anti-aging and anti-cancer benefits of dietary restriction

May 22 2009

A protein that plays a key role in tumor formation, oxygen metabolism and inflammation is involved in a pathway that extends lifespan by dietary restriction. The finding, which appears in the May 22, 2009 edition of the on-line journal *PLoS Genetics*, provides a new understanding of how dietary restriction contributes to longevity and cancer prevention and gives scientists new targets for developing and testing drugs that could extend the healthy years of life.

The protein is HIF-1 (hypoxia-inducible factor 1). It helps cells survive by "turning on" when oxygen levels are low. HIF-1 is also active in some forms of human cancer. HIF-1 overexpression is frequently detected in solid tumors; inhibition of HIF-1 has been proved to be an efficient way to prevent cancer growth. Now, scientists at the Buck Institute for Age Research have shown that HIF-1 is also a key player in dietary restriction . HIF-1 is involved in a molecular pathway known to regulate cell growth and metabolism in response to nutrients and growth factors.

"Previous studies on HIF-1 have mainly focused on its roles in oxygen metabolism and tumor development", said Buck faculty member Pankaj Kapahi, PhD, lead author of the study.

Kapahi says the study encourages the investigation of HIF-1 in nutrient sensing pathways. "The data in this study also points to HIF-1 as a likely target for regulating the protective effects of dietary restriction in mammals," said Kapahi.

"Dietary restriction is one of the most robust methods for extending lifespan and delaying age-related disease among various species."

Kapahi says the molecular mechanisms involved in how dietary restriction slows cancer and extends lifespan have been largely unknown. "This study gets us closer to understanding that process and gives us better targets for both designing and testing drugs which could mimic the effects of dietary restriction in humans," said Kapahi.

The research involved nematode worms that were genetically altered to both under and over-express HIF-1. The animals, which are the most-often used model to study aging, were fed different diets. Animals that were designed to over-express HIF-1 did not get the benefit of lifespan extension even though their diets were restricted. Animals that under-expressed HIF-1 lived longer, even when they had a nutrient-rich diet. Furthermore, it was found that the lifespan extension resulting from dietary restriction required activity in signaling pathways in the endoplasmic reticulum, the part of the cell involved in processing and the proper folding of proteins. This finding supports the theory that aging stems from the effects of misfolded proteins and opens up a rich area of investigation to examine the mechanisms by which stress in the endoplasmic reticulum affects lifespan.

Source: Buck Institute for Age Research