Study strengthens link between sirtuins proteins and life extension

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Biology professor Leonard Guarente

(PhysOrg.com) -- A new paper from MIT biology professor Leonard Guarente strengthens the link between longevity proteins called sirtuins and the lifespan-extending effects of calorie restriction.

For decades, it has been known that cutting normal calorie consumption by 30 to 40 percent can boost lifespan and improve overall health in animals such as worms and mice. Guarente believes that those effects are controlled by sirtuins — proteins that keep cells alive and healthy in the face of stress by coordinating a variety of hormonal networks, regulatory proteins and other genes.

In his latest work, published Dec. 15 in the journal *Genes and Development*, Guarente adds to his case by reporting that sirtuins bring about the effects of calorie restriction on a brain system, known as the

somatotropic signaling axis, that controls growth and influences lifespan length.

"This puts SIRT1 at a nexus connecting the effects of diet and the somatropic signaling axis," says Guarente. "This is a major shot across the bow that says sirtuins really are involved in fundamental aspects of calorie restriction."

Guarente and others believe that drugs that boost sirtuin production could help fight diseases of aging such as diabetes and Alzheimer's, improving health in later life and potentially extending lifespan. Drugs that promote sirtuin production are now in clinical trials in diabetes patients, with results expected next year.

The researchers genetically engineered mice whose ability to produce the major mammalian sirtuin SIRT1 in the brain was greatly reduced. Those mice and normal mice were placed on a calorie-restricted diet. The normal mice showed much lower levels of circulating growth hormones, demonstrating that their somatotropic signaling system was impaired, but calorie restriction had no effect on hormone levels of mice that could not produce SIRT1.

In future work, Guarente plans to investigate the mechanism by which sirtuins regulate the somatotropic axis. The work could also help researchers and companies in their search for small molecules that modulate sirtuins for maximum benefit.

More information: “Neuronal SIRT1 regulates endocrine and behavioral responses to calorie restriction,” Dena Cohen, Leonard Guarente et al. Genes and Development, Dec. 15, 2009.

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