Mimicking calorie restriction to fight obesity, type 2 diabetes

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Obesity

A Yale University-led research team has discovered how reduced expression of a particular gene protects against obesity and type 2 diabetes, possibly prolonging lifespan by mimicking the effects of calorie restriction. The study appears in the August 3 issue of *Cell Metabolism*.

It is known that excess calorie consumption leads to obesity, insulin resistance and increased mortality, whereas calorie restriction reduces accumulation of body fat and improves cellular energy balance and insulin action – reversing obesity and type 2 diabetes, delaying the aging process, and prolonging life in primates and many other species.

It has also been shown in the past that reduced expression of the so-

called “INDY” gene in D. Melanogaster flies and C. elegans worms promotes longevity in a manner similar to calorie restriction. But until now, the cellular mechanism by which this happens was unknown.

The Yale team generated a mouse with the so-called “INDY” gene deleted. Loss of the gene altered chemical levels in the cellular signaling network in a way that improved mitochondrial action in the liver, metabolism of fatty acids, and cellular energy transport. Overall, these traits protected the mice from diet-related accumulation of body fat and insulin resistance that evolve, as we age, into type 2 diabetes.

Discovering how deletion of the INDY gene would impact mitochondrial metabolism in the liver was key, because that is the main organ where the INDY gene does its work. “These findings suggest that INDY may be a novel therapeutic target for the treatment of hepatic insulin resistance, which is a major factor in the pathogenesis of type 2 diabetes ,” said lead author Gerald Shulman, M.D., Ph.D., George R. Cowgill Professor of Physiological Chemistry, Medicine and Cellular & Molecular Physiology at Yale School of Medicine and a Howard Hughes Medical Institute investigator.

Provided by Yale University