Decoding fat cells: Discovery may explain why we gain weight

December 11 2014

University of Rochester researchers believe they're on track to solve the mystery of weight gain - and it has nothing to do with indulging in holiday eggnog.

They discovered that a protein, Thy1, has a fundamental role in controlling whether a primitive cell decides to become a fat cell, making Thy1 a possible therapeutic target, according to a study published online this month by the *FASEB Journal*.

The research brings a new, biological angle to a problem that's often viewed as behavioral, said lead author Richard P. Phipps, Ph.D. In fact, some diet pills consist of antidepressants or anti-addiction medications,

and do not address what's happening at the molecular level to promote fat cell accumulation.

Although Thy1 was discovered 40 years ago and has been studied in other contexts, its true molecular function has never been known. Phipps' laboratory reported for the first time that expression of Thy1 is lost during the development of fat cells, suggesting obesity could be treated by restoring Thy1.

They're also working towards developing an anti-obesity drug, a Thy1-peptide, and have applied for an international patent to protect the invention. Phipps, who has been investigating Thy1 since 1989, is working on identifying a company to form a partnership for the drug development.

"Our goal is to prevent or reduce obesity and in this paper we've shown how to do this in principle," said Phipps, the Wright Family Research Professor in the Department of Environmental Medicine and a professor of Ophthalmology. "We believe that weight gain is not necessarily just a result of eating more and exercising less. Our focus is on the intricate network involved in fat cell development."

Researchers studied mice and human cell lines to confirm that a loss of Thy1 function promotes more fat cells. Mice lacking the Thy1 protein and fed a high-fat diet gained more weight and faster, compared to normal mice in a control group that also ate the same high-fat diet. In addition, the fatter mice without Thy1 had greater than twice the levels of resistin in their blood, a biomarker for severe obesity and insulin-resistance or diabetes. Experiments using human fatty tissue from the abdomen and eyes showed similar results.

Phipps and colleagues, including key researcher Collynn Woeller, Ph.D., research assistant professor of Environmental Medicine, are continuing

to investigate why cells with the potential to turn into fat cells loose the Thy1 protein, and why fat accumulates faster when Thy1 shuts off. It's not clear whether Thy1 levels are different in people at birth, or whether they change with time and exposure to various environmental agents.

To address the latter question, Phipps' laboratory is separately studying whether chemicals known as obesogens - such as bisphenol A (BPA), flame retardants, and phthalates - reduce Thy1 expression in human cells and promote obesity. That study is funded by the National Institute of Environmental Health Sciences. The work reported in FASEB was funded by the National Institutes of Health, as well as grants from the Rochester/Finger lakes Eye & Tissue Bank and the Research to Prevent Blindness Foundation.

An estimated 60 million people are defined as clinically obese in the United States. Diseases associated with obesity include Type 2 diabetes, various heart conditions and some cancers. Worldwide obesity has nearly doubled since 1980, according to the World Health Organization, and Phipps said the obesity epidemic is growing fastest in well-developed regions such as Asia, Latin America, and parts of the Middle East.

More information: *FASEB Journal*, www.fasebj.org/content/early/2… 257121.full.pdf+html

Provided by University of Rochester Medical Center