MedicalXpress

Study reveals how high-fat foods impact diabetes and metabolic syndrome

May 22 2012

A University of Michigan Health System study provides new clues about the health-damaging molecular changes set in motion by eating high-fat foods.

A better understanding of the body's response to indulgent eating could lead to new approaches for treating diabetes and metabolic syndrome. High-fat foods can contribute to obesity, which increases the risk for developing type 2 diabetes.

The researchers learned a key protein called Bcl10 is needed for the free fatty acids – which are found in high fat food and stored in body fat -- to impair insulin action and lead to abnormally high blood sugar.

In the laboratory study, mice deficient in Bcl10 were protected from developing insulin resistance when fed a high-fat diet. The findings will be published May 31 in *Cell Reports*.

Insulin helps control blood sugar, but insulin resistance can lead to the abnormally high blood sugar levels that are the hallmark of diabetes. Insulin resistance can occur as part of metabolic syndrome, a cluster of conditions that increase the risk for type 2 diabetes and heart disease.

As millions of Americans become overweight and obese, type 2 diabetes and metabolic syndrome are on the rise.

"The study also underscores how very short-term changes in diet such as

high-fat eating for only a few days, perhaps even less, can induce a state of insulin resistance," says senior study author Peter C. Lucas, M.D., Ph.D., associate professor of pathology at the University of Michigan Medical School.

Researchers began by investigating how free fatty acids induce inflammation and impair insulin action in the liver. It's thought the liver is a major target for the harmful effects of free fatty acids.

In the liver, free fatty acids undergo metabolism to produce diacylglycerols prior to inducing the inflammatory response. Diacylglycerols also activate NF-kB signaling which has been linked with cancer, metabolic and vascular diseases.

The team of researchers concluded that Bcl10 is required for fatty acids to induce inflammation and insulin resistance. In the study, Bcl10-deficient mice showed significant improvement in regulation of blood sugar.

"We were surprised to learn that Bcl10, a protein previously known for its critical role in immune cell response to infection, also plays a critical role in the liver's response to fatty acid," says Lucas.. "This is an example of nature co-opting a mechanism fundamental to the immune system and using it in a metabolic organ, in this case, the liver."

"These findings reveal a new and important role for Bcl10 and could lead to novel ideas for treating patients with metabolic syndrome and type 2 diabetes," says co-senior author Linda M. McAllister-Lucas, M.D., Ph.D., associate professor of pediatric hemotology/oncology.

More information: "Bcl10 Links Saturated Fat Overnutrition with Hepatocellular NF-kB Activation and Insulin Resistance," *Cell Reports* (2012), doi:10.1016/j.celrep.2012.04.006, May 31, 2012.

Provided by University of Michigan Health System