In obesity, a micro-RNA causes metabolic problems

September 20 2012

University of Illinois molecular and integrative physiology professor Jongsook Kim Kemper and her colleagues were able to reverse some of the metabolic problems associated with obesity in mice by targeting a micro-RNA. Credit: L. Brian Stauffer

Scientists have identified a key molecular player in a chain of events in the body that can lead to fatty liver disease, Type II diabetes and other metabolic abnormalities associated with obesity. By blocking this molecule, the researchers were able to reverse some of the pathology it caused in obese mice.

Their findings appear in the *Proceedings of the National Academy of Sciences*.

MiR-34a (pronounced MEER-34a), a micro-RNA, occurs at higher than normal levels in the livers of obese animals and in human patients with fatty liver disease. In the new study, researchers discovered that miR-34a gums up production of a protein receptor, called beta-Klotho, needed for metabolic signaling in the liver. This hinders normal glucose uptake, glycogen and protein synthesis and other metabolic activities.

In response to signals from the small intestine, beta-Klotho contributes to normal liver function after a meal, said University of Illinois molecular and integrative physiology professor Jongsook Kim Kemper, who led the study. But in obesity, levels of miR-34a surge much higher than normal, resulting in abnormally low levels of beta-Klotho.

"The downstream effect is more glucose in the blood, more fat in the liver," she said.

The effects are dramatic. Slices of liver tissue from obese mice are laden with fat, whereas normal mice have minimal amounts of fat in their livers.

The researchers used a complementary strand of RNA (called antisense RNA) to neutralize miR-34a in obese mice. This therapeutic approach improved "metabolic outcomes, including decreased liver fat and improved glucose level in the blood," Kemper said.

More information: "Aberrantly Elevated miR-34a in Obesity Attenuates Hepatic Responses to FGF19 by Targeting a Membrane Co-Receptor β-Klotho," *Proceedings of the National Academy of Sciences*, 2012. www.pnas.org/content/early/201 … /1205951109.abstract