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# Researchers identify protein that modulates metabolic dysfunction in obesity

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Researchers from Boston University School of Medicine (BUSM) have discovered that Sfrp5, which refers to secreted frizzled-related protein 5, is an anti-inflammatory adipokine whose expression is disrupted in animal models of obesity and type 2 diabetes. The findings, which currently appear on-line in *Science*, may provide a new way of targeting metabolic disease, specifically obesity.

Obesity is a predisposing factor for metabolic disorders such as type 2 diabetes, which is often associated with a low-grade inflammatory state in adipose tissue. Adipose tissue secretes a variety of cytokines, referred to as adipokines. Most adipokines, such as tumor necrosis factor (TNF) α, interleukin (IL)-6 and leptin, are pro-inflammatory. One prominent exception is adiponectin, an anti-inflammatory adipokine that promotes insulin sensitization and protects cardiovascular tissue from ischemic injury.

According to the researchers, because adipokine dysregulation can contribute to the pathogenesis of obesity-linked disorders, they sought to identify new adipokines by comparing the gene expression profile of adipose tissue from lean mice with that from obese mice on a high calorie diet.

"Our study shows that Sfrp5 is secreted by adipocytes and that it controls the microenvironment of white adipose tissue under conditions of obesity-induced metabolic stress. Whereas Sfrp5 deficient mice do not express a detectable phenotype when fed a normal diet, these animals

displayed aggravated fat pad inflammation and systemic metabolic dysfunction when fed a high calorie diet," explained senior author Kenneth Walsh, PhD, director of the Whitaker Cardiovascular Institute at BUSM. Conversely, the BUSM researchers found the administration of Sfrp5 to models of obese and diabetic mice improved metabolic function and reduced adipose tissue inflammation.

The researchers propose that Sfrp5 neutralizes noncanonical JNK activation by Wnt5a in macrophages and adipocytes via paracrine and autocrine mechanisms, respectively. "The JNK signaling pathway in adipocytes and macrophages has emerged as an important mediator of adipose tissue inflammation that affects systemic metabolism. Thus, the Sfrp5-JNK1 regulatory axis in fat represents a potential target for the control of obesity-linked abnormalities in glucose homeostasis," added Walsh.

Provided by Boston University