Improving obesity-induced insulin sensitivity

June 1 2012

In recent years, a growing body of evidence has linked inflammation to the development of insulin resistance. In insulin resistance, the hormone insulin is less effective in promoting glucose uptake from the bloodstream into other tissues. Obesity is a major factor that contributes to insulin resistance, which can eventually lead to type 2 diabetes. Previous studies have shown that proinflammatory molecules found in fat tissue decreases sensitivity of tissues to insulin.

To identify drug targets that will improve insulin sensitivity, Dr. Jerrold Olefsky and colleagues from the University of California in San Diego investigated the role of G protein-coupled receptor 21 (GPR21) in insulin resistance and energy homeostasis. The group compared mice without the gene encoding GPR21 to healthy control mice under normal and high-fat diet conditions. They discovered that mice lacking GPR21 had enhanced insulin sensitivity and increased energy expenditure independent of diet.

This result was attributed to the reduced migration of inflammatory cells to the liver and fat tissue in the absence GPR21. Under normal diet, absence of GPR21 in the hypothalamus caused a modest decrease in body weight. This is the first study to demonstrate the negative impact of GPR21 on inflammation and insulin sensitivity. Their findings suggest that GPR21 inhibition may improve insulin resistance and enhance energy expenditure, making GPR21 inhibitors promising treatments for diabetes.

More information: G protein–coupled receptor 21 deletion improves

insulin sensitivity in diet-induced obese mice, *Journal of Clinical Investigation*, 2012.