Multihormone reverses metabolic damage of high calorie diet

January 15 2014

Importantly, the scientists found out that treatment of obese mice with this GLP-1/Glucagon co-agonist improves metabolism and body weight associated with restored function of the weight lowering hormone leptin, even in the continued presence of a high-fat, high-sugar diet. The results are published in the current issue of the official journal of the American Diabetes Association *Diabetes*.

The adipocyte hormone leptin plays a key role in the physiology of energy and glucose metabolism. Leptin is normally secreted from adipose tissue to blood in proportion to the amount of body fat. Increased leptin levels inform the brain of stored calories and it responds to inhibit food intake, increase energy expenditure and decrease blood glucose. However, obese individuals are resistant to leptin's metabolic effects, which limits the use of leptin as an anti-obesity drug. In their new study, the group of Dr. Timo Müller (Institute of Diabetes and Obesity, Helmholtz Center Munich, Germany) discovered that treatment of diet-induced obese mice with a peptide that simultaneously activates GLP-1/glucagon receptors reversed leptin resistance, improved body weight and normalized glucose metabolism even without switching to a healthier diet.

"We are particularly encouraged to see that adding leptin produced weight loss beyond the benefits of the peptide-based, co-agonist" says Prof. Matthias Tschöp, Research Director of the Helmholtz Diabetes Center and Chair of Metabolic Diseases at Technische Universität München, Germany. The identification of this novel treatment strategy is

the result of many years of collaboration with Ambrx and Prof. Richard DiMarchi (Indiana University) who noted: "The results are inspiring, and establish a basis for validation in human studies". Dr. Christoffer Clemmensen, the lead author of the study, adds: "If this concept proves safe and efficient at least in specific subpopulations of obese patients, then we may have come a step closer to personalized prevention of type 2 diabetes".

Their findings, just published in the journal *Diabetes*, are aligned with the overall research objective of the Helmholtz Diabetes Center at Helmholtz Zentrum Munich, partner of the German Center for Diabetes Research (DZD). We aim to establish new approaches in the diagnosis, therapy and prevention of civilization's major diseases and to develop these approaches as quickly as possible in the context of translational research in order to provide specific benefits for society.

More information: Clemmensen C, Chabenne J, Finan B, Sullivan L, Fischer K, Küchler D, Sehrer L, Ograjsek T, Hofmann S, Schriever SS, Pfluger PT, Pinkstaff J, Tschöp MH, Dimarchi R, Müller TD. GLP-1/glucagon co-agonism restores leptin responsiveness in obese mice chronically maintained on an obesogenic diet. *Diabetes*. 2013 Dec 30. [Epub ahead of print] diabetes.diabetesjournals.org/ … 8/db13-1609.abstract

Provided by Helmholtz Association of German Research Centres