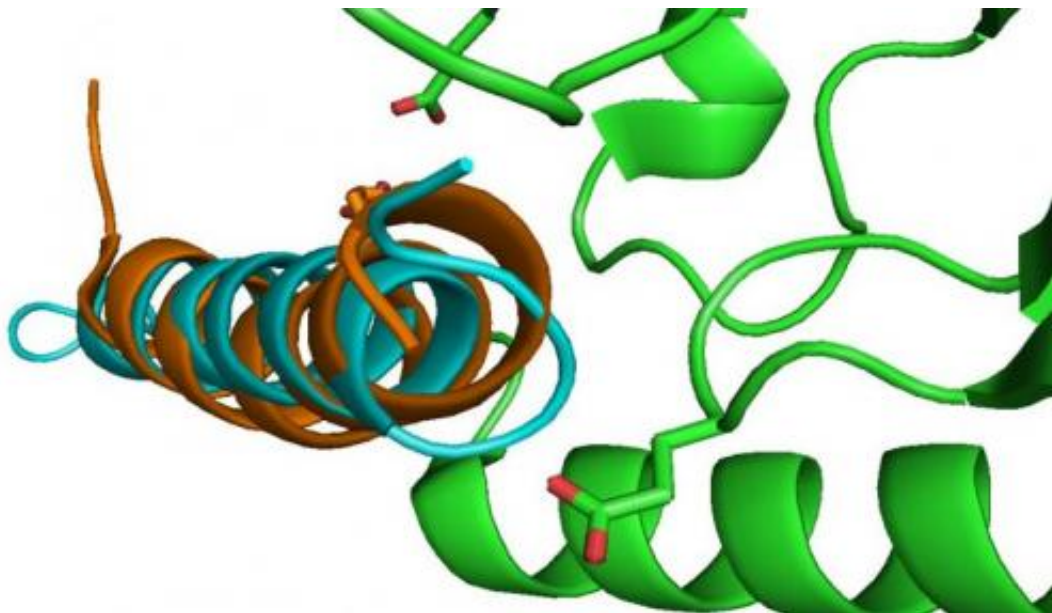


Rule of three: Hormone triplet offers hope for obesity and diabetes

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The new peptide offers a triple hormone effect in a single-cell molecule. Credit: Indiana University

A new substance that unifies the action profiles of three gastrointestinal hormones lowers the blood sugar level and reduces body fat considerably beyond existing drugs. With the discovery and validation of such novel molecules, scientists from the Helmholtz Zentrum München and the Technische Universität München, in collaboration with Indiana University, USA, have again added a new dimension to innovating treatment approaches for type 2 diabetes and obesity. The results have

been published in the journal *Nature Medicine*.

Recently, the researchers had constructed several single molecules with dual [hormone](#) action. Now, for the first time, the researchers succeeded in designing a substance that combines three metabolically active hormone components (GLP-1, GIP and glucagon) and offers unmatched potency to fight [metabolic diseases](#) in pre-clinical trials.

The team headed by physician scientist Matthias Tschöp (Helmholtz Diabetes Center at HMGU and Metabolic Diseases Chair at TUM) and peptide chemist Richard DiMarchi (Indiana University) has been cooperating for almost a decade to invent improved therapeutics for [type 2 diabetes](#) and obesity. One of their novel approaches is to design molecules that combine the effects of specific metabolic hormones. In recent years, the scientists succeeded in developing hormone-like molecular structures that incorporate efficacy of two such messengers and, consequently, can trigger more significant metabolic improvements than was previously possible with known medicinal approaches.

Triple hormone reduces body weight even more effectively and improves insulin sensitivity

The interdisciplinary team led by Tschöp and DiMarchi is now presenting a triple hormone that dramatically reduces blood glucose, appetite, and body fat in animal models while also improving fat content in the liver, cholesterol levels and calorie burning even more effectively than with previously available single action or dual action molecules. The tri-agonist can reduce body weight by around 30 percent, roughly twice as much as a dual co-agonist at the same dose, while massively improving [insulin sensitivity](#), essentially curing the rodents of obesity and diabetes.

Effect on receptors of GLP-1, GIP and glucagon

The triple hormone specifically and equally targets three receptors of GLP-1, GIP and glucagon. GLP-1 and GIP predominantly contribute to improved insulin release and a reduction of blood glucose levels. GLP-1 additionally curbs appetite. The third hormone, glucagon, primarily increases the long-term rate at which calories are burned and improves liver function. "This triple hormone effect in a single molecule shows results never achieved before. A number of metabolic control centers are influenced simultaneously, namely in the pancreas, liver, fat depots and brain," explains first author Brian Finan, who works as a chemist and pharmacologist at the Helmholtz Diabetes Center.

"This latest breakthrough shows us that we are on the right path to designing better treatments in the fight against obesity and diabetes," reports Tschöp. "Now the most important steps are clinical studies. In parallel, we are working on personalized medicines for individual patient needs, combining four, five, or more hormone components."

The objective of research at the Helmholtz Zentrum München, partner in the German Center for Diabetes Research (DZD), is to establish new approaches to the diagnosis, treatment and prevention of major widespread diseases and to further develop these as quickly as possible in the sense of translational research in order to produce concrete benefits for society.

More information: Finan, B. et al. (2014). A rationally designed monomeric peptide triagonist corrects obesity and diabetes in rodents, *Nature Medicine*, [DOI: 10.1038/nm.3761](https://doi.org/10.1038/nm.3761)

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