Adipose tissue hormone protects cells that secrete insulin, reverses damage associated with obesity

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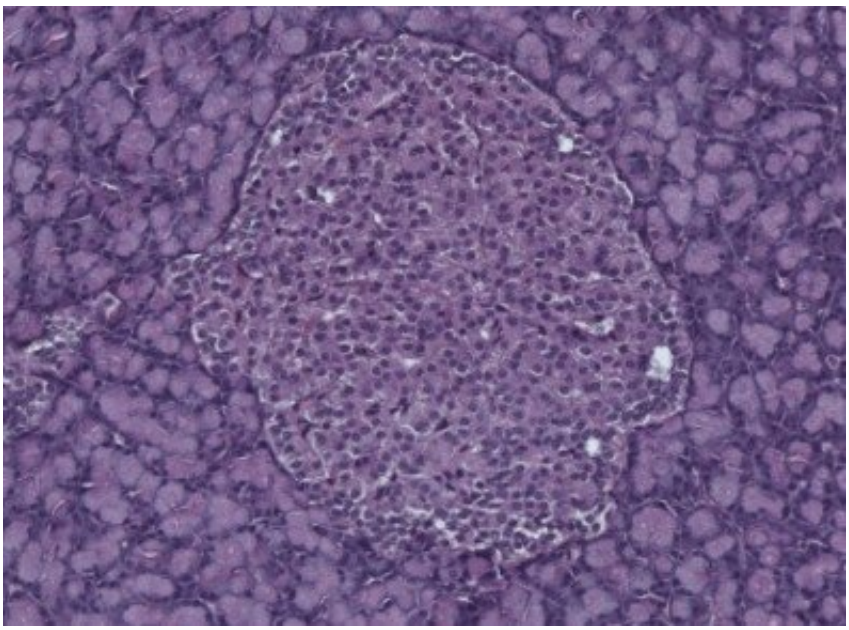

Pancreatic islet containing insulin-producing cells that can be affected by obesity. Credit: Energy Metabolism Laboratory/IQ-USP

Adiponectin, a hormone secreted by adipose tissue, plays a doubly important role in preserving pancreatic function. In lean people, it protects beta cells, which make insulin, and in obese people, it reverses damage to fatty tissue. The discovery was made by researchers at the University of São Paulo's Chemistry Institute (IQ-USP) in Brazil and is reported in an article published in the journal *Aging Cell*, showing that

adiponectin is a potential therapeutic target.

More than 1 billion people are obese worldwide, according to data made available by the World Health Organization (WHO) in 2022: 650 million adults, 340 million adolescents and 39 million children. Some 4 billion people, or more than half the world's population, will be affected by the disease in the next decade, the World Obesity Federation predicts. Obesity curtails life expectancy and increases the incidence of age-related dysfunctions, especially deregulation of pancreatic beta cells leading to inadequate secretion of insulin and type 2 diabetes.

In previous animal model trials, researchers at IQ-USP's Energy Metabolism Laboratory had shown that beta cells incubated with blood serum from lean and obese rats underwent alterations in a period of 24 hours. In lean rats, the performance of the beta cells improved because their mitochondria became more capable of producing ATP and signaling insulin secretion. ATP is a key energy-carrying molecule that fuels cellular functions. In obese rats, the integrity of the beta cells was impaired, with the opposite effect.

To confirm these findings in humans, the group analyzed blood samples from lean and obese men and women supplied by A. C. Camargo Cancer Center, an important institution in São Paulo City. "We were able to demonstrate that the lean women responded well as far as cell respiration and insulin secretion were concerned, and that the situation deteriorated in obese women as well as both lean and obese men, in that order," said Ana Cláudia Munhoz, first author of the article and a postdoctoral fellow at IQ-USP. "Gender and body fat appeared to be involved in the process, suggesting the involvement of adiponectin, which is important to mitochondrial regulation and is more abundant in women. Our laboratory trials confirmed this hypothesis."

"We found increased levels of adiponectin in lean plasma to be

responsible for preserving the functions of beta cells. This is the first time the observation has been made. In obese plasma, the hormone repaired 100% of the damage, in one of the most remarkable scientific effects I've ever seen," said Alicia Kowaltowski, last author of the article and a professor in IQ-USP's Department of Biochemistry.

According to the researchers, adiponectin may not be the only missing blood component in obese people, as diabetes is a multifactorial disease, but it is significant for its capacity to modulate the functions of beta cells .

Therapeutic target

The results of the study, which was supported by FAPESP via two projects, reinforce the importance of finding out more about the molecular mechanisms involved in obesity and their association with other health problems. This would help improve treatment and counter the stigma of "poor self-control," proving yet again that obesity is a disease caused by personal and genetic factors.

They also represent another step in the process of understanding key aspects of obesity, such as its varying prevalence in men and women, for example.

Specifically with regard to beta cells, the discovery brings good news for the future, because it shows that problems deriving from obesity are treatable and can be mitigated in a relatively short time, pointing to a promising opportunity for the development of novel therapeutic strategies.

"Adiponectin proper can't be used in treatment because the protein is already abundant in the organism, unlike insulin, but it indicates a pathway for which novel therapeutic molecules can be designed,"

Kowaltowski said. "We've already started to study drugs known to activate processes mediated by this hormone, for example."

The researchers stressed, however, that there are currently no treatments capable of raising blood levels of adiponectin, apart from losing weight and reducing central adiposity by limiting calorie intake and exercising. "It's important to bear in mind that no products sold as medication for obesity have any scientific basis right now. Patients should be careful to avoid falling for promises by charlatans on the internet," Munhoz warned.

More information: Ana Cláudia Munhoz et al, Adiponectin reverses β-Cell damage and impaired insulin secretion induced by obesity, *Aging Cell* (2023). DOI: 10.1111/acel.13827

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