

# Obesity health risk cause 'found'

BBC News  
July 11, 2009

**Scientists believe they may have uncovered a key reason why obese people have a raised risk of health complications such as type 2 diabetes.**

They blame a specific protein - pigment epithelium-derived factor (PEDF) - which is secreted by fat cells.

The Australian and US research on mice suggests blocking some of PEDF's action may reverse some complications - raising hopes of new drug treatments.

The study appears in the journal Cell Metabolism.

Because PEDF is produced by fat cells people who are overweight have higher levels of the protein in the bloodstream.

The latest research shows that the protein sends a signal to other tissues in the body, triggering development of insulin resistance - a condition that often leads to type 2 diabetes – in the muscle and liver.

Raised PEDF levels were also linked to a release of fats into the bloodstream, raising the risk of complications such as heart disease.

## Metabolism

In tests on obese mice, the researchers found that treatments designed to block the action of PEDF lowered the animals' blood fat level and reversed some of their insulin resistance.

Fat cells are known to play an important role in regulating the body's metabolism by releasing hormones and other chemicals.

This pattern of secretion is also known to change with the size of the fat cells.

**“ In light of our findings, we believe that blocking PEDF will ameliorate several obesity-related complications ”**

Dr Matthew Watt  
Monash University

The latest study set out to identify which of these secretions had a profound general impact on metabolism.

The researchers took particular interest in PEDF because it was already known that levels of the protein were raised in people with type 2 diabetes, and metabolic syndrome - a collection of risk factors including too much belly fat, high cholesterol and high blood pressure.

They found that of all the molecules secreted by fat cells PEDF was among the most abundant.

They also showed that PEDF levels fell in obese mice when they lost weight, either by using diet or drugs.

When lean mice were injected with PEDF they showed signs of developing insulin resistance and inflammation in both muscle and liver.

And in the long term, PEDF raised fat levels in the animals' blood.

These fats were transported into the muscle and liver, where they accumulated, raising the risk of insulin resistance still further.

## Complications

But when obese mice were given treatment to neutralise PEDF their sensitivity to insulin improved, reducing their risk of diabetes, and the level of fats in their blood fell.

Researcher Dr Matthew Watt, from Monash University in Australia, said: "In light of our findings, we believe that blocking PEDF will ameliorate several obesity-related complications." He said previous research had suggested that PEDF also protects against furring of the arteries and excessive blood vessel growth and helps keep the nervous system healthy.

But he said new drugs could be at least five years away.

Dr Victoria King, of Diabetes UK, said: "While this study has been carried out in mice, there has been some indication from other studies that higher levels of this protein found in overweight people with type 2 diabetes could indicate that a similar process is occurring in humans.

**“ Tackling insulin resistance directly, even in the absence of weight loss, could potentially strengthen our ability to help obese patients reduce their risk of life-shortening disease ”**

Dr Ian Campbell, medical director of the charity Weight Concern

"But this would need to be studied further and verified."

Dr Ian Campbell, medical director of the charity Weight Concern, said: "If we were able to somehow switch off or limit the activities of this, or related compounds it could open up new possibilities for drug treatments, not for obesity, but for the secondary effects."

"To date weight loss drugs though effective are often not effective enough."

"Tackling insulin resistance directly, even in the absence of weight loss, could potentially strengthen our ability to help obese patients reduce their risk of life-shortening disease."

Professor Ian MacDonald, an expert in the chemistry of nutrition at the University of Nottingham, said PEDF was one of many chemicals produced by fat cells and it was unclear how they all interacted with each other.