

Another clue to how obesity works

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(Medical Xpress) -- The effects of obesity - both on our bodies and on the health budget - are well known, and now, scientists are getting closer to understanding how the disease progresses, providing clues for future treatments.

In a study, published today in the prestigious journal [Cell Metabolism](#), researchers at Monash University in collaboration with colleagues in the United States, have revealed how resistance to the [hormone leptin](#), a key causal component of obesity, develops.

Lead author Professor Tony Tiganis, of the Monash Obesity and Diabetes Institute and Monash University's Department of Biochemistry and Molecular Biology, said our bodies produce leptin in response to increasing fat deposits.

"Acting on a part of the brain called the [hypothalamus](#), leptin instructs the body to increase [energy expenditure](#) and decrease [food intake](#), and so helps us maintain a healthy body weight," said Professor Tiganis.

"The body's response to leptin is diminished in overweight and obese individuals, giving rise to the concept of 'leptin-resistance'. We've discovered more about how 'leptin-resistance' develops, providing new directions for research into possible treatments."

Two proteins are already known to inhibit leptin in the brain and Professor Tiganis' team have discovered a third. In mice, this third protein becomes more abundant with weight-gain, exacerbating leptin-

resistance and hastening progression to morbid obesity. The study showed that the three negative regulators of leptin take effect at different stages, shedding light on how obesity progresses.

"Drugs targeting one of the negative regulators are already in clinical trials for Type 2 [Diabetes](#), however, our research shows that in terms of increasing leptin-sensitivity in obesity, targeting only one of these won't be enough. All three regulators might need to be switched off," said Professor Tiganis.

The study showed that high fat diet-induced weight gain is largely prevented in genetically-modified mice when two of the negative regulators are deleted in the brain.

"We now have to determine what happens when all three negative regulators are neutralised. Do we prevent high fat diet-induced obesity?"

Professor Tiganis said the more that is known about obesity, the better equipped scientists are to develop drugs to support good diet and exercise choices.

"Humans have a deep-seated attraction to overeating and nutrient-rich food, inherited from our hunter-gatherer ancestors. Now that food is more readily available and our lifestyles are less active, our evolutionary drive to overeat is becoming problematic."

More than four million Australians are obese and if current trends continue, by 2020, more than 80 per cent of adults and almost one third of children will be overweight or obese. Studies indicate that obesity and related health issues cost Australians more than \$56 billion a year.

"Simply telling people to eat less and exercise more is not going to be sufficient to reverse the [obesity](#) trend. There is a pressing need to

develop novel drugs that complement diet and exercise to both prevent and treat this disease," said Professor Tiganis.

Provided by Monash University

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