

## **Natural gut hormones may provide a treatment for obesity**

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Researchers from the Garvan Institute of Medical Research have shown that a hormone released naturally from the gut could be used to treat obesity and Type 2 diabetes.

After a meal, the hormone peptide YY (PYY) is released into the blood from the gastrointestinal tract. PYY then acts on the brain, contributing to a feeling of satiety and inhibiting the desire to continue eating.

These effects of PYY suggested that it could be used as a weight loss medication. The major unknown was whether or not the effects would last beyond a few weeks, one of the critical requirements of weight loss medications.

Using mice genetically engineered to produce more PYY, Professor Herbert Herzog, Head of Garvan's Neuroscience Program, and Dr Amanda Sainsbury-Salis, a senior scientist within the Neuroscience Program, showed that long-term increases in PYY can induce and maintain lower body fat levels in mice. The results were published online last week in the international journal *Neuropeptides*.

"At a time when people are considering radical treatments for obesity, including surgical intervention, we're very pleased to have identified a more natural alternative," said Dr Sainsbury-Salis. "If people respond to PYY in the same way as mice, supplements of the hormone should reduce body fat significantly over time."

"The other exciting thing about PYY is that it significantly improves a person's ability to clear glucose, or sugar, from the blood. It should therefore have the ability to prevent glucose intolerance, a known precursor of Type 2 diabetes."

In addition to reducing body fat and improving glucose tolerance, the team showed that elevated PYY also increases thyroid function, which in turn increases body temperature and metabolic rate. So when a PYY-overproducing mouse is fed the same diet as a control mouse, it has less body fat.

Dr Sainsbury-Salis believes these findings pave the way for development of PYY or PYY-like compounds as weight-loss medicines to be used in conjunction with a healthy diet and regular physical activity.

"The advantage of developing weight loss medications based on gut-derived satiety hormones is that they enhance a process that occurs naturally. It is expected, therefore, that side effects will be minimal."

Professor Herbert Herzog is also considering the other side of the equation. In other words, blocking the action of PYY as a possible treatment for the wasting associated with late-stage cancer and anorexia nervosa.

While intense research efforts are aimed at developing gut-derived satiety hormones such as PYY

into medications that will help people attain and maintain a healthy body weight, it is likely to be some years before PYY-like products reach the market.

"We don't yet know why some people produce less PYY than others, and are therefore more prone to weight gain," said Dr Sainsbury-Salis. "We do know, however, that adequate food and nutrients are required to stimulate PYY release. This highlights the importance of weight loss regimes that don't leave you feeling hungry, as well as minimizing 'empty kilojoules' such as chips and biscuits and instead choosing nutrient-rich foods."

#### **Reference**

Boey D, Lin S, Enriquez RF, Lee NJ, Slack K, Couzens M, Baldock PA, Herzog H, Sainsbury A: PYY transgenic mice are protected against diet-induced and genetic obesity. *Neuropeptides* (in press)

#### **Background references**

Boey D, Lin S, Karl T, Baldock PA, Lee NJ, Enriquez R, Couzens M, Slack K, Dallmann, R, Herzog H, Sainsbury A: PYY ablation in mice leads to the development of hyperinsulinaemia and obesity. *Diabetologia* 49: 1360-1370, 2006

Boey D, Heilbronn L, Sainsbury A, Laybutt R, Kriketos A, Herzog H, Campbell LV: Low serum PYY is linked to insulin resistance in first-degree relatives of subjects with type 2 diabetes. *Neuropeptides* 40: 317-324, 2006

#### **ABOUT GARVAN**

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Arthritis & Immunology, Osteoporosis, and Neuroscience. The Garvan's mission is to make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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