Alison Heather
Tel: +61 (2) 9295 8128

A powerful gut hormone that affects insulin and blood sugar levels

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A joint finding by Australian and British scientists shows that a gut hormone released after we eat determines the speed at which we digest food and absorb nutrients across the gut into our blood. This in turn helps regulate our insulin and blood sugar levels.

The hormone, gut peptide YY (PYY), is already known to influence how full we feel by sending signals to our brain.

The new finding is very important in that it deepens our understanding of conditions such as Type 2 diabetes, where the body becomes less able to make insulin and use it to reduce sugar in the blood.

Professor Herbert Herzog from Sydney's Garvan Institute of Medical Research, in collaboration with Professor Helen Cox from King's College London, have published their findings in the prestigious international journal, *Cell Metabolism.*

"The standard thinking at the moment is that if you eat something, it raises glucose levels in the blood, which stimulates insulin release from the pancreas, helping cells to absorb the glucose," said Professor Herzog.

"While that is true as far as it goes, our finding demonstrates that a much more complex process actually takes place."

"We show the central role that PYY plays inside the gut, orchestrating a cascade of other events that ultimately affect the energy balance of the entire body."

Endocrine cells in our gut contain PYY and other peptides such as glucagon-like peptide 1 (GLP-1). Receptors like GPR119 on the surface of these cells sense nutrients inside the gut, which helps them regulate digestion. Certain breakdown products of food, known as 'fatty acid amides', activate the GPR119 receptors, causing them to co-release PYY and GLP-1. The peptides then bind to different receptors on the gut lining that modulate nutrient and electrolyte absorption eventually leading to the uptake of nutrients and electrolytes into the blood.

"We identify a double-barrelled mechanism where the fatty acid amides present inside the gut or the blood can stimulate the endocrine cell receptor," said Professor Cox.

"It's important to note that the receptor is stimulated more when glucose is present."

“GPR119 stimulation leads to release of PYY with GLP-1 which act locally to enhance nutrient and electrolyte absorption within the gut wall before going into the bloodstream.”

“It has been known for a while that GLP-1 affects glucose tolerance, and there are various drugs on the market that stimulate the production of GLP-1, or enhance its life time in the blood” added Herzog.

“Our novel finding is that the process actually goes through the PYY system, not only through GLP-1 as thought previously. We have shown in mice without PYY that they cannot respond to fatty acid amides in the same way as mice that have PYY.”

“To begin with, we wondered if the process we were seeing might have something to do with the body’s neuropeptide Y (NPY) system, neurotransmitters that exert a powerful effect on appetite and energy balance.”

“We ruled out the involvement of the NPY system in mice by creating mice without PYY, mice without both NPY and PYY, and mice without NPY only. The loss of fatty acid amide activity was seen only in the groups of mice without PYY.”

“We believe that up until now the role of PYY has been underestimated. By showing its true importance, we highlight its potential, as well as that of GPR119, as a therapeutic target for people with metabolic disorders, including Type 2 diabetes.”

“A GPR119 agonist would be more beneficial therapeutically because it would have added value by activating both PYY and GLP-1 release and GPR119 agonists are already in clinical Phase 1 trials” summarised Professor Cox.

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 nearly 500 scientists, students and support staff. Garvan’s main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation and Neuroscience. 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.

MEDIA ENQUIRIES

Alison Heather
Science Communications Manager
Garvan Institute of Medical Research
+61 2 9295 8128
+61 434 071 326
a.heather “at” garvan.org.au