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Researchers zero in on protein that may help treat obesity, diabetes

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A newly-identified protein may hold the key to keeping appetite and blood sugar in check, according to a study by York University researchers.

Suraj Unniappan, associate professor in York's Department of Biology, Faculty of Science & Engineering, is delving into the metabolic effects of a protein called nesfatin-1, abundantly present in the brain. His studies found that rats administered with nesfatin-1 ate less, used more stored fat and became more active. In addition, the protein stimulated insulin secretion from the pancreatic beta cells of both rats and mice.

"[The rats] actually ate more frequently but in lesser amounts," says Unniappan, a member of York's neuroscience graduate diploma program, and a recipient of a Canadian Institutes of Health Research (CIHR) New Investigator Award. "In addition, they were more active and we found that their fatty acid oxidization was increased. In other words, the energy reserve being preferably used during nesfatin-1 treatment was fat. This suggests more fat loss, which could eventually result in body weight loss," he says.

The findings were reported in two recent research articles from Unniappan's laboratory: one published today in *Endocrinology* and another in March 2011 in *Journal of Endocrinology*.

Discovered by a research team from Japan in 2006, nesfatin-1 was earlier found to regulate appetite and the production of body fat when

injected into the brain of mice and rats.

Unniappan's findings indicate that the protein stimulates insulin secretion from the pancreas, a glandular organ, which contains clusters of cells called the islets of Langerhans. These islets produce several important hormones, including the primary glucose-lowering hormone, insulin.

Previously, Unniappan's team studied mice and found similar results; not only was insulin secretion stimulated, but nesfatin-1 was observed to be lowered in the pancreatic islets of mice with Type 1 diabetes and increased in those with Type 2 diabetes. In Type 1 diabetes, the body no longer produces insulin due to the destruction of cells within the pancreas. In Type 2 diabetes, the body becomes insulin resistant, and obesity often results.

Unniappan's research, conducted in the Laboratory of Integrative Neuroendocrinology, focuses on identifying and examining the biological effects of gut and brain-derived appetite-regulatory and metabolic hormones in fish and mammals.

"We call this the 'gut-brain axis,'" says Unniappan. "While the brain is involved in many factors that regulate our energy balance, the gut is also responsible for many neural and endocrine signals responsible for regulating hunger, satiety and blood sugar levels. A major question we're trying to address is how these peptides act and interact with other peptides in the endocrine network – which is so complex – in order to maintain steady blood glucose levels and body weight," he says.

A better understanding of this gut-brain axis could contribute to developing potential pharmacological interventions for diabetes and obesity.

"New hormone-based treatments that would suppress body weight and blood sugar would be very desirable. However, we are far from developing nesfatin-1 as a candidate molecule. Our current research focuses on further exploring the therapeutic potential of nesfatin-1 in metabolic diseases with debilitating complications," Unniappan says.

Provided by New York University