Fatty foods fire up hunger hormone

June 6 2009

New research led by the University of Cincinnati (UC) suggests that the hunger hormone ghrelin is activated by fats from the foods we eat—not those made in the body—in order to optimize nutrient metabolism and promote the storage of body fat.

The findings, the study's author says, turn the current model about ghrelin on its head and point to a novel stomach enzyme (GOAT) responsible for the ghrelin activation process that could be targeted in future treatments for metabolic diseases.

The laboratory study, led by Matthias Tschöp, MD, UC associate professor of psychiatry and internal medicine, is published online ahead of print Friday, June 5, 2009, in the journal *Nature Medicine*.

Ghrelin is a hormone that was believed to accumulate during periods of fasting and is found in the body in high concentrations just before meals. It is dubbed the "hunger hormone" because it has been shown that administration of pharmacological doses acts in the brain to stimulate hunger and increase food intake in animal models and humans.

The ghrelin hormone is unique in that it requires acylation (the addition of a fatty acid) by a specific enzyme (ghrelin O-acyl transferase, or GOAT) for activation. Originally it was assumed that the fatty acids attached to ghrelin by GOAT were produced by the body during fasting.

The new data by Tschöp and his team suggests that the fatty acids needed for ghrelin activation actually come directly from ingested

dietary fats. In a departure from an earlier model that was upheld for nearly a decade, Tschöp says, it appears that the ghrelin system is a lipid sensor in the stomach that informs the brain when calories are available—giving the green light to other calorie-consuming processes such as growing.

Tschöp and his team used mouse models to test the effects of over expressing the GOAT enzyme, or "knocking it out." They found that, when exposed to a lipid-rich diet, mice without GOAT accumulated less fat than normal mice, while those with over-expressed GOAT accumulated more fat mass than normal mice.

"When exposed to certain fatty foods, mice with more GOAT gain more fat," says Tschöp. "Mice without GOAT gain less fat since their brain does not receive the 'fats are here, store them' signal."

Tschöp says that although his study can't be immediately extrapolated to humans, recent human studies at the University of Virginia measured (separately) active and inactive ghrelin concentrations. Those studies showed that during fasting, active ghrelin levels were flat, but during the presence of fat from foods, ghrelin levels peaked with meals as previously described. Tschöp says these human studies support the new model for ghrelin.

"Our GOAT studies in mice offer an explanation of what could have been happening during the longer fasting periods in these human studies," Tschöp adds. "Without dietary fats, ghrelin peaks remain inactive and don't affect storage of fat.

"We are particularly interested in how ghrelin may be involved in the rapid benefits of gastric bypass surgery," says Tschöp. "This powerful obesity therapy frequently reduces appetite and improves metabolism before substantial weight loss occurs. Intriguingly, this procedure causes

food to bypass the stomach and gut sections that contain GOAT/ghrelin cells, which, based on this newly described model, would prevent ghrelin activation."

Source: University of Cincinnati Academic Health Center