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## Bariatric Surgery Better than Dieting for Glucose Control

New York, NY – April 27, 2011 – Researchers at St. Luke's and Roosevelt Hospital Center, Duke University Medical Center and Columbia University, have uncovered a new clue for why bariatric surgery is more effective than dietary remedies alone at controlling glucose levels.

This discovery, and facts gleaned from their previous studies, provides even more evidence that branched-chain amino acids are biomarkers that deserve careful scrutiny in the development and treatment of diabetes.

Physicians have observed that bariatric surgery results in improved blood sugar levels in up to 80 percent of cases, but the reason has not been entirely clear. Although considerable weight loss is part of that success, gastric bypass surgery (GBP) improves glycemic control in type 2 diabetes even before significant weight loss has occurred, which suggests alternate mechanisms related to biochemical and/or hormonal changes.

The current study showed that obese people with Type 2 diabetes undergoing GBP surgery have much lower levels of circulating branched-chain amino acids (BCAA) and the aromatic amino acids phenylalanine (Phe) and tyrosine (Tyr), compared to a matched group of obese patients with diabetes who lost an equal amount of weight by following a diet.

The results were published in *Science Translational Medicine* on April 27.

This enhanced reduction in BCAA and aromatic amino acids Phe and Tyr was linked to better improvement in glycemic (blood sugar) control in the GBP group.

Lead author Blandine Laferrère, M.D., of the New York Obesity Nutrition Research Center (NYONRC) at St. Luke's and Roosevelt Hospital Center, provided one cohort of patients for comparison and Duke University provided a cohort of obese patients without diabetes, matched also into GBP and diet groups for evaluation. Both sets of results showed the preferential reduction in amino acids in the GBP subjects, correlated with better glucose control.

"The most intriguing finding from the current study is that amino acids, particularly the branched-chain amino acids, decreased more significantly after gastric bypass surgery than after the same weight loss through a diet intervention," said Dr. Laferrère. "The next step will be to characterize the

pathways involved in these metabolic changes so we can understand how the specific metabolic signature of gastric bypass surgery is related to changes in hormones and hormone action, including gut hormones, that occur after surgery."

Senior author Christopher B. Newgard, PhD, and colleagues at the Sarah W. Stedman Nutrition and Metabolism Center at Duke University, evaluated specimens at the Center's metabolic profiling ("metabolomics") laboratory. The Center's laboratory uses mass spectrometry to measure hundreds of metabolic intermediates simultaneously in simple blood samples.

In earlier studies by the Duke group and its collaborators, clusters of branched-chain amino acids, Phe, Tyr and the breakdown products of the BCAAs were shown to be associated with insulin resistance in three independent human studies, and also with coronary artery disease in a separate case-control study.

"The evidence is mounting that BCAA and related metabolites are linked with insulin resistance and diabetes, and that they can cause metabolic dysfunction," Newgard said. "The current study shows that these metabolites are also highly responsive to a very efficacious diabetes intervention, gastric bypass surgery."

An independent study published in March of this year by a Harvard/Broad Institute group in subjects from the Framingham heart study shows that branched-chain and aromatic amino acids serve as biomarkers for risk of type 2 diabetes.

"Moving forward, we will need to design studies in the general population to completely demonstrate the value of the amino acid signature in models of risk and to come up with clinically valuable algorithms," Newgard said. "We also need to understand how BCAA and related metabolites become elevated in patients at risk for diabetes—is this genetics, diet, gut bacteria, or some combination of these factors?"

The study was supported by grants from the National Institute of Health, the American Diabetes Association, Glaxo SmithKline, and a National Institute of Mental Health Grant.

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