Public release date: 20-Jul-2009

Contact: Karen N. Peart
karen.peart@yale.edu
203-432-1326
Yale University

Yale discovery may open door to drug that cuts appetite and boosts energy

In a major advance in obesity and diabetes research, Yale School of Medicine scientists have found that reducing levels of a key enzyme in the brain decreased appetites and increased energy levels.

Reductions in the levels of the enzyme prolylcarboxypeptidase (PRCP) led to weight loss and a decreased risk of type 2 diabetes in mice, according to research published in the August issue of the Journal of Clinical Investigation. The team found that PRCP is located in the hypothalamus and regulates levels of the alpha-melanocyte stimulating hormone (alpha-MSH), which is a peptide known for inhibiting food intake and stimulating energy expenditure. Researchers found that blocking the PRCP enzyme keeps the alpha-MSH peptides from being degraded, resulting in higher levels of alpha-MSH and decreased appetite.

"Our research provides the first evidence that breaking down molecules in the brain that regulate metabolism is an important component of weight control," said senior author Sabrina Diano, associate professor in the Departments of Obstetrics, Gynecology and Reproductive Sciences, and Neurobiology. "Our findings provide a possible new target for the development of drugs to control metabolic disorders such as obesity and type 2 diabetes."

Diano and her team conducted the study in congenic mice that were naturally lean and later in mice that had PRCP removed. Animals without the PRCP enzyme were leaner and ate less food. They also had higher levels of alpha-MSH in the hypothalamus compared to control animals. The mice were put on a diet of 45 percent fat—the equivalent of eating fast food everyday—and even with this high fat diet, they did not gain as much weight as control animals on a regular diet.

Diano said the next step is to study how PRCP is regulated.

###

Other authors on the study include Nicholas Wallingford, Bertrand Perroud, Qian Gao, Anna Coppola, Erika Gyengesi, Zhong-Wu-Liu, Xiao-Bing Gao, Adam Diament, Kari A. Haus, Zia Shariat-Madar, Fakhri Mahdi, Sharon L. Wardlaw, Alvin H. Schmaier and Craig H. Warden.

Citation: Journal of Clinical Investigation, Vol. 119, No. 8 (August 2009)