Researchers find fat gene

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Rutgers researchers have identified a gene – and the molecular function of its protein product – that provides an important clue to further understanding obesity and may point the way to new drugs to control fat metabolism.

The scientists found that the human protein known as lipin is a key fat-regulating enzyme. "Lipin activity may be an important pharmaceutical target for the control of body fat in humans, treating conditions that range from obesity to the loss of fat beneath the skin, as seen in HIV patients, " said George M. Carman, a professor in Rutgers' department of food science.

In a paper published online by the *Journal of Biological Chemistry* (print version, April 7), Carman and his research team at Rutgers' Cook College describe their scientific detective work, moving from clue to clue in a series of logical connections to reach their discoveries.

Previous studies with mice showed that a lack of lipin causes a loss of body fat, whereas an excess of lipin promotes extra body fat. So researchers knew that lipin was involved in fat metabolism; they just didn't know how.

The Carman team's first revelation came with the discovery that lipin is an enzyme (phosphatidic acid phosphatase or PAP), a protein catalyst that is required for the formation of fats – triglycerides, specifically.

The breakthrough for Carman's group grew out of work with ordinary

baker's yeast; a simple single cell organism. "We isolated the PAP enzyme from yeast that corresponds in form to lipin in mammals and showed that yeast cells lacking the enzyme exhibited a 90 percent reduction in the yeast's version of fat loss," Carman said.

The group worked out the sequence of the amino acids that make up the PAP enzyme, allowing them to backtrack along the path to its origin – the gene that coded it – linking the enzyme to the yeast gene PAH1 that made it. Carman and his group went on to confirm the link by introducing the yeast gene into bacteria, with similar results.

The researchers showed that the enzyme encoded by the PAH1 gene looks and acts very much like the lipin found in mammals. The yeast PAP enzyme shares a high resemblance to the lipin protein in mammals so they logically deduced the link between PAP enzyme function and lipin.

"These findings are of major importance to the AIDS community as well as to those concerned with the obesity epidemic," said Jean Chin, a program director at the National Institute of General Medical Sciences (NIGMS), the part of the National Institutes of Health that funded the research. Carman's research is also supported by the New Jersey Agricultural Experiment Station.

Obesity in the United States has risen at an epidemic rate during the past 20 years, a condition affecting about one-third of American adults, according to the Centers for Disease Control and Prevention. One of the national health objectives for the year 2010 is to reduce the prevalence of obesity among adults to less than 15 percent.

Source: Rutgers, the State University of New Jersey