Research Highlights Role of Protein Pair in Obesity Regulation

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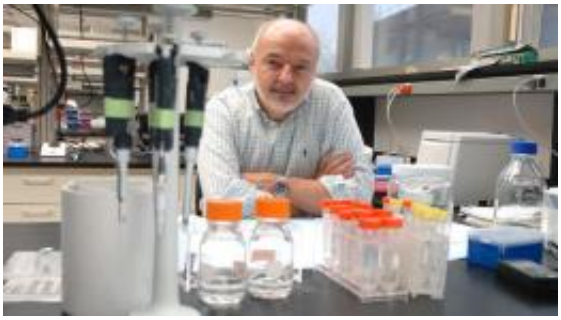

Jorge Moscat, PhD. Image: University of Cincinnati

(PhysOrg.com) -- New research by University of Cincinnati scientists implicates a new protein in obesity development and highlights a protein pair's "team effort" in regulating obesity and insulin resistance.

Jorge Moscat, PhD, chair of UC's cancer and cell biology department, says that proteins p62 and ERK are involved in adipogeneis, (the development of adipocytes, or fat cells). His new study shows precisely how this duo works together.

The study is published online in advance of print Friday, Feb. 12, 2010, in the journal EMBO Reports, and will appear in print in the March 1, 2010, edition.

Earlier research led by Moscat showed that removing or "knocking out"

p62 in mice led to the development of obesity and insulin resistance in adulthood. These mice used less energy and created more fat cells than the control group, even with the same diet and activity levels.

Targeting p62 mutations or deficiencies seemed to be a logical next step for potential obesity treatments; however, Moscat says, p62 is not an easy target due to its lack of enzymatic action. In other words, it does not catalyze reactions in a way that would be key for the success of targeted drug therapy. In addition, missing or mutated p62 has also been linked to cancer development.

Moscat and his team instead decided to focus their attention on the action of another less-understood protein, ERK, which interacts with p62.

“Thoughts about ERK’s role in obesity have been controversial,” says Moscat. “One theory suggested that it was to restrain production of fat cells. Our study shows a much more devious role for ERK.”

In the new study, Moscat and his team bred mice without p62 and ERK. These “double knockouts” did not develop obesity like the p62 knockouts did, indicating that ERK was the obesity-inducing culprit.

The team’s findings show that p62 works to suppress the action of ERK, so without p62, ERK activity goes uncontrolled.

Moscat says that ERK serves as a better target for obesity therapies because it could be inhibited without affecting p62.

Provided by University of Cincinnati

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