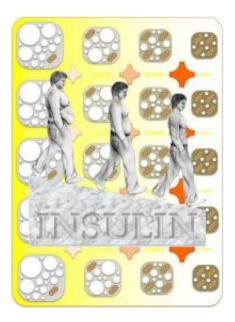


## **Could high insulin make you fat? Mouse study says yes**

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When we eat too much, obesity may develop as a result of chronically high insulin levels, not the other way around. That's according to new evidence in mice reported in the December 4th Cell Metabolism, a Cell Press publication, which challenges the widespread view that rising insulin is a secondary consequence of obesity and insulin resistance. Credit: Mehran et al., *Current Biology* 

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insulin is a secondary consequence of obesity and insulin resistance.

The new study helps to solve this chicken-or-the-egg dilemma by showing that animals with persistently lower insulin stay trim even as they indulge themselves on a high-fat, all-you-can-eat buffet. The findings come as some of the first direct evidence in mammals that circulating insulin itself drives obesity, the researchers say.

The results are also consistent with clinical studies showing that longterm insulin use by people with diabetes tends to come with <u>weight gain</u>, says James Johnson of the University of British Columbia.

"We are very inclined to think of insulin as either good or bad, but it's neither," Johnson said. "This doesn't mean anyone should stop taking insulin; there are nuances and ranges at which insulin levels are optimal."

Johnson and his colleagues took advantage of a genetic quirk in mice: that they have two insulin genes. Insulin1 shows up primarily in the pancreas and insulin2 in the brain, in addition to the <u>pancreas</u>. By eliminating insulin2 altogether and varying the number of good copies of insulin1, the researchers produced mice that varied only in their fasting blood insulin levels. When presented with high-fat food, those with one copy and lower fasting insulin were completely protected from <u>obesity</u> even without any loss of appetite. They also enjoyed lower levels of inflammation and less fat in their livers, too.

Those differences traced to a "reprogramming" of the animals' fat tissue to burn and waste more energy in the form of heat. In other words, the mice had white fat that looked and acted more like the coveted, calorieburning brown fat most familiar for keeping babies warm.

Johnson says it isn't clear what the findings might mean in the clinic just yet, noting that drugs designed to block insulin have been shown to come



with unwanted side effects. But, he added, "there are ways to eat and diets that keep insulin levels lower or that allow <u>insulin levels</u> to return to a healthy baseline each day."

Unfortunately, constant snacking is probably not the answer.

**More information:** Mehran et al.: "Hyperinsulinemia drives dietinduced obesity independently of brain insulin production." *Cell Metabolism*, <u>DOI: 10.1016/j.cmet.2012.10.019</u>

Provided by Cell Press

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