

## New diabetes treatment lowers blood sugar with less need for insulin

## February 16 2011, By Erin McColgan

Diabetes can result from either a deficiency of insulin (type 1 or insulindependent diabetes) or decreased sensitivity to insulin (type 2 diabetes). Researchers at Children's Hospital Boston have discovered a mechanism for normalizing blood sugar that doesn't involve insulin and could offer a new therapeutic approach to both kinds of diabetes.

Reporting in Nature Medicine online on February 13, Umut Ozcan, MD, and colleagues in Children's Division of Endocrinology show that a regulatory protein called XBP-1s, when activated artificially in the liver, can normalize <a href="high-blood sugar">high-blood sugar</a> in both lean, insulin-deficient type 1 diabetic mice and obese, insulin-resistant type 2 diabetic mice. This suggests that approaches aimed at increasing XBP-1s activity may benefit patients with either type of diabetes.

In previous work, Ozcan's lab identified XBP-1s as a key to the body's sensitivity to insulin, and shown that its function is impaired in the presence of obesity. Initially, XBP-1s was thought to increase <u>insulin</u> <u>sensitivity</u> and normalize blood glucose by binding to DNA and relieving stress on the endoplasmic reticulum, a cellular organ that assembles and folds proteins. When XBP-1s was artificially activated, "blood sugars in obese mice with <u>type 2 diabetes</u> came down abruptly," Ozcan says.

In the new study, Ozcan and colleagues show that XBP-1s regulates blood sugar in a second way: It causes the degradation of a protein, FoxO1, whose actions include increasing glucose output from the liver and stimulating feeding behavior in the brain. This degradation of



FoxO1, the researchers show, is independent of XBP-1s' effect on the insulin signaling system, and by itself leads to a reduction in <u>blood</u> <u>glucose levels</u> and increased <u>glucose tolerance</u> (more rapid clearing of glucose from the blood).

"Activating XBP-1s could be another approach to type 2 diabetes, and could be very beneficial for type 1 diabetes, too," says Ozcan. "Even in mice with no insulin, increased expression of XBP-1s lowered the blood glucose level significantly. This suggests that approaches that activate XBP-1s in the liver of type 1 diabetics could control blood glucose levels, with potentially much less requirement for insulin."

Ozcan's lab is now seeking practical ways to activate XBP-1s that would lend themselves to clinical development. Currently the only treatment for type 1 diabetes is insulin, which requires injections and requires close monitoring to avoid hypoglycemia. Drugs are available for type 2 diabetes, but it remains difficult to control.

## Provided by Children's Hospital Boston

Citation: New diabetes treatment lowers blood sugar with less need for insulin (2011, February 16) retrieved 26 January 2023 from <a href="https://medicalxpress.com/news/2011-02-diabetes-treatment-lowers-blood-sugar.html">https://medicalxpress.com/news/2011-02-diabetes-treatment-lowers-blood-sugar.html</a>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.