

New inflammation hormone link may pave way to study new drugs for Type 2 diabetes

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A new link between obesity and type 2 diabetes found in mice could open the door to exploring new potential drug treatments for diabetes, University of Michigan Health System research has found.

Drugs for type 2 diabetes commonly <u>target insulin</u>, which lowers <u>blood glucose levels</u>. But the U-M study suggests that <u>glucagon</u> - a pancreas-produced hormone that has the opposite effect of insulin by raising blood glucose levels - may also provide a powerful pathway to preventing and treating the increasingly prevalent disease.

Findings of the study were published this week ahead of print in *Nature Medicine*.

"Reducing sugar levels is the biggest goal for people with type 2 diabetes," says senior author Liangyou Rui, Ph.D., associate professor in the Department of Molecular and Integrative Physiology at the U-M Medical School. "We've mostly focused on controlling insulin production and action to treat diabetes but there has been very little study on the opposite hormone glucagon.

"Our study shows for the first time that obesity also affects glucagon action and that this hormone also contributes to high glucose levels found in type 2 diabetes."

Authors identified the NIK/NF-12B2 pathway, which promotes glucagon responses in obesity. NIK was abnormally activated in mice with dietary



or genetic obesity and the inhibition of liver NIK was found to cure diabetes in obese mice.

Insulin resistance - which reduces the body's ability to decrease blood glucose - has been the main hallmark of type 2 diabetes, which is the most common form of diabetes in the United States afflicting millions of Americans.

"There is a common theory that inflammation in liver and fat tissue associated with obesity causes insulin resistance and that leads to the biggest problem for type 2 diabetes: high blood glucose levels," Rui says.

"But blood glucose is also controlled by this other hormone glucagon, which signals to the liver to produce glucose. Inflammation may enhance the ability of glucagon to increase blood sugar.

"Obesity is a growing problem worldwide, leading to more cases of type 2 diabetes," Rui adds. "We hope to offer more data that can help expand options to treat this rampant disease."

Provided by University of Michigan Health System

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