

## Study identifies mechanism that leads to diabetes, blindness

September 17 2012



Insulin-secreting beta cells in the pancreas cannot make enough cyclic AMP in patients with Wolfram syndrome. As a result, the pancreas produces and secretes less insulin, and the cells eventually die. Credit: Urano lab

The rare disorder Wolfram syndrome is caused by mutations in a single gene, but its effects on the body are far reaching. The disease leads to diabetes, hearing and vision loss, nerve cell damage that causes motor difficulties, and early death.

Now, researchers at Washington University School of Medicine in St. Louis, the Joslin Diabetes Center in Boston and the Novartis Institutes for BioMedical Research report that they have identified a mechanism related to mutations in the WFS1 gene that affects insulin-secreting beta cells. The finding will aid in the understanding of Wolfram syndrome



and also may be important in the treatment of milder forms of diabetes and other disorders.

The study is published online in the journal Nature Cell Biology.

"We found something we didn't expect," says researcher Fumihiko Urano, MD, PhD, associate professor of medicine in Washington University's Division of Endocrinology, Metabolism and Lipid Research. "The study showed that the WFS1 gene is crucial to producing a key molecule involved in controlling the metabolic activities of individual cells." That molecule is called cyclic AMP (cyclic <u>adenosine</u> <u>monophosphate</u>).

In insulin-secreting beta cells in the pancreas, for example, cyclic AMP rises in response to <u>high blood sugar</u>, causing those cells to produce and secrete insulin.

"I would compare cyclic AMP to money," Urano says. "You can't just take something you make to the store and use it to buy food. First, you have to convert it into money. Then, you use the money to buy food. In the body, external signals stimulate a cell to make cyclic AMP, and then the cyclic AMP, like money, can 'buy' insulin or whatever else may be needed."

The reason patients with Wolfram syndrome experience so many problems, he says, is because mutations in the WFS1 gene interfere with cyclic AMP production in beta cells in the <u>pancreas</u>.

"In patients with Wolfram syndrome, there is no available WFS1 protein, and that protein is key in cyclic AMP production," he explains. "Then, because levels of cyclic AMP are low in insulin-secreting <u>beta</u> <u>cells</u>, those cells produce and secrete less insulin. And in nerve cells, less cyclic AMP can lead to nerve cell dysfunction and death."



By finding that cyclic AMP production is affected by mutations in the WFS1 gene, researchers now have a potential target for understanding and treating Wolfram syndrome.

"I don't know whether we can find a way to control cyclic AMP production in specific tissues," he says. "But if that's possible, it could help a great deal."

Meanwhile, although Wolfram syndrome is rare, affecting about 1 in 500,000 people, Urano says the findings also may be important to more common disorders.

"It's likely this mechanism is related to diseases such as type 2 diabetes," he says. "If a complete absence of the WFS1 protein causes <u>Wolfram</u> syndrome, perhaps a partial impairment leads to something milder, like diabetes."

Provided by Washington University School of Medicine

Citation: Study identifies mechanism that leads to diabetes, blindness (2012, September 17) retrieved 27 April 2024 from <u>https://medicalxpress.com/news/2012-09-mechanism-diabetes.html</u>

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.