Key signal that prompts production of insulin-producing beta cells points way toward diabetes cure

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This is Professor Yuval Dor of the Hebrew University of Jerusalem. Credit: The Hebrew University of Jerusalem

Researchers at the Hebrew University of Jerusalem have identified the key signal that prompts production of insulin-producing beta cells in the pancreas -- a breakthrough discovery that may ultimately help researchers find ways to restore or increase beta cell function in people with type 1 diabetes.

The work on the multi-year project was led by Prof. Yuval Dor of the Institute for Medical Research Israel-Canada of the Hebrew University, researchers from the Hadassah University Medical Center and researchers from the diabetes section of the Roche pharmaceuticals company. The study was published in a recent issue of the journal Cell Metabolism.

"Our work shows that as the glucose level is increased in the blood, it tells the beta cells to regenerate," says Dor. "It's not blood glucose per se that is the signal, but the glucose-sensing capacity of the beta cell that's the key for regeneration." This was the first time that this sensing of a high level of glucose has been shown to be the "trigger" that induces beta cells to regenerate.

In persons suffering from type 1 (juvenile) diabetes, the immune system launches a misguided attack on the insulin-producing beta cells, resulting in the cells' decline of insulin production and eventual loss of function.

Without insulin, the body's cells cannot absorb glucose from the blood and use it for energy. As a result, glucose accumulates in the blood, leaving the body's cells and tissues starved for energy. That's why people with the disease must inject insulin and monitor their blood glucose levels diligently every day. To cure type 1 diabetes, it will be necessary to develop methods to increase beta cell replication and mass, hence the potential therapeutic importance of the current study.

In their work, Dor, along with co-lead author Prof. Benjamin Glaser of the Hadassah University Medical Center, used a genetic system to destroy 80 percent of the insulin-producing cells in the pancreases of adult mice, rendering the mice diabetic.

When the researchers compared these mice with control mice, they found that those mice with diabetes and elevated blood glucose levels had regenerated a greater number of new beta cells than mice without diabetes, suggesting that glucose may be a key player in beta cell regeneration. But the researchers further found that a glucose-sensing enzyme in the cells, glucokinase, is the key molecule that triggers the beta cell regeneration.

"This means that the more work that beta cells are required to do (that is, the more 'stressed' they are), the more of themselves they make," said graduate student Shay Porat, who, along with fellow graduate student Noa Weinberg, spearheaded the study, which was funded with the support of the Juvenile Diabetes Research Foundation (JDRF). .

Because this study showed that regeneration depends on glucokinase levels, the finding may pave the way for developing a new kind of drug to modulate glucokinase or other steps in the glucose-sensing pathway to direct beta cells down the path of regeneration and replication.

And, should a mechanism be discovered that prevents the immune system from attacking beta cells in the first place, as occurs among diabetics, the combined treatment could help pave the way towards a full cure for type 1 diabetes.

Further research in this area is proceeding, with the eventual goal of progressing towards human clinical trials.

Provided by Hebrew University of Jerusalem