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Gene therapy stimulates protein that blocks immune attack and prevents Type 1 diabetes in mice

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Increasing a specific protein in areas of the pancreas that produce insulin blocks the immune attack that causes type 1 diabetes, researchers reported in the August issue of the *Journal of Clinical Investigation*, published early online.

The discovery could lead to a drug that prevents the progression of type 1 diabetes in people newly diagnosed who are in the "honeymoon" phase of the disease, when the immune system has not yet destroyed all of the insulin-producing beta cells in the pancreas.

The finding could also lead to new drugs for overcoming organ rejection in transplant patients and for improving the survival of transplanted islets - the clusters of cells in the pancreas that contain beta cells.

Normally, as the immune system successfully defeats an infection, a special type of white blood cell called T-regulatory cells produce chemical signals that turn off the immune response.

The researchers took advantage of this phenomenon as they sought to protect the beta cells from immune attack.

They used a modified virus to insert the gene for a protein called CCL22 into the beta cells of a strain of mice known to develop diabetes. The gene caused the beta cells to produce the CCL22 protein. This attracted

T-regulatory cells, which blocked the attacking immune cells and prevented most of the mice from developing type 1 diabetes.

CCL22 was discovered years ago by ovarian cancer researchers who noticed that tumours emit the protein to avoid being destroyed by the immune system.

"It's a novel way to turn down the immune system specifically in the region of the beta cells inside the pancreas, and that may be a big advantage over general immune suppression, which can have significant side effects," says Dr. Bruce Verchere, one of the study's principal investigators. He is head of the diabetes research program at the Child & Family Research Institute (CFRI) at BC Children's Hospital, Irving K Barber Chair in Diabetes Research, and professor, Department of Pathology & Laboratory Medicine and Department of Surgery at the University of British Columbia (UBC).

The study's co-lead author Dr. Joel Montane says more research is needed before the findings can be used clinically.

"Next, we need to better understand the mechanism," says Dr. Montane, a UBC post-doctoral fellow at CFRI. "We don't know exactly how CCL22 attracts T-regulatory cells to inhibit the immune response. Once we understand that, it may lead to a drug that can prevent or reverse diabetes."

"The research points to CCL22, or a modified form of it, as a potential drug to control the immune response," says Dr. Loraine Bischoff, the co-lead author. "Our strategy might also be used in other autoimmune disorders and in transplantation. The issue is how to administer it to humans. It's exciting because there are presently clinical trials using T-regulatory cells to prevent autoimmune disease."

A team of CFRI-UBC scientists, including co-principal investigator Dr. Rusung Tan, worked on this discovery.

Provided by Child & Family Research Institute