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New vaccine approach prevents/reverses diabetes in lab study

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Results of study are published in Diabetes, a journal of the American Diabetes Association

Microspheres carrying targeted nucleic acid molecules fabricated in the laboratory have been shown to prevent and even reverse new-onset cases of type 1 diabetes in animal models. The results of these studies were reported by diabetes researchers at the John G. Rangos Sr. Research Center at Children's Hospital of Pittsburgh of UPMC and Baxter Healthcare Corporation.

In a research study at Children's Hospital, the scientists injected the microspheres under the skin near the pancreas of mice with autoimmune diabetes. The microspheres were then captured by white blood cells known as dendritic cells which released the nucleic acid molecules within the dendritic cells. The released molecules reprogrammed these cells, and then migrated to the pancreas. There, they turned off the immune system attack on insulin-producing beta cells. Within weeks, the diabetic mice were producing insulin again with reduced blood glucose levels.

Results of the microsphere study are published in the June issue of *Diabetes*, the journal of the American Diabetes Association.

In type 1 diabetes, T cells from the immune system travel to the pancreas and destroy beta cells, which produce insulin. The scientists – led by Massimo Trucco, MD, and Nick Giannoukakis, PhD – found that the microspheres reprogram dendritic cells to block the signaling mechanism

that sends T cells to destroy beta cells. The microsphere research builds on previous research by Drs. Giannoukakis and Trucco in which they used dendritic cells delivered to the pancreas in another method to turn off the immune system's attack on insulin-producing beta cells, thereby allowing the cells of the pancreas to recover and begin producing insulin again.

Drs. Trucco and Giannoukakis anticipate that the latest research involving microspheres represents a significant improvement over their previous approach to extract (through a process known as leukapheresis) and reprogram the dendritic cells.

"The microspheres prevented the onset of type 1 diabetes and, most importantly, exhibited a capacity to reverse hyperglycemia, suggesting a potential to reverse type 1 diabetes in new-onset patients," said Dr. Trucco, chief of the Division of Immunogenetics at Children's. "This novel microsphere approach represents for the first time a vaccine with the potential to suppress and reverse diabetes. This finding holds true promise for clinical testing in people with type 1 diabetes."

Currently, Drs. Trucco and Giannoukakis are conducting a clinical trial of their leukapheresis-based dendritic cell approach in humans at Children's. This Phase 1 clinical trial has been approved by the U.S. Food and Drug Administration (FDA).

"Our ultimate goal is to offer this dendritic cell vaccine or microsphere-based therapy to children at risk for or newly diagnosed with type 1 diabetes. We want to make the procedure as safe and comfortable as possible," Dr. Giannoukakis said.

The trial began late last year and enrollment is ongoing. The study, which plans to enroll a total of 15 adults over age 18 with type 1 diabetes, is expected to conclude later this year.

If the leukapheresis-based approach continues to show exceptional safety, the researchers hope to launch a national clinical trial that will assess the effectiveness of the dendritic cells in pediatric patients to prevent diabetes or reverse the disease right after it is clinically confirmed. At a later date, it is anticipated that Baxter Healthcare will collaborate with Drs. Trucco and Giannoukakis in a clinical trial utilizing the unique microsphere-based approach.

Leukapheresis is a process that allows for the collection of dendritic cell precursors from the patients in the study, which takes two to four hours. After the precursors are collected, they are treated in the lab with specific growth factors that turn them into dendritic cells. The growth factors are also combined with short DNA sequences that specifically block the expression of molecules that are found at the surface of dendritic cells known as CD40, CD80 and CD86. Once these reprogrammed dendritic cells are tested in the lab, they are injected back into the patient. They then orchestrate an anti-diabetic effect by suppressing the activity of T-cells which are responsible for the impairment and destruction of the pancreatic insulin-producing cells.

“Using microspheres will be much less invasive for the patient and much more efficient for clinicians. We wouldn’t need to harvest a patient’s dendritic cells, and it would eliminate the need to genetically reprogram the dendritic cells in a sterile, off-site facility. Instead, the patient would receive the microsphere injection with a small needle in a clinic setting in a matter of minutes,” Dr. Giannoukakis said.

Source: Children's Hospital of Pittsburgh