

Gene therapy reverses type 1 diabetes in mice

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Researchers have developed an experimental cure for Type 1 diabetes, a disease that affects about one in every 400 to 600 children and adolescents. They will present their results in a mouse model of Type 1 diabetes on Sunday at The Endocrine Society's 92nd Annual Meeting in San Diego.

Using gene therapy, the team from Baylor College of Medicine in Houston tried to counter the two defects that cause Type 1 diabetes: autoimmune attack and destruction of the insulin-producing [beta cells](#). They used nonobese [diabetic mice](#), which spontaneously develop diabetes due to autoimmunity, just as humans do with Type 1 diabetes.

"A single treatment cured about 50 percent of the diabetic mice, restoring their blood sugar to normal so that they no longer need insulin injections," said study co-author Lawrence Chan, MD, DSc, chief of Baylor's diabetes, endocrinology and metabolism division.

Type 1 diabetes occurs when the body's immune system attacks and destroys the beta cells in the pancreas, the insulin "factory" of the body. The resulting near-complete deficiency of insulin—the hormone that controls blood sugar—leads to a buildup of high blood sugar and thus diabetes.

In past studies of their original gene therapy, Chan's group was able to stimulate new formation of beta cells in the liver and restore [insulin production](#) and normal blood sugar levels in more than 100 mice with chemically induced diabetes. However, in nonobese diabetic mice the

treatment failed to reverse Type 1 diabetes because the mouse's immune system killed the newly formed beta cells, he said.

In this research, which was funded by the National Institute of Diabetes, Kidney and Digestive Diseases, Chan said they "added to the original gene therapy approach a protective gene that shields the newly formed beta cells from autoimmune attack." The added gene was for interleukin-10, an important regulator of the immune system. Past studies showed that interleukin-10 can prevent diabetes development in mice but cannot reverse the disease once it has developed because of the lack of beta cells.

However, when the researchers combined the gene therapy with interleukin-10 into a single intravenous injection, the treatment showed a complete reversal of diabetes in half of the mice during more than 20 months' follow-up. Although the therapy did not reverse autoimmunity throughout the body, it protected the new beta cells from the local destructive effect of autoimmunity, Chan explained.

"We developed a protective 'moat' around the new beta cells," he said.

"We are now developing other strategies to try to fortify the newly formed beta cells and give them better weapons in addition to the moat, in order to increase the treatment's cure rate."

Why the gene therapy did not work in all the mice is unclear. However, Chan said the treated mice that did not have improvements in their blood sugar did gain weight and lived a little longer than untreated mice.

Provided by The Endocrine Society

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