Uterine stem cells used to treat diabetes in mice

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(Medical Xpress) -- Researchers funded by the National Institutes of Health have converted stem cells from the human endometrium into insulin-producing cells and transplanted them into mice to control the animals' diabetes.

The endometrium, or uterine lining, is a source of adult stem cells. Normally, these cells generate uterine tissue each month as part of the menstrual cycle. Like other stem cells, however, they can divide to form other kinds of cells.

The study's findings suggest the possibility that endometrial stem cells could be used to develop insulin-producing islet cells. These islet cells could then be used to advance the study of islet cells transplantation as a treatment for people with diabetes. If the transplantation of islet cells derived from endometrial cells is perfected, the study authors write that women with diabetes could provide their own endometrial tissue for such a transplant, sidestepping the chance of rejection posed by tissue from another person. Endometrial stem cells are readily available and can be collected easily during a simple outpatient procedure. Endometrial tissue could also be collected after hysterectomy, the surgical removal of the uterus.

"The study findings are encouraging," said Louis V. DePaolo, Ph.D., chief of the Reproductive Sciences Branch at the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), which funded the study. "Research to transplant insulin-

producing cells into patients with diabetes could proceed at a much faster pace with a relatively accessible source of donor tissue."

The study authors note that such a treatment would be more useful for people with Type 1 diabetes, in which no insulin is produced. The treatment would be less useful for Type 2 diabetes, in which insulin is usually produced, but in which cells have difficulty using the insulin that is available.

The findings appear in *Molecular Therapy*. The study was conducted by Xavier Santamaria, Efi E. Massasa, Yuzhe Feng, Erin Wolff and Hugh Taylor, M.D., all of Yale University, New Haven, Conn.

The study authors write that endometrial tissue samples could be warehoused in a tissue bank. A large number of samples would make it comparatively easy to find compatible tissue for transplant to women who no longer have a uterus and to men. According to the Centers for Disease Control and Prevention, roughly 600,000 hysterectomies are performed each year in the United States as treatment for a number of disorders and conditions.

In their study, the researchers bathed endometrial stem cells in cultures containing special nutrients and growth factors. Responding to these substances, the endometrial stem cells adopted the characteristics of beta cells, cells of the pancreas that produce insulin.

The incubation process took about three weeks. During this time, the endometrial stem cells took on the shape of beta cells and began making proteins typically made by beta cells. The researchers found that some of these cells also produced insulin.

After a meal, the body breaks food down into components like the sugar, glucose. Glucose then circulates in the blood. In response, beta cells

release insulin, which allows the body's cells to take in the circulating glucose. In their study, the researchers exposed the mature stem cells to glucose and found that, like typical beta cells, the cultured cells responded by producing insulin.

Next, the researchers injected the mature, insulin-making cells into the kidney capsule (membrane surrounding the kidney) of mice having a laboratory-induced form of diabetes. The mice had few working beta cells and very high levels of blood glucose. In mice that did not receive the stem cell therapy, blood sugar levels remained high. Additionally, the mice became lethargic and developed cataracts—both signs of untreated diabetes.

In contrast, mice receiving the cell therapy were active and did not develop cataracts. However, the treatment was not entirely effective, as the animals' blood sugar remained higher than normal. Still, the animals continued to produce some insulin for six weeks, until the researchers ended the study.

"Verifying how long this treatment stays effective is one of our next research priorities," said Dr. Taylor, the study's senior author. "We also will investigate how changing the nutrient bath or increasing the dose of injected cells could make this treatment more effective."

Dr. Taylor explained that culture and transplantation of endometrial stem cells might prove useful principally for Type 1 diabetes. In this form of the disorder, the immune system destroys the body's own insulin-producing cells. As a result, insulin is not available to bring blood glucose levels under control. Although a diabetic woman's immune system would be unlikely to reject islet cells developed from her own endometrial stem cells, it is still possible that her immune system would eventually target the new islet cells in the same way it targeted her original islet cells in the pancreas. For this reason, studies using

endometrial stem cells to treat diabetes might first need to find ways to quell the immune attack against the islet cells.

Dr. Taylor added that endometrial stem cell therapy also might one day prove most useful for patients with Type 2 diabetes. In this form of diabetes, islet cells still produce insulin, but cells have trouble using insulin. In some patients with Type 2 diabetes, beta cells eventually die off. Dr. Taylor suggested that the stem cell approach might be helpful for patients at this later stage of the disease.

This study was conducted as part of the NICHD funded nationwide Specialized Cooperative Centers Program in Reproduction and Infertility Research.

In 2010, the researchers published a study which showed that endometrial stem cells could replace brain cells lost in mice having a laboratory-induced form of Parkinson's disease.

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