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SCIENTISTS GENETICALLY ENGINEER CELLS TO PRODUCE INSULIN

DALLAS – Oct. 8, 1996 – Scientists have genetically engineered pituitary cells to produce insulin and successfully transplanted them into diabetic mice, eliminating the symptoms of diabetes.

In a study published in the August issue of *Proceedings of the National Academy of Sciences*, Dr. Christopher Rhodes, associate professor of internal medicine and pharmacology at UT Southwestern Medical Center at Dallas, said the research suggests that pituitary cells eventually could be used to re-establish secretion of insulin in people suffering from insulin-dependent diabetes mellitus, also known as type I or juvenile diabetes.

In people who have type I diabetes, the body's autoimmune system has destroyed the pancreatic beta cells, which make insulin, Rhodes said. Insulin controls glucose levels, which affect energy levels, behavior and concentration. If the pancreas no longer produces insulin, injections of the hormone are needed to regulate the body's glucose level. Over time, diabetes often causes damage to major organs and may result in premature death.

Rhodes and his colleague Myra Lipes of the Joslin Diabetes Center in Boston, looked for a way to genetically engineer production of insulin in nonpancreatic cells. "We chose the pituitary because we found that the cells have the same signaling pathways for producing hormones as the pancreatic beta cells," said Rhodes. "What we want is a normal insulin-producing cell that can be easily produced, transplanted and regulated to generate bona fide insulin in a physiologically correct manner."

The researchers created a strain of mice that spontaneously gets type-I diabetes. Then they genetically engineered pituitary cells to have the insulin gene and transplanted

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them in the diabetic mice. This resulted in the production of mature, biologically active insulin in these pituitary cells in live mice, such as would be produced in normal pancreatic beta cells.

Although the mice's pancreatic beta cells were destroyed by the rodents' autoimmune system, the pituitary cells manufacturing insulin survived in the same animals.

In addition, when the researchers transplanted a large number of the genetically altered pituitary cells into the diabetic mice, their blood glucose levels returned to normal.

Even though the successful transplantation of pituitary cells in mice is encouraging, researchers must overcome two major hurdles before the therapy is practical for humans. A way must be developed to regulate release of insulin into the body according to ever-changing glucose levels. One way this happens is with a peptide hormone called GLP-1. In a nondiabetic person, GLP-1, which is secreted by the stomach, tells the pancreas when to release insulin so glucose levels will decrease. Researchers must find a way to get that hormone or another peptide to serve the same purpose with the pituitary. Also, a way must be found to make beta cells grow faster and in larger quantities to produce enough insulin. Rhodes said further molecular manipulations may overcome both of these problems.

Rhodes recently came to UT Southwestern from Harvard Medical School and the Joslin Diabetes Center. The study was submitted for publication by National Academy of Sciences member Dr. Roger Unger, holder of the Touchstone/West Distinguished Chair in Diabetes Research at UT Southwestern and director of the Gifford Laboratories for Diabetes Research, where Rhodes now works.

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