**A Pancreas in a Capsule**

Stem-cell advocates pin their hopes on a method of treating diabetes.

By [Brian Alexander](http://www.technologyreview.com/contributor/brian-alexander/) on February 12, 2015

Fourteen years ago, during the darkest moments of the “stem-cell wars” pitting American scientists against the White House of George W. Bush, one group of advocates could be counted on to urge research using cells from human embryos: parents of children with type 1 diabetes. Motivated by scientists who told them these cells would lead to amazing cures, they spent millions on TV ads, lobbying, and countless phone calls to Congress.

Now the first test of a type 1 diabetes treatment using stem cells has finally begun. In October, a San Diego man had two pouches of lab-grown pancreas cells, derived from human embryonic stem cells, inserted into his body through incisions in his back. Two other patients have since received the stand-in pancreas, engineered by a small San Diego company called ViaCyte.+

It’s a significant step, partly because the ViaCyte study is only the third in the United States of any treatment based on embryonic stem cells. These cells, once removed from early-stage human embryos, can be grown in a lab dish and retain the ability to differentiate into any of the cells and tissue types in the body. One other study, since cancelled, treated several patients with spinal-cord injury (see “[Geron Shuts Down Pioneering Stem-Cell Program](http://www.technologyreview.com/news/426125/geron-shuts-down-pioneering-stem-cell-program/)” and “[Stem-Cell Gamble](http://www.technologyreview.com/featuredstory/424392/stem-cell-gamble/)”), while tests to transplant lab-grown retina cells into the eyes of people going blind are ongoing (see “[Stem Cells Seem Safe in Treating Eye Disease](http://www.technologyreview.com/news/531791/stem-cells-seem-safe-in-treating-eye-disease/)”).

Type 1 patients must constantly monitor their blood glucose using finger pricks, carefully time when and what they eat, and routinely inject themselves with insulin that the pancreas should make. Insulin, a hormone, triggers the removal of excess glucose from the blood for storage in fat and muscles. In type 1 diabetics, the pancreas doesn’t make it because their own immune system has attacked and destroyed the pancreatic islets, the tiny clusters of cells containing the insulin-secreting beta cells.+

The routine is especially hard on children, but if they don’t manage their glucose properly, they could suffer nerve and kidney damage, blindness, and a shortened life span. Yet despite years of research, there is still “just nothing” to offer patients, says Robert Henry, a doctor at the University of California, San Diego, whose center is carrying out the surgeries for ViaCyte.+

Henry slightly overstates the case, but not by much. There is something called the Edmonton Protocol, a surgical technique first described in the *New England Journal of Medicine* in 2000. It used islets collected from cadavers; by transplanting them, doctors at the University of Alberta managed to keep all seven of their first patients off insulin for an entire year.+

Early hopes for the Edmonton Protocol were quickly tempered, however. Only about half of patients treated have stayed off insulin long-term, and the procedure, which is still regarded as experimental in the U.S., isn’t paid for by insurance. It requires recipients to take powerful immune-suppressing drugs for life. Suitable donor pancreases are in extremely short supply.+

The early success of the Edmonton Protocol came only two years after the discovery of embryonic stem cells, in 1998. Those pressing for a diabetes cure quickly set a new goal: pair something like the Edmonton Protocol with the technology of lab-grown beta cells, the supplies of which are theoretically infinite.+



This biocompatible capsule is designed to protect manufactured pancreas cells.

“We had proof of concept that transplantation restores beta function and insulin independence,” says Richard Insel, chief scientific officer of the Juvenile Diabetes Research Foundation (JDRF), a nonprofit with 300,000 members. “So it was obvious that if we had another cell source that was replenishable, large numbers [of people] would benefit.”+

That’s why the JDRF battled the restrictions threatened by the Bush White House, and why its members were behind a 2004 voter initiative in California that created the California Institute for Regenerative Medicine, a state agency authorized to spend $3 billion on stem-cell research. The California institute has given ViaCyte six grants worth $39 million, more than it’s given any other company, and JDRF has invested another $14 million directly.   +

Although the idea of growing replacement beta cells is conceptually simple, in practice it’s proved more difficult to execute than anyone imagined. “When I first came to ViaCyte 12 years ago, cell replacement through stem cells was so obvious. We all said, ‘Oh, that’s the low-hanging fruit,’” says Kevin D’Amour, the company’s chief scientific officer. “But it turned out to be a coconut, not an apple.”+

One challenge has been getting stem cells to turn into real, functioning pancreas cells, especially the insulin-secreting beta cells. Because a recipe for doing so proved elusive, ViaCyte’s approach is to grow immature pancreas cells, counting on the body to do the work of transforming them into actual beta cells.+

The second problem is how to evade a patient’s immune system, which will attack any transplanted cell. ViaCyte’s solution is a plastic mesh capsule, which it fills with about 40 million of the immature pancreas cells it grows in its San Diego laboratory. The purpose of the capsule is to screen out the immune system’s killer T cells, which are too big to get through the fine mesh, while allowing the transplanted cells to receive nourishment from the bloodstream, as well to sense blood sugar and respond.2

Animal data that ViaCyte supplied to the U.S. Food and Drug Administration last year in order to receive approval for the human trial showed that the cells produced insulin, glucagon (secreted in response to low blood sugar), and somatostatin, a growth hormone, and successfully regulated blood sugar, at least in mice.+

Though the current human trial is meant mostly to test for safety, Henry suspects that his patients may see some reduction in their need for injected insulin. From the first patient, whose identity hasn’t been disclosed, Henry says he has already retrieved a test sack, which he says appeared to be functioning properly. Nobody is sure how long the implanted cells will survive, but it is certain that patients would have to have new implants installed periodically.  +

At least two other groups say they’ve also controlled diabetes in rodents and may soon start trials of their own. One is BetaLogics Venture, a subsidiary of the drug giant Johnson & Johnson, which last year reported reversing diabetes in mice using what its patents describe as a yarn-based scaffold in a polyester shell. Whatever the exact device is, it’s seeded with what Johnson & Johnson scientist Alireza Rezania calls “stage 7” cells— not quite mature islets, but not as immature as ViaCyte’s precursors, either.+

Douglas Melton, a biologist at Harvard University who has two children with type 1 diabetes, worries that the ViaCyte system may not work. He thinks deposits of fibrotic, scarlike tissue will glom onto the capsules, starving the cells inside of oxygen and blocking their ability to sense sugar and release insulin. Melton also thinks it might take immature cells up to three months to become fully functional. And many won’t become beta cells, winding up as other types of pancreatic cells instead.+

Melton says the “inefficiency” of the system means the company “would need a device about the size of a DVD player” to have enough beta cells to effectively treat diabetes. ViaCyte says it thinks 300 million of its cells, or about eight of its capsules, would be enough. (Each capsule holds a volume of cells smaller than one M&M candy.)    Last October, Melton’s group announced it had managed to grow fully mature, functional beta cells in the lab, a scientific first that took more than 10 years of trial-and-error research. Melton thinks implanting mature cells would allow a bioartificial pancreas to start working right away.+

To encapsulate his cells, Melton has been working with bioengineer Daniel Anderson at MIT to develop their own capsule. Anderson doesn’t want to say exactly how it works, but a recent patent filing from his lab describes a container made of layers of hydrogels, some containing cells and others anti-inflammatory drugs to prevent the capsule from getting covered with fibrotic tissue. Both Melton and Anderson are cagey about discussing their results. “We do have some successes we are very excited about,” Anderson says. “The bottom line is we have reason to believe it is possible to use Doug’s cells in our devices and cure diabetes in animals.”1

After the stem-cell wars, and then a decade of trying to turn the technology’s promises into reality, Henry says he feels convinced that “cells in bags” of some kind are going to be the answer to type 1 diabetes. He’s aware that curing rodents doesn’t guarantee the technology will help people, but he says the clinical trial he’s running is another in a series of “small steps” toward much-improved lives for millions of people. “I am just so positive that this is the future,” he says.