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Beyond Insulin: Searching for a Cure to Type 1 Diabetes

Twin challenges: Halt the autoimmune attack that destroys insulin-making cells and replace lost cells

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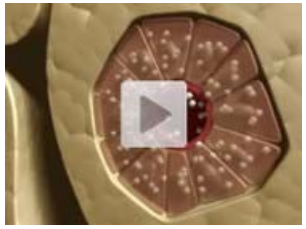
More than 80 years have elapsed since the lifesaving discovery of insulin, a hormone that has turned a once lethal disease into a chronic but manageable condition. Yet there is still no cure for type 1—aka juvenile onset—diabetes, which affects about 30,000 new Americans each year. While that won't change overnight, a series of recent breakthroughs offer hope for a long-elusive cure.


Video: What is Diabetes?

In recent weeks, two teams reported very different ways to replace insulin-secreting cells, which are instrumental in the body's processing of sugar. In type 1 diabetes, those so-called beta cells, which reside in the pancreas, get killed off in an assault by the person's own immune system. Complications can include blindness and kidney failure. Lab researchers at the University of North CarolinaChapel Hill School of Medicine morphed human skin cells into cells that make insulin. And Harvard University scientists turned noninsulin-making cells in a mouse's pancreas into rarer beta cells.

The UNC approach could theoretically offer an alternative to pancreatic cell transplantation. That experimental procedure is reserved for the sickest adult diabetics because the transplanted cells come from cadavers, and the immunosuppressive drugs needed to prevent their rejection have major downsides. If some of a patient's own cells could be converted into beta cells, rejection wouldn't be an issue, says Yi Zhang, who led the UNC research that appeared online in the *Journal of Biological Chemistry*.

The Harvard technique could enable patients to replenish their own lost cells—if it's effective in people. "Let's suppose this works," says Douglas Melton, codirector of the Harvard Stem Cell Institute, whose group's findings were published in *Nature* last week. "Is this a cure? No, it is not." Such regenerative approaches, he says, would provide only half of a cure for type 1 diabetes.

The other half is one that no amount of insulin-churning cells could fix: the immune system's relentless, misdirected attack. "There's no shortage of approaches to make new beta cells, but all of them succumb to the underlying disease," says Denise Faustman, an immunologist at Massachusetts General Hospital and Harvard Medical School. A cure must stop this assault, and Faustman's team is one of several working on the challenge.

One strategy is to intervene quickly before the autoimmune attack completely destroys a patient's insulin-making capacity. Swedish researchers reported today in the *New England Journal of Medicine* that a vaccine appeared to stall the loss of beta cell function when given to patients within six months of diagnosis, but not when treatment was delayed. However, it didn't eliminate or even reduce their need for regular doses of insulin. While the vaccine showed only a minor effect, says Faustman, who wrote an accompanying editorial in the *Journal*, it may hold promise for children, because it didn't have serious side effects associated with other therapies.

Other researchers aim to help another population: The nation's longtime type 1 diabetics whose insulin-producing capacity has flat-lined. In a controversial 2001 study, Faustman reported curing mice with advanced diabetes by giving them a simple vaccine. The animals, she reported, spontaneously regenerated insulin-making cells once the immune attack subsided. She has since launched a trial of the vaccine in adults who have completely lost the ability to make insulin.

Working independently, researchers at the Children's Hospital of Pittsburgh are injecting adult volunteers with the very immune cells that make them ill, cells that transmit the "kill" command that launches the attack on the pancreas. The scientists first remove the cells from each patient—in a three-hour process involving a needle in each arm—and, before reinjecting the cells, treat them in the lab to make them unable to communicate their orders. The experiment has already worked in diabetic mice, who recovered once their immune response was foiled. The researchers will probably have data on 15 patients sometime next year.

One of those patients is Ryan Cupps, 19, of Plum Borough, Pa., who has lived with type 1 diabetes since age 13. Even if Cupps is receiving the experimental therapy—the volunteers don't yet know who's getting a placebo treatment—he knows it may be coming too late to help him, because his immune system may have finished off his beta cells years ago. But he is hopeful that his participation may help others avoid his situation, which requires six shots of insulin and seven finger-sticks (to check his blood sugar) every day. "It would mean a whole lot to me for those newly diagnosed not to have to go through [this]," he says.

Massimo Trucco, who is heading up the trial, says that even if this experimental treatment buys patients like Cupps even a year's reprieve from the need to take insulin, he would be satisfied. Though his hopes for dramatic results are high, they're laced with uncertainty, as the path toward a cure has been littered with dead ends. "If its effects last forever, like in the mouse, I will jump for joy," he says, "but from mouse to human is always a big jump."

Tags: diabetes