New technique to 'see' and protect transplants successful in diabetic animal model

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Researchers at Johns Hopkins have found a way to overcome a major stumbling block to developing successful insulin-cell transplants for people with type I diabetes.

Traditional transplant of the cells, accompanied by necessary immune-suppressing drugs, has had highly variable results, from well- to poorly tolerated. Part of the problem, the Hopkins researchers say, is an inability to track the cells—so-called pancreatic beta cells—once they're inside the body.

Now a new technique encapsulates the insulin-producing cells in magnetic capsules, using an FDA-approved iron compound with an off-label use, which can be tracked by magnetic resonance imaging (MRI). The product, tested in swine and diabetic mice, also simultaneously avoids rejection by the immune system, likely a major reason for transplant failure. The work will be published online next week in *Nature Medicine*.

"We're really excited because we can track where we put the cells and make sure their protective housing stays intact and that the cells don't move. This could solve the mystery of why current transplantation techniques work only for so long," says one of the study's authors, Aravind Arepally, M.D., assistant professor of radiology and surgery at Hopkins.

Type I diabetes—the most common childhood sort—causes a person's immune system to destroy the pancreatic beta cells that make insulin. Without insulin, blood sugar levels can become dangerously high and lead to complications that include blindness or kidney failure. Careful monitoring of blood sugar levels paired with insulin injections can manage the condition, but transplanting healthy beta cells holds more promise for the moment-to-moment fine-tuning of insulin levels, says Arepally.

Current experimental cell transplantation techniques are done "naked and blind," only lasting a short period of time, according to co-author Jeff Bulte, Ph.D., a professor of radiology and chemical and biomolecular engineering at Hopkins. The unprotected transplanted cells are vulnerable to attack by the recipient's immune system, and researchers cannot see the cells to figure out why they stop making insulin after a while.

To address both of these challenges, the research team captured beta cells in tiny porous capsules made from a mixture of alginate, a gooey material made from seaweed, and Feridex, a magnetic iron-containing material visible under MRI. They then used a machine that oozes droplets of this mixture to surround and encapsulate individual islet clusters each containing about 500 to 1,000 insulin-producing beta cells. Once the cells are encapsulated, the shell hardens, creating a "magnetocapsule" that measures less than 1/128 of an inch across.

"They're tiny spheres with nano-scale pores just big enough too let the good stuff out but keep the bad from getting in," says lead author Brad Barnett, medical student and Howard Hughes fellow at Hopkins. The openings in the magnetocapsule are so small that the body's immune system sentinels cannot reach and attack the transplanted cells.

The team first transplanted magnetocapsules into the abdomens of mice

engineered to develop diabetes. Blood sugar levels in the animals returned to normal within a week and stayed that way for more than two months. In contrast, more than half of untransplanted diabetic mice died, and the rest had very high blood sugar levels.

To mimic human transplantation, the researchers then implanted magnetocapsules into the livers of swine with the help of MRI fluoroscopy, special reflective screens and a computer monitor that provide real-time imaging. The liver was chosen, rather than the usual pancreatic home of beta cells, because it contains many blood vessels that can deliver insulin quickly to the rest of the body.

“Getting the magnetocapsules into the right place requires hand-eye coordination normally required when playing video games,” says Arepally. The team threaded a long needle-like tube into a large vein near the upper thigh and guided the tube upward, across and into a neighboring blood vessel, ending in the body of the liver.

The pigs underwent MRI and blood tests three weeks after magnetocapsule transplantation. MRI showed that the magnetocapsules remained intact in the liver, and blood tests revealed that the cells were still secreting insulin at levels considered functional in people.

“We hope that our magnetocapsules will make tissue-type matching and immunosuppressive drugs problems of the past when it comes to cell-based therapies for type 1 diabetes,” says Bulte.

Source: Johns Hopkins Medical Institutions

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