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Pig to primate transplants show promise for diabetes

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Transplanting insulin-producing cells from embryonic pigs (above) into diabetic monkeys dramatically lowered blood sugar levels, though not quite to normal levels.

(Medical Xpress) -- Scientists exploring a potential cure for diabetes have shown that transplanting insulin-producing cells from embryonic pigs into diabetic monkeys can dramatically lower blood sugar levels, though not quite to normal levels.

Researchers at Washington University School of Medicine in St. Louis transplanted clusters of embryonic pig cells destined to become insulin-producing islet cells into three diabetic rhesus macaques. The macaques "adopted" the pig cells as their own, without the need for powerful immune suppression drugs to prevent rejection, the researchers report in the current issue of Organogenesis.

As the immature pig cells developed, they began to produce insulin, and the macaques' glucose tolerance improved.

"While we did not cure diabetes, we converted hard-to-control, or brittle, diabetes to a more manageable form of the disease using the embryonic cell transplants," says senior author Marc Hammerman, MD, the Chromalloy Professor of Renal Diseases in Medicine. "More work is necessary, but this approach presents an intriguing alternative for treating diabetes in humans. Pig cells could overcome the shortage of human islets available for transplant from deceased donors and the need for transplant patients to take anti-rejection drugs for life."

As part of the study, the researchers tried to boost insulin production in the macaques by performing a second transplant. Four weeks after transplanting the embryonic pig cells, they implanted adult insulin-producing pig islet cells into the kidneys of the macaques. The embryonic cells primed the monkeys' immune system to accept the mature islet cells, without using anti-rejection drugs, but their glucose control did not continue to improve.

Hammerman suspects this may be because they did not transplant enough adult pig islet cells or that placing them in the kidney is not an optimal location. As a comparison, the researchers also transplanted adult pig islet cells into a control group of diabetic macaques that did not receive the earlier embryonic pig cell transplants. Not surprisingly, the macaques' immune systems attacked the foreign cells and eventually rejected those cells all together.

The new study builds on earlier research in rats, reported by the same group last year in the American Journal of Pathology. In that study, the researchers used the same two-step approach to cure diabetes in rats. Unlike the macaques, rats that received both embryonic cell and islet cell transplants from the pigs could produce enough insulin to adequately

control their blood sugar.

In the current research, some of the macaques no longer needed regular, daily insulin injections after the embryonic cell transplants but still required regular glucose monitoring and insulin injections when their blood sugar was elevated.

What's most notable about the research, Hammerman says, is that the macaques did not need anti-rejection drugs.

"It's very encouraging that the pig cells became engrafted in the macaques," Hammerman says. "We've induced immune tolerance to mature islet cells by first transplanting embryonic cells from the same species."

Now, the researchers are trying the two-step approach in another group of diabetic macaques. But this time, they have increased the amount of adult islet cells being transplanted into the macaques and are placing the cells directly in the portal vein of the liver. The liver is where insulin breaks down glucose and is the same location that human islets are transplanted into patients.

"Non-human primates are much bigger than rats," Hammerman says. "It may be that we need to transplant more pig islets or transplant them in a different way to make an impact on diabetes."

More information: Rogers SA, Tripathi P, Mohanakumar T, Liapis H, Chen F, Talcott MR, Faulkner C and Hammerman MR. Engraftment of cells from porcine islets of Langerhans following transplant of pig pancreatic primordia in non-immunosuppressed diabetic rhesus macaques. *Organogenesis*. 7:154-162, 2011.