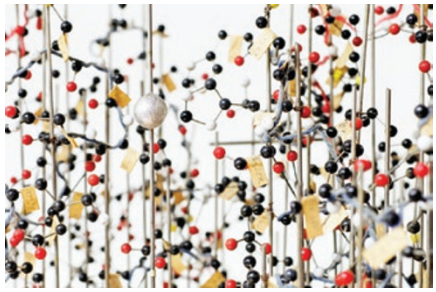
Toward a cure for diabetes

Diabetes mellitus is a chronic disease that affects at least 171 million people worldwide. Many people with diabetes are dependent on insulin and must take daily injections to regulate the levels of glucose in their blood. Failure to control blood glucose levels can result in various acute and long-term complications that can have severe health effects, including hypoglycemia, diabetic ketoacidosis, cardiovascular disease, chronic renal failure and retinal damage. Although insulin and other medications may help people to manage the disease, they are not a cure. The search for a cure continues, and new research shows promise.

A group of scientists led by Marc R. Hammerman (Washington University School of Medicine, St. Louis, MO) has shown that two-part transplants of pancreatic cells from embryonic and adult pigs can cure diabetes in rats. The cells engrafted successfully into the rats' tissues and produced enough insulin to control their blood sugar levels—without the need to administer immune-suppressive drugs to prevent transplant rejection (*Am. J. Pathol.* published online 25 June 2010; doi:10.2353/ajpath.2010.091193).



Horst Puschmann

The study used Lewis rats with diabetes induced by streptozotocin. The diabetic rats were treated with pancreatic primordial cells obtained from fetal pigs (at embryonic day 28, a very early stage of organ development). Previous studies had shown that these cells were tolerated by both rats and rhesus macaques without immune-suppressive treatments. Several weeks later, the rats were given a second transplant of pig pancreatic cells: adult islet cells. Islets are the insulin-producing cells of the pancreas. Beginning 4 weeks after islet cell transplantation and continuing for several months, rats that received both cell treatments had normal blood glucose levels. In comparison, rats that had received only embryonic cells had elevated blood glucose levels. In addition, Hammerman and his colleagues observed that the adult islet cells had successfully engrafted in rats that received both cell treatments, whereas the transplanted islet cells underwent immune rejection in rats that did not receive embryonic cells beforehand.

Next, Hammerman's group plans to test the approach in rhesus macaques. "In essence, first transplanting embryonic pig pancreatic cells enables adult pig islet implants to cure diabetes in rats without immune suppression drugs," Hammerman stated in a press release. He continued, "We are now carrying out experiments to test whether the same transplant surgery works in diabetic non-human primates without using immune suppression drugs. If it does, we hope to evaluate pig cell transplants in people with diabetes."

Monica Harrington

ENGINEERING LUNGS

Adult lung tissue, which has a limited ability to regenerate, currently can only be replaced by lung transplantation. In addition to being expensive, lung transplantation has a 10-year survival rate of only 10–20%. Moreover, there is a serious shortage of donor organs.

In an effort to develop fully functional tissue-engineered lungs for humans, a team of researchers has regenerated adult rat lung tissue in the lab (*Science* published online 24 June 2010; doi:10.1126/science.1189345). The researchers implanted these engineered lungs into rats and, for the first time, animals breathed with lab-cultivated lungs.

To produce this lung tissue *in vitro*, a research team led by Laura Niklason of Yale University (New Haven, CT) used a technique called decellularization. They used detergent to remove the cellular components of lungs, turning the lungs from red to white. The acellular adult rat lungs still maintained extracellular matrix scaffolding consisting of air passages and blood vessels.

Niklason and colleagues rinsed the acellular lungs in culture medium and moved the lungs to a culture bioreactor. They then seeded epithelial cells from newborn rats into the decellularized lungs and allowed the epithelium cells to culture on the acellular matrices for 3–5 days. Next, the researchers seeded the microvascular endothelial cells into the vascular portions of the lungs and allowed the lungs to culture. To mimic some aspects of the fetal environment, the researchers circulated fluid through the lungs. This helped improve endothelial adhesion and survival on the lung matrix. Circulating air through the lungs helped the epithelium survive and helped to clear out airway secretions. Analyses suggested that the scaffold had formed into functional lung tissue.

To test whether these engineered lungs would function, the research team removed the left lungs of four rats and implanted an engineered lung into each of them. Chest X-rays confirmed that the implanted lungs were inflating, though not as much as the right native lungs. Importantly, the implanted lungs were able to effectively exchange oxygen and carbon dioxide. About 2 hours after implantation, small blood clots began to develop in the lung's blood vessels, so the researchers euthanized the rats.

Though these results suggest that it might be possible to use decellularization to engineer human lungs in the laboratory, many issues must be resolved before this strategy can become clinically useful. Most importantly, researchers would need to find a way to cultivate a lung using the recipient's own stem cells.

Kirsten Dorans