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Researchers report possibility of using unused human pancreata to build new organs

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Researchers have been working for years to develop an artificial pancreas in the lab to help the millions of people with type 1 diabetes. But what if the answer is to "recycle" the more than 300 human pancreata from organ donors that aren't currently being used?

Online ahead of print in the *Annals of Surgery*, regenerative medicine researchers at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine and colleagues report on the potential to use human pancreata as the "hardware" of a new-generation, bio-artificial pancreas. The pancreas is a large gland near the stomach that secretes insulin to regulate the metabolism of glucose and other nutrients.

Currently, about 25 percent of the approximately 1,300 pancreata recovered for transplant cannot be used due to defects and other reasons.

"We see these unused organs as potential 'hardware." The 'software' would be the patient's own cells, so that there would be no issues with rejection," said lead author Giuseppe Orlando, M.D., Ph.D., a transplant surgeon and regenerative medicine researcher. "We believe this research represents the first critical step toward a fully human-derived artificial pancreas."

Currently, most patients who have type 1 diabetes must take injections of insulin because their bodies do not produce insulin to regulate blood sugar levels. Other options, such as a pancreas transplant or transplant of insulin-producing islet cells are rarely offered due to the lack of suitable

pancreas donors and the toxic effects of anti-rejection drugs. In the U.S., for every 10,000 patients with type 1 diabetes, only three will receive a pancreas transplant or islet transplant in their lifetime, according to the authors.

The goal of the research was to test the suitability of pancreata from organ donors as a platform for building a new bio-artificial pancreas. First, the discarded organs were washed in a mild detergent to remove all cells, a process that is known as decellularization. A similar procedure is being used by Wake Forest Baptist regenerative medicine researchers in efforts to engineer human kidneys, livers and intestine.

The goal of both projects is to develop a new, potentially inexhaustible source of organs that would not require patients to take powerful anti-rejection drugs. The idea is based on evidence that the decellularized organs contain proteins and other substances that play a vital role in the survival, welfare and function of the organ's cells.

For the study, 25 human pancreata were processed to remove cells. The researchers found that the framework of blood vessels remained intact after the washing process. In addition, the researchers are the first to report that numerous growth factors were retained in the structures. Some of these proteins are essential in blood vessel formation, cell proliferation and glucose metabolism.

In theory, these organ structures could be re-populated with a patient's own cells. Insulin-producing cells could be generated from the patient's skin cells or could come from the patient's pancreas. Cells to line the organ's blood vessels (endothelial cells) could also come from the patient's pancreas. To test the compatibility of the decellularized structures and new cells, the researchers placed both insulin-producing and endothelial cells on the decellularized structures. In both cases, the organs structures were cell-friendly and allowed the cells to attach,

function and maintain their original cell type.

Next, to test the ability of the structures to grow new blood vessels, small samples of the cell-coated pancreata structures were implanted in chicken eggs. The structures integrated well with the developing environment of the chicken egg and generated capillaries. For the first time, the authors also conducted immunological tests to understand whether the structures would be rejected by the immune system. Surprisingly, they found that the structures actually regulated the immune response, suggesting that the engineered pancreata could be used as adjuvant immunosuppressants.

"The early results are encouraging and pave the way for further investigations to understand the interactions between the organ structures and cells and to identify the optimal cell type to achieve complete regeneration of the endothelium and islets," said Orlando.

In addition to the current research, Orlando represents Wake Forest Baptist as the only U.S.-based researcher on a $9 million project to develop a cell-therapy product to treat diabetes. The four-year effort, BIOCAPAN, is funded by the European Commission. Orlando's role is to use regenerative medicine technologies to distill non-cellular materials from discarded pancreata. The research team hypothesizes that the material may support the function of insulin-producing cells and can form the basis of a new insulin-free treatment for diabetes.

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