Lab-engineered kidney project reaches early milestone

June 21 2012

Regenerative medicine researchers at Wake Forest Baptist Medical Center have reached an early milestone in a long-term project that aims to build replacement kidneys in the lab to help solve the shortage of donor organs.

In proof-of-concept research published online ahead of print in Annals of Surgery, the team successfully used pig kidneys to make "scaffolds" or support structures that could potentially one day be used to build new kidneys for human patients. The idea is to remove all animal cells – leaving only the organ structure or "skeleton." A patient's own cells would then be placed on the scaffold, making an organ that the patient theoretically would not reject.

While this is one of the first studies to assess the possibility of using whole pig kidneys to engineer replacement organs, the idea of using organ structures from pigs to help human patients is not new. Pig heart valves – removed of cells – have been used for more than three decades to provide heart valve replacements in human patients.

"It is important to identify new sources of transplantable organs because of the critical shortage of donor organs," said lead author Giuseppe Orlando, M.D., an instructor in surgery and regenerative medicine at Wake Forest Baptist. "These kidneys maintain their innate three-dimensional architecture, as well as their vascular system, and may represent the ideal platform for kidney engineering."

For the research, pig kidneys were soaked in a detergent to remove all cells, leaving behind the organ's "skeleton," including its system of blood vessels. In addition, the structure of the nephron – the kidney's functional unit – was maintained. The scaffolds were implanted in animals, where they were re-filled with blood and were able to maintain normal blood pressure, proving that the process of removing cells doesn't affect the mechanical strength of the vessels.

"There are many challenges to be met before this system could be used to engineer replacement kidneys, including problems with blood clots forming in the vessels," said Anthony Atala, M.D., co-author and director of the Wake Forest Institute for Regenerative Medicine. "The kidney is a very complex organ with at least 22 different cell types."

But, the fact that nephron structure is maintained suggests the potential to re-populate the kidney with cells, according to the scientists. They speculate that new cells introduced into the scaffold would recognize their natural niche through physical or chemical signals of the scaffold.

While the project is in its infancy, the idea represents a potential solution to the extreme shortage of donor kidneys. According to the authors, the probability in the U.S. of receiving a kidney transplant within five years of being added to the waiting list is less than 35 percent. As of late August 2011, nearly 90,000 patients in the U.S. were waiting for kidney transplants.

The science of regenerative medicine has already had success engineering skin, cartilage, bladders, urine tubes, trachea and blood vessels in the lab that were successfully implanted in patients. These structures were able to receive oxygen and nutrients from nearby vascularized tissues until they developed their own blood vessel supply.

However, the "holy grail" of regenerative medicine is to engineer more

complex organs such as the kidney, liver, heart and pancreas. These organs are very dense with cells and must have their own oxygen supply to survive. This need for a scaffold with a full vasculature is why scientists are exploring the possibility of removing cells from donor organs and replacing them with a patient's own cells.

Scientists have already used scaffolds from rodents or pigs to engineer heart, liver, lung and intestinal scaffolds. When re-populated with organ-specific cells, these "organoids" were able to produce some of the functions of native organs in the lab. The goal of the current study is to produce kidney scaffolds from the pig because of similarities to humans in terms of organ structure and size.

Provided by Wake Forest University Baptist Medical Center