New discoveries advance efforts to build replacement kidneys in the lab

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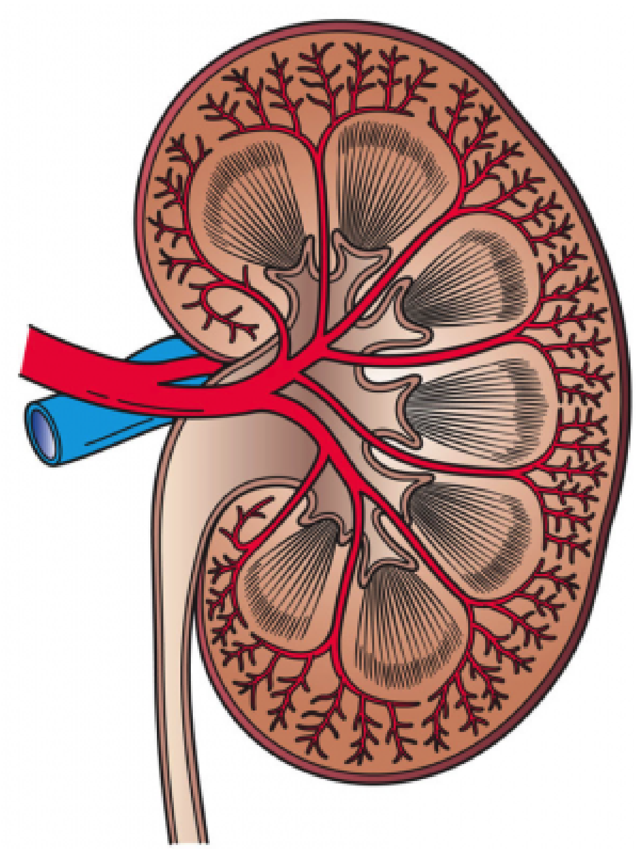

This image shows a cross section of a kidney. Credit: Holly Fischer/Wikipedia

Researchers at Wake Forest Baptist Medical Center report progress in their quest to build replacement kidneys in the lab. The teams' goal is to make use of the more than 2,600 kidneys that are donated each year, but must be discarded due to abnormalities and other factors. The scientists aim to "recycle" these organs to engineer tailor-made replacement kidneys for patients.

"We believe the two studies we are reporting provide critical information to the booming field of organ bioengineering as it applies to the kidney," said Giuseppe Orlando, M.D., Ph.D., a transplant surgeon and regenerative medicine researcher. Orlando is part of a team at the Wake Forest Institute for Regenerative Medicine aiming to recycle human kidneys. Another group at the institute is doing the same thing with pig kidneys.

The process begins by washing the discarded organs in a mild detergent to remove all cells. The idea is to replace these cells with a patient's own kidney stem cells, making a tailor-made organ that would not be rejected and wouldn't require the use of powerful anti-rejection medication. But are the organs a suitable platform for engineering after going through the process to remove cells?

To help answer that question, the researchers evaluated whether the washing process affects a small sac of capillaries in kidneys called the glomerulus. These vessels, which are vital to the kidney's role of filtering contaminants out of the body, operate at a pressure that is at least three times higher than other capillaries in the body. The scientists injected resin into the structures to measure vessel size and used pulse-wave technology to measure pressure within the vessels. The researchers also screened the kidney structures to see if they retained growth factors that play an important role in function.

In the journal *Transplantation*, the research team reports that the size, structure and function of the micro-vessels in the glomerulus are preserved after the cell-removal process. In addition, vital proteins known as growth factors that regulate cell growth and function are retained within the kidney structures.

"These growth factors play a vital role in the formation of new vessels and kidney cells," said Orlando. "The fact that they are preserved means they can potentially facilitate the repopulation of cells into the structure and reduce the potential of clot formation."

In a separate study, published in the journal *CellR4*, the team reported on the interactions that occur when stem cells are placed on kidney structures that have been through the cell removal process.

"Understanding the interaction between the kidney structure and cells, as well as the choice of cell type to use, is an important challenge to address before a viable and functioning kidney structure can be manufactured and transplanted into patients," said Orlando.

The team seeded stem cells derived from amniotic fluid onto sections of kidney structures. In this first study to describe the long-term results of this process, the scientists observed that the stem cells proliferated when placed on the structures and were functionally active as demonstrated by the fact that they secreted chemicals and growth factors involved in such critical pathways as inflammation and the formation of new blood vessels.

"These results indicate that discarded human kidneys are a suitable platform for engineering replacement kidneys and that when cells are added, the structures behave as an effective and viable biosystem," said Orlando.

The researchers' next steps are to identify the appropriate cells to regenerate the vascular compartment of the kidney as well as the compartment of the kidney responsible for blood filtration.

Provided by Wake Forest University Baptist Medical Center