Implantable artificial kidney achieves preclinical milestone

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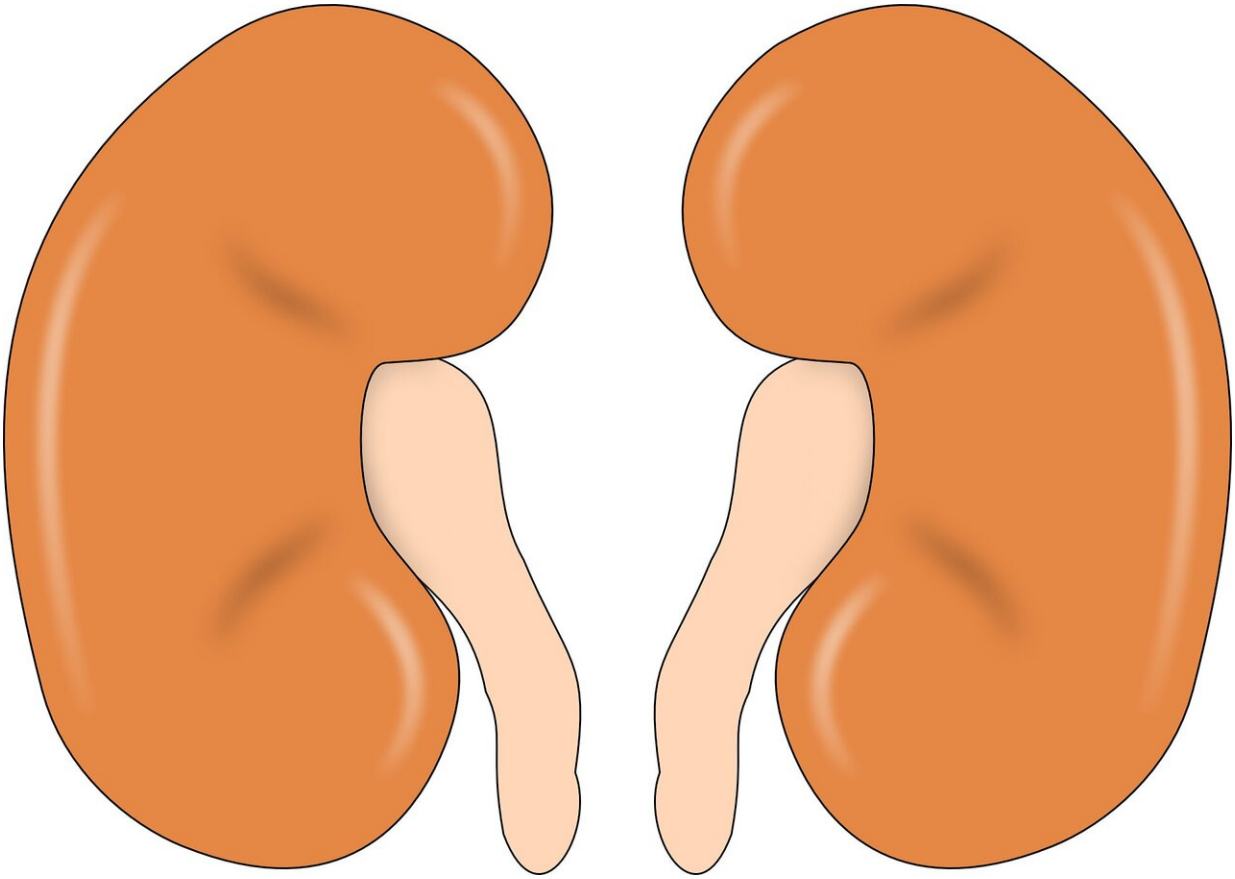

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The Kidney Project, a national effort to develop an implantable bio-artificial kidney that could eliminate the need for dialysis, will announce

a key milestone in a November 7, 2019 presentation at the American Society of Nephrology Kidney Week 2019 conference in Washington, DC.

The team will report that UC San Francisco scientists have successfully implanted a prototype kidney bioreactor containing functional human kidney cells into pigs without significant safety concerns. The device, which is about the size of a deck of cards, did not trigger an immune reaction or cause blood clots in the animals, an important milestone on the road to future human trials.

"This is the first demonstration that kidney cells can be implanted successfully in a large animal without immunosuppression and remain healthy enough to perform their function. This is a key milestone for us," said Kidney Project co-lead Shuvo Roy, Ph.D., a faculty member in the Department of Bioengineering and Therapeutic Sciences, a joint department of the UCSF Schools of Pharmacy and Medicine. "Based on these results, we can now focus on scaling up the bioreactor and combining it with the blood filtration component of the artificial kidney."

UCSF-Vanderbilt Kidney Project Aims to Eliminate Dialysis

Nearly 750,000 Americans—and two million people around the world—are treated for end-stage renal disease (ESRD), and rates of kidney disease are growing rapidly, leading to an urgent shortage of kidneys for transplant. As of 2016 there were only 21,000 donor kidneys available for transplant in the U.S. on a waiting list of nearly 100,000 and extending five to ten years.

Most patients awaiting a kidney transplant survive by undergoing long

and cumbersome dialysis treatments multiple times a week to clear toxins from their blood, but dialysis does not replace many essential kidney functions and on average, only 35 percent of dialysis patients remain alive after five years. Dialysis and other treatments for ESRD, which are universally covered by Medicare, cost $35 billion in 2016, representing seven percent of Medicare's annual budget.

The Kidney Project [pharm.ucsf.edu/kidney] is led by Roy and Vanderbilt University Medical Center nephrologist William H. Fissell, MD, who for more than a decade have been working to develop an implantable bio-artificial kidney with the goal of eliminating dialysis and easing the shortage of donor kidneys.

The implantable device being developed by The Kidney Project consists of two components: an blood filtration system called the hemofilter, which removes toxins from the blood by passing it through silicon membranes fabricated with precisely shaped nanometer-scale pores; and a bioreactor, which contains cultured human kidney cells intended to perform other kidney functions, such as maintaining adequate fluid volume and blood pressure, adjusting salt levels, and producing essential hormones.

Following promising studies in large animals, The Kidney Project's hemofiltration system is currently awaiting FDA approval for an initial clinical trial to evaluate its safety. The bioreactor technology has been tested in laboratory experiments but so far had not been implanted into animals.

Bioreactor Containing Human Kidney Cells Implanted in Pigs Without Immune Reaction or Blood Clots

In The Kidney Project's November 7 Kidney Week presentation, Rebecca Gologorsky, MD, a UCSF Surgical Innovations Fellow on the team, will show how silicon membranes inside the implanted bioreactor protect the enclosed human kidney cells from the host immune system by keeping blood-borne immune cells and proteins out of the device.

"It has been a holy grail of transplant therapies to find ways to avoid the need for lifelong immunosuppressive drugs that are often required to prevent immune rejection," Roy said. "These drugs not only expose patients to infection and other harmful side-effects but have been shown to directly harm transplanted cells and organs, eroding the therapeutic benefit of transplants over time."

Another key benefit of avoiding immunosuppression is its cost to patients, Roy says: "Medicare currently covers dialysis for life, but immunosuppressive drugs are covered for just the first three years following transplant. Many patients who receive kidney transplants ultimately lose the new organ because they weren't able to afford the immunosuppressive drugs needed to keep it healthy."

Roy's team also carefully engineered the prototype bioreactor to avoid triggering blood clots that could lead to pulmonary embolism or stroke, a major challenge faced by all patients with long-term medical implants. They achieved this by coating the silicon membrane filters that contact the blood with biologically friendly molecules and engineering the device to avoid the turbulent blood flow that can also trigger clotting.

"We couldn't use the standard blood-friendly coatings that have been developed for heart valves, catheters, and other devices because they are so thick that they would completely block the pores of our silicon membranes," Roy said. "One of our accomplishments has been to engineer a suitable surface chemistry on our silicon membranes that makes them look biologically friendly to blood."

The results, Roy says, demonstrate progress towards The Kidney Project's hoped-for clinical "trifecta": a heart-powered device that runs without batteries or other external connections that could introduce infection risk, and which can clean the blood without anti-rejection drugs or blood thinners.

The researchers now aim to scale up the prototype bioreactor to contain more cells in order to test whether the implanted device can supplement kidney function in animals with kidney failure, with the ultimate goal of eventually moving the device to human safety trials.

"Advancing a complex cell therapy like this into the clinic will not be a trivial task—for instance, it will require substantial investments in cell production and characterization in controlled GMP facilities to avoid any possibility of contamination," Roy said. "Now we've confirmed that we're on the right track to move forward with these efforts."

More information: An Immunoprotected Bioreactor for Implanted Renal Cell Therapy, Abstract TH-OR033, November 07, 2019 | 04:54 PM - 05:06 PM ET, 146 A/B, Walter E. Washington Convention Center, www.asn-online.org/education/k … px?controlId=3232240

Tunable Stiffness Polyacrylamide Hydrogels with Functionalized Matrigel for Renal Tissue Culture, Abstract SA-PO038, November 09, 2019 | 10:00 AM - 12:00 PM ET, Exhibit Hall, Walter E. Washington Convention Center,
Activation of AMPK and Inhibition of TGFß Stimulate In Vitro Transport in Human Renal Epithelial Cells, Abstract SA-PO043, November 09, 2019 | 10:00 AM - 12:00 PM ET, Exhibit Hall, Walter E. Washington Convention Center , www.asn-online.org/education/k … px?controlId=3233432

Next-Generation Renal Replacement Therapies (RRT): How Do Patients

Weigh the Risks and Benefits? Abstract SA-PO057, November 09, 2019 | 10:00 AM - 12:00 PM ET, Exhibit Hall, Walter E. Washington Convention Center, www.asn-online.org/education/k … px?controlId=3235261

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