Development of an artificial kidney for early detection of drug toxicity

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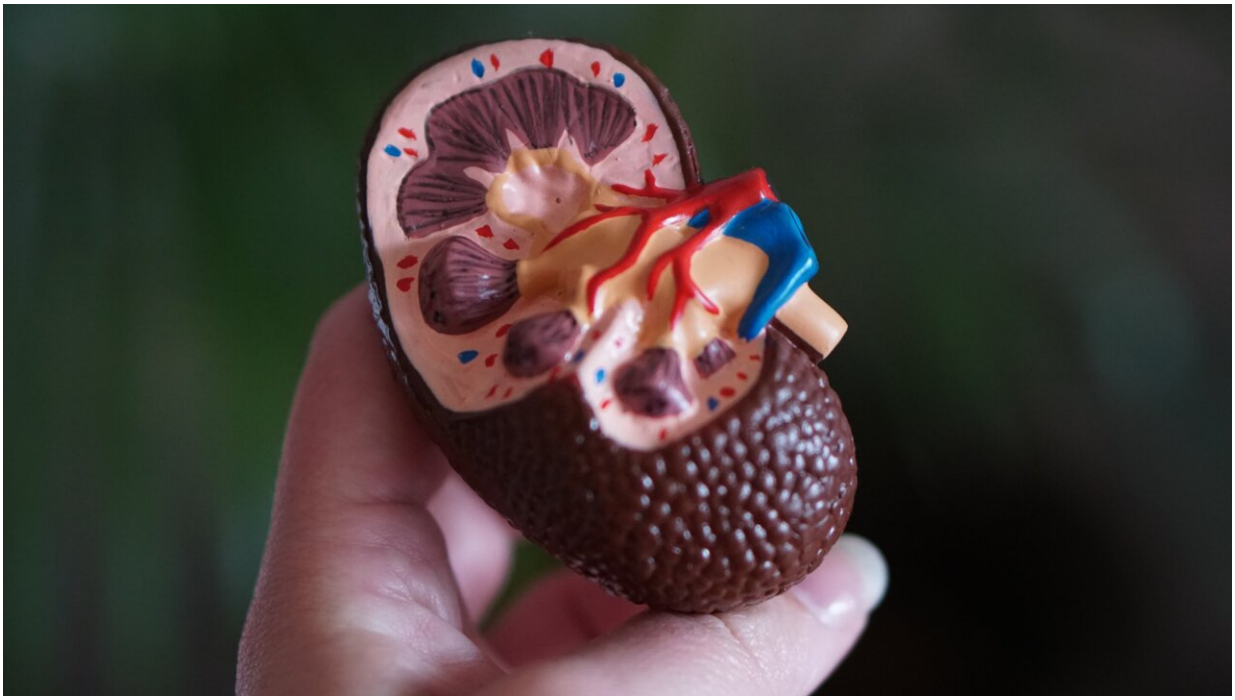

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The kidney plays a vital role in maintaining homeostasis within the body by eliminating toxic and superfluous substances in the bloodstream, including waste generated during metabolic processes, through urine. Nevertheless, toxicity can also be induced in the kidney from certain medications. Recently, a research team from POSTECH has engineered an artificial kidney that allows for the early detection of adverse drug

reactions.

The POSTECH research team led by Professor Dong-Woo Cho and Professor Jinah Jang (Department of Mechanical Engineering) fabricated a glomerular microvessel-on-a-chip, which includes glomerular endothelial cells, podocyte layers and a glomerular basement membrane (GBM) using a single step fabrication process. The research findings have been published in the journal *Biofabrication*.

Nephron is the fundamental structural and functional unit in the kidney. It encompasses a network of small blood vessels called the glomerulus, twisted into a convoluted thread-like shape, contributing to forming kidney corpuscle along with glomerular capsules. It also plays a role in removing waste from the blood. When an excessive quantity of drugs is administered, the nephron is often the first organ to exhibit drug toxicity in the body.

Given this challenge, efforts have been directed toward the development of artificial organs that can determine the degree of toxicity induced by specific drug concentrations and combinations before actual drug administration. However, it should be noted that the glomerulus is responsible not only for regulating endothelial cells but for selectively releasing proteins. This function requires interactions of podocytes and GBM proteins and is executed at a microscopic scale, making its emulation difficult.

The team successfully fabricated a glomerular microvessel-on-a-chip that recapitulates the intricate arrangement of the glomerular endothelial cells, podocyte layers, and GBM in a single step. This perfusable chip permits the co-culture of monolayer glomerular endothelium and podocyte epithelium, which demonstrate mature functional markers of glomerular cells. Moreover, the proper interactions between these cells lead to the production of GBM proteins, the key components of the

GBM in vivo. Additionally, the team assessed the selective permeability capacity, a hallmark function of the glomerular filtration barrier in this novel glomerular model as well as evaluated the response of this model to Adriamycin- and hyperglycemia-induced injury.

"We have successfully replicated glomerular units of the kidney, which offer boundless potential for drug screening and nephrotoxicity testing in clinical practice," explained Professor Dong-Woo Cho who led the study. He added, "This development will enable us to detect drug toxicity early by facilitating glomerulus disease modeling and to provide personalized treatment for patients."

More information: Narendra K Singh et al, Coaxial cell printing of a human glomerular model: an in vitro glomerular filtration barrier and its pathophysiology, *Biofabrication* (2022). DOI: 10.1088/1758-5090/acad2c

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