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NEW HIGH-THROUGHPUT SCREENING METHOD MAY UNCOVER NOVEL TREATMENTS FOR KIDNEY DISEASE

Assay screens for agents that specifically protect the cells important for blood filtration

Highlights

- Researchers have developed a system that could be used to identify novel drug candidates that protect the function of the kidney cells that are damaged in patients with chronic kidney disease.
- One drug identified through the system effectively protected the kidney cells of rodents exposed to kidney damaging agents.

More than 26 million people in the United States have chronic kidney disease.

Washington, DC (April 9, 2015) — A newly developed assay may help investigators identify novel drug candidates to protect kidney cells and prevent or treat chronic kidney disease (CKD). The advance is described in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN).

CKD affects more than 13% of adults in the United States, with diabetes, hypertension and atherosclerosis being common risk factors. Most patients rely on antihypertensive medications for treatment, and there are no therapies available that directly and specifically target the kidney.

A team led by Vineet Gupta, PhD and Jochen Reiser, MD, PhD (Rush University Medical Center) has now developed a system that can be used to identify novel drug candidates that protect the function of kidney podocytes, cells that are critical for filtering the blood. Damage to these cells is a hallmark of CKD.

“A key barrier to the rational development of podocyte-directed therapeutics has been a lack of cell-based assays for use in high-throughput drug discovery environment,” said Dr. Gupta. “Our report describes what we believe to be the first podocyte cell-based high content screening assay for the identification of novel podocyte-directed therapeutics in a high-throughput fashion.”

Using the assay, which analyzes thousands of podocytes under different conditions in multi-well plates, the investigators identified 24 small molecules that protected podocytes against injury. When they treated mice and rats with one of the molecules, called pyrintegrin, the animals' podocytes remained healthy despite being exposed to damaging agents. Pyrintegrin activates β 1 integrin, a protein that acts as a molecular bridge to help podocytes hold onto the outside of blood vessels and maintain the filtration apparatus in the kidney.

"We believe that this assay could provide the much needed boost in fueling the discovery and development of kidney directed therapeutics, development of which has significantly lacked in recent times," said Dr. Reiser.

Study co-authors include Ha Won Lee, PhD, Samia Khan, PhD, Mohd Hafeez Faridi, PhD, Changli Wei, MD, Nicholas Tardi, PhD, Mehmet Altintas, PhD, Hatem Elshabrawy, PhD, Steve Mangos, PhD, Kevin Quick, and Sanja Sever, PhD.

Disclosures: V.G. and J.R. are inventors on pending patent applications related to this study. J.R. and S.S. are cofounders and advisors of TRISAQ, a biotechnology company designed to develop novel therapeutics for kidney disease. V.G., J.R., and S.S. have the potential for financial benefit from product commercialization.

The article, entitled "A Podocyte-Based Automated Screening Assay Identifies Protective Small Molecules," will appear online at <http://jasn.asnjournals.org/> on April 9, 2015.

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Facebook: A newly developed assay may help investigators identify novel drug candidates to protect kidney cells and prevent or treat chronic kidney disease (CKD). The advance is described in the *Journal of the American Society of Nephrology*.

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