Industry Spotlight

New Method May Lead to Better CKD Testing

Researchers at Translational Genomics Research Institute (TGen) of Phonenix, AZ, have developed a promising way to isolate exosomes—tiny cell components that contain genetic and other useful information—from urine.

Exosomes are being widely studied because they may contain biomarker clues that could serve as the basis of new early diagnostic tests for chronic kidney disease (CKD). Found in urine, these cellular components may provide information about the very earliest changes in kidney function.

"Our method of extracting exosomes from urine is simple, fast, and easily adapted to clinical research, so we can ultimately help physicians provide better therapies for their patients," said Johanna DiStefano, PhD, director of TGen's Diabetes, Cardiovascular and Metabolic Diseases Division, and senior author of a report on the research that appeared in the July issue of *Kidney International*.

The plasma membrane in mammalian cells can fold into tiny containers called endosomes. Sometimes the membranes of some of the endosomes can in turn be internalized into even smaller vesicles, called multivesicular bodies. These become exosomes when the multivesicular bodies again merge, become part of the cell membrane, and break open to release their contents outside of the cell.

Exosome evaluations in urine samples would be useful in comparison to conventional kidney tissue biopsies, the group noted. "Unlike a kidney biopsy—an invasive and expensive procedure that provides only a small sample from one of two kidneys—urinary exosomes provide a full representation of the entire urinary system," said Lucrecia Alvarez, PhD, the study's lead author.

MicroRNAs (miRNAs) are important regulators of gene expression and have been linked with renal development and disease. Last year, other researchers found that in patients with severe, chronic renal failure, circulating levels of total and specific miRNAs were reduced in comparison with mild renal impairment or normal renal function. A report in *Nephrology Dialysis Transplantation* found a strong correlation exists between detected circulating miRNAs and eGFR.

In the current study, TGen researchers looked at six different methods, and found the best method for isolating exosomes was a modified protocol of an available exosome precipitation reagent called ExoQuick-TC. That reagent alone didn't yield high quantities or pure preparations of cell proteins and RNA, which would harbor biological clues. The TGen modification of the protocol led to the highest yields of miRNA and mRNA, which can subsequently be used in genetic profiling experiments, the study showed.

Currently, CKD is typically diagnosed by detecting increased levels of urinary albumin (a protein that is filtered out of urine in healthy kidneys) or of serum creatinine (a breakdown product of creatine, which is part of muscle).

The new TGen method has "strong potential for identifying and characterizing exosomal biomarkers from urine," with implications for diagnosis and treatment of chronic kidney disorders, Alvarez said.

Amgen Acquires KAI Pharmaceuticals

Amgen Inc. recently completed its acquisition of KAI Pharmaceuticals for $315 million. Initially agreed to on April 10, Amgen said the move was spurred by the "compelling" phase 2A trial results of KAI-4169, KAI's compound to treat hyperthyroidism. The deal calls for Amgen to make a loan to KAI so it can plan late-stage trials of the drug.

KAI-4169 drew attention at ASN Kidney Week in Philadelphia last November when it was reported that the drug had reduced parathyroid hormone by 33 percent in patients taking a 5-mg dose and by 49 percent in those taking a 10-mg dose. It is an experimental intravenous treatment for secondary hyperparathyroidism in patients