ATW 2022 Nov. 17(Thu)~19(Sat), 2022
CONRAD SEOUL, Seoul, Korea

Submission No.: PG11-9999
Session : Postgraduate Course 11 (Kidney/Pancreas)
Date & Time, Place : November 17 (Thu), 15:00-16:30, Room 5F-1
Session Title : New Diagnostic Tests in Kidney Transplantation

New noninvasive markers

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Developing a noninvasive clinical test to accurately diagnose kidney allograft rejection is critical to improve allograft outcomes. I will briefly review the clinical unmet needs, the clinically available biomarkers and their limitation, then I will introduce our work on urinary exosomes.

Urinary exosomes, tiny vesicles released into the urine that carry parent cells' proteins and nucleic acids, reflect the biologic function of the parent cells within the kidney, including immune cells. Their stability in urine makes them a potentially powerful tool for liquid biopsy and a noninvasive diagnostic biomarker for kidney-transplant rejection.

Using urine samples with matched biopsy samples from patients who underwent a clinically indicated kidney-transplant biopsy, we isolated urinary exosomal mRNAs and developed rejection signatures on the basis of differential gene expression. We used cross validation to assess the performance of the signatures on multiple data subsets.

We then assessed our previously described exosome multi-gene signature using a new workflow better suited for clinical laboratories, allowing for smaller urine volumes and more traditional qPCR instrumentation. Here, I will describe the application of the Exosome Transplant Rejection Urine (ExoTRU™) test, a non-invasive, urine-based exosomal mRNA assay to identify clinical and subclinical kidney transplant rejection.

We further evaluated the performance in a heterogenous cohort of patients who underwent a clinically indicated or surveillance kidney transplant biopsy. The results demonstrate the potential for a multigene classifier to stratify patients during post-transplant surveillance. Our expanded mRNA signatures in urinary exosomes not only can discriminate between patients with kidney allograft rejection but also differentiate between rejection types. Thus, enabling earlier detection of rejection and, subsequently, improve treatment management in patients with CKD.