Noninvasive protein biomarkers for detection of transplant injury in kidney transplantation

Tara Sigdel
University of California San Francisco, USA

Background: The human urinary proteome provides an assessment of kidney injury with specific biomarkers for different kidney injury phenotypes.

Method: In an effort to fully map and decipher changes in the urine proteome and peptidome after kidney transplantation, renal allograft biopsy matched urine samples were collected from 396 kidney transplant recipients. Centralized and blinded histology data from paired graft biopsies was used to classify urine samples into diagnostic categories of acute rejection, chronic allograft nephropathy, BK virus nephritis, and stable graft. Two hundred forty-five urine samples were analyzed by liquid chromatography-mass spectrometry using isobaric Tags for Relative and Absolute Quantitation (iTRAQ) reagents. From a group of over 900 proteins identified in transplant injury, a set of 131 peptides were assessed by selected reaction monitoring for their significance in accurately segregating organ injury causation and pathology in an independent cohort of 151 urine samples. Ultimately, a minimal set of 35 proteins were identified for their ability to segregate the 3 major transplant injury clinical groups.

Results: Our analysis identified a panel of 11 urinary peptides for acute rejection (93% area under the curve [AUC]), 12 urinary peptides for chronic allograft nephropathy (99% AUC), and 12 urinary peptides for BK virus nephritis (83% AUC).

Conclusion: Urinary proteome discovery and targeted validation can identify urine protein panels for rapid and noninvasive differentiation of different causes of kidney transplant injury, without the requirement of an invasive biopsy.

e: tara.sigdel@ucsf.edu