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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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Proteomics in CKD

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Proteomics has been increasingly employed in kidney disease with the goal to improve diagnosis and risk prognostication, and to provide pathophysiologic insight. This presentation prioritizes studies that have utilized multiplexed methods using nucleotide-labelled aptamers or antibodies for specific protein capture, followed by detection and quantitation based on nucleic acid oligomerization. Second, it prioritizes proteomic analyses of blood, the biofluid most frequently subject to testing in the clinic and that has been assayed in the large majority of epidemiologic studies to date. To date, these studies have identified numerous proteins associated with cross-sectional measures of kidney function, as well as with the longitudinal risk of chronic kidney disease progression. Prior to investing in dedicated animal models or randomized trials, methods that leverage the availability of genotyping in epidemiologic cohorts—including mendelian randomization—can add evidence for causal inference in CKD proteomics research. Representative signals that have emerged from the literature include an association between levels of TNFRSF1A and TNFRSF1B and worse kidney prognosis, and an association between levels of testican-2 and favorable kidney prognosis, including reduced risk of incidence CKD in population-based cohorts and reduced risk of incident ESKD among individuals with CKD. Among individuals who had undergone kidney biopsy, testican-2 levels had the strongest inverse association with glomerulosclerosis. Interestingly, profiling of renal arteriovenous samples has shown that testican-2 is released by the kidney into circulation, whereas microscopy and single-cell RNA sequencing demonstrated that testican-2 expression is highest in podocytes. Finally, testican-2 gain-of-function is beneficial, whereas testican-2 loss-of-function is detrimental, in adriamycin treated mice. Together, these findings advance the concept that testican-2 is a podocyte-derived marker and mediator of kidney health. Finally, publicly available databases (such as tissue multi-omics in KPMP) are valuable resources to complement plasma proteomic analyses.

Keywords: proteomics, aptamer, testican-2