Liquid-biopsy microRNA biomarkers to predict risk for diabetic kidney disease

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A recent study from the Madras Diabetes Research Foundation, Chennai, India and University of Lyon, France, brings new hope for using 'liquid-biopsy' exosomal microRNA biomarkers (miRNAs) from

urine to predict risk for kidney disease in diabetes patients.

Diabetic kidney disease is the leading cause of end-stage renal disease in developed as well as developing countries. While longstanding type 2 diabetes mellitus and poor glycaemic control are risk factors for diabetic nephropathy (diabetic kidney disease), South Asian ethnicity has also been linked to a relatively greater susceptibility to this complication.

"Our laboratory is committed to work on translational applications of molecular medicine and we always pick-up research topics based on 'clinical paradoxes and unmet clinical needs' in the field of diabetes and its complications" says Dr.Muthuswamy Balasubramanyam, Disease-Biologist and Dean of Research Studies at the Madras Diabetes Research Foundation, Chennai, India.

Microalbuminuria (a test to measure albumin levels in urine with a reference range of 30– 299 mg/dL) is the gold standard for detection and prediction of diabetic kidney disease in clinical practice. However, microalbuminuria has several limitations, such as sensitivity and specificity concerns as well as larger variability. Its predictive powers are also challenged, as structural changes in kidney vasculature may appear before the onset of microalbuminuria. Moreover, certain proportion of diabetic kidney disease happens even in the absence of obvious microalbuminuria. "Thus, we need to 'look beyond microalbuminuria' and explore 'early biomarkers' in order predict the risk of diabetic nephropathy in diabetic patients so that better prevention as well disease management is possible" says senior authors Dr.M.Balasubramanyam & Dr.V.Mohan.

In the study by Prabu et al, urine samples from individuals with different degrees of glucose tolerance as well as albuminuria were processed for isolation of extracellular vesicles (EVs) and profiled for expression levels of miRNAs. Altered expression levels of a panel of 4 miRNAs

(let-7i-3p, miR-24-3p and miR-27b-3p, and miR-15b-5p) were found to identify patients with microalbuminuria and thereby predicting the diabetic patients who are at risk for macroalbuminuria as well as severe kidney complications.

"In contrast to microalbuminuria test, the altered urinary miRNAs when analyzed for their biological functions by bioinformatics tools notify very early changes occurring in the kidney of diabetes patients" says Dr.Sophie Rome & Dr.M.Balasubramanyam. While the clinical use of miRNAs as liquid-biopsy assays is maturing rapidly, this study is highly promising that these genomic signatures will likely be developed into clinically-viable tests for the early detection of diabetic kidney disease. "The study also foresees for the development of simple assay systems of point-of-care approaches to adapt the testing of miRNAs from urine samples for precision medicine to predict and prevent diabetic kidney disease," says Balasubramanyam.

More information: P. Prabu et al. MicroRNAs from urinary extracellular vesicles are non-invasive early biomarkers of diabetic nephropathy in type 2 diabetes patients with the 'Asian Indian phenotype', *Diabetes & Metabolism* (2018). DOI: 10.1016/j.diabet.2018.08.004

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