

Urinary Exosomes

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Exosomes are tiny membrane-bound vesicles that are secreted by many cell types throughout the body. Their size (30–80 nm) labels them as “biological nanoparticles”. In 2004, we showed that exosomes are secreted into the urine by the cells of every renal tubule segment and by glomerular podocytes (Pisitkun T, Shen RF, Knepper MA. Proc Natl Acad Sci U S A. 2004;101:13368–73). This finding opened the door for studies to use exosome isolation as a means of enriching disease biomarkers from urine. In normal humans, we have used protein mass spectrometry (LC-MS/MS) to identify 1160 proteins that are abundant in urinary exosomes. These include 177 proteins listed on OMIM as proteins linked to genetic diseases including at least 30 that are related to specific renal disease processes, such as heritable forms of nephrotic syndrome (α -actinin-4 [MIM: 604638]; podocin [MIM: 604766]; nephrin [MIM: 602716]) and salt and water imbalance syndromes (aquaporin-2 [nephrogenic diabetes insipidus]; thiazide-sensitive Na-Cl cotransporter [MIM:263800]; bumetanide-sensitive Na-K-2Cl cotransporter [MIM:601678]; and ENaC α , β , and γ , Liddle syndrome. Mass spectrometric analysis of urinary exosomes has been used to identify biomarker proteins that can aid decision making in renal allograft patients with increasing serum creatinine (Pisitkun T, Gandolfo MT, Das S, Knepper MA, Bagnasco SM. Application of systems biology principles to protein biomarker discovery: urinary exosomal proteome in renal transplantation. Proteomics Clin Appl. 2012;6:268–78.). Here, pairs of biomarkers were identify that can discrimination between ‘rejection’ and ‘tubular damage’, and between ‘antibody-mediated rejection’ and ‘cell-mediated rejection’.