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Role of extracellular vesicles in kidney disease: from mechanism to translational application

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Tubulointerstitial injury is a histopathological feature of acute and chronic kidney diseases. Recent clinic data have provided continuing evidence to support the notion that tubulointerstitium lesions is decisive for the prognosis of renal disease. Tubule epithelial cells as the primary component of tubulointerstitial are particularly vulnerable to injury which triggers the progression of renal disease. Nevertheless, fewer studies have investigated how injured tubules communicate with interstitial and contribute to tubulointerstitial damage.

Extracellular vesicles (EVs) are initially considered as garbage bins to dispose unwanted cellular contents, however, it is increasingly recognized as the crucial intercellular communicators by transferring functional massagers. We found that upon exposure to different insults (e.g. proteinuria, hypoxia), tubule epithelial cells derived EVs selectively carried CCL2 mRNA or microRNAs which were then transferred to interstitial macrophages, inducing their infiltration and phenotype transition. Hence, EVs released by tubules participated in the progress of tubulointerstitial inflammation which may hold promise as biomarker and therapeutic target for kidney disease.

Urine EVs represents a unique source of biomarker for kidney disease due to its easy and non-invasive collection. Since the first proteomic characteristic study on urinary EVs by Pisitkun et al in 2004, it opened up new possibilities for the fluid biopsy of kidney diseases. Interestingly, those pathological EVs derived from renal cells could be detected and served as useful biomarker reflecting renal histological changes. We recently profiled the organ and cellular origin of urine EVs by long RNA transcriptome analysis which may provide new clues for future biomarker study.

Natural or engineered EVs can be exploited as delivery vectors for diverse therapeutic cargoes of interest. Recently, macrophage-derived EVs were employed for the delivery of dexamethasone to the inflamed kidney by virtue of the integrin αLβ2 and α4β1 presented on EV surface. A subsequent study also engineered macrophages to manufacture EVs overexpressing IL-10 for ameliorating renal tubular injury and renal inflammation. To improve the targeting ability, Kim-1–targeted EVs were established successfully to deliver therapeutic siRNA for acute kidney injury. These examples provide a novel insight and potential for the clinical translation of EVs in the treatment of renal disease.