CHRONIC KIDNEY DISEASE

Key role of exosomes in albumin-induced inflammation

Exosomes transfer albumin-induced inflammatory signals from tubular epithelial cells (TECs) to the interstitium, according to a new study by Lin-Li Lv, Bi-Cheng Liu and colleagues. These researchers previously reported that albuminuria causes severe TEC injury and tubulointerstitial inflammation, but the mechanism by which TEC injury induces inflammation and macrophage recruitment in the interstitium was unclear.

“We recently found that exosomes are novel biomarkers of chronic kidney disease, suggesting that they might have a role in renal tissue damage,” says Lv. “Thus, we decided to explore the potential role of exosomes released from TECs in transferring albumin-induced inflammatory signals to interstitial macrophages.”

The researchers show that acute or chronic kidney injury increased

exosome numbers in the kidneys and urine of rodents as well as the mRNA expression of inflammatory cytokines — particularly CC-chemokine ligand 2 (CCL2) — in these exosomes.

Similarly, treatment of cultured TECs with bovine serum albumin (BSA) induced the release of exosomes containing high levels of CCL2 mRNA.

Exposure of TECs to BSA increased the macrophage uptake of exosomes purified from these TECs as well as the inflammatory response and migration of the recipient macrophages. These effects were abrogated by silencing of CCL2 in the TECs prior to BSA treatment. Fluorescent labelling enabled observation of direct transfer of CCL2 mRNA from the TEC exosomes to the macrophages.

In mice, injection of exosomes from BSA-treated TECs, but not those

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from untreated TECs, into the tail vein induced renal tubular injury and inflammatory cell infiltration. CCL2 knock-down in the TECs before BSA treatment reduced the severity of renal injury induced

by exosome injection. Moreover, in patients with IgA nephropathy, urinary exosome number and exosomal CCL2 mRNA expression were increased and correlated with proteinuria and renal interstitial macrophage infiltration.

“Exosomal CCL2 mRNA represents a novel vehicle to communicate danger signals from TECs to macrophages and thereby promote inflammatory kidney damage,” concludes Liu. The researchers are now investigating the mechanism by which albumin induces increased production of TEC exosomes.

Ellen F. Carney

“Exosomal CCL2 mRNA represents a novel vehicle to communicate danger signals from TECs to macrophages”

ORIGINAL ARTICLE Lv, L.-L. et al. Exosomal CCL2 from tubular epithelial cells is critical for albumin-induced tubulointerstitial inflammation. *J. Am. Soc. Nephrol.* <https://doi.org/10.1681/ASN.2017050523> (2018)