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Cellular location and type of LRT-EV proteins identified through proteomic analysis. First column: Proteomic analysis identified the plasma membrane transporter megalin in LRT-EVs. Representative immunohistochemistry of kidney tissues collected 10 weeks post-surgery show presence of megalin (red) localized at the base of the brush border on the apical membrane in sham-operated (sham) rats. In 5/6Nx rats megalin can be seen in LRT-EVs that are within the tubule lumen and LRT-EVs emerging from the proximal tubule cells. The distribution of megalin is diffuse (yellow) or absent in some tubular cells. Image on bottom is an inset from center image. DAPI, blue; autofluorescence at 455 nm (green); Cal. bar = 100 μm.

Second column: Proteomic analysis failed to detect NHE3 in LRT-EVs. Immunohistochemistry of kidney tissue collected 10 weeks post-surgery show the presence of NHE3 (red) in sham and 5/6Nx rat proximal tubule epithelial, but not in LRT-EVs. DAPI, blue; autofluorescence at 455 nm (green); Cal. Bar = 50 μm. Adapted from Figure 2 of “Functionally Essential Tubular Proteins Are Lost to Urine-Excreted, Large Extracellular Vesicles during Chronic Renal Insufficiency” by Ryan J. Adam, Mark R. Paterson, Lukus Wardecke, Brian R. Hoffmann, and Alison J. Kriegel. KIDNEY360 1: 1107–1117, 2020. doi: 10.34067/KID.0001212020.