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Association between changes in blood, urine and stool-derived bacterial extracellular vesicles and CKD progression.

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Objectives: Gut microbiome plays an essential role in influencing host health. Extracellular vesicles (EVs) are vesicles of either plasma membrane or intracellular membranes that transport proteins, nucleic acids, and lipids. And gut bacteria-derived EVs affect host immunity as well as inflammatory pathways. In this study, the changes in bacteria-derived EVs accompanying the progression of chronic kidney disease (CKD) were discovered using various specimens.

Methods: Plasma, urine, and stool samples were collected at 0 (control), 4 (early-CKD), 8 (late-CKD) weeks from 5/6-nephrectomized rats, an animal model for CKD, and bacteria-derived EVs were discovered through 16s Next Generation Sequencing.

Results: Plasma and urine samples showed no difference in microbial diversity, while stool samples showed decreased diversity in early and late-CKD. In taxonomic profiling, Sphingomonas increased and Enterobacter decreased in the plasma of late-CKD, and Cutibacterium and Atopostipes increased sequentially from early- to late-CKD in urine. In stool, Pseudomonas gradually increased in early- and late-CKD, Clostridia_UCG-014, Ruminococcus, and Prevotellaceae_UCG-001 significantly decreased in early-CKD and maintained until late-CKD. In pathway analysis, valine, leucine, and isoleucine biosynthesis pathway was increased in plasma, whereas their degradation was increased in stool from early-CKD. In urine, elevated valine, leucine, and isoleucine degradation pathway was noted only in late-CKD. Furthermore, the metabolism of butyrate, a member of short chain fatty acid, produced by the catabolism of those branched chain amino acids, decreased significantly in urine from early-CKD and increased in stool from late-CKD. These pathway results indicated that intestinal microbial EVs may associated in synthesis and degradation of various metabolites in CKD.

Conclusions: This study revealed changes in the taxonomic profile and metabolic pathways of bacteria-derived EVs in plasma, urine and stool samples, providing evidence for the metabolic roles of bacteria-derived EVs in CKD progression.