Integrative multi-omics analyses reveal the therapeutic impact of probiotics via modulating microbial-based signatures in chronic kidney disease

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Introduction: Growing clinical evidence supports that gut dysbiosis is a major contributor to adverse chronic kidney disease (CKD) progression, resulting in generation of gut-derived uremic toxins and aggravating kidney failure. Therefore, microbiota-based therapeutic interventions could be considered potent approaches to reduce uremic toxins and alleviate CKD progression. In the present study, we integrated multi-omics analyses to investigate the mechanisms of therapeutic impact of probiotics in feline CKD.

Methods: An open-label single-arm clinical study was conducted with cats with CKD stage 2-3 for 8 weeks. Each cat collected stool, urine, and blood specimens at three time points, i.e. before, after probiotic administration for 4 and 8 weeks (one capsule per day). Each capsule contained approximately 5 billion live freeze-dried bacteria of *Lactiplantibacillus plantarum* and *Lacticaseibacillus paracasei* (Lm). Strains were selected due to their functionality against CKD progression in our previous study.

Results: After 8 weeks of Lm administration, creatinine and blood urea nitrogen were decreased in 57% and 64% of CKD cats, respectively. Lm also decreased the level of serum gut-derived uremic toxins. Alpha diversity indices were increased significantly by Lm, indicating the transition to a more diverse gut environment. Moreover, Lm changed the level of specific bacteria and metabolites in cats, and these biomarkers showed a significant correlation with adverse factors associated with kidney function.

Discussion: We demonstrated Lm downregulated gut-derived uremic toxins and improved intestinal diversity, leading to alleviated CKD progression via modulation of microbial composition and metabolite production. Bacteria and metabolites showing correlation with kidney function indicators could be utilized as novel CKD prognostic/diagnostic biomarkers. Our findings suggest these biomarkers have the potential to be developed as next-generation/precision probiotics and medicine for alleviating CKD progression.