Probiotic bifidobacteria mitigate the deleterious effects of para-cresol in a *Drosophila melanogaster* toxicity model

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Introduction: Renal impairment associated with chronic kidney disease (CKD) causes the build-up of uremic toxins that are deleterious to the patient's health status. Current standard therapies that manage toxin accumulation in CKD offer an incomplete therapeutic effect against toxins like p-cresol and p-cresyl sulfate. As these toxins continuously build-up, they contribute to the production of reaction oxygen species which can accelerate CKD progression.

Methods: Using in vitro culture techniques, strains of lactobacilli and bifidobacteria from a 24 strain synbiotic were investigated for their ability to reduce p-cresol. Toxin clearance was measured using HPLC. To assess if p-cresol clearance was maintained in vivo a *Drosophila melanogastor* model was used.

Results: Four bifidobacterial strains tested internalize p-cresol. Toxin clearance was maintained when the multi-strain product was cultured under the same conditions. Oral supplementation of toxin-clearing bifidobacteria improved longevity ($P<0.0001$) of p-cresol exposed flies compared to controls by more than twenty days. We also showed p-cresol increased reactive oxygen species in the Malpighian tubules (i.e. fly kidney) of exposed flies and two of the four bifidobacteria reduced this oxidative stress.

Discussion: Using a *Drosophila* model, this work highlights why dosing with certain probiotic strains may be clinically useful in CKD. Cost effective oral supplementation of toxin clearing probiotics may be a useful adjunct therapy in CKD and should be evaluated in humans. In addition to reducing p¬-cresol produced by the gut microbiota, the synbiotic or its components might normalize the dysbiotic gut microbiota observed in CKD patients.