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Mechanisms Underlying Anti-Diarrheal Effects of Probiotics in Models of Infectious and Inflammatory Bowel Diseases (IBD) Associated Diarrhea

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Introduction: Many Lactobacillus species have been successfully used in clinical trials to treat diarrhea in children. However, mechanisms underlying anti-diarrheal effects of probiotics are not well understood. Recent studies from our group have shown that certain lactobacillus and bifidobacterial species upregulated electrolyteabsorption in the intestine.Since Intestinal epithelial apical membrane NHE3 (Na^+/H^+ exchanger 3) and DRA (Down Regulated in Adenoma, a key Cl^-/HCO_3^- exchanger) play key roles in mediating intestinal electroneutral NaCl absorption, we sought to evaluate the efficacy of *Lactobacillus acidophilus* (LA) in counteracting NHE3 and DRA inhibition and ameliorating diarrhea in a model of *C rodentium* infection and DSS induced colitis.

Methods: FVBN mice challenged with *C. rodentium* ($1x10^9$ CFU) with or without administration of live LA ($3x10^9$ CFU) were assessed for NHE3 and DRA mRNA and protein expressio, mRNA levels of carbonic anhydrase, diarrheal phenotype (assessed by colonic weight/length ratio), myeloperoxidase (MPO) activity and proinflammatory cytokines. For colitis studies, dextran sulfate sodium (DSS in drinking water for 7 days) was used to induce colitis in C57BL/6J mice.

Results: LA counteracted *C. rodentium*-induced inhibition of colonic DRA, NHE3 and carbonic anhydrase I and IV expression, attenuated diarrheal phenotype and MPO activity. Further, LA completely blocked *C. rodentium* induction of IL-1β, IFN-γ and CXCL1 mRNA and *C. rodentium*-induced STAT3 phosphorylation. Oral gavage of live LA also showed evident alleviation of inflammatory state by reducing the weight loss, decreased colon length and colon weight in both the models. Also the inflammation as well as the decrease in DRA mRNA and protein levels caused by DSS colitis was blocked by LA.

Conclusions: Our data provide mechanistic insights into anti-diarrheal and anti-inflammatory effects of probiotics in models of infectious and chemical injury colitis.

Biography:

Dr. Dudeja is a Professor of Physiology in the Department of Medicine at University of Illinois at Chicago and a Senior Research career Scientist at the Jesse Brown VA Medical Center. His group focuses on pathophysiology of diarrheal diseases as it pertains to infectious & IBD associated diarrhea and to develop better therapeutic interventions. His recent studies have focused on defining the mechanisms underlying potential antidiarrheal effects of probiotics. He has published about ~220 original articles and has been supported by multiple grants from NIH and the Department of Veterans affairs. He serves as an Editor for "Intestinal Absorption" for Comprehensive Physiology journal and on many editorial boards including: Gastroenterology, Amer. J. of Physiol., Physiological reports and Cell. & Mol. Gastroenterology & Hepatology. He has also served on many peer review committees including National Iinstitute for Health, and Department of Veterans Affairs, USA. He has been honored by Mario Toppo Distinguished Scientist Award from the ASIOA (Assoc. of Scientists of Indian Origin in America) and is a winner of Takeda Distinguished Scientist Award of American Physiological Society for 2018. These awards honor life-time achievements of Dr. Dudeja in the area of gut-microbe interactions in pathophysiology of diarrheal diseases.