

Galacto-oligosaccharides enhance the intestinal barrier function

Yunan Hu^{1,2}, Jason W. Arnold^{2#}, Anika Rueppell², Rebecca Zasloff², Nehal Devpura^{1,2}, Scott T. Magness³, José M. Bruno-Bárcena⁴, M. Andrea Azcarate-Peril^{1,2*}

¹Department of Nutrition, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, NC, USA

²UNC Microbiome Core, Center for Gastrointestinal Biology and Disease (CGIBD), Department of Medicine, Division of Gastroenterology and Hepatology, School of Medicine, University of North Carolina at Chapel Hill, NC, USA

³Joint Department of Biomedical Engineering, University of North Carolina at Chapel Hill, and North Carolina State University, NC, USA.

⁴Department of Plant and Microbial Biology, North Carolina State University, NC, USA.

#Current address: Duke Microbiome Center, Department of Molecular Genetics and Microbiology, School of Medicine, Duke University, Durham, NC, USA

Abstract

The preservation of a functional intestinal barrier is critical for the overall host health, as increased permeability (a “leaky gut”) can lead to systemic pathologies. We have previously shown that galacto-oligosaccharides (GOS) and LacNAc-enriched GOS (humanized GOS, hGOS) modulate the gut microbiome increasing the abundance of beneficial microorganism, such as *Akkermansia*, *Bifidobacterium*, *Lactobacillus*. Here, we used old mice and young mice models combined with human primary colonic monolayers to demonstrate the effect of prebiotics on the intestinal integrity. In this study, we report that prebiotic GOS and hGOS restored intestinal permeability in young and old

mice through increased mucus production, demonstrated by increased expression of the *muc2* gene and a thicker mucus layer. *Ocln*, the gene that encodes occludin, the transmembrane protein that regulates epithelial permeability, showed different inductions in response to GOS or hGOS. Human primary colonic cells exposed to GOS and hGOS improved the integrity of the monolayers. The induction of *MUC2* and *OCN* genes in human primary colonic monolayers confirmed the findings of the experiments conducted in mice. Overall, the study highlights the mechanisms of GOS on gut health by enhancing mucus production and increasing intestinal integrity and suggests potential benefits for older individuals in improving gut barrier function.