Update from 2018's Most Valuable Presentation:
Human Milk Oligosaccharides Directly Enhance Gut Barrier Integrity to Alter Infections

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Complex oligosaccharides present in human milk (HMOs), are the result of millions of years of mammalian evolution to protect the infant from severe infections. While HMOs have many functions, two main roles are as prebiotics for specific commensal bacteria and reduction in infection through serving as receptor-decoys for pathogens thus blocking their binding to the intestine and reducing rates of infection. However, we have made a recent discovery that pre-incubation of specific HMOs like lacto-N-fucopentaose I (LNFP I) and 3' sialyllactose (3' SL) with intestinal cells directly enhances intestinal barrier integrity. We hypothesize that the well documented HMO-driven reduction in pathogen infection is modulated via two mechanistic routes, one via a direct interaction between HMO and intestinal cells thereby improving barrier function and the second through direct blocking of pathogen binding to the intestine. Pre-incubation of LNFP I and 3' SL with intestinal cells directly increases cell-cell adhesion, structural integrity and dramatically reduces internalization of pathogenic bacteria. Moreover, these HMOs directly increase transepithelial electrical resistance indicating improved tight-junction dynamics and a barrier-strengthening effect prior to pathogen encounter. Direct incubation with these HMOs also results in an alteration in the infection-dependent signaling cascade, and a dramatic reduction in pathogen-mediated chemokine expression. Using a germ-free mouse model, we have shown that 3' SL supplementation of drinking water reduces Dextran Sodium Sulfate mediated intestinal injury as determined via specific alterations in immune-markers in the mouse cecum and colon. This new evidence suggests a previously unknown protective role for HMOs directly linked to intestinal health—a finding that will enhance understanding of gut health and maturation during not only breastfeeding but can be advanced to better understand a variety of gut diseases and therapeutics across age groups.