Science Review: 2′Fucosyllactose

Human milk oligosaccharides (HMOs) are among the most abundant components in breast milk, and a growing body of research has shown they have diverse functions and are known to confer numerous health benefits and advantages to nursing infants. Emerging research has also shown that HMOs can promote health in adults, including those with gastrointestinal (GI) dysfunction.

Out of approximately 200 distinct HMO structures identified to date, 2′Fucosyllactose (2′-FL) is the most abundantly produced HMO, with an average of 2.4 grams produced per liter of milk. Formula-fed infants, weaned children, and adults are generally not exposed to dietary sources of 2′-FL; however, 2′-FL and other HMOs can also be produced using chemical synthesis or recombinant DNA technology for use in select infant formulas, dietary supplements, and medical foods.

**Mechanisms of Action**

2′-FL is one of the most simple HMOs, consisting of lactose plus a fucose group; resistant to digestion by human enzymes, 2′-FL is available as a prebiotic fuel source by gut microbiota in the colon.

With well-defined biologic mechanisms, 2′-FL is considered one of the most well-researched HMOs. Distinct mechanisms of 2′-FL include selective prebiotic effects, short-chain fatty acid production, and antimicrobial effects. 2′-FL encourages the growth of select beneficial bacteria, hinders the growth of many harmful bacteria, and thus supports GI and systemic health.

**Prebiotic and Bifidogenic Effects**

Behaving like soluble fiber, 2′-FL reaches the distal small intestine and colon intact, where it is partially fermented and serves as a source of fuel for select gut microbiota. Bacteria belonging to the genus *Bifidobacterium* are uniquely suited to metabolizing HMOs, including 2′-FL, as growth substrates. Selectively encouraging the growth of *Bifidobacterium* spp., HMOs are therefore considered “bifidogenic.”

Individuals with irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) have been shown to have significantly lower levels of *Bifidobacterium* spp. compared to healthy controls. A preliminary study of adults with IBS and IBD consuming a formulation that included 2′-FL (four grams per day) for six weeks resulted in:

- 19-fold increase in *Bifidobacterium* spp
- 17-fold increase in the species *Bifidobacterium longum*

Some preliminary research suggests that a low abundance of *Bifidobacterium* spp. in the GI tract has also been identified in other conditions including celiac disease, atopic disease, and cystic fibrosis. 2′-FL has been shown to increase *Bifidobacterium* spp. in healthy adults when taken for two weeks.

**Butyrate Production**

Bacterial fermentation of HMOs results in the production of short-chain fatty acids (SCFAs) including acetate and butyrate. When 2′-FL is metabolized by colonic bacteria, it is broken down into the SCFA acetate plus lactate; the lactate is then metabolized into butyrate by butyrate-producing gut bacteria.

By promoting intestinal butyrate production, 2′-FL promotes gut health via several mechanisms:

- Acts as a main source of energy for colonocytes and affects cellular growth and differentiation
- Affects water and electrolyte absorption and is involved in the regulation of intestinal barrier function and permeability; accelerates tight junction formation
- Modulates immune activation by suppressing nuclear factor-kappa B (NFkB) activation
- Alters visceral sensitivity and intestinal motility

**Research Highlights**

- 2′-FL shows selective prebiotic effects and promotes the growth of beneficial bacteria and healthy gut microbiota. 2′-FL promotes the production of butyrate, a key compound that plays several essential roles in the GI tract, including acting as a fuel source for colonocytes and modulation of intestinal permeability (including acceleration of tight junction formation).
- 2′-FL reduces GI infection through antimicrobial actions by acting as a decoy receptor to intestinal pathogens.
Antimicrobial Effects

2’-FL modulates epithelial immune responses and directly reduces GI infection through antimicrobial actions. Many pathogens infiltrate host cells by binding to cell surface glycans (Figure 1A). Harmful bacteria typically employ glycan-binding proteins (called adhesins or lectins) present on their surfaces to attach to and infect a host cell. HMOs including 2’-FL are similar, and in some cases identical, to intestinal cell surface glycans. This structural similarity prevents and reduces GI infection in breast-fed infants; when HMOs are present within the intestinal lumen, they act as decoys that pathogen adhesins and lectins can bind to instead of attaching to and infecting human intestinal cells (Figure 1B). Due to their ability to block pathogen attachment, HMOs have been described as “antiadhesive antimicrobials” and as part of the innate immune protection that human milk conveys.

Additional Antimicrobial Actions:

- Cell surface glycans also act as molecular targets for microbial toxins. 2’-FL has been shown to bind cholera toxin, E. coli toxins, and Shiga toxins.
- Other cell surface molecules, human blood group antigens (HBGAs), are sites of viral attachment for human noroviruses; 2’-FL has been shown to block norovirus particles from adhering to HGBA samples.
- Epidemiologic data has shown that mothers who produce higher concentrations of 2’-FL in their milk have offspring who are more protected from diarrheal illness “caused by campylobacter, caliciviruses, and stable toxin of enterotoxigenic E. coli [ETEC], and moderate-to-severe diarrhea of all causes.”
- Furthermore, by conferring a selective growth advantage to select commensal bacteria (such as Bifidobacterium spp.), 2’-FL and other HMOs also indirectly modulate the growth of pathogens.