



HUMAN MILK OLIGOSACCHARIDES

NOURISHING THE INFANT'S
DEVELOPING IMMUNE SYSTEM

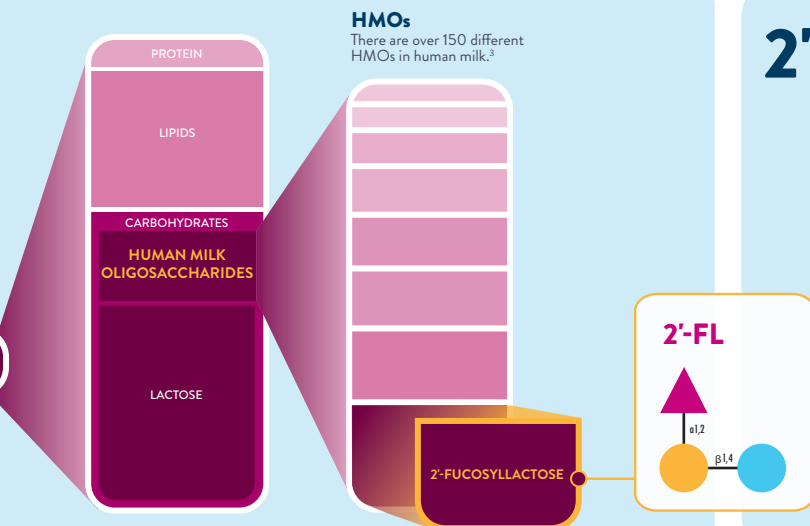
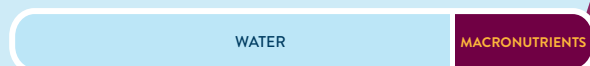
WHAT ARE HMOs?

Unique prebiotics found naturally in human milk | Food for beneficial bacteria in the infant's gut | 3rd most abundant solid component of human milk

COMPONENTS OF HUMAN MILK¹

Major nutritional components of human milk are: protein, carbohydrates, and lipids.²

HUMAN MILK



2'-FL HMO

- ✓ Approximately 75-80% of mothers secrete 2'-FL HMO in their breast milk.^{4,5}
- ✓ 2'-FL added to formula has the identical structure as 2'-FL in human milk.⁶
- ✓ Prebiotics—food for beneficial bacteria.⁷
- ✓ First clinical study with 2'-FL added to infant formula narrows the gap between human milk & infant formula.⁸

EARLY IMMUNE DEVELOPMENT

70%

of the immune system is in the digestive tract,⁹ and prebiotics support colonization of the gut which helps support immune system development.¹⁰

BENEFITS OF 2'-FL HMO EXPAND BEYOND THE GUT TO SUPPORT THE IMMUNE SYSTEM.

- A small portion of 2'-FL HMO ingested are absorbed in the infant's intestine and reach the systemic circulation.¹¹⁻¹³
- In a clinical study, 2'-FL HMO was shown to lower levels of multiple inflammatory cytokines to be more like levels in breastfed infants.⁸
- In a clinical study of infants fed formula with 2'-FL HMO,⁸ two markers of immune function associated with the severity of a respiratory infection (RSV) were more like breastfed infants than infants fed the same formula without 2'-FL HMO.*

*Using cells from infants' blood that were challenged with RSV ex vivo.

PREBIOTICS & MORE

Emerging research[†] indicates potential multifunctional benefits:

-
- COGNITION**¹⁴⁻¹⁶
 - Learning & memory
 - Long-term potentiation
 - Brain molecular markers
 - IMMUNITY**^{6,8,17-21}
 - Pathogen receptor decoy
 - Reduced symptoms of food allergy
 - Immune modulation
 - GI TOLERANCE**^{11,22-26}
 - Prebiotic
 - Gut motility
 - NEC

†Most studies were animal-based.

SUPPORTING EVIDENCE[‡]

30 STUDIES

provide preclinical and clinical evidence identifying the role of HMOs in health & development. (2000-2017)

‡Refer to references.



visit us at anhi.org
162523(2) / September 2017



REFERENCES

1. Prentice A. Constituents of human milk. United Nations University website. <http://archive.unu.edu/unupress/food/8F174e/8F174E04.htm>. Accessed February 26, 2016.
2. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. *Pediatr Clin North Am*. 2013;60(1):49-74.
3. Jantscher-Krenn E, Zherebtsov M, Nissan C, Goth K, Guner YS, Naidu N, Choudhury B, Grishin AV, Ford HR, Bode L. The human milk oligosaccharide disialyllacto-N-tetraose prevents necrotizing enterocolitis in neonatal rats. *Gut*. 2012;61(10):1417-1425.
4. Erney RM, Malone WT, Skelding MB, et al. Variability of human milk neutral oligosaccharides in a diverse population. *J Pediatr Gastroenterol Nutr*. 2000;30(2):181-192.
5. Castanys-Muñoz E, Martin MJ, Prieto PA. 2'-fucosyllactose: an abundant, genetically determined soluble glycan present in human milk. *Nutr Rev*. 2013;71(12):773-789.
6. Weichert S, Jennewein S, Hufner E, et al. Bioengineered 2'-fucosyllactose and 3-fucosyllactose inhibit the adhesion of *Pseudomonas aeruginosa* and enteric pathogens to human intestinal and respiratory cell lines. *Nutr Res*. 2013;33(10):831-838.
7. Roberfroid M. Prebiotics: the concept revisited. *J Nutr*. 2007;137(3 Suppl 2):830S-837S.
8. Goehring KC, Marriage BJ, Oliver JS, Wilder JA, Barrett EG, Buck RH. Similar to those who are breastfed, infants fed a formula containing 2'-fucosyllactose have lower inflammatory cytokines in a randomized controlled trial. *J Nutr*. 2016;146(12):2559-2566.
9. Furness JB, Kunze WA, Clerc N. Nutrient tasting and signaling mechanisms in the gut II: the intestine as a sensory organ: neural, endocrine, and immune responses. *Am J Physiol*. 1999;277(5, pt 1): G922-G928.
10. Castanys-Muñoz E, Martin MJ, Vazquez E. Building a beneficial microbiome from birth. *Adv Nutr*. 2013;7(2):323-330.
11. Bode L. Human milk oligosaccharides: every baby needs a sugar mama. *Glycobiology*. 2012;22(9):1147-1162.
12. Goehring KC, Kennedy AD, Prieto PA, Buck RH. Direct evidence for the presence of human milk oligosaccharides in the circulation of breastfed infants. *PLoS One*. 2014;9(7):e101692.
13. Marriage BJ, Buck RH, Goehring KC, Oliver JS, William JA. Infants fed a lower calorie formula with 2'FL show growth and 2'FL uptake like breast-fed infants. *J Pediatr Gastroenterol Nutr*. 2015;61(6):649-658.
14. Oliveros E, Ramirez M, Vazquez E, et al. Oral supplementation of 2'-fucosyllactose during lactation improves memory and learning in rats. *J Nutr Biochem*. 2016;31:20-27.
15. Vázquez E, Barranco A, Ramírez M, et al. Dietary 2'-fucosyllactose enhances operant conditioning and long-term potentiation via gut-brain communication through the vagus nerve in rodents. *PLoS ONE*. 2016;11(11):e0166070.
16. Vázquez E, Barranco A, Ramírez M, et al. Effects of a human milk oligosaccharide, 2'-fucosyllactose, on hippocampal long-term potentiation and learning capabilities in rodents. *J Nutr Biochem*. 2015;26(5):455-465.
17. Weichert S, Koromyslova A, Singh BK, et al. Structural basis for norovirus inhibition by human milk oligosaccharides. *J Virol*. 2016;90(9):4843-4848.

18. Ruiz-Palacios GM, Cervantes LE, Ramos P, Chavez-Munguia B, Newburg DS. *Campylobacter jejuni* binds intestinal H(O) antigen (Fuc alpha 1, 2Gal beta 1, 4GlcNAc), and fucosyloligosaccharides of human milk inhibit its binding and infection. *J Biol Chem*. 2003;278(16):14121-14120.

19. He Y, Liu S, Kling DE, et al. The human milk oligosaccharide 2'-fucosyllactose modulates CD14 expression in human enterocytes, thereby attenuating LPS-induced inflammation. *Gut*. 2016;65(1):33-46.

20. Noll AJ, Yu Y, Lasanajak Y, et al. Human DC-SIGN binds specific human milk glycans. *Biochem J*. 2016;473(10):1343-1353.

21. Wu LH, Shi BZ, Zhao QL, Wu XZ. Fucosylated glycan inhibition of human hepatocellular carcinoma cell migration through binding to chemokine receptors. *Glycobiology*. 2010;20(2):215-223.

22. Bienenstock J, Buck R, Linke H, Forsythe P, Stanisz AM, Kunze WA. Fucosylated but not sialylated milk oligosaccharides diminish colon motor contractions. *PLoS One*. 2013;8(10):e76236.

23. Ménard S, Cerf-Bensussan N, Heyman M. Multiple facets of intestinal permeability and epithelial handling of dietary antigens. *Mucosal Immunol*. 2010;3(3):247-259.

24. Gnoth MJ, Rudloff S, Kunz C, Kinne RK. Investigations of the in vitro transport of human milk oligosaccharides by a Caco-2 monolayer using a novel high performance liquid chromatography-mass spectrometry technique. *J Biol Chem*. 2001;276(37):34363-34370.

25. Eiwegger T, Stahl B, Haidl P, et al. Prebiotic oligosaccharides: in vitro evidence for gastrointestinal epithelial transfer and immunomodulatory properties. *Pediatr Allergy Immunol*. 2010;21(8):1179-1188.

26. Good M, Sodhi CP, Yamaguchi Y, et al. The human milk oligosaccharide 2-fucosyllactose attenuates the severity of experimental necrotizing enterocolitis by enhancing mesenteric perfusion in the neonatal intestine. *Br J Nutr*. 2016;116(7):1175-1187.

SUPPORTING EVIDENCE – 30 STUDIES

Erney RM, Malone WT, Skelding, et al. Variability of human milk neutral oligosaccharides in a diverse population. *J Pediatr Gastroenterol Nutr*. 2000;30(2):181-192.

Prieto PA. In vitro and clinical experiences with a human milk oligosaccharide, lacto-N-neotetraose, and fructooligosaccharides. *Foods Food Ingredients J Jpn*. 2005;(11):1018-1030.

Stepans MB, Wilhelm SL, Hertzog M, et al. Early consumption of human milk oligosaccharides is inversely related to subsequent risk of respiratory and enteric disease in infants. *Breastfeed Med*. 2006;1(4):207-215.

Newburg DS. Neonatal protection by an innate immune system of human milk consisting of oligosaccharides and glycans. *J Anim Sci*. 2009;87(suppl 13):26-34.

Wu LH, Shi BZ, Zhao QL, Wu XZ. Fucosylated glycan inhibition of human hepatocellular carcinoma cell migration through binding to chemokine receptors. *Glycobiology*. 2010;20(2):215-223.

Weichert S, Jennewein S, Hufner E, et al. Bioengineered 2'-fucosyllactose and 3-fucosyllactose inhibit the adhesion of *Pseudomonas aeruginosa* and enteric pathogens to human intestinal and respiratory cell lines. *Nutr Res*. 2013;33(10):831-838.

Vester Boler BM, Rossoni Sero MC, Faber TA, et al. In vitro fermentation characteristics of select nondigestible oligosaccharides by infant fecal inocula. *J Agri Food Chem*. 2013;61(9):2109-2119.

Yu ZT, Chen C, Kling DE, et al. The principal fucosylated oligosaccharides of human milk exhibit prebiotic properties on cultured infant microbiota. *Glycobiology*. 2013;23(2):169-177.

Yu ZT, Chen C, Newburg DS. Utilization of major fucosylated and sialylated human milk oligosaccharides by isolated human gut microbes. *Glycobiology*. 2013;23(11):1281-1292.

Bienenstock J, Buck R, Linke H, Forsythe P, Stanisz AM, Kunze WA. Fucosylated but not sialylated milk oligosaccharides diminish colon motor contractions. *PLoS One*. 2013;8(10):e76236.

Castanys-Muñoz E, Martin MJ, Prieto PA. 2-fucosyllactose: an abundant, genetically determined soluble glycan present in human milk. *Nutr Rev*. 2013;71(12):773-789.

Chow J, Panasevich MR, Alexander D, et al. Fecal metabolomics of healthy breast-fed versus formula-fed infants before and during in vitro batch culture fermentation. *J Proteome Res*. 2014;13(5):2534-2542.

Holscher HD, Davis SR, Tappenden KA. Human milk oligosaccharides influence maturation of human intestinal Caco-2Bbe and HT-29 cell lines. *J Nutr*. 2014;144(5):586-591.

Santos-Fandila A, Zafra-Gómez A, Vazquez E, Navalón A, Rueda R, Ramírez M. Ultra high performance liquid chromatography-tandem mass spectrometry method for the determination of soluble milk glycans in rat serum. *Talanta*. 2014;118:137-146.

Duska-McEwen G, Senft AP, Ruetschilling TL, Barrett EG, Buck RH. Human milk oligosaccharides enhance innate immunity to respiratory syncytial virus and influenza in vitro. *Food and Nutr Sci*. 2014;5(14):1387-1398.

He Y, Liu S, Leone S, Newburg DS. Human colostrum oligosaccharides modulate major immunologic pathways of immature human intestine. *Mucosal Immunol*. 2014;7(6):1326-1339.

Goehring KC, Kennedy AD, Prieto PA, Buck RH. Direct evidence for the presence of human milk oligosaccharides in the circulation of breast fed infants. *PLoS One*. 2014;9(7):e101692.

Marriage BJ, Buck RH, Goehring KC, Oliver JS, William JA. Infants fed a lower calorie formula with 2'FL show growth and 2'FL uptake like breast-fed infants. *J Pediatr Gastroenterol Nutr*. 2015;61(6):649-658.

Vázquez E, Barranco A, Ramírez M, et al. Effects of a human milk oligosaccharide, 2'-fucosyllactose, on hippocampal long-term potentiation and learning capabilities in rodents. *J Nutr Biochem*. 2015;26(5):455-465.

Castillo-Courtade L, Han S, Lee S, Milan FM, Buck R, Forsythe P. Attenuation of food allergy symptoms following treatment with human milk oligosaccharides in a mouse model. *Allergy*. 2015;70(9):1091-1102.

Goehring KC, Jonsson T, Marriage BJ, Prieto P, Buck RH. Infants fed formula supplemented with 2'-fucosyllactose have circulating gut flora-derived metabolites similar to breast fed infants. Presented at: Keystone Symposia: Gut Microbiota Modulation of Host Physiology; 26. March 2015; Keystone, CO.

Goehring KC, Marriage BJ, Oliver JS, Wilder JA, Barrett EG, Buck RH. Similar to those who are breastfed, infants fed a formula containing 2'-fucosyllactose have lower inflammatory cytokines in a randomized controlled trial. *J Nutr*. 2016;146(12):2559-2566.

He Y, Liu S, Kling DE, et al. The human milk oligosaccharide 2'-fucosyllactose modulates CD14 expression in human enterocytes, thereby attenuating LPS-induced inflammation. *Gut*. 2016;65(1):33-46.

Weichert S, Koromyslova A, Singh BK, et al. Structural basis for norovirus inhibition by human milk oligosaccharides. *J Virol*. 2016;90(9):4843-4848.

Oliveros E, Ramirez M, Vazquez E, et al. Oral supplementation of 2'-fucosyllactose during lactation improves memory and learning in rats. *J Nutr Biochem*. 2016;31:20-27.

Vázquez E, Barranco A, Ramírez M, et al. (2016) Dietary 2'-fucosyllactose enhances operant conditioning and long-term potentiation via gut-brain communication through the vagus nerve in rodents. *PLoS ONE*. 2016;11(11):e0166070.

Noll AJ, Yu Y, Lasanajak Y, et al. Human DC-SIGN binds specific human milk glycans. *Biochem J*. 2016;473(10):1343-1353.

Good M, Sodhi CP, Yamaguchi Y, et al. The human milk oligosaccharide 2-fucosyllactose attenuates the severity of experimental necrotizing enterocolitis by enhancing mesenteric perfusion in the neonatal intestine. *Br J Nutr*. 2016;116(7):1175-1187.

Kajzer J, Oliver J, Marriage B. Gastrointestinal tolerance of formula supplemented with oligosaccharides. *FASEB J*. 2016;30(Suppl 1):671.4

Vázquez E, Santos-Fandila A, Buck R, Rueda R, Ramírez M. Major human milk oligosaccharides are absorbed into the systemic circulation after oral administration in rats. *Br J Nutr*. 2017;117(2):237-247.

