

The diversity of HMOs impacts their functions

HMOs are known as one of the most important bioactive components in breastmilk¹

Unique, complex carbohydrates (oligosaccharides) naturally found in human milk²



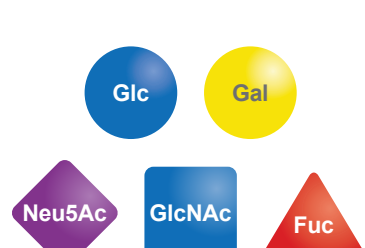
3rd largest solid component of human milk³⁻⁵:

20–25 g/L in colostrum

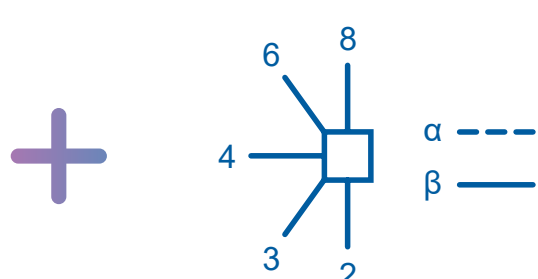
5–15 g/L in mature milk

HMOs are remarkably diverse,⁶⁻⁸ which arises from the variety of their structural features⁷⁻⁹

Composed of a vast combination of building blocks and linkages⁸



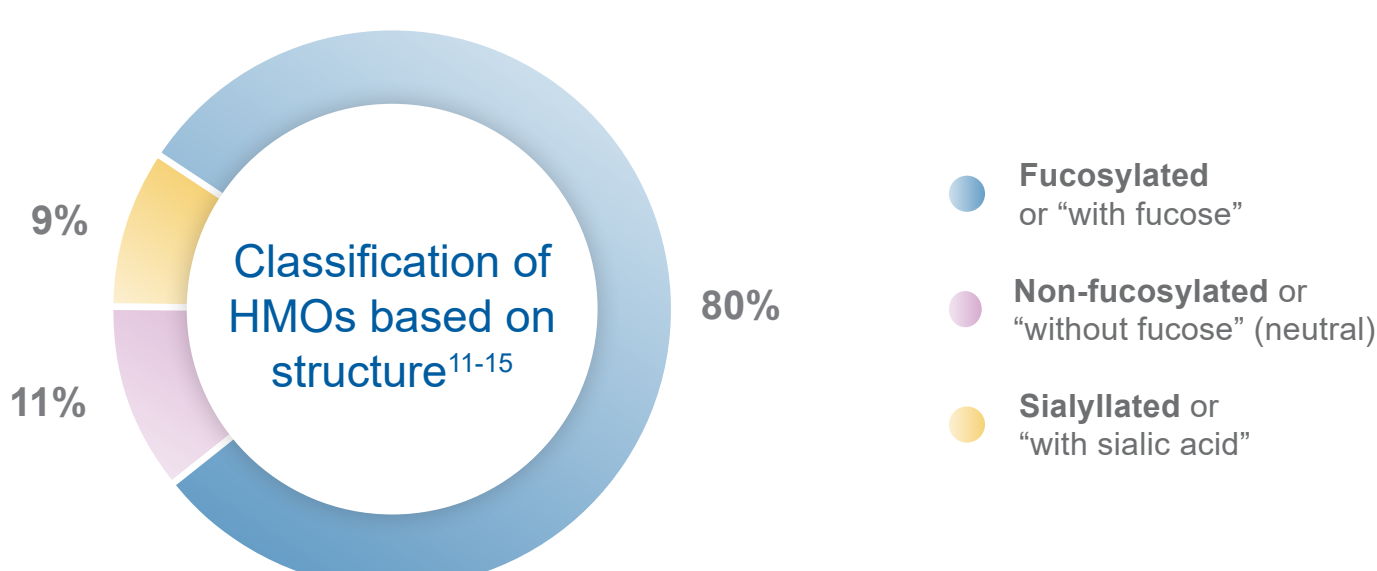
Building blocks



Linkages

Diverse range of structurally unique HMOs

Over 160 structurally unique HMOs have been identified¹⁰



The different structural features of HMOs are thought to contribute to their many functions^{1,6-9,16-23}

Emerging data on the function of different HMOs suggest benefits related to^{1,4,11-20}:



Gut and immune health



Brain and cognitive development

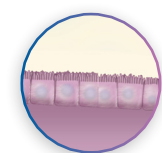
Research shows HMOs support gut and immune health on many levels



Promote the abundance of bifidobacteria²¹⁻²⁹



Inhibit and deflect fecal pathogens^{24,26,27,29}



Strengthen gut barrier function^{30,31}



Associated with less illness^{19,20,32}

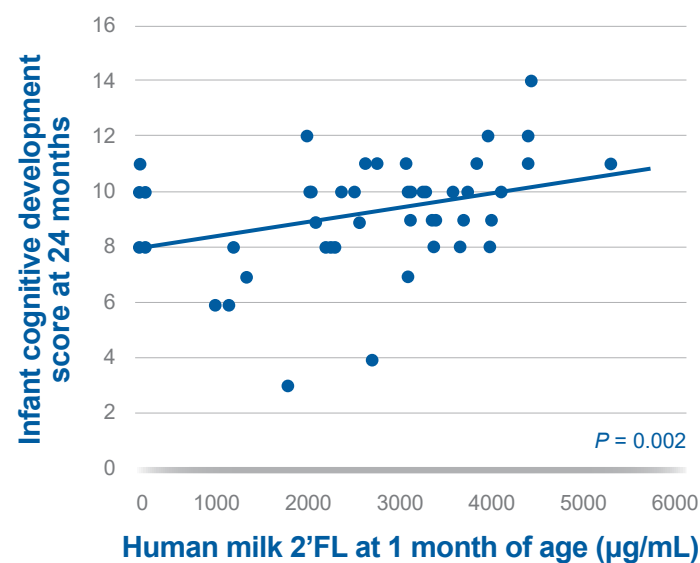


Encourage healthy immune response in the gut and systemically^{24,26,30,32-37}

Emerging research suggests HMOs support brain and cognitive development

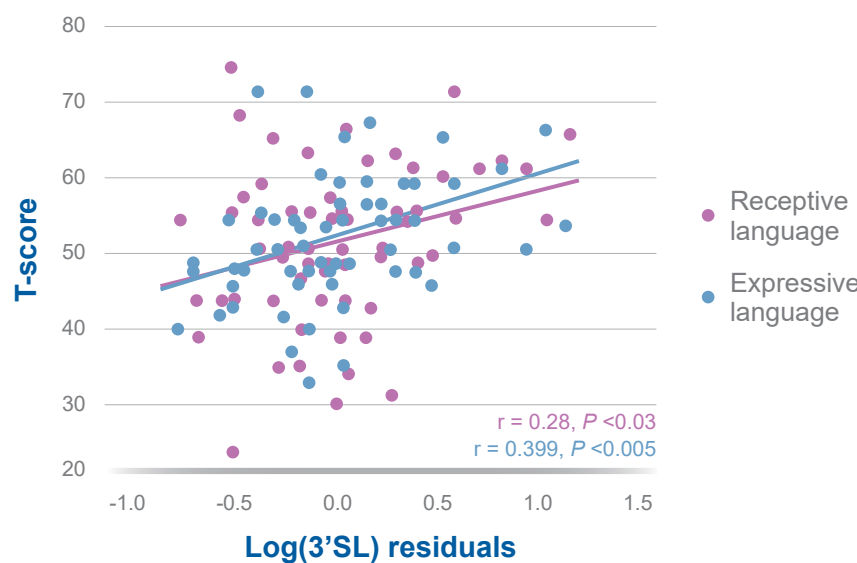
Observational studies show associations between HMO composition of human milk and cognitive development in breastfed infants^{38,39}

Higher exposure to 2'FL at 1 month results in a higher cognitive development score at 24 months of age^{38,*}



*While the assessment was done at both 1 and 6 months, the link was only observed at 1 month, but not at 6 months.

Levels of 3'SL are positively associated with receptive and expressive language scores^{39,†}



†This association between human milk 3'SL and language was observed in the subset of infants whose mothers' milk contained detectable A-Tetra HMO.

Preclinical data provide insight into the functional role of HMOs in brain and cognitive functions



3'SL and 6'SL improve executive functions and learning⁴⁰⁻⁴²



3'SL and 6'SL enrich ganglioside sialic acid (important for brain development^{4,43}) in the brain and modulate the gut microbiota⁴⁴



2'FL increases long-term potentiation and learning^{45,46}

Abbreviations: HMO = Human milk oligosaccharide; Glc = Glucose; Gal = Galactose; Neu5Ac = Sialic acid (N-acetyl-neuraminic acid); GlcNAc = N-acetyl-glucosamine; Fuc = Fucose; 2'FL = 2'-fucosyllactose; 3'SL = 3'-sialyllactose; 6'SL = 6'-sialyllactose.

References: 1. Cheng L, et al. *Crit Rev Food Sci Nutr.* 2021;61(7):1184-200. 2. Bode L. *Nutr Rev.* 2009;67(Suppl 2):S183-91. 3. Zivkovic AM, et al. *Proc Natl Acad Sci U S A.* 2011;108(Suppl 1):4653-8. 4. Bode L. *Glycobiology.* 2012;22:1147-62. 5. Kunz C, et al. *Ann Rev Nutr.* 2000;20(1):699-722. 6. Bode L. *Early Hum Dev.* 2015;91(11):619-22. 7. Ayechu-Muruzabal V, et al. *Front Pediatr.* 2018;6:239. 8. Walsh C, et al. *J Funct Foods.* 2020;72:104052. 9. Bode L, et al. *Adv Nutr.* 2012;3(3):383S-91S. 10. Urashima T, et al. *Trends Glycosci Glycotechnol.* 2018;30(172):SE51-65. 11. Austin S, et al. *Nutrients.* 2016;8(6):346. 12. Sprenger N, et al. *PLoS One.* 2017;12(2):e0171814. 13. Samuel TM, et al. *Sci Rep.* 2019;9(1):1-10. 14. Austin S, et al. *Nutrients.* 2019;11(6):1282. 15. Lefebvre G, et al. *Front Nutr.* 2020;7:225. 16. Walsh C, et al. *J Funct Foods.* 2020;72:104074. 17. Cacho NT, et al. *Front Immunol.* 2017;8:584. 18. Wiciński M, et al. *Nutrients.* 2020;12(1):266. 19. Morrow AL, et al. *J Pediatr.* 2004;145:297-303. 20. Newburg DS, et al. *Glycobiology.* 2004;14(3):253-63. 21. Smith-Brown P, et al. *PLoS One.* 2016;11(9):e0161211. 22. Lewis ZT, et al. *Microbiome.* 2015;3:13. 23. Matsuki T, et al. *Nat Commun.* 2016;7:11939. 24. Ruiz-Moyano S, et al. *Appl Environ Microbiol.* 2013;79(19):6040-9. 25. Thongaram T, et al. *J Dairy Sci.* 2017;100(10):7825-33. 26. Yu ZT, et al. *Glycobiology.* 2013;23(11):1281-92. 27. Rochat F, et al. HMO usage by infant gut bacteria seems strain and HMO-structure specific. In: *6th WCPGHAN.* June 3-6, 2020; Copenhagen, Denmark. 28. Rochat F, et al. Impact of HMOs on toddler microbiota and its activity. Abstract accepted at: 6th WCPGHAN. June 3-6, 2020; Copenhagen, Denmark. 29. Berger B, et al. *mBio.* 2020;11(2):e03196-19. 30. Angeloni S, et al. *Glycobiology.* 2005;15(1):31-41. 31. Natividad JM, et al. *Nutrients.* 2020;12(10):3047. 32. Puccio G, et al. *J Pediatr Gastroenterol Nutr.* 2017;64(4):624-31. 33. Newburg DS, et al. *J Thromb Thrombolysis.* 2016;42(1):46-55. 34. Duska-McEwen G, et al. *Food Sci Nutr.* 2014;5:1387-98. 35. Castillo-Courtade L, et al. *Allergy.* 2015;70(9):1091-102. 36. Kim J, et al. *Infect Immun.* 2018;87(1):e00694-18. 37. Goehring C, et al. *J Nutr.* 2016;146(12):2559-66. 38. Berger PK, et al. *PLoS One.* 2020;15(2):e0228323. 39. Cho S, et al. Abstract 2090. In: *6th WCPGHAN.* June 3-6, 2020; Copenhagen, Denmark. 40. Hauser J, et al. Paper presented at: 6th WCPGHAN. June 3-6, 2020; Copenhagen, Denmark. 41. Oliveros E, et al. *Nutrients.* 2018;10(10):1519. 42. Hauser J, et al. Abstract presented at: ESPGHAN 52nd Annual Meeting. June 5-8, 2019; Glasgow, Scotland. 43. ten Bruggencate SJ, et al. *Nutr Rev.* 2014;72(6):377-89. 44. Jacobi SK, et al. *J Nutr.* 2016;146(2):200-8. 45. Vazquez E, et al. *PLoS One.* 2016;11(11):e0166070. 46. Vazquez E, et al. *J Nutr Biochem.* 2015;26(5):455-65.