**Human Milk Oligosaccharides and the Infant Gut Microbiome**

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**Key Messages**

- Human milk oligosaccharides (HMOs) are diverse, biologically active components that beneficially modulate the infant microbiota as well as gut, immune, and potentially neurological development. It is now possible to produce large quantities of HMOs enabling supplementation to infant formula, with the goal of supporting the gut microbiota composition and developmental outcomes more similar to that of the breastfed infant.

- Factors Influencing Microbial Colonization

  - Infant gut colonization begins prenatally, continues during the first 2–3 years of life, and is essential for the gastrointestinal, metabolic, neural, and immune development of the infant [1]. Genetic and environmental factors, including mode of delivery, antibiotic use, and diet, shape the colonization process [1, 2]. The gut microbiota of breast- and formula-fed infants differ [3, 4] due, in part, to the high concentrations of human milk oligosaccharides (HMOs) in human milk, which are absent in infant formulas [4].

- HMOs Shape the Infant Microbiota

  - HMOs are resistant to digestion and influence the composition of the infant gut microbiome in several ways: by serving as prebiotics, by acting as substrates for fermentation to short-chain fatty acids, and by reducing pathogens (Fig. 1) [3, 4]. The gut microbiota of breastfed infants is typically dominated by bifidobacterial species, with a unique enrichment of *Bifidobacterium longum* spp. infants or *B. infantis* [2, 5]. Most bifidobacterial species that grow on HMOs only metabolize one of the predomi-nant HMOs, namely lacto-N-tetraose, whereas *B. infantis* grows well on several HMOs [6]. Genome sequencing identified that *B. infantis* is unique in that it contains all of the oligosaccharide transport proteins and enzymes needed to transport intact HMOs into the cell, where it is broken down internally [7]. In contrast, other bifidobacteria [8] and Bacteroides species [9] have the enzymes that break down the HMOs on their outer cell membrane and then transport the products into the cell for metabolism [7, 8]. If the HMO is hydrolyzed outside the cell, then other bacteria have access to these sugar compounds, which is referred to as cross-feeding [8]. Indeed, different HMOs in milk are both positively and negatively correlated with a number of bacteria in the stool of breastfed infants. Thus, HMOs have broad effects on shaping the infant microbiome, and it is possible to identify which HMO types are prebiotics for specific bacteria in the infant’s stool [2, 10].

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**References**


