Human Milk Oligosaccharides and the Mucosal Immune System

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Key Messages
Human milk oligosaccharides promote the mucosal immune protection through the microbiota and mucosal immune system.

Breastmilk is the recommended and presumed evolutionary adapted nutrition for term-born healthy infants. Numerous meta-analyses showed that breastfeeding for longer periods results in decreased risks primarily for infections, but also for diabetes and overweight, while its effect on allergies is less clear [1]. Among the breastmilk components implicated in immune protection are human milk oligosaccharides (HMOs) [2]. HMOs are elongations of the milk sugar lactose with combinations of galactose, N-acetylgalactosamine, fucose, and/or sialic acid. These elongations are structurally similar to glycans exposed on secreted mucins and cell surfaces in the form of glycolipids and glycoproteins. Cell surface glycans stabilize and modulate receptor functions commonly through the interaction with glycan-binding proteins and, due to their dominant, luminal exposure, are often primary docking sites for pathogens. The similarity of HMOs with mucin and cell surface glycans suggests that HMOs interfere with glycan-mediated processes that affect (i) the establishment of commensals, (ii) the adherence of pathogens, and (iii) mucosal cell reactivity (fig. 1).

In the intestinal epithelium, enterocytes, enteroendocrine cells, and the chemosensory Tuft cells are candidate signal transducers to the mucosal immune system. In model systems, HMOs stimulate enterocyte maturation and immune reactivity resulting in improved immune protection [3, 4]. Similarly, HMO exposure of immature human intestinal tissue shifts gene expression profiles towards immune maturation and reduced response to inflammatory stimulation [5]. About 1% of ingested HMOs reach the systemic circulation and are excreted in urine, indicating that HMOs may also directly affect mucosal immune cells lying beyond the epithelial layer. Indeed, HMOs were shown to modulate proliferation, reactivity, and migration of isolated mononuclear cells [6–8]. For such effects, a strong HMO structure-function relation is often observed, meaning that not all HMOs or other oligosaccharides act in the same way. Taken together, an HMO-modulated intestinal environment including both the mucosal immune system and intestinal microbiota might explain at least partly the immune protection provided by prolonged breastfeeding and the proposed link between HMOs and reduced infectious diarrhea [9], lower respiratory tract infection and antibiotic use [10], and delayed onset of allergic eczema in C-section born infants [11].

References

Fig. 1. Illustration on how HMOs shape the intestinal environment through their effect on commensals, pathogens, and the mucosal immune system from the epithelium to the underlying immune cells. Arrows indicate ‘activation’ and bar-headed lines indicate ‘inhibition’.