

Human milk oligosaccharides and selfish (or not selfish) *Bifidobacterium* strains

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Human milk is a rich source of components that contribute to shaping the infant gut microbiota through a variety of mechanisms. After lactose and lipids, human milk oligosaccharides (HMOs; Fig. 1) are the third most abundant components of human milk. One litre of mature human milk contains 5–20 g of these complex sugars, which often exceeds the amount of all human milk proteins combined. Oligosaccharide concentrations in colostrum are even higher [1]. To date, the molecular structures of more than 100 different HMOs have been characterized, but it is important to note that total amount and composition are highly variable between different women. In other words, not every infant who

receives human milk is exposed to the same set of HMOs with respect to total amount and structural composition. In fact, a recent cross-sectional, observational study revealed that the HMO composition of the milk of healthy women varies geographically. However, maternal genetic and environmental factors that determine HMO composition are not yet completely understood.

Once ingested, HMOs resist the low pH in the infant’s stomach as well as digestion by pancreatic and brush border enzymes. HMOs thus reach the distal small intestine and colon in an intact form, where they are available to help shape microbial communities and host–microbe interactions.

As they are not a source of calories for the host, HMOs are considered natural prebiotic compounds because they actively stimulate the growth of specific members of the infant gut microbiota. Therefore, HMOs are often considered ‘bifidogenic’, since they specifically enhance the growth of bifidobacteria, although it should be noted that only certain bifidobacterial taxa efficiently use HMOs as a sole carbon source. HMO utilization is conserved within the *Bifidobacterium longum* subsp. *infantis* lineage.

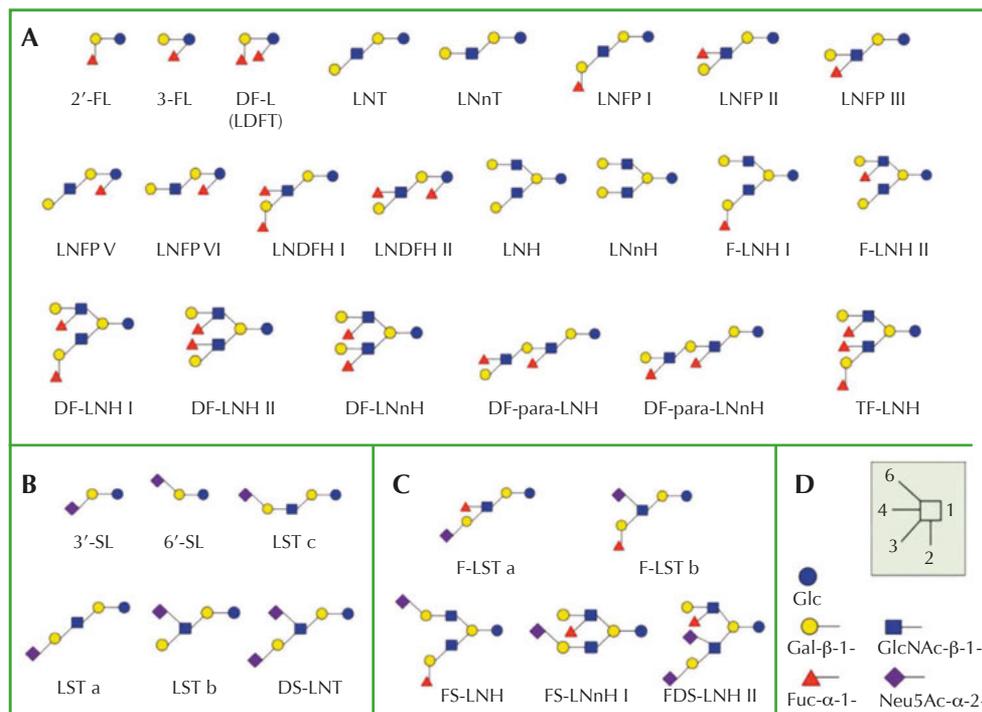


Figure 1 - Based on their chemical properties and the presence of fucose, human milk oligosaccharides can be divided into three groups: (A) neutral, (B) acid with no fucose, and (C) acid with fucose. Monomers are shown in panel D. Image from: Thurl S, Munzert M, Boehm G, Matthews C, Stahl B (2017) Systematic review of the concentrations of oligosaccharides in human milk. *Nutr Rev* 75(11):920–933

Bifidobacteria that are associated with an adult microbiota, such as *Bifidobacterium adolescentis*, are unable to use the HMO core structures. Thus, it is important to note that the 'bifidogenic' effect of HMOs is rather specific and favours *B. longum* subsp. *infantis*, and to some extent a few other infant-associated bifidobacterial, but not all bifidobacteria alike.

It is noteworthy that *B. infantis* (e.g., strain ATCC 15697) [2] is endowed with 'selfish' behaviour: it uses the products of complete HMO digestion for itself but does not share them with other components of the microbiota. In contrast, *B. bifidum* (e.g., strain PRL2010) [3] shares the products obtained by HMO digestion with other elements of the microbiota. As a direct consequence, experimentally the presence of *B. infantis* in the gut microbiota reduces its richness (alpha diversity) while the presence of strain PRL2010 increases it.

Conflict of interest

Francesco Di Pierro is the owner of Velleja Research.

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