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Spotlight

Human milk oligosaccharides and *Bifidobacterium* species

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Several bacterial species initially colonise the infant gut, but are outcompeted. Human milk oligosaccharides (HMOs) in breast milk create an environment for *Bifidobacterium* to flourish. Laursen and Roager recently showed a clear link between breast milk and the dominance of *Bifidobacterium longum subsp. infantis* in the infant gut.

The development of a healthy adult gut microbiota is strongly linked to the health and composition of the infant gut microbiota, which is shaped by several factors (Figure 1). One of these factors is whether or not a baby is breast/chest fed [1]. Laursen and Roager show a clear link between breast milk and the dominance of *Bifidobacterium longum* subsp. *infantis* in the infant gut environment [2]. However, some infants had an alternative composition of *Bifidobacterium* species, which indicates that the question of dominance or perseverance in this initial chaotic environment lies in the metabolic capacity of primary colonisers for breast milk glycans. Subsequent mouse studies explore the priority effects in a more controlled way by pitching *B. longum* subsp. *infantis* against *B. longum* subsp. *longum.*

In their report, Laursen and Roager monitored the infant gut microbiota of 16 breast-fed infants for the first 6 months of their lives. These infants were vaginally born at term and not exposed to antibiotics. The authors observed that, in the first samples, the microbial composition was very different – during the first month after birth, samples from different infants showed that strains of *Bifidobacterium breve*, *Bifidobacterium bifidum*, *Bifidobacterium catenulatum*, *Clostridium* spp, and *Escherichia coli* could all dominate initially in different infants. The sources of these initial colonisers likely vary in their origins – sometimes coming from the mother (vaginal, skin, oral, or faecal) or from the environment. After this initial phase, *B. longum* subsp. *infantis* became the most dominant bacterial species in the majority of infants (11 of 16) and this took effect between 14 and 100 days after birth. This indicates that breast milk has a strong selective influence specifically for *B. longum* subsp. *infantis*, which eclipses any priority effects the initial colonisers have. A low abundance of this species of *Bifidobacterium* has also been highlighted as a potential warning sign for the development of necrotising enterocolitis in preterm infants [3]. Furthermore, infants with severe acute malnourishment treated with *B. longum* subsp. *infantis* showed an increase in weight gain and a decrease in inflammatory markers [4].

Laursen and Roager were also able to correlate the rise in *B. longum* subsp. *infantis* with a decrease in faecal levels of fucosylated and sialylated lactose glycans. *B. longum* subsp. *infantis* has been shown to grow on the most abundant human milk oligosaccharides (HMOs) and sialic acid [5,6]. It is also likely that some *B. longum* subsp. *infantis* strains have additional colonisation factors, such as N-glycan degradation, which contribute to displacing any pioneering species/strains [4].

Interestingly, the final sample for one infant was included in the study – despite the child switching to formula – and showed a bacterial composition that echoes findings from similar previous studies. The first sample from this infant on day 30 was predominantly *B. bifidum*, but between days 45 and 172 *B. longum* subsp. *infantis* was the dominant species. The sample on day 192 represents the situation after switching to formula, and the composition was predominantly *B. longum* subsp. *longum* and *B. breve.* This jump from *B. longum* subsp. *infantis* to *B. longum* subsp. *longum* has also been observed previously with the start of weaning [7]. HMOs are difficult and expensive to synthesise, so manufacturers of infant formula largely use plant-derived galacto- and fructo-oligosaccharides instead. This, therefore, selects for *B. longum* subsp. *longum* over other strains of *Bifidobacterium* due to its capacity to degrade these glycans, and these infants have different gut microbial compositions compared with breast-fed infants.

There were a few alternatives to the *B. longum* subsp. *infantis*-dominated gut microbiota for 5 out of the 16 infants. For instance, *B. longum* subsp. *longum* dominated in one, and a mix of mostly *B. breve* with some *B. bifidum* dominated in another. These very interesting alternatives suggest that these strains together have the same glycan-degrading capacity as *B. longum* subsp. *Infantis*, and their capacity to colonise the infant gut could not be outcompeted by a *B. longum* subsp. *infantis* strain. An alternative explanation is that the particular strains of *B. longum* subsp. *infantis* in these infants did not have the same metabolic capacity as strains found in other infants where this species dominated. Cross-feeding of 3′-sialyllactose and mucin has been observed between *B. breve* and *B. bifidum*, where the latter has cell-surface-localised sialidases to remove sialic acid from these substrates. *B. breve* can use the sialic acid as a carbon source, whereas *B. bifidum* can continue processing the underlying glycans and use those monosaccharides as a carbon source [8]. Cross-feeding of HMOs has also been observed between *Bifidobacterium* species isolated from individual infants [9].

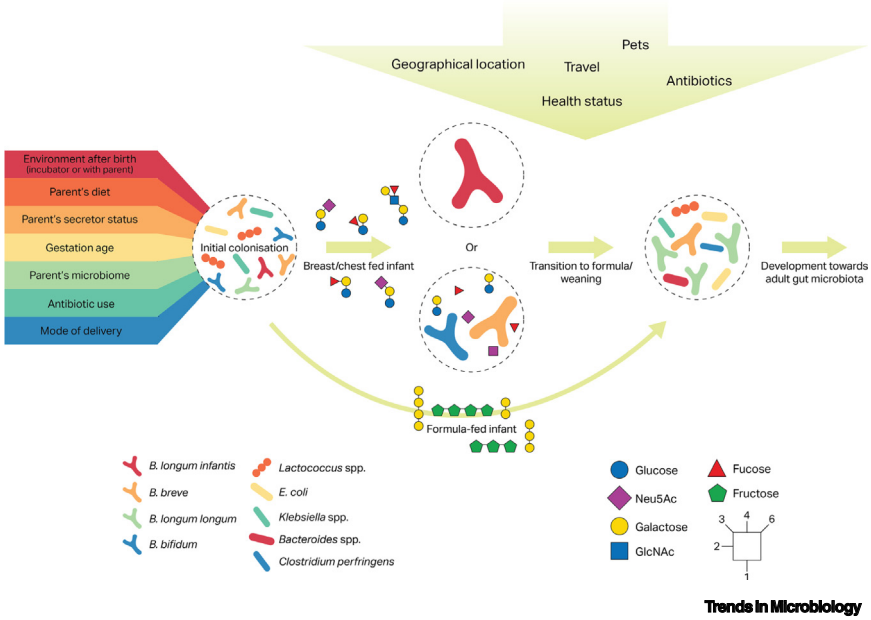

Figure 1. Early gut microbial composition is influenced by many factors. The environment that a child is born into is particularly influential – for example, whether a child was born vaginally or by caesarean section, and whether the infant can be with their parent or has to be in an incubator. Furthermore, the mother's health, microbiota, and diet also influence this. After this stage, the nutrition of the infant has a huge influence on what microbes proliferate. In particular, the glycans in human milk provide a strong selective pressure for species of *Bifidobacterium*. By comparison, formula contains plant-derived oligosaccharides which provide a selection pressure for more adult-associated bacterial species. Abbreviations: *B. bifidum, Bifidobacterium bifidum; B. breve, Bifidobacterium breve; B. longum infantis, Bifidobacterium longum subsp. infantis; B. longum longum, Bifidobacterium longum subsp. longum; E. coli, Escherichia coli; GlcNAc, N-acetylglucosamine.*

In mice, the authors were able to demonstrate that *B. longum* subsp. *infantis* could outcompete the pioneer coloniser, *B. longum* subsp. *longum*, to become the dominant species if HMOs were provided in the drinking water. This displacement was not possible without this supplement – and also not possible the other way around, with *B. longum* subsp. *longum* as the pioneering coloniser with or without the supplement. This result really highlights the power that HMOs have to shape the composition of an infant's gut microbiome.

There is also the societal approach to allowing more infants access to breastmilk. Breastfeeding can be a difficult experience, especially in public, and this is an international problem [10]. Hopefully, future generations of parents will not have the same levels of stigmatisation around breast/chest feeding that previous generations have experienced in some cultures. Scientific progress will be part of the solution, but promoting a greater respect for the needs of parents and children through changes in attitude will also contribute greatly to getting more babies more of these vital glycans. Greater access and financial support for breast milk banks would also be a huge benefit to families where breast feeding is not possible, and for premature babies in particular.

Declaration of interests

No interests are declared.

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