B. infantis Colonization Creates A Protective Environment In The Infant Gut

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The Infant Gut Microbiome

The gut microbiome plays an active role in human immune function, metabolism and neurological processes, and the composition of the gut microbiota is a factor in overall health or disease. The infant gut microbiome plays a particularly important role in human health, as it is directly involved in early immune programming and metabolic function.[1] The organisms that comprise the infant gut microbiome are initially acquired at birth, and differ dramatically depending on birth mode and infant diet.[2,3] Vaginally delivered infants are exposed to maternal vaginal and colonic microbes, allowing for rapid colonization of *Bifidobacterium* and *Bacteroides* in the breastfed infant. However, infants delivered by Cesarean-section are not exposed to the same maternal microbes as vaginally delivered infants, and are instead rapidly colonized with bacteria commonly found on the skin and the environment such as *Escherichia*, *Staphylococcus*, *Streptococcus* and *Clostridium*. This C-section associated gut dysbiosis has been linked to both acute and chronic disorders, such as colic, eczema, asthma, allergy, obesity and T1D.[4]

In addition to birth mode, infant diet plays a significant role in shaping the infant gut microbiome, as breastmilk is known to contain specific carbohydrates, called human milk oligosaccharides (HMO), that are indigestible by the infant and instead serve as food for gut microbes. The ability to metabolize HMOs differs among bacterial species, and the infant-adapted *Bifidobacterium longum* subsp. *infantis* (*B. infantis*) has been well documented to provide maximum utilization of HMO.[5] Alternatively, infant formula does not provide an equivalent food for the gut microbiota, and therefore does not support the colonization of known protective gut microbes found in the breastfed infant.[6]

Protective Effects of *B. infantis* Colonization

When *B. infantis* colonizes the infant gut during the first months of life, dramatic beneficial effects are observed in both the microbiome composition as well as intestinal biochemistry. As described above, *B. infantis* is uniquely adapted to metabolize HMO, and in turn, prevents the loss of this breastmilk component through fecal excretion. In a recent clinical study, breastfed infants who were colonized with *B. infantis* showed a 10-fold reduction in fecal excretion of HMO compared to breastfed infants who were lacking *B. infantis*.[7] This reduction in HMO excretion was further associated with improved stooling patterns, where *B. infantis* colonized infants showed significantly fewer loose, watery stools compared to controls infants.[8] The metabolism of HMO by *B. infantis* in the infant gut leads to a subsequent production of lactate and acetate, which serve as fuel for the colonocytes as well as reduce the pH of the intestinal environment, inhibiting growth of potential gut pathogens such as *Escherichia coli* and *Clostridium difficile*.[9]

In fact, in a recent clinical study breastfed infants fed *B. infantis* EVC001 (commercially available as Evivo®) showed a **93% reduction in potentially pathogenic bacteria**, along with an **85% reduction in pathogen associated virulence factors**, compared to breastfed controls.[10] Taken together, colonization of *B. infantis* in the infant gut is thought to create a protective environment, reducing the abundance and virulence of pathogenic bacteria and maximizing the utilization of breastmilk nutrients.

Restoring the Dysbiotic Infant Gut with *B. infantis*

Although the infant gut microbiome is expected to be colonized by *B. infantis* during the first months of life, modern medical and dietary practices such as C-section delivery, antibiotic use and formula feeding over the past century have disrupted the transfer of *B. infantis* from mother to infant at birth, and have led to a generational loss of *B. infantis* from the infant gut microbiome.[9] Clinical studies have now shown a marked increase in the abundance of potentially pathogenic bacteria in infants who are missing *B. infantis*, and this loss of a protective intestinal environment could have a profound impact on real time infection risk, as well as long term predisposition for auto-immune and inflammatory disorders later in life. Probiotic restoration of *B. infantis* to the infant gut microbiome has now been clinically demonstrated.[7] In this study, exclusively breastfed infants fed *B. infantis* EVC001 daily for 21 days showed stable and persistent *B. infantis* colonization throughout the supplementation period, as well as a full month after supplementation had ceased, as long as infants continued to consume breastmilk.

As we continue to better understand the critical role of the infant gut microbiome in establishing long term health trajectory, these data provide evidence that resolution of infant gut dysbiosis is possible, and stable restoration of *B. infantis* leads to significant and protective effects in the infant gut.

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