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Abstract Title:

Restoring the natural infant gut microbiome with B. infantis EVC001 significantly reduces intestinal inflammation

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Abstract Description:

Several seminal publications indicate Bifidobacterium longum subsp. infantis (B. infantis) has uniquely evolved to consume human milk oligosaccharides found in breast milk; however, recent studies indicate it is now far less abundant in infants born in industrialized nations. Therefore, setting the stage for increased abundance of potentially pathogenic bacteria and gut dysbiosis. Importantly, recent clinical studies show enteric dysbiosis during the first 100 days of life can lead to higher risk of allergic and autoimmune-mediated disorders later in life. Given the importance of the microbiome for immune system development, we investigated the effect of B. infantis EVC001 consumption on intestinal inflammation in a cohort of healthy, term infants. Forty (n=40) infants were randomly selected from the previously conducted clinical study in which healthy, exclusively breastfed infants were either fed B. infantis EVC001 daily for 21 days, starting at day 7 postpartum, or received breastmilk alone. Stool samples were collected at multiple times postnatally and analyzed for cytokine production using a multiplex system and calprotectin ELISA. Day 6 (pretreatment) fecal samples showed infants randomized to the EVC001 or control groups produced similar levels of cytokines (all adjusted P values > 0.05); however, by day 40, infants fed EVC001 produced significantly decreased cytokines, IL1□, IL8, IL22, TNF□ and IFN□ (all P < 0.01), and at day 60 postpartum IL1□, IL-6, IL-8, IL22, TNF□, and IFN□ were significantly decreased (all P < 0.01), which significantly correlated with Clostridiaceae and Enterobacteriaceae, and negatively correlated with Bifidobacteriaceae abundance. Fecal calprotectin concentration was significantly decreased in infants whose gut microbiome contained Bifidobacterium (P = 9.61e-05). This study is the first to demonstrate a significant impact of B. infantis EVC001 on immune homeostasis in breastfed infants during a critical window of immune system development. Infants fed B. infantis EVC001 produced significantly less proinflammatory cytokines and fecal calprotectin compared to

control infants. Notably, TNF□, IL1□, and IFN□, which increase intestinal permeability, were significantly elevated in control infants. This may play an important mechanistic role in explaining the chronic intestinal inflammation observed in infants not colonized with B. infantis. These critical data provide a new understanding of the role of the infant gut microbiome in immune system development and provide novel applications to address chronic inflammation through modulation of gut dysbiosis.