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How to Enrich Specific Taxa within the Gut Microbiome? Lessons from Human Milk

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Human milk contains numerous components that shape the microbial constituents of the gastrointestinal tract of infants. A prominent feature of milk is an array of oligosaccharides and glycoconjugates that are proposed to enrich a protective microbiota often dominated by bifidobacteria. Different infant-borne bifidobacteria contain specific glycosidases and transport systems required to utilize milk oligosaccharides and glycoconjugates. This suggests a co-evolutionary relationship between mammalian milk glycans, infant-borne bifidobacteria and the infant host enabling a programmed enrichment of a protective bifidobacterial-dominant community. However, two factors cloud this hypothesis. This enrichment could be driven by a “founder effect” given neonates do not have a significantly formed, or resilient, gut microbiome in early life. In addition, milk also contains numerous other effectors—such as lysozyme and lactoferrin among others—that modulate the infant gut microbiota. This makes it difficult to determine the proportional influence of milk oligosaccharides in the common bifidobacterial enrichment witnessed in humans. We have identified a number of select bifidobacterial strains that grow vigorously on specific milk oligosaccharides. Provision of wild type adult mice with both these strains and cognate milk oligosaccharides resulted in a dramatic, and persistent, enrichment of some strains to a level witnessed in human infants, albeit the effect was strain specific. The synbiotic enrichment also protected mice in a dextran sodium sulfate colitis murine model and resulted in a systemic lowering of inflammation. This work confirms that milk oligosaccharides are a driving factor in bifidobacterial enrichments in neonates and the synergy between oligosaccharides and specific bifidobacterial strains drives lower inflammation and protection. Moreover, this new model provides a path to decipher the specific genetic elements among bifidobacteria that contribute to both enrichment and protection. Further analysis of this naturally evolved system will shed light on effective pre- and probiotic tools that support a protective gut microbiota for at-risk infants and adults alike.