Sialic acid release by *Bacteroides thetaiotaomicron* from milk oligosaccharides may facilitate the growth of potentially pathogenic bacteria

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Abstract:

Human milk, as the sole nourishment food for infants, not only support infant's development but also highly influences the shaping of infant gut microbiota. Many members of the *Bacteroides*, common bacterial species in the gut, are able to utilize complex milk glycans by producing extracellular enzymes (neuraminidases and/or fucosidases) to cleave and release terminal monosaccharides such as sialic acid and fucose. In this study, we demonstrated that *Bacteroides thetaiotaomicron*, a common bacterium in the infant gut, secretes a neuraminidase that can release sialic acid from sialyated milk oligosaccharides (SMO). The experiment was performed in a minimal medium containing SMO as a sole carbons source. SMO profiling by Nano-Liquid chromatography-Chip-Quadrupole-Time-of-Flight mass spectrometry demonstrated a decrease of major SMO including 3-sialyllactose (3SL), 6-sialyllactose (6SL) and 3Hexose-1 *N*- acetylneuraminic acid after just a few hours of incubation. These results were further validated by measuring a concomitant free sialic acid increase in the medium, in concert with increased neuraminidase expression. *B. thetaiotaomicron* lacks the pathway to consume the cleaved terminal sialic acid monomers, it leaves the sialic acid in the environment, opening up the possibility for other bacterial species to consume it. To further investigate this hypothesis, we tested the ability of *Escherichia coli* to consume these free constituents (both SMO and free sialic acid) and found that while it was unable to consume complex milk oligosaccharides, it thrived on the free sugars released by *B. thetaiotaomicron*. In agreement with other studies, the ability of *Bacteroides* to release sialic acid may facilitate the growth of pathogenic bacteria that can consume sialic acid as a carbon source, but lack of ability to produce glycosidases to hydrolyze milk oligosaccharides on their own. In turn, this may lead to promote the inflammation in neonates.