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Title:

Harnessing Human Milk Oligosaccharides to Combat Group B *Streptococcus*

Abstract:

Group B *Streptococcus* (GBS) is a bacterium ubiquitous in human health that acts as both commensal and pathogen. While adults are often passively colonized with GBS, infants are particularly susceptible to invasive GBS infection and resultantly the transmission of GBS from adults to infants presents a significant risk for preterm birth and other adverse pregnancy outcomes. This heightened burden of GBS infection on neonatal health makes it of prime interest for the continued discovery and development of new antibiotics and therapeutic strategies. We have identified that the complex sugars found in breast milk, human milk oligosaccharides (HMOs), have pronounced antibacterial and antibiofilm properties against GBS. Furthermore, HMOs can be leveraged as adjuvants to increase antibiotic potency, as well as reverse antifolate antibiotic resistance within GBS. To enable further target identification studies, we have also synthesized a representative suite of bioorthogonal HMO tool molecules. Taken together, this work has developed tools and therapeutic strategies for harnessing HMOs to combat neonatal GBS infection.