EXPLORING THE MOLECULAR RECOGNITION OF MUCIN O-GLYCANS BY *SALMONELLA* SIIE ADHESIN

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Mucin O-glycan domains play a key role in the gastrointestinal tract, acting as recognition sites for bacterial adhesins. While they normally protect against pathogens, some bacteria, like *Salmonella*, use mucin O-glycans for adherence and invasion [1]. This poses a significant public health issue, especially with the rise of antibiotic-resistant strains. Understanding how *Salmonella* interacts with mucin O-glycans is critical for developing anti-adhesion strategies [1].
This research investigates the interaction between *Salmonella* and host cells, focusing on the role of the non-fibrillar SiiE adhesin in targeting Mucin-1 (MUC1) via sialic acid-containing O-glycans [2]. Understanding the specificity and molecular interactions of SiiE with mucin O-glycans is crucial for developing new anti-adhesion molecules to combat bacterial resistance. Our approach combines advanced techniques, including glycan microarrays, mucin cell-based arrays, and Nuclear Magnetic Resonance (NMR) spectroscopy, providing both high-throughput screening and detailed insights into molecular structure and dynamics. This methodology is key to revealing the molecular specificity of SiiE and advancing the development of innovative therapies against Salmonella infections.

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References:
1. T. Rehman et al., Microb. Pathog. 2019, 137, 103748.
2. Li, X. et al. PLoS Pathog. 2019, 15, e1007566