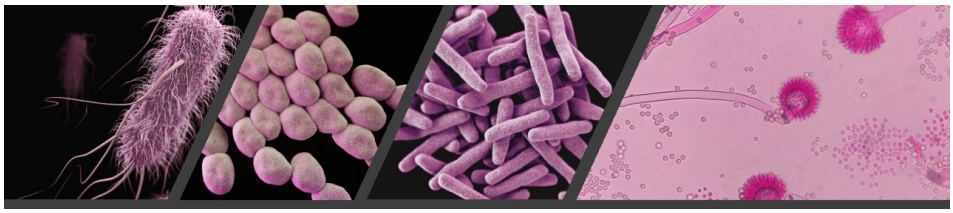

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Genetic Diversity and Lewis Antigen Status Shape Intestinal Mucus O-Glycome: A Network Perspective in TLR5-Deficient Pig Model

Friday 12 September 2025 15:00 (15 minutes)

Dissecting intestinal homeostasis requires understanding subtle interactions between host genetics, innate immunity, and the microbiota before overt disease occurs. Using genetically diverse pigs, we mapped O-glycan structures in intestinal mucus under non-induced conditions, integrating these with transcriptomic and microbiota data. Porous graphitized carbon LC-MS/MS identified ~140 distinct O-glycans across gut regions, revealing that Lewis antigen status—particularly $Le^{a/x}$ vs. $Le^{b/y}$—dominates glycan diversity, often outweighing TLR5 deficiency. Transcriptomic data showed Lewis antigen profiles and TLR5 functionality jointly shape glycosylation enzyme expression and immune signatures, indicating a bidirectional interplay between immune sensing and epithelial glycan remodeling. Microbiota changes were subtle but genotype-dependent, with specific taxa enriched in $Le^{a/x}$ animals. Combined analysis of FUT2/3 expression, a MUC13 SNP, and TLR5 deficiency revealed complex, location-specific microbial shifts, especially in the colon. These findings demonstrate that glycomics can be scaled to network-level resolution, underscoring the importance of host genetic variation in maintaining mucus barrier integrity and microbial balance, a key to preventing chronic gut disorders.

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