CHARACTERIZATION OF CARBOHYDRATE METABOLISM IN

CAMPYLOBACTER JEJUNI

by

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ABSTRACT

Previously considered asaccharolytic, it is now known that 65% of sequenced *Campylobacter jejuni* isolates possess the *fuc* operon encoding enzymes for L-fucose and D-arabinose catabolism. *C. jejuni* 11168, a *fuc+* strain, outcompetes its fucose permease mutant in colonizing a piglet model for diarrheal disease. Transfer of the *fuc* locus into a *fuc-* strain (*C. jejuni* 81-176) enables 81-176 to metabolize and swim to L-fucose and D-arabinose, suggesting that a *fuc* product is responsible for coordinating fucose detection and chemotaxis. Mutagenesis studies of the *fuc* genes suggest that a dehydrogenase coordinates carbohydrate metabolism and chemotaxis, and that the protein alone is responsible for this phenotype since transfer of the single protein into 81-176 also confers chemotaxis. A model has been established for L-fucose and D-arabinose metabolism based on growth experiments of metabolic mutants, homology comparisons to known enzymes, and NMR studies to detect metabolic products.

Fucosylated human milk oligosaccharides (HMOs) are generally considered protective against *C. jejuni* infections by serving as binding decoys; however, 16S sequencing of stool samples from children in low-to-middle-income countries (LMICs) revealed high *Campylobacter* burdens in breastfed infants. Yet there appears to be a selection against *fuc+* strains, suggesting that HMOs are preferentially bound by *fuc+* strains and thus act as decoys, but in turn allow *fuc-* strains to

proliferate. RNAseq experiments were done in order to compare the transcriptomes of 11168 and 81-176 in the presence of human breastmilk. Additionally, binding studies with liquid glycan arrays reveal 11168 binds more oligosaccharides than 81-176 and we await sequencing results to determine the carbohydrate binding preferences of these strains. Overall this work characterizes a *C. jejuni* carbohydrate metabolic pathway and identifies its involvement in chemotaxis. There is also evidence that the microbiota plays a role in L-fucose foraging by *C. jejuni* to obtain L-fucose and and that sugar-metabolizing strains may possess a different repertoire of carbohydrate adhesins that impact *C. jejuni* colonization in the gastrointestinal tract during human infections. Future work will further elucidate the role of breastfeeding in *C. jejuni* infections by examining RNAseq data and verifying that differences in metabolic and binding activities identified in the two model laboratory strains extends to the laboratory collection of human isolates from LMICs.