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Biochemical and functional analysis of modified heptoses from the capsule of *Campylobacter jejuni*

Campylobacter jejuni is a human bacterial pathogen that is a predominant cause of enteritis worldwide. Its capsule is an external polysaccharide layer important for colonization and virulence. In most strains, the capsule comprises a modified heptose whose biological roles and biosynthetic pathways are unknown. We deciphered the biosynthesis pathways for 6-deoxy-D-alto-heptose of strain 81-176 and 3,6-OMe-L-gluco-heptose of strain NCTC 11168. This allowed a direct comparison of novel C3/C5 epimerases and C4 reductases involved in these pathways. Overall, we determined the activity of 7 enzymes, revealing unexpected functions and specificities, as well as complex regulatory loops. Knockout mutagenesis studies of heptose modifying genes in strain NCTC 11168 showed that heptose modification is not necessary for capsule synthesis but affects bacterial resistance to serum and bile salts, biofilm formation, adhesion to intestinal epithelial cells and their invasion. The mutants also showed slightly decreased phagocytosis by macrophages but no defect for survival inside macrophages. We also demonstrate that heptose modifying genes are important for colonization and persistence of *C. jejuni* within the chicken intestine. Together, these findings suggest that fine tuning the capsule composition via heptose modification contributes to host pathogen interactions. This work, combining functional and biochemical data, provides grounds for the elucidation of similar pathways found in other *C. jejuni* strains, other *Campylobacter* and other pathogens. It provides new molecular tools for the synthesis of carbohydrate antigens useful for vaccination and for the screening of enzymatic inhibitors that may have antibacterial effects and could be used to decrease Campylobacteriosis.

Biography

Carole Creuzenet has completed her PhD in Biochemistry from the University of Nantes and the National Institute for Agronomical Research (France) and Postdoctoral studies from the Massachusetts Institute of Technology, USA and the University of Guelph, Canada. She is an Associate Professor at the University of Western Ontario (London, Canada) where her lab focuses on the synthesis and function of glycans found in glycolipids and glycoproteins of bacterial gastrointestinal pathogens such as *Campylobacter jejuni*, *Helicobacter pylori* and *Yersinia pseudotuberculosis*. She has published 38 papers in reputed journals including 28 in the field of glycobiology.

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