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**CAPSULAR HEPTOSE SYNTHESIS
PATHWAY OF *CAMPYLOBACTER JEJUNI*
AS A NEW TARGET TO PREVENT
CAMPYLOBACTERIOSIS**

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C*ampylobacter jejuni* (CJ) is a commensal in poultry but is also a human bacterial pathogen. It is a predominant cause of bacterial enteritis worldwide and, in developed countries, campylobacteriosis is associated with consumption of undercooked poultry meat that had been contaminated by CJ during slaughter. CJ's capsule is an external polysaccharide important for colonization and virulence that comprises a modified heptose in most strains. We investigate the biological roles and the biosynthetic pathways of these heptoses with a view to inhibit their synthesis in poultry before slaughter, which would decrease the CJ load in poultry meat and prevent harmful transmission to humans. We deciphered the activity of seven enzymes involved in modified heptoses synthesis in two CJ strains, revealing unexpected functions and specificities of novel C3/C5 epimerases and C4 reductases that could be targeted for inhibition. 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. Most importantly, we also demonstrate that heptose modifying genes are important for colonization and persistence of *C. jejuni* in chicken. These findings suggest that fine tuning the capsule composition via heptose modification contributes to host pathogen interactions and likely host specificity. This work also provides new enzyme targets to screen for inhibitors that could be used to decrease campylobacteriosis by application to chickens pre-slaughter. It also provides new tools to synthesize carbohydrate antigens useful for chicken vaccination and provides grounds for the elucidation of similar pathways of other pathogens.

BIOGRAPHY

Carole Creuzenet has completed her PhD in Biochemistry at the University of Nantes and the National Institute for Agronomical Research (France) and her postdoctoral studies at the Massachusetts Institute of Technology (USA) and the University of Guelph (Canada). She is Associate Professor at the University of Western Ontario (London, Canada) where her lab focuses on virulence factors from bacterial gastrointestinal pathogens such as *Campylobacter jejuni*, *Helicobacter pylori* and *Yersinia pseudotuberculosis*. Her focus is on glycolipids and glycoproteins as well as on novel secreted proteins and their folding partners. She has published 38 papers in reputed journals with h-index of 19.

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