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Role of capsular modified heptose in the virulence of *Campylobacter jejuni*

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Summary

The *Campylobacter jejuni* capsular polysaccharide is important for virulence and often contains a modified heptose. In strain ATCC 700819 (a.k.a. NCTC 11168), the modified heptose branches off from the capsular backbone and is directly exposed to the environment. We reported previously that the enzymes encoded by *wcaG*, *mlghB* and *mlghC* are involved in heptose modification. Here, we show that inactivation of any of these genes leads to production of capsule lacking modified heptose and alters the transcription of other capsule modification genes differentially. Inactivation of *mlghB* or *mlghC*, but not of *wcaG*, decreased susceptibility to bile salts and abrogated invasion of intestinal cells. All mutants showed increased sensitivity to serum killing, especially *wcaG::cat*, and had defects in

Introduction

Campylobacter jejuni infections are the leading cause of enteritis worldwide (Wassenaar and Blaser, 1999; Rautelin and Hanninen, 2000). Infected patients can also develop neurological complications such as Guillain–Barre and Miller Fischer syndromes (Godschalk *et al.*, 2004; 2007). Numerous factors contribute to pathogenicity of *C. jejuni* and successful host colonization, including production of toxins and glycoproteins (Szymanski *et al.*, 2002; Karlyshev *et al.*, 2004; Guerry *et al.*, 2006; Kakuda and DiRita, 2006; Vijayakumar *et al.*, 2006) and resistance to bile salts (Lin *et al.*, 2003; 2005). Flagella-mediated motility also contributes to the virulence of *C. jejuni* (Biswas *et al.*, 2007), as it facilitates colonization of the mucus layer covering the intestinal epithelium (Lee *et al.*, 1986; Beery *et al.*, 1988) and subsequent invasion of epithelial cells (Pei and Blaser, 1993; Jin *et al.*, 2001; Konkel *et al.*, 2005; Vijayakumar *et al.*, 2006). Survival of *C. jejuni* within macrophages for several days is also a key virulence factor (Kiehlbauch *et al.*, 1985; Day *et al.*, 2000), and epithelial and macrophage cell damage resulting from invasion may be critical for the inflammatory response elicited by *C. jejuni* infection (Manninen *et al.*, 1982; Newell and Pearson, 1984; Newell *et al.*, 1985; Fauchere *et al.*, 1986; Szymanski *et al.*, 1995; Biswas *et al.*, 2000). Further, the surface expression of lipooligosaccharide (LOS), which in many *C. jejuni* strains mimics human gangliosides, has been associated with autoimmune reactions implicated in the Guillain–Barre and Miller Fischer syndromes (Michu