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, mligB and mligC 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 mligB or mligC, 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 (Godschaik 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; Querry et al., 2006; Kakuda and DiRita, 2006; Vijayakumar et al., 2006) and resistance to bile salts (Jin 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 mucous 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 (Kleihauer 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. (Kleihauer,