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The *Campylobacter jejuni* glycome ☆

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Abstract

Microbial cell surface glycans in the form of glycolipids and glycoproteins frequently play important roles in cell–cell interaction and host immune responses. Given the likely importance of these surface structures in the survival and pathogenesis of *Campylobacter jejuni*, a concerted effort has been made to characterise these determinants genetically and structurally since the genome was sequenced in 2000. We review the considerable progress made in characterising the *Campylobacter* glycome including the lipooligosaccharide (LOS), the capsule and *O*- and *N*-linked protein glycosylation systems, and speculate on the roles played by glycan surface structures in the life-cycle of *C. jejuni.*

Keywords: *Campylobacter jejuni*; Glycome; Lipooligosaccharide; Capsule; Glycosylated flagellin; *N*-linked glycosylation system

Contents

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1. Introduction

The Gram-negative bacterium *Campylobacter jejuni* is the principal bacterial cause of human gastroenteritis world-wide [1]. *C. jejuni* is also the most frequent antecedent infection responsible for the post-infectious peripheral neuropathy Guillain-Barré syndrome, which is thought to be triggered by mimicry with surface exposed carbohydrate structures. The main source of transmission is through the consumption of livestock, particularly poultry where invariably flocks are heavily contaminated with up to 10^9 *Campylobacter*, yet are asymptomatic. By contrast as few as 10^2 cells is sufficient to cause severe disease in humans. Given the medical and public health importance of *Campylobacter* infection, it is remarkable that *C. jejuni* is one of the least understood enteropathogens. The lack of understanding of how the organism causes disease was the driving force for the instigation of the *C. jejuni* NCTC 11168 genome sequencing project that was completed in 2000 [2].

The sequencing of NCTC 11168 revealed a previously unexpected capacity for the organism to produce a variety of carbohydrates [2]. Subsequent analyses have demonstrated the presence of several cell surface glycoconjugates such as a novel capsule and *N*-linked glycosylation pathway, as well as providing rich data on the lipooligosaccharide (LOS) and the *O*-linked glycosylation system that decorates the flagellum (Fig. 1). A striking feature from the genome project was the presence of several hypervariable homopolymeric repeats responsible for slipped-strand mispairing and phase variation in glycan moieties present in LOS, capsule and flagella [2]. Further studies have shown that the loci responsible for the biosynthesis of these molecules are highly variable among different strains [3–7]. This is in contrast to the *N*-linked general glycosylation pathway that appears highly conserved, even among some other *Campylobacter* species [12]. Recent studies have allowed the detailed structural analysis of the glycan components of the glycolipids and glycoproteins [9], which has facilitated studies to determine gene function in the respective biosynthetic pathways [10,11]. This review will summarise the post genome genetic and structural studies on the *C. jejuni* glycolipids (LOS and capsule) and the *O*- and *N*-linked glycosylation pathways. Because there have been two recent reviews on the *Campylobacter* glycosylation systems [10,12], the emphasis on this current review will be on *Campylobacter* LOS and capsule. We will also speculate on the possible biological roles of these structural surface determinants and why some appear to be hypervariable.

2. Lipooligosaccharide (LOS)

Forming an integral part of the cell, lipid A substituted polysaccharide (PS) forms an essential cell surface structure as part of the outer leaflet of the outer membrane lipid bilayer. In addition to maintaining the structural integrity of the bacterium via a barrier function to substances entering or leaving the cell, modulation of the attached PS provides a strategy for avoidance of the host immune system. In most gram negative bacteria, lipid A is substituted with a core PS to which is attached a set of repeating subunits termed the O-chain; this structure is termed lipopolysaccharide (LPS). How-

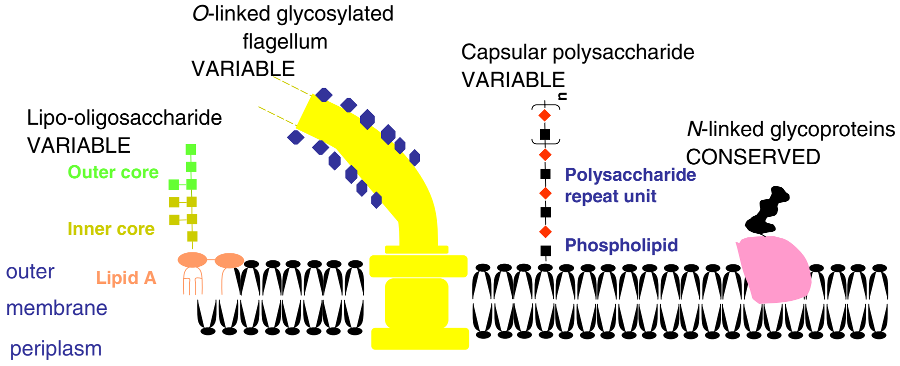

Fig. 1. The known glycolipids and glycoproteins in *C. jejuni*.