Capsular polysaccharide conformations of meningococcal serogroups W and Y

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The bacterium *Neisseria meningitides* is a causative agent of meningitis, meningococcemia, and septicemia with an estimate of over 1 million cases and 100,000 deaths annually. *N. meningitides*, is known to consist of 12 clinically significant serogroups, based on the organism's capsular polysaccharide (CPS), although only 6 groups (A, B, C, W, Y and X) have been found to be responsible for nearly all such disease.[1] The polysaccharide capsule is the main virulence factor of *N. meningitides* and the target of both conjugate and polysaccharide meningitis vaccines developed to date.

Similar polysaccharide antigen structures may elicit similar immune responses and thus provide cross protection against disease caused by related strains. Previous studies have shown that conformational analyses of oligosaccharide fragments for bacterial CPS repeat units can provide insight into vaccine cross protection between serotypes.[2] We are currently undertaking a systematic and incremental computational approach to explore the conformations of the CPS repeat units of *N. meningitides* serogroups W and Y (Figure 1).

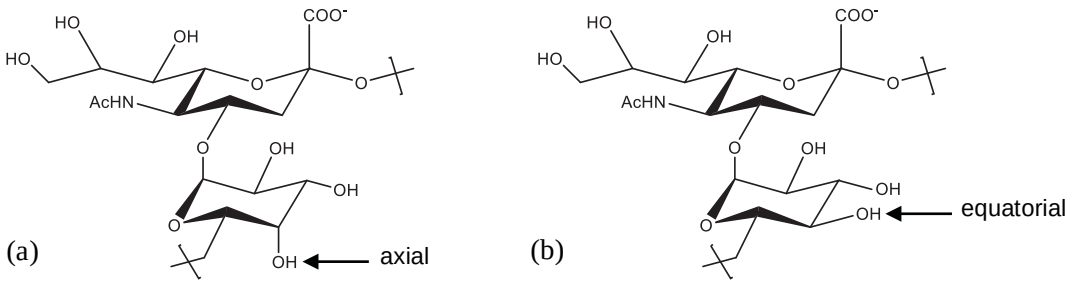

Figure 1: The de-O-acetylated capsular polysaccharide repeating unit structures of N. meningitides serogroups W (a) and Y (b).

Oligosaccharide conformation is primarily determined by orientations of the glycosidic linkages. As such, potential of mean force calculations were performed in aqueous solution to identify low energy conformations of the isolated 1→4 glycosidic linkage by rotation around the φ and ψ dihedral angles. Due to the comparative flexibility of the 2→6 linkage extended molecular dynamic (MD) simulations were conducted to obtain its preferred isolated disaccharide structure. We are currently performing MD simulations of the three repeat unit oligosaccharides in solution to investigate a conformational rationale for how a subtle structural variation between serogroups W and Y confers a difference in immunogenicity.

Keywords

Meningococcal, meningitis, capsular polysaccharide, molecular dynamics

References

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