Using Molecular Modelling to Rationalise Cross-Reactivity in the Development of Multivalent Vaccines

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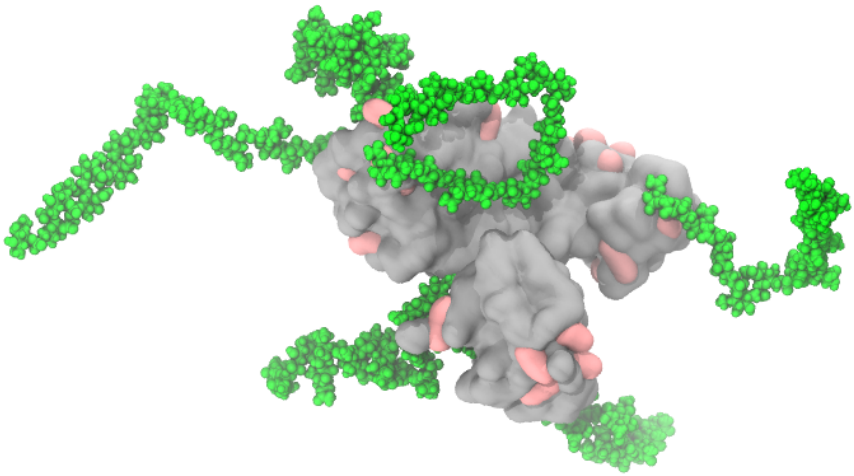
Licensed conjugate vaccines have demonstrated efficacy in preventing bacterial disease caused by *Haemophilus influenzae* type b (Hib), *Neisseria meningitidis* (Nm) and *Streptococcus pneumoniae* (Sp). The presence of multiple and emerging strains of bacteria has required the development of costly multivalent vaccines unless the antigens present elicit an immune response that provides cross-protection against infection by non-vaccine serotypes or serogroups. However, cross-protection is hard to predict, as structural similarity between carbohydrate antigens has not proven to be a reliable indicator of cross-protection. Over a series of studies, we have demonstrated that molecular modelling of structurally similar bacterial carbohydrate antigens can provide a mechanistic rationale for the existence (or absence) of cross-protection between them and thus may usefully inform the development of conjugate vaccines and further our understanding of carbohydrate immunogenicity.

The case studies comprise molecular modeling of the capsular polysaccharides for meningococcal serogroups (B and C, Y and W, A and X), key pneumococcal serotypes within serogroups 6, 15, 19 and 23 and *Haemophilus influenzae* (types a and b). Conformation as well as identification of key epitopes in the antigens, such as terminal residues and substituents, may aid in broadening vaccine coverage.



A model of CRM197 protein conjugated to 5 chains of Neisseria meningitidis serogroup A polysaccharide antigen

Bibliographic references:
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