Structural studies to guide glycoconjugate vaccine design

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Glycoconjugate vaccines are an important and successful means for prevention of infectious disease, including pneumoniae, meningitidis and salmonellosis. Understanding at atomic level the binding between microbial carbohydrates and specific functional monoclonal antibodies can direct vaccine design, particularly when synthetic carbohydrates are used. Recently we have applied structural studies to identify the minimal epitope of group B *Streptococcus* type III polysaccharide. (GBS PSIII) is a leading cause of invasive infections in pregnant women, newborns, and elderly people, and the capsule is a major virulence factor targeted for vaccine development [1]. GBS PSIII epitope has been historically considered the prototype of a complex conformational carbohydrate epitope [2]. Through an integrated approach based on competitive ELISA/Surface Plasmon Resonance/Saturation Transfer NMR/X-ray we elucidated a structural epitope consisting of a hexasaccharide constituted of a single repeating unit, and the glucosamine moiety of the next consecutive repeat unit [3]. Based on this data a conjugate vaccine from the short hexasaccharide epitope was prepared and elicited in mice functional antibodies comparably to a polysaccharide conjugate [4]. Likewise, structural studies carried out for serotypes Ia and Ib showed that the polymeric nature of the polysaccharide can strongly impact epitope presentation [5].

A similar approach allowed also to map the structural epitope of *Neisseria meningitidis* serogroup A and X, which are responsible for epidemic meningitis in the sub-Saharan region of Africa, known as meningitis belt [6],[7]. Studies are ongoing to gain this type of information also on structurally similar sialylated W and Y polysaccharides. Structural data can be exploited to guide synthetic carbohydrate vaccine design [8].

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