Semi-synthetic O25B-CRM197 conjugate vaccines give rise to functional antibodies in murine model

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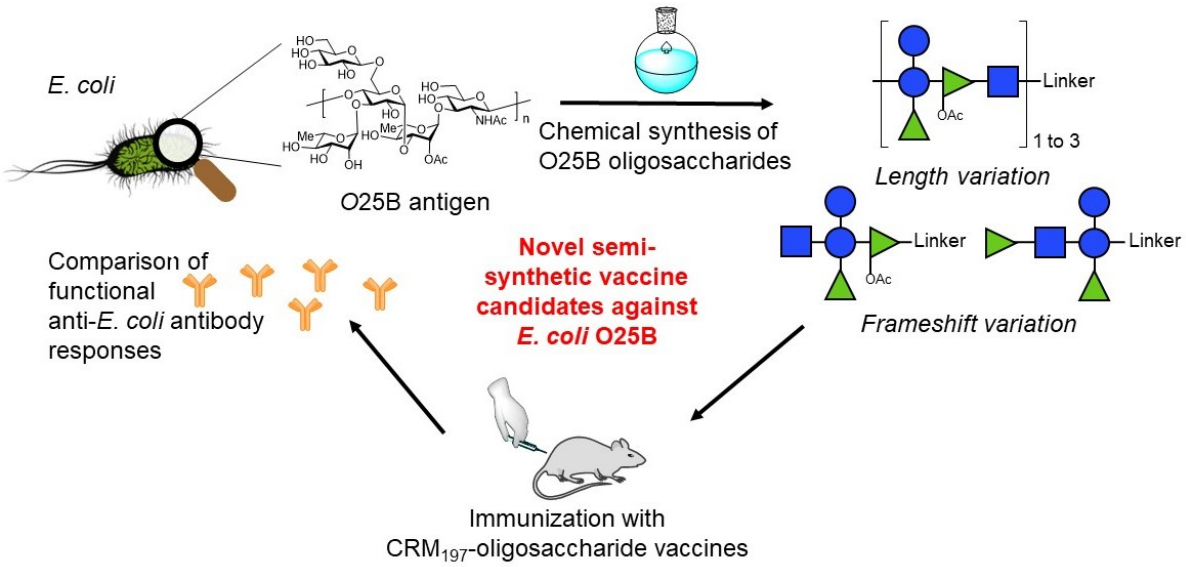
Pathogenic, multidrug resistant *E.Coli* strains causing enteric/diarrheal, urinary tract infections, sepsis and meningitis are of increasing concern worldwide. A major serotype of extraintestinal pathogenic *E.Coli* (ExPEC) is O25B, expressing an unique *O*-antigen consisting of a branched five monosaccharide repeating unit. The chemical synthesis of five fragments of various length or frameshift oligosaccharides gave access to a set of well-defined semi-synthetic glycoconjugate vaccine candidates targeting the *O*-antigen of *E.Coli* O25B serotype. The semi-synthetic glycoconjugate vaccines induced similar levels of functional IgG antibodies with opsonophagocytic activity against *E.Coli*O25B in mice as the conventional polysaccharide vaccine candidate prepared with native O25B *O*-antigen. Furthermore, it was shown that our synthetic O25B antigens can give rise to antibodies with nanomolar affinity. Moreover, we found that acetylation of a rhamnose residue as it occurs in the natural polysaccharide most likely does not influence the immunogenicity of the antigens as also our deacylated antigen elicited a strong functional IgG response. Overall, the direct comparison of the immunogenicity of a glycoconjugate vaccine prepared with isolated *O*-antigen to those prepared with chemically synthesized *O*-antigens allows a more comprehensive analysis of the binding epitopes and lays foundation for rationally designed chemically synthesized oligosaccharide-based vaccines.



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