ID: 21334

GLYCOCALIXARENES DECORATED WITH STREPTOCOCCUS PNEUMONIAE 19F CAPSULAR POLYSACCHARIDE FRAGMENTS BIND TO ANTI-19F ANTIBODIES

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Capsular polysaccharides (CPS) of encapsulated bacteria have been recognized as critical determinants of bacterial virulence and found to be able to stimulate protective immunity against infection disease, laying the bases for the development of current antibacterial vaccines. CPSs are cell-surface polymers consisting of oligosaccharide repeating units. High molecular mass repetitive polysaccharide structures are able to display simultaneously a greater number of densely displayed epitopes capable to effectively interact in a clustered form with specific antibodies. The study of the chemical determinants necessary for an effective interaction still requires detailed molecular insights. Nanomaterials or multivalent scaffolds loaded with carbohydrate antigens allow repetitive antigen display, and are emerging as promising synthetic vaccine candidates, alternative to classic polysaccharide/protein conjugate vaccines. In this framework, we have decided to explore the potential of calixarenes as scaffolds for the multipresentation of bacterial CPS fragments related to Streptococcus pneumoniae serotype 19F (SP19F). The hypothesis was to assess if such scaffolds, presenting a limited number of copies of short SP19F fragments, displayed in a multivalent form, are able to gain affinities and potencies towards the natural antibodies similar to those observed for the natural polysaccharide. Herein, we will report the preparation and biological evaluation of a family of calixarenes functionalized with saccharide fragments related to the trisaccharide repeating unit of SP19F. In particular, a calix[6]arene, functionalized with six copies of the trisaccharide repeating unit of SP19F, resulted very effective in competing with natural 19F polysaccharide in the binding to specific anti-19F antibody. This compound shows efficacies and affinities higher than those exhibited by the single trisaccharide, thus evidencing the effect of multivalency in increasing the ability of the single saccharide unit to compete with natural 19F polysaccharide in the binding to specific anti-19F antibody.