ChemForum

Centro de Química Estrutural

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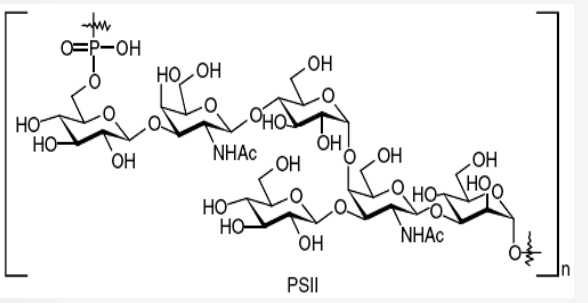
"Carbohydrate-based anti-diarrheal vaccines"



Our research efforts focus on the discovery and use of microbial-specific polysaccharides to control gastric bacterial infections in humans. Two of our main targets are *Clostridium difficile* (antibiotic associated diarrhea) and *Campylobacter jejuni* (traveller's diarrhea).

Our We discovered that *C. difficile* and *C. jejuni* produce distinctive cell-wall polysaccharides that when integrated into conjugate vaccines were capable of eliciting antibodies that prevented the disease in animal models.

C. difficile ribotypes have been found to expose a common polysaccharide (named PS-II) composed of hexasaccharide phosphate repeating blocks. After its discovery, PS-II quickly attracted the attention of many researchers as a *C. difficile* vaccine target. In our hands, a PS-II conjugate vaccine protected mice and hamsters challenged with *C. difficile* spores.

In the case of *C. jejuni,* a multivalent approach was needed, as each serotype complex expressed a specific polysaccharide. The prototype *C. jejuni* polysaccharide-based vaccine was shown to fully protect against *C. jejuni* diarrhea in a monkey model. Recently, we have discovered that certain regions of *C. jejuni* polysaccharides containing methyl phosphoramidate (MeOPN) linkages are highly immunogenic. Antibodies against a MeOPN-glycan synthetic construct reacted with the surface of *C. jejuni* and were found to have bactericidal activity. Preliminary data from a phase 1 human clinical trial has demonstrated safety in humans.

Lastly, the generation of an exciting multivalent anti-diarrheal vaccine composed of *C. jejuni/Shigella* carbohydrates and *E. coli* proteins will also be discussed.