Exploring the dual role of proteins as carrier and protective antigen in glycoconjugate vaccines

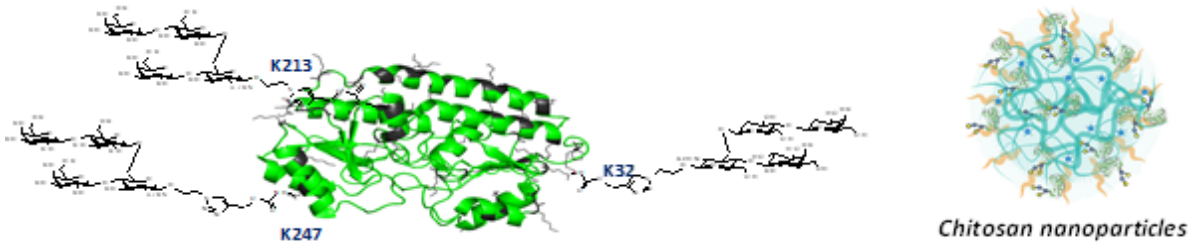
Cyrille GRANDJEAN [1], Maruthi PRASANNA [1,2], Typhaine VIOLO [1], Annie LAMBERT [1], Aline PILLOT [1], Amina FATEH [1], Laura LANEQUE [1], Ruben VARELA [3], Noemi CSABA [2], Emilie CAMBERLEIN [1]

[1] Nantes Université, CNRS, Unité en Sciences Biologiques et Biotechnologies, UMR 6286, Nantes, FRANCE, [2] Center for Research in Molecular Medicine and Chronic Diseases, University of Santiago de Compostela, SPAIN [3] Department of Biochemistry and Molecular Biology, University of Santiago de Compostela, SPAIN

cyrille.grandjean@univ-nantes.fr

Bacterial capsular glycoconjugate vaccines have proven efficient, well tolerated and safe in humans including young children and immune-compromised population.[1] Current licensed glycoconjugate vaccines are made of poly/oligosaccharides conjugated to a carrier protein which triggers a T-cell dependant immune response to the glycan owing to the activation of the T-helper cells. However, to date only a handful of carrier proteins has been validated for use in humans, a situation which raises concerns regarding pre-exposure or co-exposure to a given carrier which can lead to immune interference and reduction of the anti-carbohydrate immune response.[2] Thus, it is tempting to explore the dual role of proteins from the pathogen against which we want to develop a vaccine as carrier and protective antigen to circumvent this issue. According to this strategy, is it possible to mount a protective humoral response against both B peptide epitopes of the protein and carbohydrate antigen which compete for the same limited number of T-helper epitopes?

Considering pneumococcal infection as a model disease, we studied structure/immunogenicity relationships of a panel of glycoconjugates obtained by random[3] or controlled conjugation. In the latter case, site selective mutagenesis or unnatural amino acid incorporation was applied to prepare homogeneous glycoconjugates.[4] We also demonstrate that glycoconjugate encapsulation into chitosan nanoparticles can improve humoral response by several order of magnitudes compared to glycoconjugate administered alone.[5]



Homogeneous pneumococcal glycoconjugate (left); nanoparticle glycoconjugate vaccine (right)

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