OPTIMIZING CONJUGATION OF PATHOGEN ASSOCIATED PROTEINS FOR NOVEL GLYCOCONJUGATE VACCINES

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Increasing resistance to antibiotics renders the development of vaccines against the main pathogens involved on this silent pandemic an urgency [1]. Glycoconjugate vaccines are well established tools to prevent bacterial infections and can play a pivotal role in combating antimicrobial resistance (AMR) [2].
The articulated escape mechanisms of some antimicrobial resistant bacteria will require complex vaccine formulations for the prevention of infections from AMR pathogens. Use of proteins as carrier and antigens can support targeting multiple pathogenic mechanisms and simplify the vaccine composition.
Recently, methods for site-selective glycoconjugation have emerged, enabling to control the directionality of the conjugation step and to better preserve protein epitopes. Novel vaccine candidates based on these technologies are advancing at clinical level [2].
Carbohydrate to protein ratio, number of linked glycan moieties and directionality of the conjugation are important interconnected parameters to be considered in vaccine design.
Herein, we conceived a conjugate vaccine to target simultaneously two AMR pathogens by designing a multimeric fusion of two cytotoxins, Hla and PcrV, two potent cytotoxins from S. aureus and P. aeruginosa, respectively. A conjugation strategy based on selective targeting of a histidine tag introduced on purpose, was developed to preserve the structure and antigenicity of epitopes from the two proteins, leveraging their dual role as carrier and antigen. By comparing in animal models multimeric constructs obtained through site selective and random conjugation, we identified a lead candidate with a single attachment site inducing a robust immune response against the protein and the glycan component. These findings can guide the future design of site selective glycoconjugate vaccines.

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