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EDITORIAL

Glycoconjugate vaccines: classic and novel approaches

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Abstract

Glycoconjugate vaccines, obtained by carbohydrates covalently bound to protein carriers, have contributed to fight diseases such as meningitidis, pneumonia and typhoid fever. Despite new technologies such as RNA and adenovirus based vaccine have now reached the market, these approaches are unable to target carbohydrates which are key virulence factors.

This issue intends to provide an overview on relevant directions where the field is evolving and serve as starting point to increase interest in this exciting and fundamental part of vaccinology.

Keywords Glycoconjugates · Carbohydrates · Vaccines

Glycoconjugate vaccines are playing worldwide a major role in the prevention of infectious diseases with terrible impact on health. Today, licensed glycoconjugate vaccines are available against *Haemophilus influenzae*; meningococcus serogroups A, C, and ACWY; 10 to 13 serotypes of pneumococcus; and Salmonella typhi. These type of vaccines have demonstrated a huge impact on global infant mortality and morbidity by combating some of the historical plagues of mankind, such as meningitidis, pneumonia and typhoid fever (Rappuoli R., *Sci. Transl. Med*. 2018, 10, eaat4615).

Cost effectiveness of glycoconjugate vaccines is now well known: PCV13, the multivalent pneumococcal conjugate vaccine is a best seller and impact has recently become clear also in low-middle income countries with successful introduction of meningococcal vaccination campaigns in Africa through a program funded by PATH (*Program for Appropriate Technology in Health*).

In the current Covid-19 era, new emerging technologies such as RNA, adenovirus and other viral particle based vaccines have reached the market and will revolutionize the way vaccines are conceived, tested and produced.

However, these technologies cannot target sugars which remain a biologically relevant class of surface exposed biomolecules. New vaccines targeting O-antigens are in clinical trials for *Shigella flexneri* 2a (Cohen D. et al. *Lancet Infect. Dis.* 2020 https://doi.org/10.1016/S1473–3099(20)30488–6) and Extra Intestinal Pathogenic *E. coli* (Frenck RW et al. *Lancet Infect. Dis.* 2019, 19, 631–40) and will help to extend the clinical feasibility to different classes of bacterial carbohydrates. Recently a Phase I trial where *E. coli* expressed capsular antigens from *Staphylococcus aureus* conjugated to pathogen specific proteins has started (https://clinicaltrials.gov/ct2/show/NCT04420221?term=s+aureus+vaccine&draw=2&rank=5).

Meaningfully, these vaccines are based on novel technologies, such as synthetic carbohydrates and in vivo glycoprotein expression, named also bioconjugation, underpinning how innovation is enabling the development of new vaccines against challenging targets.

In addition, constant monitoring of serotype distribution is needed also for available vaccines which generates the need for unceasing improvement of existing formulations (Oildale N. et al. *Lancet Infect. Dis.* 2020; 21: 137–47).

The efficaciousness of glycoconjugate vaccine depends on a series of features related to the sugar and protein components, like the sugar nature, the conjugation chemistry, the protein carrier and the type of connectivity between the glycan and protein components. This drives efforts not only in developing new manufacturing processes but also analytical tools for adequate characterization of the final products.

This journal issue, which is dedicated to the memory of Paolo Costantino, who recently passed away, leaving a profound heritage in the field, aims at connecting new classic approaches for glycoconjugate preparation combining reports from innovative in silico prediction tools, advanced methodologies for sugar

This article belongs to the Topical Collection: Glycoconjugate vaccines: classic and novel approaches

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production, new conjugation methodologies both chemical and biological, identification of novel nanoparticle carriers.

Our expectation is that the selection of articles will offer an overview on relevant directions where the field is evolving and serve as starting point to increase interest in this exciting and fundamental part of vaccinology.

Declarations

Conflict of interest RA is an employee of GSK group of companies.