Synthesis of oligosaccharide libraries from GBS capsular polysaccharides for structure-based selection of vaccine candidates

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Propositions

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1. It is remarkable that, the success of glycoconjugate vaccines has not led to the elucidation of their mechanism of action (Rappuoli, R. *Sci Transl Med*, 2018, 10).

2. Establishig the minimal epitope of carbohydrate antigens is essential for the development of optimal synthetic vaccines (Adamo, R. *Accounts Chem Res*, 2017, 50, 1270-1279).

3. Research into new (chemo-enzymatic) synthesis methods and new carrier proteins is more important for the development of synthetic glycoconjugate vaccines than searching for new conjugation chemistries. (Avci F, *et al*., *mSphere*, 2019, 4:e00520-19).

4. Structural studies, such as SPR, glycoarray, STD-NMR, X-ray crystallography and microscopy are indispensable to discover small carbohydrate antigens (Carboni, F. *et al*., *PNAS*, 2017, 114(19): 5017-5022).

5. Regioselective glycosylation methods are particularly appealing when applied as one of the last steps of glycan assembly (Chapters 3 and 7).

6. More attention should be paid to the conformation of oligo- and polysaccharides to uncover structural features which are fundamental for their biological functions. (Chapters 4, 5 and 6).

7. A difference in a single glycosidic linkage can have a huge impact on the chemical and biological properties of an oligosaccharide (Chapters 4 and 5).

8. Although structural studies into oligosaccharide antigen-antibody interactions provide great insight into the activity of carbohydrate antigens, in vivo studies are required to establish their real immunogenicity (Chapters 6 and 7).

9. The multivalent exposure of (sub-)optimal short oligosaccharide epitopes on a carrier can render it as active as the native polysaccharide. (Chapter 7, Carboni et al., *J Infect Dis*, 2020, 221(6): 943-947)

10. Care should be taken in trusting the scales used by most organic chemist to establish the -often small- quantity of final compound obtained for biological testing.

11. No matter how great the talent or the effort, some things just take time.

12. Everyone wants to live on top of the mountain, but happiness and growth are found while climbing it.