Synthetic studies of glycans and glycoconjugates for regulation of immune responses

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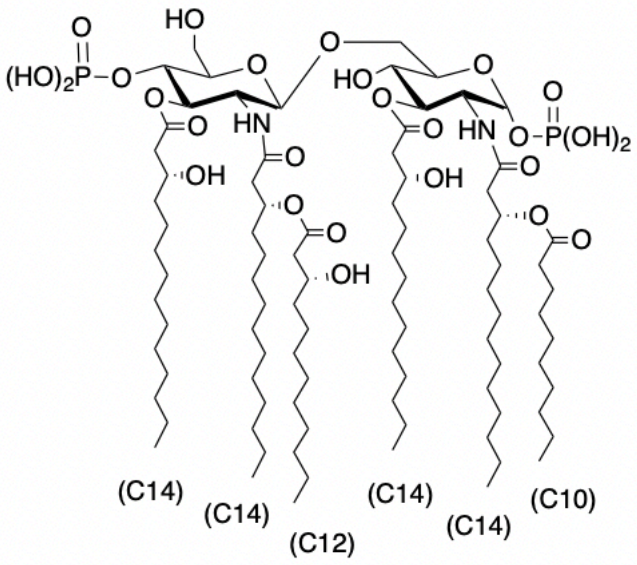
We have examined the synthesis of glycans in microbes and animals to determine the active components responsible for immunostimulatory activities, as well as their application in adjuvants and vaccines.

We have focused on developing new adjuvants using low-toxic LPS, derived from parasitic bacteria as well as the symbiotic Alcaligenes species found in the Peyer's patches, and have conducted synthesis and functional studies on its active constituent, lipid A. Our research has shown that lipid A from the symbiotic A. faecalis possesses mild immunostimulatory effects with low inflammatory properties, making it a promising candidate for a novel adjuvant.[1] Specifically, A. faecalis lipid A was found to activate both mucosal and systemic immunity, and intranasal vaccines containing this adjuvant demonstrated excellent protective effects against pathogens in a mouse model.

Furthermore, we describe the synthesis and biological activity of other low-inflammatory lipid A molecules such as Acetobacter lipid A and Campylobacter jejuni lipid A.

Self-adjuvanted vaccines, in which an antigen and an adjuvant are linked through covalent bonding or physical association, have emerged as a new strategy for vaccine development. We have prepared several self-adjuvanting vaccines that consist of an antigen, adjuvant, and T cell epitope as conjugated, liposomal, and viral capsid mimic vaccines.[2] Their efficacy in producing antibodies in mice with little inflammatory response demonstrates the potency of self-adjuvanted vaccines.



Alcaligenes faecalis lipid A

Bibliographic references:

[1] A. Shimoyama, et al. (2021), Angew. Chem. Int. Ed. Engl. (60) 10023-10031.

[2] Y. Manabe, K. Fukase, (2023), Methods Mol. Biol. (2613) 55-72.