From SF2a-TT15 to a synthetic glycan-based quadrivalent *Shigella* vaccine candidate

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The burden caused by shigellosis, a major diarrheal disease, calls for a *Shigella* vaccine that would induce broad serotype protection especially in children under five from low and middle income countries. Protective immunity is believed to be achieved to a large extent by antibodies specific for the O-antigen (O-Ag) part of the *Shigella* lipopolysaccharide. Aside the use of glycans of biological origin, vaccine candidates encompassing synthetic glycans mimicking the putative protective determinants carried by the O-Ag of selected *Shigella* serotypes was undertaken at Institut Pasteur.[1] SF2a-TT15, a semi-synthetic glycoconjugate designed to help protect against *S. flexneri* 2a[2] was well tolerated and immunogenic in healthy adult participants in a first-in-human phase 1 clinical trial.[3]

The concept of synthetic O-Ag functional mimics,[4] that serve as pillar of a vaccine candidate providing broad coverage against circulating *Shigella* strains, will be introduced. The design and optimization of monovalent glycoconjugates, combined to SF2a-TT15, pave the way to such a vaccine candidate.

Epitope mapping will underline the molecular features governing functional O-Ag mimicry by short well-defined glycans. The possible influence of chain length, end-chain residue and non-stoichiometric acetylation will be examined.

Immunogenicity data for various combinations of monovalent components will be discussed together with selection criteria to achieve a promising *Shigella* vaccine candidate featuring the best compromise between synthesis feasibility, conjugation chemistry and immunogenicity.

Bibliographic references:

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