On-resin synthesis of glycolipopeptides towards self-adjuvanting and multivalent vaccines

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Glycolipopeptides are promising scaffolds for self-adjuvanting vaccines.[1] The synthesis of these constructs is challenging due to the demanding chemistry required for fusing lipids, carbohydrates and peptides. Merging solid-phase approaches of peptides (SPPS)[2] and automated glycan assembly (AGA)[3] will enable the fully automated on-resin procedure for synthesizing *O*-linked glycopeptides. Combinations of both techniques have not been developed yet. The use of partially or fully pre-assembled glycosylated amino acids while elongating the peptide by SPPS [4] enhances epimerization. Coupling glycans to serine or threonine is limited, due to their intrinsic low reactivity and the occurrence of β-elimination. We describe a chemically optimized amino acid residue designed to overcome these drawbacks and allow for bidirectional assembly of peptides and glycans. Incorporation of unnatural amino acid is the basis for the synthesis of glycolipopeptides on solid support. Developing automated methods of the synthesis of chimeric biomolecules could lead to several applications in vaccine development and biomaterial design.

Bibliographic references:

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