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Synthesis of Glycopeptide and Glycoprotein Remodelling for Immunological Studies

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Abstract

Over the past few decades, immunologists have begun to try and develop vaccines against tumour cells. One of approach is targeting an endocytic receptor on antigen-presenting cells, which results in enhanced antigen cross-presentation. To date, there is no clear picture of the factors that are important in controlling antigen cross-presentation. The main aim of this project was to determine which structural parameters of the glycoprotein-antigen conjugate resulted in enhanced cross-presentation upon MR-ligation. Therefore, concerns the chemoenzymatic synthesis of defined glycopeptides and glycoproteins as chemical biology tools to help unravel the role(s) of the MR in antigen cross presentation.

Enzymatic degradation of locust bean gum provided a Manβ(1→4)Man disaccharide building block which in turn allowed the synthesis of N-glycan disaccharide and tetrasaccharide oxazolines. In addition, large N-glycan oligosaccharide oxazoline, $Man_9GlcNAc$-high mannose (from soybean) was accessed by semi-synthetic approaches. After this successful synthesis of N-glycans, Native glycoforms of immunological probe peptides were made by the use of ENGase enzymes (EndoA-N171A), which attached sugar oxazolines to a peptide ($OVA_{247\text{-}264A5K}$) containing a GlcNAc handle. Finally, glycoprotein remodelling of ovalbumin (OVA) was achieved with the N-glycan tetrasaccharide oxazoline donor using WT Endo A as catalyst. The synthesis of these glycopeptides and glycoproteins in homogenous form should facilitate future analysis to help define the pathway taken by an antigen after uptake by the MR.