

Targeting dendritic cells with glycosylated liposome-based vaccines for modulation of the immune system

Introduction: Glycans present on proteins and lipids (glycoproteins and glycolipids respectively) have an important role in the modulation of the immune system. In the context of cancer, specific glycans present on tumour cells induce immune tolerance, while in the context of auto immune diseases, other glycans can induce immune activation. We use these glycans to induce antigen specific tolerance or immunity by targeting dendritic cells (DCs) with liposomes covered in distinct glycans.

Methods: We construct antigen encapsulated liposomes with lipo-glycans structures that allow targeting to glycan binding receptors on DCs. These glycoliposomes also include TLR ligands for DC maturation purposes. We compare LewisY-liposomes and sialic-acid-liposomes that target DC-SIGN and Siglecs present on monocyte derived dendritic cells (moDCs) for the initiation of antigen-specific T cell responses, or oppositely, the induction of antigen-specific Treg cell-mediated tolerance. These glyco-liposomes are optimized in ex-vivo human skin model systems and in vivo mouse models for the induction/inhibition of antigen specific T cell responses in the context of anti-tumour effects or the dampening of autoimmune reactions. Alongside this line of research, we investigate whether the pre-influx of monocytes, that differentiate into moDCs, in the site of vaccination in the skin increase vaccine efficiency. Accumulation of moDCs at the site of injection, together with tissue resident DCs, may further boost DC based T cell responses. We identified specific adjuvants that are key in the mobilization of monocytes at the vaccination site. Mobilization of monocytes in situ after topical adjuvant administration is analysed with multiplex confocal microscopy in combination with histo-cytometry analysis.

Conclusion: We generate different DC-targeting glycosylated liposome-based vaccines as a platform, with immune stimulating or inhibiting functions, aimed to restore the immune system for treatment of cancer or autoimmune diseases.

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