Liposomal DNA vaccines – can we learn from nature?

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The application of liposomes as a drug delivery system is certainly not new, being first proposed by Gregoriadis in the early 70s. Since then, thousands of investigations into the application of these systems for the delivery of a range of moieties, from small molecules to large nucleic acid therapeutics have been undertaken. Due to their rather unique structure, which is composed of lipid bilayer membranes surrounding an inner aqueous core, liposomes can effectively encapsulate drugs either within their aqueous core, or within the bilayer regions, depending on their lipophilic natures. Alternatively, depending on their surface charge, drugs can also be electrostatically bound to their surface. Indeed, cationic lipids and cationic liposomes have been extensively used as gene delivery systems and more recently as vaccine adjuvants and whilst issues with biological recognition of cationic lipids can be a problem in gene therapy, for vaccination design this may be advantageous.

Within our research we have investigated cationic liposomes systems based on dimethyldioctadecylammonium bromide (DDA) and/or α,α'-trehalose 6,6'-dibehenate (TDB) as a delivery system for DNA and sub-unit antigens and considered the impact of formulation design on their efficacy to enhance immune responses has been measured. Overall, of the systems tested cationic liposome formulations incorporating TDB showed markedly increased antigen specific splenocyte proliferation and elicited cytokine production concomitant with a strong T cell driven response. The stability of these systems was dependent on the buffer used with the presence of some electrolytes having a marked detrimental effect on stability. In addition, we were looking at different immunisation regimens to evaluate the effect of heterologous DNA/subunit vaccine prime-boost strategy on promotion of immune responses. Our results show that presence of salt in the liposome formulation does not affect its biodistribution or immune response; however, incorporation of higher transition temperature lipids can provide longer retention of DNA at the site of injection. Immune study results also showed that the influence of prime-boost immunisation is not notable and subunit protein vaccines with no prime have a similar response in studied liposomes.