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Hyderabad, India***Dates:** Received: 03 July 2015; Accepted: 06 July, 2015; Published: 08 July, 2015***Corresponding author:** Syed Faisal, National Institute of Animal Biotechnology, 4th Floor Axis Clinical Building, Miyapur, Hyderabad, Telangana, 500049, India, Tel: +91-40-2304-9423; Fax: +91-40-2304-2740; E-mail: faisal@niab.org.inwww.peertechz.com**Editorial**

Liposome Adjuvants: Simultaneous Induction of Innate and Adaptive Immunity is Key to Success

availability of a variety of lipids and to accommodate different types of antigens/immunomodulators [2,6]. While liposomes have initially reached the market as drug carriers, their potential as potent vaccine adjuvants has been demonstrated against several diseases such as HIV [7] tuberculosis [8], malaria [9] and leishmaniasis [10] indicating that liposomal systems have promising future as vaccine adjuvant. Various liposome based products viz. hepatitis A vaccine have been licensed and some are in various phases of clinical trials [11,12].

Conventional liposomes (CL) find limited applications as they are inert or non-stimulatory (requires tagging with immunostimulants) and due to endocytic modes fail to deliver antigen to the cytosol for MHC I presentation and subsequent induction of a cytotoxic T cells (CTLs) response [13]. Several bacterial cell wall/membrane components or pathogen associated molecular patterns (PAMPs) have been widely exploited as immunopotentiators/ immunomodulators [14,15]. Liposomes composed of total polar lipids (TPL) isolated from various non-pathogenic and/or attenuated bacteria have shown to be very potent adjuvant/antigen delivery vehicles that can induce strong immune response correlating to significant level of protection against various infection in animal models [16-19]. These liposomes being immunostimulatory and fusogenic (IFL) were able to activate both innate and adaptive immune responses simultaneously. The simultaneous induction of both humoral and CMI by IFLs may due to their ability to be phagocytosed and target antigen to endosomes for MHCII presentation and fusion with APC to deliver antigen in cytosol for MHCI presentation leading to activation of CMI (Figure 1). Although much success has been shown by liposomes, the mechanism of their stimulating effect on innate immunity has been studied inadequately. In particular their global effects on gene transcription and the complex regulatory machinery in the cell that leads to enhanced immune responses are poorly understood. Liposomes are considered to be a sensitive adjuvant. Small changes in their properties (lipid composition, size, charge) lead to great differences in immune responses. Thus, availability of immunological profile of a liposome with a particular charge, size and lipid composition would enable rational retro-design of liposomal vaccine adjuvants. While the mechanism of most of the currently used adjuvants like alum, MF59, CpG are being explored by exploiting transcriptional gene profiling, only a few studies have reported the adjuvant mechanism of liposomes [20,21]. We have explored the adjuvant mechanism of immunostimulatory and fusogenic liposomes in mice by applying microarray-based transcriptional profiling. Our results have shown that injection of conventional (CL) or immunostimulatory/fusogenic liposomes (IFL) at mouse. Muscle or peritoneum induced distinct

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The current generation vaccines are mainly composed of highly purified antigens and tend to be poorly immunogenic, requiring potent adjuvants for their success. The adjuvants currently available suffer from various drawbacks such as low potency (inability to activate strong humoral and cell-mediated immune response) and extreme toxicity for routine clinical use in humans. In addition, not all adjuvants are effective for all antigens. The compromise between the requirement for strong adjuvant activity and an acceptable low level of toxicity has left us with limited choice of adjuvants. Although alum adjuvant has been used for decades, it is associated with severe local reaction and is unable to activate cell-mediated immunity, hence has proven unsuccessful against intracellular infections [1]. Therefore, it is very important to identify new adjuvants or improve the existing ones. The ideal adjuvant would be one that apart from activating strong humoral and cell-mediated immune response, has negligible toxicity to the host.

The success of traditional vaccines (killed and live attenuated) have been attributed to two features; their ability to stimulate innate immunity and ability to invade antigen presenting cells (APCs), thereby delivering antigen in cytosol for induction of adaptive immune response. The modern vaccines based on subunit antigens, although better defined and tend to be safer lack these two features resulting in their inability to activate strong immune response [2]. Therefore, these vaccines must include both immune potentiators and delivery systems as adjuvants for their success. Liposomes (lipid vesicles) seem to fulfill these criteria and have been widely studied as adjuvant/antigen delivery systems against various infections and have shown better performance than Freund's adjuvant or alum [3,4]. Liposomes can facilitate in vivo migration of antigens and deliver encapsulated antigen into cytosol of the antigen presenting cells for both cell-mediated as well as humoral immune responses [5]. The type and degree of immunogenicity enhancement by liposomes depends on its composition, size, charge and the type of antigens [6]. The success of Liposomes in enhancing the efficacy of subunit antigens is mainly due to protection (preventing degradation in vivo) enhanced targeting to professional APCs viz. macrophages and DCs, slow and controlled release of antigen (depot effect) leading to long lasting and sustained immune response, nontoxicity and biodegradability. The major advantage is in their versatility in the

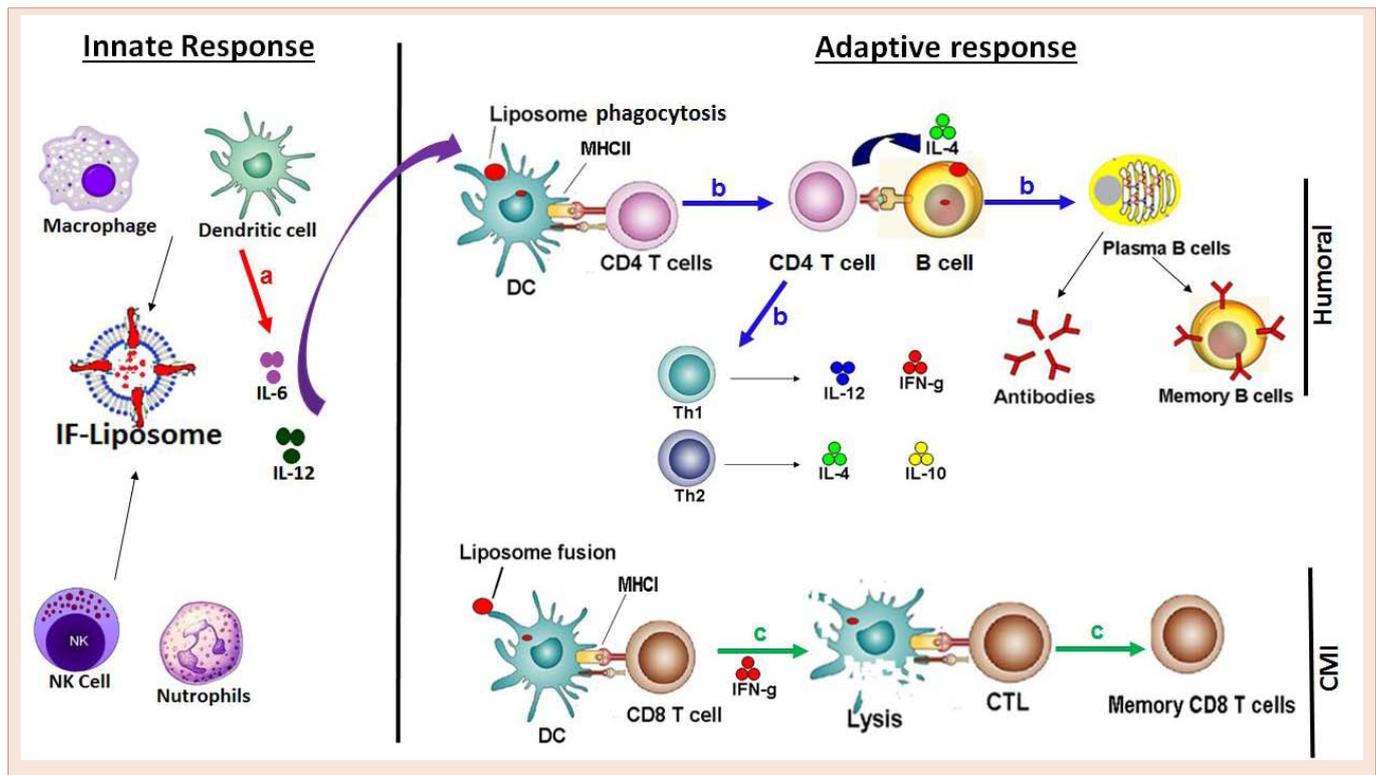


Figure 1: Simultaneous induction of innate and adaptive immune response by Immunostimulatory and fusogenic liposomes (IFLs). IFL may attract innate cells like DCs, macrophages leading to their immunostimulation and release of proinflammatory cytokines (pathway a). IFL may get phagocytosed by APCs and present antigen by MHCII molecule to CD4 T cells which may then activate and proliferate to different subtypes (Th1/Th2). CD4 T cells may also activate B cells through IL4 to produce antibodies (pathway b). IFL may get fused with APC and deliver antigen to the cytosol for presentation through MHCI to CD8 T cells which may lead to the generation of cytotoxic T cells to induce cell-mediated Immunity (pathway c).

Abbreviations: CL-Conventional Liposomes; IFL-Immunostimulatory-Fusogenic Liposomes; OVA- Ovalbumin; APC-Antigen presenting cell; CTL- Cytotoxic T cell; PAMP-Pathogen Associated Molecular Patterns; TPL-Total polar lipids; Cell mediated Immunity- CMI.

differences in magnitude and quality of innate immune responses. The innate response generated also correlated to the adaptive immune response (unpublished data).

In conclusion, immunostimulatory and fusogenic liposomes are effective and promising vaccine adjuvants which can be engineered to produce desired immune response against the particular pathogen. Exploiting new technologies to understand molecular mechanism of liposome action will pave way for the development of novel liposome-based therapeutics and prophylactics.

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