



Bacterial derived proteoliposome for allergy vaccines

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Abstract

One current approach in developing anti allergic vaccines is the use of potent adjuvants, capable of inducing Th1 or T regulatory cells. Proteoliposomes (PL) could be a suitable adjuvant. Purified *Dermatophagoides siboney* (Ds) allergens were mixed with PL and adsorbed into Al(OH)₃ and evaluated in mice. The Th1/Th2 responses were measured at classes, subclasses, cytokines, and DTH levels. Anti Ds response was deviated to a Th1 pattern, with the production of IgG2a and γ IFN. A positive DTH response and a dramatic decrease of specific IgE and IL5 were not detected. The low dose was more effective than high dose. These results clearly support the potential use of PL as possible adjuvants for anti-allergic vaccines.

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1. Introduction

IgE production by B-cells is driven by the pattern of Th2 cytokines, which overproduces IL4, inducing the class switch to IgE. One current approach in developing novel vaccines against allergy is the use of potent adjuvants, capable of stimulating the innate immune response, thus inducing Th1 or T regulatory cells. Therefore, we hypothesize that proteoliposomes (PL) derived from *Neisseria meningitidis* B, which contain native and not toxic lipopolysaccharide (LPS) as a pathogen associated molecular pattern could be a suitable adjuvant for anti-allergic vaccines.

2. Materials and methods

Purified *Dermatophagoides siboney* (Ds) allergens were mixed with PL and adsorbed into Al(OH)₃. Two doses with 0.5, 1.25, 2.25 or 5 μ g/mouse with 14 days inter-

val were administered to Balb/c mice by intramuscular (im) or subcutaneous (sc) routes. Total IgE, anti Ds IgG, IgG1 and IgG2a were measured by ELISA. Spleen cells from immunised mice were cultured and challenged in vitro with Ds and γ IFN and IL5 were detected by ELISA. Anti Ds IgE and DTH was assessed by passive cutaneous anaphylaxis (PCA) or ELISA and footpad swelling test, respectively.

3. Results and discussion

The response against Ds, when absorbed into Al(OH)₃ was characterised by a Th2 pattern being deviated to a Th1 pattern, with the production of IgG, IgG2a, γ IFN, and a DTH response with a dramatic decrease of specific IgE and no IL5 production by the incorporation of PL to the formulation. The PL dose of 0.5 μ g was the most effective being the only one that induced positive DTH and higher γ IFN levels. No significant differences were observed when i.m and s.c routes were compared. The absorption of allergen is one of the strategies to control their release and improve safety of allergen

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vaccines [1]. The incorporation of PL as potent immunomodulator can redirect the allergen and Al(OH)₃ Th2 inducer pattern to a new Th1. This could be due to the influence of LPS within the formulation but also to the constitution of PL per se [2]. In addition, the recent report of the presence of TLR in T regulatory cells [3], Th3 subtype, may explain why PL containing native LPS could effectively activate dendritic cells and naïve T cells polarizing the response to Th1 pattern. Lastly, the Th3 cells are better stimulated by low dose antigen [4] which may have been responsible for our results. These results clearly support the potential use of PL as effective and safe adjuvants for anti-allergic therapeutic vaccines, and particularly in prophylactic vaccines to be administered in early childhood.

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