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Bioprospecting and their Role in the Innovation of Vaccine Adjuvants: Mega Diversity as a Source of Competitiveness

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Abstract

Adjuvants are defined as any compound or complex molecular or supramolecular assembly that can increase the immune response when is administered in formulation with an antigen. In this way, adjuvants have the ability of act as immune enhancers, this promotes early innate immune responses which increase the effectiveness enabling antigen recognition. This topic is an important research field due to immunization with purified protein antigens typically results in the induction of a modest antibody response with little or no T-cell response, so required multiple immunizations to obtain an adequate protective response. Vaccine adjuvants is a new and innovative platform that after a century when the only adjuvants licensed for human use were hydroxide and phosphate salts of aluminium are not effective satisfactorily. Recently, natural products have been examined as potential vaccine adjuvants, which makes it an important field of research for the implementation of bioprospecting programs. For example, the plant saponin QS-21, derived from *Quillaja saponaria*, has shown to be a strongly inductor of antibody responses against cancer antigens in experimental cancer vaccines. Also, bryostatin-1 isolated from bryozoan *Bugula neritina* have the ability for induce dendritic cell activation enhancing antigen presentation and immune response. In this order of ideas, vaccine adjuvant discovery efforts are an important initiative for avoid antimicrobial drug resistance, control deadly infectious diseases and develop new anticancer strategies; so this line of research is another added value of biodiversity for the solution of the great threats of public health and a great opportunity for megadiverse countries in pharmaceutical global market.

Keywords: Immumodulatory; Adjuvants; Natural products; Vaccines

Introduction

It has been calculated that every second are given up to 30 doses of vaccines in the world, becoming the largest and most successful public health intervention available [1]. For that reason, World Health Organization (WHO) is looking for new alternatives and strategies to improve the immunization of the world population in the shortest possible time. Between them promotion of vaccination programs, increase the productive capacity of vaccines in developing countries and stimulate research and development on this particular topic [2].

In this way, the efficient delivery of antigens to antigen presenter cells (APCs), especially in dendritic cells (DCs), and the activation of APCs are some of the most important issues in the development of effective vaccines [3]. An important field in this topic is the maximization of the effectiveness of the vaccines by the discovery and optimization of new adjuvants. Adjuvants are defined as molecules or groups of molecules capable of enhancing the immune response when given in conjunction with a vaccine [4]. Adjuvants act as immunopotentiators, increasing antigen presentation and improving the response to the vaccine (Figure 1) [5]. In addition, adjuvants can be been used to improve immune responses in populations with conditions that cause an inadequate response to vaccination, as patients with renal disease [6].This topic is an important research field due to immunization with purified protein antigens typically results in the induction of a modest antibody response with little or no T cell response. Is necessary the search and development of new vaccine adjuvants for improve the protection against infectious diseases in humans and animals, this strategy should have the ability of prevent the infectious disease spread and zoonoses presence, improving the quality of life of the population [7]. Due to antigens may have low immunogenicity is important develop more powerful adjuvants for activate innate immune cells and induce high levels of immunity safely with a few doses [8]. Following this line of reasoning a good adjuvant have to comply these characteristics: non-toxic at the effective doses, stimulate a strong humoral and/or cell mediated immunity, induce immunological memory, not produce autoimmunity and hypersensitivity reactions; not cause mutagenicity, carcinogenicity and teratogenicity; non-pyrogenic and stability under the usual storage conditions [9,10].

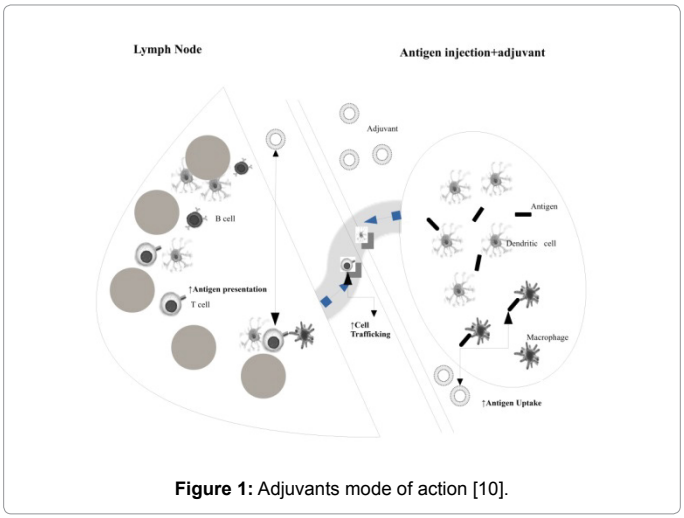

Figure 1: Adjuvants mode of action [10].

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In this order of ideas, natural products, especially medicinal plants have several reports about their biological effects on the immune system. These description of immunomodulatory activities are the starting point for the discovery of new compounds for immunotherapy [11]. For example, AS01 adjuvant is a mix of liposome, saponin (QS-21, derived from *Quillaja saponaria*) and monophosphoryl lipid A that promote antigen specific cell mediated response as well as antibody responses, and has shown the ability of increase the effectiveness of the RTS,S malaria vaccine [12]. Also, extracts from the stimulating herb *Panax ginseng* administered with ovalbumin (OVA) has shown up-regulate both T-helper lymphocytes type 1 and 2 (Th1 and Th2) as well as antibody responses; equally, extracts from *Coriolus versicolor* and *Astragalus memebranaceus* have the ability to induce antibody responses to cancer antigens in mice [13]. Another molecule with important adjuvant properties, between them DCs activation, is bryostatin-1, a lactone isolated from *Bugula neritina* [14]. Likewise, propolis has shown adjuvant action for bacterial vaccines for *Haemophilus parasuis* in pigs and *Pasteurella multocida*, *Escherichia coli* and *Klebsiella pneumoniae* in chickens [15]. Similarly, oils from plants have been patented and used as adjuvants, for example peanut oil based adjuvant was patented by Merck® and was studied for use with influenza vaccine. Equally, groundnut oil was used to enhance responses with a live Newcastle disease vaccine and increased the length of time for the protective efficacy of the vaccine compared with no adjuvant from 11 to 20 weeks [16]. In the same way is necessary solve the gap in the understanding of how some adjuvants exert their immune potentiating activities and whether the adjuvant impacts the quality of vaccine-induced protective response, due to although vaccines are the safer drugs developed, their use is young children do that the constant examination about the safety topic be high more than the other medical treatments [17]. For that reason, an important approach for toxicity screening tools is human cell-based assays that can predict *in vivo* effects of adjuvants [18].

Finally, a multidisciplinary approach in bioprospecting program seeking for new vaccine adjuvants have to evaluate new formulations with the ability of increase the immune response for antigen recognition and decrease toxicity, in this way, encapsulation of adjuvants in polymeric nanoparticles or liposomes have shown to be a promising tactic for develop innovative vaccines using immunopotentiators from natural sources [19].

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