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Vaccines: Purified Macromolecules as Vaccines and DNA Vaccines

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Abstract

Preventive vaccines work to protect an individual from infection or disease by introducing a small component or a nonharmful form of the pathogen (called the foreign antigen) into the body. The body produces an immune response to the pathogen by generating antibodies (via the humoral response), killer cells (via the cell mediated response), or both and development of immunologic memory. We reviewed the recent literature on types of vaccines and older studies were included selectively if historically relevant but none of these vaccines is ideal and can be recommended unrestrictedly therefore, the use of biotechnology could allow cheap production of valuable vaccines, while providing enhanced safety by avoidance of both human and animal viruses or other contaminants. Vaccine have been studied extensively to help eradication the infectious disease and thereby decrease the need for drugs.

Keywords: *Vaccines; Biotechnology; Immune response; humoral response; cell mediated response.*

Introduction

The terms vaccine and vaccination are derived from Variolae vaccinae (smallpox of the cow) [1]. The administration of vaccines is called vaccination. Vaccination is the most effective method of preventing infectious diseases. Vaccination is the most effective means of controlling infectious disease. It has been mainly responsible for the eradication of smallpox and for control of yellow fever, poliomyelitis and German measles in the human population, and Newcastle disease, foot and mouth disease and Marks disease in domestic animals[2].

Several factors must be considered to developing a successful vaccine. The first step is which branch of the immune system is activated, therefore the vaccine designer must recognize and considered the important differences between activation of the humoral and the cell mediated branches. A second factor is the development of immunologic memory. For example, a vaccine that induces a protective primary response may fail to induce the formation of memory cells, leaving the host unprotected after the primary response to the vaccine subsides[3].

The memory cells depends on the incubation period of the pathogen. For example, the influenza virus has a very short incubation period (1 or 2 days). Symptoms of the disease will appear at the same time as memory cells are activated therefore the maintaining high neutralizing antibody levels by repeated reimmunizations is effective for protection against influenza[4].On other hand, pathogens with longer incubation period such as poliovirus requires more than 3 days to begin infected the nervous system so it is designed to induce immunologic memory[5].

Purified macromolecules as vaccines: Some of the risks associated with attenuated or killed whole organism vaccine can be avoided with vaccines that consist of specific purified macromolecules derived from pathogens. Three general forms of such vaccines are in current use: capsular polysaccharide, toxoid, and recombinant antigens.

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Polysaccharide vaccines: Prokaryotic cells, such as bacterial cells has a hydrophilic polysaccharide capsule layer that lies outside the cell envelope of bacteria to protects the bacteria against desiccation, and it is a part of the outer envelope of a bacterial cell. The polysaccharide capsule can be the cause of various diseasesdue to prevent phagocytosis. A coating of the capsule with antibodies and/or complement may be required for phagocytosis to occur [6].

The vaccine for *Streptococcus pneumoniae* used to prevent some cases of pneumonia, meningitis, and sepsis. The vaccine induces formation of opsonizing antibodies and is administered to high-risk groups such as infants, splenectomized patients, other immune-suppressed individuals, and elderly[7]. Meningococcal vaccine consists of purified capsular polysaccharides used to prevent infection by *Neisseria meningitidis*[8].

One limitation of polysaccharide vaccine is their inability to activate $T_H$cells. They activate B cells T-independent type 2 manner, resulting in IgM production but little other class and the vaccine is ineffective in children less than 2 years old. The subcutaneous pneumococcal polysaccharide vaccine have reported the induction of IgA secreting plasma cells but the T_H cells are not involved in the response and non-responders are also common amongst older adults. Immunization is not lifelong, so individuals must be re-vaccinated at age 65 if at least 5 years after initial vaccination[9, 10].

The capsular polysaccharides conjugated with some sort of protein carrier to generated conjugated vaccine. This conjugated vaccine is highly immunogenic but non-toxic and activates T_H cells which allow for immunoglobulin type switching and can induce memory B cells but it cannot induce memory T cells specific for the pathogen. Among other things, this results in mucosal immunity and eventual establishment of lifelong immunity after several exposures[10]. For exampleof conjugated vaccine is*Haemophilus influenzae* type b vaccine (Hib) consist from type b capsular polysaccharide covalently linked to tetanus toxoid to decrease the rate of meningitis, pneumonia, and epiglottitis in children under 5 years of age[11],another example is Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein), is a sterile solution of saccharides of the capsular antigens of Streptococcus pneumoniae serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F individually conjugated to diphtheria CRM_{197} protein [12].

Toxoid vaccine: Toxoid vaccines are used when a bacterial toxinis the main cause of illness therefore, bacterial toxin are inactivated to produce bacterial toxoids in such a way that toxicity is lost but antigenicity retained. The usual method of treatment is with formaldehyde [13].Absence of toxin activity in toxoid preparations has to be demonstrated in an animal model or in cell test. The activity of the dermo-necrotic toxin of *pasteurella multocida* can be measured with the aid of Vero cells[14].

Toxoid are normally adsorbed on to an adjuvant to stimulate an immune response, usually a mineral salt such as aluminum hydroxide or mineral oil [15].

The free formaldehyde concentration must be not more than 0.05 percent m/v of free formaldehyde unless the higher concentration has been shown to be safe[15].

In some cases anacultures was used to obtain both antibacterial and antitoxic immunity because in some cases where high levels of challenge lead to large quantities of toxin which overwhelm the antitoxic activity. A typical example of this was seen in *Clostridium perfringens* type C and *Cl. Chauvoei*[16].

When the immune system receives a vaccine containing a harmless toxoid, it learns how to fight off the natural toxin. The immune system produces antibodies that lock onto and block the toxin. Vaccines against diphtheria, Botulism and, tetanus are examples of toxoid vaccines[17].

The obtaining sufficient quantities of the purified starting materials with toxoid vaccine is difficulty due to one the problems with toxoid vaccine is consisting from purified macromolecules. This problem has been overcome by cloning the exotoxin genes and the expressing them in easily growth host cells therefore large quantities of the exotoxin can be produced, purified, and subsequently inactivated[18].

Recombinant antigen vaccines: The alternative vaccines which are more safe and effective such as highly purified recombinant proteins, subunits of pathogens or DNA vaccine for replacing these conventional vaccines[19]. The recombinant antigen vaccines are the DNA encoding any immunogenic protein can be cloned and expressed in a variety of expression systems for antigenic protein components, such as bacteria, yeast, mammalian cells and insect cells. Bacterial expression systems are the most used due to the ease of handling and

to their capacity for high level expression. However, for antigens in which post-translational modifications (e.g., glycosylation) are necessary, the use of mammalian or insect cells should be considered [20, 21].

The current vaccines are produced by expressing the hepatitis B surface antigen (HBsAg) in yeast cells then purified by conventional biochemistry techniques. The HBsAg assembles into virus-like particles (VLPs), which are extremely immunogenic [22, 23, 24]. Furthermore, yeast cells are responsible for the post-translational modification of proteins, being capable of rendering proteins glycosylated.

The recombinant antigen vaccines has several advantages when compared with traditional vaccines, such as safety and production cost, most of them present weak or poor immunogenicity when given alone, and thereby require the use of adjuvants such as aluminum salt to elicit a protective and long-lasting immune response[25].

DNA Vaccines: DNA vaccination is a technique for protecting against disease by injection plasmid DNA encoding antigenic proteins into the muscle of the recipient so some cells will take up that DNA and directly expressed the encoded protein antigen[26]. The cells secrete the antigens and display them on their surfaces. In other words, the body's own cells become vaccine-making factories, creating the antigens necessary to stimulate both humoral antibody response and a cell-mediated response. The surprising about injected DNA vaccine is expressed by the muscle cells with much greater efficiency than in tissue culture. The DNA appears either to maintain for long periods in an episomal form or integrated into the chromosomal DNA[27].

The viral antigen is also expressed by dendritic cells by take up the plasmid DNA and expresses the viral antigen, therefore the DNA vaccines have valuable potentials of dendritic cells. Dendritic cells can be present the vaccine antigens on MHC class I and II products because it is ability to transduced with DNA vaccine and the presenting of cellular antigen by dendritic cells allow dendritic cells to expand and sustain vaccine memory in the CD4 helper and CD8 killer compartments[26, 27].

DNA vaccine offer advantages over many existing vaccines. There is no risk for infection, no denaturation or modification on the encoded antigen because it is expressed in the host in its natural form, obviates need for peptide synthesis, expression and purification of recombinant proteins and use of toxic adjuvants, refrigeration is not required for handling and storage of the plasmid DNA, andDNA vaccines are relatively easy and inexpensive to design and produce[26, 28].

Several DNA vaccines are available for veterinary, including the influenza virus and West Nile virus. Currently no DNA vaccines have been approved for human use. Research is investigating the approach for malaria, AIDS, influenza, and herpesvirus in humans, as well as for several cancers[28]. New experimental trials of DNA vaccines will mix gene for antigenic proteins with cytokines or chemokines to enhance the immune response to the optimum pathway. For example, IL-12 gene may be included in a DNA vaccine because the expression of IL-12 will stimulate TH1 type immunity induced by the vaccine[29,30].

To determine the DNA vaccine ADVAX could induce efficient antiviral CD4+ T cell responses mediated by shared high-affinity TCRs. efficient antiviral CD4+ T cell responses mediated by shared high-affinity TCRs therefore, the DNA vaccination by electroporation primed for TCR clonotypes that were associated with HIV control, highlighting the potential of this vaccine delivery method [31].

Some disadvantage might prevent their universal application, for example, only protein can be immunogen that is mean the DNA vaccine are not useful for non-protein antigen such as pneumococcal and meningococcal infection, use protective polysaccharide antigens. Another shortcoming are coming from the risk of affecting genes controlling cell growth, possibility of inducing antibody production against DNA, potential for atypical processing to bacterial and parasite proteins, and inability to use DNA vaccine as oral vaccine or those given as nasal spray, that are applied to mucosal surfaces[32, 33].DNA vaccines also present a slight risk of potentially disrupting normal cellular processes because the introduction of foreign DNA into the body could affect a cell's normal protein expression pathways[34].

Two concerns regarding the effectiveness of the vaccine itself revolve around the body's reaction to the vaccine. The first is the chance of an immune response against the DNA itself, or the DNA delivery vector, which would defeat the point of the vaccine as a whole. If such a reaction were to occur, no protein immunogens would be expressed, and there would be no immune

response to those immunogens. Secondly there is a chance that the body develops a resistance or tolerance towards the protein the vaccine introduces [35, 36].

DNA vaccine consist of DNA can be administered with a needle. Recently, Cationic derivatives of polyprenols were used as effective DNA vaccine carriers in chickens and mice result, induced strong humoral response to the antigen encoded by the DNA vaccine plasmid. Another method called gen gunthat uses high-pressure gas to shoot microscopic gold particles coated with DNA directly into cells[37].

Conclusion

Purified macromolecules as vaccines,and DNA vaccines have been studied extensively as a future vaccine to help eradication the infectious disease development, and thereby decrease the need for drugs.

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Conflict of Interest: None

Ethical Clearance: The study protocol conformed to the ethical guidelines of the 1975 Helsinki Declaration and the approval was obtained from ethical committee of Middle East University-Amman-Jordan.

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