DNA Vaccines for Inducing Immune Responses in Mucosal Tissues

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Abstract -

DNA vaccines represent an innovative approach allowing the induction of humoral and cell-mediated antigen-specific immune response in systemic and mucosal compartments. A DNA vaccine is a type of vaccine that transfect a specific antigen-coding DNA sequence into the cells of an organism as a mechanism to induce an immune response.. DNA vaccines elicit CD8 T cell responses in most experiments through cross-presentation of antigen. Because most pathogens invade hosts through mucosal surfaces, the induction of mucosal and systemic immunity is of paramount importance. Although systemic DNA vaccination exhibits high efficiency, generally weaker immune responses are induced by mucosal DNA administration. However, systemic immunization with selected viral and bacterial vaccines may also protect against mucosal infections. Furthermore, in contrast to high immunogenicity confirmed in small experimental animals, human DNA vaccines require further optimization to exhibit a protective effect. Therefore, various systems for the delivery of DNA vaccines and various immune-modulatory molecules co-administered with DNA vaccines have been developed to optimize the immune response and protection. This review is a short insight on DNA vaccines and their delivery methods.

Key words - DNA vaccine, CD8 T cell, humoral, cell mediated

Introduction -

Conventional vaccines contain either specific antigens from a pathogen, or attenuated viruses which stimulate an immune response in the vaccinated organism. DNA vaccines are members of the genetic vaccines, because they contain a genetic information (DNA or RNA) that codes for the cellular production (protein biosynthesis) of

an antigen. DNA vaccines contain DNA that codes for specific antigens from a pathogen. The DNA is injected into the body and taken up by cells, whose normal metabolic processes synthesize proteins based on the genetic code in the plasmid that they have taken up. Because these proteins contain regions of amino acid sequences that are characteristic of bacteria or viruses, they are recognized as foreign and when they are processed by the host cells and displayed on their surface, the immune system is alerted, which then triggers immune responses (Alarcon et al 1999 and Robinson et al, 2000). Alternatively, the DNA may be encapsulated in protein to facilitate cell entry. If this capsid protein is included in the DNA, the resulting vaccine can combine the potency of a live vaccine without reversion risks.

Methodology:

Plasmid vector design:- DNA vaccines elicit the best immune response when high-expression vectors are used. These are plasmids that usually consist of a strong viral promoter to drive the in vivo transcription and translation of the gene (or complementary DNA) of interest (Mor et al). Polycistronic vectors (with multiple genes of interest) are sometimes constructed to express more than one immunogen, or to express an immunogen and an immune stimulatory protein (Lewis and Babiuk 1999).

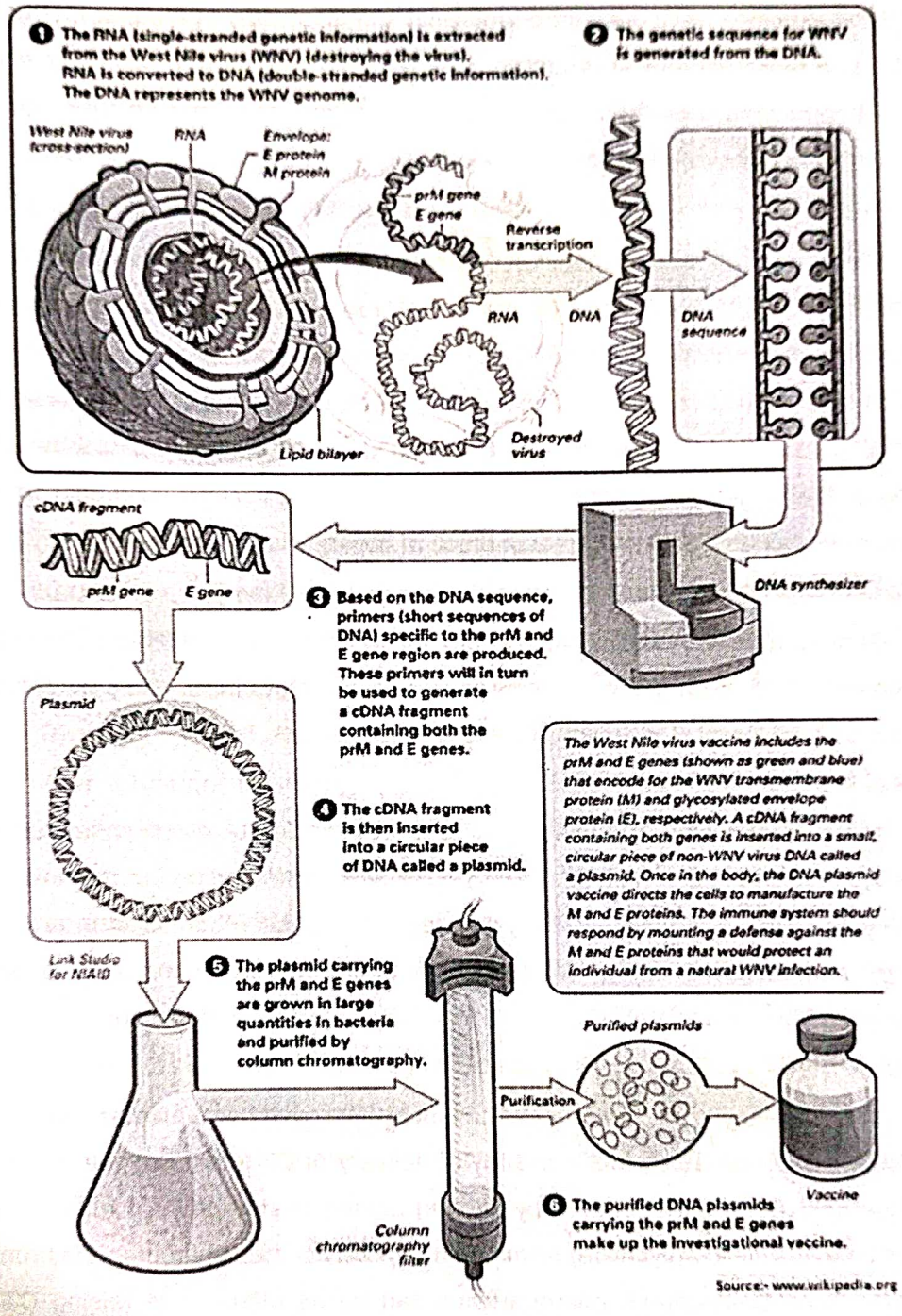
Mechanism of plasmids action:

Once the plasmid inserts itself into the transfected cell nucleus, it codes for a peptide string of a foreign antigen. On its surface the cell displays the foreign antigen with both histocompatibility complex (MHC) classes I and class II molecules. The antigen-presenting cell then travels to the lymph nodes and presents the antigen peptide and costimulatory molecule signalling to T-cell, initiating the immune response (Kutzler and Weiner 2008).

Vaccine insert design

Immunogens can be targeted to various cellular compartments to improve antibody or cytotoxic T-cell responses. Secreted or plasma membrane-bound antigens are more effective at inducing antibody responses than cytosolic antigens, while cytotoxic T-cell responses can be improved by targeting antigens for cytoplasmic degradation and subsequent entry into the major histocompatibility complex (MHC) class I

pathway(Robinson and Pertmer 2000).



Vaccine Delivery:

DNA vaccines have been introduced into animal tissues by multiple methods. In 1999, the two most popular approaches were injection of DNA in saline: by using a standard hypodermic needle, or by using a gene gun delivery.[30] Several other techniques have been documented in the intervening years.

Saline injection

Injection in saline is normally conducted intramuscularly (IM) in skeletal muscle, or intradermally (ID), delivering DNA to extracellular spaces. This can be assisted either 1) by electroporation (Widera et al 2000); 2) by temporarily damaging muscle fibres with myotoxins such as bupivacaine; or 3) by using hypertonic solutions of saline or sucrose (Alarcon et al 1999). Immune responses to this method can be affected by factors including needle type, needle alignment, speed of injection, volume of injection, muscle type, and age, sex and physiological condition of the recipient(Alarcon et al 1999).

Gene gun

Gene gun delivery ballistically accelerates plasmid DNA (pDNA) that has been absorbed onto gold or tungsten microparticles into the target cells, using compressed helium as an accelerant (Lewis and Babiuk 1999).

Mucosal surface delivery

Alternatives included aerosol instillation of naked DNA on mucosal surfaces, such as the nasal and lung mucosa (Lewis and Babiuk 1999) and topical administration of pDNA to the eye (Dahesia et al 1997) and vaginal mucosa. Mucosal surface delivery has also been achieved using cationic liposome-DNA preparations, biodegradable microspheres (Chen et al 1997) .

Conclusion:

The efficiency of DNA immunization can be improved by stabilising DNA against degradation, and increasing the efficiency of delivery of DNA into antigen-presenting cells. This has been demonstrated by coating biodegradable cationic microparticles (such as poly (lactide-co-glycolide) formulated with cetyl trimethyl ammonium bromide) with DNA. Such DNA-coated microparticles can be as effective at raising CTL as recombinant viruses, especially when mixed with alum. Particles 300 nm in diameter

appear to be most efficient for uptake by antigen presenting cells (Robinson and Pertmer 2000).

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