NUCLEIC ACID VACCINES

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Introduction

The most revolutionary approach to vaccination, stems from the discovery that DNA itself can be used as a vaccine. Lie and colleagues in 1993 reported that direct injection of a gene from influenza virus, induced protective immune response in immunized mice. This was a novel concept of vaccination and since then the technology of DNA Vaccination has become well established and widely spread in the research community as a method for infectious disease prophylaxis.

Review of literature

Robenson et al (1993) immunized chicks with DNA containing the Haemagglutinin (HA) gene of influenza virus strain H7N7. Chicks were given primary immunization with 100µg of DNA vaccine followed by a booster dose of another 100µg of the same DNA vaccine one month later and challenged with 100 lethal doses of homologous virus 1-2 weeks post-booster. A significantly high protection was observed in immunized chicks compared to non-immunized chicks.

Jiang et al (1998) used a plasmid DNA containing VP gene of Canine parvo virus to immunize dogs. The vaccinated dogs were completely protected against a virulent homologous Canine parvo virus challenge.

Dogs immunized with plasmid containing the nucleocapsid , fusion and attachment protein genes of a virulent Canine Distemper (CD) virus strain developed virus neutralizing antibodies. Vaccinated dogs were protected against challenge with virulent CD (Cherpillod et al, 2000)

Mode of action

In contrast to vaccines that employ recombinant bacteria or virus, genetic vaccines consist only of DNA (as plasmids) or RNA (as mRNA), which is taken up by cells and translated into proteins. In case of gene-gun delivery, plasmid DNA is precipitated on to an inert particle (generally gold beads) and forced into cells with a helium blast. Transfected cells then express the antigen encoded on the plasmid resulting in an immune response. Like live or attenuated vaccines, DNA vaccines effectively engage both MHC-1 and MHC-2 pathway allowing for the induction of CD8+ and CD4+ T-cells. Whereas in case where antigen is present in soluble form, such as recombinant protein, it generally induces only antibody response. In addition to the use of plasmid DNA for prophylactic vaccination against infectious diseases, DNA vaccines may be useful as a treatment of individuals chronically infected with viruses.Eg; HIV and Hepatitis virus strain B and C.

Genetic vaccination through the delivery of RNA has also been investigated,but to lesser extent than DNA vaccination. RNA expression is short lived, and is thus less effective in inducing an immune response. The preparation and administration of RNA is troublesome because of the low stability of the RNA. One advantage of the RNA strategy is that there is no risk of integration of the delivered gene into the host genome.

DNA vaccines consist of plasmid DNA expression vectors of E.coli origin which encode the antigen or antigens of interest under the control of strong viral promoters recognized by the mammalian host. When the plasmid DNA is administered to an animal, the antigen is expressed insitu, leading to an antigen specific immunity. This method offers a number of attractive qualities; simplicity of production of large quantities of pure DNA, the breath of applicability to various pathogens, the ability to induce cellular immune responses through MHC Class I presentation, and the potential to manipulate the immune response through the co- delivery of

genes encoding immunologically relevant molecules.

Genetic vaccines can be delivered into the host by several routes and methods. The main methods of plasmid-DNA delivery to the skin are by needle injection or by gene-gun delivery. These two methods differ in several aspects. Needle injection requires relatively large amount of plasmid, whereas the amount of plasmid required for gene –gun delivery immunization has been titrated down to few nanograms. At least 100 fold less plasmid DNA is required for the induction of protective immune response when administered adsorbed to gold particles and delivered by a gene- gun when compared with inoculation of plasmid DNA in saline using a syringe and needle. The gold particles directly penetrate the skin due to the force of delivery, thereby increasing the rate of transfection without having to rely on the uptake of DNA by the host cell itself.

Advantages

Ø Purity, physio-chemical stability and simplicity

Ø Relatively low cost of production ,distribution and delivery

Ø Inclusion of multiple antigens in a single plasmid

Ø Expression of antigen in the natural form

Ø T_H, T_C as well as antibody response is elicited

Ø Induction of immunity in the presence of maternal antibodies.

Disadvantages

Ø Concern related to possible integration into chromosomal DNA, leading to insertional mutagenesis and oncogenesity

Ø Induction of autoimmune diseases including anti-DNA antibody

Ø Cost of proving safety will be significant for animals in the human food chain

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