DNA VACCINES: NEW APPLICATIONS OF BIOTECHNOLOGY TO INFECTIOUS DISEASES

Robert Whalen

Director of Research, French National Center of Scientific Research, Paris, France,
E-mail: whalen@pasteur.fr The ONA Vaccine Web: http://www.genweb.com/Dnavax/

Introduction

Although direct gene transfer into tissues is a relatively inefficient process, it is nonethetess possible to synthesize enough of a foreign protein after injection of purified plasmid DNA expression vector to induce an immune response, The expression of several types of antigens from a large number of pathogens has shown that the immune responses induced are broad-based, These responses include induction of antibodies as well as the production of cytotoxic and helper T lymphocytes, and they result in long- lasting T-cell memory in the animal.

In several cases, the immunity resulting from such DNA-based immunization is able to protect the animal from challenge by the pathogenic organism. Thus, such DNA vaccines have been clearly demonstrated to be a realistic approach to vaccine development, and further work in this field can concentrate on the practical maters of formulation of such novel vaccines so that they can be used safely and reliably for human and veterinary vaccination purposes, Several phase I/II clinical trials are currently underway to evaluate the safety and immunogenicity of DNA vaccines in humans.

Such a methodology has many advantages with respect to vaccine developmment, The ability to immunize with a simple ONA plasmid allows researchers to test many ideas using a very simple methodology. The plasmids can be introduced by intramuscular or intradermal needle injection, or the DNA can be delivered after absorption to gold particle and then bombarded into the epidermis. The use of the latter technology, often referred to as a "gene gun", appears to give very efficient DNA uptake, and strong immune responses can be achieved with a few micrograms or less of DNA. This technology has also allowed the sirnultaneous introduction of thousands of clones of potentially antigenic genes, in an approach called "expression-library immunization".

Results and Discussion

In our experimental work, plasmids encoding the envelope protein of the hepatitis B virus give strong immune responses, and these results wilt serve to illustrate the potential of DNA vaccines. Intramuscular irnrnunization induces a particular effective T cell priming which can protect chimpanzees from disease after challenge by the hepatitis B virus. Other results indicate that a DNA vaccine encoding HBV proteins could be effective in treating chronic hepatitis B, which is a great public health problem in Asia, Africa and many other countries. It is clear that plasmid DNA itself functions as an immunostimulatory molecule, and in particular accounts for the induction of a T-helper type I phsnotype characterized by the secretion of the cytokines interferon-gamma and interleukin-2.

Conclusion

High quality plasmid DNA is relatively easy to prepare, using straightforward fermentation and chromatography methods. The DNA itself is very stable, and this aspect, combined with the inexpensive production process, could result in DNA vaccines which are affordable in most aceas of the world, Indeed, the manufacturing expertise required should be implemented in as many countries as possible, to provide foc "vaccine independence" and the ability to move quickly to produce vaccines relevant to each country's specific infectious diseases problems.

1. Donnelly JJ, Ulrner JB, Shiver JW, Liu MA. DNA vaccines. Annu Rev Immunol 1997;15:617-648.

2. Pisetsky DS. Immune activation by bacterial DNA: a new genetic code. Immunity 1996;5:303-310.

3. Whalen RG. DNA vaccines for emerging infectious diseases. Emerging Infectious Oiseases 1996;2:168-175. Available online at: <http://www.cdc.gov/ncidod/EID/vol2no3/whalen.htm>