Recombinant DNA vaccines: Prevention from Covid-19 and Other Pandemics

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Abstract -

The use of recombinant proteins allows the targeting of immune responses focused against few protective antigens. There are a variety of expression systems with different advantages, allowing the production of large quantities of proteins depending on the required characteristics. Live recombinant bacteria or viral vectors effectively stimulate the immune system as in natural infections and have intrinsic adjuvant properties. DNA vaccines, which consist of non-replicating plasmids, can induce strong long-term cellular immune responses. Prime-boost strategies combine different antigen delivery systems to broaden the immune response. In general, all of these strategies have shown advantages and disadvantages, and their use will depend on the knowledge of the mechanisms of infection of the target pathogen and of the immune response required for protection. Recombinant DNA vaccines offer new potential for reducing the burden of diseases like Covid-19, SARS, hepatitis, polio and diarrhoea especially in developing countries like India where administering vaccines is major issue.In this review, we discuss some of the major breakthroughs that have been achieved using recombinant vaccine technologies, as well as new approaches and strategies for vaccine development, including potential shortcomings and risks.

Keywords : DNA vaccines, Covid-19, SARS, Viral vectors, Plasmids.

Introduction -

Toward development of r DNA and edible vaccines, transgenes of various antigens and antibodies have been expressed successfully in plants, and have been shown to retain their native functionalities. Categories of Vaccines Recombinant vaccines fall into three basic categories: live genetically modified organisms, recombinant inactivated vaccines, and genetic vaccines Production of edible subunit-based recombinant vaccine proteins in the form of leaves, seeds or fruit is expected to be cost effective, and products will be easily stored and transported under limited refrigeration

without degradation. Administration of commercial edible vaccines will require significantly less labor and technical training of medical and veterinary personnel. Oral ("edible") delivery of subunit vaccine proteins has been shown more efficient compared to subcutaneous or intramuscular injection vaccines due to the increased chance of provoking mucosal immune responses, which in turn stimulate cell mediated responses. Most current vaccines owe their success to their ability to target pathogens that have low antigenic variability and for which protection depends on antibody-mediated immunity. This is the case for polio, tetanus, diphtheria, measles, and hepatitis B, among others (Plotkin,2001; Ada,2005; robbinson, 2005). As a consequence, vaccines capable of generating neutralizing or opsonizing antibodies against these pathogens were successful.

On the other hand, important cell-mediated immunity against intracellular pathogens (which in most cases leads to chronic infections) is much more difficult to obtain using current vaccine strategies. The live attenuated pathogen vaccines, which are capable of eliciting this type of response, although not often, may offer potential risks that cannot be overlooked, such as virulence in susceptible hosts and potential reversal of attenuation.

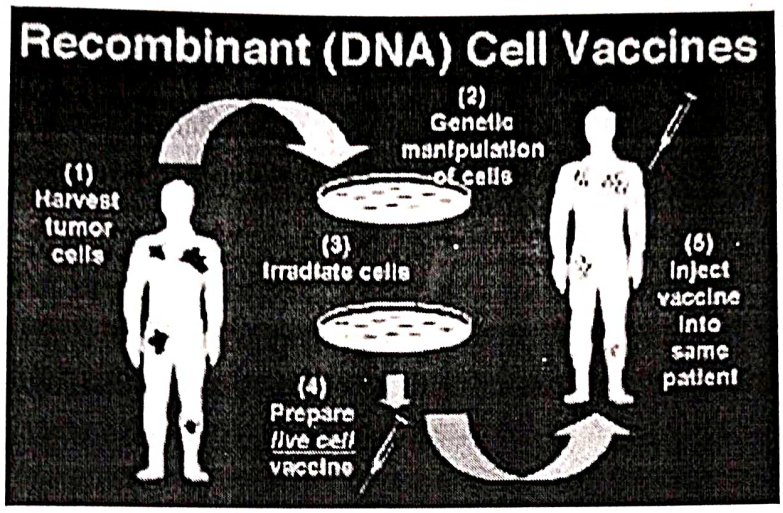
Recombinant vaccines rely on the capacity of one or multiple defined antigens to induce immunity against the pathogen, when administered in the presence of adjuvants or when expressed by plasmids or harmless bacterial/viral vectors. Recombinant protein vaccines permit the avoidance of several potential concerns raised by vaccines based on purified macromolecules, such as the risk of co-purification of undesired contaminants or reversal of the toxoids to their toxigenic forms, if considering diphtheria or tetanus toxoid vaccines, for example. Another fundamental issue overcome by this technology is the complexity involved in obtaining sufficient quantities of purified antigenic components.

However, one of the main challenges in the development of these new strategies of immunization consists of designing vaccines that elicit the appropriate kind of immune response to confer immunity mainly to intracellular pathogens and especially to those that establish chronic, often lifelong infections. For this, the knowledge of the biology of highly conserved antigens involved in pathogenesis and of the immune mechanisms that should be elicited for protection must be obtained to rationally design vaccine strategies that can overcome the low protective immunity naturally generated by infection (Lemaire *et al* 2012).

DNA vaccines - The direct injection of a naked DNA plasmid into muscle as a vaccine system with the ability to induce an immune response and protection after challenge is now well established, since this approach has been used to express numerous antigens from different pathogens with promising results (Wolff *et al* 1993). A DNA vaccine (or genetic vaccine as it is also called) consists of a plasmid containing: 1) one origin of replication of Escherichia coli, for the amplification of the plasmid; 2) a strong promoter, generally from cytomegalovirus; 3) multiple cloning sites, in which one can insert the gene to be expressed, and 4) an antibiotic as selection marker (Ulmer *et al* 1999). The idea behind the DNA vaccine system is that the antigen can be expressed directly by the cells of the host in a way similar to that occurring during viral infection. As a result, the antigens can be processed as proteins synthesized in the cytoplasm, and the fragmented peptides presented to the immune system by class I MHC molecules. In addition, if the protein is exported or secreted, it can be processed by class II MHC molecules and, as a result, mount a specific antibody response (Oliviera *et al* 1999).

Initially, DNA vaccines were administrated either by intramuscular (im) injection or using a DNA particle delivery system called Gene Gun (Yang *et al* 1990). Unlike im injection, which requires micrograms of plasmid DNA and several doses, the Gene Gun system requires nanogram levels of plasmid DNA to induce the same level of immune response. However, the type of immune response induced in response to the same antigen by the two systems was shown to be distinct. While im injection raised predominantly a Th1 response, Gene Gun immunization induced a mixed Th1/Th2 or a Th2 shifted profile. These findings are particularly important in vaccine design, as it is desirable to establish previously the kind of immune response required for protection against a specific pathogen (Oliviera *et al* 2009). DNA vaccines have several properties that could represent advantages over other immunization procedures: there is no risk of infection, contrary to attenuated vaccines; they elicit both humoral and cell-mediated immunity, and they are capable of inducing long-lived immune responses and increased cytotoxic T-cell responses. In addition, DNA vaccines avoid problems associated with producing recombinant protein vaccines, such as inadequate folding of target molecules or high purification cost of recombinant proteins. Although DNA vaccines present many advantages, some concerns regarding suitability and capability should be investigated,

such as the possibility of production of anti-DNA antibodies, integration of DNA plasmid into the cell genome (now considered a remote possibility), and low efficiency of transfection of the cells in vivo (Belakova *et al* 2007).



The Serum Institute of India Pvt Ltd CoviShield COVID-19 (AZD1222) (C19VAZ) vaccine, formerly known as ChAdOx1 nCoV-19, is made from a virus (ChAdOx1 recombinant), a weakened version of a common cold virus (adenovirus). In addition, genetic material has been added to the ChAdOx1 construct, which is used to make proteins from the SARS-CoV-2 coronavirus called Spike glycoprotein (S).

Conclusion - Nonetheless, considerable advances in the fields of immunology, molecular biology, recombinant DNA, microbiology, genomics, bioinformatics, and related areas have provided novel insights to help elucidate important pathogenic mechanisms involved in these infectious diseases and in pathogen interaction with the host. Altogether, these advances have led to the development of several new vaccine strategies with promising results. It seems now clear that an integrated approach will be necessary to foster continued progress in the immunology field, which probably constitutes the limiting factor for the development of new vaccines.

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