VACCINES PART : 3

E - MODULE

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RECOMBINANT VECTOR VACCINES

- Genes that encode major antigens of especially virulent pathogens can be introduced into attenuated viruses and bacteria.
- The attenuated organism serves as vector replicating within the host and expressing the gene product of the pathogen.
- These are mainly of two types:

  1.Viral vector vaccine

  2.Bacterial vector vaccine

VACCINIA VIRUS AS VECTOR

- The vaccinia virus can replicate in the host cell cytoplasm (of the infected cells) rather than the nucleus. This is possible since the vaccinia virus possesses the machinery for DNA replication, transcription-DNA polymerase, RNA polymerase etc.
- The foreign genes inserted into the vaccinia virus can also be expressed along with the viral genome. Thus, the foreign DNA is under the control of the virus, and is expressed independently from the host cell genome.

Vaccines against Viruses- Vaccinia Virus

- Vaccinia viruses is basically the vaccine that was originally used by Jenner for the eradication of smallpox.
- Vaccinia virus contains a double-stranded DNA (187 kb) that encodes about 200 different proteins. The genome of this virus can accommodate stretches of foreign DNA which can be expressed along with the viral genes.

VIRUS VECTOR VACCINES

- Most of the work on the development of live viral vaccines has been carried out on Vaccinia virus.
- Other viruses such as adenovirus, poliovirus and varicella-zoster virus are also being tried as recombinant vaccines.
- Scientists are attracted to develop a recombinant poliovirus as it can be orally administered. It might take many more years for the recombinant viral vaccines to become a reality for human use.

VACCINIA VIRUS AS VECTOR

- The vaccinia viruses are generally harmless, relatively easy to cultivate and stable for years after lyophilization (freeze-drying). All these features make the vaccinia virus strong candidates for vector vaccine
- The cloned foreign genes (from a pathogenic organism) can be inserted into vaccinia virus genome for encoding antigens which in turn produces antibodies against the specific disease-causing agent.

RECOMBINANT VACCINIA VIRUS

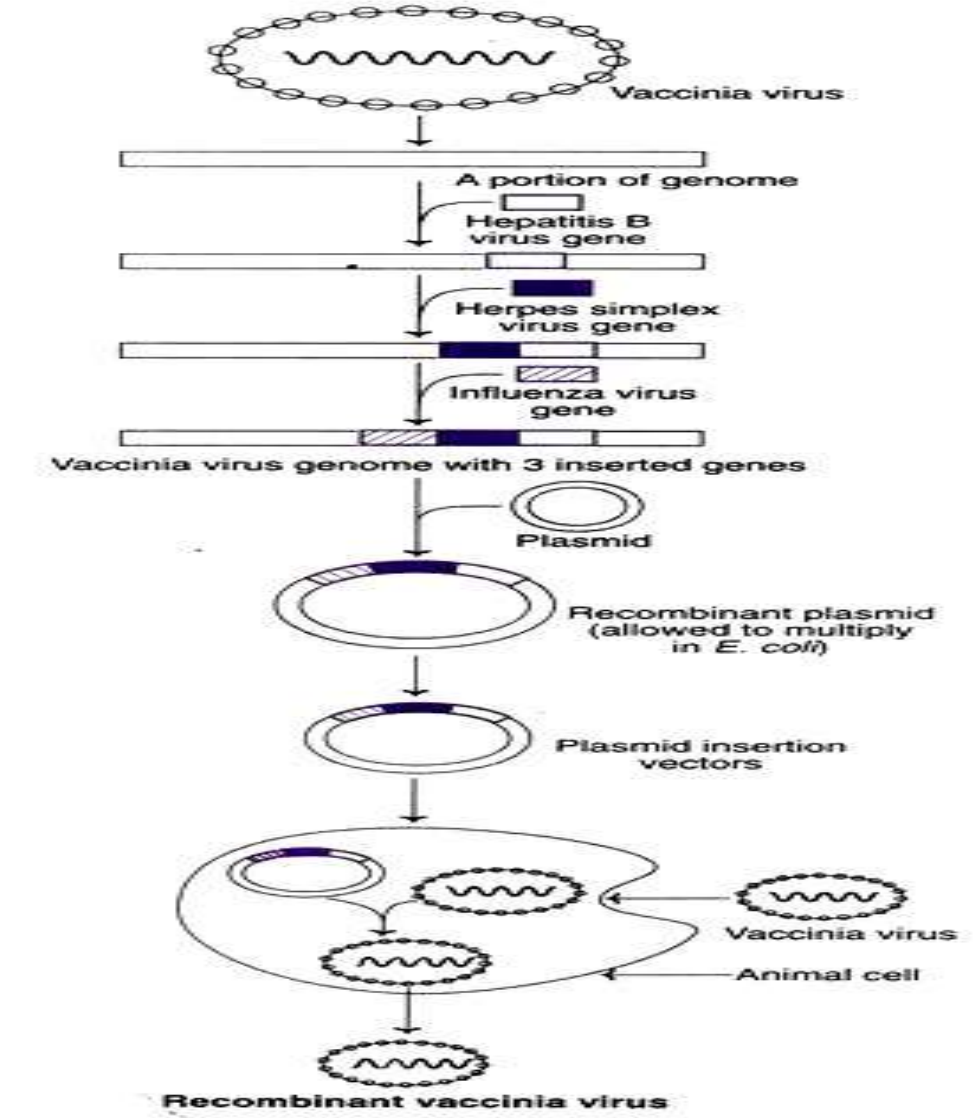


Fig. 16.8 : Production of recombinant vaccinia virus.

VECTOR VACCINE

- Antigen genes for certain diseases have been successfully incorporated into vaccinia virus genome and expressed.
- Thus, vector vaccines have been developed against hepatitis, influenza, herpes simplex virus, rabies, angular stomatitis virus and malaria.
- However, none of these vaccines has been licensed for human use due to fear of safety.

VECTOR VACCINE

- The **advantage** with vector vaccine is that it stimulates B-lymphocytes (to produce antibodies) and T-lymphocytes (to kill virus infected cells). This is in contrast to a subunit vaccine which can stimulate only B-lymphocytes.
- Thus, vaccinia virus can provide a high level of immuno protection against pathogenic organisms.
- Another advantage of vaccinia virus is the possibility of vaccinating individuals against different diseases simultaneously.
- This can be done by a recombinant vaccinia viruses which carries genes encoding different antigens.

RECOMBINANT VACCINIA VIRUS

Advantages:

1. Authenticated antigens that closely resemble natural antigens can be produced.
2. The virus can replicate in the host cells. This enables the amplification of the antigens for their action on B-lymphocytes and T-lymphocytes.
3. There is a possibility of vaccinating several diseases with one recombinant vaccinia virus.

RECOMBINANT VACCINIA VIRUS

Disadvantages:

- 1. The most important limitation is the yet unknown risks of using these vaccines in humans.
- 2. There may be serious complications of using recombinant viral vaccines in immunosuppressed individuals such as AIDS patients.

BACTERIAL VECTOR VACCINE

- Attenuated strains of bacteria have been also used to carry genes of virulent pathogens.
- The DNA encoding the antigenic determinants is inserted into the attenuated bacterial genome.
- The bacteria then express the antigen along with its own protein. The production and expression of antigen by the bacterial virus inside the host body stimulates the immune system.
- Salmonella typhimurium, the causative agent of food poisoning is being explored as a vector and is currently in human trials.

BACTERIAL VECTOR VACCINE

Advantages

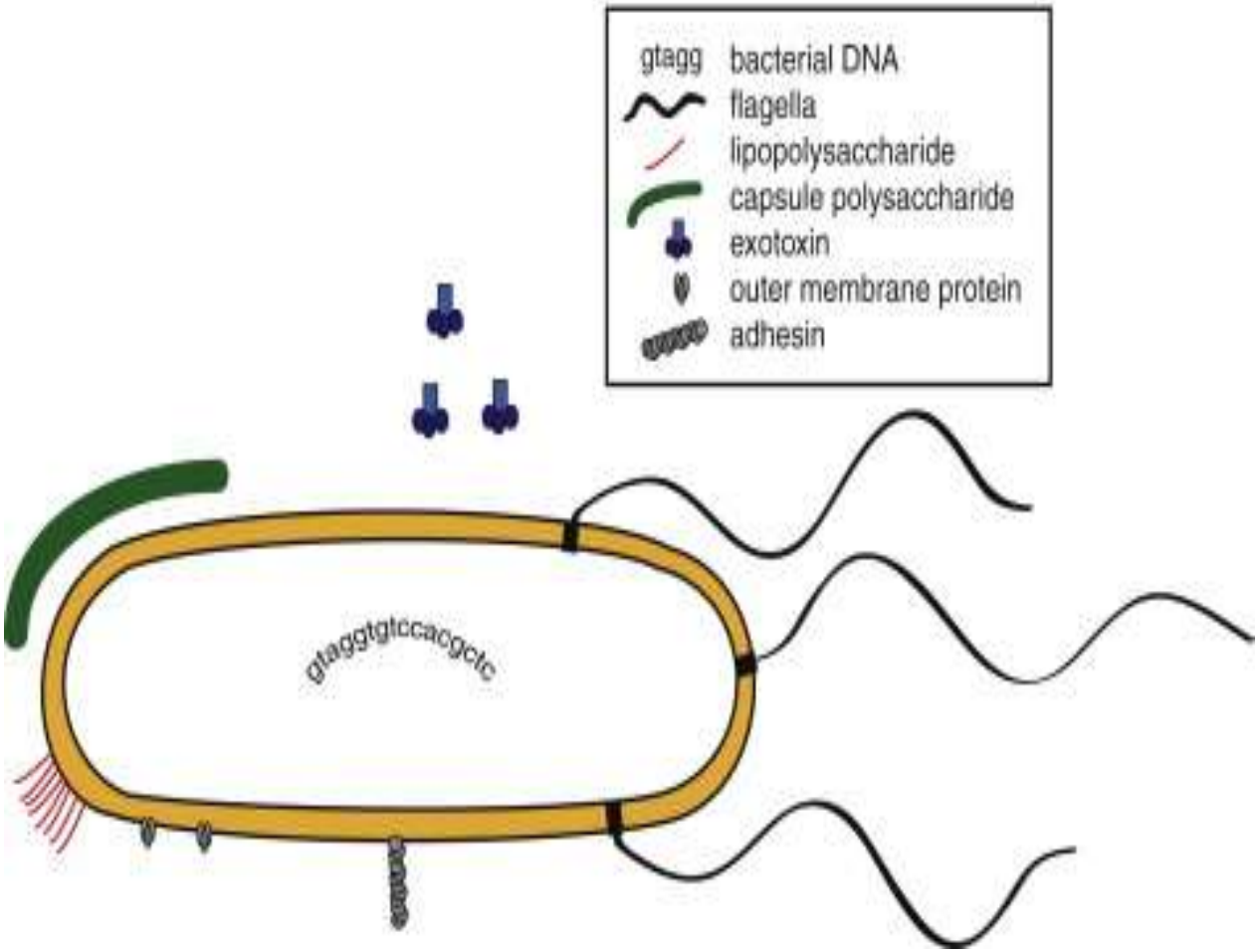
- Attenuated strains are easily available and genes can be easily manipulated.
- The use of bacterial vaccine will produce immune responses both against the vector as well as inserted antigen.
- Both types humoral and cell mediated immune responses are produced. IgA or mucosal immunity is also produced as some bacteria are present in gastrointestinal tract.

BACTERIAL VECTOR VACCINE

Disadvantages

- Reversion and emergence of virulent strains.
- Rejection and elimination of bacterial vector before it can express the recombinant protein.
- Antigen formed inside the bacteria may be lysed by bacterial enzymes.

BACTERIAL COPONENTS FOR VACCINE DESIGN



NUCLEIC ACID VACCINES

- Another approach to vaccination involves introducing genetic material encoding the antigen against which an immune response is sought.
- The body's own cells then use this genetic material to produce the antigens.
- Potential advantages of this approach include the stimulation of broad long-term immune responses, excellent vaccine stability and relative ease of large-scale vaccine manufacture.

DNA VACCINES

- Genetic immunization by using DNA vaccines is a novel approach that came into being in 1990. The immune response of the body is stimulated by a DNA molecule.
- A DNA vaccine consists of a gene encoding an antigenic protein, inserted onto a plasmid, and then incorporated into the cells in a target animal.
- The plasmid carrying DNA vaccine normally contains a promoter site, cloning site for the DNA vaccine gene, origin of replication, a selectable marker sequence and a terminator sequence.

DNA VACCINES

- The plasmid vaccine carrying the DNA (gene) for antigenic protein enters the nucleus of the inoculated target cell of the host. This DNA produces RNA, and in turn the specific antigenic protein.
- The antigen can act directly for developing humoral immunity or as fragments in association with major histocompatibility complex (MHC) molecules for developing cellular immunity.

DNA VACCINES

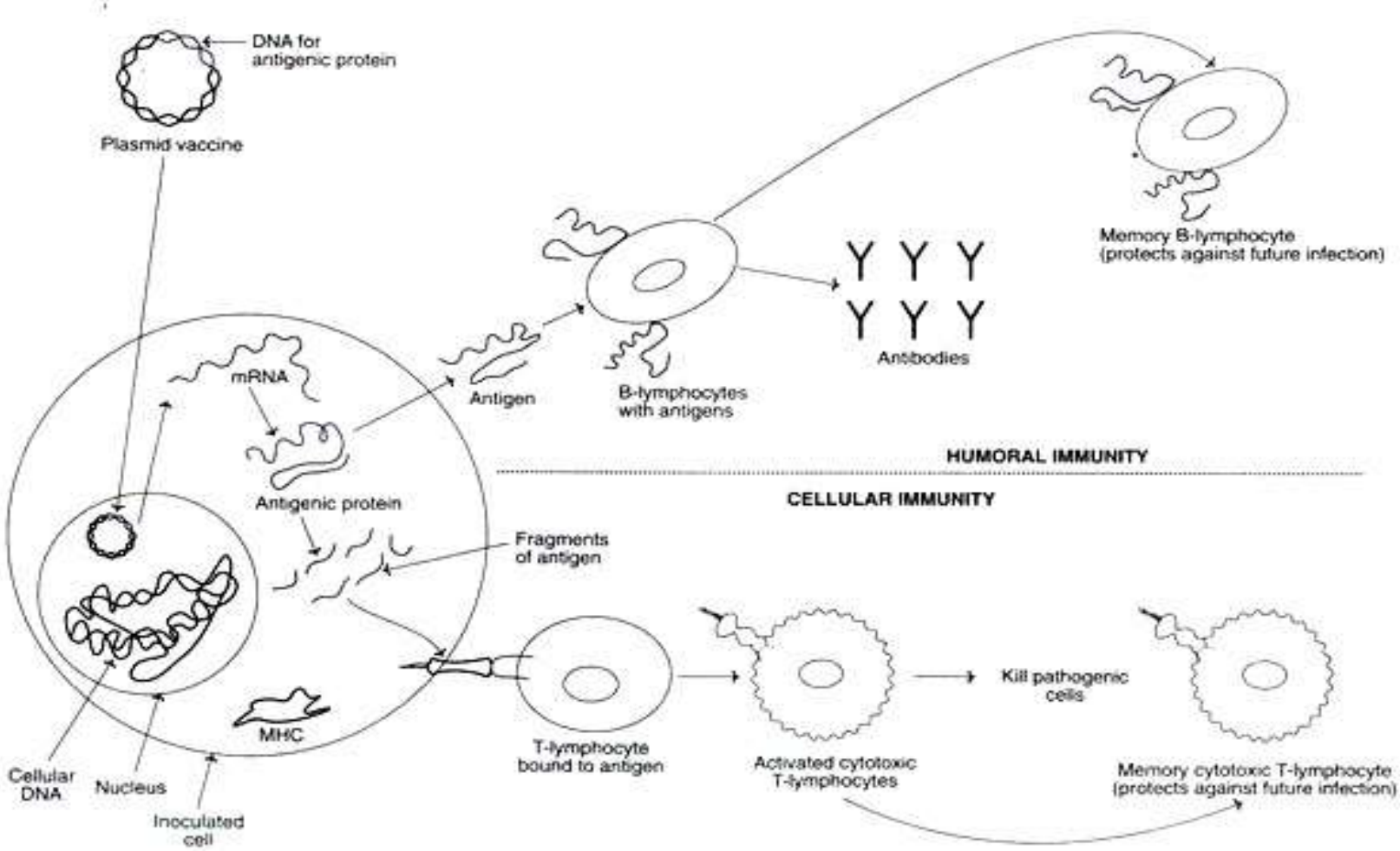


Fig. 16.5 : DNA vaccine and mechanism of its action in developing immunity (MHC–Major histocompatability complex molecule)

Screening of pathogenic genome for selecting DNA vaccines

- The ultimate goal of scientists is to choose the right DNA fragment from the pathogen to serve as a vaccine for the strongest immune response against the invading pathogen.
- The pathogen's DNA can be broken into fragments and a large number of vaccines DNA—plasmids can be prepared.
- The immune response for each one of the DNA vaccines can be studied by injecting the pathogen
- . By screening the DNA fragments of the pathogenic genome, it is possible to choose one or few DNA vaccines that can offer maximal immune protection.

DNA VACCINES

Advantages

1. The difficult and costly procedures of purifying antigens or creating recombinant vaccines are not necessary.
2. DNA vaccines are very specific in producing the target proteins (antigens or antibodies). Thus, the immune response generated is only against the specific pathogen.
3. DNA vaccines elicit much higher immune response compared to other kinds of vaccines.
4. DNA vaccines are more stable for temperature variations (low or high) than the conventional vaccines. Thus, the storage and transport problems associated with vaccines are minimal.
5. The delivery methods to the host are simpler for DNA vaccines.
6. Easy to manufacture in large amounts.

DNA VACCINES

Disadvantages

1. The fate of the DNA vaccine in the host cells is not yet clear. There is a possibility of this DNA getting integrated into the host genome and this may interrupt the normal functions.
2. Insertion of foreign DNA may cause cell to become cancerous. So there also exists a danger of cancer due to DNA vaccines.
3. The post-translational modification of the gene (DNA vaccine) product in host cells may not be the same as that found in the native antigen.
4. Immunologic tolerance may be induced.
5. Not effective against polysaccharide antigens.

DNA VACCINE ADMINISTRATION

DNA vaccine—plasmids can be administered to the animals by one of the following delivery methods:

i. Nasal spray

ii. Intramuscular injection

iii. Intravenous injection

iv. Intradermal injection

v. Gene gun or biolistic delivery (involves pressure delivery of DNA-coated gold beads).

Present status of DNA vaccines

Since 1990, scientist world-over have been trying to develop DNA vaccines against various diseases in experimental animals.

Genetic immunization has been done against a number of pathogenic organisms. These include influenza A virus, rabies virus, hepatitis B virus, bovine herpes virus, HIV type I, and Plasmodium species (malarial parasite).

RNA VACCINES

- Scientists are also working on to use RNA molecules as vaccines. These RNAs can readily synthesize the antigenic proteins and can generate immunity.
- But RNAs are less stable than DNAs and it poses a major problem for RNA vaccine manufacturing and distribution.
- Therefore, the progress in the development of RNA vaccines has been slow compared to DNA vaccines.

SYNTHETIC VACCINES

- Among new vaccine strategies one is synthetic vaccines as Peptide sequences of protein antigens can be chemically synthesized in laboratory.
- A whole protein molecule is large molecule and there can be technical difficulties in synthesizing it so, small parts containing antigenic determinants can be synthesized.
- But the major drawback is that these are poorly immunogenic.

VACCINE AGAINST AIDS

- The reason for the non-availbility of vaccine against AIDS is that the HIV has high frequency of mutations.
- Therefore the vaccines developed cannot bind to the new virus strain i.e., mutated one.
- Despite these limitations, scientists have not lost hope, and research is going on all over the world to develop vaccine against AIDS.

IDEAL VACCINE

- It should be able to generate both memory T and B cells which can produce acceltated and immediate protection to the host.
- It should provide lifelong immunity with single dose.
- It should have less side effects.
- It shouid be inexpansive,easy to store and transport.

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