# GENETICALLY MODIFIED OR GENETICALLY ENGINEERED VACCINES:

1. Recombinant protein vaccines or recombinant subunit vaccines.
2. Recombinant DNA vaccines or simply “DNA vaccines”.
3. Ghost cell vaccines.
4. Recombinant vector vaccines.
5. Knock-out vaccine or gene deletion vaccines.

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## 1. RECOMBINANT PROTEIN VACCINES OR RECOMBINANT SUBUNIT VACCINES:

The gene encoding the immunogenic epitope of a pathogen is cloned into a plasmid vector using recombinant DNA technology that is then transformed into a bacterial host cell. In the host bacterial cell, the gene is expressed that is purified and used as a vaccine. As shown in Fig. 1. These recombinant subunit vaccines are more immunogenic than killed vaccines.

## 2. RECOMBINANT DNA VACCINES OR SIMPLY “DNA VACCINES”

The gene encoding the immunogenic epitope of a pathogen is cloned into a plasmid vector using recombinant DNA technology as like that of Recombinant protein vaccines but in this case the recombinant DNA is not transformed into a bacterial cell but is directly injected into the animal by intra-muscular route. The recombinant DNA is internalized by muscles cells and local dendritic cells (local antigen presenting cells). In the muscle cells the recombinant DNA is taken inside the nucleus and the gene of epitope present in the recombinant vector is expressed. The protein (epitope) comes out of cell and is reacted by the antibody present on the membrane of B cells leading to its activation. On the other hand some of the epitopes move to the lysozomes where they are degraded into antigenic peptides that are loaded on MHC class I and expressed on the cell surface that is recognized by T-cell receptor (TCR) present on the cytotoxic T lymphocytes (CTLs) leading to their activation. In case of the recombinant DNA that is internalized by antigen presenting cell (APCs), is expressed in the same way in the nucleus of APCs. The epitopes generated inside the APCs follow three types of pathways.

1. MHC class I pathway
2. MHC class II pathway
3. Humoral immune response

In the MHC-I pathway, the antigenic peptides generated by lysozomal degradation of antigens are loaded onto the MHC class I molecules and expressed on the cell surface that is recognized by CTLs leading to their activation.

In MHC class II pathway, the antigenic peptides generated by lysozomal degradation of antigens are loaded onto the MHC class II molecules and expressed on the cell surface that is recognized by Helper T lymphocytes ($T_H$ cells) leading to their activation. The $T_H$ cells then differentiates into $T_{H1}$ cells that help in activation of CTLs and $T_{H2}$ cells that help in activation of B lymphocytes.

In Humoral immune response, some of the epitopes generated comes out of the cell intact. These intact epitopes are recognized by membrane bound antibodies of B cells leading to their activation. See Fig. 3 and Fig. 4.

Advantages of DNA vaccines:

1. The DNA vaccines have long shelf life and do not require cold chain.
2. They can stimulate both the arms of immune system.

Disadvantages of DNA vaccines:

1. Extracellular degradation of recombinant DNA.
2. Destruction of recombinant DNA in lysozome.
   *These disadvantages can be nullified by the use of delivery systems such as liposomes, nanoparticles etc.*

3. GHOST CELL VACCINES

The Ghost cell vaccines are created by completing extracting the DNA from the bacterial cell. The empty bacterial cell devoid of DNA is said to be ghost cells. The bacteriophage PhiX174 has a gene called "Lysis gene E". This gene when expressed in the bacterial cell upon infection of bacterial cell by the bacteriophage PhiX174, causes the formation of transmembrane tunnel that causes emptying of the cellular content including DNA. The resultant remnant of empty bacterial cell is called Ghost cell. The resulting empty cell envelope retains all the morphological, structural and immunogenic features of the cell envelope of a living cell. In case of killed cells that are used as killed vaccines do not express many of the immunogenic epitopes due to destruction of these during the process of killing the organism. While in case of ghost cell vaccine, all the immunogenic epitopes are retained. See Fig. 5.

4. RECOMBINANT VECTOR VACCINES.

The Recombinant vector vaccines are made by inserting the gene responsible for formation of immunogenic epitopes in a target pathogen (viral or bacterial) into another avirulent virus or avirulent bacteria (called vector). Now the vector would carry express the immunogenic epitopes of the pathogen. This recombinant vector when it is injected into the animal, it would be able to generate immune response against the target pathogen using the expressed epitope in the vector. The organisms that are used as vector are *Lactobacillus*, BCG strain of *Mycobacterium* spp., Adenovirus, vaccinia virus etc.

5. KNOCK-OUT VACCINE OR GENE DELETION VACCINES

These are the live vaccines obtained by deleting the virulent gene or the gene responsible for virulence or the pathogenesis. Hence the virulent pathogen becomes avirulent. However, this method cannot be used for all the pathogens as in some pathogens, the virulent genes are also required for the survival of the cell. So, if the virulent genes are removed, the organism would not survive. Such vaccines are able to stimulate both the arms of immune system (HI and CMI).

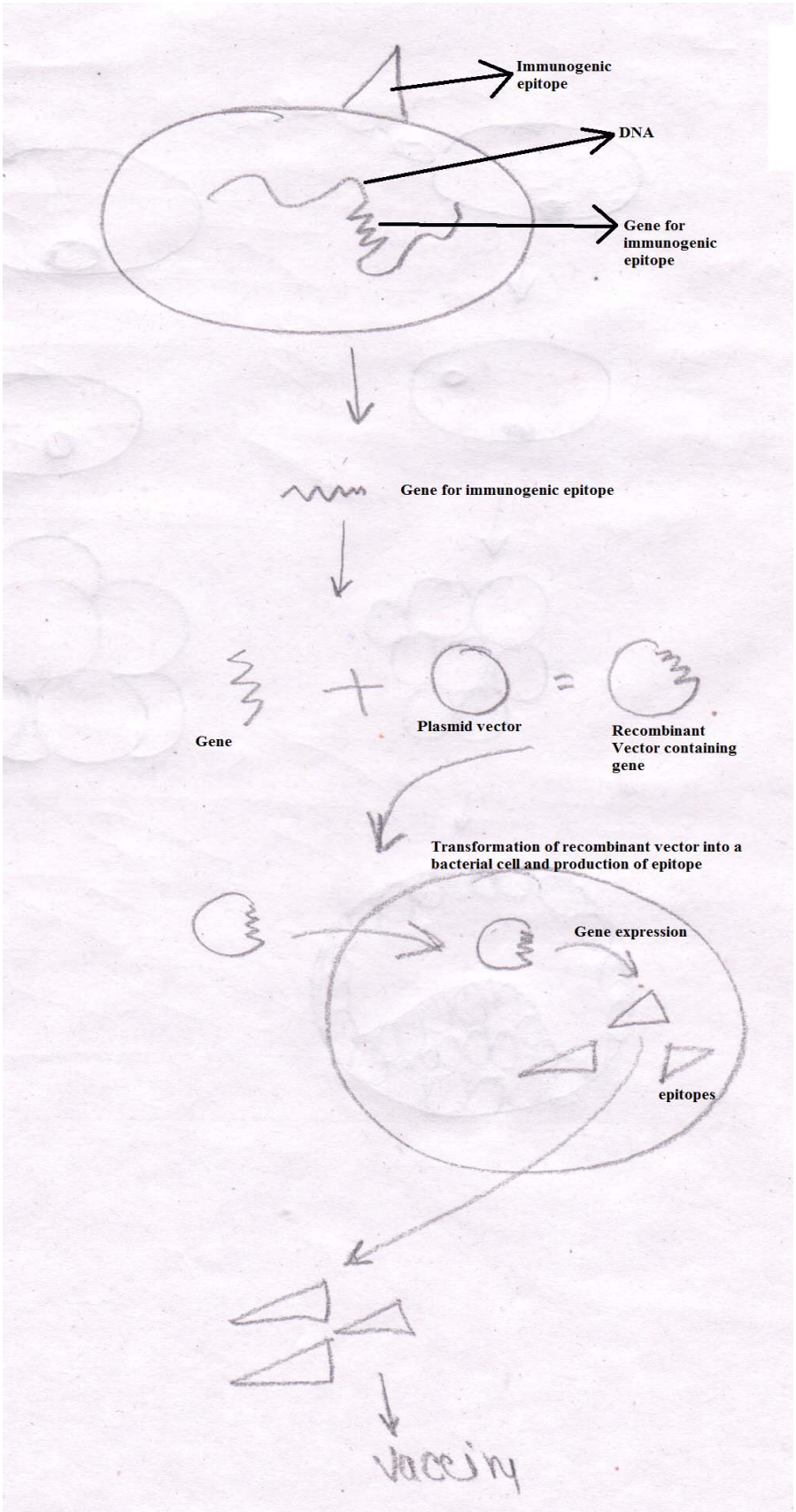


Fig 1: RECOMBINANT SUBUNIT VACCINES

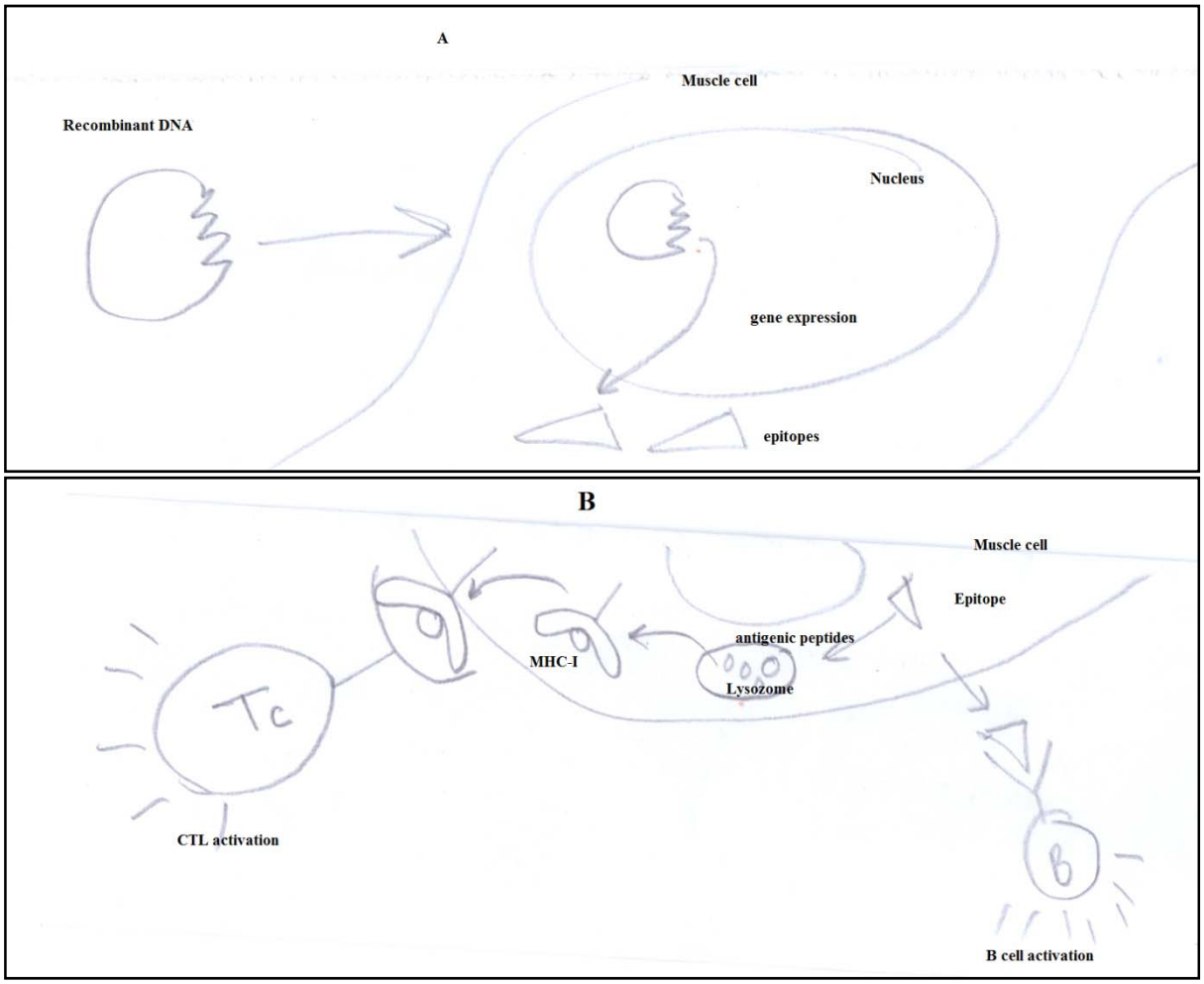


Fig. 2. Internalization of recombinant DNA by Muscle cells

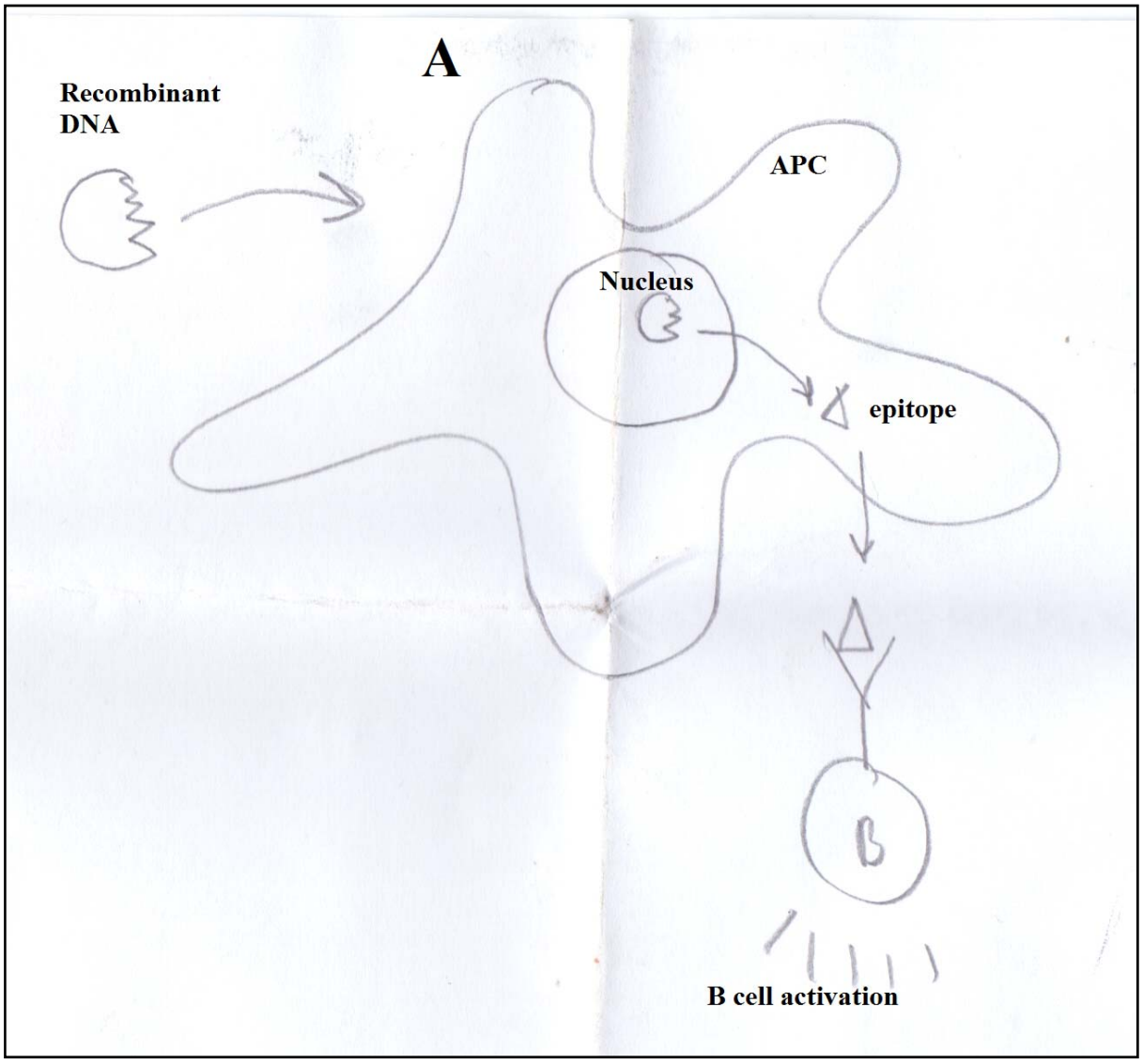


Fig. 3. B cell activation by the recombinant DNA internalized by antigen presenting cells (APCs)

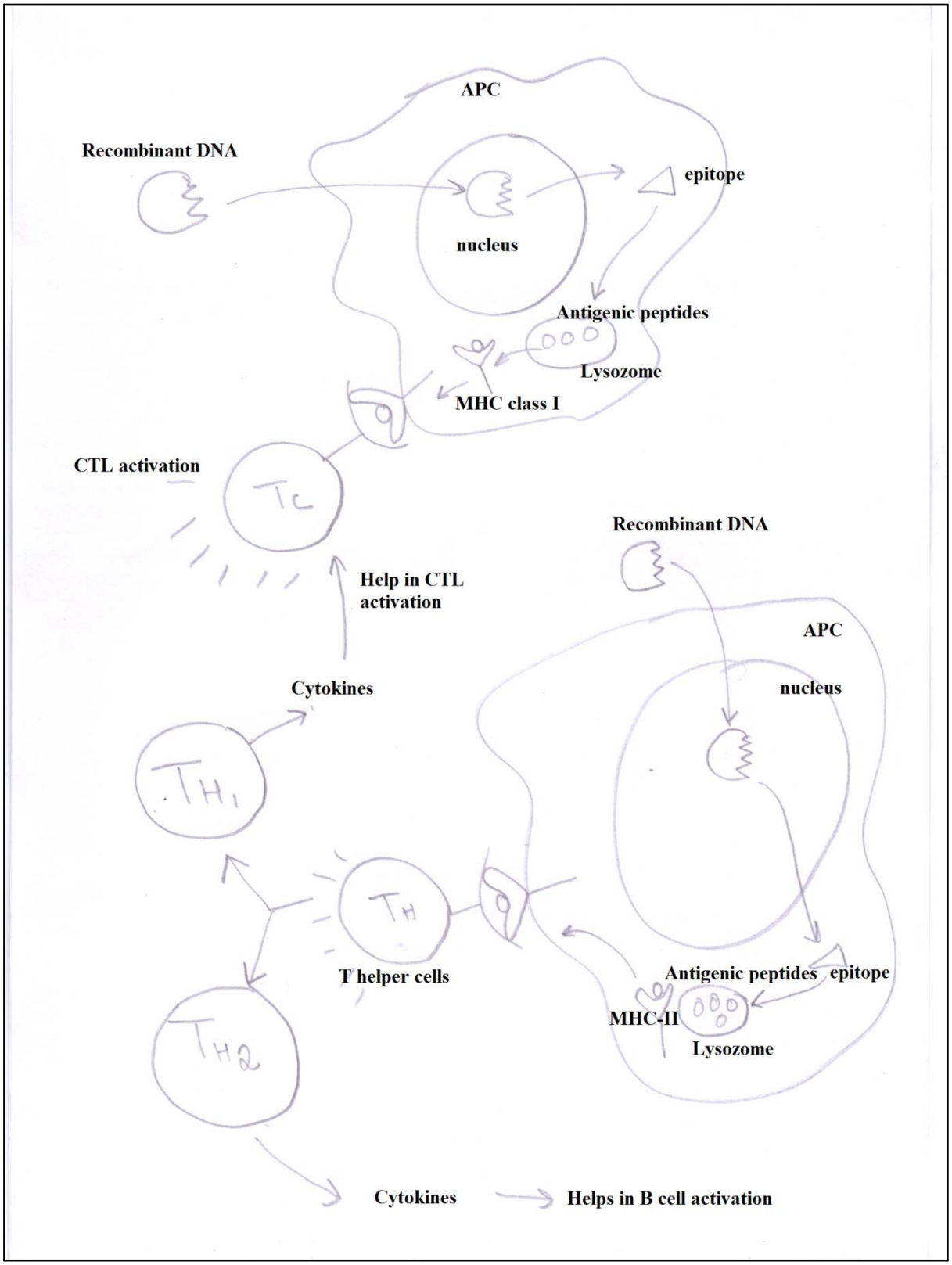


Fig. 4. Activation of cell mediated immune response by the recombinant DNA internalized by antigen presenting cells (APCs) through the activation MHC class I and Class II pathways.

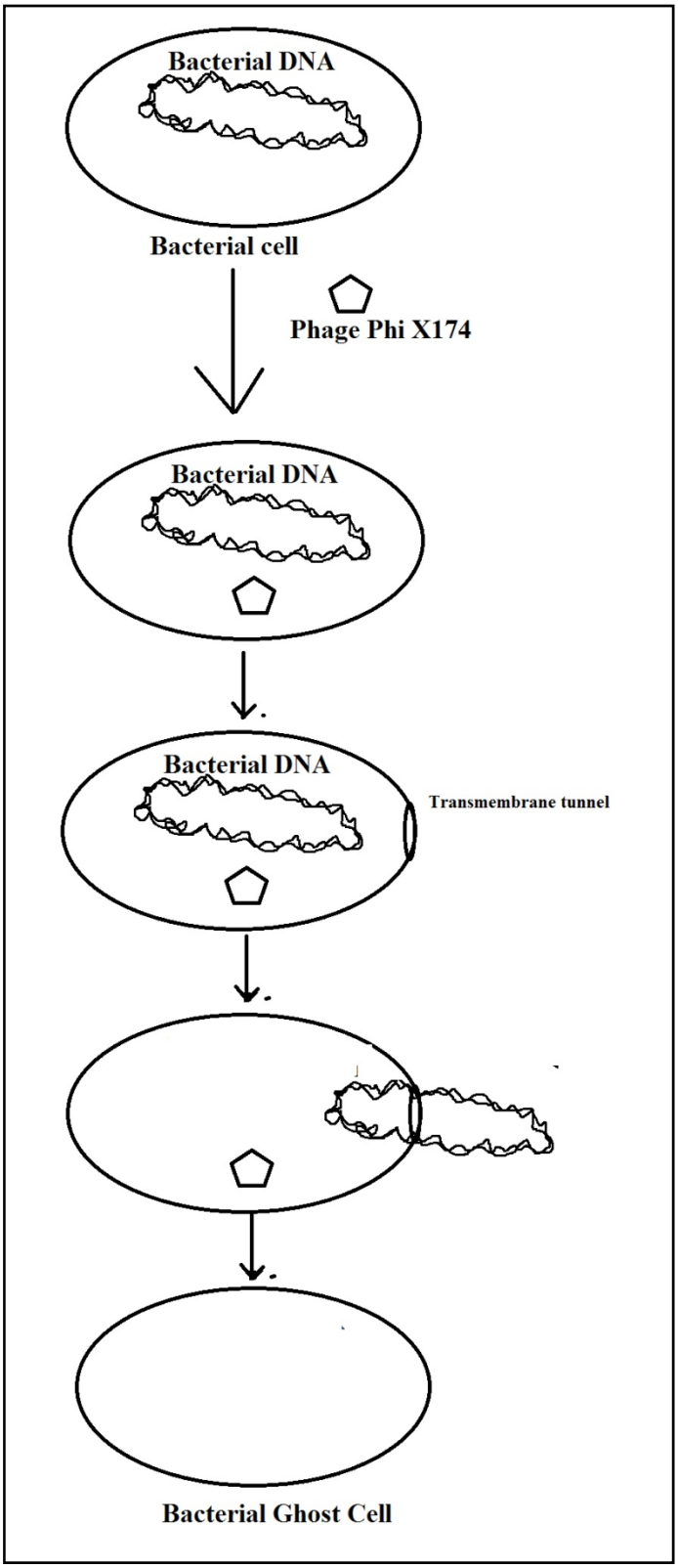


Fig. 5. Formation of ghost bacterial cell

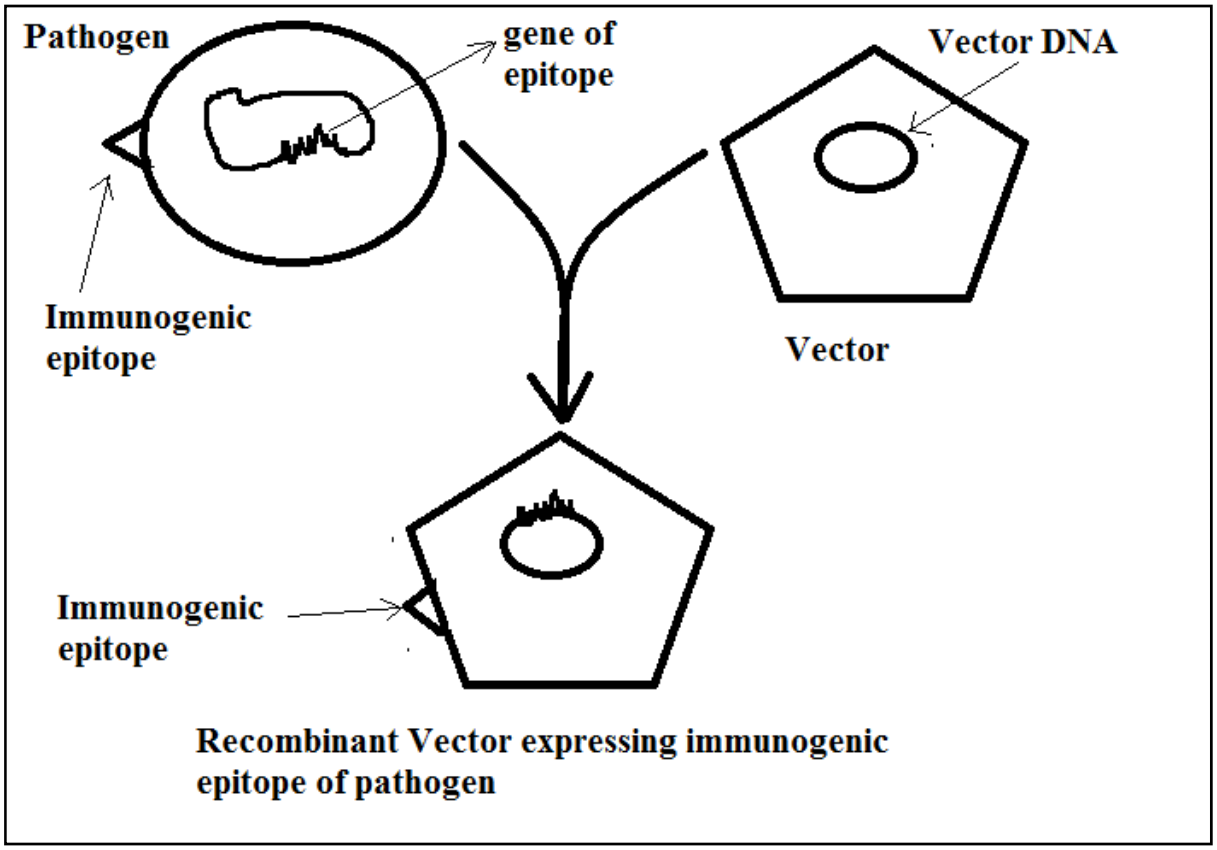


Fig. 6. Recombinant vector vaccine.