IMMUNOLOGY

VACCINES

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VACCINES

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- TOPIC:
  - RECOMBINANT VECTOR
  - DNA VACCINES
  - SYNTHETIC PEPTIDE VACCINE
  - MULTIVALENT VACCINE

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- Vaccines are either antigen /antibody that induce artificial immunity
- The vaccinated individual become immunized to that antigen
- Vaccination is them most cost effective method of preventing infectious disease
- Most of the vaccines used to prevent future infections and few are therapeutic as in the case of cancer

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TYPES

- PASSIVE
- ACTIVE

- If antibodies are given to the person , it is called passive immunization
- It doesn't activate immune system , but gives immediate protection for short time ,it generate Weak response with no memory
- Eg; injection of anti tetanus serum gives protection to tetanus

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Vaccines for passive immunization

vaccine	disease
Horse- anti toxin	diphtheria
Horse anti toxin	botulism
Pooled immune igG	Hepatitis A&B
Pooled immune igG	Measles
Pooled immune igG	rabies
Horse anti toxin,tetanus toxoid	tetanus
Horse anti venum	Snake bite
Horse anti venum	Spider bite
Monoclonal anti RSV	Rsv infection(**Respiratory syncytial virus)**
Monoclonal antibody drugs	Cancer and auto immune disease

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- If antigens are used for vaccination it called active immunization
- It gives protective immunity for longer period
- It retains immunological memory and elicits a high response
- Vaccines used for active immunization:

❖ Live attenuated vaccine

- virulent micro organism can convert to non virulent organism
- But retain power of multiplication in host but lose pathogenity

❖ Killed inactivated vaccine

- pathogen inactivated by heat/chemicals
- It is capable to replication in host
- Eg ; salmonella typhi
- Improper inactivation causes intact infectious organism

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❖ Virus like particle

- It consist of viral protein but lack of nucleic acid
- It isn’t infectious
- Eg: hepatitis B vaccine
- more recently viral like particle used as pre- clinical vaccine against chikungunya

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TYPES OF VACCINES

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1.MULTIVALENT VACCINES

- Vaccines may be monovalent or multivalent
- a monovalent vaccine designed to immunize against a single antigen or single micro organism
- A multivalent vaccine is designed to immunize against two or more strains of the same organism / two or more different organisms
- For rapid and strong immune response a monovalent vaccine is preferable
- Numerous multivalent vaccines are now available
- The combined diphtheria/tetanus/pertussis (DTS)- a triple antigen vaccine is used in routine vaccination program
- Another combination of vaccines – measles/mumps/rubella (MMR) vaccine with hepatits A+B and hepatitis A+ typhoid are also given as combination of vaccines
- The combination of vaccines administered as a single injection

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- They provide protection against one or more disease
- The pentavac PFS is a single dose prefilled syringe (PFS) are available it contains :-purified diphtheria and tetanus toxoid ,inactivated pertrussis bacteria &purified Hbs Ag from genetically engineered yeast and capsular poly saccharide of haemophilus influenza type b chemically conjugated with tetanus toxoid along with thiomersal as preservative

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- Approaches to produce multivalent vaccines are two types:

❑Attach monoclonal antibodies to a solid support (Matrix) and then react it with antigen to produce *solid matrix-antibody-antigen (SMAA) complex* This resulting complex is used as vaccines.

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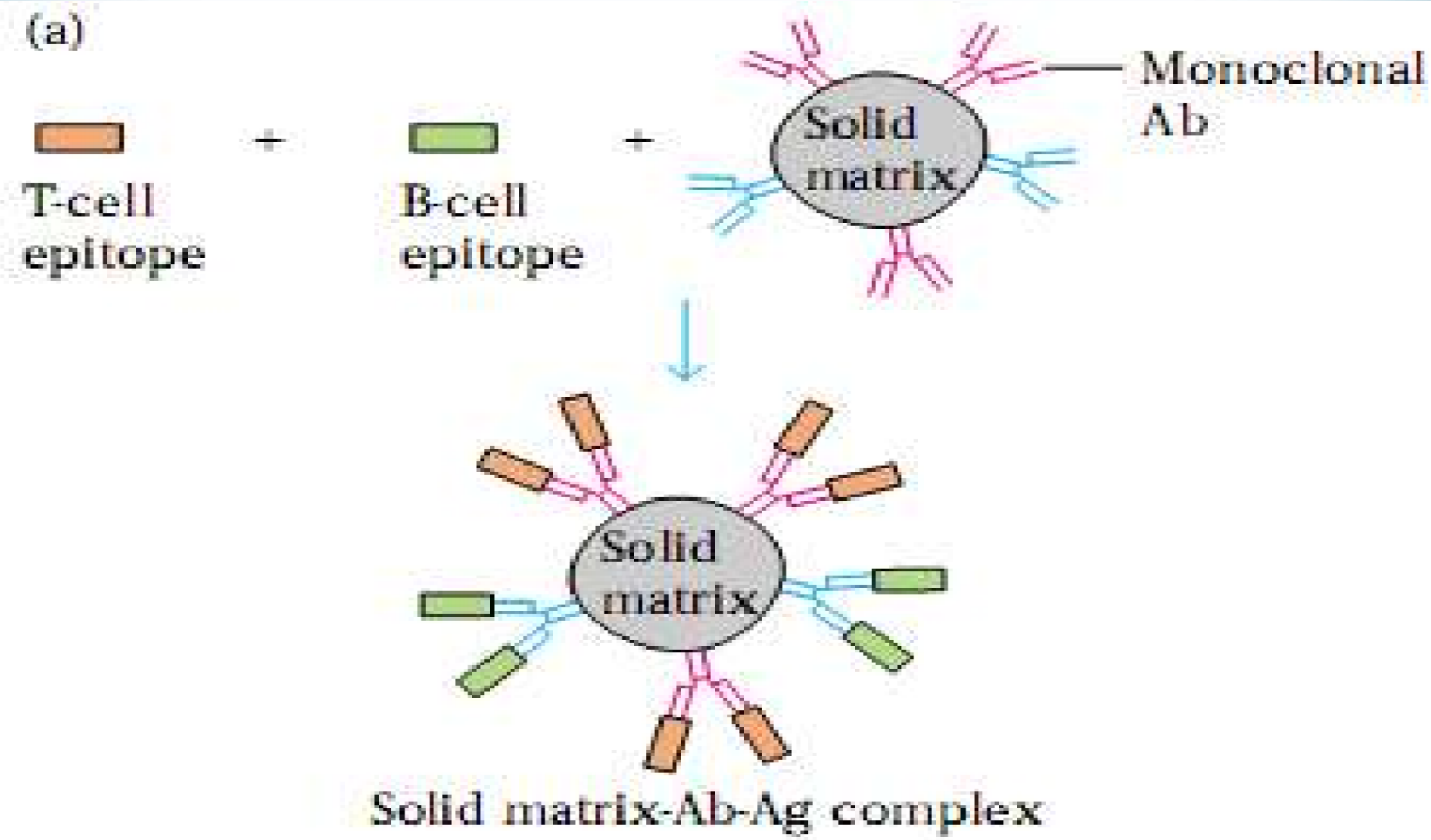
(a)
T-cell epitope
+
B-cell epitope
+
Solid matrix
Monoclonal Ab
Solid matrix
Solid matrix-Ab-Ag complex

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- *Multivalent vaccines* can also be prepared by incorporating protein antigens into protein micelles/lipid vesicles(liposome) /into immunostimulating complexes(*Immuno stimulating complexes(ISCOMs)* are lipid carriers prepared by mixing protein or peptide antigens with detergent and a glycoside called *Quil A*) using detergent.

- In ISCOMs, the long fatty-acid tails of the external detergent layer are adjacent to the hydrophobic residues of the centrally located antigen molecules

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- ISCOMs and liposomes can deliver antigens inside cells, so they mimic endogenous antigens.
- Subsequent processing by the cytosolic pathway and presentation with class I MHC molecules induces a cell-mediated response.

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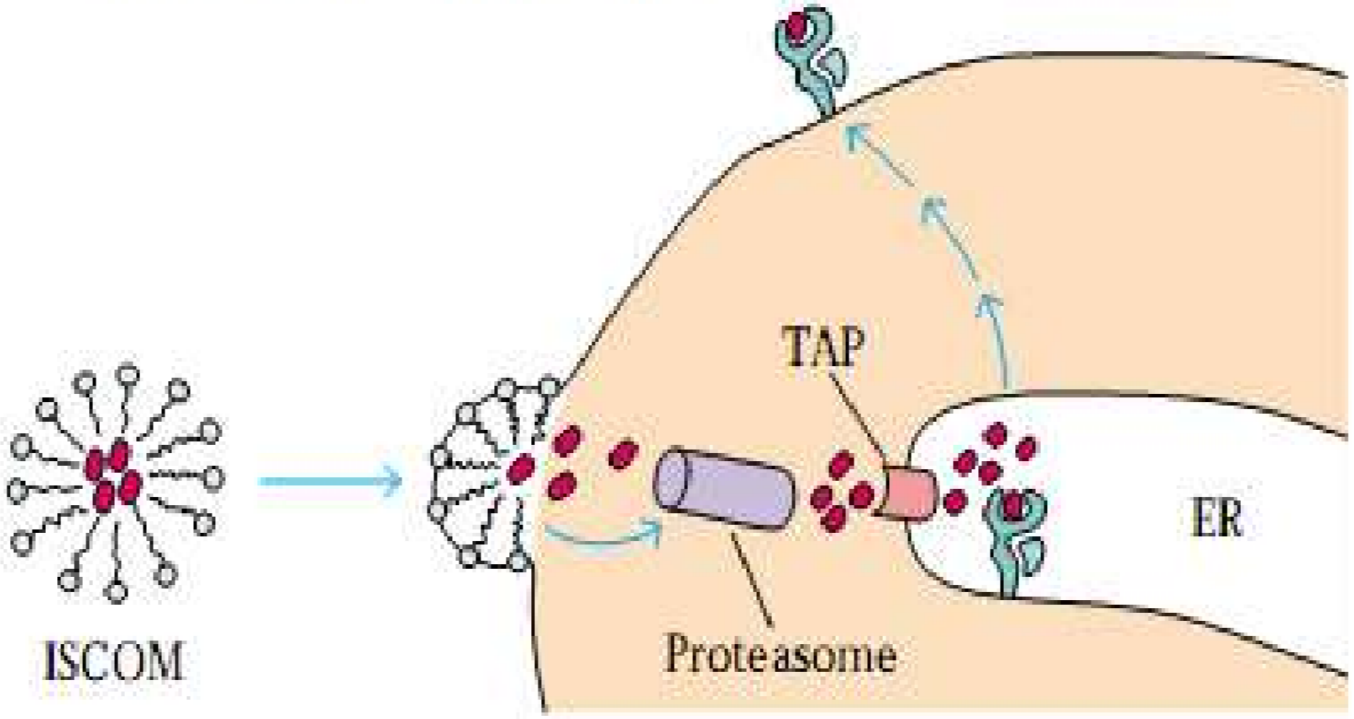
(c) ISCOM delivery of antigen into cell



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2.Synthetic peptide vaccines

- identify the peptide sequences that trigger a protective immune response and to use completely synthetic versions of these as the vaccine substance.
- Because they would be synthetic, there would be no risk of mutation or reversion, little or no risk of contamination by pathogenic or toxic substances, and chemical manipulation of the peptide structure could possibly increase stability and decrease unwanted side effects
- Peptides are not as immunogenic as proteins.

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- It is difficult to elicit both humoral and cellular immunity to them.
- Conjugates and adjuvants can assist in raising protective immunity to peptides
- Construction of synthetic peptide vaccines requires an understanding of the nature of T-cell and B-cell epitopes.
- Amino acid sequence of antigens and its three dimensional structure are studied well.

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- Hydrophilic sequences and B-cell epitopes are identified and synthetic peptides corresponding to B-cell epitopes are prepared.
- Surface antigen of hepatitis B virus-HBsAg's synthetic peptide produced by cyclic repeats of 139-147 amino acids
- A successful peptide vaccine must include immunodominant T-cell epitopes for the production of *memory TH cells*.
- Polymorphism of MHC molecules and variety of peptides are to be considered.

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- The suppressor peptides must be eliminated from the synthetic vaccines.
- This approach enables immunologists to produce defined vaccines that may permit selective activation of either humoral or the cell mediated branch of the immune system.

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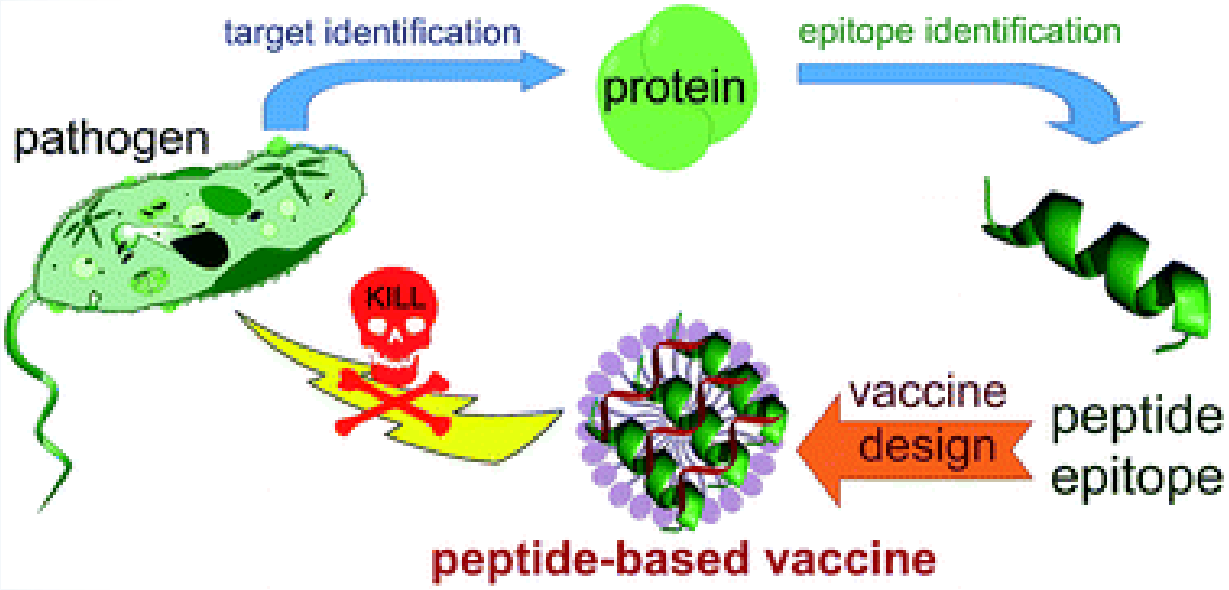
target identification
protein
epitope identification
pathogen
KILL
vaccine
design
peptide
epitope
peptide-based vaccine

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3.DNA VACCINES

- DNA of antigen is used for vaccination
- plasmids are easily constructed and cloned in E coli in large amounts using recombinant DNA technology
- They are purified and injected to muscle with gene gun
- The DNA is taken up by the muscle cells and encoded protein antigen is expressed, leading to both humoral response and cell-mediated response.
- The DNA is integrated to the chromosomal DNA or maintained for long periods in an episomal form.

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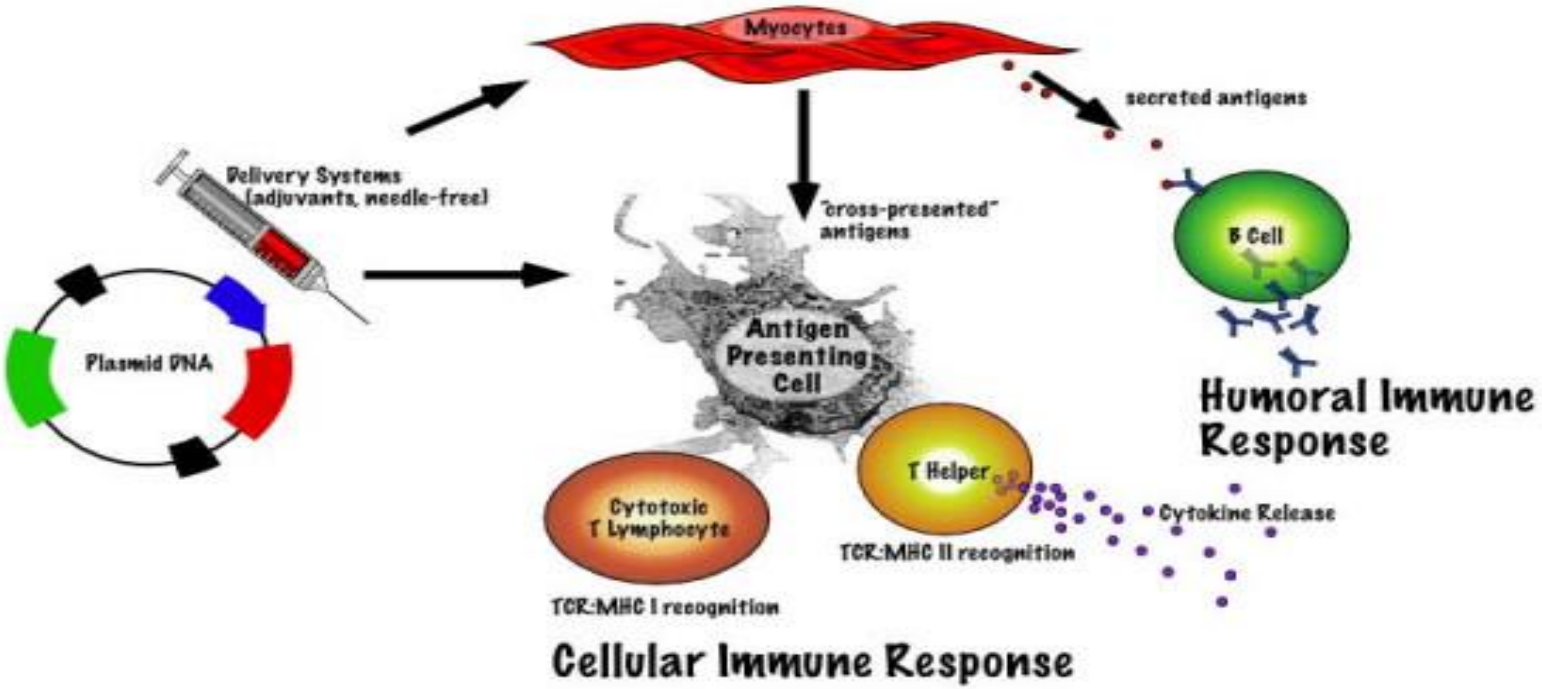
Mechanisms of Action of DNA Vaccines



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- Advantages

In DNA vaccines, the encoded protein is expressed in natural form without any denaturation.

Both arms of immune response are activated.

It has a prolonged efficiency with immunological memory.

Refrigeration is not required.

- Disadvantages

Only protein antigens can be used

Many of the polysaccharide antigens cannot be used in this method.

DNA vaccines cannot be administered orally, as nasal spray and on mucosal surfaces.

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4.RECOMBINANT VECTOR VACCINES

- Genes encoding major antigens of especially virulent pathogens are introduced into attenuated viruses or bacteria.
- This attenuated organism serves as a vector.
- It replicates within a host and express gene product of the pathogen.

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- *Vaccinia virus, canarypox virus, attenuated polio virus, adenoviruses,* attenuated strains of *salmonella* and *BCG* strain of *mycobacterium bovis* etc are used as vectors.

- The canarypox virus has been tried recently as a vector vaccine because it is a large virus that can easily been engineered to carry multiple genes.

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Preparation of recombinant vaccine

Vaccines

- Recombinant Vector Vaccines

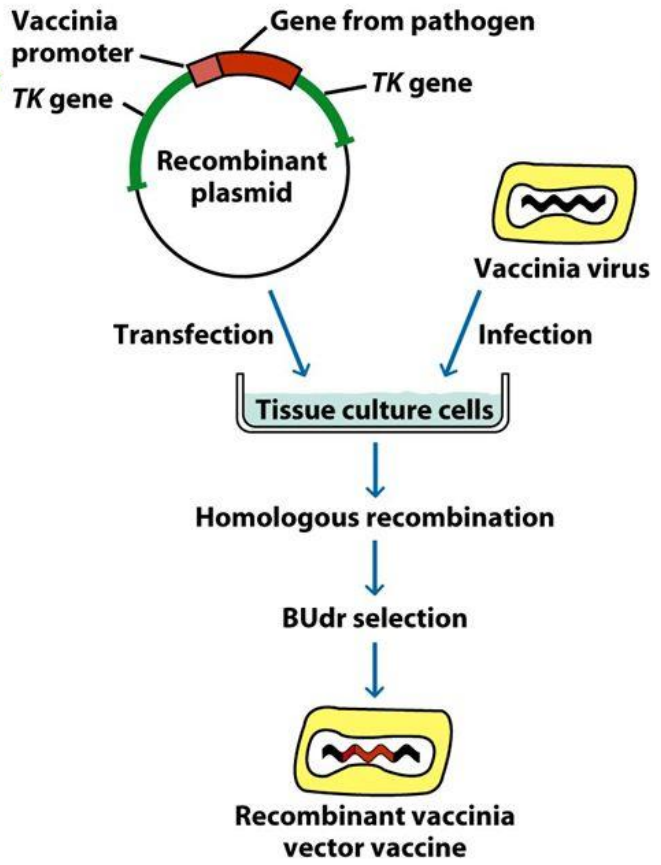

Figure 19-8 part 2
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- The gene that encodes the desired antigen is inserted in to a plasmid vector adjacent to a vaccinia promoter and flanked on either side by the Thymidine kinase (T K) gene.
- When tissue culture cells are incubated simultaneously with vaccinia virus and the recombinent plasmid
- the antigen gene and promoter are inserted into the vaccinia virus genome by homologous recombination at the site of the non-essential TK gene
- resulting in a TK^{-}recombinant virus
- Cells containing the recombinant vaccinia virus are selected by addition of Bromodeoxyuridine (Budr),which killsTK^{+} cells

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- These recombinant vector vaccines can be introduced into an individual simply by scratching the skin
- It induces cell mediated immunity and antibody-mediated immunity.
- **Advantage:**vector replicates in the host cells, which serves to maximize the cell-mediated immunity to the expressed antigens

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