VACCINOLOGY

- History
- Concept of Vaccination
- Trends of Vaccine
  - First Generation Vaccine
  - Second Generation Vaccine
  - Third Generation Vaccine
  - Fourth Generation Vaccine
- Subunit vaccine
- Where we are?

Vaccines-Historical Perspective

- **7th century**- Indian Buddhists' drank snake venom to protect against snake bite.
- **10th century**- Variolation to prevent smallpox in China and Turkey.
- **Early 1700s**- Variolation introduced into England.
- **1760-70**- The Jennerian era.
- **1875-1910**- Dawn of Immunological Science.
- **1910-30**- Early bacterial vaccines, toxins and toxoids.
- **1930-50**- Early viral vaccines: yellow fever and Influenza.
- **1950-1970**- The tissue culture revolution: poliomyelitis, measles, mumps and rubella.
- **1970-1990**- Dawn of the molecular era: hepatitis B, Streptococcus pneumonia, Hemophilus influenza B.
- **Today**- Glycoconjugate vaccines, rotavirus vaccine, human papilloma virus vaccine and herpes zoster vaccine.

Edward Jenner

- First to publish and test immunity by challenge with smallpox
- 1796, inoculated a person, 5 years later vaccination became popular
- Invented smallpox vaccine

Dawn of Immunological Science 1875-1910

Louis Pasteur

- 1881 anthrax vaccine
- 1882 85000 sheep immunized.
- Introduced use of vaccinia virus
- Invented rabies vaccine

Robert Koch

1896 Discovery of *Vibrio cholerae*, killed whole-cell bacterial vaccines

Concept of Vaccination

- **To *protect* those at highest risk**

  (selective immunisation **strategy**)

  or

- **To *eradicate*, *eliminate* or *control* disease**

  (mass immunisation **strategy**)

Currently, it is estimated that vaccination saves the lives of *3 million* children a year

- **Eradication**
  - Infection (pathogen) has been removed worldwide e.g. Smallpox, Rinderpest eradication
- **Elimination**
  - Disease has disappeared from one area but remains elsewhere e.g. polio, measles
- **Control**
  - Disease no longer constitutes a significant public health problem e.g. neo-natal tetanus

Classification

Vaccines:

1. Killed (inactivated)vaccines
2. Live attenuated(weakened)vaccines
3. Toxoids
4. Subunit vaccines
5. Recombinant

Killed vaccines

- These consist of microorganisms killed by heat or chemical
- They generally requires to be given by a series of injections for primary immunization
- The immunity is relatively shorter lasting

  e.g. cholera and meningococcal A&G vaccine

Live attenuated vaccines

- These consist of live bacteria or virus which have been rendered avirulent
- They are grow and multiply in the body of the host to a limited extent
- Live vaccine usually produce long lasting immunity.

  e.g. sabin vaccine ,typhoid oral vaccine

Trends of Vaccine

First Generation

- Live/ Attenuated e.g. Measles, ND etc.
- Inactivated/ Killed e.g. Influenza, Polio

Second Generation

- Subunit e.g. Hepatitis B, Influenza etc.
- Toxoid e.g. Tetanus, Diphtheria etc.
- Conjugate e.g. Anti-cancer vaccine etc.

Third Generation

- Nucleic Acid Vaccine

Fourth Generation

- Recombinant vector e.g. Influenza, Polio
- Genetic manupulated vaccine e.g. BHV, MDV
- Chimera vaccine e.g. BHV & Brucella

First Generation

Live/ Attenuated Vaccine

Tissue culture
Embryonated eggs
Unnatural Live animal host
Unnatural media

Viral:

Lasota vaccine
Influenza vaccine
Oral polio vaccine (Sabin)

Bacterial:

BCG (Bacillus Calmette–Guérin) vaccine

- Administered via injection or natural route (oral, respiratory)
- Humoral immunity (IgG) in bloodstream
- Secretory IgA response
- Good induction of cellular immunity
- Not require adjuvant
- Generally induces long-term immunity
- Vaccine strain may spread to other animals
- Immunodeficient hosts might become ill
- Vaccine may mutate (revert) towards virulence
- May recombine with other viruses in host.
- Heat labile
- More expensive

Killed Vaccine

Chemical
Thermal
Radioactive

Viral:

Influenza vaccine
Rabies vaccine
Hepatitis A vaccine

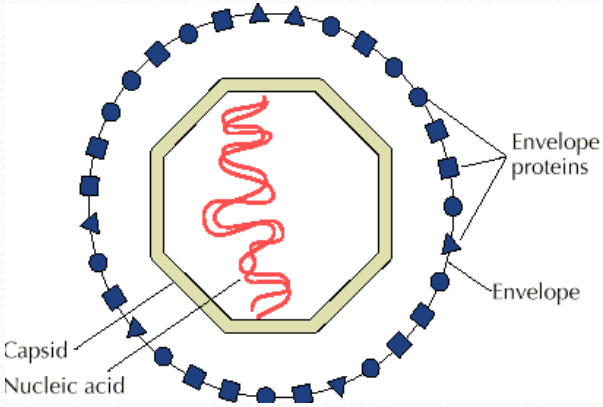
Bacterial:

Cholera vaccine

- Administered via injection
- Produces humoral immunity (IgG) in bloodstream
- Absense of living virus permits use in immunodeficient hosts
- Absence of revert back to virulent pathogen
- No spread of live pathogen to other animals
- Stable (not heat labile)
- Less expensive
- Variable induction of cellular immunity
- Requires adjuvant
- Repeated booster shots required

Second generation vaccine

Subunit/Peptide Vaccines



Not use entire pathogenic agent

Components of pathogenic organism

Generated after the disruption of the pathogen

Heterologus expression

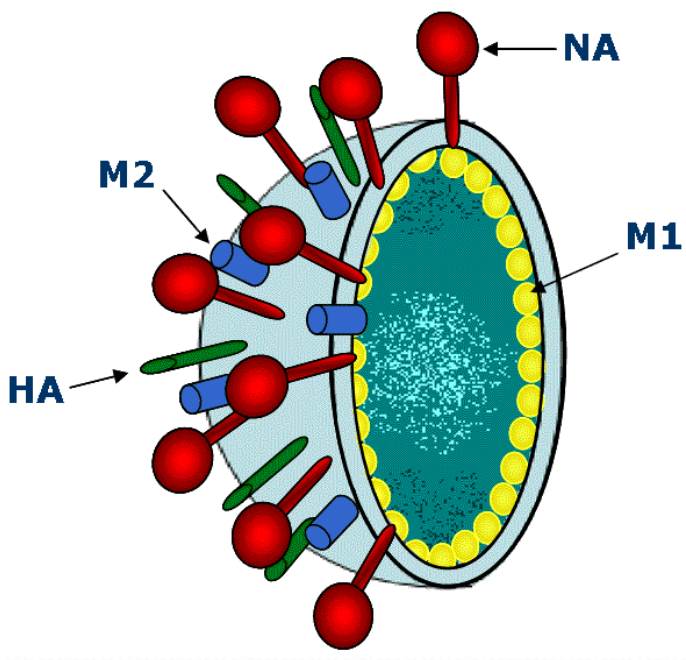
Viral: capsid or envelope

IBD Vaccine (VP2)
FMD Vaccine (VP1)

Bacterial: Outer membrane protein

Salmonella vaccine

Virus-like Particle (VLP)



Structurally similar to virus

Immunologically similar to virus

Do not contain genetic material

Non-infectious

IBD VLP

JE VLP

BT VLP

Edible vaccine

Transgenic plant expressing immunogenic protein

Banana &Tomato: Hepatitis A

Toxoid vaccine

Tetanus and Diphtheria Vaccine

Conjugate Vaccine

Bacterial outer coat polysaccharide carrier protein

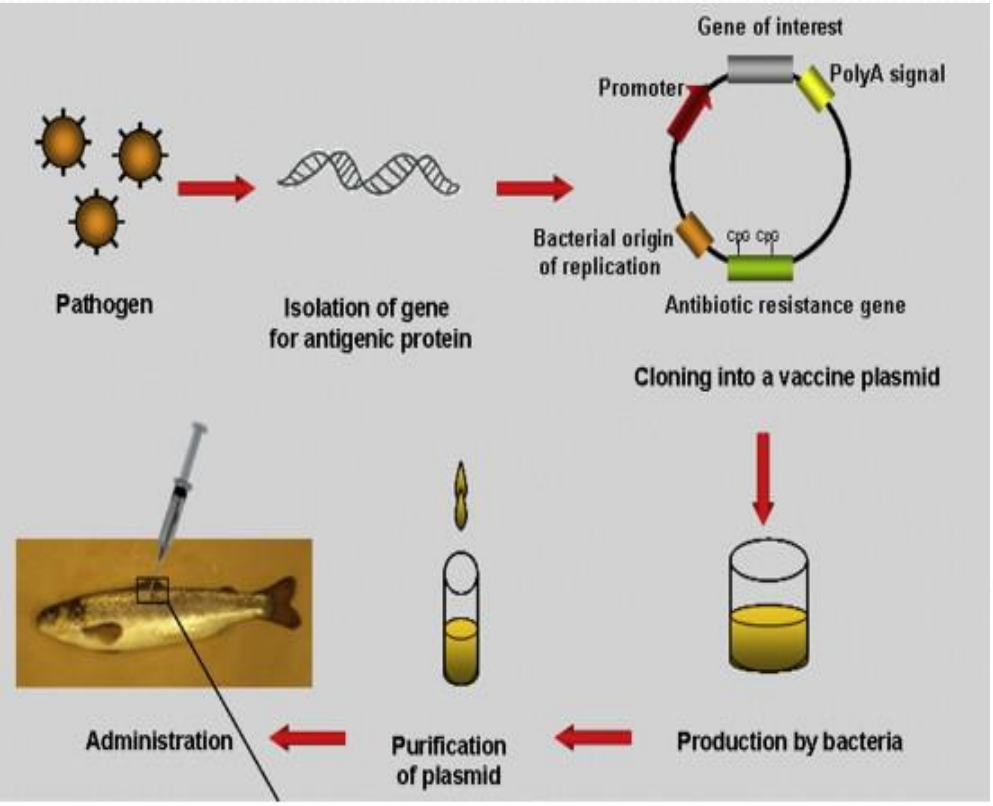
Haemophilus influenzae type B vaccine

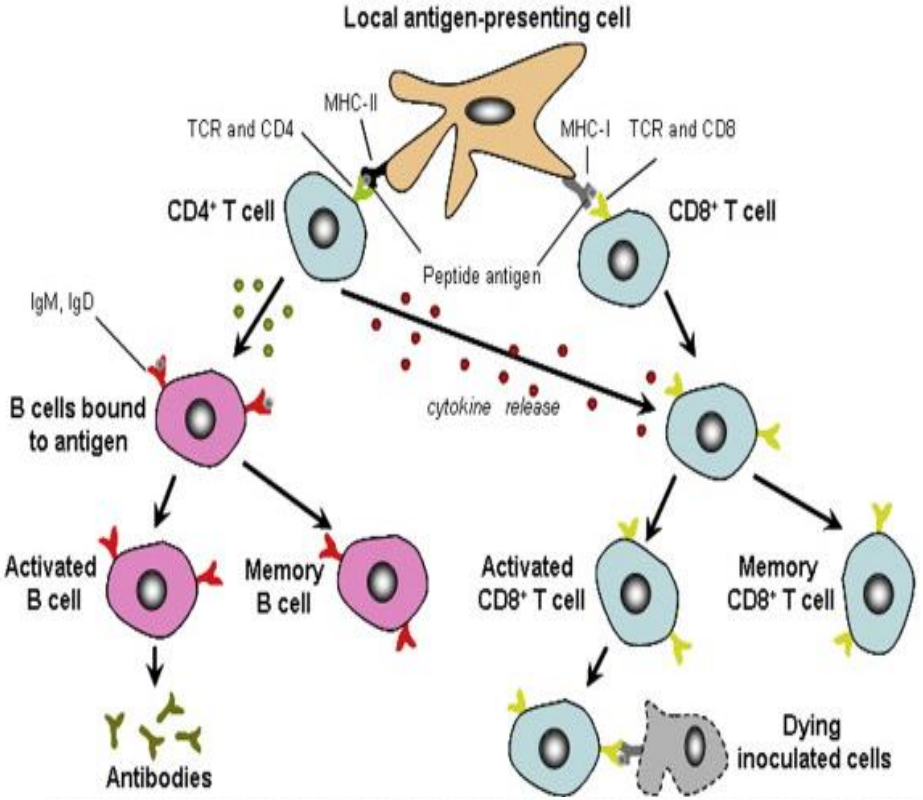
Third Generation Vaccine

Nucleic Acid Vaccine

DNA Vaccine
Vaccine

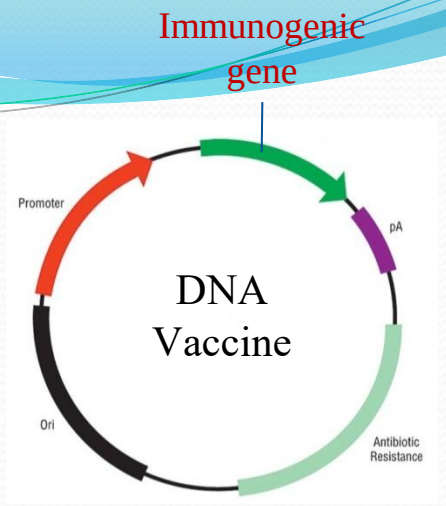
RNA



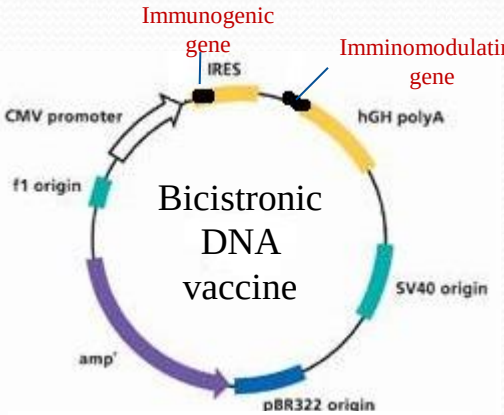


22272 Articles cited in Pubmed

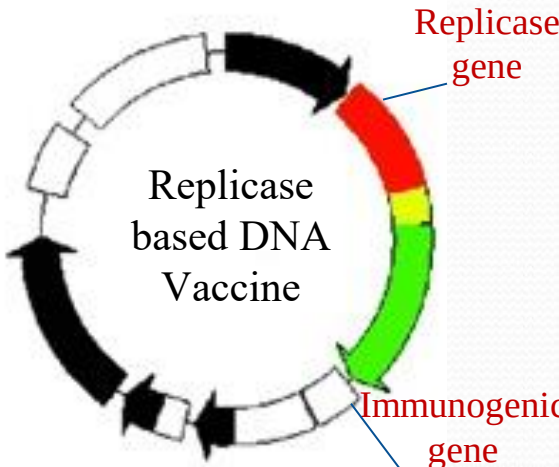
Conventional DNA Vaccine



Bicistronic DNA vaccine



Self replicating/ Replicase based DNA Vaccine



RNA vaccine

mRNA encaptured in liposome

Fourth generation vaccine

Virus vector-based vaccines

Non-pathogenic viruses expressing pathogenic proteins

Vaccinia virus, Adenovirus

Easy to produce in culture

Infect broad spectrum of cell types

Low risk of integration into chromosomal DNA

Gene-deleted marker vaccine

Viral:

BHV vaccine (gE deleted)
MDV vaccine (gE deleted)
Pseudorabies vaccine (gE deleted)

Bacterial:

Salmonella vaccine (*aroA* deleted)

Chimera vaccine

Chimera microbes produced by fusion of genes of two pathogen

JEV-CSFV Chimera
BHV -Brucella Chimera

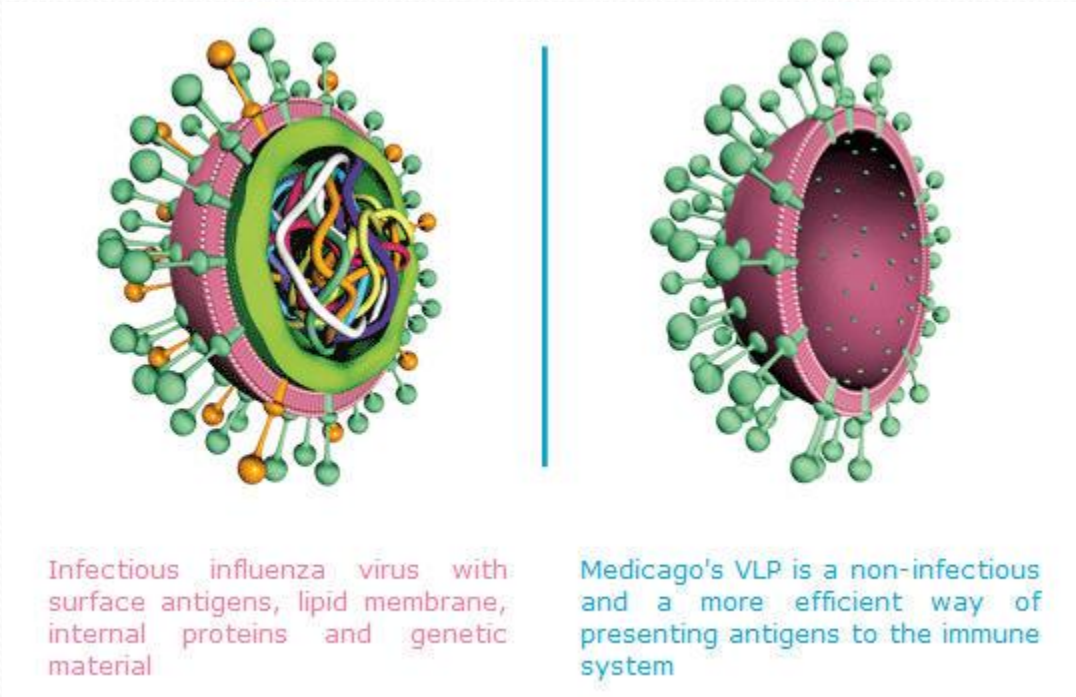
Anti-idiotype Vaccine

Subunit vaccine

- Heterologous expression vaccine
  - Bacterial Expression System
  - Yeast Expression System
  - Insect cell Expression System
  - Mammalian cell Expression System
  - Plant Expression System
- Synthetic peptide vaccines

- **“Structural” vaccination**

Virus-like particles (VLPs)



Infectious influenza virus with surface antigens, lipid membrane, internal proteins and genetic material

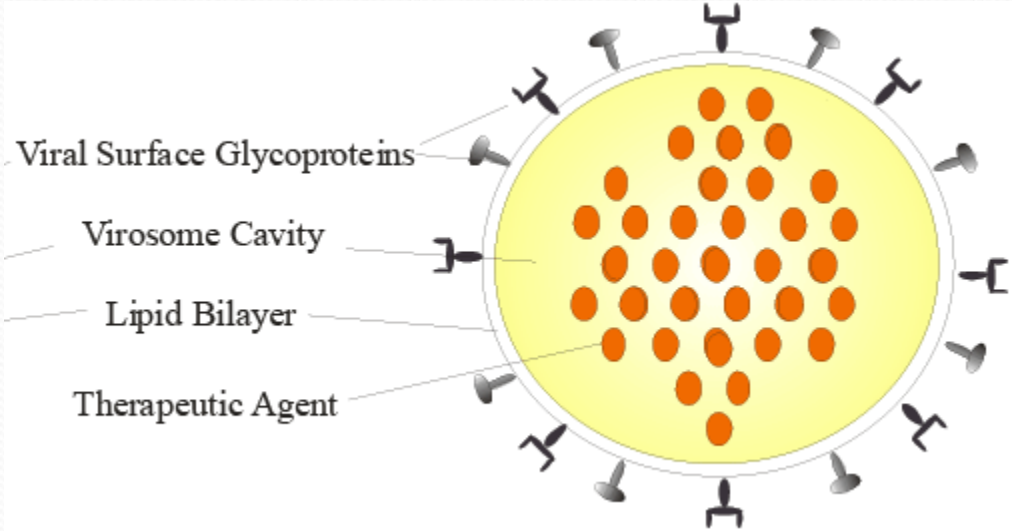
Medicago's VLP is a non-infectious and a more efficient way of presenting antigens to the immune system

- **Virosomes**

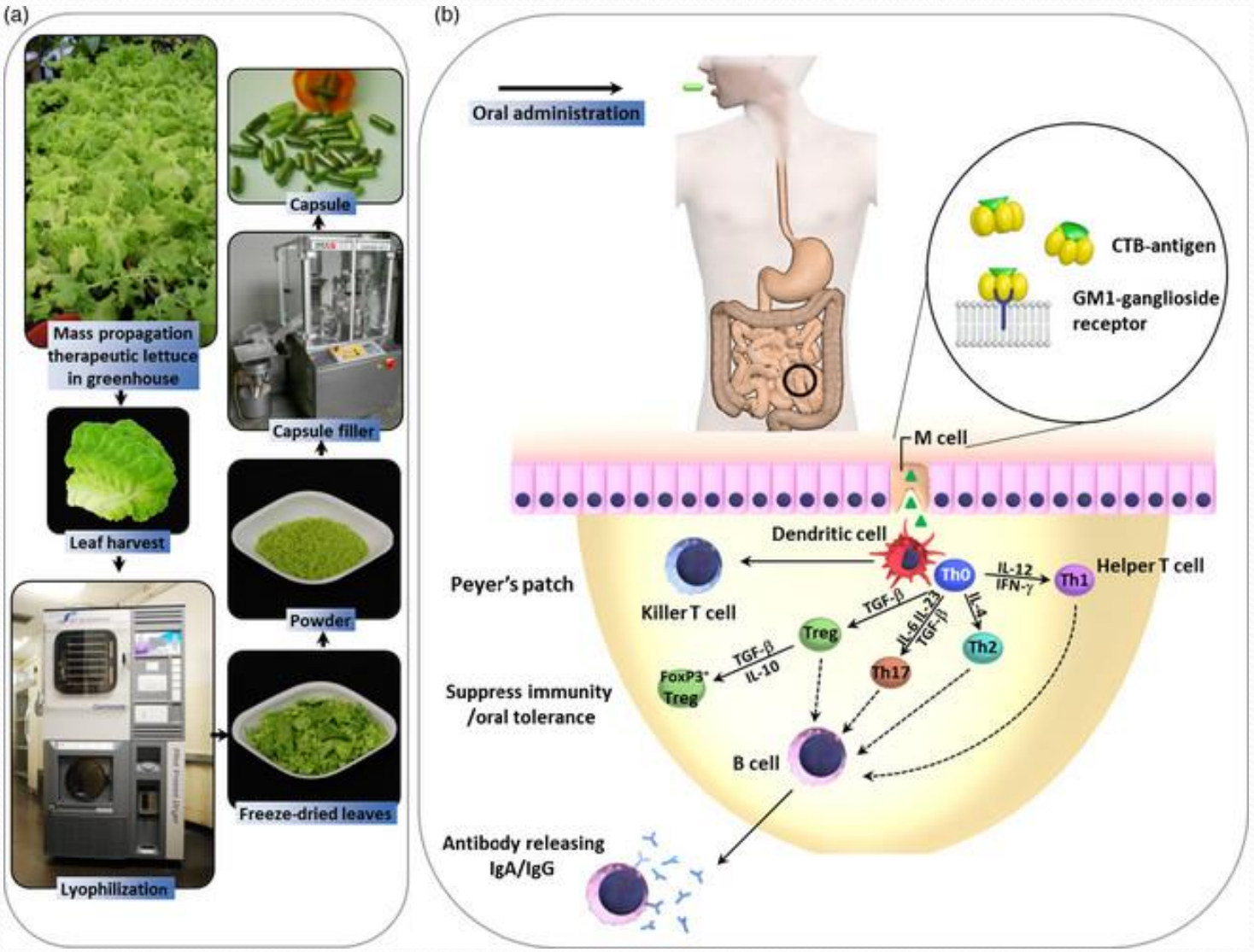
  Quillaja saponaria

  Quil A: **saponins**

  Liposome



- **Plant-made vaccines**



Enteric pathogens

Viral

Norwalk virus capsid protein (NVCP),

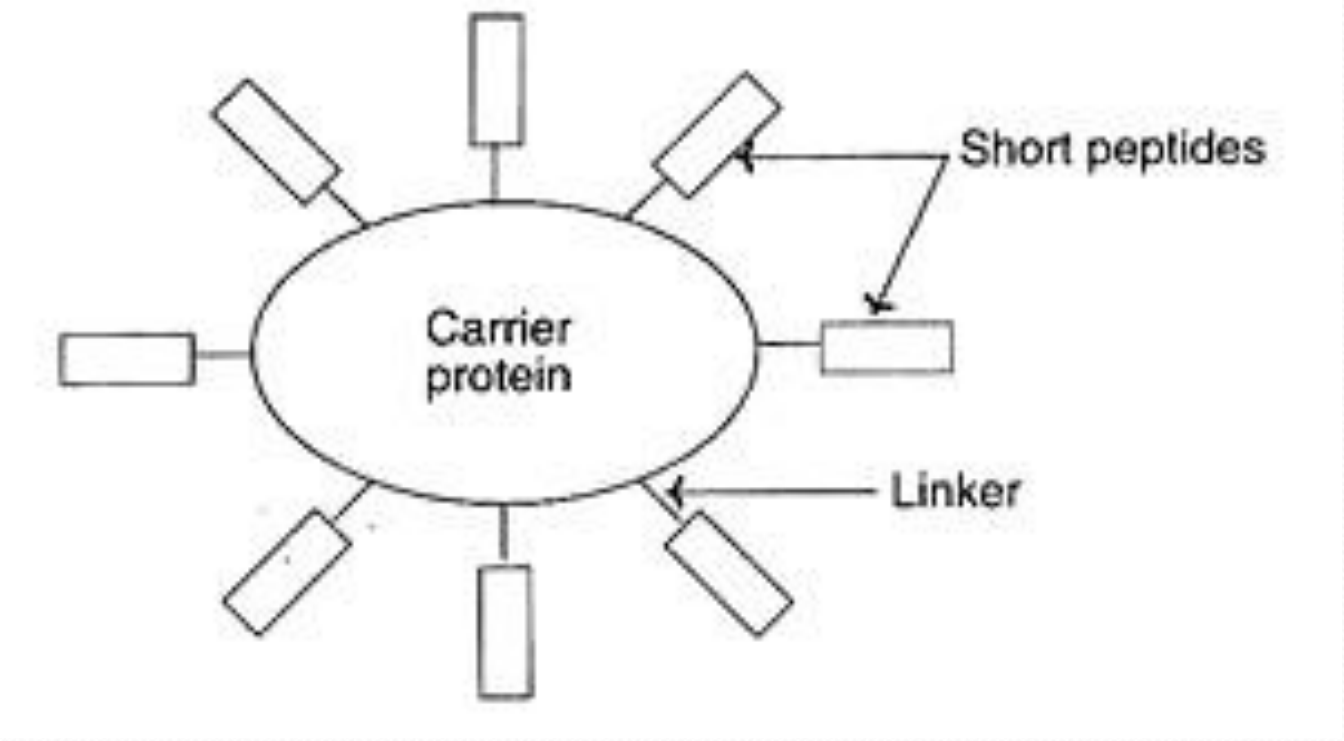
Rotavirus capsid protein

Bacterial

Cholera toxin B subunit (CTB): Ganglioside-binding protein

Eschericia coli heat-labile toxin B subunit (LTB)

- **Synthetic peptide vaccines**



Foot and mouth disease virus (FMDV)
Influenza virus haemagglutinin (HA)

Where we are?

- **Development of gene-deleted BHV Marker vaccine**
- **Development of VLP of JEV as vaccine candidate**
- **Generation of Sub-viral Particle of IBDV as candidate vaccine**