

## Chapter 11-Vaccines

Traditional vs. rDNA vaccines

- Subunit vaccines
- Attenuated vaccines
- Vector vaccines

### Traditional vaccines and their drawbacks

- Traditional vaccines are either inactivated or attenuated infectious agents (bacteria or viruses) injected into an antibody producing organism to produce immunity
- Drawbacks include: inability to grow enough agent, safety concerns, reversion of attenuated strains, incomplete inactivation, shelf life may require refrigeration

Recombinant DNA technology can create better, safer, reliable vaccines

- Immunologically active, non infectious agents can be produced by deleting virulence genes
- A gene(s) encoding a major antigenic determinant(s) can be cloned into a benign carrier organisms (virus or bacteria)
- Genes or portions of genes encoding major antigenic determinants can be cloned in expression vectors and large amounts of the product purified and used as a **subunit** or **peptide vaccine**, respectively

Table 11.1 Some human disease agents for which rDNA vaccines are being developed

Pathogenic agent	Disease
Varicella-zoster virus	Chicken pox
Hepatitis A and B viruses	High fever, liver damage
Herpes simplex virus type 2	Genital ulcers
Influenza A and B viruses	Acute respiratory disease
Rabies virus	Encephalitis
Human immunodeficiency virus	AIDS
<i>Vibrio cholerae</i>	Cholera
<i>Neisseria gonorrhoeae</i>	Gonorrhea
<i>Mycobacterium tuberculosis</i>	Tuberculosis
<i>Plasmodium</i> spp.	Malaria
<i>Trypanosoma</i> spp.	Sleeping sickness

Fig. 11.1 Typical animal virus structure

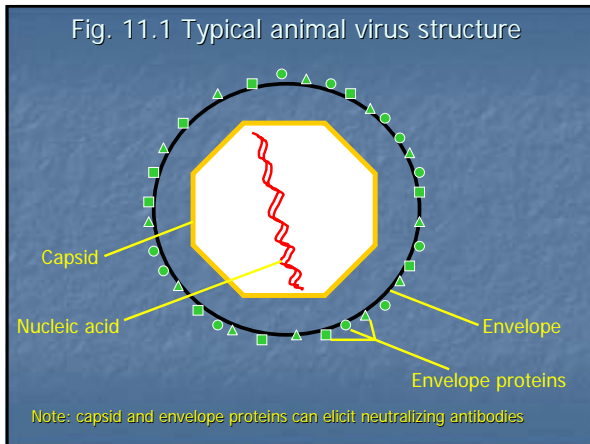
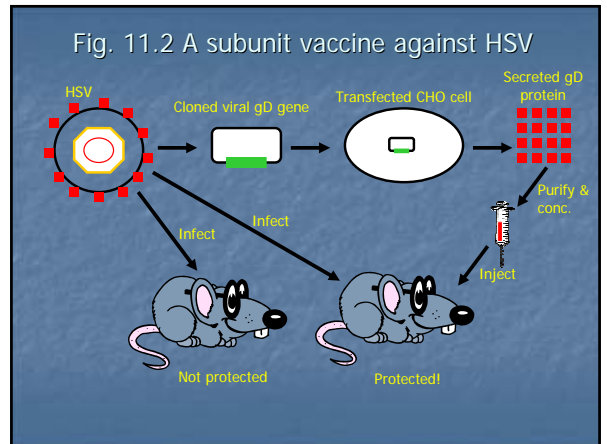


Fig. 11.2 A subunit vaccine against HSV



A similar approach was used to create a subunit vaccine against foot-and-mouth disease virus (FMDV)

- FMDV has a devastating effect on cattle and swine
- The successful subunit vaccine is based on the expression of the **capsid viral protein 1 (VP1)** as a fusion protein with the bacteriophage MS2 replicase protein in *E. coli*
- The FMDV genome consists of a 8kb ssRNA; a cDNA was made to this genome and the VP1 region identified immunologically (see Fig. 11.4)

Fig. 11.6 Structure of a peptide vaccine, representing yet another rDNA approach

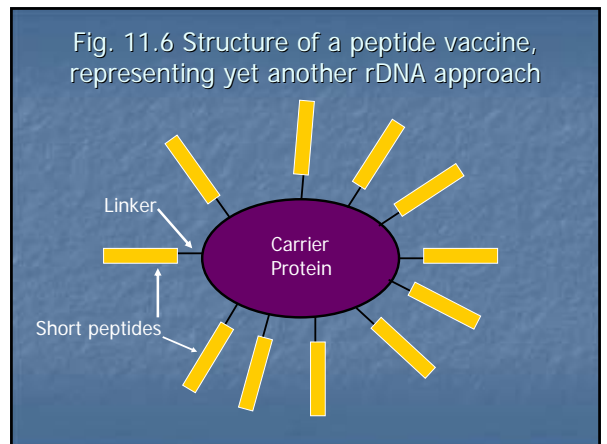


Fig. 11.10 Genetic immunization: DNA vaccines represent another rDNA approach

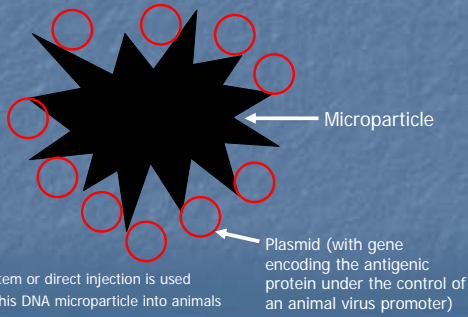


Table 11.2 Advantages of genetic immunization over traditional vaccines

- Culturing of dangerous infectious agents is avoided
- No chance to revert to virulence
- Avoid any side effects of attenuated vaccines in young or old (immunocompromised) animals
- Production is inexpensive since there is no need to produce or purify protein
- Storage is inexpensive since DNA is stable
- One plasmid could encode several antigens/vaccines or several plasmids could be mixed and administered simultaneously

### Attenuated vaccines

- Attenuated vaccines traditionally use nonpathogenic bacteria or viruses related to their pathogenic counterparts
- Genetic manipulation may also be used to create attenuated vaccines by deleting a key disease causing gene from the pathogenic agent
- Example: the enterotoxin gene for the A1 peptide of *V. cholerae*, the causative agent of cholera, was deleted; the resulting bacterial was non pathogenic and yet elicits a good immunoprotection (some side effects noted however)

### Vector vaccines

- Here the idea is to use a benign virus as a vector to carry your favorite antigen gene from some pathogenic agent
- The **vaccinia virus** is one such benign virus and has been used to express such antigens
- Properties of the vaccinia virus: 187kb dsDNA genome, encodes ~200 different proteins, replicates in the cytoplasm with its own replication machinery, broad host range, stable for years after drying
- However, the virus genome is very large and lacks unique RE sites, so gene encoding specific antigens must be introduced into the viral genome by homologous recombination (see Fig. 11.16)