



VACCINE DEVELOPMENT USING RECOMBINANT DNA TECHNOLOGY

Animal Agriculture's
Future through
Biotechnology

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CAST

The Science Source for Food,
Agricultural, and Environmental Issues

Vaccines Represent one of the Greatest Success Stories in Biology

- Edward Jenner in 1798 used cowpox virus to immunize people against smallpox
- Smallpox eradicated



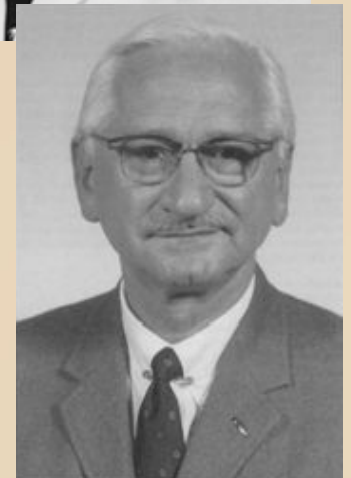
Vaccines Represent one of the Greatest Success Stories in Biology

Killed and Attenuated Polio Vaccines

- Jonas Salk: Killed Vaccine
- Albert Sabin: Live Vaccine
- Polio almost eradicated



Jonas Salk



Albert Sabin

Vaccines Represent one of the Greatest Success Stories in Biology

- Rinderpest has decimated cattle and wild populations of buffalo, giraffe, and wildebeest
- The virus was last detected in 2001 in wild buffaloes in Meru National Park in Kenya



Vaccines Represent one of the Greatest Success Stories in Biology

Other Animal Diseases that Conceivably could be Eradicated



Foot and Mouth Disease



Peste des Petits Ruminants

Remainder of Talk

1. Compare conventional vs recombinant DNA vaccines
2. Describe the different classes of recombinant DNA vaccines
3. Describe recombinant DNA vaccines for different animals (cattle, sheep, goats, swine, poultry, fish and companion animals)
4. Future trends and developments

Conventional vs Recombinant DNA Vaccines

Conventional

- Chemical or physical inactivation (Killed)
- Laboratory induced changes to weaken pathogen (Live Attenuated)
- Isolate related and attenuated (Live Attenuated)

Problem: Limited resources and possibility of reversion

Recombinant DNA

- Recombinant generated subunit or DNA vaccines (killed)
- Gene deleted pathogens (Live)
- Vector-based organisms designed to deliver foreign gene products (Live)

Advantage: Safe and possible to design vaccine to order

Subunit Vaccines (Cat. I)

Gene coding for antigen



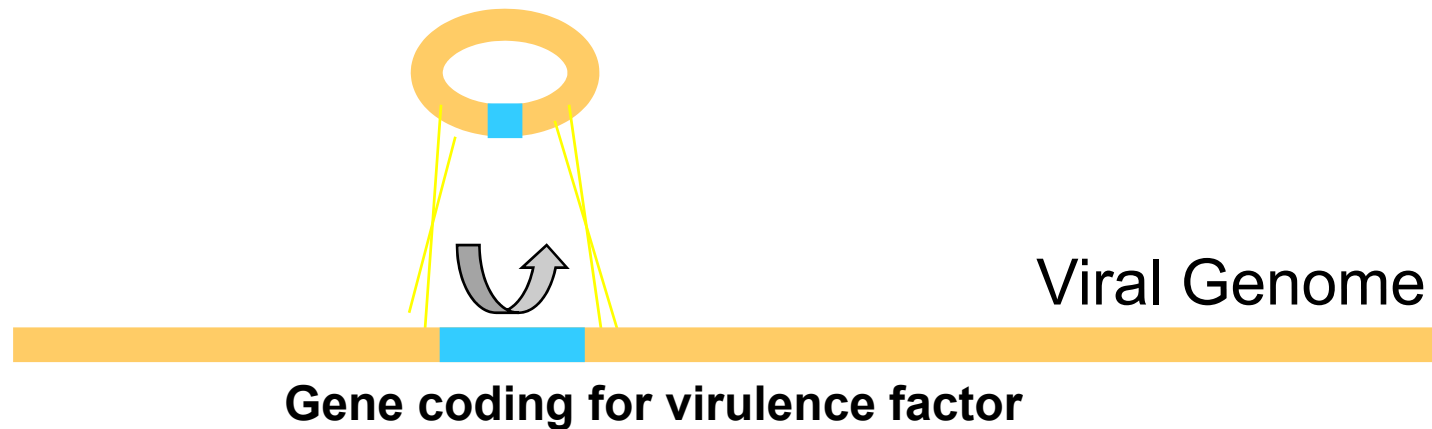
Viral Genome



Pro: Safe

Con: Low levels; Not as protective as live vaccine

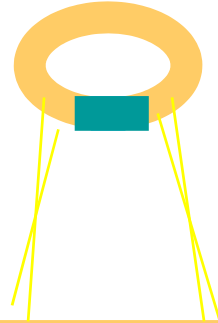
Knockout Mutants (Cat. II)



Pro: Differentiating Infected from Vaccinated Animals (DIVA);
Usually highly protective

Con: Potential for reversion

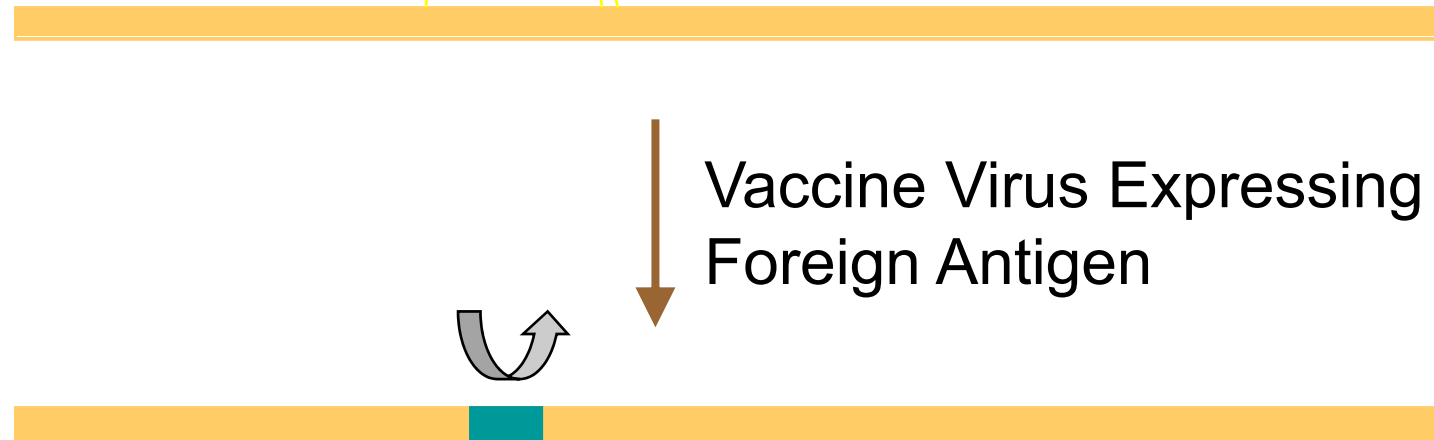
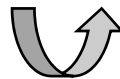
Viral Vectors (Cat. III)



Attenuated or Vaccine Virus



Vaccine Virus Expressing Foreign Antigen

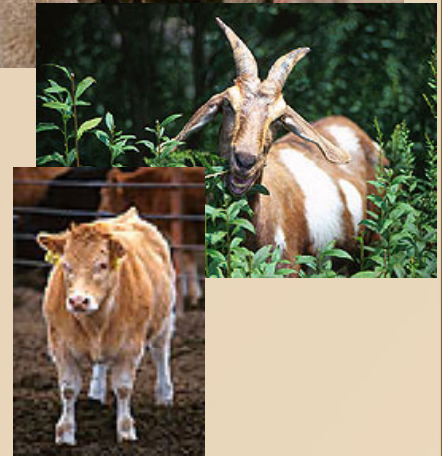


Pro: Polyvalent Vaccines; Usually highly protective; Safe

Con: none

Recombinant Vaccines for Cattle, Sheep, and Goats

- There are no U.S. licensed recombinant vaccines
- EU licensed naturally occurring gE deletion of bovine infectious rhinotracheitis
- E2 gene deleted bovine viral diarrhea virus protects against BVD and does not produce infectious virus
- Gene deleted bovine respiratory syncytial virus protects against shipping fever and does not produce infectious virus
- FanC subunit of *E. coli* expressed in soybeans as possible oral vaccine for *E. coli* induced diarrhea in cattle, sheep and goats
- Capripox vaccine used as vector to protect against rinderpest and peste-des-petits ruminants



Recombinant Vaccines for Swine

- Licensed gI and gX deleted pseudorabies virus for DIVA-based eradication of pseudorabies in U.S.
- Subunit vaccine of toxin fragments from *Pasteurella multocida* resulted in improved survival
- Pseudorabies virus vaccine used as vector to express spike gene from coronavirus transmissible gastroenteritis virus
- Human adenovirus used as vector to deliver hemagglutinin and nucleoproteins from swine influenza virus



Recombinant Vaccines for Poultry

- There are 11 U.S. licensed rDNA poultry vaccines
- Fowlpox virus vectored vaccines for avian influenza, Newcastle disease, avian encephalomyelitis, laryngotracheitis, and *Mycoplasma gallisepticum*
- Marek's disease virus vectored vaccines for Newcastle disease, laryngotracheitis, and infectious bursal disease
- Double deletion mutant of *Salmonella typhimurium*
- Deletion mutant of laryngotracheitis virus expressing hemagglutinin gene from avian influenza



Recombinant Vaccines for Fish

- There are no U.S. licensed recombinant vaccines
- Canada licensed first DNA vaccine for infectious haemopoetic necrosis virus in salmon
- Two subunit vaccines are effective against viral hemorrhagic septicemia in trout
- DNA vaccines for infectious salmon anemia virus show promise
- Recombinant protein vaccines for infectious pancreatic necrosis virus have shown some protective efficacy for salmon



Recombinant Vaccines for Companion Animals

- There are a number of canarypox-vectored U.S. licensed recombinant vaccines
- Canarypox-vectored canine vaccines for Lyme disease, canine distemper, and canine rabies
- Canarypox-vectored feline vaccines for leukemia and feline rabies
- Canarypox-vectored horse vaccines for West Nile and equine influenza
- DNA vaccine expressing human tyrosinase-encoding gene to enhance long-term survival in canine malignant melanoma



Future Developments

- Identification and utilization of better immunogens and new vaccines for diseases for which no currently available vaccines exist
- Better vaccine delivery methods: oral, intranasal, and needle-free systems allowing mass vaccinations
- Use of immunomodulators in vector-based vaccines: CpG motifs and cytokines
- Viral vectors to deliver small interfering RNAs (siRNA)
- Expression of foreign proteins in plants and the development of edible vaccines
- Vaccines developed for non-infectious agents: control and prevent cancer; vaccines to induce long lasting contraception

**Vaccination has been
one of the major success
stories in biology**

**The future of animal
vaccines promises to be
even more rewarding**

