Why is it so difficult to make a vaccine for ASF?

Virus:
- one of the largest viruses; > 150 genes, 170 proteins (Ebola virus has 7 proteins)
- > 20 different genotypes
- Different hosts, different life-cycles
- Hardy virus, can survive in extreme pH and temperature variations
- Difficult to grow the virus in culture
- Requires special facilities, limited funding available
Why is it so difficult to make a vaccine for ASF?

Immune response:
- > 40 genes involved in modulating immune response
- Inhibits cell death (apoptosis)
- Infects and replicates in macrophages; kills B and T cells
- Passive transfer of serum antibodies provides protection
- T cell response crucial for protection
- Single genotype protection

Reis et al. 2017
Can fit about 10,000 viruses on the rim of a coin

About 100 nm
Architecture of the ASF virus
Vaccine types in development?

- **Live attenuated** (genetically modified)
  - Gene-deletion mutant
  - Natural mutants

- **Subunit** vaccines
  - Protein cocktails

- **Vector-based** vaccines
  - Viral vector for delivery of genes

- DNA vaccine
- Inactivated virus
Genetically attenuated viruses

- Live virus, but less virulent (less disease causing)
  - Pirbright, UK (double-deletion)
  - Madrid Spain (double-deletion)
  - Plum Island, US (triple-deletion)
  - Harbin Institute, China (double-deletion)

- Vaccine viruses with 1-3 deletions described so far
- Level of protection quite good against the same genotype, although usually short term protection

**BUT:**
- Safety: not enough = weak response; too much = induces disease
- Shedding of the virus (environment, natural reservoirs, etc.)
- Genetic stability
- No DIVA marker established yet; difficult to grow in culture
Naturally attenuated vaccines - Vaccination of wild boar

- April 2019
- Attenuated, non-hemadsorbing p72 genotype II ASFV Lv17/WB/Rie1
- 12 wild boar piglets per group
- 9 immunized, 3 through contact
- Orally immunized with $10^4$ TCID$_{50}$
- After 30 days all animals were exposed to shedder animals for infection

Barasona et al. 2019
Protein cocktails

- Very safe, no viable virus
  - Mwangi (Kansas)- delivery via adeno
  - Dixon (Pirbright)

- Neither of the cocktails showed complete protection

- Latest data from Pirbright looks very promising, started out with 38 proteins down to 5 proteins

- How to improve protein cocktails?
  - Viral vectors
  - Adjuvants
Viral vectors

- Only few ASF genes selected
- Incorporated in another virus
- Other virus is used to deliver the genes (vector)
- Very safe, no viable ASF virus
- Examples: Adenovirus, Canarypox, Modified Vaccinia, etc.
- Has the advantage of inducing good immunity while not using live ASF virus
Will we ever use a vaccine in North America?

- Not likely:
  - Safety of live-attenuated vaccines and risk of transmission
  - No DIVA marker available
  - No companion diagnostic

- Protein cocktail or vectored vaccine more likely, however, none of them there yet

- Antivirals?
Antivirals

- Drugs that can reduce replication of the virus
- Reduced shedding and reduced transmission
- But: how long does the effect last?
- How to administer?
- Cost?
Summary

- Live-attenuated vaccines are becoming available to protect against current strains
- Will be used in China and other parts of Asia, not a viable option for Canada
- Subunit vaccines (protein cocktail) or viral vector only possibility for Canada, however, no promising candidates at the moment, will likely take a few years
- Antivirals can help to contain outbreaks. Cull infected animals. Nearby animals could be treated to reduce viral spread
Thank you