

Alphavirus Replicon Vaccines for Marburg and Ebola Viruses

Performed through

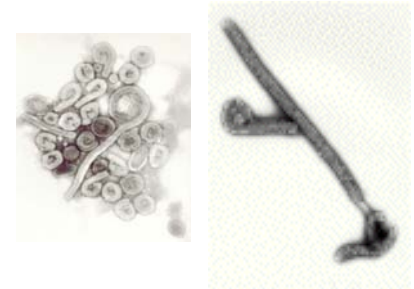
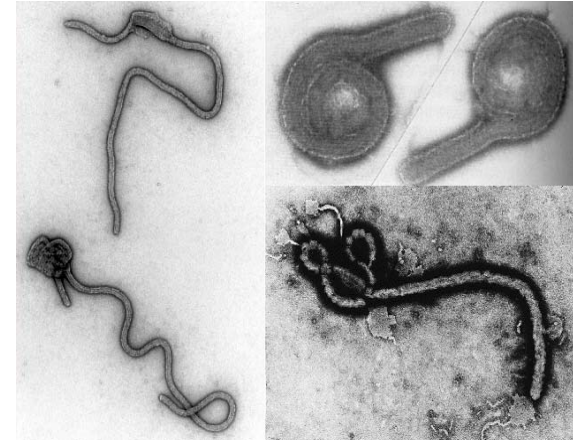
- (1) NIH Grant No. U01 AI056438 to AlphaVax, and
- (2) A Cooperative Research and Development Agreement (CRADA) between AlphaVax and the US Army Medical Research Institute for Infectious Diseases (USAMRIID) at Fort Detrick, MD.



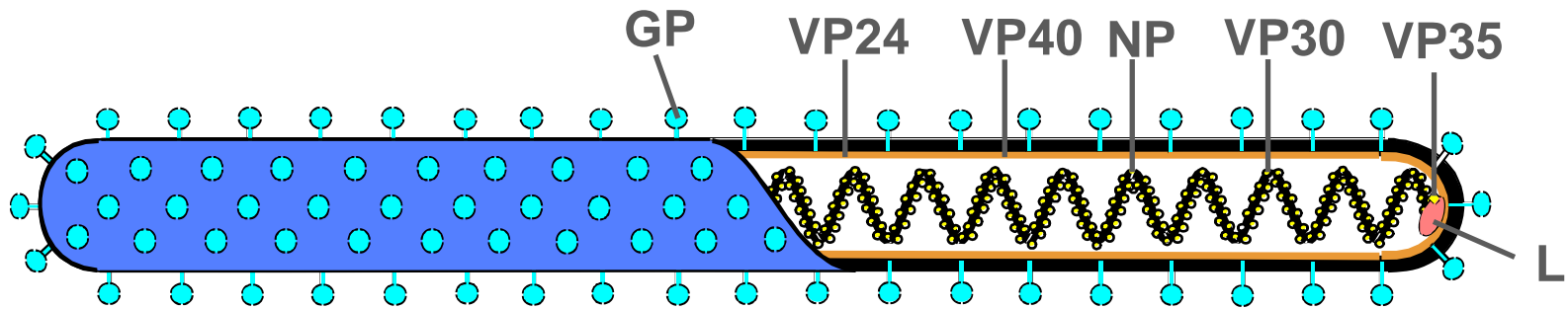
Filovirus Hemorrhagic Fevers

Ebola and Marburg Viruses

- First reported case 1976, Zaire
- Category A Bioterrorism Agents (CDC)
- Negative sense, enveloped, ssRNA virus
- Filamentous morphology
- Epidemiology
 - Natural host is unknown
 - Transmission associated with close contact (blood or body fluids)
- Clinical Features
 - Incubation period: 4-21 days
 - Abrupt onset of nonspecific symptoms
 - Liver function impaired
 - Bleeding & dysregulated coagulation (clotting)
 - Death/shock 6-9 days after onset
 - Case fatality rates high (40-90%)



Structure and Genetic Organization of Filoviruses



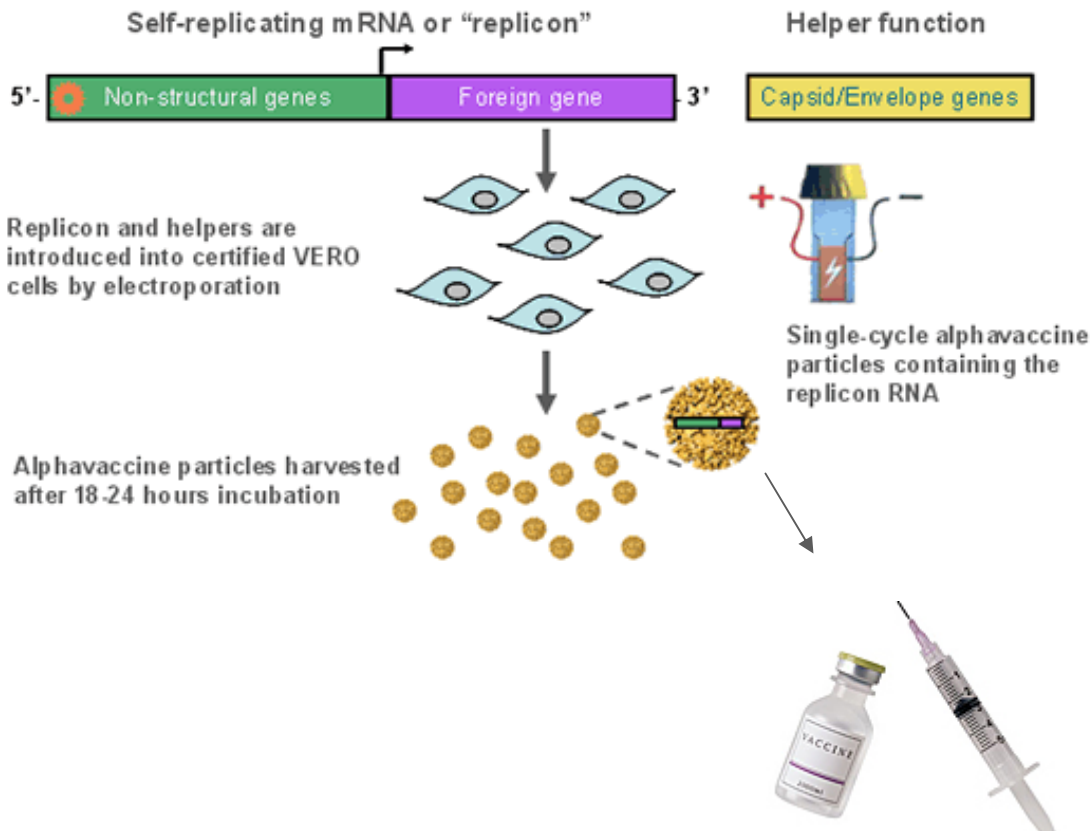
Organization of the Filovirus Genome



NP	Major nucleocapsid protein
VP35	Phosphoprotein, IFN antagonist
VP40	Membrane-associated matrix protein
GP	Transmembrane glycoprotein
sGP	Secreted glycoprotein
VP30	Ribonucleoprotein associated (minor)
VP24	Membrane-associated protein (minor)
L	RNA-dependent RNA polymerase

- Single-strand negative sense
- RNA of ~19 kilobases
- Produces 7 mRNAs upon infection

Alphavirus Replicon Particle Vaccines (“VRP”)



VRP Advantages:

- High antigen expression and targeting to dendritic cells (potent Antigen Presenting Cells)
- Induction of broad humoral and cellular responses
- Multivalent VRP vaccines easily constructed
- Single-cycle RNA based expression vector
- Scalable and economic production process developed
- Sound clinical safety profile
- Lack of pre-existing immunity in population.

VRP Vaccine Candidates for Ebola and Marburg Viruses – Summary Results

- **A single vaccination with VRP expressing the glycoprotein (“GP”) of either the Marburg (“MBG”) or Ebola (“EB”) virus protects against intramuscular or aerosol challenge with the homologous filovirus in non-human primates**
- **Vaccination with VRP expressing MBG GP from one strain of the MBG virus also provided protection against two other MBG strains**
- **Work to date supports the establishment of a possible correlate of protection based on VRP vaccine-induced GP-specific antibody levels in serum for assessing the efficacy of vaccines for use in humans**