1 Types of Viral Genomes (Baltimore Classification)

All types of viruses make mRNA (messenger RNA) which allows them to make proteins

+ sense: The genome can be translated directly into proteins

− sense: Other strand must be transcribed (turned into + sense) to make viral proteins

The type of genome can give clues as to how the virus replicates and evolves

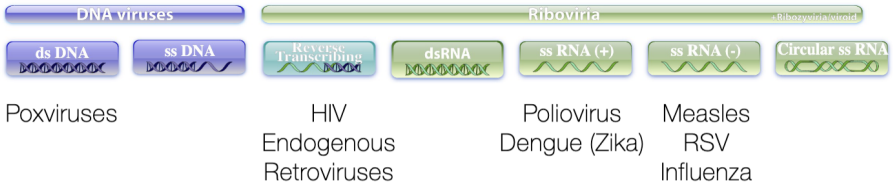

Figure 1: Viral genomes

2 Poxviruses

Family: *Poxviridae*

Double Stranded DNA genome

Replicates in the cytoplasm of the cells

Extremely large virus (Virion can be seen with just light microscopy)

Subfamily: *Chordopoxvirinae*

Genus: *Orthopoxvirus*

Examples: Vaccinia virus, Cowpox virus, Mpox (Monkeypox) virus, Raccoonpox virus, Variola virus

Note: First vaccine and the only human virus that has ever been completely eradicated

2.1 Genome

Many RNA viruses are ∼10 kb in size

Poxviruses have 170-250 kb of a linear, dsDNA genome

1. Tightly packed genome
2. Genes are not overlapping and do not have introns
3. Replicate in the cell cytoplasm (no splicing)
4. Encode many immunomodulatory genes
5. Over 100 ORFs (open reading frames) (genes that encode proteins)

2.1.1 Immunomodulation

Infected cells that sense viral infection release interferons (IFNs)

Poxviruses make a decoy receptor, binding to the IFN (similar to a neutralizing antibody)

3 Smallpox

Transmission: Respiratory droplets, 'fomites', close contact

Lethality: ∼30% plus significant scarring

Ancient disease of humans

1. Over 3000 years ago in India, China, and Africa
2. Endemic in Asia by 1000 A.D.
3. Endemic in every European country by the end of the 19th century
4. Large epidemics in Europe (1200-1600) and the Americas (1507-1524)

Ex: Estimated 40% of Tenochtitlan (pop: 200,000) died from Smallpox in 1520

Ancient remains can be used to sequence and date Smallpox using phyogenetics

Viking age Variola Virus discovered in 2020

3.1 Variolation

Early form of vaccination for Smallpox

16th century: First reference to inoculation with dried pox in China (likely also used in India)

Variolation: Dried material from infected persons ground up and placed under skin or inhaled

Risk of Death: 14% → 2%

Risks: 2-3% of people develop severe smallpox infection and spread disease

3.2 Early Vaccines

1790s: Observation that milkmaids exposed to cowpox did not develop smallpox

Edward Jenner inoculated his gardener's son with cowpox and showed that the boy did not become sick after infection with smallpox scabs

Called the process vaccination (vacca: latin for cow)

3.3 Vaccinia Virus

Poxviruses infect a wide range of mammalian species

Smallpox Vaccine: Live-attenuated viruses with unknown origins and attenuation history

Vaccinia virus-MVA is more closely related to monkeypox than smallpox

3.4 Orthopoxvirus Diversity

Cross-species transmission of poxviruses can occur

1. Cowpox from cows to humans
2. Monkeypox from small mammals to humans
3. Buffalopox from water buffaloes to humans
4. Spread within humans limited after transmissions

Despite genetic diversity, infection with one orthopoxvirus can confer protective immunity against another

3.5 Eradication

Smallpox officially declared eradicated in 1980

Led to the end of smallpox vaccination

>70% of the global population is not immune to smallpox (or other related poxviruses)

3.6 Mpox

Can trigger fevers, aches, and painful fluid-filled skin lesions (can be fatal)

Mpox endemic in parts of Africa (Likely a rodent reservoir / spillover in 2022)

Endemic: Majority non-sexual transmission

2022 (Americas and Europe): Majority sexual encounters in gay populations

3.6.1 Case Fatality Rate (CFR)

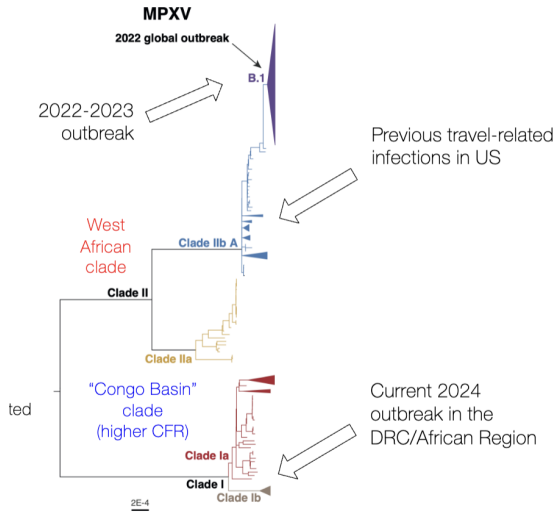

Figure 2: Different versions of MPXV

Notes:

1. Not all infections are detected
2. Less severe cases not documented
3. Other heath conditions

3.6.2 Modern Vaccines

Smallpox vaccine protects against Mpox infection (Relatedness and immune cross-reactivity)

Current Challenge: Lack of vaccine supply where it is needed (Ex: DRC)