

Meeting 2 of the Committee on Current State of Research, Development, and Stockpiling of Smallpox MCMs

December 1, 2023

Overview of Mpox Virus Research in the Laboratory of Viral
Diseases, NIAID

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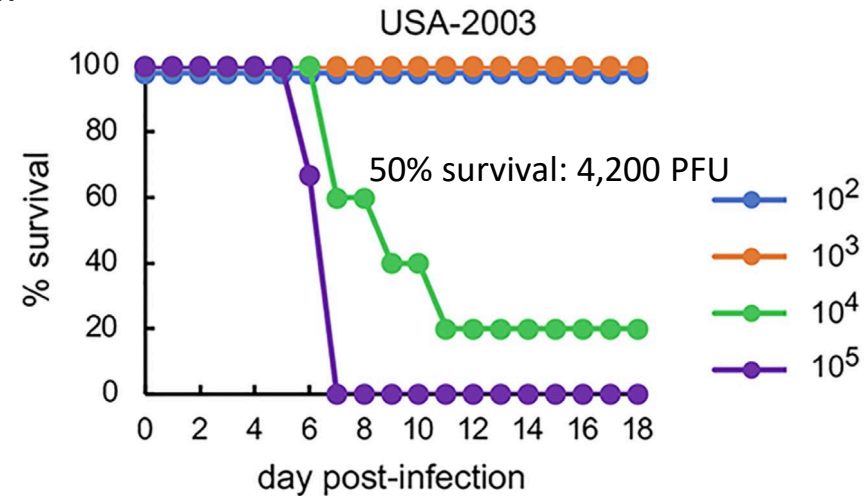
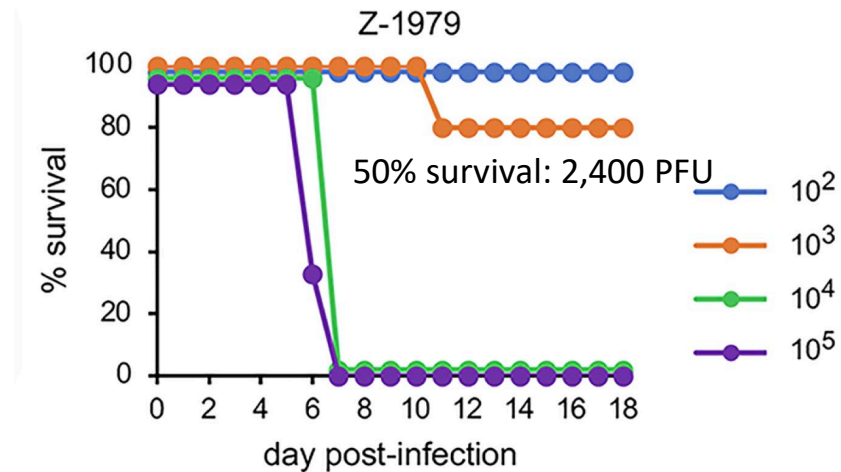
Development of CAST/EiJ Mouse Model

- Commercially available wild-derived Inbred mouse strain
- Susceptible to severe infection with mpox virus, cowpox virus, vaccinia virus, Akhmeta virus and mild infection with variola virus
- Develops strong IgG and T cell responses to vaccination or infection
- Low basal level of NK cells correlates with virus susceptibility
- Uses: investigate virulence, vaccines, therapeutics

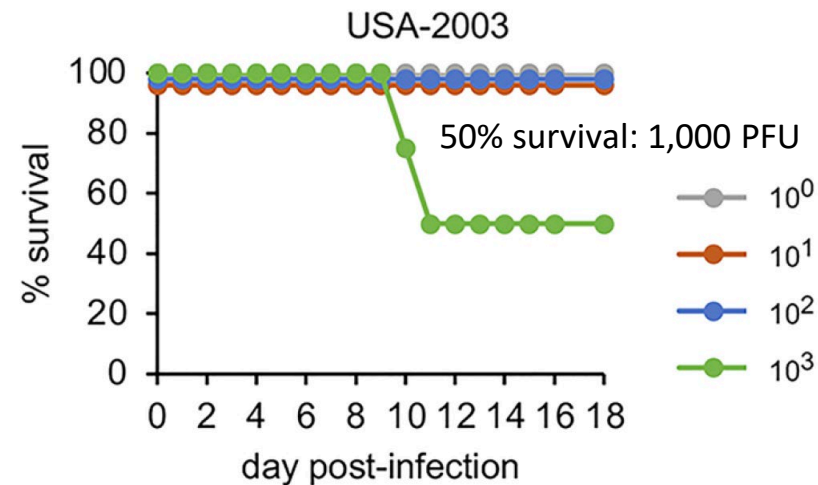
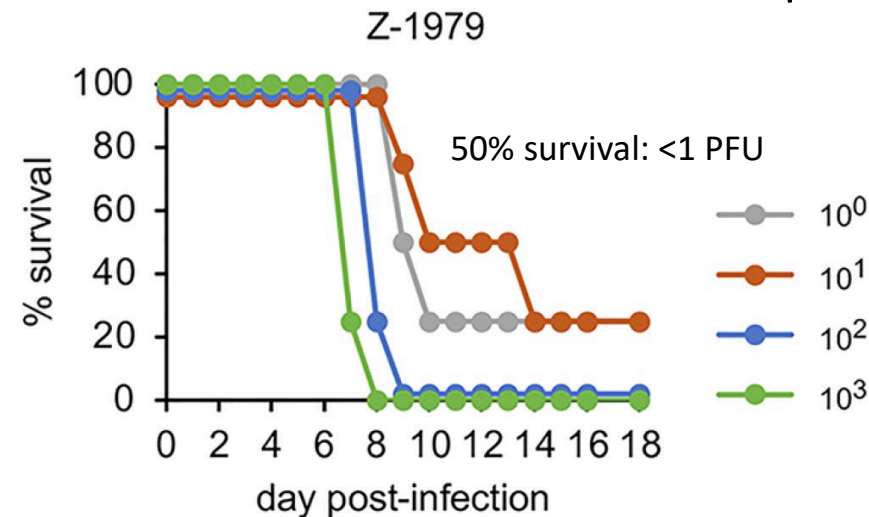
Earl, Americo, Moss 2012; Americo et al 2014; Earl et al 2015; Earl, Americo, Moss 2017; Gallardo-Romero et al 2019; Earl, Americo, Moss 2020; Morgan et al 2020

Clade I (Z-790) is more Virulent than Clade IIa (USA-2003) in CAST/EiJ mouse

Intranasal



Intraperitoneal

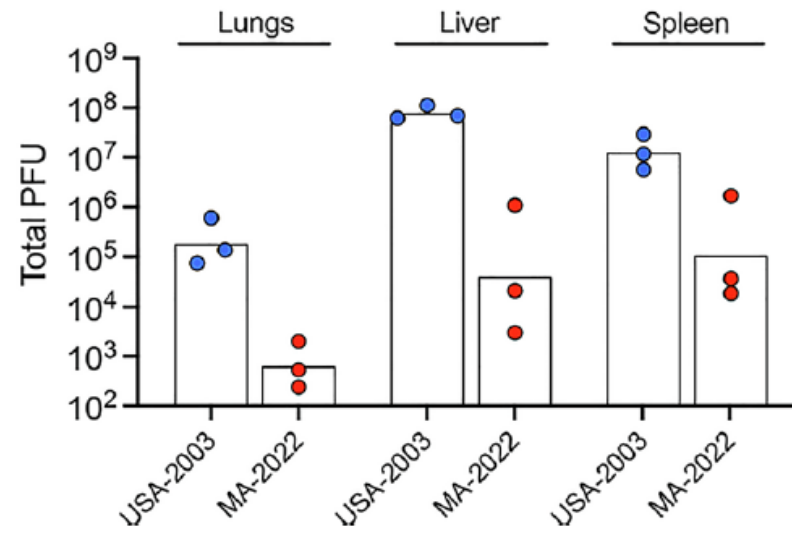
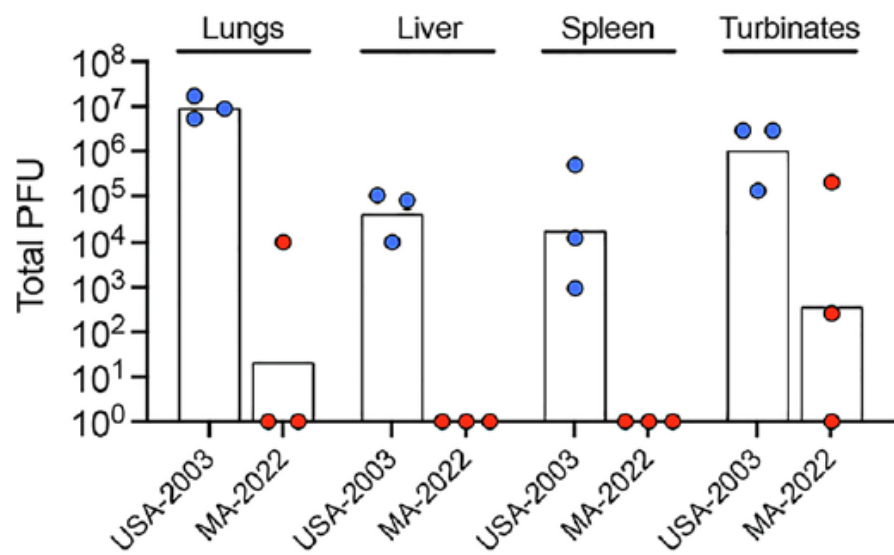
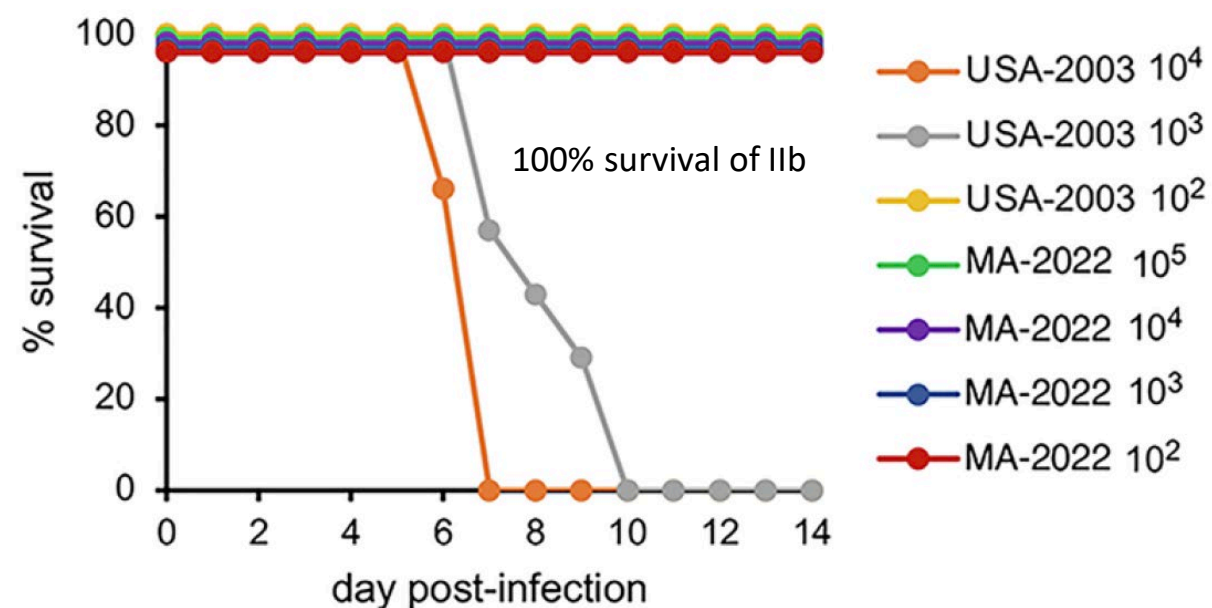
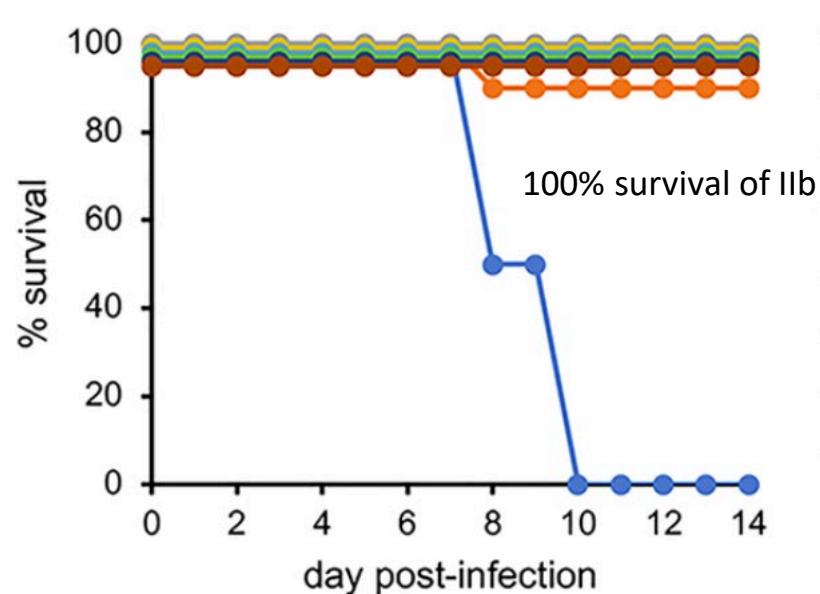


Clade IIa (USA-2003) is More Virulent than Clade IIb (MA-2022)

Intranasal

in CAST/EiJ Mouse

Intraperitoneal



Smallpox/Mpox Vaccines

ACAM 2000 – replication-competent vaccinia virus derived from Dryvax vaccine, administered by skin prick with 2×10^5 infectious units. Advantage: low dose, easily manufactured. Disadvantage: potential severe side effects particularly in immunodeficient.

Jynneos – replication-deficient Modified Vaccinia Virus Ankara (MVA) strain, administered subcutaneously with 10^8 infectious units. Advantage: Safe even in immunocompromised. Disadvantage: high dose and preparation in avian cells.

mRNA 1769 – lipid nanoparticle containing 4 mpox virus mRNAs expressing membrane proteins of mature virion (A29 and L1) and extracellular virion (A35 and B6) administered intramuscularly, in phase I trials (ClinicalTrials.Gov). Advantage: induces high neutralizing antibodies to mpox and vaccinia virus in animal models, potentially safe and easily manufactured.

Components of mRNA 1769 Protect Mice Against Lethal Vaccinia Virus Challenge (Collaboration between Moderna and NIAID)

