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# SAFETY, DURABILITY AND PROTECTION OF A SINGLE-DOSE TNX-801 MPOX VACCINE

**Sina Bavari, Ph.D.**

**World Vaccine Congress, Amsterdam**
**October 14, 2025**

1625 World Vaccine Congress Presentation PO6108

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# TALK OVERVIEW

**1) Background**

**2) TNX-801 characteristics *in vitro* and *in vivo***

**compare to other pox virus vaccines: well-tolerated, and far less reactogenic**

**3) TNX-801 immunogenicity and efficacy in animal models**

*TNX-801 is in the pre-IND stage of development and has not been approved for any indication.

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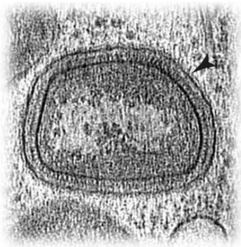
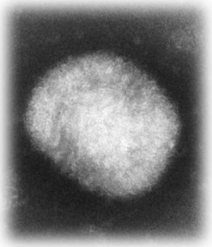
# POXVIRUSES

- Double stranded DNA, ~128-456 kb size
- Virions: enveloped, brick-shaped
- Size: ~220 to 450 nm long × 140 to 260 nm wide × 140 to 260 nm thick
- Infect vertebrate or invertebrate hosts
- Genus *Orthopoxvirus*:
  - Human Pathogens:
    - VARV: Case fatality rate ~30 to 50%
    - MPXV: Case fatality rate ~ 0.1 to 11%
  - Vaccines:
    - Vaccinia, Cowpox, Horsepox
    - Horsepox virus: ***TNX-801***





PLOS ONE

RESEARCH ARTICLE

Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments

Ryan S. Noyce[1], Seth Lederman[2], David H. Evans[1]*

1 Department of Medical Microbiology & Immunology and Li Ka Shing Institute of Virology, University of Alberta, Edmonton, Alberta, Canada, 2 Tonix Pharmaceuticals, Inc., New York, New York, United States of America

Noyce RS, Lederman S, Evans DH. *PLoS One*. 2018. 19;13(1):e0188453.

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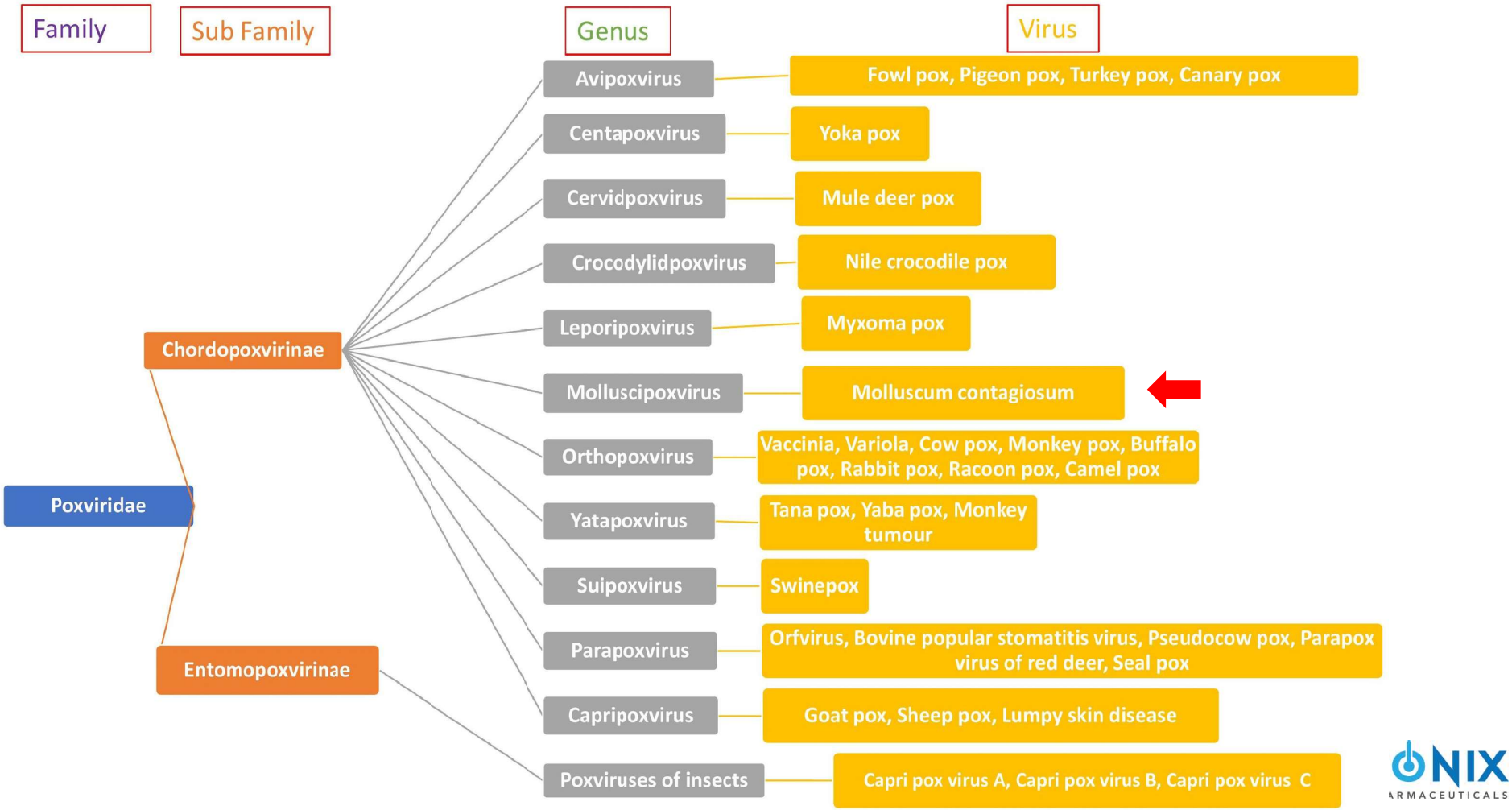
# POXVIRUSES: UBIQUITOUS IN THE ENVIRONMENT



# MONKEYPOX VIRUS (MPOX)

- **Endemic in Central and West Africa**
- **Two Clades:**
  1) Clade I (DRC)
  2) Clade IIa (West Africa) and IIb (Nigeria)
- **Human Case Fatality Rate:**
  - Clade I – ~11%
  - Clade IIa – ~3%
  - Clade IIb – ~<0.1%
- **Clade IIb – 2022 Outbreak**
  - 122 Countries
  - ~100,000 Confirmed Cases

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# VARIOLA VIRUS (SMALLPOX)

- **Oldest written record – ~3,500 years**
- **Oldest sequences – ~1,400 years**
- **Human Case Fatality Rate: ~30%**
- **20$^{th}$ century – ~250 to 500 million deaths**
- **Eradication: 1980**

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# EDWARD JENNER- SMALLPOX VACCINE (1796)

- **Jenner observed milkmaids were protected from smallpox, reasoned that infection with an illness similar to smallpox but less deadly could protect one against smallpox**
  - **"Cowpox" was the name of a disease in cows that could transfer to humans and cause sores**
  - **Jenner "vaccinated" (from *vacca*, Latin for "cow") a patient with pustule matter from "cowpox" sores on a milkmaid's hands; that patient remained healthy when challenged with smallpox virus**
- **Jenner suspected that the agent causing cowpox, which he called vaccinia originated in horses and had been transferred from horses to cows' udders by dirty hands[1]**

[1]Esparza J, et al. *Vaccine*. 2020. 38(30):4773-4779.
Photo: The College of Physicians of Philadelphia. Accessed July 15, 2021. /www.historyofvaccines.org

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# SMALLPOX VACCINES

- **Vaccine: Cowpox origin[1]**
- **Serial passaging: Humans, cows, and horses (143 years)**
- **Vaccine: Vaccinia Virus (1939) closely related to cowpox but serologically distinct[2]**
- **Multiple Vaccinia virus-based vaccines developed**
- **Smallpox eradication**

[1]Esparza J, et al. *Vaccine.* 2020. 38(30):4773-4779.
[2]Downie AW. 1939. *Br J Exp Pathol* 20:158–176.



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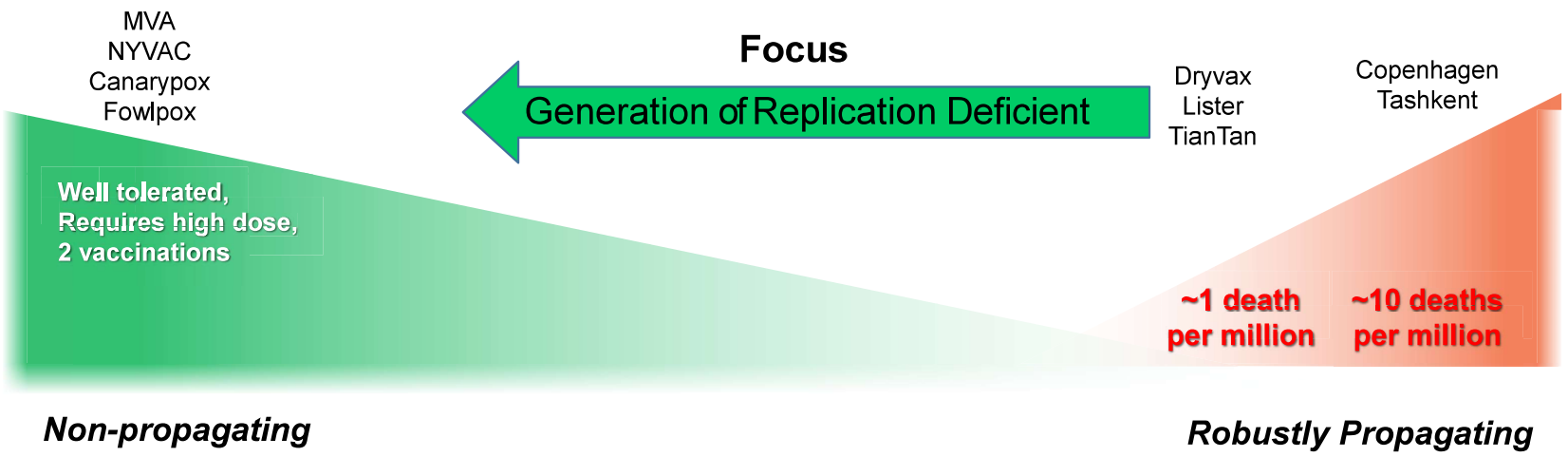
# BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES



# BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES

# 4 PRONG APPROACH TO MPOX/SMALLPOX VACCINE (TNX-801)

1) **Well-tolerated**

2) **Single dose**

3) **Durable**

4) **Protection against mpox disease (lesions)**

# TNX-801 *IN VITRO* AND *IN VIVO* CHARACTERISTICS: IMPROVED SAFETY AND REACTOGENICITY COMPARED TO OTHER REPLICATING VACCINIA-BASED VACCINES

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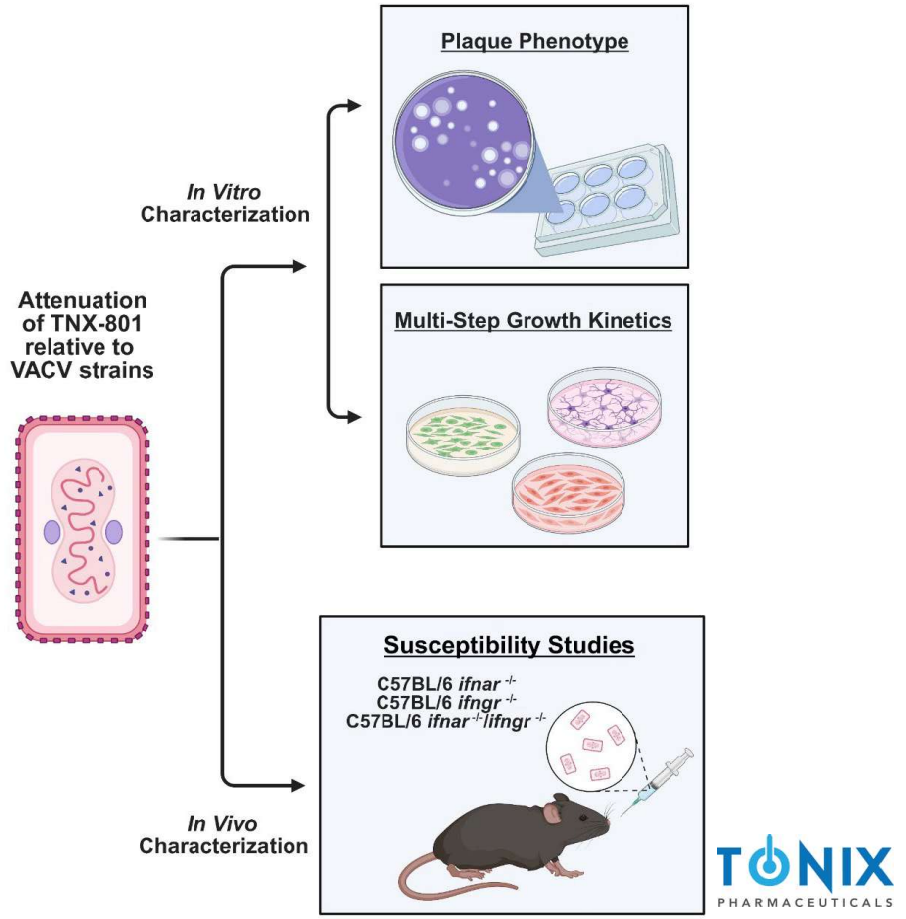
Recombinant chimeric Horsepox virus (TNX-801) is attenuated relative to Vaccinia virus strains in both *in vitro* and *in vivo* models

Stephanie V. Trefry,[1] Mayanka Awasthi,[1] Christy N. Raney,[1] Amy L. Cregger,[1] Chase A. Gonzales,[1] Brittney L. Layton,[1] Robert N. Enamorado,[1] Nelson A. Martinez,[1] Deborah S. Gohegan,[1] Masoudeh Masoud-Bahnamiri,[1] Jennifer Y. Cho,[1] Dawn M. Myscofski,[1] Tinoush Moulaei,[1] Natasza E. Ziółkowska,[1] Scott J. Goebel,[1] Seth Lederman,[1] Sina Bavari,[1] Farooq Nasar[1]

AUTHOR AFFILIATION See affiliation list on p. 23.




Trefry SV, et al. *mSphere*. 2024. 9(12):e0026524.

# *IN VITRO* TNX-801 GROWTH

- **Investigate growth characteristics of TNX-801 *in vitro* relative to VACV strains**
  - Positive Control: VACV-Western Reserve (WR), VACV-International Health Department (IHD)
  - Older vaccines used in smallpox eradication:
    1) VACV-Lister (Lis)
    2) VACV-New York City Board of Health (NYCBH)
  - New Vaccine: TNX-801
  - Non-replicating control: MVA
- ***In vitro* Assays:**
  1) **Plaque phenotype – BSC-40 and Vero-E6**
  2) **Replication Kinetics**
     - Immortalized non-human primate cell lines
     - Human primary cells from two main route of poxvirus transmission
       - Dermal and respiratory tracts

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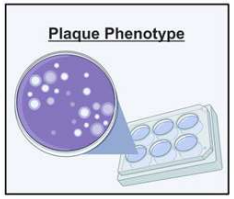
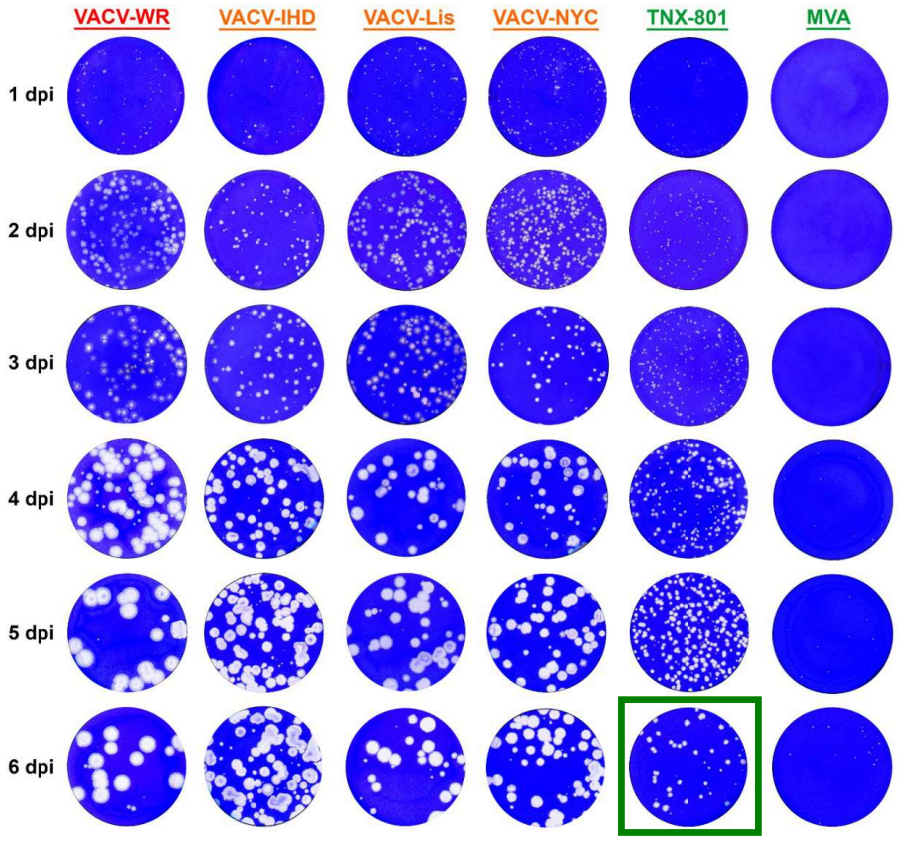
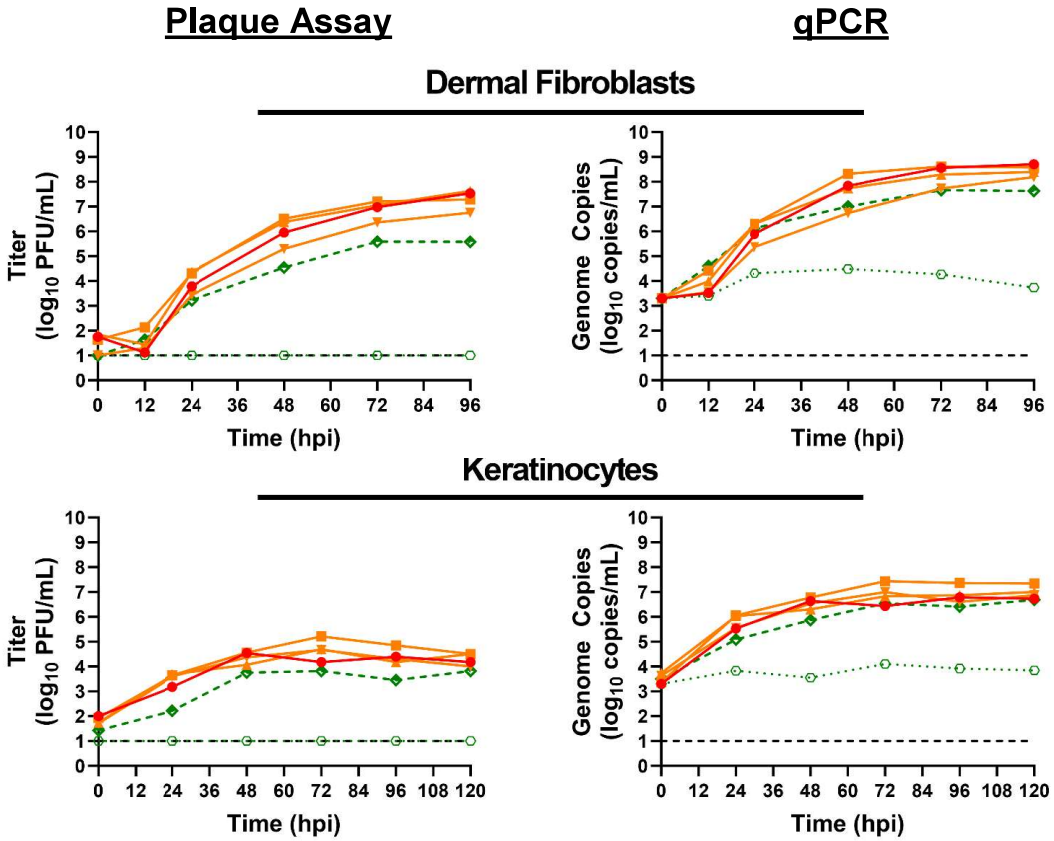
# TNX-801 DISPLAYS SMALL PLAQUE PHENOTYPE AS COMPARED TO OTHER REPLICATING VACCINA VIRUSES

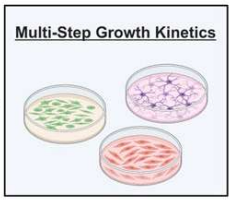



VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

# TNX-801: REPLICATION IN PRIMARY HUMAN CELLS (DERMAL TRACT)




VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

***Similar results were obtained with human primary cells from the respiratory tract***

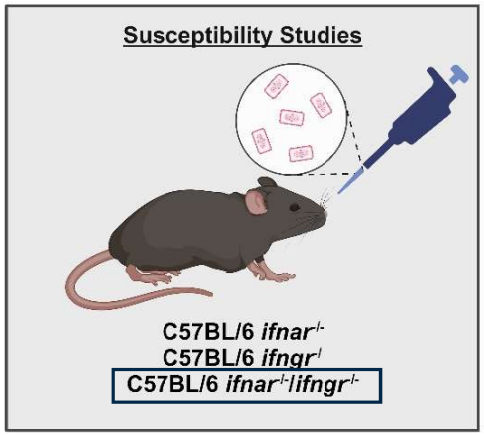
**TNX-801: *~27- to 119-fold* more attenuated than VACV based vaccines**

# *IN VIVO RESPONSES TO* TNX-801:WELL-TOLERATED AND LACKS REACTOGENICITY

- **Investigate attenuation of TNX-801 *in vivo* relative to VACV based vaccines**
  - Immunocompromised Mice (C57BL/6 *ifnar*$^{-/-}$, C57BL/6 *ifngr*$^{-/-}$, C57BL/6 *ifnar*$^{-/-}$/*ifngr*$^{-/-}$)
    - Interferon receptor knockout model
    - Sensitive to virus infection

  - **Positive Control:** VACV-WR, VACV-IHD
  - **Older vaccines:** VACV-Lis, VACV-NYCBH
  - TNX-801
  - **Route:** Intranasal

- **Parameters measured:**
  1) Disease Score
  2) Temperature
  3) ***Weight loss***
  4) ***Survival***

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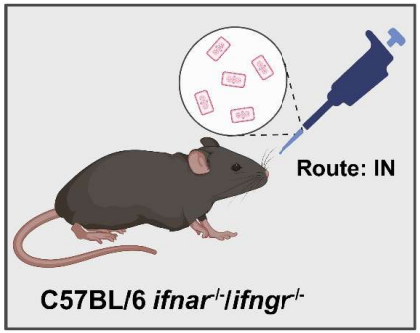
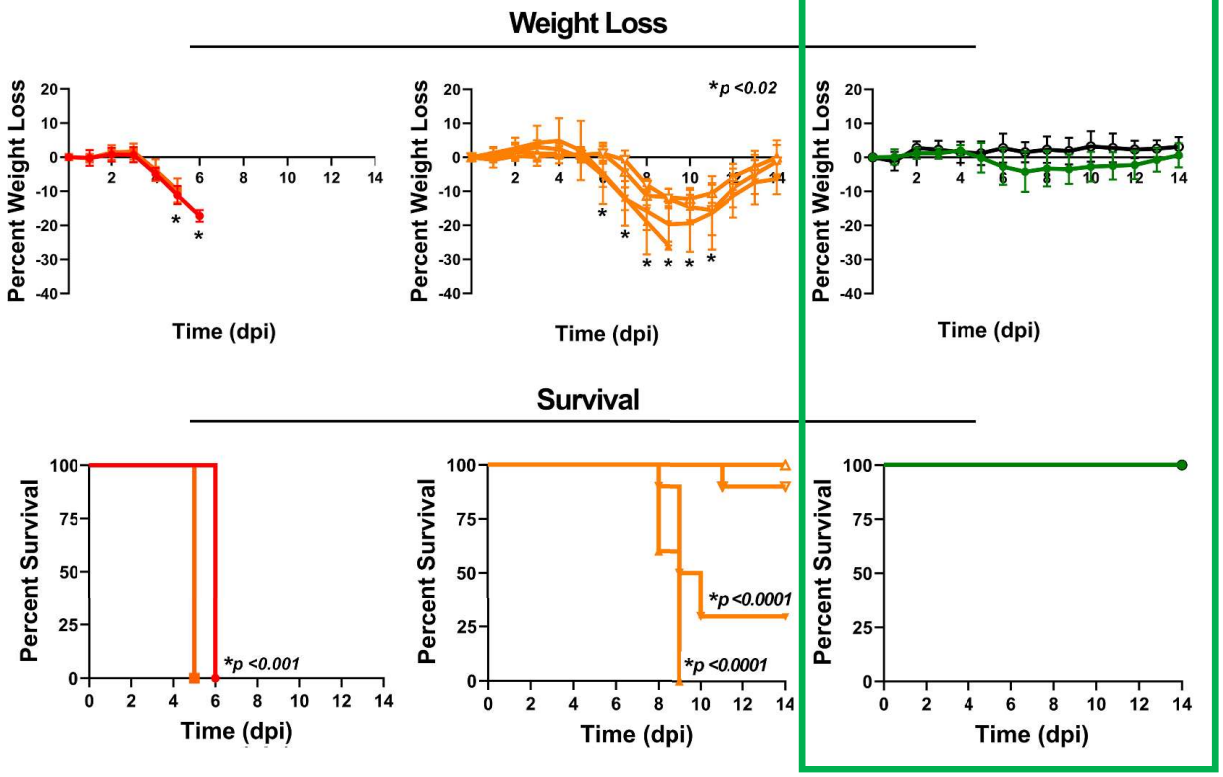
# TNX-801 LACKS LETHALITY ASSOCIATED WITH OLDER SMALLPOX VACCINE STRAINS (LIS, NYCBH)




VACV-WR, IHD
~$10^3$ PFU

VACV-Lis, NYCBH
~$10^4$ and $10^3$ PFU

TNX-801*, Mock
~3 x $10^8$ PFU




***TNX-801 is up to 100,000-fold more attenuated***



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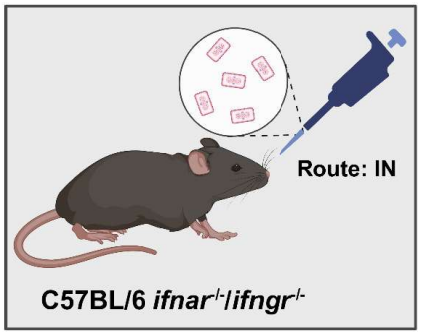
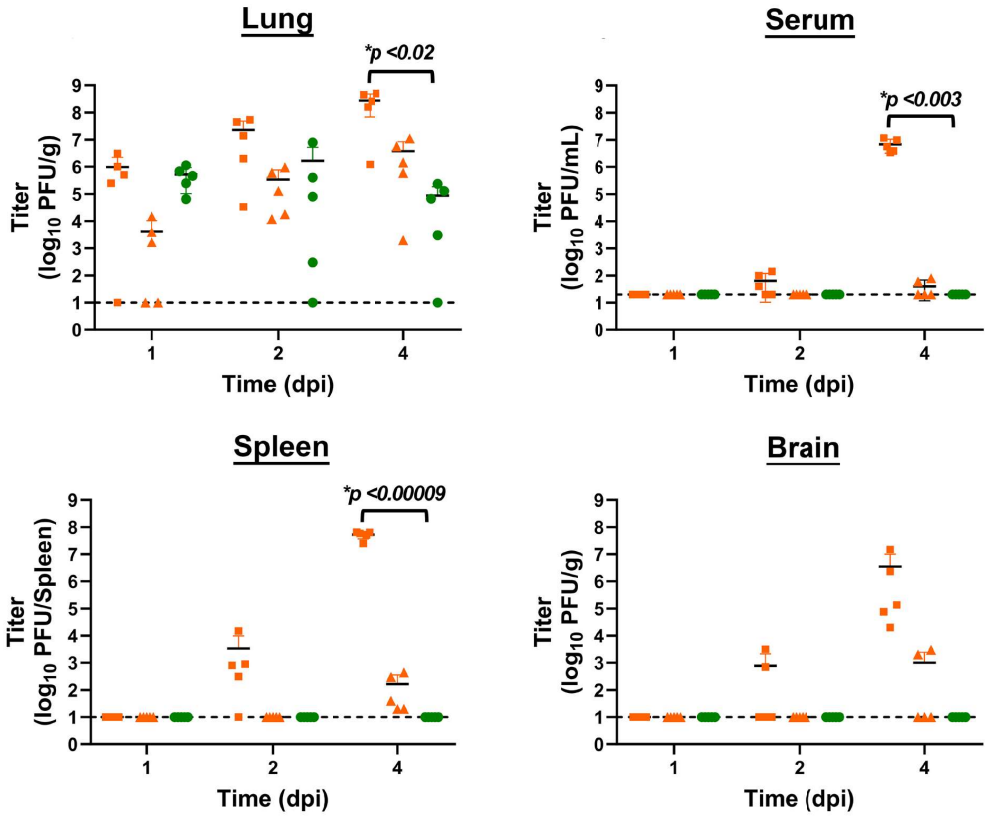
# TNX-801 INFECTION DISPLAYS LIMITED REPLICATION




VACV-IHD ~$10^6$ PFU (■)

VACV-NYCBH ~$10^6$ PFU (▲)

TNX-801 ~$10^8$ PFU (●)



# CONCLUSION: *IN VITRO GROWTH* AND *IN VIVO REACTOGENICITY AND TOLERABILITY*

**TNX-801 plaques and in vitro growth is similar to MVA**

**TNX-801 is up to 100,000 safer than older vaccina-based vaccines in IFN-KO mice**

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Editor's Pick | Biotechnology | Research Article

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**Is TNX-801 efficacious against deadly MPXV clade 1 and is the immunity long-lasting**

Trefry SV, et al. *mSphere*. 2024. 9(12):e0026524.

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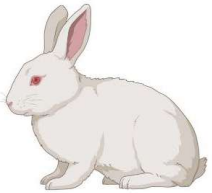
# TNX-801 IMMUNOGENICITY AND EFFICACY IN ANIMAL MODELS (SINGLE DOSE)

1)  → MPXV Clade Ia

2)  → RPXV

3)  → MPXV Clade IIa

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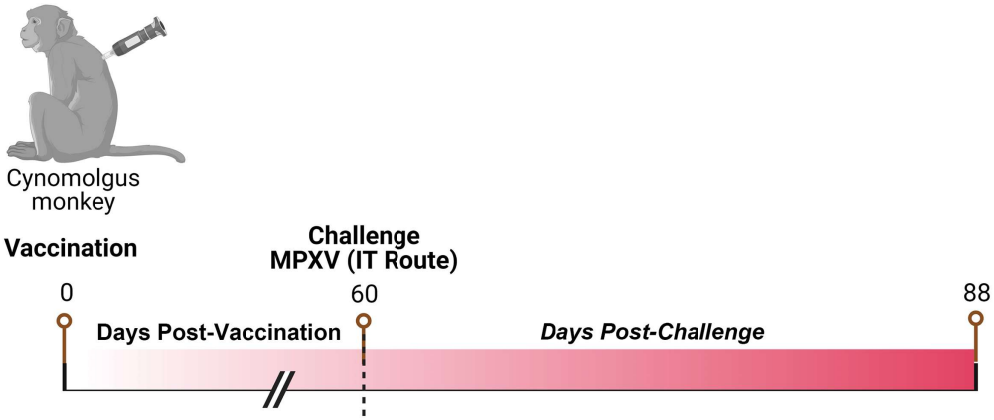
# NHP IMMUNOGENICITY AND EFFICACY STUDY DESIGN




viruses

MDPI

*Article*

**Single Dose of Recombinant Chimeric Horsepox Virus (TNX-801) Vaccination Protects Macaques from Lethal Monkeypox Challenge**

Ryan S. Noyce [1], Landon W. Westfall [2,†], Siobhan Fogarty [3], Karen Gilbert [2], Onesmo Mpanju [4], Helen Stillwell [3,‡], José Esparza [5], Bruce Daugherty [3], Fusataka Koide [2], David H. Evans [1] and Seth Lederman [3,*]

| Vaccination | | | | | Challenge | | |
|---|---|---|---|---|---|---|---|
| Group | Treatment | n | Dose (PFU) | Route | *Virus* | *Dose (PFU)* | *Route* |
| 1 | TNX-801 (High) | 4 | $4 \times 10^6$ | PERCUT | *MPXV (Zaire)* | $10^5$ | *IT* |
| 2 | TNX-801 (Low) | 4 | $5 \times 10^5$ | PERCUT | *MPXV (Zaire)* | $10^5$ | *IT* |
| 3 | rVACV | 4 | $1 \times 10^5$ | PERCUT | *MPXV (Zaire)* | $10^5$ | *IT* |
| 4 | Mock | 4 | - | PERCUT | *MPXV (Zaire)* | $10^5$ | *IT* |

**rVACV = Plaque pick from ACAM2000 (Approved Vaccine)**

Noyce RS, et al. *Viruses*. 2023. 15(2):356.

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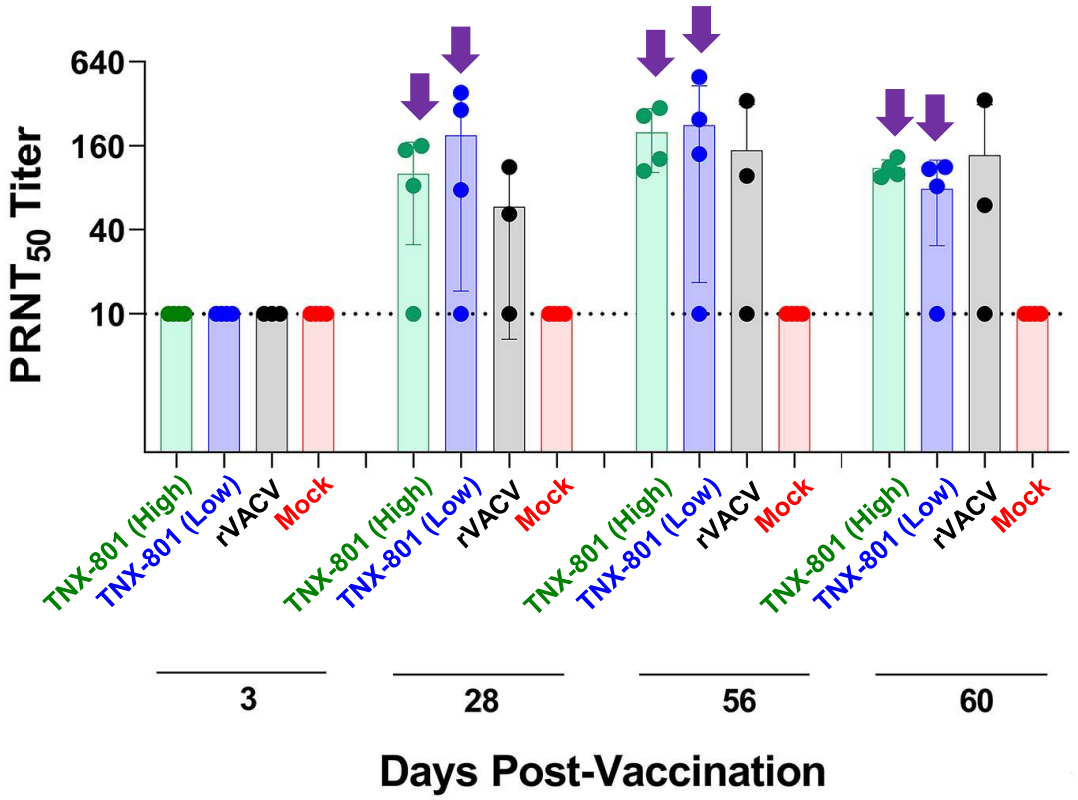
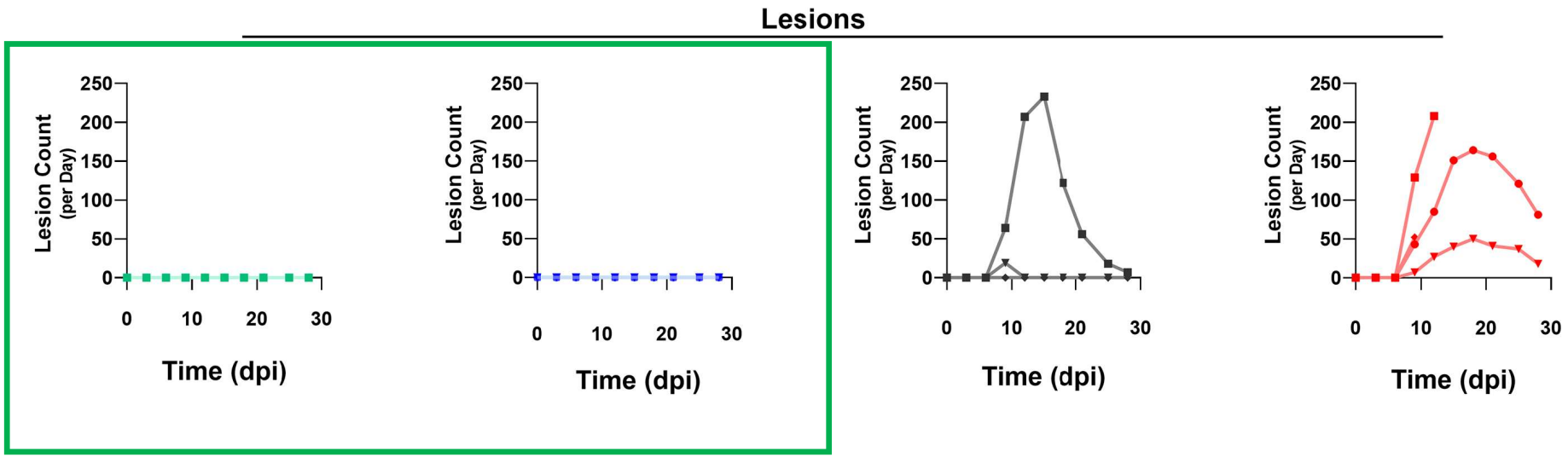
# NHP IMMUNOGENICITY: TNX-801 INDUCES NEUTRALIZING ANTIBODY RESPONSE

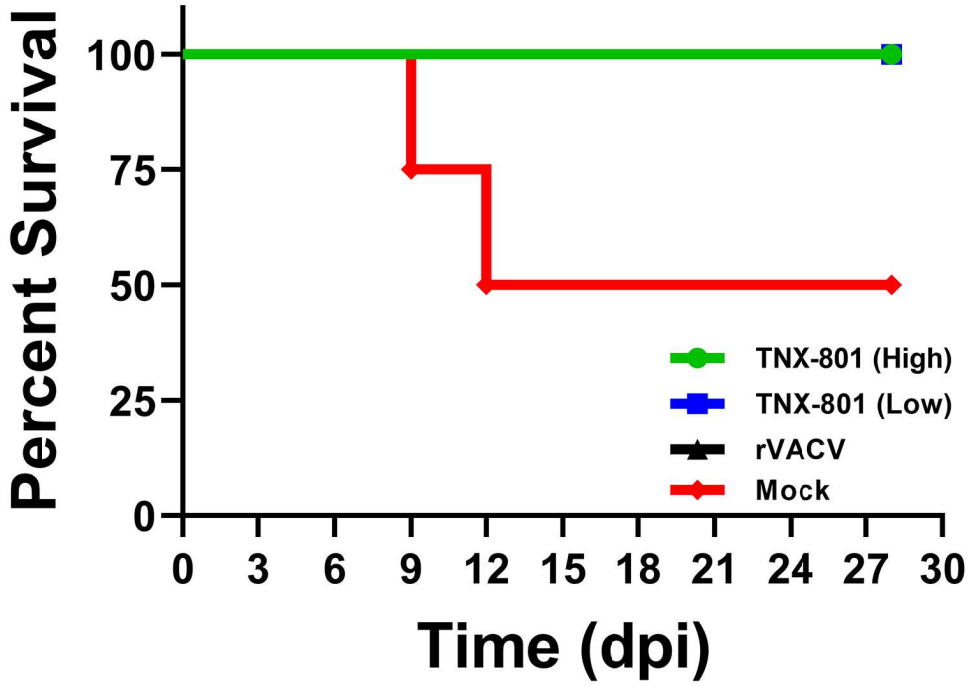


# TNX-801 PROVIDES PROTECTION AGAINST MPOX DISEASE




***NO LESIONS in TNX-801 vaccinated groups***

# TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE I CHALLENGE




***NO LETHALITY in TNX-801 vaccinated groups***

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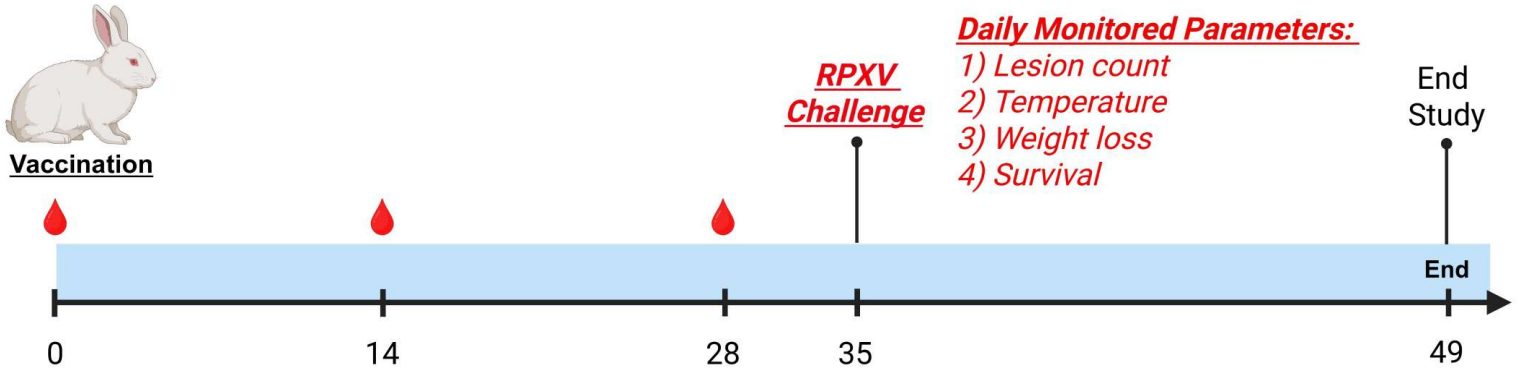
# A SINGLE VACCINATION OF TNX-801 PROTECTS AGAINST MPXV WHEN VACCINATION WAS PERFORMED BY USING BIFURCATED METHOD:

# HOW ABOUT OTHER METHODS OF VACCINATION?

# TNX-801 VACCINATION VIA ALTERNATIVE ROUTES (ID, SC, IM): STUDY DESIGN




| Treatment | Route | Dose (PFU) | Number of Animal per Group |
|---|---|---|---|
| TNX-801 | ID | $10^6$ | 6 (3M/3F) |
| TNX-801 | ID | $10^5$ | 6 (3M/3F) |
| TNX-801 | SC | $10^6$ | 6 (3M/3F) |
| TNX-801 | SC | $10^5$ | 6 (3M/3F) |
| TNX-801 | IM | $10^6$ | 6 (3M/3F) |
| TNX-801 | IM | $10^5$ | 6 (3M/3F) |
| Mock | - | - | 6 (4M/2F) |

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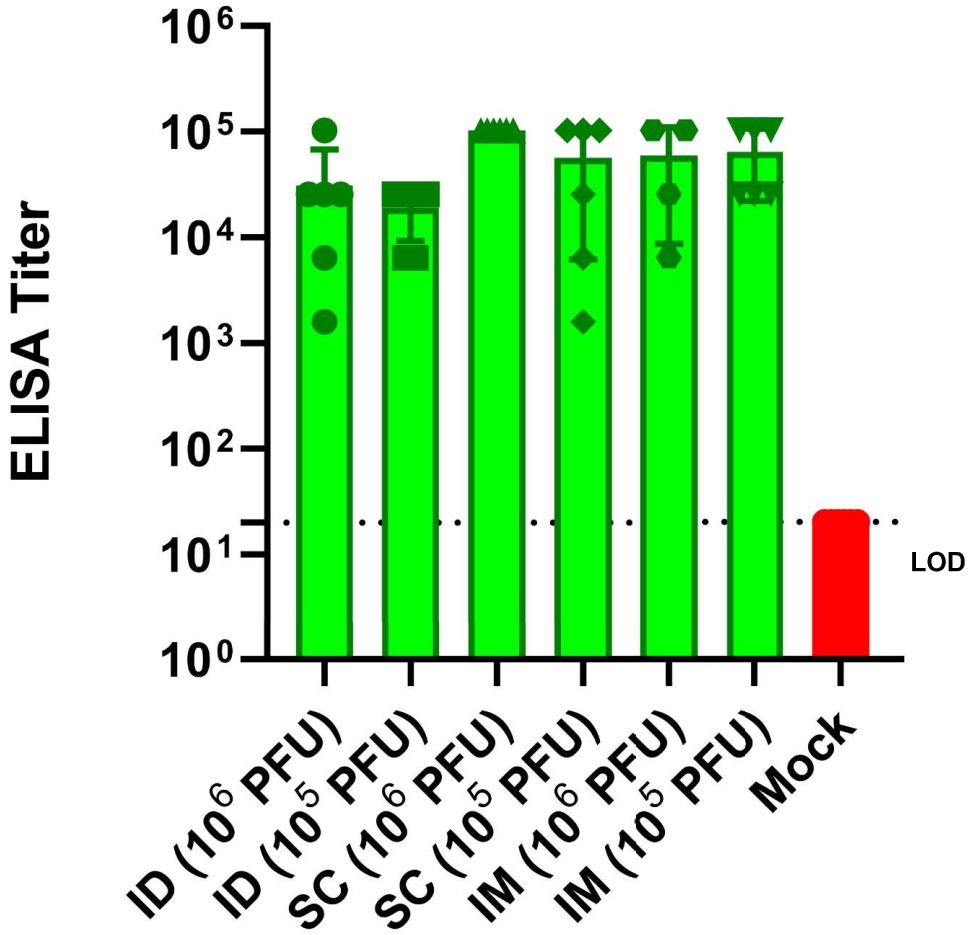
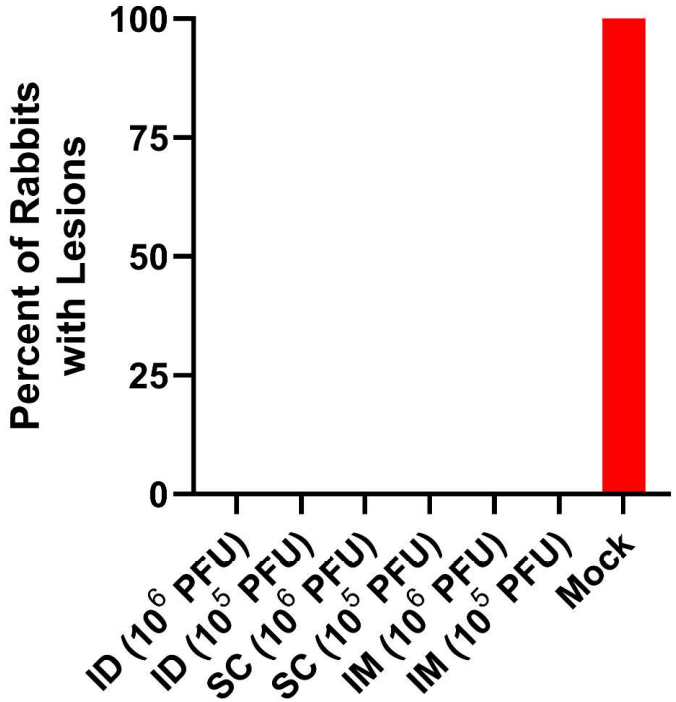
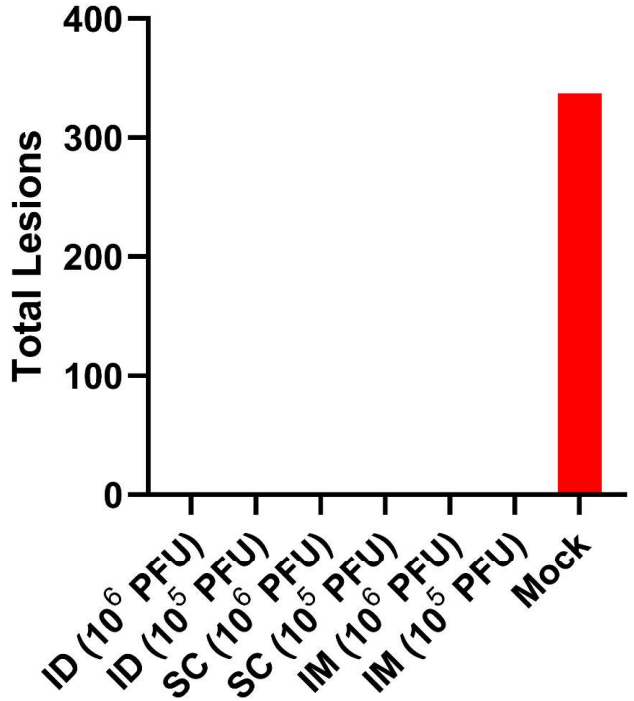
# IMMUNOGENICITY: DAY 28 ANTI-VACV (MVA) TITERS




***Comparable IgG titers regardless of Route or Dose***

# ALL ROUTES OF TNX-801 VACCINATION PROTECTS AGAINST CLINICAL DISEASE (LESIONS)




***NO LESIONS in TNX-801 vaccinated groups***

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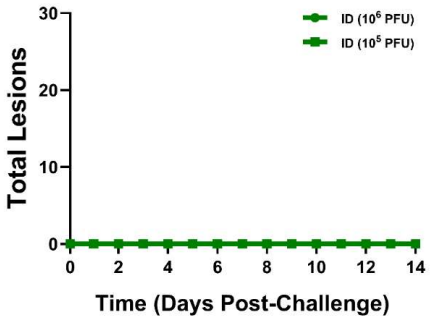
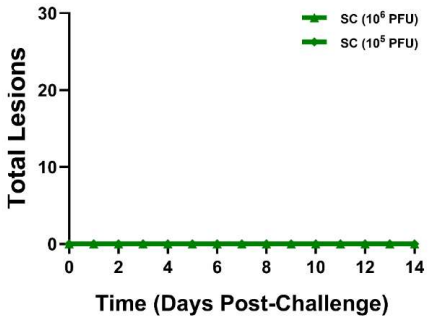
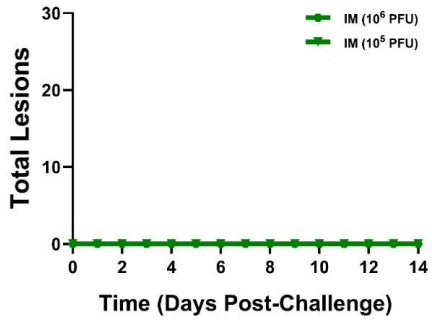
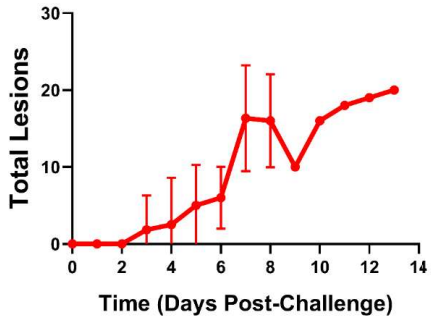
# ALL ROUTES OF TNX-801 VACCINATION PROTECTS AGAINST CLINICAL DISEASE (LESIONS)



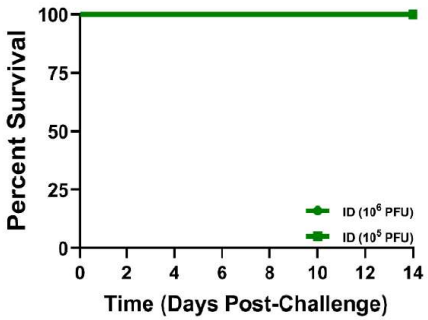



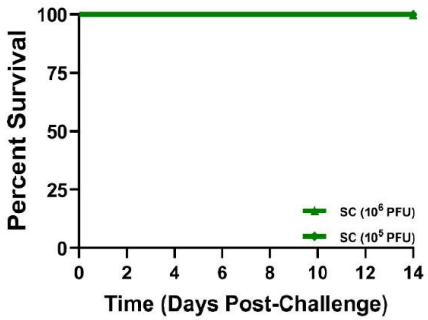



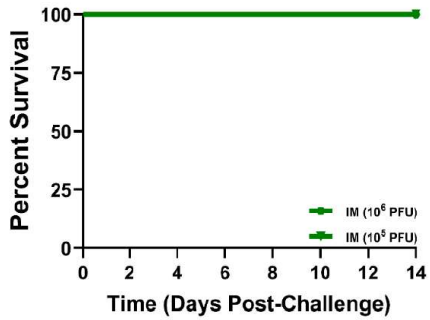



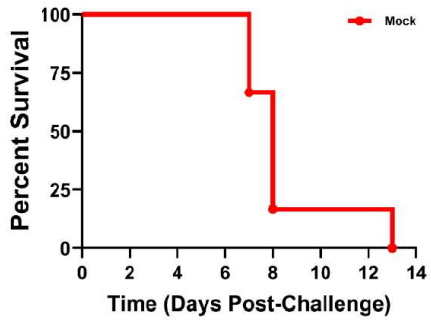

***NO LESIONS in TNX-801 vaccinated groups***

# ALL ROUTES OF TNX-801 VACCINATION PROTECTS AGAINST LETHAL RPXV CHALLENGE




***<u>TNX-801 was well tolerated and NO LETHALITY in TNX-801 vaccinated groups</u>***

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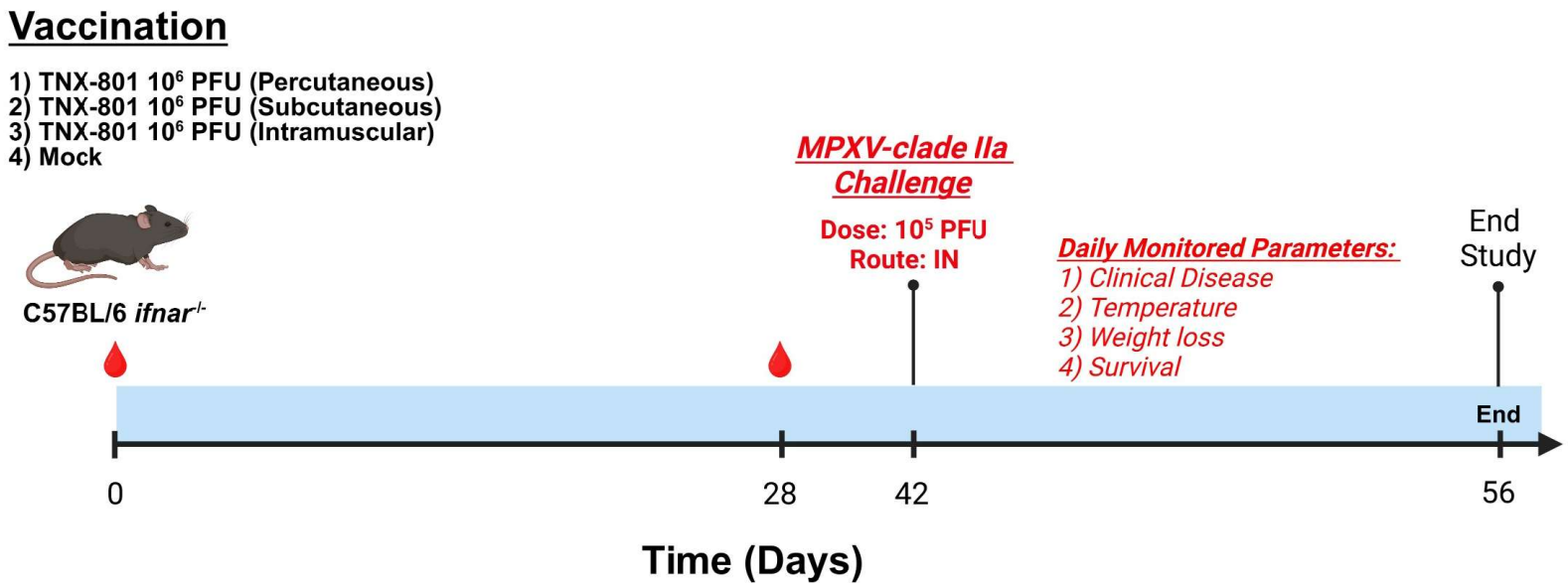
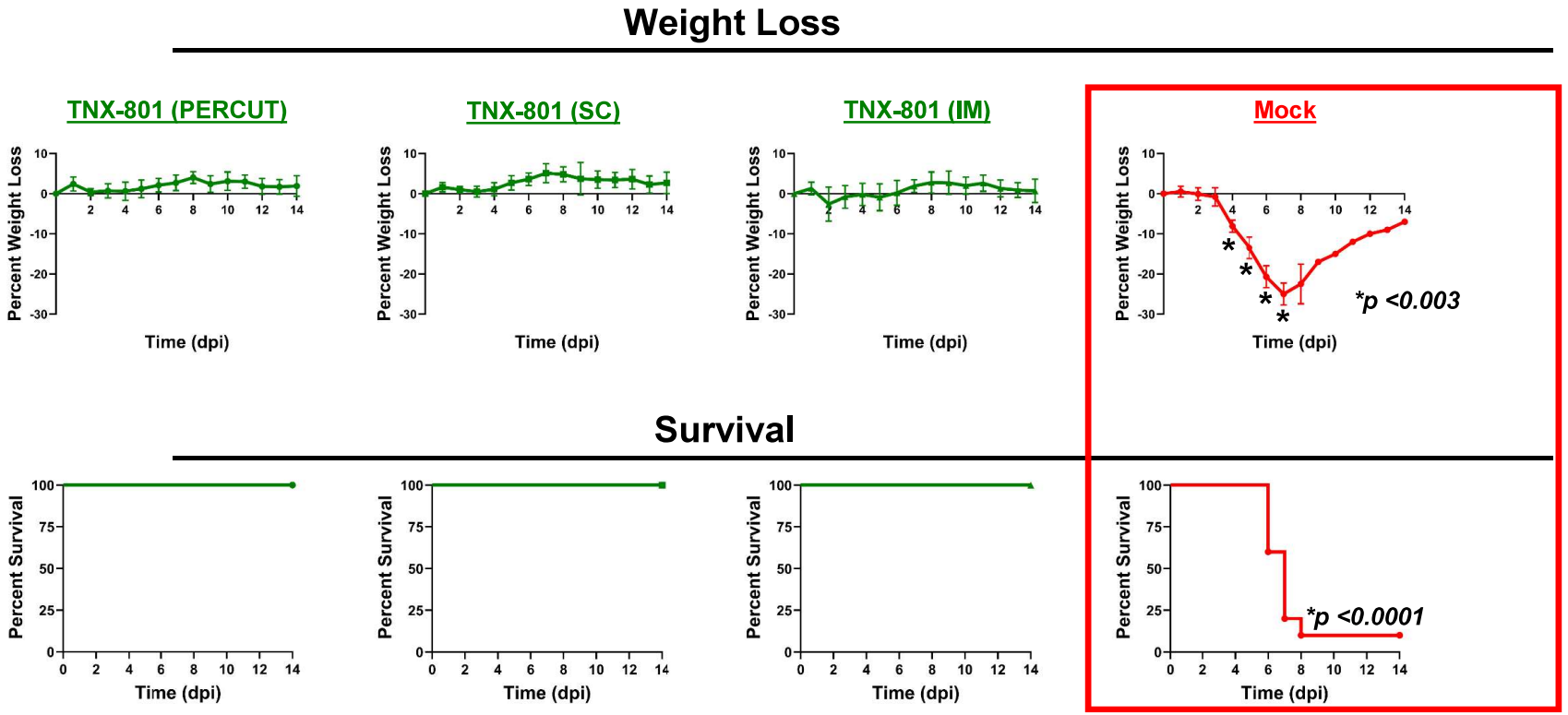
# TNX-801 ADMINISTRATION PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE IIA CHALLENGE: DIFFERENT ROUTES



# ALL ROUTES OF TNX-801 VACCINATION PROTECTED AGAINST LETHAL MONKEYPOX CLADE IIA CHALLENGE



# TNX-801 ADMINISTRATION IS WELL-TOLERATED PROVIDES PROTECTION AGAINST LETHAL RPXV MONKEYPOX CLADE IIA CHALLENGE: WHEN THE VACCINE WAS ADMINISTERED BY IM, SQ, OR ID

# HOW ABOUT OTHER MODES OF DELIVERY SUCH AS MICRONEEDLE ARRAY PATCHES (MAPS)?

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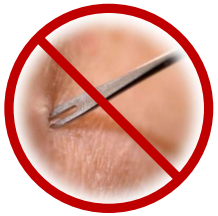
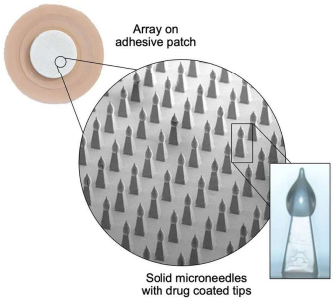
# ALTERNATIVE DELIVERY OF TNX-801 USING MICRONEEDLE ARRAY PATCHES (MAPS)



- ❑ Movement away from current standard bifurcated percutaneous delivery
- ❑ Established network with MAP industry leaders
- ❑ Potential for self-administration and increased acceptability
- ❑ Improved stability and transport




*solid-coated microneedles*

*dissolvable microneedles*

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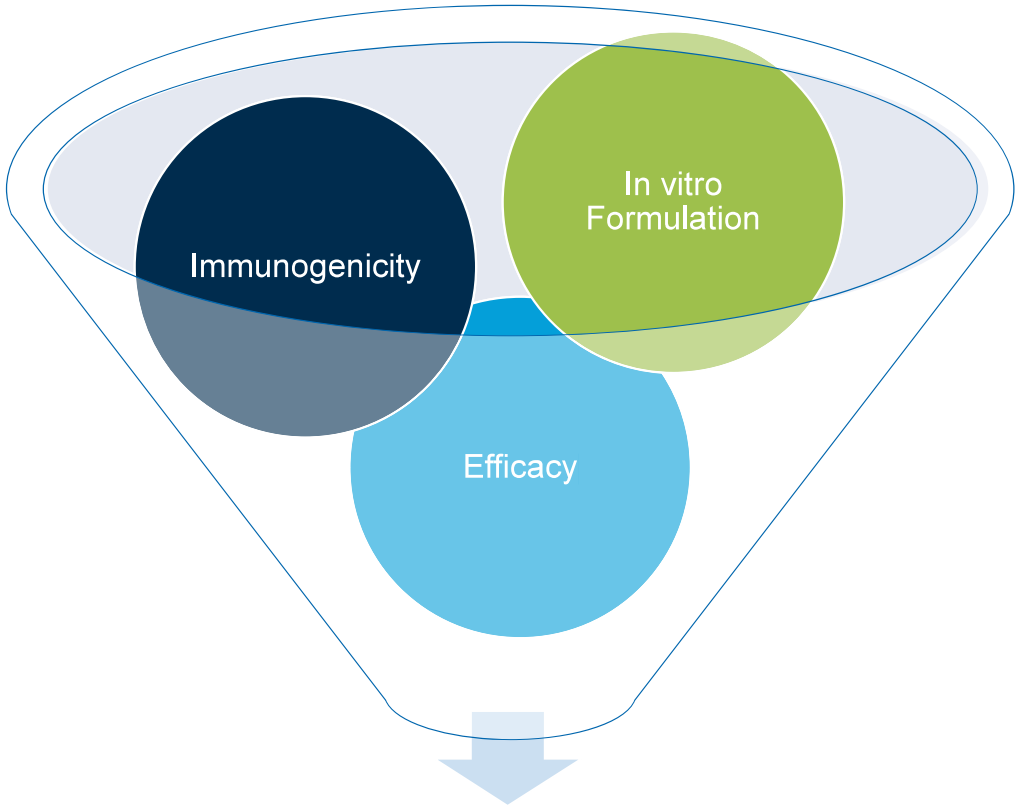
# ESTABLISHED PIPELINE TO DETERMINE OPTIMAL MAP VACCINE FORMULATION




**Rationally selected and optimized MAP with desired biophysical properties, immunogenicity and efficacy profiles**



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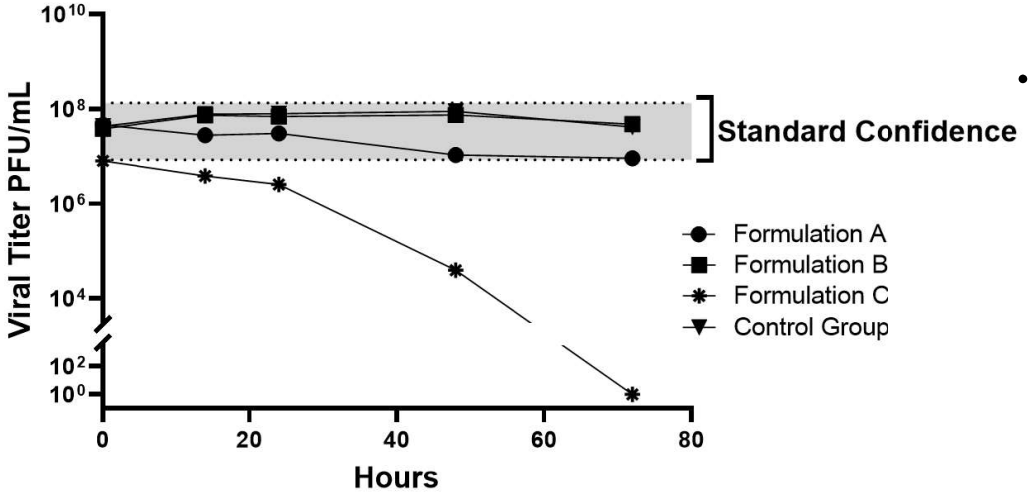
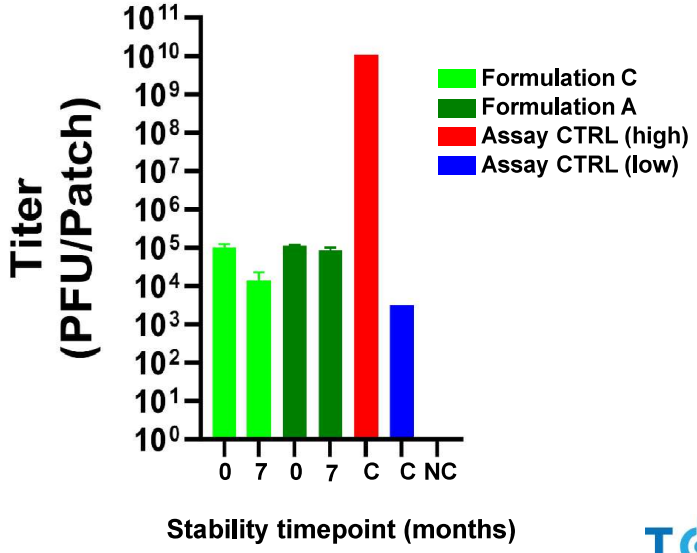
# IDENTIFICATION OF TNX-801 MAP FORMULATIONS WITH POTENTIAL FOR EXTENDED STABILITY

- Multiple MAP formulations tested for effects on in-vitro TNX-801 growth properties

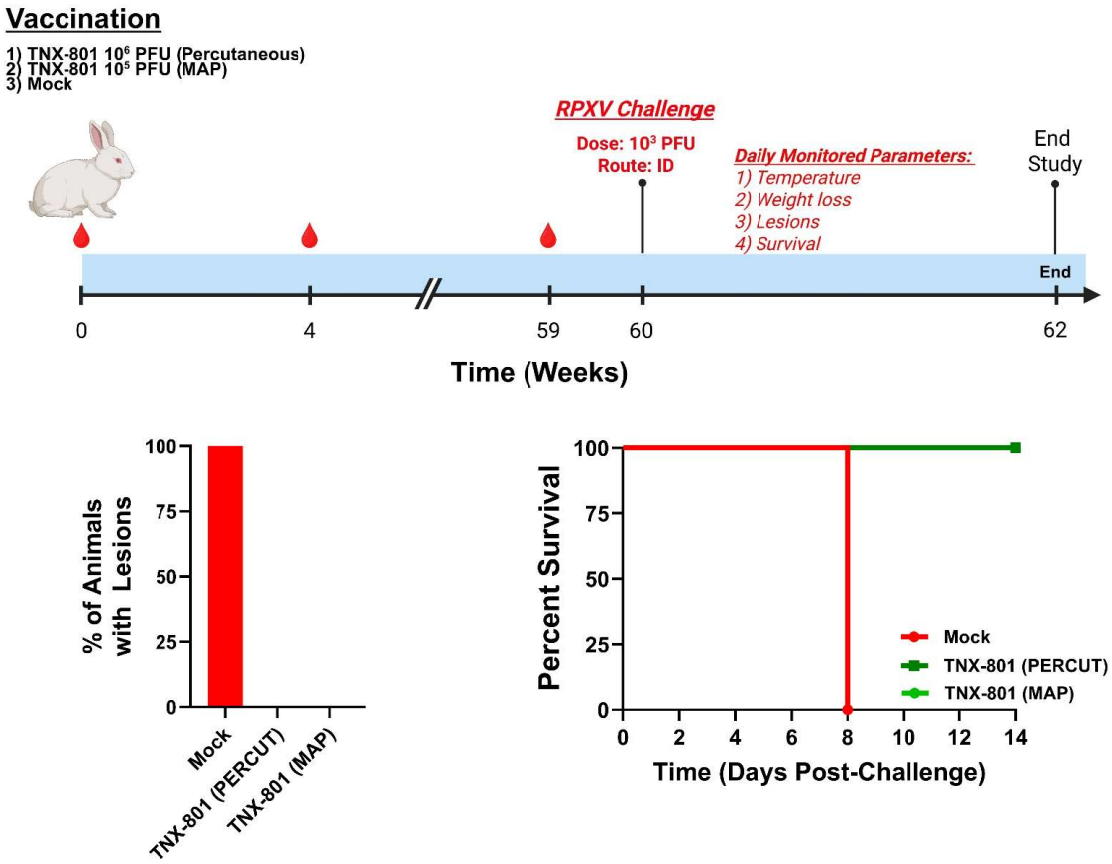



*Representative data on 3 formulations*

- TNX-801 was formulated with Kindeva's solid hollow MAP and then tested at **7 months post 4°C storage**.
- Potency of TNX-801 was measured by plaque assay and compared to fleshly formulated TNX-801/MAPs
- Stability testing is still on-going



# TNX-801 PROVIDES DURABLE PROTECTION AGAINST LETHAL RABBIT POX CHALLENGE: 14 MONTHS (PERCUT AND KINDEVA MAP)



# TNX-801 SAFETY

- ***In vitro***:
  - **Small plaque phenotype**
  - **Up to 100-fold lower replication than VACV strains**
  - **Primary cells from dermal and respiratory tracts**
- ***In vivo***:
  - **Well tolerated in mice, rabbits, hamsters, and NHPs**
  - **Minimal or no disease in immunocompromised murine models**
  - **up to 100,000-fold safer than VACV-based vaccines**
  - **Minimally replicates at site of delivery**

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# TNX-801 IMMUNOGENICITY, EFFICACY, AND DURABILITY OF PROTECTION AFTER A SINGLE DOSE

- **Evaluated in multiple animal models**
  - **Mouse, Rabbit, and NHP (Cynomolgus)**

- **Elicits IgG and/or neutralizing responses and protects**
  - **Various route percutaneous, subcutaneous, intramuscular, and intradermal**
  - **Microneedle delivery**

- **Provides 100% protection against lesions**
  - **Rabbit and NHP models**
  - **Rabbit model: 6- and 14-months**

- **Provides 100% protection against lethal challenge**
  - **Models: Mouse, Rabbit, and NHP**
  - **Viruses: VACV, RPXV, MPXV clade Ia and IIa**

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