



NYC Builds Bio+ Vanquishing the Virus

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Potential COVID-19 Vaccine¹

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TNX-1800 (modified horsepox virus)^{2,3}

- Pre-clinical and pre-IND stage
- Live virus vaccine designed on our horsepox vaccine platform⁴ to express the SARS-CoV-2 Spike (S) protein
- Milestones:
 - 4th Quarter 2020 – Non-human primate testing results expected⁵

¹ COVID-19 = Coronavirus disease 2019

² Collaboration with Southern Research and University of Alberta

³ Experimental new biologic, not approved for any indication

⁴ TNX-801 is unmodified horsepox virus, which is in development as a vaccine to protect against smallpox and monkeypox

⁵ We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

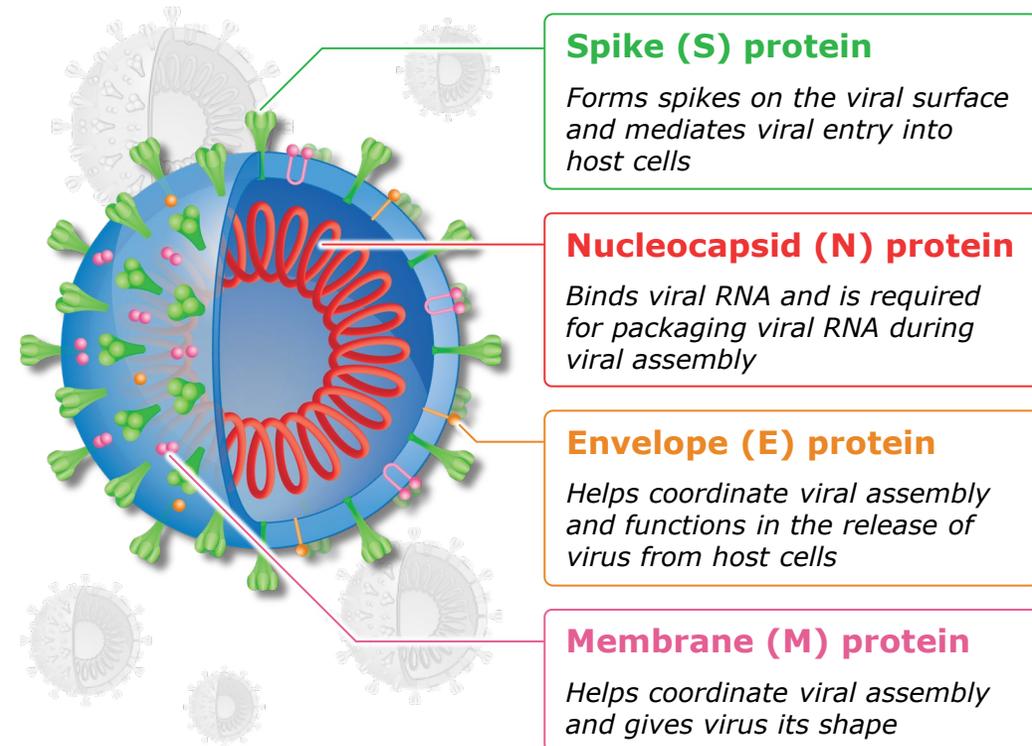


Considerations in SARS-CoV-2 Vaccination Strategies: Choice of Antigen

- CoVs are characterized by spike (S) proteins projecting from the virion surface¹
- Antibodies generated against S proteins in SARS-CoV provide full protection against infection, though the duration of protection is unclear^{2,3}

An optimal SARS-CoV-2 vaccine would also induce a potent T cell response to **improve** viral clearance and **promote** long-lived protection^{4,5}

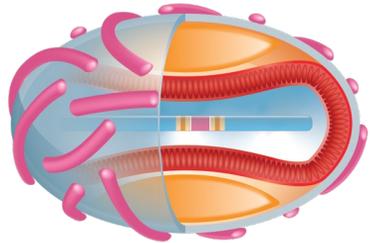
Structure of SARS-CoV-2^{1,6}



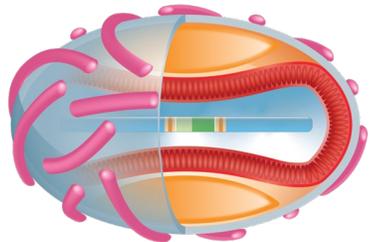
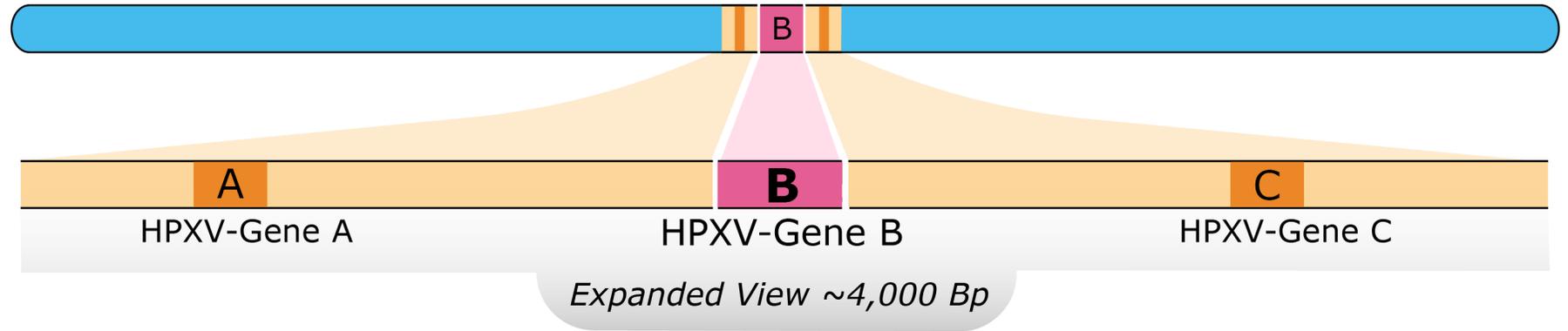
1. Ashour HM, et al. *Pathogens*. 2020;9(186):1-15.
2. Enjuanes L, et al. *Virus Res*. 2008;133(1):45-62.
3. Tang F, et al. *J Immunol*. 2011;186(12):7264-7268.
4. Zhao J, et al. *J Virol*. 2010;84(18):9318-9325.
5. Channappanavar R, et al. *J Virol*. 2014;88(19):11034-11044.
6. The Economist. Accessed March 30, 2020. <https://www.economist.com/briefing/2020/03/12/understanding-sars-cov-2-and-the-drugs-that-might-lessen-its-power>



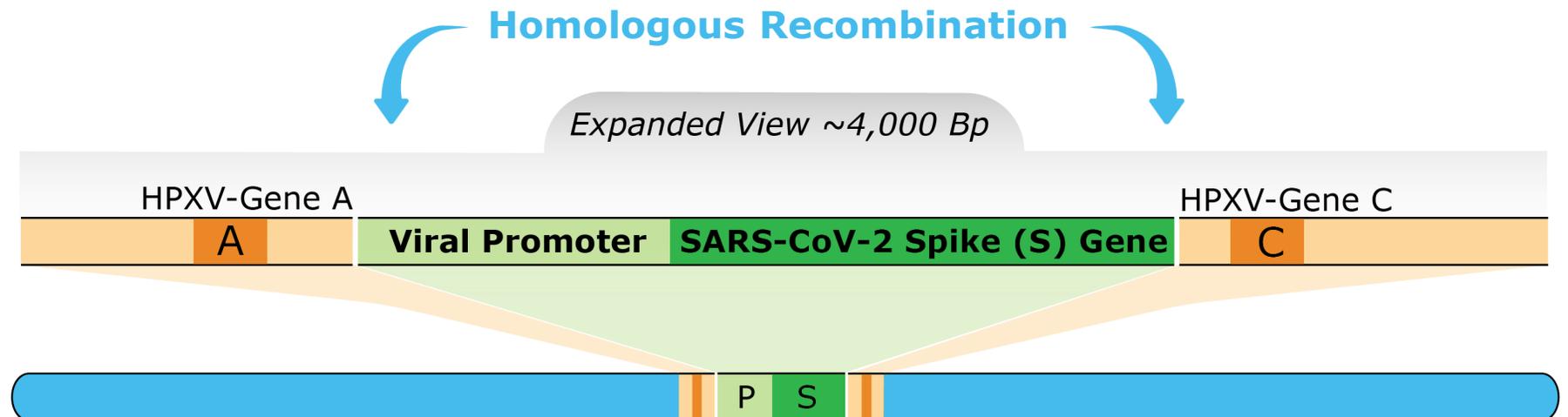
TNX-1800 is Based on a Horsepox Virus (HPXV) Vector Designed to Express SARS-CoV-2 S Protein



Horsepox
sHPXV
~200,000 Bp



TNX-1800*
rHPXV/SARS-CoV-2S
~200,000 Bp

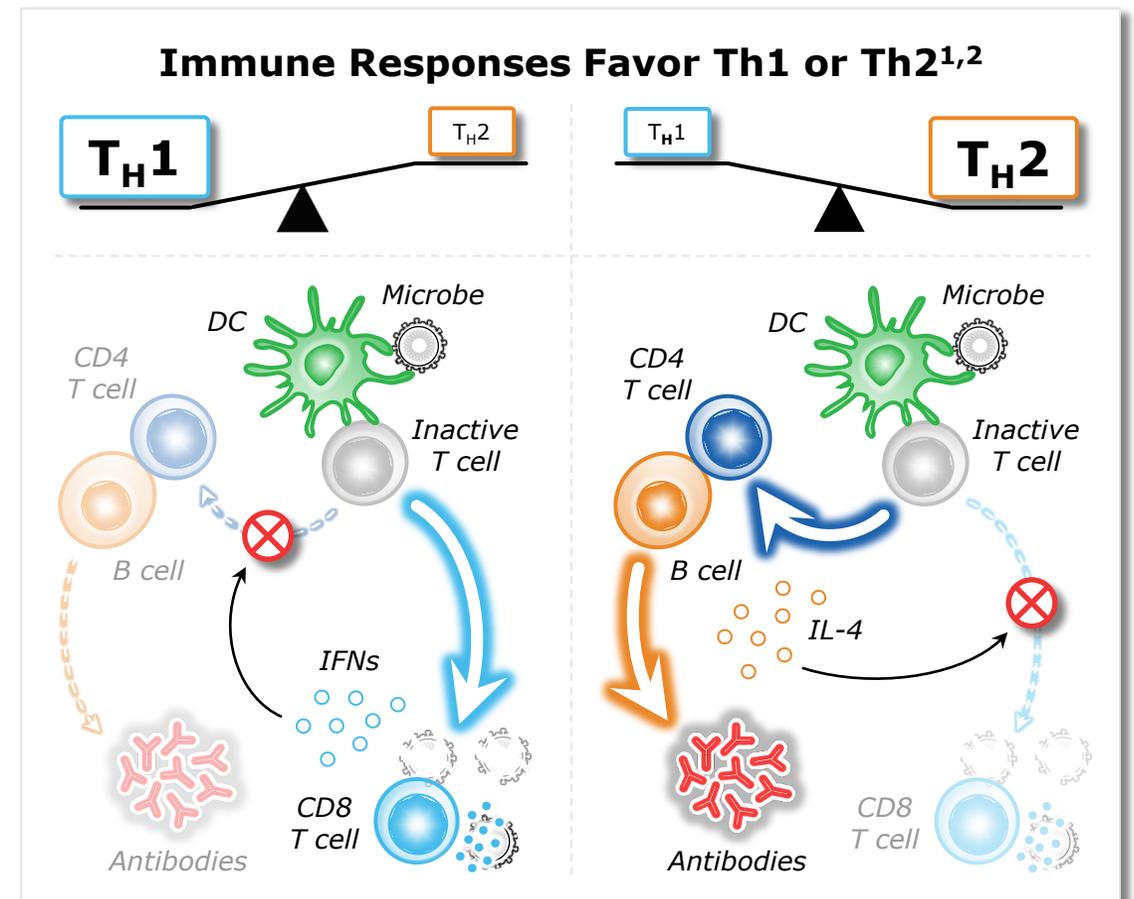


*TNX-1800 is at the pre-IND stage of development



The T_H1/T_H2 Decision: The Immune System Chooses a Cellular or Humoral Response

- T_H1 (cellular) and T_H2 (humoral) responses are characterized by unique cytokine patterns^{1,2}
- The immune response favors T_H1 or T_H2 immunity, a decision based in part on which cytokines (eg, IFNs or IL-4) are produced early in the adaptive response^{1,2}
- Some infections are only well controlled by T_H1 T cell-mediated immunity^{1,3}
- In 20 healthy recovered CoV-2 volunteers, only T_H1 T cell-mediated immunity was observed⁴



1. Bretscher PA. *Scand J Immunol.* 2014;79(6):361-376.
2. Kaiko GE, et al. *Immunology.* 2008;123(3):326-338.
3. Prompetchara E, et al. *Asian Pac J Allergy Immunol.* 2020;38(1):1-9.
4. Grifoni A., et al. *Cell* (2020), doi: <https://doi.org/10.1016/j.cell.2020.05.015>.

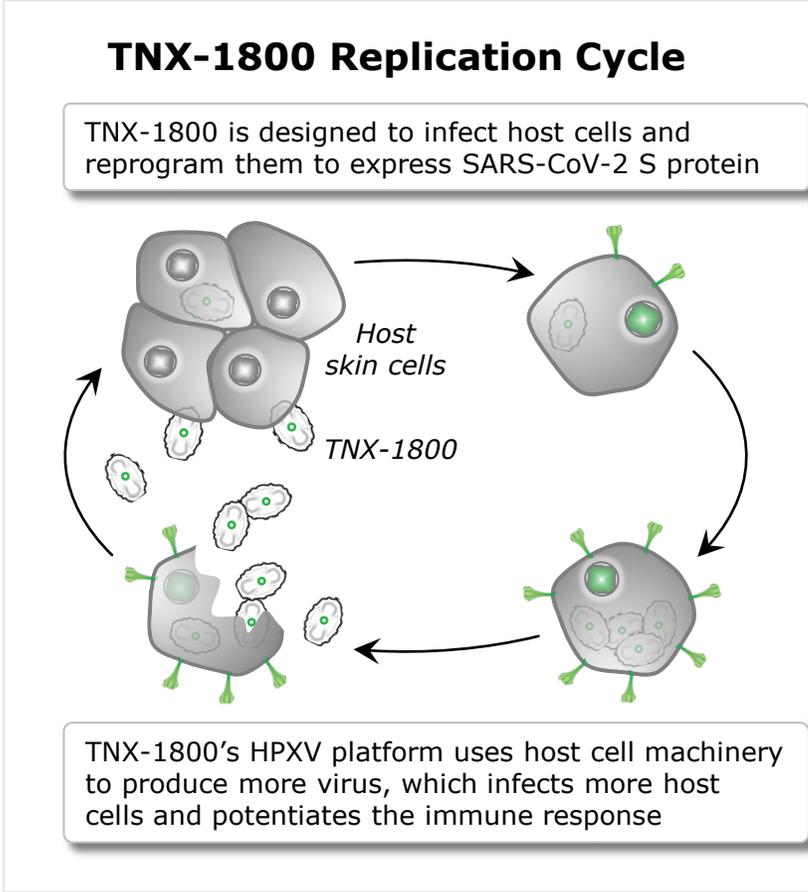


Advantages of Live, Replicating HPVX as a Vector Platform for Vaccines

- TNX-1800–infected host cells are designed to produce SARS-CoV-2 S protein, activating an immune response against those proteins
- TNX-1800 is based on a live, replicating vaccine (HPXV) platform, which induces a robust immune response

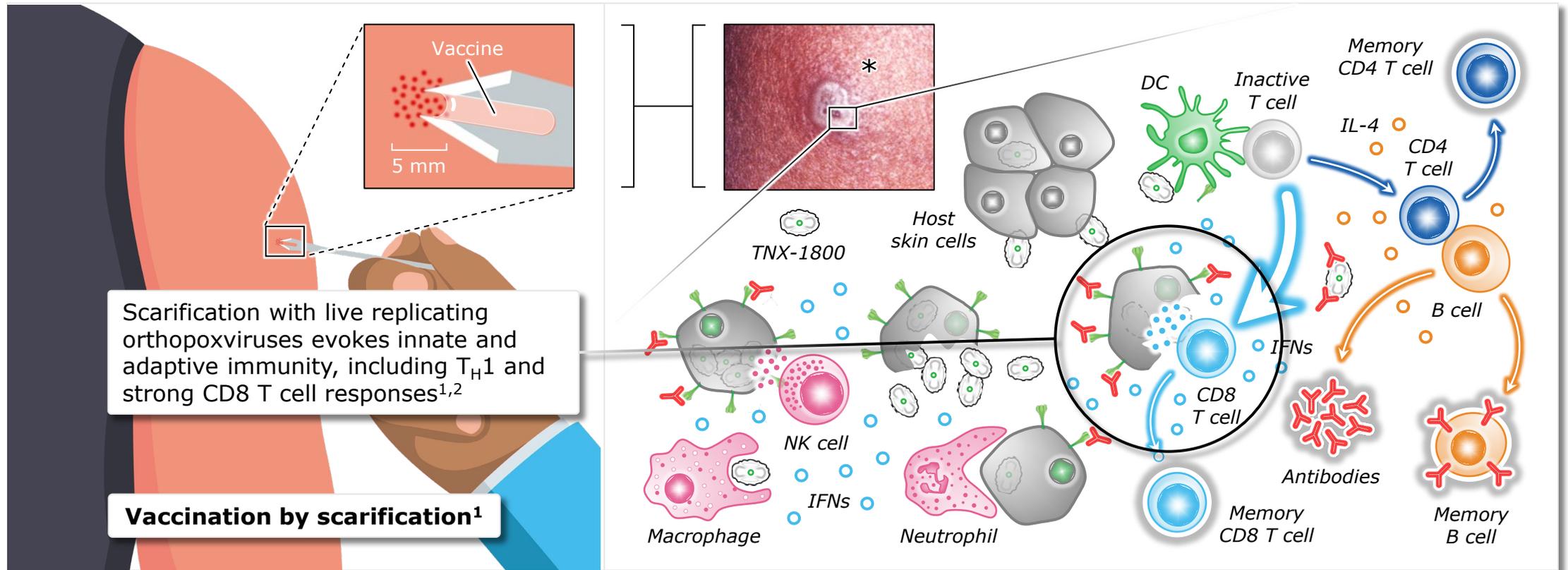
HPXV can serve as a platform for general vaccine development:

- ✓ *Capacity for large and diverse viral DNA inserts*
- ✓ *Vaccines can be rapidly generated and readily manufactured at scale*





TNX-1800 is Designed to Induce Robust T_H1 Cellular Immunity



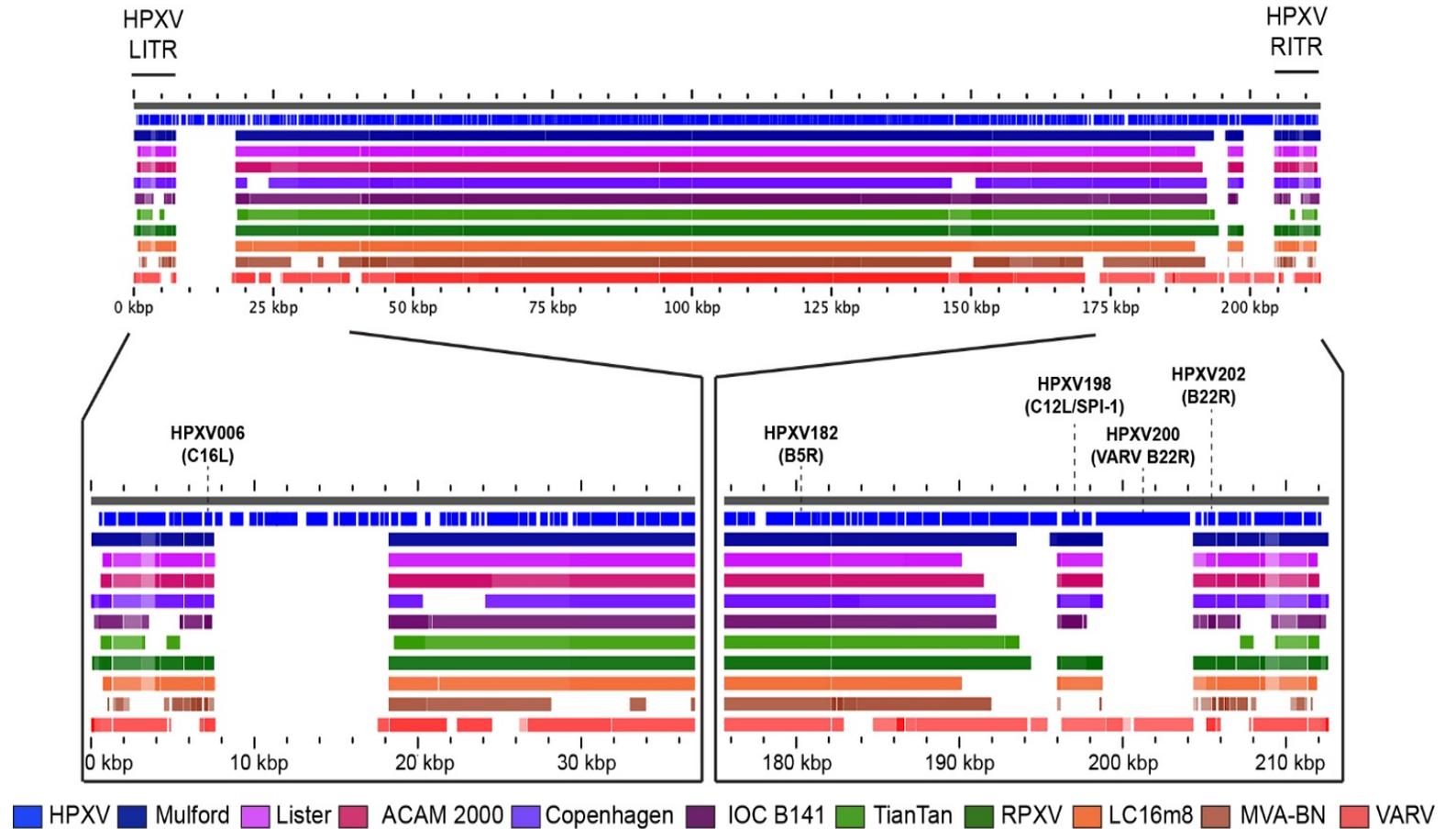
*Example of major cutaneous reaction, or "take," resulting from a replication-competent live-virus vaccine delivered via scarification, indicating successful vaccination^{1,3}

1. Fulginiti VA, et al. *Clin Infect Dis.* 2003;37(2):241-250.
2. Liu L, et al. *Nature Med.* 2010;16(2):224-228.
3. Centers for Disease Control and Prevention. Accessed April 15, 2020. <https://phil.cdc.gov/Details.aspx?pid=3276>



Relationship Between Horsepox, Certain Vaccinia Strains and Variola

Legend: Alignment of orthopoxvirus genomes and location of horsepox (HPXV) genes within telomeres. Orthopoxvirus genomes were aligned using the program GView (<https://server.gview.ca>). The actual nucleotide sequence of each gene within the genome was compared to the coding sequence (CDS) of each gene within the horsepox (HPXV) reference genome (NCBI Accession DQ792504) and the following orthopoxvirus genomes (VACV Mulford 1902 - MF477237; VACV Lister - AY678276; VACV ACAM2000 - AY313847; VACV Copenhagen - M35027; VACV IOC-B141 - KT184690; VACV TianTan - KC207810; Rabbitpox virus (RPXV) Utrecht - AY484669; MVA-BN - DQ983238; VACV LC16m8 - AY678275; Variola virus (VARV) (Bangladesh 1975 - L22579). The white gaps in the HPXV reference sequence represent non-coding sequences within the genome. The percent identity (PID) cutoff was set to 85%, meaning that only matches with PID values over 85% are displayed. Abbreviations: BLAST = Basic Local Alignment Search Tool; LITR = left inverted terminal repeat (ITR); RITR= right ITR.





Development of TNX-1800 as a COVID-19 Vaccine

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Collaboration with Southern Research

- Southern Research will develop and test TNX-1800, which is designed to express Spike (S) protein from the virus that causes COVID-19, which is called SARS-CoV-2.
- We plan to test whether vaccination of animals with TNX-1800 will elicit an immune response to the S protein from SARS-CoV-2 and if so, whether such an immune response will protect mice and non-human primates against a challenge with SARS-CoV-2 virus
- We expect to receive data from small animal experiments and from primates in the fourth quarter of 2020¹

Further Development

- The further development of TNX-1800 for human clinical trials will require manufacturing according to Good Manufacturing Practice, or GMP
- TNX-1810, TNX-1820 and TNX-1830² are in early development as vaccines to elicit almost pure T cell responses vaccines

¹We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

²TNX-1810, -1820 and -1830 are experimental new biologics, at the pre-IND and pre-clinical stage of development and are not approved for any indication



Thank you!