

Potential SARS Virus Vaccines

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Potential SARS Virus Vaccines

First Generation

- Whole Inactivated virus (Salk)
- Live attenuated (Sabin)

Second Generation

- Gene-based vaccines (DNA, ADV, poxvirus, etc.)
- Recombinant subunit (protein)
- Peptide-based

Accelerated vaccination for Ebola virus haemorrhagic fever in non-human primates

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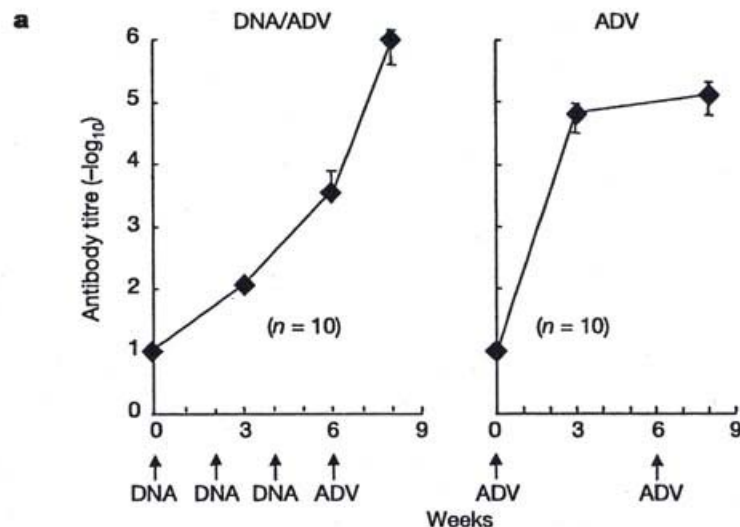
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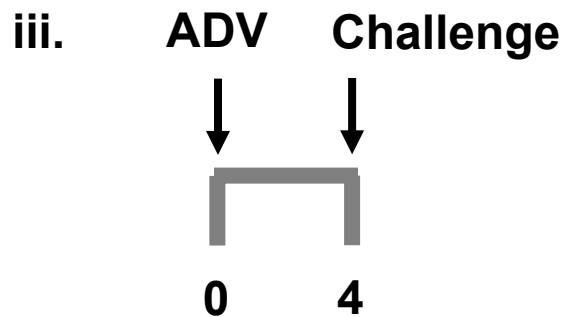
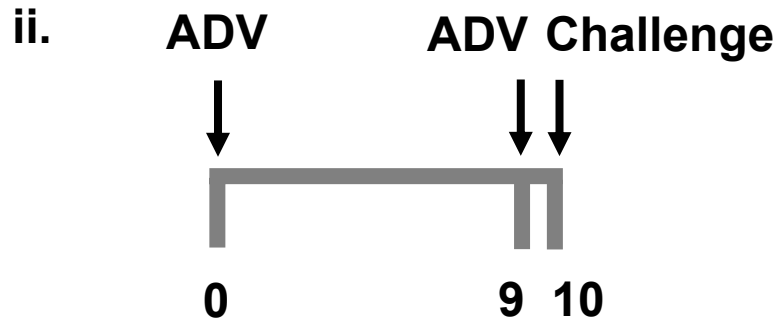
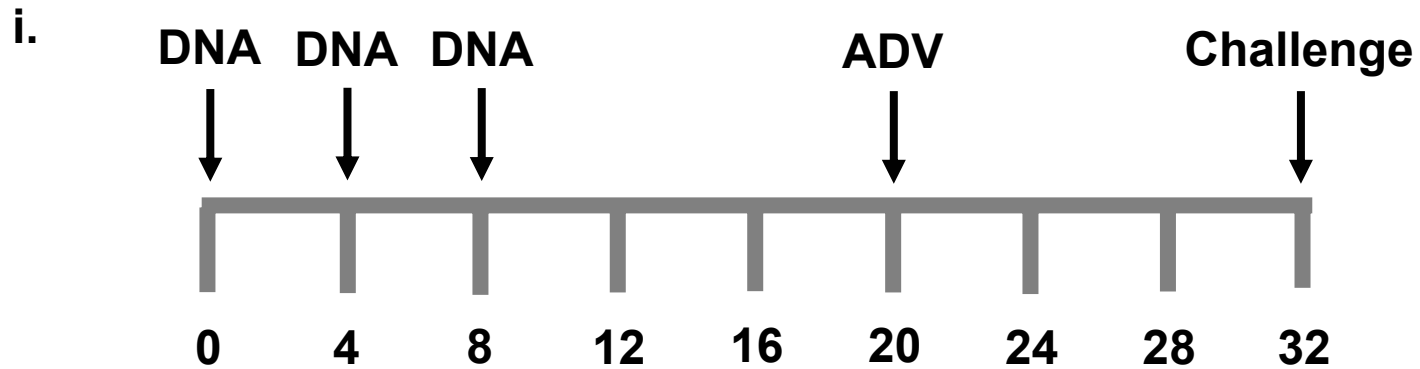
Containment of highly lethal Ebola virus outbreaks poses a serious public health challenge. Although an experimental vaccine has successfully protected non-human primates against disease¹, more than six months was required to complete the immunizations, making it impractical to limit an acute epidemic. Here, we report the development of accelerated vaccination against Ebola virus in non-human primates. The antibody response to immunization with an adenoviral (ADV) vector encoding the Ebola glycoprotein (GP) was induced more rapidly than with DNA priming and ADV boosting, but it was of lower magnitude. To determine whether this earlier immune response could nonetheless protect against disease, cynomolgus macaques were challenged with Ebola virus after vaccination with ADV-GP and nucleoprotein (NP) vectors. Protection was highly effective and correlated with the generation of Ebola-specific CD8⁺ T-cell and antibody responses. Even when animals were immunized once with ADV-GP/NP and challenged 28 days later, they remained resistant to challenge with either low or high doses of virus. This accelerated vaccine provides an intervention that may help to limit the epidemic spread of Ebola, and is applicable to other viruses.

CD4⁺ T cells at this time (data not shown). Both CD8⁺ cellular and humoral immune responses therefore were associated with protection.

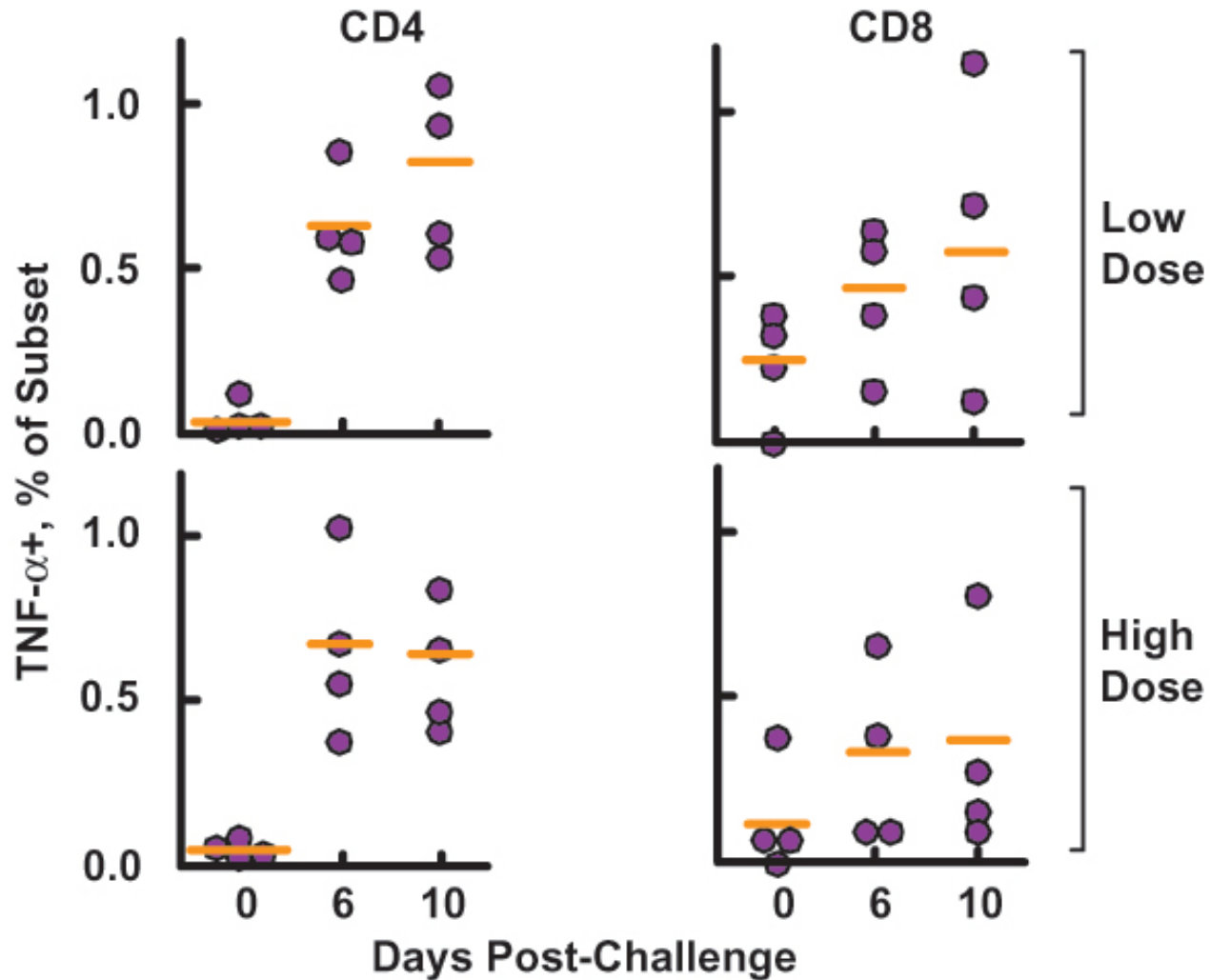
A second adenoviral immunization did not substantially increase the Ebola-specific immune responses (data not shown), raising the notion that the primary immunization was sufficient to confer protection. To address this possibility, a single immunization was given, and animals were challenged one month afterwards (Fig. 1b, bottom panel). Both at low and high viral challenge doses, animals were completely protected against infection (Fig. 4a). In this case, changes in the intracellular IFN- γ response in T lymphocytes were not consistently seen (data not shown); however, Ebola-specific T-cell responses were detected with intracellular tumour-necrosis factor (TNF)- α . CD8 responses were observed before challenge or were induced soon thereafter in five of eight animals, once again correlating with protection against infection (Fig. 4b, right). In contrast, CD4⁺ responses, not detectable before inoculation, increased after challenge (Fig. 4b, left). Immunoglobulin- γ (IgG)



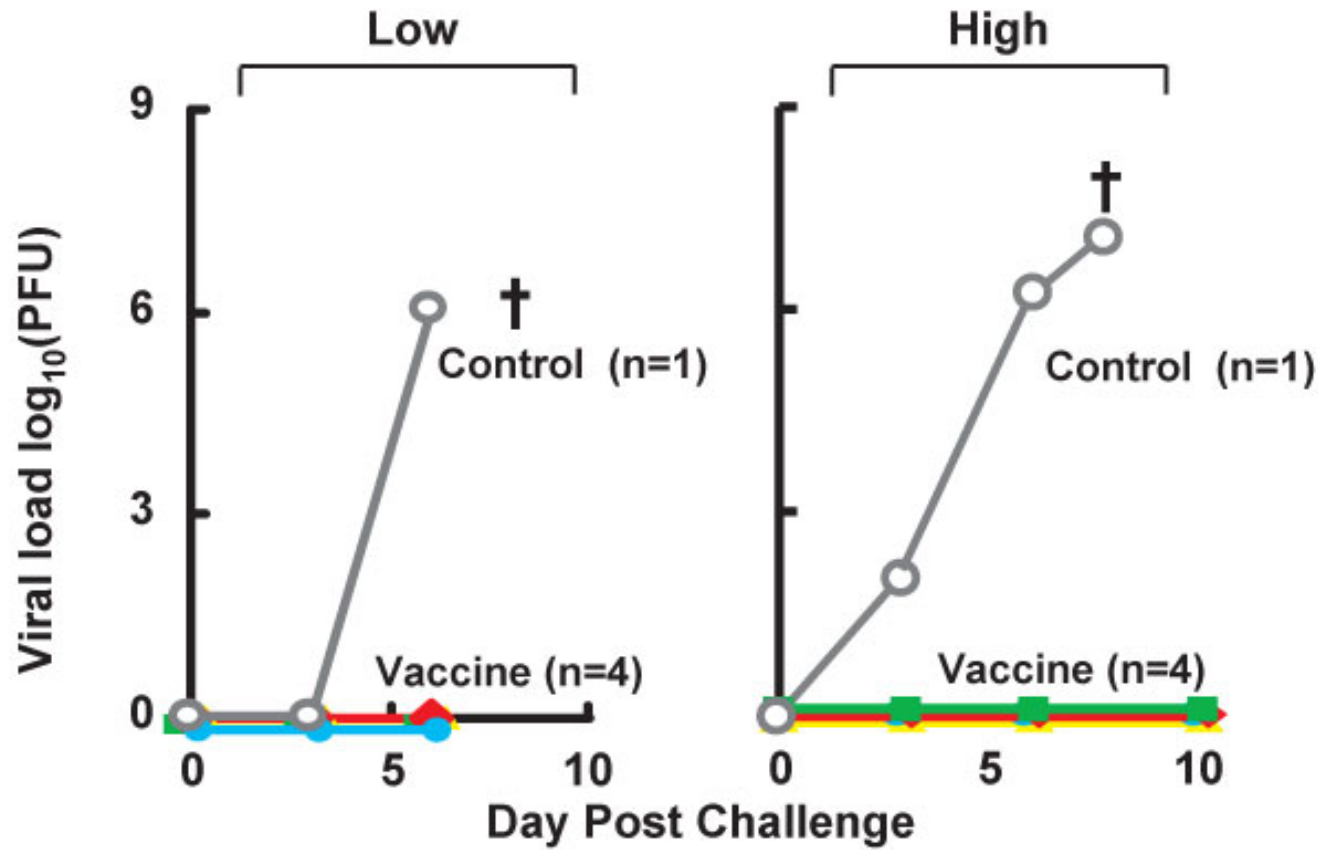
Ebola Virus Vaccine Immunization Protocol



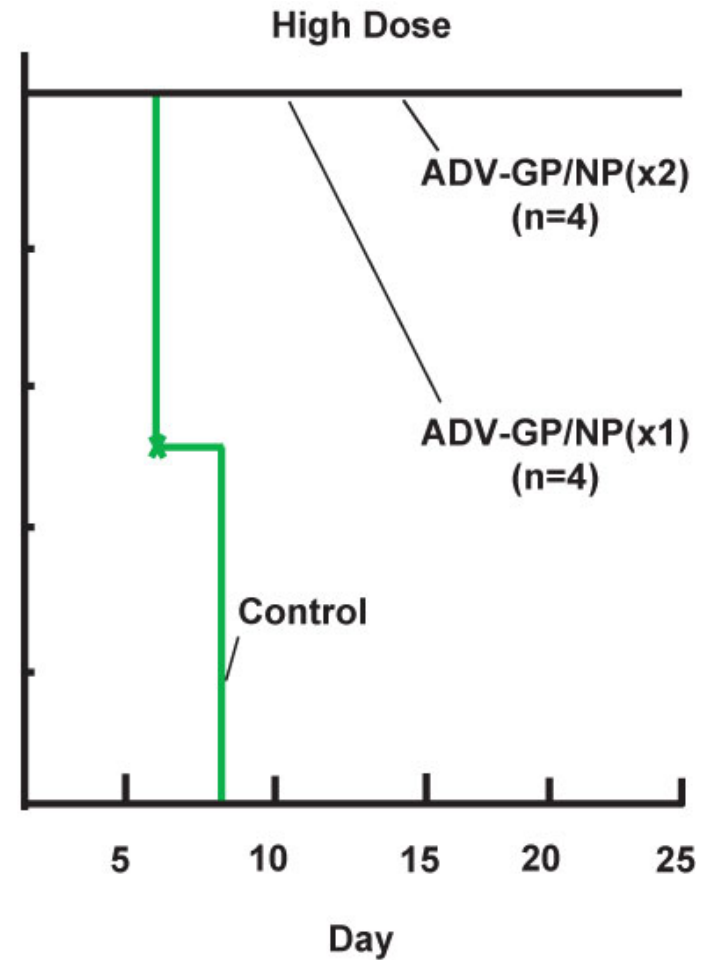
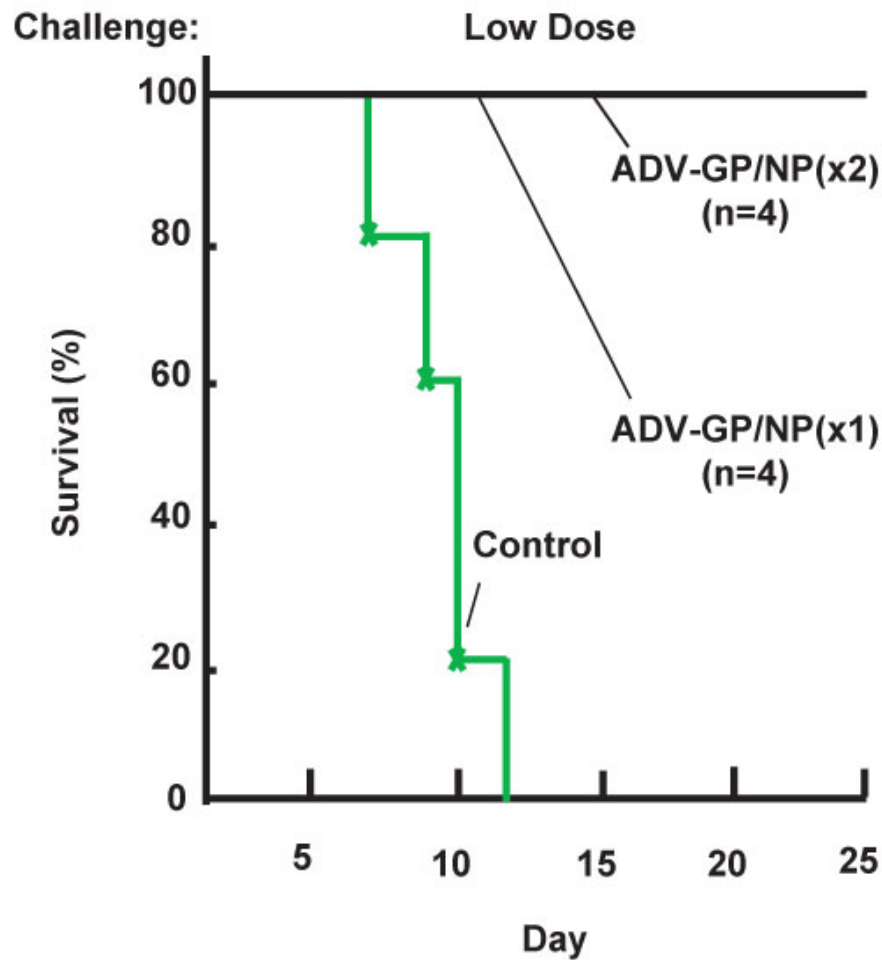
Immune Response in Non-human Primates After a Single Adenoviral Immunization



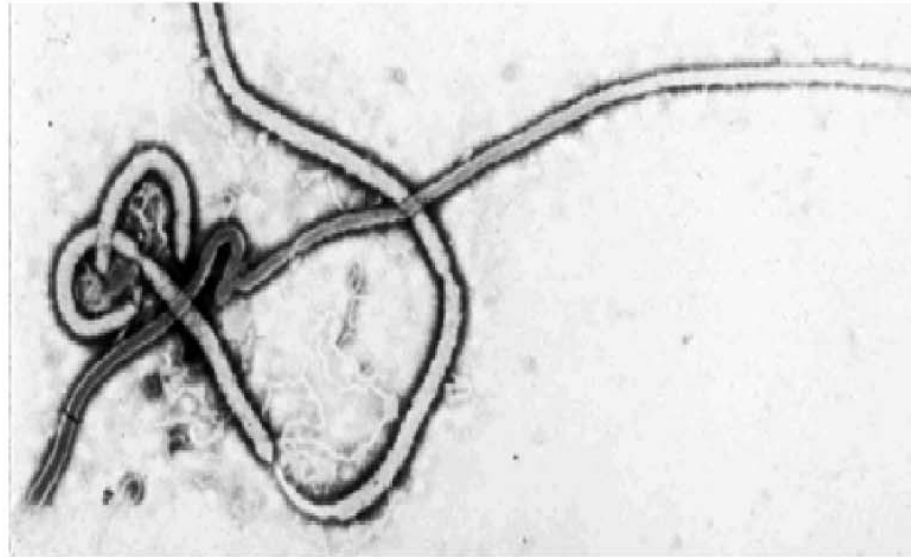
Protection Against Lethal Challenge in Non-human Primates Using a Single Adenoviral Immunization (4 Week Challenge)



Cumulative Survival Adenoviral Immunizations



How Might Hemorrhagic Fever Virus Vaccines Be Used?

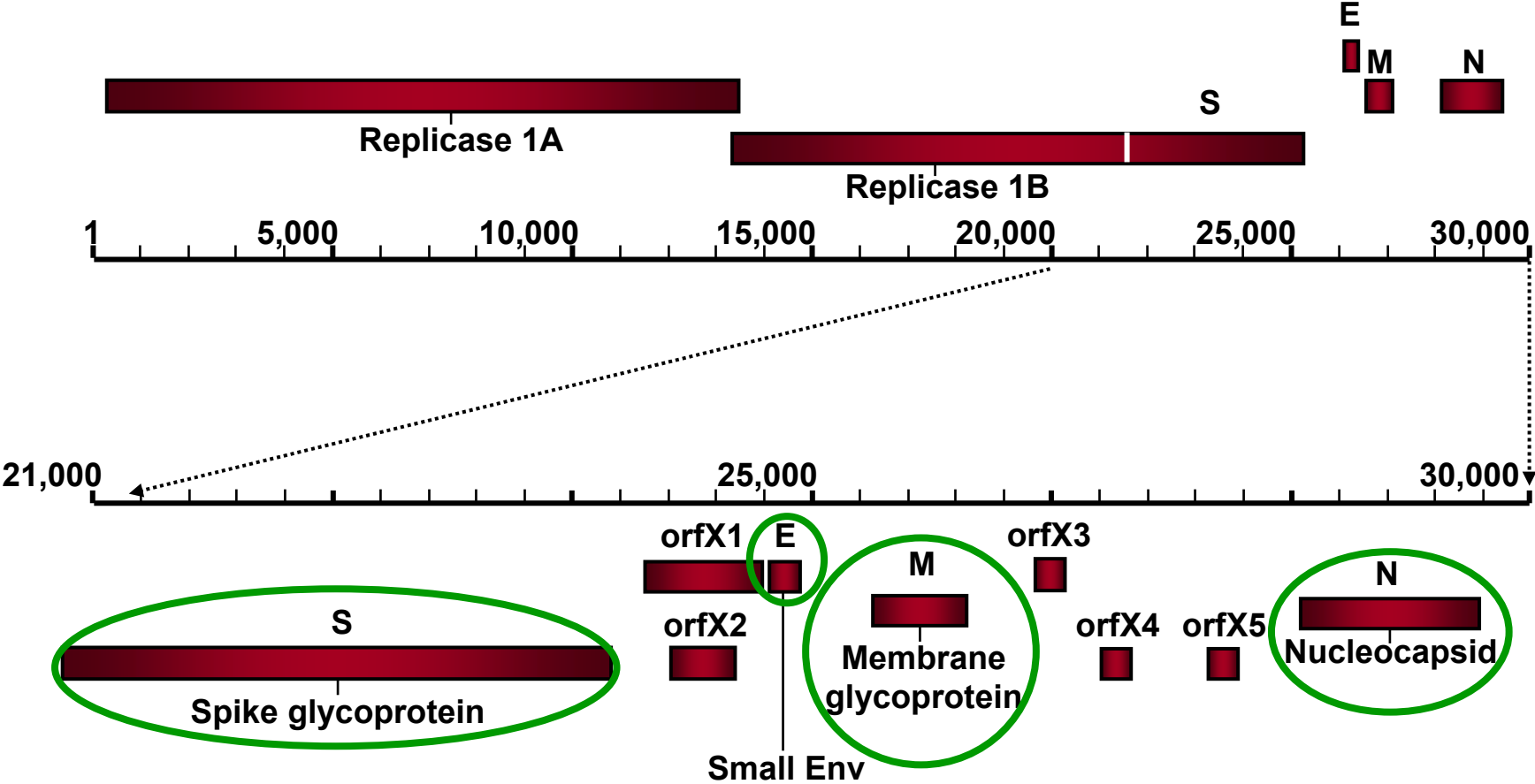


Acute Outbreak Vaccination: ADV

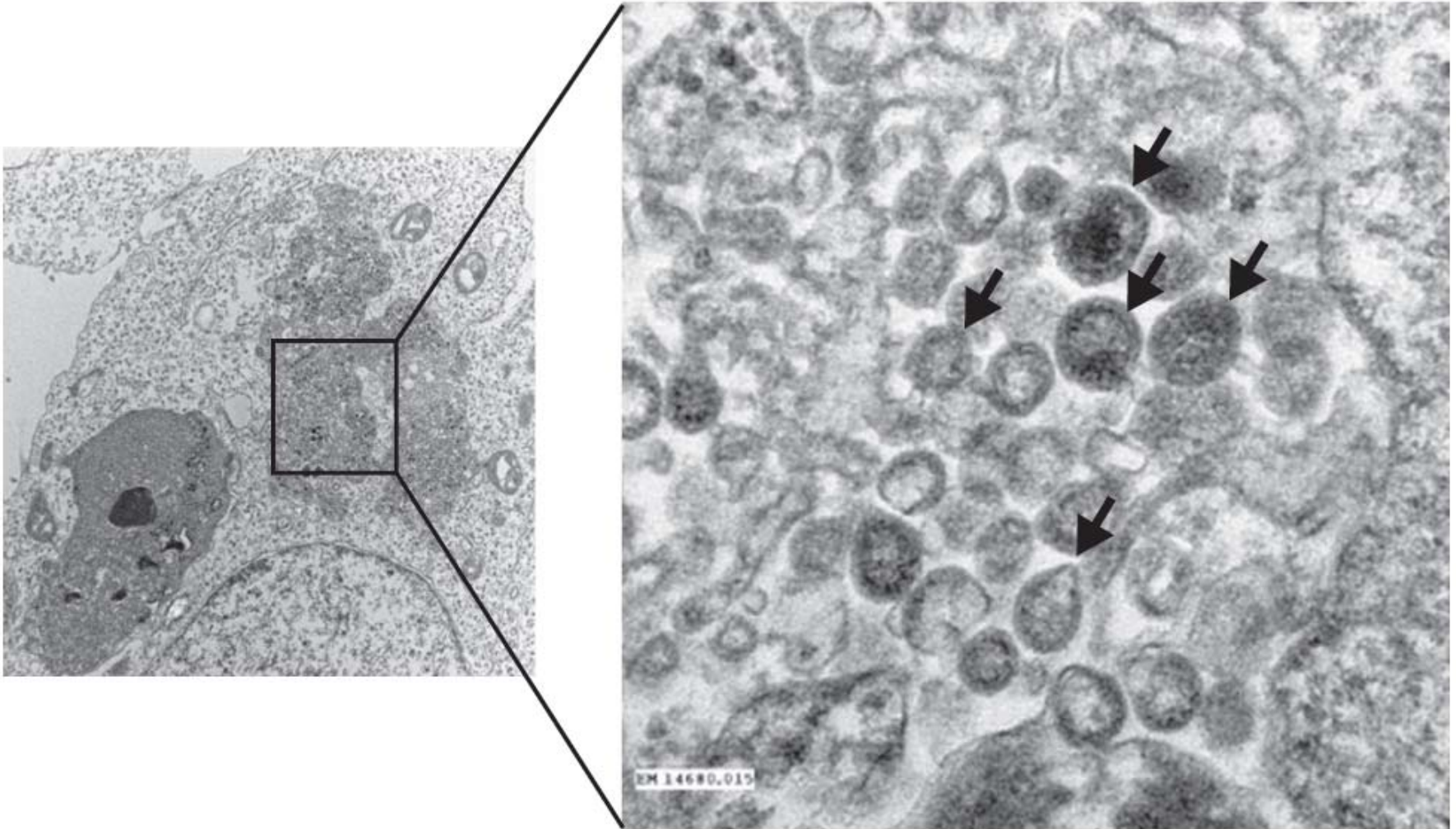
**Preventive Vaccines (e.g.
military recruits, hospital
workers)**

**DNA + ADV, or other
"prime-boost"
combinations**

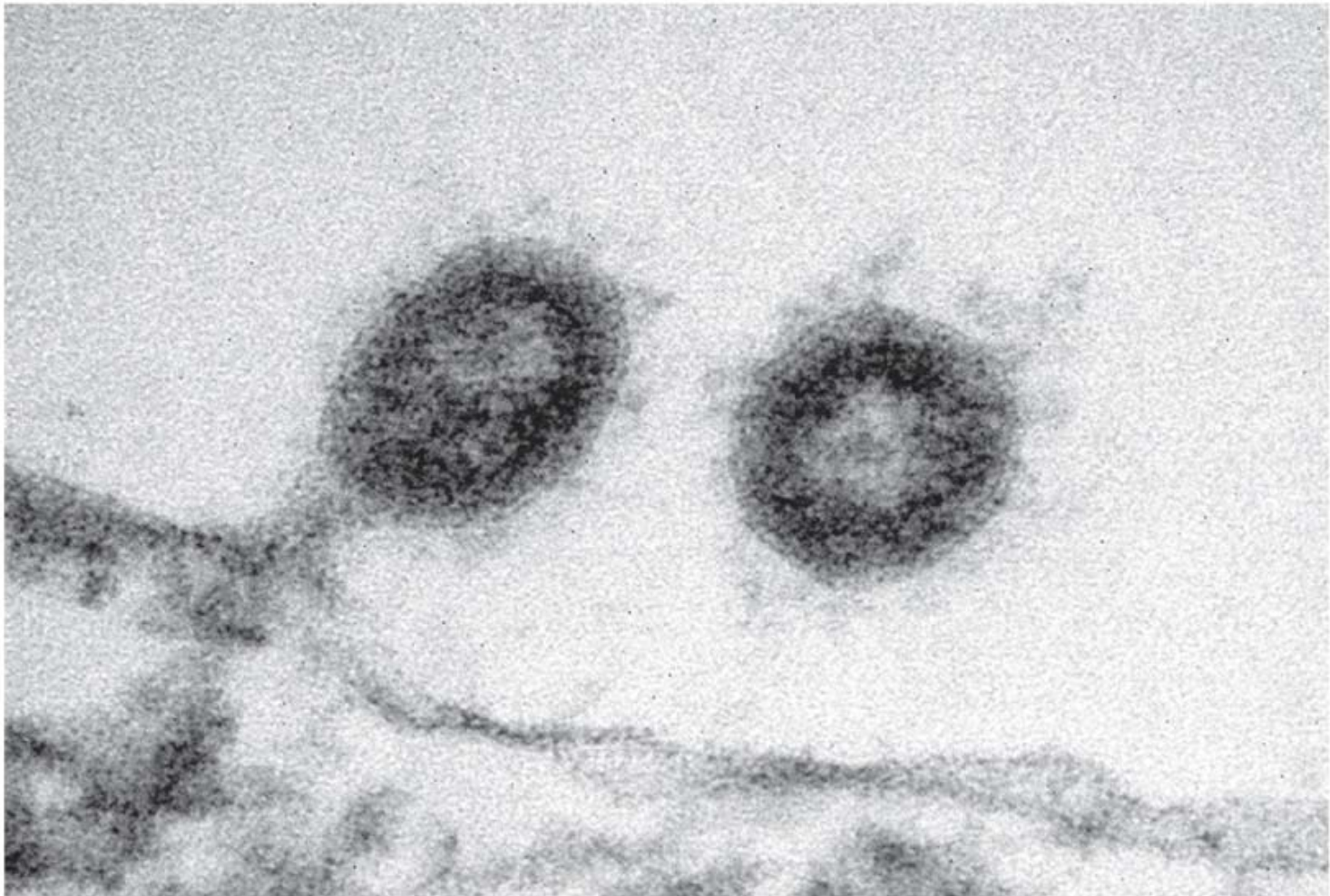
The SARS-CoV Genome



Electron micrograph of SARS-CoV capsids in transfected 293T cells.



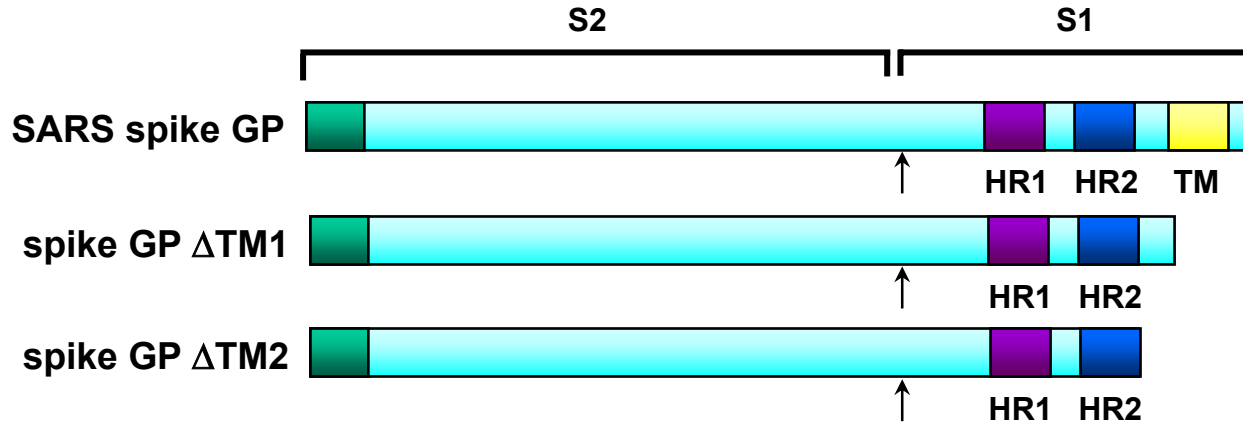
Formation of Coronavirus-like Particle by Inclusion of S Glycoprotein Expression Vector



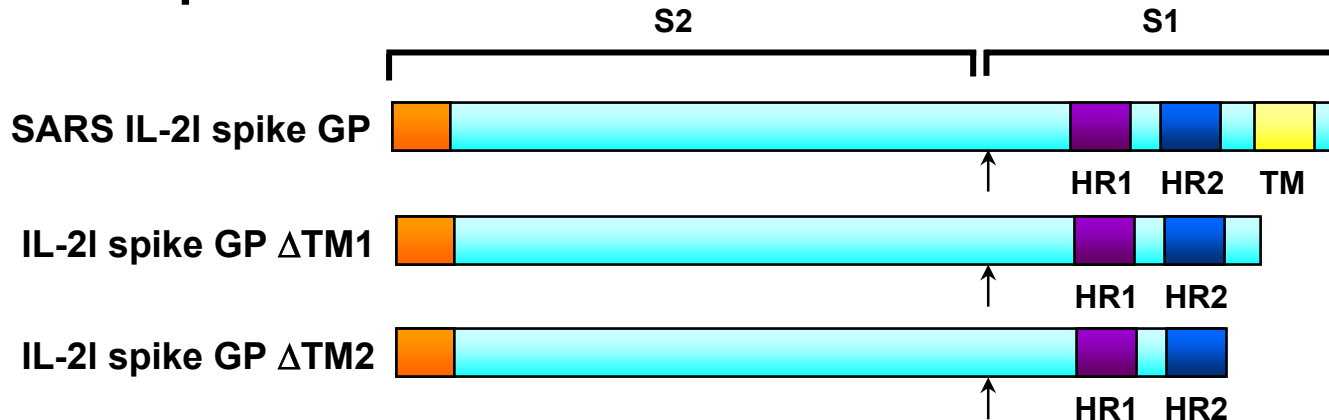
100 nm

SARS Vaccine Vectors (DNA and ADV)

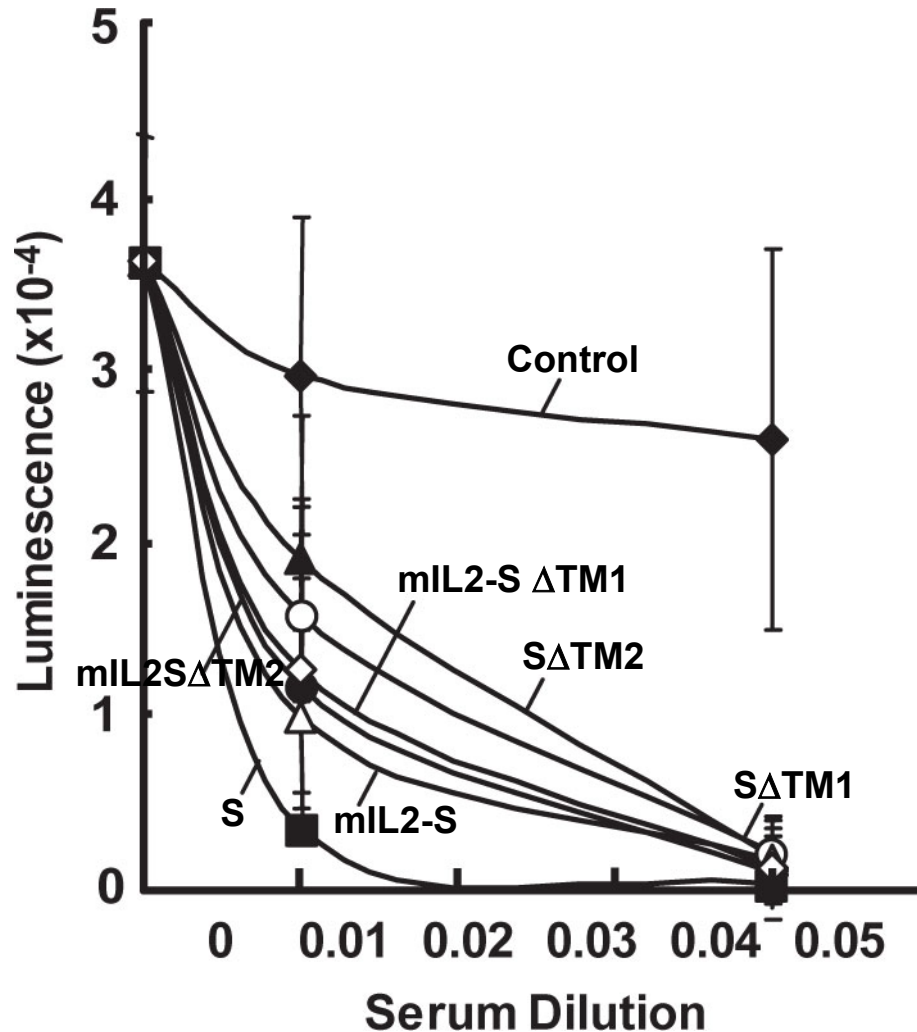
Native Leader Sequence



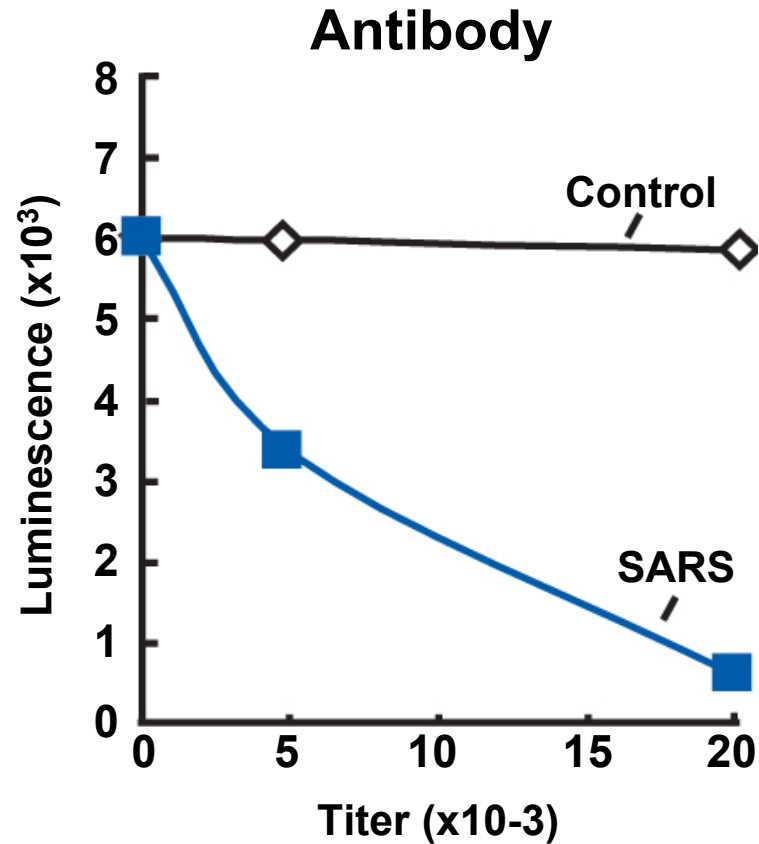
IL-2 Signal Sequence



Inhibition of Viral Gene Transfer by Mouse Immune Antisera



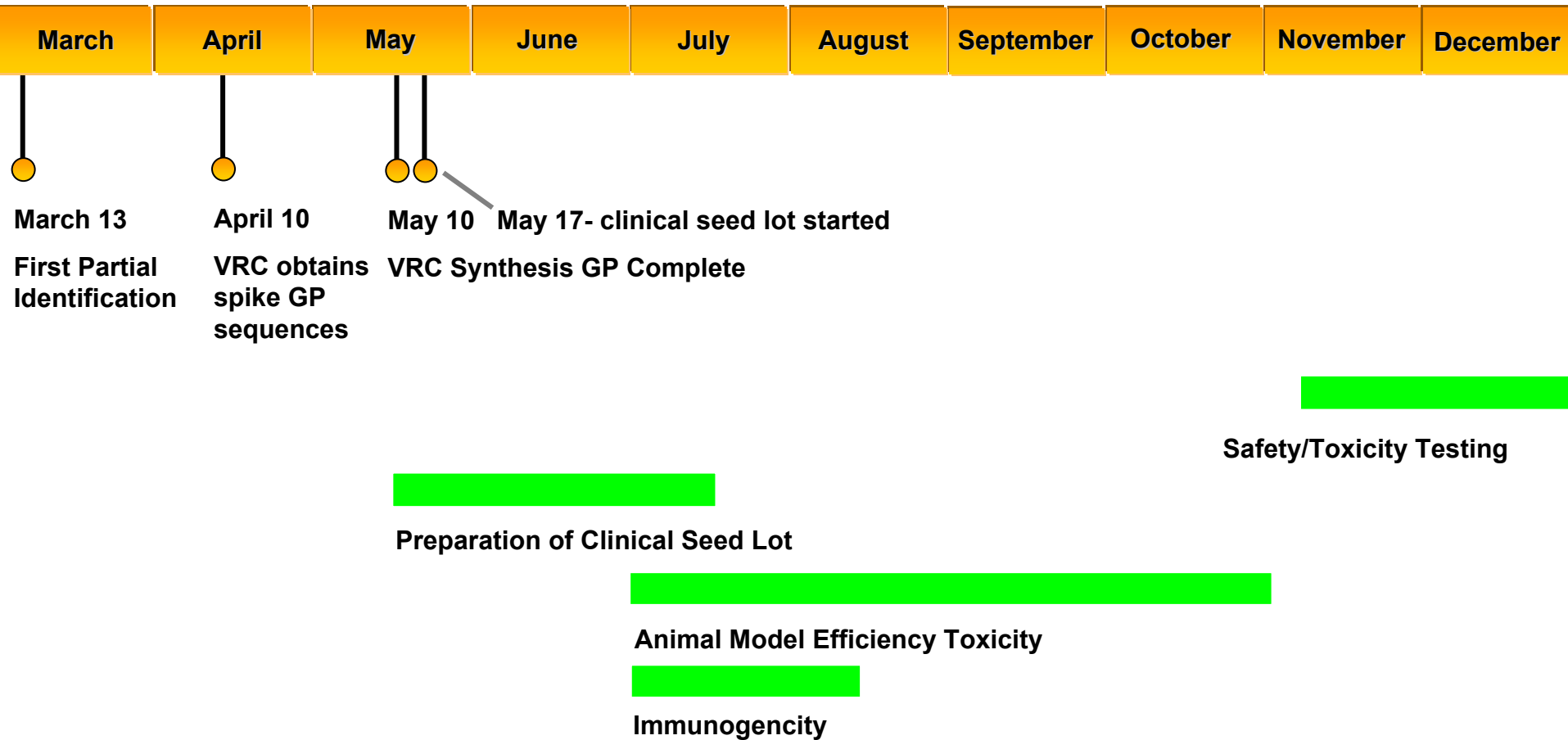
Inhibition of SARS-CoV S Pseudotype Infection by a Antisera From a Recovered Patient



Advantages of Gene-based SARS Vaccines

- rapid onset of action**
- ring vaccination for acute outbreaks**
- cell-mediated and humoral immunity**
- can boost with inactivated virus vaccine**

VRC SARS 2003 Virus Vaccine Timeline



Acknowledgements

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SARS-CoV Mouse Studies NIAID, NIH

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