

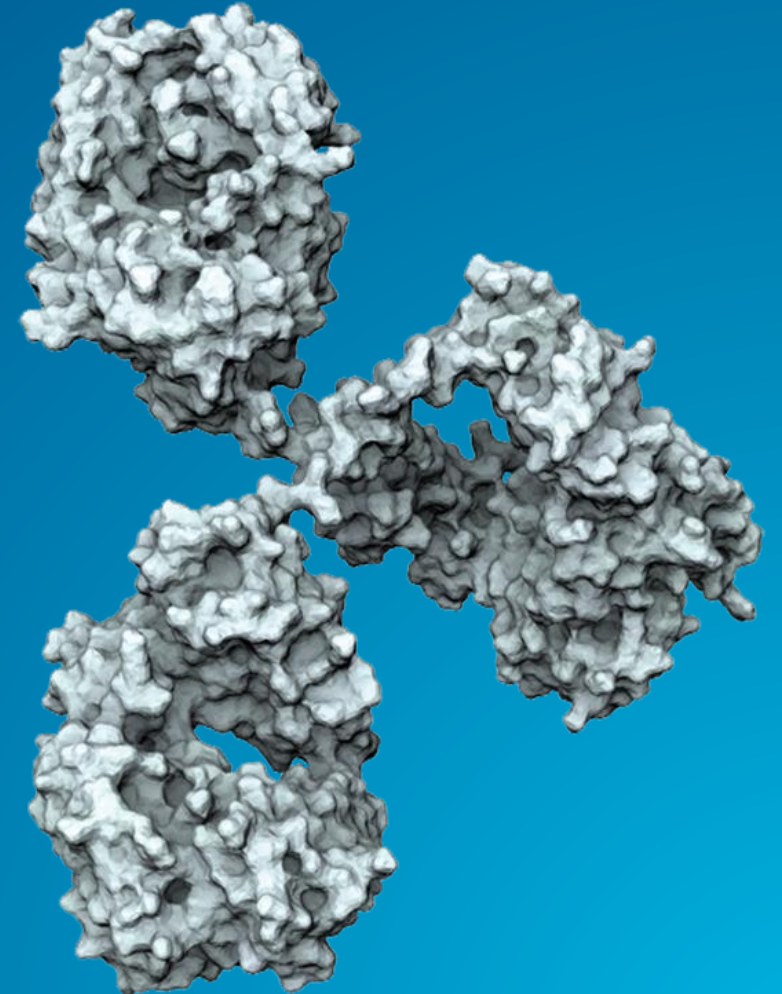


Translating **science** into
global health impact

HIV Vaccine Development: Current Approaches

Dr. Vincent Muturi-Kioi

GHVE Annual Stakeholders' Meeting | 28th November 2023



IAVI gratefully acknowledges the generous support provided by the following major funders



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As of July 2023

Outline

The Burden of Disease

Challenges in HIV Vaccine Development

Strategies for Vaccine Development

HIV; Burden of Disease

HIV remains a major health issue globally

As much as ever, the world needs an efficacious HIV vaccine

Global number of people living with HIV in 2022

39.0 million

Number of people newly infected worldwide - 2022

1.3 million

Number of AIDS-related deaths in 2022

680 000

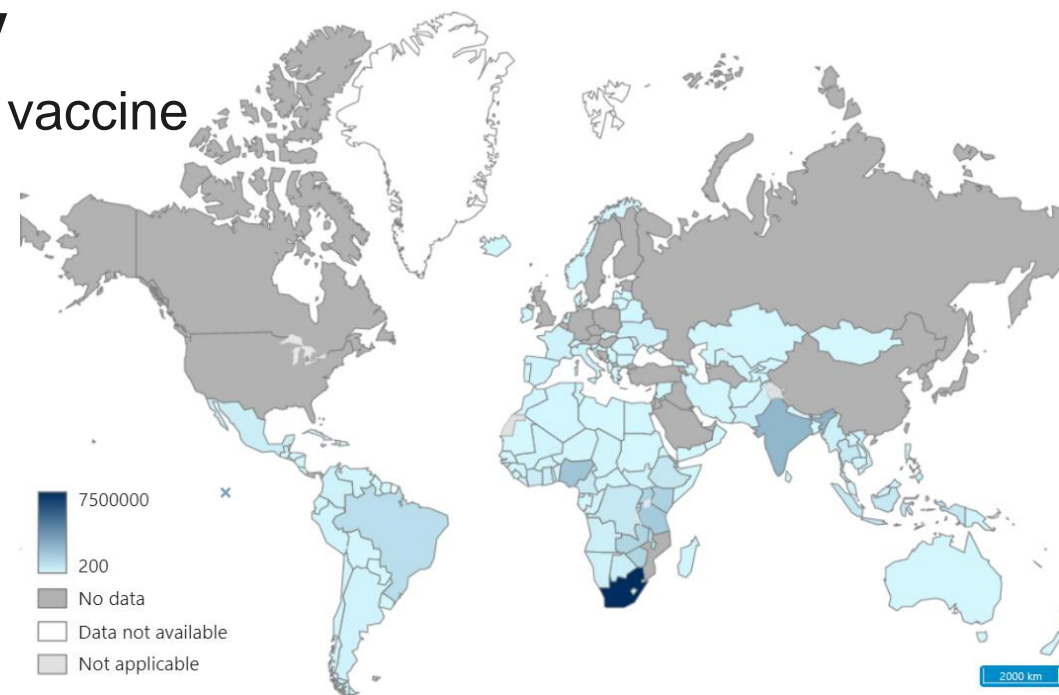
African Region remains most severely affected

60% of global new infections

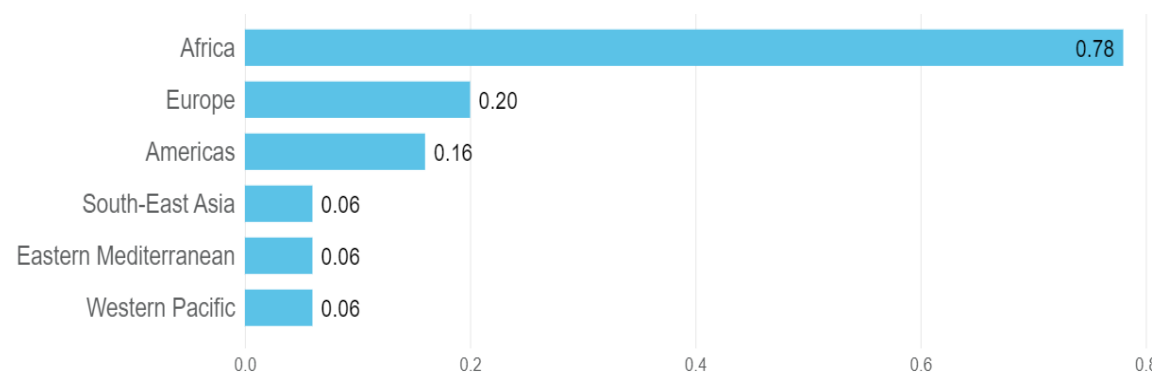
Women and girls accounted for 46% of all new infections in 2022.

130 000 new infections in children in 2022

UNAIDS 2023: https://www.unaids.org/en/resources/documents/2023/UNAIDS_FactSheet



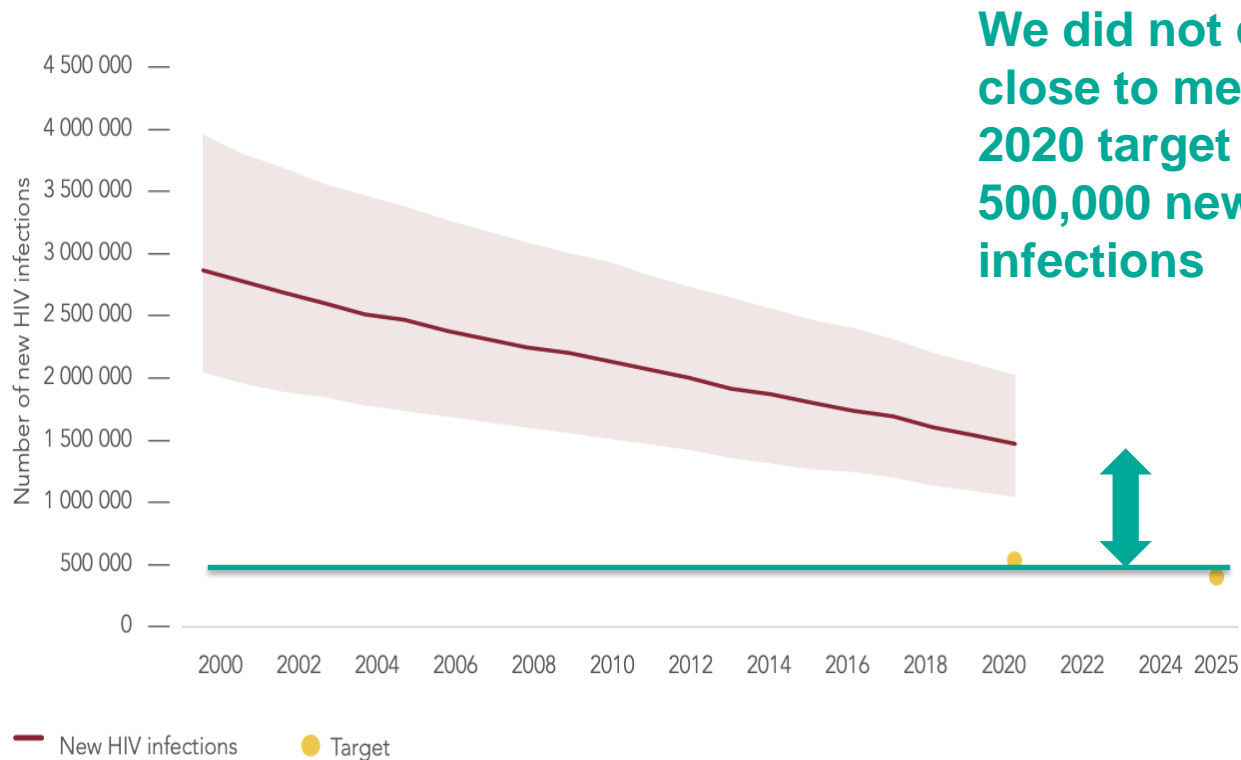
Number of people living with HIV



New HIV infections (per 1000 population)

Unrelenting HIV incidence and unmet goals reinforce the need for new prevention tools

FIGURE 0.5 | NEW HIV INFECTIONS, GLOBAL, 2000–2020, AND 2020 AND 2025 TARGETS



Source: UNAIDS epidemiological estimates, 2021 (<https://aidsinfo.unaids.org/>).

The development of new prevention tools that provide longer lasting protection, including efficacious vaccines, and long-acting ARVs and broadly neutralizing antibodies for PrEP, will be essential

Risks to future progress in decreasing incident infection rates:

- Demographic changes (“youth bulge”)
- Increasing number of people in need of treatment
- Risk of drug resistance
- Donor fatigue and competing global priorities

An effective HIV vaccine would be transformative

An HIV vaccine could:

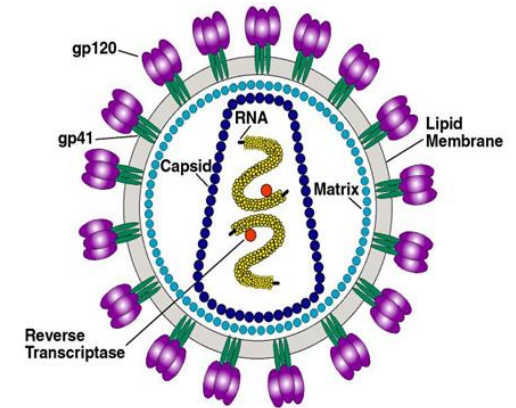
- Provide long-lasting protection with a limited number of doses within a discrete timeframe *before* window of HIV infection risk.
- Be distributed widely and confidentially (and not apparent to partners, parents and peers).
- Overcome challenges of behavior change and adherence.
- Protect all people at risk of HIV infection, including those most vulnerable to HIV who may be difficult to reach with other prevention interventions.



Challenges in HIV Vaccine Development

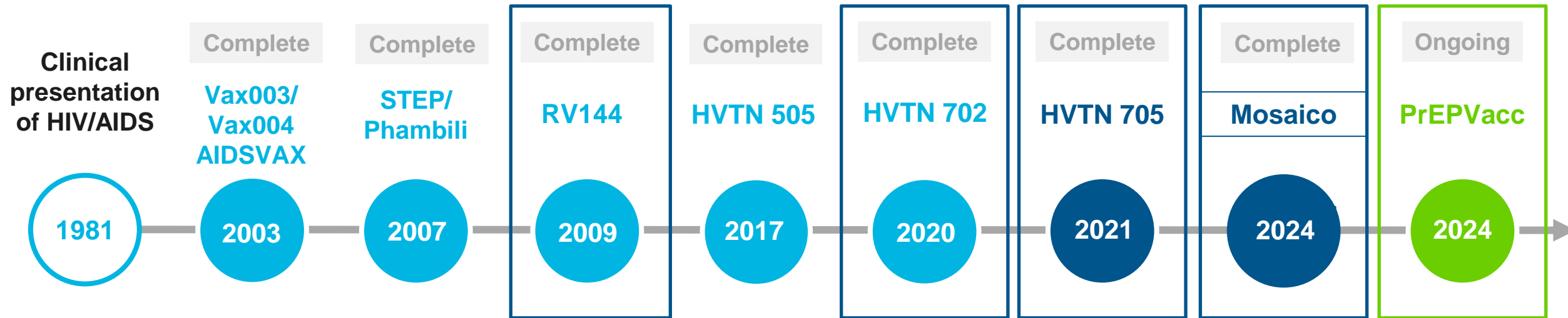
Traditional vaccine approaches have failed for HIV

- HIV is hyper variable (the result of active, ongoing replication and “error-prone” replication processes).
- Once HIV infects, it maintains persistent infection for life. There are no examples of natural clearance of infection and no “natural immunity”.
- HIV evades, avoids or escapes from antiviral antibodies and T cell responses
- HIV attacks and directly infects key immune effector cells (CD4 T cells and some “antigen presenting” cells).
- Common animal models have uncertain value in reliably predicting efficacy of vaccine candidates in humans.



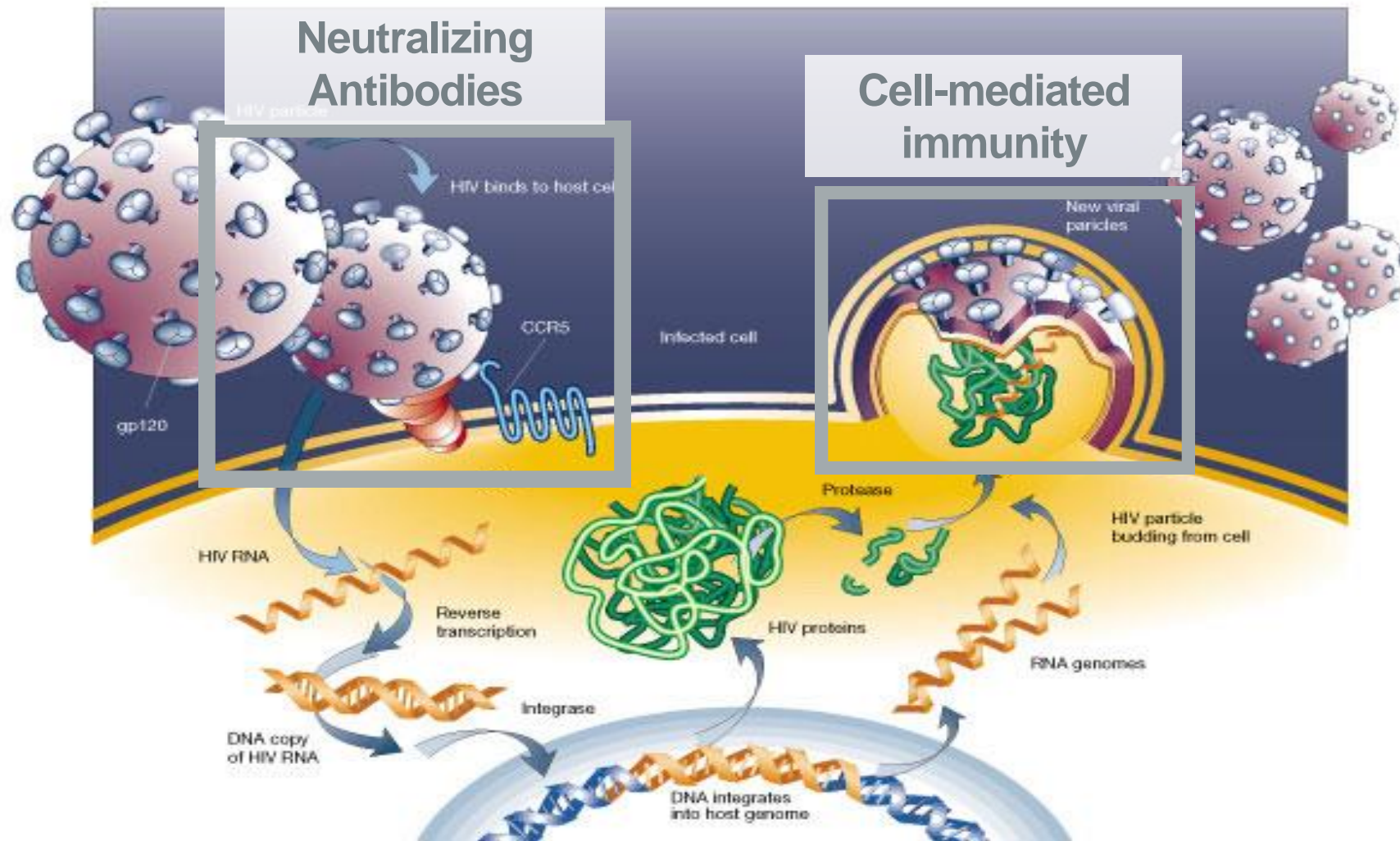
HIV Vaccine Strategies- Picture of Success?

HIV vaccine efficacy trials to date.



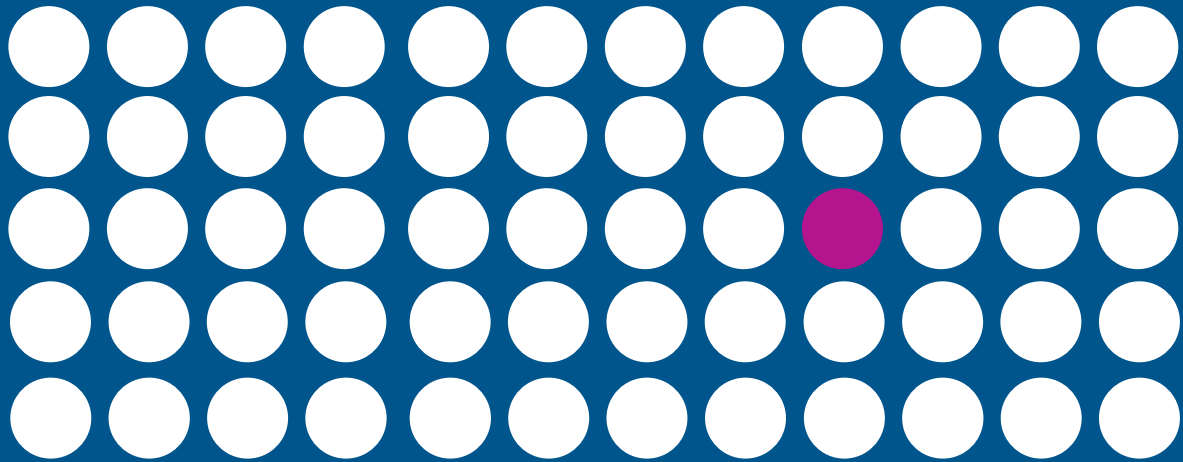
Nine Phase II/III clinical trials have been completed since the discovery of HIV/AIDS. These vaccine candidates were designed using an **empirical approach** where different parts of the virus were formulated to stimulate either B- or T-cell response following vaccination.

An effective HIV Vaccine will likely need to stimulate **Neutralizing Antibodies** and **Cell Mediated Immunity**



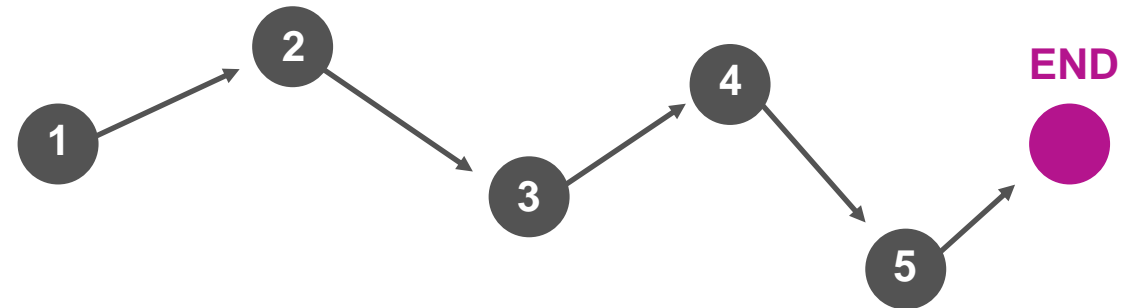
IAVI is prioritizing a rational approach to HIV vaccine design

EMPIRICAL APPROACH



Test different vaccine candidates; if one demonstrates **protection efficacy**, then identify correlates of protection.

RATIONAL DESIGN APPROACH



Identify a **correlate of protection**, then create a strategy to elicit that correlate of protection by rational design.

Vaccines to Induce bnAbs against HIV

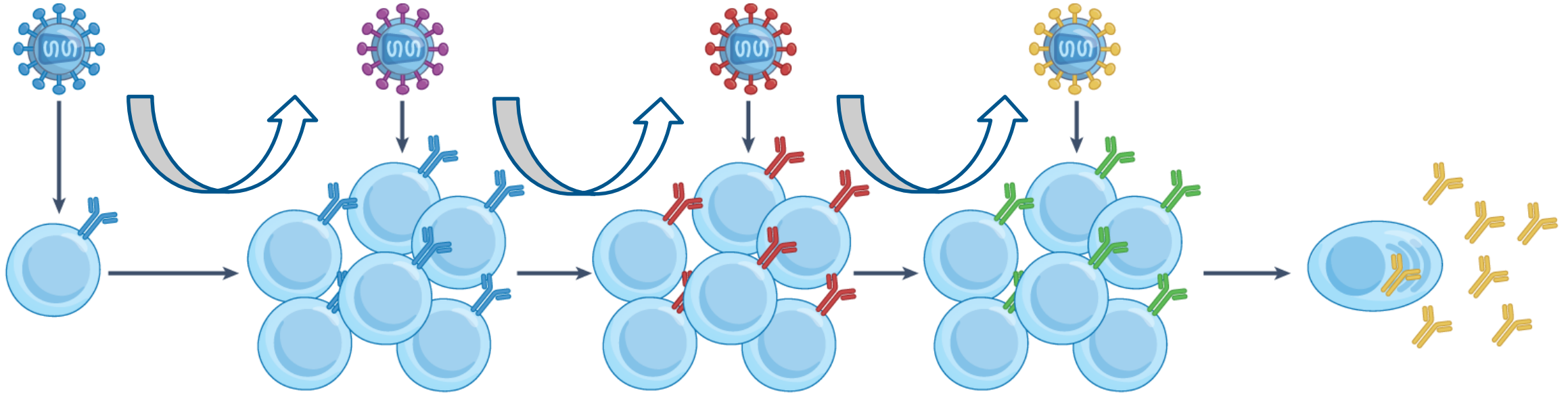
Major approaches to bnAb-based HIV vaccine design to be tested in humans in the coming years

Lineage-based vaccine design – sequence of immunogens derives from sequence of Env variants in a longitudinal case study of bnAb development from natural infection. Priming immunogen selected to bind UCA for one lineage.
Trials: prime/boost for CH103, CH235, DH270 lineages from Haynes and colleagues

Germline-targeting vaccine design – priming immunogen engineered to broadly activate diverse precursors within a bnAb class (spanning many lineages); boost immunogens are successively more native-like.
Trials: priming VRC01-class responses, three different immunogens from Schief, Sanders, Stamatatos and their colleagues; priming BG18-class responses by Schief and colleagues

Immunofocusing vaccine design – immunogen sequence designed to focus responses to one or more particular epitopes, but “germline agnostic”.
Trials: Fusion peptide vaccine by Kwong, Mascola and colleagues

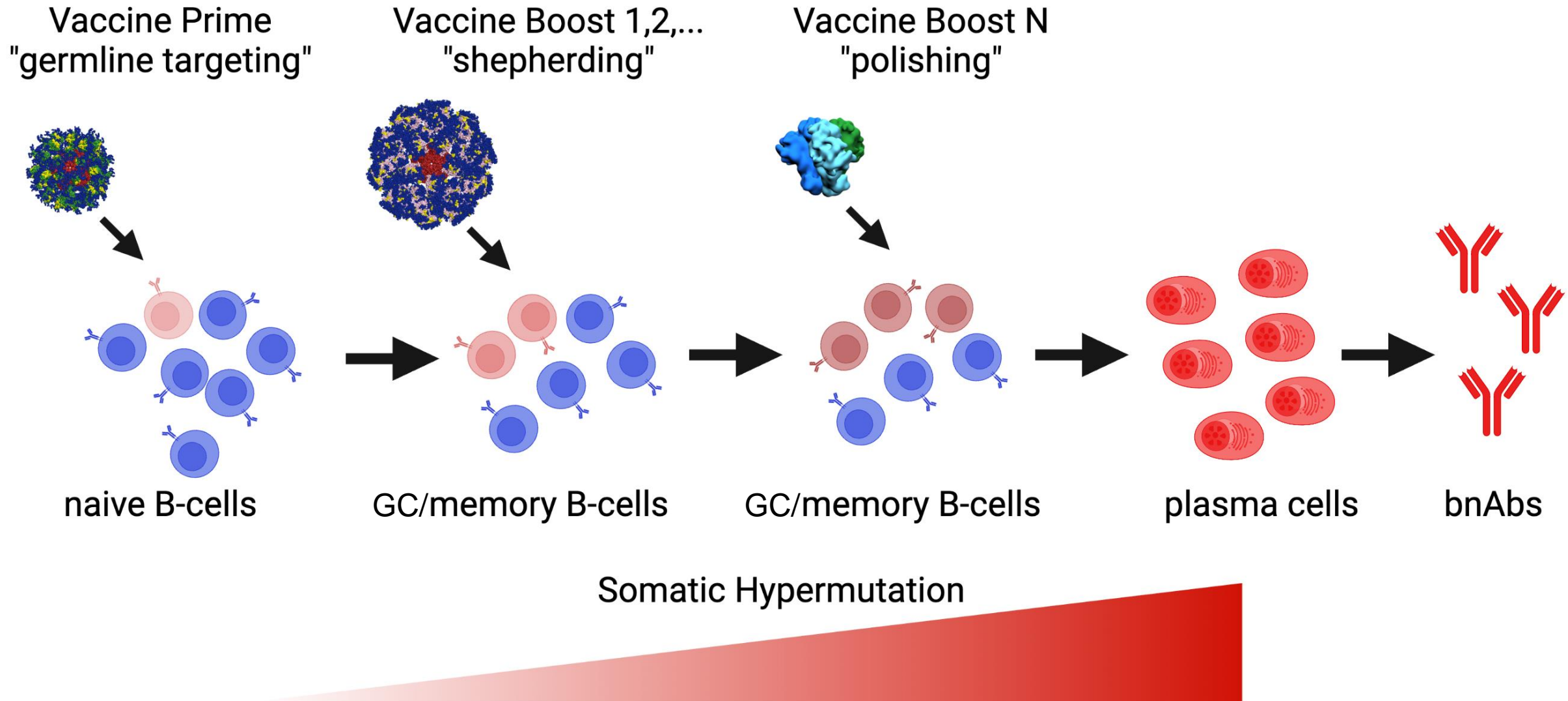
We've learned from PLWH.



Host-virus co-evolution, viral escape drives production of bnAbs

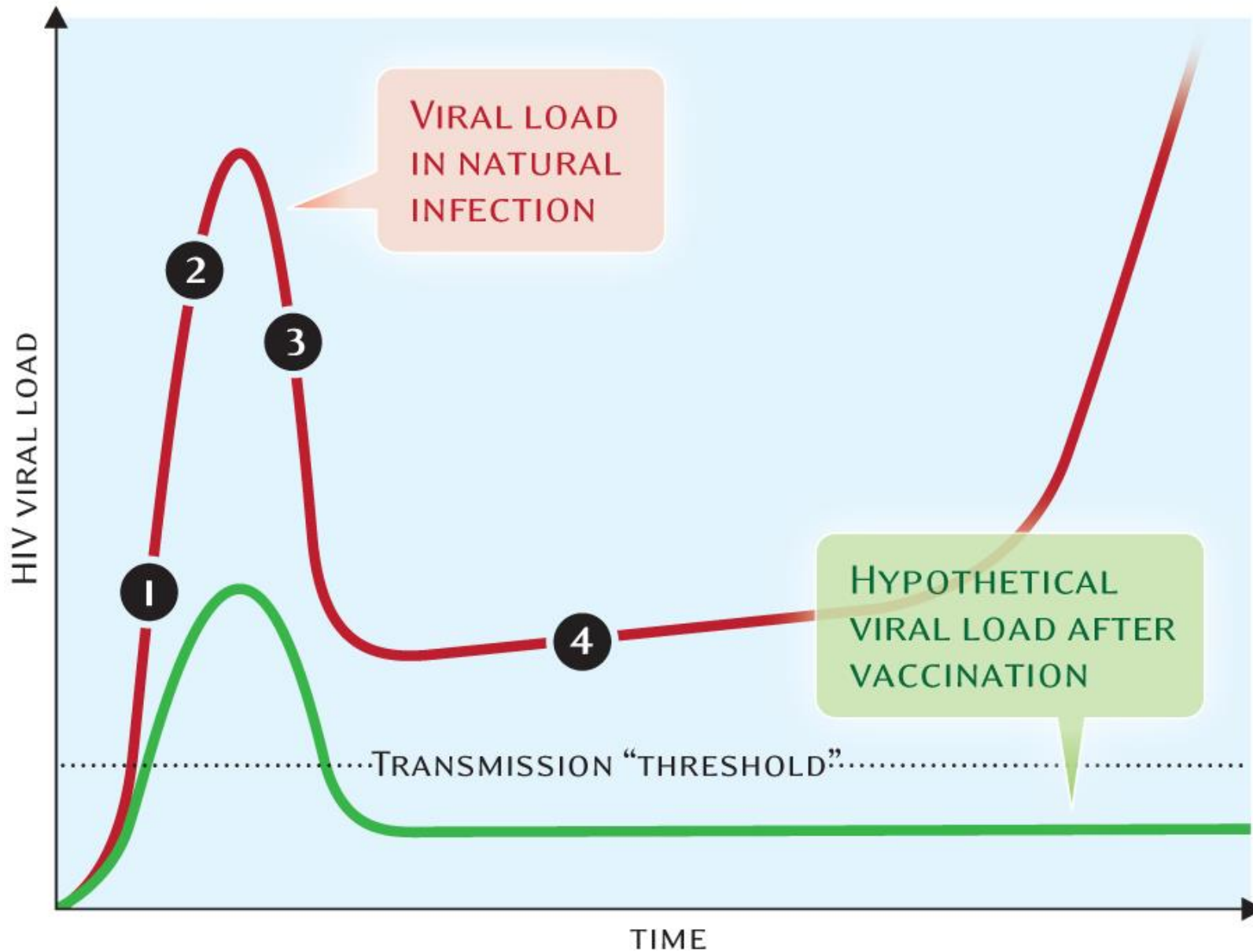
- bnAbs neutralize diverse isolates, some up to 99% of all isolates
- bnAbs can provide sterilizing immunity in animal models
- bnAbs can protect in humans
- If a vaccine can elicit bnAbs, it could prevent HIV infection

A sequence of different vaccines may be needed.



Vaccines to Induce Cell Mediated Responses

Cell-Mediated Immunity (CMI) in HIV Infection



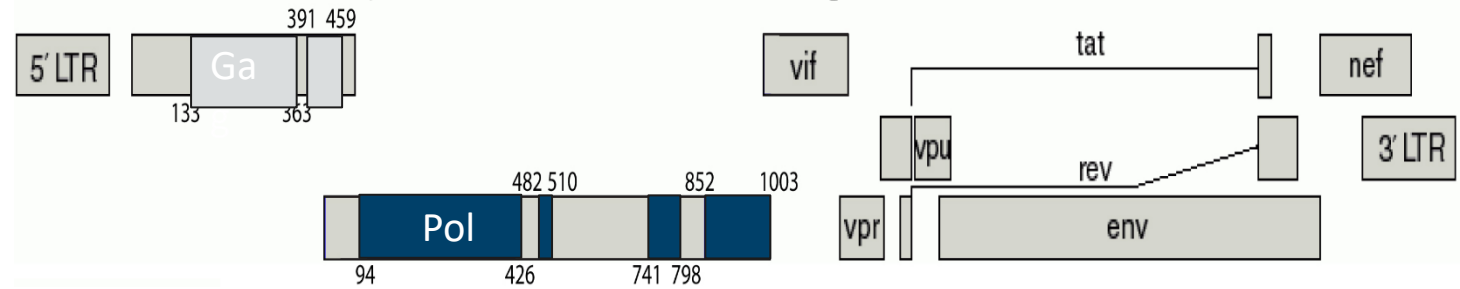
CMI Approaches for Coping with viral diversity

The mosaic vaccines: computational design of small sets of artificial viral proteins to provide optimal coverage of the diverse forms of HIV.

Conserved region vaccines: focuses on conserved regions with minimal diversity across all forms of HIV

Networked epitope vaccines: focus on highly networked mutation-constrained regions in the HIV proteome

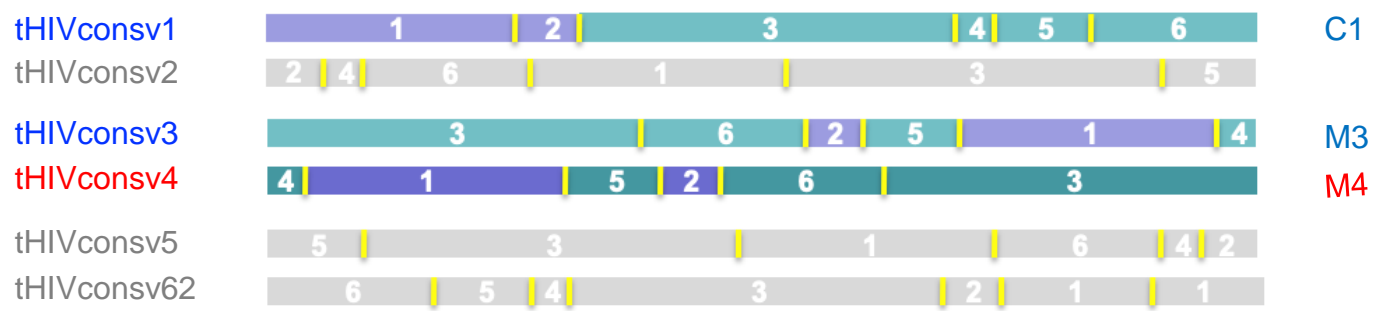
Six highly functionally conserved regions of the HIV-1 proteome



Computed bi-valent mosaic



Reshuffled regions for synthetic immunogen genes



Courtesy of Tom Hanke – University of Oxford

Summary

- HIV continues to cause a high burden of disease around the world.
- Demographic changes coupled with high incidence in specific groups could reverse gains in epidemic control
- A vaccine used together with other available interventions could end the pandemic.
- Traditional vaccine development strategies have failed for HIV
- A successful strategy will likely require eliciting bnAb and CMI responses and there are several promising strategies currently in development

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