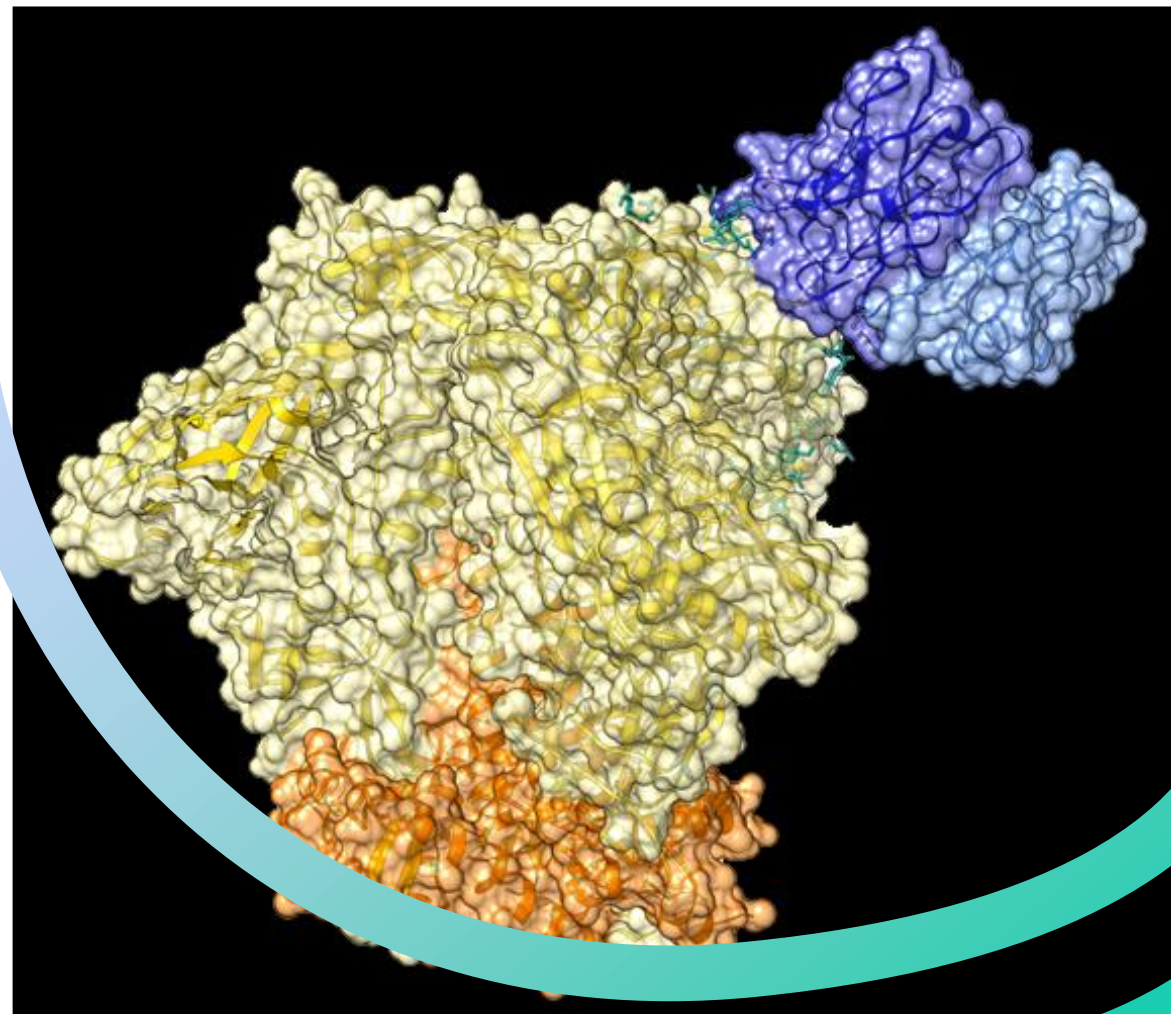


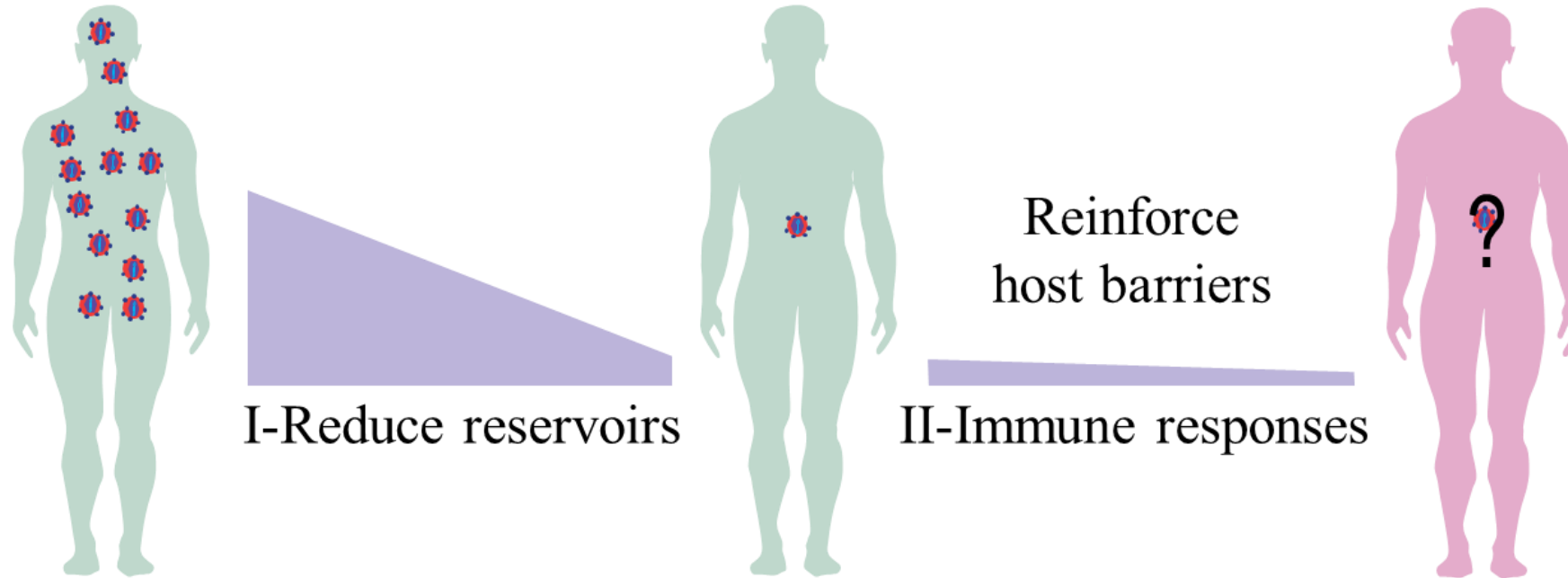
Role of bNAbs in remission of HIV-1 infection

Asier Sáez-Cirión

Viral Reservoirs and Immune Control Unit



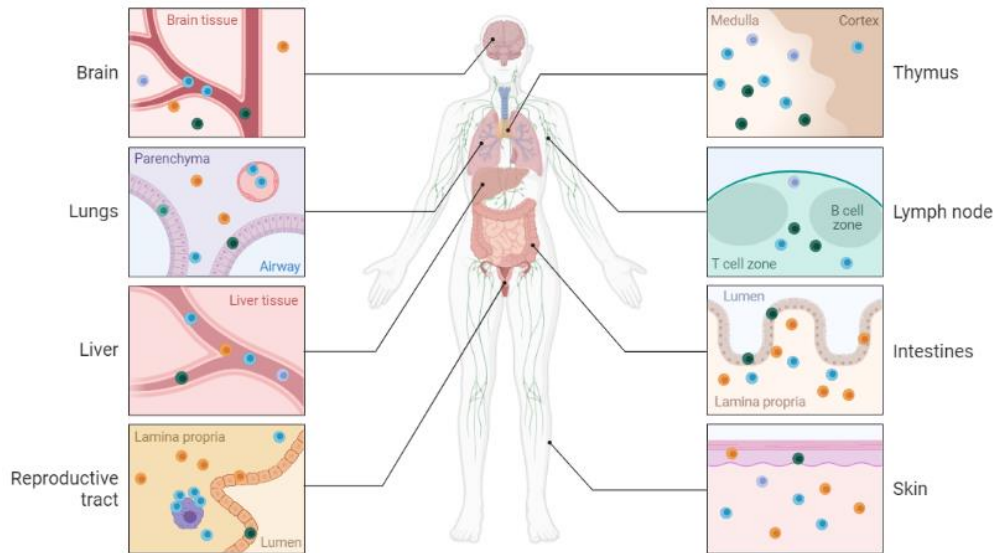
HIV cure strategies will require a combined strategy



HIV cure: a hurdle race

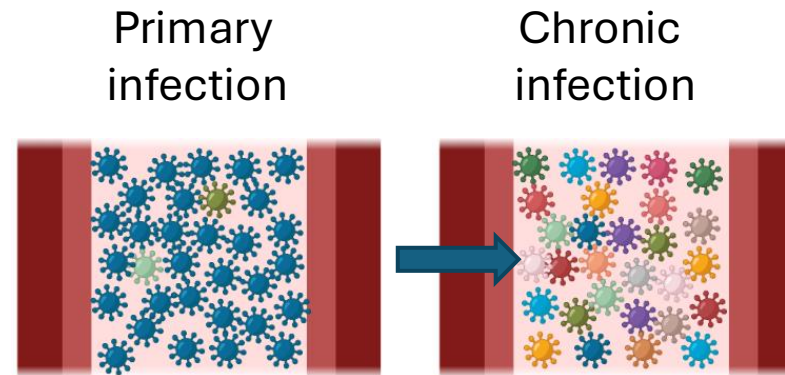
I- Viral reservoirs

Multiple sites of infection with diverse properties of target cells, which are programmed to last



Mueller & Mackay, *Nat Rev Immunol* 2016

Viral variants rapidly accumulate after infection



Impossibility to distinguish latently infected cells

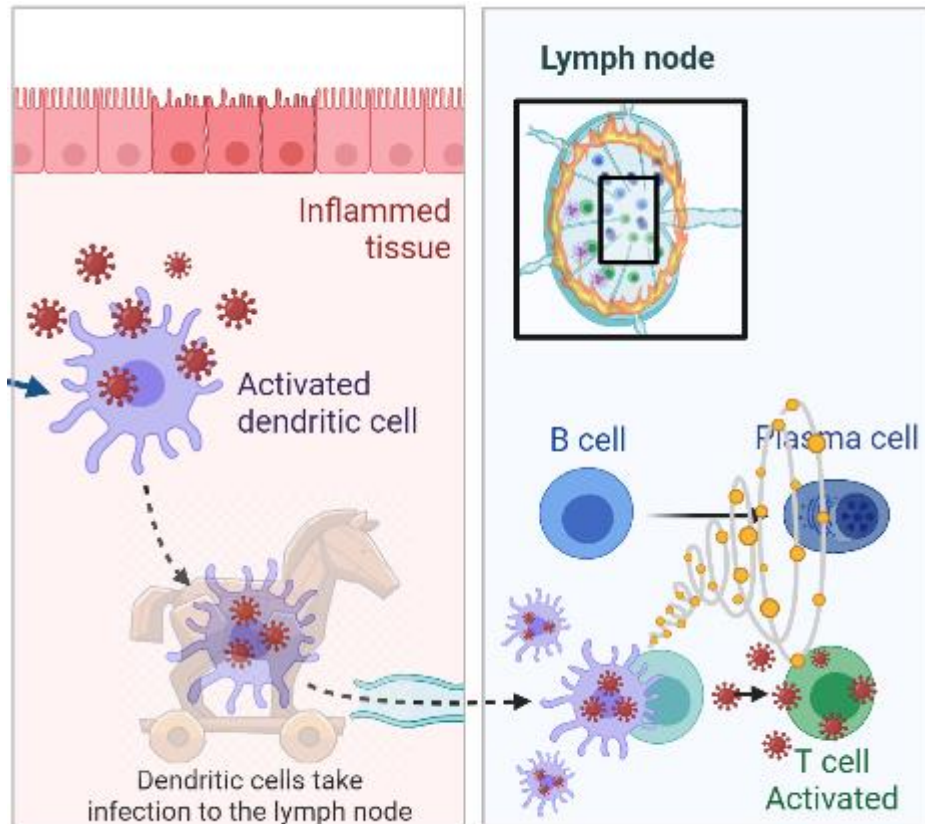


Infected cells have heterogeneous and dynamic characteristics

HIV cure: a hurdle race

II- Immune responses

Viral replication in lymphoid organs



Altered training of immune responses

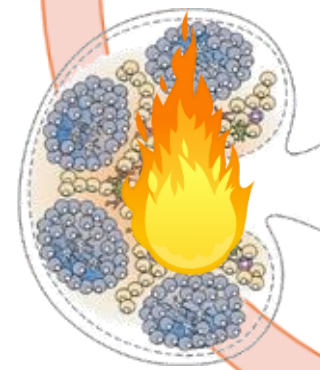


Emerging of escaping variants



Damaged lymphoid organs

Uncontrolled viremia



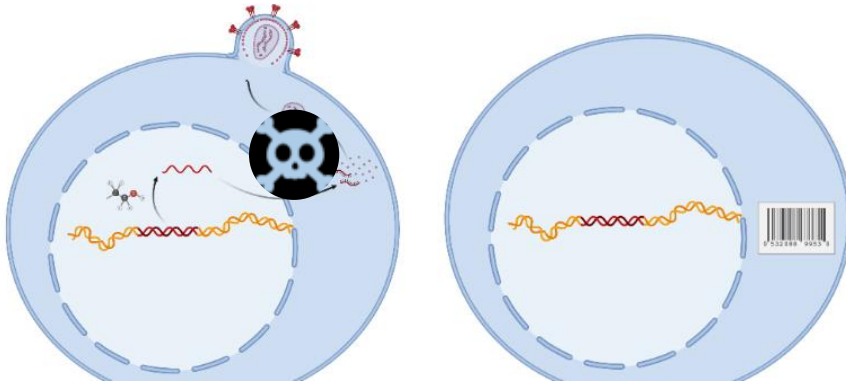
Inflammation, fibrosis, disrupted architecture

Immune exhaustion



Strategies targeting the viral reservoir

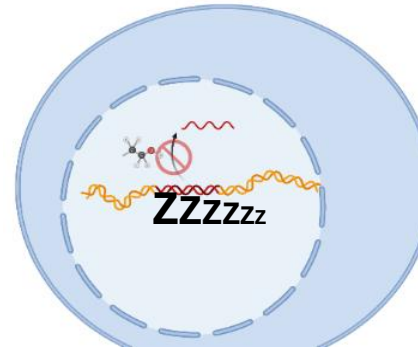
Kill infected cells



Replication-
induced death

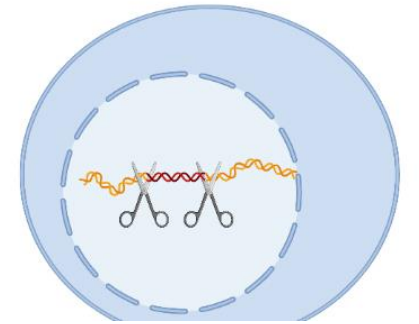
Targeting cell
characteristics

Repress the provirus



Transcription
inhibitors

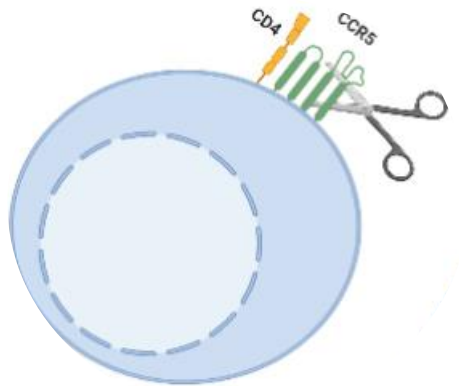
Remove the provirus



Gene editing

Strategies seeking to reinforce host barriers

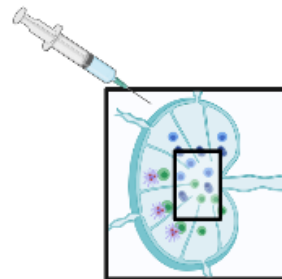
Inducing intrinsic resistance



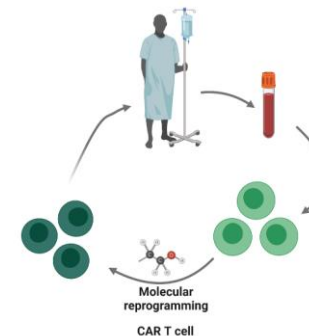
Immunotherapies



Therapeutic vaccines

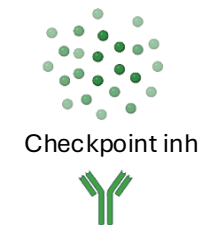


Cell Therapies



Immune modulators

Cytokines, agonists,
Immunosuppressants



bNAbs



HIV cure: an increasing number of clinical trials

Ongoing interventional studies



NA	Phase I	Phase II	Phase III/IV	Total
7	34	33	3	77

<https://www.treatmentactiongroup.org/cure/trials/>

22 monoclonal antibodies (bNAbs)
12 including vaccine candidates
12 Cell therapies (including CAR cells)
9 Cell modulators (BCL2 inhibitors, jak/kinase inh, mTOR...)
9 ART based (early treatment, intensification, ATI...)
6 other gene editing technologies
4 Latency reversal agents
4 TLR7/TLR9 agonists
4 cytokines
2 Immune checkpoint inhibitors

bNAbs, versatile tools against HIV-1 infection

Neutralizing



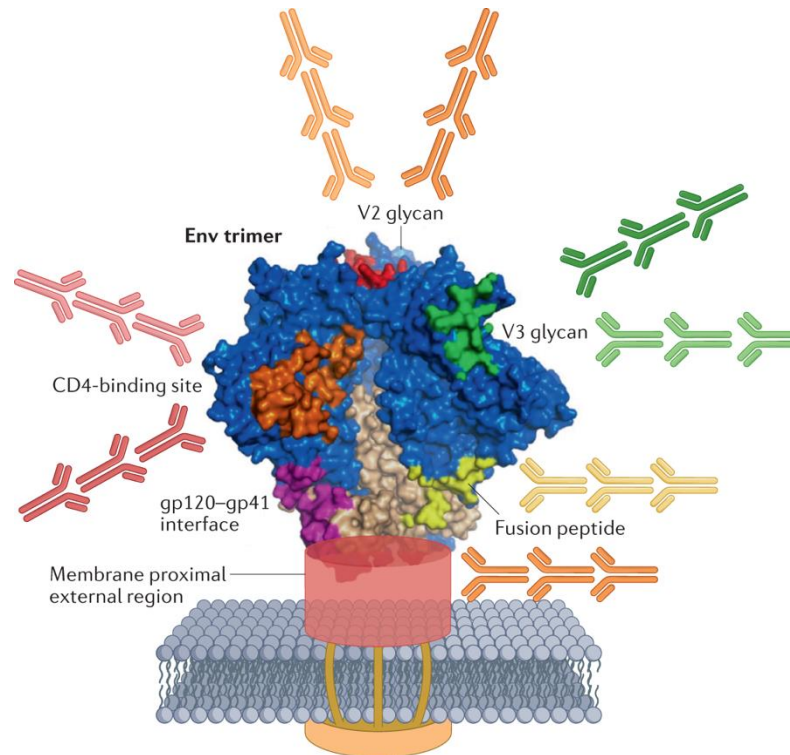
Cross neutralizing



Broadly neutralizing

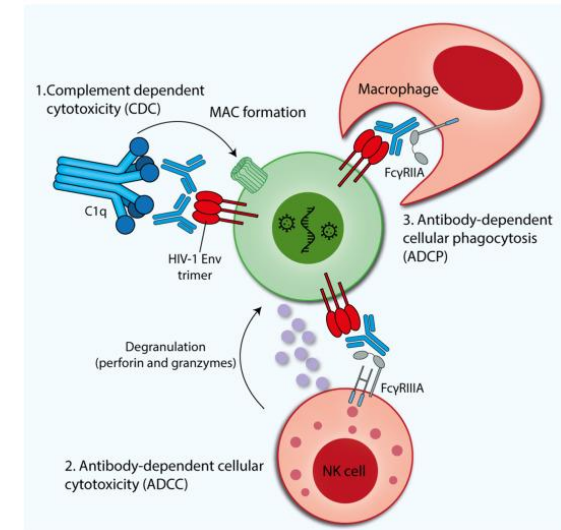


Identification of several vulnerable sites, targets of bNAbs



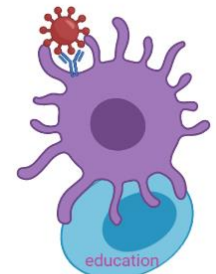
Haynes et al Nat Rev Immunol 2023

Beyond neutralization



Schriek et al Antiviral Res 2024

Vaccinal effects?

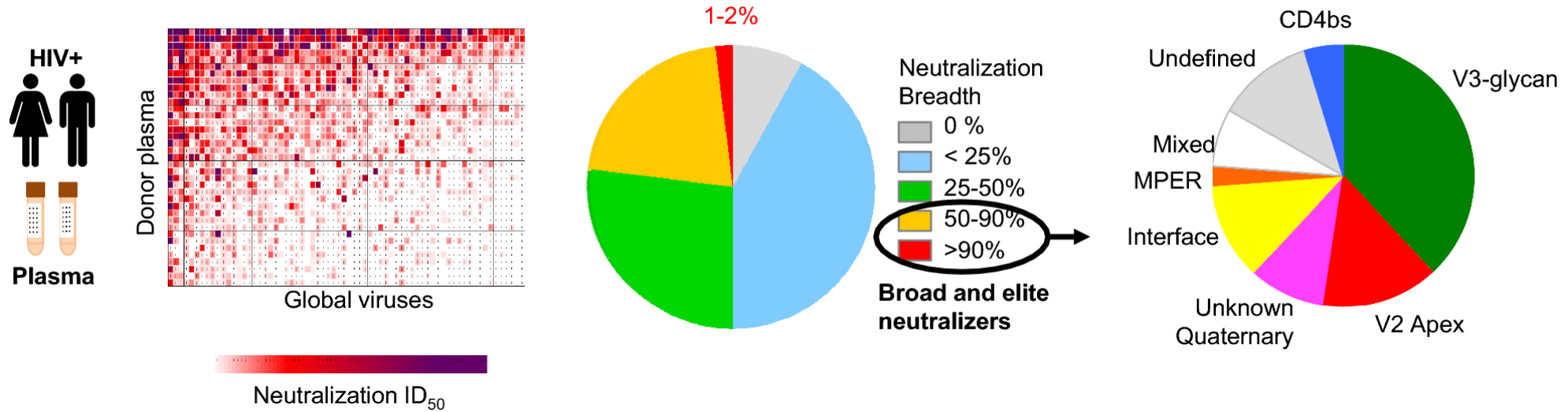


Development of broadly neutralizing antibodies in rare individuals

Screening of plasma for breadth →

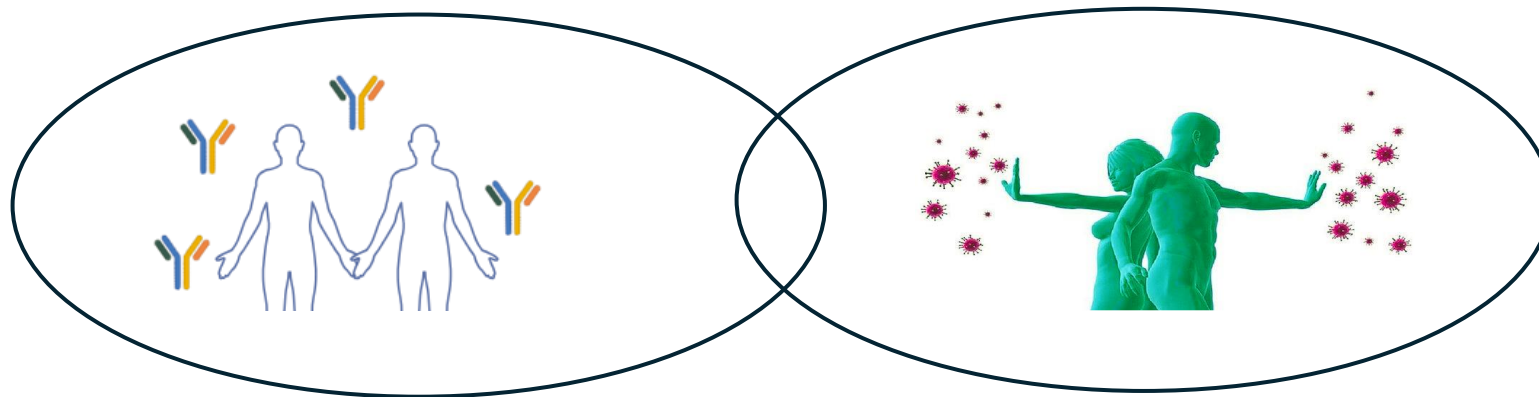
Classification of broad neutralizers →

Mapping the targets of bNAbs

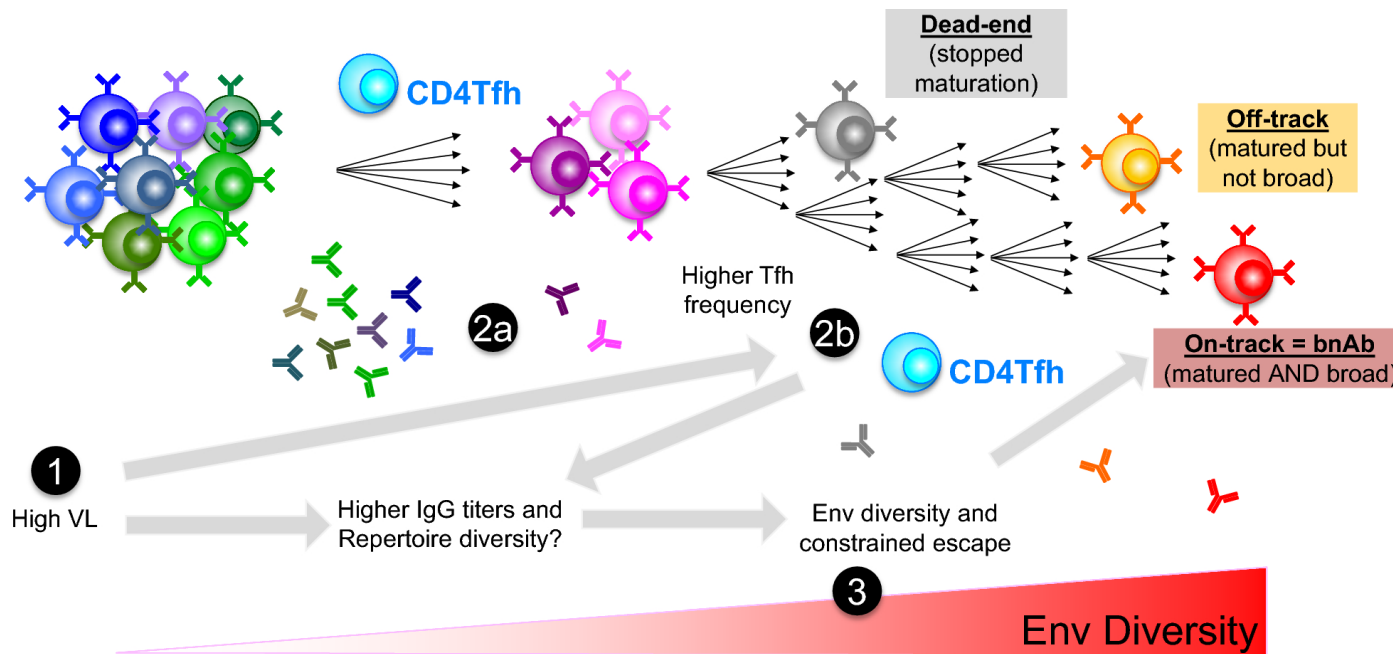


Landais & Moore Retrovirology 2018

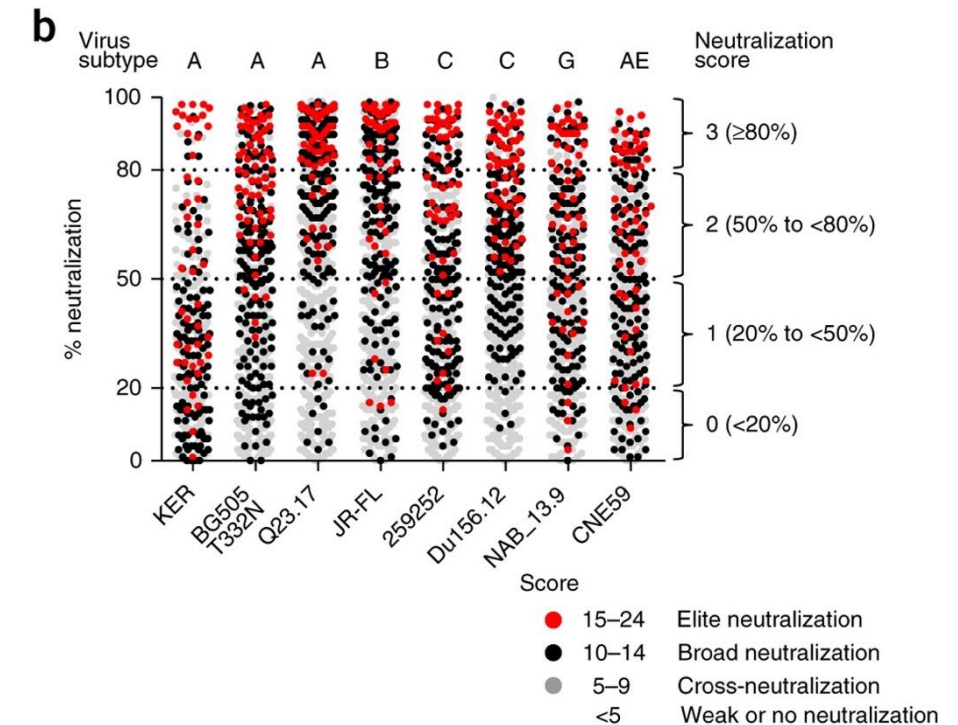
Elite neutralizer ≠ Elite controller



Determinants of bNAb development, exposure to antigens and viral diversity



4,484 individuals from the Swiss HIV Cohort Study

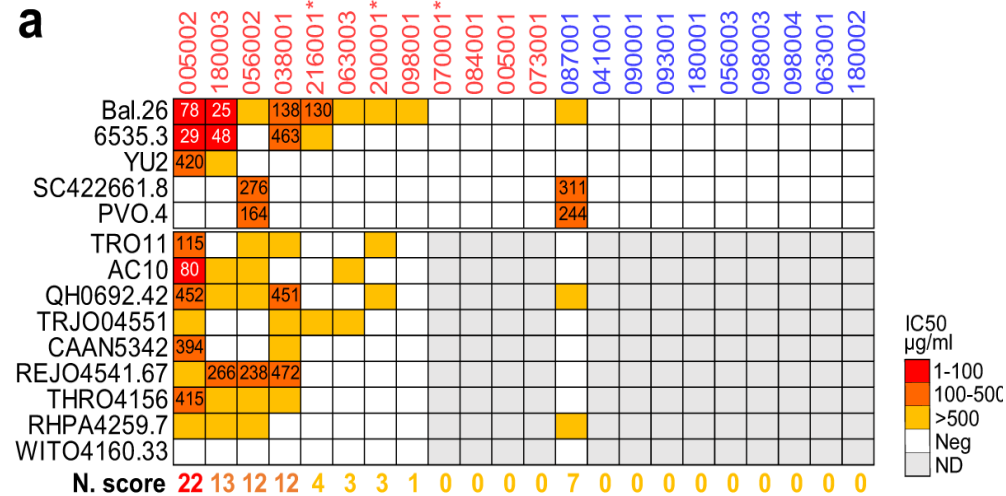


Parameters driving bNAb evolution:
viral load,
length of untreated infection
viral diversity

Higher rates of bNAbs among black participants

Coordinated antibody response in people controlling HIV-1 without ART

Cross neutralizing activity found in some PTCs related to sporadic viral exposure



Molinos-Albert et al Nat Com 2022; Cell Host Micr 2023

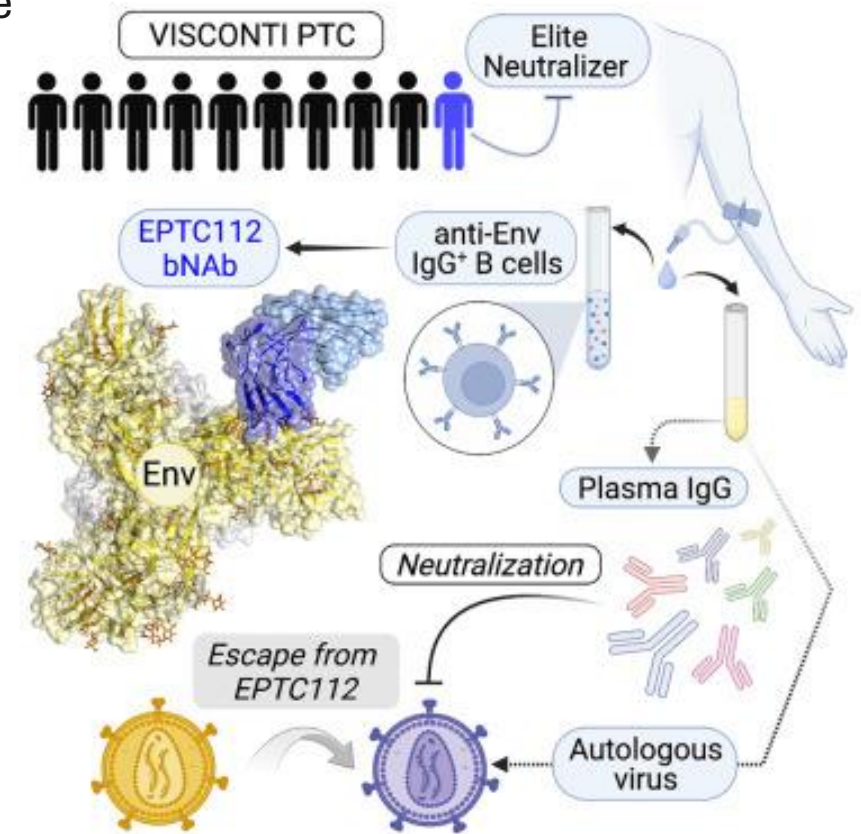
Despite low viremia :

High frequency of HIV-specific memory B cells

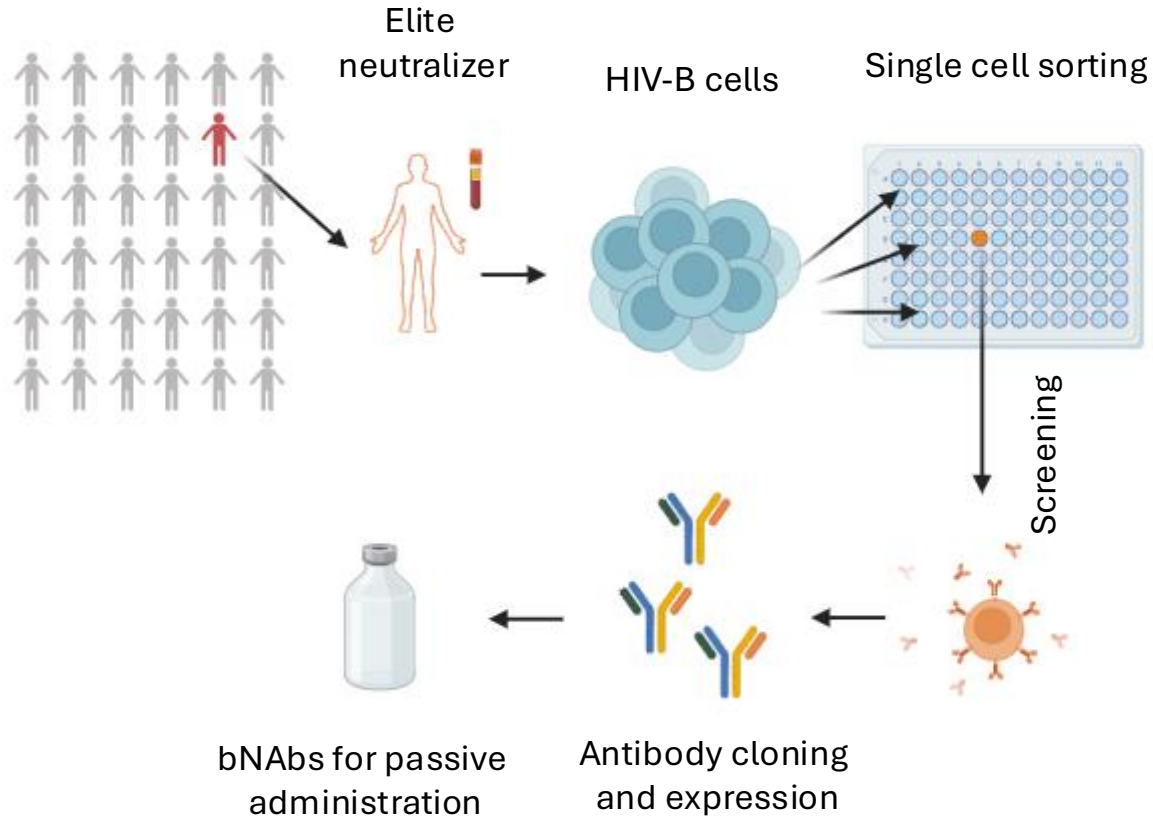
Rossignol et al CellRep 2021; Molinos-Albert et al Nat Com 2022

Autologous neutralizing antibodies increase with early ART and shape HIV rebound after treatment interruption

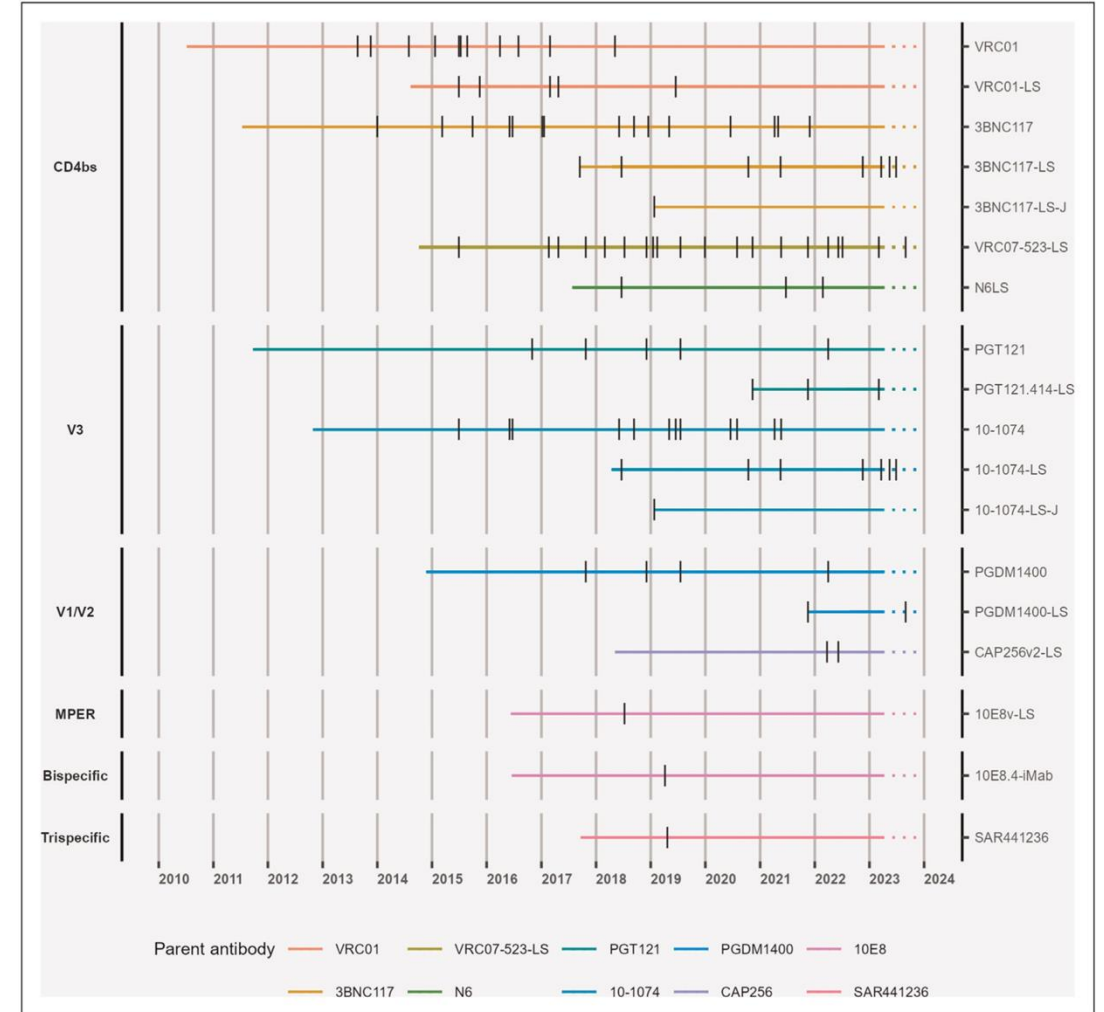
Esmailzadeh et al Sci Trans Med 2023 Fugamallo et al medRxiv 2025



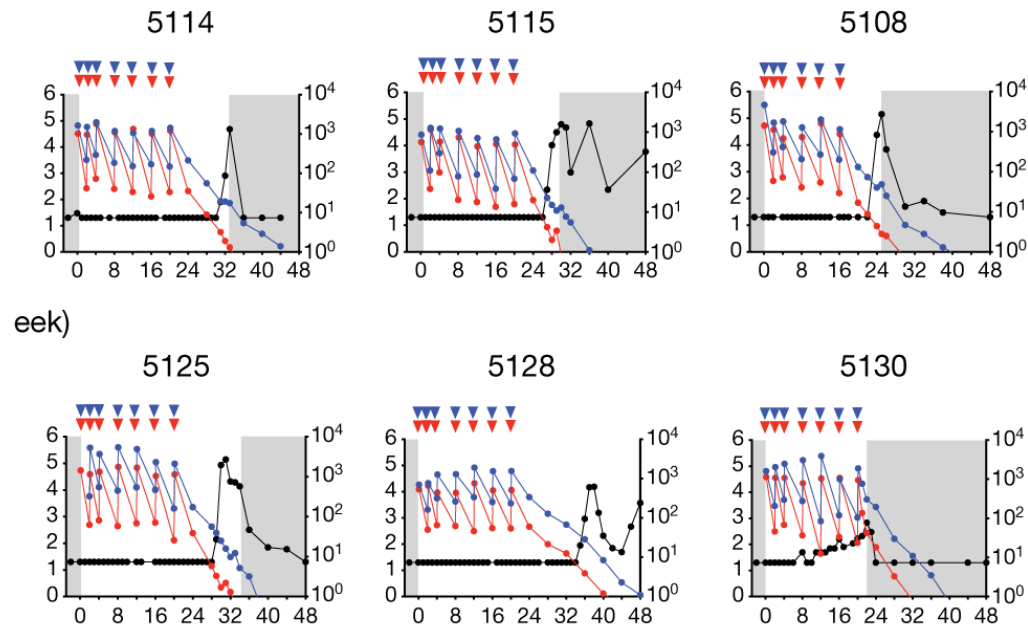
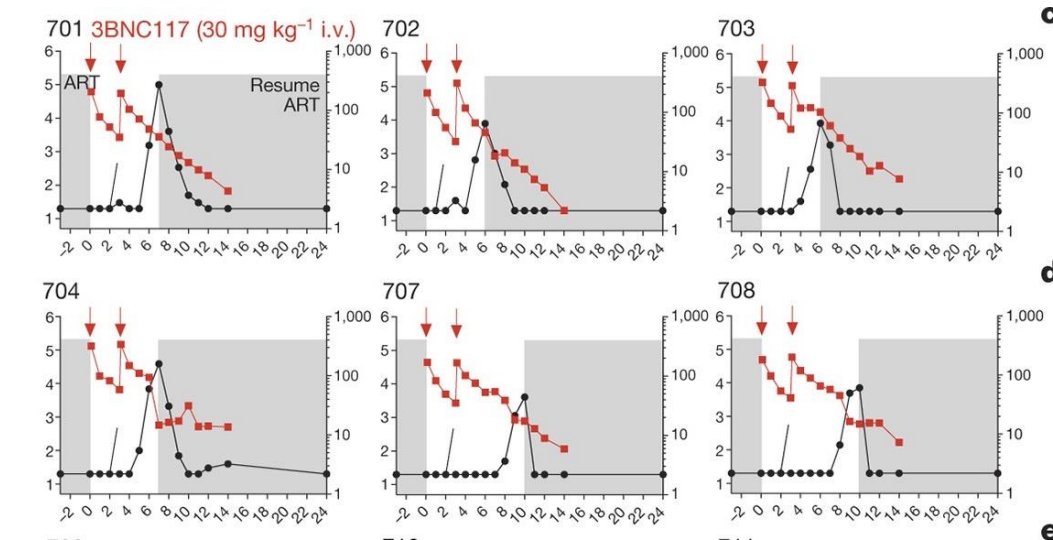
bNAbs for passive administration protocols



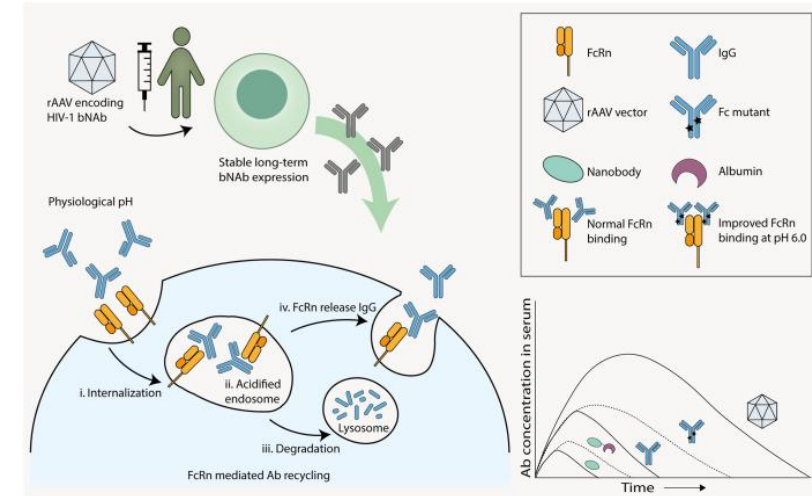
bNAbs in clinical trials



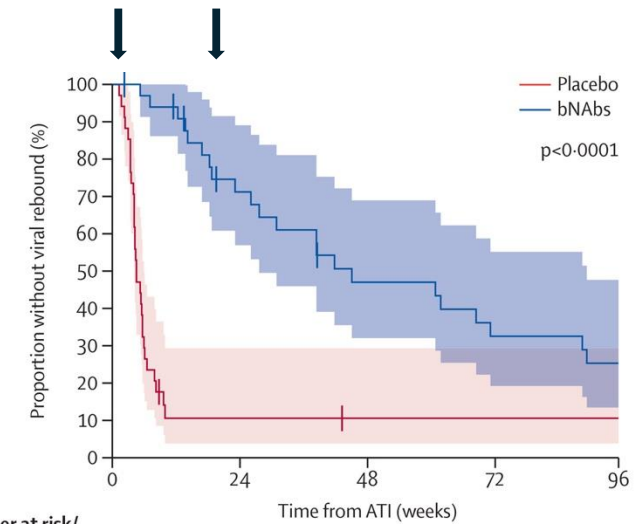
bNAbs: maintenance of viral suppression after ART discontinuation



Extending the half life of antibodies

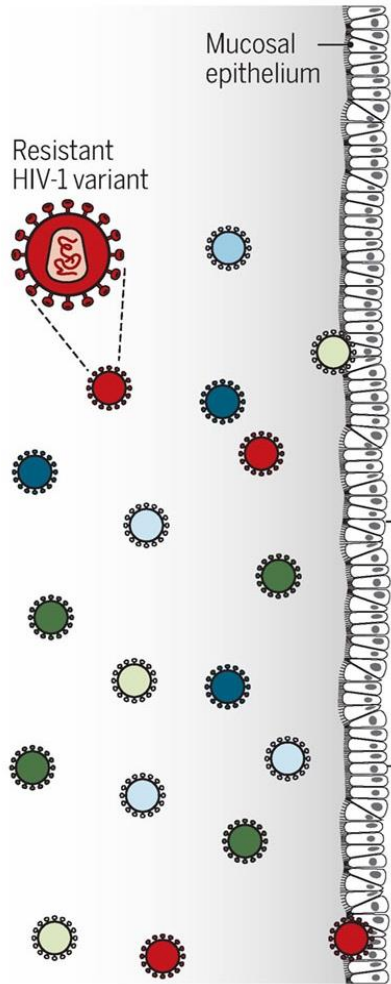


Schriek et al Antiviral Res 2024



Lee et al Lancet HIV 2026

bNAbs for prevention of HIV-1 infection

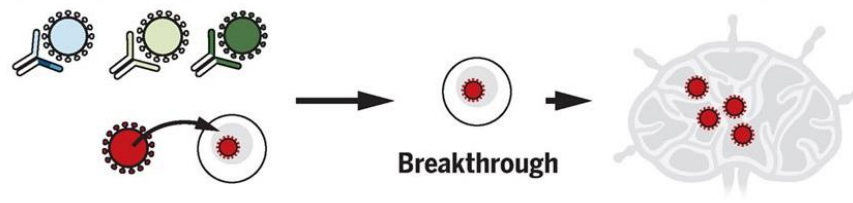


Limitations

Cold change storage

Intravenous
administration

Broad but not perfect

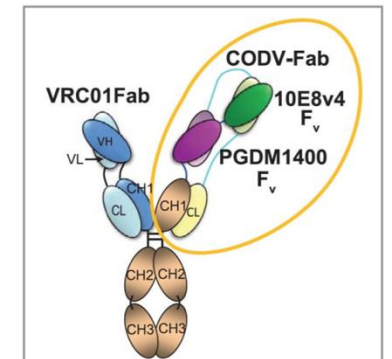


subcutaneous
administration

In clinical trials



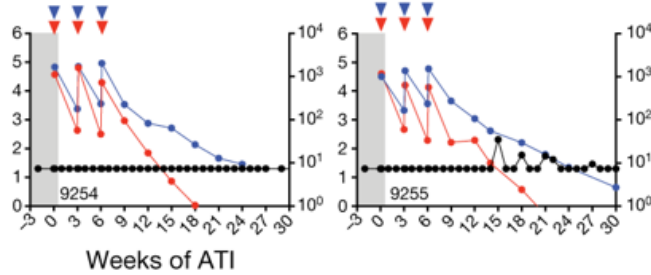
bNAbs + lenacapavir



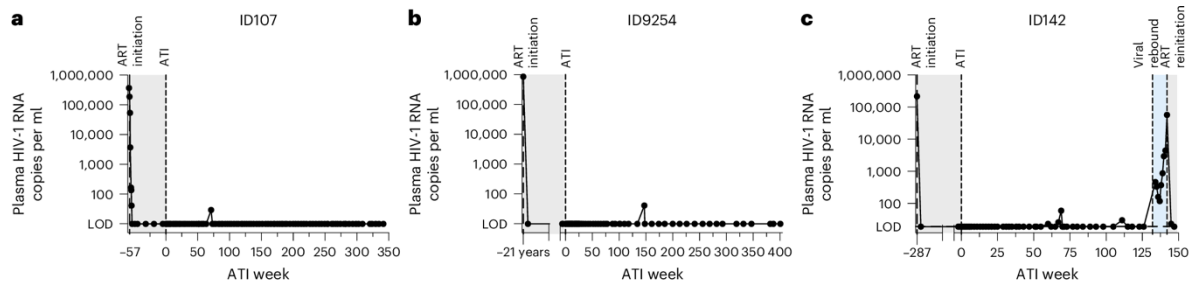
Trispecific Ab

Post Intervention controllers

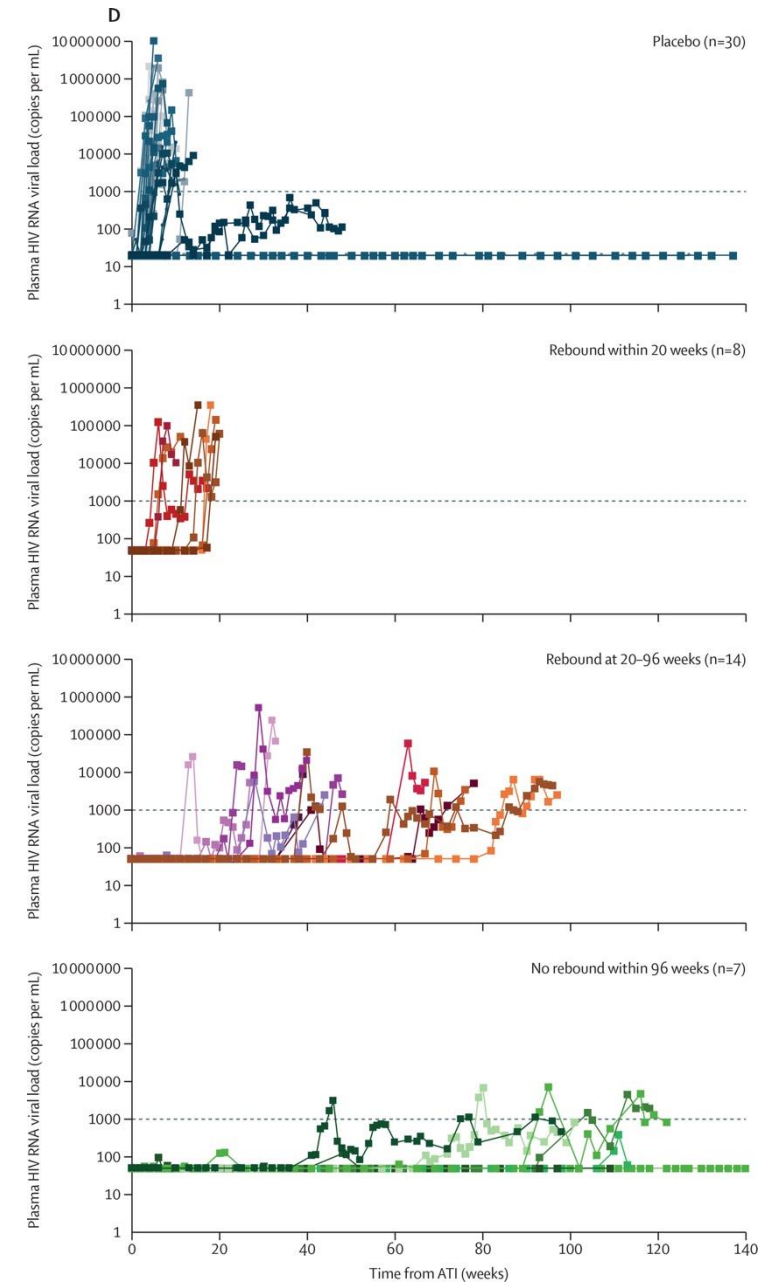
People maintaining undetectable viremia despite bNAbs waning titers



Mendoza et al Nature 2018

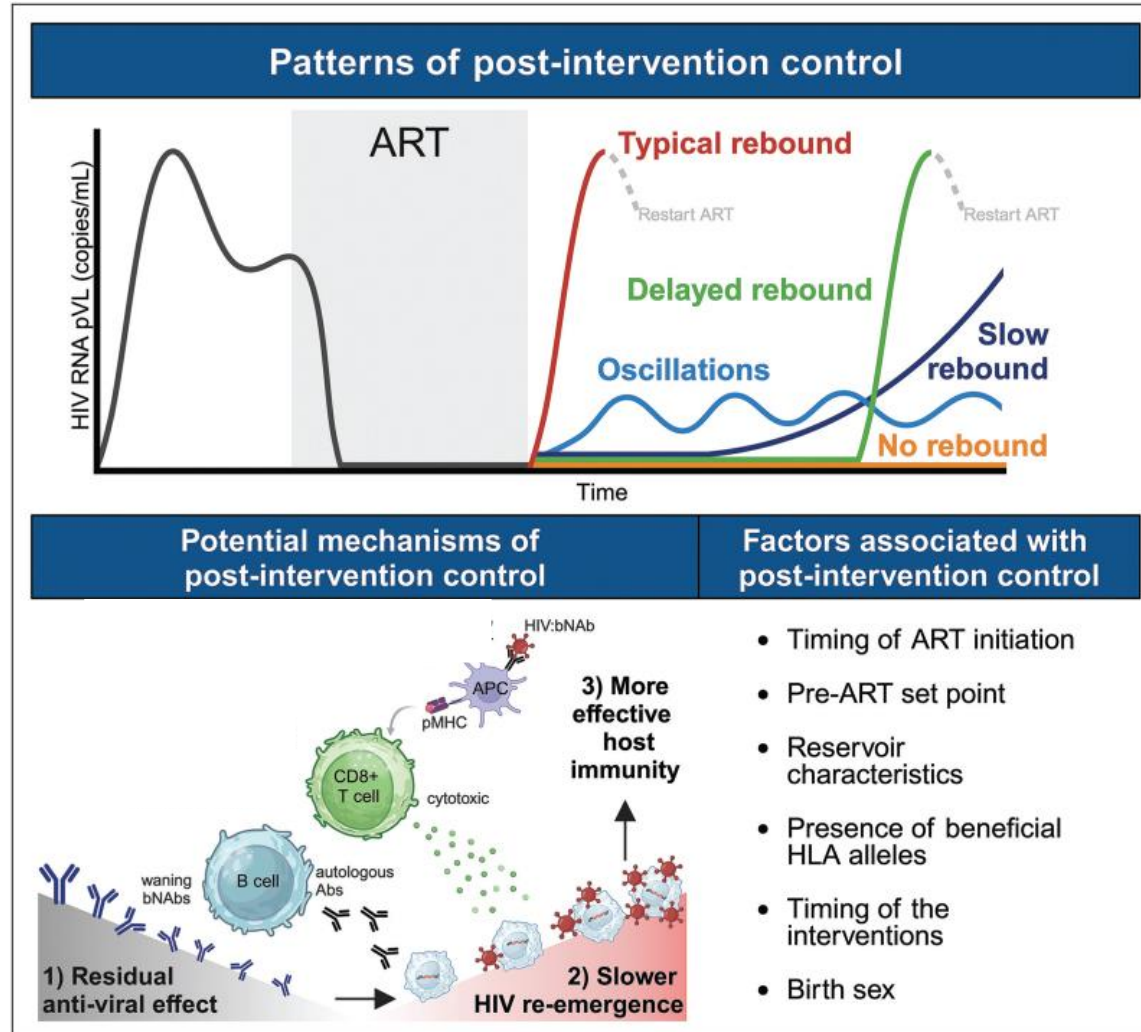


Fisher et al Nat Immunol 2026

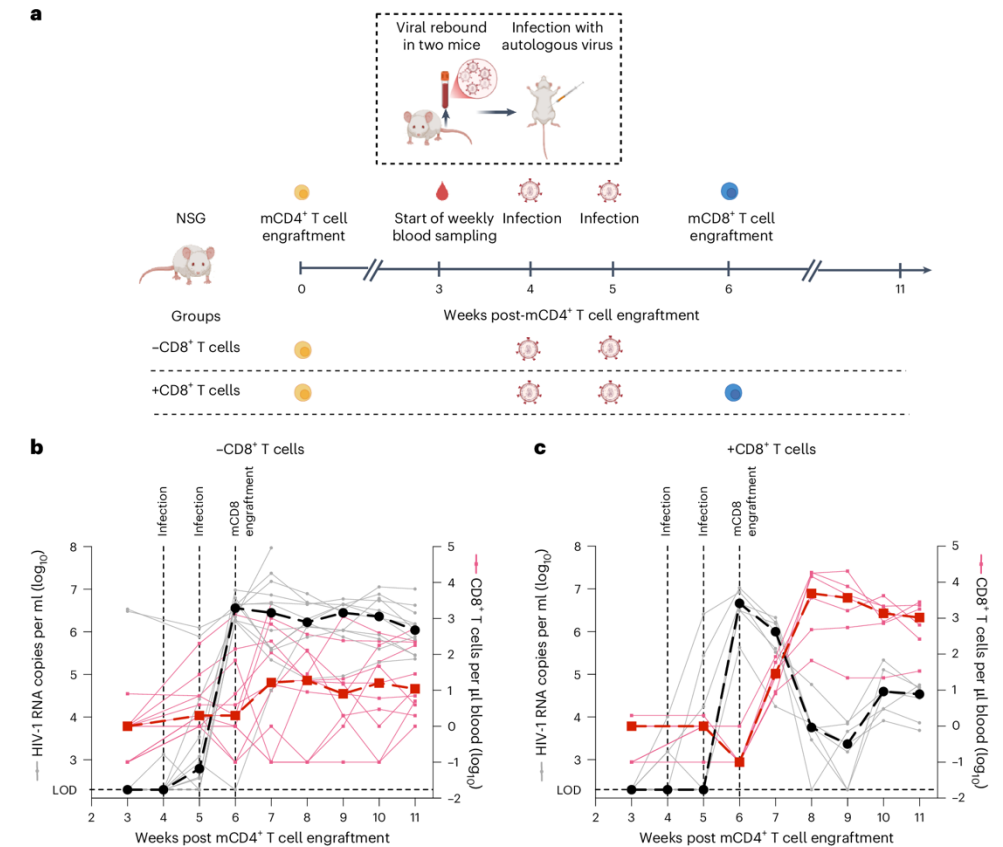


Lee et al Lancet HIV 2026

Mechanisms associated with post-intervention control?



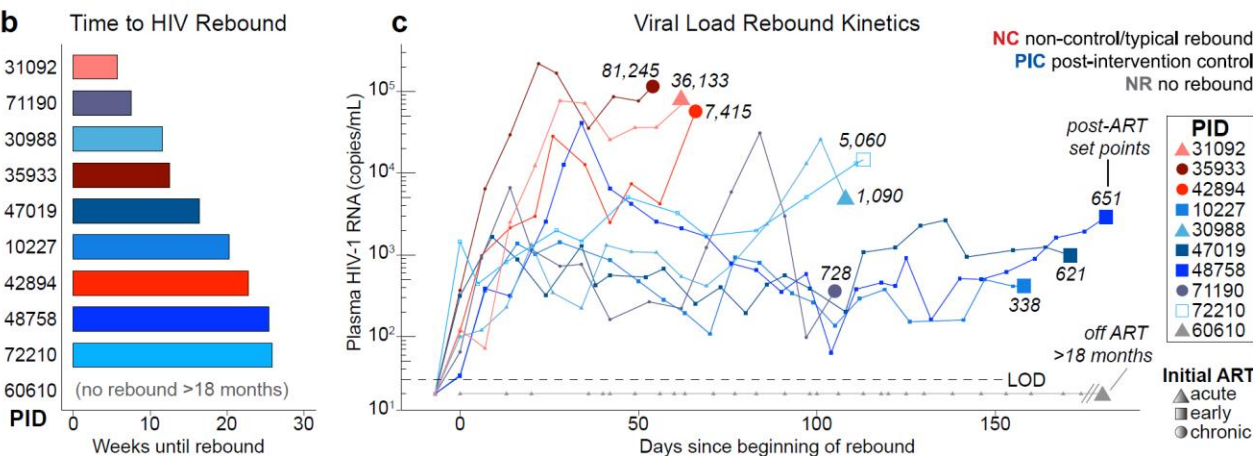
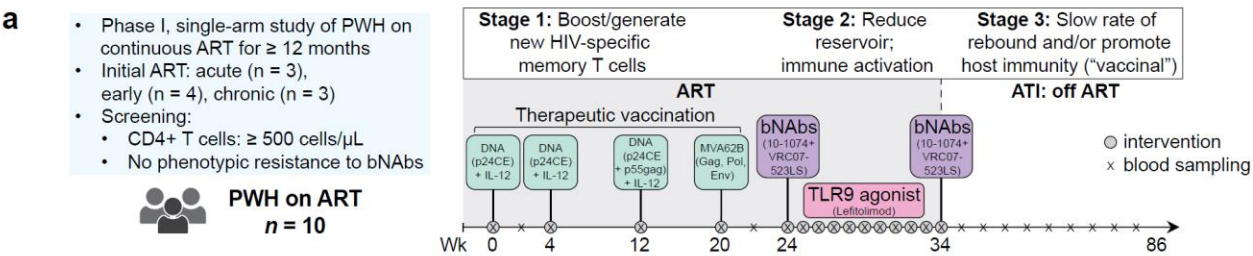
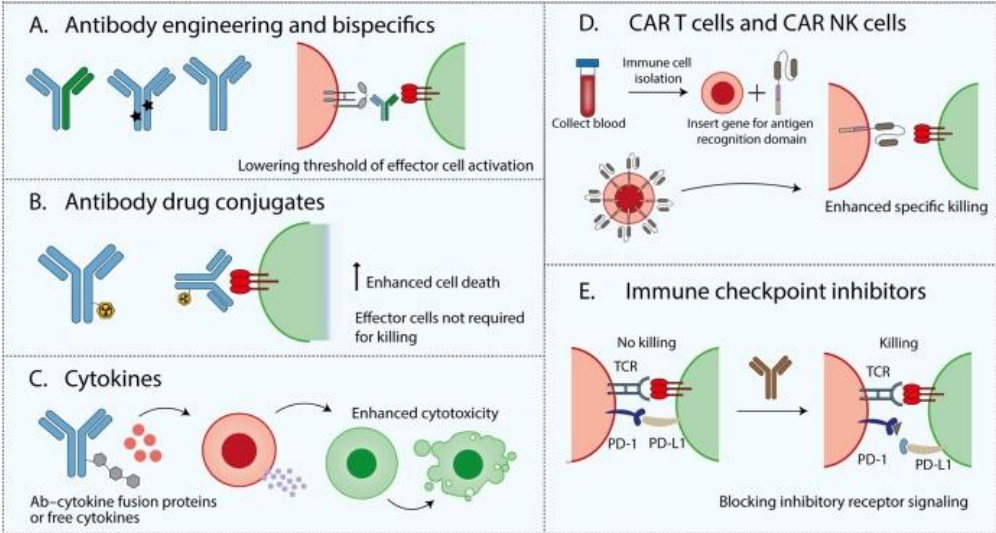
Key role of CD8+ T cell responses



It is likely that efficacy will come from combinations

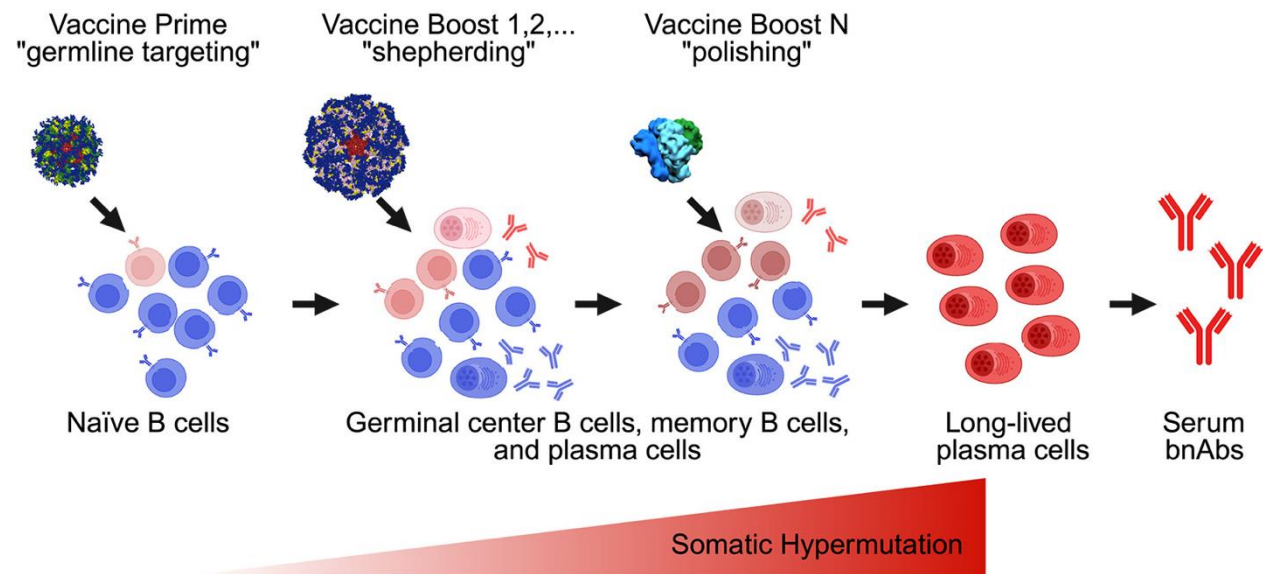


Combination immunotherapy induces post-intervention control of HIV



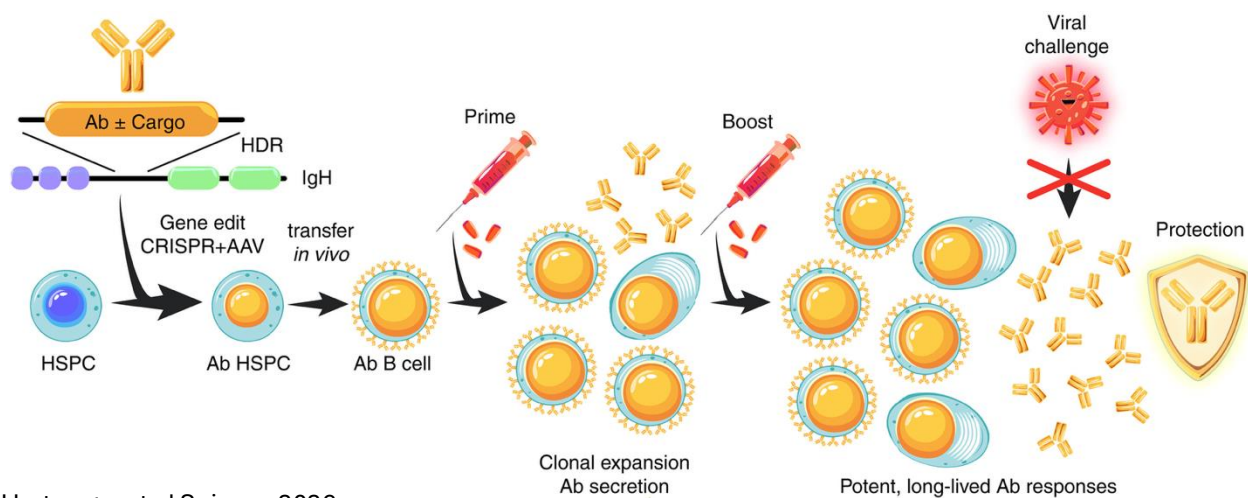
Beyond passive administration, the bNAbs in the HIV cure agenda

Germline-targeting vaccine strategies to induce bnAbs



Willis et al Science 2025

Gene editing to generate bnAbs cell factories



Hartweiger et al Science 2026

ANRS 176 RHIVIERA 02: Potential for HIV remission of ART and broadly neutralizing antibodies delivered during primary HIV-1 infection



Potentiate the beneficial impact of early ART administration towards HIV remission

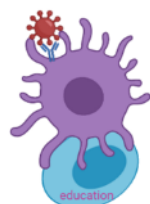
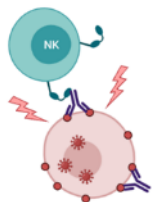
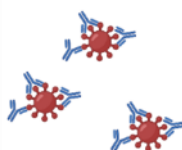


broadly neutralizing antibodies bNAbs

Block the virus

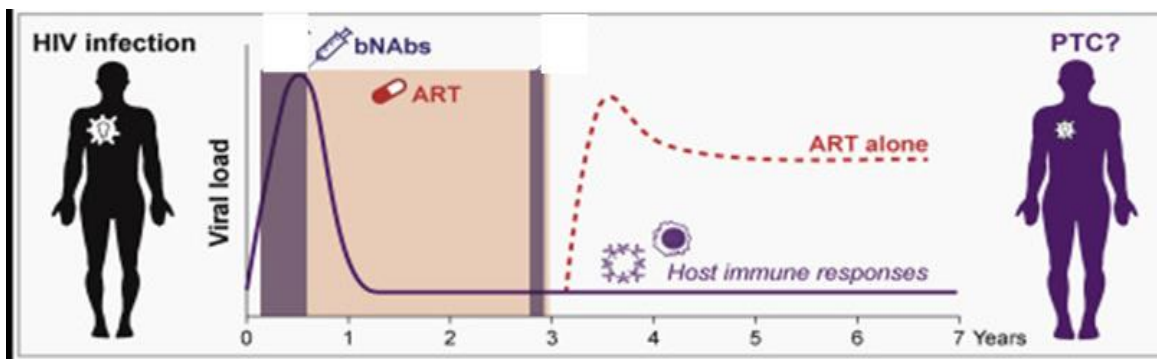
Facilitate the elimination of infected cells

“vaccinal” effect



ANRS 176 RHIVIERA 02: primo-bNAbs

Impact of ART + dual long-acting HIV-specific bNAbs (3BNC117-LS & 10-1074-LS) during primary infection on post-treatment HIV control



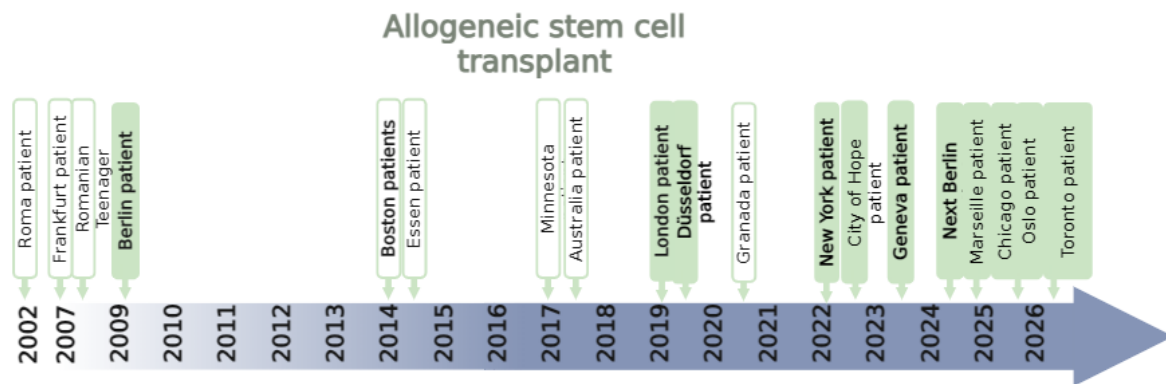
PI: Cecile Goujard, CS: Asier Sáez-Cirión; CMG: Laurence Meyer



Collab: Michel Nussenzweig

Hugo Mouquet

Inclusions in progress (49 out of 69),
14 participants already underwent ATI



Romuald, the “Geneva” patient

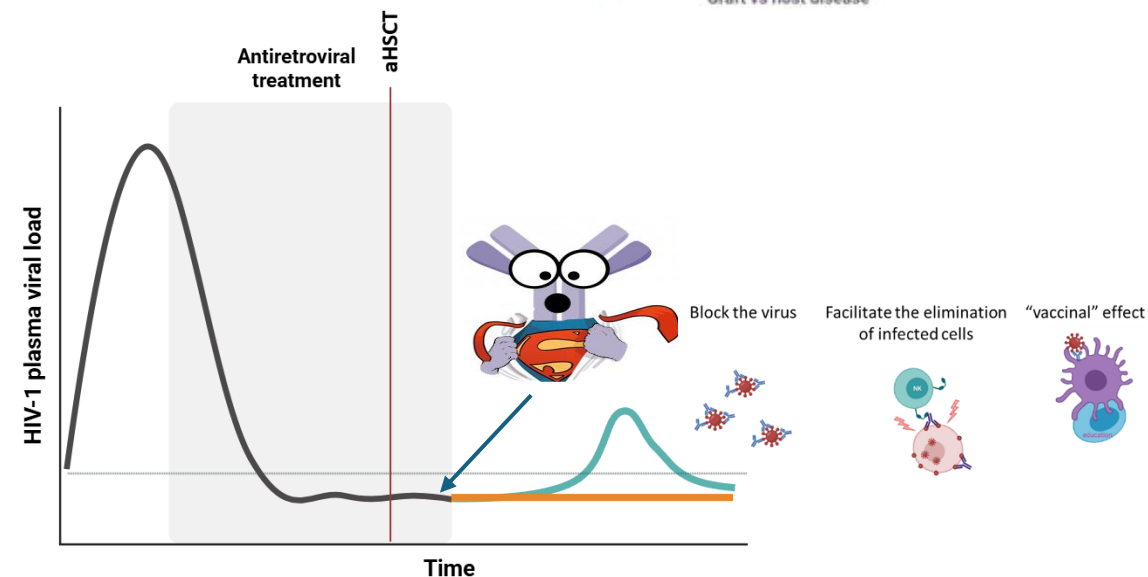
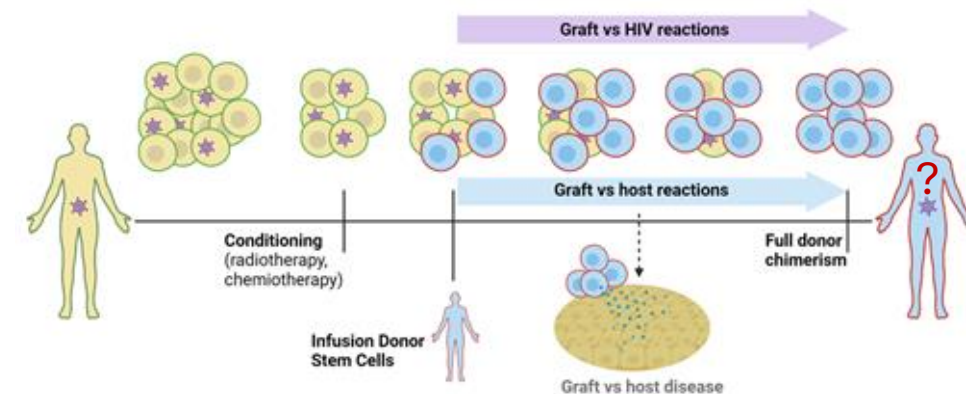


55 months of undetectable viremia without ART after CCR5WT allo-HSCT

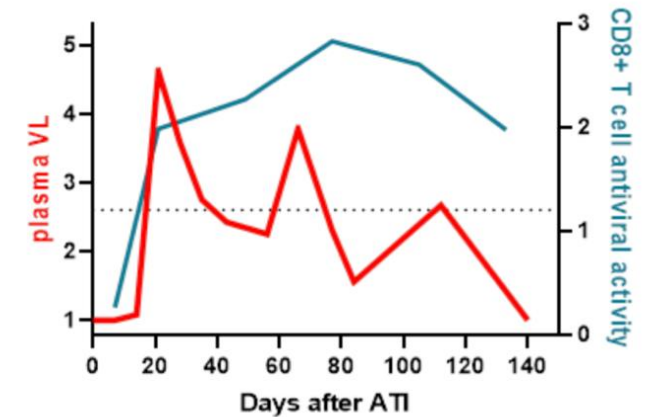
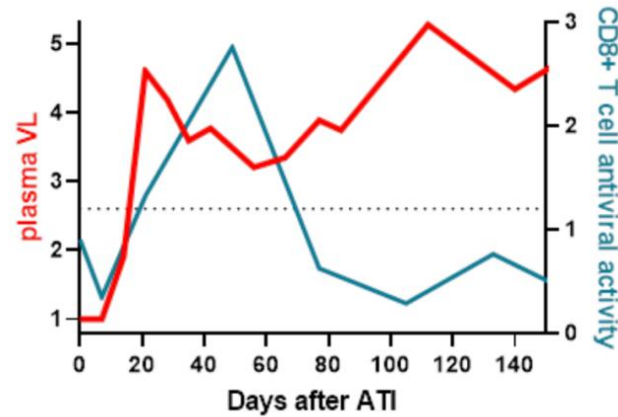
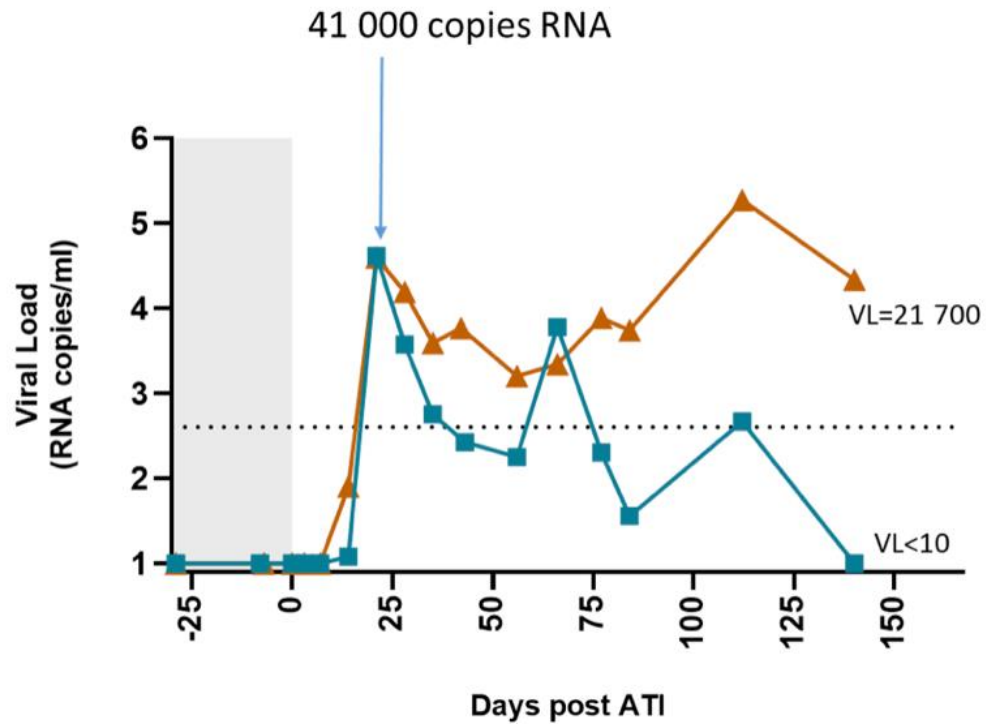
- Biphenotypic sarcoma (extramedullary myeloid tumor),
- **Allo-HSCT July 2018 CCR5WT/WT donor**
- Stop ART **November 2021**

Allogenic Transplant and Antibodies to Cure HIV

10 PLWH after CCR5WT allo HSCT



Monitoring viral rebound



Viral rebound after ART interruption does not preclude subsequent viral control

ANRS RHIVIERA CONSORTIUM

A Multidisciplinary Research Initiative Towards Control of Reservoirs and HIV Remission



rhiviera.com

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Quanterix

