HIV vaccines in development

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Overview

- Global status of HIV vaccine research
- Scientific challenges
- New-generation vaccine platforms

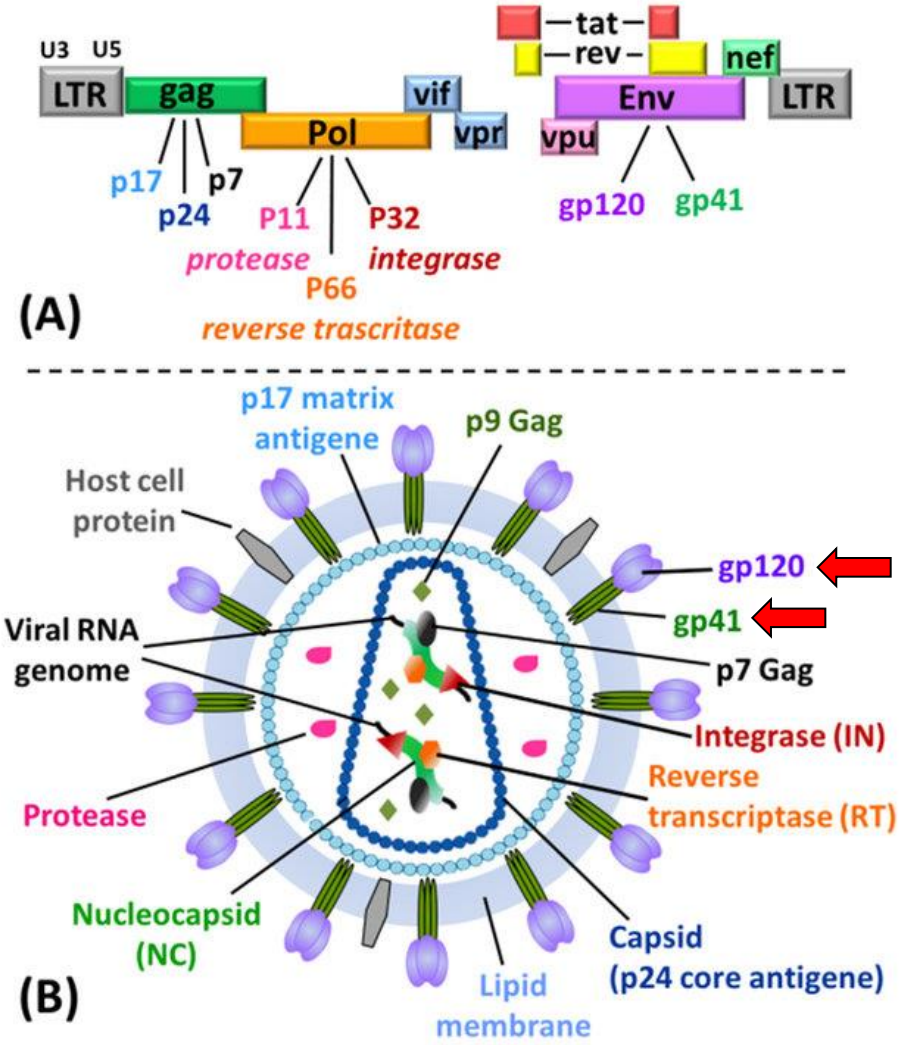
Why an HIV Vaccine Remains Essential?

- Antiretroviral therapy (ART) and PrEP are powerful tools, but not a definitive end to the pandemic.

- A safe and effective vaccine is the cornerstone for achieving sustainable epidemic control.

- Core Question: After 40+ years of research, what makes an HIV vaccine uniquely difficult?

HIV genome (A) and structure (B)



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Core Challenges in HIV Vaccine Development

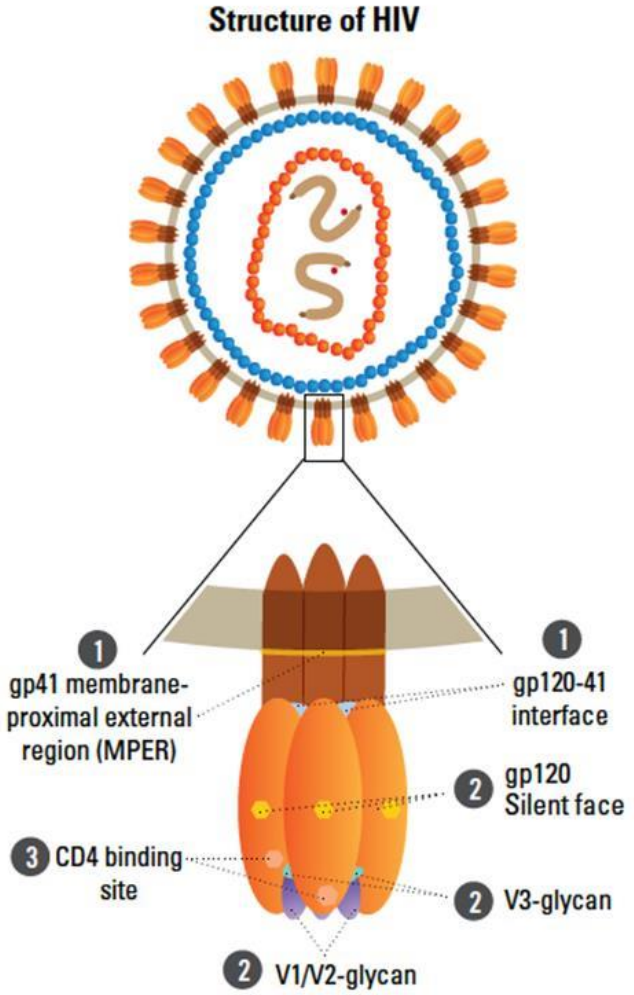
- Extreme Diversity: Rapid mutation and global genetic diversity.
- Immune Attack: Direct infection of CD4+ T-helper cells.
- Viral Latency: Establishment of a permanent viral reservoir.
- Glycan shield on Env protein.
- No Natural Cure.

From Empirical Trials to Rational Design

- Past: Testing immunogens based on natural infection responses.
- Present & Future: Structure-based rational design.
- Focus on guiding the immune system to produce specific, potent, and broad responses.
- The leading target: Broadly Neutralizing Antibodies (bNAbs).

Broadly neutralizing antibodies (bNAbs)

- Specialized antibodies that bind to and neutralize multiple strains of HIV
- Numerous bNAbs discovered since 2009
- Five main targets of bNAbs on the virus envelope



Broadly Neutralizing Antibodies (bNAbs)

- Target conserved epitopes across HIV strains

  Examples: VRC01, 3BNC117, 10E8

- Use for prevention (PrEP) and therapeutic trials

Germline-Targeting Approach

- Aim: initiate bNAb maturation pathways
- Key candidate: eOD-GT8
- IAVI G001 trial results: successful B-cell activation

- Germline targeting is the design of immunogens that first activate the rare naïve B-cell precursors and then, through multiple sequential booster immunizations, guide their maturation toward the production of broadly neutralizing antibodies (bnAbs).

- This strategy mimics the natural co-evolution of the immune system but follows an engineered and highly targeted developmental pathway.

The bNAb Pathway: A Guided Approach

- Goal: Induce antibodies that neutralize a wide swath of global HIV strains.
- Method: Sequential immunization with engineered protein immunogens.
- These immunogens act as "primers" and "boosters" to guide B-cell maturation.
- Proof-of-Concept: The IAVI G001 trial (2022) successfully activated target B-cell precursors in 97% of recipients.

Diverse Platforms in the Pipeline

- mRNA Platform
- Enables rapid iteration of immunogen designs (e.g., Moderna/IAVI/NIH trials).

- Viral Vectors (e.g., CMV)
- Designed to elicit powerful, persistent tissue-resident T-cell immunity.

- Combination Strategies
- Prime-boost regimens targeting both antibodies and T-cells.

Learning from Clinical Trial Outcomes

Trial (Phase)	Outcome	Key Lesson
Mosaico (III)	Halted (2023)	T-cell responses alone are insufficient for reliable protection.
PrEPVacc (II/III)	Halted (2023)	Highlights the critical importance of immunogen design.
IAVI G001 (I)	Success (2022)	Proof that guiding naive B-cells is feasible.

- Each trial, successful or not, provides essential data to refine the roadmap.

Long-Acting bNAbs for Prevention

- Direct administration of pre-made, potent bNAbs.
- Proof-of-Concept: Antibody Mediated Prevention (AMP) trials.

- Next Generation: More potent and longer-lasting bNAb combinations (e.g., VRC07-523LS + CAP256V2LS) are in trials.

- A bridge or complement to an active vaccine.

The Road Ahead: Integration and Persistence

- The bNAb-guided pathway is the most promising strategic direction.
- Platforms like mRNA will accelerate immunogen testing.
- A final vaccine will likely be multi-component.
- It will be part of a larger prevention toolkit (alongside ART, PrEP, bNAbs).

Conclusion

- HIV vaccine development remains one of the greatest scientific challenges.
- Major breakthroughs: bnAbs, germline targeting, mRNA platforms.
- Early human trials show clear biological success, though not yet clinical protection.
- Optimism for next-generation vaccines based on sequential bnAb induction.
- Sustained global investment and collaboration are non-negotiable for success.

با سپاس از توجه شما

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