The Battle Against HIV Immune Evasion: Could Vaccines Be Possible One Day?

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Introduction

- In 1984, the Human Immunodeficiency Virus (HIV) was determined to be the causative agent of AIDS, with the first cases reported in 1981 [3].
- HIV-1 and HIV-2 are two main types of HIV and both lead to the Acquired Immunodeficiency Syndrome (AIDS0 [14].
- There have been around 84.2 million infections and 40.4 million deaths [16].

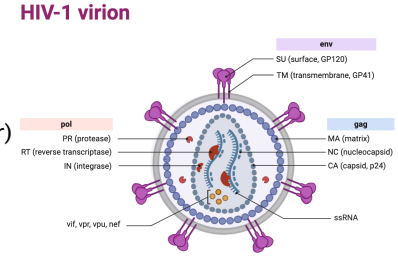

Figure 1: HIV-1 virion (BioRender)

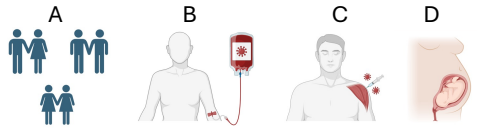

Figure 2: Modes of HIV transmission. Panel A: sexual intercourse, panel B: blood transfusion, infected needles or syringes, from mother to child during pregnancy (Pictures from BioRender).

Methods

A literature review of primary and secondary journal articles was conducted to establish the consensus that HIV immune evasion causes obstacles in vaccine research.

Infection of CD4+ T cells & AIDS

- CD4+ T cells or helper T cells are white blood cells that help coordinate the immune system to destroy viruses and/or bacteria during an infection.
- HIV primarily attacks CD4+ T cells to weaken the immune system [12].
- Retroviruses such as HIV use the process of reverse transcription to integrate their genomes into the host cell genome which facilitates viral replication [7].
- The normal count of CD4+ T cells is between 500 and 1500 cells/mm^3 [2].
- AIDS is diagnosed once the CD4+ T cells count drops under 200 cells/mm^3 [2]. If HIV is detected before the cell count reaches that level and treatment is initiated, HIV is likely to not progress into AIDS.
- Antiretroviral therapy is available for HIV-positive individuals that works by suppressing the virus and lowering the viral load as a result.

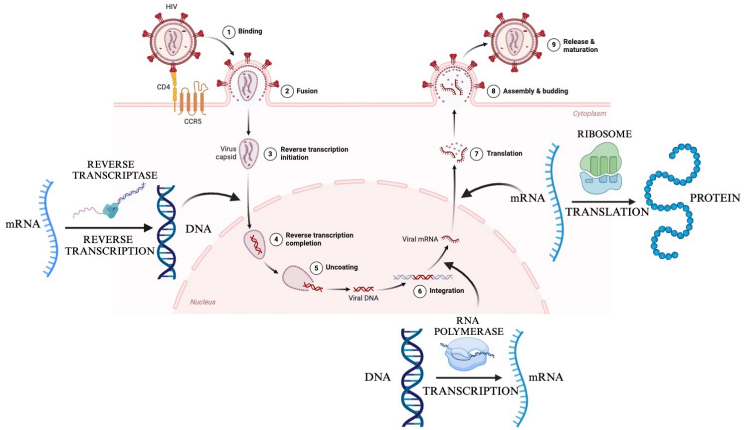

Figure 3: Mechanism of HIV replication cycle inside a CD4+ T cell using reverse transcription (BioRender).

HIV-Antibody Interaction

- HIV-1 has a mutation rate of 10^{-4} to 10^{-5} mutations/base pair/cycle which is 10,000 to 100,000 times faster than the mutation rate of the eukaryotic genome (10^{-8} to 10^{-9} mutations/base pair/cycle) [9].
- Mutations cause genetic changes in the viral envelope glycoproteins gp120 and gp41 where non-neutralizing antibodies bind and prevent neutralizing antibodies and T cells from recognizing the virus [10].

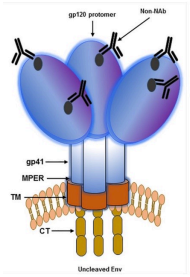

Figure 4: Illustration of the envelope glycoproteins gp120 and gp41 (Modified from [1]).

Scientific Advancement and Future Directions

- RV144 vaccine candidate in Thailand (2009).
  - Combination of ALVAC-HIV (prime vaccine) and AIDSVAX B/E (booster).
  - Efficacy of 60% at 12 months post trial that dropped to 31% after 3 and a half years without intensification of the infection [6].

Scientific Advancement and Future Directions

- mRNA vaccine tested on macaques designed to co-express HIV-1 glycoproteins and Simian Immunodeficiency Virus Gag proteins and generate virus-like particles [17].
  - 79% less likely to develop an HIV infection.
  - Induction of CD4+ T cell response and neutralizing antibodies.
- In March 2022, the National Institute of Allergy and Infectious Diseases launched a Phase I clinical trial for three mRNA vaccines (HVTN 302 study) [11].

Conclusions & Significance

- HIV vaccine research will take time, commitment, association of researchers [15].
- Unequal accessibility to antiretroviral therapy and risk of side effects and drug resistance [5].
- An HIV vaccine is estimated to cost between $500 per dose for a five-dose series, with the cost of antiretroviral therapy reaching $36,000 a year per patient in 2018 [8].

Acknowledgments & References

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Scan me!