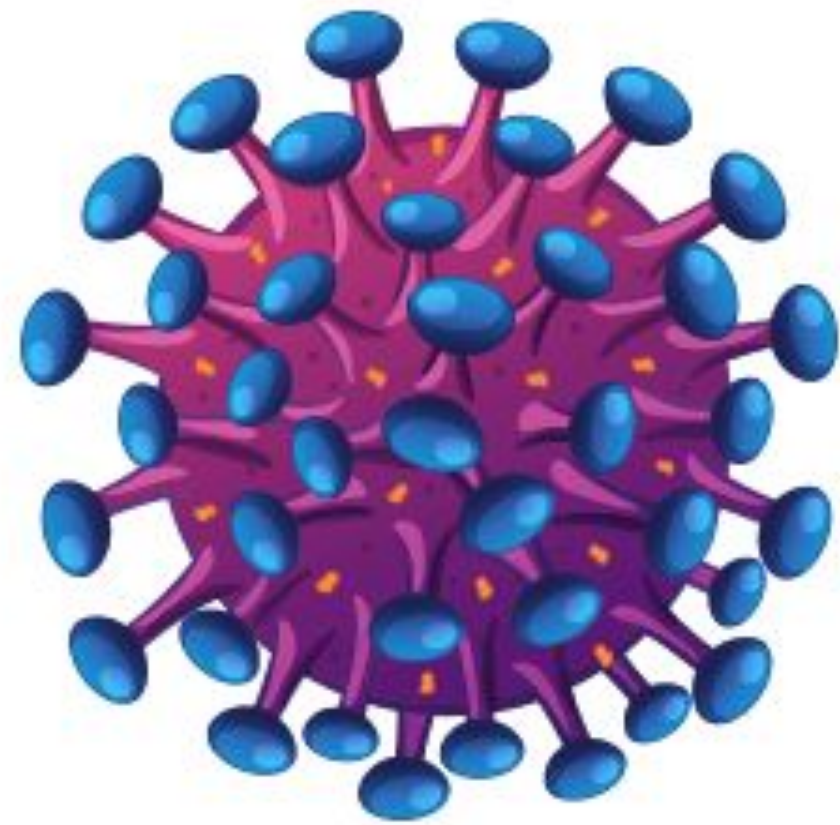


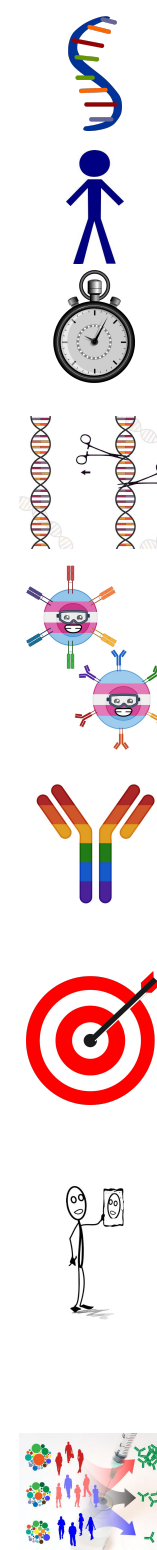


What is HIV?

HIV (Human Immunodeficiency Virus) is an epidemic virus responsible for over 38 million infections worldwide. HIV infects and kills **T cells**, a critical cell type for a healthy immune system.



Over time, infection with HIV (and loss of T cells) can lead to **AIDS**, or acquired immunodeficiency syndrome. This disease is characterized by immune failure and vulnerability to infections and cancers. This disease is responsible for 650,000 deaths worldwide per year.



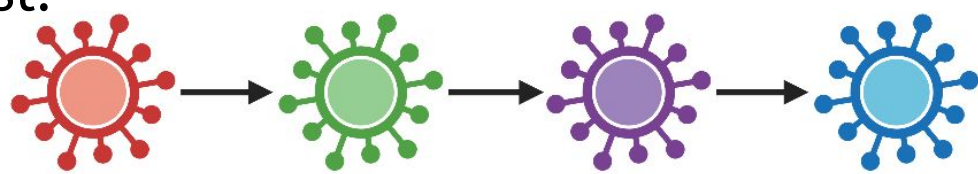
| SARS-CoV-2 | HIV |
|--|---|
| Single stranded RNA | Single stranded RNA |
| Largely cleared by infected individuals | Not cleared by infected individuals |
| Slow mutation rate | Extremely high mutation rate |
| Doesn't integrate into host genome | Integrates into host genome within 72h of transmission |
| Adaptive immune response can clear | Adaptive immune response unable to clear infected cells |
| Vaccine strategy: induce neutralizing antibodies | Vaccine strategy: induce neutralizing antibodies |
| Vaccine antibody target: Spike protein on outside of virus | Antibody target: Envelope protein surrounding outside of virus |
| No similar host targets to spike protein | HIV envelope mimics the outside of host cells |
| Broadly neutralizing antibodies induced within 10 days of COVID-19 symptoms/2 weeks of vaccination | Broadly neutralizing antibodies not readily induced by vaccination or infection |

Challenges

Researchers have been trying to produce an HIV-1 vaccine since the 1980s, but have faced several challenges:

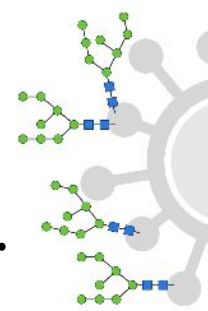
1. Mutations

HIV-1 mutates extremely quickly, providing a tough "moving target" to vaccinate against.



2. A sugar "shield"

HIV-1 is decorated with sugars called glycans which hide it from the immune system, because they look like the sugars on our own cells.



3. A permanent infection

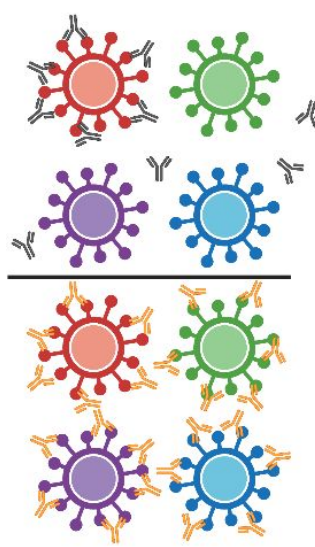
Some viruses, like SARS-CoV2, are naturally cleared by the immune system. A good vaccine for these diseases works by preparing the immune system to respond to infection.



In contrast, HIV-1 infection is permanent. Thus, a good vaccine must completely prevent infection. This is a particularly high bar for protection.

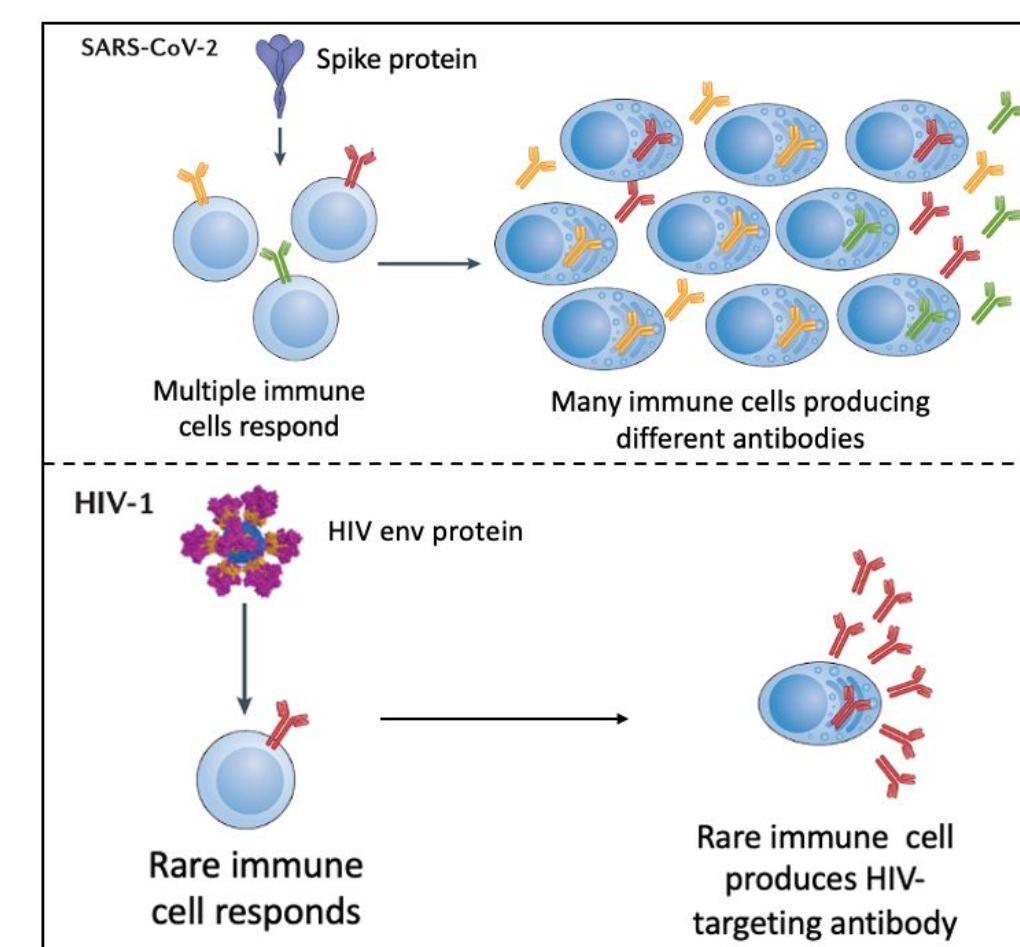
The goal: broadly neutralizing antibodies (bnAbs)

Many antibodies can bind to some HIV, but are quickly evaded by mutations (gray). The goal is to instead produce broadly neutralizing antibodies (orange). Like a master key opens many locks, these bnAbs can bind to an array of differently mutated HIV.



Successes & Improvements

- Antiretroviral drug therapies** have effectively turned AIDS into a chronic disease with a near normal lifespan
 - Pre- (PrEP) and post-exposure (PEP) prophylaxis
- Developing **cell-based immunotherapies** as potential treatment post-HIV infection
 - Immune cell therapy for HIV by Dr. Mehri McKellar at Duke University
- mRNA vaccines** have induced low levels of plasma HIV-1 targeted antibodies in rhesus macaques
 - Effective in the COVID-19 vaccines and shows promise for HIV vaccines
- Immune vaccine stimulants** induce HIV-1 specific antibody production in macaques, leading to protection from infection
 - Investigating ways to stimulate strong immune cell responses
- New strategies for combating HIV's high mutation rate
 - Small group testing of HIV patients to identify new HIV mutations for rapid vaccine design



Modified from Haynes B., Nature Reviews Immunology, 2021

Future Directions



Creation of the Duke Center for HIV Structural Biology

- Within 5 years will create 3D models of how HIV enters host cell and evades immune system to drive better vaccine strategies
- Clinical Trials
 - 4 ongoing or recently completed Phase I Clinical Trials to evaluate safety of different vaccine candidates
 - Next one has preliminary data for a novel vaccine candidate expected in October 2022!

Acknowledgements



A special thanks to Dr. Wilton Williams, Dr. Barton Haynes, Dr. Kevin Saunders, Zekun (Charlie) Mu for their ongoing work on HIV/AIDS at Duke and their help in creating this poster.

