**HIV Vaccine Progress: At Duke**

**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.

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**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.

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**Successes & Improvements**

1. **Antiretroviral drug therapies** have effectively turned AIDS into a chronic disease with a near normal lifespan
   - Pre- (PrEP) and post-exposure (PEP) prophylaxis

2. **Developing cell-based immunotherapies** as potential treatment post-HIV infection
   - Immune cell therapy for HIV by Dr. Mehri McKellar at Duke University

3. **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

4. **Immune vaccine stimulants** induce HIV-1 specific antibody production in macaques, leading to protection from infection
   - Investigating ways to stimulate strong immune cell responses

5. **New strategies for combating HIV’s high mutation rate**
   - Small group testing of HIV patients to identify new HIV mutations for rapid vaccine design

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**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!

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**SARS-CoV-2**

- Single stranded RNA
- Largely cleared by infected individuals
- Slow mutation rate
- Doesn’t integrate into host genome
- Adaptive immune response can clear
- Vaccine strategy: induce neutralizing antibodies
- Vaccine antibody target: Spike protein on outside of virus
- No similar host targets to spike protein
- Broadly neutralizing antibodies induced within 10 days of COVID-19 symptoms/2 weeks of vaccination

**HIV**

- Single stranded RNA
- Not cleared by infected individuals
- Extremely high mutation rate
- Integrates into host genome within 72h of transmission
- Adaptive immune response unable to clear infected cells
- Vaccine strategy: induce neutralizing antibodies
- Antibody target: Envelope protein surrounding outside of virus
- HIV envelope mimics the outside of host cells
- Broadly neutralizing antibodies not readily induced by vaccination or infection

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**Modified from Haynes B., Nature Reviews Immunology, 2021**

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