thewellproject

HIV Drugs and the HIV Lifecycle

Last updated: August 30, 2024

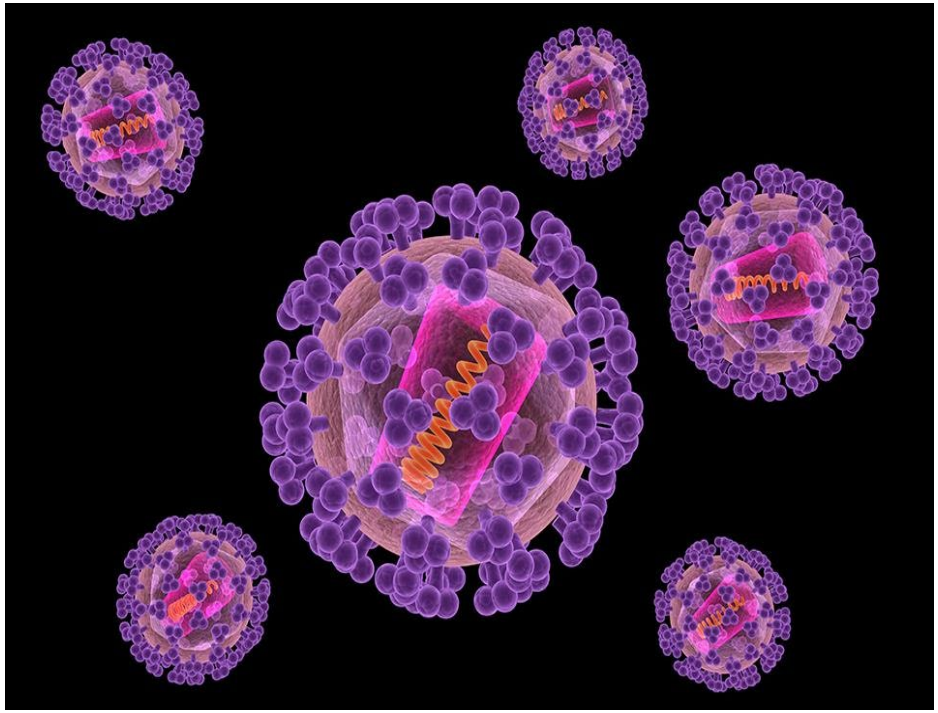
Together, we can change the course of the HIV epidemic…one woman at a time.

#onewomanatatime #thewellproject

HIV Drugs and the HIV Lifecycle

HIV must go through a number of steps to make copies of itself; these steps are called the ***HIV lifecycle***

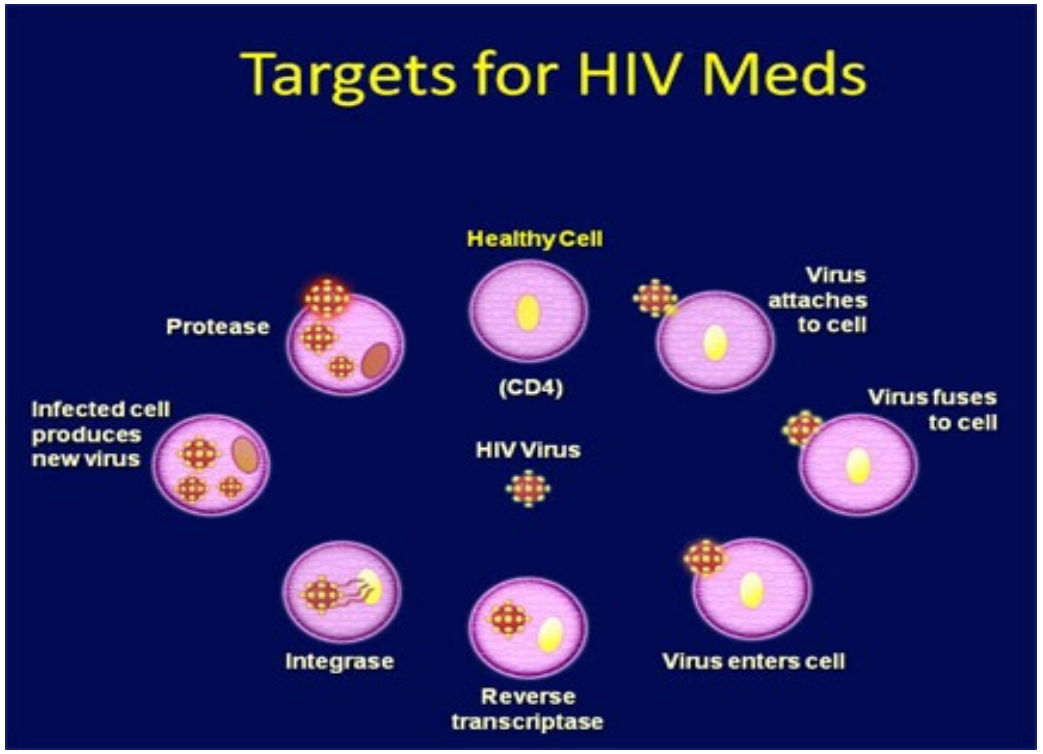
- **All HIV drugs work by interrupting different steps in HIV's lifecycle**
- HIV drugs can't cure HIV, but can help you stay healthy and keep you from transmitting HIV to others
- HIV infects CD4 cells (a type of white blood cell) and other cells
- HIV turns CD4 cells into factories, producing thousands of copies of the virus
- CD4 cells are destroyed in the process



The HIV Lifecycle

The steps HIV goes through to complete the process of reproducing itself are:

- Binding and fusion
- Reverse transcription
- Integration
- Transcription
- Assembly
- Budding



The HIV Lifecycle

Binding and Fusion: HIV begins to enter a CD4 cell by binding, or attaching itself, to a specific point, called a **CD4 receptor**, on the cell's surface

- HIV must then bind to a second **receptor**, either the CCR5 co-receptor or the CXCR4 co-receptor
- This allows the virus to join, or merge, with the CD4 cell in a process called **fusion**
- After fusion, HIV releases its **RNA** (HIV's genetic material) and **enzymes** (proteins causing chemical reactions) into the CD4 cell

The HIV Lifecycle

Reverse Transcription: HIV's RNA contains the "instructions" that will reprogram the CD4 cell to produce more virus

- In order to be effective, HIV's RNA must be changed into DNA
- An HIV enzyme called **reverse transcriptase** changes the HIV RNA into HIV DNA

Integration: Next, the newly formed HIV DNA enters the nucleus (command center) of the CD4 cell

- Another HIV enzyme called **integrase** combines or “integrates” HIV's DNA with the CD4 cell's DNA

The HIV Lifecycle

Transcription: Once the virus is integrated into the CD4 cell, it commands the CD4 cell to start making new HIV proteins

- The proteins are the building blocks for new HIV viruses
- They are produced in long chains

Assembly: An HIV enzyme called **protease** cuts the long chains of HIV proteins into smaller pieces

- As the smaller protein pieces come together with copies of HIV's RNA, a new virus is put together (assembled)

Budding: The newly assembled virus pushes ("buds") out of the original CD4 cell

- This new virus can now target and infect other CD4 cells

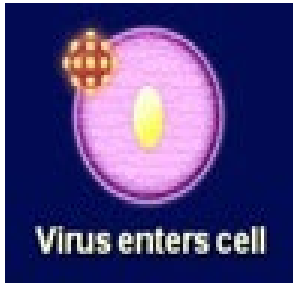
Approved HIV Drugs

- Different **classes or groups** of HIV drugs block different steps in HIV's lifecycle
- FDA has approved **several classes of HIV drugs:**
  - Entry Inhibitors
  - Post-attachment Inhibitor
  - Integrase Inhibitors
  - Nucleoside and Nucleotide Reverse Transcriptase Inhibitors
  - Non-Nucleoside Reverse Transcriptase Inhibitors
  - Protease Inhibitors
  - Capsid Inhibitor
  - Boosting Agents
  - Fixed-Dose Combinations

Entry and Integrase Inhibitors

Entry Inhibitors:

Stop HIV from entering CD4 cell

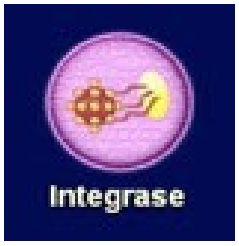


- **Fusion inhibitor:** Fuzeon (enfuvirtide or T-20)
- **CCR5 antagonist**: Selzentry (maraviroc)
- **Attachment inhibitor:** Rukobia (fostemsavir)
- **Post-attachment inhibitor:** Trogarzo (ibalizumab)

Integrase Inhibitors:

Interfere with HIV's **integrase** enzyme

- bictegravir (in a combination pill)
- elvitegravir (in several combination pills)
- Isentress (raltegravir)
- Tivicay (dolutegravir)
- Vocabria (cabotegravir or CAB)



NRTIs (“Nukes”)

Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTIs or "nukes"):

- Interfere with HIV's **reverse transcriptase** enzyme
  - Emtriva (emtricitabine or FTC)
  - Epivir (lamivudine or 3TC)
  - Retrovir (zidovudine or AZT)
  - tenofovir alafenamide fumarate (TAF) (in several combination pills, also sold separately as Vemlidy for treatment of hepatitis B)
  - Videx (didanosine or ddI) (no longer used in the US)
  - Viread (tenofovir disoproxil fumarate or TDF)
  - Zerit (stavudine or d4T) (no longer used in the US)
  - Ziagen (abacavir)

NNRTIs ("Non-Nukes")

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs or "non-nukes"):

- Like NRTIs, interfere with HIV's reverse transcriptase enzyme
- There are a number of approved NNRTIs:
  - Edurant (rilpivirine or RPV)
  - Intelence (etravirine or ETR)
  - Pifeltro (doravirine or DOR)
  - Rescriptor (delavirdine)
    (no longer used in the US)
  - Sustiva (efavirenz) (only in combination pill)
  - Viramune (nevirapine)

Protease Inhibitors ("PIs")

Protease Inhibitors (PIs):

- Interfere with HIV's **protease** enzyme
  - Aptivus (tipranavir)
  - Crixivan (indinavir) (no longer used in the US)
  - Invirase (saquinavir) (no longer used in the US)
  - Lexiva (fosamprenavir)
  - Norvir (ritonavir, generally used as boosting agent)
  - Prezista (darunavir)
  - Reyataz (atazanavir)
  - Viracept (nelfinavir)

Capsid Inhibitor

Capsid Inhibitor:

- Interferes with the shell that protects HIV's genetic material. It can work at different stages of the HIV lifecycle.
  - Sunlenca (lenacapavir)

Boosting Agents

Boosting Agents:

- Drugs do not affect HIV's lifecycle
- Instead, they improve, or 'boost', the level of other HIV drugs in the blood stream so they can be taken at a lower dose
- Approved boosting agents:
  - Norvir (ritonavir)
  - Tybost (cobicistat)

Fixed-Dose Combinations

Fixed-dose drugs **combine 2 or more HIV drugs from 1 or more classes in just 1 pill (or injection)**

- Atripla (Sustiva + Emtriva + Viread)
- Biktarvy (bictegravir + Emtriva + tenofovir alafenamide)
- Cabenuva (Vocabria + Edurant; available as a monthly injection)
- Cimduo (Epivir + Viread)
- Combivir (Retrovir + Epivir)
- Complera (Emtriva + Viread + Edurant)
- Delstrigo (Pifeltro + Epivir + Viread)
- Descovy (Emtriva + tenofovir alafenamide)
- Dovato (Tivicay + Epivir)
- Epzicom (Epivir + Ziagen)
- Evotaz (Reyataz + Tybost)
- Genvoya (elvitegravir + Tybost + Emtriva + tenofovir alafenamide fumarate)
- Juluca (Tivicay + Edurant)
- Kaletra (lopinavir + Norvir)
- Odefsey (Emtriva + tenofovir alafenamide + Edurant)
- Prezcobix (Prezista + Tybost)
- Stribild (Emtriva + Viread + elvitegravir + Tybost)
- Symfi and Symfi Lo (contains less Sustiva) (Sustiva + Epivir + Viread)
- Symtuza (Prezista + Tybost + Emtriva + tenofovir alafenamide)
- Triumeq (Ziagen + Tivicay + Epivir)
- Trizivir (Retrovir + Epivir + Ziagen)
- Truvada (Emtriva + Viread)

Combining HIV Drugs

- Healthcare providers combine drugs from different classes in order to attack HIV at more than one step in its lifecycle
  - HIV can **mutate** when it reproduces, which could stop HIV drugs from working
  - When this happens, we say that HIV has become **resistant** to that drug
- If you take only one drug (monotherapy) or a few drugs from the same class, HIV can become resistant to that drug or drug class
- **HIV has a much harder time developing mutations and resistance when you take a combination of drugs from different classes**
- Fixed-dose combinations: take three drugs in one pill

thewellproject

What Does This Mean for You?

Combination therapy with drugs that block HIV at different steps of its lifecycle can prevent the production of new virus.

Most importantly, it means **slower disease progression and longer life** for people living with HIV.

thewellproject

Learn More!

- To learn more, please read the full fact sheet on this topic:
  - HIV Drugs and the HIV Lifecycle
- For more information on approved HIV drugs:
  - The Well Project's HIV Drug Chart
- For more fact sheets and to connect to our community of women living with HIV, visit:
  - www.thewellproject.org
  - www.facebook.com/thewellproject
  - www.twitter.com/thewellproject
  - www.instagram.com/thewellprojecthiv
  - www.youtube.com/thewellprojecthiv