HIV Drugs and the HIV Lifecycle

August 15, 2018

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

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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 by preventing HIV from reproducing
- Once HIV is in the body, it infects CD4 cells (a type of white blood cell) and other cells
- HIV turns CD4 cells into factories, producing thousands of copies of HIV
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

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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
Different classes or groups of HIV drugs block different steps in HIV's lifecycle. The U.S. Food and Drug Administration (FDA) has approved six classes of HIV drugs:

- Entry Inhibitors
- Integrase Inhibitors
- Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTIs or "nukes")
- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs or "non-nukes")
- Protease Inhibitors (PIs)
- Boosting Agents
**Entry Inhibitors:**

Stop HIV from entering CD4 cell

Different types of entry inhibitors

- **Fusion inhibitor:** Fuzeon (enfuvirtide)
- **CCR5 antagonist:** Selzentry (maraviroc)
- **Post-attachment inhibitor:** Ibalizumab

**Integrase Inhibitors:**

Interfere with HIV's **integrase** enzyme

There are 3 approved integrase inhibitors:

- Isentress (raltegravir)
- Tivicay (dolutegravir)
- Vitekta (elvitegravir)

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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 Biktarvy, Descovy and Genvoya)
  - Videx (didanosine or ddI)
  - Viread (tenofovir disoproxil fumarate or TDF)
  - Zerit (stavudine or d4T)
  - 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)
  - Rescriptor (delavirdine)
  - Sustiva (efavirenz)
  - Viramune (nevirapine)
Protease Inhibitors (PIs):

- Interfere with HIV's **protease** enzyme
  - Aptivus (tipranavir)
  - Crixivan (indinavir)
  - Invirase (saquinavir)
  - Kaletra (lopinavir plus ritonavir)
  - Lexiva (fosamprenavir)
  - Norvir (ritonavir)
  - Prezista (darunavir)
  - Reyataz (atazanavir)
  - Viracept (nelfinavir)

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Fixed-dose drugs combine 2 or more HIV drugs from 1 or more classes in just 1 pill for easier dosing:

- Atripla (Sustiva plus Emtriva plus Viread)
- Biktarvy (Bictegravir plus Descovy)
- Combivir (Retrovir plus Epivir)
- Complera (Emtriva plus Viread plus Edurant)
- Descovy (Emtriva plus tenofovir alafenamide (TAF))
- Epzicom (Epivir plus Ziagen)
- Evotaz (Reyataz plus Tybost)
- Genvoya (Vitekta plus Tybost plus Emtriva plus tenofovir alafenamide fumarate (TAF))
- Juluca (Tivicay plus Edurant)
- Odefsey (Emtriva plus tenofovir alafenamide (TAF) plus Edurant)
- Prezcobix (Prezista plus Tybost)
- Stribild (Emtriva plus Viread plus Vitekta plus Tybost)
- Triumeq (Ziagen plus Tivicay plus Epivir)
- Trizivir (Retrovir plus Epivir plus Ziagen)
- Truvada (Emtriva plus Viread)
**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)
Combining HIV Drugs

- Health care 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 that belong to the same class, HIV can develop mutations that make it resistant to that drug or drug class
- **HIV has a much harder time changing enough to develop drug mutations and resistance when you take a combination of drugs from different classes**
What Does This Mean for You?

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

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