THE HIV LIFE CYCLE

Understanding How Antiretroviral Medications Work
DEFINITIONS

- **Host**: The animal or cell that another organism lives in. In HIV, human CD4 T-cells are the host for HIV.

- **Nucleus**: The core of CD4 T-cells, it contains human DNA.
DEFINITIONS

- **DNA:** The chemical make-up of living things. DNA contains 2 copies of information.

- **RNA:** the chemical make up of living things. RNA contains only 1 copy of information and needs another copy to replicate.

- **HIV:** A virus that can only survive in host cells. It carries with it RNA, but must make DNA to replicate.
DEFINITIONS

- **Retrovirus**: A type of virus that has RNA instead of DNA as its genetic material. It uses an enzyme called reverse transcriptase to become part of the host cell’s DNA. This allows many copies of the virus to be made in the host cell.
DNA versus RNA
Several steps must occur for the HIV to replicate

- Entry of virus into host cell
- Copying RNA into DNA
- Hiding HIV DNA in host cell nucleus
- Multiplication of the virus within cell
- Budding of virus
AFRITAB
HIV binds to receptors on CD4 T-cell

A message is sent to the CD4 T-cell to let the virus in
Fusion

Once bound, the virus is allowed to dump its contents into the CD4 T-cell.

Included in its contents are HIV RNA and reverse transcriptase.
The HIV RNA is turned into double-stranded DNA within the CD4 T-cell.

The enzyme reverse transcriptase aids in this process.
Once the DNA is formed, it hides itself in the human DNA housed in the CD4 T-Cell nucleus.
- Copies of HIV DNA are made and released from the nucleus in small ‘packages’
- Each of the small ‘packages’ contains information for creating a new HIV
ASSEMBLY

- The protease enzyme in the cell combines the DNA ‘packages’ to create active virus
Once the new HIV is formed, it pushes itself out of the CD4 T-cell.

The virus steals part of the CD4 T-cells protective coating.
HIV Life Cycle - The Big Picture

1. Attachment
   - HIV binds to receptors on the CD4 T-cell.
   - A message is sent to the CD4 T-cell to let the virus in.

2. Fusion
   - Once bound, the virus is allowed to dump its contents into the CD4 T-cell.
   - Included in its contents are HIV RNA and reverse transcriptase.

3. Reverse Transcription
   - The HIV RNA is turned into double-stranded DNA within the CD4 T-cell.
   - The enzyme *reverse transcriptase* aids in this process.

4. Integration
   - Once the DNA is formed, it hides itself in the human DNA housed in the CD4T-cell nucleus.

5. Transcription
   - Copies of HIV DNA are made and released from the nucleus in small packages.
   - Each of the small packages contains information for creating a new HIV.

6. Assembly
   - The *protease* enzyme in the cell combines the DNA ‘packages’ to create active virus.

7. Budding
   - Once the new HIV is formed, it pushes itself out of the CD4 T-cell.
   - The virus steals part of the CD4 T-cell protective coating.
HIV

- Virus is in the bloodstream but also hides in other cells (e.g. lymph nodes)
  - Drugs don’t reach these sequestered cells*
  - That’s why there is no cure
- Virus destroys CD4 cells which lead to:
  - Immune suppression
  - Opportunistic infections and AIDS

*HIV hides in cells in certain organs which are “protected” by the body: lymph nodes, the brain, reproductive organs. Not enough meds can get to those cells.
HIV Life Cycle - Worksheet

A. HIV binds to receptors on the CD4 T-cell.
   - A message is sent to the CD4 T-cell to let the virus in.

B. HIV is formed, it pushes itself out of the CD4 T-cell
   - The virus steals part of the CD4 T-cell protective coating.

F. Once bound, the virus is allowed to dump its contents into the CD4 T-cell.
   - Included in its contents are HIV RNA and reverse transcriptase.

R. The HIV RNA is turned into double-stranded DNA within the CD4 T-cell.
   - The enzyme reverse transcriptase aids in this process.

I. Once the DNA is formed, it hides itself in the human DNA housed in the CD4 T-cell nucleus.
   - Included in the contents are HIV DNA and reverse transcriptase.

T. Copies of HIV DNA are made and released from the nucleus in small packages’.
   - Each of the small packages contains information for creating a new HIV.

A. The protease enzyme in the cell combines the DNA ‘packages’ to create active virus.
   - The virus steals part of the CD4 T-cell protective coating.

B. HIV is formed, it pushes itself out of the CD4 T-cell
   - The virus steals part of the CD4 T-cell protective coating.
HOW MEDICATIONS WORK:

Drug Classes and Medications
FUSION INHIBITORS

- Inhibit first step of HIV replication
- Prevent fusion of HIV to CD4 T-cell
- Virus is prevented from using host for replication

- Enfuviritide (Fuzeon®)-BID
- Maraviroc (Selzentry®)-BID
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)

- Inhibit reverse transcriptase—the enzyme responsible for turning HIV RNA into DNA
- Prevents virus from replicating
- Delavirdine (Rescriptor®)-3x daily
- Nevirapine (ViramuneXR®)-daily
- Efavirenz (Sustiva®)-daily
- Etravirine (Intelence®)-2x daily
- Rilpivirine (Edurant®)-daily
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

- Inhibit reverse transcriptase. Drug binds to the enzyme at a different place than the NNRTIs

- Lamivudine (Epivir®)-1 to BID
- Zidovudine (Retrovir®)-BID
- Abacavir (Ziagen®)-1 to BID
- Emtricitabine (Emtriva®)-daily
- Didanosine (VidexEC®)-1 to BID
- Tenofovir (Viread®)-daily
- Stavudine (Zerit®)-BID
- Tenofovir + Emtricitabine (Truvada®) -daily
- Abacavir + Lamivudine (Epizom®)- daily
- Zidovudine + Lamivudine (Combivir®)- BID
- Abacavir + Zidovudine + Lamivudine (Trizivir®)- BID
INTEGRASE INHIBITORS

- Newest class of drugs that work within the cell nucleus.
- Blocks viral DNA and keeps HIV from binding to the host cell DNA.
- Prevents viral replication.

- **Raltegravir (Isentress) – 1 to BID**
PROTEASE INHIBITORS

- Prevent the piecing together of HIV DNA into small ‘packages’
- Prevents formation of new HIV

- Fosamprenavir (Lexiva®) - 1 to BID
- Indinavir (Crixivan®) - 1 to 3x
- Saquinavir (Invirase®, Fortovase®) - BID
- Lopinavir + Ritonavir (Kaletra®) - daily
- Atazanavir (Reyataz®) - daily
- Nelfinavir (Viracept®) - 2 to 3x
- Tipranavir (Aptivus®) - BID
- Ritonavir (Norvir®) - 1 to bid
- Prezista (Darunavir®) - 1 to bid
SINGLE TABLET REGIMENS

- Efavirenz + Tenofovir + Emtricitabine (Atripla®)- daily
- Rilpivirine + Tenofovir + Emtricitabine (Complera®)- daily
- Elvitegravir + Cobicistat + Tenofovir + Emtricitabine (Stribild®)- daily
Medications at Work in the HIV Life Cycle

1. **Fusion Inhibitors**
   - Inhibit first step of HIV replication.
   - Prevent fusion of HIV to CD4 T-cell.
   - Virus prevented from using host for replication.

2. **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
   - Inhibit reverse transcriptase—the enzyme responsible for turning HIV RNA into DNA.
   - Prevents virus from replicating.

3. **Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**
   - Inhibit reverse transcriptase. This drug binds to the enzyme at a different place than the NNRTIs.
   - Prevents virus from replicating.

4. **Integrase Inhibitors**
   - Blocks viral DNA and keeps HIV from binding to the host cell DNA.
   - Prevents virus from replicating.

5. **Protease Inhibitors**
   - Prevents the piecing together of HIV DNA into small ‘packages’.
   - Prevents the formation of new HIV.

6. **Attachment**
   - Entry of the virus into the cell.

7. **Fusion**
   - Virus fusion to the cell membrane.

8. **Reverse Transcription**
   - Reverse transcriptase enzyme converts RNA to DNA.

9. **Integration**
   - Integration of viral DNA into host cell DNA.

10. **Transcription**
    - Viral RNA is transcribed into DNA.

11. **Assembly**
    - Viral proteins are assembled into new virions.

12. **Budding**
    - Viruses are released from the cell.
GOALS OF THERAPY

- Suppress HIV VL to <50 copies/ml for as long as possible
- Improve quality of life
- Preserve medications for future use
- Restore immune function
PRINCIPLES OF HAART

- HIV has 1 goal: replication
- Triple-drug therapy
  - “Block” virus in several different ways
  - Slow down viral replication
  - Allow immune system to ‘recover’