Overview of the HIV Life Cycle

David H. Spach, MD
Editor-in-Chief, National HIV Curriculum
Professor of Medicine
Division of Allergy and Infectious Diseases
University of Washington

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Dr. Spach does not have any disclosures.
HIV Life Cycle

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HIV Life Cycle

1. **ENTRY**
   - Host cell
   - HIV

2. **Cytoplasmic Transport & Nuclear Import**
   - Host cell
   - HIV core
   - Nuclear pore
   - Envelope Glycoprotein (gp120, gp41)
   - CD4 receptor
   - CCR5 coreceptor

3. **Reverse Transcription**
   - Host cell
   - HIV RNA
   - Single-stranded HIV DNA
   - Nuclear pore
   - Integrase
   - Host DNA
   - HIV DNA
   - Proviral DNA
   - Host enzyme
   - Host cell RNA polymerase
   - Host DNA
   - HIV genomic mRNA

4. **Integration**
   - NUCLEUS
   - HIV DNA
   - Integrase
   - Host DNA
   - HIV genomic mRNA
   - HIV Gag-Pol polyprotein
   - HIV envelope glycoprotein

5. **Transcription**
   - NUCLEUS
   - HIV DNA
   - Proviral DNA
   - Host enzyme
   - Host cell RNA polymerase
   - Host cell mRNA
   - HIV mRNA
   - Spliced HIV envelope
   - Host cell ribosome

6. **Translation**
   - HOST CELL
   - HIV matrix
   - HIV core
   - Envelope Glycoprotein (gp120, gp41)
   - CD4 receptor
   - CCR5 coreceptor

7. **Assembly**
   - BUDDING & MATURATION
   - Mature HIV virion
   - HIV Gag-Pol polyprotein
   - HIV envelope glycoprotein

8. **Budding & Maturation**
   - Mature HIV virion
   - HIV Gag-Pol polyprotein
   - HIV envelope glycoprotein

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HIV Life Cycle

Entry
HIV Envelope Glycoprotein
Entry

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Entry

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Entry

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Entry

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CD4 binding site

CD4 receptor

Envelope glycoprotein
- gp41
- gp120

CCR5 coreceptor

HIV

Host cell
Entry: Attachment

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Entry

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Entry: Coreceptor Binding

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Entry

Host cell

gp41

HIV

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Illustration: Cognition Studio Inc., and David H. Spach, MD
Illustration: Cognition Studio, Inc. and David H. Spach, MD
Entry

Illustration: Cognition Studio, Inc. and David H. Spach, MD
Entry

HIV matrix shell

HIV core

Host cell

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Entry: Fusion

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HIV Life Cycle
Cytoplasmic Transport and Nuclear Import
Cytoplasmic Transport and Nuclear Import

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Cytoplasmic Transport and Nuclear Import

- HIV core
- Integrase
- Reverse transcriptase
- Genomic HIV RNA

Host cell
Nucleus
Cytoplasmic Transport and Nuclear Import
Cytoplasmic Transport and Nuclear Import

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Cytoplasmic Transport and Nuclear Import

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Cytoplasmic Transport and Nuclear Import

Host cell

Microtubule

Nucleus
Cytoplasmic Transport and Nuclear Import

Host cell

Nucleus

Microtubule

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Cytoplasmic Transport and Nuclear Import

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Cytoplasmic Transport and Nuclear Import

HIV Core
Nuclear Pore Complex
Cytoplasmic ring
Central channel
Nuclear ring
Nuclear basket
Host cell
Cytoplasm
Nucleus

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Cytoplasmic Transport and Nuclear Import

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HIV Life Cycle

Reverse Transcription

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Reverse Transcription

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Reverse Transcription

HIV RNA

HIV DNA
Reverse Transcription

HIV RNA → Reverse Transcriptase → HIV DNA
Reverse Transcription

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Reverse Transcription

Intracellular Pool of Nucleotides

HIV RNA

HIV DNA
Reverse Transcription

Intracellular Pool of Nucleotides

HIV RNA

- Phosphate
- Pentose
- Nitrogenous Base

HIV DNA

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# Reverse Transcription

<table>
<thead>
<tr>
<th>Human Nucleotides</th>
<th>DNA and RNA</th>
<th>DNA Only</th>
<th>RNA Only</th>
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<tbody>
<tr>
<td>Adenine</td>
<td><img src="image" alt="Adenine" /></td>
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<tr>
<td>Guanine</td>
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<tr>
<td>Cytosine</td>
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<tr>
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<tr>
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Reverse Transcription

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Reverse Transcription

HIV RNA Template

Host cell

Host Cell Nucleotides

Reverse Transcriptase

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Reverse Transcription

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Reverse Transcription

Illustration: David H. Spach, MD
Reverse Transcription

HIV RNA Template

Host cell

Reverse Transcriptase

Host Cell Nucleotides

Illustration: David H. Spach, MD
Reverse Transcription

HIV RNA Template

Host cell

Reverse Transcriptase

Host Cell Nucleotides

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Reverse Transcription

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Single-Stranded HIV DNA

HIV reverse transcriptase

HIV RNA

Nuclear pore

Host cell cytosol

Host cell nucleus
Reverse Transcription

- **HIV core**
- **Double-Stranded HIV DNA**
- **Nuclear pore**
- **Host cell nucleus**
Reverse Transcription

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Nuclear Transport and Reverse Transcription

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Integration

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Integration

Host cell DNA

HIV integrase

HIV DNA

Intasome

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Integration

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Integration

Catalytic core region

3’OH

HIV DNA

Host cell DNA

Nucleus

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Integration

Illustration: Cognition Studio, Inc., and David H. Spach, MD

Host cell DNA

HIV DNA

Nucleus
Integration

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Integration

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Integration

HIV provirus

Host cell DNA

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HIV Life Cycle
Transcription
Transcription

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Transcription

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Transcription

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Transcription

- HIV genomic RNA
- HIV mRNA
- HIV DNA

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Transcription

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Transcription

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Transcription

Host cell RNA polymerase

HIV genomic RNA

Unspliced mRNA

Trans-activator of transcription (Tat)

Partially-spliced mRNA transcript

Nucleus

Full-Length RNA transcript

Fully-spliced mRNA transcript
Transcription

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Translation

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Translation

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Translation

Rev

Unspliced mRNA transcripts

Partially-spliced mRNA transcripts

Nucleus

Host cell cytosol
Translation

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Translation

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Translation

Endoplasmic reticulum

Cytosol

Ribosome

HIV mRNA

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Translation

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Translation

HIV envelope precursor protein (gp160)
Oligosaccharides
Signal peptide

Endoplasmic reticulum
HIV mRNA
Ribosome
Cytosol

Illustration: Cognition Studio, Inc., and David H. Spach, MD
HIV envelope precursor protein (gp160)

Endoplasmic reticulum

HIV mRNA

Ribosome

Glycan Shield

Signal peptide

Cytosol
Translation

Cytosol

Endoplasmic reticulum

HIV mRNA

Ribosome

HIV envelope precursor protein (gp160)

Signal peptidase

Signal peptide

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Translation

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Translation

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Translation

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gp120-gp41 pair

Noncovalent bond

1 2 3
Translation

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Translation

HIV Gag polyprotein

95% of the time

Host cell cytoplasm

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Assembly

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Assembly

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Assembly

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Assembly

HIV Matrix

Host Cell Membrane

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Assembly

Host Cell Membrane

HIV Matrix

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Assembly

Host Cell Membrane

HIV Matrix

Myristyl Group (sequestered)
Assembly

phosphatidylinositol-4,5-bisphosphate

Host Cell Membrane

Basic domain

HIV Matrix

Myristyl Group (sequestered)

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Assembly

Illustration: David H. Spach, MD

Host Cell Membrane

phosphatidylinositol-4,5-bisphosphate

Myristyl Group (sequestered)

Basic domain

HIV Matrix
Assembly

phosphatidylinositol-4,5-bisphosphate

Host Cell Membrane

Myristyl Group (exposed)

HIV Matrix

Illustration: David H. Spach, MD
Assembly

Host Cell Membrane

phosphatidylinositol-4,5-bisphosphate

Myristyl Group (exposed)

HIV Matrix
Assembly

HIV Envelope

HIV Envelope

Host Cell Membrane

HIV Matrix

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HIV Matrix

HIV p6

HIV Vpr

Host Cell Membrane

HIV Envelope

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HIV Life Cycle
Budding and Maturation
Budding and Maturation

Host cell cytosol

HIV Gag

HIV Matrix

HIV budding
Budding and Maturation

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Host cell cytosol

HIV maturation

Gag Clustering
Budding and Maturation

Host cell cytosol

HIV maturation

Capsid-Capsid Binding
Budding and Maturation

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Budding and Maturation

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Budding and Maturation

Illustration: Cognition Studio, Inc., and David H. Spach, MD
Budding and Maturation

Illustration: Cognition Studio, Inc., and David H. Spach, MD

Gag and Gag-Pol polyprotein processing
Budding and Maturation

Processing of Gag Polyprotein

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Illustration: Cognition Studio, Inc., and David H. Spach, MD
Budding and Maturation

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HIV Capsid and Core Formation

Monomers → Polymers

- Hexamer
- Pentamer
Budding and Maturation

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HIV

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HIV Life Cycle

Human T-cell Lymphocyte

Source for T-cell Image: NIAID/HIH
HIV Life Cycle

Human T-cell Lymphocyte

Source for T-cell Image: NIAID/NIH
HIV Life Cycle

Human T-cell Lymphocyte

HIV
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