

# HIV lifecycle

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HIV is a virus. Viruses are microscopic germs that are unable to reproduce (replicate) by themselves. Instead they need to find and infect a cell that will act as a host in which new viruses can be made.

When HIV is outside a cell it is known as a virion and is surrounded by a protective envelope. The envelope surrounds a number of viral proteins and some genetic material – a ‘blueprint’ containing all the information necessary to make new viruses.

Viruses can be divided into two forms: those whose genetic material is made of DNA, and those whose genetic material consists of RNA (such as HIV). RNA viruses are called retroviruses. HIV is a retrovirus and the reproductive process of HIV and other retroviruses involves an additional step that is not needed by DNA viruses.

## Fusion

Viruses often have a specific cell in the host human, animal or plant that they particularly like to infect. The main cells that HIV infects are those carrying a molecule called CD4 on their surface. CD4 is found on immune cells, most particularly on T-helper cells, which co-ordinate the immune system, and on macrophages, cells which roam the body engulfing bacteria and other germs.

HIV gets inside these cells by binding to the CD4 receptor using a molecule on the surface of the virus called gp120. Once HIV has bound to CD4, it activates other proteins on the surface of the human cell known as CCR5 and CXCR4 in order to complete its fusion with the cell.

Anti-HIV drugs which are designed to attack this stage of the HIV lifecycle are called fusion inhibitors. T-20 (enfuvirtide, *Fuzeon*) is the only fusion inhibitor currently available and works well when used with other anti-HIV drugs. Its use is reserved for people who have taken a lot of anti-HIV drugs in the past. T-20 binds to the virus.

Drugs are currently being developed that stop HIV binding with CCR5 receptors on the surface of cells. One drug, maraviroc (*Celsentri*) has been approved for people starting or changing HIV treatment.

## Reverse transcription

Once fusion has occurred, the inside of the virus (the RNA and some important enzymes) is absorbed into the human cell. A viral enzyme called reverse transcriptase performs the process required to translate HIV’s genetic material (RNA) into DNA.

Three classes of anti-HIV drugs target this stage: nucleoside reverse transcriptase inhibitors, AZT/zidovudine (*Retrovir*), ddI/didanosine (*Videx*), 3TC/lamivudine (*Epivir*), d4T/stavudine (*Zerit*), abacavir (*Ziagen*), and FTC/emtricitabine (*Emtriva*); non-nucleoside reverse transcriptase inhibitors, efavirenz (*Sustiva*), nevirapine (*Viramune*), and etravirine (*Intence*), and the nucleotide reverse transcriptase inhibitor tenofovir (*Viread*).

AZT/3TC are available in a combination pill called *Combivir*, abacavir/3TC in a pill called *Kivexa*, AZT/abacavir/3TC in a pill called *Trizivir*, FTC/tenofovir in a pill called *Truvada* and FTC/tenofovir/efavirenz in a pill called *Atripla*.

## Integration

The newly formed viral DNA is then integrated with the DNA of the human host cell using a viral enzyme called integrase. This allows HIV to ‘re-programme’ the human cell to make more HIV. New drugs called integrase inhibitors, are being developed and, raltegravir (*Isentress*) has been approved for people starting or changing treatment.

## Transcription

In this stage, the two strands of DNA divide and form a new strand of viral RNA, sometimes called messenger RNA.

## Translation

Next the protein building blocks, which will go on to form the new HIV particle, are assembled within the human cell. These blocks are laid out in turn through the translation of the information contained in the messenger RNA.

## Viral assembly

The protein building blocks are then cut into smaller pieces by a viral enzyme called protease. These pieces form the structure of the new HIV particle, including each of the enzymes and proteins needed to repeat the reproductive process. Once this assembly has occurred, the new viral particle buds off the human cell, floats off into the bloodstream and is able to infect other cells. It is estimated that about 10.3 billion new HIV virions are produced every day in people who are not on HIV treatment.

The protease inhibitors recommended for use are all ‘boosted’ by taking them with a small dose of a second protease inhibitor called ritonavir (*Norvir*). These protease inhibitors are: atazanavir (*Reyataz*), darunavir (*Prezista*), fosamprenavir (*Telzir*), lopinavir/ritonavir (*Kaletra*), saquinavir (*Invirase*) and tipranavir (*Aptivus*).

There are two other protease inhibitors that are now rarely used: indinavir (*Crixivan*) and nelfinavir (*Viracept*).