**Retrovirus**

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| ***Retroviruses*** | |
| [http://upload.wikimedia.org/wikipedia/commons/thumb/f/f3/Hiv_gross.png/220px-Hiv_gross.png](http://en.wikipedia.org/wiki/File:Hiv_gross.png) | |
| HIV retrovirus schematic of cell infection, virus production and virus structure | |
| [**Virus classification**](http://en.wikipedia.org/wiki/Virus_classification) | |
| Group: | Group VI ([ssRNA-RT](http://en.wikipedia.org/wiki/SsRNA-RT_virus)) |
| Order: | *Unassigned* |
| Family: | ***Retroviridae*** |
| **Genera** | |
| **Subfamily**: *Orthoretrovirinae*   * [*Alpharetrovirus*](http://en.wikipedia.org/wiki/Alpharetrovirus) * [*Betaretrovirus*](http://en.wikipedia.org/wiki/Betaretrovirus) * [*Deltaretrovirus*](http://en.wikipedia.org/wiki/Deltaretrovirus) * [*Epsilonretrovirus*](http://en.wikipedia.org/wiki/Epsilonretrovirus) * [*Gammaretrovirus*](http://en.wikipedia.org/wiki/Gammaretrovirus) * [*Lentivirus*](http://en.wikipedia.org/wiki/Lentivirus)   **Subfamily**: *Spumaretrovirinae*   * [*Spumavirus*](http://en.wikipedia.org/wiki/Spumavirus) | |

*Retroviridae* is a [family](http://en.wikipedia.org/wiki/Virus_classification) of [enveloped viruses](http://en.wikipedia.org/wiki/Enveloped_virus) that replicate in a host cell through the process of [reverse transcription](http://en.wikipedia.org/wiki/Reverse_transcription). A **retrovirus** is a single-stranded [RNA virus](http://en.wikipedia.org/wiki/RNA_virus) that stores its nucleic acid in the form of an [mRNA](http://en.wikipedia.org/wiki/MRNA) genome (including the [5' cap](http://en.wikipedia.org/wiki/5%27_cap) and 3' [PolyA tail](http://en.wikipedia.org/wiki/PolyA_tail)) and targets a host cell as an [obligate parasite](http://en.wikipedia.org/wiki/Obligate_parasite). Once inside the host cell [cytoplasm](http://en.wikipedia.org/wiki/Cytoplasm) the virus uses its own [reverse transcriptase](http://en.wikipedia.org/wiki/Reverse_transcriptase) enzyme to produce[DNA](http://en.wikipedia.org/wiki/DNA) from its [RNA](http://en.wikipedia.org/wiki/RNA) genome, the reverse of the usual pattern, thus *retro* (backwards). This new DNA is then [incorporated](http://en.wikipedia.org/wiki/Retroviral_integration) into the host cell [genome](http://en.wikipedia.org/wiki/Genome) by an [integrase](http://en.wikipedia.org/wiki/Integrase) enzyme, at which point the retroviral DNA is referred to as a [provirus](http://en.wikipedia.org/wiki/Provirus). The host cell then treats the viral DNA as part of its own [genome](http://en.wikipedia.org/wiki/Genome), translating and transcribing the viral genes along with the cell's own genes, producing the proteins required to assemble new copies of the virus. It is difficult to detect the virus until it has infected the host. At that point the infection will persist indefinitely.

In most viruses, DNA is [transcribed](http://en.wikipedia.org/wiki/Transcription_(genetics)) into RNA, and then RNA is [translated](http://en.wikipedia.org/wiki/Translation_(genetics)) into [protein](http://en.wikipedia.org/wiki/Protein). However, retroviruses function differently – their RNA is reverse-transcribed into DNA, which is integrated into the host cell's genome (when it becomes a [provirus](http://en.wikipedia.org/wiki/Provirus)), and then undergoes the usual transcription and translational processes to express the genes carried by the virus. So, the information contained in a retroviral gene is used to generate the corresponding protein via the sequence: RNA → DNA → RNA → polypeptide. This extends the fundamental process identified by [Francis Crick](http://en.wikipedia.org/wiki/Francis_Crick), (one gene-one peptide), in which the sequence is: DNA → RNA → peptide, (proteins are made of one or more polypeptide chain e.g. haemoglobin is a four chain peptide).

Retroviruses are proving to be valuable research tools in molecular biology and have been used successfully in gene delivery systems.[[1]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-KurthBannert-1)

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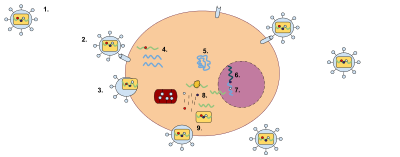
**Structure**

[Virions](http://en.wikipedia.org/wiki/Virions) of retroviruses consist of enveloped particles about 100 nm in diameter. The virions also contain two identical single-stranded [RNA](http://en.wikipedia.org/wiki/RNA) molecules 7–10 [kilobases](http://en.wikipedia.org/w/index.php?title=Kilobases&action=edit&redlink=1) (kb) in length. Although virions of different retroviruses do not have the same morphology or biology, all the virion components are very similar.[[2]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-she-2)

The main virion components are:

* [Envelope](http://en.wikipedia.org/wiki/Viral_envelope): composed of lipids (obtained from the host [plasma membrane](http://en.wikipedia.org/wiki/Plasma_membrane) during budding process) as well as glycoprotein encoded by the env gene.
* [RNA](http://en.wikipedia.org/wiki/RNA): consists of a [dimer](http://en.wikipedia.org/wiki/Dimer_(chemistry)) RNA. It has a cap at the 5' end and a poly(A) tail at the 3' end. The RNA genome also has terminal noncoding regions, which are important in replication, and internal regions that encode virion proteins for [gene expression](http://en.wikipedia.org/wiki/Gene_expression). The 5' end includes four regions, which are R, U5, PBS, and L. The R region is a short repeated sequence at each end of the genome used during the [reverse transcription](http://en.wikipedia.org/wiki/Reverse_transcription) to ensure correct end-to-end transfer in the growing chain. U5, on the other hand, is a short unique sequence between R and PBS. PBS (primer binding site) consists of 18 bases complementary to 3' end of tRNA primer. L region is an untranslated leader region that gives the signal for packaging of the genome RNA. The 3' end includes 3 regions, which are PPT (polypurine tract), U3, and R. The PPT is a primer for plus-strand DNA synthesis during [reverse transcription](http://en.wikipedia.org/wiki/Reverse_transcription). U3 is a sequence between PPT and R, which serves as a signal that the provirus can use in [transcription](http://en.wikipedia.org/wiki/Transcription_(genetics)). R is the terminal repeated sequence at 3' end.
* [Proteins](http://en.wikipedia.org/wiki/Protein): consisting of gag proteins, [protease](http://en.wikipedia.org/wiki/Protease) (PR), pol proteins and env proteins. [Group-specific antigen](http://en.wikipedia.org/wiki/Group-specific_antigen) (gag) proteins are major components of the viral [capsid](http://en.wikipedia.org/wiki/Capsid), which are about 2000–4000 copies per virion. Protease is expressed differently in different viruses. It functions in proteolytic cleavages during virion maturation to make mature gag and pol proteins. Pol proteins are responsible for synthesis of viral DNA and integration into host DNA after infection. Finally, env proteins play a role in association and entry of virion into the host cell.[[3]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-se-3) Possessing a functional copy of an env gene is what makes retroviruses distinct from retroelements.[[4]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-4) The env gene serves three distinct functions: enabling the retrovirus to enter/exit host cells through endosomal membrane trafficking, protection from the extracellular environment via the lipid bilayer, and the ability to enter cells. The ability of the retrovirus to bind to its target host cell using specific cell-surface receptors is given by the surface component (SU) of the env, while the ability of the retrovirus to enter the cell via membrane fusion is imparted by the membrane-anchored trans-membrane component (TM). Thus the env protein is what enables the retrovirus to be infectious.

**Multiplication**

[](http://en.wikipedia.org/wiki/File:Life_Cycle_of_a_Retrovirus.svg)

A retrovirus has a membrane that contains glycoproteins, which are able to bind to a receptor protein on a host cell. Within the cell there are two strands of RNA that have three enzymes, protease, reverse transcriptase, and integrase (1). The first step of replication is the binding of the glycoprotein to the receptor protein (2). Once these have been bound the cell membrane degrades and becomes part of the host cell, and the RNA strands and enzymes go into the cell (3). Within the cell, reverse transcriptase creates a complementary strand of DNA from the retrovirus RNA and the RNA is degraded, this strand of DNA is known as cDNA (4). The cDNA is then replicated, and the two strands form a weak bond and go into the nucleus (5). Once in the nucleus, the DNA is integrated into the host cells DNA with the help of integrase (6). This cell can either stay dormant, or RNA may be synthesized from the DNA and used to create the proteins for a new retrovirus (7). Ribosome units are used to transcribe the mRNA of the virus into the amino acid sequences which can be made into proteins in the Rough Endoplasmic Reticulum. This step will also make viral enzymes and capsid proteins (8). Viral RNA will be made in the nucleus. These pieces are then gathered together and are pinched off of the cell membrane as a new retrovirus (9).

When retroviruses have integrated their own genome into the [germ line](http://en.wikipedia.org/wiki/Germline), their genome is [passed on](http://en.wikipedia.org/wiki/Inheritance) to a following generation. These [endogenous retroviruses](http://en.wikipedia.org/wiki/Endogenous_retrovirus) (ERVs), contrasted with [exogenous](http://en.wikipedia.org/wiki/Exogenous_DNA) ones, now make up 5-8% of the human genome.[[5]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-5) Most insertions have no known function and are often referred to as "[junk DNA](http://en.wikipedia.org/wiki/Junk_DNA)". However, many endogenous retroviruses play important roles in host biology, such as control of gene transcription, cell fusion during [placental](http://en.wikipedia.org/wiki/Placenta) development in the course of the [germination](http://en.wikipedia.org/wiki/Germination) of an [embryo](http://en.wikipedia.org/wiki/Embryo), and resistance to exogenous retroviral infection. Endogenous retroviruses have also received special attention in the research of [immunology](http://en.wikipedia.org/wiki/Immunology)-related pathologies, such as [autoimmune diseases](http://en.wikipedia.org/wiki/Autoimmune_disease) like [multiple sclerosis](http://en.wikipedia.org/wiki/Multiple_sclerosis), although endogenous retroviruses have not yet been proven to play any causal role in this class of disease.[[6]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-6)

While transcription was classically thought to occur only from DNA to RNA, [reverse transcriptase](http://en.wikipedia.org/wiki/Reverse_transcriptase) transcribes RNA into DNA. The term "retro" in retrovirus refers to this reversal (making DNA from RNA) of the [central dogma of molecular biology](http://en.wikipedia.org/wiki/Central_dogma_of_molecular_biology). Reverse transcriptase activity outside of retroviruses has been found in almost all [eukaryotes](http://en.wikipedia.org/wiki/Eukaryote), enabling the generation and insertion of new copies of [retrotransposons](http://en.wikipedia.org/wiki/Retrotransposon) into the host genome. These inserts are transcribed by enzymes of the host into new RNA molecules that enter the cytosol. Next, some of these RNA molecules are translated into viral proteins. For example, the *gag* gene is translated into molecules of the capsid protein, the *pol* gene is translated into molecules of reverse transcriptase, and the *env*gene is translated into molecules of the envelope protein. It is important to note that a retrovirus must "bring" its own reverse transcriptase in its [capsid](http://en.wikipedia.org/wiki/Capsid), otherwise it is unable to utilize the enzymes of the infected cell to carry out the task, due to the unusual nature of producing DNA from RNA.

Industrial drugs that are designed as protease and [reverse transcriptase inhibitors](http://en.wikipedia.org/wiki/Reverse_transcriptase_inhibitor) are made such that they target specific sites and sequences within their respective enzymes. However these drugs can quickly become ineffective due to the fact that the gene sequences that code for the protease and the reverse transcriptase quickly mutate. These changes in bases cause specific codons and sites with the enzymes to change and thereby avoid drug targeting by losing the sites that the drug actually targets.

Because reverse transcription lacks the usual [proofreading](http://en.wikipedia.org/wiki/Proofreading_(biology)) of DNA replication, a retrovirus [mutates](http://en.wikipedia.org/wiki/Mutate) very often. This enables the virus to grow [resistant](http://en.wikipedia.org/wiki/Immunology) to antiviral pharmaceuticals quickly, and impedes the development of effective [vaccines](http://en.wikipedia.org/wiki/Vaccines) and inhibitors for the retrovirus.[[7]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-7)

One drawback of retroviruses, such as the Moloney retrovirus, involves the requirement for cells to be actively dividing for transduction. As a result, cells such as neurons are very resistant to infection and transduction by retroviruses. There is concern that insertional mutagenesis due to integration into the host genome might lead to cancer or leukemia. This is unlike [*Lentivirus*](http://en.wikipedia.org/wiki/Lentivirus), a genus of *Retroviridae*, which are able to integrate their RNA into the genome of non-dividing host cells.

**Transmission**

* Cell-to-cell[[8]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-8)
* Fluids
* Airborne, like the [Jaagsiekte sheep retrovirus](http://en.wikipedia.org/wiki/Jaagsiekte_sheep_retrovirus).

**Genes**

Retrovirus genomes commonly contain these three [open reading frames](http://en.wikipedia.org/wiki/Open_reading_frames) that encode for proteins that can be found in the mature virus:

* [*group-specific antigen*](http://en.wikipedia.org/wiki/Group-specific_antigen) (gag) codes for core and structural [proteins](http://en.wikipedia.org/wiki/Protein) of the virus;
* [*polymerase*](http://en.wikipedia.org/wiki/Polymerase) (pol) codes for [reverse transcriptase](http://en.wikipedia.org/wiki/Reverse_transcriptase), [protease](http://en.wikipedia.org/wiki/Protease) and [integrase](http://en.wikipedia.org/wiki/Integrase); and,
* [*envelope*](http://en.wikipedia.org/wiki/Env_(gene)) (env) codes for the retroviral coat proteins.

**Provirus**

This DNA can be incorporated into host genome as a provirus that can be passed on to progeny cells. The retrovirus DNA is inserted at random into the host genome. Because of this, it can be inserted into [oncogenes](http://en.wikipedia.org/wiki/Oncogene). In this way some retroviruses can convert normal cells into cancer cells. Some provirus remains latent in the cell for a long period of time before it is activated by the change in cell environment.

**Early evolution**

Studies of retroviruses led to the first demonstrated synthesis of DNA from RNA templates, a fundamental mode for transferring genetic material that occurs in both[eukaryotes](http://en.wikipedia.org/wiki/Eukaryote) and [prokaryotes](http://en.wikipedia.org/wiki/Prokaryote). It has been speculated that the RNA to DNA transcription processes used by retroviruses may have first caused DNA to be used as genetic material. In this model, the [RNA world hypothesis](http://en.wikipedia.org/wiki/RNA_world_hypothesis), cellular organisms adopted the more chemically stable DNA when retroviruses evolved to create [DNA](http://en.wikipedia.org/wiki/DNA) from the [RNA](http://en.wikipedia.org/wiki/RNA)templates.

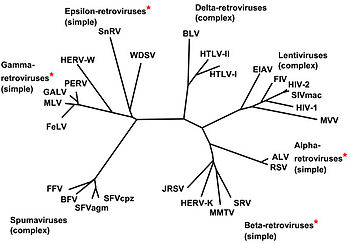
**Gene therapy**

[Gammaretroviral](http://en.wikipedia.org/wiki/Gammaretrovirus) and [lentiviral](http://en.wikipedia.org/wiki/Lentiviral) [vectors](http://en.wikipedia.org/wiki/Vector_(molecular_biology)) for [gene therapy](http://en.wikipedia.org/wiki/Gene_therapy) have been developed that mediate stable genetic modification of treated cells by chromosomal integration of the transferred vector genomes. This technology is of use, not only for research purposes, but also for clinical gene therapy aiming at the long-term correction of genetic defects, e.g., in stem and progenitor cells. Retroviral vector particles with tropism for various target cells have been designed. Gammaretroviral and lentiviral vectors have so far been used in more than 300 clinical trials, addressing treatment options for various diseases.[[1]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-KurthBannert-1)[[9]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-Desportm-9)

**Cancer**

Retroviruses that cause tumor growth include [*Rous sarcoma virus*](http://en.wikipedia.org/wiki/Rous_sarcoma_virus) and [*Mouse mammary tumor virus*](http://en.wikipedia.org/wiki/Mouse_mammary_tumor_virus). Cancer can be triggered by proto-oncogenes that were mistakenly incorporated into proviral DNA or by the disruption of cellular proto-oncogenes. Rous sarcoma virus contains the [src gene](http://en.wikipedia.org/wiki/Src_(gene)) that triggers tumor formation. Later it was found that a similar gene in cells is involved in cell signaling, which was most likely excised with the proviral DNA. Nontransforming viruses can randomly insert their DNA into proto-oncogenes, disrupting the expression of proteins that regulate the cell cycle. The promoter of the provirus DNA can also cause over expression of regulatory genes.

**Classification**

[](http://en.wikipedia.org/wiki/File:Phylogeny_of_Retroviruses.jpg)

Phylogeny of Retroviruses

**Exogenous**

These are infectious RNA-containing viruses which are transmitted from human to human.

The following genera are included here:

* Genus [*Alpharetrovirus*](http://en.wikipedia.org/wiki/Alpharetrovirus); type species: [*Avian leukosis virus*](http://en.wikipedia.org/wiki/Avian_leukosis_virus); others include [*Rous sarcoma virus*](http://en.wikipedia.org/wiki/Rous_sarcoma_virus)
* Genus [*Betaretrovirus*](http://en.wikipedia.org/wiki/Betaretrovirus); type species: [*Mouse mammary tumour virus*](http://en.wikipedia.org/wiki/Mouse_mammary_tumour_virus)
* Genus [*Gammaretrovirus*](http://en.wikipedia.org/wiki/Gammaretrovirus); type species: [*Murine leukemia virus*](http://en.wikipedia.org/wiki/Murine_leukemia_virus); others include [*Feline leukemia virus*](http://en.wikipedia.org/wiki/Feline_leukemia_virus)
* Genus [*Deltaretrovirus*](http://en.wikipedia.org/wiki/Deltaretrovirus); type species: [*Bovine leukemia virus*](http://en.wikipedia.org/wiki/Bovine_leukemia_virus); others include the cancer-causing [*Human T-lymphotropic virus*](http://en.wikipedia.org/wiki/Human_T-lymphotropic_virus)
* Genus [*Epsilonretrovirus*](http://en.wikipedia.org/wiki/Epsilonretrovirus); type species: [*Walleye dermal sarcoma virus*](http://en.wikipedia.org/w/index.php?title=Walleye_dermal_sarcoma_virus&action=edit&redlink=1)
* Genus [*Lentivirus*](http://en.wikipedia.org/wiki/Lentivirus); type species: [*Human immunodeficiency virus 1*](http://en.wikipedia.org/wiki/HIV); others include [*Simian*](http://en.wikipedia.org/wiki/Simian_immunodeficiency_virus), [*Feline*](http://en.wikipedia.org/wiki/Feline_immunodeficiency_virus)immunodeficiency viruses
* Genus [*Spumavirus*](http://en.wikipedia.org/wiki/Spumavirus); type species: [*Simian foamy virus*](http://en.wikipedia.org/wiki/Simian_foamy_virus)

These were previously divided into three subfamilies (*Oncovirinae*, *Lentivirinae*, and *Spumavirinae*), but are now divided into two: *Orthoretrovirinae* and*Spumaretrovirinae*. The term [oncovirus](http://en.wikipedia.org/wiki/Oncovirus) is now commonly used to describe a cancer-causing virus.

Retroviruses were in 2 groups of the [Virus\_classification#Baltimore\_classification](http://en.wikipedia.org/wiki/Virus_classification#Baltimore_classification).

**Group VI viruses**

All members of [Group VI](http://en.wikipedia.org/wiki/Virus_classification#Baltimore_classification) use virally encoded [reverse transcriptase](http://en.wikipedia.org/wiki/Reverse_transcriptase), an RNA-dependent DNA polymerase, to produce DNA from the initial virion RNA genome. This DNA is often integrated into the host genome, as in the case of retroviruses and [pseudoviruses](http://en.wikipedia.org/wiki/Pseudoviridae), where it is replicated and [transcribed](http://en.wikipedia.org/wiki/Transcription_(genetics)) by the host.

Group VI includes:

* Family [*Metaviridae*](http://en.wikipedia.org/wiki/Metaviridae)
* Family [*Pseudoviridae*](http://en.wikipedia.org/wiki/Pseudoviridae)
* Family *Retroviridae* — Retroviruses, e.g. [*HIV*](http://en.wikipedia.org/wiki/HIV)

**Group VII viruses**

Both families in [Group VII](http://en.wikipedia.org/wiki/Virus_classification#Baltimore_classification) have DNA genomes contained within the invading virus particles. The DNA genome is transcribed into both mRNA, for use as a transcript in protein synthesis, and pre-genomic RNA, for use as the template during genome replication. Virally encoded [reverse transcriptase](http://en.wikipedia.org/wiki/Reverse_transcriptase) uses the pre-genomic RNA as a template for the creation of genomic DNA.

Group VII includes:

* Family [*Hepadnaviridae*](http://en.wikipedia.org/wiki/Hepadnaviridae) — e.g. [*Hepatitis B virus*](http://en.wikipedia.org/wiki/Hepatitis_B_virus)
* Family [*Caulimoviridae*](http://en.wikipedia.org/wiki/Caulimoviridae) — e.g. [*Cauliflower mosaic virus*](http://en.wikipedia.org/wiki/Cauliflower_mosaic_virus)

**Endogenous**

Endogenous retroviruses are not formally included in this classification system, and are broadly classified into three classes, on the basis of relatedness to exogenous genera:

* Class I are most similar to the gammaretroviruses
* Class II are most similar to the betaretroviruses and alpharetroviruses
* Class III are most similar to the spumaviruses.

**Treatment**

[Antiretroviral drugs](http://en.wikipedia.org/wiki/Antiretroviral_drugs) are medications for the treatment of infection by retroviruses, primarily [HIV](http://en.wikipedia.org/wiki/HIV). Different classes of antiretroviral drugs act on different stages of the [HIV](http://en.wikipedia.org/wiki/HIV) [life cycle](http://en.wikipedia.org/wiki/Biological_life_cycle). Combination of several (typically three or four) antiretroviral drugs is known as highly active anti-retroviral therapy (HAART).[[10]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-pmid10908497-10)

**Treatment of veterinary retroviruses**

[*Feline leukemia virus*](http://en.wikipedia.org/wiki/Feline_leukemia_virus) and [*Feline immunodeficiency virus*](http://en.wikipedia.org/wiki/Feline_immunodeficiency_virus) infections are treated with [biologics](http://en.wikipedia.org/wiki/Biologic_medical_product), including the only immunomodulator currently licensed for sale in the United States, [Lymphocyte T-Cell Immune Modulator](http://en.wikipedia.org/wiki/Lymphocyte_T-Cell_Immune_Modulator) (LTCI).[[11]](http://en.wikipedia.org/w/index.php?title=Retrovirus&printable=yes#cite_note-11)

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**External links**

* [ViralZone](http://www.expasy.org/viralzone/) A [Swiss Institute of Bioinformatics](http://en.wikipedia.org/wiki/Swiss_Institute_of_Bioinformatics) resource for all viral families, providing general molecular and epidemiological information (follow links for *"Retro-transcribing viruses"*)
* [Retrovirus Animation](http://www.1lec.com/Microbiology/Replication%20Cycle%20of%20a%20Retrovirus/index.html) (Flash Required)
* [Retrovirology](http://www.retrovirology.com/) Scientific journal
* [Retrovirus life cycle chapter](http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/R/Retroviruses.html) From Kimball's *Biology* (online biology textbook pages)
* Coffin, John M; Varmus, Harold E, eds. (1997). [*Retroviruses*](http://www.ncbi.nlm.nih.gov/books/NBK19376/). Cold Spring Harbor Laboratory. [ISBN](http://en.wikipedia.org/wiki/International_Standard_Book_Number) [0-87969-571-4](http://en.wikipedia.org/wiki/Special:BookSources/0-87969-571-4). NBK19376.
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