Retroviruses

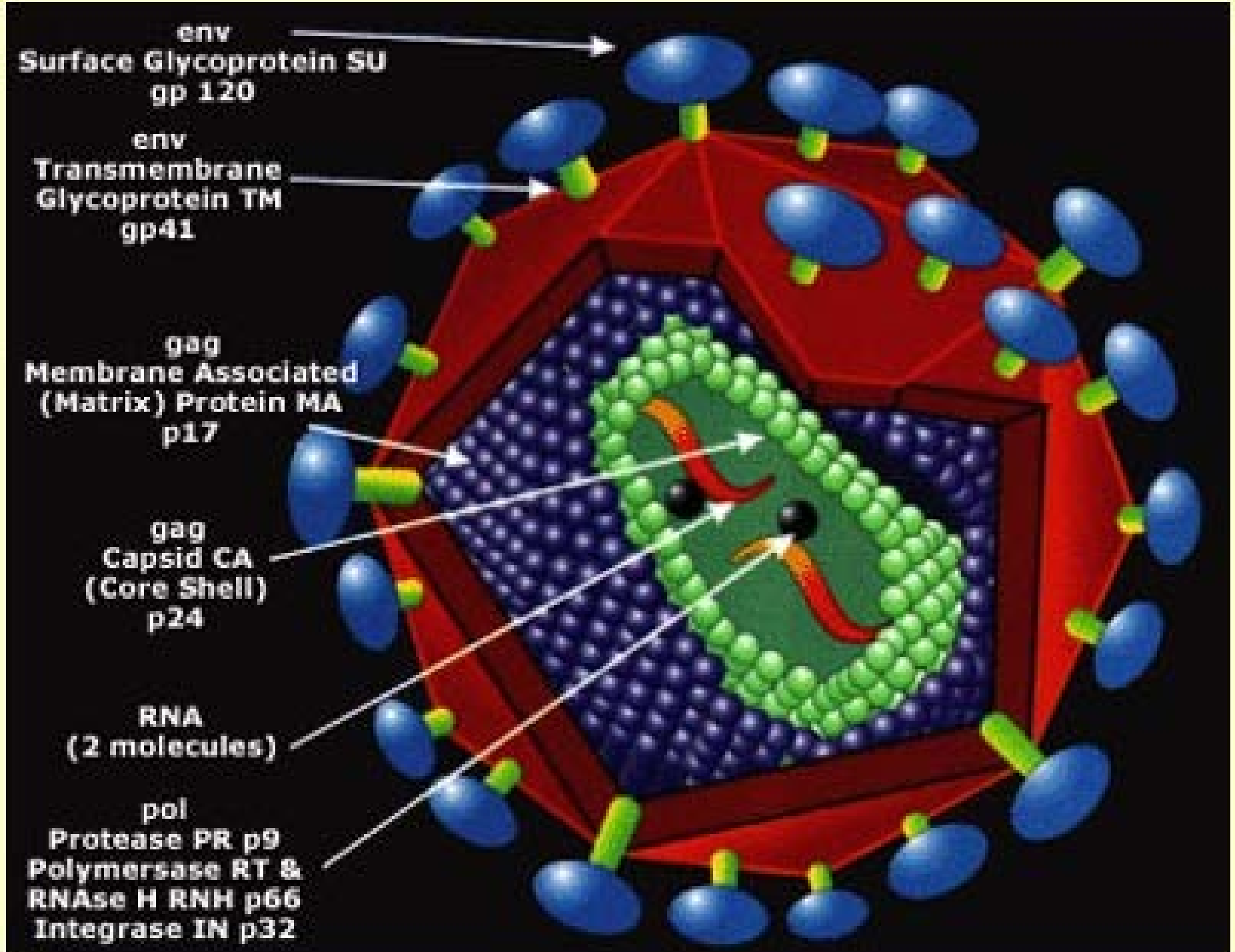
By- Dr. Ekta Khare

Department of Microbiology,

Chhatrapati Shahu Ji Maharaj University, Kanpur

Retroviruses

- Retroviruses are a group of viruses with RNA genomes that carry the enzyme reverse transcriptase and form a DNA copy of their genome during their reproductive cycle.
- Various retroviruses are capable of causing human diseases, like AIDS and some kinds of cancer.
- Retrovirus virons consist of the outer lipid envelope of glycoprotein.
- The virons contain two identical single-stranded RNA molecules that are present as a dimer.
- Although the virons do not have the same biology or morphology, their components are very similar.


env
Surface Glycoprotein SU
gp 120
env
Transmembrane
Glycoprotein TM
gp41
gag
Membrane Associated
(Matrix) Protein MA
p17
gag
Capsid CA
(Core Shell)
p24
RNA
(2 molecules)
pol
Protease PR p9
Polymersase RT &
RNAse H RNH p66
Integrase IN p32

Infection cycle

- On infection, the single stranded RNA viral genome (~10,000 nucleotides) and the enzyme enter the host cell.
- The reverse transcriptase first catalyzes the synthesis of a DNA strand complementary to the viral RNA, then degrades the RNA strand of the viral RNA-DNA hybrid and replaces it with DNA.
- The resulting duplex DNA often becomes incorporated into the genome of the eukaryotic host cell.
- These integrated (and dormant) viral genes can be activated and transcribed, and the gene products—viral proteins and the viral RNA genome itself—packaged as new viruses.

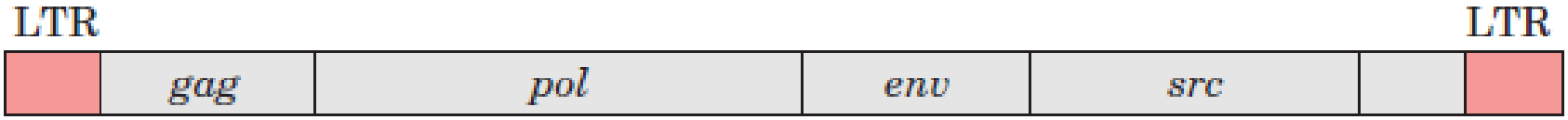
Structure and Replication of Viral Genome

- At each end of the linear RNA genome are long terminal repeat (LTR) sequences of a few hundred nucleotides.
- Transcribed into the duplex DNA, these sequences facilitate integration of the viral chromosome into the host DNA and contain promoters for viral gene expression.
- Reverse transcriptases catalyze three different reactions:

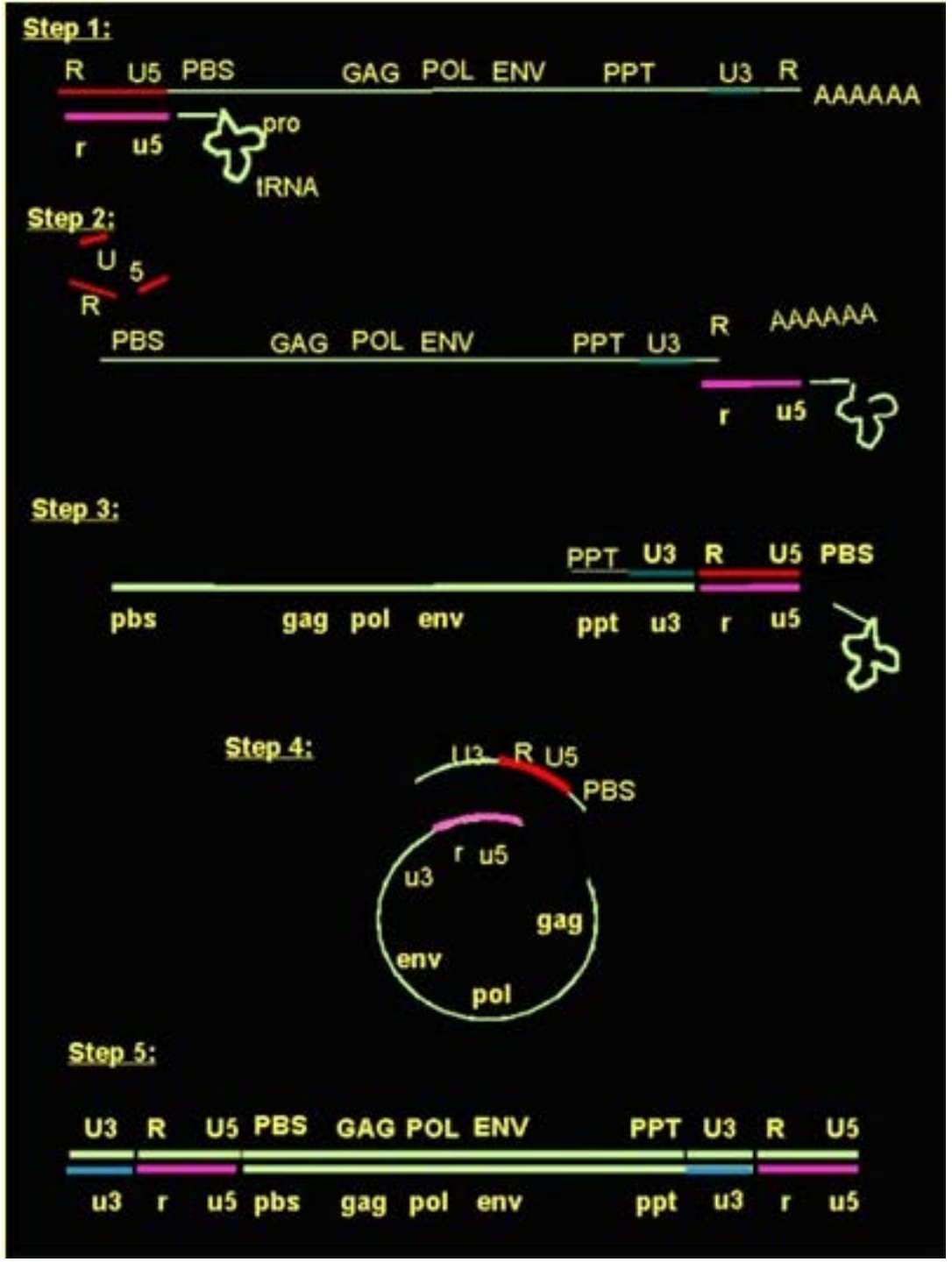
  (1) RNA-dependent DNA synthesis, (2) RNA degradation,

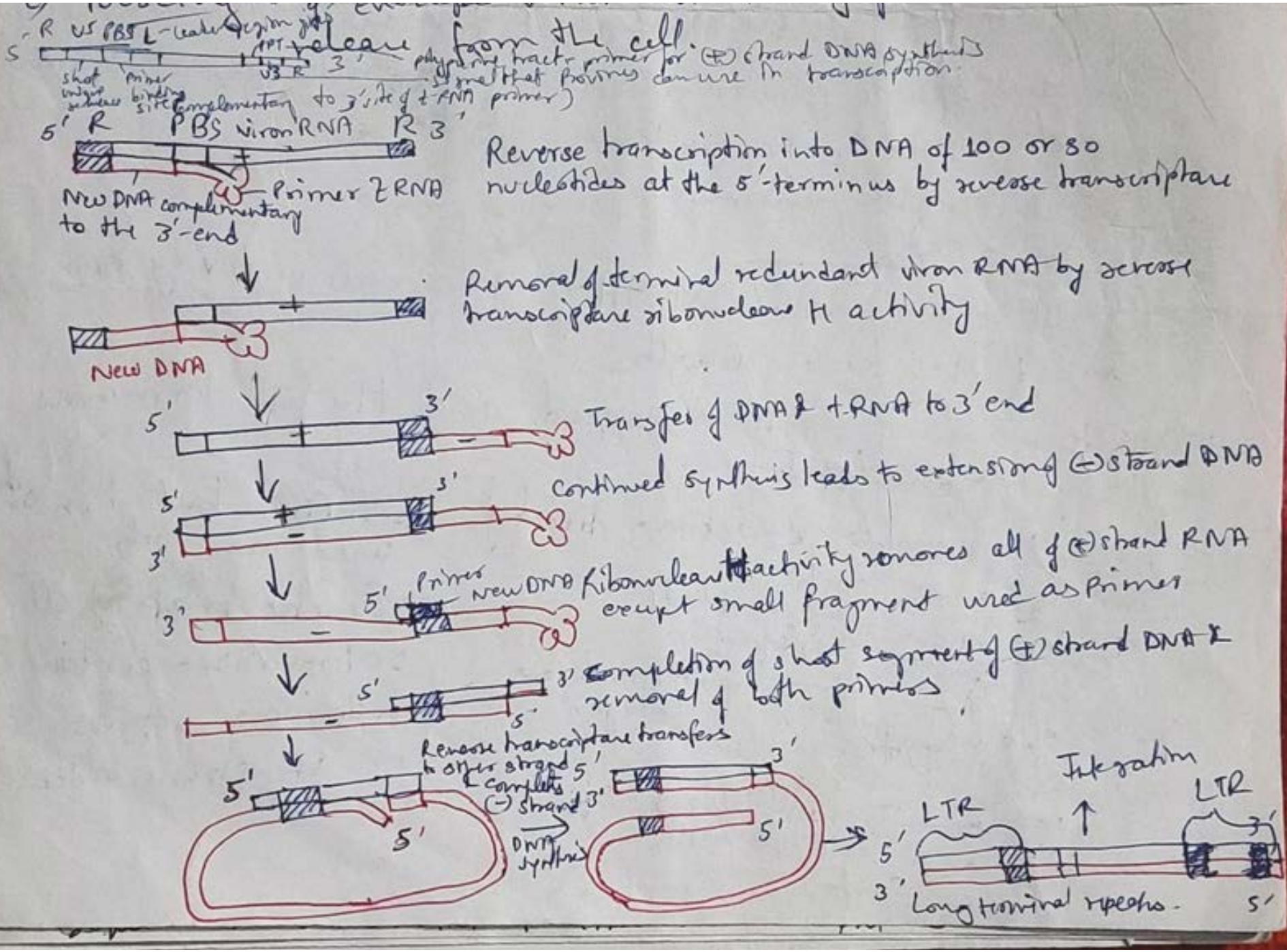
  (3) DNA-dependent DNA synthesis.
- For DNA synthesis to begin, the reverse transcriptase requires a primer, a cellular tRNA obtained during an earlier infection and carried within the viral particle.
- This tRNA is base-paired at its 3’ end with a complementary sequence in the viral RNA. The new DNA strand is synthesized in the 5’ to 3’ direction, as in all RNA and DNA polymerase reactions.
- Reverse transcriptases, like RNA polymerases, do not have 3’ to 5’ proofreading exonucleases.
- A consequence is a higher mutation rate and faster rate of viral evolution, which is a factor in the frequent appearance of new strains of disease-causing retroviruses.

- Some retroviruses, classified as RNA tumor viruses, contain an oncogene that can cause the cell to grow abnormally.
- The first retrovirus of this type to be studied was the Rous sarcoma virus (also called avian sarcoma virus)



Reverse Transcription of Retrovirus--Conversion of single stranded RNA genome to Double-stranded DNA





release from the cell.

polypurine tract primer for (+) strand DNA synthesis
(small RNA portions can use in transcription)

Reverse transcription into DNA of 100 or 80 nucleotides at the 5'-terminus by reverse transcriptase

Removal of terminal redundant viron RNA by reverse transcriptase ribonuclease H activity

Transfer of DNA & t-RNA to 3' end

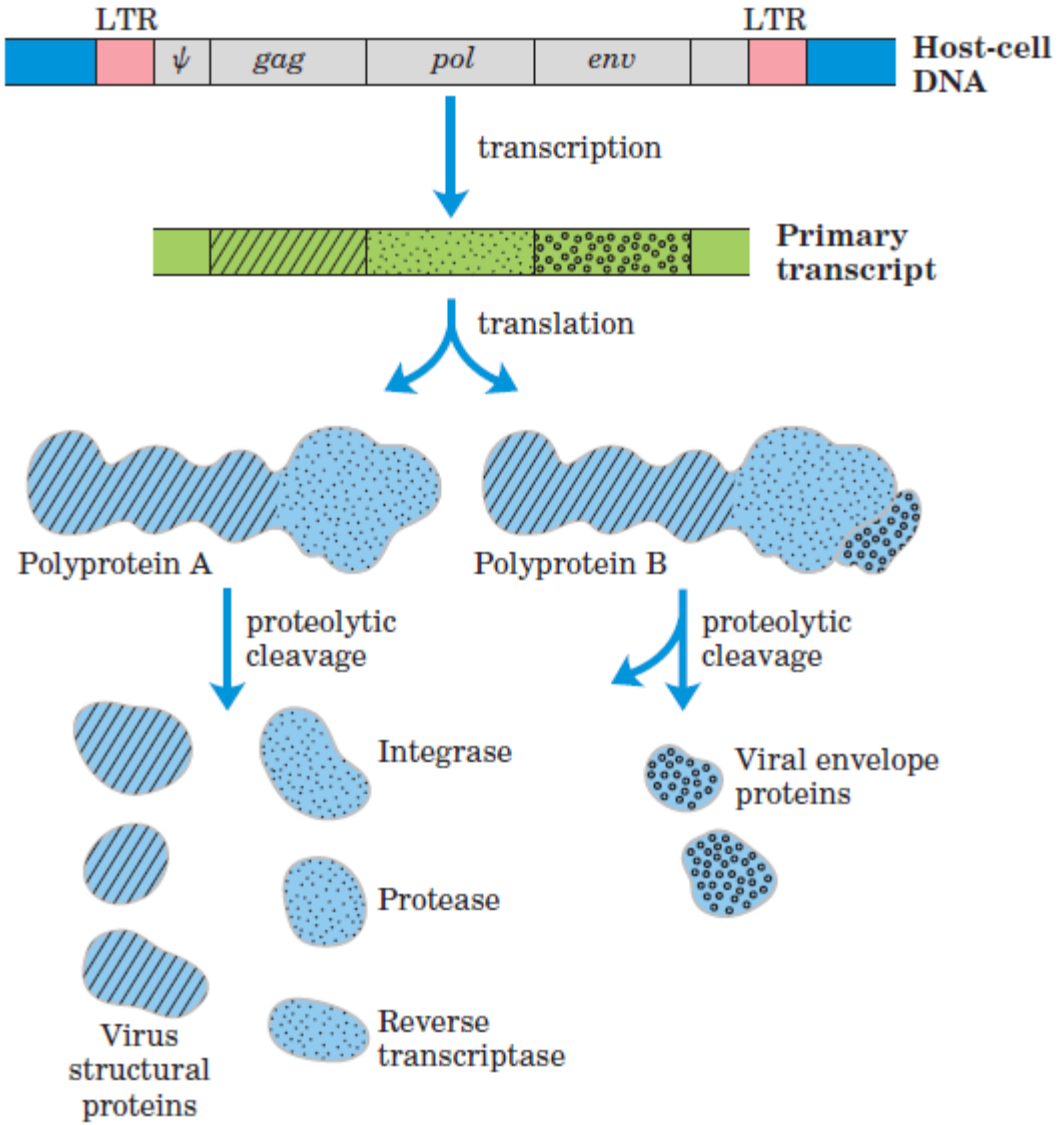
Continued synthesis leads to extension of (+) strand DNA

Ribonuclease H activity removes all of (+) strand RNA except small fragment used as primer

- The LTR of all retroviruses, located at each end of the provirus as a direct repeat containing the U3, R, and U5 regions, functions as an eukaryotic transcription unit.
- The U3 region contains the viral promoter and enhancer elements.
- The R region includes the mRNA initiation site (+1) and ends at a polyadenylation termination site.
- The function of the U5 region is not well understood.
- It separates the R region from the tRNA primer binding site used to initiate reverse transcription.
- The integrated provirus is larger than the viral genome but its complexity is the same because of duplication of U3 and U5 during its synthesis.

Gene products of an integrated retroviral genome

- Retroviruses typically have three genes: *gag* (derived from the historical designation group associated antigen), *pol*, and *env*.
- Transcription of the retroviral DNA produces a primary transcript encompassing the *gag*, *po*l, and *env* genes.
- Translation produces a polyprotein, a single long polypeptide derived from the *gag* and *pol* genes, which is cleaved into six distinct proteins.
- The proteins derived from the *gag* gene make up the interior core of the viral particle.
- The *pol* gene encodes:
  - the protease that cleaves the long polypeptide,
  - an integrase that inserts the viral DNA into the host chromosomes,
  - reverse transcriptase
- Splicing of the primary transcript yields an mRNA derived largely from the *env* gene, which is also translated into a polyprotein, then cleaved to generate viral envelope proteins.



Structure and gene products of an integrated retroviral genome. The long terminal repeats (LTRs) have sequences needed for the regulation and initiation of transcription. The sequence denoted is required for packaging of retroviral RNAs into mature viral particles.