Double Stranded DNA Viruses

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Double Stranded DNA Viruses

- Most of these viruses must enter the host nucleus before they can replicate.
- It is because they use the host cell‘s polymerases when replicating their viral genome.
- They can induce the cell to undergo cell division, which further leads to transformation of the cell, and ultimately, to cancer.
- Examples include: polyomaviruses, papillomaviruses, adenoviruses, herpesviruses, poxviruses, *etc*.

Polyomaviruses

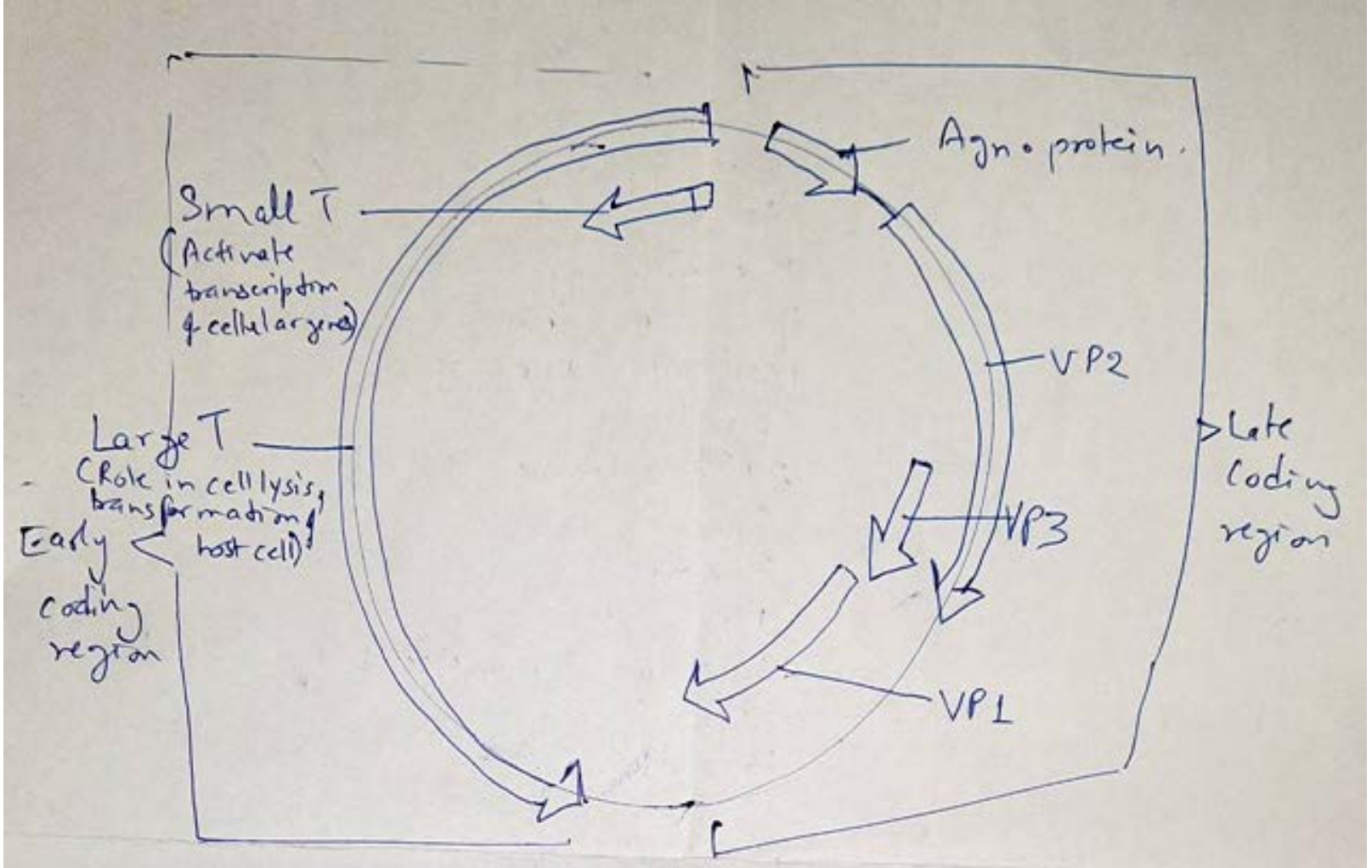
- Some viruses induce tumors (oma means tumor).
- **Simon virus 40 (SV40)** first isolated from monkeys)- used as vector for moving genes into eukaryotic cells.
- SV40: nonenveloped particle 45nm in dia.
  - Icosahedral head containing 72 protein subunits.
  - No enzymes in viron
  - One mol. of dsDNA of 5243bp – circular (super coiled configuration).
  - Replicates in nucleus, protein synthesis in cytoplasm and assembly in nucleus.

Replication

- Replication of virion can be divided into two distinct positions: Early & Late
- Before replication begins – early proteins synthesized.
- **During early stage**-Inside the cell nucleus, the cellular RNA polymerase II acts to promote early gene expression.
- Early coding region of viral DNA transcribed to single RNA molecule (primary transcript made by cellular RNA polymerase).
- Processed into two mRNAs (a large one and a small one)
- Introns excised out of the pri. RNA transcript.
- mRNA capped and translated to yield to proteins
- Large T antigen: 5% goes to plasma membrane and 95% returns to nucleus and binds 3 viral DNA sites I, II and III
- Binding site I and II autoregulate early RNA synthesis
- Binding site I initiates DNA replication at the origin of replication. Protein-protein interaction between T-antigen and DNA polymerase-alpha directly stimulate replication.

...Replication

- **Late SV40 mRNA** synthesized using the strand complementary to that used for early mRNA synthesis.
- Transcription begins at promotor near origin of replication.
- Late RNA processed by splicing, capping and polyadenylation.
- mRNA corresponding to 3 coat proteins VP1, VP2, VP3 (overlapping genes)
- mRNAs transported to cytoplasm and translated to viral coat proteins.
- Coat proteins transported back to nucleus and assembly of viron takes place.
- Eventual release of viral particles is cytolytic and results in cell death.



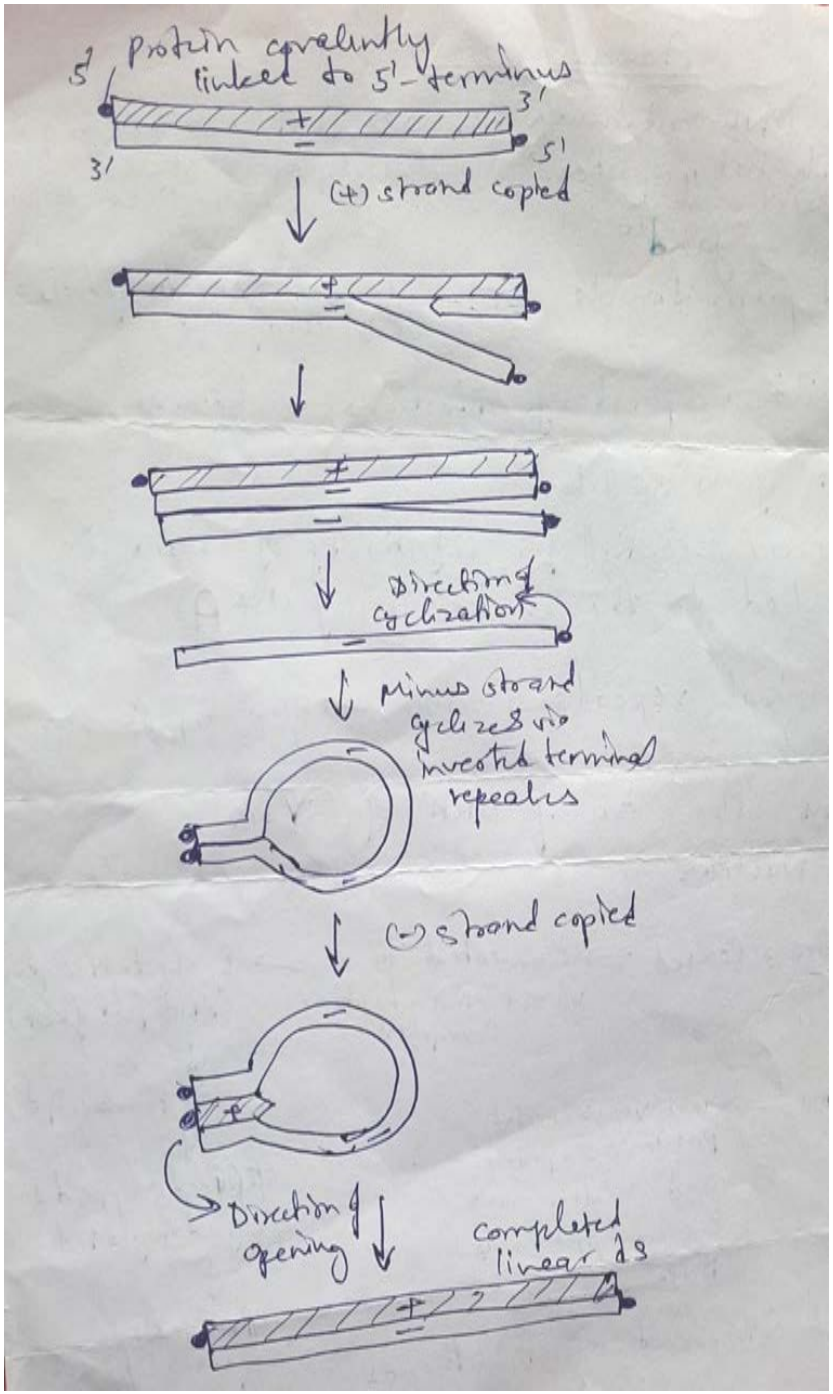
Large T also binds and inactivates tumor suppressor proteins (p^{53}, p^{105-Rb}) – causes cell to leave G1 phase and enter into S phase which promotes DNA replication.

Adenoviruses

- Icosahedral DNA-containing viruses that have unique molecular biological properties.
- Icosahedral protein shell (70-100 nm dia, 252 capsomers) surrounding a protein core that contains linear-ds DNA genome of ~36 kb.
- First isolated from tonsils and adenoid glands of humans.
- Cause mild respiratory infections in humans.
- A protein component essential for infectivity of DNA is covalently linked to the 5’-terminus of DNA.
- DNA has inverted terminal repeats of 100-1800 bp (varies with viral strains).

Replication in Nucleus

- In nucleus core releases and viral genomic DNA converted to a viral DNA-histone complex.
- Early transcription takes place by host RNA polymerase and primary transcripts spliced, capped and polyadenylated to several mRNAs.
- Early proteins involves in replication of DNA genome.
- Late proteins codes for coat proteins.
- Replication begins at either end or at both ends.


5'
protein covalently linked to 5'-terminus
3'
3'
5'
(+) strand copied
Direction of cyclization
Minus strand circularized via inverted terminal repeats
(-) strand copied
Direction of opening
completed linear ds