ONCOGENIC VIRUSES/ oncoviruses

Prof.Dr.Fawziah Ali

Cells Transformation become cancer

- Almost all of substances causing genetic changes are cancerous to eukaryote cells.
- Substances that caused cellular DNA changes and possess effect to the genome: oncogenic
- Oncogene was first founded by J. Michael Bishop & Harold E. Varmus (American Microbiologist) --- cancer that causing by virus
- The gene of cancer carry by the host (chicken): *src* gene

- Host oncogene (proto-oncogene) was activated by microorganisms/chemicals/high energy radiation
- DNA viral able to integrate to the DNA host and causes host characteristic changes are Oncogenic Virus

Oncogenic DNA viruses

- Adenoviridae
- Herpesviridae
- Poxviridae
- Papovaviridae
- Hepadnaviridae
- papillomavirus

Oncogenic DNA viruses code oncoprotein:

- Important for virus replication
- Control cellular growth

Oncogenic RNA viruses

- Family of Retroviridae
- Retrovirus
- Reverse transcriptase ----- form DNA (provirus) from RNA
- *Human T-cell leukemia viruses* (HTLV-1 & HTLV-2)
- *Feline leukemia virus* (FeLV)

RNA tumor viruses

 Highly oncogenic (direct-transformation). Virus carry an **oncogene** of cellular origin.
These virus is referred to as **acute transformation agent** for inducing tumors in vivo **after a very short latency period**.
 Weakly oncogenic (slow transforming). Virus **do not contain an oncogene**, and induce tumor **after long incubation periods latency by indirect-transformation.**
Can not produce transformation of culture cells

 Both DNA and DNA (provirus) of RNA viruses genome - integrate to host genome alter the host metabolisms process and over growth

Carcinogenesis

- Carcinogenesis is a gradual process, multistep process
- Tumor develop slowly, need a long time
- The mutation rate suggested between 3-8 times
- Need multiple genetic changes to change normal cell become malignant
- Virus can be initiator neoplastic process
- Cellular transformation may be defined as a stable, heritable change in the growth control of cells

The most prominent changes associated with transformed cells include:

- Alterations in cell growth pattern

Growth to higher cell density; increased rate growth; decreased requirement for serum growth factors; decreased cell adhesion to a substrate; enhanced ability to grow in semisolid medium (anchorage independent)

- Alterations in cell surface

Increased rate of transport of cell nutrients; increased secretion of protease or protease activator; changes in composition of glycoprotein and glycolipid, etc.

- Alternations in intracellular components and biochemical process

Increase metabolic rate; increased glycolysis; activation or repression of certain cellular genes, etc.

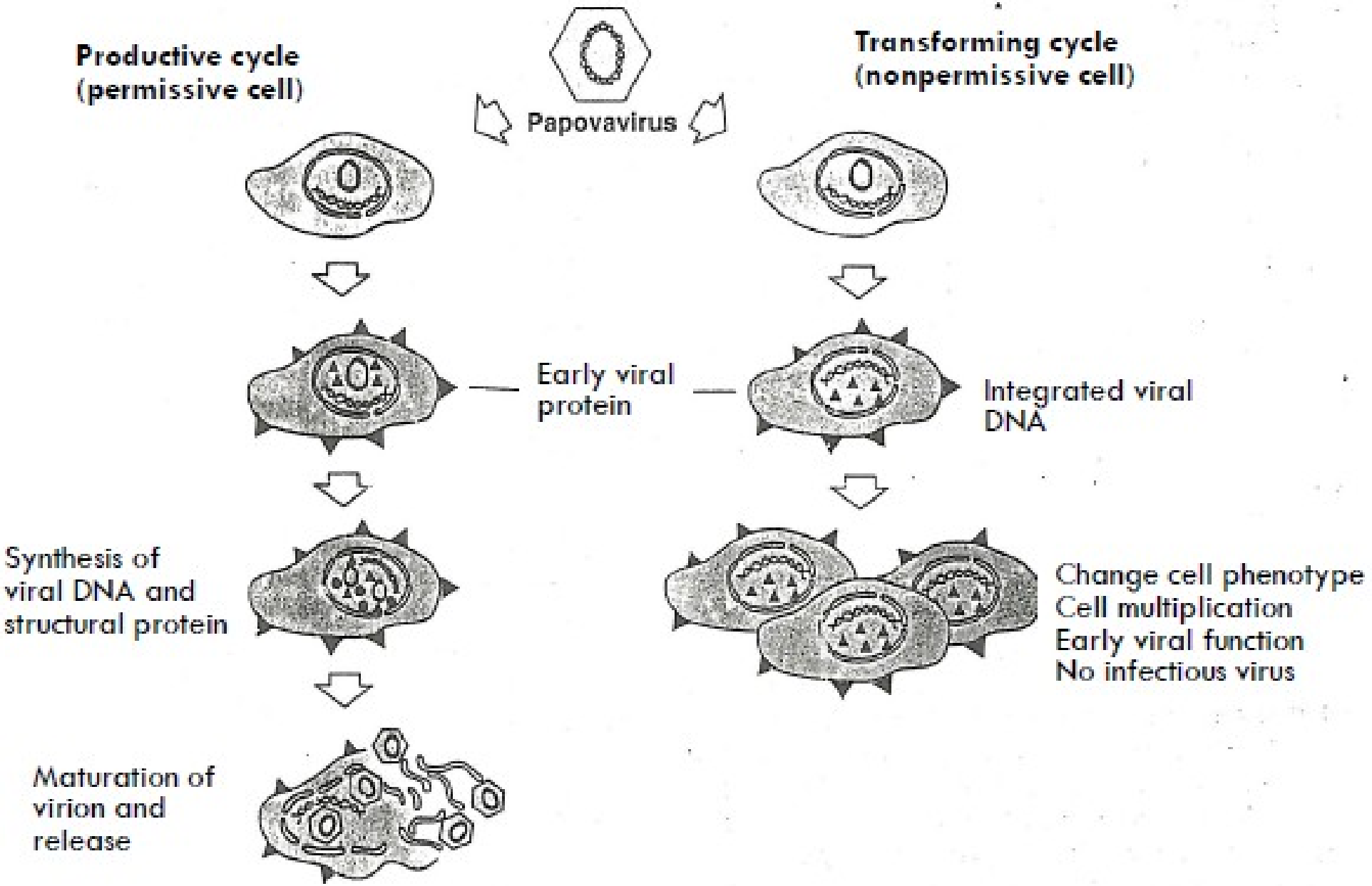
- Tumorigenicity

Production of tumor when transformed cell are injected to appropriate test animal

- DNA tumor viruses
  - Replicate in certain cell of natural hosts, but rarely produce tumors in those host

- RNA tumor viruses
  - RNA viruses usually cause cancers in their natural host.
  - Replicate and transformed the homologous cells, because viral replication is not cytolytic.

- Integration of tumor virus nucleic acid in a host cell
- Mechanisms of cell transformation by viruses
- The tumor virus introduces a new transforming gene into the host cell ---- or ---
- The virus induce or alter the expression of pre-existing cellular gene
- Results of the both mechanisms is that the cells losses control of normal regulation of growth process


Productive cycle
(permissive cell)
Papovavirus
Transforming cycle
(nonpermissive cell)
Early viral
protein
Integrated viral
DNA
Synthesis of
viral DNA and
structural protein
Change cell phenotype
Cell multiplication
Early viral function
No infectious virus
Maturation of
virion and
release

Interaction between oncogenic virus with the host

A. Persistent infection

- The molecular mechanisms of viral oncogenesis are complex & involve the induction chronic inflammation ---- disruption host genetic & epigenetic integrity ---- homeostasis -----interference with cellular DNA repair mechanisms ---- genome instability ---- cell cycle dysregulation
- Long infection may caused the virus develop a control to modify the growth host cells --- depend to the host defence mechanisms

In biology, epigenetics is **the study of stable phenotypic changes (known as marks) that do not involve alterations in the DNA sequence**.

B. Host immune responses

- Immune deficient individual more sensitive to the cancer cells, especially CMI

C. Host cell resistance to the viral infection

- Involving surface receptor of the host cell

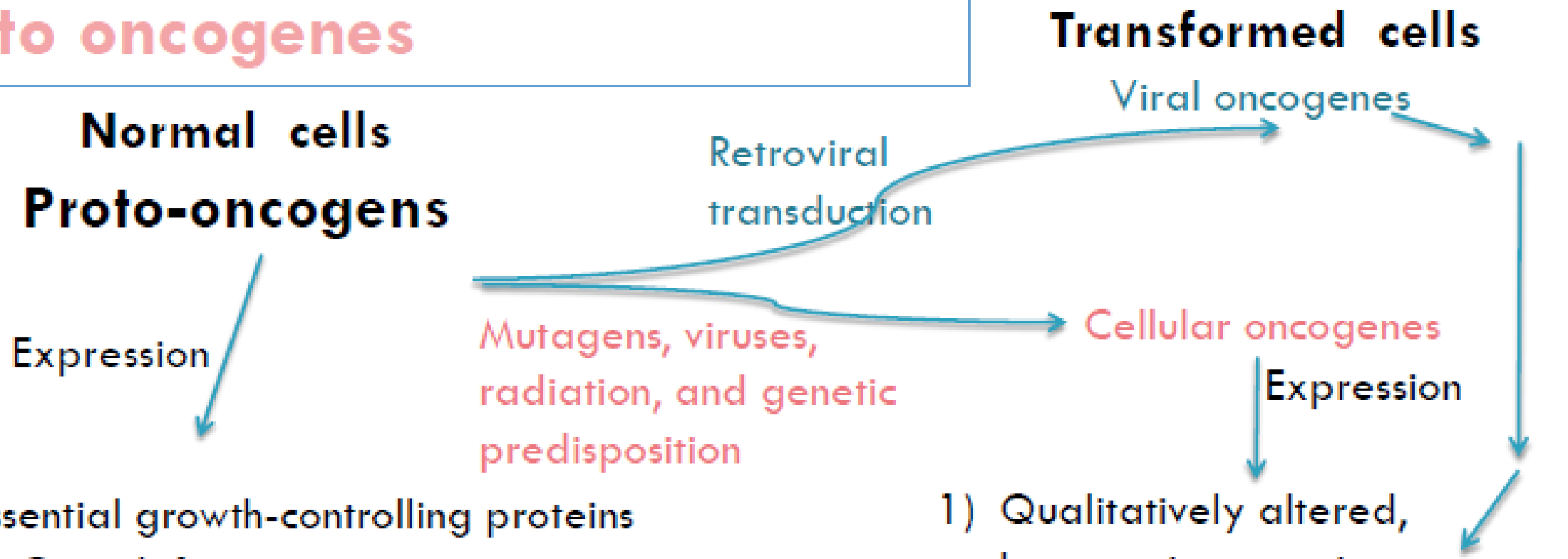
D. Nucleic acid retention in the host cells

- Stable genetic changes from normal cells become neoplastic cells require viral gene retention in the host cell ---- caused by integration of viral gene to the host genome.

Mutation may involved genes of:

- Growth factor (PDGF)
- Growth factor-receptor (*Neu)*
- Signal transduction *(Src)*
- Transcription factor *(Jun)*
- Tumor supressor *(p53)*
- Apoptosis *(Bcl2)*

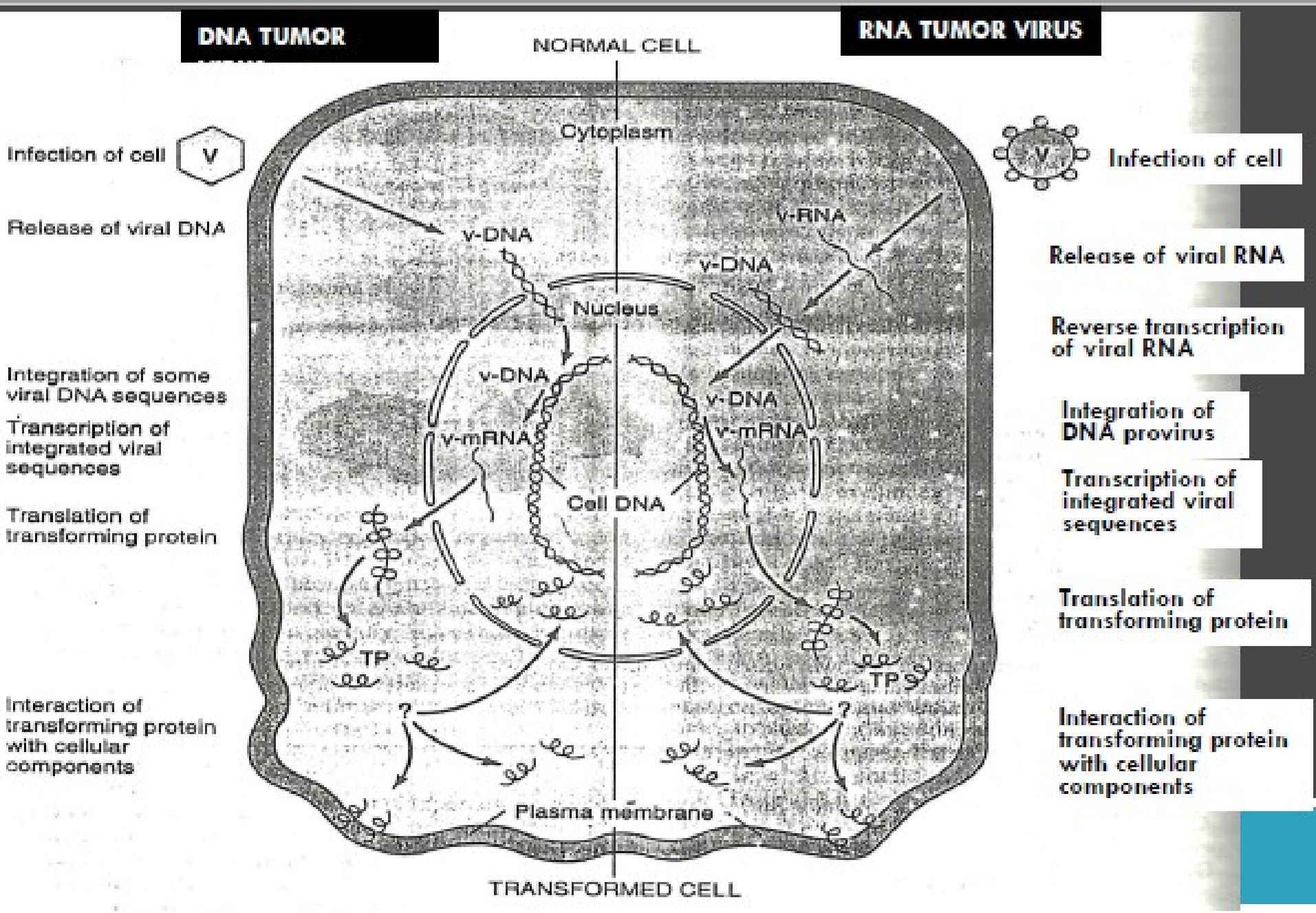
Conversion of proto-oncogenes into oncogenes



Essential growth-controlling proteins

- Growth factors
- Growth-factor receptors
- Signal transduction
- Intranuclear factors
- Regulation of programmed cell death

1) Qualitatively altered, hyperactive proteins
2) Quantitative alterations (gene amplification or translocation) resulting in increased or decreased levels of product


DNA TUMOR
NORMAL CELL
RNA TUMOR VIRUS
Infection of cell
V
Release of viral DNA
Integration of some viral DNA sequences
Transcription of integrated viral sequences
Translation of transforming protein
Interaction of transforming protein with cellular components
Cytoplasm
v-DNA
v-RNA
Nucleus
v-mRNA
Cell DNA
TP
?
Plasma membrane
TRANSFORMED CELL
Infection of cell
Release of viral RNA
Reverse transcription of viral RNA
Integration of DNA provirus
Transcription of integrated viral sequences
Translation of transforming protein
Interaction of transforming protein with cellular components