TUMOUR VIRUSES
&
ONCOGENESIS

Tumour Viruses

- **Tumour viruses are those viruses which when introduced into an appropriate host can produce tumour.**
- **It is well proved that viruses cause cancer in animals.**
- **However, proving causal relationship between viruses and human cancer is controversial.**

Relation between Viruses & Tumours

- **The virus can be isolated from tumor cells at some stages of development.**
- **Detection of viral nucleic acid or viral encoded protein in tumour cells.**
- **The ability of the virus to cause transformation of cultured cells or tumour in laboratory animals.**
- **Decrease in incidence of some tumours by prevention of the related virus.**

Relation between Viruses & Tumours

- **Tumour viruses can cause cellular transformation, known as a stable heritable changes of cell characters.**
- **Transformed cells contain either the whole or part of the viral genome, usually integrated into the cell DNA. Sometimes, it is present as a free plasmid-like entity.**
- **Transformed cells do not produce viruses and detection of the integrated specific viral sequence can only be done by recombinant DNA techniques.**

Characteristics of Transformed Cells 1

1. **Alteration in cell growth patterns:**
   - Increase in the rate of growth.
   - Decrease requirements of serum.
   - Loss of contact inhibition.

2. **Alteration in cell surface:**
   - Increase rate of transport of cell nutrients.
   - Increase secretion of proteases.
   - Acquisition of new surface antigens most of them are virus specific.
   - Changes in the composition of glycoproteins and glycolipids, including the presence of viral encoded proteins.

Characteristics of Transformed Cells 2

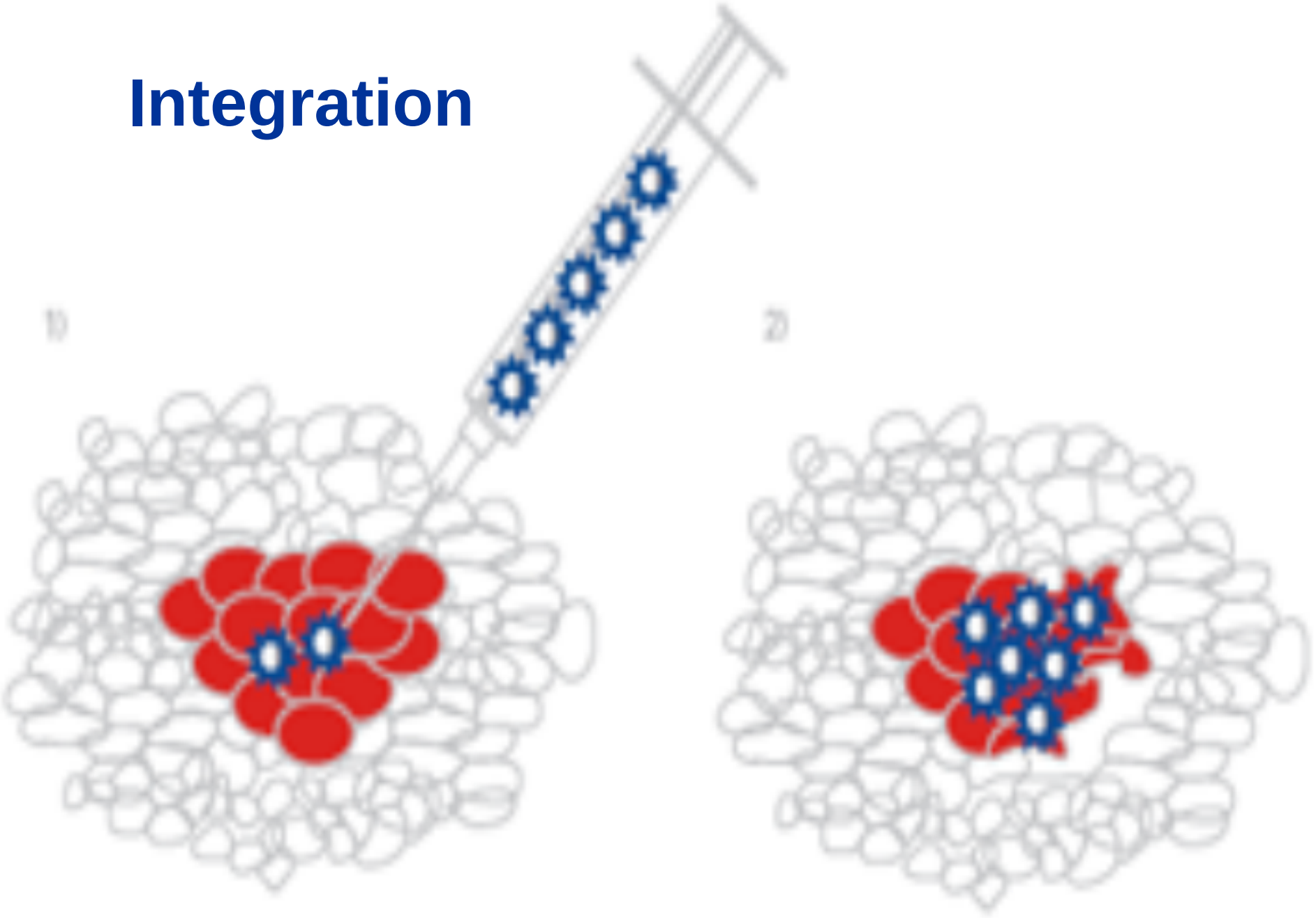
3. **Alteration in intracellular components:**
   - Increased metabolic rate and glycolysis.
   - Decreased levels of cyclic AMP.
   - Increased secretion of plasminogen-activator.

4. **Tumourigenicity:** The ability to produce tumour when injected into appropriate test animals.

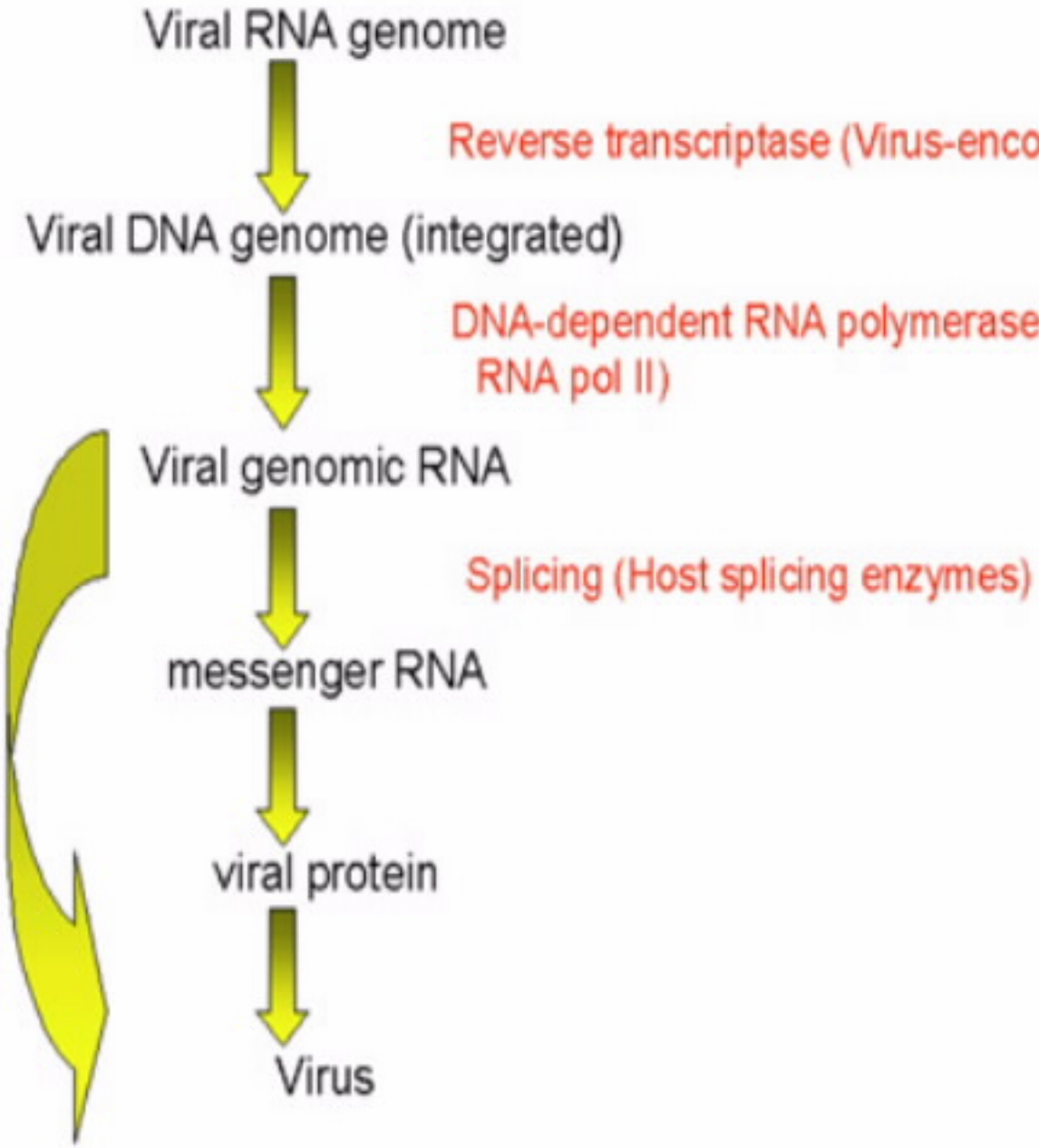
Mechanism of Cell Transformation

- **Tumour viruses mediate changes in cell behavior by means of a limited amount of genetic information integrated in the cell chromosome:**
  - **DNA Viruses: A portion of the viral DNA becomes integrated in the host cell genome.**
  - **RNA Viruses : The reverse transcriptase makes a DNA copy of the viral RNA which is then integrated into the cell genome.**

Integration



RNA Tumor Viruses



The Integrated Viral Genes Cause Transformation through:

1. **The virus introduces a new "transforming gene" into the cell (viral oncogene).**

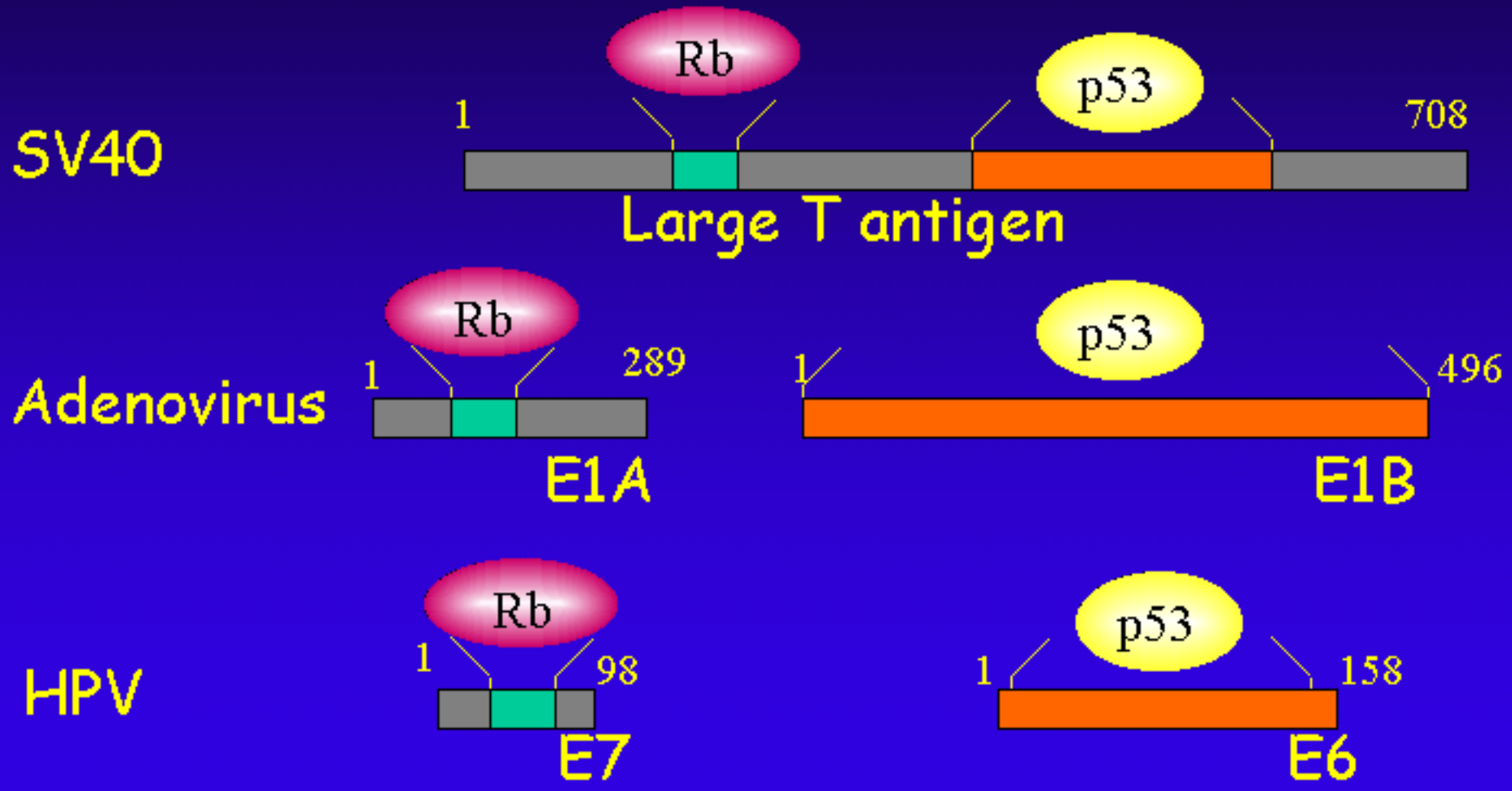
2. **The virus induces or alters the expression of a pre-existing cellular gene "proto-oncogene" by:**
   - **Insertional mutation: over expression of a proto-oncogene may occur as a result of insertion of a viral promoter "enhancer gene" adjacent to cellular oncogene.**
   - **Translocation of the proto-oncogene from its normal regulatory sequence, where it becomes adjacent to a strong promoter.**
   - **Gene amplification.**
   - **Mutation.**

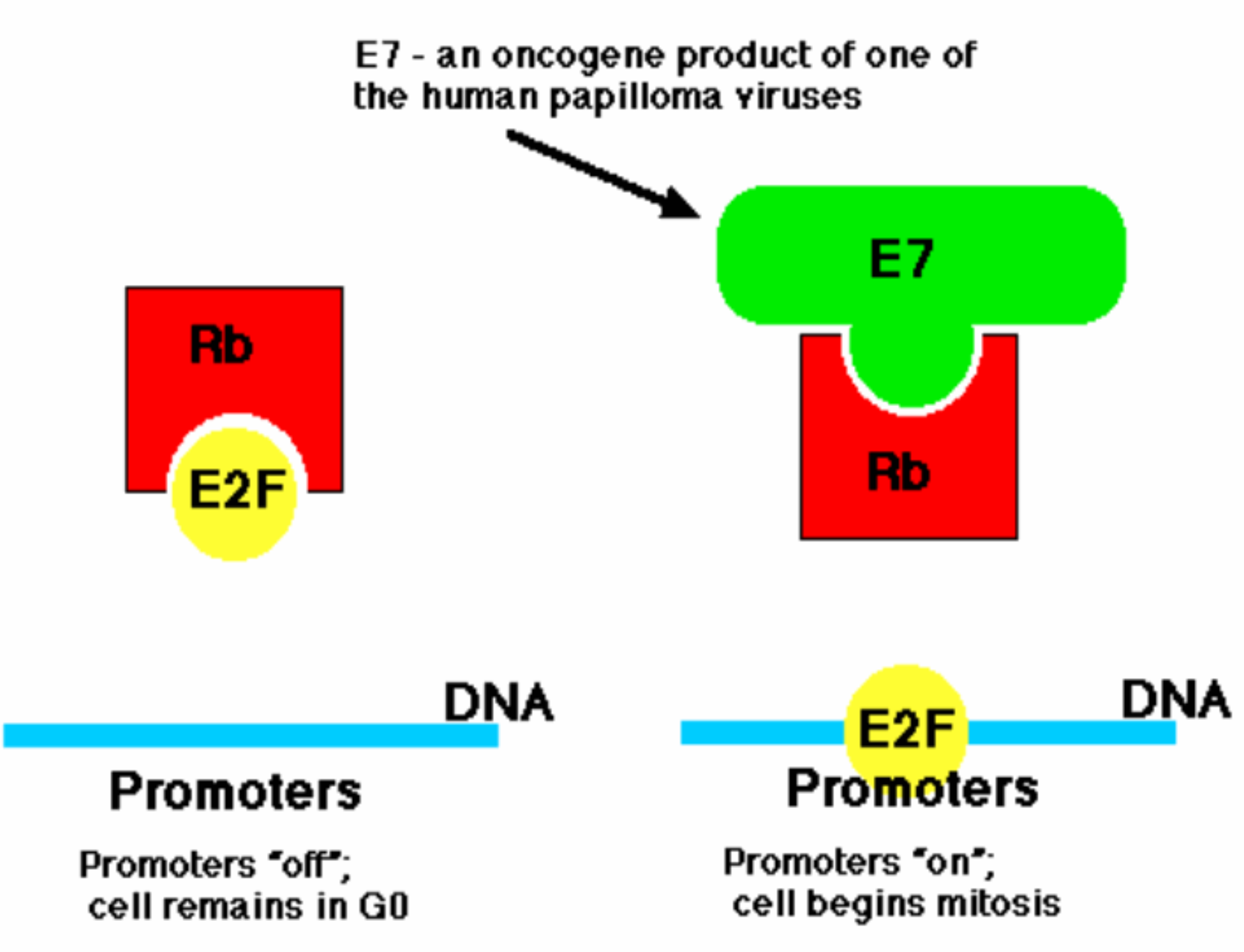
The integrated viral genes cause transformation through:

3. Viral proteins may **inactivate tumour suppressor genes (anti-oncogenes).**

   e.g., The Rb gene and the P53 gene appear to be altered in at least 50% of human tumours.

DNA tumor viruses bind multiple cellular proteins




E7 - an oncogene product of one of the human papilloma viruses
E7
Rb
Rb
E2F
DNA
DNA
E2F
Promoters
Promoters
Promoters "off"; cell remains in G0
Promoters "on"; cell begins mitosis

I. DNA Tumour Viruses

1. **Herpes viruses:**
   - Herpes simplex type 2 is related to carcinoma of the cervix.
   - Epstein Barr virus is linked to Burkitt ’s lymphoma. There is EB viral DNA in tumour cells.
   - Human Herpes virus 8 is related to Kaposi ’s sarcoma.

2. **Hepatitis B virus** has been strongly implicated in development of HCC.

I. DNA Tumour Viruses

3. Human papilloma virus can cause warts, laryngeal papilloma or carcinoma of the cervix.

4. Adenoviruses can cause transformation in rodent cells. No association of adenoviruses with human neoplasms has been found.

5. Poxviruses ; as molluscum contagiosum virus produces small benign growths in human skin.

II. RNA Tumour Viruses

1. HCV: is strongly related to HCC.

2. Human T-cell Lymphotropic Virus (HTLV-1); a retrovirus which causes tumours of the reticuloendothelial and haematopoietic systems.


Thank You