



# TUMOR VIRUSES

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**Presented by: Dr. Asma**

# TUMOR VIRUSES

Viruses that produce tumor in their natural host/experimental animals or which induce malignant transformation of cells on culture. Also

called as oncoviruses.

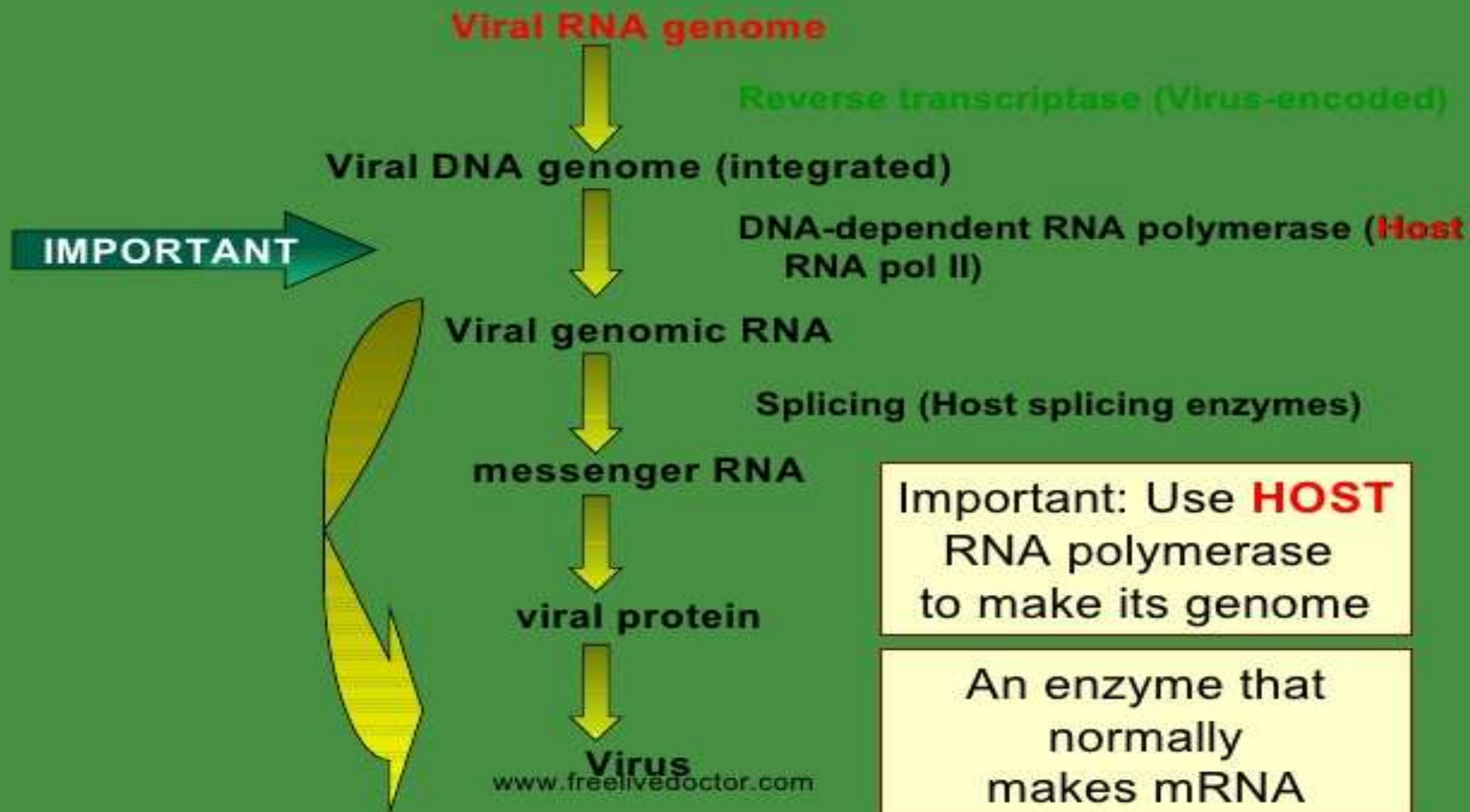
**RNA Tumor Viruses**

All RNA tumor viruses are retroviruses, with the exception of hepatitis C virus (HCV).

**DNA tumor Viruses**

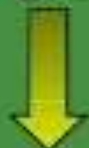
They are grouped in four families, namely, SV40 and polyomavirus, papilloma viruses (HPV), adenoviruses, and herpesviruses.

# RNA Tumor Viruses



# DNA Tumor Viruses

DNA genome



mRNA

Host RNA  
polymerase II



Host enzymes

protein



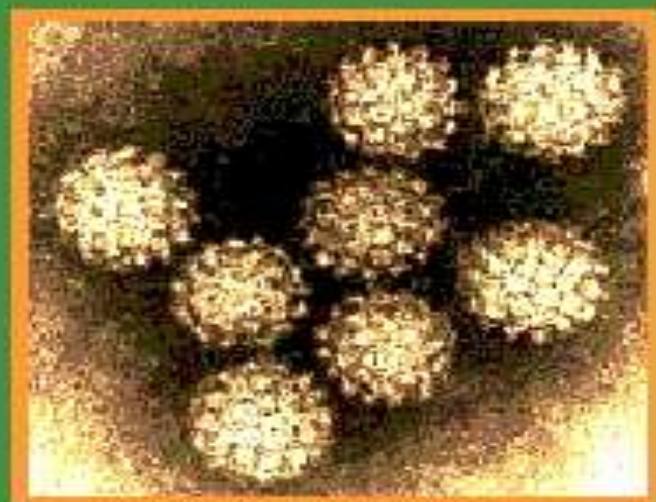
virus

**OR TRANSFORMATION**

In transformation usually only **EARLY** functions are expressed

# DNA Tumor Viruses In Human Cancer

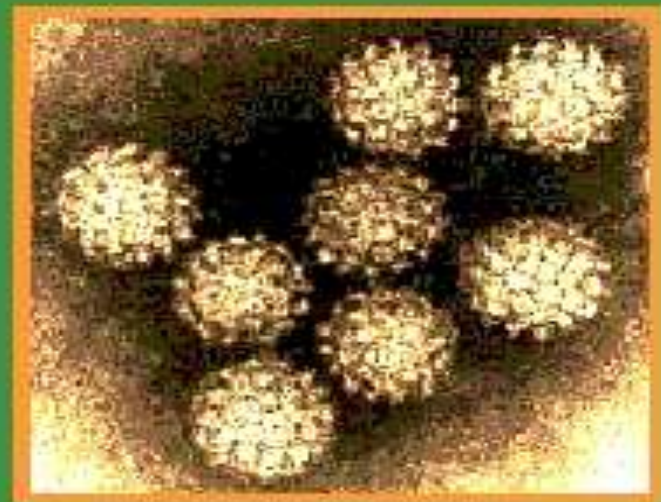
## Papilloma Viruses



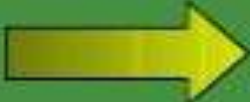
- cause natural cancers in animals
- cause benign warts
- ubiquitous
- epitheliotropic - most human tumors are malignancies of epithelial cells

# DNA Tumor Viruses In Human Cancer

## Papilloma Viruses



- Epidermodysplasia verruciformis

wart  malignant squamous cell carcinoma

# DNA Tumor Viruses In Human Cancer



## Papilloma Viruses

urogenital cancer

wart



malignant squamous cell carcinoma

**Papilloma viruses are found in 91% of women with cervical cancer**

Squamous cell carcinoma:

Larynx

Esophagus

Lung

All histologically similar

10% of human cancers may be HPV-linked

# DNA Tumor Viruses In Human Cancer

## Papilloma Viruses

- >100 types identified - most common are types **6 and 11**
- Most cervical, vulvar and penile cancers are ASSOCIATED with types **16 and 18** (70% of penile cancers)

EPIDEMIOLOGICAL STUDIES **BUT:**  
HPV 16 and HPV 18 do transform human keratinocytes

Effective Vaccine  
(quadrivalent recombinant HPV 6, 11, **16 and 18** proteins made in  
yeast - Gardasil)



# Papilloma Viruses

- The important transforming genes in papilloma viruses are: E6 and E7
- Early genes - Not encoding structural proteins
- **Oncogenes**

# DNA Tumor Viruses In Human Cancer

## Polyoma Viruses

- Simian virus 40 - juvenile hamster sarcomas, transformation
- Polyoma - mouse leukemia, in vitro transformation
- Human polyomas (JC and BK) - monkey sarcoma, transformation

Possible association of BK with human prostate cancer

*Polyoma virus transforms cells when the genome is incomplete*

**Early functions are necessary - ONCOGENES**

JC: **PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)**

# DNA Tumor Viruses In Human Cancer

## Adenoviruses

Highly oncogenic in animals

Only part of virus integrated

Always the same part

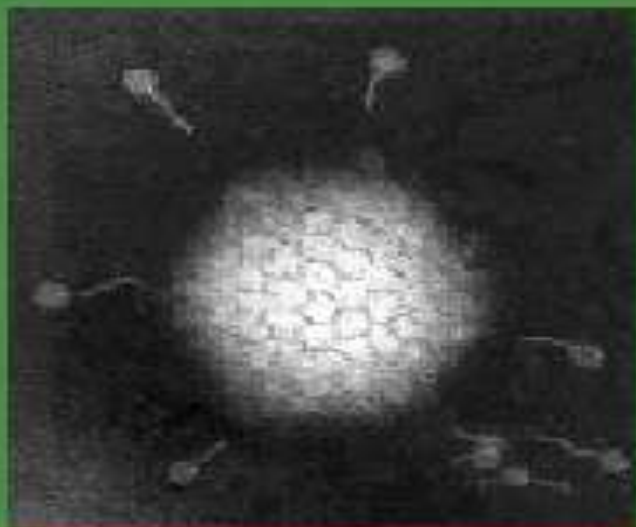
**Early functions**

E1A region: 2 T antigens

E1B region: 1 T antigen

**E1A and E1B = Oncogenes**

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# DNA Tumor Viruses In Human Cancer

## ONCOGENE

A gene that codes for a protein that potentially can transform a normal cell into a malignant cell

An oncogene may be transmitted by a virus in which case it is known as a VIRAL ONCOGENE

**v-onc**

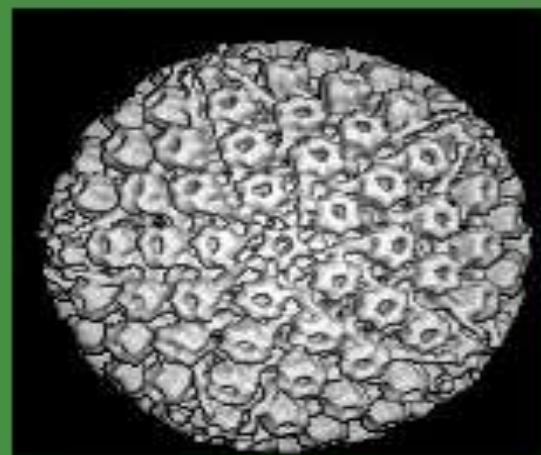
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# DNA Tumor Viruses In Human Cancer

## Herpes Viruses

**Considerable evidence for role in human cancer**

- Some very tumorigenic in animals
- Integrated viral DNA found in small proportion of tumor cells: “hit and run”



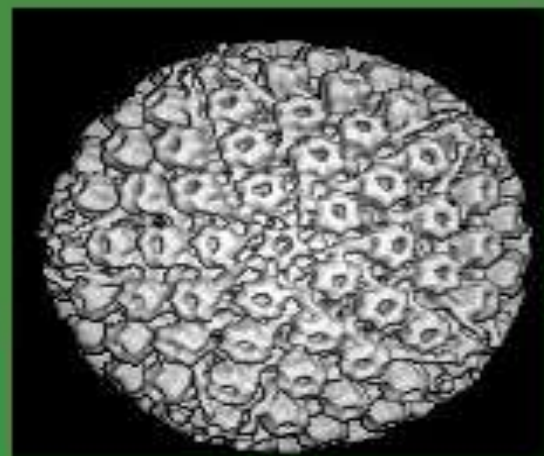
# DNA Tumor Viruses In Human Cancer

## Epstein-Barr Virus



- **Burkitt's Lymphoma**
- **Nasopharyngeal cancer**
- **Infectious mononucleosis (glandular fever)**
- **Transforms human B-lymphocytes *in vitro***

- Burkitt's lymphoma: malarial infested regions
- Nasopharyngeal cancer: China, SE Asia – diet?



# DNA Tumor Viruses In Human Cancer

Human herpes virus – 8  
Kaposi's Sarcoma Herpes Virus

Kaposi's sarcoma

## Hematologic malignancies

- Primary effusion lymphoma
- Multicentric Castleman's disease (MCD) – a rare lymphoproliferative disorder (AIDS)
  - MCD-related immunoblastic/plasmablastic lymphoma
- Various atypical lymphoproliferative disorders



# DNA Tumor Viruses In Human Cancer

## Hepatitis B Virus



**DNA genome**



**RNA polymerase II**

Host enzyme

**RNA Provirus**



**Reverse transcriptase**

Viral enzyme

**DNA genome**



# DNA Tumor Viruses In Human Cancer

Hepatitis B continued

- **Vast public health problem**
- **10% of population in underdeveloped countries are chronic carriers**
- **Long latency**

# DNA Tumor Viruses In Human Cancer

## Summary

- Can transform cells or have lytic life cycle
  - Often integrate into host genome
- In transformation often **ONLY early genes** are transcribed
- These are genes that are **also necessary** for a **PRODUCTIVE** infection
  - True viral genes

# RNA Tumor Viruses

## RNA Genome - Retroviruses

RNA-dependent DNA Polymerase encoded by virus

### REVERSE TRANSCRIPTASE



RNA genome



Reverse transcriptase



DNA genome



Integrase



Integrates

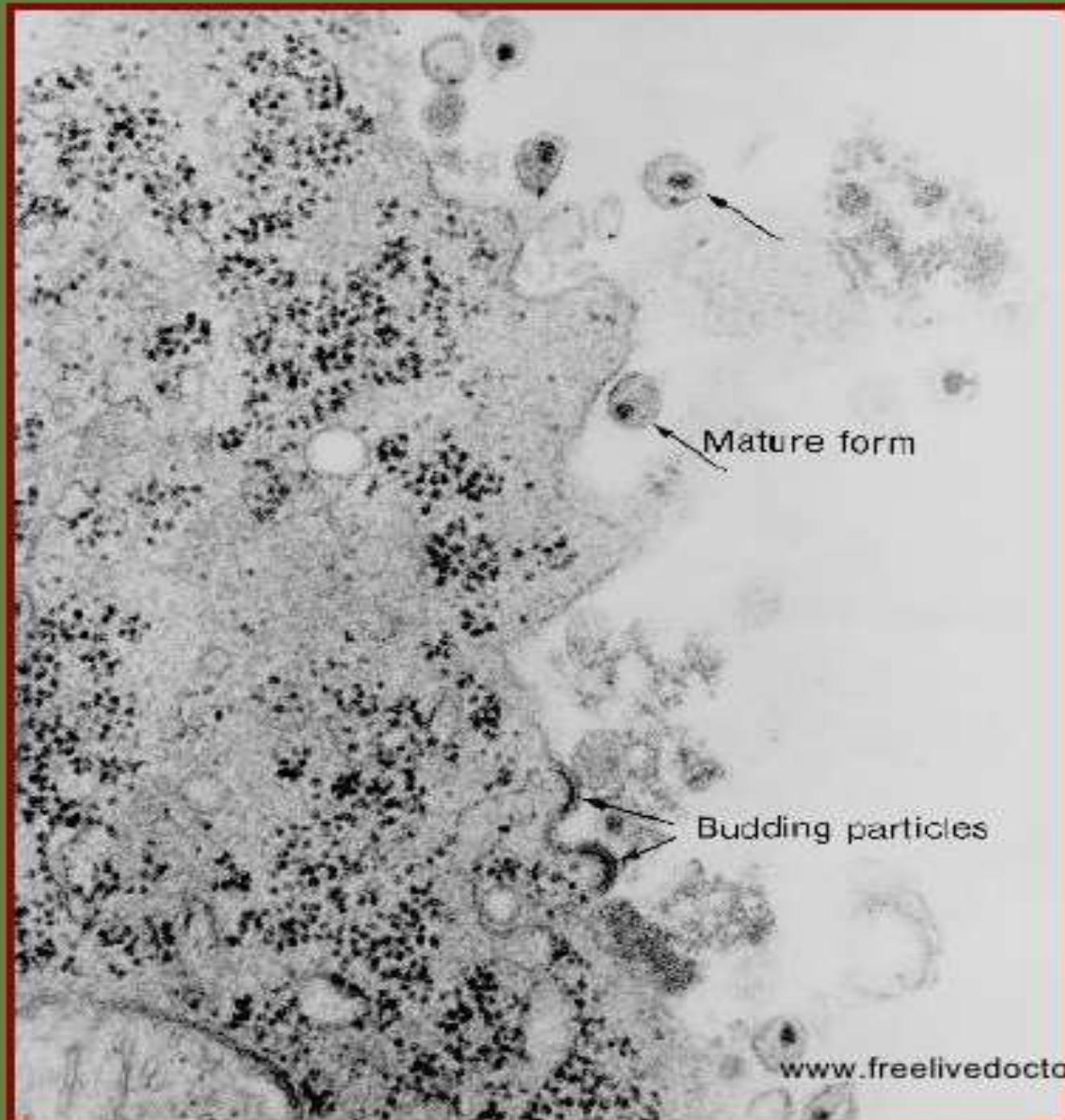


Host RNA polymerase II



RNA genome

# RNA Tumor Viruses



# RNA Tumor Viruses

A normal retrovirus has:

**3 genes**

**GAG** : internal proteins

**ENV**: Envelope glycoproteins

**POL**: Enzymes

Reverse transcriptase – RNase H

Integrase

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**Protease**

# RNA Tumor Viruses

## RNA is:

- Diploid
- Capped and polyadenylated
- **Positive** sense (same as mRNA)

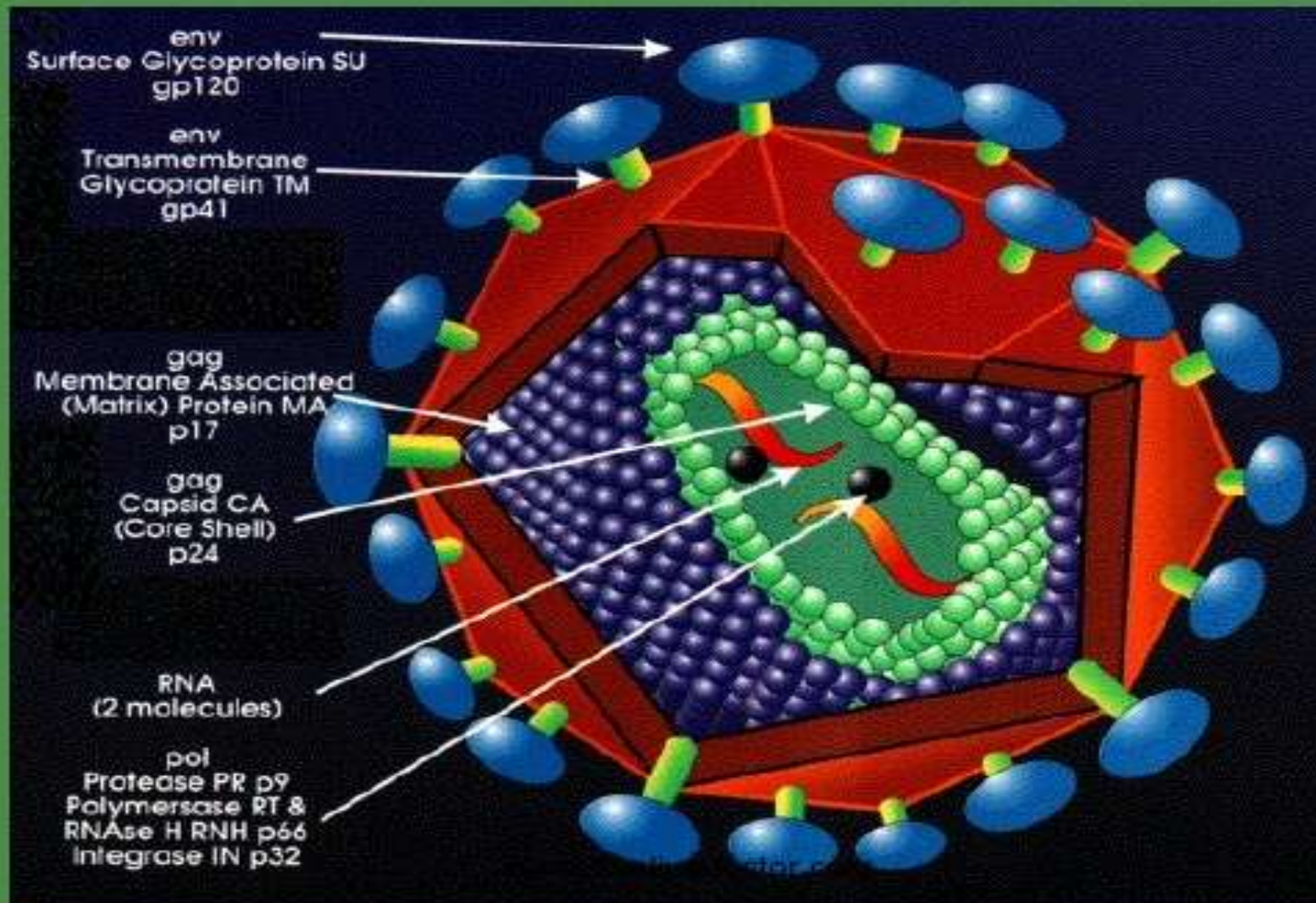
Viral RNA cannot be read as mRNA  
(even though same sense)

New mRNA must be made

Virus must make **negative sense DNA** before proteins are made

Therefore virus must carry **REVERSE TRANSCRIPTASE**  
into the cell

# RNA Tumor Viruses



# RNA Tumor Viruses

## Groups of Retroviruses

- **Oncovirinae**

← important

Tumor viruses and similar

- **Lentiviruses**

← important

Long latent period

Progressive chronic disease

Visna    HIV



# RNA Tumor Viruses

Retroviruses known to cause human cancer

- **Human T cell lymphotropic virus -1 (HTLV-1)**

Adult T cell leukemia, Sezary T-cell leukemia

Africa, Caribbean  
S. America (Peru, Bolivia)

Some Japanese Islands

Okinawa, Kiyushu, Shikoku (12 - 16% infection rate)

# RNA Tumor Viruses

## Human T cell lymphotropic virus -1 (HTLV-1)

UNITED STATES AND OTHER WESTERN COUNTRIES  
IV DRUG USERS

US rate of infection about one tenth of that of HIV  
BUT half as prevalent as HIV in IV drug users

Also causes: Tropical spastic paraparesis

- (affects the gray and white matter of the spinal cord - myelopathy)
- 1-4% of infected people

Immunosuppression

# RNA Tumor Viruses

Parental RNA

Reverse transcriptase

RNA/DNA Hybrid

Reverse transcriptase

Linear DNA/DNA duplex

Circular Duplex DNA

Integrase

Host DNA polymerase

Integration

Replication (DNA genome in cell)

Host RNA pol II

Host splicing enzymes

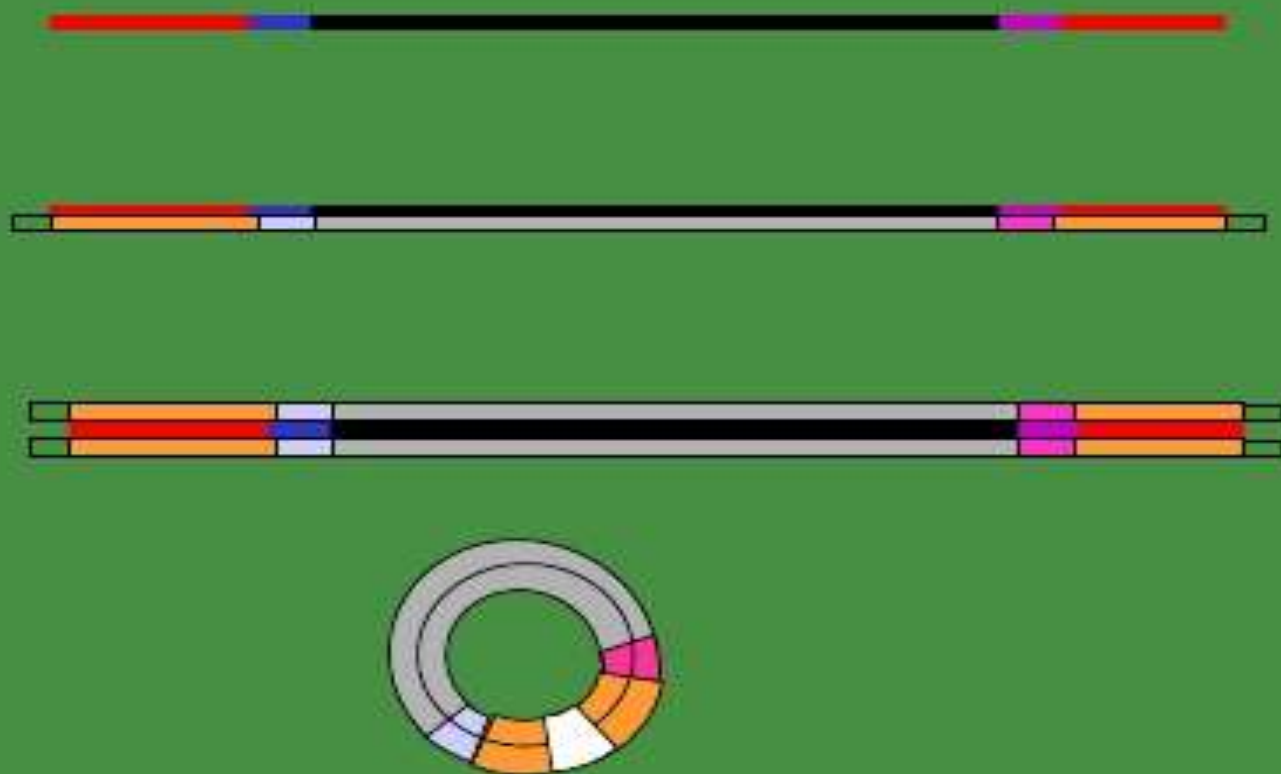
Transcription

Viral RNA genome

mRNA

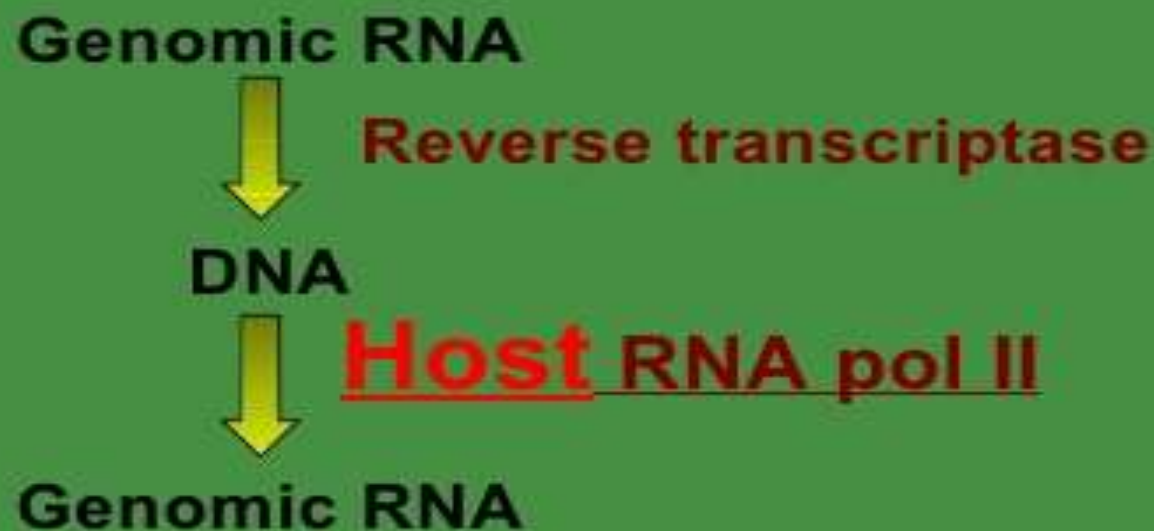
protein

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# RNA Tumor Viruses

Drawback to this lifestyle

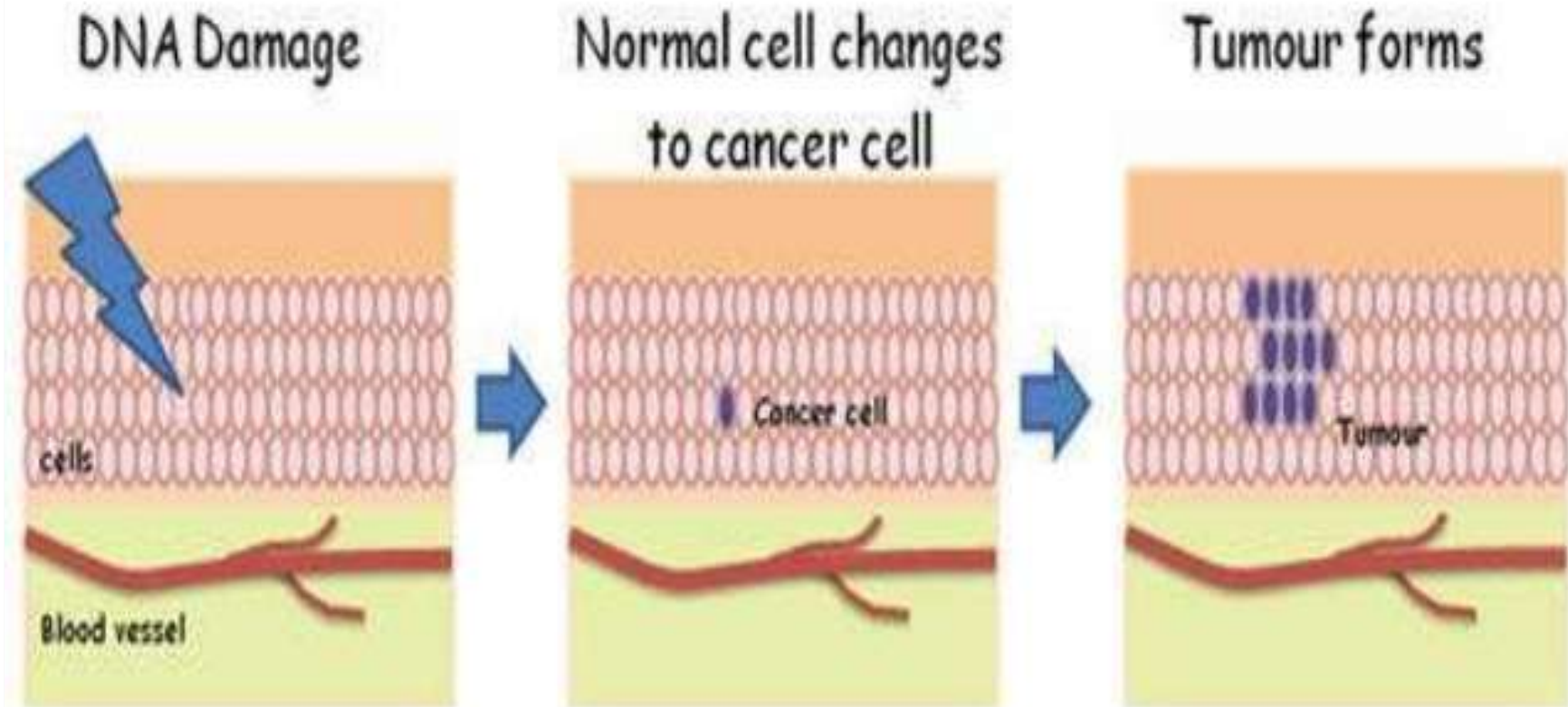


Pol II is a **host enzyme** that, in the uninfected cell, makes mRNA

When making mRNA, pol II **does not copy** entire gene to RNA

# GROWTH OF CANCER CELLS

Damaged DNA responsible for cancer



Thank You