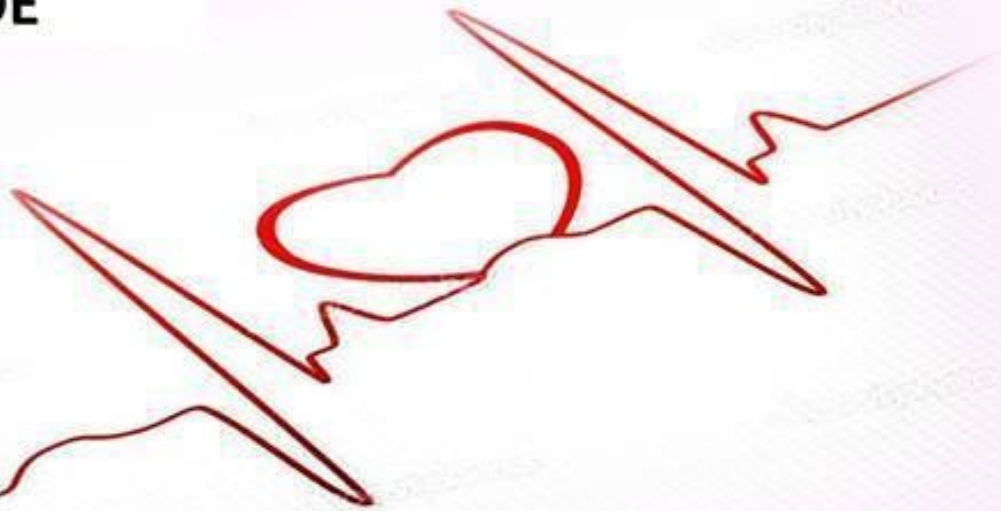


**SHEET**



**SLIDE**




Slide :20- Carcinogens



Doctor: Dr. Mazen





Etiology of cancer  
*Carcinogenic agents*

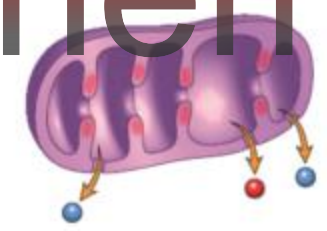
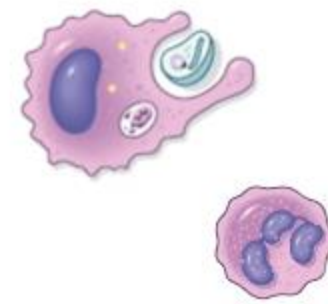
Radiant



Microbial



Chemical

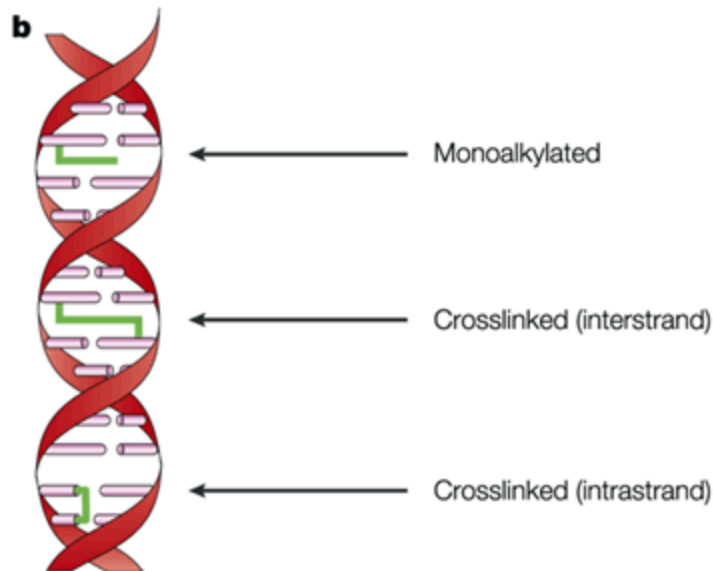
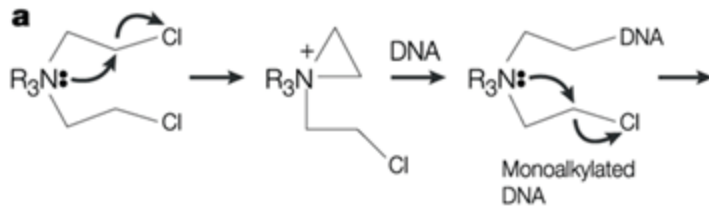




## Chemical

Chimney sweeps & scrotal cancer





## Chemical

### Direct acting

Generally weak

No metabolic conversion required

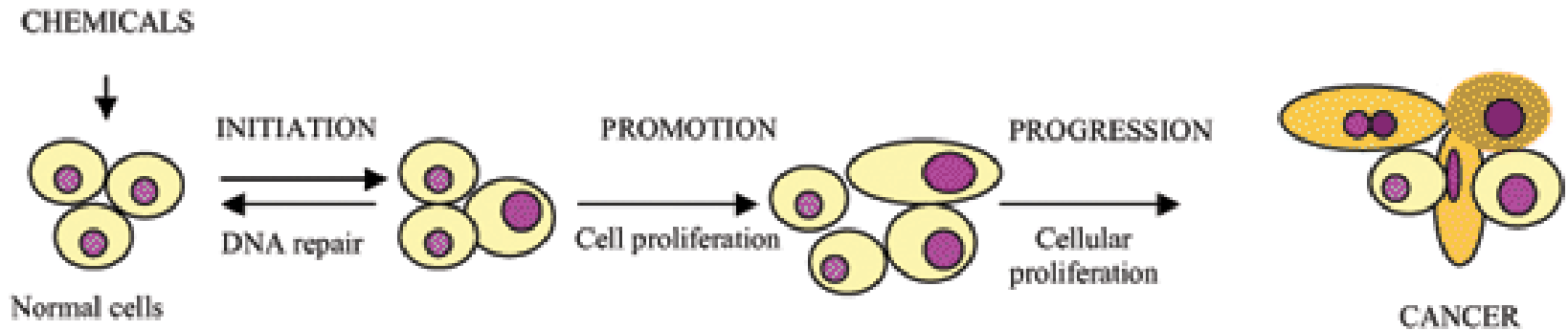
e.g. Alkylating agents

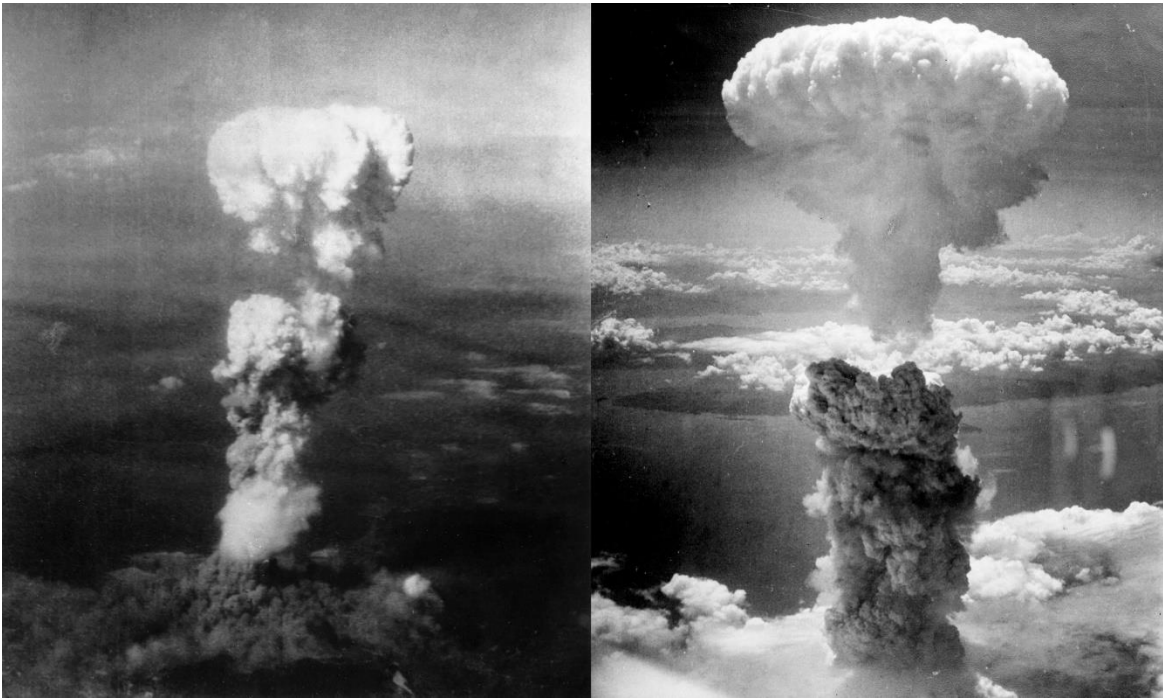
### Indirect acting

Require metabolic conversion (e.g. P450)

e.g. Polycyclic hydrocarbons (fossil fuel /cigarettes)

# Initiation Promotion Progression





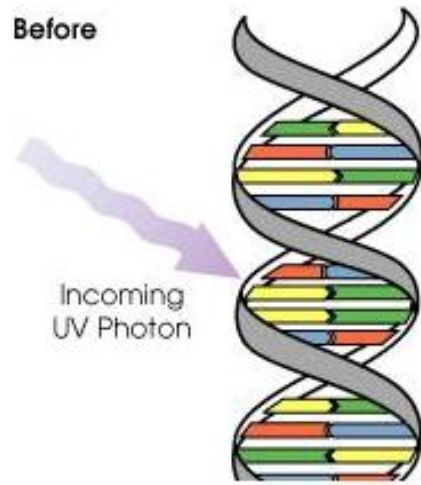
## Radiation

UV, X-rays, nuclear

- Chromosome breakage
- Translocations
- Point mutations



Before



Incoming  
UV Photon

After



## Skin Cancer & UV

Non-melanoma -  
Accumulative exposure

Melanoma - Intense  
intermittent exposure

Risks:

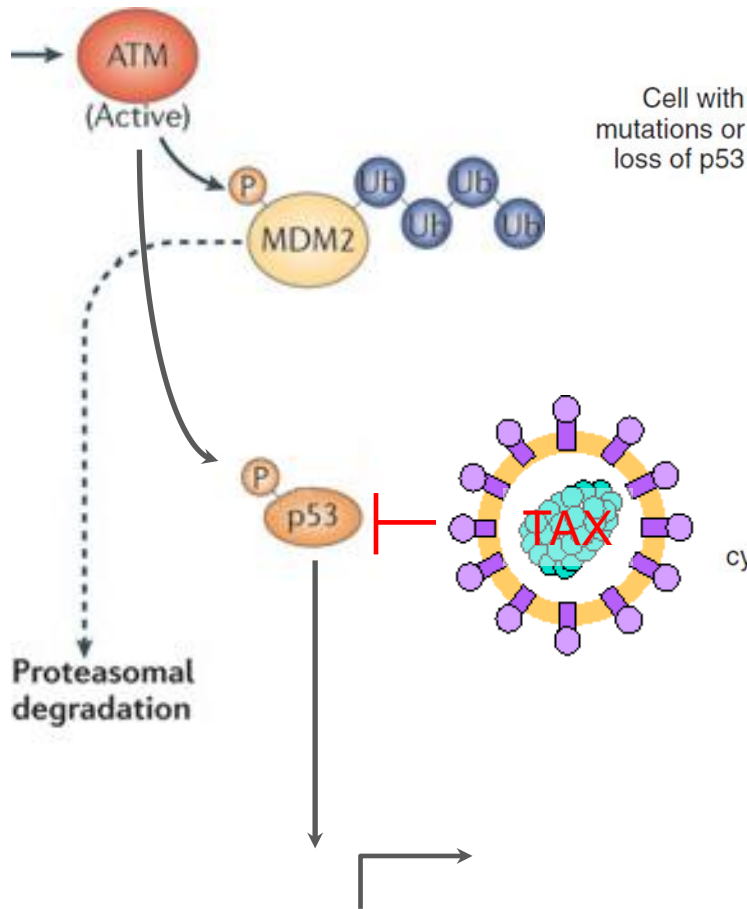
- Fair skin
- Geography
- Personal habits



Search ID: rjo1235







## Microbial

### HTLV-1 (retrovirus)

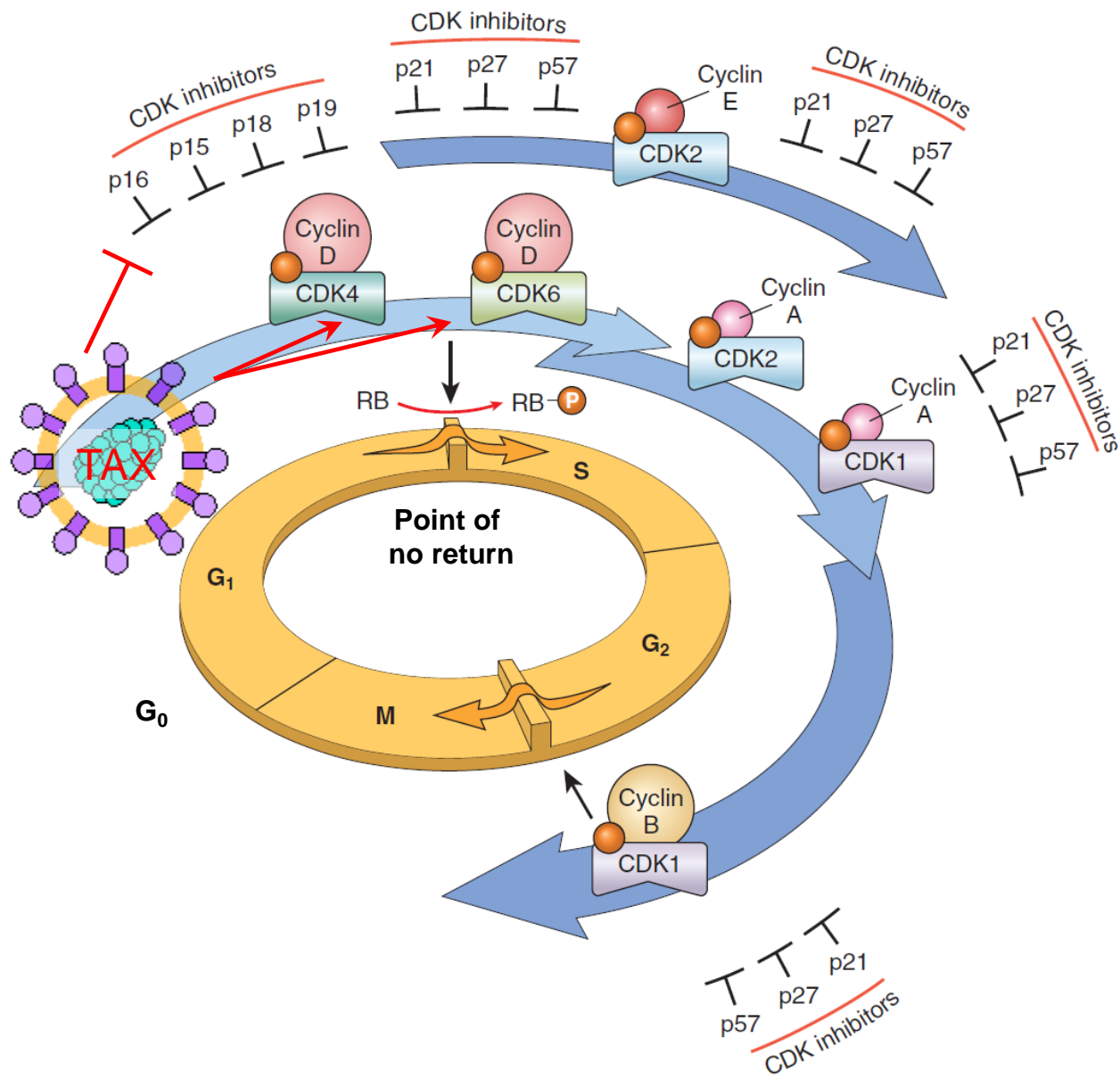
T cell leukemia/  
lymphoma 3-5% (Japan  
Caribbean)

Sex/Blood/Breastfeeding

Long latency 20-50yrs

CD4+ T cell  
transformation

No viral  
oncogene/oncogene  
integration site



## Microbial

### HTLV-1 (retrovirus)

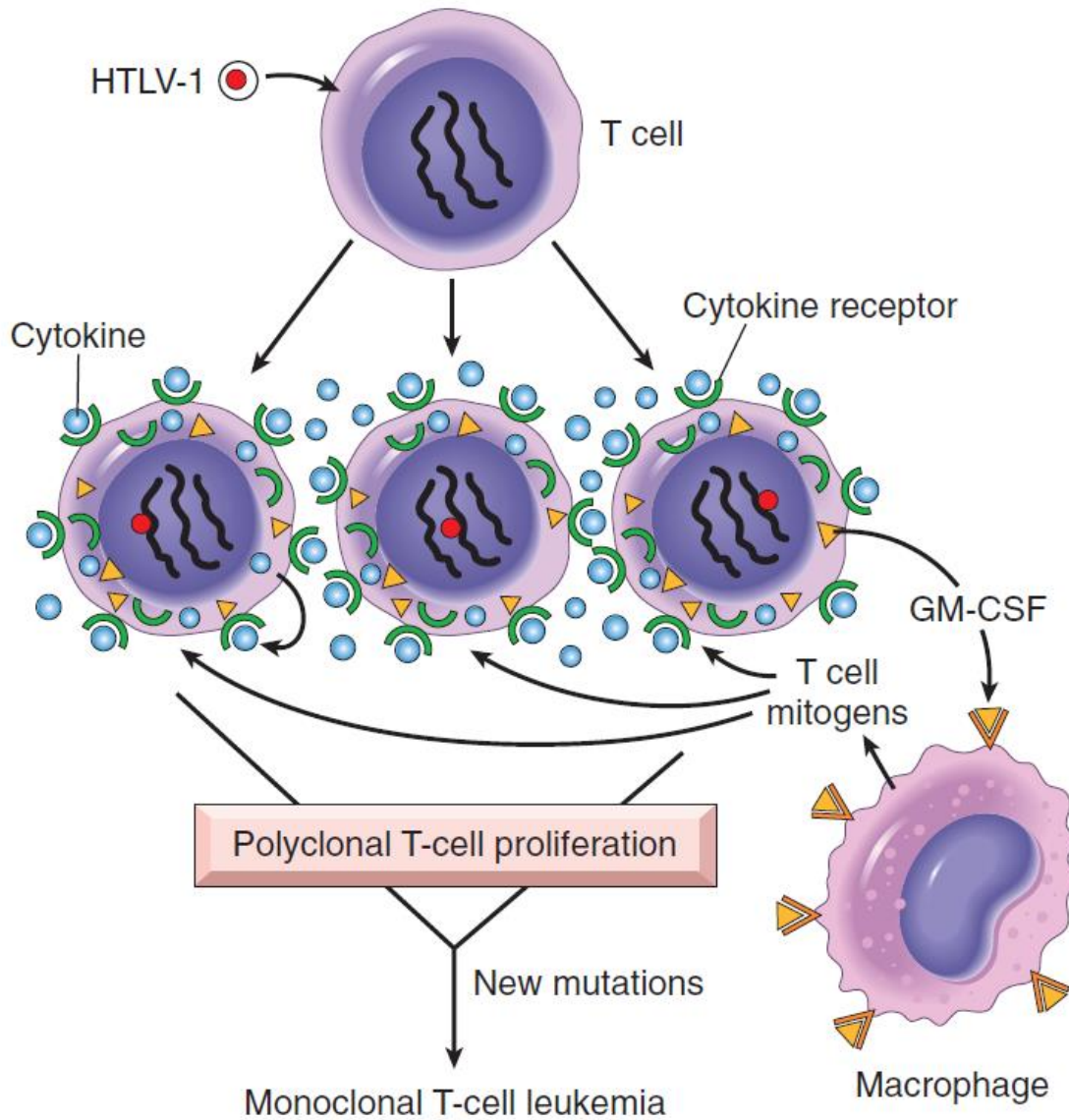
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## Microbial

### HPV (DNA)

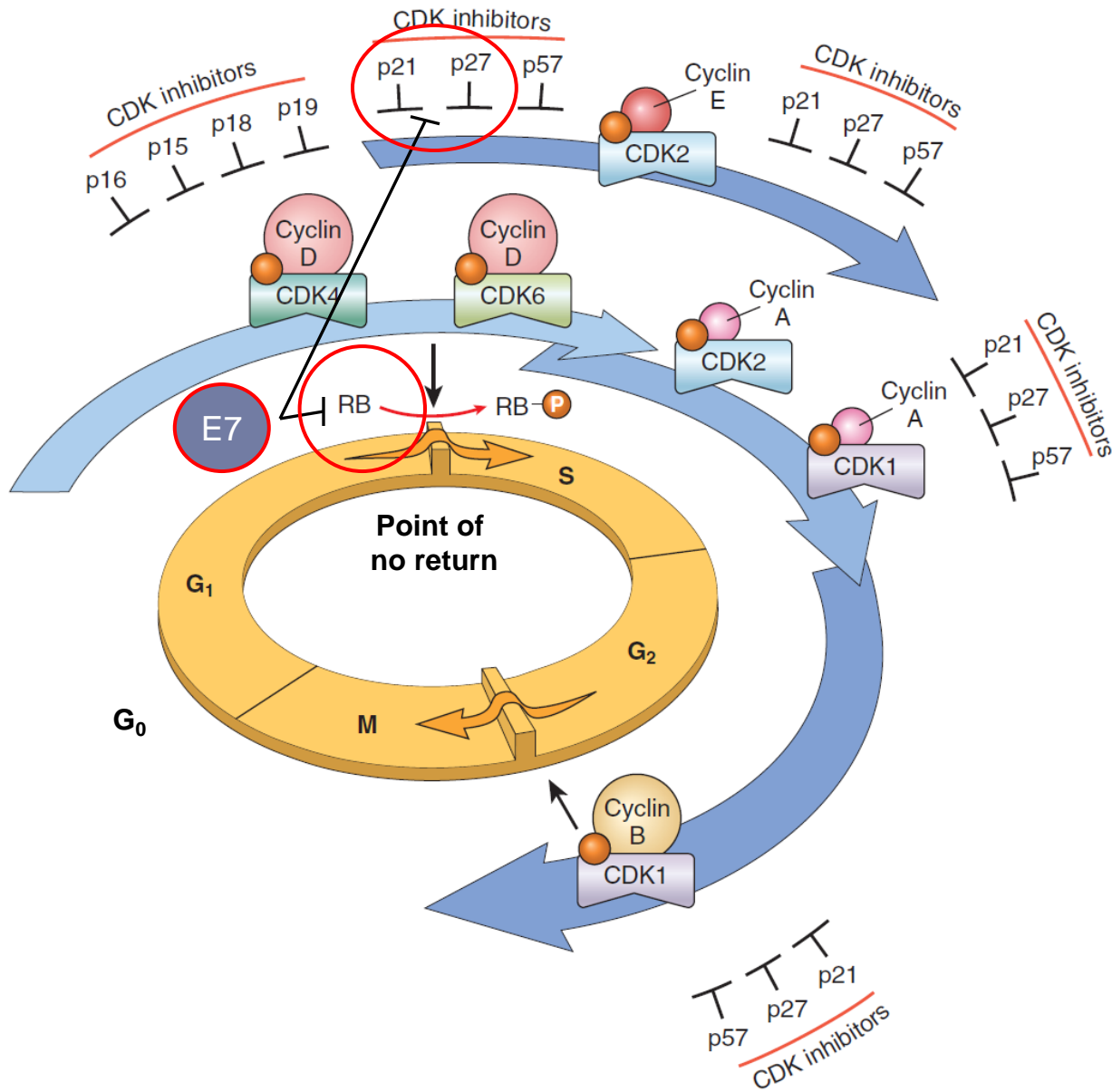
Several types

- 1,2,4,7 Warts
- 6,11 Genital warts
- 16,18 SCC (cervix & anogenital)

Viral proteins responsible

- E6
- E7





## Microbial

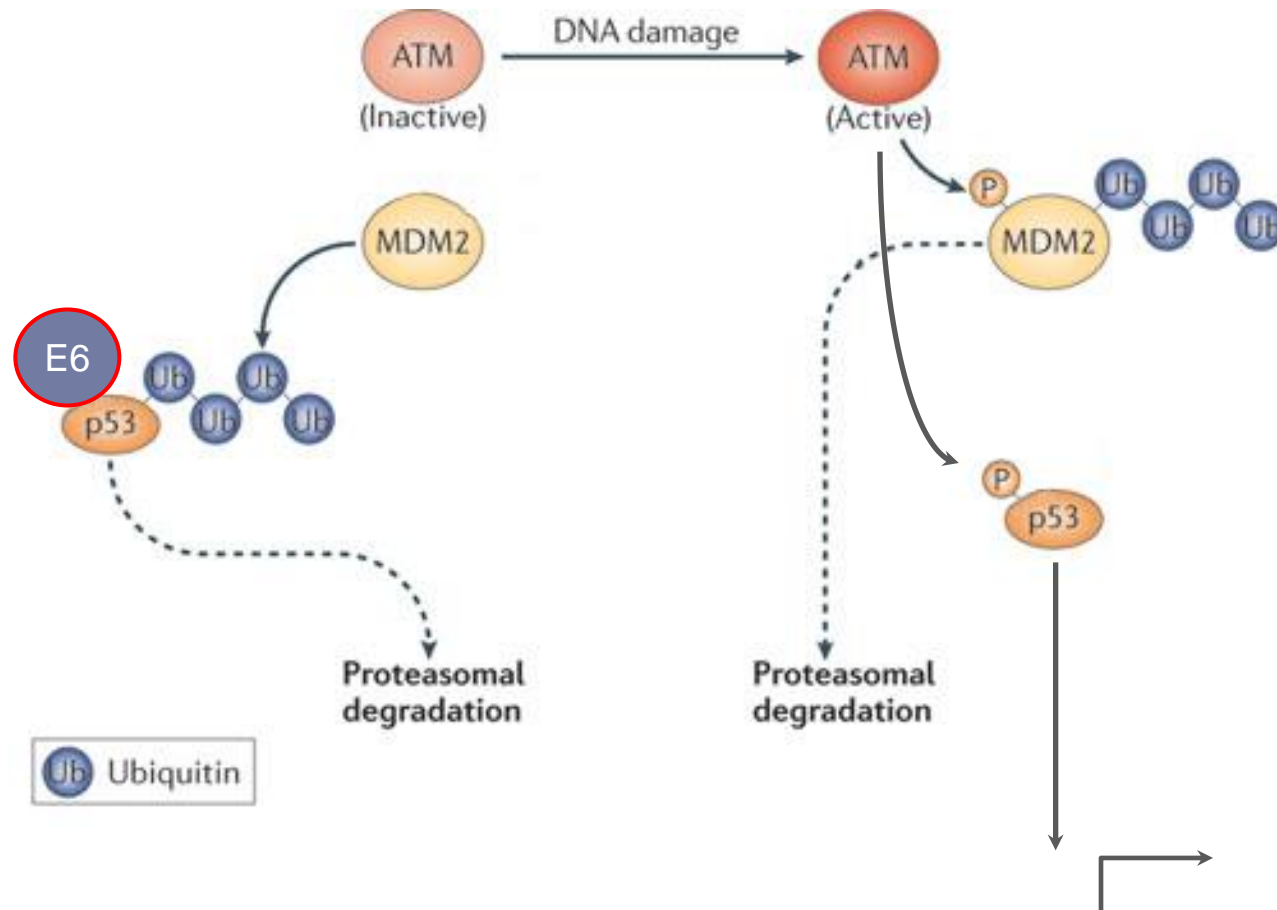
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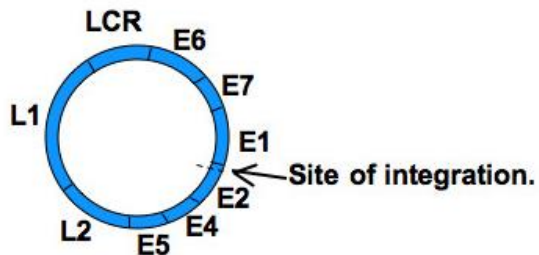
**Infectious  
Viral particles**

**Shedding virus  
particles**

**Transformation  
zone**

**Active  
Differentiation**

**Viral genome**



**E6/E7 Over expression.  
Viral genome integration.**

**Microbial**

**HPV (DNA)**

Several types

- 1,2,4,7 Warts
- 6,11 Genital warts
- 16,18 SCC (cervix & anogenital)

Viral proteins responsible

- E6
- E7

# Necessity & Sufficiency

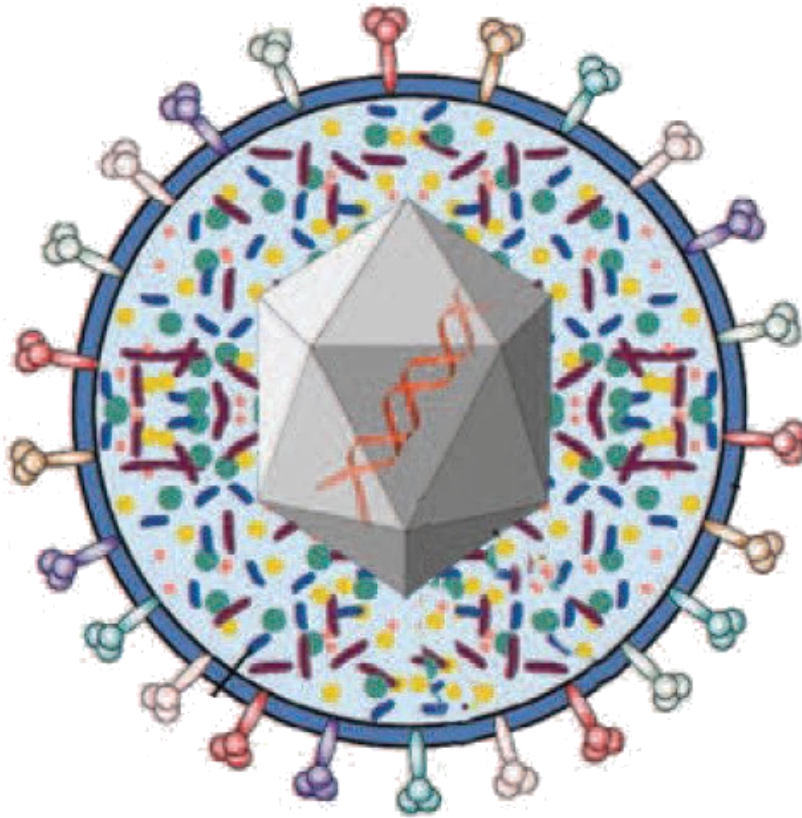
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Oxygen is necessary for human life.  
However, Oxygen alone is not sufficient.

Pouring freezing water on your “friend” is  
sufficient to wake him/her up, but not  
necessary. There are other ways.







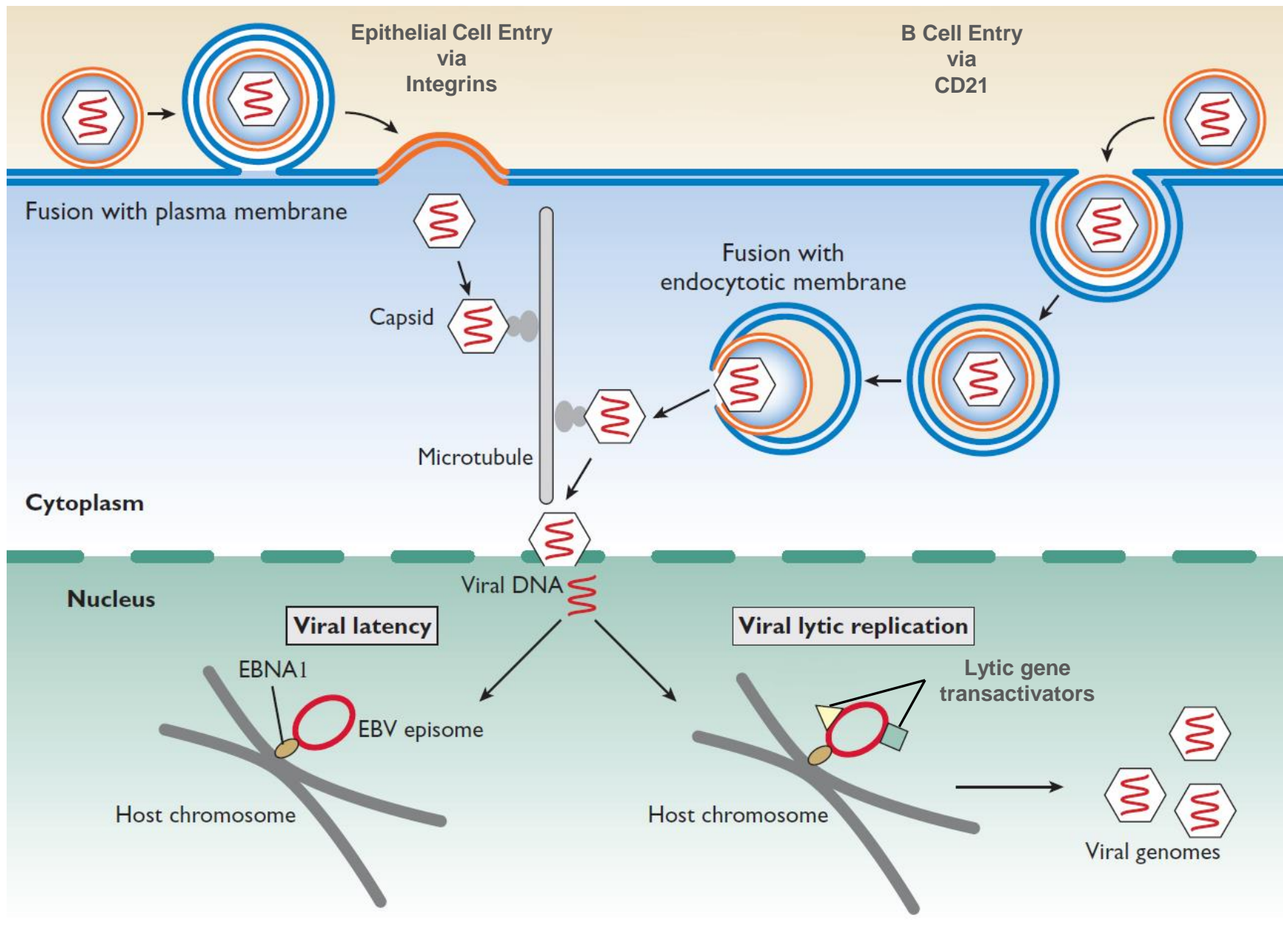
## Microbial

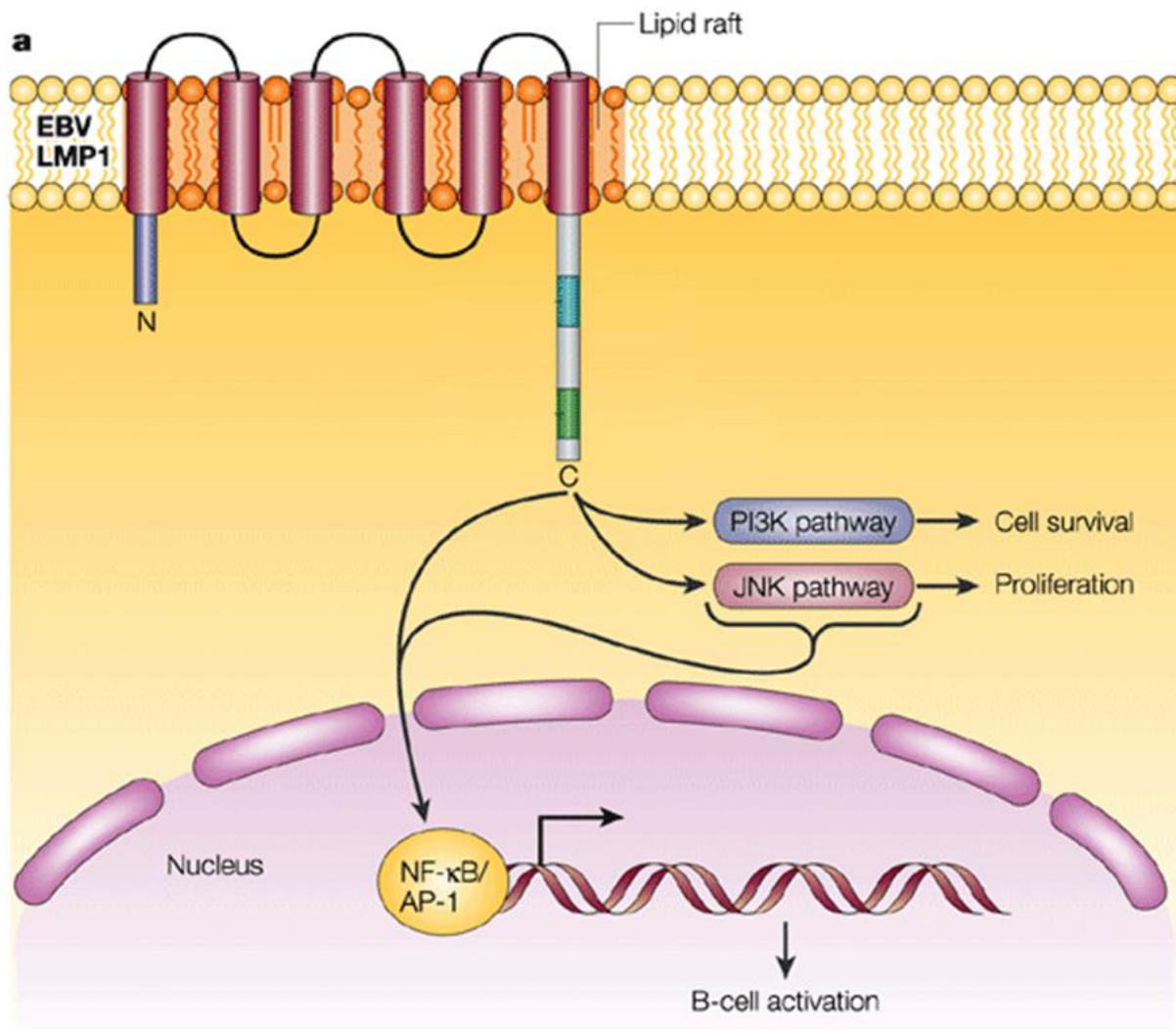
### EBV (DNA)

1<sup>st</sup> virus linked to a human tumor (Burkitt lymphoma)

Wide range of B, T & NK lymphomas as well as some carcinomas & sarcomas

Endemic in Africa (BL)  
Endemic in SEA (NPC)





## Microbial

EBV (DNA)

LMP1 - viral oncogene

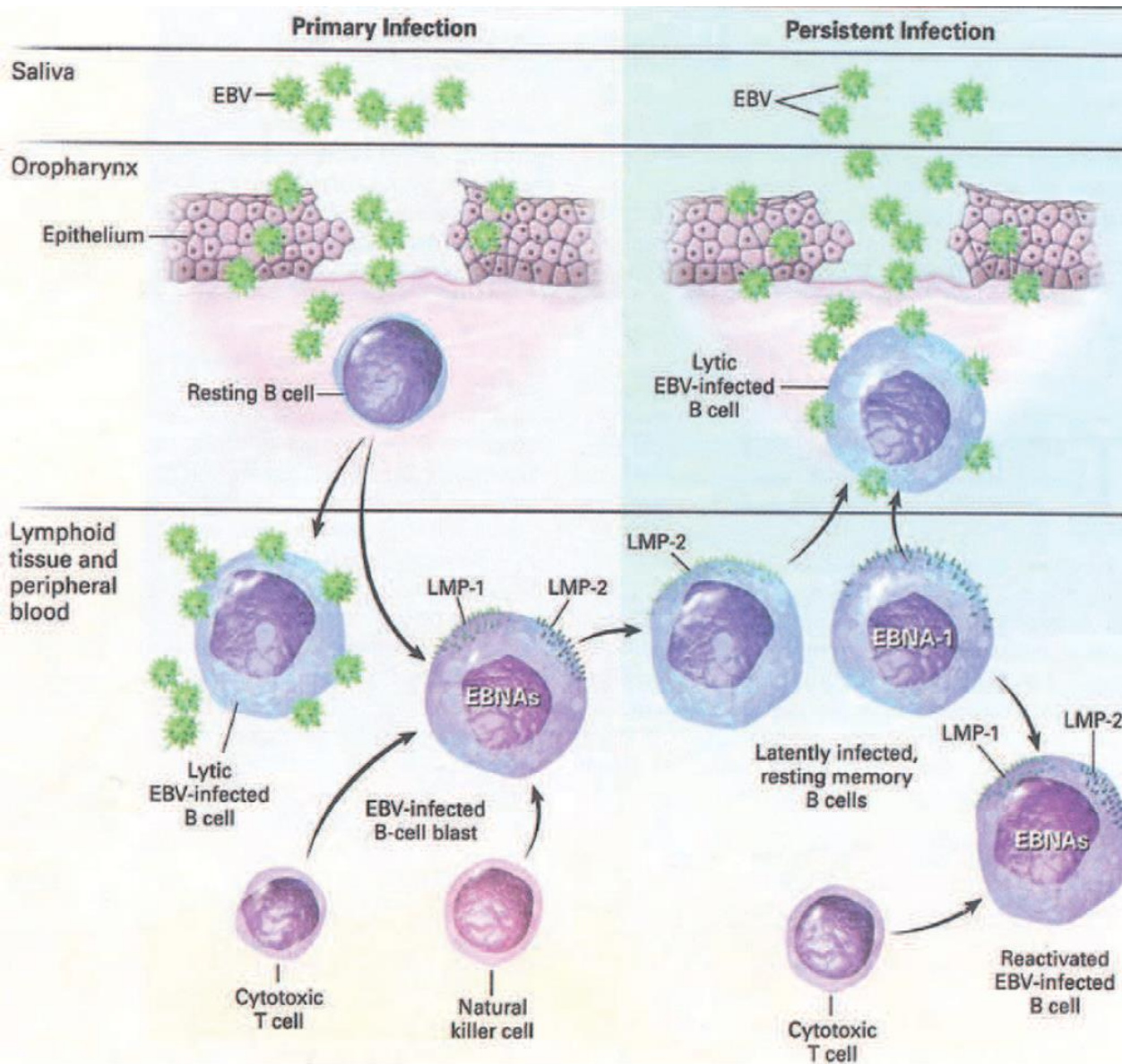
Mimics CD40 signalling  
(TNF receptor)

- JAK/STAT
- NF- $\kappa$ B

Inhibits apoptosis by  
activating Bcl-2

## EBNA2

- $\uparrow$  CyclinD
- $\uparrow$  src proto-oncogene



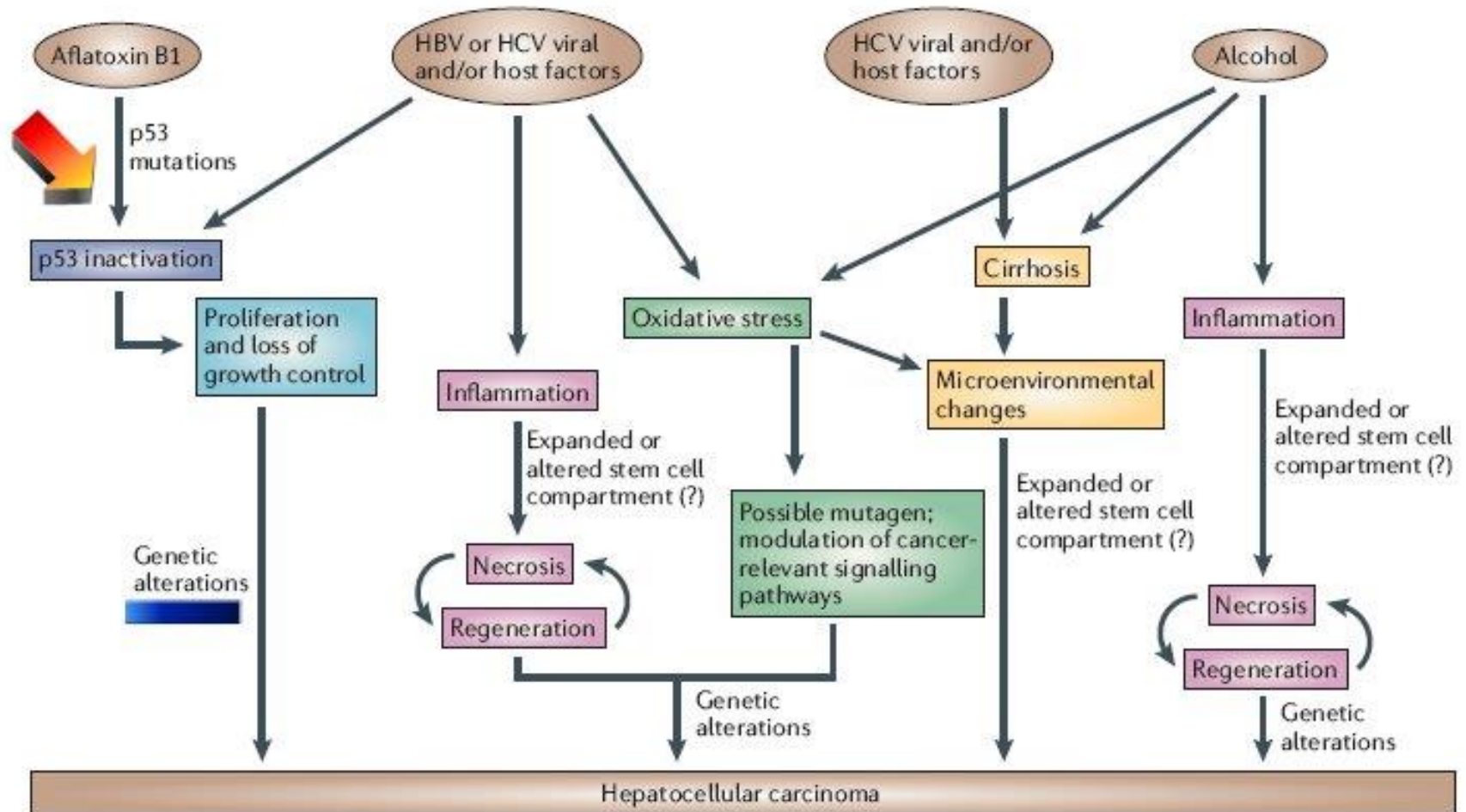
## Microbial

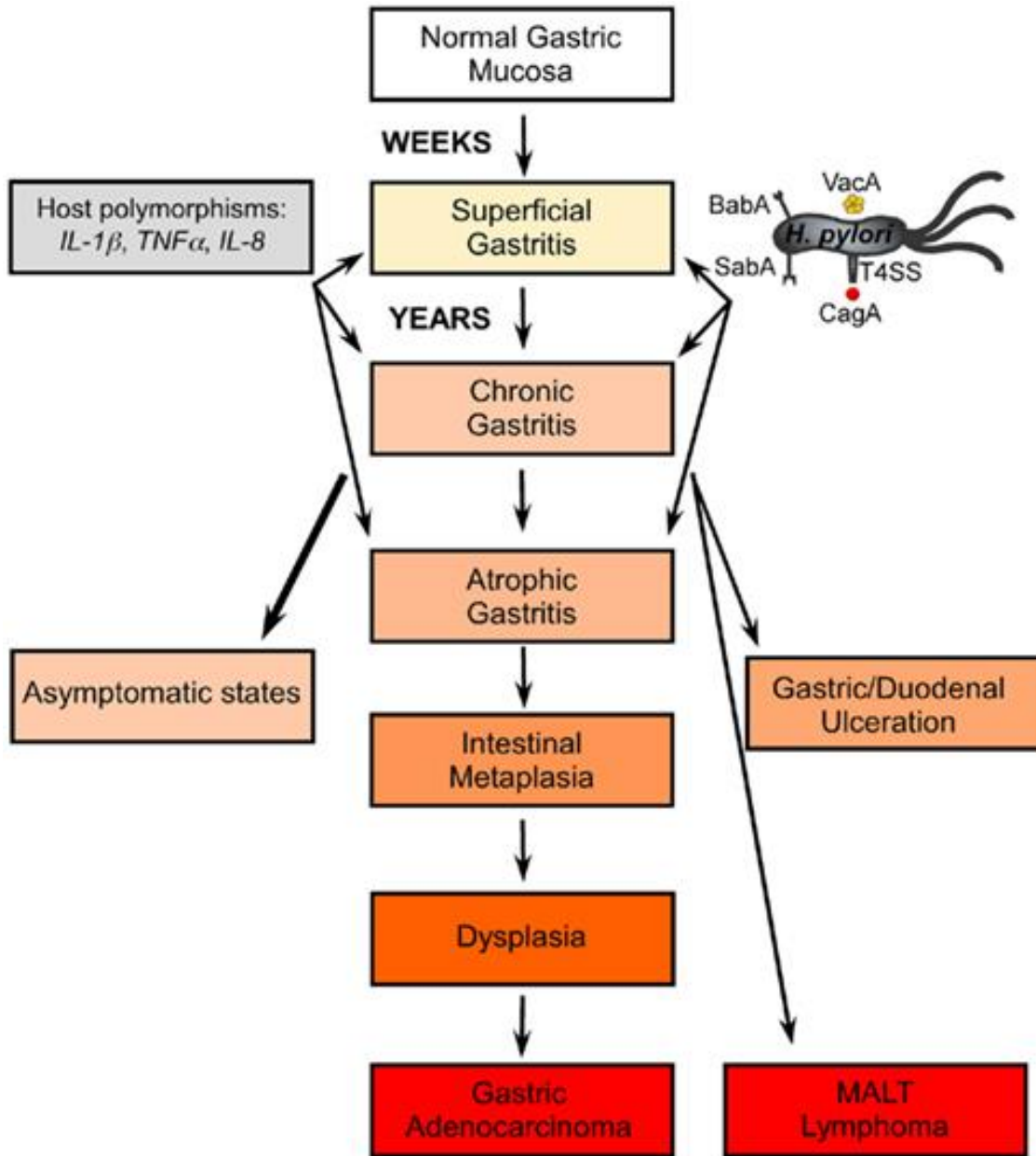
EBV (DNA)

vIL10 - viral cytokine

- Pirated (evolution)
- Inhibits M/M T cell activation

# Microbial HBV/HCV (DNA/RNA)





## Microbial

### Helicobacter pylori

Gastric adenocarcinomas  
& MALT lymphomas

Similar scenario to HBV  
(chr. inflammation/ROS)