Virus-associated human cancers

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Content

Virus	Cancer
Hepatitis B Virus (HBV)	Hepatocellular Carcinoma (HCC)
Hepatitis C Virus (HCV)	
Human T-cell Lymphotropic Virus Type I (HTLV-1)	Adult T-Leukemia/Lymphoma (ATL)
Kaposi's Sarcoma-associated herpesvirus (KSHV)	Kaposi's Sarcoma (KS)
Epstein-Barr Virus (EBV)	Nasopharyngeal Carcinoma (NPC)
Human Papillomavirus (HPV)	Cervical Cancer

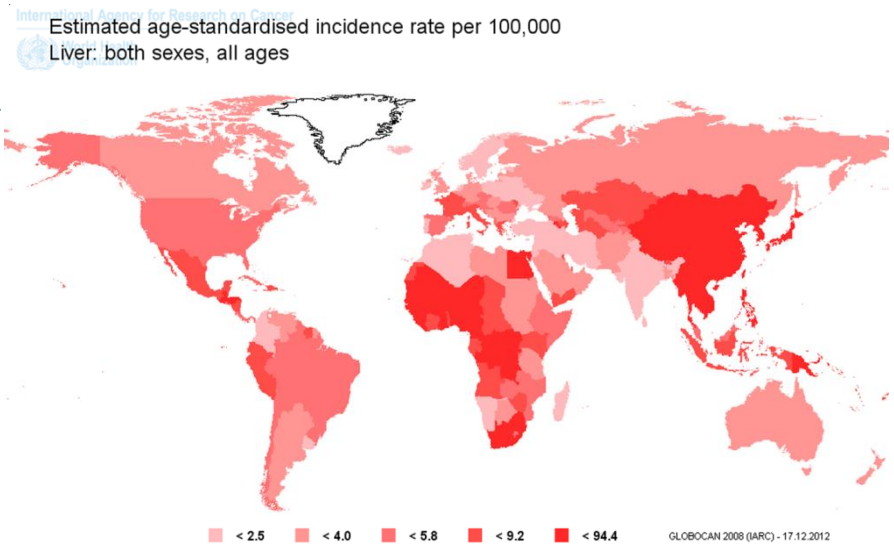
Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)

- Hepatocellular carcinoma (HCC)
  - Epidemiology
- Structure of HBV and HCV
  - Mechanism of pathogenesis

Hepatocellular carcinoma (HCC)

Epidemiology

- Eastern and Southeast Asia
- Sub-saharan Africa



Incidence

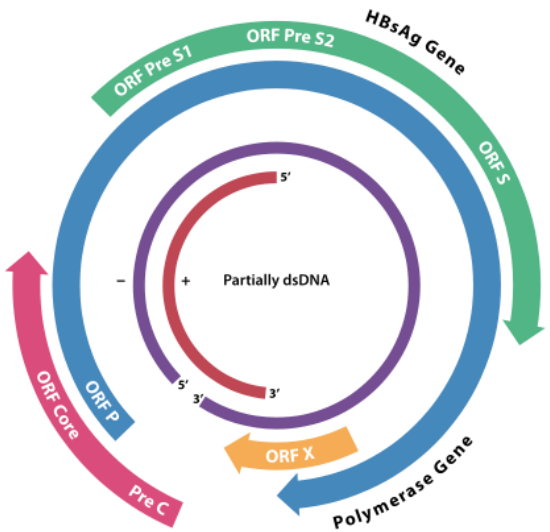
- 310,000 annually
- 140,000 in China alone
  - Infect during neonatal period → chronic → HCC
  - Infect in adulthood → seldom chronic → rare in tumor formation
- Predominant in men

Hepatocellular carcinoma (HCC)

- HBV
  - Perinatal transmission
  - Unsafe blood transfusion
  - Unsafe sexual contact

Hepatitis B Virus (HBV)

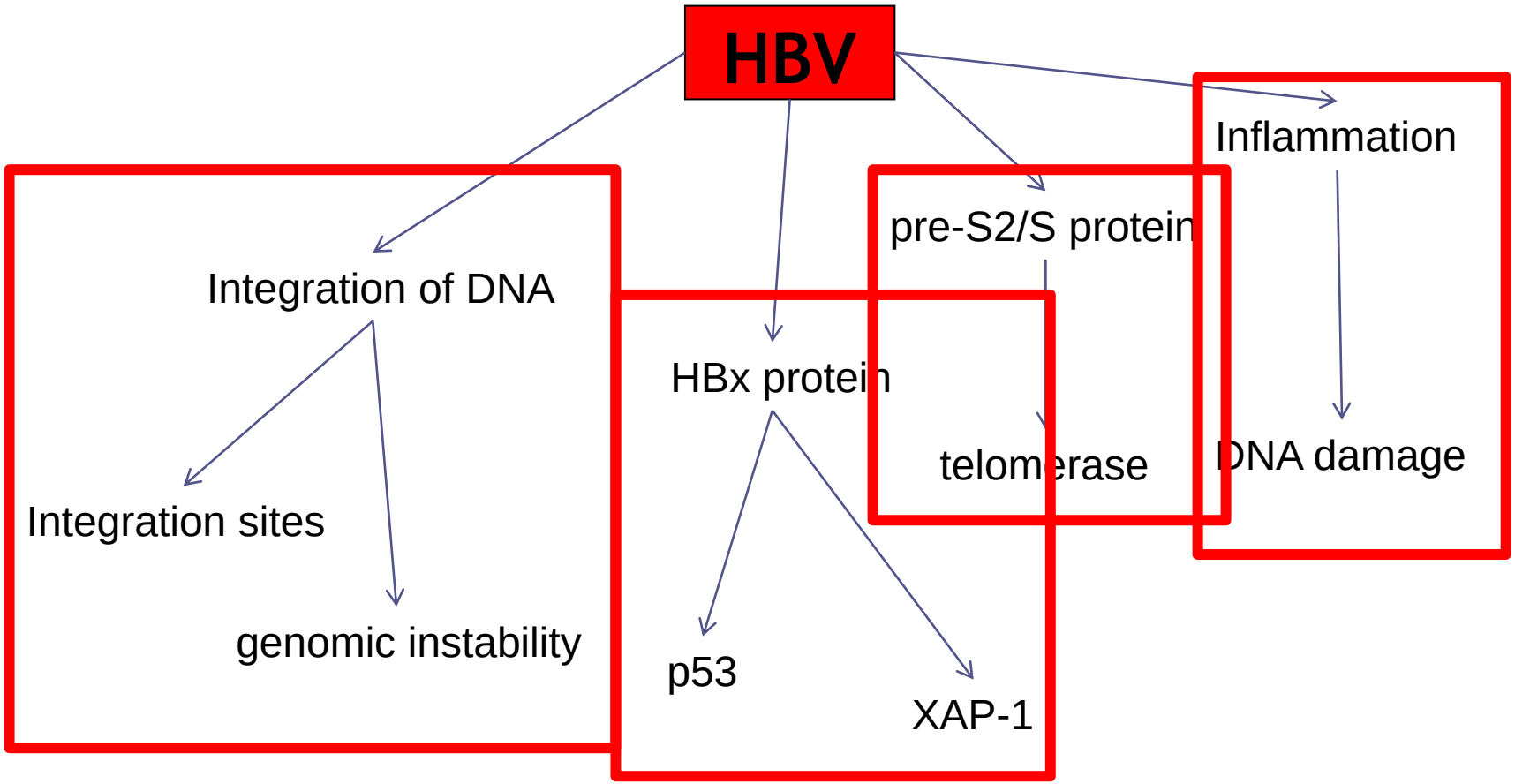
- Structure
  - Enveloped (HBsAg)
  - Nucleocapsid (HBcAg)
  - Viral genome: partially double-stranded DNA
  - 4 ORFs:
    enveloped,
    core,
    polymerase,
    X protein



Organisation of the hepatitis B virus genome

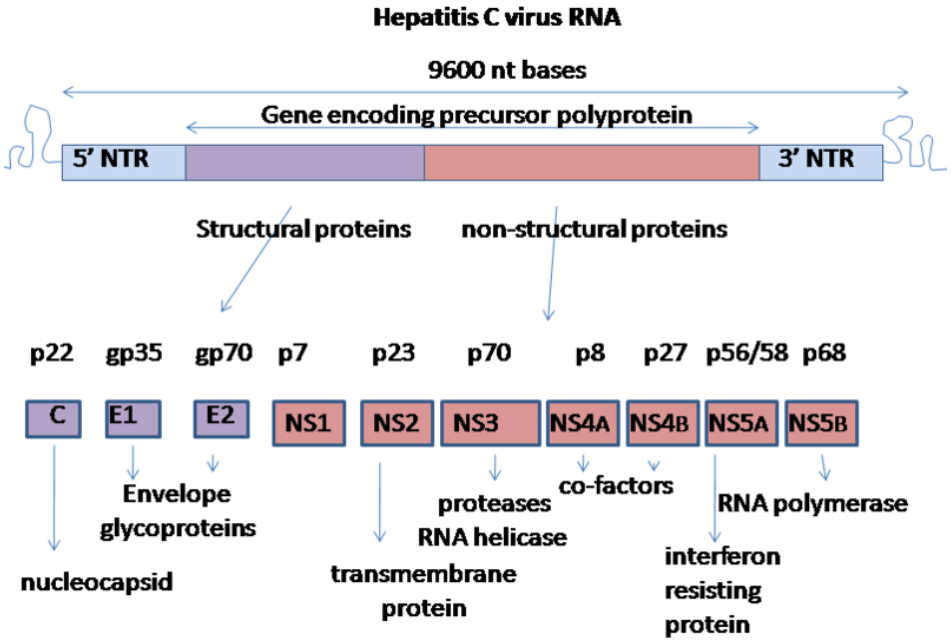
Hepatitis B Virus (HBV)

Mechanism of pathogenesis

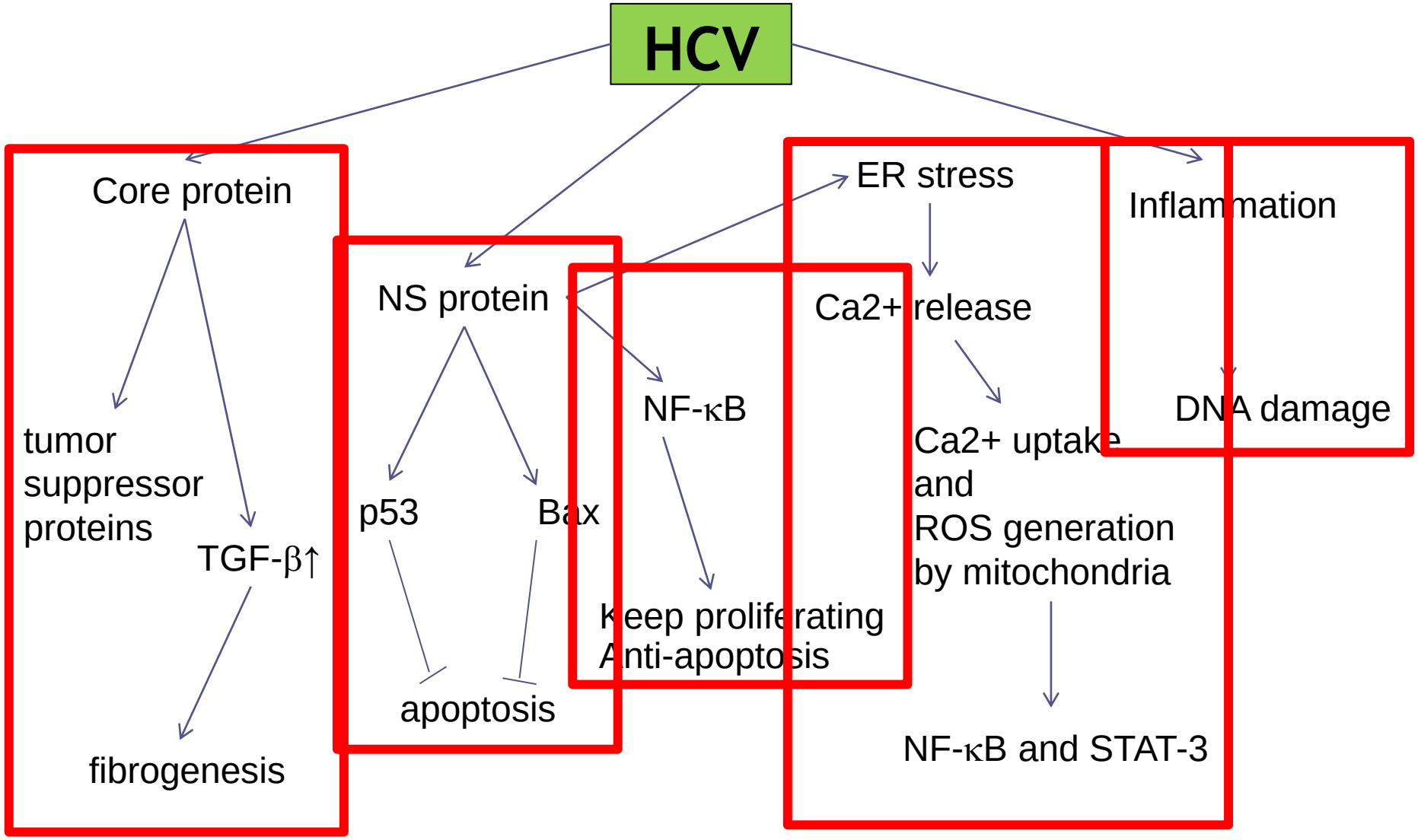


Hepatitis C Virus (HCV)

- Structure
  - Enveloped: with 2 envelope glycoprotein E1, E2
  - Single positive-stranded RNA: (+)ssRNA
  - Encode:
    structural
      core protein
      envelope glycoprotein
        E1 and E2
    and non-structural protein
      p7, NS proteins



Hepatitis C Virus (HCV)



Human T-cell Lymphotropic Virus Type I (HTLV-I)

- Structure
- Adult T-Leukemia (ATL)
  - Epidemiology
    Transmission
  - Pathogenesis of ATL

Human T-cell Lymphotropic Virus Type I (HTLV-I)

- Structure
  - Single-stranded RNA virus
  - Delta-retrovirus
  - Carry genetic information for structural proteins and enzymes (gag, env, pol, pX region)
  - pX region encode viral regulatory proteins e.g. Tax, HTLV-1 bZIP factor (HBZ) etc
  - Target on CD4+ T-cell

→ Adult T-Leukemia (ATL)

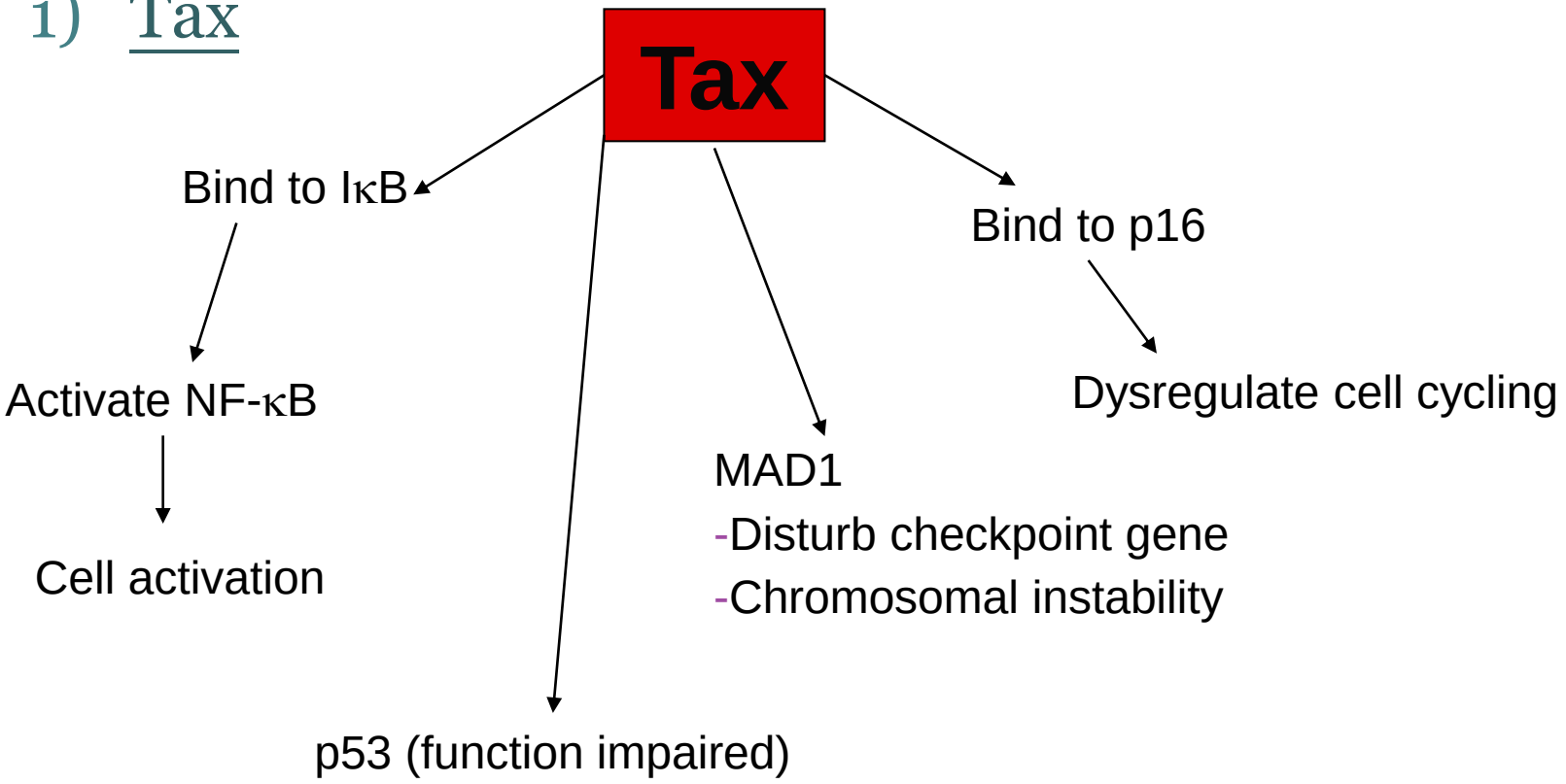
Human T-cell Lymphotropic Virus Type I (HTLV-I)

- Adult T-Leukemia (ATL)
  - Epidemiology
    - 1 million HTLV-1 carriers in Japan (90, 12)
    - Incidence of ATL among HTLV-1 carriers
      61/100,000 HTLV-1 carriers (2010)
    - Annual incidence:
      8.7/100,000 men (age>30 years) (95-04)
      5.5/100,000 women (age>30 years) (95-04)
    - Mortality: 1,000 people die of ATL each year in Japan (98-08)
  - Transmission:
    - sexual contact, breastfeeding, blood transfusion

Human T-cell Lymphotropic Virus Type I (HTLV-I)

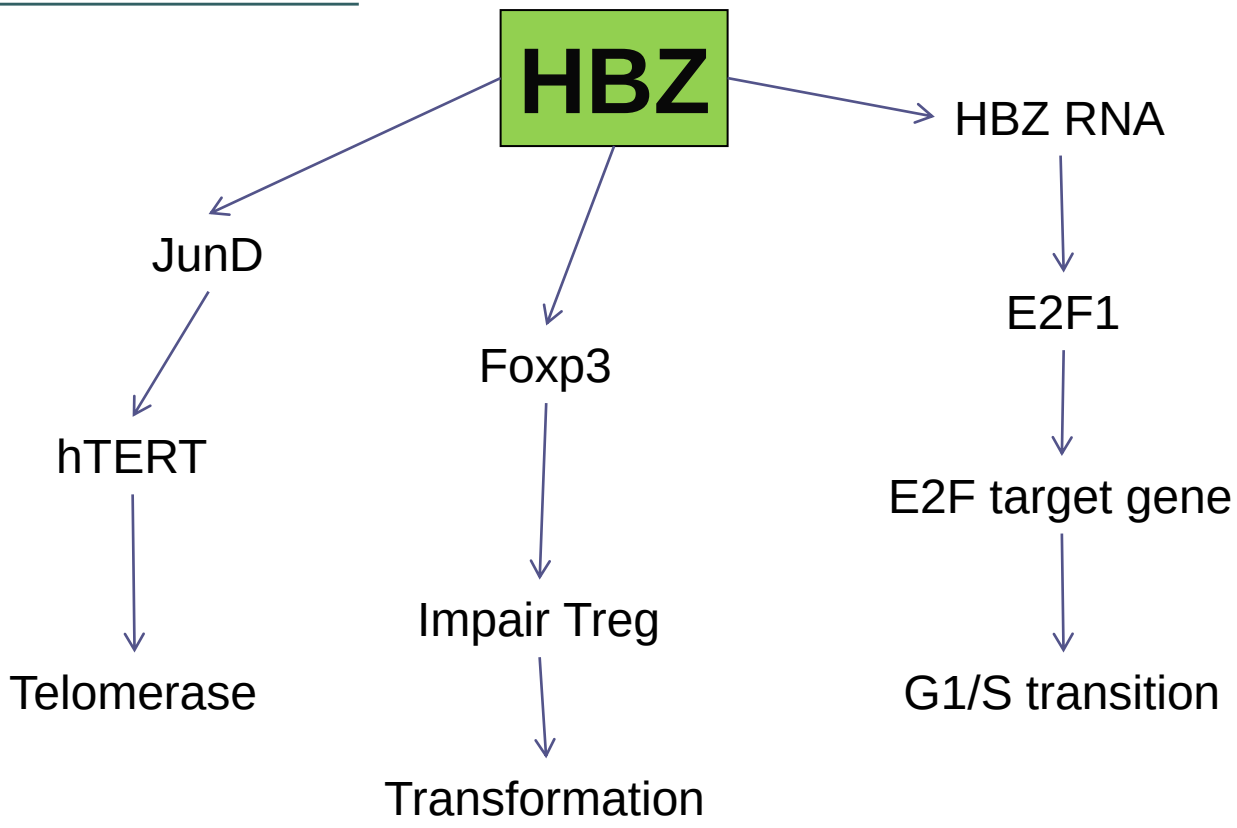
Pathogenesis of ATL

1) Tax



Human T-cell Lymphotropic Virus Type I (HTLV-I)

2) HTLV-1 bZIP factor



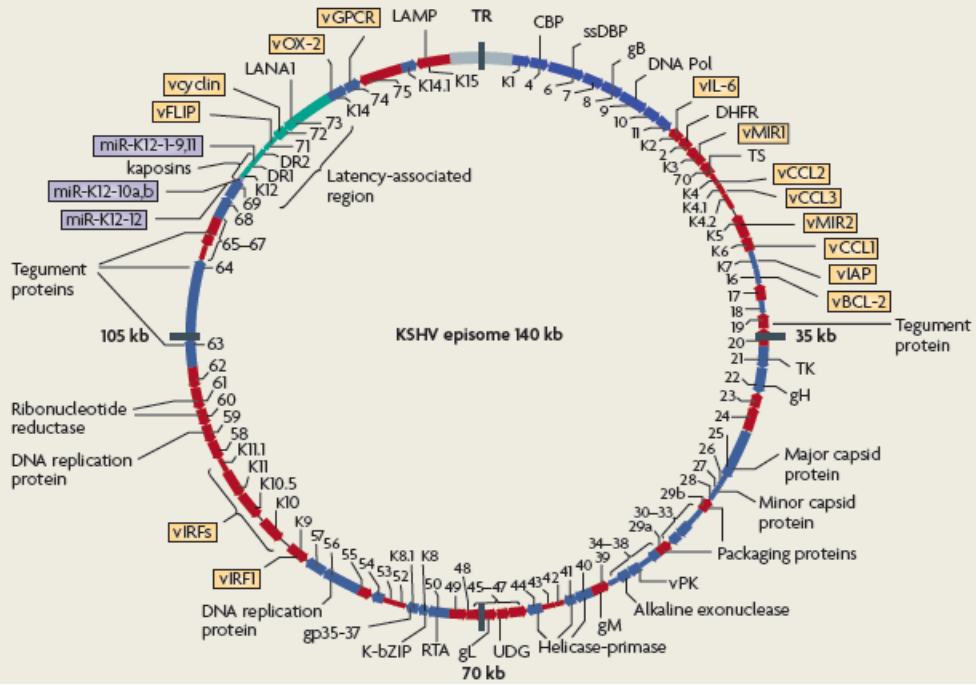
Kaposi's sarcoma-associated herpesvirus(KSHV)

- Structure
- Classification of Kaposi’s Sarcoma (KS)
- Pathogenesis of KS

Kaposi's sarcoma-associated herpesvirus (KSHV)

Structure

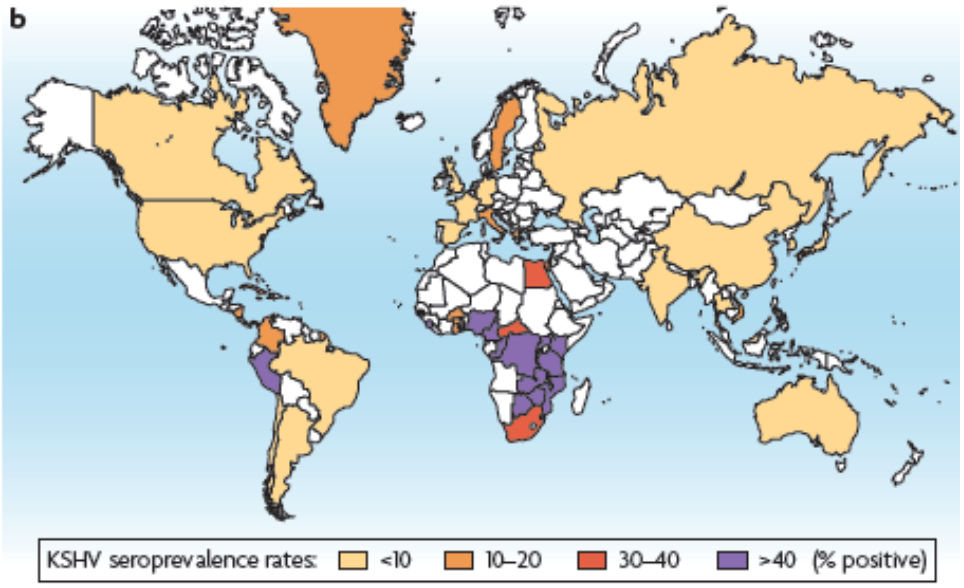
- Double-stranded DNA
- Early lytic genes
  - Viral proteins for DNA replication or viral gene expression
- and Late Lytic genes
  - Viral structural proteins for viral particle assembly



Kaposi's sarcoma-associated herpesvirus(KSHV)

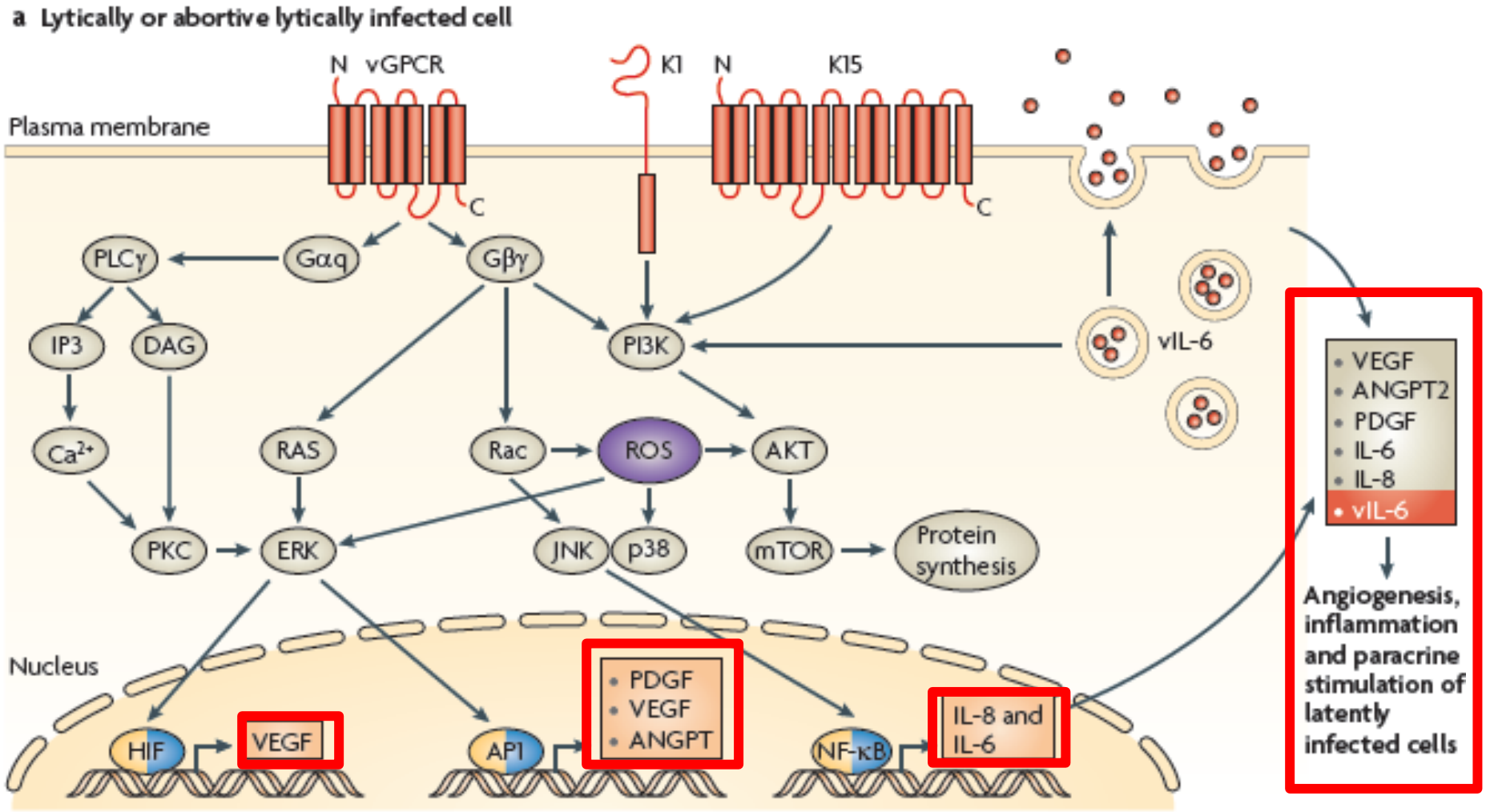
KS Classification

- Classic KS
  elderly men of Mediterranean or Eastern European Jewish
- Endemic KS
  Central and Eastern Africa
- AIDS-related KS
- Iatrogenic KS
  immunosuppressed individuals after organ transplant

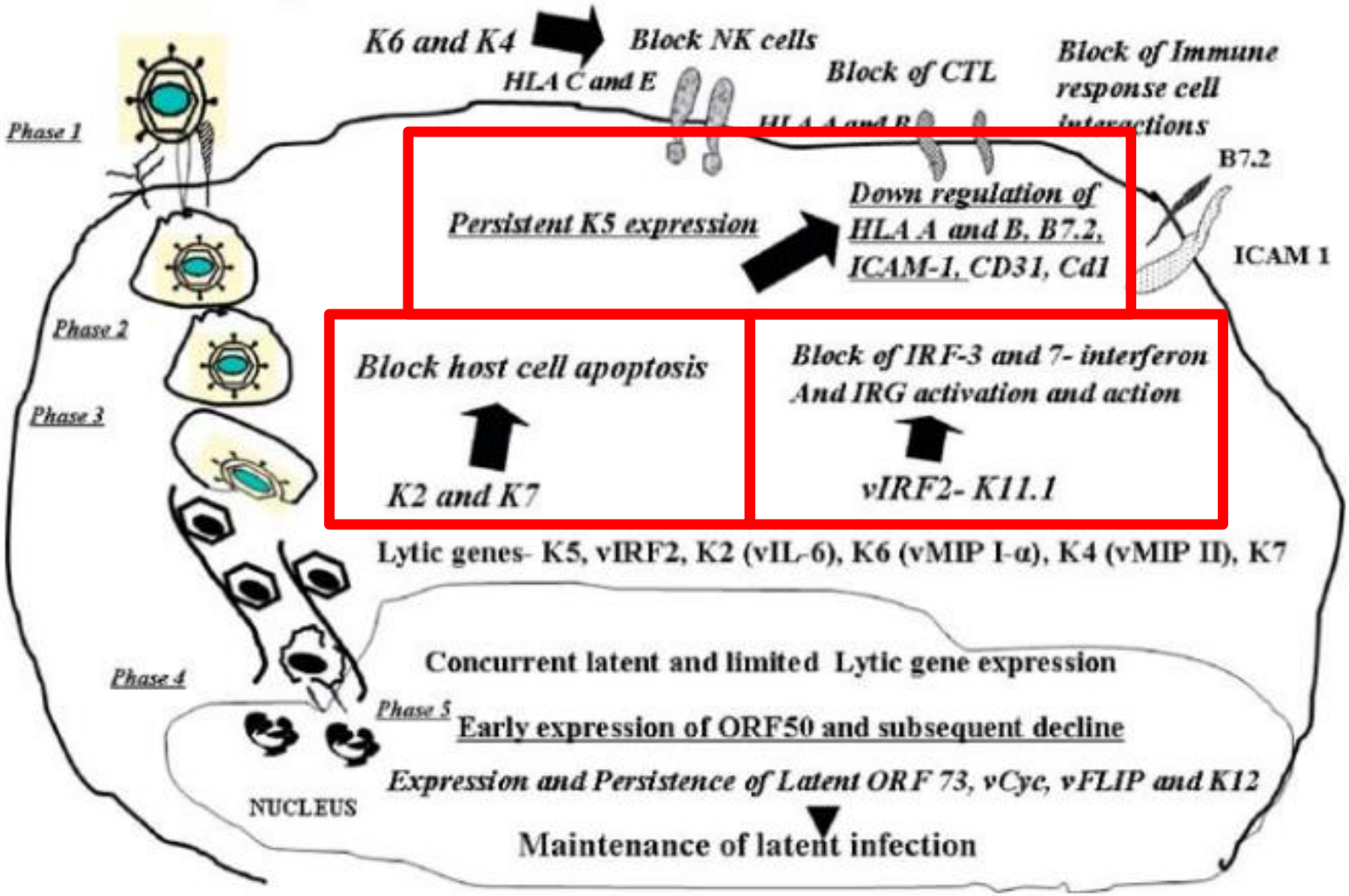


Kaposi's sarcoma-associated herpesvirus(KSHV)

Pathogenesis of KS



Kaposi's sarcoma-associated herpesvirus(KSHV)



Epstein–Barr virus (EBV)

- Structure
- Nasopharyngeal carcinoma (NPC)
- Pathogenesis of NPC

Epstein-Barr virus (EBV)

- Structure
  - Enveloped double-stranded DNA
  - Infect human B-lymphocyte, epithelial cells
  - Infect 90% population worldwide

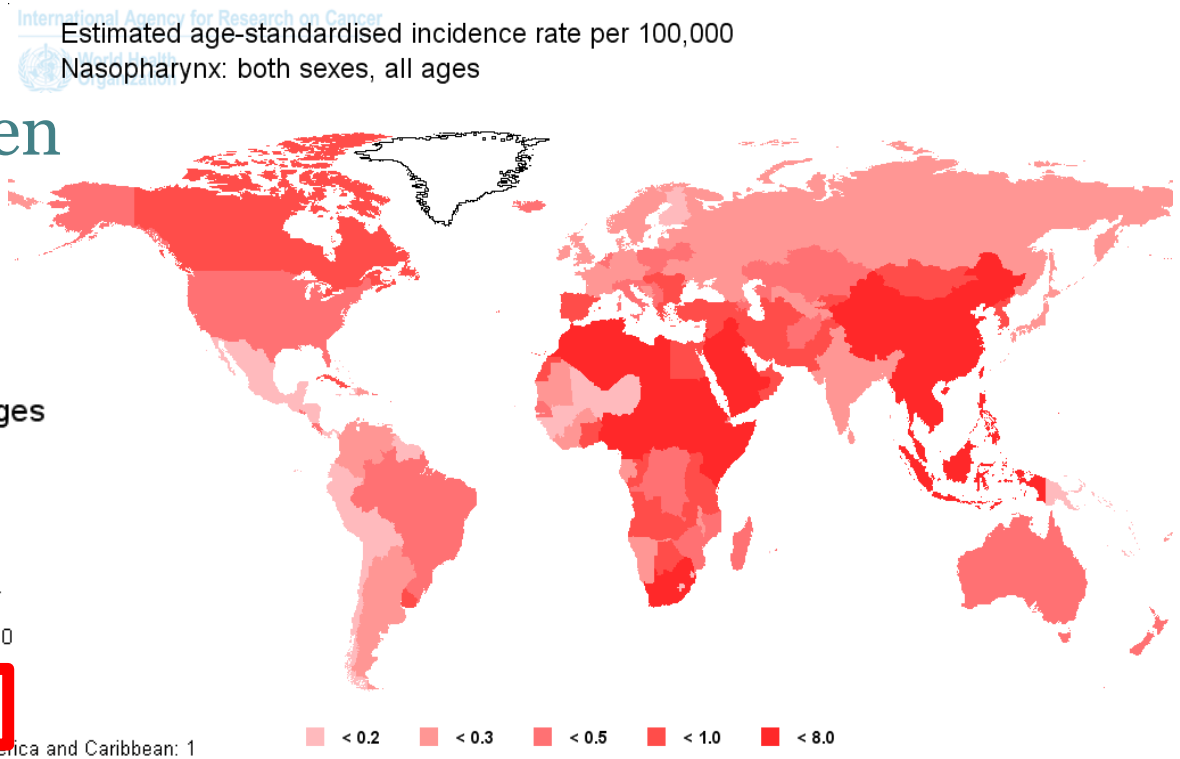
→ **Nasopharyngeal carcinoma (NPC)**

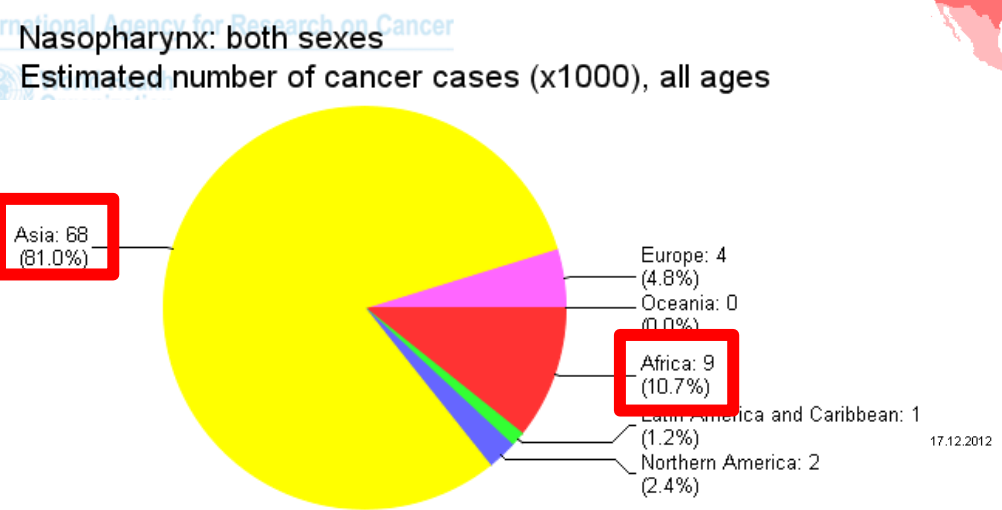
→ Burkitt's lymphoma (BL)

Epstein-Barr virus (EBV)

Nasopharyngeal carcinoma (NPC)

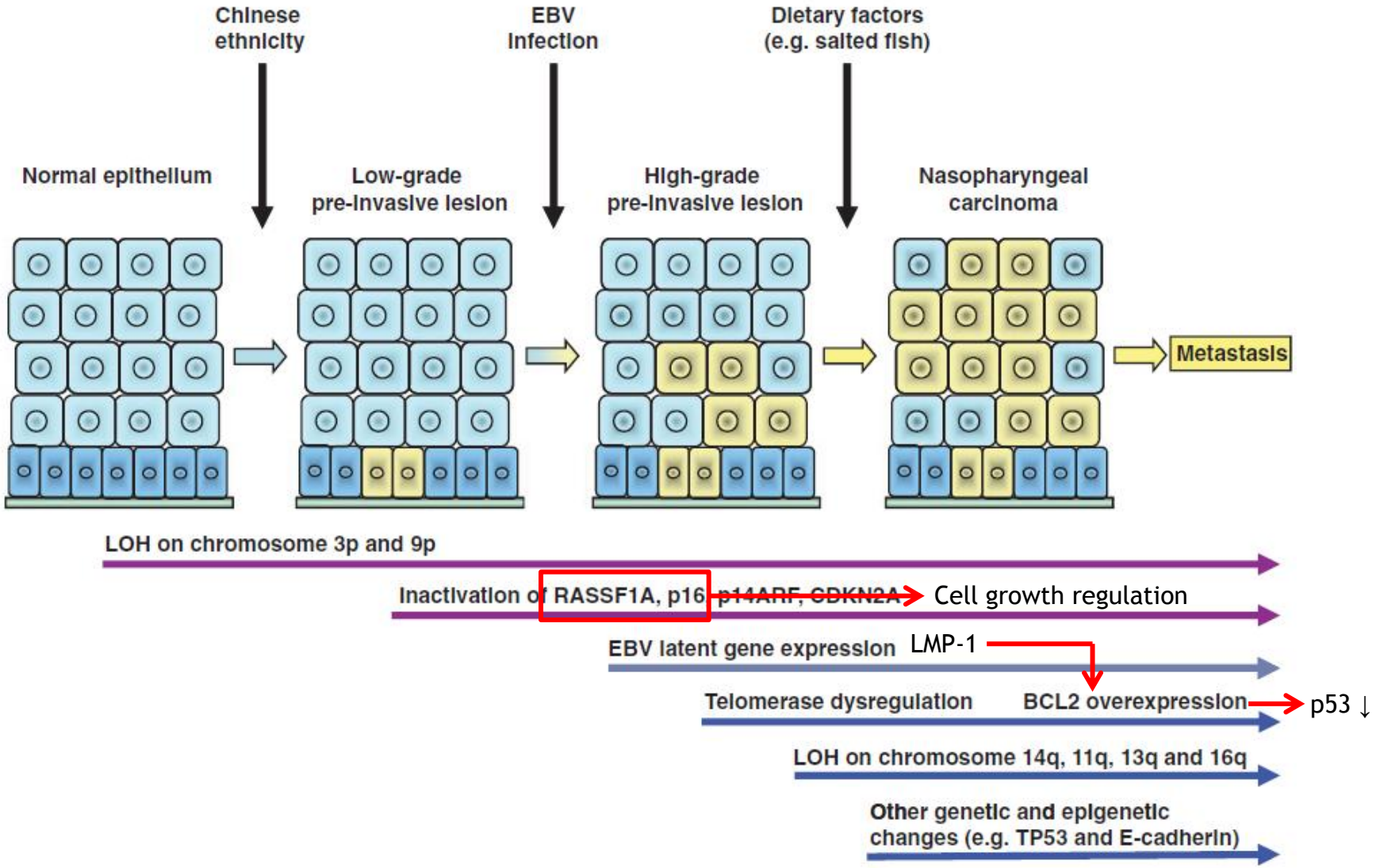
- Incidence: over 20/100,000 in Southern China
- Peak: 50-60 year
- Predominant in Men





Epstein-Barr virus (EBV)

Pathogenesis of NPC



Human papillomavirus (HPV)

- Structure
- Global burden of HPV
- Cervical cancer
- Pathogenesis of Cervical cancer

Human papillomavirus (HPV)

- Structure
  - Circular
    double-stranded DNA virus
  - Genome: about 8000 base pairs
  - 3 regions: early, late, long control region (LCR)
  - Encode viral proteins:
    Early: E6, E7, E1, E2, E4, E5
    Late: L1, L2
    LCR: contain promoter and enhancer for viral replication

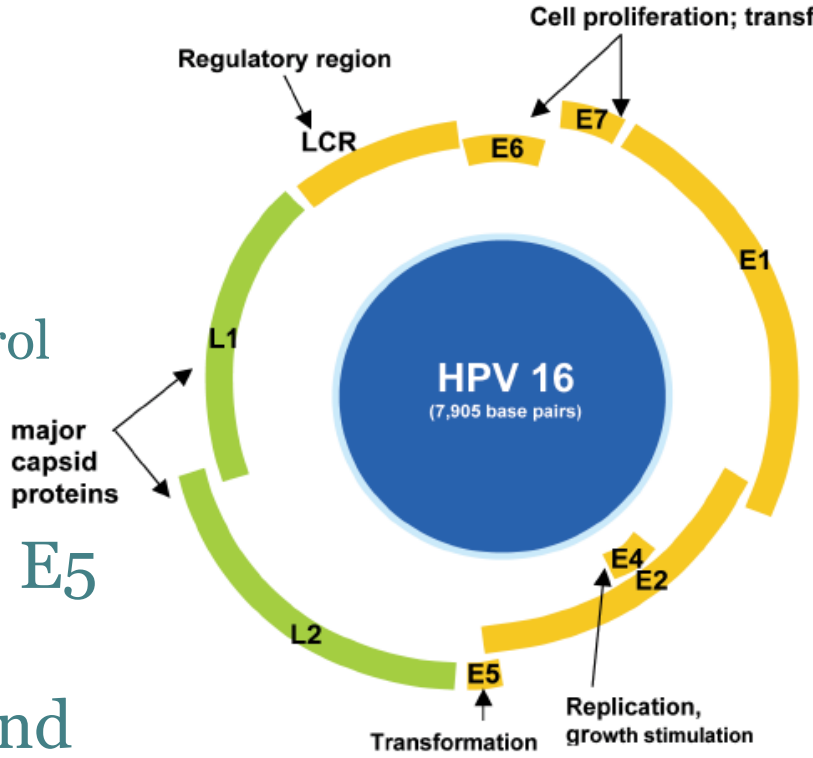
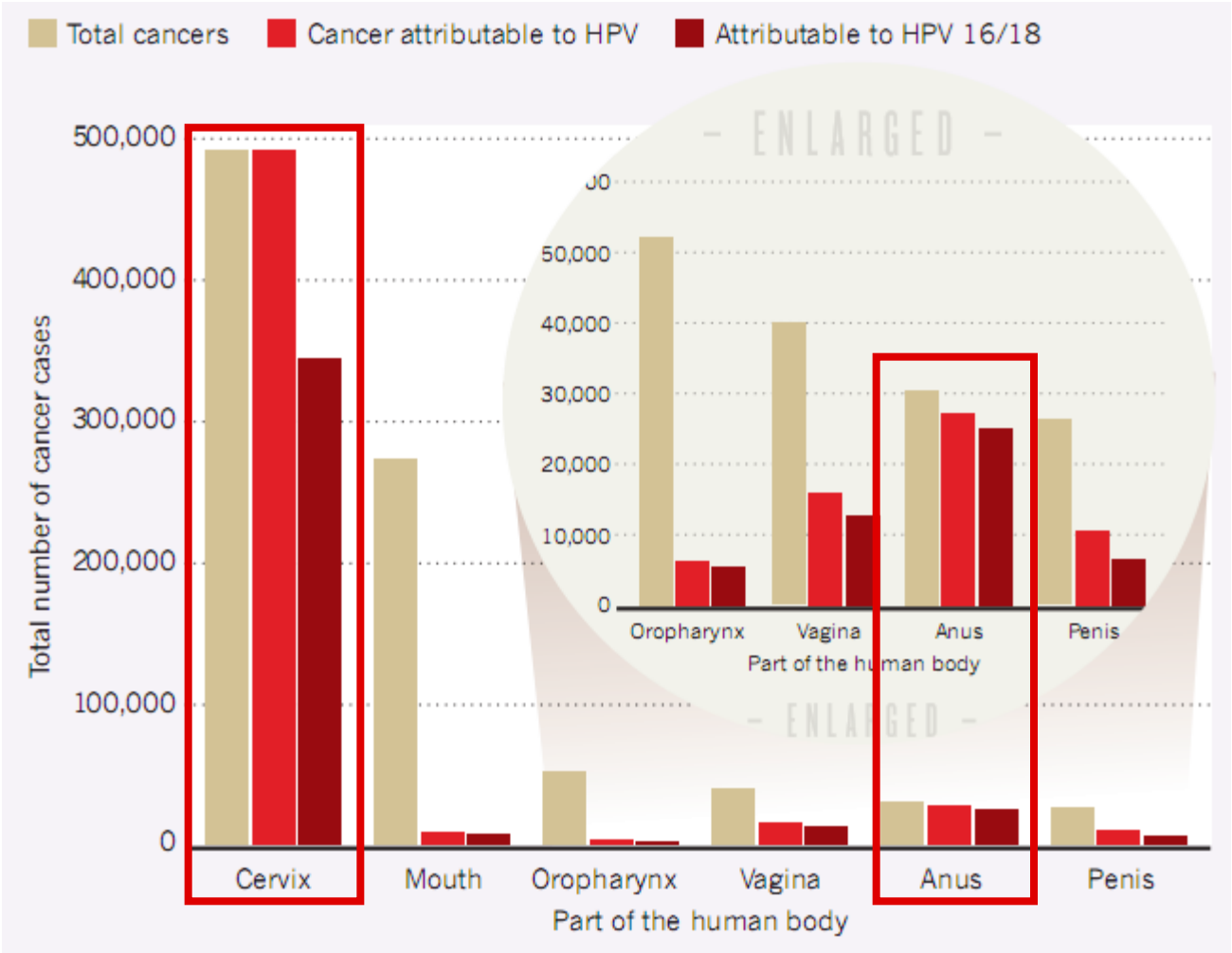


Figure 1 General organization of the HPV genome.

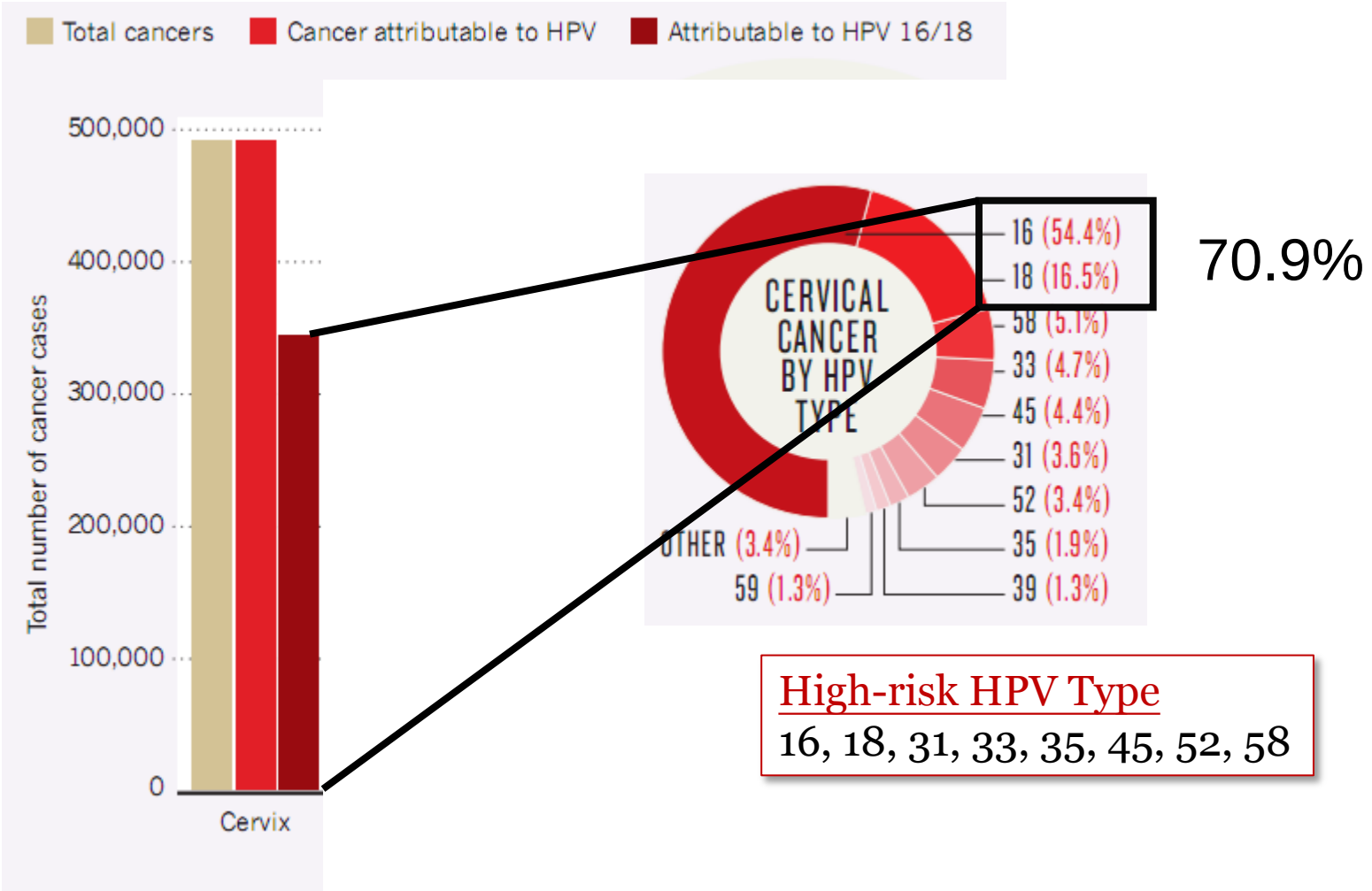
Human papillomavirus (HPV)

- HPV-associated cancers



Human papillomavirus (HPV)

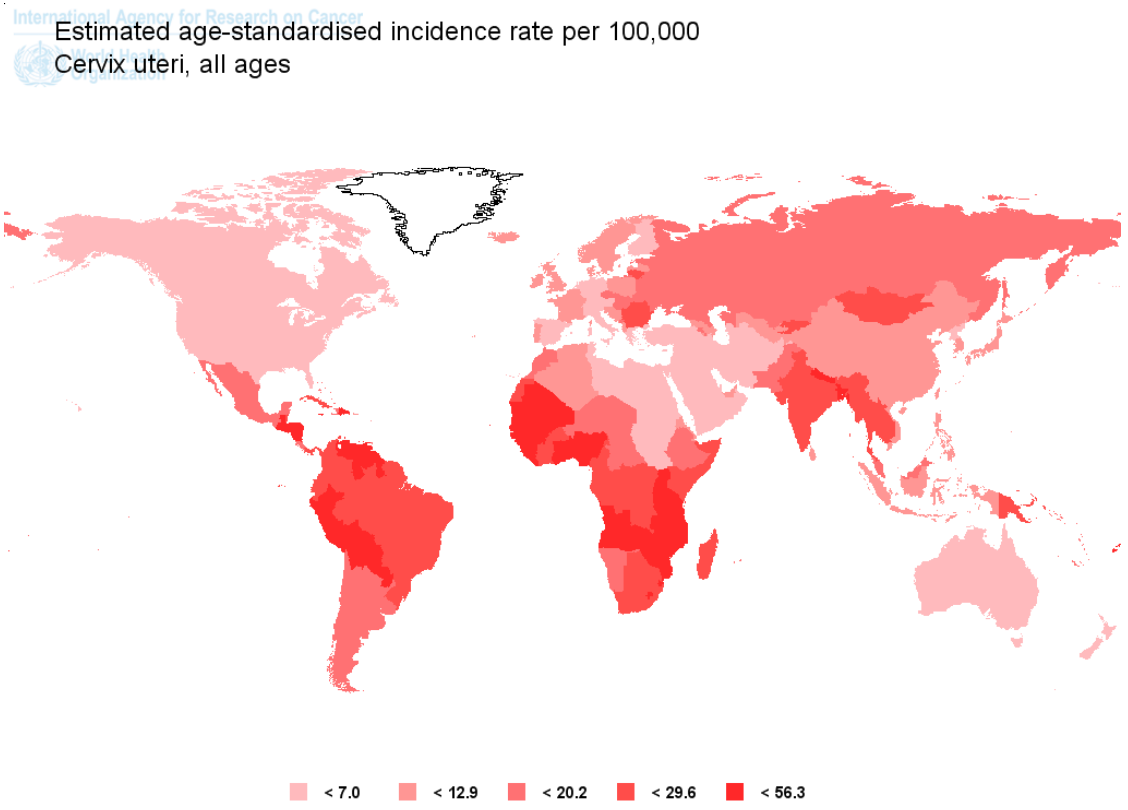
- HPV-associated cancers



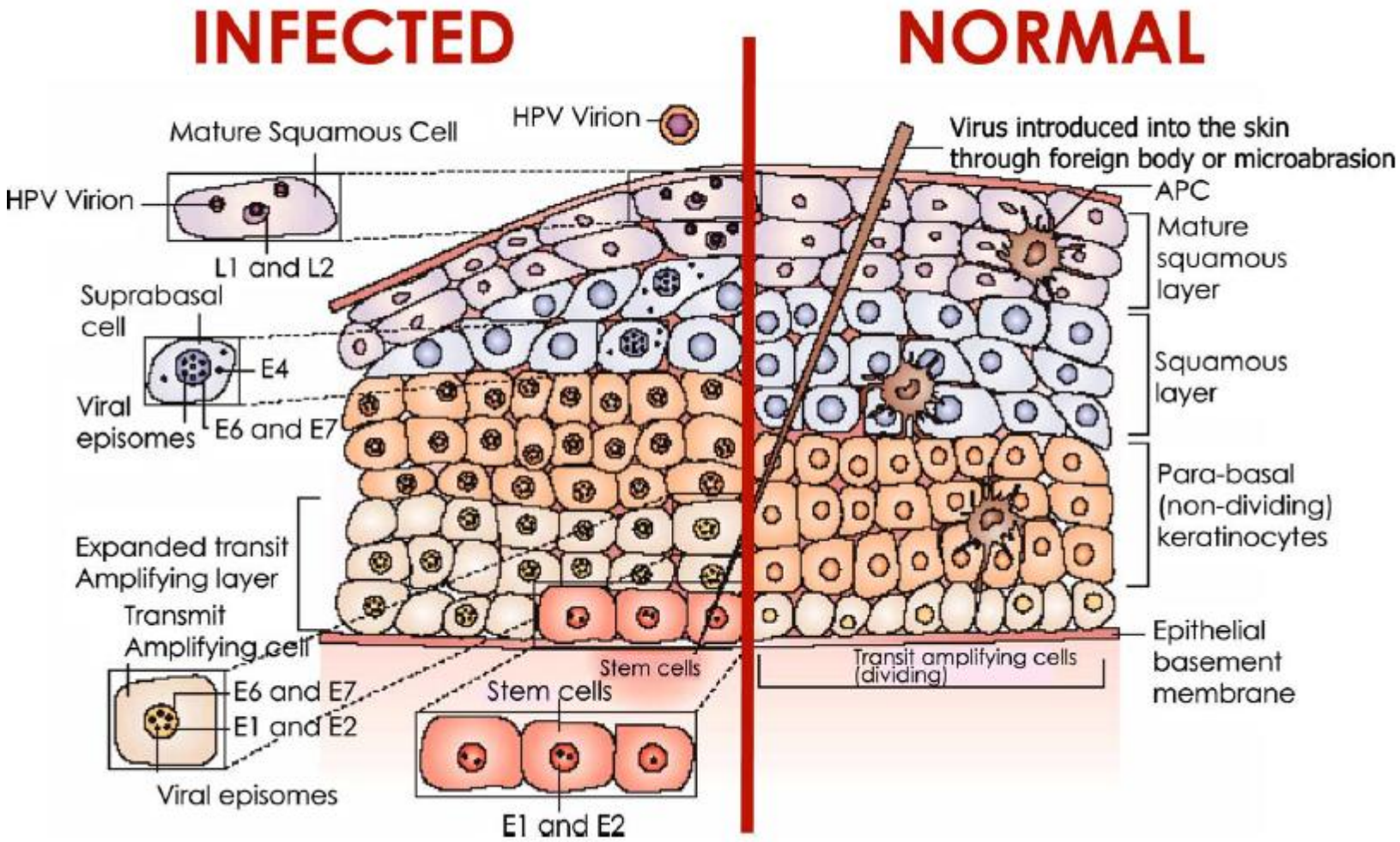
Human papillomavirus (HPV)

Cervical cancer

- Incidence: 493,243 women per year
- Mortality: 273,505 women
- In Asia and America:
  2nd most frequent cancer in women (age 15-44)
- In Africa:
  Most frequent cancer in women and women aged 15-44

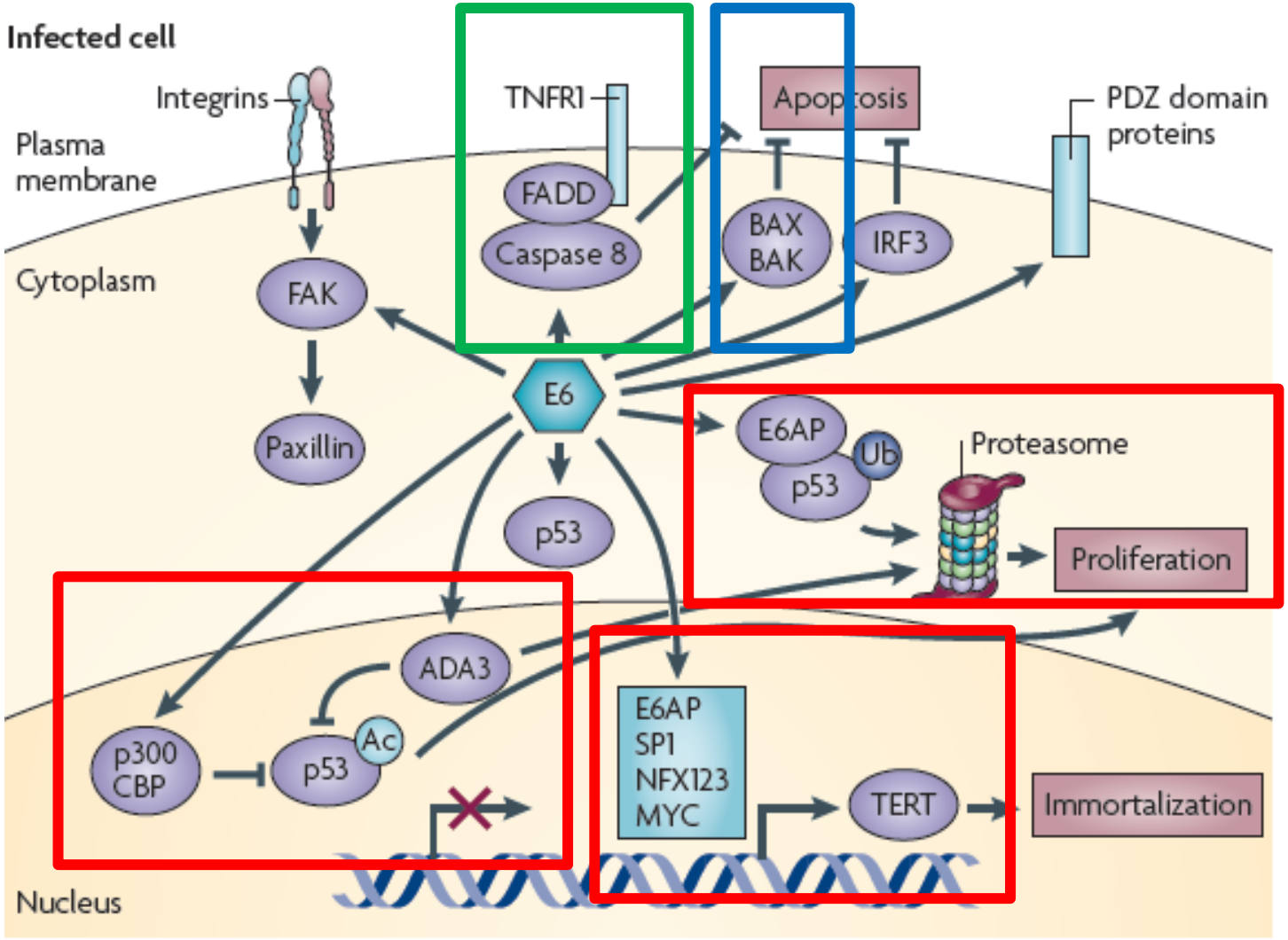


Human papillomavirus (HPV)



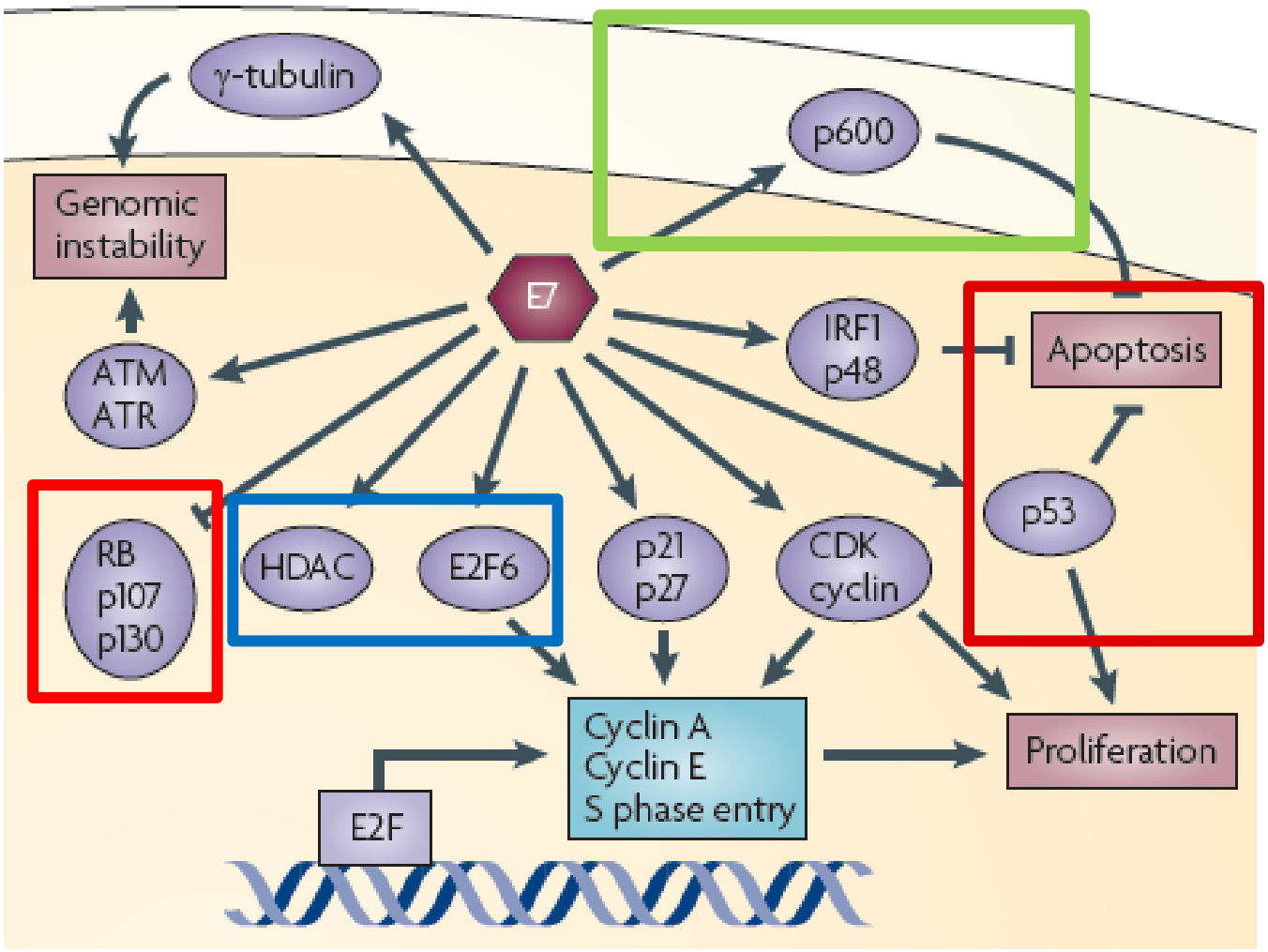
Human papillomavirus (HPV)

E6 oncoprotein



Human papillomavirus (HPV)

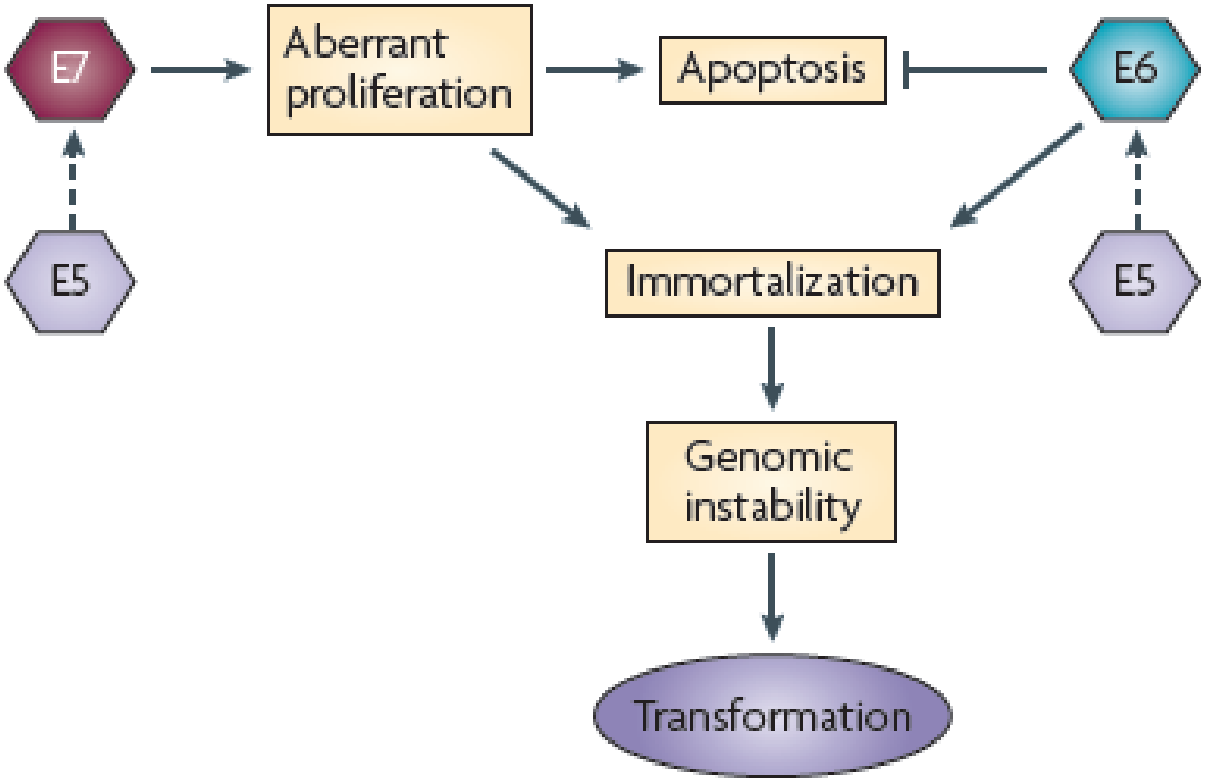
E7 oncoprotein



Human papillomavirus (HPV)

E5 oncoprotein

- Expressed together with either E6 or E7
  → greater tumor burden



Summary

Virus	Cancer
Hepatitis B Virus (HBV)	Hepatocellular Carcinoma (HCC)
Hepatitis C Virus (HCV)	
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Kaposi's Sarcoma-associated herpesvirus (KSHV)	Kaposi's Sarcoma (KS)
Epstein-Barr Virus (EBV)	Nasopharyngeal Carcinoma (NPC)
Human Papillomavirus (HPV)	Cervical Cancer

- Cell activation, proliferation
- Inhibit apoptosis : targeting p53 and other proteins

END

Thank you.