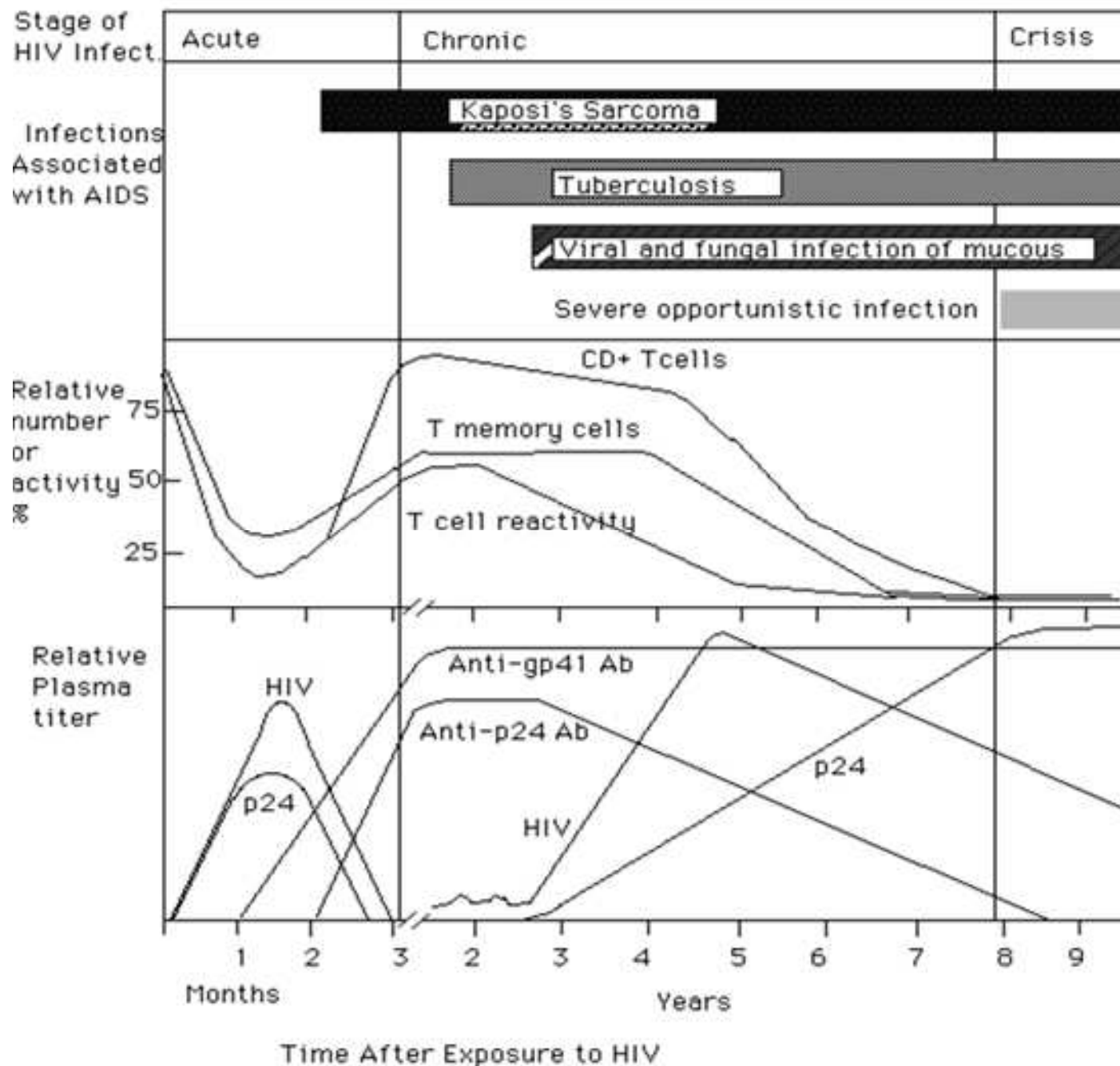


# AIDS-hez társult tumorok

**Nagy Károly**  
Orvosi Mikrobiológiai Intézet  
Semmelweis Egyeteme, Budapest



## A HIV fertőzés és az AIDS kialakulását kísérő események



# AIDS-hez társult malignitások

- Non-Hodgkin's lymphomák

  - immunoblastic lymphomák

  - diffuse large cell lymphomák

- Kaposi's sarcoma

- Primary effusion lymphomák

- Castleman's disease

- Hodgkin's lymphomák

- Squamous cell carcinoma

- Egyéb (ritka)

# Kaposi Mór



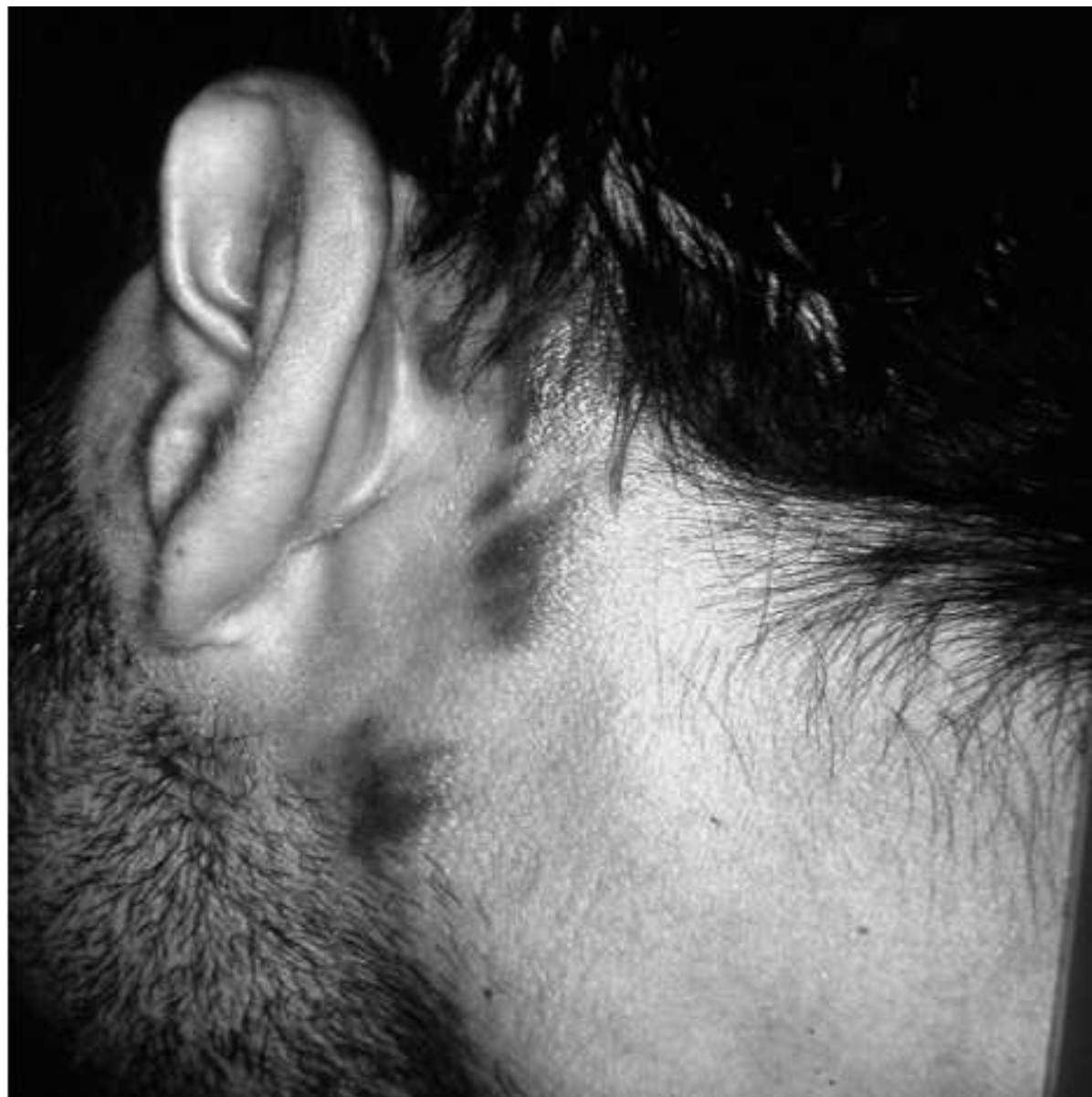
**Kaposvár**

**1837 – 1902**

**Vienna**



## AIDS-hez társult Kaposi sarcoma



## AIDS-hez társult Kaposi sarcoma



***Gammapherpesviridae***

***Rhadinoviruses***

HVS

EHV2

KSHV  
(HHV-8)

EBV  
(HHV-4)

Lymphocryptovirus

***Alphaherpesviridae***

HSV1 (HHV-1)

HSV2 (HHV-2)

EHV1

PRV

VZV (HHV-3)

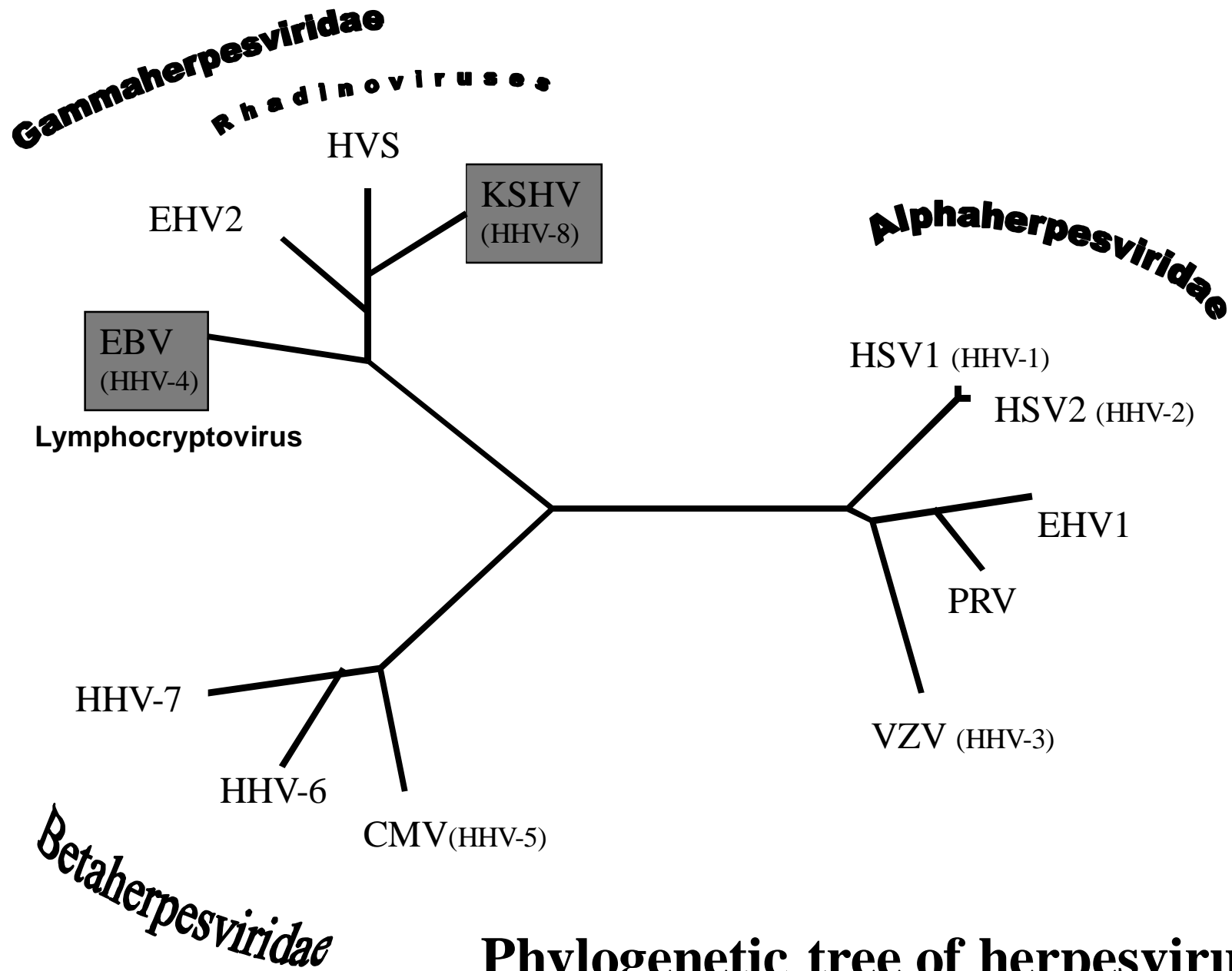
HHV-7

HHV-6

CMV (HHV-5)

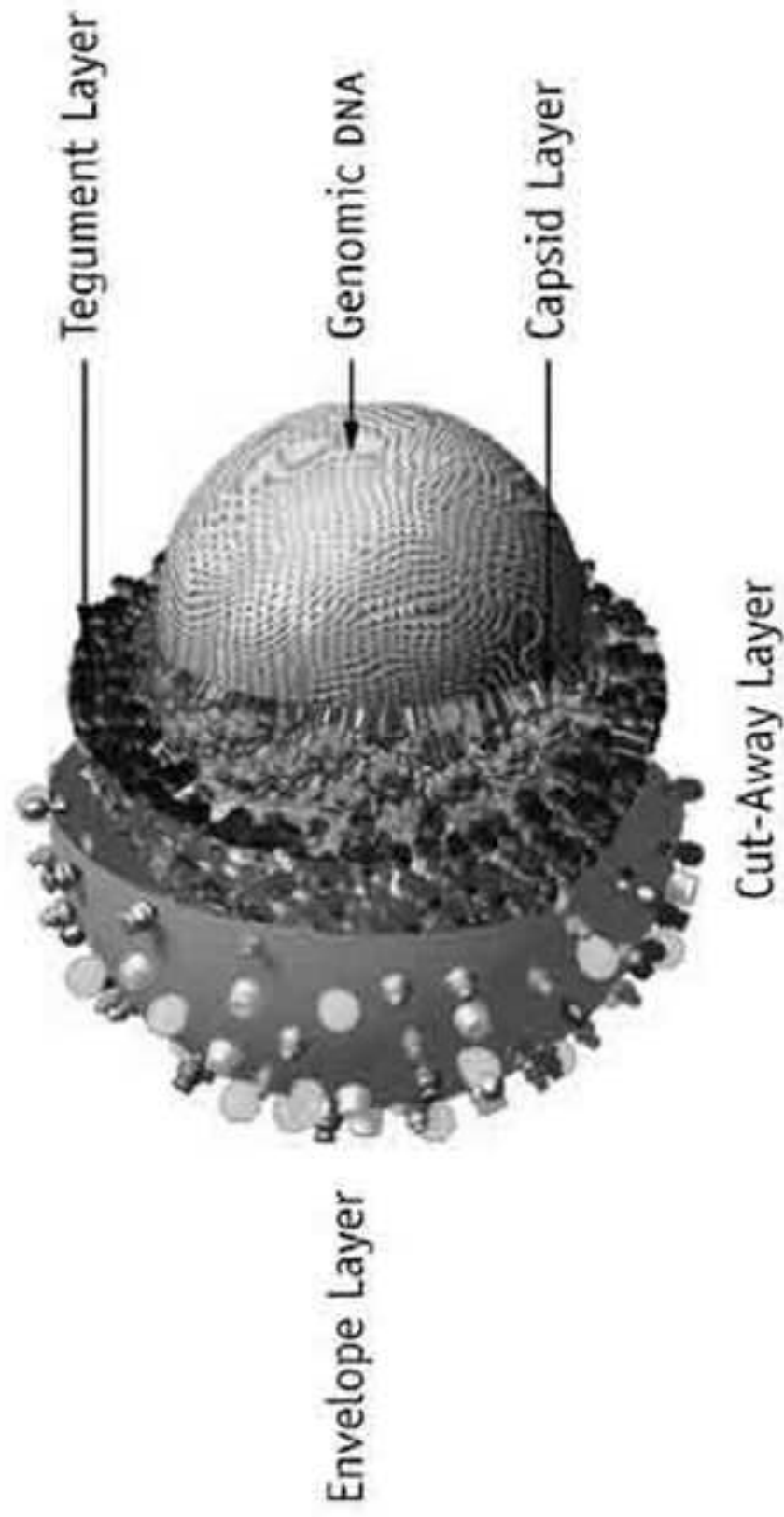
***Betaherpesviridae***

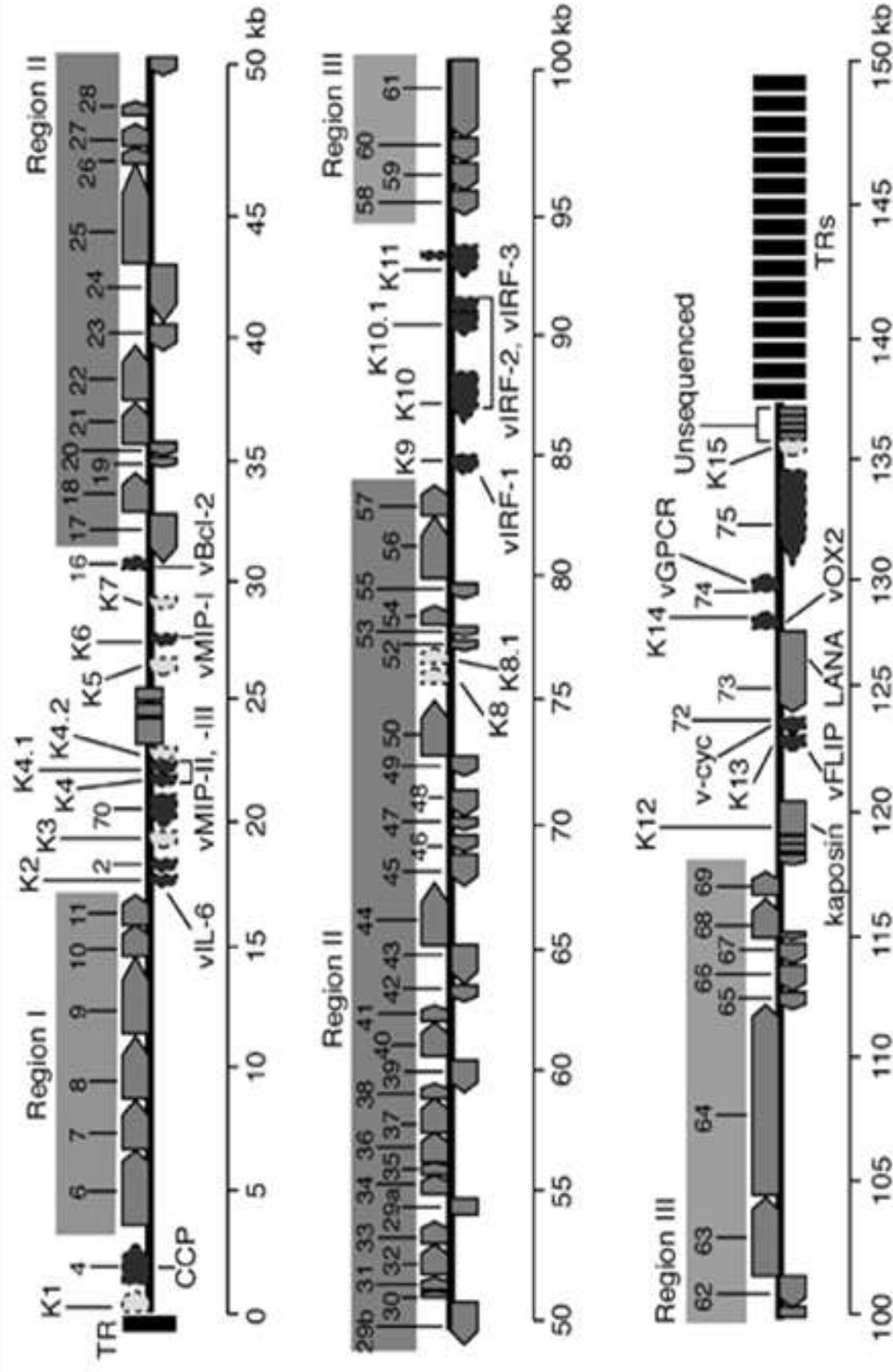
**Phylogenetic tree of herpesviruses**





## Kaposi's Sarcoma-Associated Herpesvirus (KSHV)





## The human herpesvirus 8 (HHV-8) genome


Expert Reviews in Molecular Medicine ©2001 Cambridge University Press

## Seroprevalence of HHV-8 antibodies\* in KS risk groups and in the general population

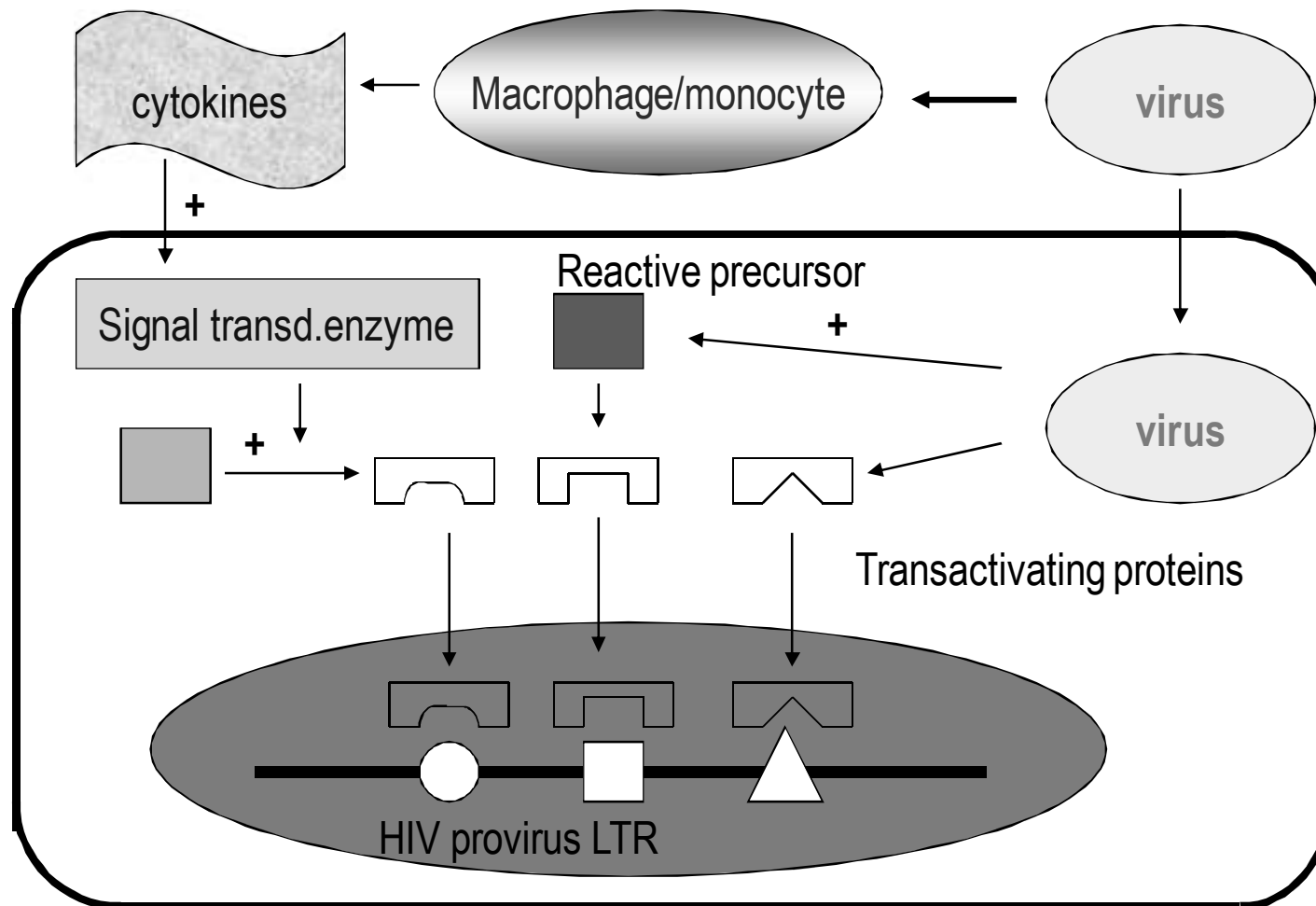
Groups	Sample	HHV-8 ab positive	
	#	#	%
Classic KS	28	25	~ 90
HIV+ / KS -	108	24	22.2
HIV - / KS -	90	1	1
STD patients	80	1	1.2
Dialysis patients	521	8	1.6
Healthy population	570	12	2.1
	1.397	71	

\* to LANA , by IIF and WB

## Association of HHV-8 and Kaposi's sarcoma

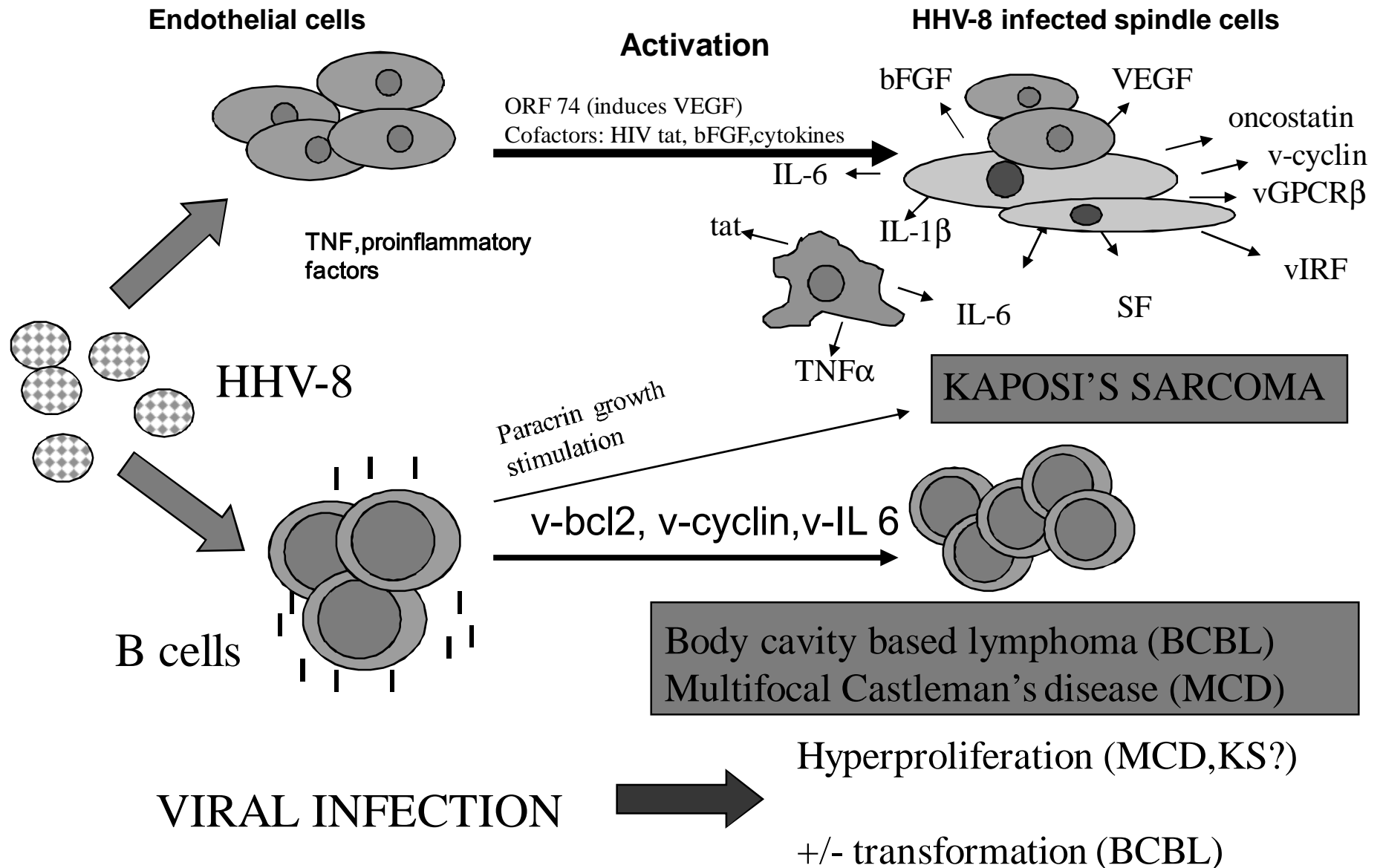
	Central Europe	Western Europe/USA
AIDS associated KS	7-10 %	25-30 %
HHV-8 DNA in KS lesion	>95%	>95 %
HHV-8 seroprevalence	22-25%	25-30 %
Iatrogenic KS	~22%	~ 5 %
per cent of all posstransplant tumor		
HHV-8 DNA in KS lesion	>90 %	>90 %
HHV-8 seroprevalence in population	~2%	1 - 4 %
HHV-8 sequence variability		
?	ORF26	97.5 %
	ORF 1	~95 %

# HERPESVIRUSES AS CO-FACTORS FOR OR PROMOTERS OF HIV INFECTION



Binding sites for transcriptional factors in HIV LTR

# TUMOR INDUCTION BY HHV-8



*Viral etiology of AIDS  
related malignancies*

***Additional factors in the etiology of AIDS related malignancies:***

- Immune suppression
- Immune dysregulation
- Molecular lesions of cancer-related genes
- P53 degradation
- LMP1 (TNFR) controls by growth and differentiation
- Inflammatory cytokines (vIL-6 vs. hIL-6)
- Adhesion molecules
- Growth factors



- Kaposi's sarcoma
- Primary effusion lymphomas
- Castleman Disease (multicentric  
angiolympho-proliferative hyperplasia)
- Non-Hodgkin lymphomas
  - B-immunoblastic lymphomas
  - small non-cleaved lymphomas (Burkitt  
lymphoma)
  - diffuse large cell lymphomas
- Hodgkin lymphomas
- Cervical cancers

**Oncogenic  
herpesviruses:**

**KSHV(HHV-8)**

**EBV(HHV-4)**

**Lenti-retroviruses:  
HIV-1**

**Human papilloma viruses:**

**HPV-16    HPV-18**

**Human T-cell leukemia  
virus:**

**HTLV-1**

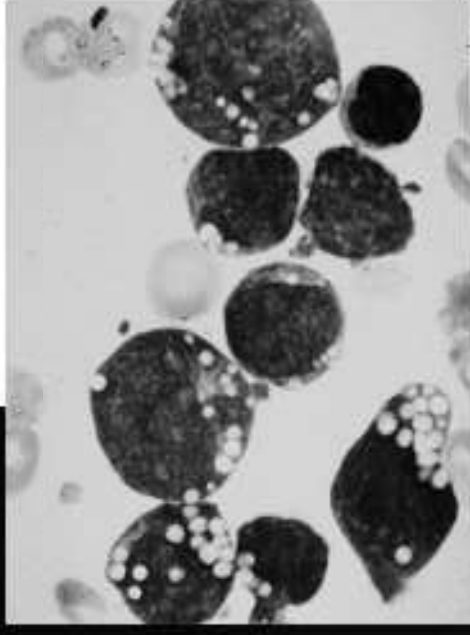
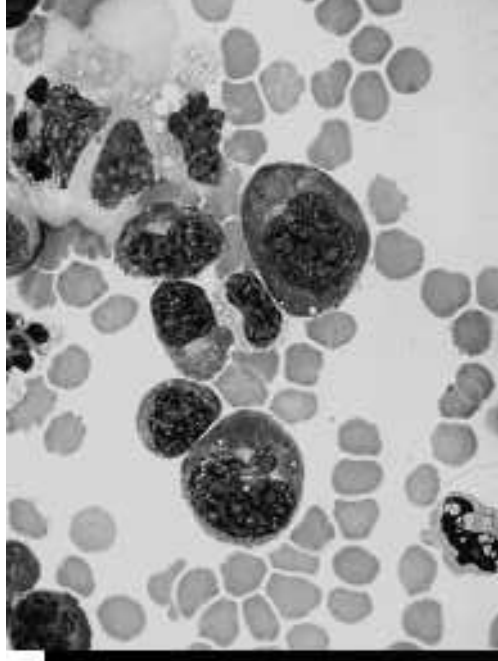
# Burkitt's Lymphoma vs Small Noncleaved Non-Burkitt's

## Burkitt's lymphoma

- High-grade tumor
- Uniform appearance of abnormal cells
- t(8;14); t(8;22) or t(8;2)
- Endemic in equatorial Africa

## Small noncleaved non-Burkitt's

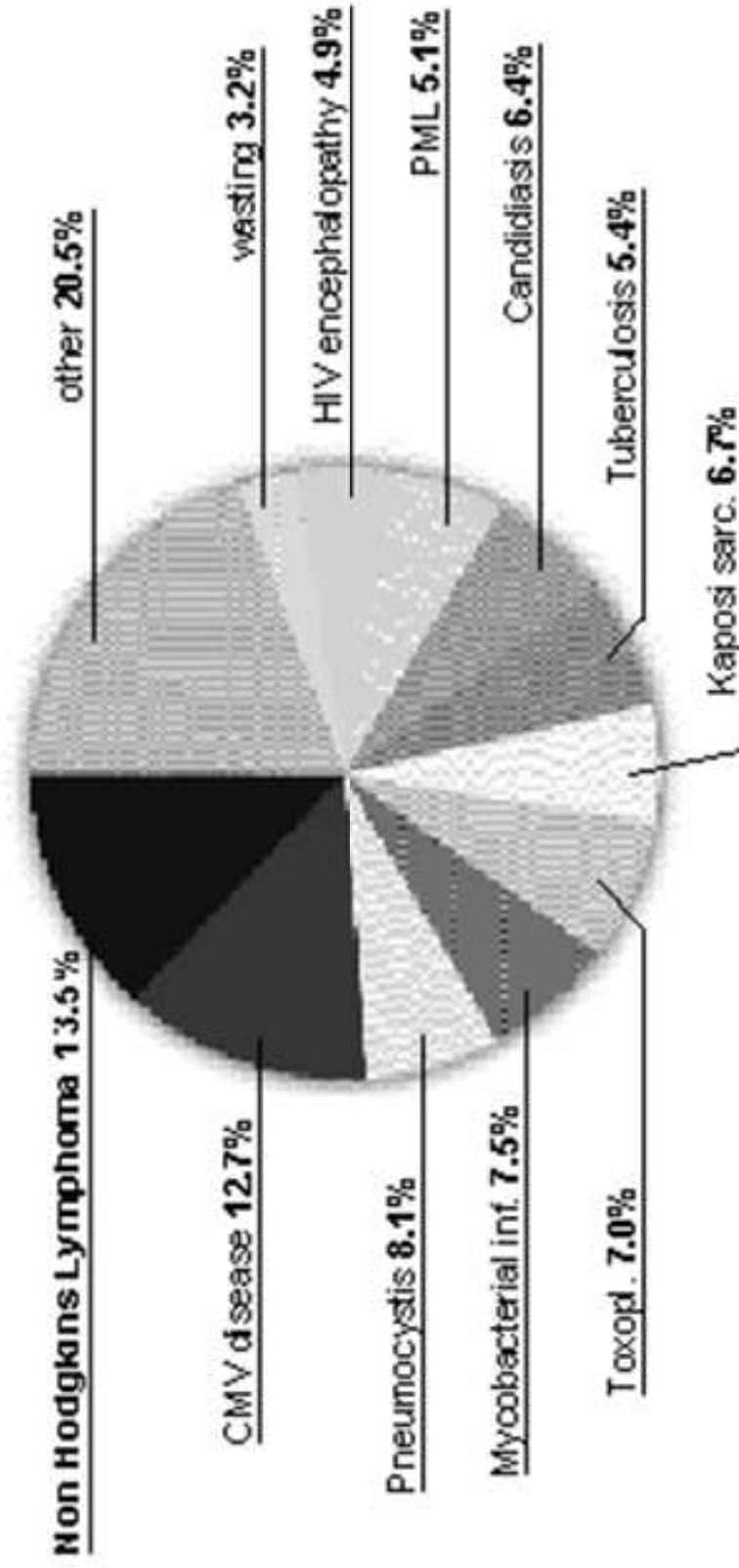
- High-grade tumor
- Variability in size and shape of abnormal cells
- t(8;14); t(8;22) or t(8;2)



## MOST COMMON AIDS-DEFINING DISEASES

among 217 AIDS-related deaths

figure 4



Charlotte Lewden, French "Mortalité 2000" study group, 9th CROI, Seattle, 25-28 February 2002 Abs. 753