

# *Viral subversion of the immune system*

*G. Gillet and A. Vanderplasschen*

*Immunology - Vaccinology  
Faculty of Veterinary Medicine  
University of Liège  
Belgium*

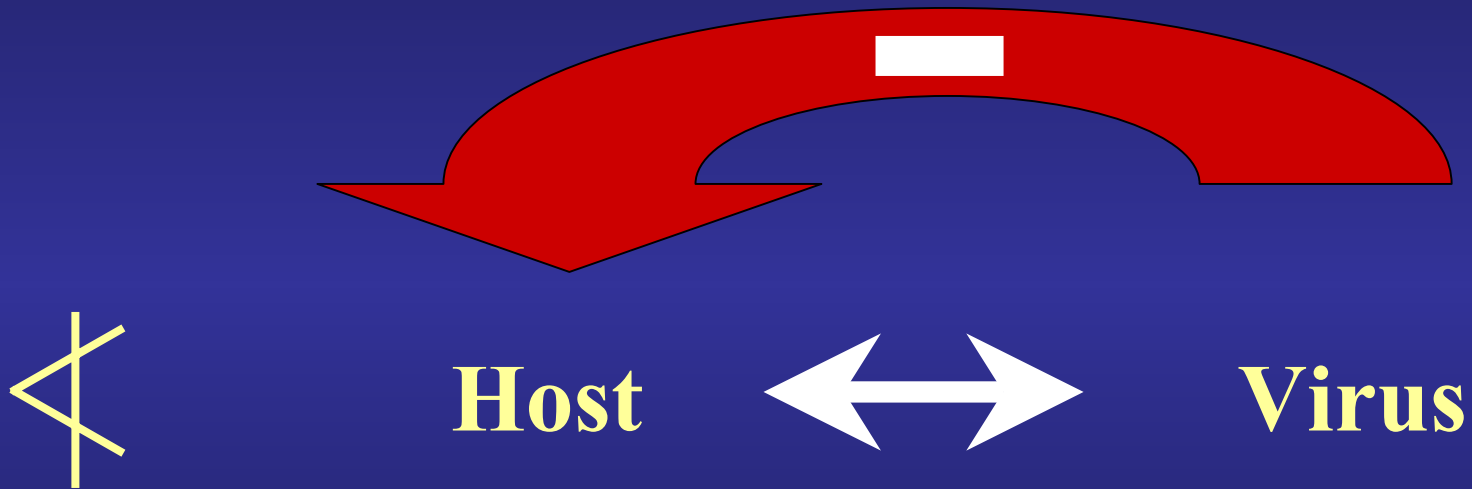


# Darwinism

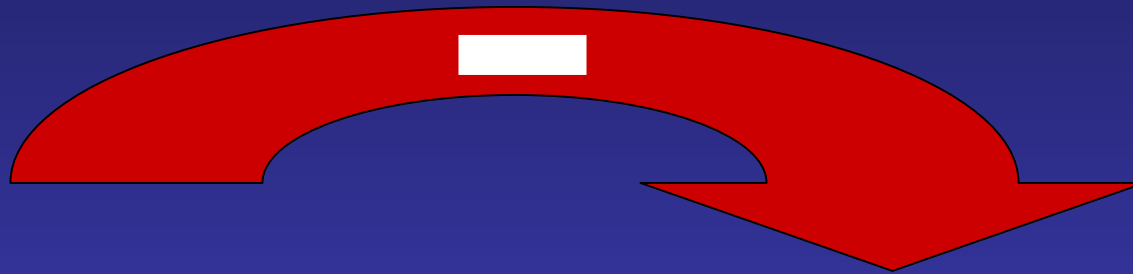
**1/ Generation of a genetic diversity**

**2/ Selection of the most adapted  
individuals**

# Darwinism and the host/virus relationship



# Darwinism and the host/virus relationship



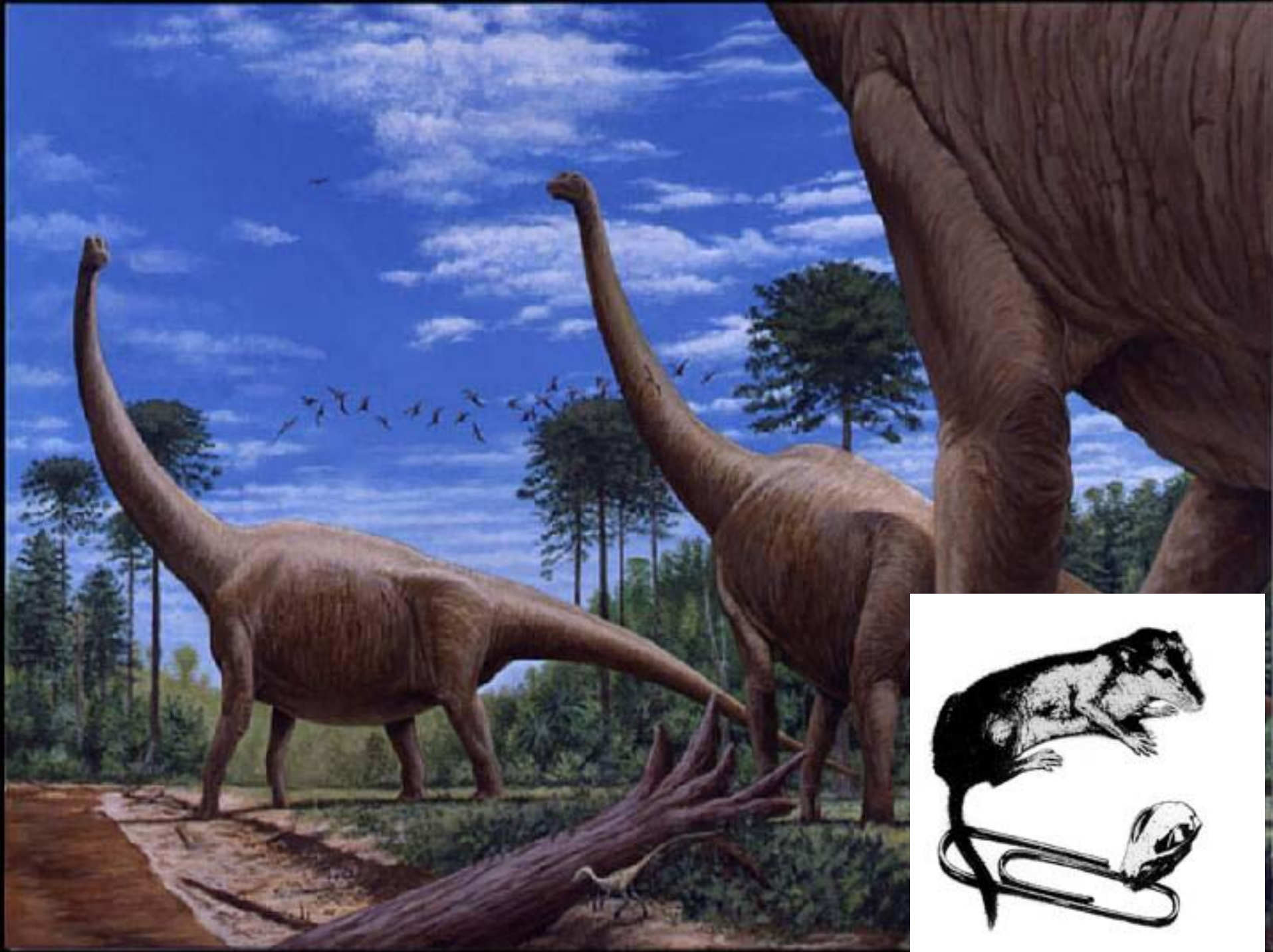
Host

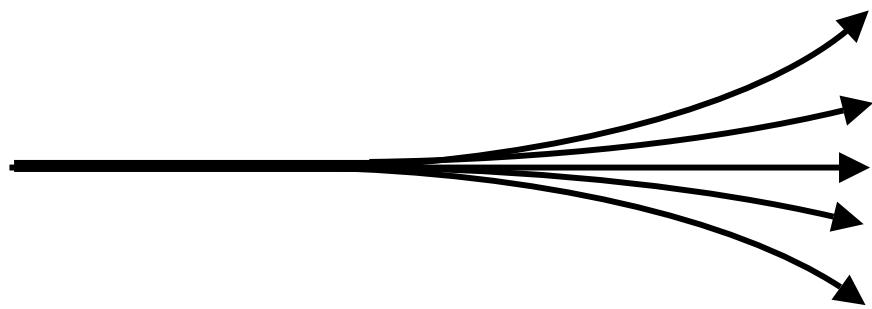
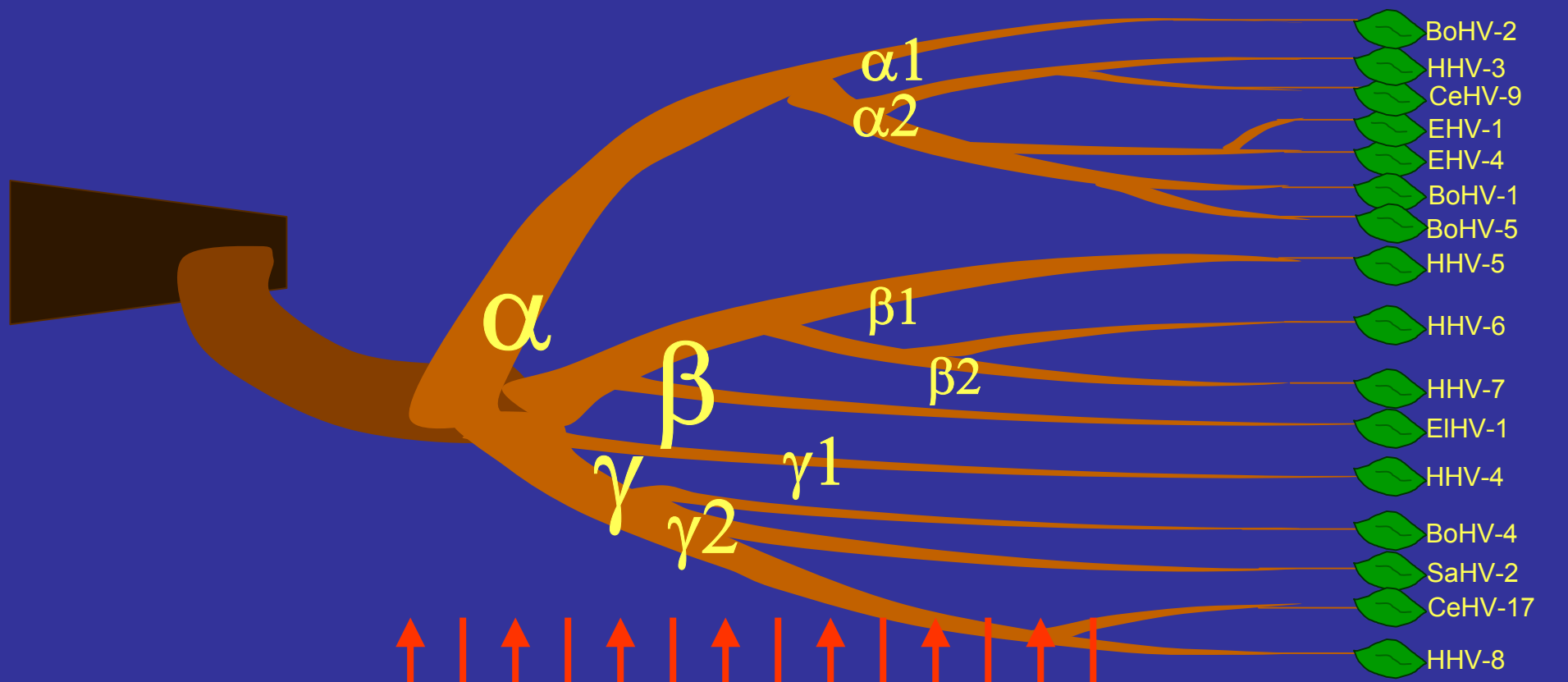


Virus



**Immune evasion**





# **Viral subversion of the immune system**

~~Passive~~ and active strategies

# **Viral subversion of the immune system**

## **Active strategies**

**Viral interference with MHC class I pathway**

**Viral evasion of Natural Killer cells**

**Viral inhibition of MHC class II antigen presentation**

**Viral interference with cytokines, chemokines**

**Viral inhibition of apoptosis**

**Virus complement evasion strategies**

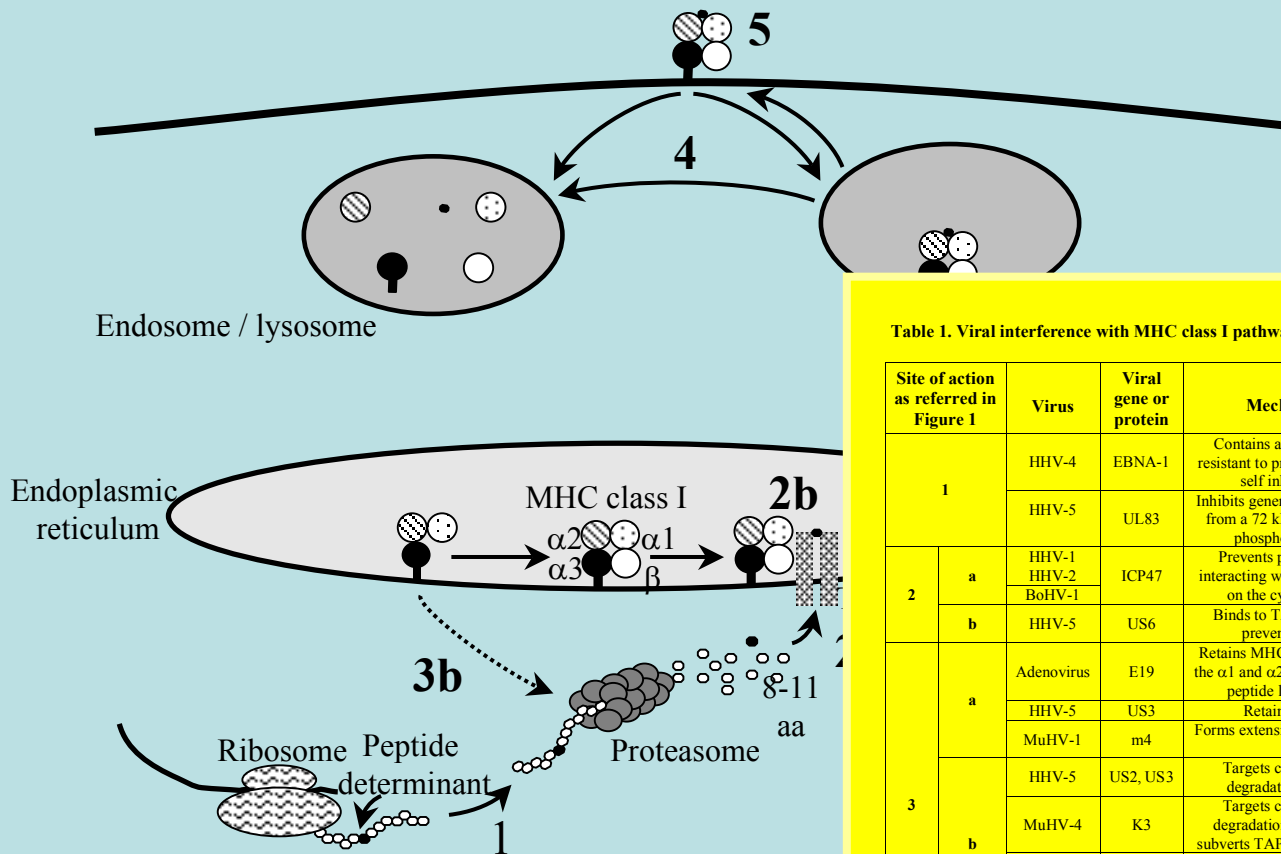
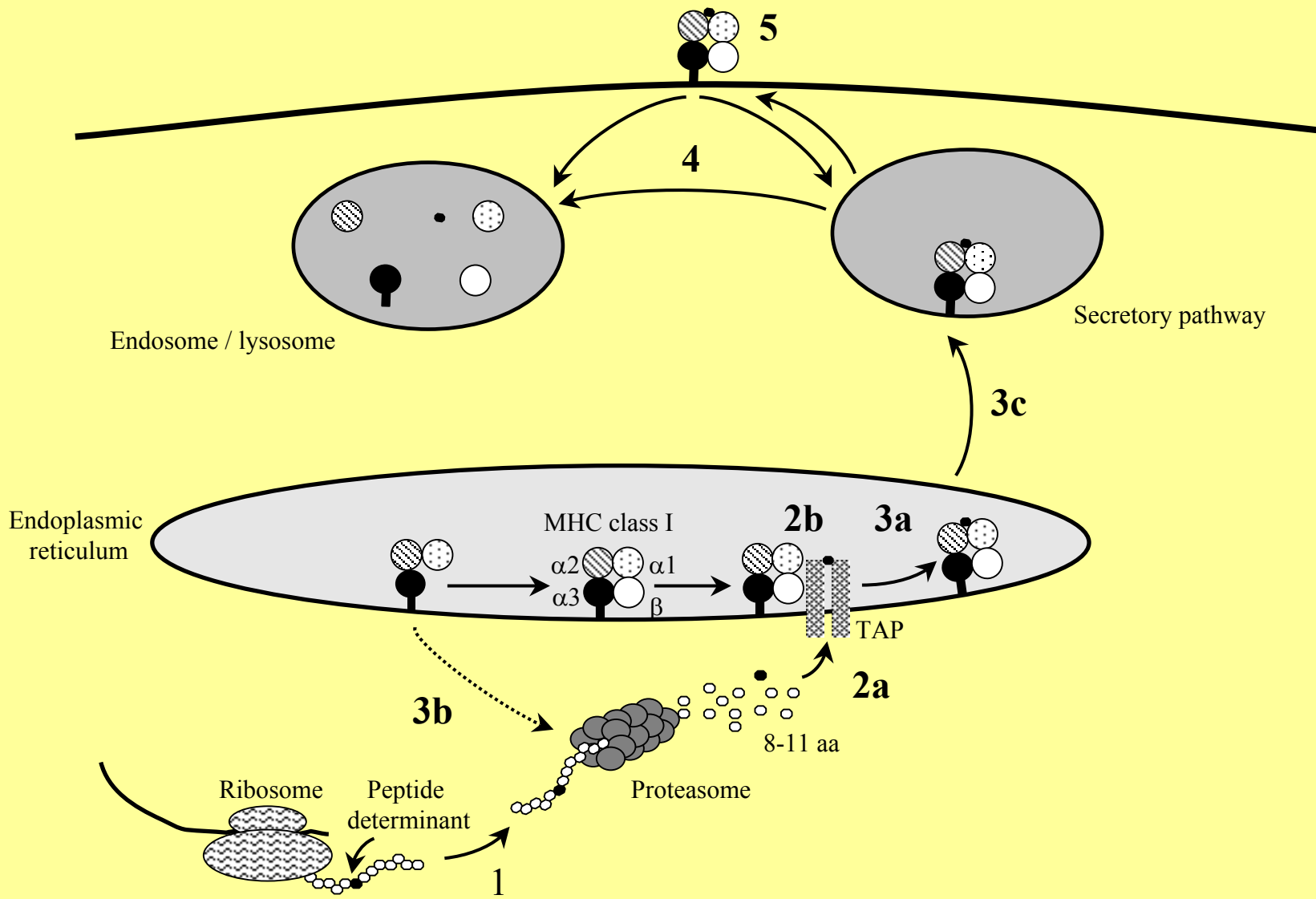


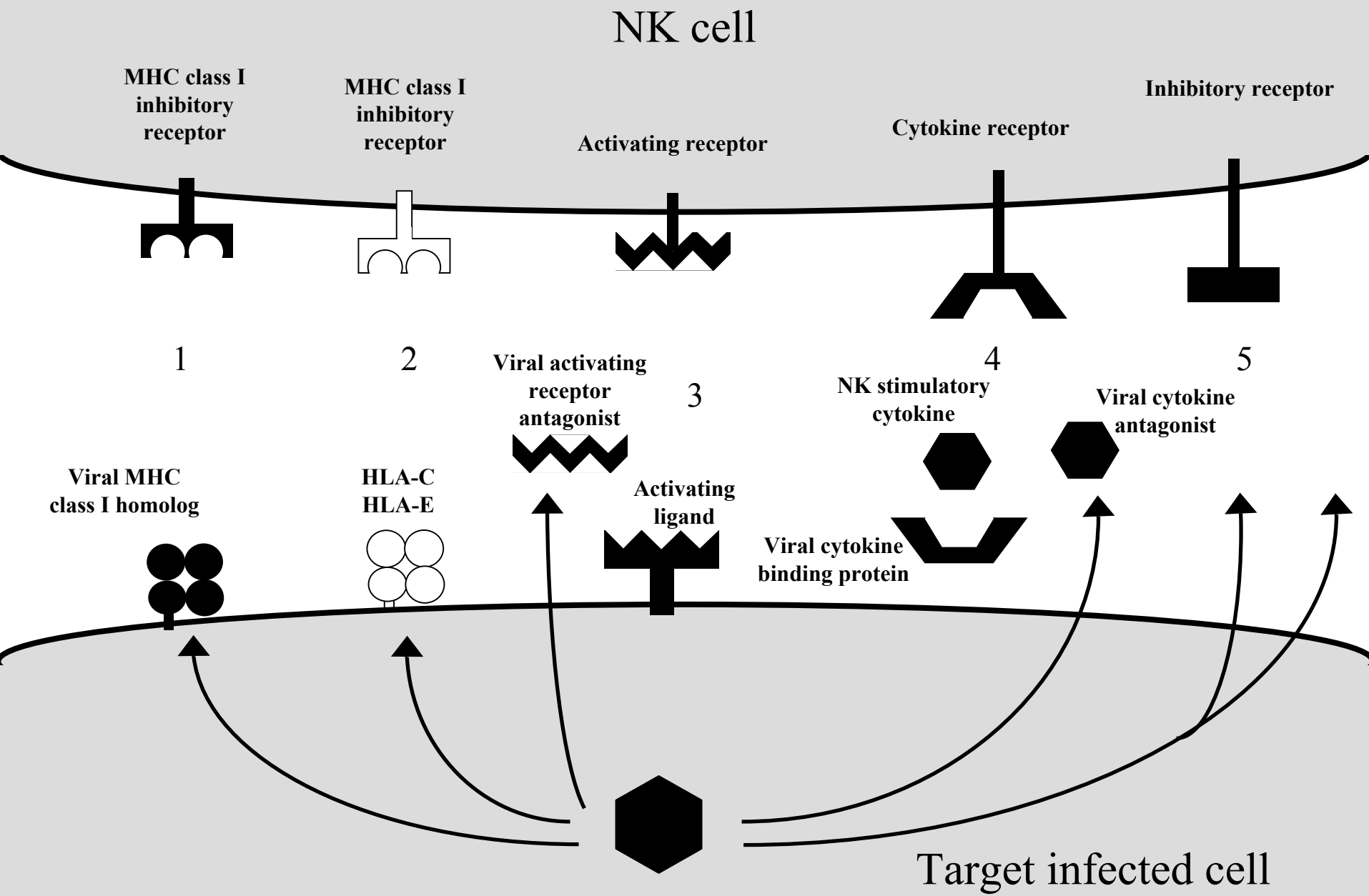
Table 1. Viral interference with MHC class I pathway.

Site of action as referred in Figure 1	Virus	Viral gene or protein	Mechanism of action	Reference source	
1	HHV-4	EBNA-1	Contains a sequence that renders it resistant to proteasome degradation and self inhibition of synthesis	(2, 3)	
	HHV-5	UL83	Inhibits generation of antigenic peptides from a 72 kDa transcription factor by phosphorylation of the latter	(4)	
2	HHV-1 HHV-2 BoHV-1	ICP47	Prevents peptide translocation by interacting with both TAP 1 and TAP 2 on the cytosolic side of the ER	(5, 6) (7)	
	HHV-5	US6	Binds to TAP in the ER lumen and prevents peptide transport	(8-11)	
3	Adenovirus	E19	Retains MHC-I in the ER by binding to the α1 and α2 regions (could also inhibit peptide loading of the MHC-I)	(12-15)	
		US3	Retains MHC-I in the ER	(16, 17)	
		m4	Forms extensive complexes with MHC-I in the ER	(18)	
	b	HHV-5	US2, US3	Targets class 1 heavy chains for degradation by the proteasome	(19)
		MuHV-4	K3	Targets class 1 heavy chains for degradation by the proteasome and subverts TAP/Tapsin associated class I	(20, 21)
		HIV-1	Vpu	Destabilizes newly synthesized class 1 molecules and targets for degradation	(22)
		HTLV-1	p12(I)	Targets class 1 heavy chains for degradation by the proteasome	(23)
	c	MuHV-1	m152	Retains MHC-I within the ER-transGolgi intermediate compartment	(24)
	4	MuHV-1	m06	Prevents the MHC-I from reaching the cell surface	(25)
HIV, SIV		nef	Accelerates endocytosis of class 1 complexes (specific targeting of HLA A and B locus)	(26, 27)	
EHV-1		?	Enhanced endocytosis of MHC-I from the surface	(28)	
HHV-8		K3, K5	Targets the MHC-I to lysosomes	(29)	
5	MuHV1	m4	Inhibits T CD8+ cell recognition	(30)	

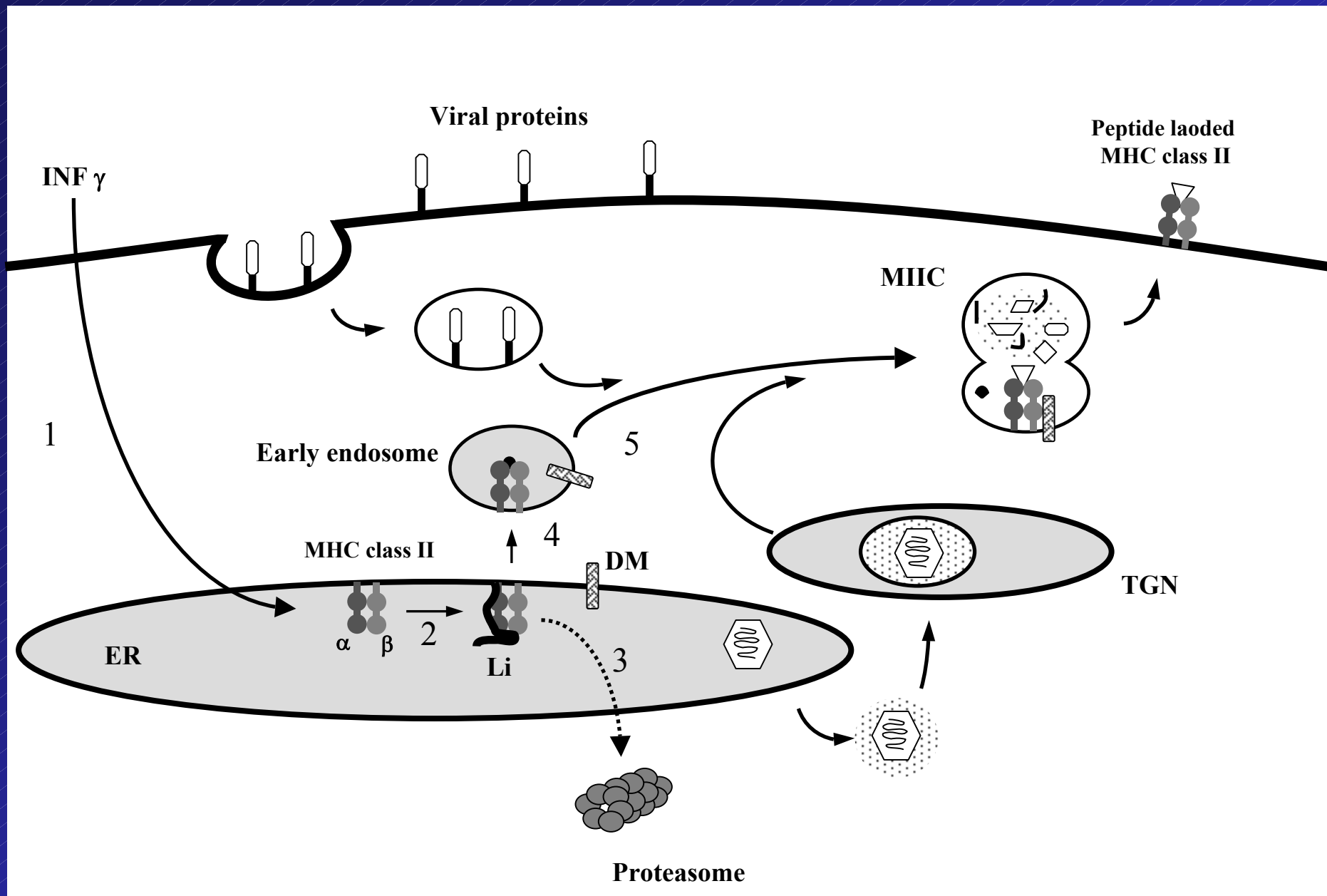
# **Viral interference with MHC class I pathway**



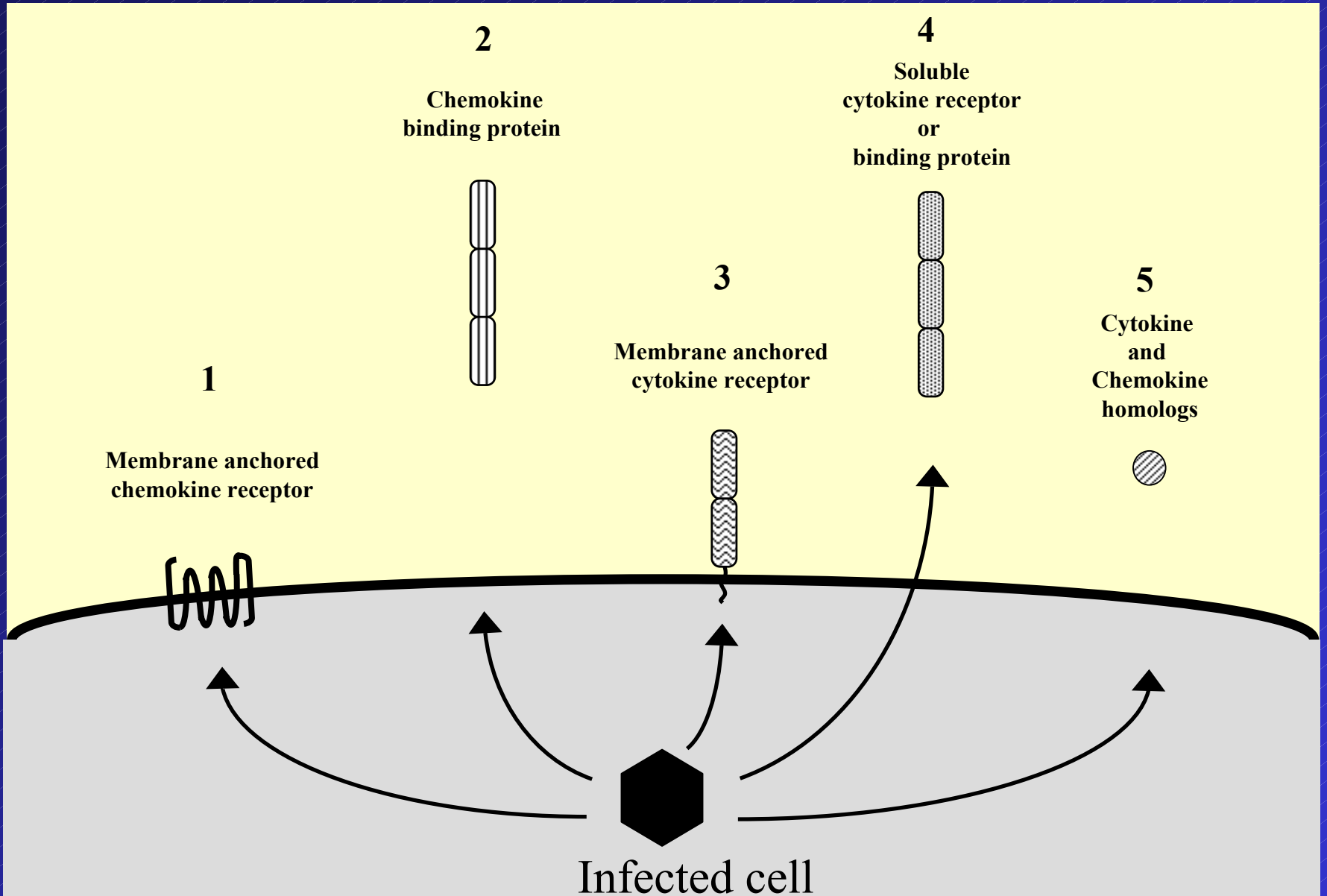
# **Viral evasion of Natural Killer cells**



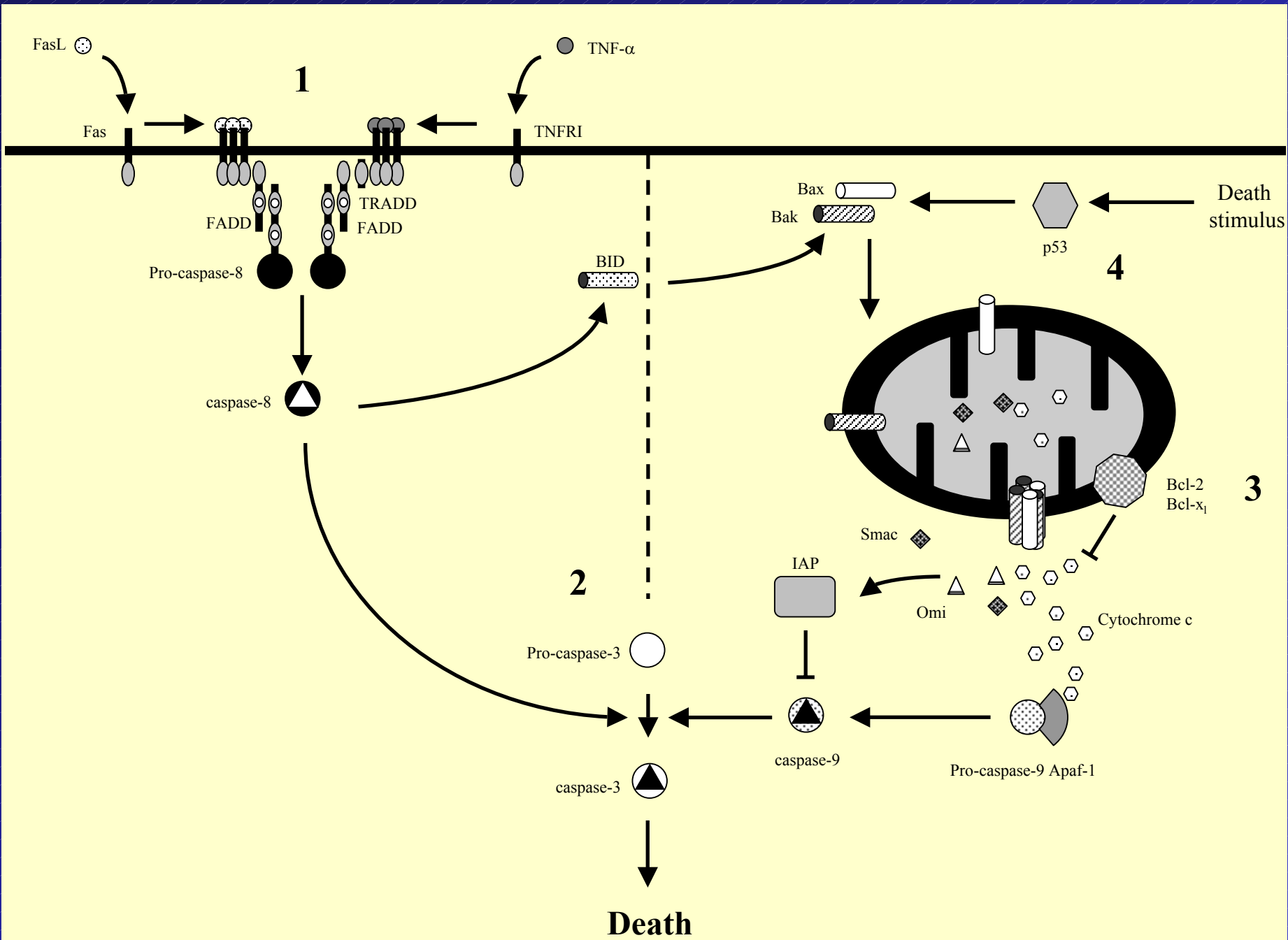
# **Viral inhibition of MHC class II antigen presentation**



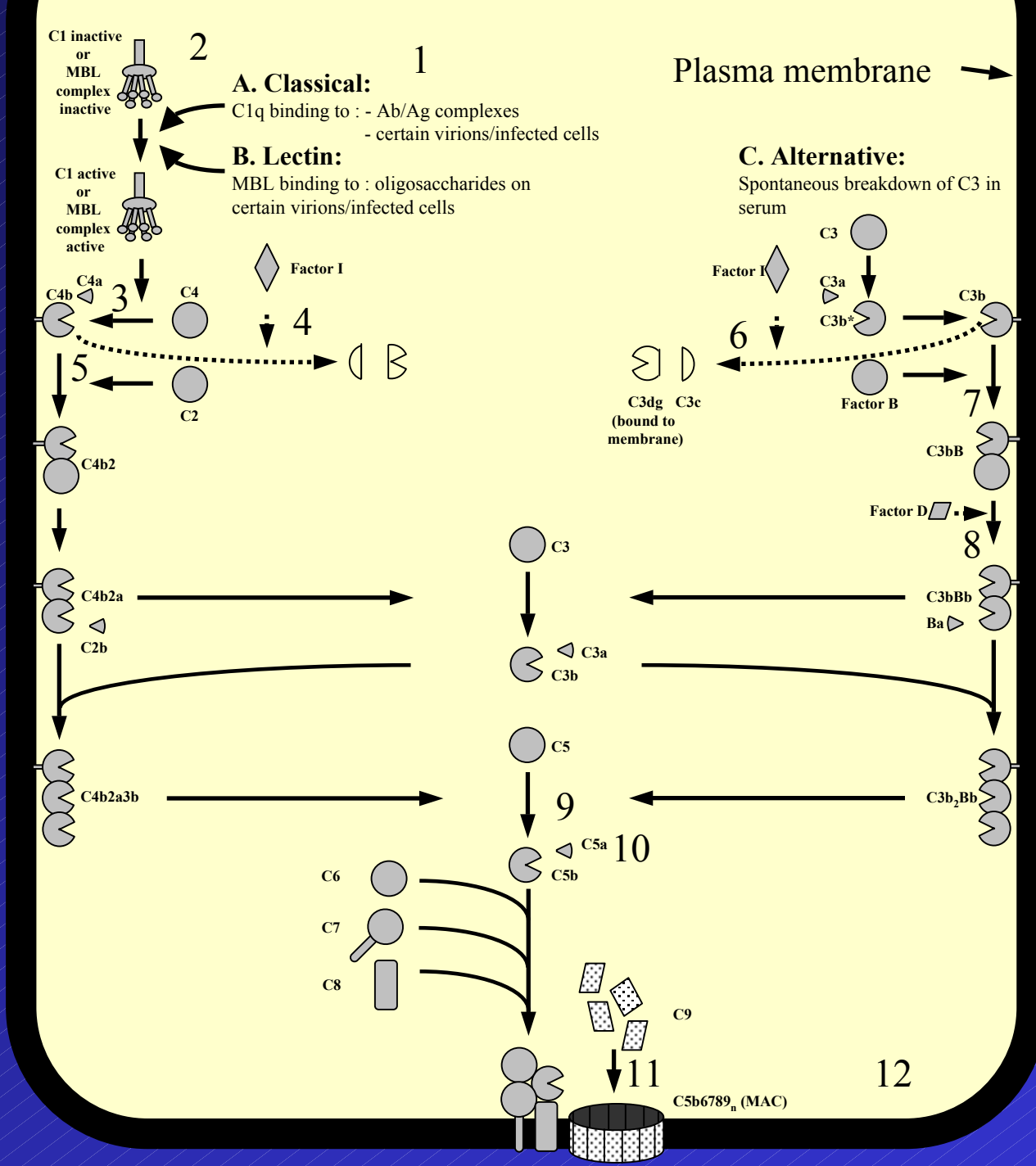
# **Viral interference with cytokines, chemokines**



# **Viral inhibition of apoptosis**



# **Virus complement evasion strategies**



# Conclusion

**Viruses have acquired many strategies to interfere with many components of the immune system**

**Viruses live on the edge**

Impair the host immune response to replicate and to avoid eradication

Respect the host immune response in order to insure their host's (and hence their own) survival

## Deletion of the vIL-1 $\beta$ R gene from vaccinia virus

VV wt  
vIL-1 $\beta$ R<sup>+</sup>



VV v $\Delta$ B15R  
vIL-1 $\beta$ R<sup>-</sup>

