

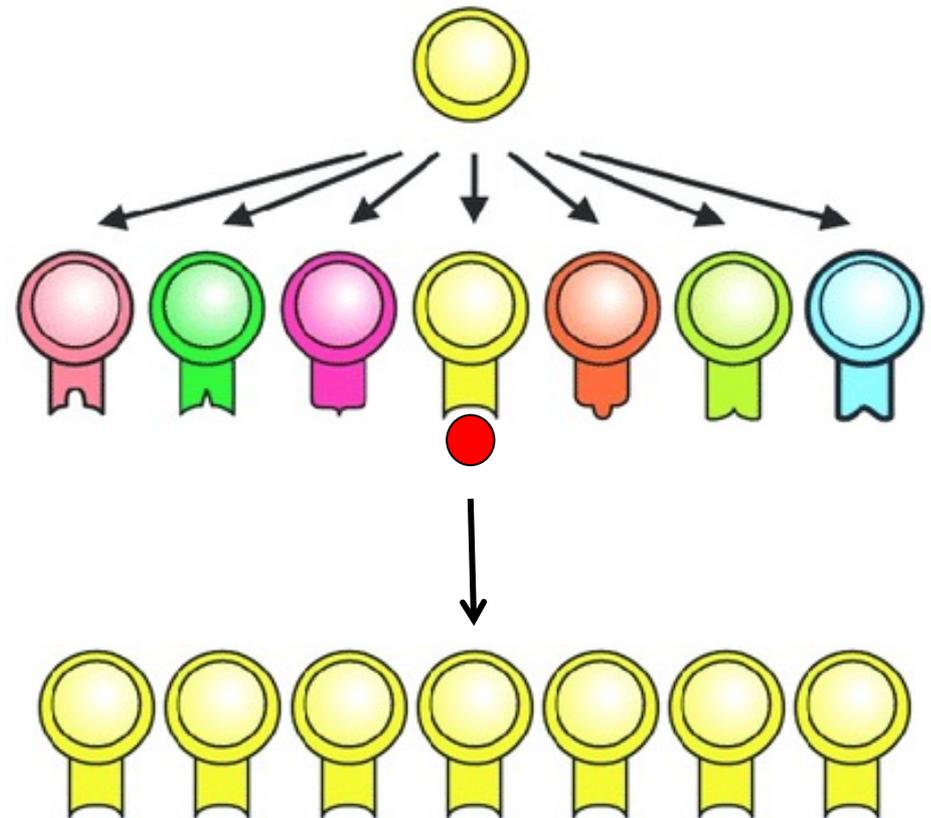
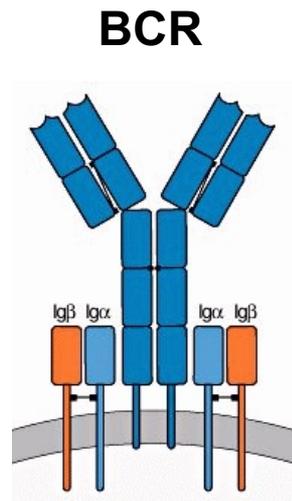
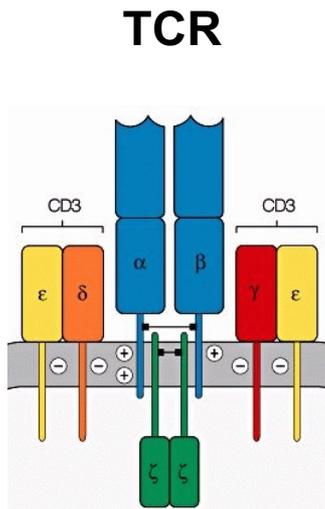
Estrutura do MHC, processamento e apresentação de antígenos

Prof. Dr. Gustavo P. Amarante-Mendes
Disciplina BMI-0256 – Imunologia
Nutrição Noturno - 2021

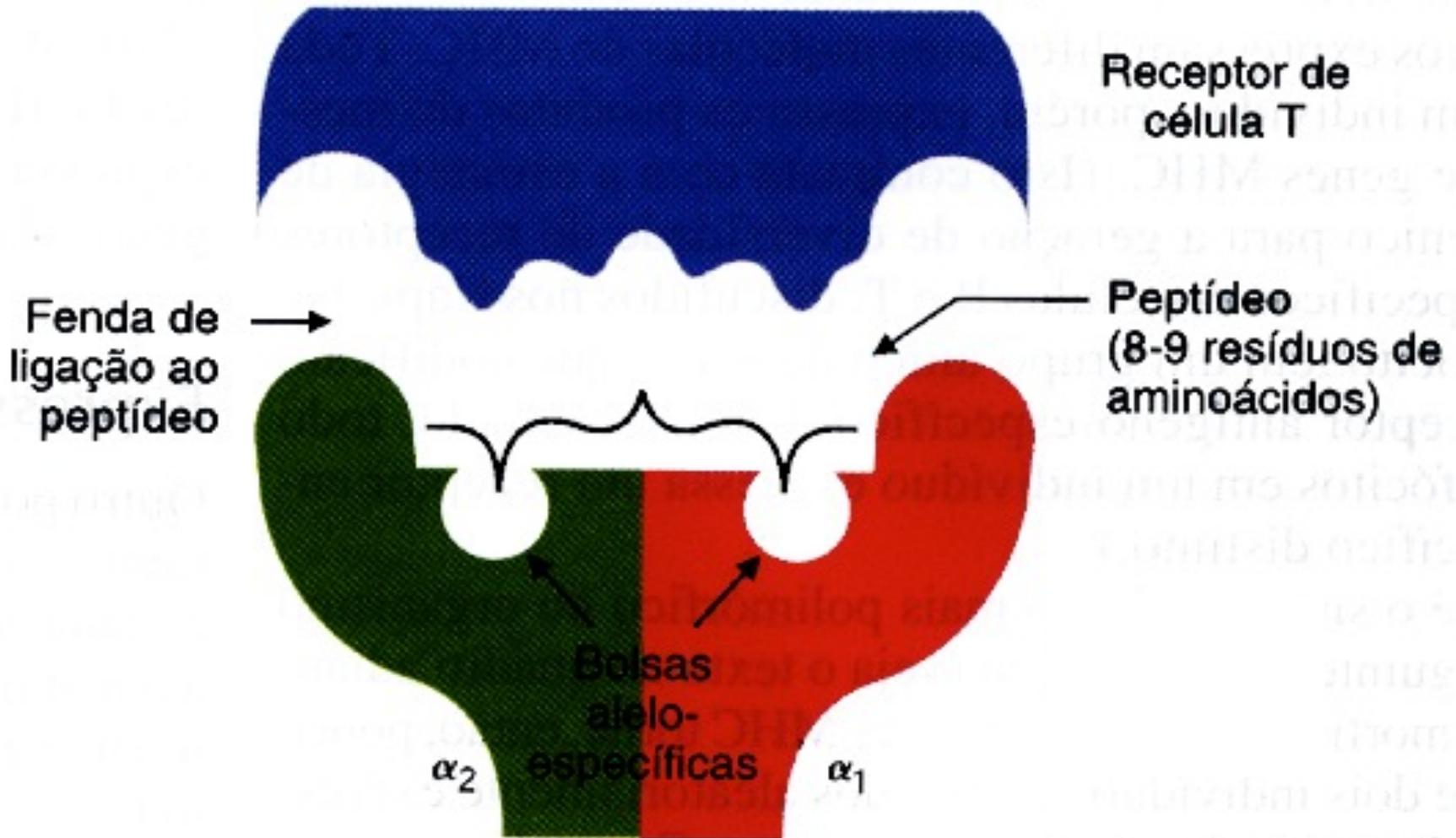


Estratégia de reconhecimento pela Imunidade Adaptativa

- Altíssima especificidade – reconhece “particularidades”
- Distribuição clonal

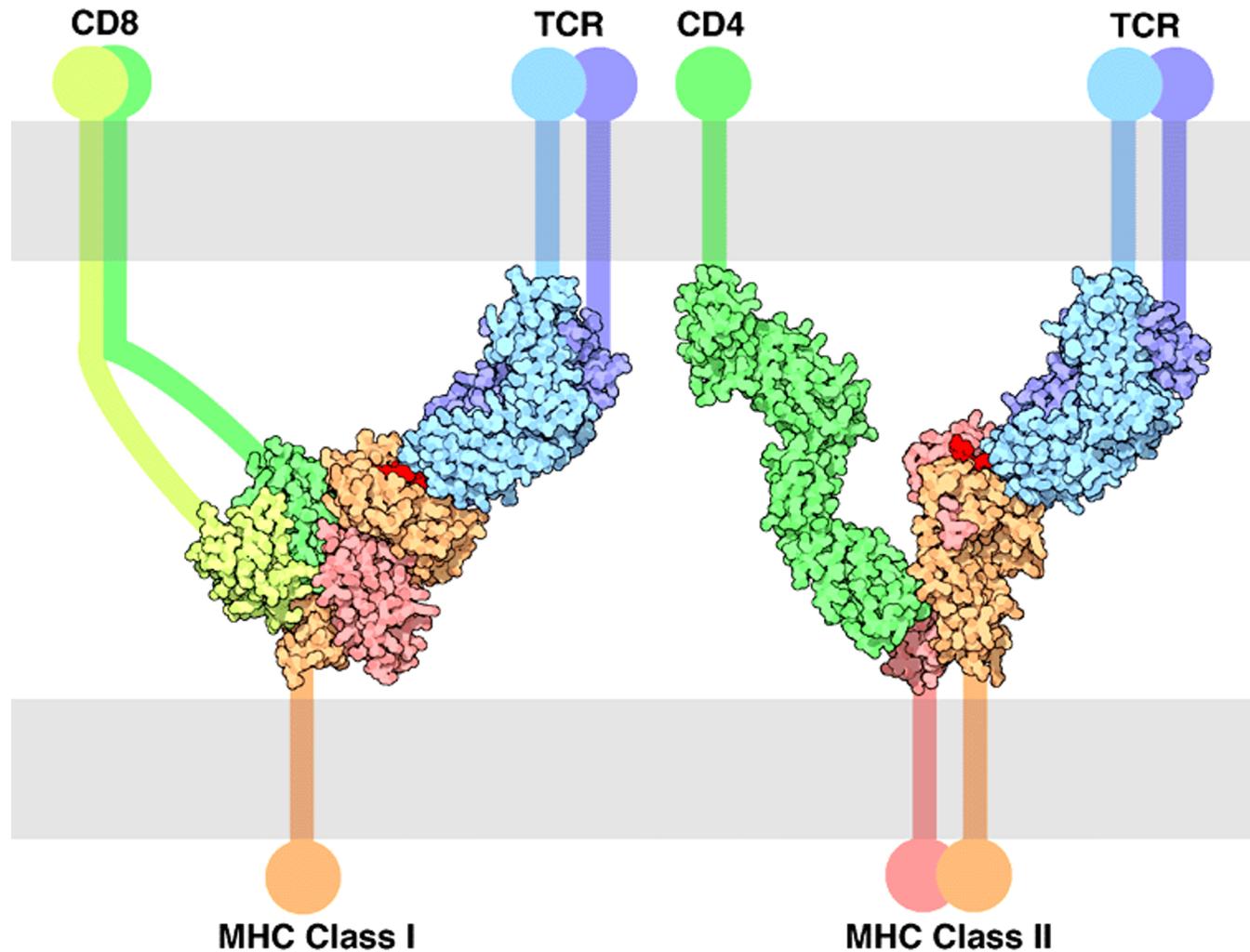


Interação TCR-MHC+peptídeo



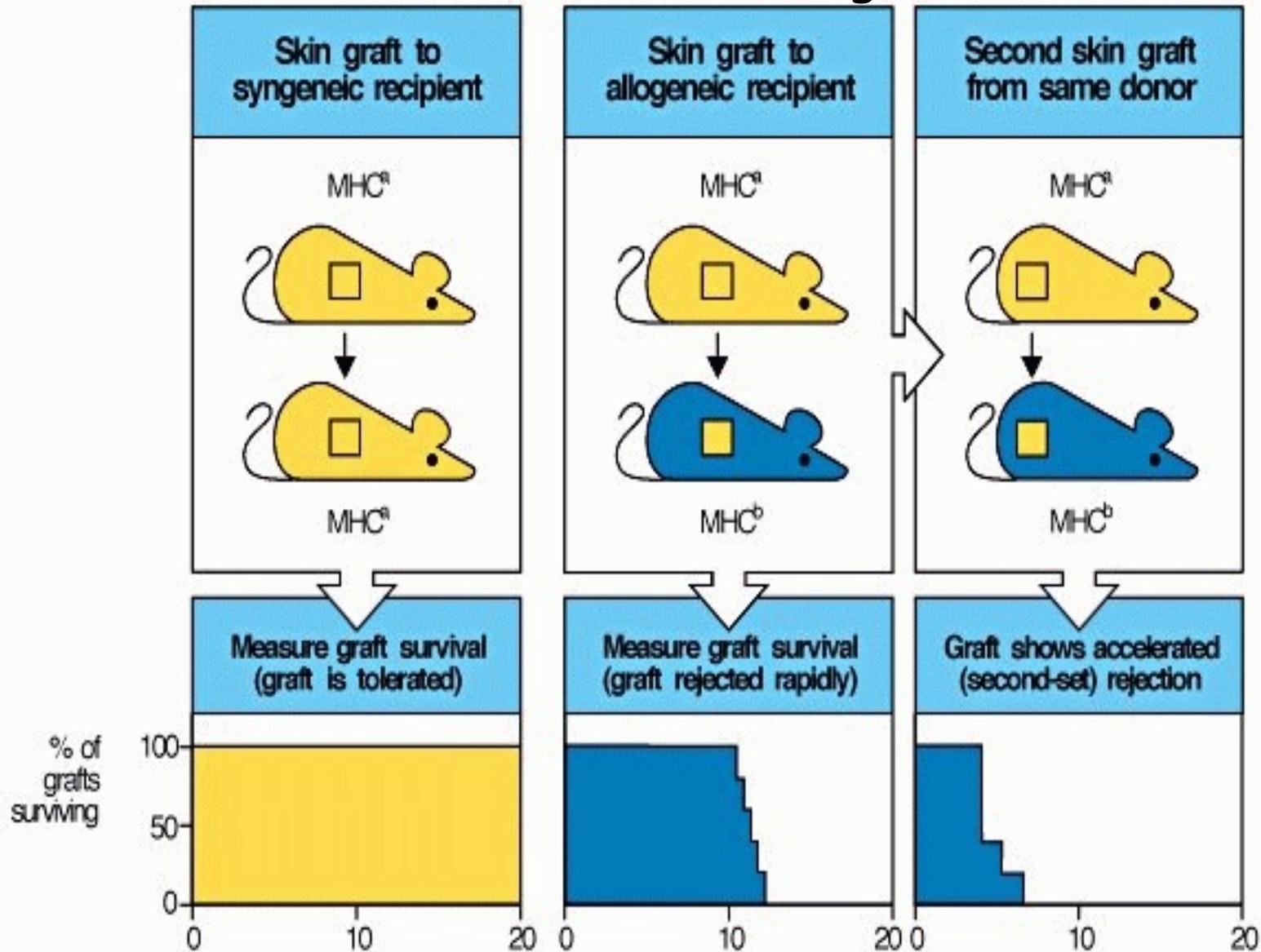
Interação TCR-MHC+peptídeo

Receptores e Co-receptores

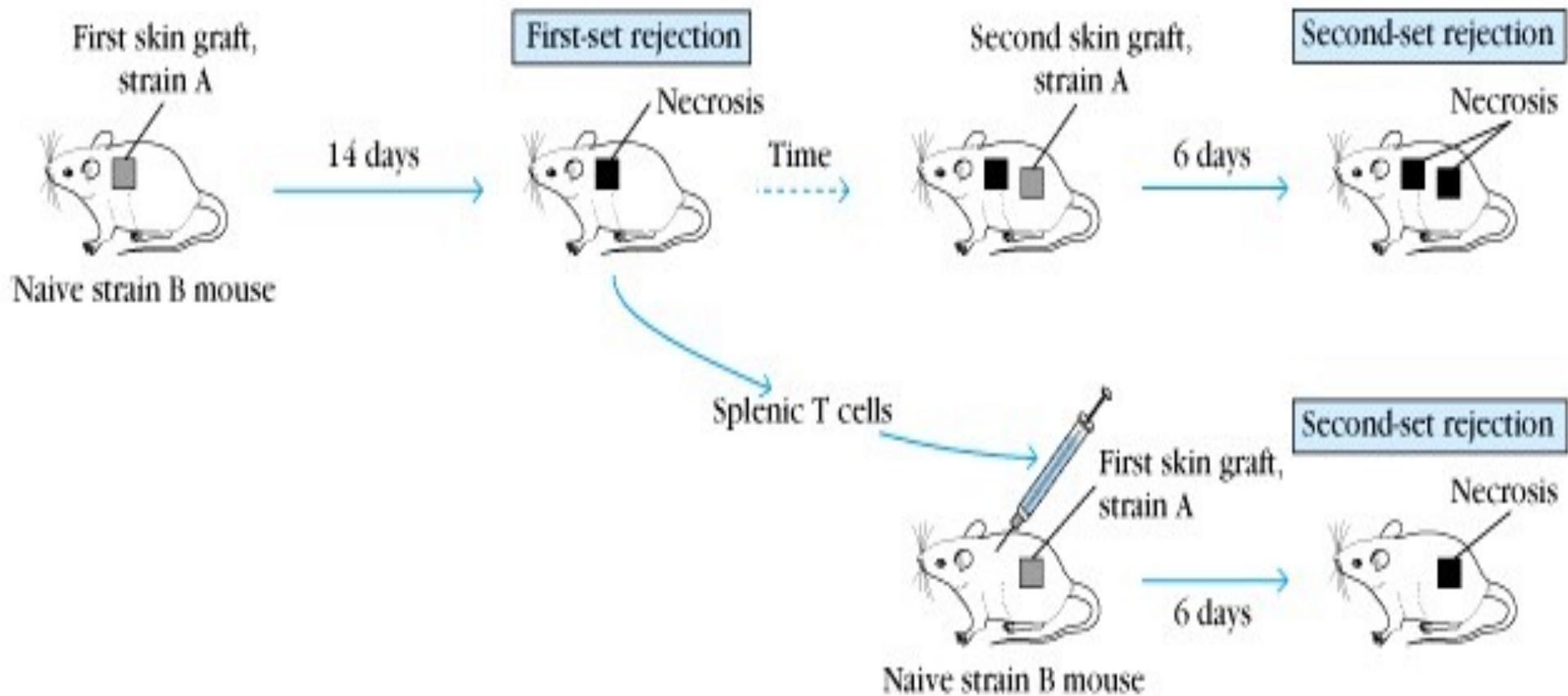


HISTOCOMPATIBILIDADE

Peter Gorer (1930s) and George Snell (1940-50s)



Linfócitos T “transferem” rejeição



Rejeição de transplantes

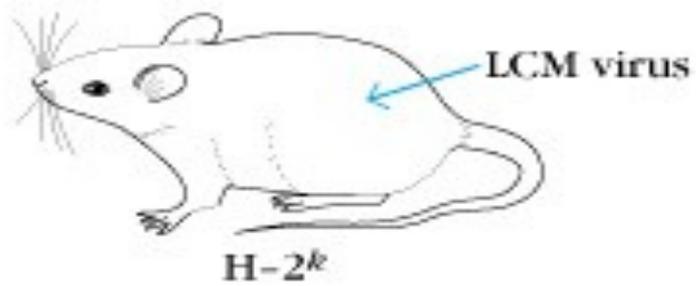
Resposta Imune Adaptativa

Mediada por linfócitos T

Contra aloantígenos

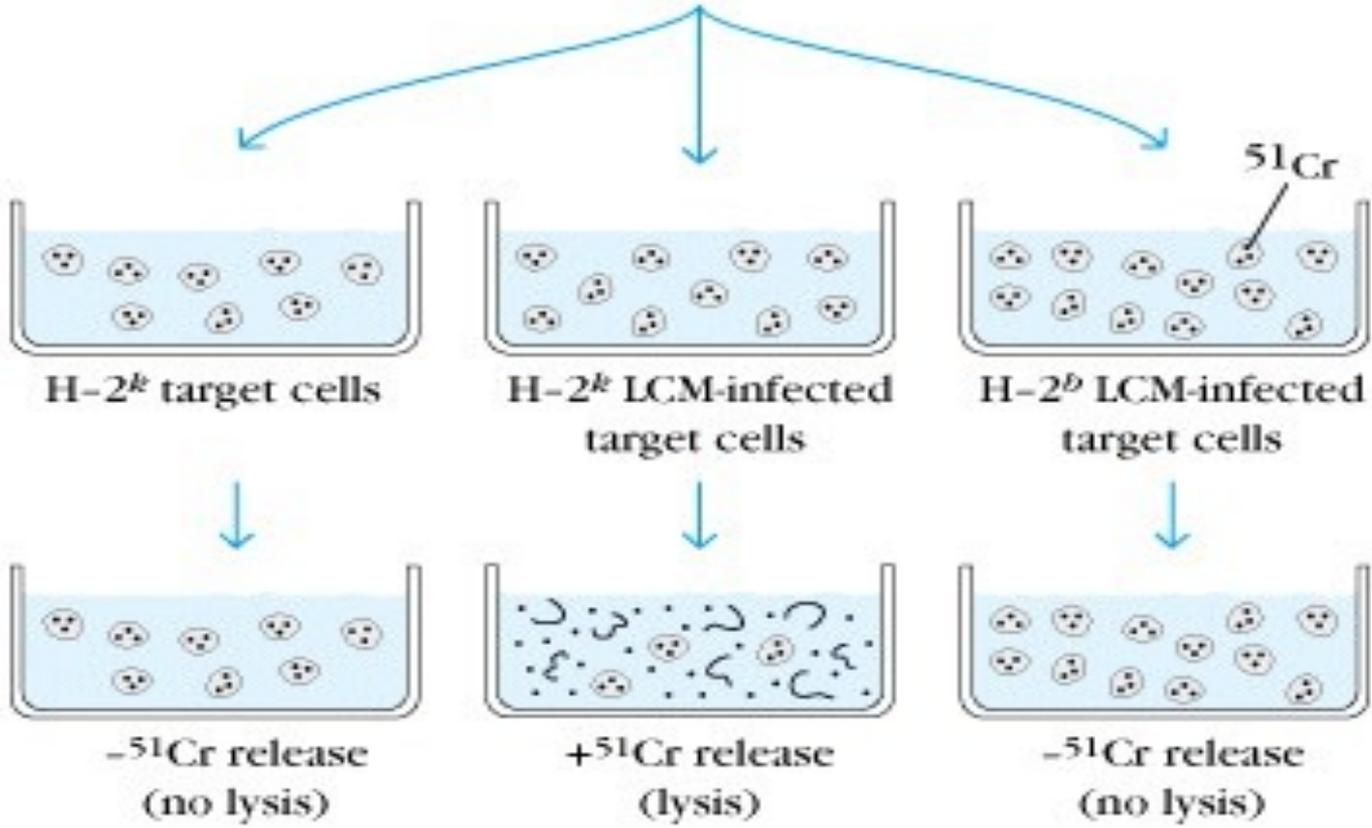
(sobretudo o MHC)

Restrição ao MHC



Zinkernagel &
Doherty
(Nobel em 1996)

Spleen cells
(containing T_c cells)



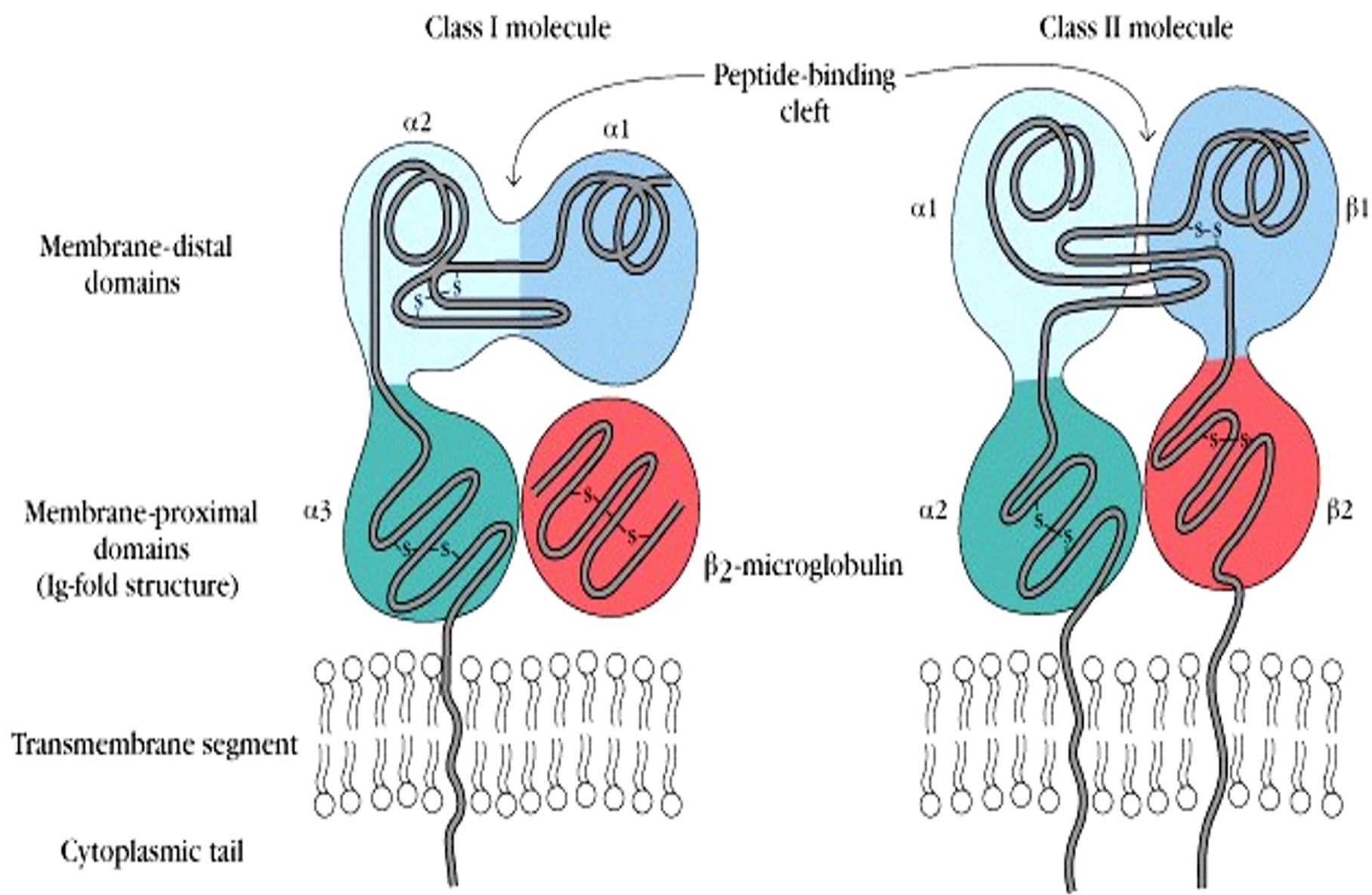
Características das moléculas do MHC

Proteínas Altamente Polimórficas

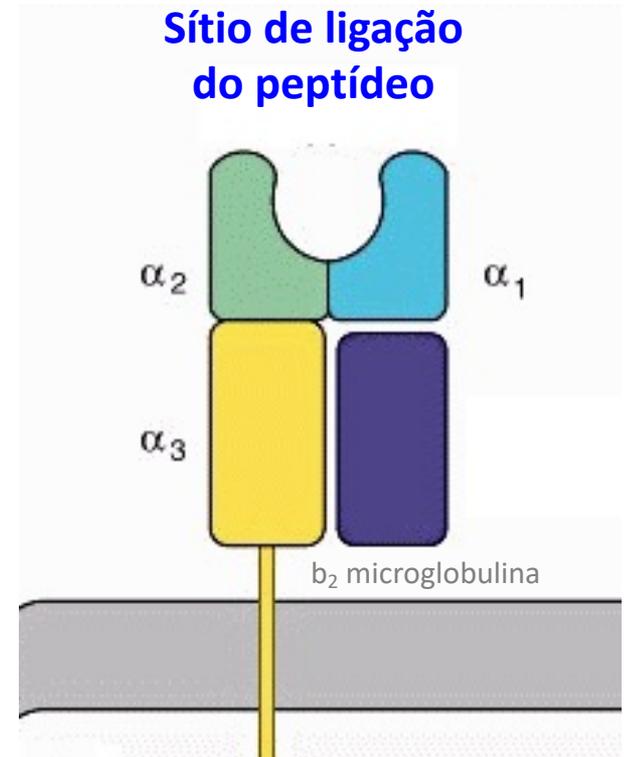
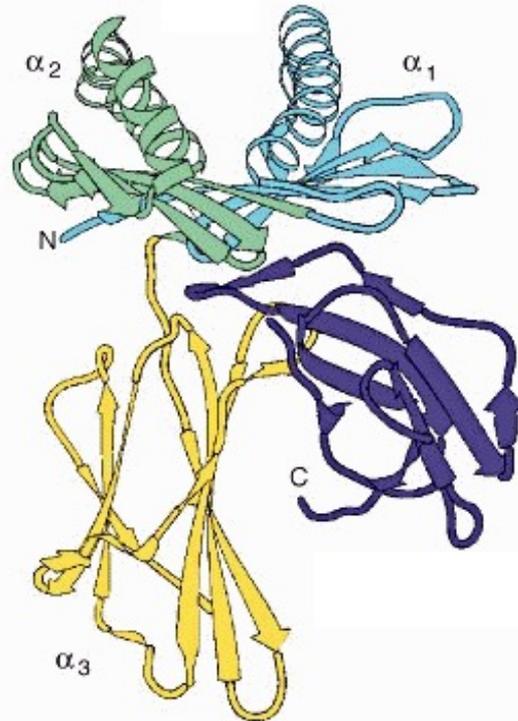
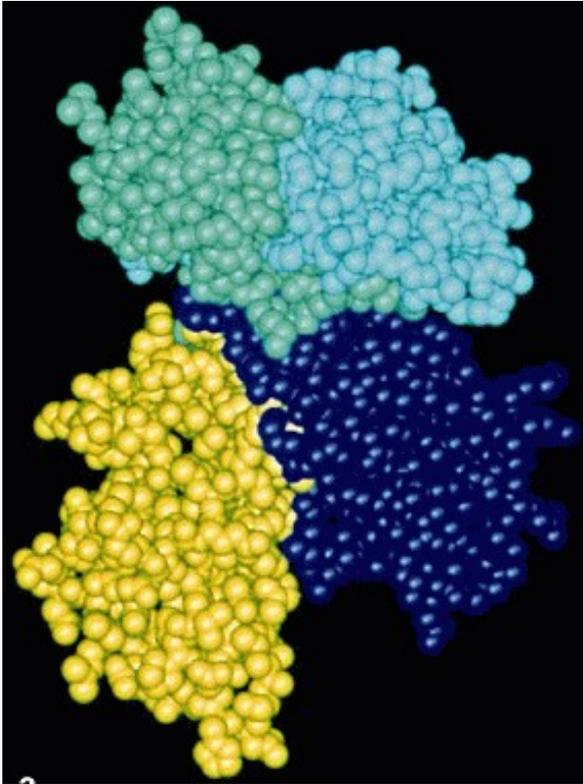
Sistema Poligênico

Expressão co-dominante

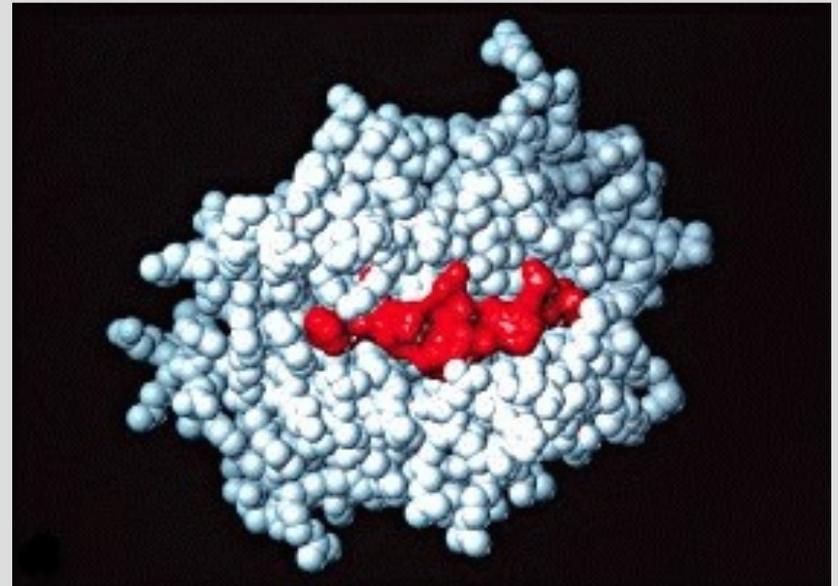
Herdadas em blocos (“HAPLÓTIPOS”)



Estrutura da molécula de MHC classe I



Ligação do peptídeo à molécula de MHC classe I



H ⁺ N	T	Y	Q	R	T	R	A	L	V	COO ⁻
H ⁺ N	S	Y	F	P	E	I	T	H	I	COO ⁻
H ⁺ N	K	Y	Q	A	V	T	T	T	L	COO ⁻
H ⁺ N	S	Y	I	P	S	A	E	K	I	COO ⁻

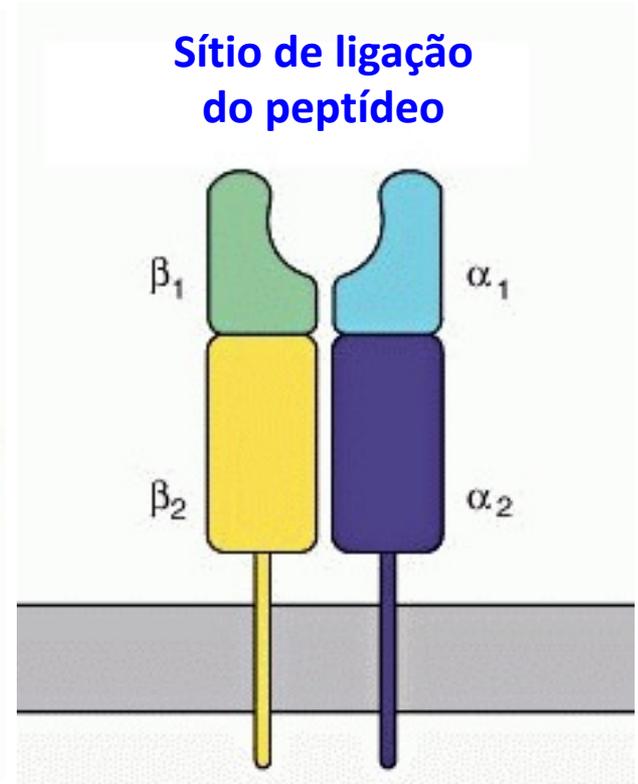
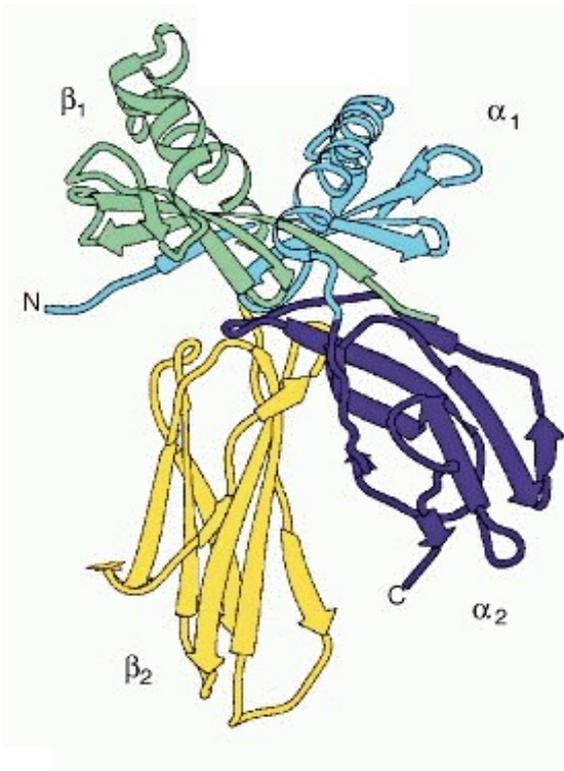
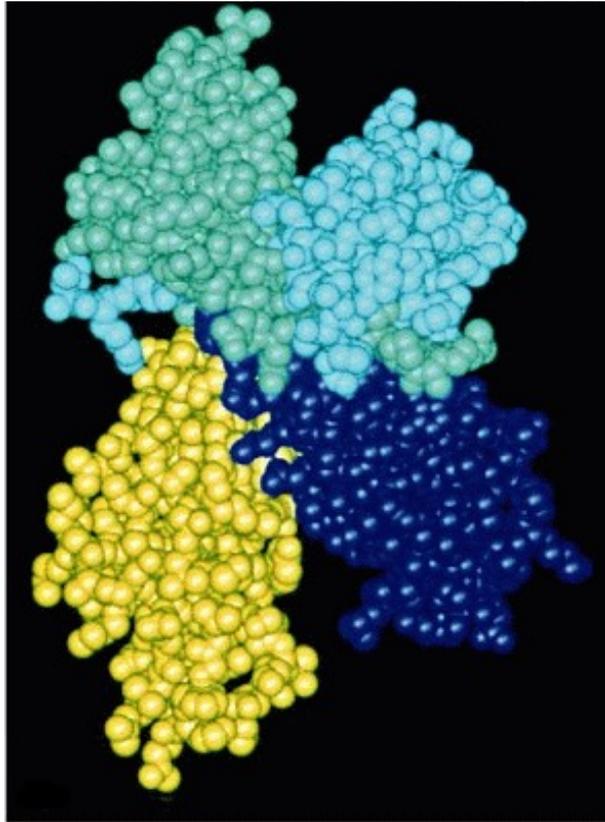
8-10 aa

Ligam ~ 2000 peptídeos

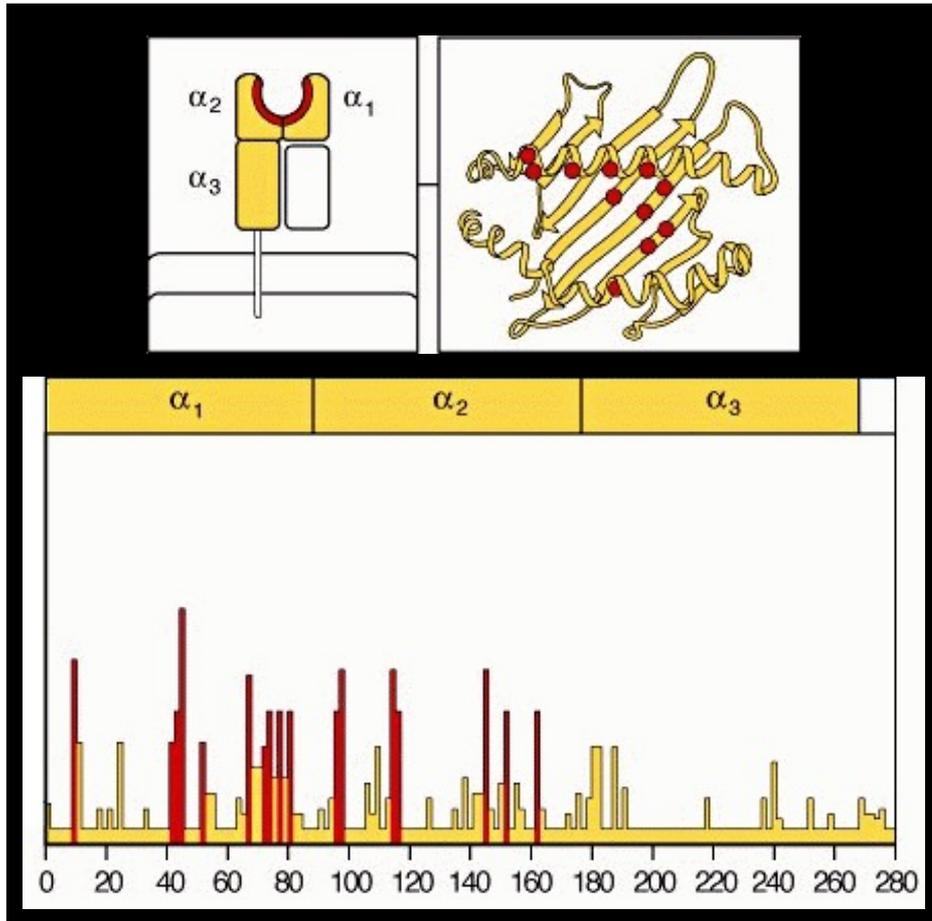
10^5 de cada variante alélica por célula

apresentação ~ 100-4000 cópias

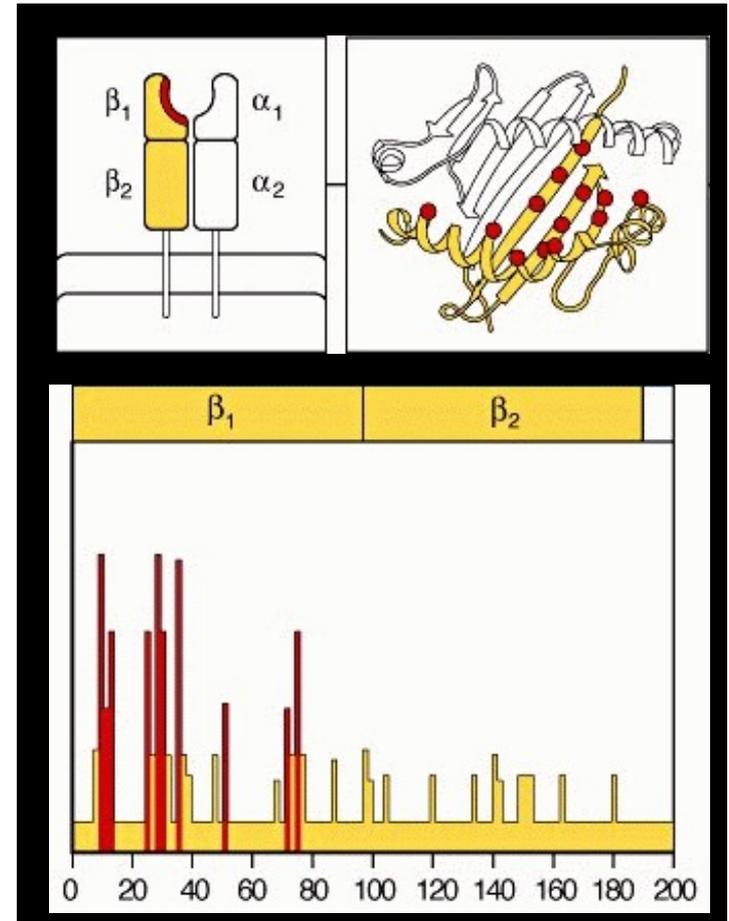
Estrutura da molécula de MHC classe II



Localização da variação alélica



Molécula de MHC classe I



Molécula de MHC classe II

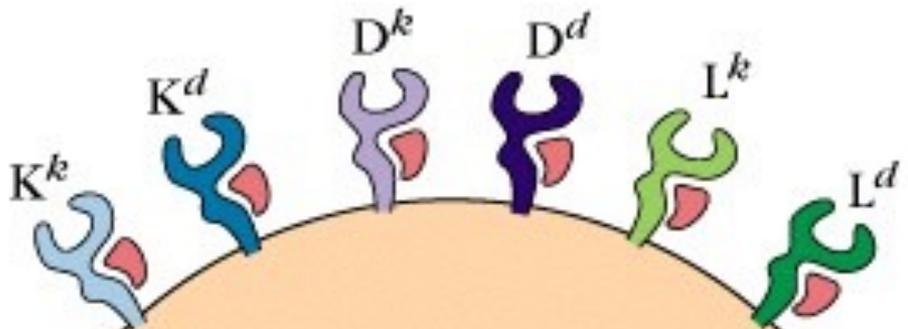
Mouse H-2 complex (Chromosome 17)

Complex	H-2						
MHC class	I	II		III		I	
Region	K	IA	IE	S		D	
Gene products	H-2K	IA $\alpha\beta$	IE $\alpha\beta$	C' proteins	TNF- α TNF- β	H-2D	H-2L

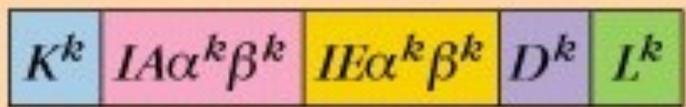
Human HLA complex (Chromosome 6)

Complex	HLA								
MHC class	II			III			I		
Region	DP	DQ	DR	C4, C2, BF			B	C	A
Gene products	DP $\alpha\beta$	DQ $\alpha\beta$	DR $\alpha\beta$	C' proteins	TNF- α TNF- β	HLA-B	HLA-C	HLA-A	

Class I molecules



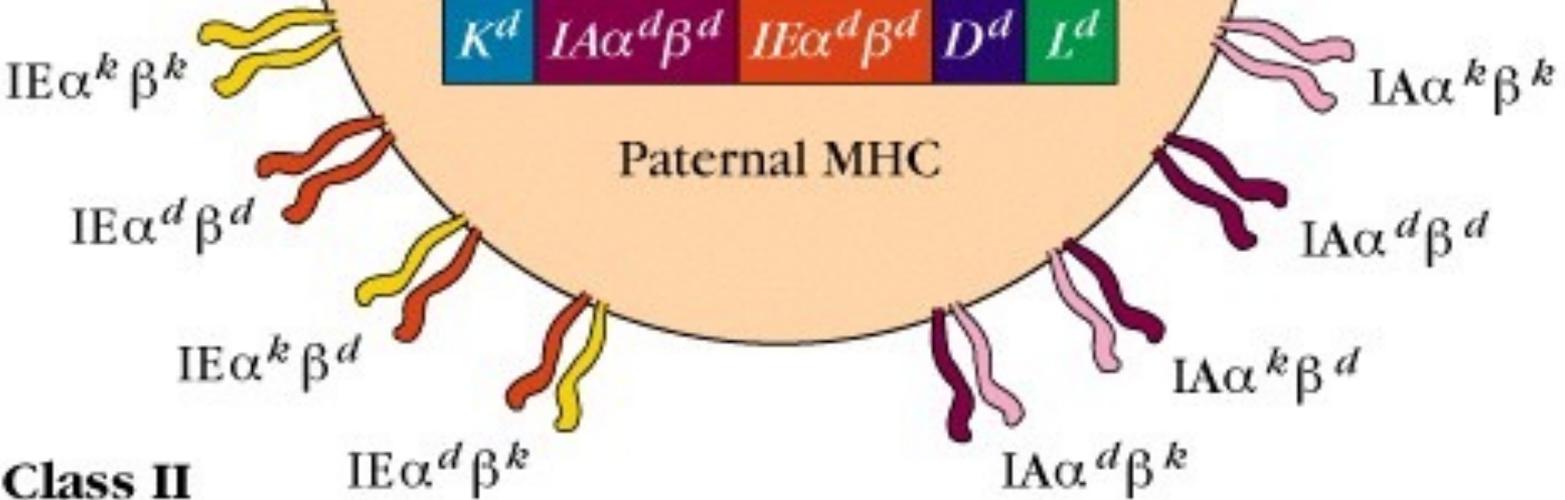
Maternal MHC



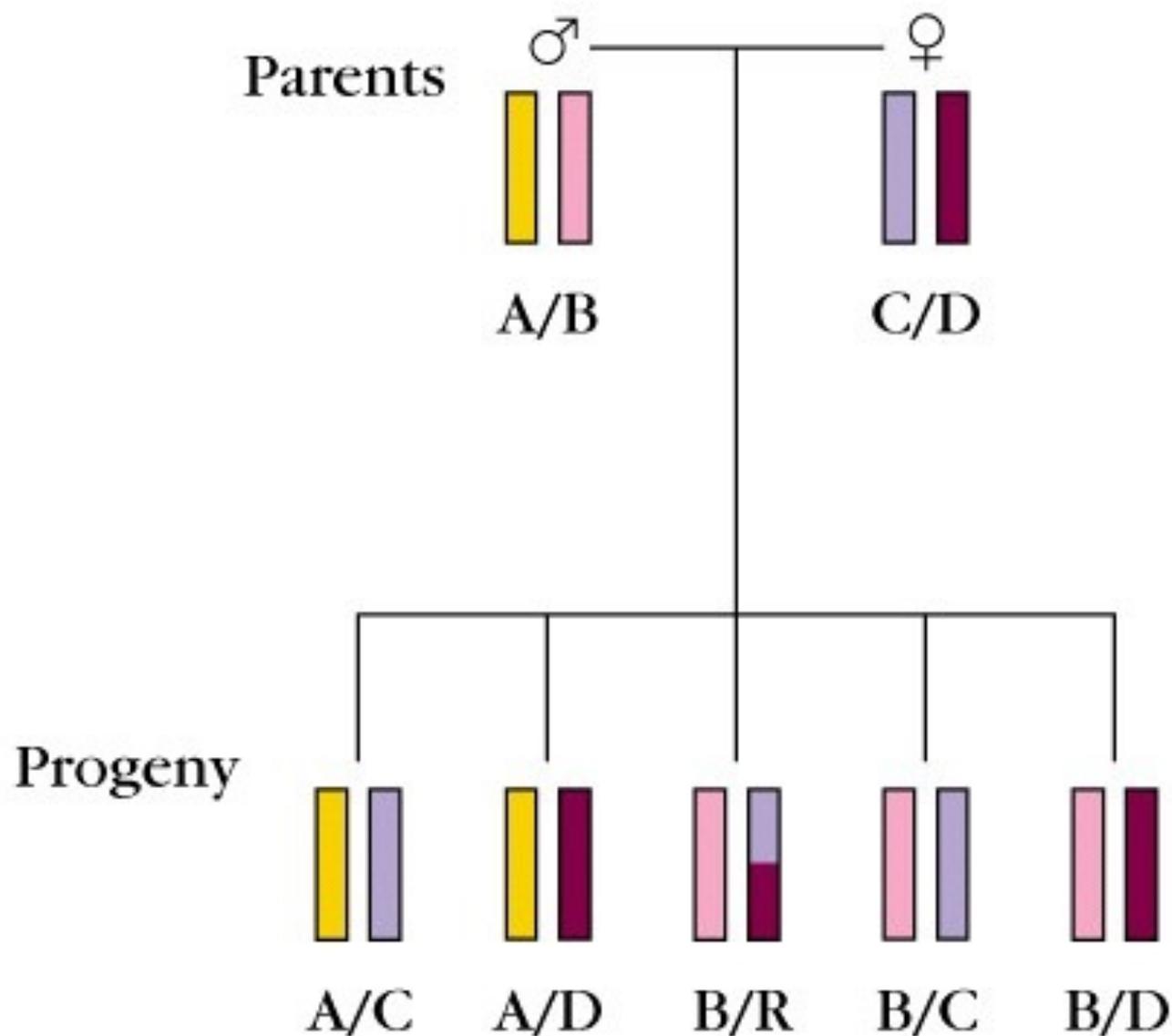
Paternal MHC



Class II molecules



(c) Inheritance of HLA haplotypes in a typical human family

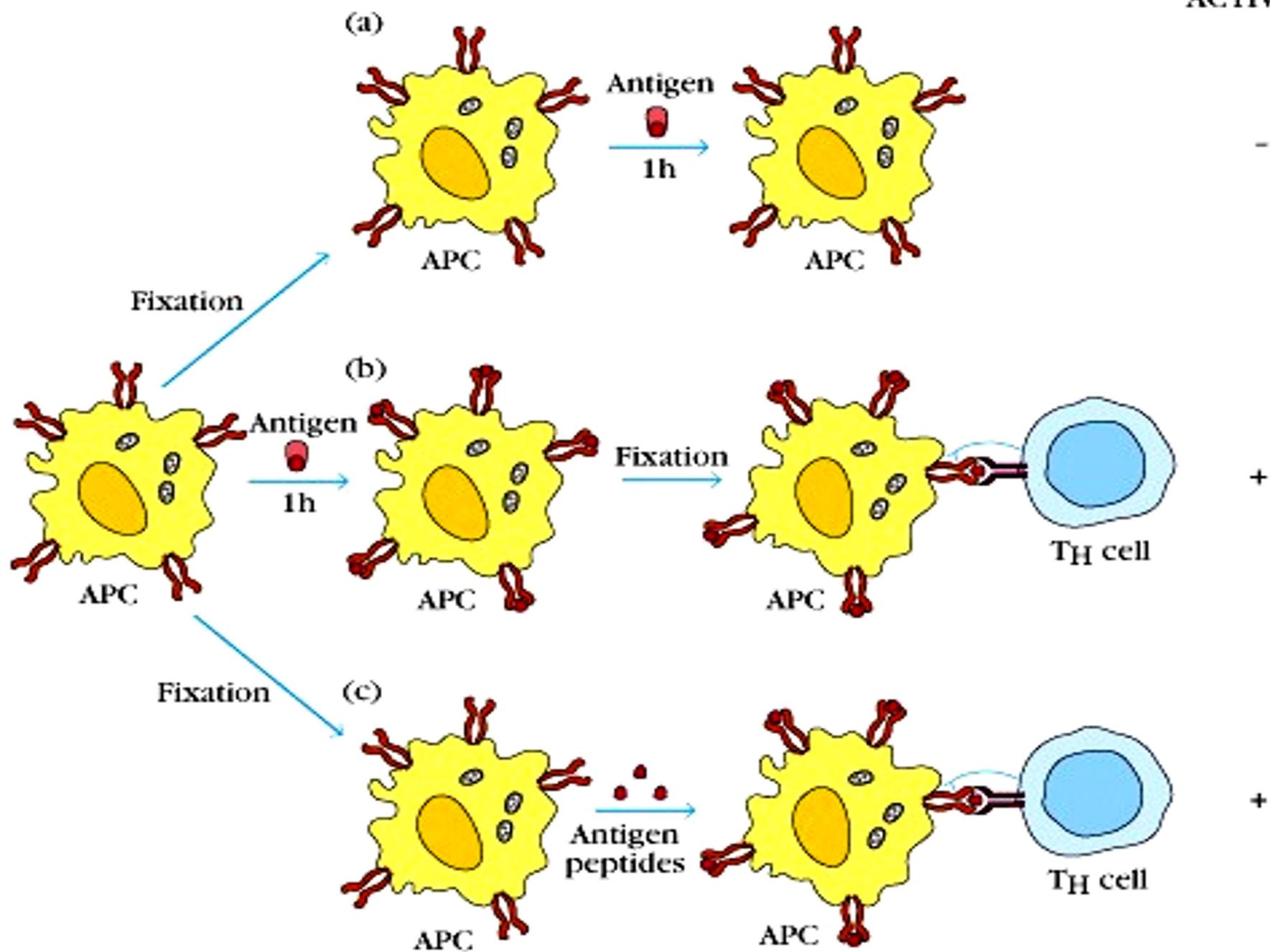


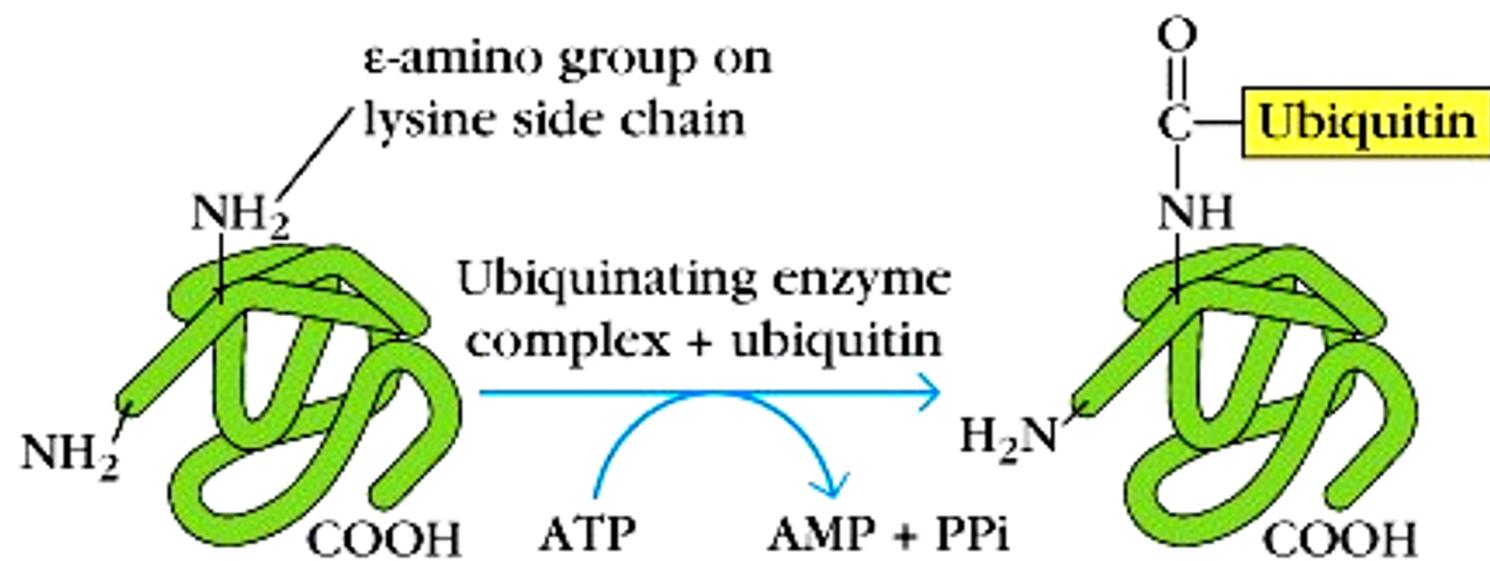
Polimorfismo das moléculas de MHC classe I e classe II

100 (K) x 100 (IAa) x 100 (IAb)
x 100 (IEa) x 100 (IEb) x 100 (D)

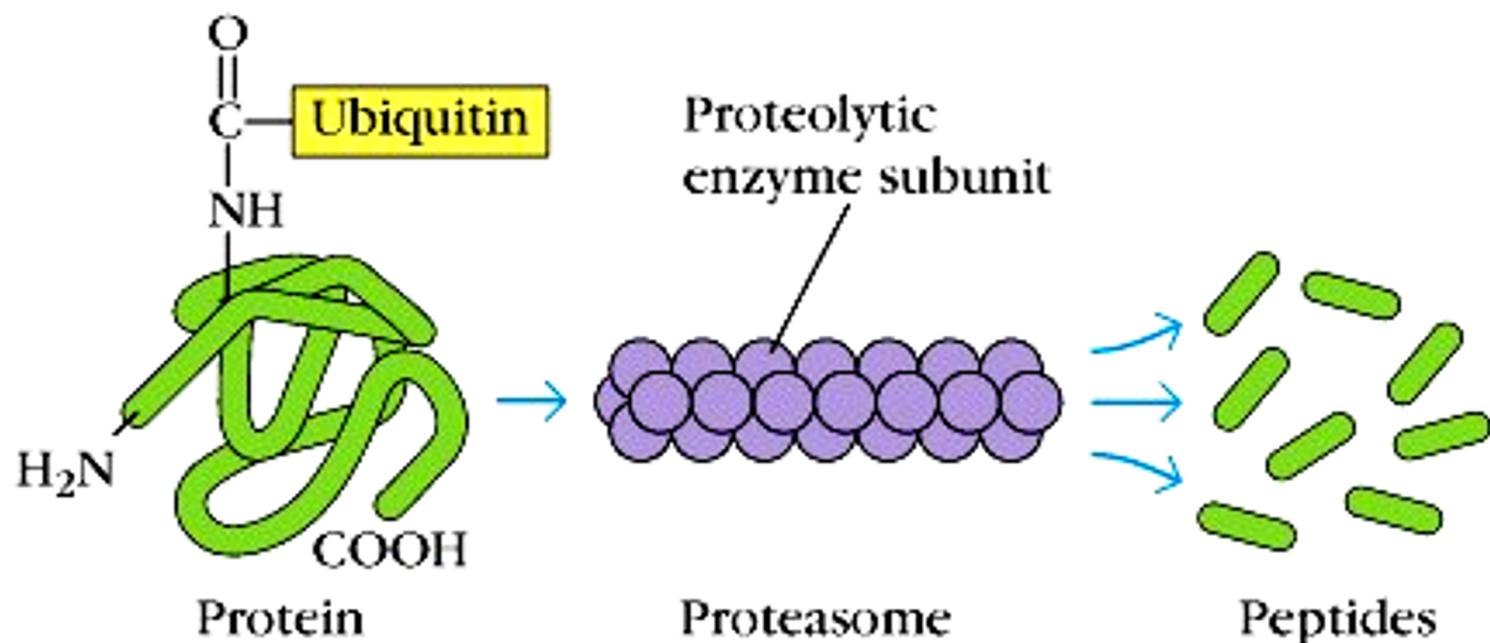
= 10^{12} !!!!

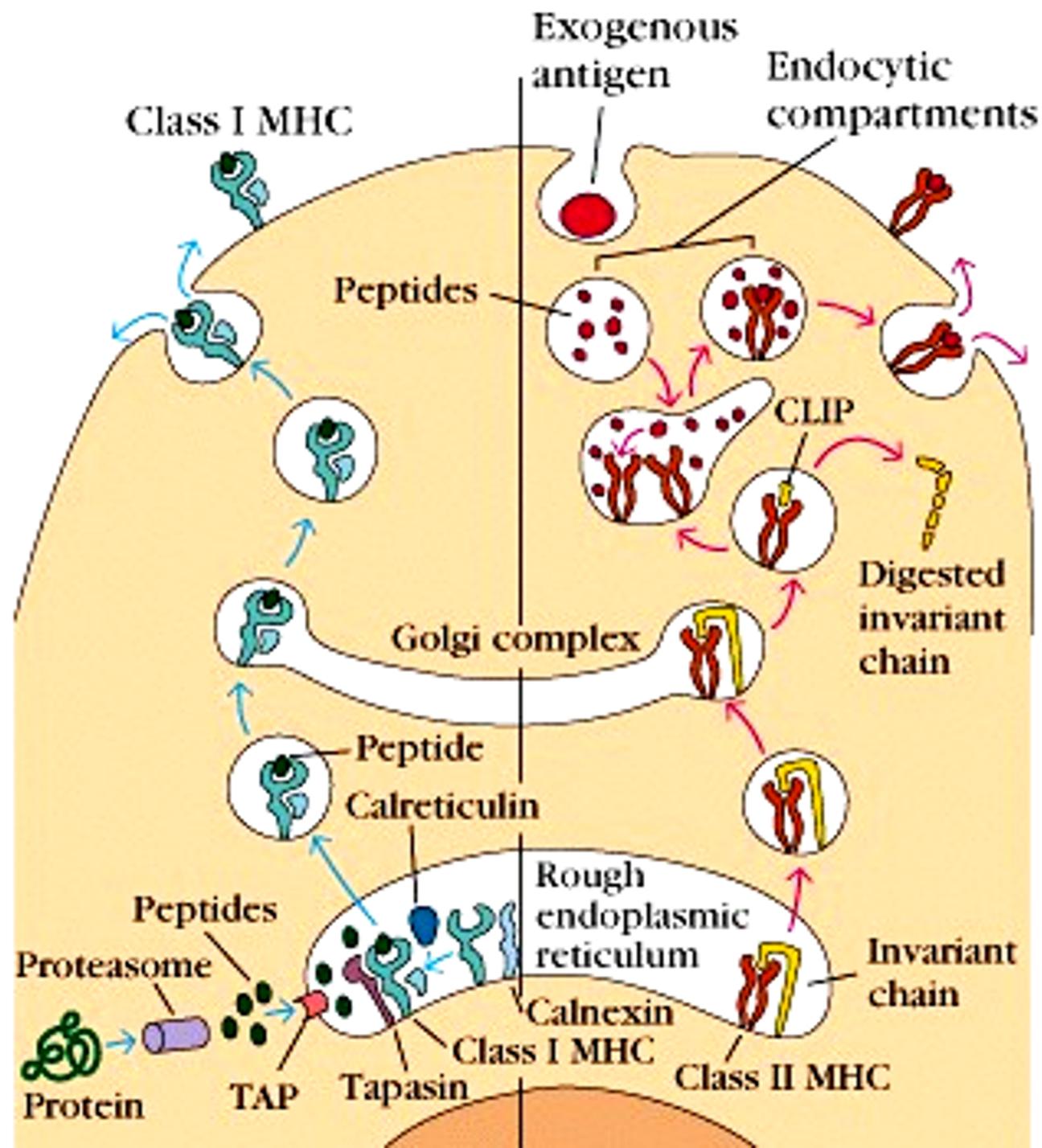
EXPERIMENTAL CONDITIONS

T-CELL
ACTIVATION

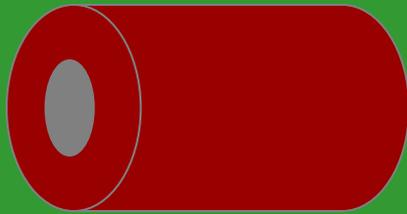
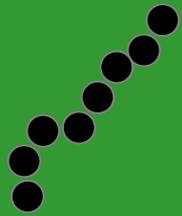


(b)

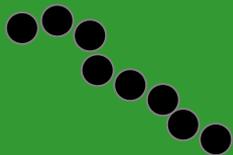
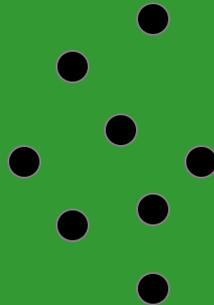




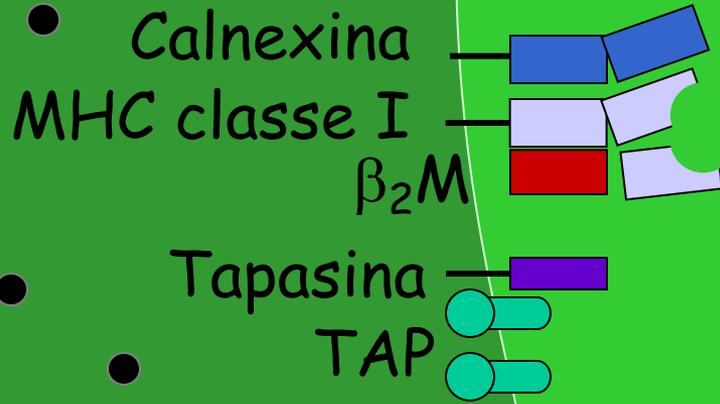
Degradação de substâncias presentes no citosol



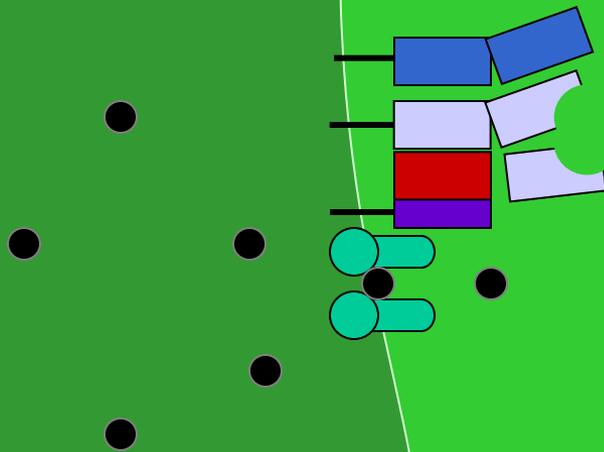
Proteosomas



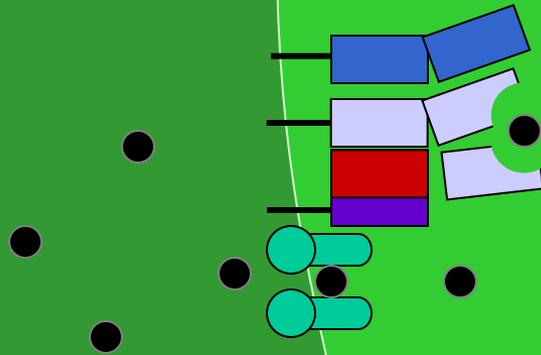
Tráfego de peptídeos presentes no citosol



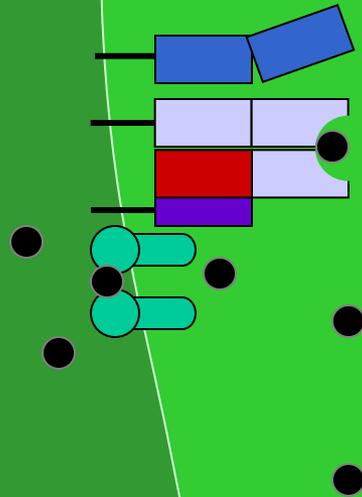
Tráfego de peptídeos presentes no citosol



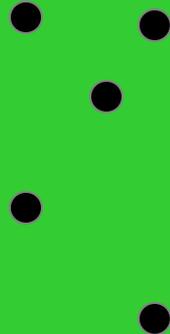
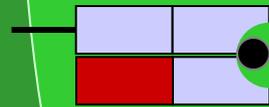
Tráfego de peptídeos presentes no citosol



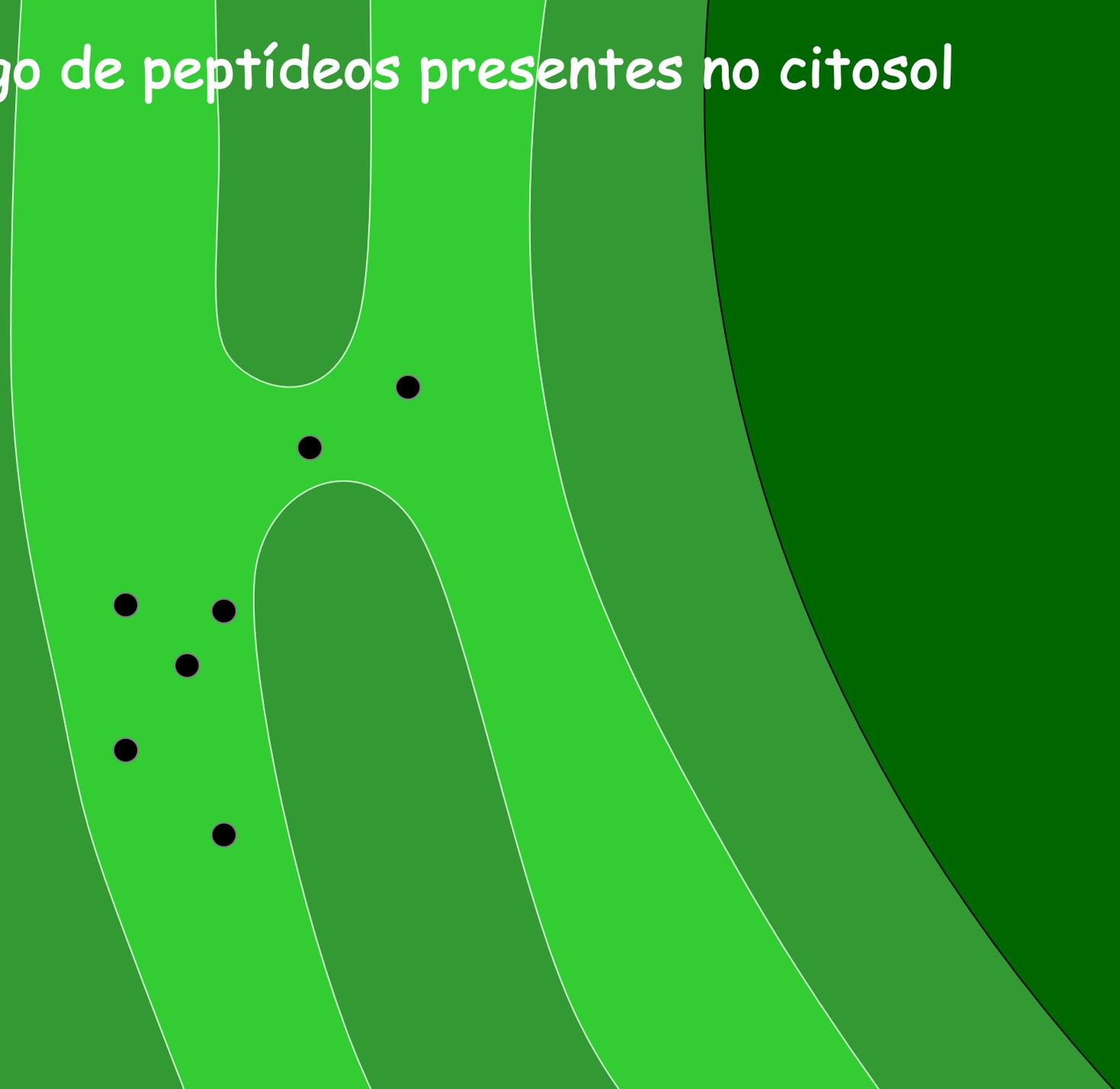
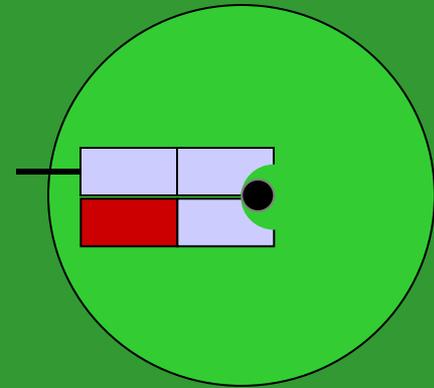
Tráfego de peptídeos presentes no citosol

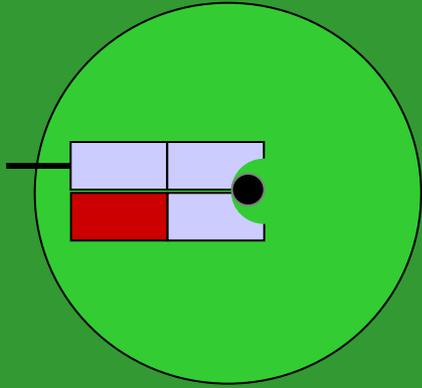


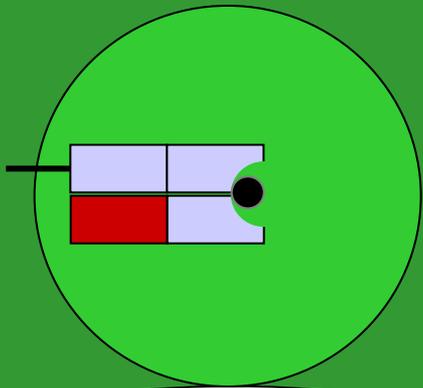
Tráfego de peptídeos presentes no citosol

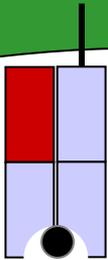


Tráfego de peptídeos presentes no citosol

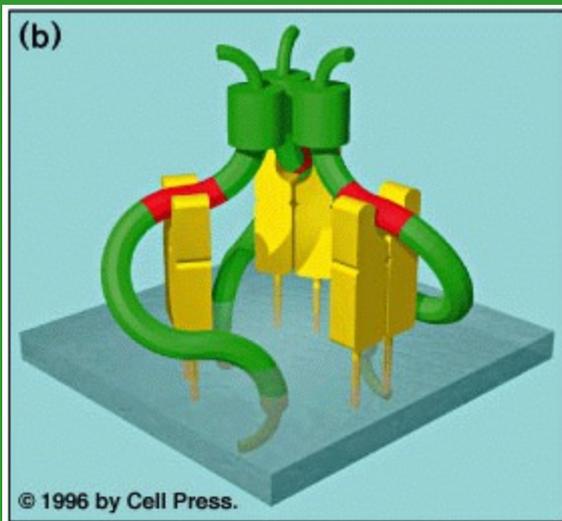
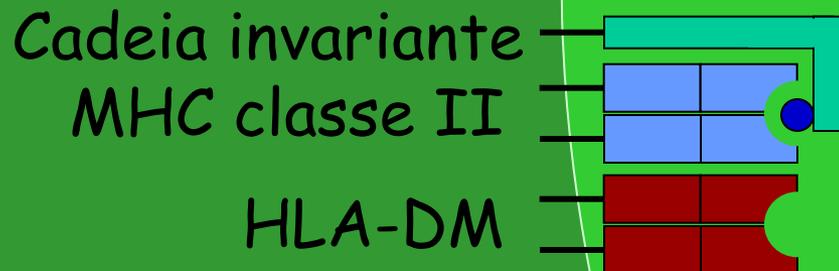




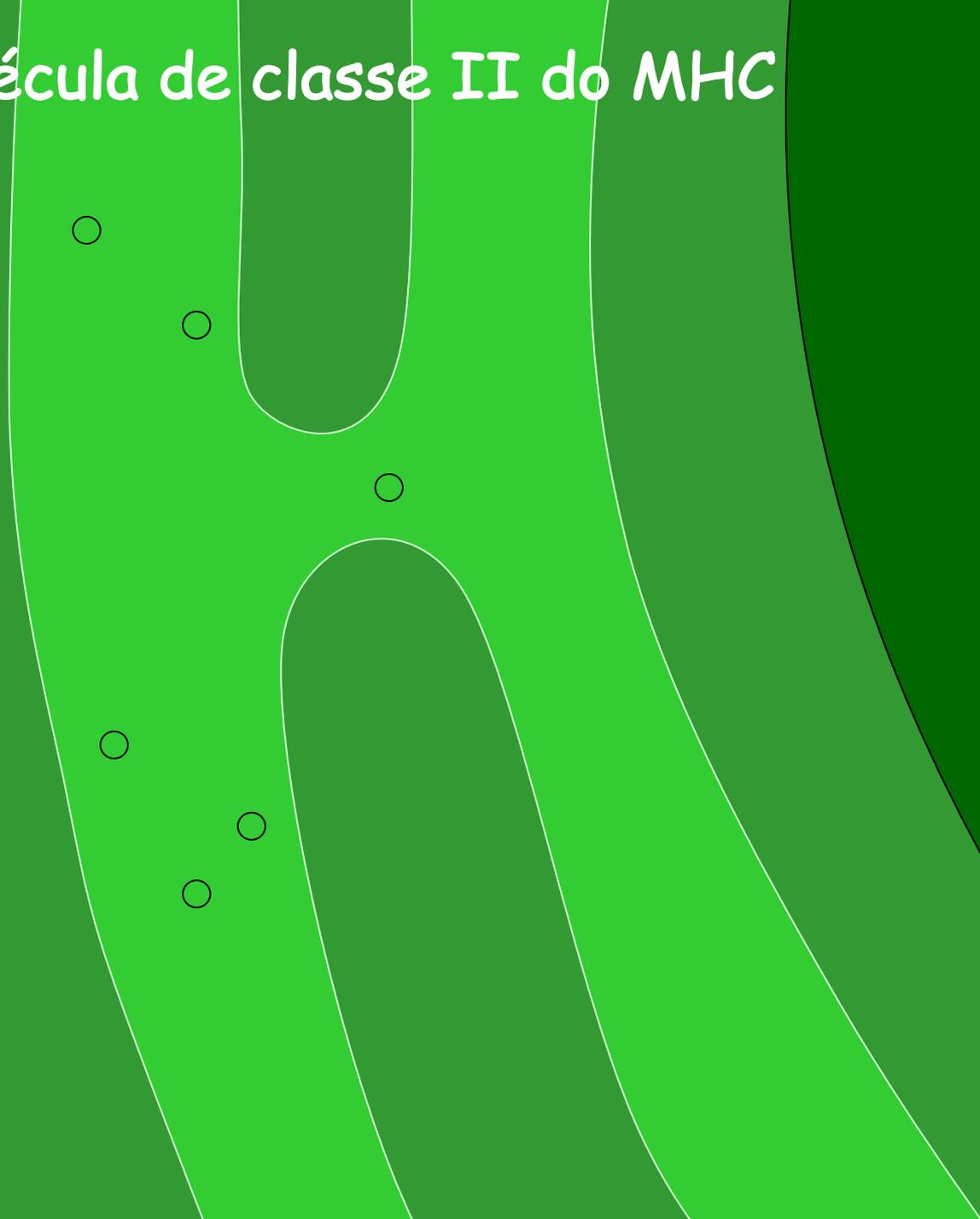
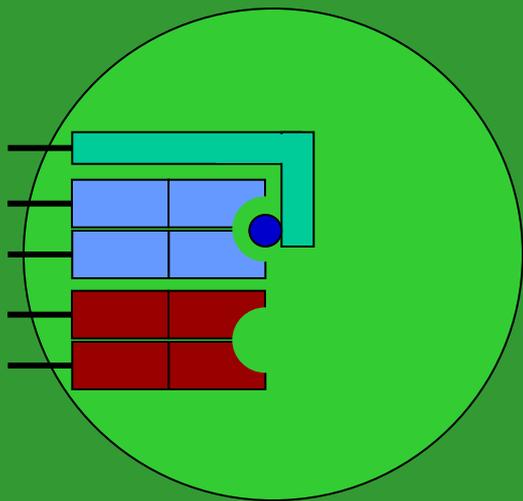




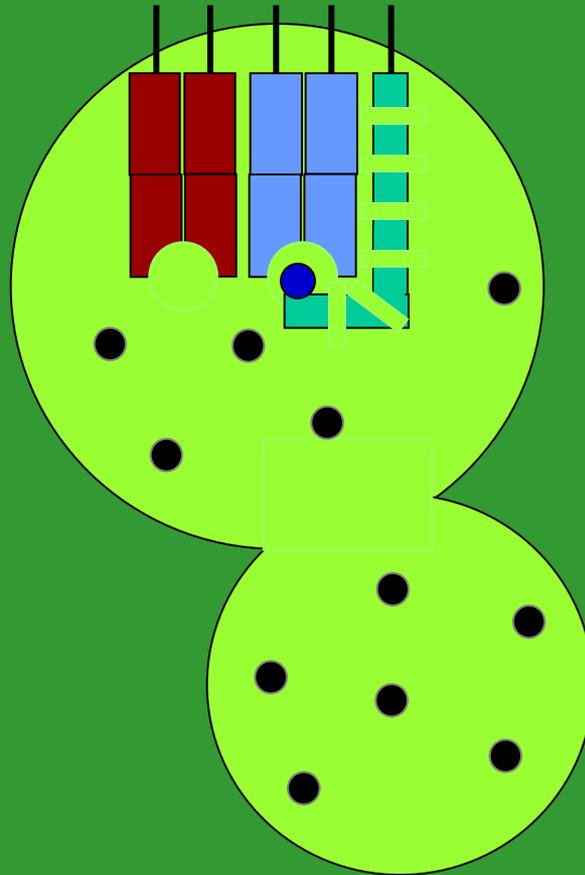
Síntese da molécula de classe II do MHC



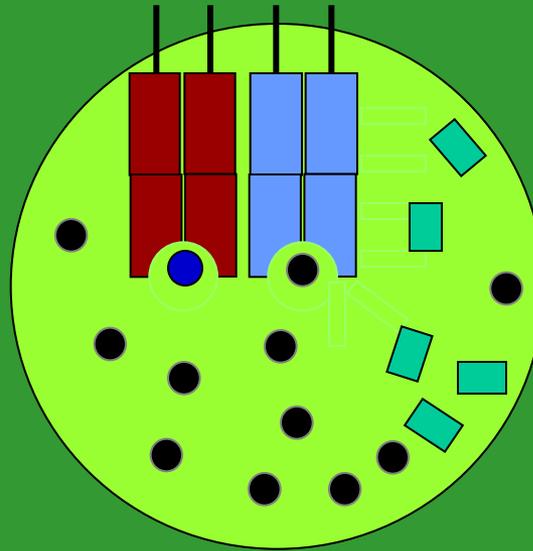
Síntese da molécula de classe II do MHC



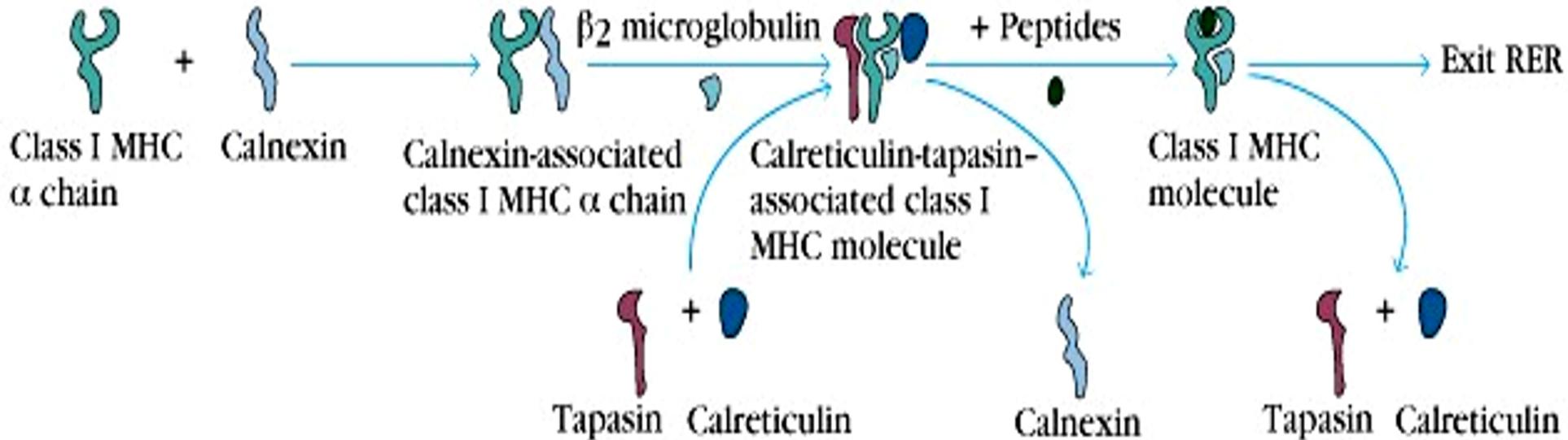
Degradação da cadeia invariante

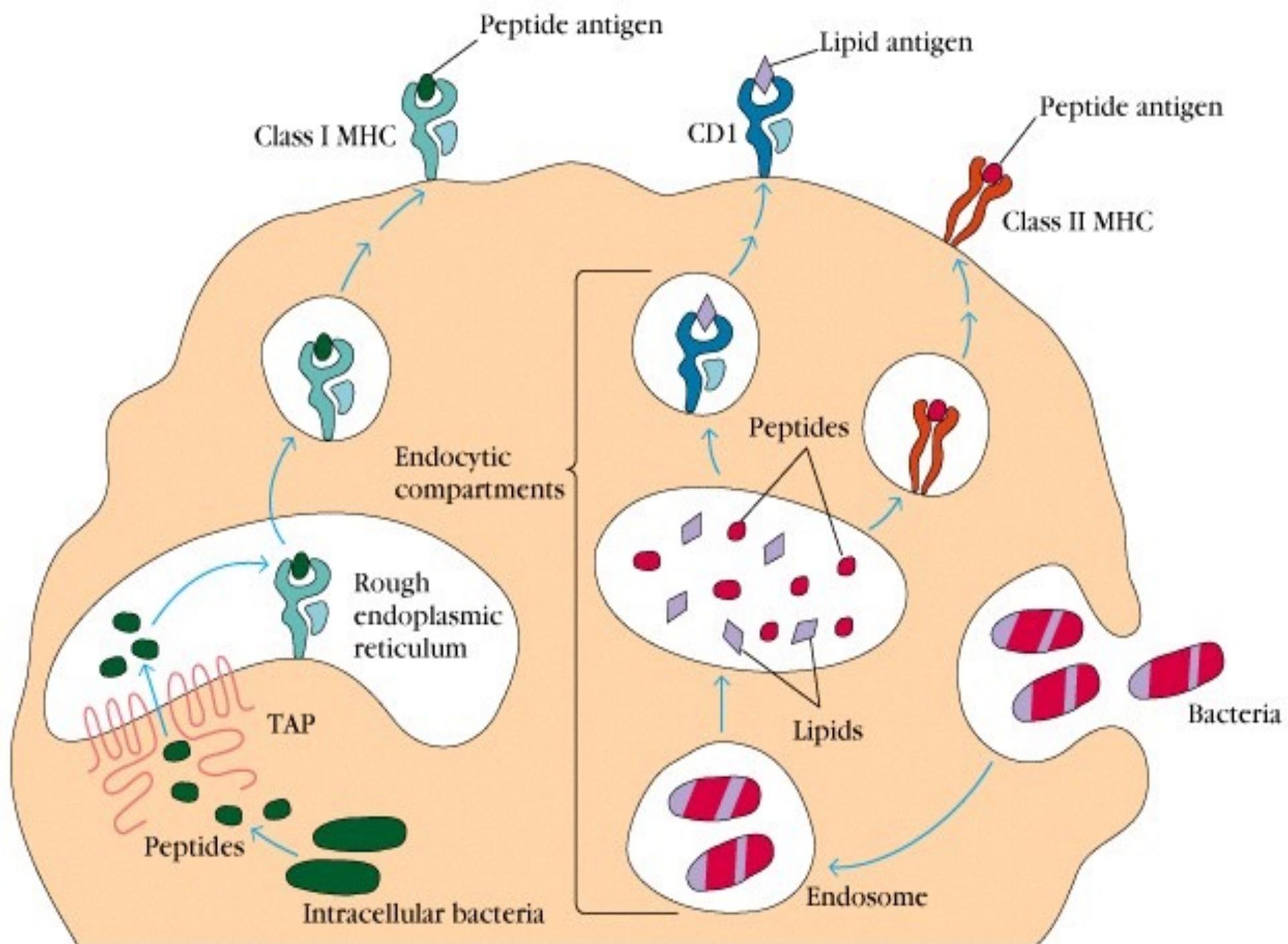


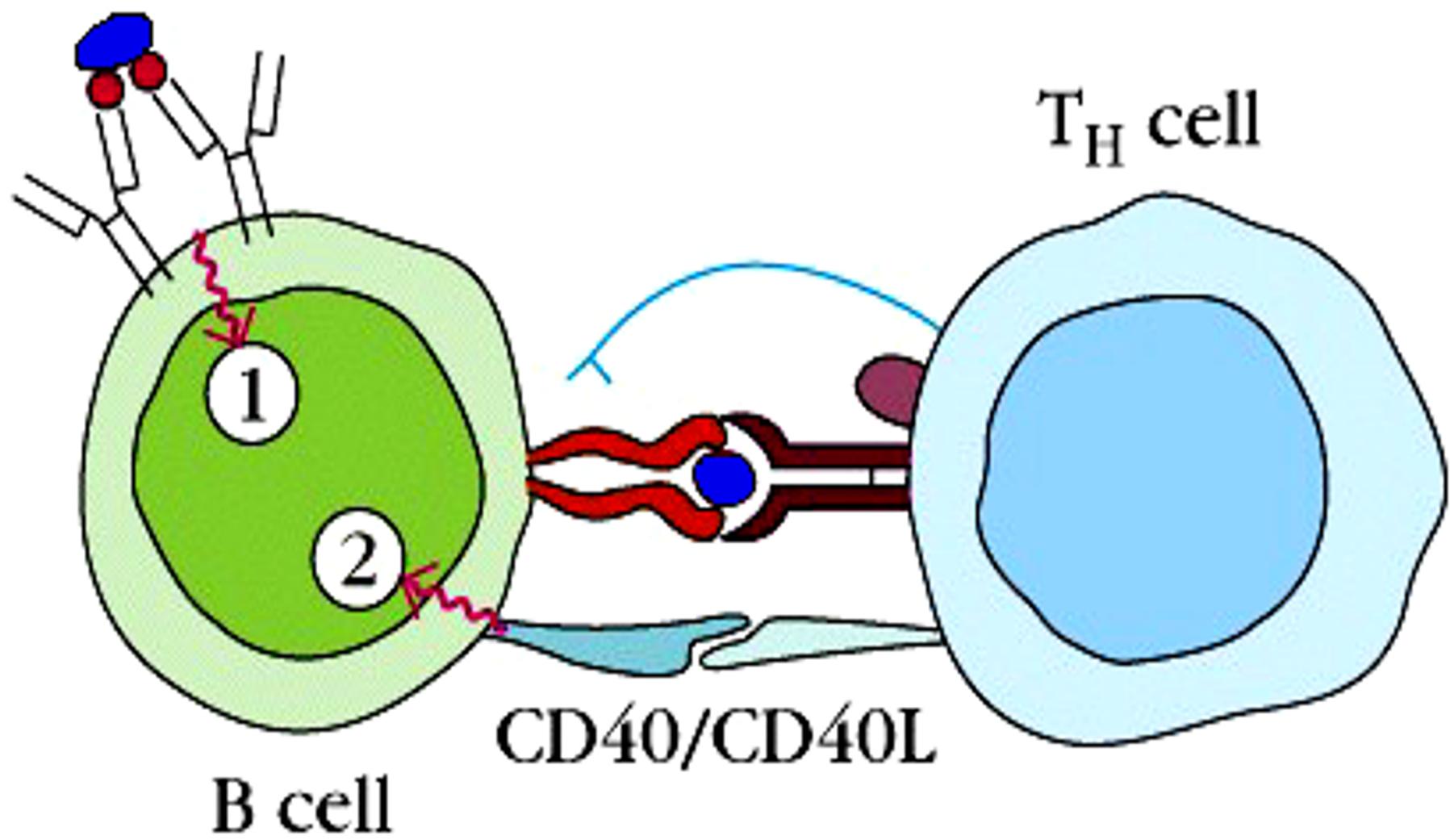
Apresentação do peptídeo na superfície celular

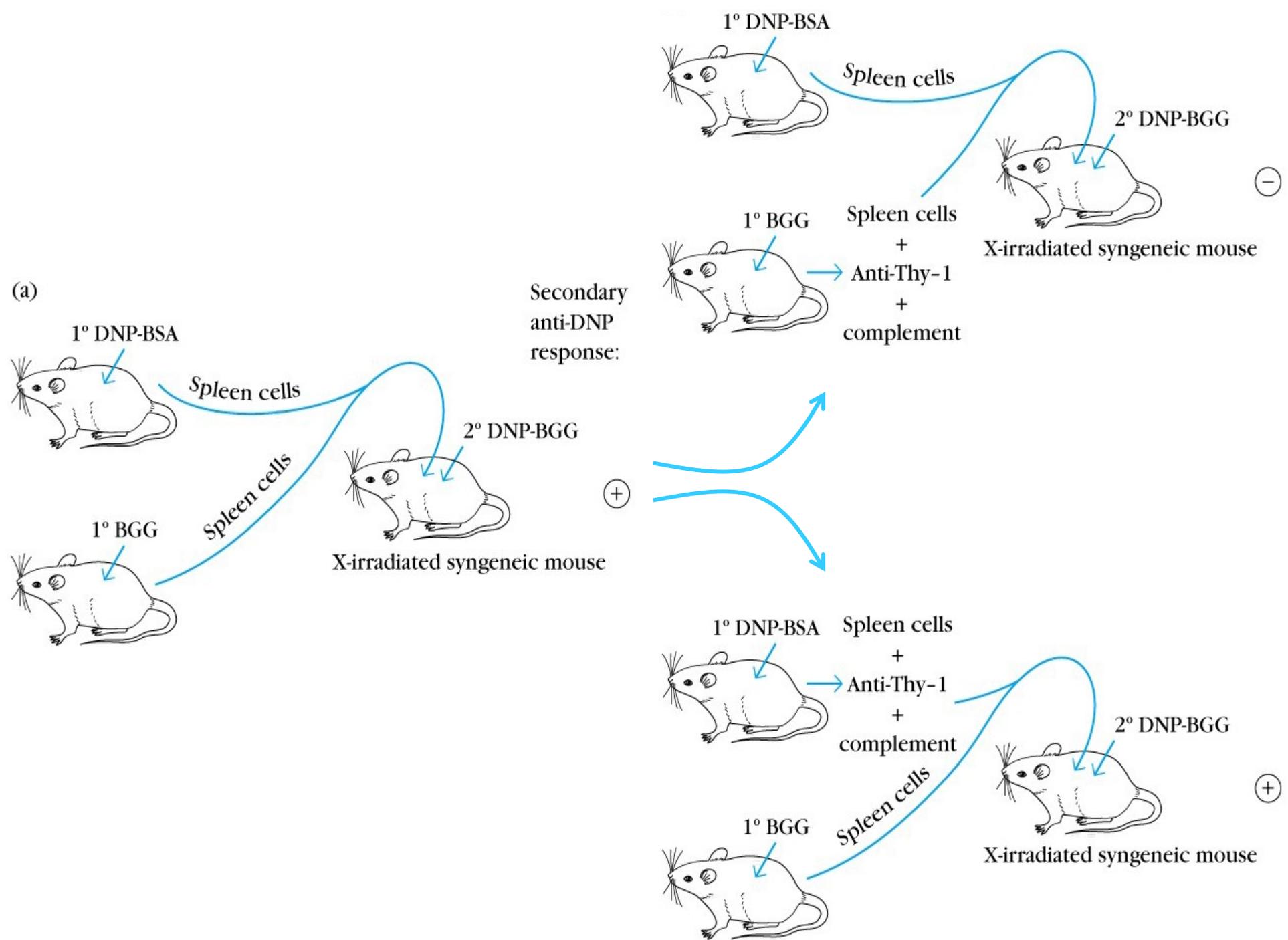


Formação do complexo associado à molécula de MHC classe I

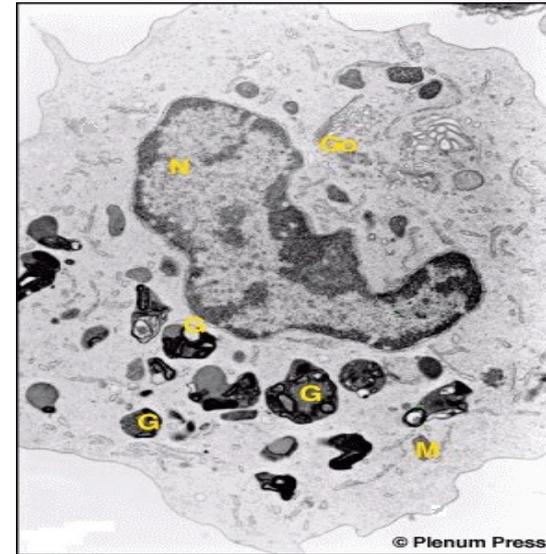
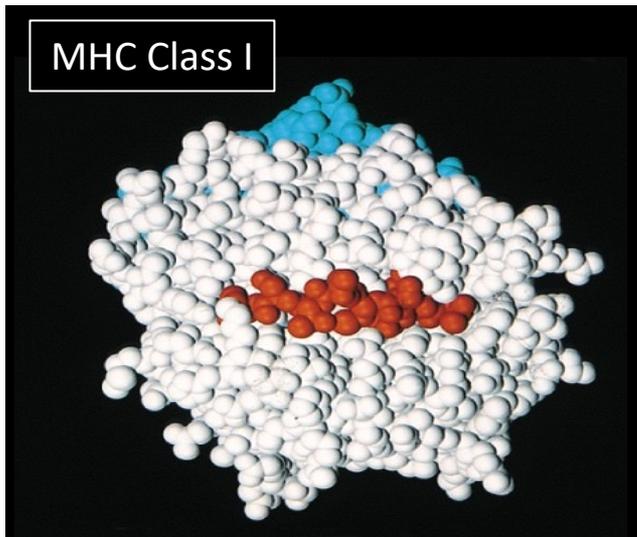




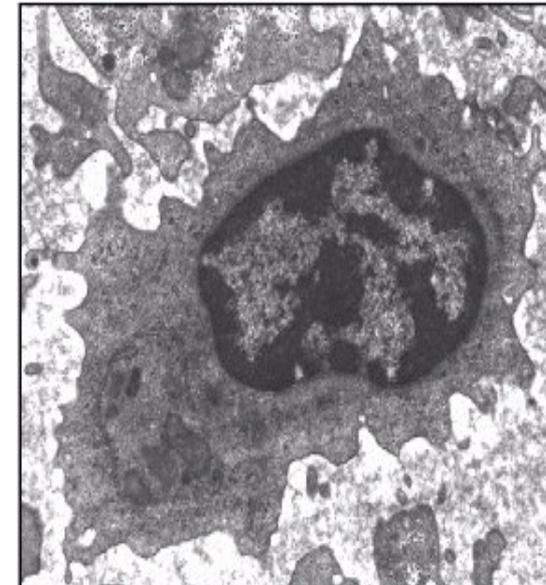
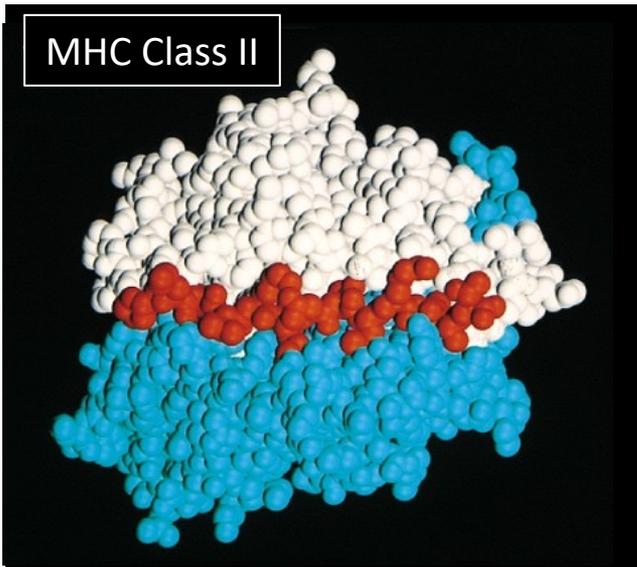




Interação TCR-MHC+peptídeo



Linfócito T CD8+



Linfócito T CD4+

Interação TCR-MHC+peptídeo

Receptores e Co-receptores

