

Apresentação de antígenos e receptores de linfócitos T e B

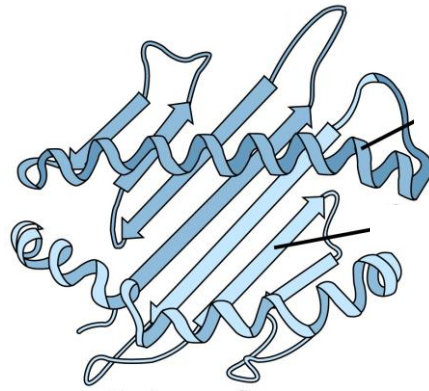
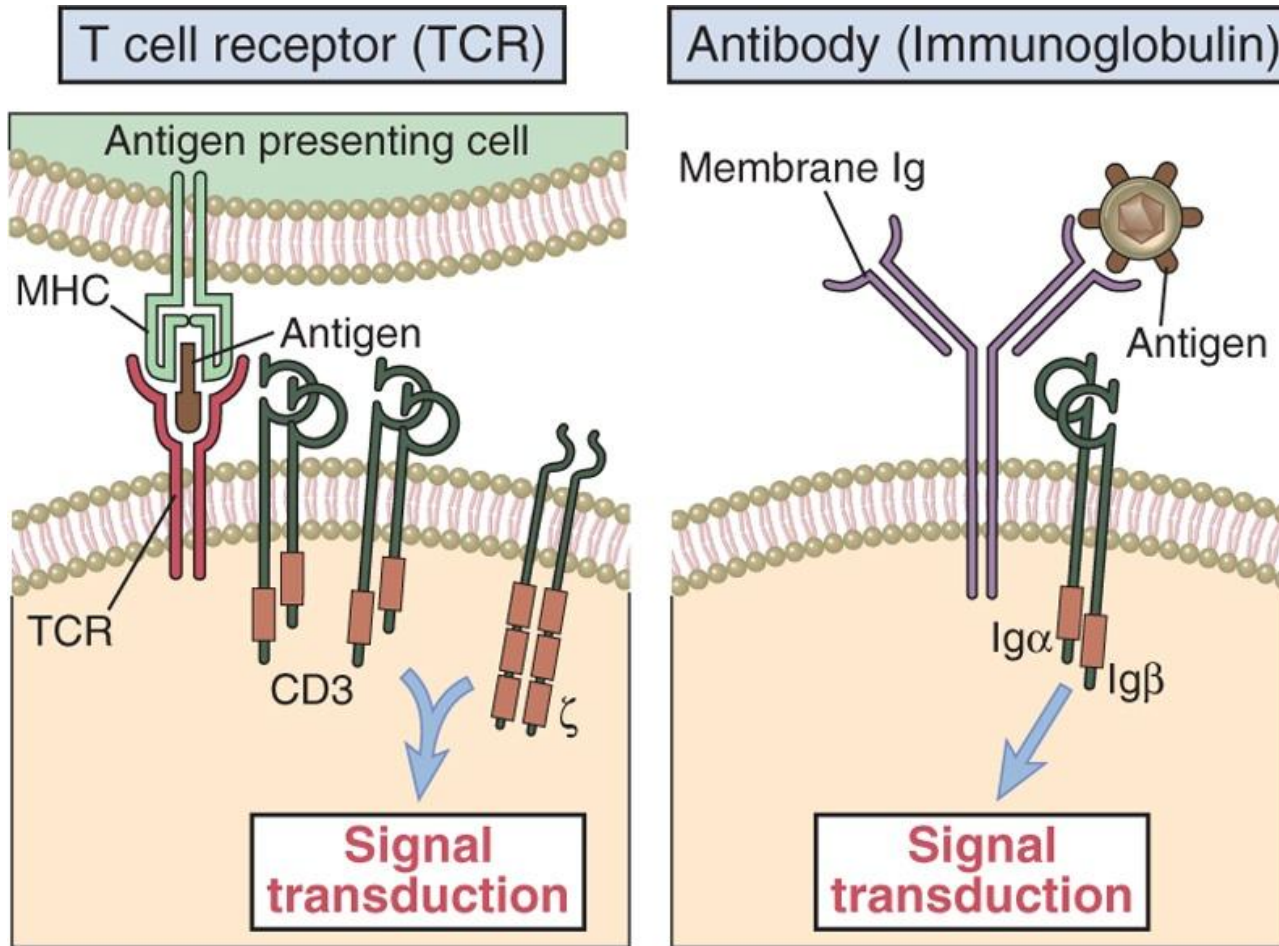


Figure 8-10
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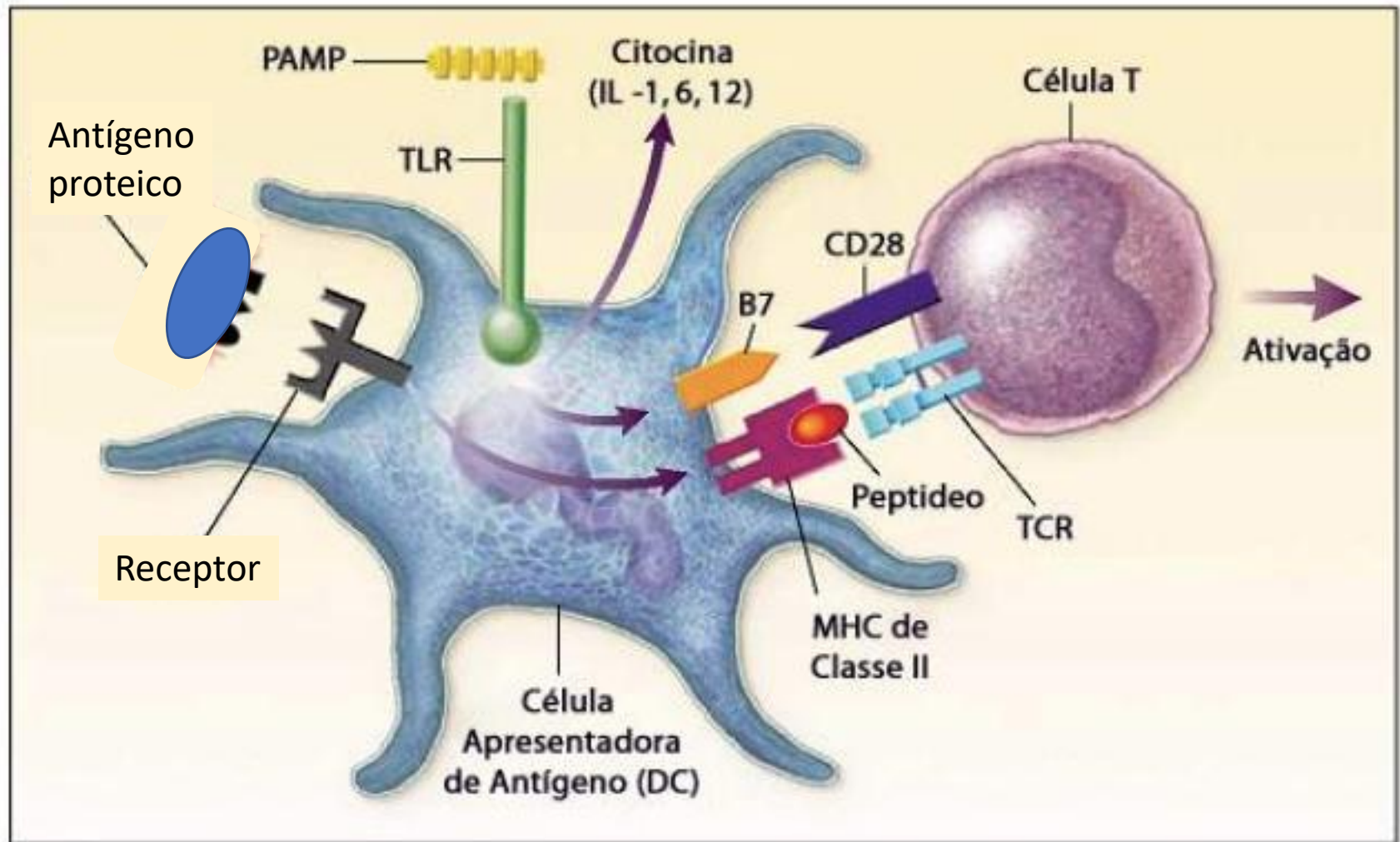
Sergio Costa Oliveira

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ICB – USP

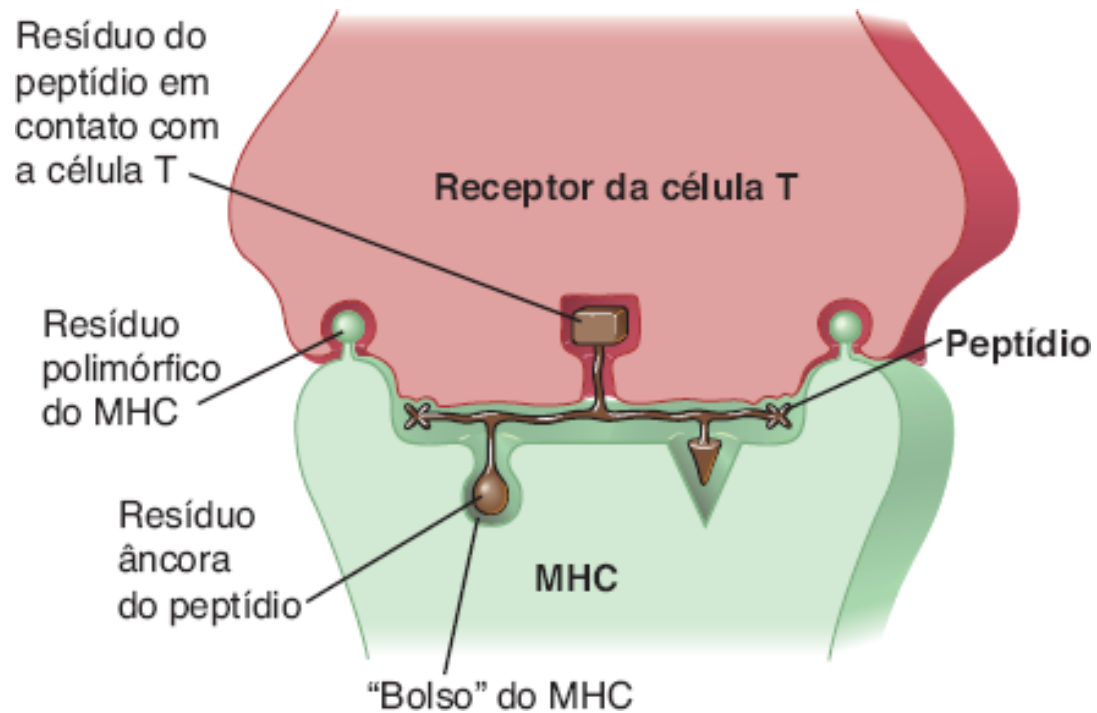
Os linfócitos B e T reconhecem antígenos de forma diferente



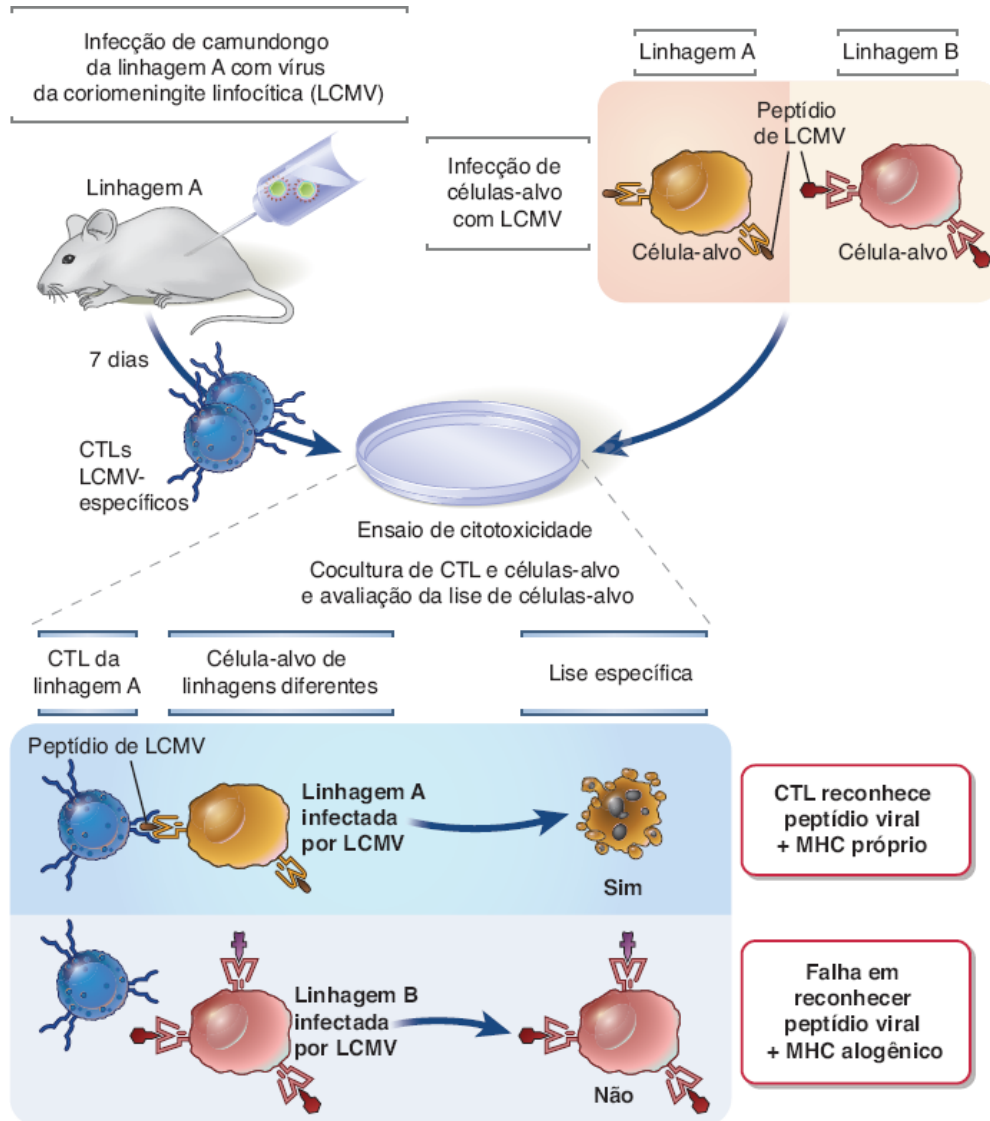
Os linfócitos T reconhecem peptídeos apresentados pela molécula do MHC na superfície de uma célula apresentadora



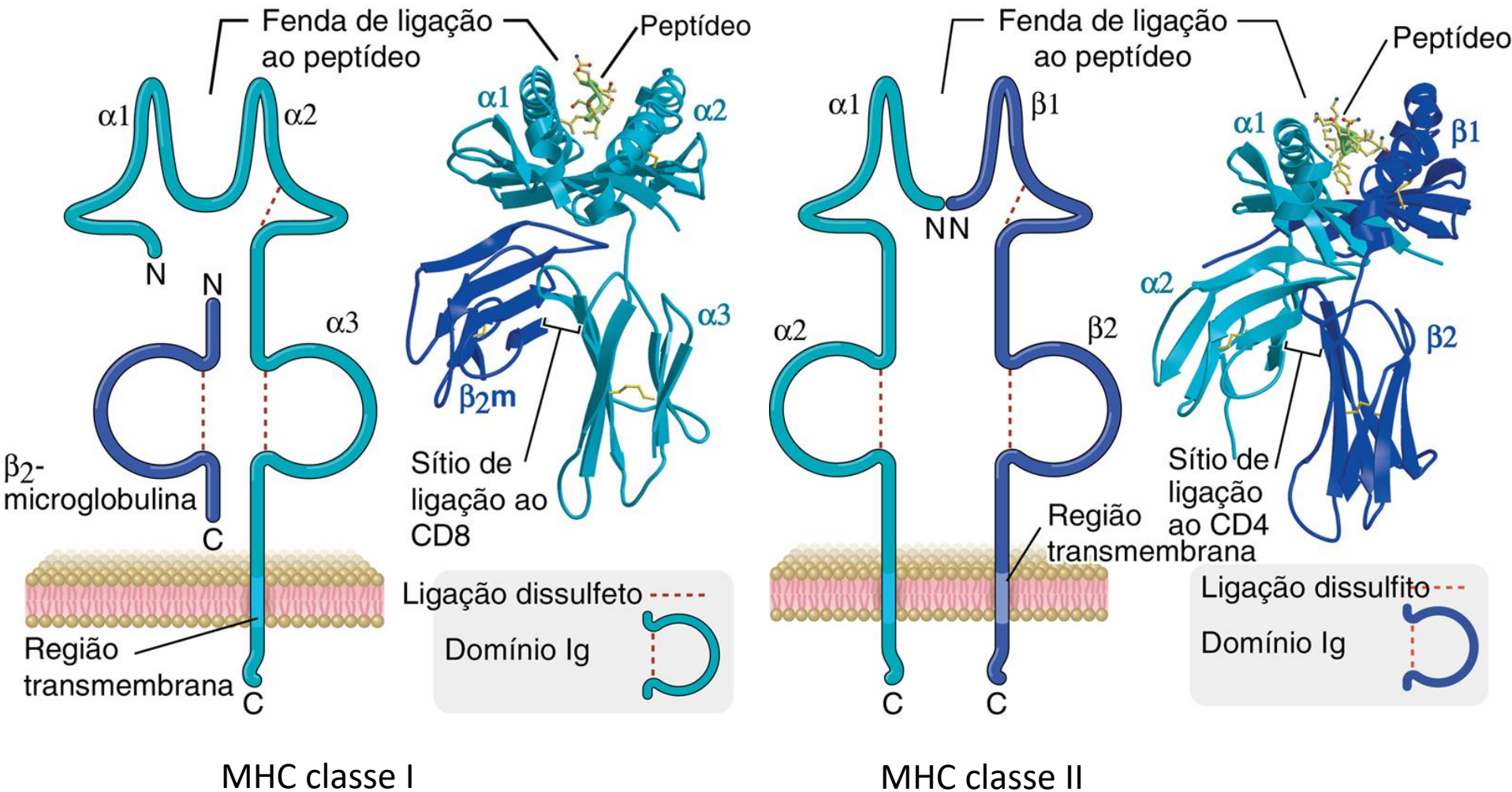
Interação TCR e MHC



Restrição ao MHC



As moléculas de MHC I e II



Estrutura molecular e expressão do MHC

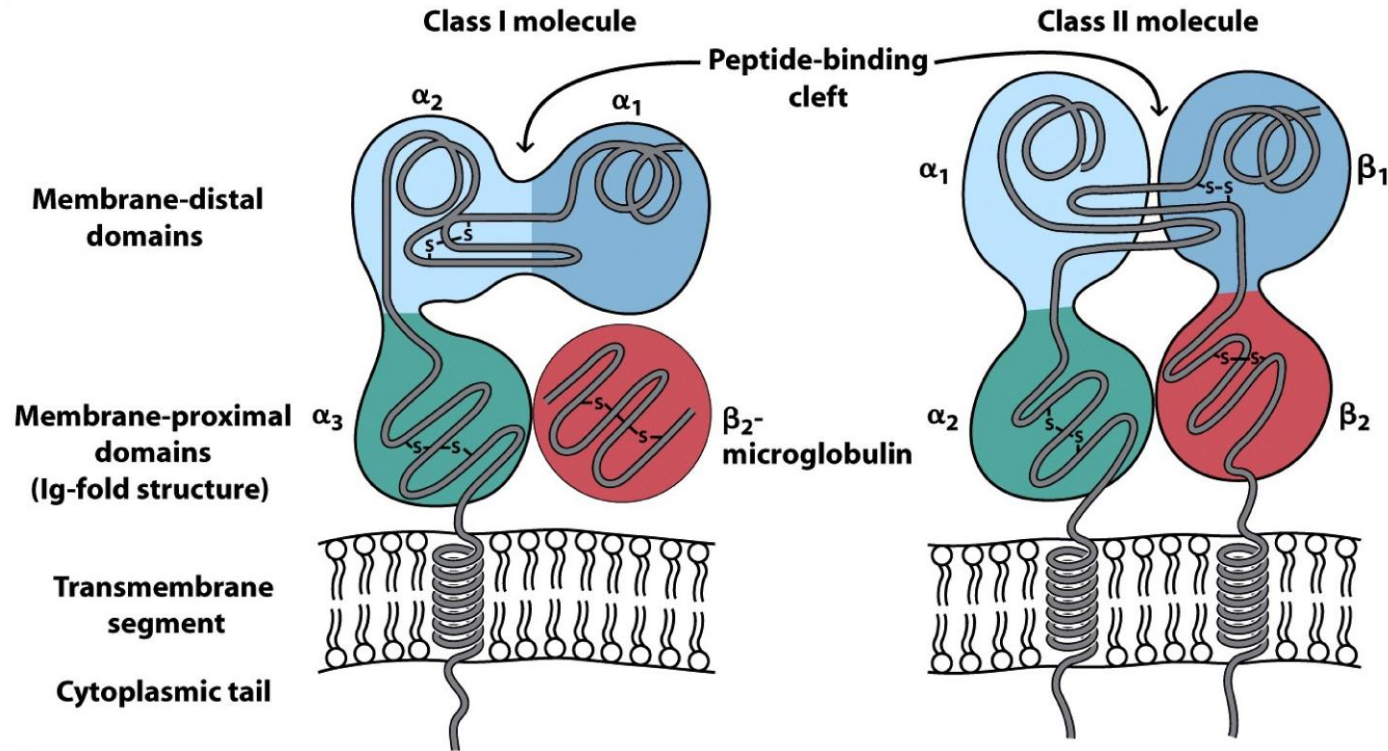


Figure 8-3
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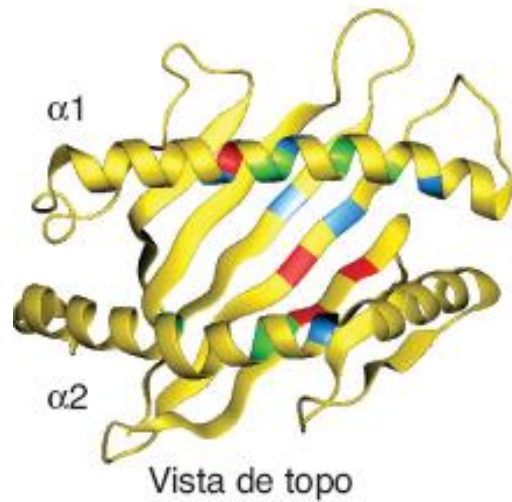
Expressão

Todas as células
nucleadas

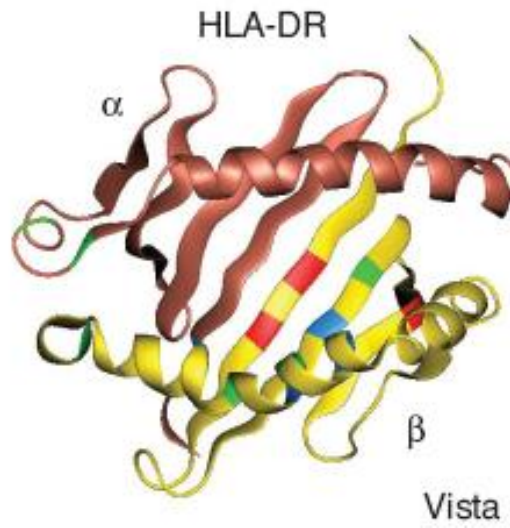
Células apresentadoras
de antígenos

Vista da fenda do MHC I e II

HLA de classe I



HLA de classe II



HLA-DQ

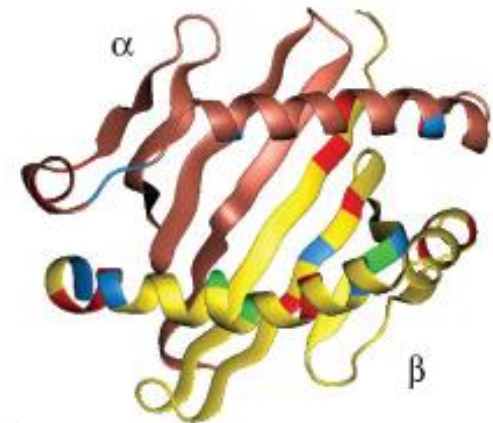


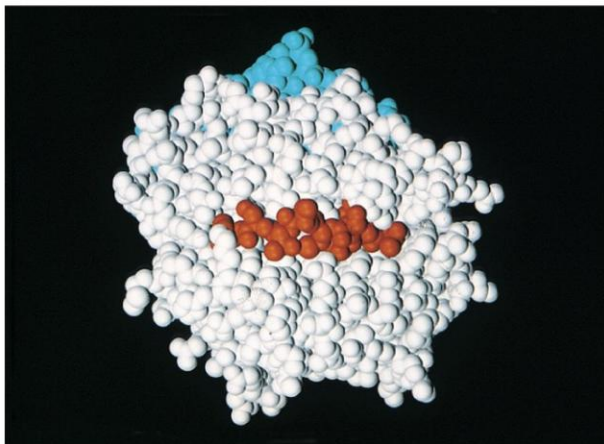
TABLE 8-3 Antigen-presenting cells		
Professional antigen-presenting cells	Nonprofessional antigen-presenting cells	
Dendritic cells (several types)	Fibroblasts (skin)	Thymic epithelial cells
Macrophages	Glial cells (brain)	Thyroid epithelial cells
B cells	Pancreatic beta cells	Vascular endothelial cells

Table 8-3
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TABLE 8-2 Peptide binding by class I and class II MHC molecules		
	Class I molecules	Class II molecules
Peptide-binding domain	$\alpha 1/\alpha 2$	$\alpha 1/\beta 1$
Nature of peptide-binding cleft	Closed at both ends	Open at both ends
General size of bound peptides	8–10 amino acids	13–18 amino acids
Peptide motifs involved in binding to MHC molecule	Anchor residues at both ends of peptide; generally hydrophobic carboxyl-terminal anchor	Anchor residues distributed along the length of the peptide
Nature of bound peptide	Extended structure in which both ends interact with MHC cleft but middle arches up away from MHC molecule	Extended structure that is held at a constant elevation above the floor of MHC cleft

Table 8-2
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(a) Class I MHC



(b) Class II MHC

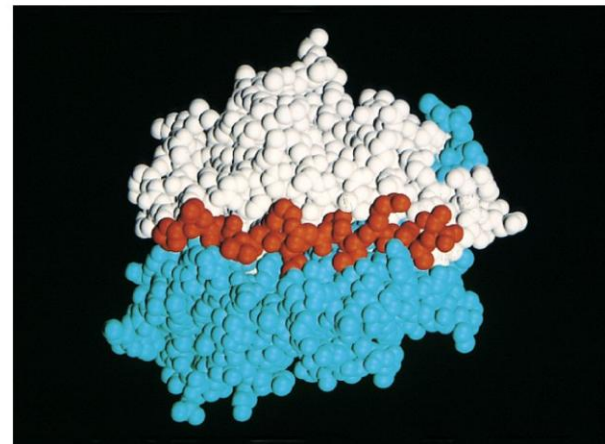
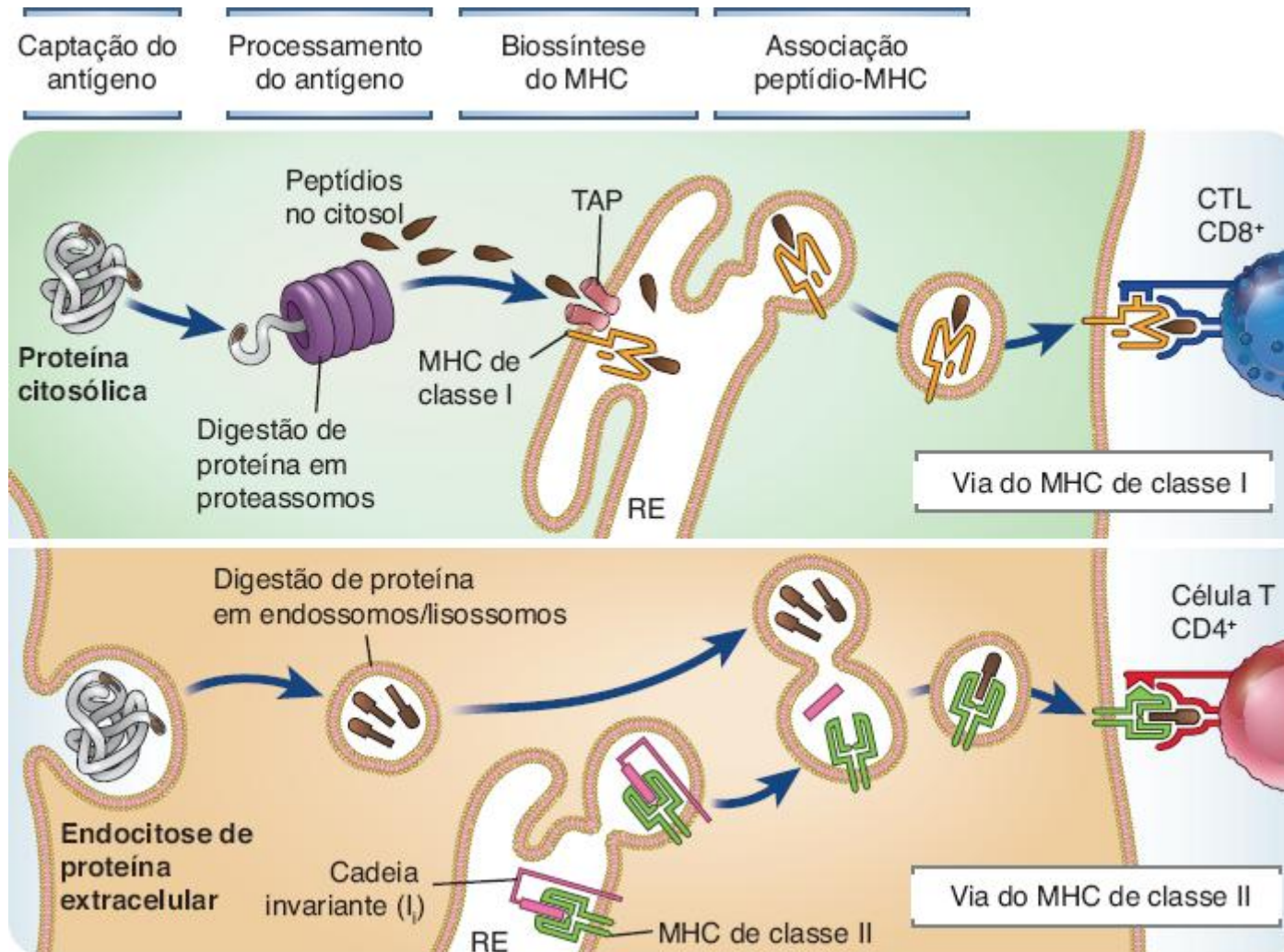
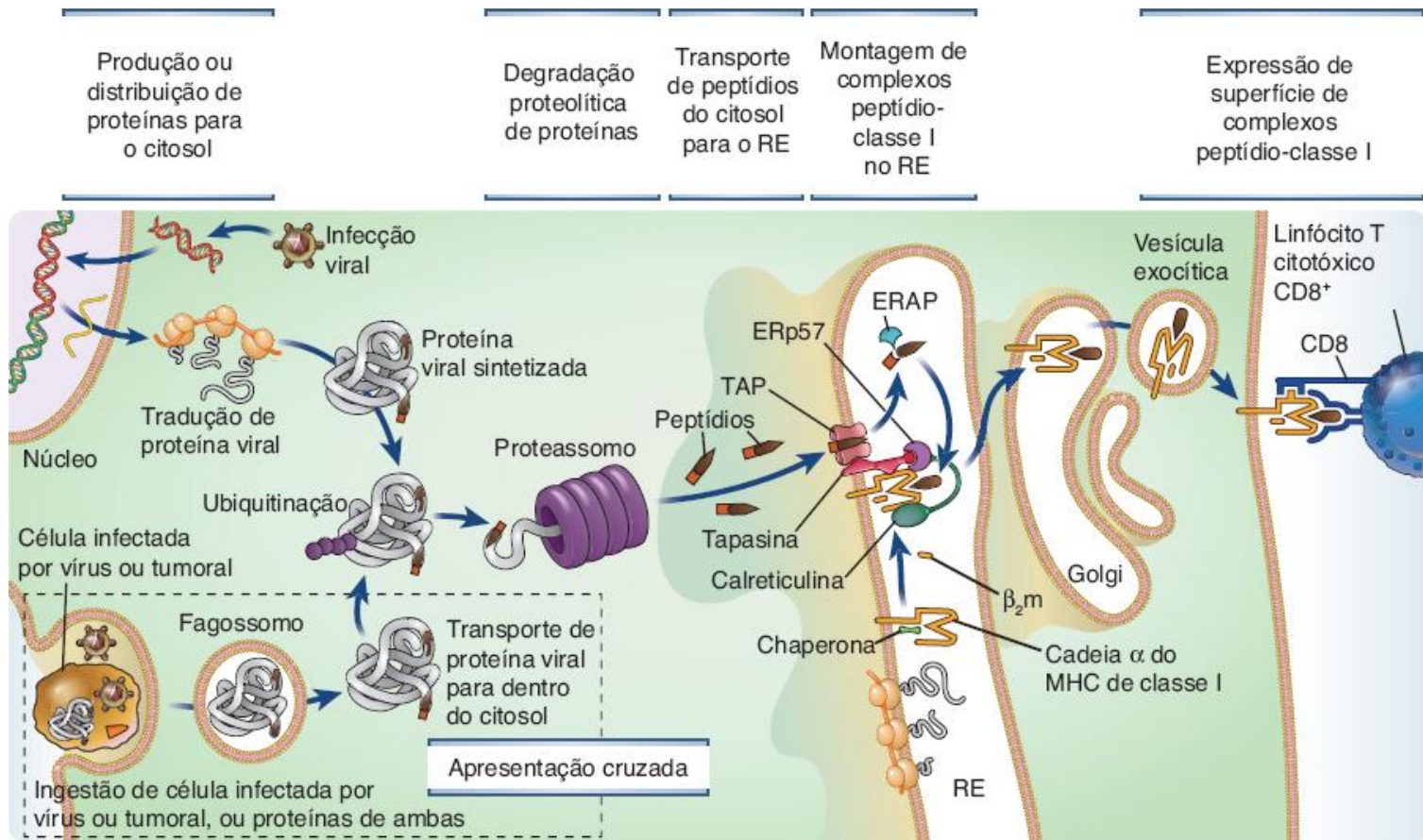


Figure 8-7
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Vias de Processamento e Apresentação de antígenos



Via MHC de Classe I



Via MHC de Classe II

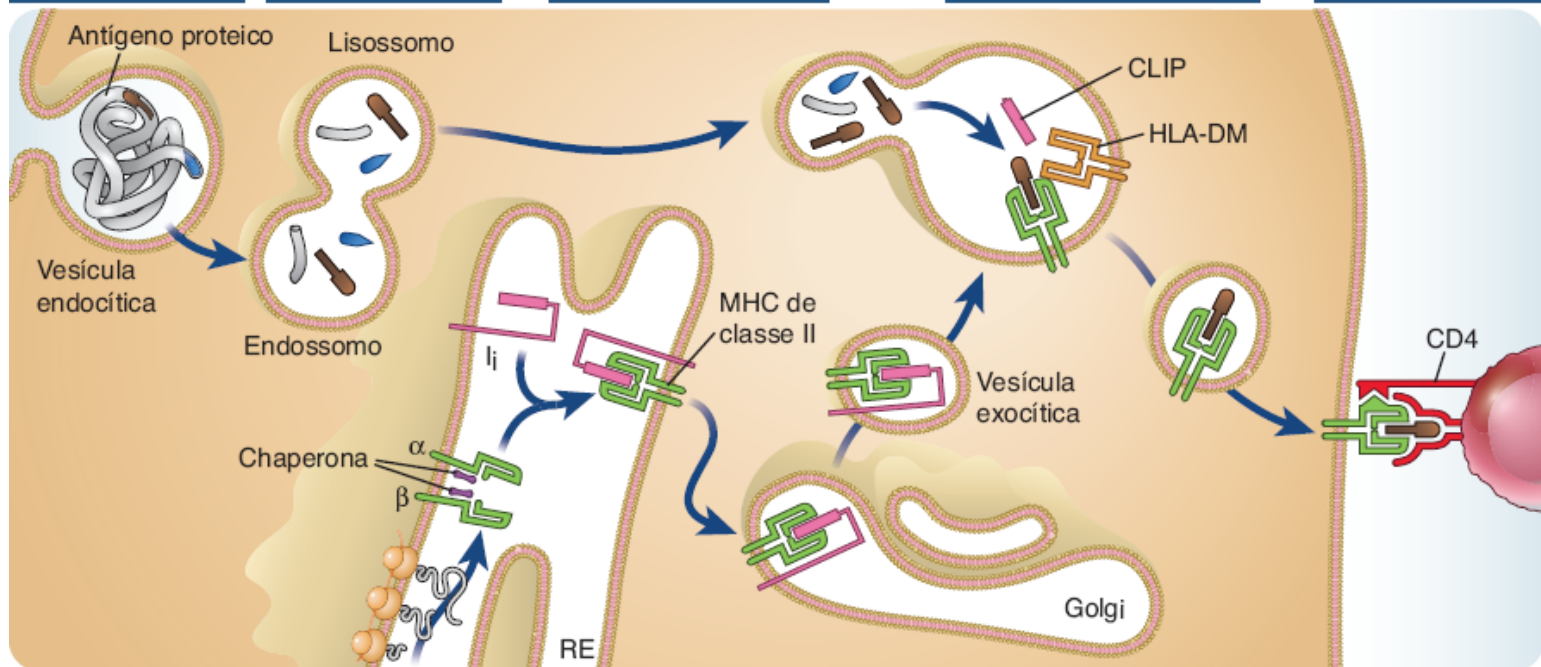
Captação de proteínas extracelulares dentro de compartimentos vesiculares de APC

Processamento de proteínas internalizadas em vesículas endossômicas/ lisossômicas

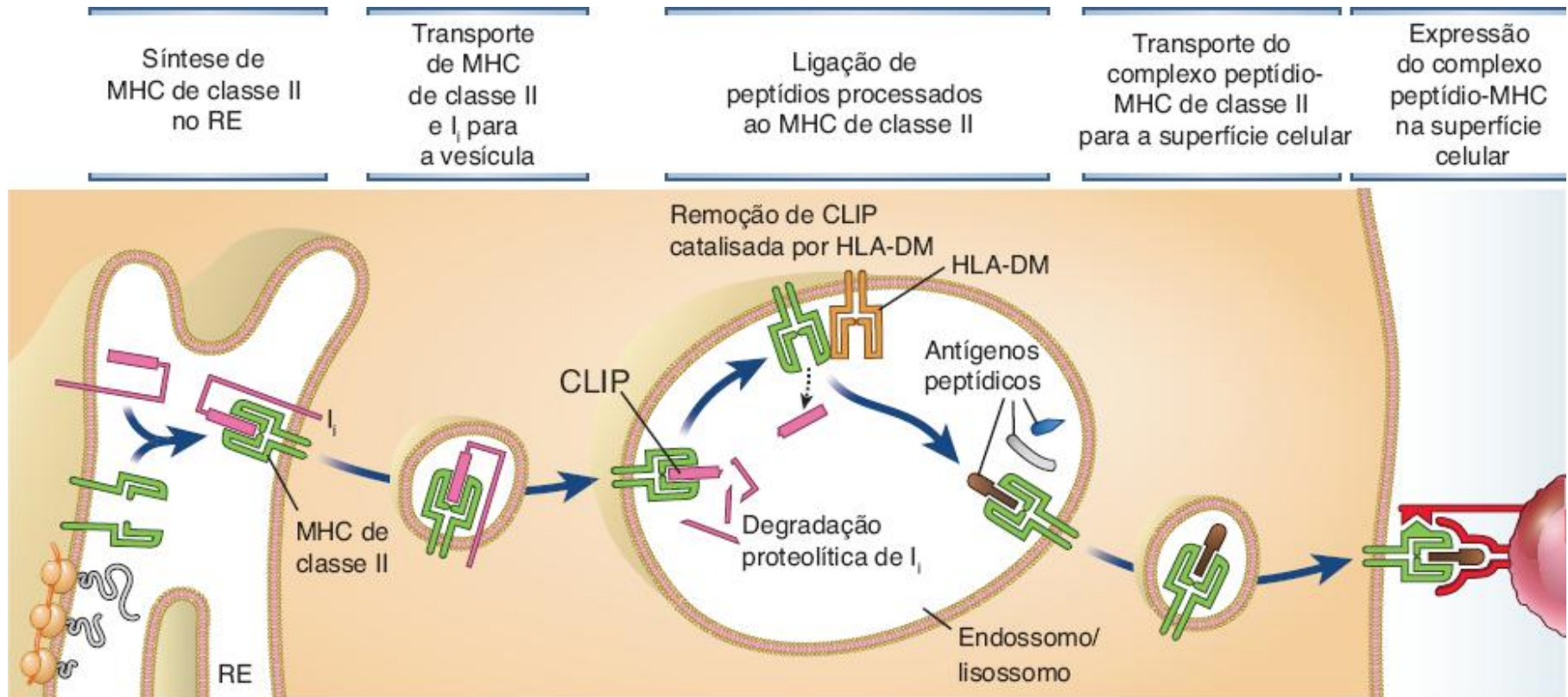
Biossíntese e transporte de moléculas do MHC de classe II para os endossomos

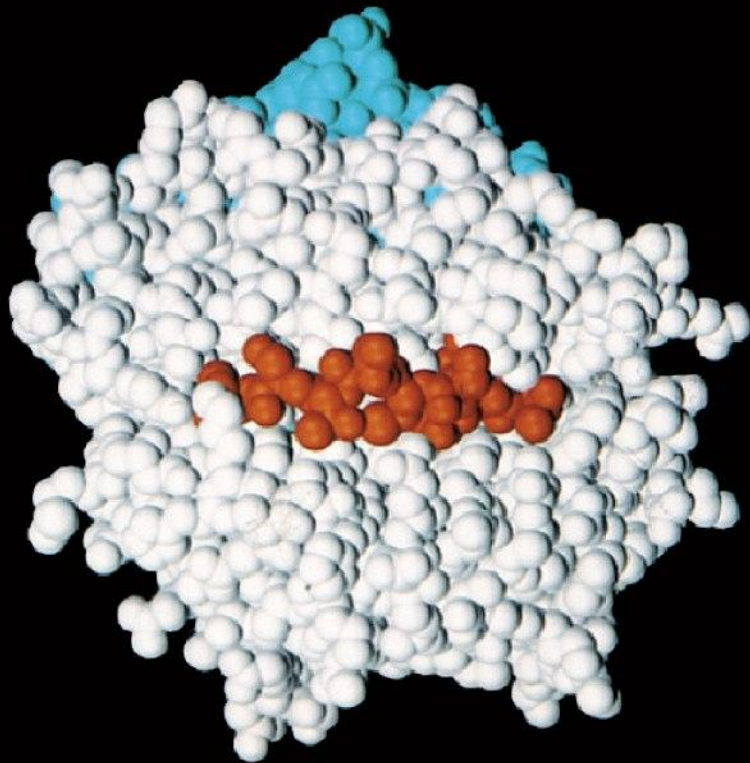
Associação de peptídios processados com moléculas do MHC de classe II em lisossomos

Expressão de complexos peptídeo-MHC na superfície celular

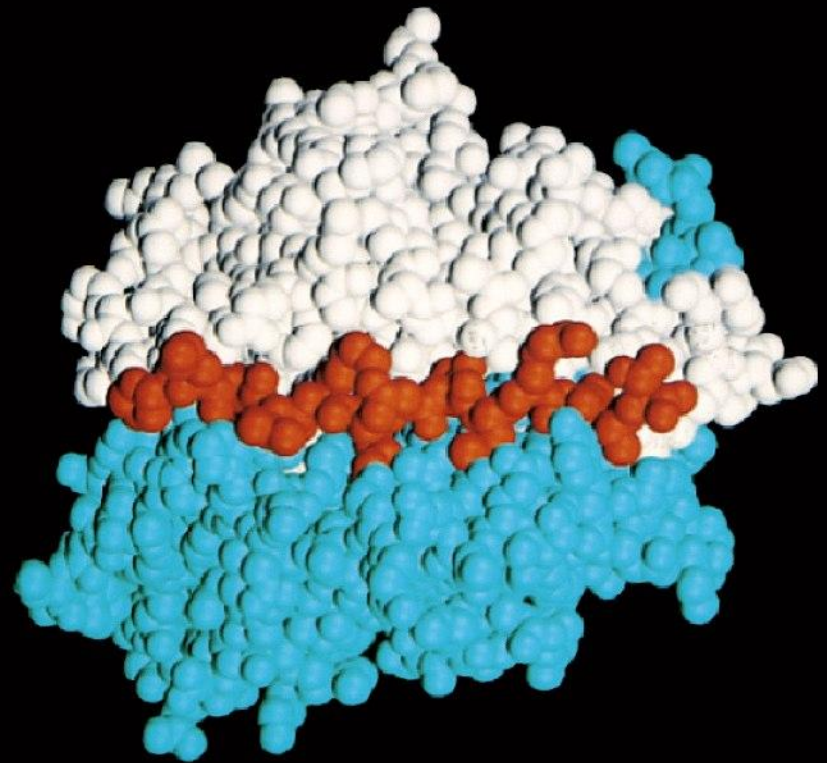


Cadeia Invariante associada ao MHC II





Class I MHC



Class II MHC

Mouse H-2 complex

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*

*Not present in all haplotypes

Human HLA complex

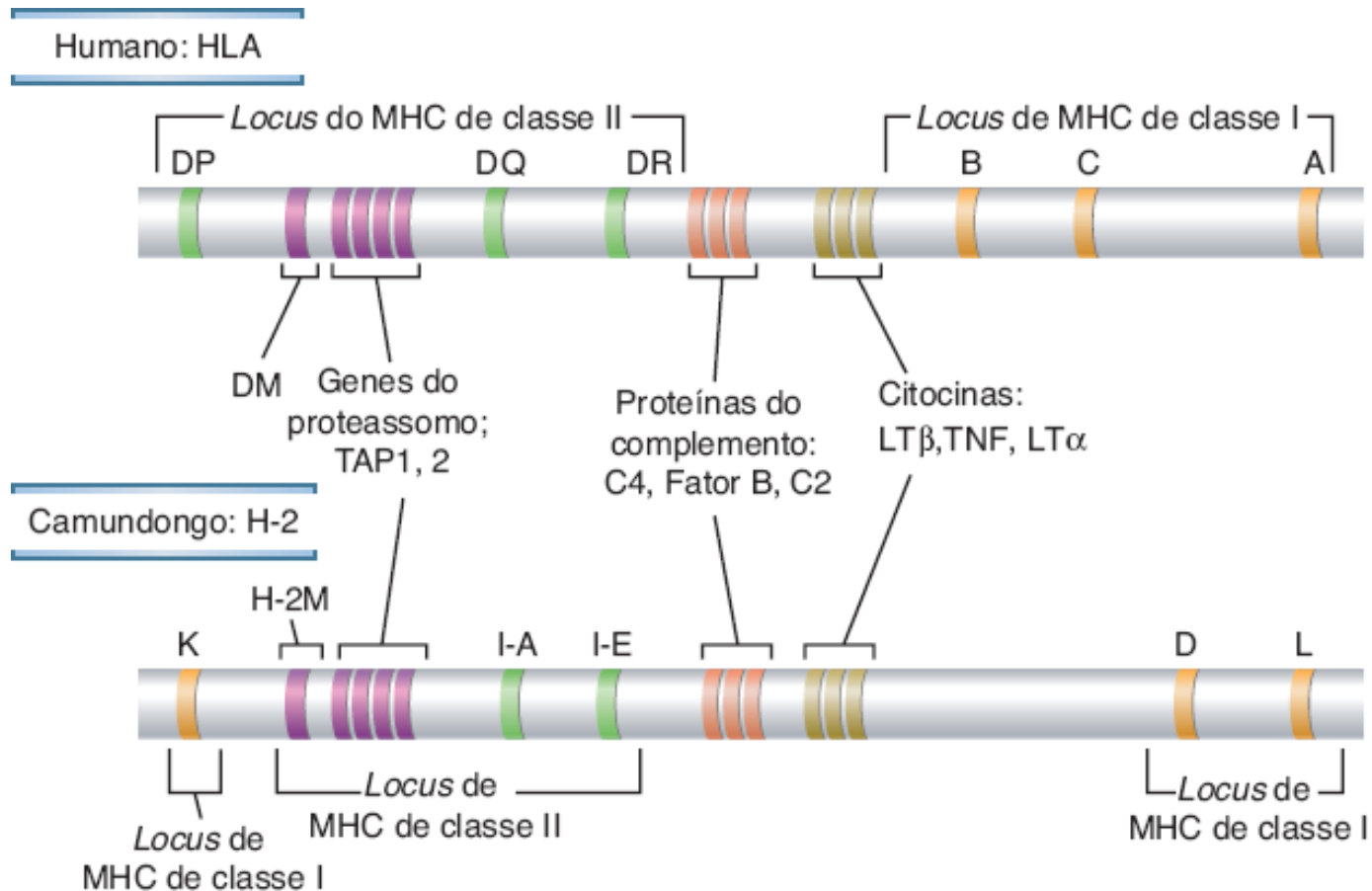
Complex	HLA							
MHC class	II			III		I		
Region	DP	DQ	DR	C4, C2, BF		B	C	A
Gene products	DP $\alpha\beta$	DQ $\alpha\beta$	DR $\alpha\beta$	C' proteins	TNF- α TNF- β	HLA-B	HLA-C	HLA-A

Figure 8-1

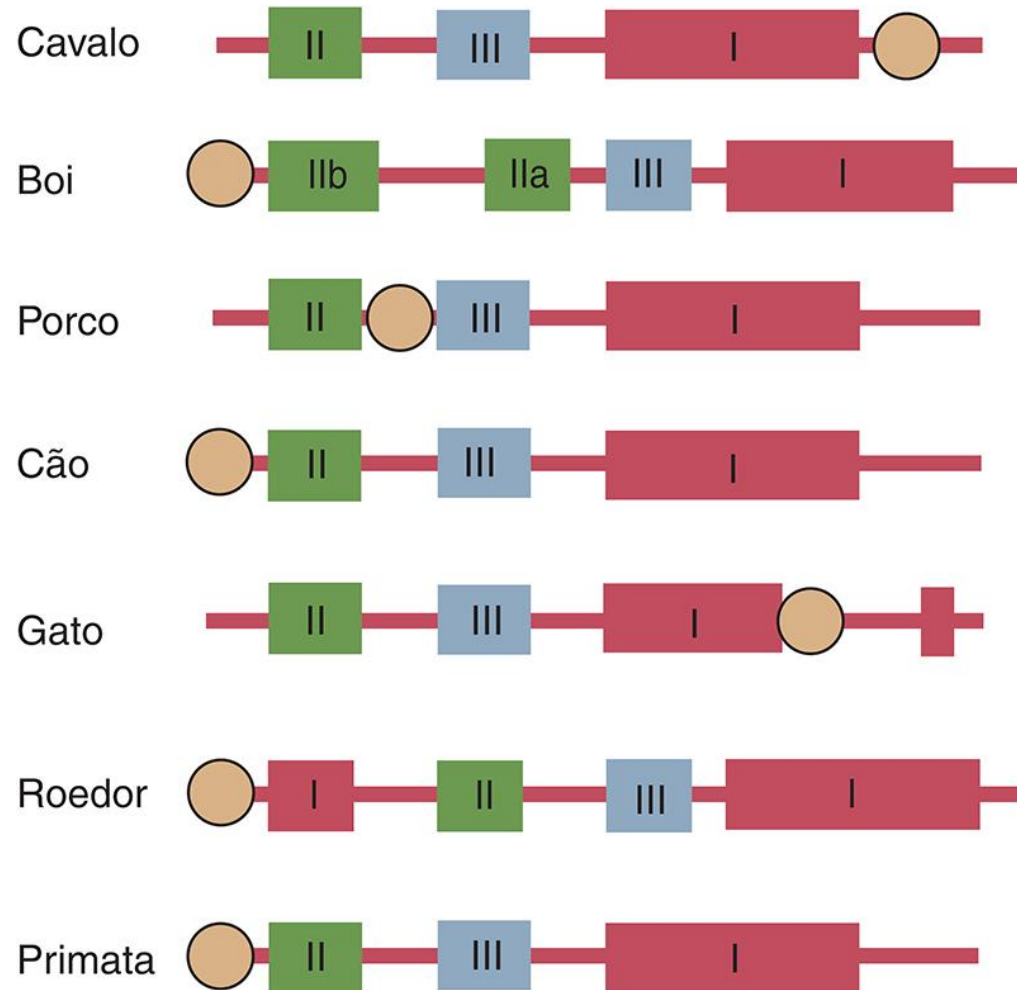
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Estrutura Genômica do MHC



Estrutura Genômica do MHC dos animais domésticos



Herança dos
haplótipos de
HLA

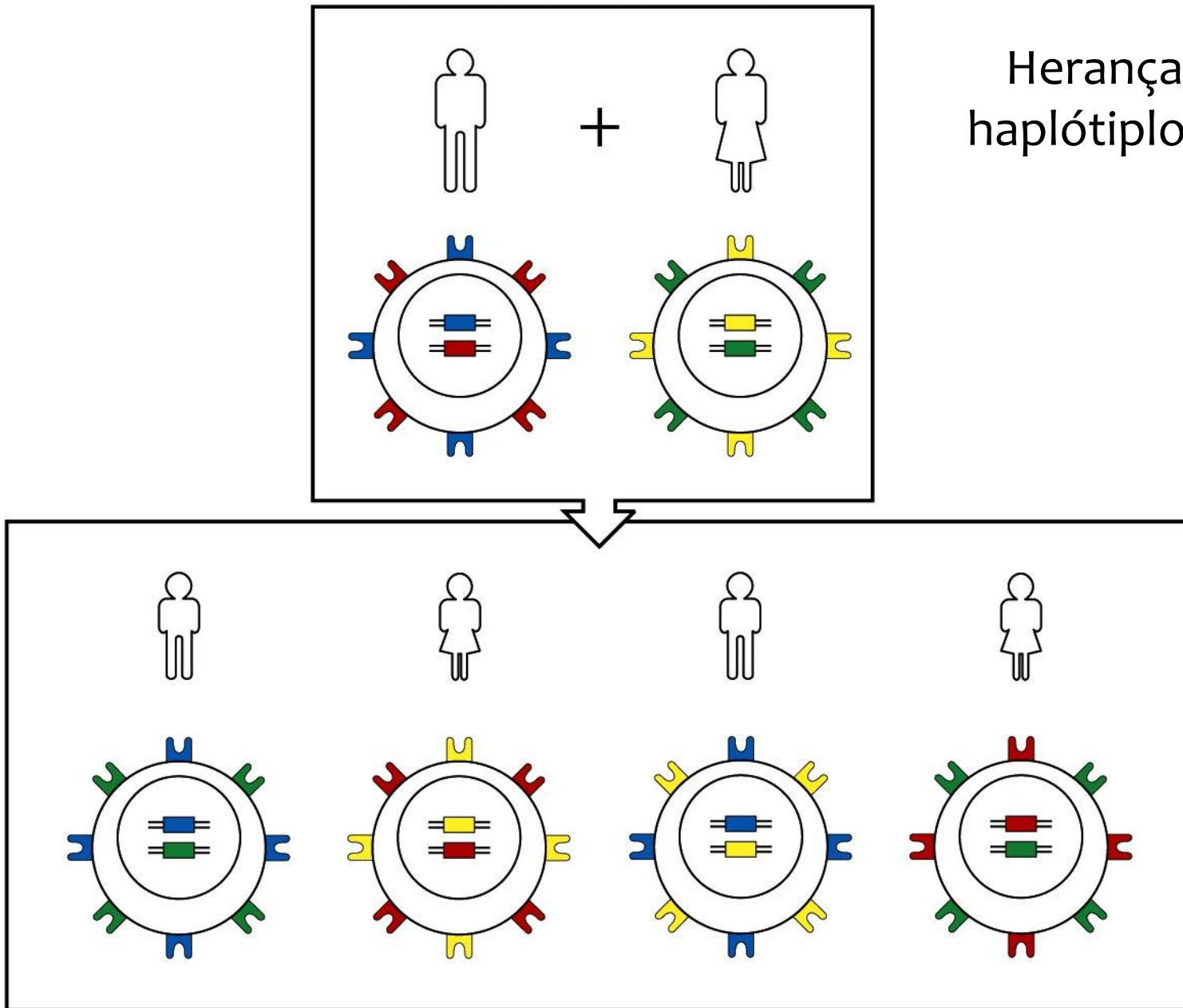


Figure 5-15 Immunobiology, 7ed. (© Garland Science 2008)

Polimorfismo e poligenia no HLA

TABLE 8-3

Genetic diversity of MHC loci in the human population

MHC CLASS I	
HLA locus	Number of allotypes (proteins)
A	1448
B	1988
C	1119
E	3
F	4
G	16
MHC CLASS II	
HLA locus	Number of allotypes (proteins)
DMA	4
DMB	7
DOA	3
DOB	5
DPA1	17
DPB1	134
DQA1	47
DQB1	126
DRA	2
DRB1	860
DRB3	46
DRB4	8
DRB5	17

Source: Data obtained from <http://hla.alleles.org>, a Web site maintained by the HLA Informatics Group based at the Anthony Nolan Trust in the United Kingdom, with up-to-date information on the numbers of HLA alleles and proteins.

Haplótipo

Materno

Paterno

MHC I

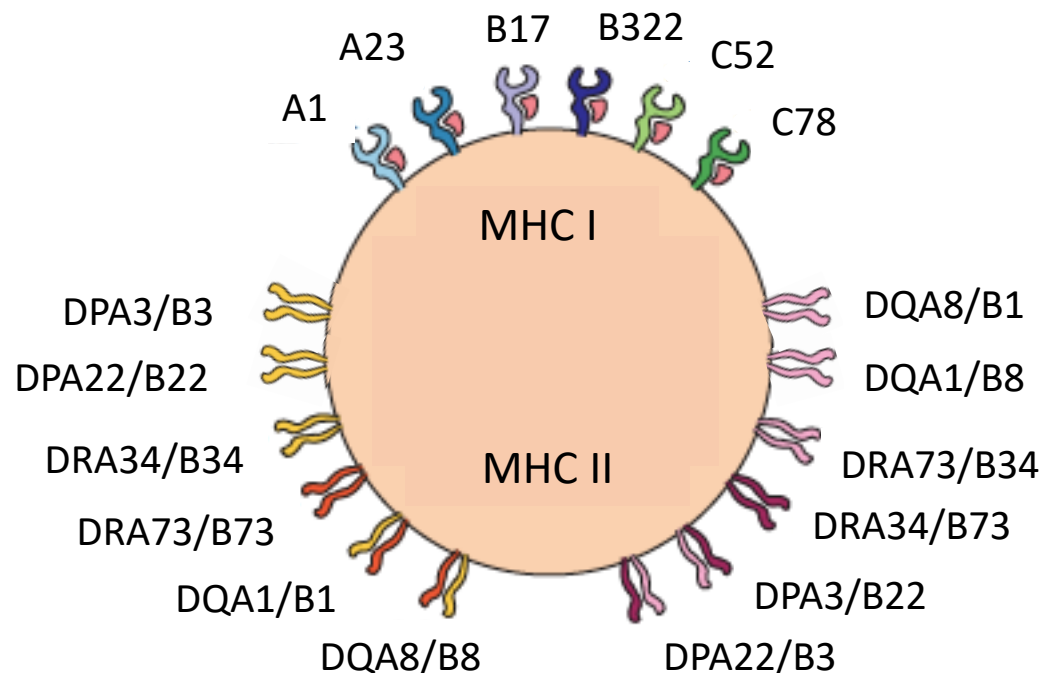
A1/B17/C52

A23/B322/C78

MHC II

DP3/DR34/DQ1

DP22/DR73/DQ8



O polimorfismo dos genes do MHC se concentra na região da fenda

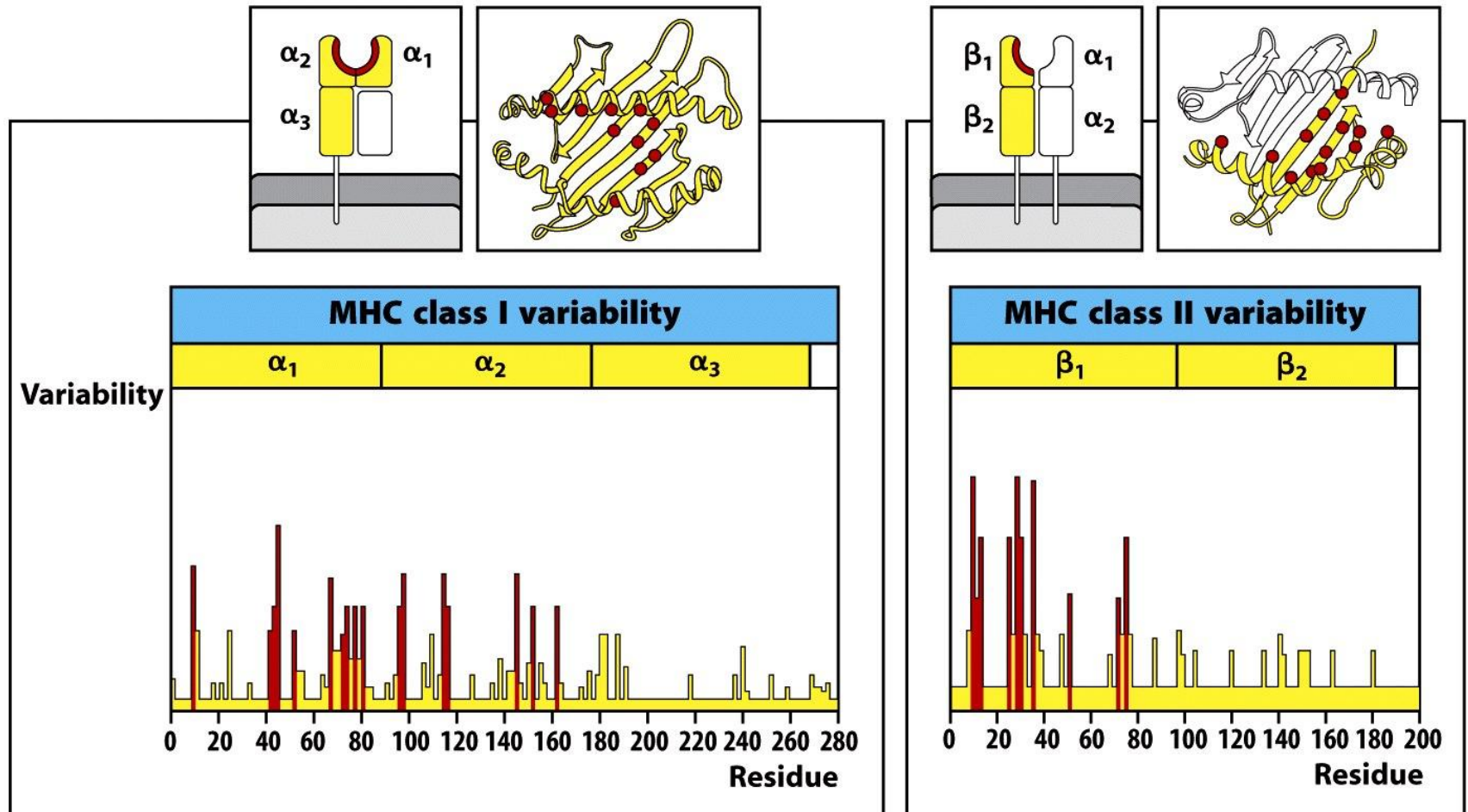


Figure 5-18 Immunobiology, 7ed. (© Garland Science 2008)

MHC restriction

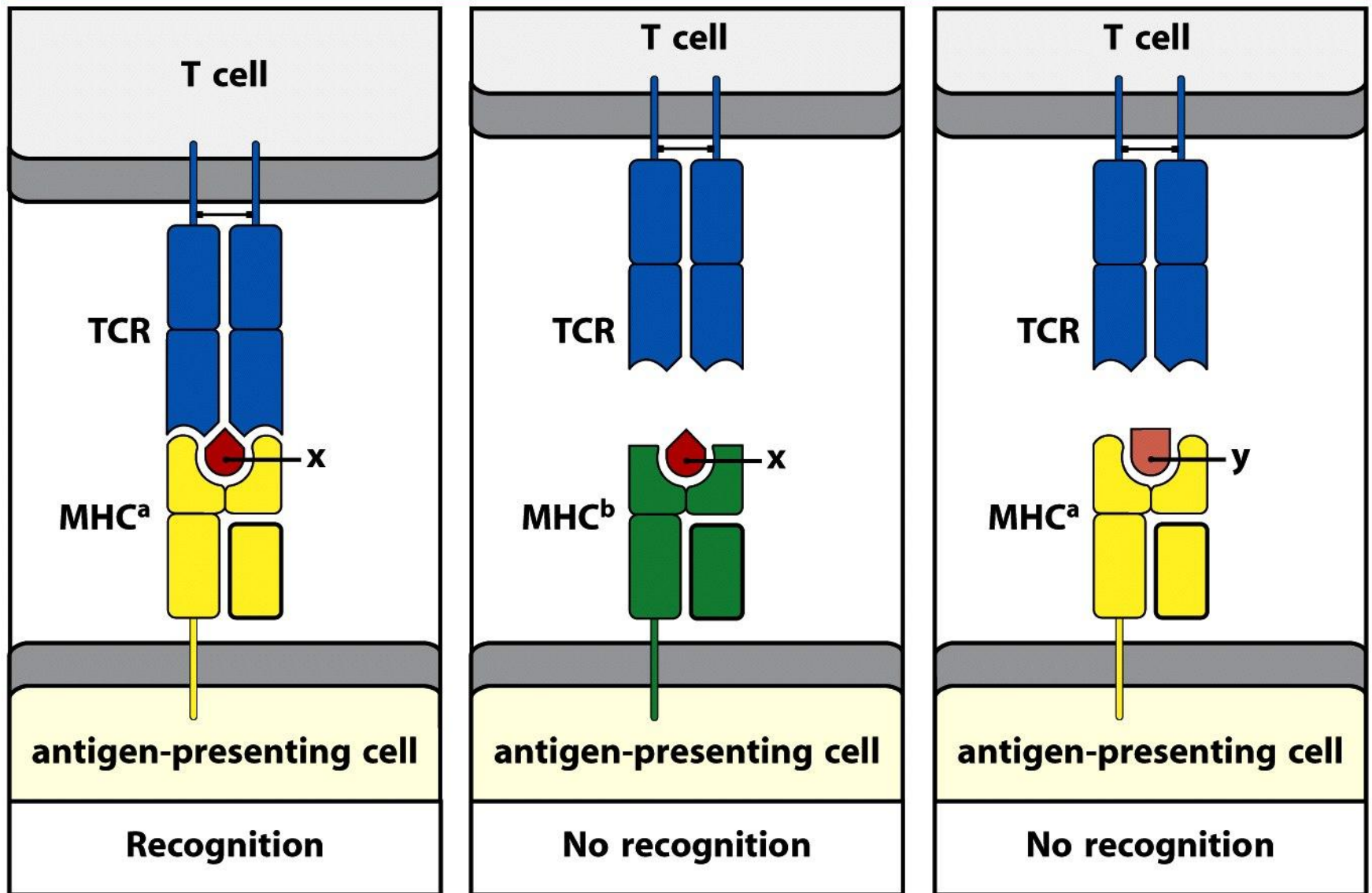
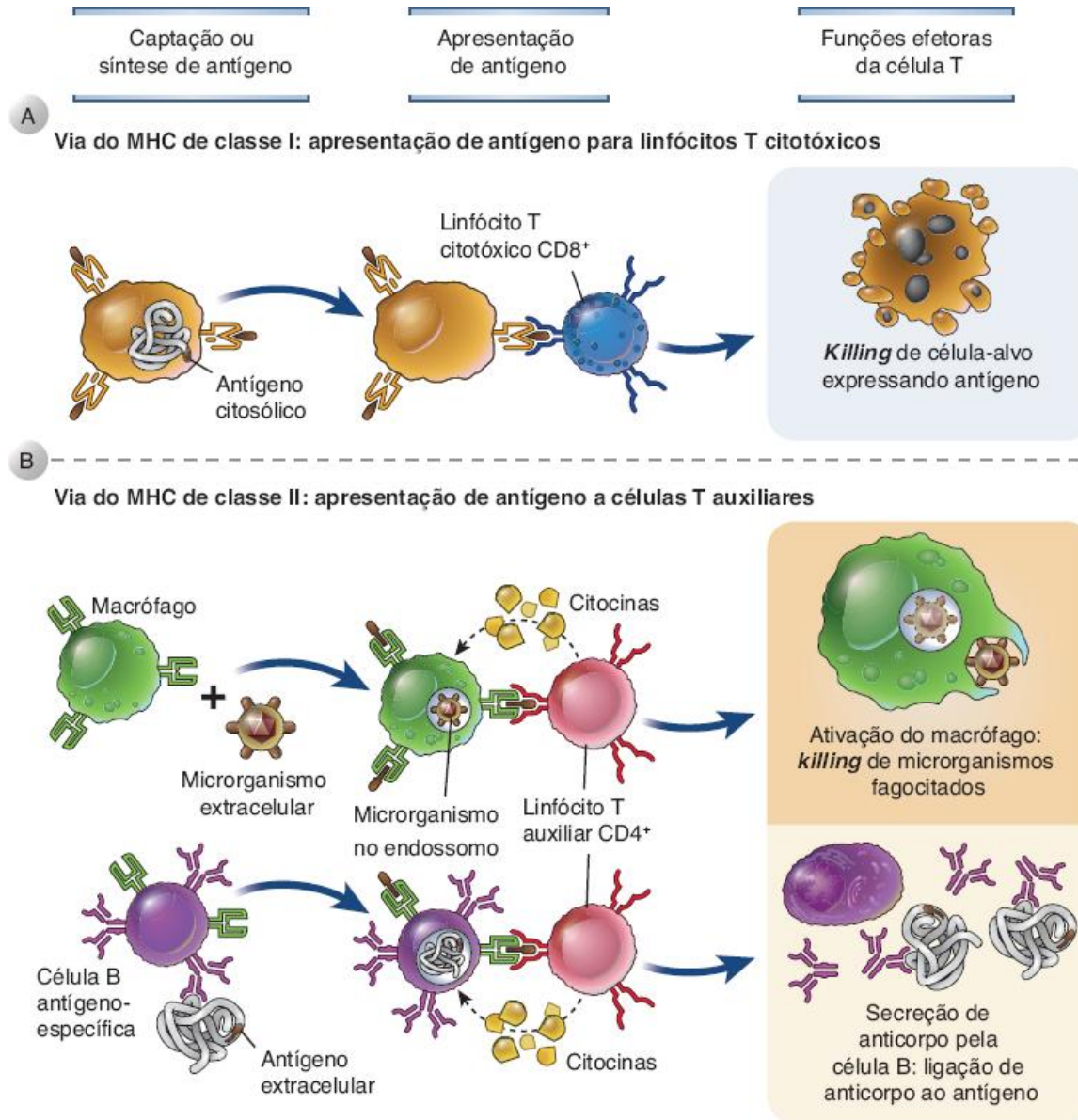


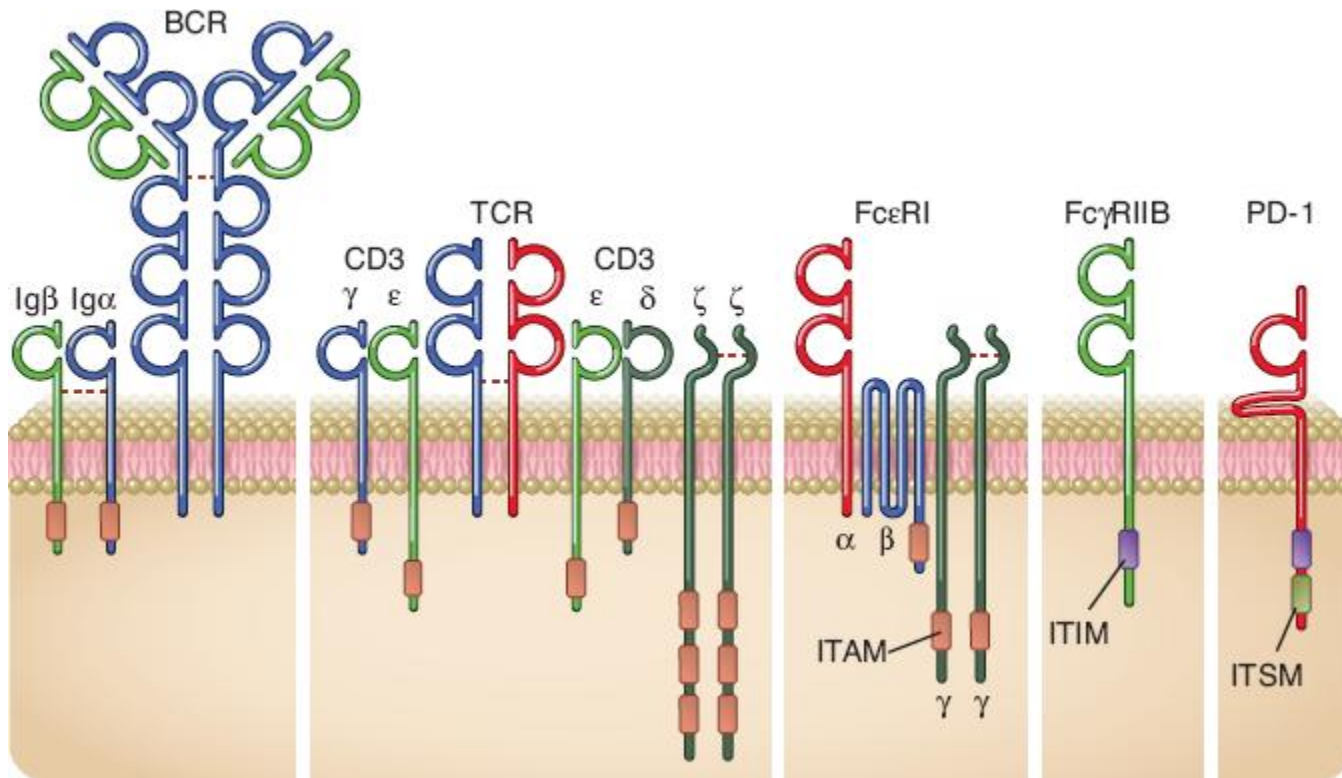
Figure 5-20 Immunobiology, 7ed. (© Garland Science 2008)

Resultado da Apresentação de Antígeno

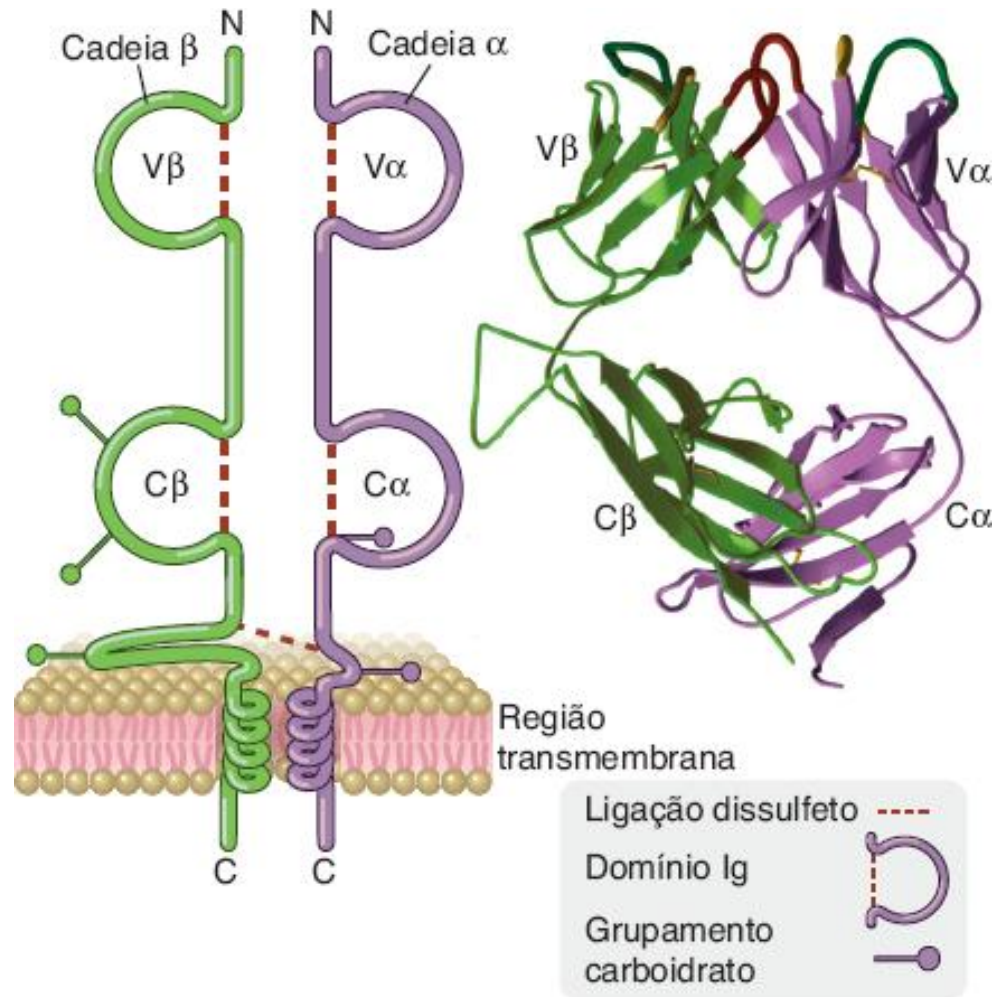


Receptores de Linfócitos T e B

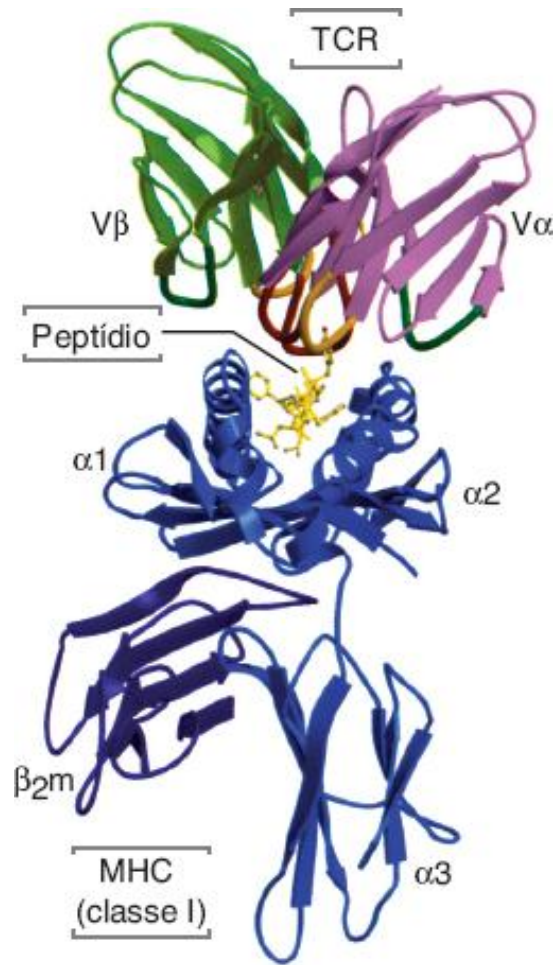
Membro da família de receptores



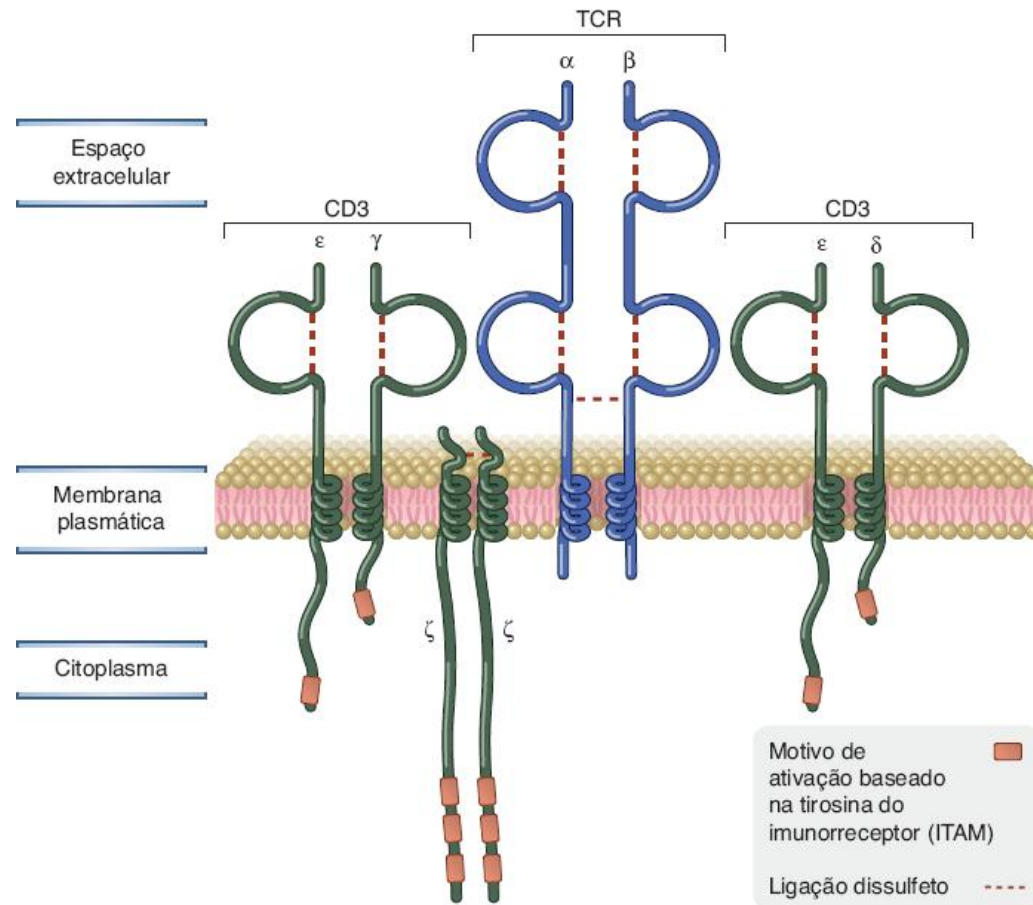
Receptor do Linfócito T



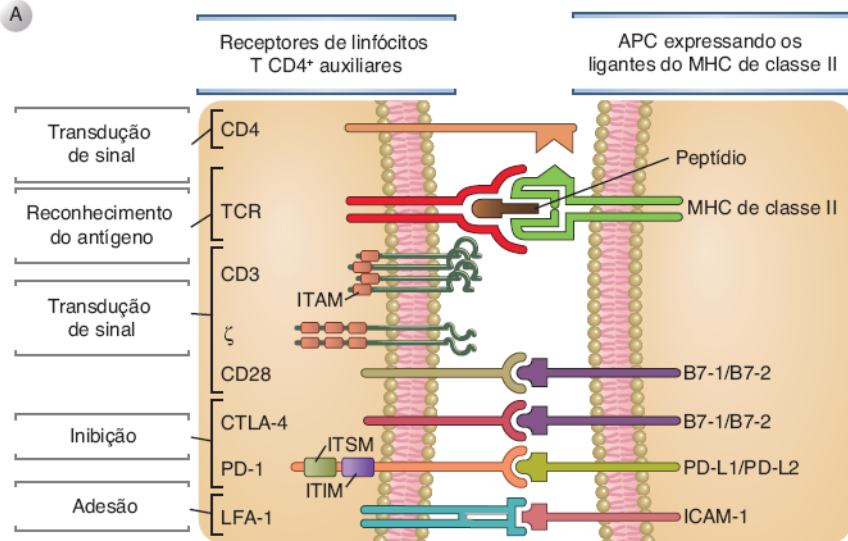
Ligação do TCR ao MHC



Complexo do TCR



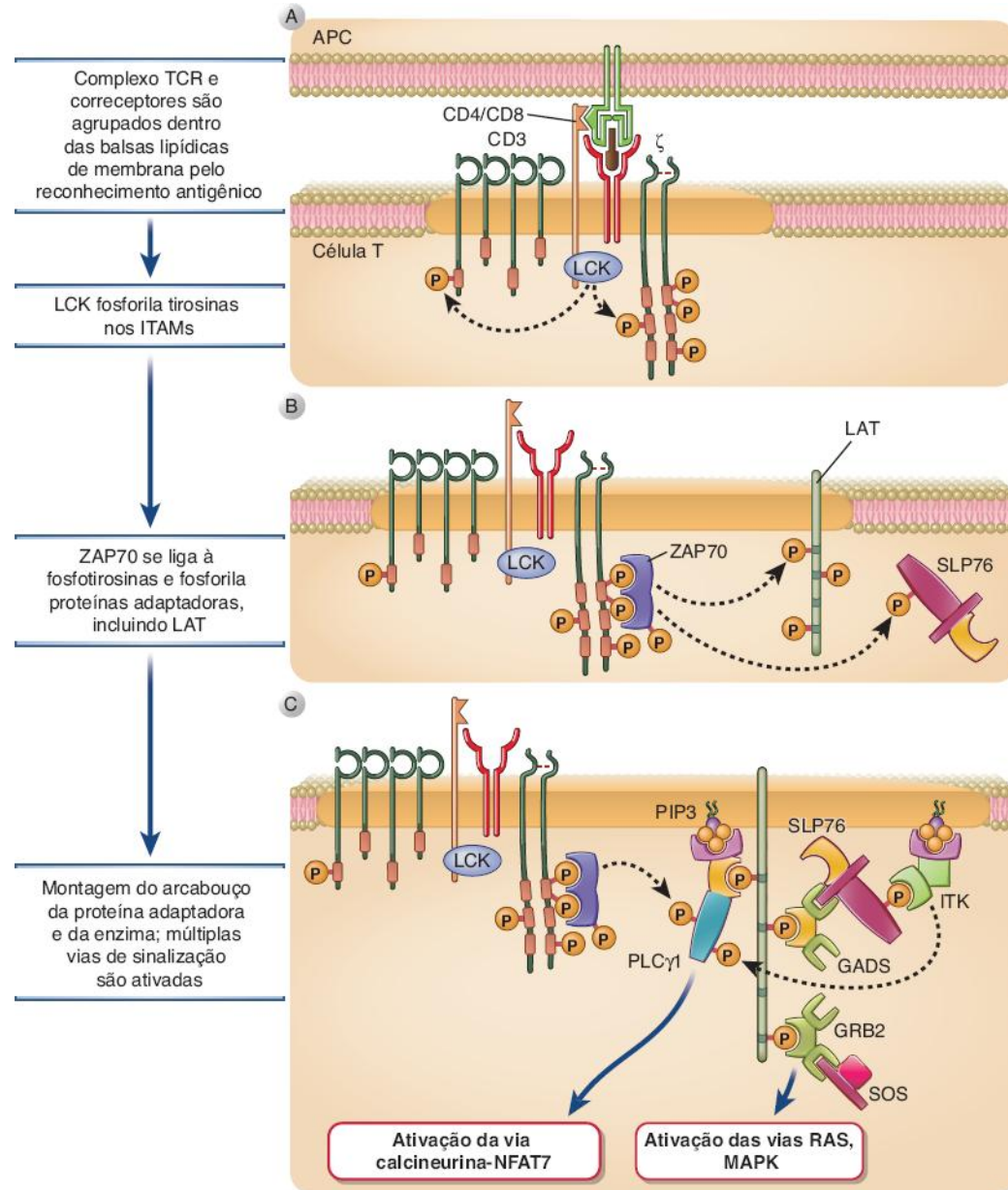
Ligantes e Receptores



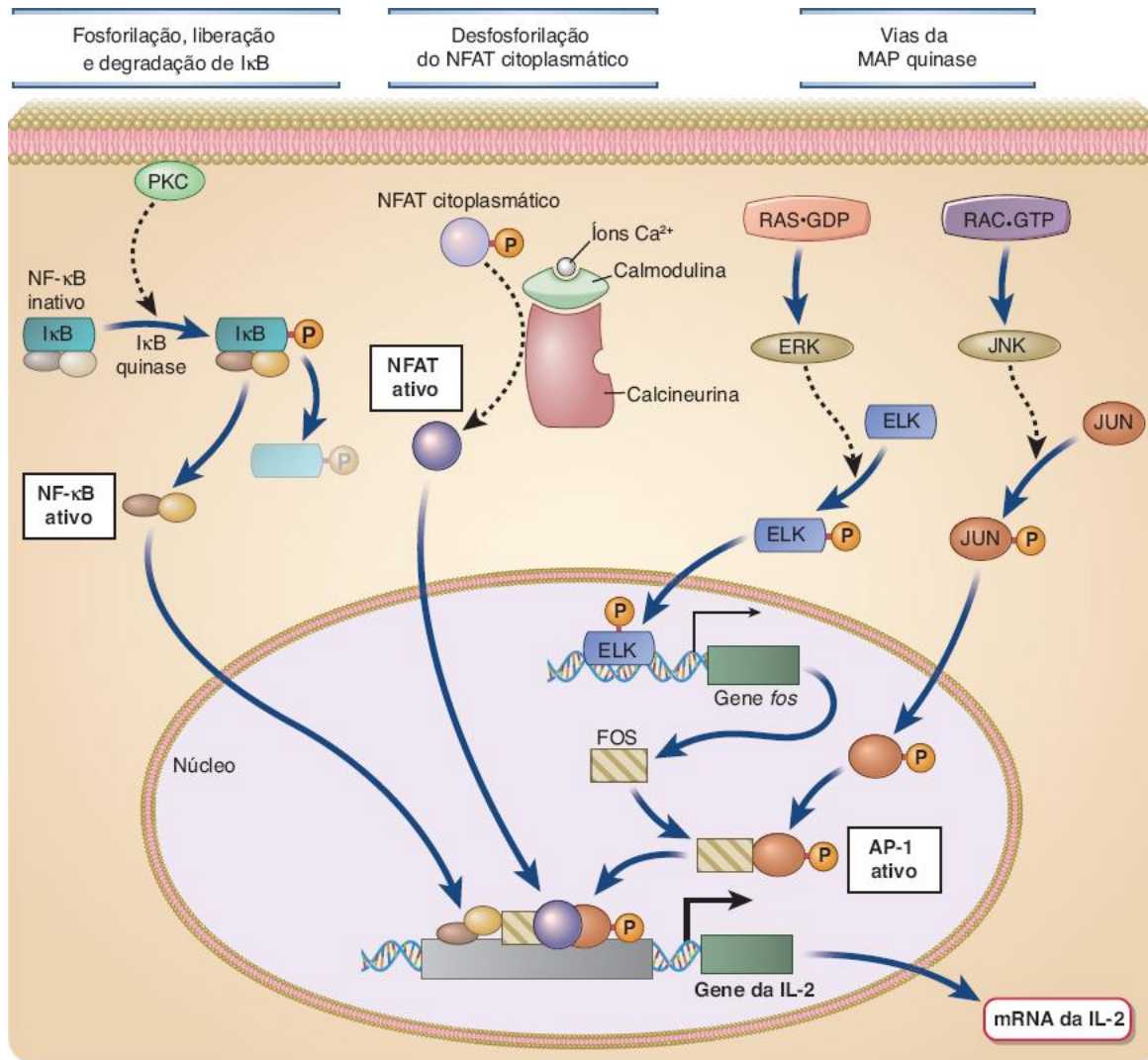
B

Molécula da célula T	Função	Ligante	
		Nome	Expresso em
CD3	Transdução de sinal pelo complexo TCR	Nenhum	
ζ	Transdução de sinal pelo complexo TCR	Nenhum	
CD4	Transdução de sinal	MHC de classe II	Células apresentadoras de antígeno
CD8	Transdução de sinal	MHC de classe I	Todas as células nucleadas
CD28	Transdução de sinal (coestimulação)	B7-1/B7-2	Células apresentadoras de antígeno
CTLA-4	Inibição	B7-1/B7-2	Células apresentadoras de antígeno
PD-1	Inibição	PD-L1/PD-L2	Células apresentadoras de antígeno, células teciduais, células tumorais
LFA-1	Adesão	ICAM-1	Células apresentadoras de antígeno, endotélio

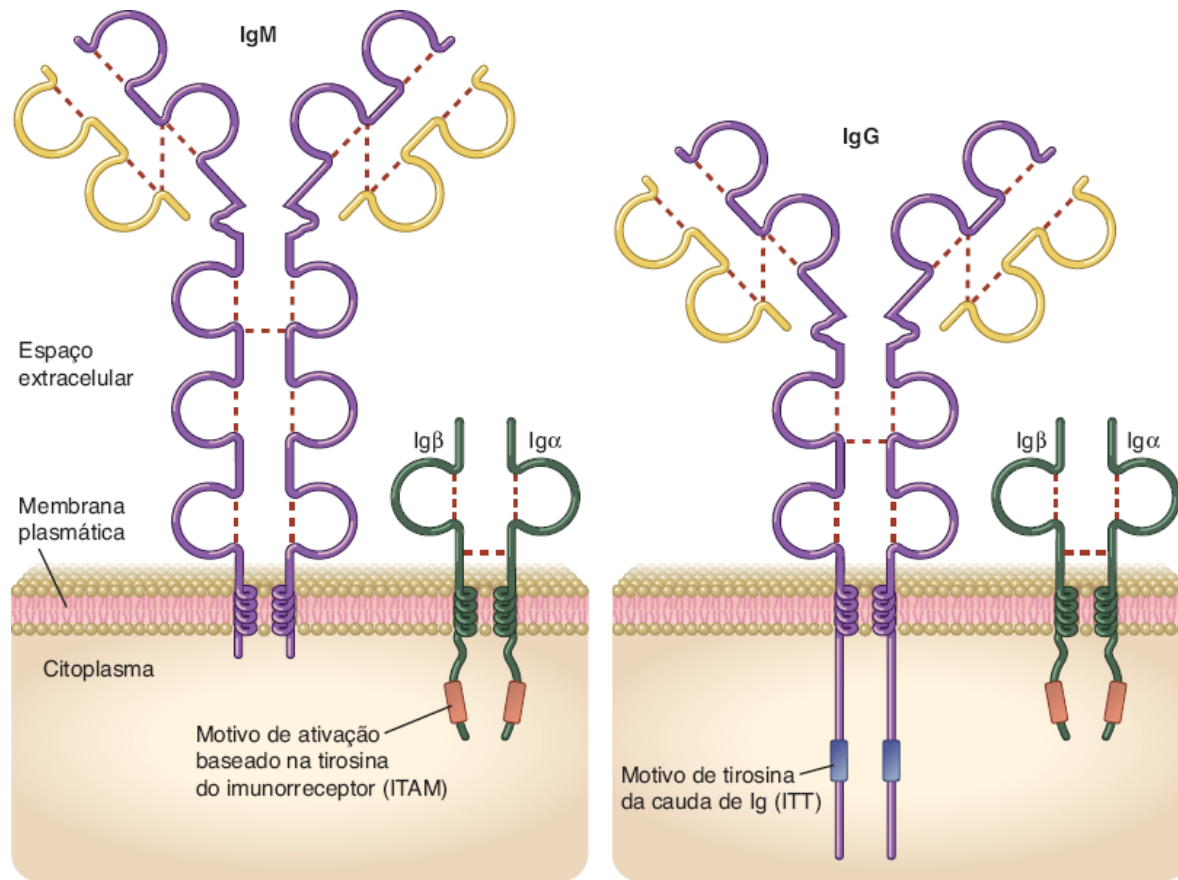
Fosforilação de Tirosinas LCK e ZAP70



Fatores de transcrição dos linfócitos T



Receptores dos Linfócitos B



Sinais de ativação do linfócito B

