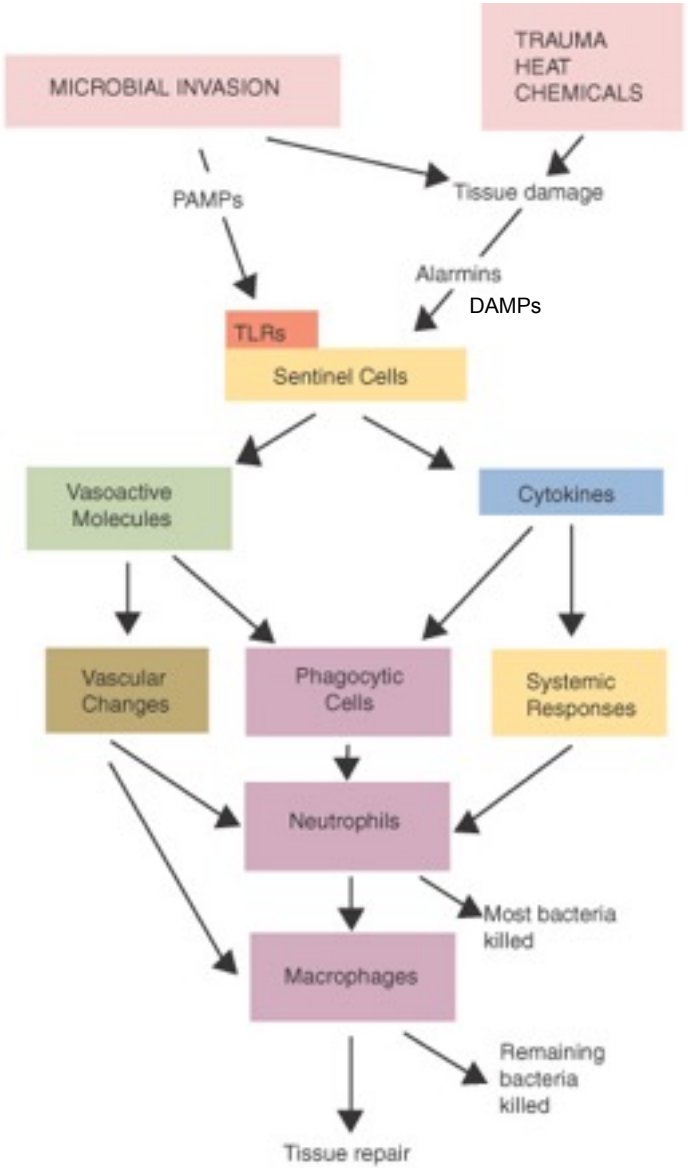



**FIGURE 2-1** An overview of the essential features of acute inflammation, an innate mechanism for focusing cells and other defensive mechanisms. It is triggered by microbial invasion and tissue damage.

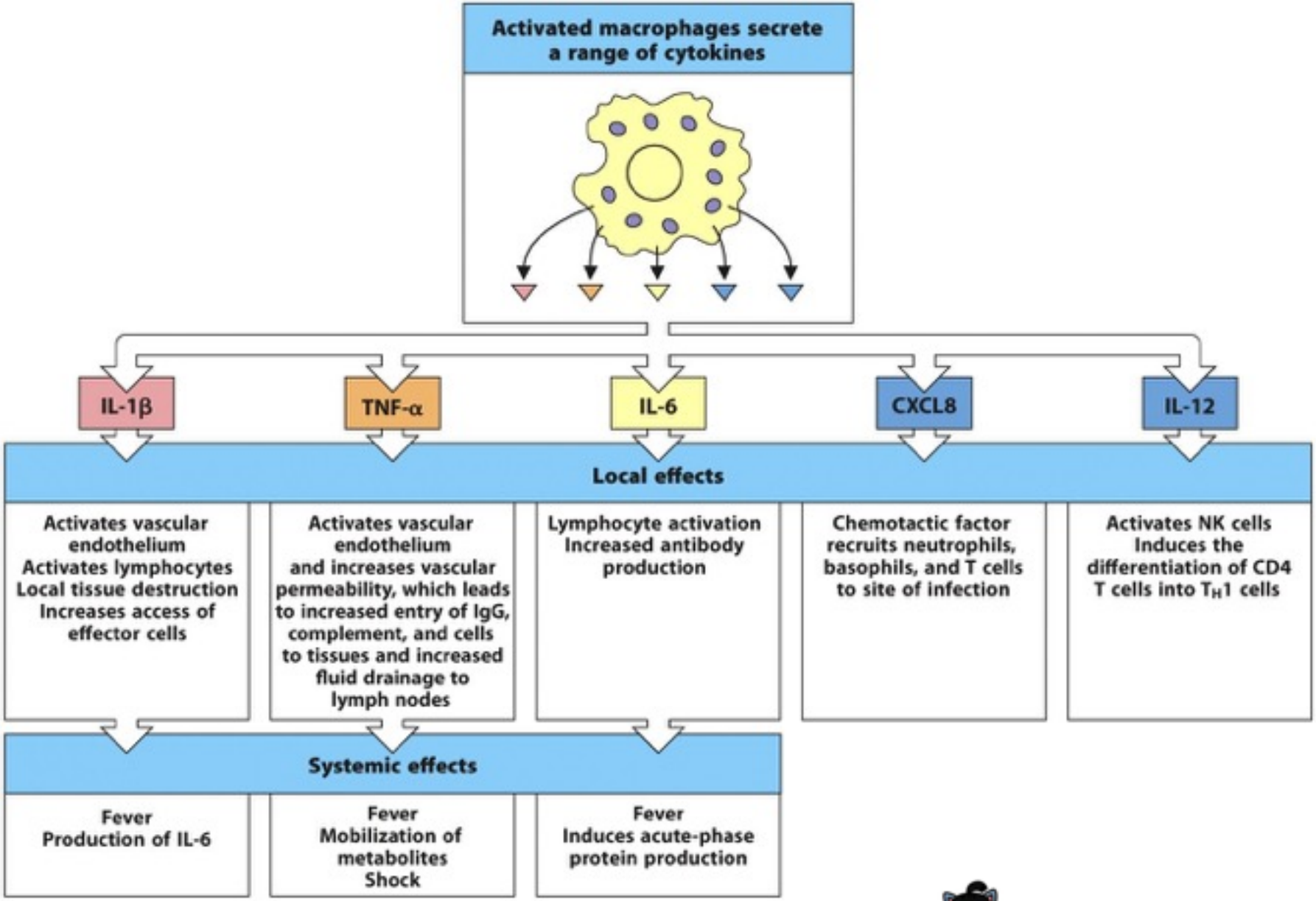



Figure 3.21 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

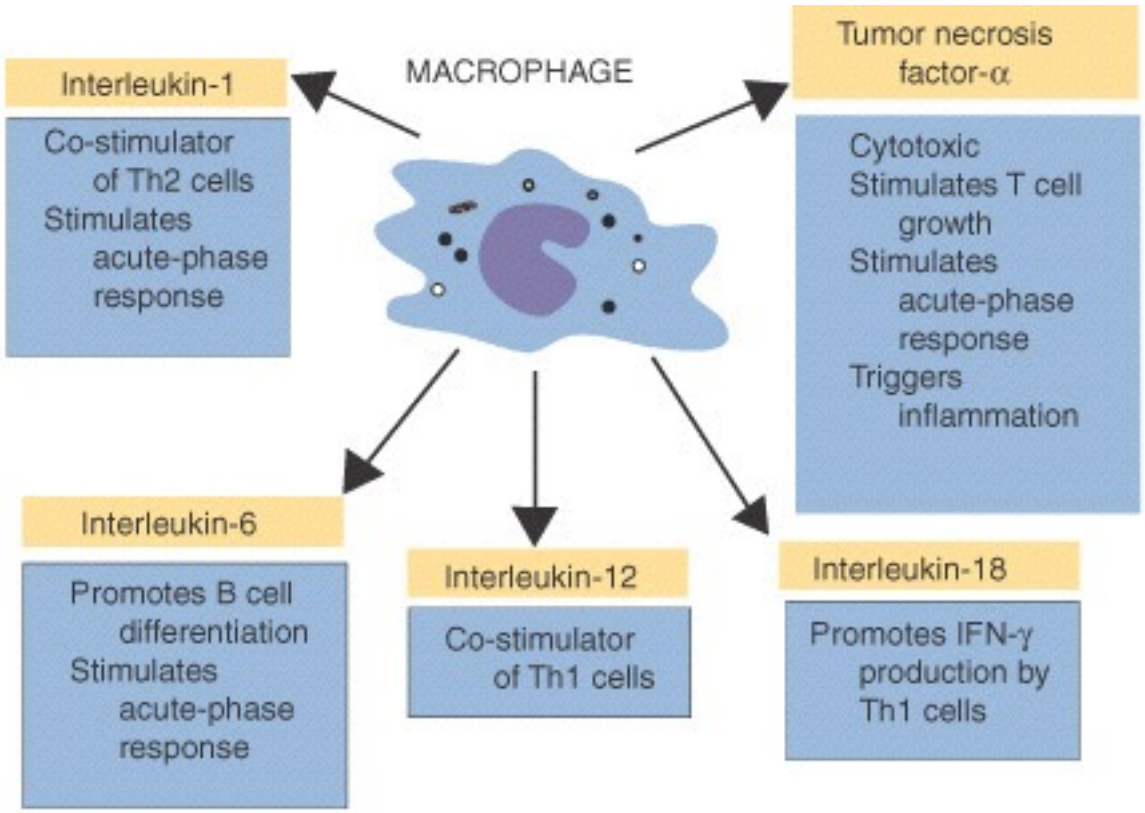



**FIGURE 4-1** The cytokines secreted by macrophages and their functions.



conceito importante!

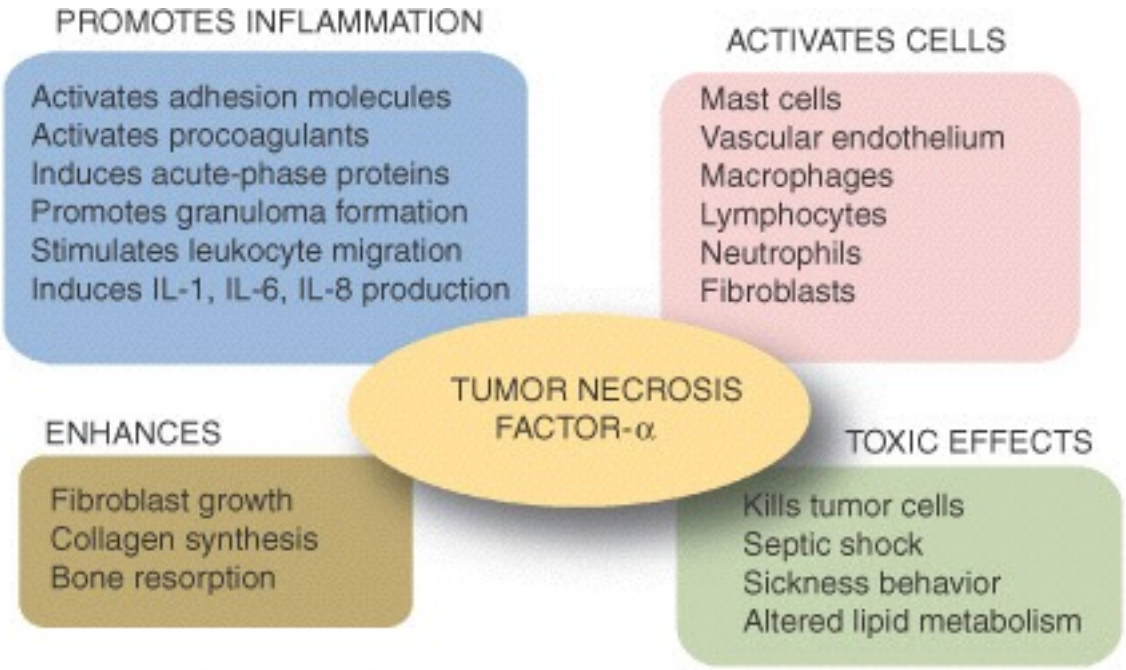



**FIGURE 2-13** Some of the properties of tumor necrosis factor-α.



conceito importante!

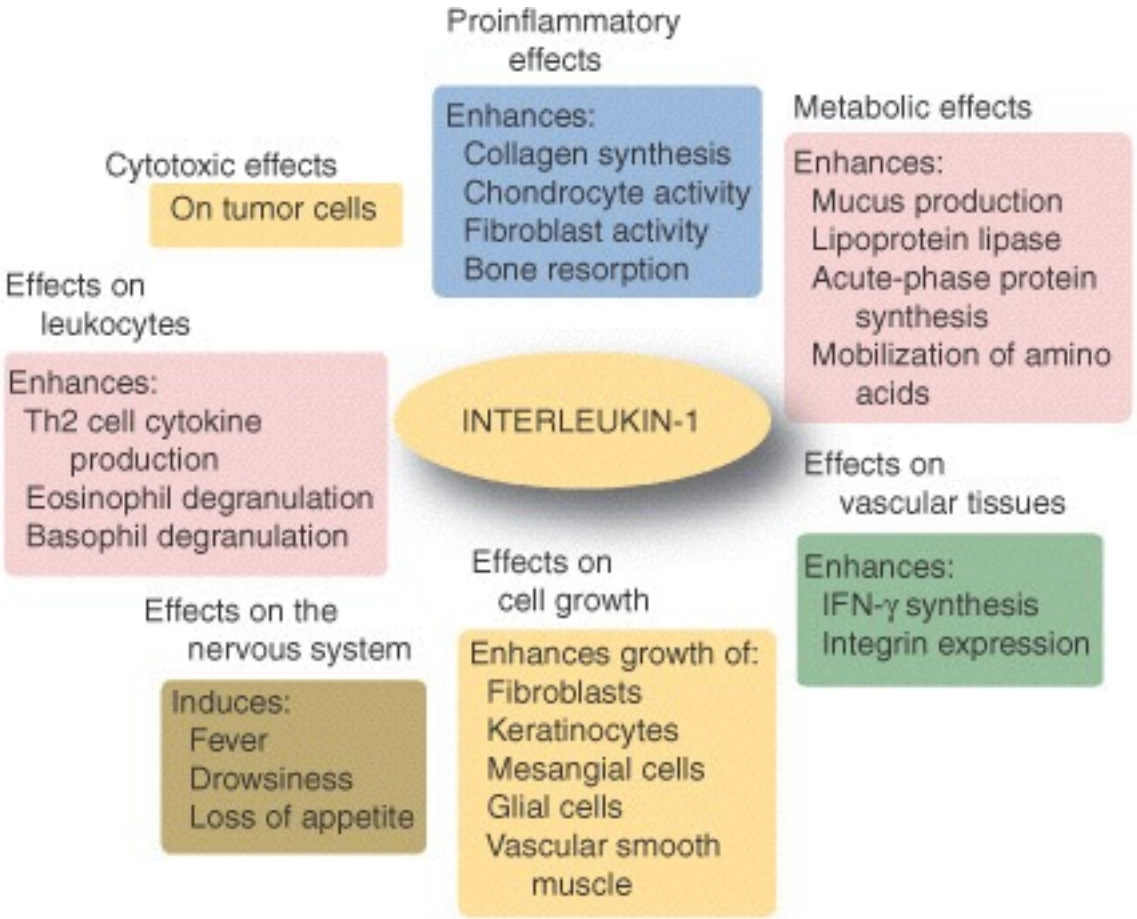



**FIGURE 2-15** Some of the effects of interleukin-1 on the cells of the body.



conceito importante!

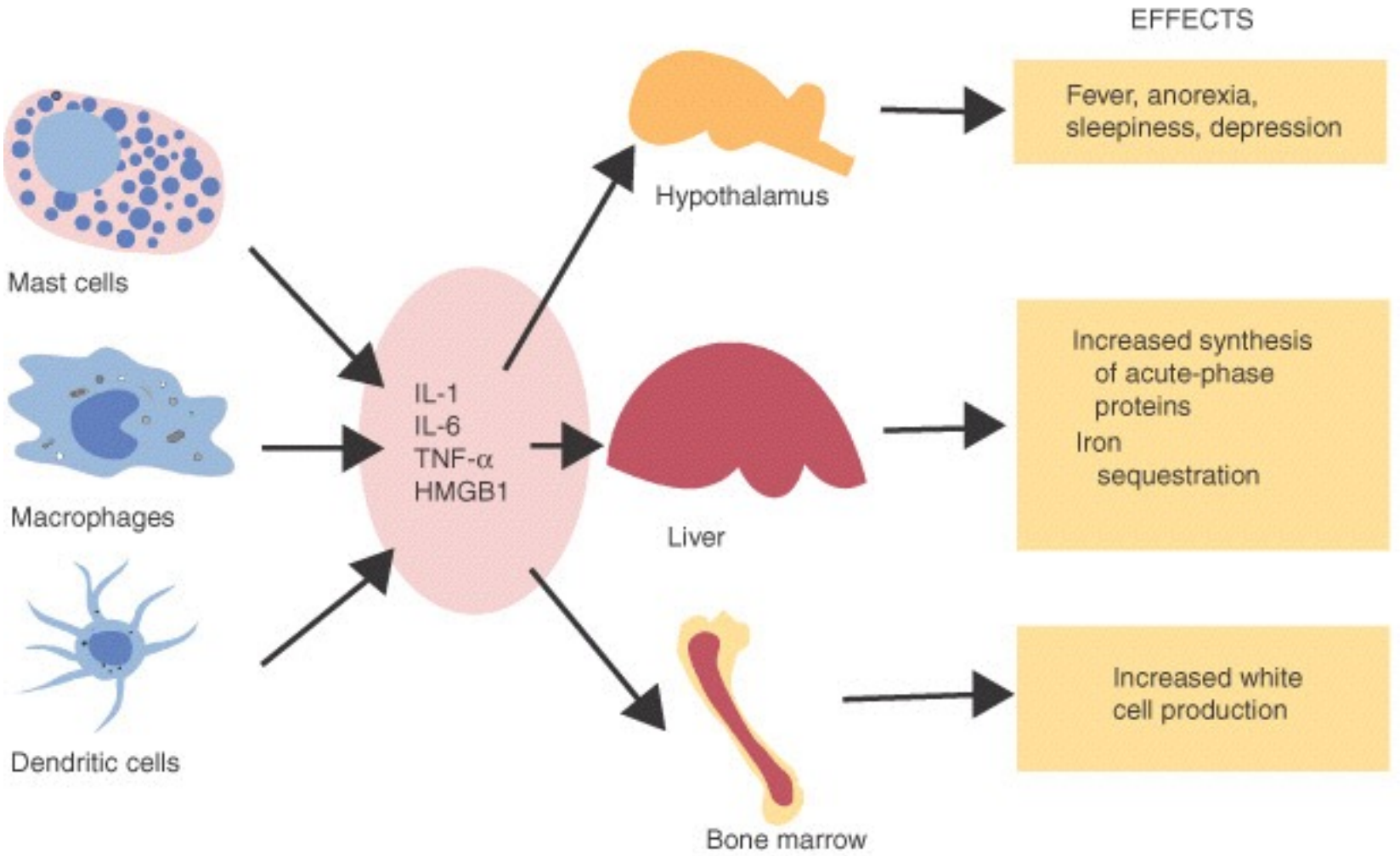
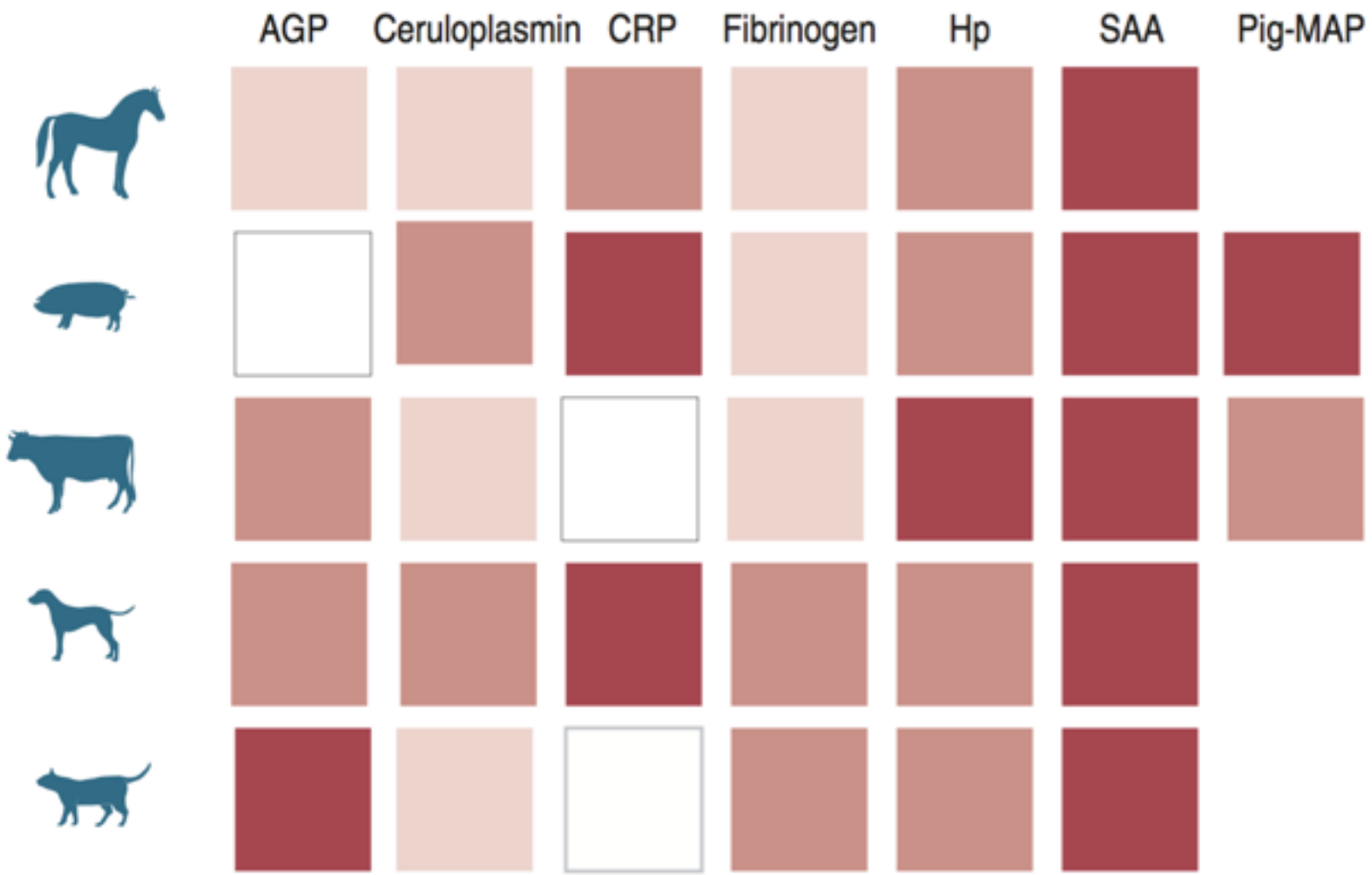



**FIGURE 4-13** Sickness behavior is part of the response of the body to inflammatory stimuli. Multiple systemic effects are due to the four major cytokines secreted by sentinel cells, mast cells, macrophages, and dendritic cells. The major sickness-inducing cytokines are interleukin-1 *(IL-1)*, IL-6, tumor necrosis factor-α *(TNF-α)*, and high mobility group box protein-1 *(HMGB1)*.



conceito importante!




AGP = glicoproteína ácida
CRP = proteína C reativa
Hp = haptoglobulina
SAA = amilóide A
MAP = major acute protein

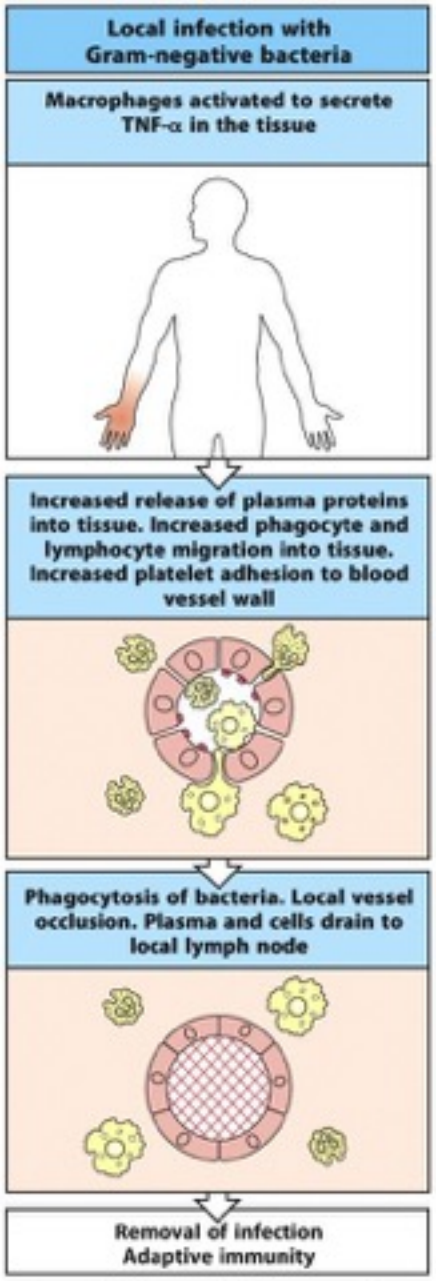
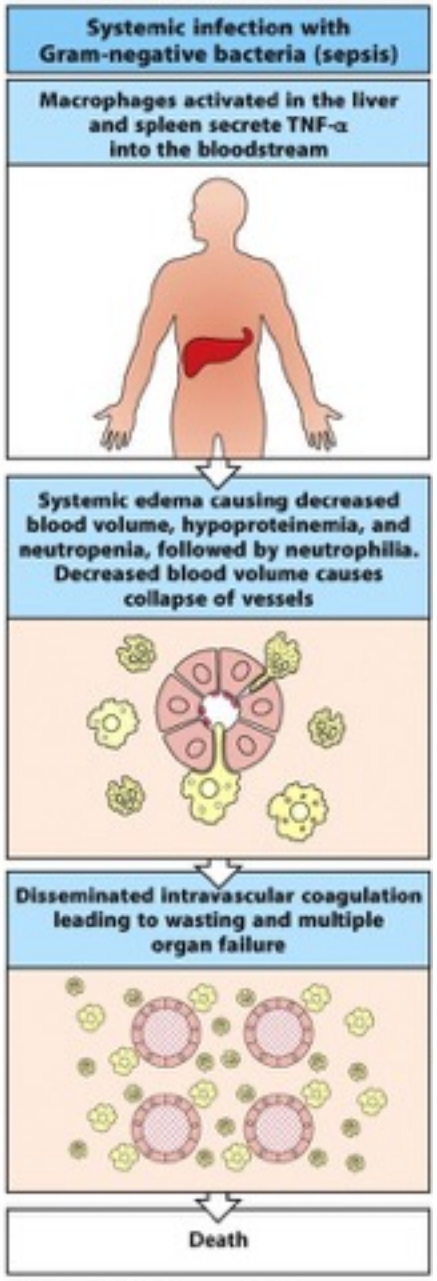



Figure 3.26 Janeway's Immunobiology, 8




Bed. (© Garland Science 2012)

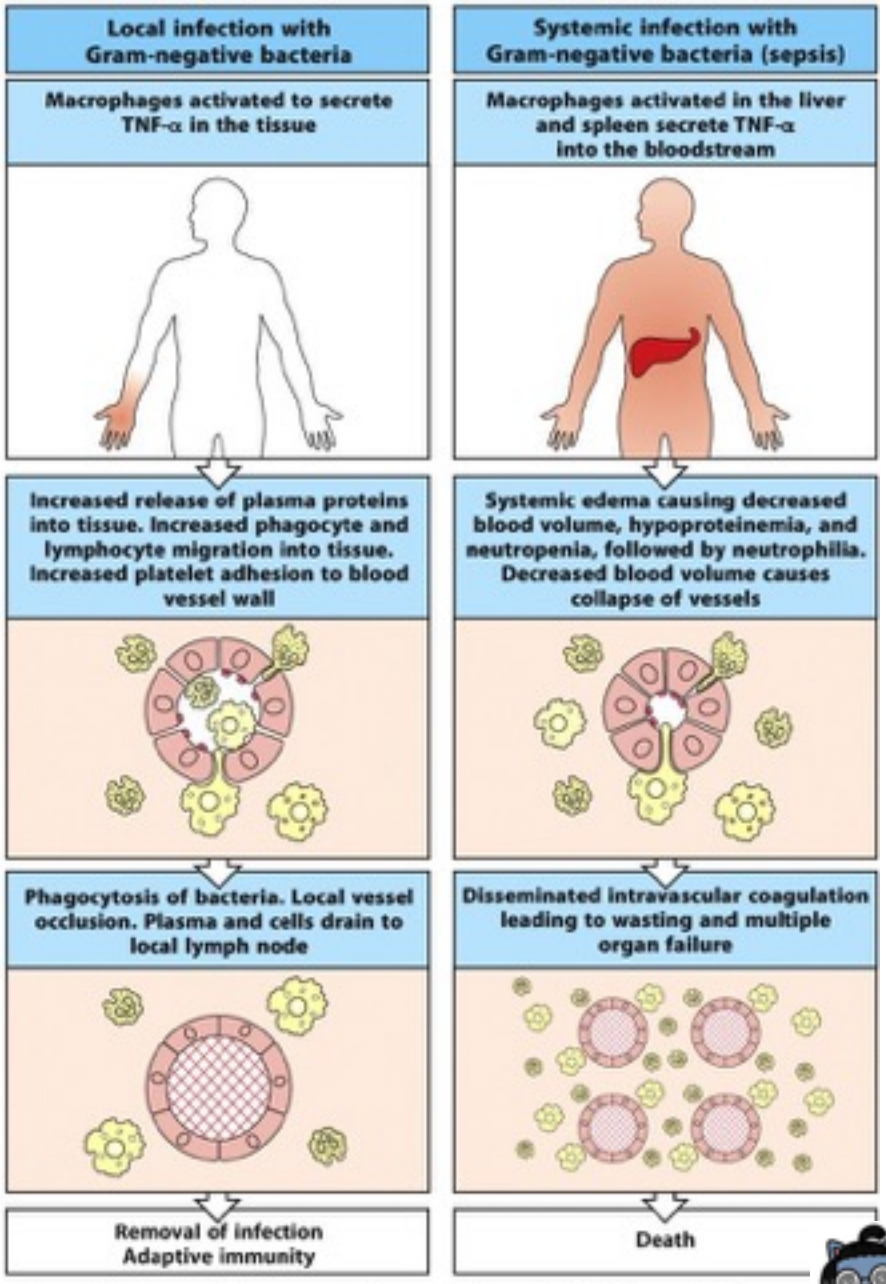



Figure 3.26 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

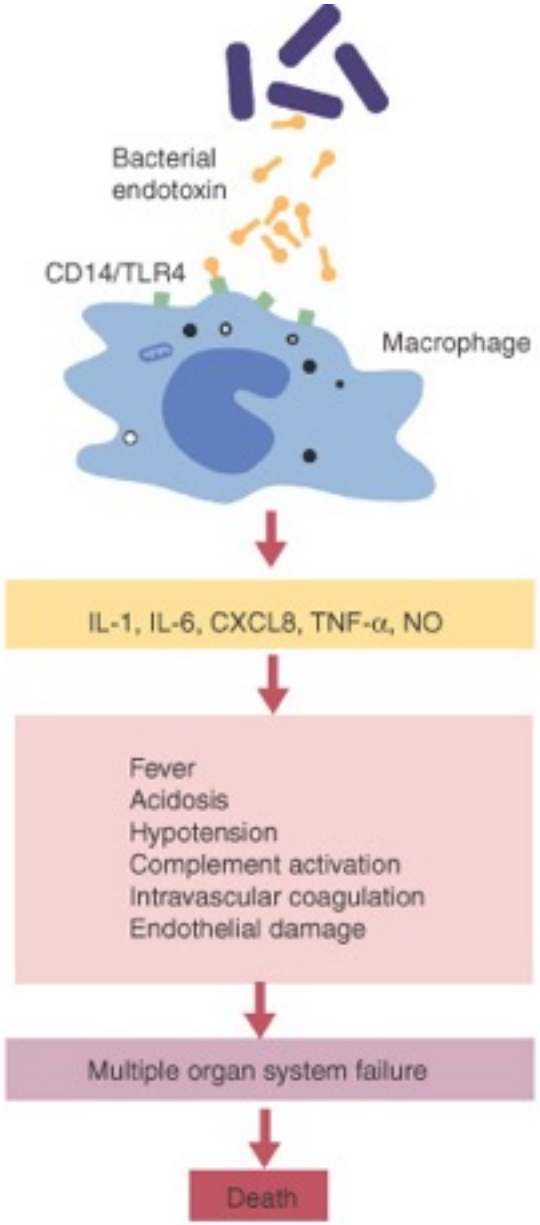
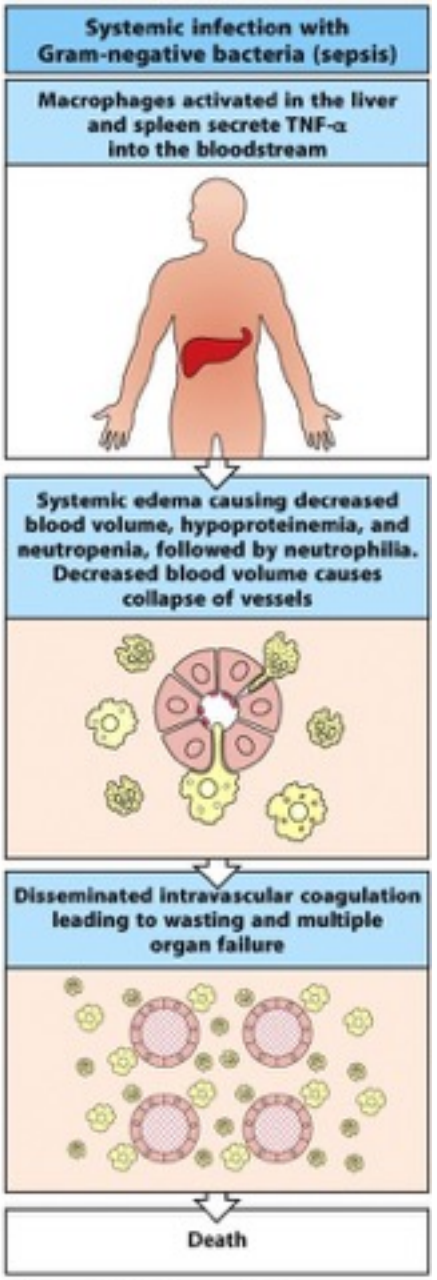



**FIGURE 4-16** The pathogenesis of the systemic inflammatory response syndrome.






conceito importante!

1st description of clinical manifestations of sepsis by Hippocrates (460-377 BC)

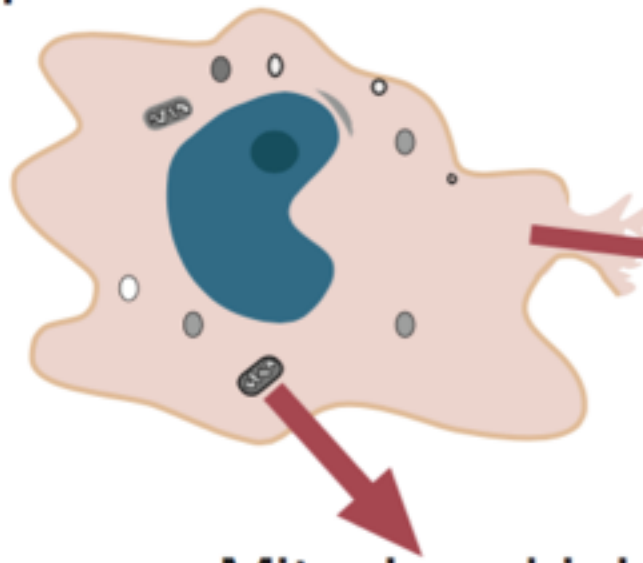
# Não confundir

PAMP com DAMP

conceito importante!

## EXTRACELLULAR DAMPs

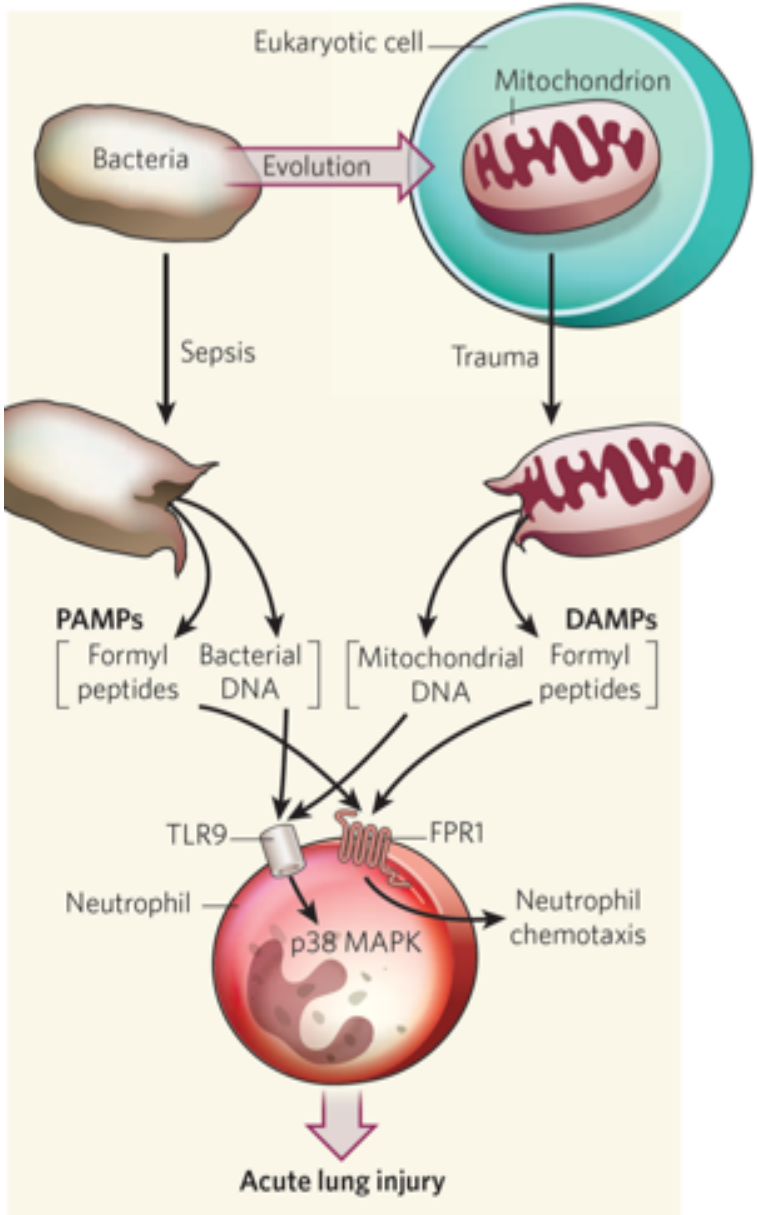
Hyaluronic acid
Heparan sulfate
Fibrinogen
Collagen-derived paptides
Fibronectin
Laminin
Elastin



Mitochondrial DNA

## INTRACELLULAR DAMPs

HMGB1
Uric acid
Chromatin
Heat-shock proteins
Adenosine
Galectins
S100 proteins
Cathelicidins
Defensins
N-formyl peptides
Lactoferrin
Heat-shock proteins




CLINICAL IMMUNOLOGY

# Culprits with evolutionary ties

Carolyn S. Calfee and Michael A. Matthay

**The cellular organelles we know as mitochondria are thought to have originated as symbiotic bacteria. Indeed, the two use common mechanisms to trigger innate immune responses to injury and infection, respectively.**

nature Vol 464|4 March 2010 doi:10.1038/nature08780

LETTERS

## Circulating mitochondrial DAMPs cause inflammatory responses to injury

Qin Zhang[1], Mustafa Raoof[1], Yu Chen[1], Yuka Sumi[1], Tolga Sursal[1], Wolfgang Junger[1], Karim Brohi[2], Kiyoshi Itagaki[1] & Carl J. Hauser[1]

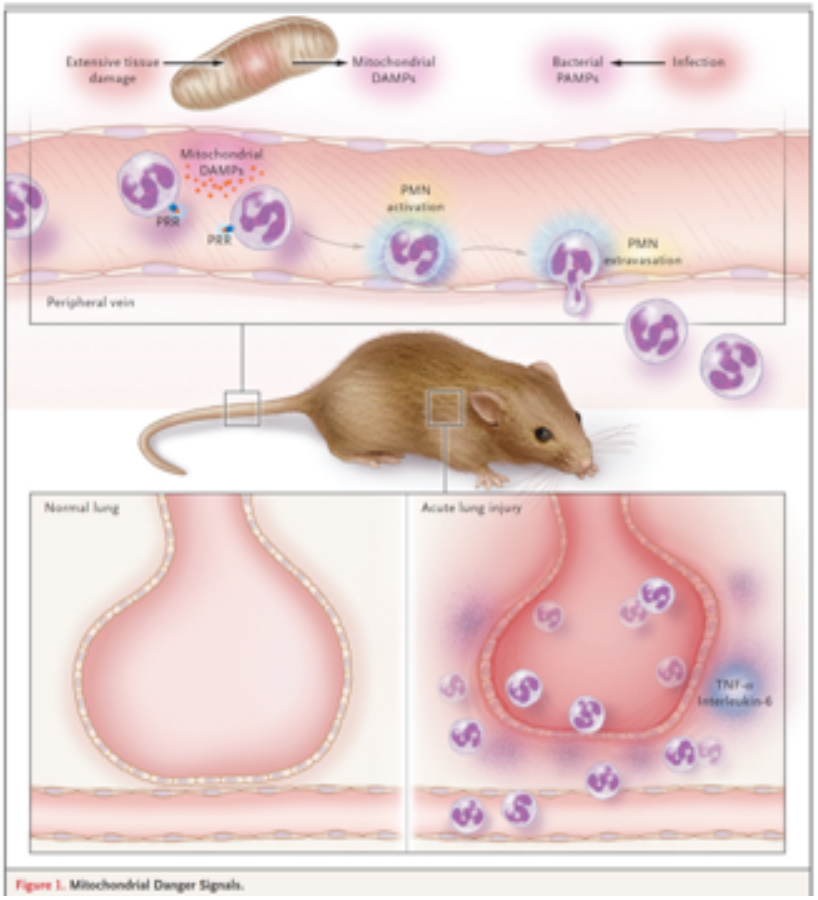



Figure 1. Mitochondrial Danger Signals.

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL IMPLICATIONS OF BASIC RESEARCH

## The Mitochondrion — A Trojan Horse That Kicks Off Inflammation?

Angelo A. Manfredi, M.D., and Patrizia Rovere-Querini, M.D., Ph.D.

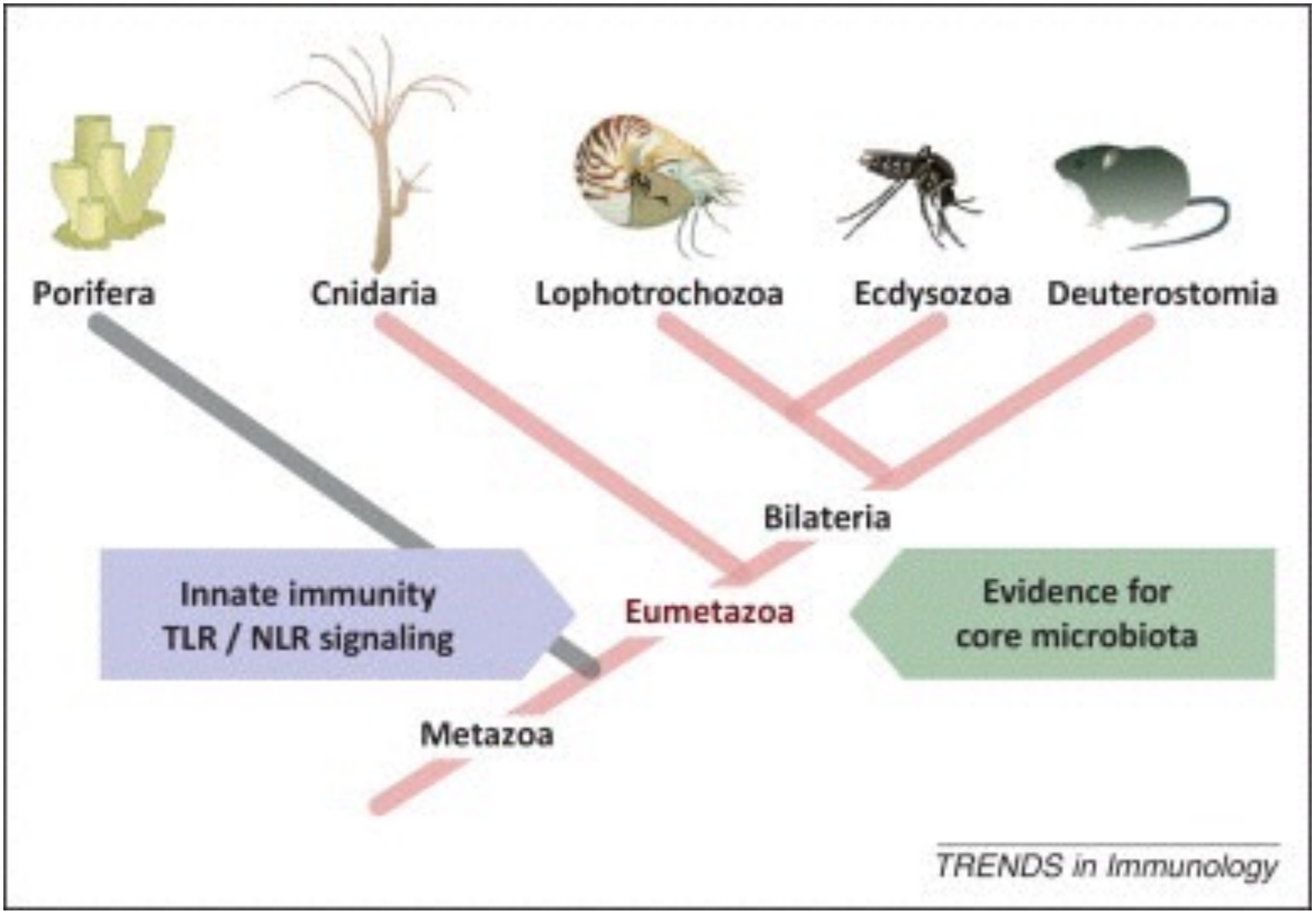



Figure 1. The early occurrence of Cnidaria on Earth. Cnidarians such as the freshwater polyp Hydra serve as models for studying the evolution of innate immunity and host–microbe interactions.

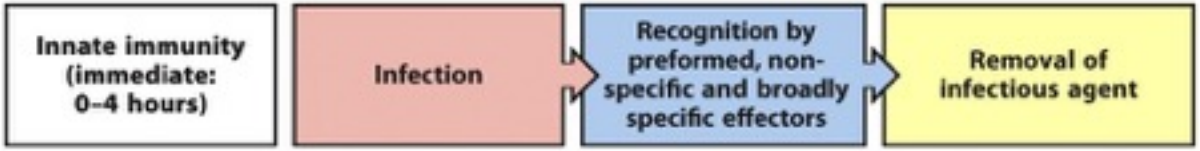
Thomas C.G. Bosch
**Rethinking the role of immunity: lessons from Hydra**
Trends in Immunology, Volume 35, Issue 10, 2014, 495–502

B C R

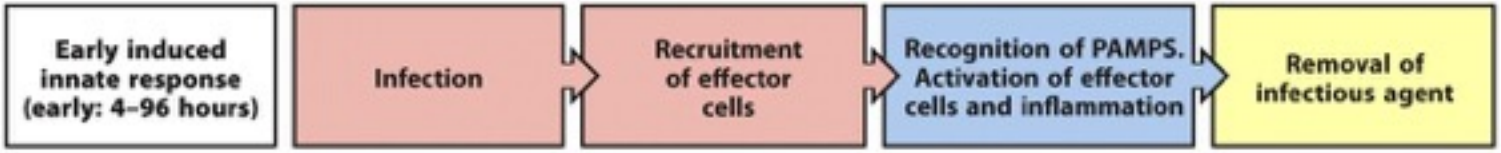
T C R

M H C

S E X




conceito importante!


conceito importante!

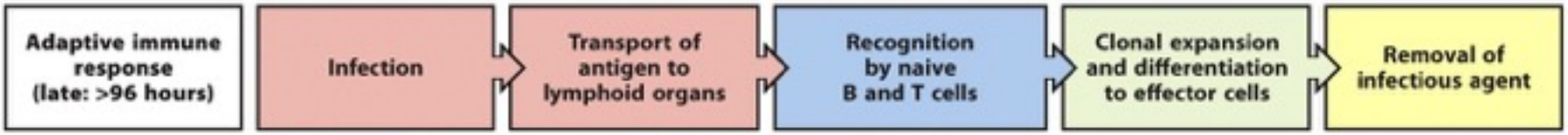




Figure 2.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)


conceito importante!

| Receptor characteristic | Innate immunity | Adaptive immunity |
|---|---|---|
| Specificity inherited in the genome | Yes | No |
| Expressed by all cells of a particular type (e.g. macrophages) | Yes | No |
| Triggers immediate response | Yes | No |
| Recognizes broad classes of pathogens | Yes | No |
| Interacts with a range of molecular structures of a given type | Yes | No |
| Clonal distribution | No | Yes |
| Able to discriminate between even closely related molecular structures | No | Yes |

Figure 3.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

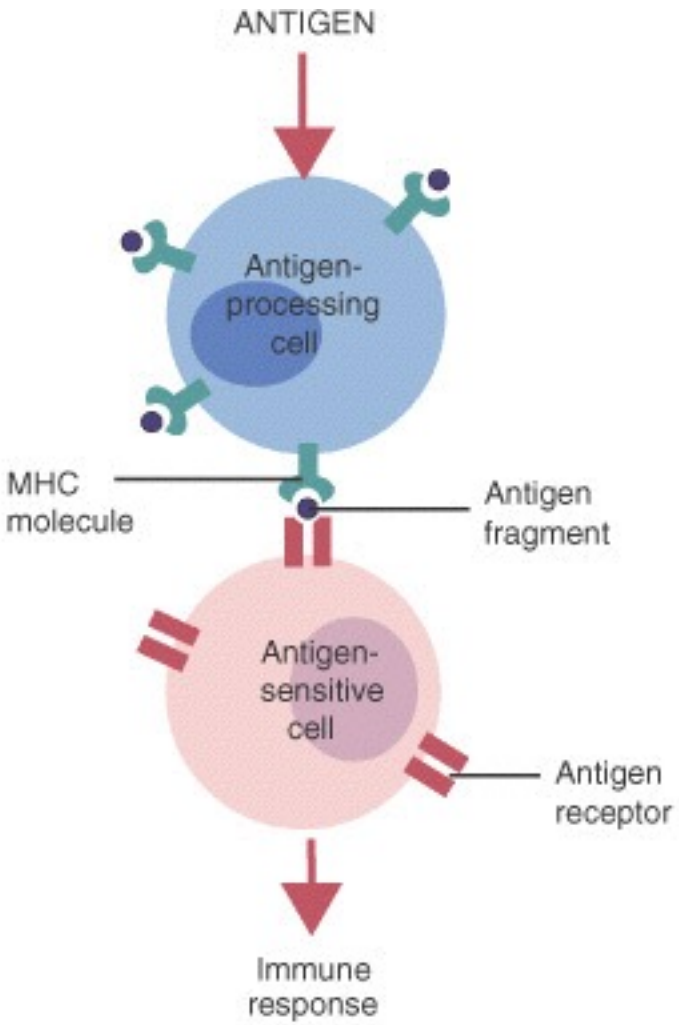
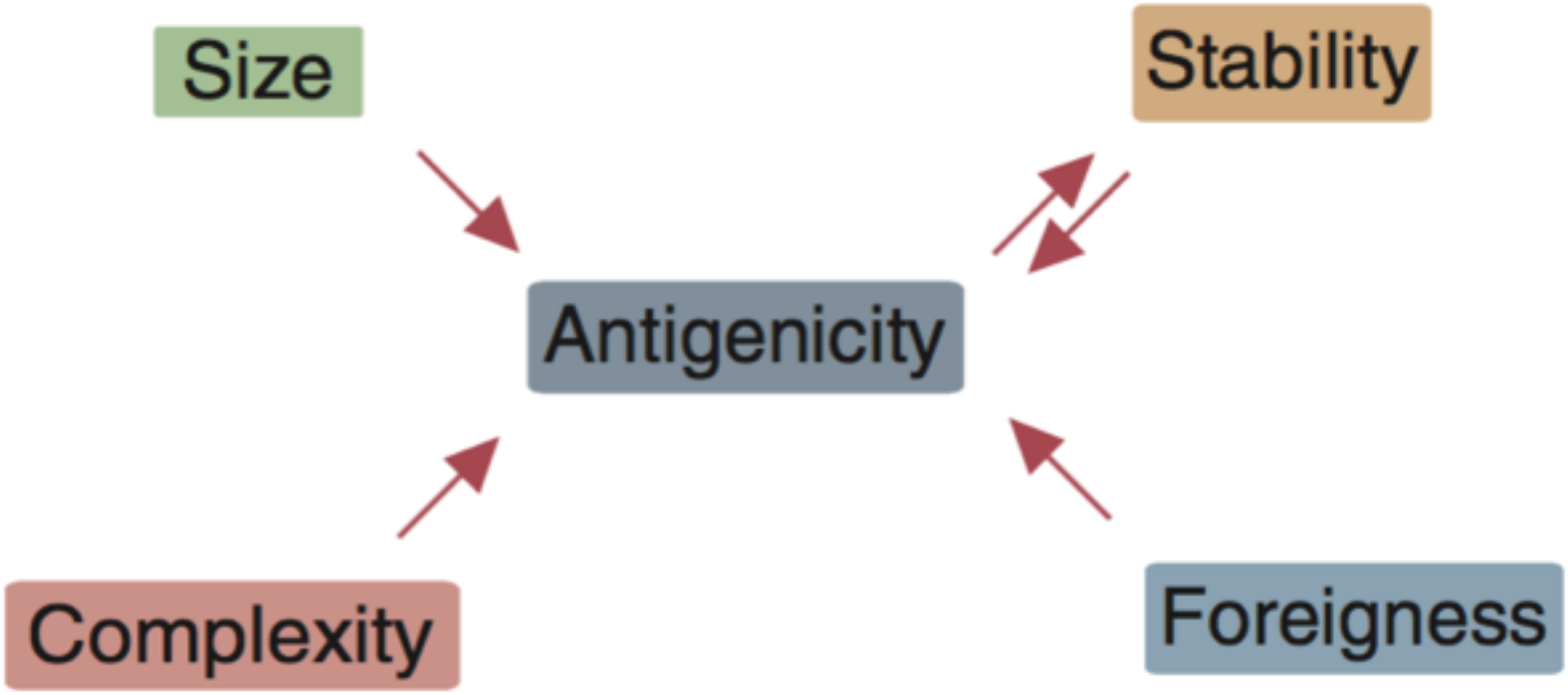
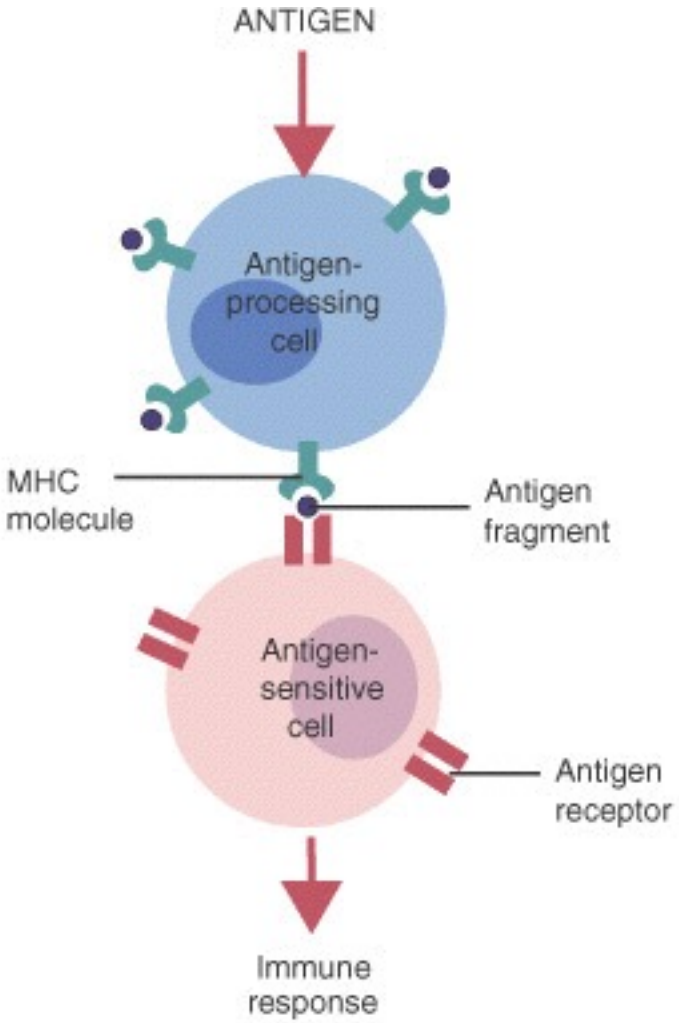



**FIGURE 9-1** The key initial step in any immune response is the presentation of antigens by antigen-processing cells to antigen-sensitive cells. This step is performed by major histocompatibility complex *(MHC)* molecules located on the surface of antigen-processing cells.

# O que é um antígeno?




conceito importante!



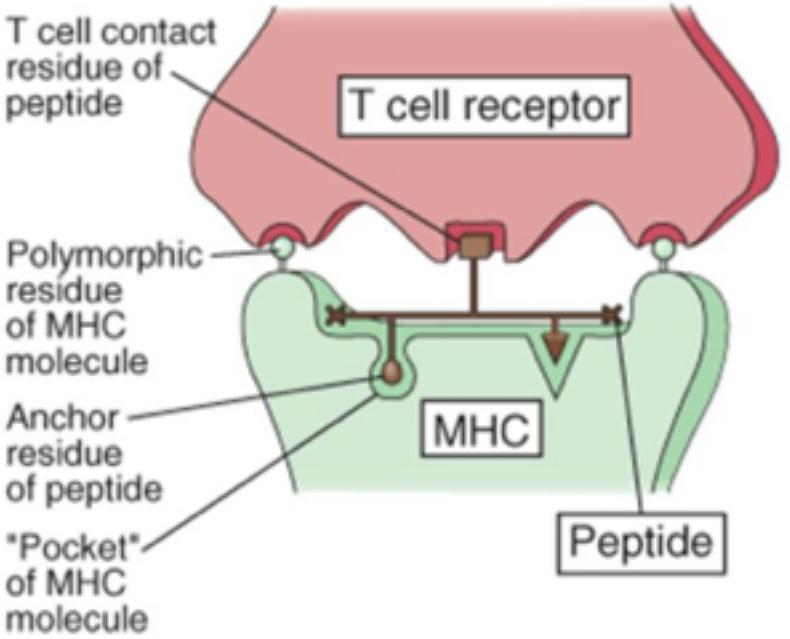




**FIGURE 9-1** The key initial step in any immune response is the presentation of antigens by antigen-processing cells to antigen-sensitive cells. This step is performed by major histocompatibility complex *(MHC)* molecules located on the surface of antigen-processing cells.

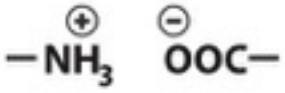
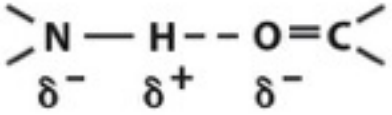
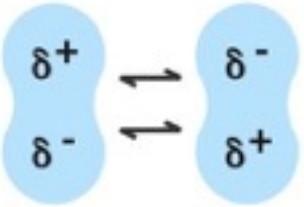
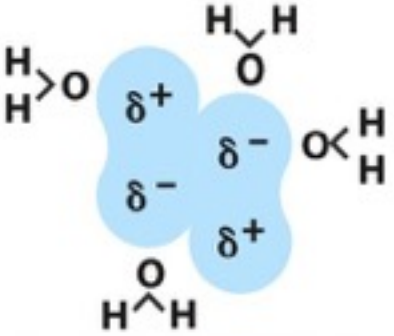
| Noncovalent forces | Origin | |
|---|---|---|
| Electrostatic forces | Attraction between opposite charges |  |
| Hydrogen bonds | Hydrogen shared between electronegative atoms (N,O) |  |
| Van der Waals forces | Fluctuations in electron clouds around molecules polarize neighboring atoms oppositely |  |
| Hydrophobic forces | Hydrophobic groups interact unfavorably with water and tend to pack together to exclude water molecules. The attraction also involves van der Waals forces |  |

Figure 4.9 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

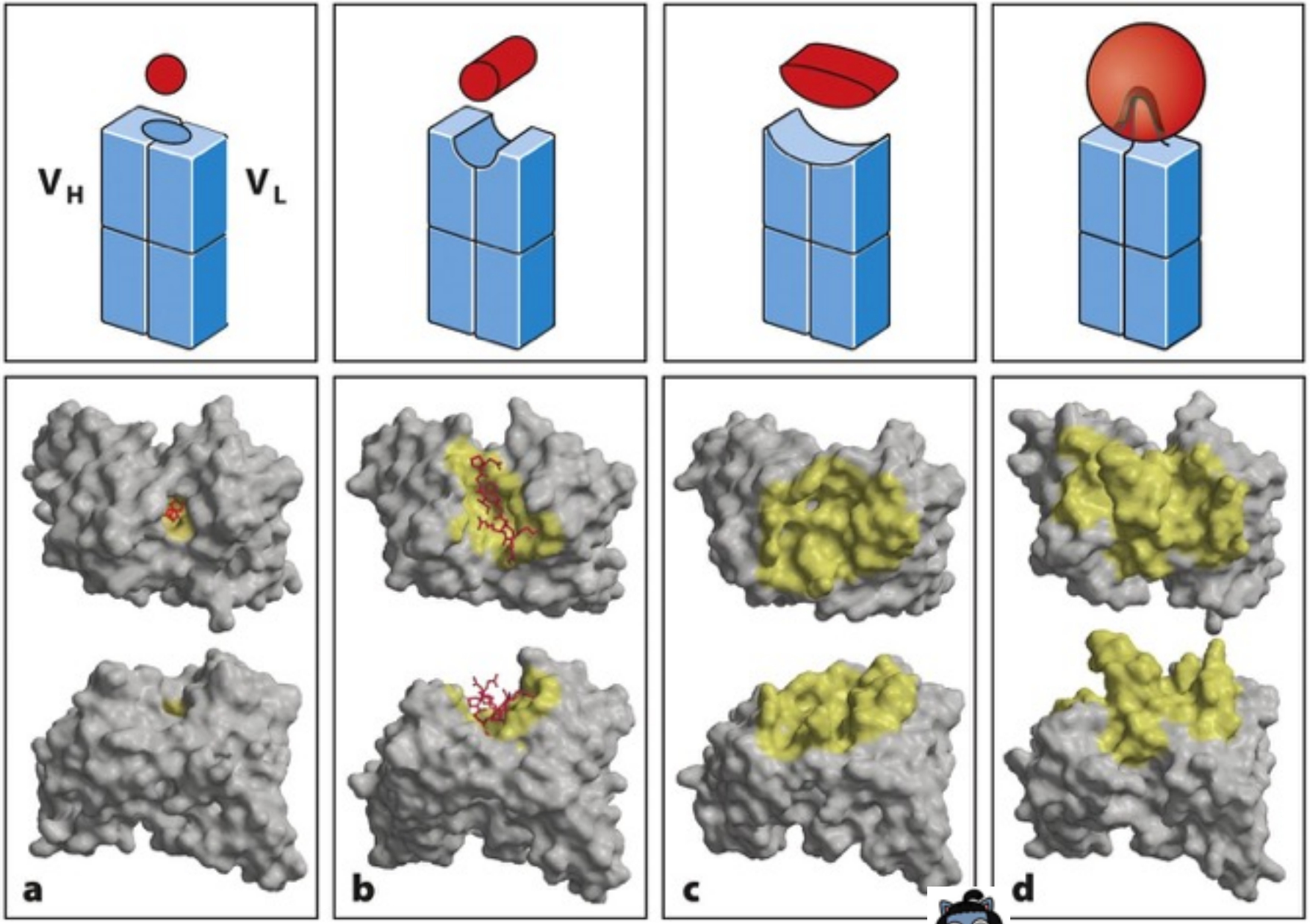



Figure 4.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

# O que é epítopo?

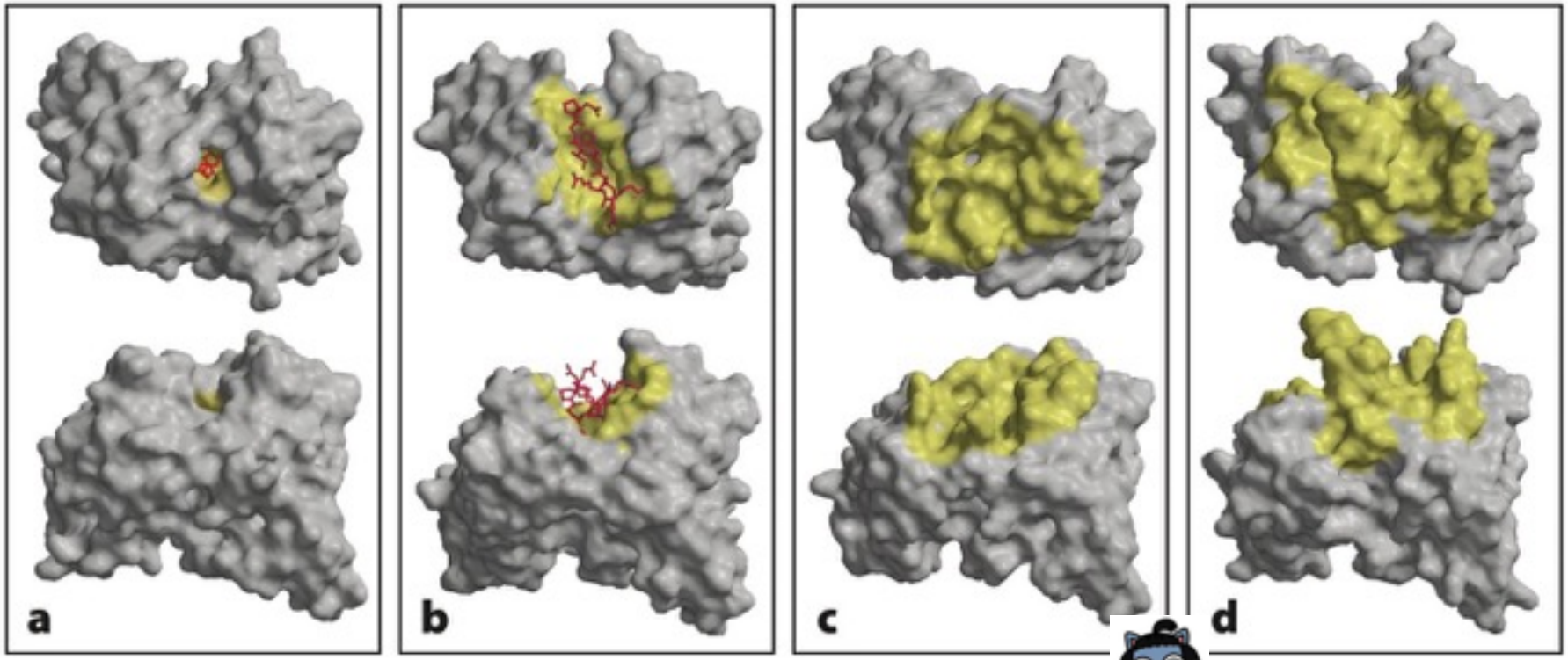
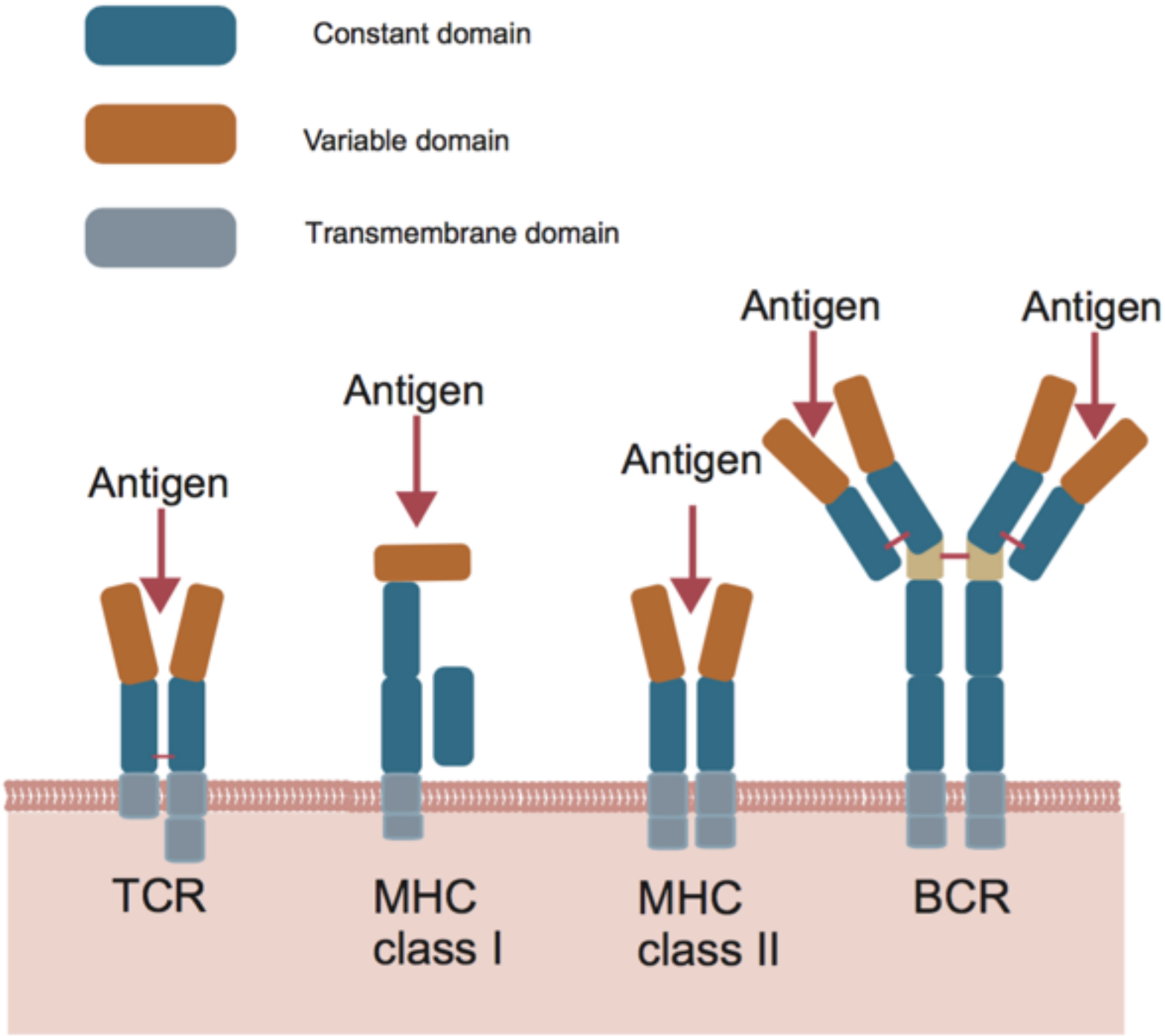



Figure 4.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

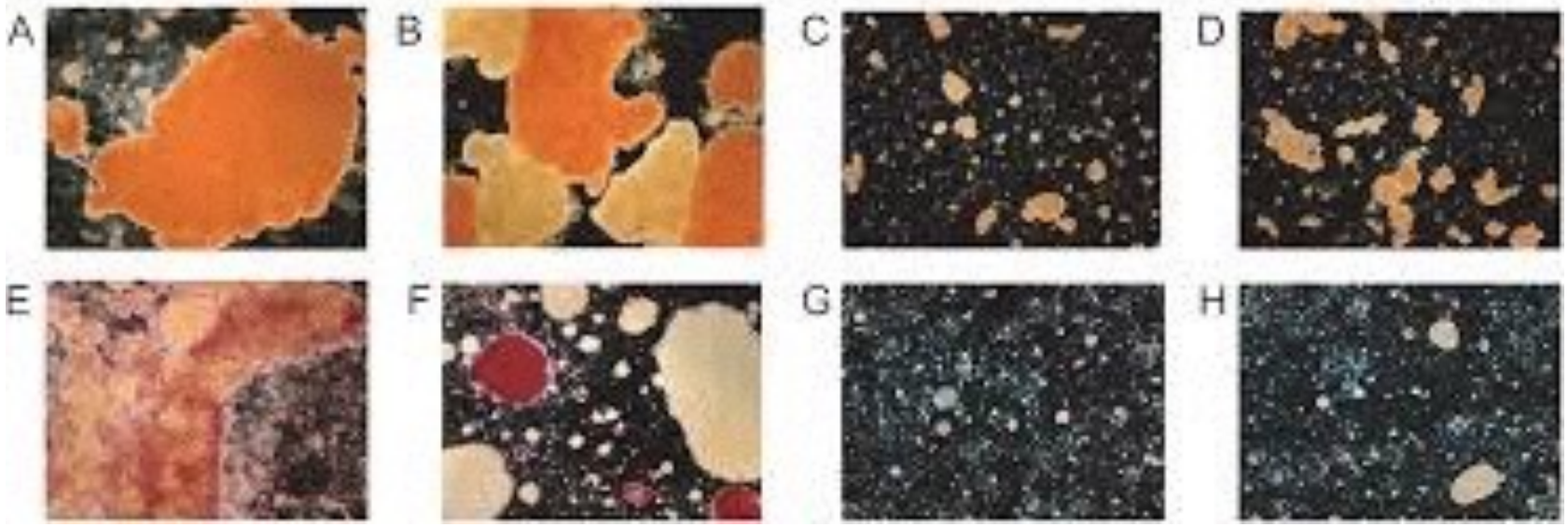


conceito importante!

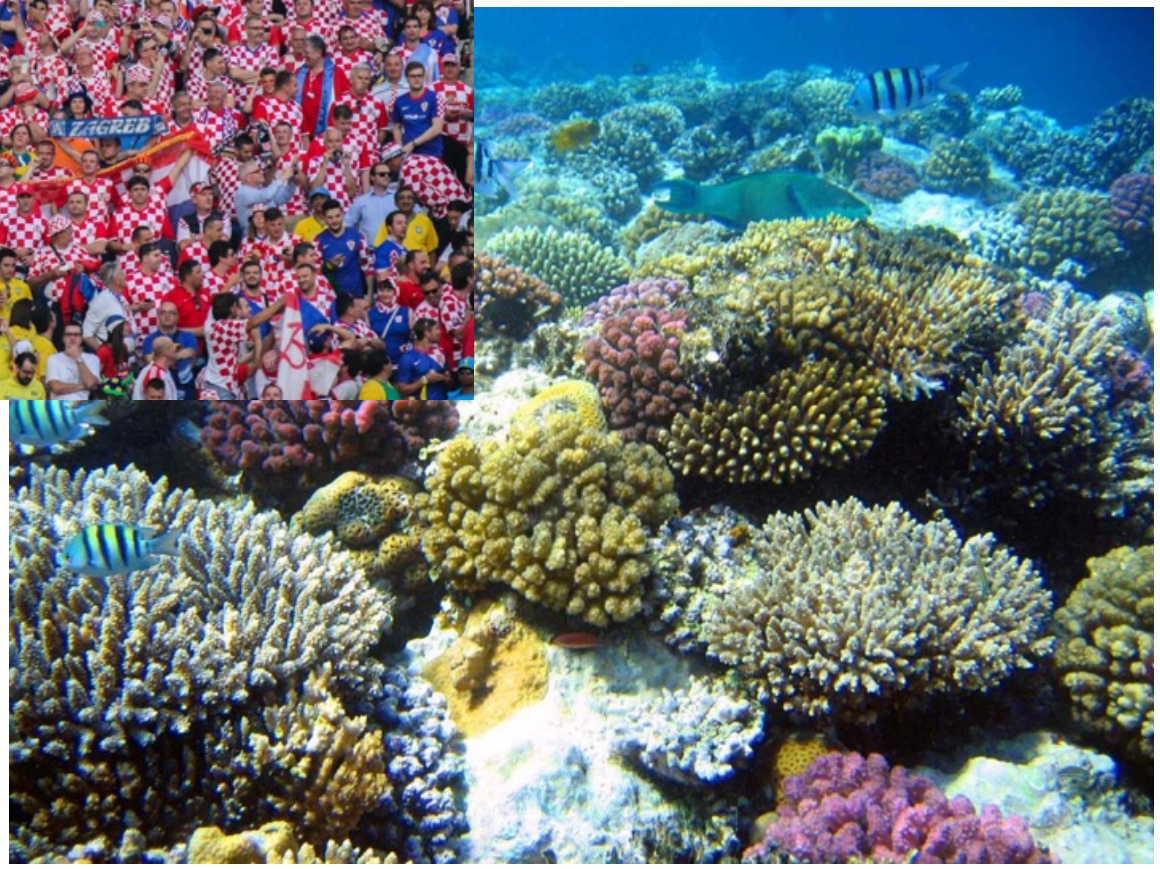

Constant domain
Variable domain
Transmembrane domain
Antigen
Antigen
Antigen
Antigen
Antigen
TCR
MHC
class I
MHC
class II
BCR


TOP
SECRET

Como é que as células do sistema imune discriminam quais são as células próprias (pertencem ao mesmo time) das não-próprias (jogam em times diferentes)?


the same type
different types
no calcium
antibody
A
B
C
D
E
F
G
H

# As moléculas do Complexo de Histocompatibilidade Principal (MHC) identificam as “famílias"

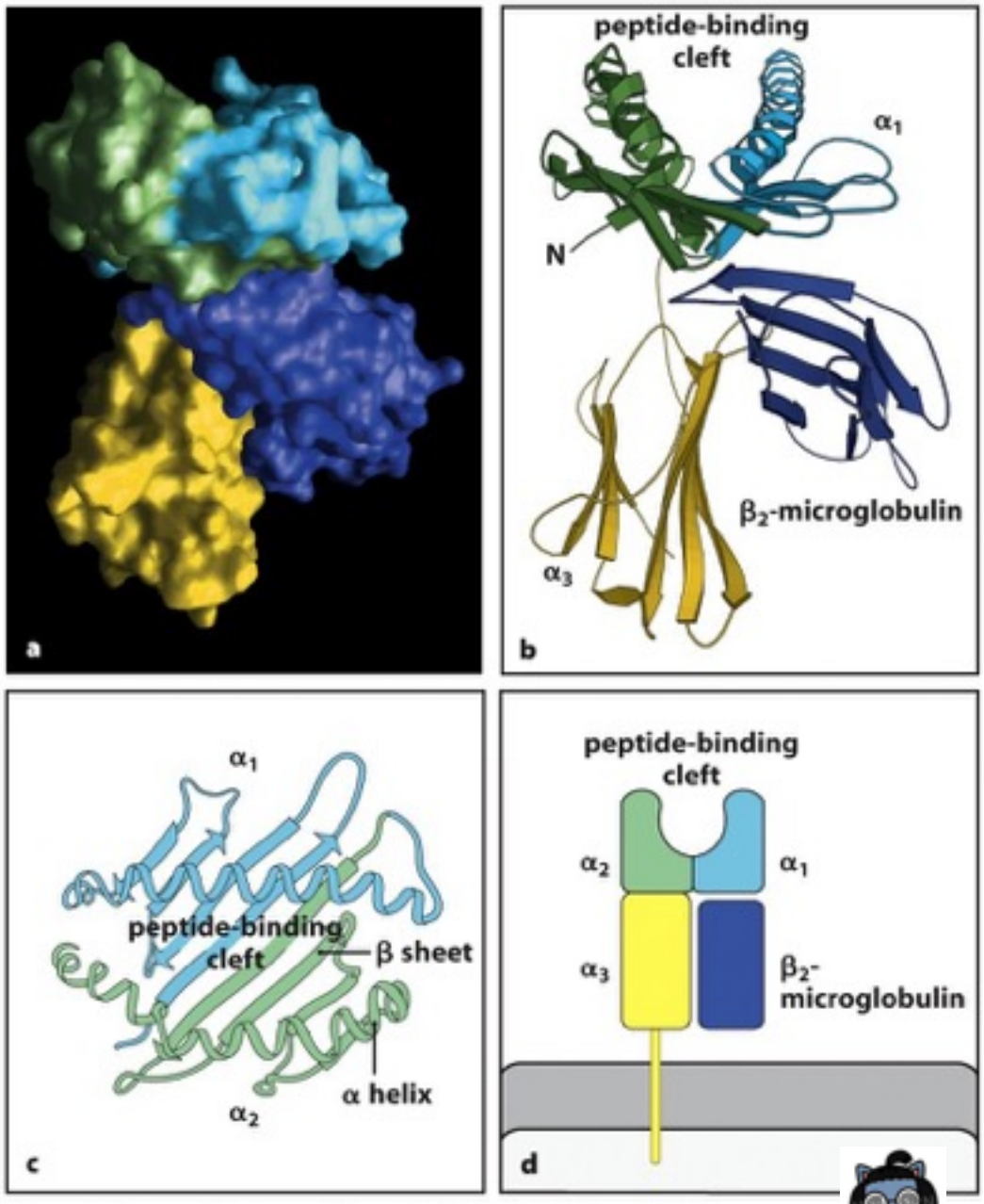


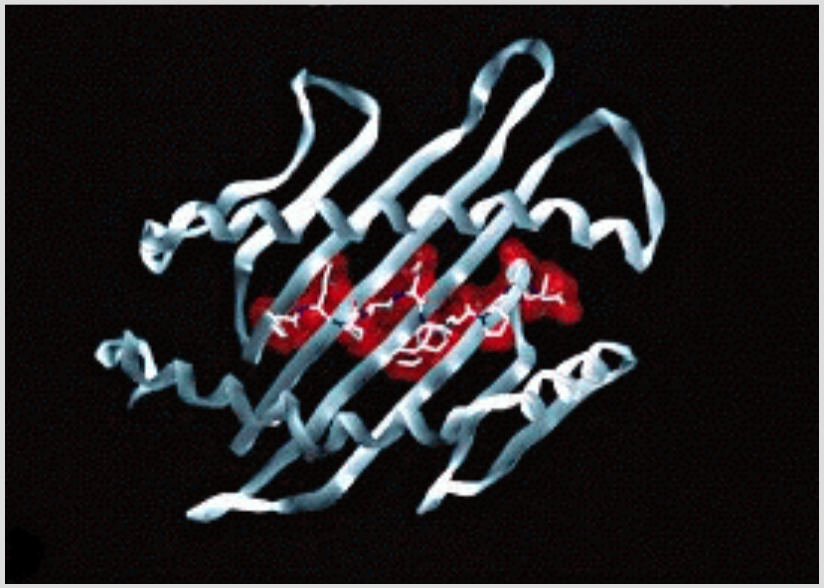

Figure 4.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

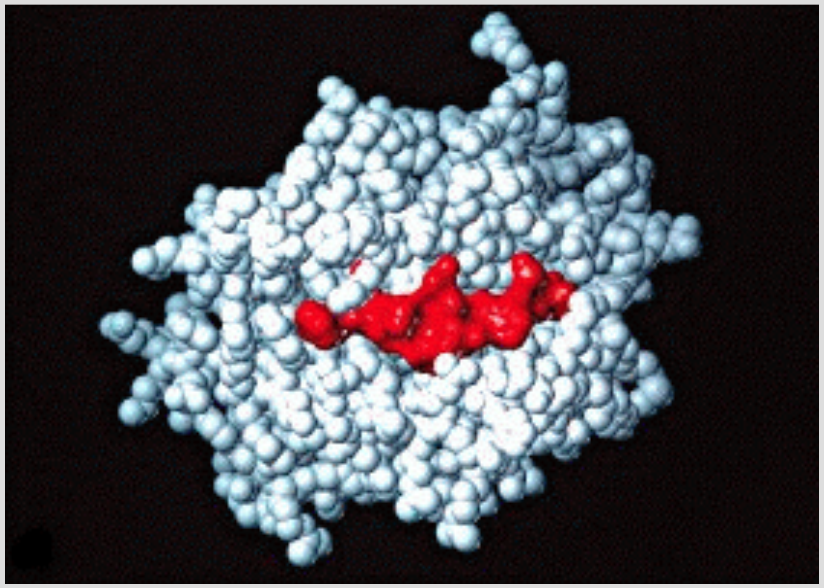
Major
Histocompatibility
Complex

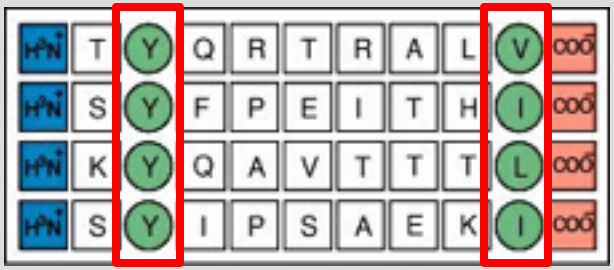
classe I

conceito importante!

A ligação do peptídeo, de aproximadamente nove aminoácidos, ao MHC classe I depende principalmente dos aminoácidos localizados em duas posições da molécula.








conceito importante!

* tamanho
* carga elétrica
* formato (cadeias laterais)
* aminoácidos de ancoragem

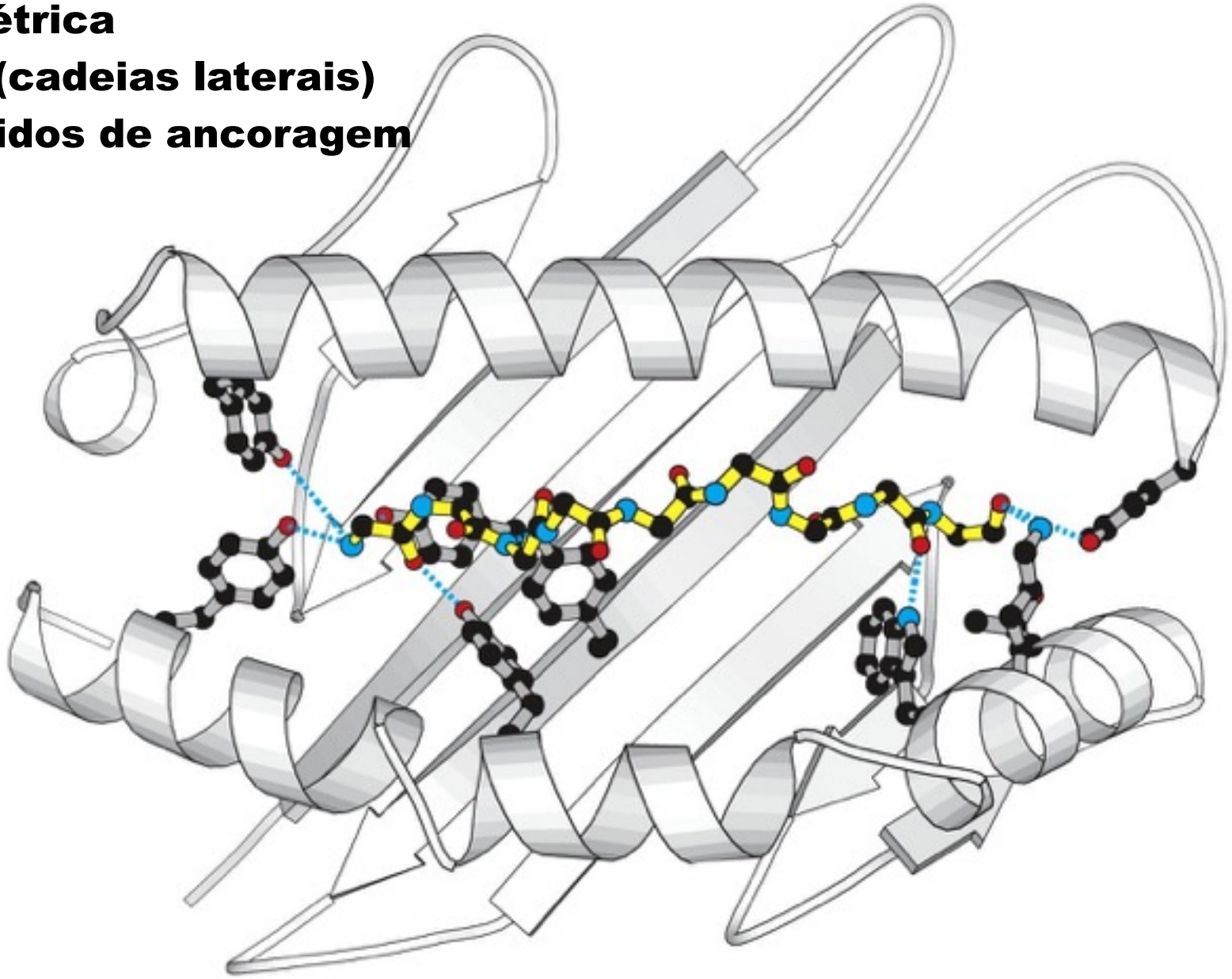


Figure 4.18 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

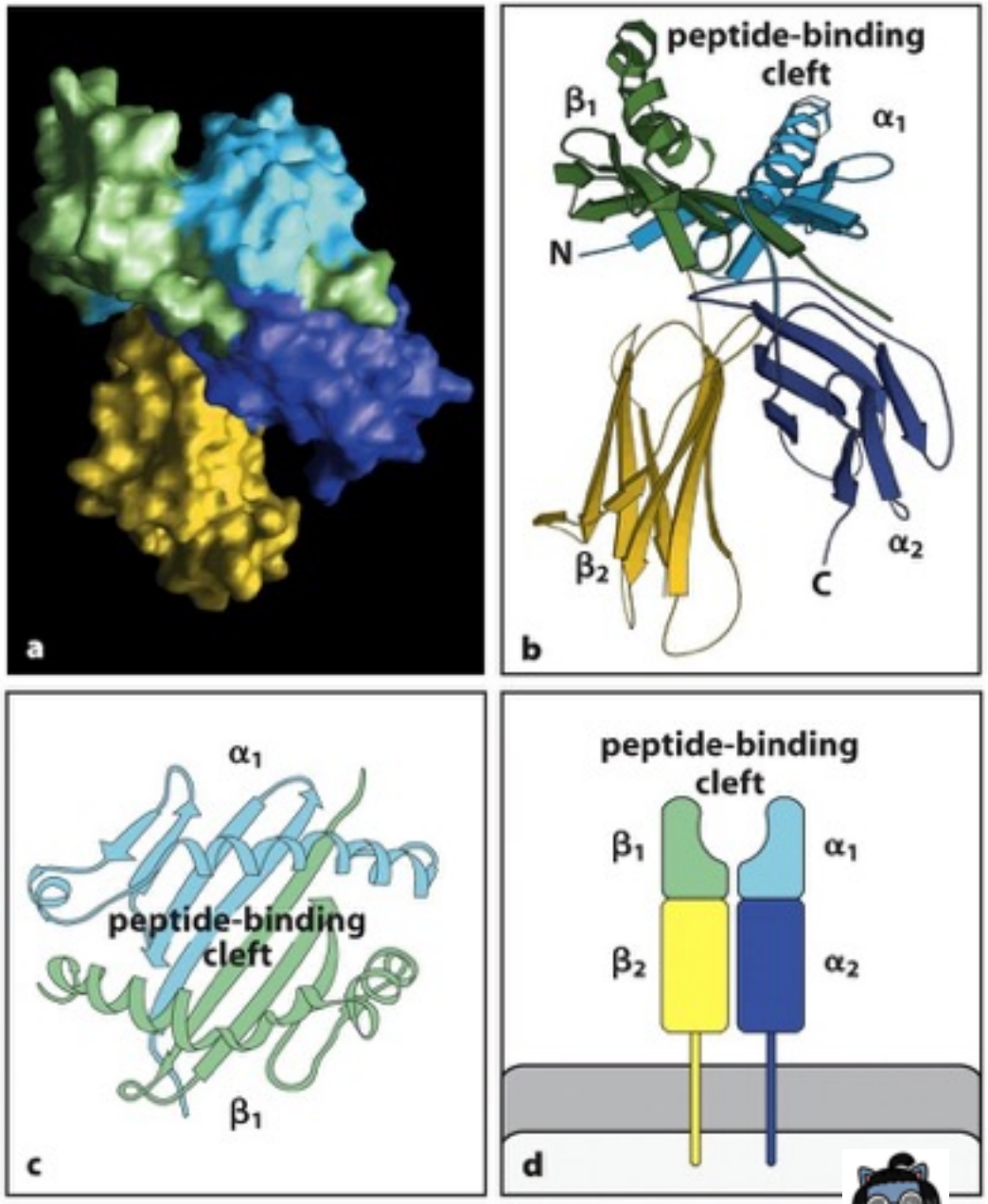


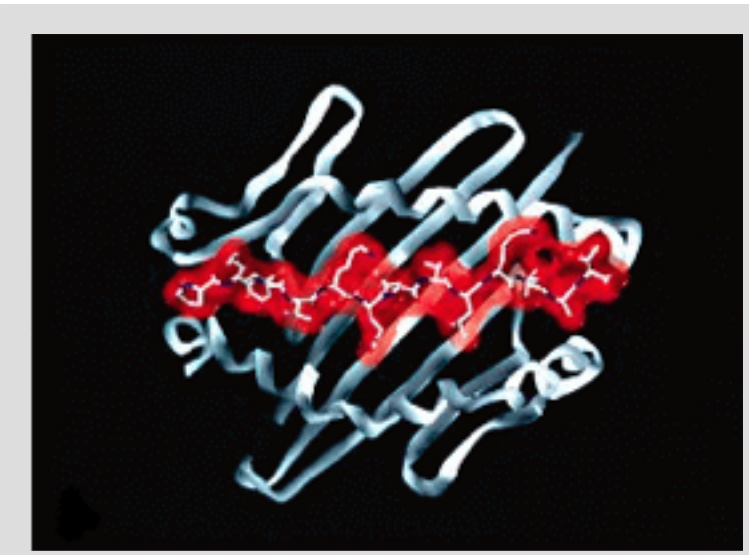

Figure 4.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

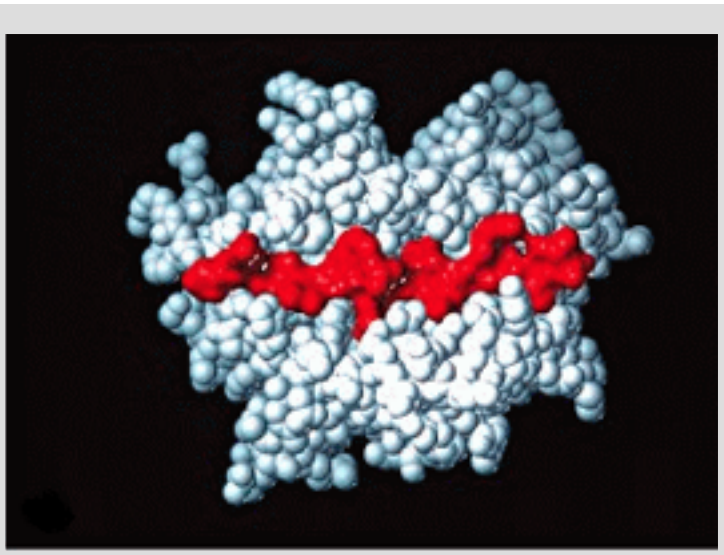
Major
Histocompatibility
Complex

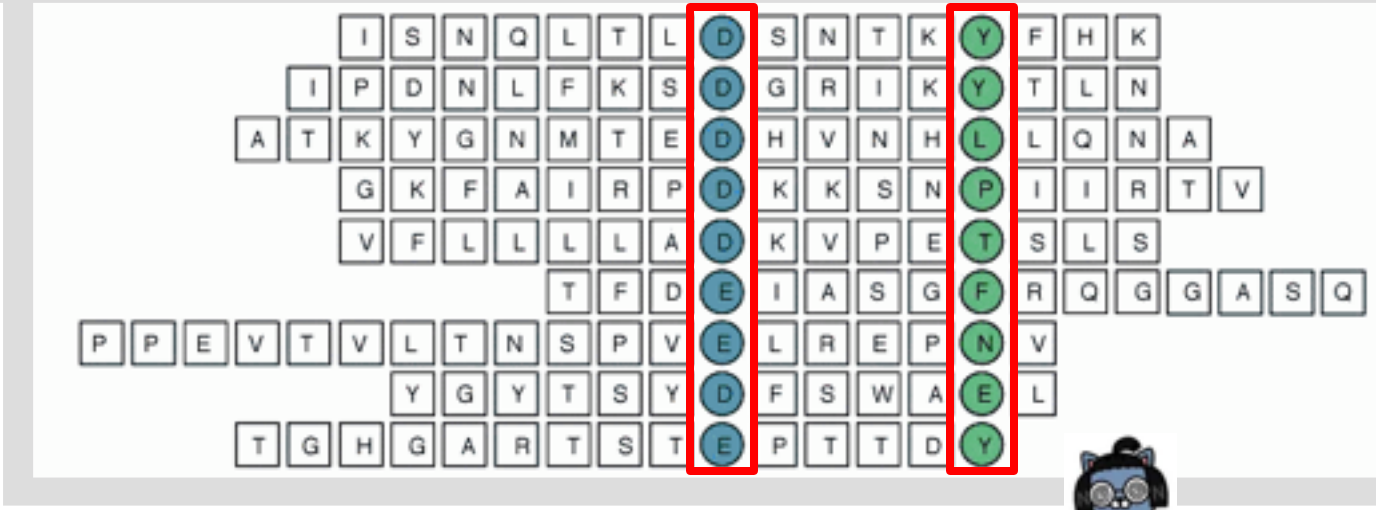
classe II

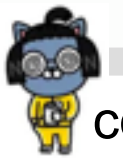
conceito importante!

A ligação do peptídeo à molécula de MHC classe II também depende principalmente de dois aminoácidos mas a fenda é mais permissiva quanto ao tamanho do peptídeo por ser aberta nas laterais.







conceito importante!

* carga elétrica
* formato (cadeias laterais)
* aminoácidos de ancoragem

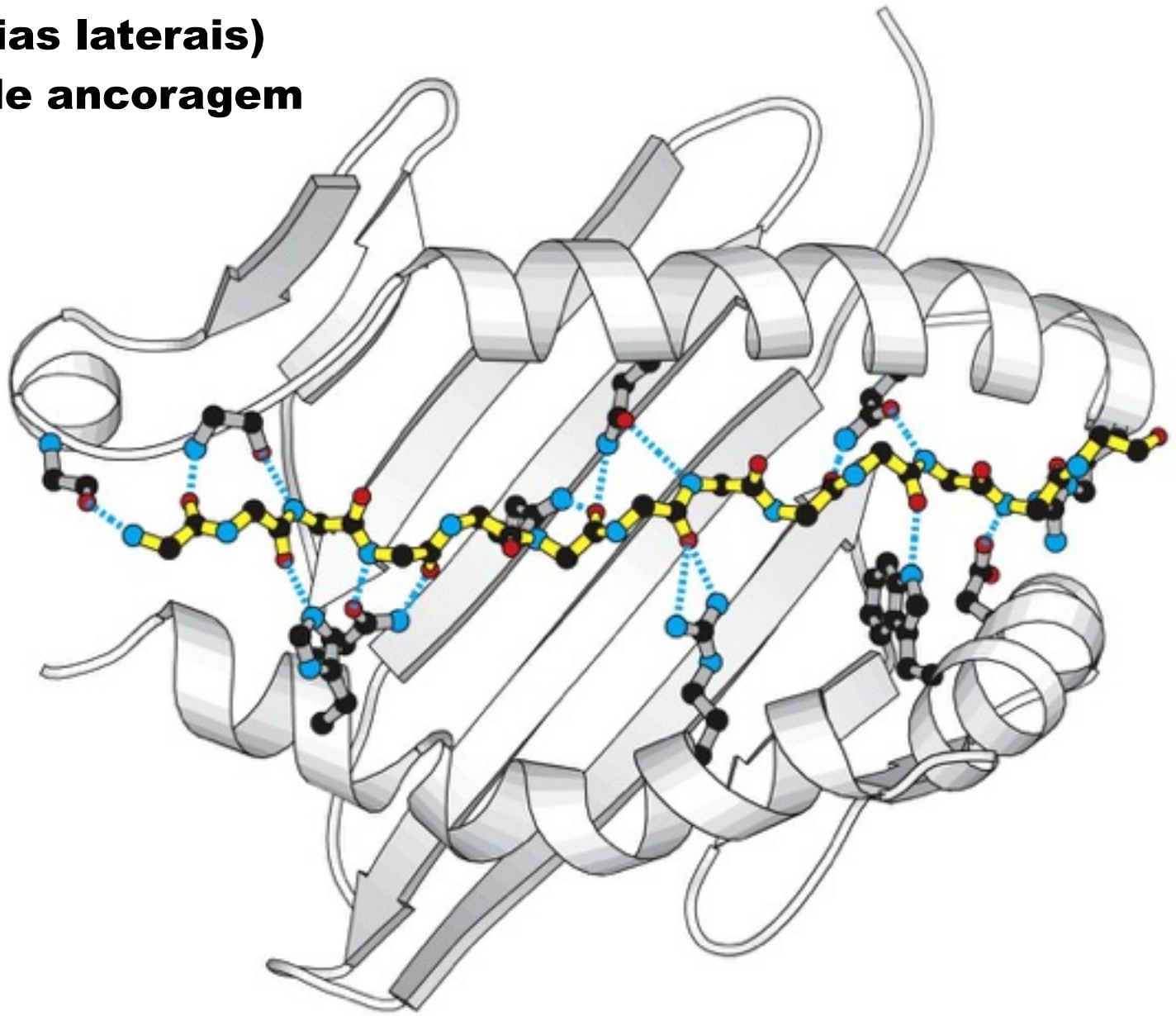


Figure 4.20 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

MHC-I


MHC-II

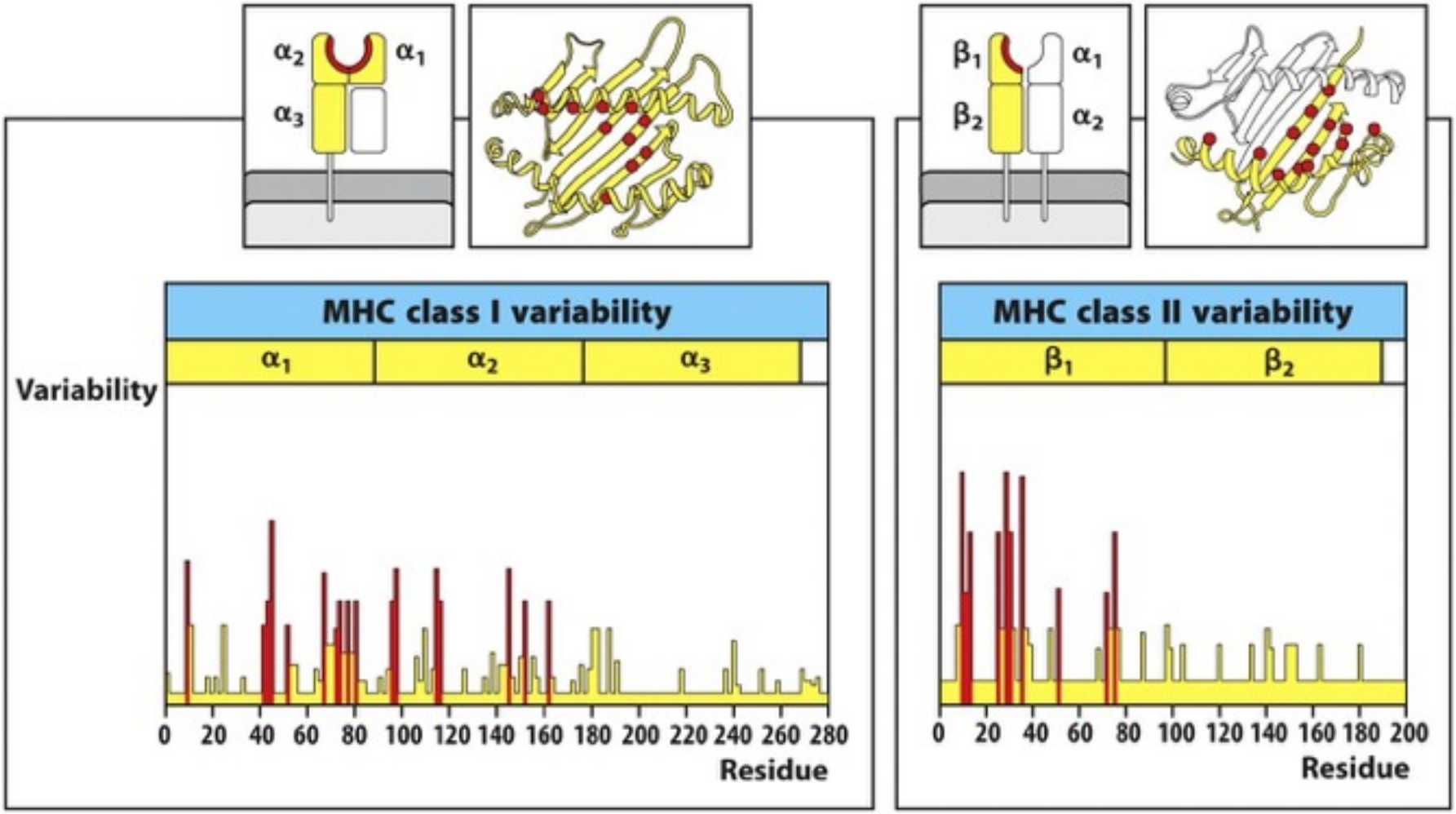
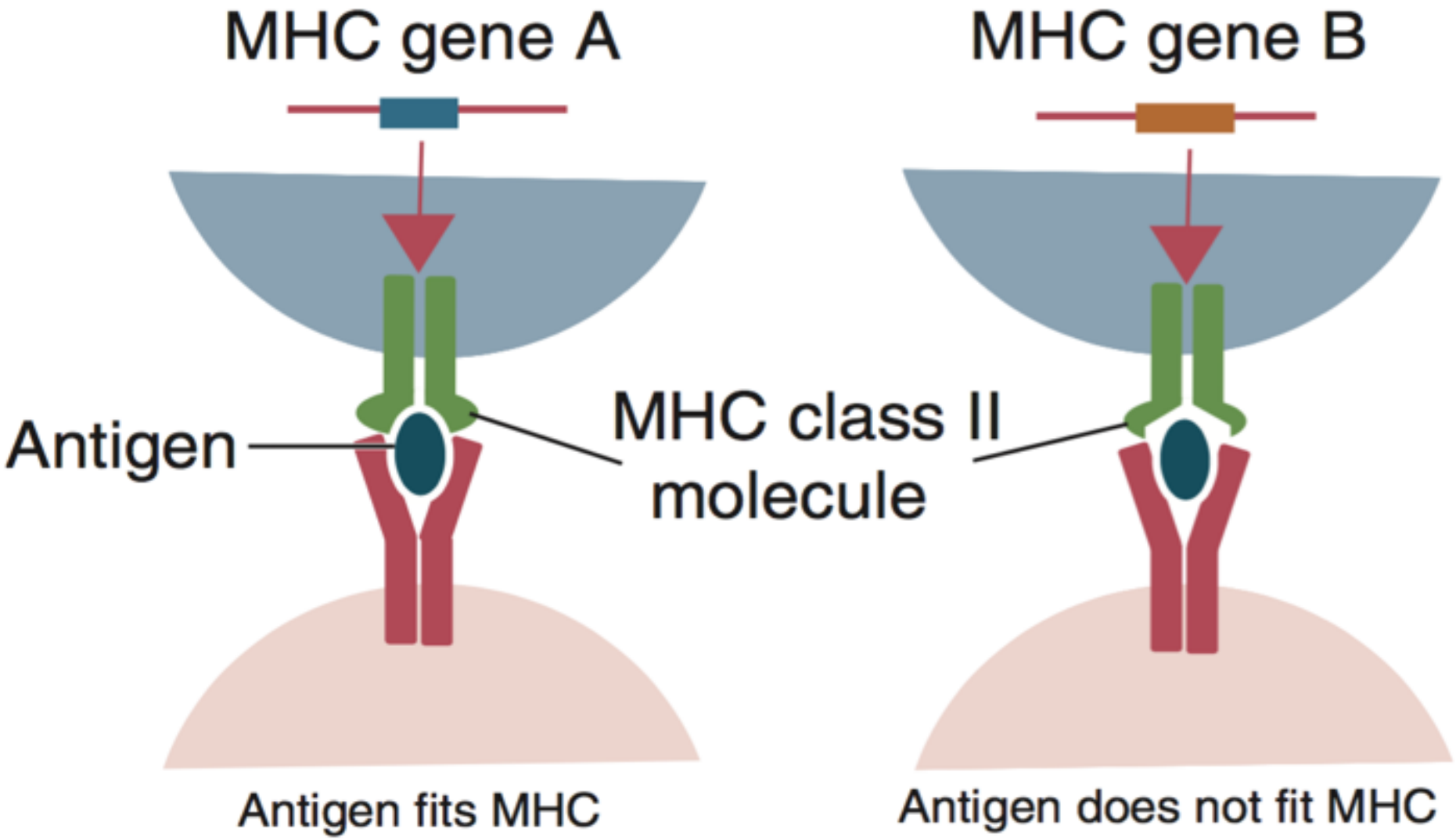
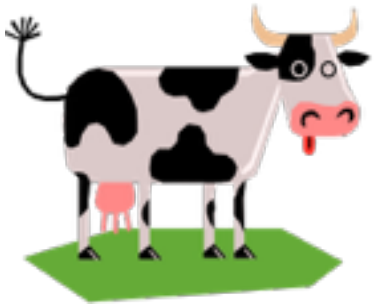



Figure 6.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)


MHC gene A
MHC gene B
Antigen
MHC class II molecule
Antigen fits MHC
Antigen does not fit MHC
Immune response
No immune response

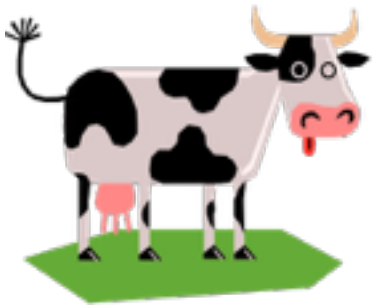
# MHC II e susceptibilidade ao vírus da leucemia bovina (leucose bovina)



**MHC II DRB3**

**Ácido glutâmico 70** (polar ácido)
**Arginina 71** (polar básico)

**RESISTENTE**



**MHC II DRB3**

**Valina 75** (apolar)
**Asparagina 76** (neutro)
**Treonina 77** (neutro)
**Tirosina 78** (neutro aromático)

**SUSCEPTÍVEL**

# As moléculas de MHC são polimórficas e poligênicas

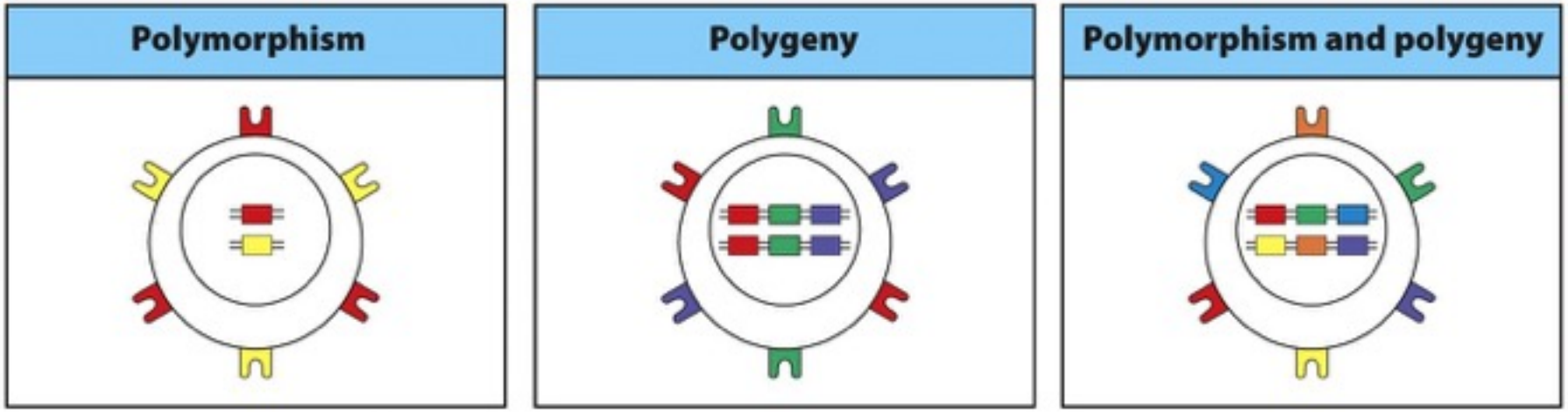



Figure 6.17 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Este indivíduo consegue apresentar um número maior de moléculas diferentes por ser heterozigoto.

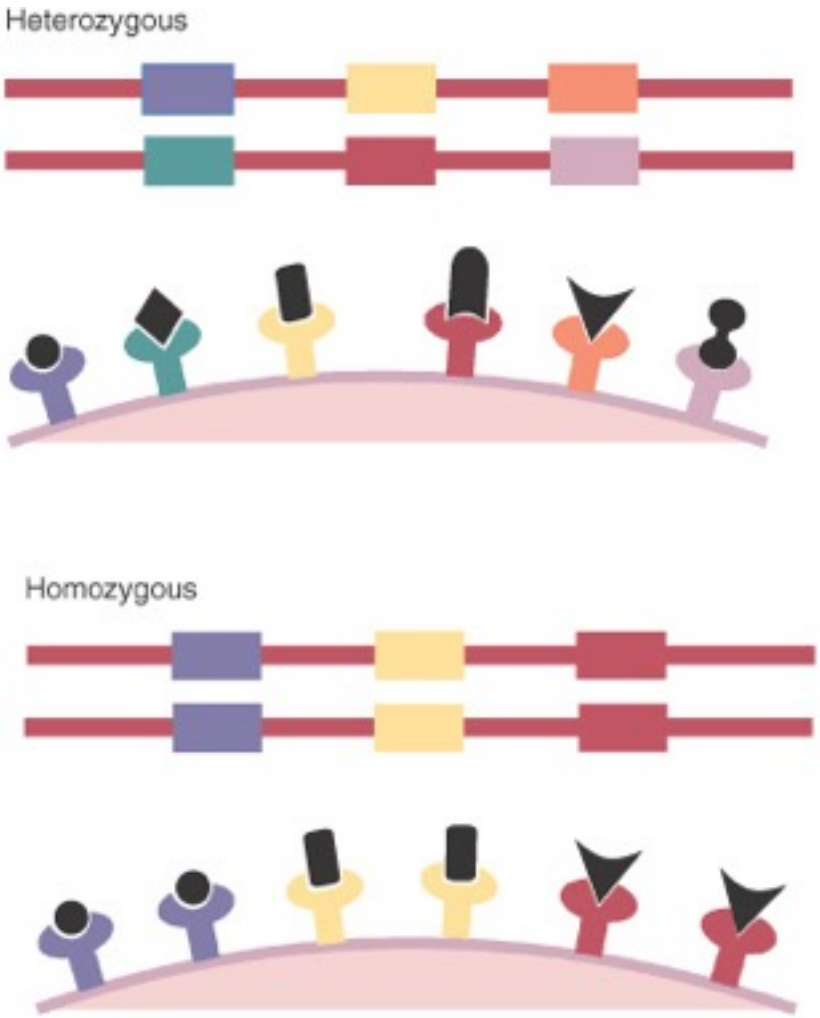



**FIGURE 9-13** Heterozygous animals with two types of major histocompatibility complex (MHC) molecule coded for at each locus express six different antigen-presenting molecules on the cell surface. Therefore they generate a more diverse and effective immune response than homozygous animals with only one MHC molecule coded for at each locus. An example of heterozygote advantage.

# 1,7 x $10^{18}$ combinações gênicas possíveis para MHC (humanos)

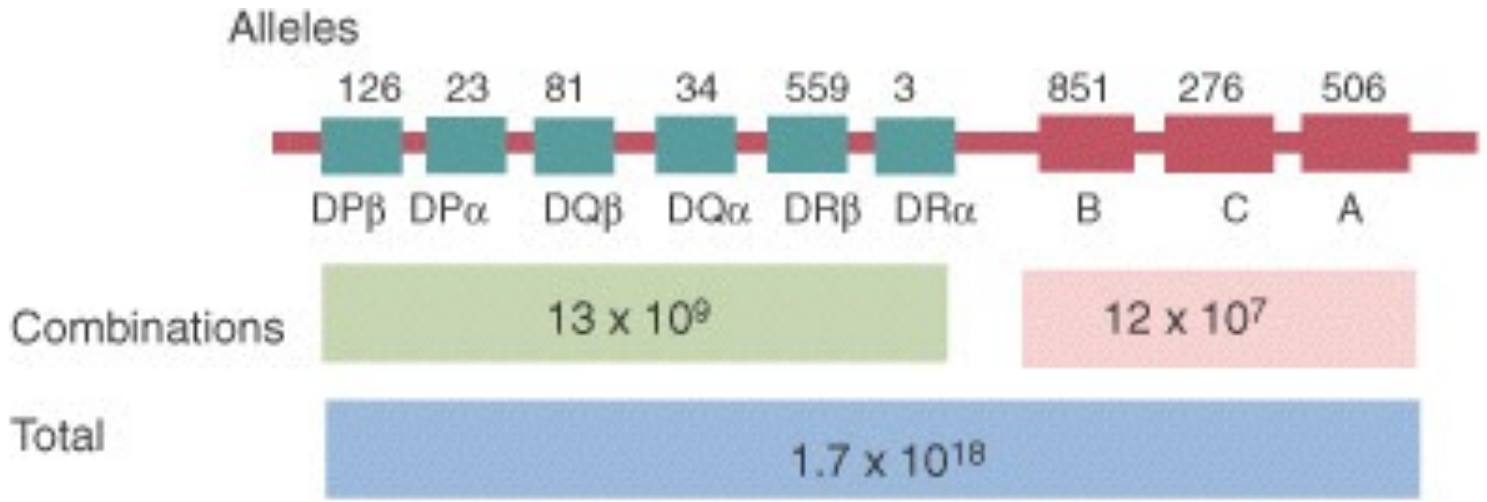
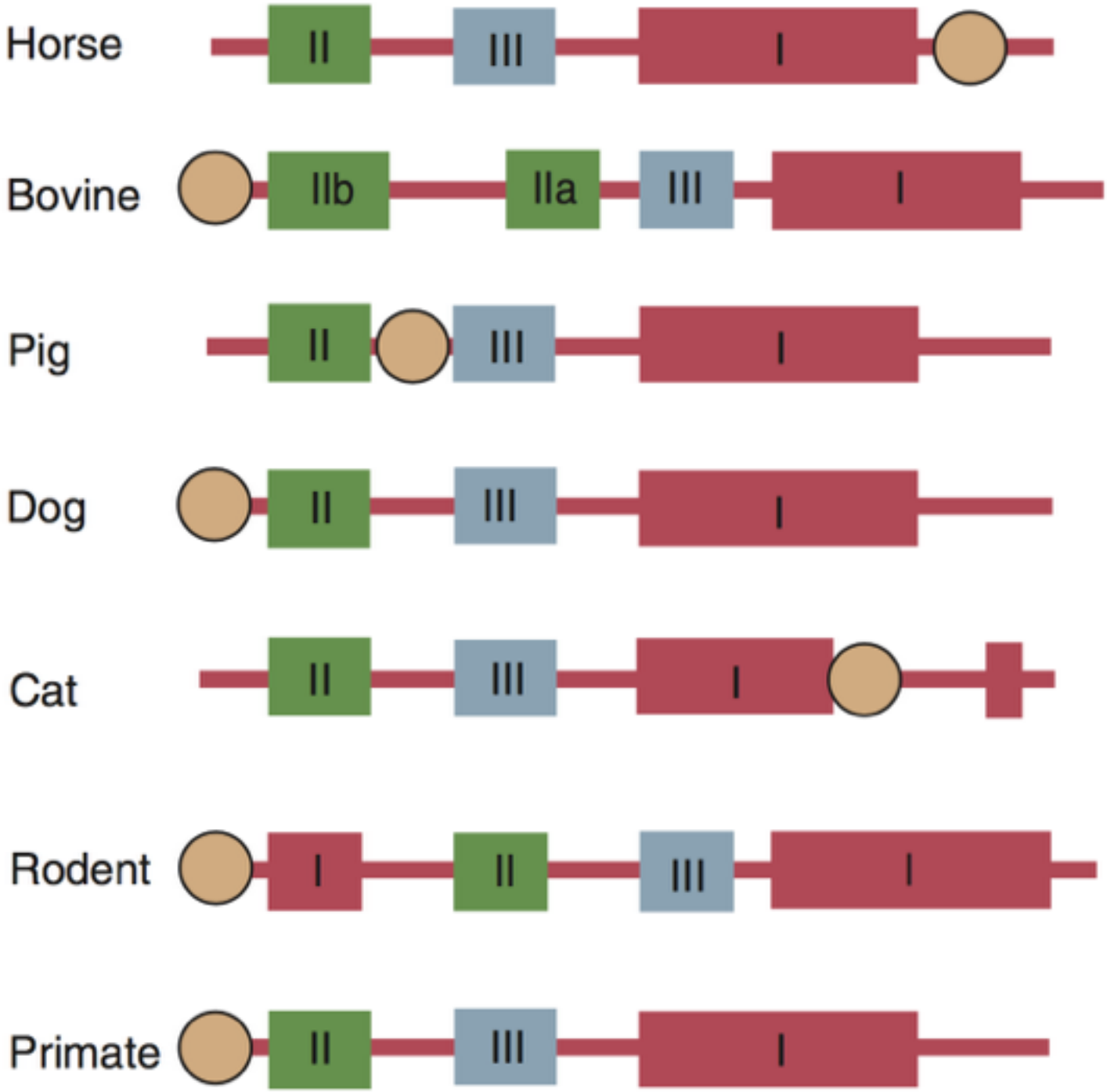
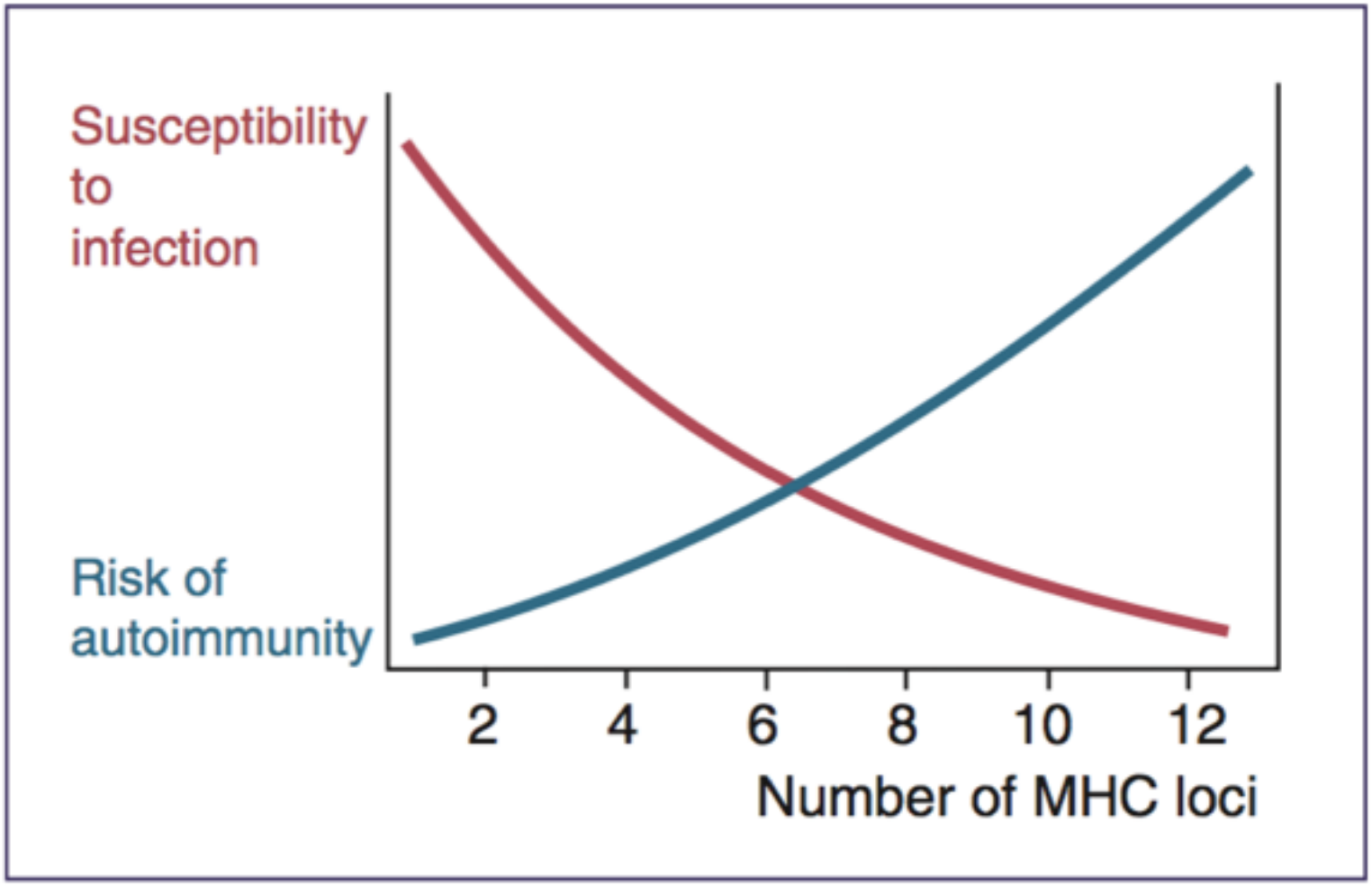



**FIGURE 9-15** An example of how major histocompatibility complex (MHC) polymorphism can generate an enormous number of different MHC haplotypes. The numbers above each locus are the number of identified alleles in the human MHC as of January 2007. The number of different combinations can be determined by multiplying all of them together. Thus there are $13 \times 10^9$ class II combinations, $12 \times 10^7$ class I combinations, and $1.7 \times 10^{18}$ total possible combinations, more than sufficient to give every human a unique haplotype.


Horse
II
III
I
Bovine
IIb
IIa
III
I
Pig
II
III
I
Dog
II
III
I
Cat
II
III
I
Rodent
I
II
III
I
Primate
II
III
I


Susceptibility to infection
Risk of autoimmunity
2
4
6
8
10
12
Number of MHC loci

| Tissue | MHC class I | MHC class II |
|---|---|---|
| **Lymphoid tissues** | | |
| T cells | +++ | +* |
| B cells | +++ | +++ |
| Macrophages | +++ | ++ |
| Dendritic cells | +++ | +++ |
| Epithelial cells of the thymus | + | +++ |
| **Other nucleated cells** | | |
| Neutrophils | +++ | – |
| Hepatocytes | + | – |
| Kidney | + | – |
| Brain | + | –† |
| **Nonnucleated cells** | | |
| Red blood cells | – | – |

Figure 4.27 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

*

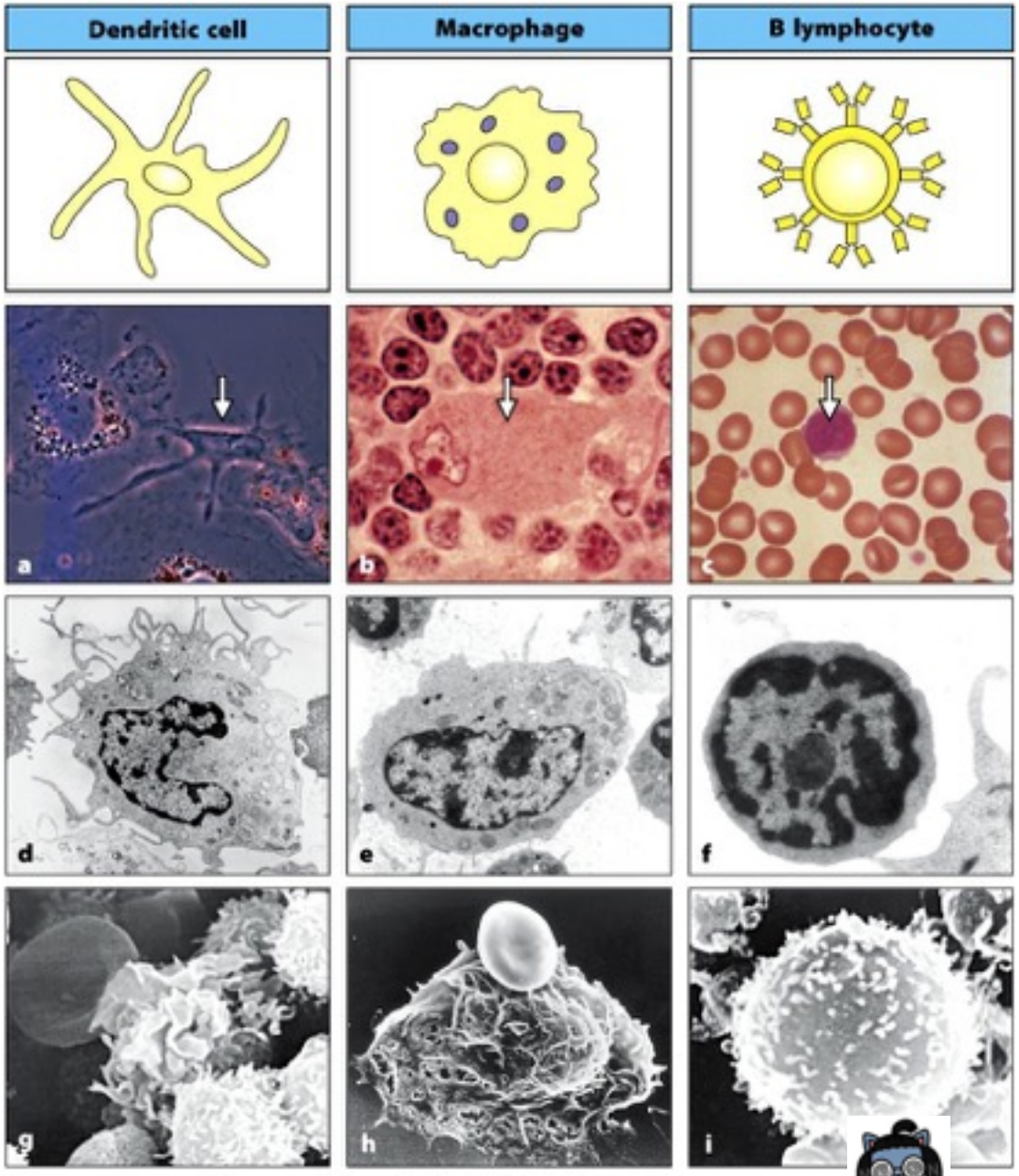



Figure 1.22 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

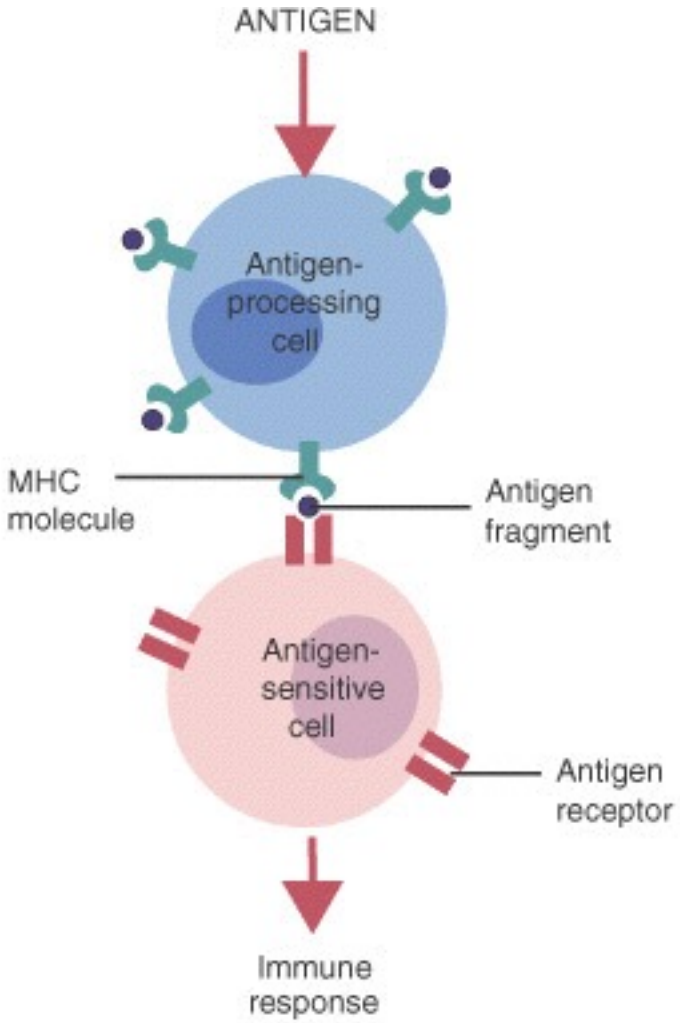
Antigen
Presenting
Cell

Células
aPresentadoras
de Antígeno

expressam
MHC-II
além do
MHC-I

conceito importante!

conceito importante!



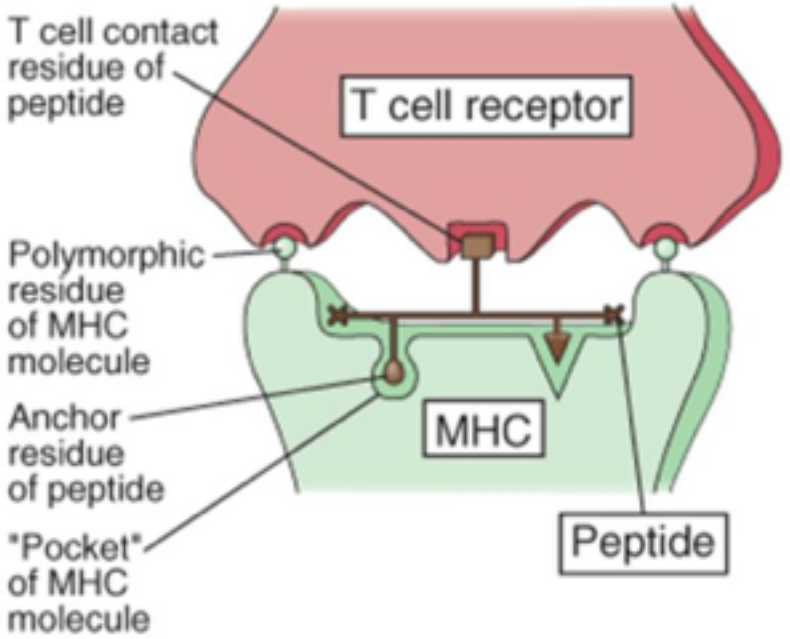
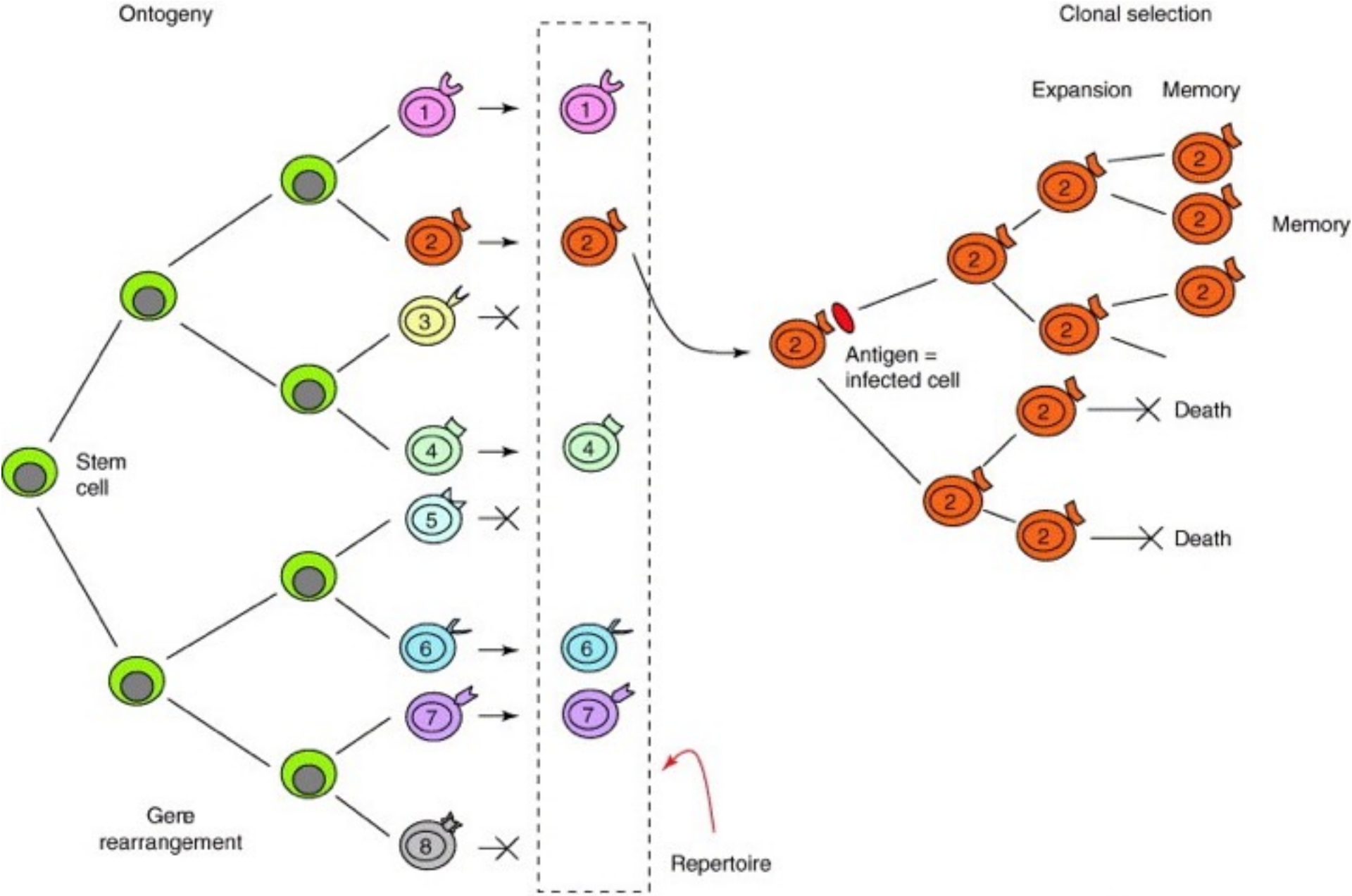
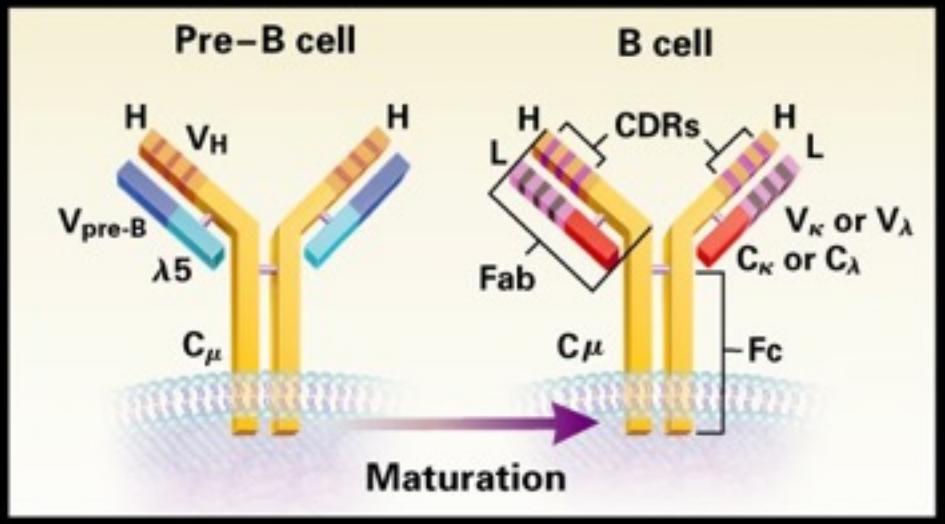



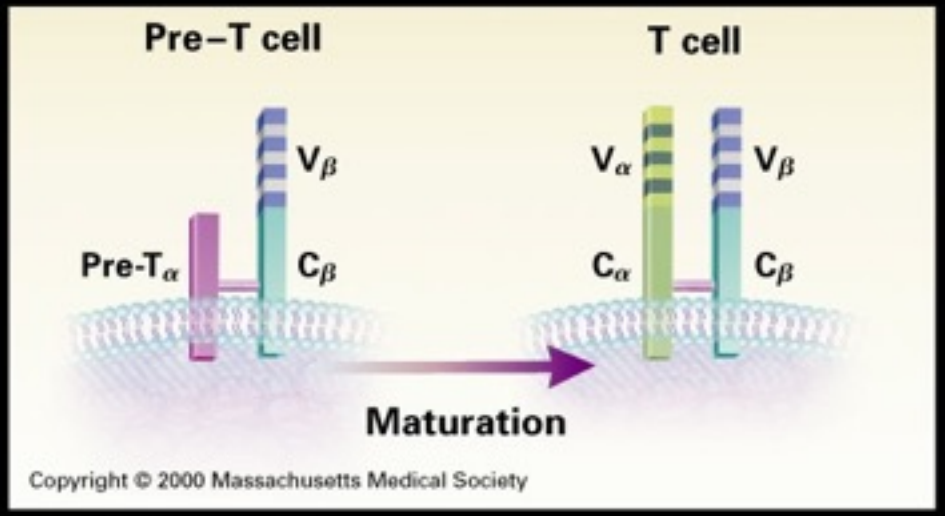

**FIGURE 9-1** The key initial step in any immune response is the presentation of antigens by antigen-processing cells to antigen-sensitive cells. This step is performed by major histocompatibility complex *(MHC)* molecules located on the surface of antigen-processing cells.


STAR WARS
EPISODE II
ATTACK OF THE
CLONE AMPLIFIERS


Ontogeny
Clonal selection
Expansion
Memory
Memory
Stem cell
Gene rearrangement
Antigen = infected cell
Death
Death
Repertoire
1
2
3
4
5
6
7
8

# Structure of Immature and Mature B-Cell and T-Cell Antigen Receptors






Delves PJ, Roitt IM.
The Immune System (Part1).
N Engl J Med 2000;343:37-49.

The New England Journal of Medicine

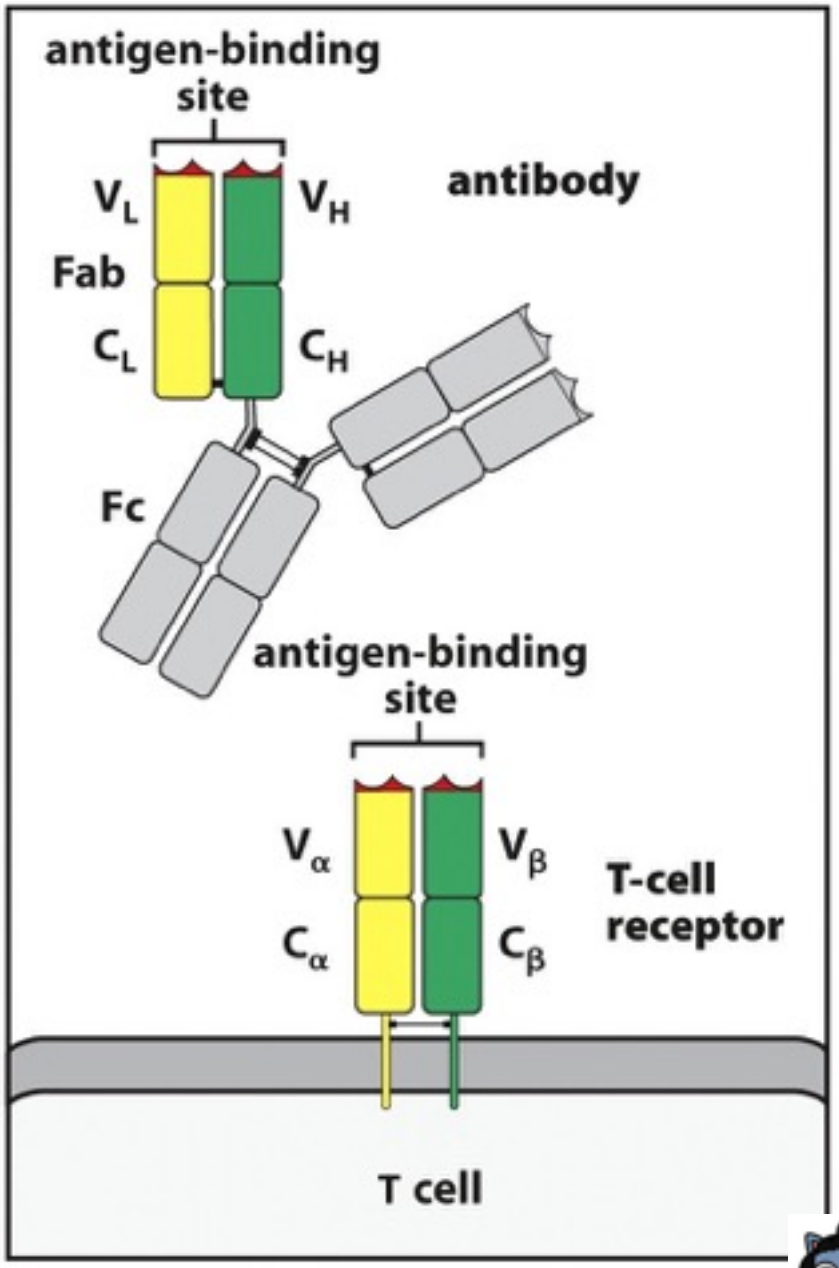



Figure 4.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

B
Cell
Receptor

T
Cell
Receptor

conceito importante!

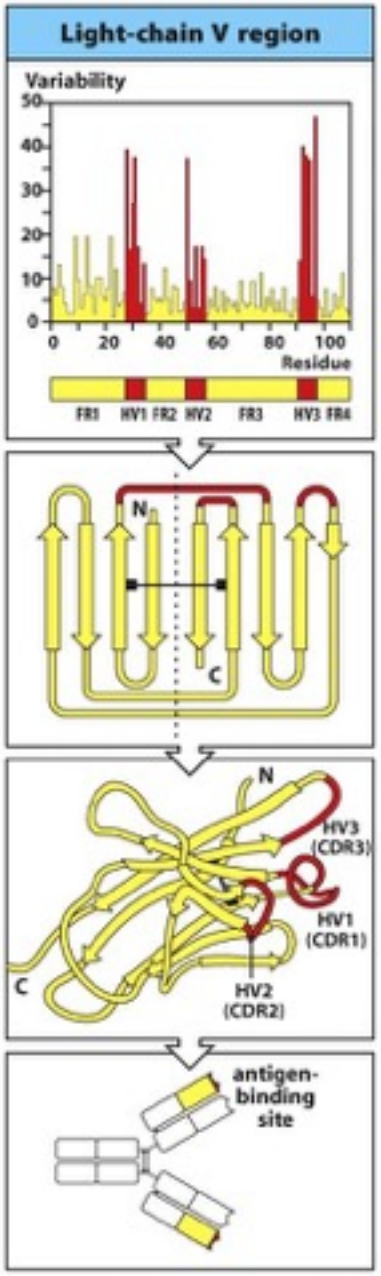



Figure 4.7 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

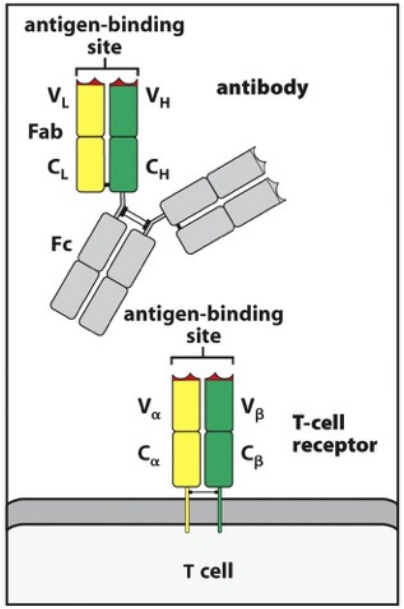



Figure 4.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

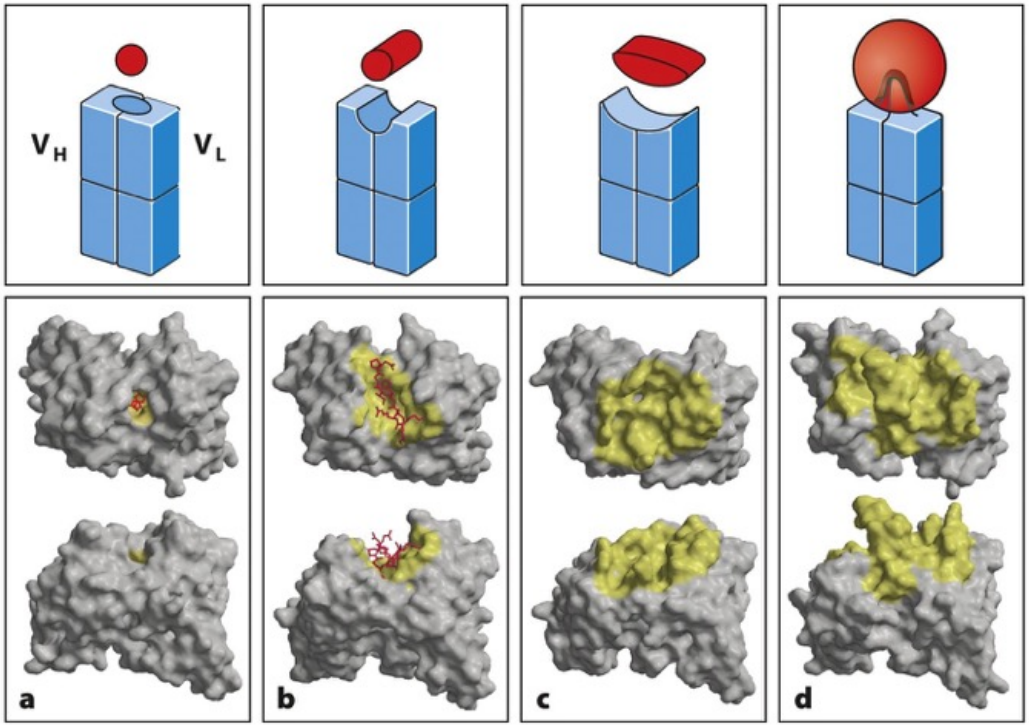
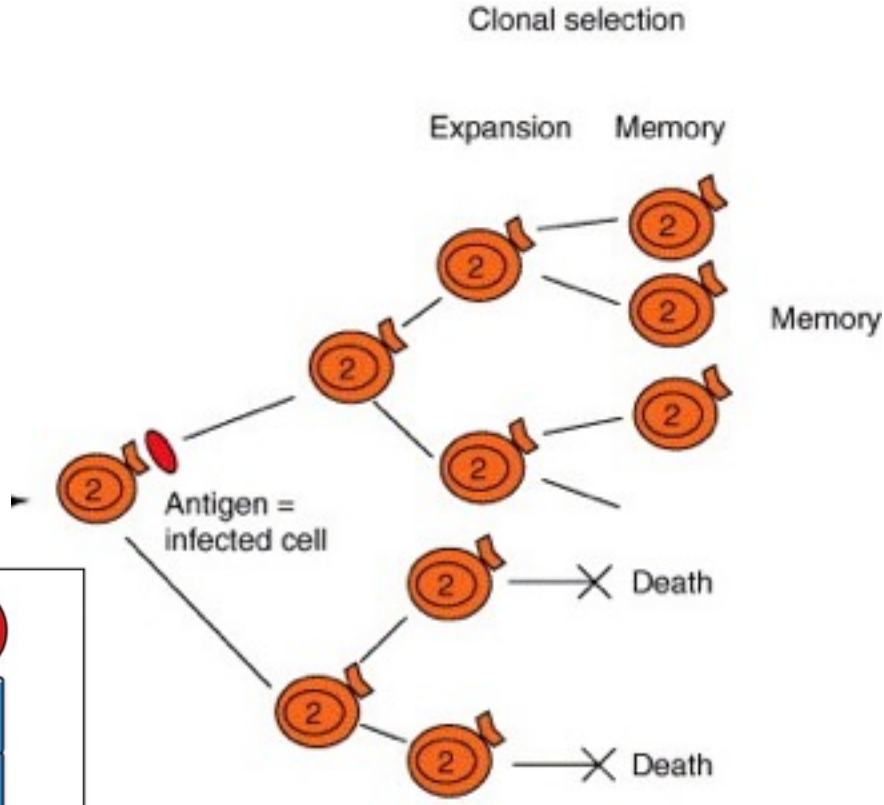
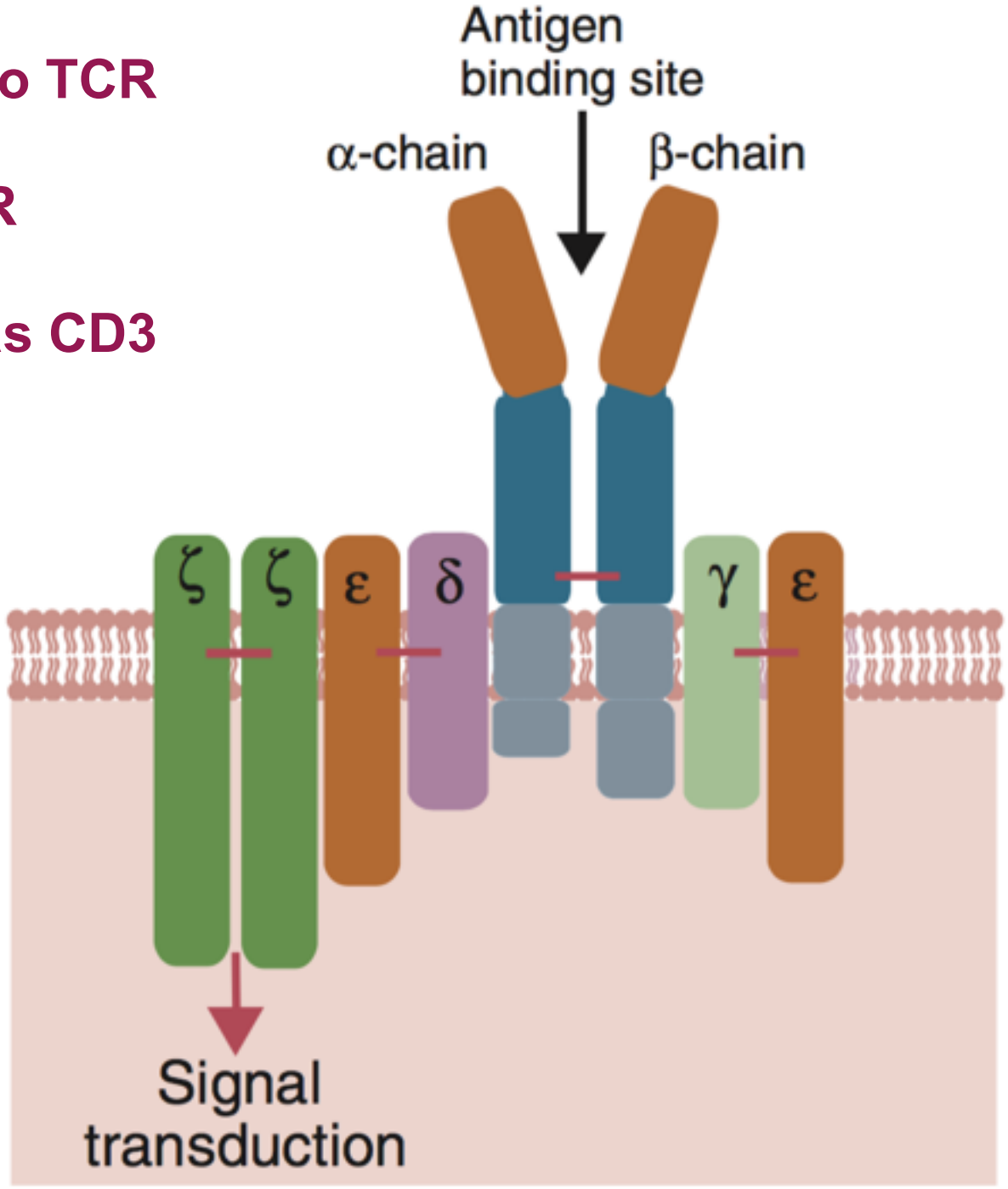



Figure 4.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

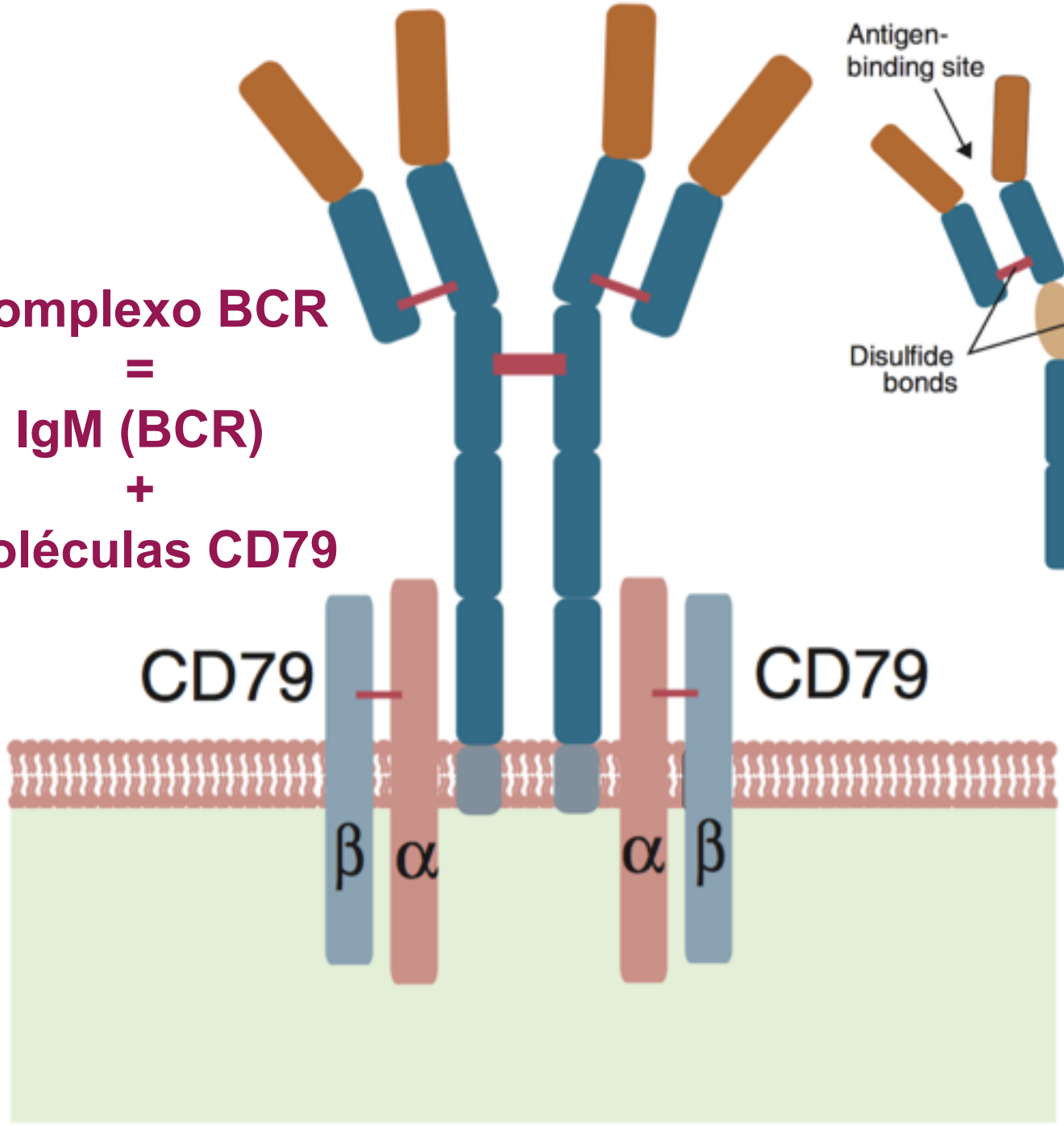


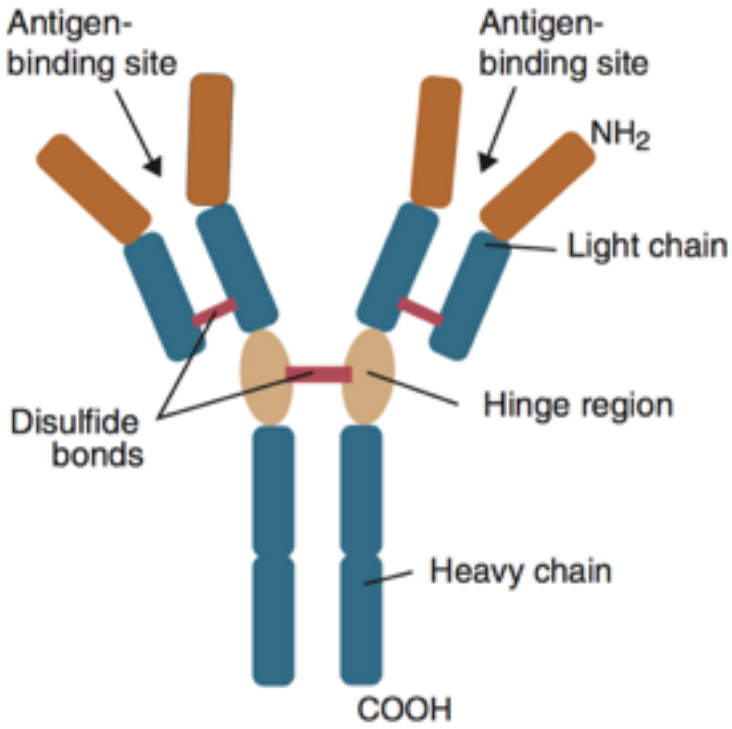

TRENDS in Ecology & Evolution

**Complexo TCR**
**=**
**TCR**
**+**
**moléculas CD3**



**Complexo BCR**
**=**
**IgM (BCR)**
**+**
**moléculas CD79**



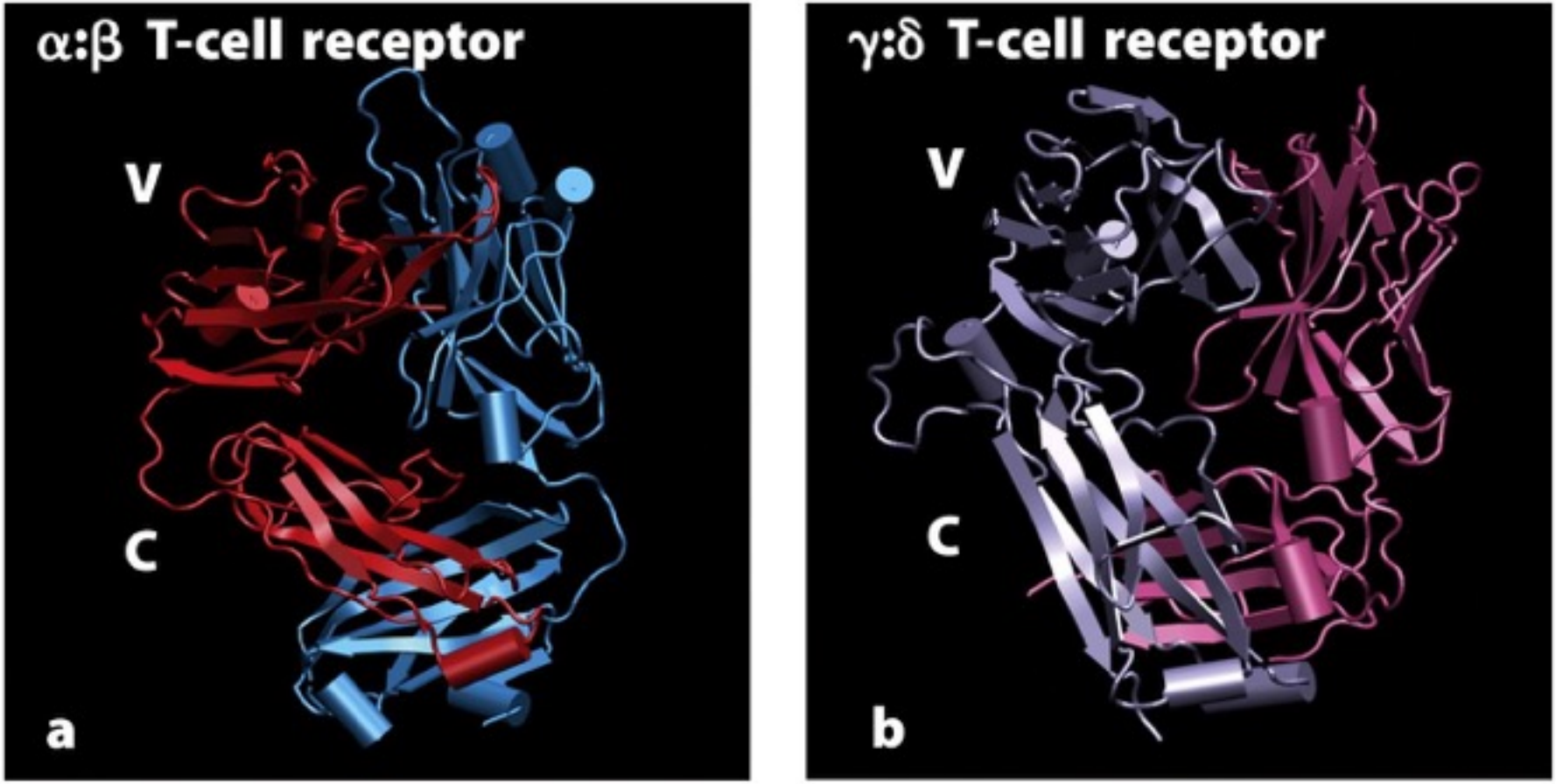
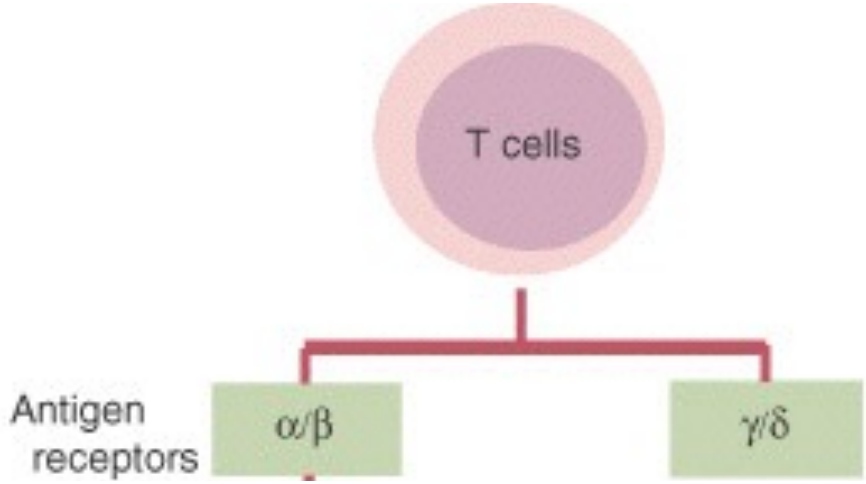



Figure 4.28 Janeway's Immunobiology, 8ed. (© Garland Science 2012)




conceito importante!

**$1{,}8 \times 10^{16}$ regiões variáveis diferentes para BCR (humanos)**

**$5 \times 10^{15}$ regiões variáveis diferentes para TCRalfa/beta (humanos)**

se 1 gene = 1 proteína,
não existe espaço no genoma mamífero para conter todos os genes necessários

Como resolver este problema?

| Receptor characteristic | Innate immunity | Adaptive immunity |
|---|---|---|
| Specificity inherited in the genome | Yes | No |
| Expressed by all cells of a particular type (e.g. macrophages) | Yes | No |
| Triggers immediate response | Yes | No |
| Recognizes broad classes of pathogens | Yes | No |
| Interacts with a range of molecular structures of a given type | Yes | No |
| Encoded in multiple gene segments | No | Yes |
| Requires gene rearrangement | No | Yes |
| Clonal distribution | No | Yes |
| Able to discriminate between even closely related molecular structures | No | Yes |

Figure 3.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

ww2.icb.usp.br/icb/cdh/

Apps NCBI Apple iCloud Facebook Twitter Wikipedia Yahoo! » Outros favoritos

HOME Graduação Pós-Graduação Pesquisa Extensão Concursos Departamentos Acesso Rápido Telefones O que procura OK

Universidade de São Paulo
INSTITUTO DE CIÊNCIAS BIOMÉDICAS
Excelência em Ensino e Pesquisa

## COMISSÃO DE DIREITOS HUMANOS

CDH ICB-USP

A CDH foi criada para acolher, articular e difundir discussões em prol da diversidade e pluralidade. É objetivo da CDH incentivar ações no ICB-USP calcadas no respeito à diversidade, seja ela de gênero, cor e/ou orientação sexual, bem como combater qualquer forma de discriminação e assédio.

Criada pela Diretoria em 23 de janeiro de 2018, por meio da portaria interna "002/2018", a CDH-ICB busca responder a uma demanda da comunidade do ICB-USP para o estabelecimento de um canal de acolhimento e discussão contra assédio de qualquer natureza e em prol do diálogo sobre temas que impactam diretamente nas políticas de diversidade e direitos humanos no ambiente do ICB-USP.

Para tanto, a CDH busca atuar de forma transversal e em rede com outras Comissões estatutárias e de apoio, ouvidoria, estruturas departamentais, entidades e associações estudantis, órgãos da USP e parceiros externos.

A voz de todos é bem-vinda!

Somos um grupo designado pela Diretoria e por nossos pares, com representantes de graduandos, pós-graduandos, docentes e funcionários do ICB-USP para atuarmos em prol da valorização da diversidade, pluralidade e dos Direitos Humanos no ICB-USP, e como via de mão dupla, na sociedade de forma geral.

Trabalhamos para acolher e orientar pessoas que se sentiram lesadas e desrespeitadas em seus direitos, combater qualquer forma de discriminação e assédio, bem como atuar de forma educativa, valorizando o respeito e a igualdade.

- Tipos de violência
- Assédio sexual
- Direitos humanos
- Vídeos

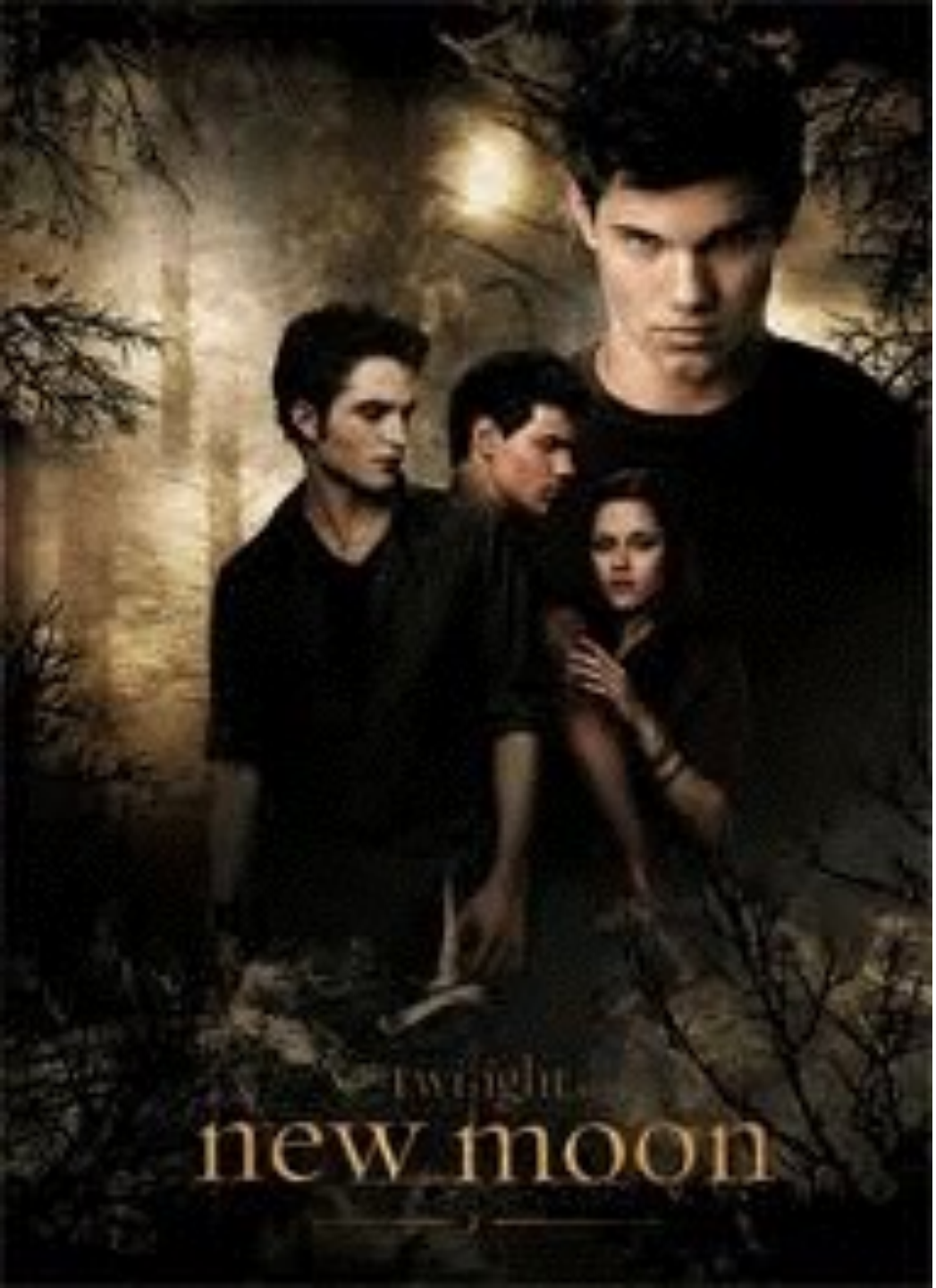
**Questionário on-line**

Você está satisfeito com a convivência aqui no ICB?
Clique aqui e responda nosso questionário sobre as interações das pessoas que estudam e trabalham com você, são só 5 minutos!
Você não precisa se identificar, o questionário é anônimo.
Responda até o dia 30/05

**Acesse**

- Membros da comissão de direitos humanos
- Cartilha: Assédio moral e sexual, Previna-se
- Cartilha: Violência de gênero na Universidade
- USP Mulheres
- Rede não cala! USP
- Rede de defesa de direitos das meninas e das mulheres do Estado de São Paulo
- Assédio sexual vindo de colegas de trabalho é mais traumático
- Mulheres

← Voltar




O Grande mistério da saga Twilight…

Bella preferirá o vampiro Edward, cujos bolores nunca viram a luz do sol, ou o lobisomem Jacob, cuja pelagem densa está sempre úmida?

Qual dos dois cheira melhor?
Qual dos dois combina melhor com seu MHC?
E como ela descobrirá?