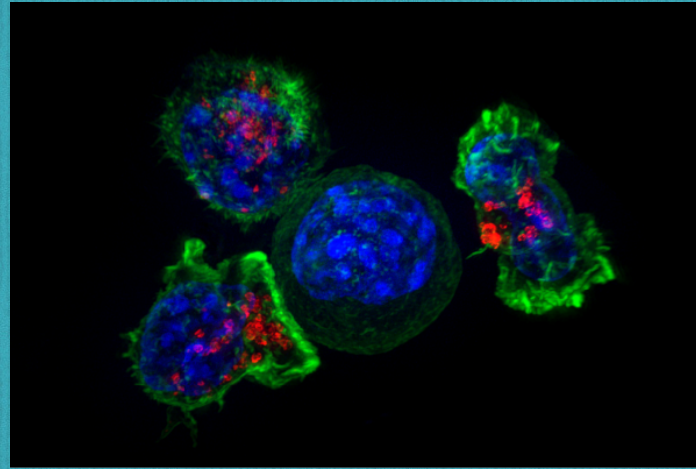
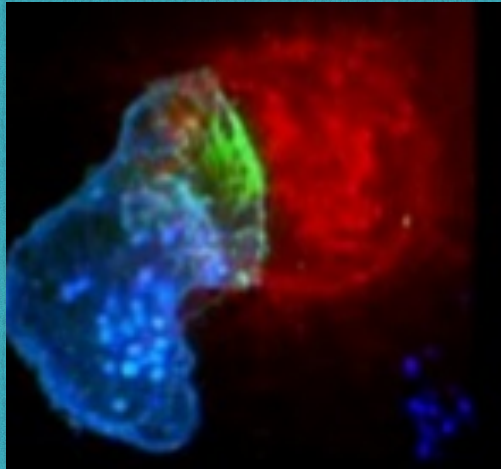


Curso de Ciencias Biologicas
Disciplina BMI-296 – Imunologia basica



Aula 9 – Geração e ativação dos linfócitos B

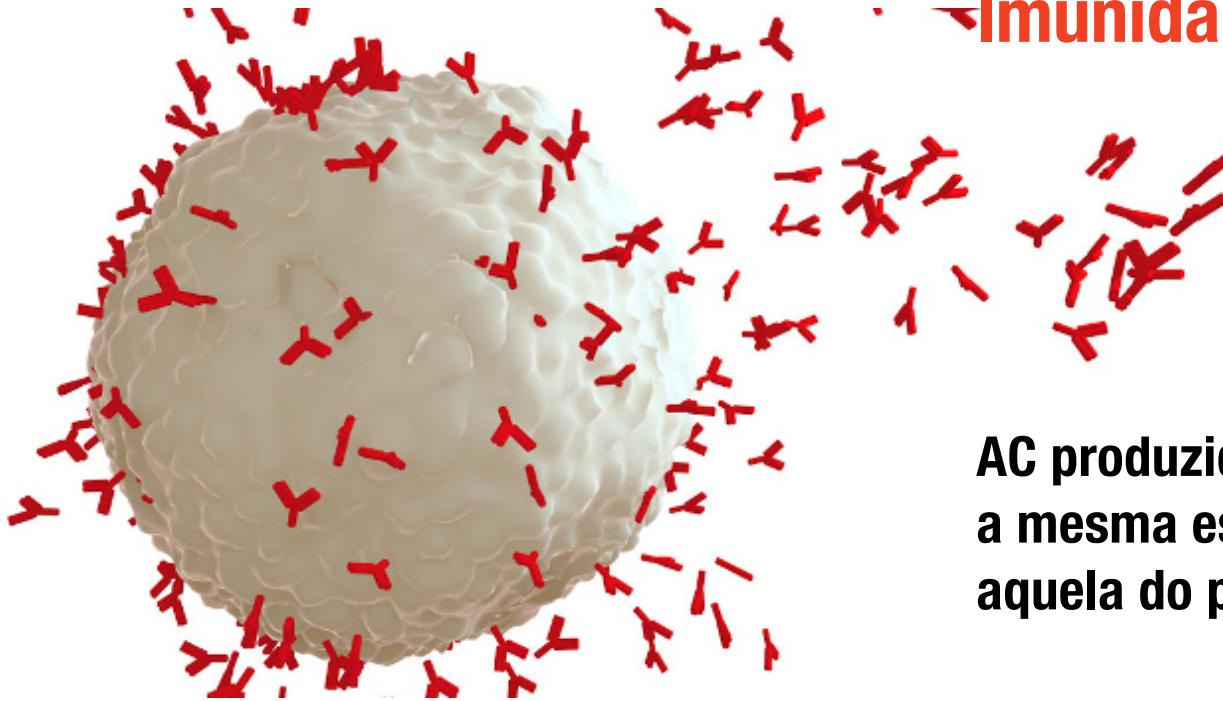
Alessandra Pontillo

Lab. Imunogenetica/Dep.Imunologia/ICB/USP

Linfocitos B

Producao de anticorpos

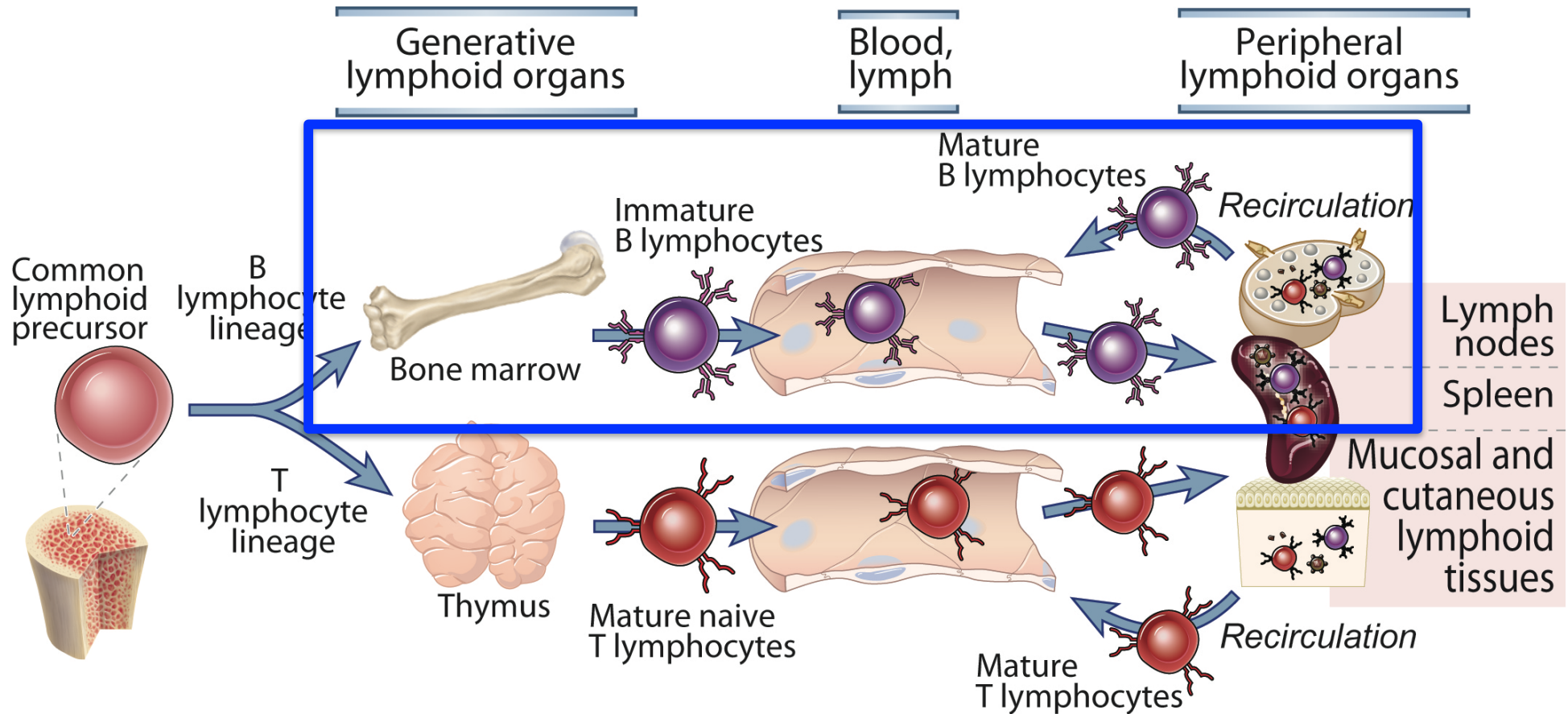
Imunidade adquirida humoral



AC produzidos por um L.B tem todos a mesma especificidade (V) que é idêntica aquela do próprio BCR

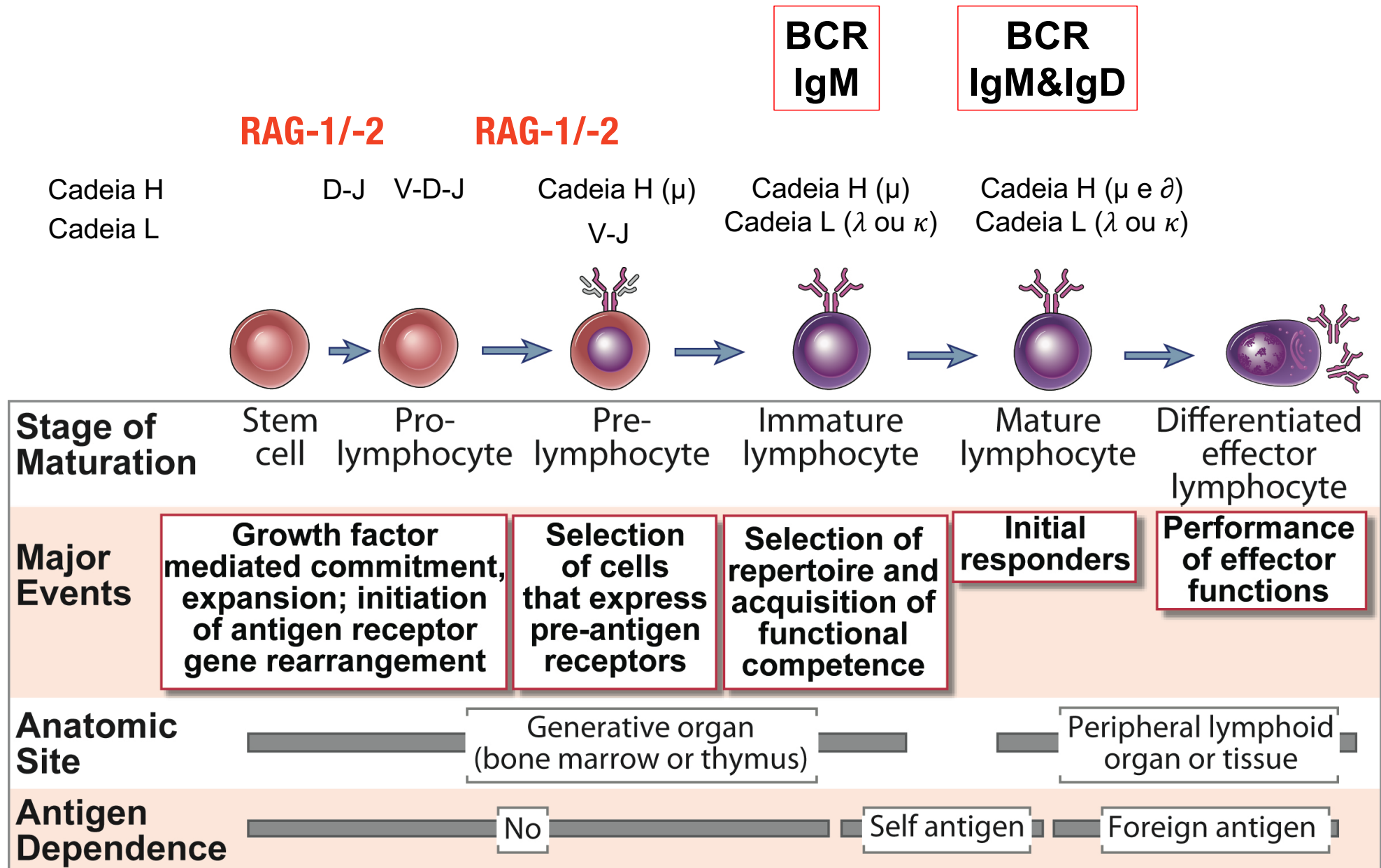
Reconhecem Ag e medeiam varias funções efetoras

Desenvolvimento Linfocitos B



Formação do receptor
→elevada especificidade de cada clone
→tolerância a "self"

Desenvolvimento Linfocitos B



Desenvolvimento Linfocitos B

Construção do BCR

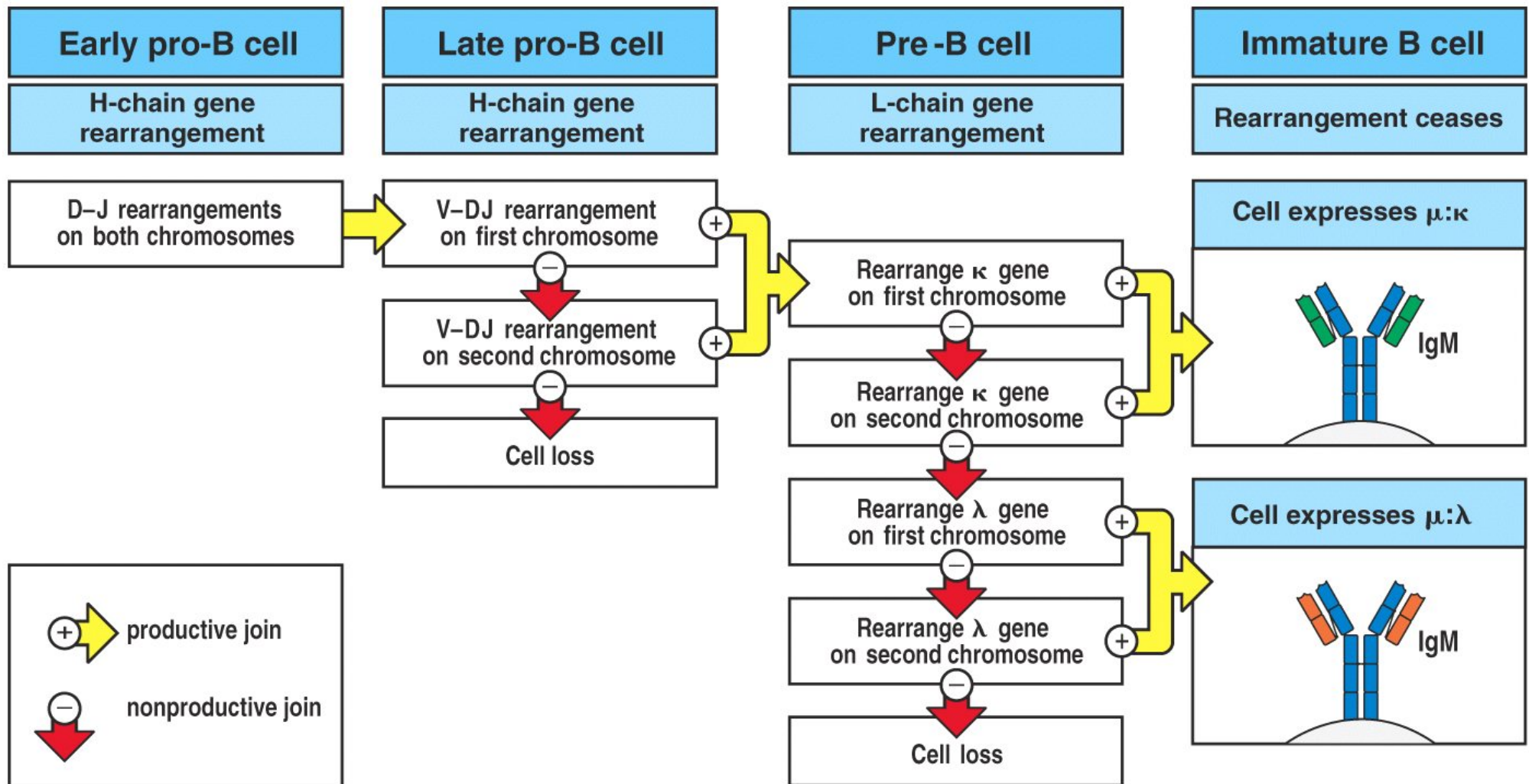
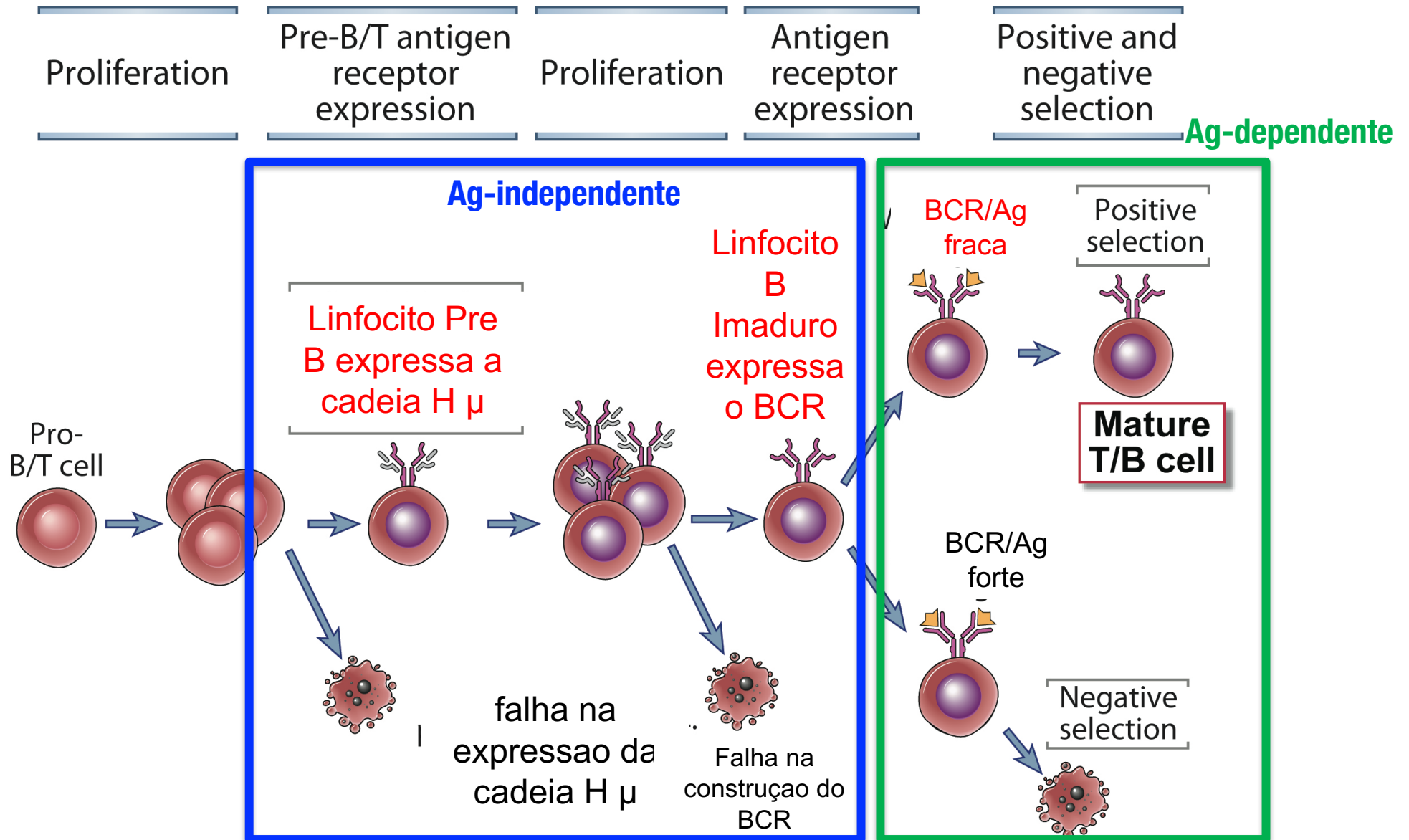


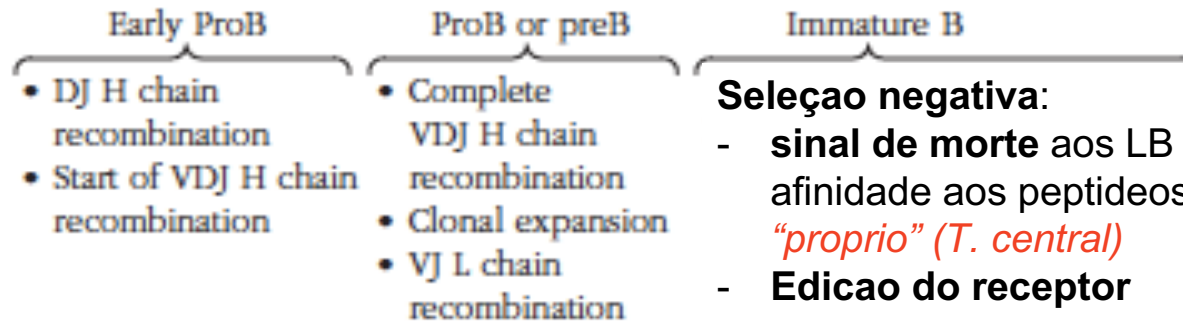
Figure 7-15 Immunobiology, 6/e. (© Garland Science 2005)

Desenvolvimento Linfocitos B

Seleção do BCR

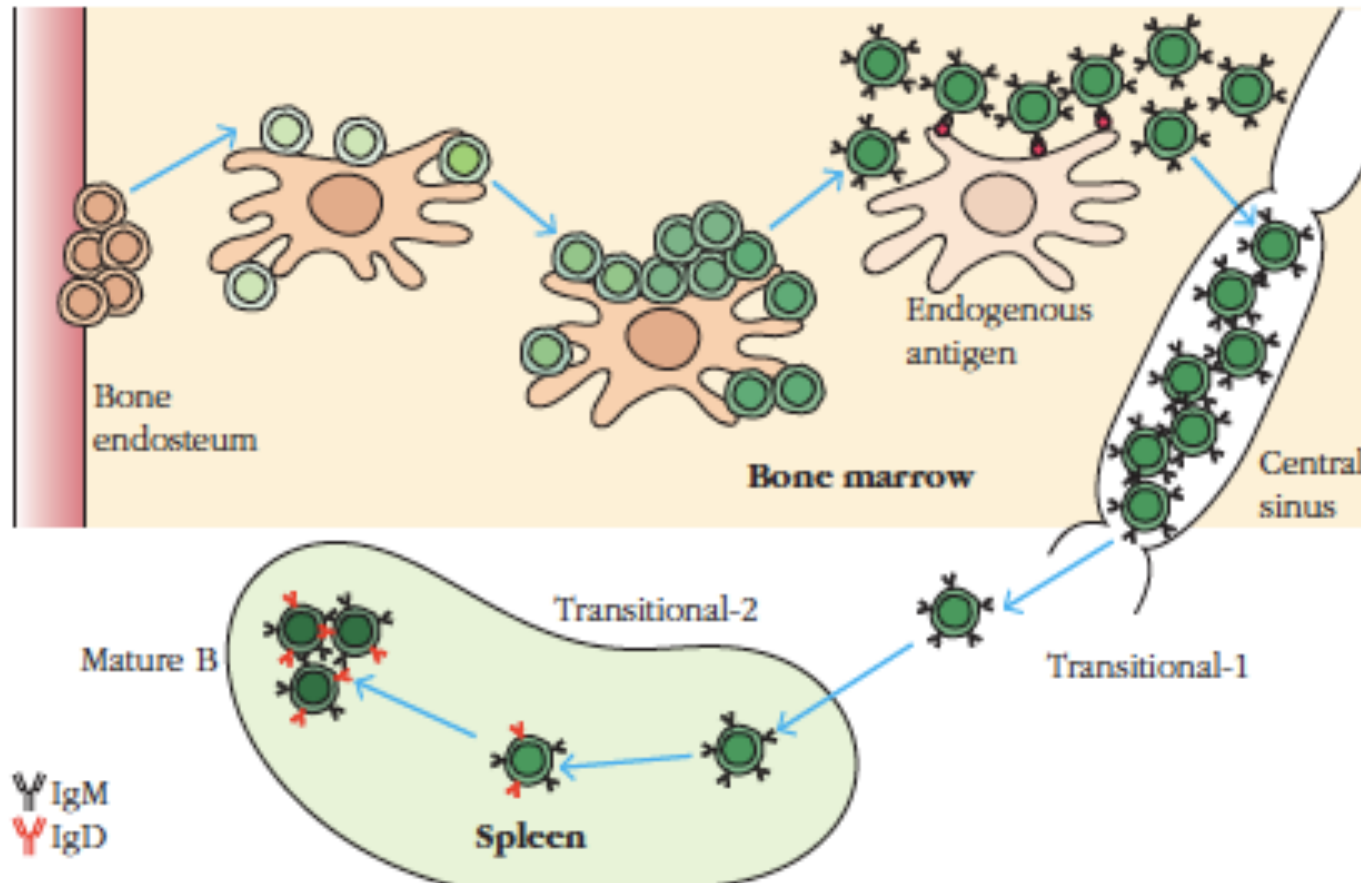


Desenvolvimento Linfocitos B

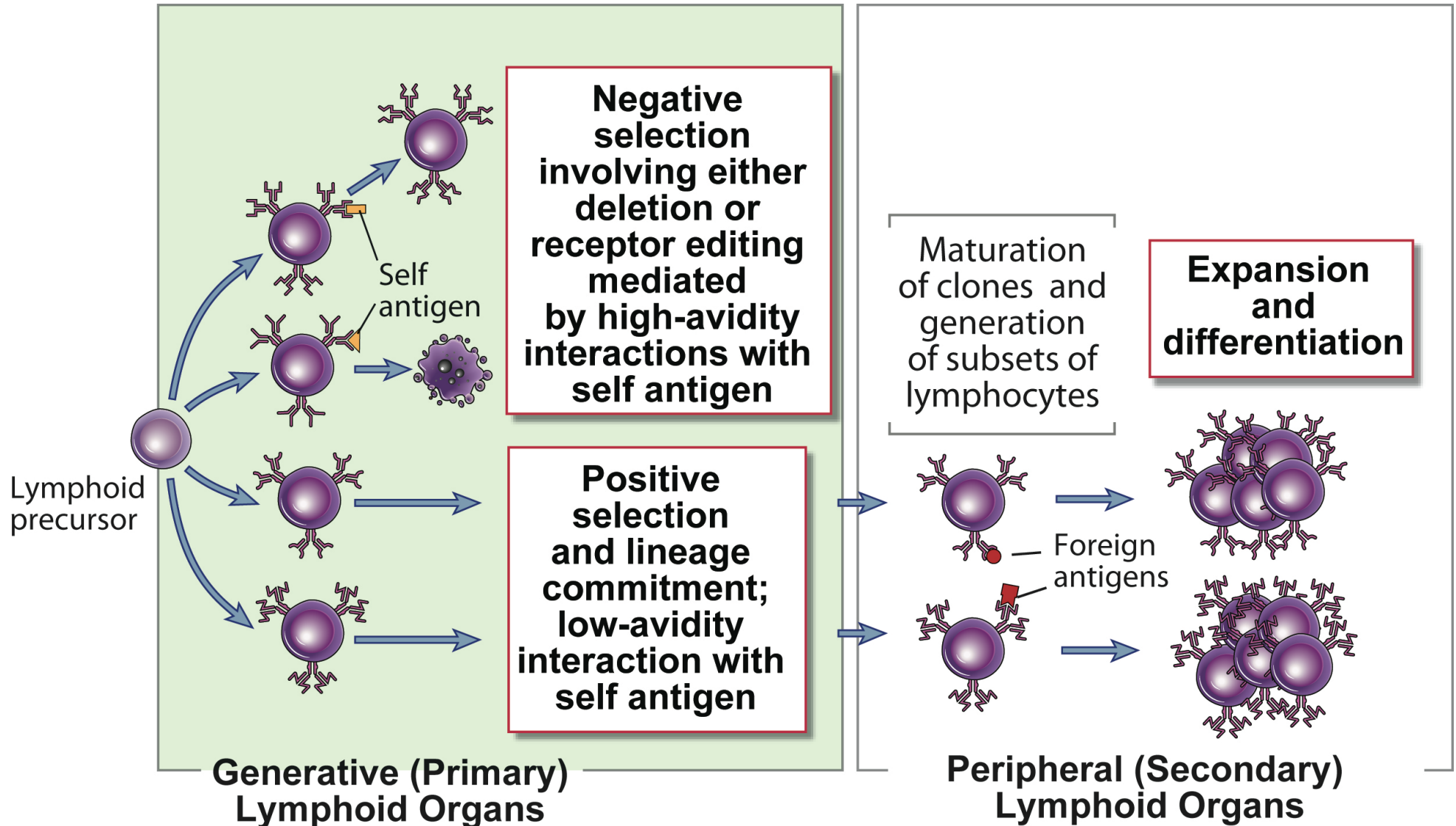


Seleção negativa:

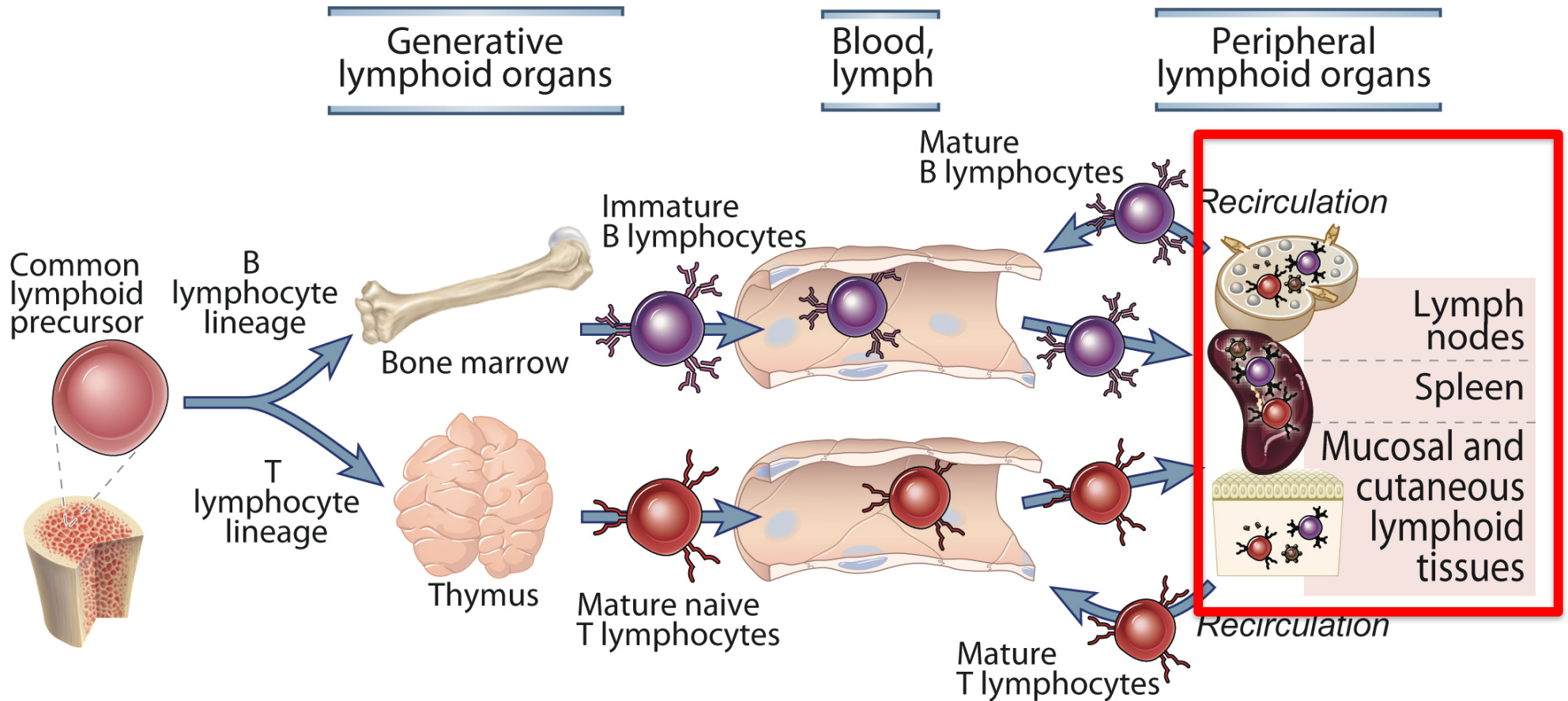
- **sinál de morte** aos LB com BCR com elevada afinidade aos peptideos proprios → *tolerância ao "proprio" (T. central)*
- **Edicao do receptor**



Ativação dos Linfócitos B



Ativação Linfocitos B

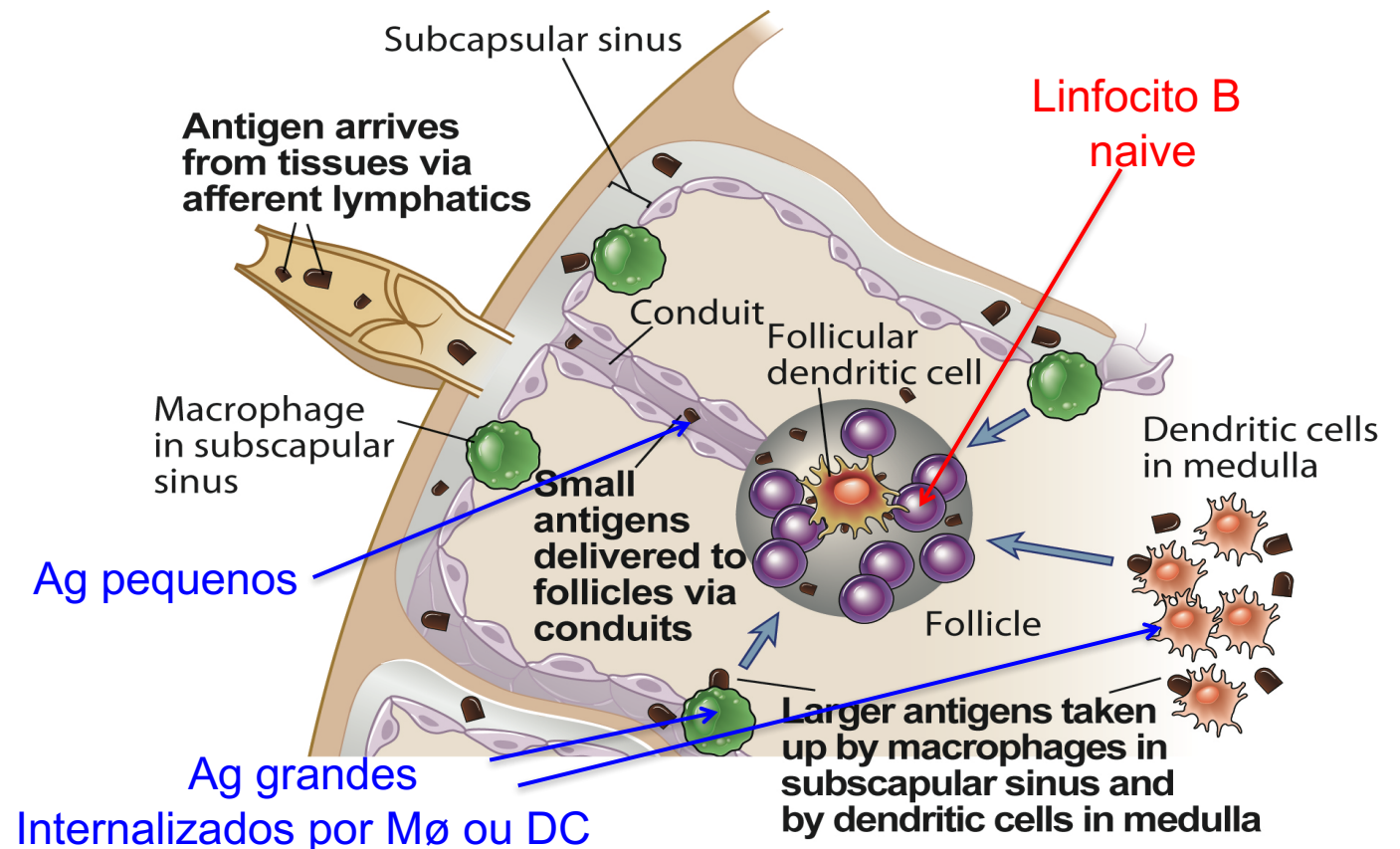


Recirculação dos linfocitos "naive"
Encontro com Ag
→ Ativação do linfocito
→ Resposta ao Ag
→ Geração de memória

Ativação Linfocitos B

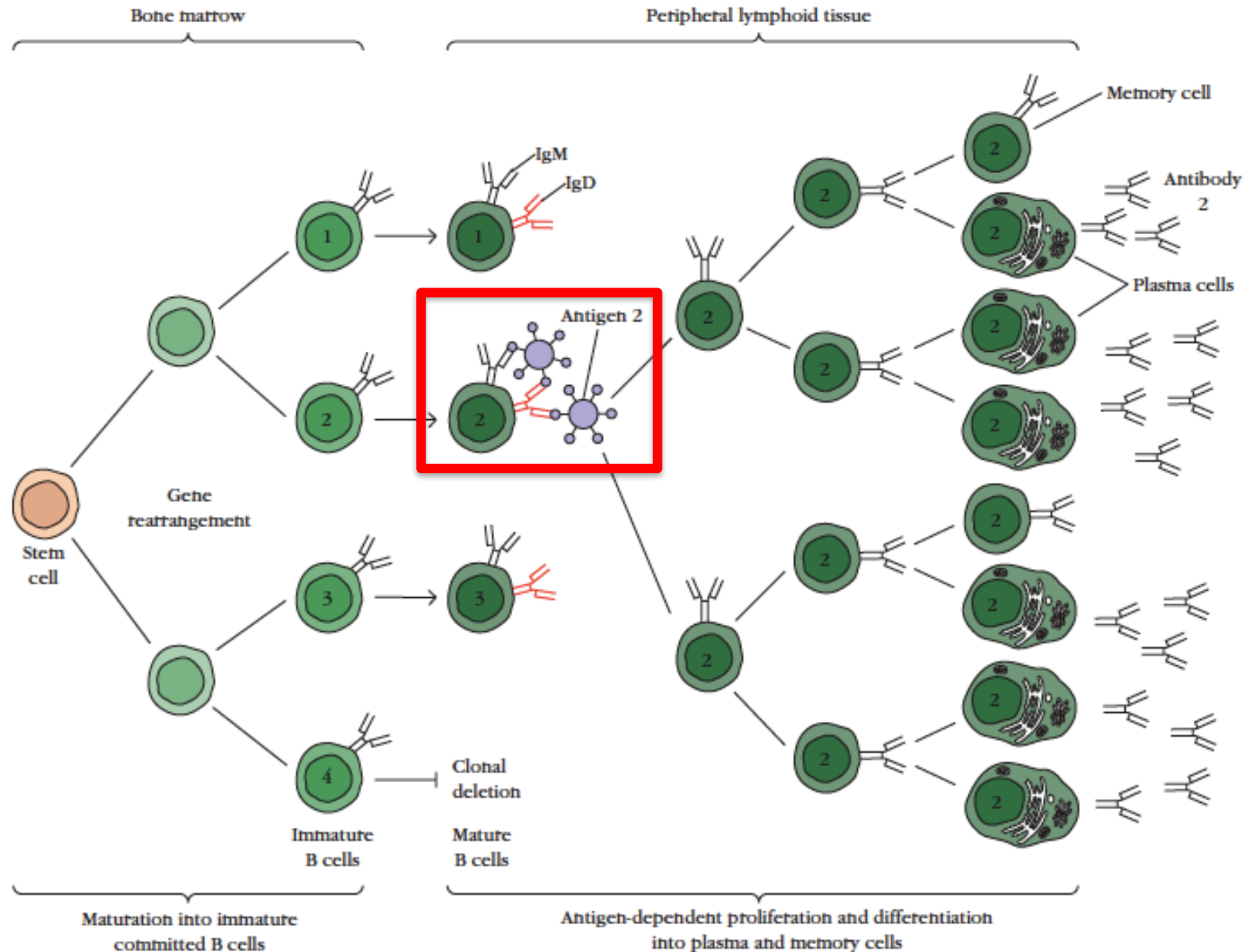
RECONHECIMENTO DO Ag

- * Ag solúveis <70kDa chegam a zona de B pelos condutos e interagem diretamente com os B
- * MØ subcapsular e DC medular capturam Ag maiores ou microrganismos inteiros e podem ativar os B
- * Complexos Ag/Ac+complemento liga Rec (CR2)



Ativação Linfocitos B

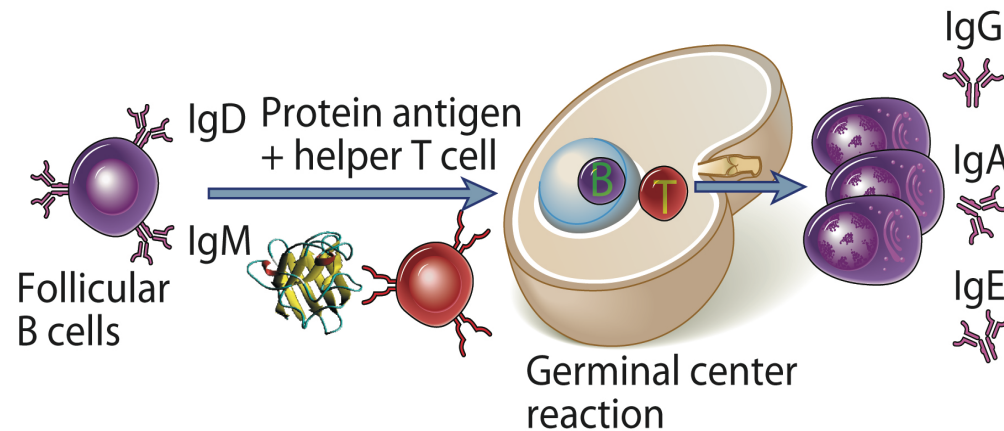
EXPANSÃO CLONAL



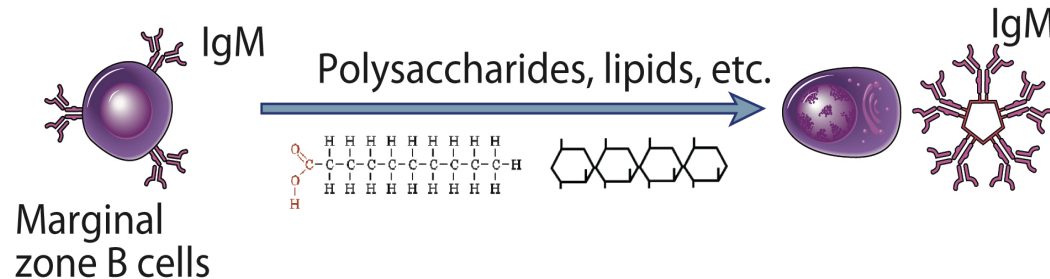
Ativação Linfocitos B

Diferentes tipos de sinal do Ag

**Baço e
outros OL**

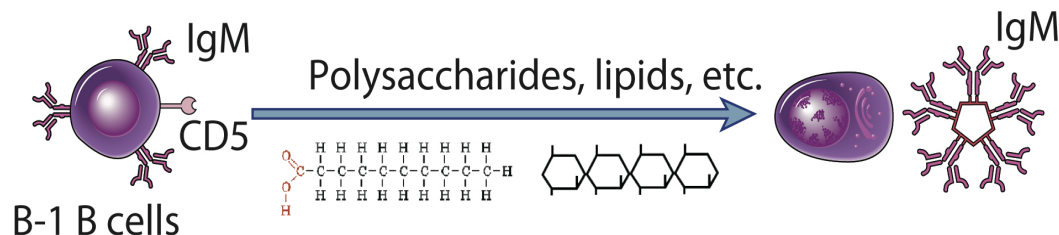


T-dependente:
plasmacell de vida
longa, isotipo
switchado, Ac de
elevada afinidade



T-independente:
plasmacell de vida
curta, **IgM**

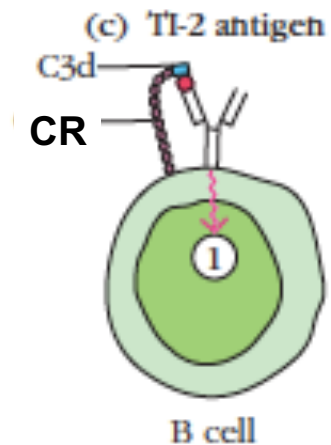
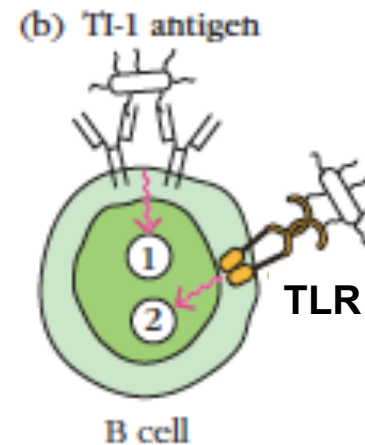
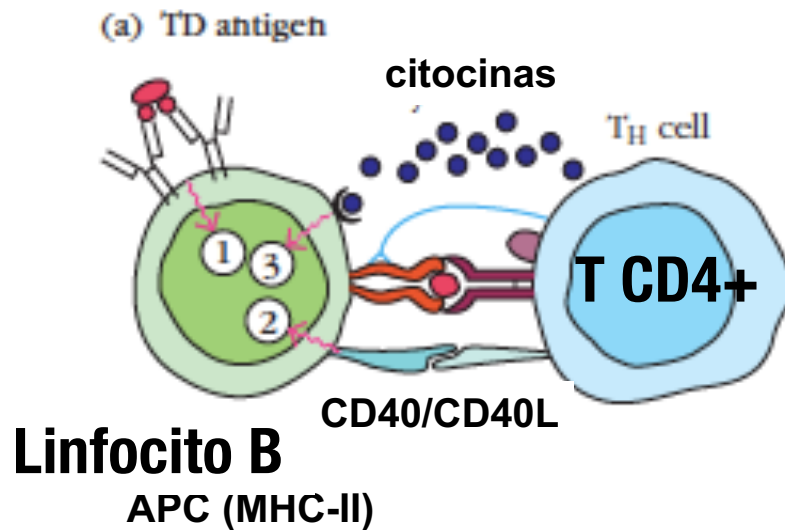
**Mucosas,
cavidade
peritoneal**



T-independente:
plasmacell de vida
curta, **IgM**

Ativação Linfocitos B

Diferentes tipos de sinal do Ag



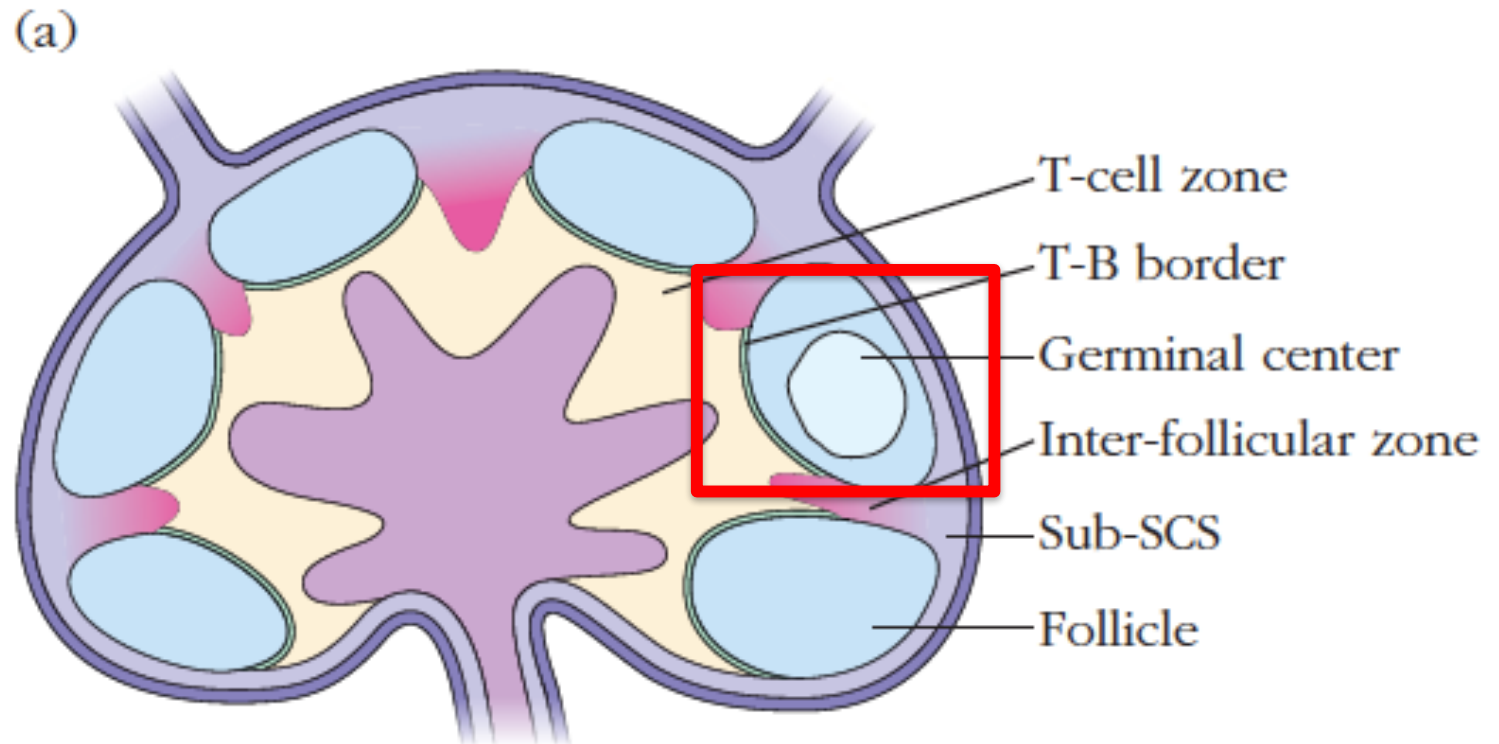
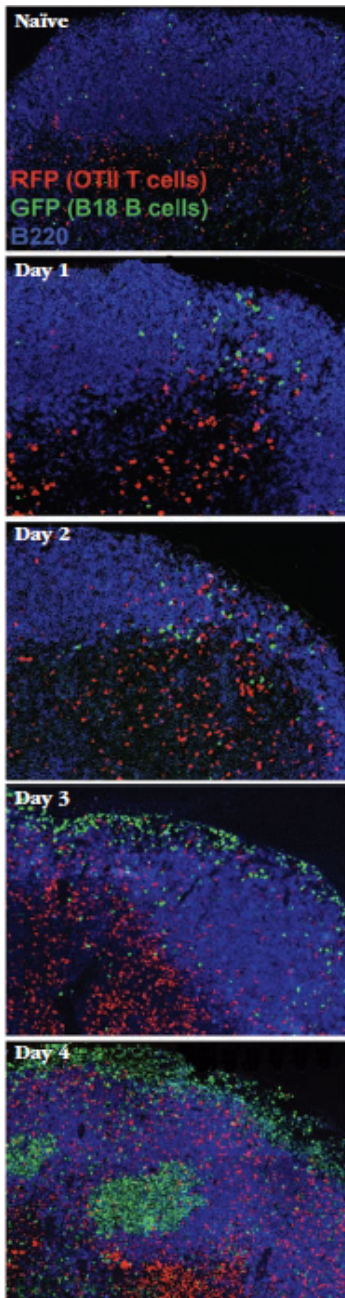
T-independente (TLRs, CRs):
plasmacell de vida curta, IgM

T-dependente:

- ✓ CD4+ativado e diferenciado ajuda a ativação do LB
- ✓ estimulam troca de isotipo, maturação de afinidade e geração de plasmacel de vida longa e cel de memória → mais “sofisticada” resposta humoral
- ✓ Ag proteicos! (Ag/MHC-II)

Ativação Linfocitos B

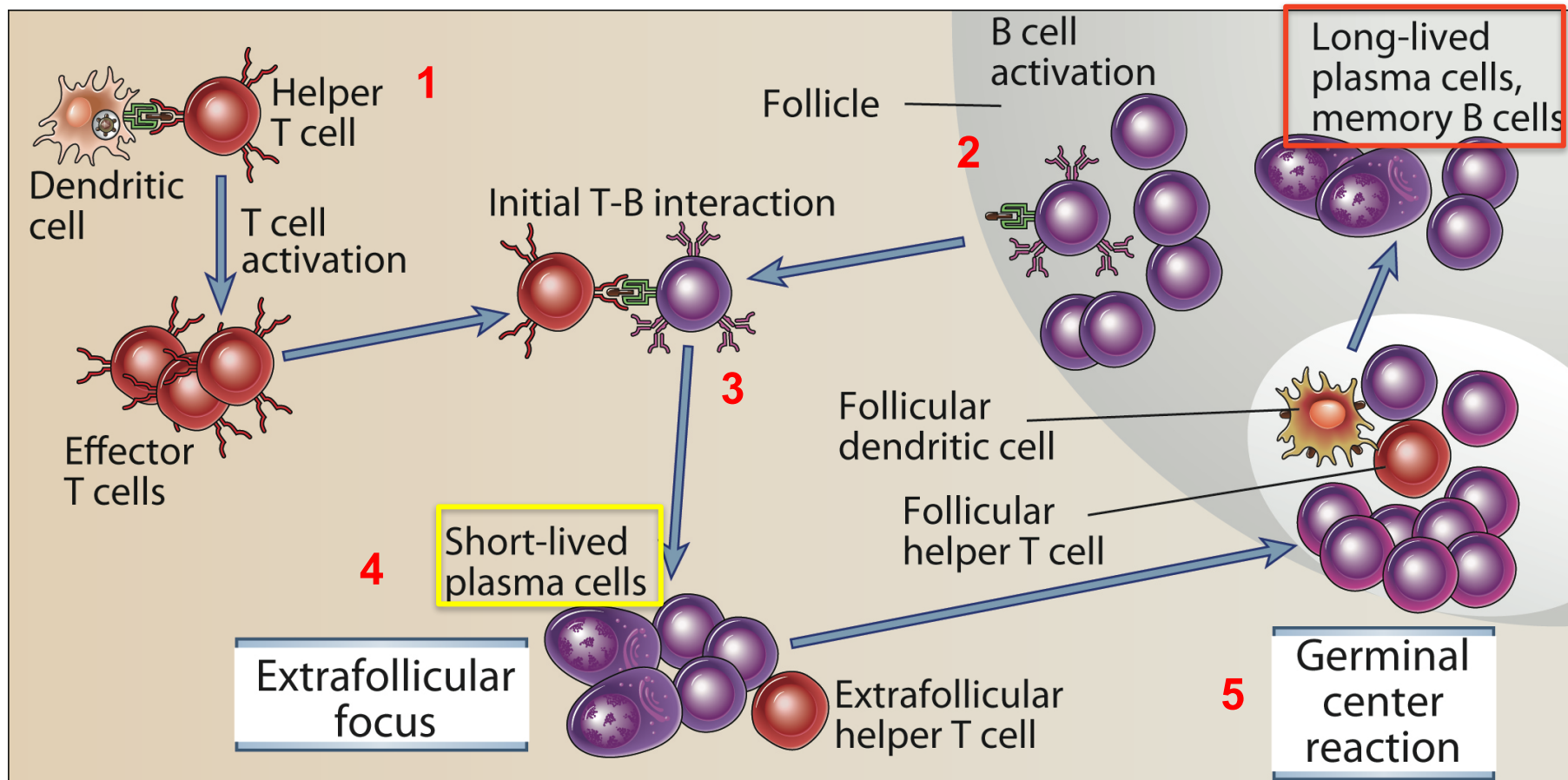
Ativação T-dependente...tem lugar



Ativação Linfocitos B

ATIVAÇÃO EXTRA-FOLICULO (3-4 dd)

CENTRO GERMINAL (6-10 dd)



Mudança de isotipo;
Hipermutação somática limitada;
Afinidade de AC baixa;
Plasmocitos de vida curta (3d)

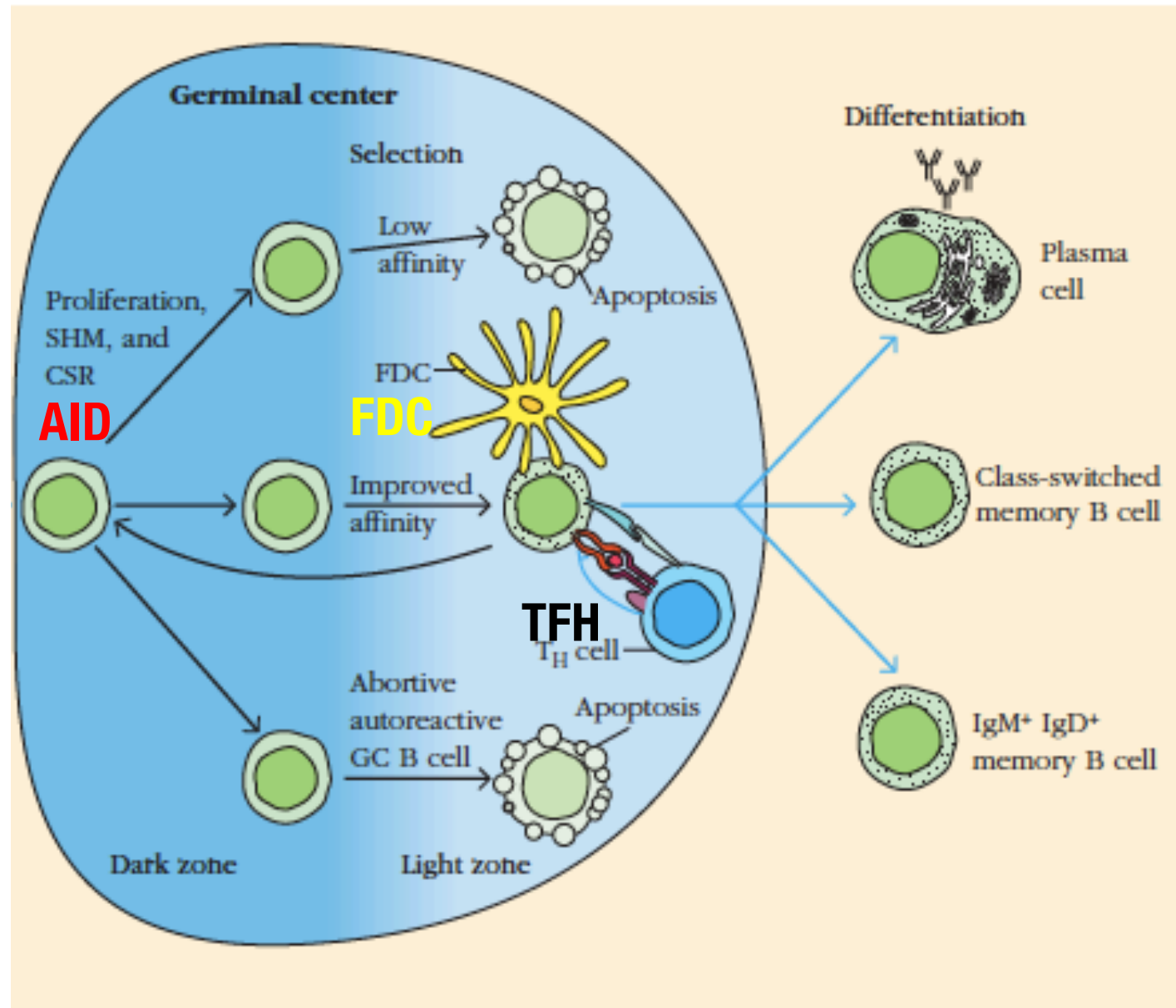
Mudança de isotipo;
Hipermutação somática elevada;
Maturação da afinidade → AC com alta afinidade
Plasmocitos de vida longa & Cel B memória

Ativação Linfocitos B

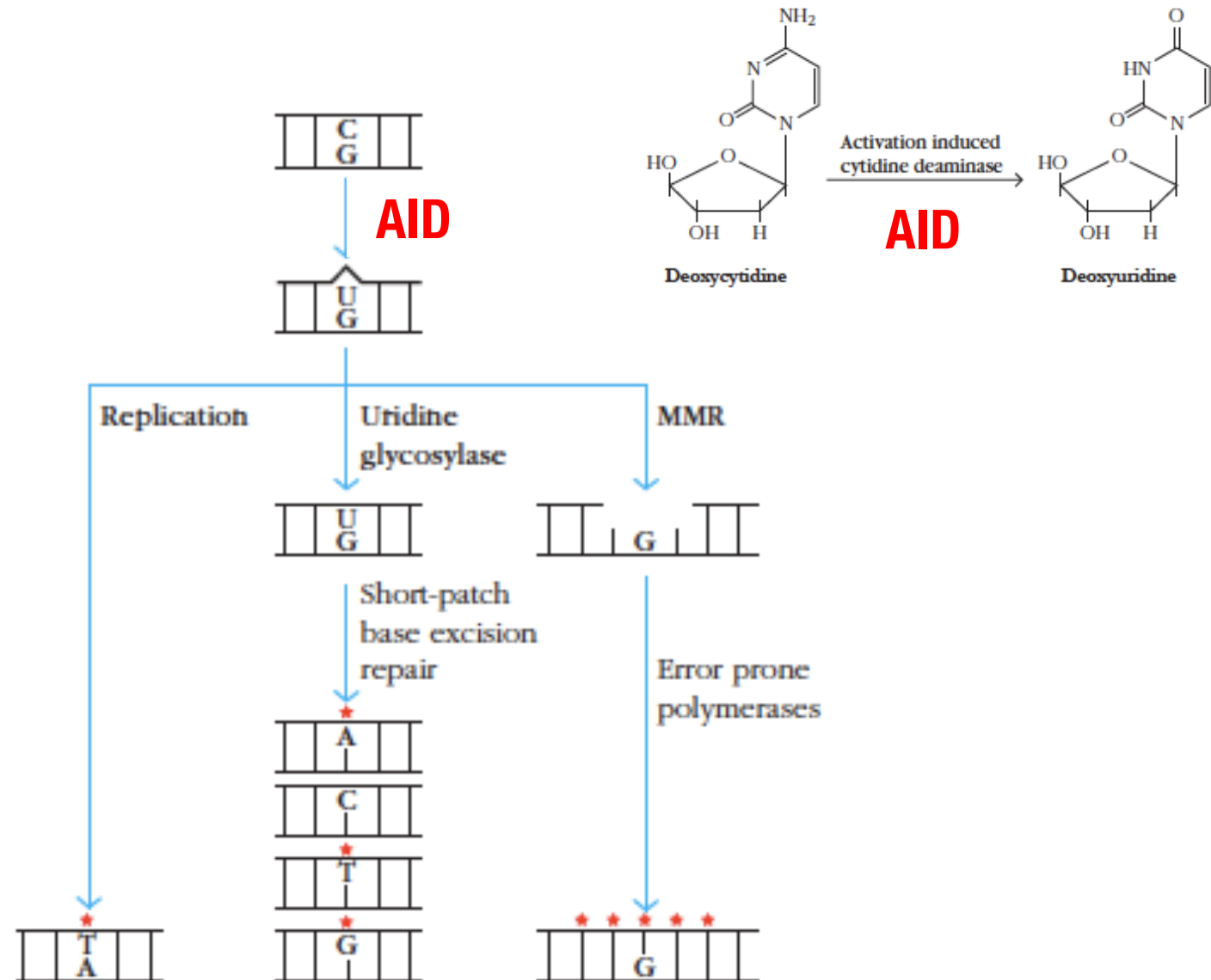
CENTRO GERMINAL

L.B.

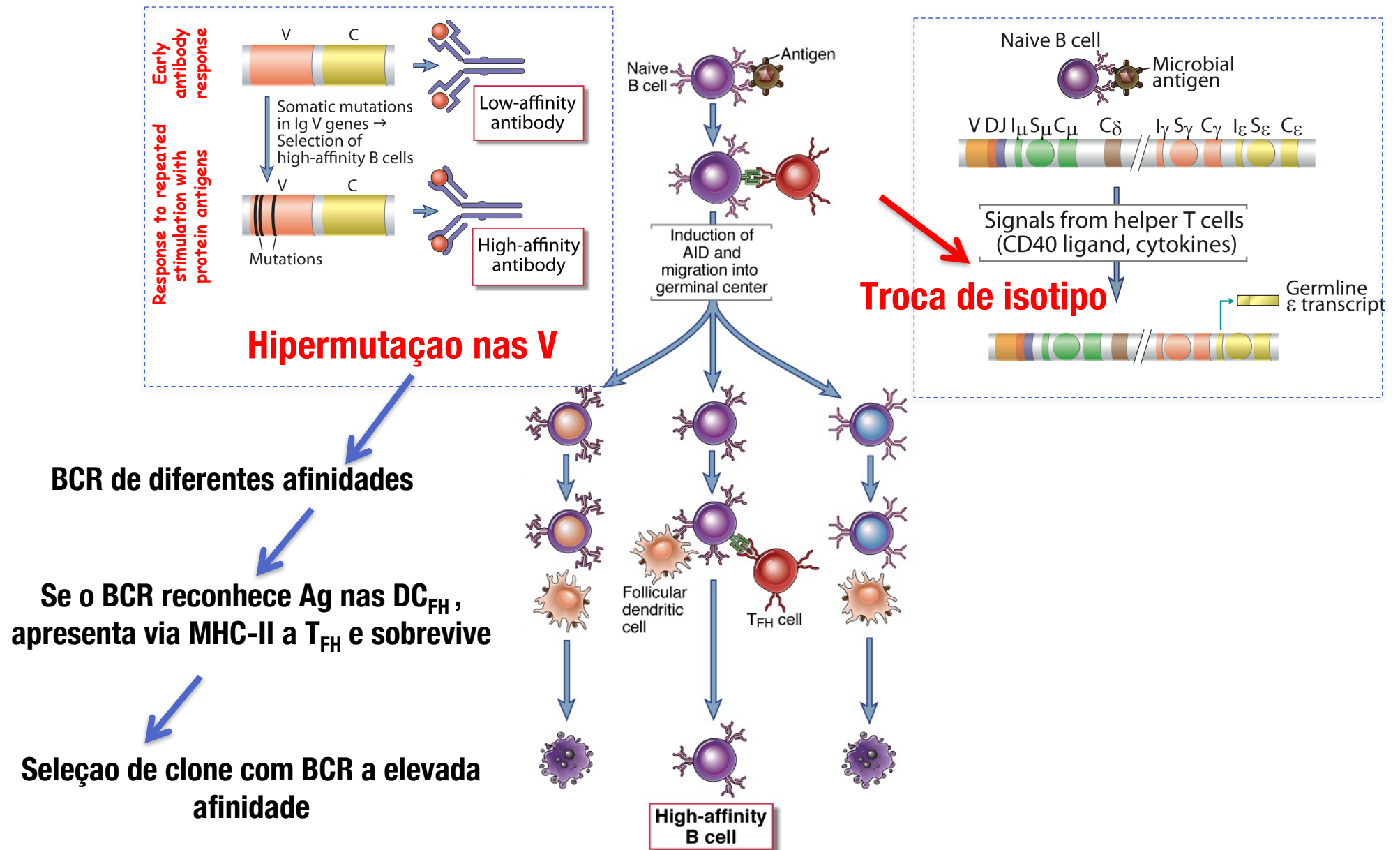
- ✓ Proliferação
- ✓ Hipermutação somática (→ BCR testado pelas FDC)
- ✓ Switch isotípico (→ classe depende do tipo de patógeno)



Ativação AID e hipermutação

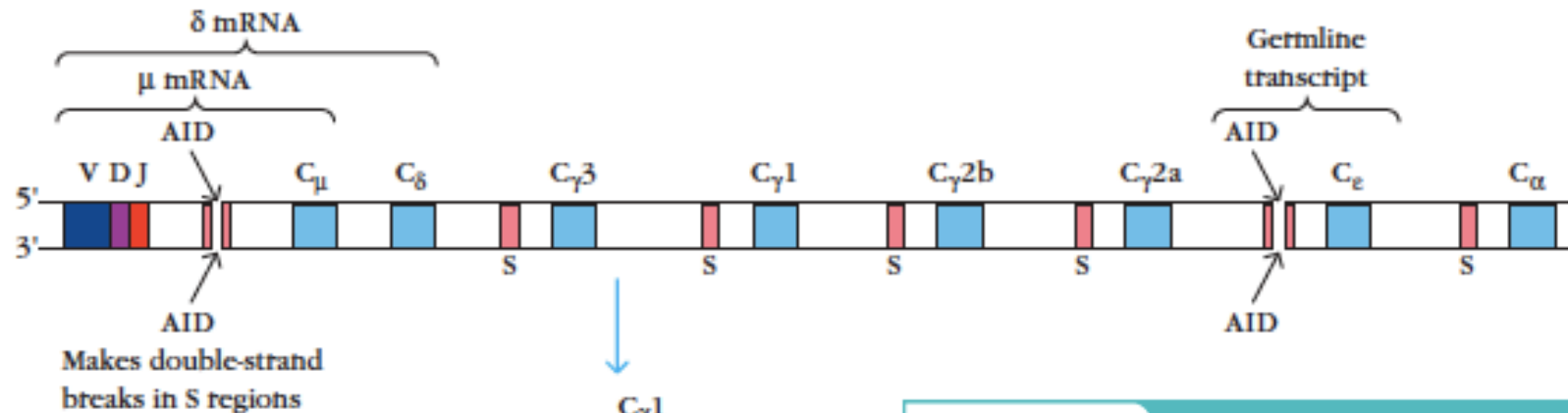


Hipermutação & Switch isotipico

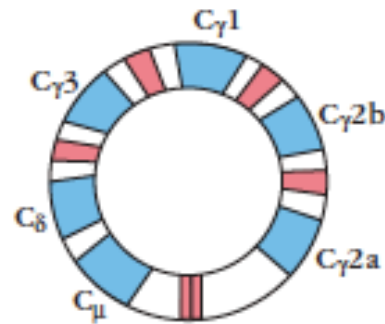


Switch isotipico

Heavy chain genes in IgM-expressing cells



Class switch recombination (requires DSBs)



Heavy chain genes in IgE-expressing cell

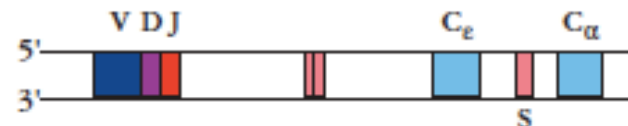


TABLE 12-1

Specific cytokines signal B cells to undergo CSR to different heavy-chain classes

Cytokine signal	Isotype synthesized by target B cell
IL-4	IgG1, IgE
TGF-β	IgA, IgG2b
IL-5	IgA
IFN-γ	IgG3, IgG2a

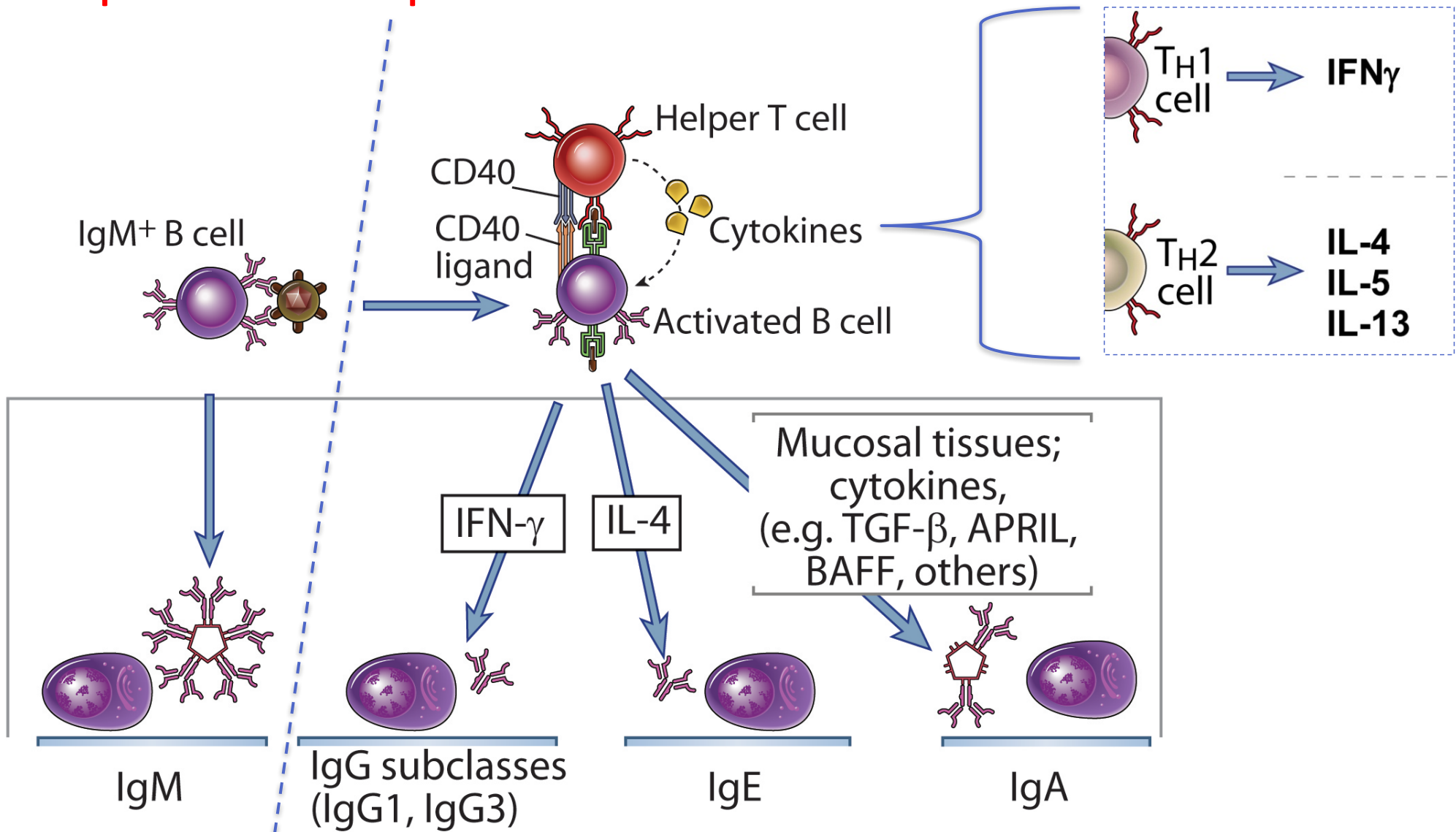
Ativação Linfocitos B TD e TI

TABLE 12-4 Functional differences among mature B-cell subsets

Attribute	Conventional B2 B cells	B-1 B cells	Marginal zone B cells
Major sites	Secondary lymphoid organs	Pleural and peritoneal cavity; also spleen	Marginal zones of spleen in mice; primates also have MZ cells in other locations
V region diversity	Highly diverse	More restricted diversity	Moderate diversity
Rapidity of antibody response	Slow; plasma cells appear 7–10 days post stimulation	Rapid; plasma cells appear as early as 3 days after stimulation	Rapid; plasma cells appear as early as 3 days after stimulation
Surface IgD?	High levels of IgD	Low levels of IgD	Low levels of IgD
Somatic hypermutation	Yes	No	Yes in primates; possibly in rodents
Requirements for help from other cell types	Provided by T cells	No, although T and other cells can enhance response	Dendritic cells and neutrophils can enhance response (see Box 12-2)
Participate in germinal center reaction?	Yes	No	Possibly, although with slower kinetics than follicular B cells
Isotypes produced	All isotypes	Predominantly IgM	Predominantly IgM
Immunological memory	Yes	Very little	Yes; source of IgM-producing memory cells

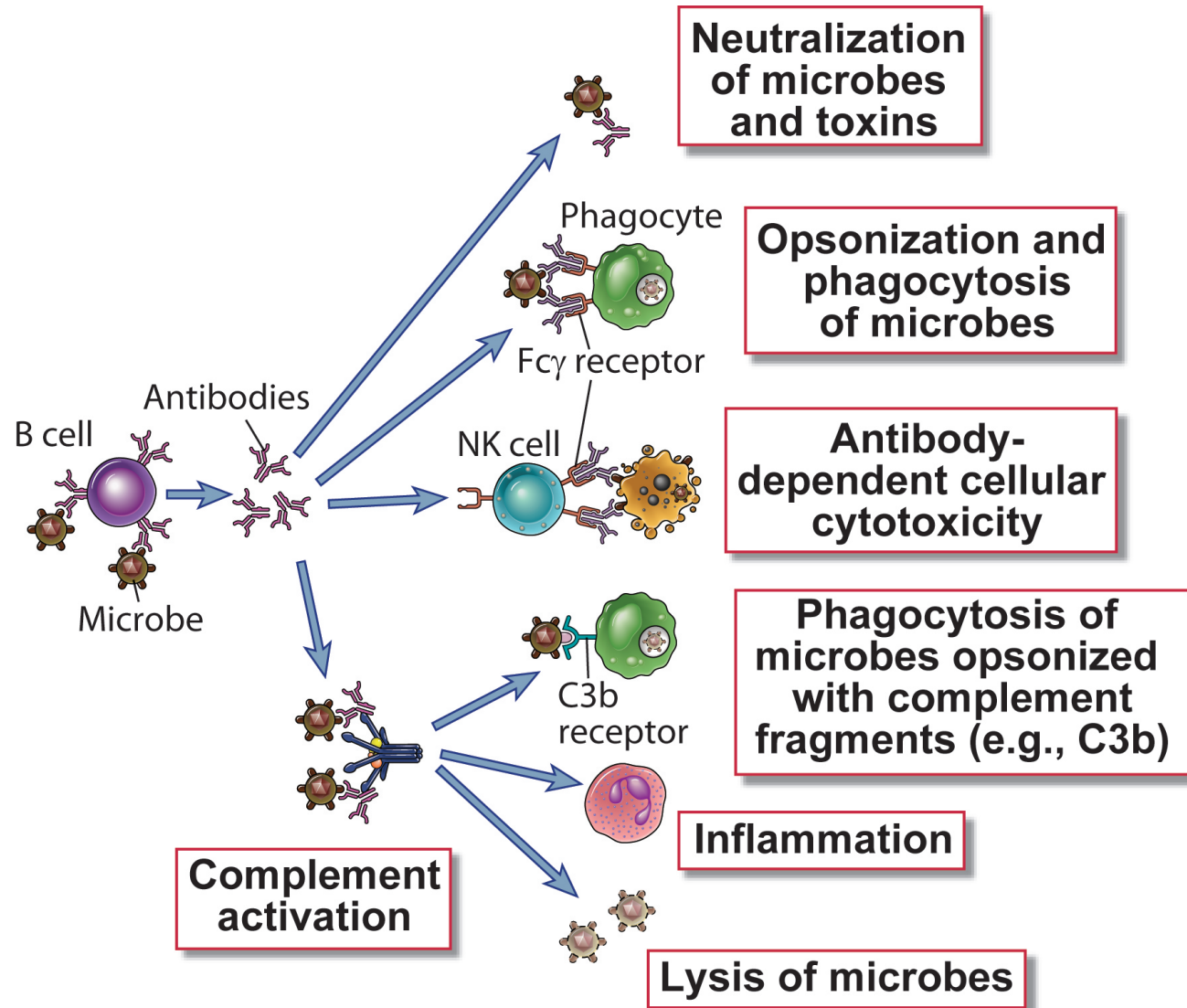
Ativação Linfócitos B e AC

Tipo de CD4+ e isotipos

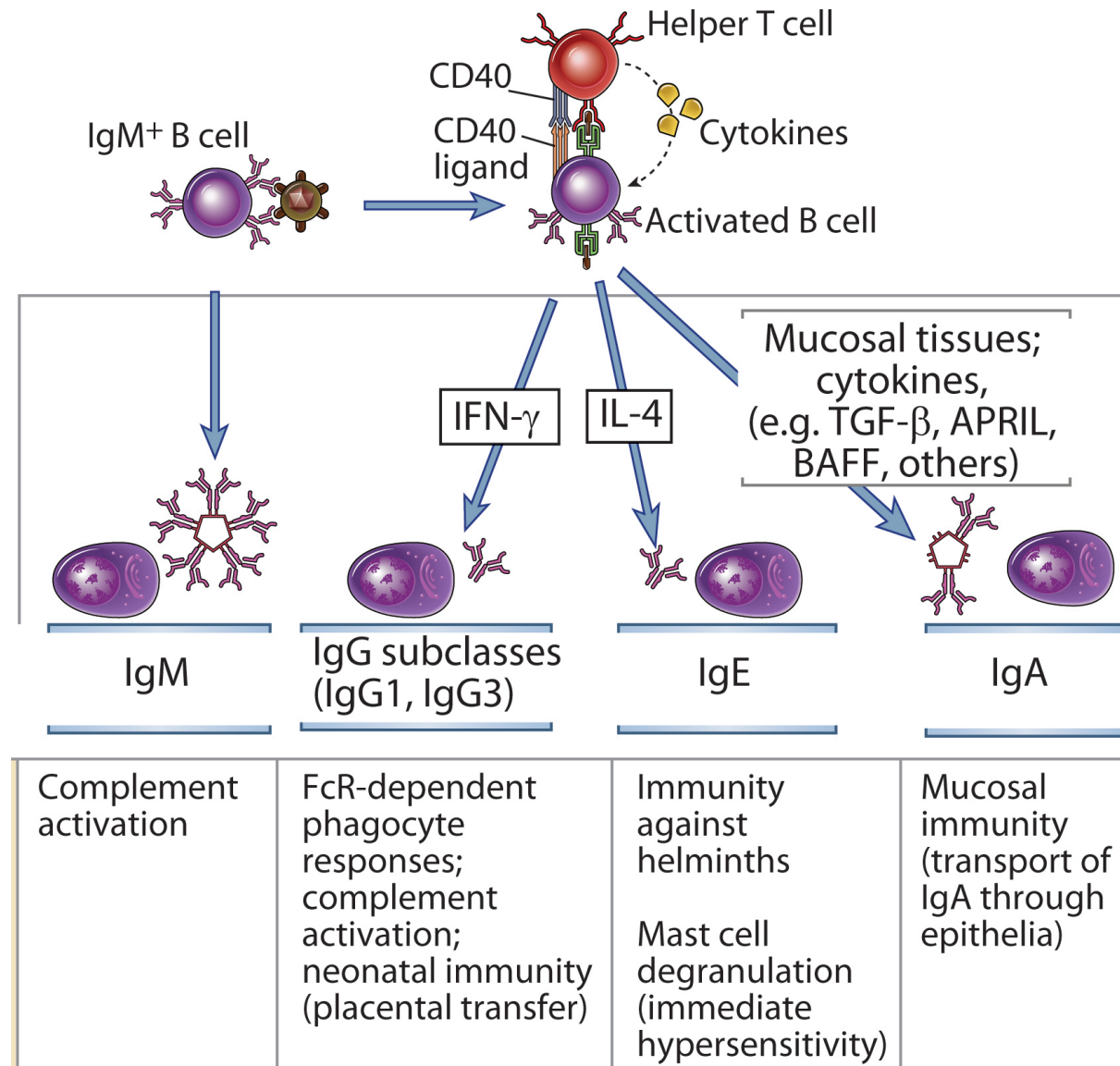


Funcao efetora dos Linfocitos B

= FUNCAO EFETORA DOS AC



Funcao efetora dos Linfocitos B



Ativação dos linfócito B

Activation of naive lymphocytes and initiation of adaptive immune responses

Secondary (peripheral) lymphoid organs

Lymph node

Spleen

Effector T lymphocytes and antibodies

Delivery via blood of effector cells and antibodies to site of infection

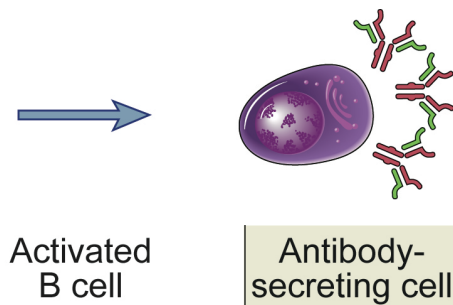
Mucosa/skin

Activation of effector T cells in infected tissues

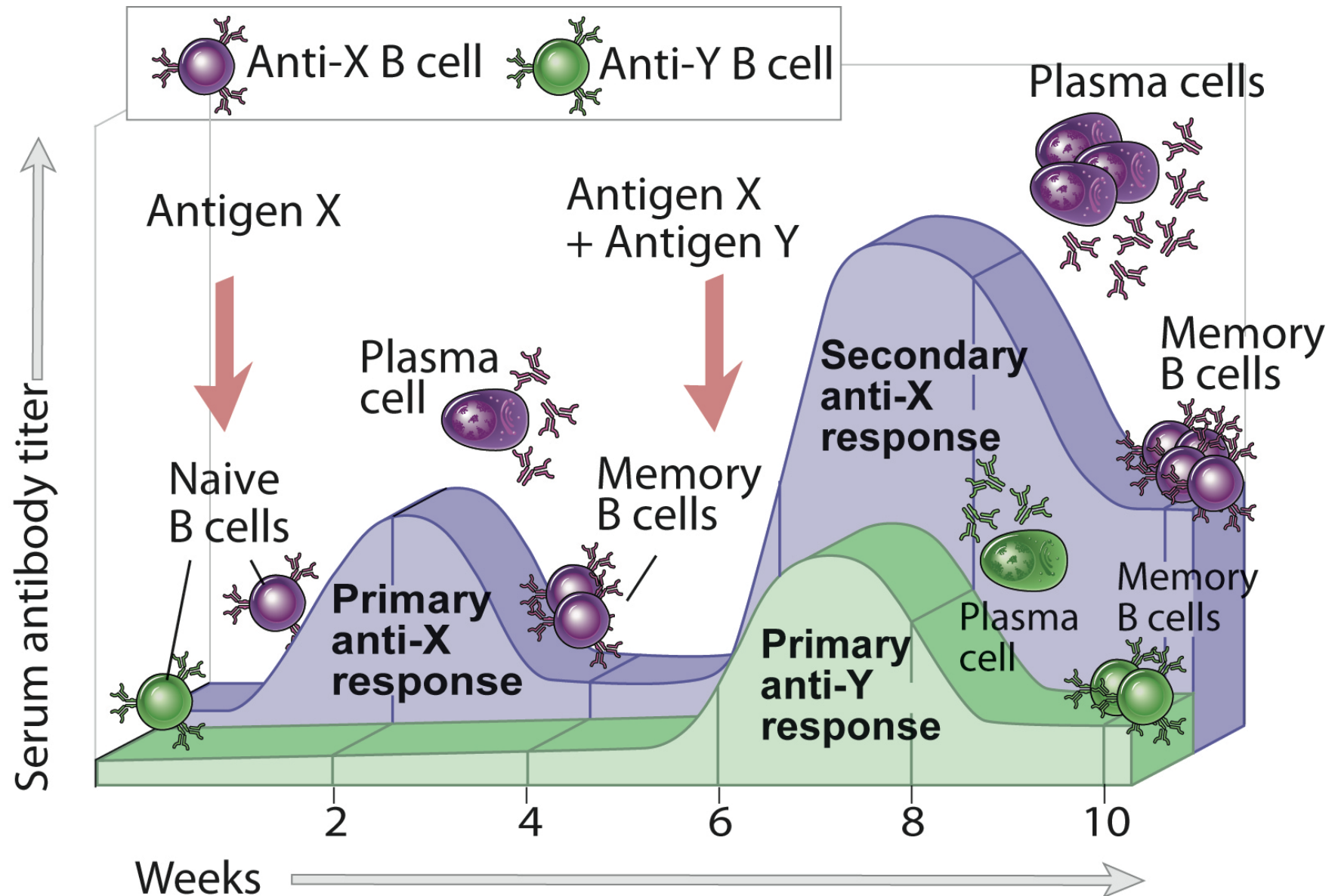
Antigens/microbes

linfócitos B diferenciam a plasmacelulas e produzem Ac

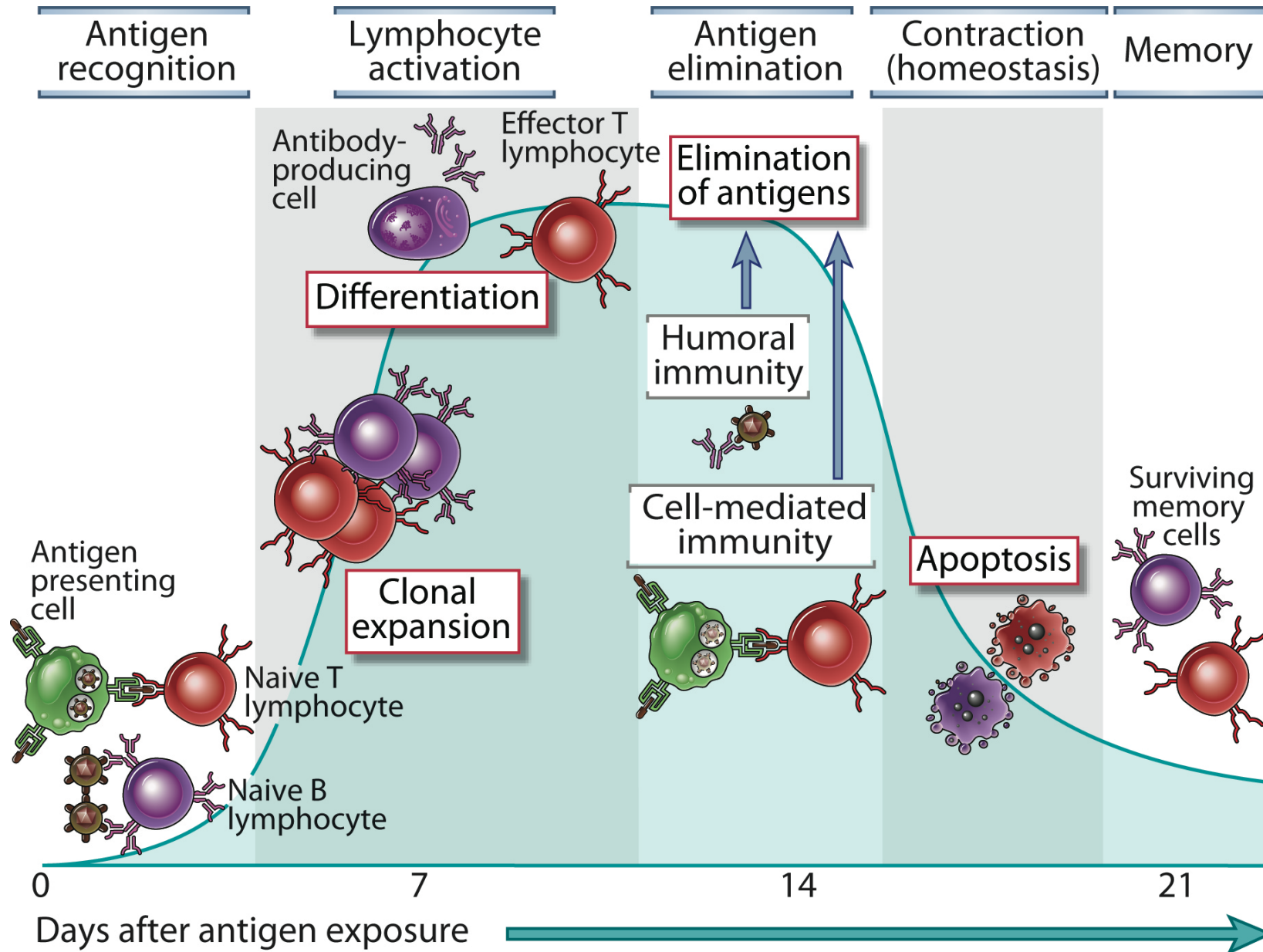
Anticorpos no sítio de infecção



Cinetica da ativação Linfocitos B



Resposta mediada por Linfocitos B



Linfocitos B & AC & idade

