Basic Immunology

Lecture 18

Maintenance of the immunological memory and its role in immune response regulation. Comparison of the primary and secondary immune response.

Why is memory important?

- Ability of the adaptive (specific) IR
- Results protection against infections (diseases)
- The phenomenon is used for vaccination
- Ability to respond more rapidly and effectively to the same antigen → secondary, tertiary IR

Why is memory response more effective?

Clonal proliferation of antigen specific cells results a lot of:

-> effector cells -> death by apoptosis

-> memory cells -> survival

-> increase in frequency of antigen specific cells

1. T and B cells with highest affinity BcR and TcR have a chance to contact with the antigen and get signals overcome the apoptotic mechanisms

2. Antigen presenting cells are different

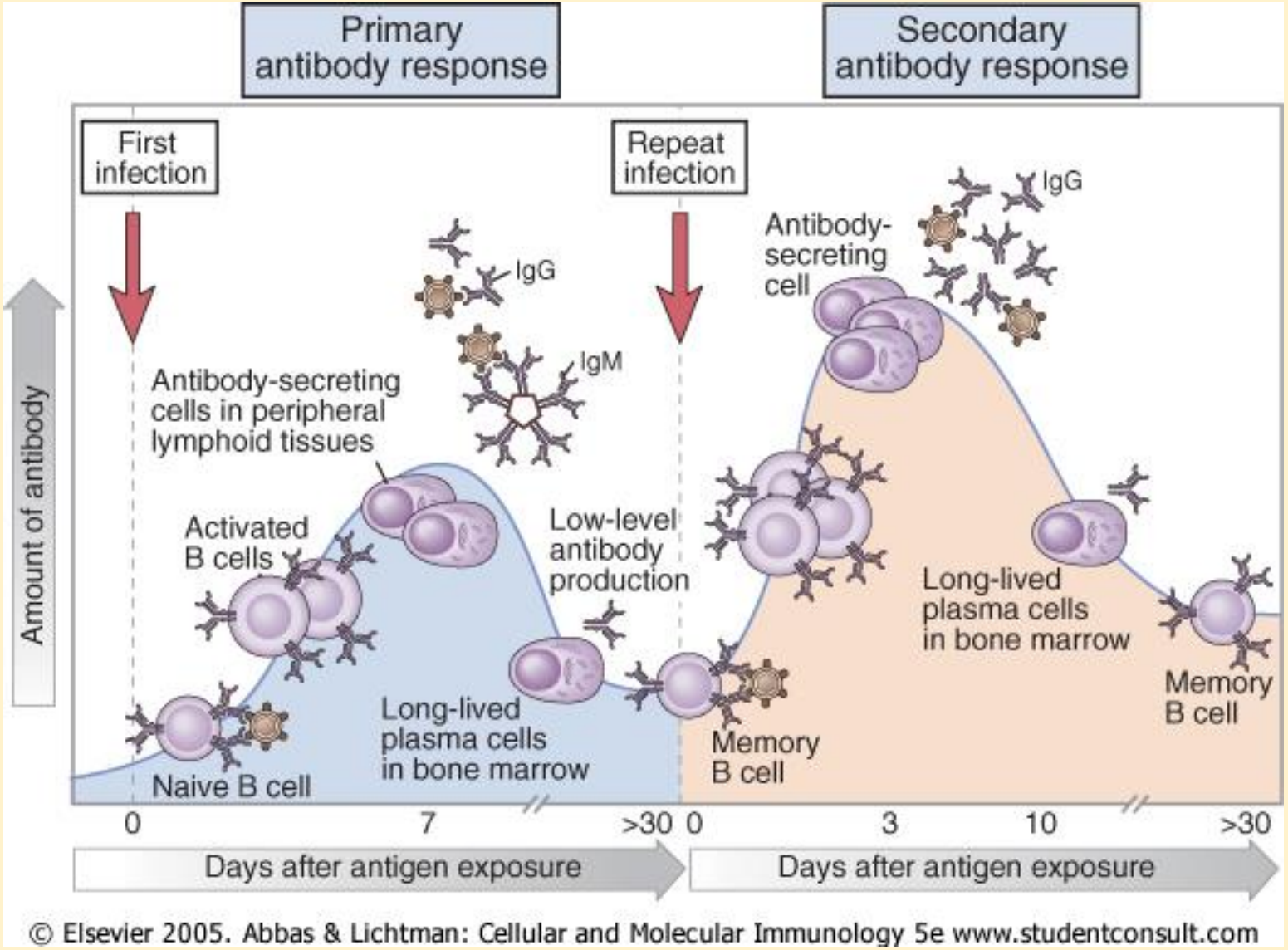
3. Homing behavior of lymphocytes is different

4. Surface adhesion molecules are different

5. CD45 isoform is different

B cell memory

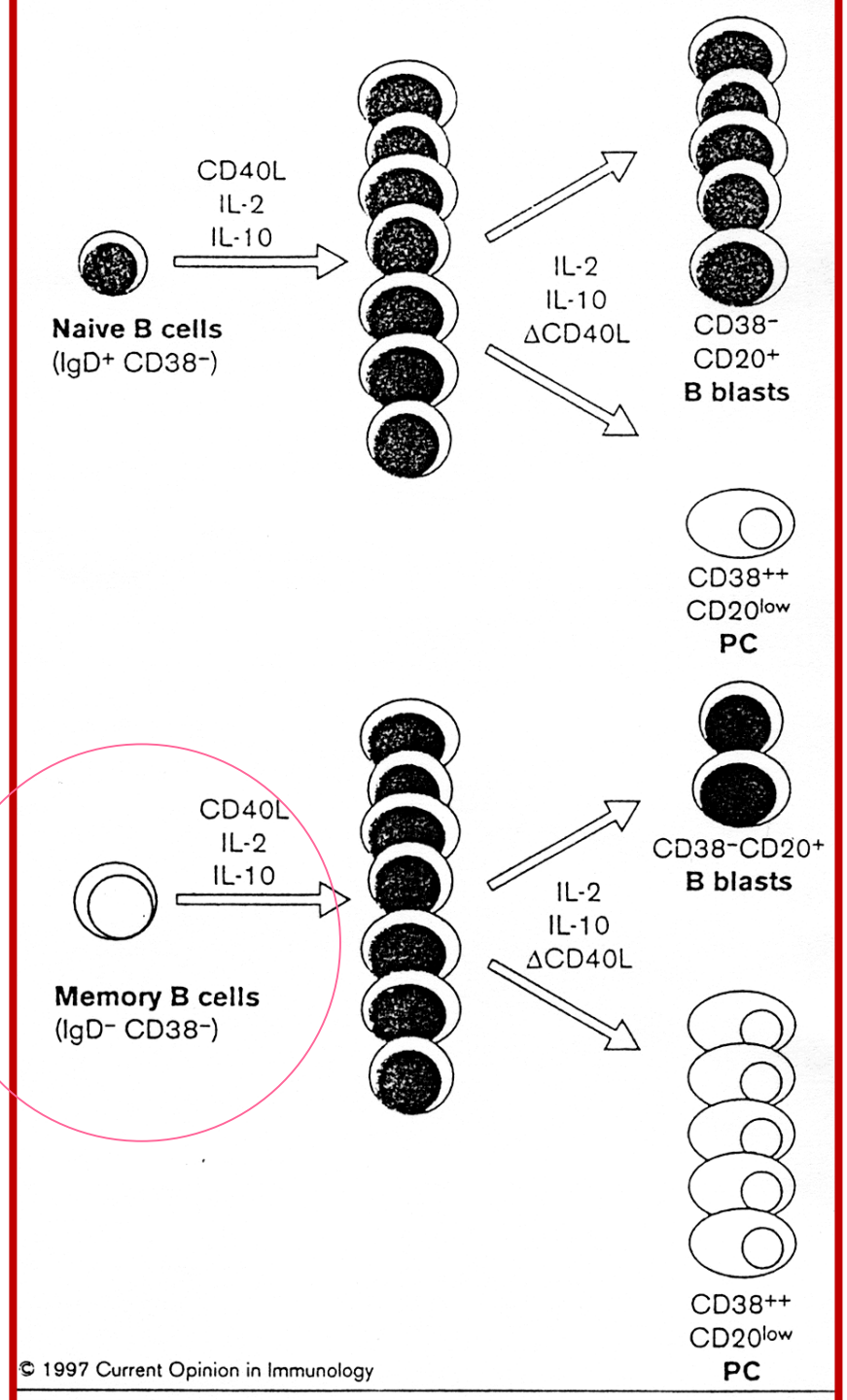
Primary and secondary B cell response



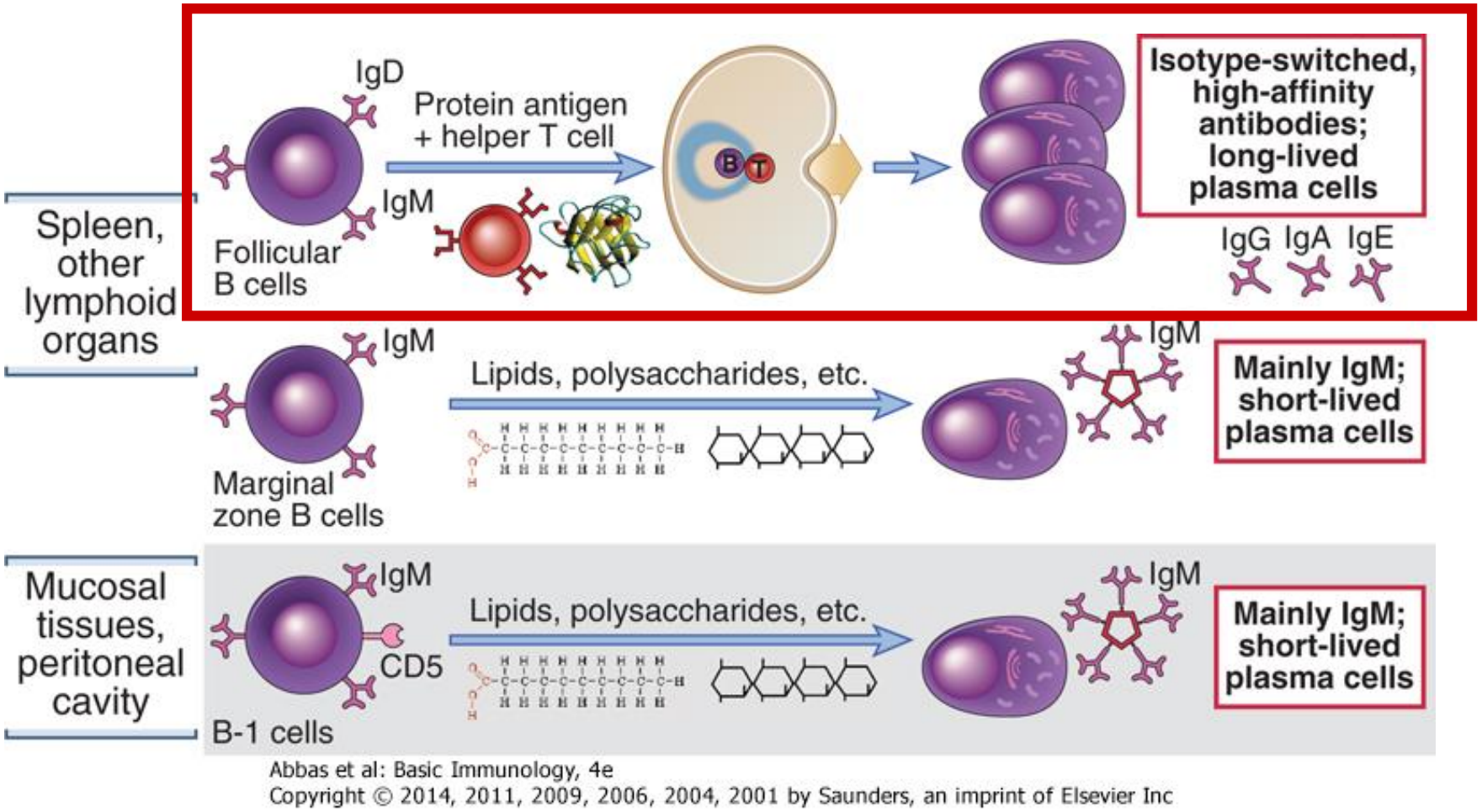
Primary response, naive B cell activation

→ more memory B cells are generated

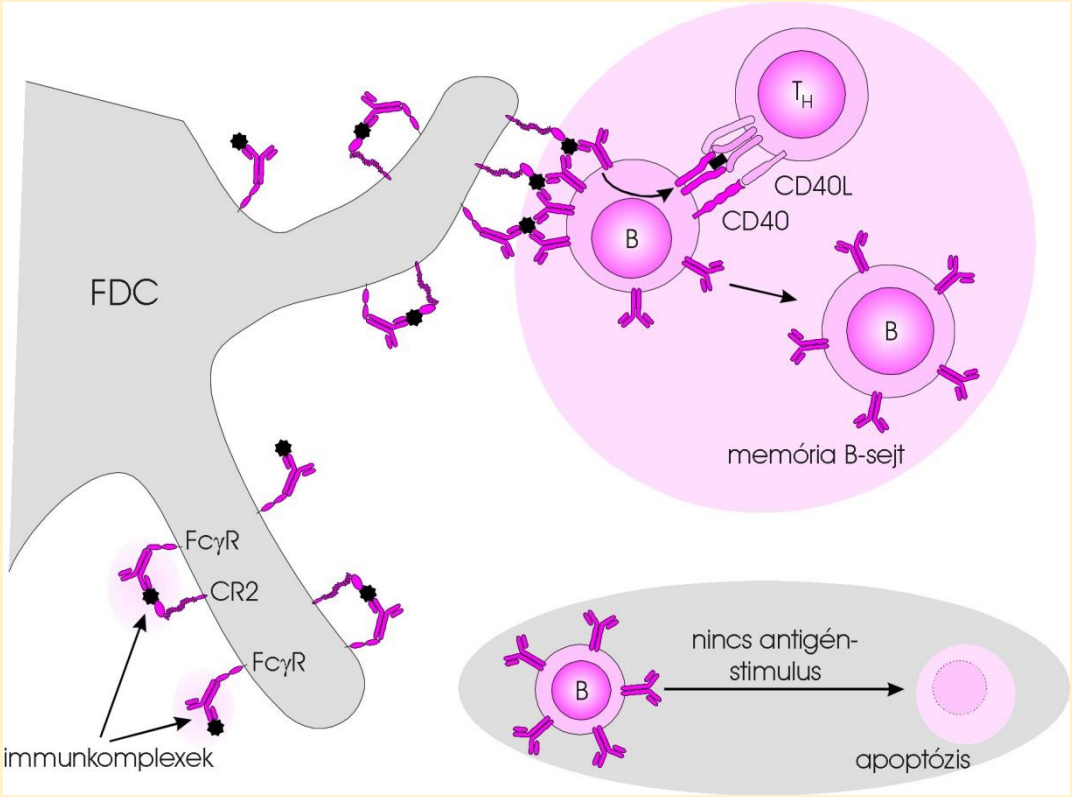
Secondary, memory B cell response → mostly plasma cells are generated (5x more)



TD and TID antigen response



1. T and B cells with highest affinity BcR and TcR have a chance to contact with the antigen and get signals overcome the apoptotic mechanisms



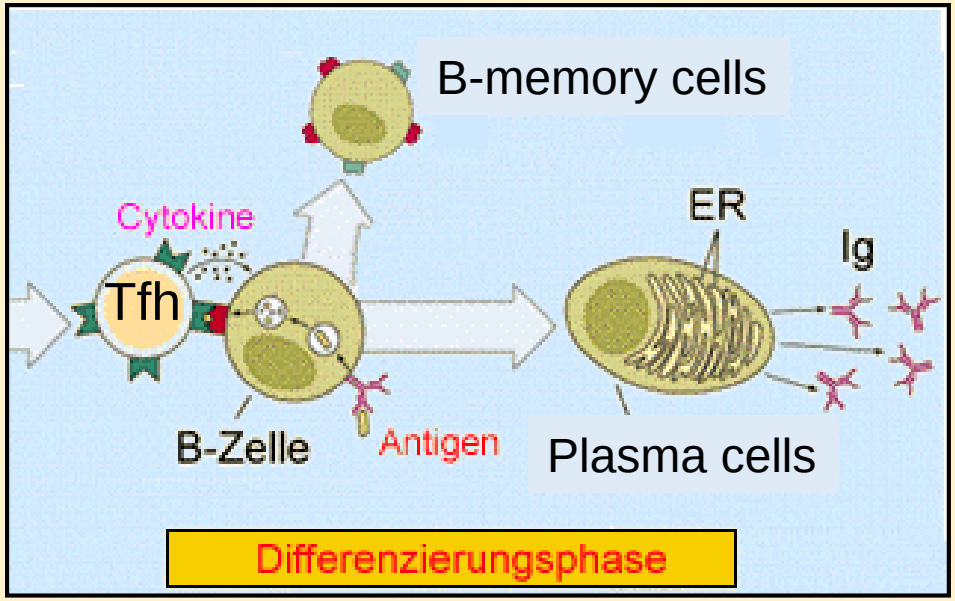
What gives the survival signal?

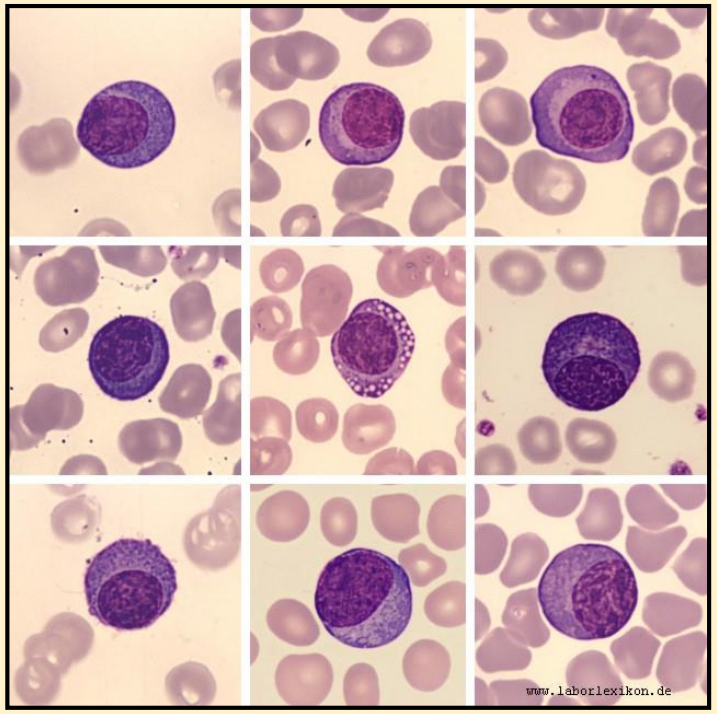
Minute amount of antigen present as IC on FDC or infected cells induce the division and survival of memory cells?

Cross-reactive antigens?

Idiotype-specific antibodies

Plasma cells



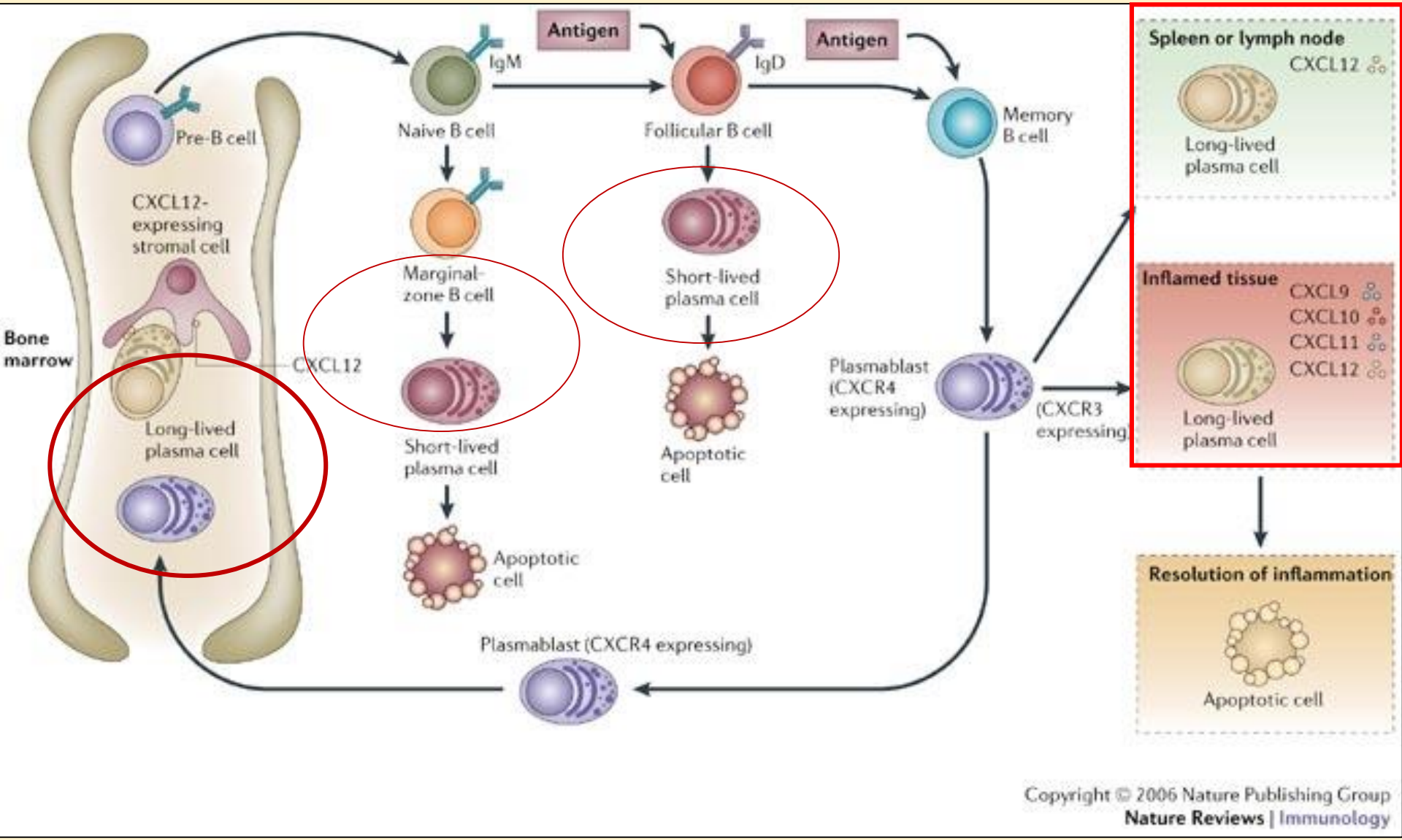


Cytokines: IL-2, IL-4, IL-5, IL-6, IL-10, IL-13…
CD40L-CD40 Signal

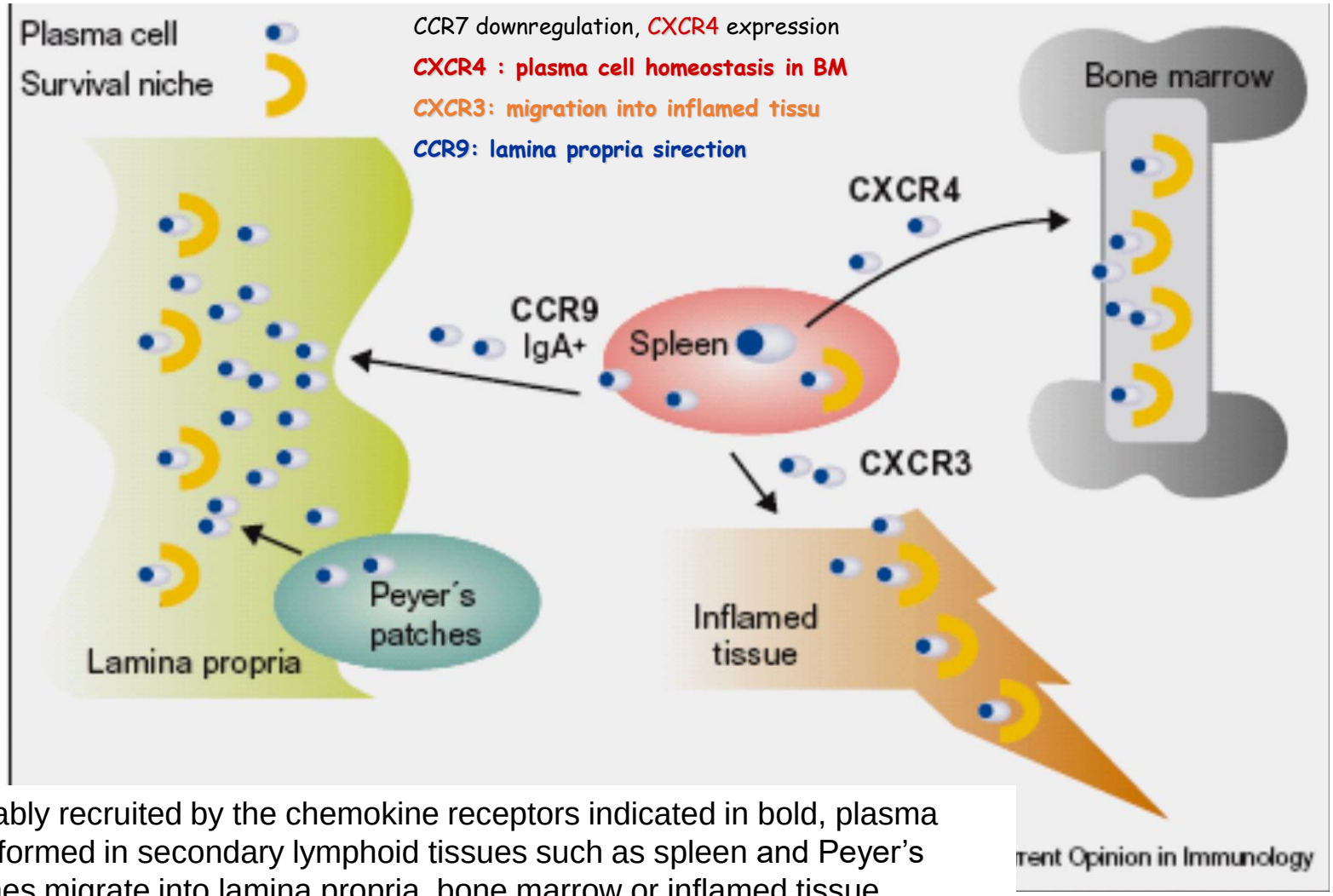
Plasma cells: CD38++

Where?
Bone marrox perivascular sinus
Mucosa Lamina Propria
Spleen red pulp
Lymph node medulla

Plasma cells



Possible regulation of plasma cell homeostasis by survival niches



Probably recruited by the chemokine receptors indicated in bold, plasma cells formed in secondary lymphoid tissues such as spleen and Peyer's patches migrate into lamina propria, bone marrow or inflamed tissue.

Long-lived plasma cells

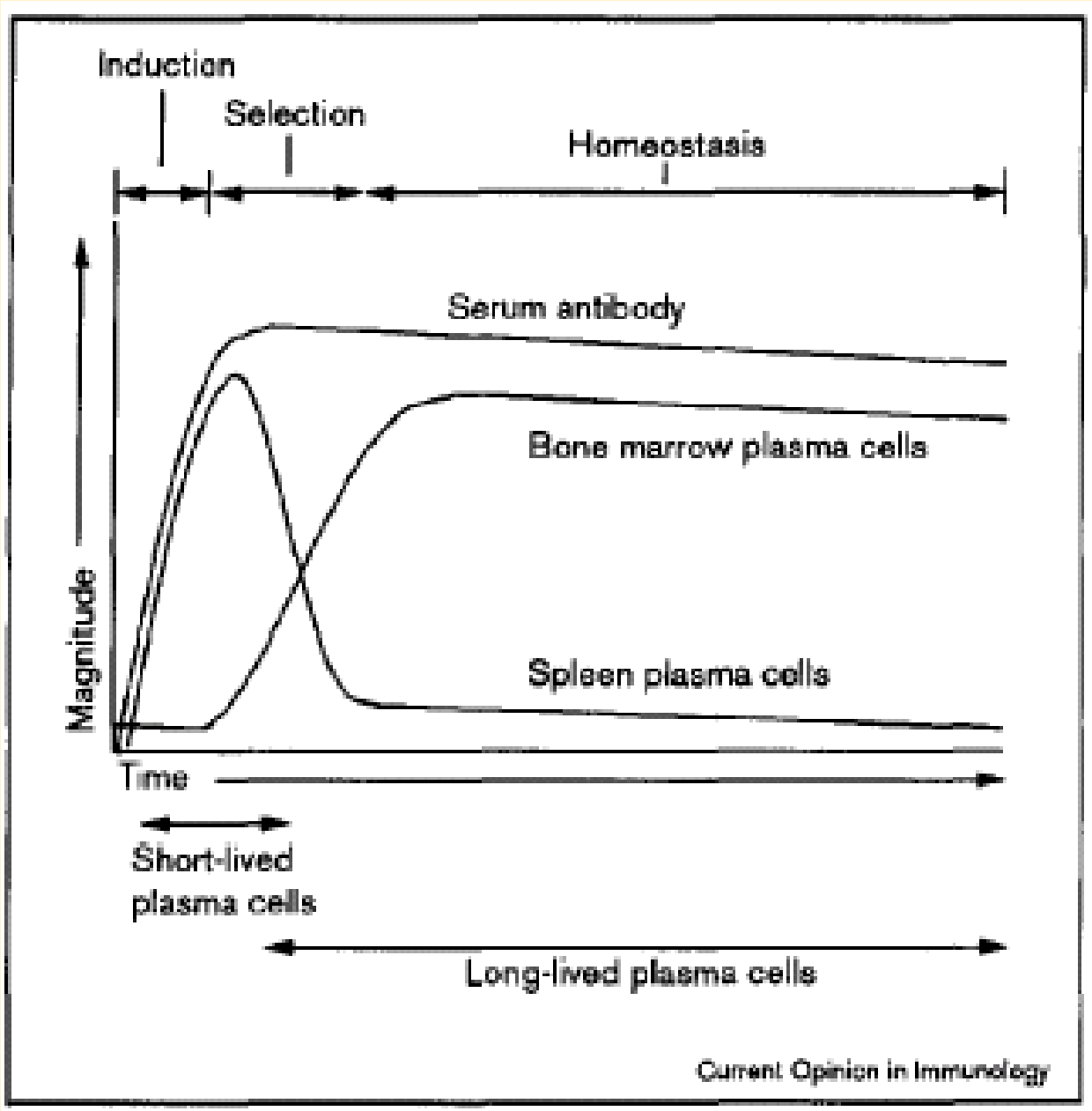


TABLE 11-4 COMPARISON OF PRIMARY AND SECONDARY ANTIBODY RESPONSES

Property	Primary response	Secondary response
Responding B cell	Naive (virgin) B cell	Memory B cell
Lag period following antigen administration	Generally 4–7 days	Generally 1–3 days
Time of peak response	7–10 days	3–5 days
Magnitude of peak antibody response	Varies depending on antigen	Generally 100–1000 times higher primary response
Isotype produced	IgM predominates early in the response	IgG predominates
Antigens	Thymus-dependent and thymus-independent	Thymus-dependent
Antibody affinity	Lower	Higher

BcR changes during memory formation !

TABLE 11-7 COMPARISON OF NAIVE AND MEMORY B CELLS

Properties	Naive B cell CD27- IgD+	Memory B cell CD27+ IgD-
Membrane markers		
Immunoglobulin	IgM, IgD	IgM, IgD(?), IgG, IgA, IgE
Complement receptor	Low	High
Anatomic location	Spleen	Bone marrow, lymph node, spleen
Life span	Short-lived	May be long-lived
Recirculation	Yes	Yes
Receptor affinity	Lower average affinity	Higher average affinity due to affinity maturation*
Adhesion molecules	Low ICAM-1	High ICAM-1

*Affinity maturation results from somatic mutation during proliferation of centroblasts and subsequent antigen selection of centrocytes bearing high-affinity mIg.

T cell memory

Memory T-cell types

Naive T cell	Effector T cells	Memory T cells
CD45RA+	CD45RO+	CD45RO+
CD25lo	CD25hi	CD25lo
CD127hi	CD127lo	CD127hi
CD44lo	CD44hi	CD44hi

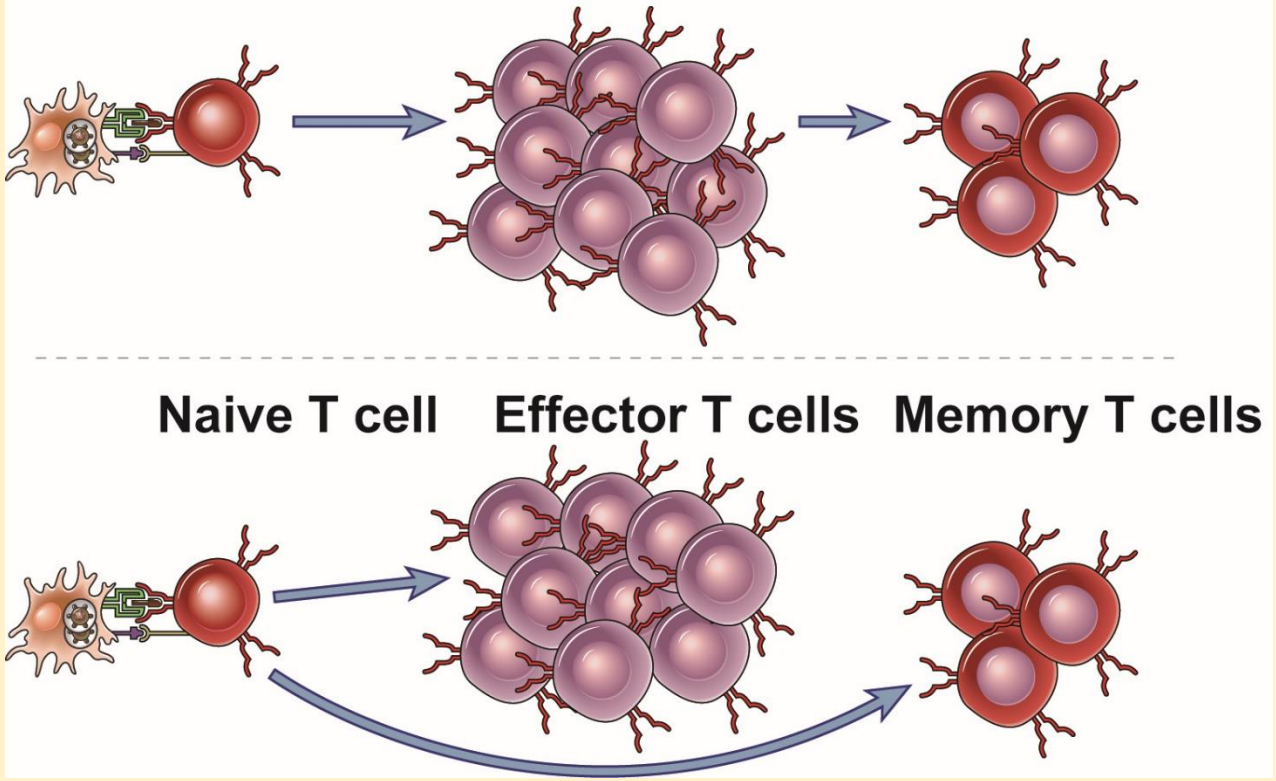
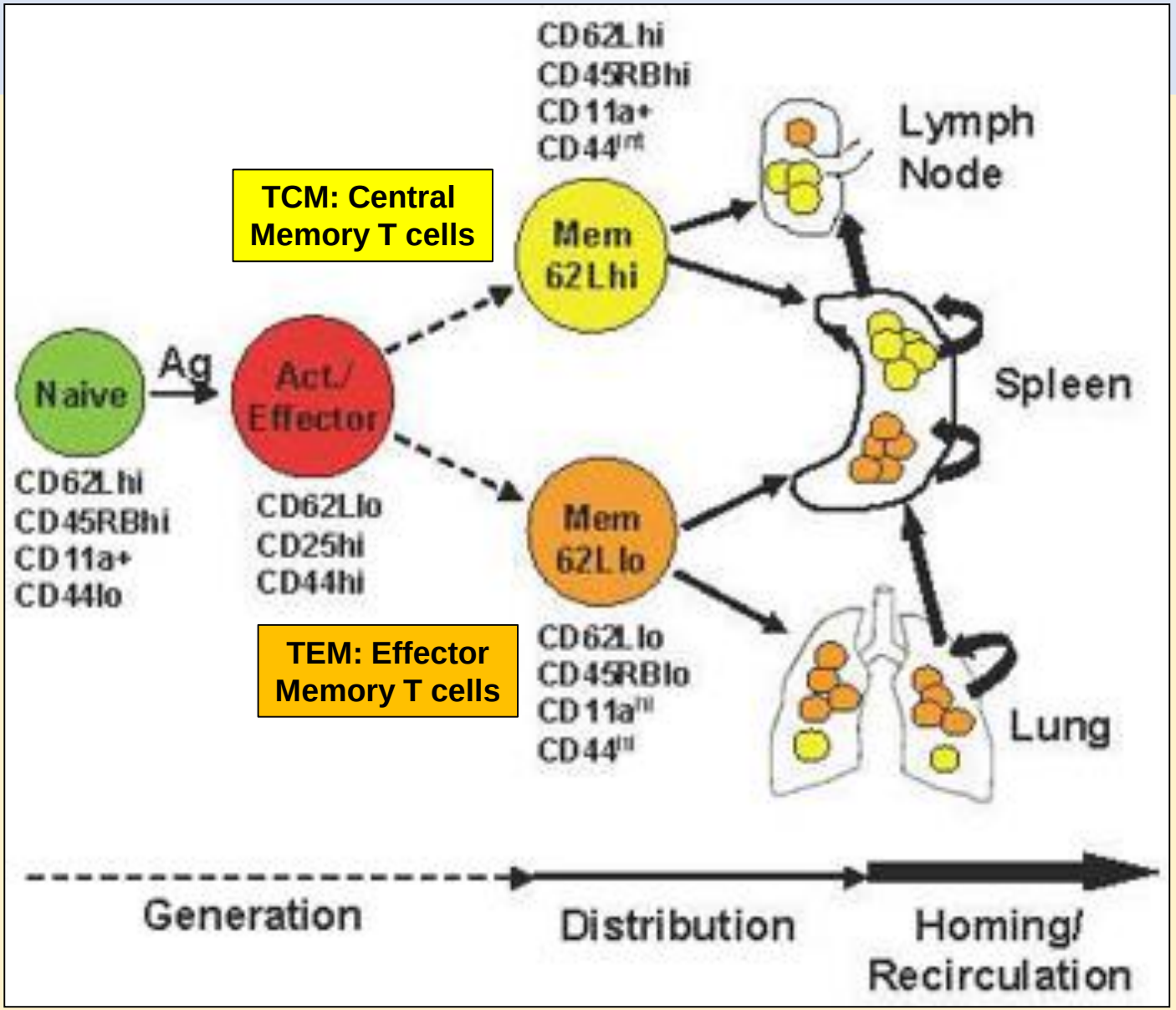
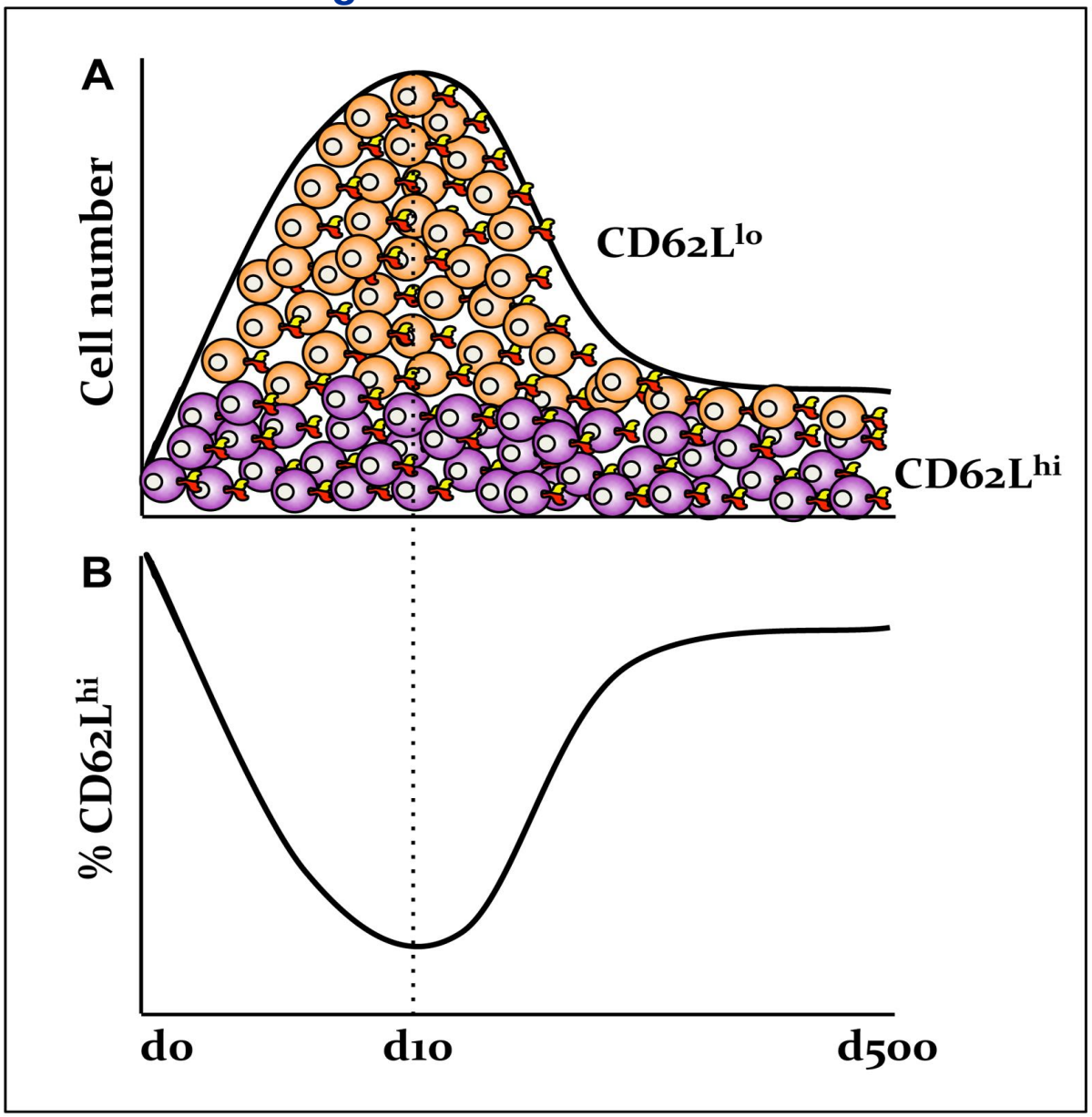


Fig. 9-19

Memory T cell types



Preferential survival of antigen-specific memory CD62LhiCD8+ T cells following influenza virus infection.

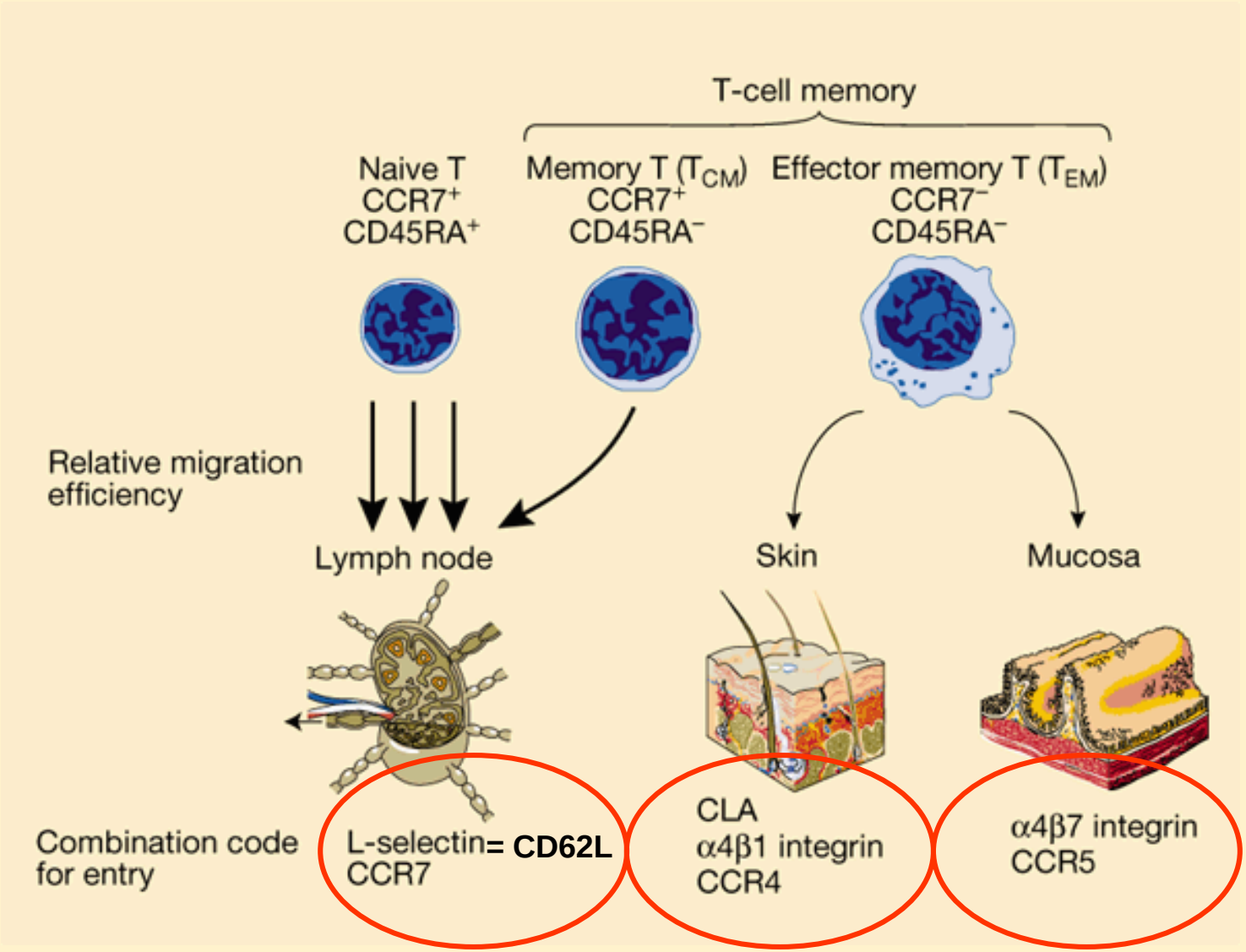


TEM

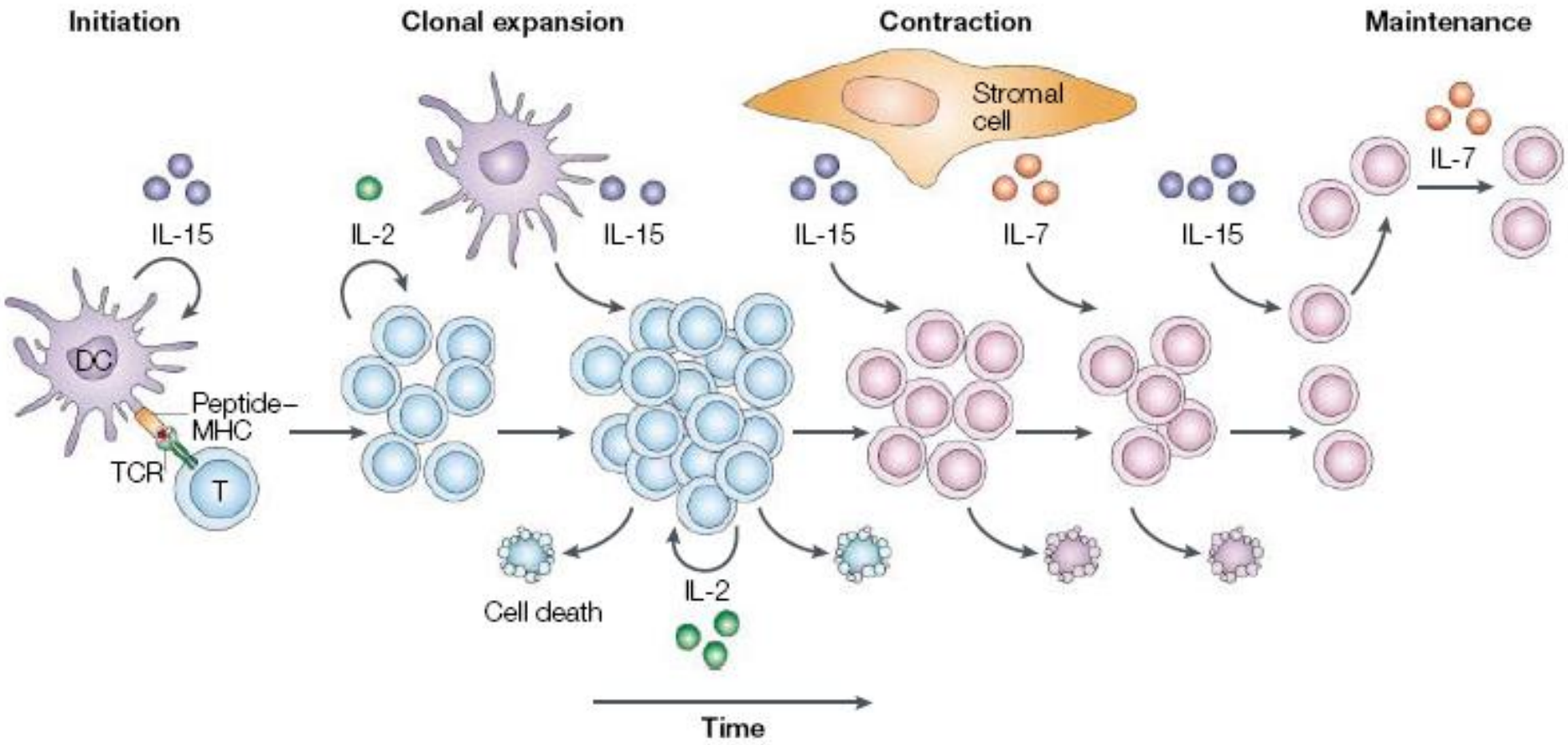
TCM

Figure 1 Kedzierska et al

Immunological memory is systemic



The checkpoints of memory T cell survival



Memory T cells: IL-15-dependent proliferation, IL-7 dependent survival

Surface adhesion molecules are different

- **Downregulation of: L-selectin**
- **Upregulation of:**
  - **VLA-4 (ligand of VCAM)**
  - **LFA-1, CD2, LFA-3**
  - **CD44 (hyaluronic acid receptor)**

Homing of memory T cells

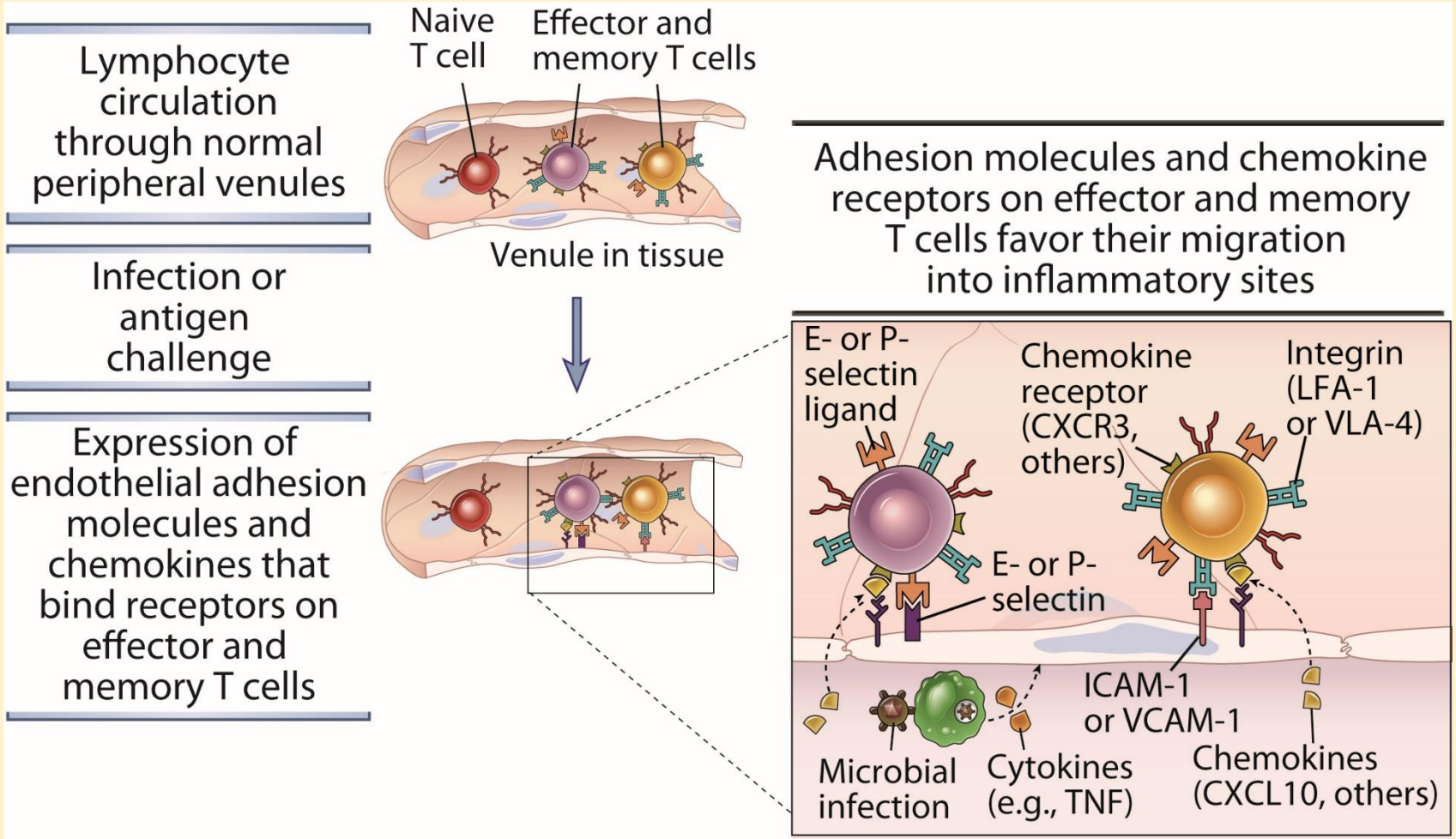
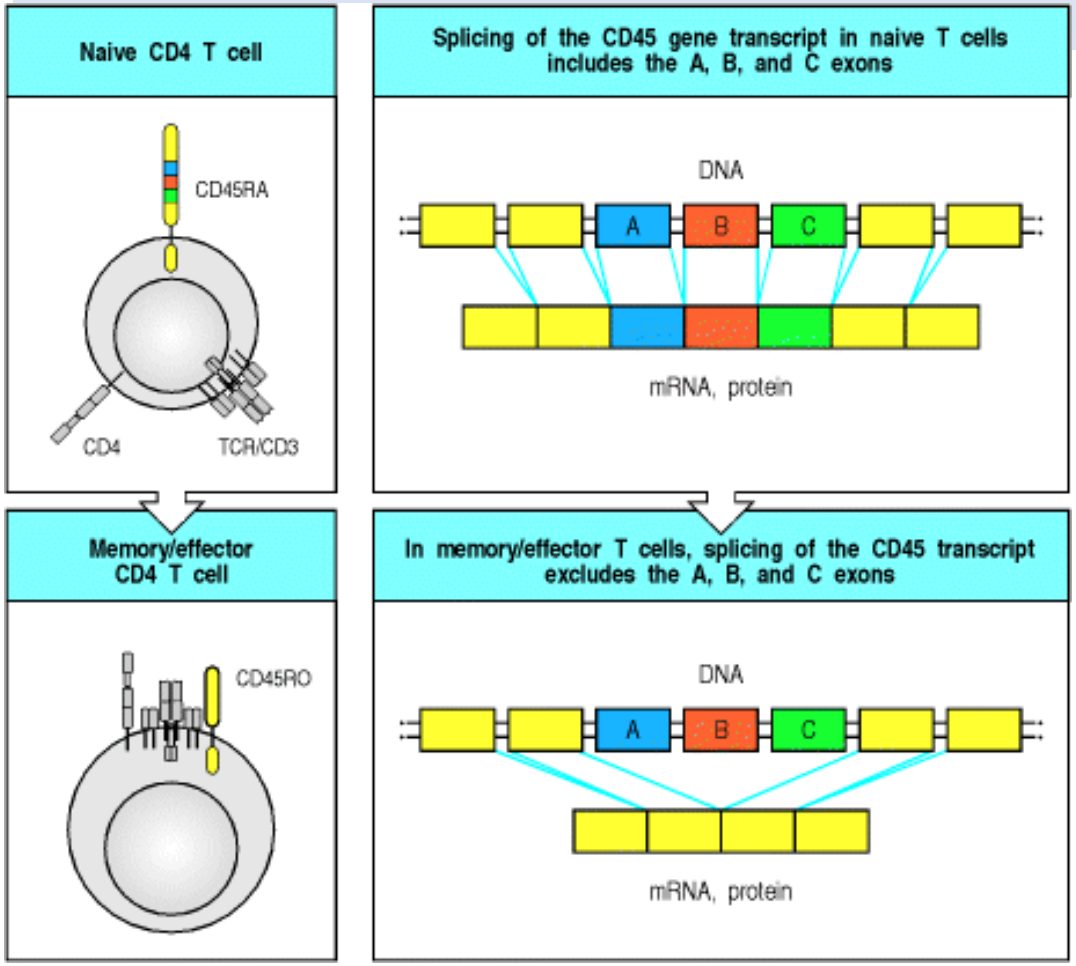


Fig. 10-3

CD45 isoforms on naive and memory T cells



Naive T cells: CD45-RA

Memory T cells: CD45-RO

→shorter extracellular domain→ can associate much better to TcR → more effective signal Transduction

CD45 is important in cell activation, regulation of signal transduction - ***tyrosine –foszfatase*** ***domain -dephosphorylation***

Components of immunological memory

The result of antigen-specific cell proliferation:

- **effector cells → apoptosis**
- **memory cells → survival TEM, TCM, BMEM +PLASMA CELLS**
- **memory cell with increased frequency (M/E)**

1. **T/B cells with the highest affinity can bind to residual or re-entrant antigen with the highest chance of survival. Cells/clones?**
2. **Different CD45 isoform**
3. **Altered cell surface adhesion molecule composition.**
4. **B cell becomes the main antigen-presenting cell.**
5. **Lymphocyte recirculation pattern differs.**

Cells of the evolutional (species specific) memory: NATURAL IMMUNITY

- **CD5-positive (B-1) B cells**: production of low-affinity polyreactive antibodies against common bacterial polisaccharide antigens; autonom self-renewal; dominant B cell type in newborn
- **γ/δ T cells, NKT cells**: restricted TcR specificity, bacterial glycolipid antigen recognition with non-conventional MHC-like molecules: CD1, MR. Effector and memory phenotype