



The development of B lymphocytes

Dr. Glorivee Rosario-Pérez
BIOL 4056



Introduction



The life cycle of B cells

Generation of B cells in bone marrow.

Elimination of self-reactive B cells in bone marrow.

Activation of B cells by foreign antigen in secondary lymphoid tissues.

Differentiation to antibody-secreting plasma cells and memory B cells in secondary lymphoid tissues.

The life cycle of B cells cont.

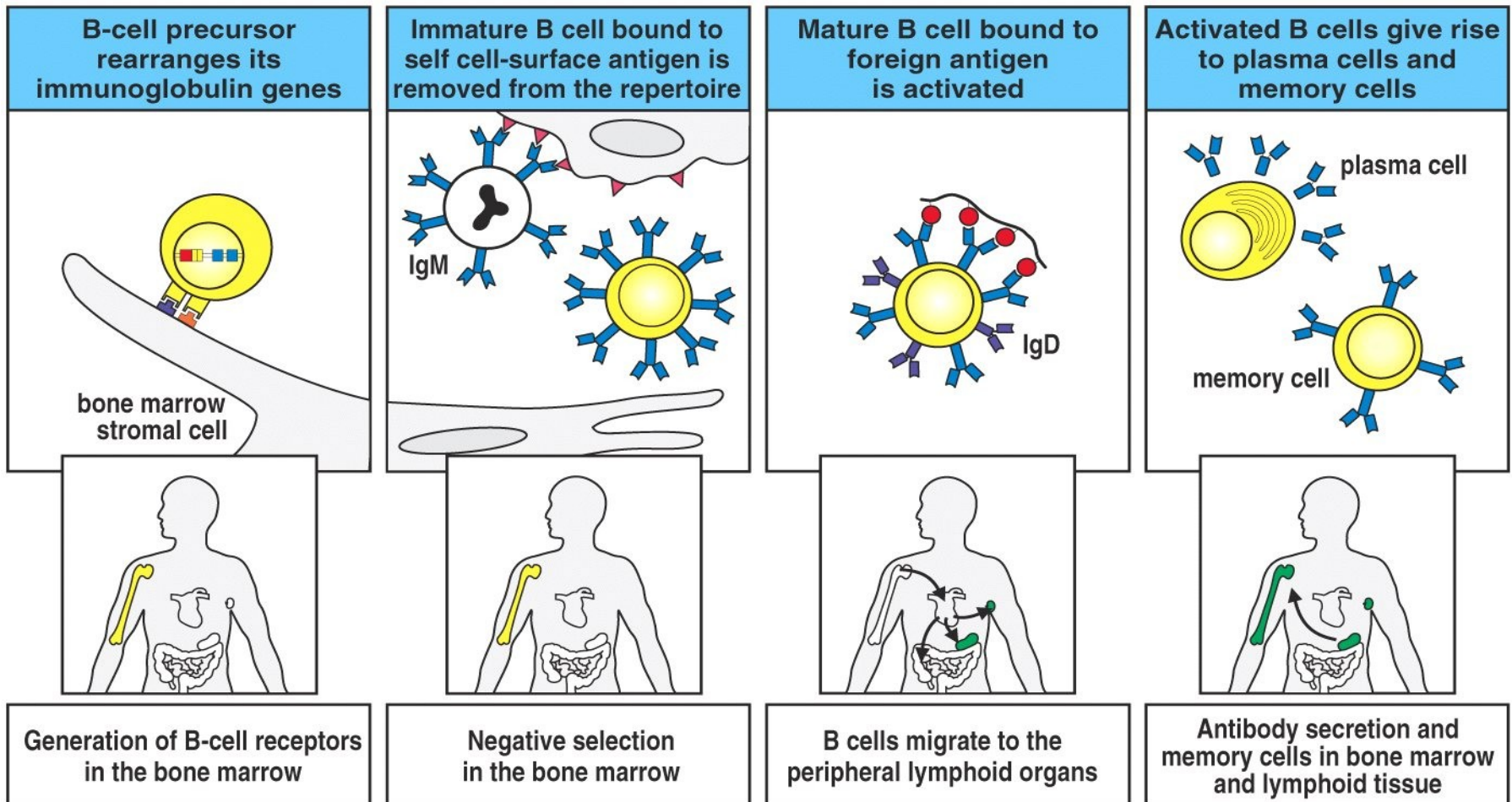


Figure 7-1 Immunobiology, 6/e. (© Garland Science 2005)

The development of B cells in the bone marrow



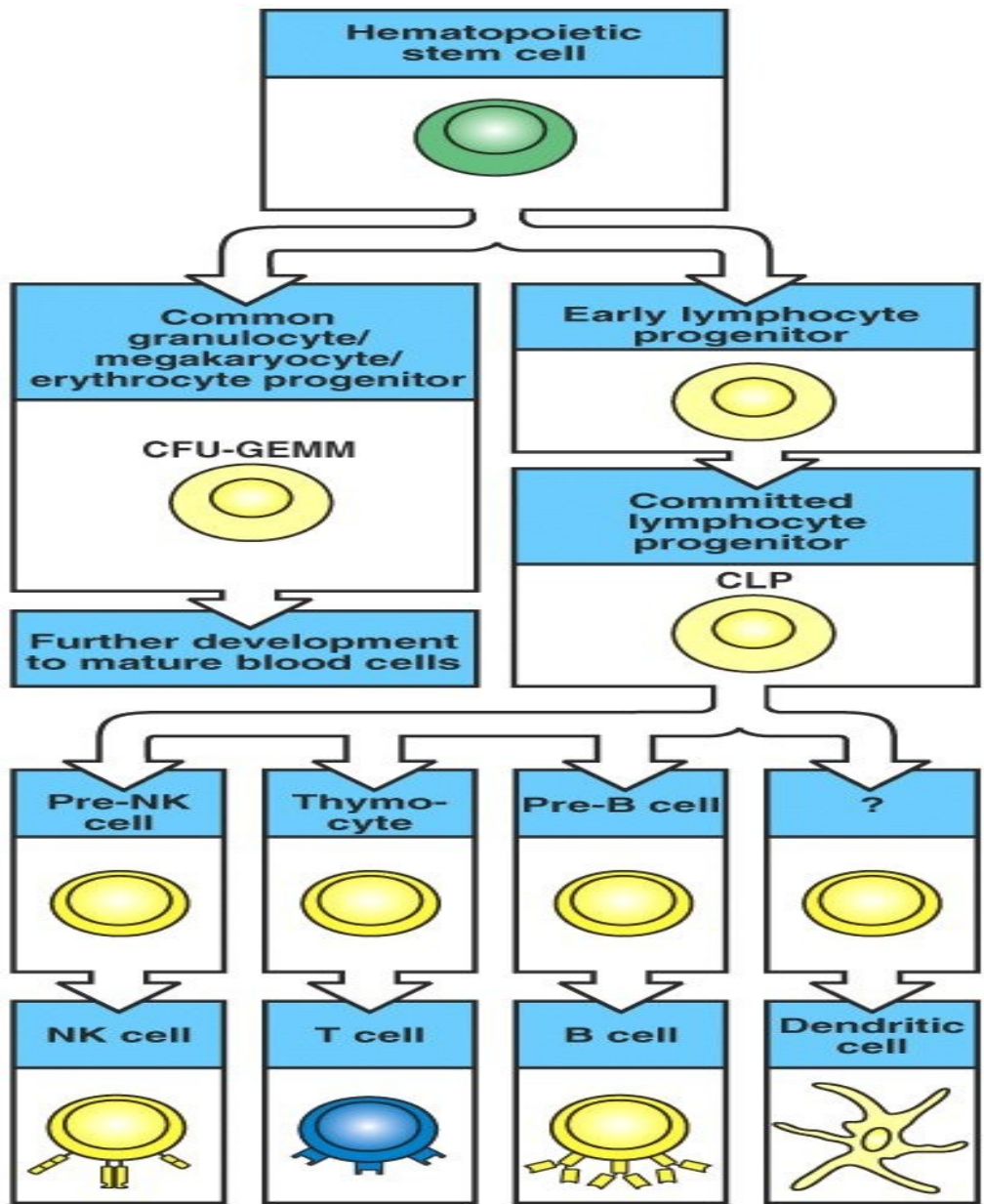


Figure 7-3 Immunobiology, 6/e. (© Garland Science 2005)

B cell development : rearrangement and expression of immunoglobulin genes

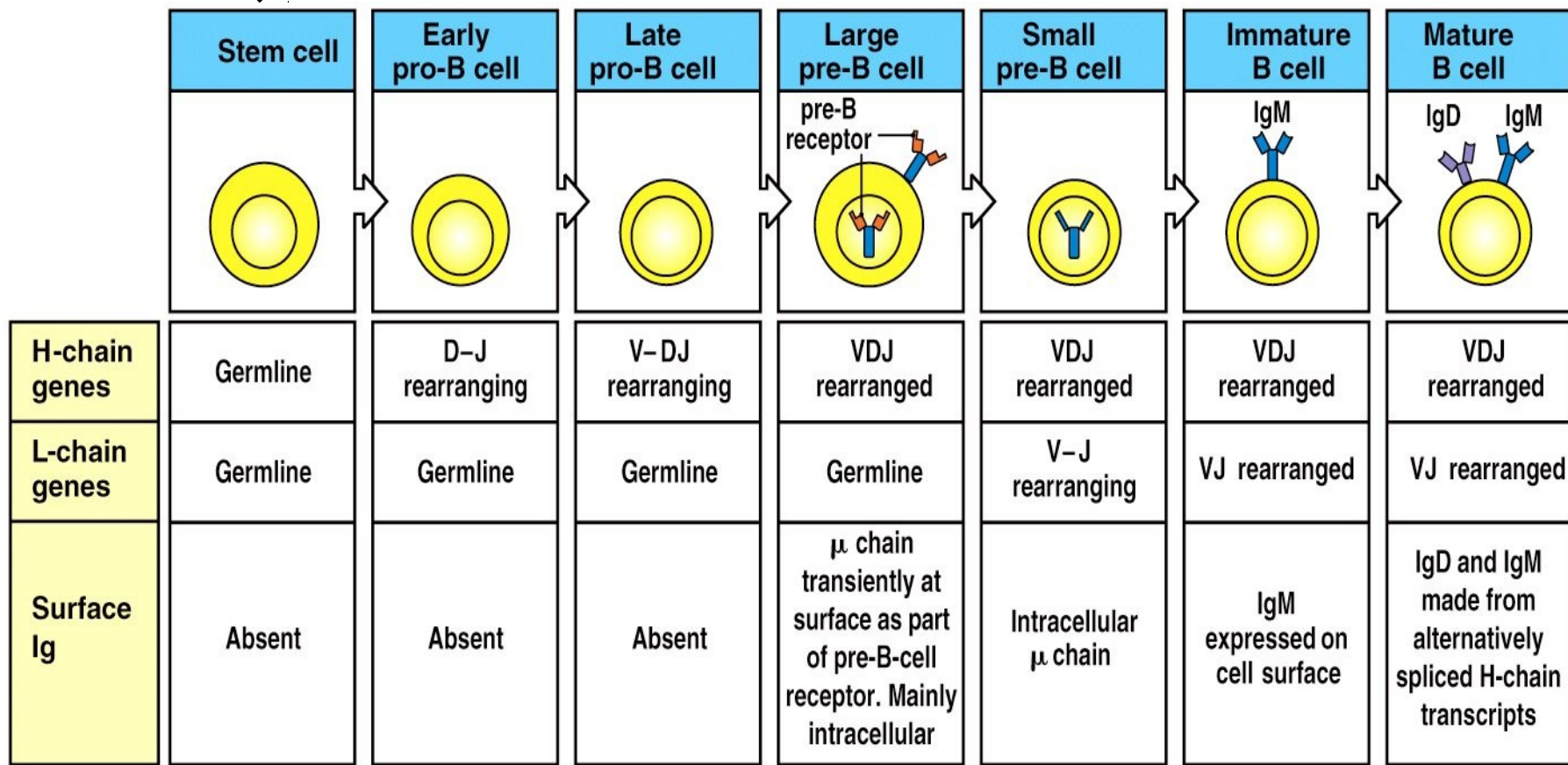


Figure 7-6 Immunobiology, 6/e. (© Garland Science 2005)

B cell development : rearrangement and expression of immunoglobulin genes cont.

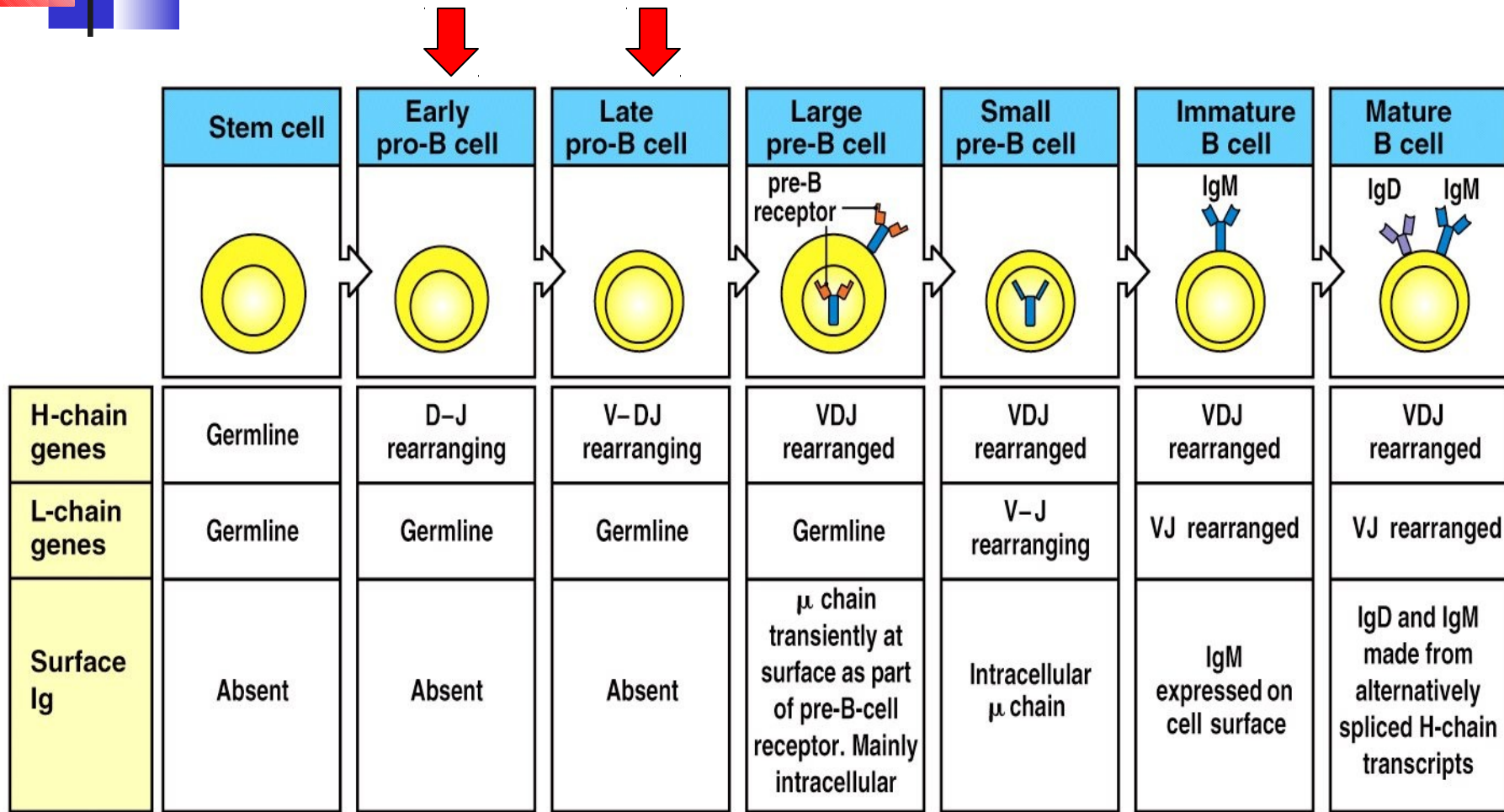


Figure 7-6 Immunobiology, 6/e. (© Garland Science 2005)

B cell development : rearrangement and expression of immunoglobulin genes cont.

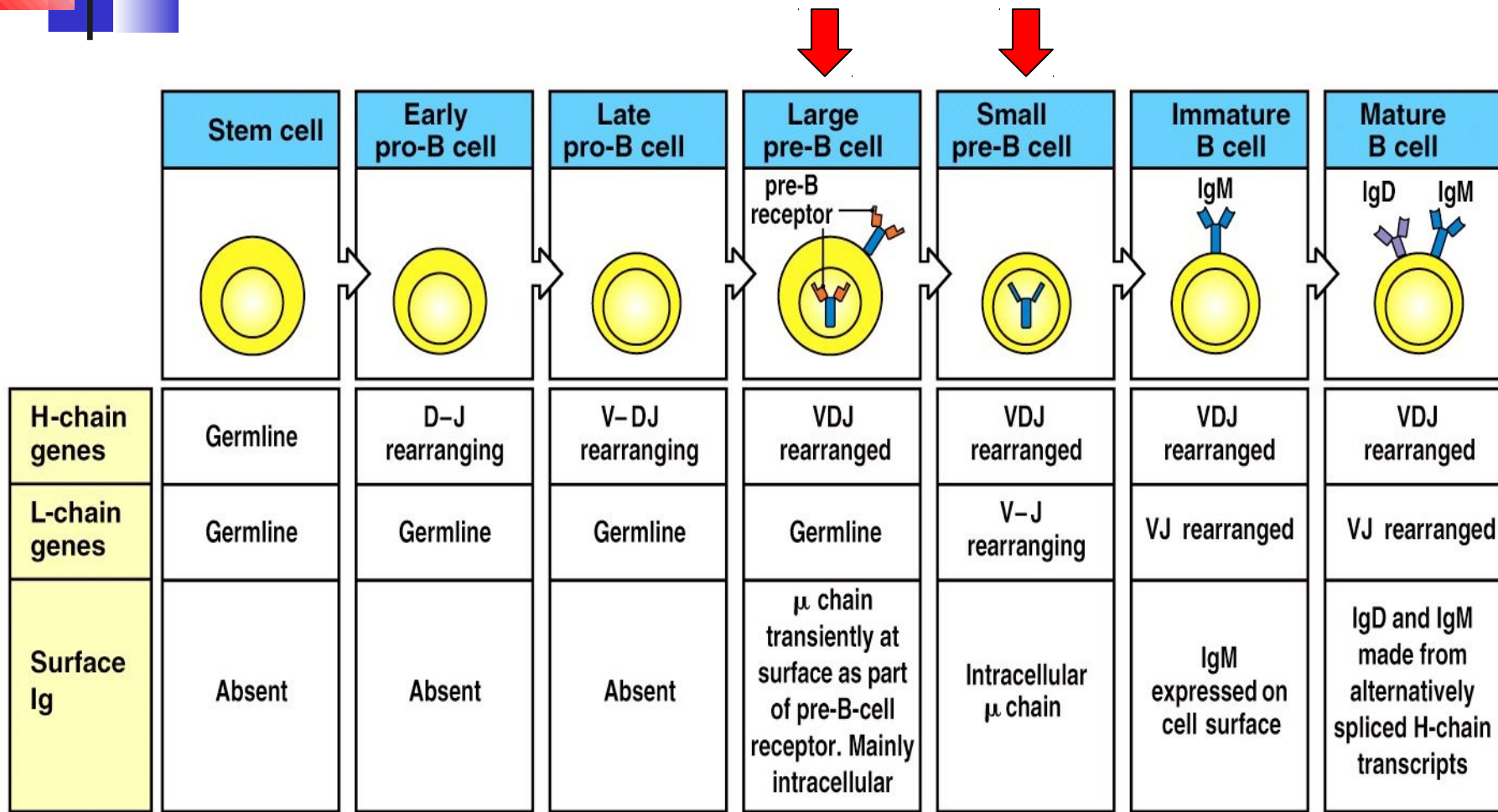
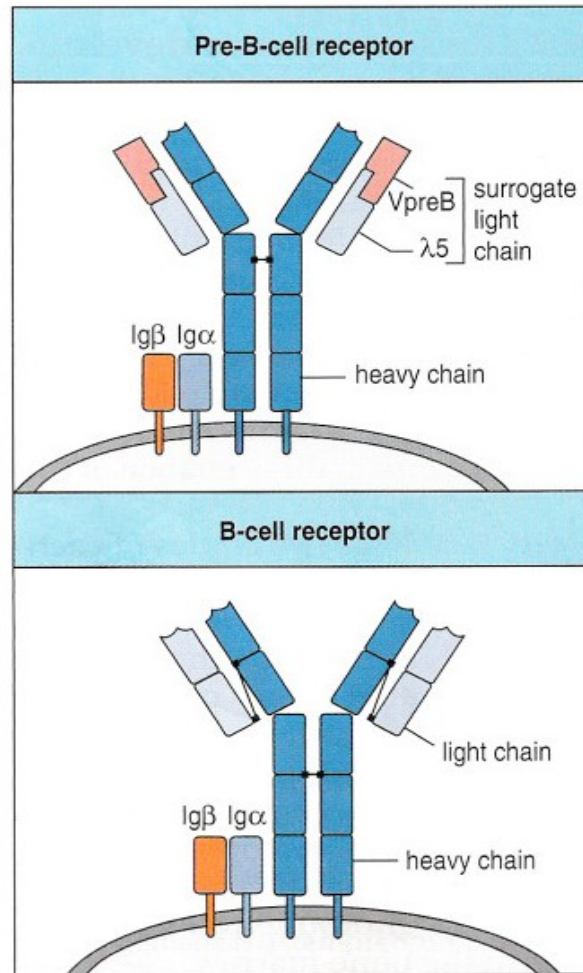


Figure 7-6 Immunobiology, 6/e. (© Garland Science 2005)

B cell development : rearrangement and expression of immunoglobulin genes cont.



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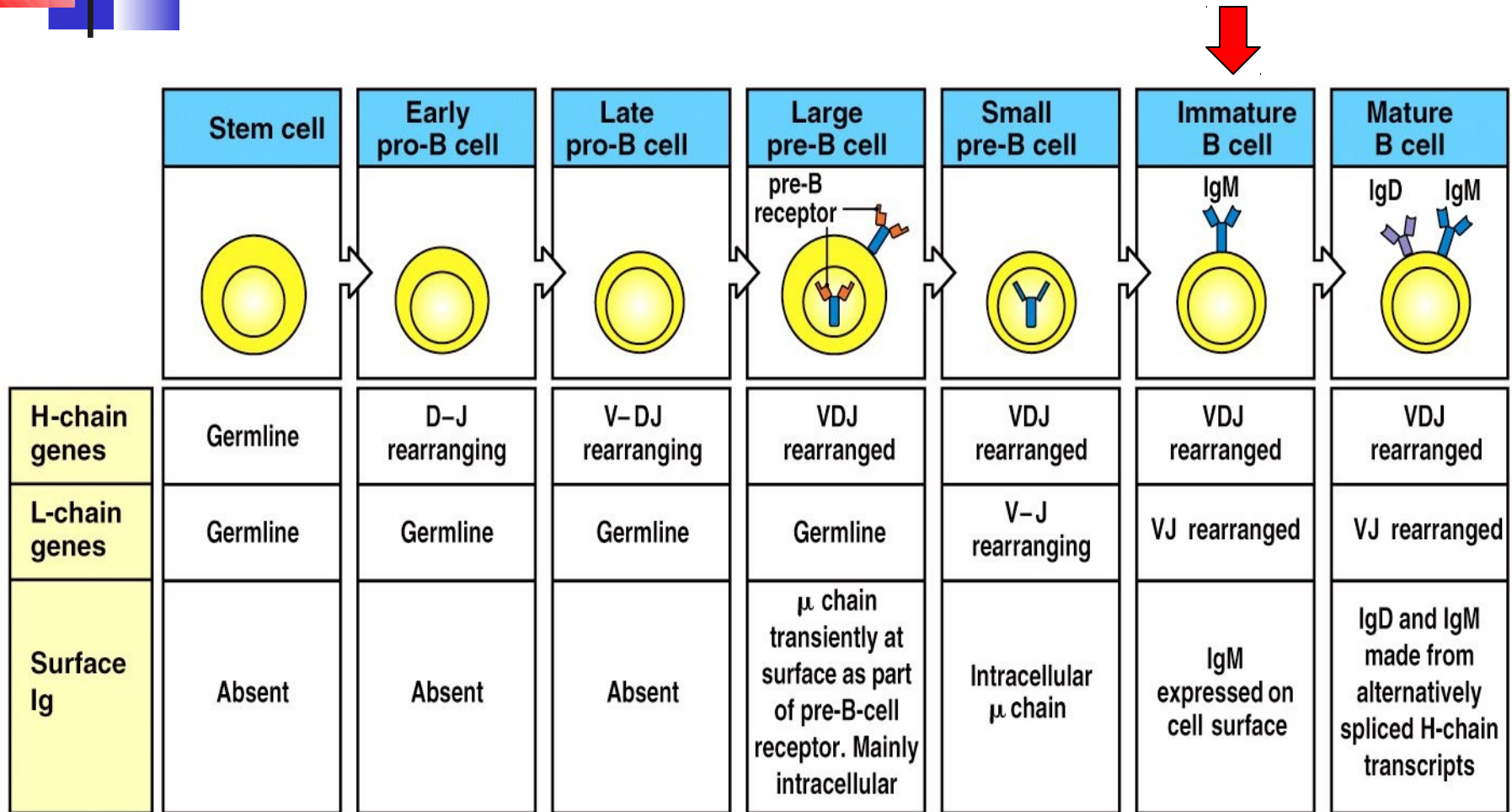


Figure 7-6 Immunobiology, 6/e. (© Garland Science 2005)

B cell development : rearrangement and expression of immunoglobulin genes cont.

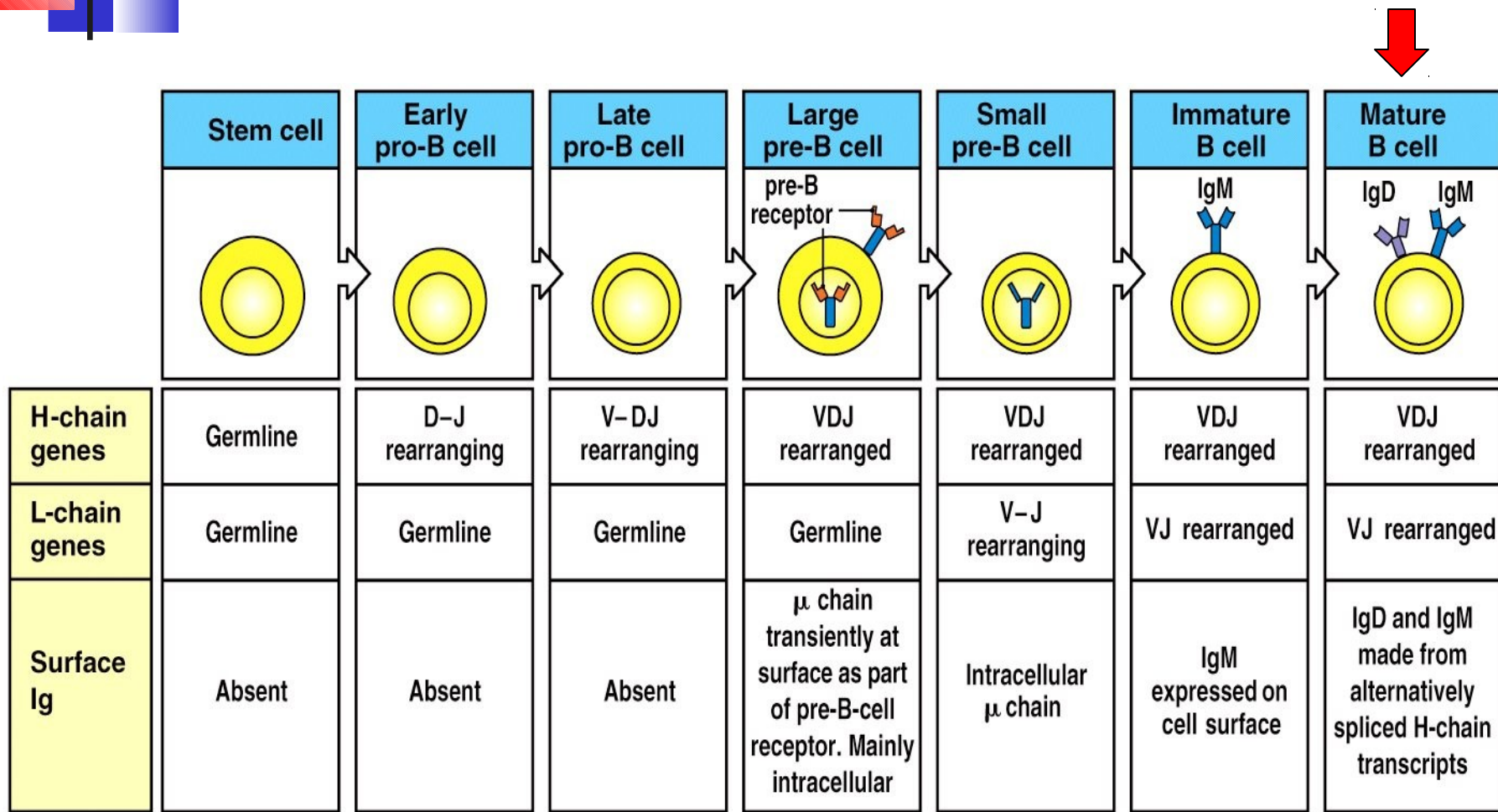
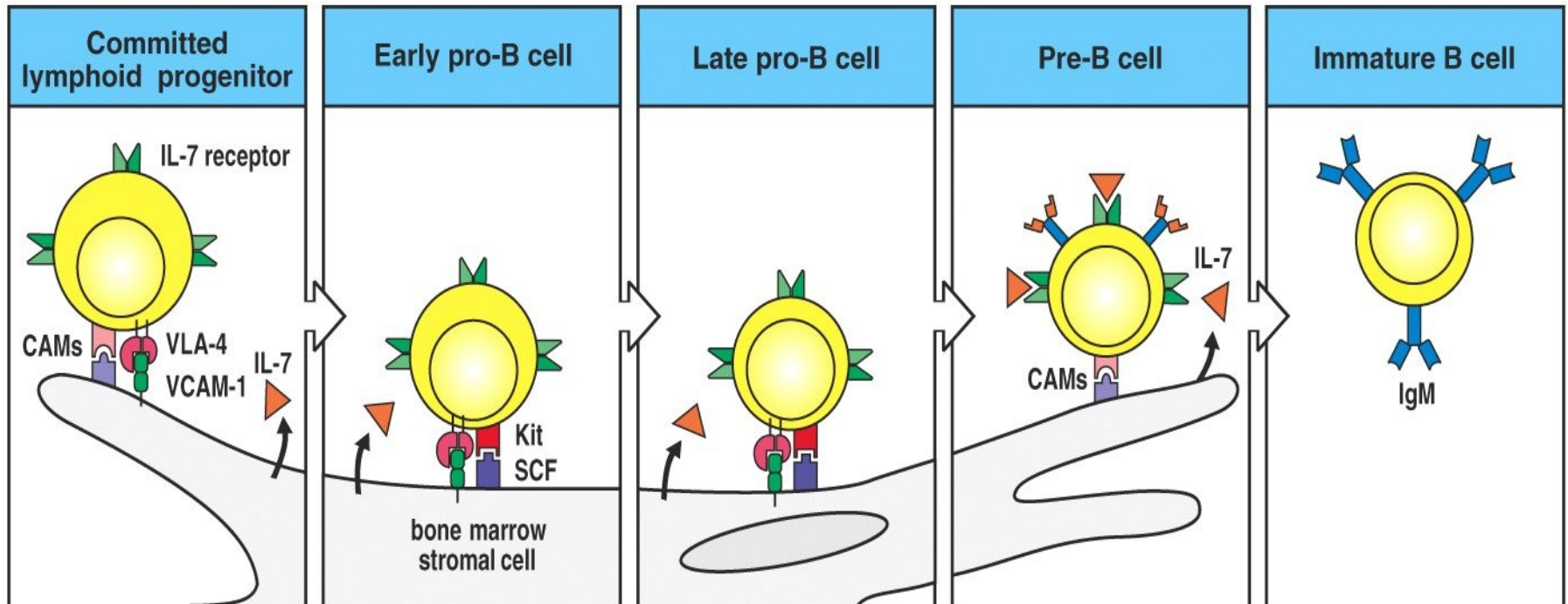


Figure 7-6 Immunobiology, 6/e. (© Garland Science 2005)

Bone marrow stromal cells



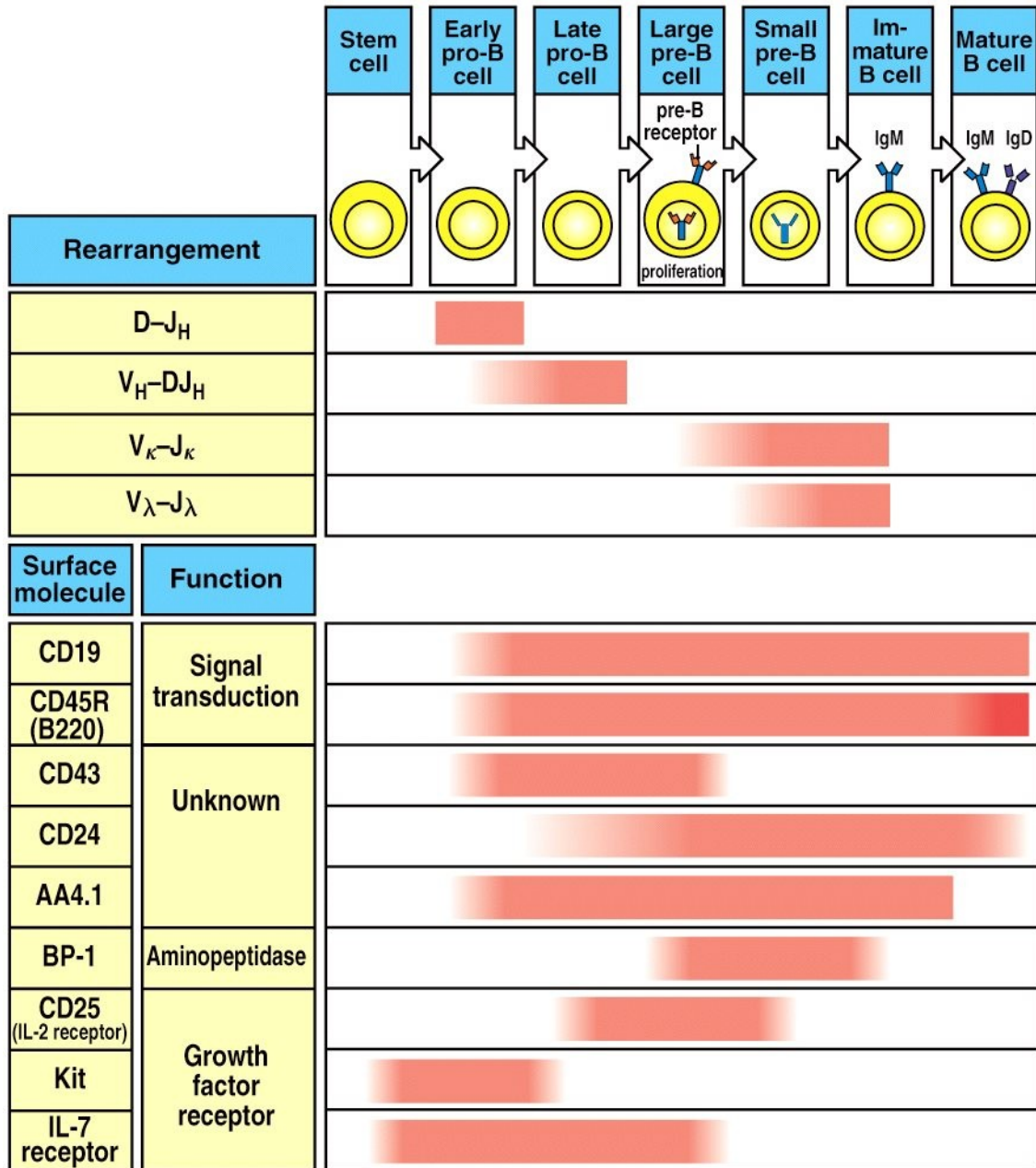
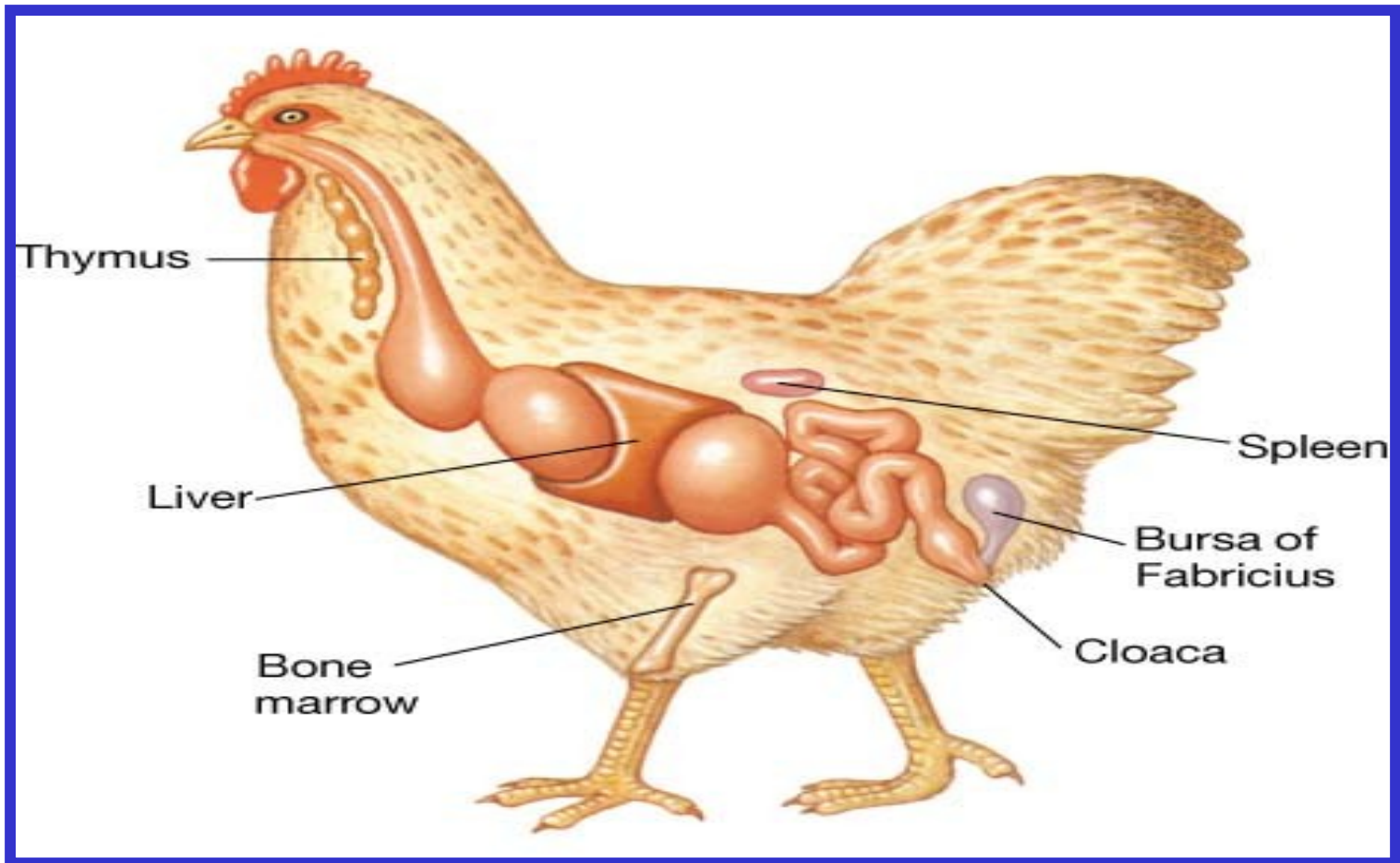


Figure 7-7 Immunobiology, 6/e. (© Garland Science 2005)

B cell development in chicken



The survival of a developing B cell

- Unproductive rearrangements
 - Gene rearrangements that cannot be translated into a protein.
- Productive rearrangements
 - Rearrangements that preserve a correct reading frame and give rise to a complete and functional immunoglobulin chain.

The survival of a developing B cell

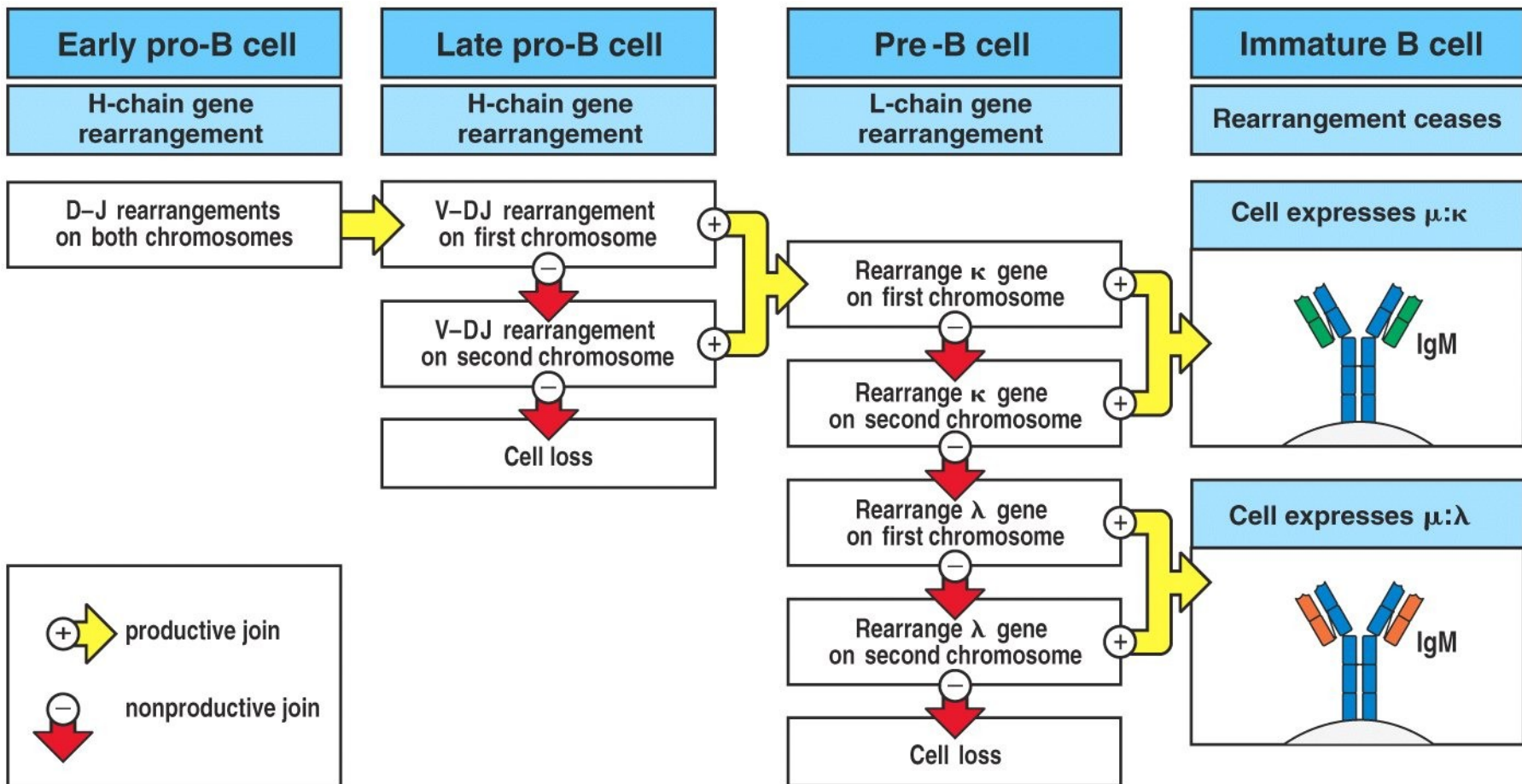


Figure 7-15 Immunobiology, 6/e. (© Garland Science 2005)

Cell-surface expression of the products of rearranged immunoglobulin genes

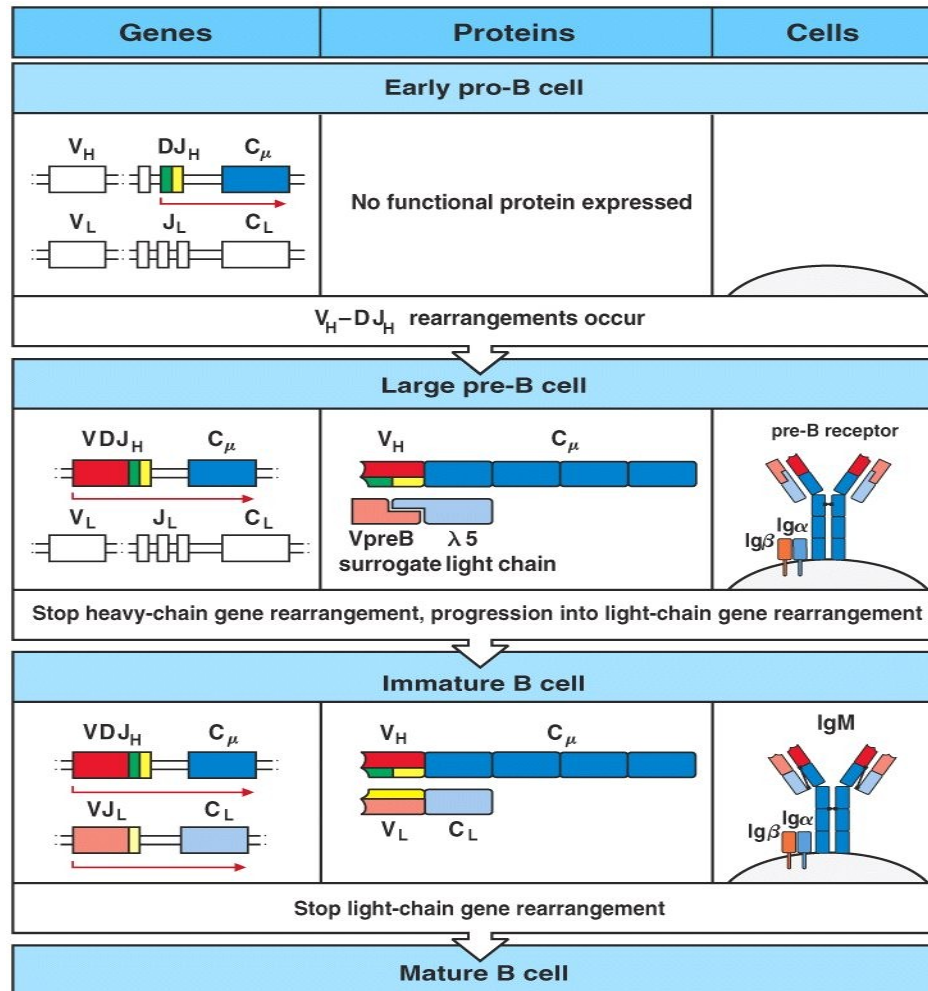
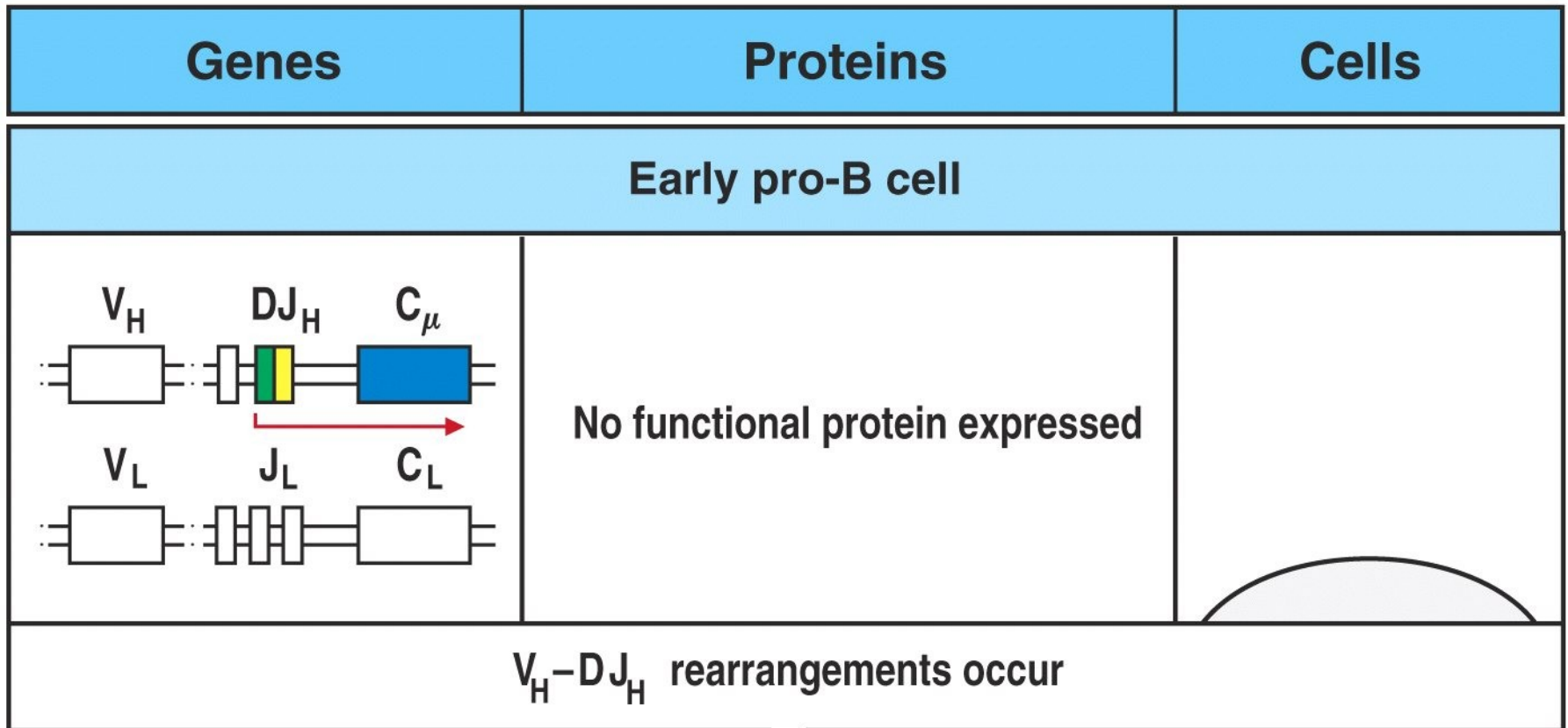


Figure 7-17 Immunobiology, 6/e. (© Garland Science 2005)

Cell-surface expression of the products of rearranged immunoglobulin genes cont.



Cell-surface expression of the products of rearranged immunoglobulin genes cont.

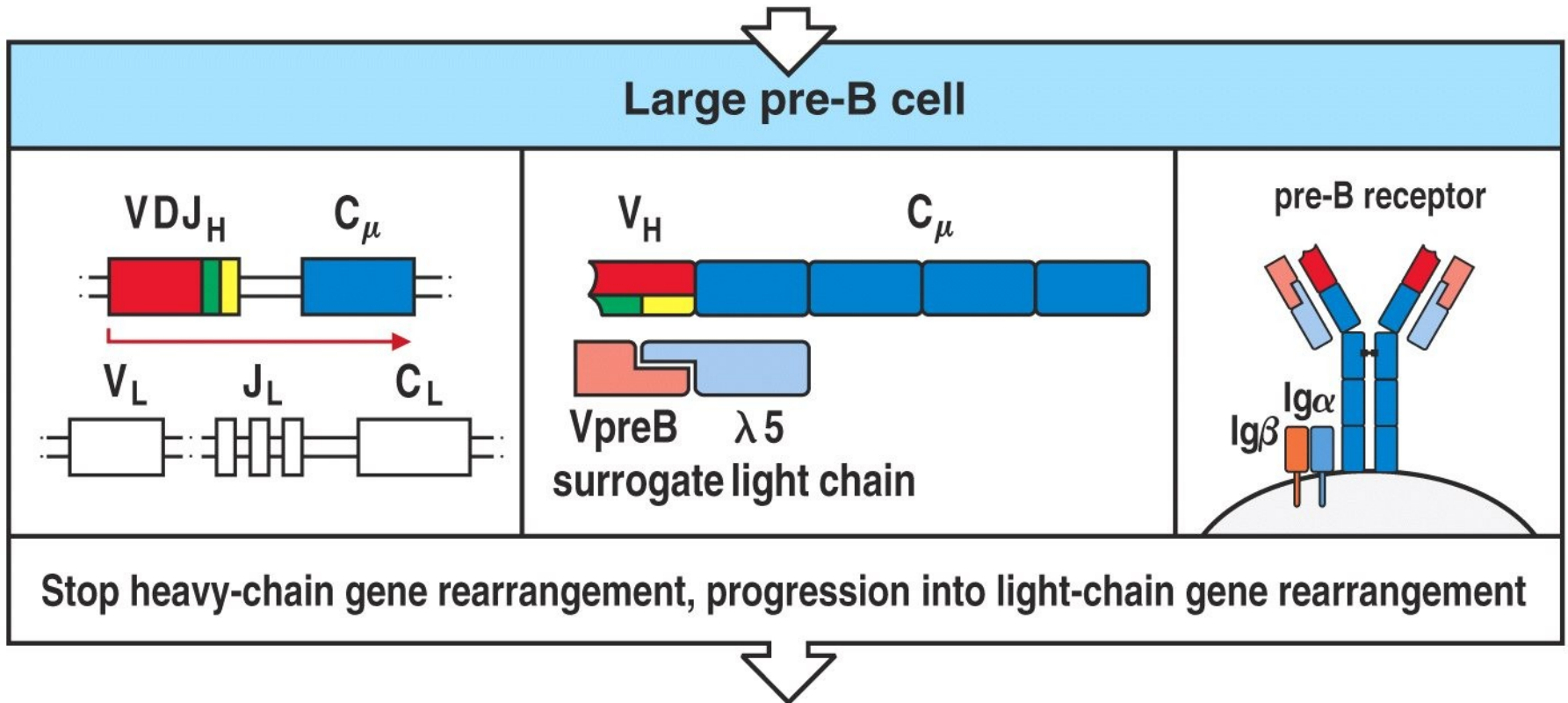


Figure 7-17 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Cell-surface expression of the products of

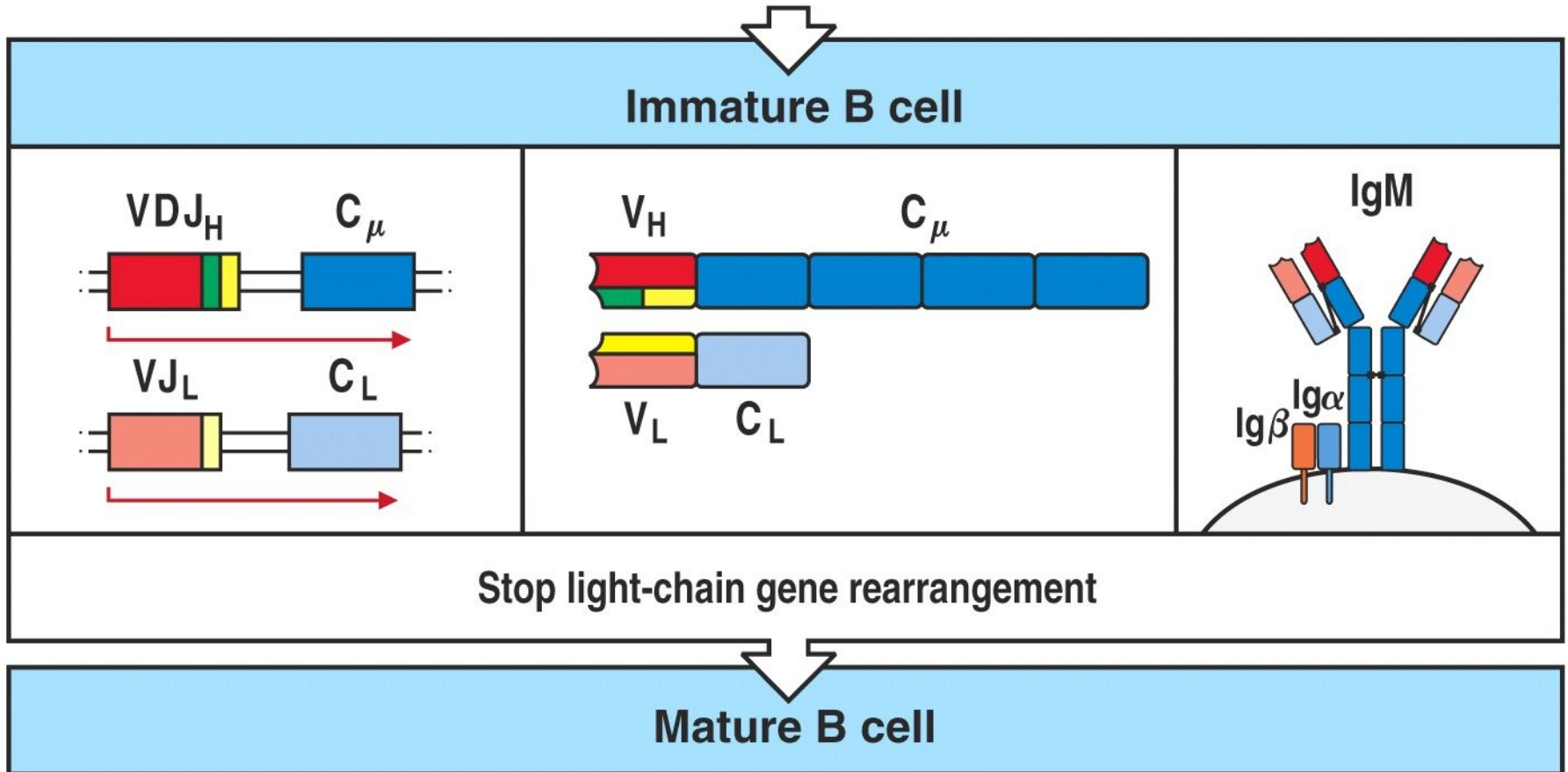


Figure 7-17 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Cell-surface expression of the products of rearranged immunoglobulin genes cont.

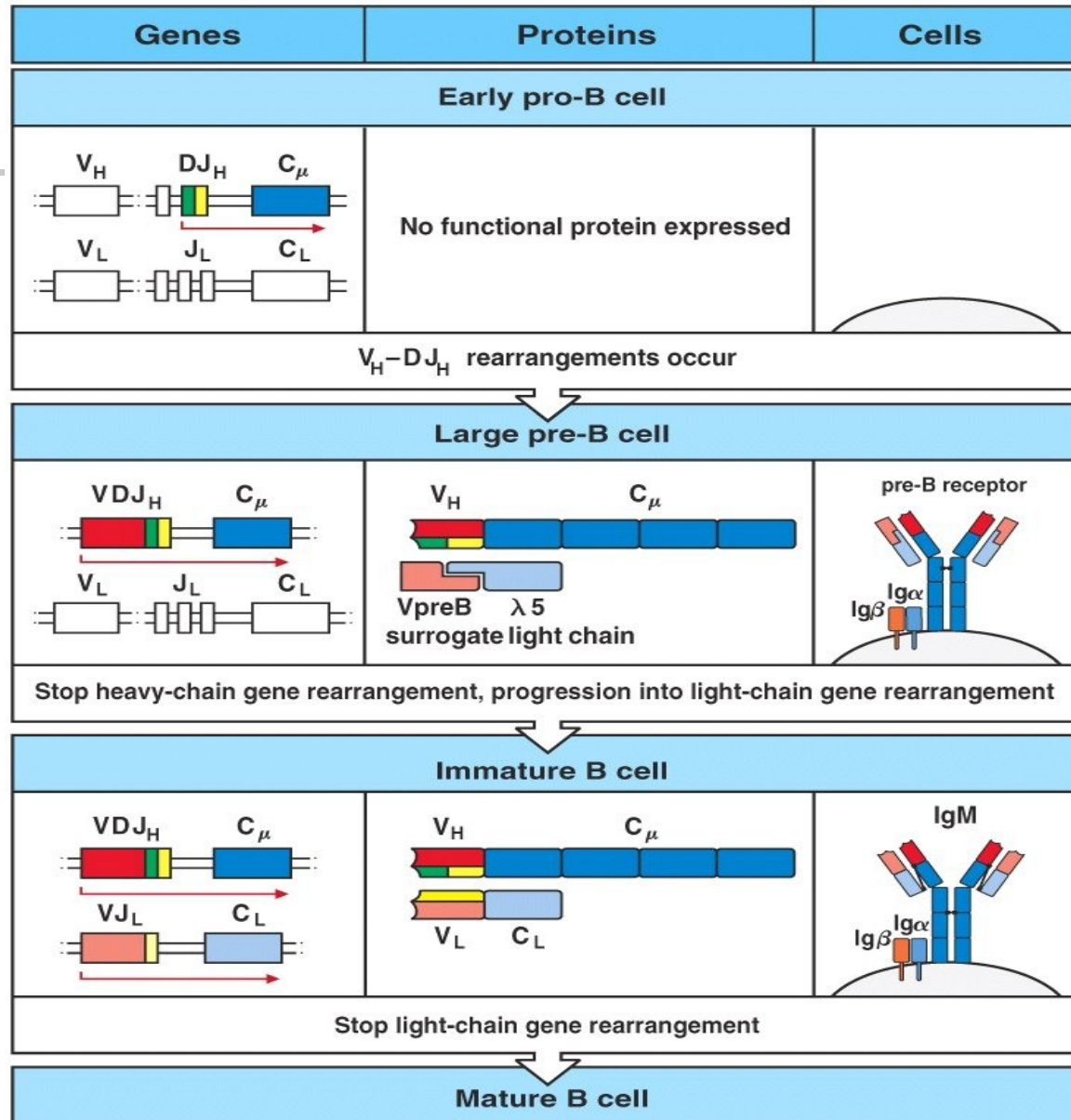


Figure 7-17 Immunobiology, 6/e. (© Garland Science 2005)

Repeated rearrangements are possible at the light-chain loci

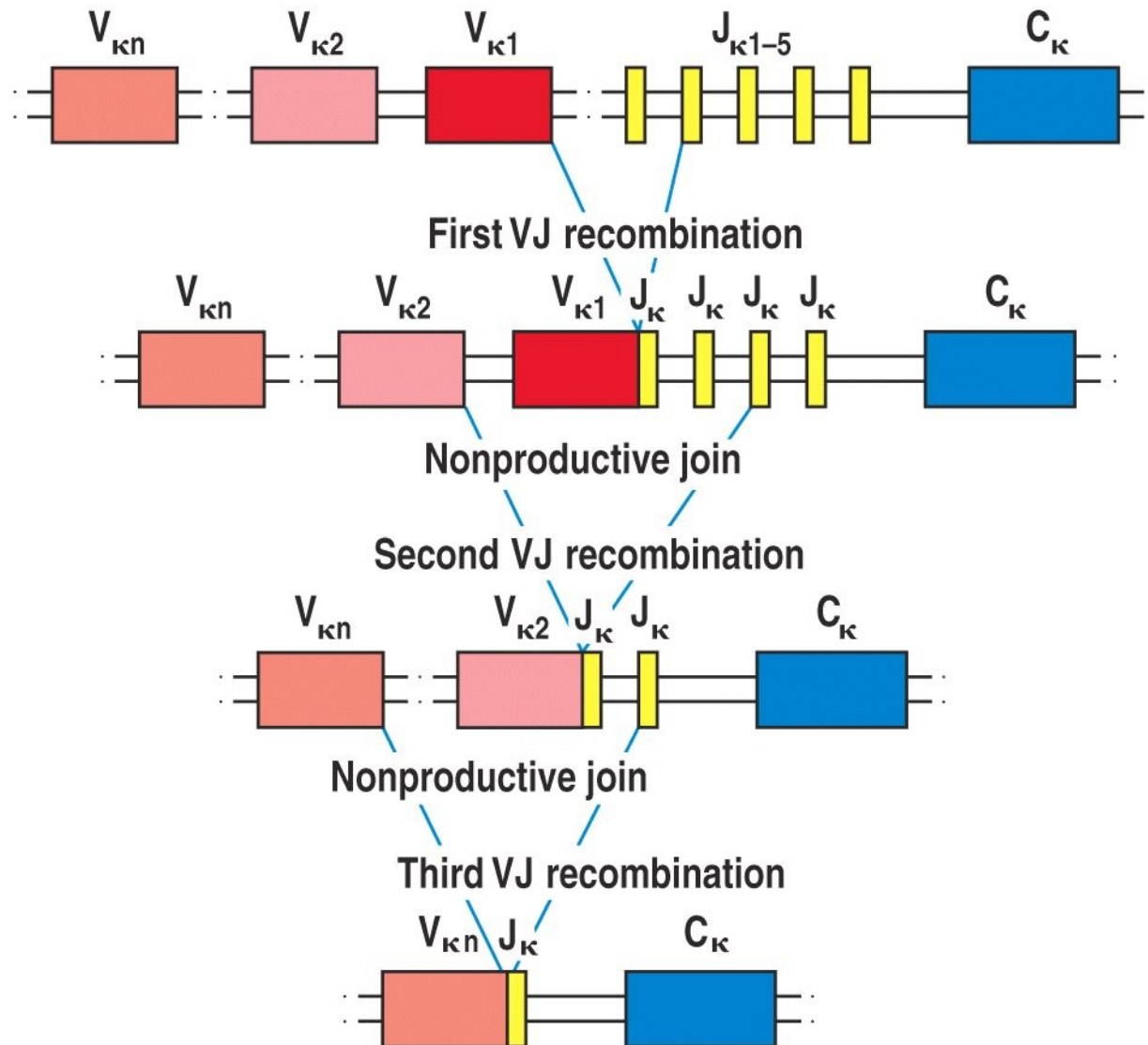


Figure 7-18 Immunobiology, 6/e. (© Garland Science 2005)

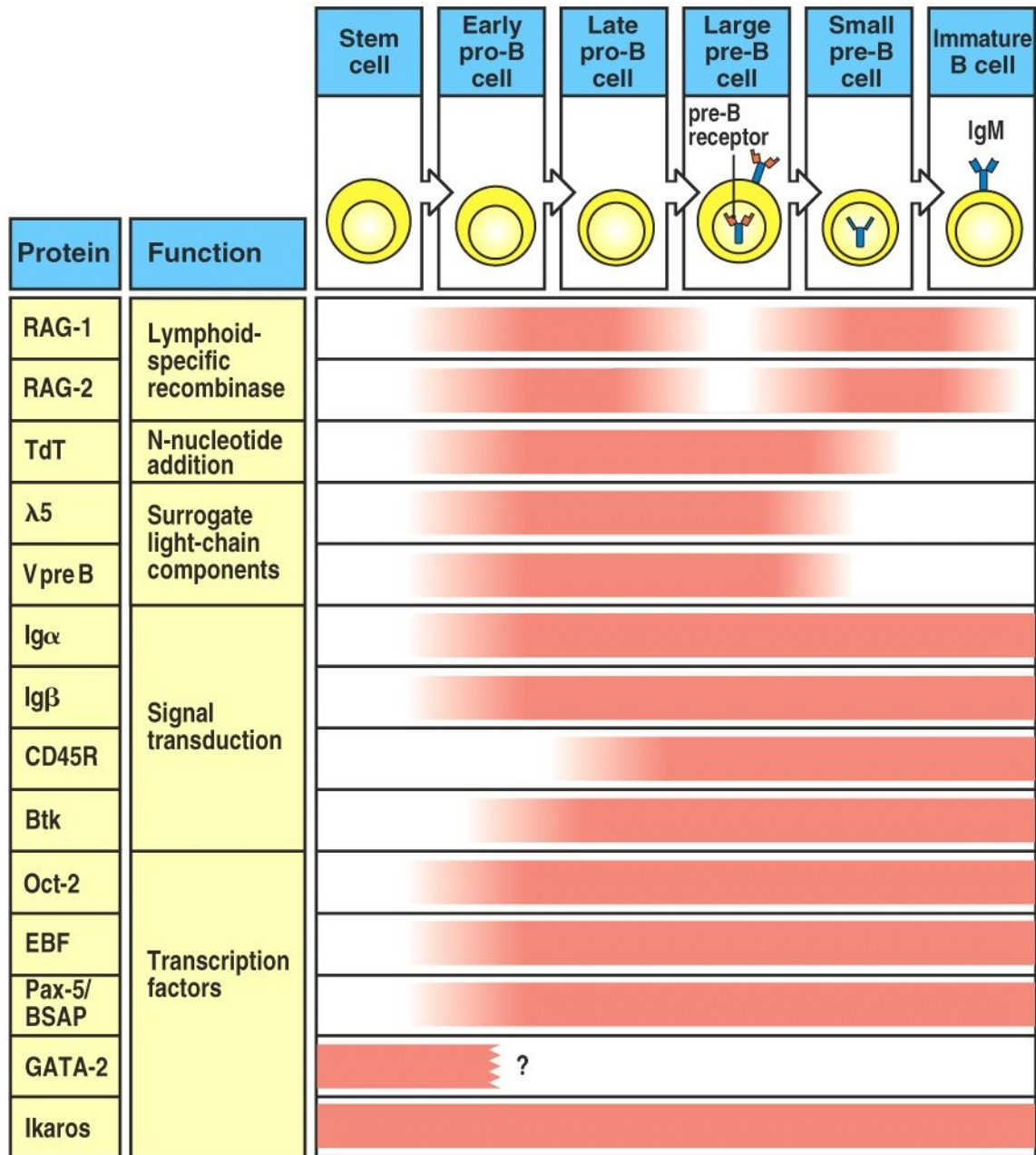


Figure 7-19 Immunobiology, 6/e. (© Garland Science 2005)

Selection and development of the B cell repertoire



Deletion or inactivation of immature B cells

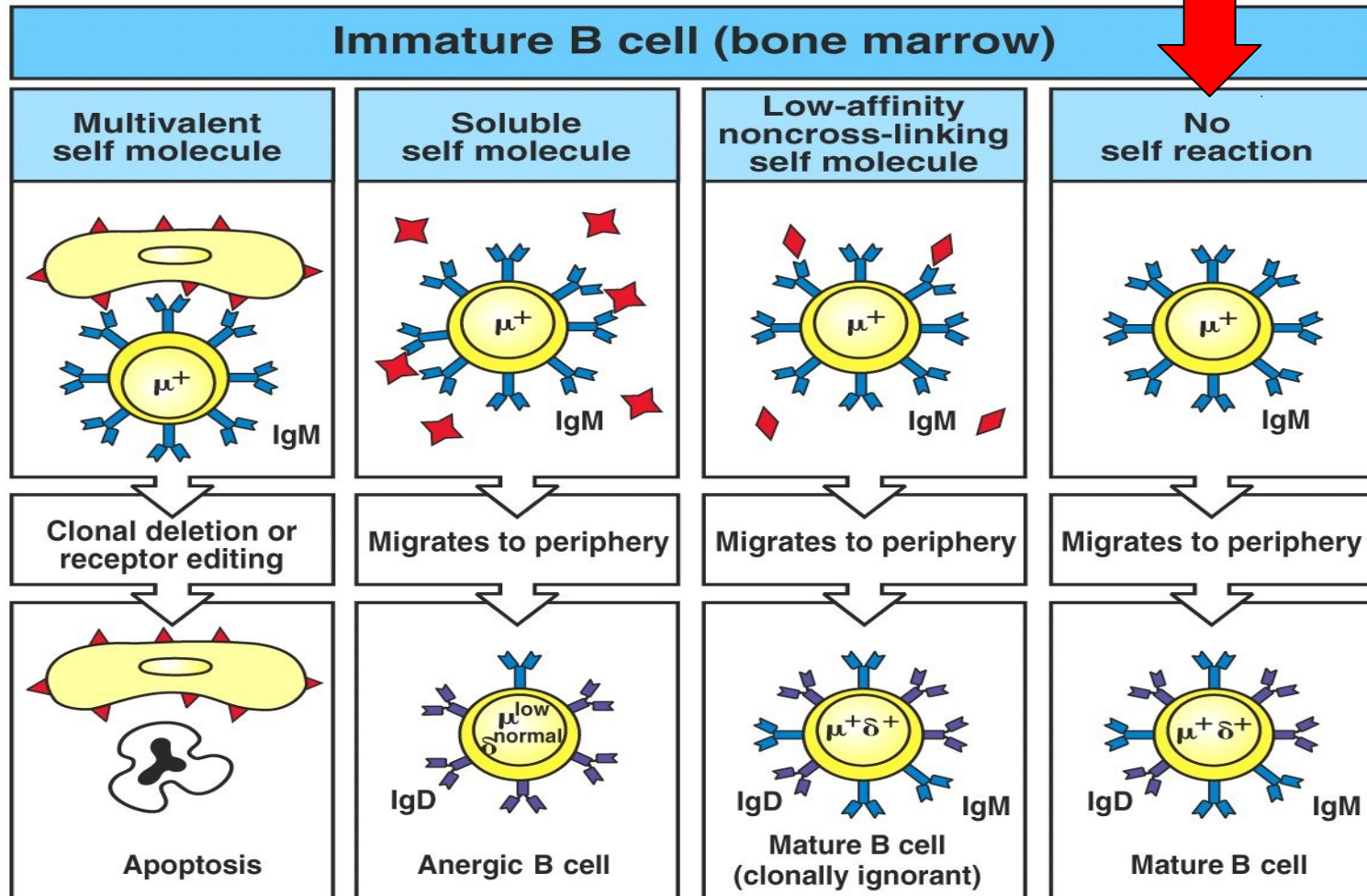


Figure 7-26 Immunobiology, 6/e. (© Garland Science 2005)



Self-antigens

- Mature B cells whose receptors bind to normal components (self-antigen) of the human body.
- If such B cells were allowed to mature they could make potentially disease-causing antibodies.
- Self-antigens:
 - Glycoproteins
 - Proteoglycans
 - Glycolipids

Deletion or inactivation of immature B cells cont.

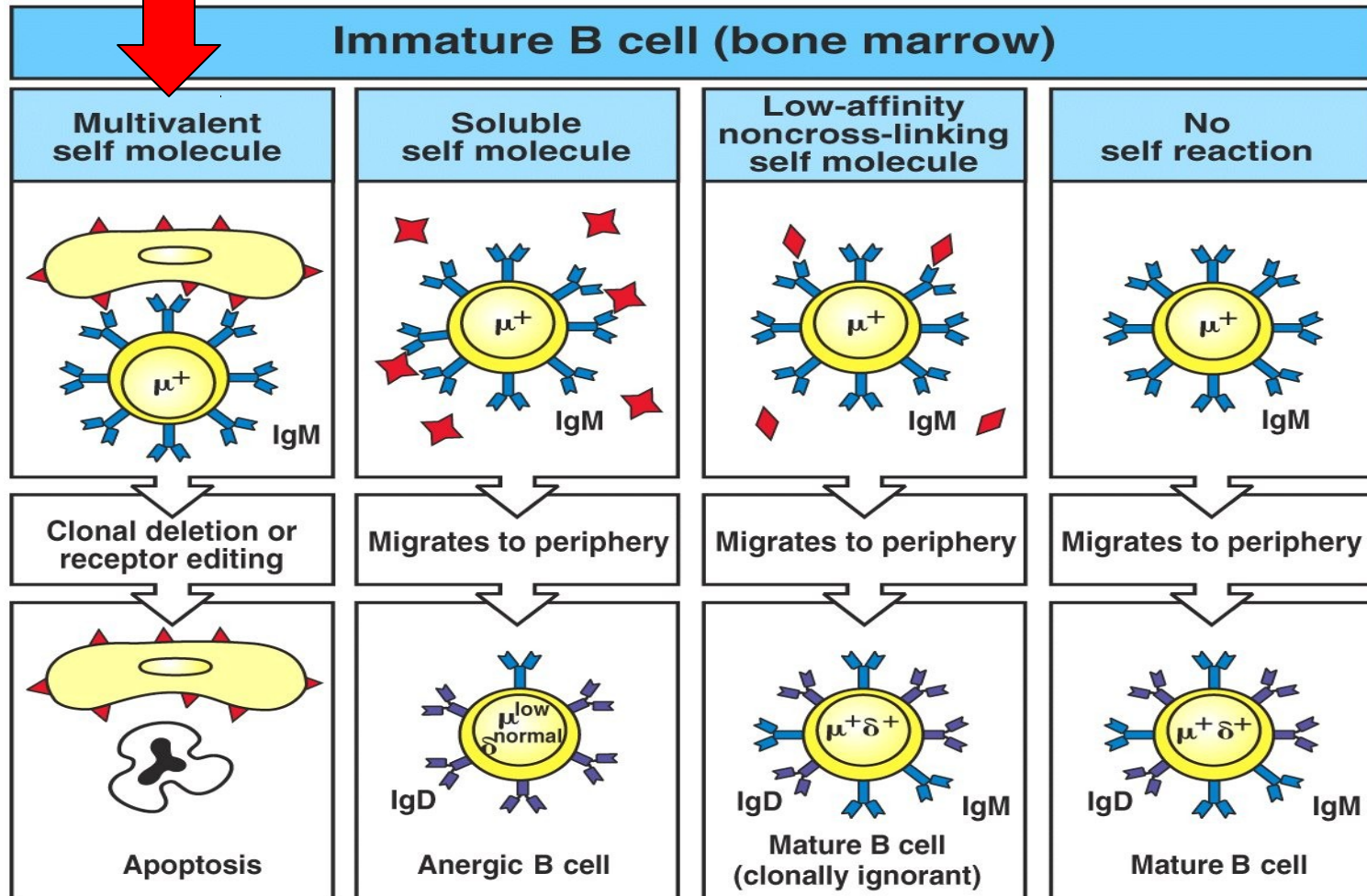


Figure 7-26 Immunobiology, 6/e. (© Garland Science 2005)

Deletion or inactivation of immature B cells cont.

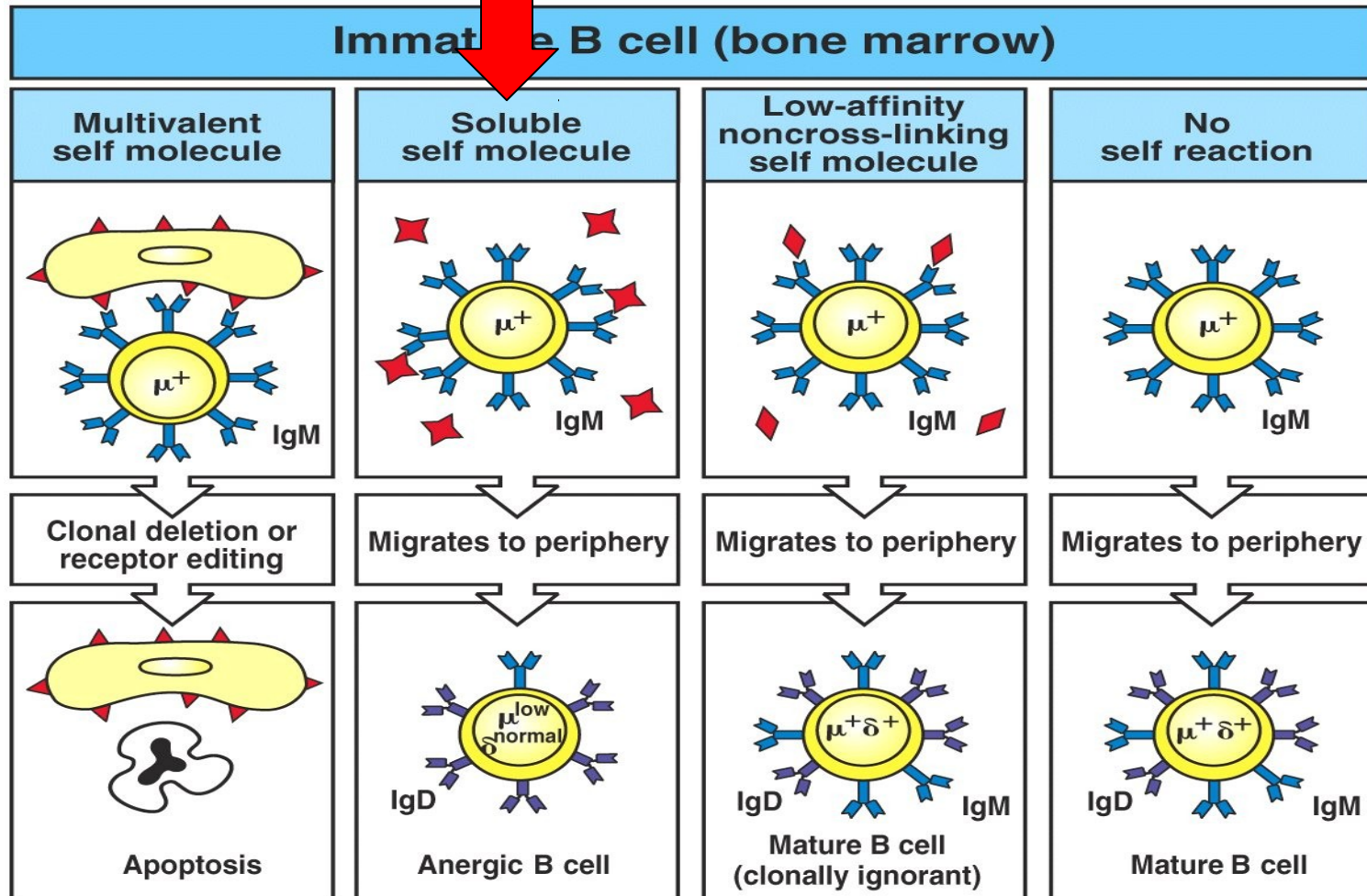


Figure 7-26 Immunobiology, 6/e. (© Garland Science 2005)

Self-reactive B cells

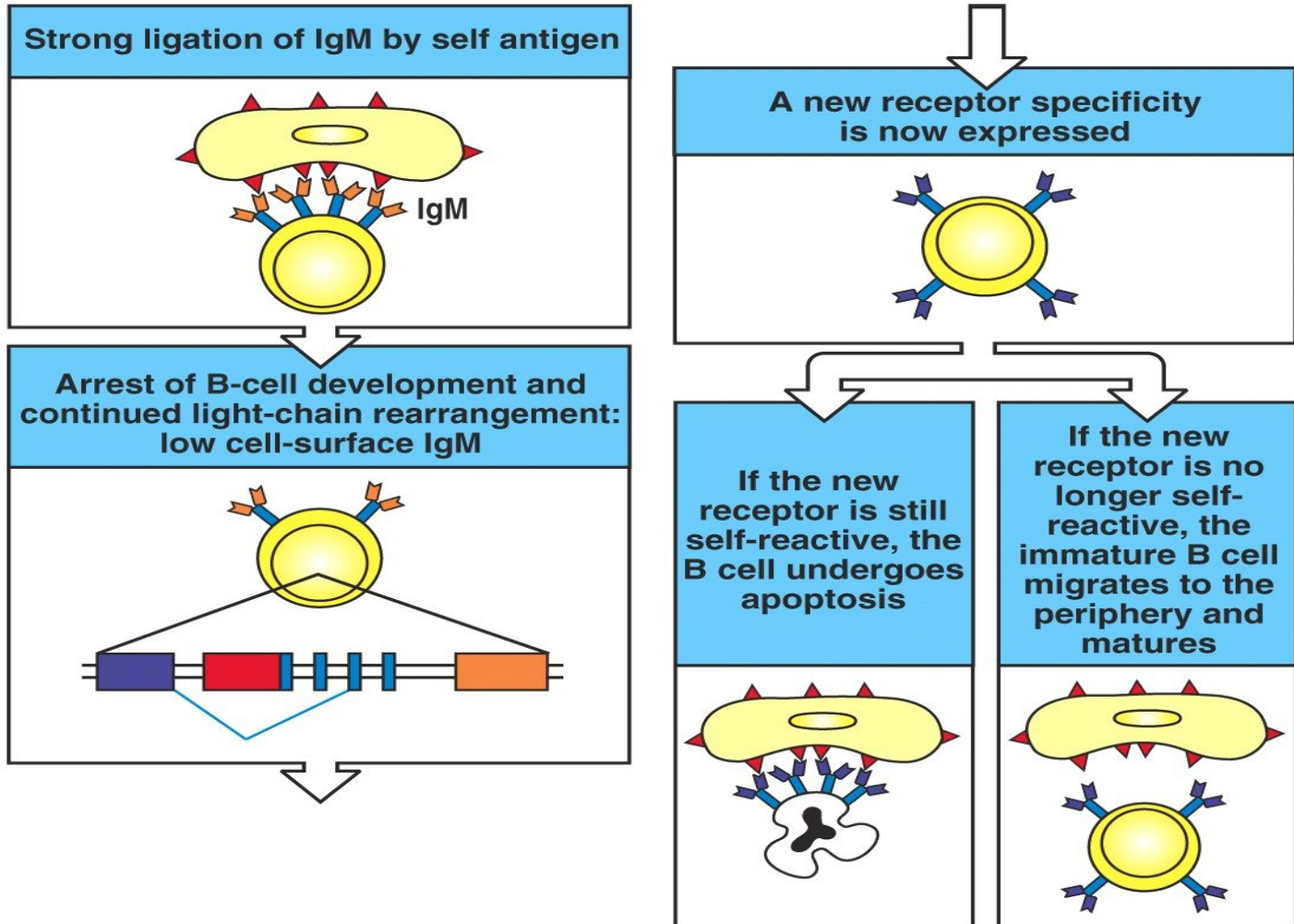
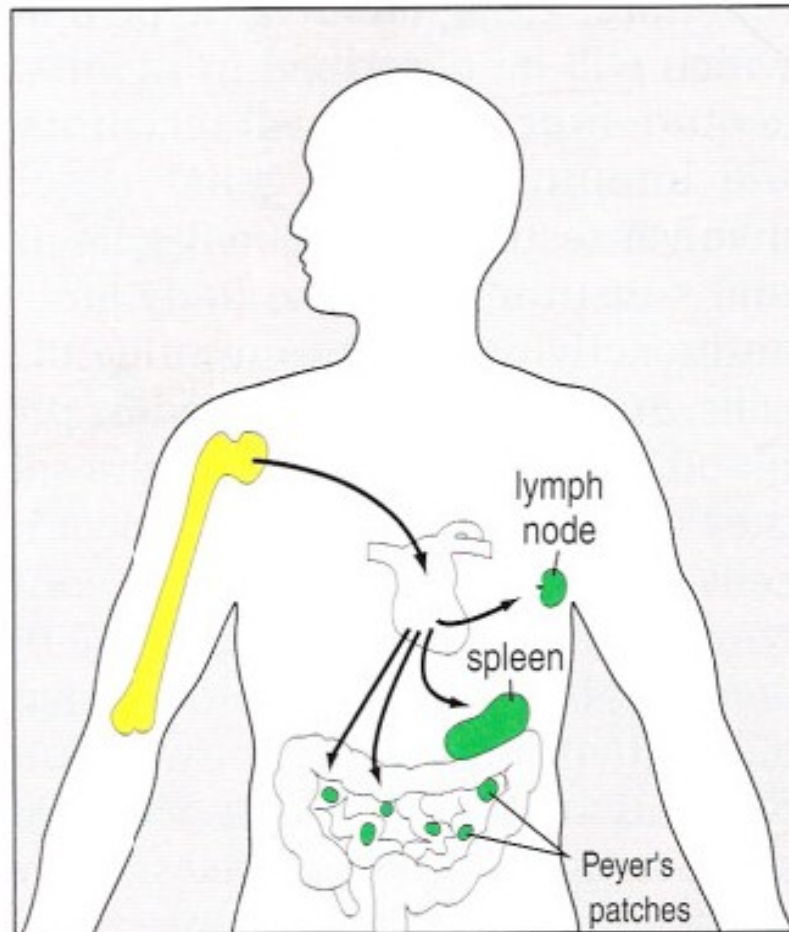
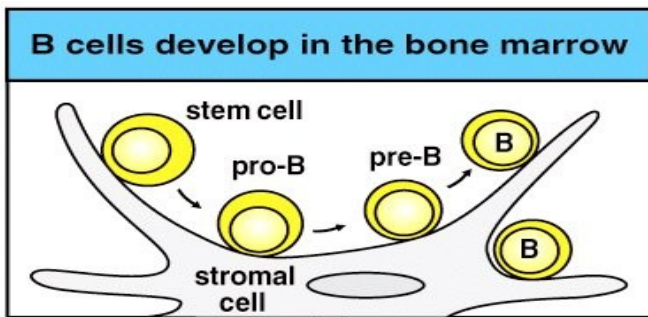


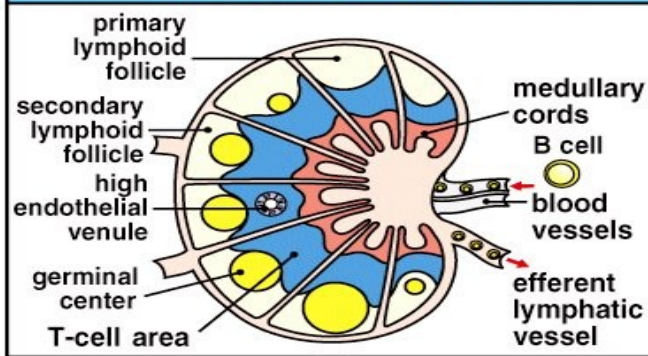
Figure 7-27 Immunobiology, 6/e. (© Garland Science 2005)

Mature and naïve B cells

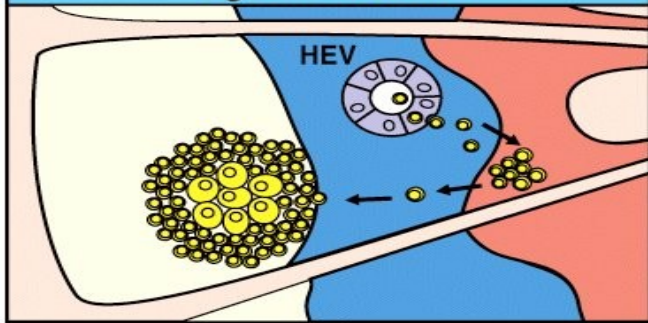




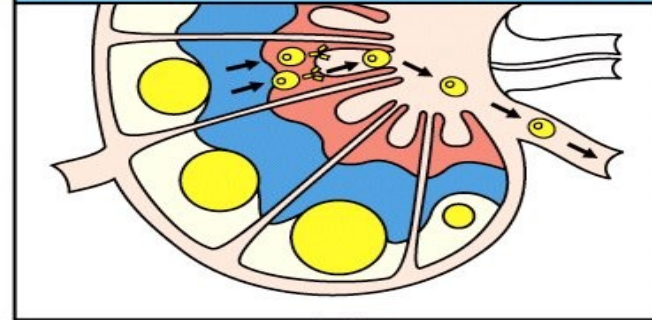
Mature B cells travel to the lymph node via the bloodstream and leave via the efferent lymph



B cells that encounter antigen at the T-cell/B-cell border become activated. They form primary foci in the medullary cords. Some cells then migrate to the primary follicle, forming a germinal center



Plasma cells migrate to the medullary cords or leave via the efferent lymphatics



Plasma cells migrate to the bone marrow

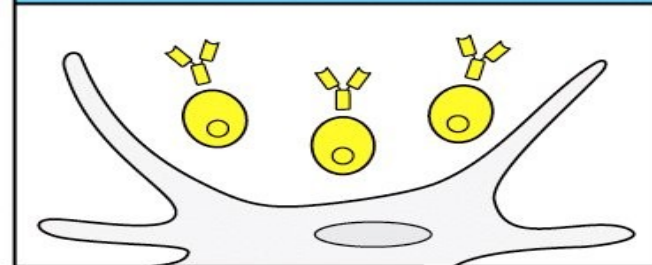


Figure 9-11 Immunobiology, 6/e. (© Garland Science 2005)

Mature and naïve B cells

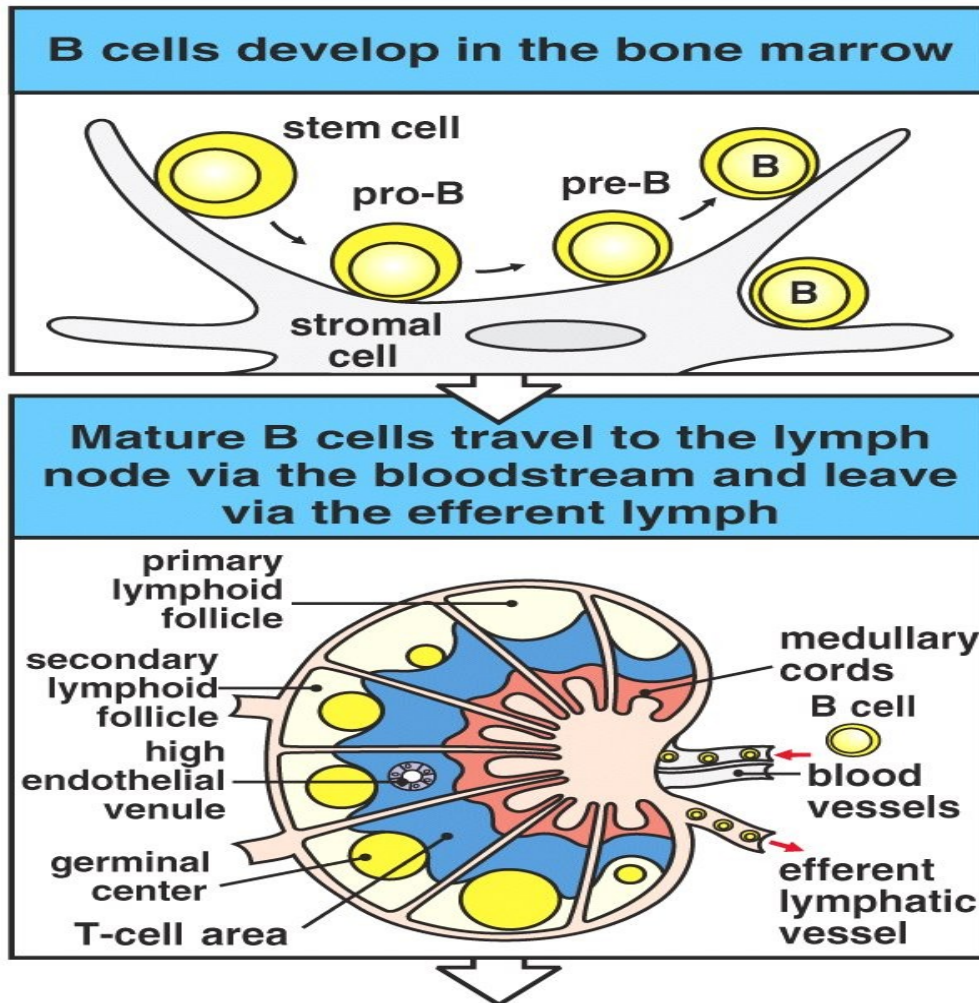


Figure 9-11 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

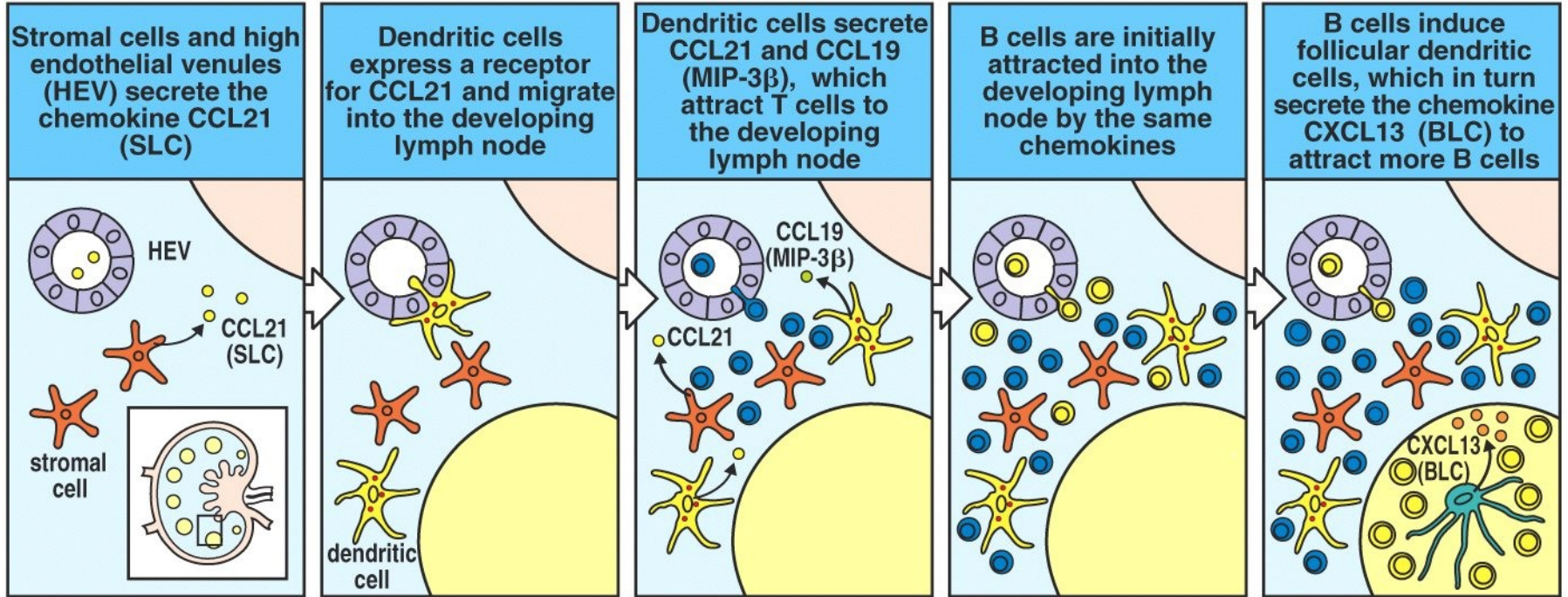
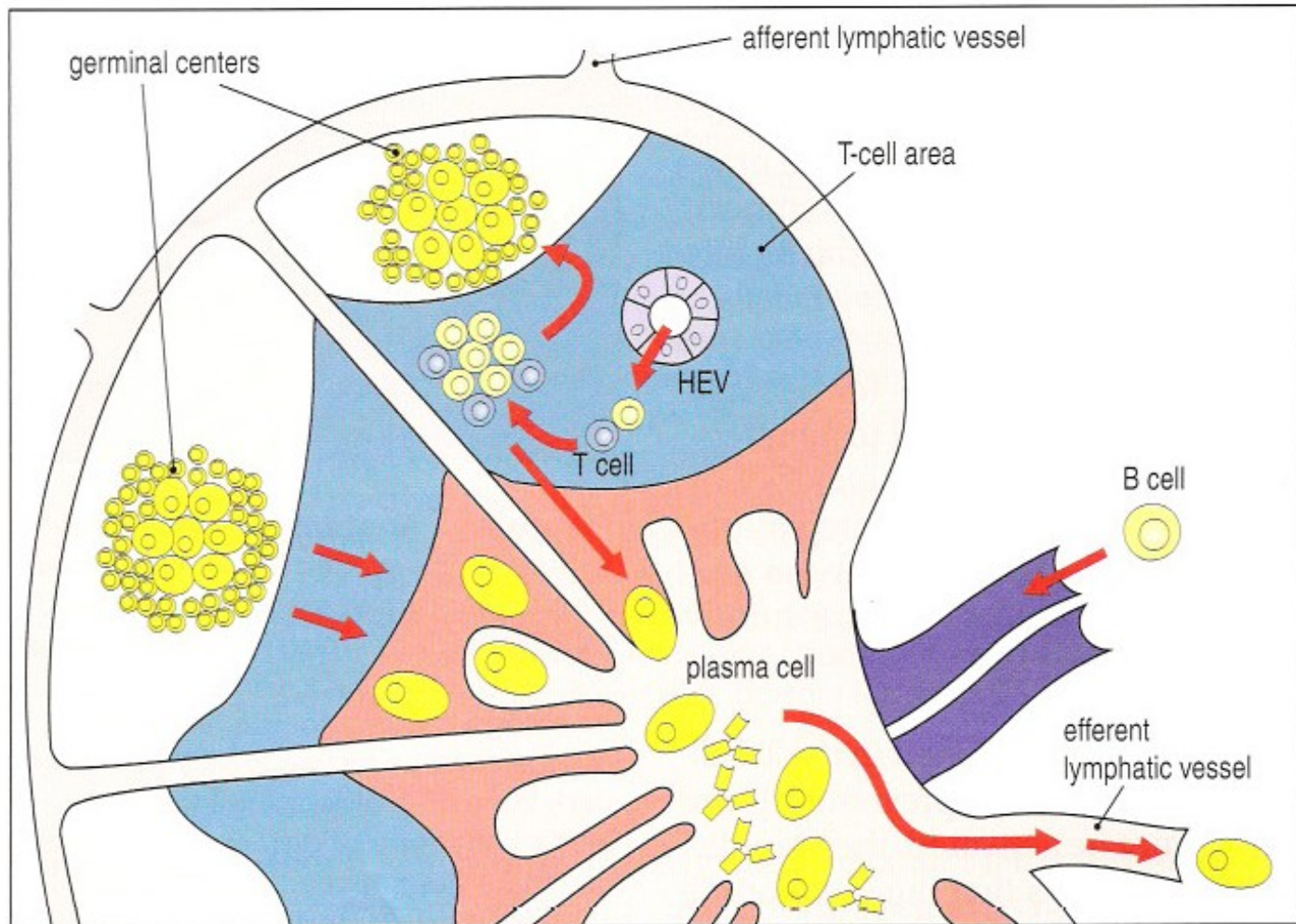


Figure 7-39 Immunobiology, 6/e. (© Garland Science 2005)

Encounter with antigen



Encounter with antigen

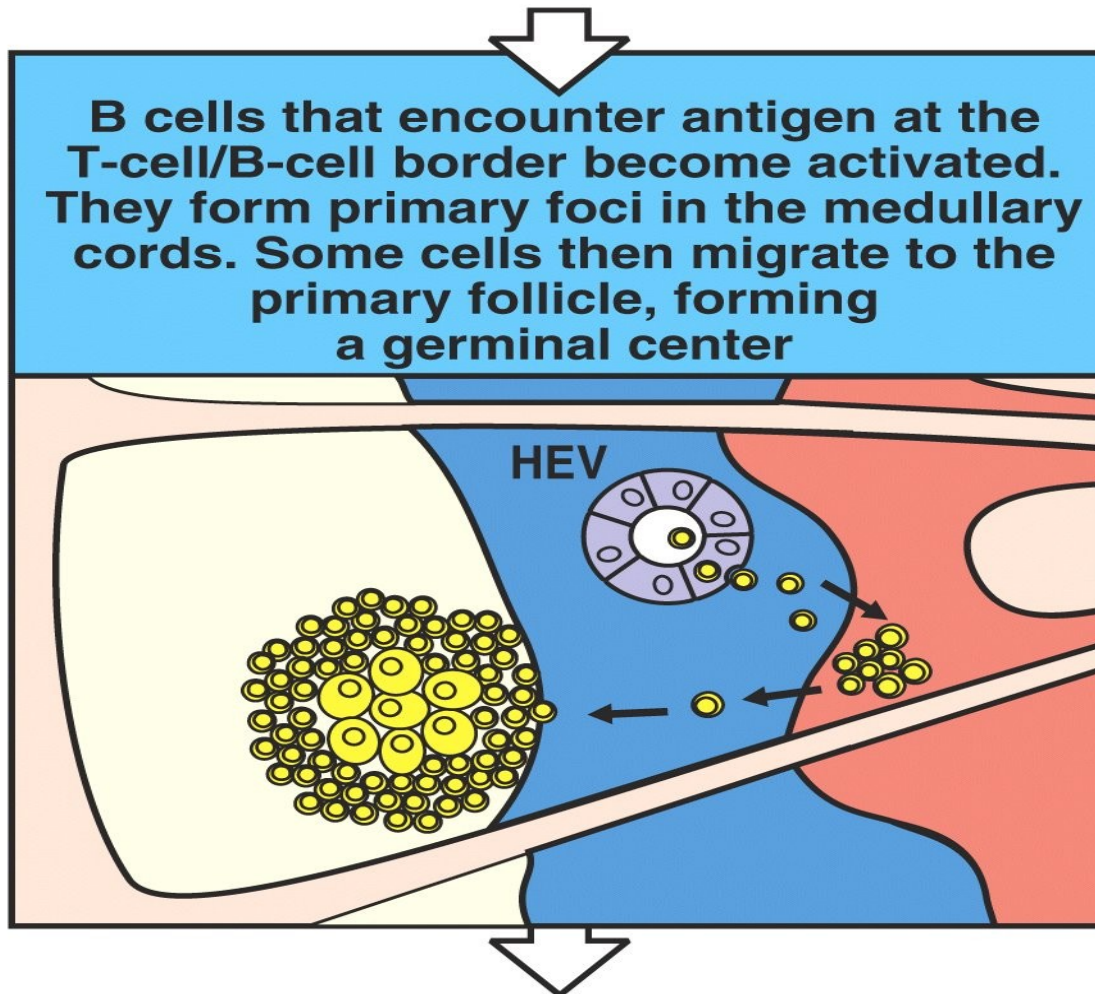


Figure 9-11 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Encounter with antigen

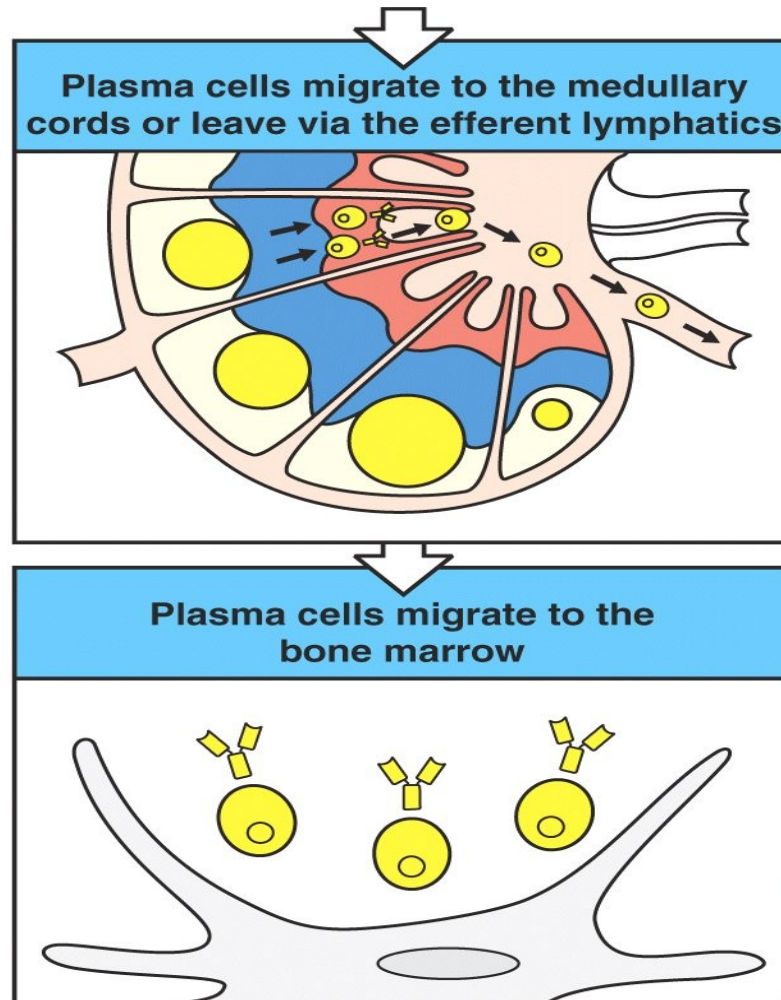


Figure 9-11 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)



Memory cells

- Persist for long periods of time.
- They are much more easily activated on encountering antigen than naïve B cells.
- Rapid activation and differentiation into plasma cells (secondary antibody response). More quickly and stronger than the primary immune response.



Plasma cells

B cells



Plasma cells








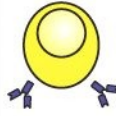
Name of tumor	Normal cell equivalent		Location	Status of Ig V genes
Acute lymphoblastic leukemia	Lymphoid progenitor		Bone marrow and blood	Unmutated
Pre-B cell leukemia	Pre-B cell			Unmutated
Mantle cell lymphoma	Resting naive B cell		Periphery	Unmutated
Chronic lymphocytic leukemia (CLL)	Activated or memory B cell			Usually unmutated
Follicular center cell lymphoma Burkitt's lymphoma	Mature memory B cell Resembles germinal center B cell			Mutated, intracлонаl variability
Hodgkin's lymphoma	Germinal center B cell			Mutated +/- intracлонаl variability
Waldenström's macroglobulinemia	IgM-secreting B cell			Mutated, no variability within clone
Multiple myeloma	Plasma cell. Various isotypes			Bone marrow

Figure 7-42 Immunobiology, 6/e. (© Garland Science 2005)



Summary

Summary

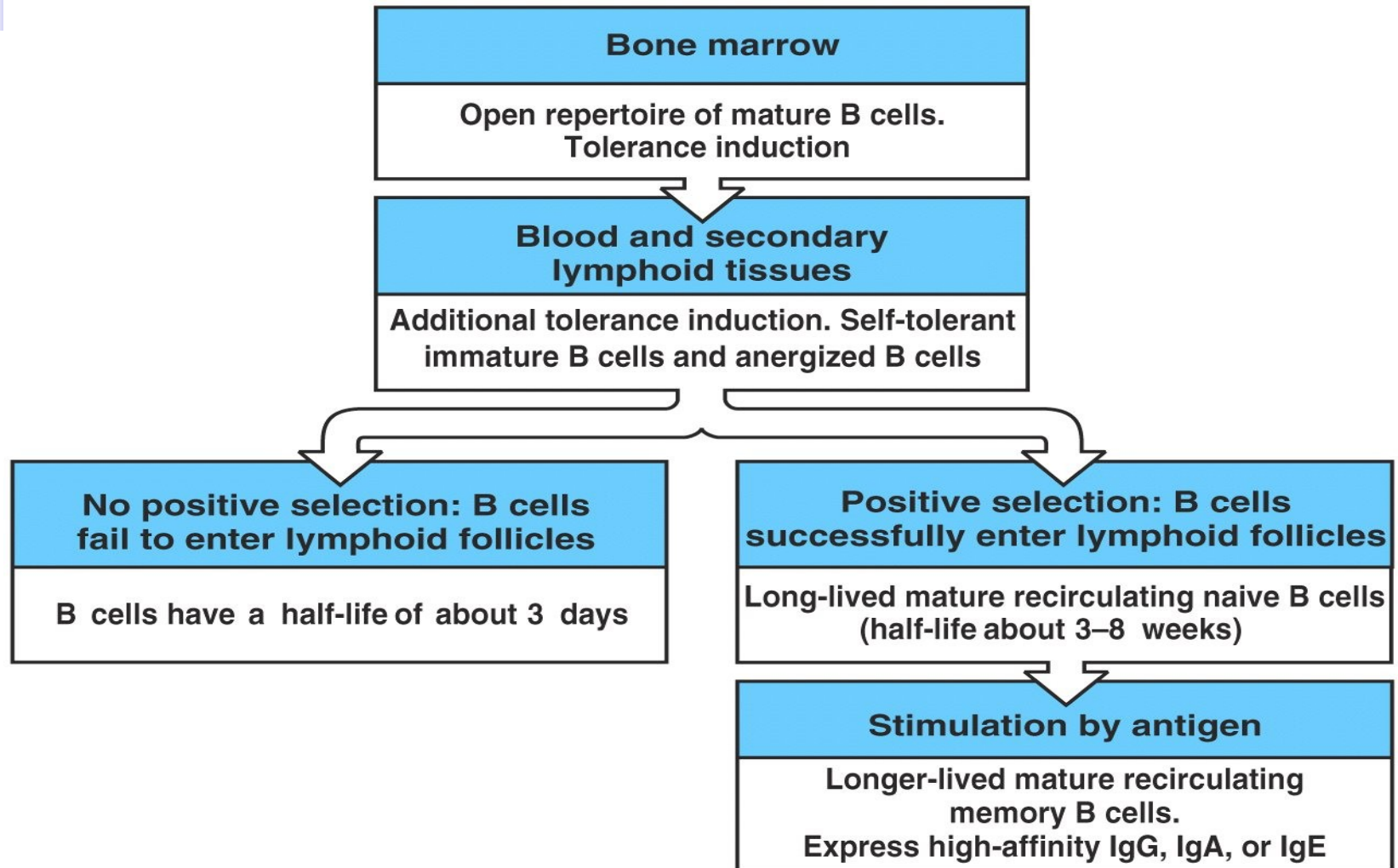


Figure 7-40 Immunobiology, 6/e. (© Garland Science 2005)

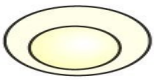
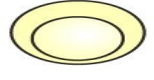

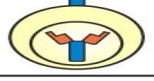

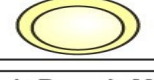




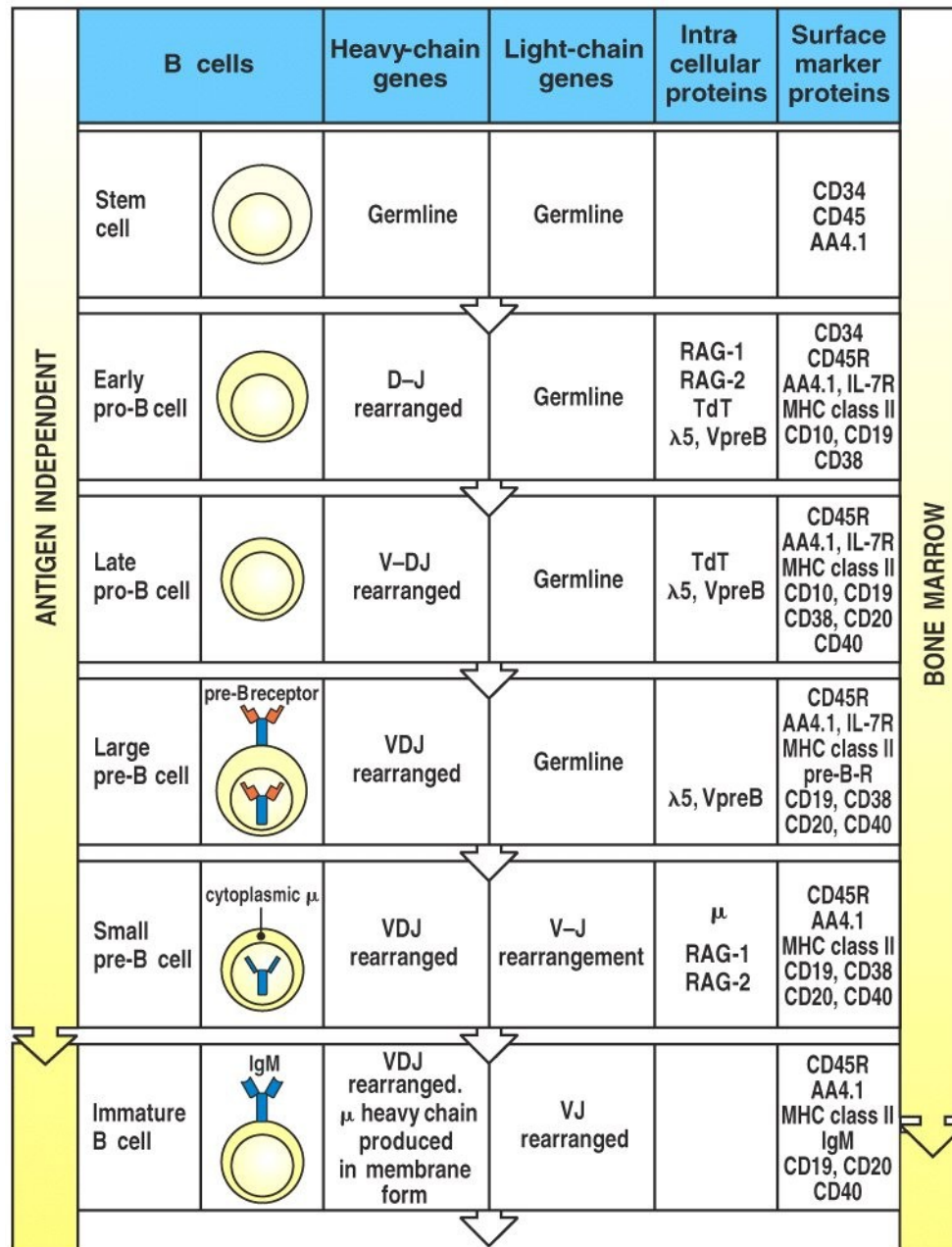
		B cells	Heavy-chain genes	Light-chain genes	Intra cellular proteins	Surface marker proteins		
ANTIGEN INDEPENDENT	Stem cell		Germline	Germline		CD34 CD45 AA4.1	BONE MARROW	
	Early pro-B cell		D-J rearranged	Germline	RAG-1 RAG-2 TdT λ 5, VpreB	CD34 CD45R AA4.1, IL-7R MHC class II CD10, CD19 CD38		
	Late pro-B cell		V-DJ rearranged	Germline	TdT λ 5, VpreB	CD45R AA4.1, IL-7R MHC class II CD10, CD19 CD38, CD20 CD40		
	Large pre-B cell	pre-B receptor 	VDJ rearranged	Germline	λ 5, VpreB	CD45R AA4.1, IL-7R MHC class II pre-B-R CD19, CD38 CD20, CD40		
	Small pre-B cell	cytoplasmic μ 	VDJ rearranged	V-J rearrangement	μ RAG-1 RAG-2	CD45R AA4.1 MHC class II CD19, CD38 CD20, CD40		
ANTIGEN DEPENDENT	Immature B cell	IgM 	VDJ rearranged. μ heavy chain produced in membrane form	VJ rearranged		CD45R AA4.1 MHC class II IgM CD19, CD20 CD40	PERIPHERY	
	Mature naive B cell	IgD IgM 	VDJ rearranged. μ chain produced in membrane form. Alternative splicing yields $\mu + \delta$ mRNA			CD45R MHC class II IgM, IgD CD19, CD20 CD21, CD40		
	Lymphoblast	IgM 	Alternative splicing yields secreted μ chains		Ig	CD45R MHC class II CD19, CD20 CD21, CD40		
	Memory B cell	IgG 	Isotype switch to C γ , C α , or C ϵ . Somatic hypermutation	Somatic hypermutation		CD45R MHC class II IgG, IgA CD19, CD20 CD21, CD40		
TERMINAL DIFFERENTIATION	Plasma blast and Plasma cell	IgG 	Alternative splicing yields both membrane and secreted Ig	VJ rearranged	Ig	CD135 Plasma cell antigen-1 CD38		

Figure 7-46 Immunobiology, 6/e. (© Garland Science 2005)



BONE MARROW

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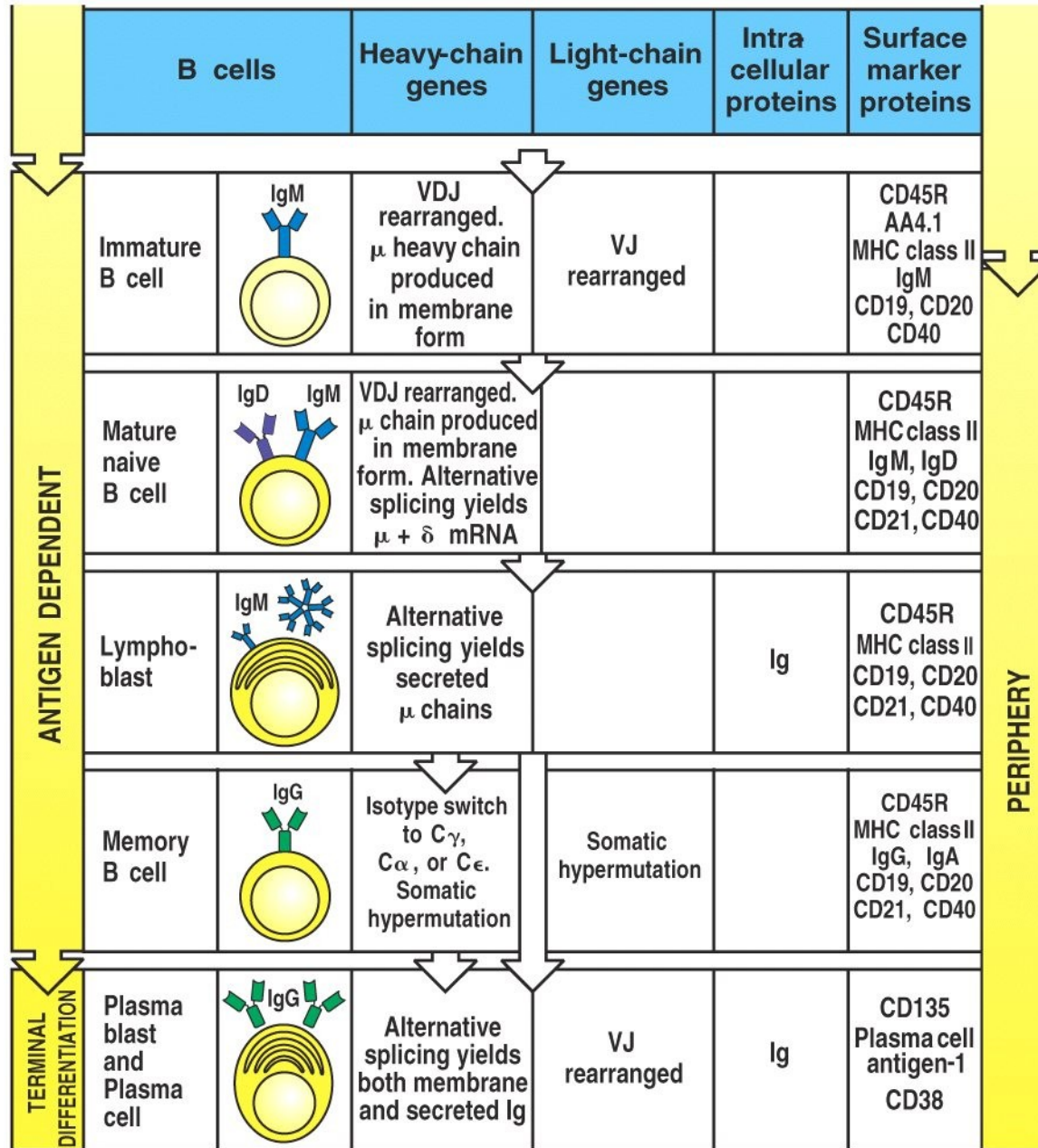


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