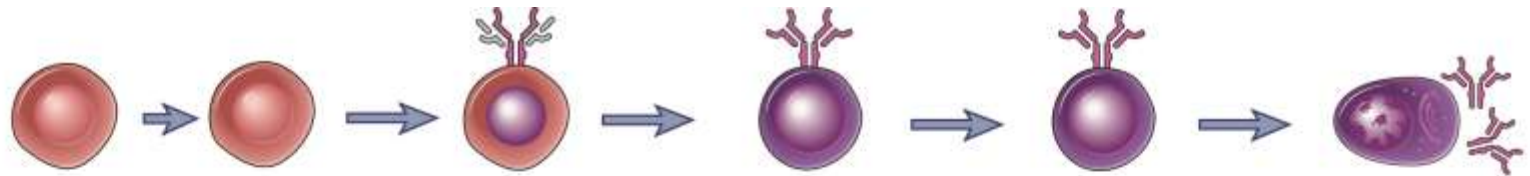




Stages of Lymphocyte Maturation



Stage of Maturation	Stem cell	Pro-lymphocyte	Pre-lymphocyte	Immature lymphocyte	Mature lymphocyte	Differentiated effector lymphocyte
Major Events	Growth factor mediated commitment, expansion; initiation of antigen receptor gene rearrangement		Selection of cells that express pre-antigen receptors	Selection of repertoire and acquisition of functional competence	Initial responders	Performance of effector functions
Anatomic Site	Generative organ (bone marrow or thymus)				Peripheral lymphoid organ or tissue	
Antigen Dependence	No			Self antigen	Foreign antigen	

Fig. 8-1

Distinct Lineages of Lymphocyte Maturation

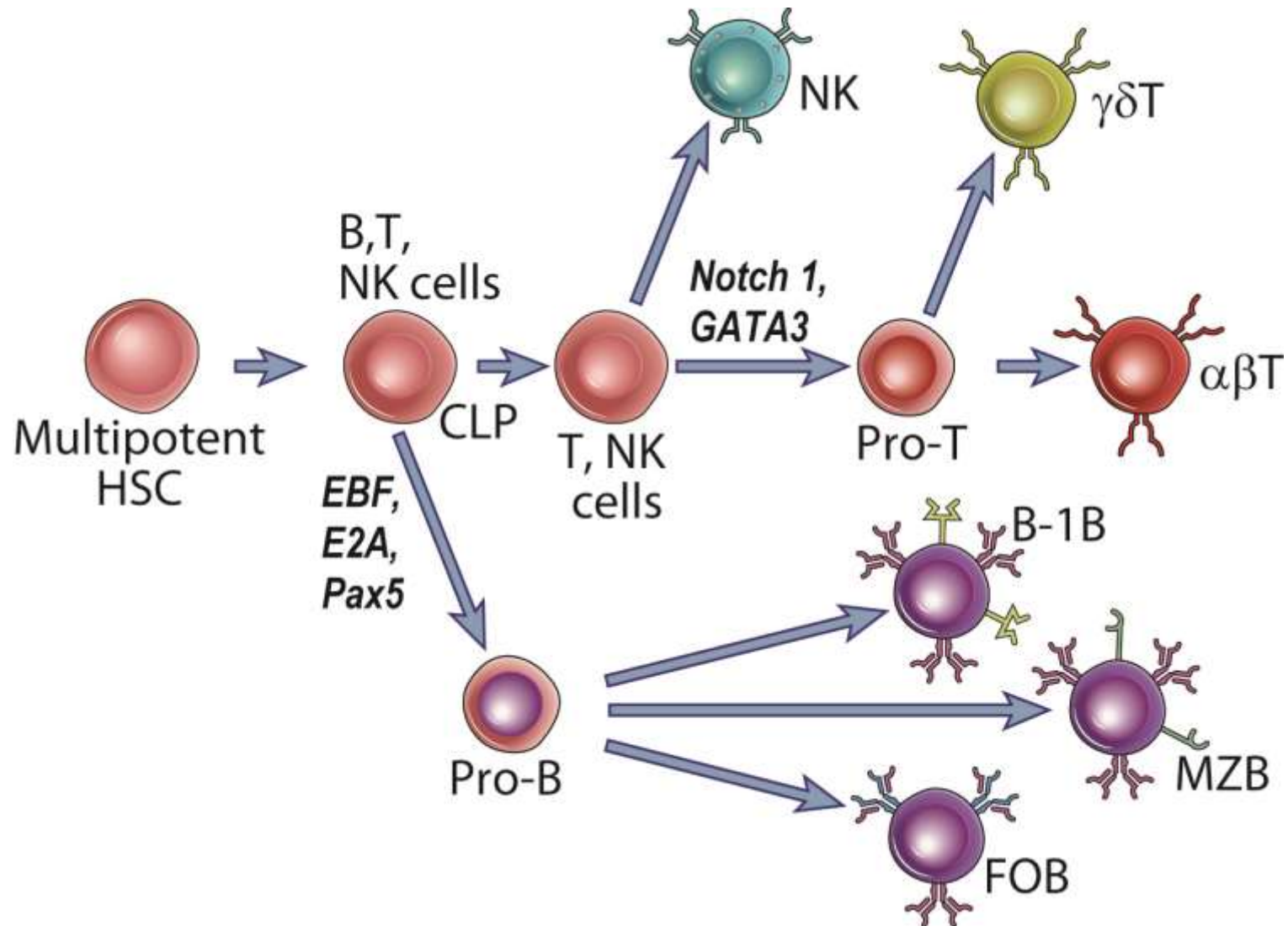


Fig. 8-2

Checkpoints in Lymphocyte Maturation

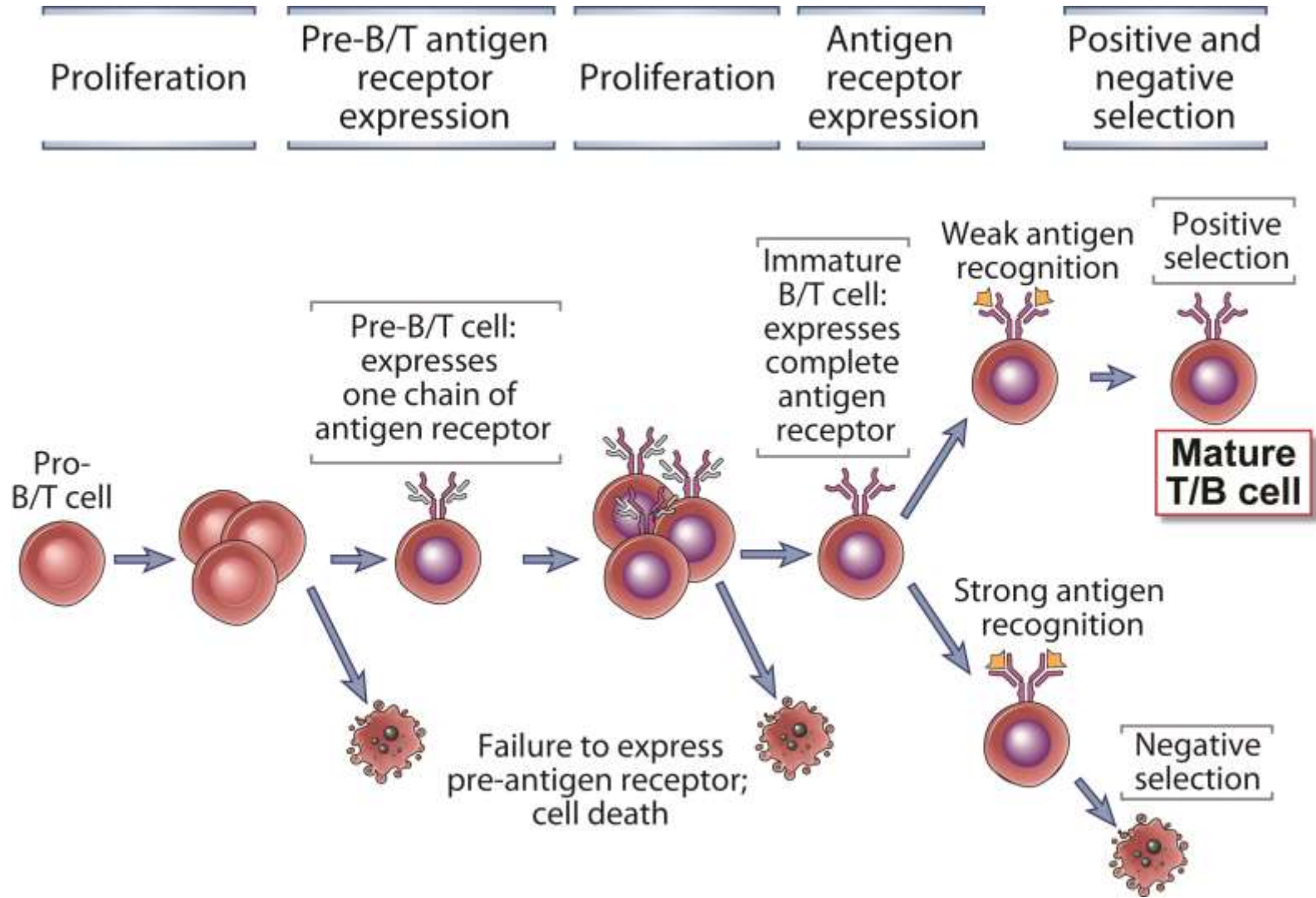


Fig. 8-3



Pos. and Neg. Selection of Lymphocytes

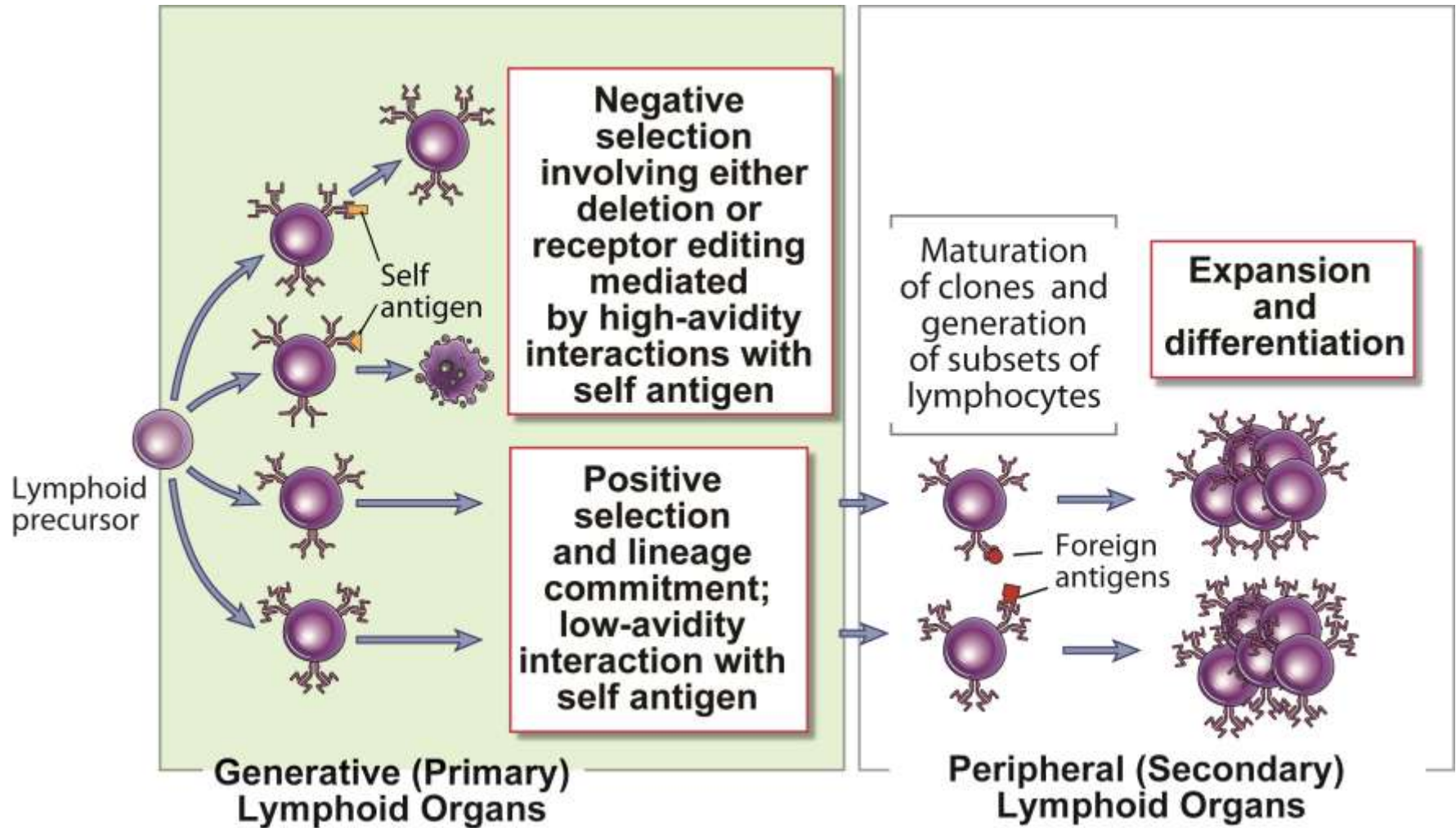


Fig. 8-4



Germline Organization of Human Ig Loci

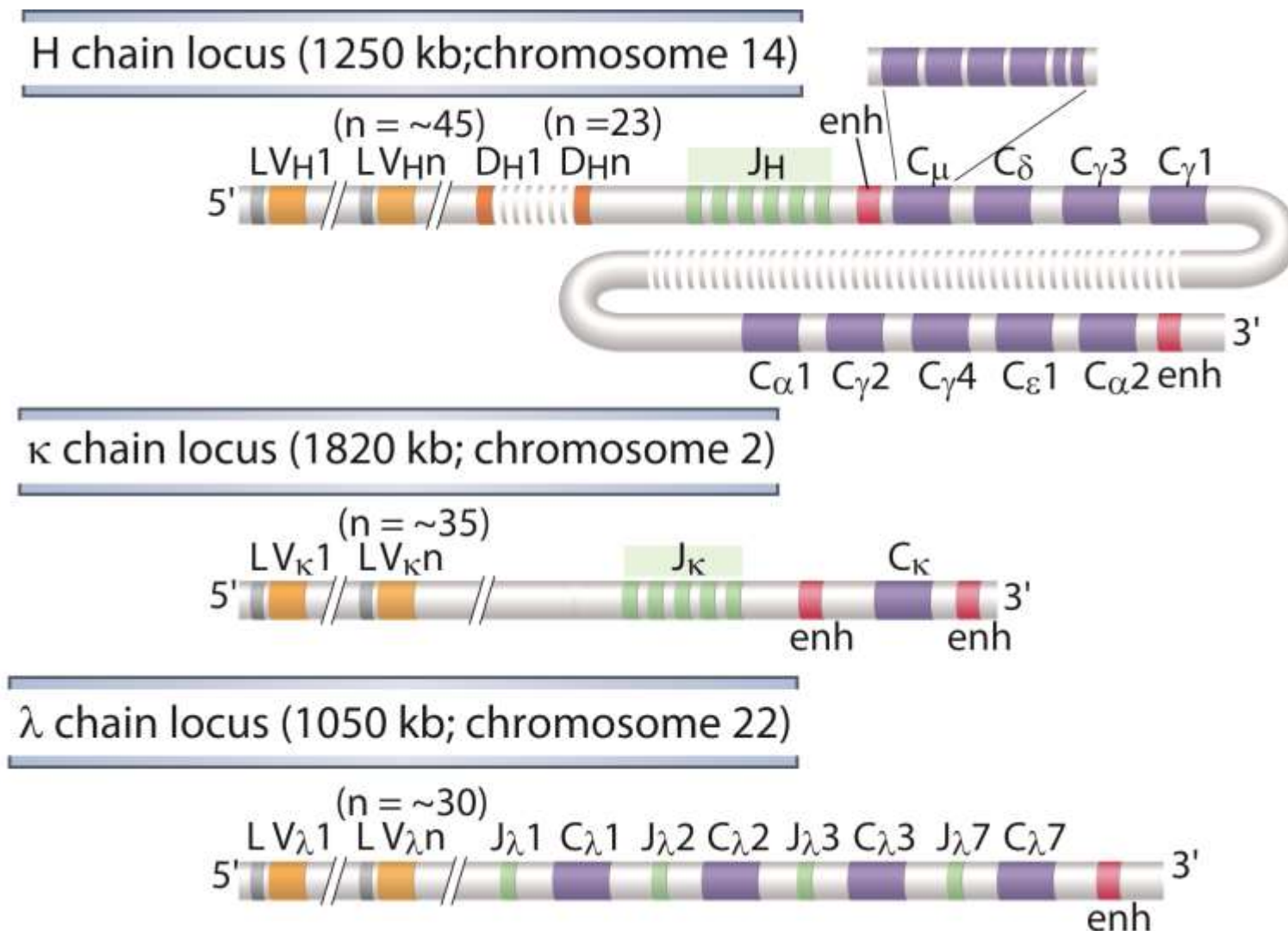


Fig. 8-5



Domains of Ig and TCR proteins

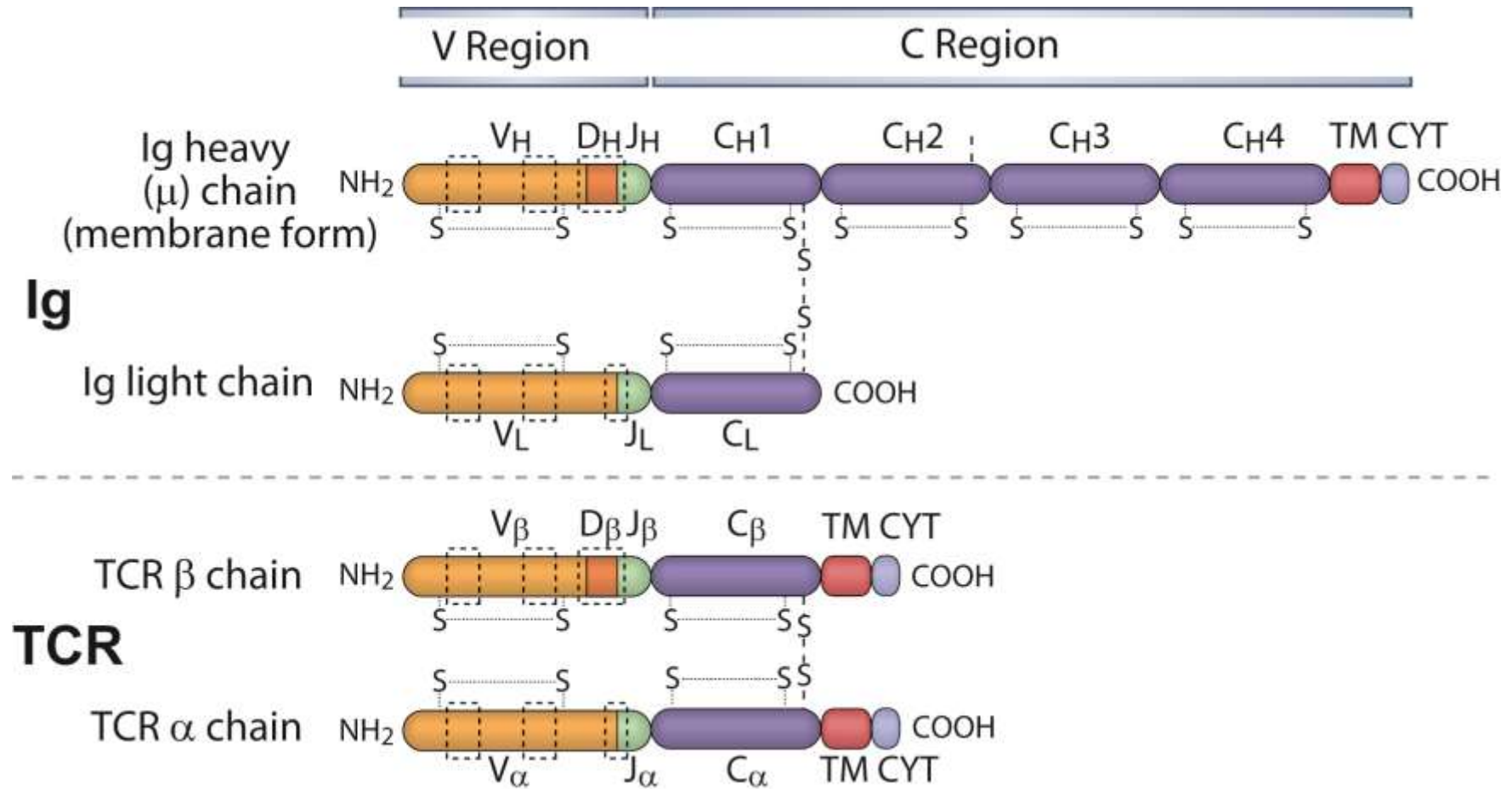
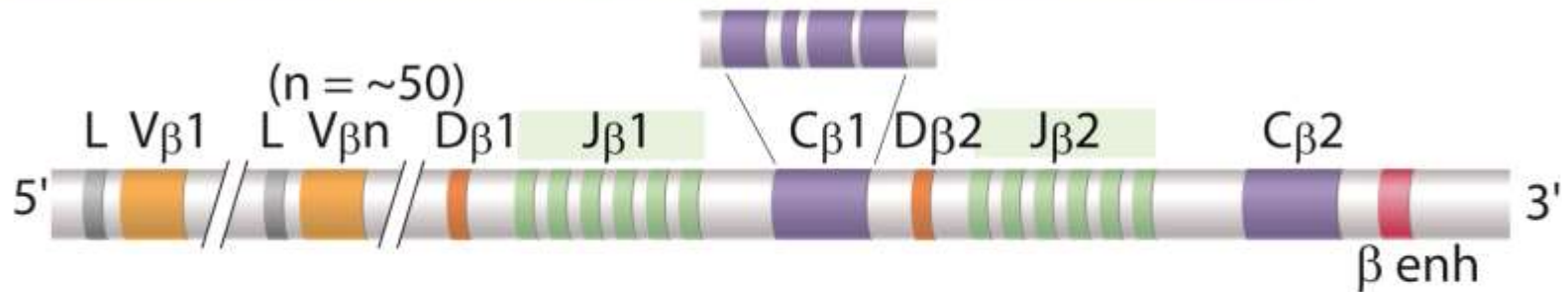


Fig. 8-6



Germline Organization of Human TCR Loci (1)

Human TCR β chain locus (620 kb; chromosome 7)



Human TCR α chain locus (1000 kb; chromosome 14)

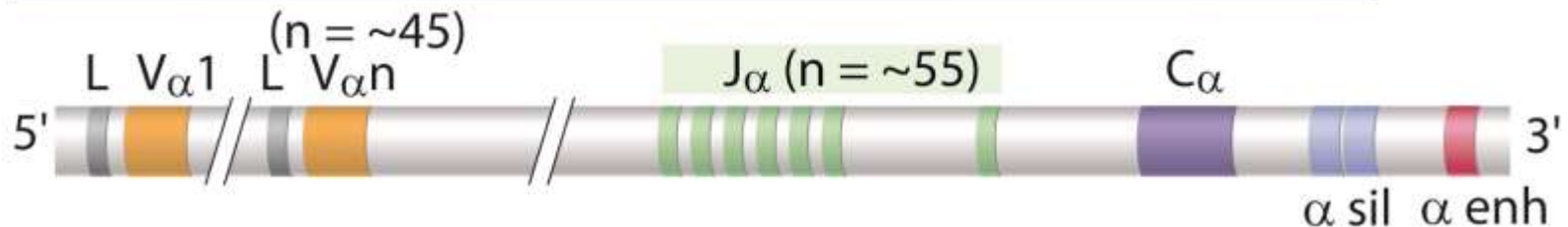


Fig. 8-7

Germline Organization of Human TCR Loci (2)

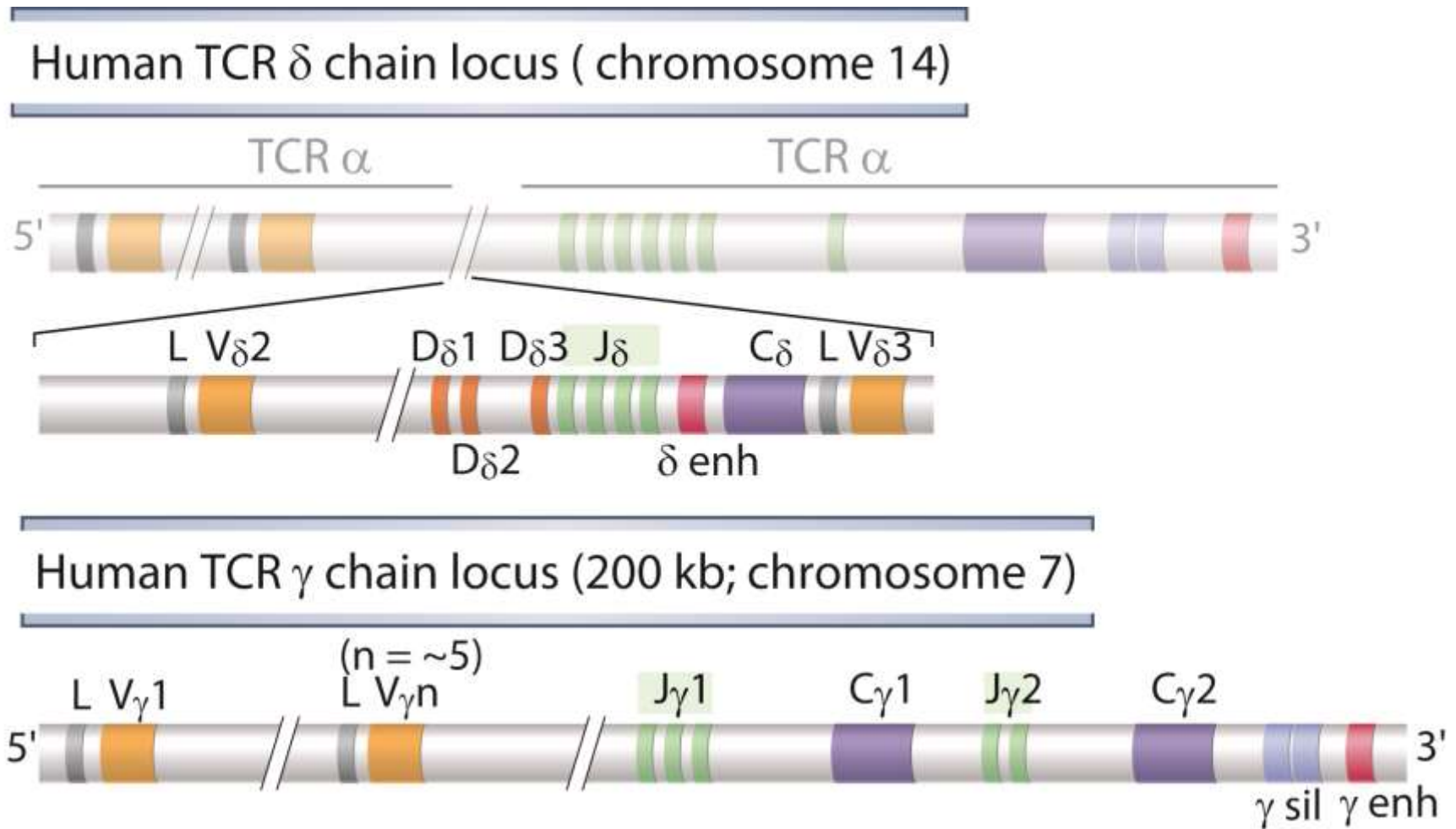


Fig. 8-7

Antigen receptor Gene Rearrangements

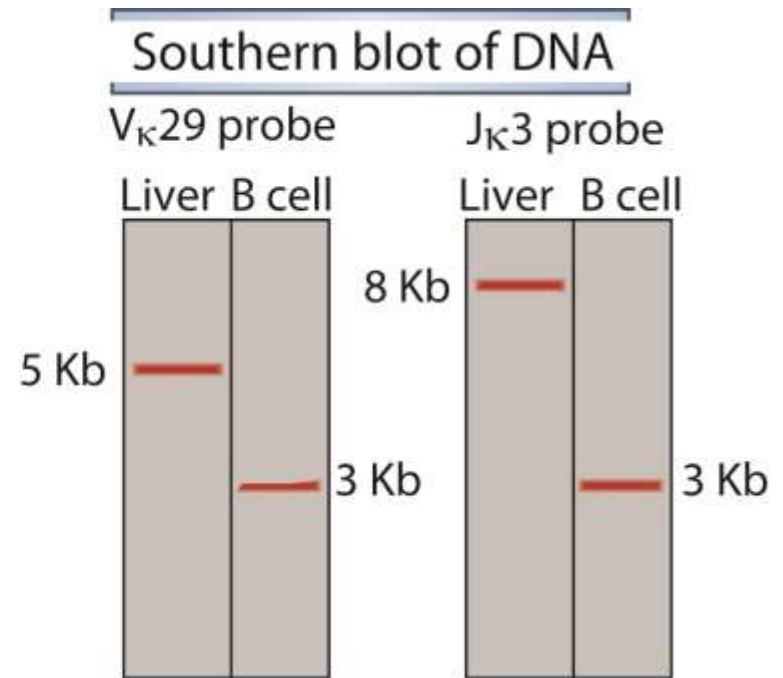
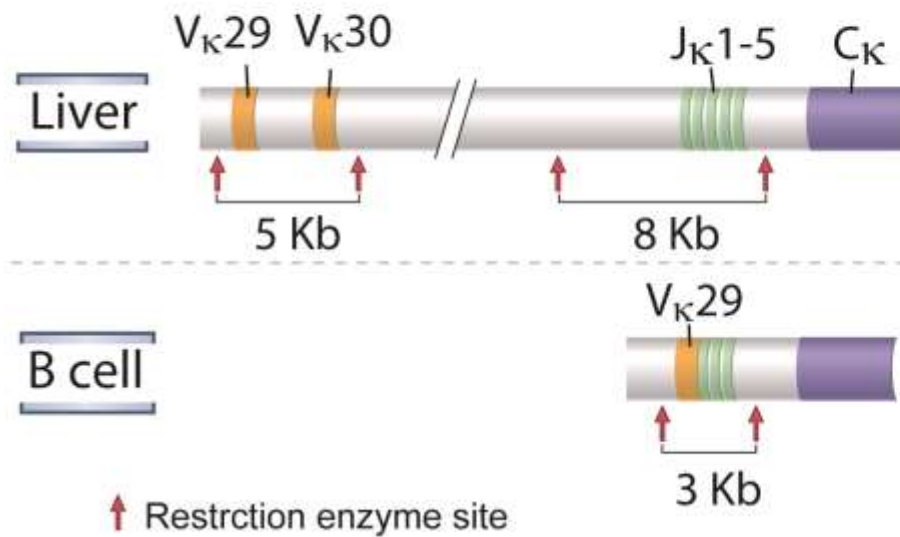
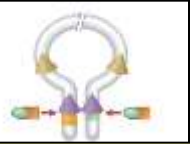


Fig. 8-8



Diversity of Antigen Receptor Genes

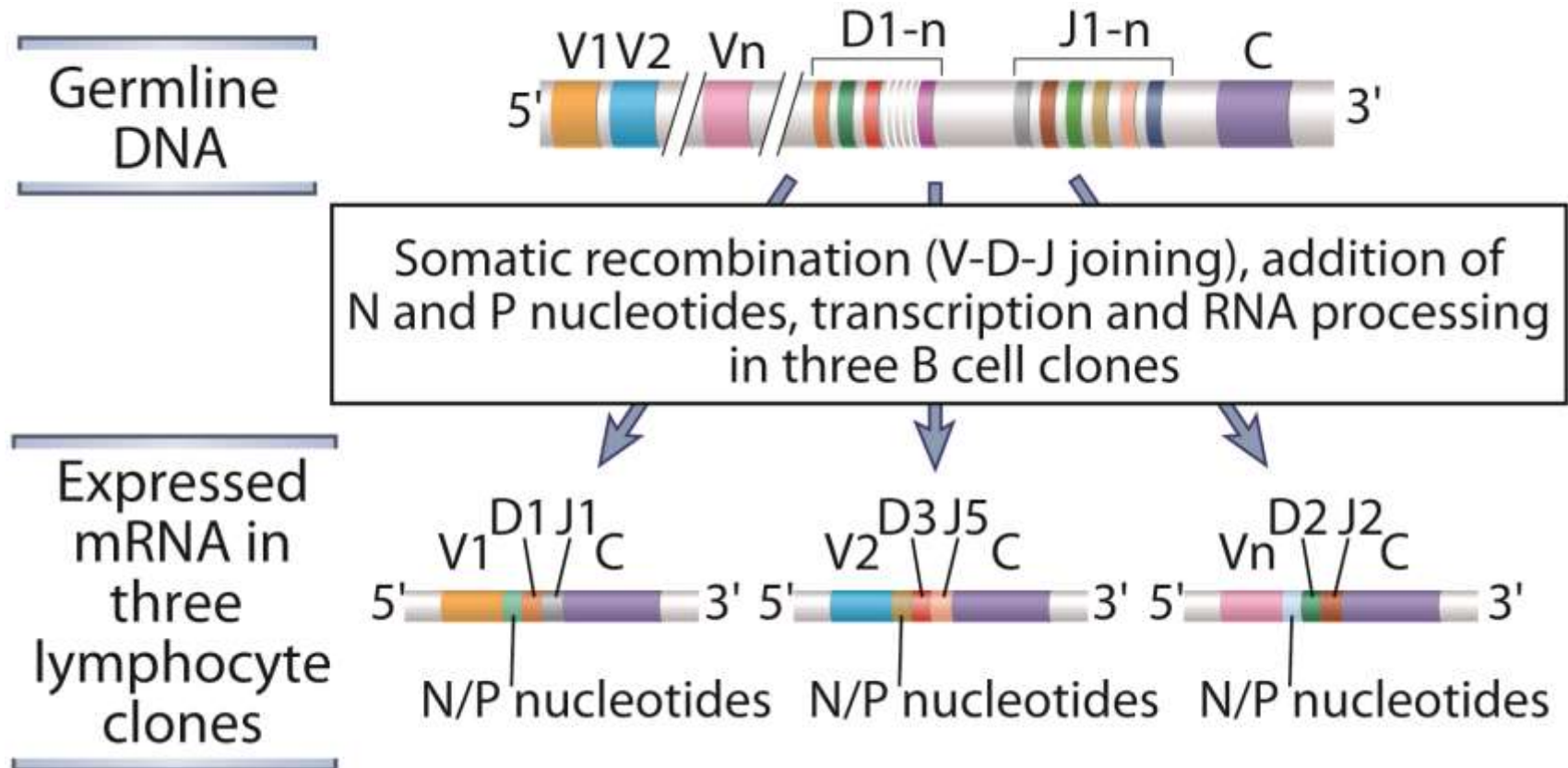
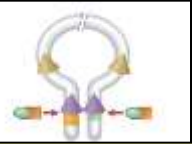


Fig. 8-9



V(D)J Recombination (1)

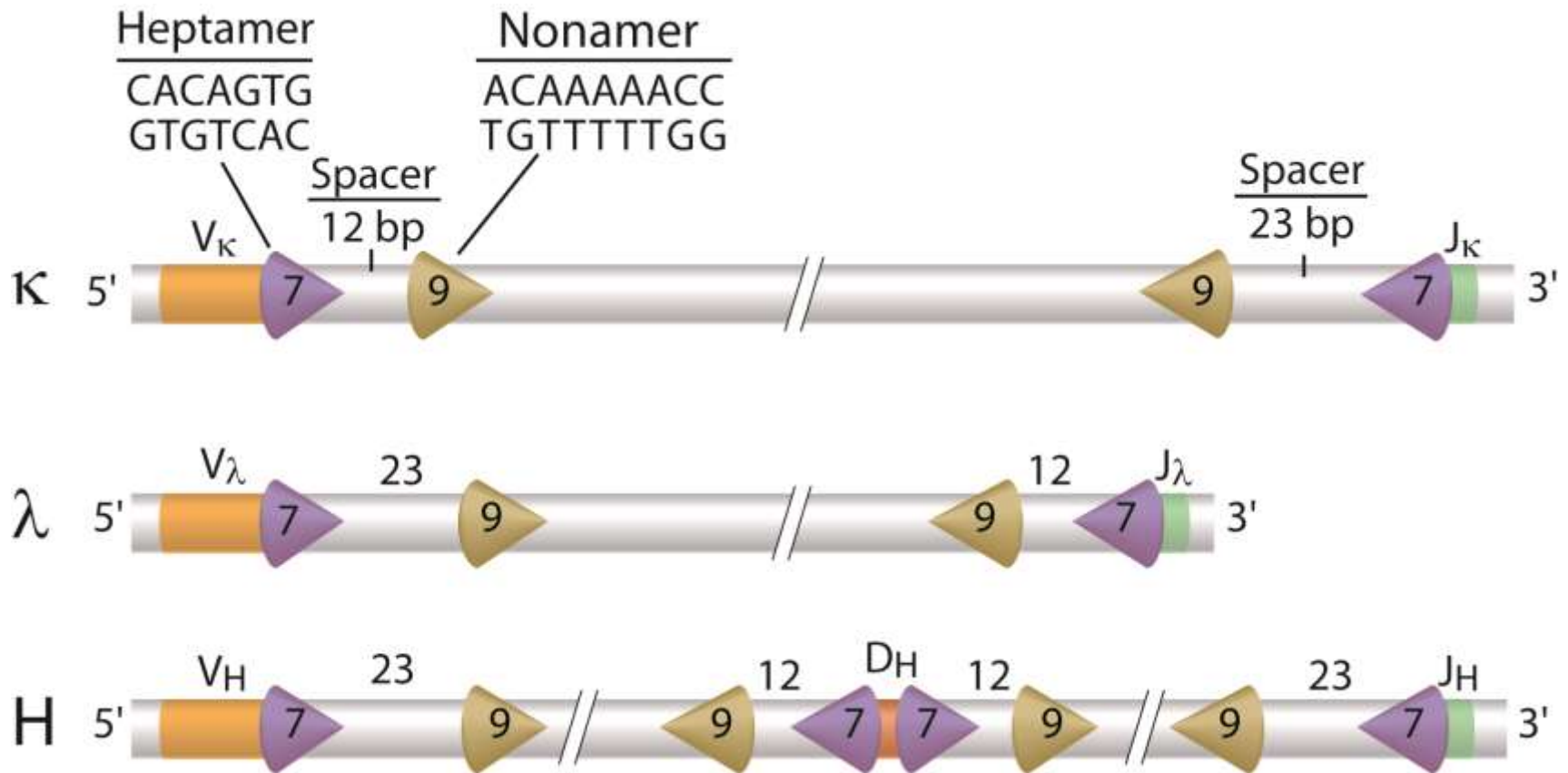
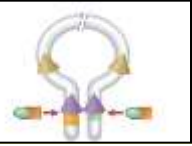


Fig. 8-10A



V(D)J Recombination (2)

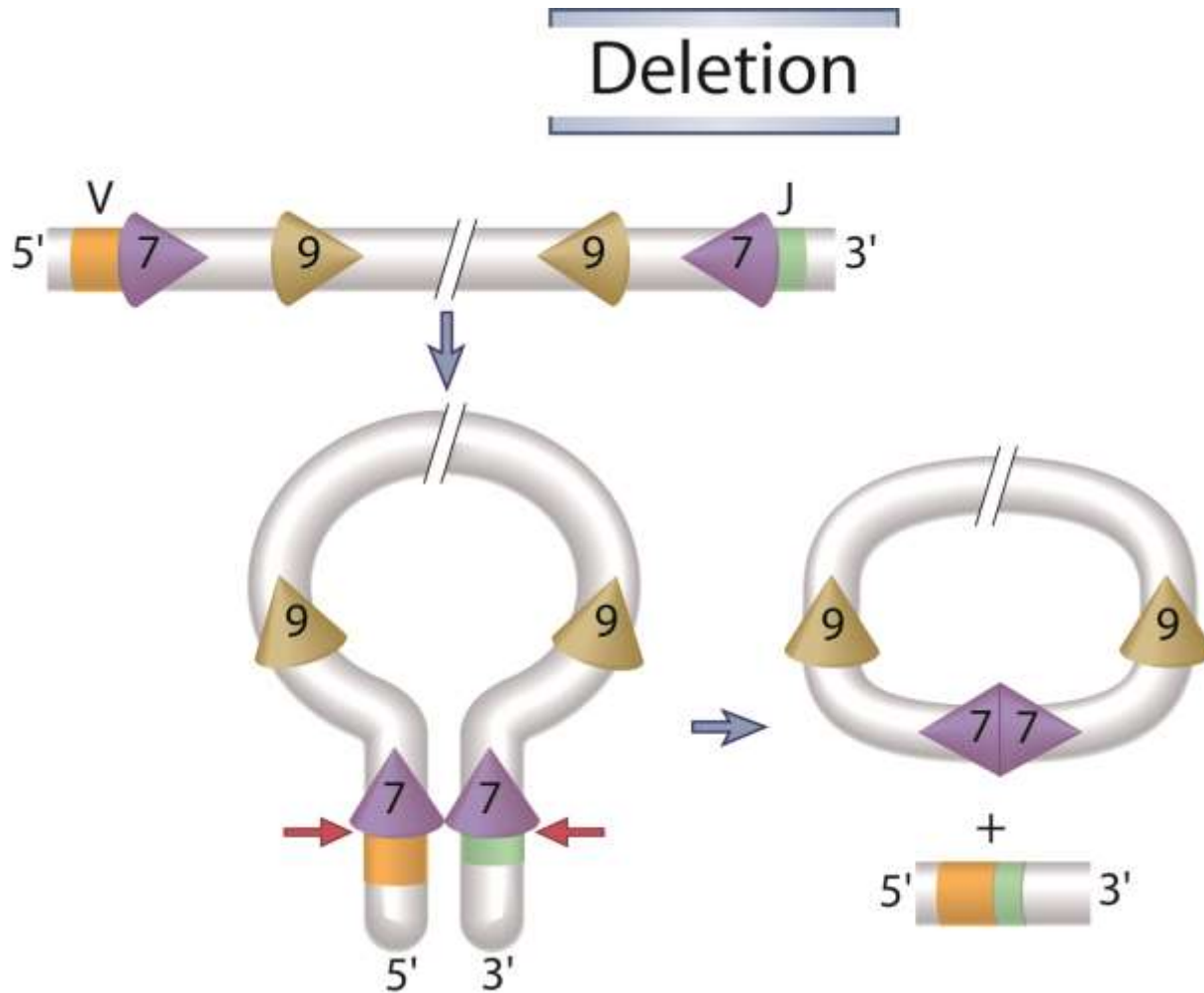
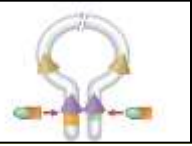


Fig. 8-10B



V(D)J Recombination (3)

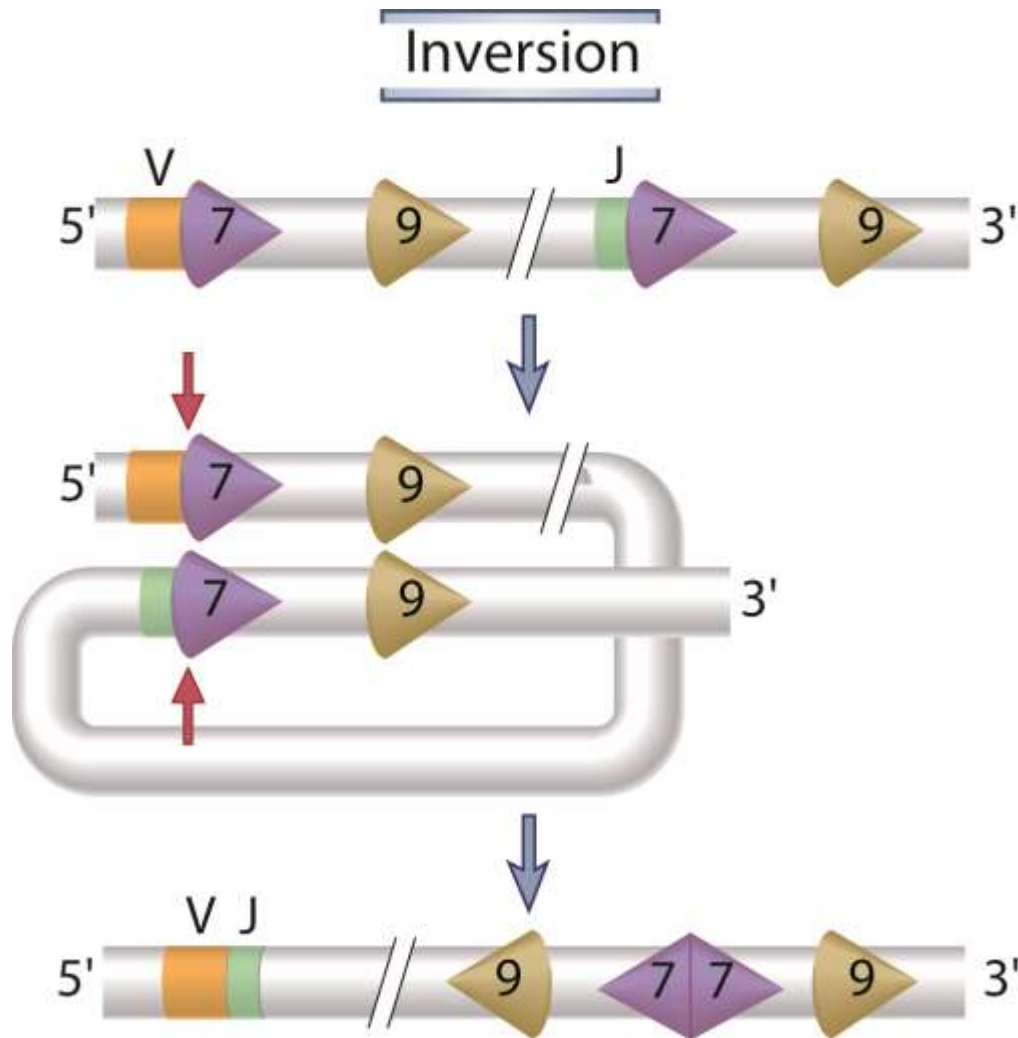


Fig. 8-10C



Transcriptional Regulation of Ig Genes

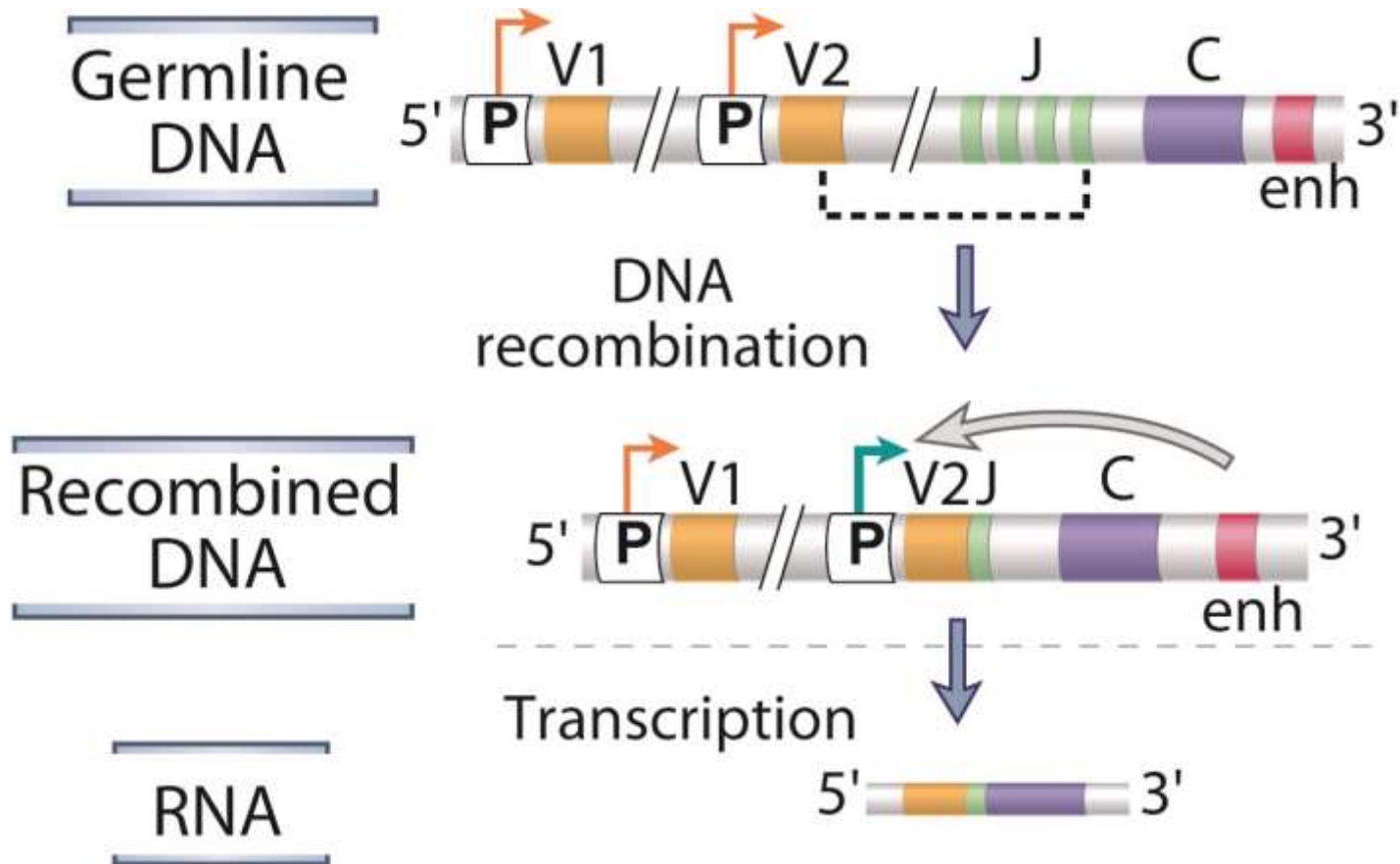


Fig. 8-11

Events During V(D)J Recombination (1)

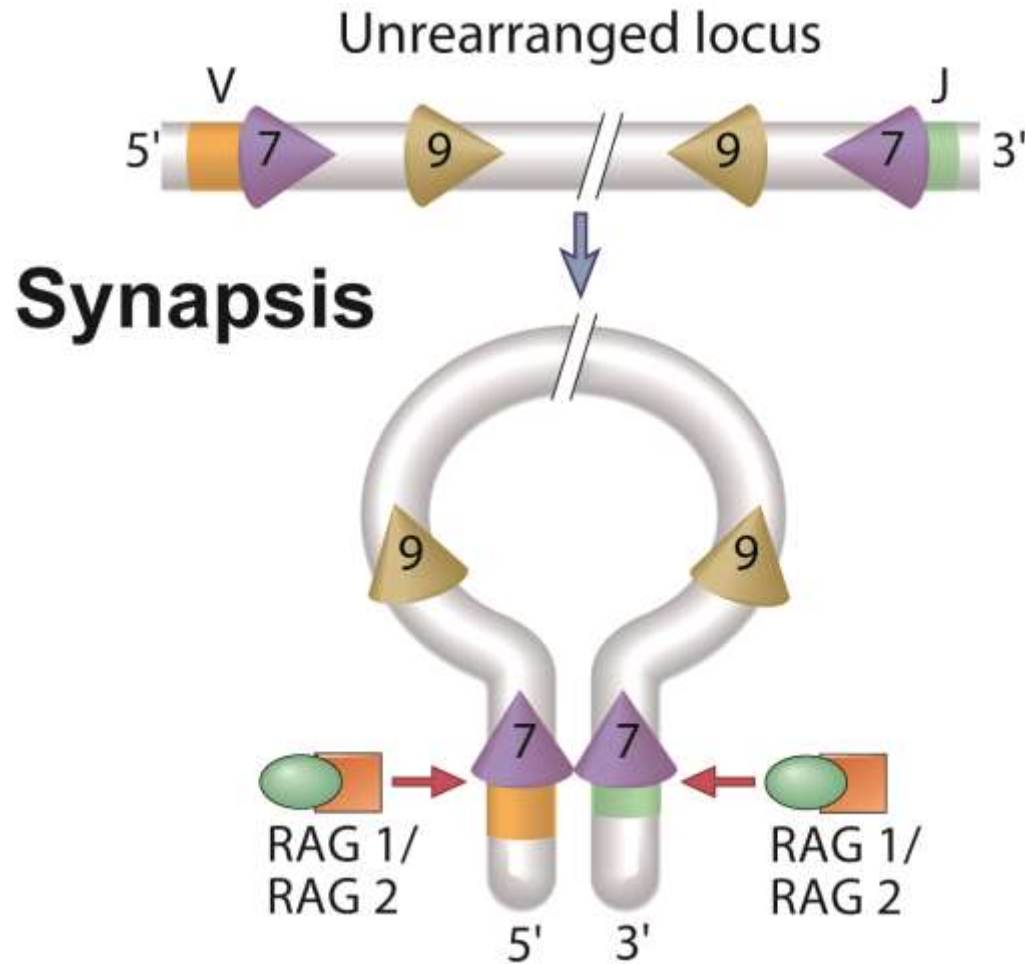


Fig. 8-12

Events During V(D)J Recombination (2)

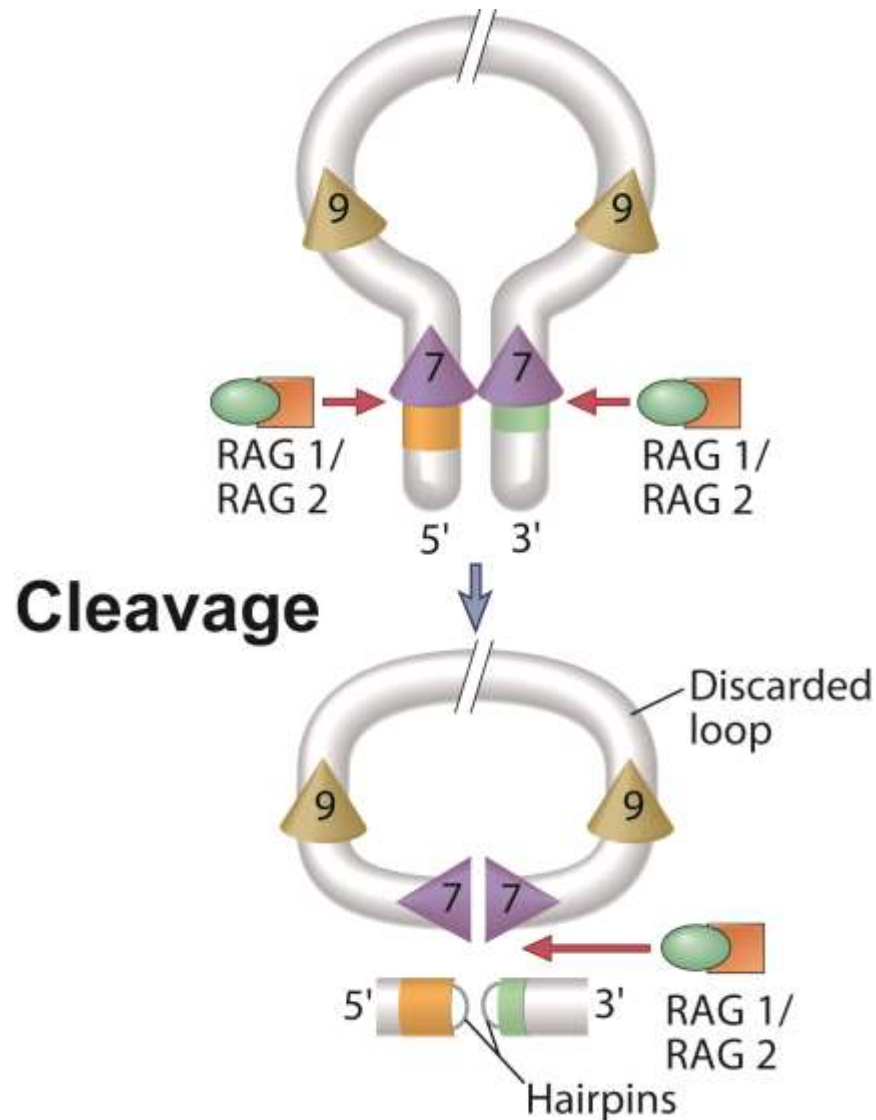
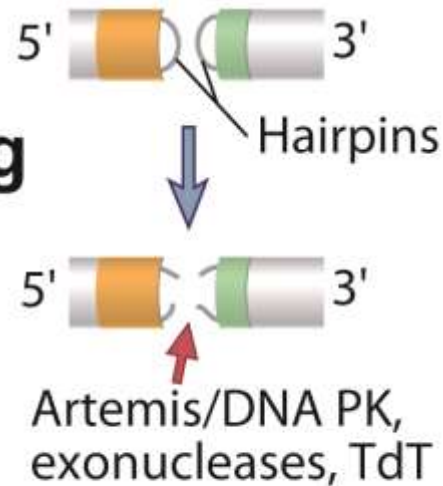


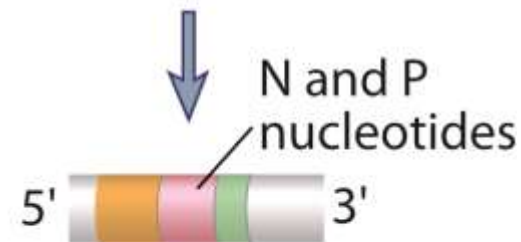
Fig. 8-12

Events During V(D)J Recombination (3)

**Hairpin opening
and end-
processing**



Joining



Ku70/Ku80/DNA-PK
XRCC4/DNA LigaseIV

Fig. 8-12



Junctional Diversity

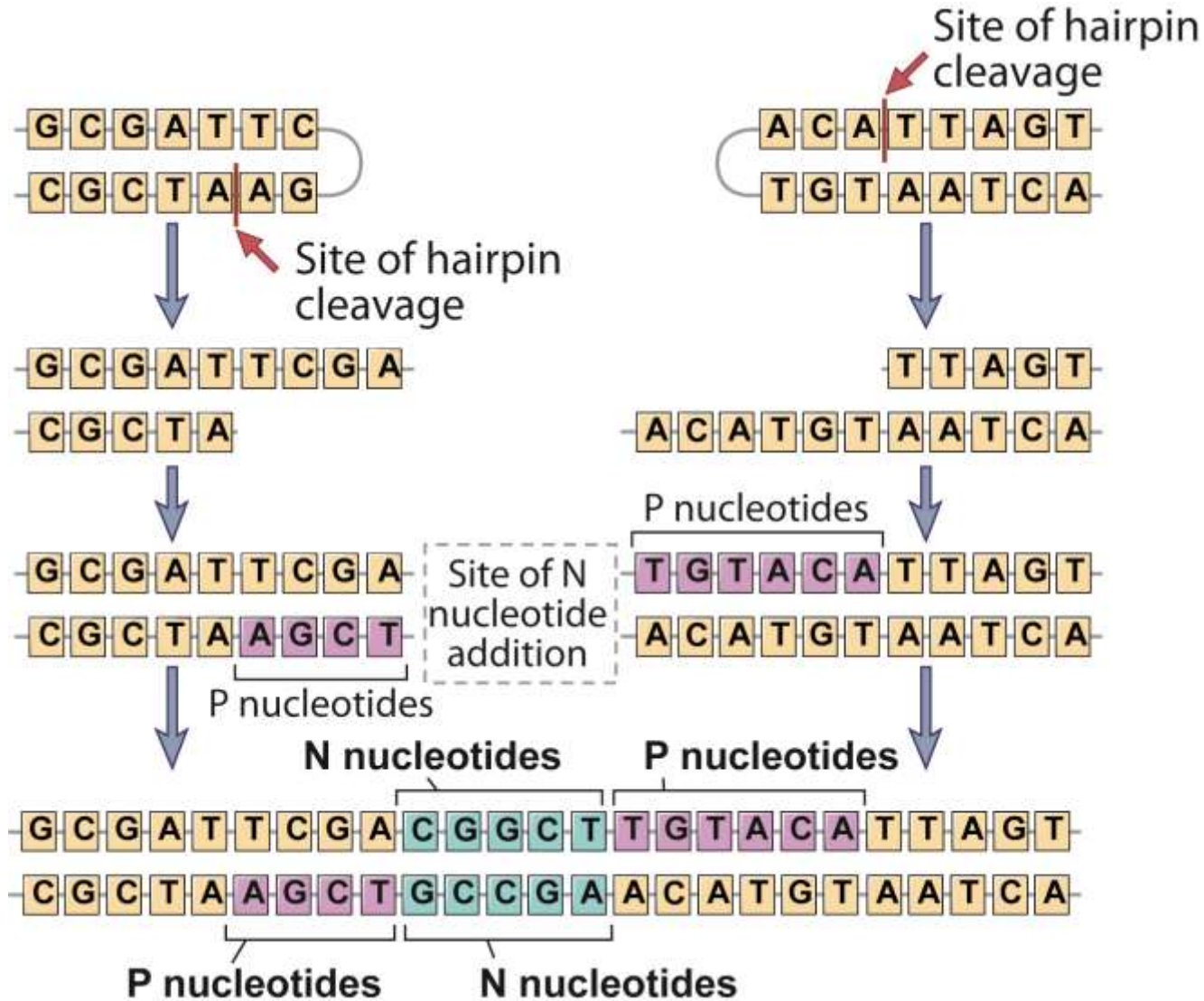
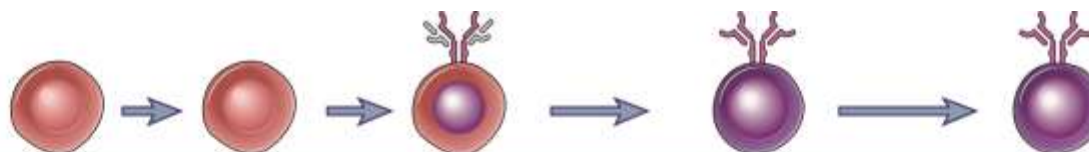


Fig. 8-13



Stages of B Cell Maturation



Stage of maturation	Stem cell	Pro-B	Pre-B	Immature B	Mature B
Proliferation	[Bar]		[Bar]		
RAG expression		[Bar]		[Bar]	
TdT expression		[Bar]			
Ig DNA, RNA	Ggermline DNA	Germline DNA	Recombined H chain gene (VDJ); μ mRNA	Recombined H chain gene (VDJ), κ or λ genes (VJ); μ or κ or λ mRNA	Alternative splicing of VDJ-C RNA to form C_μ and C_δ mRNA
Ig expression	None	None	Cytoplasmic μ and pre-B receptor – associated μ	Membrane IgM (μ + κ or λ light chain)	Membrane IgM and IgD
Surface markers	CD43 ⁺	CD43 ⁺ CD19 ⁺ CD10 ⁺	B220 ^{lo} CD43 ⁺	IgM ^{lo} CD43 ⁻	IgM ^{hi}
Anatomic site	[Bar] Bone marrow			[Bar] Periphery	
Response to antigen	None	None	None	Negative selection (deletion), receptor editing	Activation (proliferation and differentiation)

Fig. 8-14



Ig Gene Recombination

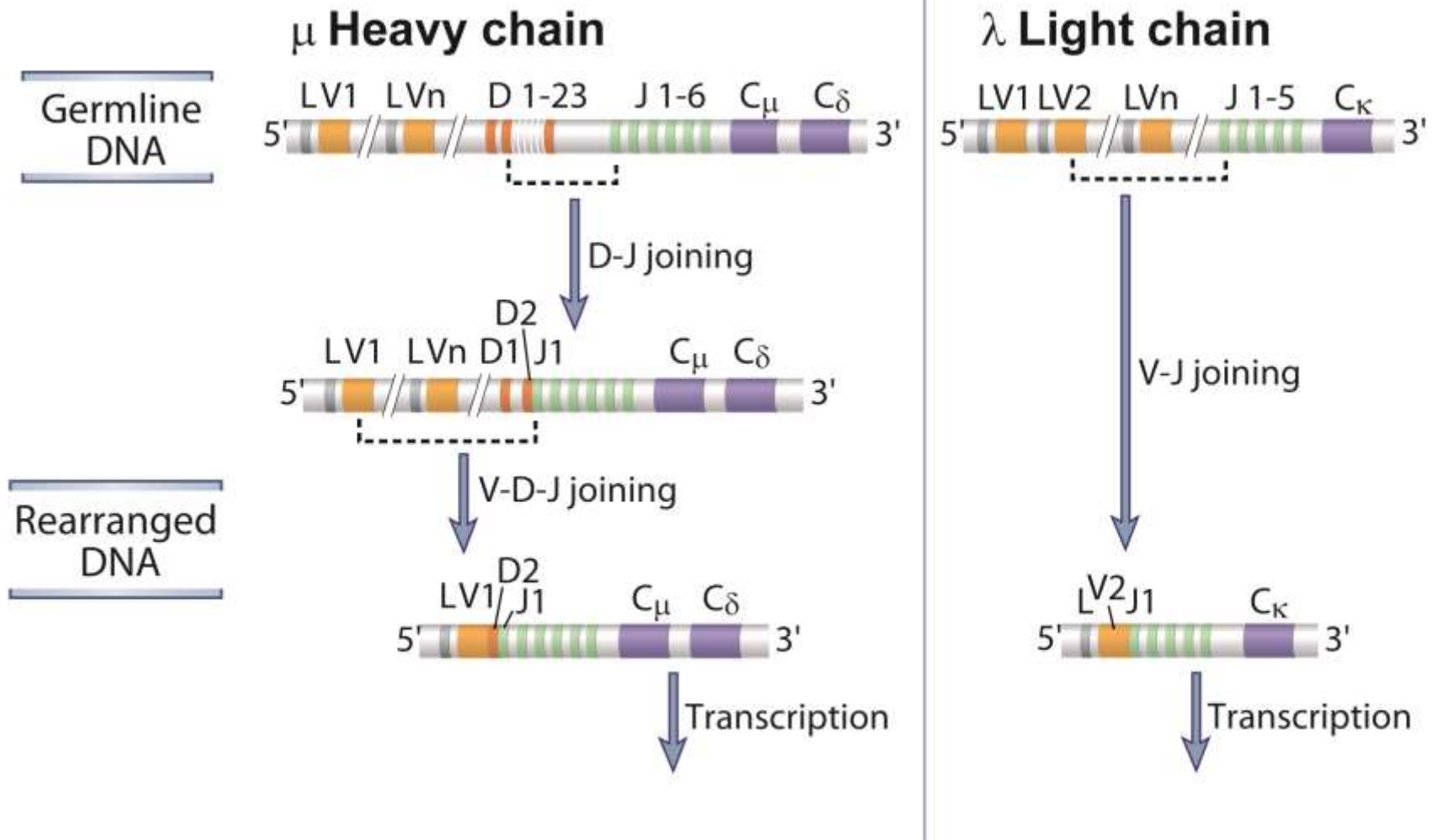


Fig. 8-15A



Ig Gene Expression

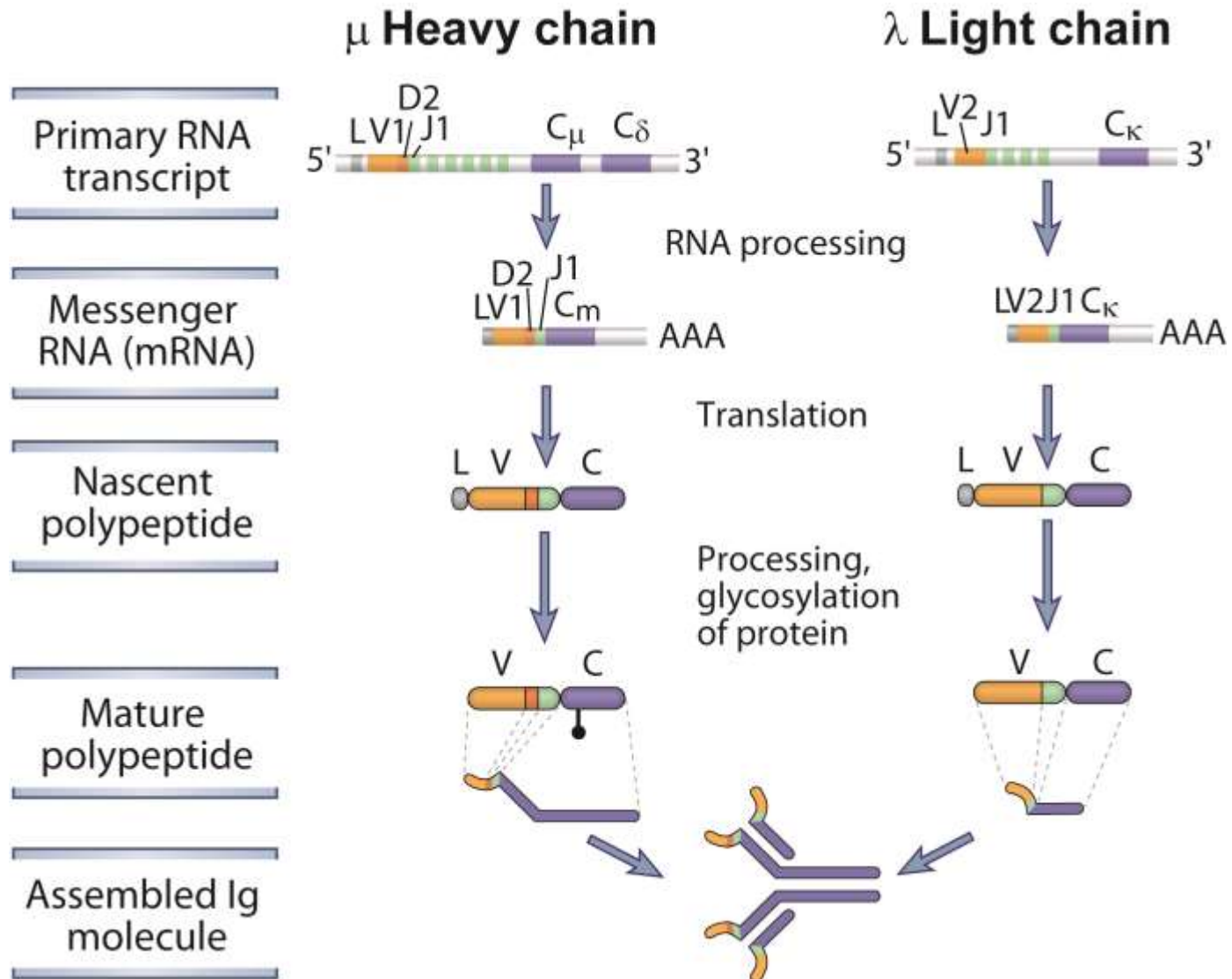


Fig. 8-15B



Pre-B cell and Pre-T cell Receptors

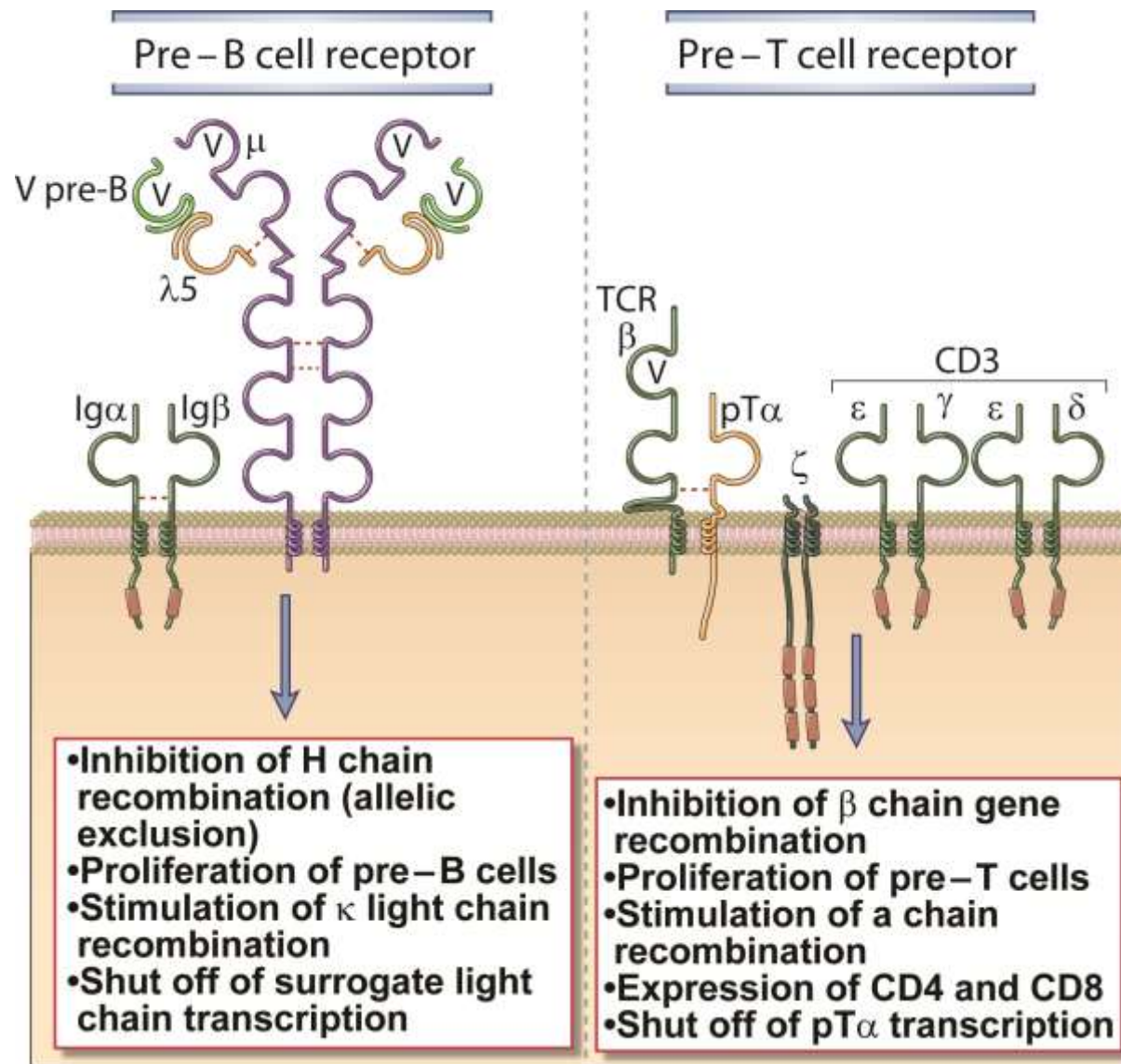


Fig. 8-16



B Lymphocyte Subsets

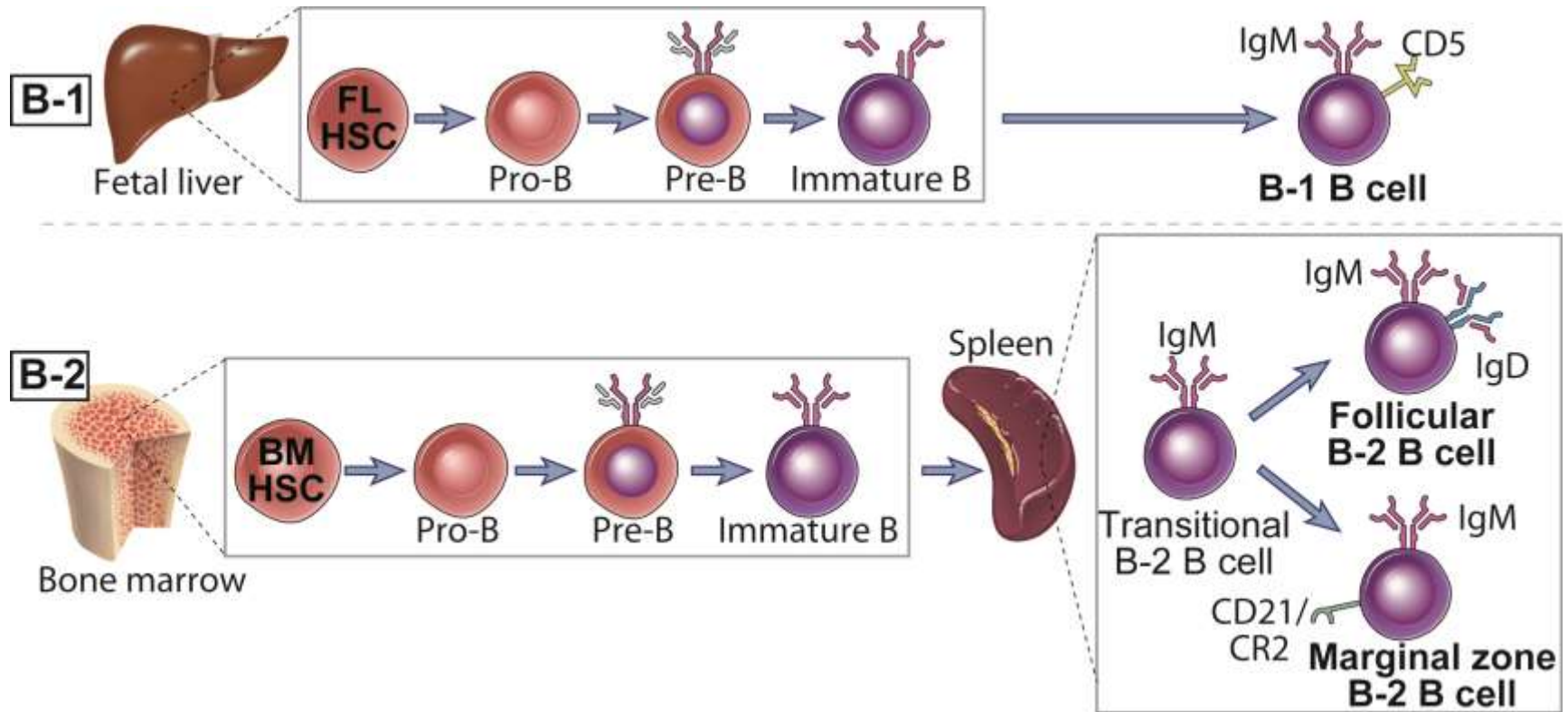
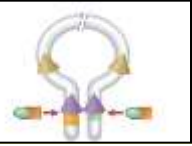


Fig. 8-17



Coexpression of IgM and IgD.

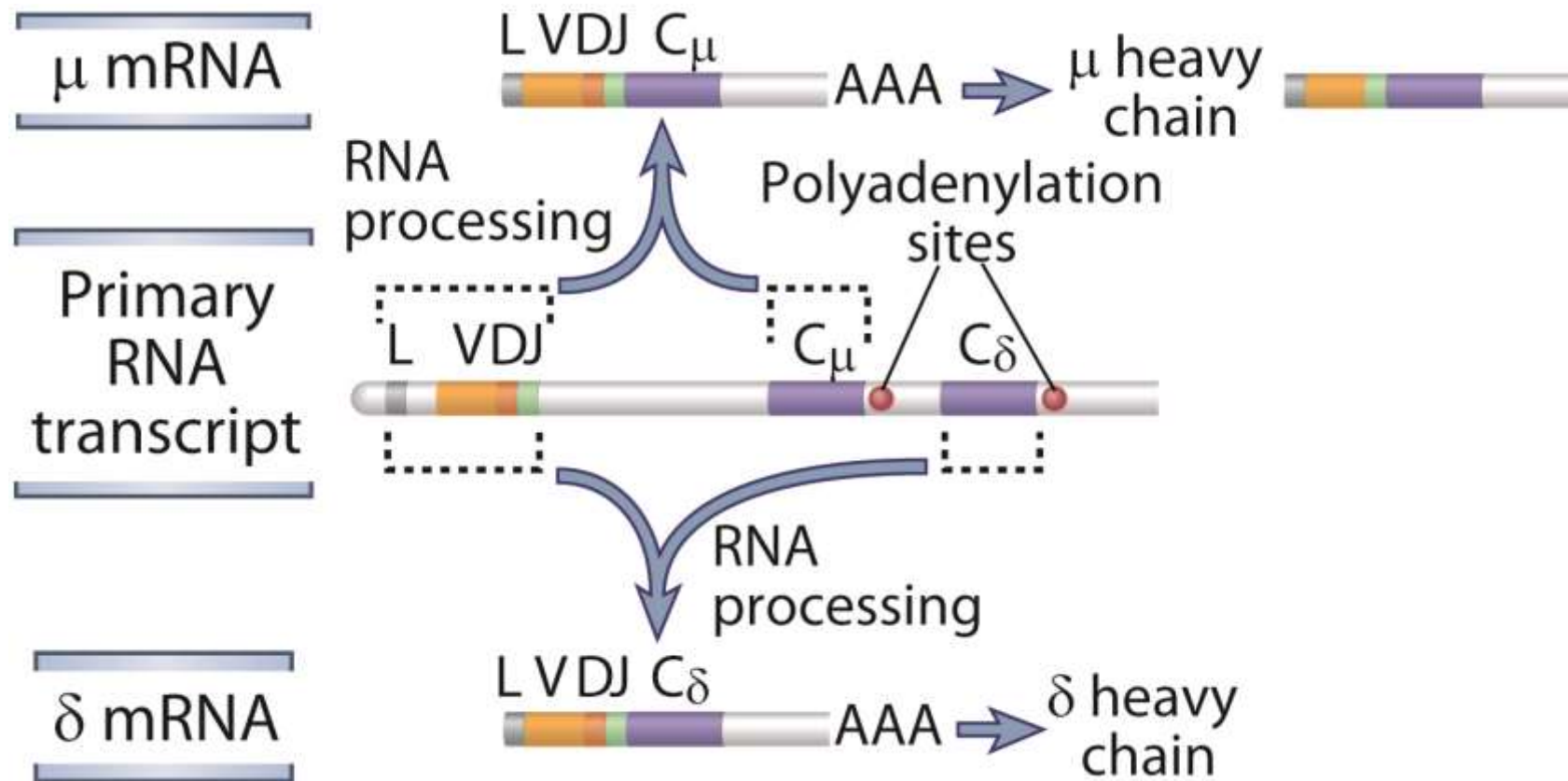
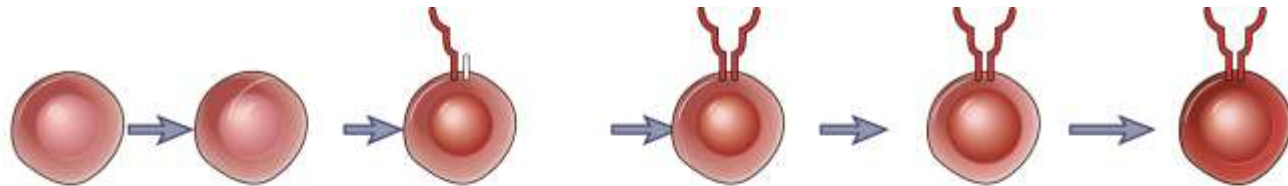


Fig. 8-18

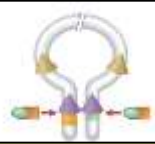


Stages of T Cell Maturation



Stage of maturation	Stem cell	Pro-T	Pre-T	Double positive	Single positive immature T cell	Naive mature T cell
Proliferation	■		■			
RAG expression		■		■		
TdT expression		■				
TCR DNA, RNA	Germline DNA	Germline DNA	Recombined β chain gene [V(D)J-C]; β chain mRNA	Recombined β , α chain genes [V(D)J-C]; β and α chain mRNA	Recombined β , α chain genes [V(D)J-C]; β and α chain mRNA	Recombined β , α chain genes [V(D)J-C]; β and α chain mRNA
TCR expression	None	None	Pre-T receptor (β chain/pre-T α)	Membrane $\alpha\beta$ TCR	Membrane $\alpha\beta$ TCR	Membrane $\alpha\beta$ TCR
Surface markers	c-kit ⁺ CD44 ⁺ CD25 ⁻	c-kit ⁺ CD44 ⁺ CD25 ⁺	c-kit ⁺ CD44 ⁻ CD25 ⁺	CD4 ⁺ CD8 ⁺ TCR/CD3 ^{lo}	CD4 ⁺ CD8 ⁻ or CD4 ⁻ CD8 ⁺ TCR/CD3 ^{hi}	CD4 ⁺ CD8 ⁻ or CD4 ⁻ CD8 ⁺ TCR/CD3 ^{hi}
Anatomic site	Bone marrow	Thymus				Periphery
Response to antigen	None	None	None	Positive and negative selection		Proliferation and differentiation

Fig. 8-19



Maturation of T cells in the Thymus

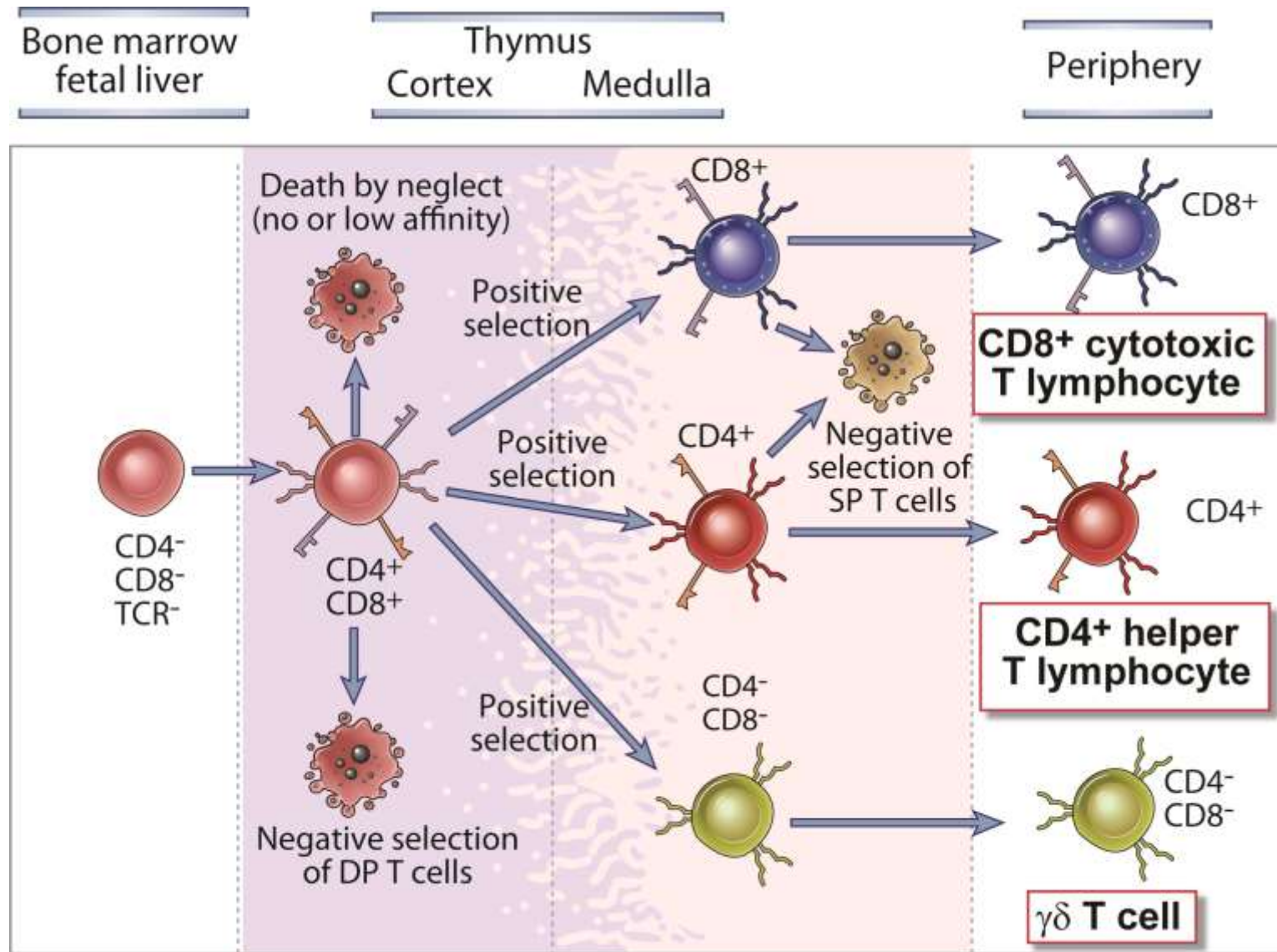


Fig. 8-20

TCR α and β Chain Gene Recombination

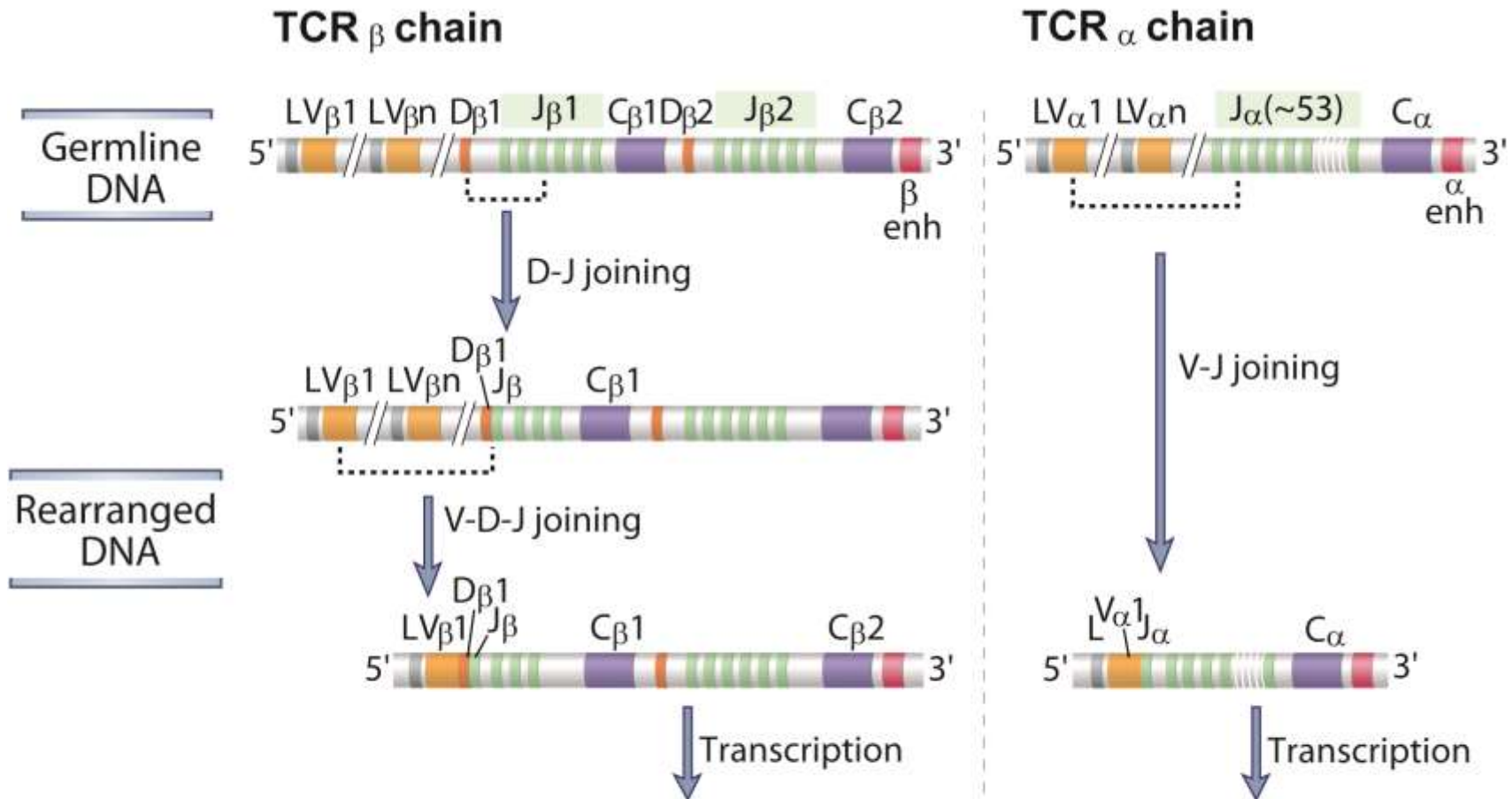
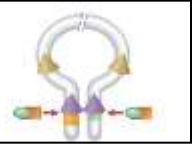


Fig. 8-21A



TCR α and β Chain Gene Expression

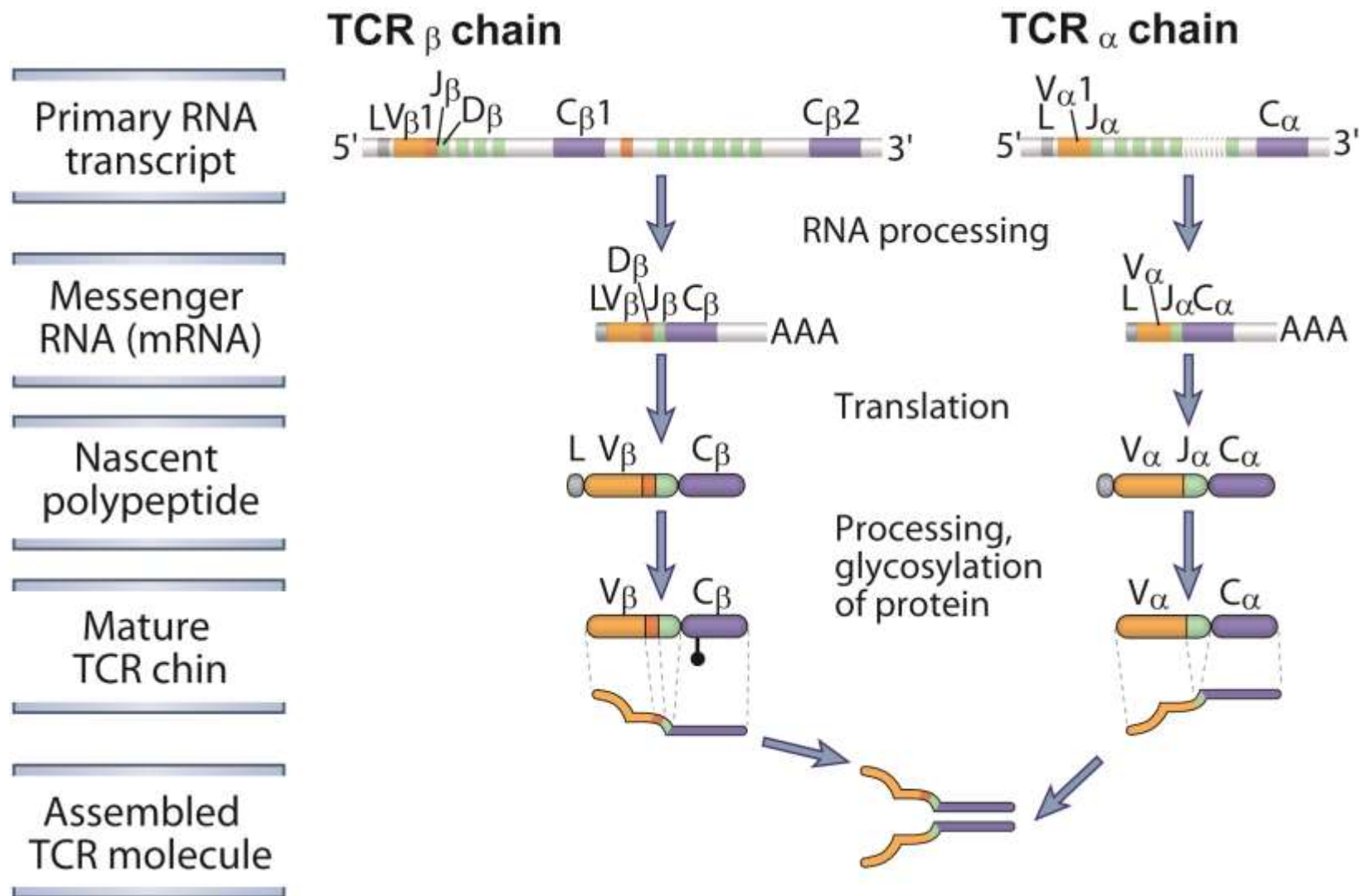


Fig. 8-21B

T Cell CD4 and CD8 Expression in the Thymus

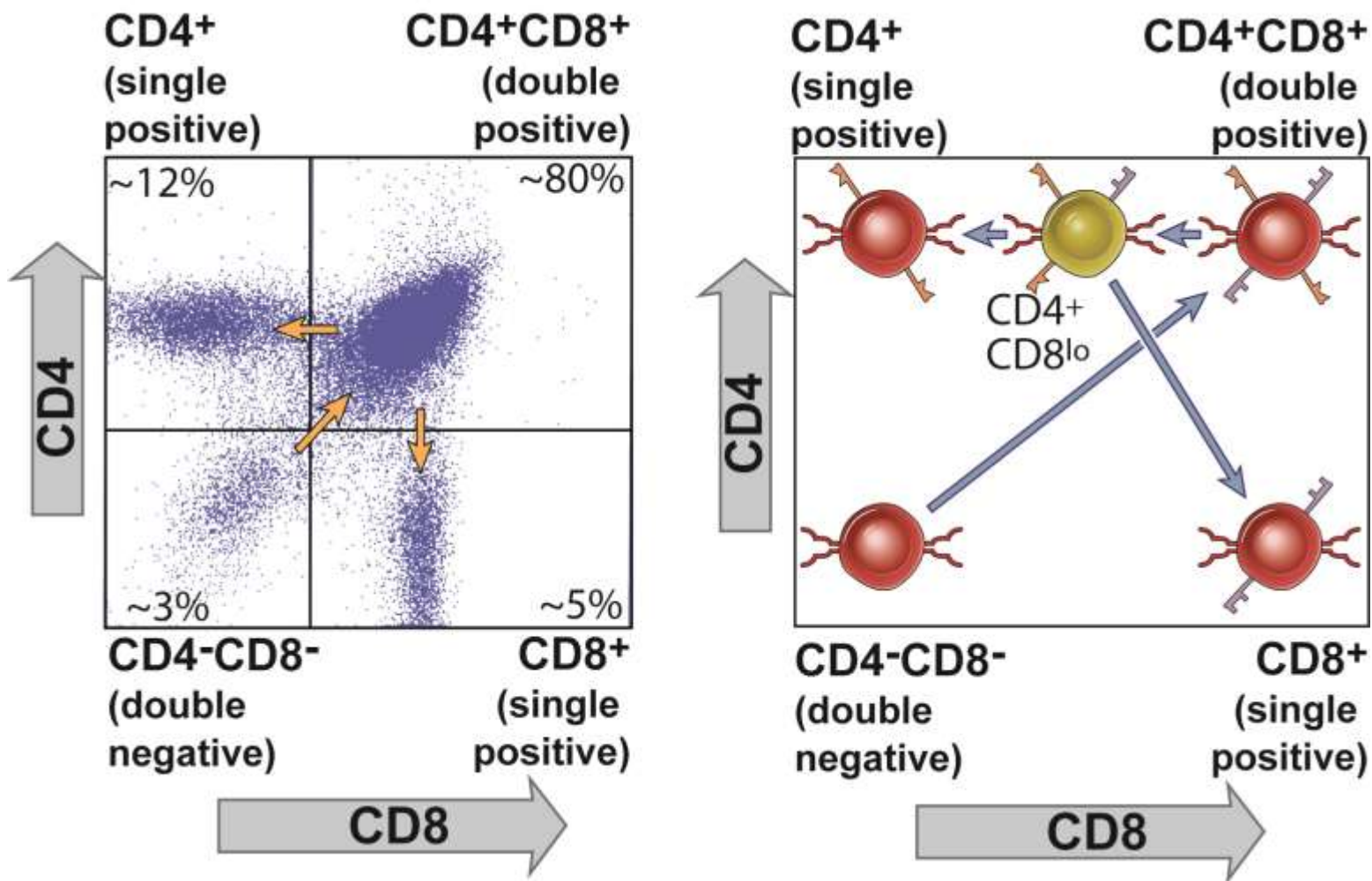


Fig. 8-22