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Transplant Surgery and Immunology

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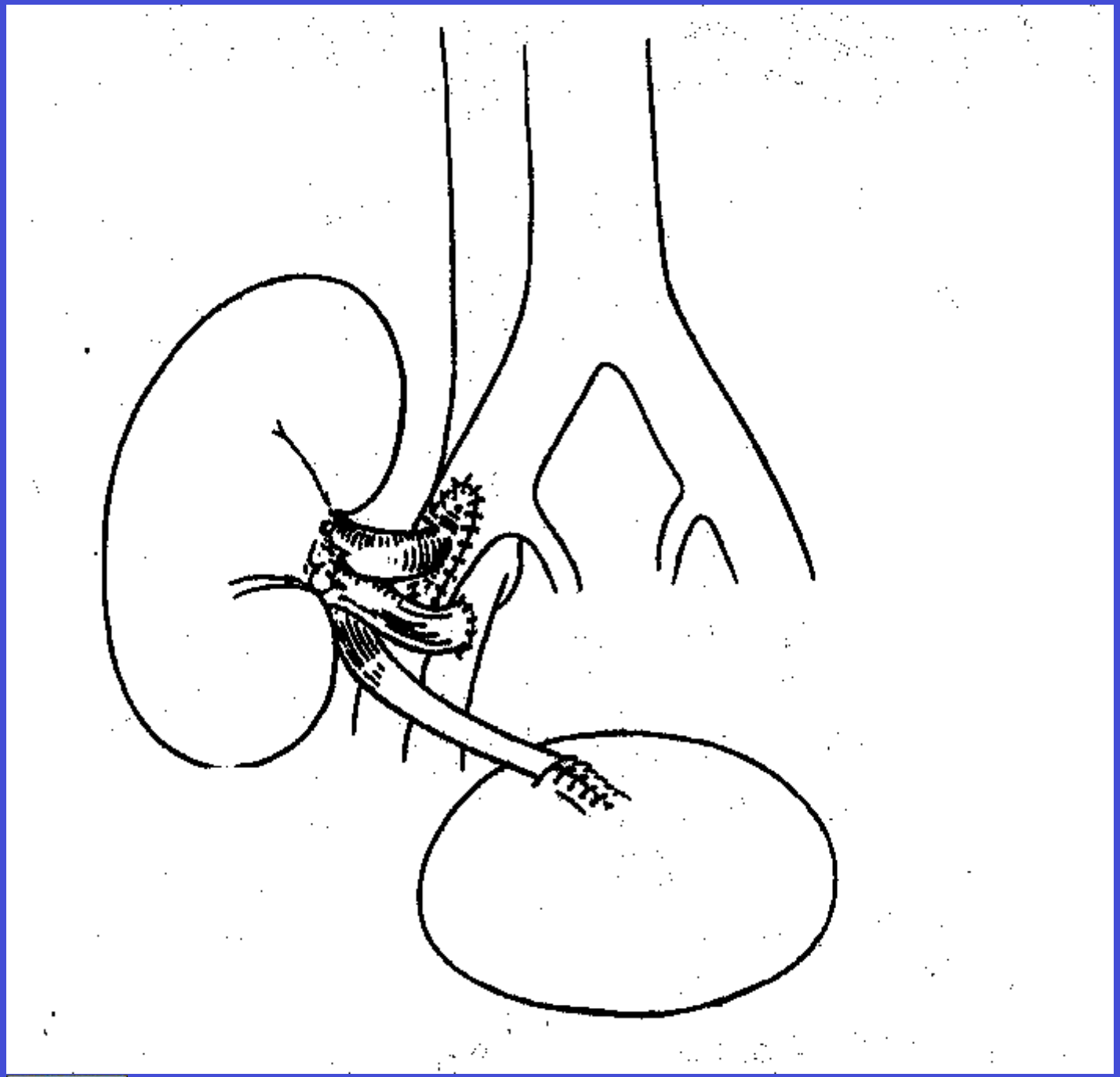
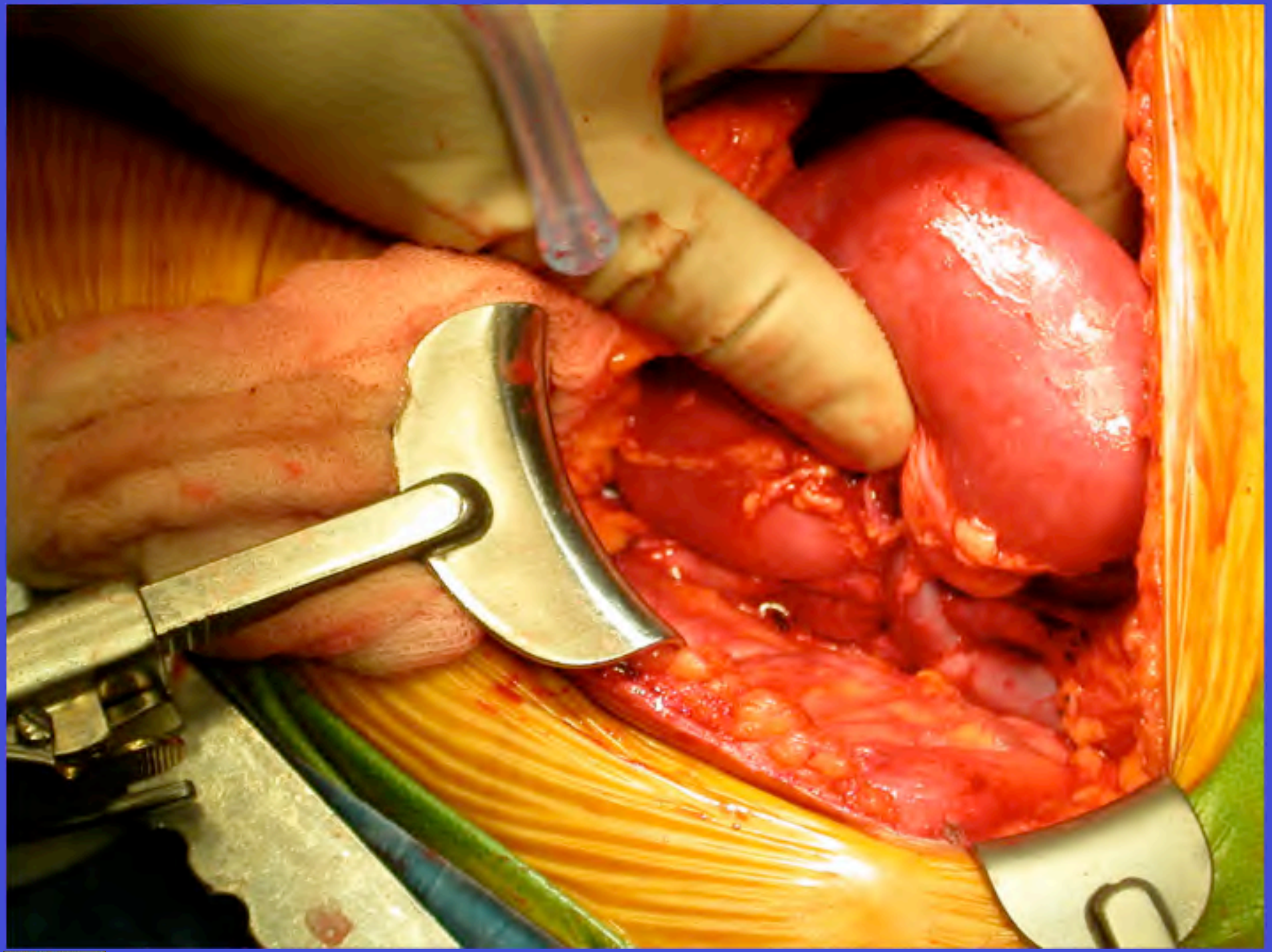
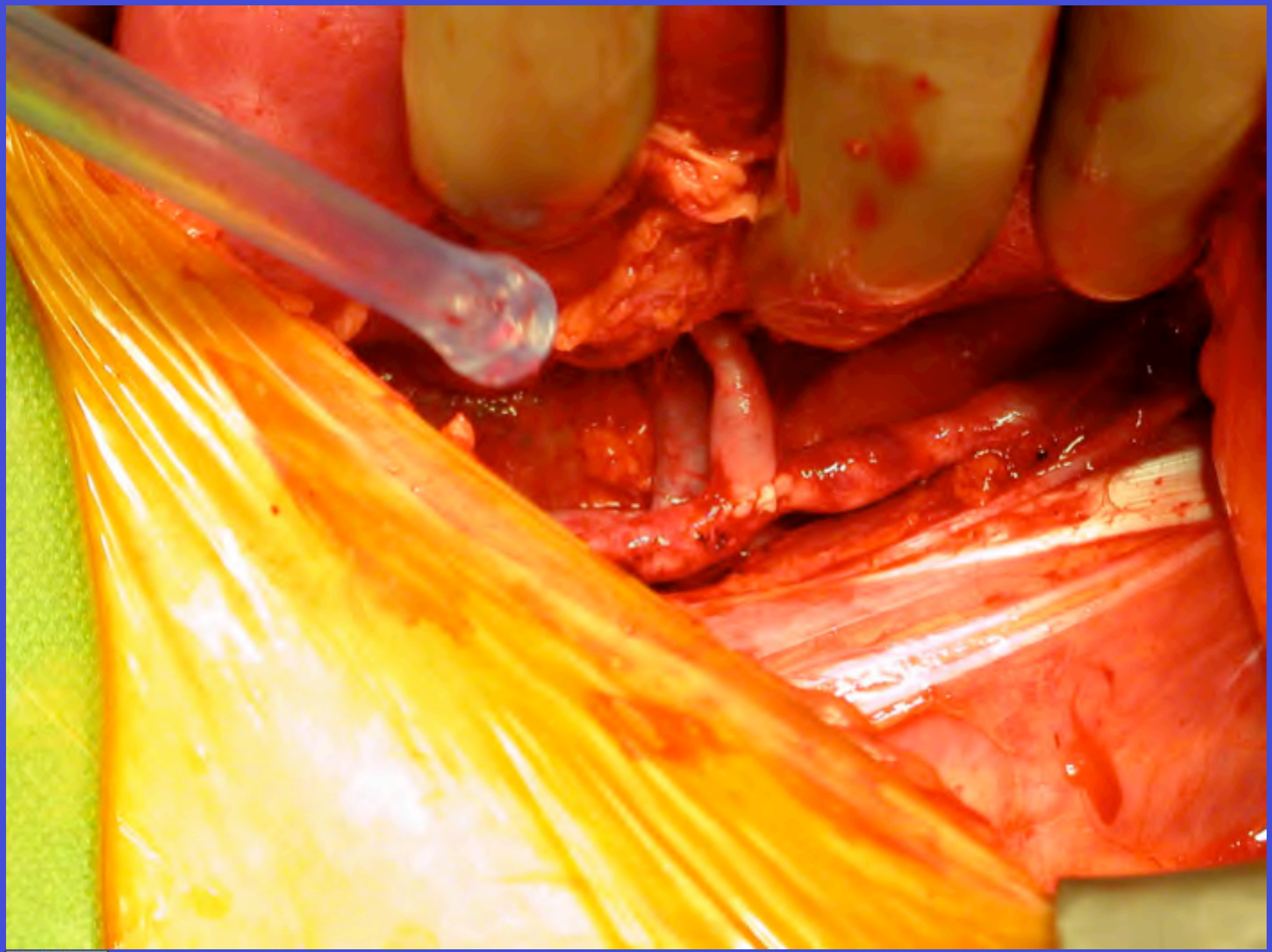
Fall 2008

Renal Transplantation
Technical Consideration



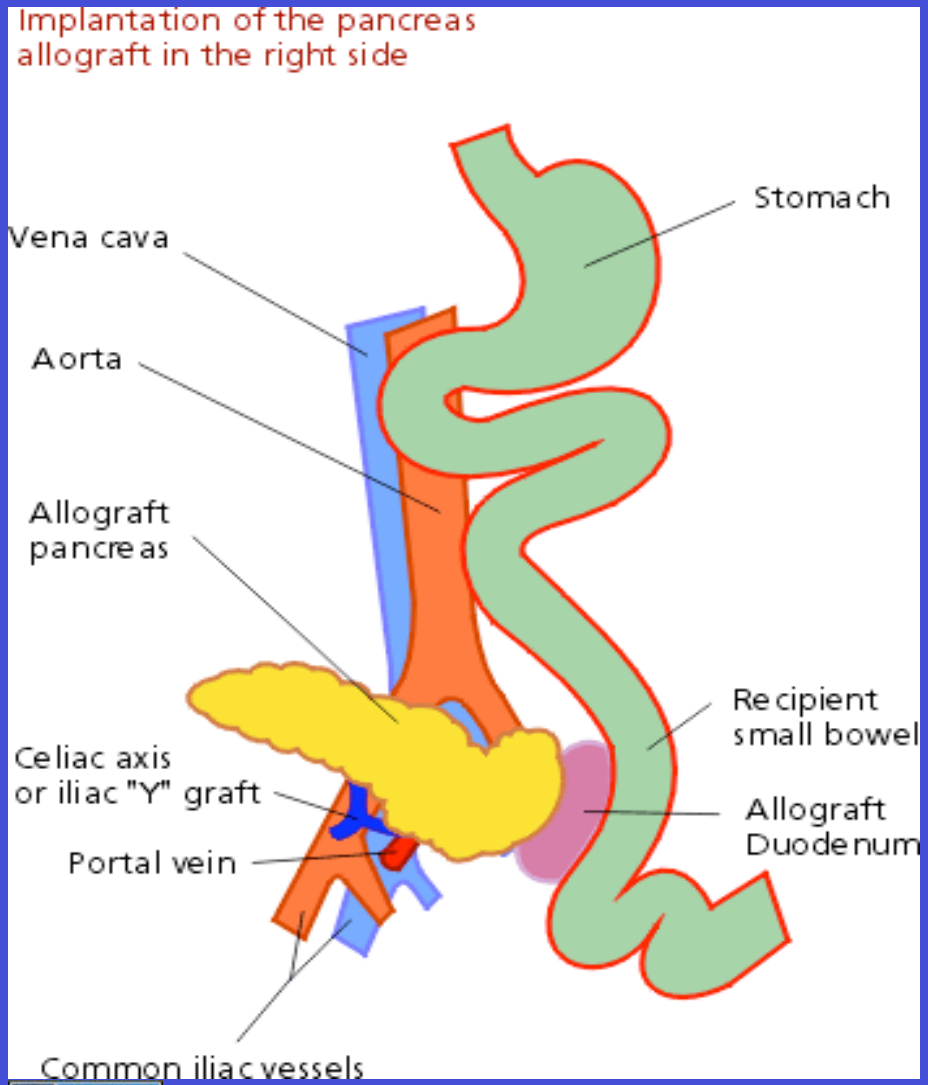




Surgical Complications

- Vascular
  - Arterial
  - Venous
- Ureteral leak/stenosis
- Wound
  - Hematoma
  - Lymphocele

Pancreas Transplantation



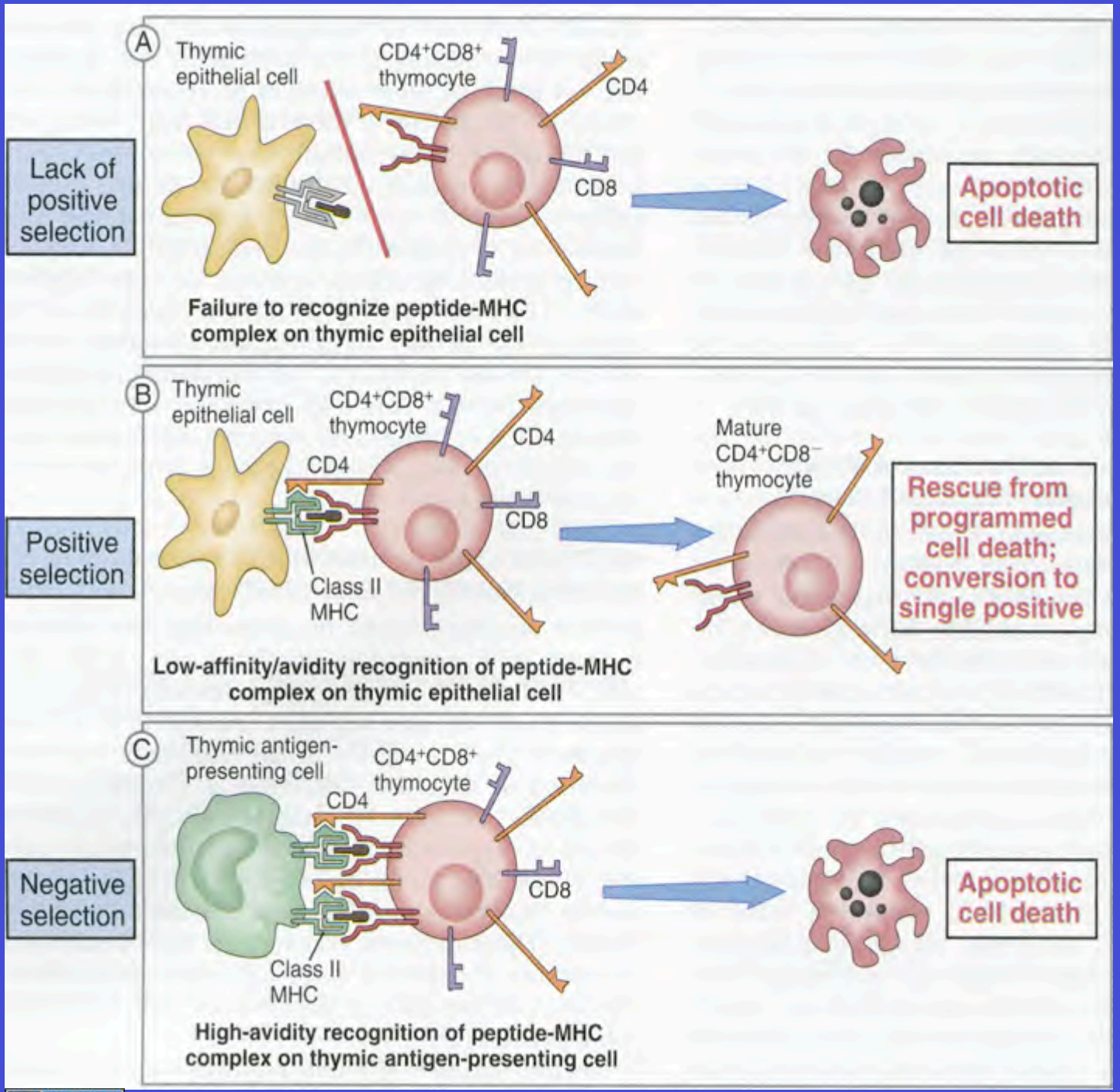
Transplant Immunology

The Biology of the Alloresponse

Learning Objectives

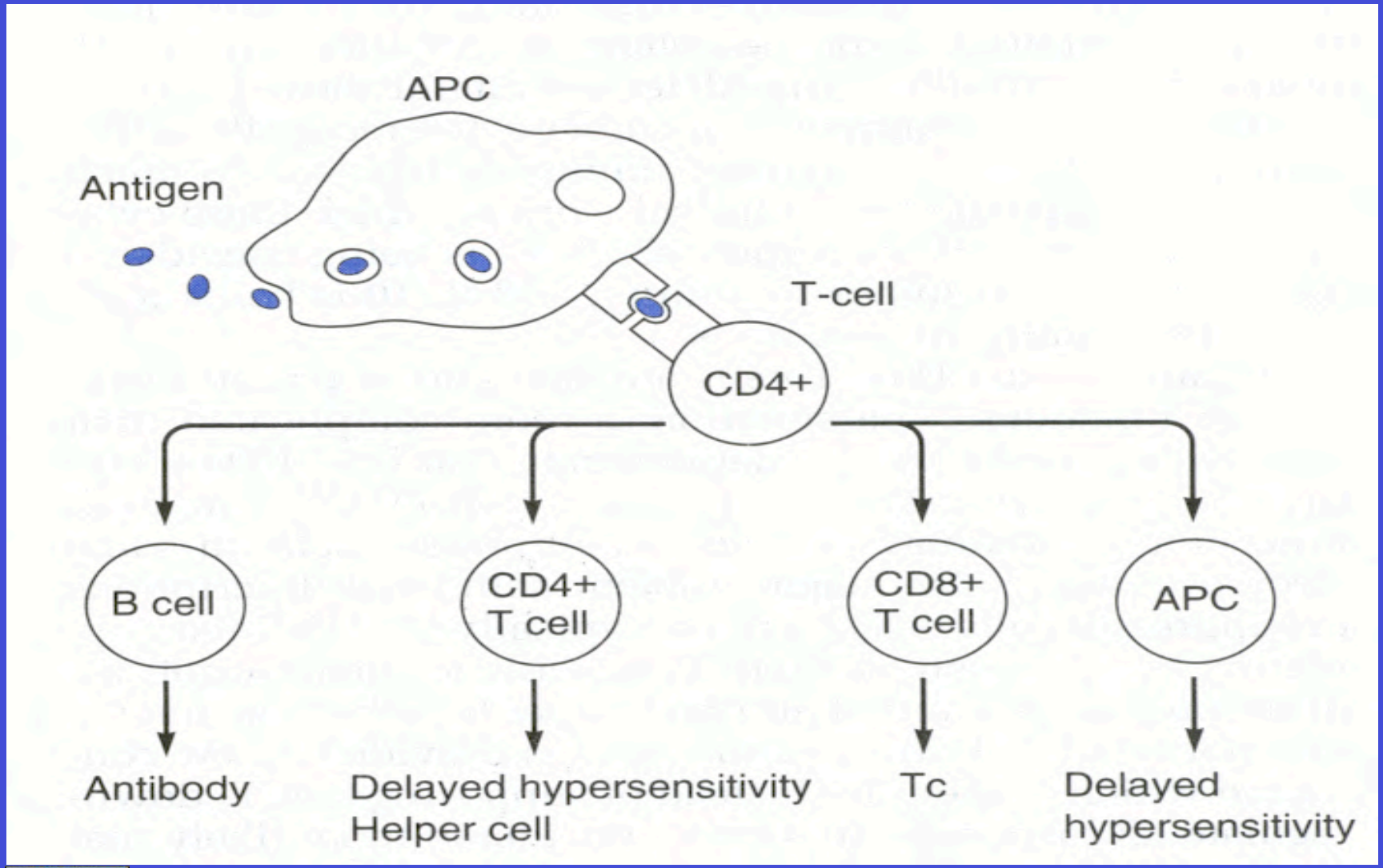
- To understand the role of the MHC
- To understand the 3 signals needed for T-cell activation
- To understand the mechanisms of transplant rejection
- To understand how transplant rejection is prevented

Thymic Selection



 Abbas,Lichtman, Pober: Cellular & Molecular Immunology, 4th Ed

Central Paradigm for Cellular Initiation of an Immune Response



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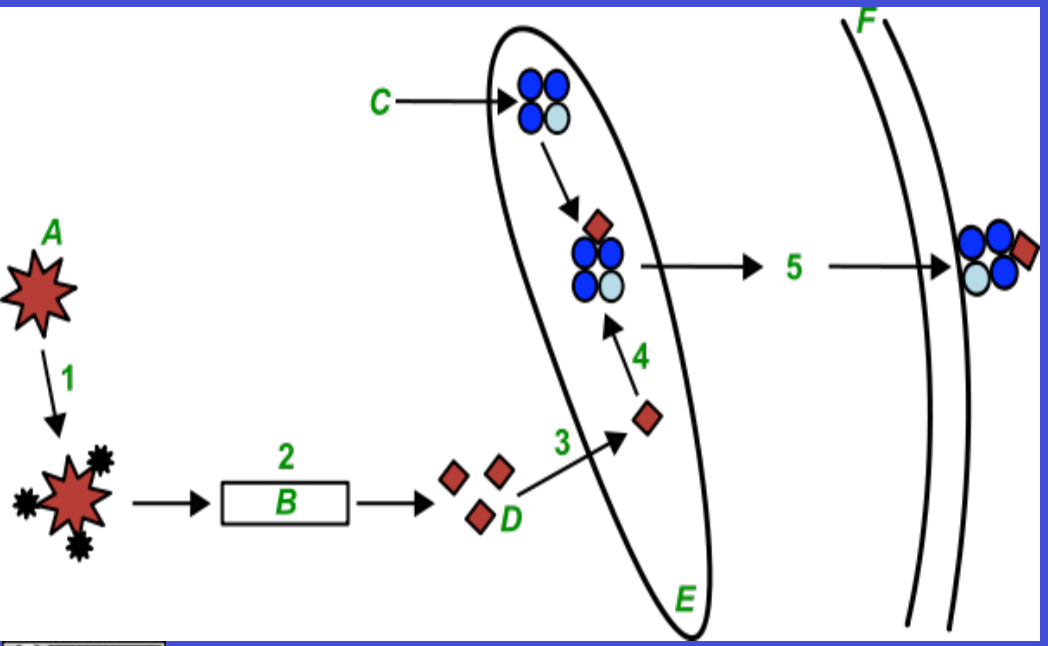
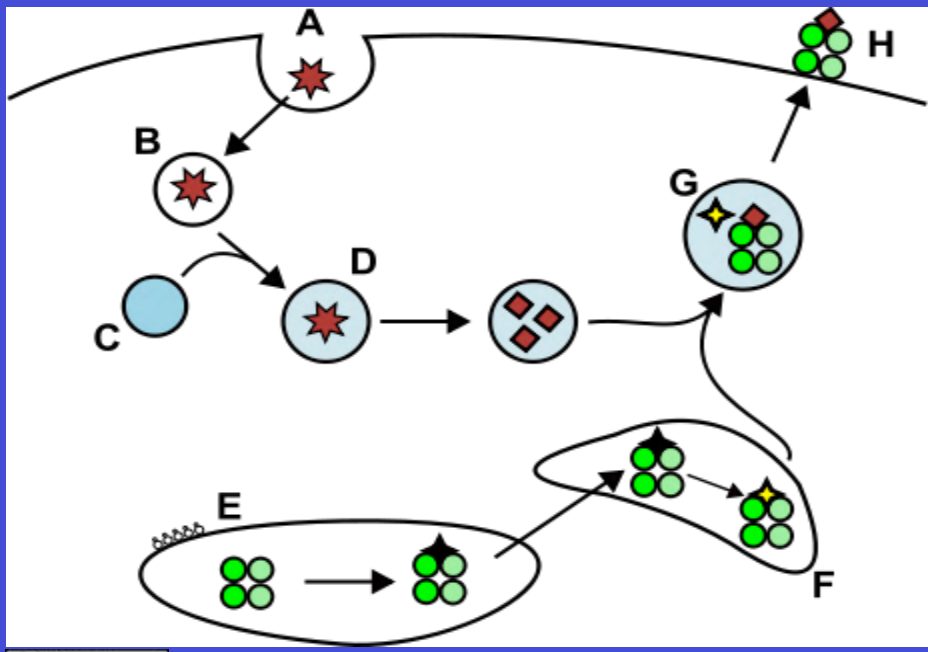
Antigen Processing and Presentation





- **MHC I antigen processing**
  - A Protein
  - B Proteasome
  - C MHC class I protein sythesis
  - D Peptides for presentation
  - E ER
  - F Plasma membrane

1. Ubiquitination
2. Protein degradation to peptides by proteasome
3. Transporting peptides to the lumen of ER by ABC transporters
4. Binding of peptides in a groove of MHC I complex
5. Antigen presentation on plasma membrane

- **MHC II antigen processing**
  - A Foreign protein
  - B Endosome
  - C Lysosome
  - D Late endosome/Phagolysosome
  - E Rough ER
  - F Golgi apparatus
  - G CLIP for antigen exchange
  - H Antigen presentation at plasma membrane

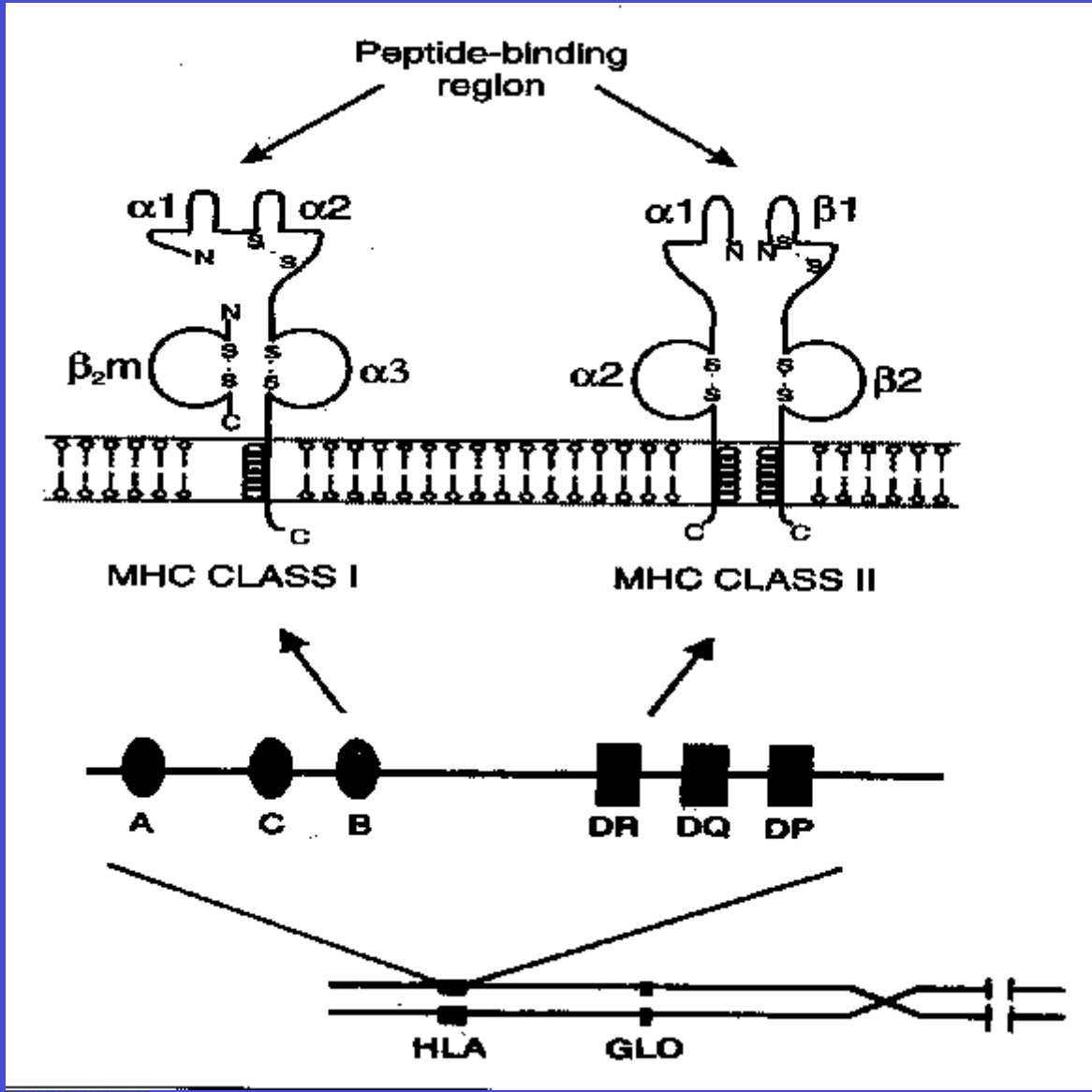
Antigen Presenting Cells

- Dendritic cells
- Macrophages
- B Lymphocytes
- Vascular endothelial cells
- Various epithelial and parenchymal cells

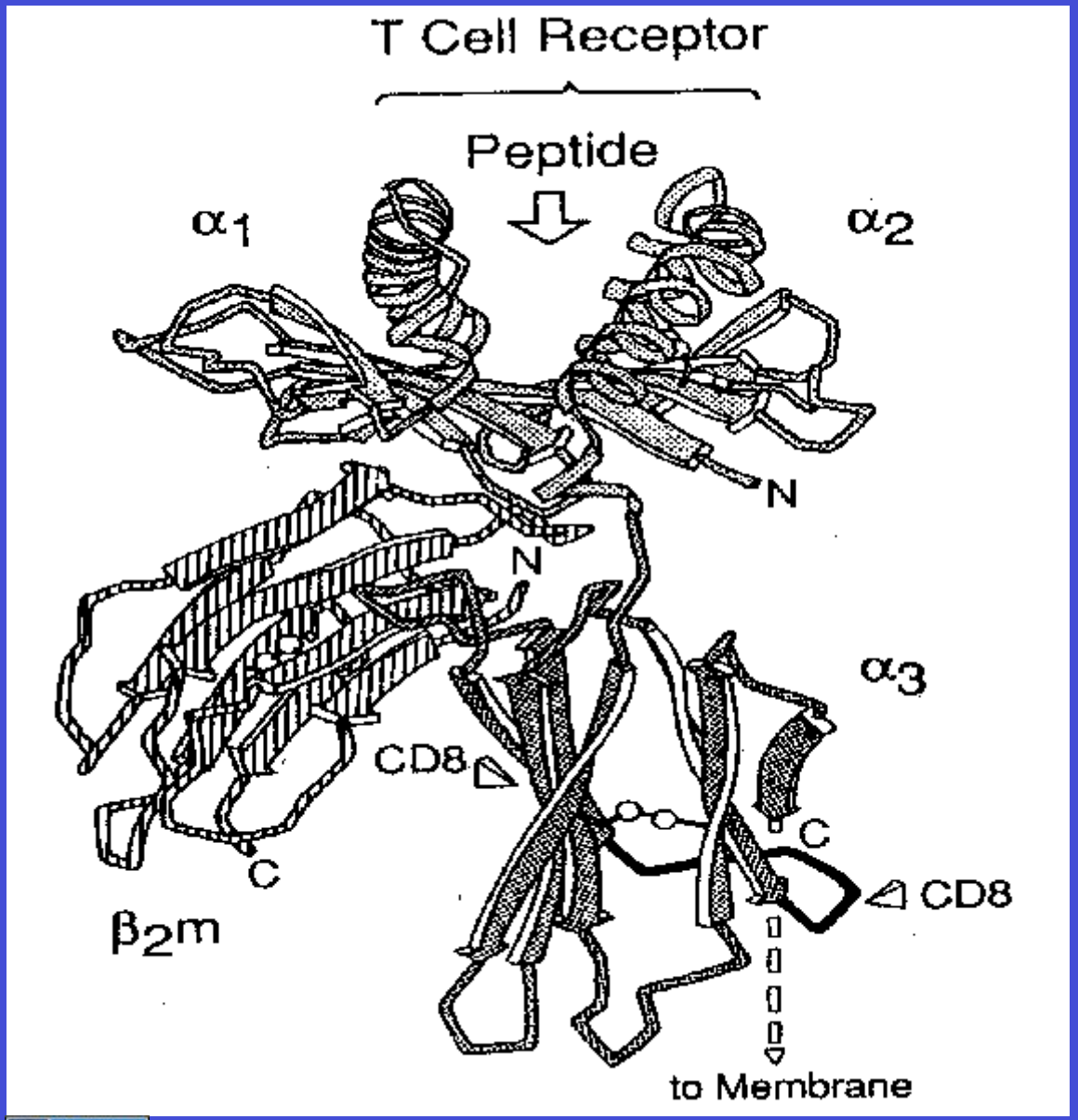
Antigen Presentation on APC

- Occurs through the major histocompatibility complex (MHC)
- The MHC are a group of genes that are responsible for the recognition of the graft as foreign
- The principal function of MHC is to present foreign antigen fragments that can be recognized by specific antigen receptors on T cells

MHC Class I and Class II



MHC Class I Molecule (HLA A2)



MHC Class I and II

- Class I is presented on all nucleated cells and recognized by CD8+ T cells
- Class II is presented on APC and recognized by CD4+ T cells

Human Leukocyte Antigen (HLA)

HLA's are polymorphic cell-surface molecules (alloantigens) that are encoded by the MHC genes

TABLE 7-1.

HLA Antigen Specificities

A	B	B	C	DR	DQ	DP
A1	B5	B5103	Cw1	DR1	DQ1	DPw1
A2	B7	B52(5)	Cw2	DR103	DQ2	DPw2
A203	B703	B53	Cw3	DR2	DQ3	DPw3
A210	B8	B54(22)	Cw4	DR3	DQ4	DPw4
A3	B12	B55(22)	Cw5	DR4	DQ5(1)	DPw5
A9	B13	B56(22)	Cw6	DR5	DQ6(1)	DPw6
A10	B14	B57(17)	Cw7	DR6	DQ7(3)	
A11	B15	B58(17)	Cw8	DR7	DQ8(3)	
A19	B16	B59	Cw9(w3)	DR8	DQ9(3)	
A23(9)	B17	B60(40)	Cw10(w3)	DR9		
A24(9)	B18	B61(40)		DR10		
A2403	B21	B62(15)		DR11(5)		
A25(10)	B22	B63(15)		DR12(5)		
A26(10)	B27	B64(14)		DR13(6)		
A28	B35	B65(14)		DR14(6)		
A29(19)	B37	B67		DR1403		
A30(19)	B38(16)	B70		DR1404		
A31(19)	B39(16)	B71(70)		DR15(2)		
A32(19)	B3901	B72(70)		DR16(2)		
A33(19)	B3902	B73		DR17(3)		
A34(10)	B40	B50(21)		DR18(3)		
A36	B4005	B51(5)		DR51		
A43	B41	B5102		DR52		
A66(10)	B42	B75(15)		DR53		
A68(28)	B44(12)	B76(15)				
A69(28)	B45(12)	B77(15)				
A74(19)	B46	B7801				
	B47					
	B48	Bw4				
	B49(21)	Bw6				

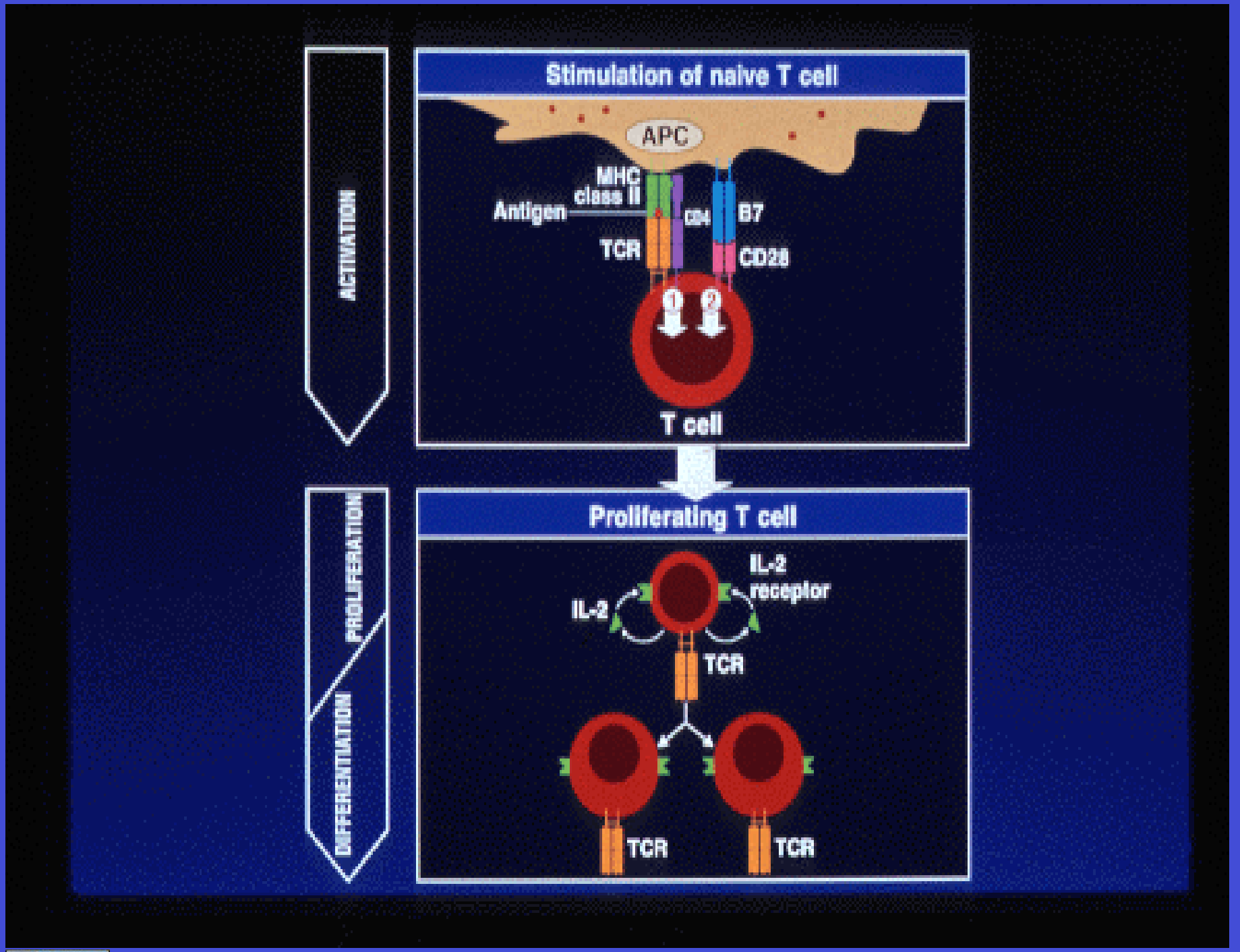
Antigens listed in parentheses are the broad antigens; antigens followed by broad antigens in parentheses are the antigen splits.

MHC Polymorphism

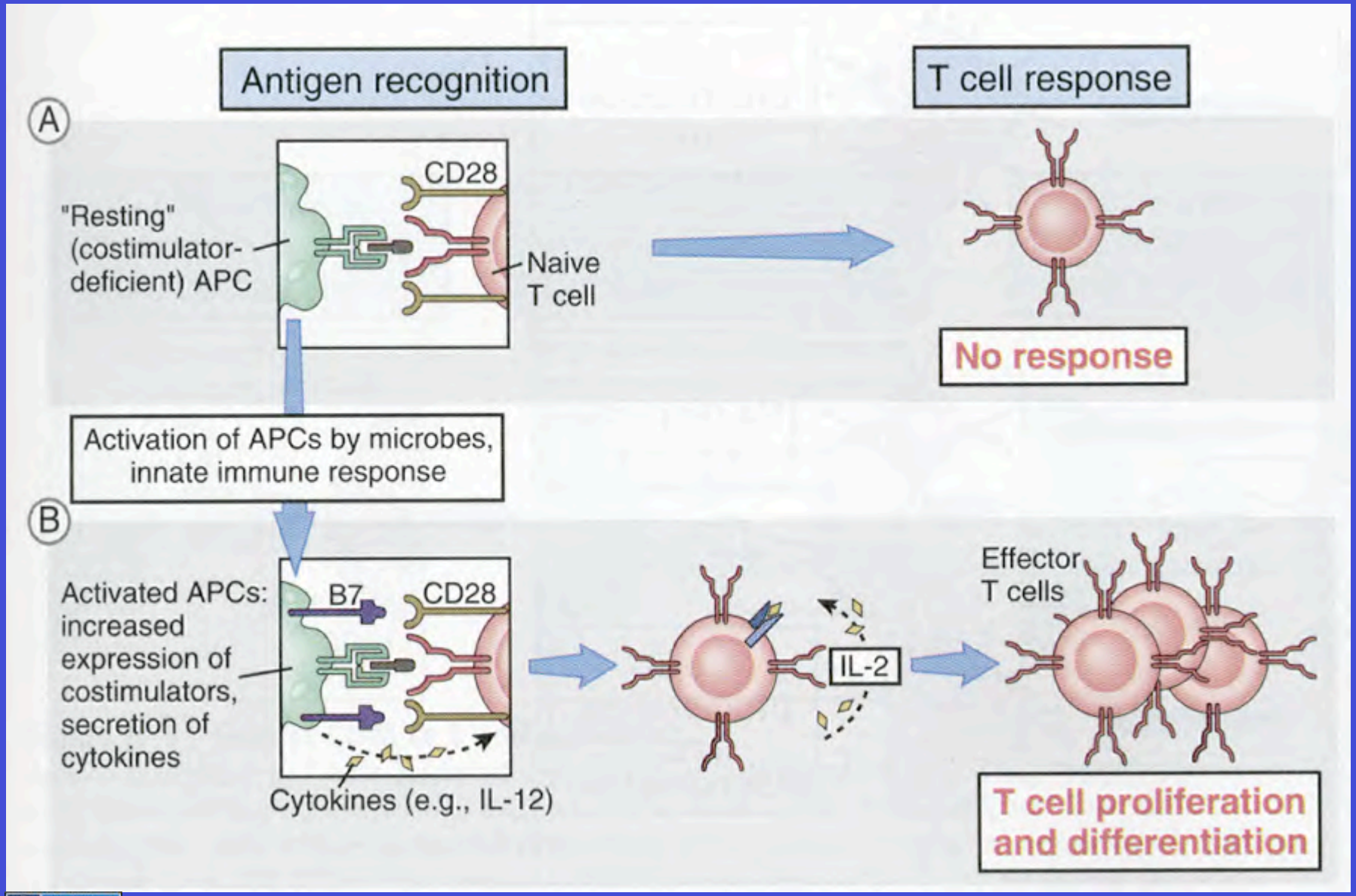
- MHC molecules are highly polymorphic to allow extraordinary levels of diversity in functionally important regions (peptide binding site) without losing structural integrity
- The large number of polymorphic MHC molecules expressed by an individual permits binding of an extensive range of structurally different peptides

Three Signals of Tcell Activation

- Antigen presentation and recognition (provides specificity – essential but not sufficient)
- Costimulation – needed for T-cell proliferation
- Autocrine proliferation



Role of Co-stimulation in T Cell Activation



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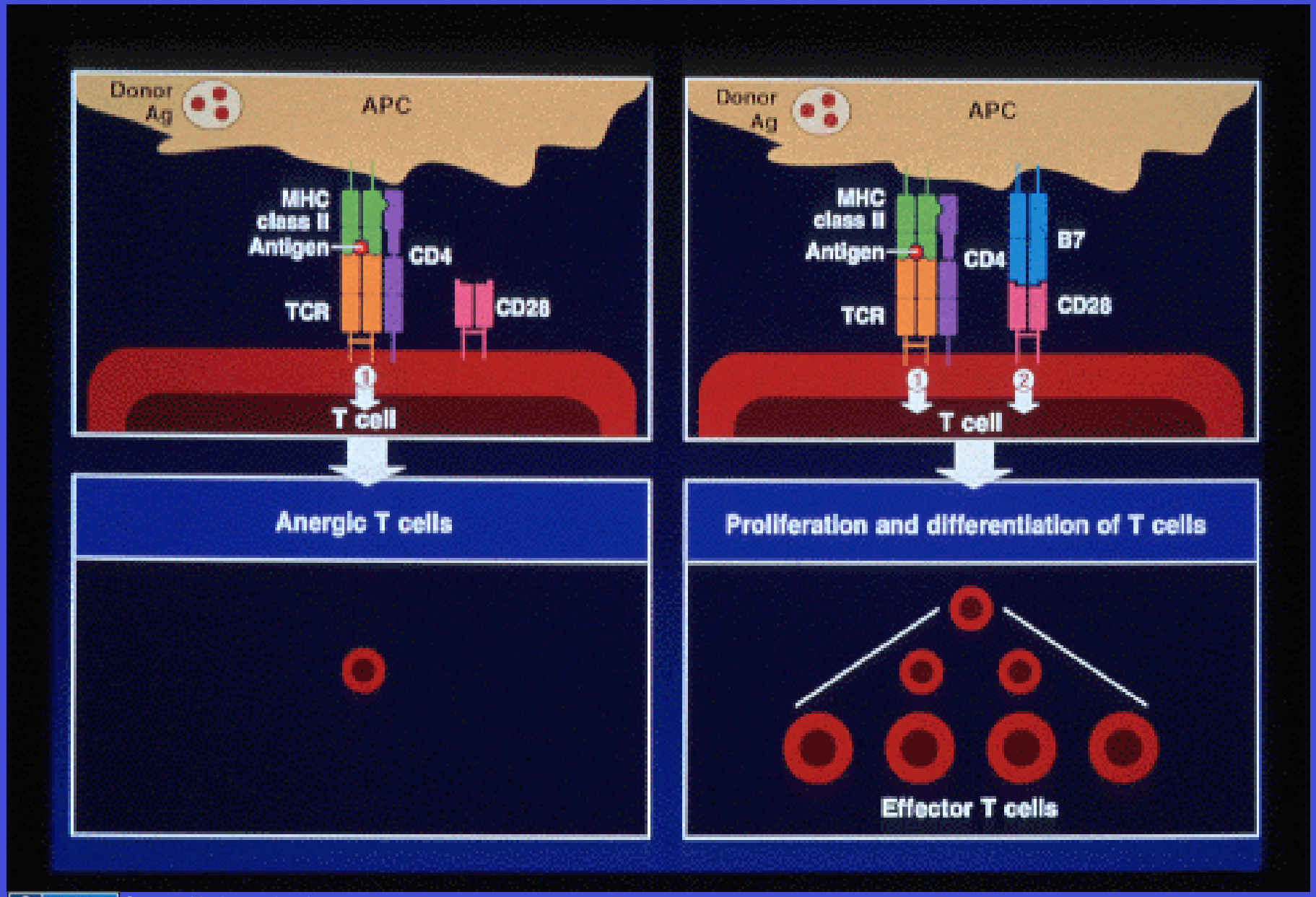
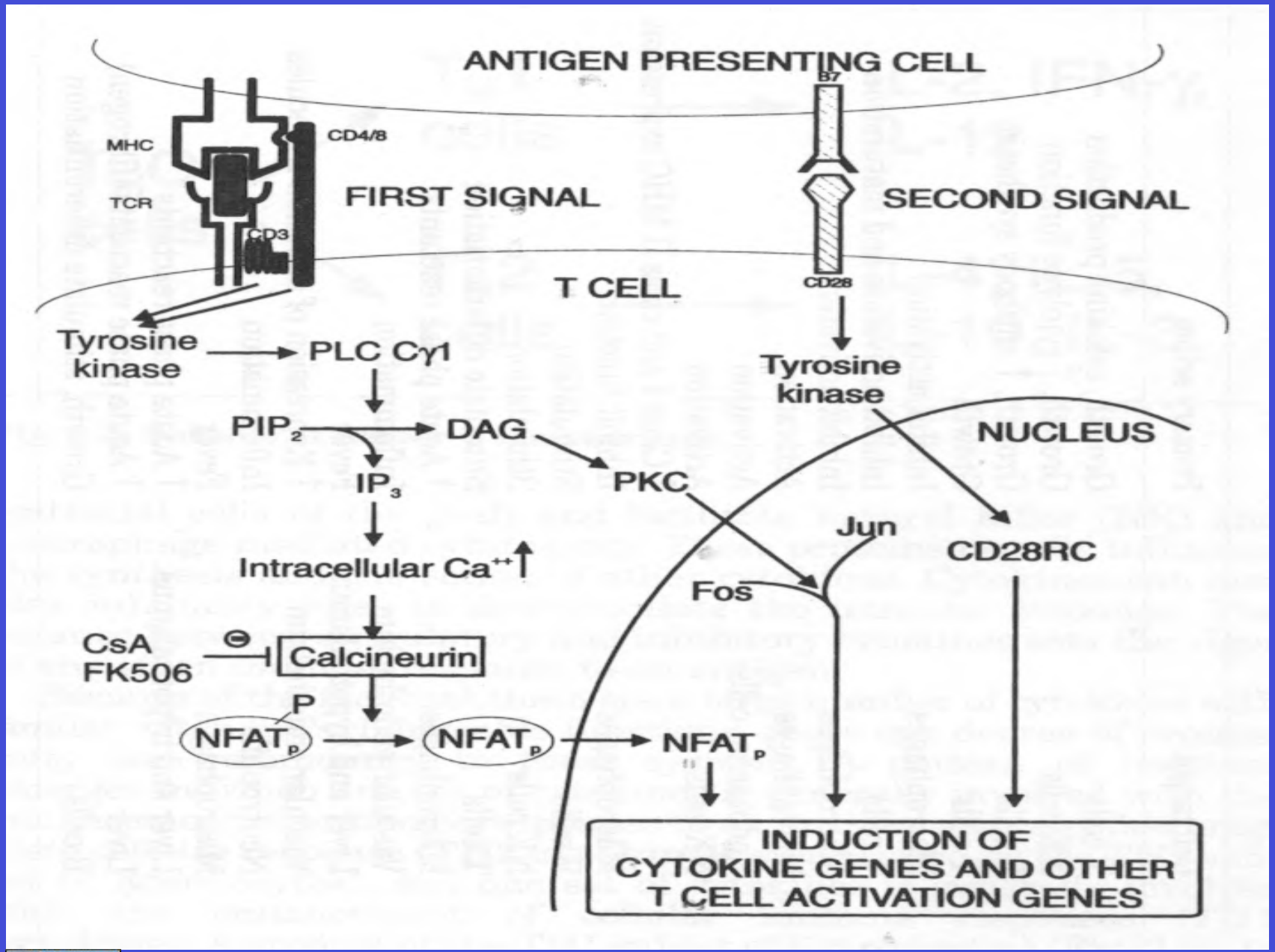
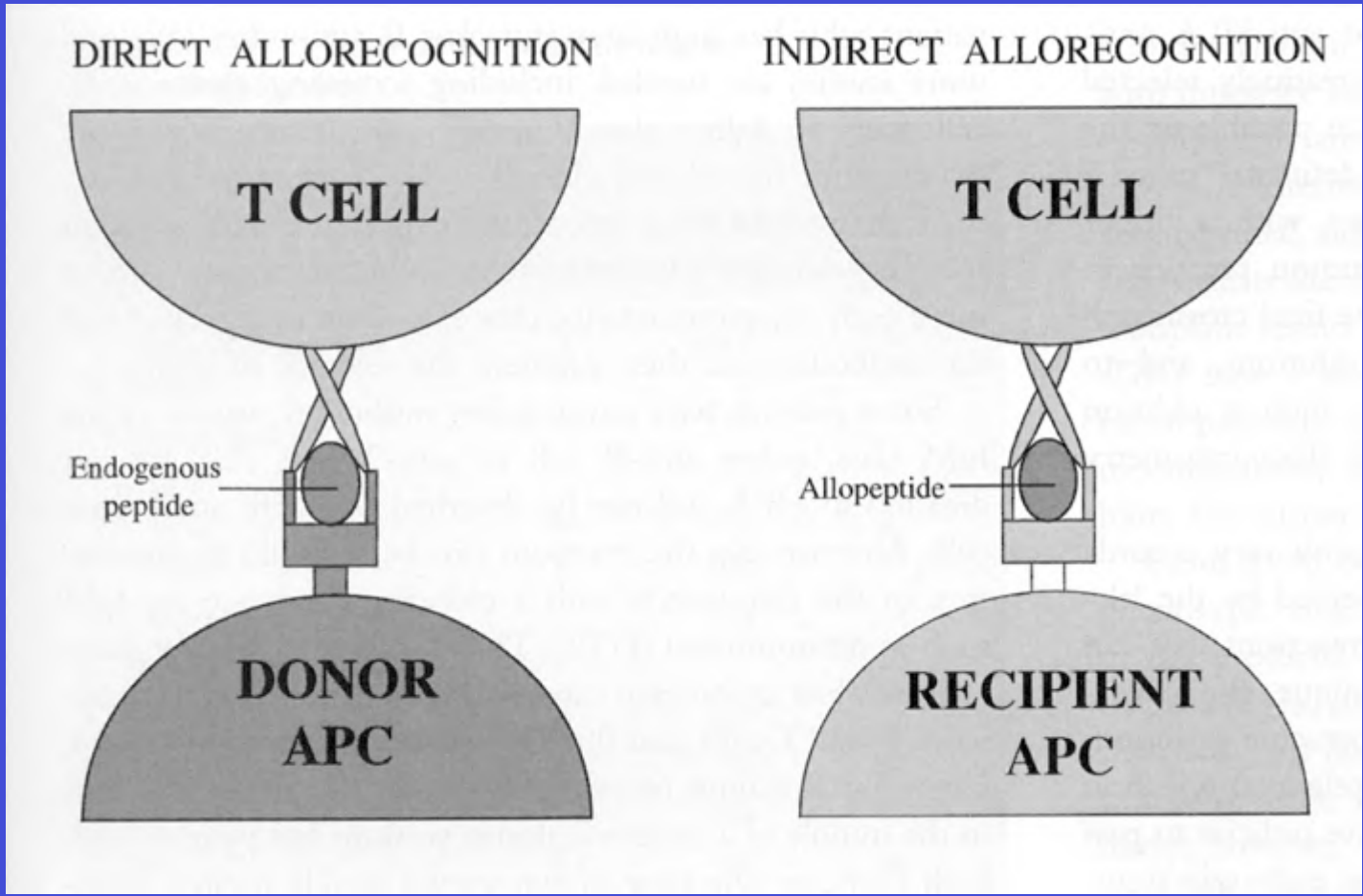


Intracellular signaling pathways in T cell activation



Allorecognition
Direct vs Indirect



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