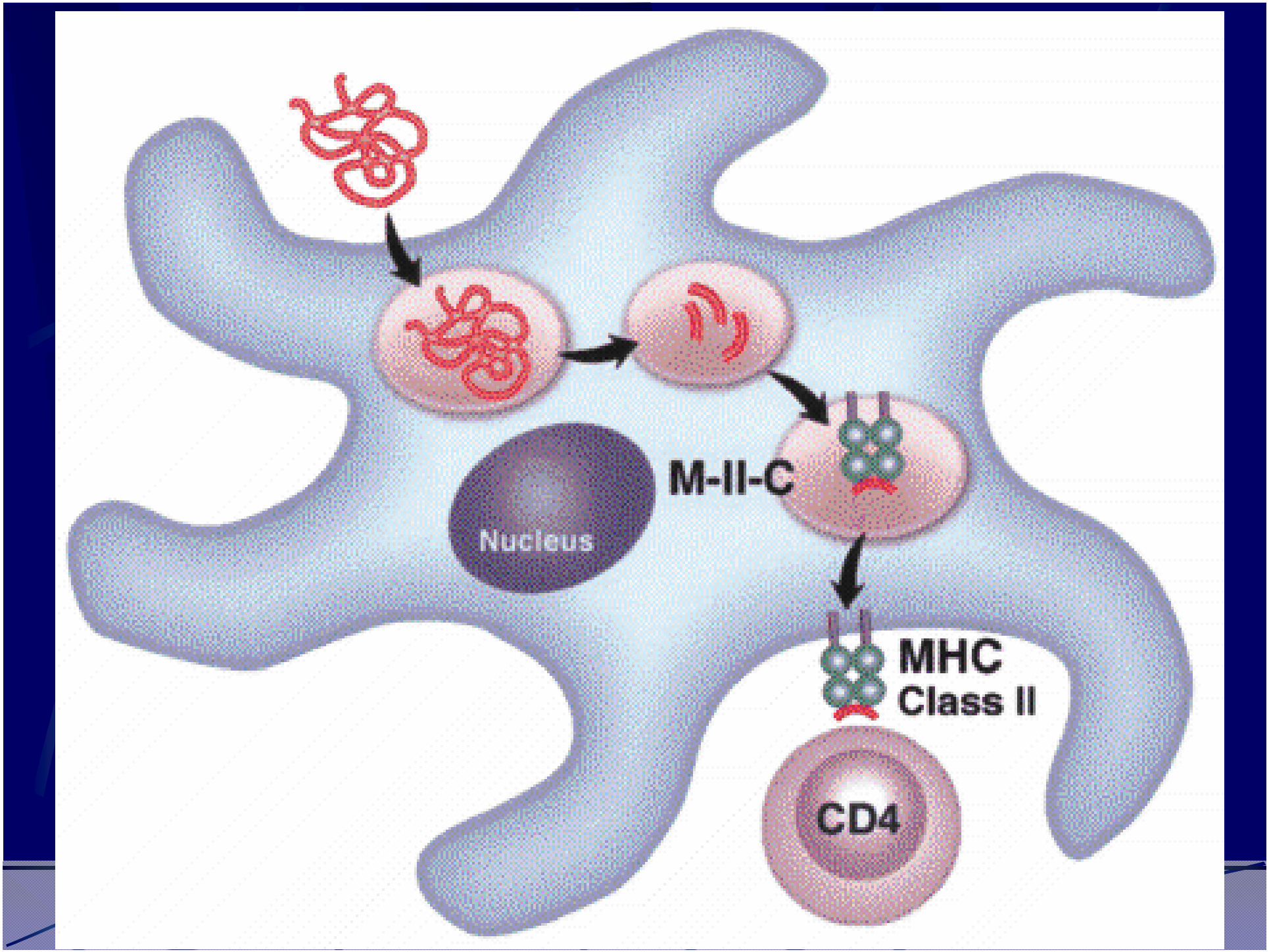
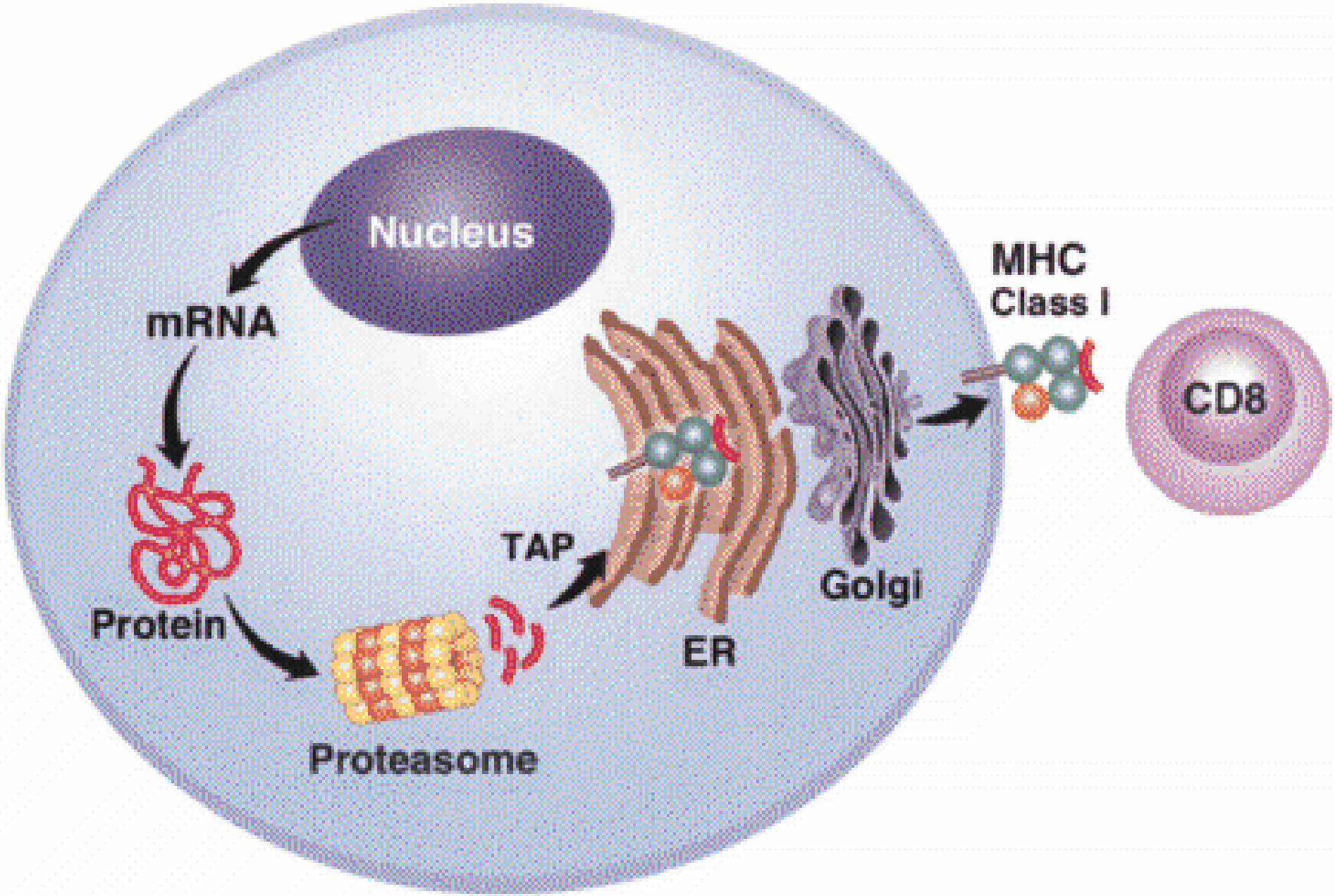
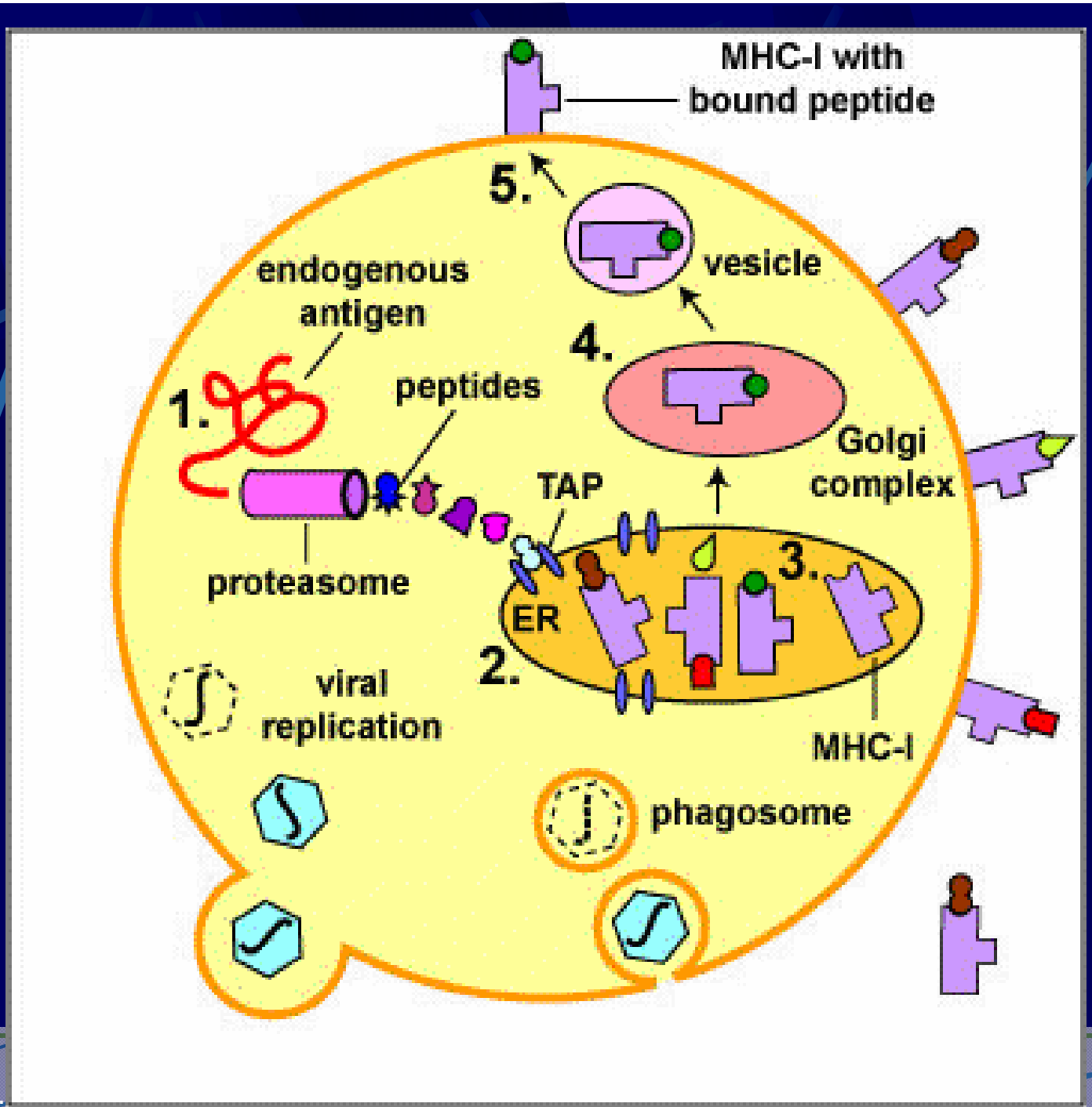
Главный комплекс гистосовместимости

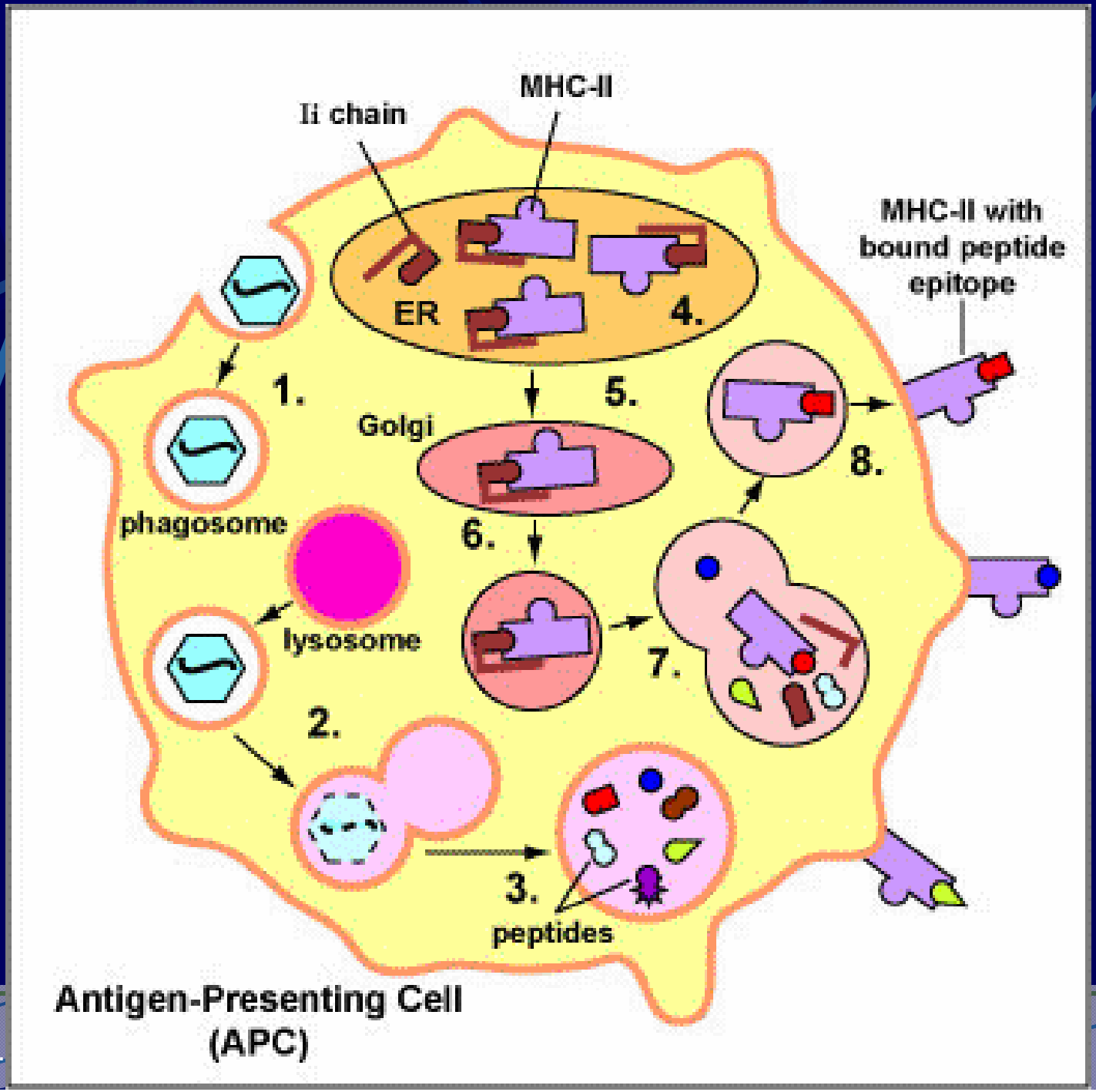
2

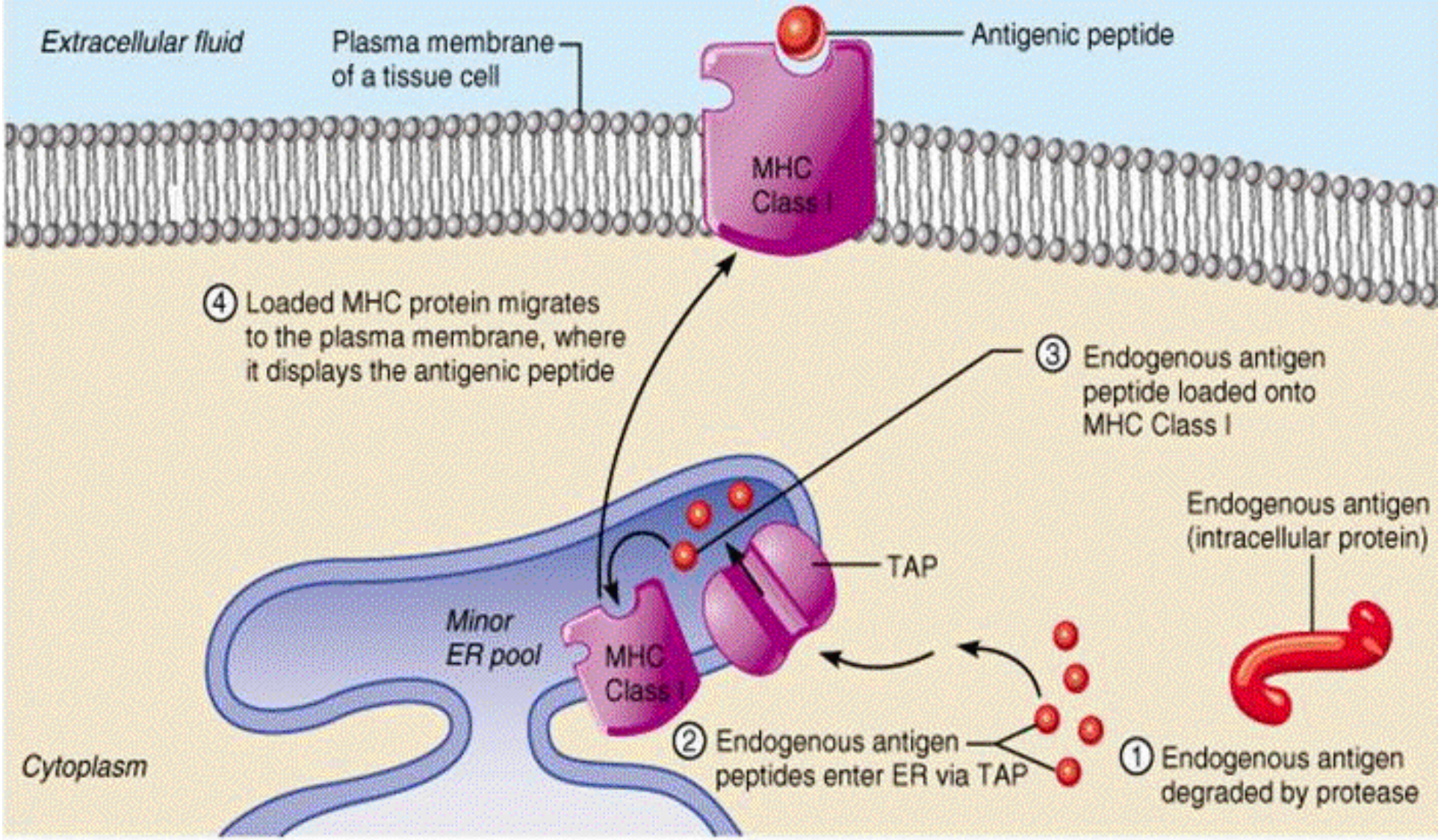
Подготовлено
доцентом Ю.И.Будчановым

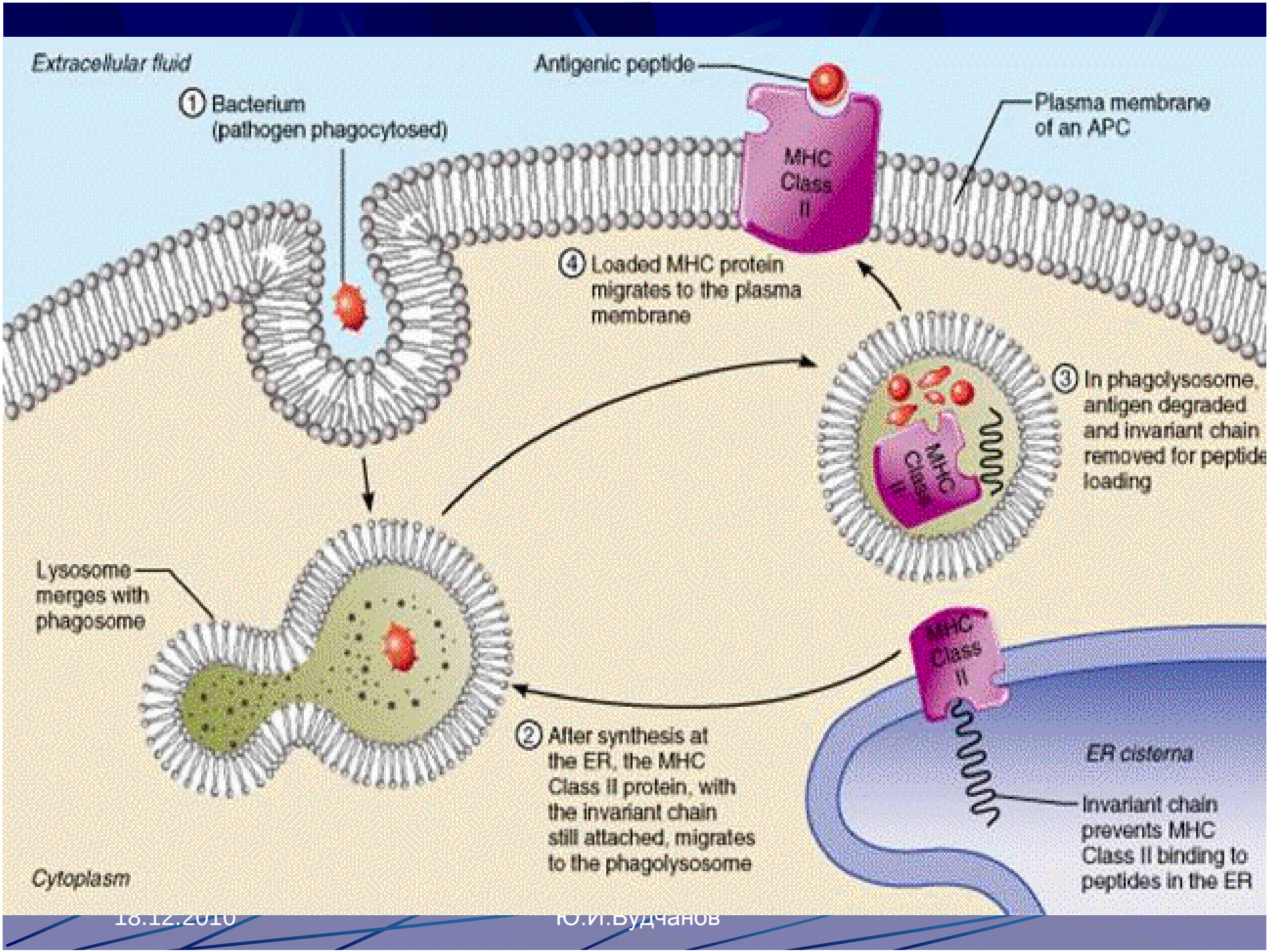

Nucleus
M-II-C
MHC
Class II
CD4

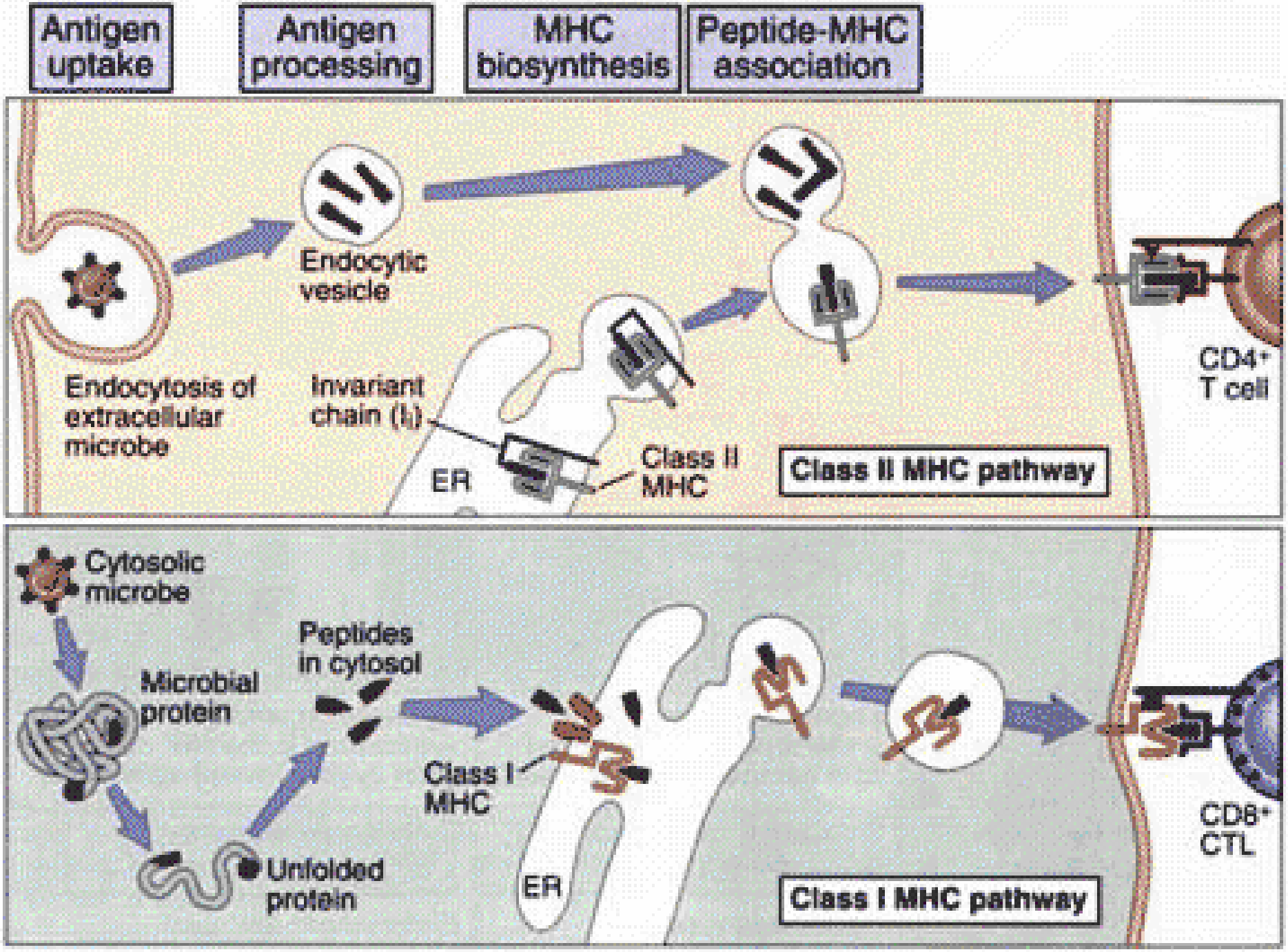

Nucleus
mRNA
Protein
Proteasome
TAP
ER
Golgi
MHC
Class I
CD8

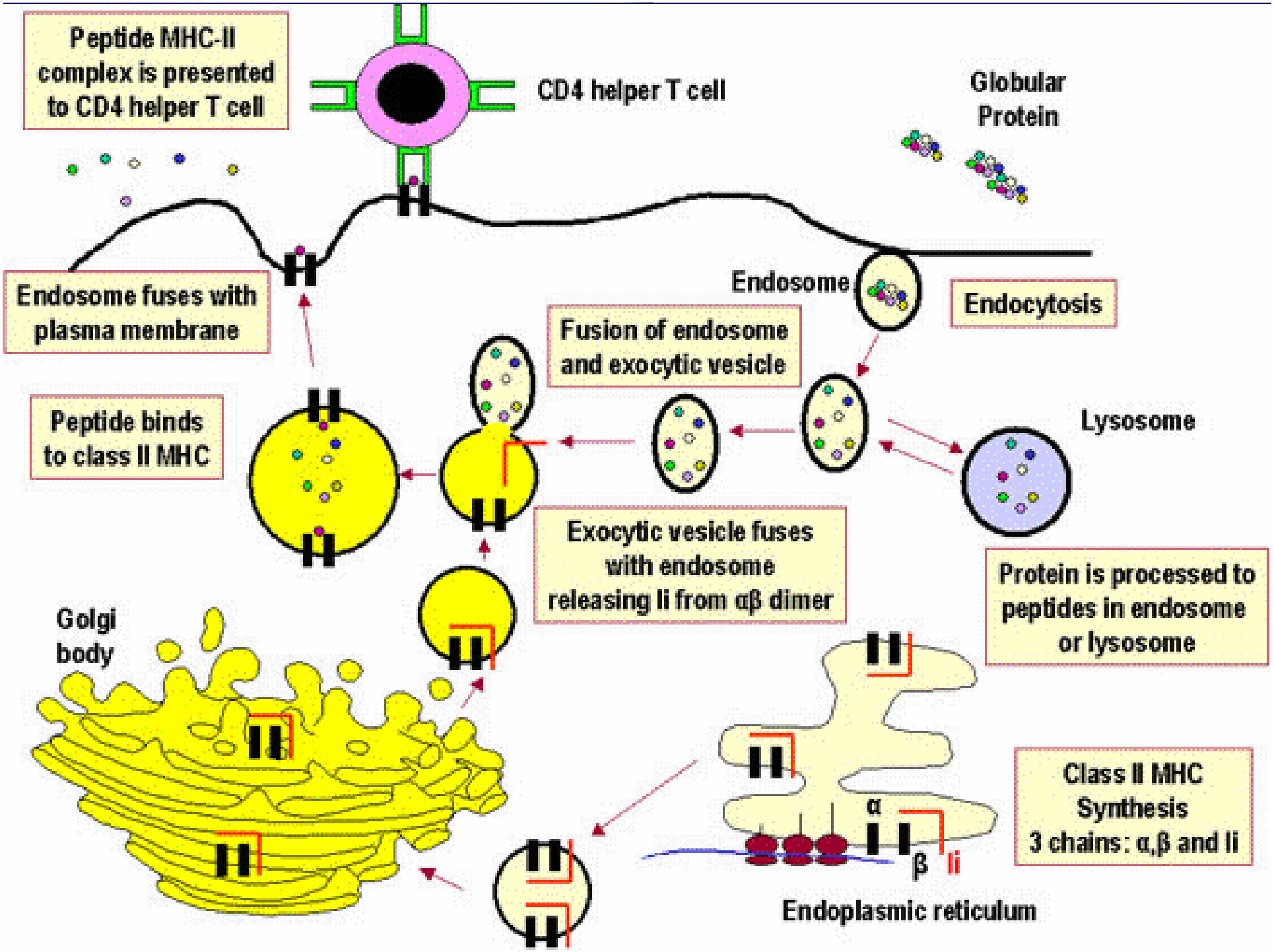

MHC-I with
bound peptide
5.
vesicle
endogenous
antigen
4.
1.
peptides
Golgi
complex
TAP
3.
proteasome
ER
2.
viral
replication
MHC-I
phagosome

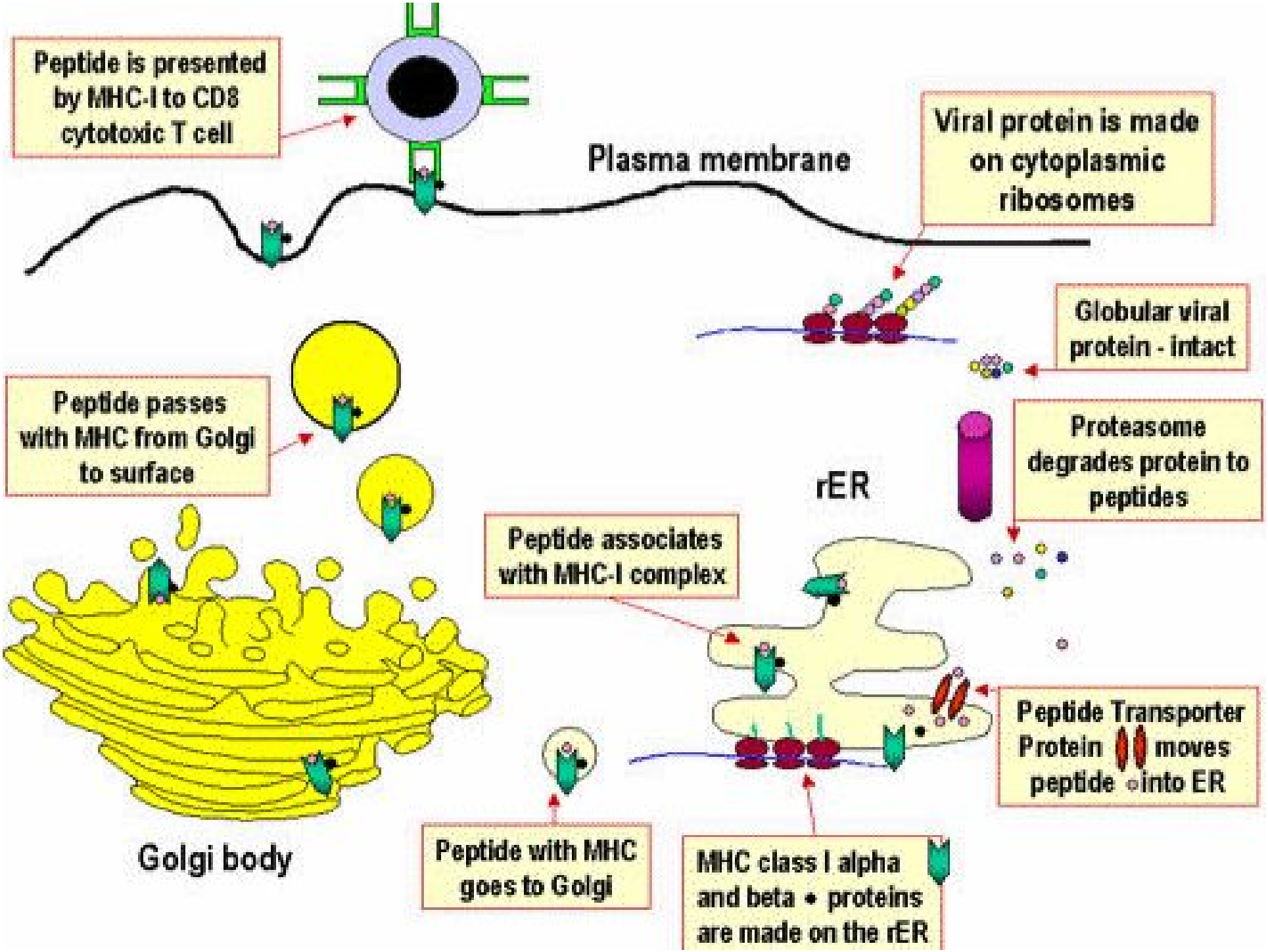

MHC-II
Ii chain
MHC-II with
bound peptide
epitope
ER
4.
1.
5.
Golgi
8.
phagosome
6.
lysosome
7.
2.
3.
peptides
Antigen-Presenting Cell
(APC)

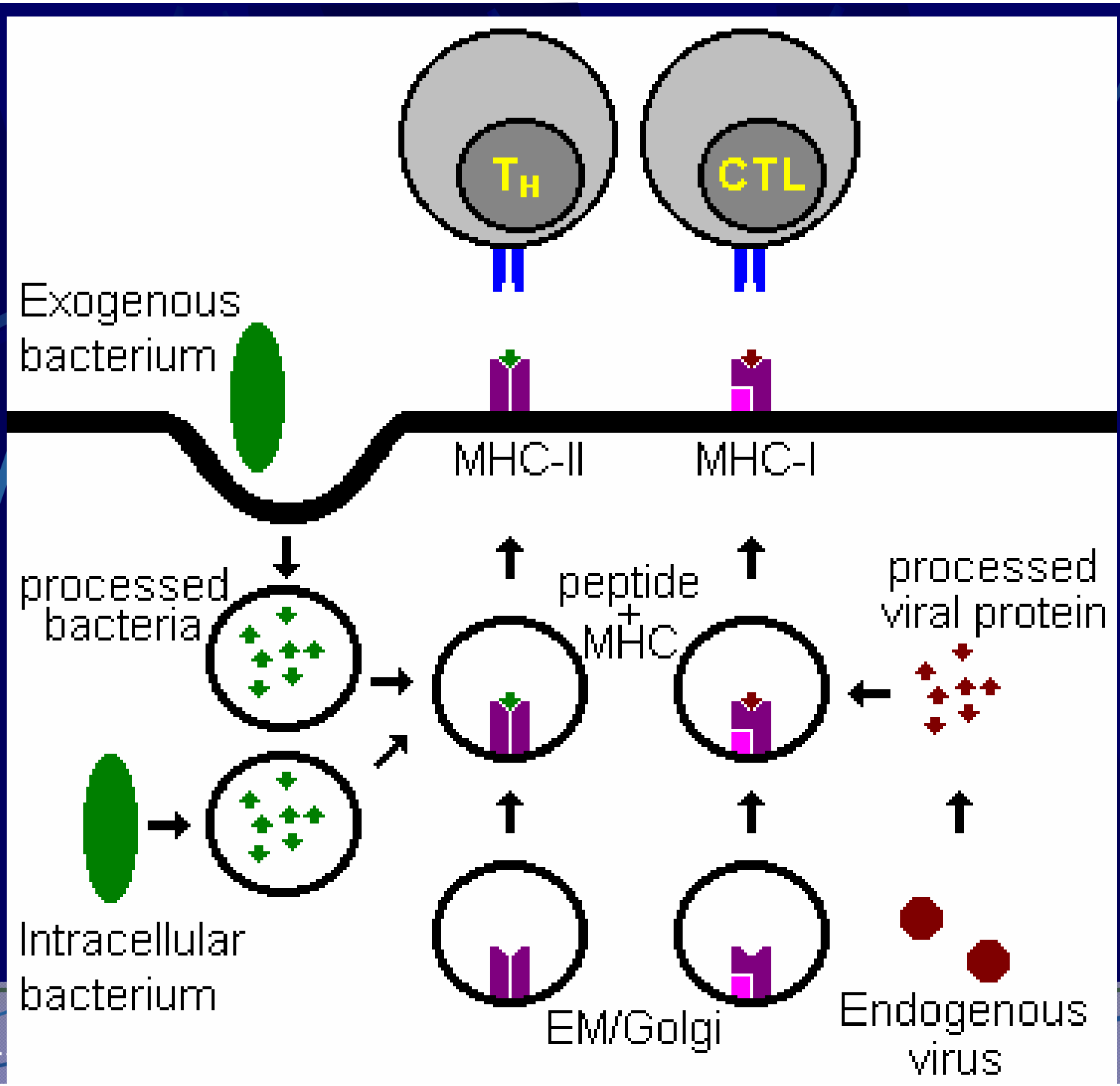

Extracellular fluid
Plasma membrane of a tissue cell
Antigenic peptide
MHC Class I
④ Loaded MHC protein migrates to the plasma membrane, where it displays the antigenic peptide
③ Endogenous antigen peptide loaded onto MHC Class I
Endogenous antigen (intracellular protein)
TAP
Minor ER pool
MHC Class I
② Endogenous antigen peptides enter ER via TAP
① Endogenous antigen degraded by protease
Cytoplasm

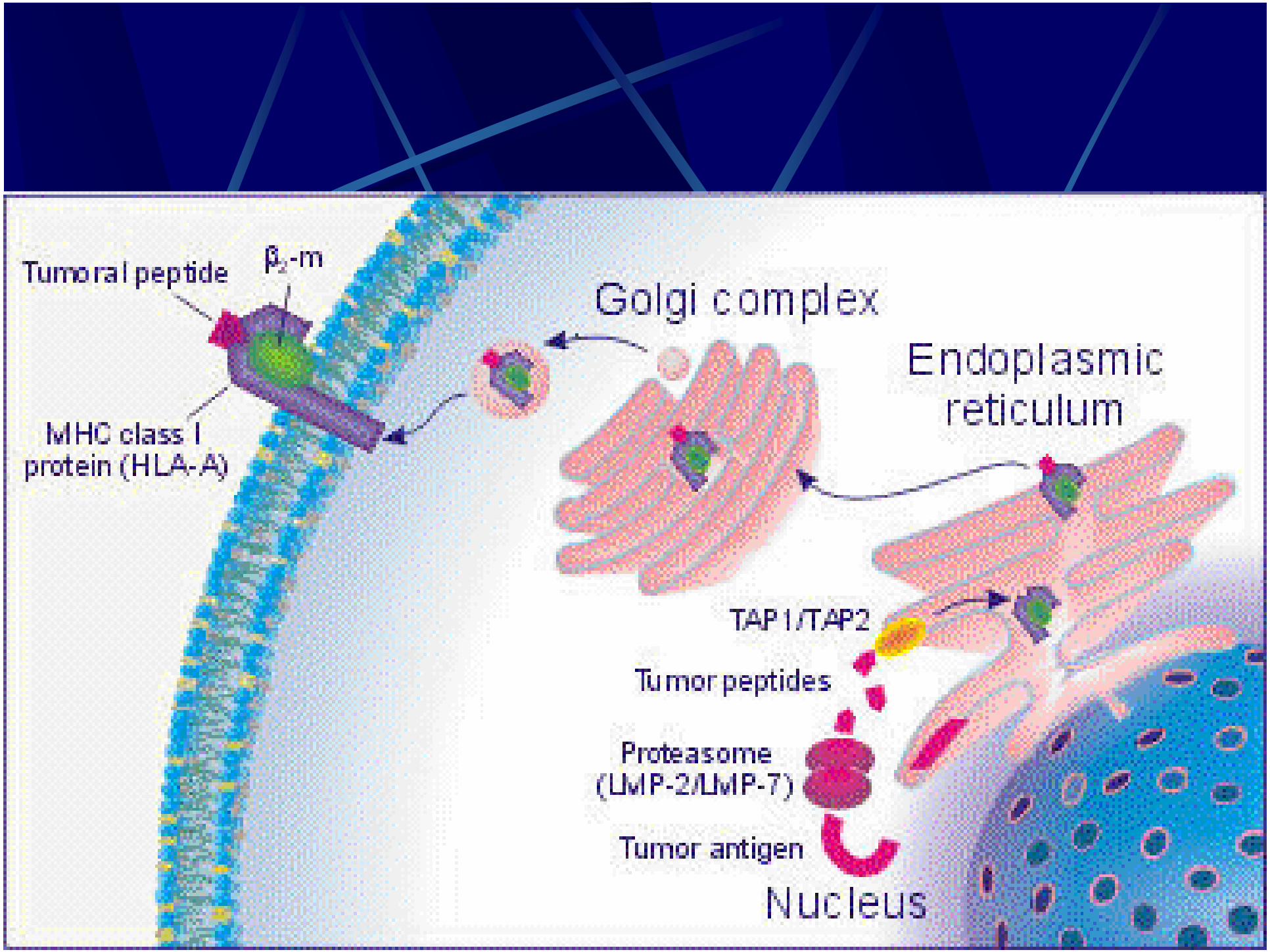

Extracellular fluid
Antigenic peptide
1 Bacterium (pathogen phagocytosed)
Plasma membrane of an APC
MHC Class II
4 Loaded MHC protein migrates to the plasma membrane
3 In phagolysosome, antigen degraded and invariant chain removed for peptide loading
Lysosome merges with phagosome
2 After synthesis at the ER, the MHC Class II protein, with the invariant chain still attached, migrates to the phagolysosome
ER cisterna
Invariant chain prevents MHC Class II binding to peptides in the ER
Cytoplasm

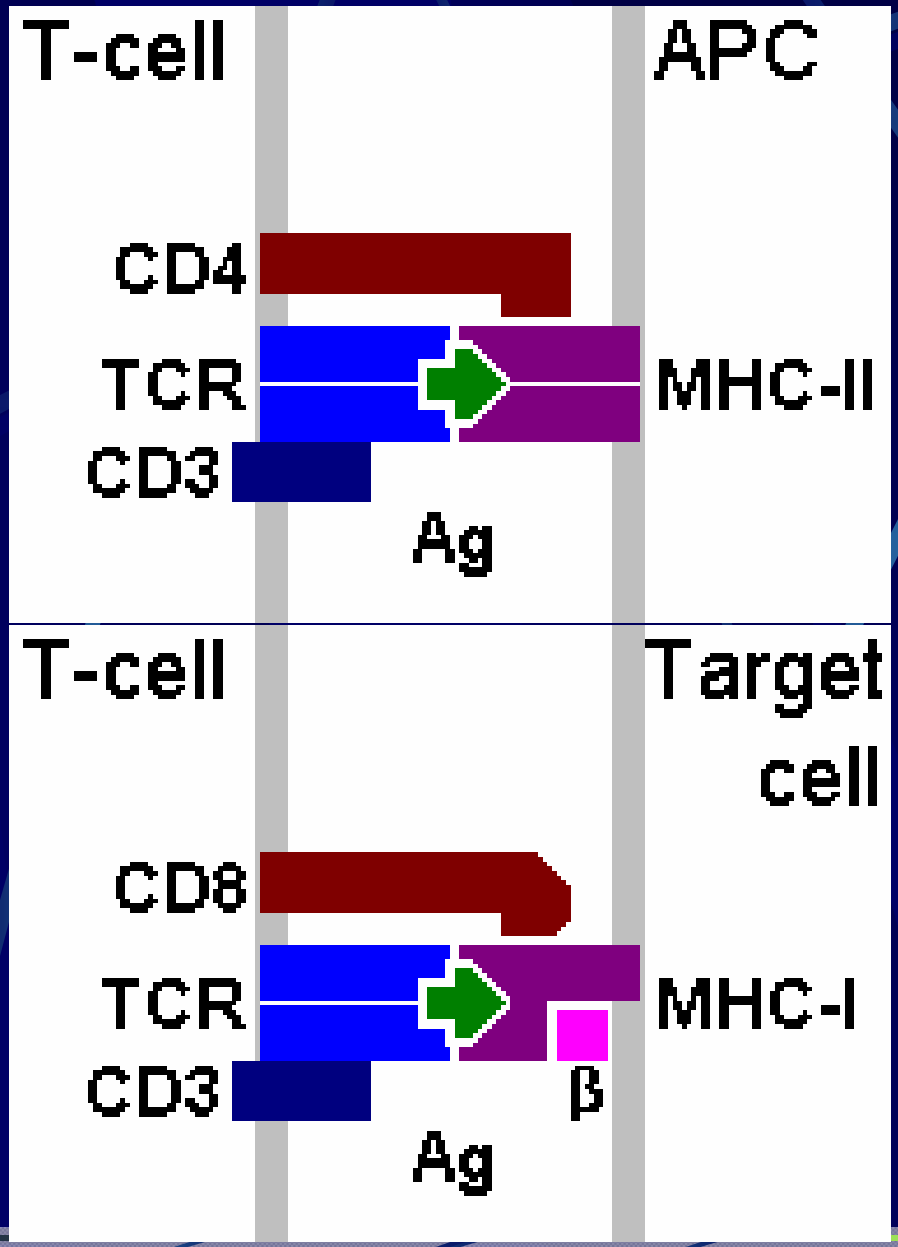

Antigen uptake
Antigen processing
MHC biosynthesis
Peptide-MHC association
Endocytic vesicle
Endocytosis of extracellular microbe
Invariant chain (Ii)
ER
Class II MHC
Class II MHC pathway
CD4+ T cell
Cytosolic microbe
Microbial protein
Peptides in cytosol
Unfolded protein
Class I MHC
ER
Class I MHC pathway
CD8+ CTL

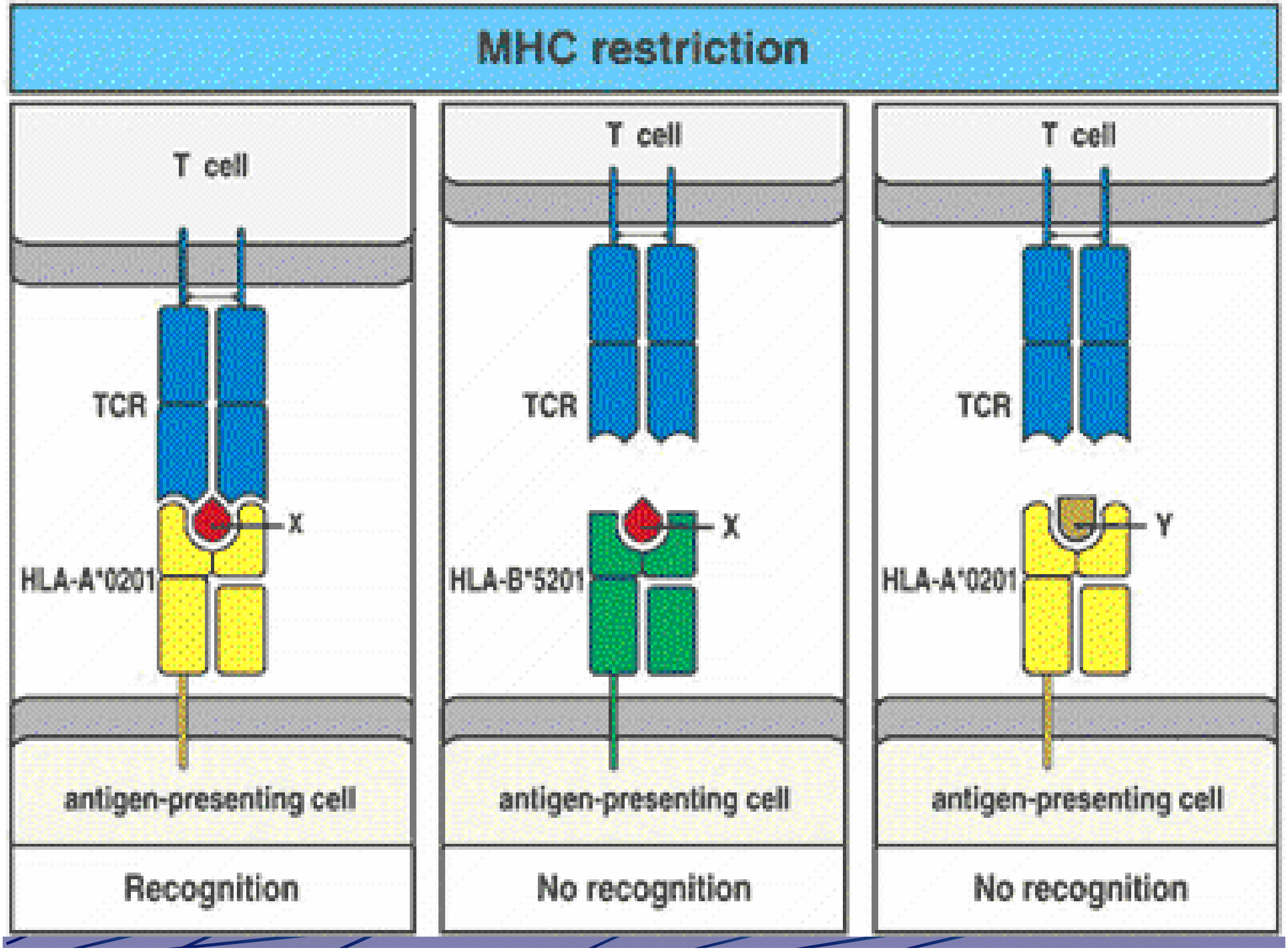

Peptide MHC-II complex is presented to CD4 helper T cell
CD4 helper T cell
Globular Protein
Endosome fuses with plasma membrane
Endosome
Endocytosis
Fusion of endosome and exocytic vesicle
Peptide binds to class II MHC
Lysosome
Exocytic vesicle fuses with endosome releasing Ii from αβ dimer
Protein is processed to peptides in endosome or lysosome
Golgi body
Class II MHC Synthesis 3 chains: α,β and Ii
α
β
Ii
Endoplasmic reticulum

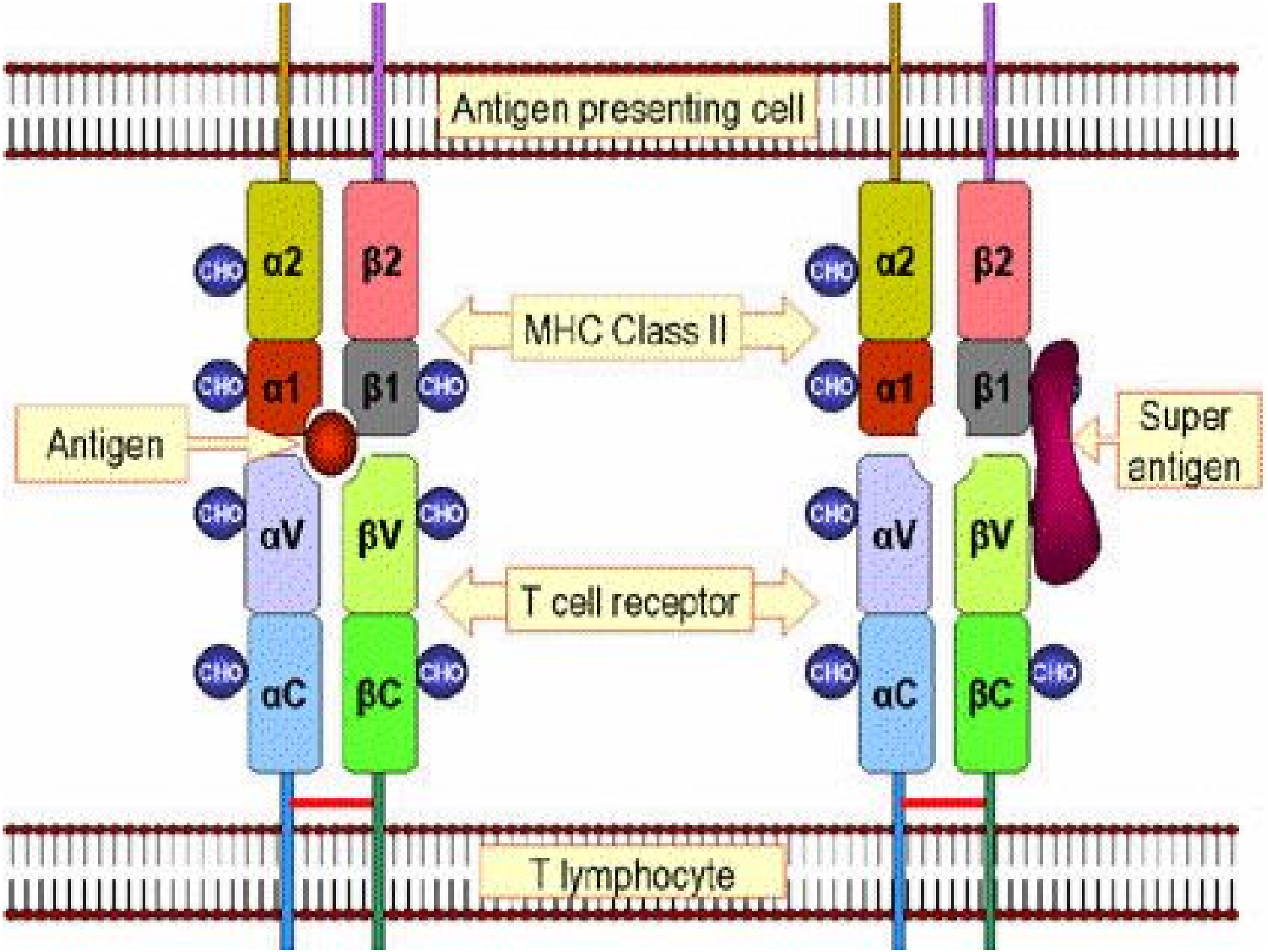

Peptide is presented by MHC-I to CD8 cytotoxic T cell
Plasma membrane
Viral protein is made on cytoplasmic ribosomes
Globular viral protein - intact
Proteasome degrades protein to peptides
Peptide passes with MHC from Golgi to surface
rER
Peptide associates with MHC-I complex
Peptide Transporter Protein moves peptide into ER
Golgi body
Peptide with MHC goes to Golgi
MHC class I alpha and beta • proteins are made on the rER

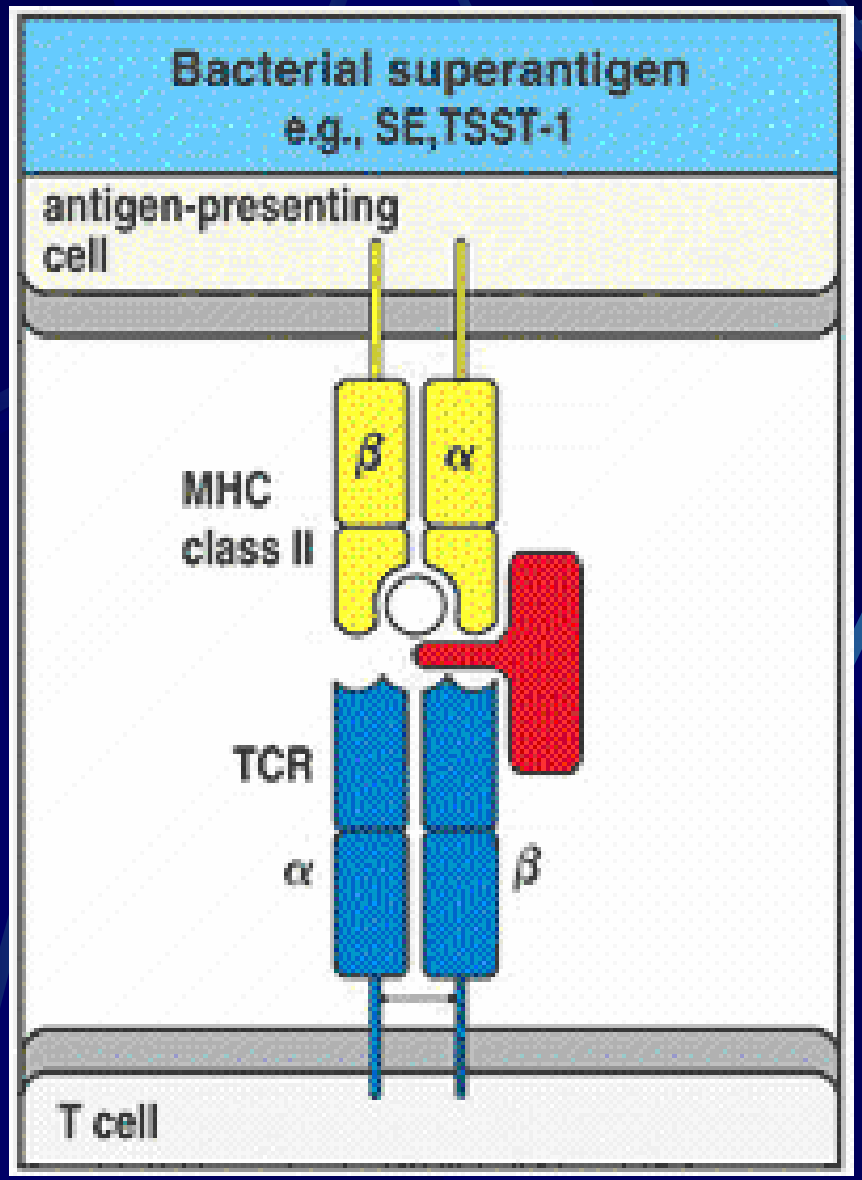

TH
CTL
Exogenous bacterium
MHC-II
MHC-I
processed bacteria
peptide + MHC
processed viral protein
Intracellular bacterium
EM/Golgi
Endogenous virus


Tumoral peptide
β2-m
MHC class I protein (HLA-A)
Golgi complex
Endoplasmic reticulum
TAP1/TAP2
Tumor peptides
Proteasome (LMP-2/LMP-7)
Tumor antigen
Nucleus


T-cell
APC
CD4
TCR
MHC-II
CD3
Ag
T-cell
Target cell
CD8
TCR
MHC-I
CD3
β
Ag


MHC restriction
T cell
TCR
X
HLA-A*0201
antigen-presenting cell
Recognition
T cell
TCR
X
HLA-B*5201
antigen-presenting cell
No recognition
T cell
TCR
Y
HLA-A*0201
antigen-presenting cell
No recognition


Antigen presenting cell
α2
β2
CHO
MHC Class II
α1
β1
Antigen
Super antigen
αV
βV
T cell receptor
αC
βC
T lymphocyte



Суперантиген

HLA и болезни

TABLE 1. ASSOCIATION BETWEEN THE PRESENCE OF VARIOUS HLA MARKERS AND SELECTED AUTOIMMUNE DISEASES.

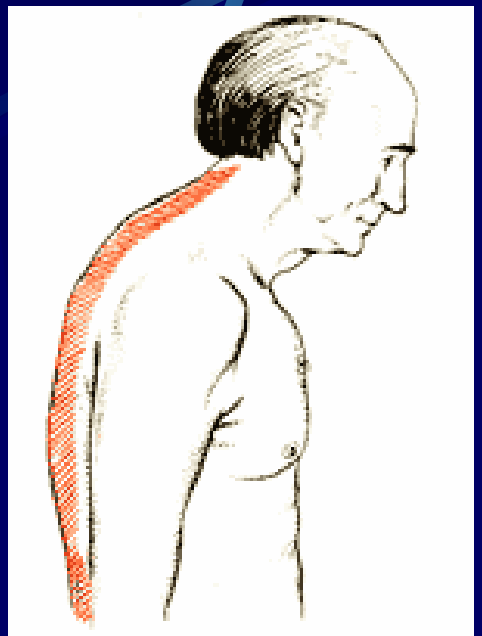
DISEASE	ASSOCIATED HLA MARKER*	RELATIVE RISK OF DISEASE†
Ankylosing spondylitis	B27	87.4
Reactive arthropathy, including Reiter's syndrome	B27	37.0
Rheumatoid arthritis	DR4	4.2
Behçet's syndrome	B51	3.8
Systemic lupus erythematosus	DR3	5.8
Insulin-dependent (type 1) diabetes mellitus	DR3	3.3
	DQB1*0201	2.4
	DR4	6.4
	DQB1*0302	9.5
	DR2	0.19
	DRB*1501‡	
	DRB*0101‡	
	DQB1*0602	0.15
Idiopathic Addison's disease	DR3	6.3
Graves' disease	DR3	3.7
Hashimoto's disease	DR11	3.2
Postpartum thyroiditis	DR4	5.3
Celiac disease	DR3	10.8
	DQB1*0201‡	
	DQA1*0501‡	
	DR7, 11	6.0–10.0
	DR7, DQB1*0201‡	
	DR11, DQA1*0501‡	
Dermatitis herpetiformis	DR3	15.9
Sicca syndrome	DR3	9.7
Myasthenia gravis	DR3	2.5
	B8	3.4
Idiopathic membranous glomerulonephritis	DR3	12.0
Goodpasture's syndrome	DR2	15.9

Ассоциация заболеваний

с HLA антигенами.

Определяет предрасположенность человека к ряду болезней

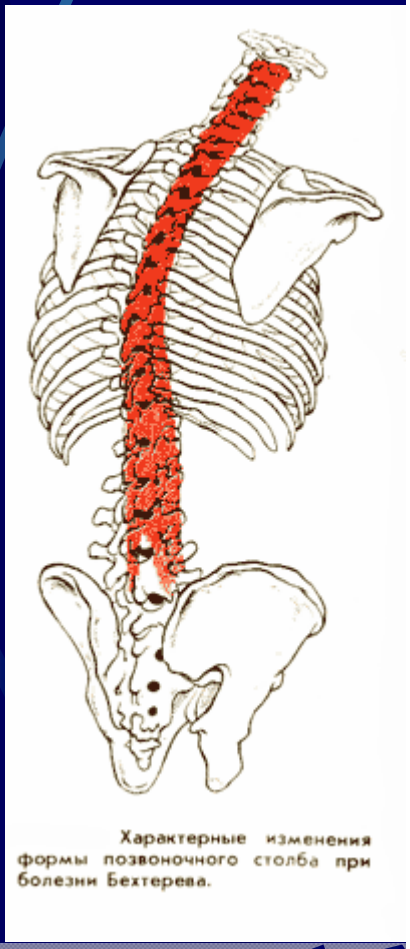
Анкилозирующий спондилит



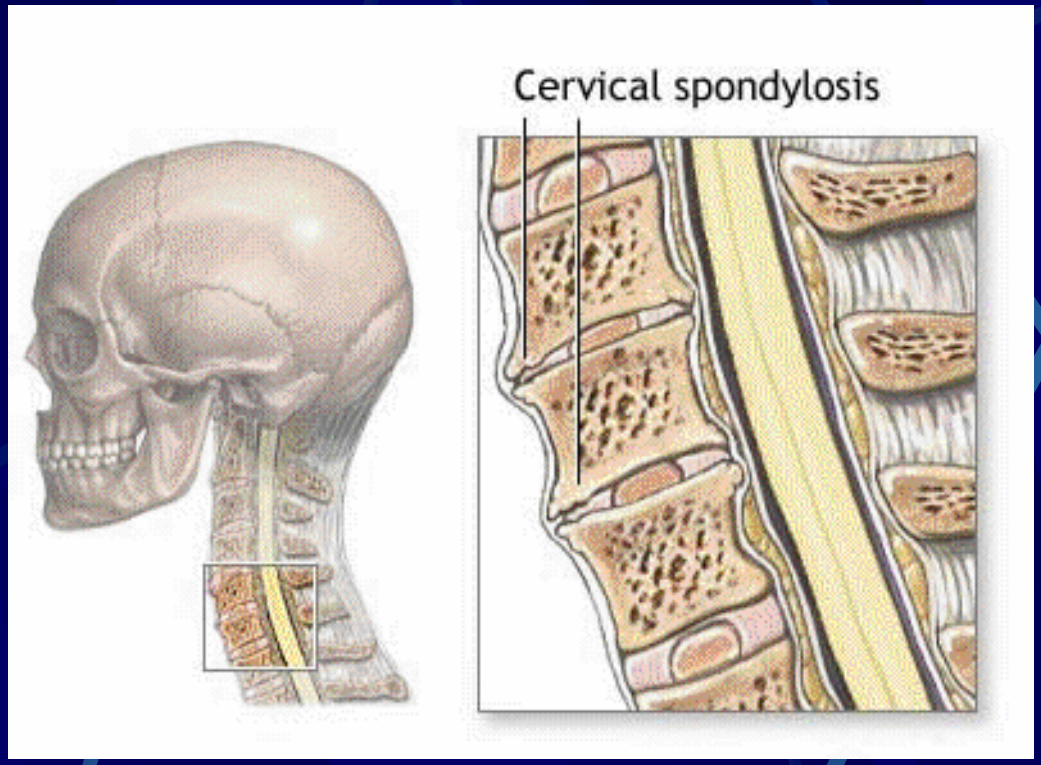
Возможное распространение болей и изменение формы позвоночника при болезни Бехтерева.

Болезнь обычно дает о себе знать уже в позднем подростковом возрасте. Первыми признаками ее бывают нерезкие боли в крестцовом отделе позвоночника, а также иногда в паху и в области внешней стороны бедер.

Характерная изменения

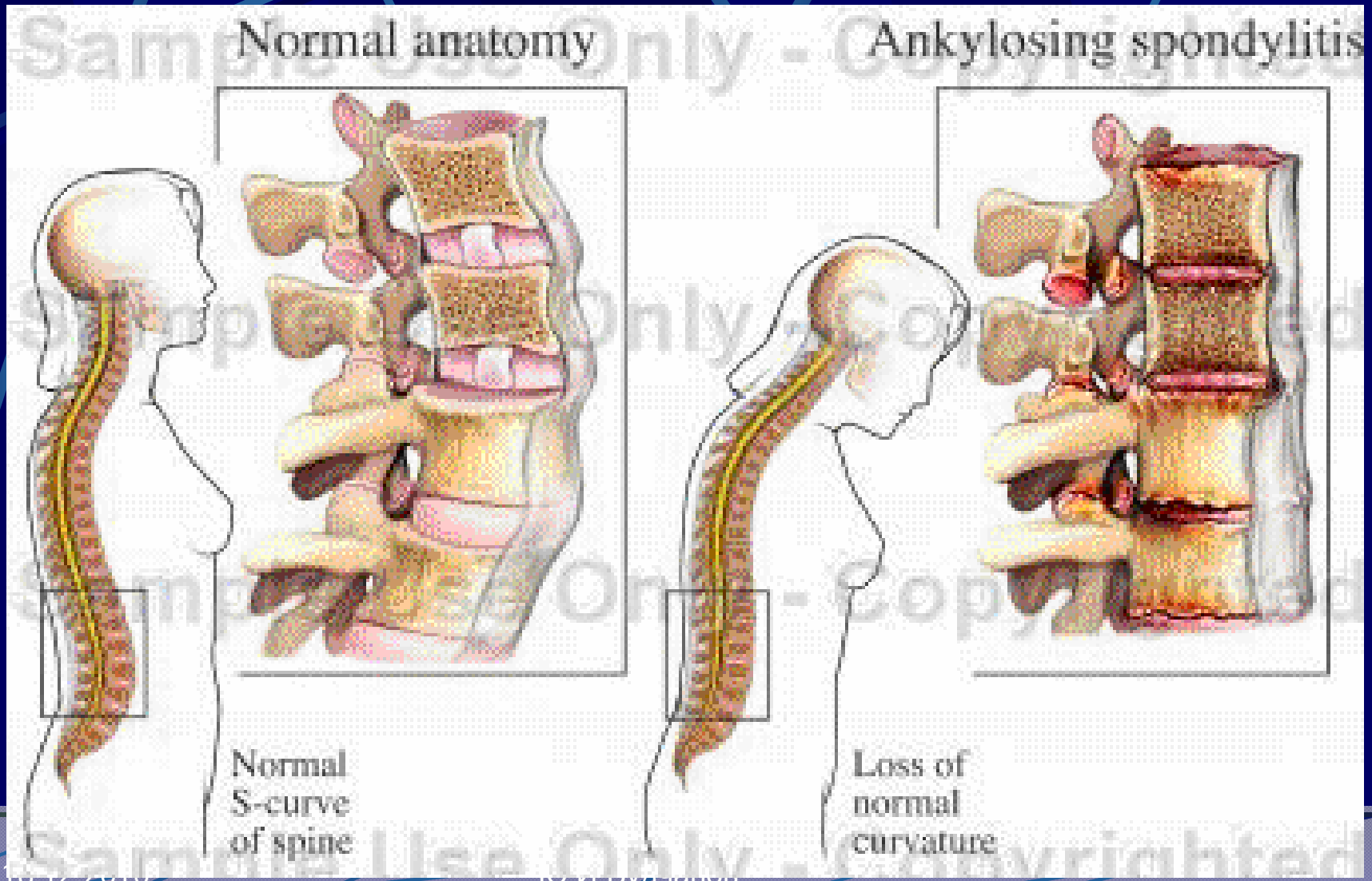


Характерные изменения формы позвоночного столба при болезни Бехтерева.

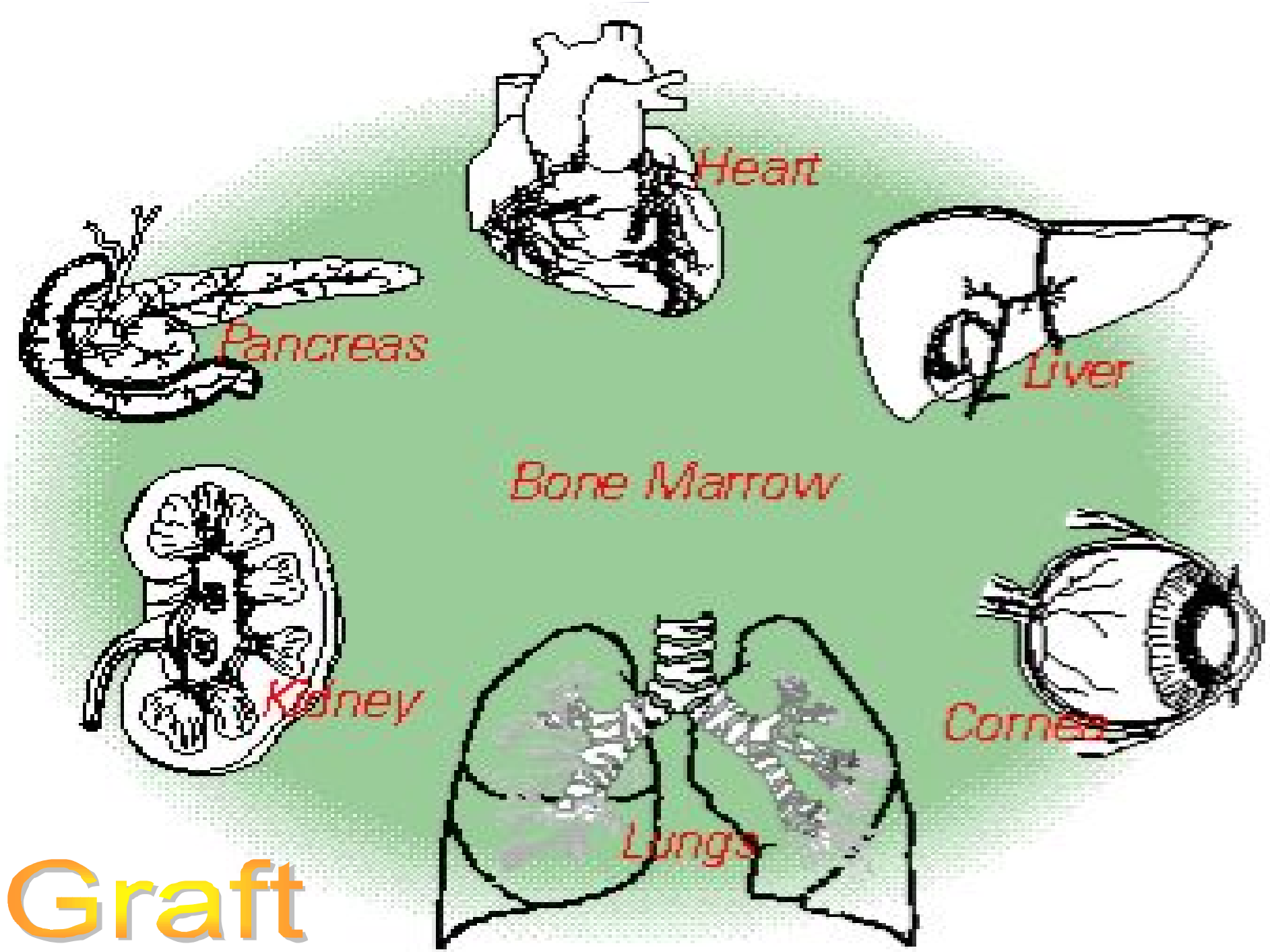


Анкилозирующий спондилит

Длительный аутоиммунный воспалительный процесс приводит к обызвествлению связок позвоночника. Воспаление поражает межпозвонковые и реберно-позвоночные суставы, а также поперечные отростки грудных позвонков. Это также ведет к уменьшению подвижности грудной клетки и появлению болей при глубоком дыхании.



Болезнь Бехтерева



Graft

Tissue graft survival

Tissue transplanted	5-year graft survival*	No. of grafts in USA (1999)
Kidney	80–90%	13,429 (12,483)
Liver	40–50%	4698
Heart	70%	2234 (2185)
Lung	30–40%	934 (885)
Cornea	~70%	~40,000†
Bone marrow	80%	23,500‡

Fig 13.29 © 2001 Garland Science

These are averages. How well the donor and recipient are matched for MHC and minors has a big impact on graft survival.

Most transplants require lifelong immunosupression with **cyclosporin A or FK506.**

These drugs have many affects on the immune system but, overall, are not too toxic

Cytotoxic T cell recognizes complex of viral peptide with MHC class I and kills infected cell

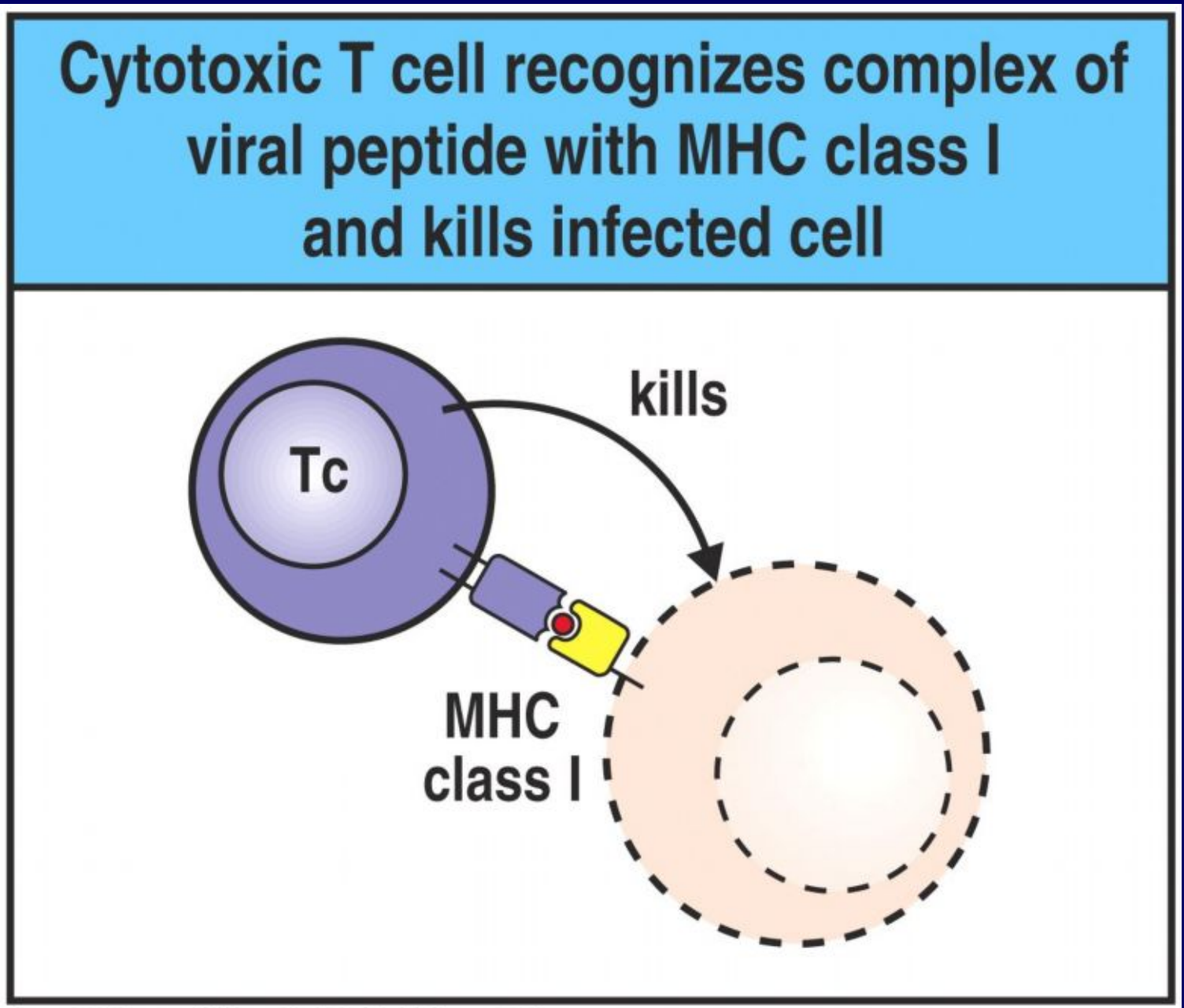
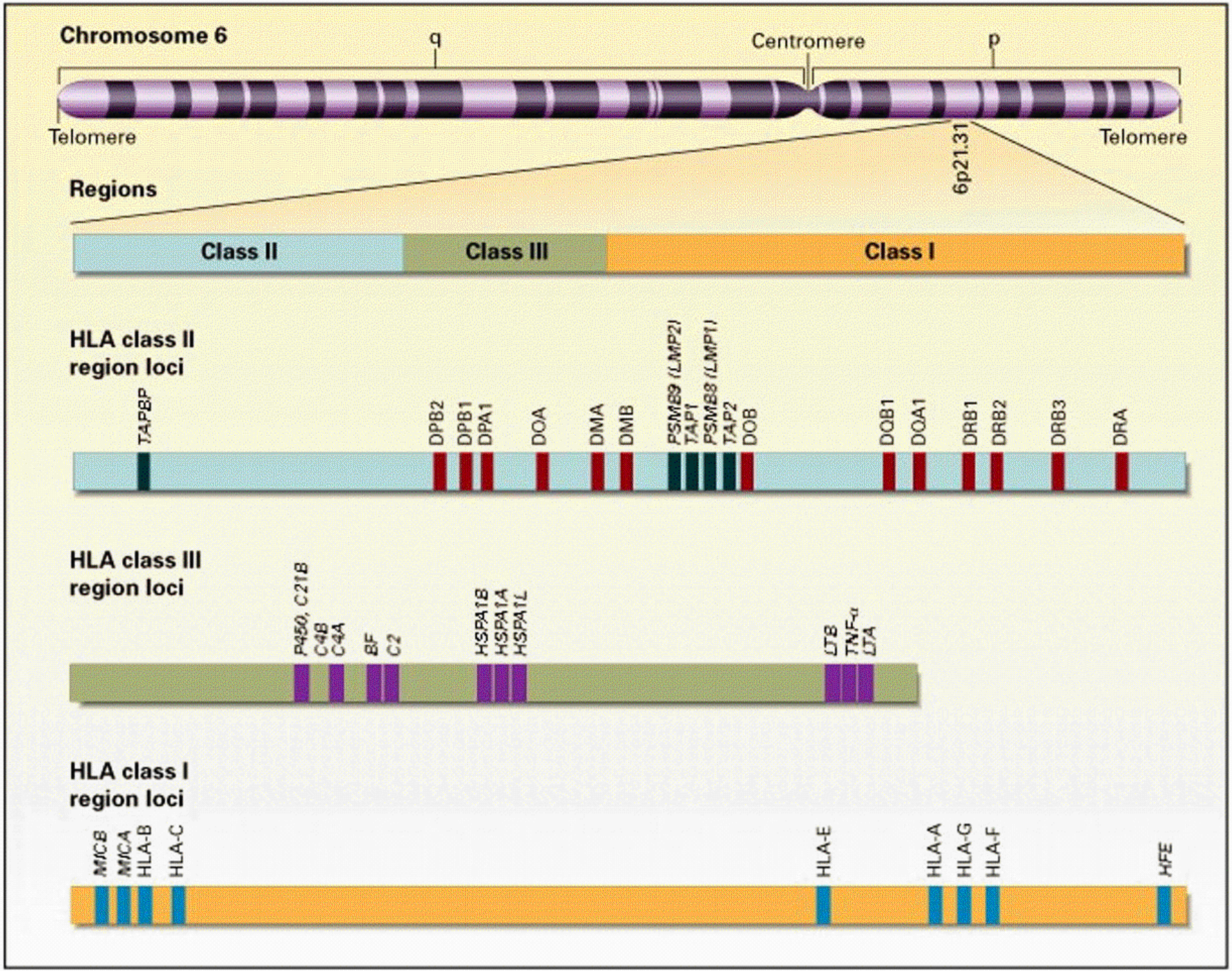


Figure 1-30 Immunobiology, 6/e. (© Garland Science 2005)

	Локус	Кол-во аллелей, выявленных молекулярно-генетическим ДНК-типированием	Кол-во аллелей, выявленных серологическим, клеточно-опосредованным типированием
Класс I	HLA-A	209	28
	HLA-B	414	61
	HLA-C	101	10
	HLA-E	6	-
	HLA-F	1	-
	HLA-G	15	-
Класс II	HLA-DRA	2	-
	HLA-DRB1	273	24
	HLA-DRB2	1	
	HLA-DRB3	30	
	HLA-DRB4	10	
	HLA-DRB5	15	
	HLA-DRB6	3	
	HLA-DRB7	2	
	HLA-DRB8	1	
	HLA-DRB9	1	
	HLA-DQA1	21	9
	HLA-DQB1	45	
	HLA-DPA1	19	6
	HLA-DPB1	93	
	HLA-DQA	8	-
	HLA-DQB	8	-
	HLA-DMA	4	-
	HLA-DMB	6	-
	TAP1	6	-
	TAP2	4	-
	MICA	51	-
	ВСЕГО	*1349*	*138*


Chromosome 6
q
Centromere
p
Telomere
Telomere
6p21.31
Regions
Class II
Class III
Class I
HLA class II region loci
TAPBP
DPB2
DPB1
DPA1
DOA
DMA
DMB
PSMB9 (LMP2)
TAP1
PSMB8 (LMP1)
TAP2
DOB
DQB1
DQA1
DRB1
DRB2
DRB3
DRA
HLA class III region loci
P450, C21B
C4B
C4A
BF
C2
HSPA1B
HSPA1A
HSPA1L
LTB
TNF-α
LTA
HLA class I region loci
MICB
MICA
HLA-B
HLA-C
HLA-E
HLA-A
HLA-G
HLA-F
HFE