Introduction to immunology: outline

1. Classification of immune responses

2. Specificity of adaptive immune responses:
    1. Antigen receptor diversity
    2. Major histocompatibility complex

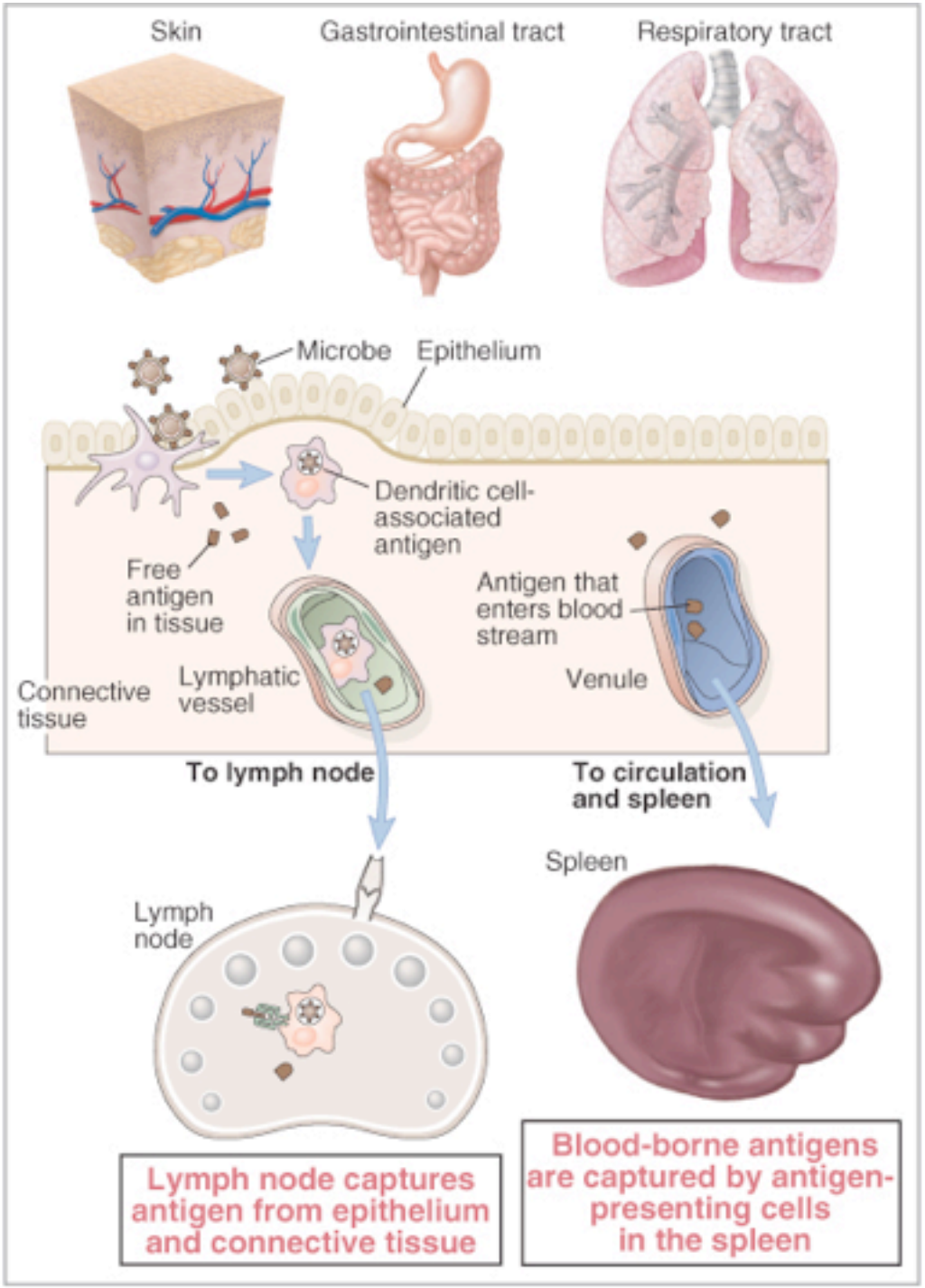
3. Antigen processing/presentation

4. T-cell development and tolerance

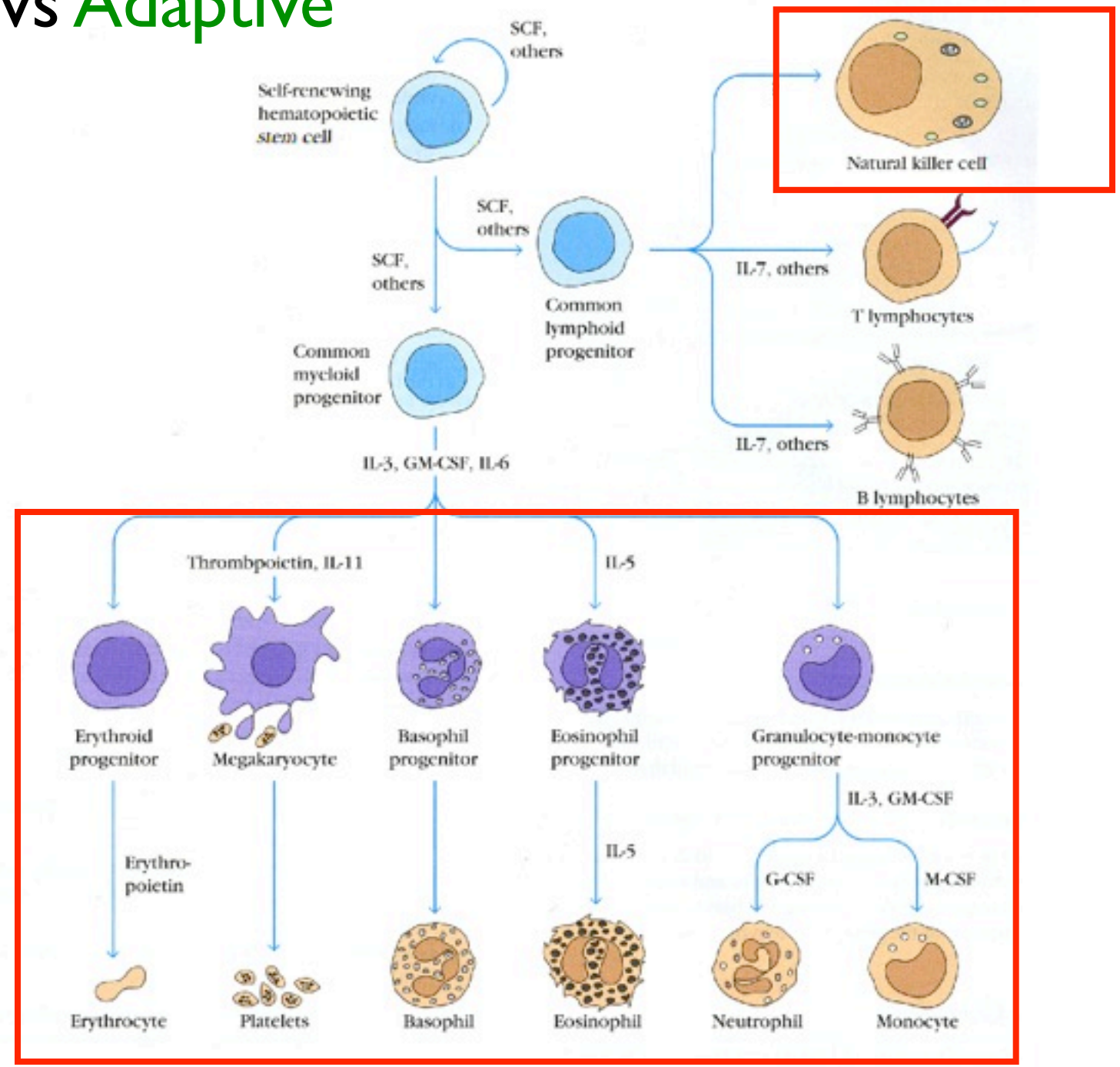
5. Innate immunity

6. Lymphocyte trafficking

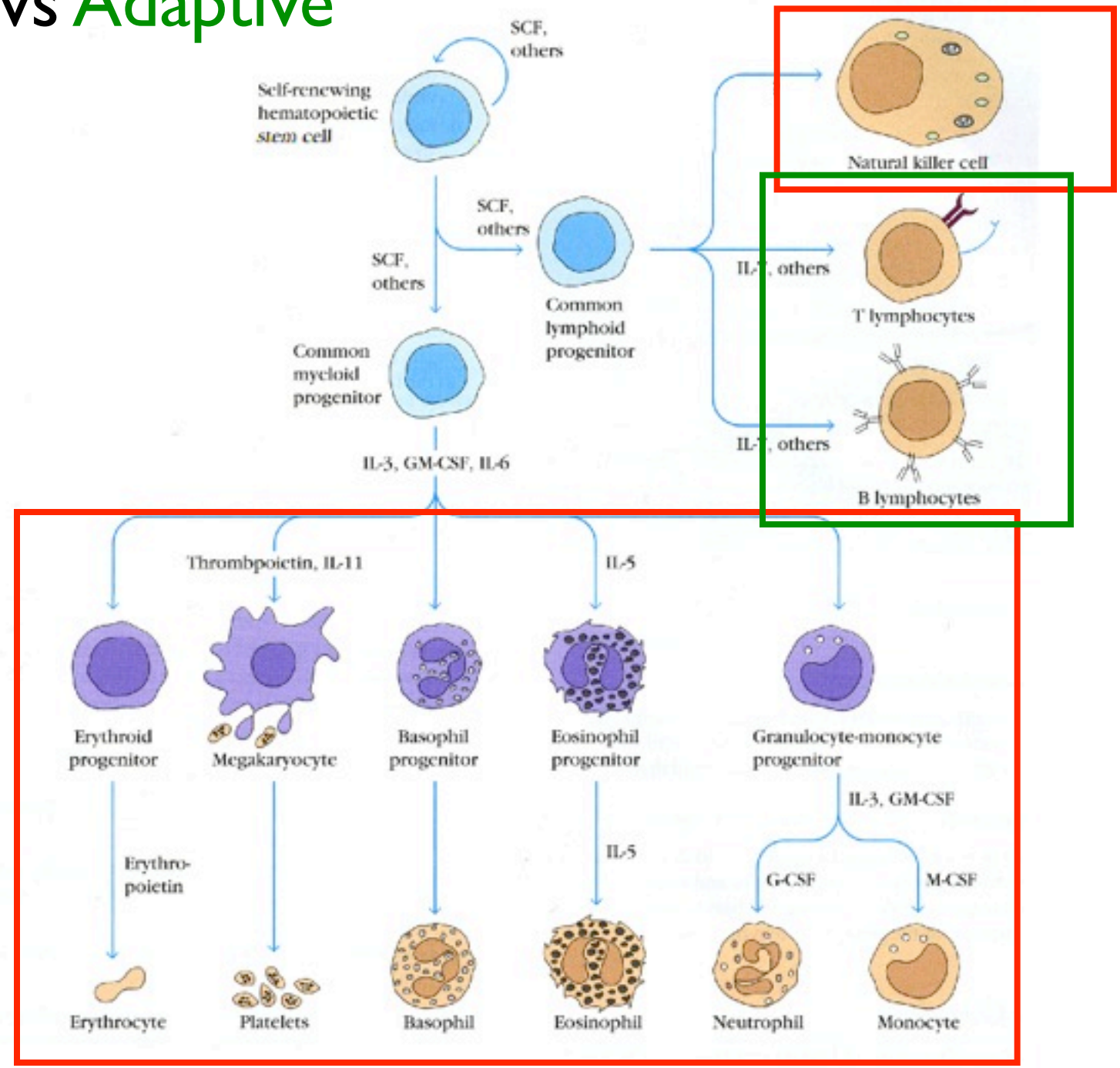
7. Cytokines and chemokines


Skin
Gastrointestinal tract
Respiratory tract
Microbe
Epithelium
Dendritic cell-associated antigen
Free antigen in tissue
Antigen that enters blood stream
Connective tissue
Lymphatic vessel
Venule
To lymph node
To circulation and spleen
Spleen
Lymph node
Lymph node captures antigen from epithelium and connective tissue
Blood-borne antigens are captured by antigen-presenting cells in the spleen

Innate vs Adaptive



Innate vs Adaptive



Innate and adaptive immunity

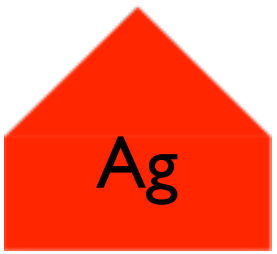
INNATE IMMUNITY

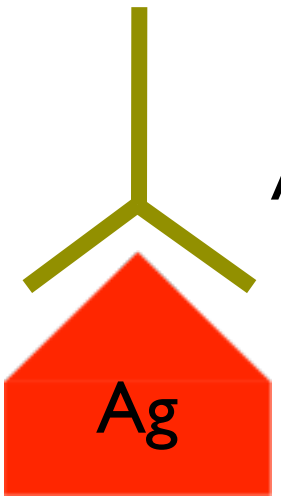
Present from birth
Not antigen-specific (TLR)
Not enhanced by second exposure
Has no memory

ADAPTIVE IMMUNITY

Learnt from experience
Antigen-specific
Enhanced by second exposure
Has memory

Use cellular and humoral components
POORLY EFFECTIVE IF NOT IN PAIR

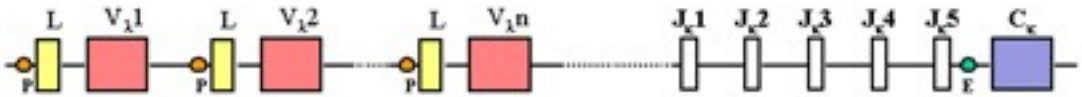

Ag



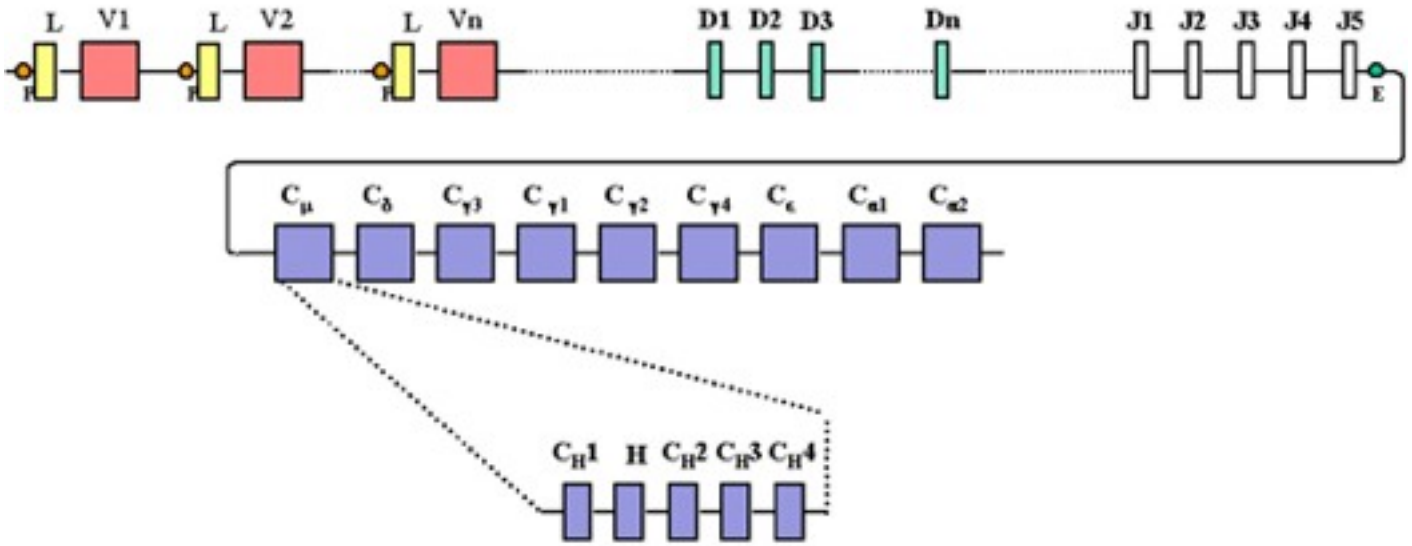
Antigen receptor

Lambda light chain genes; n=30

Kappa light chain genes; n=300

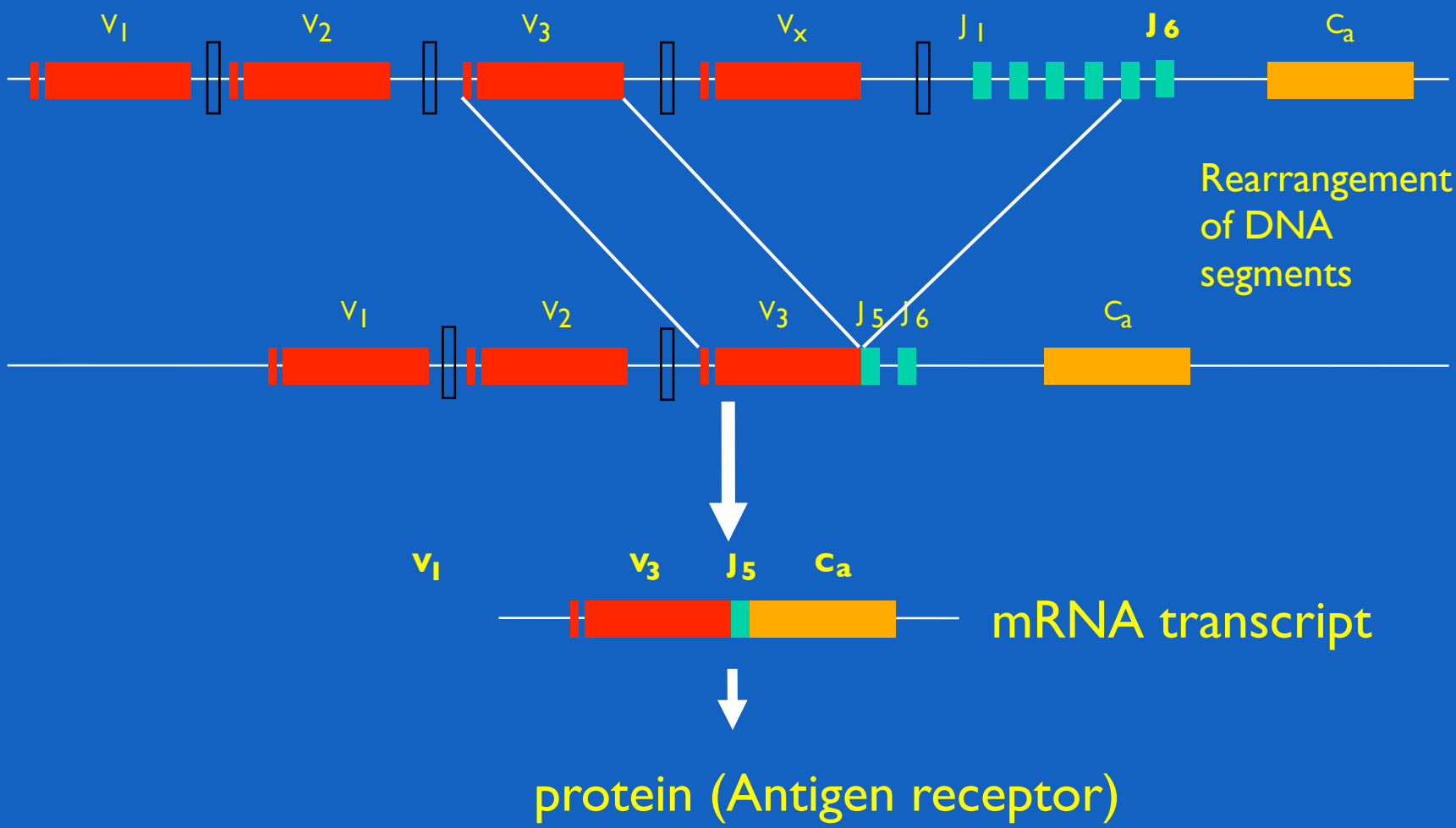


Heavy chain genes; Vn=1000, Dn=15



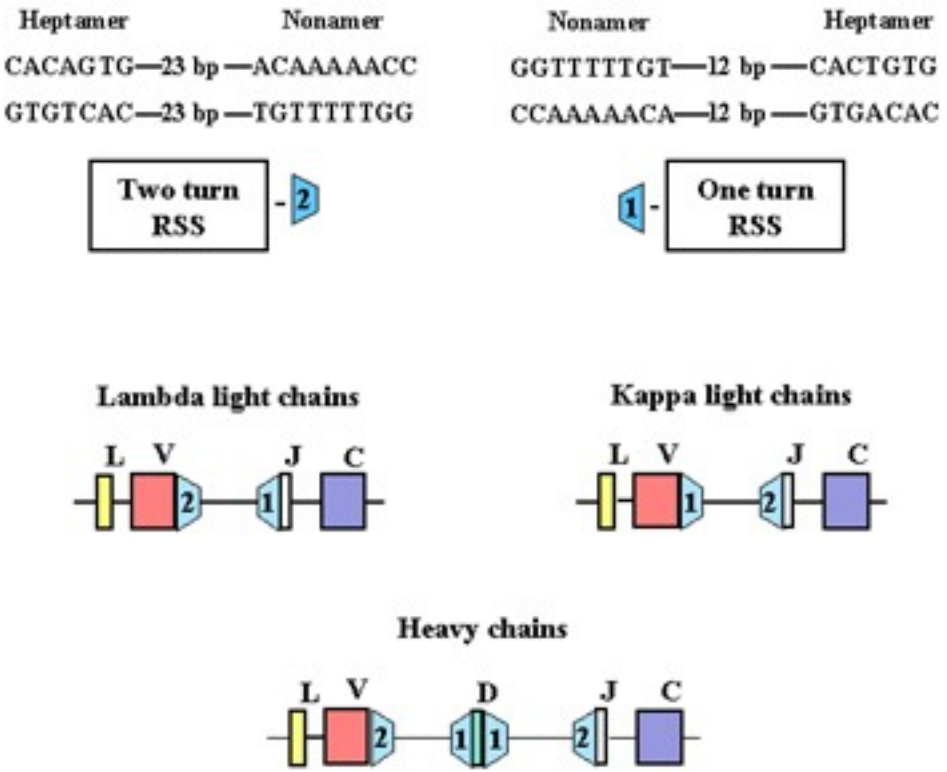
Introns separate exons coding for H chain domains

Generation of diversity



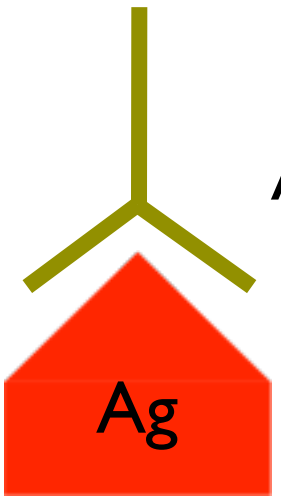
Mechanism of DNA Rearrangements

- Recombination signal sequences (RSS)
  - Nonmer
  - Heptamer
  - 1 or 2 turn signals
- Rag-1 and Rag-2

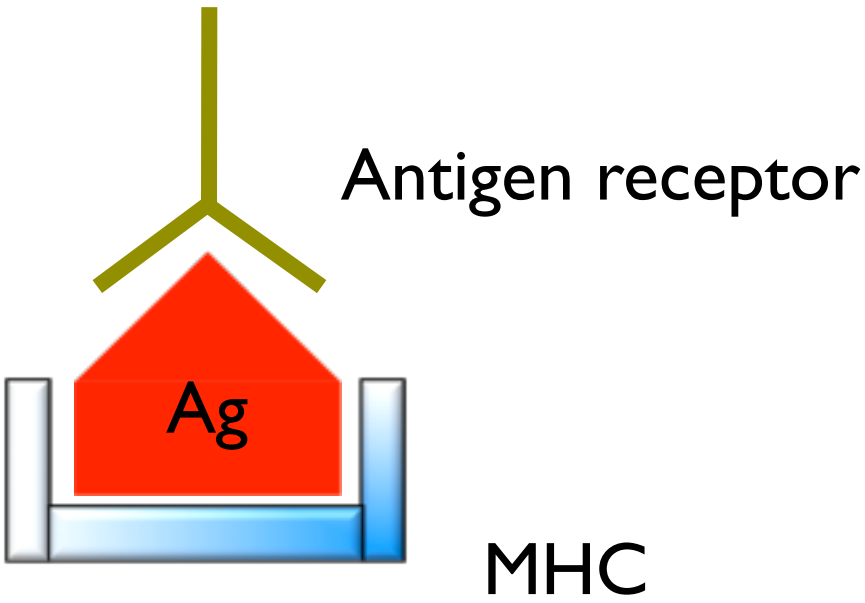


Origin of antibody diversity

- Multiple V genes
- V-J and V-D-J joining
- Junctional diversity
- N region insertions
- Somatic mutations
- Combinatorial association (HC-LC pairing)
- Cross-reactivity



Antigen receptor

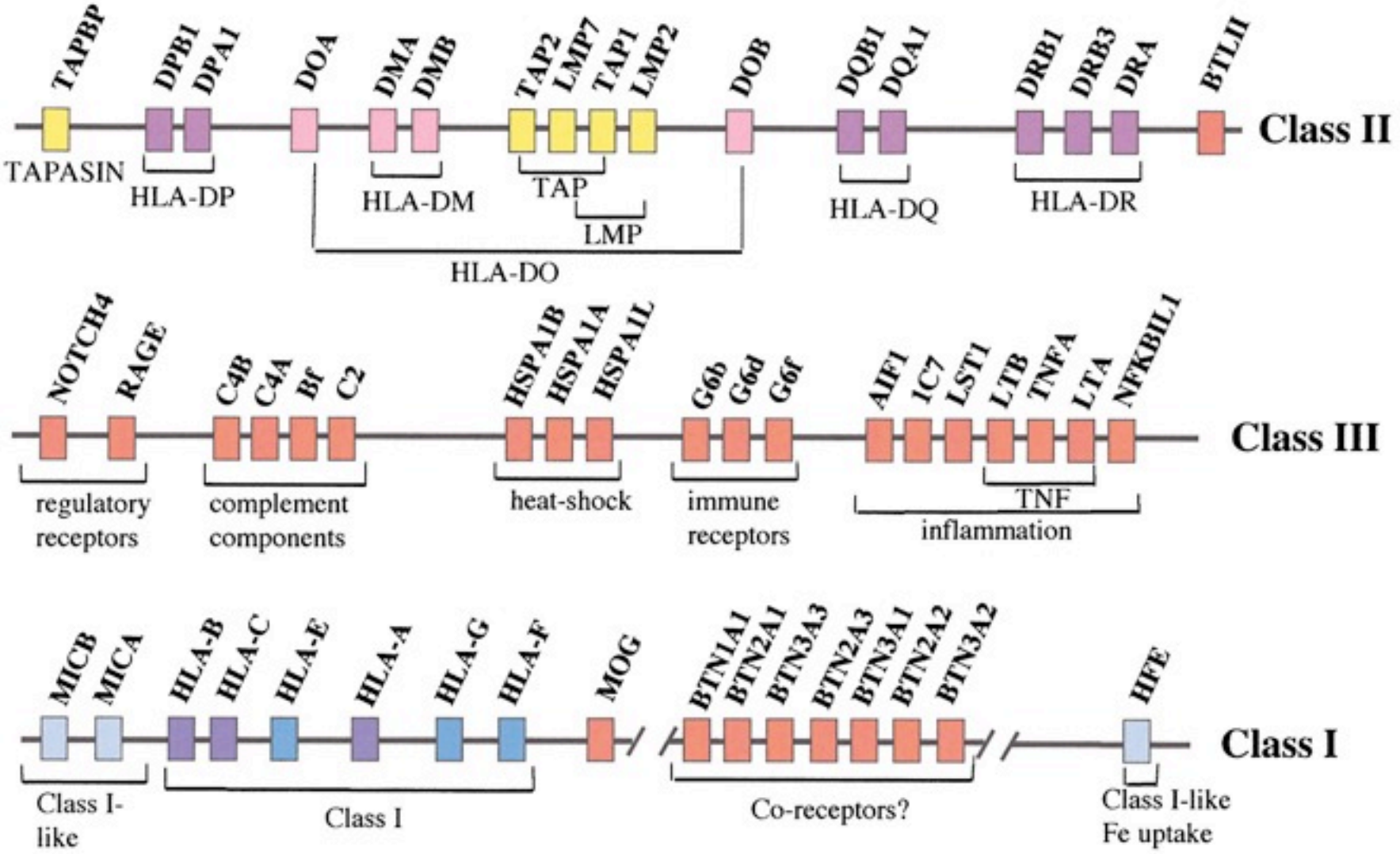

Antigen receptor
Ag
MHC

Specificity of B and T lymphocytes: MHC makes the difference

- Antibodies recognise native, intact antigen particles

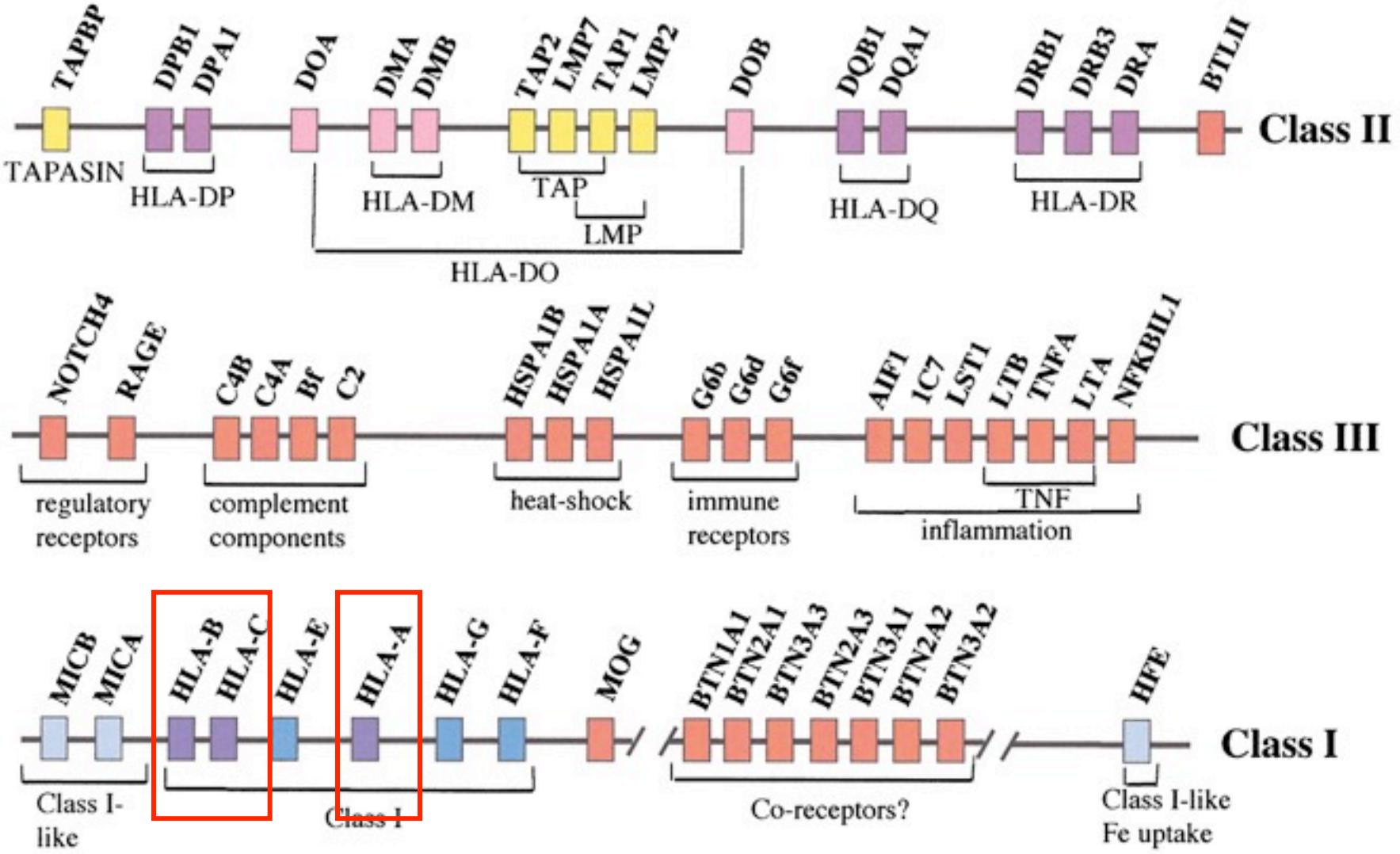
- T cells recognise digested and selected antigenic fragments (peptides) on antigen presenting cells

Genomic organization of MHC molecules



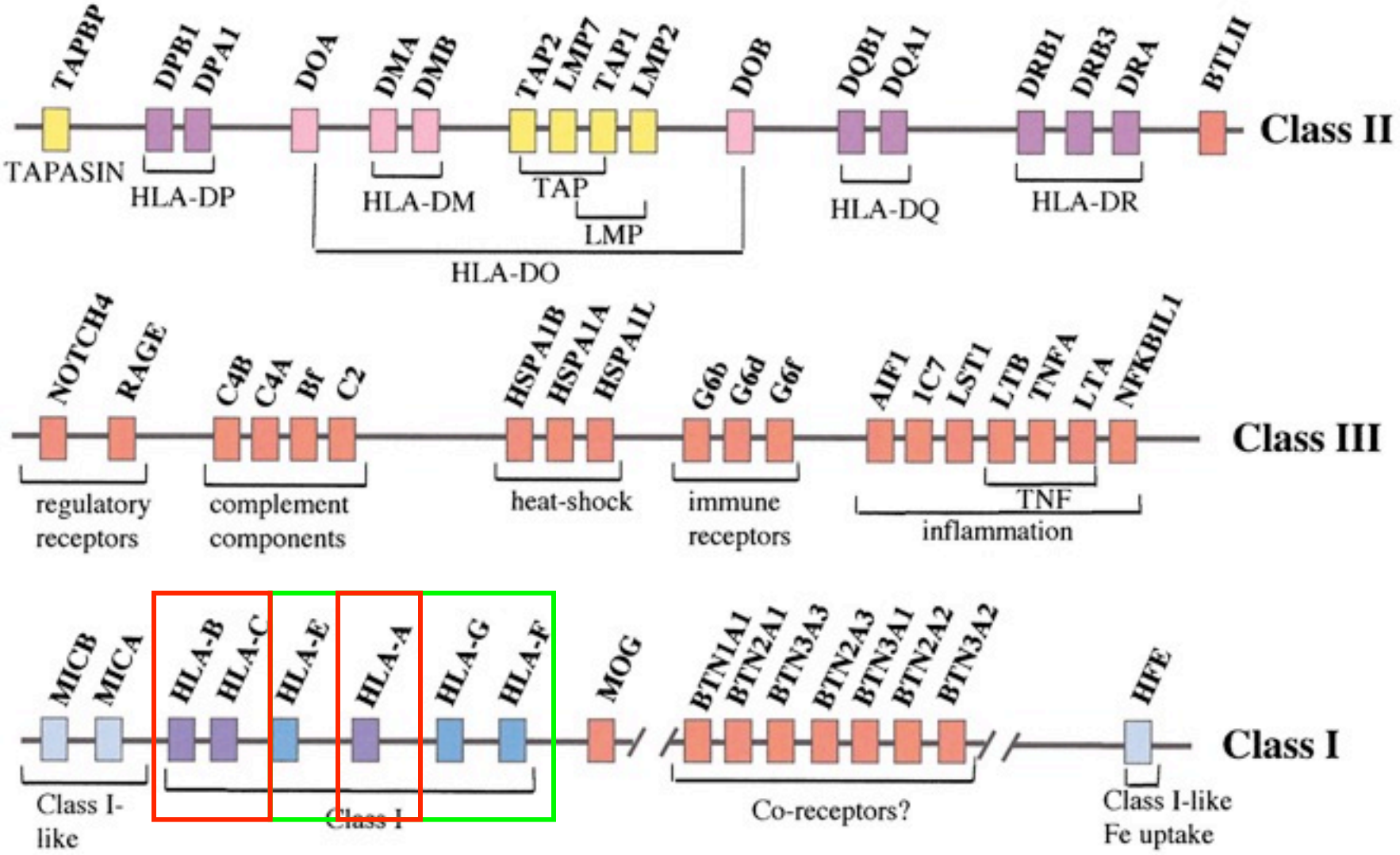
Immunity (2001) Vol. 15, p.363-374

Genomic organization of MHC molecules



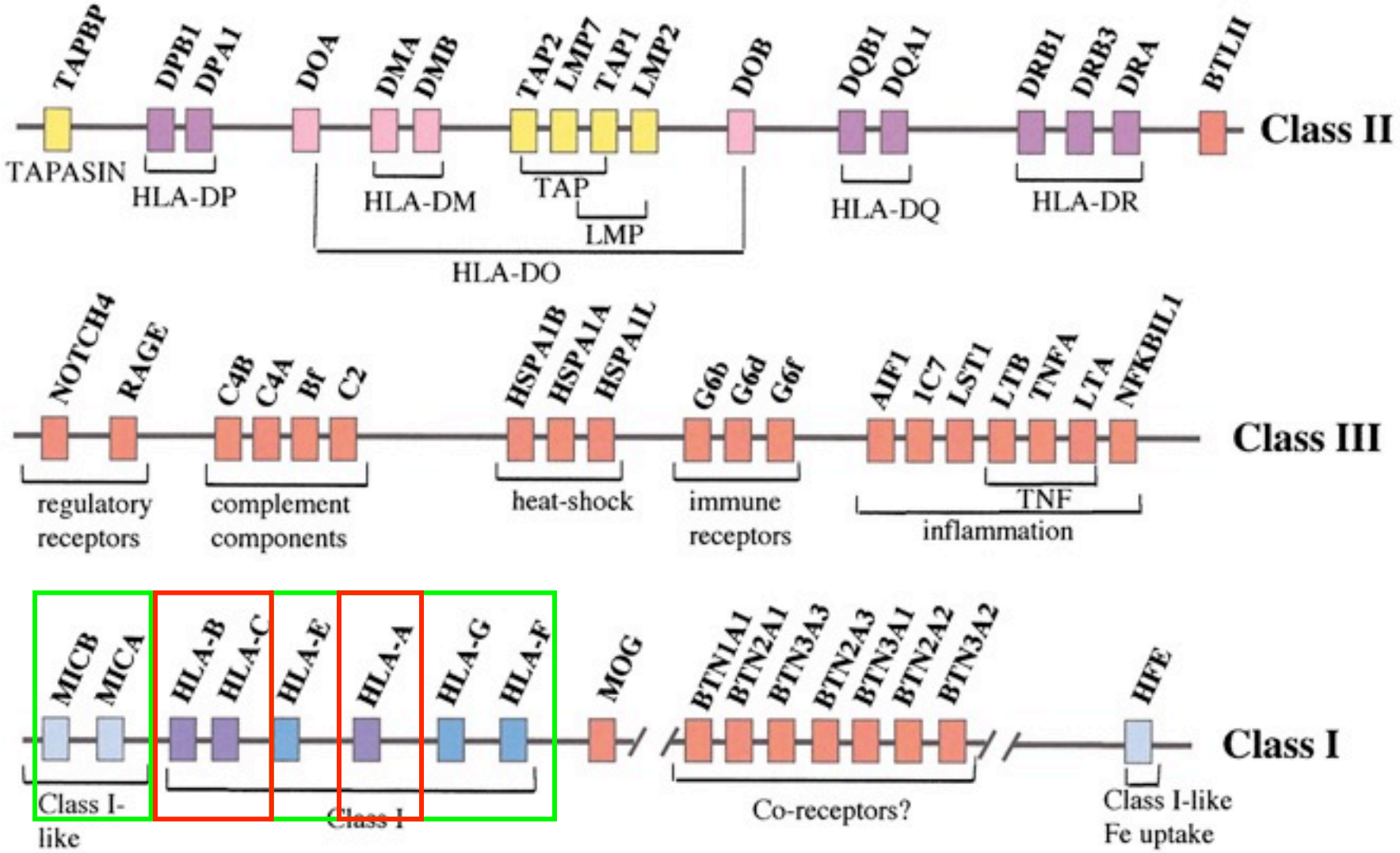
Immunity (2001) Vol. 15, p.363-374

Genomic organization of MHC molecules



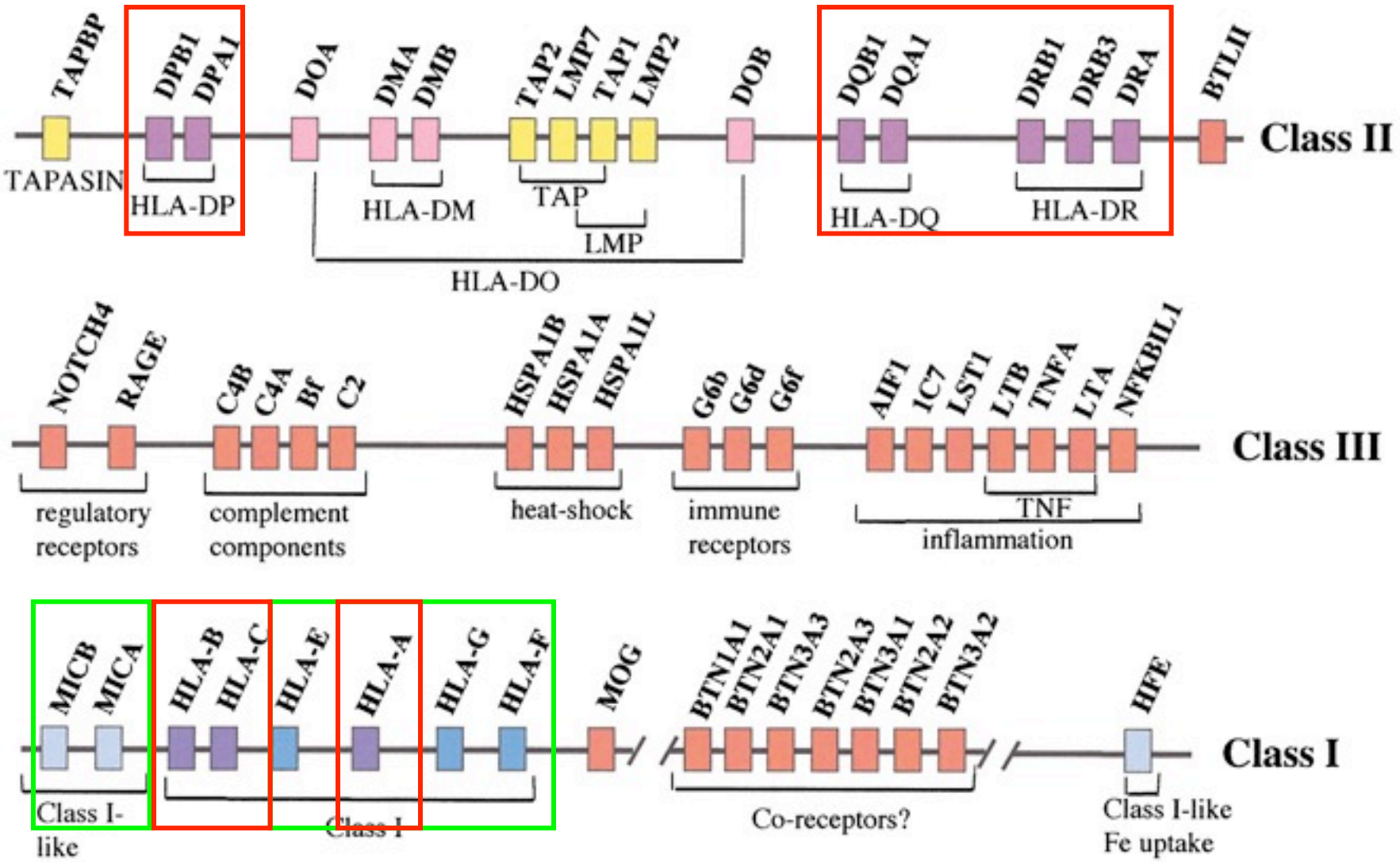
Immunity (2001) Vol. 15, p.363-374

Genomic organization of MHC molecules



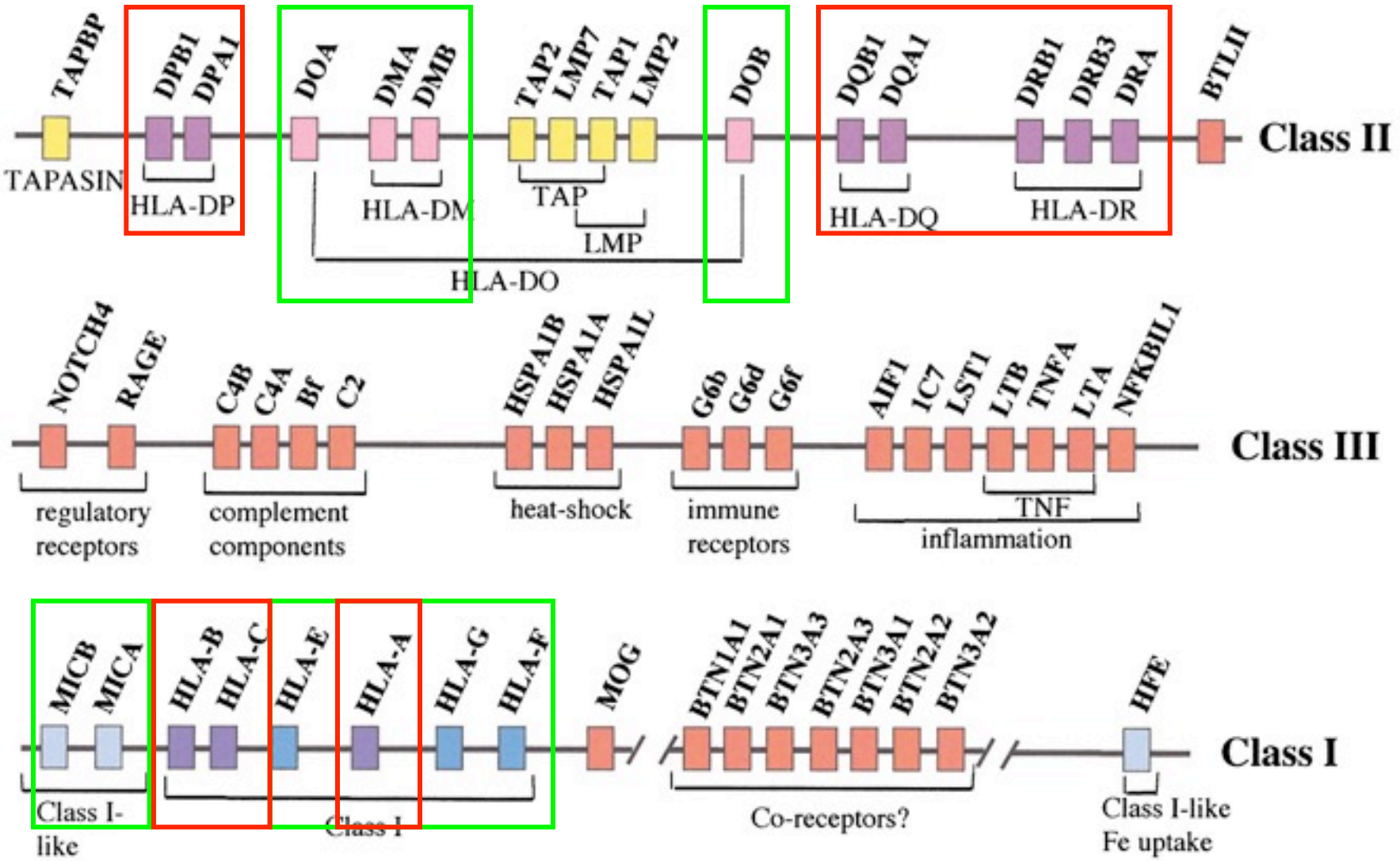
Immunity (2001) Vol. 15, p.363-374

Genomic organization of MHC molecules



Immunity (2001) Vol. 15, p.363-374

Genomic organization of MHC molecules



Immunity (2001) Vol. 15, p.363-374

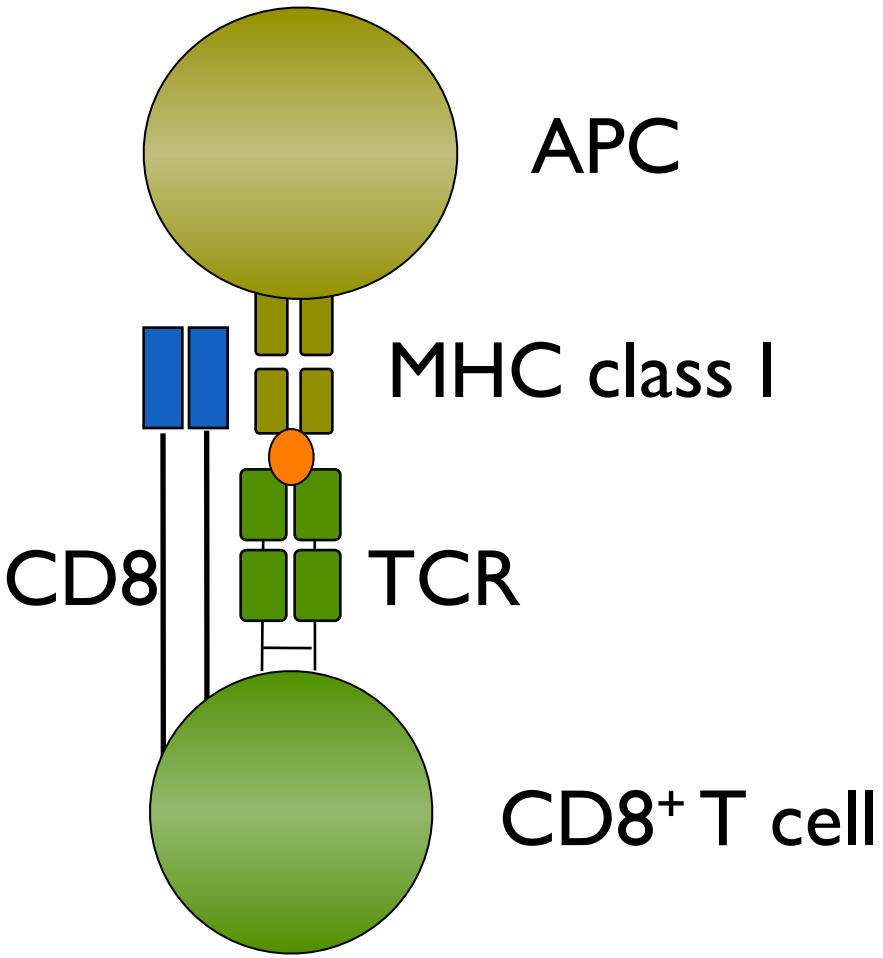
Expression of HLA molecules

Class I	Almost all nucleated cells; not on villous trophoblast

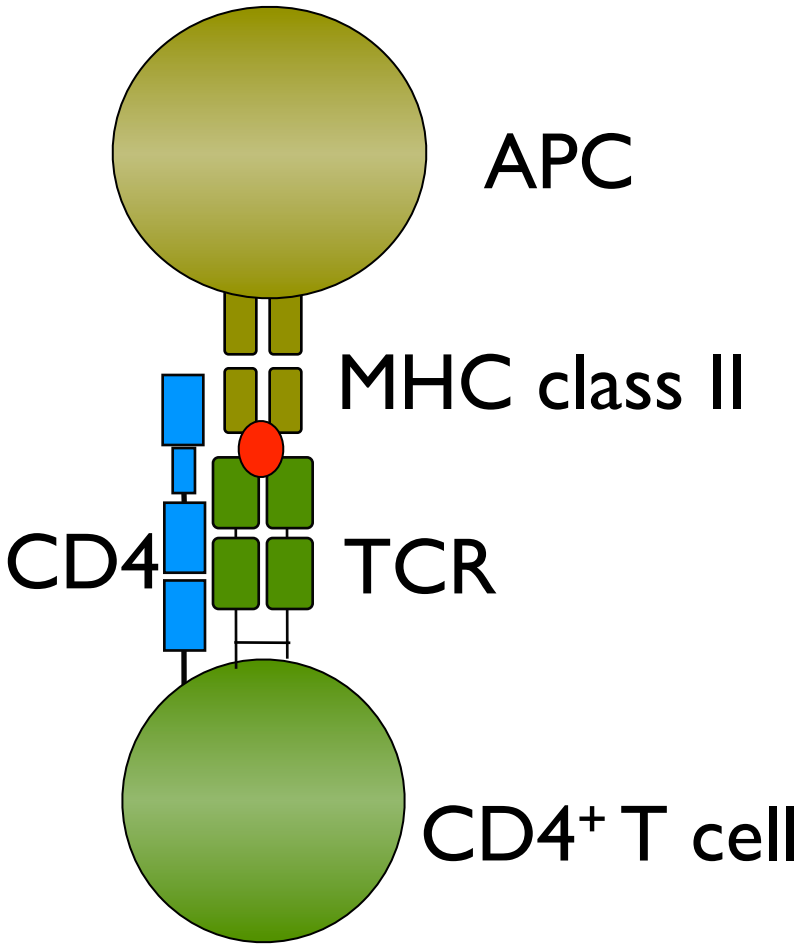
Expression of HLA molecules

Class I	Almost all nucleated cells; not on villous trophoblast
Class II	Antigen presenting cells. Its expression can be induced in other cell types

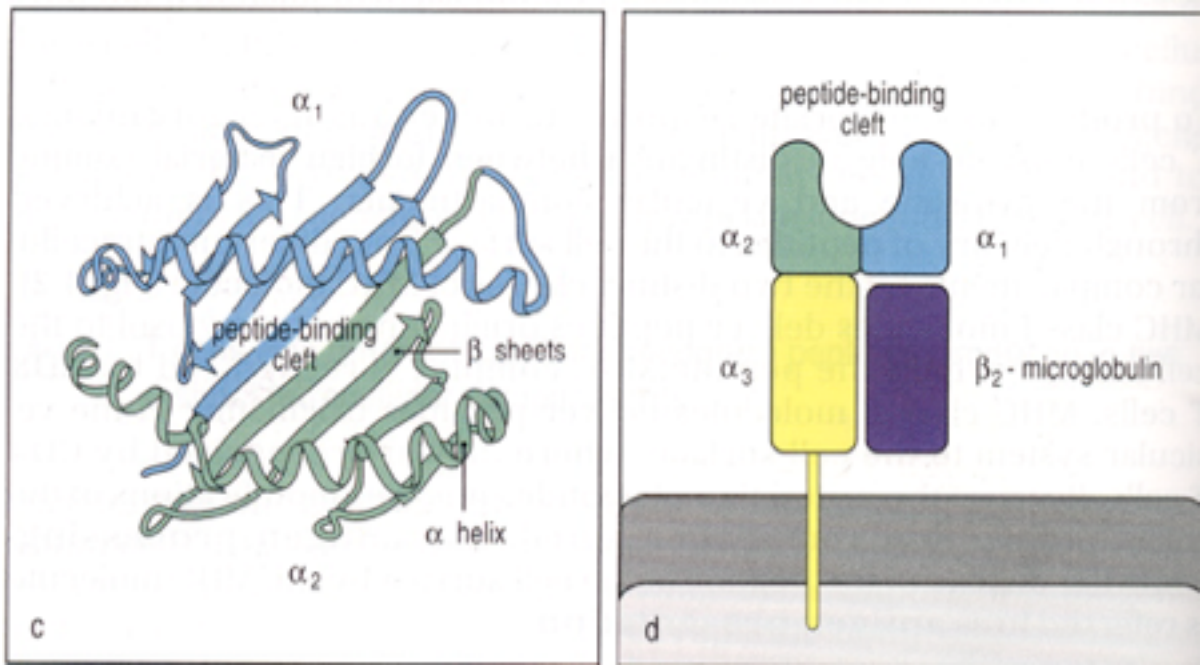
CD8+ T cells



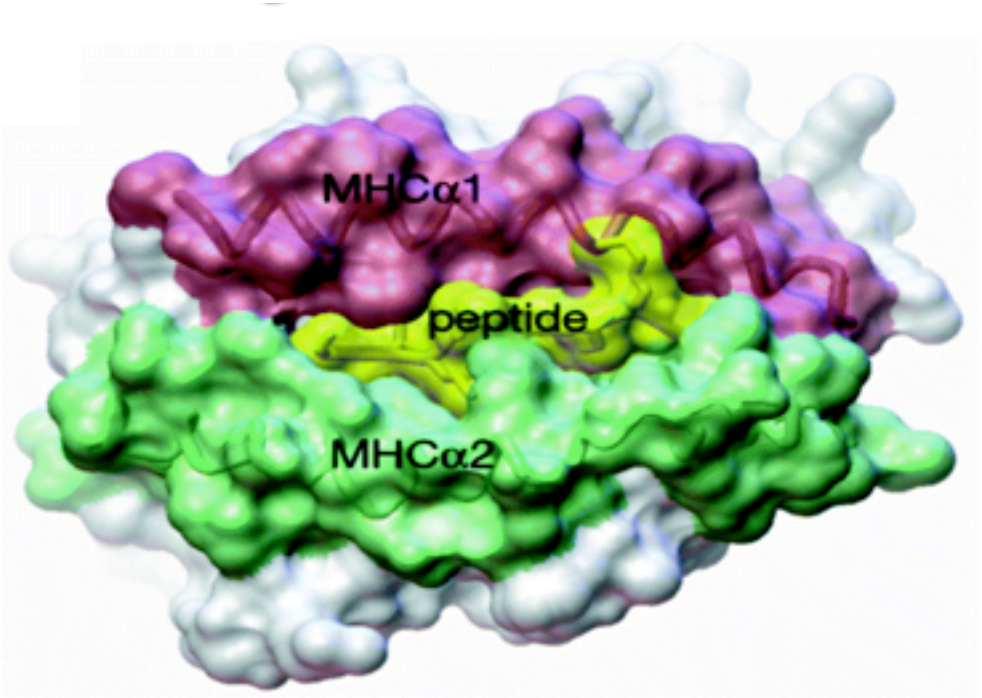
CD4+ T cells



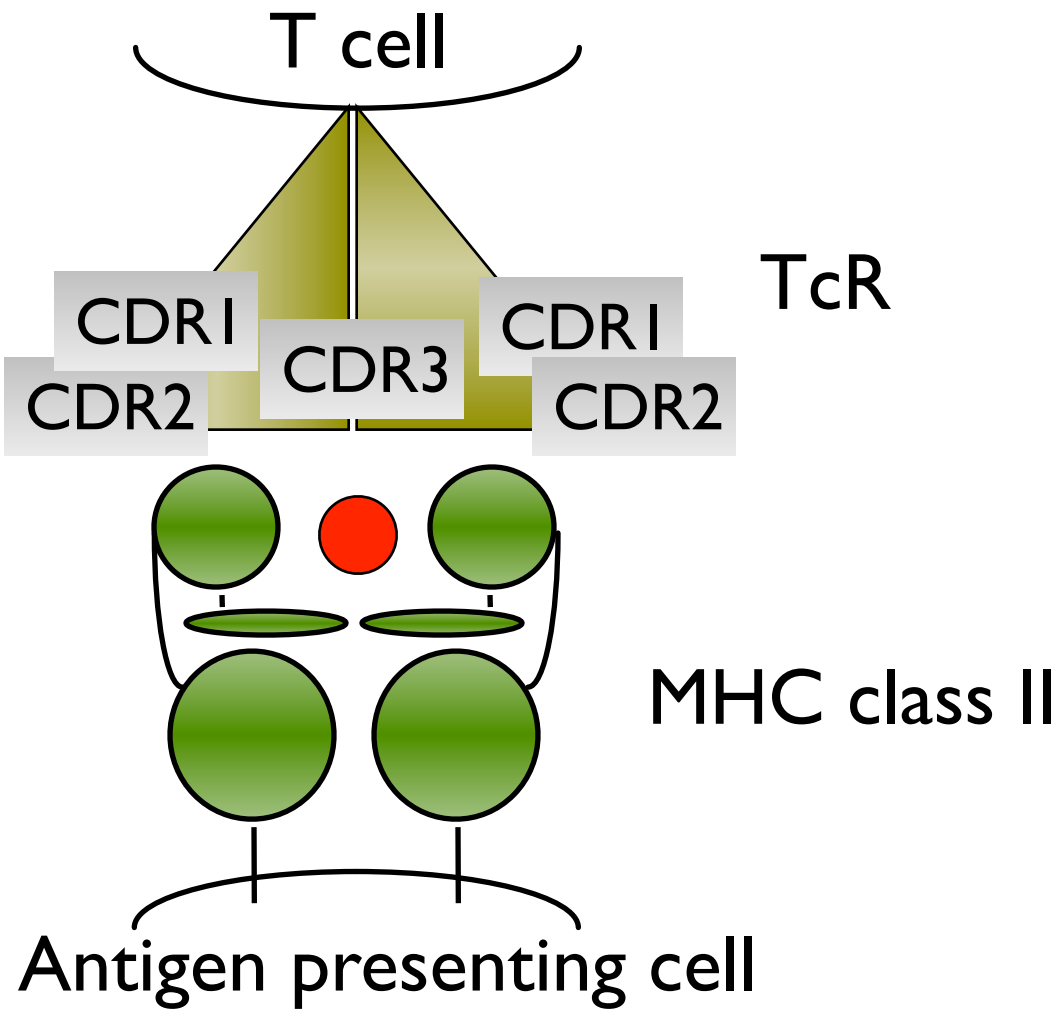
MHC-Class I molecule



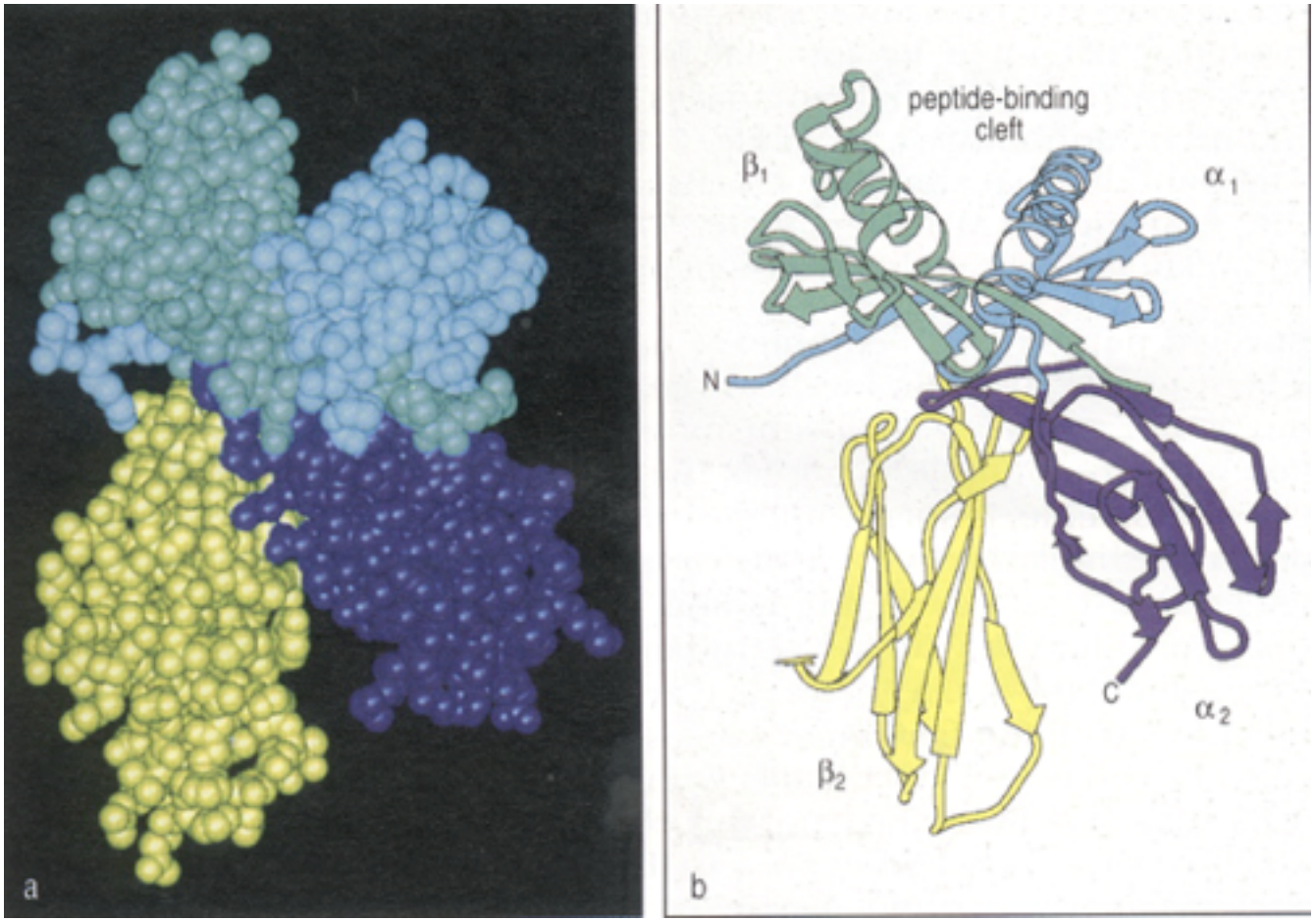
- Two noncovalently linked polypeptide chains: α (MHC-encoded) and β_2 (non MHC-encoded)
- Two strands of α-helix and 8 strands of β-sheet
- Ends of the peptide binding cleft are closed


MHCα1
peptide
MHCα2

TCR structure-MHC recognition



MHC-Class II molecule



- Two noncovalently linked polypeptide chains: α (32-34kD) and β (29-32kD). Both polymorphic in domain I
- Heterozigosity and pairing
- Peptide is required for stable expression

MHC genes are immune response genes

1. Graft rejection

MHC^a

MHC^b

Skin graft		
	Syngeneic	Allogeneic
Graft rejection	No	Yes

2. Immune responses to foreign proteins

MHC^a

MHC^b

Immunisation	R	NR

Antigen processing: basic concepts

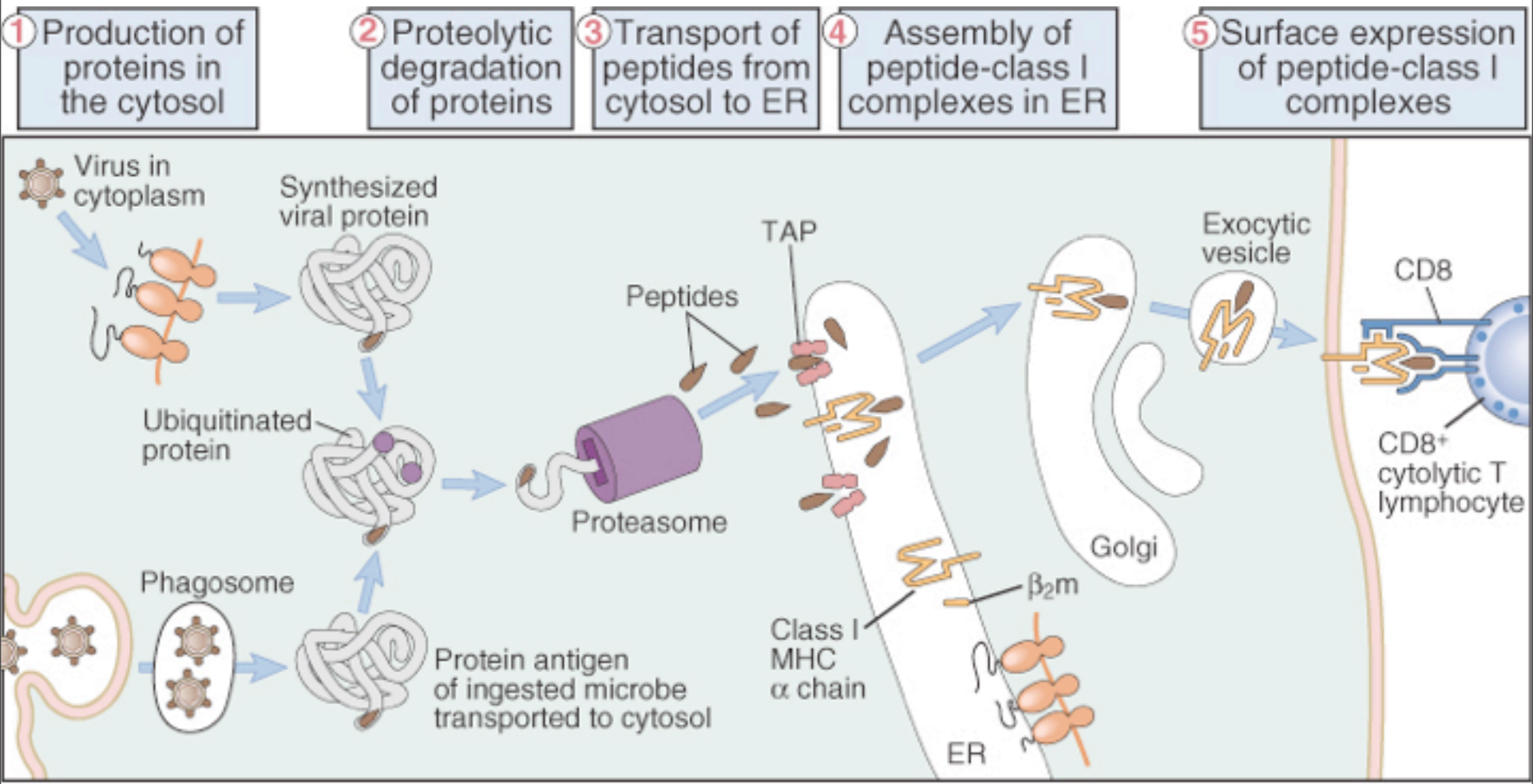
• T cells recognise foreign peptide antigens only if these peptides are bound to the MHC molecules of that individual: MHC restriction

• CD4+ T cells recognise peptides presented by MHC class II, whereas CD8+ T cells recognise peptides in association with MHC class I

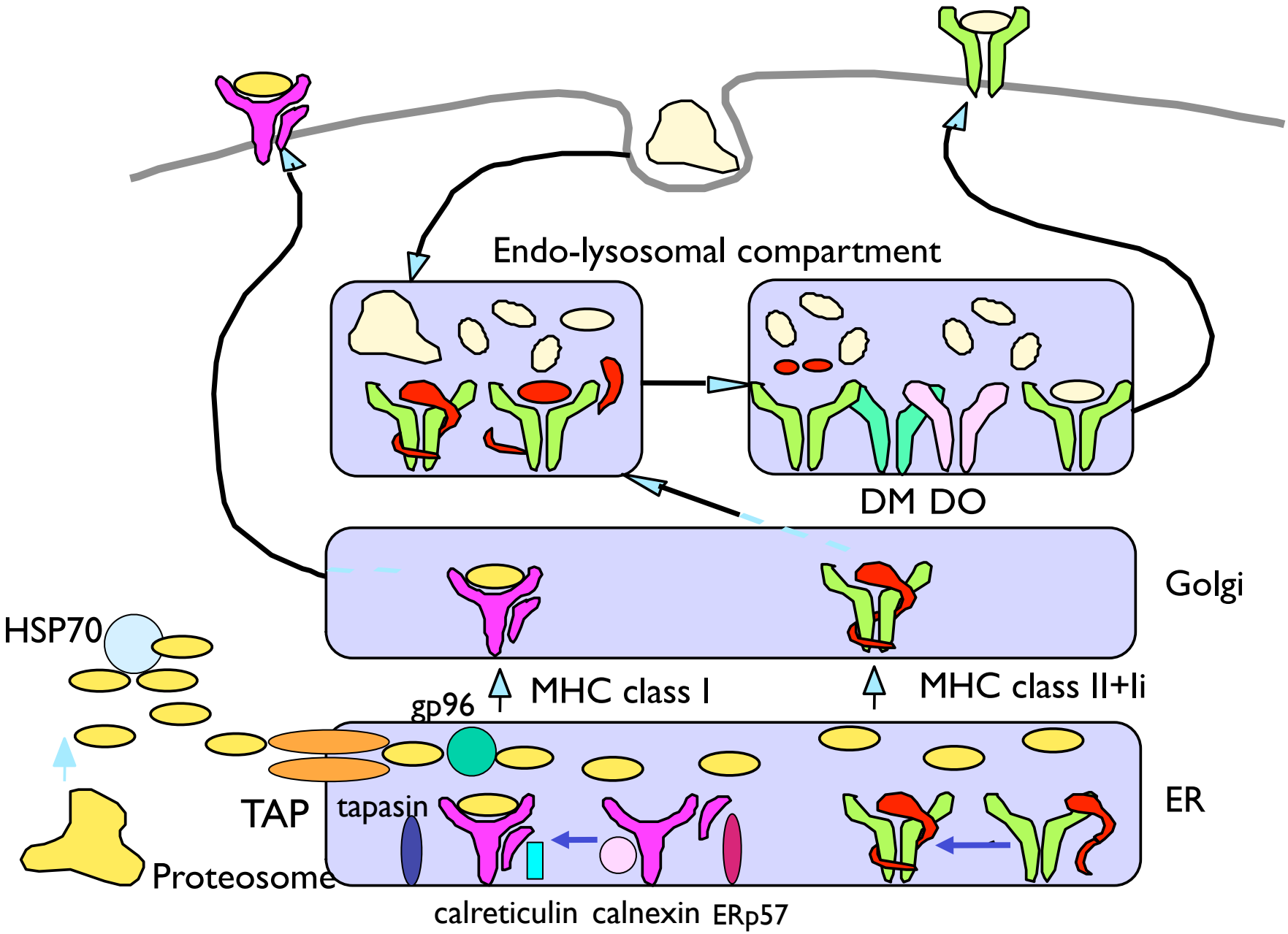
• MHC molecules are specialised: class I molecules display the inside of the cell, class II display the outside of the cell.

• Cross-priming: Dendritic cells have the capacity to present exogenous antigen with MHC class I molecules

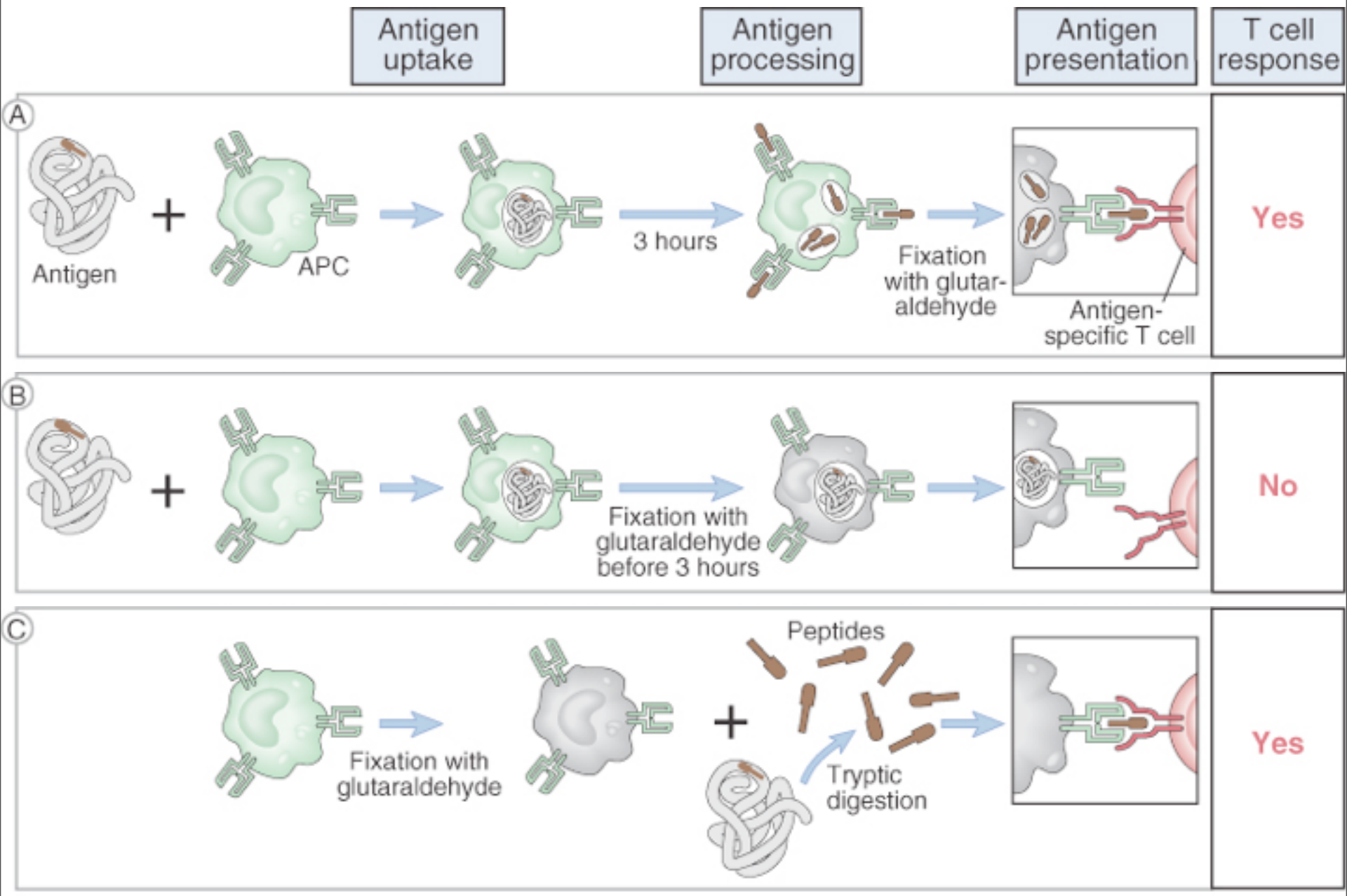
MHC Class I antigen processing

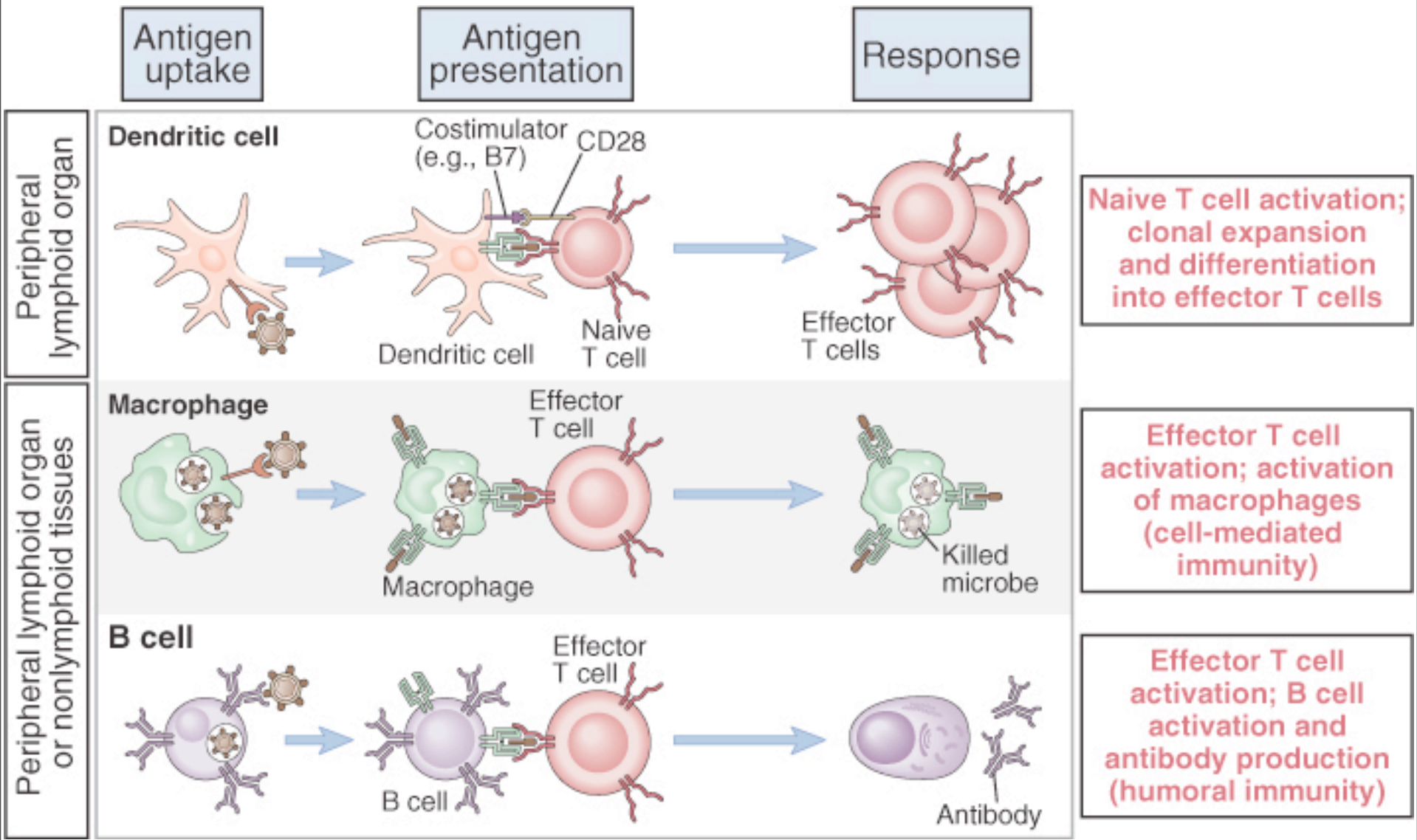


MHC Class II antigen processing

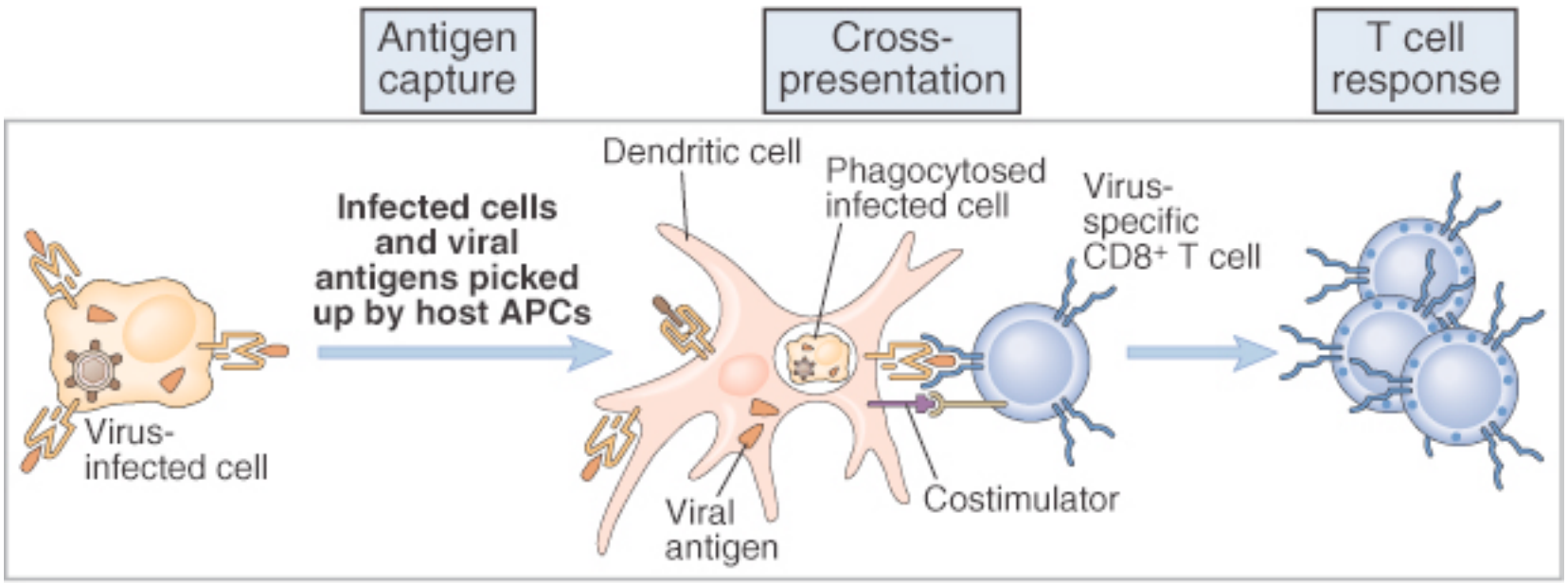


ANTIGEN PROCESSING REQUIRES TIME AND METABOLISM



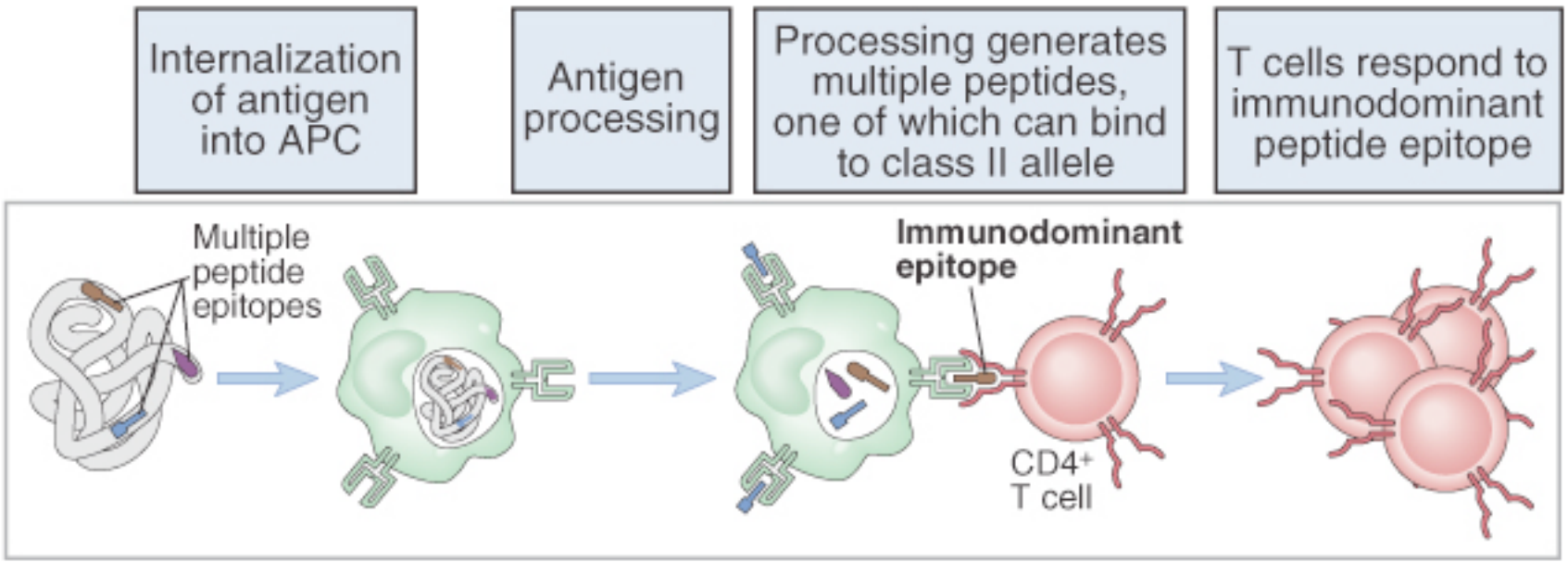

Antigen uptake
Antigen presentation
Response
Peripheral lymphoid organ
Peripheral lymphoid organ or nonlymphoid tissues
Dendritic cell
Costimulator (e.g., B7)
CD28
Dendritic cell
Naive T cell
Effector T cells
Naive T cell activation; clonal expansion and differentiation into effector T cells
Macrophage
Effector T cell
Macrophage
Killed microbe
Effector T cell activation; activation of macrophages (cell-mediated immunity)
B cell
Effector T cell
B cell
Antibody
Effector T cell activation; B cell activation and antibody production (humoral immunity)

Feature	Myeloid DCs CD8 negative	Plasmacytoid DCs	Myeloid DCs CD8 positive
Surface markers	CD11c-high, CD11b-high	CD11c-low, CD11b-negative, B220-high	$CD8\alpha^+$, CD11c-low/high, CD11b-negative
Growth factors for *in vitro* derivation	GM-CSF, Flt3-ligand	Flt3-ligand	Flt3-ligand?
Expression of Toll-like receptors (TLRs)	TLR-4, 5, 8 high	TLR-7, 9 high	TLR-3 high
Major cytokines produced	TNF, IL-6	Type I interferons	IL-12
Ability to cross-present	+/-	+/-	++
Postulated major functions	Induction of T cell responses against most antigens	Innate immunity and induction of T cell responses against viruses	Activation of $CD8^+$ T cells by cross-priming

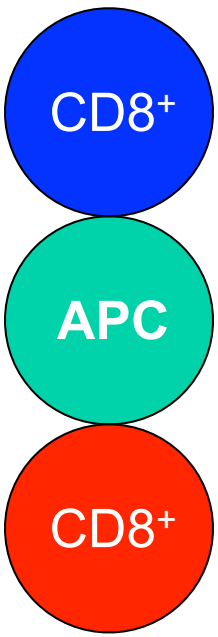

Antigen capture
Cross-presentation
T cell response
Dendritic cell
Phagocytosed infected cell
Virus-specific CD8+ T cell
Infected cells and viral antigens picked up by host APCs
Virus-infected cell
Viral antigen
Costimulator

Immunogenicity of protein antigens

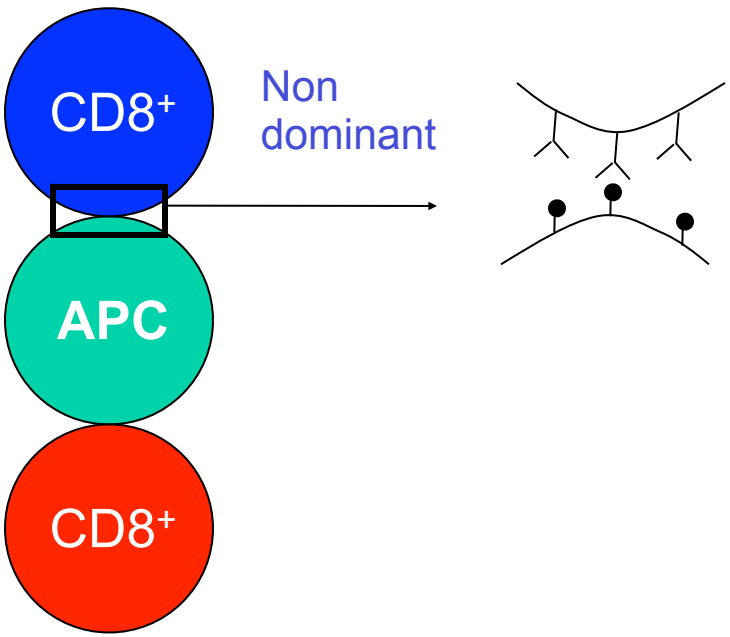
- Immunodominance
- Determinant selection


Internalization of antigen into APC
Antigen processing
Processing generates multiple peptides, one of which can bind to class II allele
T cells respond to immunodominant peptide epitope
Multiple peptide epitopes
Immunodominant epitope
CD4+ T cell

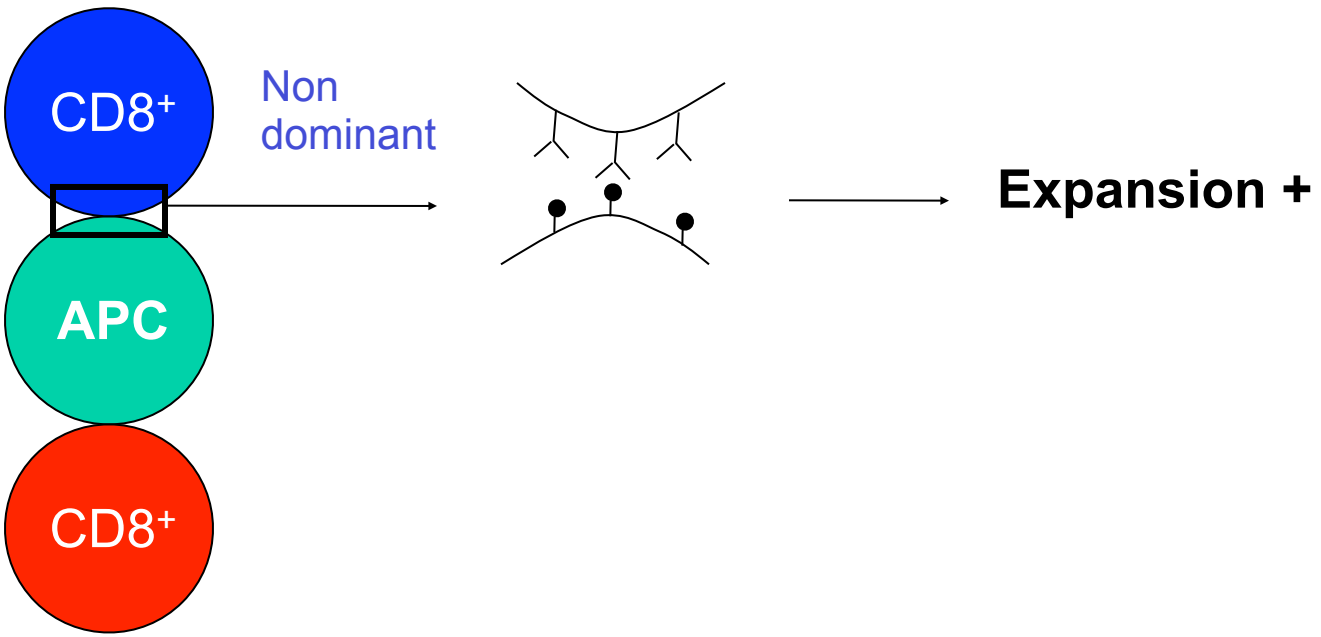
Immunodominance



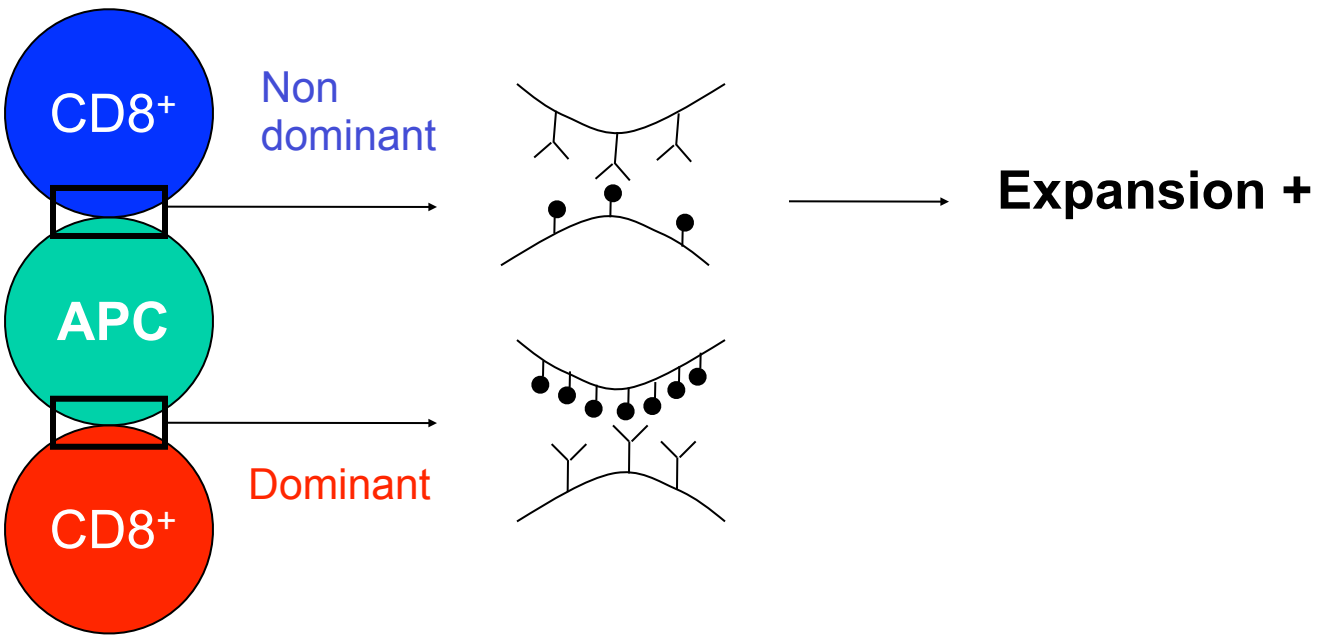
Immunodominance



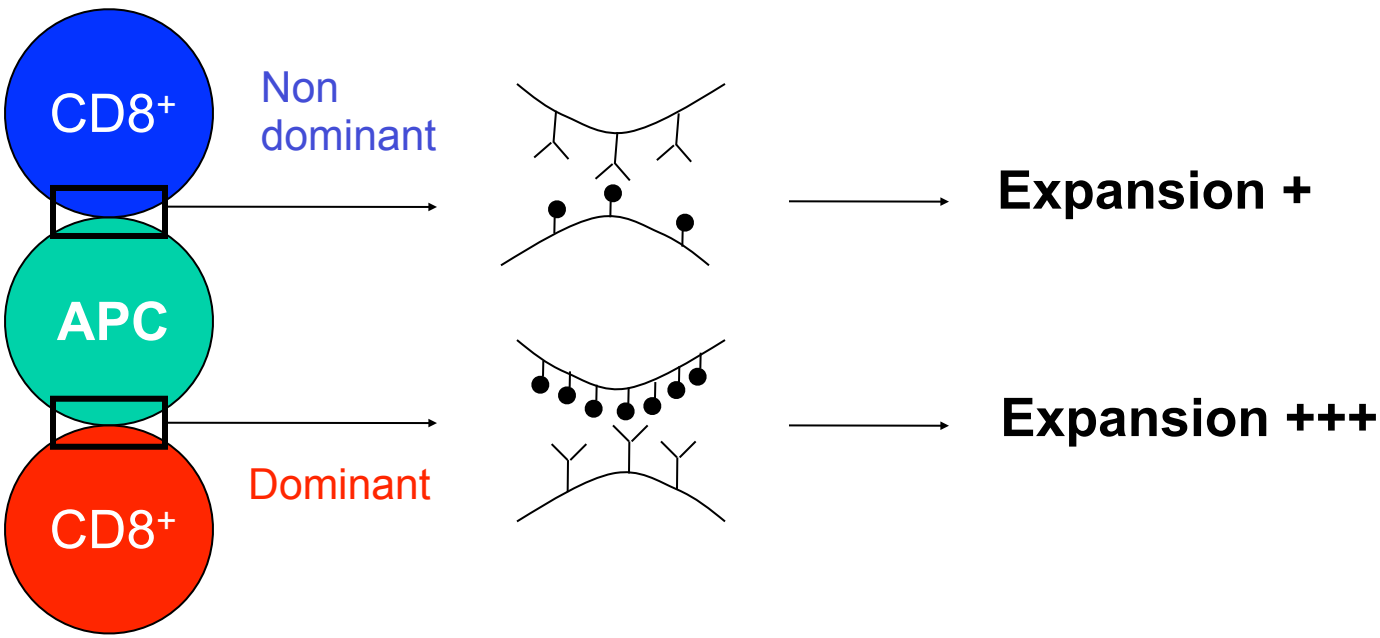
Immunodominance



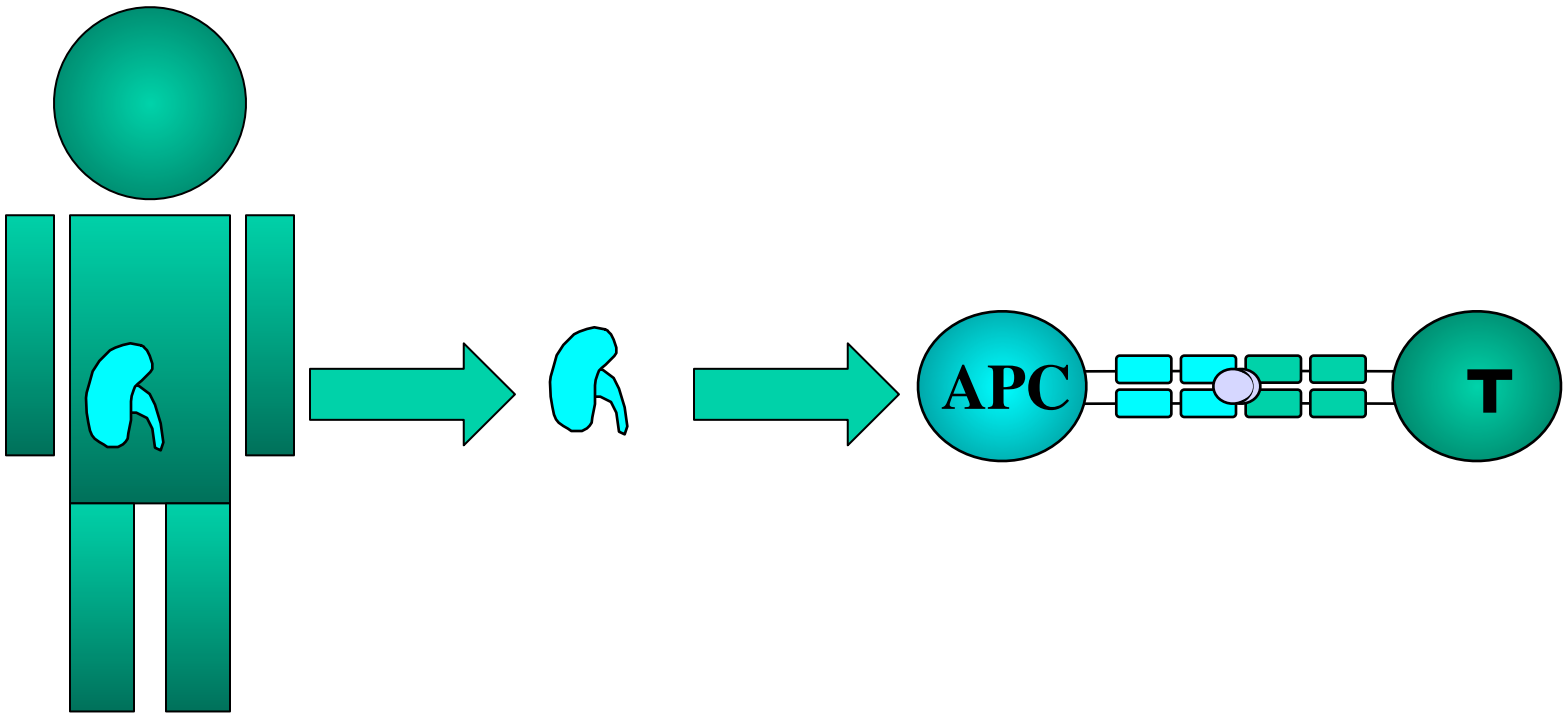
Immunodominance



Immunodominance



Allorecognition



Recognition of the graft MHC alloantigens by T lymphocytes is the major trigger of immunological rejection of organ transplants

The phenomenon of allorecognition

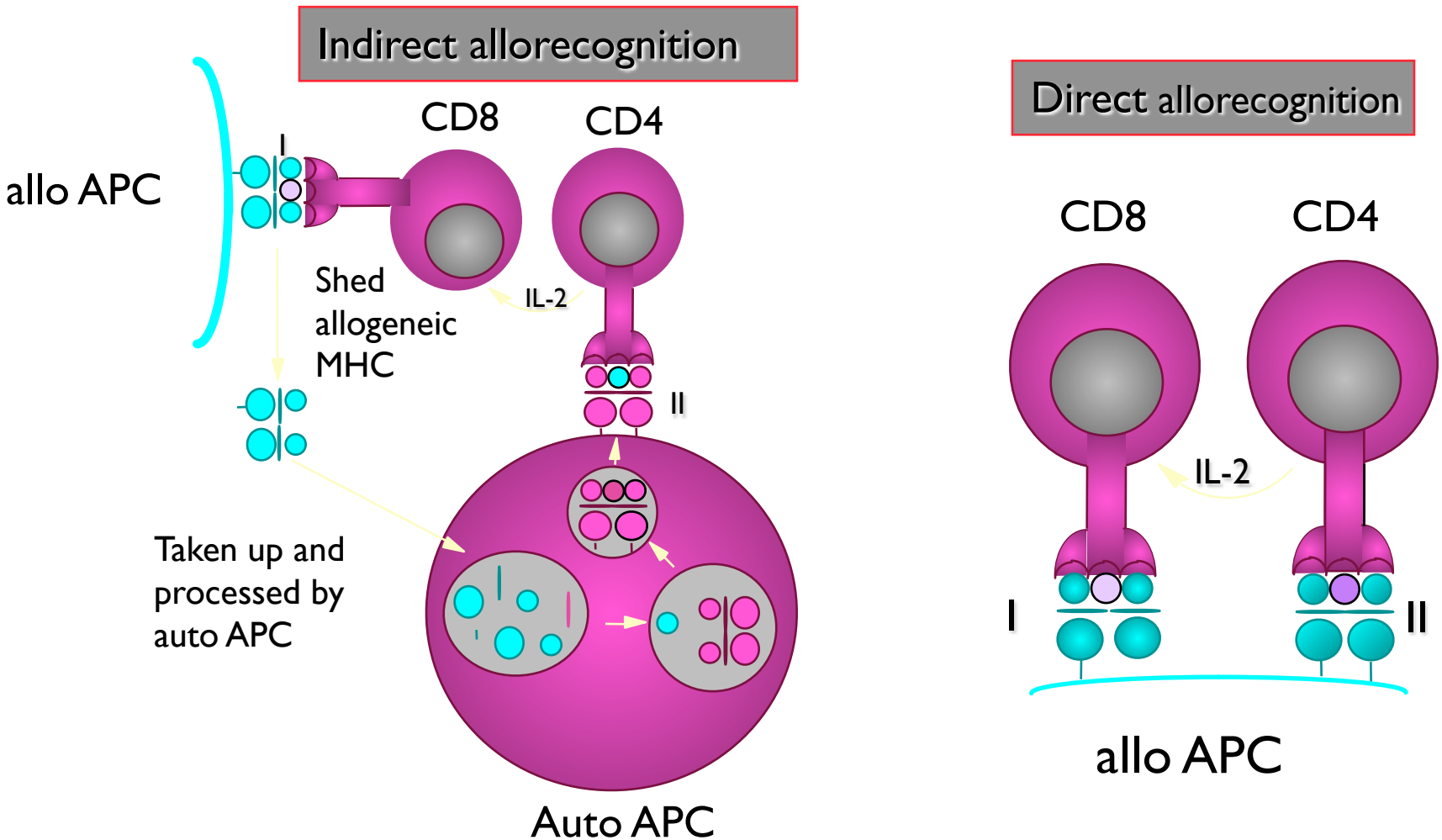
MHC-incompatible cells induce uniquely strong primary immune responses.

In vivo -> HVG and GVH reaction

In vitro -> MLR

This reflects the high precursor frequencies of T cells with anti-MHC allospecificity.

Allorecognition: the two pathways



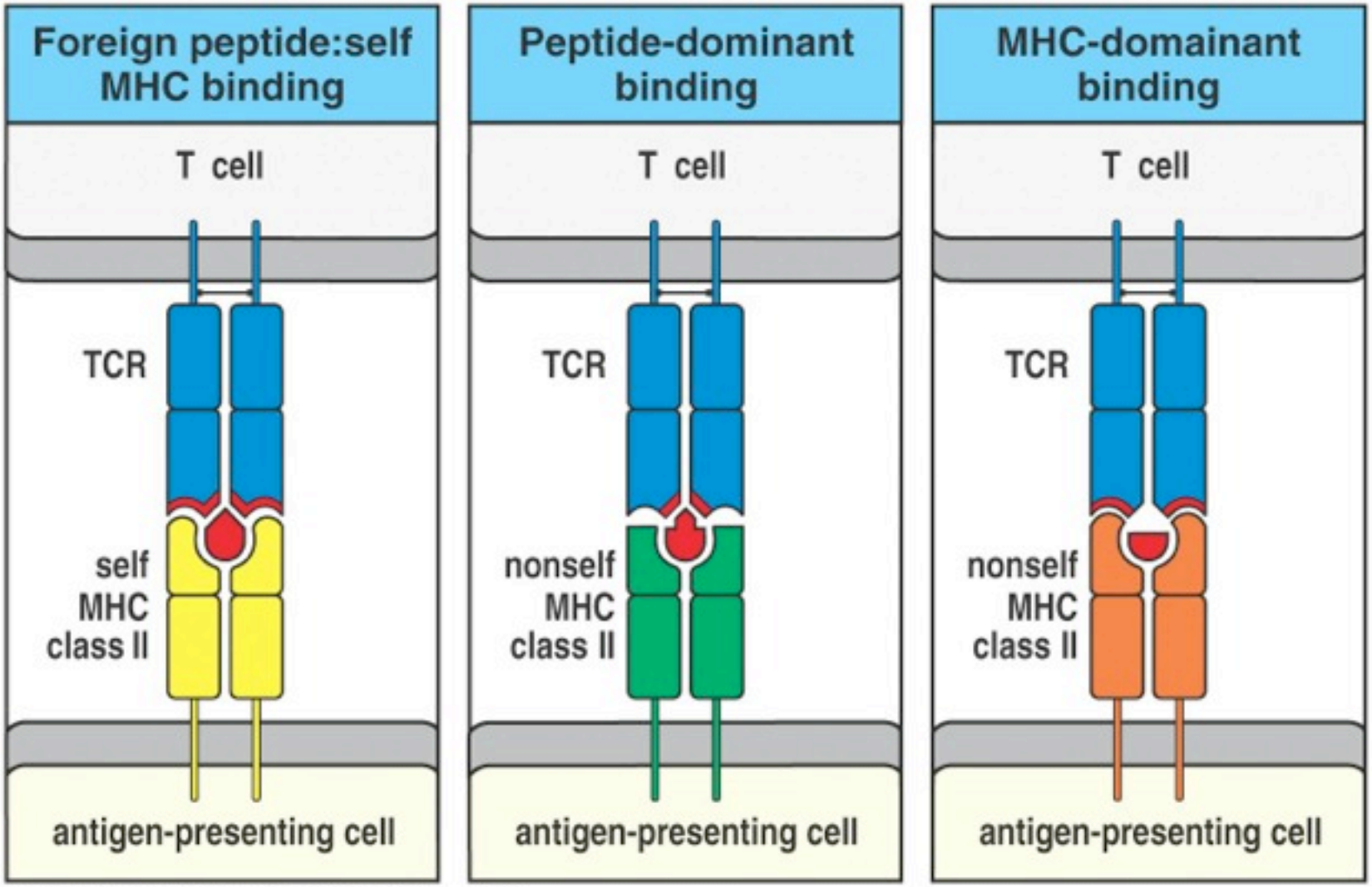


Figure 5-18 Immunobiology, 6/e. (© Garland Science 2005)

HLA and Disease associations

Autoimmune disease

- HLA-B27 and ankylosing spondylitis
- HLA-DQB1*0602 and narcolepsy

Infectious disease

- Malaria
- HIV

Response to non-self proteins

- Insulin
- Coagulation FVIII

Insulin dependent diabetes mellitus

Risk factor: IDDM1

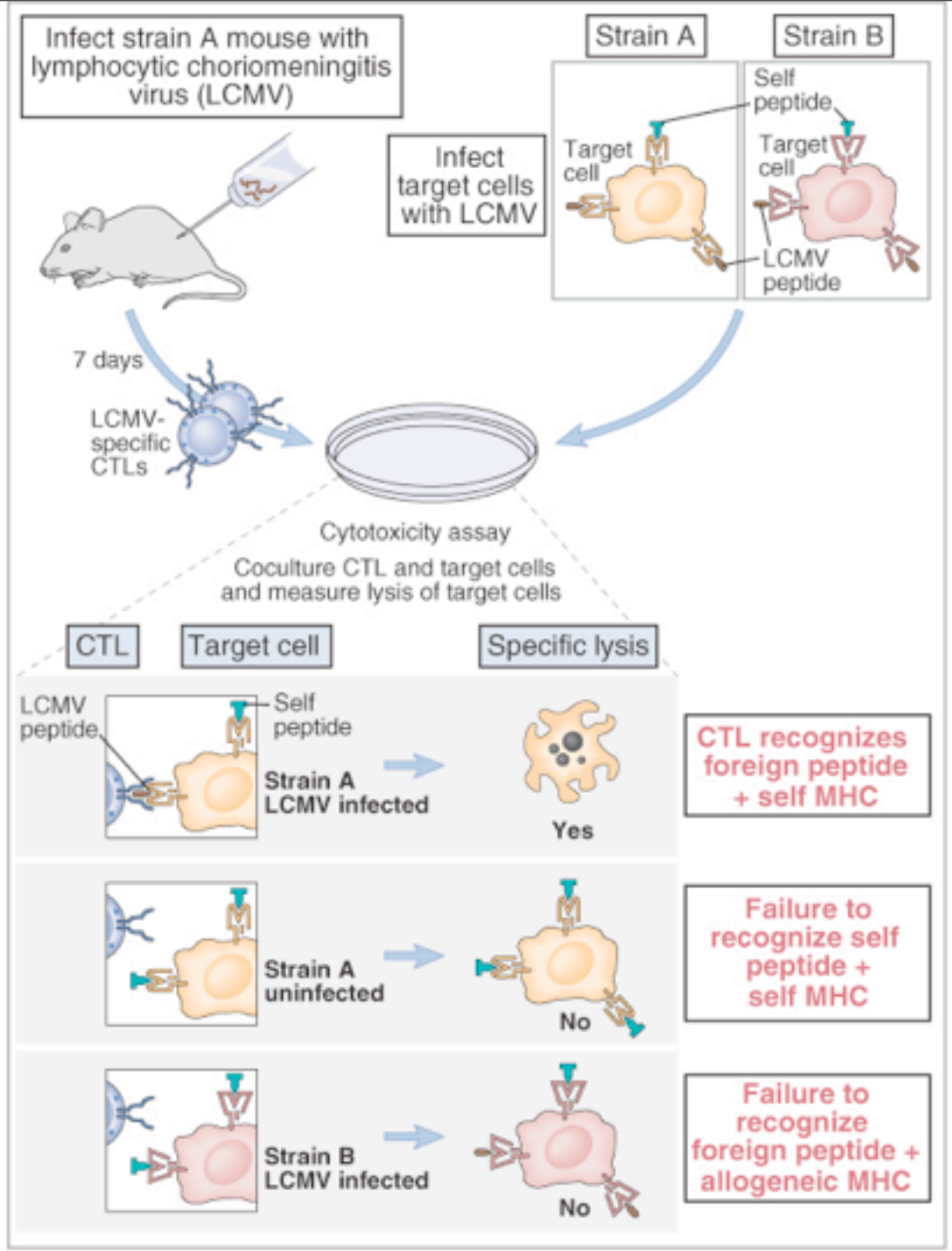
MHC class II β chains with valine, serine, alanine at position 59

Aspartic acid at position 59 is protective

Protection is dominant

Protective class II alleles can delete autoreactive T cells in the thymus (JEM 186:1059, 1997)

Thymocyte development


Infect strain A mouse with lymphocytic choriomeningitis virus (LCMV)
Strain A
Strain B
Self peptide
Target cell
Target cell
Infect target cells with LCMV
LCMV peptide
7 days
LCMV-specific CTLs
Cytotoxicity assay
Coculture CTL and target cells and measure lysis of target cells
CTL
Target cell
Specific lysis
LCMV peptide
Self peptide
Strain A LCMV infected
Yes
CTL recognizes foreign peptide + self MHC
Strain A uninfected
No
Failure to recognize self peptide + self MHC
Strain B LCMV infected
No
Failure to recognize foreign peptide + allogeneic MHC

Process of Self MHC Restriction in the Thymus

Process of Self MHC Restriction in the Thymus

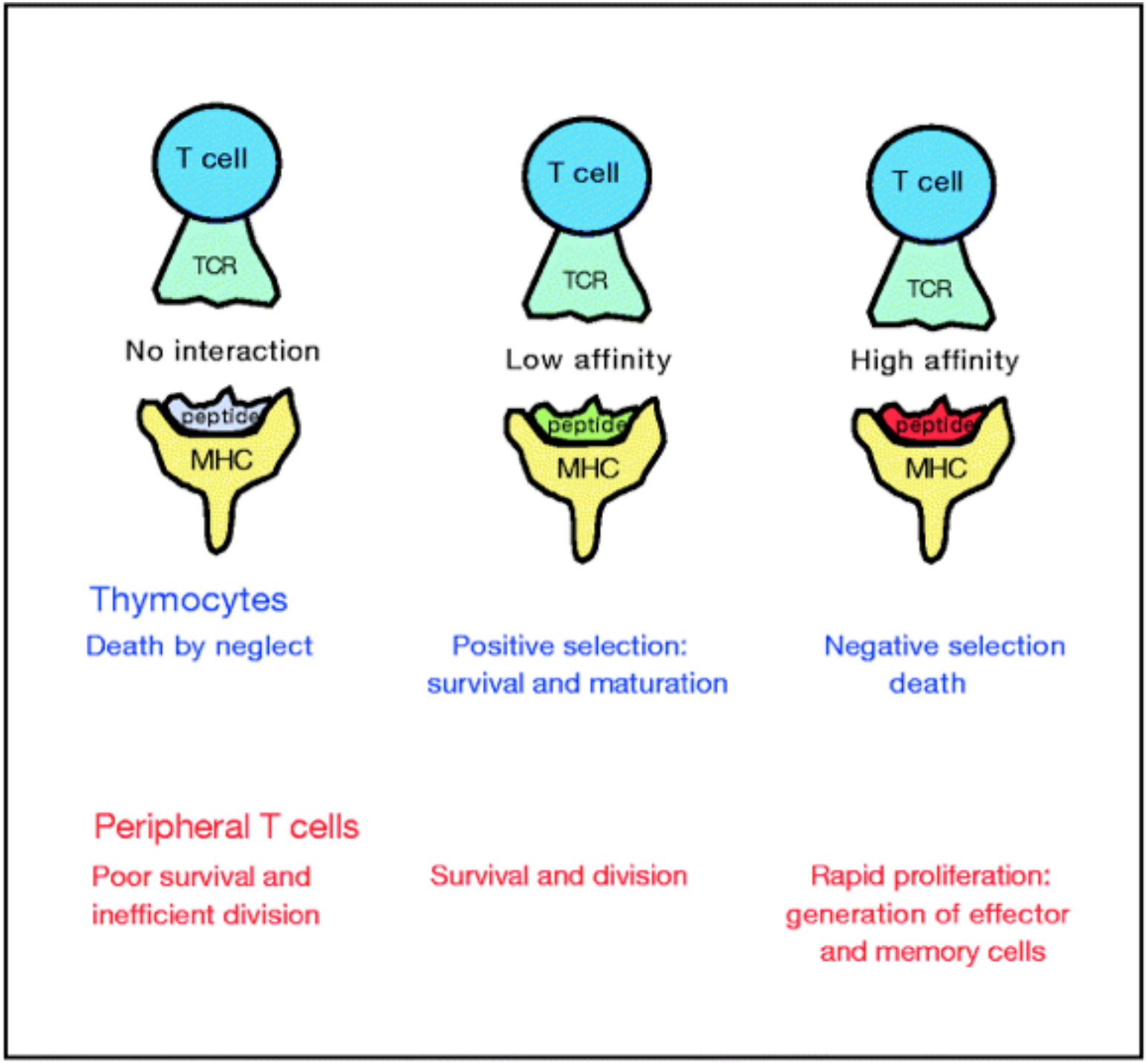
- T cells with TCR recognizing self MHC molecules are retained ("positive selection")

Process of Self MHC Restriction in the Thymus

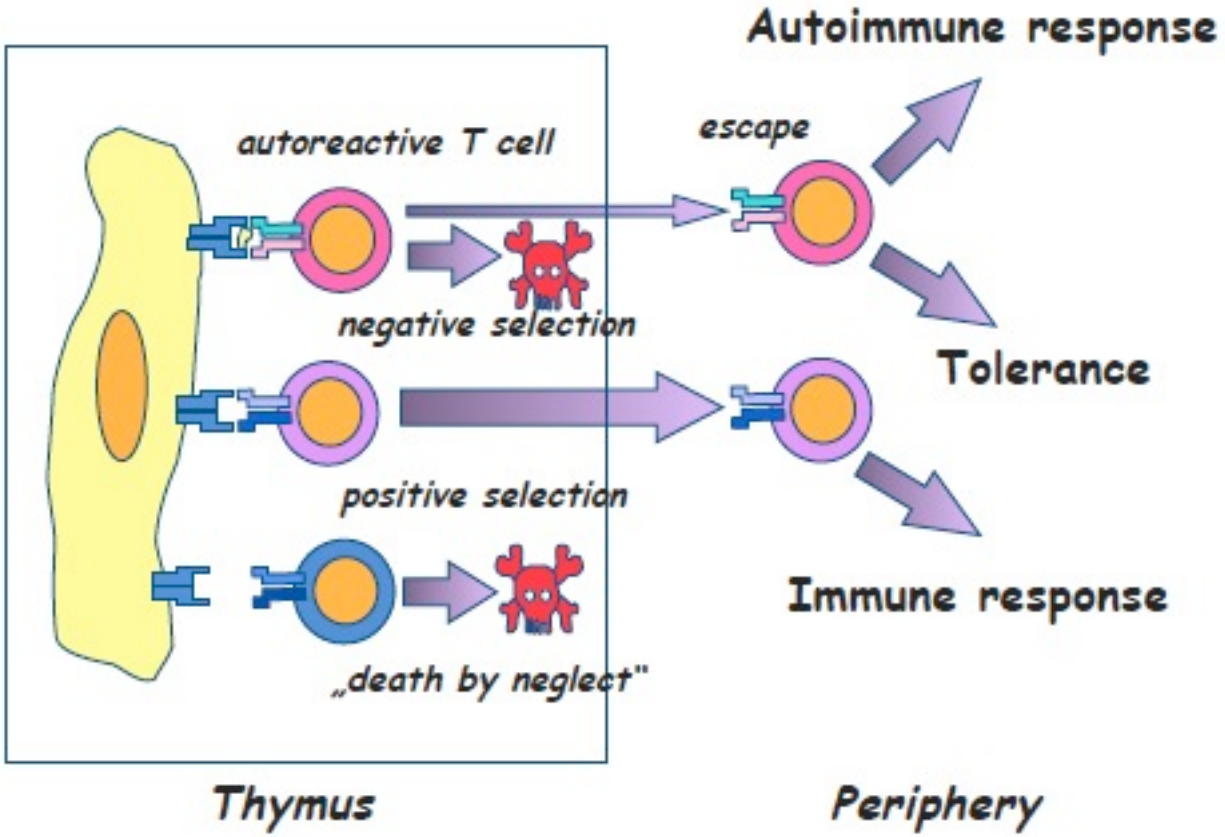
- T cells with TCR recognizing self MHC molecules are retained ("positive selection")
- Retained T cells with TCR recognizing self peptide associated with self MHC are eliminated ("negative selection")

Process of Self MHC Restriction in the Thymus

- T cells with TCR recognizing self MHC molecules are retained ("positive selection")
- Retained T cells with TCR recognizing self peptide associated with self MHC are eliminated ("negative selection")
- Self MHC-restricted T cells are released

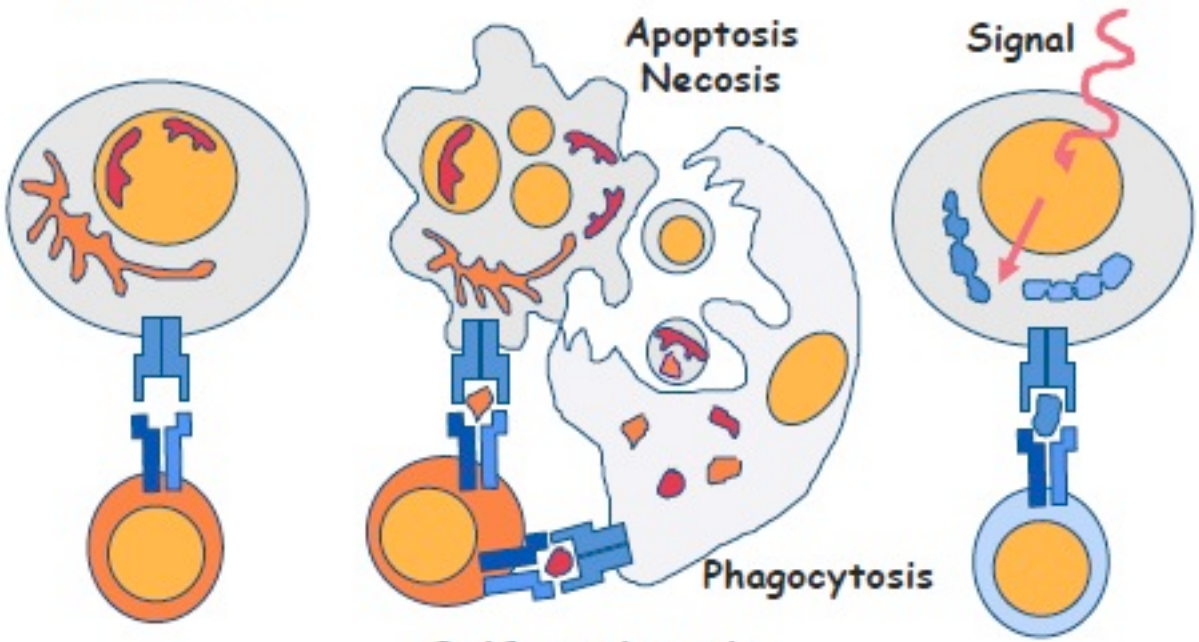

T cell
TCR
No interaction
peptide
MHC
T cell
TCR
Low affinity
peptide
MHC
T cell
TCR
High affinity
peptide
MHC
Thymocytes
Death by neglect
Positive selection:
survival and maturation
Negative selection
death
Peripheral T cells
Poor survival and
inefficient division
Survival and division
Rapid proliferation:
generation of effector
and memory cells

Central thymic deletion is incomplete



Immunological ignorance

Recognition of "hidden" auto-antigens

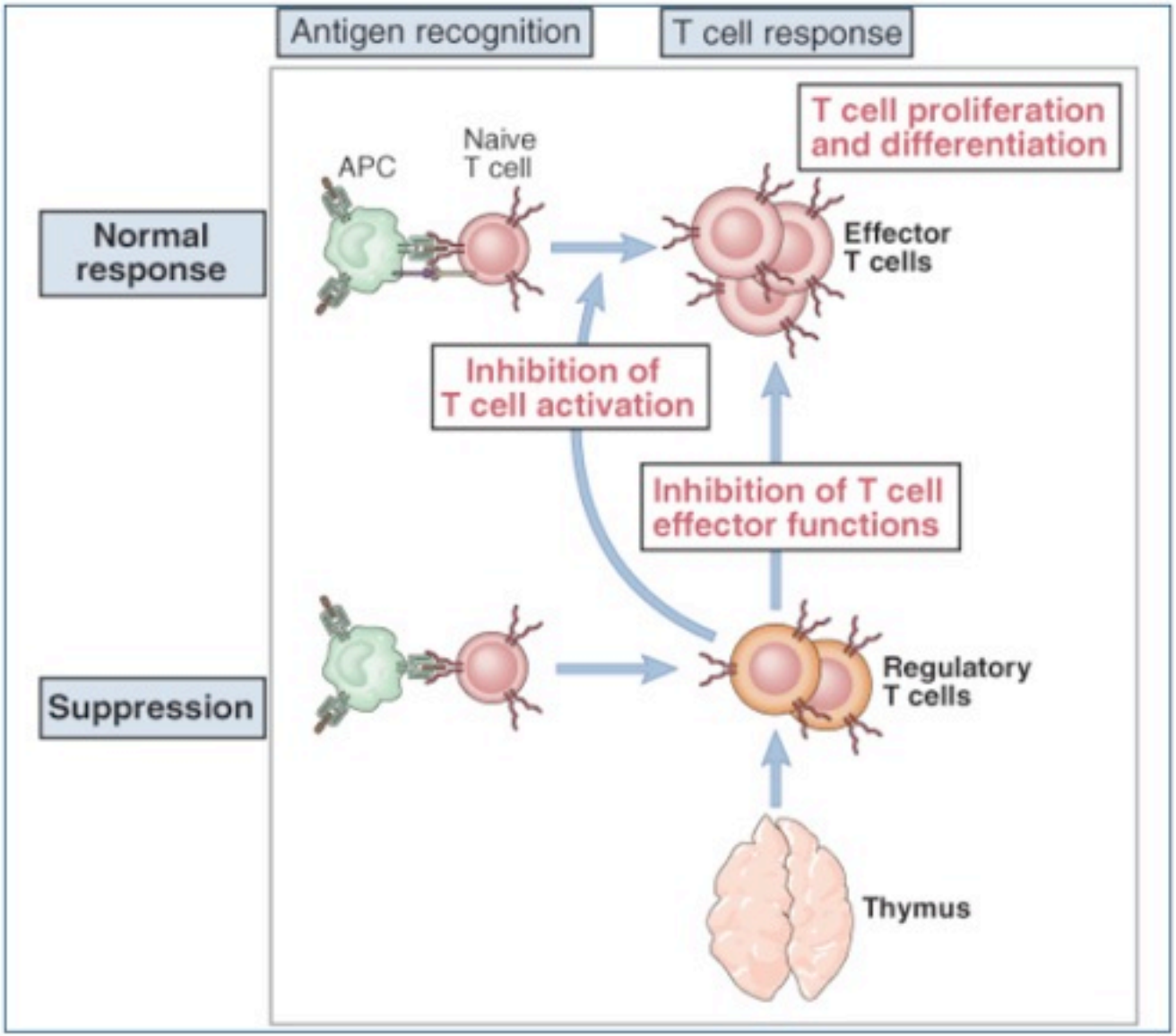


Self-antigen is in a hidden form

Self-antigen is released during excessive cell death

Self-antigen expression is induced

Regulatory T cells



CD4+CD25+ Regulatory T cells

CD4+CD25+ Regulatory T cells

- Characterised by: FoxP3+CTLA-4+CD127-FR4+

CD4+CD25+ Regulatory T cells

- Characterised by: FoxP3+CTLA-4+CD127-FR4+
- T-cell subset of thymic origin

CD4+CD25+ Regulatory T cells

- Characterised by: FoxP3+CTLA-4+CD127-FR4+
- T-cell subset of thymic origin
- Anergic and immunosuppressive

CD4+CD25+ Regulatory T cells

- Characterised by: FoxP3+CTLA-4+CD127-FR4+
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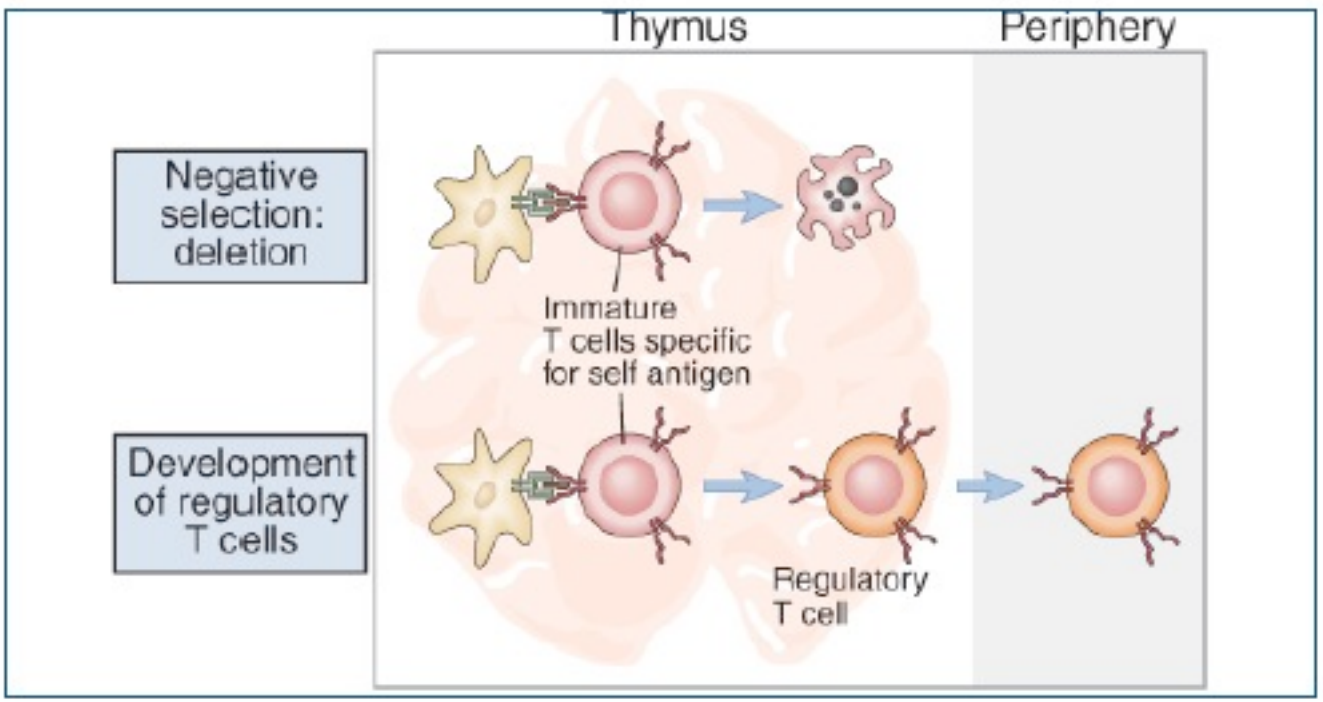
- Anergic and immunosuppressive
- Its removal enhances autoimmunity

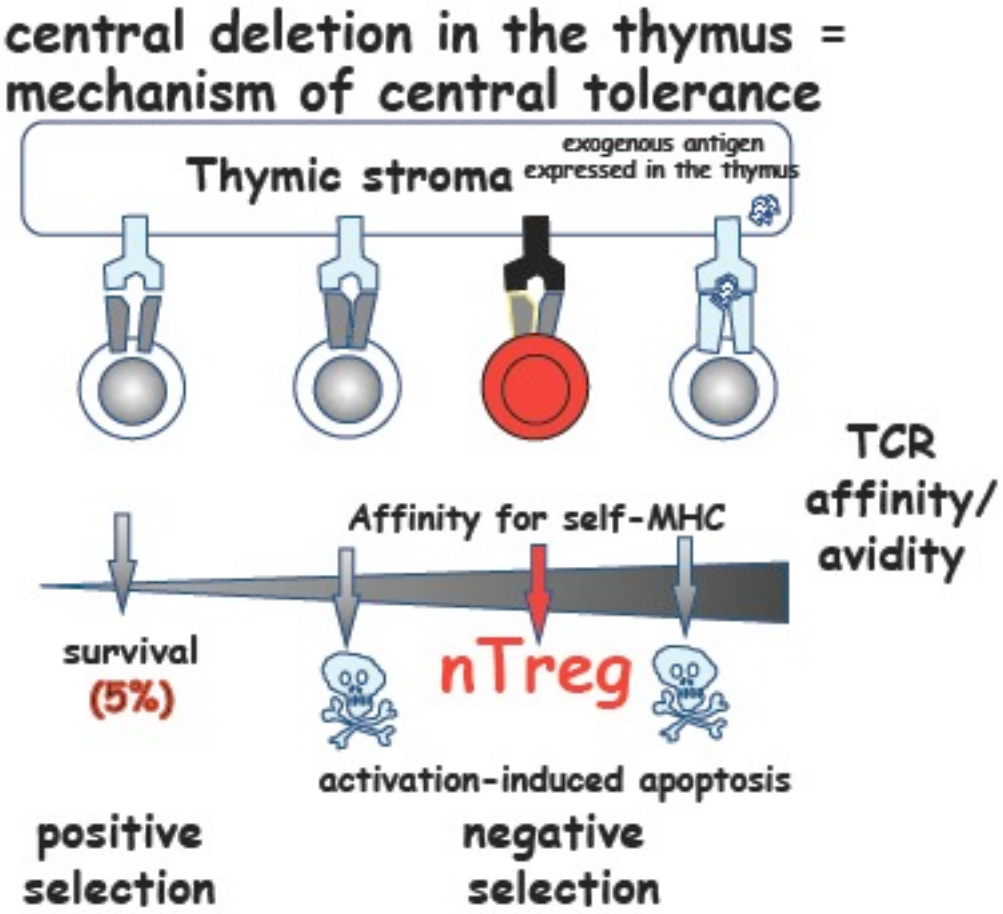
CD4+CD25+ Regulatory T cells

- Characterised by: FoxP3+CTLA-4+CD127-FR4+
- T-cell subset of thymic origin
- Anergic and immunosuppressive
- Its removal enhances autoimmunity
- Its removal enhances tumour immunity

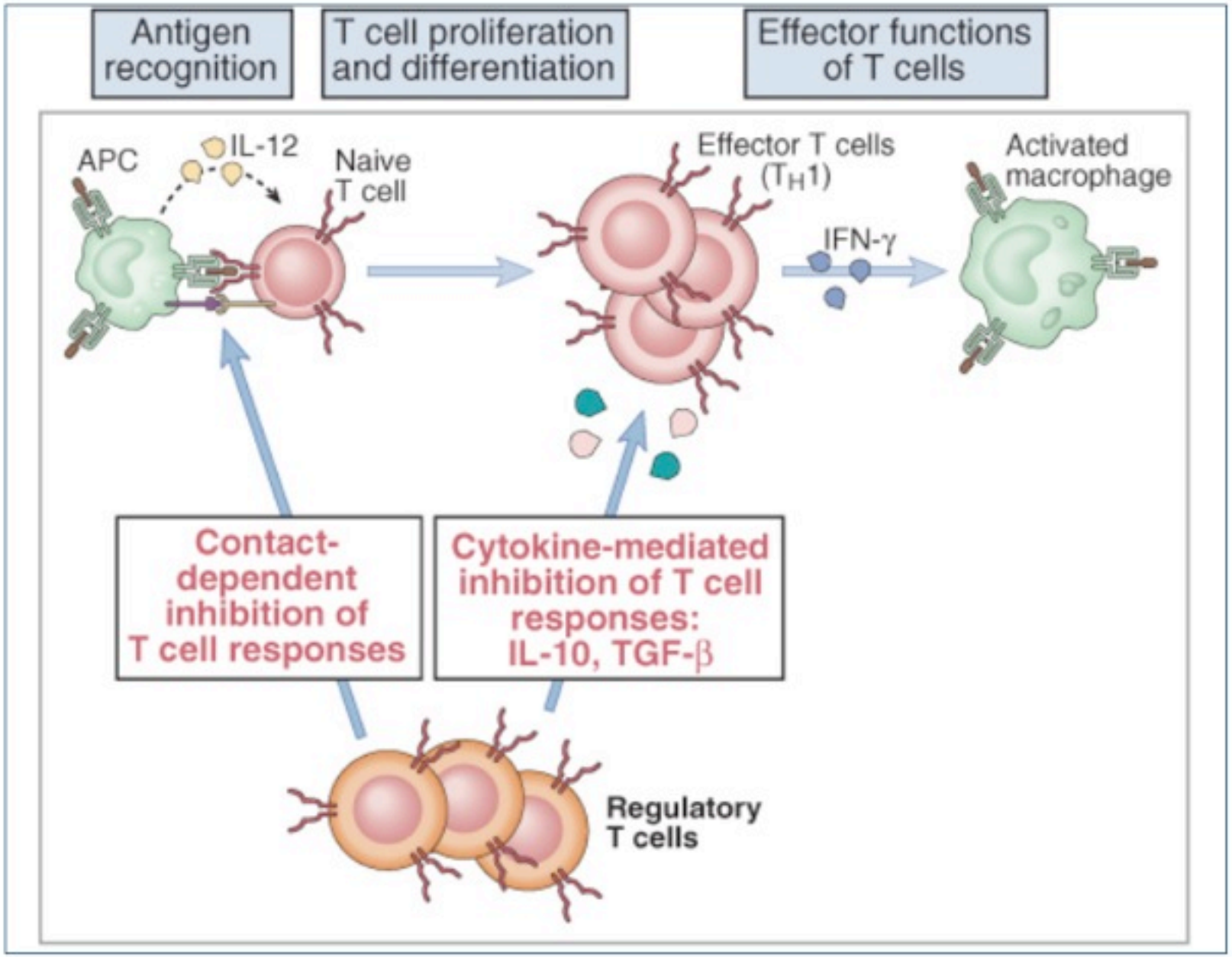
Autoreactive regulatory T cells are NOT negatively selected (CD4+25+ Treg and CD8aa+ intraepithelial lymphocytes)



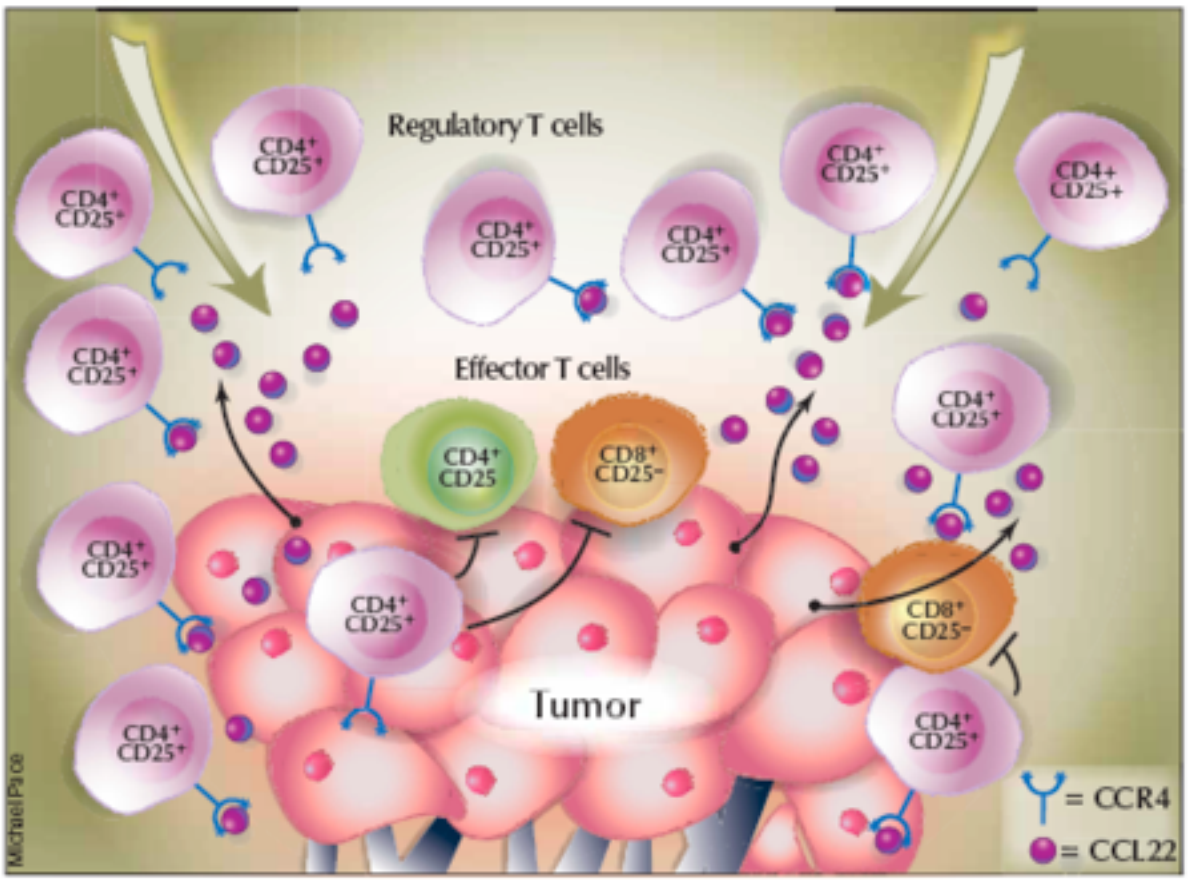
Natural regulatory T cell Selection



Mechanisms of action of regulatory T cells.

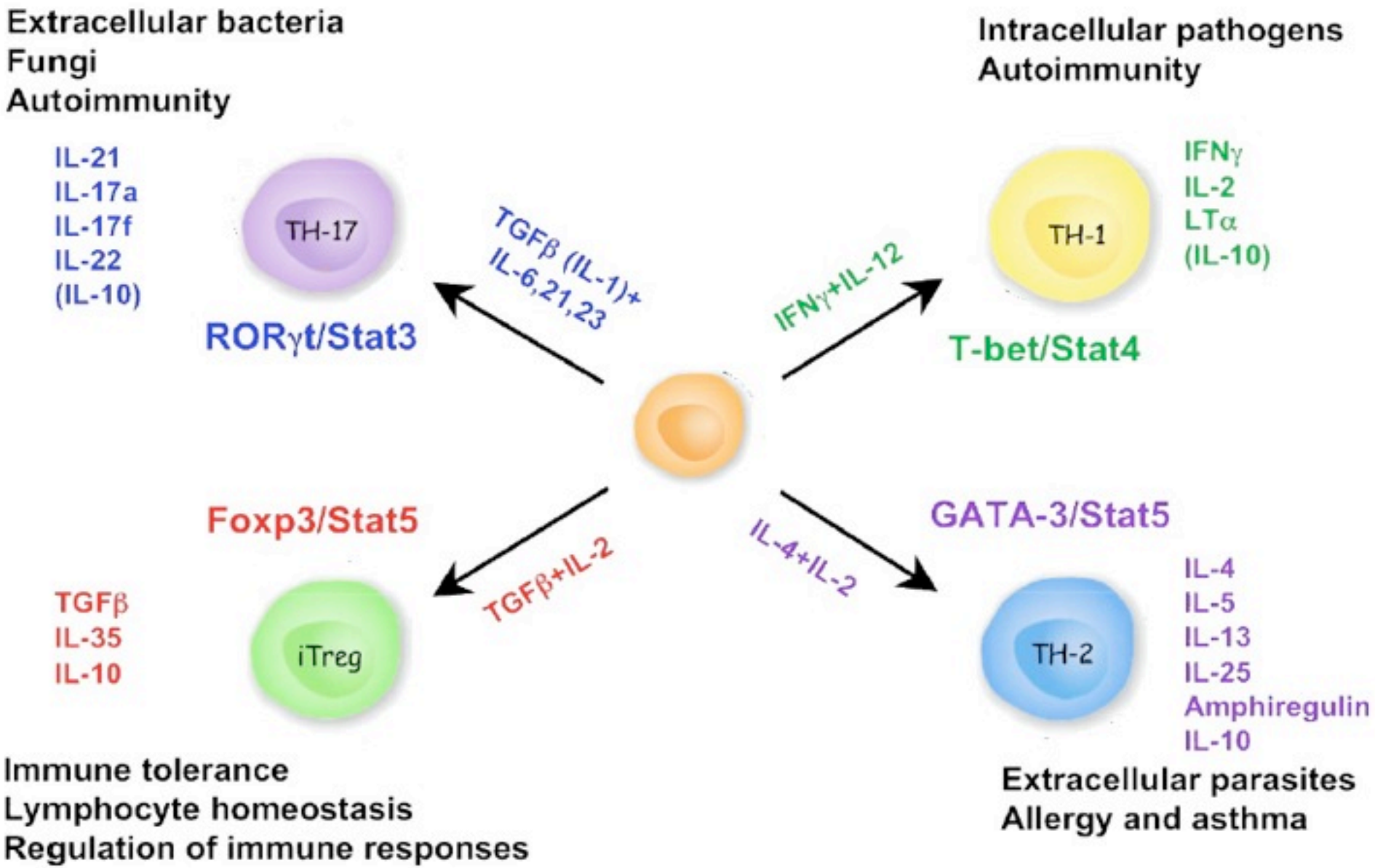


Treg affect clinical outcome and response to treatment in patients with tumours



Nat Med 10:942, 2004

TGFβ and IL-2 induced T reg differentiation



T-cell trafficking

Journal of Pathology
J Pathol 2008; **214**: 179–189
Published online in Wiley InterScience
(www.interscience.wiley.com) **DOI:** 10.1002/path.2269

Invited Review

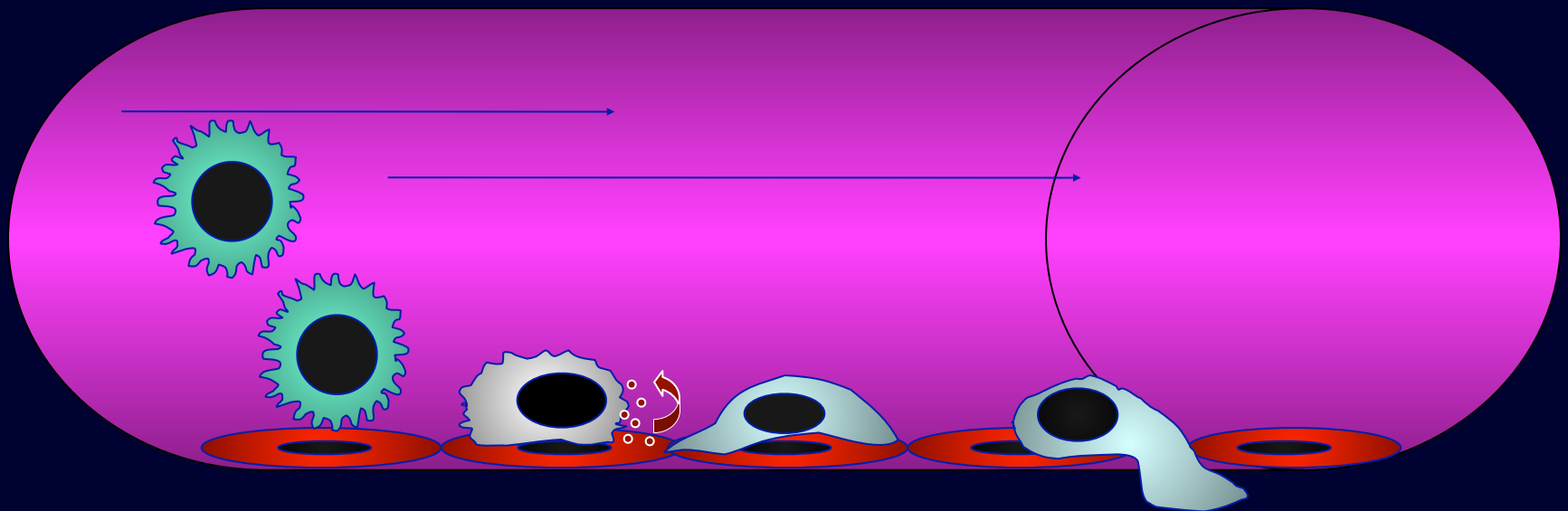
The highway code of T cell trafficking

FM Marelli-Berg,[1]* L Cannella,[2] F Dazzi[2] and V Mirenda[3]

Extravasation events

Specialized molecules expressed by lymphocytes and endothelial cells regulate lymphocyte migration into tissues

How cells localize into tissues

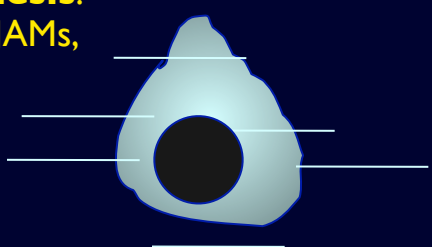


i. **Tethering/ rolling**: selectins integrins

ii. Exposure to chemokines (**activation**)

iii. **Firm adhesion**: integrins

iv. **Diapedesis**: CD31, JAMs, CD99



v. **Tissue infiltration**: integrins, chemokines, MMPs laminin 8/10

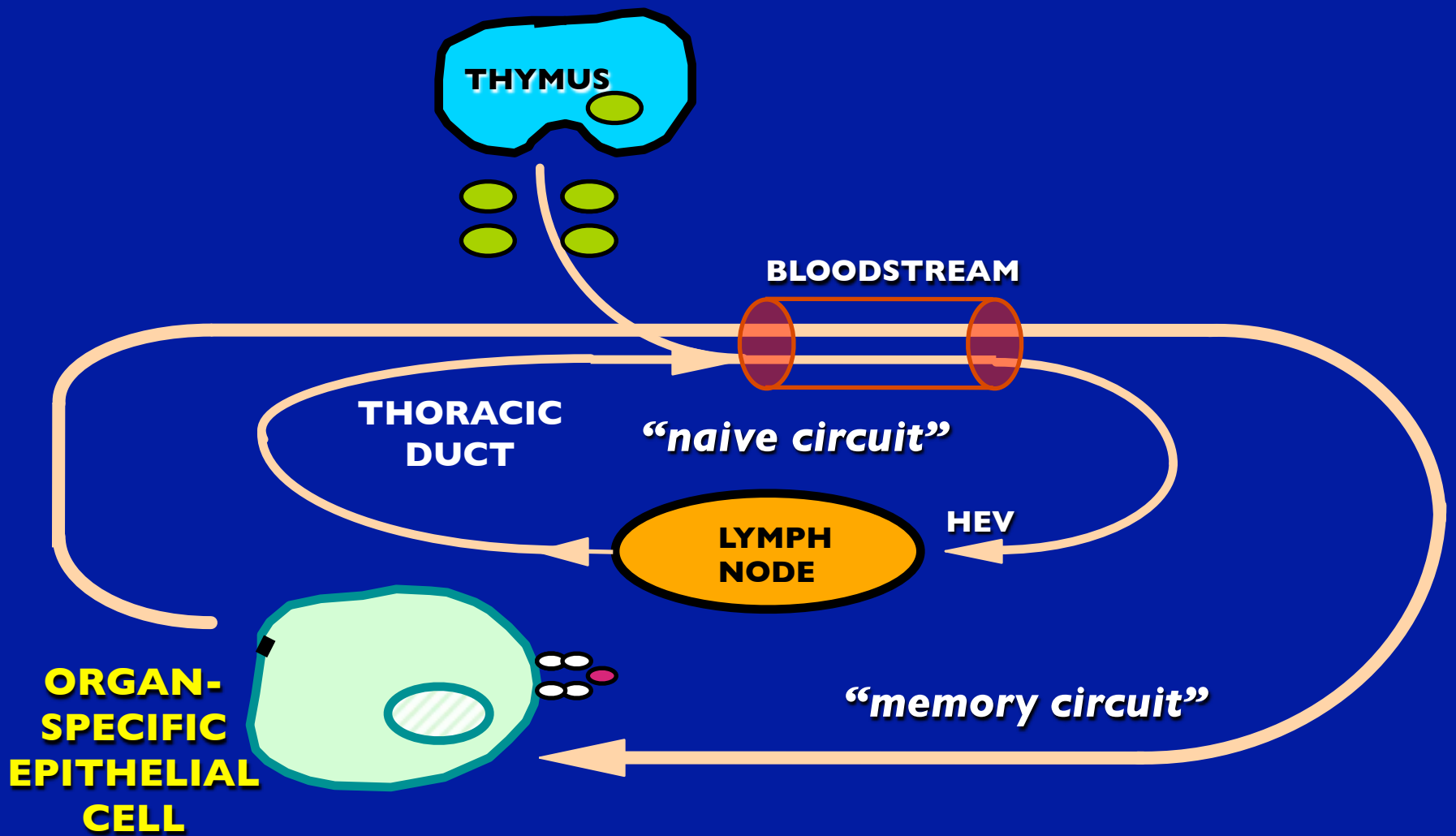
Priming results in the differentiation of memory T cell subsets

Effector memory T cells (CD45RO+, CCR7-, CD62L-)

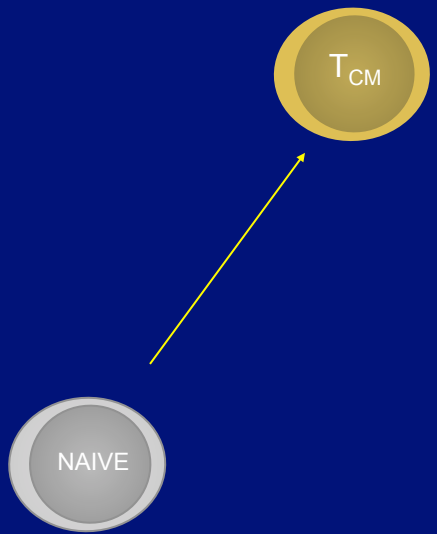
Central memory T cells (CD45RO+, CCR7+, CD62L+)

Follicular homing T cells (CD45RO+, CCR7-, CD62L-, CXCR5+)

Naïve and memory T cells have different patterns of recirculation.



Trafficking features: LN - PP - blood
Vessel type: HEV
Tethering/rolling: L-selectin (PNAd)
$\alpha_4\beta_7$(MAdCAM-1) in MLN
Integrin activation: CCR7 (CCL19/CCL21)
Firm adhesion: LFA-1 (ICAM-1)
$\alpha_4\beta_7$(MAdCAM-1) in PP



Trafficking features: LN - PP - bone marrow
Vessel type: HEV, sinusoid/venules in bone marrow
Survival: long-term
Tethering/rolling: L-selectin (PSGL-1)
$\alpha_4\beta_7$(MAdCAM-1) for MLN
PSGL-1 (P-/E-selectin) in bone marrow
Integrin activation: CCR7 (CCL19/CCL21)
CXCR4 (CXCL12)
Firm adhesion: LFA-1 (ICAM-1)
$\alpha_4\beta_7$ (MAdCAM-1) in PP

Trafficking features: LN - PP - blood
Vessel type: HEV
Tethering/rolling: L-selectin (PNAd)
$\alpha_4\beta_7$(MAdCAM-1) in MLN
Integrin activation: CCR7 (CCL19/CCL21)
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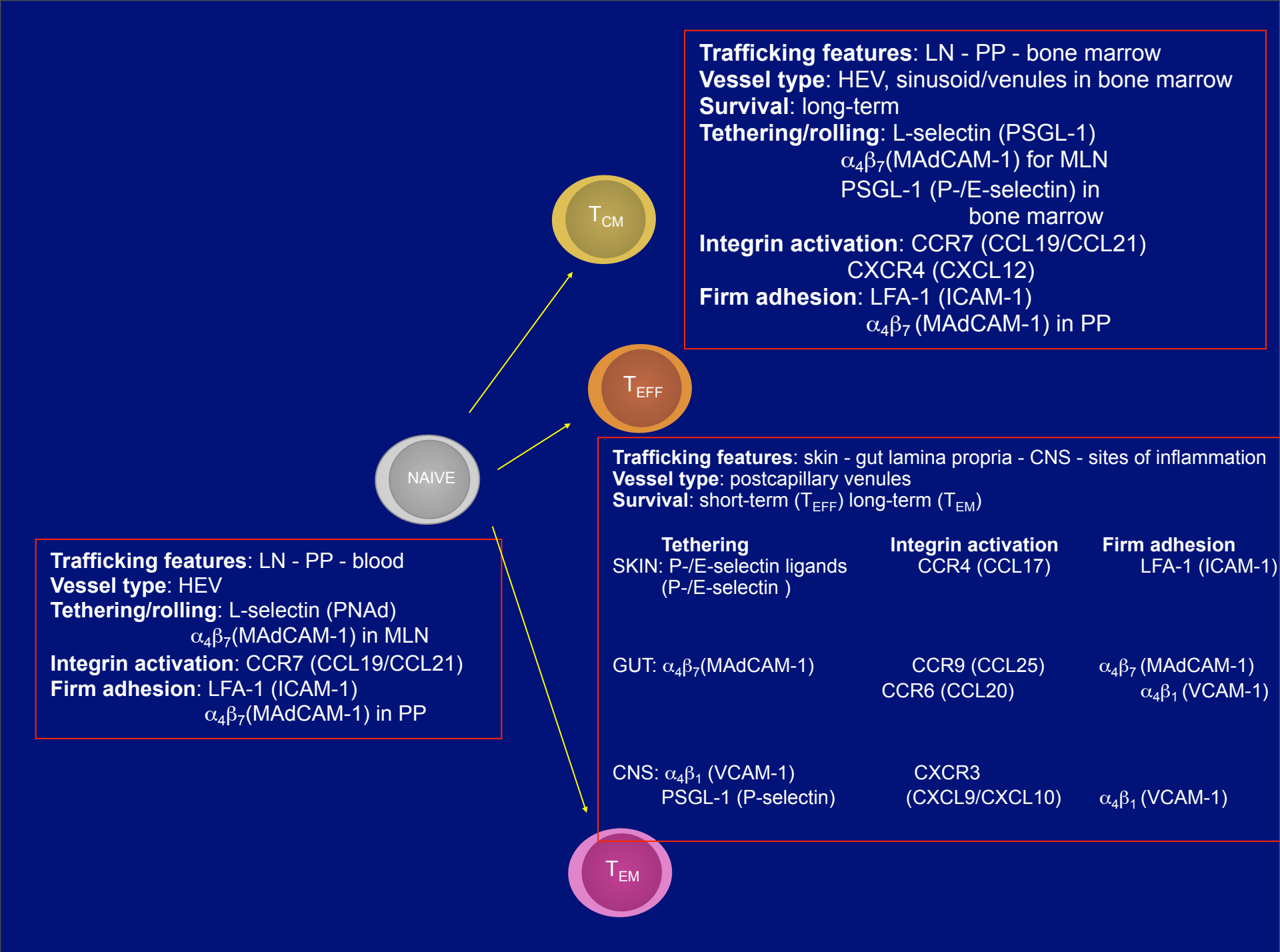
$\alpha_4\beta_7$(MAdCAM-1) in PP


Trafficking features: LN - PP - bone marrow
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$\alpha_4\beta_7$ (MAdCAM-1) in PP
T_{CM}
T_{EFF}
NAIVE
T_{EM}
Trafficking features: skin - gut lamina propria - CNS - sites of inflammation
Vessel type: postcapillary venules
Survival: short-term (T_{EFF}) long-term (T_{EM})
Tethering
Integrin activation
Firm adhesion
SKIN: P-/E-selectin ligands (P-/E-selectin)
CCR4 (CCL17)
LFA-1 (ICAM-1)
GUT: $\alpha_4\beta_7$(MAdCAM-1)
CCR9 (CCL25)
CCR6 (CCL20)
$\alpha_4\beta_7$ (MAdCAM-1)
$\alpha_4\beta_1$ (VCAM-1)
CNS: $\alpha_4\beta_1$ (VCAM-1)
PSGL-1 (P-selectin)
CXCR3 (CXCL9/CXCL10)
$\alpha_4\beta_1$ (VCAM-1)
Trafficking features: LN - PP - blood
Vessel type: HEV
Tethering/rolling: L-selectin (PNAd)
$\alpha_4\beta_7$(MAdCAM-1) in MLN
Integrin activation: CCR7 (CCL19/CCL21)
Firm adhesion: LFA-1 (ICAM-1)
$\alpha_4\beta_7$(MAdCAM-1) in PP

T cell homing and disease

Disease	Key effector cell	Proposed leukocyte receptors for endothelial traffic signals		
		L-selectin, ligand	GPCR	Integrin[a]
Acute inflammation				
Myocardial infarction	Neutrophil	PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
Stroke	Neutrophil	L-selectin, PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
Ischemia-reperfusion	Neutrophil	PSGL-1	CXCR1, CXCR2, PAFR, BLT1	LFA-1, Mac-1
T_H1				
Atherosclerosis	Monocyte	PSGL-1	CCR1, CCR2, BLT1, CXCR2, CX3CR1	VLA-4
	T_H1	PSGL-1	CXCR3, CCR5	VLA-4
Multiple sclerosis	T_H1	PSGL-1 (?)	CXCR3, CXCR6	VLA-4, LFA-1
	Monocyte	PSGL-1 (?)	CCR2, CCR1	VLA-4, LFA-1
Rheumatoid arthritis	Monocyte	PSGL-1	CCR1, CCR2	VLA-1, VLA-2, V LFA-1
	T_H1	PSGL-1	CXCR3, CXCR6	VLA-1, VLA-2, V LFA-1
	Neutrophil	L-selectin, PSGL-1	CXCR2, BLT1	LFA-1[b]
Psoriasis	Skin-homing T_H1	CLA	CCR4, CCR10, CXCR3	VLA-4[c], LFA-1
Crohn disease	Gut-homing T_H1	PSGL-1	CCR9, CXCR3	$\alpha_4\beta_7$, LFA-1
Type I diabetes	T_H1	PSGL-1 (?)	CCR4, CCR5	VLA-4, LFA-1
	CD8	L-selectin (?), PSGL-1 (?)	CXCR3	VLA-4, LFA-1
Allograft rejection	CD8	PSGL-1	CXCR3, CX3CR1, BLT1	VLA-4, LFA-1
	B cell	L-selectin, PSGL-1	CXCR5, CXCR4	VLA-4, LFA-1
Hepatitis	CD8	PSGL-1	CXCR3, CCR5, CXCR6	VLA-4
Lupus	T_H1	None	CXCR6	VLA-4[d]
	Plasmacytoid DC	L-selectin, CLA	CCR7, CXCR3, ChemR23	LFA-1, Mac-1
	B cell	CLA (?)	CXCR5, CXCR4	LFA-1
T_H2				
Asthma	T_H2	PSGL-1	CCR4, CCR8, BLT1	LFA-1
	Eosinophils	PSGL-1	CCR3, PAFR, BLT1	VLA-4, LFA-1
	Mast cells	PSGL-1	CCR2, CCR3, BLT1	VLA-4, LFA-1
Atopic dermatitis	Skin-homing T_H2	CLA	CCR4, CCR10	VLA-4, LFA-1

Luster et al.,Nature Immunology **6**, 1182 - 1190

Luster et al.,Nature Immunology **6**, 1182 - 1190

TABLE 1. Clinical Trials Targeting Leukocyte Integrins and Their IgSF Ligands[a]

Indication	Target	Result	Drug	Company	Ref.
Asthma	$\alpha_1\beta_2$	Negative	Efalizumab	Genentech/Xoma	[114]
	$\alpha_4\beta_1$	*Negative*	BIO1211	Biogen Idec/Merck	[18]
	$\alpha_4\beta_1/\alpha_4\beta_7$	*Positive*	R411	Roche	[115]
Burns	ICAM-1	Negative	Enlimomab	Boehringer Ingelheim	[96]
Inflammatory bowel disease					
Crohn's	α_4	Positive	Natalizumab	Biogen Idec/Elan Pharmaceuticals	[116]
	$\alpha_4\beta_7$	*Negative*	MLN02	Millennium/Genentech	[117]
	ICAM-1	Negative	Alicaforsen	ISIS Pharmaceuticals	[118, 119]
Ulcerative colitis	$\alpha_4\beta_7$	*Positive*	MLN02	Millennium/Genentech	[120]
Multiple sclerosis	α_4	Positive	Natalizumab	Biogen Idec/Elan Pharmaceuticals	[121]
	β_2	*Negative*	Rovelizumab	ICOS	[122]
Myocardial infarction (MI)	β_2	Negative	Erlizumab	Genentech	[123]
	β_2	Negative	Rovelizumab	ICOS	[124]
Psoriasis	$\alpha_1\beta_2$	Positive	Efalizumab	Genentech/Xoma	[125–127]
Psoriatic arthritis	$\alpha_1\beta_2$	*Negative*	Efalizumab	Genentech/Xoma	[128]
Rheumatoid arthritis (RA)	$\alpha_1\beta_2$	*Negative*	Efalizumab	Genentech/Xoma	[129]
	ICAM-1	Negative	Alicaforsen	ISIS Pharmaceuticals	[130]
Stroke	$\alpha_M\beta_2$	Negative	Neutrophil inhibitory factor	Pfizer	[131]
	β_2	*Negative*	Rovelizumab	ICOS	[132]
	ICAM-1	Negative	Enlimomab	Boehringer Ingelheim	[95]
Transplant	$\alpha_1\beta_2$	Negative	Odulimomab	IMTIX/Pasteur Merieux Serums at Vacins	[133, 134]
	ICAM-1	Negative	Enlimomab	Boehringer Ingelheim	[135]
Traumatic shock	β_2	*Negative*	Rovelizumab	ICOS	[136]
	β_2	Negative	Erlizumab	Genentech	[137]

[a] Completed Phase II or III trials. Results from unpublished trials are indicated in *italics*. Genentech (San Francisco, CA); Xoma (Berkeley, CA); Biogen Idec (Cambridge, MA); Merck (Rahway, NJ); Roche (Nutley, NJ); Boehringer Ingelheim (Pearl River, NY); Elan Pharmaceuticals (Dublin, Ireland); Mellennium (Cambridge, MA); ISIS Pharmaceuticals (Carlsbad, CA); ICOS (Bothell, WA); Pfizer (Groton, CT); IMTIX (Austria) Pasteur Merieux Serums et Vacins (France).

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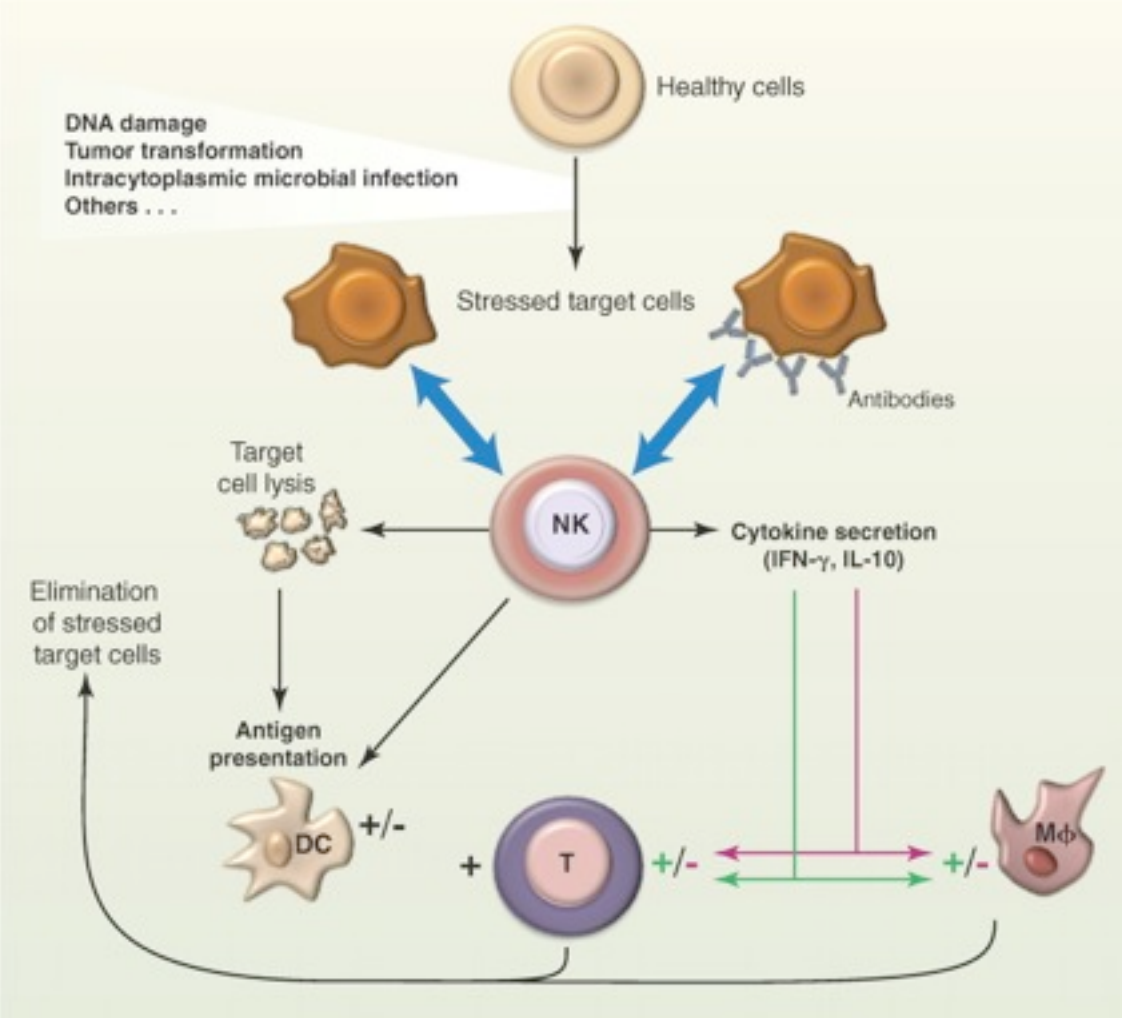
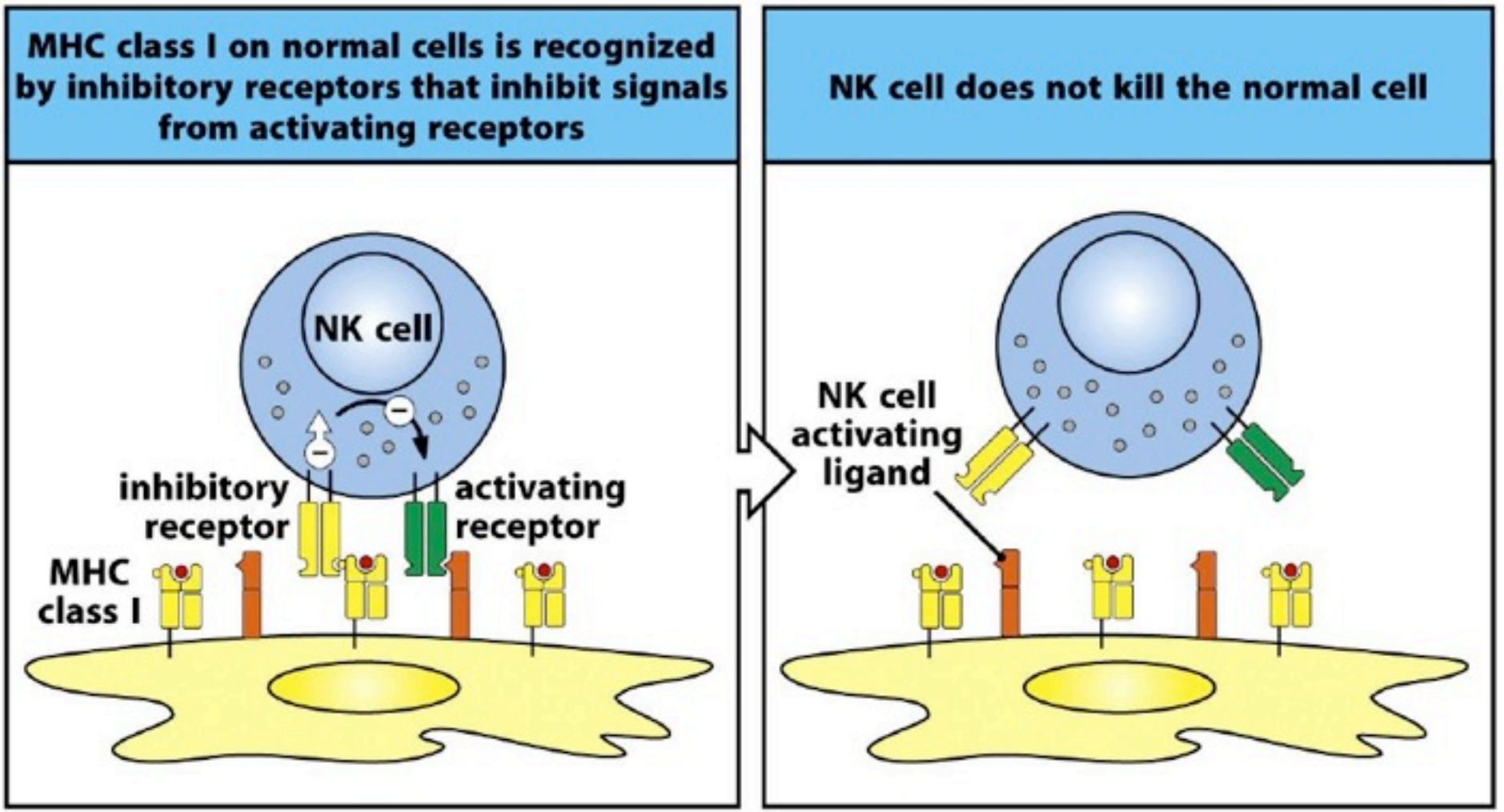
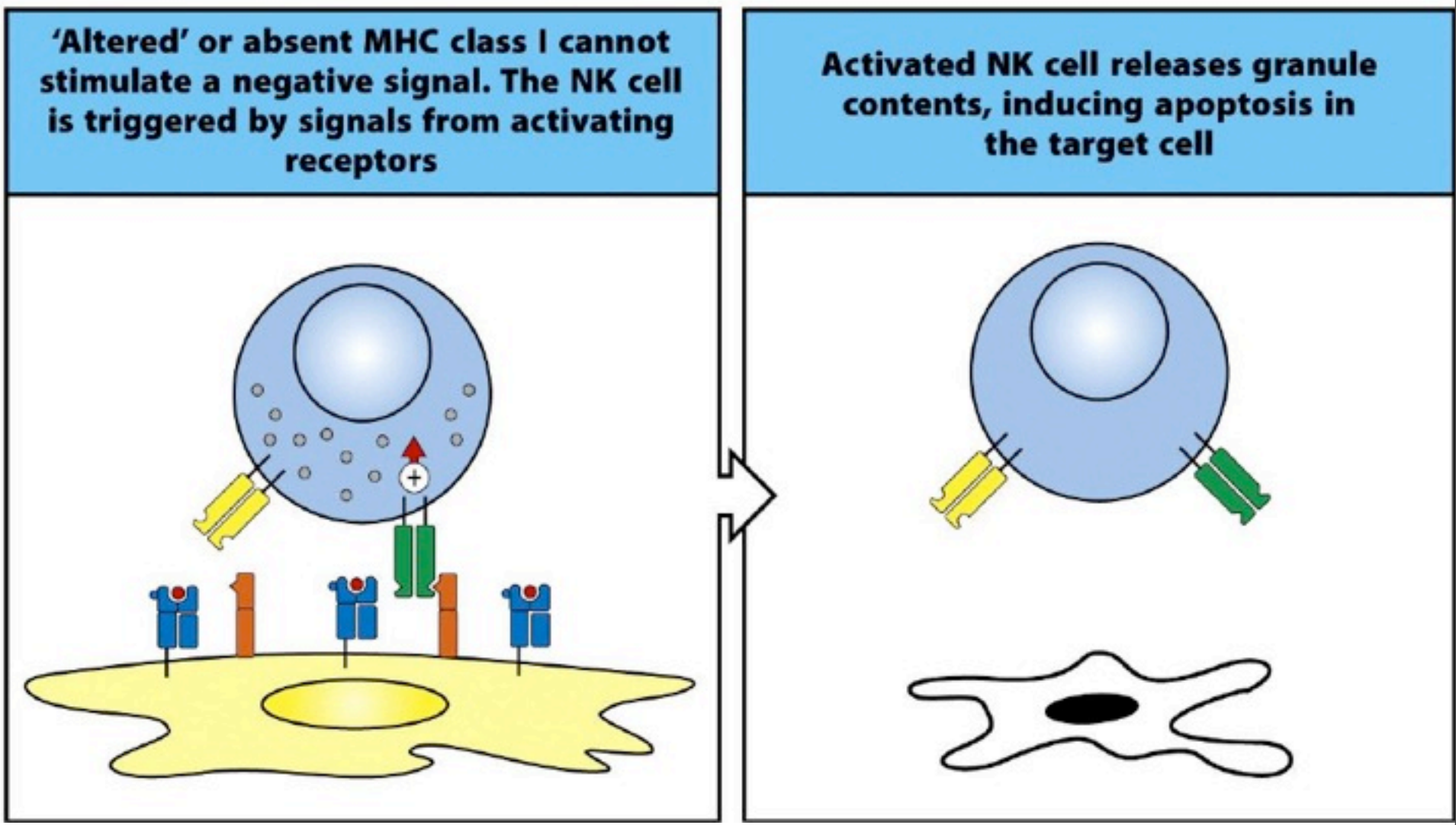
The biological functions of NK cells



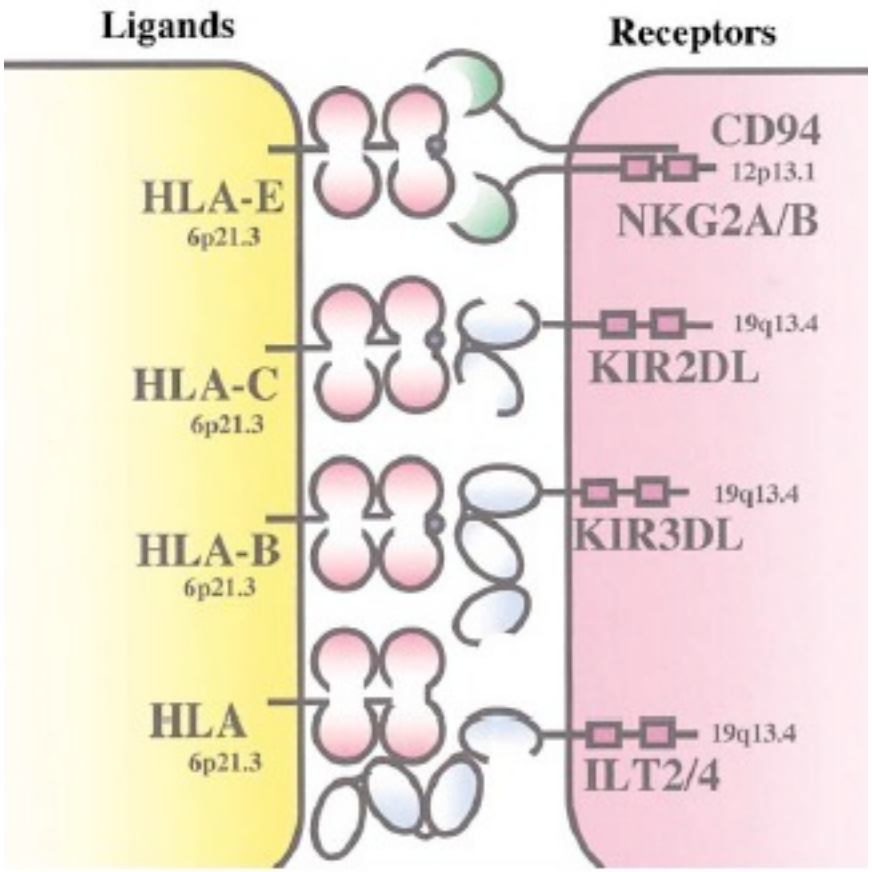
E Vivier et al. Science 2011;331:44-49

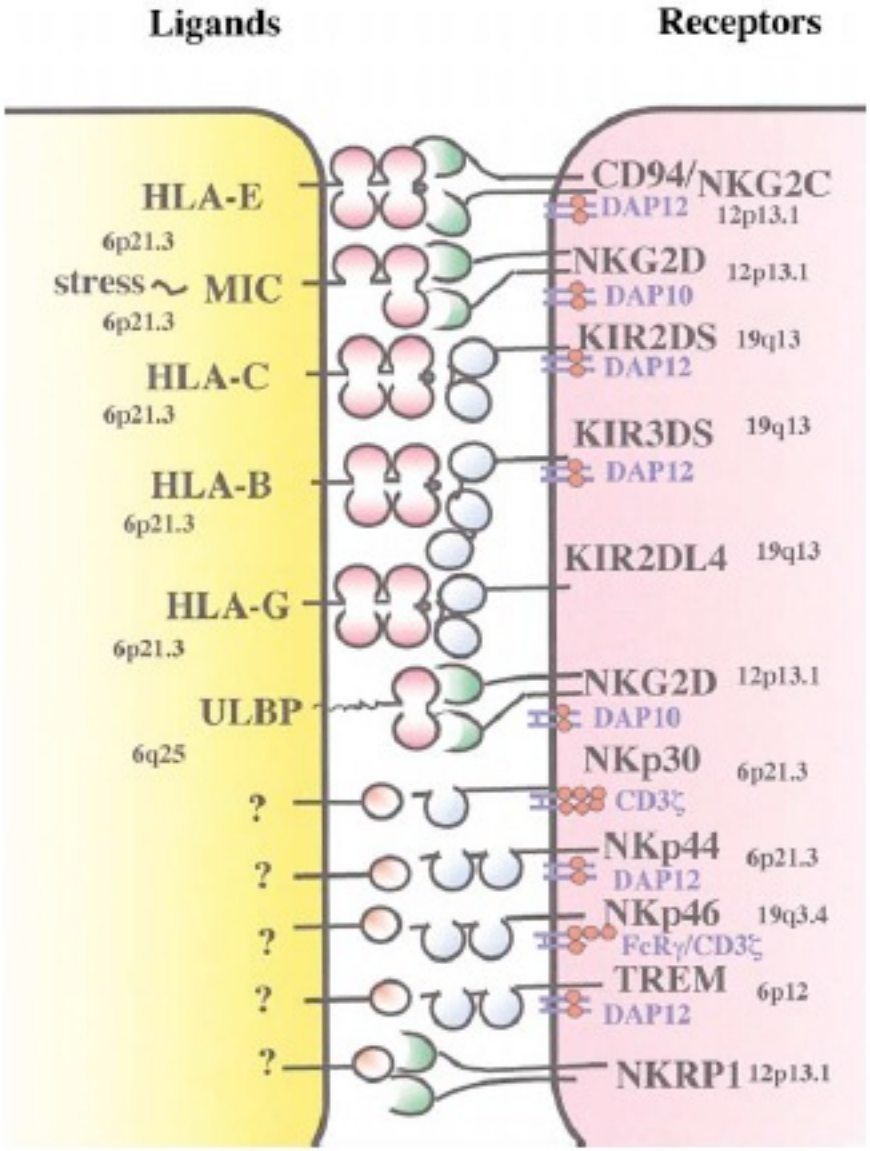

MHC class I on normal cells is recognized by inhibitory receptors that inhibit signals from activating receptors
NK cell
inhibitory receptor
activating receptor
MHC class I
NK cell does not kill the normal cell
NK cell activating ligand


'Altered' or absent MHC class I cannot stimulate a negative signal. The NK cell is triggered by signals from activating receptors
Activated NK cell releases granule contents, inducing apoptosis in the target cell

Activating receptors

Inihibitory receptors

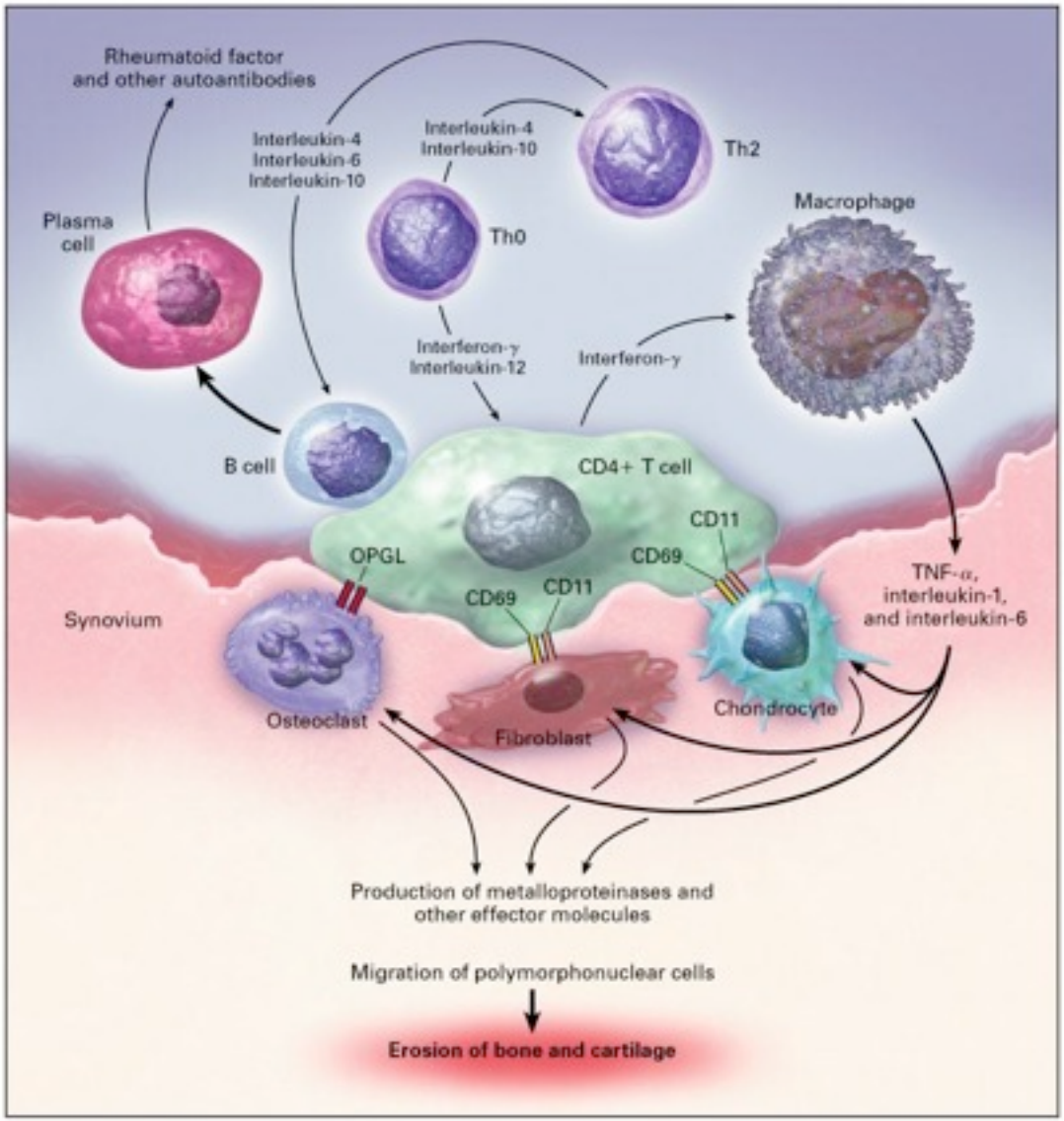




Biological functions of cytokines

1. Innate and adaptive immune responses
2. Haemopoiesis
3. Inflammation
4. Proliferation and differentiation
5. Wound healing

Cytokine Signaling Pathways Involved in Inflammatory Arthritis



Choy E and Panayi G. N Engl J Med 2001;344:907-916

Olsen N and Stein C. N Engl J Med 2004;350:2167-2179

Th1/Th2 in human diseases

- Transplantation rejection and tolerance
- Successful pregnancy and recurrent abortions
- Allergic disorders
- Autoimmune disorders
  - Thyroiditis
  - Multiple sclerosis
  - Type 1 or indulin-dependent diabetes
  - Systemic sclerosis
- Chronic inflammatory gastrointestinal disorders

Chemokines

Mediator of acute inflammation to infections.

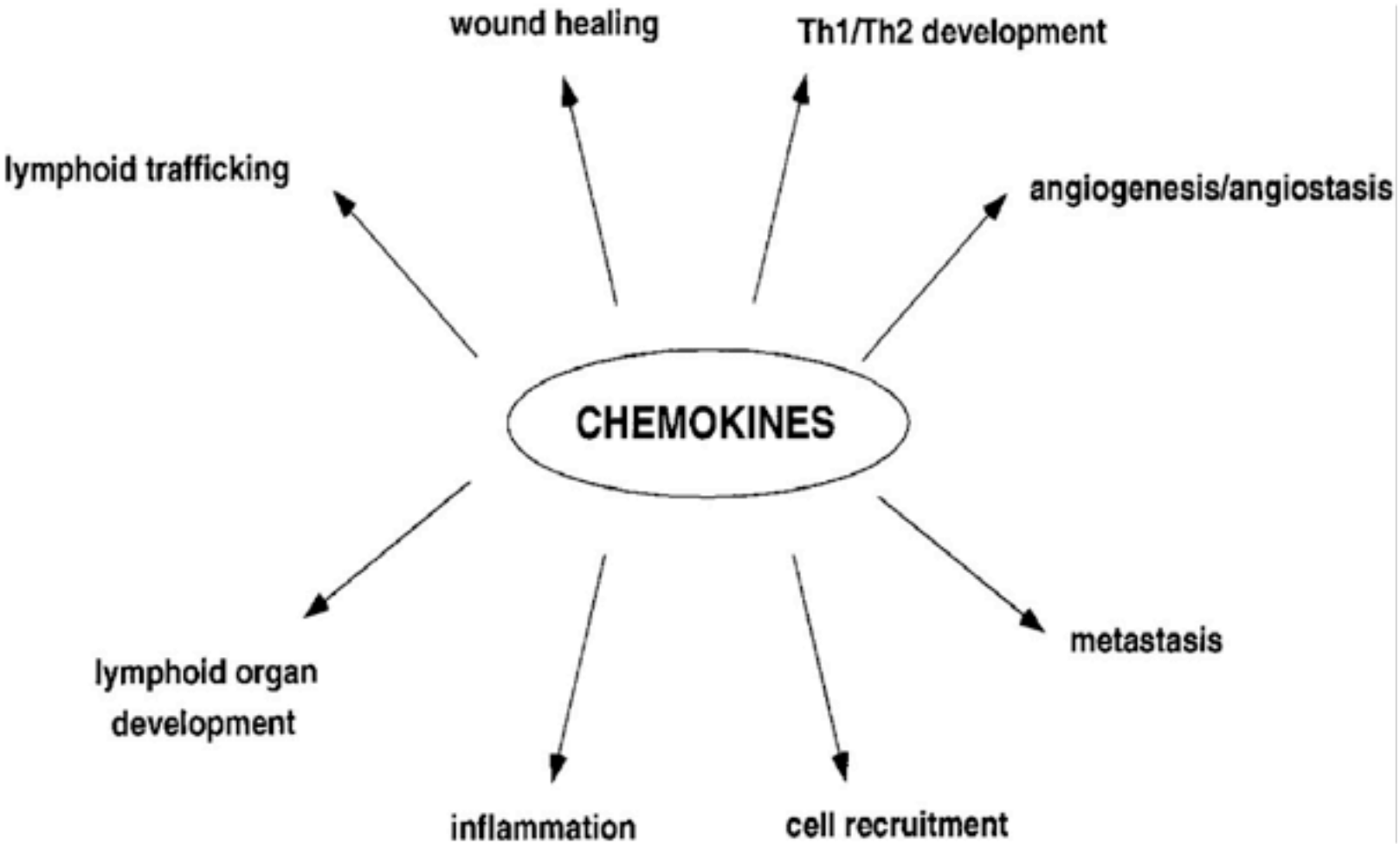
Production:

– Produced by leukocytes, epithelial and endothelial cells, fibroblasts. Induced by microbes, TNF, IL-1, Ag-stimulated T cells. Some constitutive (lymph traffic)

– CC (act on neutrophils) and CXC (monocytes, lymphocytes, eosinophils).

– 10 receptors for CC, 6 for CXC. They are rapidly down regulated by exposure to the chemokine.

Biological effects of chemokines



Summary of chemokine receptors, their ligands and function

Receptor	Ligand	Function
CCR1	RANTES, MIP-1α, MCP-3, HCC-1,-2,-3	Recruitment of monocytes
CCR2	MCP-1,-3,-4	Macrophage migration
CCR3	Eotaxin-1,-2,-3, RANTES, MCP-2,-3,-4	Parasitic defense
CCR4	MDC, TARC	Skin homing
CCR5	MIP-1α, MIP-1β, RANTES	Macrophage and memory T cell migration
CCR6	MIP-3α	Dendritic cell migration
CCR7	MIP-3β, 6CKine	Lymphoid tissue homing
CCR8	TARC, I-309	Monocyte migration
CCR9	TECK	Gut homing
CCR10	CTACK	Skin homing
CXCR1	IL8, GCP-2, ENA-78	Monocyte and neutrophil migration
CXCR2	IL8, GCP-2, ENA-78, NAP-2	Neutrophil migration
CXCR3	MIG, IP-10, I-TAC	Effector T cell migration
CXCR4	SDF-1α, SDF-1β	Naïve T cell and B cell migration
CXCR5	BLC/BCA-1	B cell migration
CXCR6	CXCL16	DC-T cells interactions
CX_3CR1	Fractalkine	Monocyte migration
XCR1	Lymphotactin, SCM-1β	Unknown