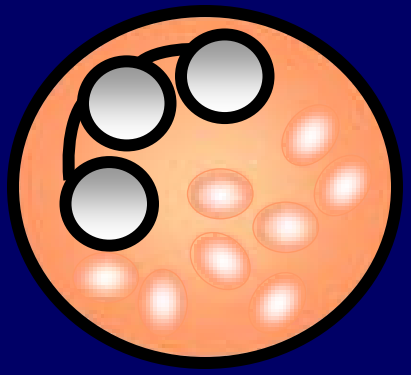
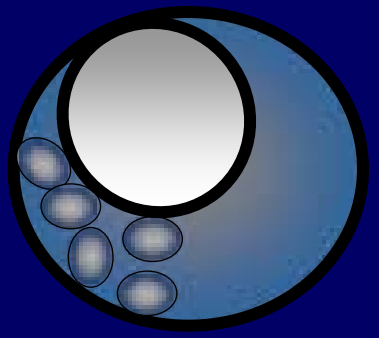
Cells of **innate** immunity

PMN



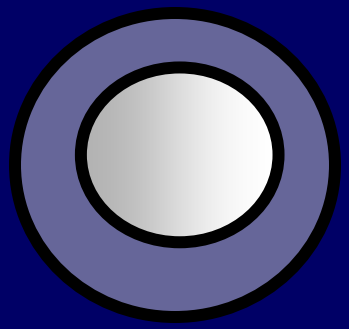
Macrophage

NK



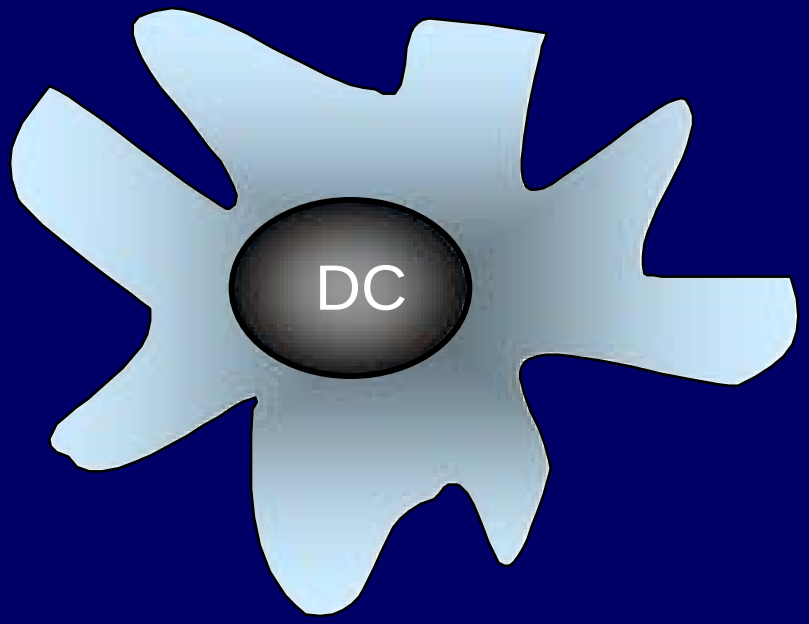
Cells of **acquired** immunity

Lymphocyte

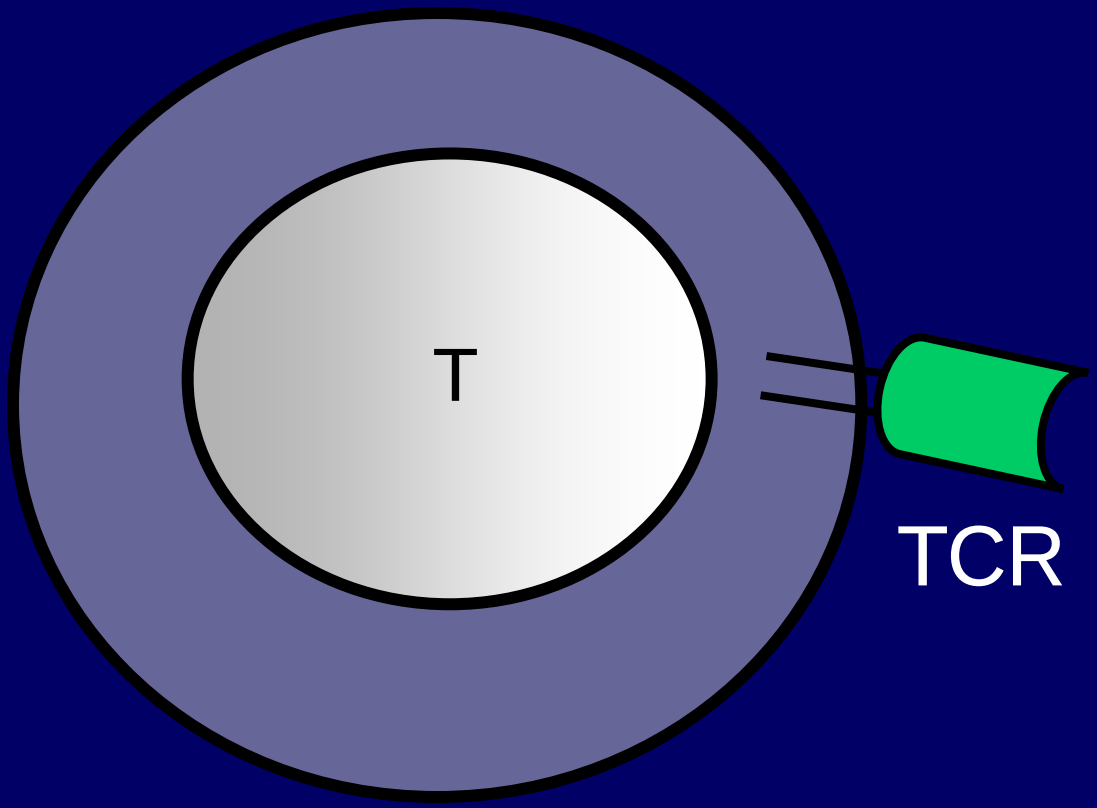


T cell CD4+, CD8+
B cells

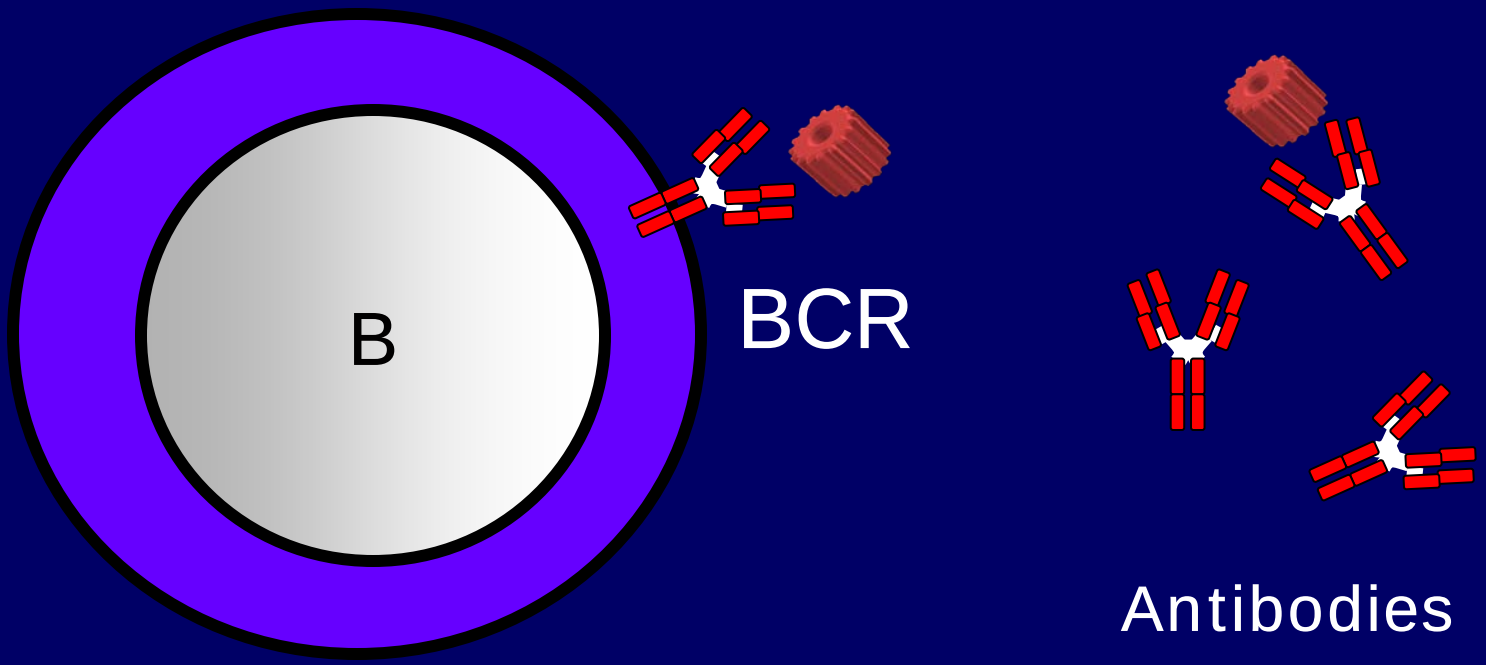
Dendritic cell



T cell

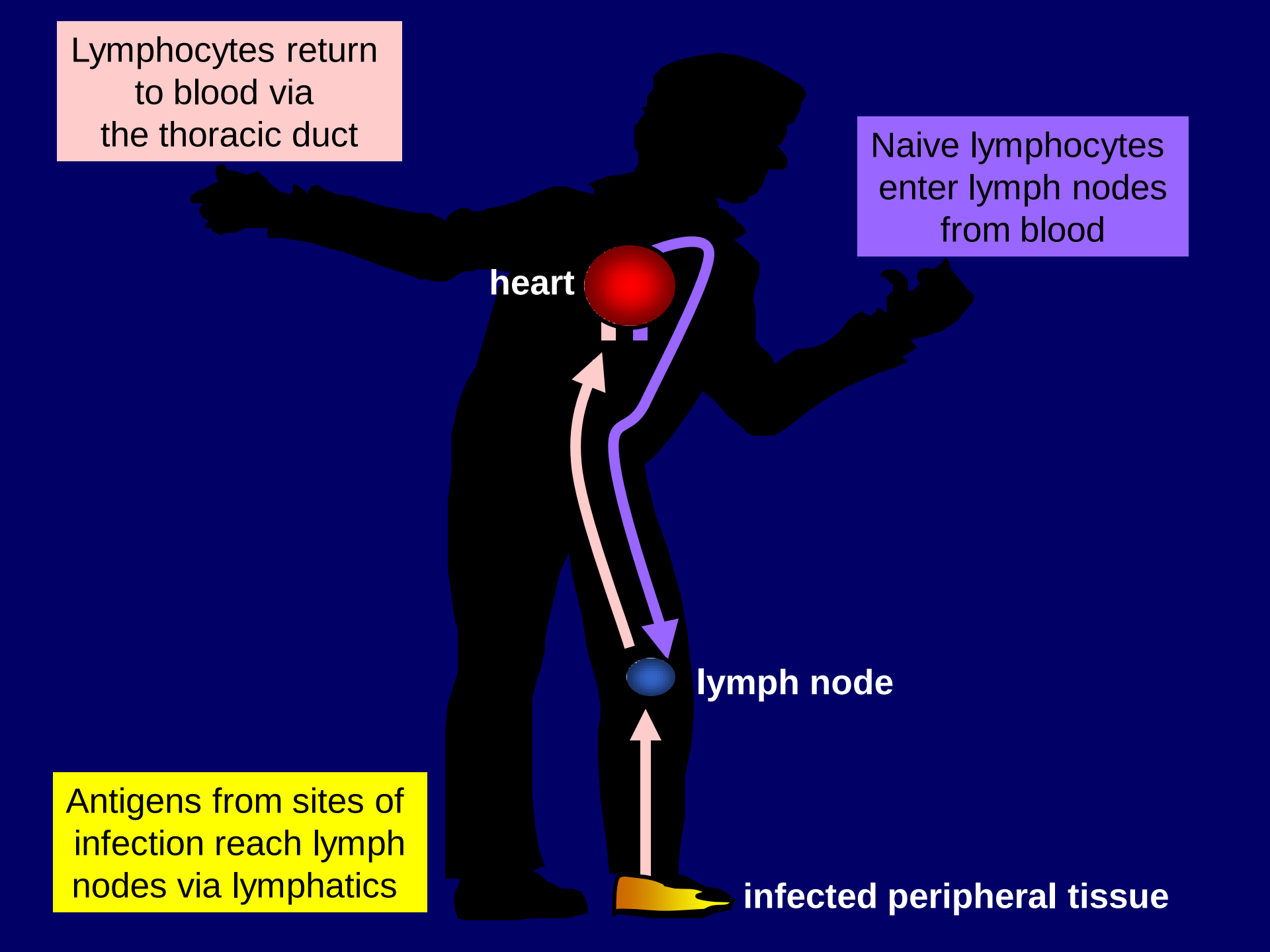


B cell

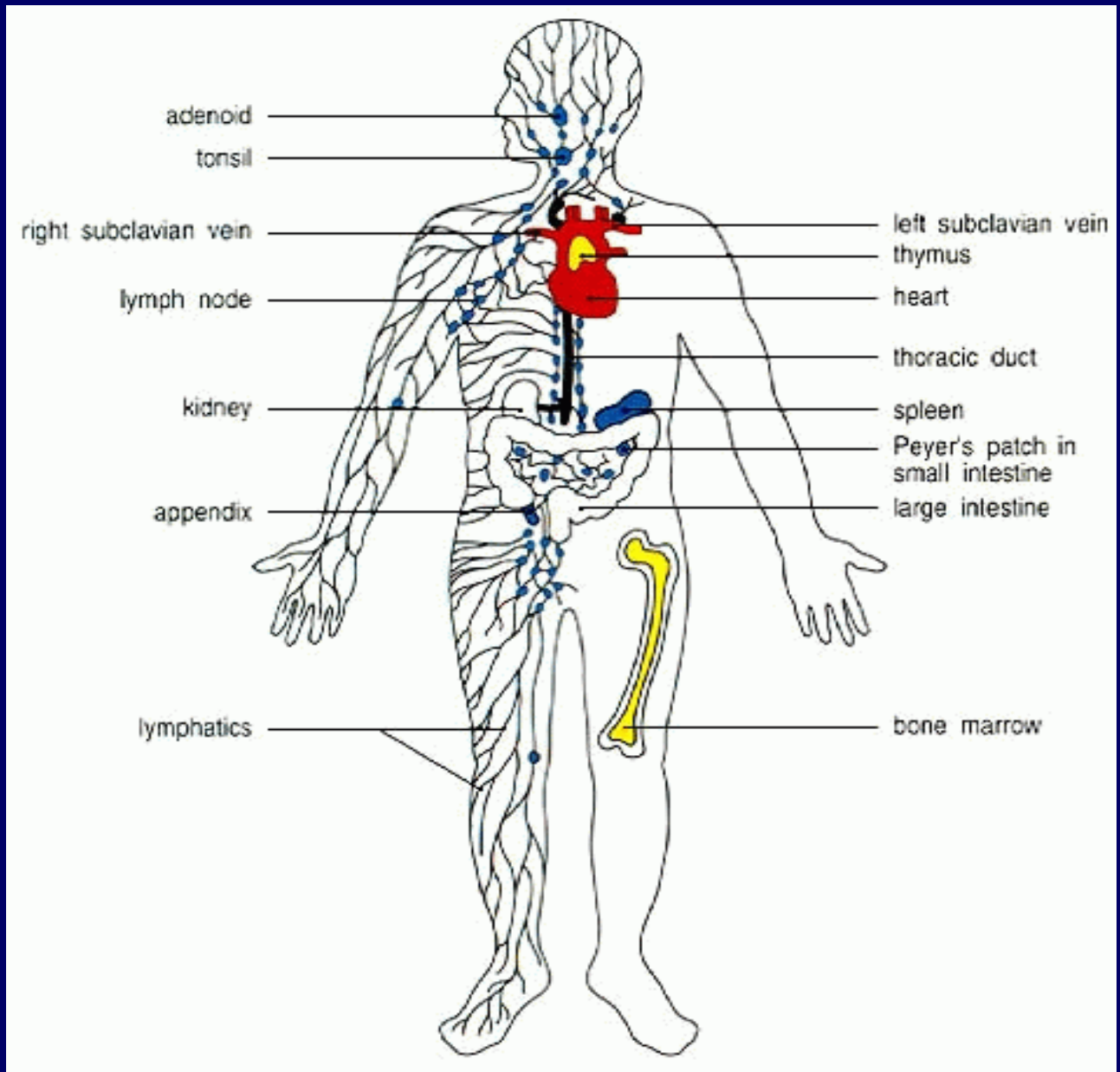


Locations of immune cells

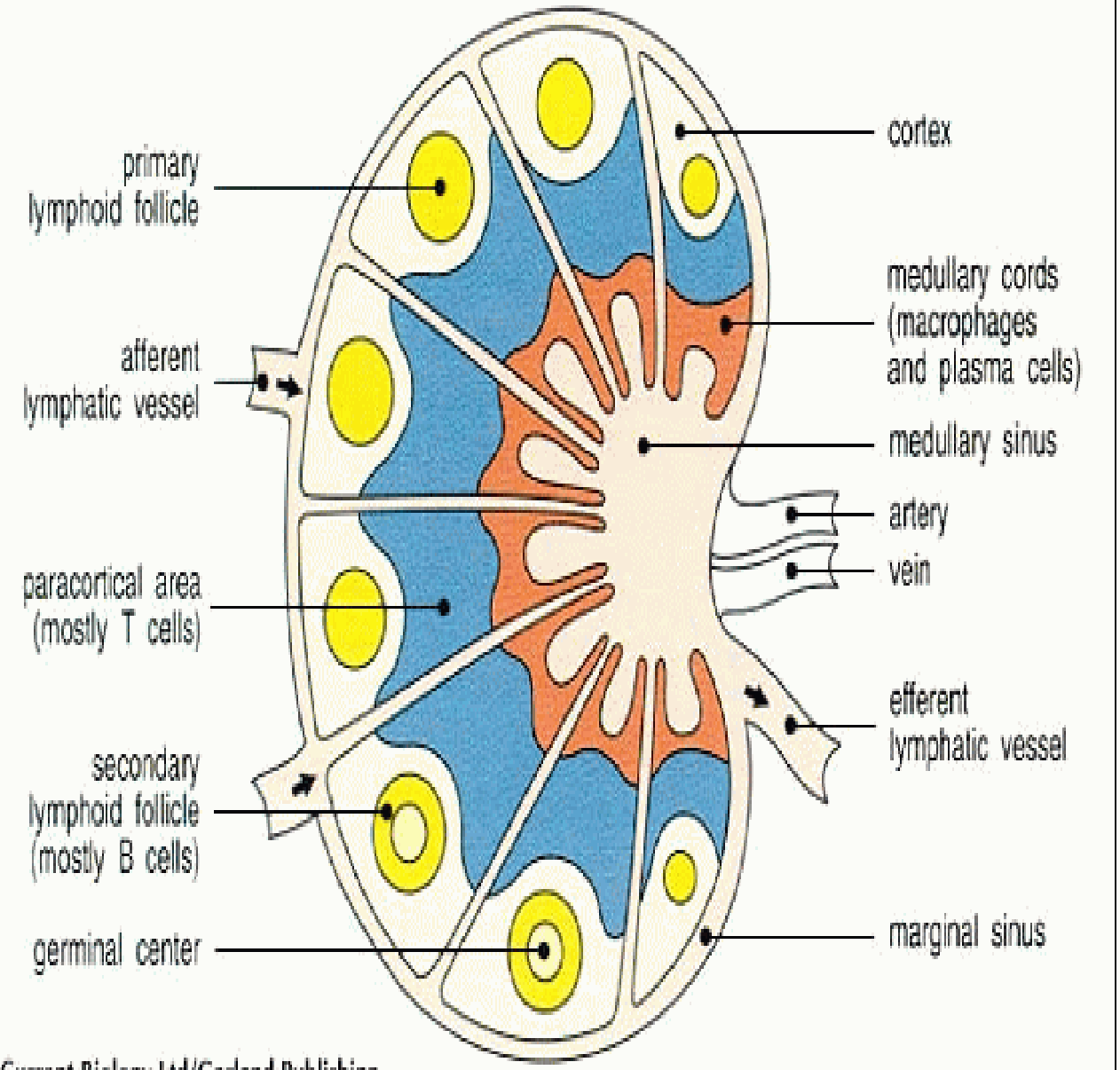
- Blood and lymph
- Defined collections in lymphoid organs
- On the periphery


Lymphocytes return to blood via the thoracic duct
Naive lymphocytes enter lymph nodes from blood
heart
lymph node
Antigens from sites of infection reach lymph nodes via lymphatics
infected peripheral tissue

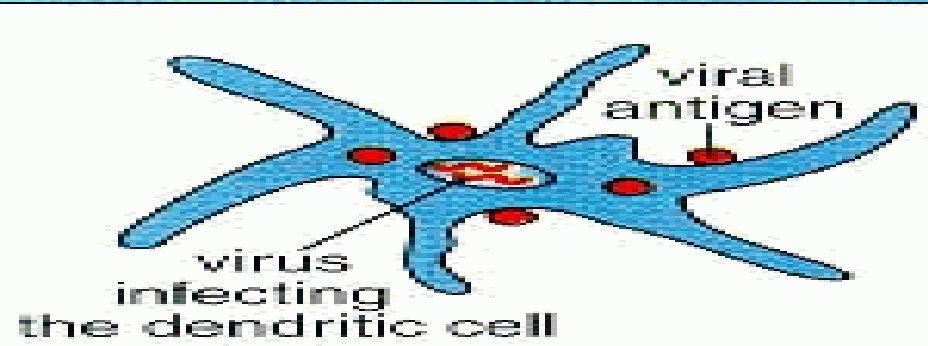
Human lymphoid organs

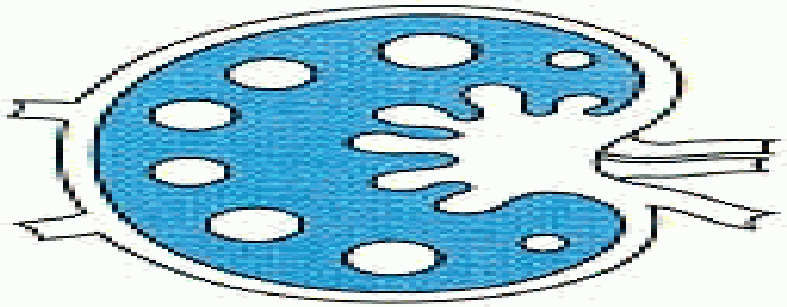


The lymph node

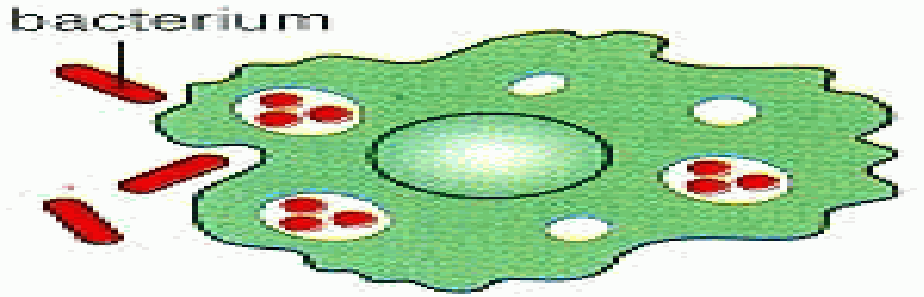


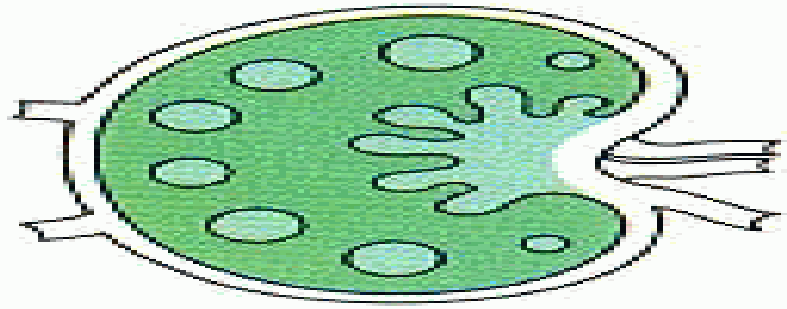
Dendritic cells (interdigitating reticular cells)



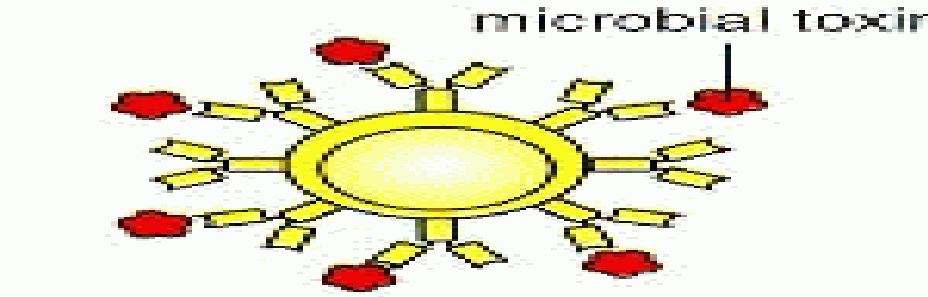


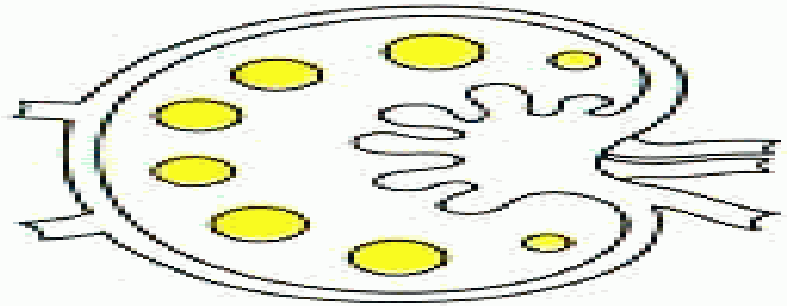
Macrophages



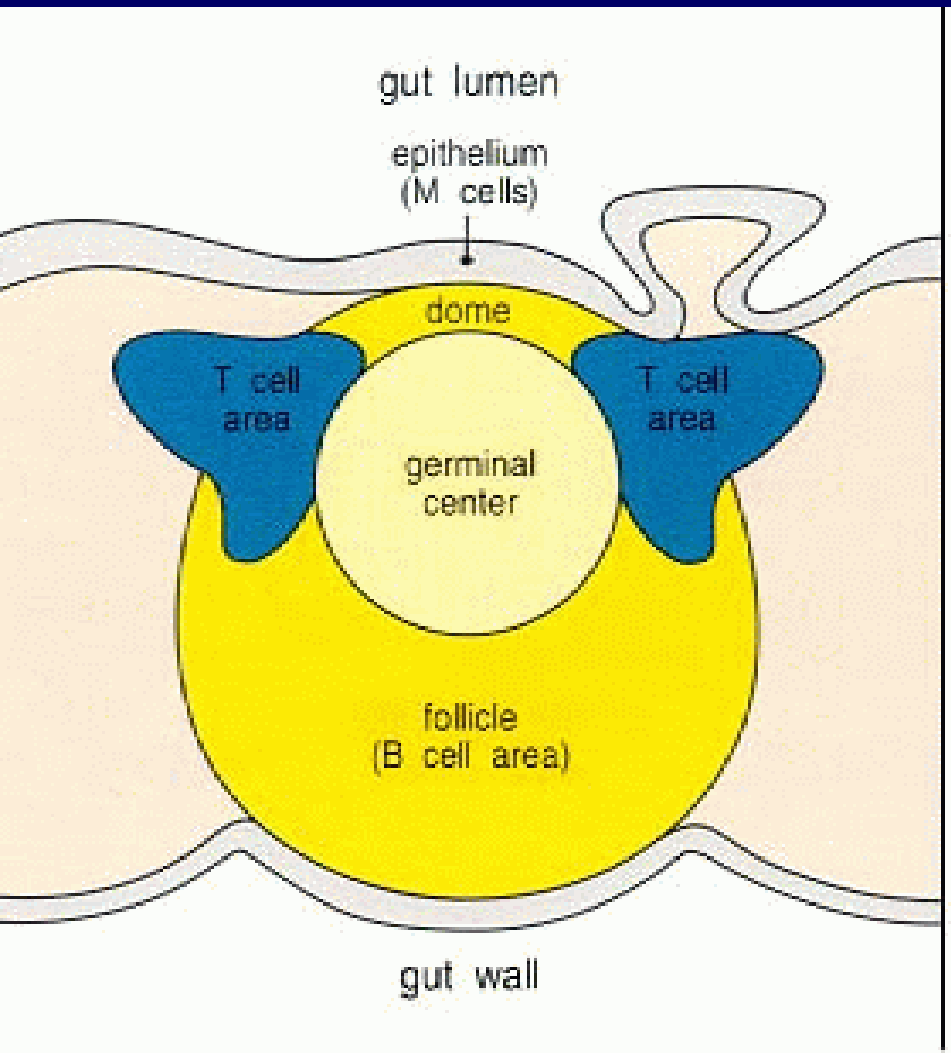


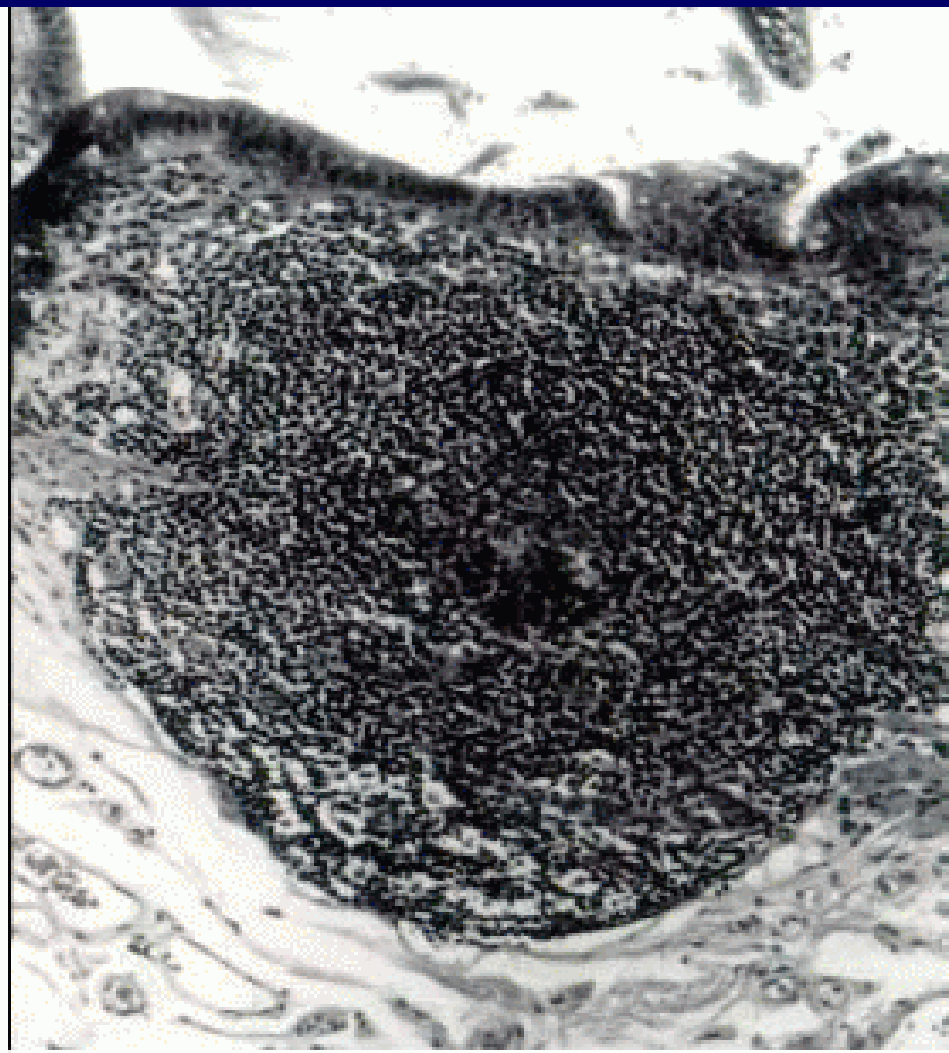
B cells



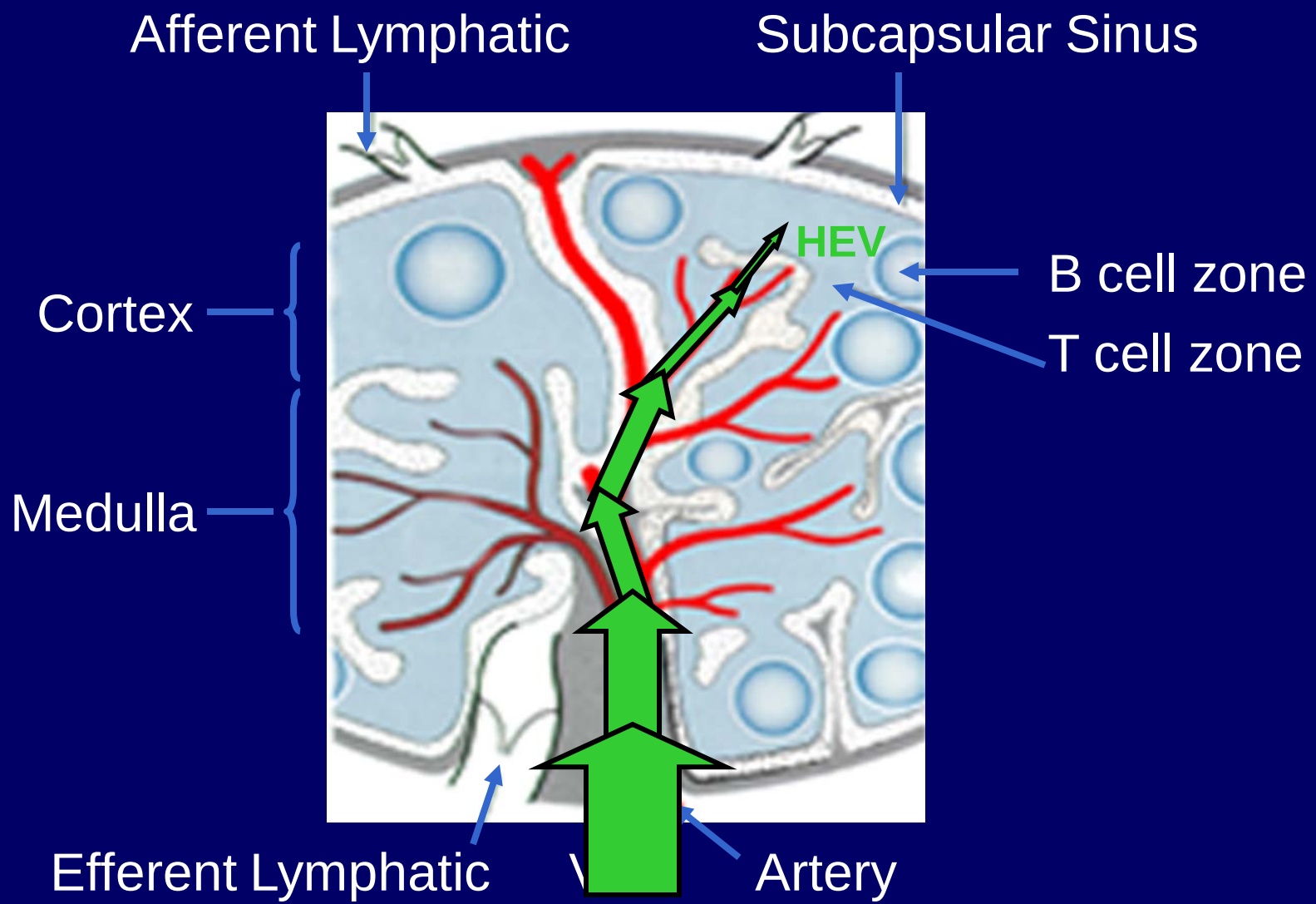


Typical gut-associated lymphoid tissue in schematic and light microscopic.



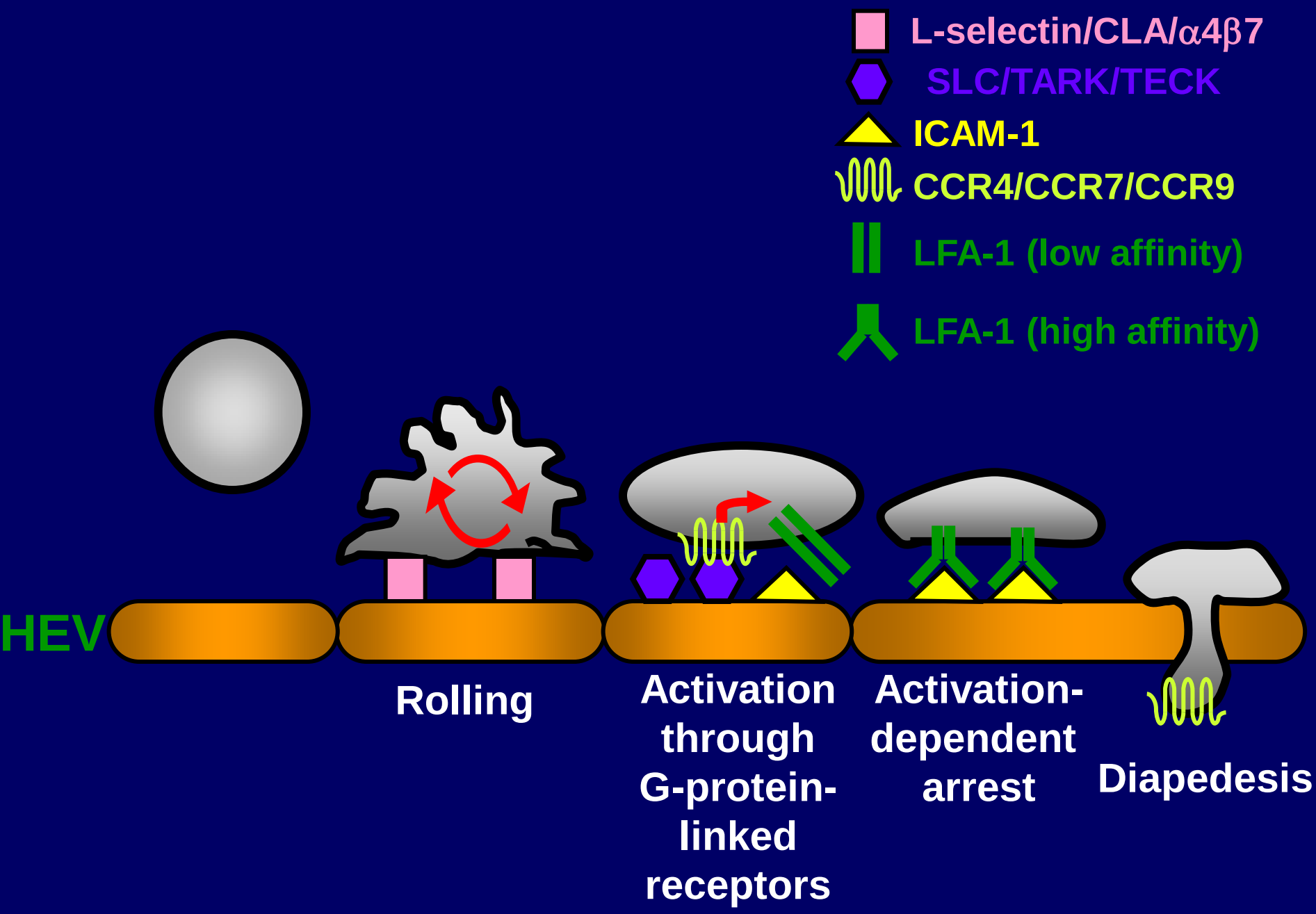


Lymphocytes enter PLN via blood

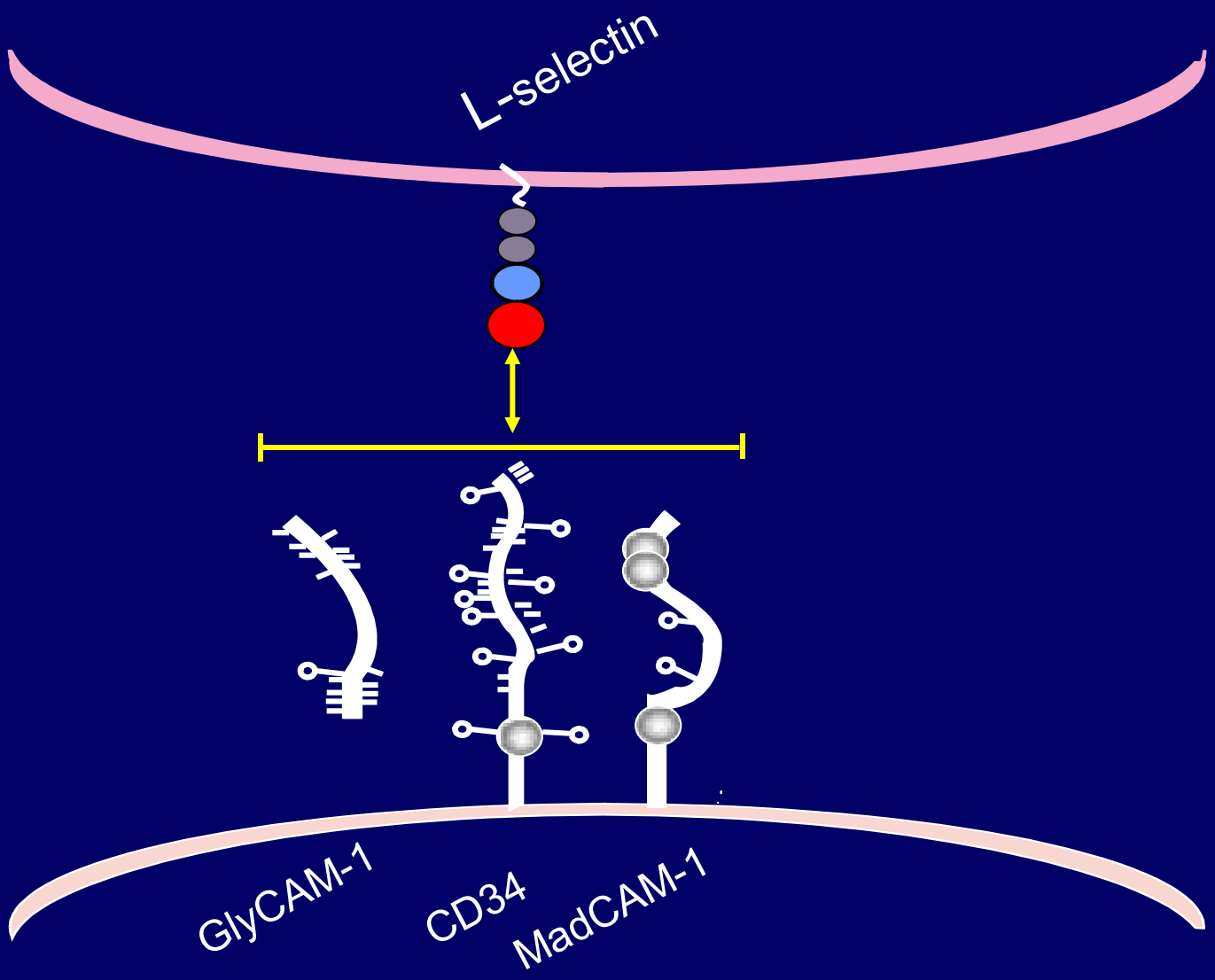


Homing to Peripheral Lymph Nodes (PLN)

- Step 1: Rolling via L-selectin (CD62L): PNAd interaction
- Step 2: Activation via G-protein-coupled receptor (ChR)
- Step 3: Sticking via CD11a/CD18 (LFA-1)


L-selectin/CLA/α4β7
SLC/TARK/TECK
ICAM-1
CCR4/CCR7/CCR9
LFA-1 (low affinity)
LFA-1 (high affinity)
HEV
Rolling
Activation through G-protein-linked receptors
Activation-dependent arrest
Diapedesis

Some Selectin Ligands



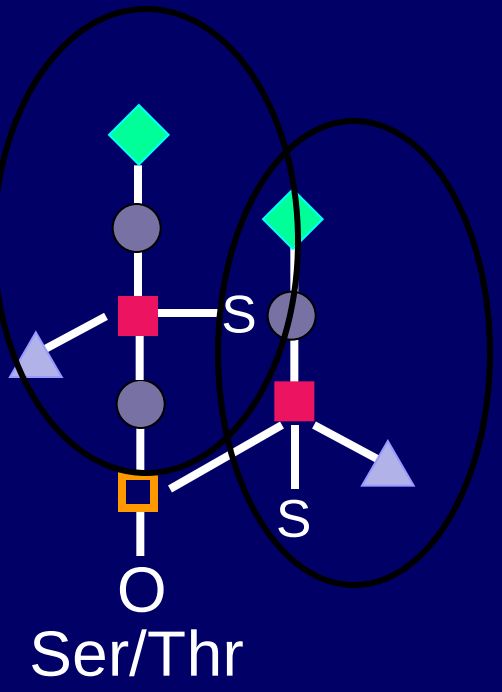
L selectin ligands on PLN HEV

- CD34 (mouse and human)
- GlyCAM-1 (mouse)
- Podocalyxin (human)
- Endomucin (mouse and human)

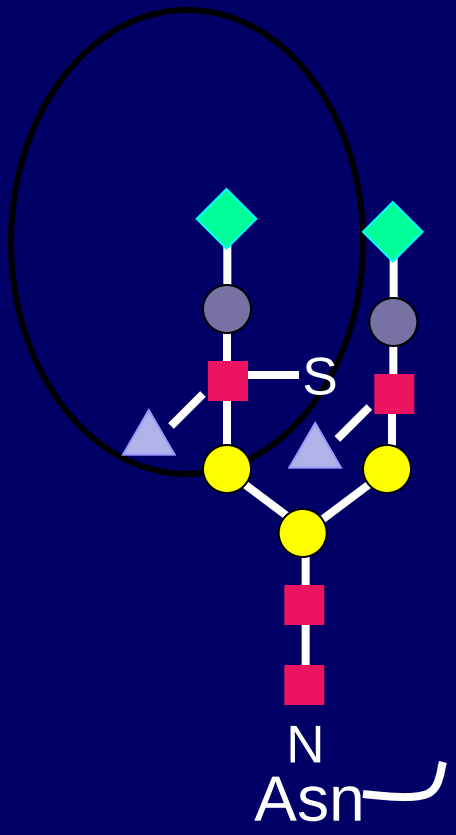
Sialomucins (glycoproteins with multiple O-linked glycans)

O-glycans and N-glycans decorate CD34

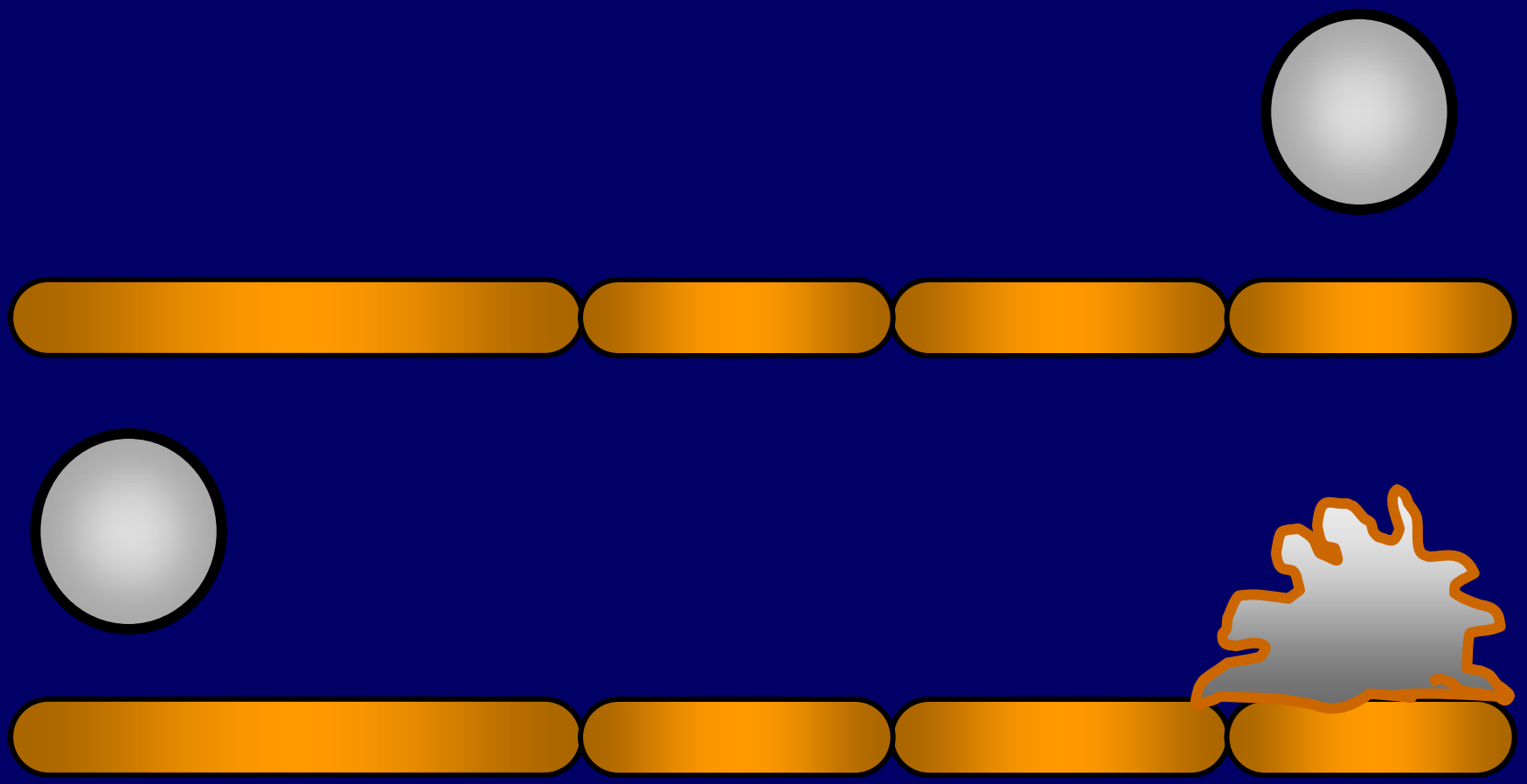
6-sulfo sLe^X on *O*-glycan



6-sulfo sLe^X on *N*-glycan



Rolling



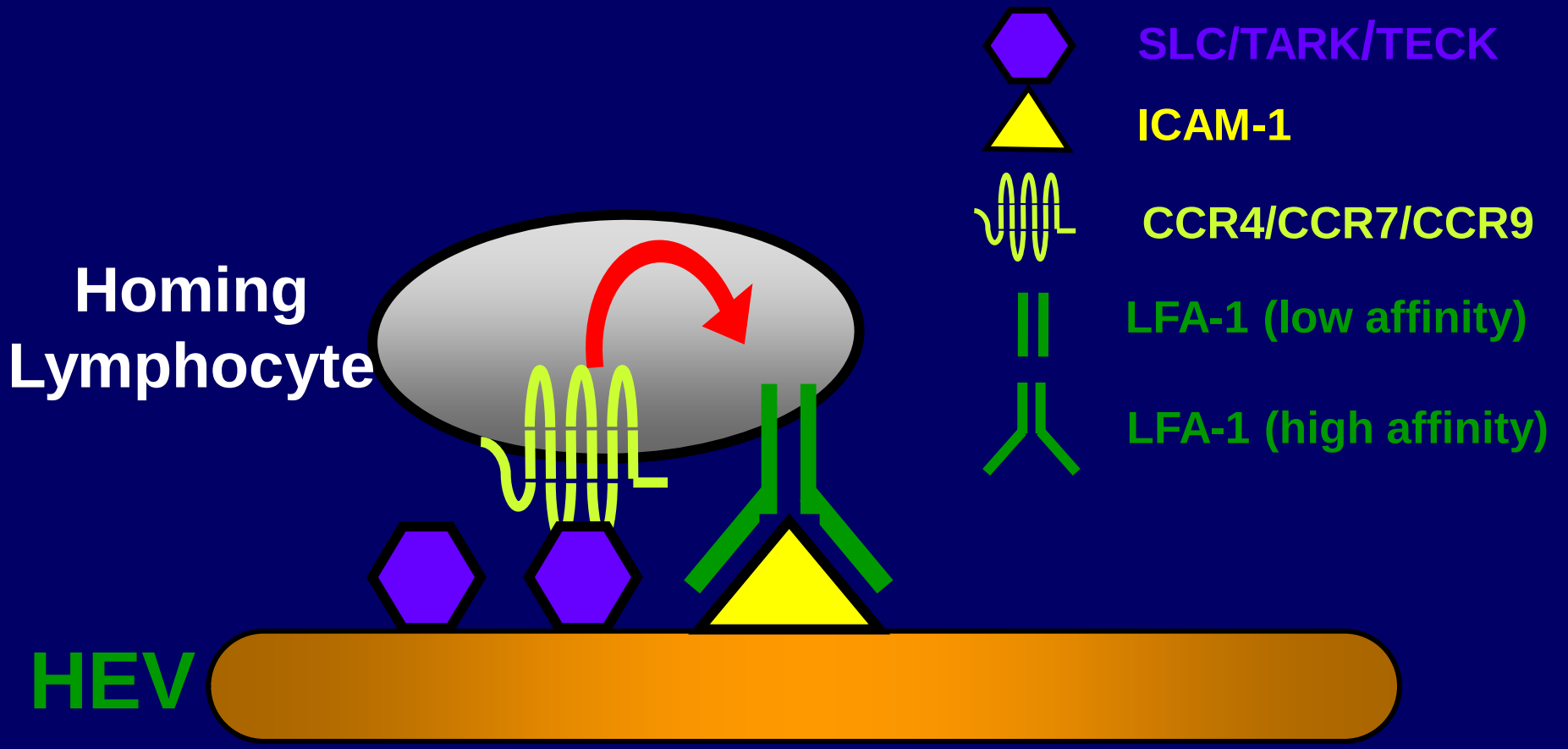
Chemokines

CC	MCP-1, 2, 3, 4	Monocyte chemotactic peptide 1, 2, 3, 4
	RANTES	Regulated on activation, normal T cell expressed and secreted
	MIP-1α, -1β	Macrophage inflammatory protein 1α, 1β
	Eotaxin	Eosinophil chemoattractant protein
	I309	Intercrine-β glycoprotein 309
	TARC	Thymus and activation-regulated chemokine
	MDC	Macrophage-derived chemokine
	LARC	Liver and activation-regulated chemokine
	ELC	EBL1-ligand chemokine
	SLC (CCL21)	Secondary lymphoid tissue chemokine

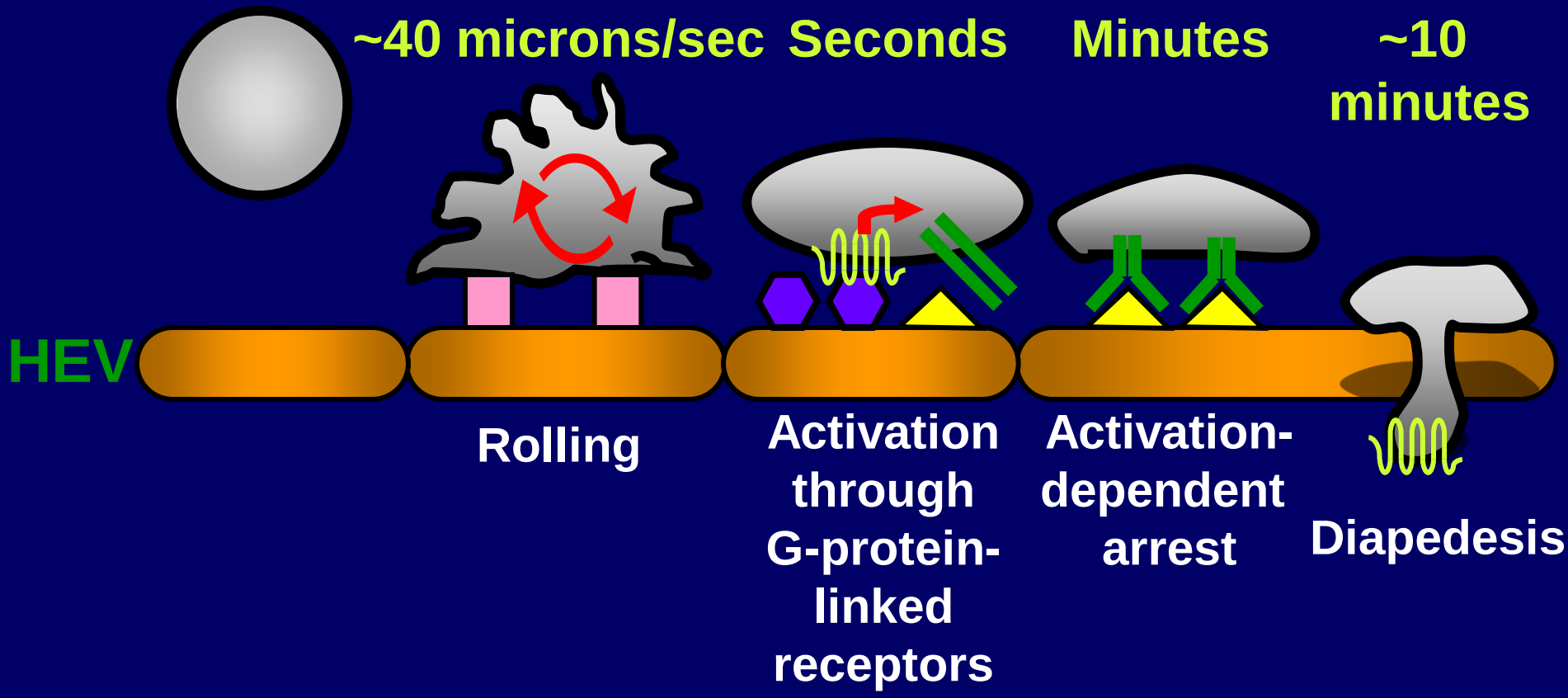
Chemokines

CXC	IL-8	Interleukin-8
	GRO α, β, γ	Growth releated protein α, β, γ
	NAP-2	Neutrophil-activating peptide 2
	ENA-78	Epithelial cell-derived neutrophil-activating peptide 78
	GCP-1	Granulocyte chemotactic protein 2
	IP-10	IFNγ–inducible 10 kDa protein
	MIG	Monocyte/Mac activating IFNγ–inducible protein
	I-TAC	IFNγ–inducible, T cell activating α chemokine
	SDF-1	Stromal cell-derived factor 1
	BCA-1 (CXCL13)	B cell-attracting chemokine 1

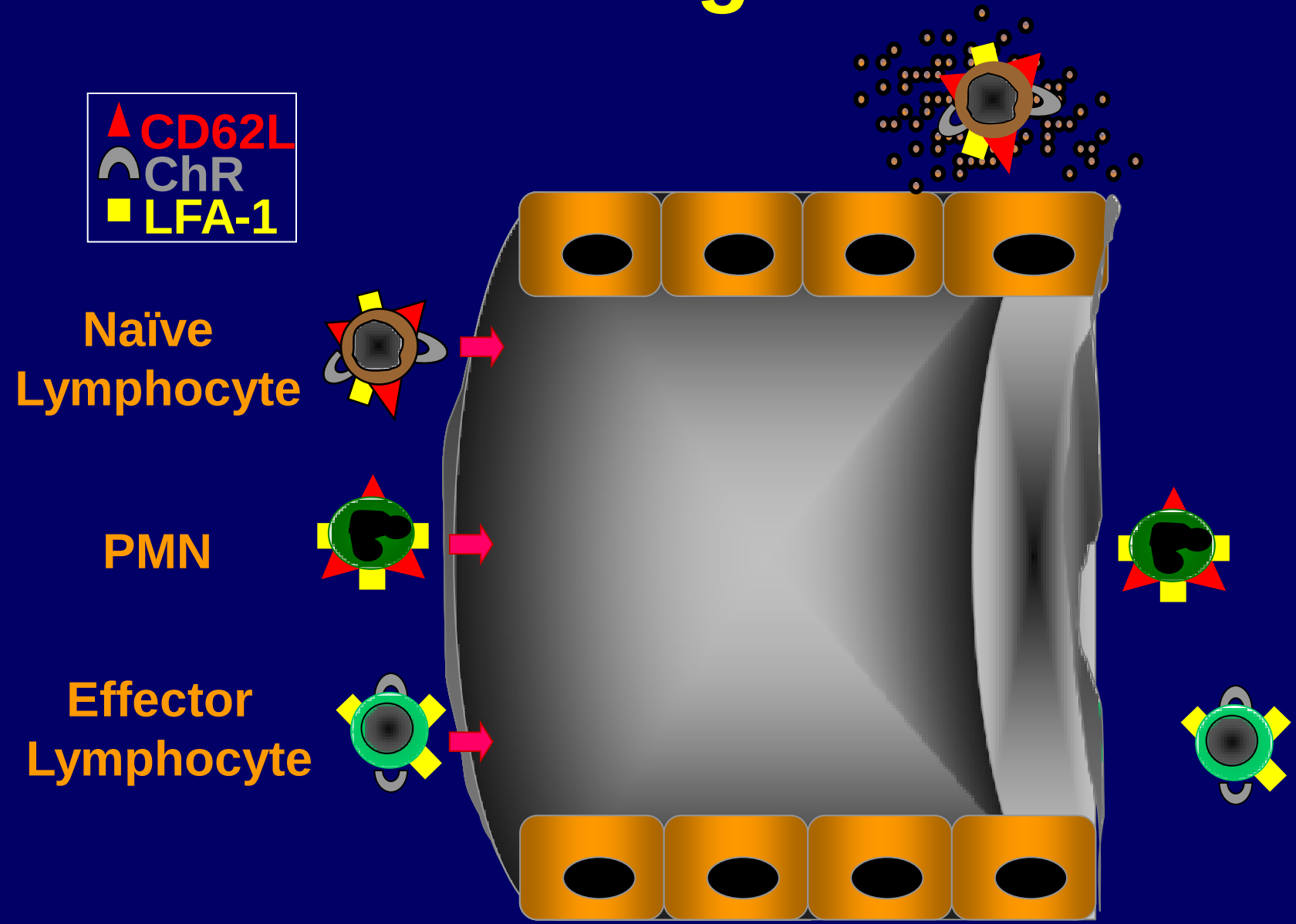
Activation through **G-protein-linked receptor** results in transition of **LFA-1** from low to high affinity state



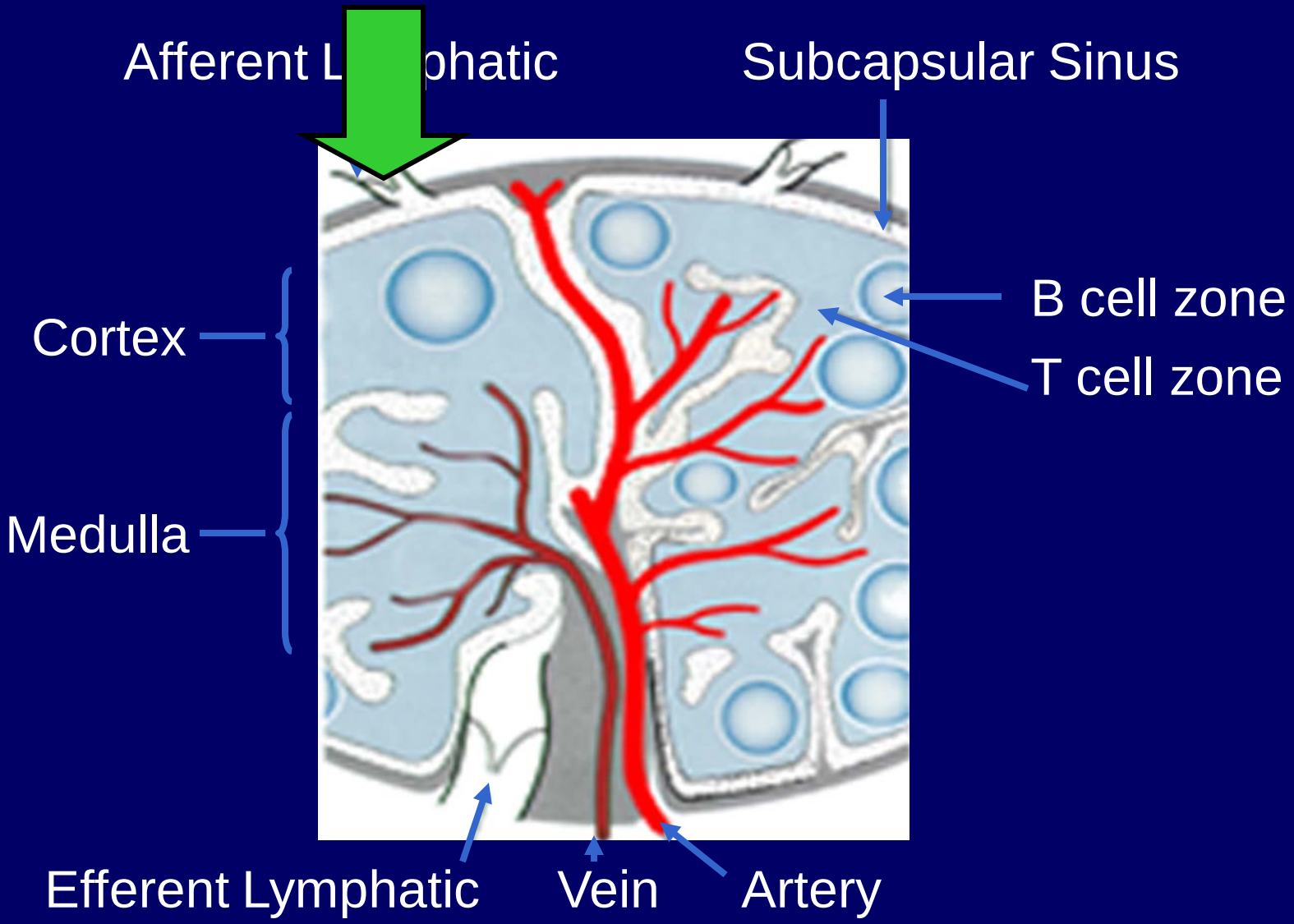
The speed and timescale of lymphocytes traversing HEVs from the blood

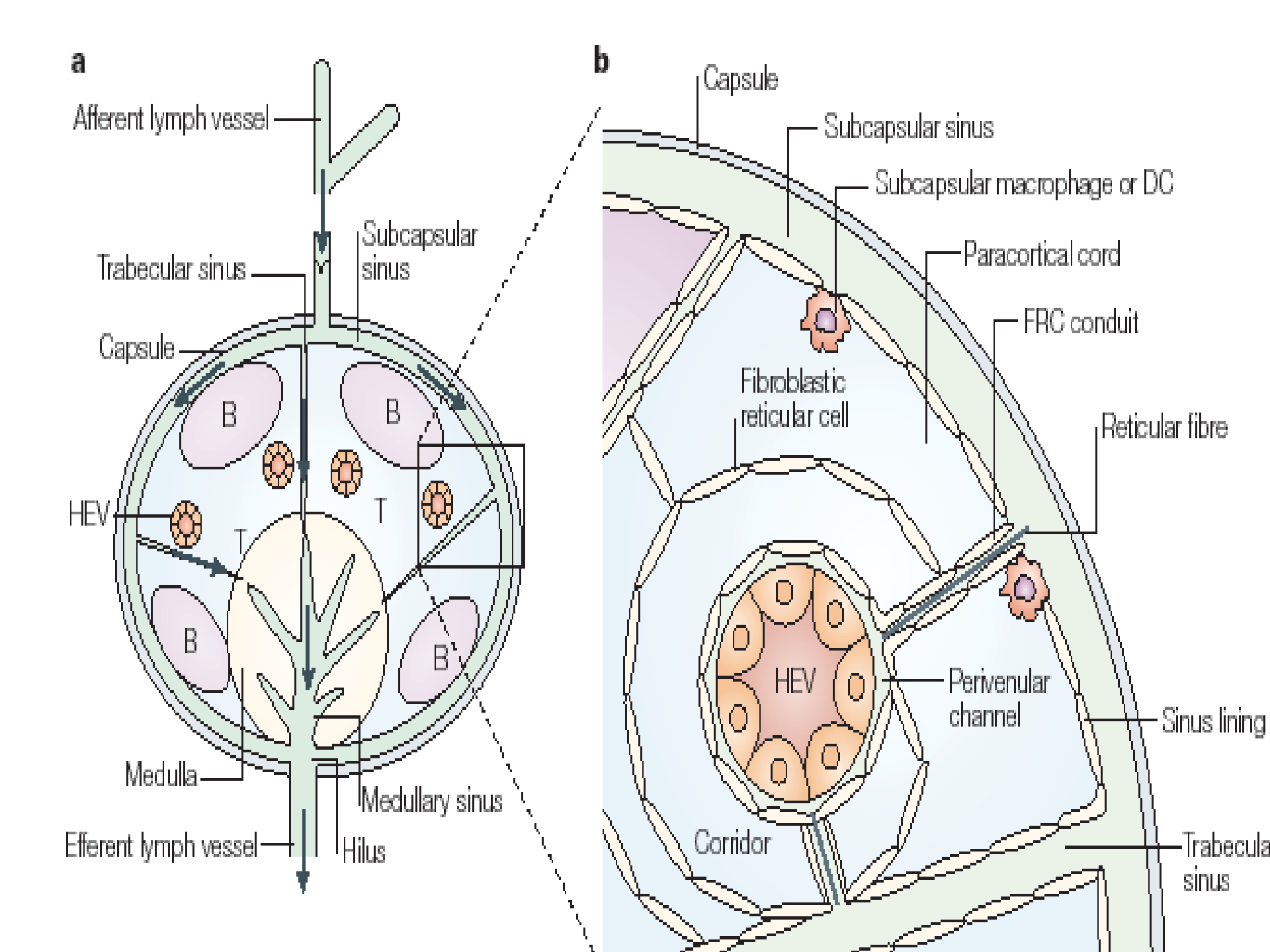


Homing to PLN

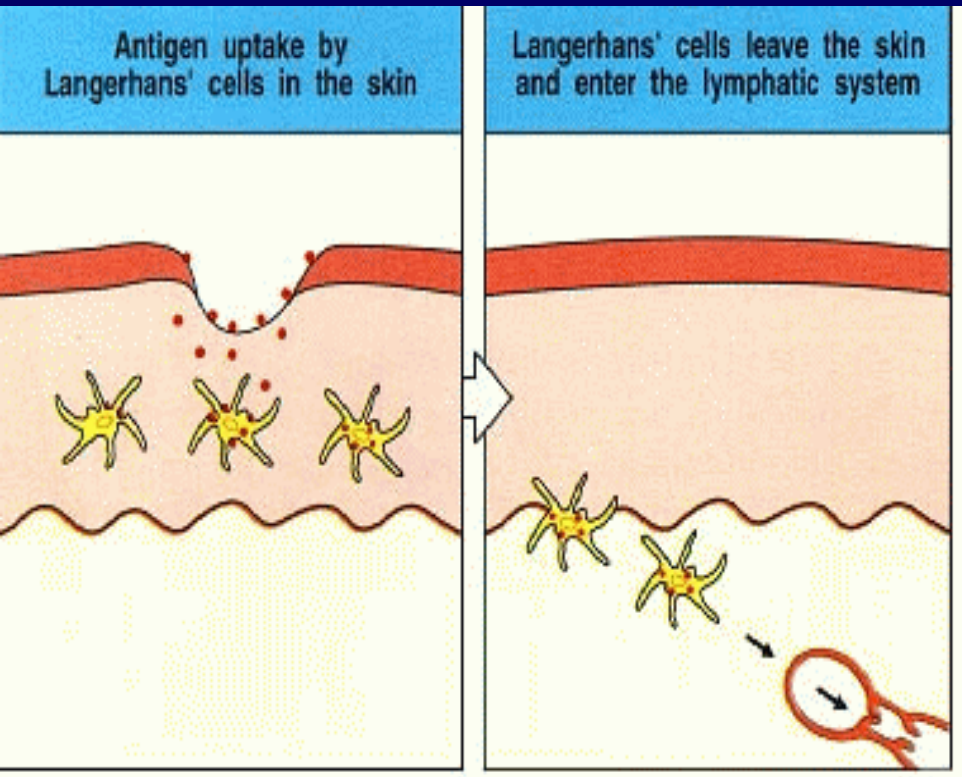


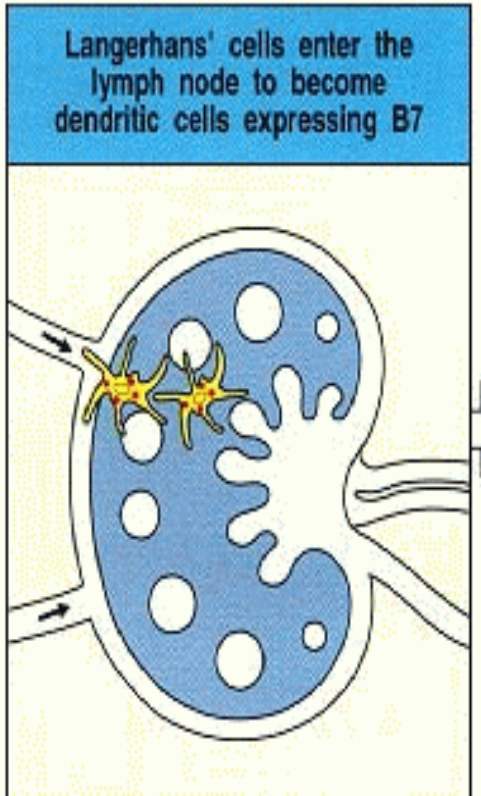
Antigens enter PLN via lymph

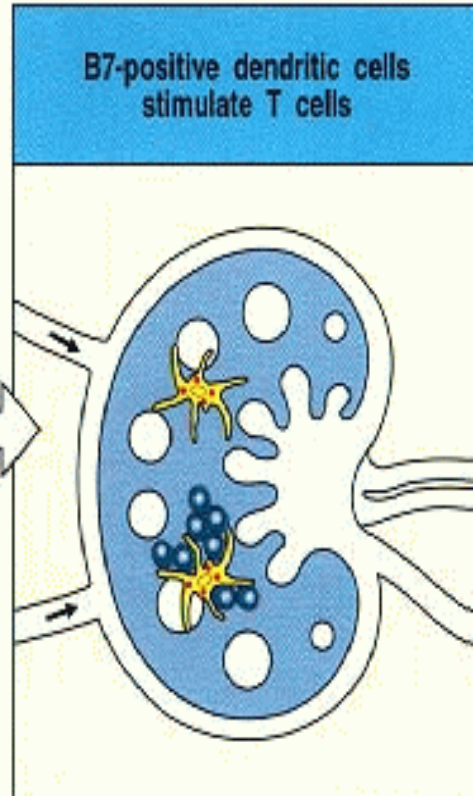



a
Afferent lymph vessel
Subcapsular sinus
Trabecular sinus
Capsule
B
B
T
T
HEV
B
B'
Medulla
Medullary sinus
Efferent lymph vessel
Hilus
b
Capsule
Subcapsular sinus
Subcapsular macrophage or DC
Paracortical cord
FRC conduit
Fibroblastic reticular cell
Reticular fibre
HEV
Perivenular channel
Sinus lining
Corridor
Trabecula sinus

Langerhans' cells can take up antigen in the skin and migrate to lymphoid organs where they present it to T cells



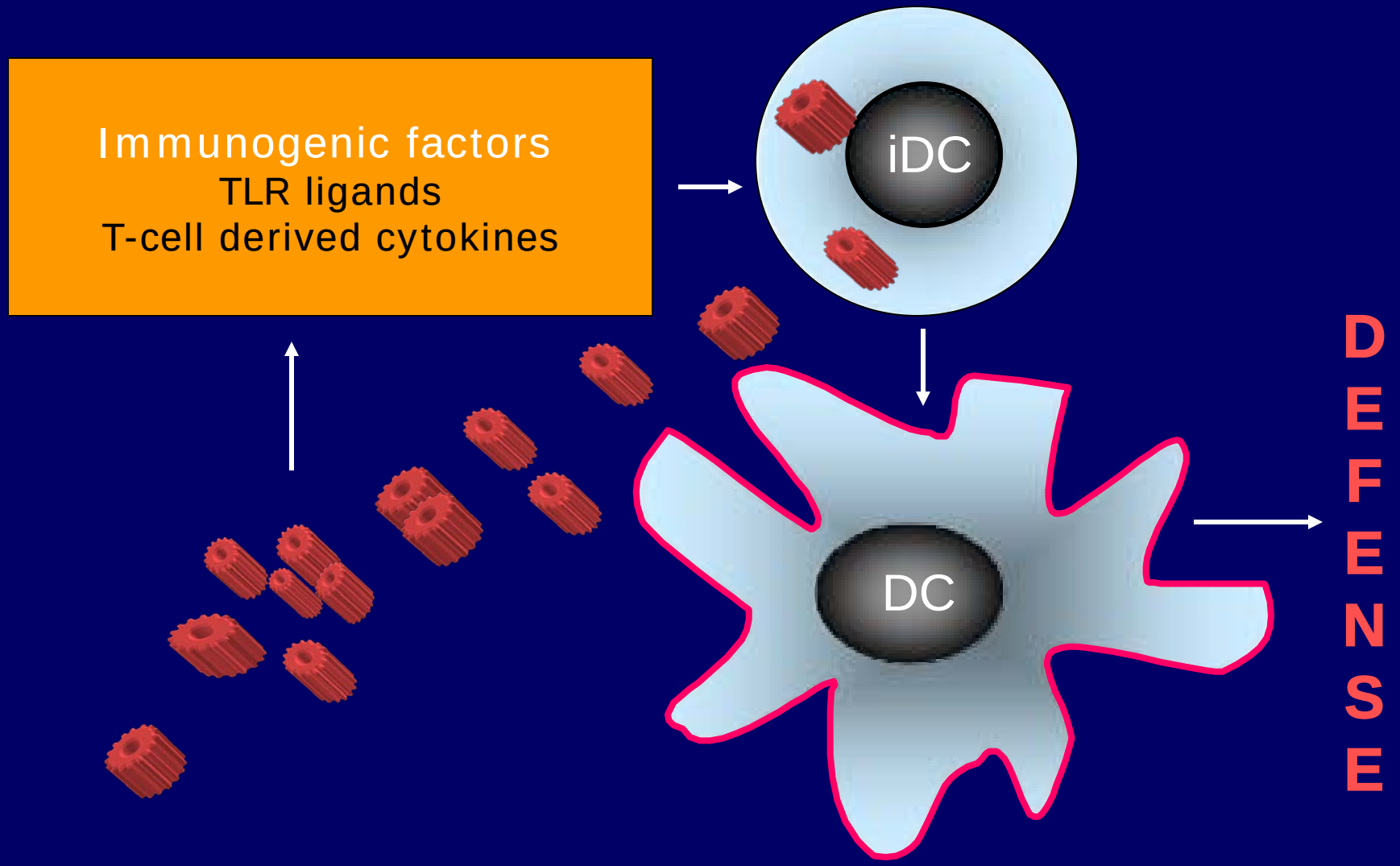




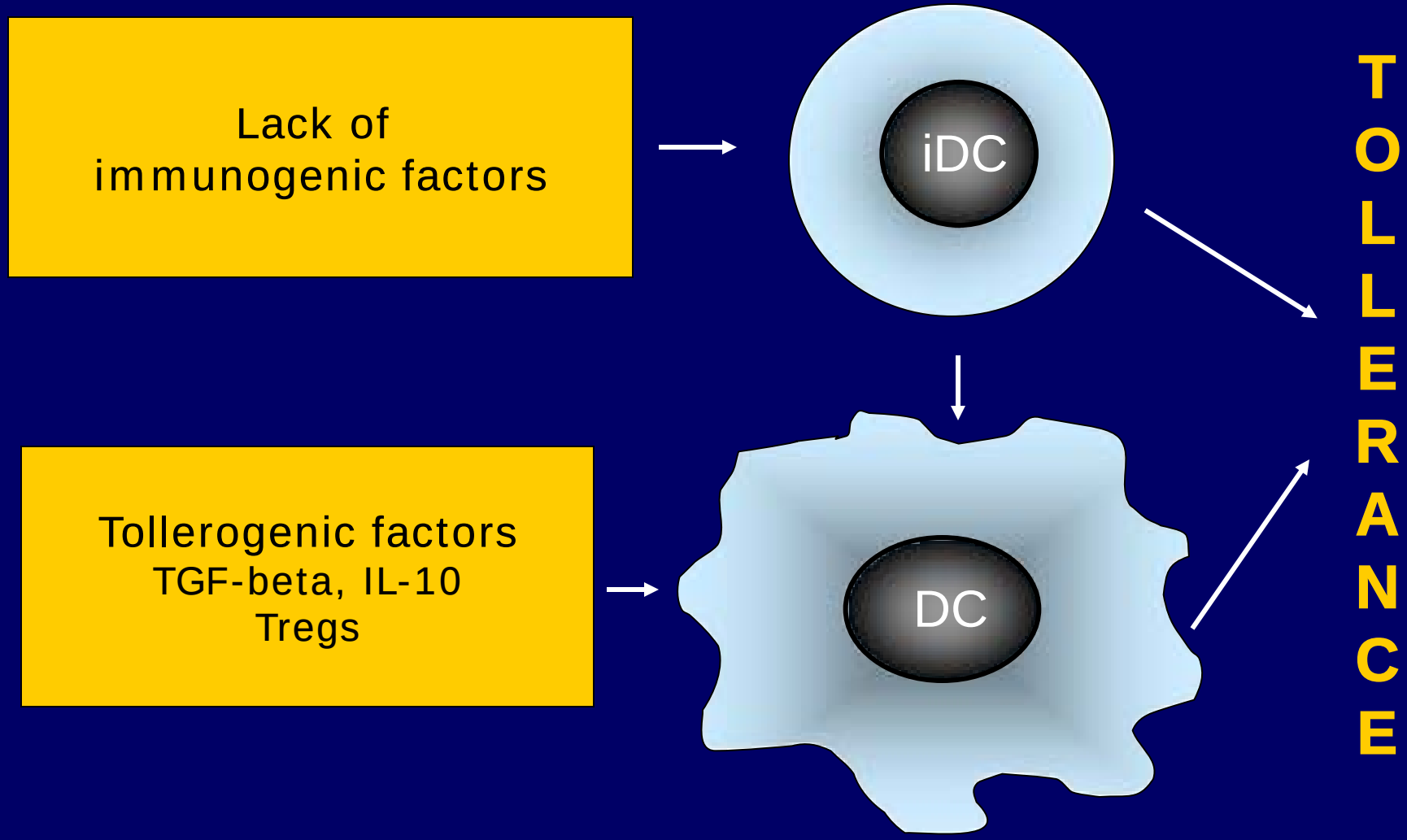
Dendritic cells (DC)

- **Human blood**
  - Myeloid DC $CD11c^{+}$ DC
  - Plasmacytoid DC $CD11c^{-}$, $CD123^{+}$ DC

DC in immune responses



DC in immune tollerance



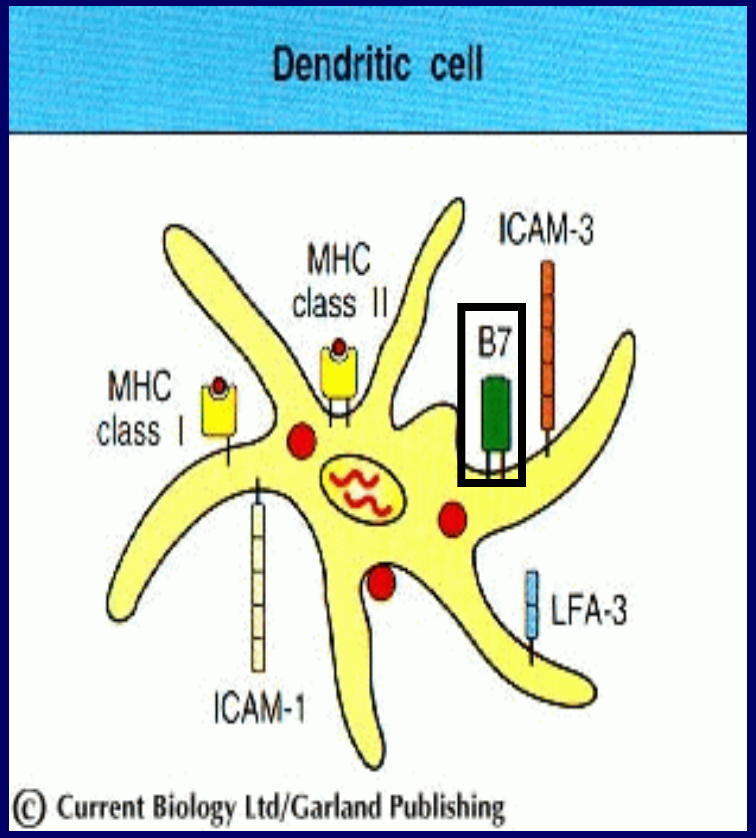
Maturation of DC

- Antigen processing by lowering the pH of endocytic vacuoles, activating proteolysis and transporting peptide-MHC complexes on the cell surface
- Remodeling cell surface (co-stimulatory molecules B7, TNF, Notch)

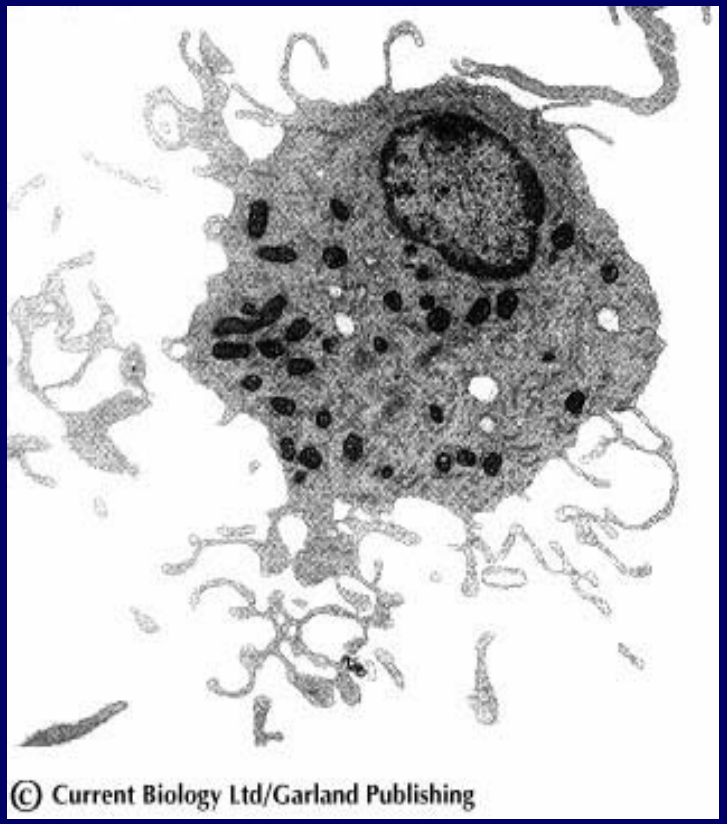
Some stimuli for DC maturation

- Microbial products (Toll-like)
- Lymphocytes, NK, neutrophils (CD40)
- Cytokines (TNF, interferons, TLSP)
- Endogenous ligands (uric acid)
- Immune complexes (FcR)

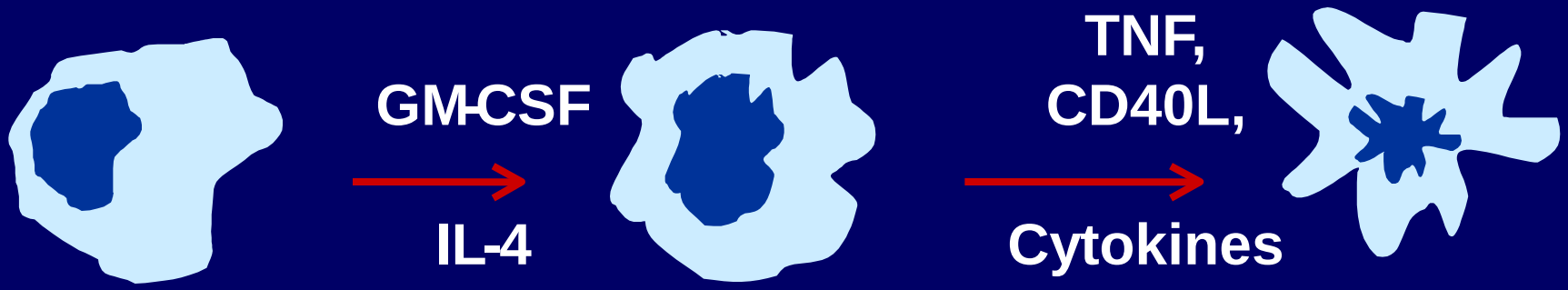
Dendritic cells are highly efficient inducers of T-cell activation



Dendritic cells in lymphoid tissue have high levels of co-stimulatory activity



Cytokine-Driven Differentiation of Human Monocyte Into Mature DC



Precursor

HLA-DR^{low}
CD86^{low}
P55, CD83^{low}
CD1a^{low}
CD68^{high}
CD25^{low}

Immature DC

HLA-DR^{moderate}
CD86^{moderate}
P55, CD83^{low}
CD1a^{high}
CD68^{high}
CD25^{low}

Mature DC

HLA-DR^{high}
CD86^{high}
P55, CD83^{high}
CD1a^{low}
CD68^{spot}
CD25^{high}

T-cell immunity is driven by:

- Peptide-MHC complex (signal one)
- High B7-2/CD86 expression (signal two)
- Cytokines (IL-12, Intγ)

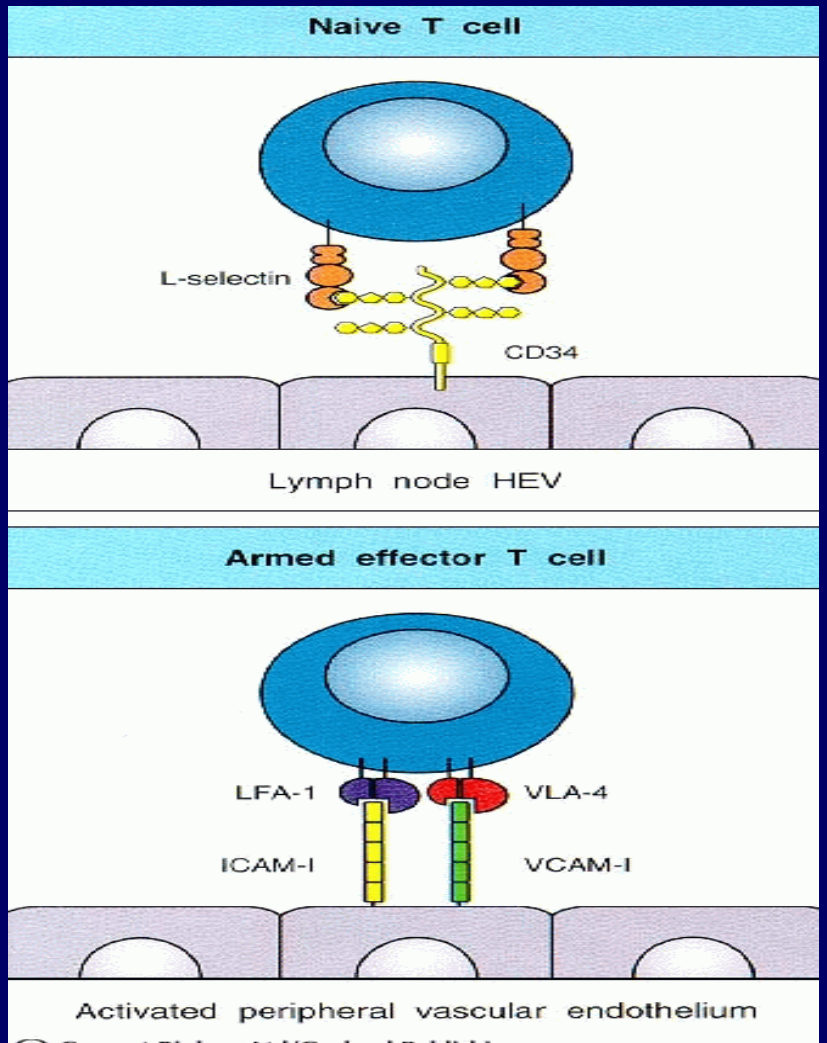
  or
- Membrane-associated TNF family receptors (CD40)
- TNF family members (CD70, OX40)

Inflammation

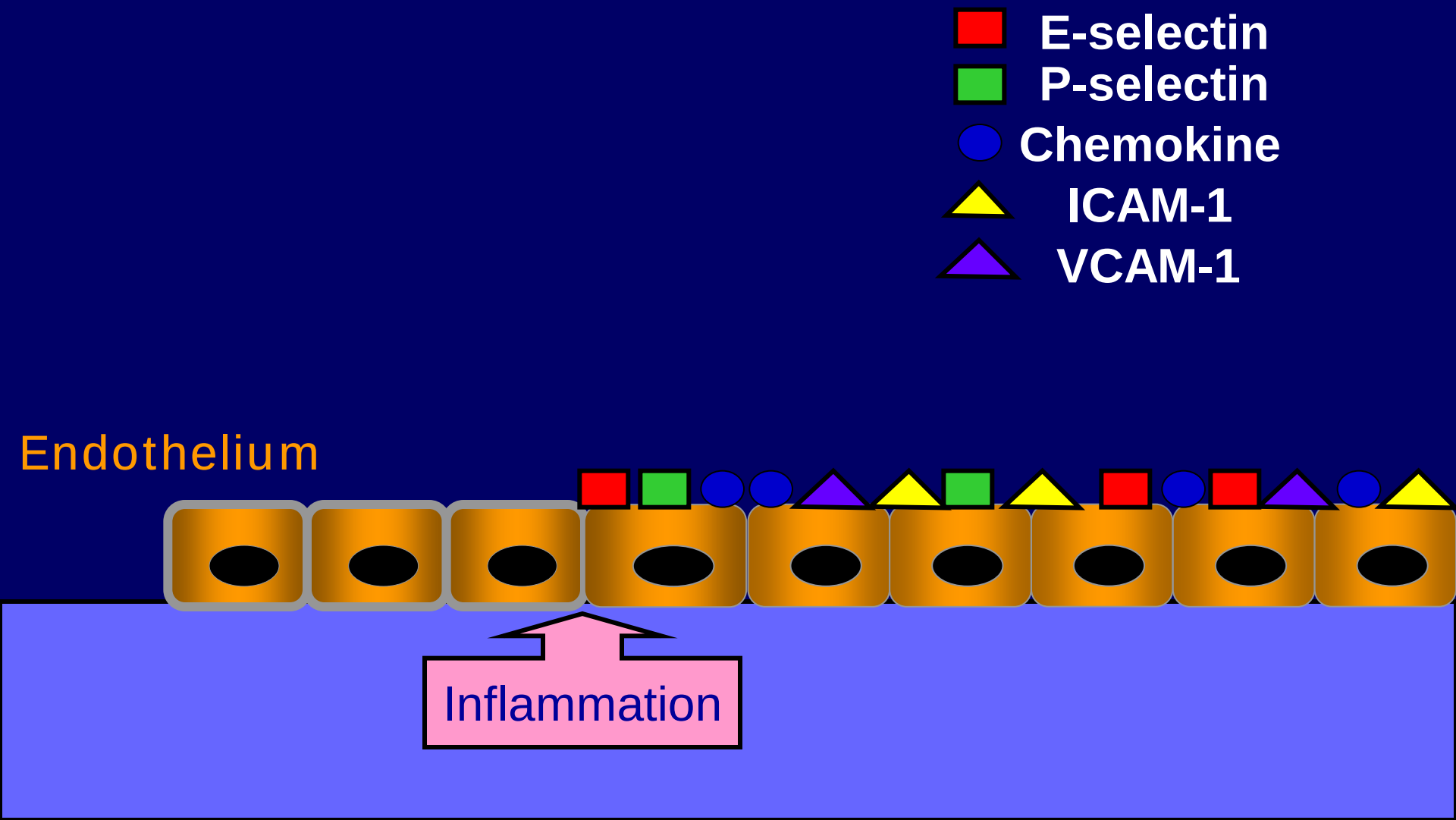
Expression pattern of naïve and activated lymphocytes

CD4	CD62L	VLA-4	LFA-1	CD2	CD4	TCR	CD44	CD45 RA	CD45 RO
N	+	-	+	+	+	+	+	+	-
A	-	+	++	++	+	+	++	-	+

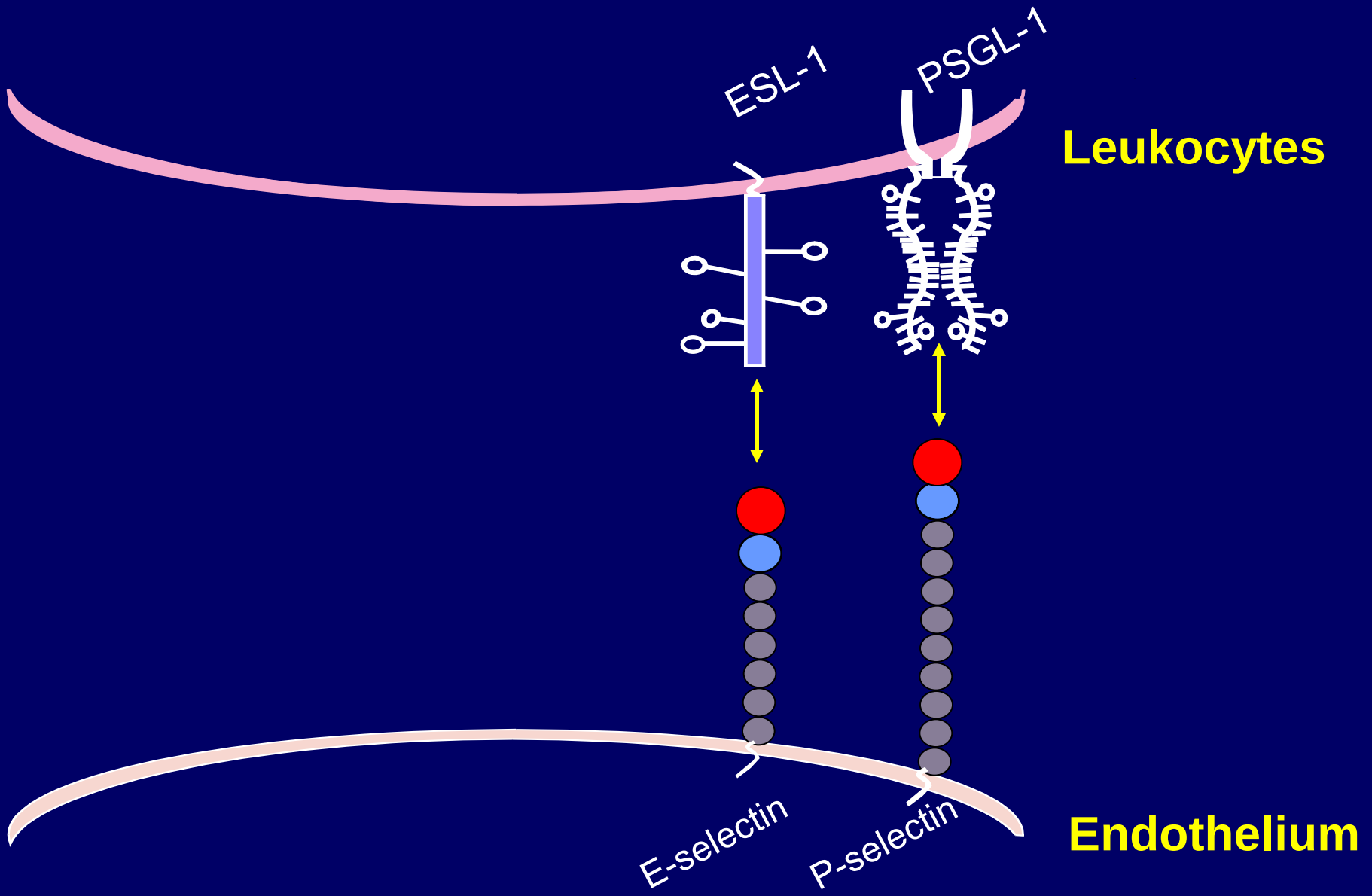
Armed effector T cells change their surface molecules so that they can home to sites of infection via the blood.



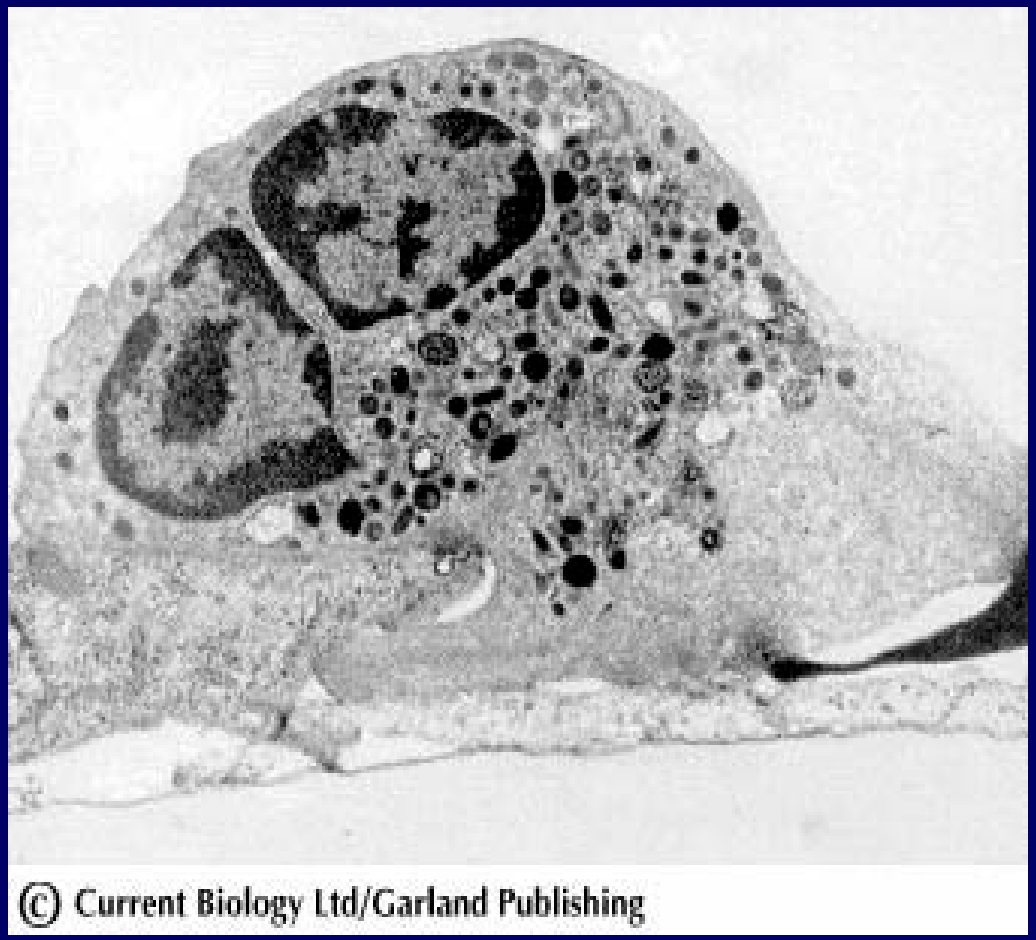
„Inflamed endothelium”



Selectin Ligands



Phagocytic leukocytes are directed to sites of infection through interactions between adhesion molecules induced by cytokines.



Role of PSGL-1 in leukocyte trafficking