Immunology 5

Cells and organs of specific immunity
Development of lymphocytes

Cells and organes

Lymphocytes

- T cells
- B cells → plasmatic cells
- NK cells

Lymphoid tissues and organes

- primary (thymus, bome marrow)
- secundary (spleen, lymphatic nodes, MALT)
- lymphatic vessels

Development of lymphocytes

- T lines
- - structure of thymus
- - development of αβ T cells
- - development of γδ T cells
- - development of NK cells
- B lines
- - bone marrow
- - B-1 and B-2 cells

Cells of specific immunity

- Unlike in **nonspecific immunity** (granulocytes, monocytes,...)
- cells **specific immunity** LYMPHOCYTES – are not morphologically recognisable
- with the exeption of size
  - small - 4 - 7μm
  - medium - 7 – 11μm
  - big – 11 – 15μm

Differencies based on specific **receptors** and **organes** in which they develope

Cells of specific immunity – executors of activities

They contain molecules (receptors) – indicating the function

Specialised in primary organes – thymus or bone marrow

Reside in specialised area – secudary organs - spleen, lymphatic nodes, accumulation of lymphocytes)

Can develope further - differentiation

Transported to infected area

Lymphocytes

- recognition of self and non-self – somatically generated epitope-specific receptores (TCR and BCR)
- they are generated de novo by recombination of genes in every individual T and B lymphocytes **before** exposition to antigen
- Based on site of differentiation and on receptors:

T cells and naturall killers T - in thymus - (TCR)

B cells – bone marrow - (BCR)

(no cell surface specific receptors – NK cells)

Thymus derived cells
T lymphocytes

- most important players of specific immunity
- direct effectors and regulators of activity of other cells

Produced in bone marrow: not mature T cell – prothymocyte

Migrates in thymus - thymocyte, where *TCR are produce*.

Skreening of ability to recognise self and non-self.

Most of them are *eliminated*, others are *indicated* to be T cells and *leave* thymus and *enter* to ciruculation

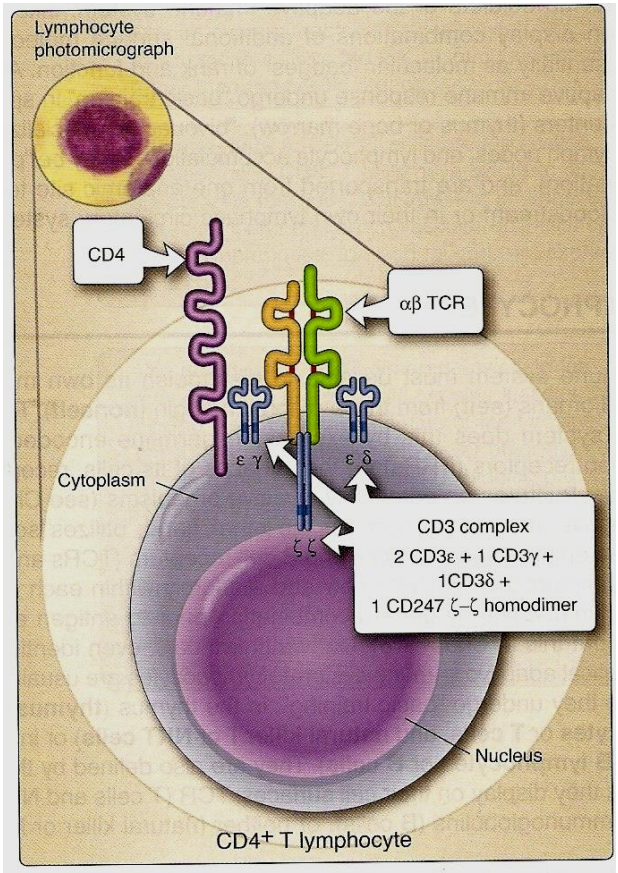
Contain surface receptors TCR

CD3

CD4 or CD8

- CD4 T cell

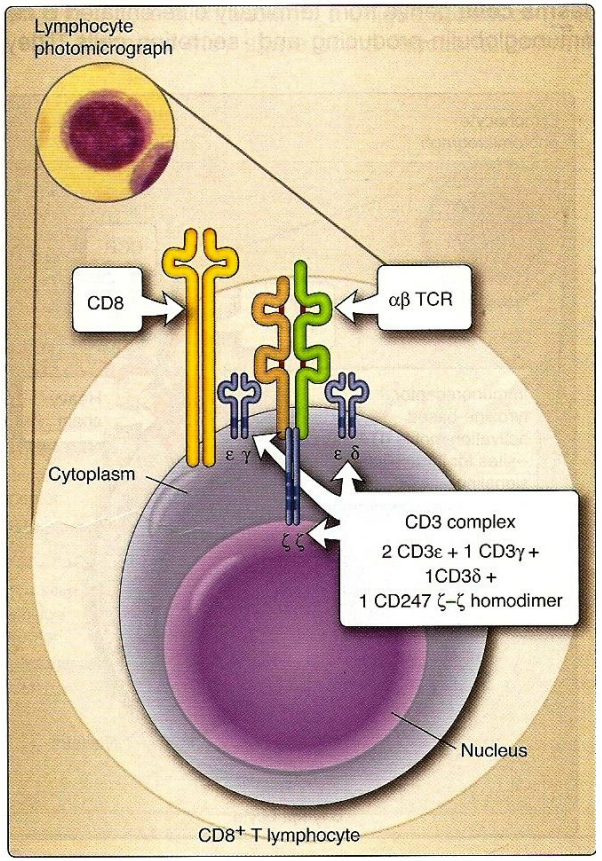
- 2/3 of all T cells containging CD3
- CD4 cell surface molecule – recognise part of **MHC II** molecule that is not part of peptid binding site
- Functionally – helper



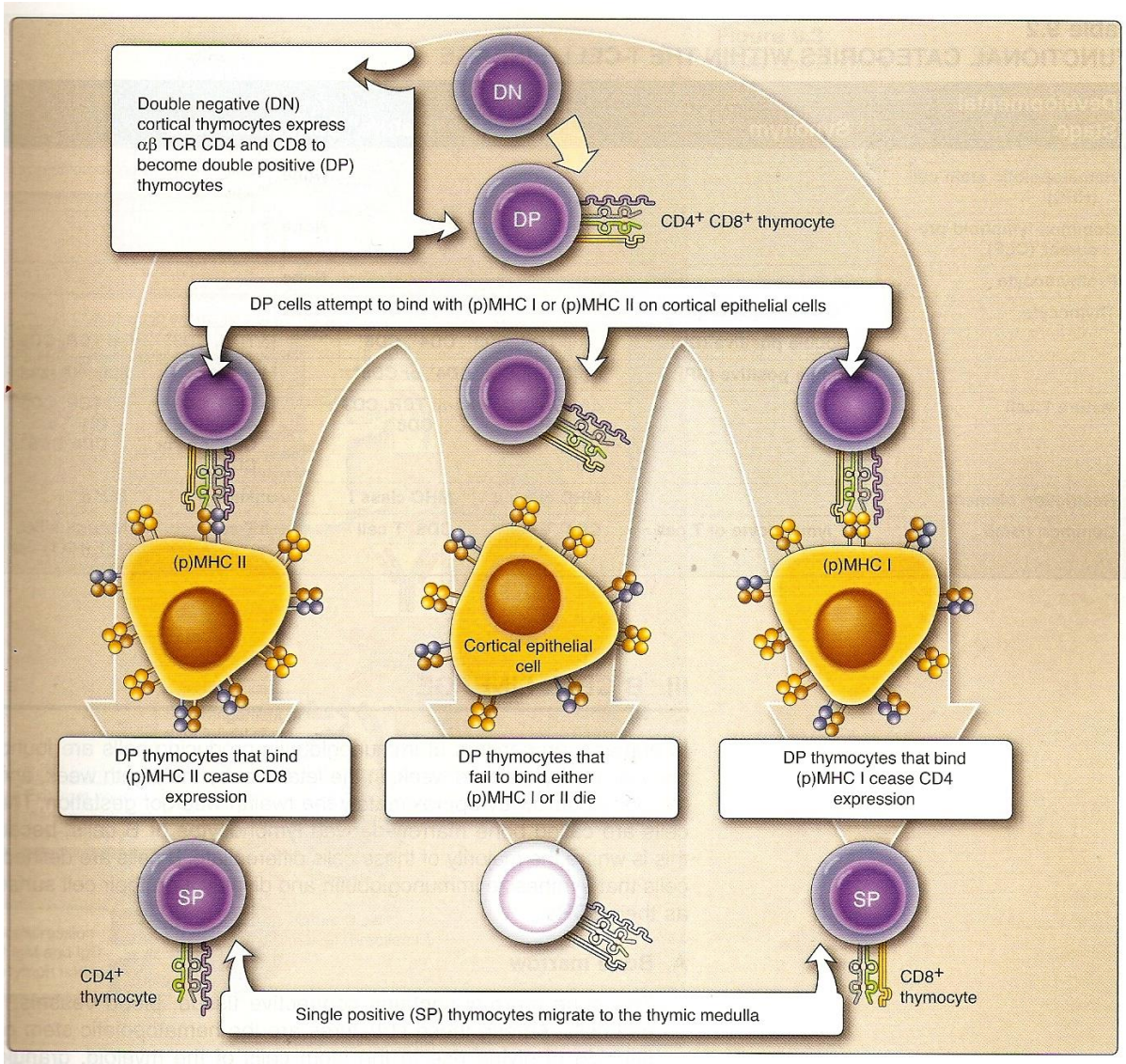
- CD8 T cells

- 1/3 of all T cells containing CD3
- CD8 cell surface molecule – recognise part of **MHC I** molecule that is not designated to bind peptids
- Functionally :
  Tc cytotoxic – eliminate virus or i.c.bacteria infected cells

  Ts supreesor – increase and control reactions of specific immunity

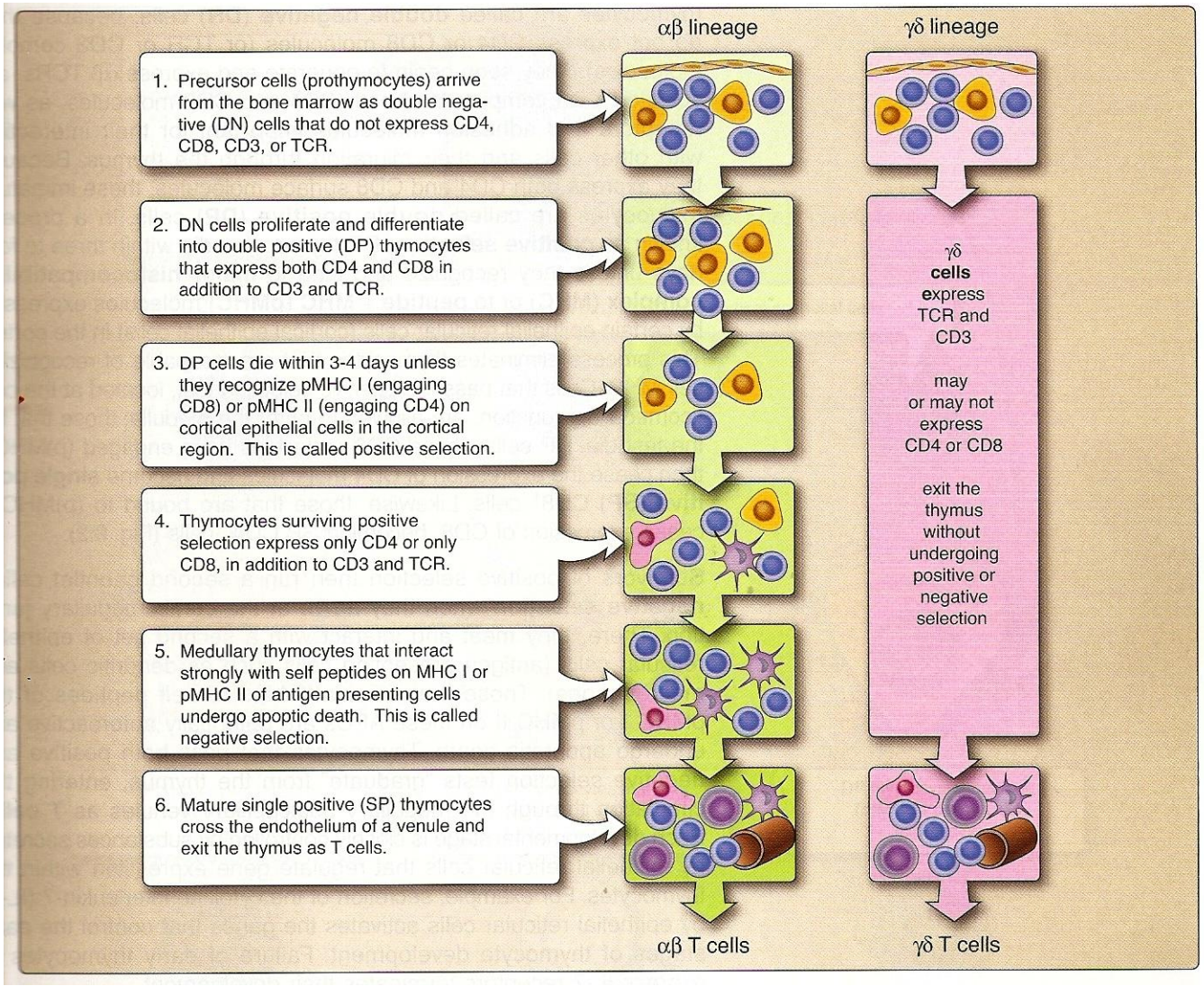


Differentiation of T cells



T line

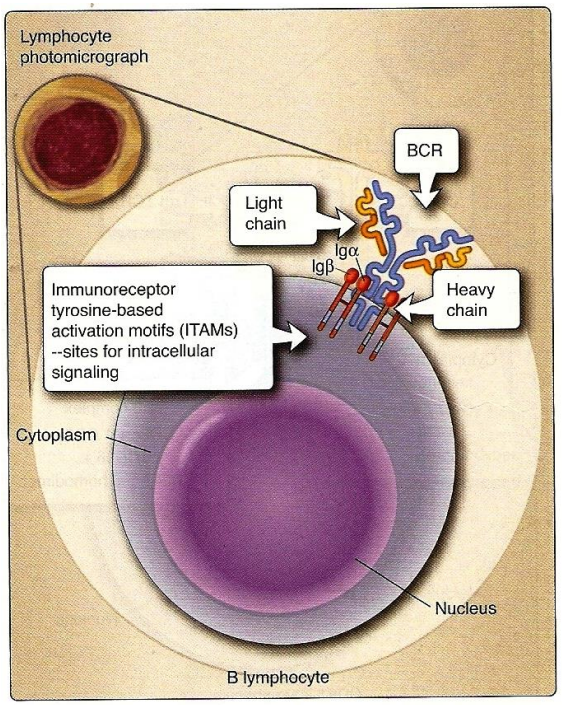
- αβ T cells
- γδ T cells
- NKT cells



Cells produced in bone marrow only B - lymphocytes

- Not all cells produced in bone marrow migrate to thymus
- Some differentiate in bone marrow further and are precursors of cells producing immunoglobulins
- **B lymphocytes – B cells** – synthetise immunoglobulin, that is then situated on the cell surface as BCR.
- Differenciated mature B cell synthetises and secretes immunoglobulines

- B cells

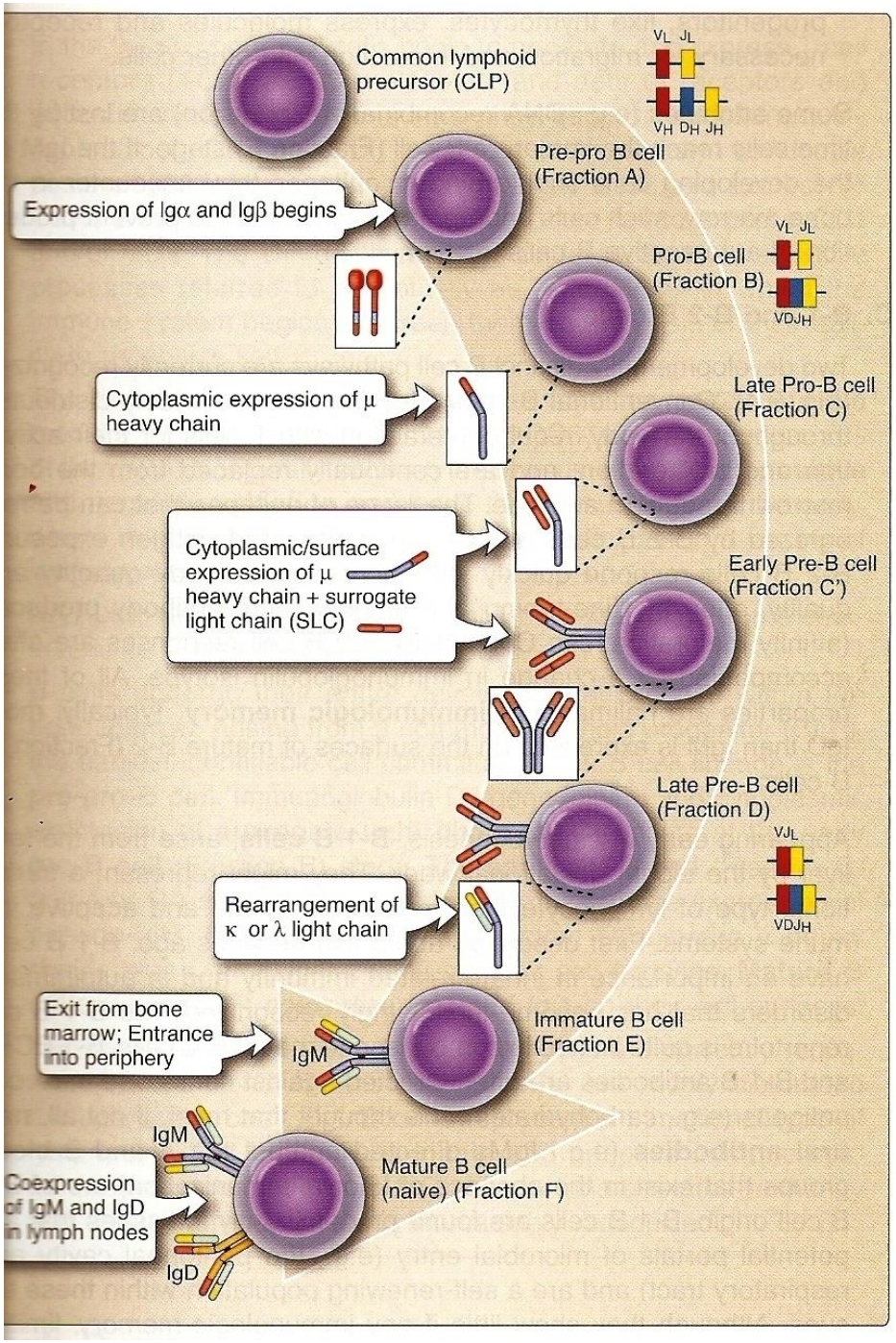


- develope from pluripotent steam hematopoetic cell in bone marrow
- do ônot migrate to thymus
- exist in 2 lines B-1 and B-2

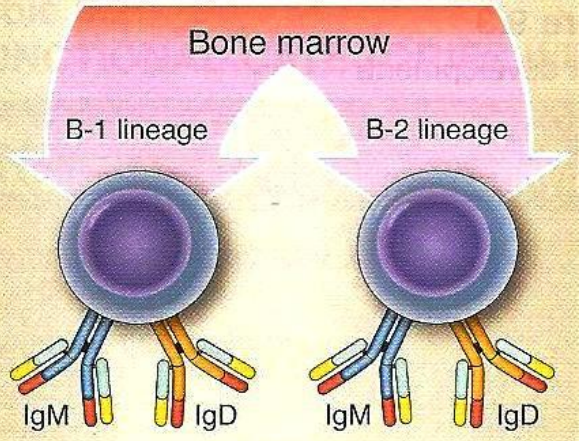
B-1: population present in pleural and peritoneal cavities, connected to inborne immunity
important in autoimmue disorders

B-2: produced during perinatal period, constantly produced in bone marrow and present in lymphoid organs and tissues.

Every B cell is specific, produce Ig of unique specificity, recognising one unique epitop Big diversity

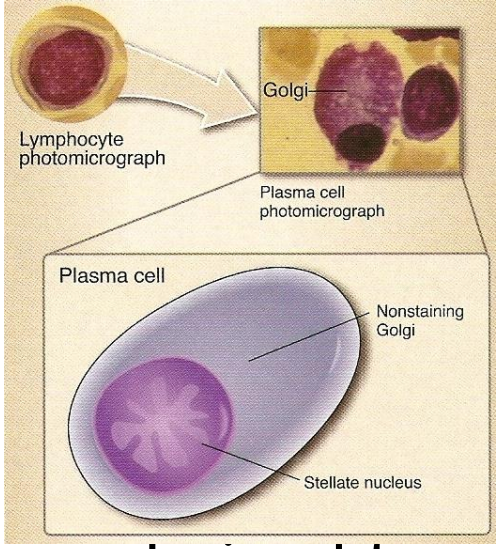


Development of B cells



Arise	Fetal	Perinatal/ Postnatal
Location	Respiratory & GI systems	Widespread
Diversity	Low	High
Memory	Little/none	Yes
Usual target	Carbohydrates	Proteins
Dominant isotype on surface of naive B cell	IgM>IgD = B1	IgD>IgM = B2
Isotype switch	Limited	Typical
Require T cell help	Almost never	Almost always
Replace-ment	Self-renewing in periphery	Continuously replaced from bone marrow

B-1, B-2



- Plasmatic cells

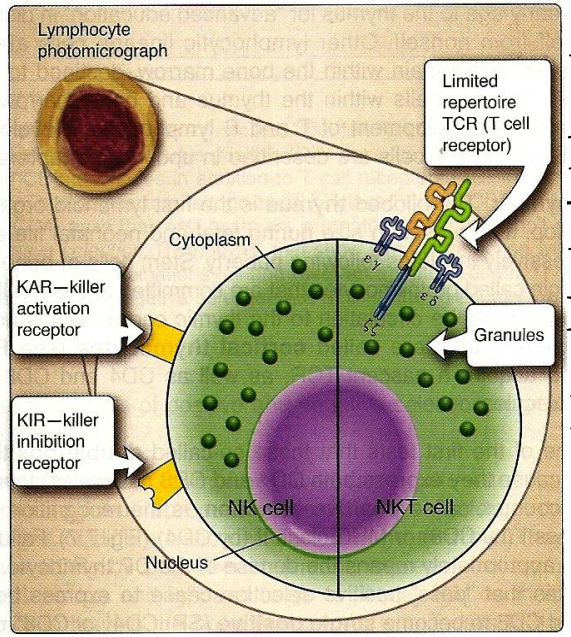
- derived from terminally differentiated B cells
- produce and secrete immunoglobulines
- in the momente, when they start to produce and secrete Ig, they stop to use immunoglobuline molecule as BCR
- they are bigger and have bigger metabolic activity
- produce big ammounts of Ig
- survive 30 days
- basofil cytoplasma.

NK cells – natural killers

- 5% - 10% periferal blood lymphocytes
- do not have markers (receptors) as T cells (CD3, TCR) and B cells (Ig)
- kill cells infected by viruses and tumor cells without previous sensibilisation
- granular cyroplasma

- NK vs. NKT cells

- contain KAR
  a KIR receptores
  recognise cells
  that have to be
  killed



unique subtype
functional charateristics
TCR of restricted
repertoire
respond to lipids
glykolipids and
hydrophobic molecules
presented by nonclassical
molecules MHC I (CD1) and
secrete big ammounts of
cytokines (ex.IL-4)

Lymphoid tissues and organes

- Leukocytes exist in body as:

- isolated tissue and circulation
- agglomaration of cells – Peyer´s plaques
- lymphoid organes – thymus, spleen, lymphatic nodes

Organes:

- primary – *thymus and bone marrow*– production and differentiation of cells
- secundary – *spleen, LU, agglomaration of lymfoid cells* – filter immunogens and are meeting point for immunocompetent cells to contact each other and stimulate immune reactions

Primary organes

Thymus and bone marrow

- education centers for lymphocytes
- recognition of self and non self – T cells
- cells in bone marrow – B cells

Stromal cells – regulation of developement

Primary organes: thymus

- organ developing in fetal and neonatla period
- involution on adolescence

- Stem cells in bone marrow migrate to cortex of thymus (*prothymocytes*) – (c*ortical thymocytes)* – where they gain TCR and CD4 and also CD 8 – *double positive thymocytes*
- next stage is positive selection – recognise MHC I or MHC II and then express only just CD4 or CD8 and become single positive.
- Migrate to medular part. In this stage (negative seletion) – those that cooperate with MHC are designed for **apoptosis.** Other continue in development – 5% of all

Primary organes: bone marrow

- early differenciation in bone marrow of future – imunoglobulines producing lymphocytes – B cels
- produce BCR by rearrangement of DNA and expose IgM before leaving bone marrow
- interraction with stromal cells in medullar part regulate the development of B cells
- In bone marrow accidentally produced BCR on some B cells can recognise and bind self molecules – they where self-reactíve cells designed in medulla for *apoptosis*

Secundary organes and tissues

- filtres to eliminate foreign structures, dead cells, agregates of proteins
- circulation facilitate cells via these organes

- Spleen, lymphatic nodes, tonsils and Peyer´s plaques

Spleen, Mucous Associated Lymphatic Tissue

- Spleen: the biggest lymphoid organe cleans blood and concentrates antigens., contains many plasmatic cells, T and B cells
- MALT, tonsils – potencial places of invasion of microbes

Lymphatic nodes

- periferal and secundary lymphoid organes
- accumulation of leukocytes
- filtration of cleaning of lymphe
- site for contact of ly, mono, dendritic cells to iniciate immunity reaction

Contain cortex (superficial - Bcells, deep – Tcells, germinal centrum) and medulla + retricular net (phagocyting reticular or dendritic cells)

Circular lymphatic system

- capillary net harvesting lymph
- Lymph – watery liquid containing leu and rest of cells
- Vessels in intestin contain chylus drained to lymphatic nodes
- They meet to produce ductus thoracicus, that drain to blood