

Breast Cancer.

ERT, PRVE, Her. neu.

i) gene expression profiling

ii) molecular classification of Cancer.

→ Molecular classification of Breast Ca based on gene expression profiling

Q FISH Congenital malformation - metaphase

Oncological specimens - Interphase

2 variants - i) Chromosomal painting (entire human genome on same chromosome)

fluorochrome painted on entire genome of one chromosome

Q 2) Multicoloured FISH - entire genome on all gen chromosome

Spectral Karyotyping simultaneously
Spectral Karyotyping - fluorochromes Computer generalized

Immunology

Immunity

Innate

Acquired

- Birth / 1st line of defence
- Non memory
- Non-Specific

- memory ⊕
- Specific ⊕

- B T cells

T cells

MHC Complex

NK-T cells variant

of T-cell.

- epithelial cell

- Neutrophil, Dendritic cells.

Macrophage

- NK cells

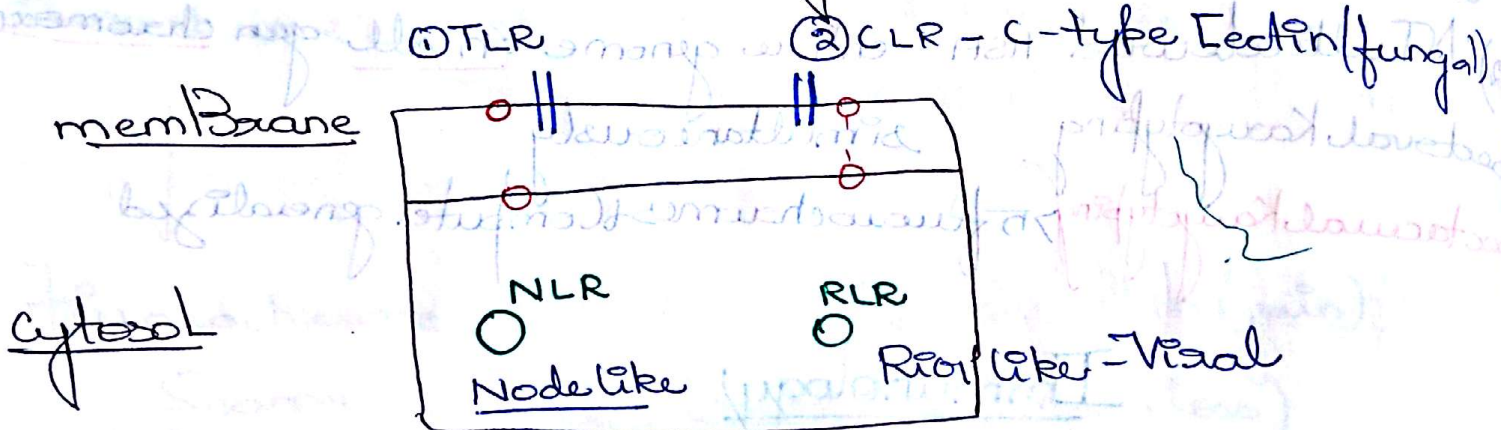
Complements

C-Reactive proteins

- Pattern Recognition Receptors.

[PRR]

Q. Pattern Recognition Receptor.



i) metabolic byproducts

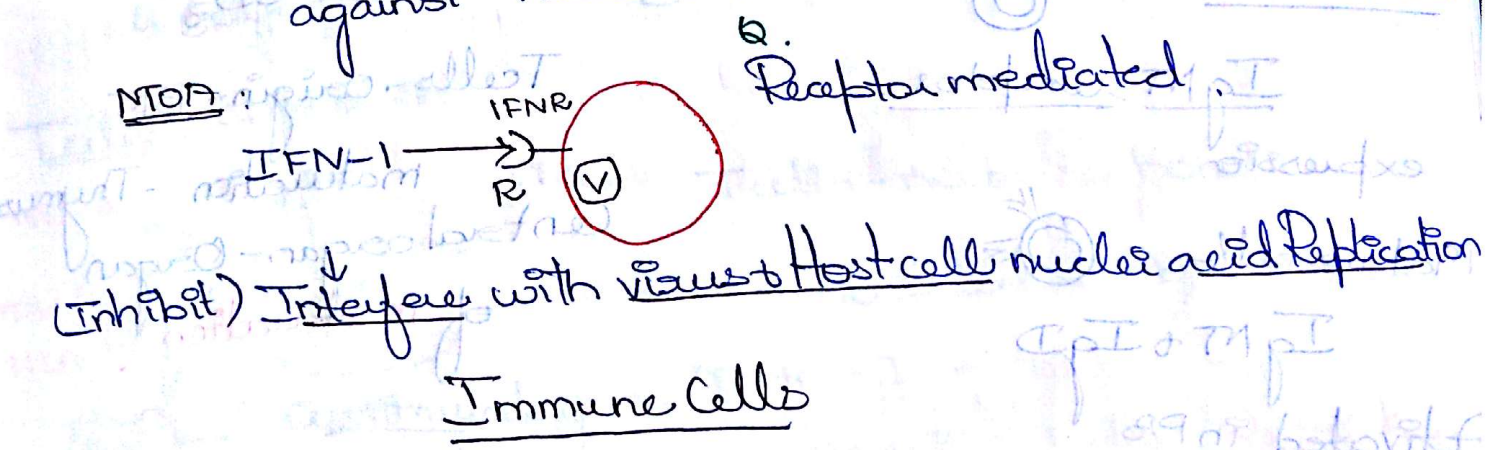
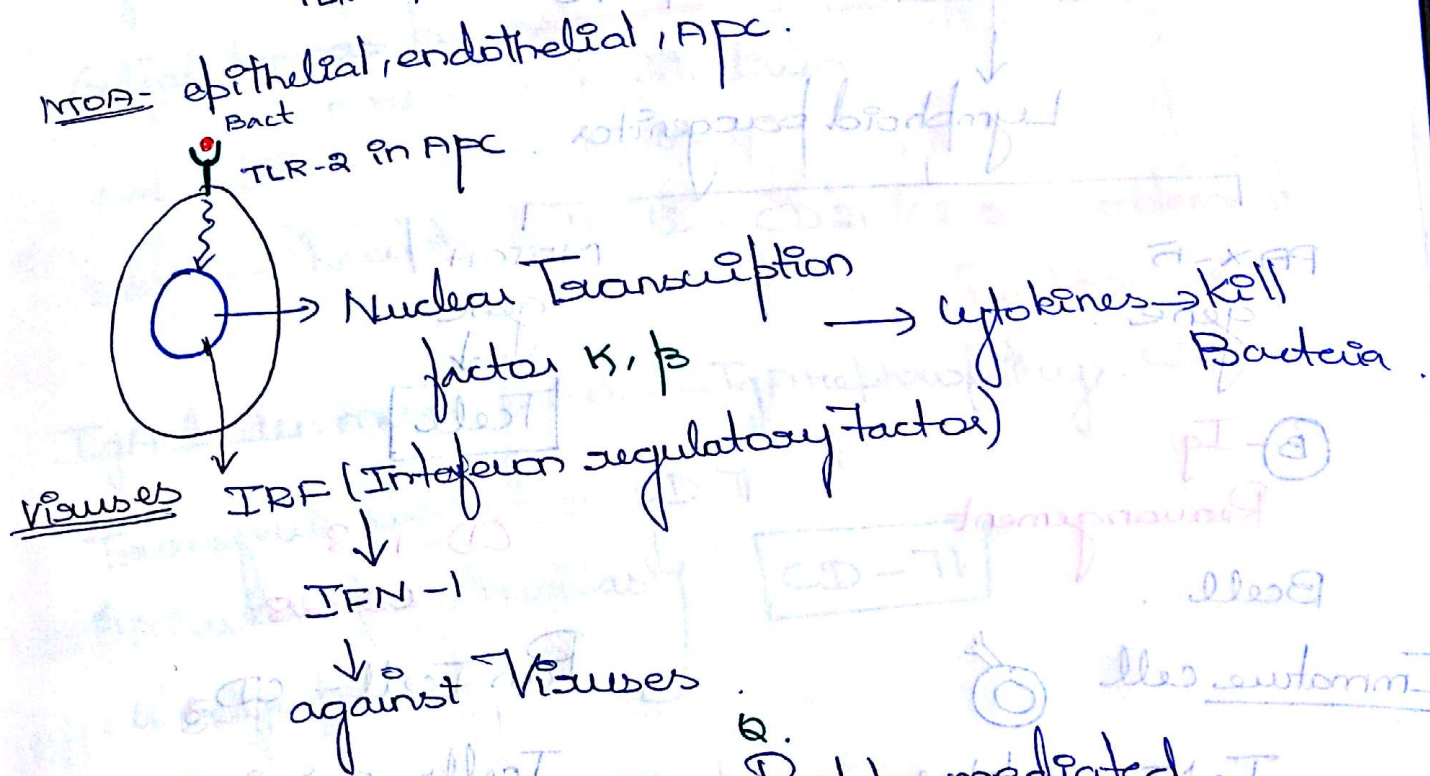
- lipoic acid (involved in GALT pathogenesis)

ii) Flagellated organisms

iii) Tonic disturbances

iv) also associated with NOD-like Receptors.

Toll-like Receptor - TLR:
 TLR-2 → Gram +ve, Leptospira, fungal infection
 TLR-4 → Gram -ve (endotoxin)



i) Lymphoid.

- T-cell 60-70%
- B-cell 20-30%

ii) APC

iii) NK Cell

Large granular lymphocytes

↓

5-10%

Lymphoid cells

origin - Stem cells (CD34+ve)

∴ mature cells 34-ve

Lymphoid progenitor

PAX-5 gene

ⓑ-Ig
Rearrangement
Bcell

Immature cell

IgM receptor
expression

Mature cell
IgM + IgD

Activated in PB

IgA
IgM; IgD
CD-10-CALLA

CD markers - CD-10, 19

CD-19-24 Pan Bcell - CD19

3-1415C, 33 - Monocyte/macrophage
CD-14

NOTCH gene
↓
Tcell

CD-1-8
CD-28

Pan Tcell - CD3

Tcells - origin - BM.
maturation - Thymus
Central organ - Organ
of maturation

NTyeloid markers - NTPO > CD117

Glial tumors, present on neuronal epithelium - CD133

NK cell - CD16, CD56

EBV → Receptor on B cell - CD21 / CR2 - complement Receptor - 2.

IgA laden mesangial cells - IgA nephropathy. CD71

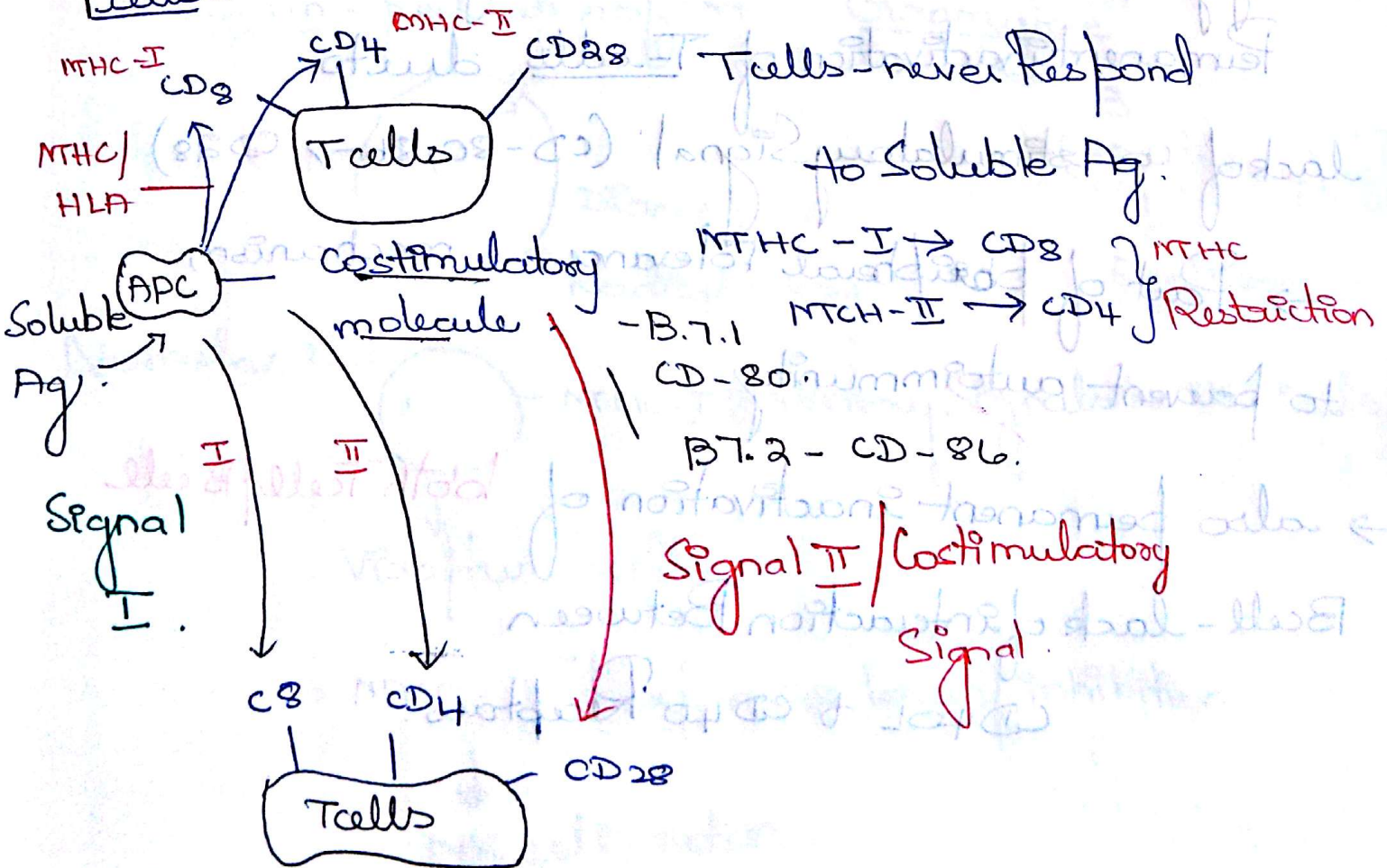
Transferrin Receptor - CD71

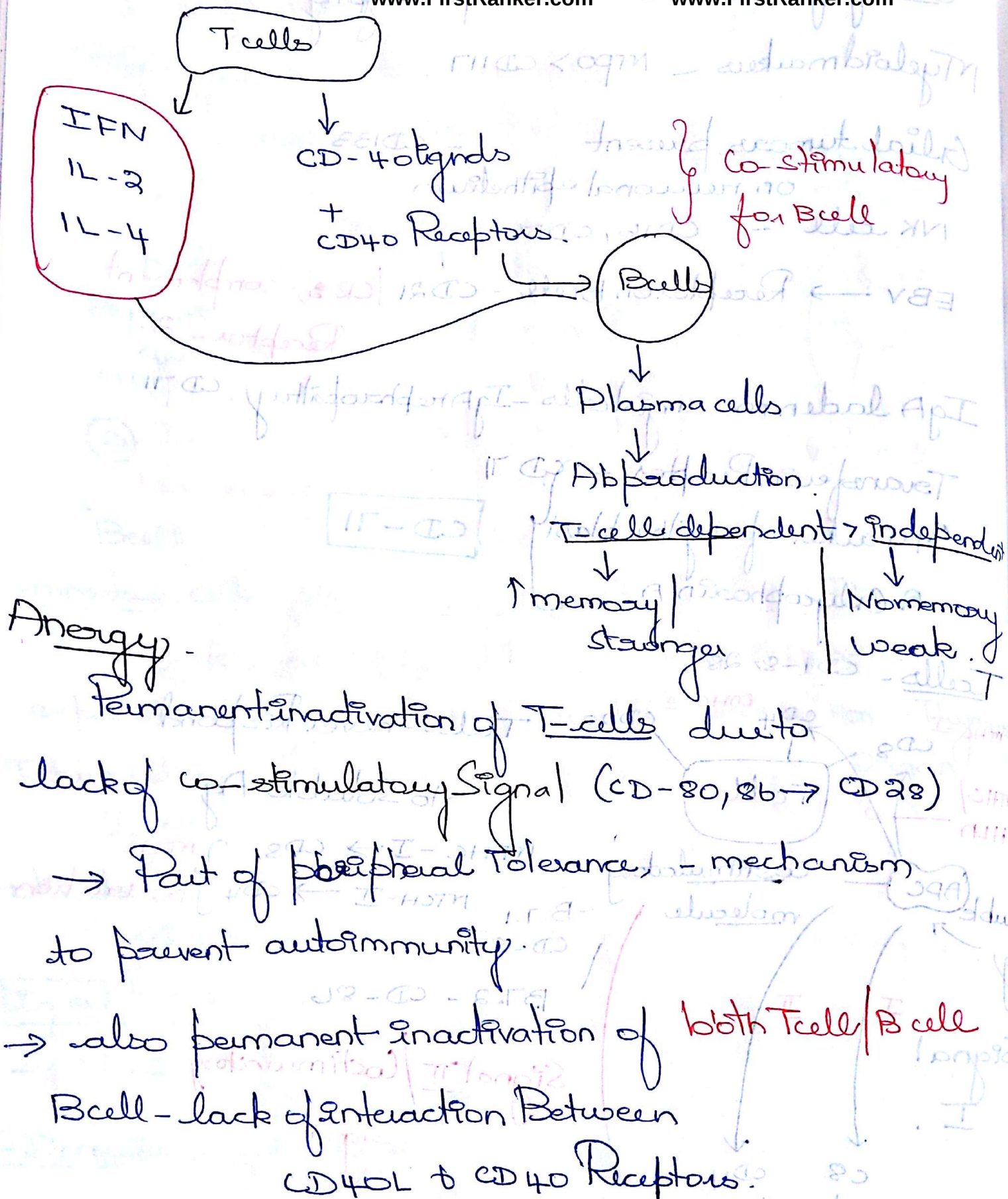
A marker of erythroblast

A Glycophorin A

CD-71

T cells - CD1-8, 28



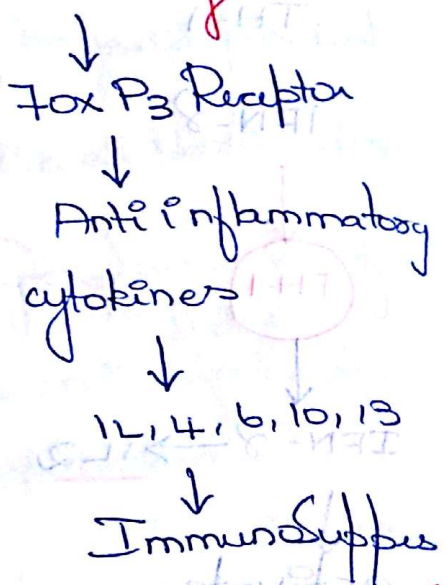
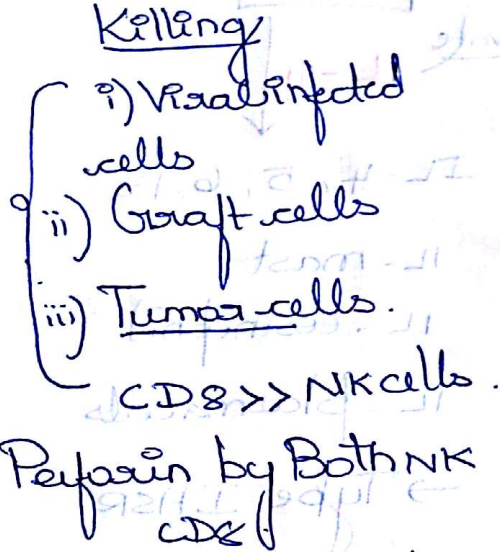
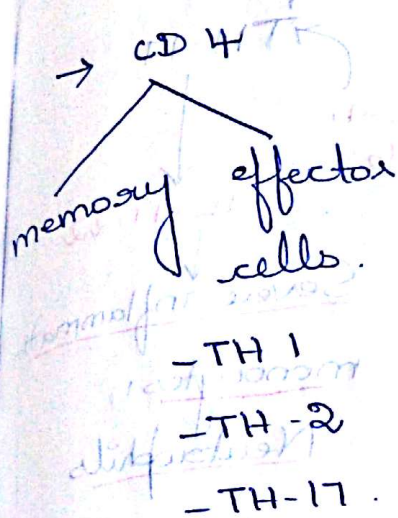


Types of T cells

Helper T cell

CD 8
cytotoxic
CD 8

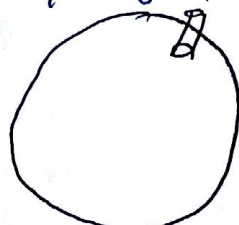
Suppressor / Regulatory
Self Ag
CD 4 T Regy



Perforin - granzyme mediated cell damage = **CD 8 > NK cells**

Perforin - perforation of CM

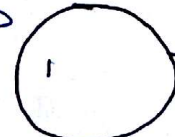
Granzyme



Direct face
Radical Injury

B.
(FAS / FASL)
↓
Apoptosis

Normal cells

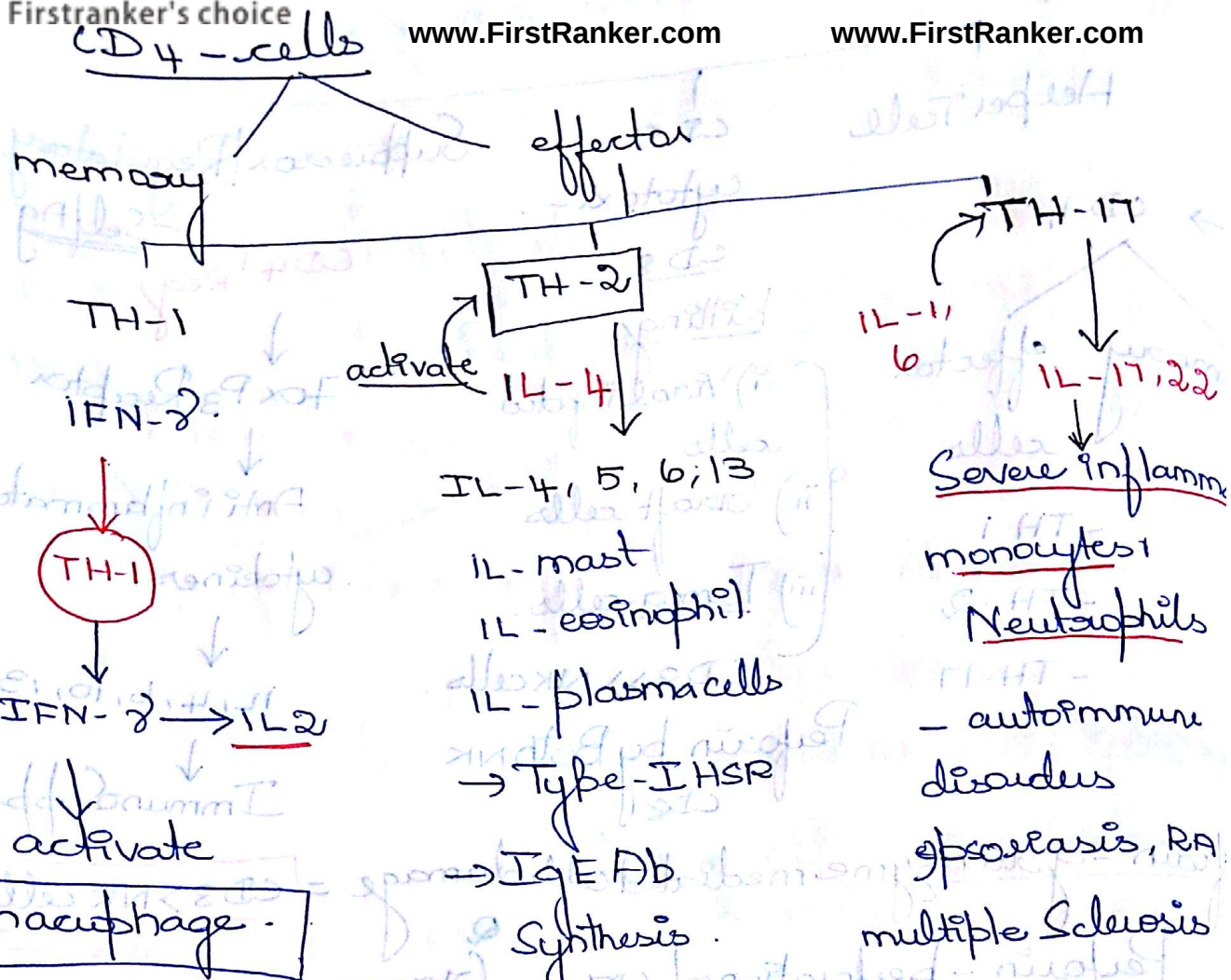


MHC - I inhibitory Signals to NK - cells

Viral / tumor cells

MHC - I ↓ expression loss of inhibition.

↓
NK cell action



- 1) Granuloma formation $\rightarrow$ Parasites
- 2) Type IV HSR.
- 3) Intracellular killing.
- 4) GIVHD

Professional
MHC-II

- a) Immature Dendritic cells - Langerhans
- b) **Mature DC** - most potent.
- c) Macrophage
- d) B cells.

i) Epithelial cells (few)

eg - thyroid epithelial cells.

b) Thymic epithelial cells.

~~Thymocytes - precursor of T cells~~

c) m-cells - microfold cells.

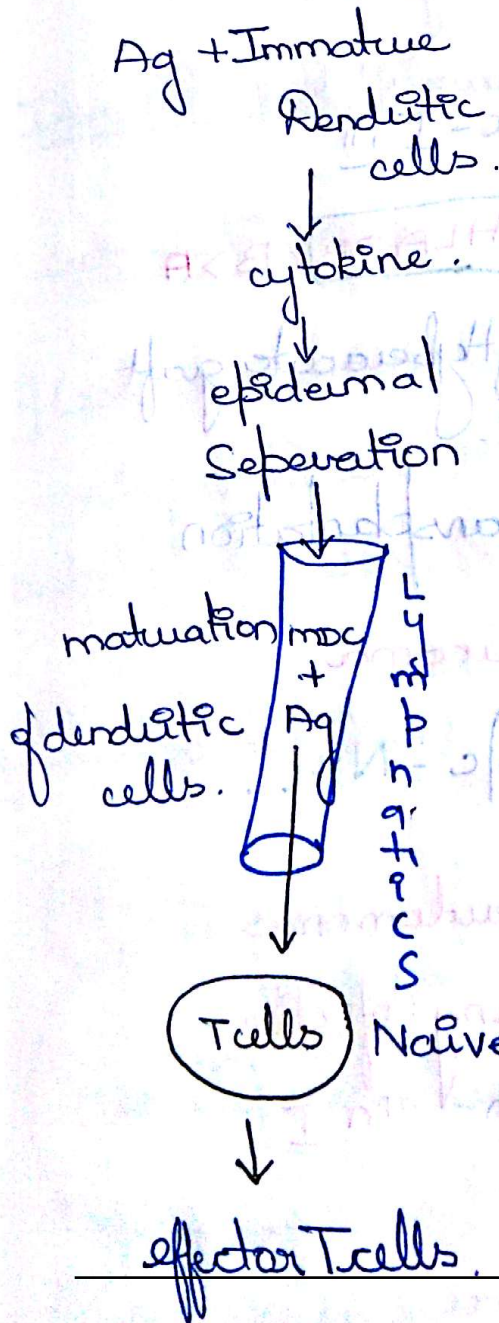
S. Intestine - Peyer patches

ii) All endothelial cells

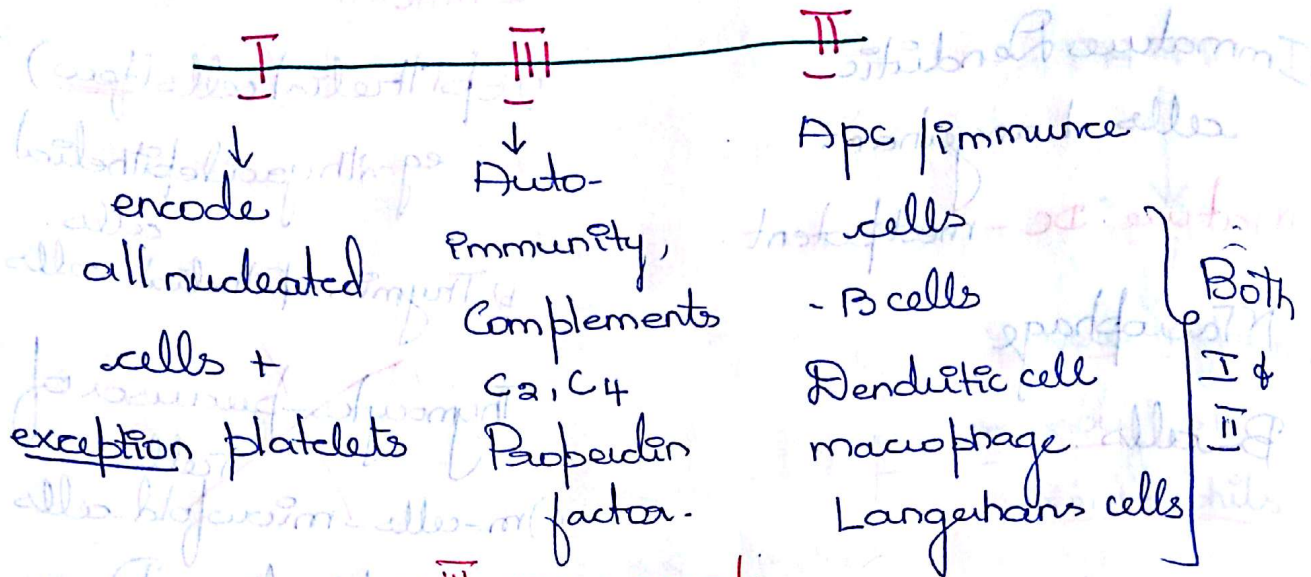
iii) All glial cells - astrocytes
oligodendrocytes
ependymal cells

iv) Pancreatic Islet cells.

v) Fibroblasts



HLA:



III - never encode

C3
HSP, TNF- α .

Graft Rejection

GVHD

- CD4 T, CD8 T, Both MHC - I, II

Before organ Transplantation - m/c - **HLA DR** > B > A

Due to HLA-DR typing - $\downarrow$ Risk of Hyperacute graft rejection.

m/c Cancer associated with Organ Transplantation

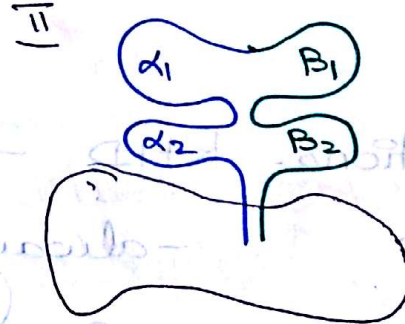
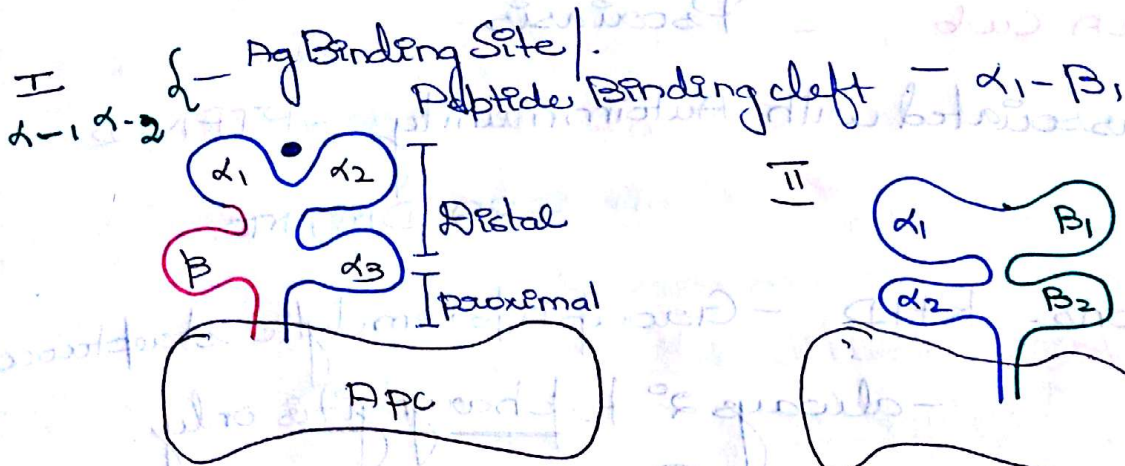
Skin Ca (SCC) > NHL > Kaposi Sarcoma

[general m/c - Skin Ca - Bcc] HIV-m/c - NHL

Lung Transplant - m/c Cause of death - Pseudomonas

Lung Transplant m/c Cause of death - **Lung infection**
M. I

important in - Renal Transplant



Autoimmunity

Loss of Immunological Tolerance (Both Central + Peripheral)

Immunological Tolerance - (1) Non Responsiveness to self antigens.

Central Tolerance

Peripheral Tolerance

1) Central deletion
- By apoptosis, kills auto reactive cells. **Negative Selection**

1) Anergy

2) Regulatory T cell

3) Physiological Apoptosis

4) Ag - Sequestration

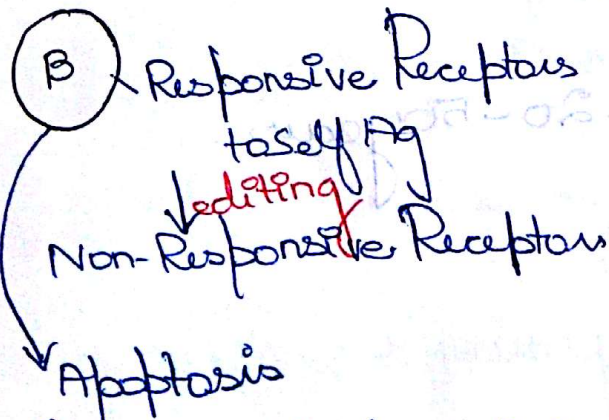
i) Brain

ii) eye

iii) Testis

Immune privileged sites

2) Receptor editing



If not able to form non responsive receptors

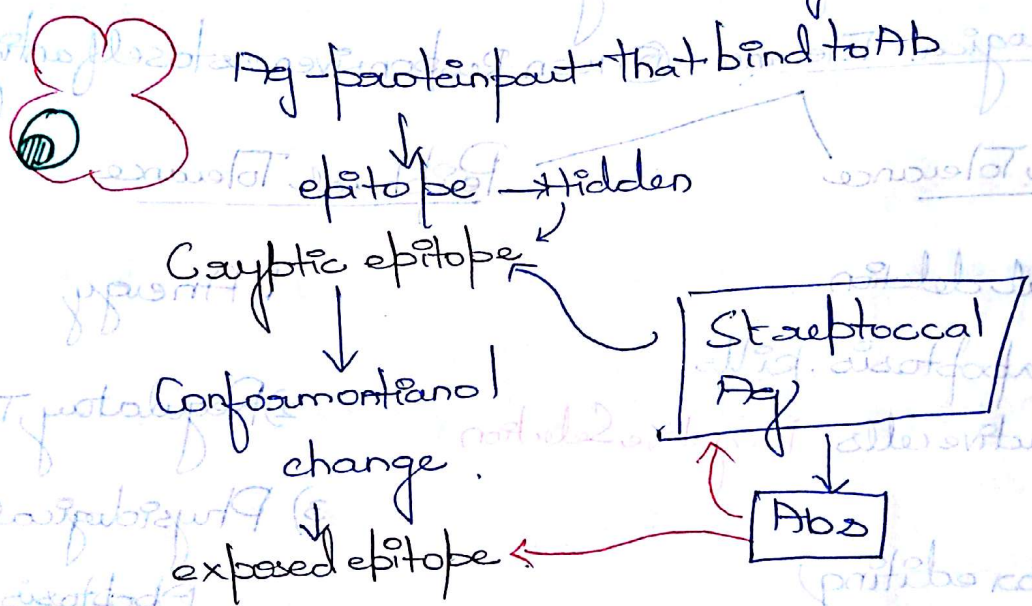
Mechanisms

→ HLA-B-27 - Ankylosing Spondylitis
HLA Cw6 - Psoriasis.

2) Gene associated with Autoimmunity - PTPN-22
- RA, DM, MS.

3) Infections - RHD - Group A β Hemolytic streptococci.
- always 2° to pharyngitis only.

mechanism - Cross Reactivity.
molecular mimicry.



Autoimmunity: Females > Males.

Reproductive age - 20-50 years.

SLE

Oral ulcers
Malar Rash.

Phototoxicity Ro - SS-A

Myocarditis - Ro Ab

→ Shrinking lung Syndrome - Ro Ab

→ SLE with Raynaud's phenomena - anti U, RNP

Neonatal Lupus with congenital Heart block - Ro Ab / SS-A

Ro + LA - both
(present)

most specific ↑

Lung - m/c present - pleuritis

Cardiac - m/c pericarditis, most specific - Libman Sacks

Musculoskeletal System - non erosive arthritis

Hematology - Ab { RBC - AIHA
Plt - I.T. thrombocytopenia
WBC

→ Renal - lupus nephritis

→ CNS - Psychosis - Anti-Ribosomal Pab

m/c System involved - musculoskeletal System

Hematology - 85%

m/c presentation - Arthralgia - 95%

m/c Cause of Death - myocardial infarction

m/c co within 10 years of onset - Nephritis & infection

Antibody-

- 1) Most Sensitive - ANA (
- 2) Most Specific - Sm Ab - only 3% (>> 90%
95% present
- 3) Most Specific & Sensitive - Anti dsDNA
- 4) Best Correlation of Prognosis - Anti dsDNA

Indirect immunofluorescence -

- 1) RIM / peripheral  dsDNA Abs.

Bright yellow

- 2) Diffuse Staining / Homogenous 
Histone Antibodies

- 3) Speckled - green background & dark spots  - Smith Abs.

→ m/c immunofluorescence - SLE :

- A) Centromeric pattern - spots green, Background dark.

Cytoplasmic
perinuclear ANCA



Special drug induced

→ Drug - procainamide } Anti Histone.
Hydralazine

Drug induced Lupus - Renal/CNS involvement rare

Nucleus with Homogeneous chromatin

↓ Hematoxylin Body - LE Body.

Peripheral Blood

Bone marrow.

never seen
in urine

Phagocytic cell Take up LE Body



Scleroderma - / Systemic Sclerosis.

Sclerosis - collagen deposition.

→ 20 - 30 years/F.

! Hallmark of pathogenesis of Scleroderma - microvascular injury.

↑ platelets.

↓
TGF- β , PDGF- α (imp. fibrogenic cytokines)

Subcutaneous fibrosis + Ca^{2+} deposition

Diffuse (Total)

anti-DNA

Topoisomerase

Localised



anti-centromere-Ab

CREST / Scleroderma

→ RNA polymerase-III Ab

associated with acute Renal

crisis / Cancer

→ Most Sensitive -

Anti Nuclear antibodies

→ most Specific - Anti-DNA-Topoisomerase

3) NTixed Connective Tissue disease

- SLE

- polymyositis

- Scleroderma

- polymyositis. Sjogren Syndrome (Rare)

Anti-UI RNP (Ribonucleoprotein)

4) Sjogren Syndrome

40-60 years / Female

1° Sjogren

2° Sjogren associated with autoimmune diseases.

- glandular
- extra-glandular
- Day-eye
- Keratoconjunctivitis
- Sicca
- Xerostomia-day mouth.
- Chronic Inflammation (polyclonal)
- Chronic Inflammation → **Marginal zone B cell lymphoma**
- (m/c)
 - i) arthritis
 - ii) Hepatitis
 - iii) Splenomegaly

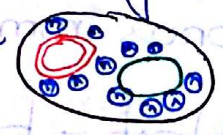
- RA (m/c)
- SLE
- Chronic active Hepatitis / autoimmune Hepatitis → PBC.

Δ Sjogren Serology

- SS-A - Ro - most Sensitive
- SS-B LA (most Specific)

Biopsy

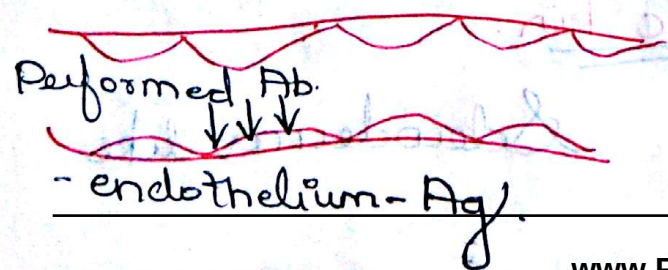
Site → minor Salivary gland of lips.
earliest perivascular periductal lymphocytic infiltrate



Graft Rejection

- 1) Hyperacute Graft Rejection: m/c in Renal transplants within minutes > Hours.

- due to preformed Abs (in Host) - i) Multiparous women ii) Previous H/o Transfusion iii) H/o Transplant.



2) Acute Graft Rejection - II > IV HSR

Humoral

Ab → endothelial Ag

Type-II HSR

Cellular

C₄, CD₈

Type-IV HSR

→ Blood vessel - Complement deposition } C₄d Diagnostic

3) Chronic Graft Rejection - CD₄T / CD₈T

Type-IV HSR

4) Graft Versus Host Disease

a/k/a - Runt's disease [Cattle / pig]

Donor immunity - very good immunocompetent

Host - poor immunity

m/c associated with stem cell immunity

Chronic

Acute

< 100 days

> 100 days

Organs affected - All organs

Rare - lungs m/c Skin

Skin - Simple erythematous

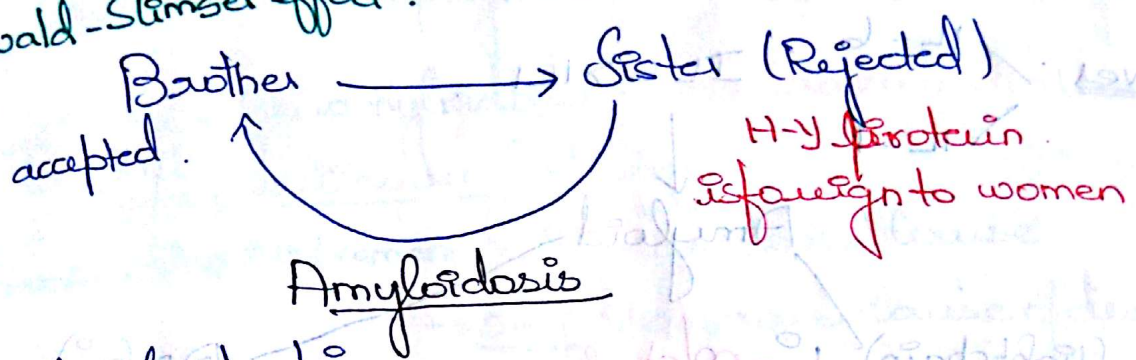
Scleroderma like

Sex-linked B-lymphocyte Rejection

Tetracosapeptide

Ubiquitously transcribed
H-Y linked disorder

Leitchwald - Slimmer effect.



Amyloid - glycoprotein.

Chromosome - 21

length - indefinite length.
diameter - 7-10nm
Non branching fibrils

electron microscopy

B-pleated Sheets - X-Ray diffraction microscope

Congo-Red Stain

Ordinary
(Red/Pink)

Polarized microscope

Fibrin/Collagen/Hyaline
also Red

Apple-green birefringence
(Diagnostic)

→ Amyloid always extracellular, acellular, pink

Other stains:

Thioflavin-T

Hyaline

Toluidine Blue

Methyl violet

Crystal violet

→ Silver methenamine

www.FirstRanker.com

www.FirstRanker.com

Toluidine Blue - also stain for mast cells

Liver / IL-6 IL-6 > IL-1

IL-1

Amyloid

AL (light chain) 1° - m/c type

Plasma cell disorders.

Multiple myeloma

Cardiac failure

Overall cause - Cardiac failure

m/c Cause of morbidity → Renal failure

Gingival Amyloidosis - multiple myeloma (1°)

Para-neoplastic: Renal cell Ca, Hodgkins Lymphoma

Hemodialysis - Aβ₂ microglobulin

APAP^{sc} → Prion disease

A. Cal → calcitonin - medullary Ca of thyroid

A IAPP Islet associated polypeptide - Type II Diabetes

Familial

- 1) Familial amyloidotic polyneuropathy (mutant Transthyretin)
 - 2) Systemic Senile amyloidosis - wild Transthyretin (non-mutant)
 - [Senile Cardiac amyloidosis]
- No extra cardiac involvement - Benign clinical course
→ CHF - very rare cause of death

Organ Involvement

- m/c - Renal Amyloidosis - m/c Presentation Nephrotic Syn (50%)
Hypertension (20%)
- earliest site affected i) mesangial matrix.
ii) Capillary Basement membrane

- Splenic - 1) Diffuse (Red pulp) - Laradaceous spleen
La REDaceous.
- 2) Follicles (Localized) - white pulp - Sago Spleen.

Liver amyloidosis: 1st - Space of disse - (perisinusoidal)

Best Site for Biopsy - Abdominal fat pad aspirate - Rectal B.

Because - capillaries are first affected)

Sensitivity - 80%.

Isolated organ amyloidosis - Specific organ - choice of B.

∴ Senile Systemic amyloidosis → Cardiac Biopsy