

Breast Cancer.

i) gene expression profiling - eg. ERT, PR, HER. neu.

ii) molecular classification of Cancer.

→ Molecular classification of Breast Ca based on gene expression profiling

a) FISH Congenital malformation - metaphase

Oncological Specimens - Interphase

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

fluorescence painted on entire genome of one chromosome

a

2) Multicoloured FISH - entire genome on all gen chromosomes

Spectral Karyotyping

simultaneously

Spectral Karyotyping

fluorescence Computer generalized.

Immunology

Immunity

Innate

Acquired

- Birth / 1st line of defence

- memory ⊕

- Non memory

- Specific ⊕

- Non-Specific

- B 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]

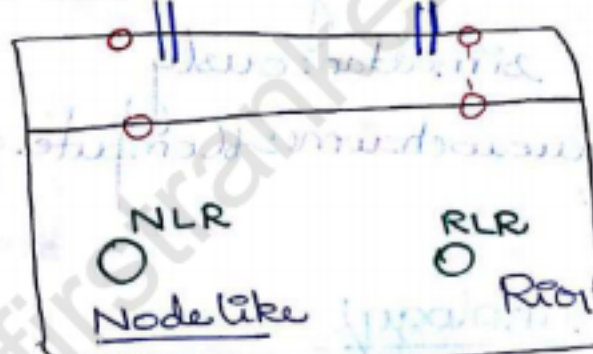
Pattern Recognition Receptor.

① TLR

② CLR - C-type Lectin (fungal)

membrane

cytosol



i) metabolic byproducts

- lactic acid (involved in GI tract pathogenesis)

ii) Flagellated organisms

iii) Tonic disturbances

iv) also associated with NOD-like Receptors.

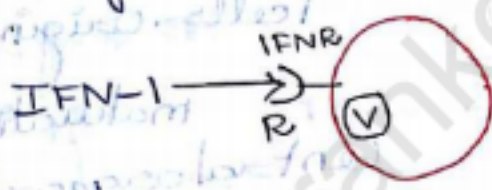
Toll-like Receptor - TLR: Best defined PRR.
 TLR-2 → Gram +ve, Leptospira, fungal infection
 TLR-4 → Gram -ve (endotoxin)

MOA: epithelial, endothelial, APC.
 Bact
 TLR-2 in APC



→ cytokines → kill Bacteria
 IRF (Interferon regulatory factor)
 IFN-1
 against Viruses

MOA



Receptor mediated

(Inhibit) Interfere with virus Host cell nuclear acid Replication

Immune Cells

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

Reassortment

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

3-14/15C, 33 - Monocyte/macrophage

CD-14

NOTCH gene

Tcell

CD-1-8

CD-28

Pan Tcell - CD3

Tcells - Origin - BMT

maturation - Thymus

Central organ - Organ of maturation

Myeloid markers - MPO > 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

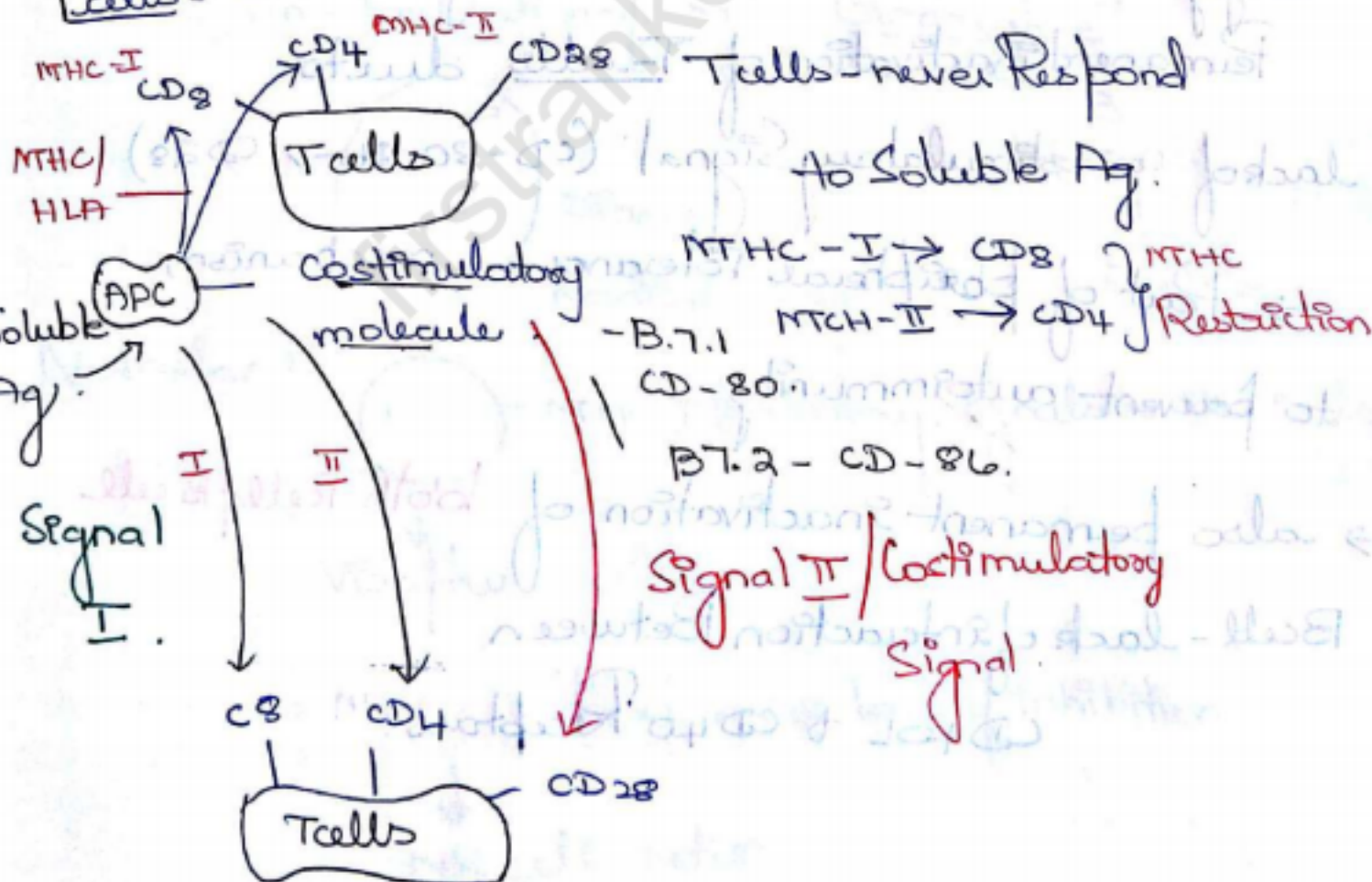
Transferrin Receptor - CD71

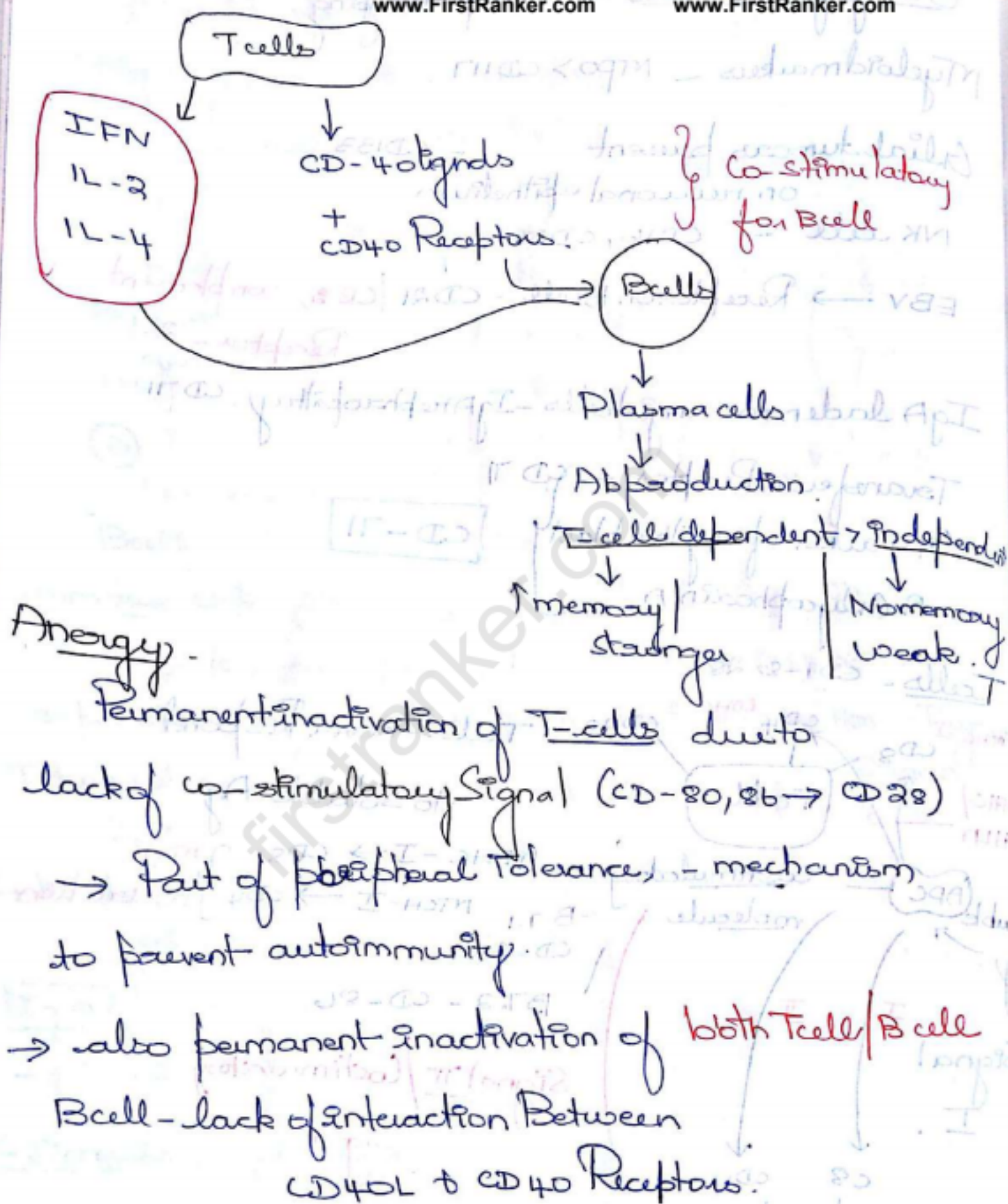
Marker of erythroblast

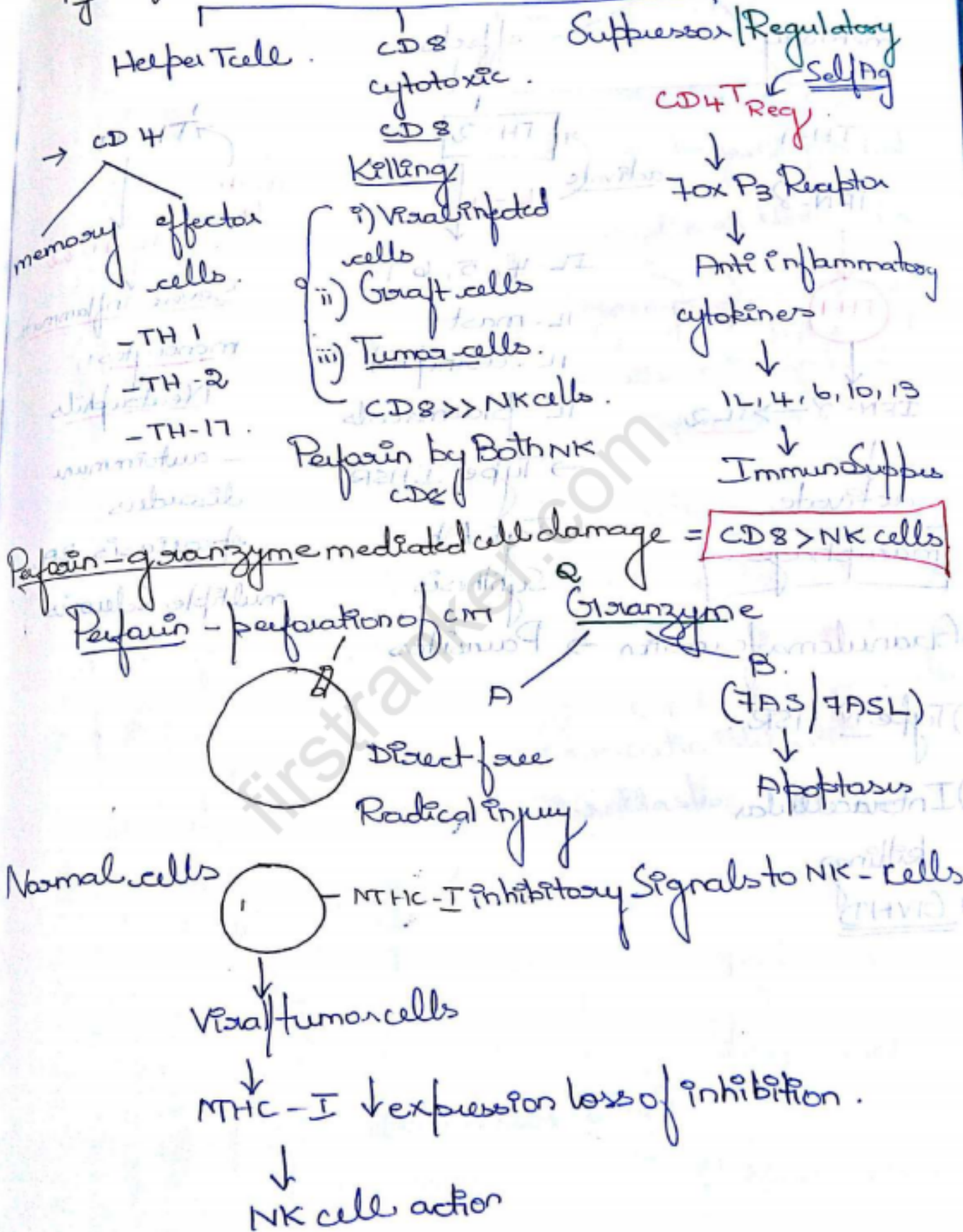
Glycophorin A

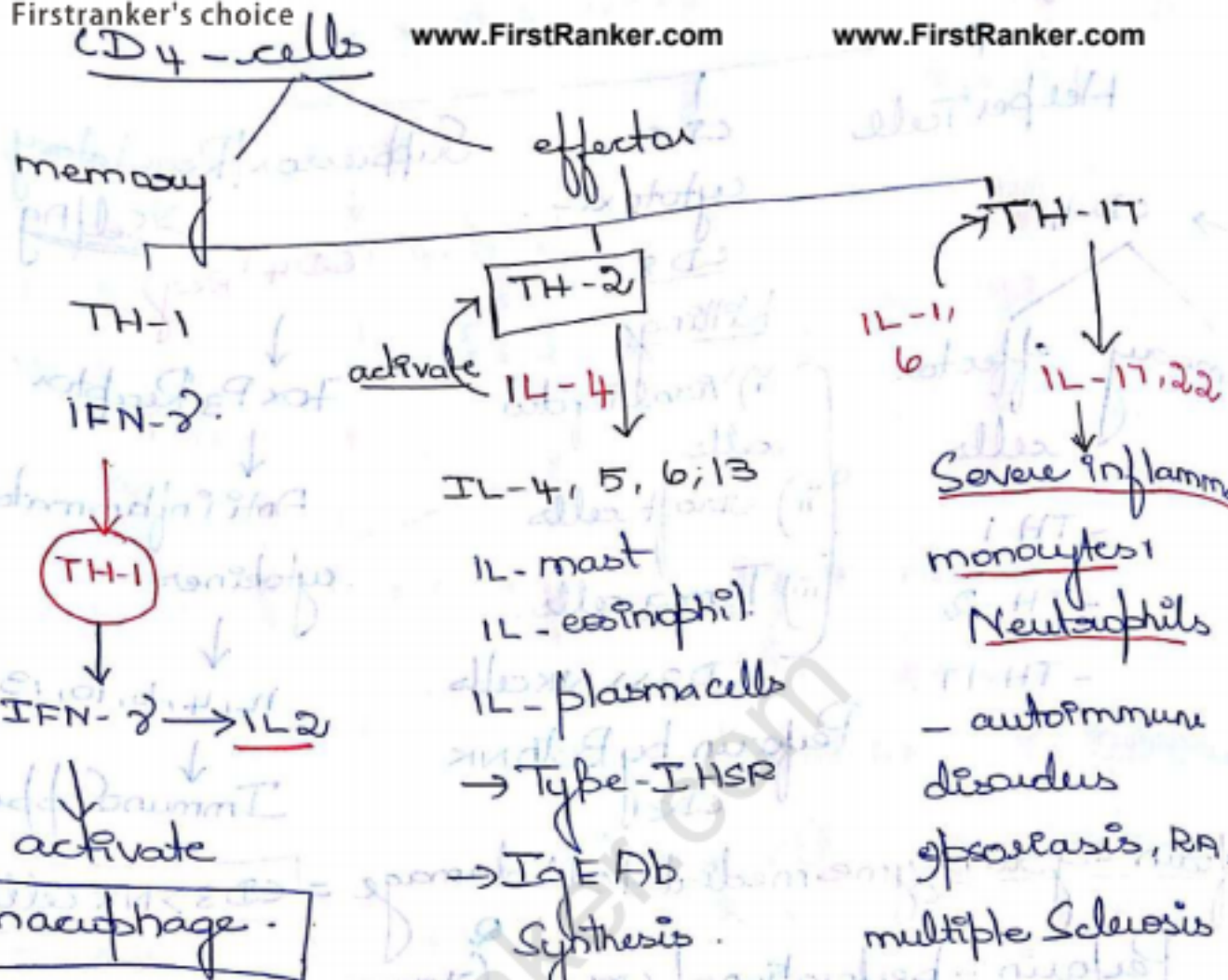
CD-71

T cells - CD1-2, 28.









- 1) Granuloma formation → Parasites
- 2) Type IV HSR
- 3) Intracellular killing
- 4) GIVHD

Professional
MHC-II

- Immature Dendritic cells - Langerhans
- Matue DC - most potent.
- Macrophage
- B-cells.

i) Epithelial cells (few)

eg - thyroid epithelial cells.

ii) Thymic epithelial cells.

~~Thymocytes - precursor of T cells~~

iii) m-cells - microfold cells.

S. Intepithelium - Peyer patches

iv) All endothelial cells

v) All glial cells - astrocytes
oligodendrocytes
ependymal cells

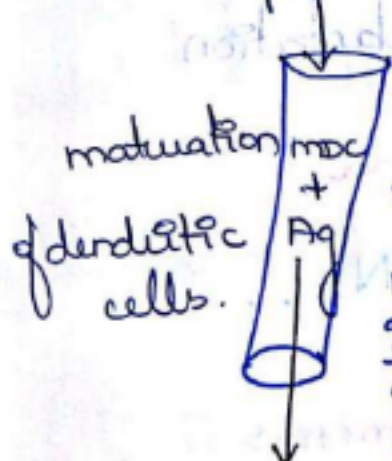
vi) Pancreatic Islet cells.

vii) Fibroblasts

Ag + Immature
Dendritic
cells.

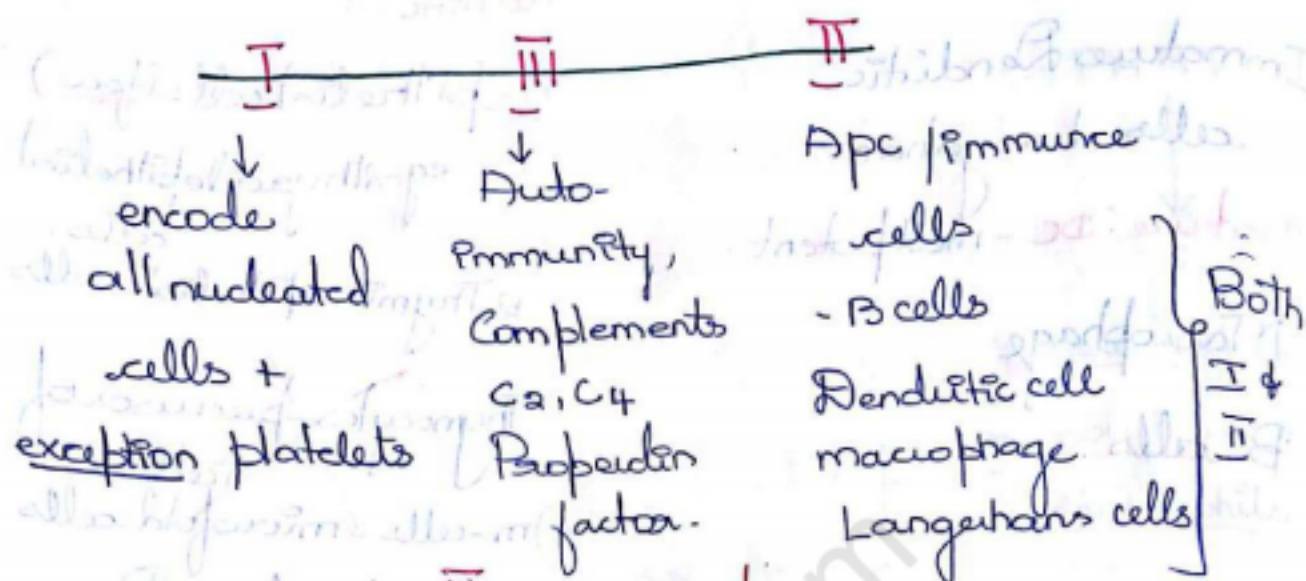
↓
cytokine.

↓
epidermal
Seperation



Naïve T cells (not exposed to Ag)

↓
effector T cells.



Graft Rejection

GVHD

C3
HSP, TNF- α .

- CD4 T, c8T, Both MHC - I, II

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

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

m/c Cancer associated with Organ Transplantation

SkinCa (SCC) > NHL > Kaposi Sarcoma

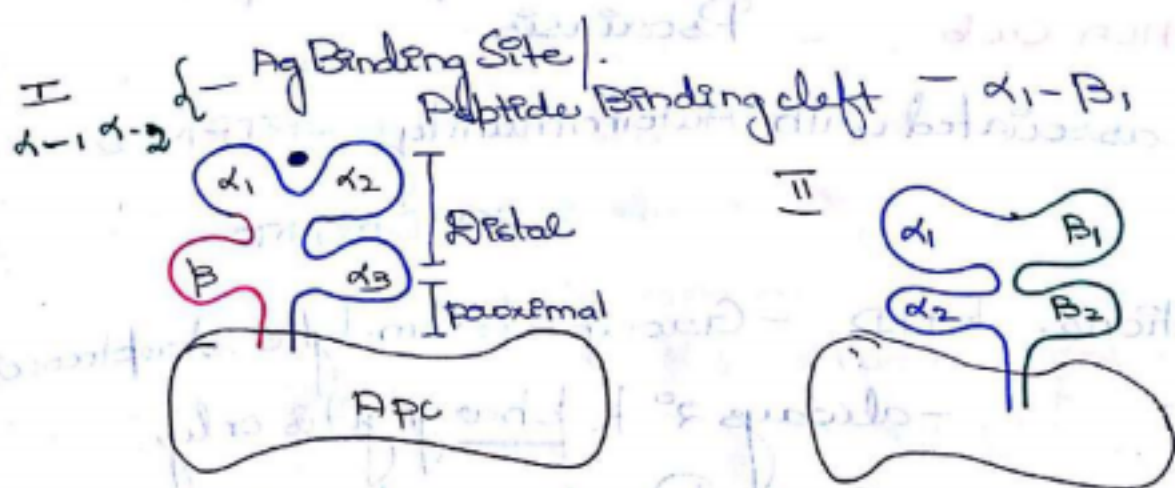
[general m/c - SkinCa - Bcc] HIV-m/c - NHL

Lung Transplant - m/c Cause of death - **Pseudomonas**

Lung Infection

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

size important, not
important in - Renal Transplant



Autoimmunity

Loss of Immunological Tolerance (Both central & peripheral)

Immunological Tolerance - (1) turn 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

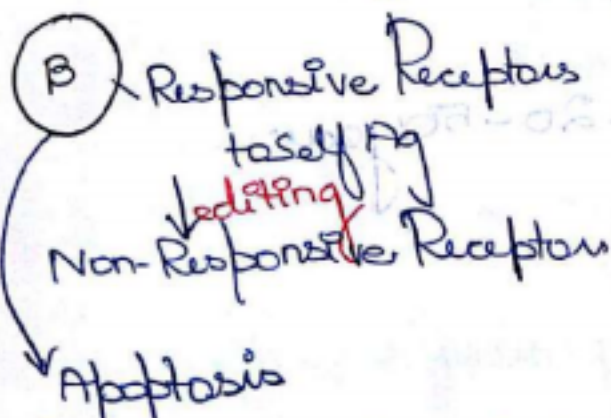
4) Ag - Sequestration

i) Brain

ii) eye

iii) Testis

Immune privileged sites



If not able to form non responsive

Genetic 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.



Ag - protein part that bind to Ab

epitope → hidden

Cryptic epitope

Conformational change

exposed epitope

Streptococcal Ag

Ab

Autoimmunity: Females > Males.

Reproductive age - 20-50 years.

Oral ulcers

Malar Rash.

Phototoxicity Ro - SS-A

Myocarditis - Ro Ab

→ Shrinking lung Syndrome - Ro Ab

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

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 P ab

m/c System involved - musculoskeletal System

Hematology - 85%

m/c presentation - Arthralgia - 95%

m/c Cause of Death - myocardial infarction

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

Antibody-

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

Indirect immunofluorescence -

- 1) RIT/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
LE-cell



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

→ RNA polymerase-III Ab

associated with acute Renal

crisis / Cancer

Localised



anti-centromere-Ab

CREST / Scleroderma

→ NTest 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

associated with
autoimmune diseases

→ RA (m/c)

→ SLE

→ Chronic active

Hepatitis / autoimmune
Hepatitis → PBC.

→ Marginal zone B cell lymphoma

glandular

Ray-eye

Keratoconjunctivitis

Sicca

→ Xeroderma-day
mouth.

Chronic Inflammation →
(polyclonal)

Δ Sjogren

Serology

SS-A - Ro - most Sensitive

SS-B LA (most Specific)

Graft Rejection

i) 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.

Preformed Ab
↓ ↓ ↓
- endothelium - Ag.

Biopsy

Site → minor Salivary gland
of lips.

earliest - perivascular
periductal lymphocytic
infiltrate



2) Acute Graft Rejection - $\text{II} > \text{IV}$ HSR

Humoral

Ab $\rightarrow$ endothelial Ag

Type-II HSR

$\rightarrow$ Blood vessel - Complement deposition

Cellular

C_4, CD_8

Type-IV HSR

$\left. \begin{array}{l} \text{Blood vessel - Complement deposition} \\ \text{Type-II HSR} \end{array} \right\} \text{C}_4 \text{ Diagnostic}$

3) Chronic Graft Rejection - $\text{CD}_4 \text{ T} / \text{CD}_8 \text{ T}$

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 CD_4 T cell immunity

Acute /

< 100 days

Chronic

> 100 days

Organs affected - All organs

Rare - lungs m/c skin

Skin - Simple erythematous

Scleroderma like

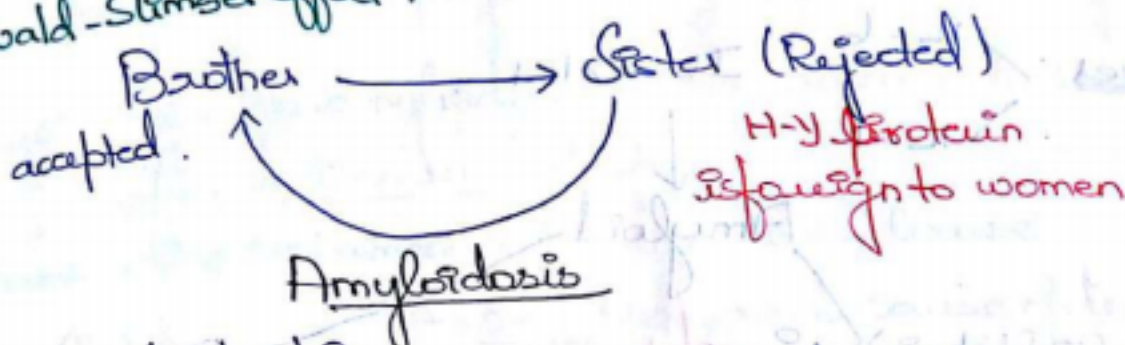
Sex-linked dominant

www.FirstRanker.com

www.FirstRanker.com

Tetrapeptide H-Y linked disorder

Archwald-Slimser effect.



Amyloid - glycoprotein.

Chromosome - 21

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

} electron microscopy.

Pleated Sheets - X-Ray diffraction microscope.

Congo-Red Stain

Ordinary

(Red/Pink)

Fibrin/Collagen/Hyaline
also Red

Polarized microscope.

Apple green birefringence
(Diagnostic)

→ Amyloid always extracellular, acellular, pink

Other stains:

Hyaline.

Thioflavin-T.

Toluidine Blue.

Methyl violet

Crystal violet

→ Silver methenamine: used for amyloidosis

Bluidine Blue - also stain for mast cells

Liver / IL-6 IL-6 > 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°)

Pan-
neoplastic: Renal cell Ca,
Hodgkins
Lymphoma

Hemodialysis - Aβ₂ microglobulin

APAP → Psion disease

A. Cal → calcitonin - medullary Ca of thyroid

AIAPP 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

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

Splenic

- 1) Diffuse (Red pulp) - Lacunaceous 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 - Redal B.

Because - capillaries are first affected)

Sensitivity - 80%.

Isolated organ amyloidosis - Specific organ - choice of Bx

∴ Senile Systemic amyloidosis → Cardiac Biopsy