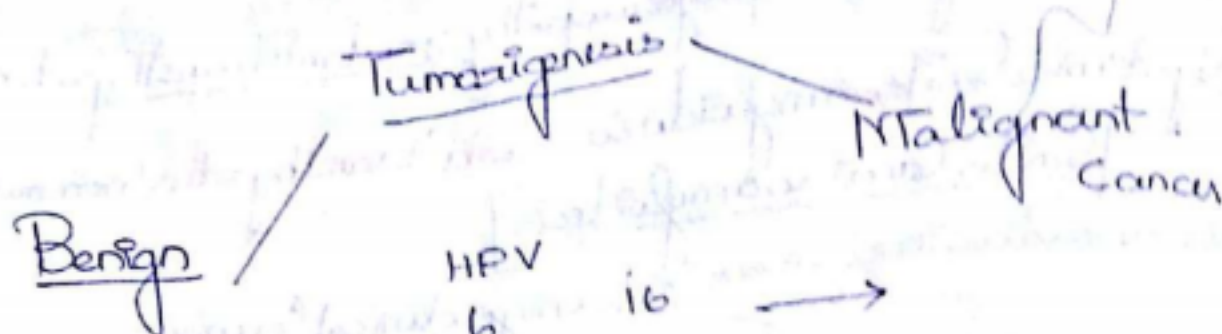




Characteristic-

1) Rate of growth - Monoclonal

Hematoma - Benign tumor
- clonal in origin

Hematoma } non-neoplastic
Chondroma } polyclonal

[abnormal tissue in
① anatomical site]



ectopic Rests of
normal tissue.

2) Metastasis - Sure sign of malignancy

exception

RCC

Glioma

Metastasis ⊕

Carcinoma

pheochromocytoma
pituitary
Parathyroid

homot

Adenoma

Routes

Lymphatic

Hematogenous

Sarcoma

epithelial tumors

* Alveolar Rhabdomyosarcoma

except -

RCC > HCC

→ Osteogenic Sarcoma

- Rhabdomyosarcoma

embryo

Pleomorph

Angioinvasive

* → Synovial Sarcoma

Alveolar

FirstRanker.co

→ Completely Irreversible

N/C Ratio - 1
Amplified

Complete loss of differentiation

Ca-In situ-
Basement membrane
Intact

-Hallmark of malignancy
mets $\ll$ Anaplasia

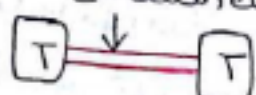
+) Protooncogene $\xrightarrow{\text{mutation}}$ Oncogene

- 1) Protooncogene mutation → Oncogene
 2) Self Sufficiency [don't require growth factor]
 3) Resistant to growth inhibitory signals (Tumor Suppressors)
 4) Evasion from apoptosis [Bcl-2 antiapoptotic expression]
 5) Limitless Replicative potential (Telomerase)
 6) Angiogenesis (m/c Cause - Hypoxia) - HIF-1 gene → VEGF, bFGF
 without angiogenesis limit of growth 1-2mm
 ↓
 disorganized B.V.
 6) Metastasis - m/essential factor → Angiogenesis
 Balance } Metastatic gene ↑↑ | Anti-metastatic gene ↓↓
 b/w } → ezrin (RMS) (first to discover)
 → miR-10b
 Snail, Twist → Breast Carcinoma
 i) NMT-23.
 ii) miR-226, 335
 iii) KAI-1 - prostate Ca
 iv) KISS - melanoma

EMT - Epithelial mesenchymal Transition

- also associated with wound Healing & Repair, Organ fibrosis.

e-cadherin [B/w normal/tumor cells]



↓ epithelial downregulation (e-cadherin)

Tumorous cells

1) Detachment.

2) Degradation of ECM. By.

proteases - i) plasmin

ii) MMP

MMP₂

MMP₉

Better.

Break ECM +

Synthesis of BV

3) Attachment with ECM

① - integrin + ↑ Synthesis of ECM protein

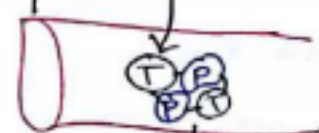
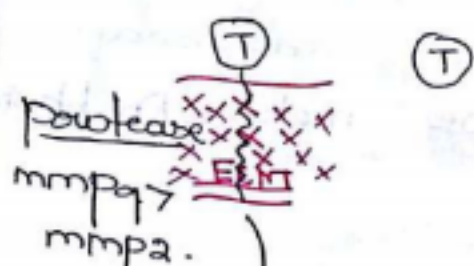
mesenchymal upregulation

[collagen, Laminin, Vitronectin, Fibronectin]

4) Tumor emboli. in BV mostly associated

Cell + platelet

Organ.



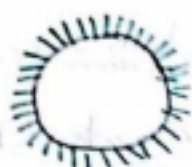
Detachment
Degradation
attachment



Antitumor cells - CD8, NK cells, NT macrophages

i) Ag - ve Tumor cells

ii) glycocalyx coating



iii) Ca cell $\leftarrow$ (Circled) - express FAS/FASL $\rightarrow$ undergo apoptosis

vii) Ca-metabolism - **Aerobic glycolysis** (Warburg effect)

Warburg $\rightarrow$ 1921

$\downarrow$
Nobel prize - 1931

, Basis of PET Scan.

Gene Repair Defect - Chromosomal instability Syndrome.

Bq - Bloom Syndrome

F - Fanconi

A - Ataxia Telangiectasia

X - Xeroderma pigmentosa (nucleotide excision repair Defect)

Lynch Syndrome $\rightarrow$ AD

Homologous DNA defect disorder.
AR

uv light
 $\downarrow$
Skin

Pyrimidine Dimer

$\rightarrow$ Repaired by excision $\rightarrow$ $\therefore$ accumulated in XP.

Skin Ca

Lynch Syndrome - DNA mismatch Repair gene defect
(Spell checker) ↓
microsatellite instability < Stomach
Colon
Chromothripsis - Dramatic Chromosomal
Catastrophy

Random damage of chromosome

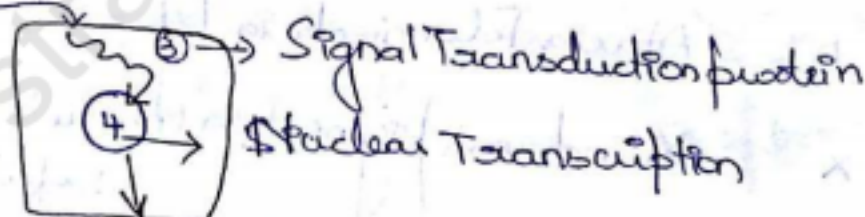
- activation of oncogenes
- inhibition of Tumor Suppressors

eg: Osteosarcoma, Glioma

Protooncogenes: Helps in normal proliferation & differentiation

1) growth factor

2) GF - R



⑤ Cyclin & Cyclin Dependent Kinase

Cell Cycle - $G_0 \rightarrow G_1 \rightarrow S \rightarrow G_2 \rightarrow M$

Any Protooncogene $\rightarrow$ oncogene - affect Cell Cycle

↓
Tumorigenesis

- i) PDGIF
- ii) FGF
- iii) HGF
- iv) TGF- α (TGF- β -tumour suppressor gene)

2) Growth factor Receptor group

- i) ERBB-1: Adenocarcinoma of lung
- ii) ERBB-2 [Her-2/neu] - Breast Ca.
- iii) RET - Protooncogene - medullary Ca of thyroid.
- iv) C-KIT - GIST, melanoma, Seminoma, myeloid Cancers.

CD-117

3) Signal Transduction Protein

- a) RAS - m/c oncogene mutation in Human Cancer.

P53 $\rightarrow$ 50% Human Ca $\rightarrow$ 53%

RAS - 20-30%

P53 $\rightarrow$ RAS

Ca. Pancreas - m/c mutation. KRAS (60-70%) $\ll$ p-16 (95%)
m/c oncogene mutation - KRAS.

2) ABL

BCR-ABL

CML
(good)

ALL
(poor)

$>60\%$ Skin Ca $\rightarrow$ BRAF

③ BRAF $\rightarrow$ 60% Skin Ca (melanoma)

$>90\%$ Human Ca $\rightarrow$ BRAF

↳ Langerhan Cell Histiocytosis (monoclonal)

1) JAK - 2 - Polycythemia vera

NOTCH - T cell leukemia

4) Nuclear Transcription Factor -

Myc; Fos; Jun

↓
n-myc amplification

↓
neuroblastoma (Bad) }
medulloblastoma }

C-myc - Burkitt's lymphoma
Translocation

5) Cyclin + Cyclin Dependent kinase -

Cyclin

D₁

Bcl-1

mantle cell lymphoma

D₂

(Bcl-2)

follicular lymphoma

CDK4 mutation

glioblastoma

melanoma

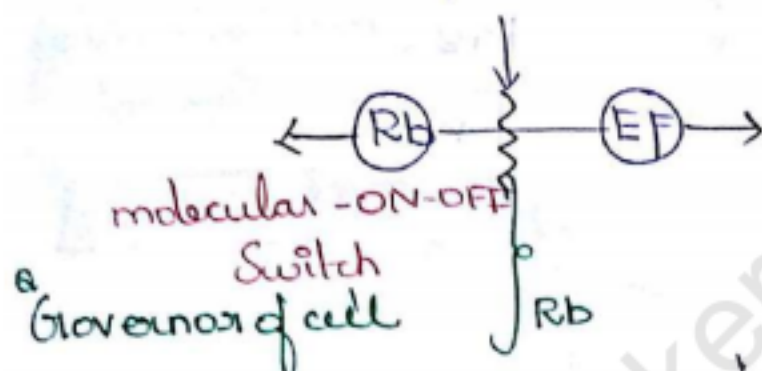


[OFF] $\rightarrow$ Rb + EF-2 (inactive) [EF-elongation factor]

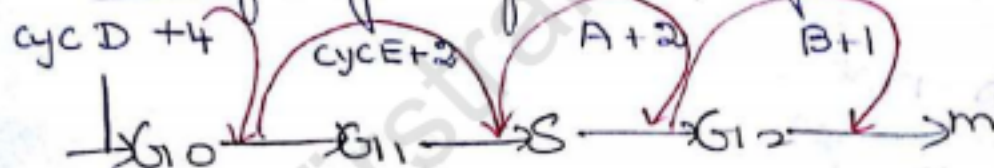
D+4 $\rightarrow$ O2 phosphorylation

$\uparrow$ ATP

Rb- allows
G₁ $\rightarrow$ S



Removal of elongation factor - progression of cell cycle



mid G₁ phase - Cyclin - D Synthesis

Check point - G₁ S

errors before DNA
replication

G₂ M

after DNA
replication errors.

Cyclin A $\ll$ Cyclin B

Cip-kip family

(Cip-waf)

- Non specific inhibitor

P21, P27, P29

P53 induce → P21

[indirect
cell cycle
inhibitor] G1-S → G2-M

P16INK4a

- Specific inhibitor

Cyclin D + K4
K6

P15

P16

P18

P19

Tumor Suppressor Gene

BRCA-1 : Ch-17

BRCA-2 → Ch-13

male Breast Ca { BRCA 2 & BRCA1
Ovarian tumor }

BRCA-1 medullary Breast Ca.

↓

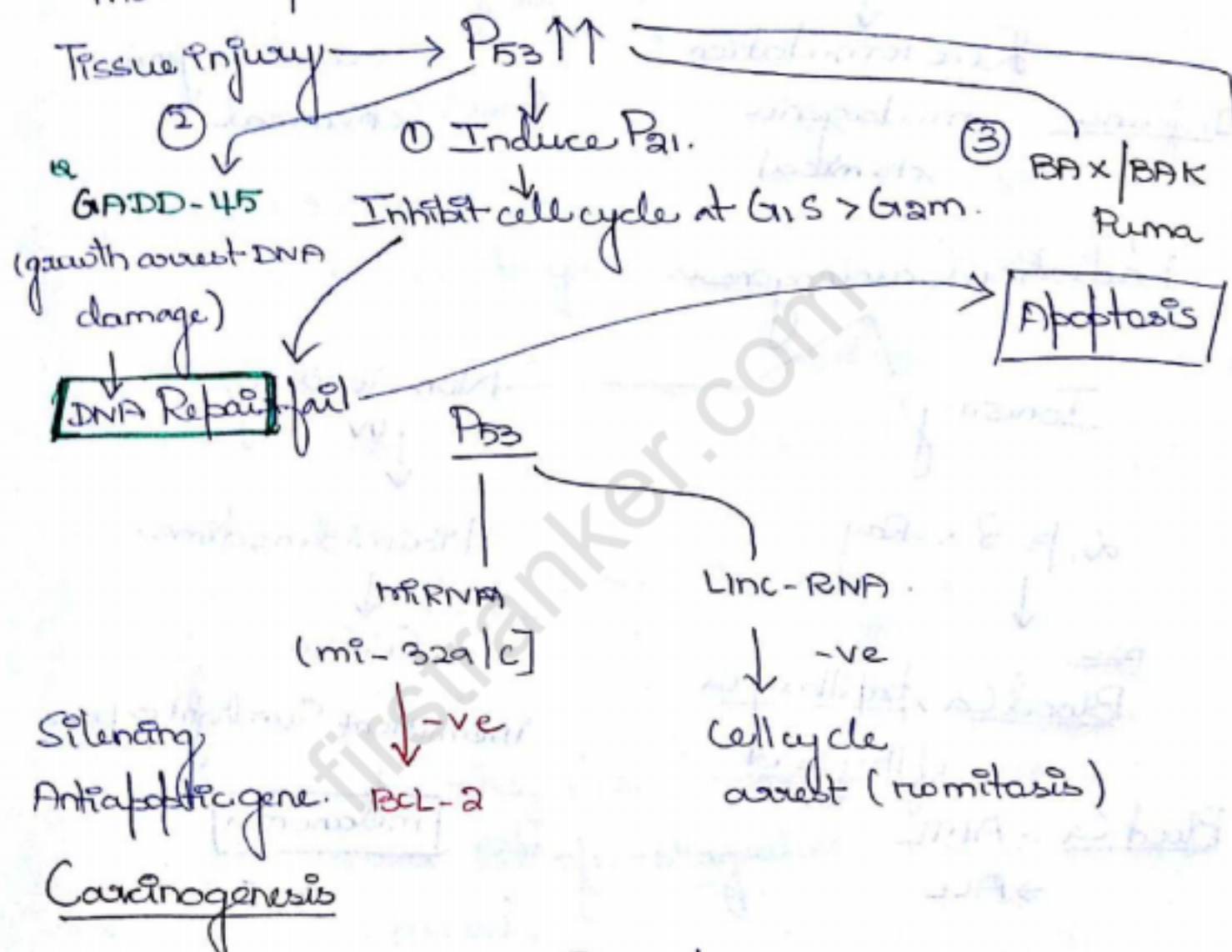
Triple negative [ER-ve, PR-ve, Her-2-ve]

BRCA-2 = ER+, PR+ve Her-2-ve

P53: Ch-Hp molecular weight - 53k Dalton

Li-Fraumeni Syndrome → multiple Ca.

guardian of genome
molecular policeman



1) Chemical Carcinogenesis- Benzopyrene

↓
Tissue damage

• P53 ↑↑

↓
Liver.

• Cyt - P-450

Somatic mutation.

DNA Repair

↑
nucleophilic.

↑
Carbonium Ion

↑
epoxide

Benzopyrene

www.FirstRanker.com

Salmonella typhimurium
Chemical + (normal Histidine negative)

Histidine +ve

Histidine -ve

Due to mutation

non mutagenic

Inference - mutagenic chemical

chemical

Radiation Carcinogenesis

Tonising

Non-Tonising

α, β, γ X-Ray

uv

Plasmid dimer

mc

Blood Ca $\rightarrow$ papillary Ca of thyroid

Skin Ca

Intermittent Sun light exposure

Blood Ca - AML

melanoma

$\rightarrow$ ALL

$\rightarrow$ CML

CLL is not associated with radiation

→ Microbe 1st established → H. pylori gastric adenocarcinoma > NHL

m/c NHL lymphoma of stomach - DLBCL > MALToma

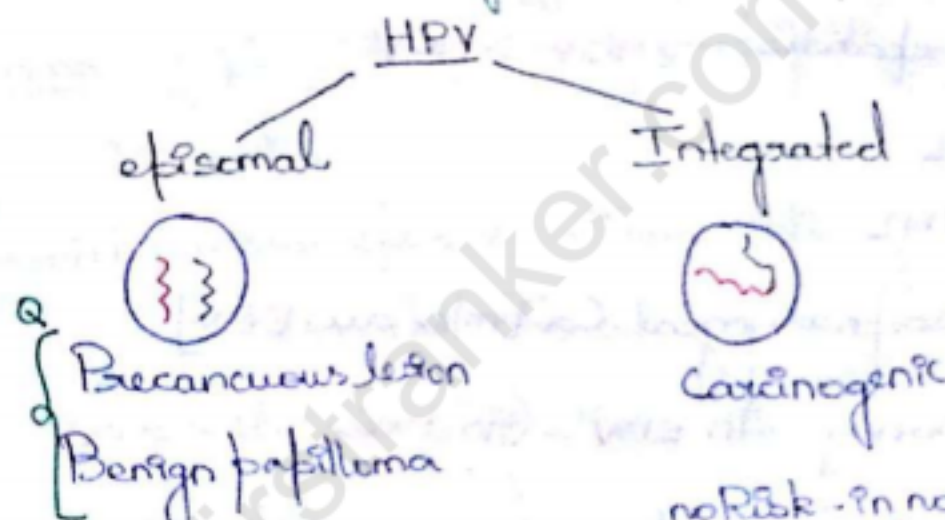
NTALT - m/c site ileum (Peyer's patches)

NTALToma - m/c site - stomach

→ HPV - 6, 11 - Papilloma 16, 18 - Carcinoma

E₆ → inactivate P₅₃

E₇ → inactivate Rb gene



HPV → Risk for esophageal SCC - only in endemic regions

Leukoplakia - Risk of esophageal SCC

Vit - A, Zn, Se - protective

HBV

↓
DNA

Nuclear
damage

↓
10 years

HCC

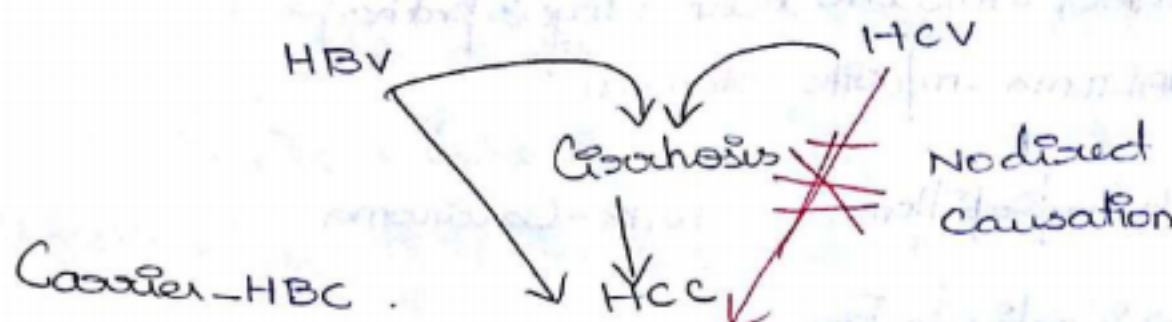
HBV > HCV

HCV → 21-30 yrs

HBV can also cause HCC directly, even without cirrhosis

undergoing Cirrhosis

But HCV - donot cause direct HCC.



Chronicity, Cirrhosis → HCV

Transfusion Hepatitis → HBV > HCV

→ EBV:

HL
NHL

Nasopharyngeal Ca [m/c w/ EBV]

m/c malignancy with EBV - Gastric adenocarcinoma

Tumour diagnosis approach

1) Tumour markers - Never confirm diagnosis

Uses - prognosis,

Response to Rx

→ may correlate to size of tumour.

eg- α -HCG - not a marker.

↓
FSH / LH / TSH

β -HCG → Chorio Carcinoma.

↓
variant

Fibromellar variant - (N)-AFP; Neurotension marker

→ α -FP - Non Seminomatous; max elevation yolk sac tumor/ended
Seminomatous - LDH, PLAP 15% - arise from Syncytiotrophoblast
15% - β -HCG.

Yolk Sac tumor - α FP, α -1 antitrypsin.

CD30+ve, C-KIT-ve: embryonal Ca.

N melanoma - m/Sensitive - S-100; m/Specific HMB-45.

→ Vimentin.

→ mitf-1 (microphthalmia Transcription factor-1)
↓
Choroidal melanoma.

Cytokeratin - for epithelial cancers.

Ca15 → Breast Ca

Ca19.9 → pancreas, Colon

Ca125 - Ovarian tumor (not used for Screening)

↓
only for prognosis.

II FNAC: Size: 22G - 27G.

4± 1) Patient's consent.

2) Bleeding Diathesis

3) H/o anaphylaxis

4) Testicular malignancy

→ To rule out infatality

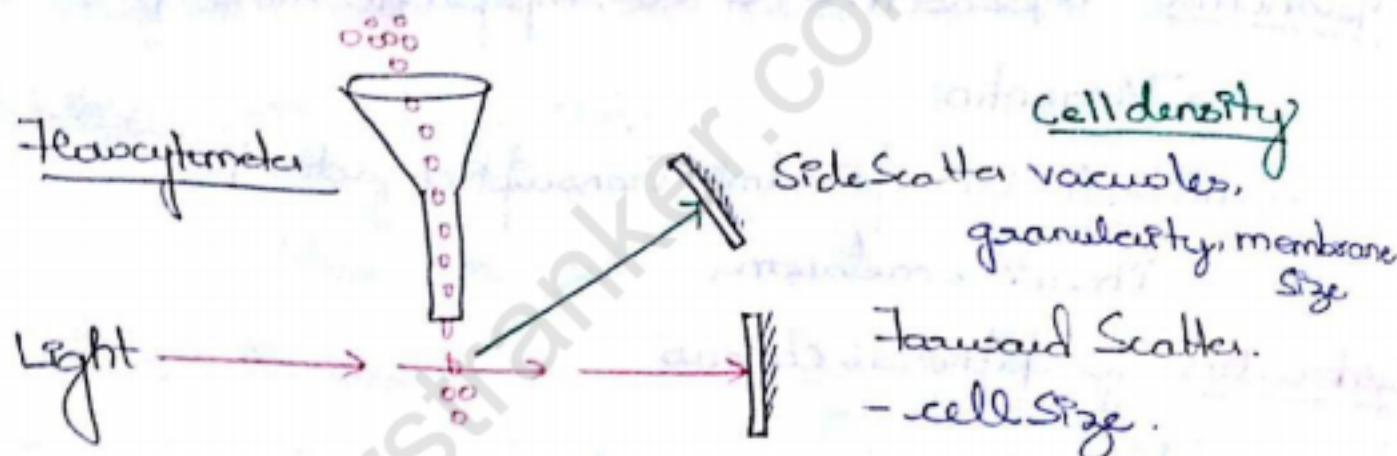
→ Follicular adenoma vs Follicular Carcinoma - FNAC not useful.
Confirm - only by tissue Biopsy

III Immunophenotyping - Study of CD markers.

Flow cytometry - ideal for lymphocytosis.

→ simultaneous provide Immunophenotyping

∴ IOC → CLL, ANTL.



IV Immunohistochemistry - IHC

Artificial (cloned Ab) → Tumor Ag - complex under microscope.

Basis - Intermediate filament

1) Cytokeratin (epithelial tumors)

→ Carcinoma (any Carcinoma)

2) Vimentin - Connective tissue

melanoma, Sarcoma

RNTS

RNTS myogenin > myo D-1 > Desmin.

4) Neurofilament -

a) Neuroendocrine tumor [NET]

→ Carcinoid

→ Pheochromocytoma / Paraganglioma

→ Small cell Ca of lung.

→ Neuroblastoma.

b) Neuronal tumor of Brain

→ ganglioglioma

→ gangliocytoma

→ Neurocytoma.

5) Glial Fibrillary Acidic Protein - GFAP

→ Glial tumor of brain - Astrocytoma.

↓
Oligodendroglioma
ependymoma.