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WHAT YOU ARE NOT READING & NOBODY IS TEACHING YOU

THE PATHOLOGY COMIC BOOK

70 high-yield panels — straight off the whiteboard, into your exam.

For FRCPath Part 1, FRCPath Part 2, NEET-SS Pathology & MD/DNB Pathology

FRCPath Part 1 | FRCPath Part 2 | NEET-SS Pathology | MD/DNB Pathology

"Scroll AI content. Study from the OG master."

By Dr. Maitrayee Roy & Dr. Akshay Bali — eLearning FRCPath

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Before You Dive In...

Somewhere between a whiteboard marker running dry and a 2 a.m. Instagram scroll, the eLearning FRCPath team has been quietly building the pathology cheat sheet nobody handed you in med school. This book is that entire feed, rescued from your camera roll and put in an order that actually makes sense — bone leads into skin, lung leads into lymphoma, kidney leads into colon. Every panel keeps its original artwork exactly as posted. The little caption underneath is just us narrating — think of it as the sarcastic senior resident standing over your shoulder while you revise. Read it once for fun. Read it again for the marks.

Table of Contents

Meet Your Instructors

The pathologists behind every whiteboard scrawl in this book.

MR

Dr. Maitrayee Roy

MD FRCPath (Histopathology)

Experienced pathologist with a demonstrated history of working in the hospital & health care industry. Skilled in Histopathology, Hematopathology, Chemical Pathology.

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MD DipRCPath (Histopathology)

Experienced pathologist with a demonstrated history of working in the hospital & health care industry. Skilled in Histopathology, Hematopathology, Chemical Pathology.

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01

BONE & SOFT TISSUE PATHOLOGY

The lesions that look alike under the scope until one marker ruins the disguise.

8 panels • maps to:

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WHAT YOU ARE NOT READING & NOBODY IS TEACHING YOU

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MDM2 SAVES THE DIAGNOSIS

In bone & soft tissue lesions, **morphology can be misleading.**
MDM2 helps you make the right call.

THE DIAGNOSTIC DILEMMA

Well-differentiated liposarcoma (WDLS)

vs.

Benign lipoma
Atypical lipomatous tumor (ALT)

They look alike under the microscope!

MDM2 TO THE RESCUE

- **MDM2** gene amplification present in WDLS / ALT
- Detected by IHC or FISH
- Highly specific and diagnostically decisive

MDM2

POSITIVE MDM2 = Think WDLS / ALT

When morphology is equivocal, don't guess. **DO THE TEST.**

One marker.
One correct diagnosis.
Big difference in patient care.

TAKE-HOME MESSAGE:
MDM2 is not just a marker, it's a decision maker.

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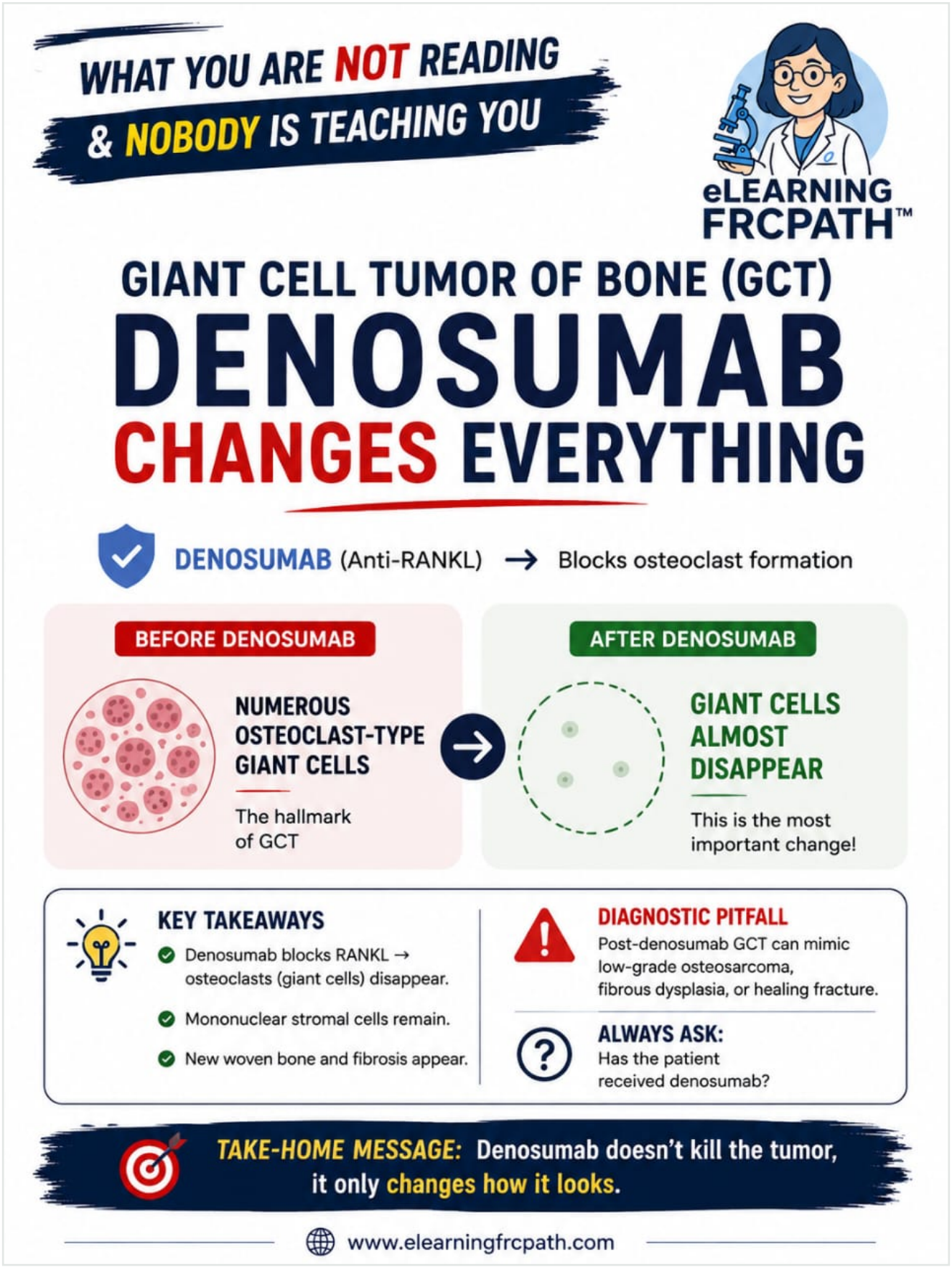
The exam will hand you a bland spindle cell lesion and dare you to call it benign. MDM2 is the friend who stops you making that mistake.



Plot twist: the drug doesn't kill the tumor. It just gives it a really convincing disguise. Don't fall for it.

WHAT YOU ARE NOT READING & NOBODY IS TEACHING YOU

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H3F3A MUTATION IS NOT UNIQUE TO GIANT CELL TUMOR

COMMON MUTATION

H3F3A G34W

~90–95% of GCTs

RARE MUTATIONS

G34L G34M G34R G34V

Same codon, different amino acid

WHY IT MATTERS

Antibody detects only G34W.

- ✕ G34L = negative
- ✕ G34M = negative
- ✕ G34R = negative

Still true GCTs!

PRACTICAL EXAMPLE

Morphology classic but H3G34W stain

NEGATIVE

Could be non-W mutation. Confirm by sequencing.

MORPHOLOGY + MOLECULAR TESTING = ACCURATE DIAGNOSIS

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One negative stain and half the class writes "not GCT" on the answer sheet. The other half keeps the marks.

WHAT YOU ARE NOT READING AND NOBODY IS TEACHING YOU!

SERIES

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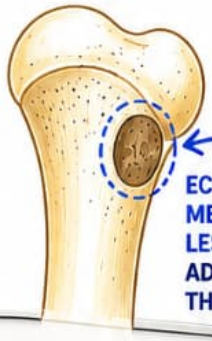
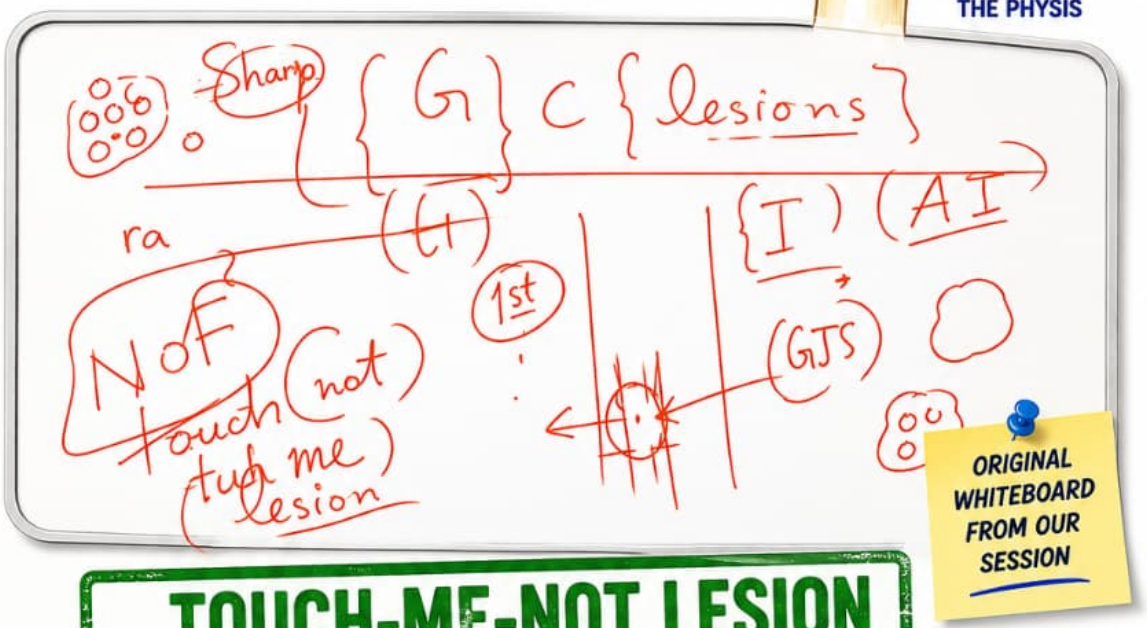
NON-OSSIFYING FIBROMA (NOF)

FIBROUS CORTICAL DEFECT



ECCENTRIC METAPHYSEAL LESION ADJACENT TO THE PHYSIS



TOUCH-ME-NOT LESION

It is most commonly diagnosed in the second decade of life (ages 10 to 15).

TOUCH-ME-NOT LESION

Incidental, asymptomatic finding in growing children.

NO TREATMENT NEEDED!

RADIOLOGICAL FEATURES

Well-defined, eccentric metaphyseal lytic lesion adjacent to the physis with sclerotic rim.

HISTOPATHOLOGICAL PITFALL

Histology can mimic GCT of bone.

ALWAYS CORRELATE WITH RADIOLOGY.

REAL PATHOLOGY. REAL LEARNING. REAL CONFIDENCE.

Also known as: the lesion your radiologist spots by accident and your report is happy to leave alone.

WHAT YOU ARE NOT READING & NOBODY IS TEACHING YOU

4 SOFT TISSUE TUMOR RULES THAT WILL FAIL YOU IN THE EXAM

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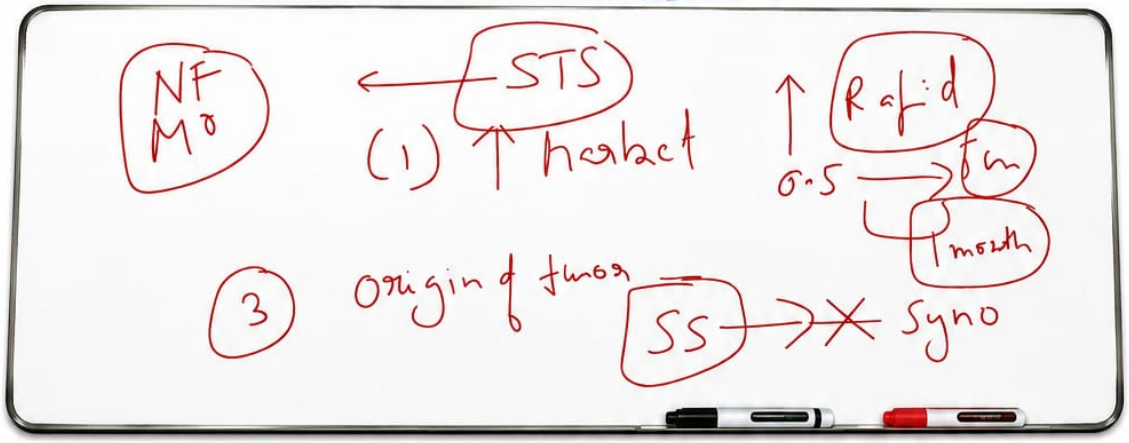
What they teach VS. *what actually happens.*



1 ATYPIA + MITOSIS ≠ MALIGNANCY

Benign entities like Nodular Fasciitis can show marked atypia & mitoses yet remain strictly benign.

2 RAPID GROWTH ≠ MALIGNANCY

Benign soft tissue lesions can grow fast.
Examples: Nodular Fasciitis, Myositis Ossificans.

3 TUMOR NAME ≠ CELL OF ORIGIN

Names can mislead.
Example: Synovial Sarcoma does not arise from synovial membranes or cells.

4 SAME HISTOLOGY ≠ SAME TUMOR

Identical histology can belong to completely different entities.
Use context, IHC, and molecular tools.

RULES EXIST. EXCEPTIONS DEFINE EXPERTISE.

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Four things your textbook swears are always true. The exam has other ideas.

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Smart Pathology. Exam Ready.

WHAT YOU ARE NOT READING AND NOBODY IS TEACHING YOU SERIES

SATB2 | THE DEVELOPMENTAL SIGNAL BEHIND ITS SURPRISING POSITIVITY

A MASTER REGULATOR OF CRANIOFACIAL DEVELOPMENT

COMMON USES OF SATB2 (EVERYONE IS AWARE OF)

1. OSTEOBLASTIC / BONE TUMORS

- Osteosarcoma (especially osteoblastic)
- Osteoblastoma
- Osteoid osteoma

2. GASTROINTESTINAL ORIGIN TUMORS

- Colorectal adenocarcinoma (high sensitivity & specificity)
- Appendiceal adenocarcinoma

KEY TAKE-HOME (THE CLASSIC ONE)

SATB2 positivity strongly supports osteoblastic differentiation or colorectal / appendiceal origin.

WHY SATB2 LIGHTS UP ODONTOGENIC TUMORS

SATB2 is essential for development of the craniofacial skeleton and teeth.

- Neural crest cell differentiation
- Osteoblast differentiation
- Maxillary and mandibular development
- Tooth morphogenesis

Odontogenic tumors arise from tissues participating in tooth development (odontogenic epithelium & ectomesenchyme).

They retain the embryonic transcriptional profile, including SATB2 expression.

SATB2 POSITIVITY = DEVELOPMENTAL MEMORY

Odontogenic tumors remember their embryonic roots.
That's why SATB2 shows up.

SCROLL AI CONTENT. STUDY FROM THE OG MASTER.

SATB2 turning up in a jaw tumor is basically running into your dentist at the gym.

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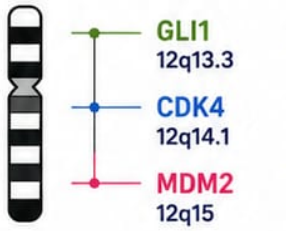
WHAT YOU'RE NOT READING & NOBODY IS TEACHING YOU

THINK BEYOND MORPHOLOGY

GLI1-ALTERED TUMORS VS SOLITARY FIBROUS TUMOR

	GLI1-ALTERED TUMORS (GLI1 amplification / GLI1 fusion)	SOLITARY FIBROUS TUMOR (SFT)
GENETIC ALTERATION	GLI1 amplification or GLI1 fusion	NAB2::STAT6 gene fusion
CELL PATTERN	Nested epithelioid or spindle cells	Patternless spindle cells
VASCULATURE	Branching ("staghorn") vessels	Branching (hemangiopericytoma-like) vessels
STAT6 IMMUNOSTAIN	STAT6 NEGATIVE	STAT6 NUCLEAR POSITIVE

12q13–15: DIAGNOSTIC TRAP



Large 12q13–15 amplicon
↓
Co-amplification of GLI1 + CDK4 + MDM2

MDM2 amplification can occur as part of the same 12q13–15 amplicon as GLI1.
Not every MDM2-amplified tumor is dedifferentiated liposarcoma.
Correlate morphology.

PITFALL

MDM2 AMPLIFICATION ≠ DEDIFFERENTIATED LIPOSARCOMA

Correlate morphology + molecular findings.

THINK BEYOND MORPHOLOGY. THINK GLI1.
CONFIRM WITH RNA SEQUENCING OR FISH.

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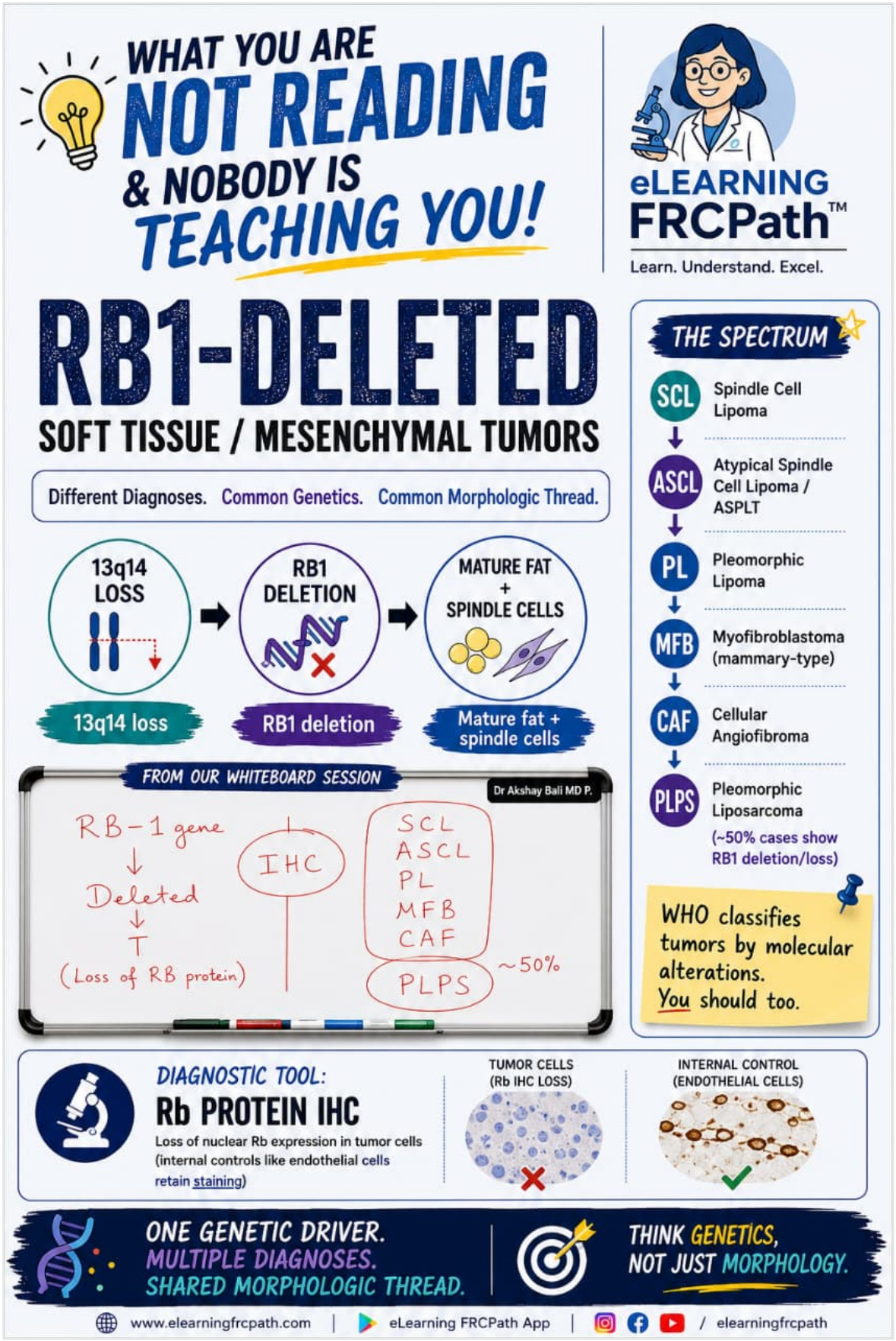
Two staghorn-vessel tumors walk into a lab. Only STAT6 knows which one's which.



One gene deletion, six different names on the request form. RB1 really does get around.

02

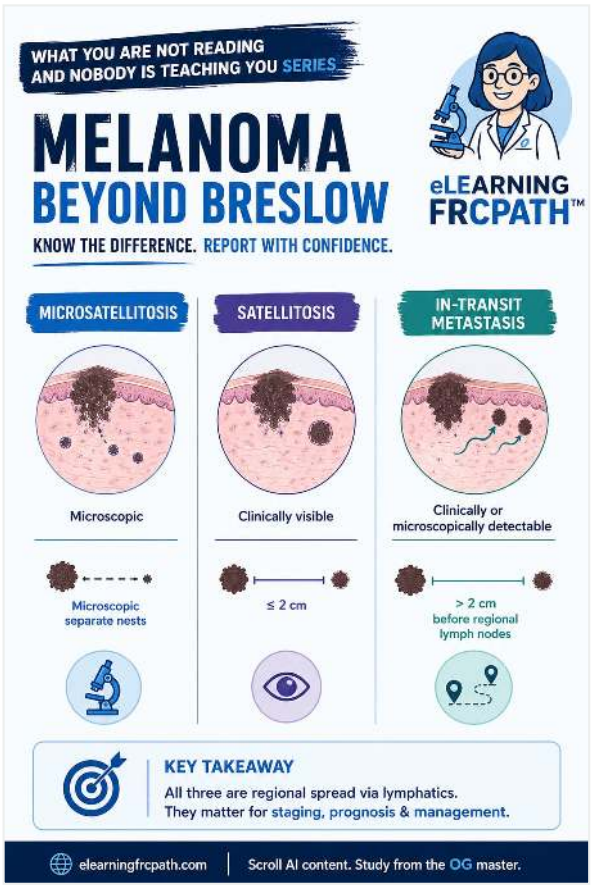
SKIN & MELANOCYTIC PATHOLOGY

Melanoma, Spitz tumors, and the junctions that hold your skin together.

4 panels • maps to:

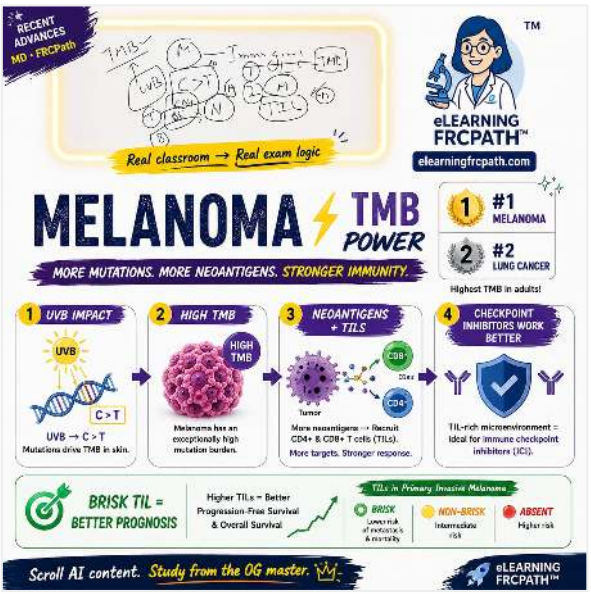
FRCPath Part 2

Double Feature: Melanoma, Two Ways



2cm doesn't sound like much until it's the line between a satellite and a metastasis.

VS



Melanoma racks up more mutations than a first-year's differential list. For once, that's actually good news.

Two panels, one sun-damaged genome.

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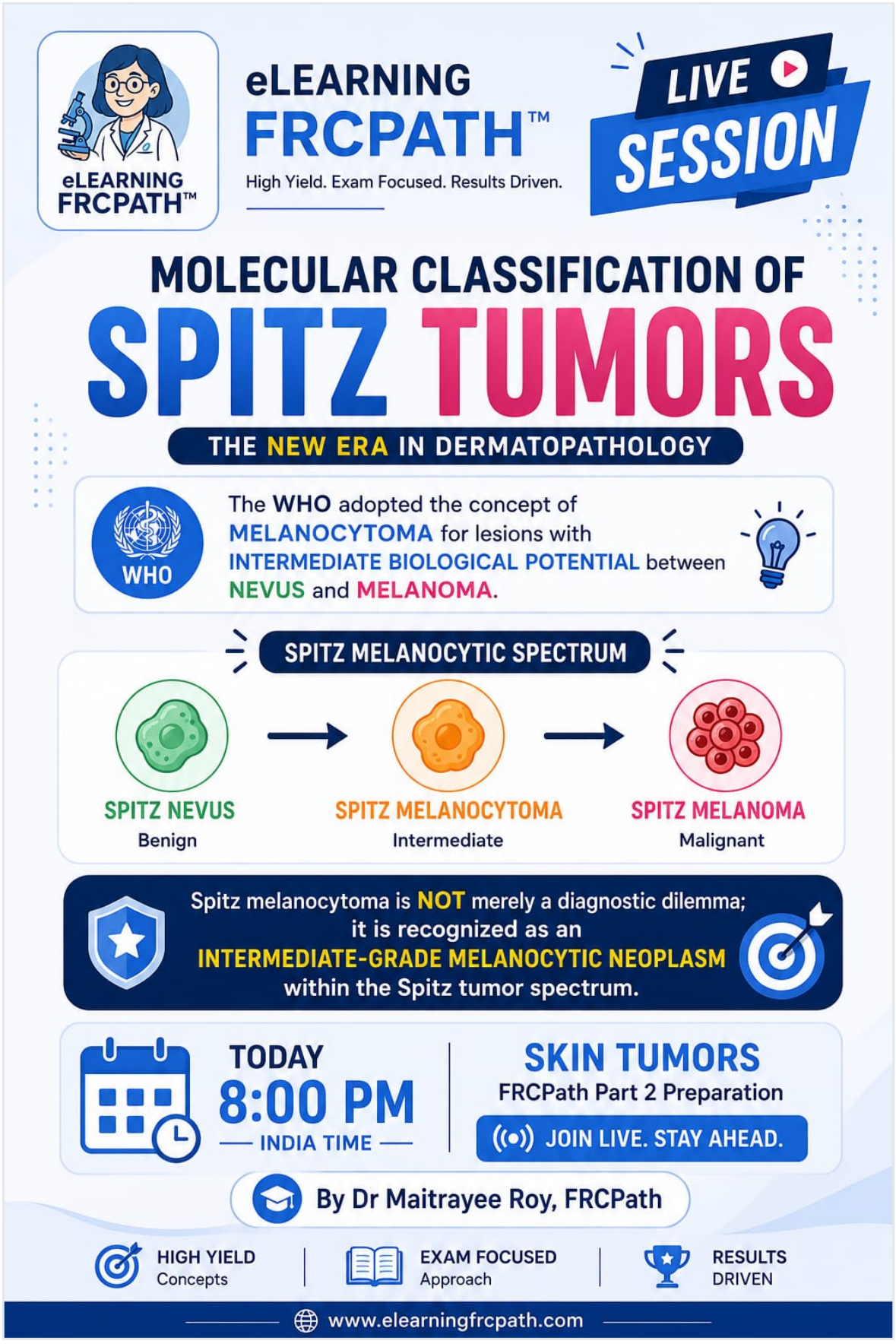

WHO finally admitted what every dermpath fellow already suspected: sometimes a Spitz lesion just won't pick a side.

STRONG BASICS LEAD TO STRONG HISTOPATHOLOGY

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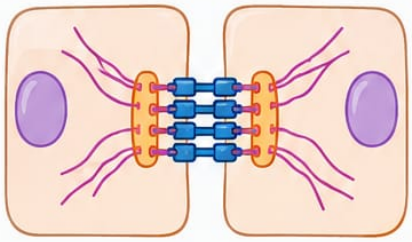
DESMOSOMES vs HEMIDESMOSOMES

DESMOSOMES

Cell to Cell Adhesion



- Links adjacent epithelial cells
- Provides mechanical strength
- Found between epithelial cells

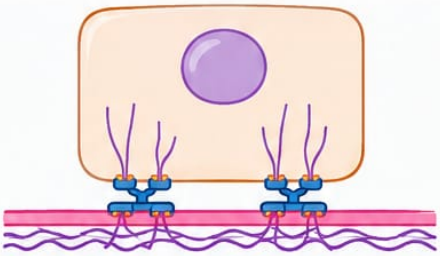
WHEN IT FAILS?

Pemphigus Vulgaris

- Autoantibodies vs Desmoglein
- Desmosomes destroyed
- Loss of cell-to-cell adhesion (Acantholysis)
- Intraepidermal (suprabasal) blister
- Positive Nikolsky sign

HEMIDESMOSOMES

Cell to Basement Membrane Adhesion



- Anchors cells to basement membrane
- Maintains tissue stability
- Found at basal surface

WHEN IT FAILS?

Bullous Pemphigoid

- Autoantibodies vs BP180 (Collagen XVII) and BP230
- Hemidesmosomes disrupted
- Epidermis separates from basement membrane
- Subepidermal blister
- Negative Nikolsky sign

DESMO = DUO (Two cells together)
HEMI = HALF (One cell attached to basement membrane)

STRONG BASICS. CLEAR CONCEPTS. CONFIDENT PATHOLOGIST.

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Desmo means duo, hemi means half. Mix that up on exam day and you'll have a blister of your own.

03

HEMATOLYMPHOID PATHOLOGY

Reed-Sternberg cells, popcorn cells, and the markers that tell them apart.

4 panels • maps to:

FRCPath Part 1 FRCPath Part 2

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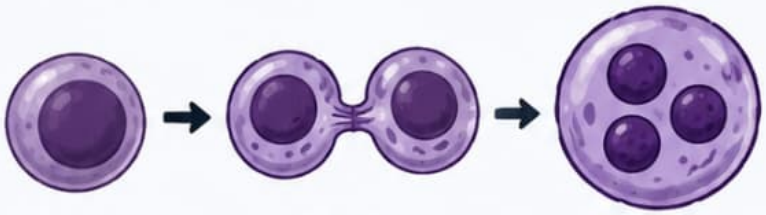
WHAT YOU ARE NOT READING

™

AND NOBODY IS TEACHING YOU

SERIES

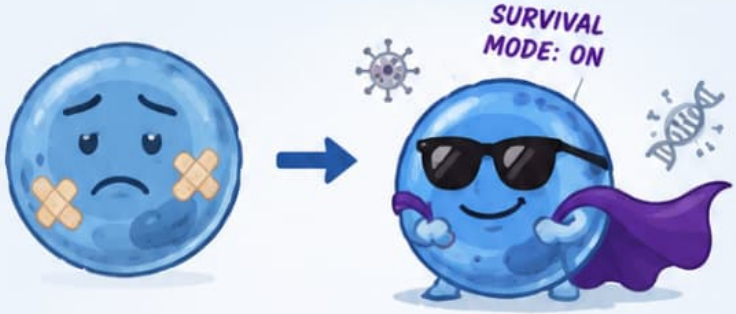
HOW REED-STERNBERG CELLS ARE BORN



RS CELLS FORM BY INCOMPLETE CYTOKINESIS & RE-FUSION OF DAUGHTER HODGKIN CELLS.
NOT BY FUSION OF TWO INDEPENDENT NEOPLASTIC CELLS.

A CRIPPLED B-CELL THAT CHEATED DEATH

A transforming event—often driven by EBV infection or NF-κB pathway mutations—rescues the cell from death and turns it cancerous.



LINEAGE INFIDELITY: GLOBAL LOSS OF B-CELL IDENTITY

RS CELLS:

- ✕ LOSE CD19 & CD20
- ✕ LOSE IMMUNOGLOBULINS
- ✕ SHUT DOWN B-CELL MASTERS (E2A, PU.1, OCT-2)

BEYOND THE TEXTBOOK. BEYOND THE ORDINARY. STUDY THE REALITY.

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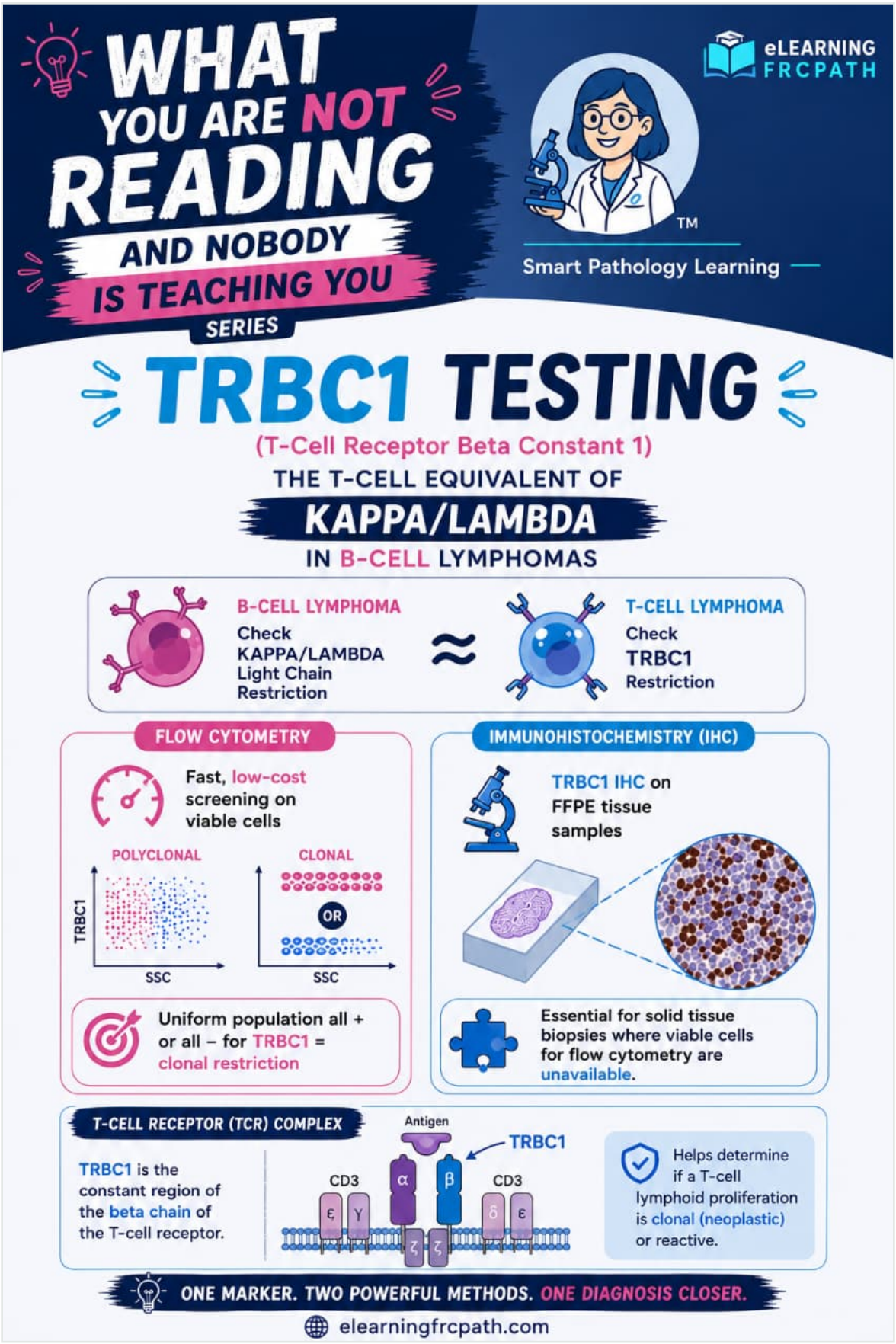
Reed-Sternberg cells aren't a merger of two cells. It's one cell that tried to divide, gave up halfway, and got famous anyway.

BCL-2 isn't on that report for decoration. It's the actual reason the cell refuses to die on schedule.



T cells finally got their own version of kappa/lambda. Took long enough.

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NLPHL IS A MISNOMER!™

THE TRUTH BEHIND THE NAME

B

NODULAR LYMPHOCYTE-PREDOMINANT B-CELL LYMPHOMA

An indolent mature B-cell lymphoma.

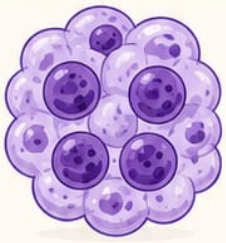
LP ("POPCORN") CELLS RETAIN B-CELL PROGRAM

CD20 PAX5 OCT2 BOB1

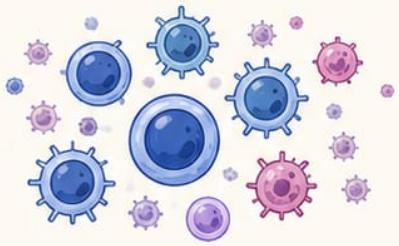
Unlike Reed–Sternberg cells of classical Hodgkin lymphoma.

ITS DEADLIER BROTHER

T-CELL/HISTIOCYTE-RICH LARGE B-CELL LYMPHOMA



Vs



IN BOTH, THE MALIGNANT CELLS ARE FEW.

SEA OF REACTIVE NON-NEOPLASTIC CELLS

TUMOUR CELLS HIDE IN PLAIN SIGHT

"THE CELLS THAT GRAB YOUR ATTENTION ARE OFTEN NOT THE TUMOUR. | THE TUMOUR IS THE CELL YOU'RE STRUGGLING TO FIND."

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BEYOND MEMORIZATION. | BEYOND TEXTBOOKS. | STUDY THE REAL BIOLOGY.

The actual tumour cells are the ones you can barely find in a sea of reactive lymphocytes. Typical.

04

THORACIC & LUNG PATHOLOGY

PD-L1, liquid biopsy, and every molecular subtype the lung throws at you.

8 panels • maps to:

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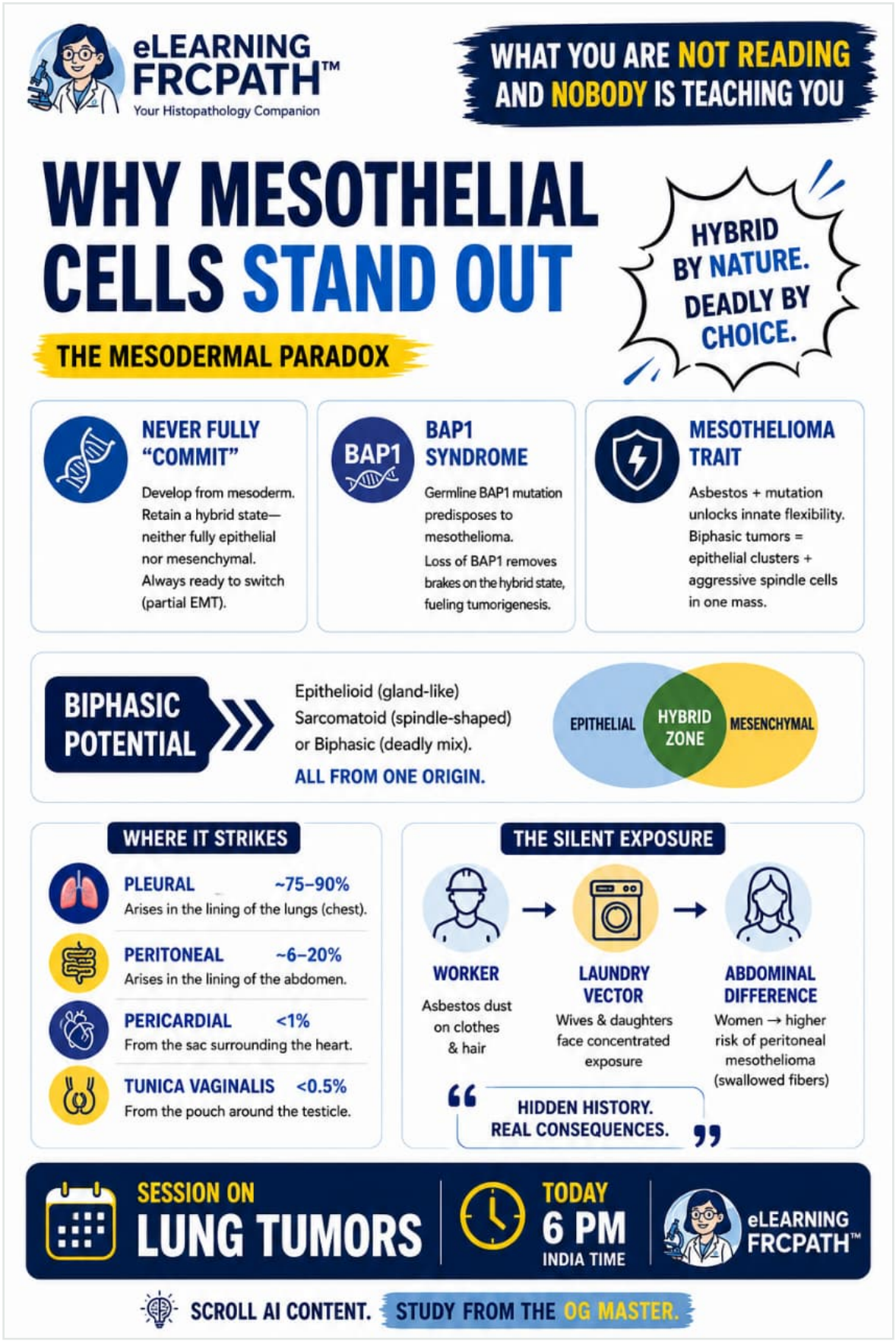
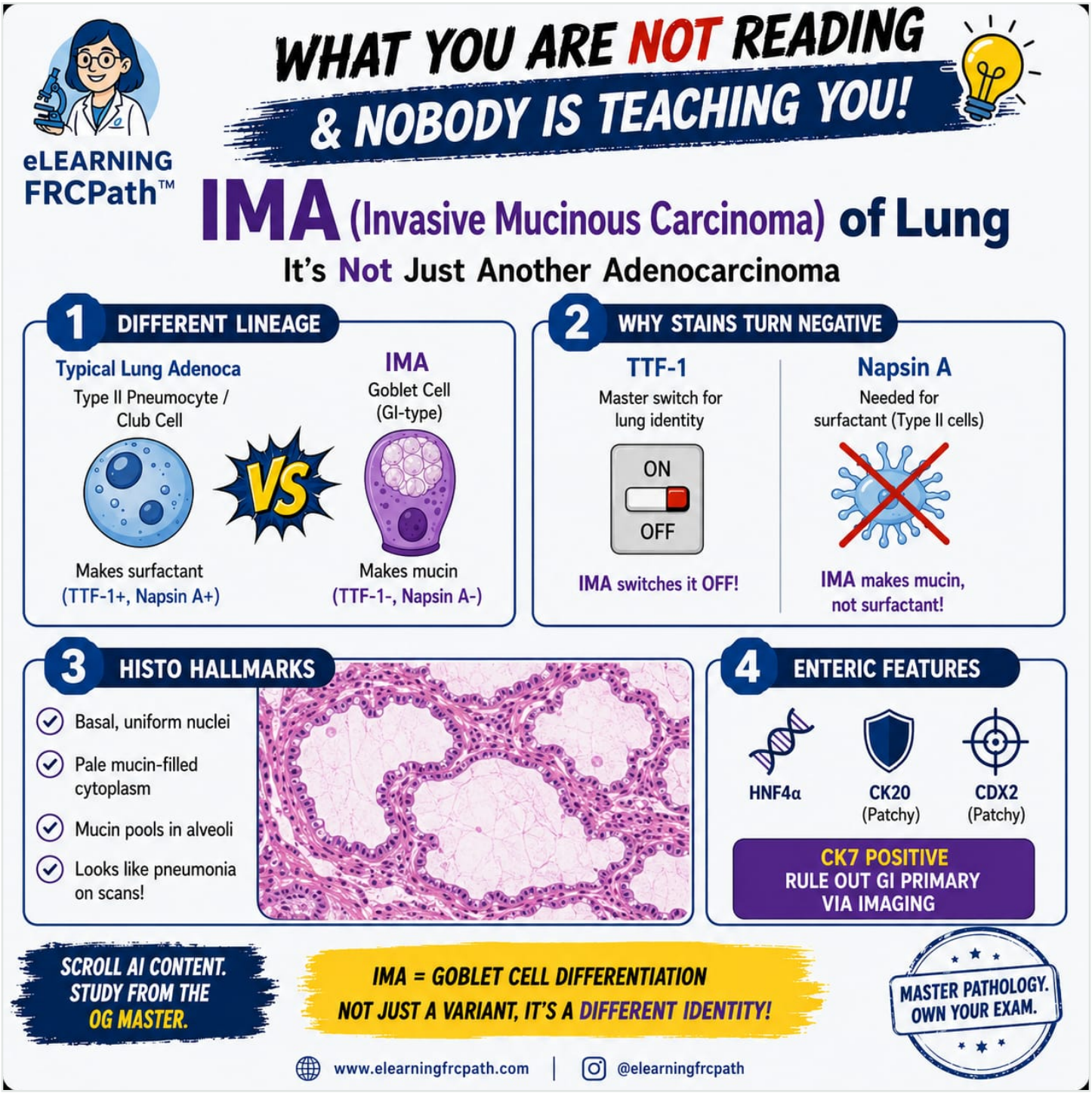


Mesothelial cells can't fully commit to being epithelial or mesenchymal. Honestly, relatable.



Looks like pneumonia on the CT, behaves like a goblet cell under the scope. Lung adenocarcinoma having an identity crisis.

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GET OVER PD-L1

PD-L1 ALONE DOES NOT DECIDE ICI THERAPY.

1 PD-L1 IS NO LONGER THE WHOLE STORY

- PD-L1 IHC alone is an imperfect predictive biomarker.
- PD-L1-high tumors can fail, PD-L1-negative can respond.

Current research integrates:

- TMB
- TILs
- Gene-expression signatures
- ctDNA
- Spatial immune profiling
- AI-based digital pathology

→ Better prediction of benefit

2 PERIOPERATIVE IMMUNOTHERAPY IS CHANGING CURE RATES

PD-1 inhibitors are now used:

BEFORE SURGERY (Neoadjuvant) | AFTER SURGERY (Adjuvant)

Significantly improved event-free survival in:

- NSCLC
- Melanoma
- Bladder Cancer
- Renal Cell Carcinoma

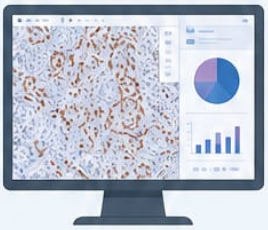
3 COMBINATION THERAPY IS THE FUTURE

Beyond PD-1 blockade alone

- PD-1 + CTLA-4
- PD-1 + VEGF inhibitors
- PD-1 + Antibody-Drug Conjugates (ADCs)
- PD-1 + Chemotherapy
- PD-1 + Radiotherapy
- PD-1 + STING agonists

→ Superior outcomes in selected patients

4 AI IS TRANSFORMING PD-L1 INTERPRETATION



- Improves PD-L1 scoring reproducibility
- Quantifies immune-cell distribution
- Predicts immunotherapy response from H&E in some studies
- Reduces interobserver variability

5 NEW IMMUNE CHECKPOINTS ARE EMERGING

PD-1 is no longer the only checkpoint. New targets include:

LAG-3 | TIGIT | TIM-3 | VISTA | B7-H3

Especially important for patients resistant to PD-1 therapy.

BEYOND PD-L1. TOWARDS PRECISION.

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PD-L1 used to be the whole answer. Now it barely gets half the marks.

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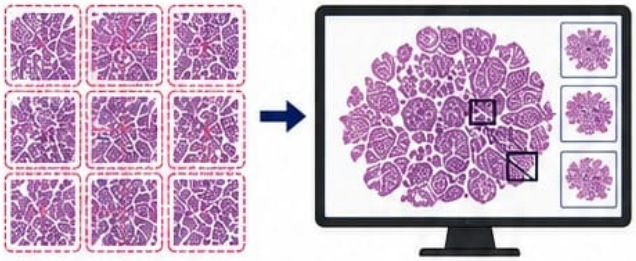
Recent advances for MD exam

STITCHING (TILE SCANNING) VS LINE SCANNING

STITCHING (TILE SCANNING)

Captures multiple overlapping tiles and stitches them to create the whole slide image.



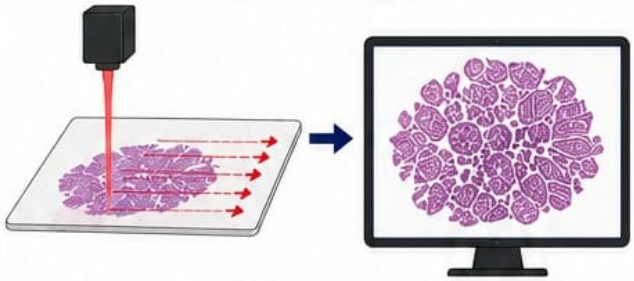
Multiple overlapping tiles captured

Stitched whole slide image

- Stop-and-go stage movement
- Requires complex stitching algorithms
- Relatively slower
- Stitching artifacts possible

LINE SCANNING

Captures the slide line by line with continuous movement to build the whole image.



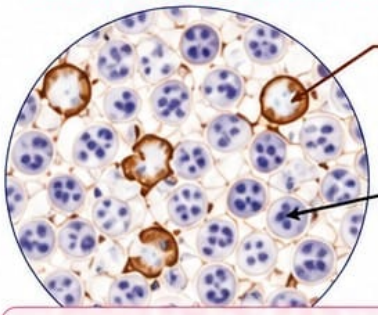
Line by line capture with continuous movement

Assembled whole slide image

- Continuous stage movement
- Minimal stitching; line alignment
- Generally faster
- Line/banding artifacts possible

PD-L1 TPS IN NSCLC

PD-L1 IHC – INDIVIDUAL CELL ASSESSMENT



$$TPS = \frac{\text{PD-L1 positive viable tumor cells (with membranous staining)}}{\text{Total viable tumor cells}} \times 100$$

- Only viable tumor cells counted
- Partial or complete membranous staining
- Immune cells, necrosis & cytoplasmic staining not included

Staining intensity (weak, moderate, strong) DOES NOT affect TPS. Any membranous staining at any intensity is considered positive.

KEY CUTOFFS & SIGNIFICANCE

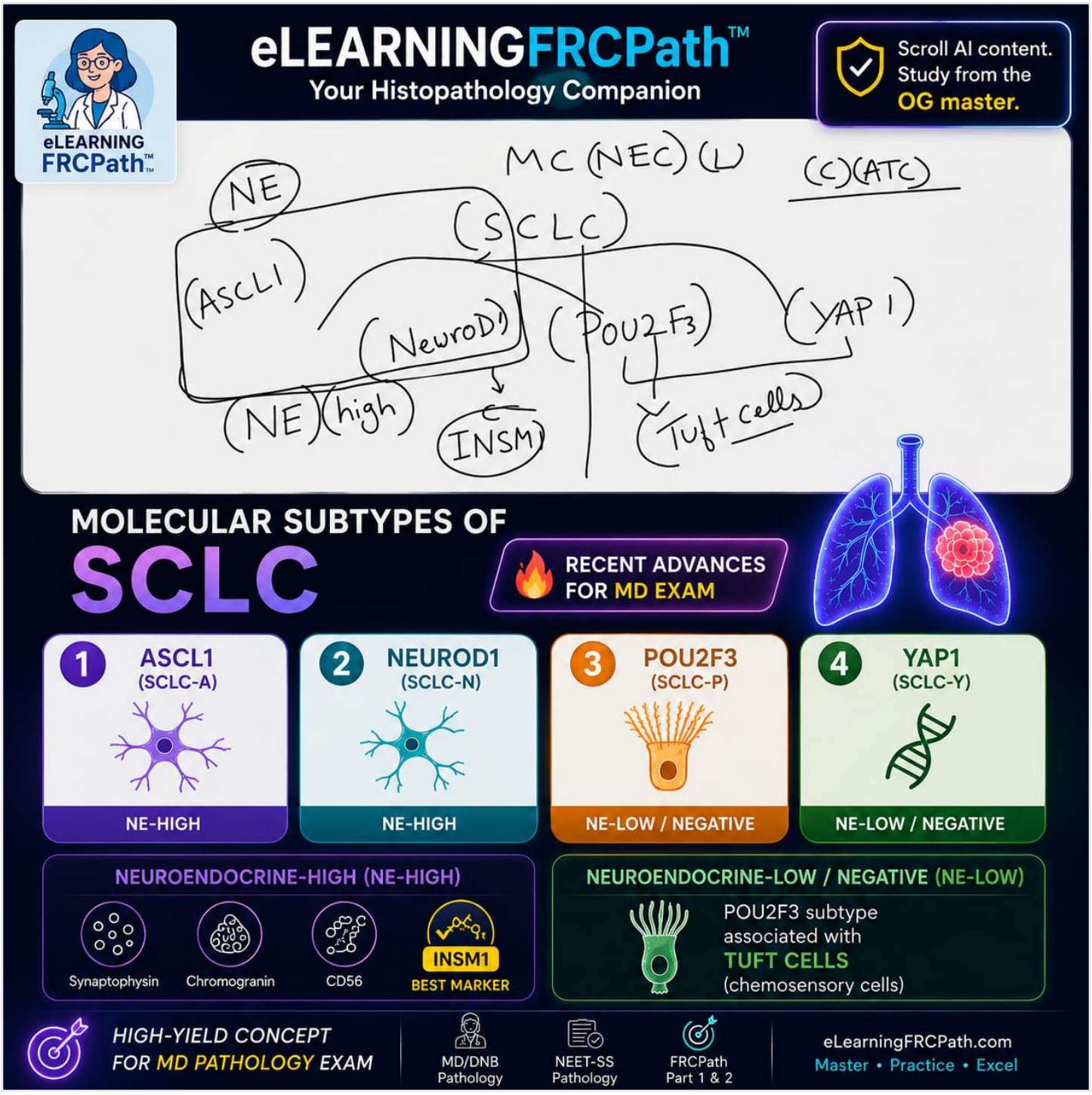
< 1% — Negative
Not eligible for PD-1 inhibitor monotherapy based on PD-L1 expression alone.

1–49% — Low PD-L1 expression
May be eligible for immunotherapy, often in combination with chemotherapy.

≥ 50% — High PD-L1 expression
Eligible for PD-1/PD-L1 inhibitor monotherapy in appropriate advanced NSCLC (no targetable driver mutations).

TPS ≥ 50% = High PD-L1 expression → Eligible for PD-1/PD-L1 inhibitor monotherapy in NSCLC

Two ways to turn a glass slide digital, and one very specific cutoff the exam always circles back to.



Four transcription factors, four completely different personalities of small cell lung cancer. INSM1 is still the dependable one.

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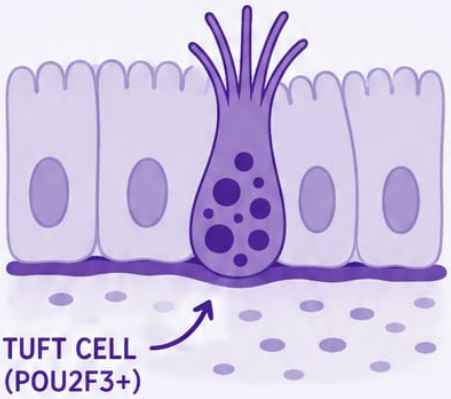
PATH TO GLOBAL EXCELLENCE

WHAT YOU ARE NOT READING
AND NOBODY IS TEACHING YOU
SERIES

NOT ALL NEUROENDOCRINE TUMORS ARE POSITIVE FOR CONVENTIONAL NEUROENDOCRINE MARKERS!

Neuroendocrine tumors are a diverse group.

In small cell tumors, especially lung, and in POU2F3-type NENs arising from tuft cells, many can be **NEGATIVE** for conventional markers like Synaptophysin and Chromogranin.



TAKEAWAY: If Synaptophysin & Chromogranin are negative in small cell tumors, especially lung, think POU2F3 and do IHC!

Scroll AI content.
Study from the OG MASTER.

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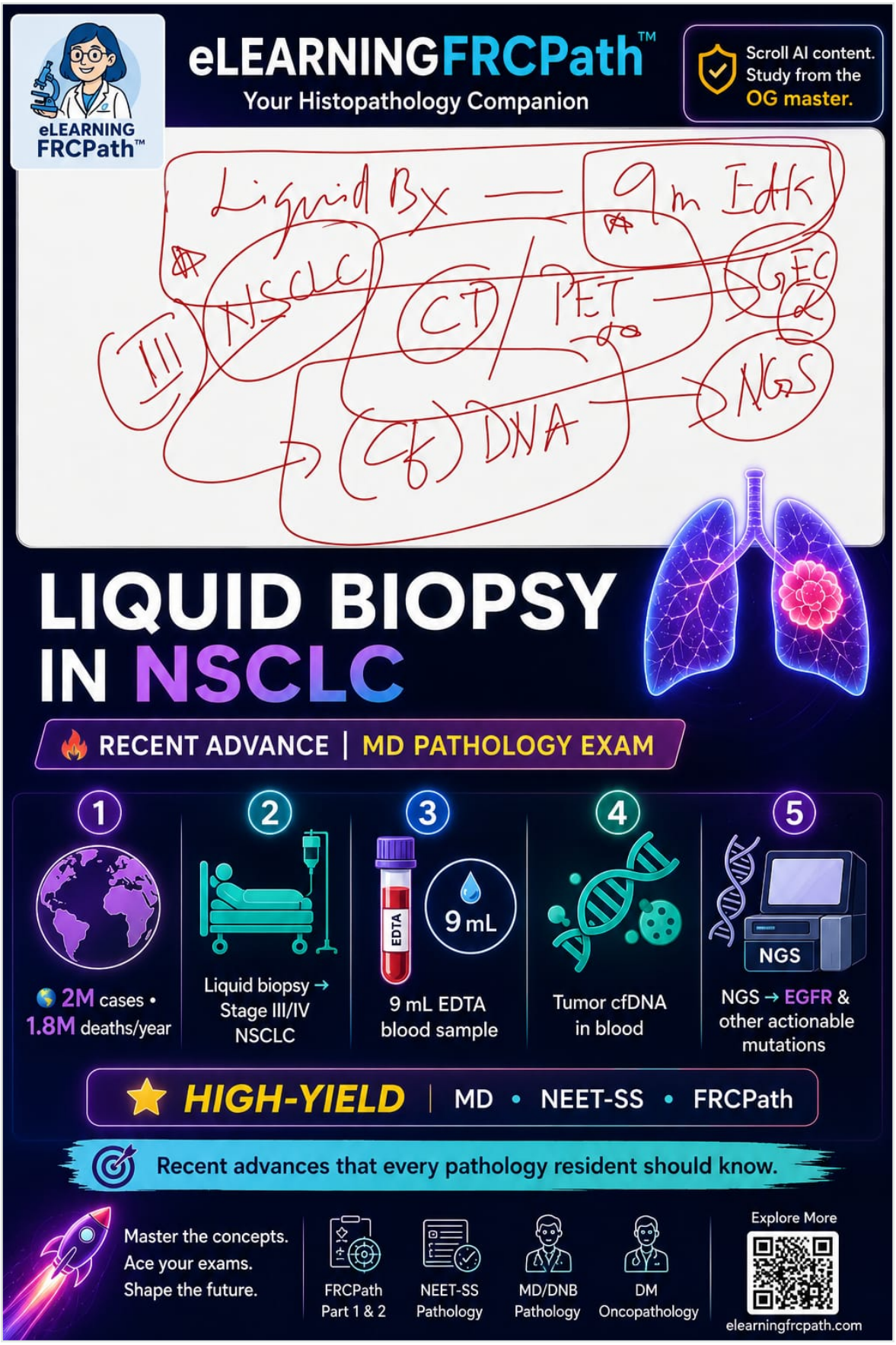
PATH TO GLOBAL EXCELLENCE

Synaptophysin and chromogranin both go quiet, and it's still a neuroendocrine tumor. Blame the tuft cells.



9 mL of blood versus a needle biopsy. Ask the patient which one they'd rather have.

A negative first-line panel isn't the finish line. It's the "please continue" sign.

05

CELL BIOLOGY & MECHANISMS OF DISEASE

How cells actually die, scar, and switch their genes off.

5 panels • maps to:

FRCPath Part 1 | MD/DNB Pathology

THINGS HAVE MOVED BEYOND *APOPTOSIS.*

BUT ARE YOU UPDATED?

Modern pathology is decoding more.
So should you.

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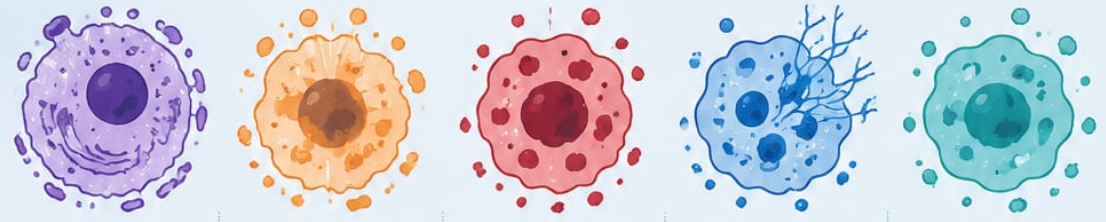
CELL DEATH: MORE THAN ONE WAY



APOPTOSIS	NECROPTOSIS	PYROPTOSIS	NETOSIS	AUTOPHAGY
Programmed Cell Death	Regulated Necrosis	Inflammatory Cell Death	Webs That Trap & Protect	Cellular Self-Cleaning

KEY PLAYERS YOU MUST KNOW

- **CASPASE 3** — Executioner of Apoptosis
- **CASPASE 1** — Master of Pyroptosis
- **MLKL** — Driver of Necroptosis
- **MPO** — Key Enzyme in NETosis

STAY AHEAD. STAY UPDATED.

We cover what really matters — regularly.

AT eLEARNINGFRCPATH™

HIGH-YIELD CONCEPTS · UPDATED TOPICS · EXAM FOCUSED · MADE BY EXPERTS

Learn Smarter. Score Higher.

Turns out cells have almost as many ways to die as pathology has ways to test you on it.

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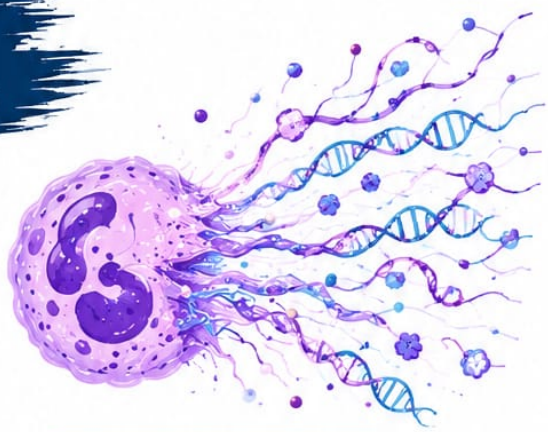
WHAT YOU ARE NOT READING AND NOBODY IS TEACHING YOU SERIES

NETOSIS

THE DOUBLE EDGED SWORD OF NEUTROPHILS



NETosis is a specialized form of programmed neutrophil cell death (vital NETosis can occur without immediate cell death)

NETS ARE MADE OF

- Decondensed chromatin (DNA & histones)
- Neutrophil Elastase (NE)
- Myeloperoxidase (MPO)
- Antimicrobial proteins

WHAT NETS DO

- **Trap and kill** microorganisms
- **Cause collateral tissue injury** by histones, proteases and reactive oxygen species
- **Activate endothelial cells** leading to endothelial dysfunction and microvascular damage
- **Promote microthrombosis** and ischemic injury

DISEASES WHERE NETOSIS MATTERS

- Sepsis
- Acute Respiratory Distress Syndrome (ARDS)
- COVID-19
- Vasculitis
- Ischemia–Reperfusion Injury

NETOSIS PROTECTS AGAINST INFECTION

BUT DAMAGES OUR OWN TISSUES

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SCROLL AI CONTENT. STUDY FROM THE OG MASTER.

Neutrophils throwing their own DNA out like a net. Great against bacteria, rough on the neighbourhood.

WHAT YOU ARE NOT READING

AND NOBODY IS TEACHING YOU

Pyroptosis IN ARDS

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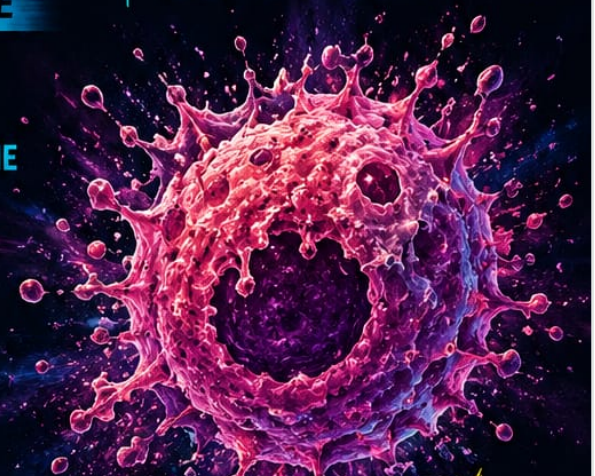
ARDS is now increasingly viewed as a disease driven by interconnected inflammatory cell-death pathways—particularly **PYROPTOSIS** and **NETOSIS**—rather than neutrophil-mediated injury alone.

THE PYROPTOSIS CASCADE

1. **DAMPs & PAMPs** activate **NLRP3 INFLAMMASOME**
2. This activates **CASPASE-1**
3. **CASPASE-1** cleaves **GASDERMIN D**
4. N-terminal fragment of **GASDERMIN D** forms **PORES** in the cell membrane
5. Cells **SWELL** and **RUPTURE** Massive release of IL-1β, IL-18 and DAMPs



INFLAMMATION UNLEASHED!

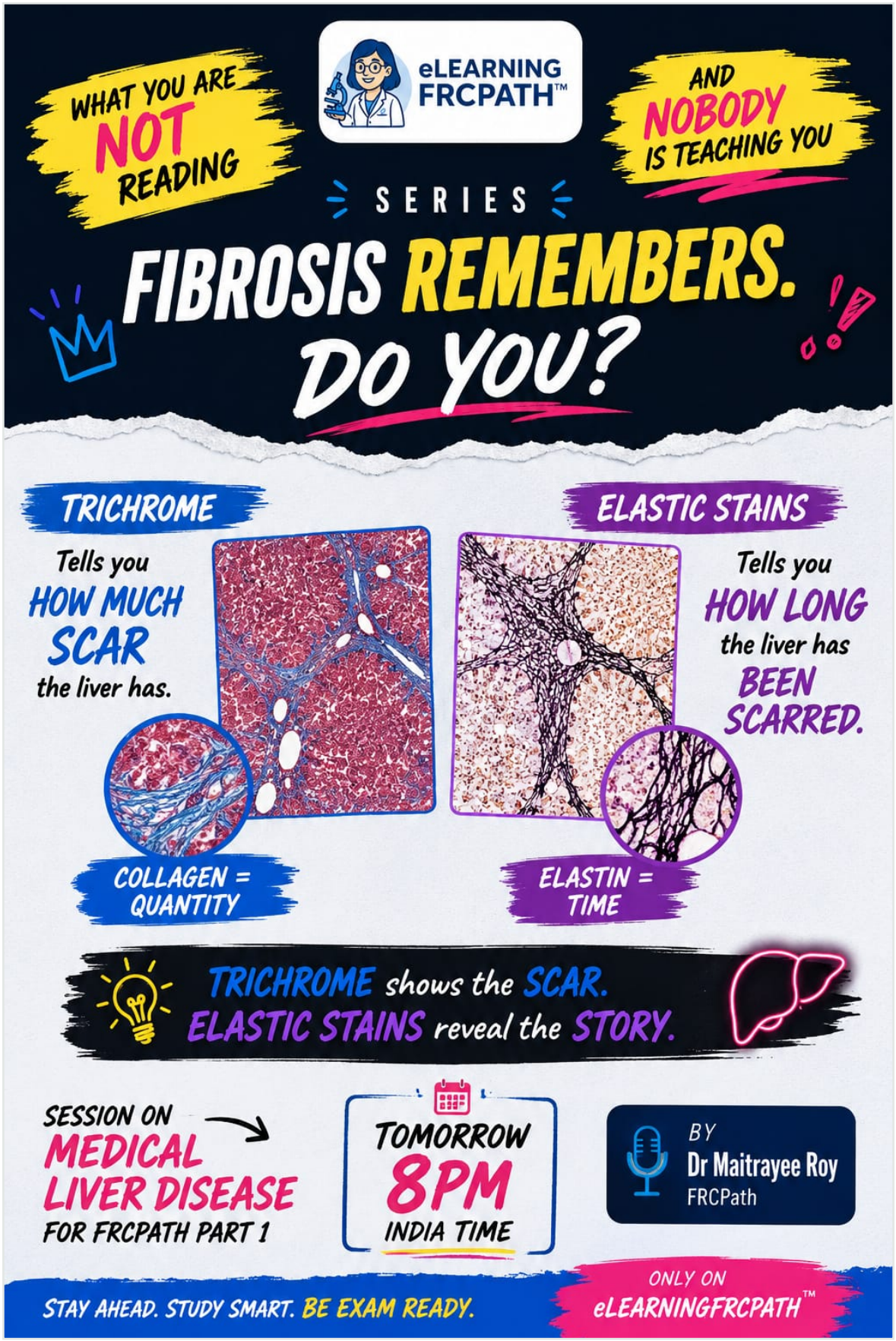
- Alveolar-capillary barrier **BREAKDOWN**
- Pulmonary **EDEMA**
- **CYTOKINE STORM** AMPLIFICATION
- **DIFFUSE ALVEOLAR DAMAGE**

THE VICIOUS LOOP:
Pyroptosis → NETosis → More Inflammation
A self-propagating cycle driving severe ARDS

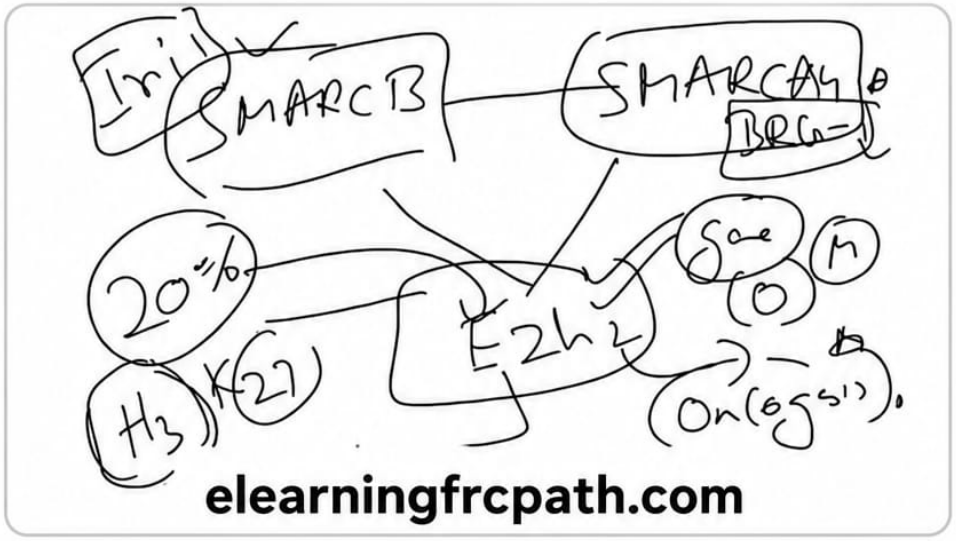
FUTURE THERAPIES:
Target NLRP3 • Caspase-1 • Gasdermin D
IL-1 Blockade • PAD4 Inhibition

SCROLL AI CONTENT. STUDY FROM THE OG MASTER.

One pore in the membrane, and suddenly the whole lung is having a very bad day.



Trichrome counts how much damage happened. Elastic stain tells you how long ago it started. Together, basically the liver's diary.



THE EPIGENETIC BALANCE OF CANCER

When the balance breaks, cancer wins.

1 THE CORE INTERACTION

SMARCB1 and SMARCA4 work together as a chromatin-remodeling powerhouse.

SMARCB1 (INI1) + SMARCA4 (BRG1)

They regulate genes by controlling chromatin access.

2 THE DOWNSTREAM TARGET

Working together, they control the expression of EZH2 (a histone methyltransferase).

EZH2

3 THE ONCOGENIC MECHANISM

If EZH2 is mutated or overexpressed, it drives oncogenesis (tumor development).

4 GENETIC ALIASES

Clinical / diagnostic names you'll see in reports.

SMARCB1	→ INI1
SMARCA4	→ BRG1

5 THE EPIGENETIC MARK

EZH2 adds trimethyl groups to H3K27 → H3K27me3. This mark silences genes.

me3

H3 K27 me3

= Transcriptional Silencing

6 WHEN THE BALANCE BREAKS

If SMARCB1 or SMARCA4 is defective, EZH2 goes "UNCHECKED."

→ Hyper-methylation
→ Gene silencing
→ Malignancy

SMARCB1 SMARCA4 ⊣ EZH2

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LEARN. REVISE. CRUSH IT.

SMARCB1 and SMARCA4 keep EZH2 in check. The second they clock out, EZH2 throws a party nobody invited.

06

GYNECOLOGIC PATHOLOGY

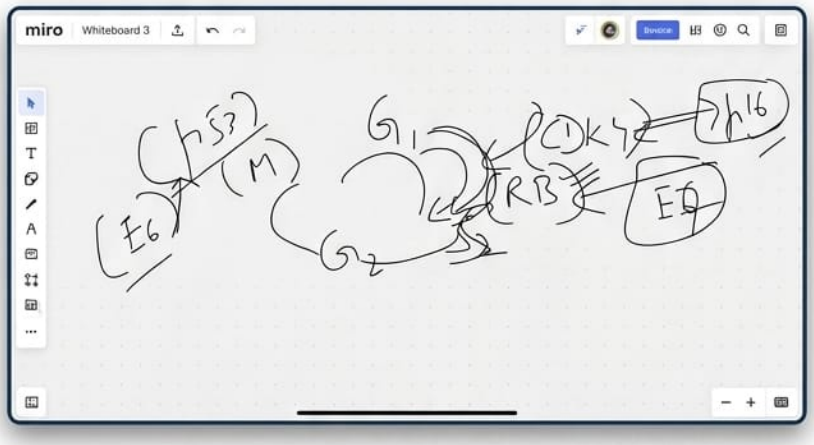
Cervix, ovary and endometrium — where the exam loves to get specific.

12 panels • maps to:

FRCPath Part 1

ELearningFRCPath

CUT THE COMPETITION: CRUSH THE HPV PATHWAY.



1. HPV'S DUAL THREAT

E7 DEGRADES RB
E6 DESTROYS p53

LIBERATING E2F

2. THE FEEDBACK LOOP

HYPERPROLIFERATION = STRESS!
p16 SURGE TO SLOW DOWN

p16

E2F STAYS UNBOUND! (p16 FAILS TO BIND)

3. CLINICAL EDGE

BLOCK p16 EXPRESSION IS KEY FOR DIAGNOSIS (HSIL/CxCa)

MASTER THE FEEDBACK, OWN THE FRCPath EXAM.

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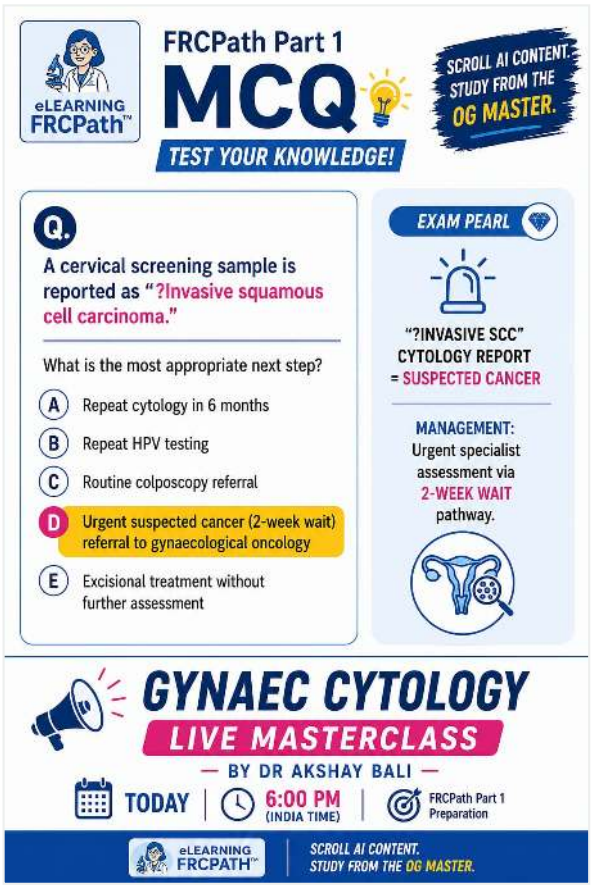
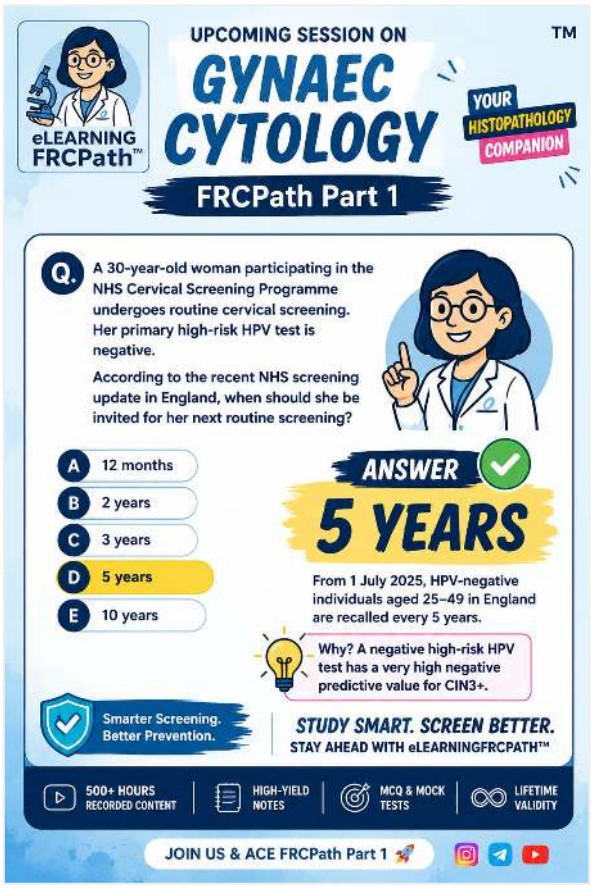
E6 takes out p53, E7 takes out Rb. HPV really came in swinging with a two-for-one deal.

Pop Quiz: Gynaec Cytology



"?Invasive SCC" on a cytology report is not a maybe. It's a two-week-wait referral wearing a disguise.

+



A negative HPV test just bought her five years off, not five months of worry.

Two cards, zero excuses for missing this on the exam.

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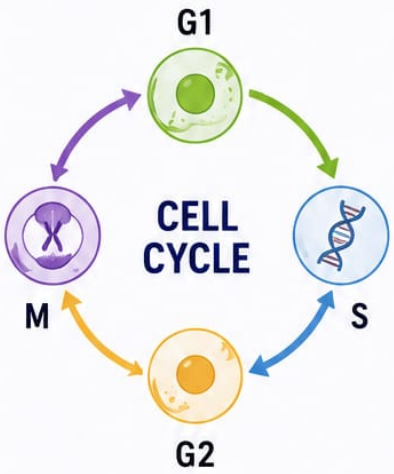
— Your Histopathology Companion —

WHAT YOU ARE NOT READING AND NOBODY IS TEACHING YOU SERIES

p16 OVEREXPRESSION



Diffuse p16 positivity is a marker of CELL-CYCLE DEREGULATION, not proof of HPV infection or cervical origin.

Always interpret p16 in conjunction with morphology and a broader immunohistochemical panel.

p16 OVEREXPRESSION CAN BE SEEN IN:

- Cervical SCC/HSIL
- HPV-associated Oropharyngeal SCC
- Anal, Vulvar, Vaginal, Penile SCC
- Urothelial Carcinoma
- High-grade Serous Ovarian Carcinoma
- Endometrial Serous Carcinoma

⚠ p16 positivity reflects Rb pathway inactivation, not necessarily HPV infection or cervical origin.

KNOW BEYOND THE TEXTBOOK

THINK LIKE AN EXAMINER

FOCUS ON WHAT REALLY MATTERS

LEARN. REVISE. RECALL. REPEAT.

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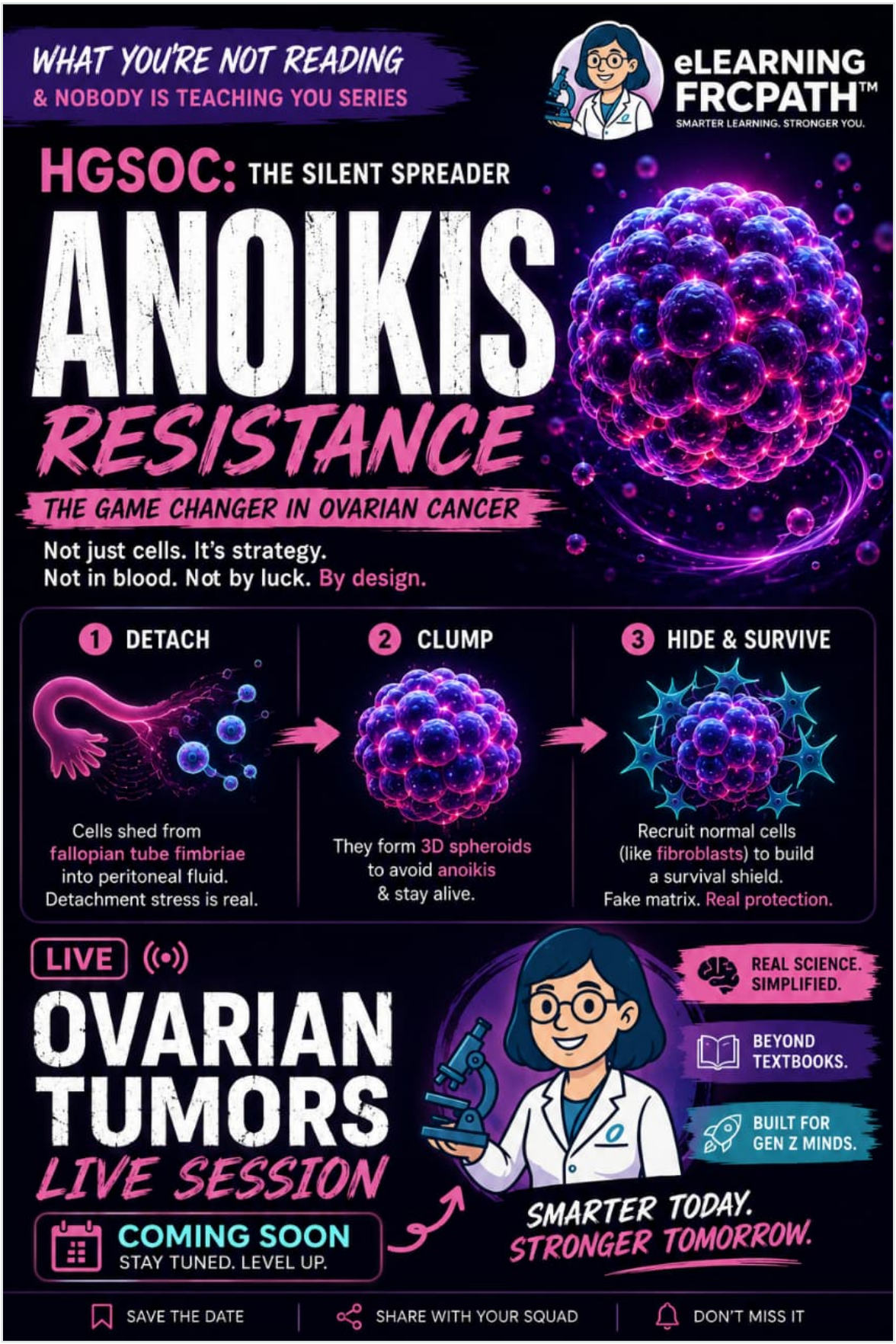
p16 positive means the cell cycle broke. It doesn't, by itself, tell you who broke it. Read the room.



Detach, clump up, recruit a few fibroblasts as bodyguards. Ovarian cancer cells have an actual survival strategy, and it's a good one.

DID YOU KNOW?

BRCA NEGATIVE CAN STILL BE HRD POSITIVE!

BRCA1/2 negative in blood and tumor, but **HRD positive** due to other HR gene alterations.

1. BLOOD TEST	2. TUMOR TEST	3. HRD TEST
BRCA1/2 NEGATIVE	BRCA1/2 NEGATIVE	HRD POSITIVE

WHY CAN THIS HAPPEN?

Alterations in other HR genes can cause HRD.

RAD51C · RAD51D · PALB2 · ATM · ATR · BRIP1 · CHEK2 · FANCA · FANCD2 · FANCL · NBN

HRD SCORE (GENOMIC SCARS)

HRD Score = LOH + TAI + LST

LOH	TAI	LST
Loss of Heterozygosity	Telomeric Allelic Imbalance	Large-Scale State Transitions
18	15	12

HRD SCORE = 18 + 15 + 12 = 45

(≥42 = HRD Positive*)

TAKEAWAY

HRD-positive tumors may still benefit from **PARP inhibitor therapy**, even if BRCA is negative.

LEARN • REVISE • EXCEL eLEARNING FRCPATH™

Clean BRCA result, broken repair pathway anyway. The tumor found a workaround.

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EXPANSILE INVASION IN OVARIAN MUCINOUS TUMORS

WHO CRITERIA YOU MUST KNOW

DEFINED AS:

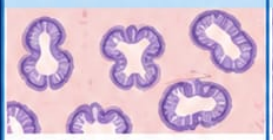
- Confluent glandular/ cribriform growth
- With minimal intervening stroma
- Measuring ≥5 mm in greatest linear dimension

OR

- Occupying an area ≥10 mm²

SIZE MATTERS. STROMA MATTERS.

Once this threshold is exceeded, the lesion is classified as **EXPANSILE INVASIVE MUCINOUS CARCINOMA** rather than borderline tumor.

BORDERLINE TUMOR	EXPANSILE INVASIVE CARCINOMA
	
Glands separated by stroma	Confluent glands with minimal/no stroma

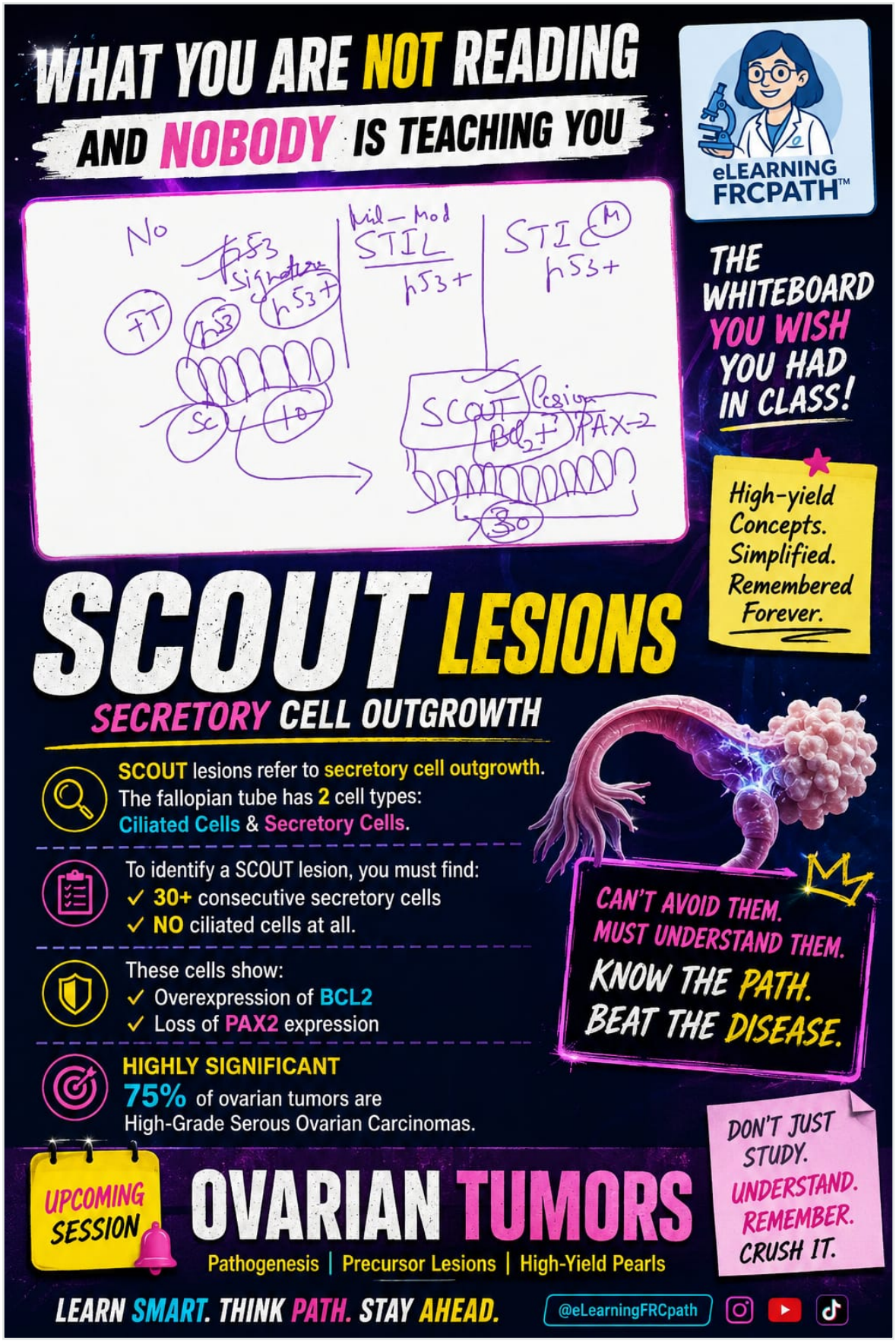
UPCOMING SESSION

OVARIAN TUMORS

High yield. Exam focused. Pathology made simple.

STAY AHEAD. PATH SMART. with eLEARNINGFRCPATH™

5mm is all it takes to flip "borderline" into "call the oncologist."



Thirty secretory cells in a row, zero ciliated cells in sight. The fallopian tube's way of raising an early red flag.

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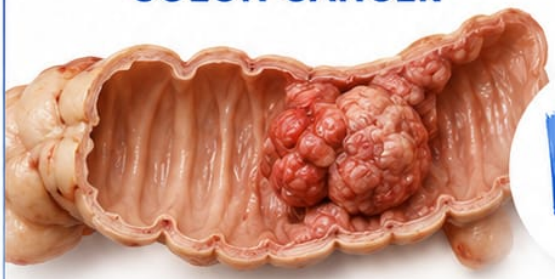
TWO CANCERS. TWO GATEKEEPERS. TWO LEGENDS.

APC

THE FAMOUS ONE

THE GATEKEEPER OF **COLON CANCER**



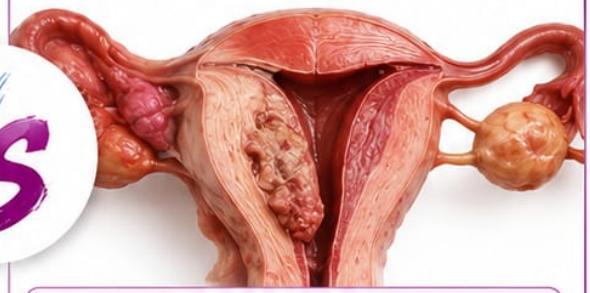
APC loss is the **earliest step** in colorectal cancer.

Classic. Taught. Well known.

PTEN

THE LESSER KNOWN VILLAIN

THE GATEKEEPER OF **ENDOMETRIAL CANCER**



PTEN loss is the **most common and earliest mutation** in endometrial carcinoma.

Real. Powerful. Underappreciated.

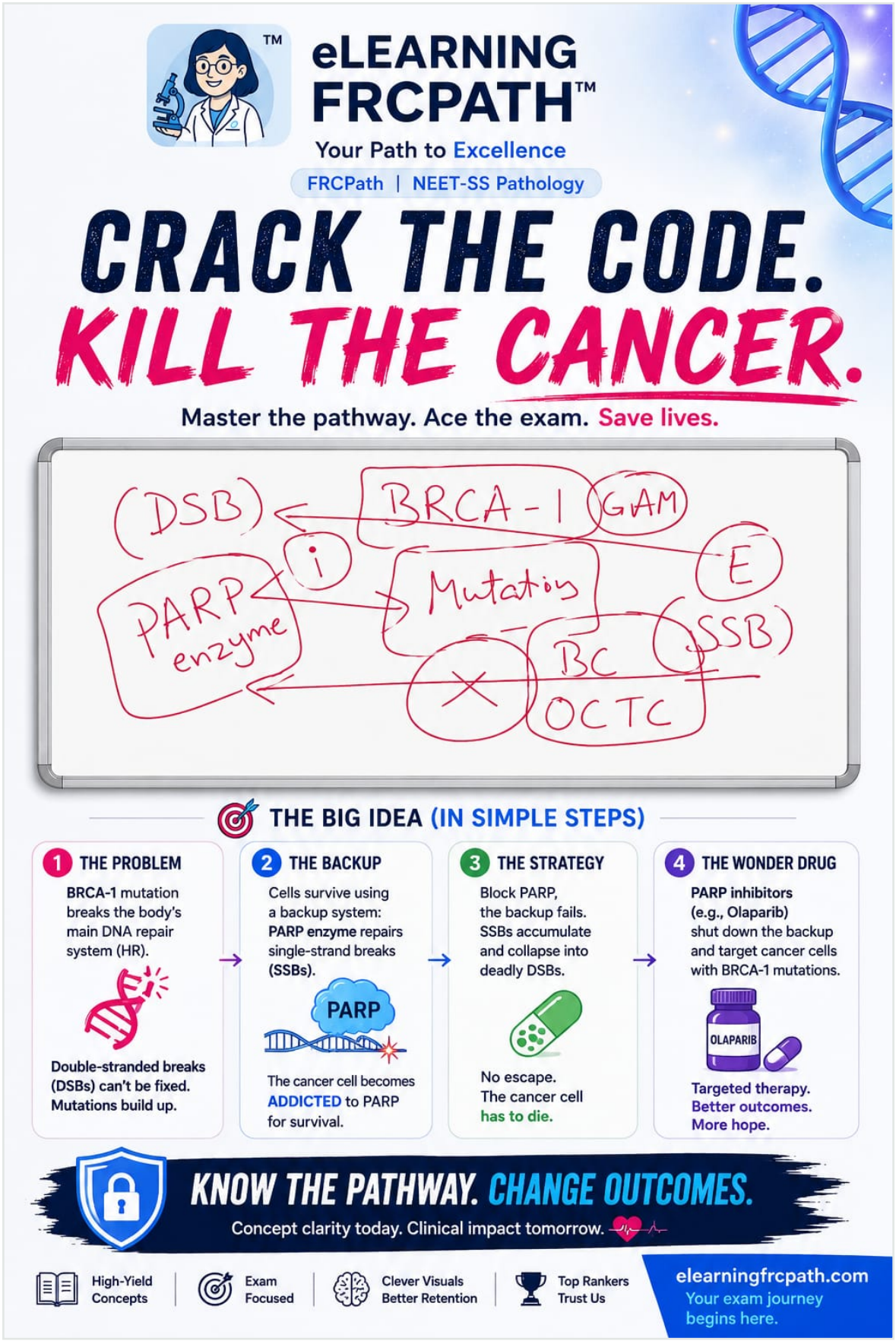
VS

IF APC = COLON CANCER, THEN PTEN = ENDOMETRIAL CANCER.

KNOW THE PATH. | RESPECT THE GATEKEEPERS. | CRACK THE EXAM.

eLEARNINGFRCPATH™ – LEARNING THAT HITS DIFFERENT.

APC gets all the textbook fame for colon cancer. PTEN has quietly been running the same show in the endometrium the whole time.



Take away the backup DNA repair system, and the cancer cell genuinely has nowhere left to go. That's the entire strategy.

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THE BIG TRAP

NOT ALL ENDOMETRIAL TUMORS ARE ER/PR POSITIVE!

CONVENTIONAL THINKING IS WRONG.

Not all endometrial carcinomas arise from the estrogen pathway.

HIGH-GRADE ENDOMETRIAL CARCINOMAS

USUALLY ER/PR NEGATIVE

CLEAR CELL CARCINOMA

ER – PR –

Napsin A +
HNF1β +

SEROUS CARCINOMA

ER – PR –

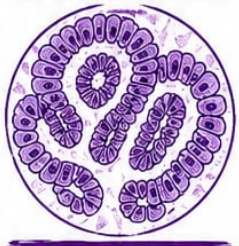
p53 abnormal
p16 diffuse +

MESONEPHRIC-LIKE ADENOCARCINOMA

ER – PR –

TTF-1 +
GATA3 +

ENDOMETRIOID CARCINOMA (ESTROGEN-DRIVEN)



ER + PR +

Often PTEN, PIK3CA, MMR, POLE

DON'T ASSUME ER/PR POSITIVITY.
ALWAYS USE A PANEL. THINK MORPHOLOGY + IHC + MOLECULAR.

QUICK CHECK

Uterine carcinoma ER/PR negative? → Check PAX8 → Use panel: TTF-1, GATA3, Napsin A, HNF1β, p53, p16 → Arrive at the correct diagnosis

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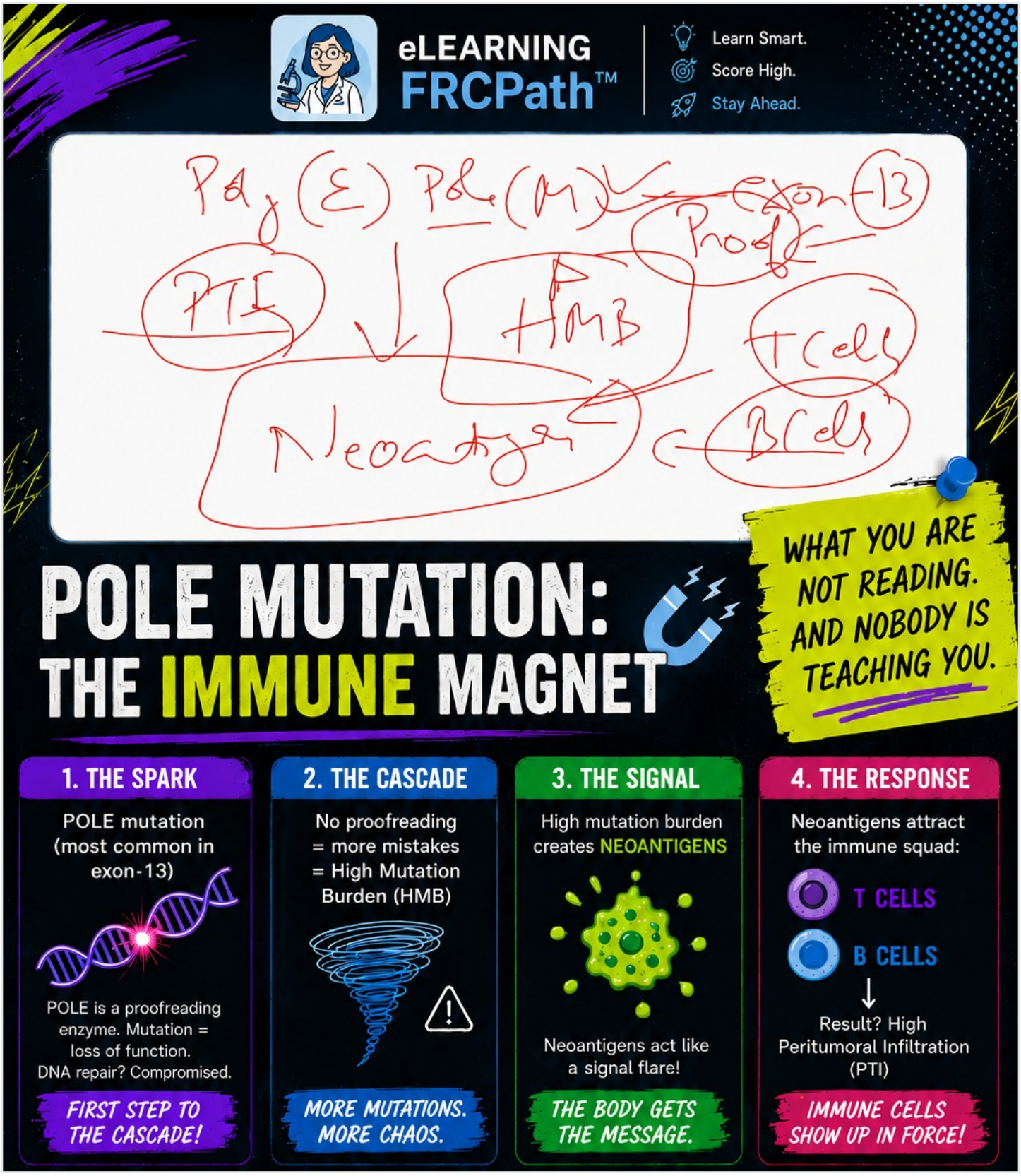
LEARN SMART. DIAGNOSE BETTER. EXCEL ALWAYS.

Assuming every endometrial cancer is hormone-driven is exactly how marks get lost on this question.



A proofreading enzyme breaks, mutations pile up, and somehow that mess is why the immune system shows up in force. Cancer biology, everyone.

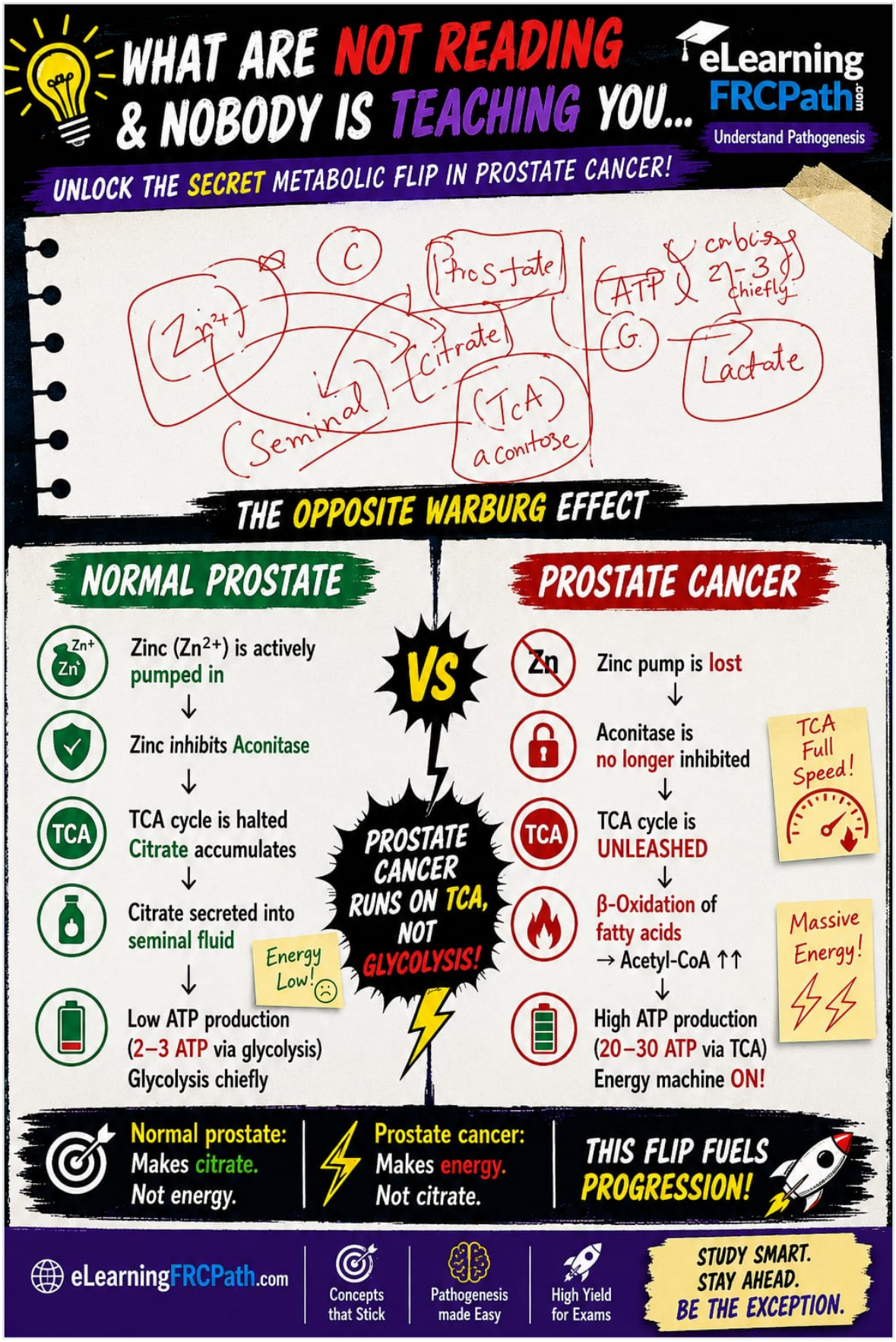
07

GENITOURINARY PATHOLOGY: PROSTATE & BLADDER

Gleason grades, PTEN, and the variants that change management.

7 panels • maps to:

NEET-SS Pathology | FRCPath Part 1



Normal prostate cells make citrate and call it a day. Cancer cells flip the switch and start making energy instead. Overachievers.

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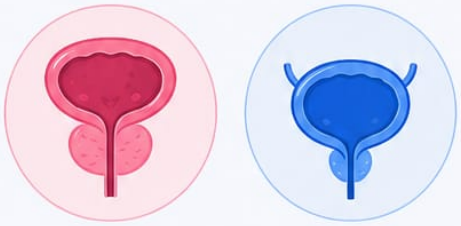
High Yield. Exam Focused. Results Driven.

CLASS TODAY!

PATHOLOGY POWER HOUR

PROSTATE & URINARY BLADDER



HIGH YIELD

EXAM FOCUSED

RESULTS DRIVEN

KEY GRADING DIFFERENCES

FEATURE	TURP / ENUCLEATION SPECIMEN	RADICAL PROSTATECTOMY (RP) SPECIMEN
Primary Pattern	Most common pattern.	Most common pattern.
Secondary Pattern	Highest grade pattern present (even if it accounts for < 5%).	Second most common pattern.
Minor High-Grade (< 5%)	Directly included in the main Gleason Score as the secondary number.	Reported separately as a Tertiary Pattern; does not change the core Gleason Score/Grade Group.
Minor Low-Grade (< 5%)	Ignored.	Ignored.

TODAY 6:00 PM — INDIA TIME —

BE THERE. LEARN BETTER. SCORE HIGHER.

JOIN LIVE. STAY AHEAD.

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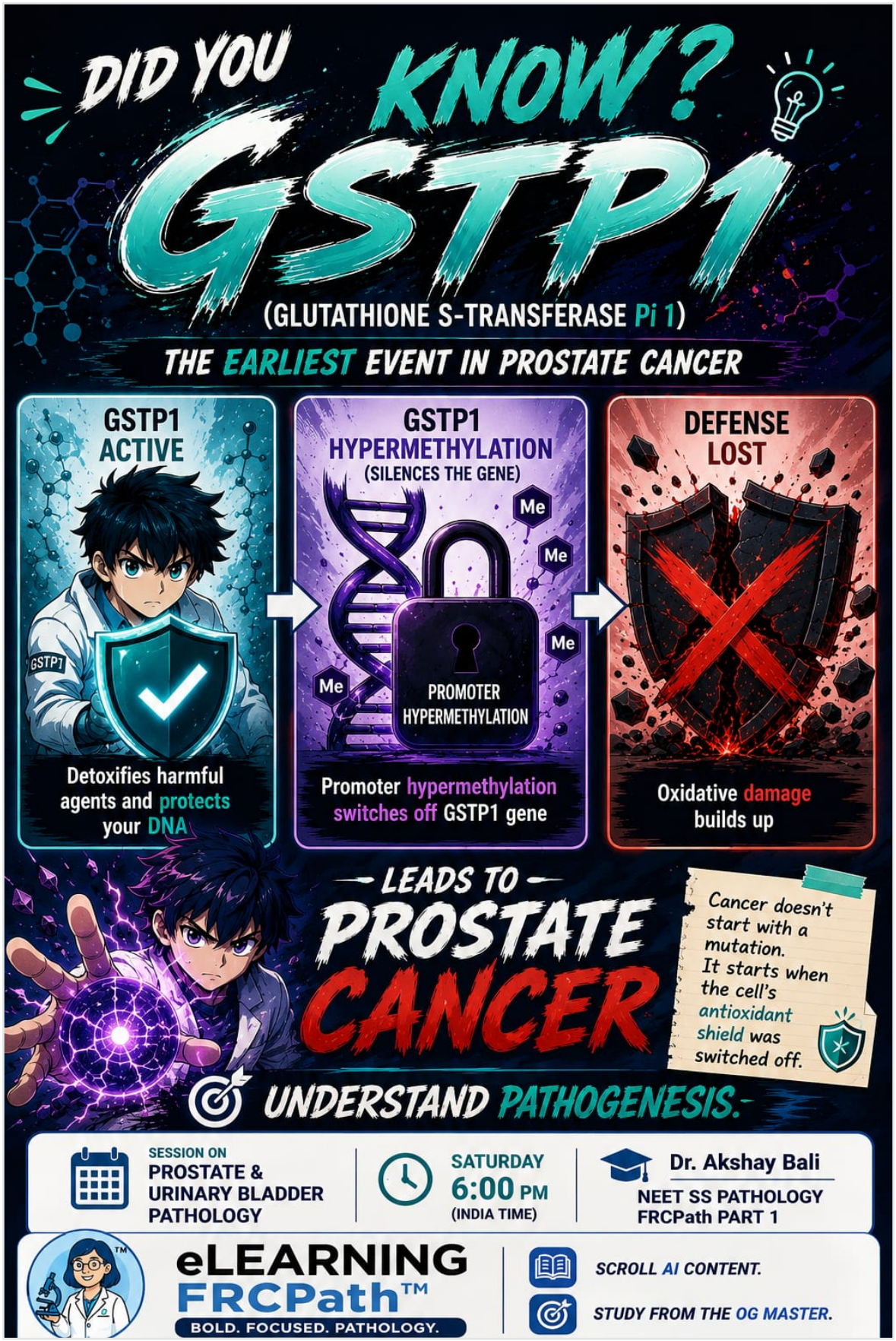
Same 5% tumor, two completely different rules depending on which specimen it landed in. The exam loves this exact detail.



Cancer doesn't always start with a bang. Sometimes it starts with the antioxidant shield quietly getting switched off.

IDC-P vs CRIBRIFORM ADENOCARCINOMA

SAME CRIBRIFORM. DIFFERENT CRIME SCENE.

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IDC-P
(INTRADUCTAL CARCINOMA OF PROSTATE)

LUXURY APARTMENT

Inside the pre-existing duct

- Basal cells present (at least focally)
- Intraductal location (within ducts/acini)
- Marked nuclear pleomorphism common
- Comedonecrosis common

CRIBRIFORM ADENOCARCINOMA
(INVASIVE)

PRISON BREAK

Invades the stroma

- Basal cells absent
- Stromal invasion present
- Gleason Pattern 4 (Cribriform = Pattern 4)

COMEDONECROSIS

Dead cell trap in the center (Comedonecrosis) can occur in BOTH.

NOT A RELIABLE DIFFERENTIATOR!

QUICK GUIDE

BASAL CELLS PRESENT?
Think IDC-P
(Intraductal)

VS

BASAL CELLS ABSENT?
Think Cribriform Adenocarcinoma
(Invasive, Gleason Pattern 4)

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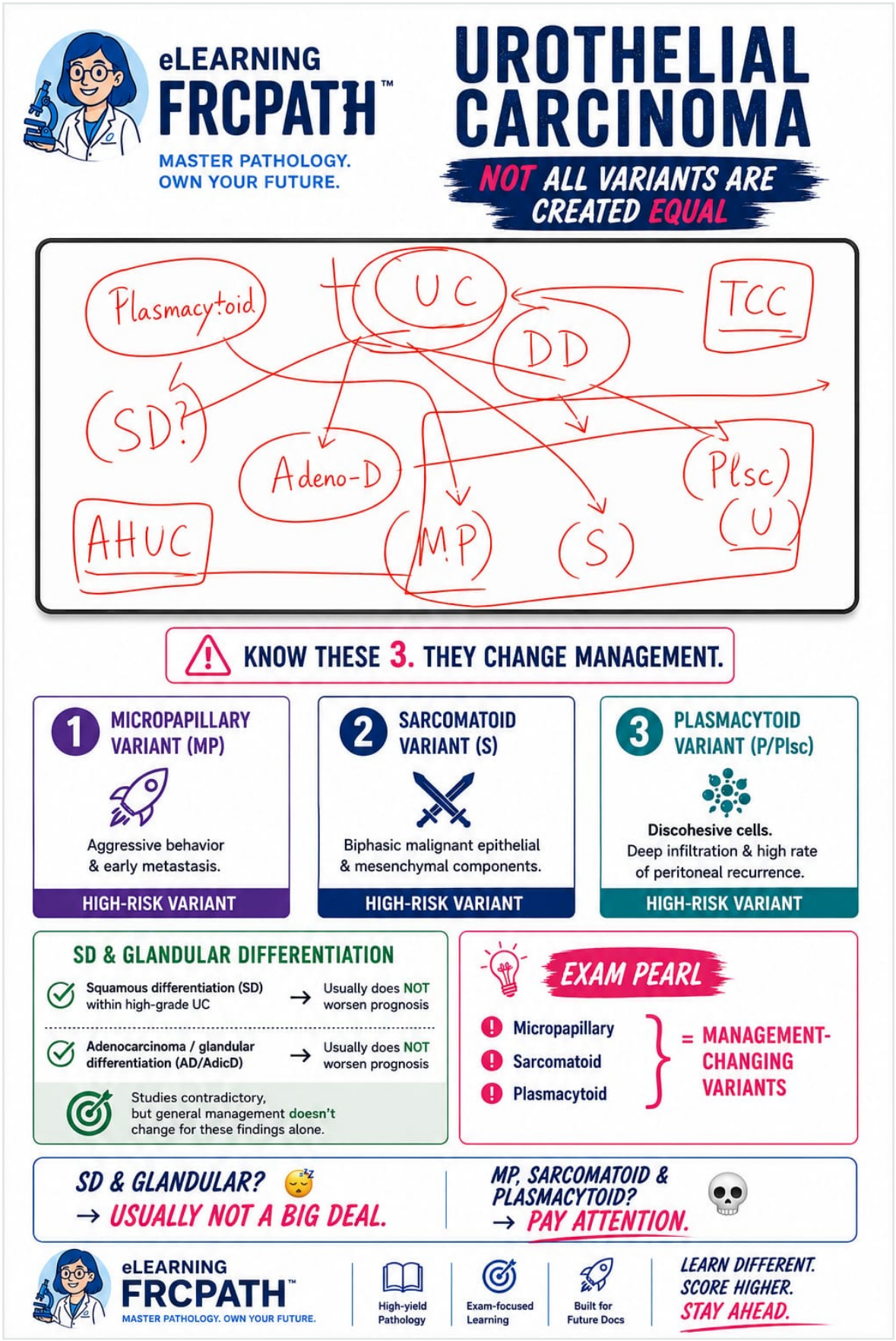
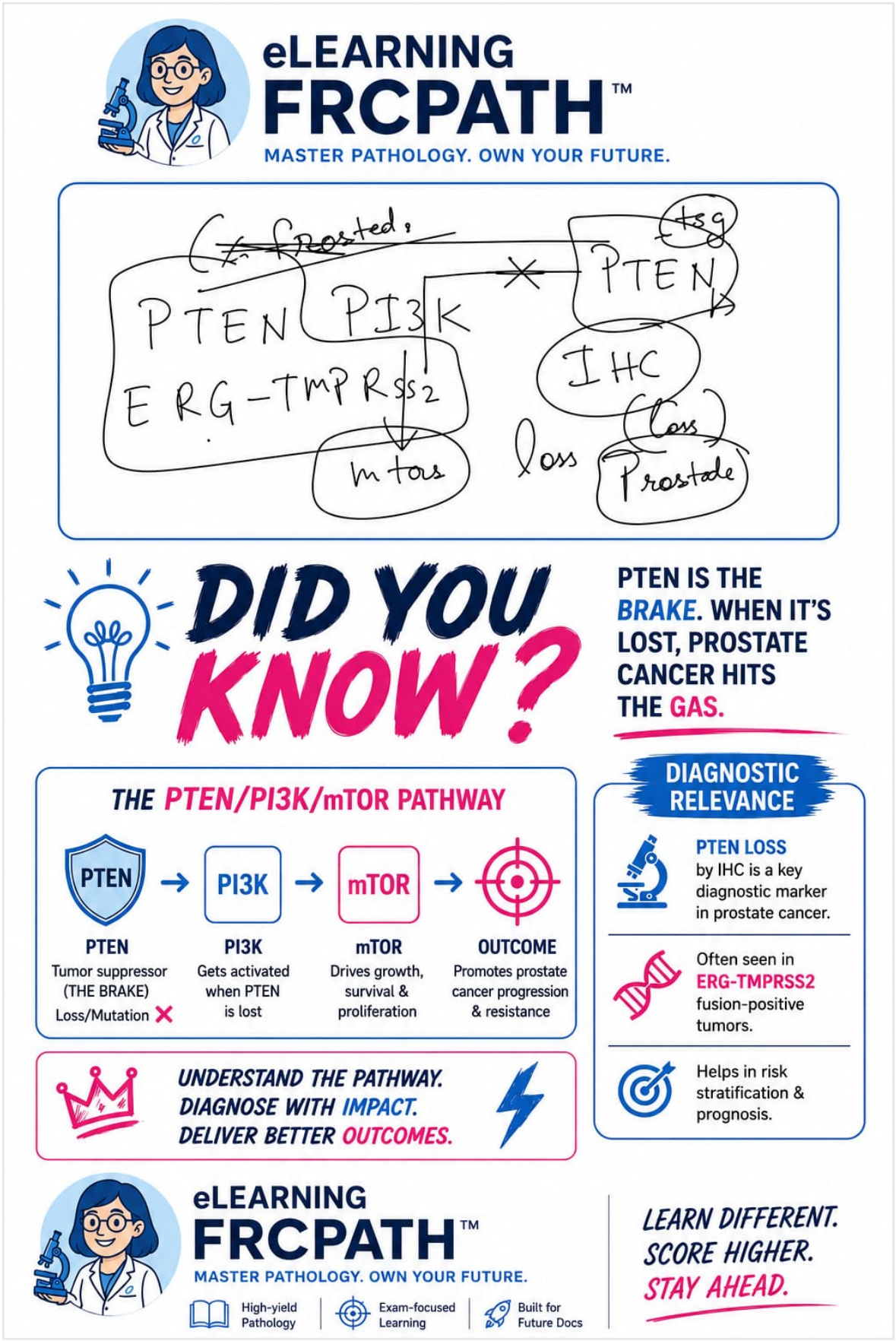
Scroll AI content.
Study from the OG master.

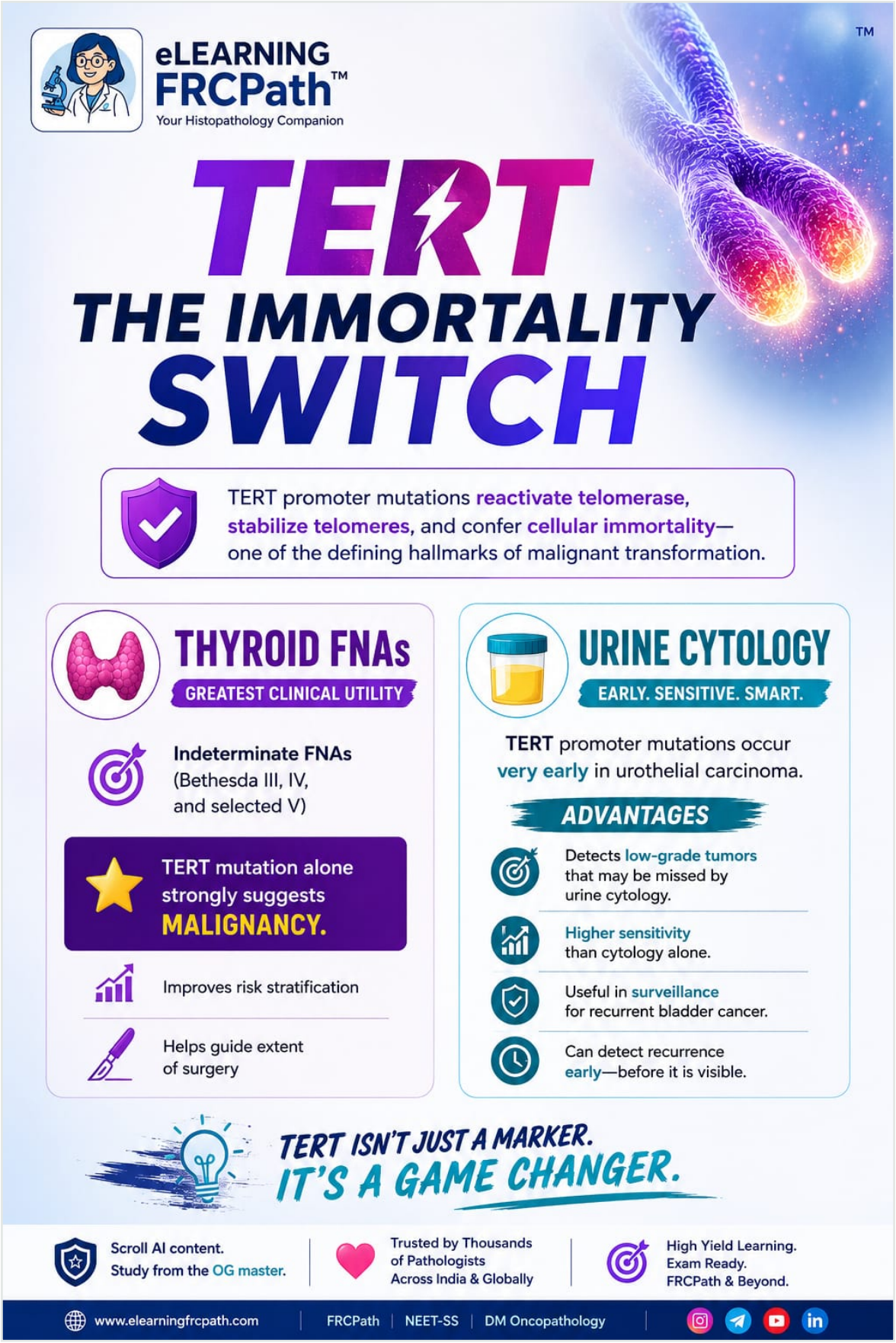
Same cribriform pattern, same ugly nuclei. Only one of them actually broke out of the duct — the basal cells are the bouncers who decide which.



Micropapillary, sarcomatoid, plasmacytoid. Three words that quietly rewrite the whole management plan.



PTEN is the brake pedal. Lose it, and prostate cancer finds the accelerator.



One mutation in a promoter region and the cell simply forgets how to grow old. Thyroid and bladder both fall for it.

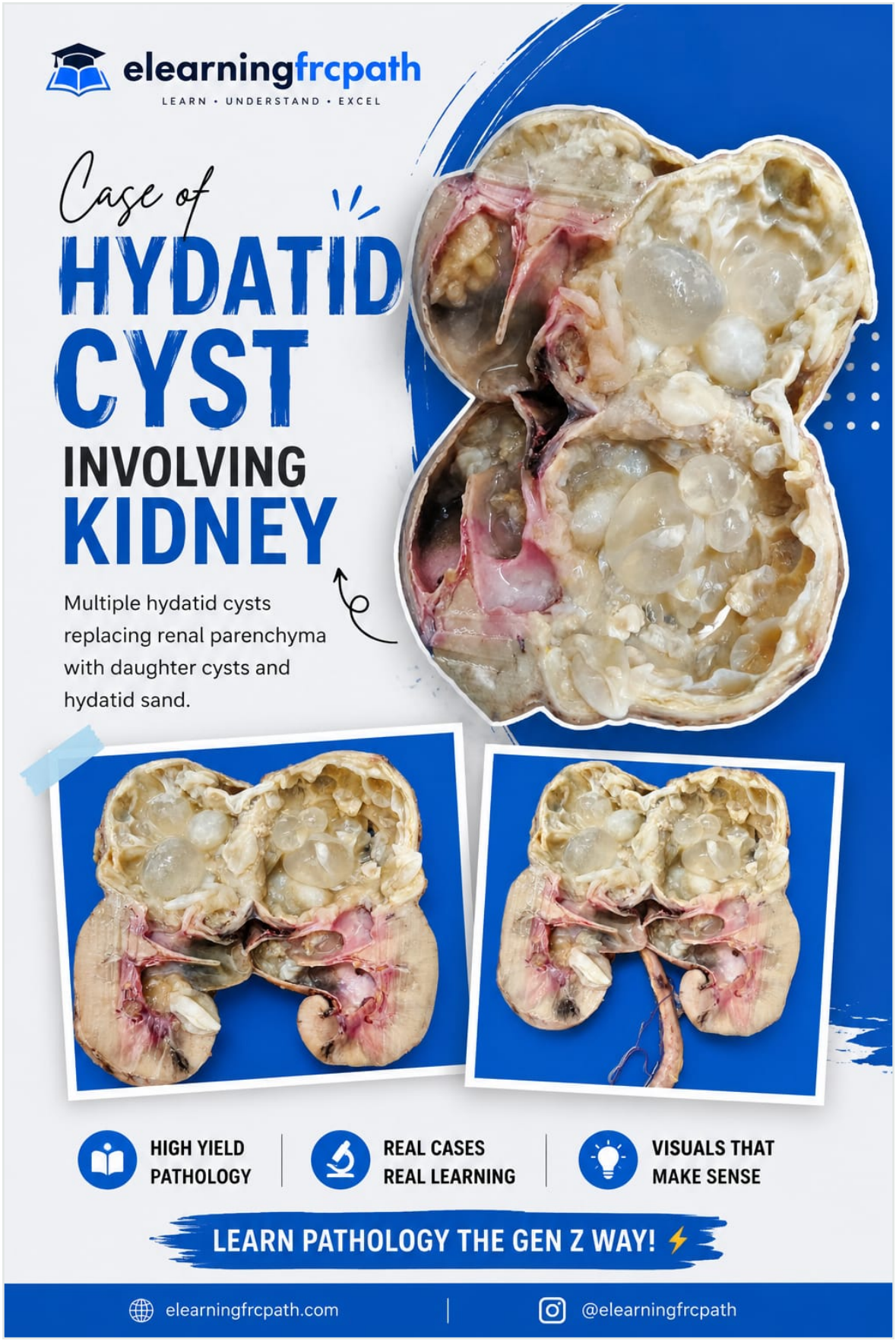
08

RENAL PATHOLOGY: MEDICAL & NEOPLASTIC

From glomeruli to pediatric renal tumors — the biggest chapter in the book, for a reason.

15 panels • maps to:

NEET-SS Pathology | FRCPath Part 2



Daughter cysts, hydatid sand, and a gross specimen photo that never fails to make the whole room go quiet.

Titer drops, patient goes into remission. Titer creeps back up, so does the proteinuria. PLA2R does not do subtlety.

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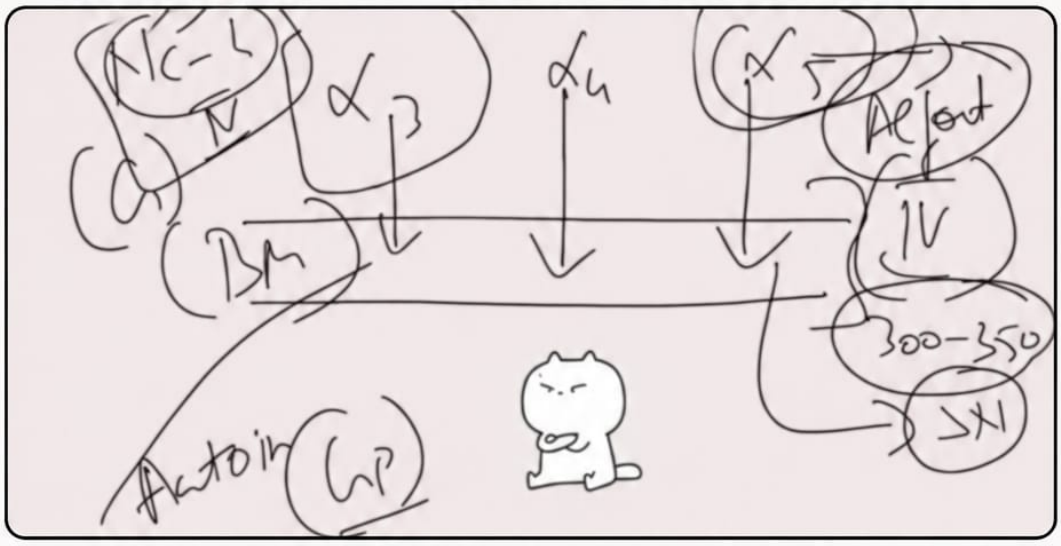
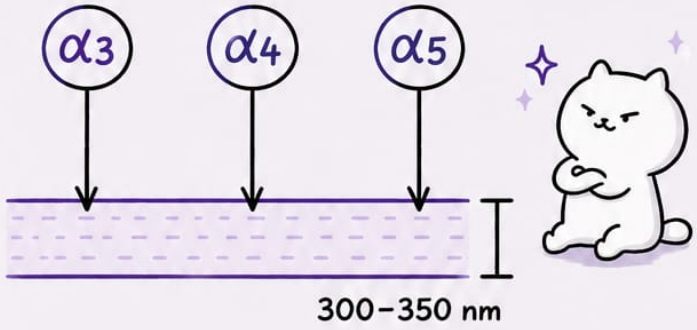


1. STRUCTURE & NORMAL CHARACTERISTICS

- ☆ **Key Component:** GBM is composed of Type IV collagen.
- ☆ **Normal Thickness:** 300 – 350 nm
- ☆ **Alpha Chains:** Type IV collagen consists of α3, α4, α5 chains.



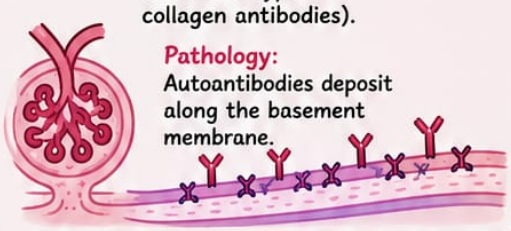
2. ASSOCIATED CLINICAL SYNDROMES

GOODPASTURE SYNDROME

Classification: Autoimmune disorder.

Mechanism: Autoantibodies target the α3 chain (NC1) of Type IV collagen (anti-NC3 Type IV collagen antibodies).

Pathology: Autoantibodies deposit along the basement membrane.



ALPORT SYNDROME

Classification: Genetic disorder (X-linked).

Mechanism: Defective gene that fails to properly code for the α5 chain of Type IV collagen.

Clinical Triad:

- **Glomerular Dysfunction** (hematuria, proteinuria)
- **Sensorineural Deafness** (progressive hearing loss)
- **Eye Defects** (lenticonus, retinopathy)

KNOW THE MEMBRANE. DIAGNOSE WITH CONFIDENCE.

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Same collagen chain — attacked by antibodies in one disease, never built properly in the other. The kidney loses either way.

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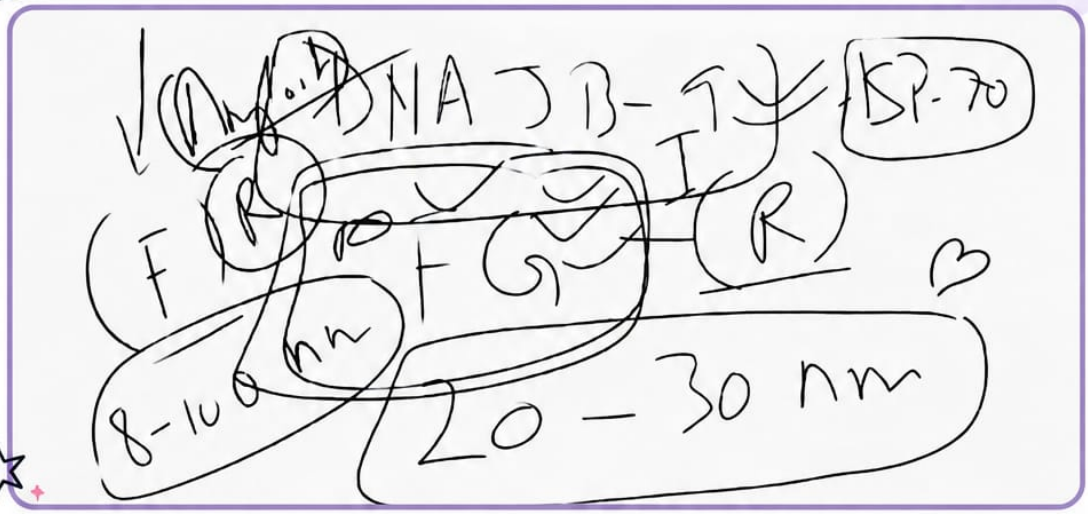
LEARN SMARTER, NOT HARDER

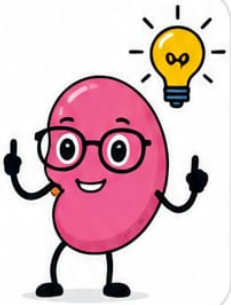


FGN VS. AMYLOIDOSIS

KNOW THE DIFFERENCE. DIAGNOSE WITH CONFIDENCE.

KEY DIAGNOSTIC MARKER

- DNAJB9 has been identified as a highly specific diagnostic biomarker for fibrillary glomerulonephritis (FGN).
- It is a member of the Heat Shock Protein 70 (HSP-70) co-chaperone family.
- DNAJB9 serves as an immunohistochemistry (IHC) marker to accurately differentiate FGN from other mimicking renal diseases.



ULTRASTRUCTURAL DIFFERENCES (FIBRIL SIZE)

While both diseases feature extracellular, randomly arranged fibril deposits, they differ significantly under electron microscopy:

	FIBRILLARY GLOMERULONEPHRITIS (FGN)	VS.	AMYLOIDOSIS
FIBRIL DIAMETER	20 – 30 nm		8 – 10 nm
ARRANGEMENT	Randomly arranged		Randomly arranged
PREVALENCE	Very rare renal disease		More common

PATHOLOGY IS COOL. YOU'VE GOT THIS!

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FOLLOW & LEARN!

Both look like a tangle of random fibrils on EM. Only the ruler — and DNAJB9 — settles the argument.

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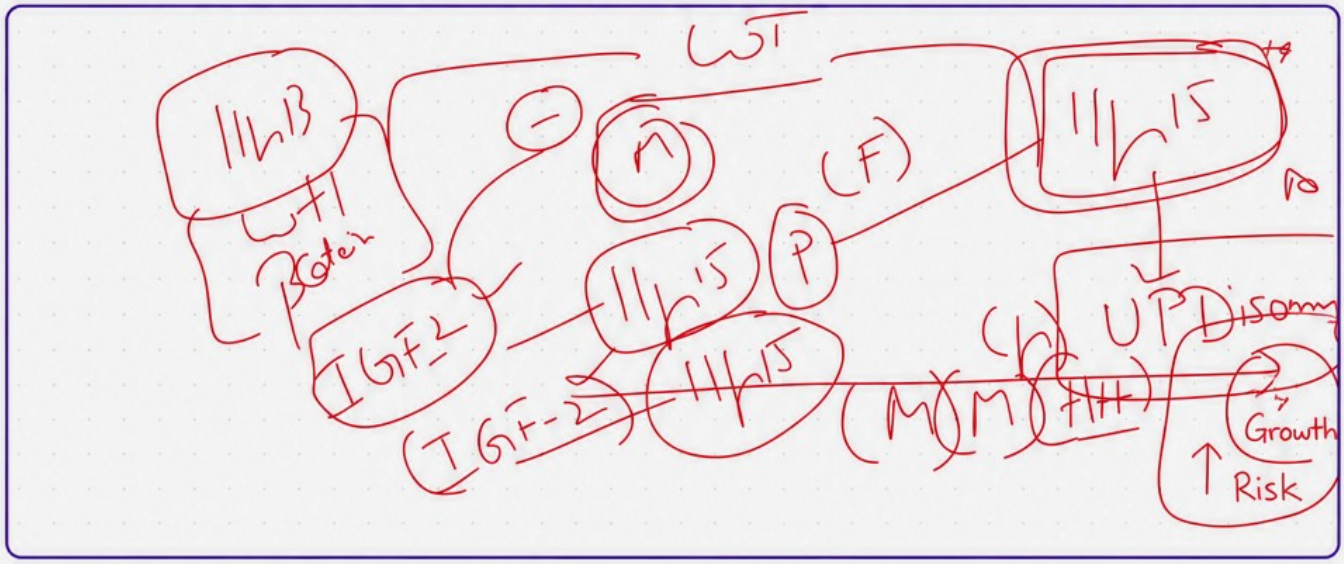
Master Pathology. One Concept at a Time

WHAT YOU ARE NOT READING AND THEY ARE NOT TELLING YOU

#Pathology ThatSticks

WILMS TUMOR PATHOGENESIS FOCUS



THE 2 MAJOR GENETIC PATHWAYS

11p13 PATHWAY

- Germline mutation in **WT1** gene
- May involve β-catenin (**CTNNB1**)

↓

Developmental arrest
(Intralobar nephrogenic rests)

11p15 PATHWAY

- Driven by Paternal Uniparental Disomy **(pUPD)**
- Both copies of 11p15 come from the father

↓

Overgrowth signal
(Perilobar nephrogenic rests)

Two different problems, one common outcome:

Persistent nephrogenic progenitors → Wilms tumor

Two completely different genetic wrong turns, same destination. Nephrogenic rests really don't like being told to stop growing.

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WHAT YOU ARE NOT READING
AND THEY ARE NOT TELLING YOU

THE FILTER THAT KEEPS PROTEIN OUT

THE GLOMERULAR SLIT DIAPHRAGM

THE DREAM TEAM OF THE FILTRATION BARRIER

NEPHRIN
(GENE: NPHS1)

The main gatekeeper. Controls the filtration of albumin and other proteins.

+

PODOCIN
(GENE: NPHS2)

The supporter. Lives inside the podocyte foot processes and connects directly to nephrin.

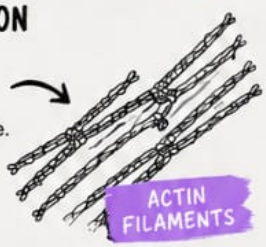
+

CD2AP
(GENE: CD2A)

The connector. Brings structure and stability to the slit diaphragm.

THE POWER CONNECTION

- These proteins link up with **actin filaments** (the cell's skeleton) inside the podocyte.
- This gives strength, shape, and protection to the filtration barrier.



WHEN THE CODE BREAKS

Mutations in NPHS1 or NPHS2 disrupt this framework.

RESULT?

COMPROMISED FILTRATION BARRIER → PROTEIN LEAK → FSGS & CONGENITAL NEPHROTIC SYNDROME

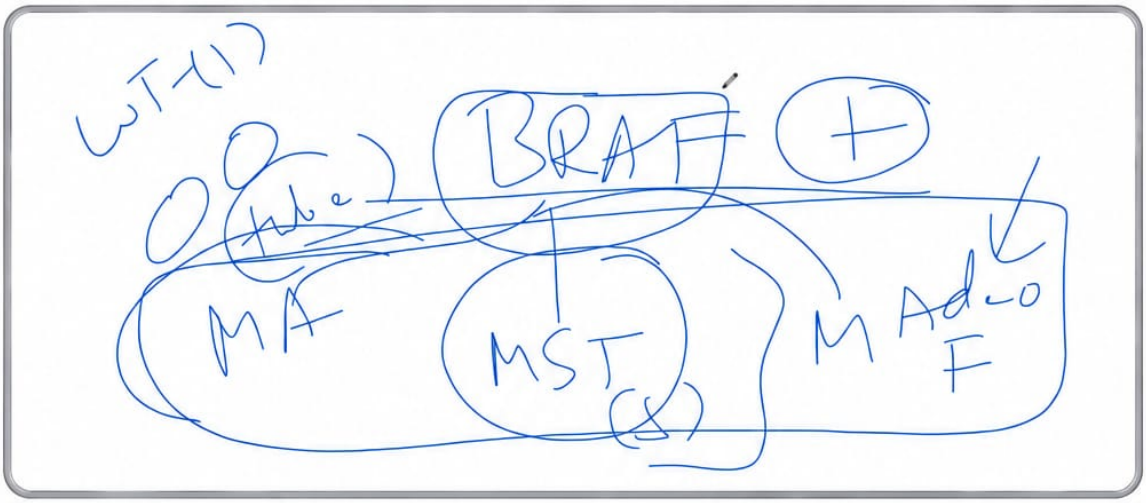
BIOLOGY ISN'T BORING, IT'S BRILLIANT

REMEMBER:
Tiny proteins.
Big impact.
Life-long consequences.

UPCOMING CLASS
MEDICAL KIDNEY DISEASE
Don't miss it!
Save the date & level up!

STUDY SMART. THINK DEEP. STAY CURIOUS.

Nephrin, podocin and CD2AP hold the whole filtration barrier together. Break one, and the protein just walks straight out.



BRAF-POSITIVE METANEPHRIC TUMORS

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LEARN. VISUALIZE. EXCEL.

THE "BROTHERHOOD" OF THE KIDNEY

THREE TUMORS. ONE GENE. DIFFERENT VIBES....

GEN Z EDITION

They may look different, but BRAF+ is their flex.

1 METANEPHRIC ADENOMA (MA)

- Morphology: Small tubules
- IHC: WT-1 positive
- BRAF is the real MVP
- Diagnosis flex: Highly specific with BRAF

PROGNOSIS: EXCELLENT

2 METANEPHRIC STROMAL TUMOR (MST)

- Morphology: Spindle cells
- Distinct but still in the crew
- BRAF+ keeps it in the family
- Indolent & chill (aka excellent prognosis)

PROGNOSIS: EXCELLENT

3 METANEPHRIC ADENOFIBROMA (MAdF)

- Morphology: Unique glandular + stromal mix
- Different look, same BRAF+ story
- Still part of the metanephric fam

PROGNOSIS: EXCELLENT

THE BIGGER PICTURE

Different morphologies. Same BRAF-driven pathway.
Diagnosis = Morphology + BRAF IHC. Easy.

SAME GENE DIFFERENT DRIP

KEY TAKEAWAYS FOR GEN Z PATHOLOGY

- Know the 3 brothers: MA, MST, MAdF
- BRAF+ is the glue that holds them together
- Excellent prognosis = good vibes only
- Morphology is the look, BRAF is the hook

STUDY SMART, NOT HARD.

Understand the story.
Crush the exam.

100

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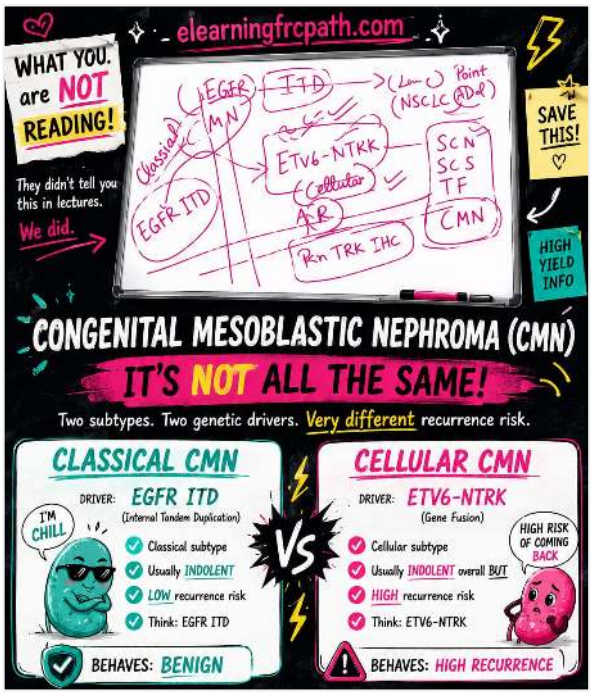
THREE TUMORS. ONE GENE. DIFFERENT VIBES.... | BRAF+ = THE FLEX

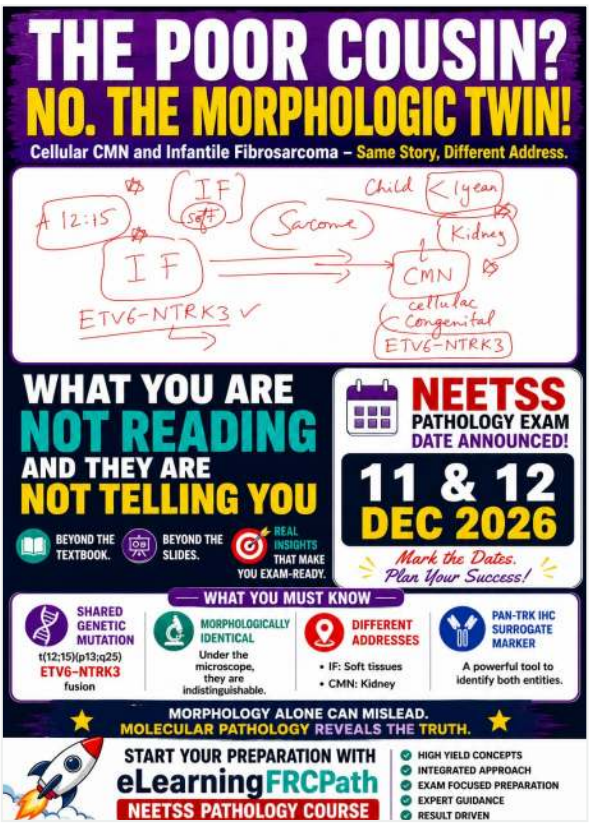
Three tumors, three completely different looks, one shared BRAF mutation running the show backstage.

Side by Side: Congenital Mesoblastic Nephroma



Same tumor name, two very different personalities. One's chill. The other one keeps coming back.

VS



Identical under the microscope, same fusion gene, different postcode. Morphology alone would never have caught this.

Same name, different personalities — and the exam knows it.

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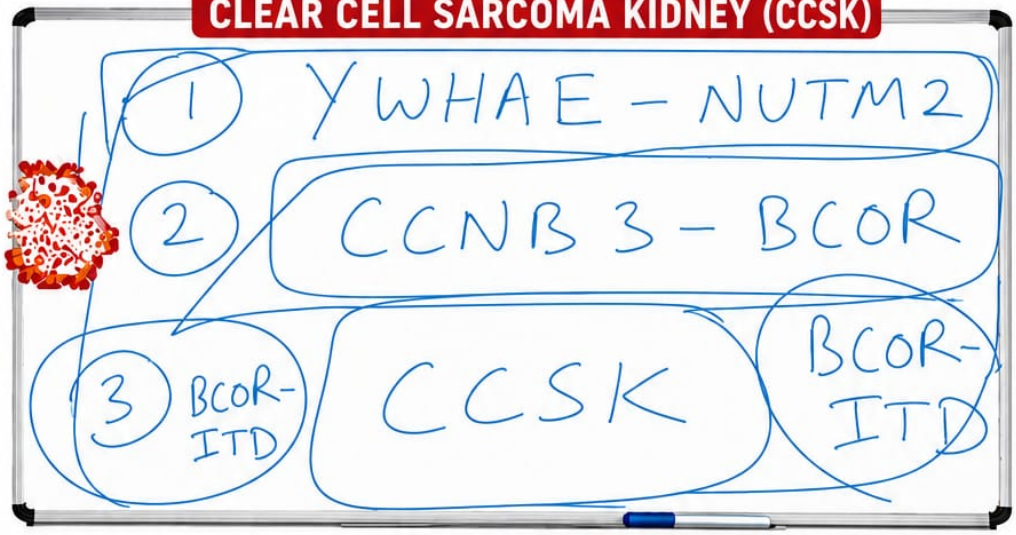
PEDIATRIC RENAL TUMORS

MOLECULAR PATHOBIOLOGY FOR CLEAR CELL SARCOMA KIDNEY (CCSK)



WHAT YOU ARE NOT READING AND THEY ARE NOT TELLING YOU.

ONE FAMILY. THREE HITS. MUTUALLY EXCLUSIVE.

1 BCOR-ITD
(INTERNAL TANDEM DUPLICATION)

MOST COMMON ALTERATION IN CCSK

2 YWHAE-NUTM2
FUSION

SPECIFIC CHROMOSOMAL TRANSLOCATION

3 CCNB3-BCOR
FUSION

DISTINCT MOLECULAR VARIANT

CROSSOVER INTO GYNECO-PATH
High-grade Endometrial Stromal Sarcomas (ESS) are frequently defined by the same molecular signatures (YWHAE fusions and BCOR alterations).

BONE & SOFT TISSUE CONNECTION
Tumors with CCNB3-BCOR fusion are now recognized as a distinct disease entity – not just "round cell sarcoma" anymore.

THE GOLDEN RULE: THESE 3 ALTERATIONS ARE MUTUALLY EXCLUSIVE. IF A TUMOR HAS ONE, IT WON'T HAVE THE OTHER TWO.

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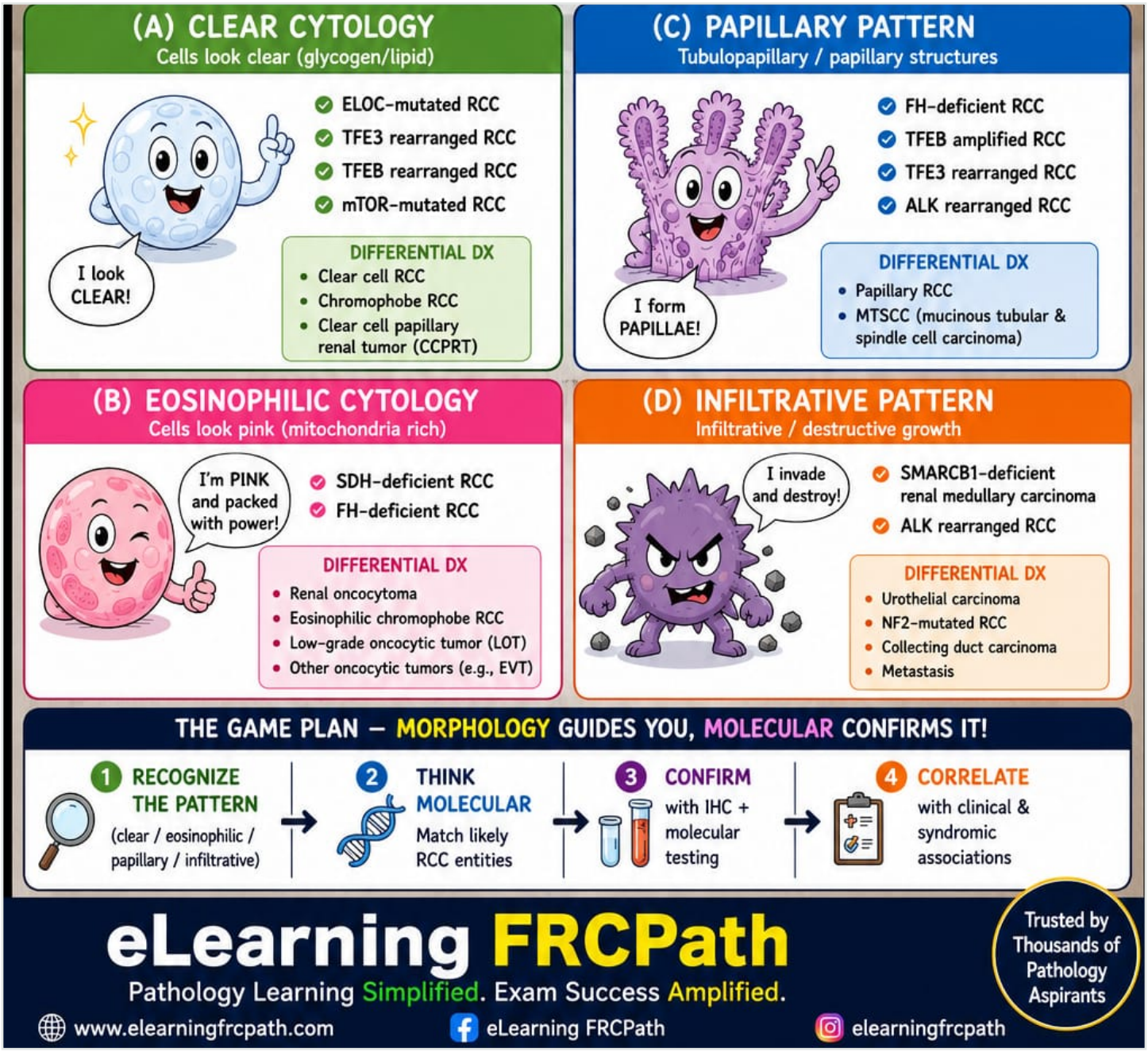
DEEP LEARNING. | REAL UNDERSTANDING. | EXAM DOMINANCE.

NEETSS PATHOLOGY EXAM
DEC 11TH
YOUR D-DAY. OWN IT.

PATHOLOGY THAT MAKES SENSE. | CONCEPTS THAT STICK. | RANKERS TRUST US.

One family of mutations, three members, and a strict no-overlap policy. CCSK does not do combos.



Clear, pink, papillary or invasive — the cytoplasm hands you the first clue before molecular testing even opens its mouth.

WHAT YOU ARE NOT READING AND THEY ARE NOT TELLING YOU

SERIES

eLearning FRCPath
High-Yield Pathology Learning

THE REAL STORY BEHIND MiTF FAMILY RCC, PEComas, CATHEPSINS & HMB45

EXAM FACTS
- MiT/TFE PATHWAY
- LYSOSOMES
- MELANOSOMES
- CATHEPSIN K
- HMB45

HIGH-YIELD!

THE MiT/TFE – LYSOSOME – MELANOSOME AXIS

1. MiT/TFE ACTIVATION
- Translocation / mutation / amplification / mTOR dysregulation (TSC1/2 loss)
- → Constitutive nuclear activation

2. LYSOSOMAL EXPANSION
- CLEAR network upregulation
- Lysosomal biogenesis, autophagy, trafficking
- ↑ Cathepsins (Cathepsin K, L, B)

3. MELANOSOME-RELATED PROGRAM
- Melanosomes are lysosome-related organelles (LROs)
- ↑ PMEL (gp100), TYR, MART1, Melan-A
- → HMB45 positivity

4. TUMOR PHENOTYPE
- Eosinophilic, granular cytoplasm
- Nested /alveolar patterns
- Co-expression of Cathepsin K + HMB45 ± Melan-A

5. mTOR / TSC CONNECTION
- TSC1/2 loss → mTOR activation
- TFEB/TFE3 escape cytoplasmic retention
- Translocate to nucleus → program ON

WHERE YOU SEE THIS AXIS

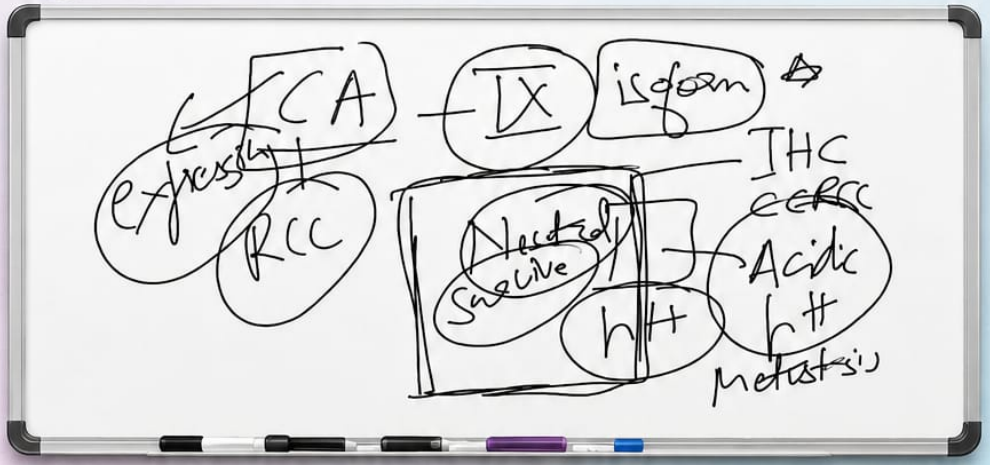
- PEComas (AML, LAM, PEComa NOS)
- TFEB-rearranged RCC
- TFE3-rearranged RCC
- Epithelioid Angiomyolipoma (AML)
- Eosinophilic Vacuolated Tumors (TSC)
- Eosinophilic Solid & Cystic RCC
- Other mTOR/TSC-associated Eosinophilic Renal Tumors

DIFFERENT NAMES. SAME BIOLOGIC PROGRAM.

PEComas, TFE3-rearranged RCC and HMB45 positivity all trace back to the same lysosome-melanosome program. Small world.

WHAT YOU ARE NOT READING

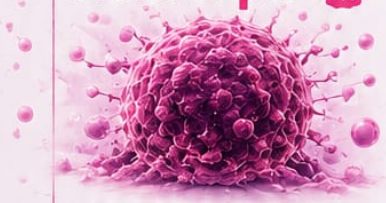
AND THEY ARE NOT TELLING YOU IS.....



THE NORMAL JOB OF CARBONIC ANHYDRASE (CA) IS TO MAINTAIN pH.
BUT IN CARCINOMA CELLS—ESPECIALLY RCC—IT FLIPS THE SCRIPT
TO HELP TUMORS GROW, SURVIVE, AND SPREAD.

EXTRACELLULAR
(OUTSIDE THE CELL)

MAINTAINS AN
ACIDIC pH



THE ACIDIC ENVIRONMENT
ACTS LIKE A CORROSIVE FORCE:

- DEGRADES THE SURROUNDING MATRIX
- BREAKS DOWN BARRIERS
- CLEARS A PATH FOR INVASION

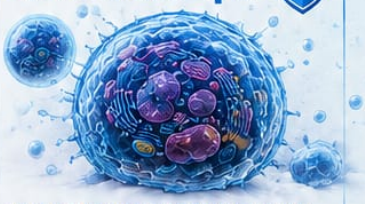
DIRECTLY PROMOTES METASTASIS

CA-IX

- DOUBLE GAME. SINGLE GOAL.
- OUTSIDE: DESTROY & INVEST.
- INSIDE: PROTECT & PERSIST.
- RESULT: AGGRESSIVE CANCER THAT SPREADS & SURVIVES.

INTRACELLULAR
(INSIDE THE CELL)

MAINTAINS A
NEUTRAL pH



KEEPS THE CELL'S INTERNAL WORLD
STABLE AND PROTECTED:

- PRESERVES ENZYME FUNCTION
- PROTECTS CELLULAR MACHINERY
- ENSURES SURVIVAL IN HARSH CONDITIONS

FUELING TUMOR GROWTH & SURVIVAL

THE BOTTOM LINE

CA-IX is not just a marker.
It's a master switch in RCC.
Target it. Understand it.
Disrupt it.
That's how we stop it.

KNOWLEDGE IS POWER.
QUESTION MORE.
LEARN DEEPER.

STAY CURIOUS.
STAY AHEAD.
YOUR NEXT DISCOVERY
COULD SAVE LIVES.

elearning FRC PATH

LEARN BEYOND.
LEAD BEYOND.

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Carbonic anhydrase's day job is keeping pH balanced. In renal cell carcinoma, it moonlights as a metastasis enabler.

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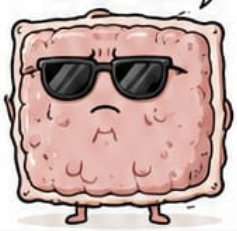
Your Path. Our Purpose.

EOSINOPHILIC RENAL TUMORS WHO'S WHO?

	LOT (Low-grade Oncocytic Tumor)	ONCOCYTOMA	CHROMOPHOBE RCC	EVT (Eosinophilic Vacuolated Tumor)
	I'm chill & low-grade. CK7 yes, CD117 no!	I'm benign & classic. CD117 is my superpower!	I've got plant cell borders & raisinoid nuclei!	I'm vacuolated & on the mTOR spectrum!
				
ARCHITECTURE	Solid / Nested	Nested / Tubular	Solid sheets	Solid nests
CYTOPLASM	Eosinophilic	Dense granular oncocytic	Pale eosinophilic with perinuclear halos	Eosinophilic with prominent vacuoles
NUCLEI	Bland, low-grade	Round, uniform	Irregular "raisinoid"	Large nucleoli common
CLUE	Hybrid LOT phenotype	Central scar (gross)	Wrinkled nuclei + halos	Intracytoplasmic vacuoles
CK7	POSITIVE (diffuse)	NEGATIVE / Focal	POSITIVE (diffuse)	FOCAL / PATCHY
CD117 (KIT)	NEGATIVE	POSITIVE	POSITIVE	POSITIVE

Four pink, granular tumors that all deserve their own name instead of one shared shrug.

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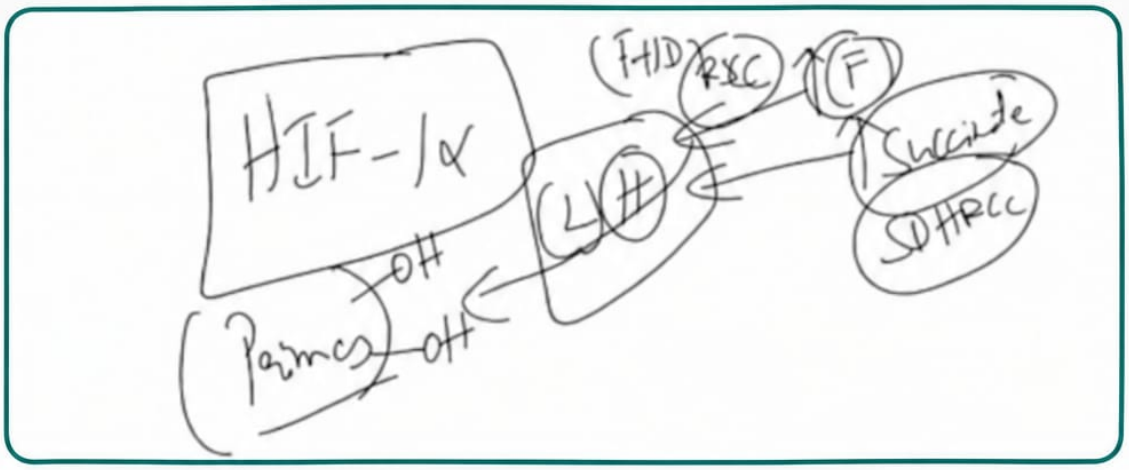


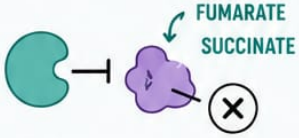
MECHANISM OF HIF-1α REGULATION

HIGH-YIELD MADE SIMPLE

1 HYDROXYLATION

The enzyme **prolyl hydroxylase** adds a hydroxyl group (–OH) to HIF-1α, priming it for degradation.

2 INHIBITION



This hydroxylase enzyme is inhibited by high cellular levels of **fumarate** or **succinate**.

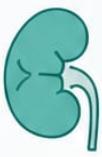
3 EFFECT

Inhibition prevents hydroxylation, leading to HIF-1α stabilization and activation of genes that drive tumorigenesis.

⚠ PATHOLOGICAL IMPLICATIONS

The accumulation of these metabolites due to enzyme deficiencies leads to specific cancers:

FH DEFICIENCY



Fumarate Hydratase (FH) Deficiency: Causes fumarate to accumulate, leading to Fumarate Hydratase-deficient RCC (FH-RCC).

SDH DEFICIENCY

Succinate Dehydrogenase (SDH) Deficiency: A similar mechanism where succinate accumulation inhibits the hydroxylase, contributing to tumorigenesis (often associated with hereditary paraganglioma-pheochromocytoma syndromes).

FOCUS. LEARN. ACE FRCPath.

Trusted by Pathology Aspirants for FRCPath & NEET SS

SCAN TO LEARN MORE!

Block the hydroxylase, stabilize HIF-1a, and the tumorigenesis switch flips before anyone notices.

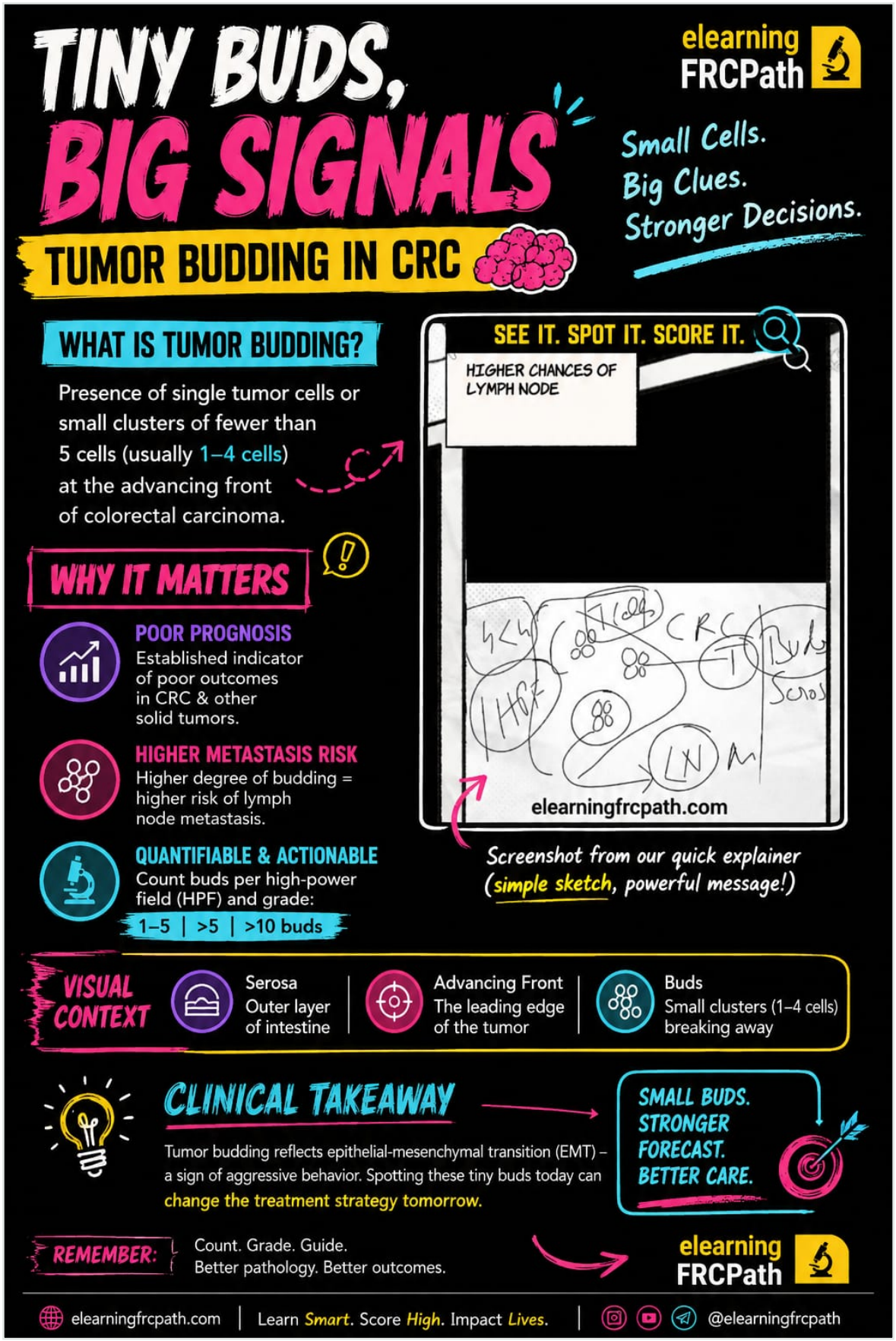
09

GASTROINTESTINAL PATHOLOGY

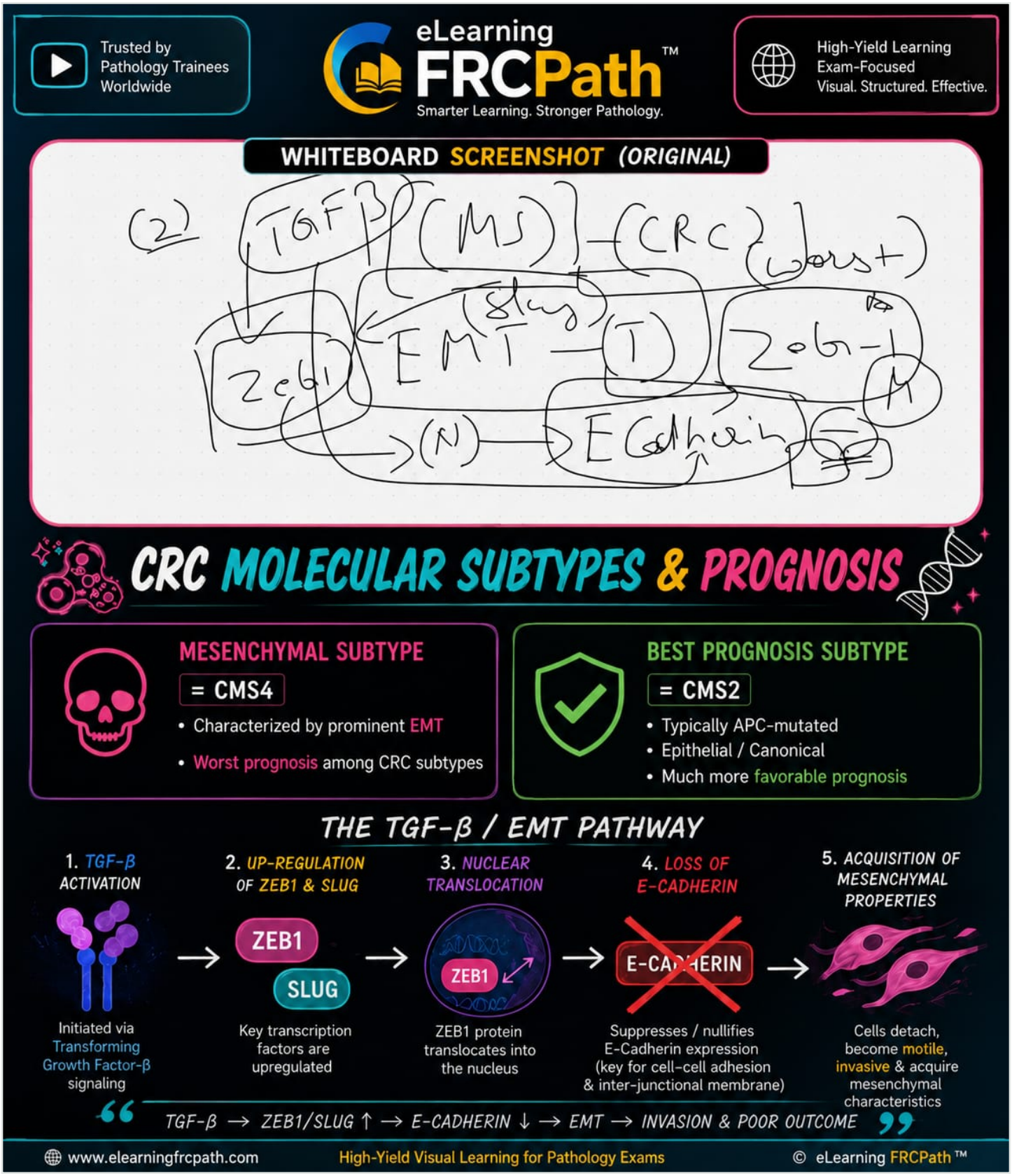
Colon cancer's favorite tricks, and the syndrome you should never miss.

5 panels • maps to:

NEET-SS Pathology | FRCPath Part 1



One to four cells breaking off at the invasive front. Small detail, huge difference to the prognosis line of the report.



Same organ, same word "colorectal," wildly different outcomes depending on which CMS subtype shows up.

Snail, Slug and ZEB1 sound like a band lineup. They're actually why colon cancer cells learn to let go and invade.

LYNCH SYNDROME

aka HNPCC THINK EARLY. THINK FAMILIES. THINK LYNCH.

HIGH YIELD ALERT!

1 AGE-BASED SCREENING

Any patient diagnosed with COLORECTAL CARCINOMA (CRC) before the age of **50** should be investigated for HNPCC.

GEN Z NOTE

YOUNG AGE + CRC = CHECK FOR LYNCH!

2 HISTOLOGICAL FEATURES IN PATIENTS UNDER 60

Certain patterns in colorectal tumors strongly suggest HNPCC.

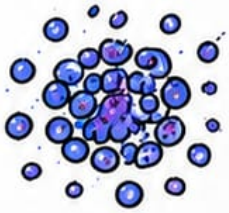
SIGNET-RING MORPHOLOGY

Cells that resemble a signet ring due to a large mucus vacuole.

MUCINOUS MORPHOLOGY

A tumor that produces significant amounts of extracellular mucus.

LYMPHOCYTIC REACTION



Specifically, a Crohn's-like reaction, where lymphoid aggregates are present at the tumor's advancing edge.

Colorectal cancer before 50 isn't bad luck until someone proves otherwise. Check for Lynch first.

PDGFRA MUTATIONS IN GIST PATIENTS

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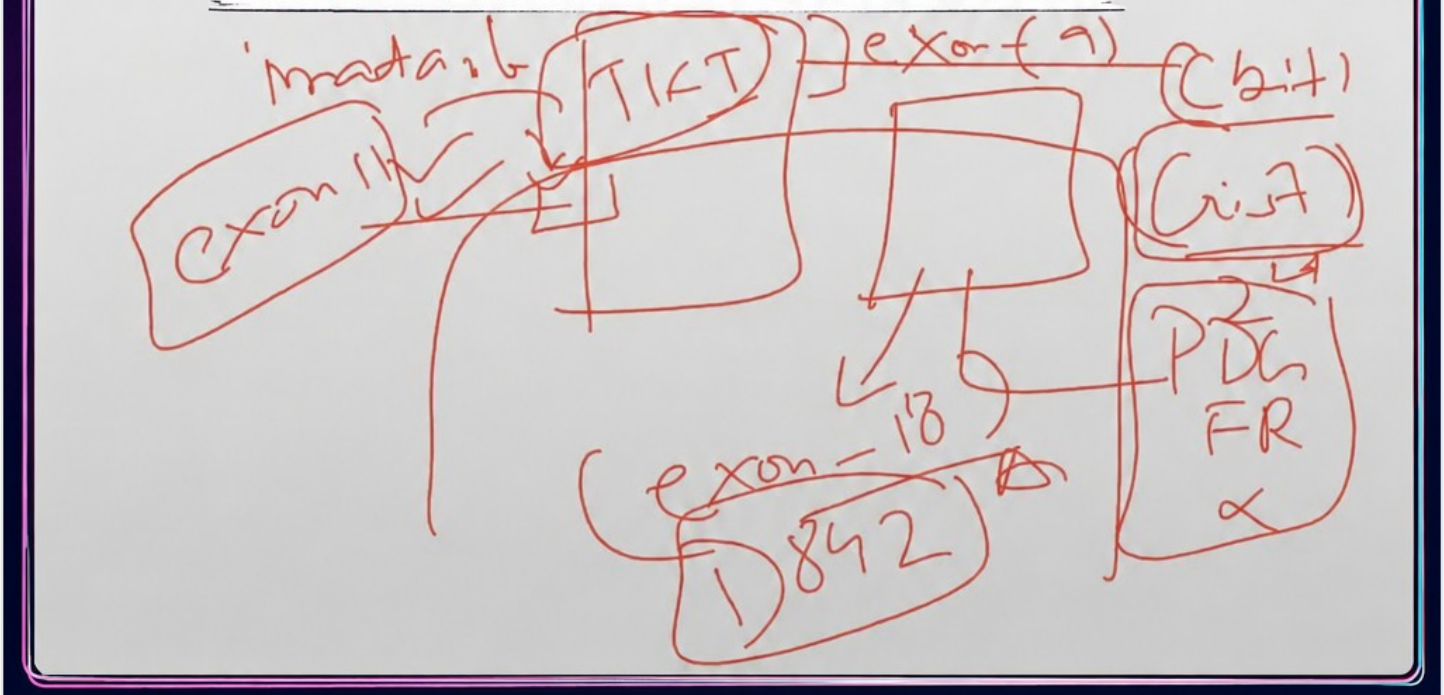
LEARN TODAY LEAD TOMORROW

WHITEBOARD EXPLAINED BY ELEARNINGFRCPATH.COM



PDGFRA MUTATIONS DRIVE A DISTINCT SUBSET OF GISTs — KNOW THEM, TARGET THEM!

WHERE DO THEY OCCUR?

- Predominantly in exon 18 of PDGFRA gene
- Key hotspot: **D842V** mutation

COMMON PDGFRA MUTATIONS

- **D842V** (Exon 18) – most common
- **D842Y** (Exon 18)
- **D842H** (Exon 18)

IMATINIB RESPONSE

D842V mutation is **RESISTANT** to Imatinib

Exon 18's D842V mutation shrugs off imatinib like it's nothing. Know this one before the exam does.

10

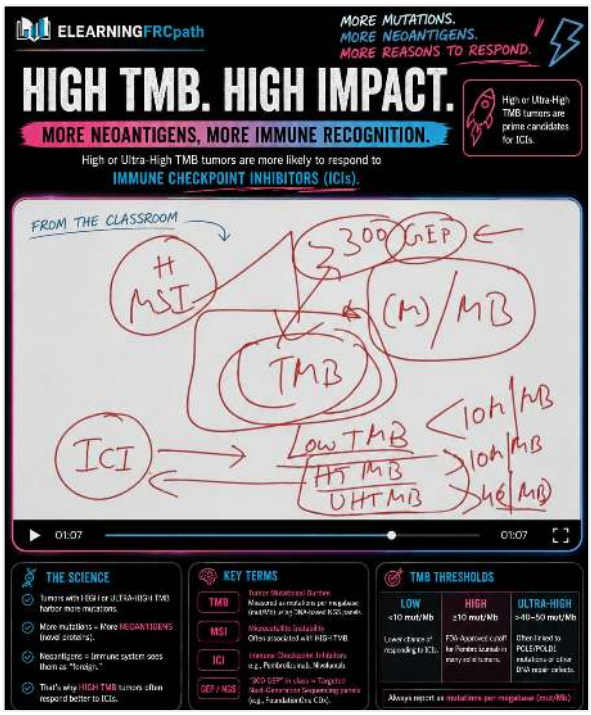
BONUS: IMMUNO-ONCOLOGY & ABOUT ELEARNING FRCPATH

One last high-yield concept, then meet the people behind this book.

2 panels • maps to:

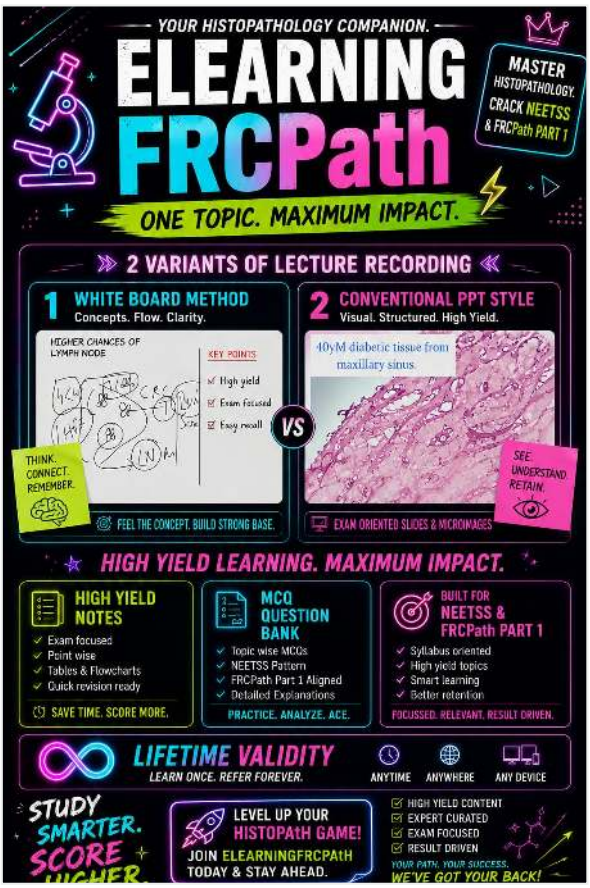
FRCPath Part 1 | FRCPath Part 2 | NEET-SS Pathology

Closing Spread



More mutations means more neoantigens means more reasons for the immune system to finally notice the tumor.

→



Messy whiteboard or clean slide deck — however it clicks for you, the goal's the same: walk into that exam and actually know it.

That's a wrap. Now go make those 70 panels count.

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Keywords: FRCPath exam preparation, NEET-SS pathology, histopathology high-yield notes, MD/DNB pathology