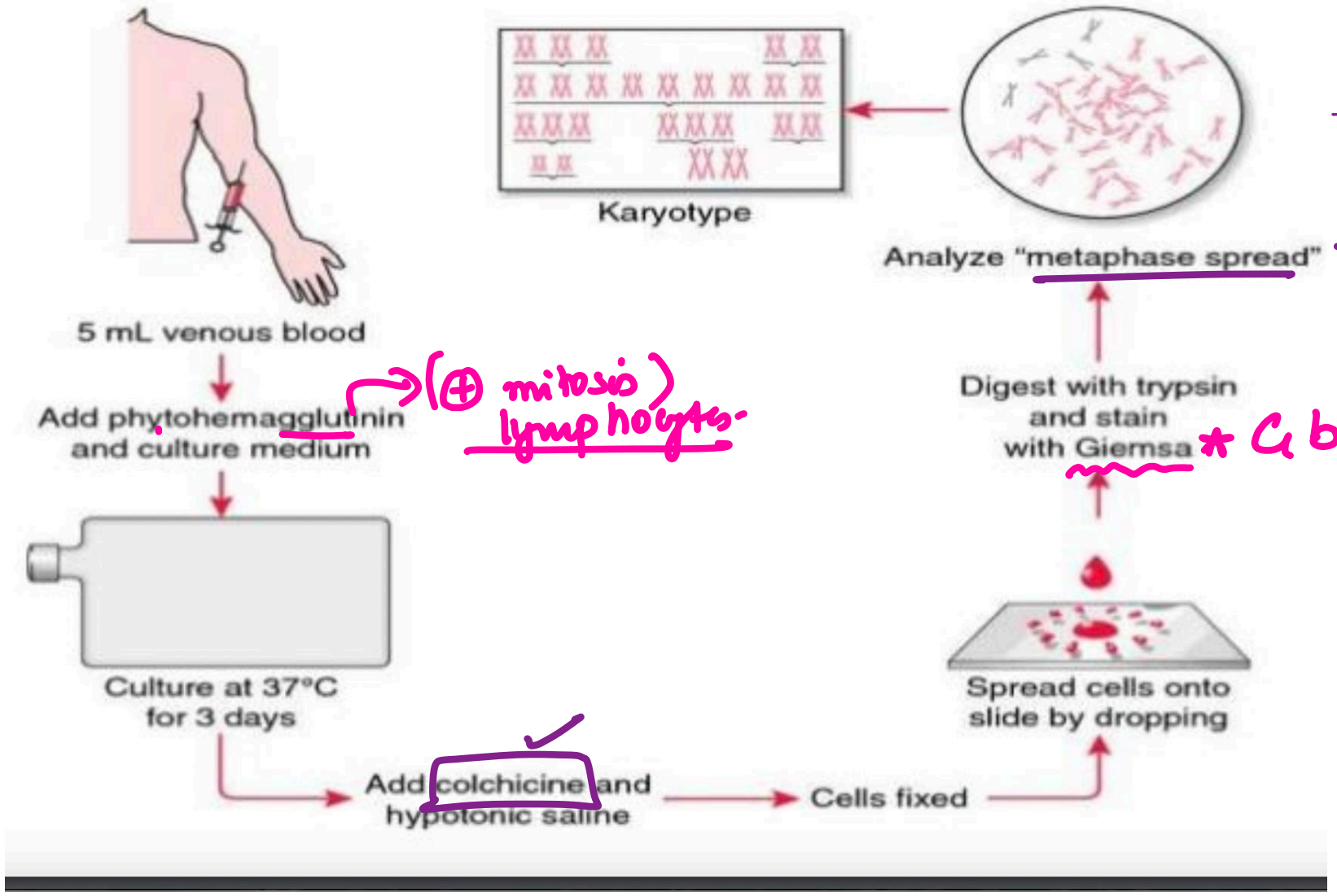
BIOCHEMISTRY BINGE REVISION

Medsynapse by Dr. Nikita



Karyotyping
- metaphase
colchicine

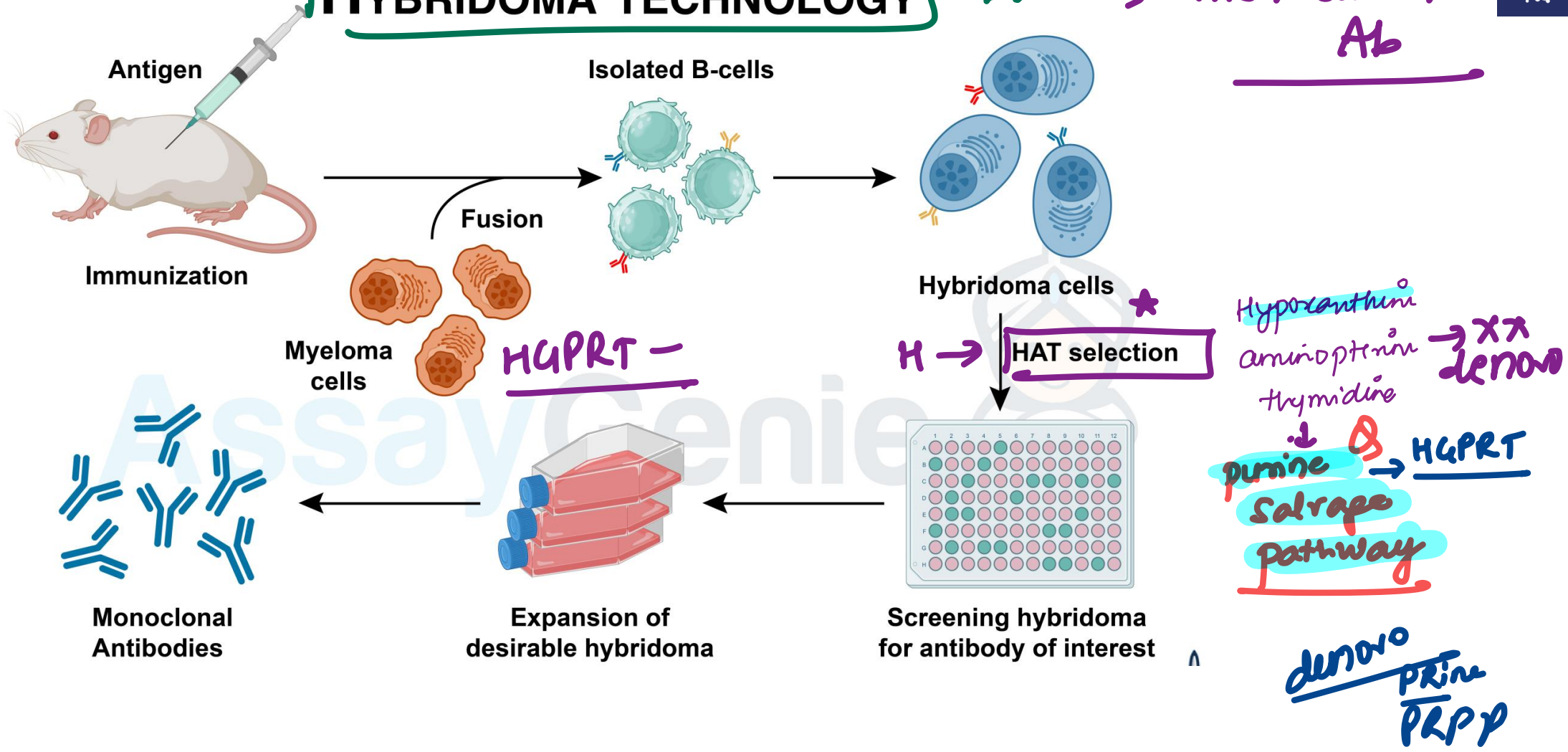
(⊕ mitosis) lymphocytes.

G banding

C.I

FISH

HYBRIDOMA TECHNOLOGY

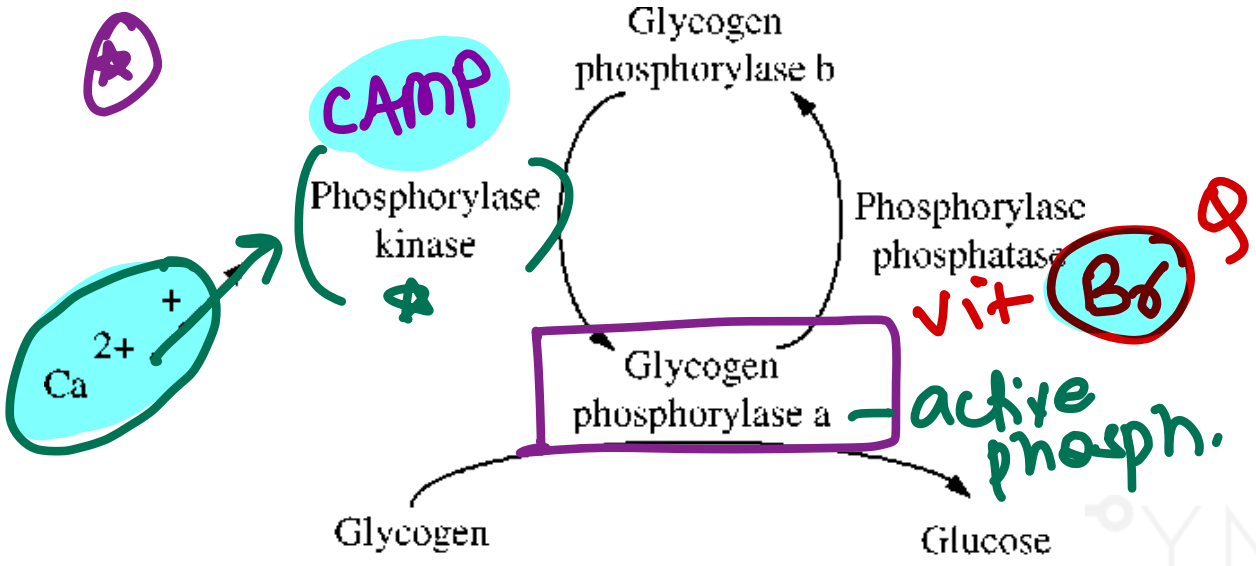


** → monoclonal Ab

Hypoxanthine
aminopterin
thymidine
→ XX denovo

purine salvage pathway → HGPRT

denovo pathway PRPP



inh for:

- Glycogen phosphorylase → both liver & muscle
- gluco. 6 phosphatase → von Gierke → liver only

vit B6

active phosph.

* active in phosphorylated Glycogen phosphorylase

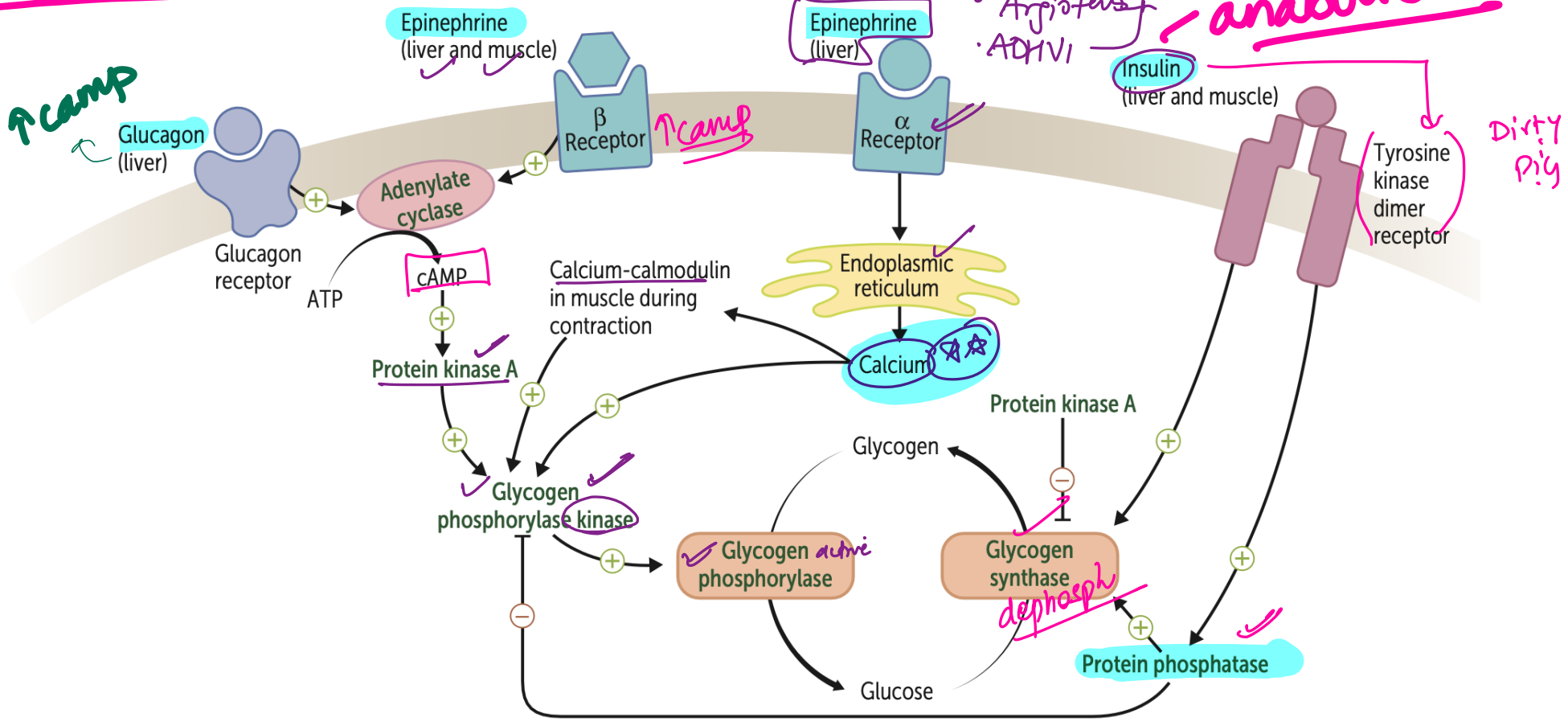
↓

glycogenolysis

⊕ fasting

⊕ fosphorylated.

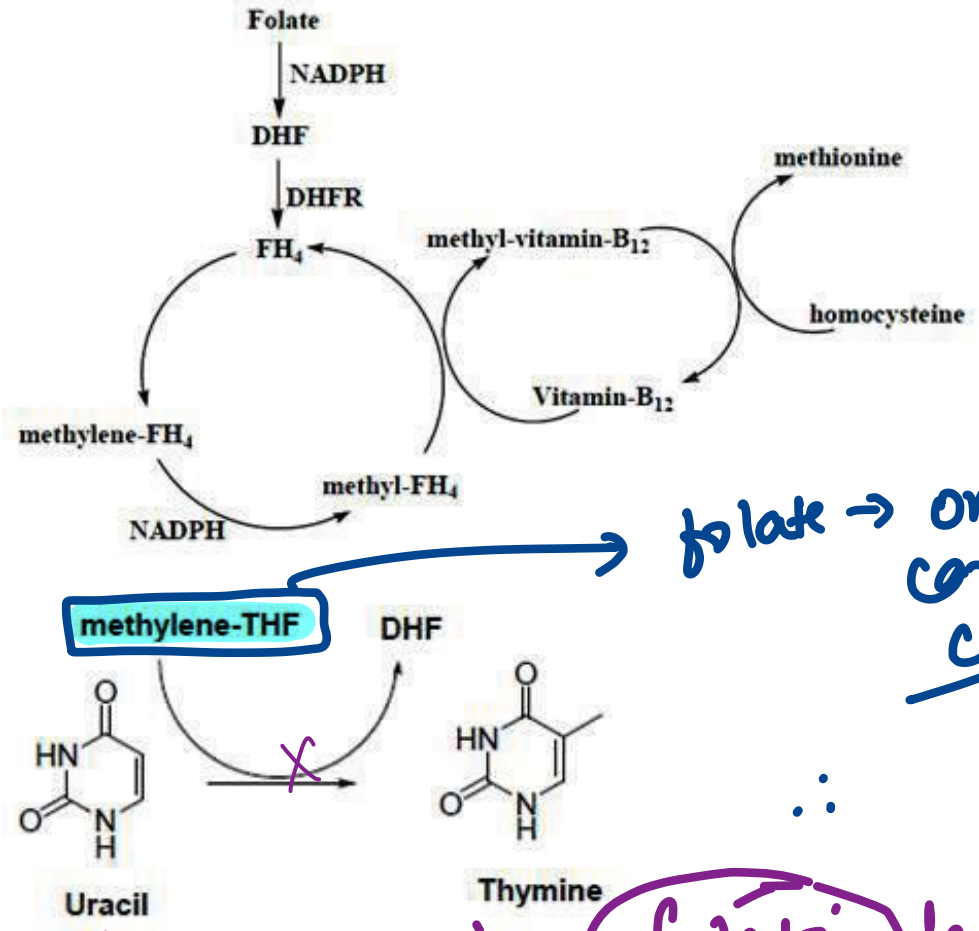
Glycogen regulation by insulin and glucagon/epinephrine



glucagon → ↑ camp → ↑ heart ⊕

→ Rx for β blocker toxicity

β1 ✓ ANP ✱ (β → ↑cAMP glucagon.)



P4Q

DNA · XU

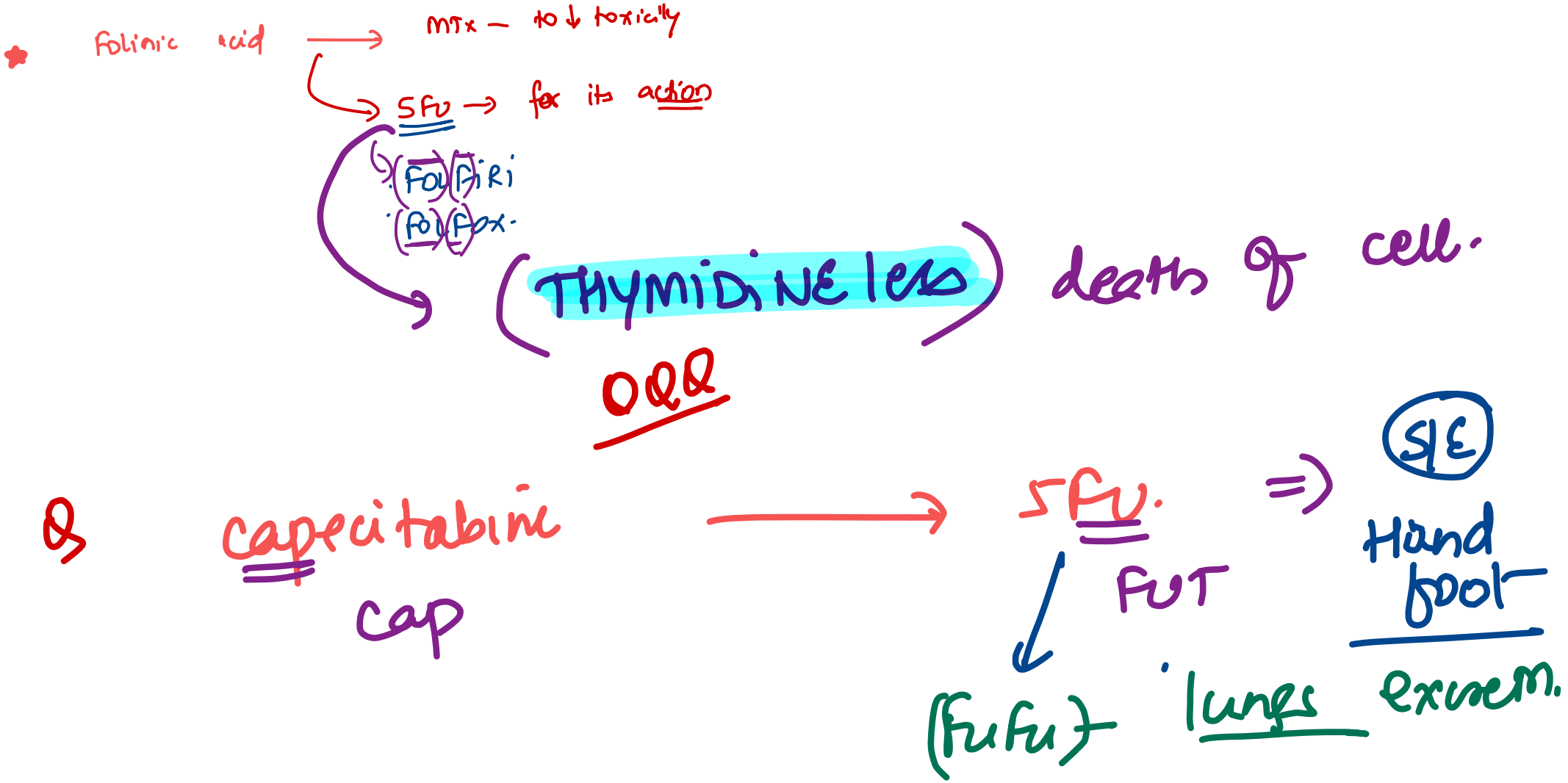
purine → AG

pyri → CUT

folate → one carbon carrier

∴

↳ in DNA if folate def ☆


Folinic acid
MTX — to ↓ toxicity
5Fu → for its action
FOLFIRI
FOLFOX
THYMIDINE less
death of cell.
OR
& capecitabine
cap
5fu.
FUT
(FuFu)
SE
Hand foot
lungs
exam.

Nucleoside = base + (deoxy)ribose (sugar).
Nucleotide = base + (deoxy)ribose + phosphate; linked by 3′-5′ phosphodiester bond.

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Deamination reactions:
Cytosine → uracil
Adenine → hypoxanthine
Guanine → xanthine
5-methylcytosine → thymine

Uracil found in RNA; thymine in DNA.
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5′ end of incoming nucleotide bears the triphosphate (energy source for the bond). α-Phosphate is target of 3′ hydroxyl attack.

Pure **A**s **G**old.
CUT the **pyr**amid.
Thymine has a **methyl**.
C-G bond (3 H bonds) stronger than A-T bond (2 H bonds). ↑ C-G content → ↑ melting temperature of DNA. "**C-G** bonds are like **C**razy **G**lue."

Amino acids necessary for **pur**ine synthesis (cats **purr** until they **GAG**):
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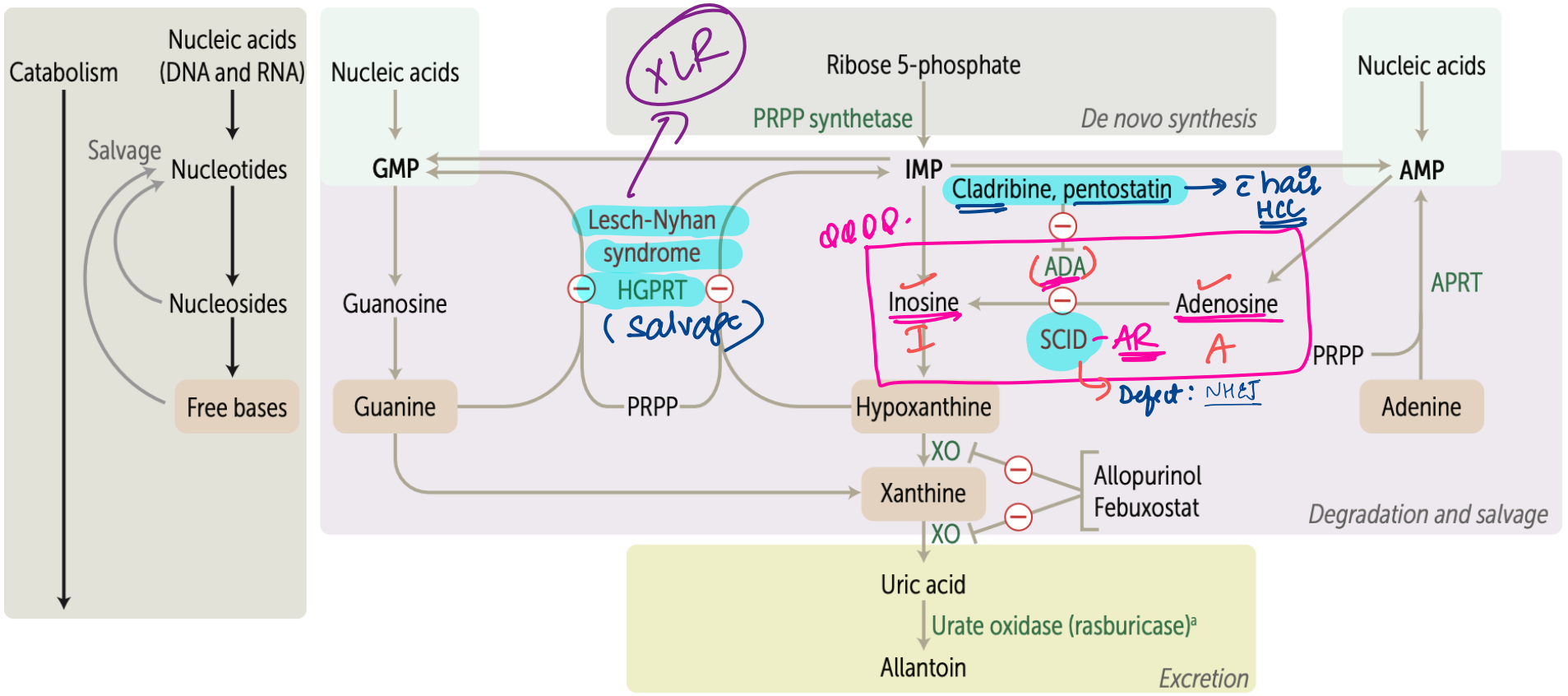
Aspartate
Glutamine



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Regulation of gene expression

Promoter	Site where RNA polymerase II and multiple other transcription factors bind to DNA upstream from gene locus (AT-rich upstream sequence with TATA and CAAT boxes, which differ between eukaryotes and prokaryotes). Promoters increase ori activity.	Promoter mutation commonly results in dramatic ↓ in level of gene transcription.
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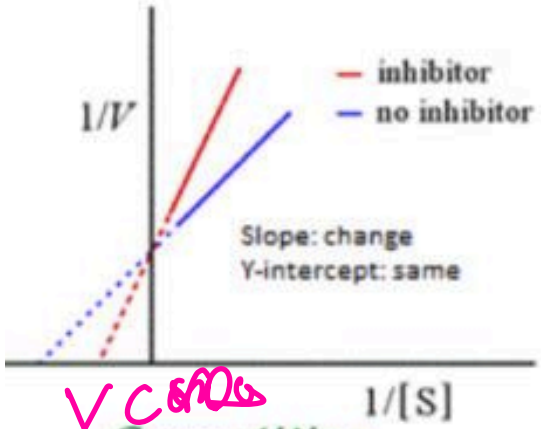
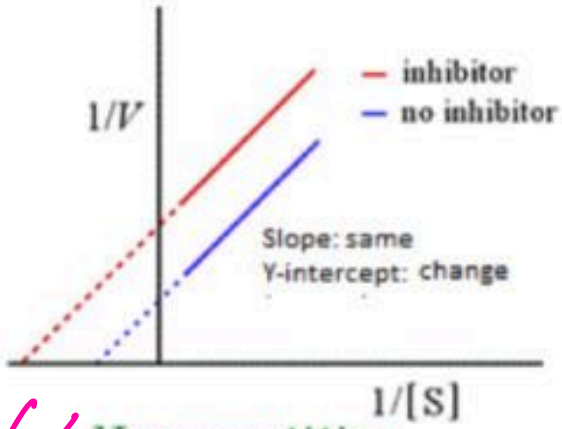
Epigenetics	Changes made to gene expression (heritable mitotically/meiotically) without a change in underlying DNA sequence.	Primary mechanisms of epigenetic change include DNA methylation, histone modification, and noncoding RNA.

QQQ.

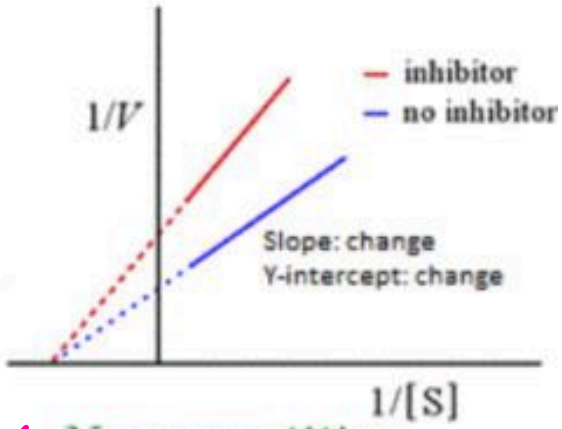
Lineweaver-Burk plots for enzyme inhibition



Competitive inhibition
K_M increased
V_{max} unaffected



Uncompetitive inhibition
K_M reduced
V_{max} reduced



Noncompetitive (Mixed) inhibition
K_M unaffected
V_{max} reduced

- Competitive
  - Km ↑
  - Vmax same
- TCA → malonate → complex ② ⊖ ETC
  - ⊖ SD.
  - iron MSD.

Rate-determining enzymes of metabolic processes

PROCESS	ENZYME	REGULATORS
Glycolysis	Phosphofructokinase-1 (PFK-1)	AMP ⊕, fructose-2,6-bisphosphate ⊕ ATP ⊖, citrate ⊖
Gluconeogenesis	Fructose-1,6-bisphosphatase 1	AMP ⊖, fructose-2,6-bisphosphate ⊖
TCA cycle	Isocitrate dehydrogenase	ADP ⊕ ATP ⊖, NADH ⊖
Glycogenesis	Glycogen synthase	Glucose-6-phosphate ⊕, insulin ⊕, cortisol ⊕ Epinephrine ⊖, glucagon ⊖
Glycogenolysis	Glycogen phosphorylase	Epinephrine ⊕, glucagon ⊕, AMP ⊕ Glucose-6-phosphate ⊖, insulin ⊖, ATP ⊖
HMP shunt	Glucose-6-phosphate dehydrogenase (G6PD)	$NADP^+$ ⊕ NADPH ⊖
De novo pyrimidine synthesis	Carbamoyl phosphate synthetase II	ATP ⊕, PRPP ⊕ UTP ⊖
De novo purine synthesis	Glutamine-phosphoribosylpyrophosphate (PRPP) amidotransferase	AMP ⊖, inosine monophosphate (IMP) ⊖, GMP ⊖
Urea cycle	Carbamoyl phosphate synthetase I	N-acetylglutamate ⊕
Fatty acid synthesis	Acetyl-CoA carboxylase (ACC)	Insulin ⊕, citrate ⊕ Glucagon ⊖, palmitoyl-CoA ⊖
Fatty acid oxidation	Carnitine acyltransferase I	Malonyl-CoA ⊖
Ketogenesis	HMG-CoA synthase (HOMG! I'm starving!)	
Cholesterol synthesis	HMG-CoA reductase	Insulin ⊕, thyroxine ⊕, estrogen ⊕ Glucagon ⊖, cholesterol ⊖

TCA → ATP ⊖ / NADH ⊖

• Insulin → anabolic
- ⊕ glycogenesis
- ⊕ cholesterol synth

except (
- Ketogenesis /
- gluconeogenesis
)

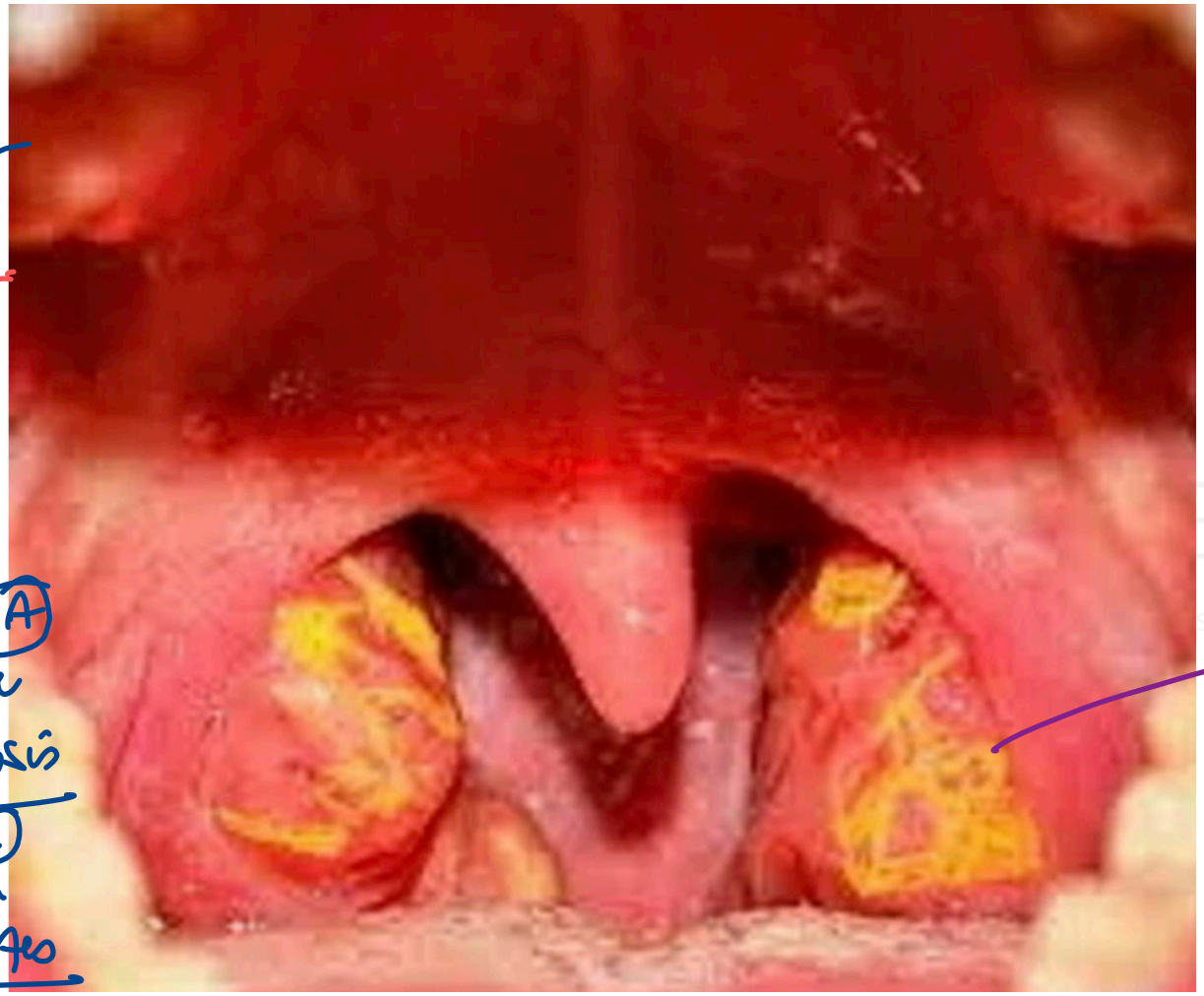
VS

abetalipoprot

- MTP defect
- HDL (N)

- Rest ↓

- Retinitis pigmentosa (vit A)
- acanthocytosis (vit E)
- Lipid laden enterocytes



HDL (healthy)

reverse cholest

↳ LCAT

↳ apo Ai quality

orange tonsils

Tang

Tangier's

ABCA1 def.

Peroxisome

Membrane-enclosed organelle involved in:

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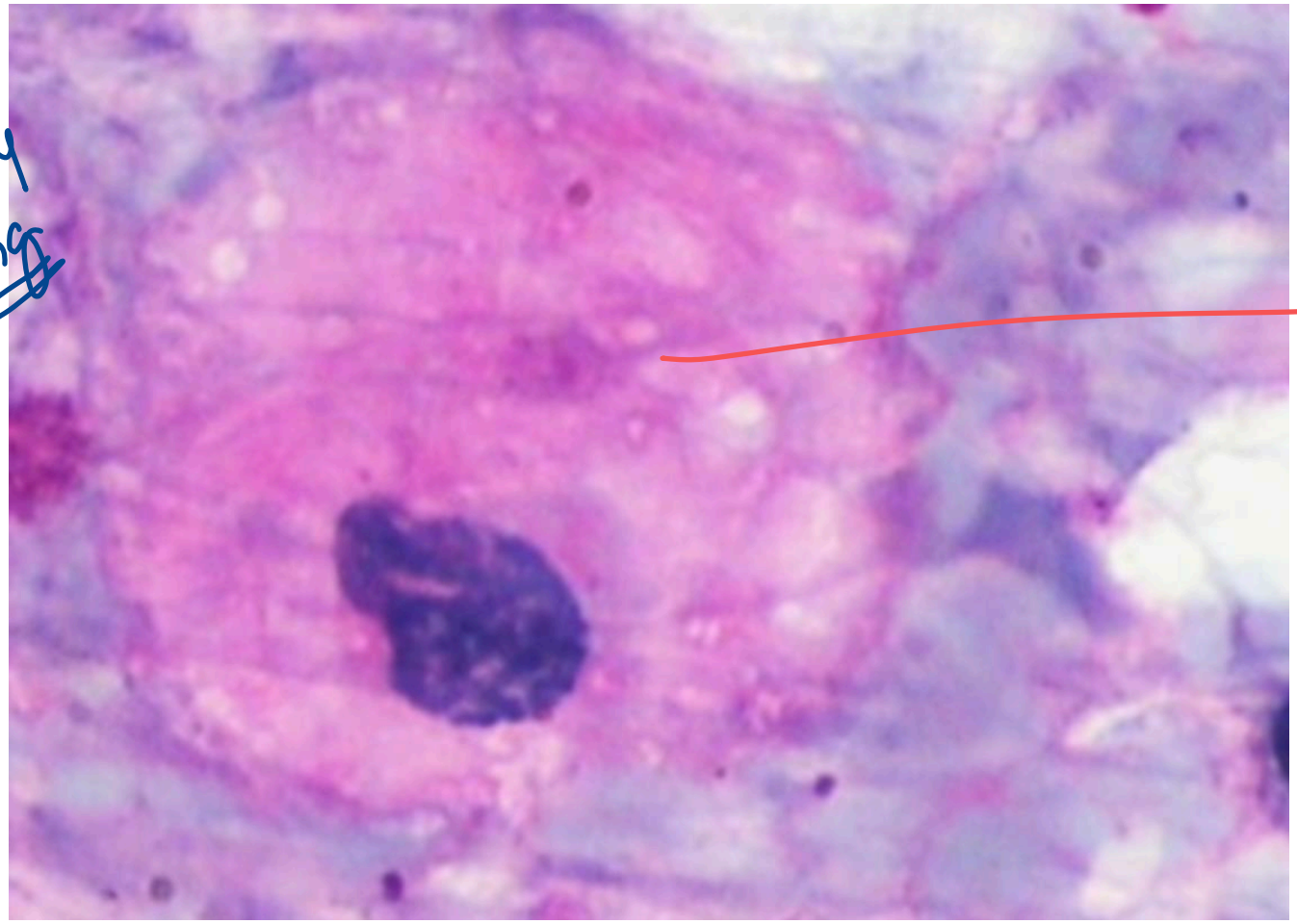


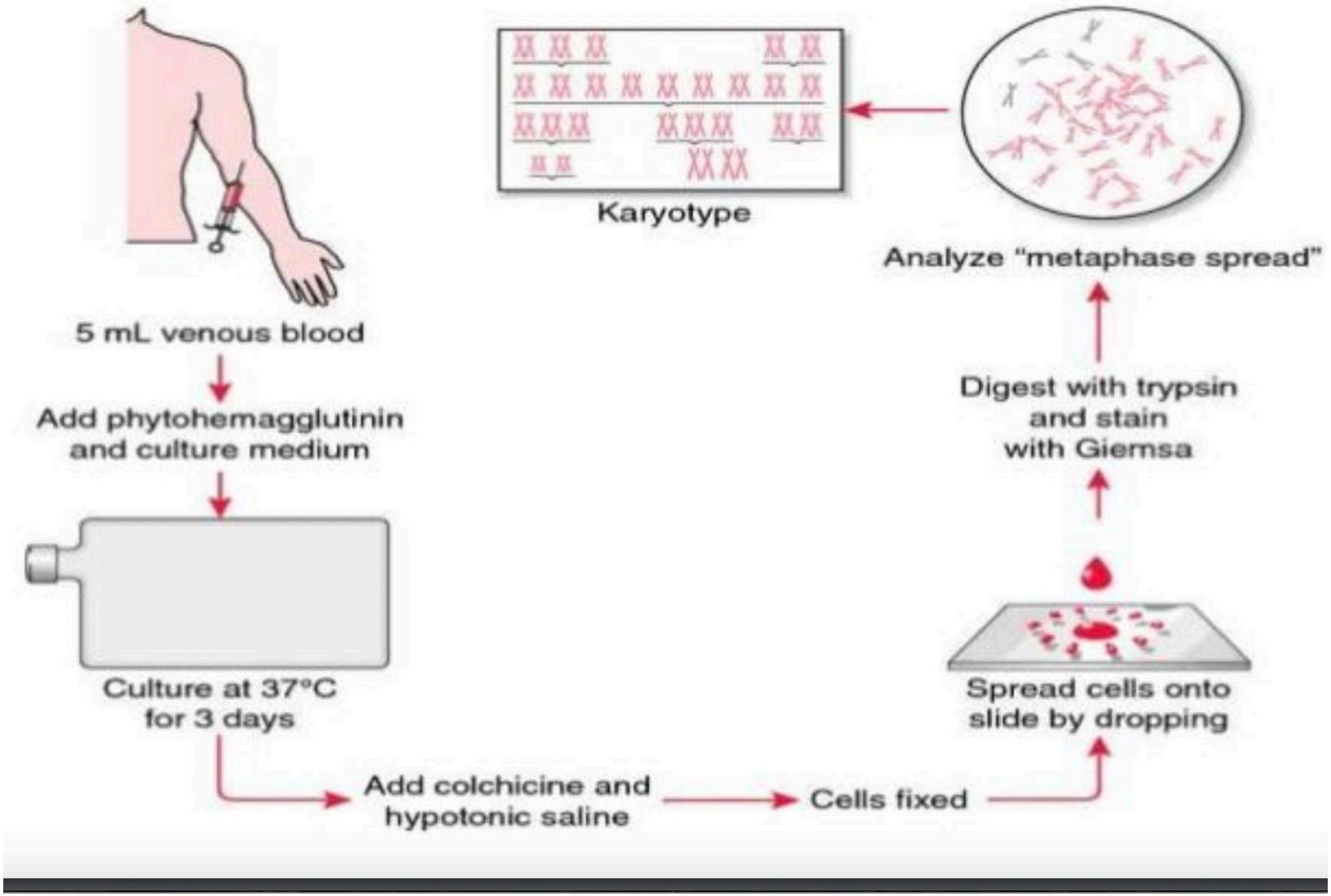
- CR
  - TS → tiny
  - NP → big

crumpled gaucher

AR

bone pain

β-glucosidase



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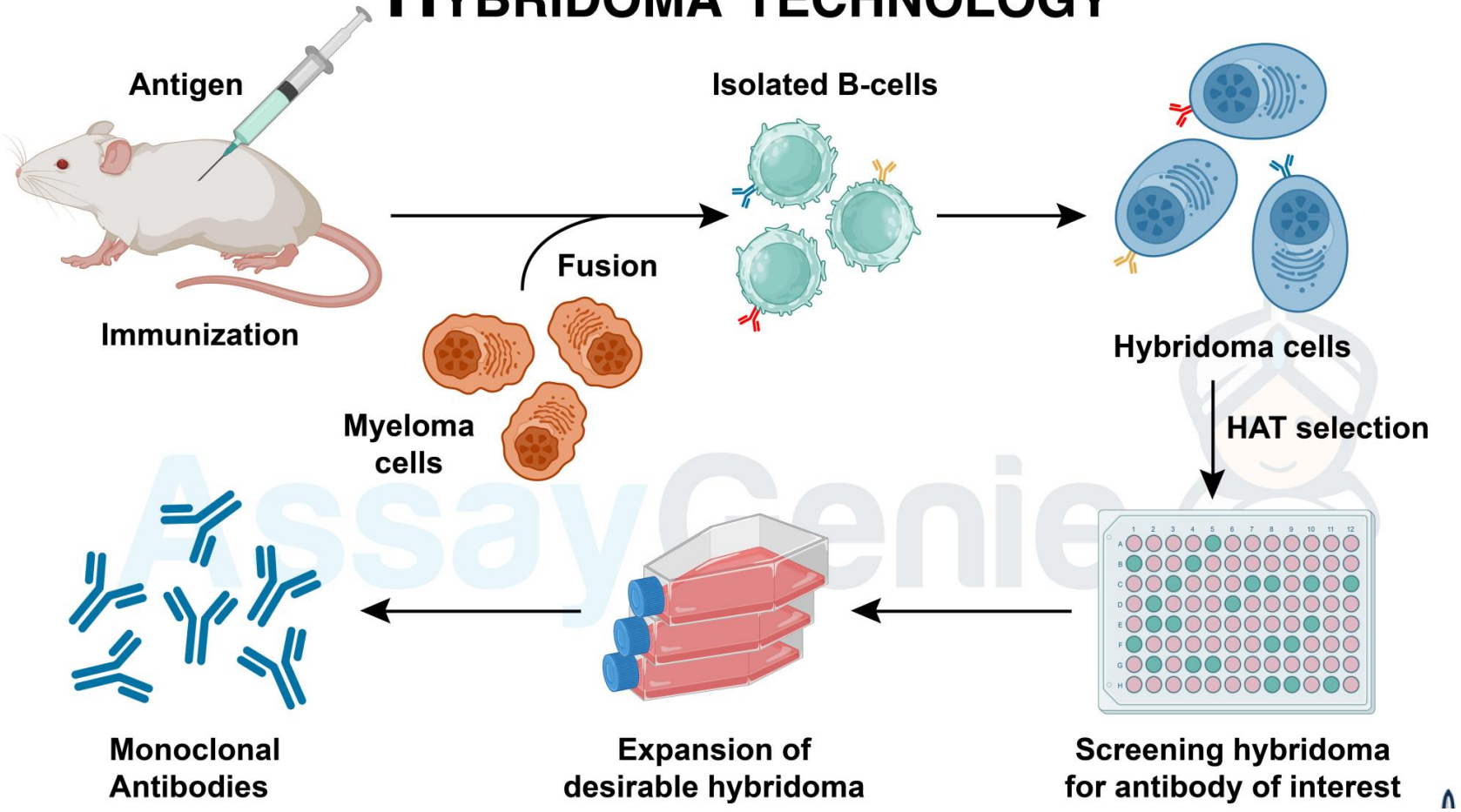
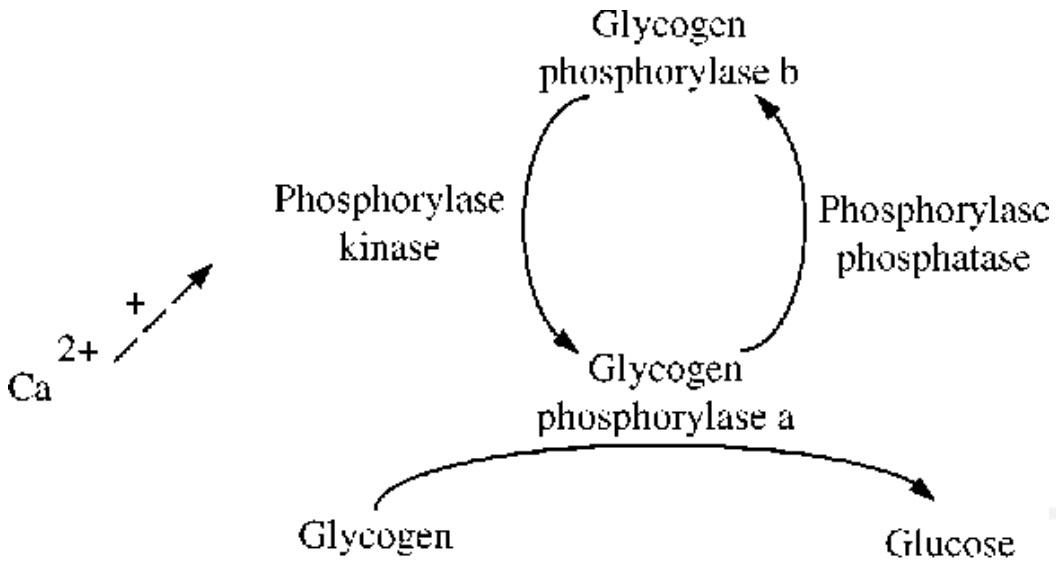
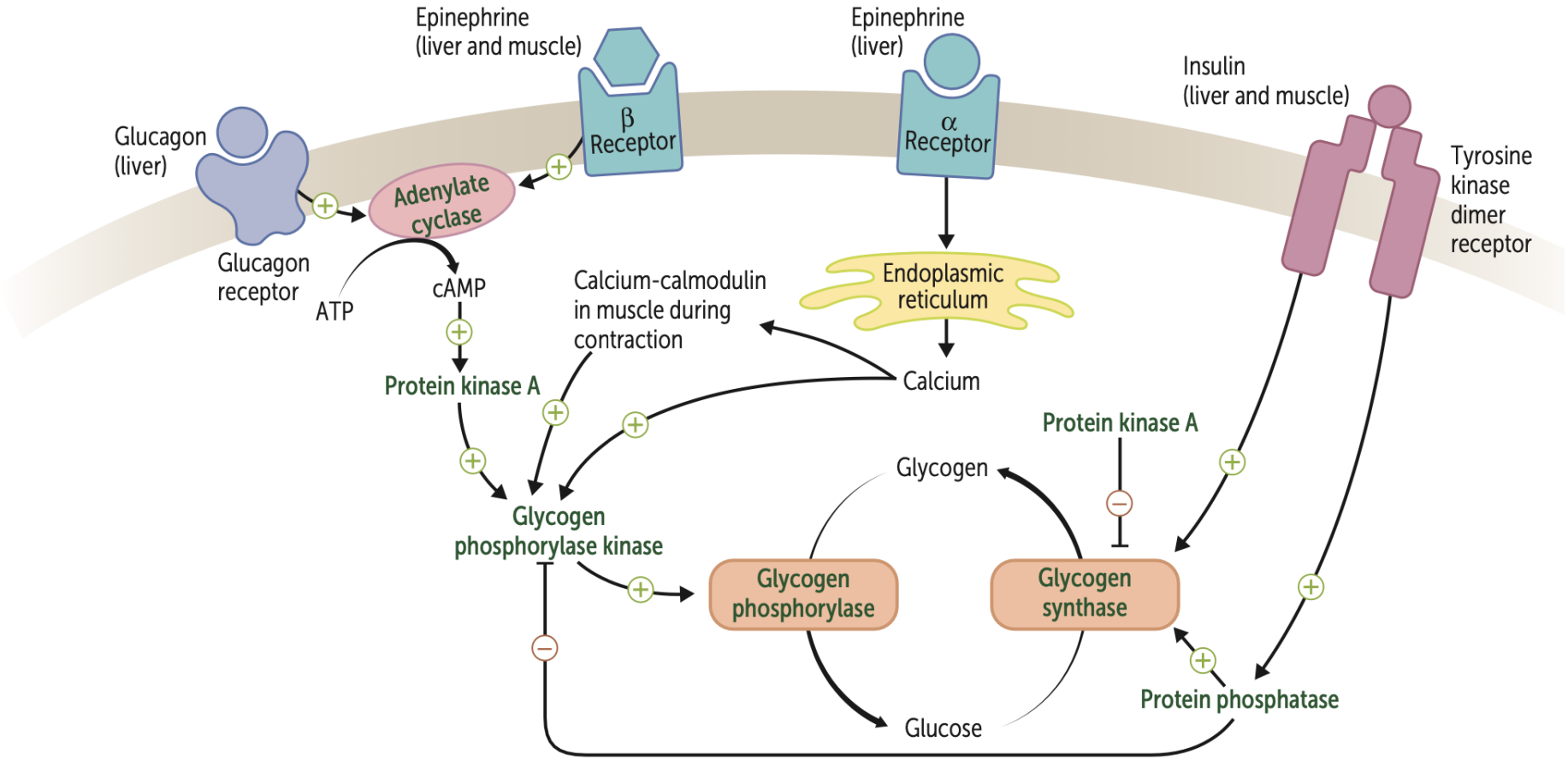
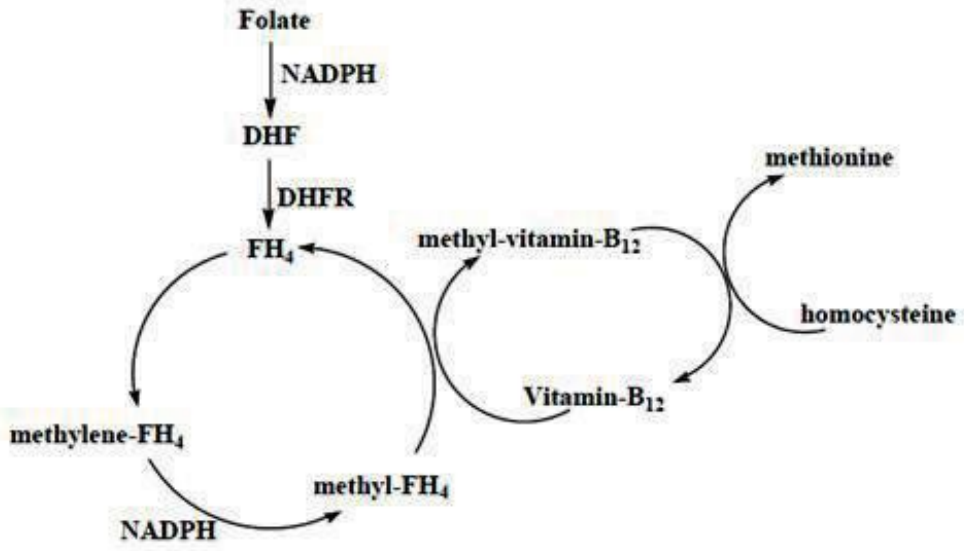




Glycogen regulation by insulin and glucagon/epinephrine





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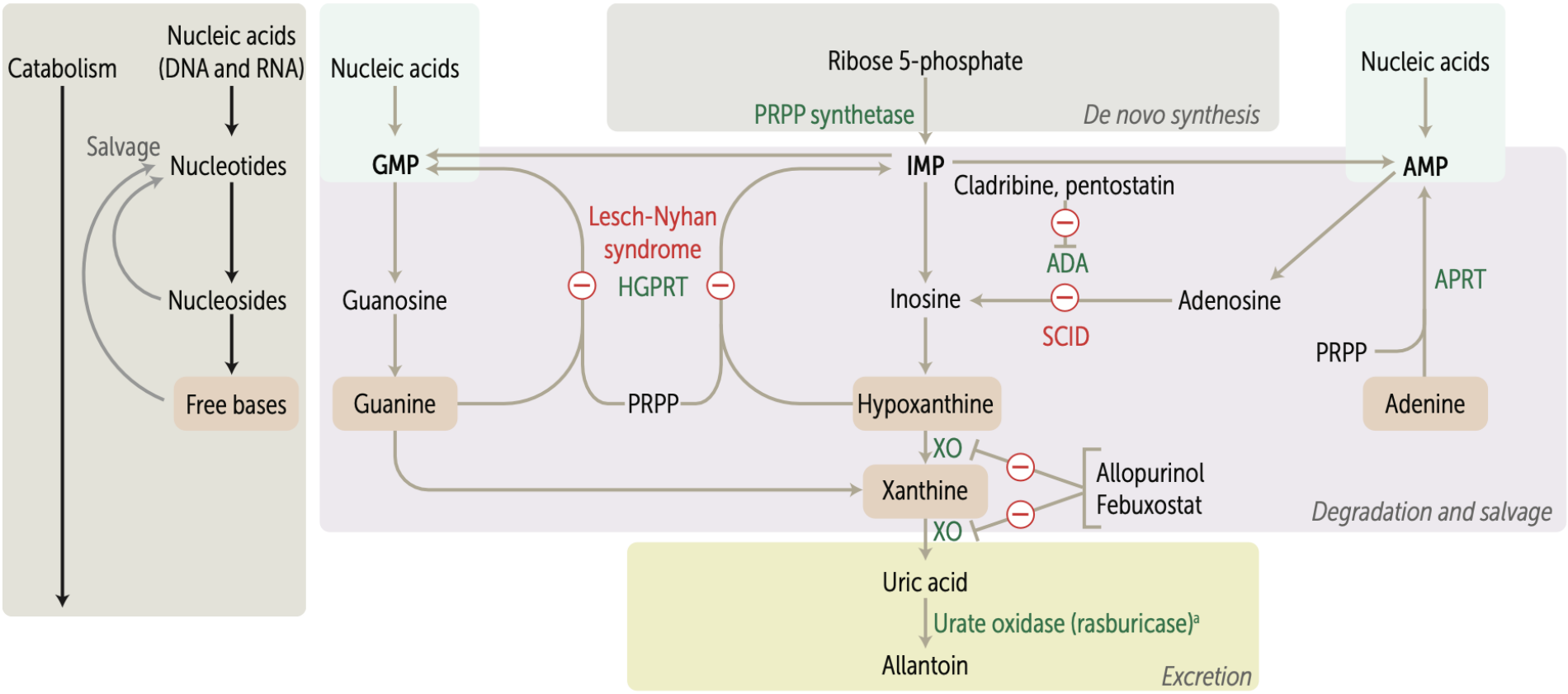

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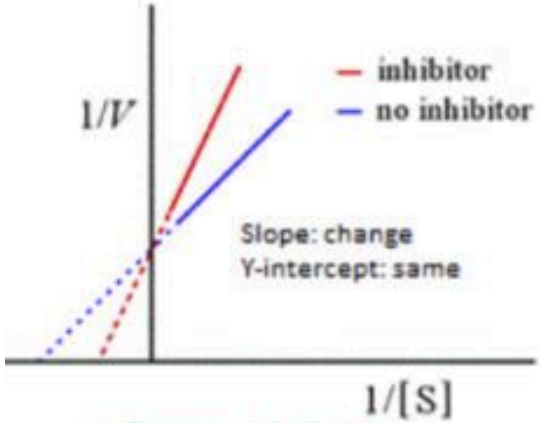

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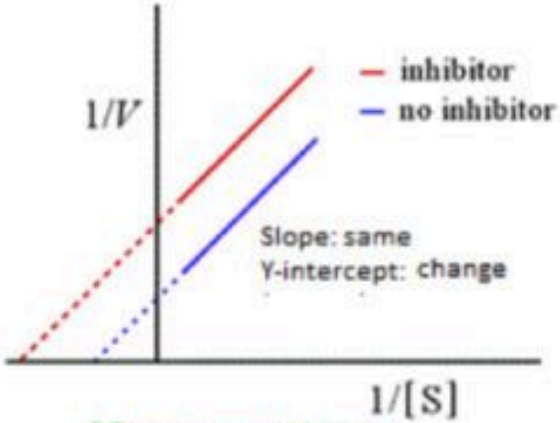

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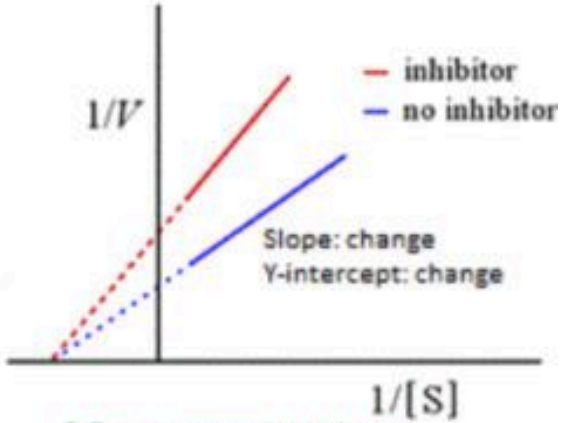

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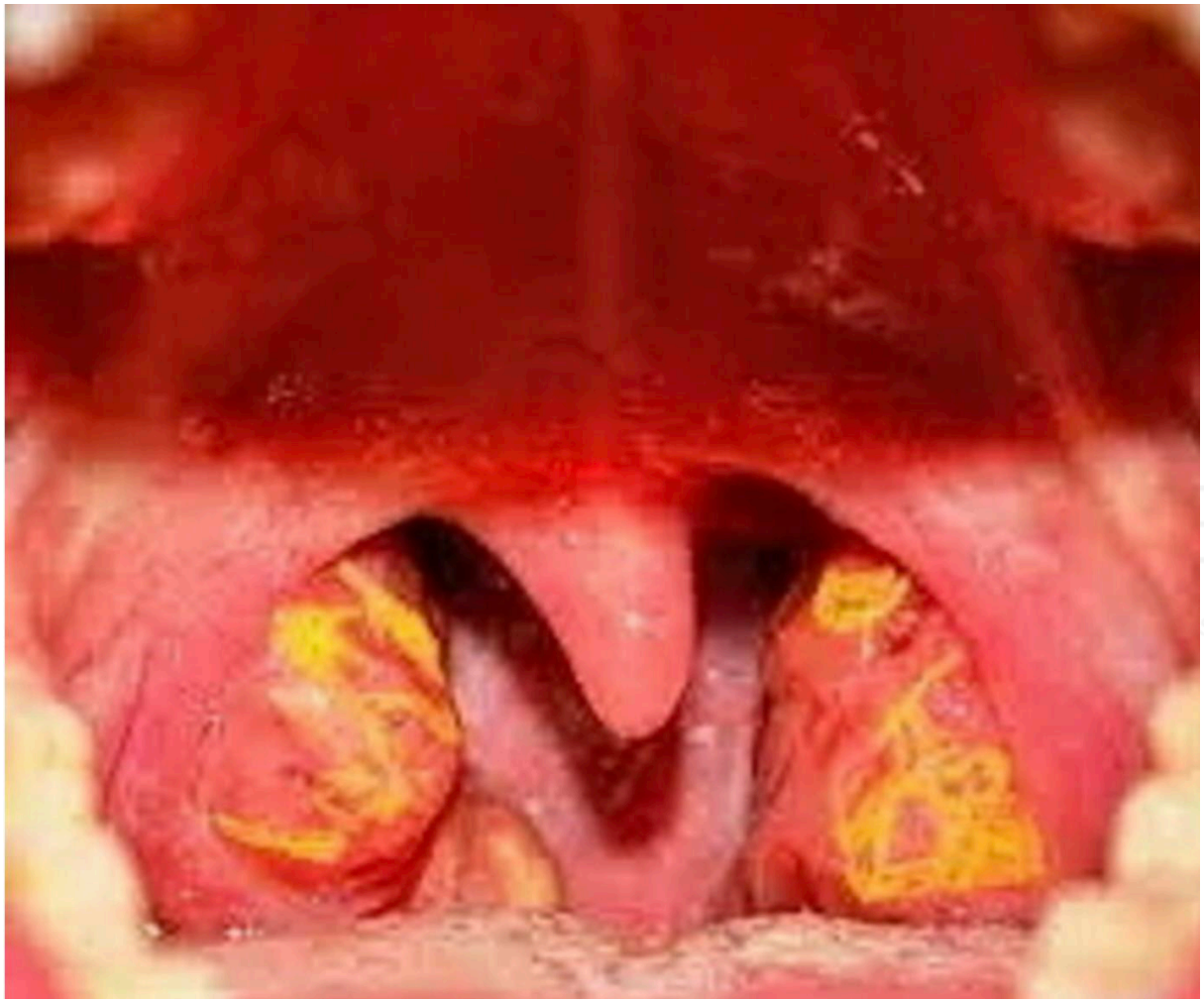

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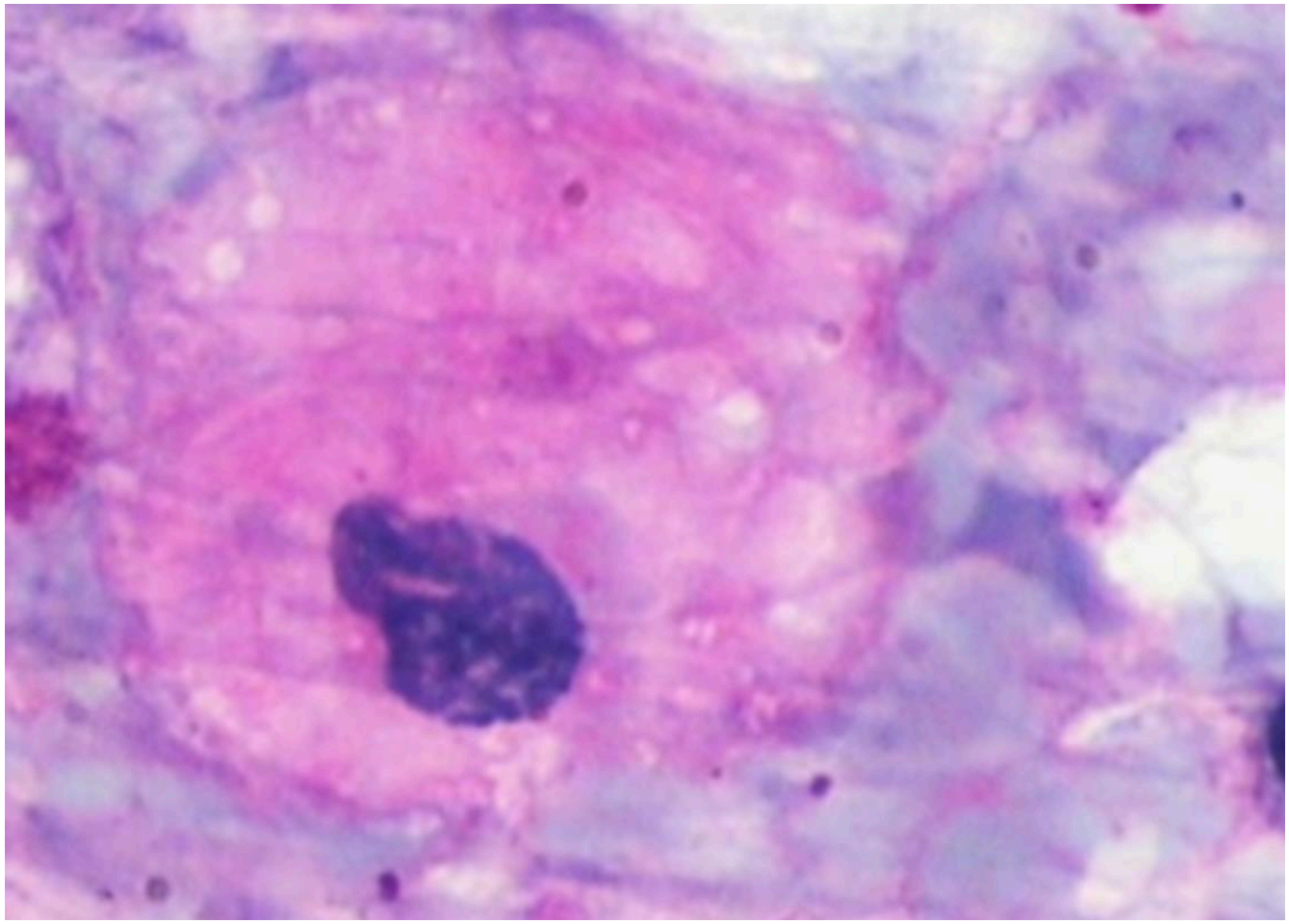
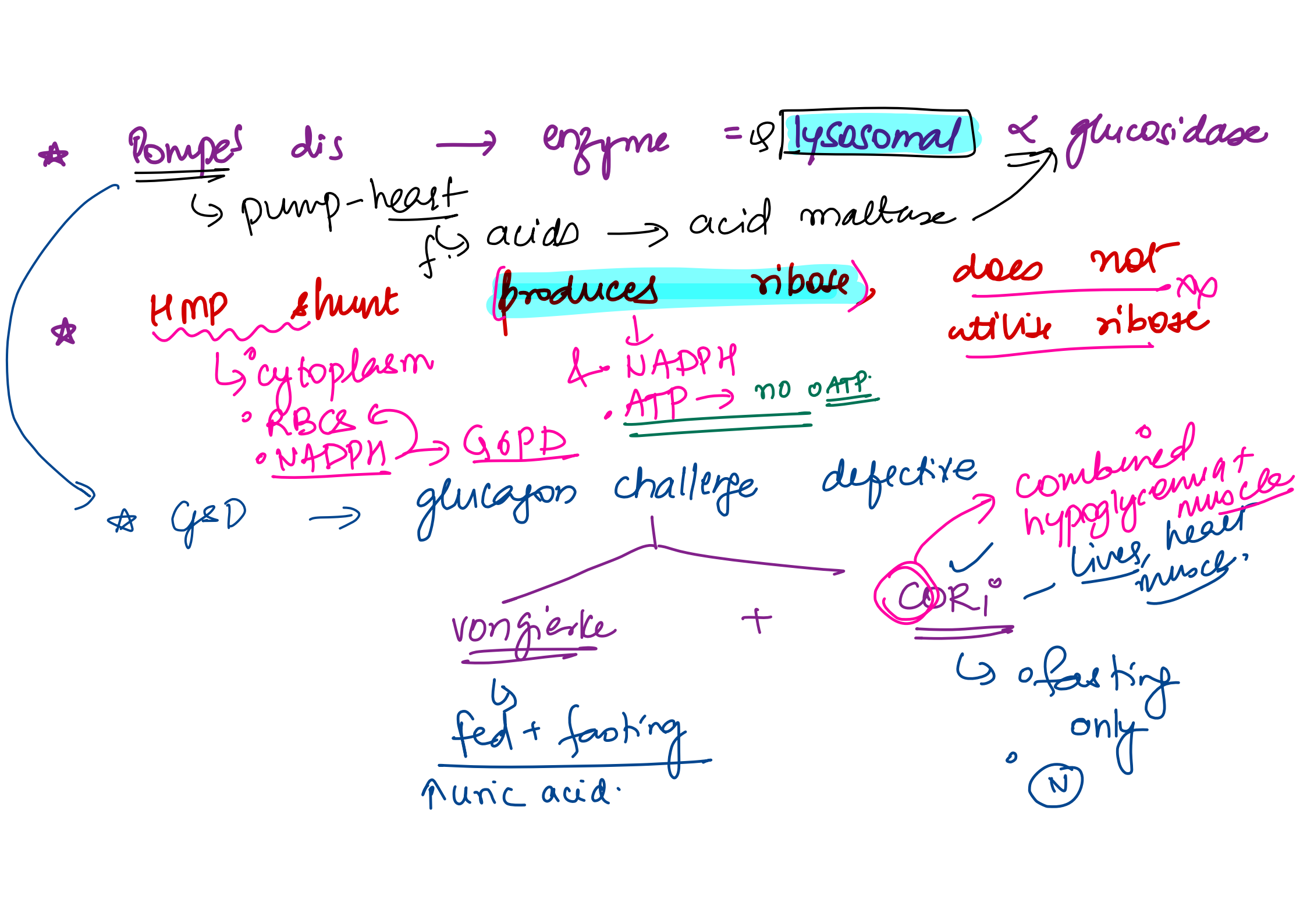



Pompe's dis → enzyme = lysosomal α glucosidase
↳ pump-heart
↳ acidD → acid maltase
HMP shunt
produces ribose
does not utilize ribose
↳ cytoplasm
↓
& NADPH
• RBCs
• NADPH → G6PD
• ATP → no ATP
G&D → glucagon challenge defective
combined hypoglycemia + muscle
CORI
lives, heart muscle
von gierke
+
↳ fasting only
↳ fed + fasting
↑uric acid
N

★ max Specific dynamic allowance / thermic effect is max in PROTEINS (egg) in summer

★ COLLAGEN : ① Most abundant a.a = Glycine (C-G) at every 3rd posn.

② Triple helical structure.

Proline lysine

③ Hydroxylase → vit C – collagen

④ Lysyl Oxidase → Cu → (Menkes) → ATP7A
copper ↓ cross linking → X linked.

★ 2, 3 BPG binds to deoxyHb → globin chain of Hb.
O_2 binds to heme

→ shifts to ↑ → Rt shift
R_f – Raised

★ Acidosis → ↓ 2,3 BPG.
ACD → stored blood

* **Substrate** is complementary to active sit of enzyme.

* A.a restricted in MSUD :
  - in homocystinuria → restrict
    - supplem → cysteine
    - Methionine ↳ forms homocysteine
  - Burnt Sugar odour : maple syrup ***
  - Selenocysteine : 21st aa : selenium
    - Enzymes :
      - Glutathione peroxidase
      - Thioredoxin reductase
      - Deiodinase

UGA — peroxidase — Perfect thigh — (thiolo)

× Lysine

Live
- leucine
- isoleucine
- valine

✡ selenocyst ⟶ UGAS UGA uganda

pyrolysine → UAG.

AAG

① Phospholipids:

- Mitochondria (powerhouse) → Cardiolipin (C-G)
  (Diphosphatidyl glycerol)
  Def → Barth syndrome
- Brain → cephalin (phosphatidyl ethanolamine)
  (1 ethanol brain)
- HMD → Dipalmitoyl (DPL) lecithin
- atherosclerosis → LDL → lecithin (oxidised lecithin)

② Lives lacks THIOPHORASE and ∴ cannot use ketone bodies.

- vit C synth ~~xxx~~ → gulonolactone oxidase: C-G
  ↓
  Ketogenesis =

① RNA synthesis : · Clone of Coding strand (same)
· Reverse of template stand.

Template eg. → 5' CATTCG 3' } complement
RNA · 3' GUAAGC 5'
ie 5' CGAAUG 3' coding

• coding DNA / RNA are complem to template

② FISH (Cannot) determine DNA sequence alteration

✓ RFLP, Pyrosequencing

× Flow cytometry
↳ CD marker

CLL
CD5+ CD23+

③ DNA repair :

Try new zero coke

① Xeroderma pig → NEX.

② HNPCC → MMR: (MLH1/MSH2) MMM.

③ SCID → NHEJ

④ Double stranded break repair

CRISPR Cas9 NHEJ > HR

NHEJ → KU70

HR → ATM → ataxia.
BRCA

④ Hybridoma technology uses Salvage (HAT medm)

of purine synthesis (HGPRT dependent)

* To detect DNA - protein interaction : DNA footprinting

vs DNA fingerprinting : uses RFLP for paternity testing
familial

& gene func → Northern blot (RNA product).

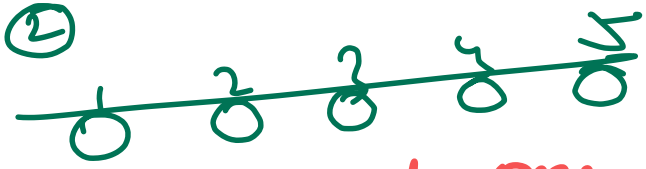
* Humane genome project :

- 1990 – 2003 : ~ 13yrs
- Total : 20500 genes approx
- First generation sequencing like Sangers was used (Not next generation)
  L = array techniques.
-

★ Banding : Karyotyping

- dicentric → C centromere
- Fluorescent (quenched) → Q (quinacrine)
- Routine → G band (general)
- Telomere → T

★ Nested PCR (specific) : multiple primers



- Multiplex PCR : for multiple genes at one time
- Digital droplet PCR : for low freq. mutant allele
- Sanger technique → sequencing → dideoxy NTP
  ↳ stops elongn.

vs PCR → • deoxy NTP
• Mg^{+} • Taq polymerase

* Deficiency of folate leads to misincorporation of uracil into DNA.
  - one carbon carrier: folate

* Cystic fibrosis mutation:
  - chrom 7, AR, sweat chloride ↑↑.
  - potentiator CFTR → (IVA) factor
  - ABPA, pseudo, fat soluble vit def

ΔF508, CFTR
(F) phenylalanine
phenylalanine Cl^- channel

* Chimeric DNA is used for: organ transplant. QQ

* RNA editing does not happen in 5' to 3' direction

- Sickle cell → β mutn: Missense. β6 glu → valine
  - DMD → frameshift
- CRISPR – cas9: NHEJ
- mRNA to ribosome binding: by (guanyl cap)
  Tail → 3' end – polyA → post transcriptn. co transcriptn. → mG – cap 5' end.
- Palindrome: AAGCTT (2° rest. endonucleases acts)
  AGCGCC xxxx (not palind)
- Klenow fragment (DNA polym. (I)) lacks: (5'–3' exonuclease) (clean no)
- Rothera test for ketones

* Phenylbutyrate is used in urea cycle disorders ∵ it scavenges nitrogen.

(phenyl butyl glutamine)

↳ more water soluble excreted.

* Not seen in low (fasting) insulin — glucagon:

Odd man out

a) glycogen bkdown → fasting

b) ketogenesis → fasting

c) glycogen storage → fed

d) gluconeogenesis → fasting

① Xanthurenic aciduria = def of vit B6 (kynurenine)

② megaloblastic anemia ↓ (N) MMA → B9 def.

③ vit E
- def → ~(vit K toxicity) Hemolytic anemia (∵ antioxidant) · B12 def ↑↑ MMA
- toxicity → ~ vit K deficiency (hemorrhage)

④ (Raw egg) → ↗ vit Biotin → carboxylation enzyme def → (Pyruvate carboxylase)
↳ enzyme of gluconeogenesis

⑤ RBC transketolase → vit B1

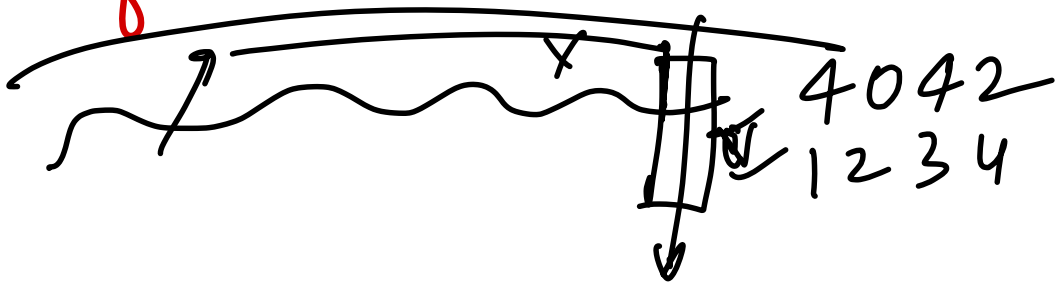
* (Cyt. P450) utilises NADPH during phase 1 reaction
(Hydroxylation) of xenobiotics detoxification

↓
oxidn/reductn
hydrolysis

cholesterol
steroid
glutathione → SER

oligomycin

* Increased H+ ions in intermembrane space of mitochondria due to →



↓ oxidative phosphorylation
(by oligomycin)
Fo - comp V

* (fructosamine) → glycated albumin (nonenzymated)

- alternative to HbA1c → 8-12 wks control

(2-3 wks control) 3wks

HbA1c

↓

g → best → ion exchange (HPLC) affinity chromatog.