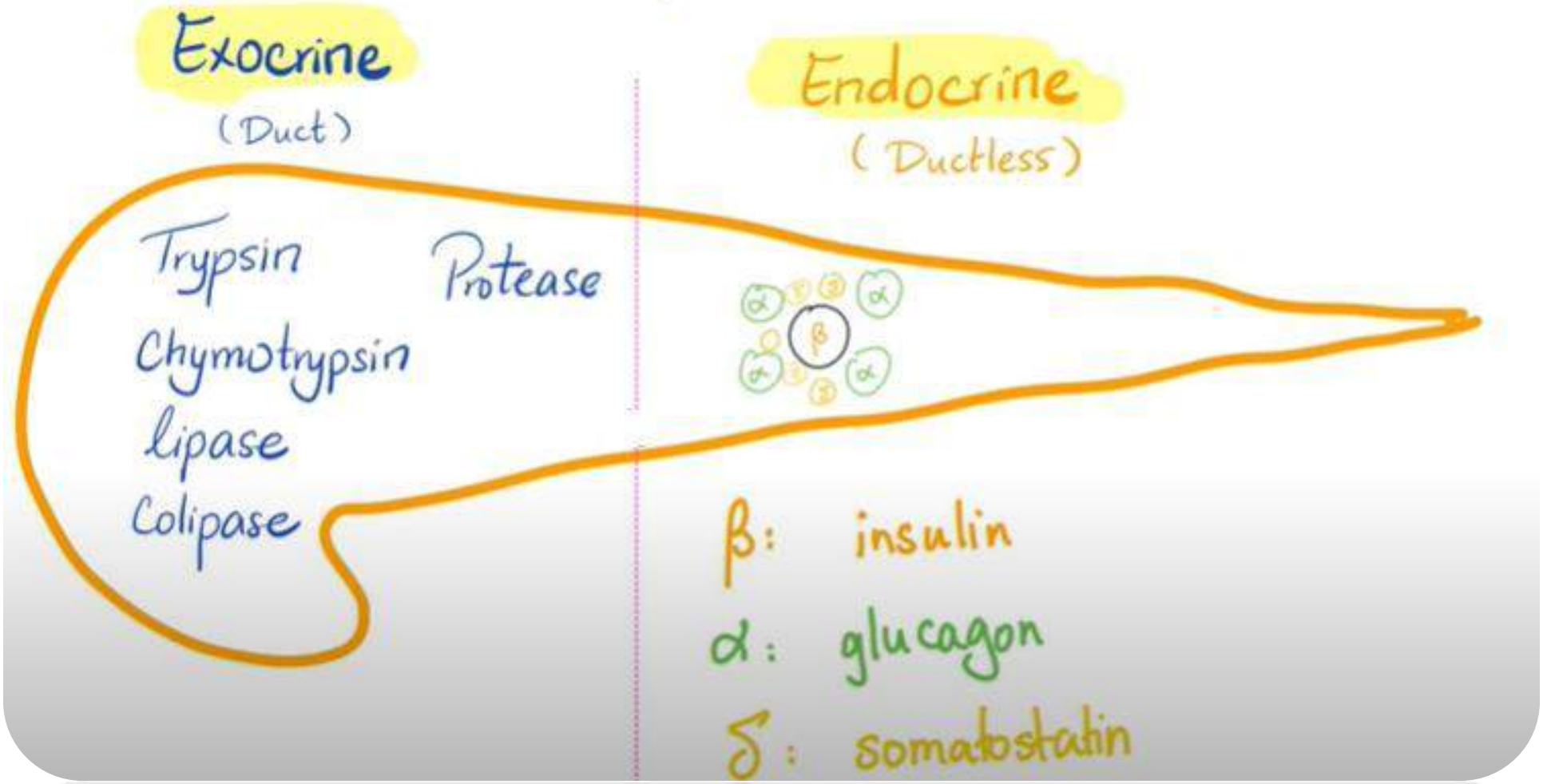
Pancreatic hormones and blood glucose regulation

DR. Arwa Rawashdeh

- Thyroid, adrenal cortex , gonads obeys hypothalamus and anterior pituitary
- Parathyroid , adrenal medulla and pancreas Don’t

The pancreas

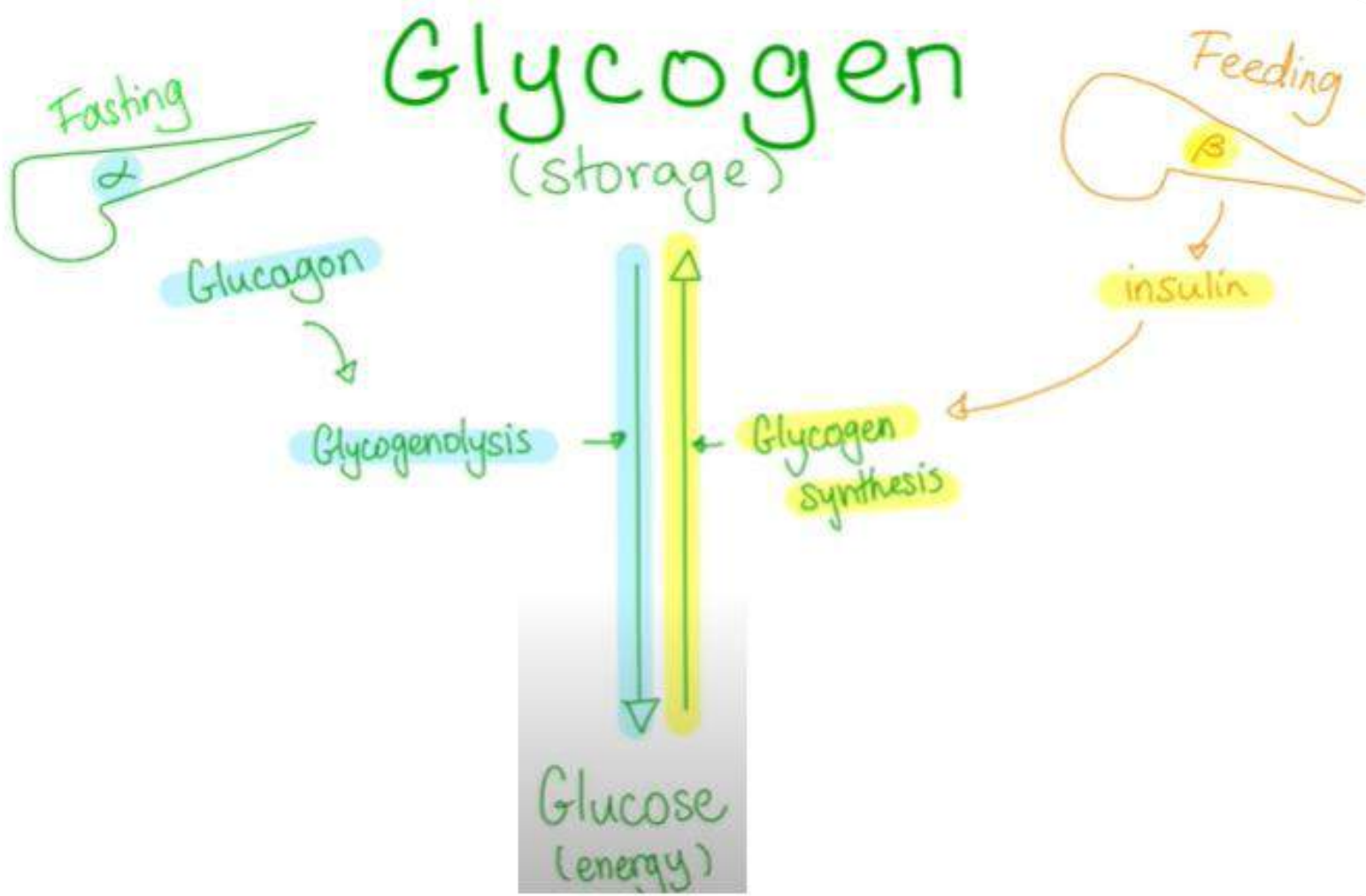


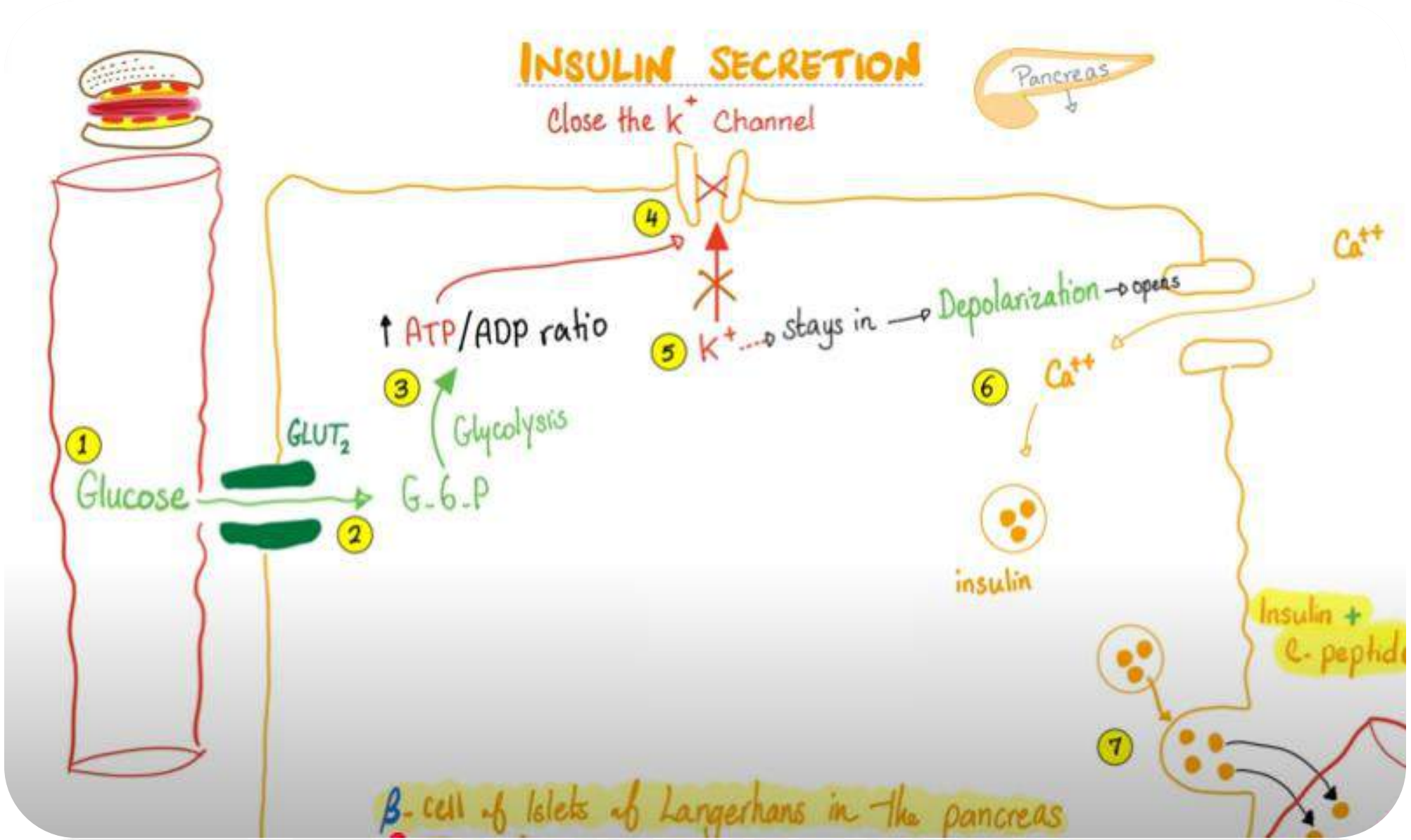
- Glucagon (α) → ↑↑ glucose in the blood.

Type 1 Diabetes Type 2 Diabetes

- Insulin (β) → ↓↓ glucose in the blood.

- Somatostatin (δ) → a "universal inhibitor".


Glycogen
(storage)
Fasting
α
Feeding
β
Glucagon
insulin
Glycogenolysis
Glycogen synthesis
Glucose
(energy)


INSULIN SECRETION
Pancreas
Close the k+ Channel
4
↑ ATP/ADP ratio
5 K+ ... stays in
Depolarization → opens
Ca++
3
Glycolysis
1
GLUT2
Glucose
G-6-P
2
6
Ca++
insulin
Insulin +
C-peptid
7
β-cell of Islets of Langerhans in the pancreas

Insulin VS Glucagon

Insulin	Glucagon
* Protein Anabolic	* Protein Catabolic
* Glycogen Anabolic	* Glycogen Catabolic
* Fat Anabolic	* Fat Catabolic

Anti- Ketogenic

dephosphonylates −Ⓟ

rate- limiting enzymes

⊕ Phosphatase "Protein-Phosphatase-1"

↓ cAMP

Pro- ketosis

Phosphonylates +Ⓟ

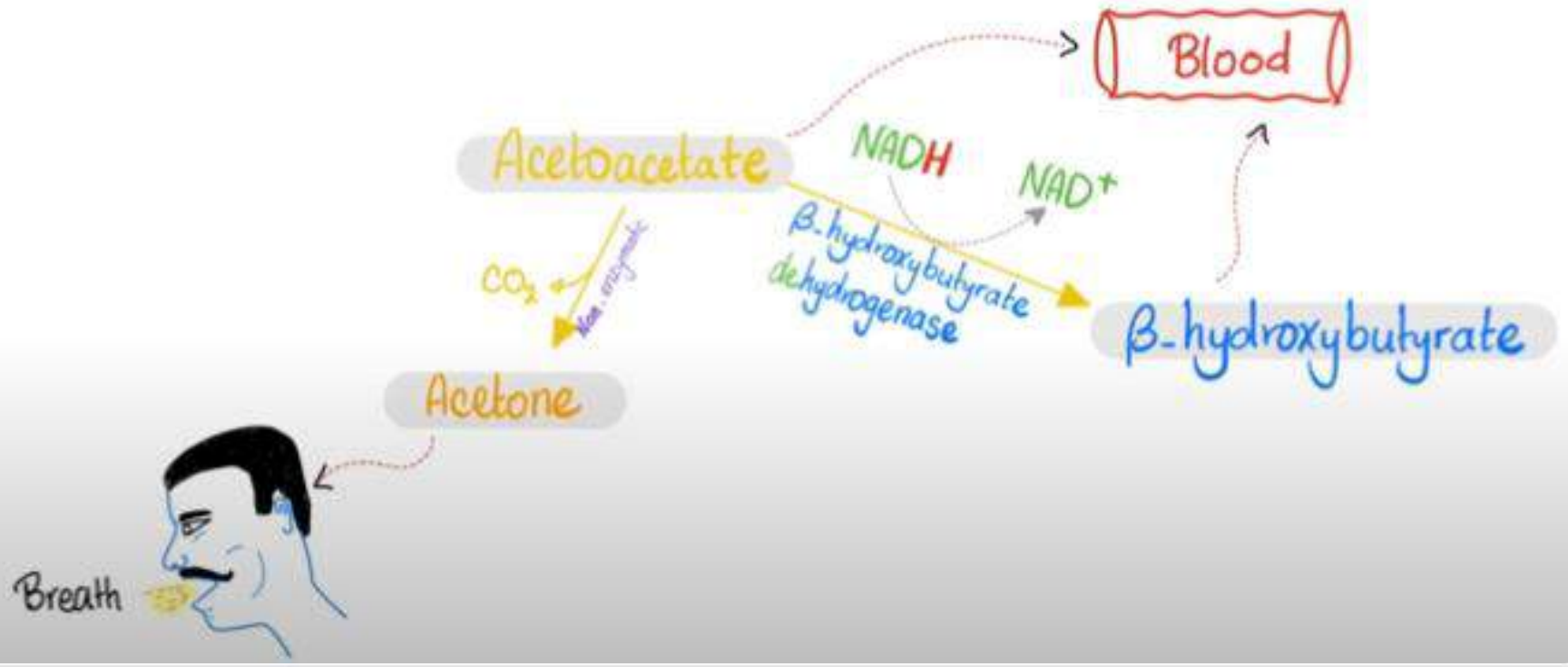
rate- limiting enzymes

⊕ Kinase "Protein Kinase A"

↑ cAMP

What are the Ketone bodies ?!

Acids



I

Type I DM → No insulin → Ketosis → Diabetic Keto-acidosis

II

Type II DM → Insulin is present (early) → No ketosis → Hyperosmolar Hyperglycemic Non-Ketotic Syndrome (HHNKS)

How does Glucagon work ?!

Glucagon is a water-soluble hormone

Hormone Signal Transduction Pathway

Intracellular Receptors

Steroid Hormones
Thyroid Hormones
Vitamin D

Cell Surface Receptors

G-protein Coupled Receptor

- Acetylcholine
- Catecholamines
- Glucagon
- Serotonin
- Secretin

Ligand-Gated Ion Channels

- Acetylcholine
- $GABA_A$

Enzyme-Linked Receptor

Receptor Tyrosine Kinase (RTK)

MAPK Pathway

- Insulin
- Growth Factors

Receptor Protein Serine Kinase/ Threonine Kinase

- TGF-β (cytokine)

Nonreceptor Tyrosine Kinase (NRTK)

JAK/STAT

Growth Hormone (GH) & Prolactin

Hematopoietic cytokines
EPO
TPO
G-CSF

Immunomodulating cytokines
IL-2
IL-6
IFN

2nd messenger

cAMP

Hypothalamus Hormones
GHRH
CRH
V_2 receptor (ADH)

Pituitary Hormones
ACTH
MSH
TSH
FSH
LH

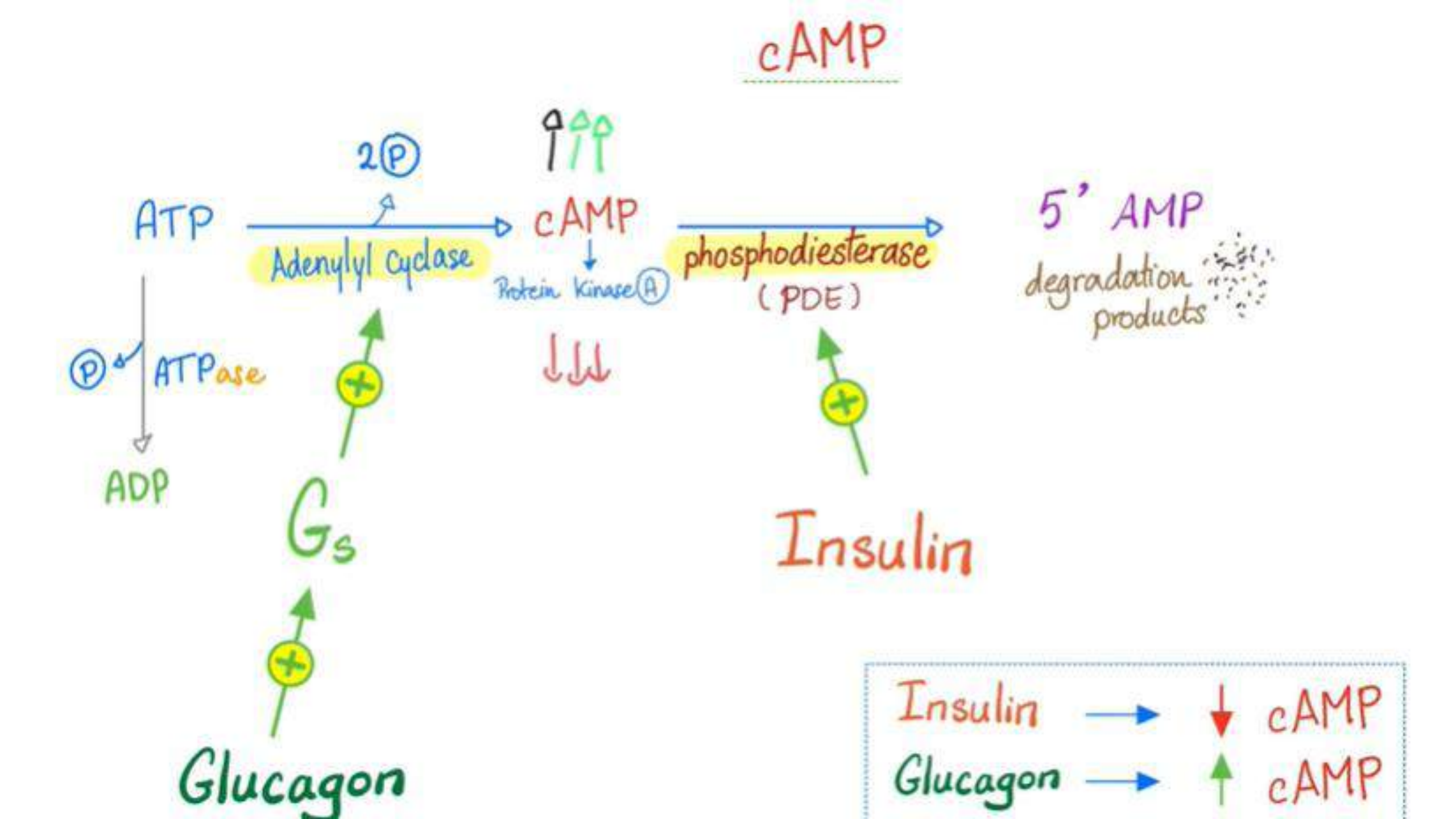
Other Hormones
PTH
Calcitonin
Glucagon
H_2 receptor of Histamine
hCG

IP_3 & DAG

Hypothalamus Hormones
TRH
GnRH
V_1 receptor (ADH)
Oxytocin

Other Hormones
H_1 receptor (Histamine)
Angiotensin II
Gastrin

cGMP (NO)


cAMP
2Ⓟ
ATP
Adenylyl Cyclase
cAMP
Protein Kinase Ⓐ
phosphodiesterase
(PDE)
5' AMP
degradation products
Ⓟ
ATPase
ADP
Gs
Insulin
Glucagon
Insulin → ↓ cAMP
Glucagon → ↑ cAMP

A Tale of 2 worlds

Insulin World

VS

Glucagon World

Insulin

Glucagon
Cortisol
Epinephrine
Thyroxine

→ Glucagon as an "antidote" for β-blocker.

- If β-blocker TOXICITY ? → Give Glucagon reverses the β-blocker symptoms, but without interfering with β receptors.
  ↓↓ cAMP
  ↑↑ cAMP

GROWTH HORMONE (GH) = Somatotropin

(polypeptide hormone)

Insulin-like action

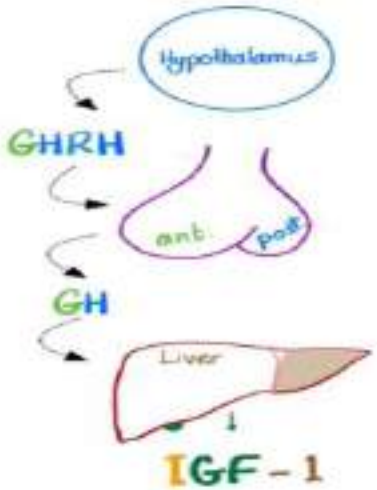
ANABOLIC

JAK-STAT

- similar to pro-insulin
- insulin-like receptors
- ↓↓ glucose & FFA

} like insulin

Receptor Tyrosine Kinase (RTK) & Insulin-Receptor Substrate (IRS)



ANTI_insulin actions

STRESS HORMONE

CARBOHYDRATE CATABOLIC — DIABETOGENIC

JAK-STAT

↑↑ Glycogenolysis

↑↑ Gluconeogenesis

→ ↑↑ glucose

FAT CATABOLIC — KETOGENIC

JAK-STAT

↑↑ Ketogenesis

Lipids → Lipolysis → F.F.A / ketone bodies