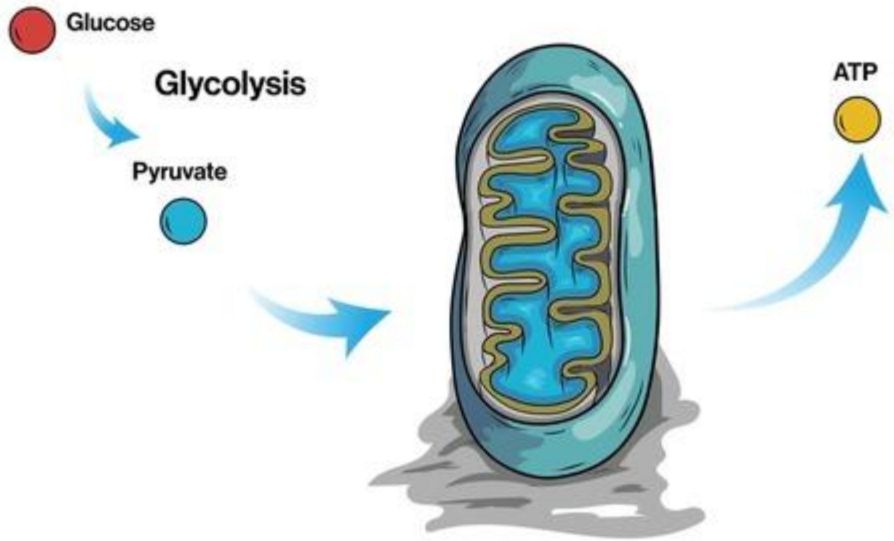
CARBOHYDRATES METABOLISM



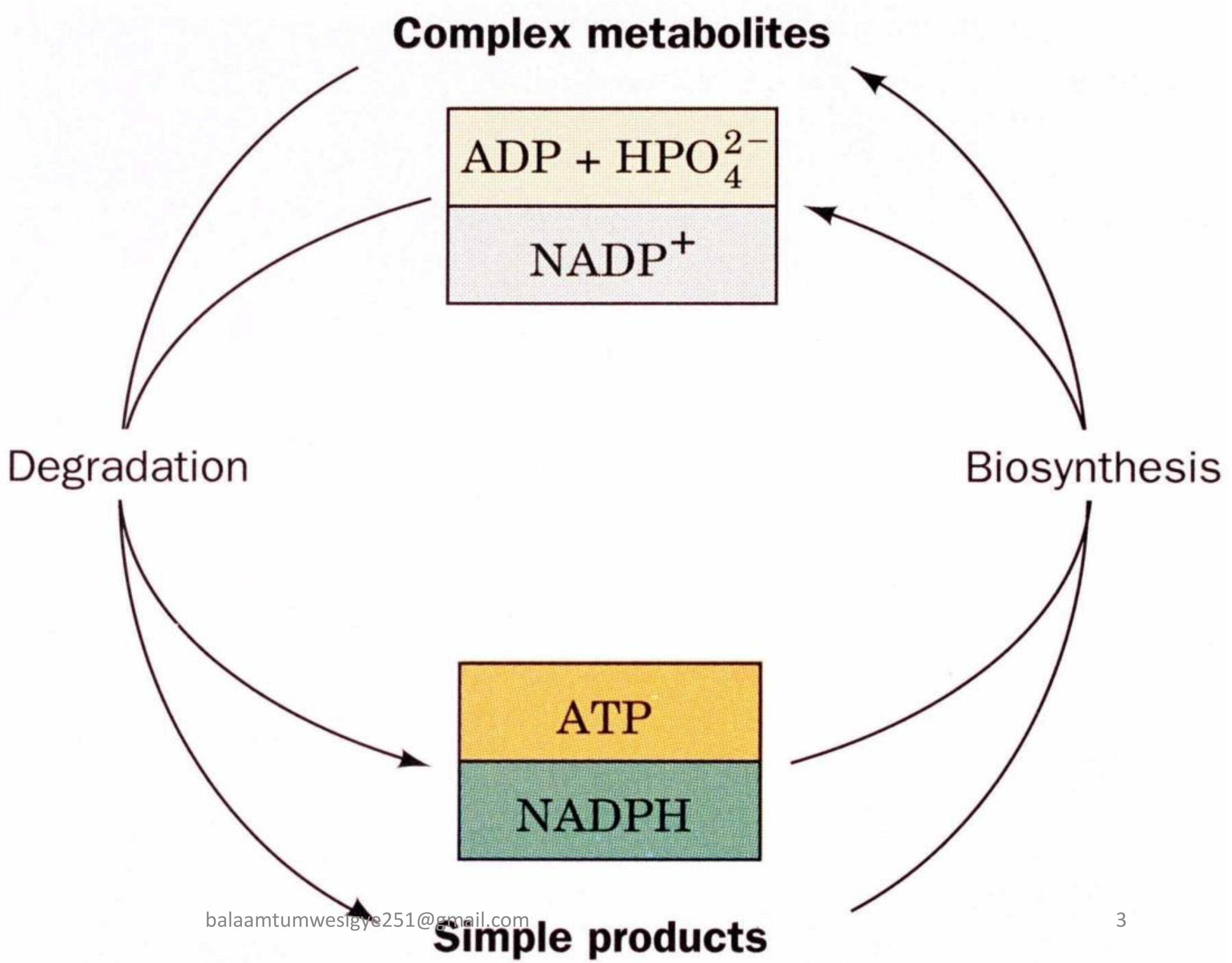
Metabolism

Metabolism is the overall process through which living systems acquire and utilize free energy to carry out their functions.

The coupling of exergonic reactions of nutrient breakdown to the endergonic processes is required to maintain the living state.

How do living things acquire the energy needed for these functions ?

Look at this


Complex metabolites
ADP + HPO$_4^{2-}$
NADP$^+$
Degradation
Biosynthesis
ATP
NADPH
Simple products

Overview of glucose metabolism

Glucose metabolism is the process by which the body uses and regulates glucose for energy.

Glucose, obtained from dietary carbohydrates, is the main energy source, especially for the brain.

It is either:

- Broken down to produce ATP (energy)
- Stored as glycogen in liver and muscles
- Synthesized when needed (gluconeogenesis)

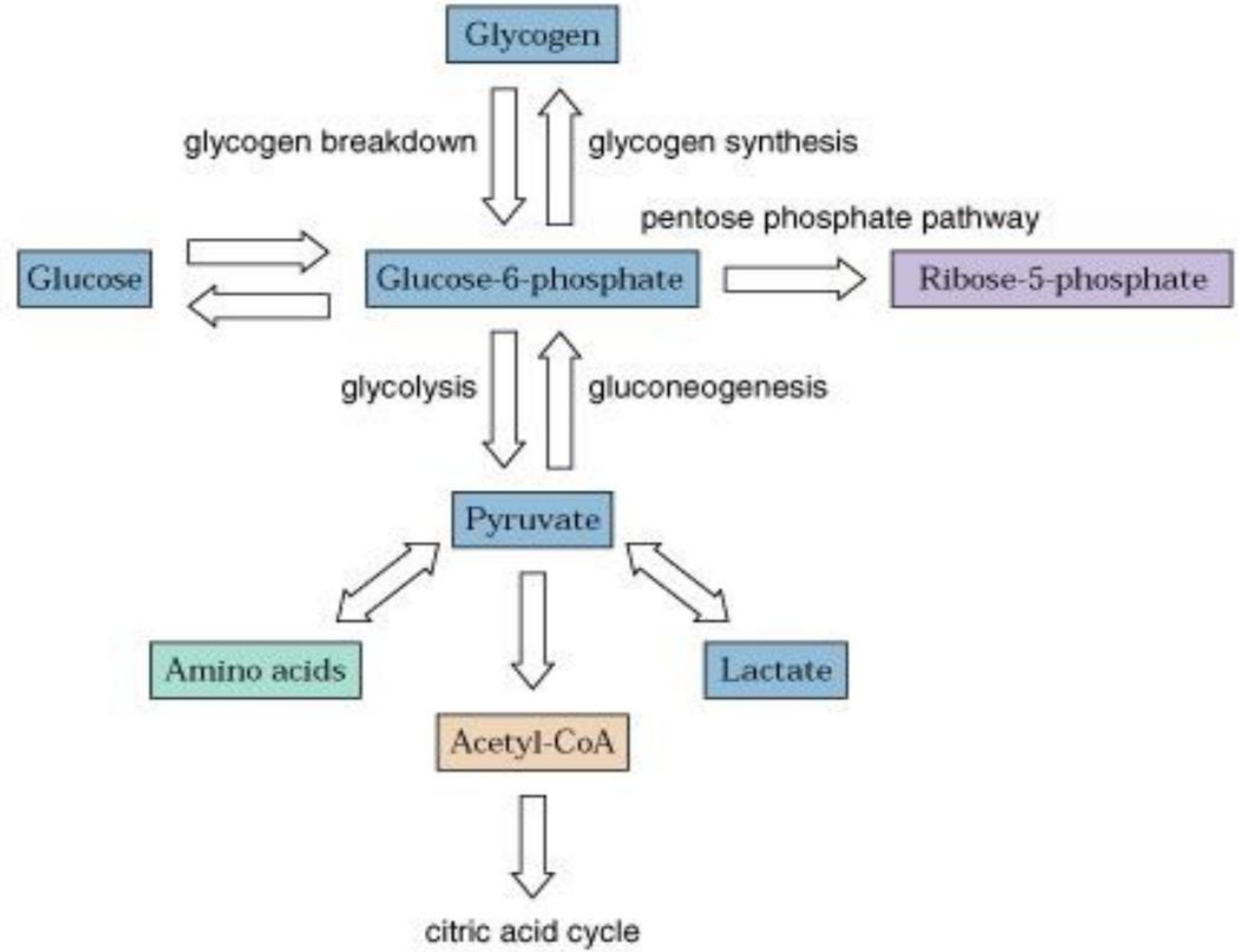
Con’t

Key pathways include:
Glycolysis
Citric acid cycle
Oxidative phosphorylation

Regulated by hormones:Insulin (lowers blood glucose)
Glucagon (raises blood glucose)

Proper regulation is essential; imbalance can lead to Diabetes Mellitus

Overview


Glycogen
glycogen breakdown
glycogen synthesis
pentose phosphate pathway
Glucose
Glucose-6-phosphate
Ribose-5-phosphate
glycolysis
gluconeogenesis
Pyruvate
Amino acids
Lactate
Acetyl-CoA
citric acid cycle

Glycolysis

The break down of glucose (carbohydrate) glucose (C6) to pyruvate (C3); occurs in the cytoplasm of the cell.

In presence of oxygen, the pyruvate enters the mitochondria and is completely oxidized to $CO_2$and H_2O.

In absence of oxygen (i.e. anaerobic conditions), the pyruvate is temporarily converted into lactic acid.

Glycolysis is carried out by a group of ten glycolytic enzymes summarized in 10 reactions as follows:

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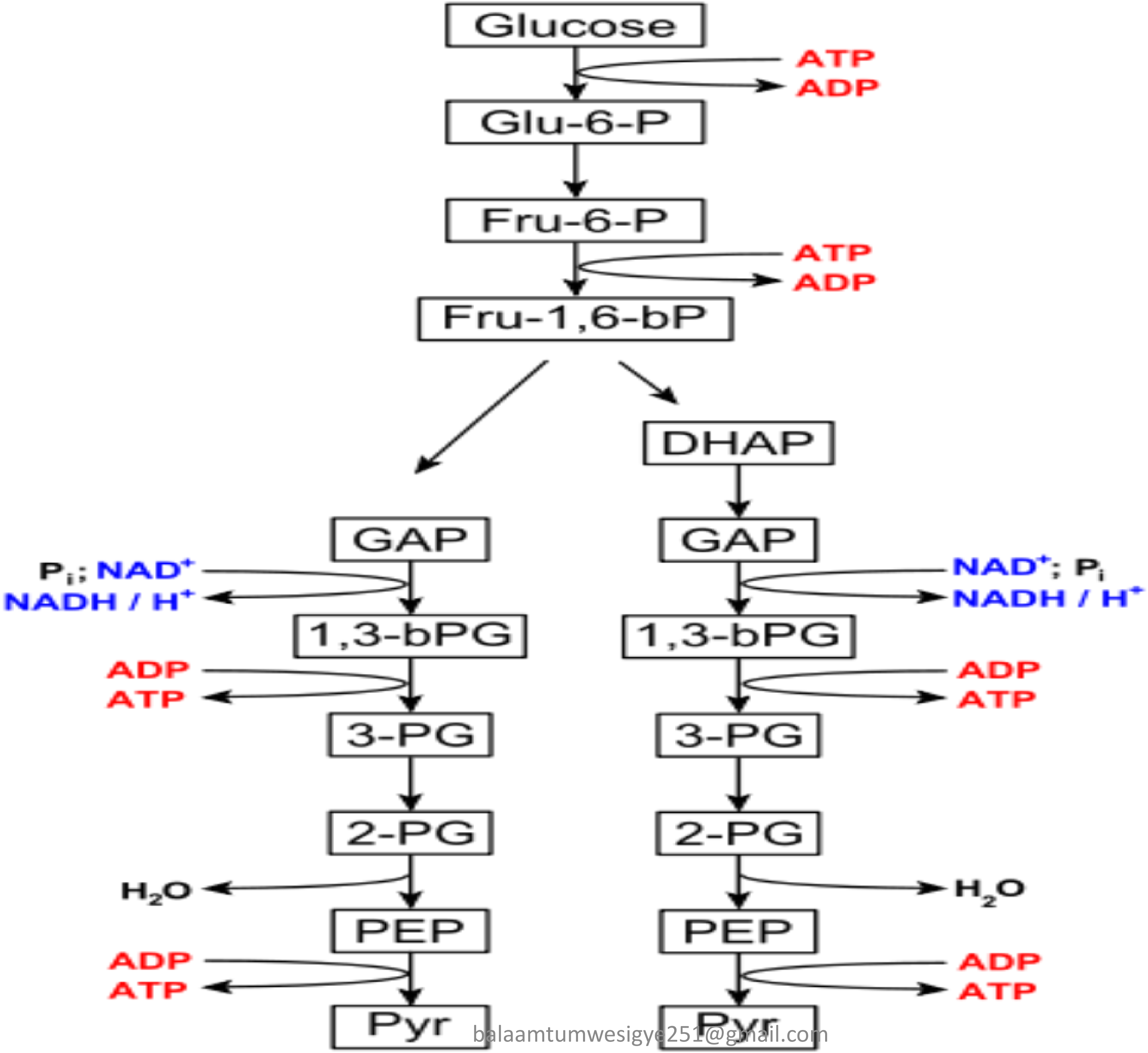
Glucose
ATP
ADP
Glu-6-P
Fru-6-P
ATP
ADP
Fru-1,6-bP
DHAP
GAP
GAP
P_i; NAD^+
$NADH / H^+$
NAD^+; P_i
$NADH / H^+$
1,3-bPG
1,3-bPG
ADP
ATP
ADP
ATP
3-PG
3-PG
2-PG
2-PG
H_2O
H_2O
PEP
PEP
ADP
ATP
ADP
ATP
Pyr
Pyr

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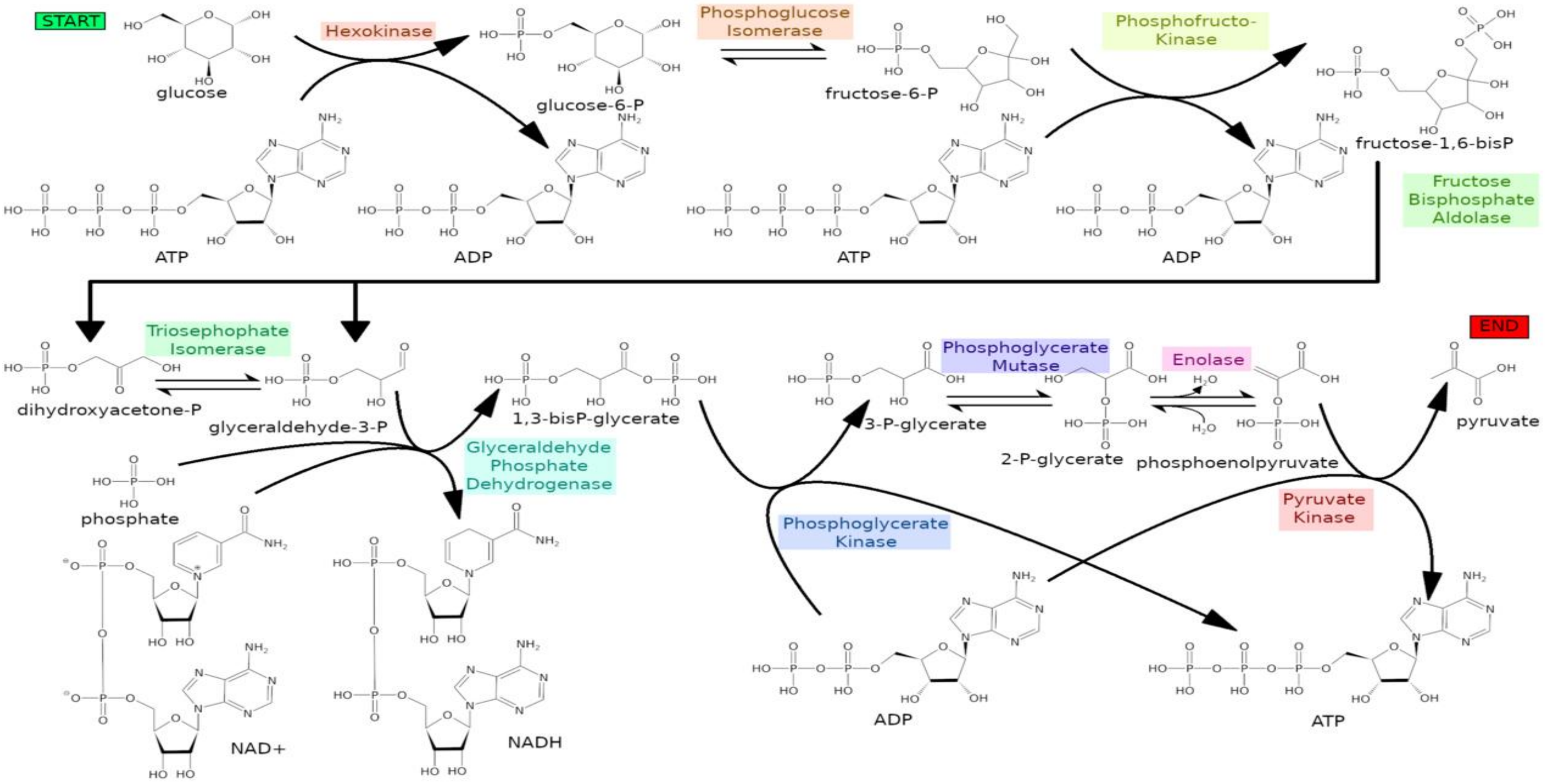
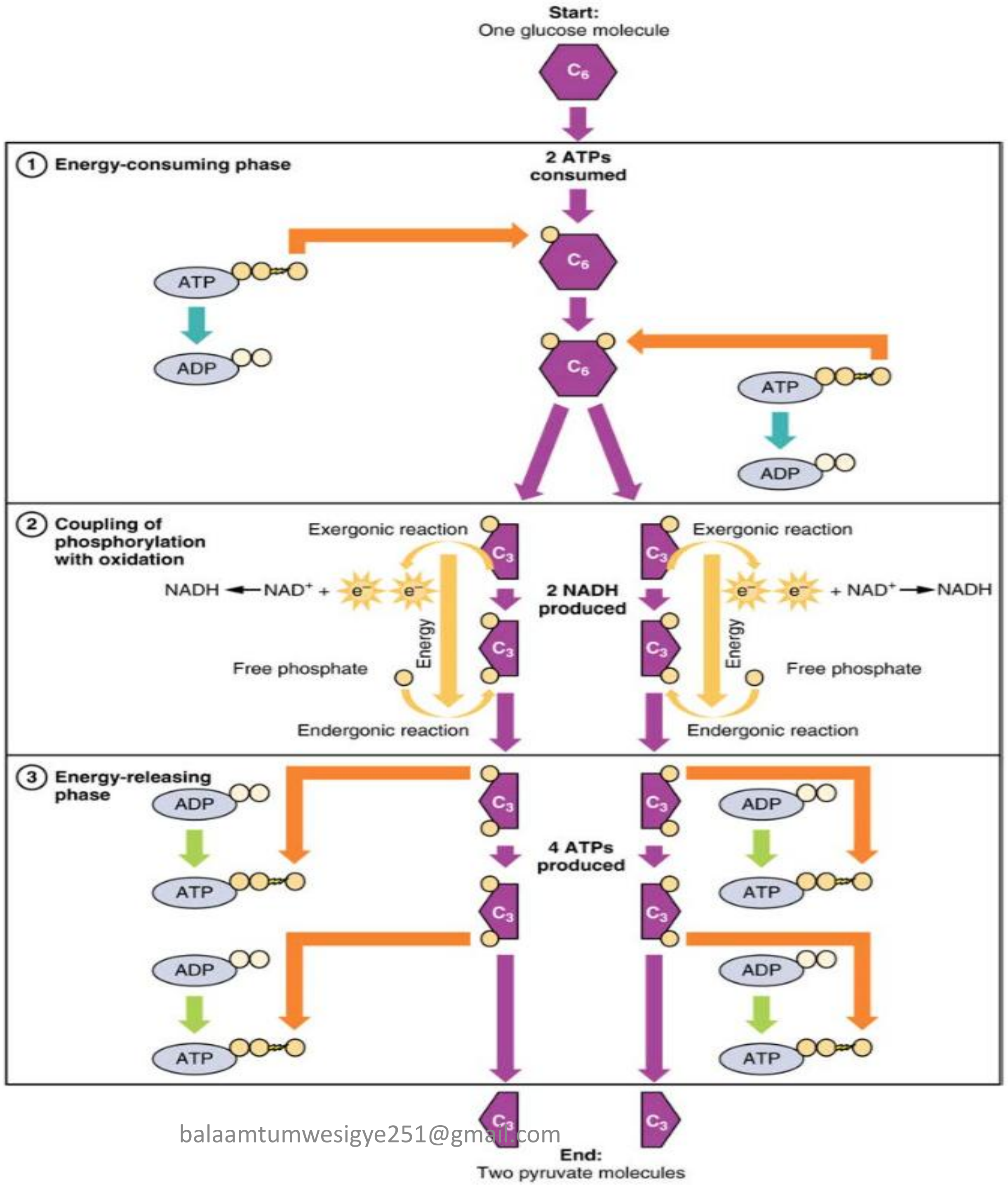

START
glucose
Hexokinase
glucose-6-P
Phosphoglucose Isomerase
fructose-6-P
Phosphofructo-Kinase
fructose-1,6-bisP
ATP
ADP
ATP
ADP
Fructose Bisphosphate Aldolase
Triosephophate Isomerase
dihydroxyacetone-P
glyceraldehyde-3-P
1,3-bisP-glycerate
phosphate
Glyceraldehyde Phosphate Dehydrogenase
NAD+
NADH
3-P-glycerate
Phosphoglycerate Mutase
2-P-glycerate
Enolase
phosphoenolpyruvate
END
pyruvate
Phosphoglycerate Kinase
Pyruvate Kinase
ADP
ATP

More explained



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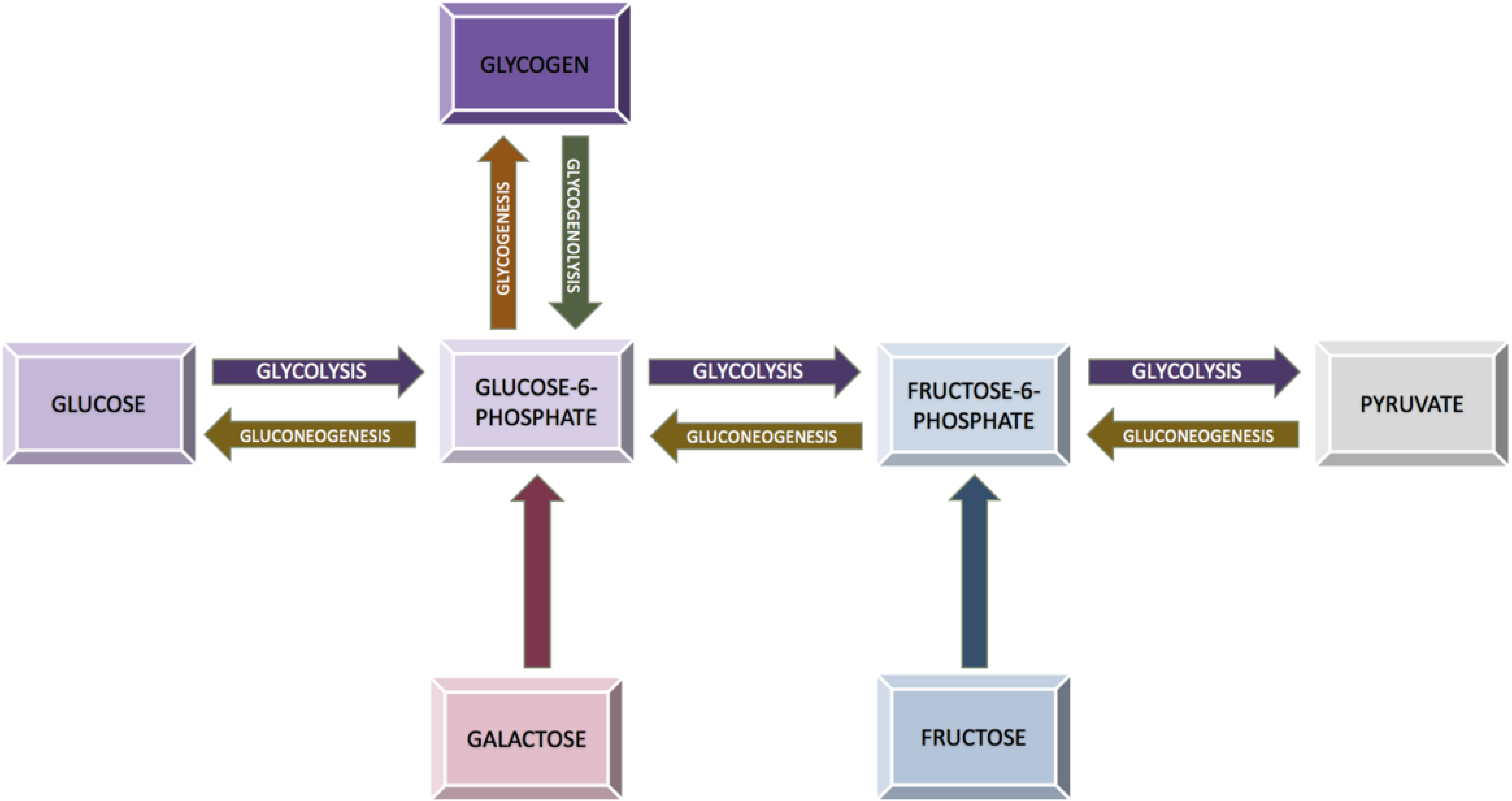
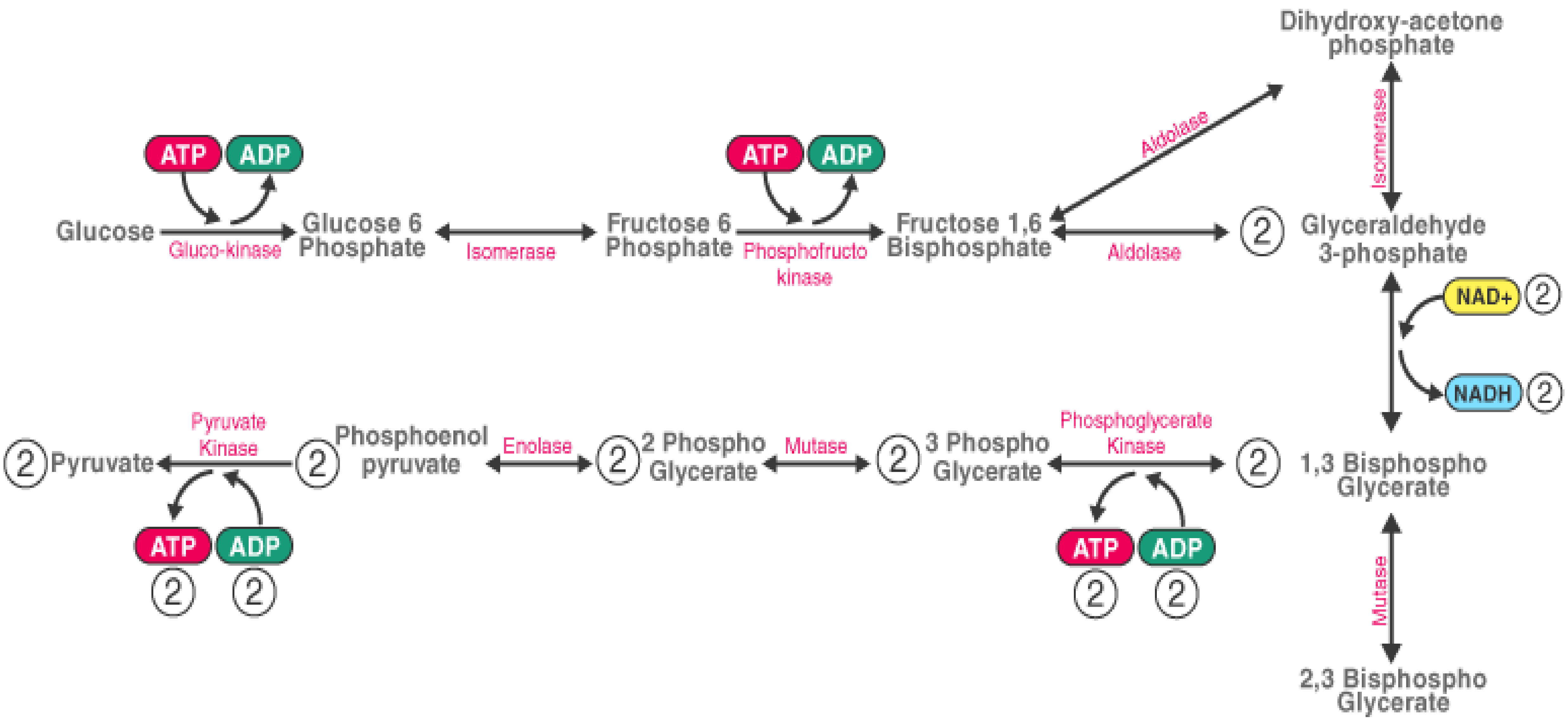
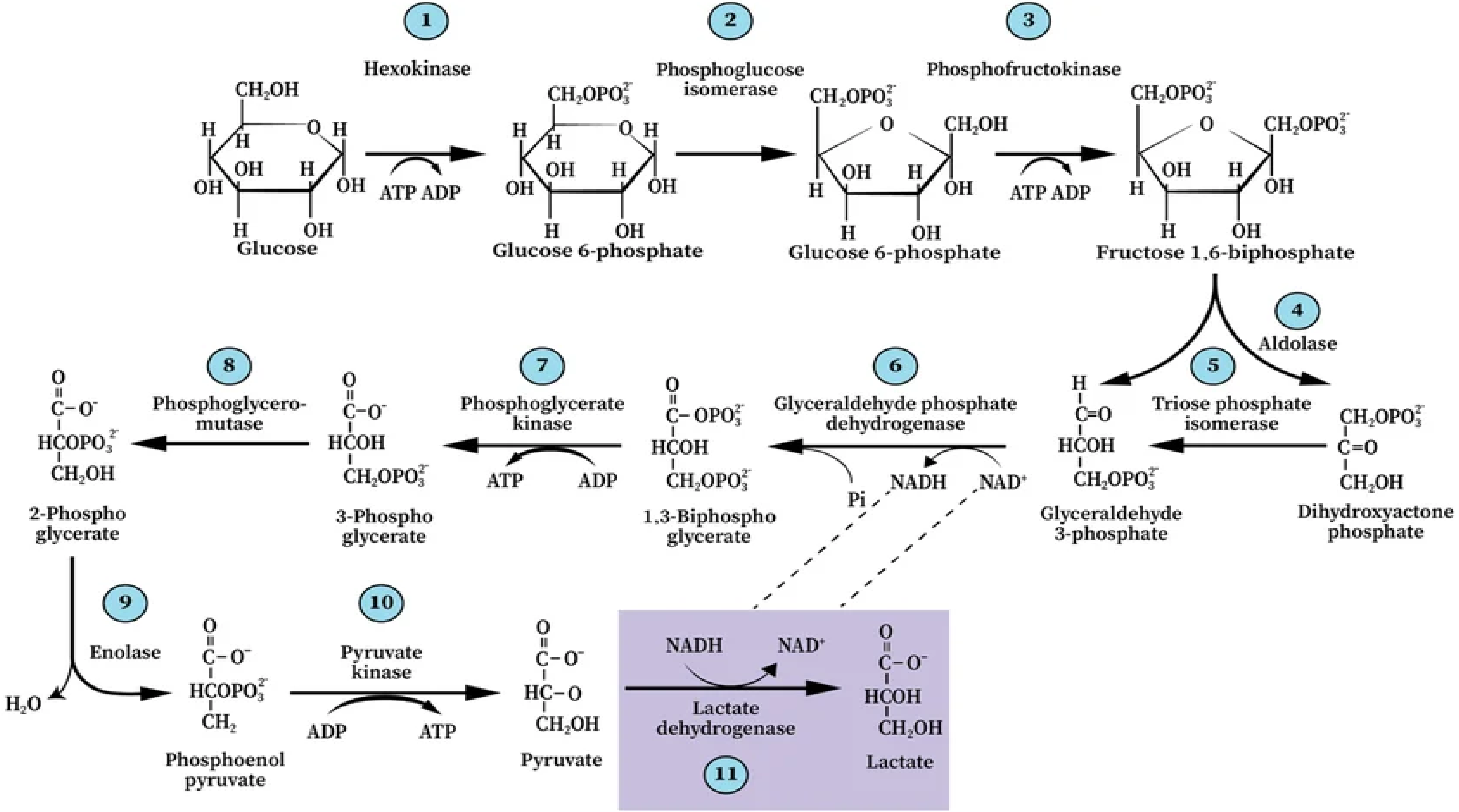

GLYCOGEN
GLYCOGENESIS
GLYCOGENOLYSIS
GLUCOSE
GLYCOLYSIS
GLUCONEOGENESIS
GLUCOSE-6-PHOSPHATE
GLYCOLYSIS
GLUCONEOGENESIS
FRUCTOSE-6-PHOSPHATE
GLYCOLYSIS
GLUCONEOGENESIS
PYRUVATE
GALACTOSE
FRUCTOSE

PATHWAY OF GLYCOLYSIS





1
Hexokinase
2
Phosphoglucose isomerase
3
Phosphofructokinase
Glucose
ATP ADP
Glucose 6-phosphate
Glucose 6-phosphate
ATP ADP
Fructose 1,6-biphosphate
4
Aldolase
5
Triose phosphate isomerase
6
Glyceraldehyde phosphate dehydrogenase
7
Phosphoglycerate kinase
8
Phosphoglycero-mutase
Glyceraldehyde 3-phosphate
Dihydroxyactone phosphate
Pi
NADH
NAD+
1,3-Biphospho glycerate
ATP
ADP
3-Phospho glycerate
2-Phospho glycerate
9
Enolase
H_2O
Phosphoenol pyruvate
10
Pyruvate kinase
ADP
ATP
Pyruvate
NADH
NAD+
Lactate dehydrogenase
11
Lactate

TCA CYCLE

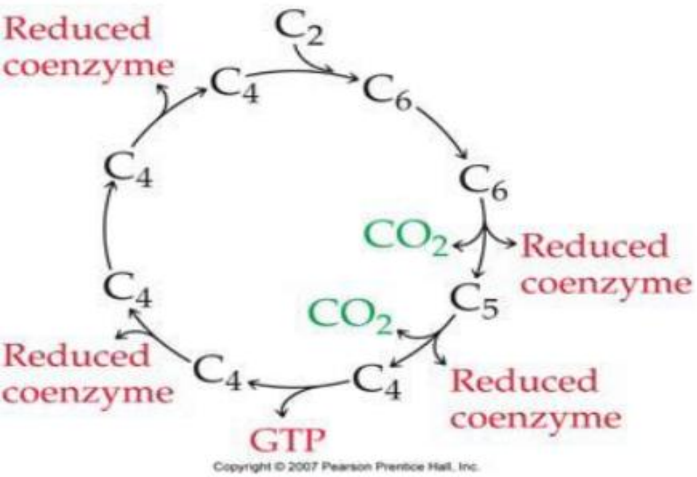
TCA CYCLE

Also known as the Citric acid cycle, Krebs cycle or the central oxidative pathway.

Occurs inside the mitochondria in the matrix only in presence of oxygen.

It requires supply of coenzymes NAD+ and FAD which receive H or electrons and transfer them to O2 via the electron transport chain

TCA Cycle


Reduced coenzyme
C2
C4
C6
C4
C6
CO2
Reduced coenzyme
C4
CO2
C5
Reduced coenzyme
C4
C4
Reduced coenzyme
coenzyme
GTP
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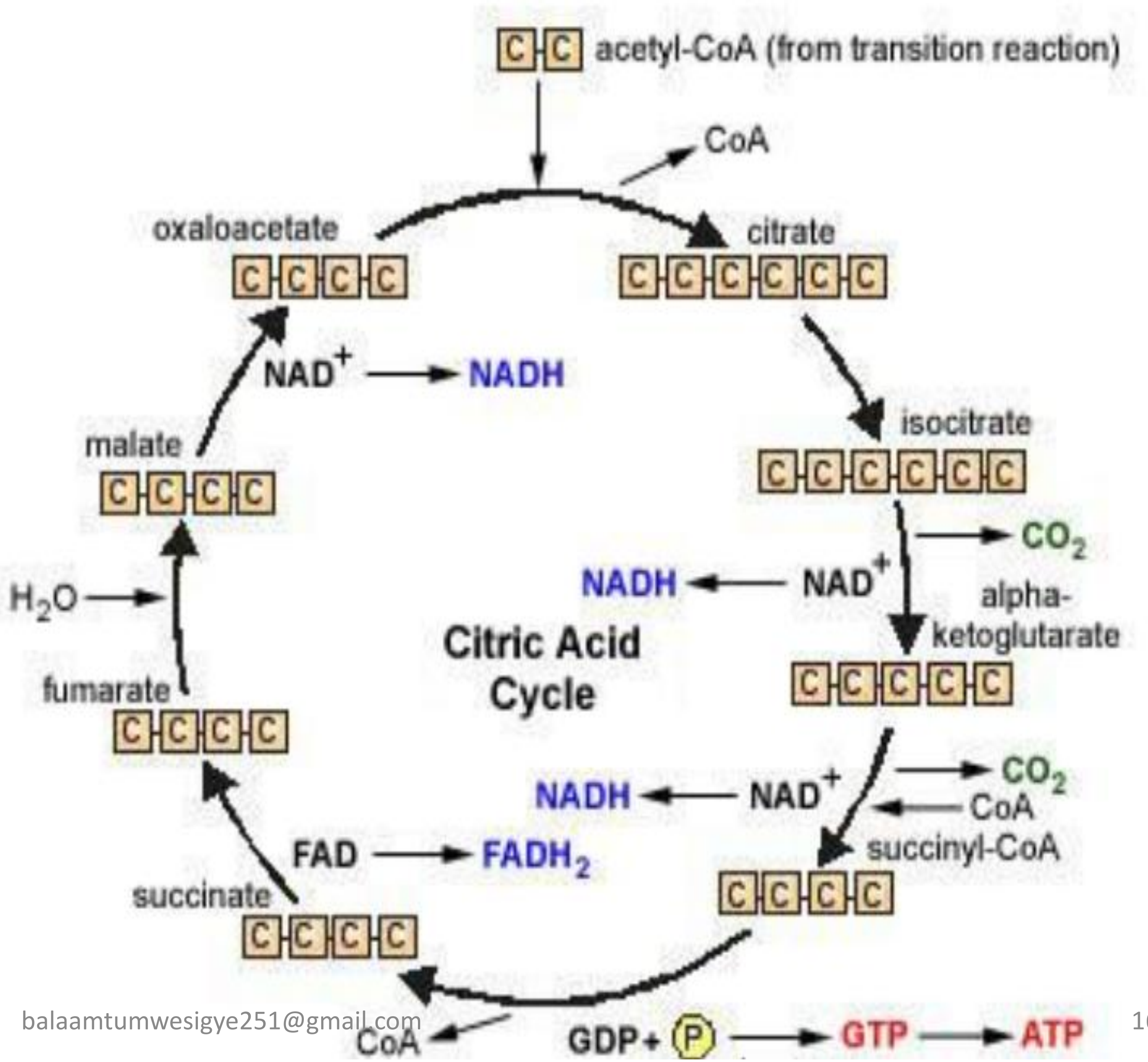
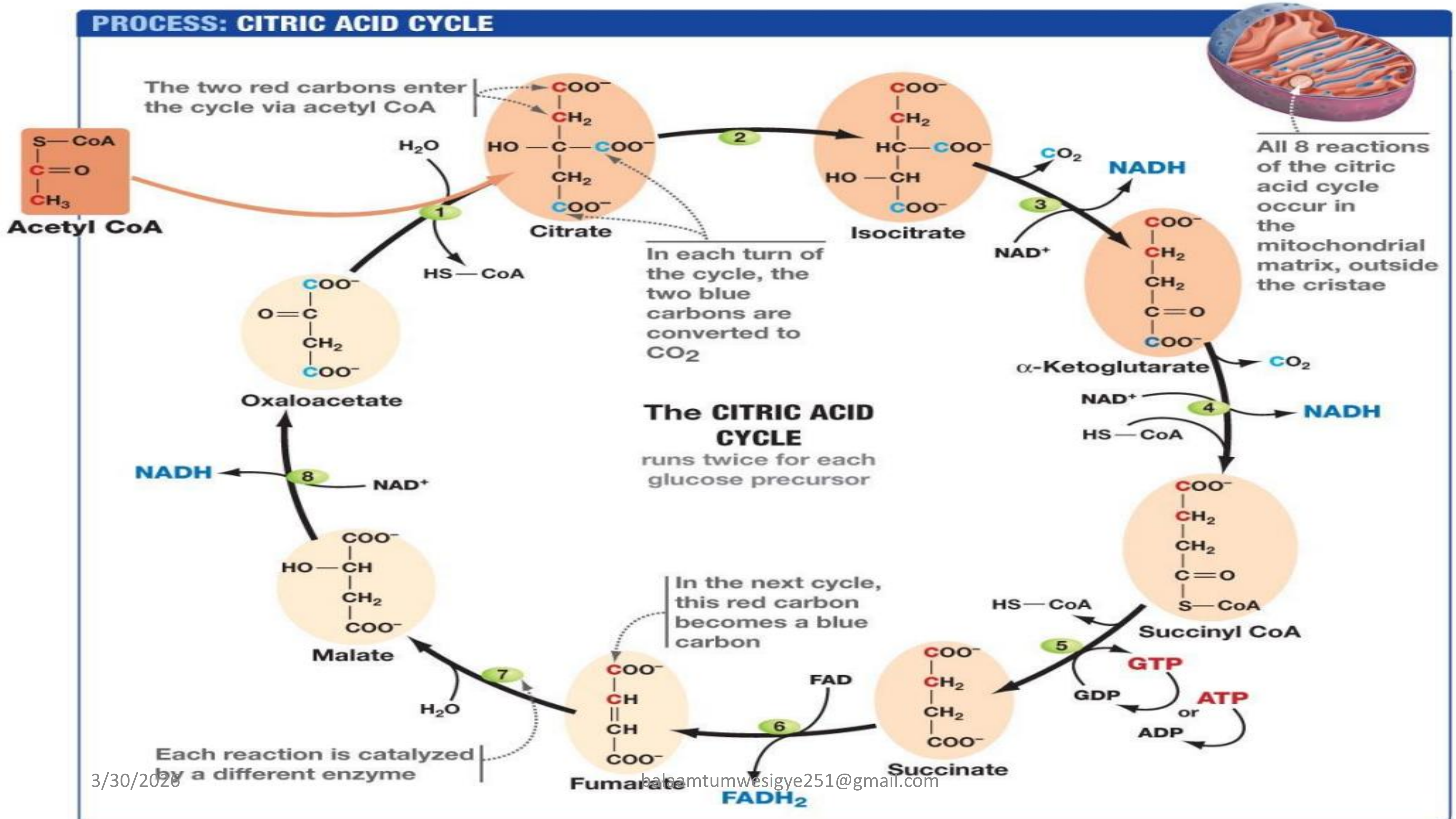

acetyl-CoA (from transition reaction)
CoA
oxaloacetate
citrate
NAD+
NADH
isocitrate
malate
CO2
NADH
NAD+
alpha-ketoglutarate
H2O
Citric Acid Cycle
fumarate
NADH
NAD+
CO2
CoA
succinyl-CoA
FAD
FADH2
succinate
CoA
GDP + P
GTP
ATP

Tricarboxylic acid cycle



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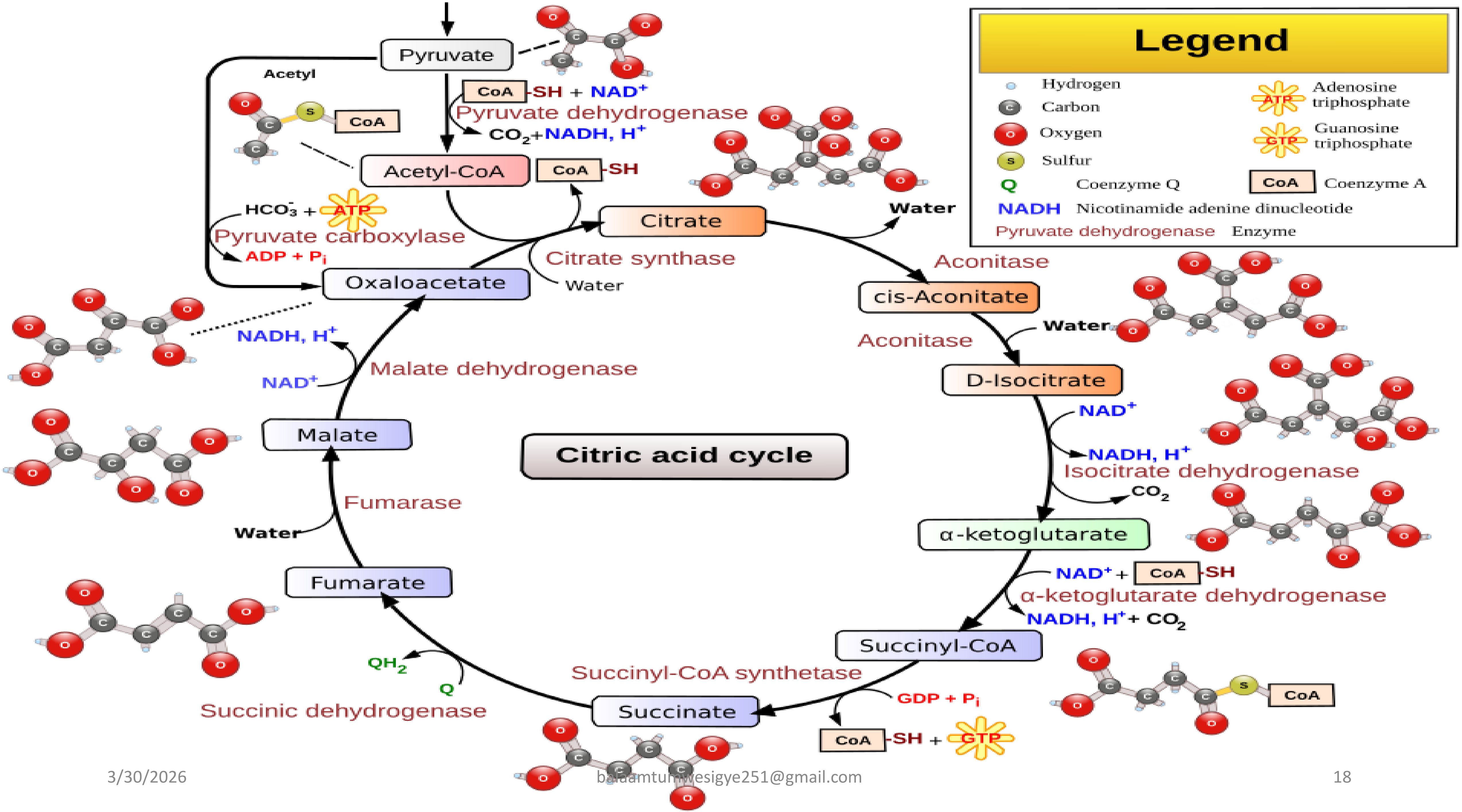


Legend
Hydrogen
Carbon
Oxygen
Sulfur
Q Coenzyme Q
NADH Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase Enzyme
ATP Adenosine triphosphate
GTP Guanosine triphosphate
CoA Coenzyme A
Citric acid cycle
Pyruvate
Acetyl
CoA-SH + NAD+
Pyruvate dehydrogenase
CO2+NADH, H+
Acetyl-CoA
CoA-SH
HCO3- + ATP
Pyruvate carboxylase
ADP + Pi
Oxaloacetate
Citrate
Citrate synthase
Water
Aconitase
cis-Aconitate
Water
Aconitase
D-Isocitrate
NAD+
NADH, H+
Isocitrate dehydrogenase
CO2
α-ketoglutarate
NAD+ + CoA-SH
α-ketoglutarate dehydrogenase
NADH, H+ + CO2
Succinyl-CoA
Succinyl-CoA synthetase
GDP + Pi
CoA-SH + GTP
Succinate
Succinic dehydrogenase
Q
QH2
Fumarate
Fumarase
Water
Malate
Malate dehydrogenase
NAD+
NADH, H+

The Electron Transport Chain

Final stage of **cellular respiration**

Occurs in the **inner mitochondrial membrane**

Main function: **produce ATP (energy)**

Requires **oxygen (aerobic process)**

Key components

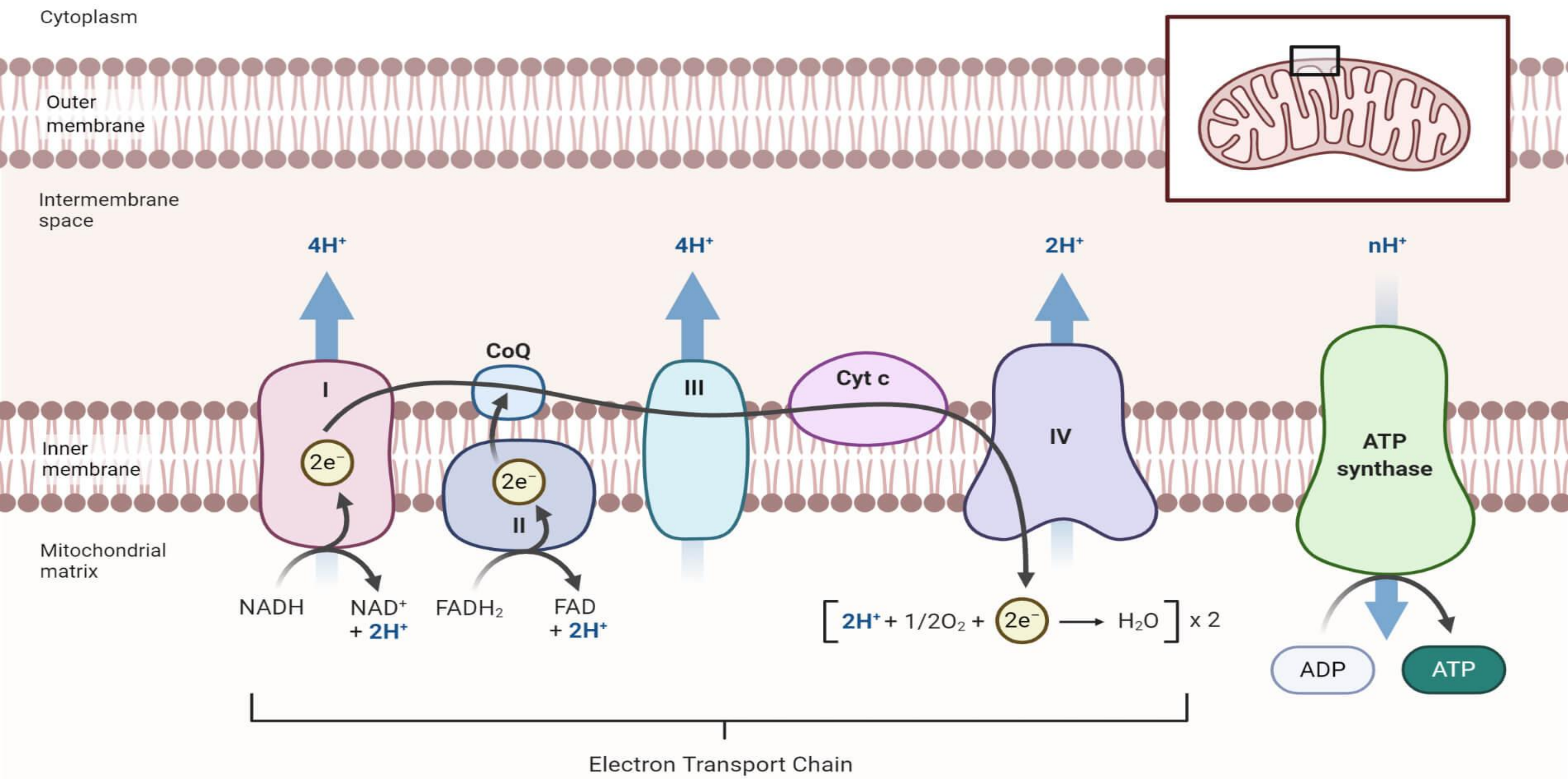
Electron carriers: NADH and $FADH_2$

Protein complexes: Complex I, II, III, IV

Mobile carriers: Coenzyme Q (ubiquinone), Cytochrome c

Enzyme: ATP synthase

Final electron acceptor: Oxygen (O_2)


Cytoplasm
Outer membrane
Intermembrane space
4H+
4H+
2H+
nH+
CoQ
I
III
Cyt c
IV
ATP synthase
Inner membrane
2e−
2e−
II
Mitochondrial matrix
NADH
NAD+ + 2H+
FADH2
FAD + 2H+
[2H+ + 1/2O2 + 2e− → H2O] x 2
ADP
ATP
Electron Transport Chain

How it works

NADH and $FADH_2$ donate electrons

Electrons move through protein complexes

Energy released pumps H^+ ions across membrane

Proton gradient is created

H^+ flows back through ATP synthase → ATP is made

Oxygen combines with electrons + H^+ → Water (H_2O)

Importance of ETC

Produces ~28–34 ATP molecules

Most efficient energy-producing step

Maintains proton gradient for ATP synthesis

Without oxygen → ETC stops → no ATP → cell death

PENTOSE PHOSPHATE PATHWAY PPP

Pentose Phosphate Pathway (PPP)

The pentose phosphate pathway (PPP)

Also called the hexose monophosphate (HMP) shunt

Is an alternative metabolic pathway that branches off from glycolysis.

It takes place in the cytoplasm and plays a crucial role in maintaining cellular health and supporting biosynthesis.

Pentose Phosphate Pathway

- Is an alternative pathway for oxidation of glucose.
- Used to produce five carbon (Pentose) sugars e.g. ribulose, xylulose and ribose
- Used in RNA and DNA synthensis.

PPP

- The PPP has two main phases:

1. Oxidative Phase (irreversible)

Converts glucose-6-phosphate into ribulose-5-phosphate

Produces:

- NADPH (very important reducing agent) & CO_2

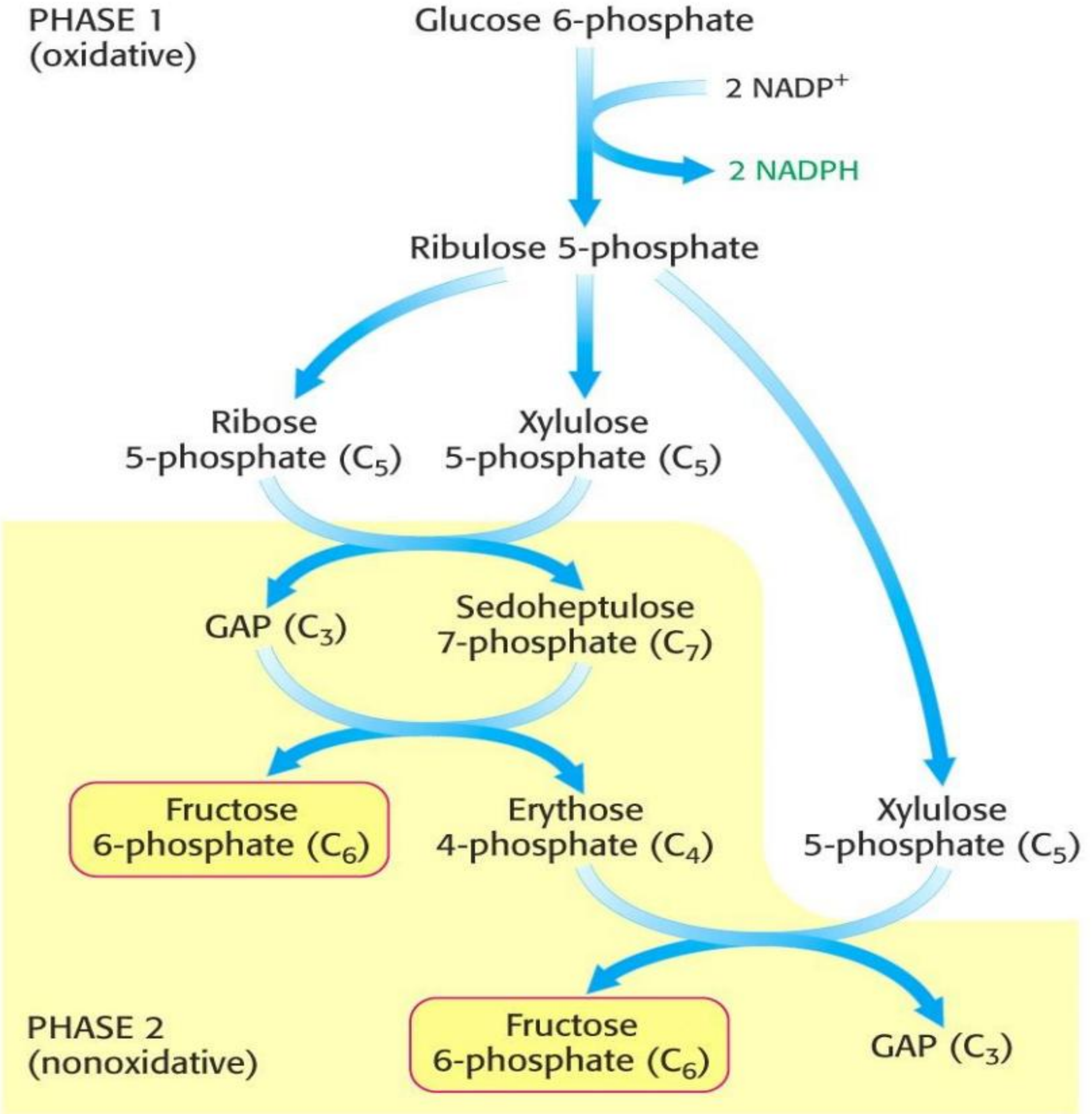
Key enzyme: Glucose-6-phosphate dehydrogenase (G6PD)

2. Non-oxidative Phase (reversible)

Converts ribulose-5-phosphate into: Ribose-5-phosphate (for nucleotide synthesis)

Intermediates like fructose-6-phosphate and glyceraldehyde-3-phosphate (which re-enter glycolysis)

The pentose pathway can be divided into two phases



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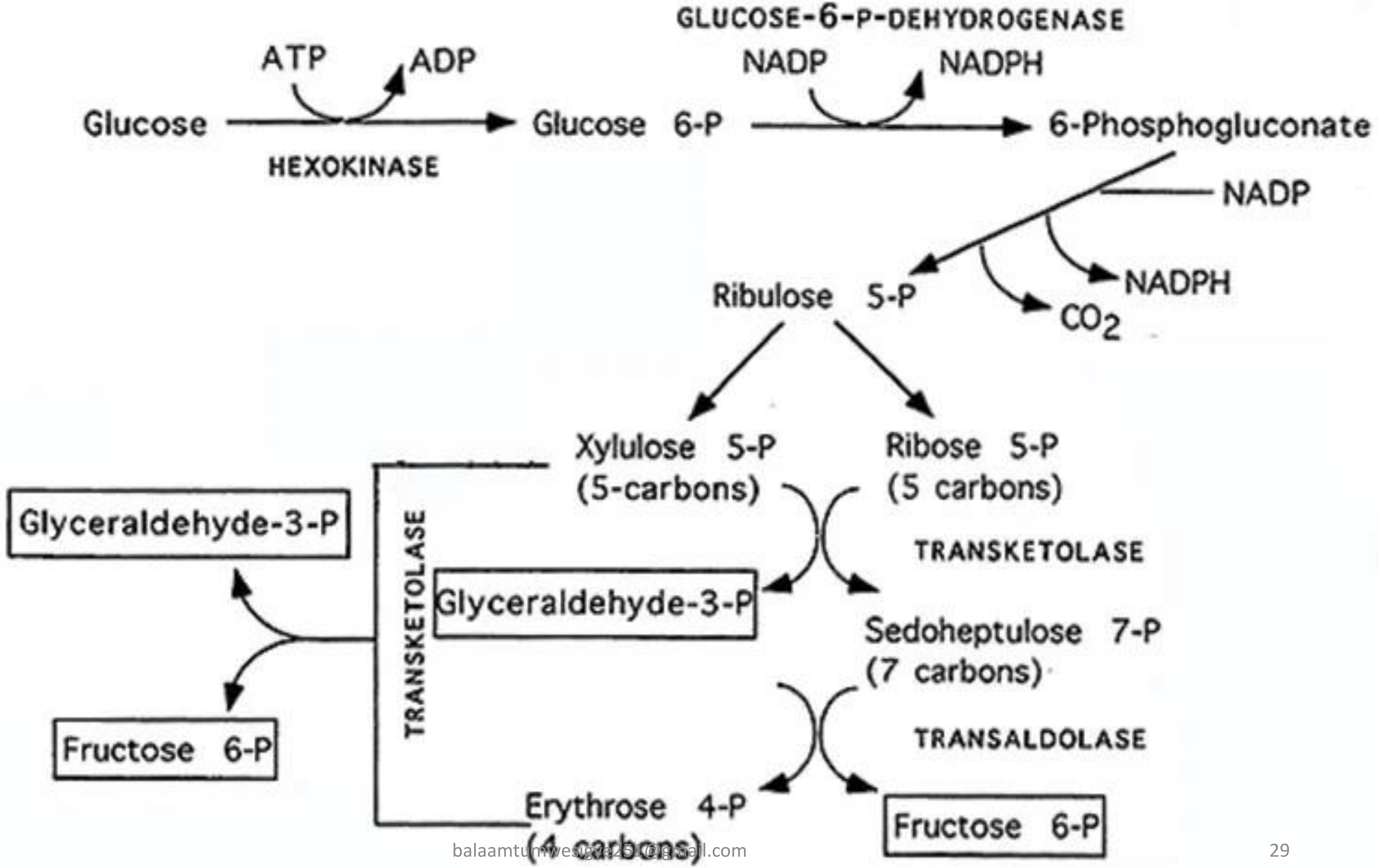
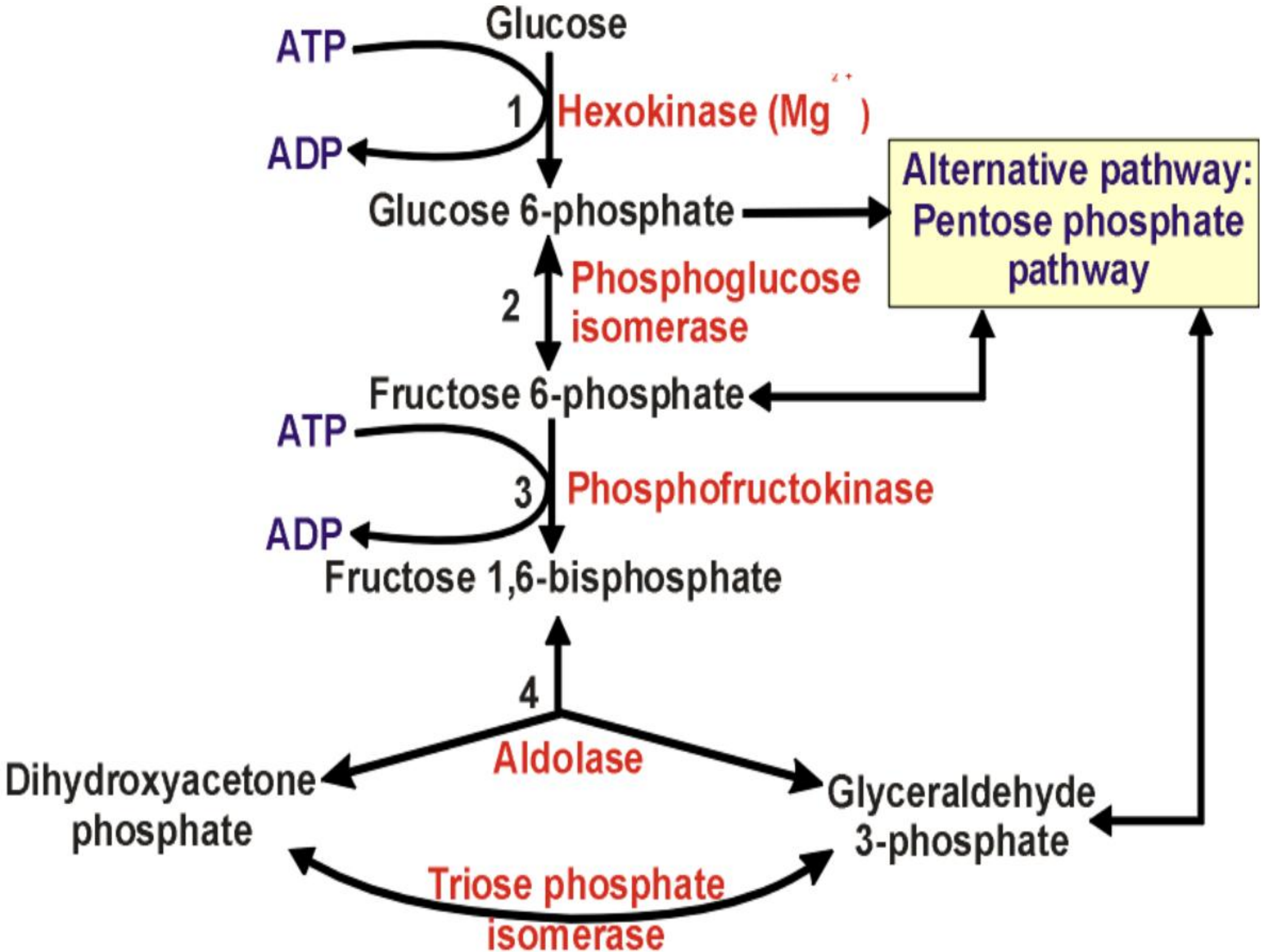

GLUCOSE-6-P-DEHYDROGENASE
ATP
ADP
NADP
NADPH
Glucose
HEXOKINASE
Glucose 6-P
6-Phosphogluconate
NADP
NADPH
CO_2
Ribulose 5-P
Xylulose 5-P
(5-carbons)
Ribose 5-P
(5 carbons)
TRANSKETOLASE
Glyceraldehyde-3-P
TRANSKETOLASE
Glyceraldehyde-3-P
Sedoheptulose 7-P
(7 carbons)
TRANSALDOLASE
Fructose 6-P
Erythrose 4-P
(4 carbons)
Fructose 6-P

Why is it called a shunt?



Key Functions of the PPP

1. Production of NADPH

NADPH is essential for:

1. **Biosynthetic reactions** (fatty acid and cholesterol synthesis)
2. **Detoxification** (e.g., in the liver via cytochrome P450 systems)
3. **Antioxidant defense**

   Maintains reduced glutathione to neutralize reactive oxygen species

this is critical in:

- ✓Red blood cells (to prevent oxidative damage)
- ✓Liver and adipose tissue

Functions simplified

TABLE 20.2 Pathways requiring NADPH

Synthesis

Fatty acid biosynthesis

Cholesterol biosynthesis

Neurotransmitter biosynthesis

Nucleotide biosynthesis

Detoxification

Reduction of oxidized glutathione

Cytochrome P450 monooxygenases

ABLE 20.4 Tissues with active pentose phosphate pathways

Tissue	Function
Adrenal gland	Steroid synthesis
Liver	Fatty acid and cholesterol synthesis
Testes	Steroid synthesis
Adipose tissue	Fatty acid synthesis
Ovary	Steroid synthesis
Mammary gland	Fatty acid synthesis
Red blood cells	Maintenance of reduced glutathione

•

NADH & NADPH

NADH	NADPH
NADH is the reduced form of NAD	NADPH is the reduced form of NADP
NAD+ is the oxidized form	NADP+ is the oxidized form
Involved in cellular respiration	Involved in photosynthesis
Produced in glycolysis and Krebs cycle	Produced in the light reaction of photosynthesis
Used in the electron transport chain to produce ATP by oxidative phosphorylation	Used in the Calvin cycle to assimilate carbon dioxide
Do not contain a free phosphate group	Contains a free phosphate group in the 2' position of the ribose, which is attached to the adenine moiety
Involved in anabolic reactions	Involved in catabolic reactions
Less abundant than NAD+	Most abundant form inside the cell

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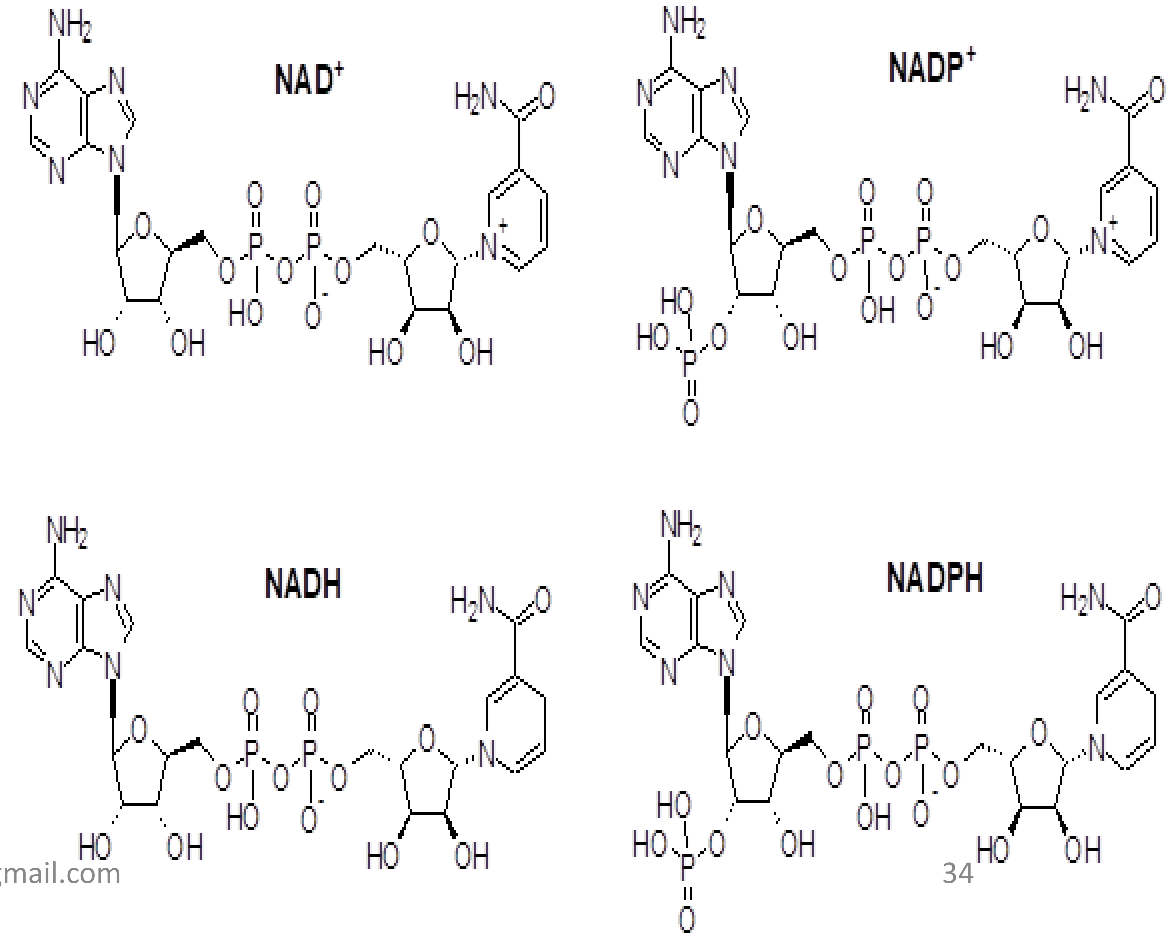


CLINICAL RELEVANCE

G6PD Deficiency

A genetic condition affecting the enzyme G6PD

Leads to reduced NADPH production

Causes increased susceptibility to oxidative stress

What is G6PD Deficiency?

Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) is a **genetic disorder** where the body lacks enough functional **Glucose-6-phosphate dehydrogenase**, the key enzyme in the **pentose phosphate pathway**.

This enzyme is responsible for producing **NADPH**, which is essential for protecting cells; especially red blood cells; from oxidative damage.

Why NADPH is So Important?

In red blood cells (RBCs):

NADPH keeps **glutathione** in its **reduced form**

Reduced glutathione neutralizes **reactive oxygen species (ROS)** like hydrogen peroxide

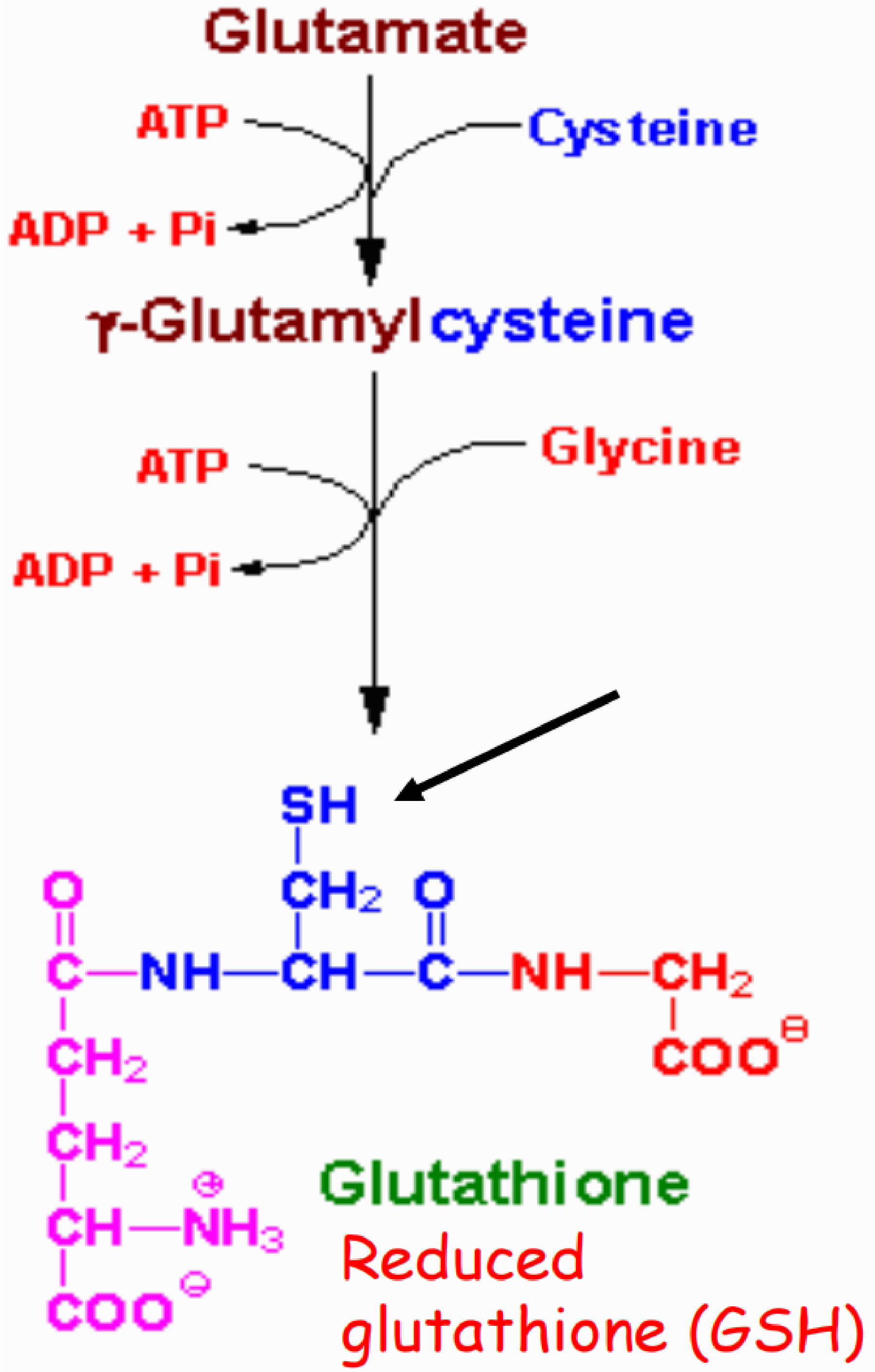
Without enough NADPH:

- ROS accumulate
- Cell components (especially hemoglobin and membrane) get damaged

Glutathione and NADPH
What is Glutathione?
Why is it important?
How is it related to NADPH?

Glutathione is a tripeptide composed of glutamate, cysteine, glycine.

Reduced glutathione (GSH) maintains the normal reduced state of the cell.



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Glutathione Functions-1

- It serves as a reductant (reducing agent).
- Conjugates to drugs making them water soluble.
- Involved in amino acid transport across cell membranes.
- Cofactor in some enzymatic reactions.
- – rearrangement of protein disulfide bonds.

Glutathione Functions-2

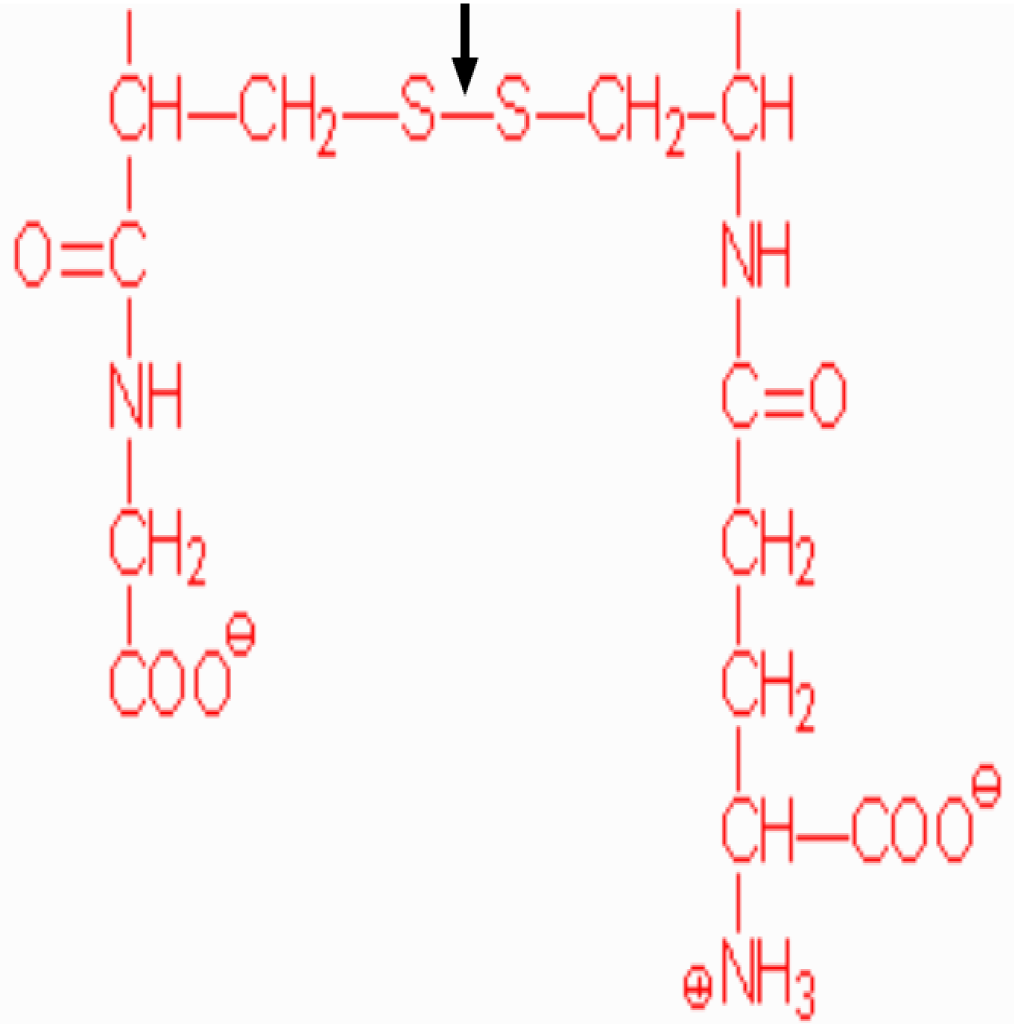
The sulfhydryl of GSH is used to reduce peroxides (ROS) formed during oxygen transport.

– Reactive oxygen species (ROS) can damage macromolecules (DNA, RNA, and protein) and ultimately lead to cell death.

The resulting oxidized form of GSH is two molecules linked by a disulfide bridge (GS-SG).

Glutathione

The enzyme glutathione reductase uses NADPH as a cofactor to reduce GS-SG back to two moles of GSH. Thus, the pentose pathway is linked to the supply of adequate amounts of GSH.



Glutathione disulfide (GSSG)

What Happens in G6PD Deficiency?

1. ↓ G6PD enzyme activity
2. ↓ NADPH production
3. ↓ Reduced glutathione
4. ↑ Oxidative stress
5. Damage to RBCs → rupture (**hemolysis**)

Why Red Blood Cells Are Most Affected

RBCs **lack mitochondria**

They rely **entirely** on the pentose phosphate pathway for NADPH

So they are highly vulnerable when G6PD is deficient

⚠️ Hemolytic Anemia

The main clinical effect is **Hemolytic anemia**, where red blood cells are destroyed faster than they can be produced.

The growth of Plasmodium falciparum (malaria parasite) fails in G6PD deficient individuals. EXPLAIN HOW THIS HAPPENS.

Triggers of Hemolysis

People with G6PD deficiency are usually normal **until exposed to oxidative stress**.

1. 💊 Drugs

Certain medications increase oxidative stress:

- ❑Antimalarials (e.g., **Primaquine**)
- ❑Sulfa drugs (e.g., **Sulfamethoxazole**)
- ❑Some painkillers and antibiotics

👉 **Example:**
A patient takes primaquine for malaria → oxidative stress rises → RBCs break down → sudden anemia.

FAVISM

- Individuals with **G6PDH** deficiency must not eat Fava beans.
- Pythagora's stay away from fava beans
- Erythrocytes lyse = dark or black urine.

Foods (Fava Beans)
This is called Favism
Fava beans contain oxidant compounds
☞ Example:Someone eats fava beans → within hours to days develops:Dark urine
Weakness
Jaundice