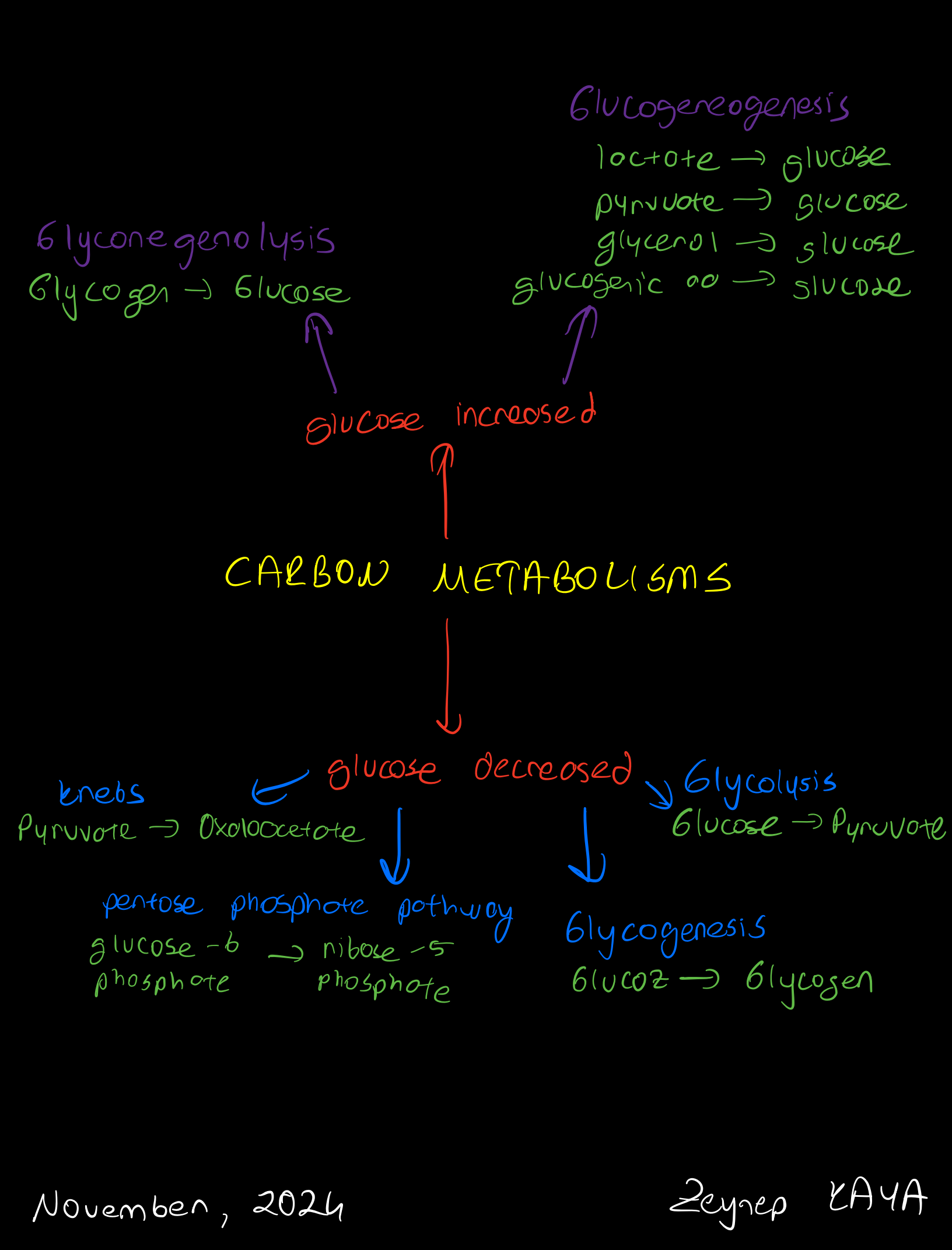


November, 2024

Zeynep KAYA

Carbon Metabolism

Glycolysis

intro = glucose versatile precursor biosynthetic reaction
expected glucose level 70-100

Glucose → oxidation → glycolysis → pyruvate
→ oxidation → pentose phosphate → ribose 5 phosphate
→ storage → → glycogen

glycolysis general = Glucose ⟶ 2 pyruvate
↓ ↓
2 NADH 2 ATP

↳ in cells with mitochondria and adequate supply of energy

Glucose ⟶ lactate

↳ anaerobic glycolysis

↳ just bcs pyruvate not enter mito.

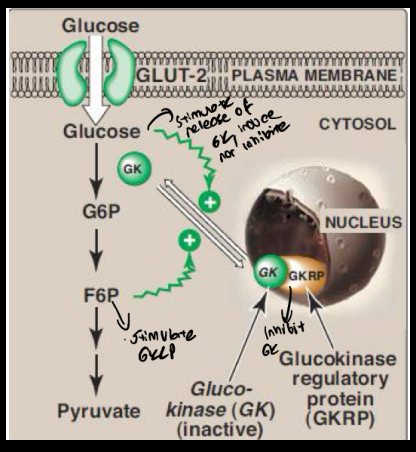
reaction of glycolysis = energy investment → phosphorylated
energy generation → synthesize of ATP, pyruvate NADH

Step ① - HEXOKINASE, GLUCOKINASE

Glucose $\xrightarrow[\text{hexokinase}]{ATP \xrightarrow{Mg^{+2}} ADP}$ Glucose-6-phosphate

- Regulatory Enzyme - irreversible

	Hexokinase	Glucokinase
	- most tissue	- in liver parenchymal cells, β cells of pancreas
Km	- low	- high
Vmax	- low	- high
inhibition by G6P	- yes	- no
inducible	- no	- yes (insulin)
	- intracellular glucose concent.	- blood glucose cont.

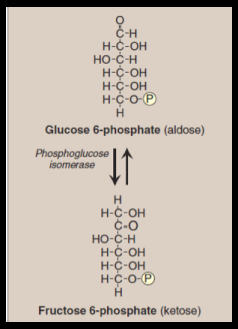


→ glucokinase indirectly inhibited by fructose 6 phosphate

Step ② - PHOSPHO GLUCOSE ISOMERASE

Glucose-6-phoshate ⇌ Fructose-6-phoshate

phosphoglucose isomerase

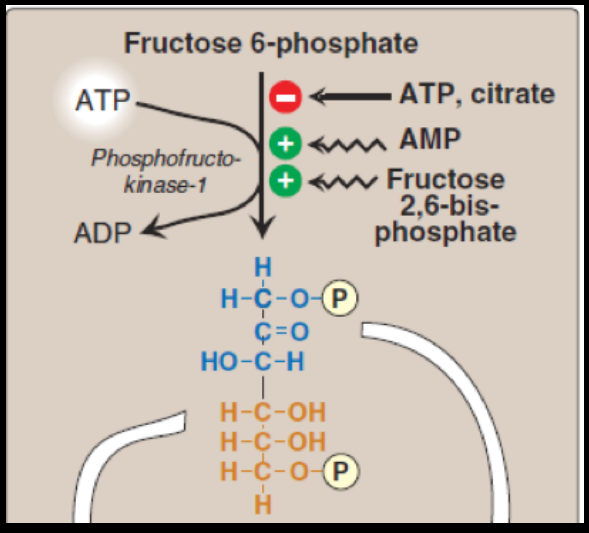


Step ③ - PHOSPHOFRUCTOKINASE-1

Fructose-6-phosphate ⟶ Fructose 1,6-bisphosphate

ATP → ADP

- Regulatory Enzyme - irreversible

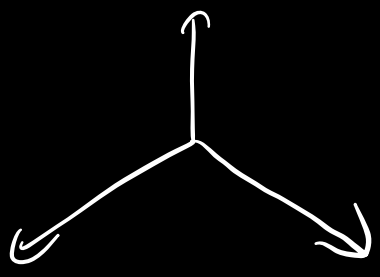


→ Regulation of PFK-1

→ Fructose 2,6 biphosphate the most potent activator

Step ④ - ALDOLASE

Fructose 1,6- bisphosphate



Glyceraldehyde 3-phosphate

Dihydroxyacetone phosphate

triose phosphate isomeros

Step ⑤ - TRIOSE PHOSPHATE ISOMERASE

Dihydroxyacetone phosphate ⟷ Glyceraldehyde 3-phosphate

triose phosphate isomeros

Step ⑥ GLYCERALDHYDE 3-PHOSPHATE DEHYDROGENASE

Glyceraldehyde 3-phosphate + Pi + NAD → NADH → 1-3 biphosphoglycerate

Glyceraldehyde 3-phosphate dehydrogenas

Step (7) PHOSPHOGLYCERATE KINASE

1,3 biphosphoglycerate ⇌ (ADP → ATP; phosglycerate kinase) 3-phosphoglycerate

FIRST ATP GENERATION OCCURS

Step (8) PHOSPHOGLYCERATE MUTASE

3-Phosphoglycerate ⇌ (phosphoglycerate mutase) 2-phosphoglycerate

Step (9) ENOLASE

2-Phosphoglycerate ⇌ (enolase; → H_2O) Phosphoenolpyruvate

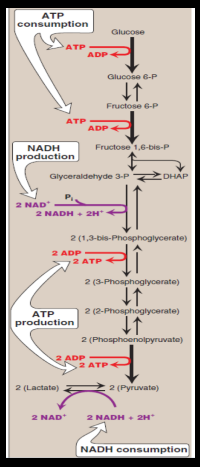
Step (10) PYRUVATE KINASE

Phosphoenolpyruvate → (ADP → ATP; pyruvate kinase) pyruvate

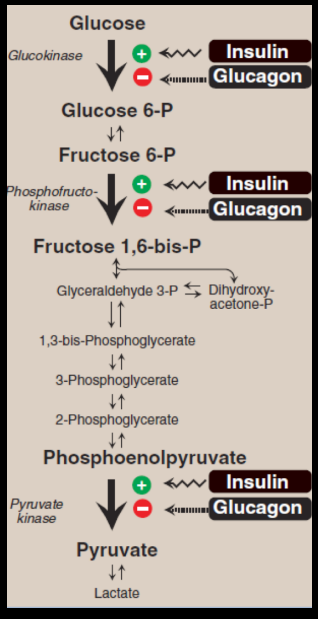
- Regulatory Enzyme - irreversible
- SECOND ATP GENERATION OCCURS

extra notes

- in liver pyruvate kinase is activated by fructose 1,6 bisphosphate
- Hemolytic anemia caused
  - ① glucose 6 phosphate dehydrogenase
  - ② pyruvate kinases



→ Anaerobic glycolysis no net NADH.



→ Hormonal regulation of glycolysis

Glycogen Metabolism

Utilize glycogen to fat

- fatty acids cannot metabolized anaerobically
- all humans cannot convert fat to glucose
- muscle cannot do fat as efficiently as glycogen

Glucose Obtained

- diet
- degradation of glycogen → rapid
- gluconeogenesis → slow

Glycogen

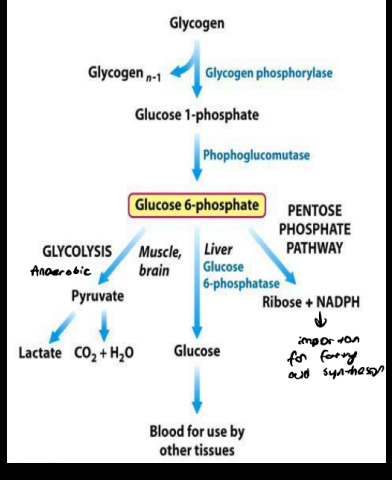
- buffer to maintain blood glucose level
- glucose from them energy for strenuous activity
- found in liver and skeletal muscle

Step ① - HEXOKINASE

$$\text{Glucose} \xrightarrow[\text{ATP} \curvearrowright \text{ADP}]{\text{hexokinase}} \text{Glucose-6-phosphate}$$

fate of Glucose 6-P

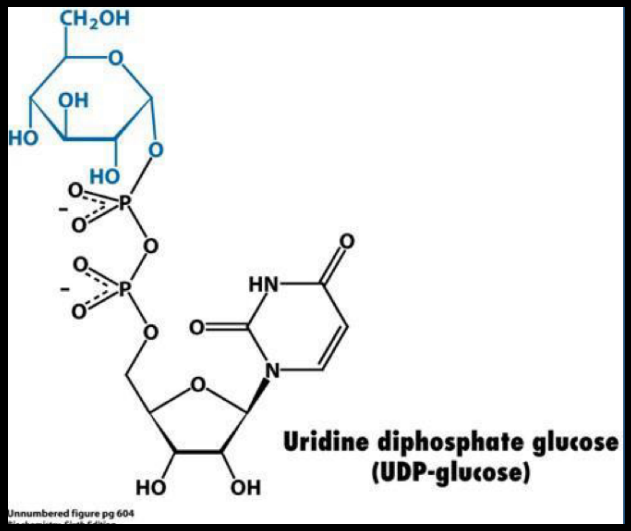
- glycolysis
- pentose phosphate pathway
- glycogen synthesis
- degradation to free glucose



1- activation of glucose

UDP glucose, glucose donor in biosynthesis of glycogen

ACTIVATED FORMS OF GLUCOSE

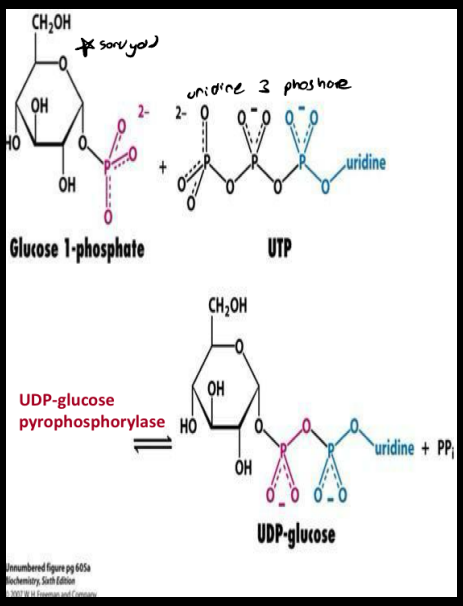


2 - synthesis of UDP glucose

glucose 1- phosphate + UTP

→ UDP - glucose

UDP - glucose pyrophosphorylase

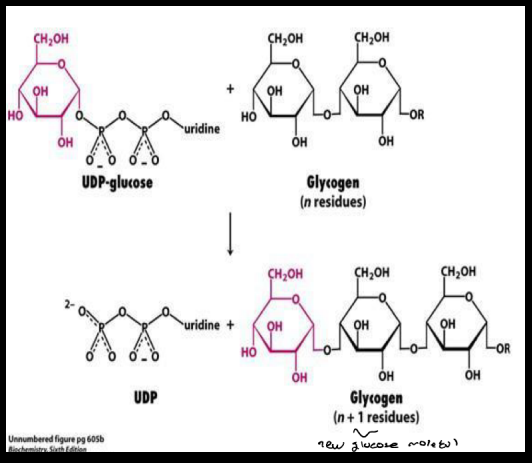


3- adding UDP

UDP - glucose + Glycogen (n residues)

→ UDP + Glycogen (n+1 residues)

ATP → ADP



Glycogenin
- primer function
- enzyme
- produces, α(1→4) linked glucosyl chain
- glucose receptor absence of glycogen fragment

Step ② Initiation - GLYCOGEN SYNTHESIS

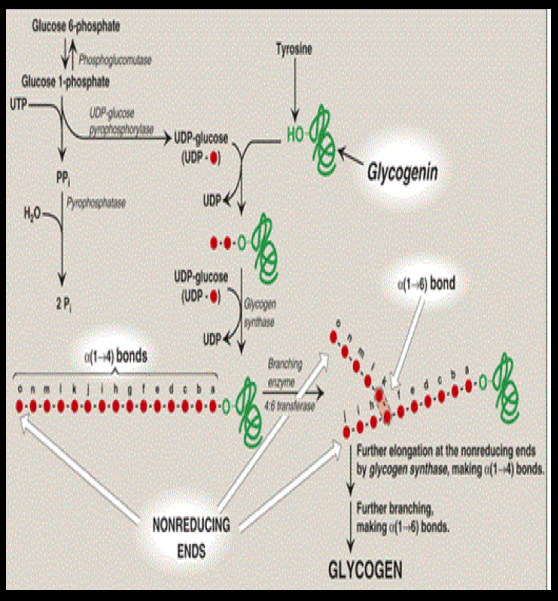
- moving a (1→4) bonds
- elongate existing chain
- each subunit of glycogenin catalyzes eight glucose units.
- synthesis of a primer to initiate

Step ③ Elongation - GLYCOGEN SYNTHESIS

- new glucosly residues added to non reducing end
- formation of a (1,4) linkage

Step ④ Glycogen Branching TRANSGLUCOSIDASE

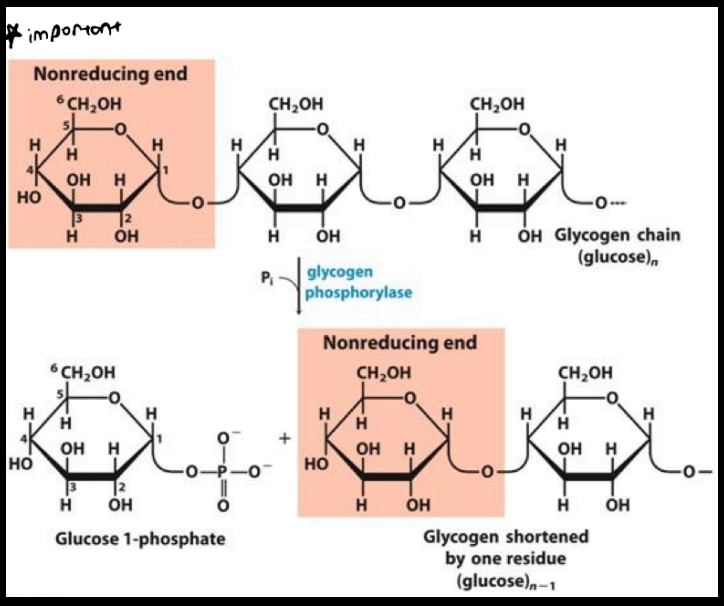
- amlyo - (1,4) -> (1,6)
- increases solubility
- increases terminal residues → site for action of synthase and phosphonylase
- rapid storage
- provide degradation of glycogen



Glyconegenolysis

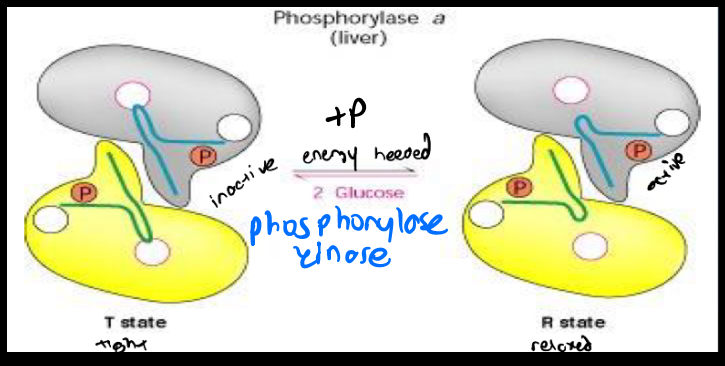
genenal = not reversal
a seperate set of cytosolic enzymes

stony begins

1. 

primary product
glucose 1-phosphate
breaking
α-(1→4) glycosidic bond
enzyme
Glycogen Phosphonylose

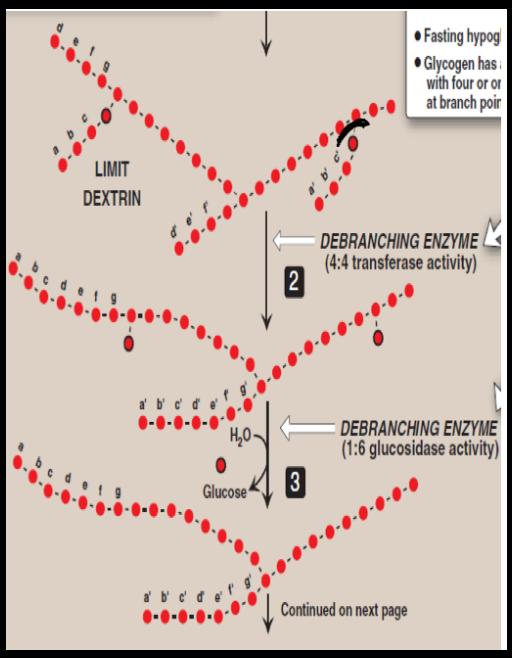
Glycogen Phosponlyose
- Pyridoxal phosphate (PLP), required as coenzym
- Allosteric enzyme.

phosphonylose b 

phosphonylose a

✡ Glycogen Phosphonylose cleaves glucosyly residues from glycogen until four glucosly residues remain on each chain → LIMIT DEXTRIN

(2)



Debranching Enzyme

- first, 4:4 transferase removes the outer 3 out of the 4 residues on limit dextrin
- remaining single residues cleaved by 1:6 glucosidase releasing → one free glucose

(3) Conversion of G 1-p to G 6-p

Glucose 1-phosphate ⟶ Glucose 6-phosphate
phosphoglucomutase

↳ common in muscle and liver

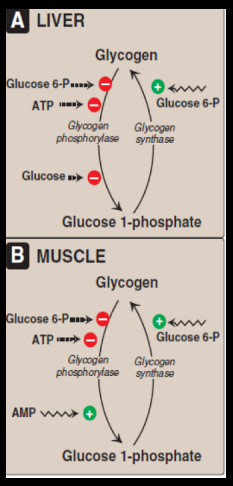
Glucose 6-phosphate ⟶ into endoplasmic reticulum
transferred by
Glucose 6-phosphate translocase

Glucose 6-phosphate ⟶ glucose
glucose 6-phosphatase

↳ just in liver

✱ muscle connot produce glucos bcs lack of glucose 6-phosphatase
↳ glucose 6-phosphate enters glycolysis
↳ energy for muscle contraction
↳ * reminder: phosphonylated glucose is not transported out of the muscle cells

Regulation of Glyconeogenolysis



LIVER

↑ Glucose
↑ G-6P
↑ ATP

MUSCLE

↑ AMP

Glycogen

Glyconeogenolysis

glycogen phosphonylase

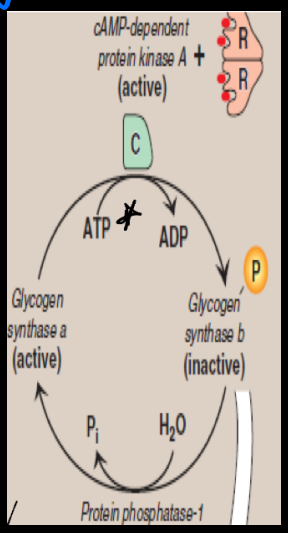
- Glucogon
- Norepinefnin
- Epinefnin

protein kinase A
PKA

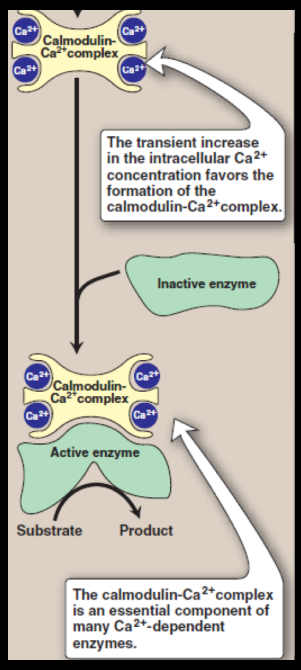
Glucose

Glycogenesis

glycogen synthase



phosphonylose kinose B $\xrightarrow{+P}$ phosphonlouse kinose A



→ when there is urgent need for ATP in muscles.

→ the Co^{2} binds CALMODULIN complex activates muscle and hepatic phosphonylose kinose b

Glycogen Storage Diseases

↳ formation of glucose that is abnormal structure

↳ excessive amounts of normal glycogen

Ia - Von Gierges Disease → Glucose 6-phosphates

Ib - → Glucose 6-P translocase

II - Pompe's disease → Acid maltose

↳ (1-3%) of glycogen degraded by lysosomal enzyme, a C(1→4)-glucosidase by acid maltase

↳ only lysosomal storage disease

III - Cori's disease → Debranching enzyme

IV - Anderson disease → Branching enzyme

V - McArdle disease → Glycogen Phosphorylase (muscle)

Glucogeneogenesis

general = synthesize glucose from non-carbonhydrat precursors.

anobolic pathway
in liver %90, kidney %10
↳ prolonged fast kidney up to %40

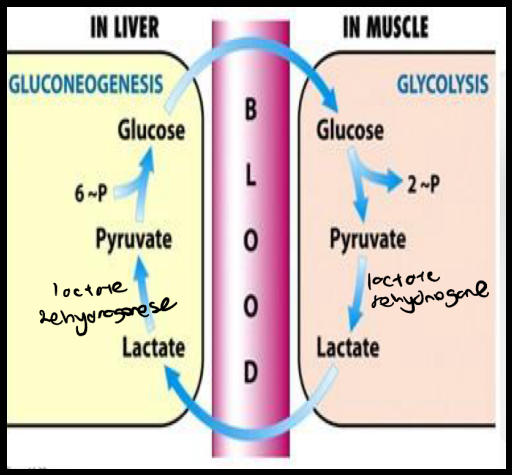
glucose major source

- brain
- nerveous system
- erythrocytes
- testes
- renal medulla
- embryonic tissues

substrate for gluconeogenesis

1. loctate
2. pyruvate
3. glycerol, from catabolisms of triacylglycerol
4. e-ketoacids, from catabolism of glucogenic aa

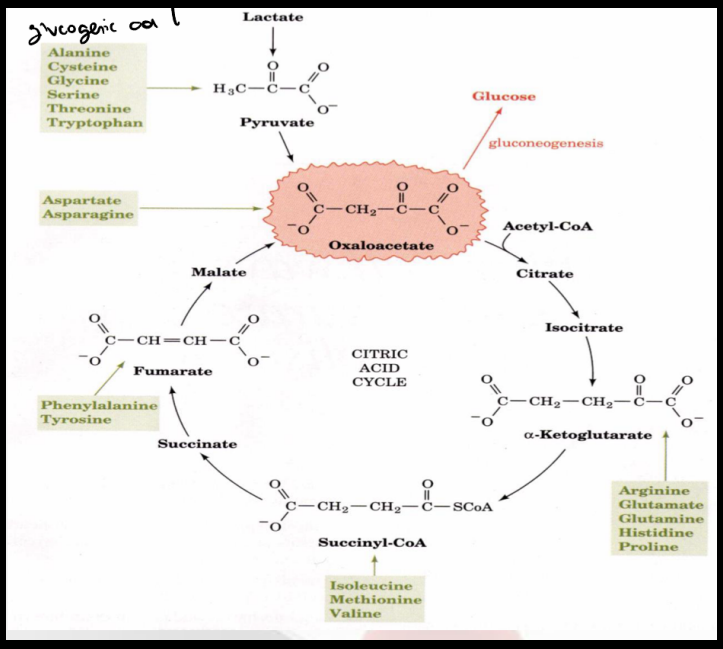
1) Loctate as a substrate



→ THE CORI CYCLE

→ loctate formed during strenuous exercise and the tissue lacking mitochondria

④ Amino acids as a substrate

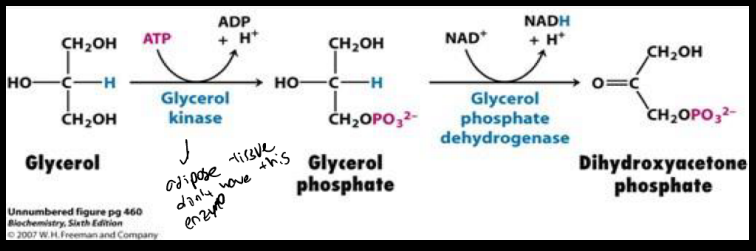


→ glucogenic aa converted into glucose

→ ketogenic aa converted into ketone bodies

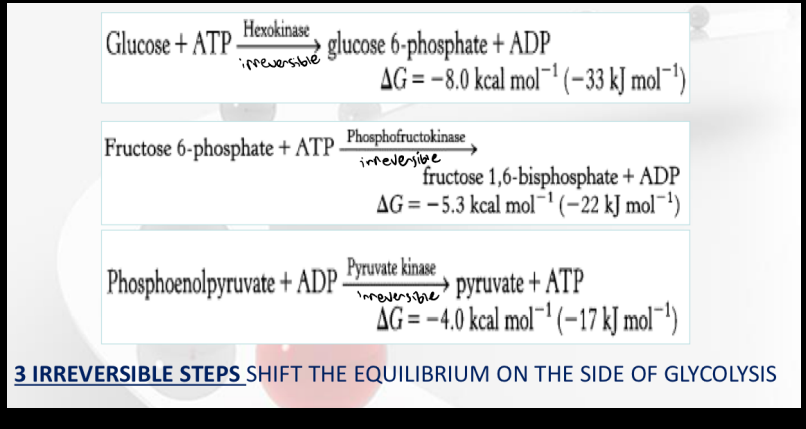
→ the source of pyruvate and oxaloacetate for gluconeogenesis is mainly aa catabolism

③ Glycerol as a substrate



→ source of glycerol hydrolysis of triacylglycerols in adipose tissues

→ adipose tissues lack enzyme glycerol kinase.



→ this three steps are irreversible in glycolysis

! in gluconeogenesis three major barries are bypassed by successive steps.

Successive Steps in order

Step ① PYRUVATE CARBOXYLASE

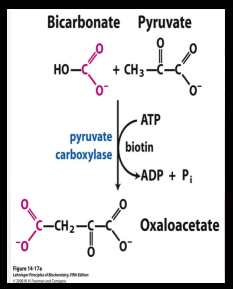
Bicarbonate + Pyruvate + CO_2 + H_2O ⟶ Oxaloacetate

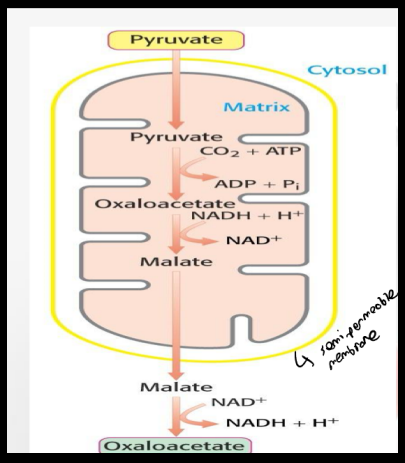
pyruvate carboxylase

ATP → ADP

biotin

in mitochondrial matrix



! 

→ Oxaloacetate can't pass out of the mitochondria it is converted to malate

Step ② PEP CARBOXYKINASE

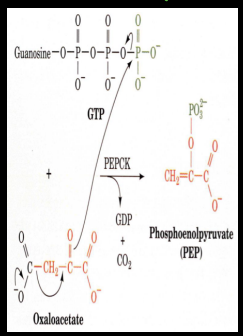
Oxaloacetate ⟶ Phophoenolpyruvate + CO_2

PEPCK

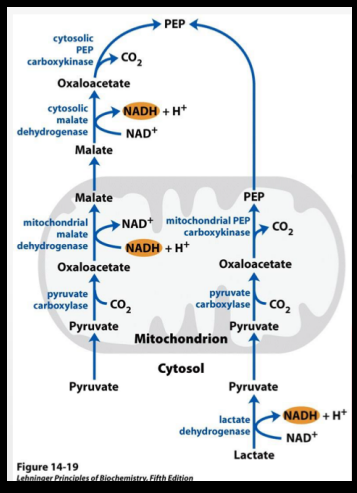
GTP → GDP

in the cytosol

reversible



! Alternative pathway



→ Cytosolic NADH is generated in LDH reaction and not have to be shuttled out of the mitochondrion.

Step (3) FRUCTOSE 1,6 - BISPHOSPHATASE

Fructose 1,6 bisphosphate $+H_2O$ → Fructose - 6 phospate $+P_i$

Fructose 1,6 bisphosphatase

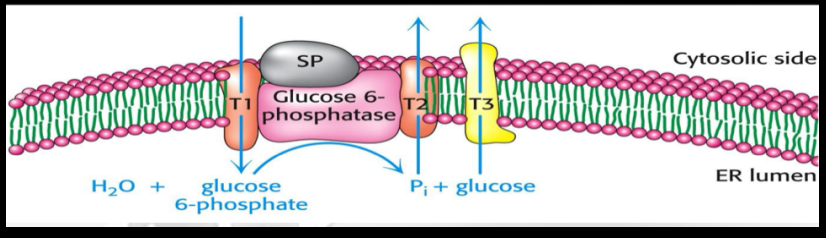
Irreversible

- Mg^{+2} dependent enzyme
- present in liver kidney skeletal muscle
  absent from heart and smooth muscle

Step (4) GLUCOSE 6 - PHOSPHATASE

Glucose 6 phosphate $+H_2O$ → Glucose $+P_i$

- not occur in cytoplasm transported into the lumen of the endoplasmic reticulum.



T_1 - transport glucose 6 phosphate into the lumen of ER

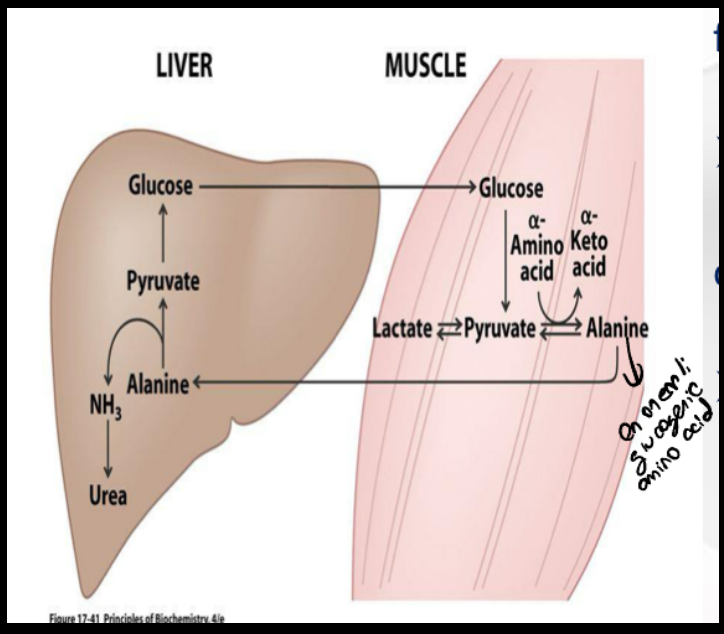
T_2 - transport P_i to cytosol

T_3 - transport glucose to the cytosol

T_4 - Ca^{+2} binding protein → stobilizing protein essential for phosphato activity

* Just found on liver and lesser extent kidney

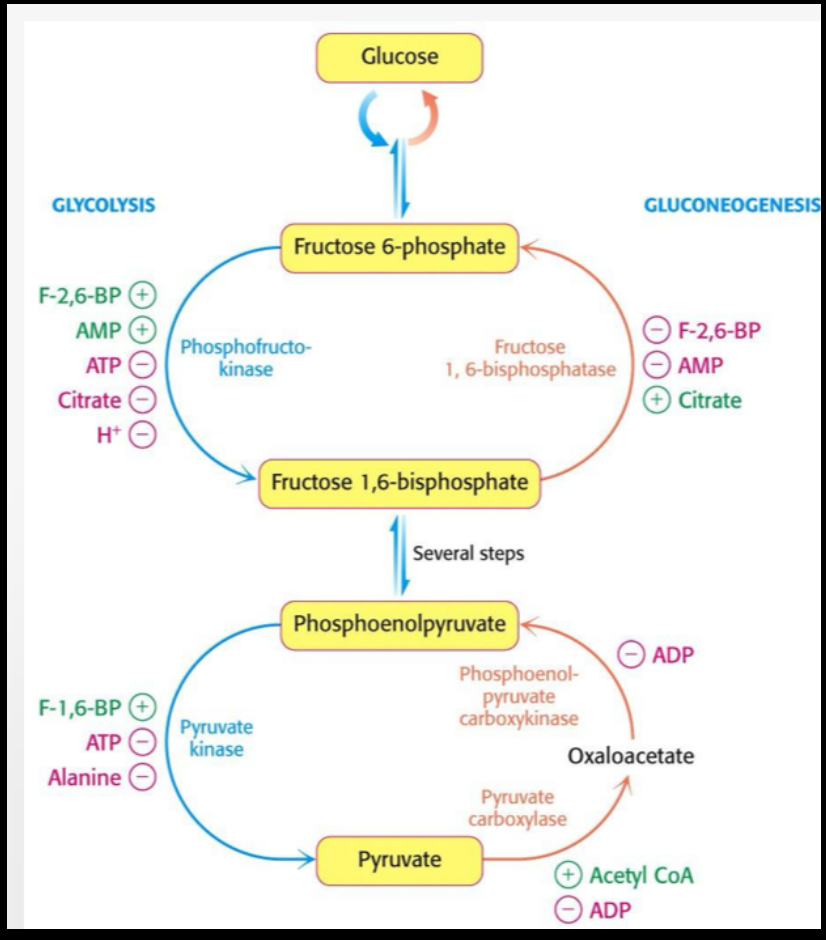
An Extra - Glucose - alanine cycle



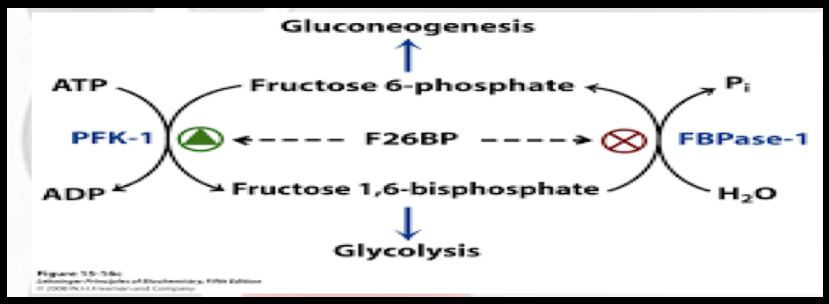
→ alanine produced by transamination
↳ transfer of one αα group one molecule to another

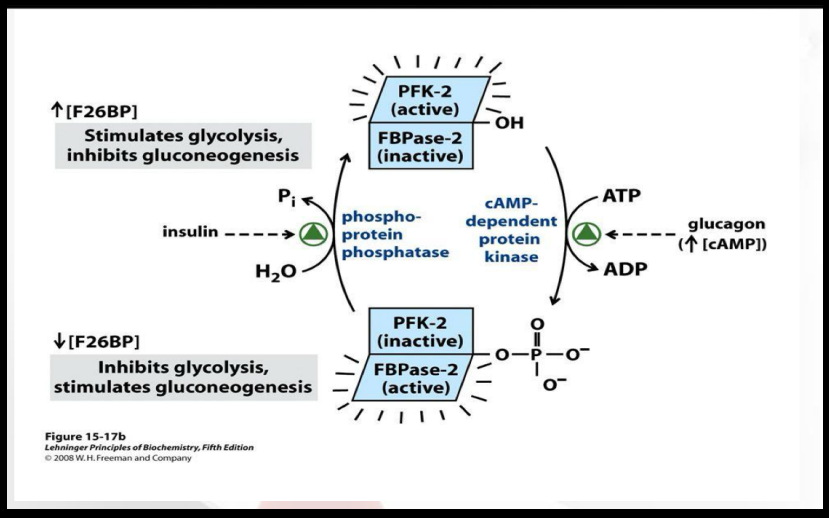
→ in active muscle lactate used in this way

Regulation of Gluconeogenesis



allosteric regulation of gluconeogenesis.





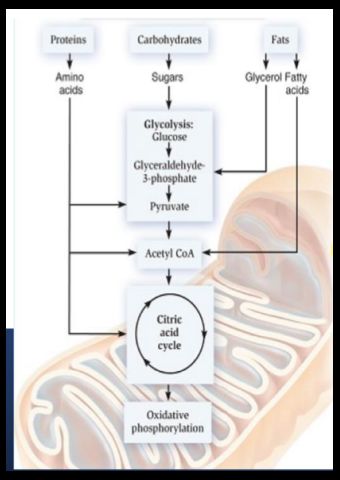
! F2,6-BP formed catolyzed by (PFK-2) phospho fructo kinase 2

! hydrolyzed F-6-BP by Fructose Bisphosphotase (FB Base -2

- F2,6-BP binds to allosteric site on PFK1 increase affinity for F6-P, reduces affinity for allosteric inhibitors ATP and citrate

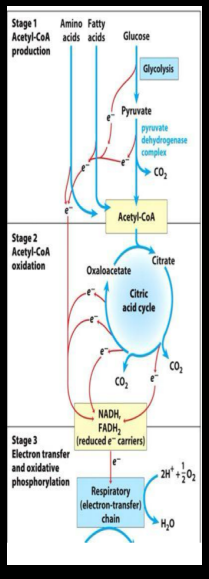
- PFK-1 inactive in the absence of F2,6-BP
- F2,6 BP activates PFK-1 → stimulate glycolysis
- F2,6 BP inhibits FBPASE-1 → slow gluconeogenesis,

Krebs Cycle



general info

- consume O_2, produce CO_2
- captures energy stored in lipids and aa.
- acetyl coA obtained from diverse sources
- intermediates can be used to synthesize different compounds

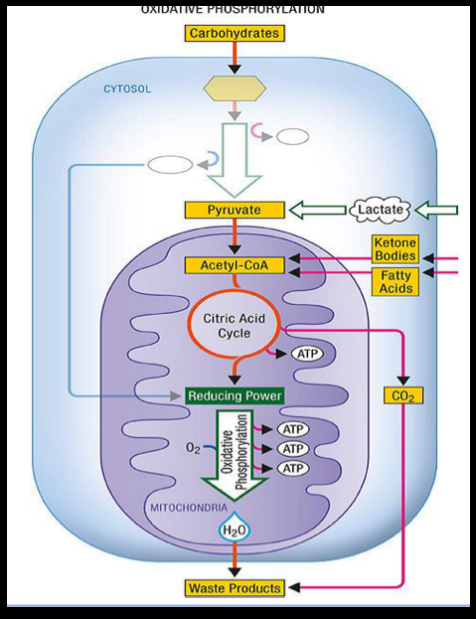


steps of krebs cycle

1- Acetyl CoA production (from organic fuels)

2- Acetyl CoA oxidation (in TAC to produce CO_2)

3- Electron transfer and oxidative phosphorylation (give their e^-'s to O_2 forming ATP)



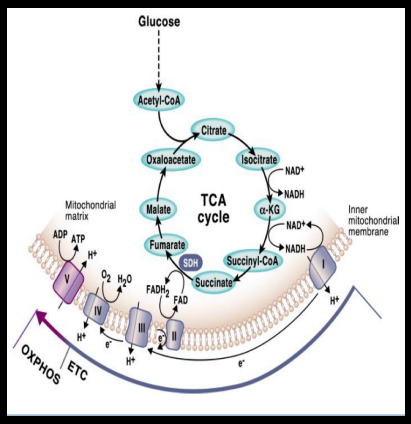
location

1- Glycolysis in cytoplasma

2- TCA cycle in mitochon. matrix

3- Just succinate dehydrogenase in mitochondrial inner membrane

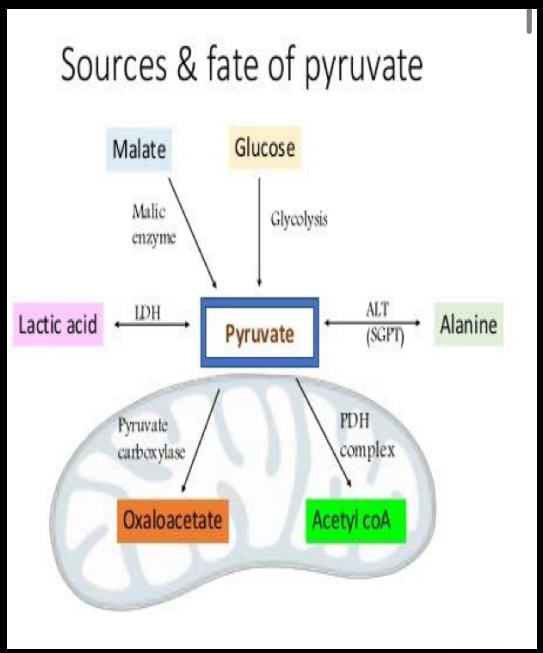
4- Oxidative phosphorylation in inner membrone



by a series of reactions

- a number of reducing equivalents are removed

↳ oxidized to water in respiratory chain



fate of pyruvate

oxidative decarboxylation

① ⟶ acetil CoA

② +2H+ ⟶ lactate (anaerobic)

③ +NH3+ ⟶ alanine (aa synt.)

④ CO_2 ⟶ oxaloacetate (gluconeogenesis)

alcoholic fermentation

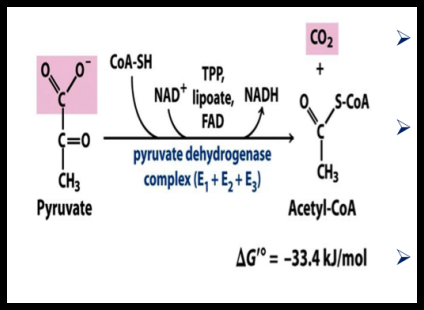
⑤ ⟶ ethanol + CO_2

① Pyruvate to Acetil CoA

pyruvate ⟶ (oxidative decarboxylation) ⟶ Acetil CoA + CO_2

pyruvate dehydrogenase complex ($E_1 + E_2 + E_3$)

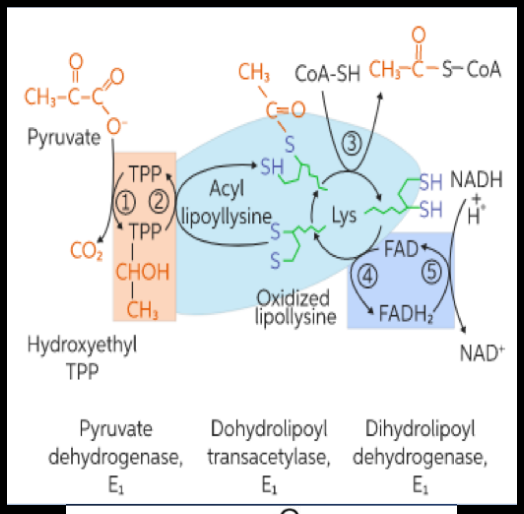
$NAD^+ \longrightarrow NADH$

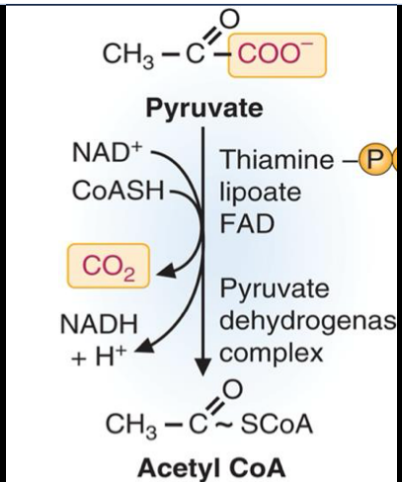


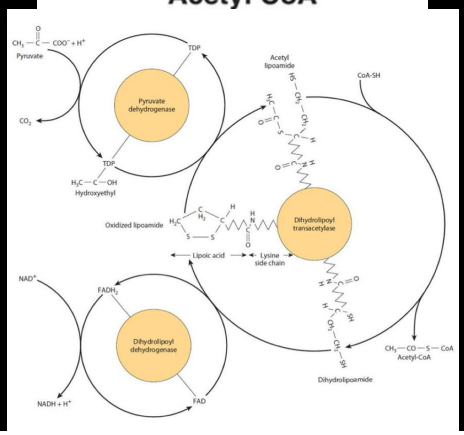
⟶ pyruvate transported mitochon. by a proton symporter

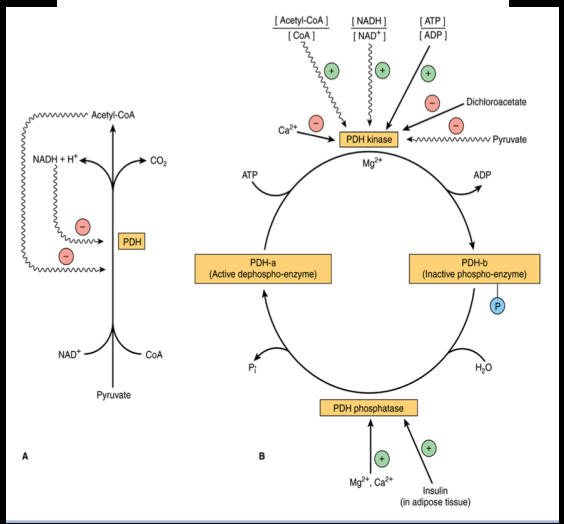
⟶ decarboxylated by PDH to form acetyl CoA

⟶ inneversible reaction









PDH complex

1- Pyruvate dehydrogenase
2- Dihydrolipoly transacetylase
3- Dihydrolipoly dehydrogenase

PDH requires 5 coenzymes

→ prosthetic groups = TBP, lipoate FAD
→ co-substrates = NAD+, CoA-SH

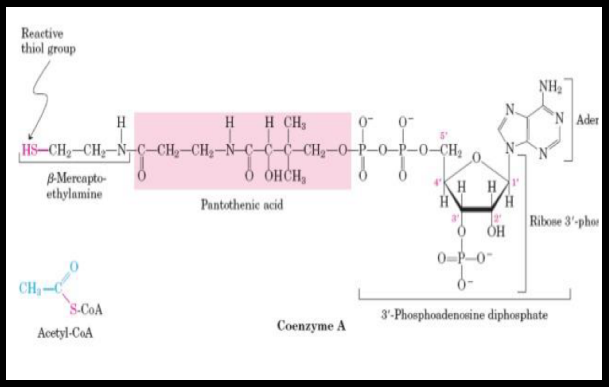
TPP - Thiomine (B_1)
FAD - Riboflavin (B_2)
NAD - Niacin (B_3)
CoA - Panthothenic acid (B_5)

How it works

→ lipoic acid join by an amide link to enzyme complex
→ it forms a long flexible arm to rotate btw active sites of enzymes

Regulation of PDH

→ inhibited by Acetyl-CoA and NADH
→ PDH kinase - phosphorylated ↳ inactive
PDH Phosphatase - dephos. ↳ active
→ inhibited by ATP



An Extra = Structure of CoA

→ associate, complete function, disso-

→ function: accept and carry acetyl groups

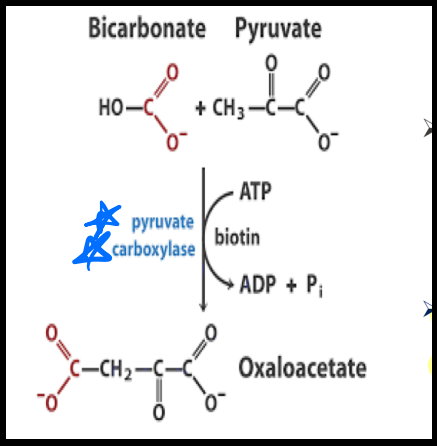
→ thioesters: high acyl group transfer potential

② Pyruvate to lactate

pyruvate $\xrightarrow[\text{lactate dehydrogenase}]{NADH \rightarrow NAD}$ lactate

! regeneration of NAD sustains the continued glycolysis under anaerobic conditions

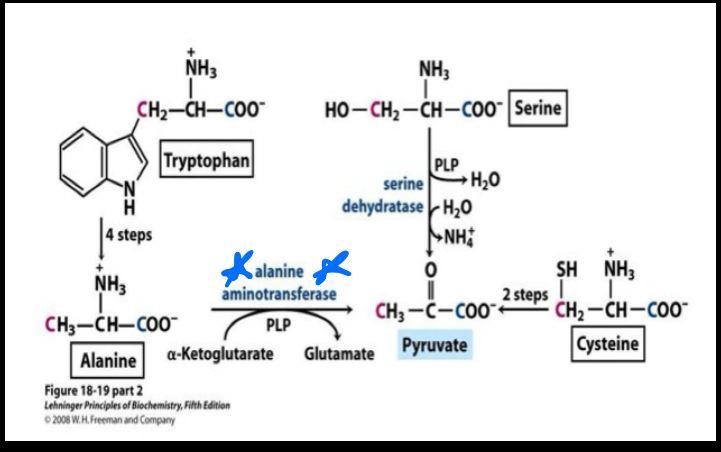
③ Pyruvate to oxaloacetate



→ biotin is coenzyme

→ oxaloacetate used for synthesis of: aspartate, phosphoenolpyruvate or utilized in TAC

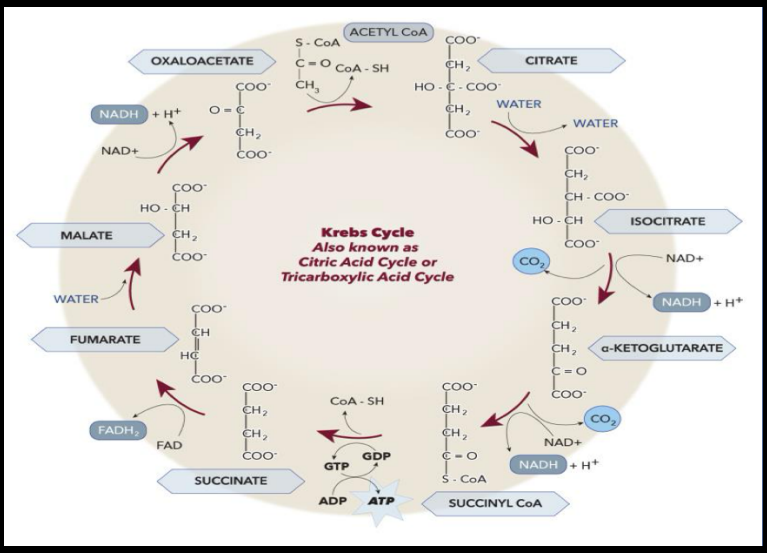
④ Pyruvate to Alanine



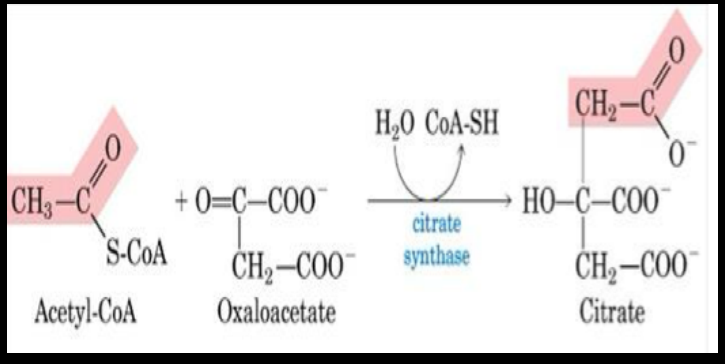
→ transsomination

→ important for catabolism and synthesis of non-essential aa.

Krebs Cycle Step by Step



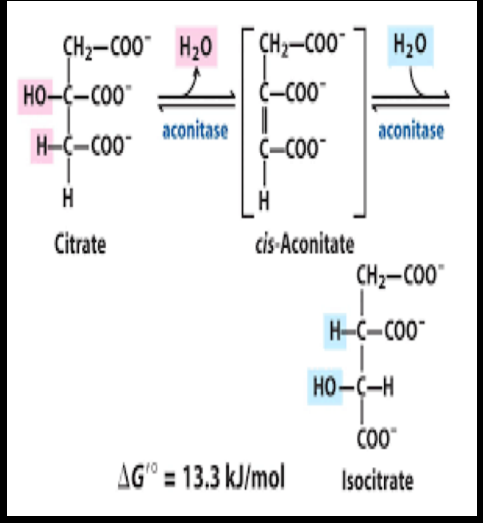
Step ① Citrate Synthase



- uses acid / base catalysis
  - ↳ ① carbonyl of oxaloacetate is good electrophile
  - ② methyl group converted to methylene

- activity largely depends on oxaloacetate.
- irreversible

Step ② Aconitase



- isomeration by dehydration
- two steps → ① dehydration cis aconitate
  → ② rehydration isocitrate

- this asymmetric behavior provides Citrate in the cytosol as a source of acetyl CoA for fatty acid synthe.

Aconitose extras:

- water removal from citrate addition to cis aconitate catalyzed by iron-sulfur center
  - ↳ function as electron carrier
  - ↳ act both substrate bindin catalyzing
- when Fe is deficient, aconitose loses its FeS center acquire new role in Fe homeostasis

Cytosolic Aconitose a regulator of protein synthesis

transferrin carries Fe in blood (-Fe)

transferrin receptor receive, endocytoses Fe

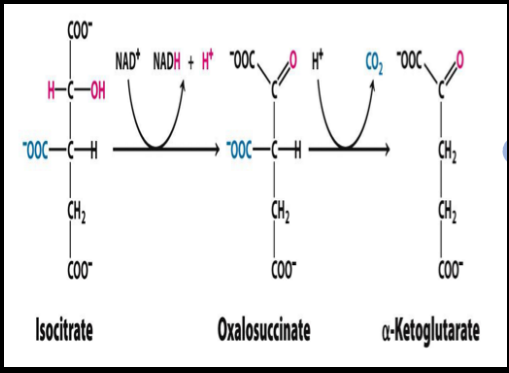
ferritin stores excess Fe in the cell

apoaconitose regulates protein levels by stabilize or unstabilize the mRNA of transferrin receptor or ferritin

! fluoroacetate → strong inhibitor of aconitose

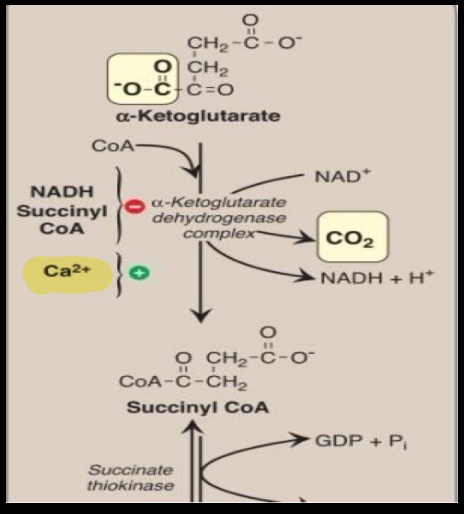
- fluoroacetyl - CoA condenses with oxaloacetate to form fluorocitrate, which inhibits aconitose, cause citrate accumulate.
- anticancer agents, industrial chemicals (pesticides)

Step ③ Isocitrate Dehydrogenase



- CO_2 generated
- irreversible

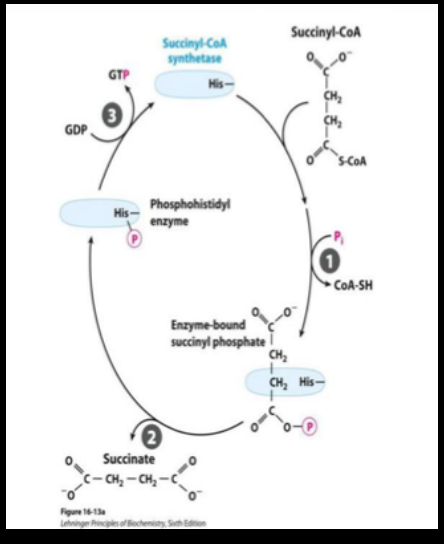
Step ④ α-ketoglurate Dehydrogenase Complex



- net full oxidation of all carbons of glucose
- irreversible

e ketoglutorate dehydrogenase comp.

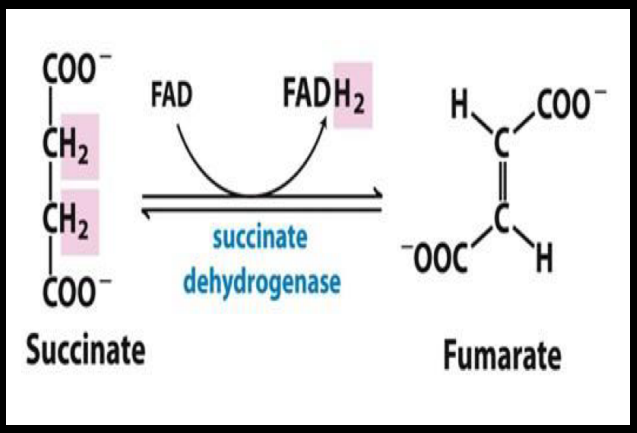
- thiomin disphosphate, lipoate, NAD+, FAD and CoA → same as PDH comp.



substrate level phosphonilation

- Succinly coA → high energy thioester bond
- this bond allows for incorporation of inorganic phosphate into ADP or GDP
- goes through phospho enzyme intermediate
- produces GTP, converted ATP directly ATP
- reversible

Step (5) Succinate Dehydrogenase

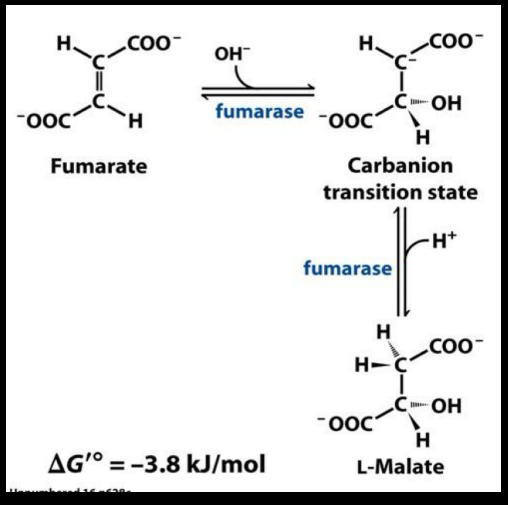


Succinate dehydrogenase

- flavoprotein
- bind to mitochondrial inner membrane
- three different iron - sulfur cluster and FAD

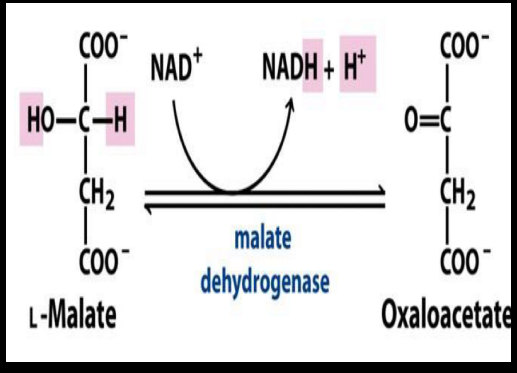
- Electron pass from succinate through the FAD and iron sulfur center before entering ETS.

Step (6) Fumarase



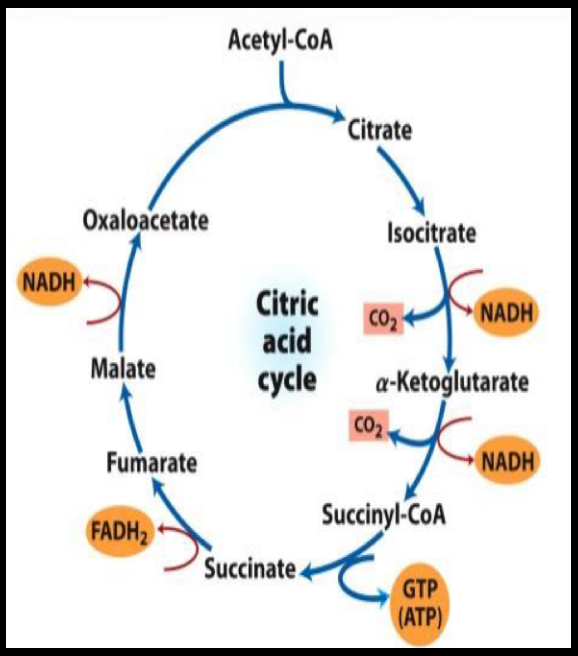
- addition of water is always trans, forms L-malate
- cannot work on malate

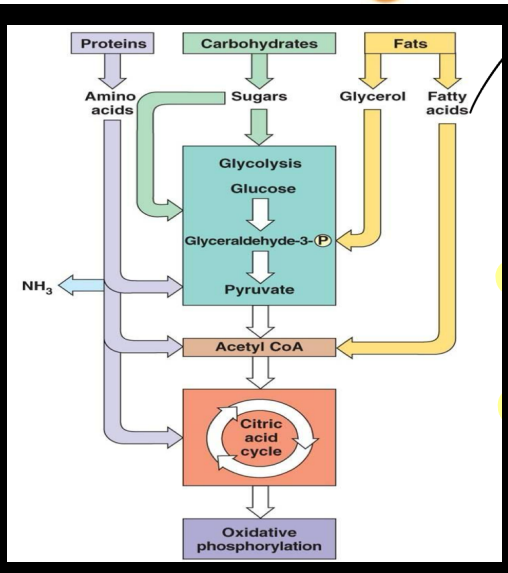
Step (7) Malate Dehydrogenase

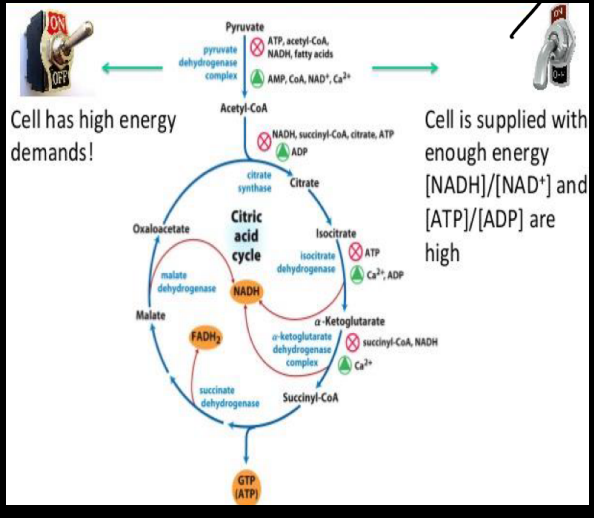


- regenerates oxaloacetate
- oxaloacetate concentration kept very low by citrate synthase

Overview to Krebs Cycle







- net oxidations of two carbons to CO_2
- generates 1 GTP
- 3 NADH, 1 $FADH_2$ generated
- the efficiency of oxidation of glucose is nearly 40%

importance of it

① final catabolic pathway for carbohydrates, lipids and protein

② glucose, fatty acids and many amino acids can be synthesized from intermediates

③ Capture of energy as ATP

regulation of it

1- regulatory enzyme → inactive in the absence of acetyl coA

2- more acetyl coA, more activity

irreversible steps

PDH, citrate synthase, IDH, α-KDH

inhibitors: NADH, ATP

activators: NAD, AMP

* Co^{+2} in muscles activates cycle

Direct and Indirect ATP Yield

TABLE 16–1 Stoichiometry of Coenzyme Reduction and ATP Formation in the Aerobic Oxidation of Glucose via Glycolysis, the Pyruvate Dehydrogenase Complex Reaction, the Citric Acid Cycle, and Oxidative Phosphorylation

Reaction	Number of ATP or reduced coenzyme directly formed	Number of ATP ultimately formed*
Glucose → glucose 6-phosphate	−1 ATP	−1
Fructose 6-phosphate → fructose 1,6-bisphosphate	−1 ATP	−1
2 Glyceraldehyde 3-phosphate → 2 1,3-bisphosphoglycerate	2 NADH	3 or 5†
2 1,3-Bisphosphoglycerate → 2 3-phosphoglycerate	2 ATP	2
2 Phosphoenolpyruvate → 2 pyruvate	2 ATP	2
2 Pyruvate → 2 acetyl-CoA	2 NADH	5
2 Isocitrate → 2 α-ketoglutarate	2 NADH	5
2 α-Ketoglutarate → 2 succinyl-CoA	2 NADH	5
2 Succinyl-CoA → 2 succinate	2 ATP (or 2 GTP)	2
2 Succinate → 2 fumarate	2 $FADH_2$	3
2 Malate → 2 oxaloacetate	2 NADH	5
Total		30–32

*This is calculated as 2.5 ATP per NADH and 1.5 ATP per $FADH_2$. A negative value indicates consumption.

†This number is either 3 or 5, depending on the mechanism used to shuttle NADH equivalents from the cytosol to the mitochondrial matrix; see Figures 19–30 and 19–31.

Table 16-1
Lehninger Principles of Biochemistry, Sixth Edition
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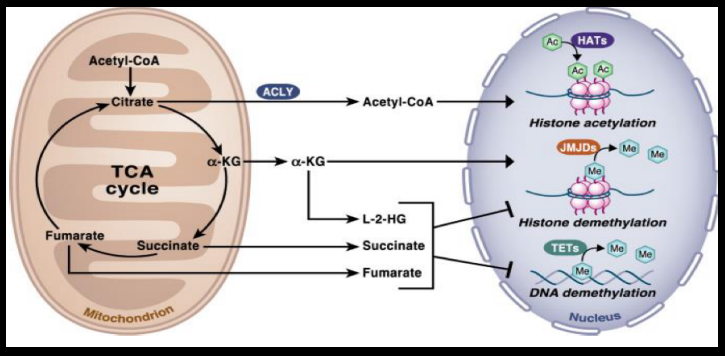
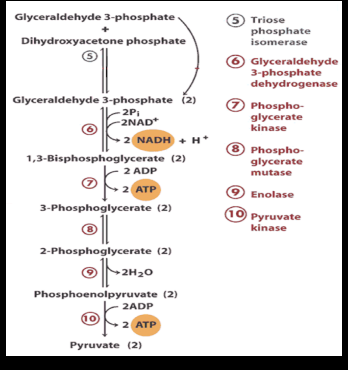
New Roles for TCA cycle intermediates



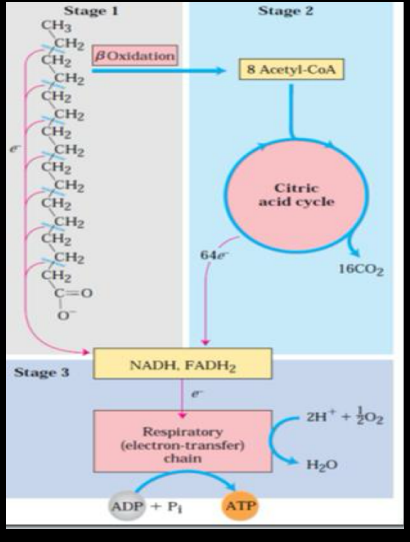
As a signaling molecules
↳ controlling chromatin modifica. DNA methylation, the hypoxic response and immunity

Catabolic roles



Carbonhydrates

all the carbonhydrates can be converted into glucose by glycolytic pathway and TAC



lipids

- oxidation of fatty acids → Acetil CoA
- propionyl coA formed from fatty acids
  ↳ converted into succinyl coA
- glycerol released from lipids
  ↳ can be converted into pyruvate by glycolytic pathway

aminoacids

GLYCINE
ALANINE
SERINE
THREONINE
CYSTEINE
TRYPTOPHAN
HYDROXYPROLINE
↓
PYRUVATE

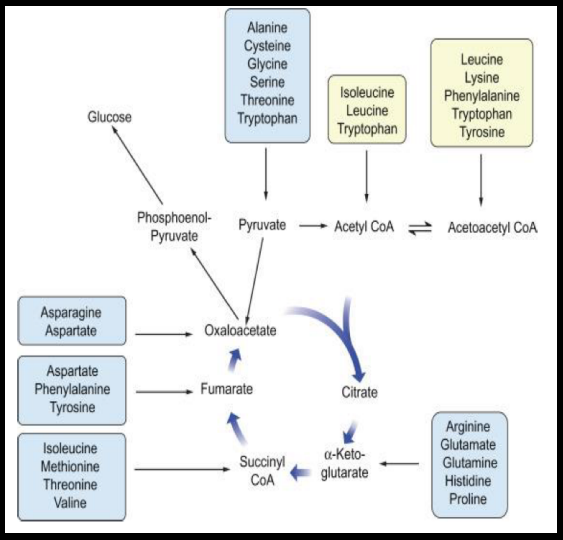
GLUTAMINE
ARGININE
HISTIDINE
PROLINE
↓
GLUTAMATE
↓
α-KETOGLUTARATE

VALINE
ISOLEUCINE
METHIONINE
↓
SUCCINYL CoA

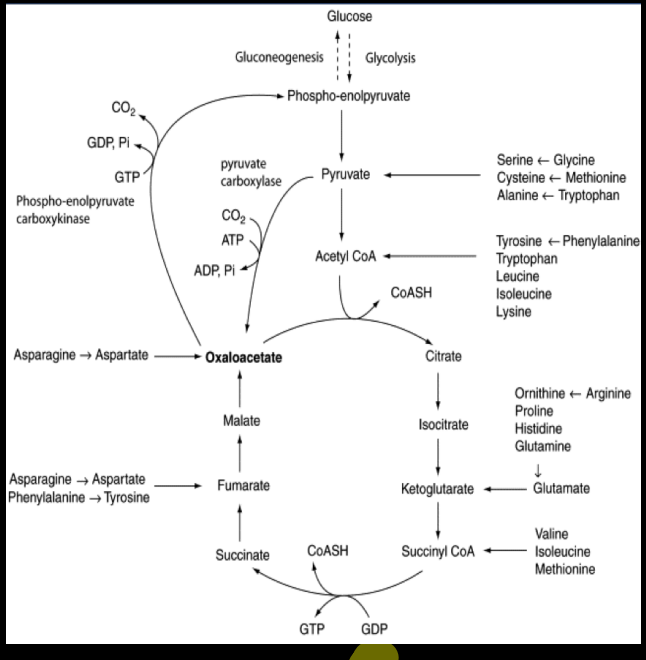
LEUCINE
LYSINE
↓
Acetyl CoA

PHENYLALANINE
TYROSINE
↓
FUMARATE

ASPARAGINE
ASPARTATE
↓
OXALOACETATE

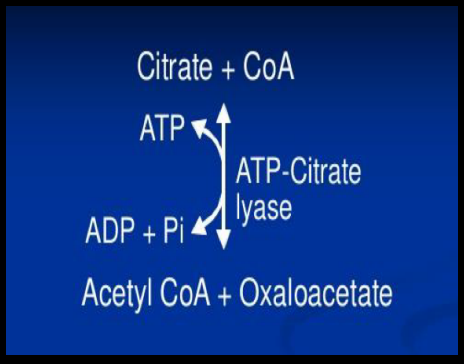


anabolic roles



(1)

- glucose, fatty acids, may be synthesized from intermediates of krebs cycle
- interconvention of nutrients
- all intermediates converted to oxaloacetate
- oxaloacetate substrate for ← gluconeogenesis to produce glucose



② • fatty acids synthesized from acetyl CoA

• acetcyl coA formed in mitochondria but fatty acids are synthesized in cytosol.

• Acetyl CoA cannot pass mitochondrial membrane but citrate can

• Acety CoA converted into citrate in mitochondria

• Citrate goes to cytosol cleaved into acetyl coA + oxaloacetate

• this way acetyl coA used for fatty acid synthesis

~~ABCA~~ Bcs krebs cycle perform both anabolic and catabolic functions → it is amphibolic pathway

Pentose Phosphate Pathway

General info: - all cell types and tissues
- in liver %30 glucose metabolized by it
- occurs in cytoplasm
- produces NADP
  - fatty acid synthesis
  - oxidative stress homeos.
  - cytchrome P450 enzymes
- not produce ATP

form NADPH, the synthesis of ribose

- happen in two state

① Oxidative nonreversible

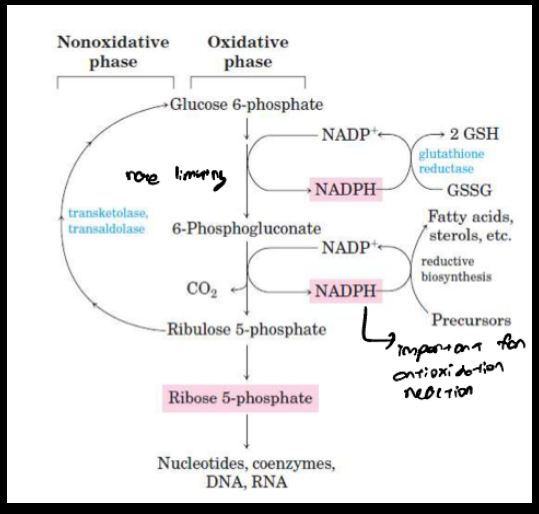
dehydrogenation and decarboxylation

- Ribolose 5- Phosphate

② Nonoxidative reversible

mainly two enzymes transketolase transaldolase

- Glucose 6- Phosphate



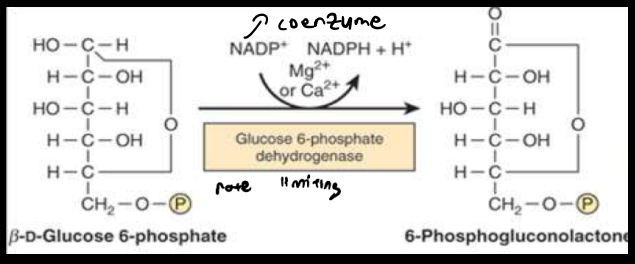
① Oxidative nonreversible

final product = ribulose 5-phosphate, CO_2, two molecules of NADPH for each molecule of glucose-6 phosphate.

important at = ① in liver and opise active in
↳ NADPH dependent synthesis of fatty acids
② in testes, ovaries, placenta adrenal cortex
↳ NADPH dependent synthesis of steroid hormons
③ in erythrocytes
↳ NADH to keep glutathione reduced

irreversible oxidative reaction

Step ① GLUCOSE 6 PHOSPHATE DEHYDRO.



Step ② ① 6-PHOSPHOGLUCONOLACTONE HYDROLASE
② 6-PHOSPHOGLUCONATE DEHYDROGENASE

1) 6 phosphoglucolactone —①→ 6-phosphogluconate
2) 6-phosphogluconate —②→ Ribulose-5-phosphate + NADPH

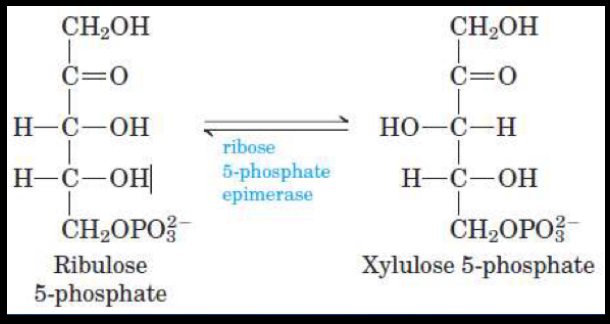
1) irreversible, not rate limiting
2) reversible, rate limiting

! regulation of G6PD → NADPH, insulin inhibits

reversible
nonoxidative reaction

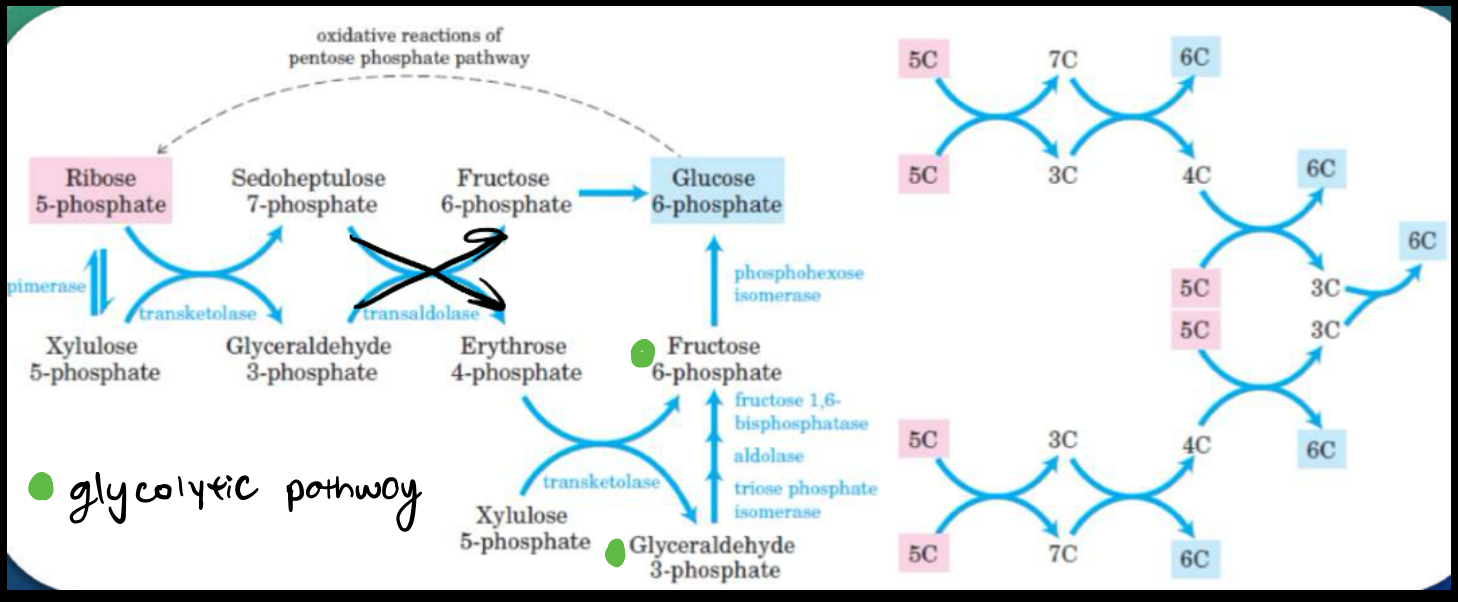
goal = permit ribulose 5-phosphate to be converted
ribose 5-phosphate or intermediate of glycolysis
(6C fructose 6-phosphate
3C glyceraldehyde 3-phosphate)

step ① RIBOSE 5-PHOSPHATE EPIMERASE



! transketolase = transfers two carbon (2C) units in thiamine pyrophosphate (TPP) requiring reaction.

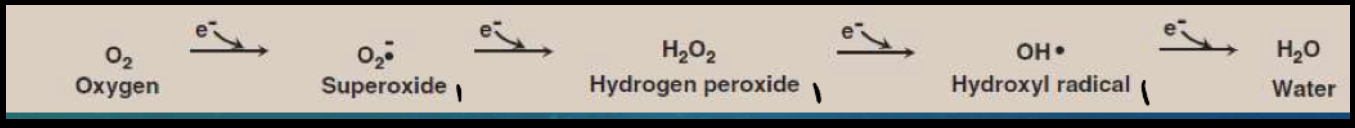
transaldolase = transfers three carbon (3C) units



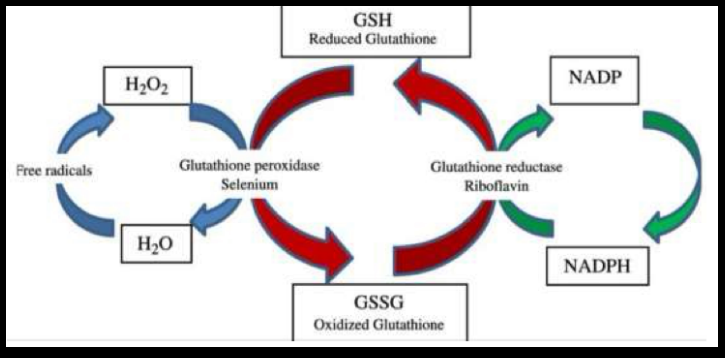
Uses of NADPH

① NADPH provides reducing power for biosynthetic rxn.
↳ NADPH - dependent biosynthesis of fatty acids and steroid hormons

② Reduction of hydrogen peroxide



- reactive oxigen intermediates → injury, cancer, aging inflammatory disease



→ the cell regenerate reduced glutathione in Glutathione Reductase using NADPH as a reducing equivalents.

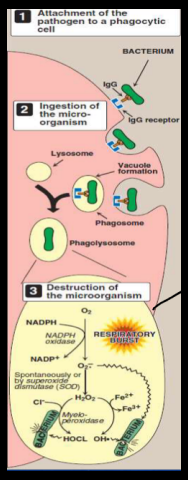
→ thus indirectly provides electrons for the reduction of hydrogen peroxide.

③ Cytochrome P450 Monooxygenase System

mitochondrial system = in steroidogenic tissues, used to hydroxlate intermediates in the conversion of cholesterol to steroid hormones

microsomal system = associated with the membranes of smooth ER → the detoxification of foreign compounds.

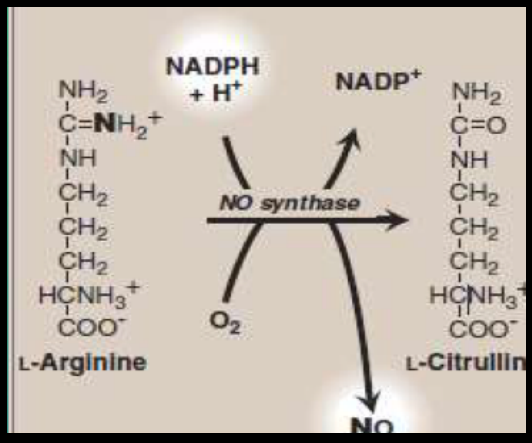
④ Phagocytosis by White Blood Cell



→ oxygen independent = use pH changes in phagolysosomes and lysosomal enzymes to destroy pathogen

→ oxygen dependent = include enzymes NADPH oxidase and myeloperoxidase (MPO) work together in killing bacteria

⑤ Synthesis of Nitric Oxide

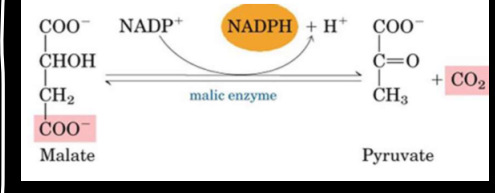


→ NO is endothelium relaxing factor causes vasodilation by relaxing vascular smooth muscle.

→ act as neurotransmitter prevent platelet aggregation plays essential role in macrophage function.

G6PD Deficiency

- inherited disease characterized by hemolytic anemia caused by the inability to detoxify oxidizing agents.
- most common enzyme abnormality
- impair ability to produce NADPH
- result in a decrease in the cellular detoxification
- treated by → oxidant drugs
  → favism (fava beans)
  → infection



↳ Alternative NADPH source