

GLICOLISI

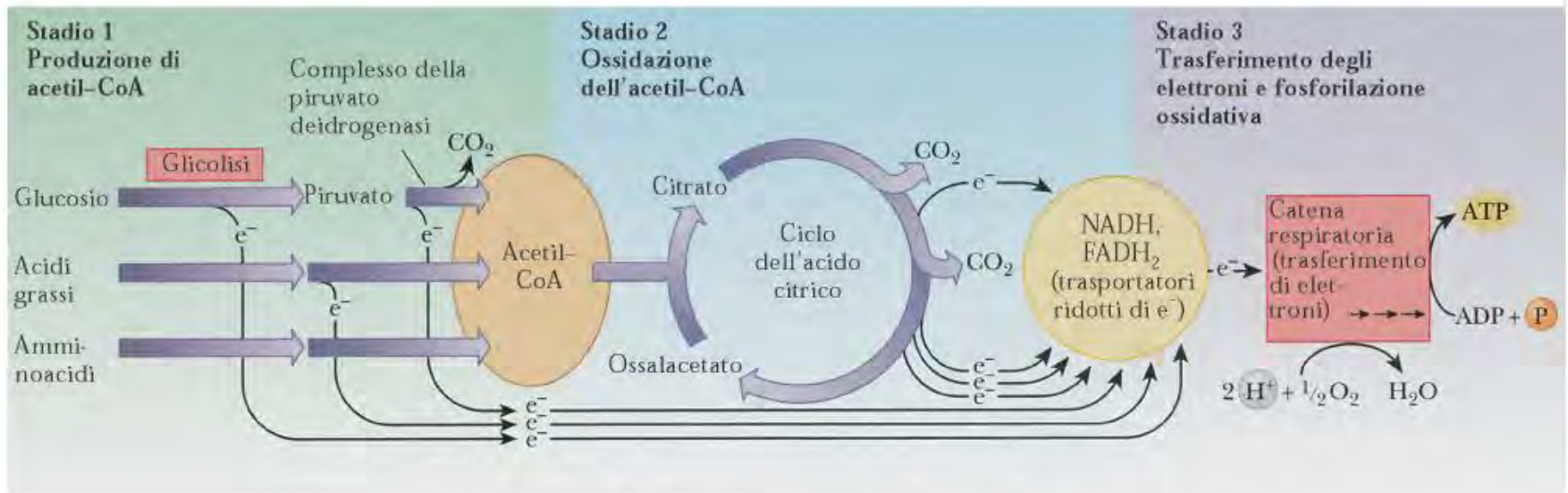
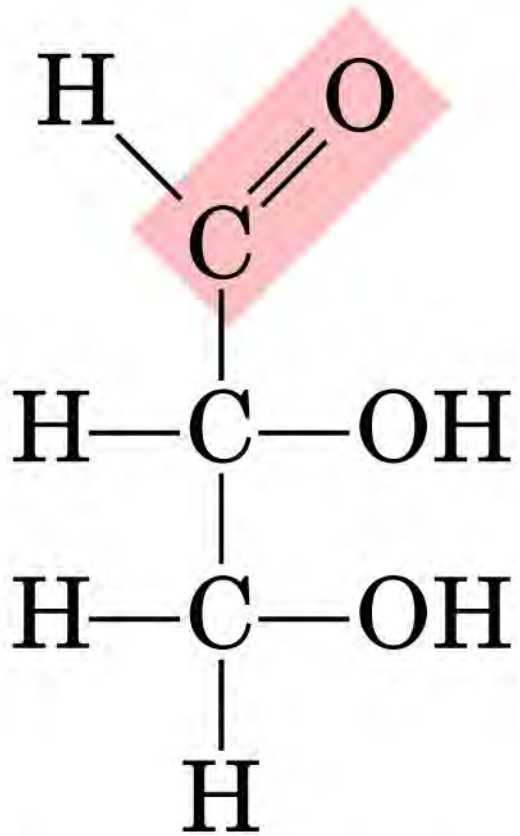
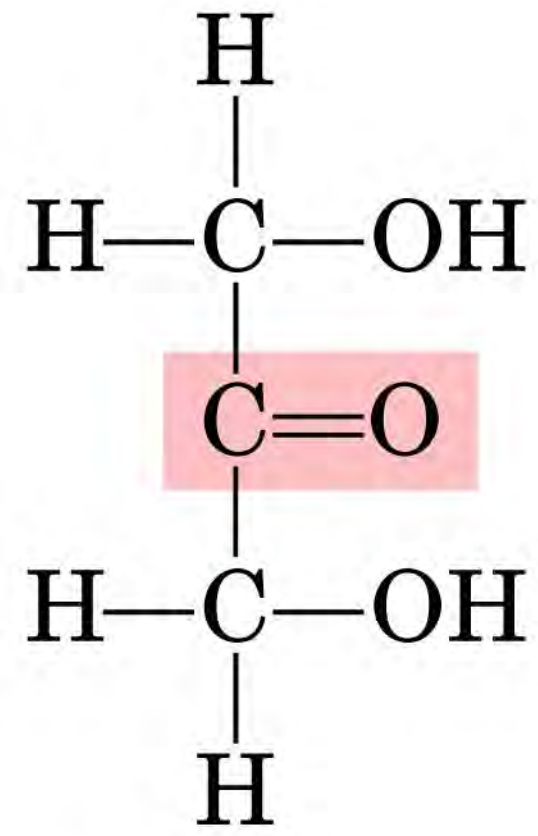


FIGURA 16.1

Il ciclo dell'acido citrico ha un ruolo centrale nel catabolismo. Gli amminoacidi, gli acidi grassi e il glucosio possono produrre tutti acetil-CoA nello stadio 1 del catabolismo. Nello stadio 2, l'acetil-CoA entra nel ciclo dell'acido citrico. Gli stadi 1 e 2 producono trasportatori di elettroni ridotti (qui mostrati come e^-). Nello stadio 3, gli elettroni entrano nella catena di trasporto degli elettroni, che produce ATP.

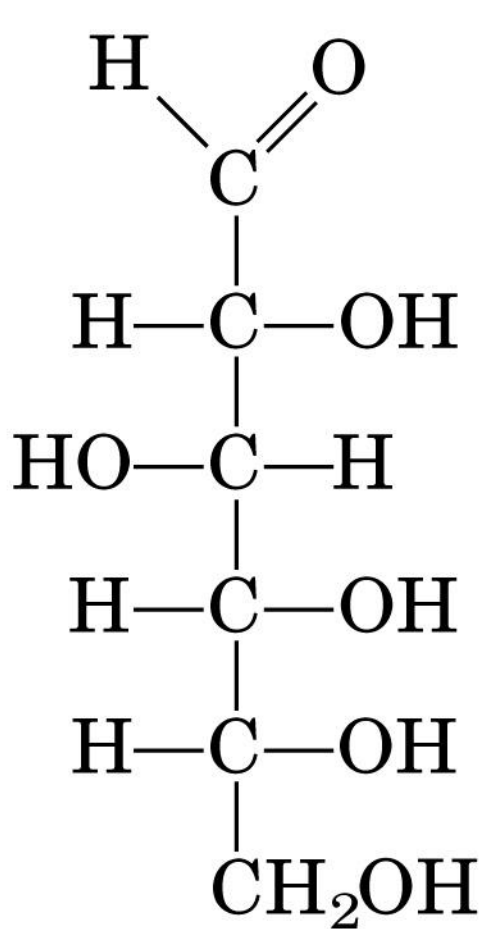


Glyceraldehyde,
an aldotriose

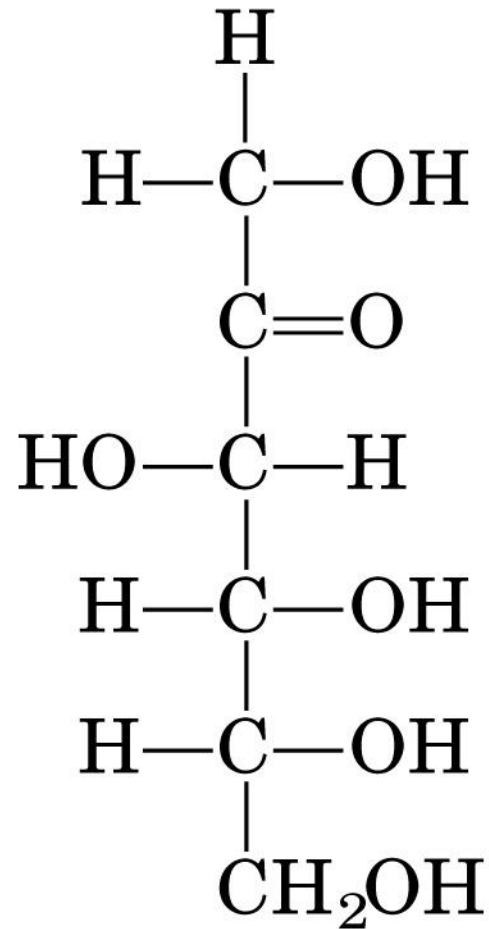


Dihydroxyacetone,
a ketotriose

(a)

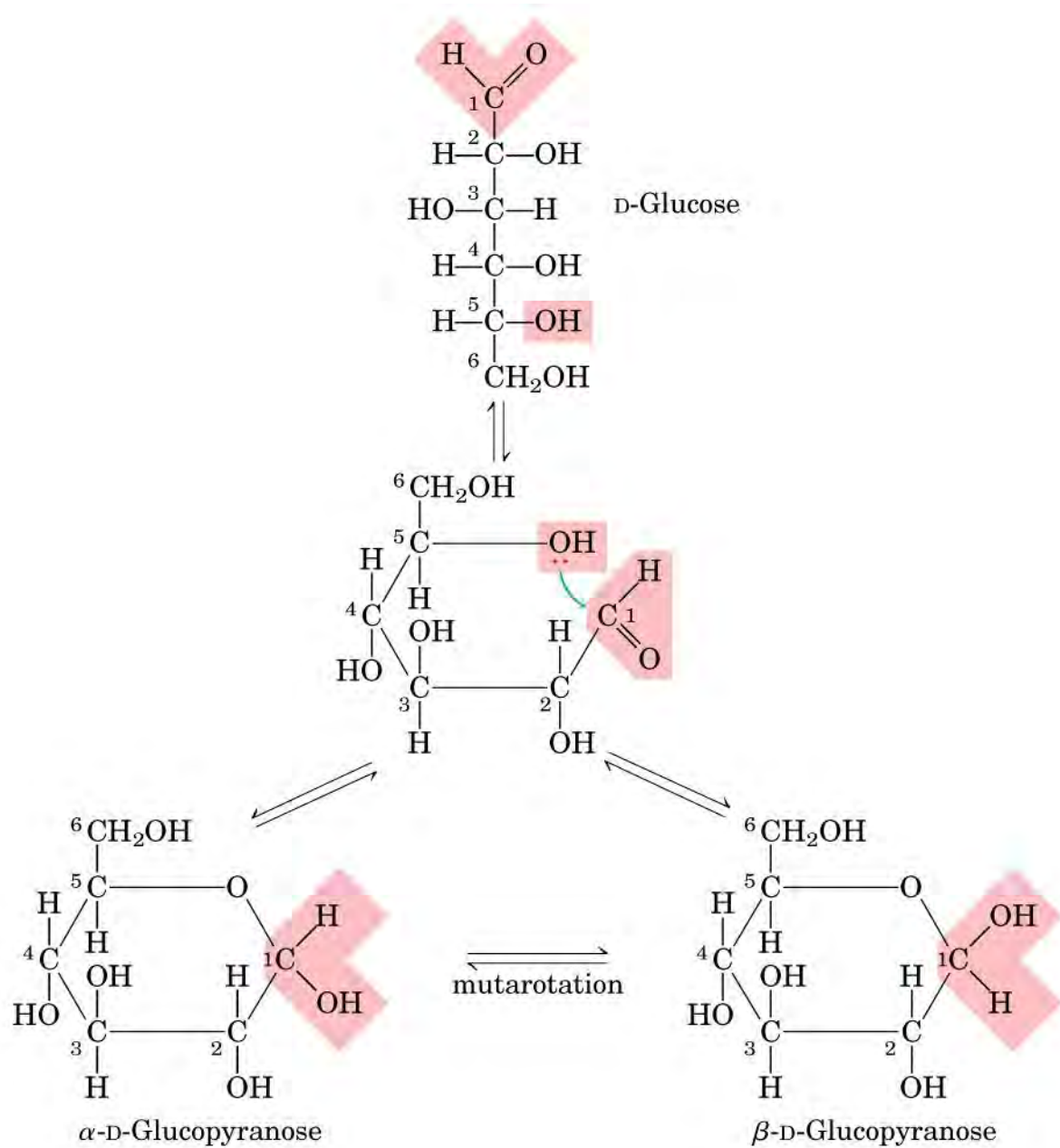


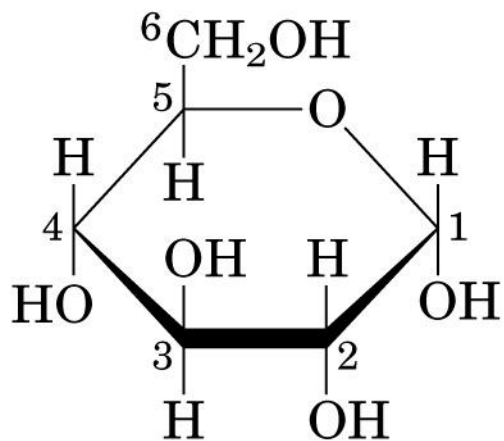
D-Glucose,
an aldohexose



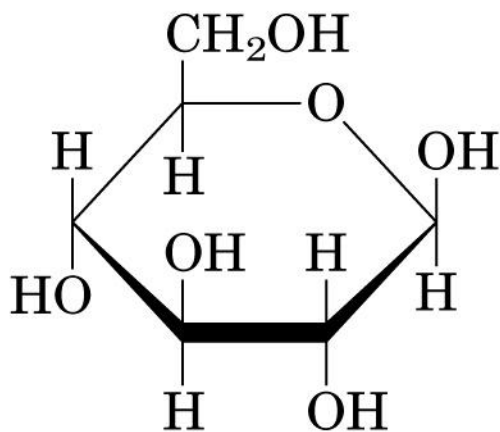
D-Fructose,
a ketohexose

(b)

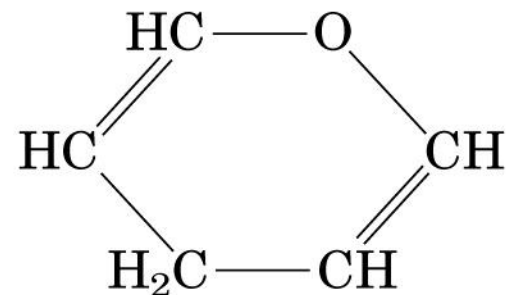




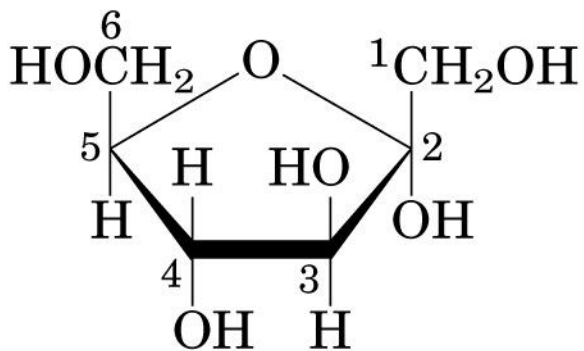
α -D-Glucopyranose



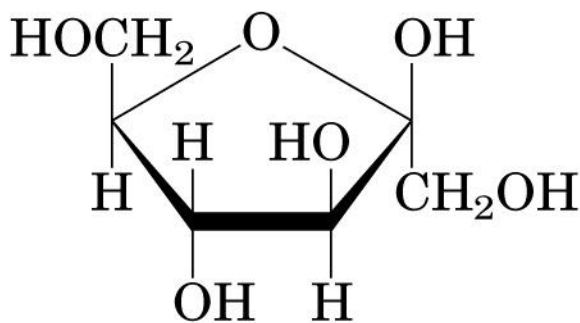
β -D-Glucopyranose



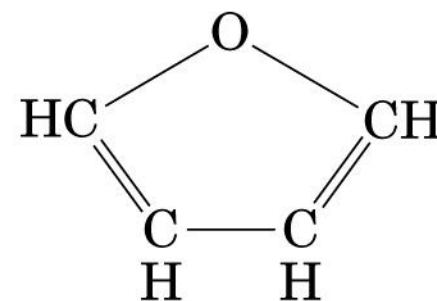
Pyran



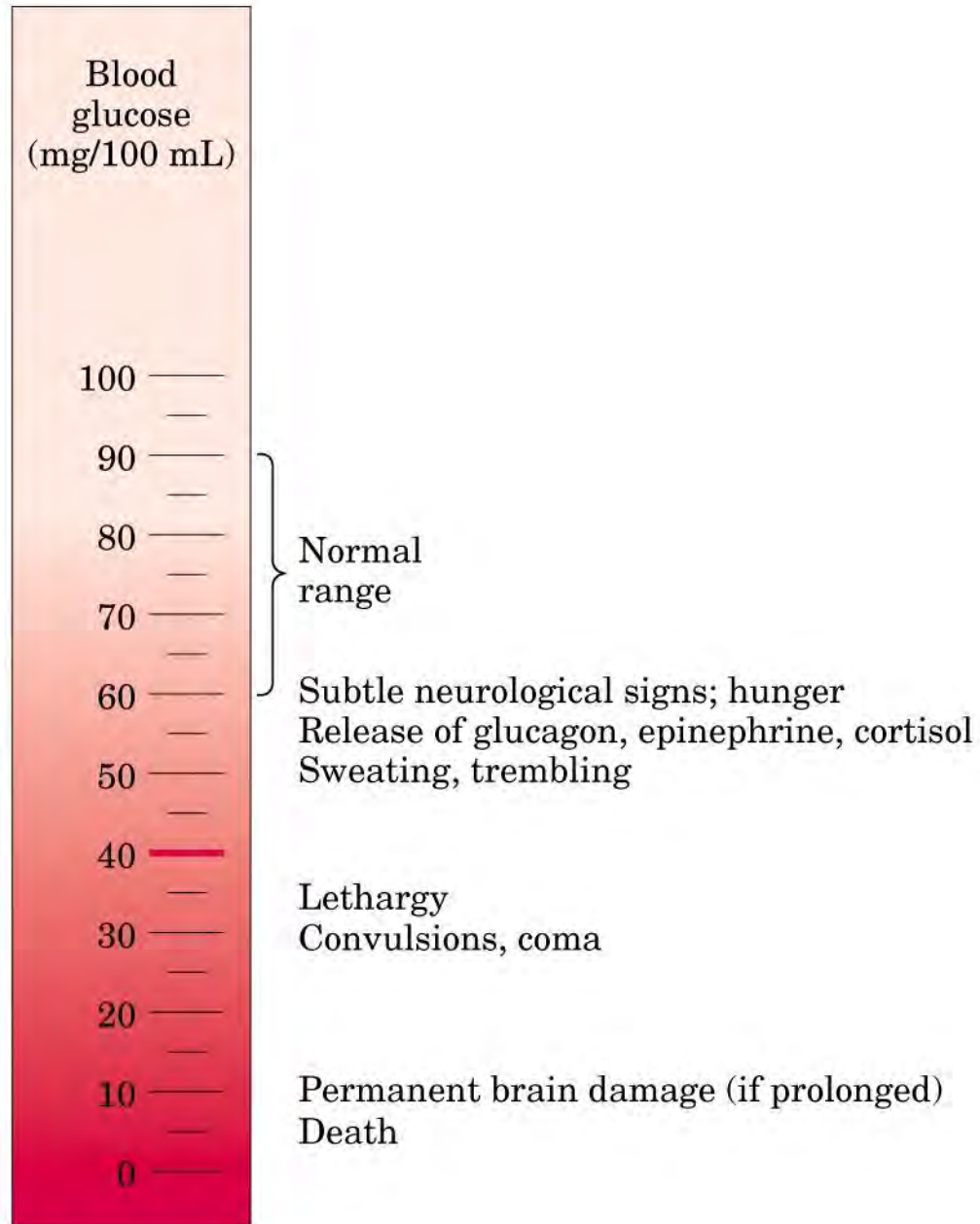
α -D-Fructofuranose

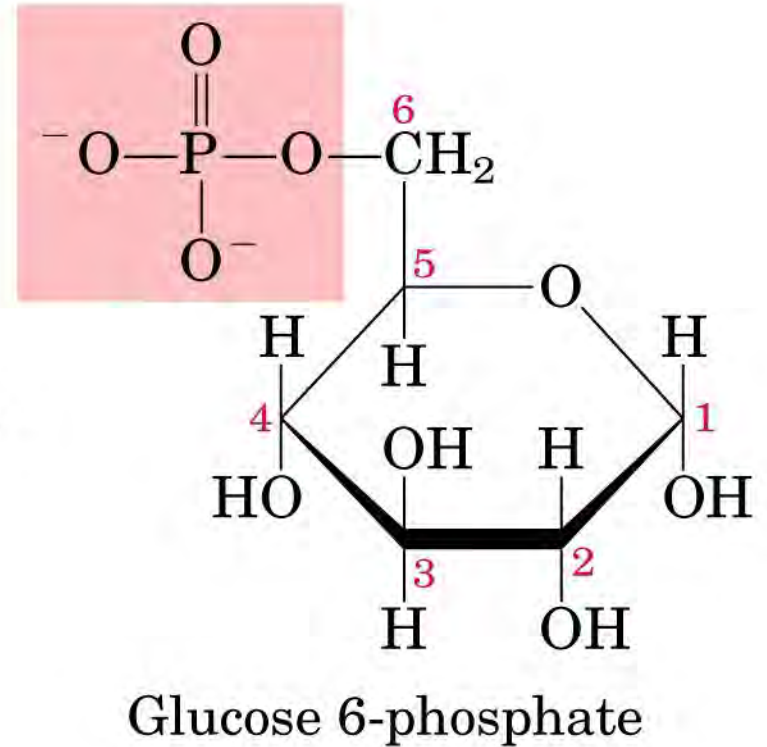
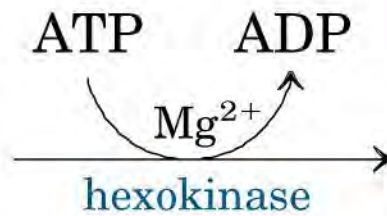
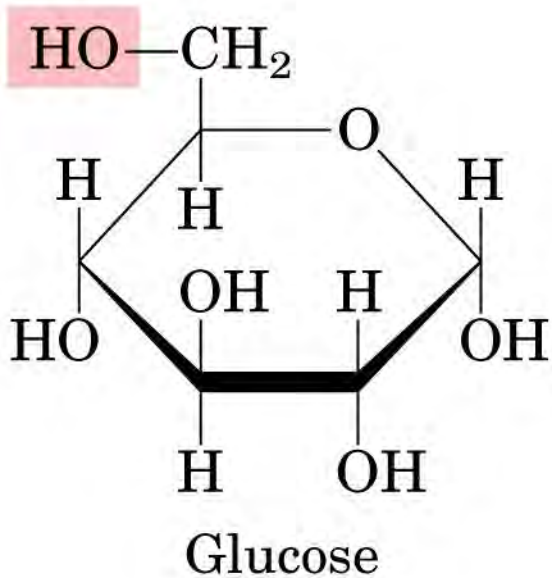


β -D-Fructofuranose

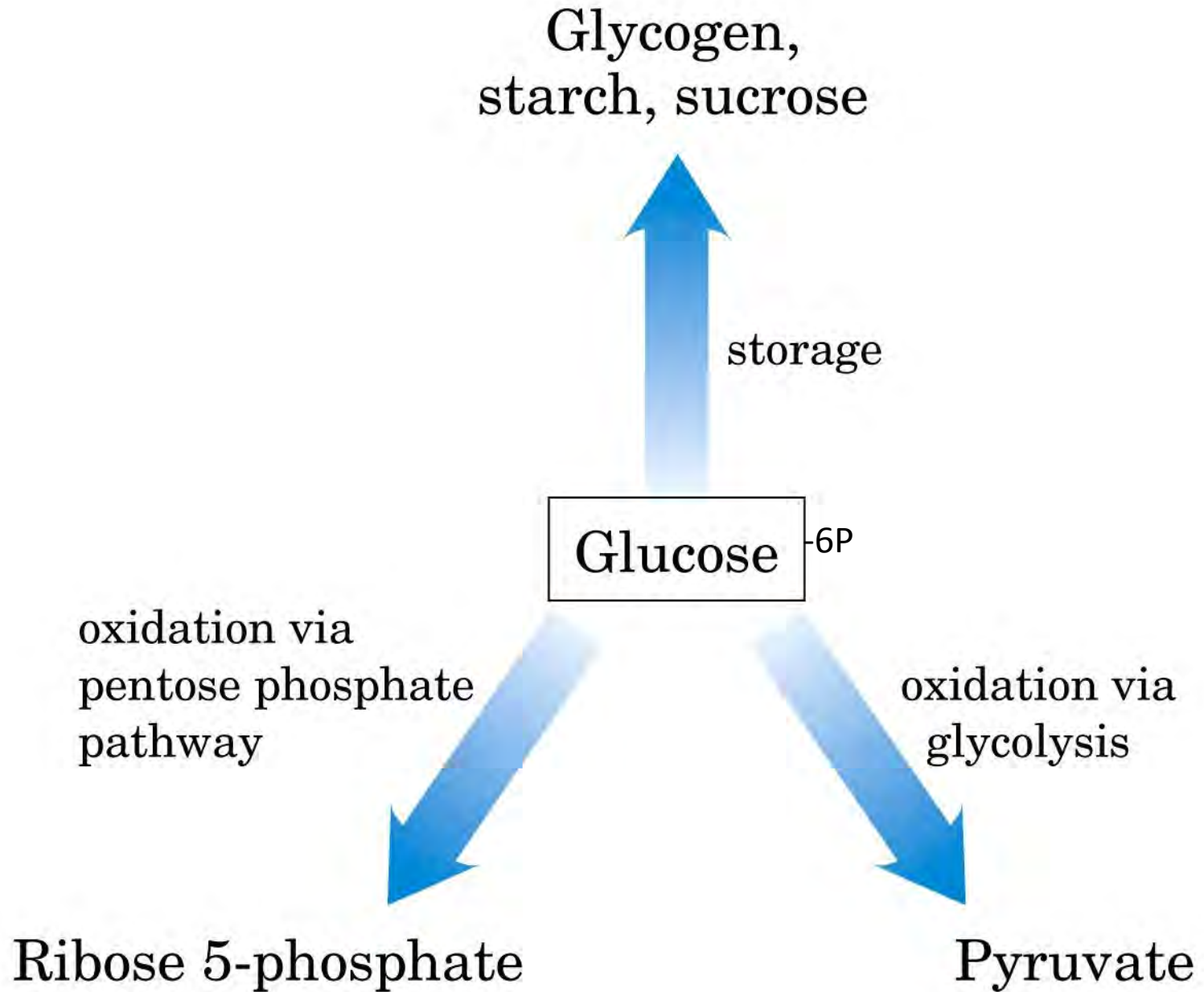


Furan



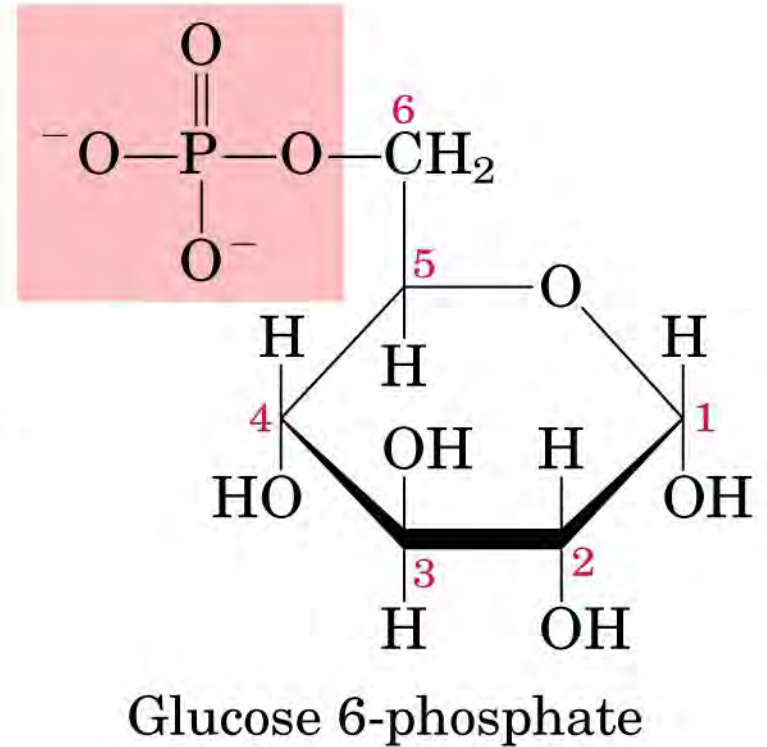
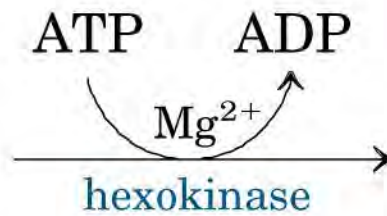
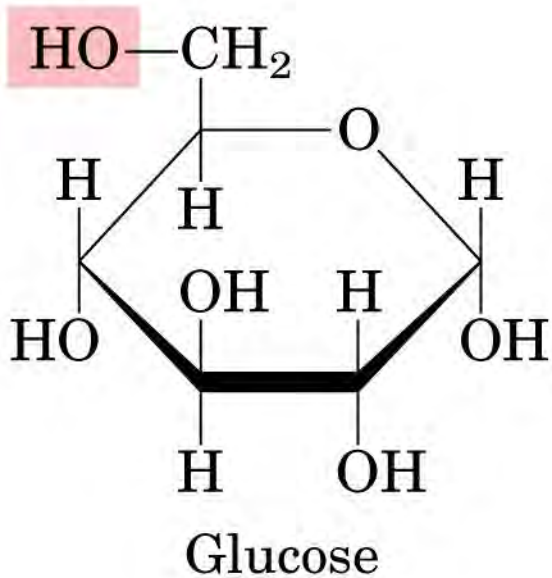


$$\Delta G'^{\circ} = -16.7 \text{ kJ/mol}$$

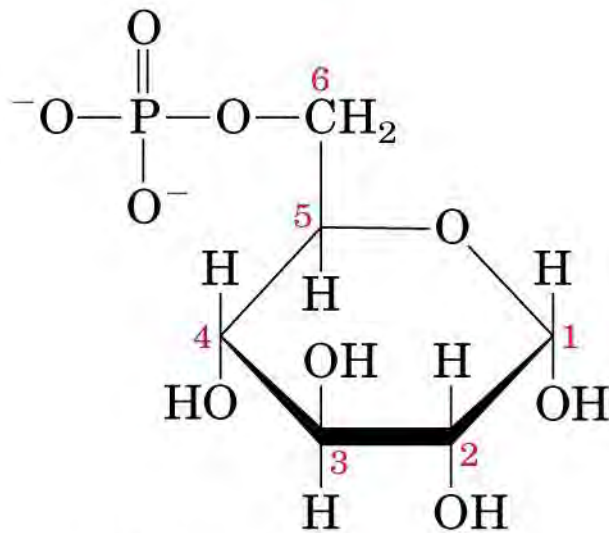


GLICOLISI

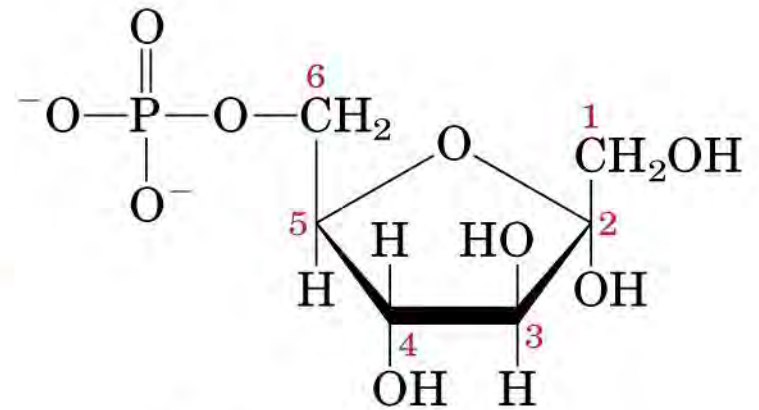
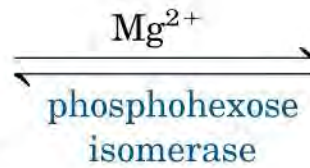
- via metabolica più antica (sia filogeneticamente che storicamente)
- avviene nel citosol
- non necessita di per sé O_2 , quindi può avvenire anche
in condizioni anaerobiche
- fermentazione: glicolisi in condizioni anaerobiche
- il glucosio è un combustibile essenziale ed il fegato è
deputato al controllo dei livelli ematici di glucosio (glicemia)



$$\Delta G'^{\circ} = -16.7 \text{ kJ/mol}$$

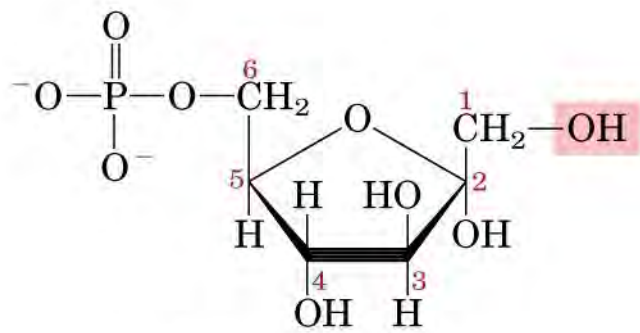


Glucose 6-phosphate

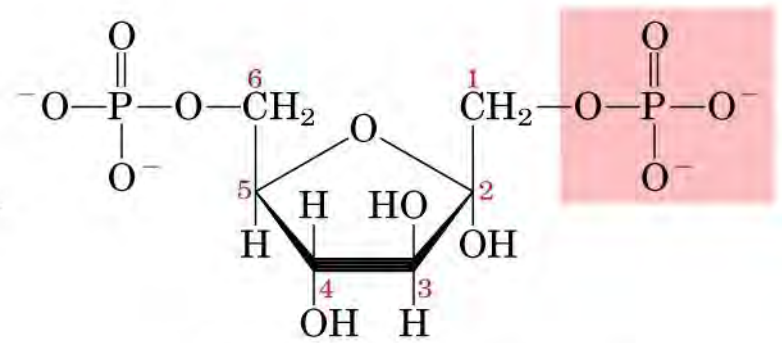
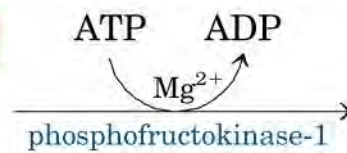


Fructose 6-phosphate

$$\Delta G'^{\circ} = 1.7 \text{ kJ/mol}$$

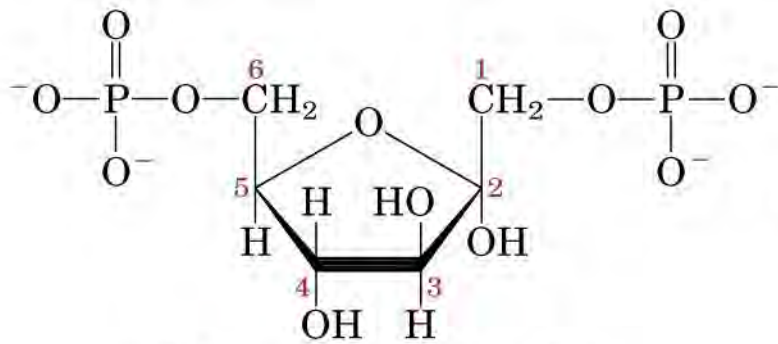


Fructose 6-phosphate

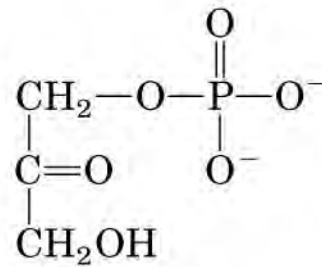


Fructose 1,6-bisphosphate

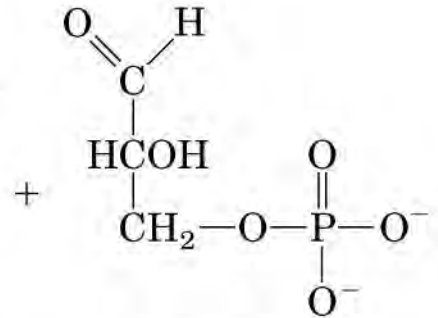
$$\Delta G'^{\circ} = -14.2 \text{ kJ/mol}$$



Fructose 1,6-bisphosphate

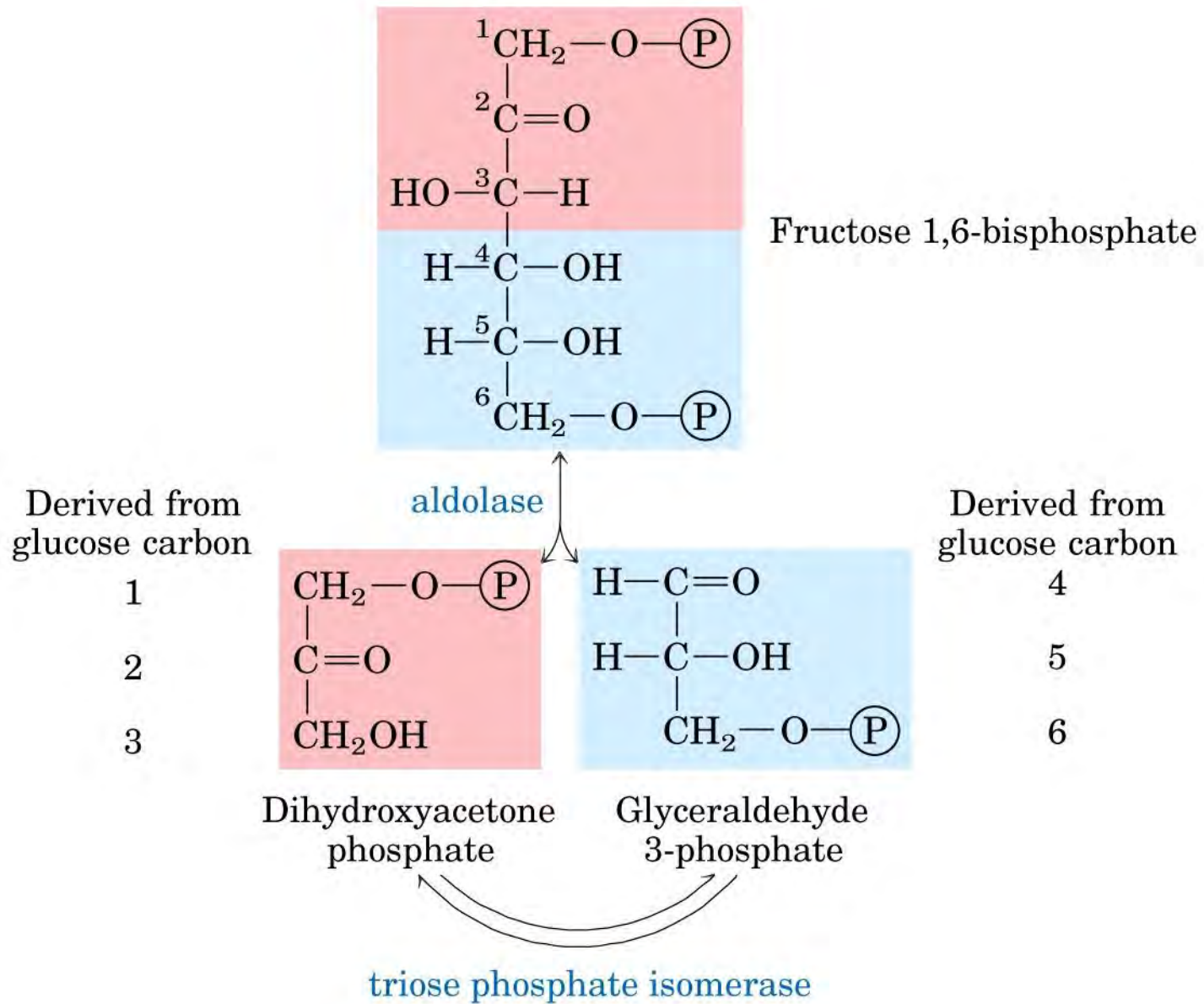


Dihydroxyacetone phosphate

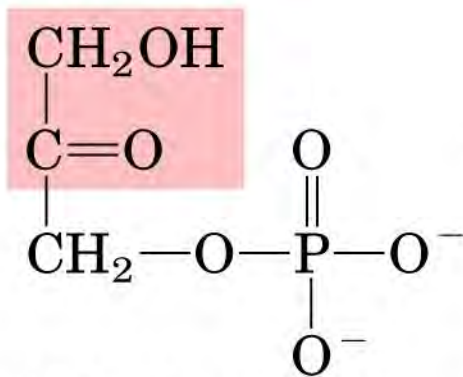


Glyceraldehyde 3-phosphate

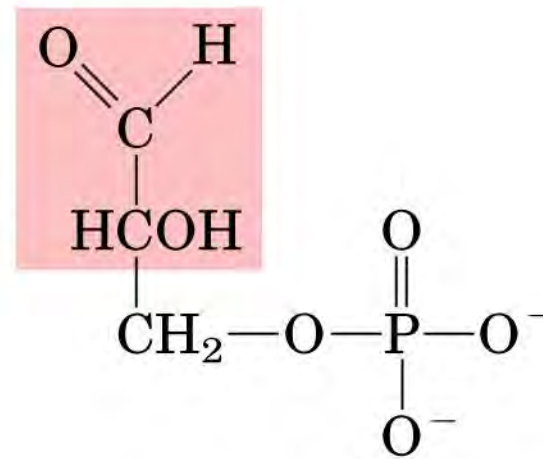
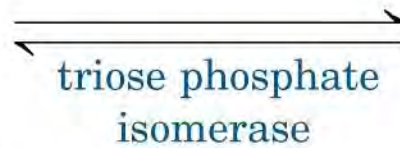
$$\Delta G'^{\circ} = 23.8 \text{ kJ/mol}$$



(a)

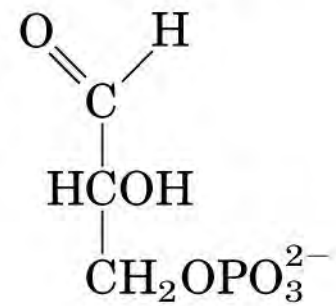


Dihydroxyacetone
phosphate

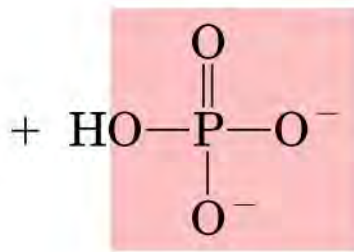


Glyceraldehyde
3-phosphate

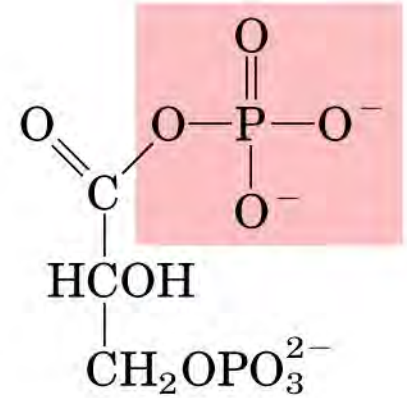
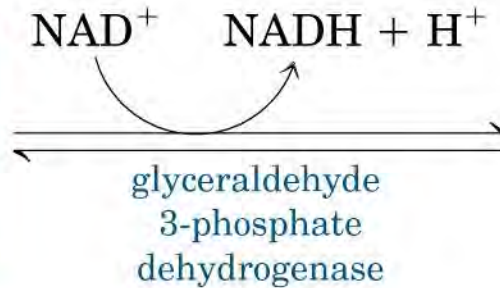
$$\Delta G'^{\circ} = 7.5 \text{ kJ/mol}$$



Glyceraldehyde
3-phosphate

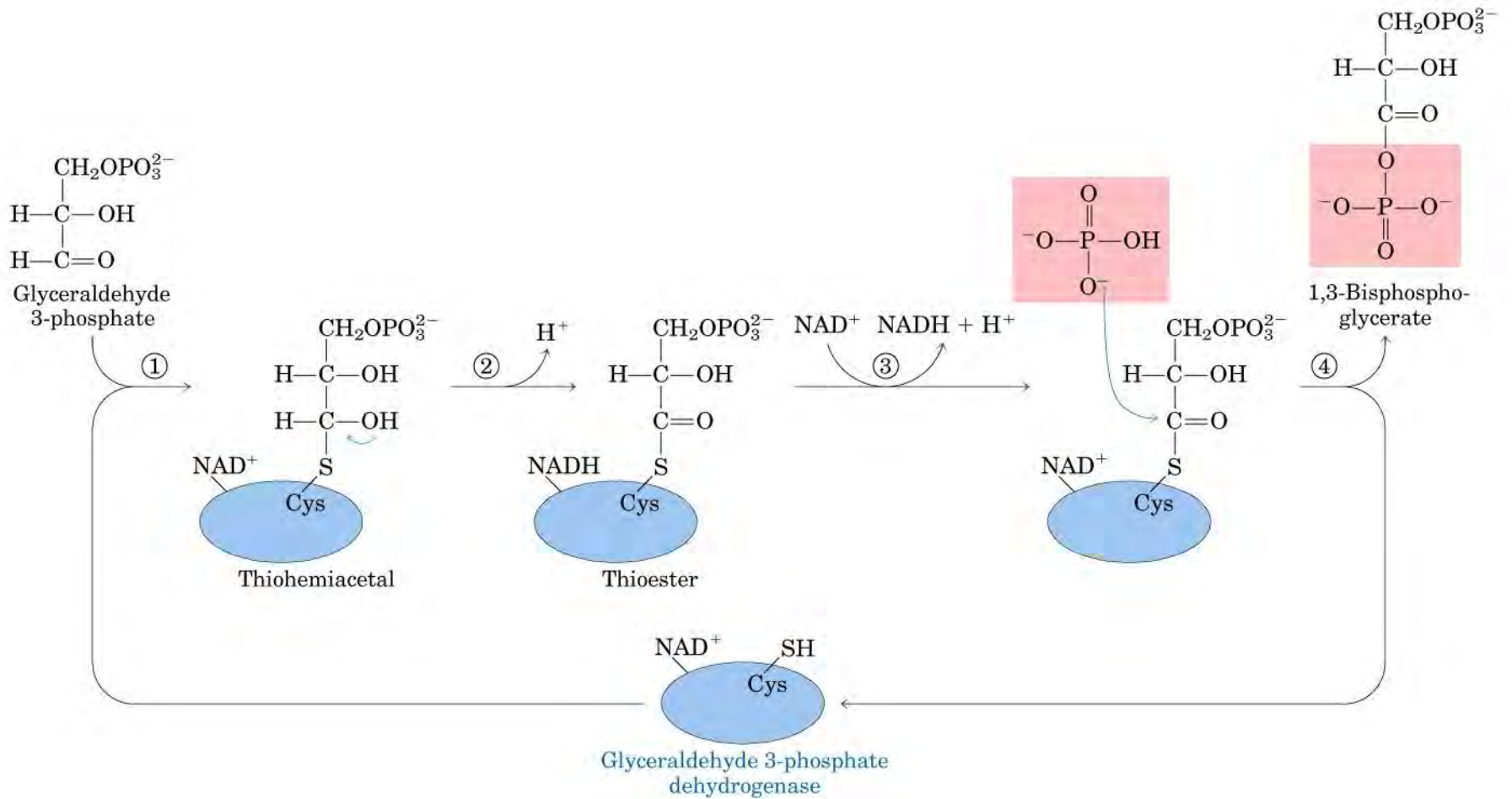


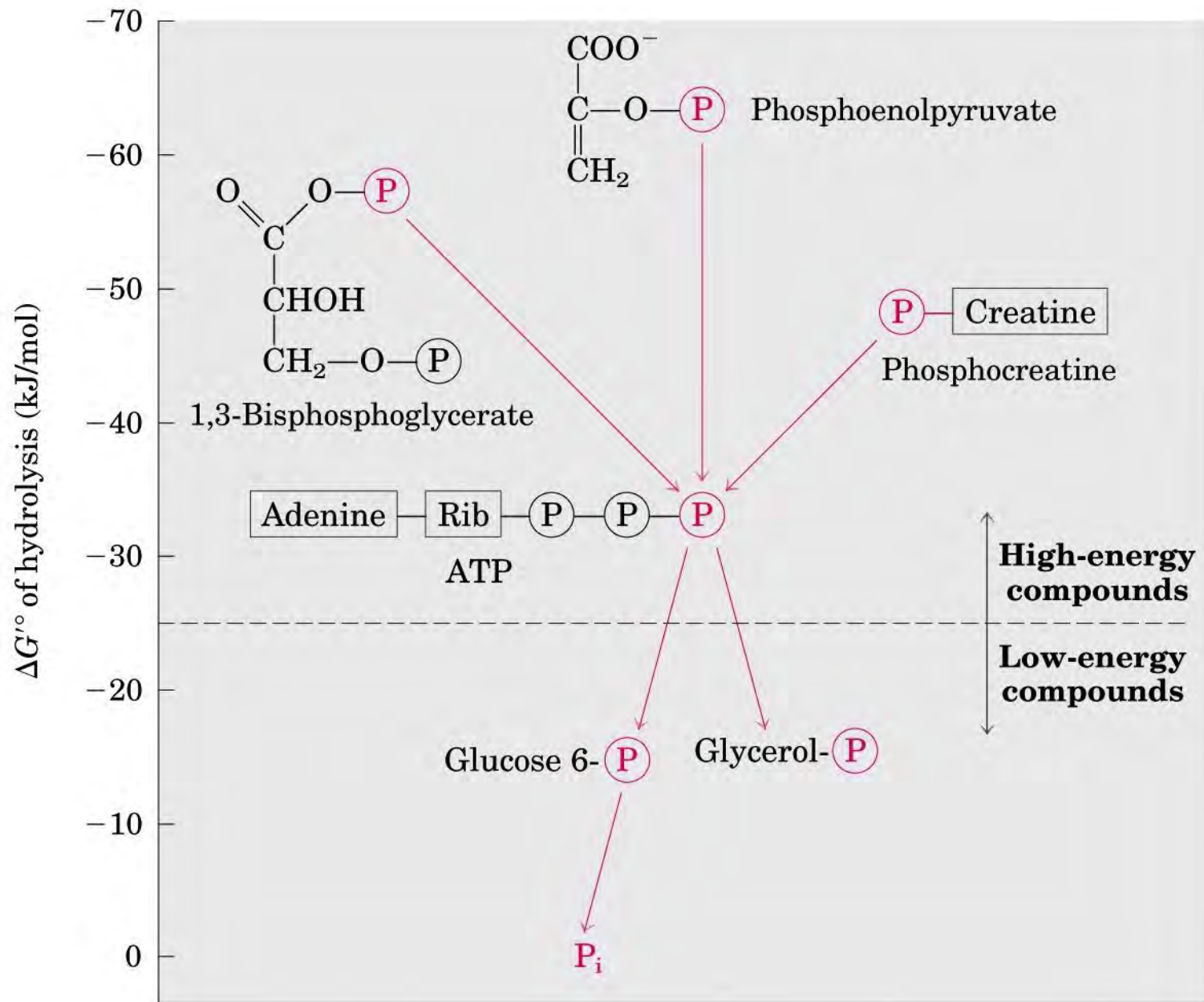
Inorganic
phosphate

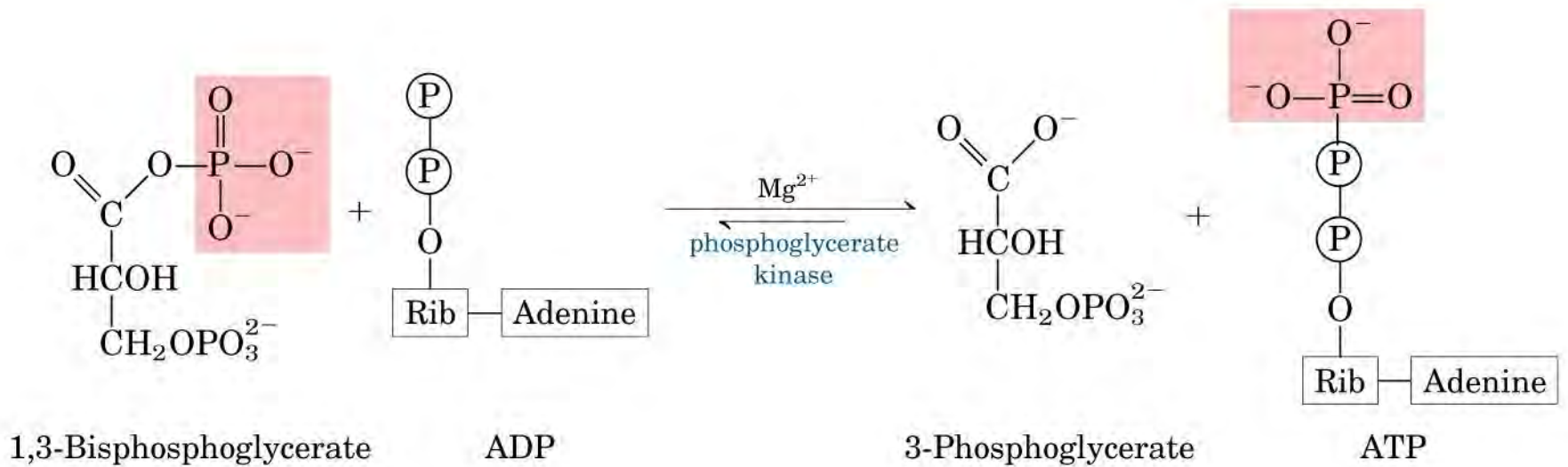


1,3-Bisphosphoglycerate

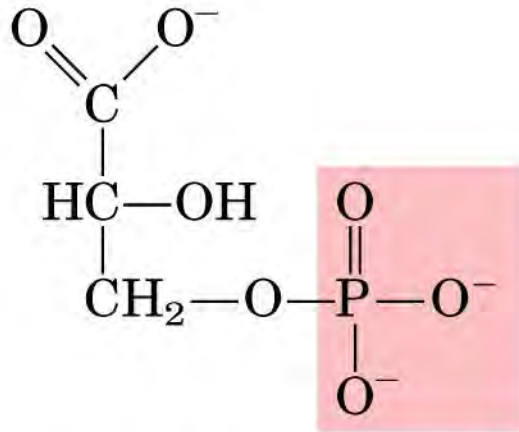
$$\Delta G'^{\circ} = 6.3 \text{ kJ/mol}$$



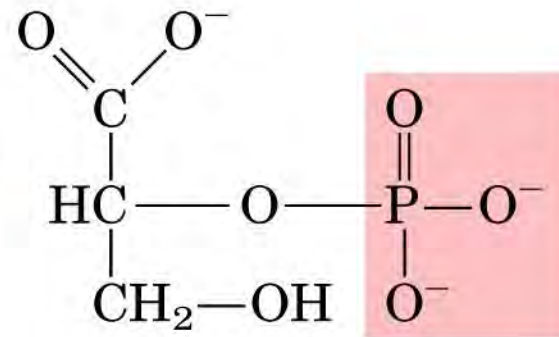
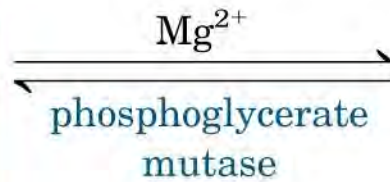




$$\Delta G'^{\circ} = -18.5 \text{ kJ/mol}$$

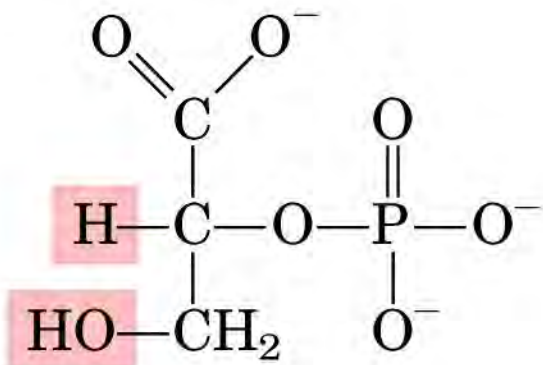


3-Phosphoglycerate

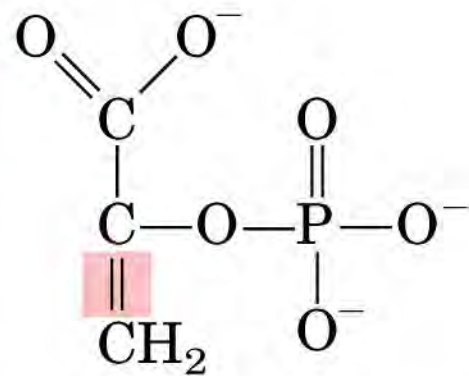
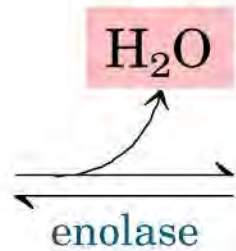


2-Phosphoglycerate

$$\Delta G'^{\circ} = 4.4 \text{ kJ/mol}$$

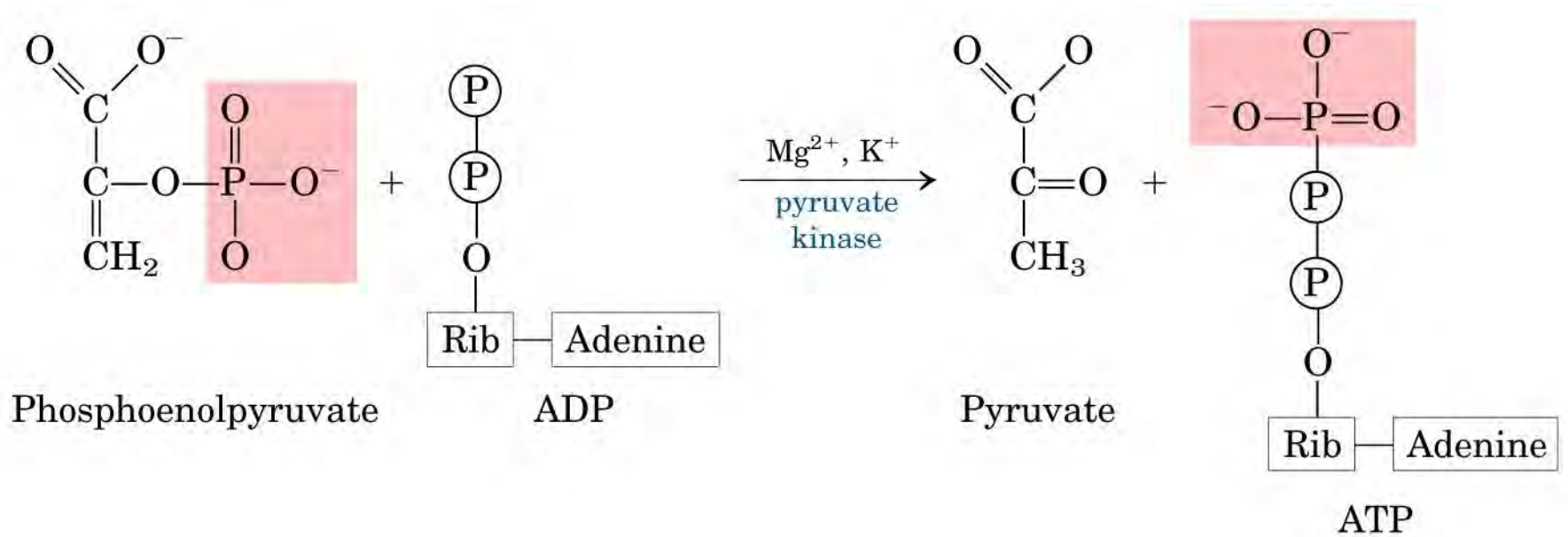


2-Phosphoglycerate

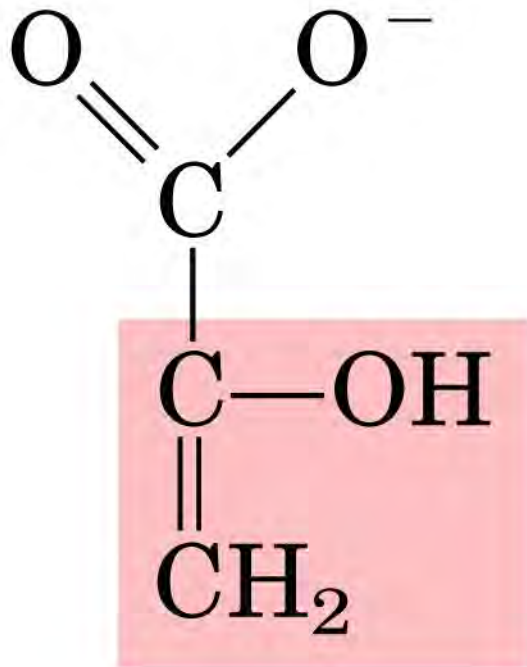


Phosphoenolpyruvate

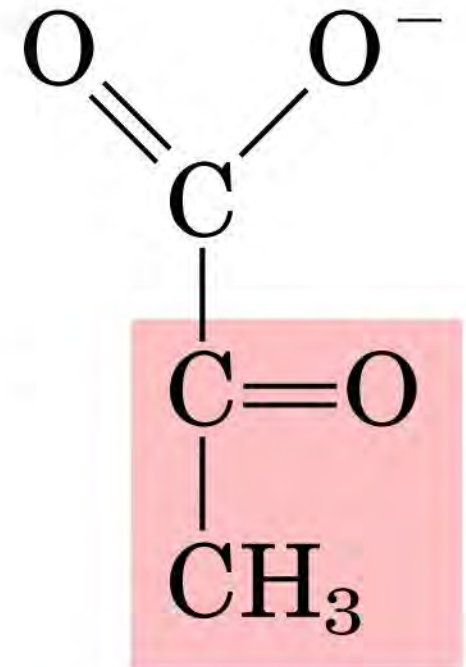
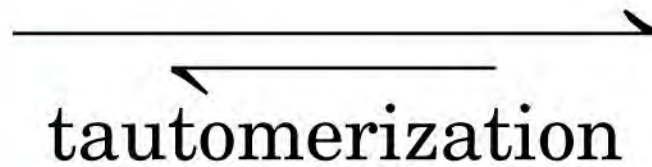
$$\Delta G'^{\circ} = 7.5 \text{ kJ/mol}$$



$$\Delta G'^{\circ} = -31.4 \text{ kJ/mol}$$

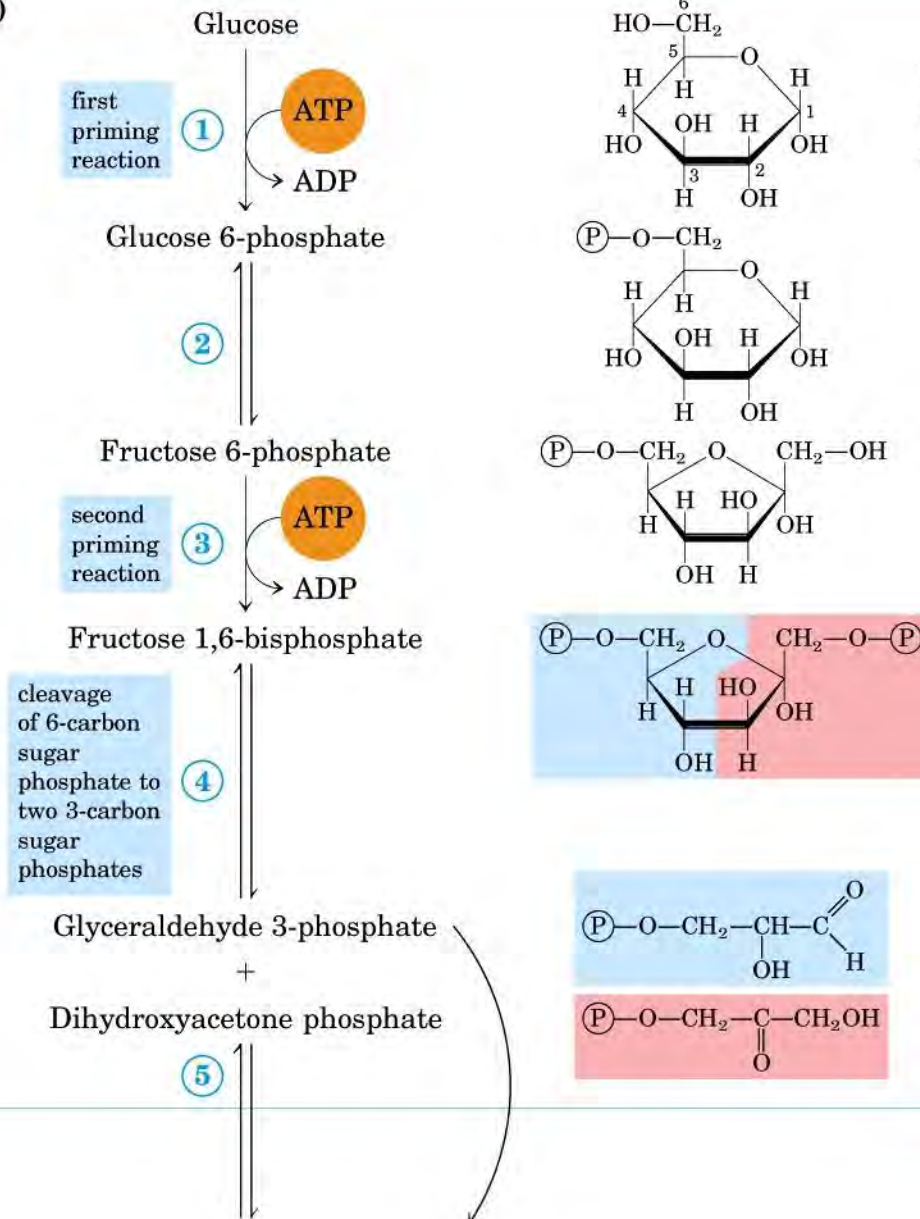


Pyruvate
(enol form)



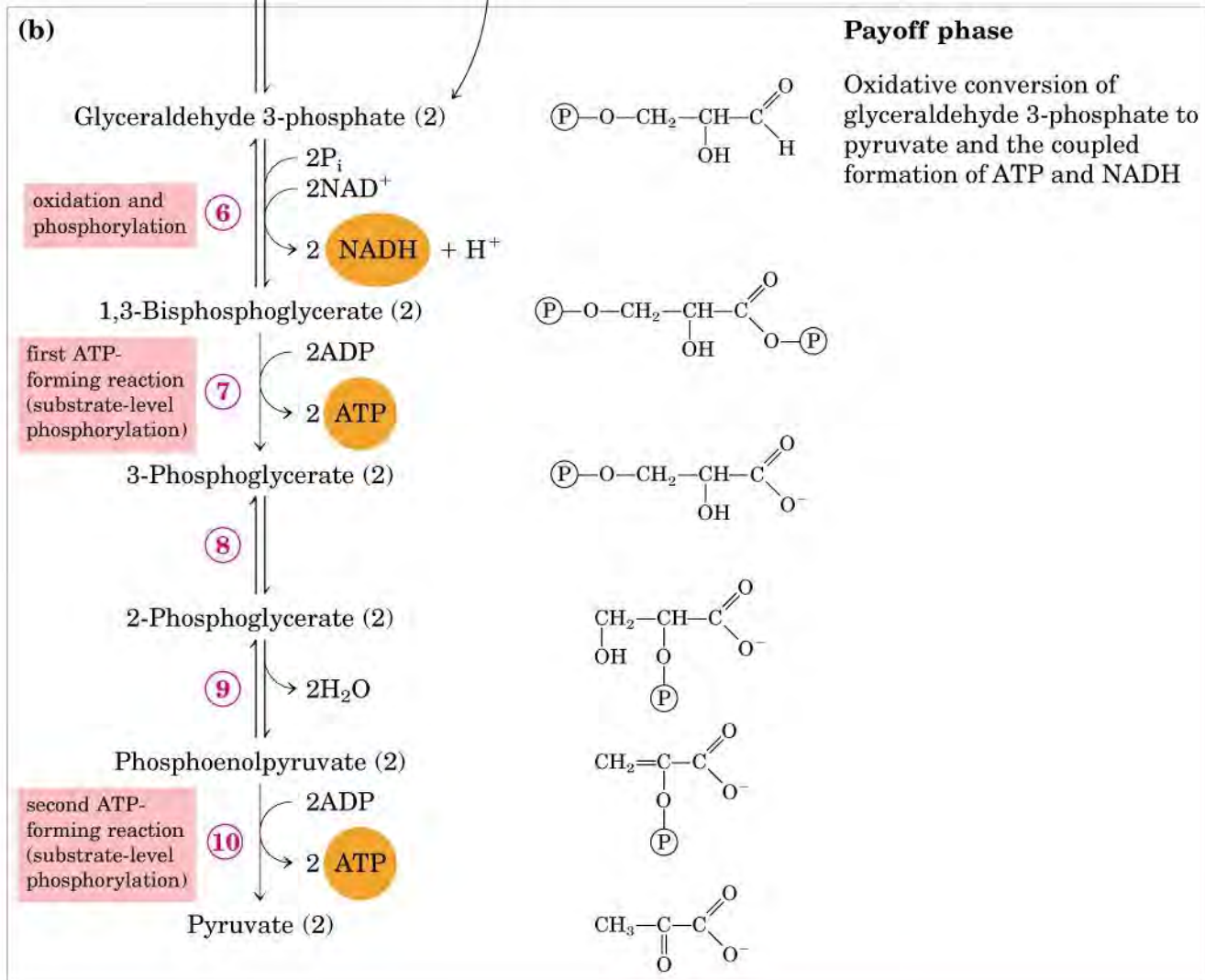
Pyruvate
(keto form)

(a)



Preparatory phase

Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate



Glicolisi

Bilancio energetico

- 2 molecole di ATP
- 2 molecole di NADH + H⁺
- 2 molecole di piruvato

GLUCONEOGENESI

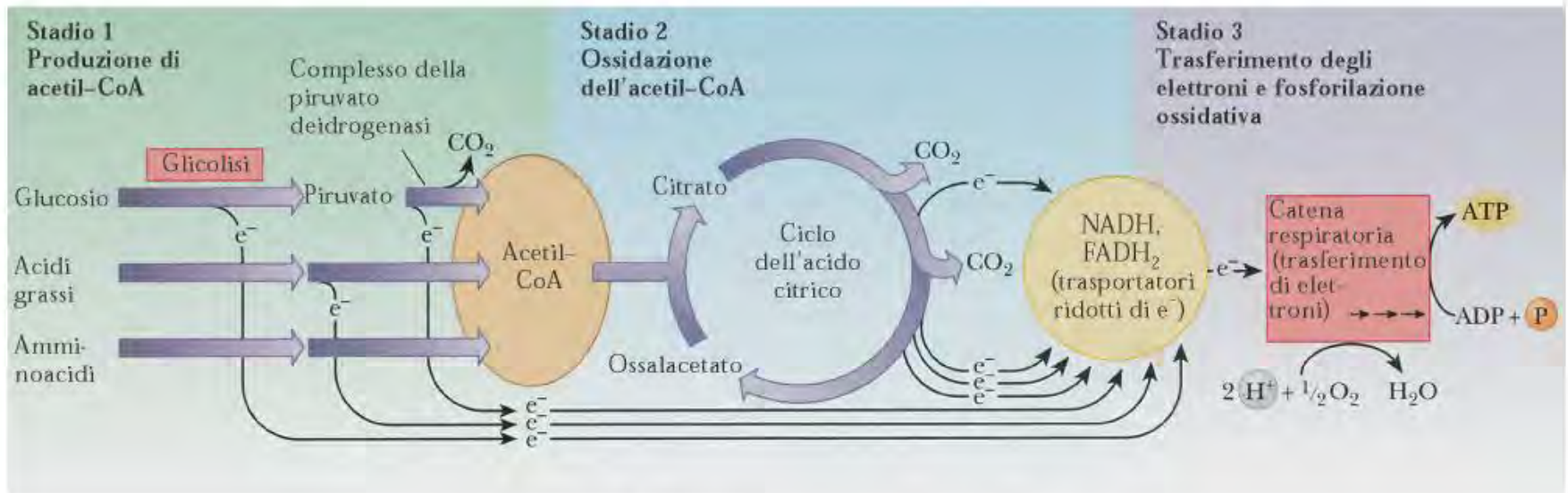
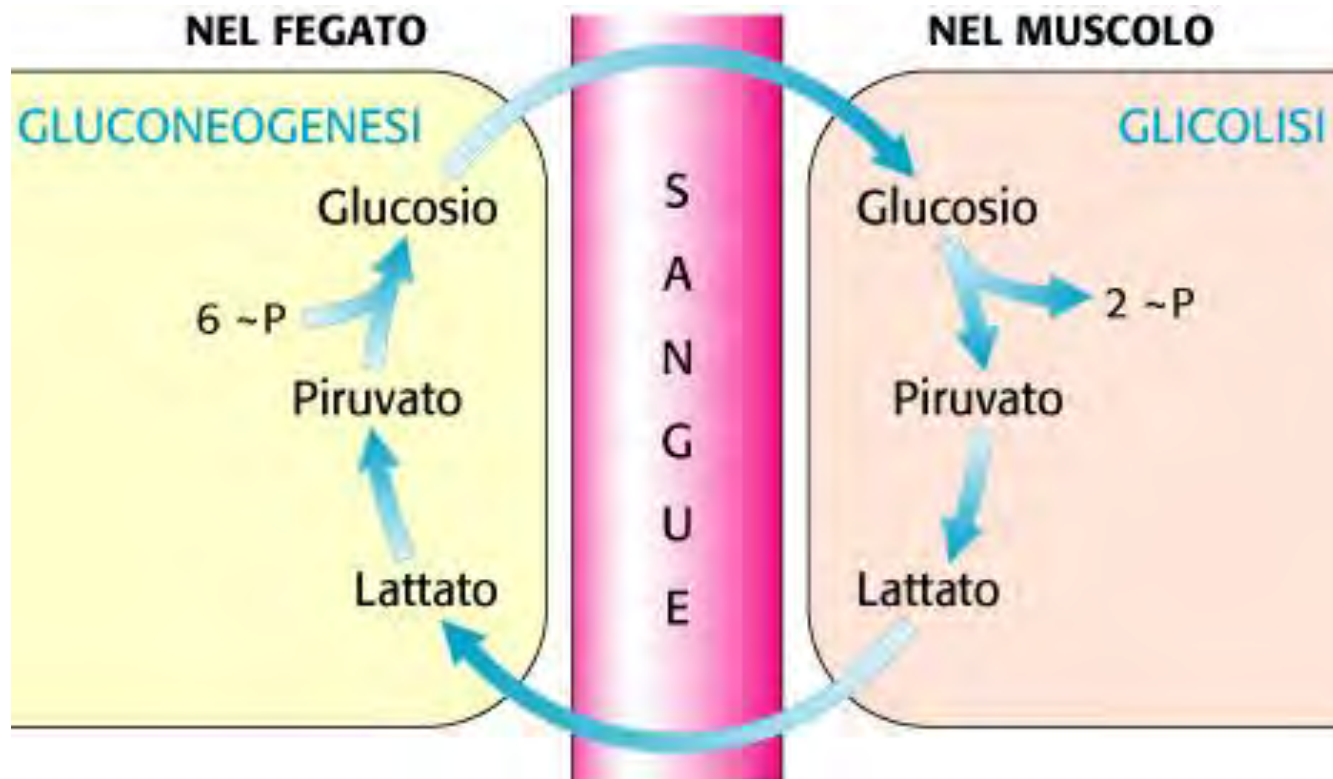


FIGURA 16.1

Il ciclo dell'acido citrico ha un ruolo centrale nel catabolismo. Gli amminoacidi, gli acidi grassi e il glucosio possono produrre tutti acetil-CoA nello stadio 1 del catabolismo. Nello stadio 2, l'acetil-CoA entra nel ciclo dell'acido citrico. Gli stadi 1 e 2 producono trasportatori di elettroni ridotti (qui mostrati come e^-). Nello stadio 3, gli elettroni entrano nella catena di trasporto degli elettroni, che produce ATP.



LA GLUCONEOGENESI

Sintesi de novo di molecole di glucosio

Avviene nel fegato a partire da
lattato,
piruvato
ossalacetato

che derivano dal catabolismo anaerobico del glucosio (in altri tessuti)
o da catabolismo degli aminoacidi

Rappresenta il principale meccanismo con cui il fegato produce e
immette nel sangue glucosio durante il digiuno

Non è esattamente l'inverso della glicolisi,
anche se molte reazioni sono comuni

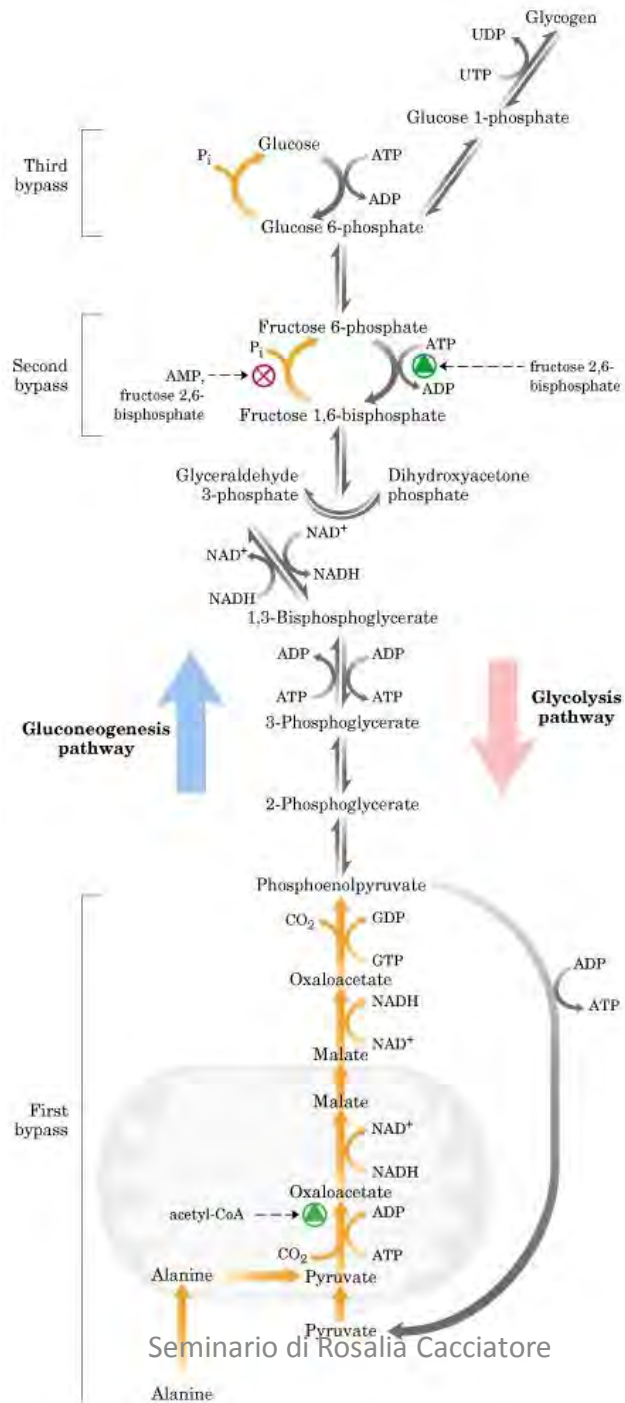


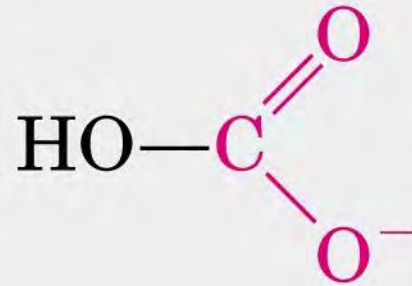
table 20-1

Free-Energy Changes of Glycolytic Reactions in Erythrocytes*

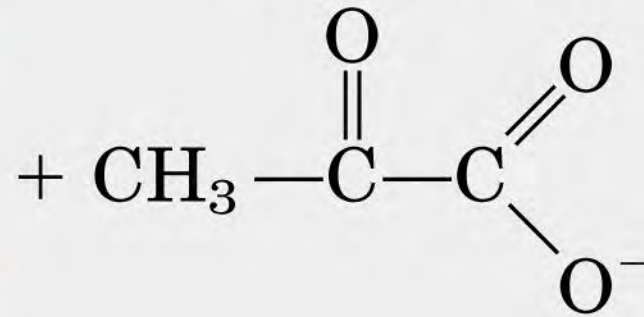
Glycolytic reaction step	$\Delta G'^{\circ}$ (kJ/mol)	ΔG (kJ/mol)
① Glucose + ATP \longrightarrow glucose 6-phosphate + ADP + H ⁺	-16.7	-33.4
② Glucose 6-phosphate \rightleftharpoons fructose 6-phosphate	1.7	-2.5
③ Fructose 6-phosphate + ATP \longrightarrow fructose 1,6-bisphosphate + ADP + H ⁺	-14.2	-22.2
④ Fructose 1,6-bisphosphate \rightleftharpoons dihydroxyacetone phosphate + glyceraldehyde 3-phosphate	23.8	-1.25
⑤ Dihydroxyacetone phosphate \rightleftharpoons glyceraldehyde 3-phosphate	7.5	2.5
⑥ Glyceraldehyde 3-phosphate + P _i + NAD ⁺ \rightleftharpoons 1,3-bisphosphoglycerate + NADH + H ⁺	6.3	-1.7
⑦ 1,3-Bisphosphoglycerate + ADP \rightleftharpoons 3-phosphoglycerate + ATP	-18.8	1.25
⑧ 3-Phosphoglycerate \rightleftharpoons 2-phosphoglycerate	4.4	0.8
⑨ 2-Phosphoglycerate \rightleftharpoons phosphoenolpyruvate + H ₂ O	7.5	-3.3
⑩ Phosphoenolpyruvate + ADP + H ⁺ \longrightarrow pyruvate + ATP	-31.4	-16.7

* $\Delta G'^{\circ}$ is the standard free-energy change, as defined in Chapter 14 (see p. 494). At pH 7.0, ΔG is the free-energy change calculated from the actual concentrations of glycolytic intermediates present under physiological conditions in erythrocytes. The glycolytic reactions bypassed in gluconeogenesis are shown in red.

Bicarbonate



Pyruvate



pyruvate
carboxylase

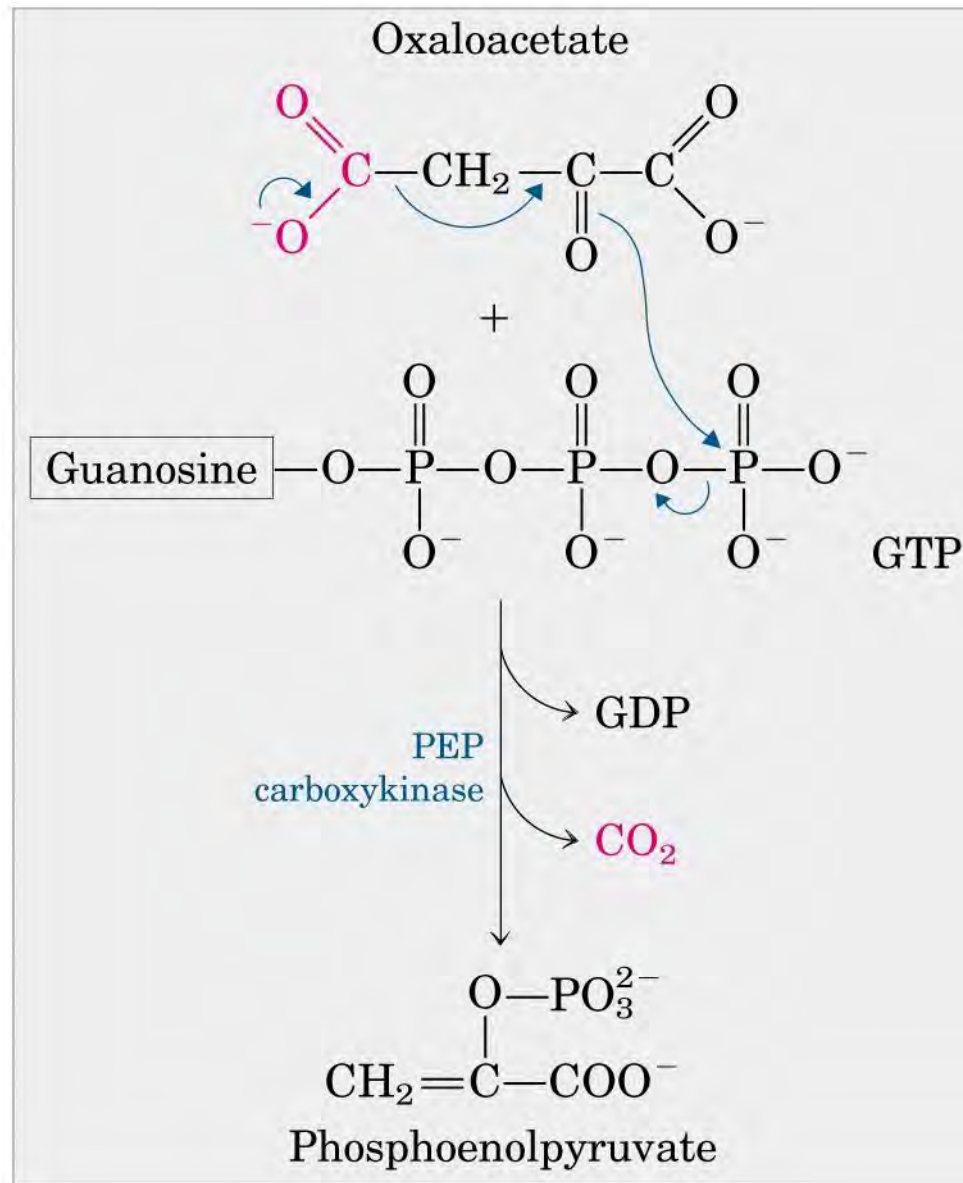
ATP

biotin

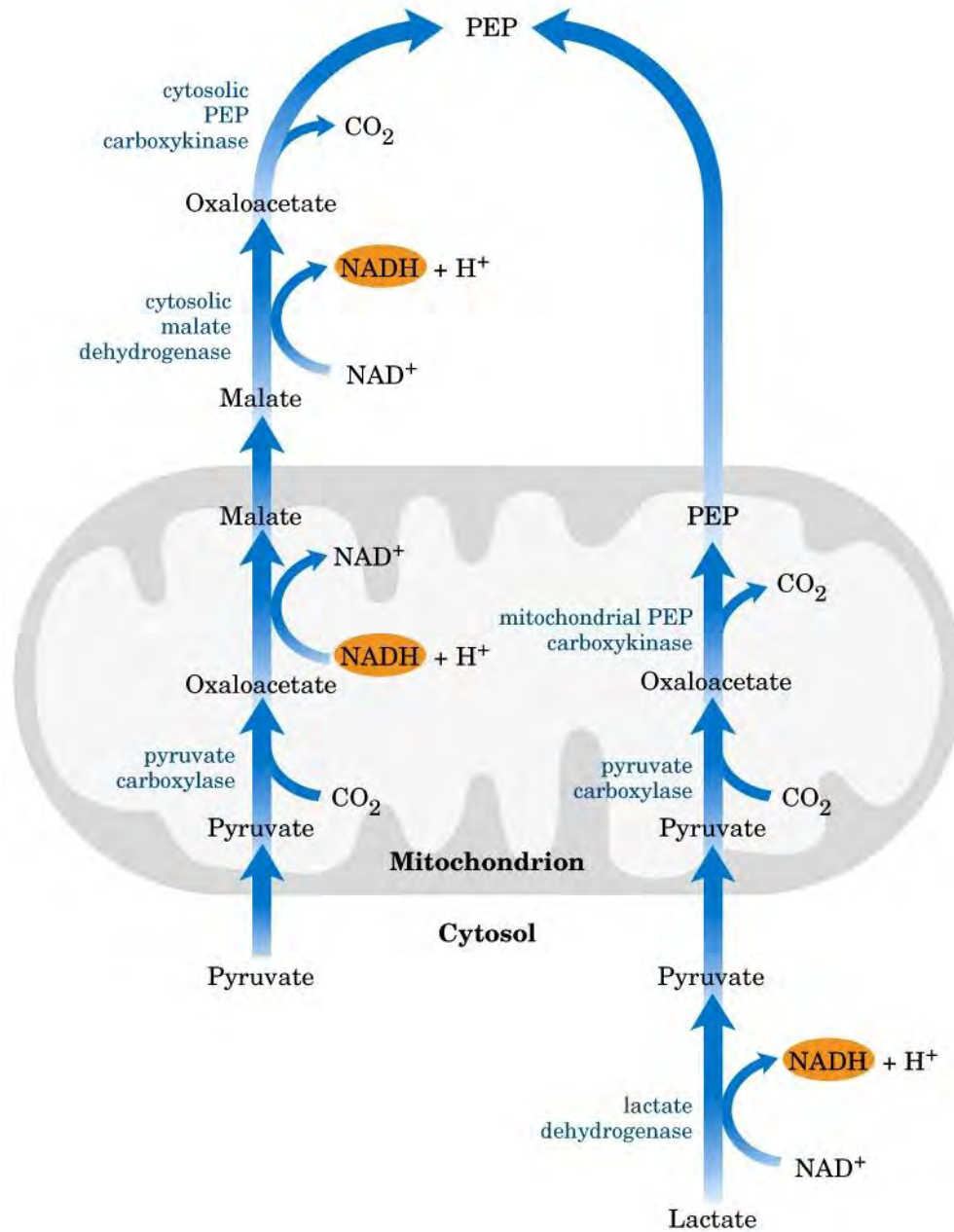
ADP + P_i

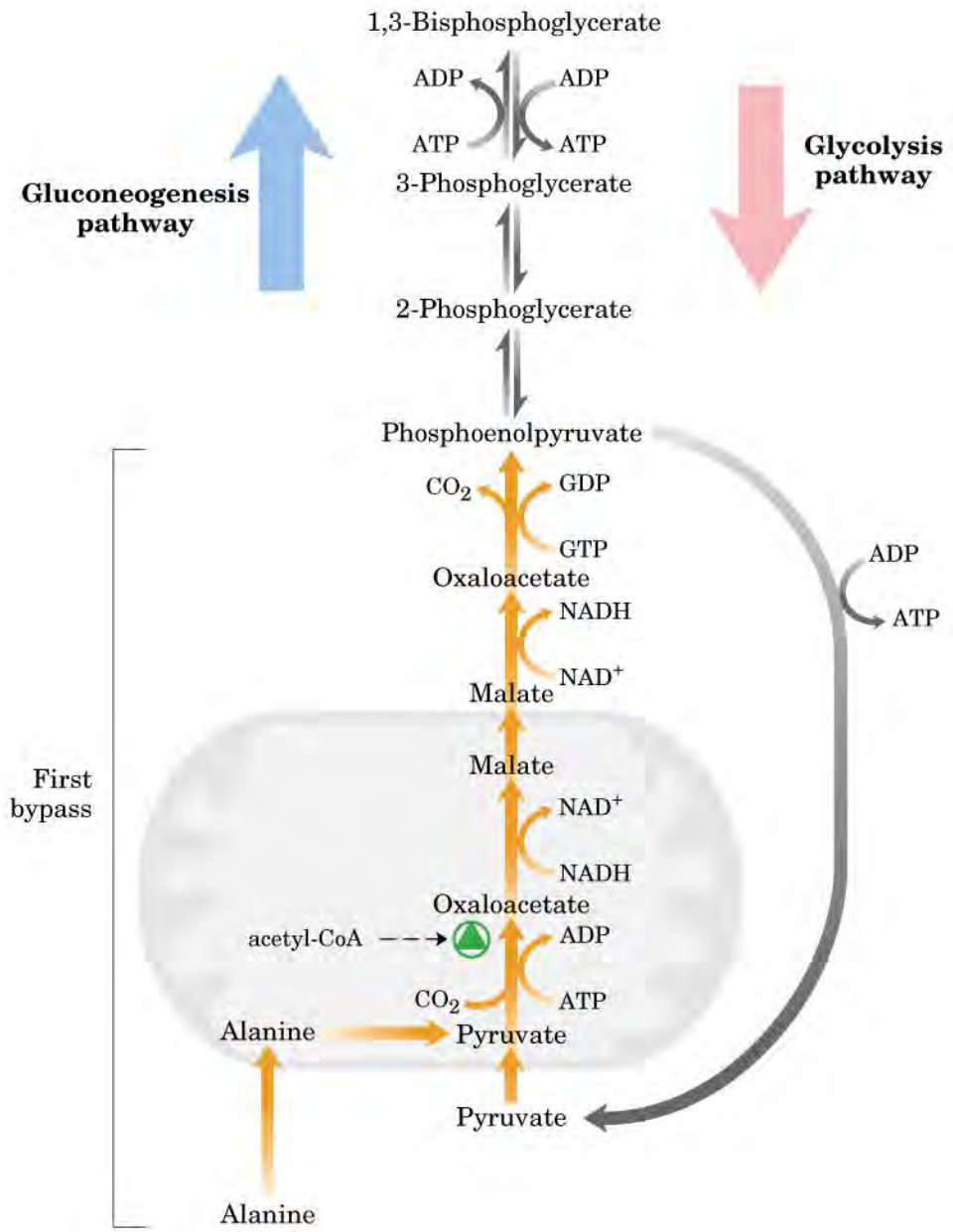
Oxaloacetate

(a)



(b)





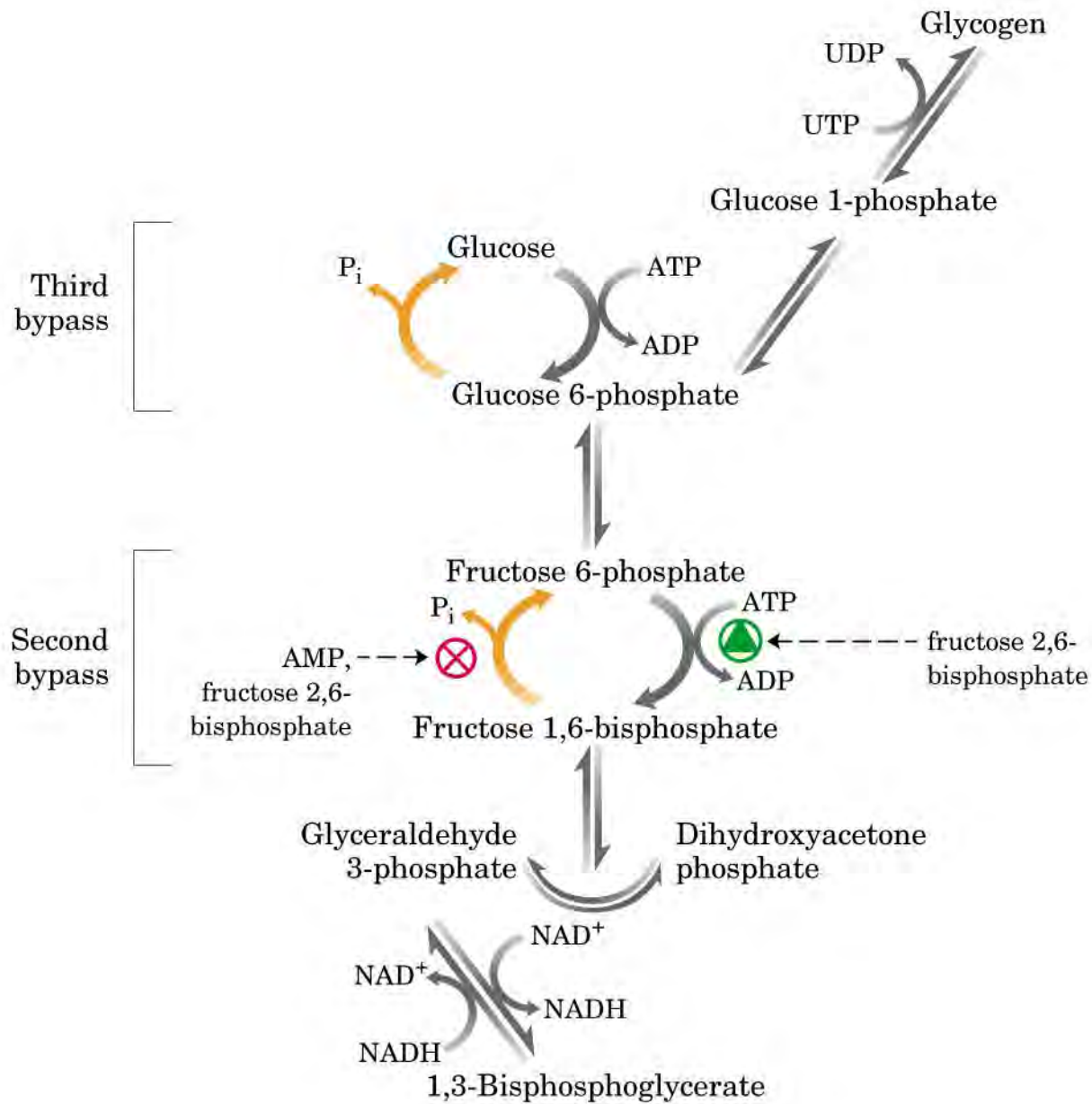


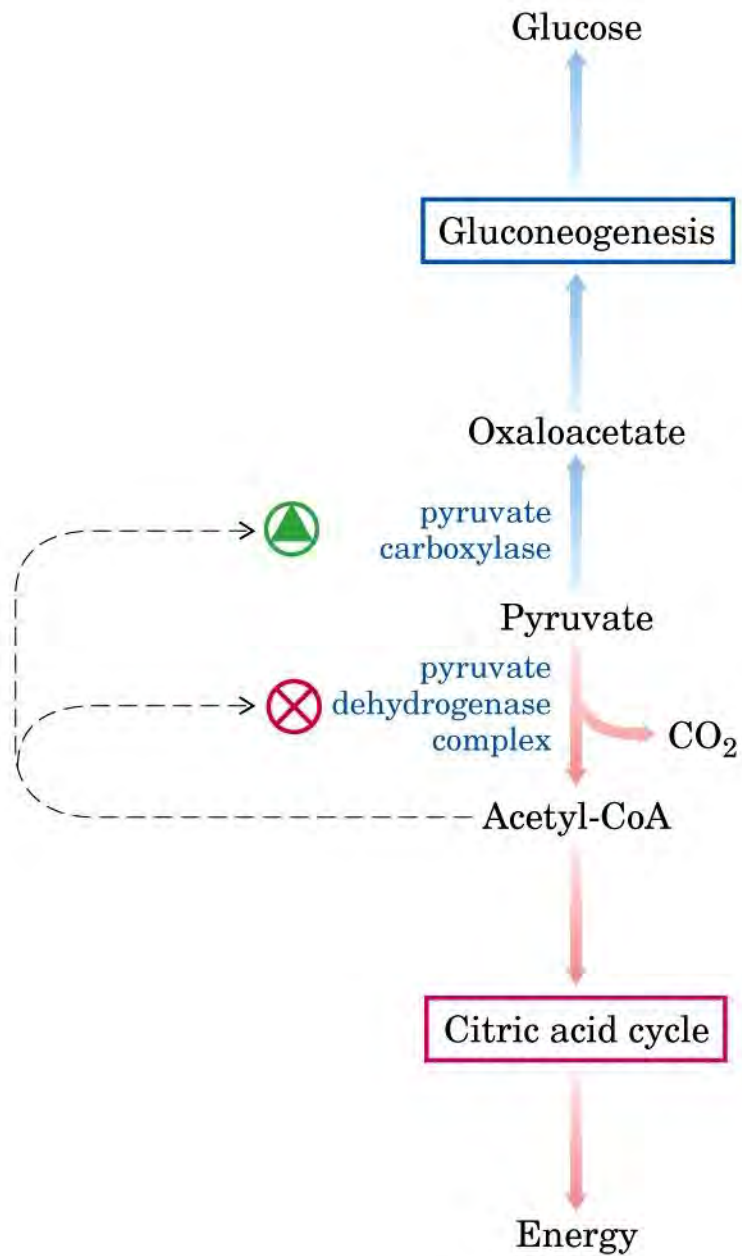
table 20-2

Sequential Reactions in Gluconeogenesis Starting from Pyruvate*

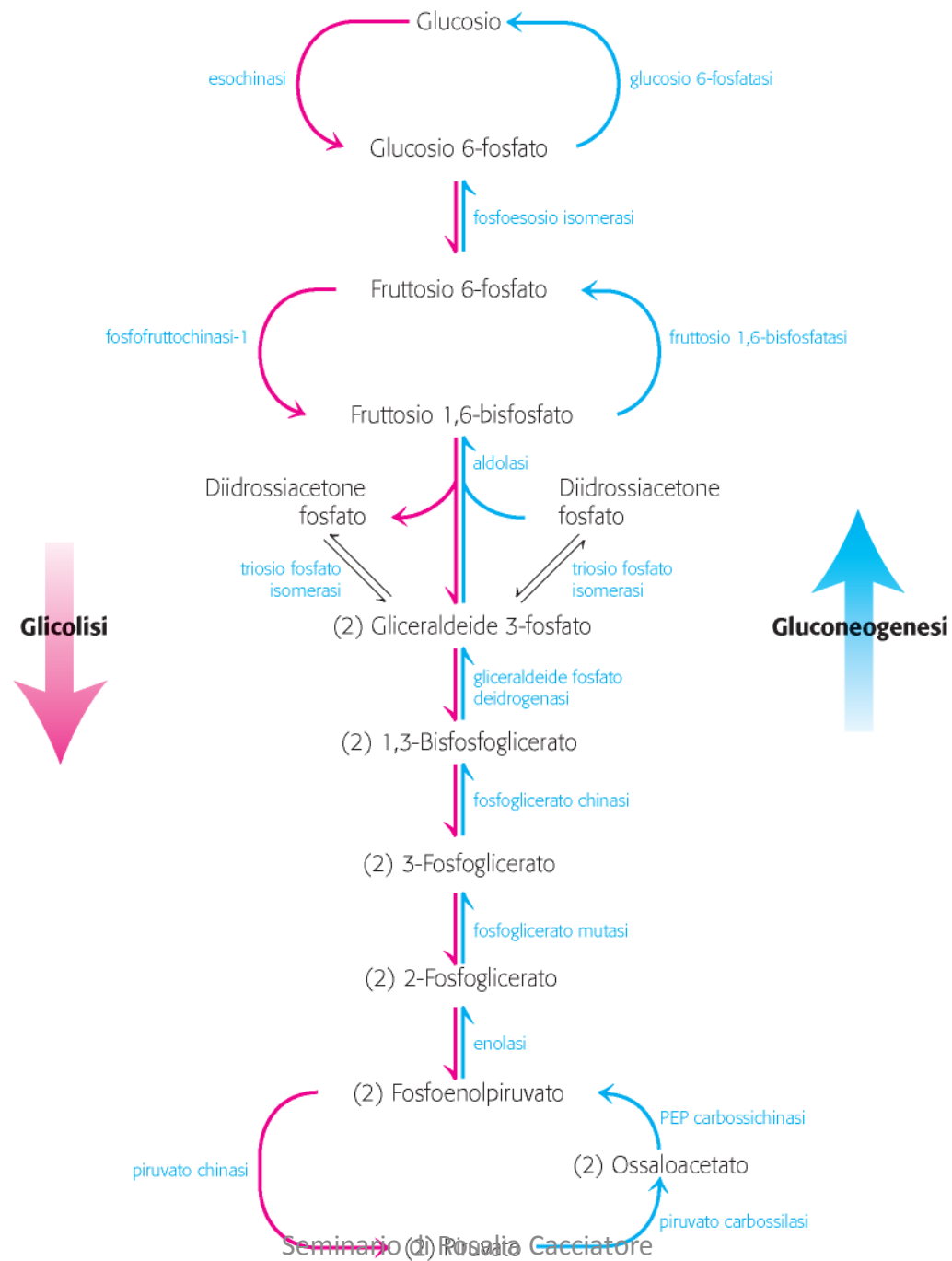
Pyruvate + HCO ₃ ⁻ + ATP → oxaloacetate + ADP + P _i + H ⁺	×2
Oxaloacetate + GTP ⇌ phosphoenolpyruvate + CO ₂ + GDP	×2
Phosphoenolpyruvate + H ₂ O ⇌ 2-phosphoglycerate	×2
2-Phosphoglycerate ⇌ 3-phosphoglycerate	×2
3-Phosphoglycerate + ATP ⇌ 1,3-bisphosphoglycerate + ADP + H ⁺	×2
1,3-Bisphosphoglycerate + NADH + H ⁺ ⇌ glyceraldehyde 3-phosphate + NAD ⁺ + P _i	×2
Glyceraldehyde 3-phosphate ⇌ dihydroxyacetone phosphate	
Glyceraldehyde 3-phosphate + dihydroxyacetone phosphate ⇌ fructose 1,6-bisphosphate	
Fructose 1,6-bisphosphate + H ₂ O → fructose 6-phosphate + P _i	
Fructose 6-phosphate ⇌ glucose 6-phosphate	
Glucose 6-phosphate + H ₂ O → glucose + P _i	
<i>Sum:</i> 2 Pyruvate + 4ATP + 2GTP + 2NADH + 4H ₂ O → glucose + 4ADP + 2GDP + 6P _i + 2NAD ⁺ + 2H ⁺	

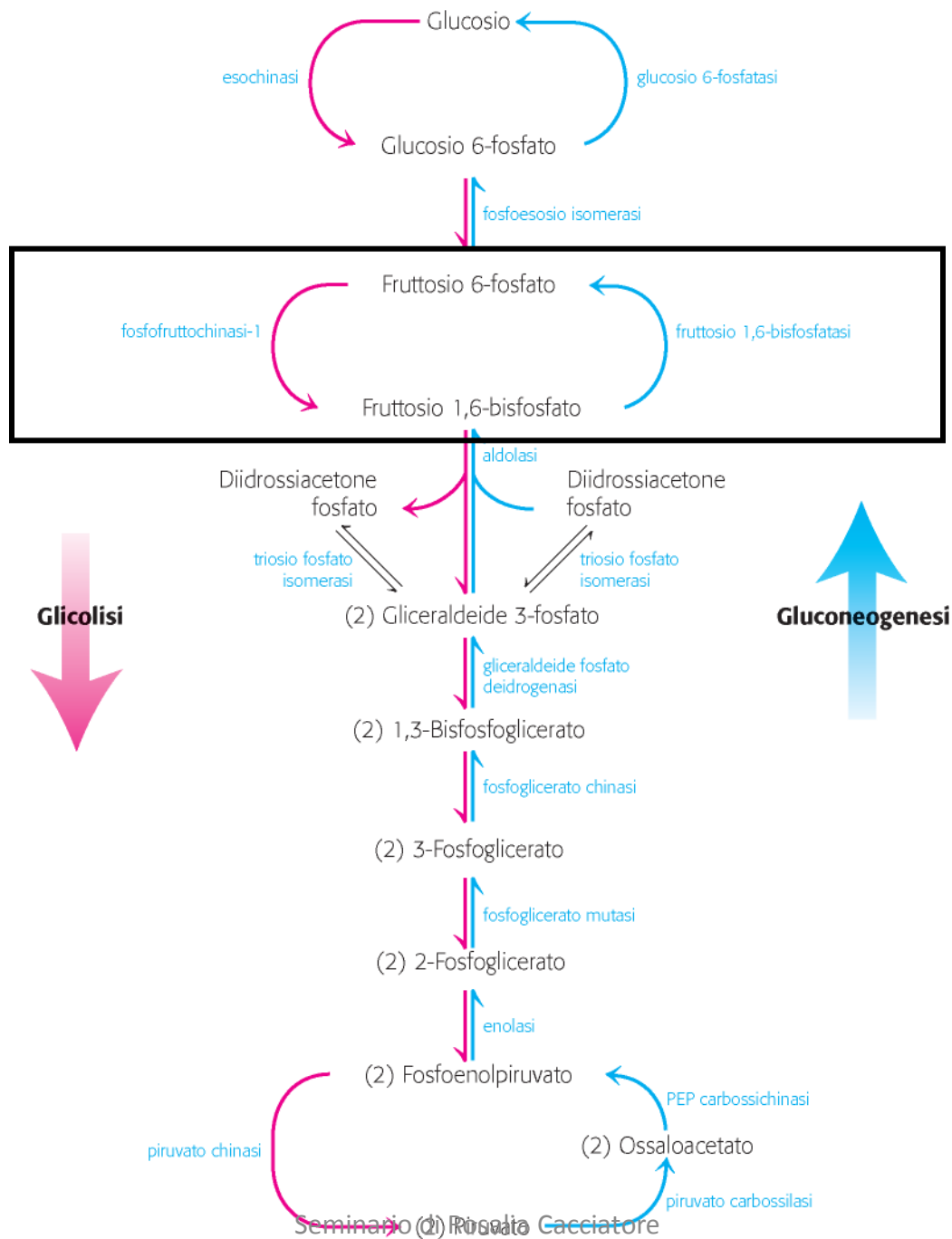
*The bypass reactions are in red; all other reactions are reversible steps of glycolysis. The figures at the right indicate that the reaction is to be counted twice, because two three-carbon precursors are required to make a molecule of glucose. Note that the reactions required to replace the cytosolic

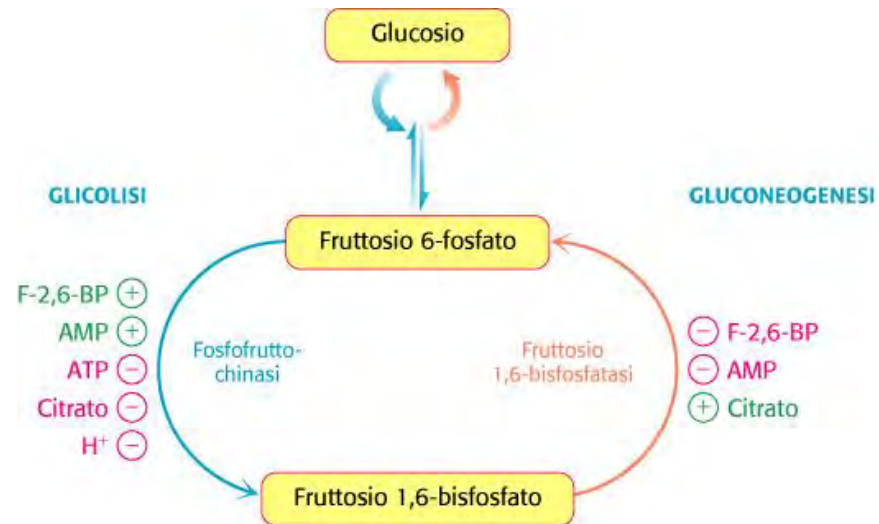
NADH consumed in the glyceraldehyde 3-phosphate dehydrogenase reaction (the conversion of lactate to pyruvate in the cytosol or the transport of reducing equivalents from mitochondria to the cytosol in the form of malate) are not considered in this summary.



**REGOLAZIONE
DELLA GLICOLISI
E DELLA GLUCONEOGENESI
NEL FEGATO
DA PARTE DEL GLUCAGONE**





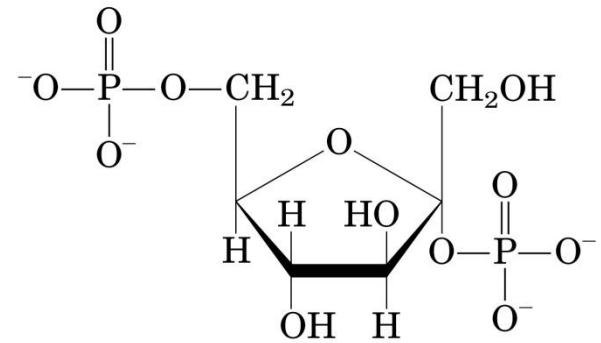


IL FRUTTOSIO 2,6 BISFOSFATO E' UN

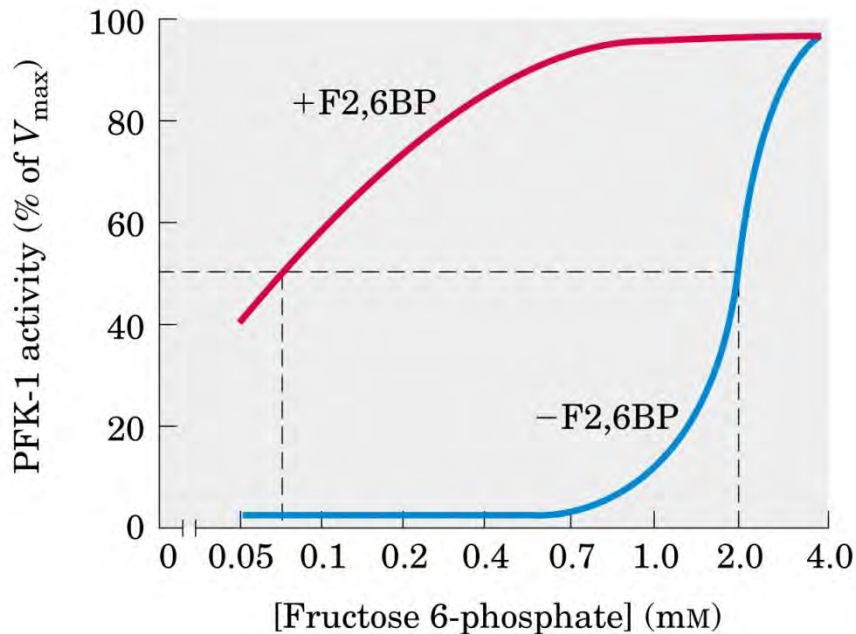
ATTIVATORE ALLOSTERICO DELLA PFK-1
(quindi stimola la glicolisi)

E UN

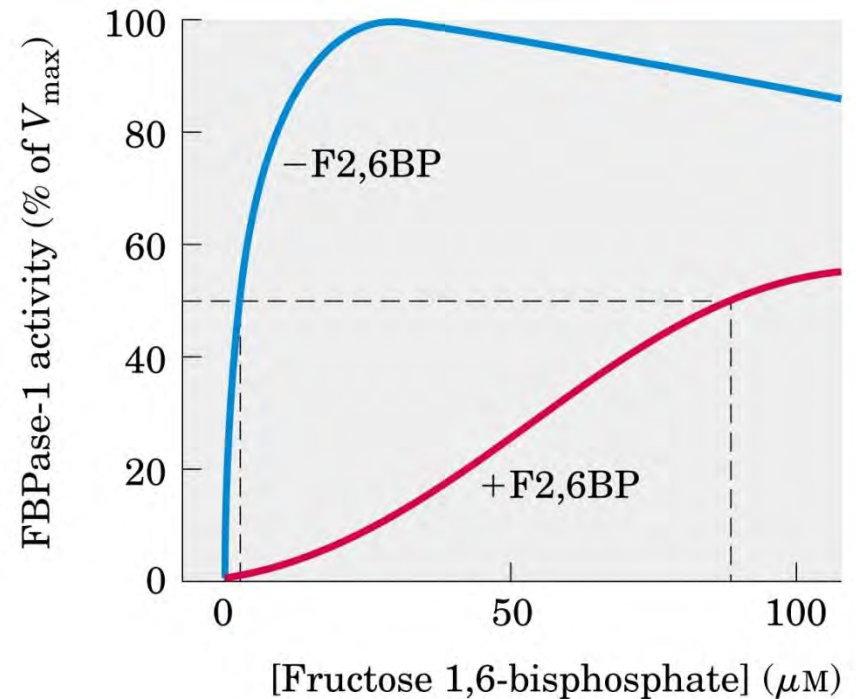
INIBITORE ALLOSTERICO DELLA FBPasi-1
(quindi inibisce la gluconeogenesi)



Fructose 2,6-bisphosphate



(a)



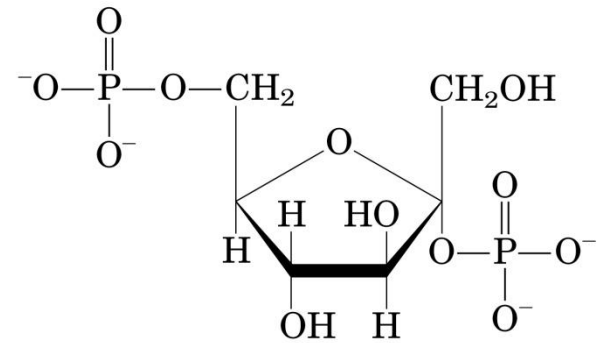
(b)

IL FRUTTOSIO 2,6 BISFOSFATO E' UN

**ATTIVATORE ALLOSTERICO DELLA PFK-1
(quindi stimola la glicolisi)**

E UN

**INIBITORE ALLOSTERICO DELLA FBPasi-1
(quindi inibisce la gluconeogenesi)**



Fructose 2,6-bisphosphate

**I LIVELLI DI FRUTTOSIO 2,6 BISFOSFATO
SONO REGOLATI DAL GLUCAGONE**

IL GLUCAGONE

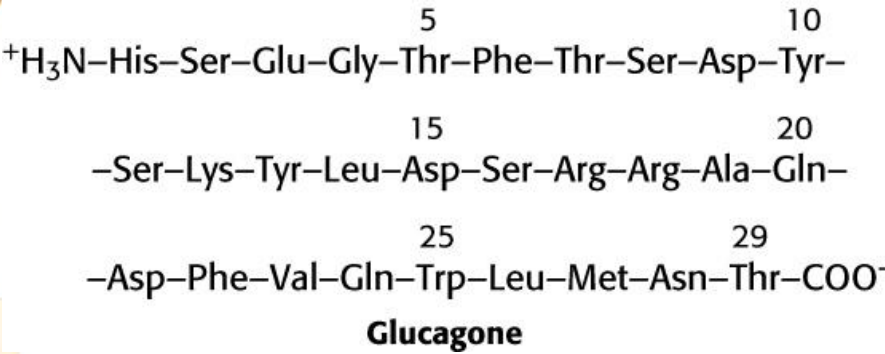
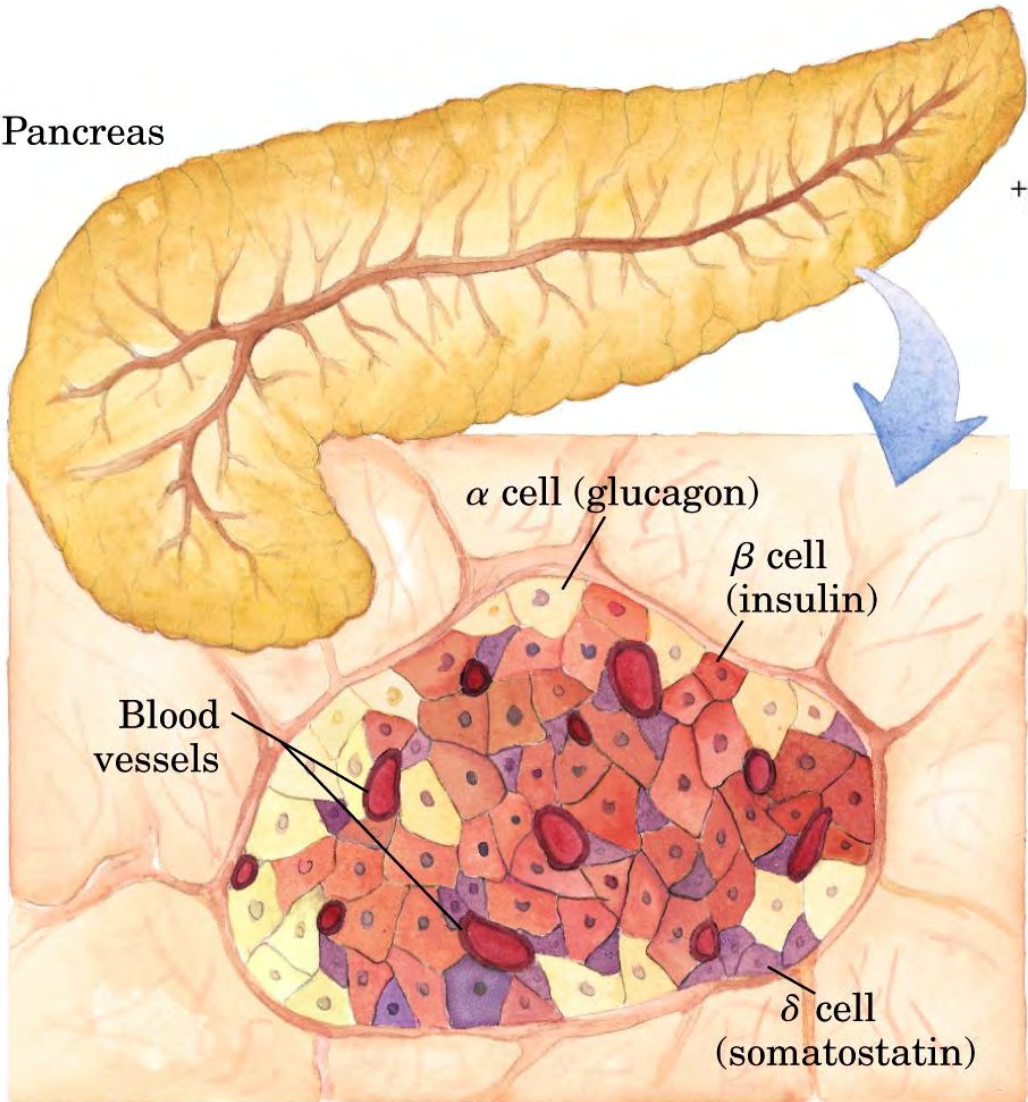
RIDUCE I LIVELLI DI FRUTTOSIO 2,6 BISFOSFATO

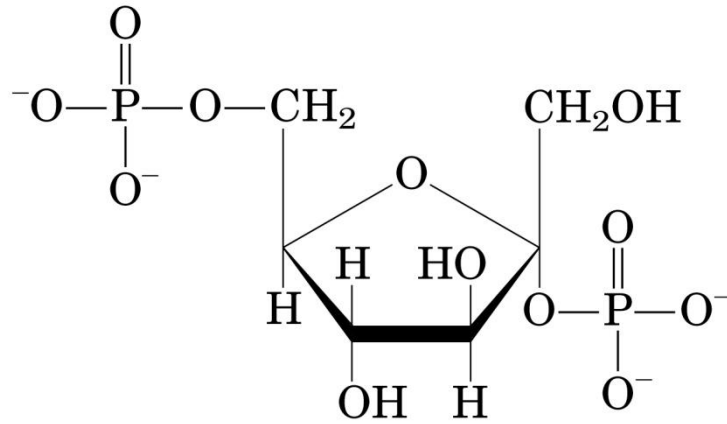
E QUINDI

STIMOLA LA GLUCONEOGENESI ED

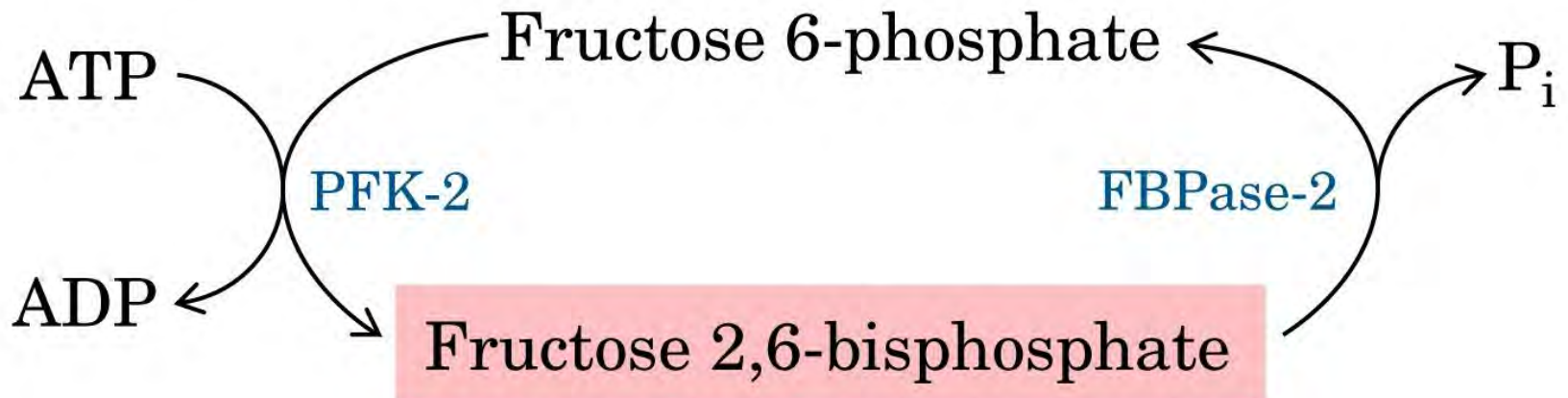
INIBISCE LA GLICOLISI NEL FEGATO

Pancreas

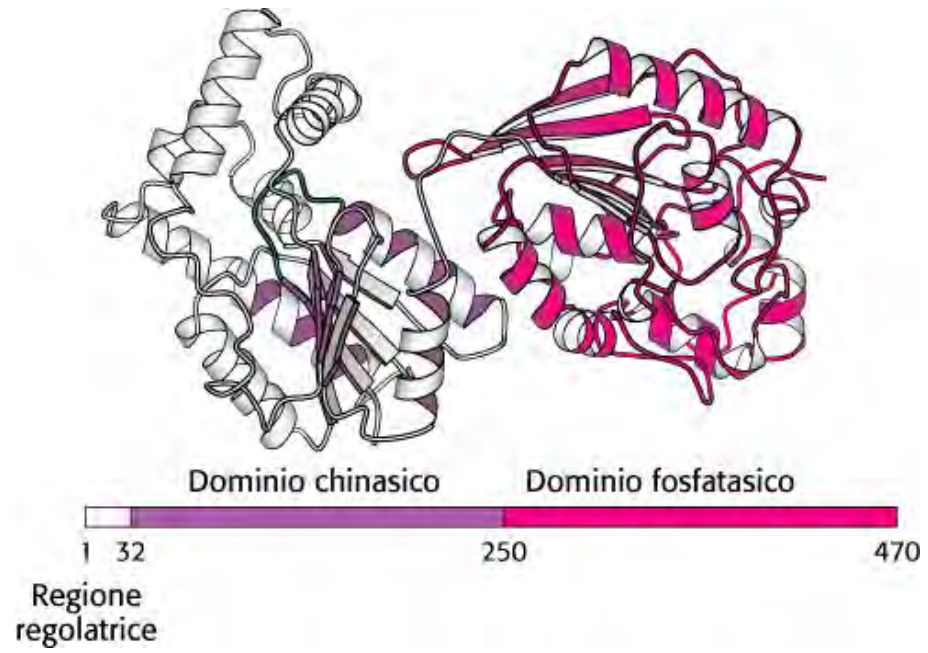


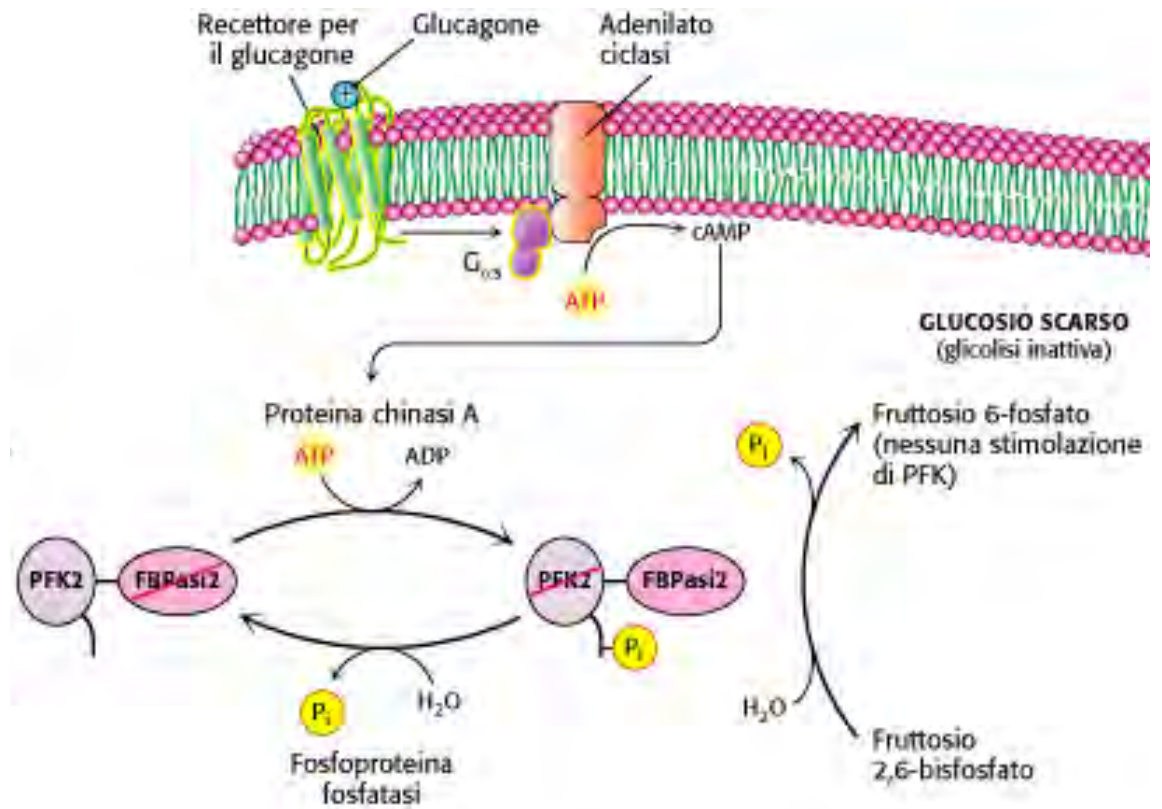


Fructose 2,6-bisphosphate



(a)

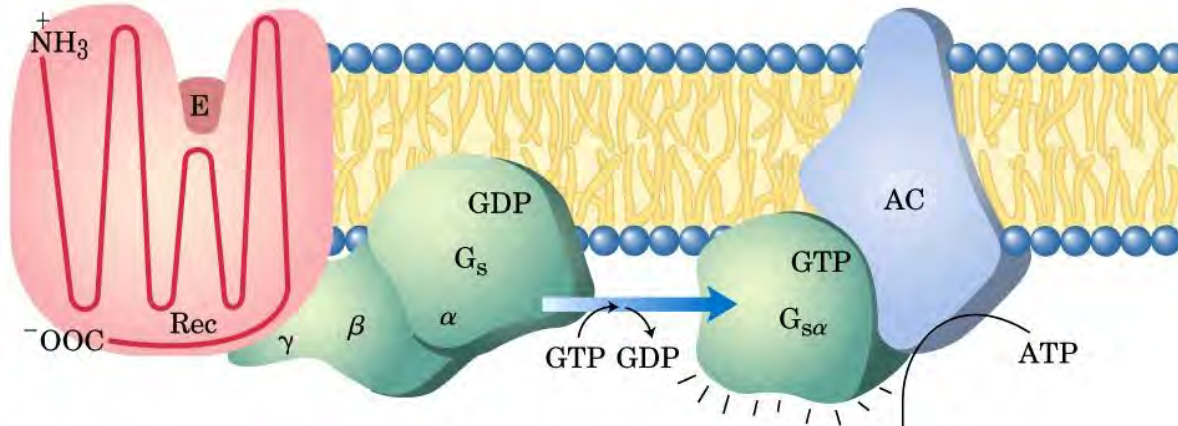




RECETTORE PER L'ADRENALINA, PROTEINE G, ED ADENILATO CICLASI

①

Epinephrine binds to its specific receptor.



②

The occupied receptor causes replacement of the GDP bound to G_s by GTP, activating G_s .

③

G_s (α subunit) moves to adenylyl cyclase and activates it.

④

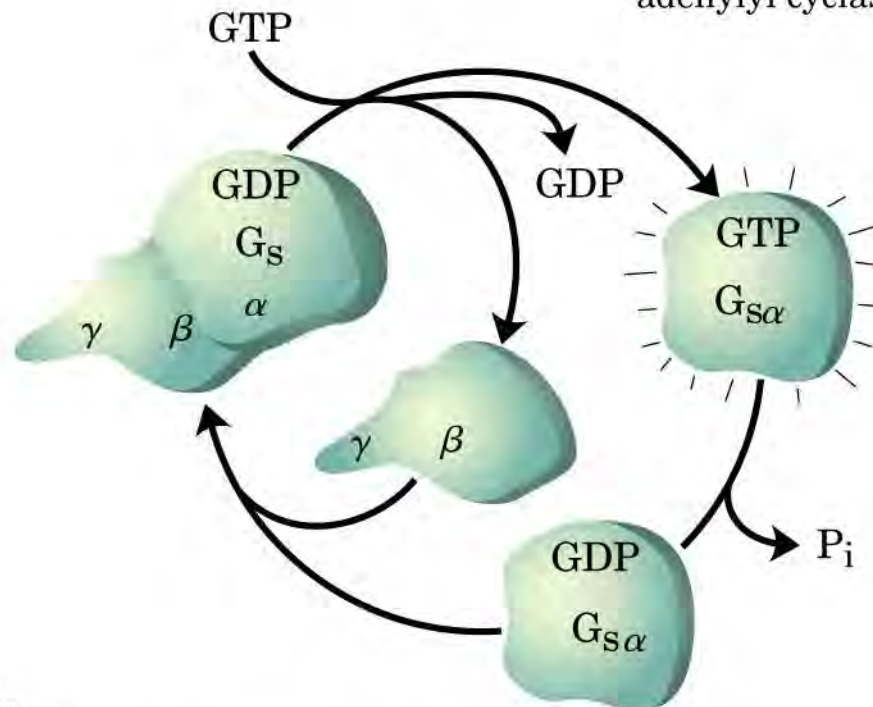
Adenylyl cyclase catalyzes the formation of cAMP.

cAMP

① G_S with GDP bound is turned off; it cannot activate adenylyl cyclase.

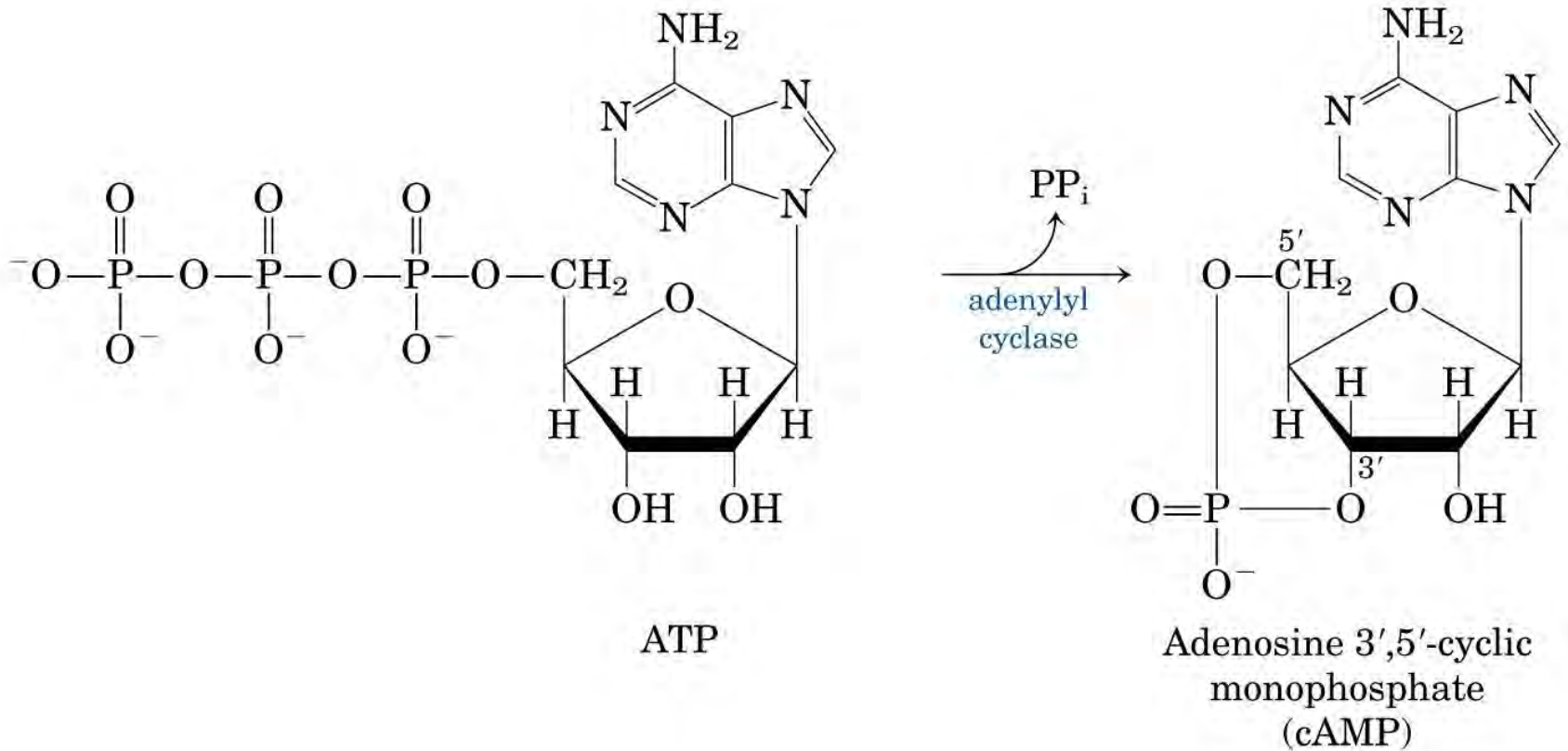
② Contact of G_S with hormone-receptor complex causes displacement of bound GDP by GTP.

③ G_S with GTP bound dissociates into α and $\beta\gamma$ subunits. $G_{S\alpha}$ -GTP is turned on; it can activate adenylyl cyclase.

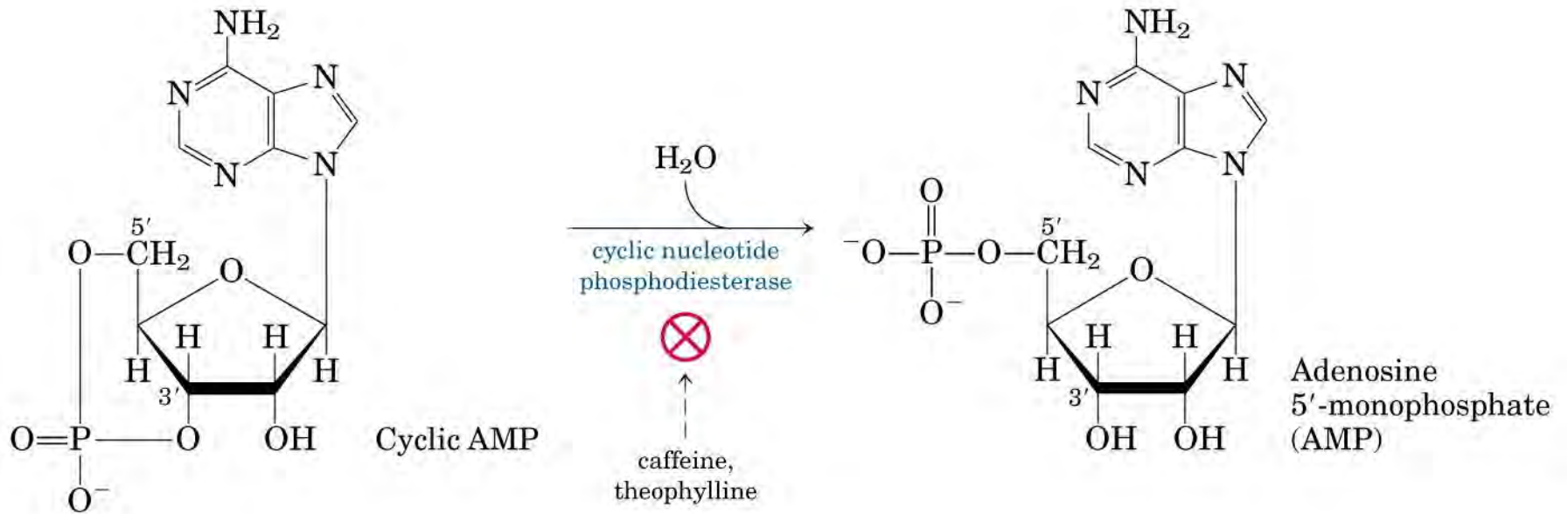


④ GTP bound to $G_{S\alpha}$ is hydrolyzed by the protein's intrinsic GTPase; $G_{S\alpha}$ thereby turns itself off. The inactive α subunit reassociates with the β , γ subunits.

AMP CICLICO (cAMP) sintesi



AMP CICLICO (cAMP) degradazione

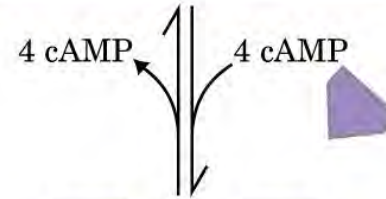
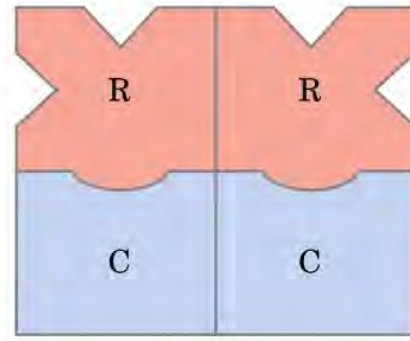


Il cAMP attiva la protein chinasi cAMP-dipendente (PKA)

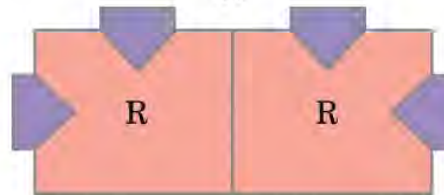
Inactive PKA

Regulatory subunits:
empty cAMP sites

Catalytic subunits:
substrate-binding
sites blocked by
autoinhibitory
domains of R subunits



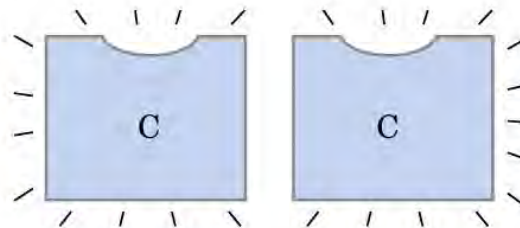
Regulatory subunits:
autoinhibitory
domains buried



+

Active PKA

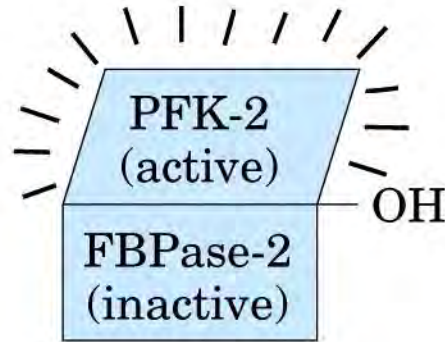
Catalytic subunits:
open substrate-
binding sites



(a)

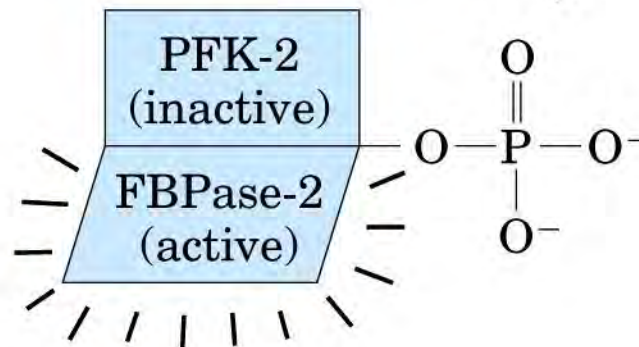
↑ [Fructose 2,6-bisphosphate]

Stimulates glycolysis,
inhibits gluconeogenesis

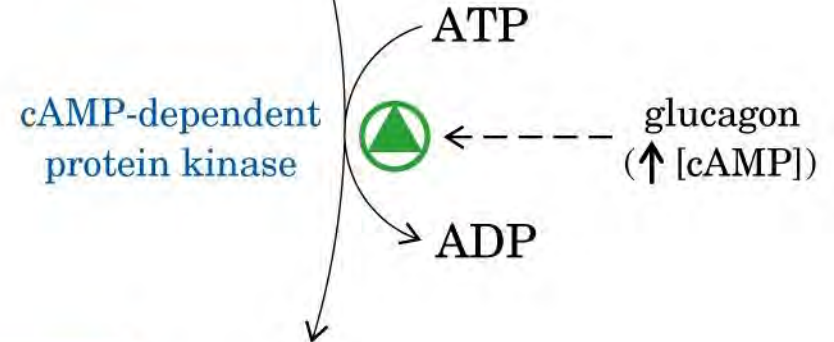


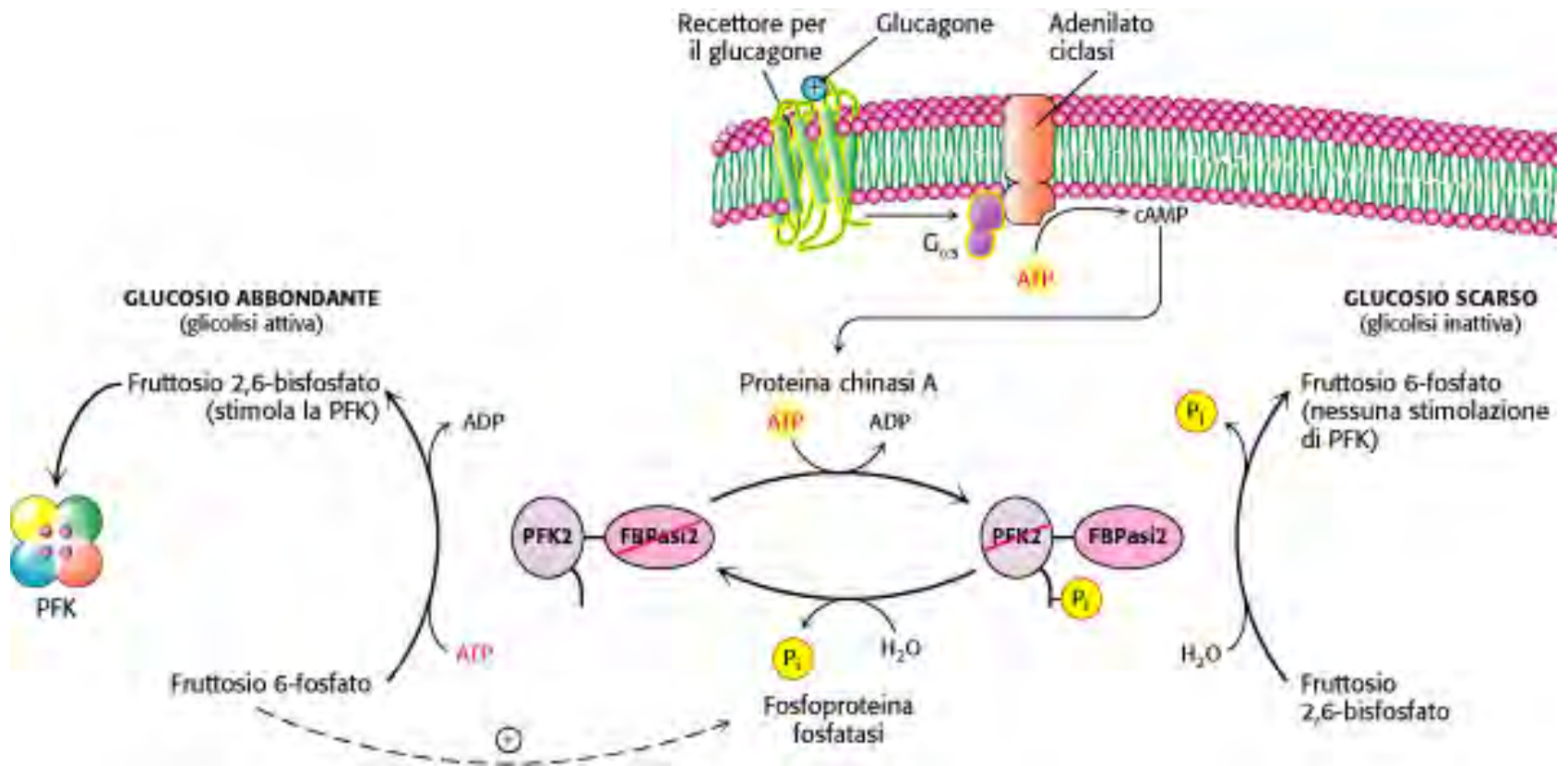
↓ [Fructose 2,6-bisphosphate]

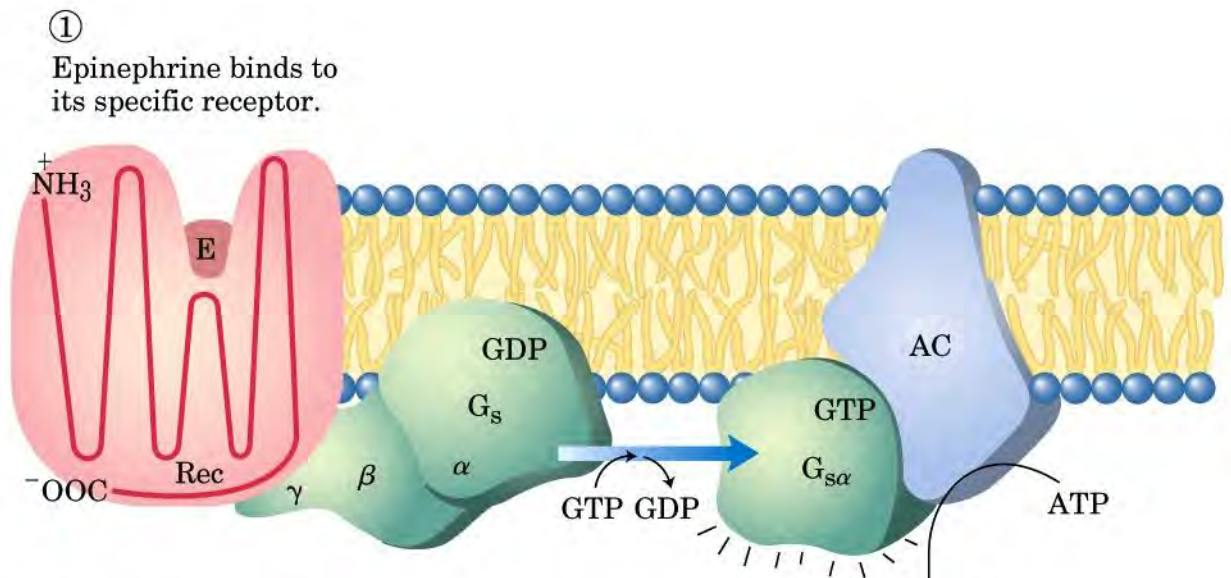
Inhibits glycolysis,
stimulates gluconeogenesis



(b)





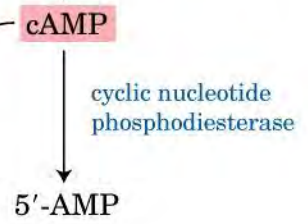


② The occupied receptor causes replacement of the GDP bound to G_s by GTP, activating G_s .

③ G_s (α subunit) moves to adenylyl cyclase and activates it.

④ Adenylyl cyclase catalyzes the formation of cAMP.

⑤ PKA is activated by cAMP.



⑥ Phosphorylation of cellular proteins by PKA causes the cellular response to epinephrine.

⑦ cAMP is degraded, reversing the activation of PKA.