Universidade de São Paulo

Metabolismo

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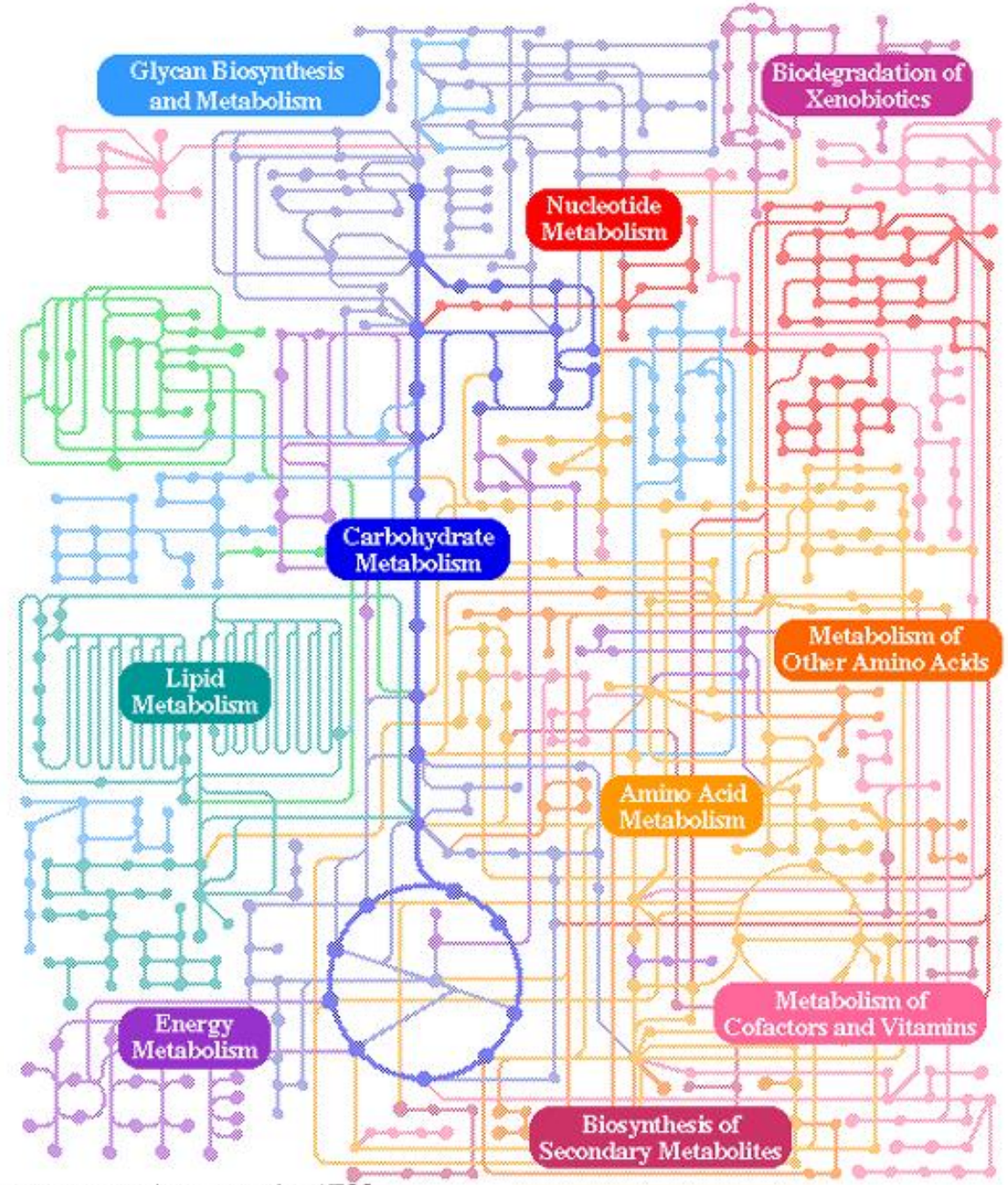
Bioquímica e Metabolismo Animal

Metabolismo

- Soma de todas as reações bioquímicas catalisadas por enzimas que ocorrem nos organismos vivos
  - obtenção e utilização de energia
  - síntese de moléculas estruturais e funcionais
  - crescimento e desenvolvimento celular
  - remoção de produtos de excreção

Metabolismo

- Energia química extraída de nutrientes simples
  - carboidratos, proteínas e lipídeos
- Processos químicos celulares
  - rede de reações enzimáticas interligadas
- A energia liberada conservada
  - ATP (trifosfato de adenosina)
  - NADPH (nicotinamida adenina dinucleotídeo fosfato)
- Biossíntese a partir de precursores simples



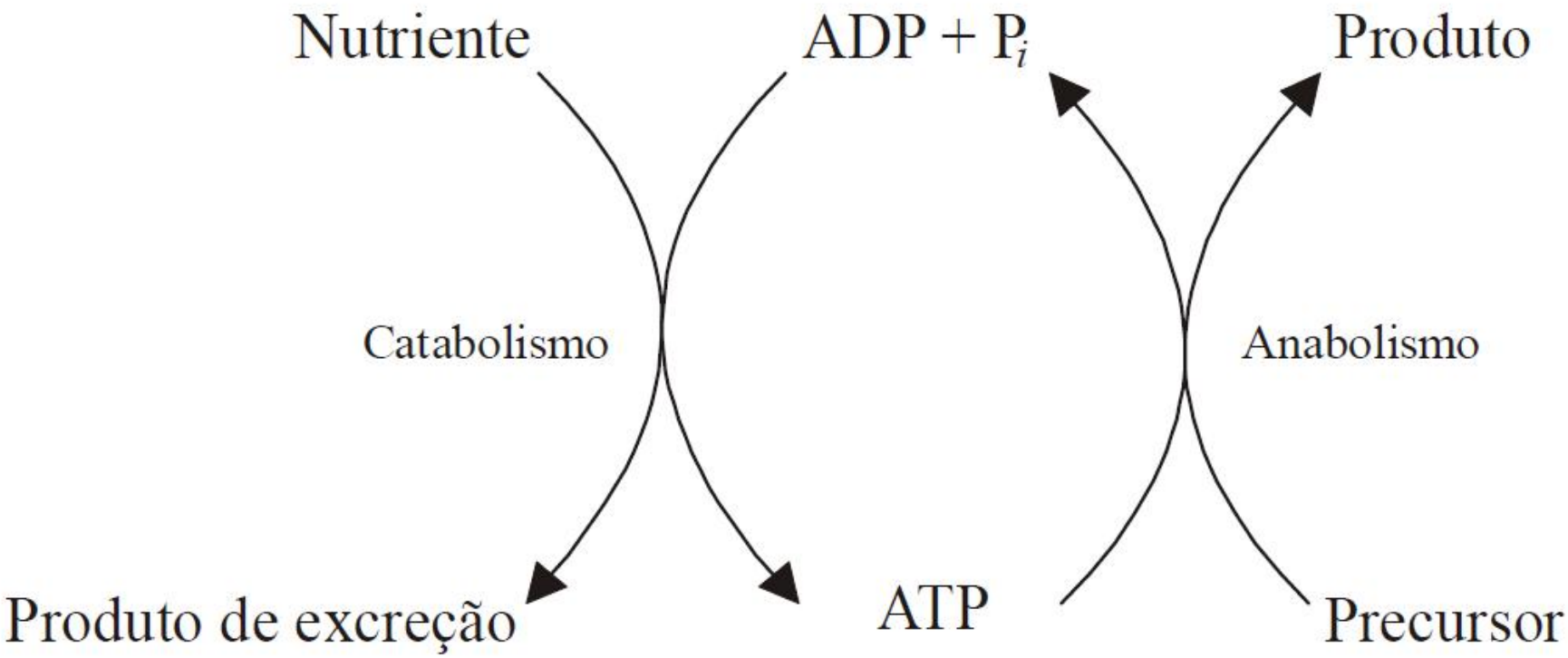
01100 5/31/04 Image source from KEGG

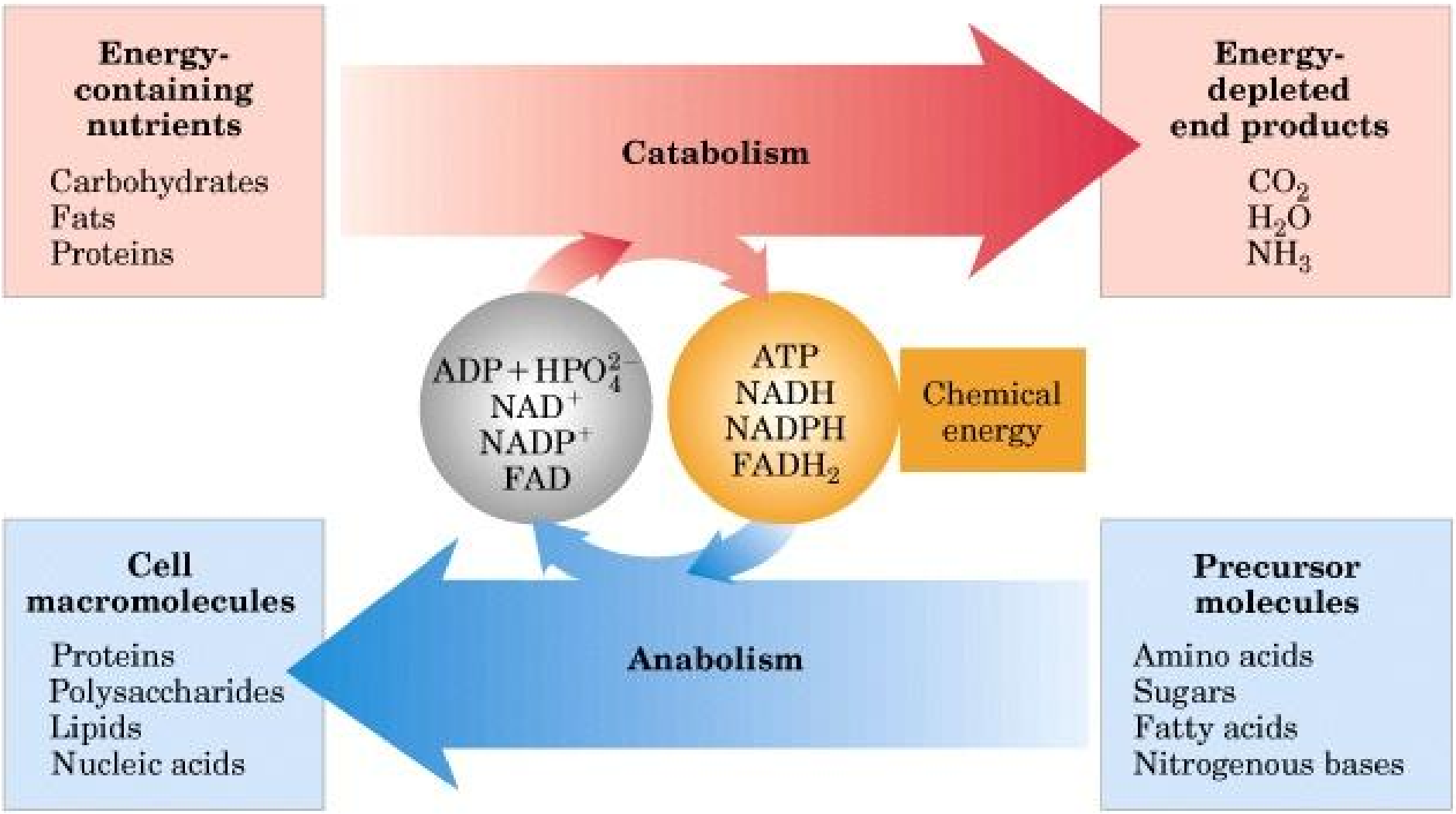
Metabolismo

- Catabolismo: processos de degradação
  - Nutrientes complexos degradados para geração de energia
  - Oxidação exergônica

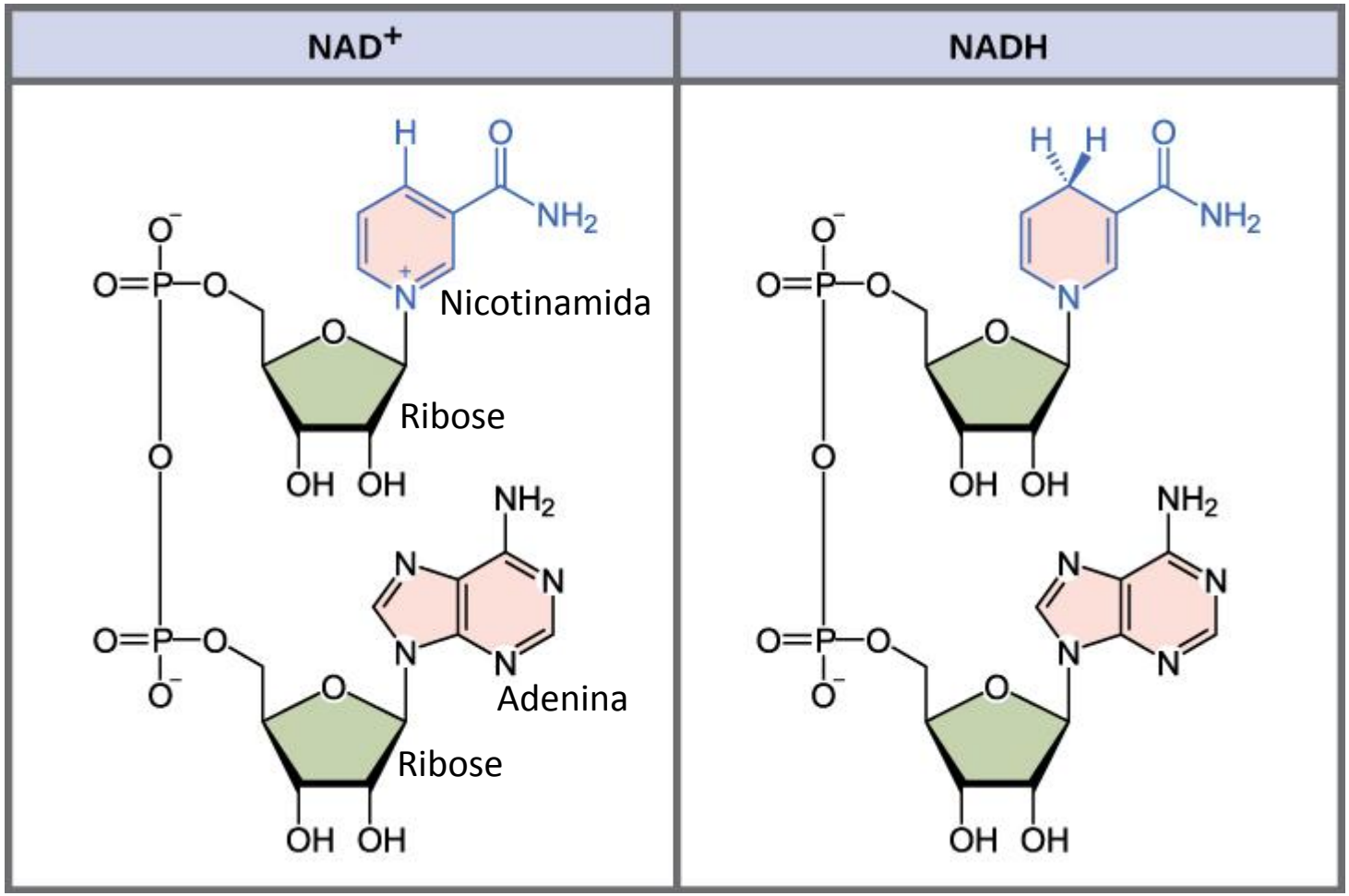
- Anabolismo: processos de biossíntese
  - Síntese endergônica de moléculas biológicas a partir de precursores simples
  - Acopladas a processos exergônicos através de compostos de alta energia

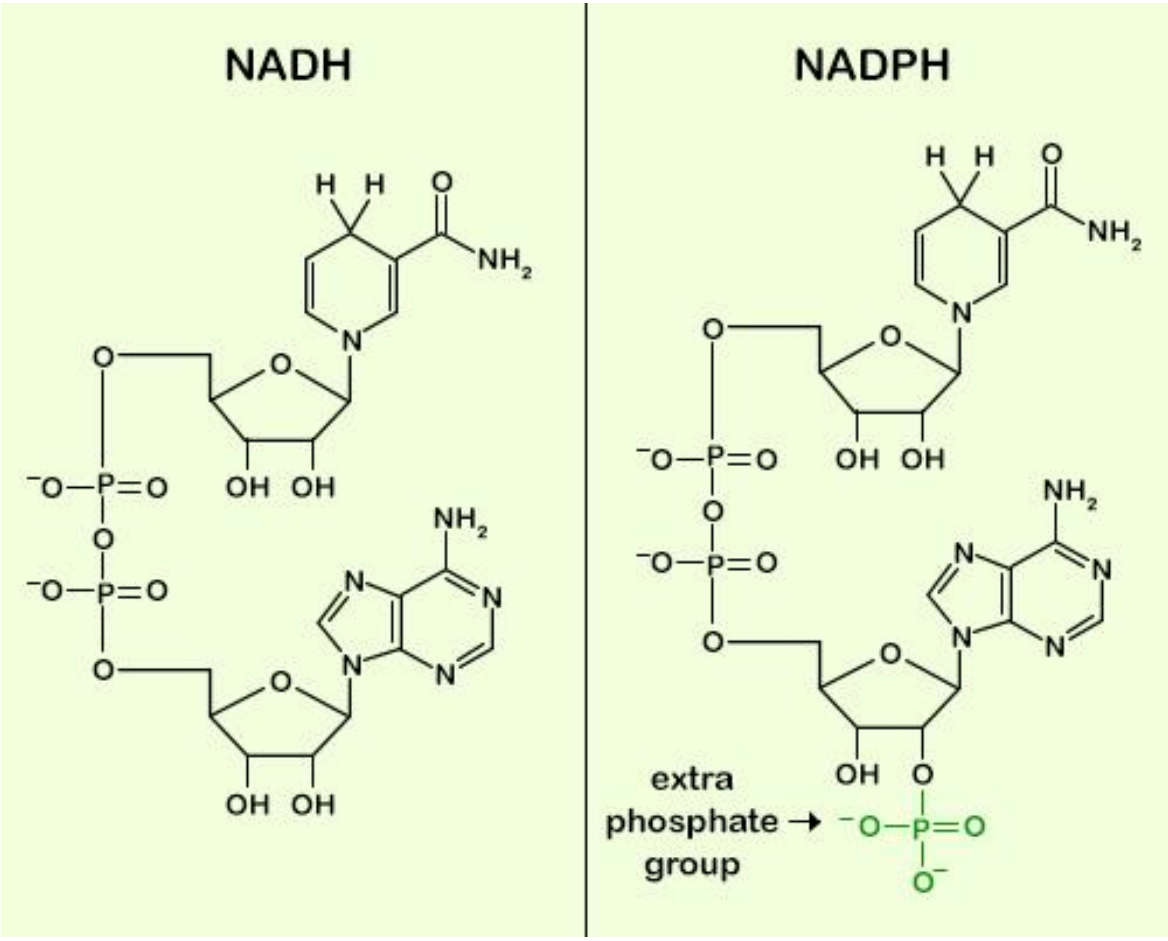
Metabolismo




Energy-containing nutrients
Carbohydrates
Fats
Proteins
Catabolism
Energy-depleted end products
CO_2
H_2O
NH_3
$ADP + HPO_4^{2-}$
NAD^+
$NADP^+$
FAD
ATP
NADH
NADPH
$FADH_2$
Chemical energy
Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Anabolism
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases

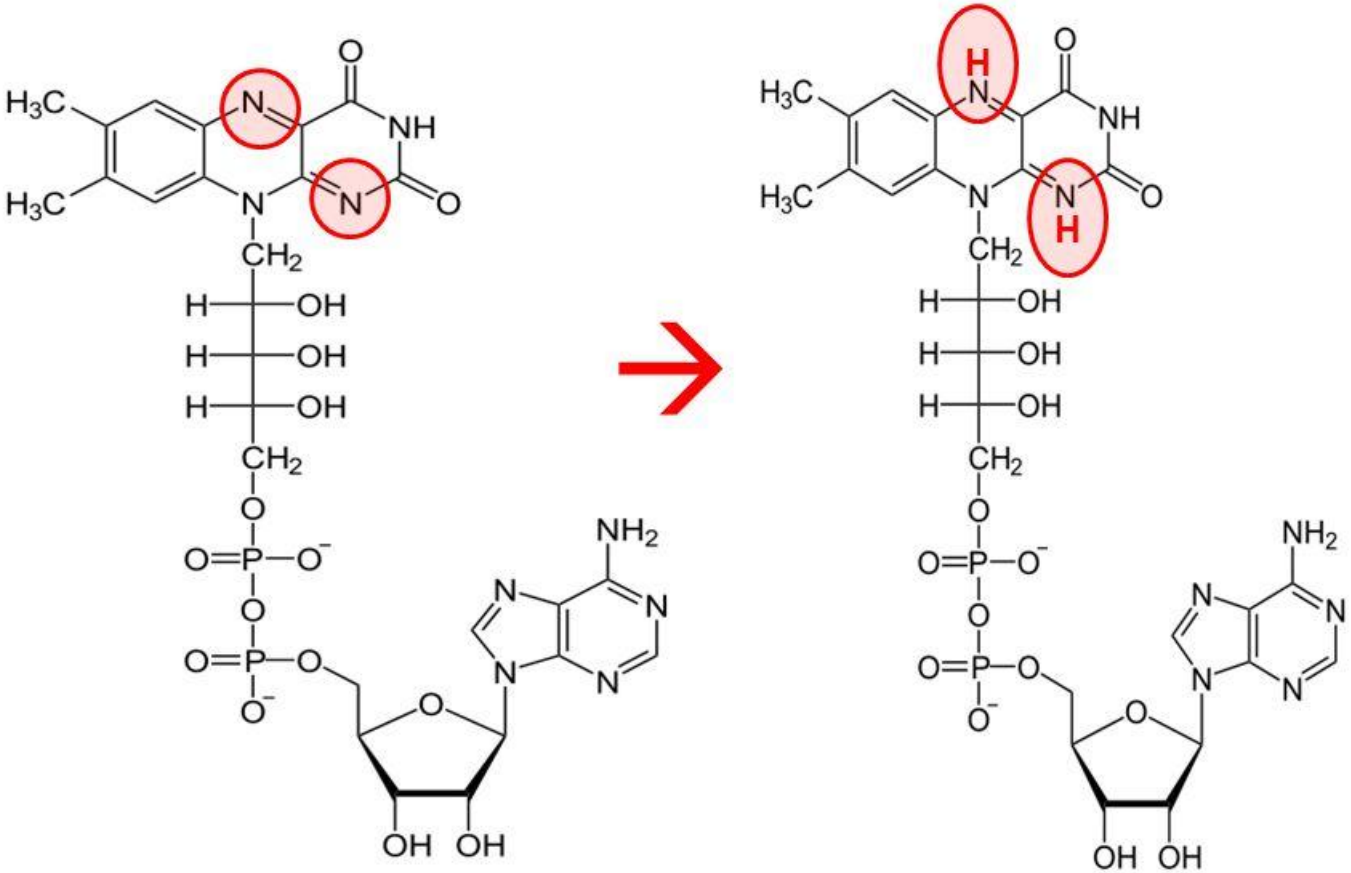
Nicotinamida Adenina Dinucleotídeo

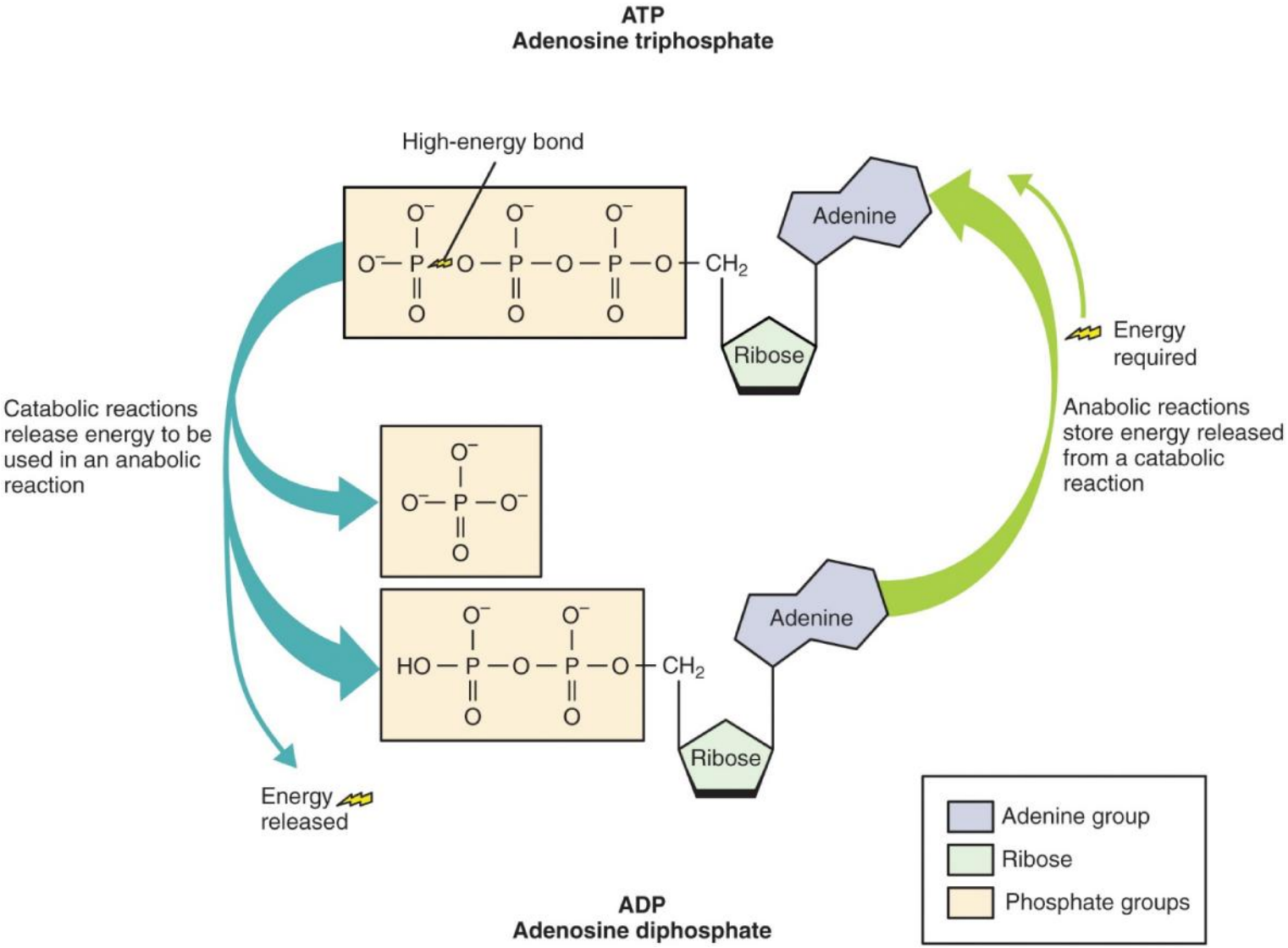



NADH
NADPH
extra
phosphate
group

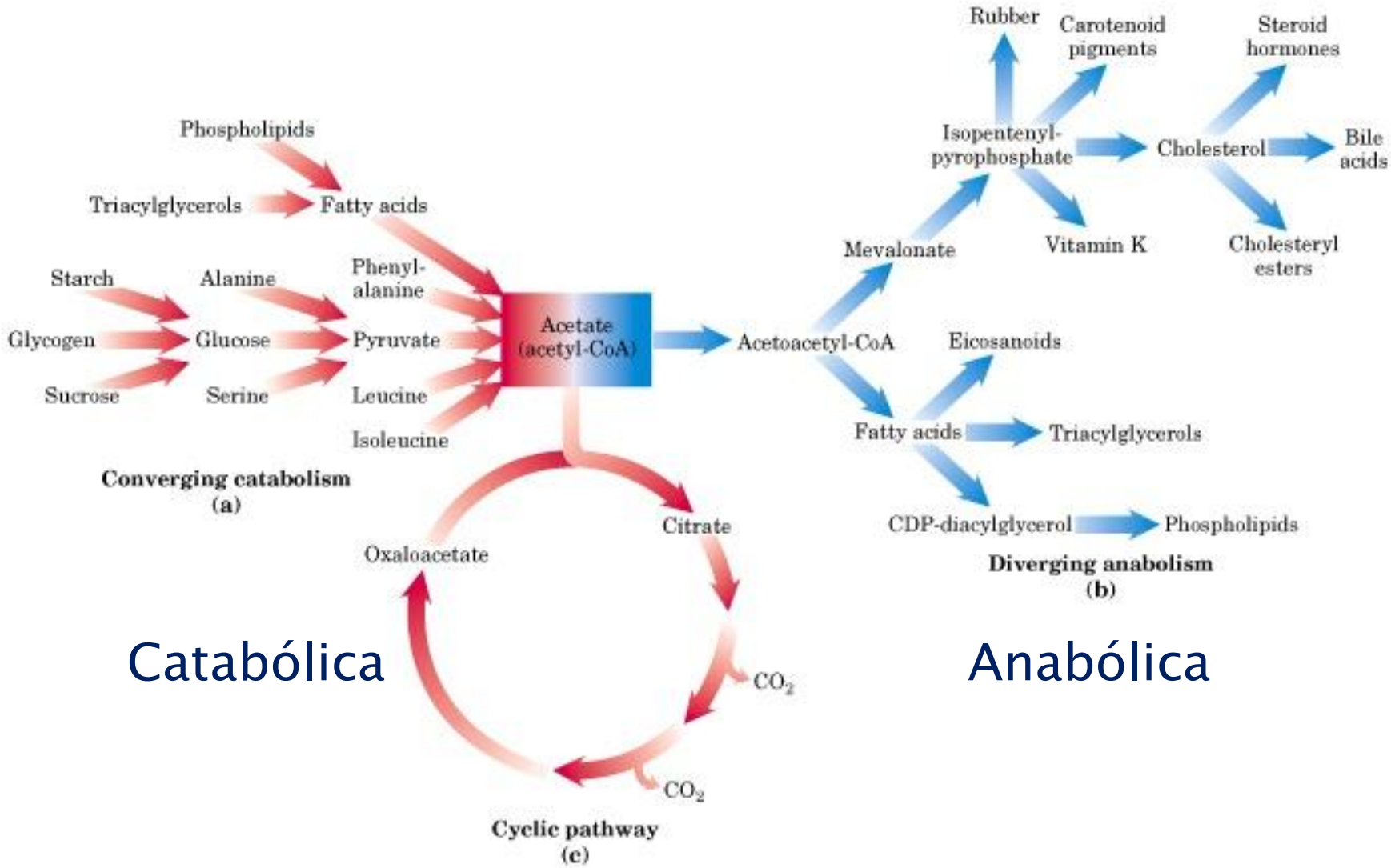
FAD→FADH2

Flavin Adenine Dinucleotide




ATP
Adenosine triphosphate
High-energy bond
Adenine
Ribose
Energy required
Catabolic reactions release energy to be used in an anabolic reaction
Anabolic reactions store energy released from a catabolic reaction
Adenine
Ribose
Energy released
Adenine group
Ribose
Phosphate groups
ADP
Adenosine diphosphate

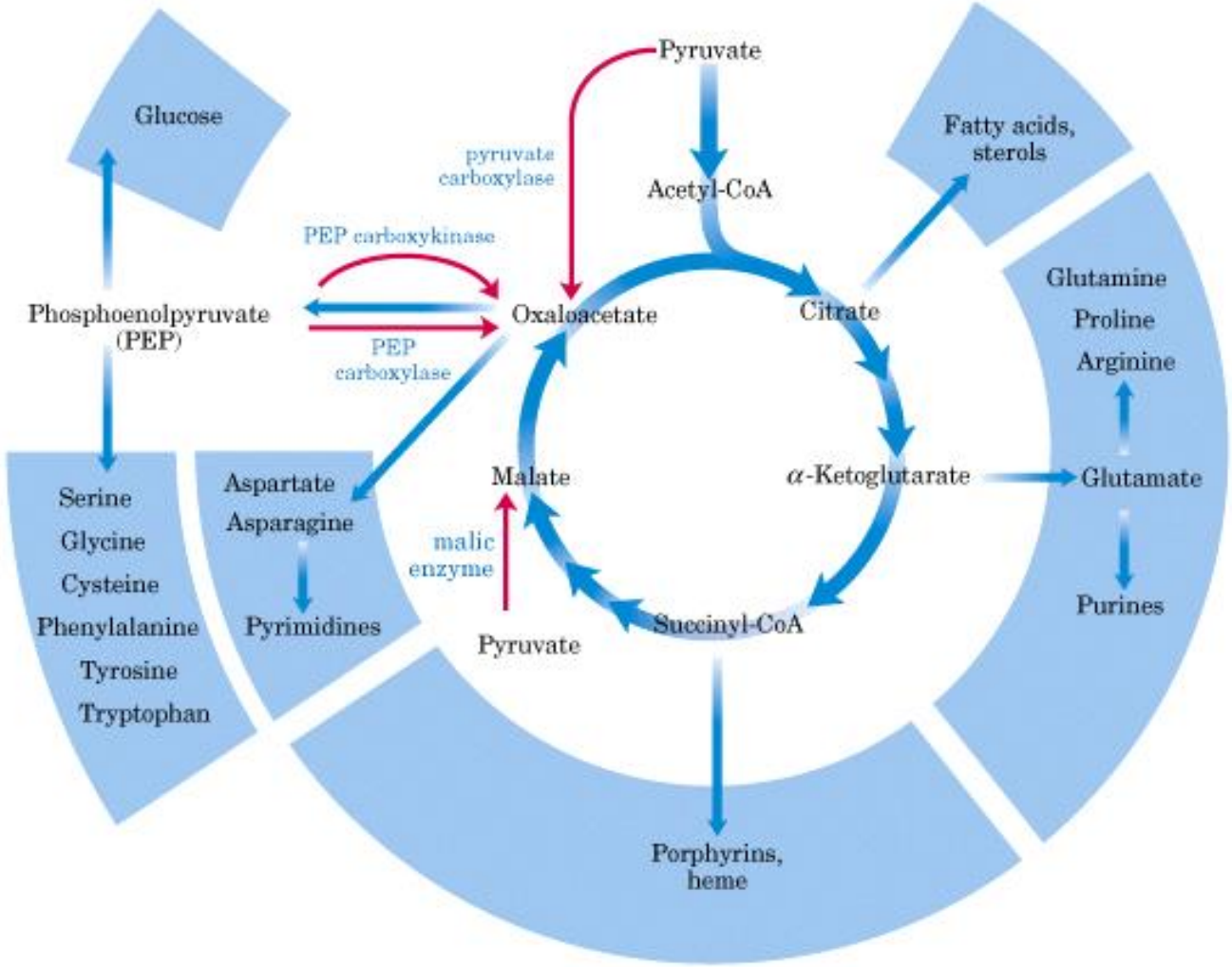
3 tipos de rotas não-lineares:
Convergente, cíclica ou divergente



Catabólica

Anabólica

- Rota anfibólica
  - Catabolismo de CHO, ác. graxos, aminoácidos
  - Precursores para diversas rotas biosintéticas



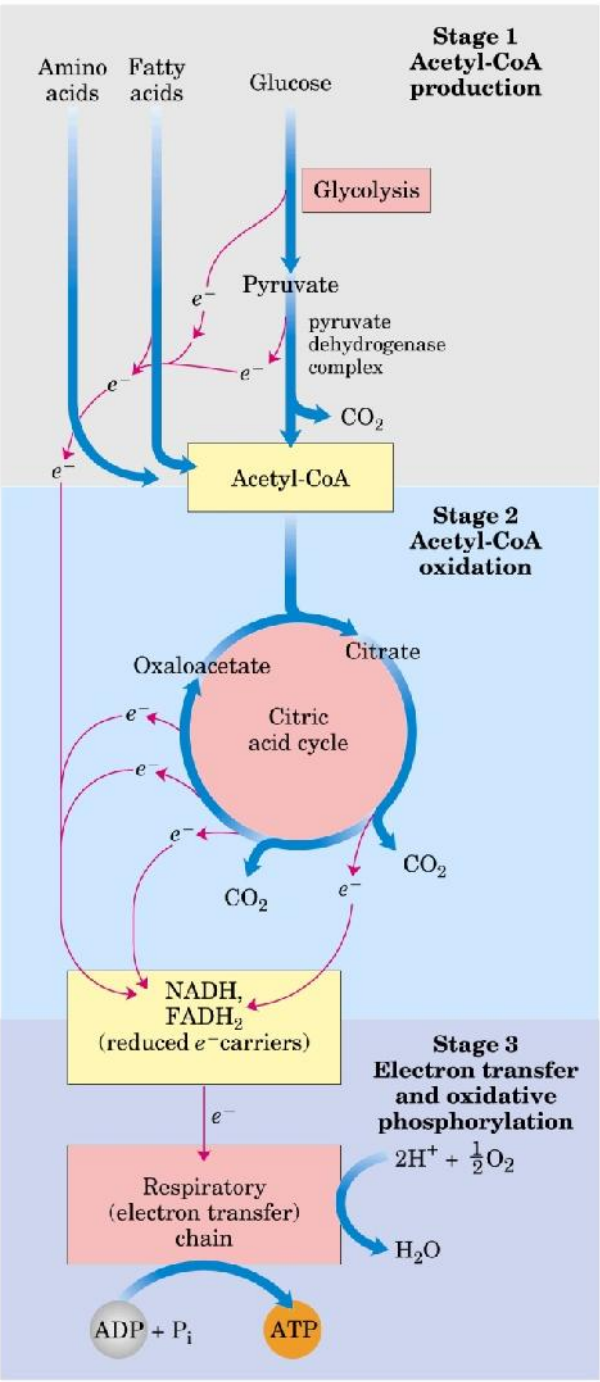
Mudança de energia livre (ΔG) expressa a força que leva reação (condições padrões: 25°C, 1 atm) em direção ao equilíbrio.

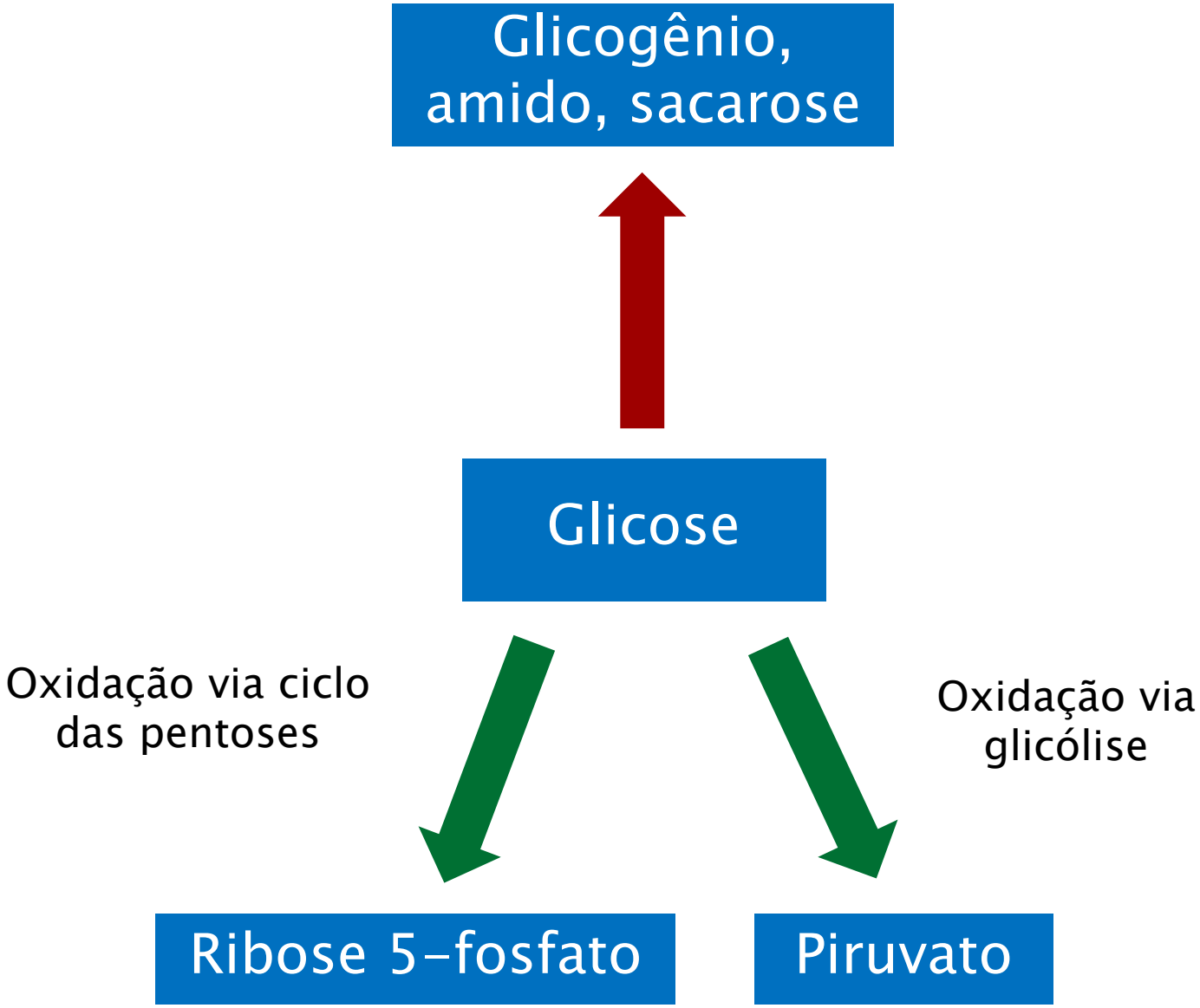
$$\Delta G'^{\circ} = -RT \ln K'_{eq}$$

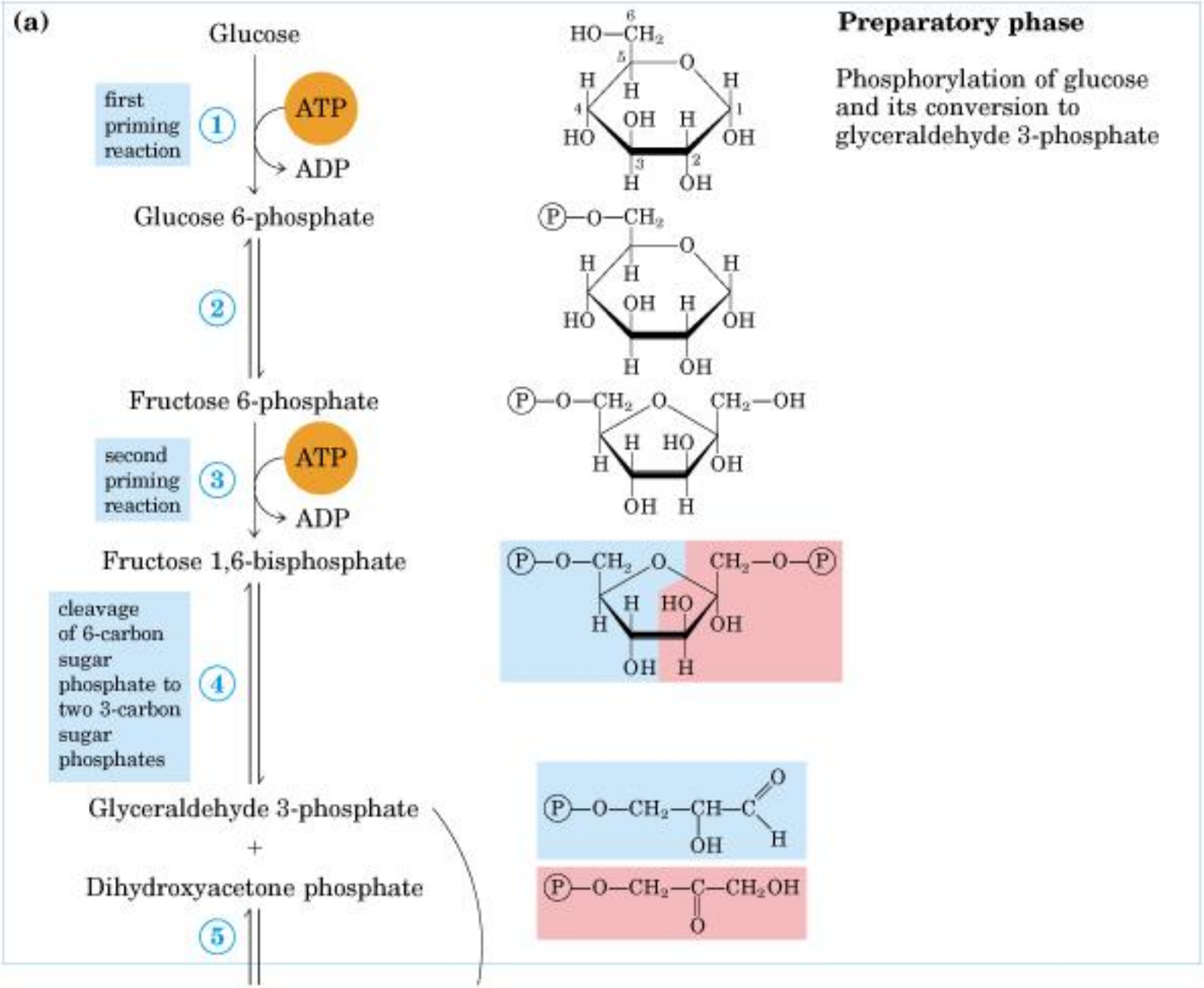
Relationships among K'_{eq}, $\Delta G'^{\circ}$, and the Direction of Chemical Reactions under Standard Conditions

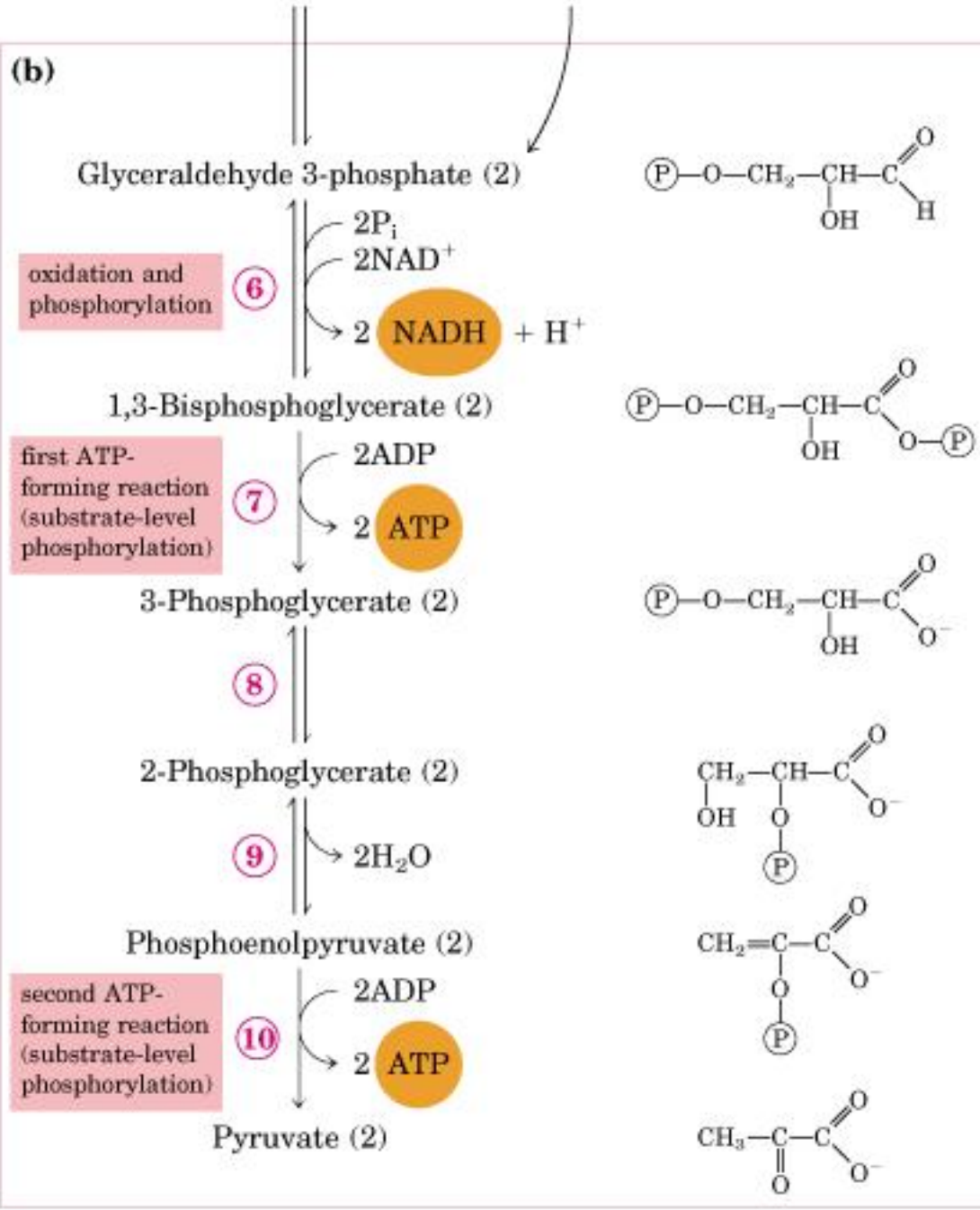
When K'_{eq} is	$\Delta G'^{\circ}$ is	Starting with 1 M components the reaction
>1.0	Negative	Proceeds forward
1.0	Zero	Is at equilibrium
<1.0	Positive	Proceeds in reverse

Metabolismo de carboidratos


Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
CO_2
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Oxaloacetate
Citrate
Citric acid cycle
CO_2
CO_2
NADH, $FADH_2$
(reduced e^-carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
$2H^+ + \frac{1}{2}O_2$
Respiratory (electron transfer) chain
H_2O
ADP + P_i
ATP


Glicogênio, amido, sacarose
Glicose
Oxidação via ciclo das pentoses
Oxidação via glicólise
Ribose 5-fosfato
Piruvato


(a)
Glucose
first priming reaction
1
ATP
ADP
Glucose 6-phosphate
2
Fructose 6-phosphate
second priming reaction
3
ATP
ADP
Fructose 1,6-bisphosphate
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
4
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate

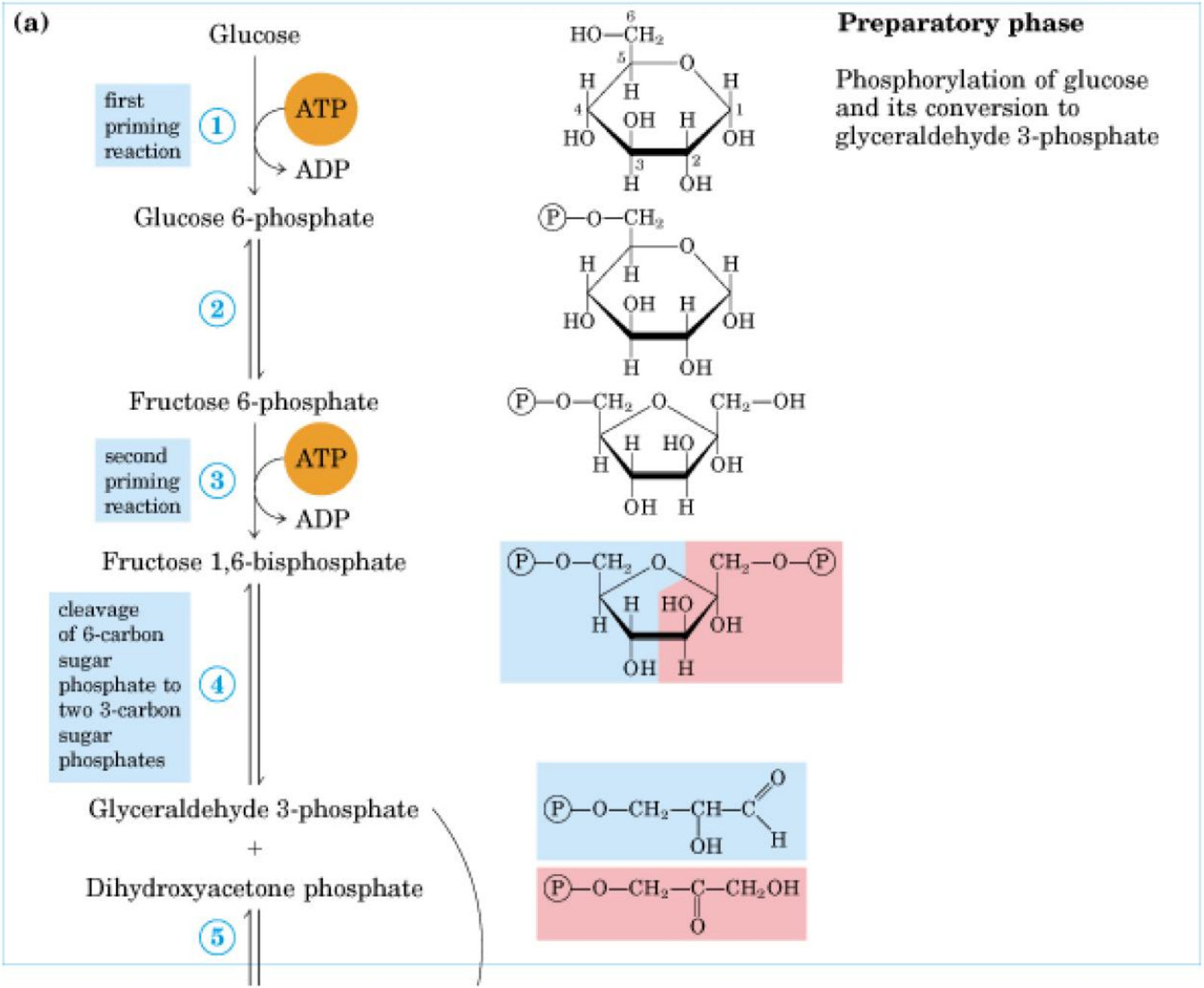


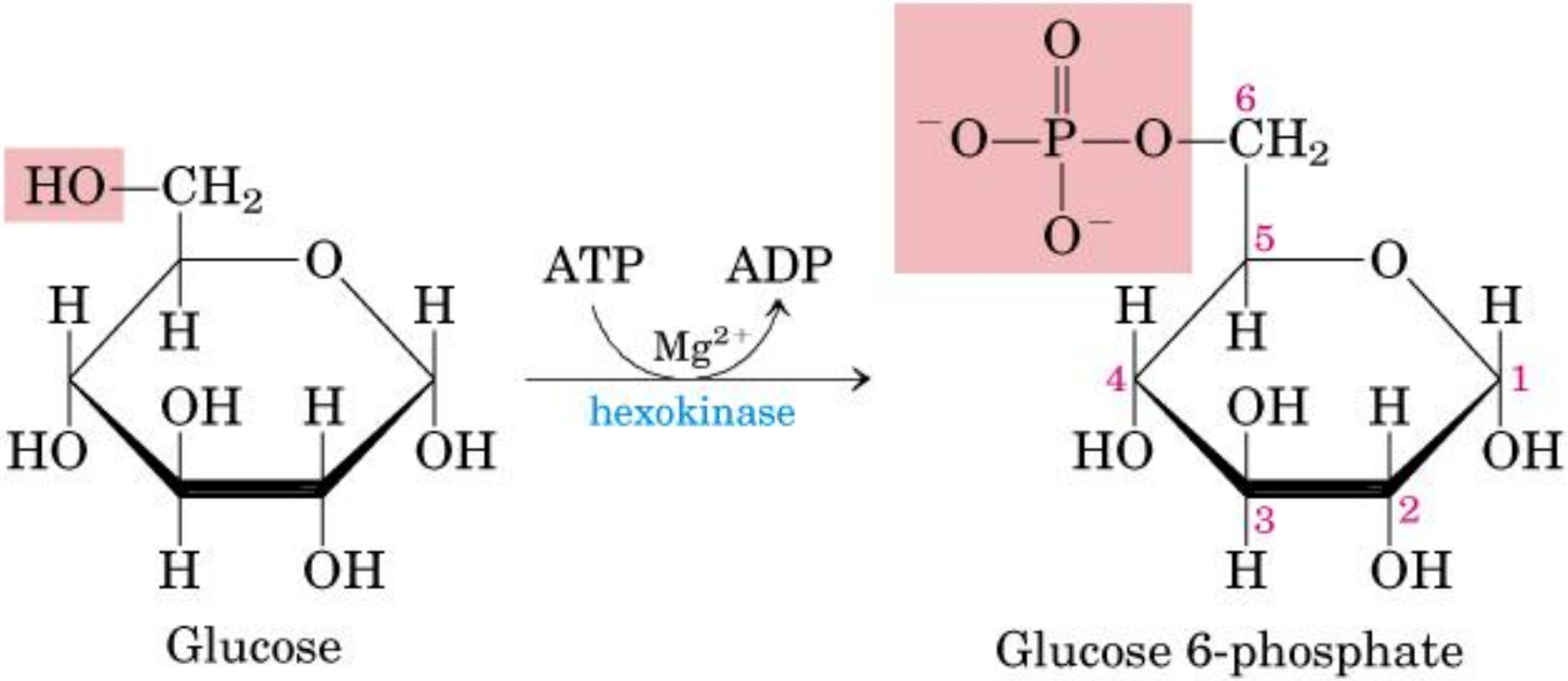
Payoff phase

Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH

Intermediários fosforilados

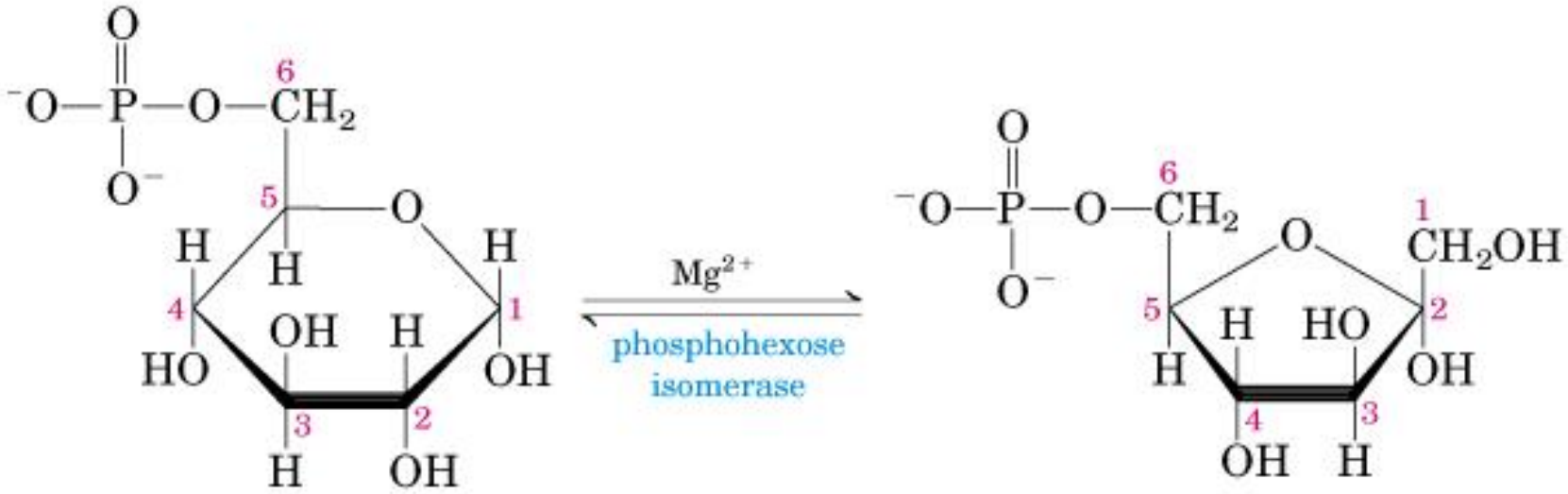
- Qual a importância do grupo fosforil?
  - Ionizáveis em pH 7, resultando em intermediários com carga negativa: não deixam a célula
  - Grupo fosforil é componente essencial na conservação enzimática de energia metabólica
  - Energia resultante da ligação de grupos fosfatos a sítio ativo de enzimas reduz energia de ativação.
    - Formam complexos com Mg^{2+}: sítios de ligação de várias enzimas são específicos para esses complexos


(a)
Glucose
first priming reaction
1
ATP
ADP
Glucose 6-phosphate
2
Fructose 6-phosphate
second priming reaction
3
ATP
ADP
Fructose 1,6-bisphosphate
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
4
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5
Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate



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

Hepatócitos: glucokinase
Controle alostérico pelo produto

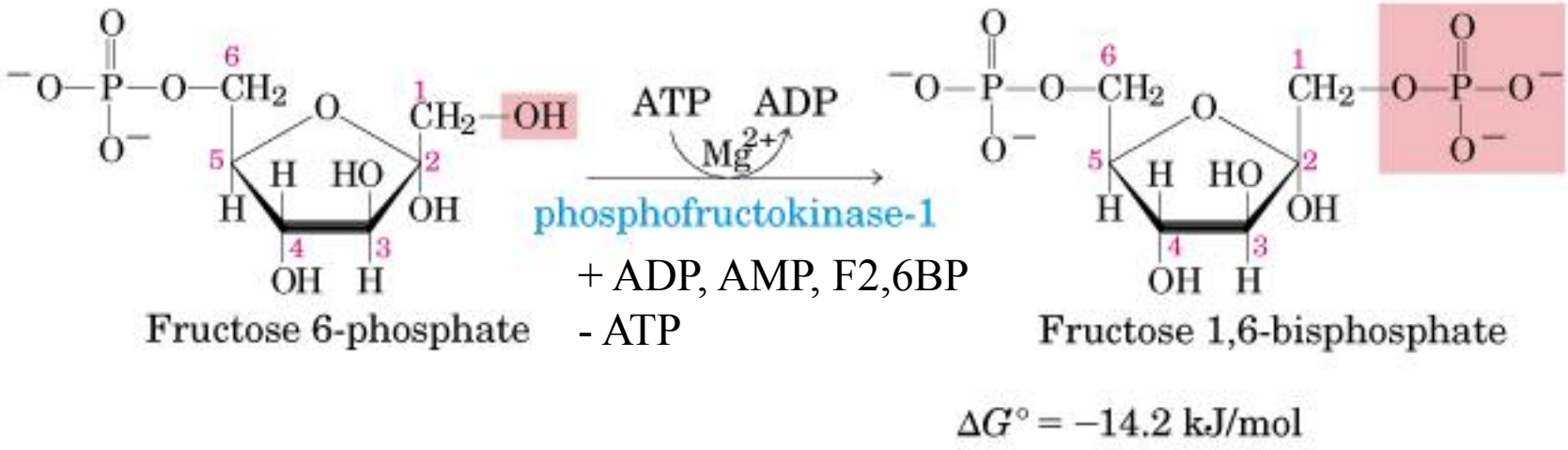


Glucose 6-phosphate

Fructose 6-phosphate

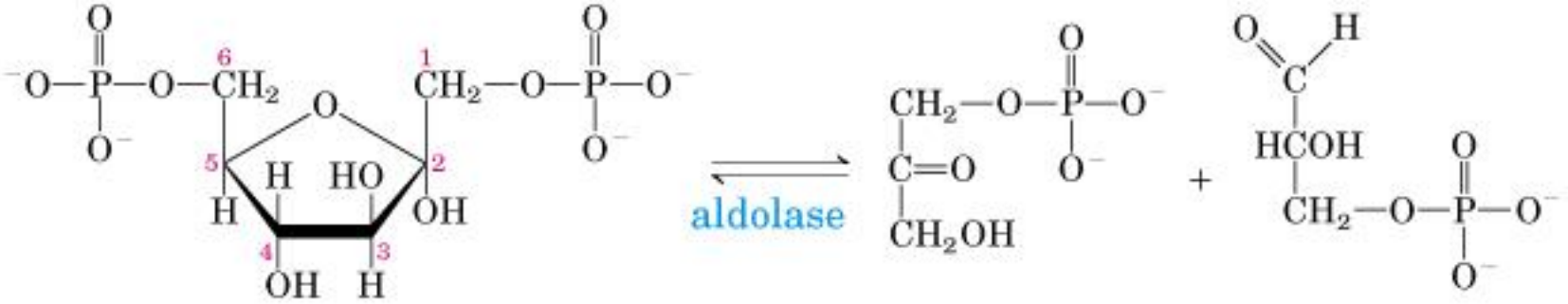
$\Delta G'^{\circ} = 1.7$ kJ/mol

Ponto de regulação



+ ADP, AMP, F2,6BP
- ATP

$\Delta G^\circ = -14.2$ kJ/mol

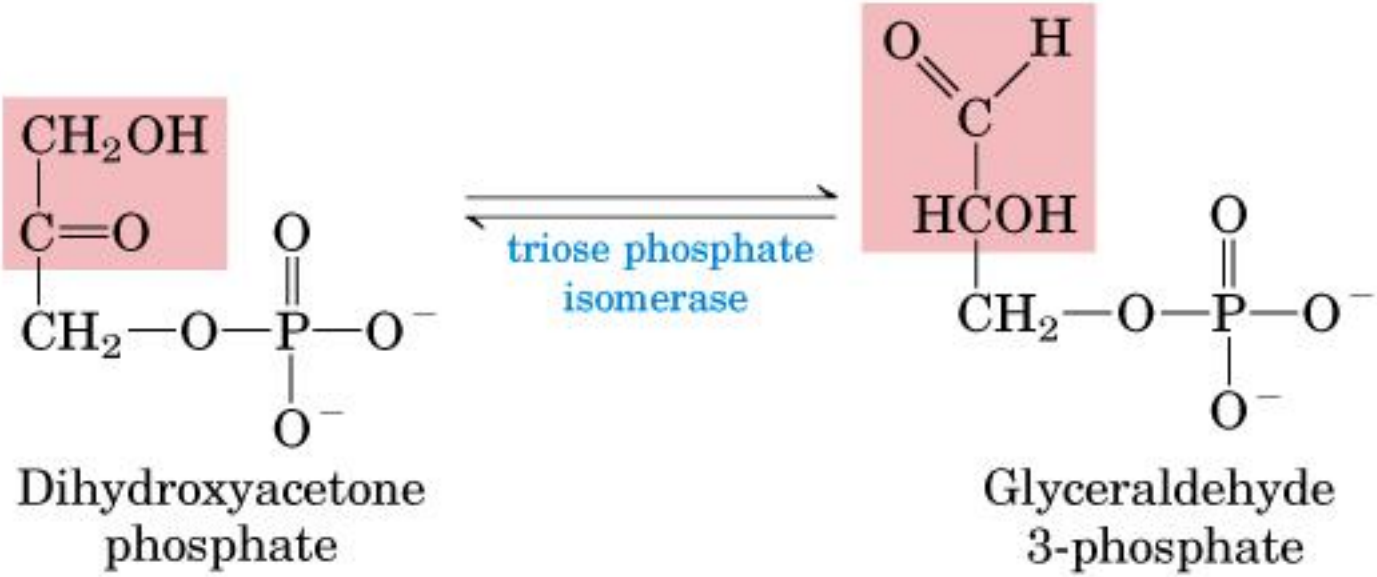


Fructose 1,6-bisphosphate

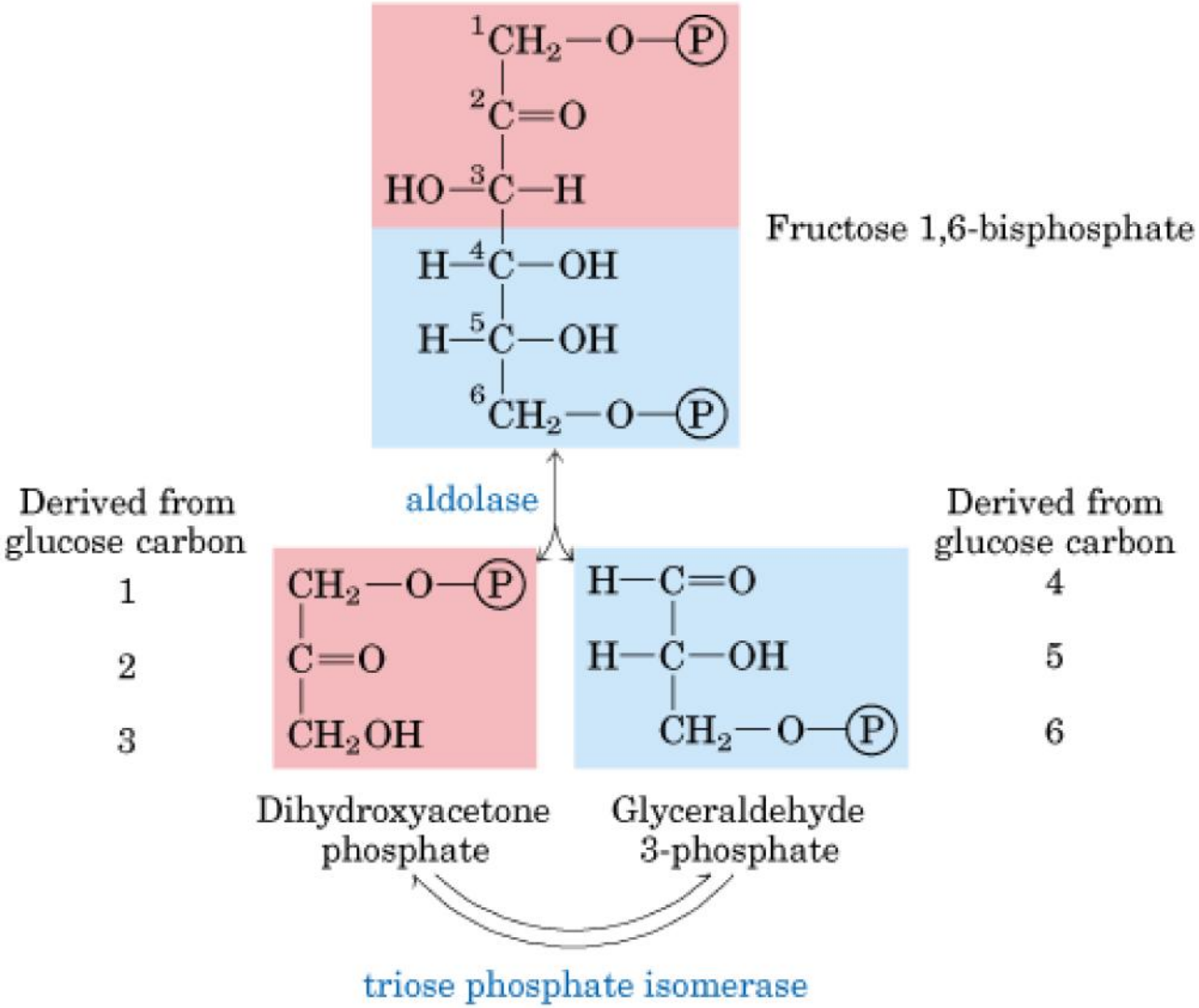
Dihydroxyacetone phosphate

Glyceraldehyde 3-phosphate

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



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


Fructose 1,6-bisphosphate
aldolase
Derived from glucose carbon
1
2
3
Derived from glucose carbon
4
5
6
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate
triose phosphate isomerase

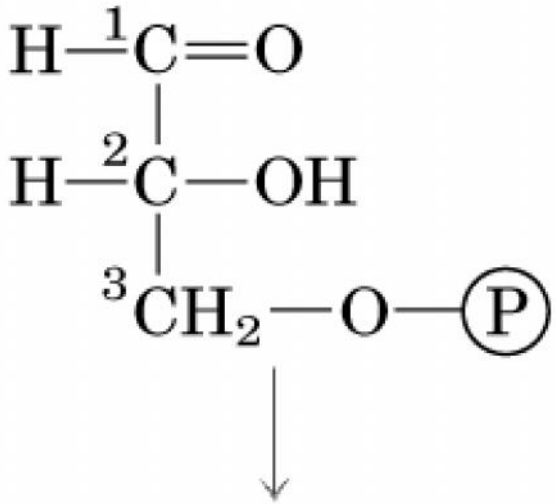
(a)

Derived from glucose carbons

4 or 3

5 or 2

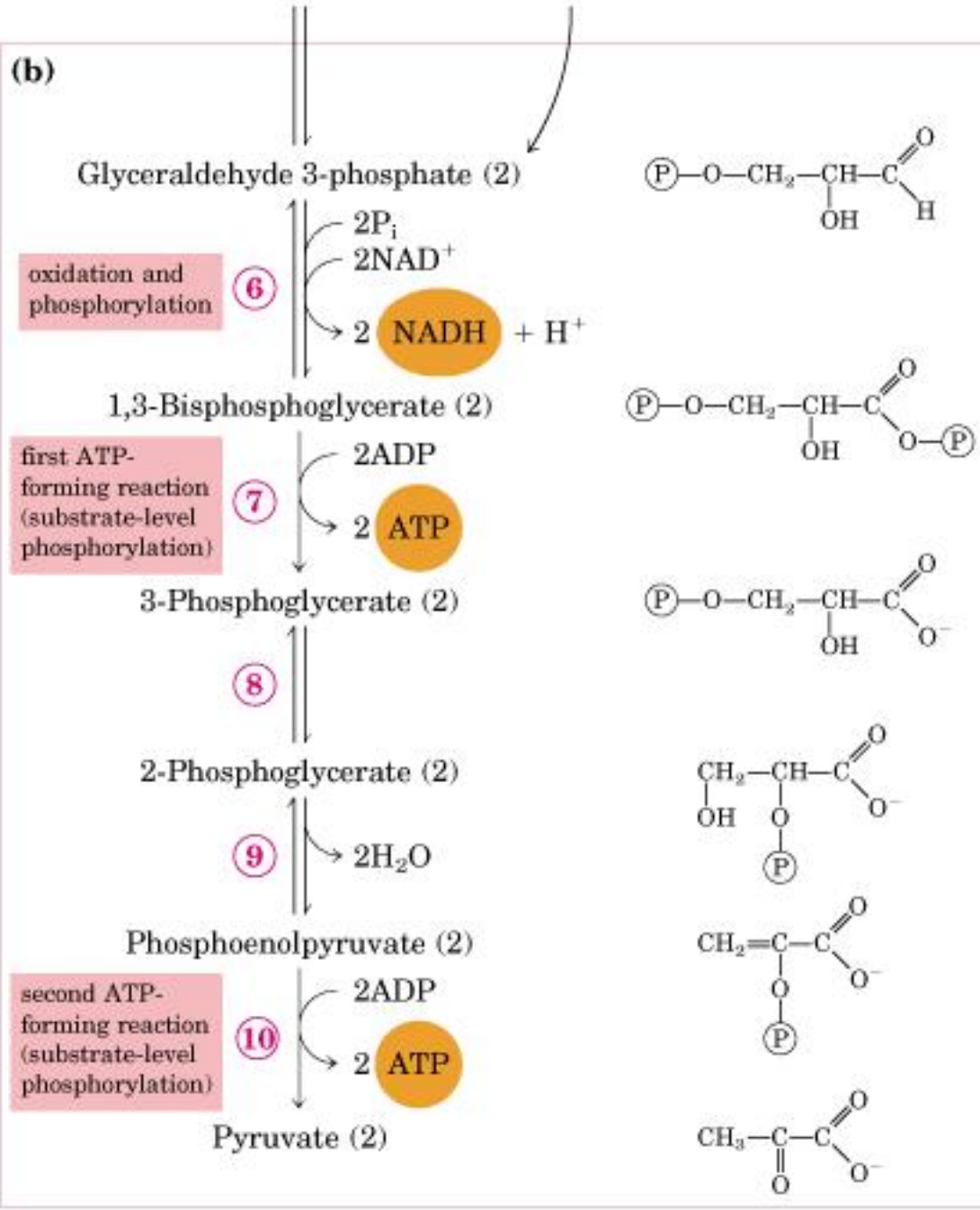
6 or 1



D-Glyceraldehyde 3-phosphate

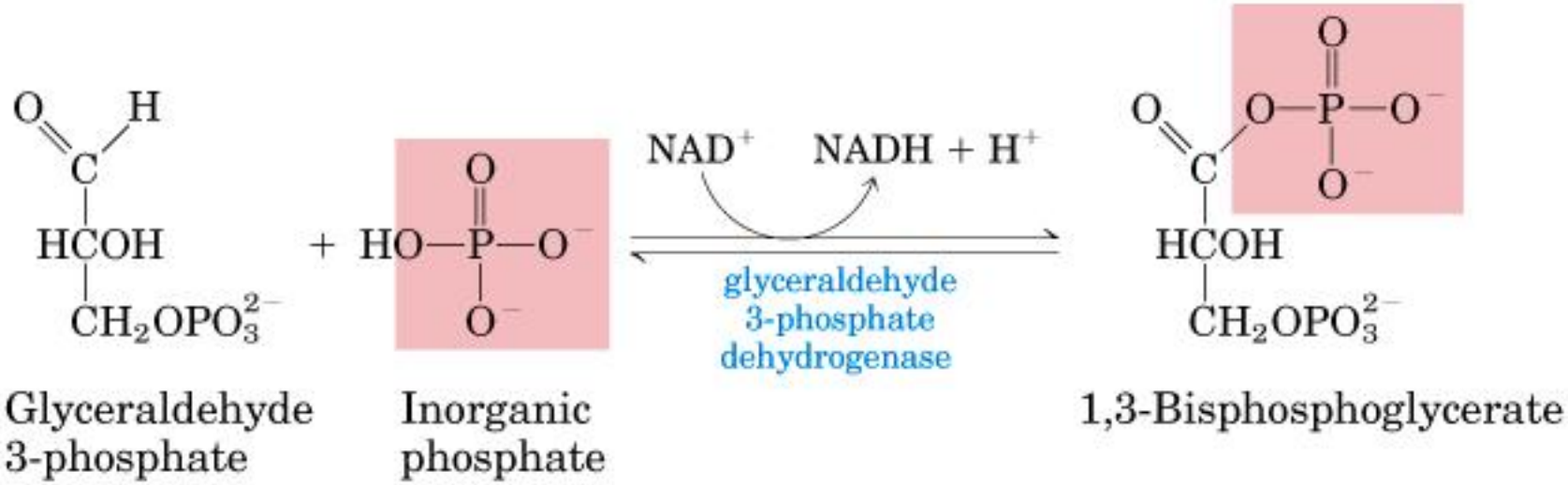
Subsequent reactions of glycolysis

(b)

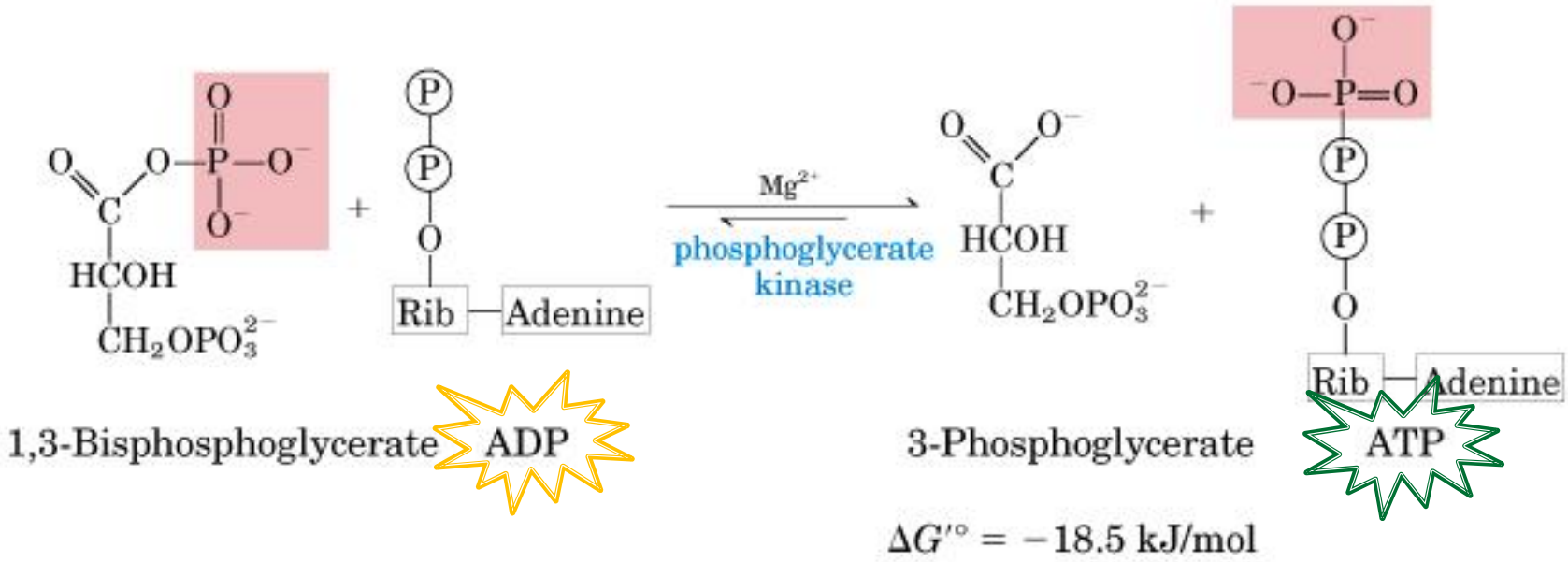


Payoff phase

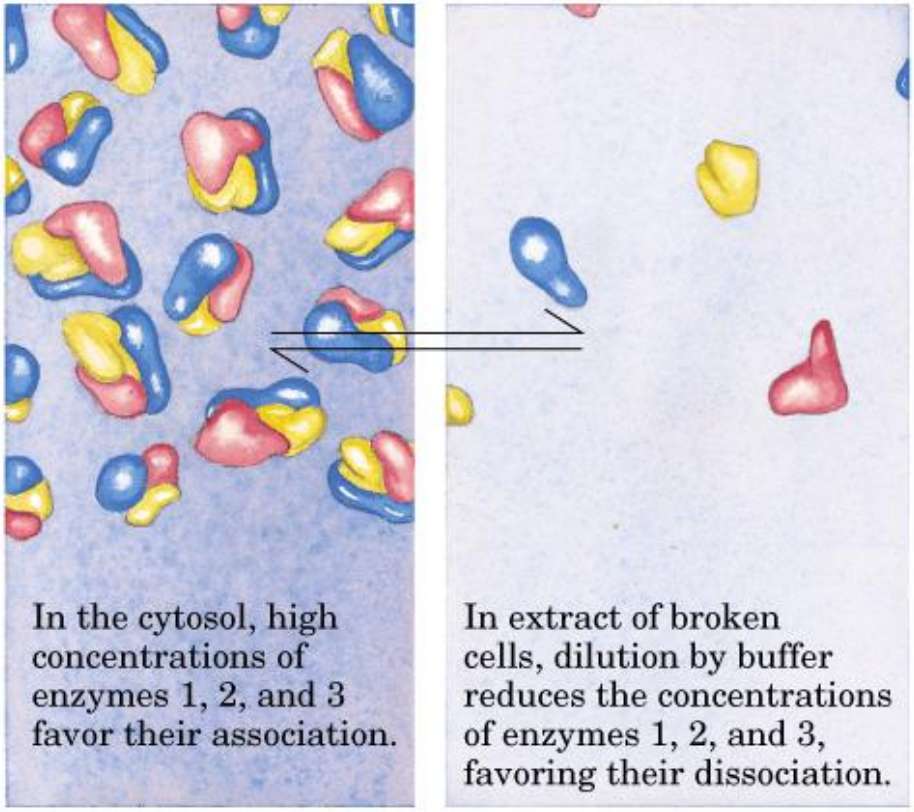
Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH

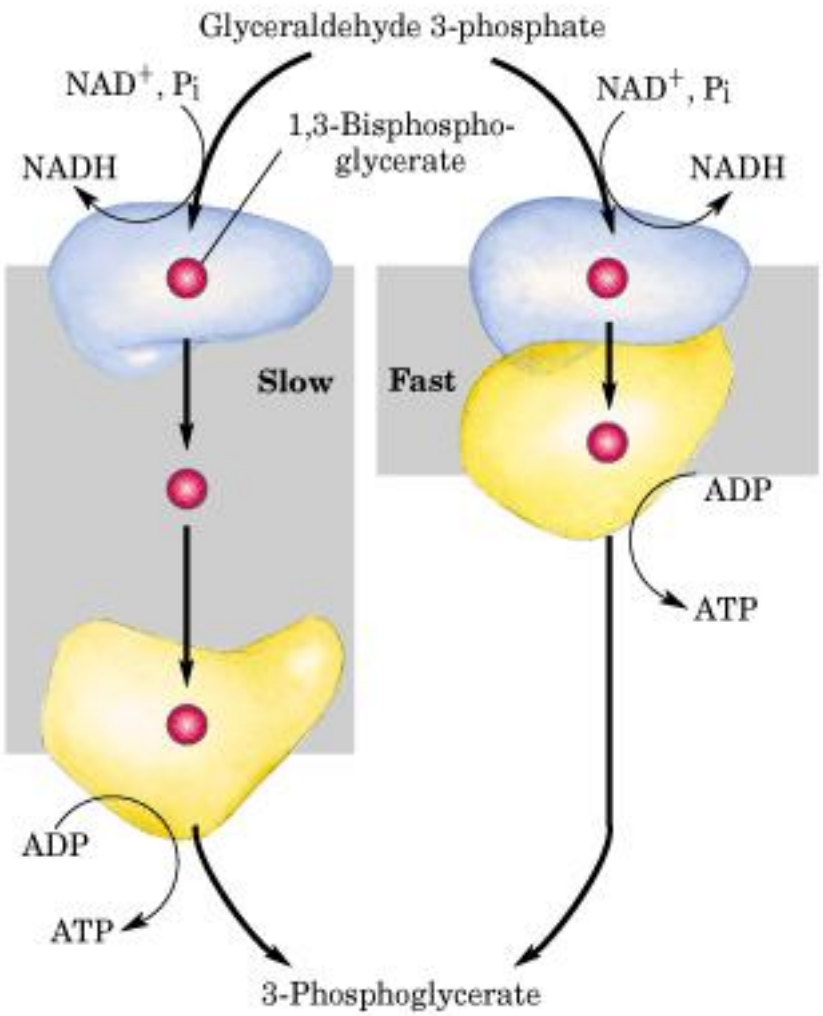


$\Delta G'^{\circ} = 6.3$ kJ/mol



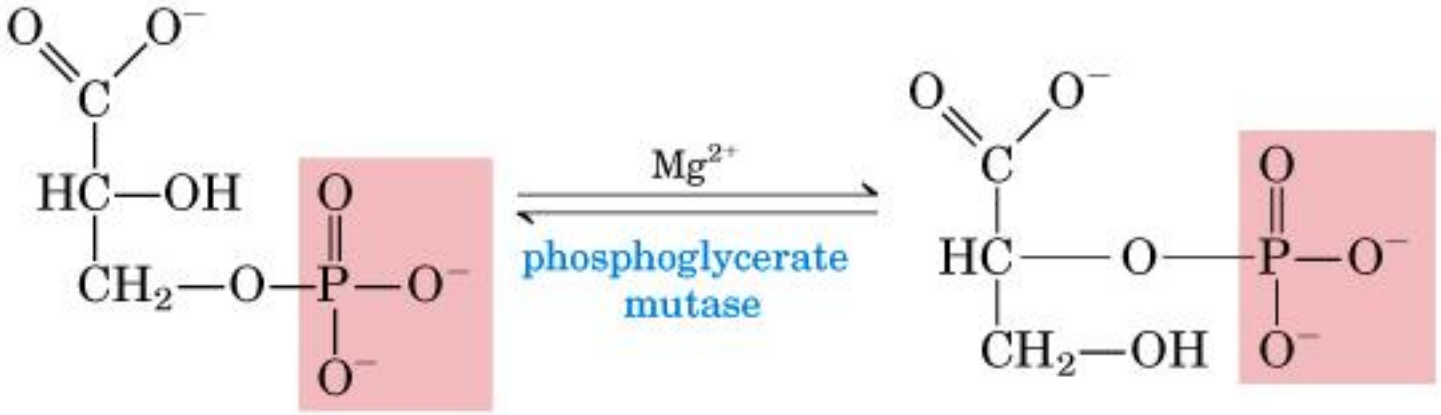
Fosforilação em nível de substrato


In the cytosol, high concentrations of enzymes 1, 2, and 3 favor their association.
In extract of broken cells, dilution by buffer reduces the concentrations of enzymes 1, 2, and 3, favoring their dissociation.



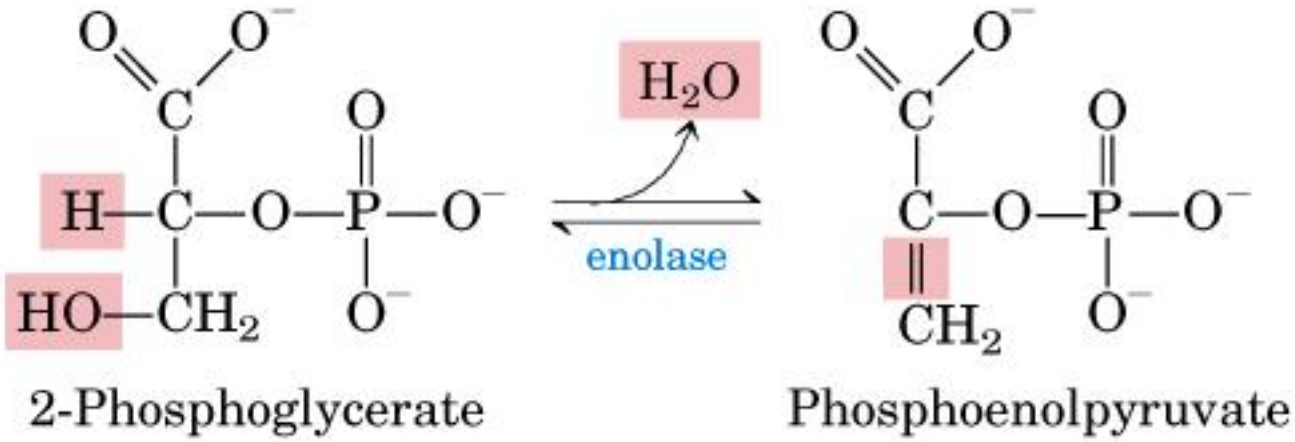
Sequential action of two separate enzymes: the product of the first enzyme (1,3-bisphosphoglycerate) diffuses to the second enzyme.

Substrate channeling through a functional complex of two enzymes: the intermediate (1,3-bisphosphoglycerate) is never released to the solvent.

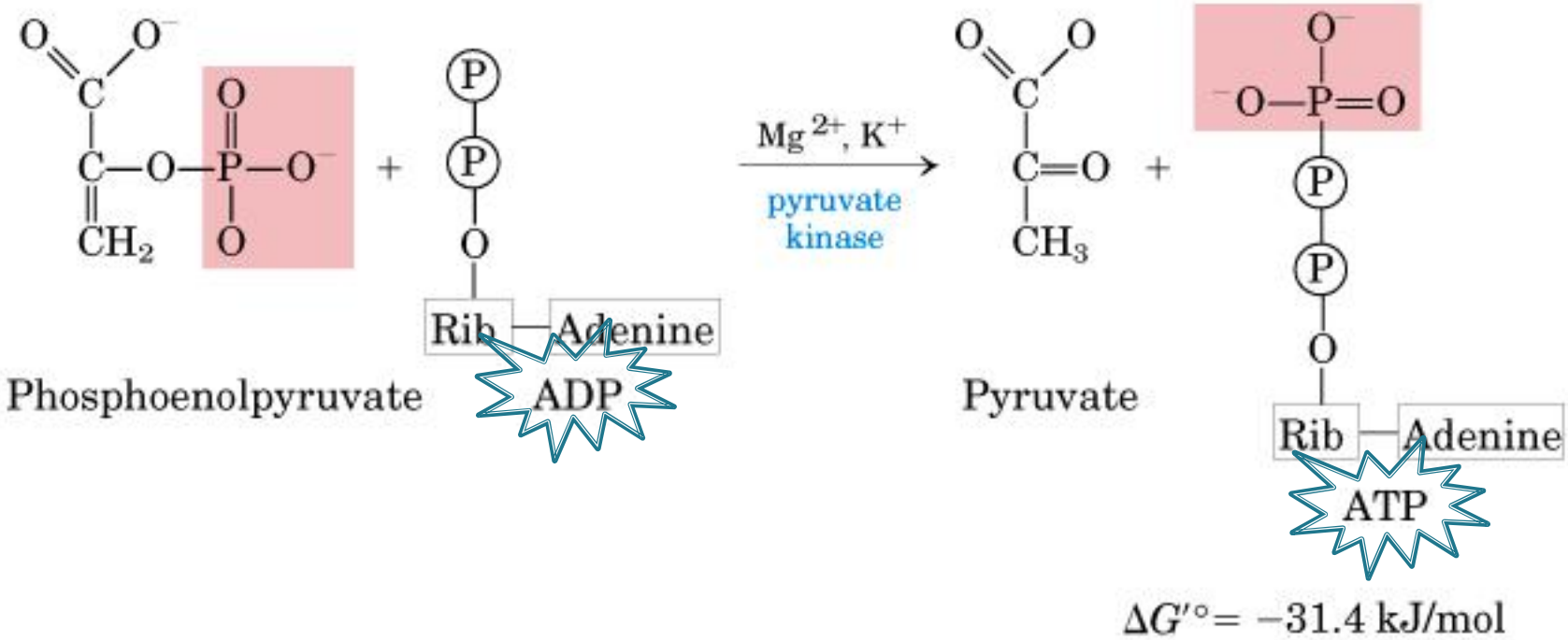


3-Phosphoglycerate 2-Phosphoglycerate

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

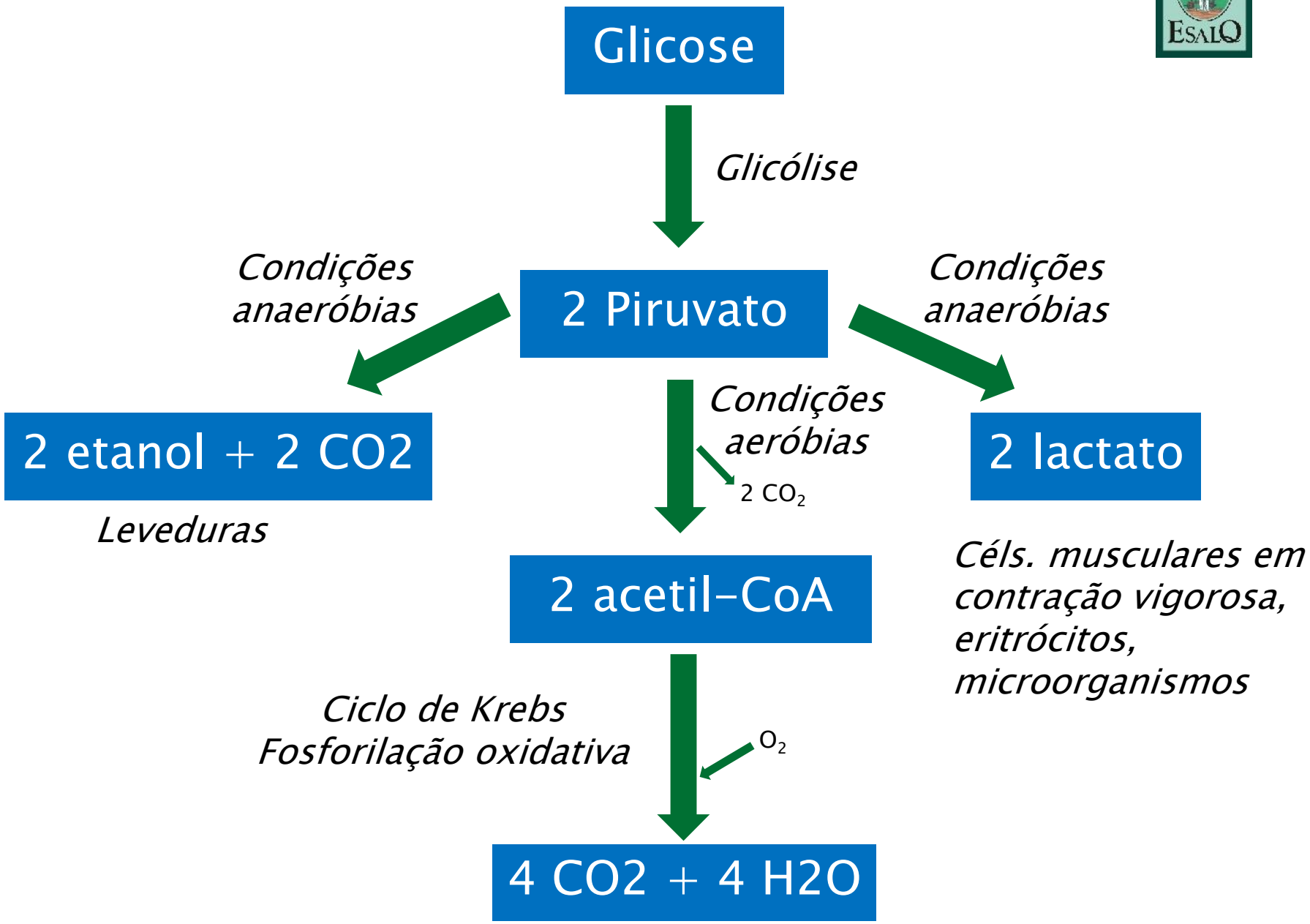


$\Delta G'^{\circ} = 7.5$ kJ/mol



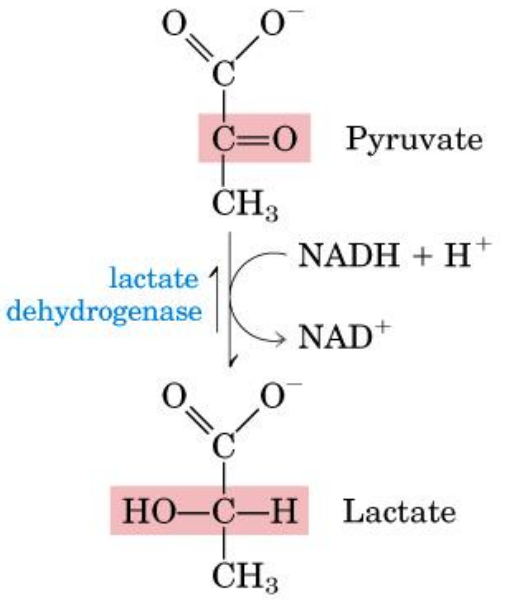
Fosforilação em nível de substrato

Destino do Piruvato



Destino do Piruvato: Lactato

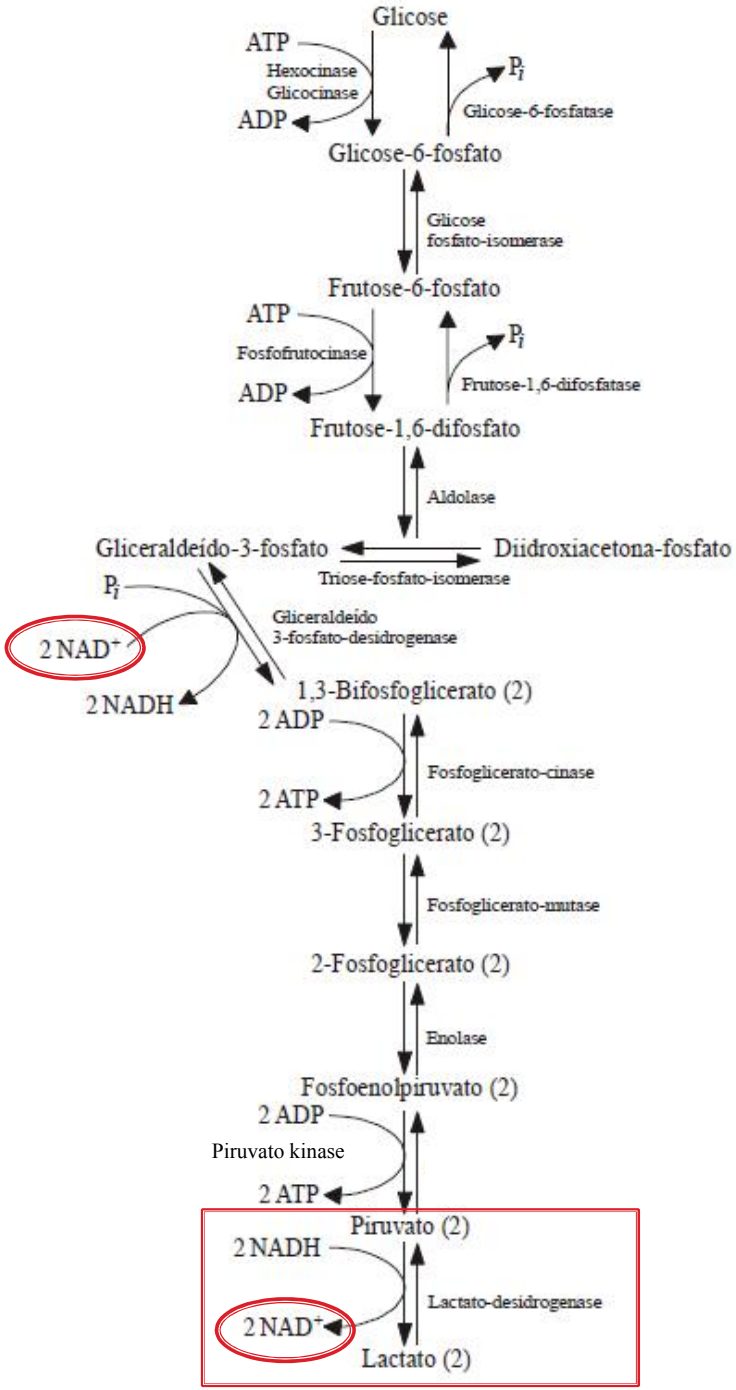
- Na ausência de O_2, NADH não será reoxidado a NAD^+ na oxidação fosforilativa



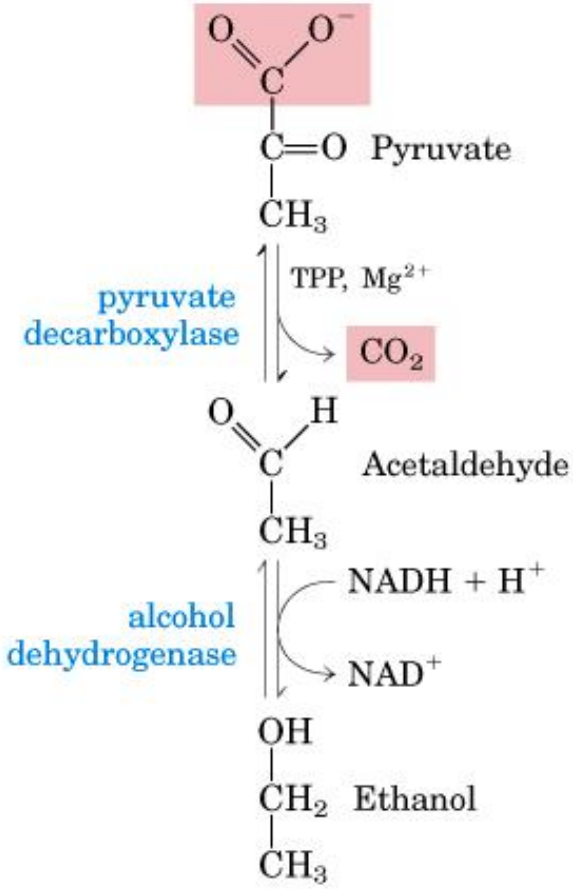
$\Delta G'^{\circ} = -25.1$ kJ/mol

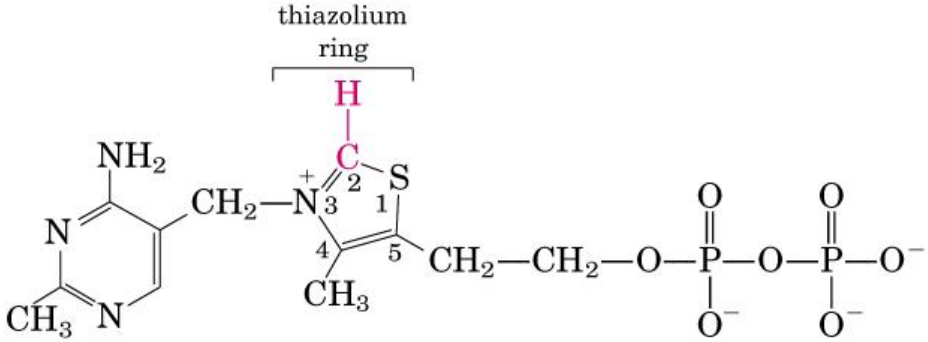
5 isoenzimas da desidrogenase lática
H_4, M_4, H_2M_2, H_3M e HM_3

Coração: H4, lactato $\rightarrow$ piruvato
Músculos: M4, piruvato $\rightarrow$ lactato


Glicose
ATP
Hexocinase
Glicocinase
ADP
P_i
Glicose-6-fosfatase
Glicose-6-fosfato
Glicose
fosfato-isomerase
Frutose-6-fosfato
ATP
Fosfofrutocinase
ADP
P_i
Frutose-1,6-difosfatase
Frutose-1,6-difosfato
Aldolase
Gliceraldeído-3-fosfato
Diidroxiacetona-fosfato
Triose-fosfato-isomerase
P_i
2 NAD+
Gliceraldeído
3-fosfato-desidrogenase
2 NADH
1,3-Bifosfoglicerato (2)
2 ADP
2 ATP
Fosfoglicerato-cinase
3-Fosfoglicerato (2)
Fosfoglicerato-mutase
2-Fosfoglicerato (2)
Enolase
Fosfoenolpiruvato (2)
2 ADP
Piruvato kinase
2 ATP
Piruvato (2)
2 NADH
2 NAD+
Lactato-desidrogenase
Lactato (2)

Destino do Piruvato: fermentação alcóolica

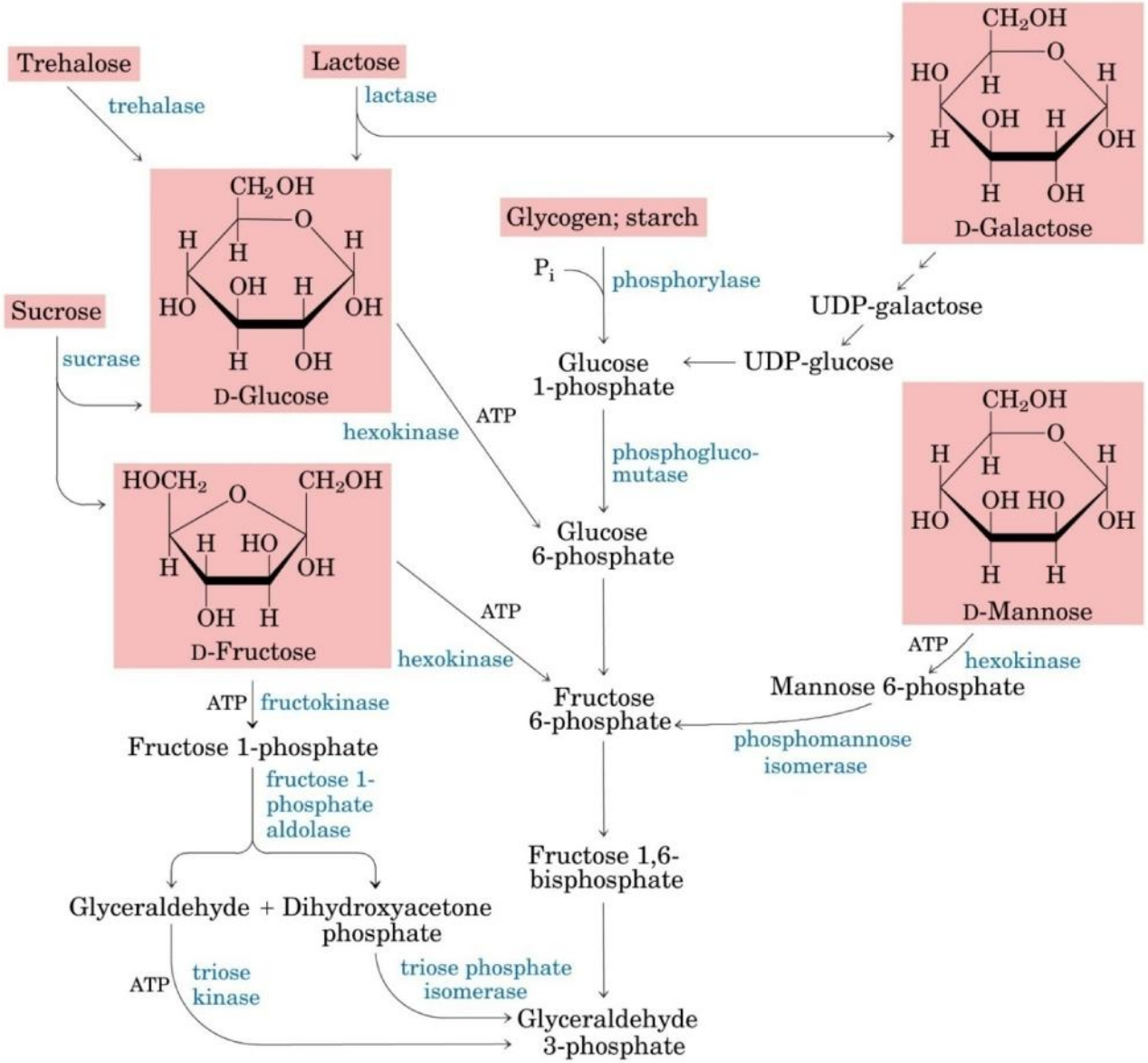




Thiamine pyrophosphate (TPP)

(a)

Vários carboidratos tem seu destino catabólico na glicólise



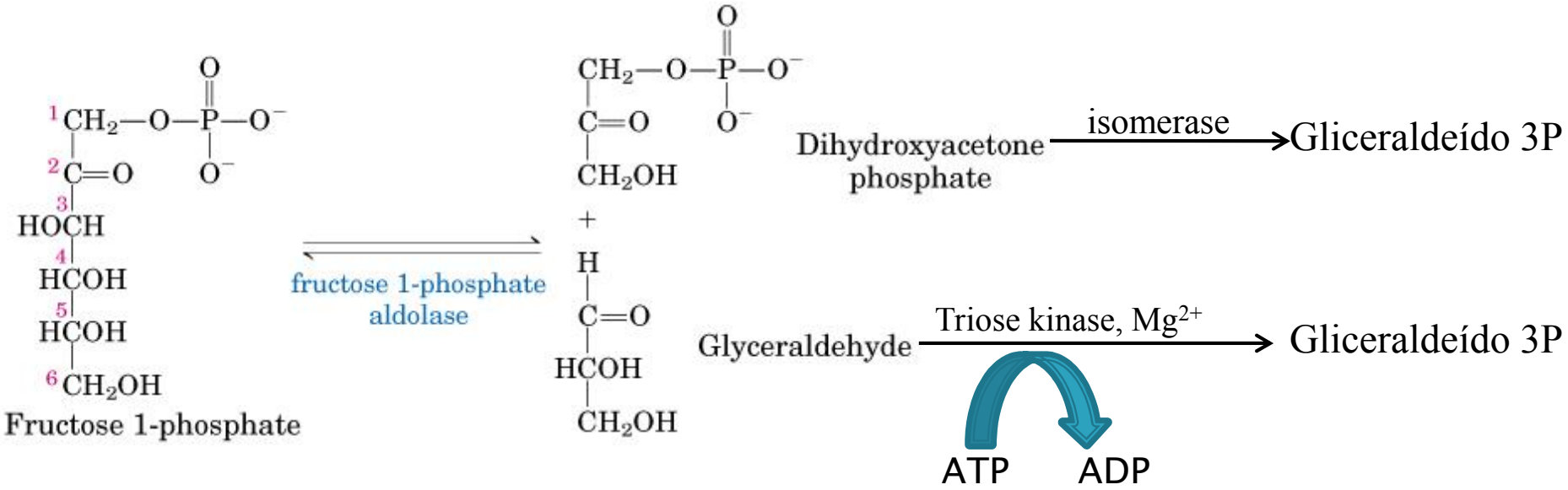
Hexoses precisam ser fosforiladas

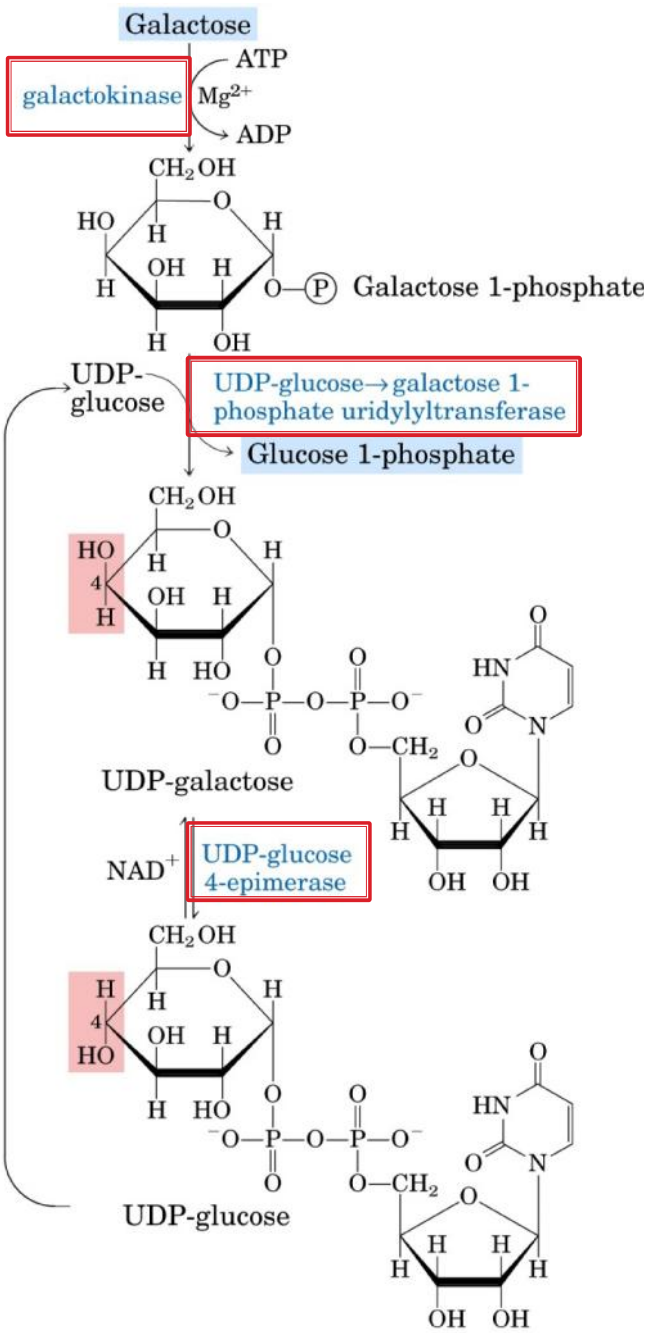
Hexokinase: (músculos e rins)

$$\text{Frutose} + \text{ATP} \xrightarrow{Mg^{2+}} \text{Frutose 6-fosfato} + \text{ADP}$$

Fructokinase: (fígado)

$$\text{Frutose} + \text{ATP} \xrightarrow{Mg^{2+}} \text{Frutose 1-fosfato} + \text{ADP}$$

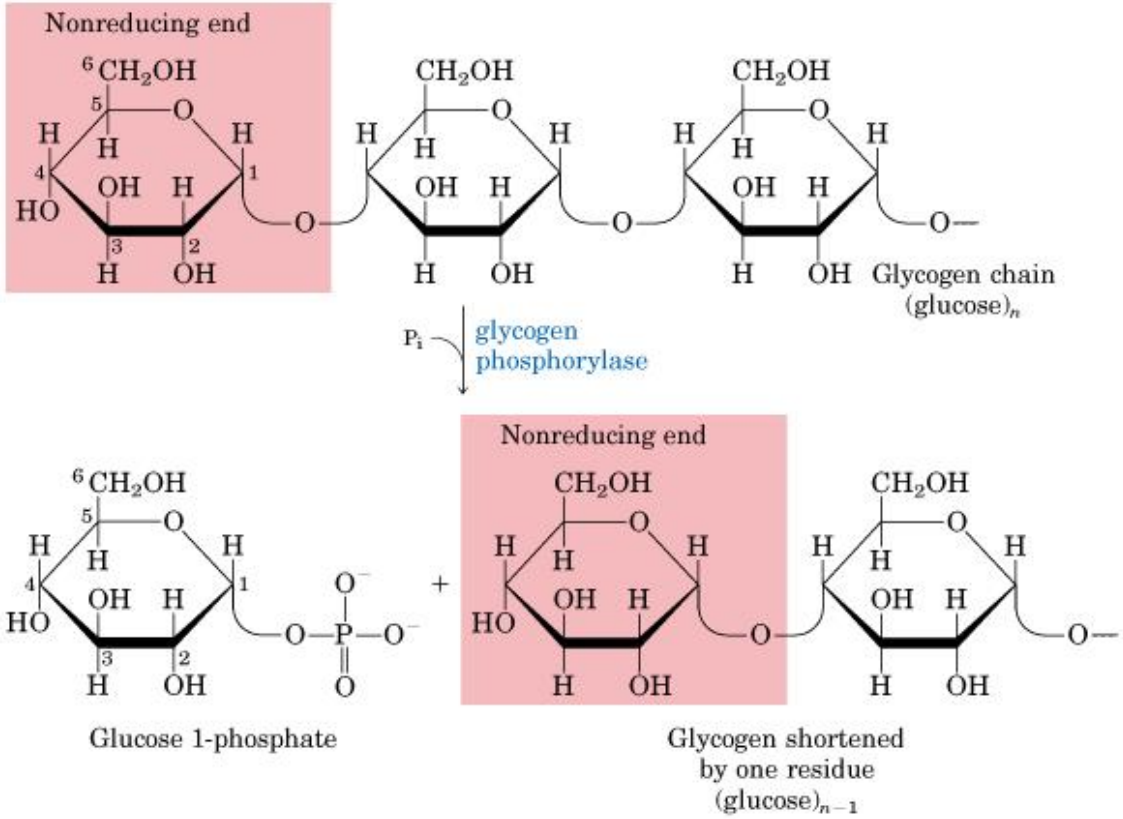

Fructose 1-phosphate
fructose 1-phosphate aldolase
Dihydroxyacetone phosphate
isomerase
Gliceraldeído 3P
Glyceraldehyde
Triose kinase, Mg2+
Gliceraldeído 3P
ATP
ADP

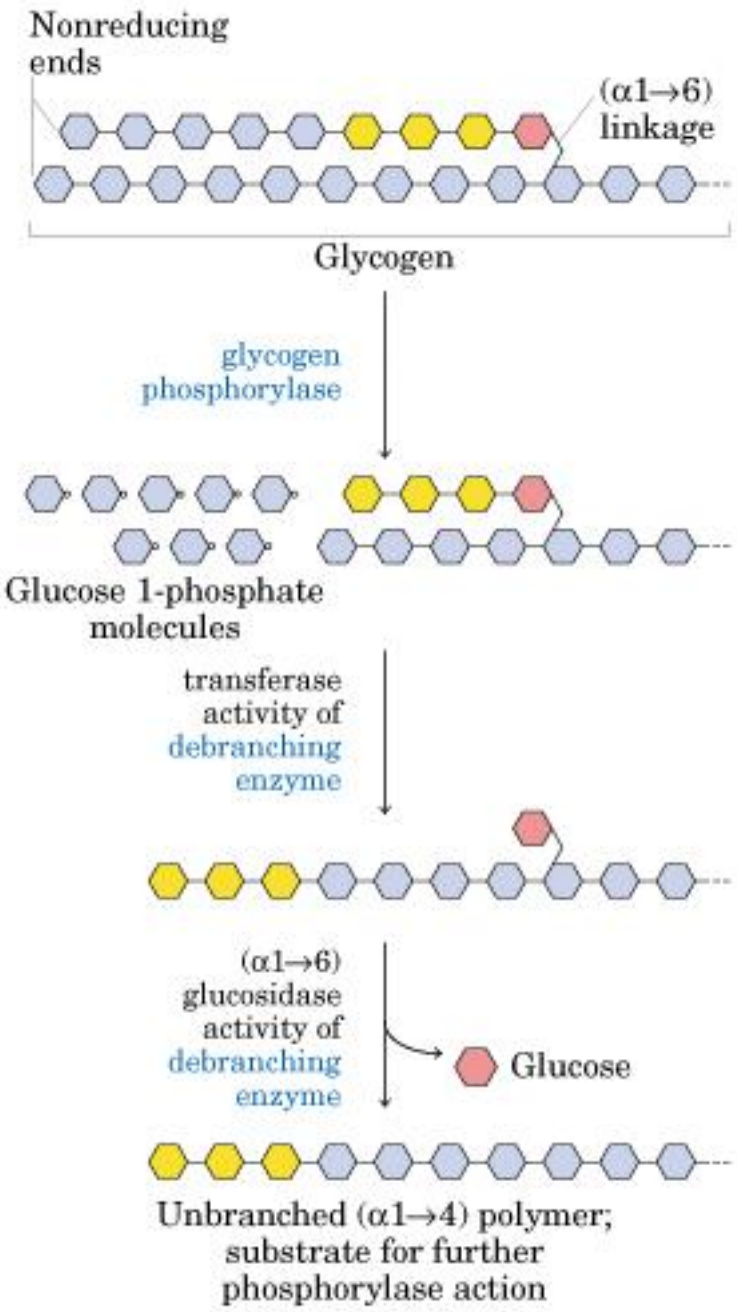


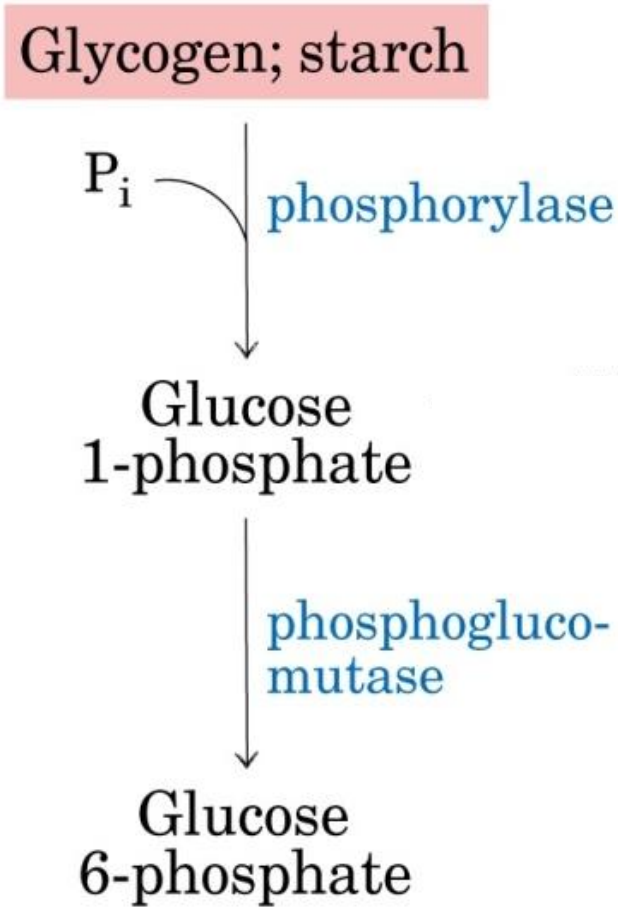
Galactosemia

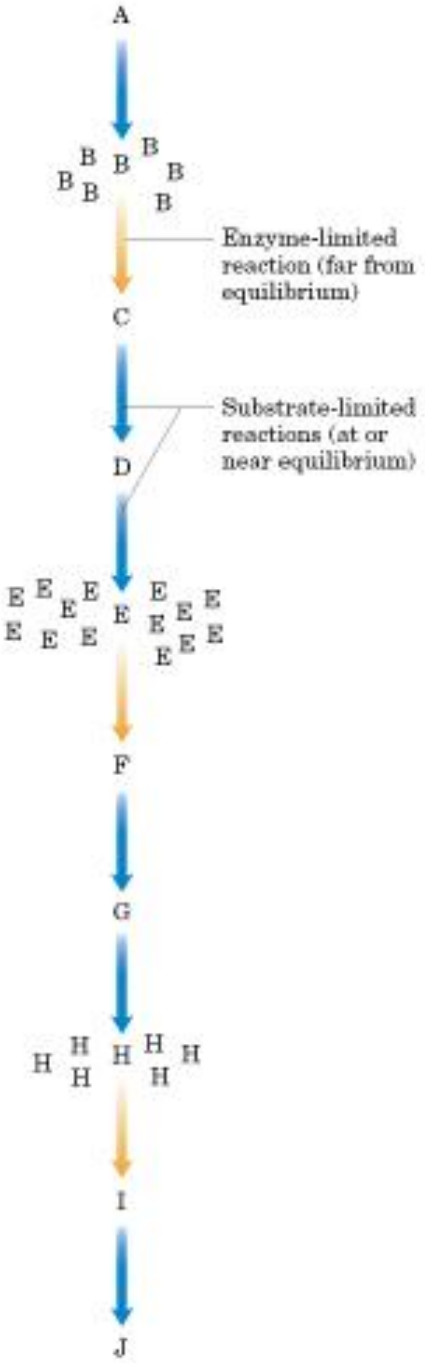
Glicogênio

- Ação de duas enzimas:
  - Fosforilase
    - Glicogênio
    - Amido
  - fosfoglucomutase




Nonreducing ends
(α1→6) linkage
Glycogen
glycogen phosphorylase
Glucose 1-phosphate molecules
transferase activity of debranching enzyme
(α1→6) glucosidase activity of debranching enzyme
Glucose
Unbranched (α1→4) polymer; substrate for further phosphorylase action


Glycogen; starch
P_i
phosphorylase
Glucose 1-phosphate
phosphoglucomutase
Glucose 6-phosphate



- Reações limitadas por substrato:
  - Atividade enzimática é suficientemente alta, substrato entra em equilíbrio com produto assim que substrato é fornecido

- Reações limitadas por enzimas:
  - Sua taxa afeta toda a rota metabólica (*etapa ou passo limitante, rate-limiting step*)
    - Reguladores alostéricos
    - Controle hormonal da atividade enzimática
    - Enzimas regulatórias estão localizadas em pontos de ramificação de rotas
    - Pontos de regulação: reações irreversíveis

Regulação do catabolismo

- Produção e manutenção de concentrações:
  - ATP
  - Precursores para processos de síntese

  - Alterações de demanda
    - Ajustes nas taxas de fluxo das rotas: enzimas-chave

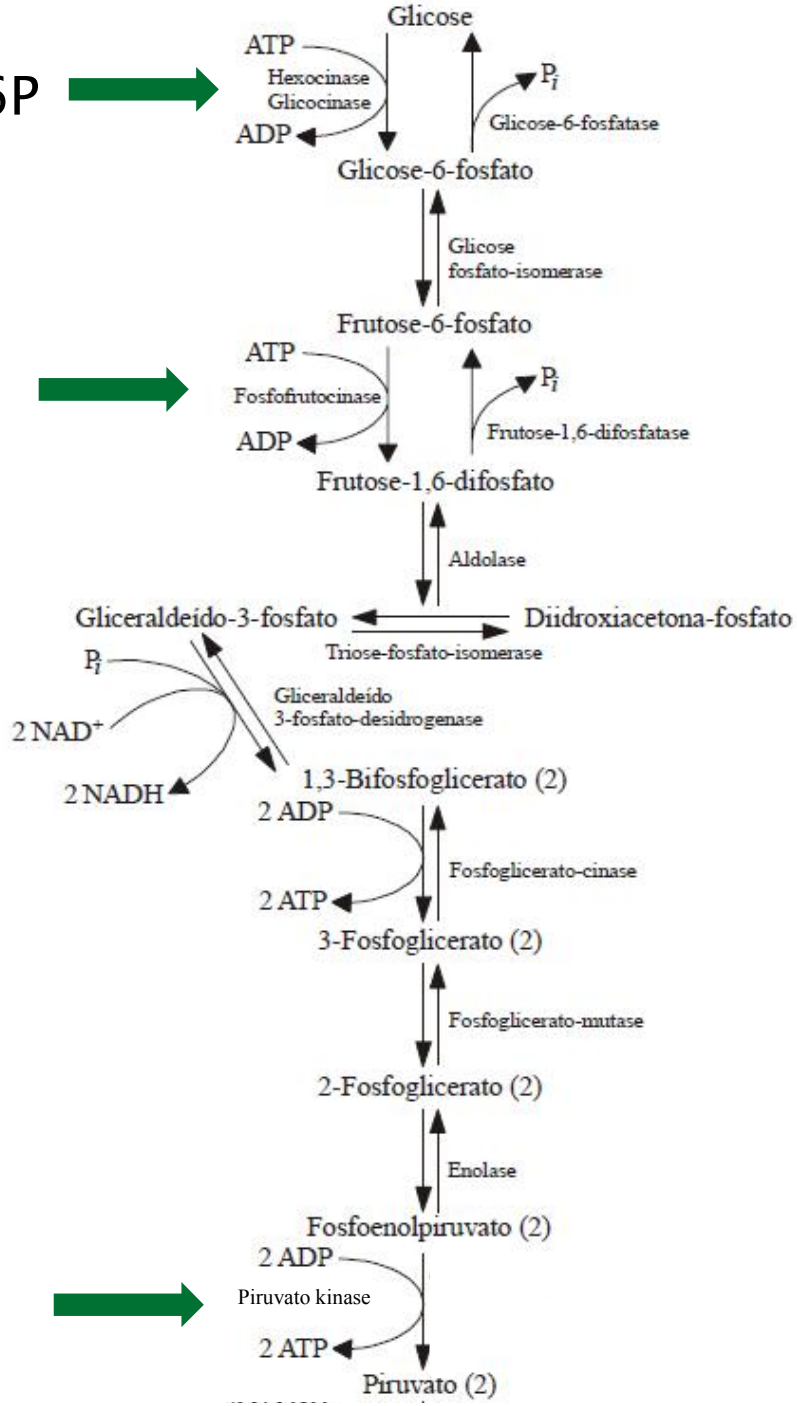
    - Músculo e fígado:
      - Glicogênio fosforilase
      - Hexokinase
      - Fosfofructokinase-1
      - Piruvato kinase

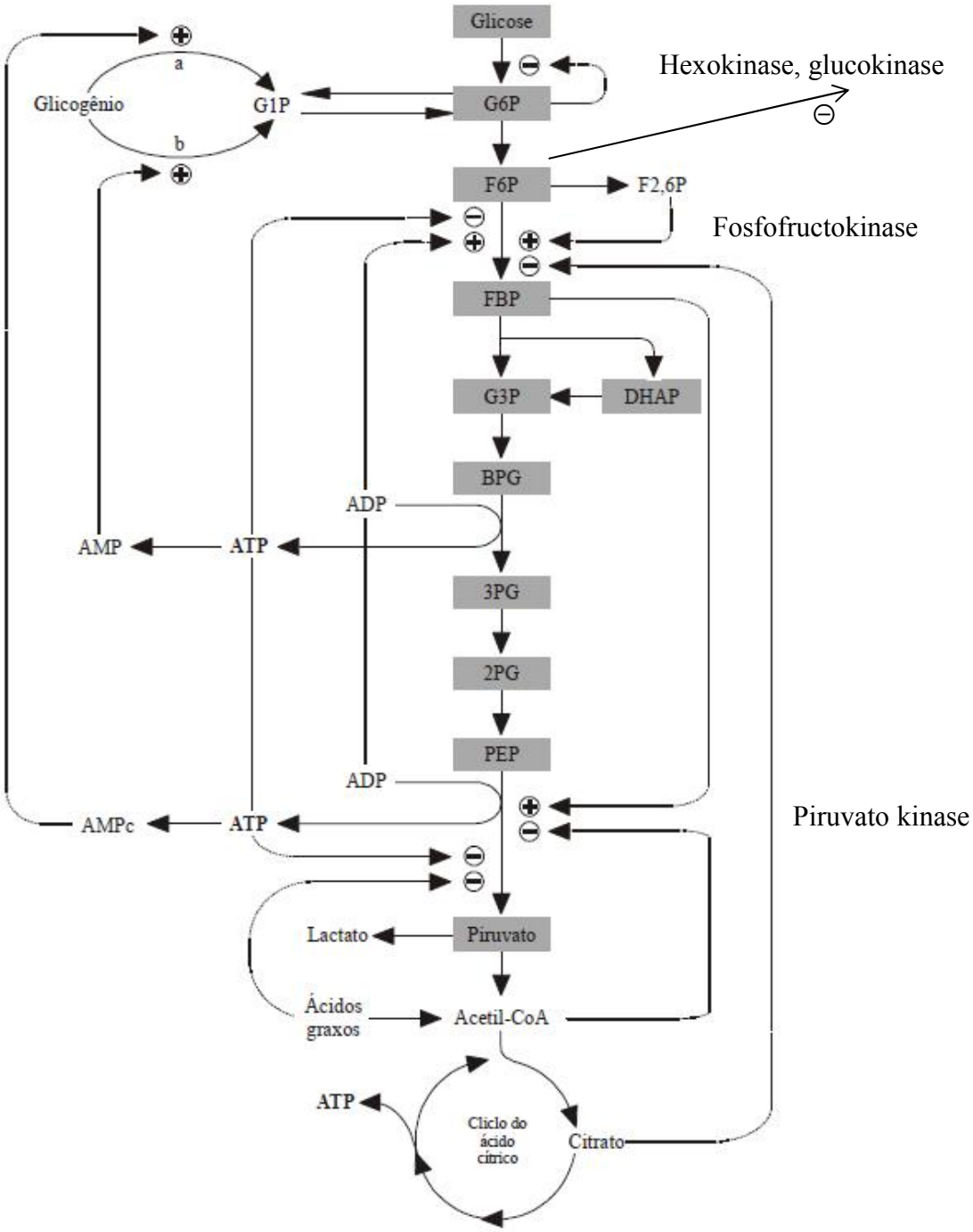
Efetores alostéricos

⊖ G6P

⊕ AMP, frutose 2,6 BP
⊖ ATP, citrato

⊕ AMP
⊖ ATP, acetil-CoA, AGCL





+ Insulina
- glucagon

Via das pentoses-fosfato

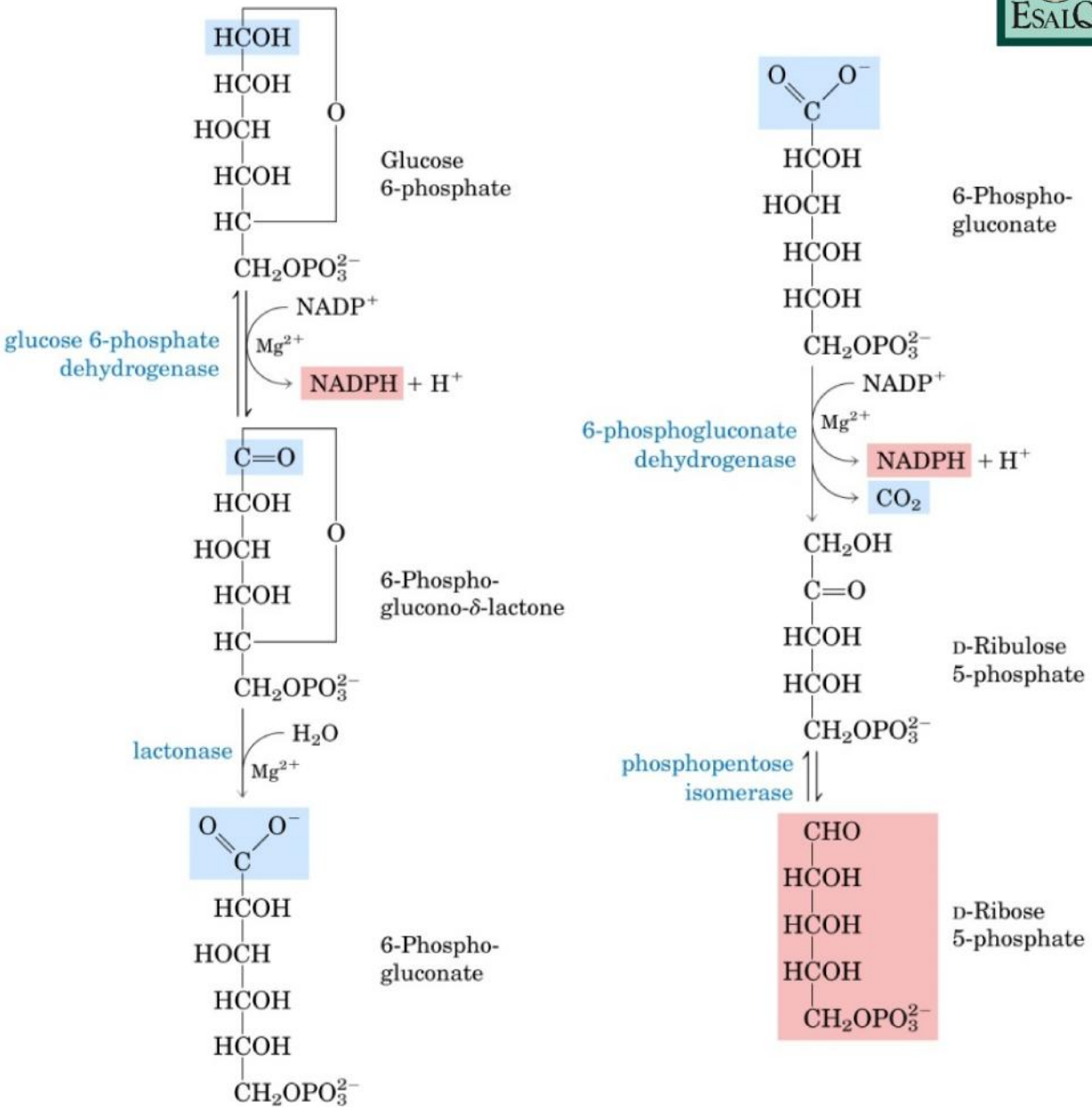
- Via alternativa a glicólise
  - NADPH: agente redutor necessário para vias anabólicas
    - Tecidos produzindo AG ou esteroides
  - Ribose 5-fosfato: componente de nucleotídeos e ác. Nucléicos
- Etapa oxidadiva:

Glicose-6P +2 $NADP^+$ + H_2O → Ribose 5P + CO_2+ 2 **NADPH** + $2H^+$

- Etapa não-oxidativa: isomerização e condensação de açúcares

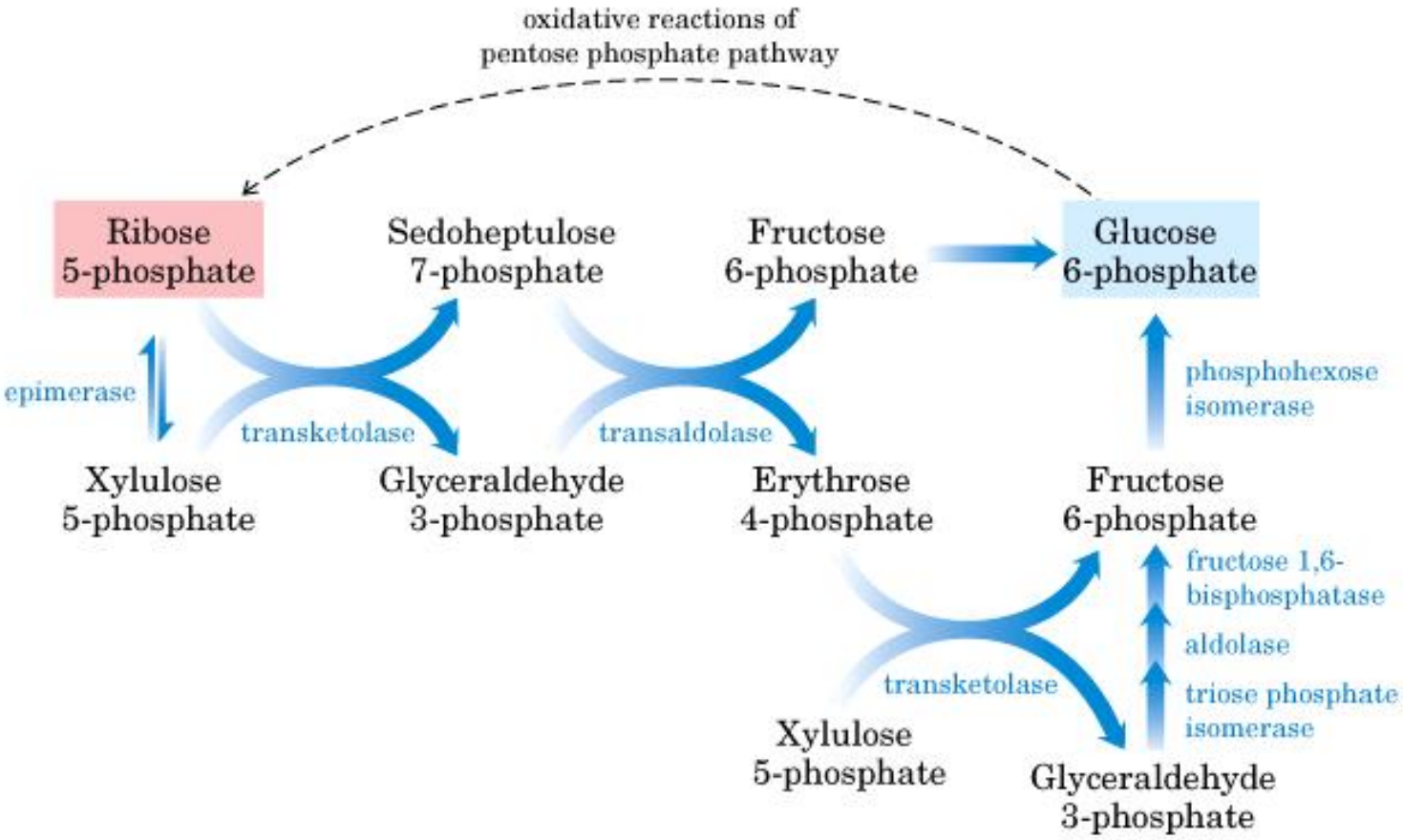
Etapa oxidativa

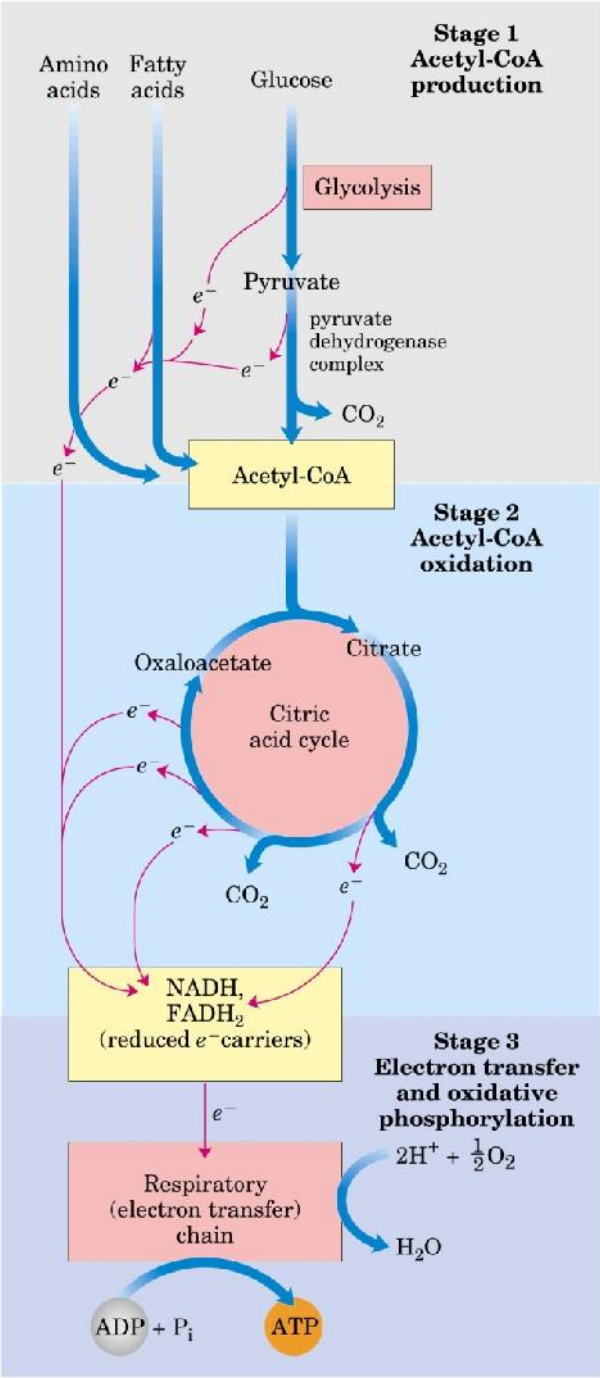
Passo limitante

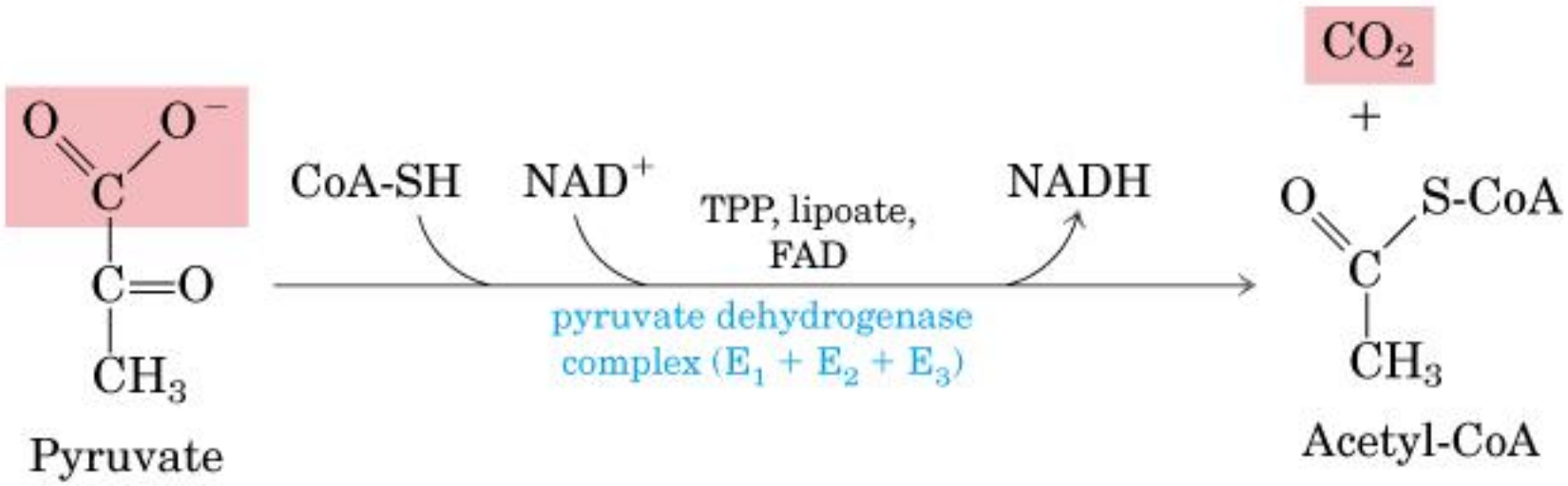


Etapa não-oxidativa

- Reciclagem de glucose 6-fosfato
  - Tecidos com exigência em NADPH e não Ribose 5P



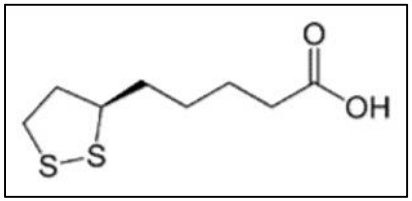

Stage 1
Acetyl-CoA
production
Amino acids
Fatty acids
Glucose
Glycolysis
Pyruvate
pyruvate dehydrogenase complex
CO_2
Acetyl-CoA
Stage 2
Acetyl-CoA
oxidation
Oxaloacetate
Citrate
Citric acid cycle
CO_2
CO_2
NADH, $FADH_2$
(reduced e^-carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
$2H^+ + \frac{1}{2}O_2$
Respiratory
(electron transfer)
chain
H_2O
ADP + P_i
ATP

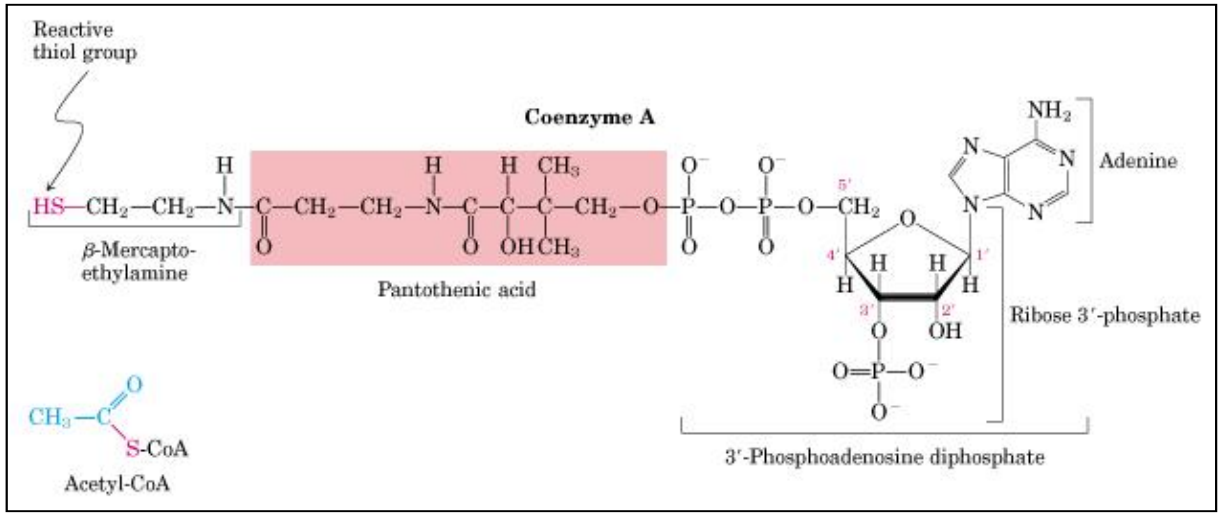


$\Delta G'^{\circ} = -33.4$ kJ/mol

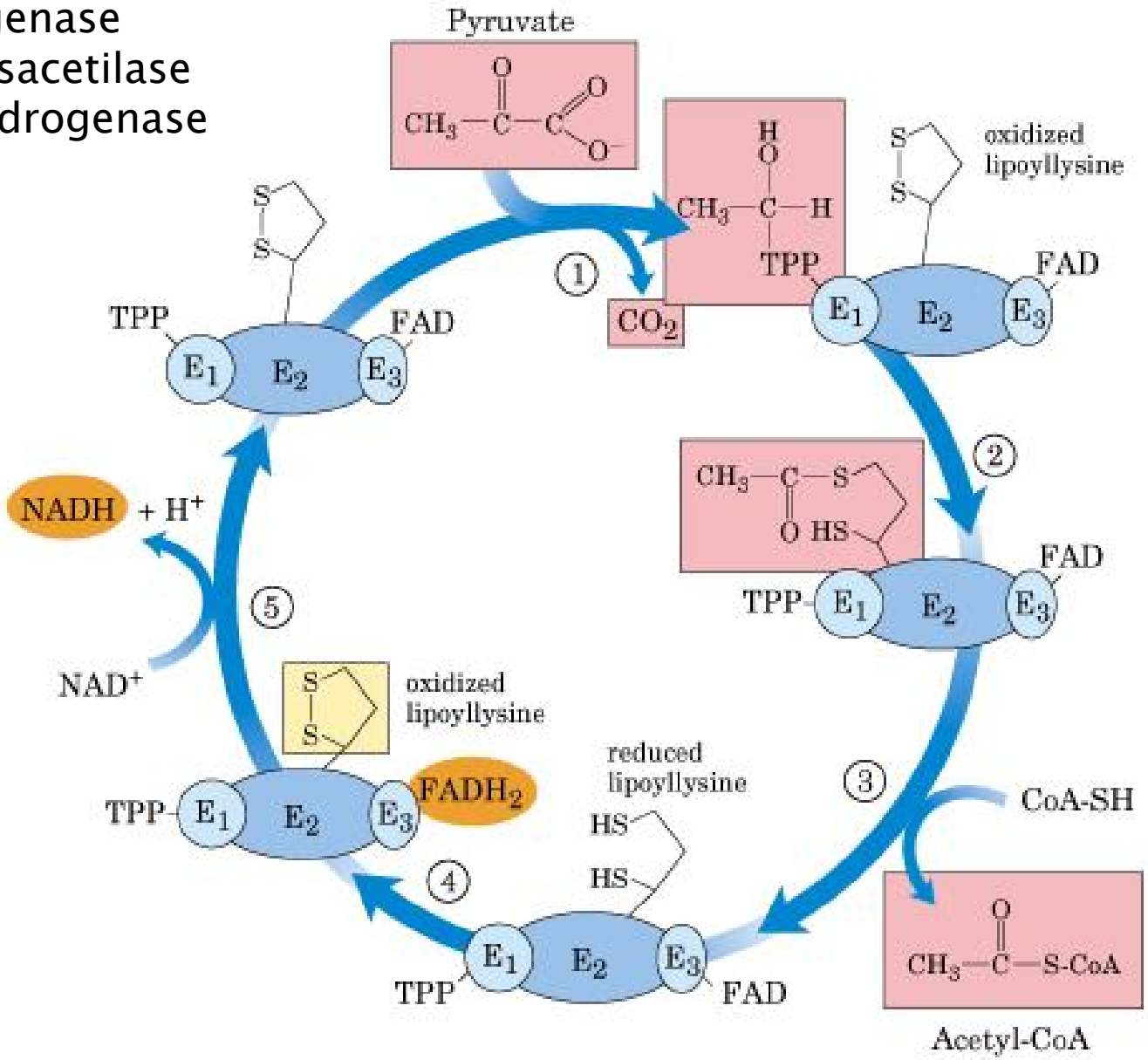
Complexo enzimático

- Exigência de 5 coenzimas
  - TPP: **tiamina** pirofosfato (vit B1)
  - FAD: Dinucleotídeo flavina adenina (**riboflavina – B2**)
  - NAD: Dinucleotídeo nicotinamida adenina (**niacina – B3**)
  - Coenzima A (**pantotenato – B5**)
  - Lipoato

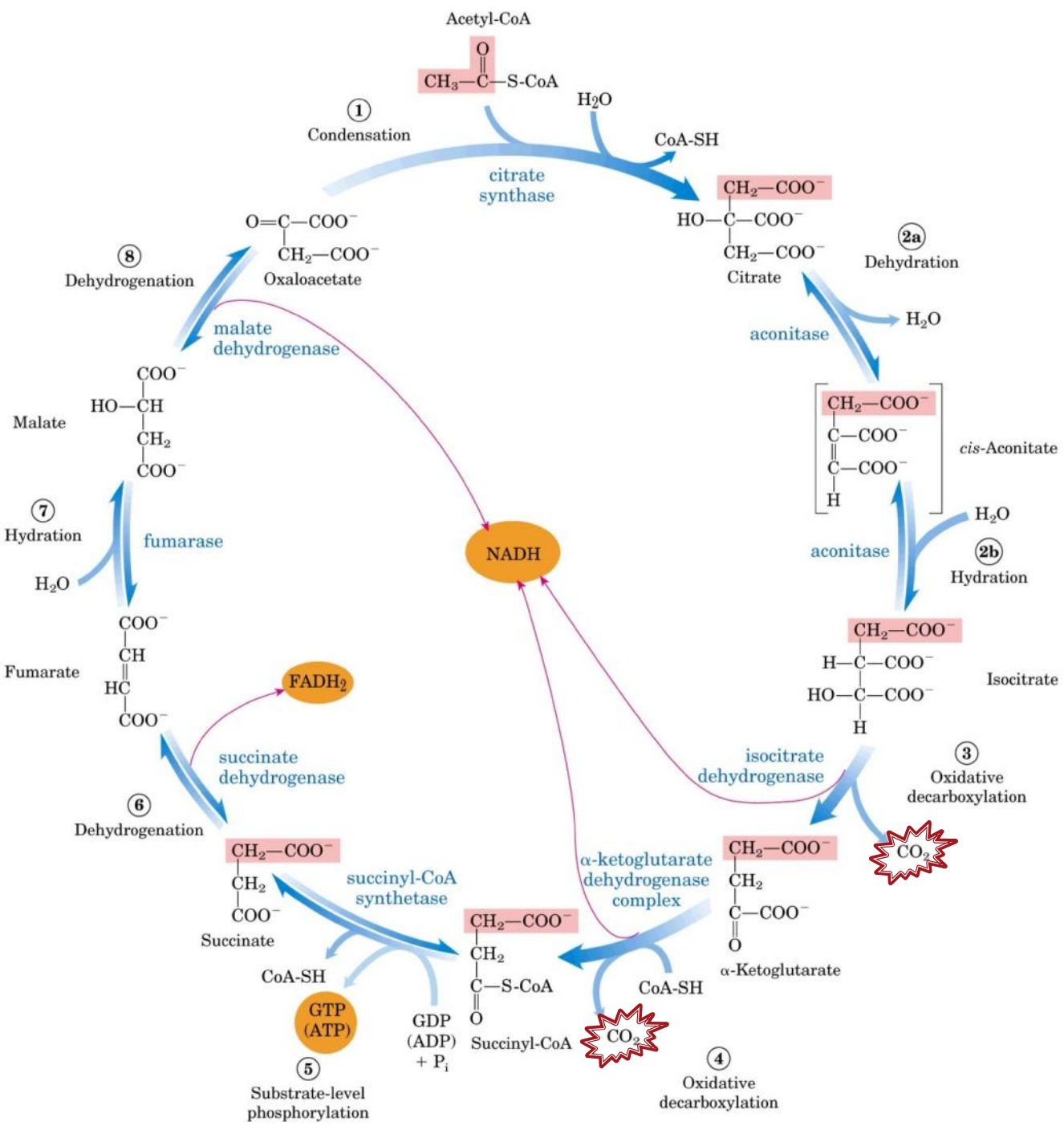




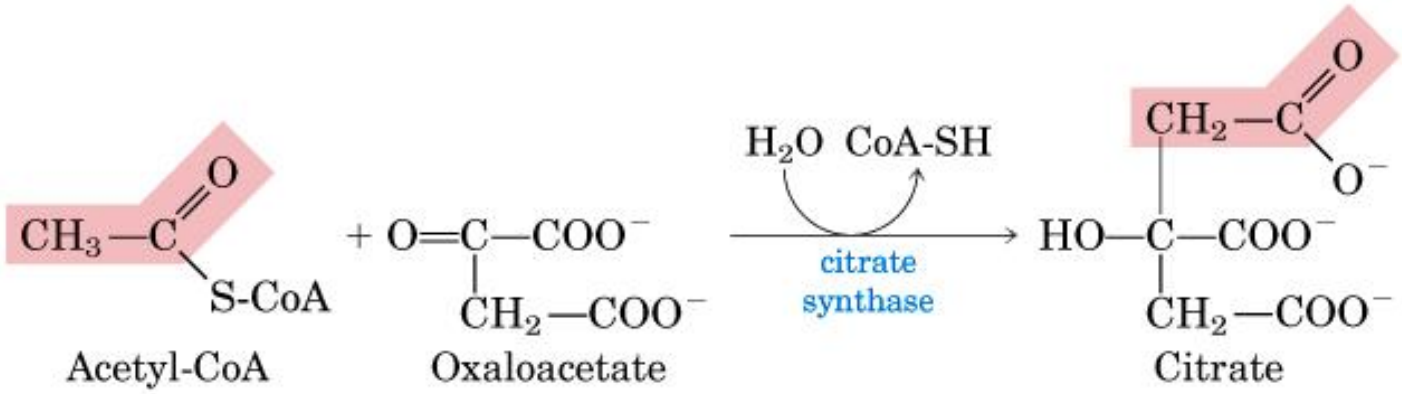
E1: Piruvato desidrogenase
E2: Dihidrolipoil transacetilase
E3: Dihidrolipoil desidrogenase



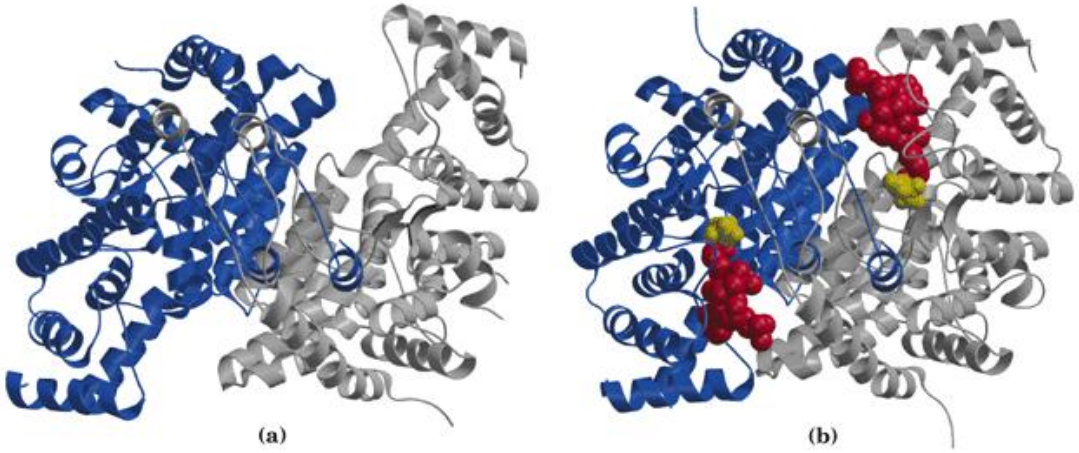
1: Descarboxilação do piruvato
2: Transferência do grupo acetil para grupo lipolisina oxidada
3: Transesterificação com formação de Acetil-CoA


Acetyl-CoA
CH3—C—S-CoA
H2O
CoA-SH
1
Condensation
citrate synthase
CH2—COO⁻
HO—C—COO⁻
CH2—COO⁻
Citrate
2a
Dehydration
H2O
aconitase
cis-Aconitate
H2O
aconitase
2b
Hydration
Isocitrate
isocitrate dehydrogenase
3
Oxidative decarboxylation
CO2
α-ketoglutarate dehydrogenase complex
α-Ketoglutarate
CoA-SH
CO2
4
Oxidative decarboxylation
Succinyl-CoA
succinyl-CoA synthetase
GDP (ADP) + Pi
GTP (ATP)
5
Substrate-level phosphorylation
CoA-SH
Succinate
6
Dehydrogenation
succinate dehydrogenase
FADH2
Fumarate
7
Hydration
H2O
fumarase
Malate
8
Dehydrogenation
malate dehydrogenase
Oxaloacetate
NADH

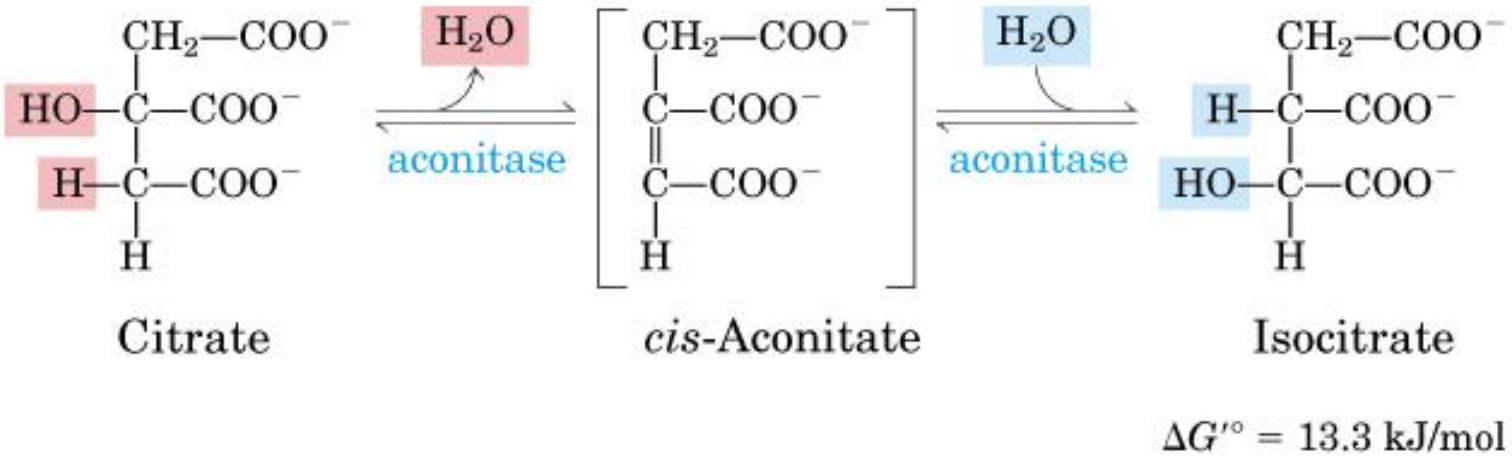
Formação de citrato



$\Delta G'^{\circ} = -32.2$ kJ/mol

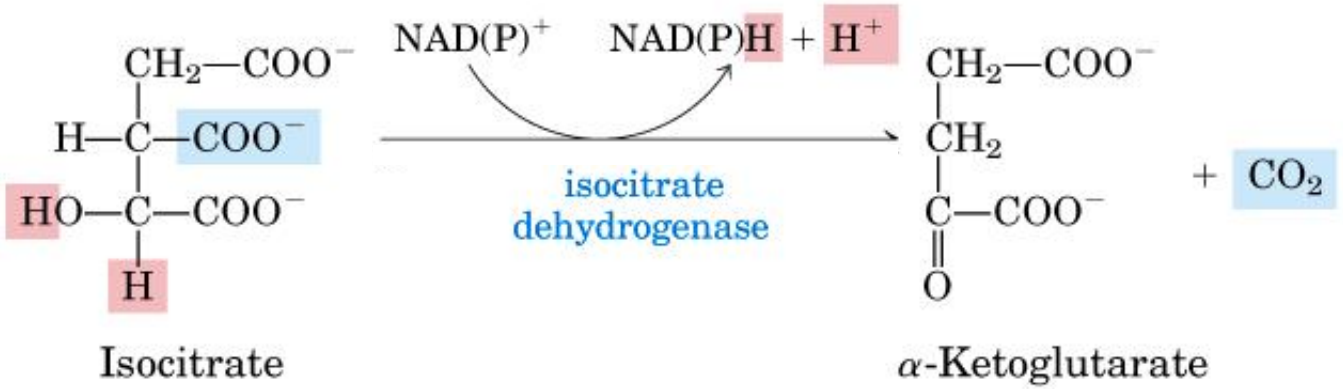


Formação de Isocitrato



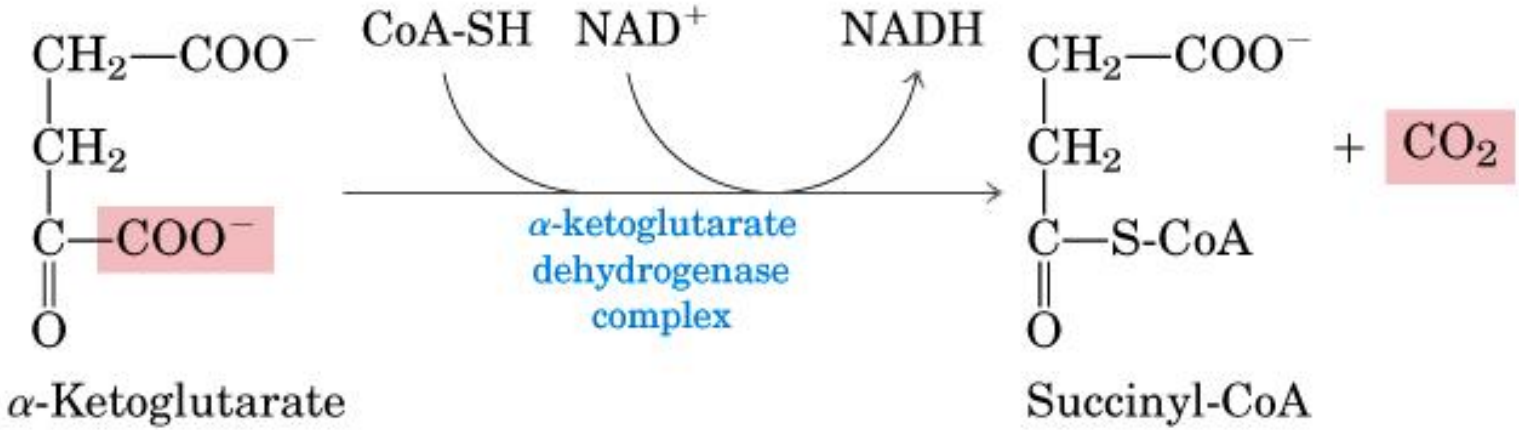
Em pH 7,4 e temperatura de 25°C: 10% isocitrato !

Oxidação de isocitrato em α-cetoglutarato



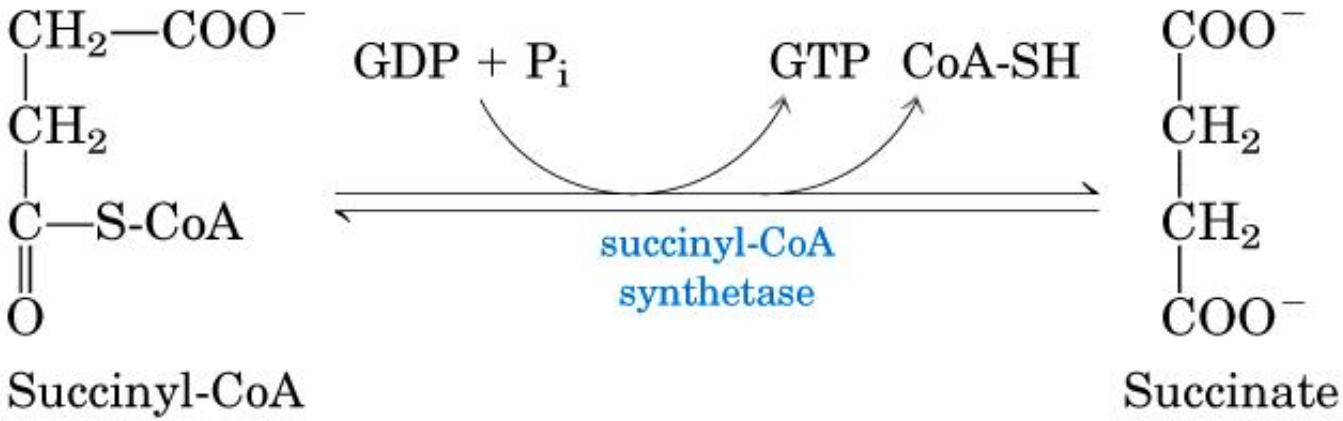
$\Delta G'^{\circ} = -20.9$ kJ/mol

Oxidação de α-cetoglutarato em succinil-CoA

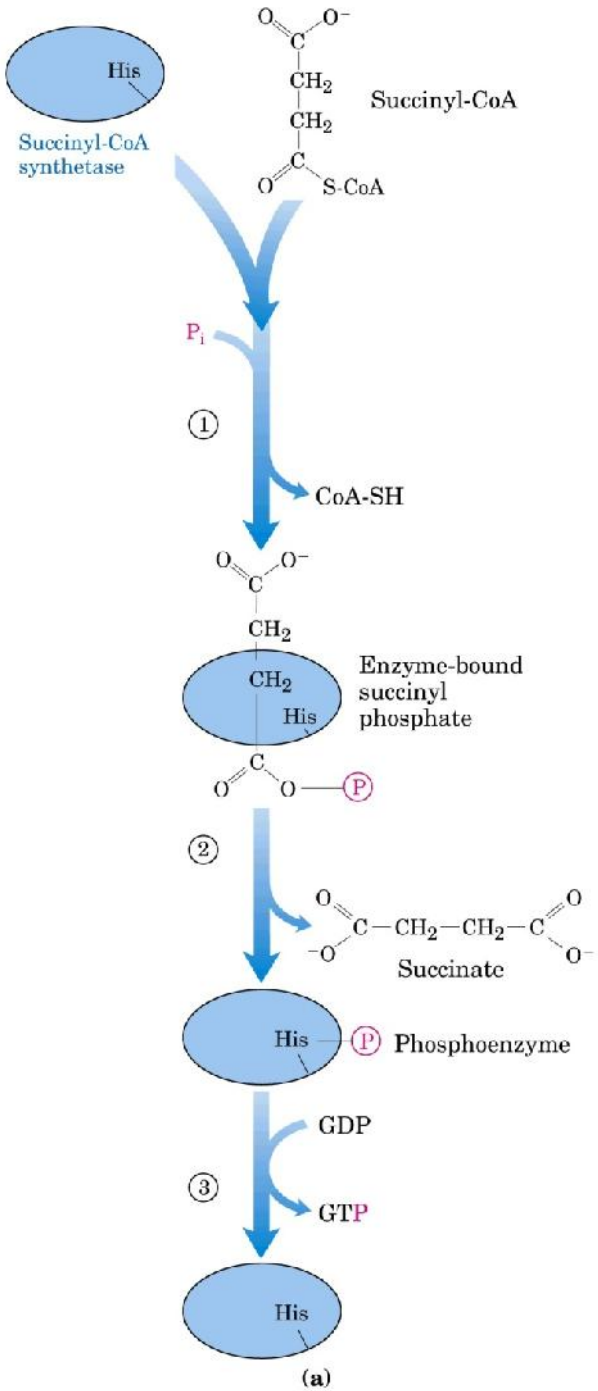


$\Delta G'^{\circ} = -33.5$ kJ/mol

Conversão de succinil-CoA em succinato

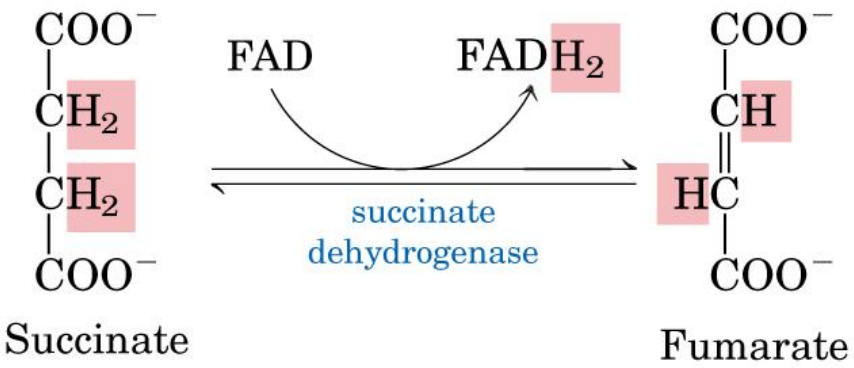


$$\Delta G'^{\circ} = -2.9 \text{ kJ/mol}$$



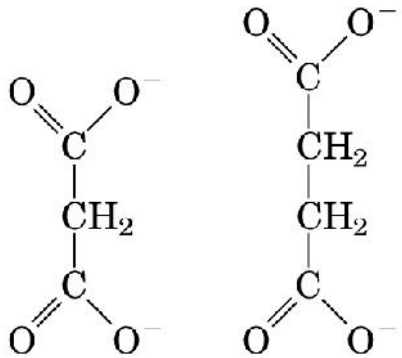
$$GTP + ADP \xrightarrow{Mg^{2+}} GDP + ATP$$

Oxidação de succinato em fumarato

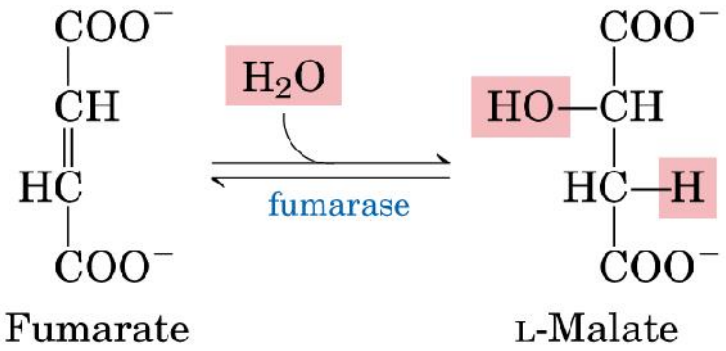


$\Delta G'^{\circ} = 0$ kJ/mol

- Enzima ligada a membrana mitocondrial
- Malonato é inibidor competitivo da enzima

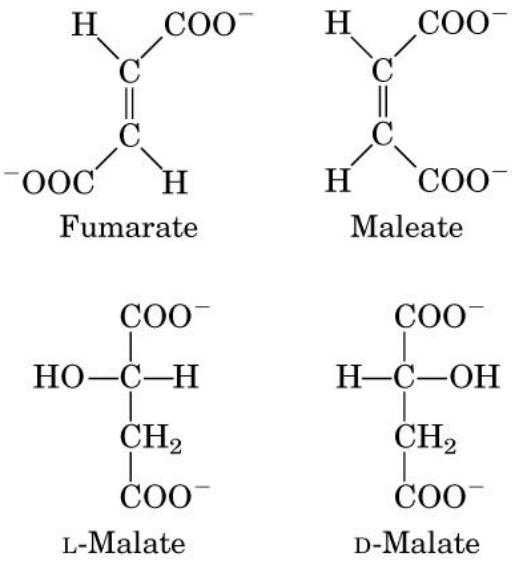


Hidratação de fumarato a malato

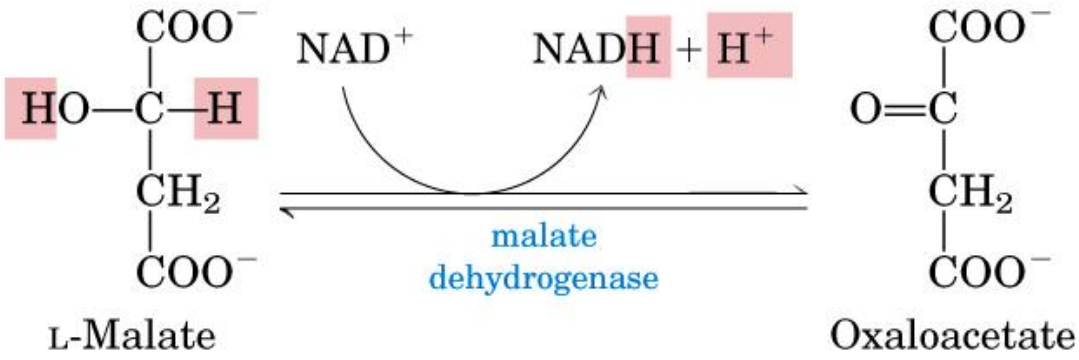


$\Delta G'^{\circ} = -3.8$ kJ/mol

- Enzima estereoespecífica



Oxidação de malato a oxaloacetato



$\Delta G'^{\circ} = 29.7$ kJ/mol

- Rota anfibólica
  - Catabolismo de CHO, ác. graxos, aminoácidos
  - Precursores para diversas rotas biossintéticas

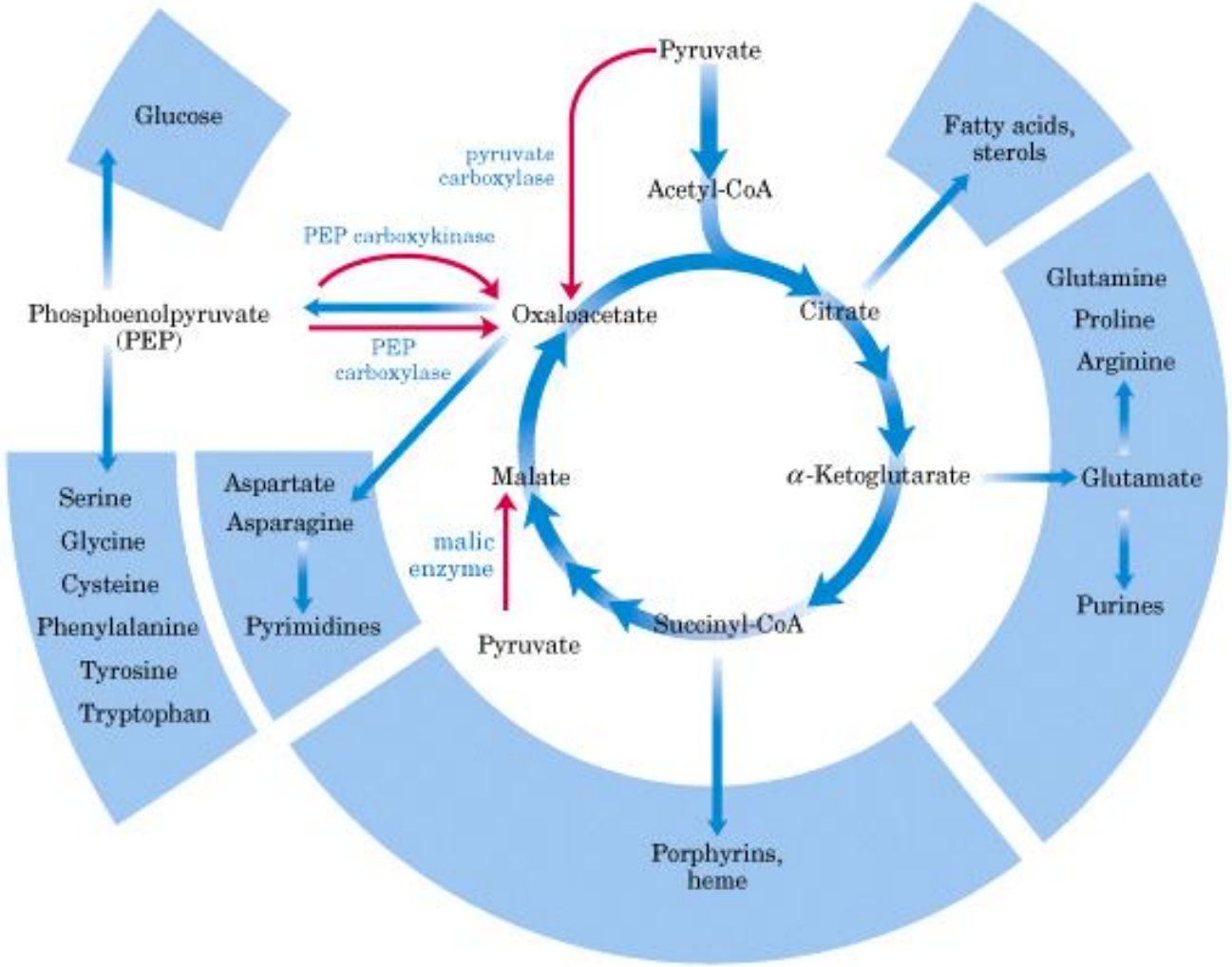
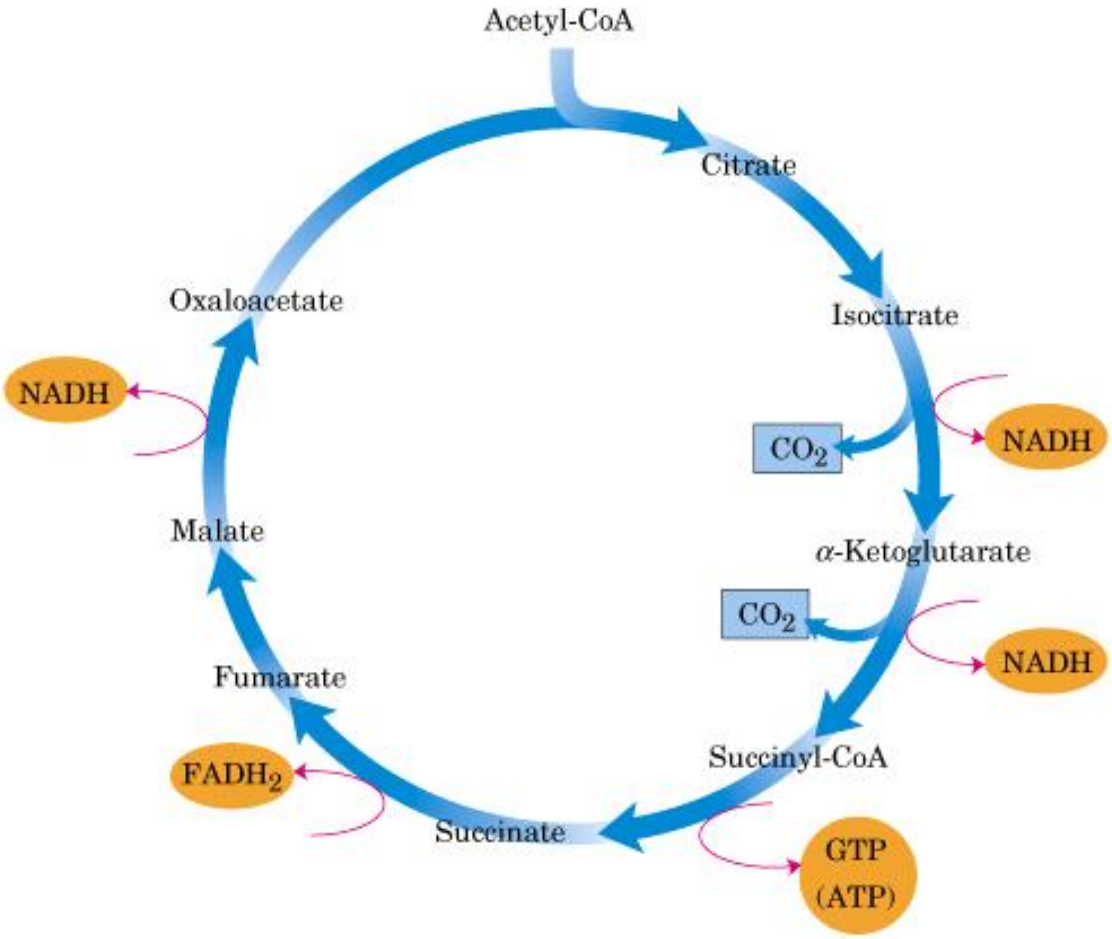


table 16–2

Anaplerotic Reactions

Reaction	Tissue(s)/organism(s)
Pyruvate + HCO_3^- + ATP $\xrightleftharpoons{\text{pyruvate carboxylase}}$ oxaloacetate + ADP + P_i	Liver, kidney
Phosphoenolpyruvate + CO_2 + GDP $\xrightleftharpoons{\text{PEP carboxykinase}}$ oxaloacetate + GTP	Heart, skeletal muscle
Phosphoenolpyruvate + HCO_3^- $\xrightleftharpoons{\text{PEP carboxylase}}$ oxaloacetate + P_i	Higher plants, yeast, bacteria
Pyruvate + HCO_3^- + NAD(P)H $\xrightleftharpoons{\text{malic enzyme}}$ malate + $NAD(P)^+$	Widely distributed in eukaryotes and prokaryotes

Piruvato carboxilase: inativa em baixas [acetil-CoA]
PEP carboxykinase: + 1,6 frutose bifosfato



- Oxidação fosforilativa:
  - NADH: 2,5 ATP
  - $FADH_2$: 1,5 ATP
  - GTP (ATP)

- Cada ciclo:
  - 3 NADH: 7,5 ATP
  - FADH2: 1,5 ATP
  - GTP (ATP)

- 10 ATP

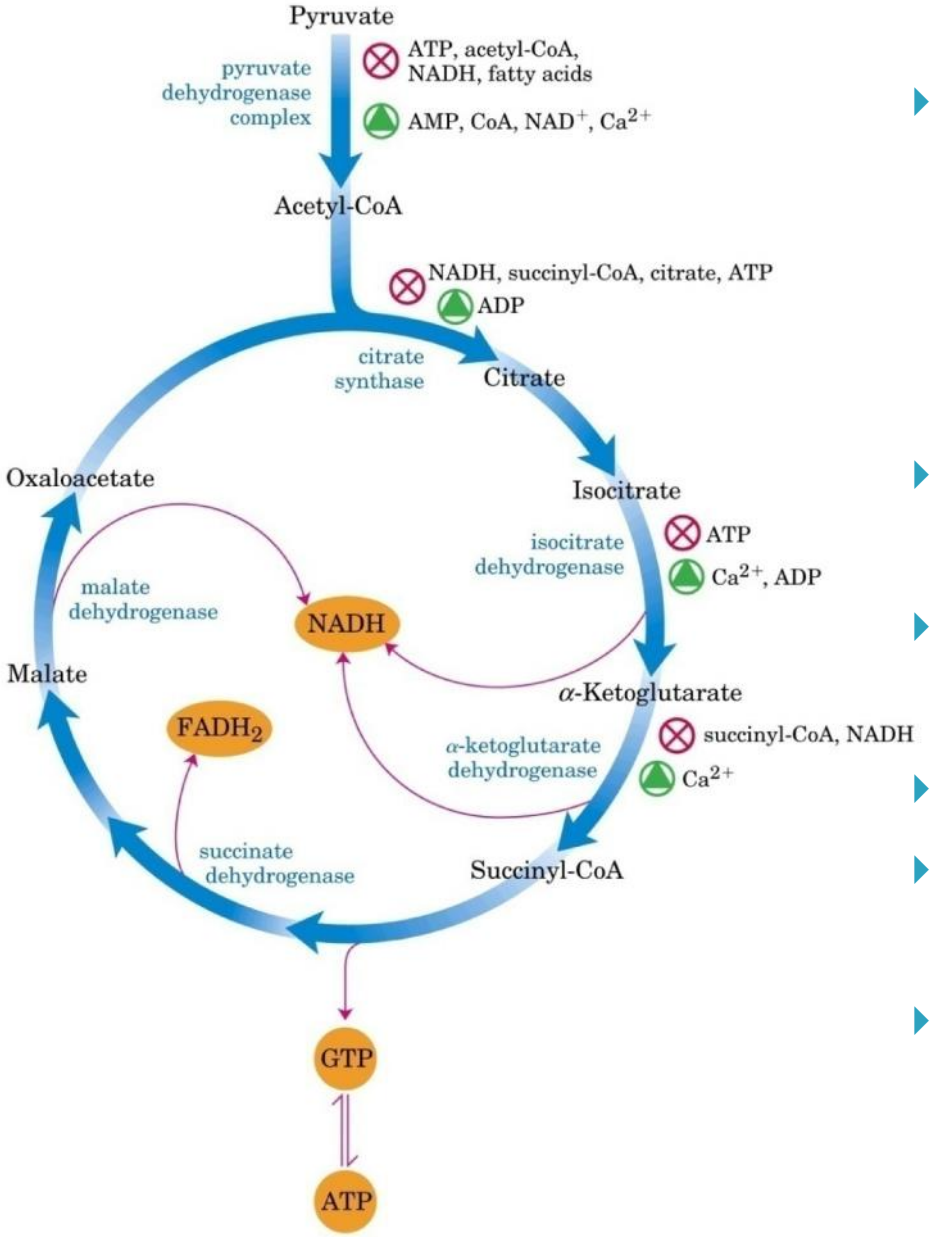
table 16–1

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

Reaction	Number of ATP or reduced coenzymes 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	3–5
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.

Regulação do ciclo de Krebs



- Manutenção da produção de intermediários e de produtos de forma a manter célula estável

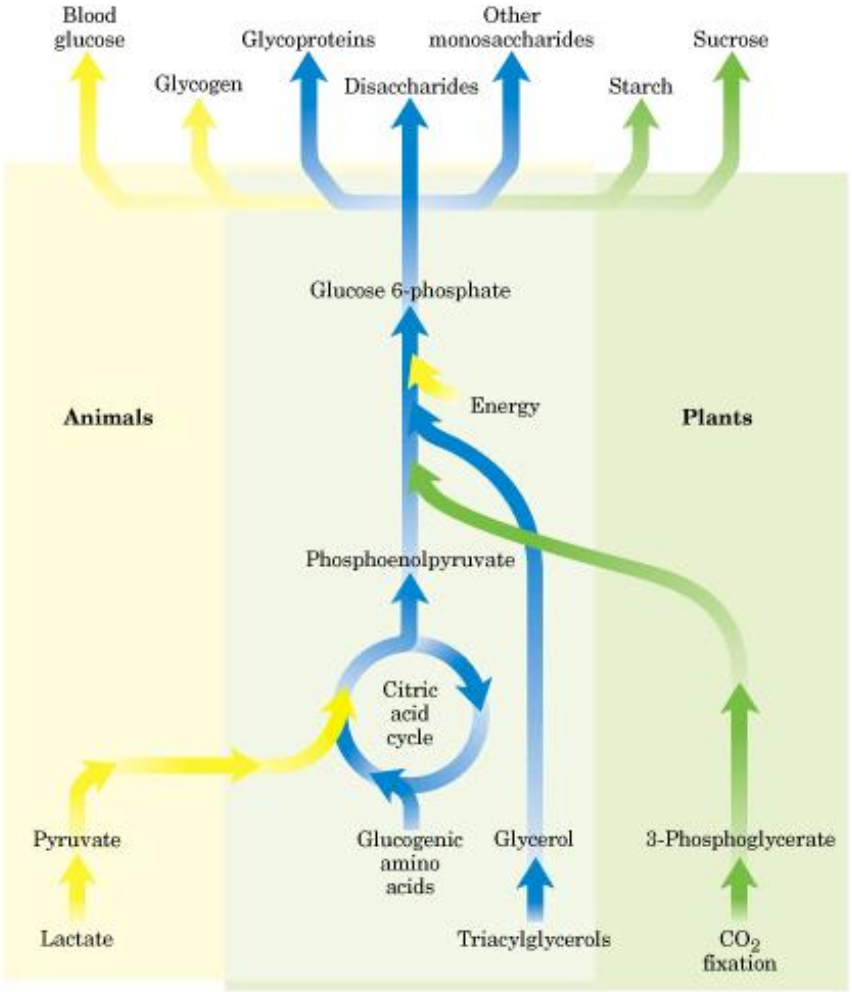
- Conversão de piruvato a acetil-CoA
- Entrada de acetilCoA no ciclo

- Disponibilidade de substrato
- Inibição por acúmulo de produto
- Regulação alostérica

Anabolismo

Síntese de CHO

- Biosíntese de glucose
  - Cérebro e sist. Nervoso
  - Eritrócitos, medula renal, tec. embrionários



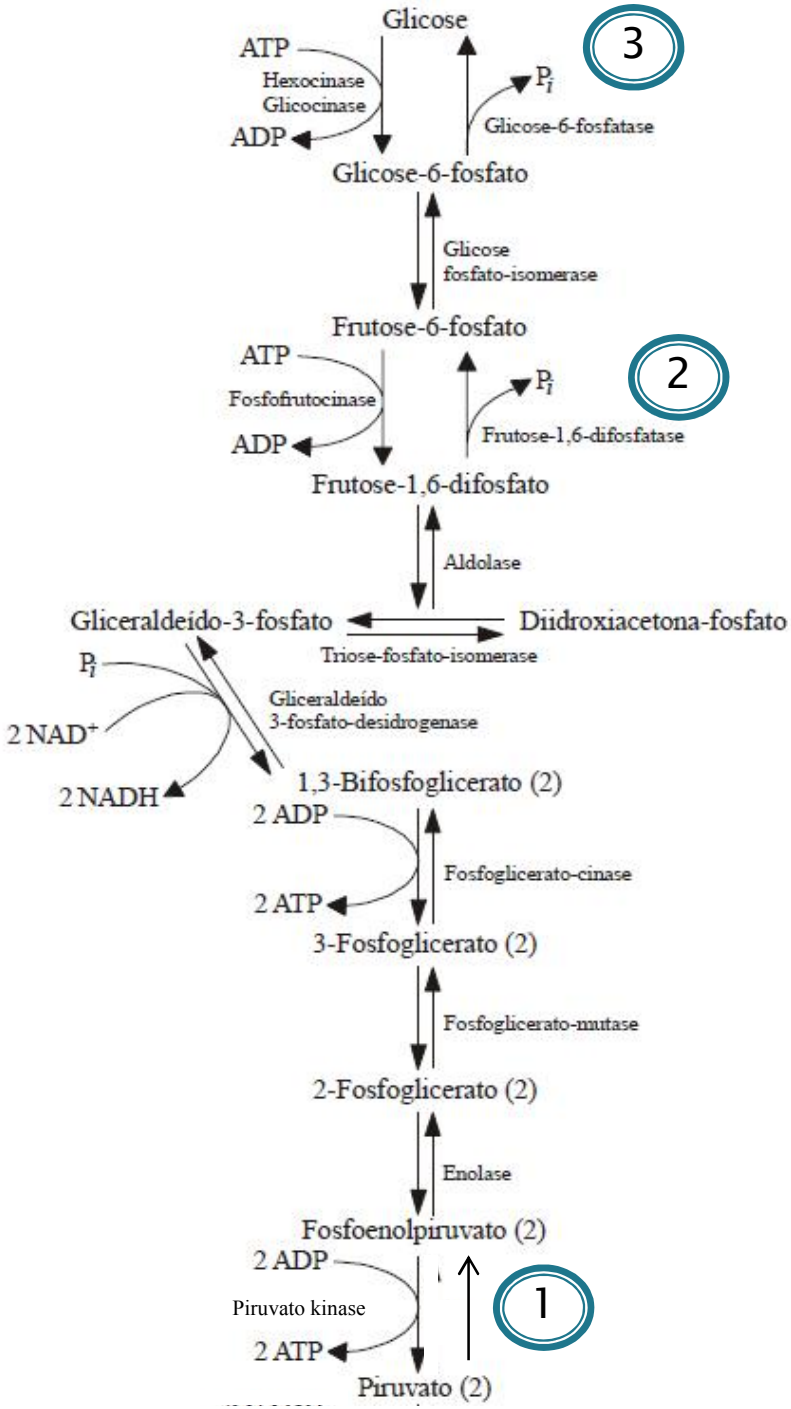
Gluconeogênese

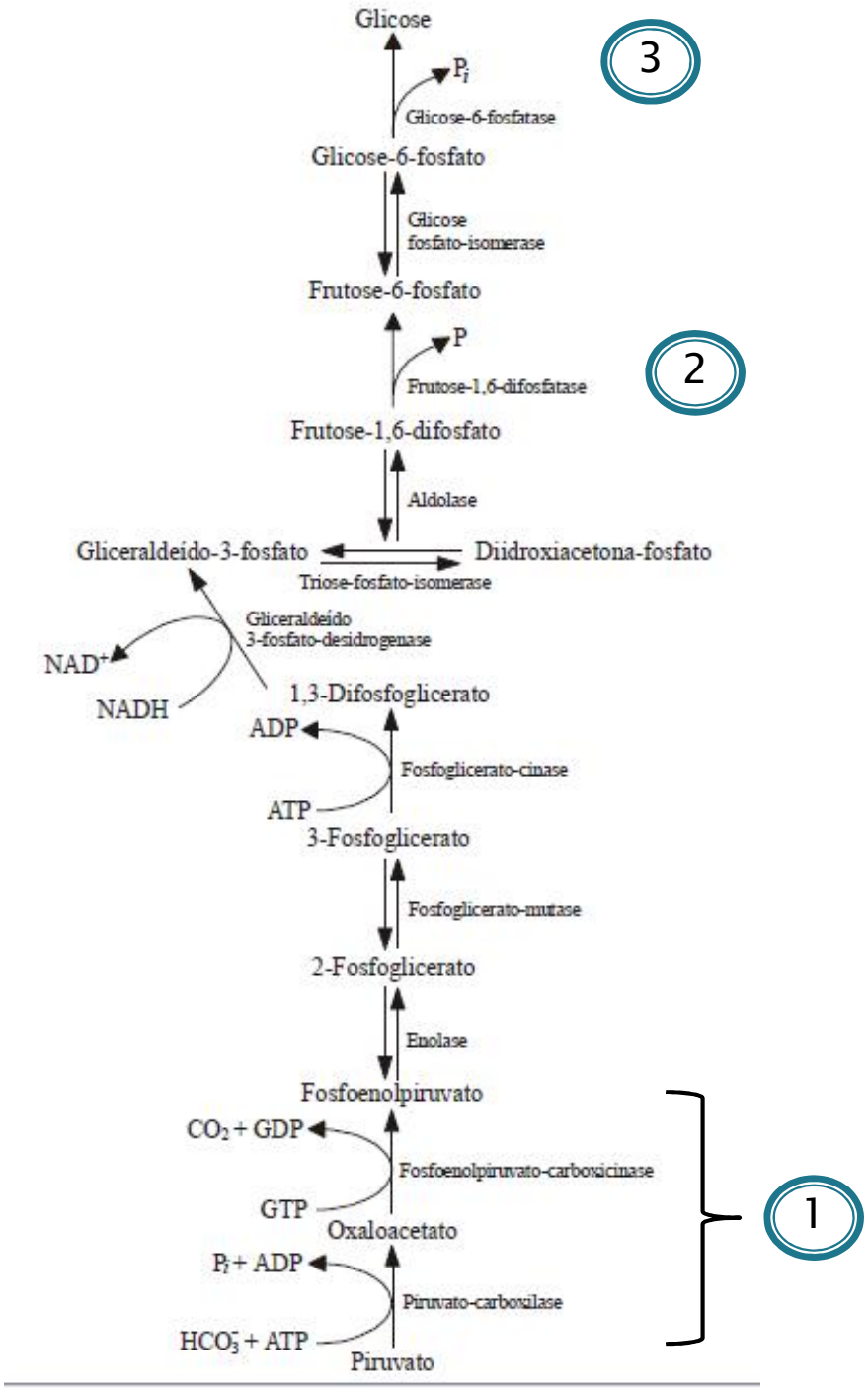
- Formação de glicose a partir de precursores não-carboidratos
  - Lactato, piruvato, glicerol e aa

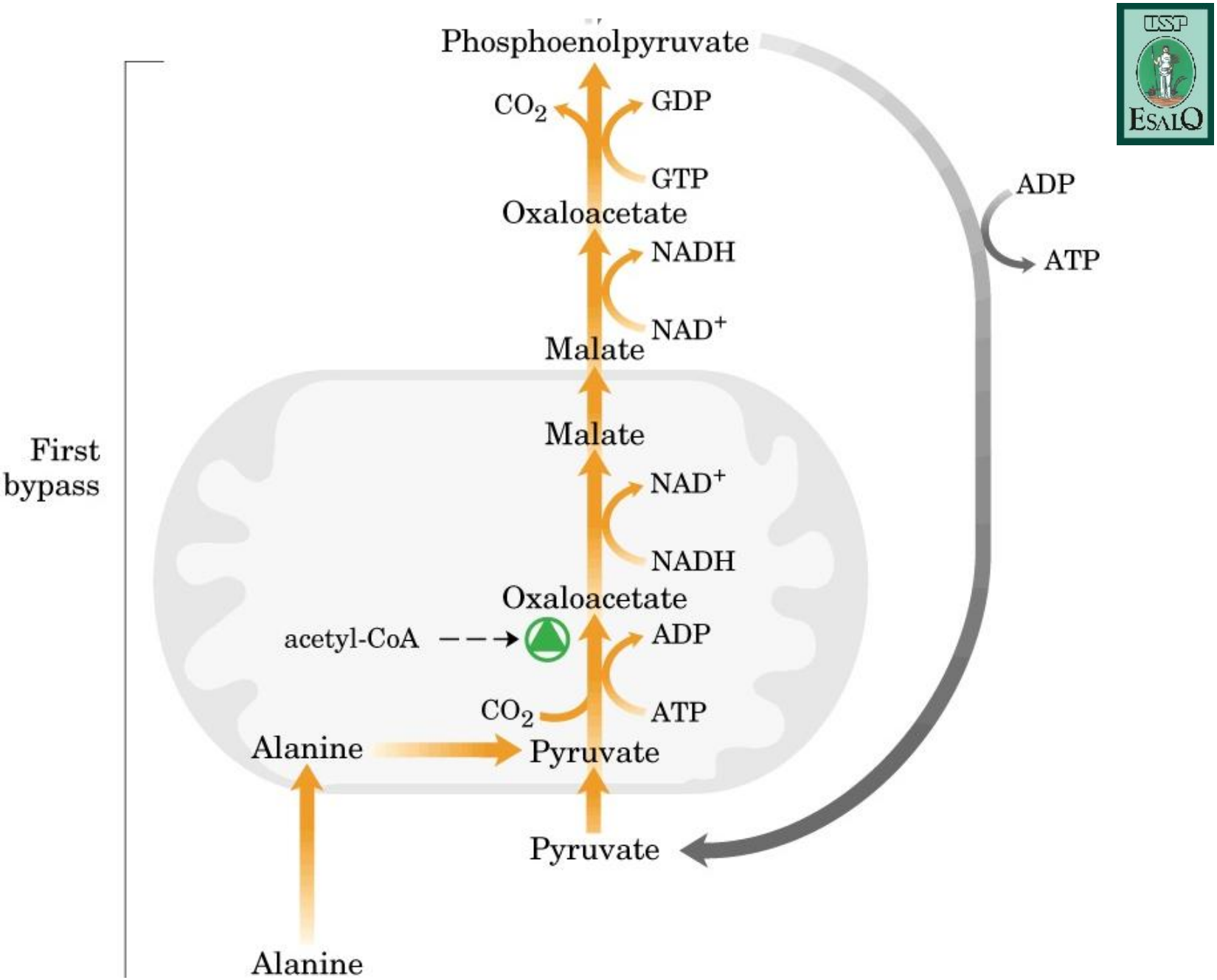
  - Fígado
  - Rins

  - Ocorre depois de glicogenólise completa

  - Cérebro e eritrócitos: glicose, corpos cetônicos
  - Músculos: glicose a partir de glicogênio, AG e corpos cetônicos

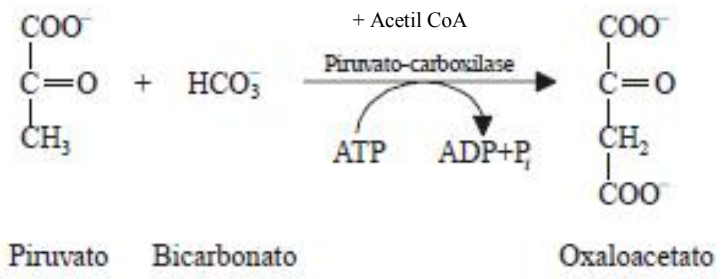

Glicose
ATP
Hexocinase
Glicocinase
ADP
P_i
Glicose-6-fosfatase
3
Glicose-6-fosfato
Glicose
fosfato-isomerase
Frutose-6-fosfato
ATP
Fosfofrutocinase
ADP
P_i
Frutose-1,6-difosfatase
2
Frutose-1,6-difosfato
Aldolase
Gliceraldeído-3-fosfato
Diidroxiacetona-fosfato
Triose-fosfato-isomerase
P_i
2 NAD+
2 NADH
Gliceraldeído
3-fosfato-desidrogenase
1,3-Bifosfoglicerato (2)
2 ADP
2 ATP
Fosfoglicerato-cinase
3-Fosfoglicerato (2)
Fosfoglicerato-mutase
2-Fosfoglicerato (2)
Enolase
Fosfoenolpiruvato (2)
2 ADP
Piruvato kinase
2 ATP
1
Piruvato (2)


Glicose
P_i
Glicose-6-fosfatase
3
Glicose-6-fosfato
Glicose
fosfato-isomerase
Frutose-6-fosfato
P
Frutose-1,6-difosfatase
2
Frutose-1,6-difosfato
Aldolase
Gliceraldeído-3-fosfato
Diidroxiacetona-fosfato
Triose-fosfato-isomerase
Gliceraldeído
3-fosfato-desidrogenase
NAD+
NADH
1,3-Difosfoglicerato
ADP
Fosfoglicerato-cinase
ATP
3-Fosfoglicerato
Fosfoglicerato-mutase
2-Fosfoglicerato
Enolase
Fosfoenolpiruvato
CO_2 + GDP
Fosfoenolpiruvato-carboxicinase
GTP
Oxaloacetato
P_i + ADP
Piruvato-carboxilase
HCO_3^- + ATP
Piruvato
1


Phosphoenolpyruvate
CO_2
GDP
GTP
Oxaloacetate
NADH
NAD^+
Malate
Malate
NAD^+
NADH
Oxaloacetate
acetyl-CoA
ADP
CO_2
ATP
Alanine
Pyruvate
Pyruvate
Alanine
First bypass
ADP
ATP

1 Conversão de piruvato em PEP

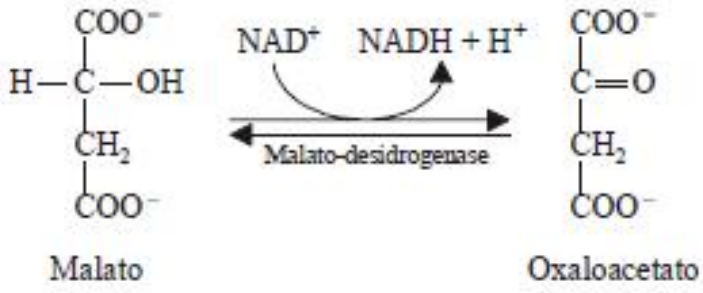
- Na mitocôndria:



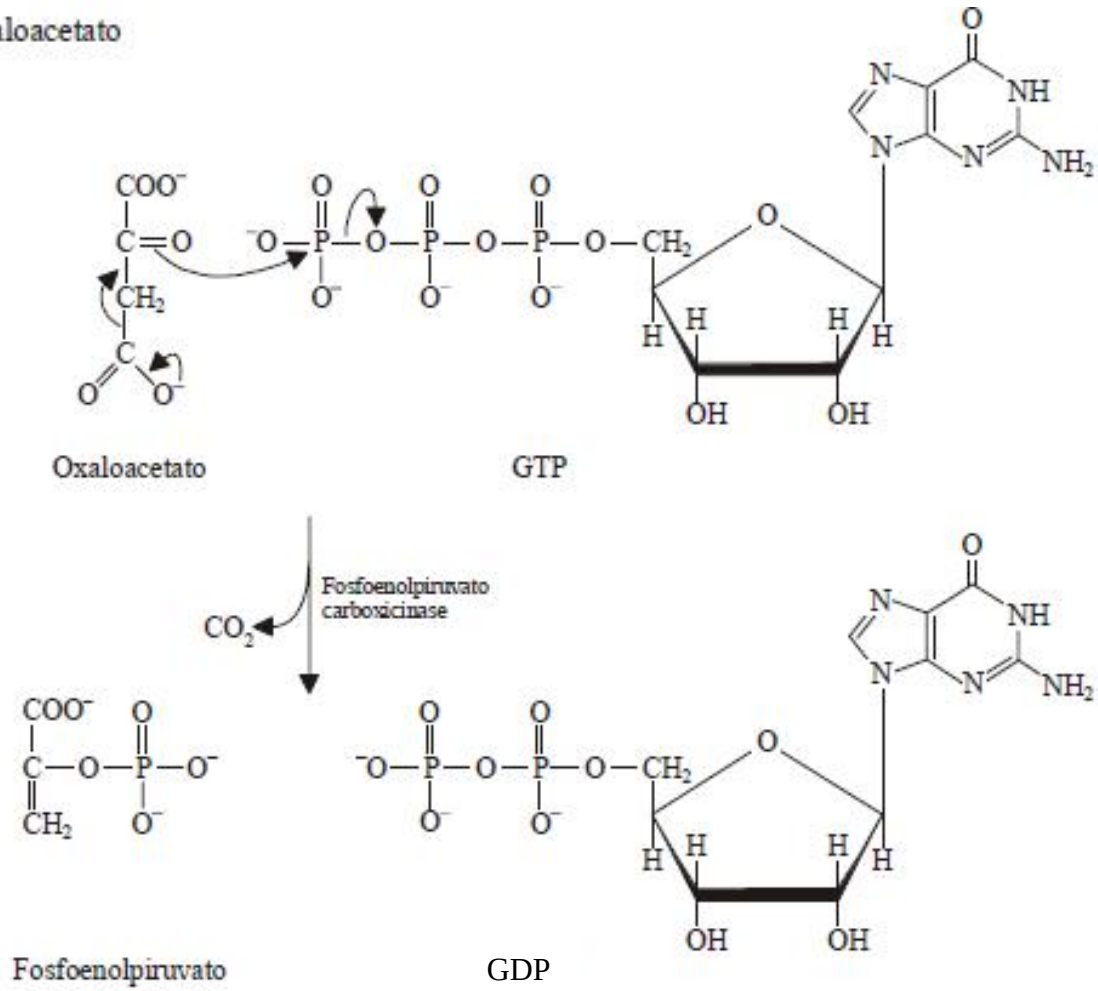
- Membrana mitocôndria impermeável ao oxaloacetato:

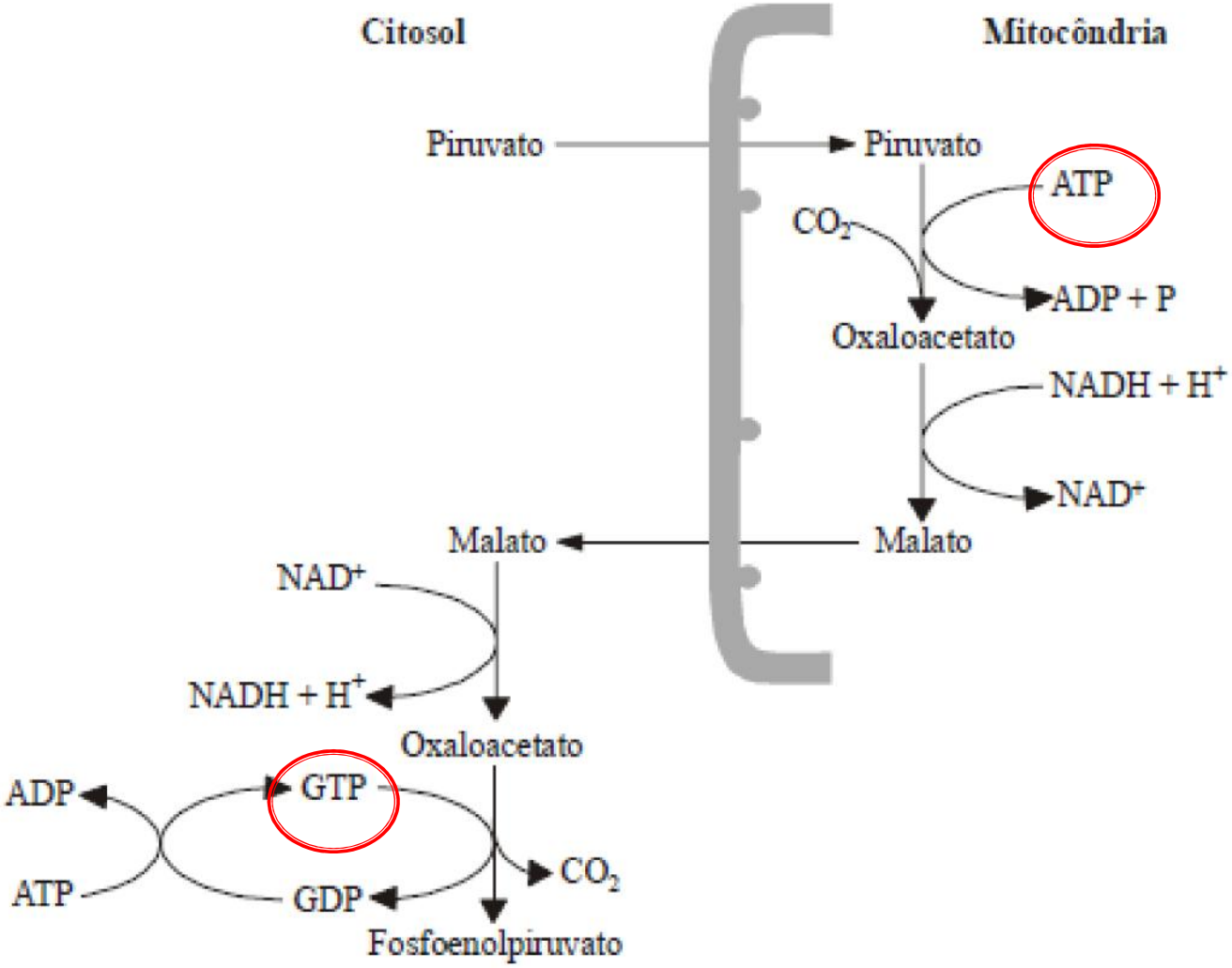
$$\text{Oxaloacetato} + \text{NADH} + \text{H}^+ \xleftrightarrow{\text{Malato desidrogenase}} \text{Malato} + \text{NAD}^+$$

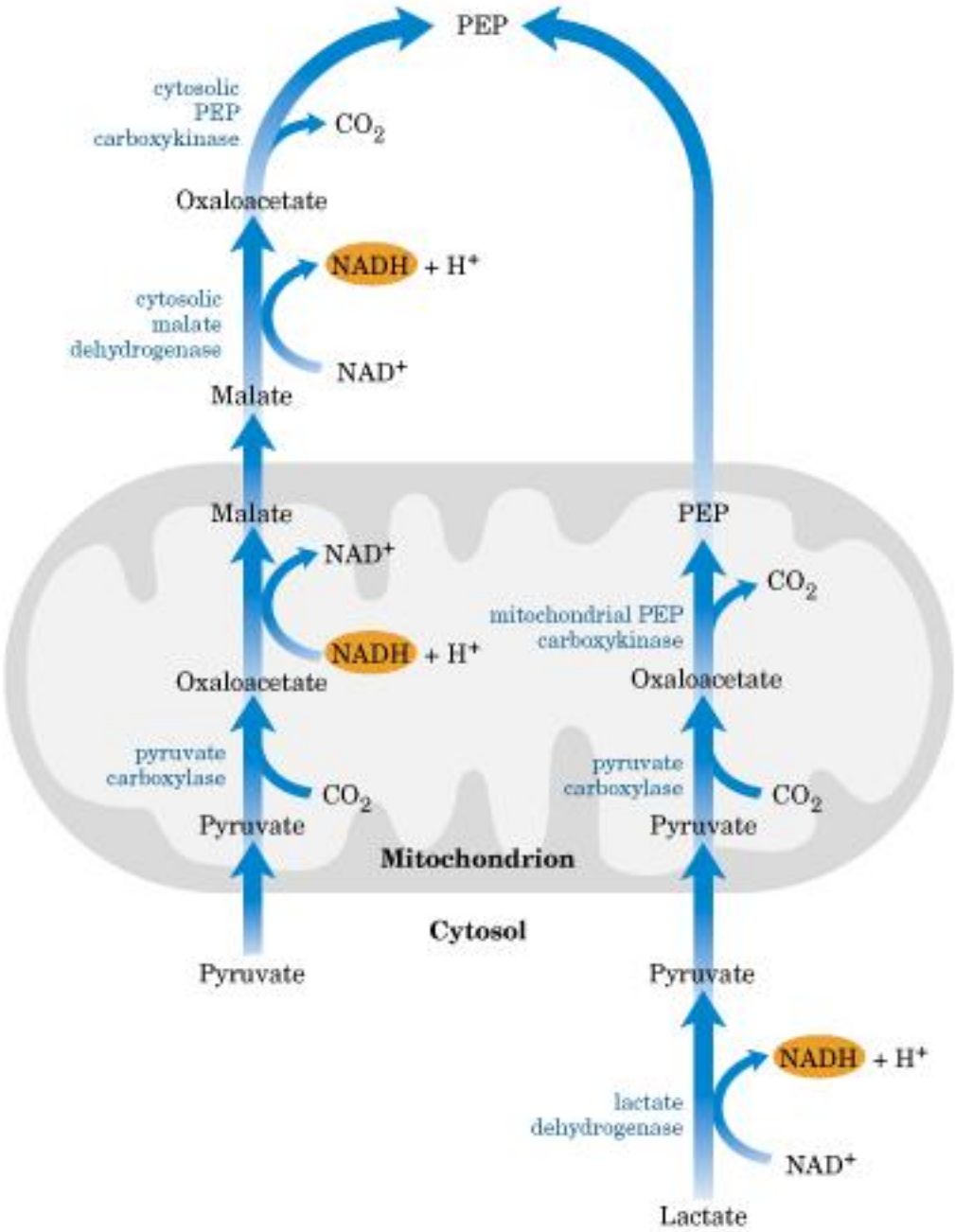
- Transferência do malato para o citosol

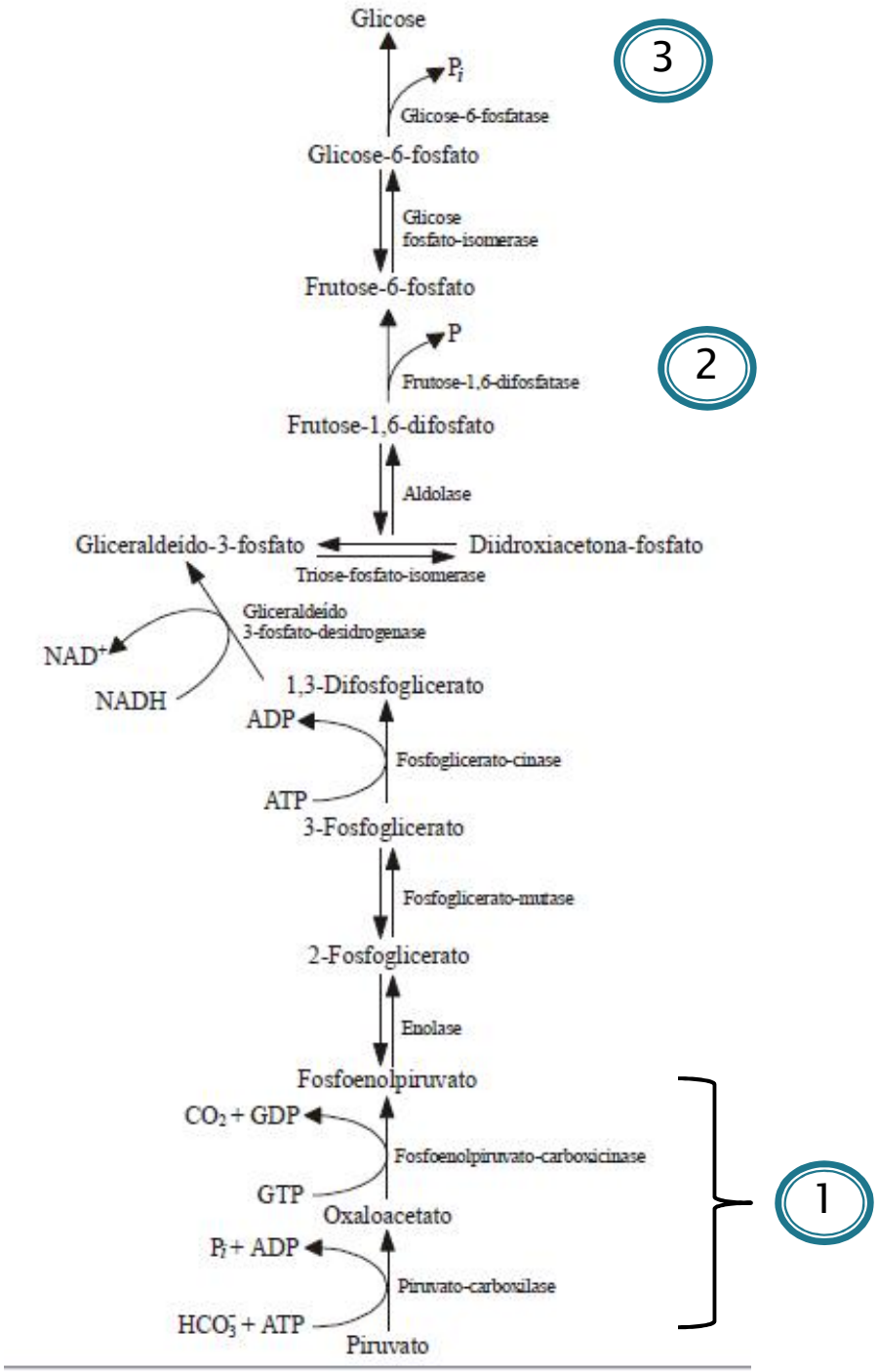


- Descarboxilação e ligação com grupo fosforil




Citosol
Mitocôndria
Piruvato
Piruvato
ATP
CO_2
ADP + P
Oxaloacetato
NADH + H^+
NAD^+
Malato
Malato
NAD^+
NADH + H^+
Oxaloacetato
ADP
GTP
ATP
GDP
CO_2
Fosfoenolpiruvato


PEP
cytosolic
PEP
carboxykinase
CO_2
Oxaloacetate
NADH + H^+
cytosolic
malate
dehydrogenase
NAD^+
Malate
Malate
NAD^+
NADH + H^+
Oxaloacetate
PEP
CO_2
mitochondrial PEP
carboxykinase
Oxaloacetate
pyruvate
carboxylase
CO_2
Pyruvate
pyruvate
carboxylase
CO_2
Pyruvate
Mitochondrion
Cytosol
Pyruvate
Pyruvate
NADH + H^+
lactate
dehydrogenase
NAD^+
Lactate

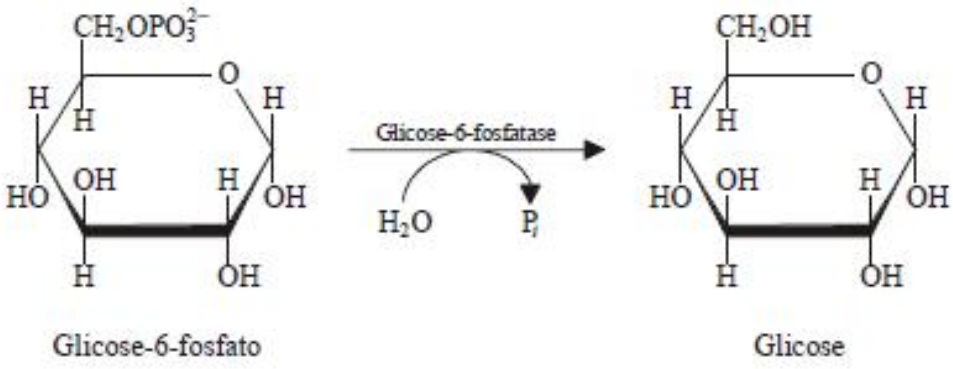

Glicose
P_i
Glicose-6-fosfatase
Glicose-6-fosfato
Glicose fosfato-isomerase
Frutose-6-fosfato
P
Frutose-1,6-difosfatase
Frutose-1,6-difosfato
Aldolase
Gliceraldeido-3-fosfato
Diidroxiacetona-fosfato
Triose-fosfato-isomerase
Gliceraldeido 3-fosfato-desidrogenase
NAD^+
NADH
1,3-Difosfoglicerato
ADP
Fosfoglicerato-cinase
ATP
3-Fosfoglicerato
Fosfoglicerato-mutase
2-Fosfoglicerato
Enolase
Fosfoenolpiruvato
CO_2 + GDP
Fosfoenolpiruvato-carboxicinase
GTP
Oxaloacetato
P_i + ADP
Piruvato-carboxilase
HCO_3^- + ATP
Piruvato
3
2
1

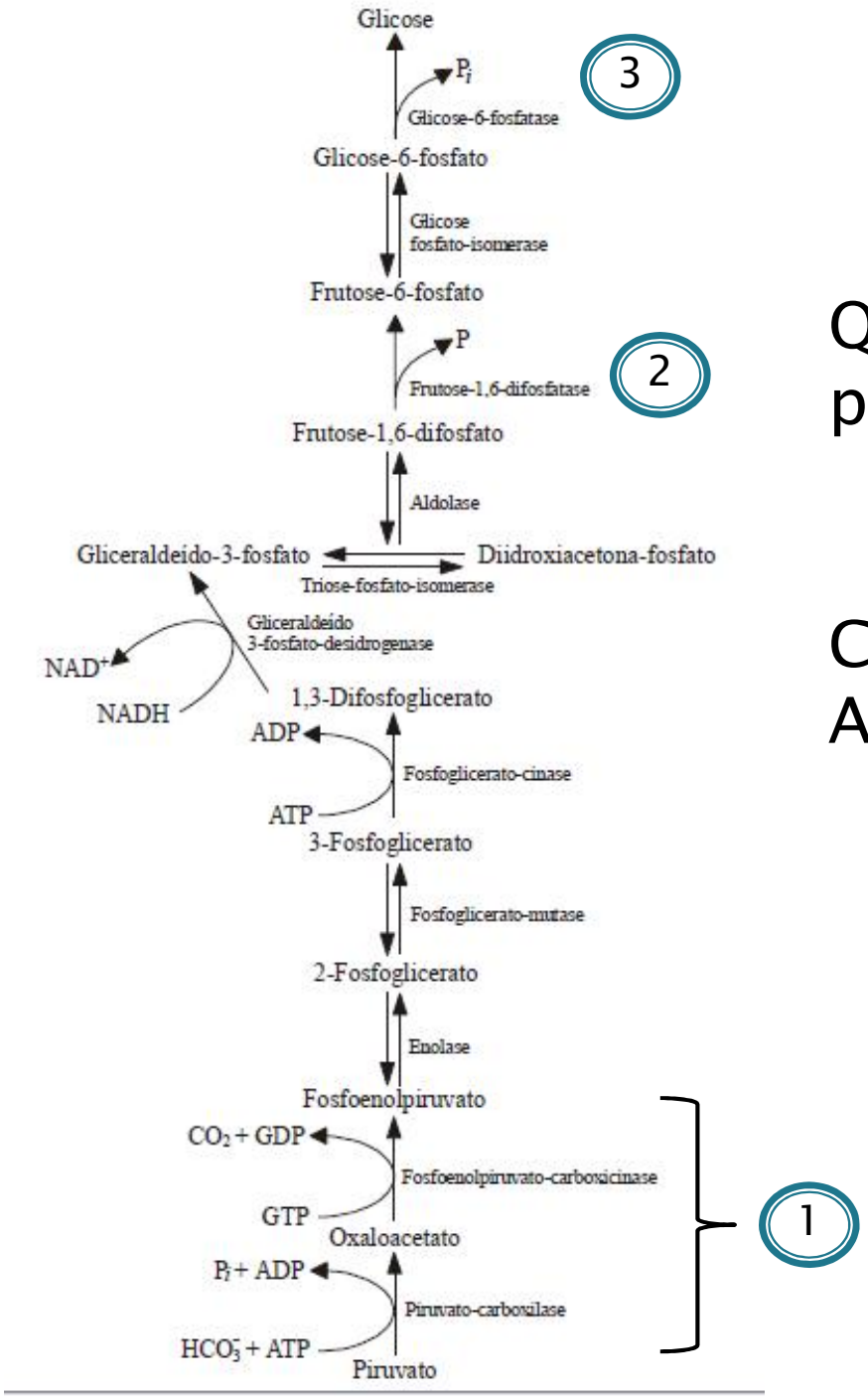
2

Frutose 1,6 bifosfato + H2O $\xrightarrow{\text{Frutose 1,6 bifosfatase}}$ frutose 6 fosfato + Pi

+ citrato
- AMP
- frutose 2,6 BP

3 Formação de glicose a partir de glicose 6P



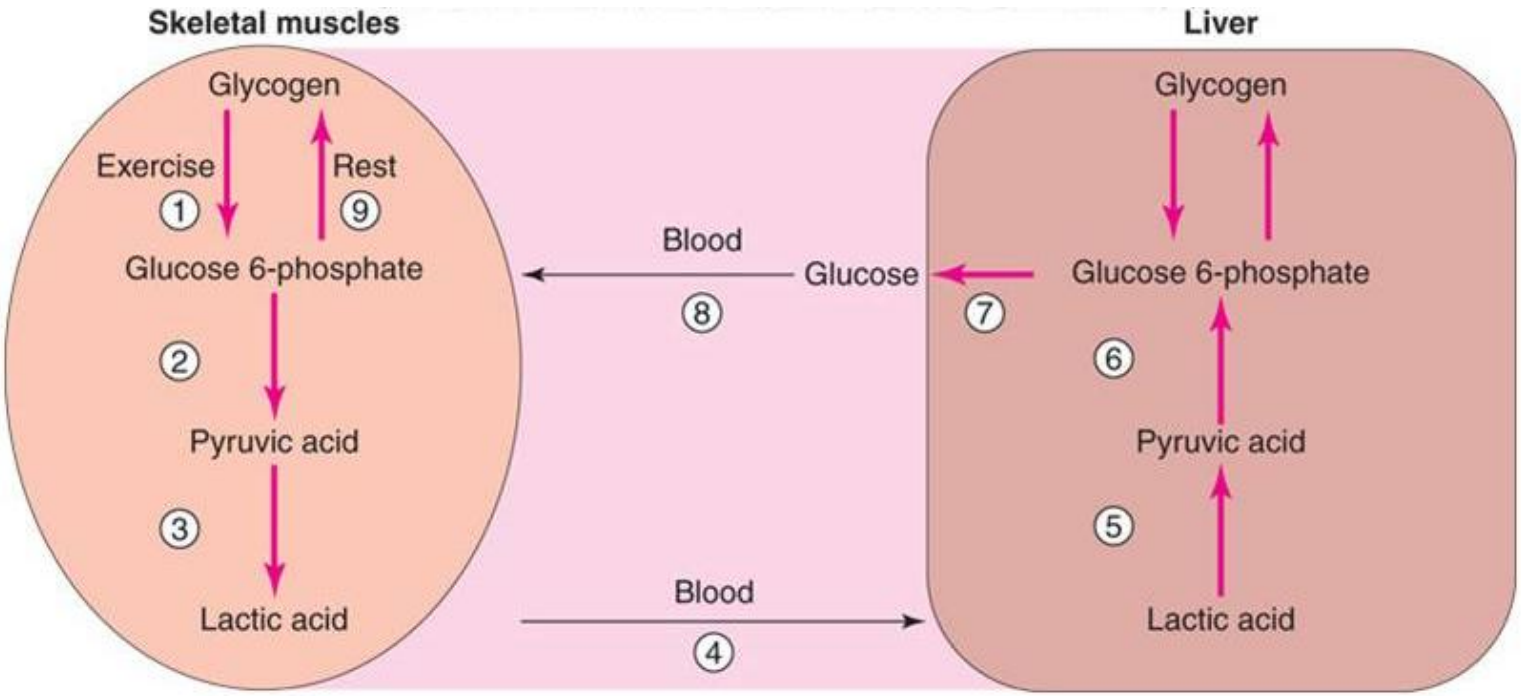


Qual é o consumo de ATP para formar 1 glicose?

Consumo de até 60% do ATP gerado no fígado.

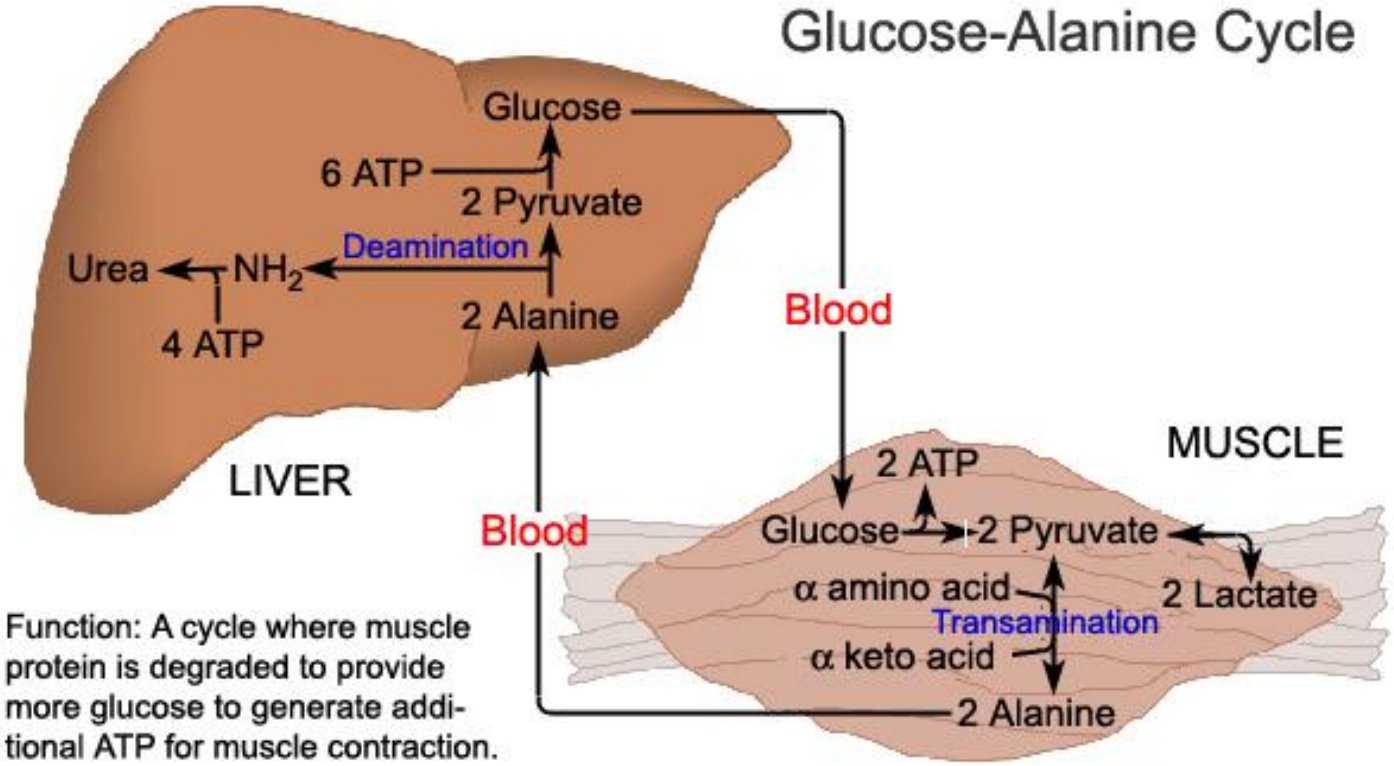
Precursores gluconeogenese

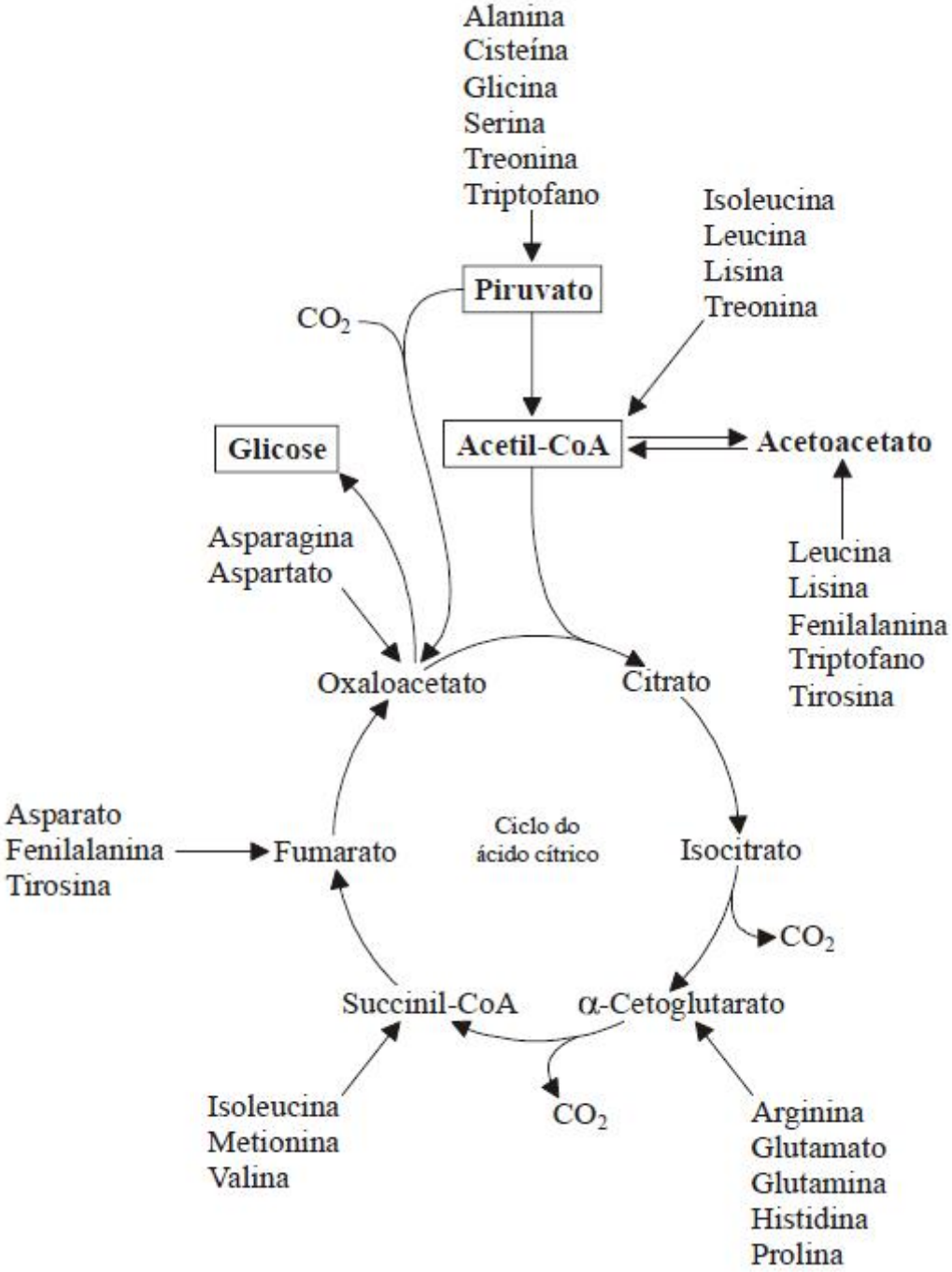
- Lactato: eritrócitos e células musculares



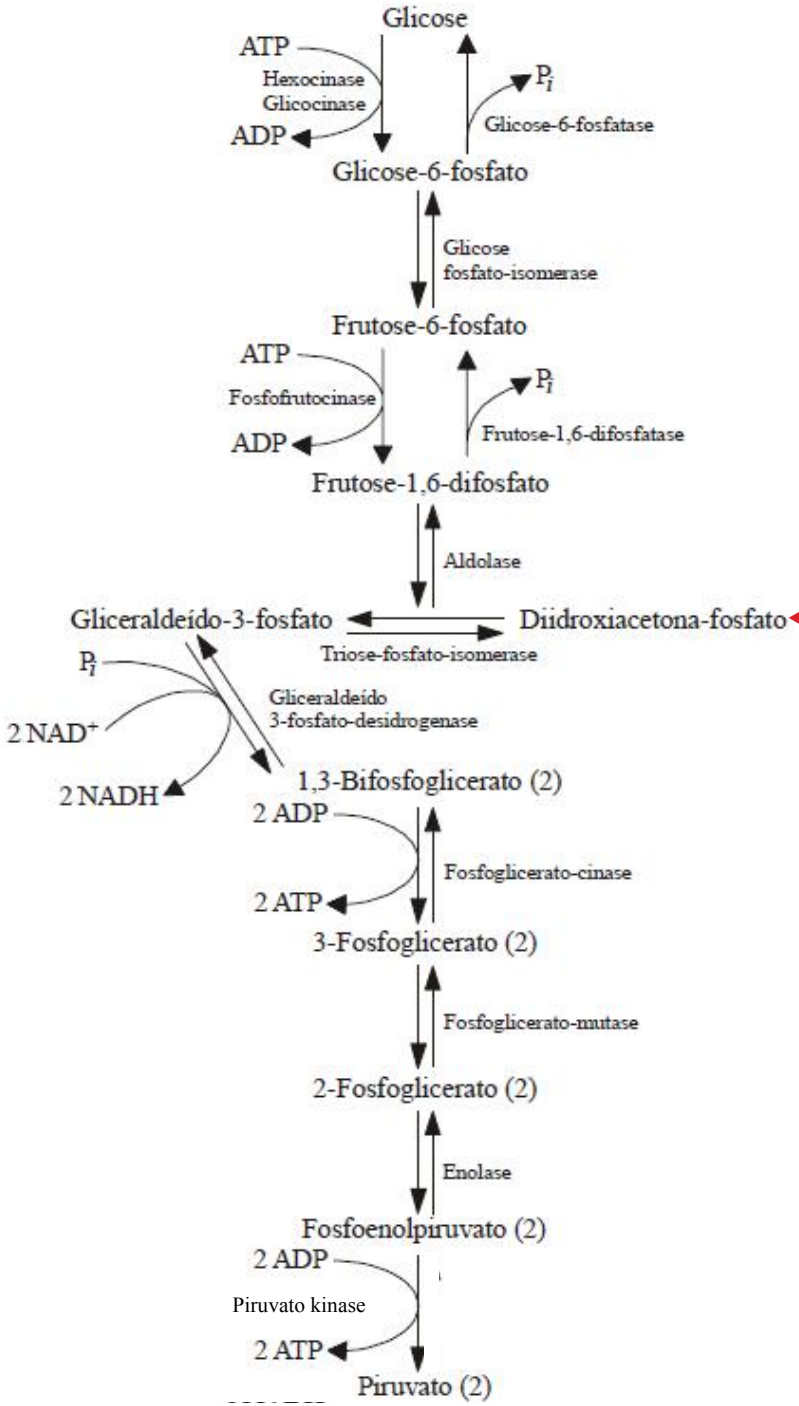
2 lactato + 6 ATP + 6 H2O → glicose + ADP + 6 Pi + $4H^+$

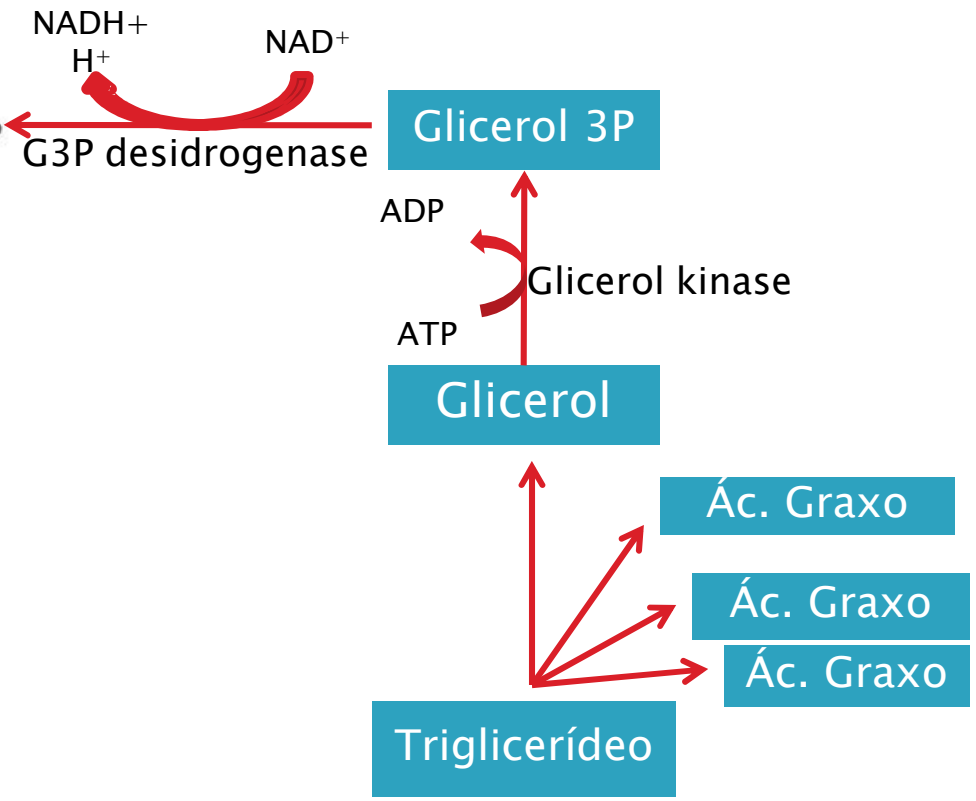
- Alanina: aminoácido gluconeogênico mais importante



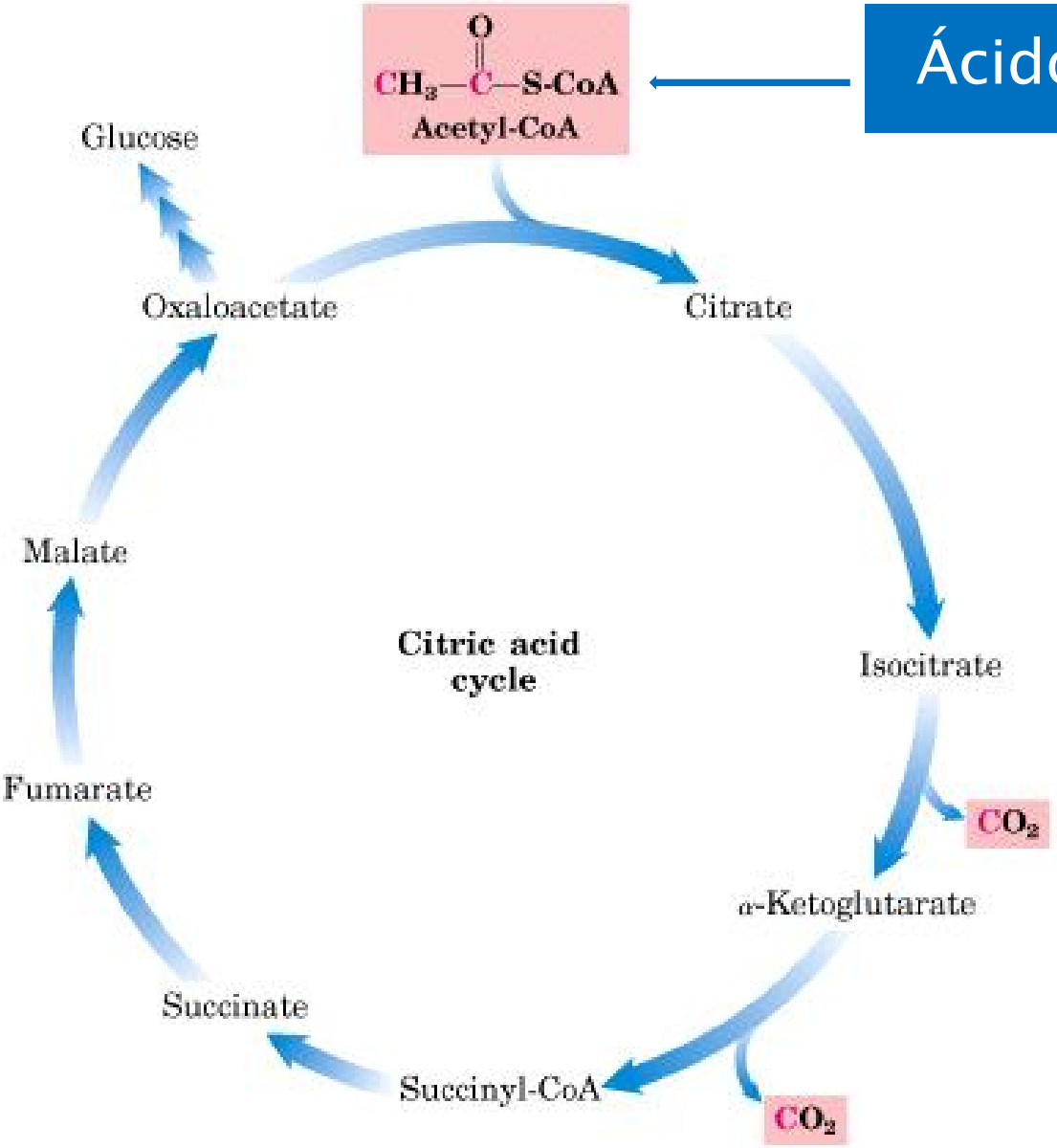

Alanina
Cisteína
Glicina
Serina
Treonina
Triptofano
Piruvato
CO_2
Isoleucina
Leucina
Lisina
Treonina
Glicose
Acetil-CoA
Acetoacetato
Asparagina
Aspartato
Leucina
Lisina
Fenilalanina
Triptofano
Tirosina
Oxaloacetato
Citrato
Asparato
Fenilalanina
Tirosina
Fumarato
Ciclo do
ácido cítrico
Isocitrato
CO_2
Succinil-CoA
α-Cetoglutarato
Isoleucina
Metionina
Valina
CO_2
Arginina
Glutamato
Glutamina
Histidina
Prolina

Glicerol: produto da hidrólise dos triglicerídeos no tec. adiposo



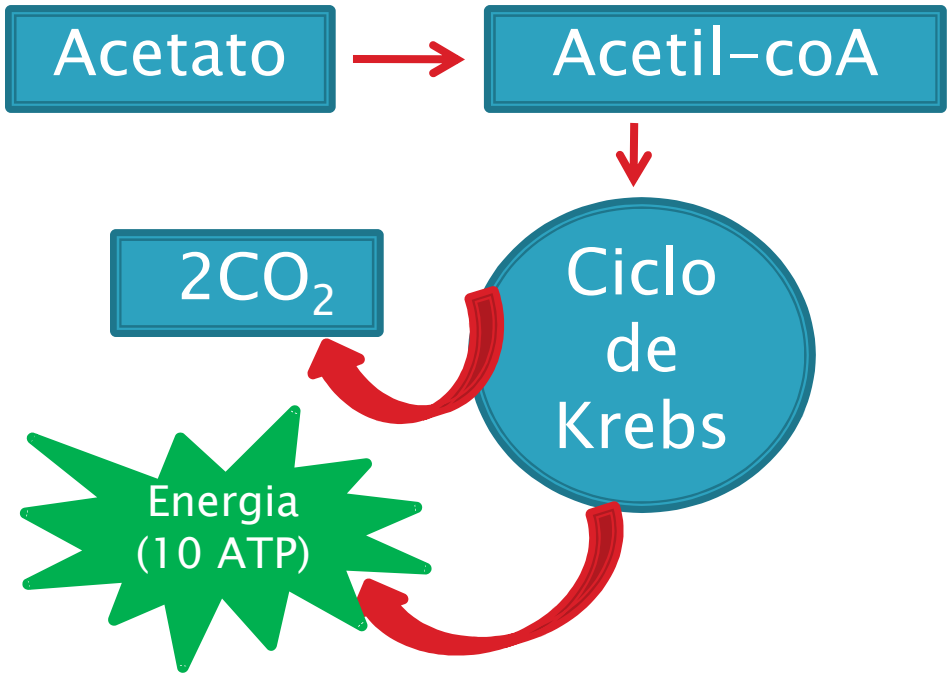


Ácidos Graxos



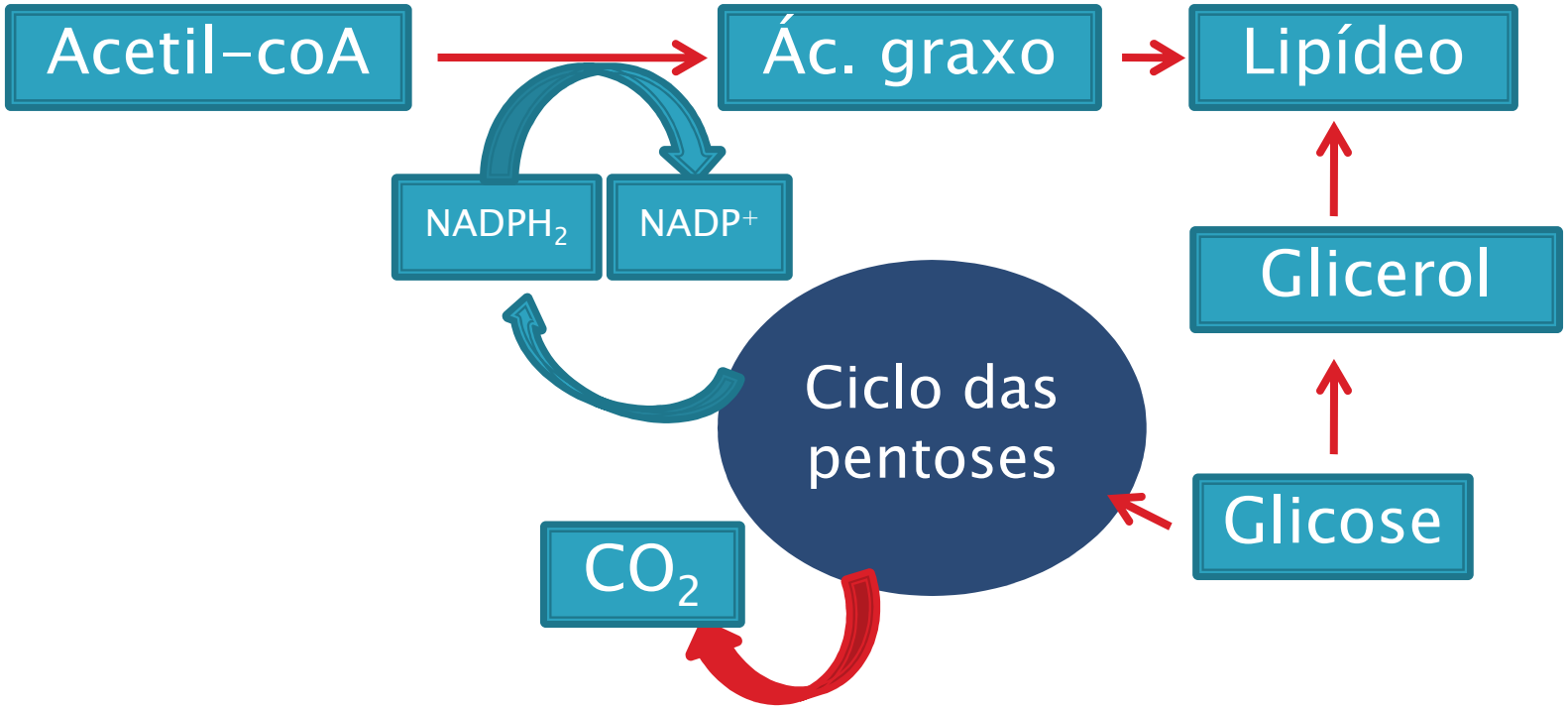
Ruminantes: Ác. Graxos voláteis

- Acetato
  - Fonte de energia



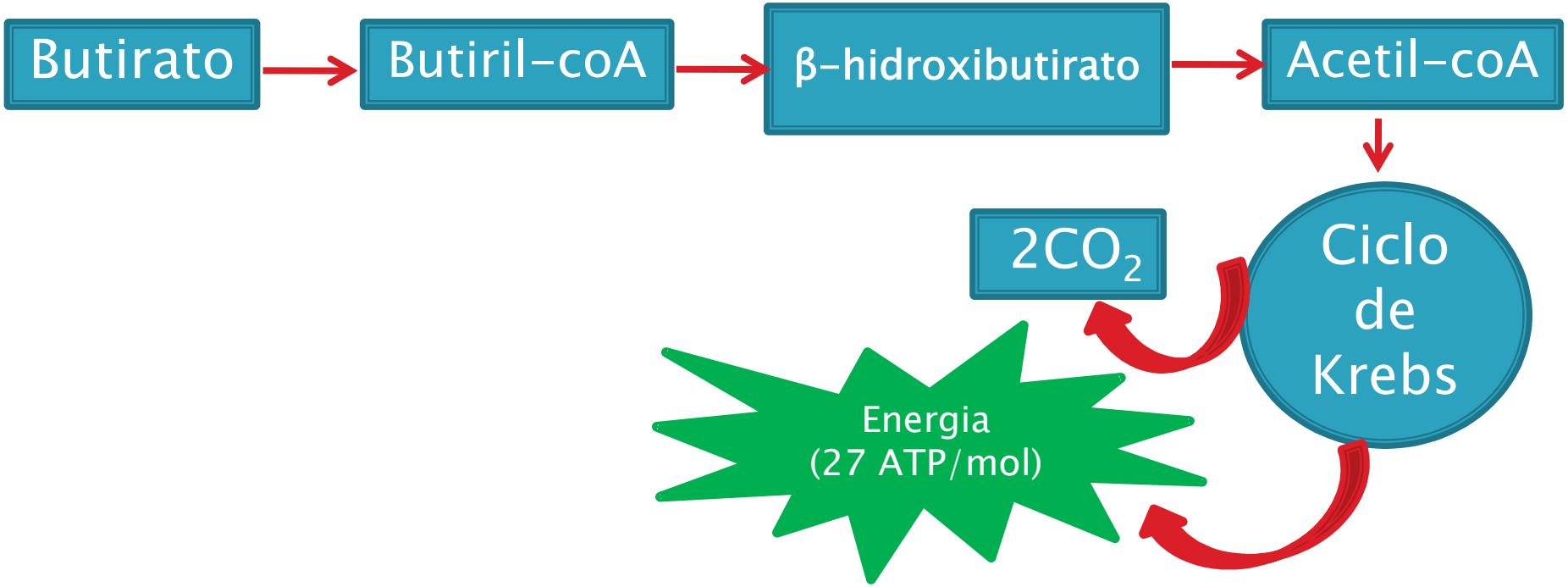
Ruminantes: Ác. Graxos voláteis

- Acetato
  - Síntese de lipídeos



Ruminantes: Ác. Graxos voláteis

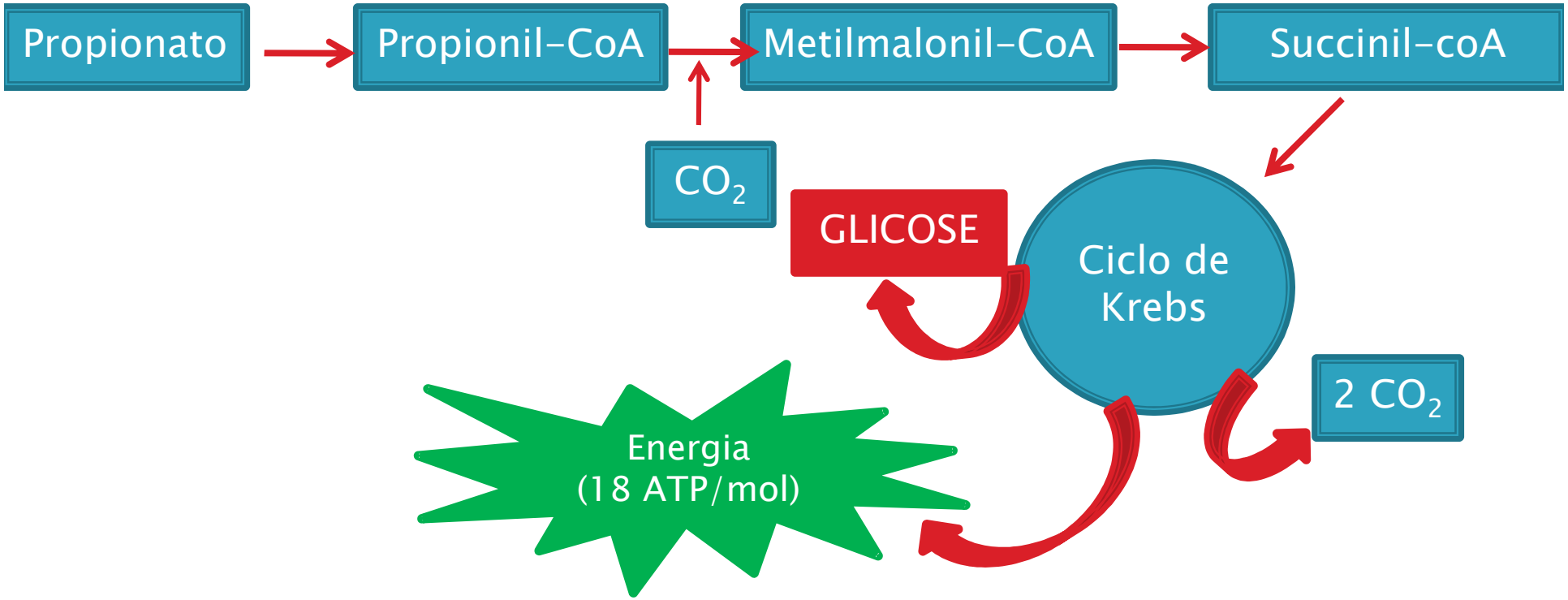
- Butirato
  - Fonte de energia



• Parte do butirato também é utilizado para iniciar a síntese de lipídeos

Ruminantes: Ác. Graxos Voláteis

- Propionato
  - Fonte de glicose (energia)

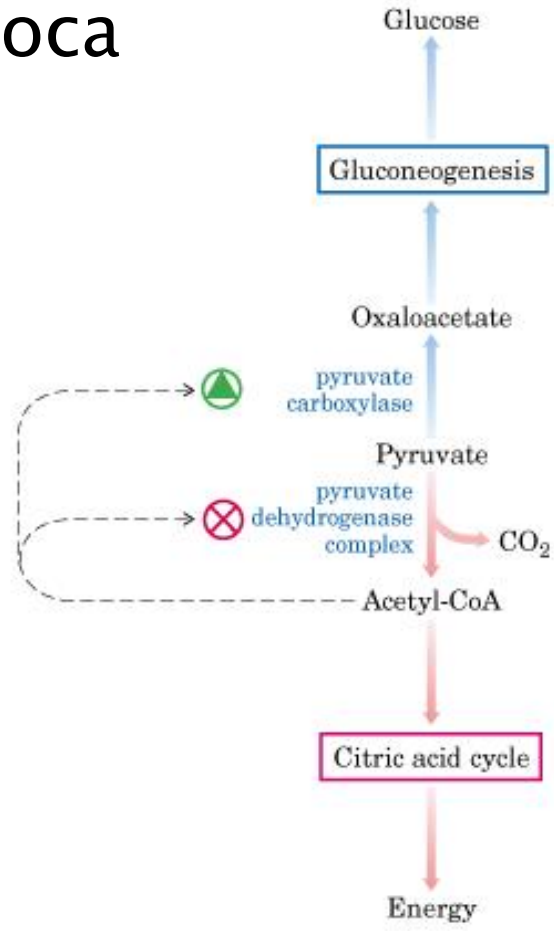


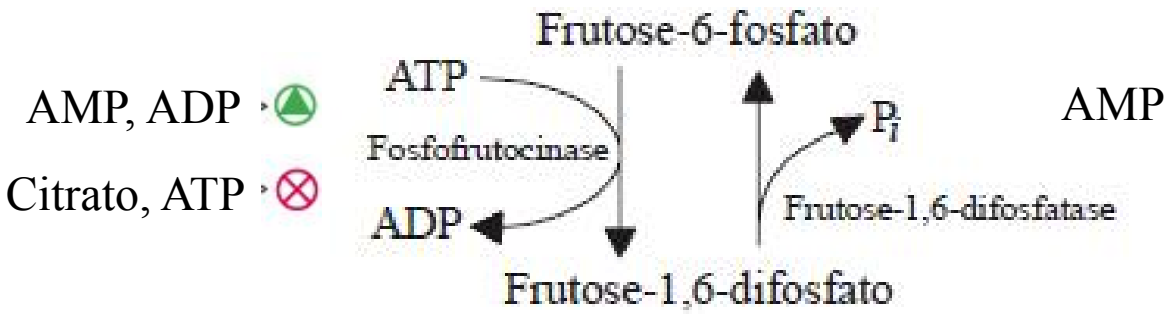
Utilização de AGV no metabolismo de ruminantes

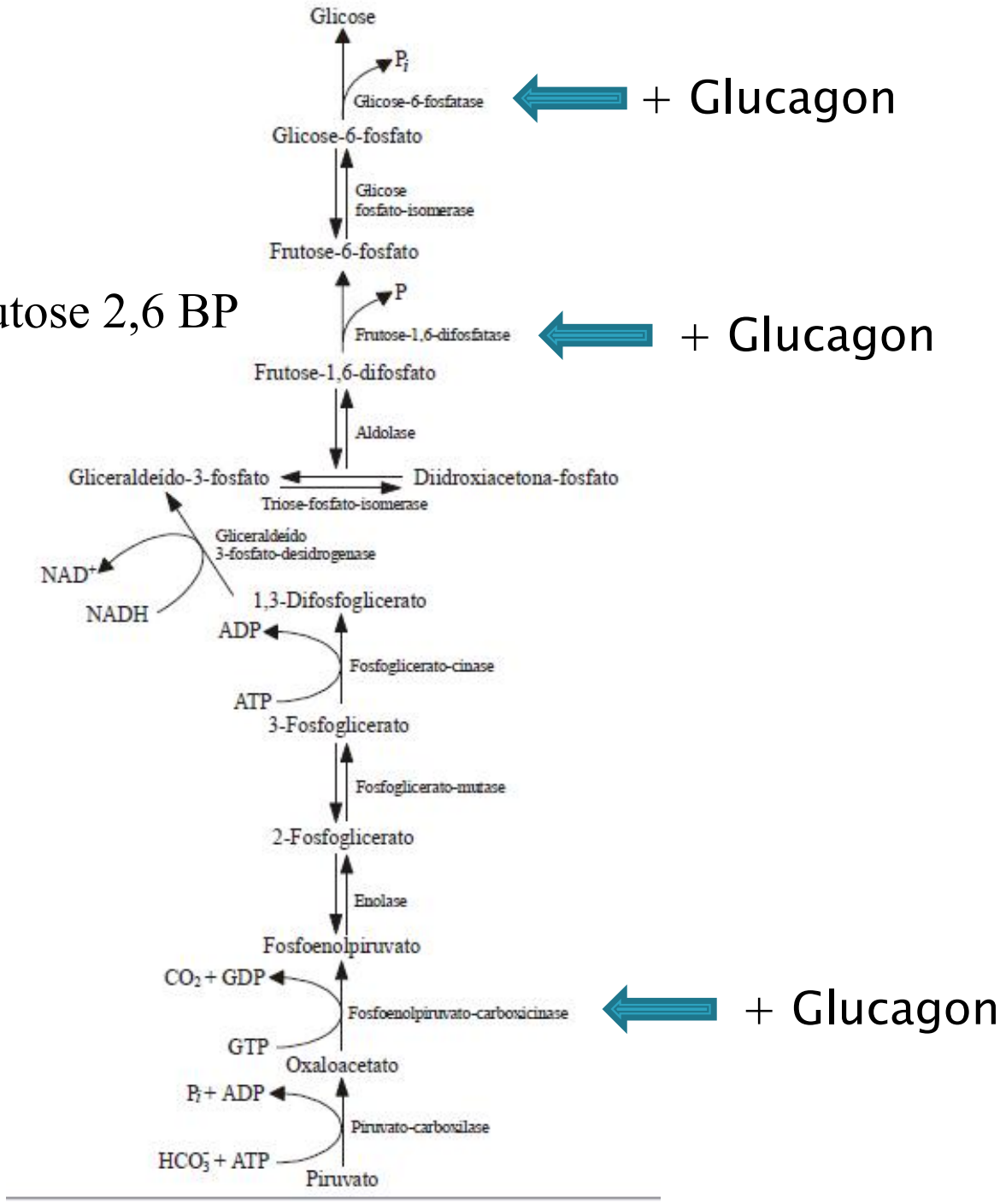
- Acetato
  - Energia
  - Fonte de Carbono para síntese de ác. graxos
    - Tecido adiposo
    - Glândula mamária
- Propionato
  - Energia
  - Precursor de glicose
- Butirato
  - Energia
  - Fonte de Carbono para síntese de ác. graxos

Glicólise x Gluconeogenese

- Regulação coordenada e recíproca
  - Destino do Piruvato
    - Regulação alostérica
  - 2º. By-pass
    - Frutose 1,6 bifosfatase






Glicose
P_i
Glicose-6-fosfatase
+ Glucagon
Glicose-6-fosfato
Glicose
fosfato-isomerase
Frutose-6-fosfato
Frutose 2,6 BP
P
Frutose-1,6-difosfatase
+ Glucagon
Frutose-1,6-difosfato
Aldolase
Gliceraldeido-3-fosfato
Diidroxiacetona-fosfato
Triose-fosfato-isomerase
Gliceraldeido
3-fosfato-desidrogenase
NAD^+
NADH
1,3-Difosfoglicerato
ADP
Fosfoglicerato-cinase
ATP
3-Fosfoglicerato
Fosfoglicerato-mutase
2-Fosfoglicerato
Enolase
Fosfoenolpiruvato
CO_2 + GDP
Fosfoenolpiruvato-carboxicinase
+ Glucagon
GTP
Oxaloacetato
P_i + ADP
Piruvato-carboxilase
HCO_3^- + ATP
Piruvato