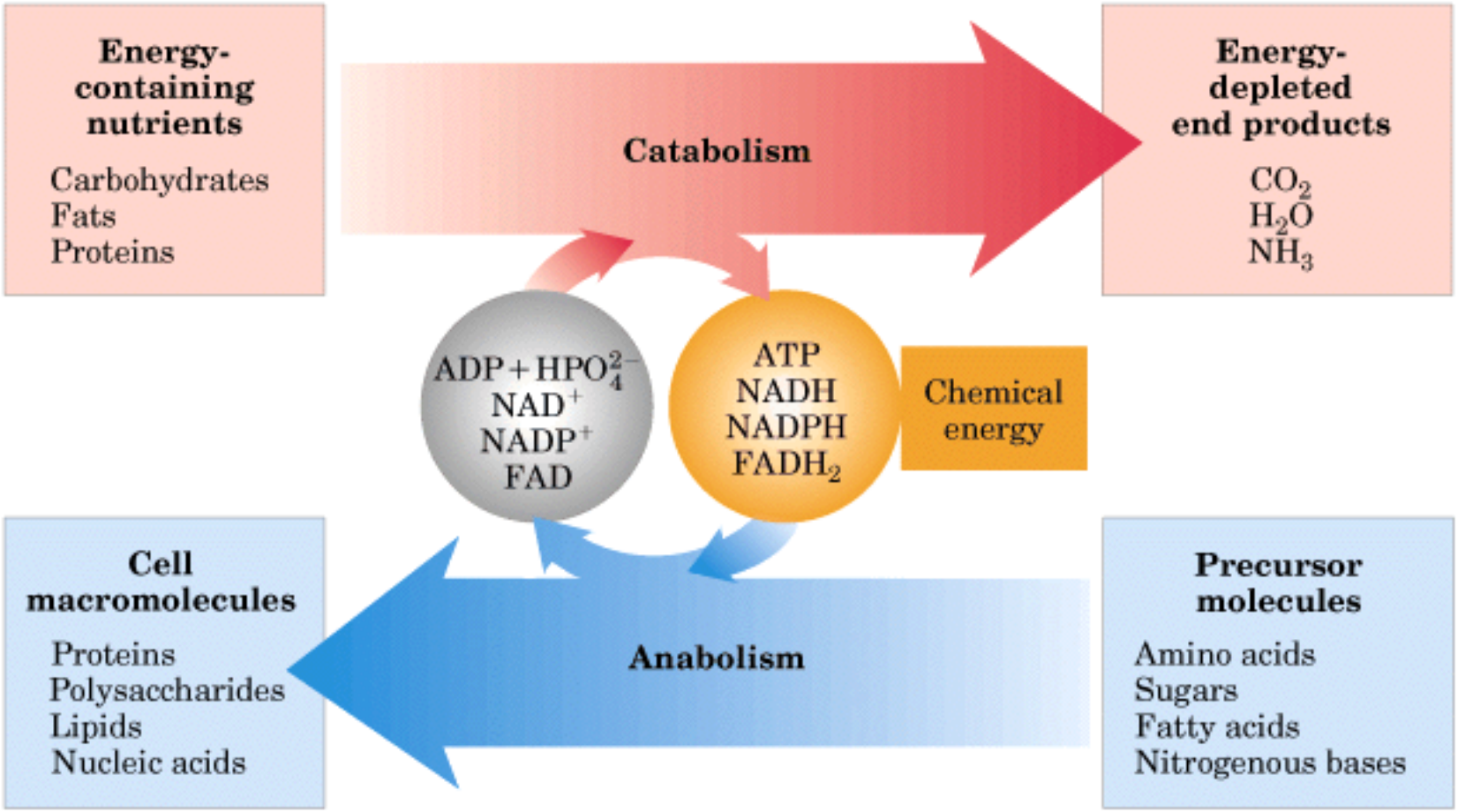
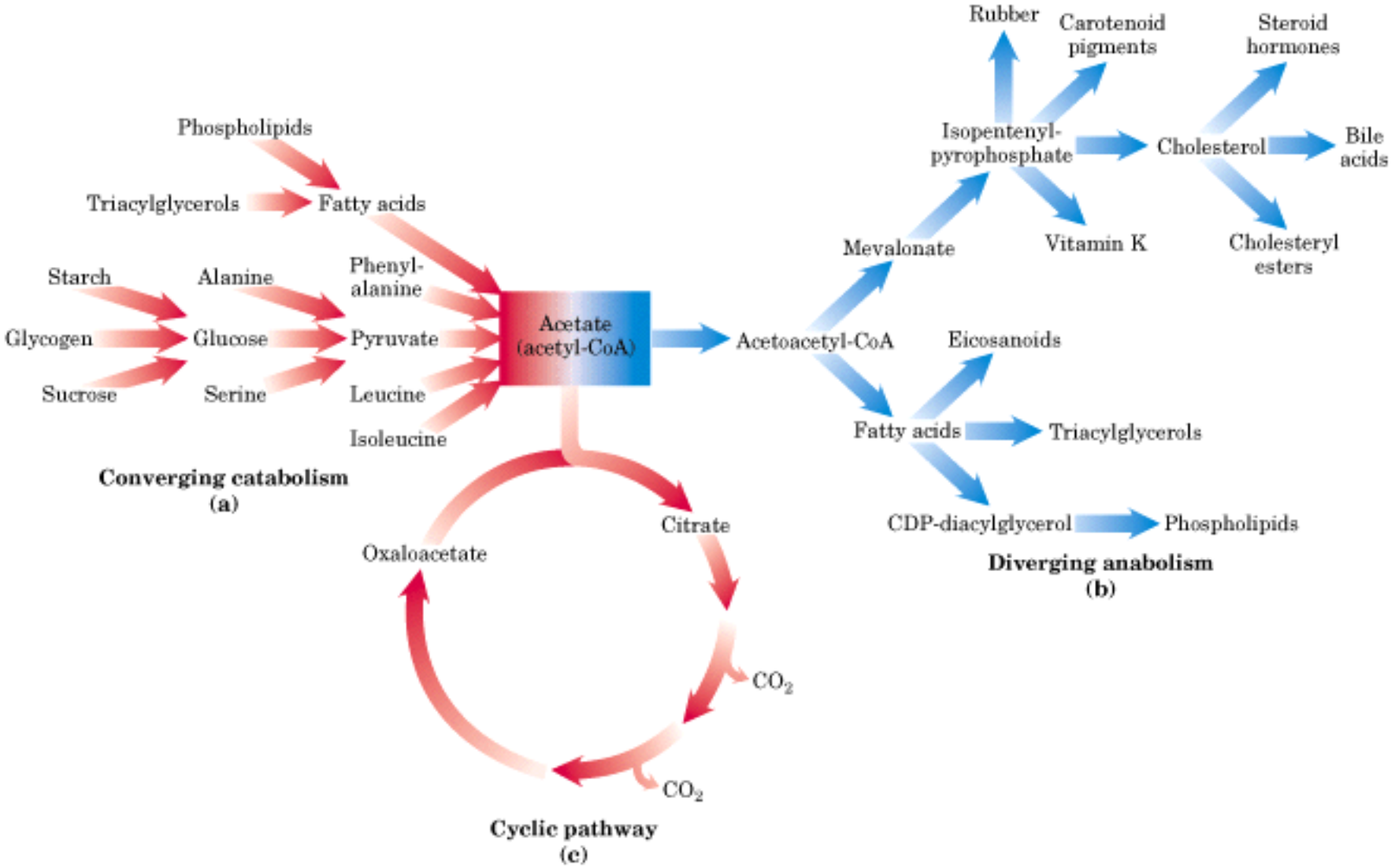
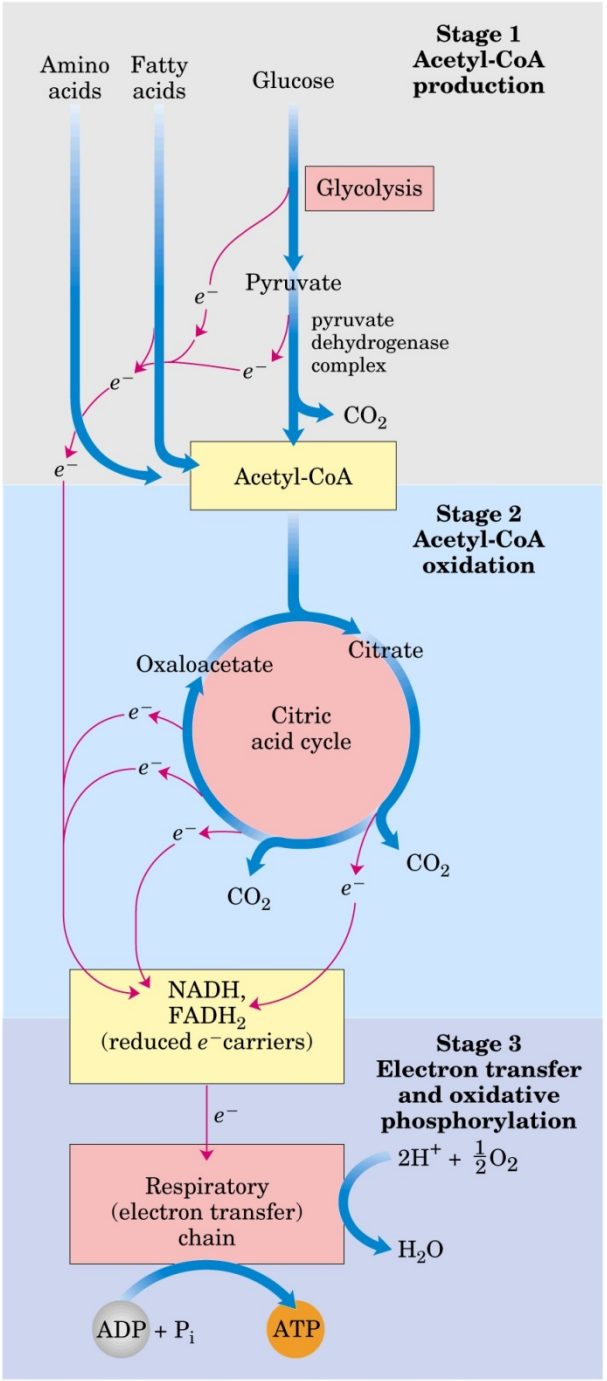

Energy-containing nutrients
Carbohydrates
Fats
Proteins
Catabolism
Energy-depleted end products
CO_2
H_2O
NH_3
$ADP + HPO_4^{2-}$
NAD^+
$NADP^+$
FAD
ATP
NADH
NADPH
$FADH_2$
Chemical energy
Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Anabolism
Precursor molecules
Amino acids
Sugars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


Phospholipids
Triacylglycerols
Fatty acids
Starch
Glycogen
Sucrose
Alanine
Glucose
Serine
Phenyl-alanine
Pyruvate
Leucine
Isoleucine
Acetate (acetyl-CoA)
Converging catabolism
(a)
Acetoacetyl-CoA
Mevalonate
Rubber
Carotenoid pigments
Isopentenyl-pyrophosphate
Vitamin K
Steroid hormones
Cholesterol
Bile acids
Cholesteryl esters
Eicosanoids
Fatty acids
Triacylglycerols
CDP-diacylglycerol
Phospholipids
Diverging anabolism
(b)
Citrate
Oxaloacetate
CO_2
CO_2
Cyclic pathway
(c)

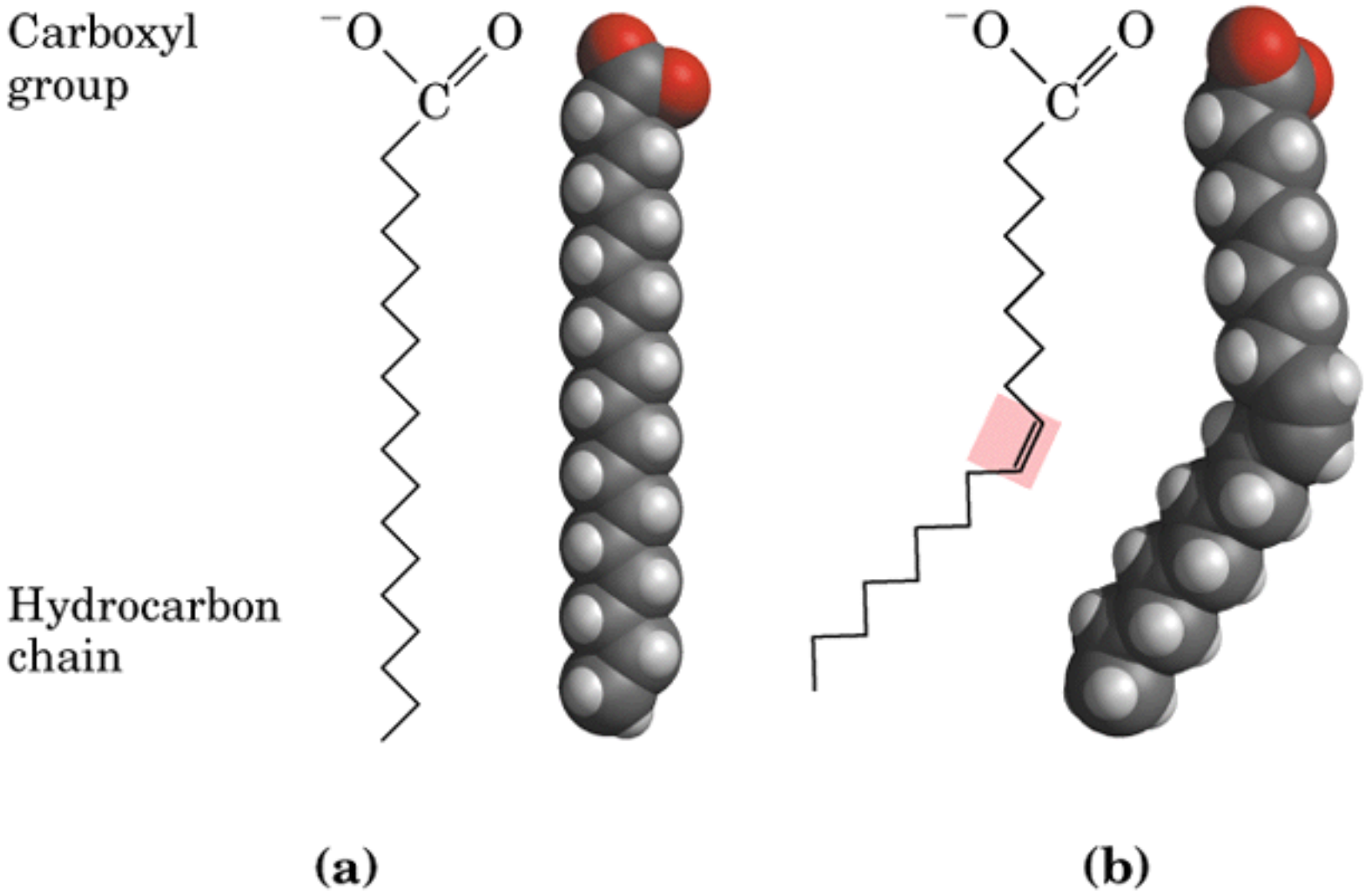


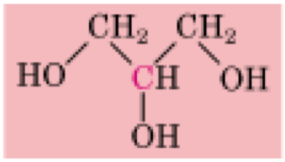
Acetil CoA

ATP

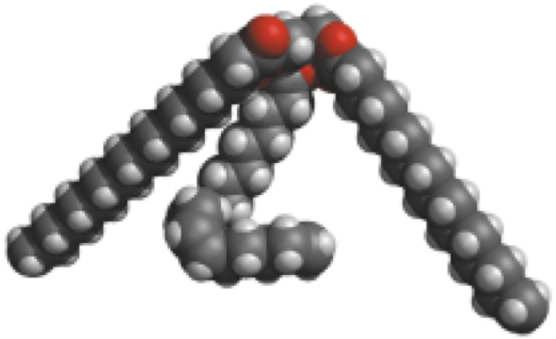
Fontes de Ácidos Graxos

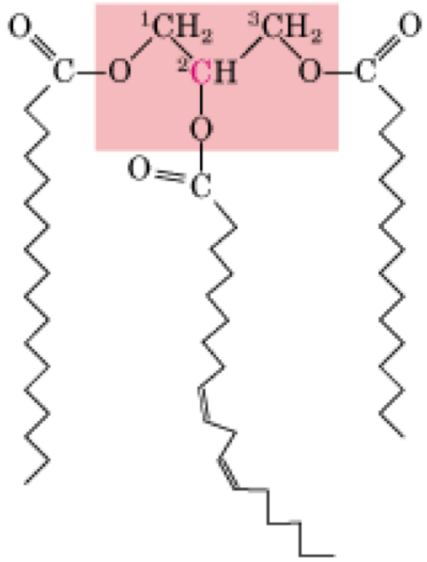
- Dieta
- Estoque de gorduras
- Síntese de outras fontes


Carboxyl group
Hydrocarbon chain
(a)
(b)



Glycerol





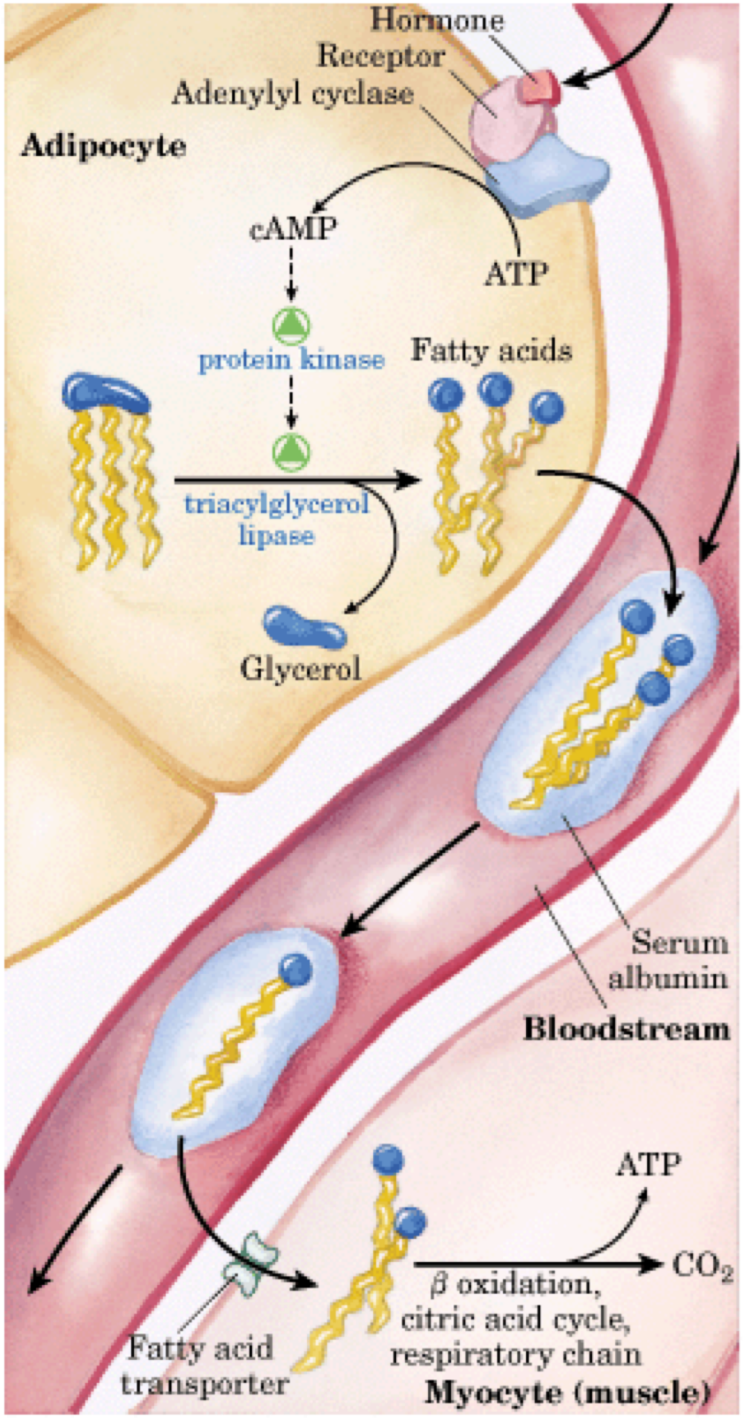
1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

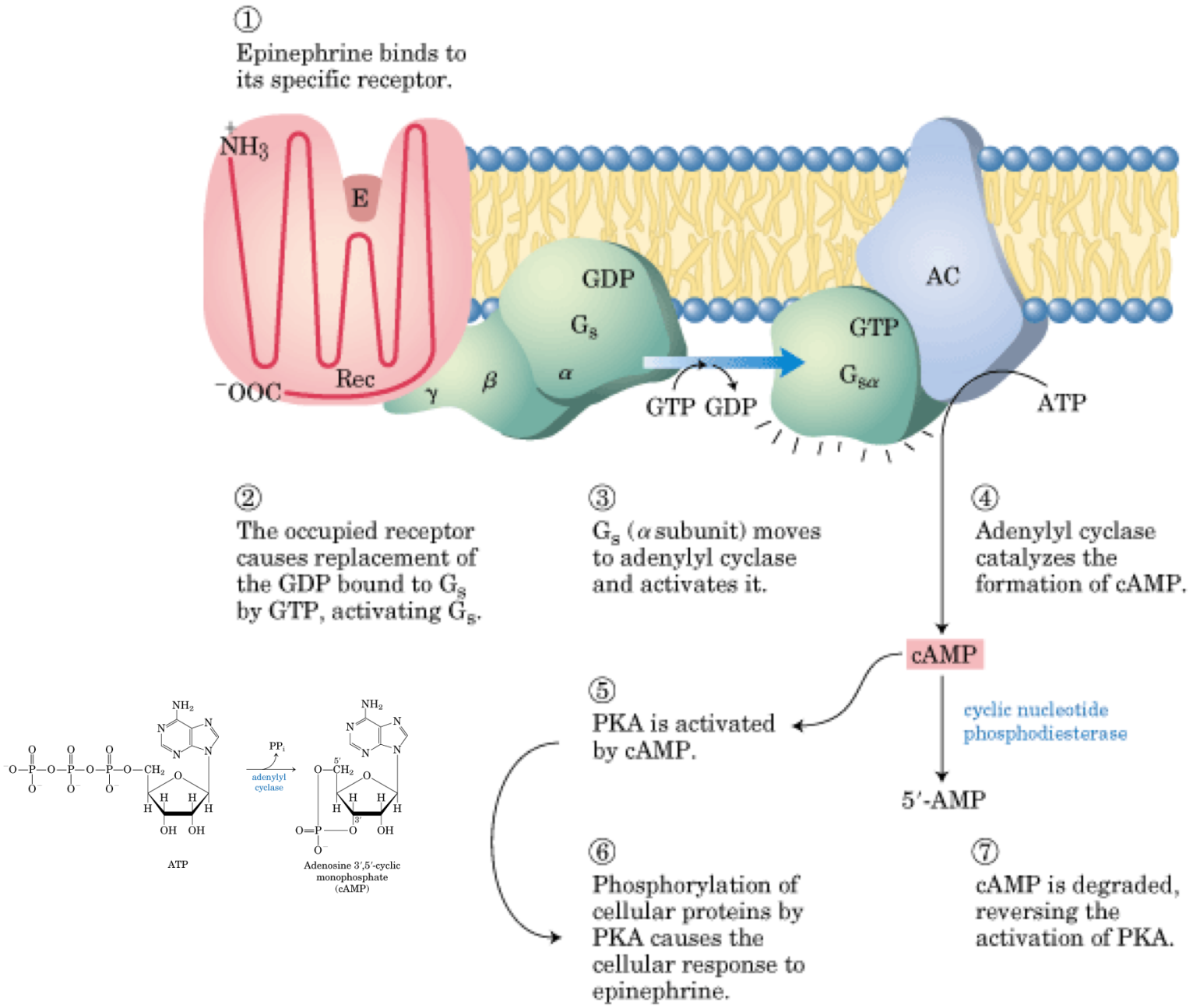
Hormônios sinalizam a mobilização de gorduras estocadas

- Os hormônios adrenalina e glucagon ativam a adenilato ciclase na membrana plasmática dos adipócitos.

- Os ácidos graxos liberados dos adipócitos entram na corrente sanguínea onde ligam-se a albumina.

- Os AG são transportados para tecidos como músculo, coração e córtex renal.

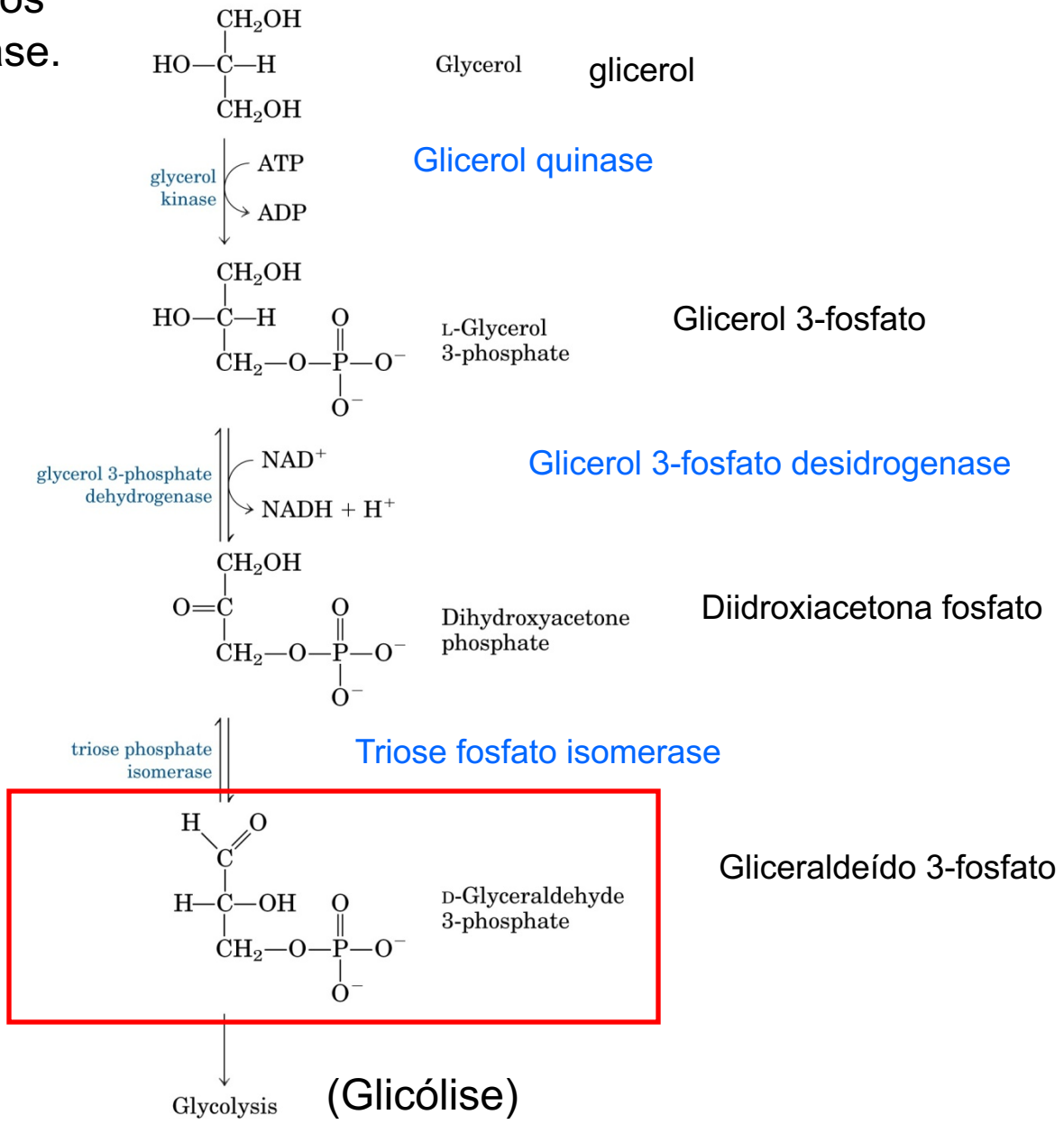

Hormone
Receptor
Adenylyl cyclase
Adipocyte
cAMP
ATP
protein kinase
Fatty acids
triacylglycerol lipase
Glycerol
Serum albumin
Bloodstream
ATP
CO_2
β oxidation, citric acid cycle, respiratory chain
Fatty acid transporter
Myocyte (muscle)


①
Epinephrine binds to its specific receptor.
NH3
E
⁻OOC
Rec
GDP
Gs
γ
β
α
GTP GDP
GTP
Gsα
AC
ATP
②
The occupied receptor causes replacement of the GDP bound to Gs by GTP, activating Gs.
③
Gs (α subunit) moves to adenylyl cyclase and activates it.
④
Adenylyl cyclase catalyzes the formation of cAMP.
cAMP
cyclic nucleotide phosphodiesterase
5′-AMP
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.
PPi
adenylyl cyclase
ATP
Adenosine 3′,5′-cyclic monophosphate (cAMP)

O glicerol não pode ser aproveitado pelos adipócitos que não tem glicerol quinase.

É liberado na circulação .

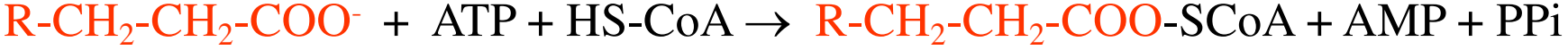
No fígado e em outros tecidos é convertido em diidroxiacetona fosfato.



Os ácidos graxos precisam ser ativados

- Por ser a ligação C-C nos AG relativamente estável, eles são ativados antes da oxidação.

- O AG é convertido em acil-CoA em reação de 2 passos pela acilCoA sintetase.

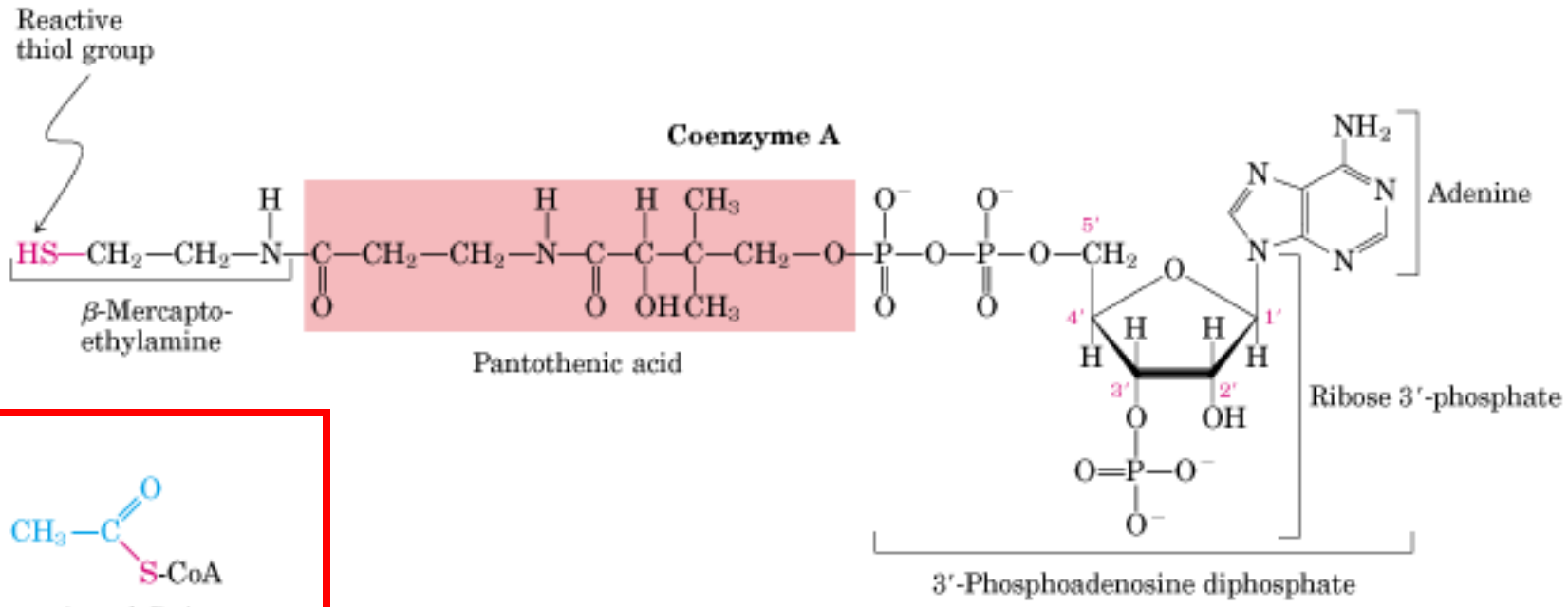


As acil-CoA são compostos ricos em energia.

A ligação tioéster é formada as custas da quebra de uma ligação Anidrido fosfórico ATP $\rightarrow$ AMP +PPi

O Pirofosfato é hidrolisado a 2 Pi (2 fosfatos) numa ligação irresversível, que torna o processo todo irreversível

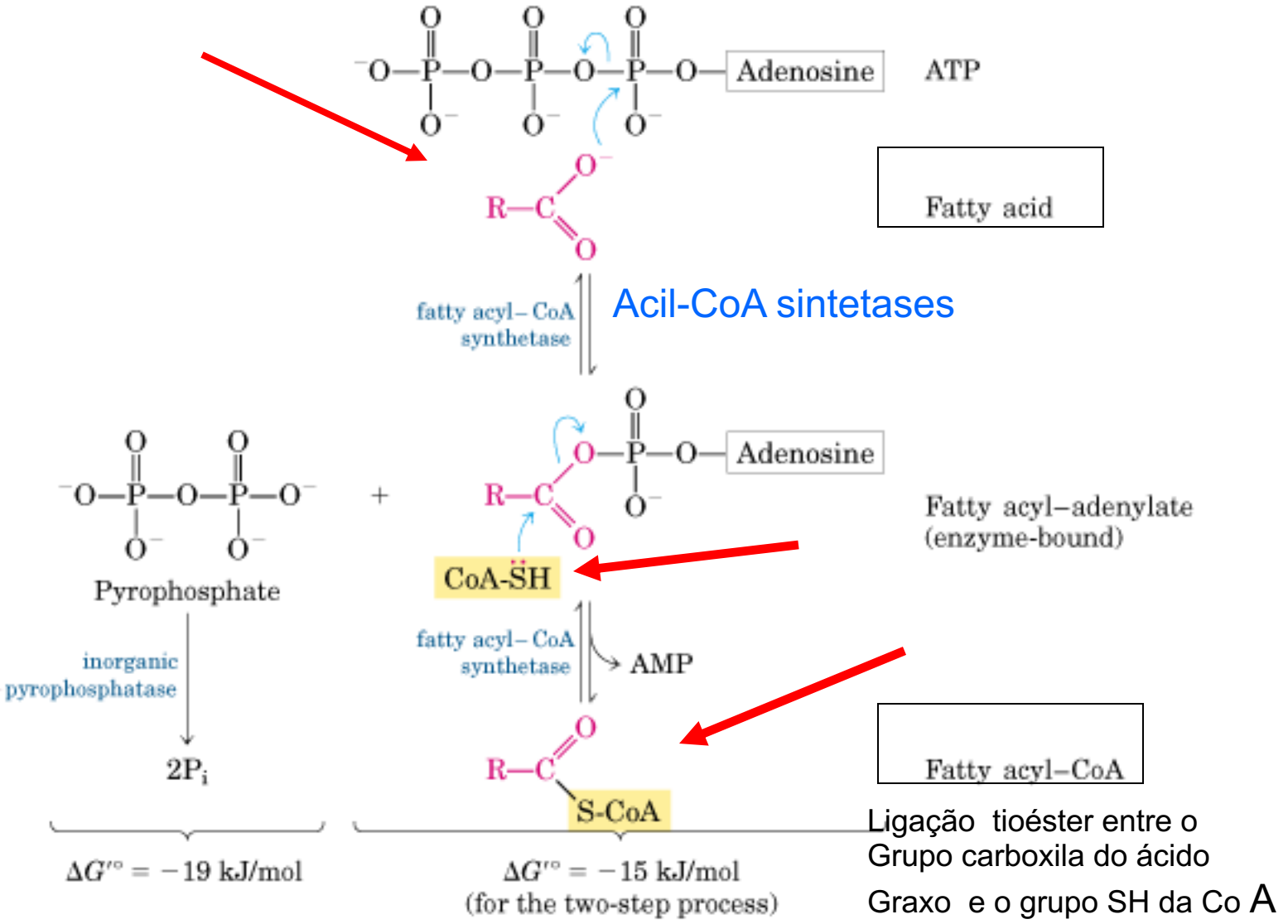
$$R\text{-}CH_2\text{-}CH_2\text{-}COO^- + ATP + HS\text{-}CoA \rightarrow R\text{-}CH_2\text{-}CH_2\text{-}COO\text{-}SCoA + AMP + PPi$$


Reactive thiol group
Coenzyme A
β-Mercapto-ethylamine
Pantothenic acid
Adenine
Ribose 3′-phosphate
3′-Phosphoadenosine diphosphate

S-CoA

Acetyl-CoA

Ácido graxo + ATP + HS-CoA → Acil-CoA + AMP + PPi

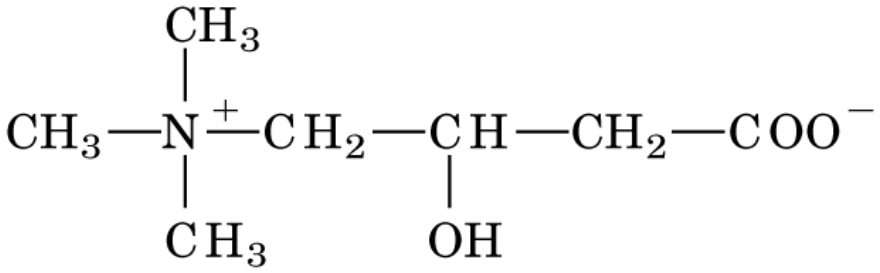


Ligação tioéster entre o Grupo carboxila do ácido Graxo e o grupo SH da Co A

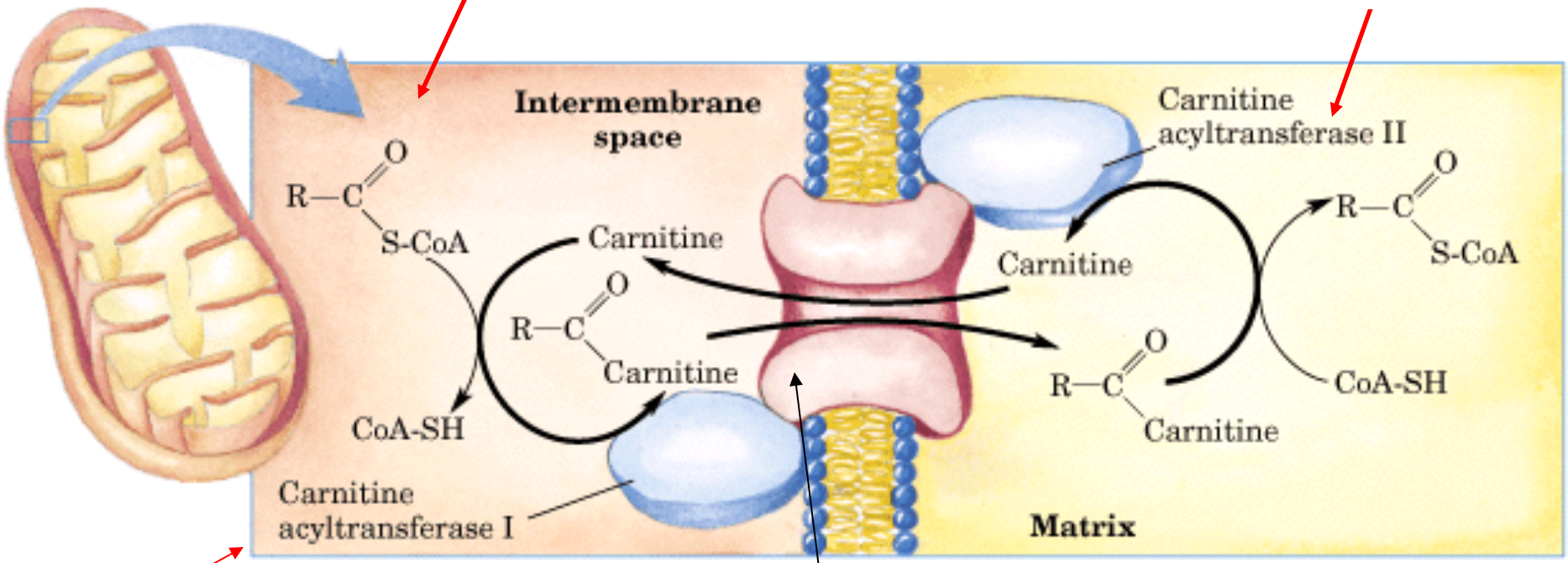
Os ácidos graxos ativados são transportados para a matriz mitocondrial.

A membrana mitocondrial interna é impermeável a acil-CoA.

Sintetizada a partir de aminoácidos



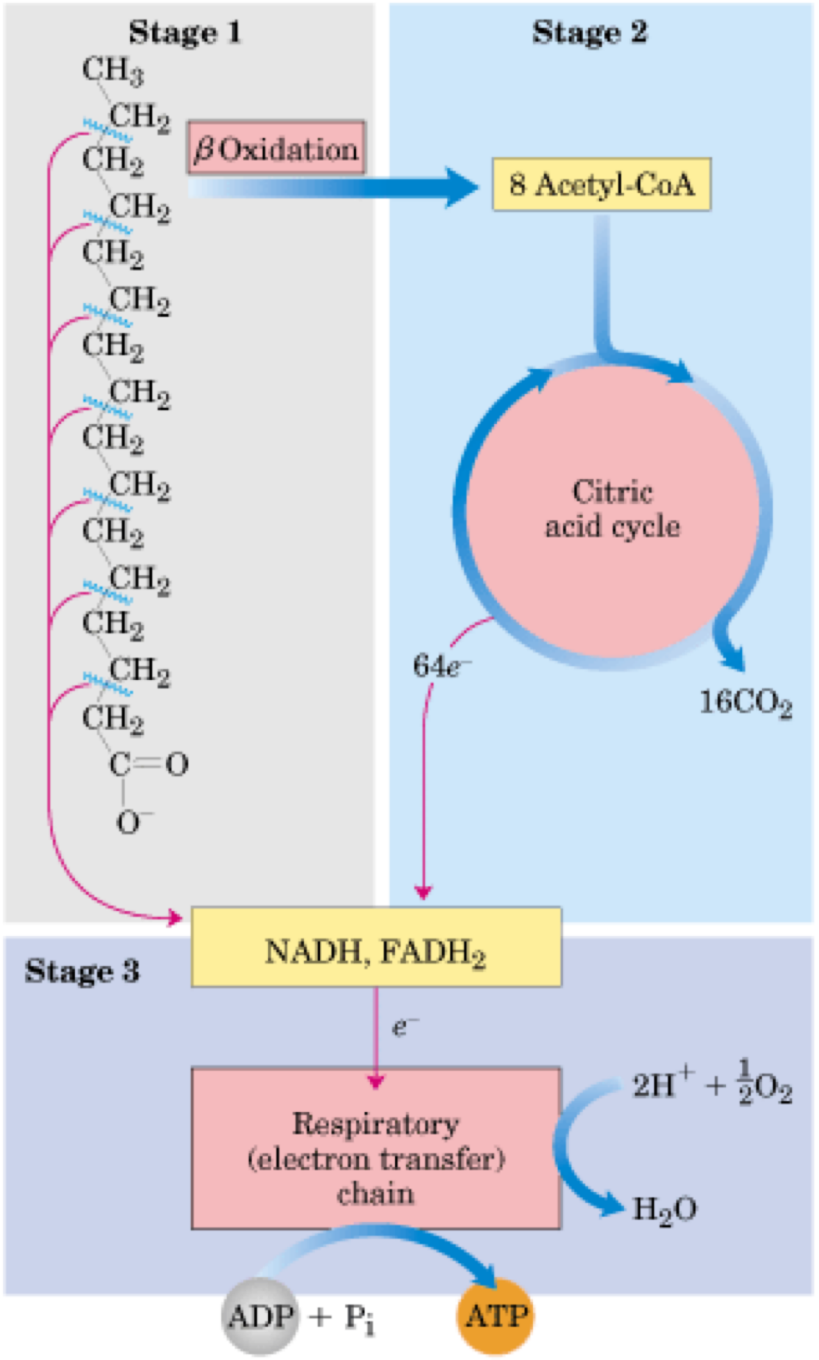
Carnitina acil-transferase II



Carnitina acil-transferase I

Translocase

Na β-oxidação, acil-CoA é oxidada a Acetil-CoA produzindo NADH e $FADH_2$



1-Oxidação da acil-CoA a enoil-CoA

Acil-CoA desidrogenase

2- Hidratação da dupla formando 3-hidroxiacil-CoA

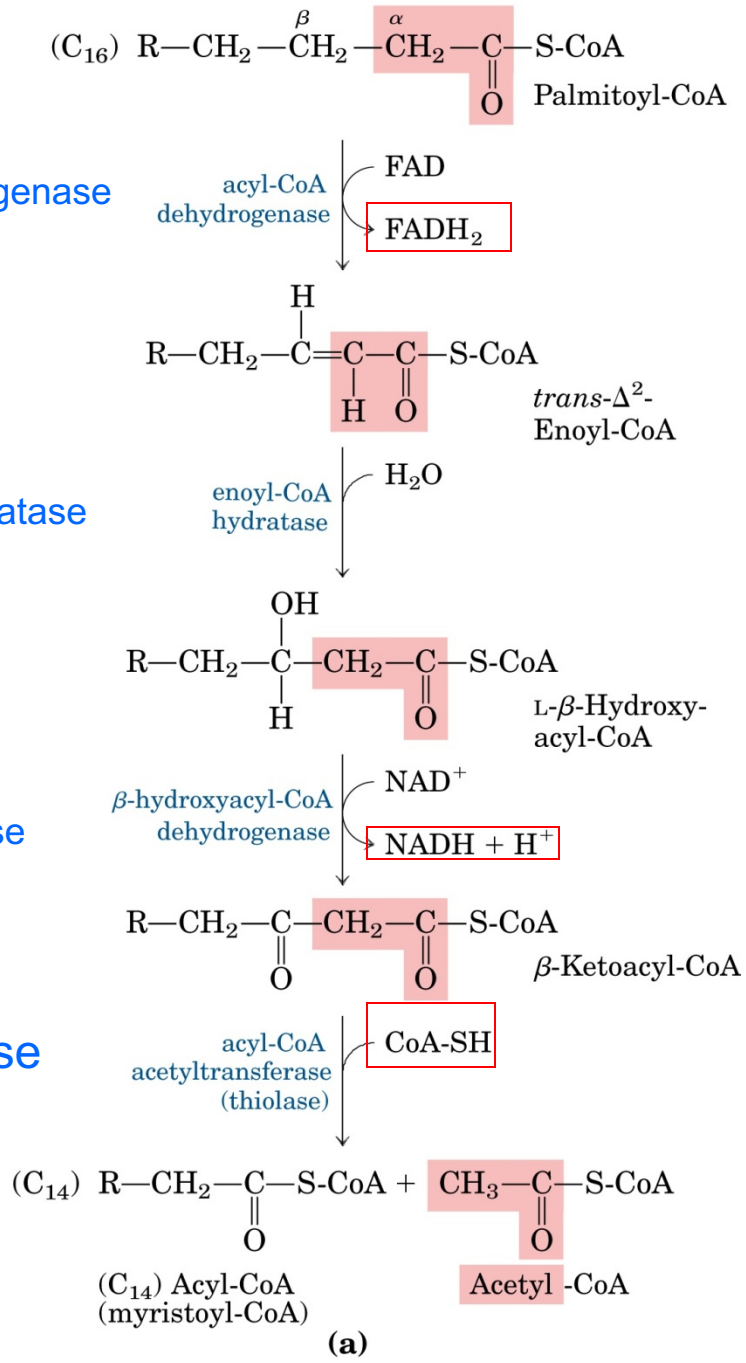
enoil-CoA hidratase

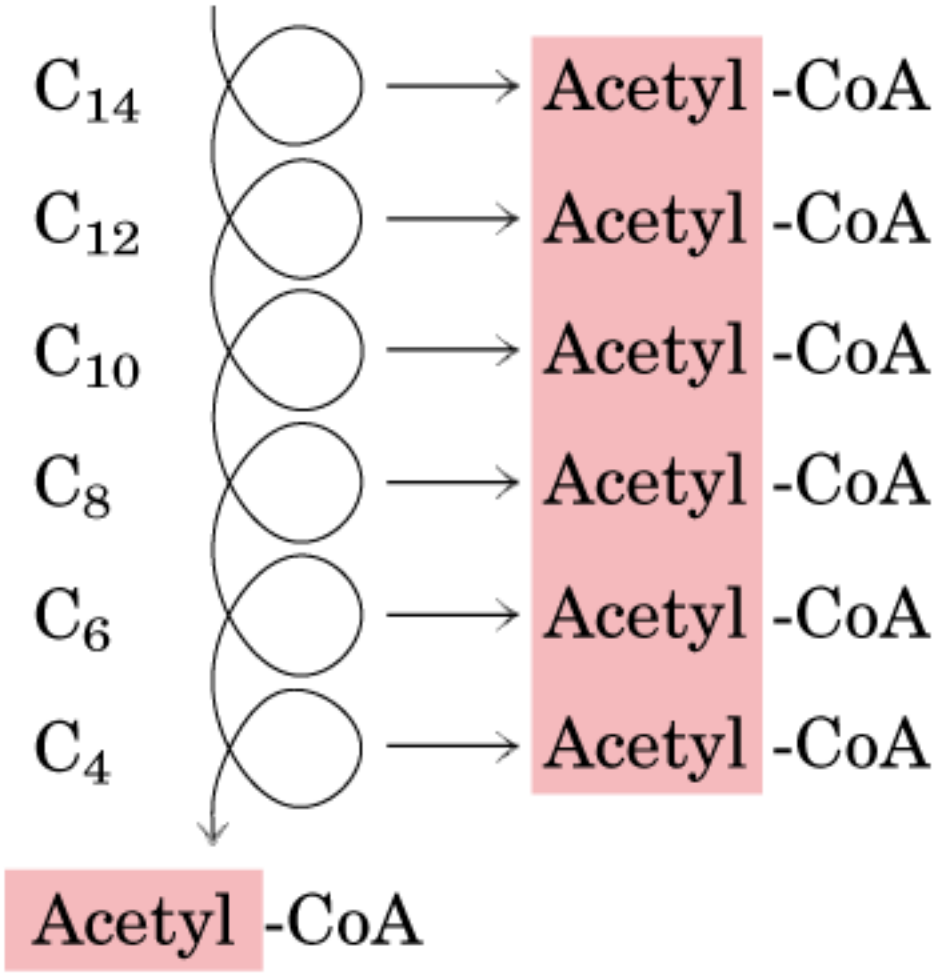
3-Oxidação de um grupo hidroxila a carbonila

β-hidrociacil-CoA desidrogenase

4-cisão da β-cetoacil-CoA por uma Reação com uma molécula de CoA

tiolase




C_{14}
C_{12}
C_{10}
C_8
C_6
C_4
Acetyl -CoA
Acetyl -CoA
Acetyl -CoA
Acetyl -CoA
Acetyl -CoA
Acetyl -CoA
Acetyl -CoA

(b)

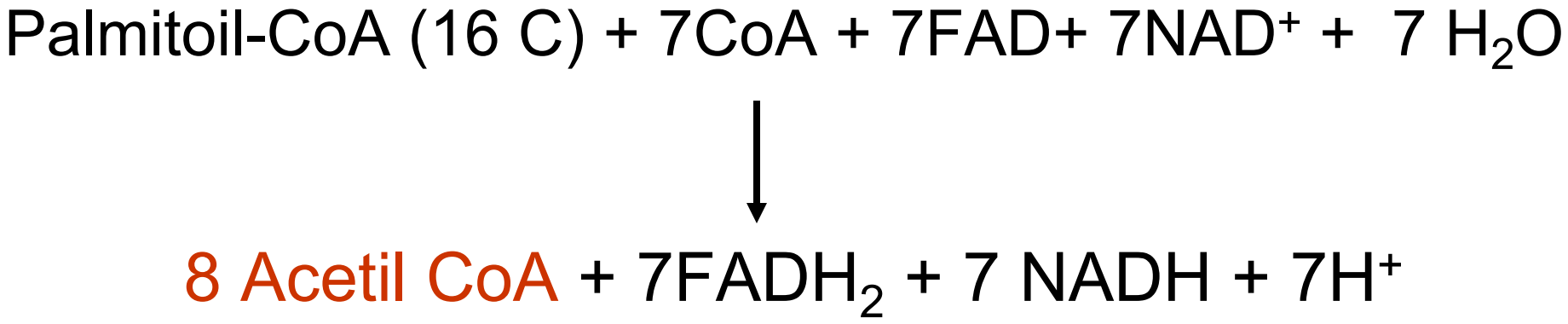

Palmitoil-CoA (16 C) + 7CoA + 7FAD+ 7NAD+ + 7 H2O
8 Acetil CoA + 7FADH2 + 7 NADH + 7H+

table 17–1

Yield of ATP during Oxidation of One Molecule of Palmitoyl-CoA to CO_2 and H_2O

Enzyme catalyzing the oxidation step	Number of NADH or $FADH_2$ formed	Number of ATP ultimately formed*
Acyl-CoA dehydrogenase	7 $FADH_2$	10.5
β-Hydroxyacyl-CoA dehydrogenase	7 NADH	17.5
Isocitrate dehydrogenase	8 NADH	20
α-Ketoglutarate dehydrogenase	8 NADH	20
Succinyl-CoA synthetase		8†
Succinate dehydrogenase	8 $FADH_2$	12
Malate dehydrogenase	8 NADH	20
Total		108

*These calculations assume that mitochondrial oxidative phosphorylation produces 1.5 ATP per $FADH_2$ oxidized and 2.5 ATP per NADH oxidized.

†GTP produced directly in this step yields ATP in the reaction catalyzed by nucleoside diphosphate kinase (p. 578).

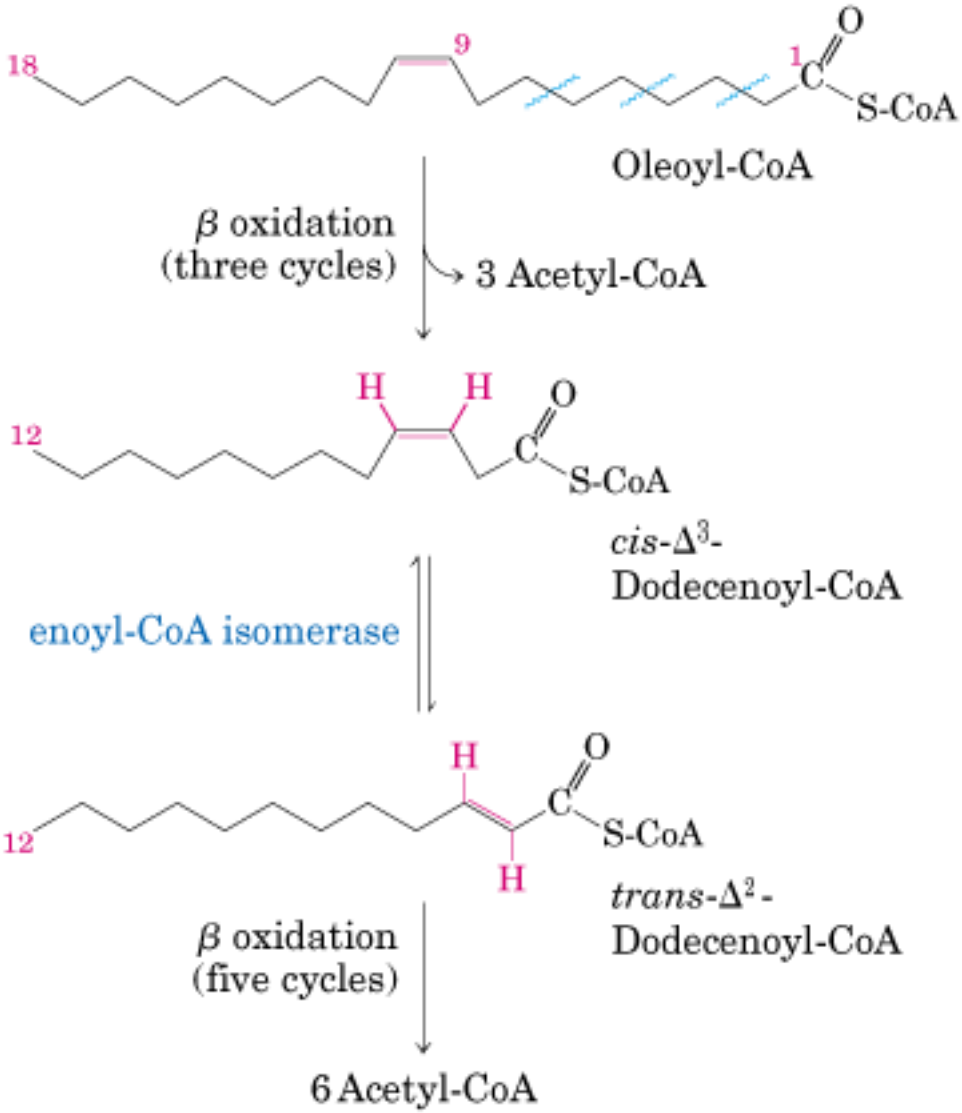
Rendimento energético da oxidação de ácido palmítico (C16)

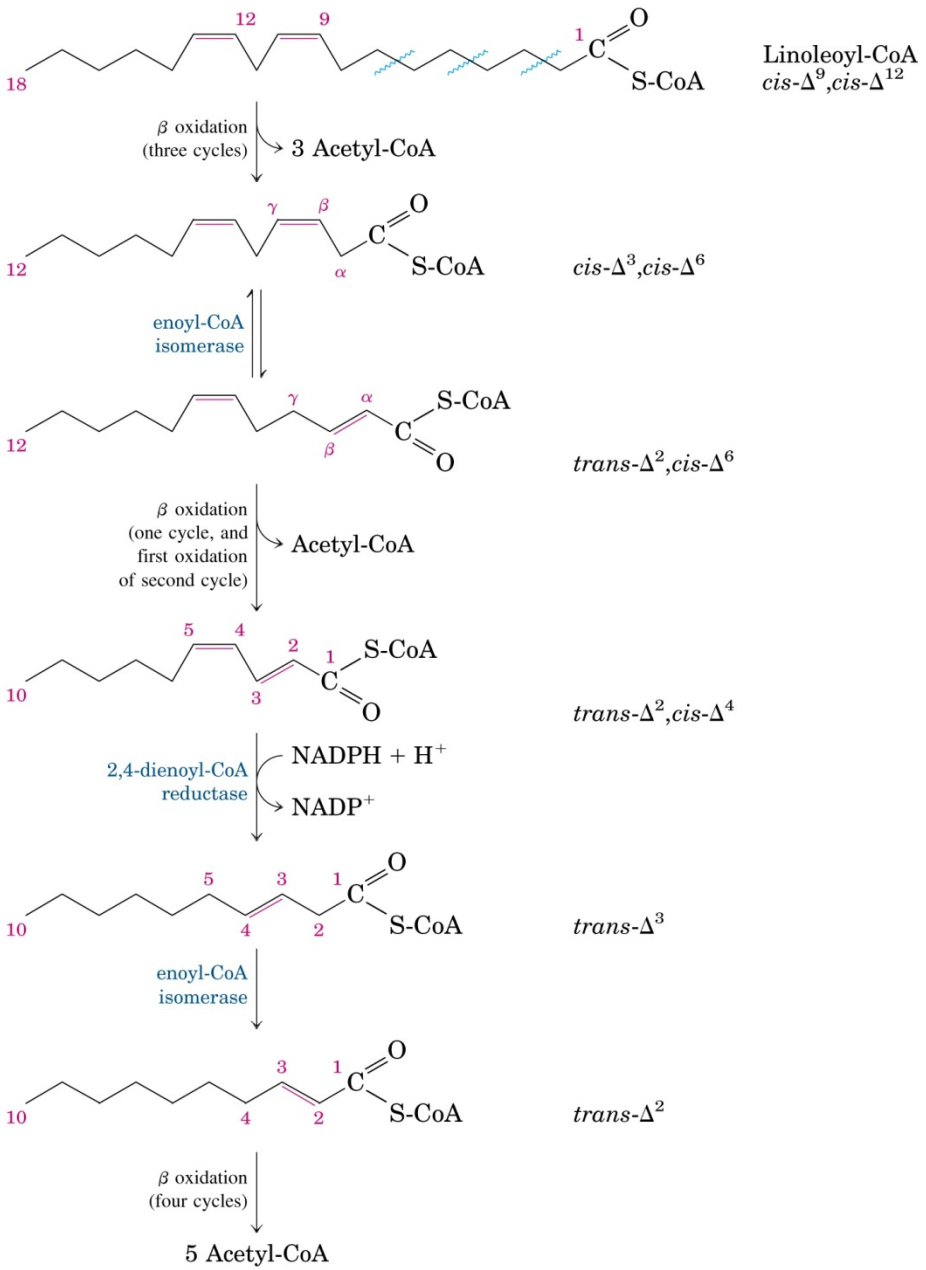
Produtos da β-oxidação	Produtos da oxidação de 8 acetil- CoA no Krebs	Total β-oxidação + Krebs	ATP
8-acetil-CoA			
7 NADH	24 NADH	31 NADH	93
7$FADH_2$	8 $FADH_2$	15 $FADH_2$	30
	8 GTP	8 GTP	8
Total			131

- ATP da ativação (2 ligações ricas em energia) = 2 ATP = 129

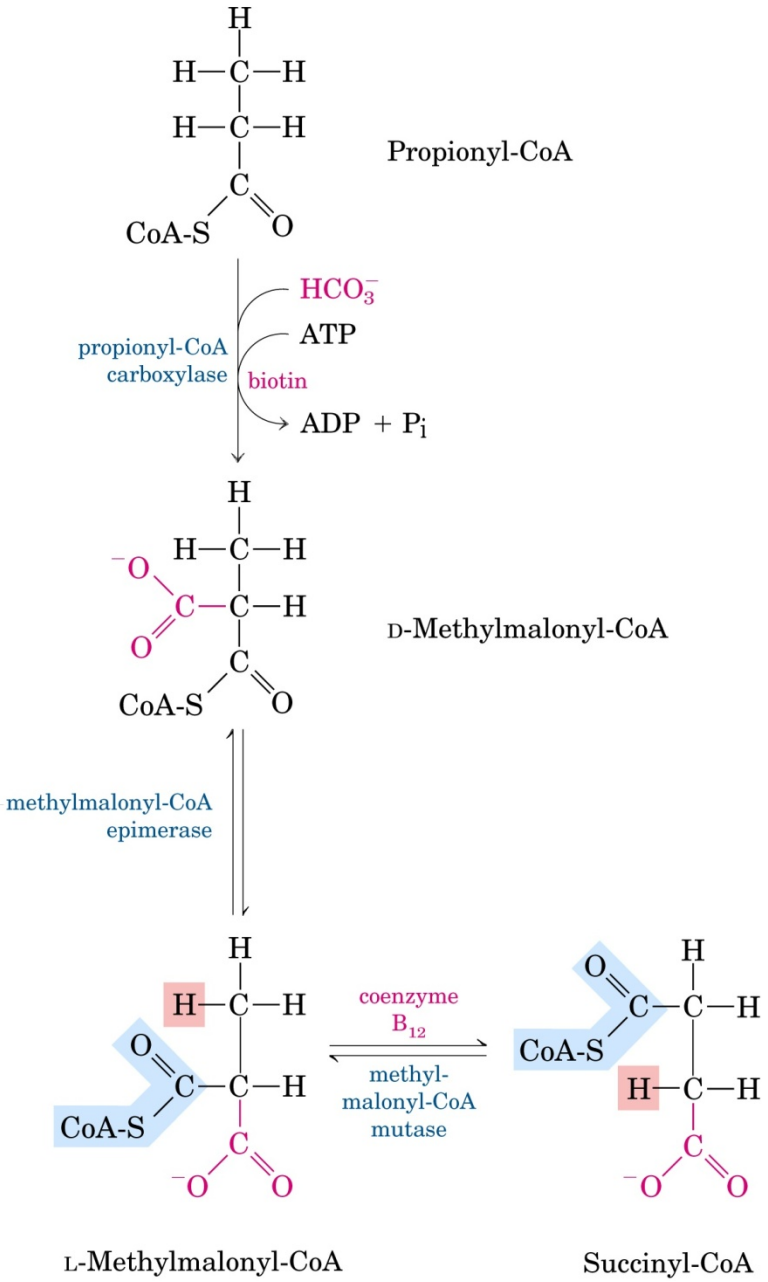
A oxidação de ácidos insaturados requer enzimas adicionais

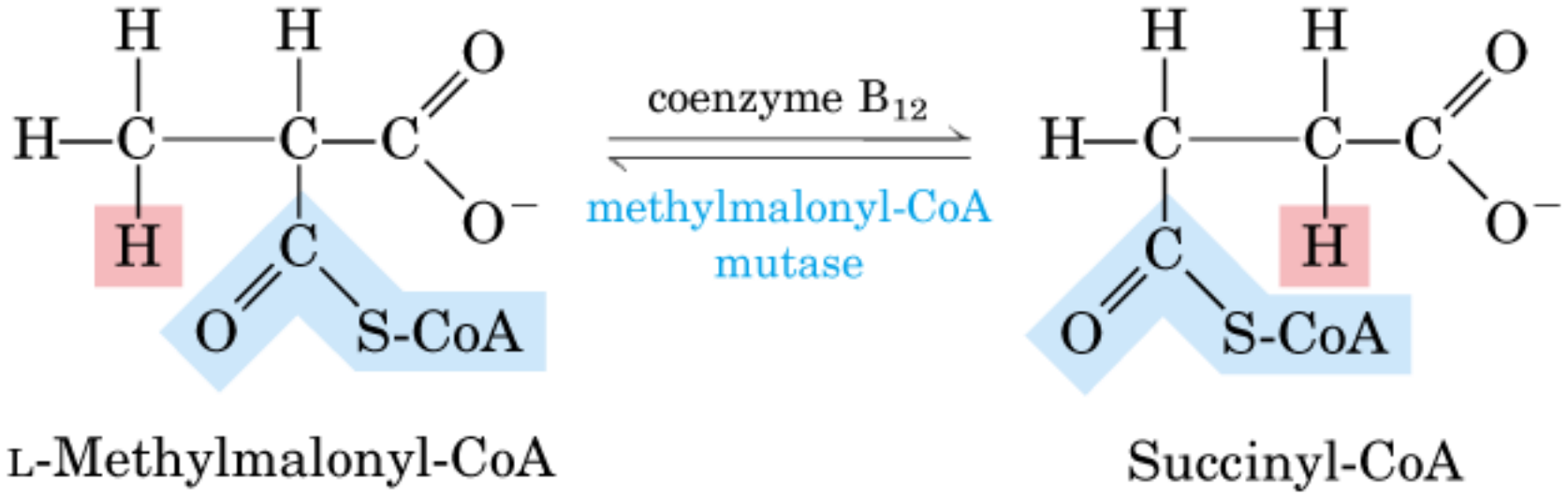
Os AG insaturados são comuns em tecidos animais e vegetais e suas configurações são quase sempre cis




Linoleoyl-CoA
cis-Δ9,cis-Δ12
β oxidation
(three cycles)
3 Acetyl-CoA
cis-Δ3,cis-Δ6
enoyl-CoA
isomerase
trans-Δ2,cis-Δ6
β oxidation
(one cycle, and
first oxidation
of second cycle)
Acetyl-CoA
trans-Δ2,cis-Δ4
2,4-dienoyl-CoA
reductase
NADPH + H+
NADP+
trans-Δ3
enoyl-CoA
isomerase
trans-Δ2
β oxidation
(four cycles)
5 Acetyl-CoA

AG com número ímpar de C

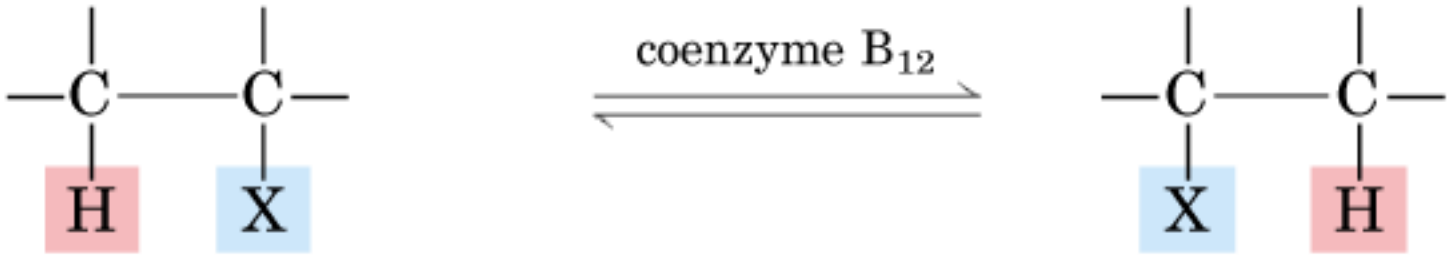




L-Methylmalonyl-CoA

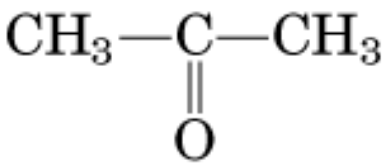
Succinyl-CoA

(a)

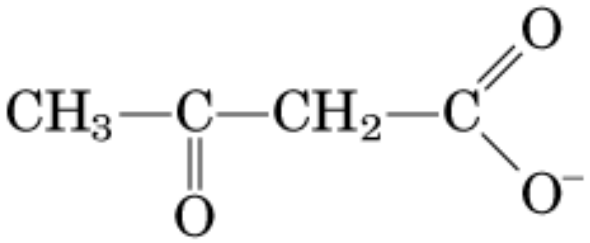


(b)

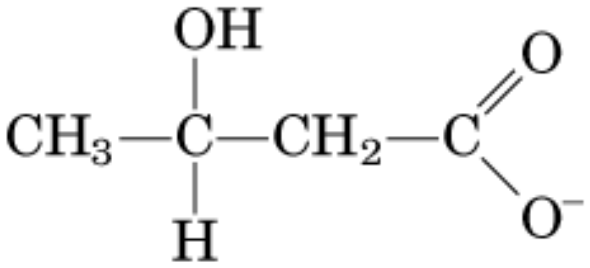
Os corpos cetônicos veículo de transferência de carbonos oxidáveis
Do fígado para outros tecidos



Acetone



Acetoacetate



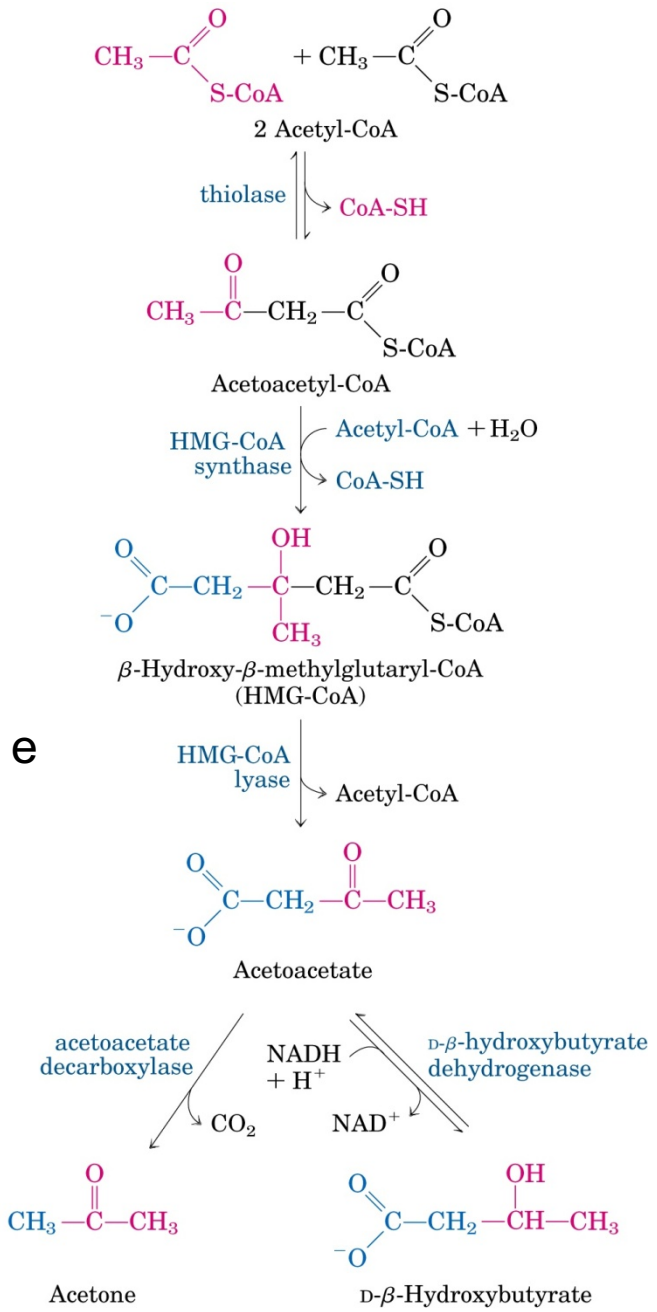
D-β-Hydroxybutyrate

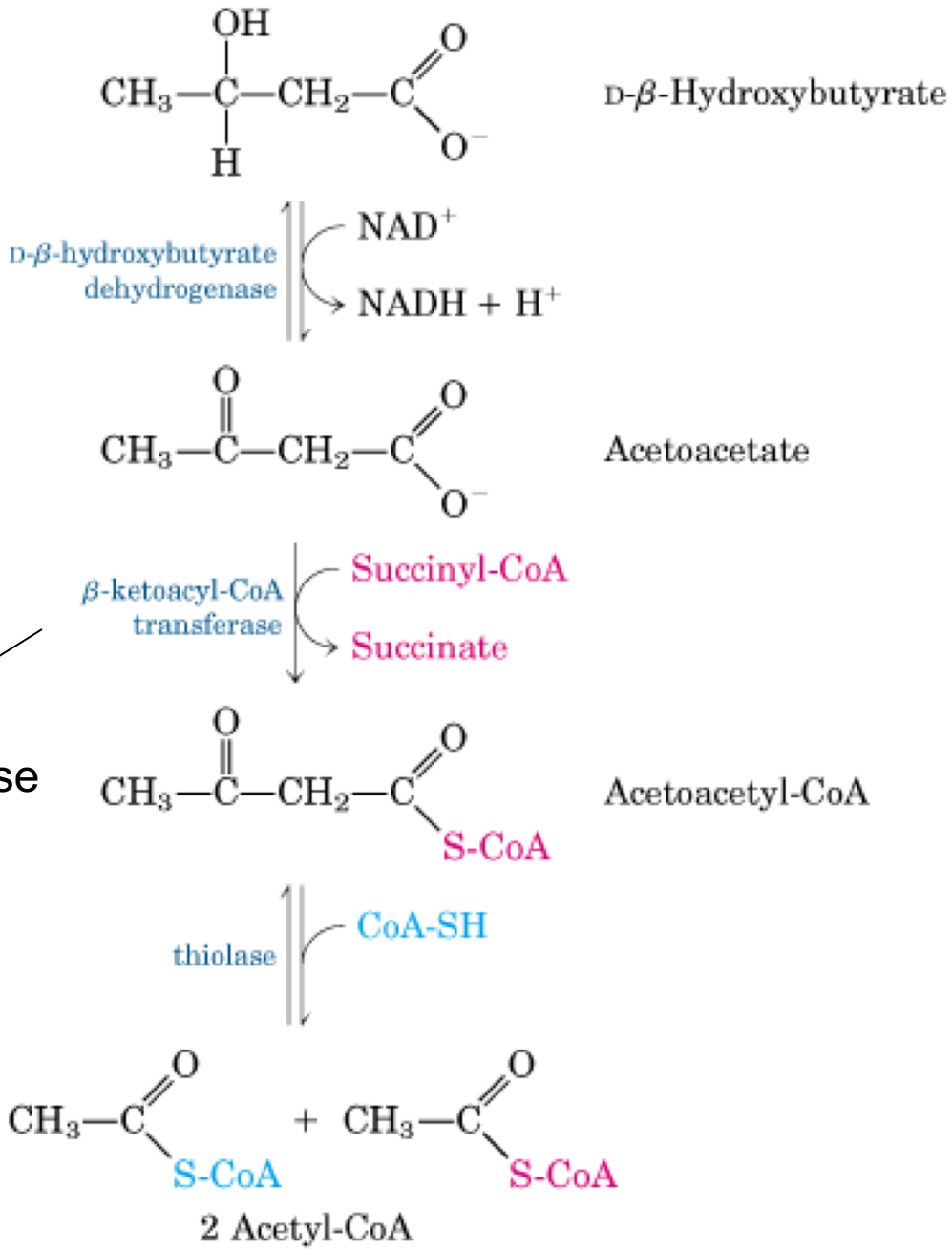
Cetogênese- fígado
Matriz mitocondrial

No fígado acetil-CoA pode
ser convertida a corpos cetônicos
oxidados por tecidos extra-hepáticos,
principalmente coração e músculo
esquelético

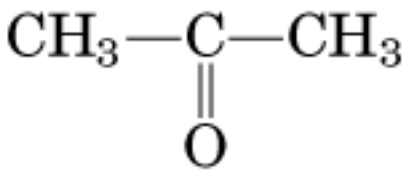
Cetose= elevada concentração de
Corpos cetônicos no plasma (cetonemia) e
na urina (cetonúria)

Cetonemia resulta em acidose

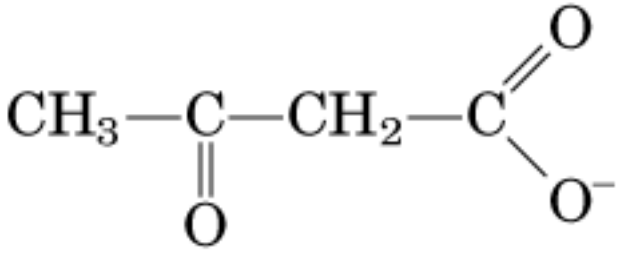




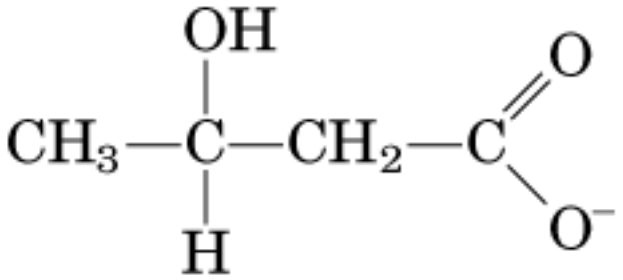
β-cetoacil transferase
Ausente no fígado



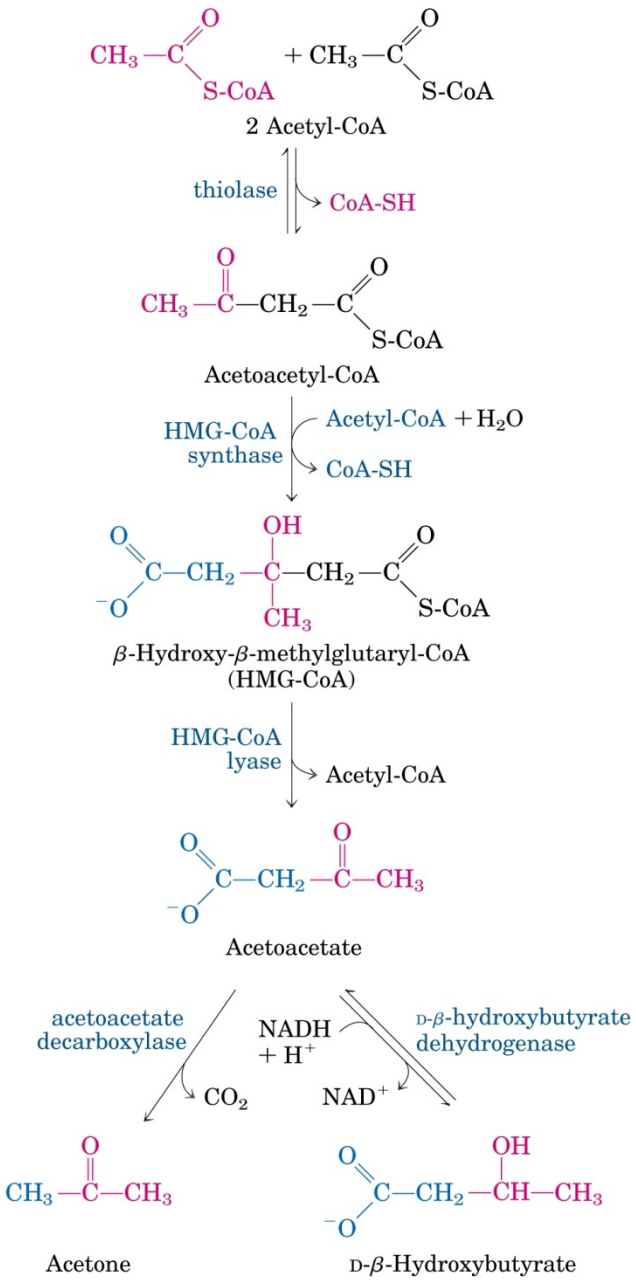
Acetone

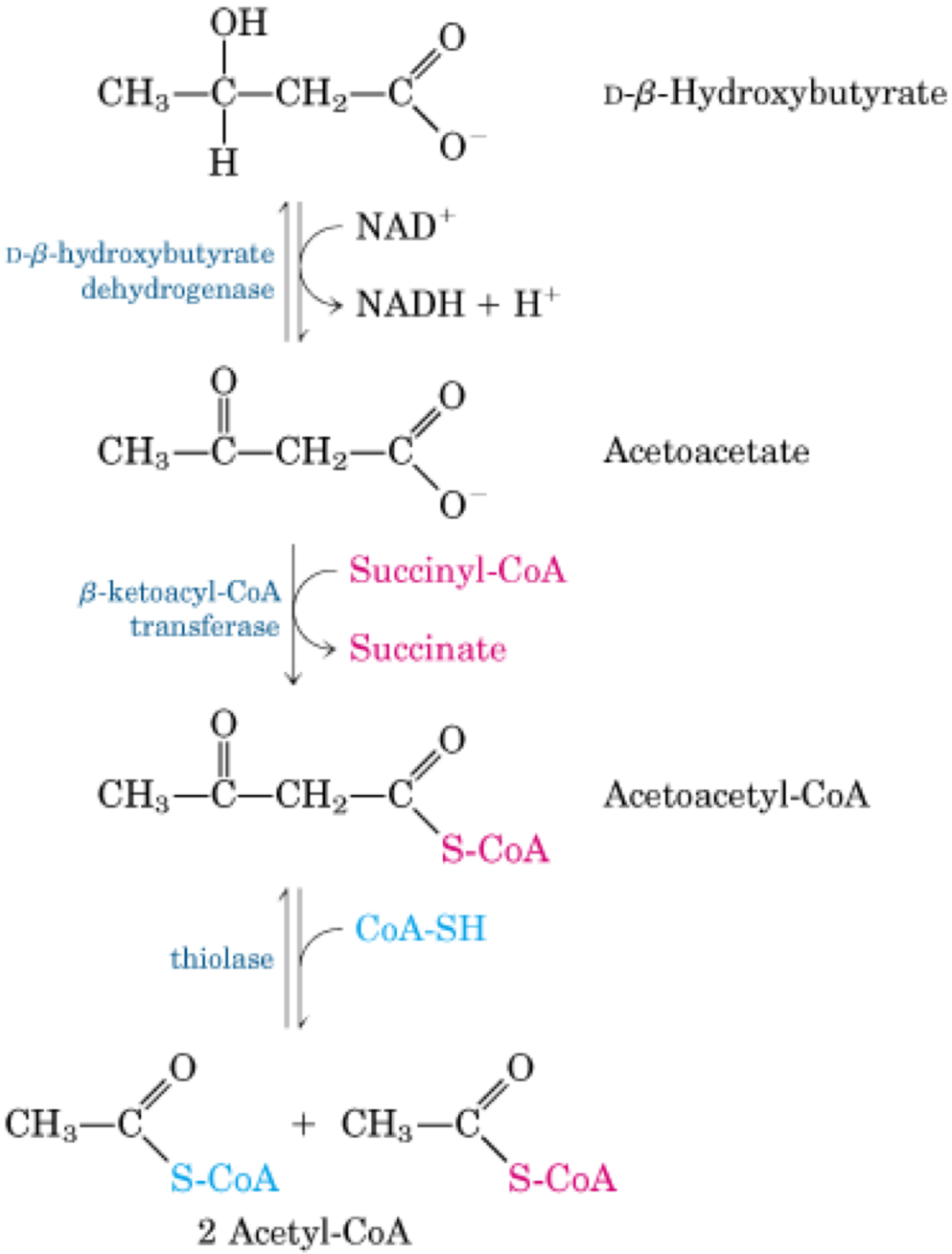


Acetoacetate



D-β-Hydroxybutyrate


2 Acetyl-CoA
thiolase
CoA-SH
Acetoacetyl-CoA
HMG-CoA synthase
Acetyl-CoA + H2O
CoA-SH
β-Hydroxy-β-methylglutaryl-CoA (HMG-CoA)
HMG-CoA lyase
Acetyl-CoA
Acetoacetate
acetoacetate decarboxylase
CO2
NADH + H+
NAD+
D-β-hydroxybutyrate dehydrogenase
Acetone
D-β-Hydroxybutyrate


D-β-Hydroxybutyrate
D-β-hydroxybutyrate dehydrogenase
NAD+
NADH + H+
Acetoacetate
β-ketoacyl-CoA transferase
Succinyl-CoA
Succinate
Acetoacetyl-CoA
S-CoA
thiolase
CoA-SH
S-CoA
S-CoA
2 Acetyl-CoA

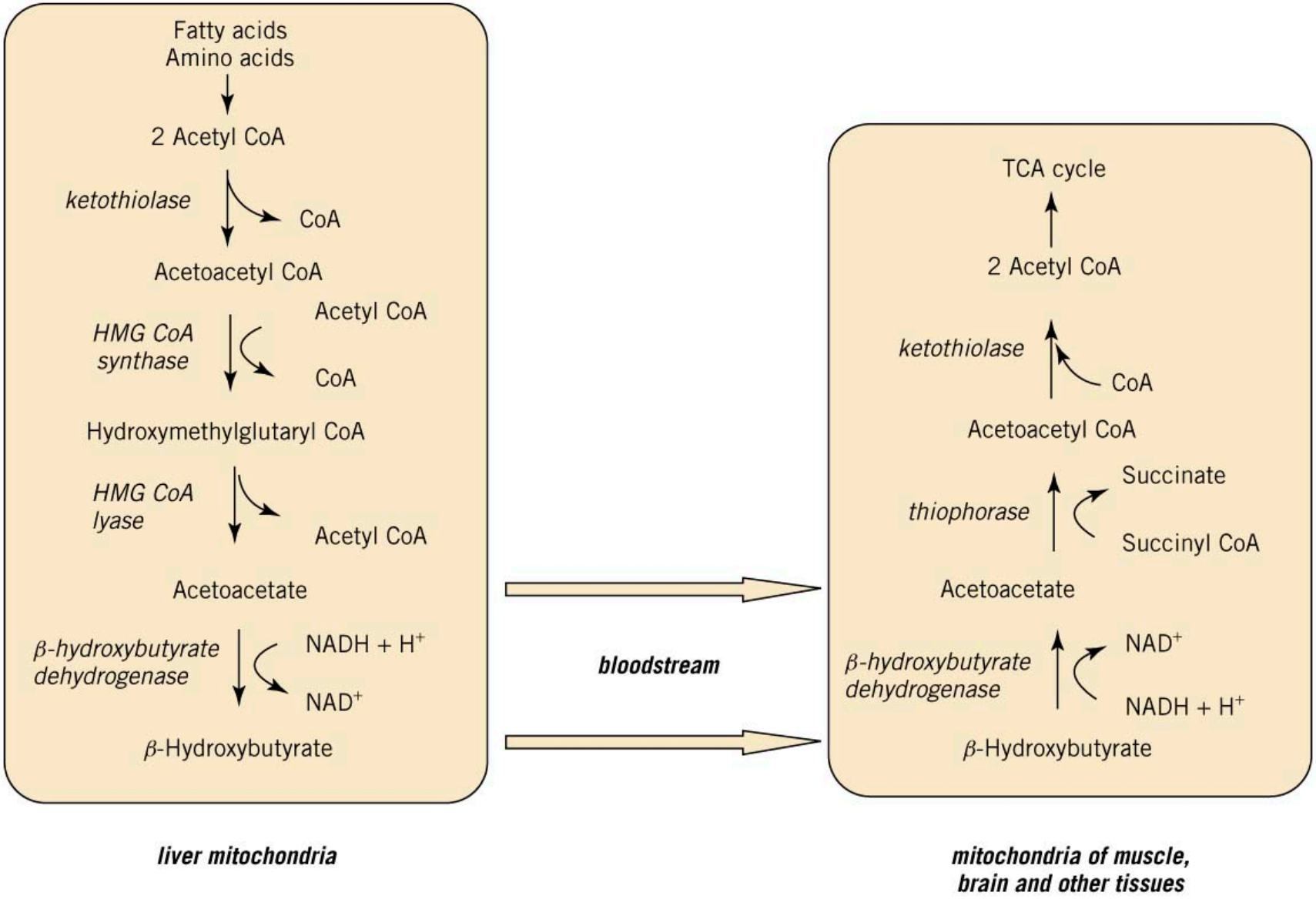


Figure 17.26. Ketone body synthesis and utilization.

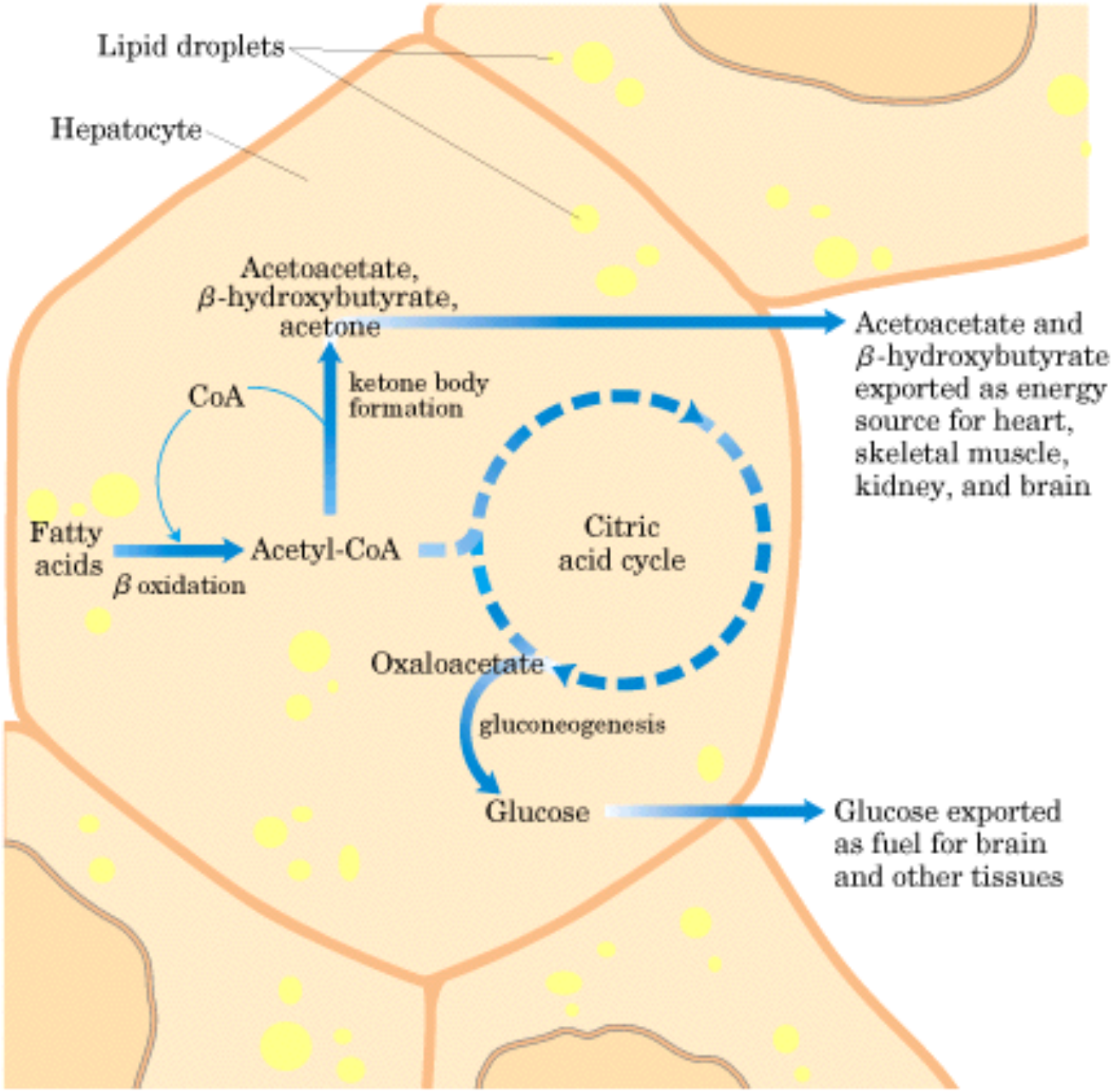

Lipid droplets
Hepatocyte
Acetoacetate, β-hydroxybutyrate, acetone
Acetoacetate and β-hydroxybutyrate exported as energy source for heart, skeletal muscle, kidney, and brain
CoA
ketone body formation
Fatty acids
β oxidation
Acetyl-CoA
Citric acid cycle
Oxaloacetate
gluconeogenesis
Glucose
Glucose exported as fuel for brain and other tissues

table 17–2

Ketone Body Accumulation in Diabetic Ketosis

	Urinary excretion (mg/24 h)	Blood concentration (mg/100 mL)
Normal	≤125	<3
Extreme ketosis (untreated diabetes)	5,000	90

Cetoacidose

A cetoacidose diabética é uma complicação aguda grave, potencialmente mortal

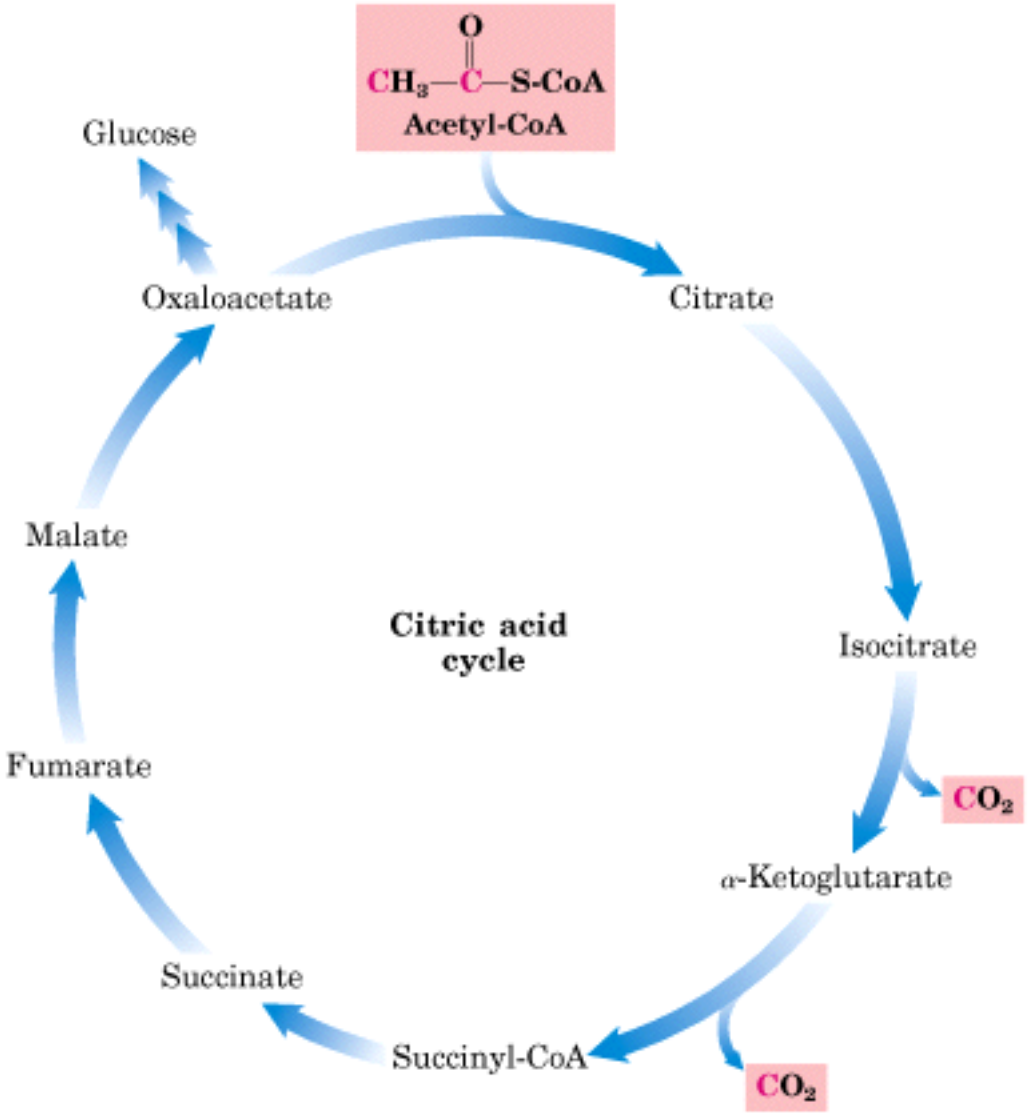
Baixa relação insulina/glucagon

Estímulo da beta-oxidação

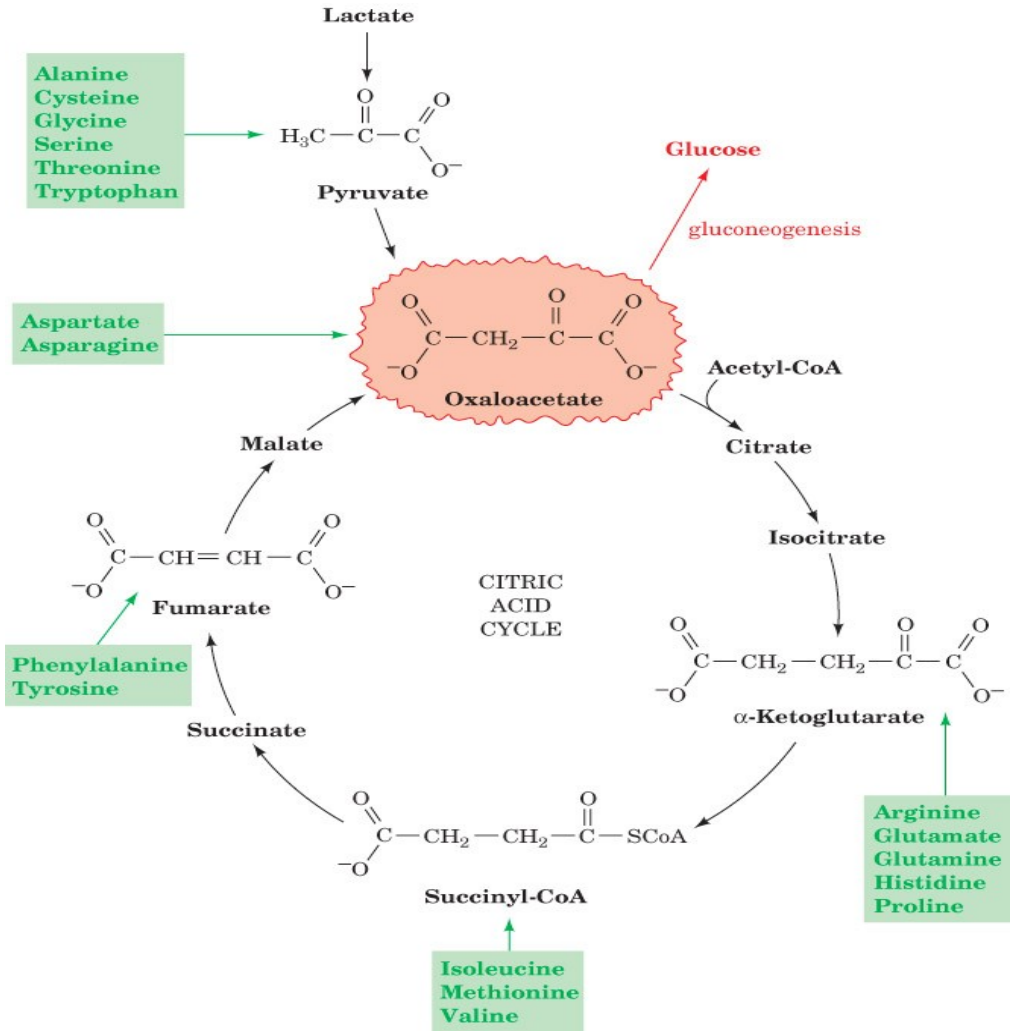
Aumento da neoglicogênese

Diminuição relativa da velocidade do ciclo de Krebs

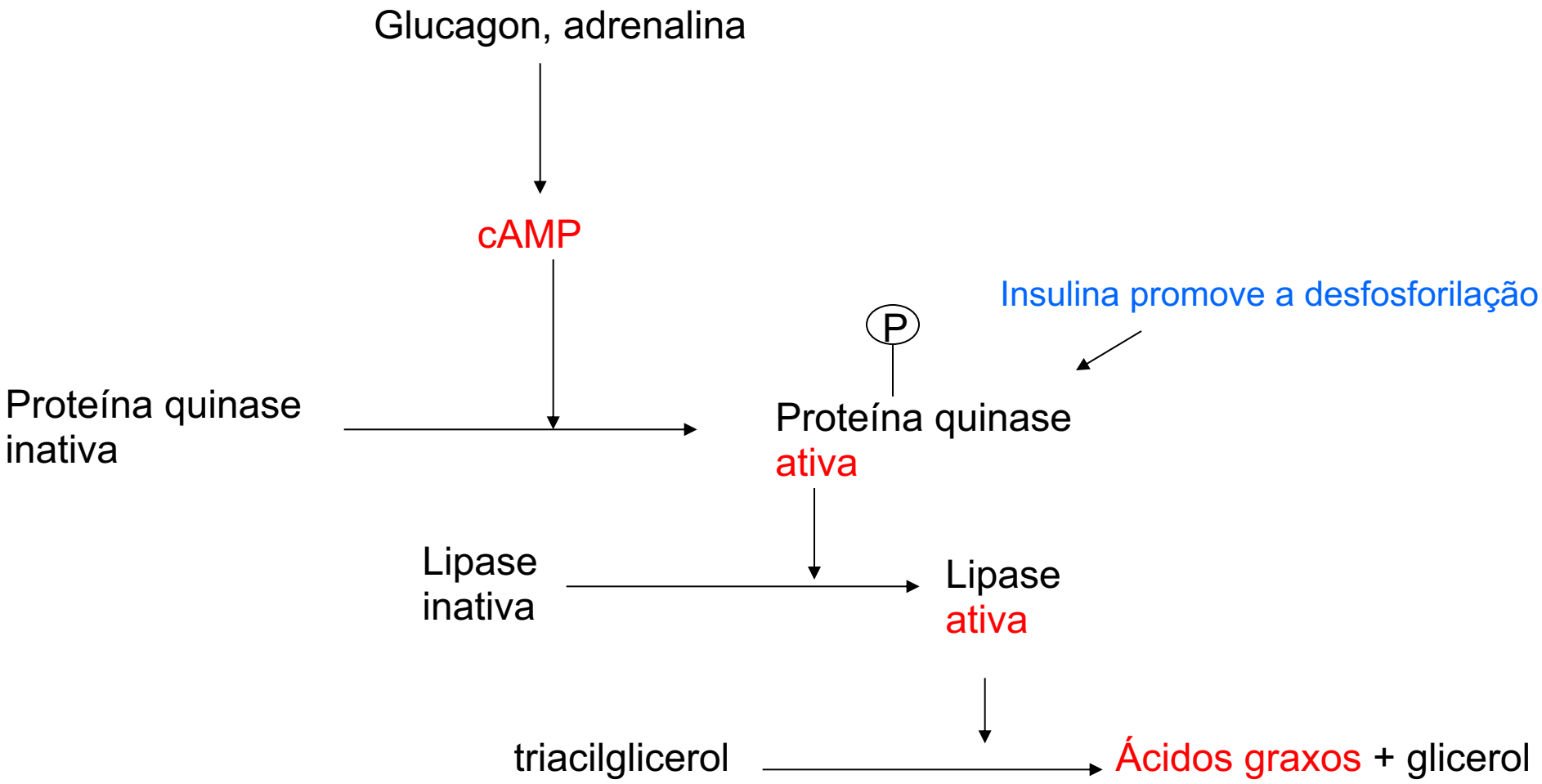
Formação de corpos cetônicos


O
CH3—C—S-CoA
Acetyl-CoA
Glucose
Oxaloacetate
Citrate
Isocitrate
CO2
α-Ketoglutarate
CO2
Succinyl-CoA
Succinate
Fumarate
Malate
Citric acid cycle

Pathways converting lactate, pyruvate, and citric acid cycle intermediates to oxaloacetate.



No jejum, o glucagon determina a degradação de ácidos graxos



Verificar em quais das seguintes situações haverá estímulo da formação de corpos cetônicos:

a) Dieta rica em carboidratos e normal em lipídeos
b) Jejum
c) Dieta rica em lipídeos e normal em carboidratos
d) Diabetes