

BLOQUE III: TEMA 16

METABOLISMO DE LÍPIDOS

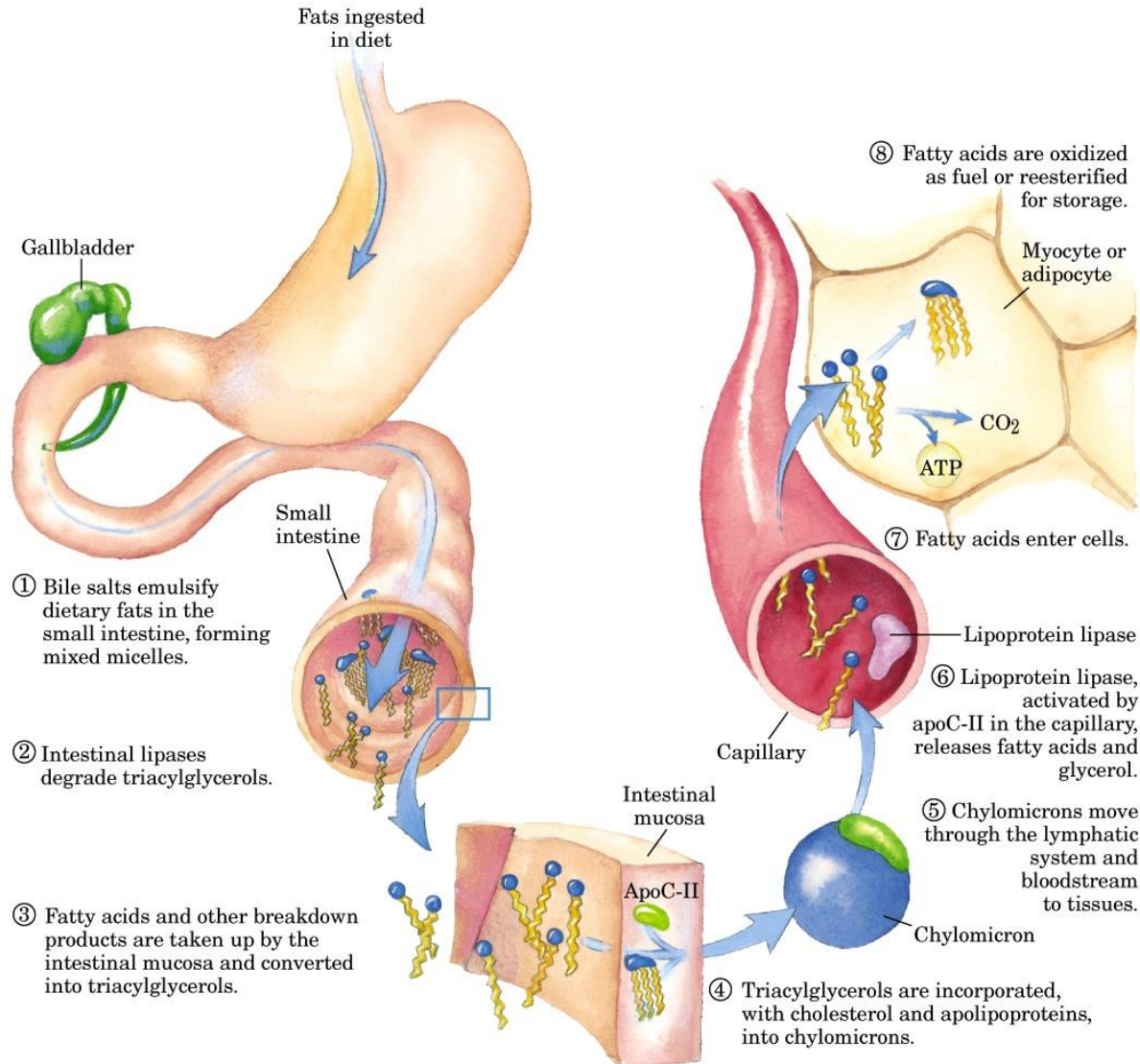
“L’autor/L’autora s’acull a l’article 32 de la Llei de propietat intel·lectual vigent respecte de l’ús parcial d’obres alienes com ara imatges, gràfics o altre material contingudes en les diferents diapositives, donat el caràcter i la finalitat exclusivament docent i eminentment il·lustrativa de les explicacions a classe d’aquesta presentació,”

“El autor/La autora se acoge al artículo 32 de la Ley de Propiedad Intelectual vigente respecto al uso parcial de obras ajenas, como imágenes, gráficos u otro material contenido en las diferentes diapositivas., dado el carácter y la finalidad exclusivamente docente y eminentemente ilustrativa de las explicaciones en clase de esta presentación,”

ÍNDICE

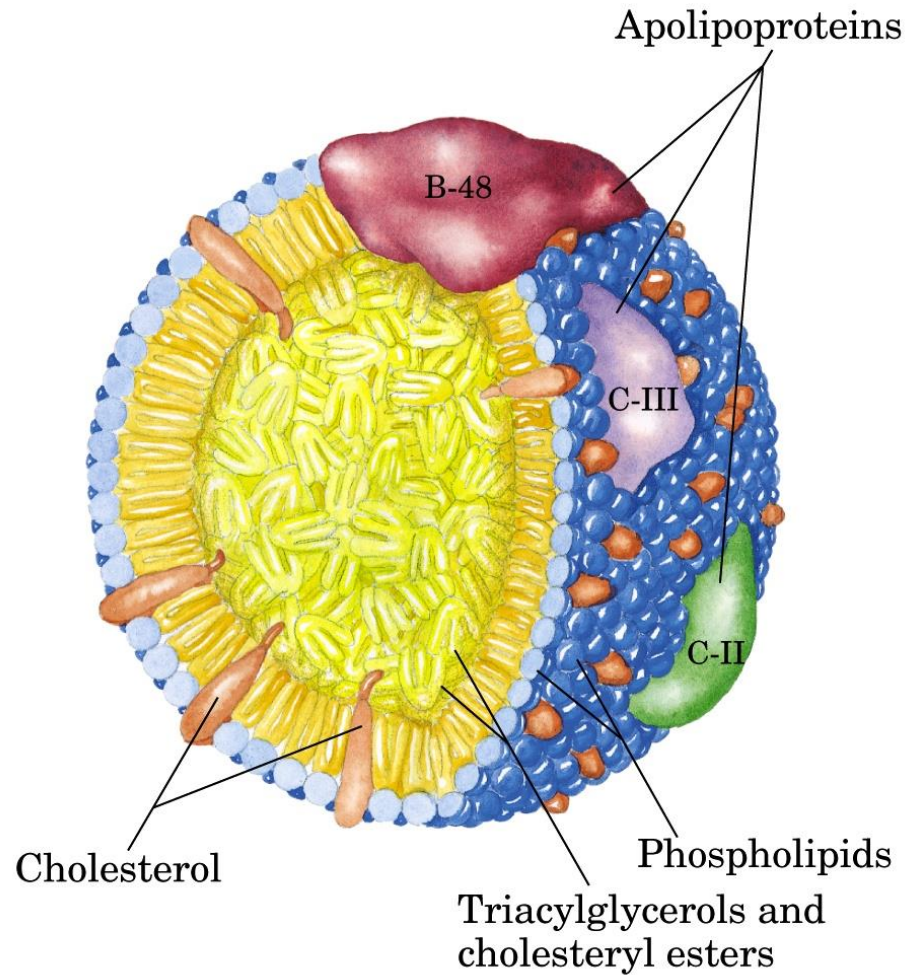
- Digestión y absorción de ácidos grasos
- Lipoproteínas
- Beta-oxidación
- Síntesis de cuerpos cetónicos
- Síntesis de ácidos grasos
- Síntesis de colesterol
- Regulación del metabolismo lipídico

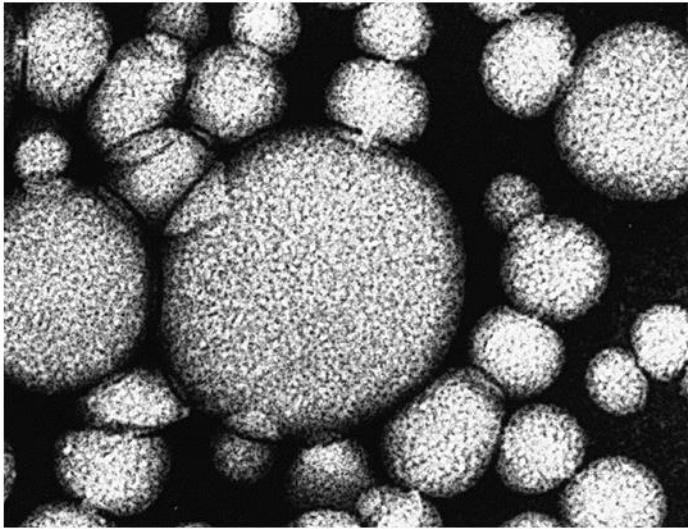
Digestión y absorción de grasas



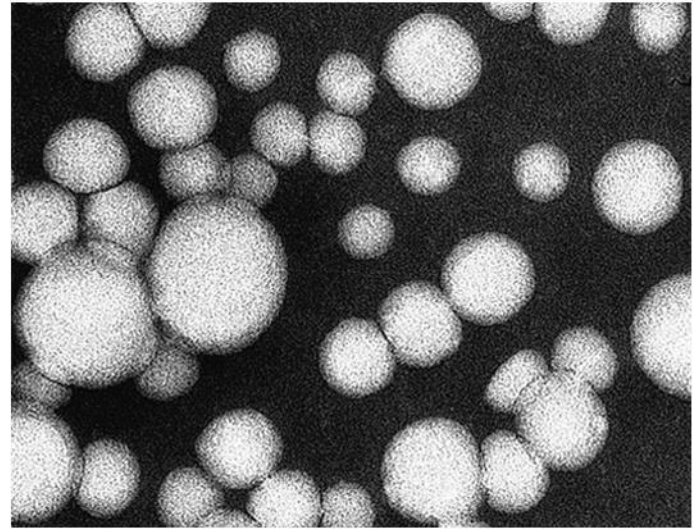
LIPOPROTEÍNAS

Estructura molecular
de un quilomicrón

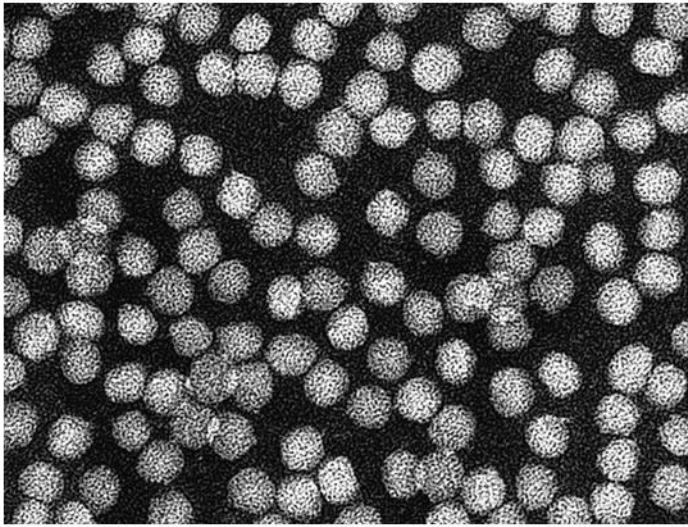




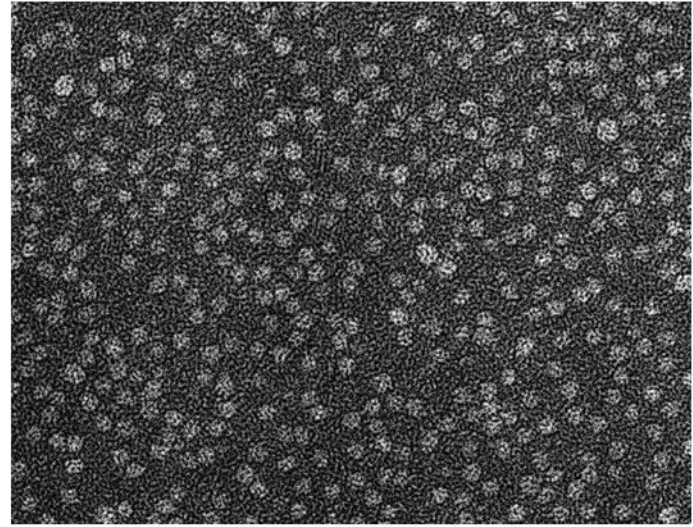
Chylomicrons (x60,000)



VLDL (x180,000)



LDL (x180,000)



HDL (x180,000)

(b)

LIPOPROTEÍNAS

table 21-2

Major Classes of Human Plasma Lipoproteins: Some Properties

Lipoprotein	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95-1.006	10	18	7	12	50
LDL	1.006-1.063	23	20	8	37	10
HDL	1.063-1.210	55	24	2	15	4

Source: Modified from Kritchevsky, D. (1986) Atherosclerosis and nutrition. *Nutr. Int.* 2, 290-297.

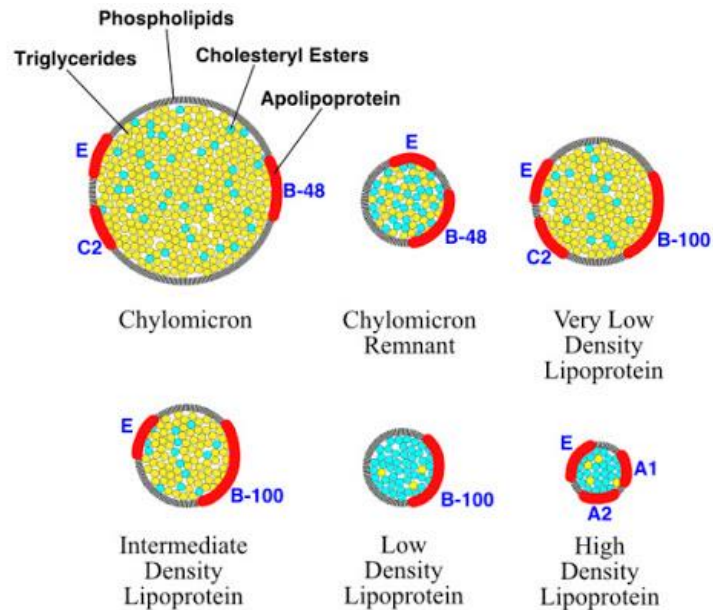


Figure 2.1: Approximate relative sizes and compositions of the six major classes of lipoproteins. The specific apolipoprotein components of each lipoprotein are also indicated.

LIPOPROTEÍNAS

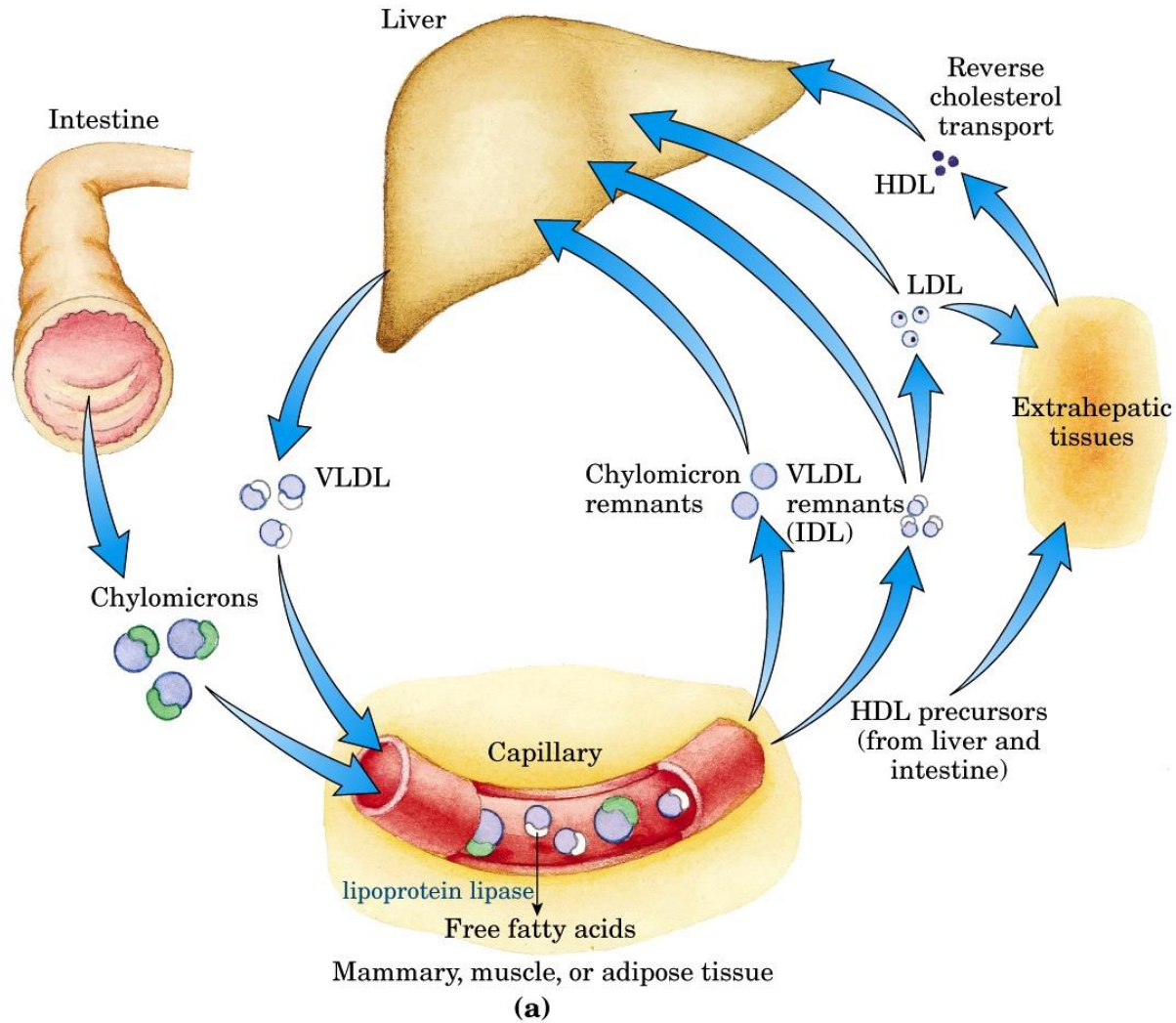
table 21-3

Apolipoproteins of the Human Plasma Lipoproteins

Apolipoprotein	Molecular weight	Lipoprotein association	Function (if known)
ApoA-I	28,331	HDL	Activates LCAT; interacts with ABC transporter
ApoA-II	17,380	HDL	
ApoA-IV	44,000	Chylomicrons, HDL	
ApoB-48	240,000	Chylomicrons	
ApoB-100	513,000	VLDL, LDL	Binds to LDL receptor
ApoC-I	7,000	VLDL, HDL	
ApoC-II	8,837	Chylomicrons, VLDL, HDL	Activates lipoprotein lipase
ApoC-III	8,751	Chylomicrons, VLDL, HDL	Inhibits lipoprotein lipase
ApoD	32,500	HDL	
ApoE	34,145	Chylomicrons, VLDL, HDL	Triggers clearance of VLDL and chylomicron remnants

Source: Modified from Vance, D.E. & Vance, J.E. (eds) (1985) *Biochemistry of Lipids and Membranes*. The Benjamin/Cummings Publishing Company, Menlo Park, CA.

LIPOPROTEÍNAS



LIPOPROTEÍNAS

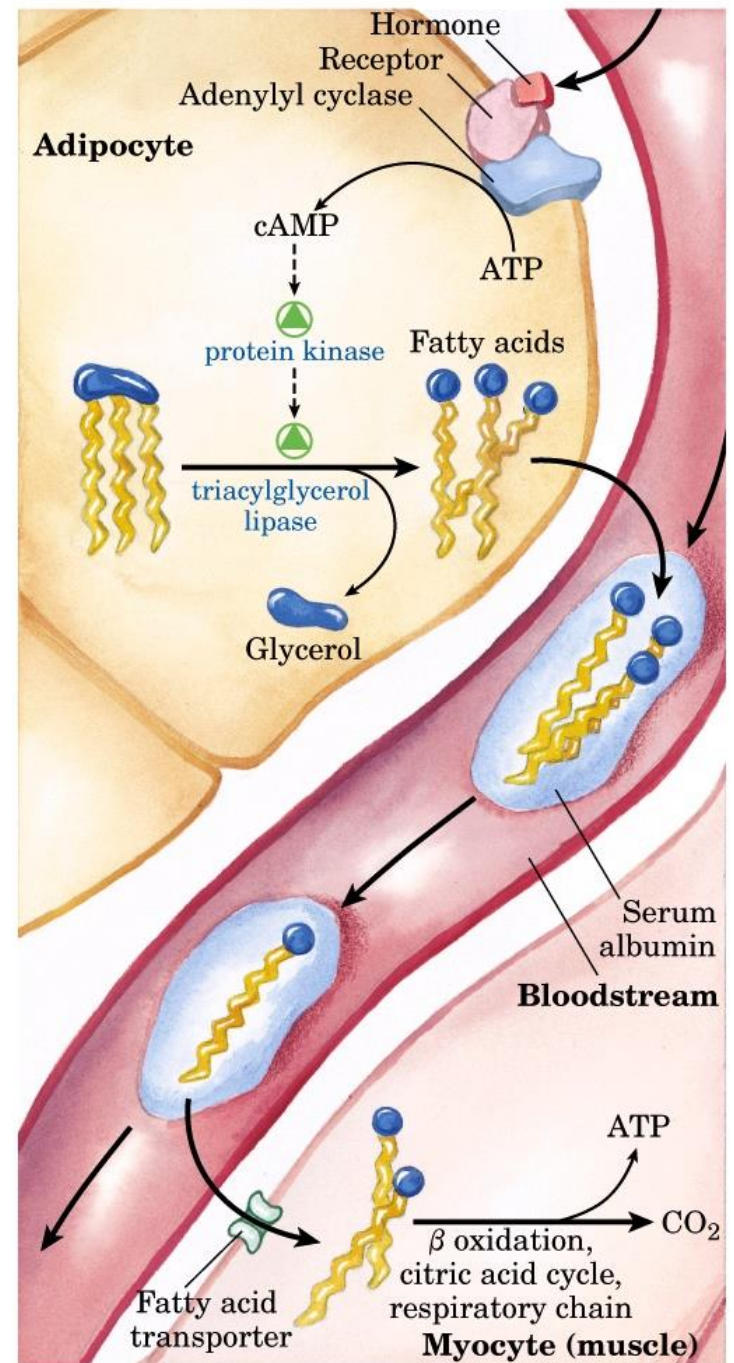


Blood plasma
after fast

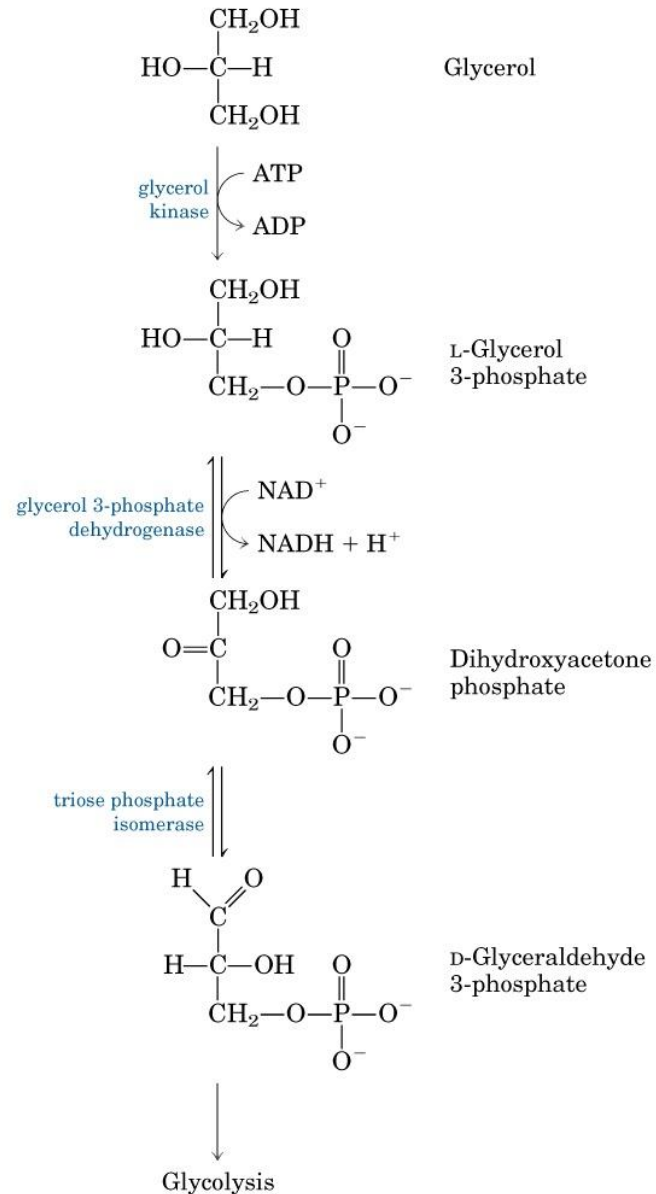
Blood plasma
after meal

(b)

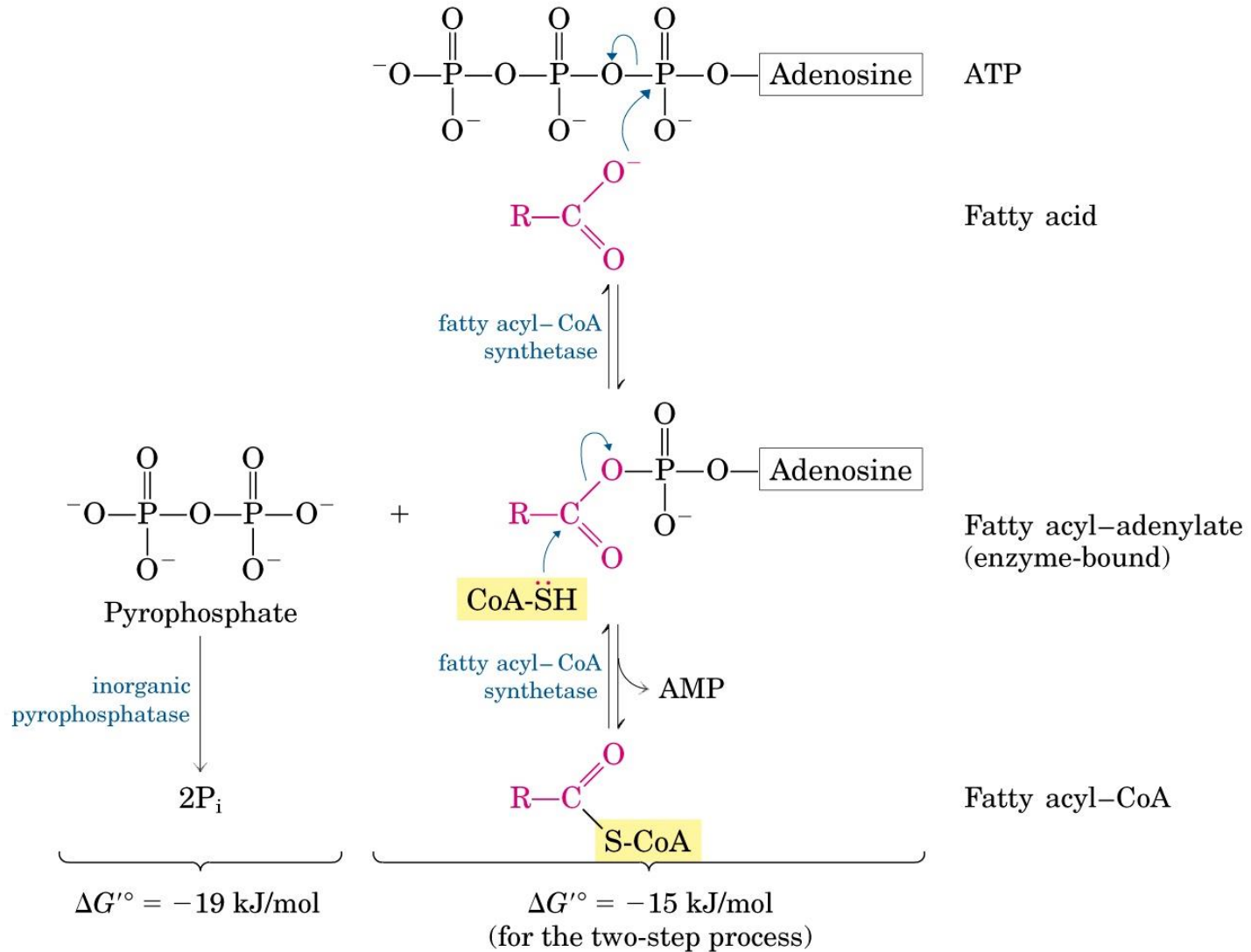
Movilización de triglicéridos



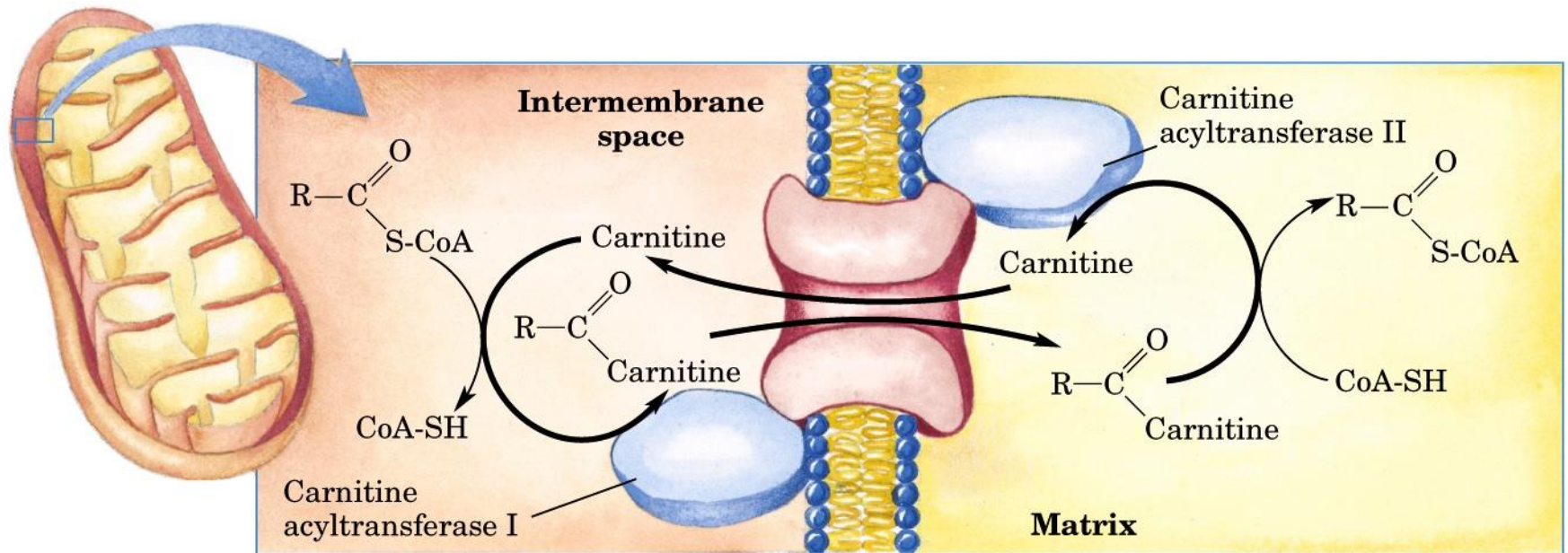
Entrada del glicerol en la ruta glucolítica

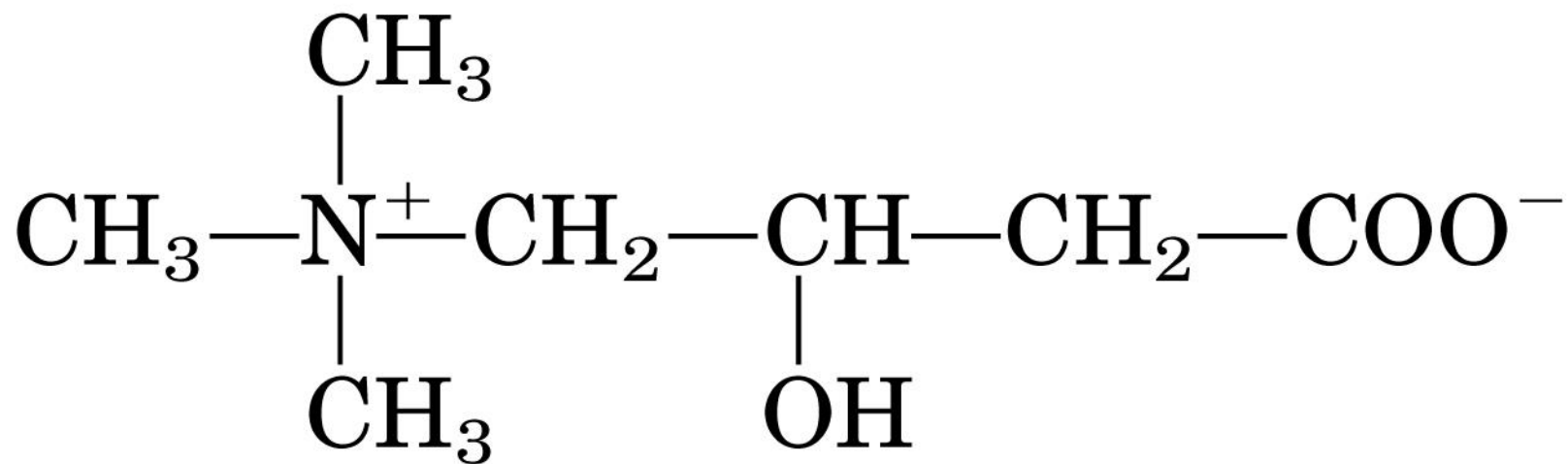


Activación de los ácidos grasos



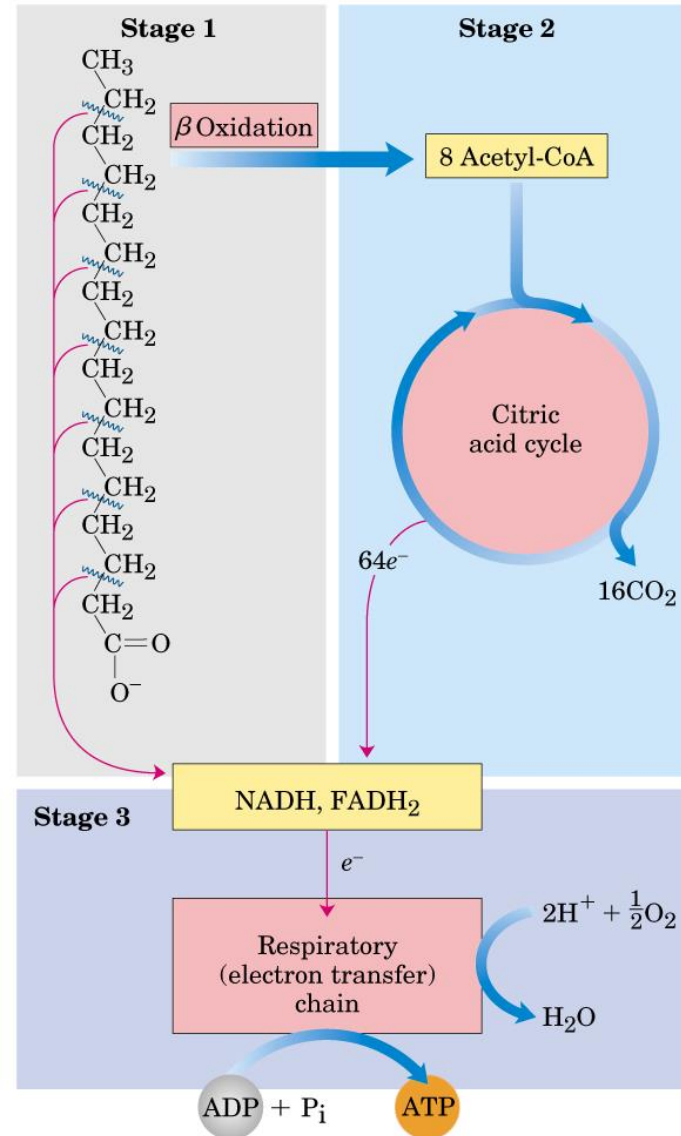
Entrada de los ácidos grasos en la mitocondria a través del transportador acil-carnitina/carnitina



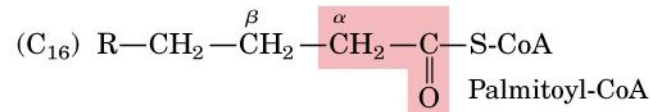
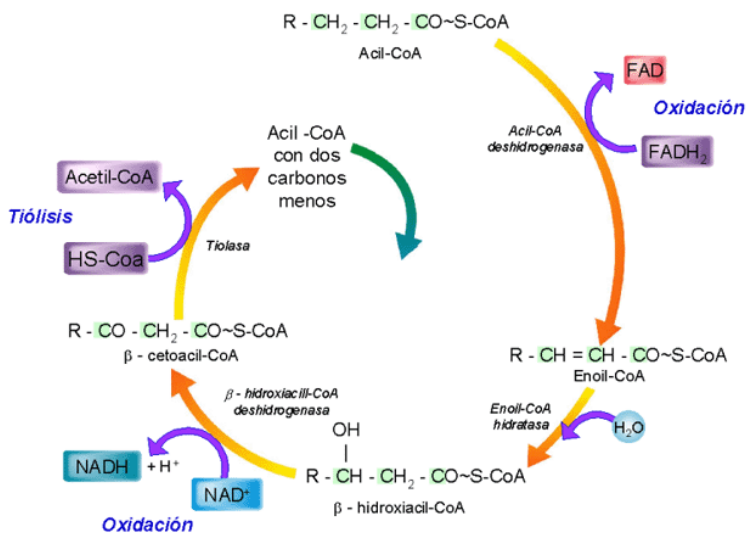


Carnitine

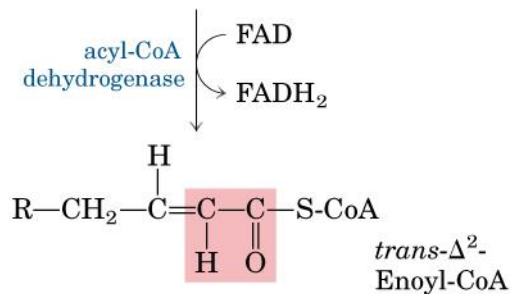
OXIDACIÓN DE LOS ÁCIDOS GRASOS



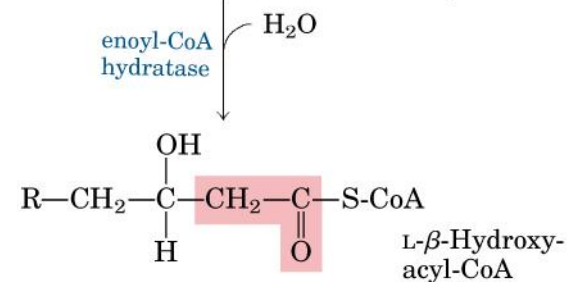
β -oxidación de ácidos grasos saturados



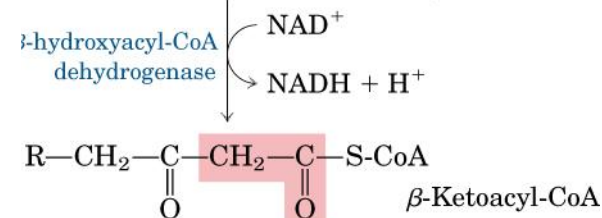
3C y 14e⁻



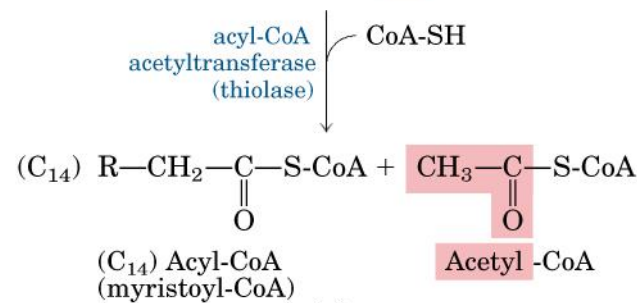
3C y 12e⁻



3C y 12e⁻



3C y 10e⁻



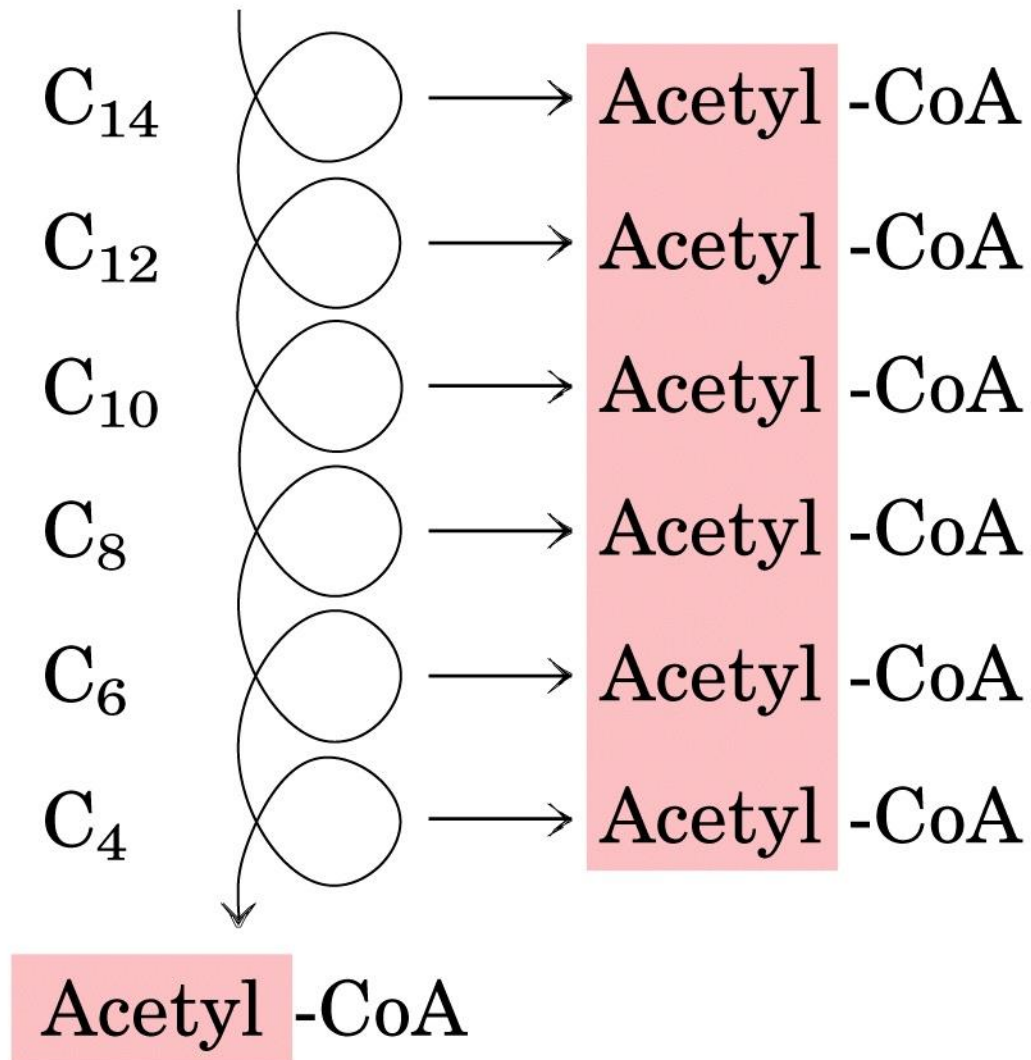
C _{β} : 1C y 2e⁻

C _{α} : 2C y 8e⁻

Al ciclo de Krebs

(a)





(b)

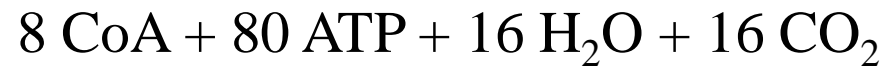
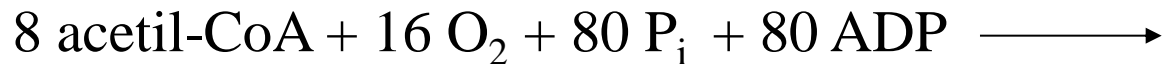


table 17-1

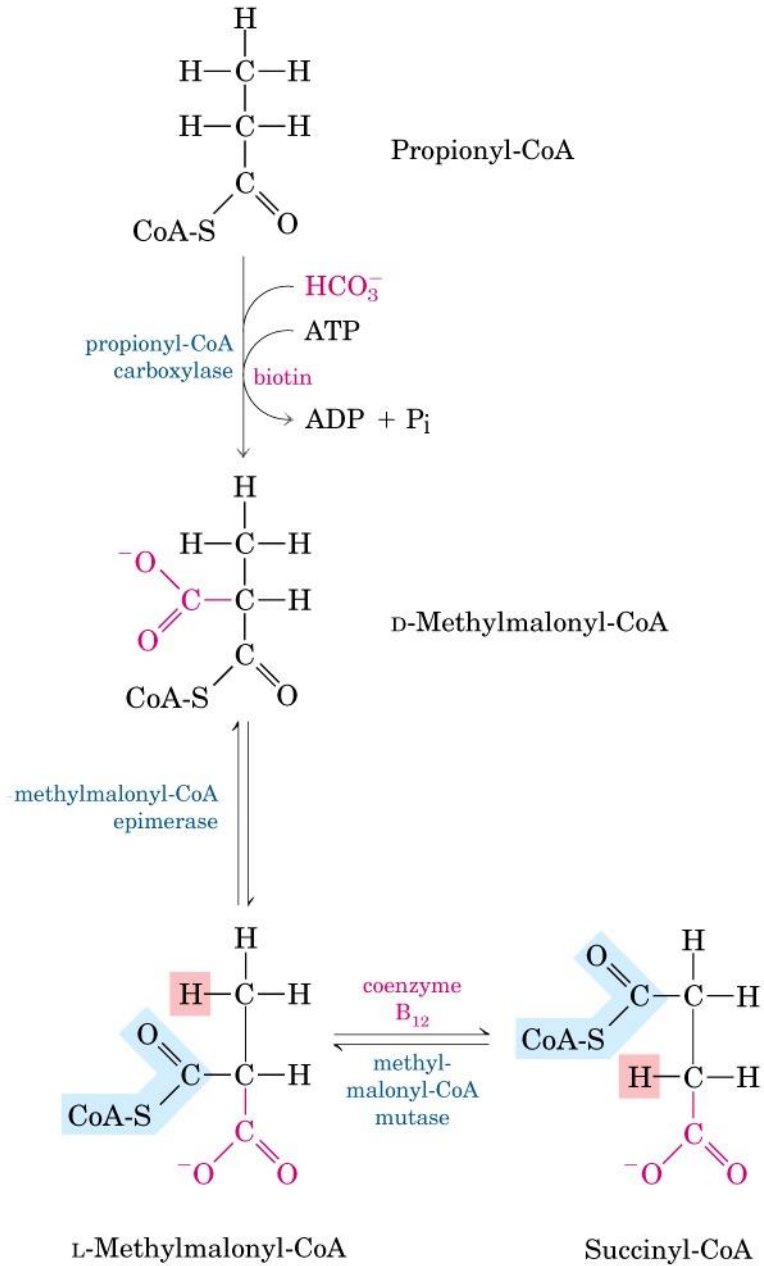
Yield of ATP during Oxidation of One Molecule of Palmitoyl-CoA to CO₂ and H₂O

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		<u>108</u>

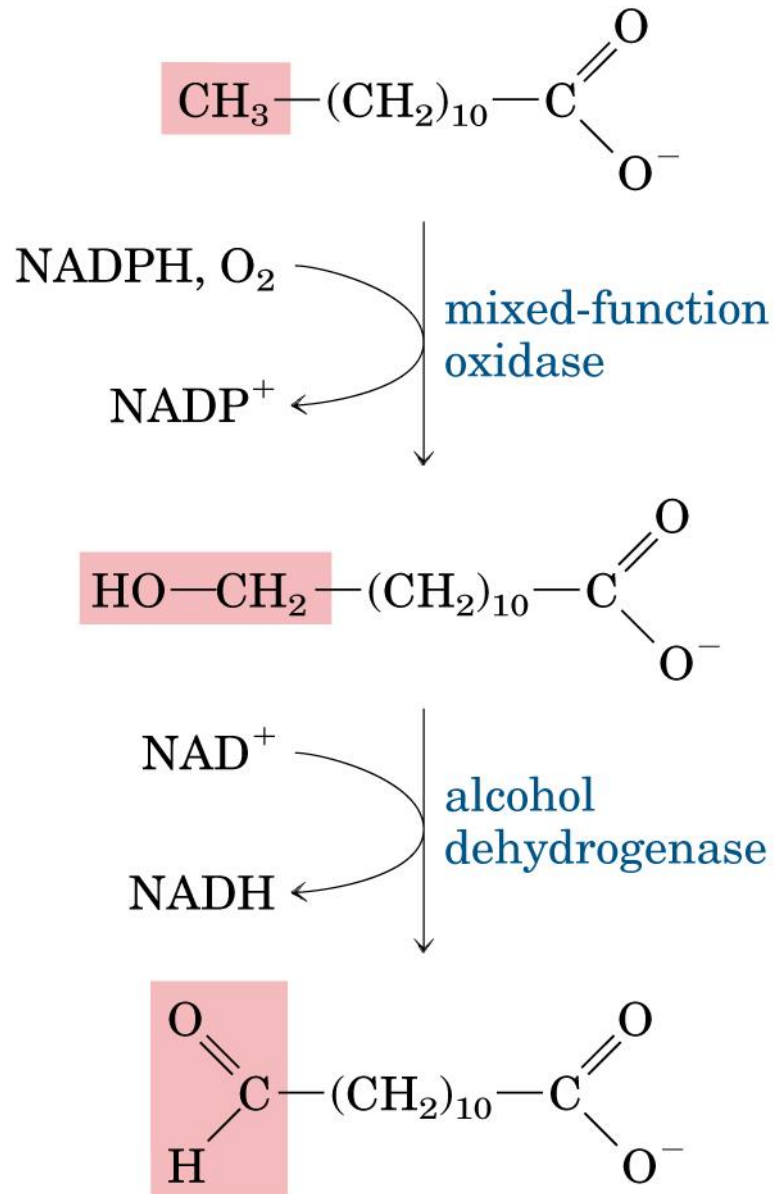
*These calculations assume that mitochondrial oxidative phosphorylation produces 1.5 ATP per FADH₂ oxidized and 2.5 ATP per NADH oxidized.

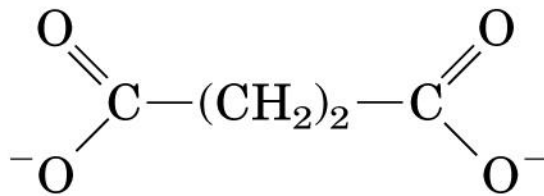
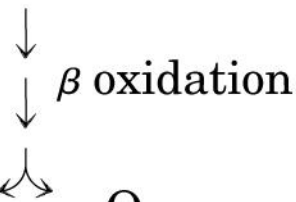
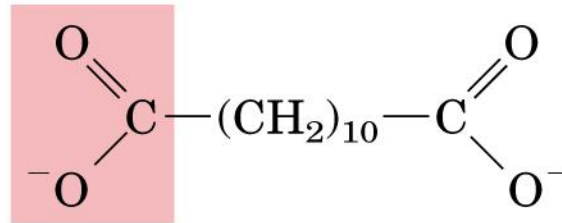
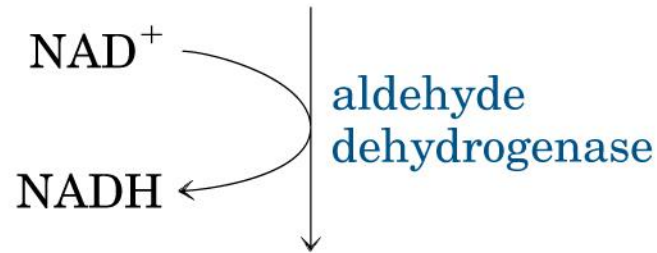
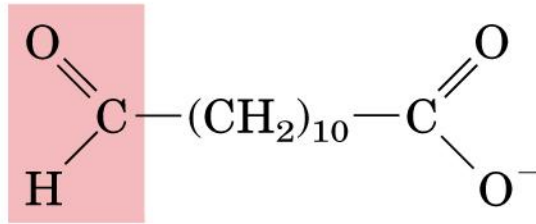
[†]GTP produced directly in this step yields ATP in the reaction catalyzed by nucleoside diphosphate kinase (p. 578).

Oxidación de un ácido graso de cadena impar

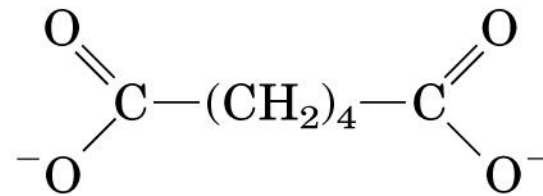


ω -Oxidación de ácido grasos en el retículo endoplasmático



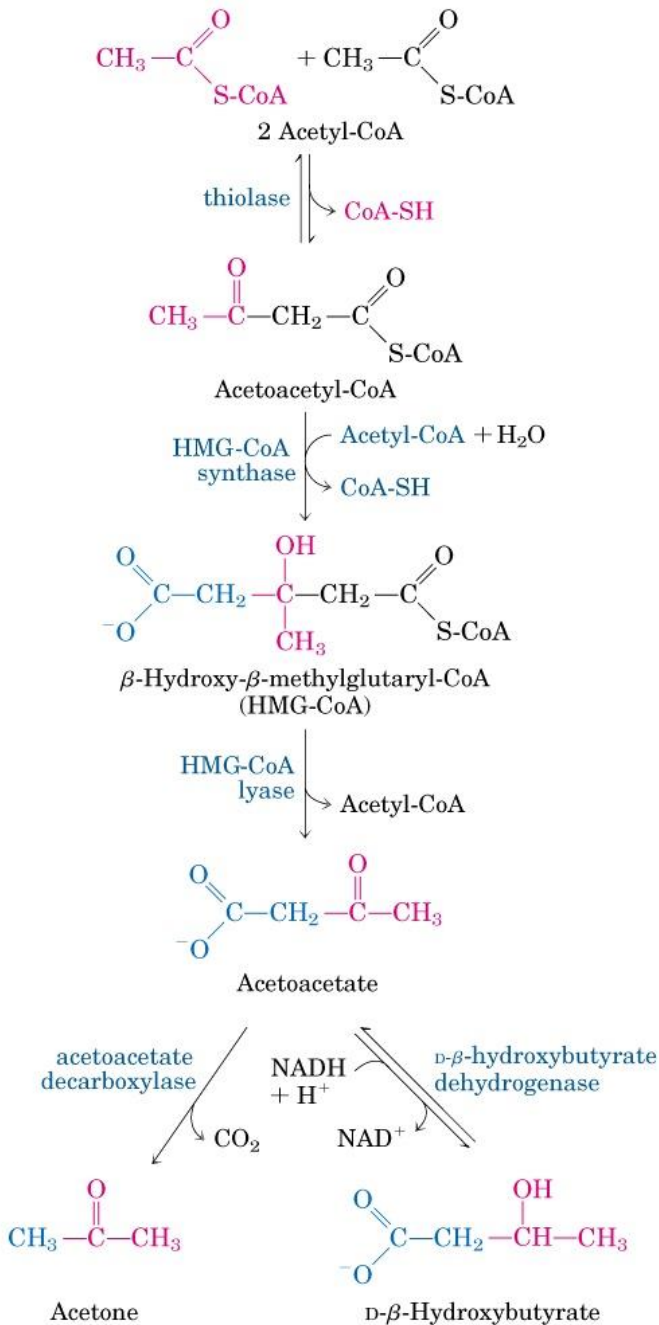


Succinate



Adipate (adipic acid)

BIOSÍNTESIS DE CUERPOS CETÓNICOS EN HÍGADO



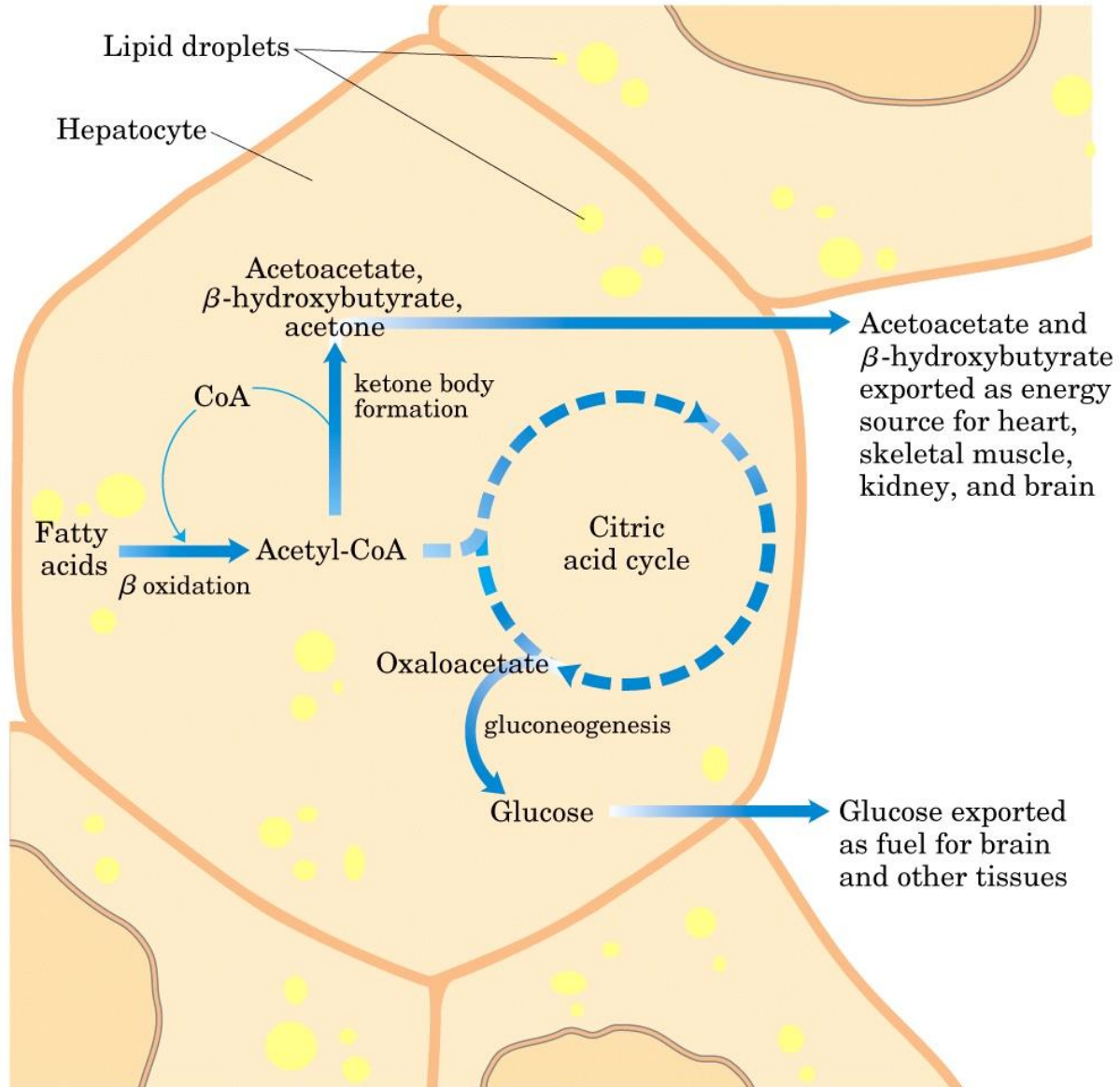
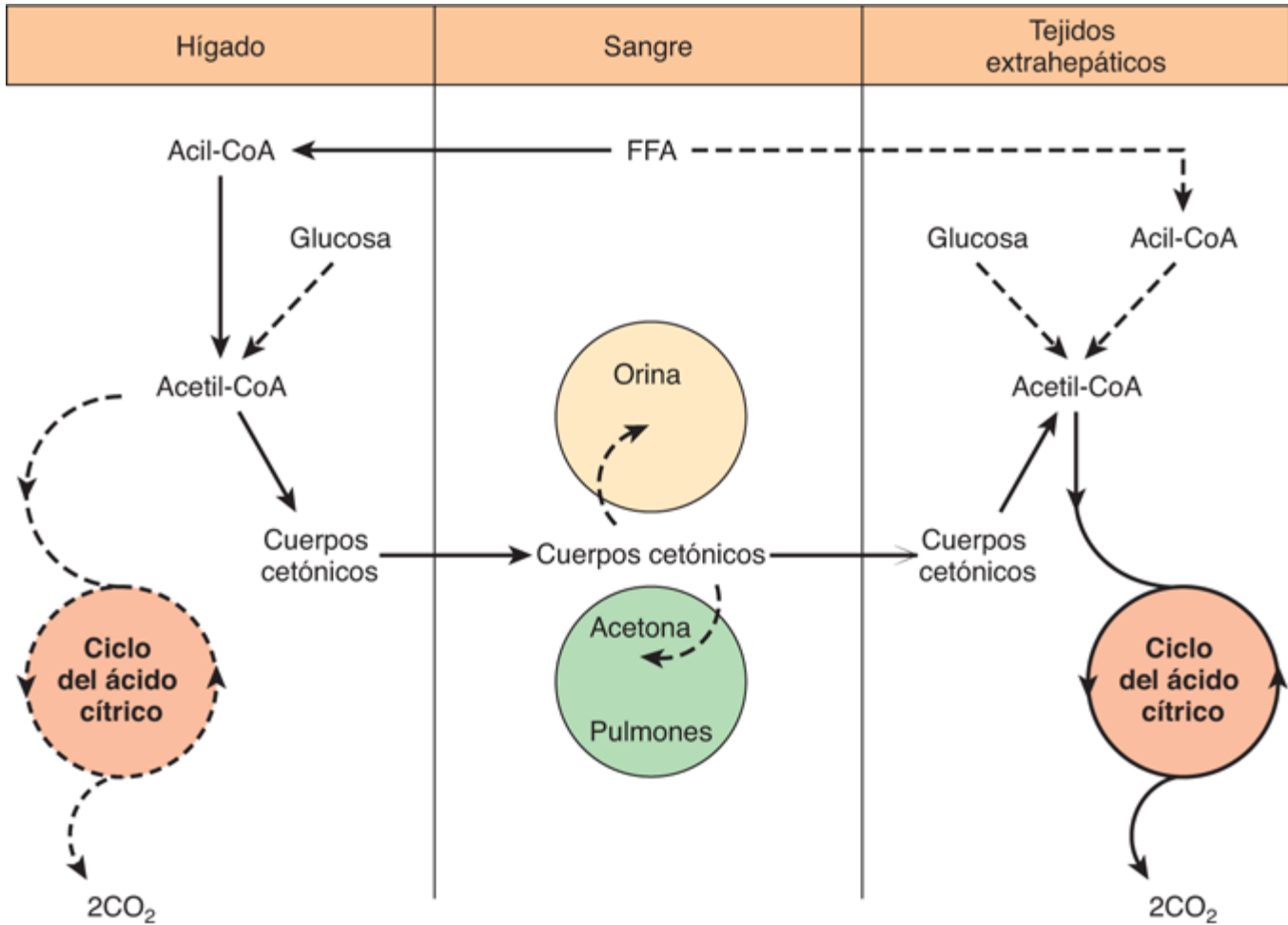


table 17-2

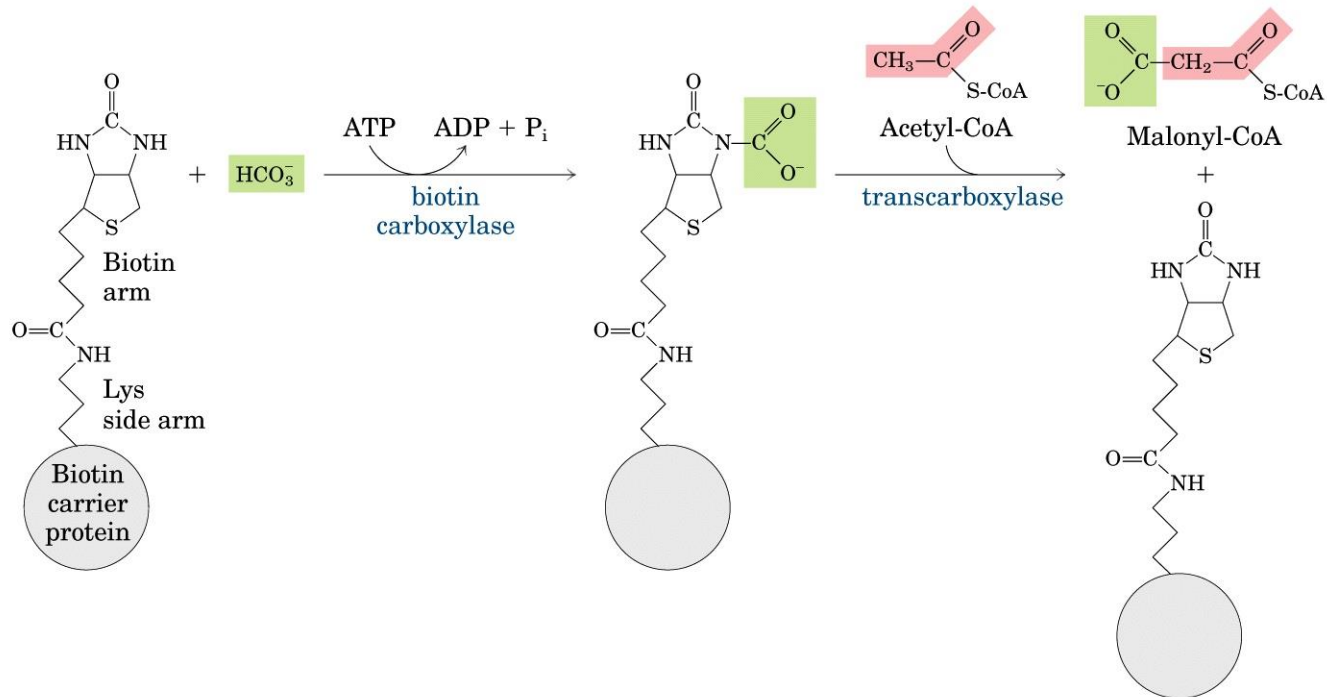
**Ketone Body Accumulation
in Diabetic Ketosis**

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

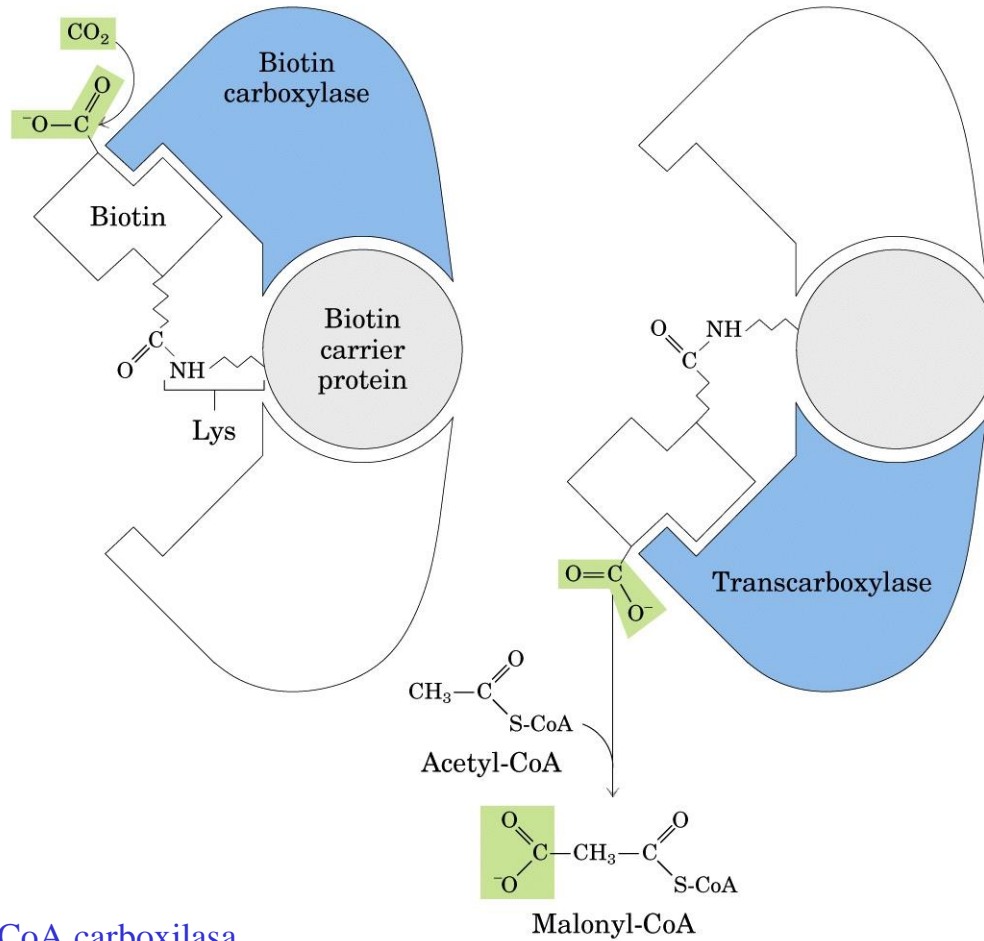


Fuente: Robert K. Murray, David A. Bender, Kathleen M. Botham, Peter J. Kennelly, Víctor W. Rodwell, P. Anthony Weil: *Harper. Bioquímica ilustrada*, 29a edición: www.accessmedicina.com
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BIOSÍNTESIS DE ÁCIDOS GRASOS: MALONIL-CoA

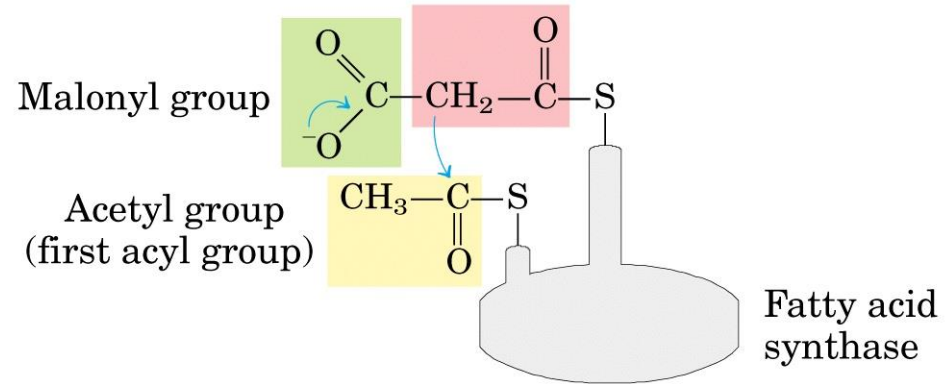
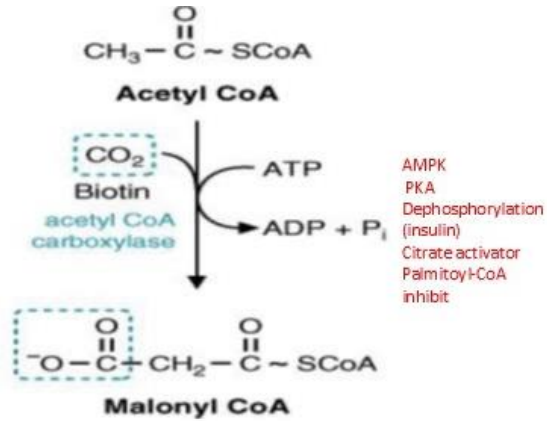


Acetil-CoA carboxilasa

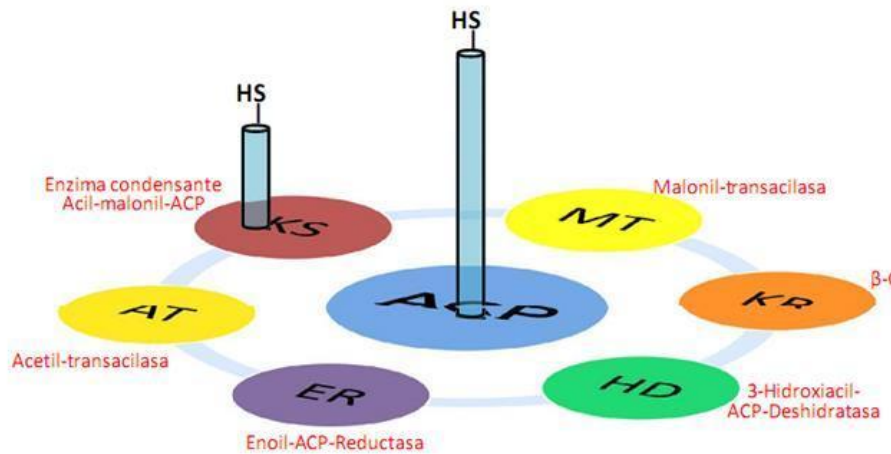


Acetyl-CoA carboxilasa

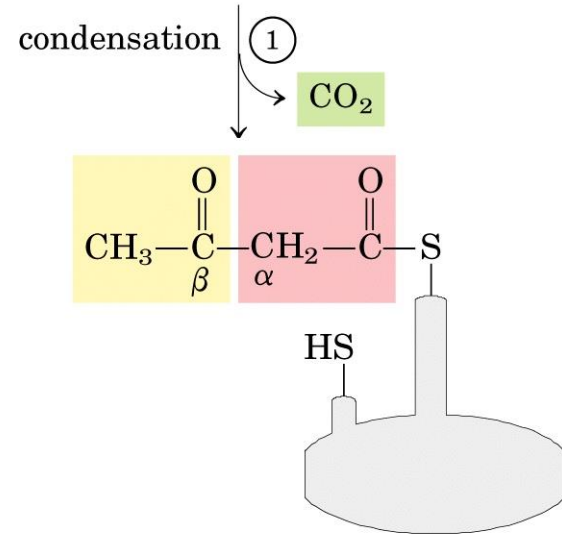
BIOSÍNTESIS DE ÁCIDOS GRASOS

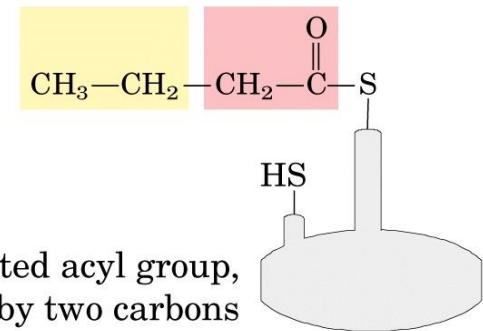
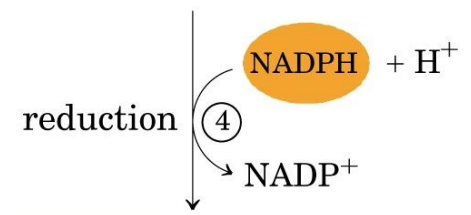
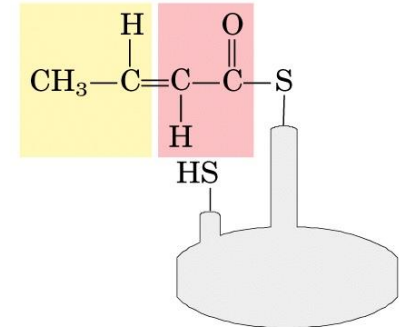
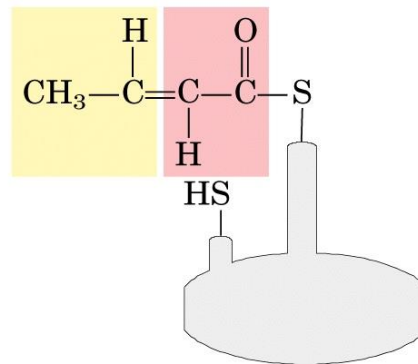
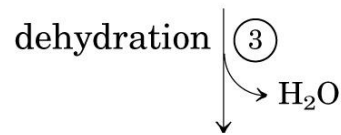
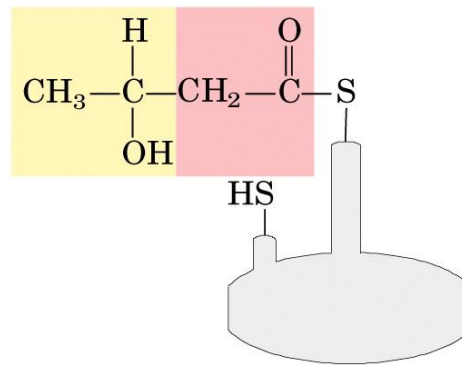
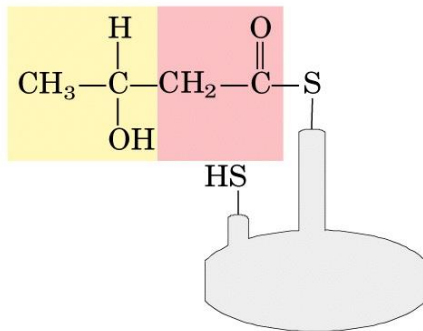
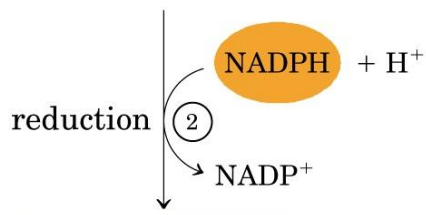
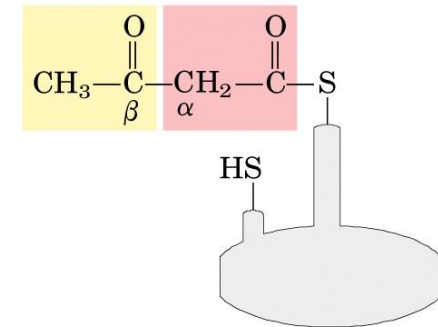


Ácido graso sintasa



COMPLEJO ENZIMÁTICO ÁCIDO GRASO SINTASA





BIOSÍNTESIS DE ÁCIDOS GRASOS

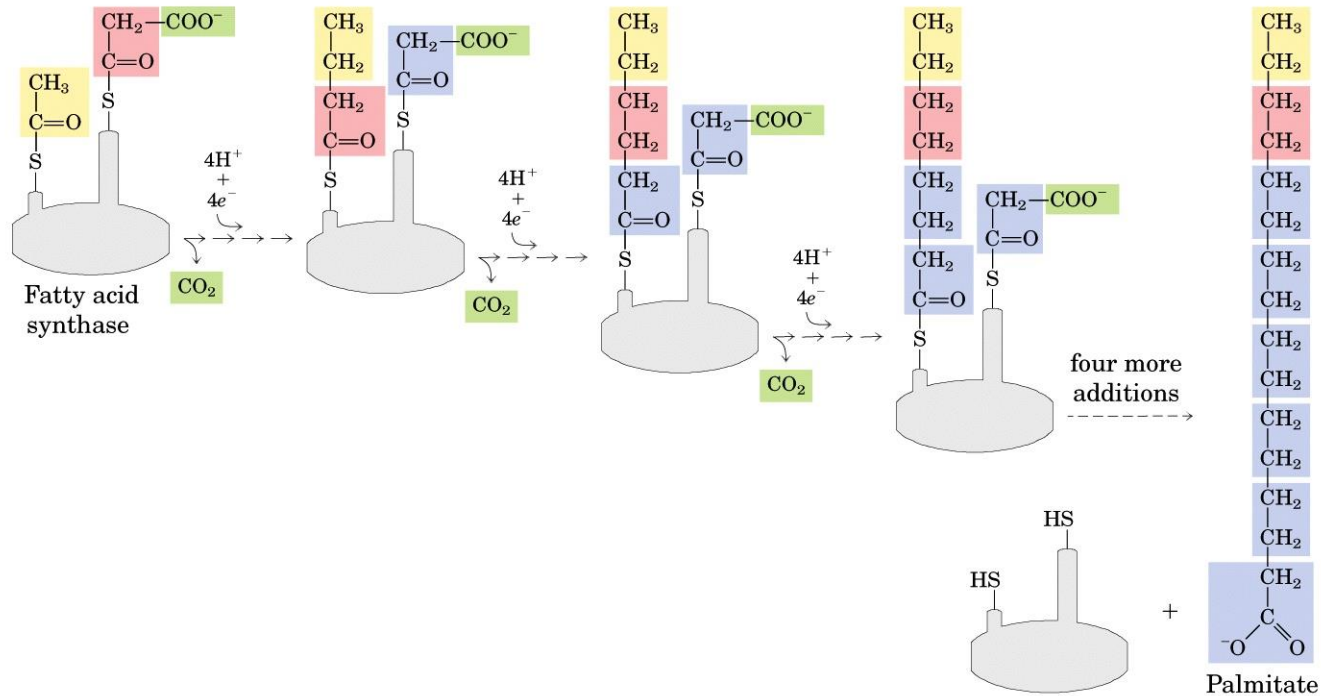
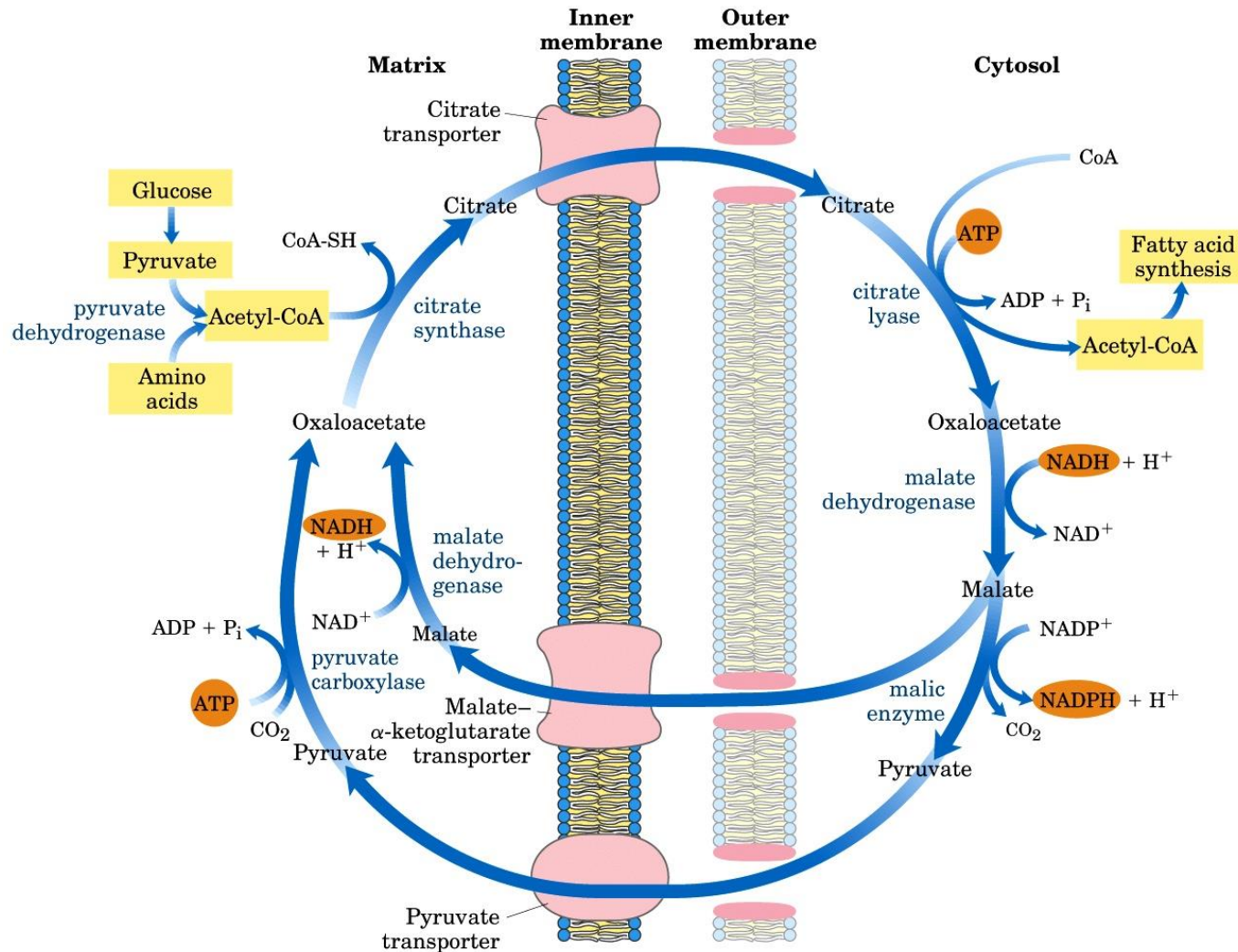


table 21–1

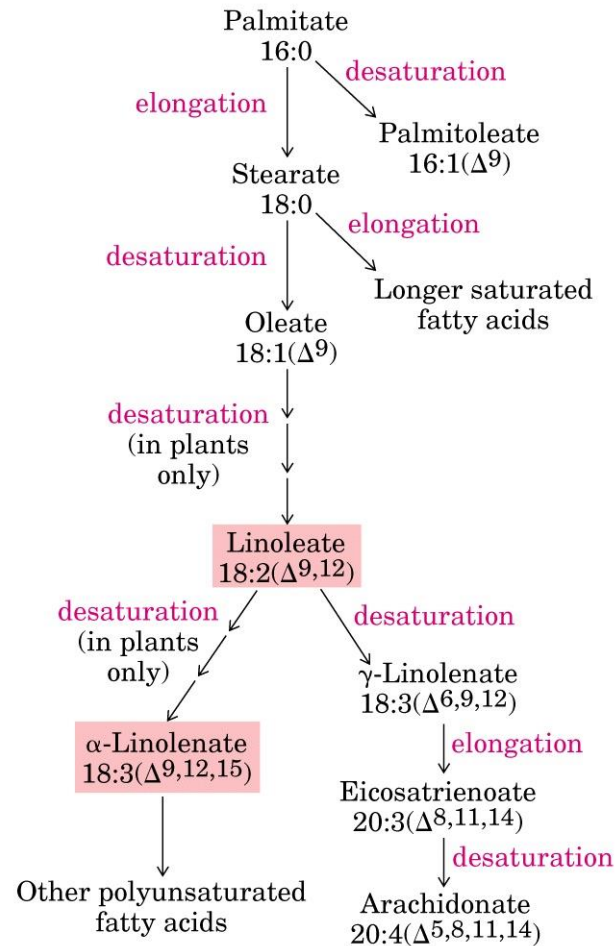
Proteins of the Fatty Acid Synthase Complex of *E. coli*

Protein	Role
Acyl carrier protein (ACP)	Carries acyl groups in thioester linkage
Acetyl-CoA–ACP transacetylase (AT)	Transfers acyl group from CoA to Cys residue of KS
β -Ketoacyl-ACP synthase (KS)	Condenses acyl and malonyl groups (there are at least three isozymes of KS)
Malonyl-CoA–ACP transferase (MT)	Transfers malonyl group from CoA to ACP
β -Ketoacyl-ACP reductase (KR)	Reduces β -keto group to β -hydroxy group
β -Hydroxyacyl-ACP dehydratase (HD)	Removes H ₂ O from β -hydroxyacyl-ACP, creating double bond
Enoyl-ACP reductase (ER)	Reduces double bond, forming saturated acyl-ACP

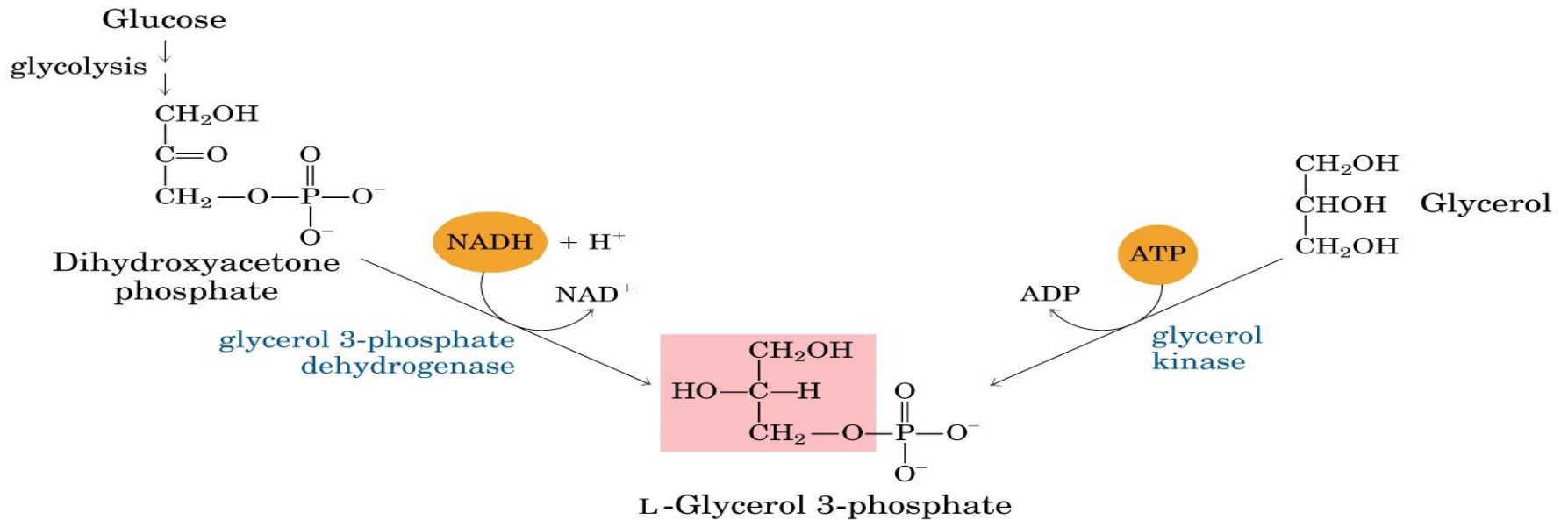
Lanzadera para la transferencia de grupos acetilo desde la mitocondria al citosol

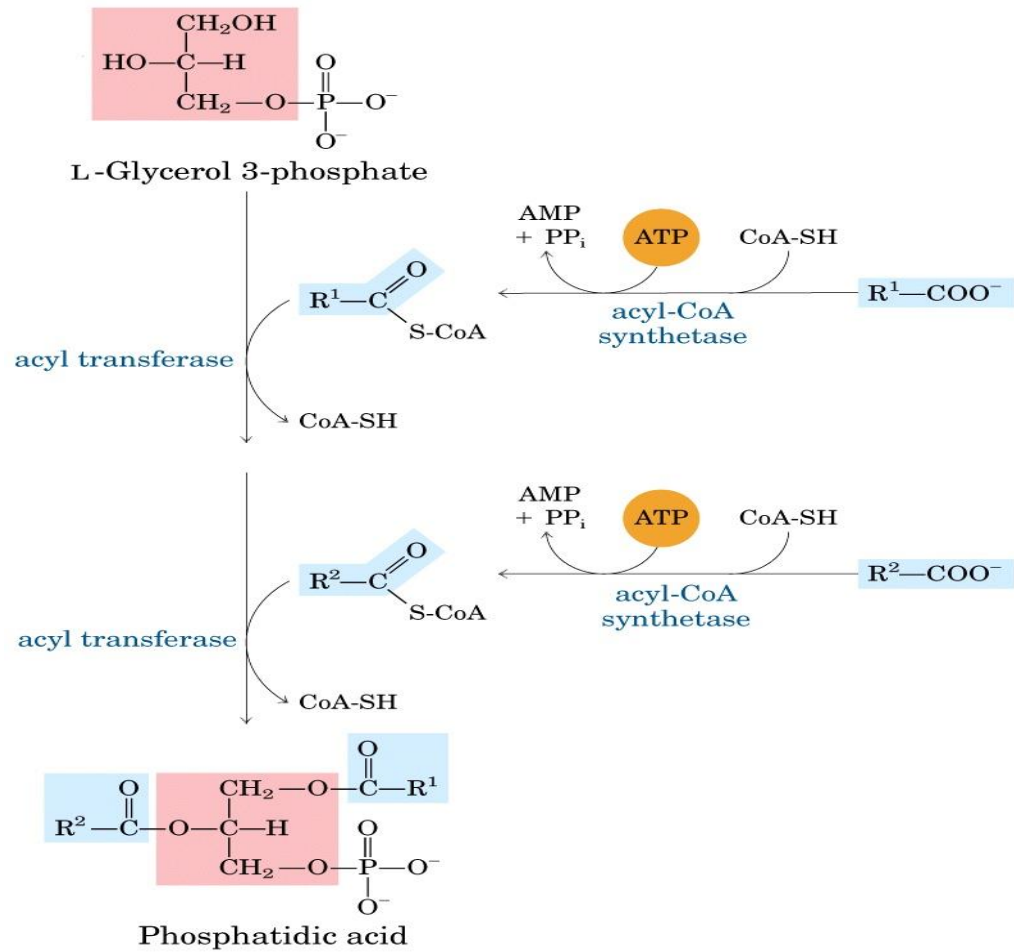


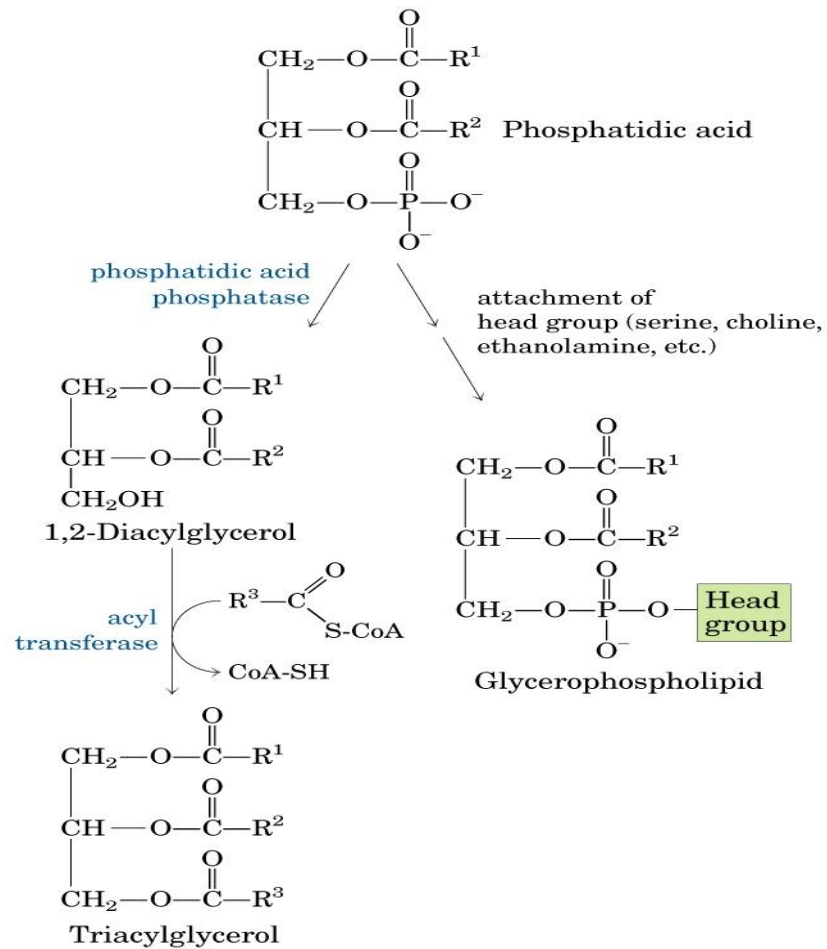
RUTAS DE SÍNTESIS DE OTROS ÁCIDOS GRASOS



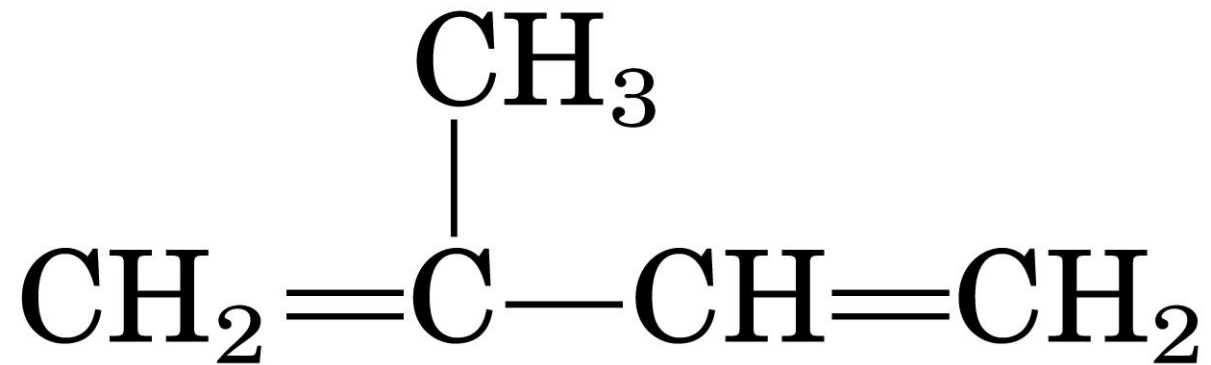
RUTAS DE SÍNTESIS DE TRIGLICÉRIDOS





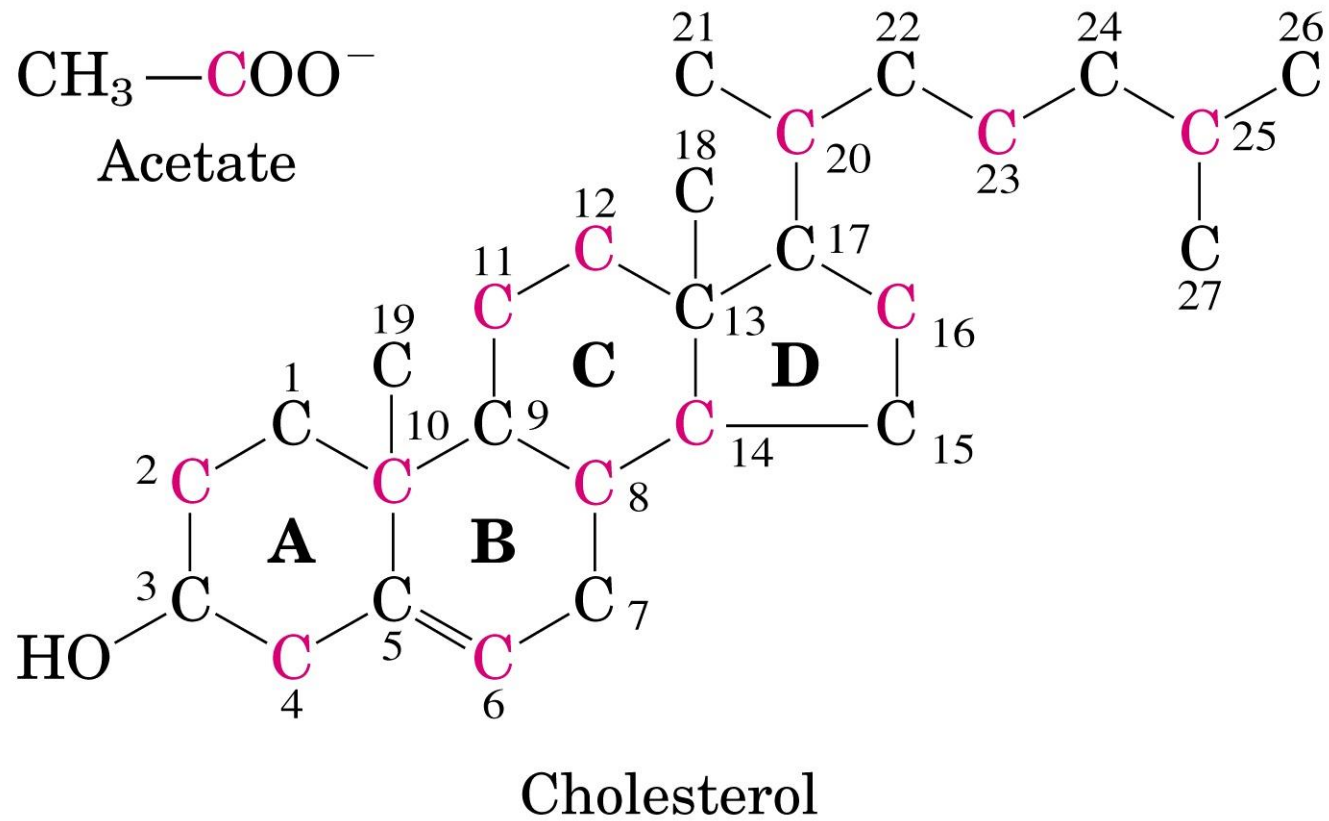


BIOSINTESIS DEL COLESTEROL

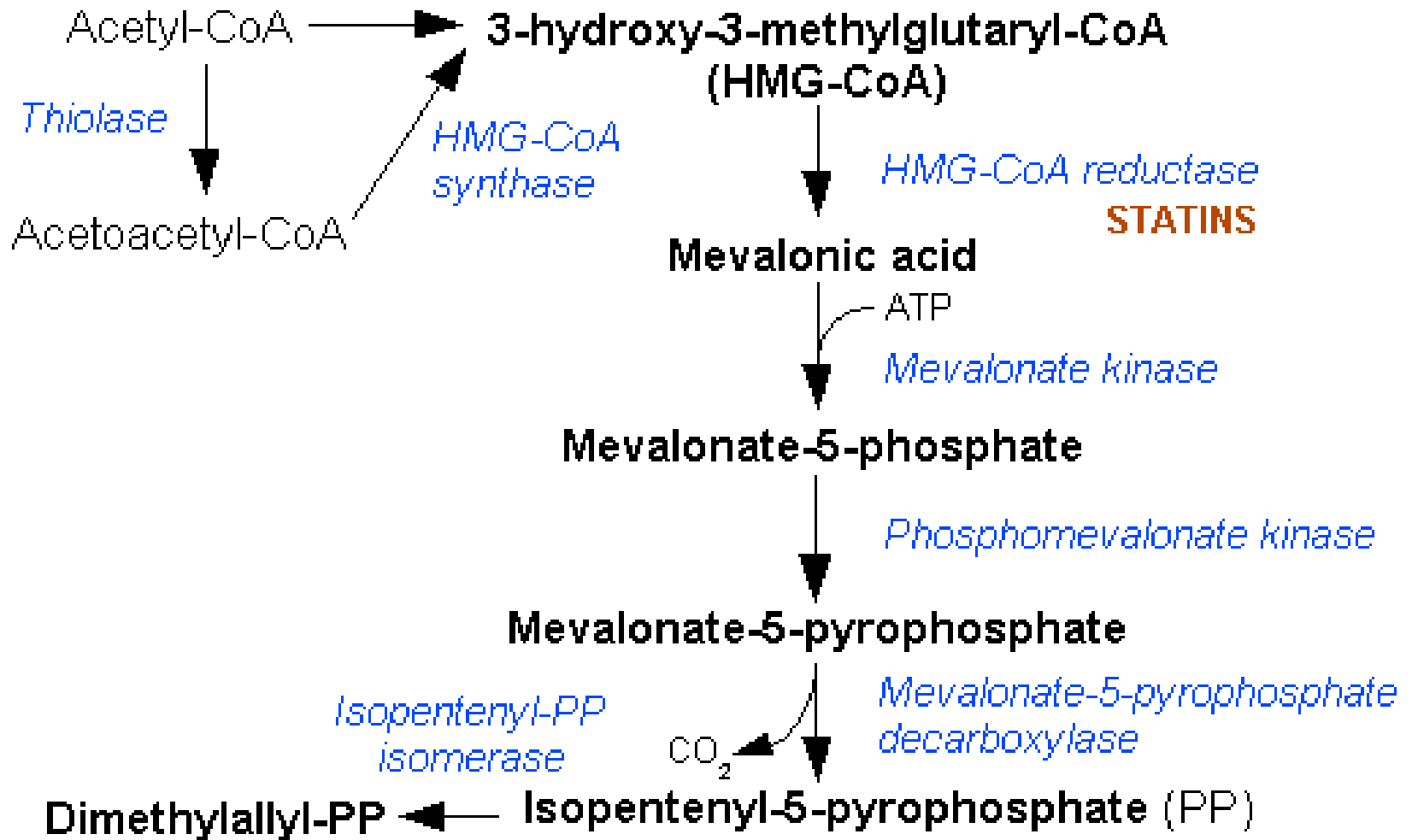


Isoprene

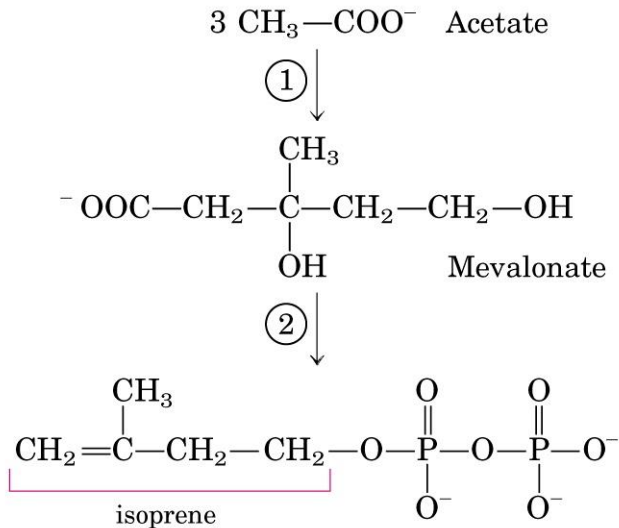
Origen de los átomos de carbono del colesterol



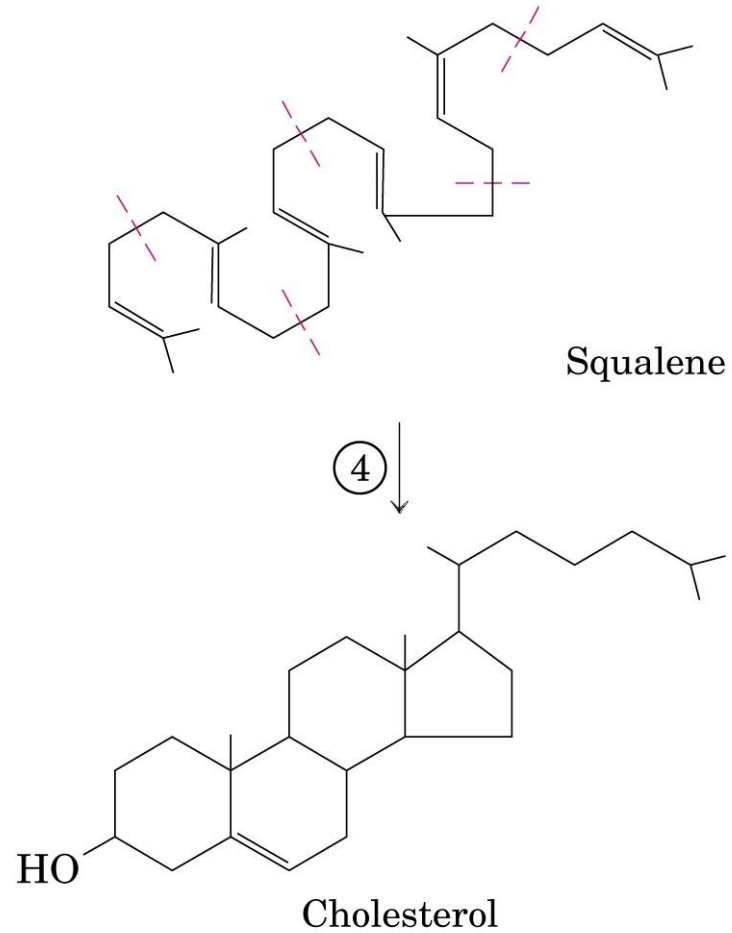
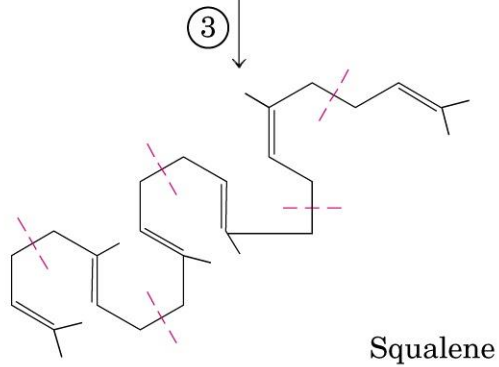
Resumen de la biosíntesis del colesterol



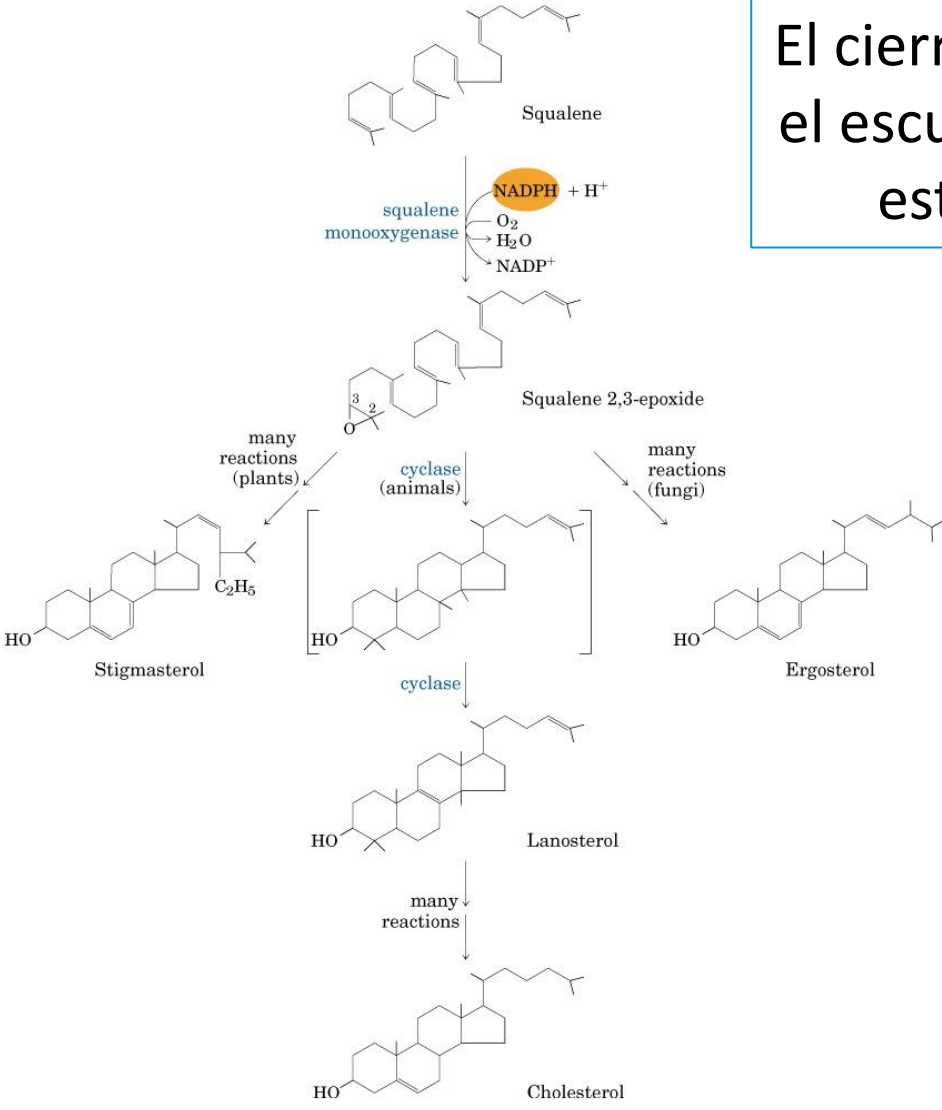
Resumen de la biosíntesis del colesterol

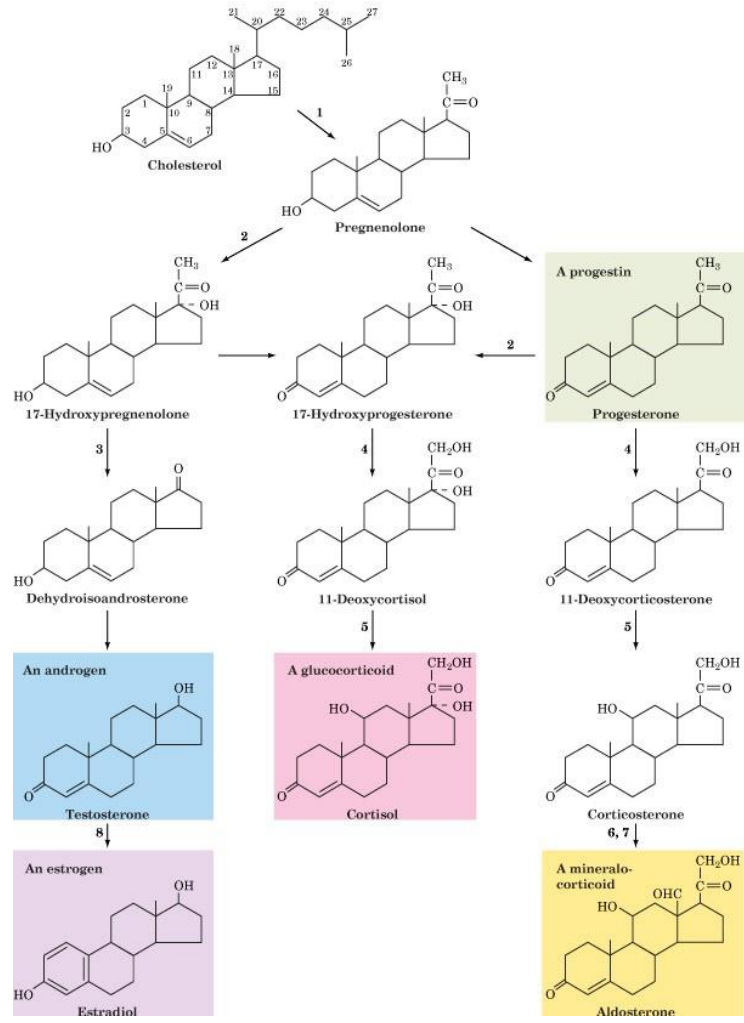


Activated isoprene



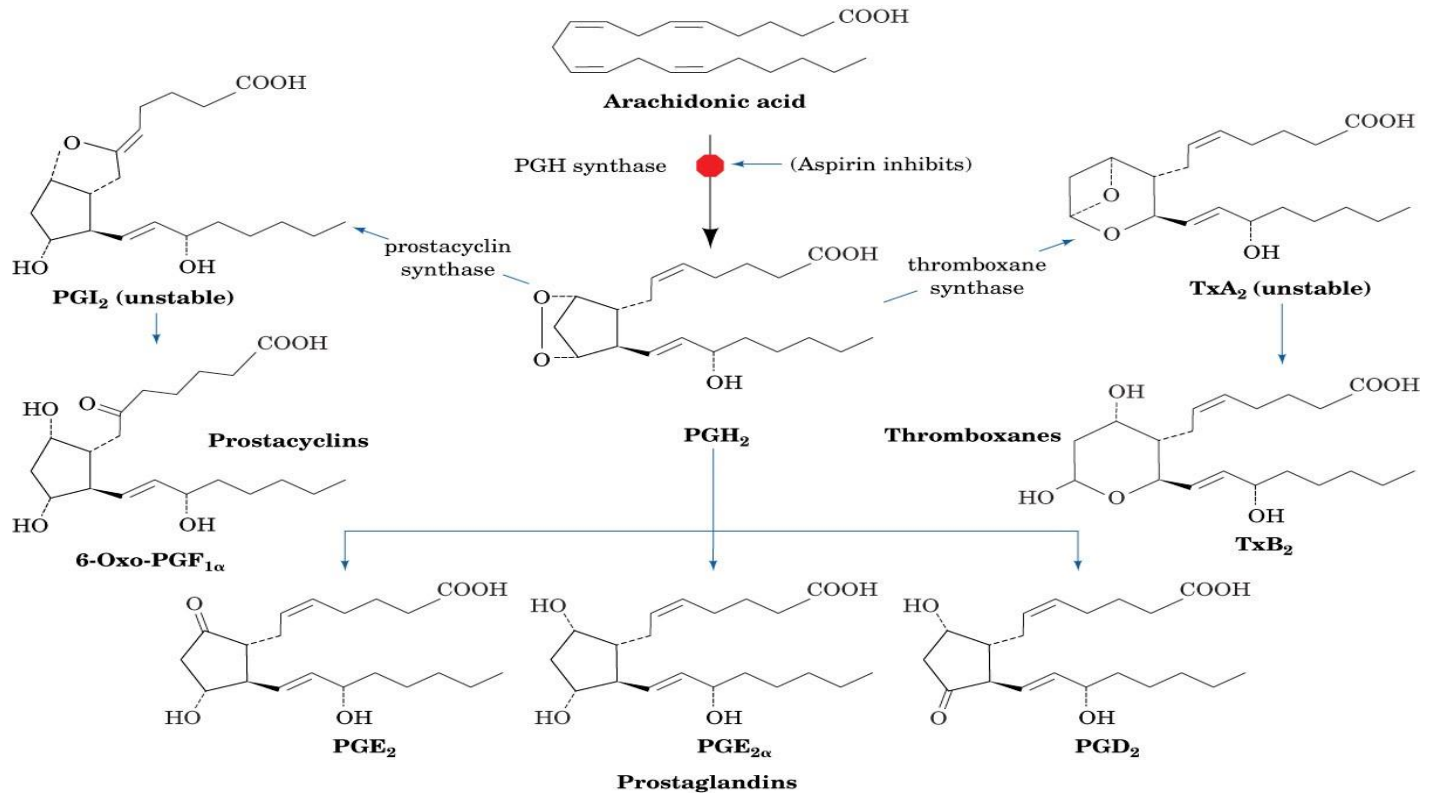
El cierre de los anillos convierte el escualeno lineal en el núcleo esteroideo condensado



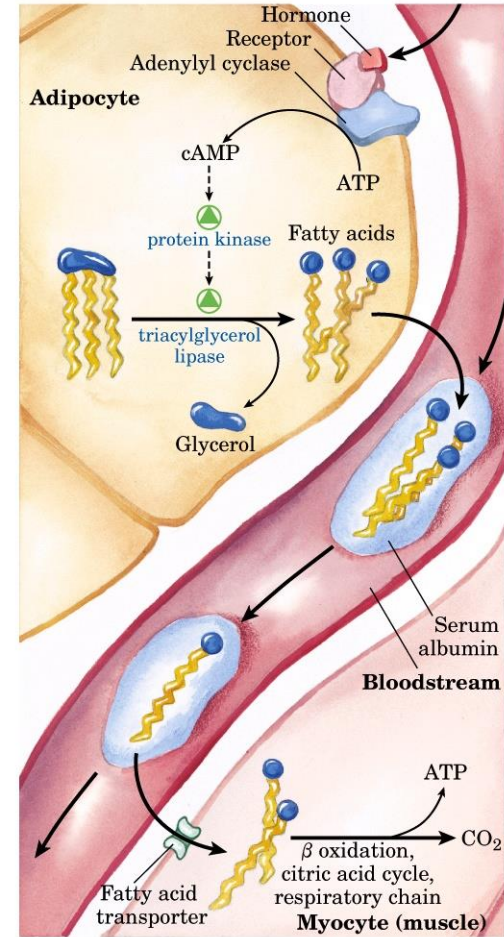
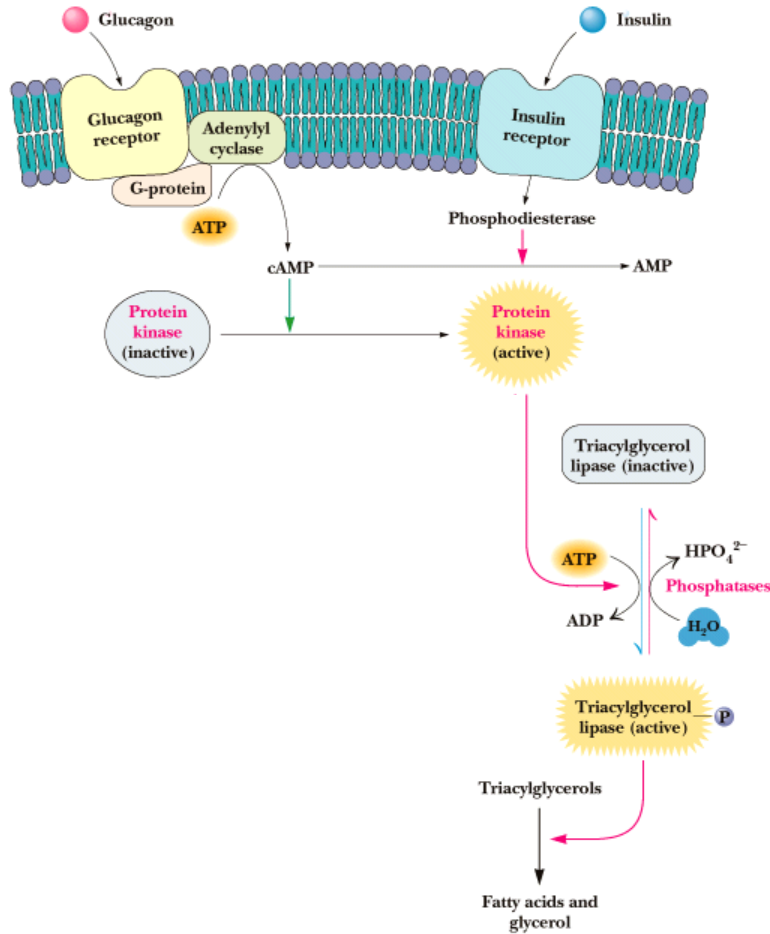


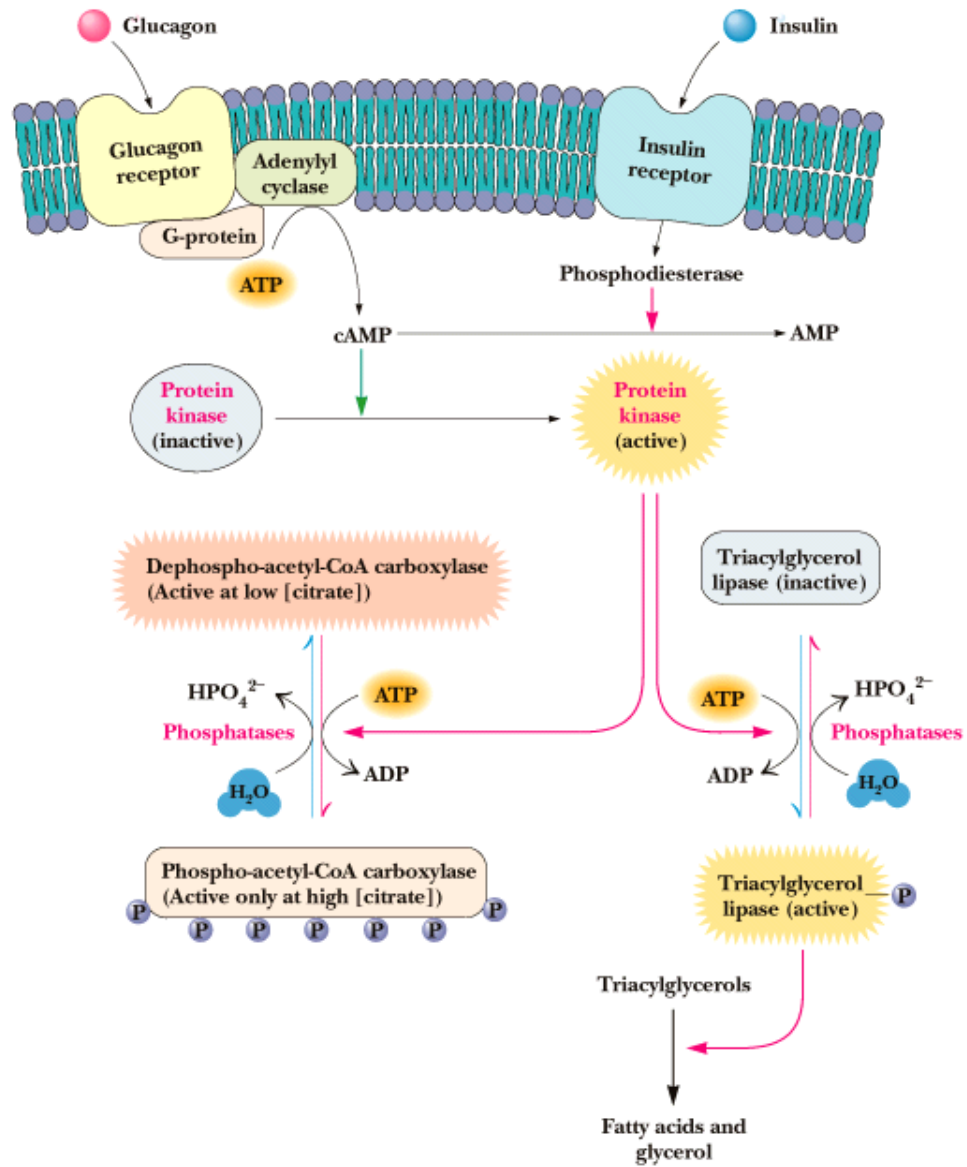
Biosíntesis de prostaglandinas

The cyclic pathway of arachidonic acid metabolism.



REGULACIÓN DE LA OXIDACIÓN DE ACIDOS GRASOS





Regulación de la síntesis de Ácidos grasos

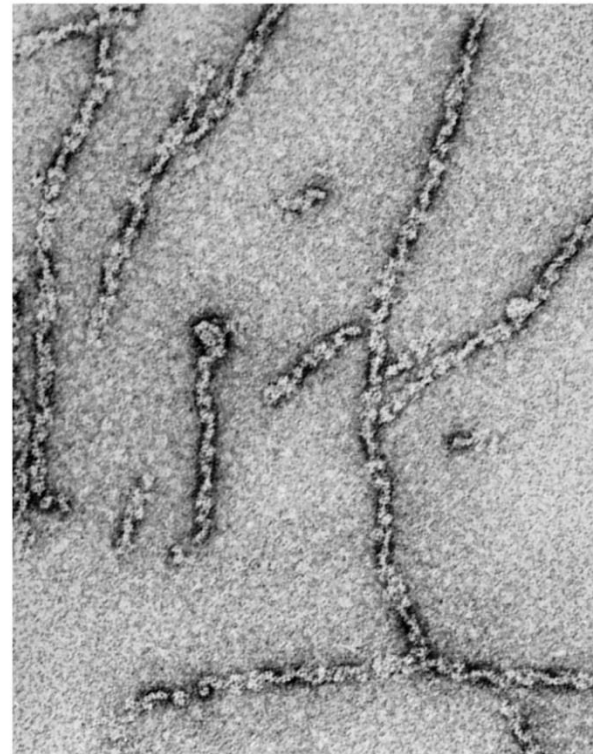
Modificadores alostéricos, fosforilación y hormonas

- El malonil-CoA bloquea la carnitina acil-transferasa y por tanto inhibe la beta-oxidation
- Citrato activa a la acetil-CoA carboxilasa
- Los acil graso-CoAs inhiben a la acetil-CoA carboxilasa
- Las hormonas regulan a la acetil-CoA carboxilasa
- Glucagon activa lipasas/inhibe acetil-CoA carboxilasa
- Insulina inhibe lipasas/activa acetil-CoA carboxilasa

Acetil-CoA Carboxilasa

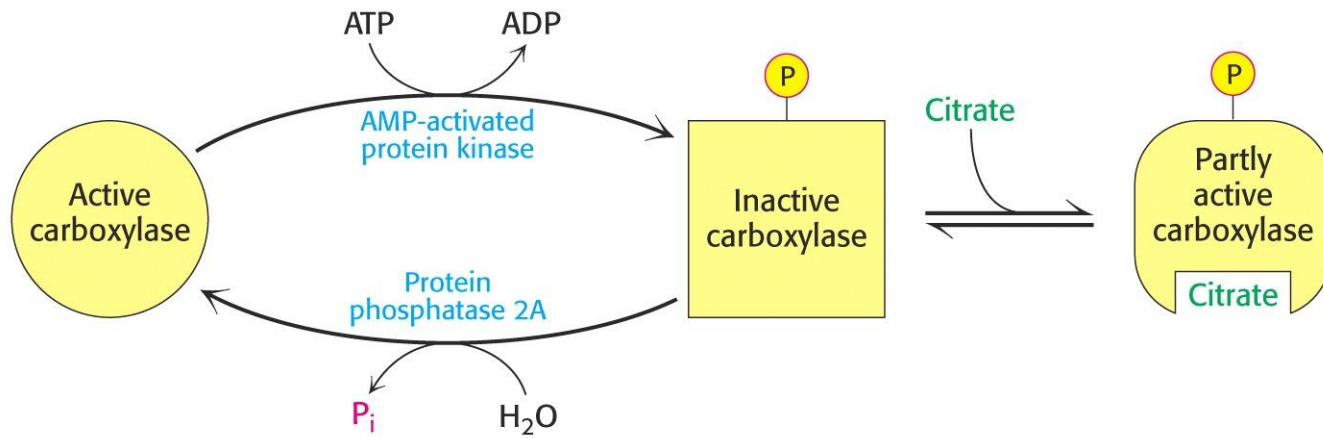


(b)



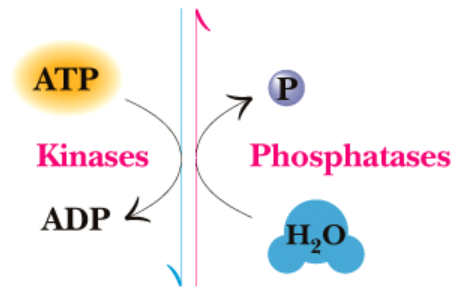
100 nm

Acetil-CoA Carboxilasa

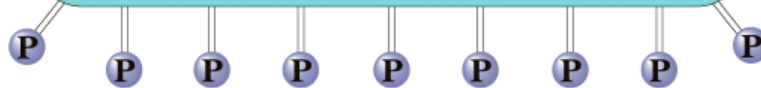


Acetil-CoA Carboxilasa

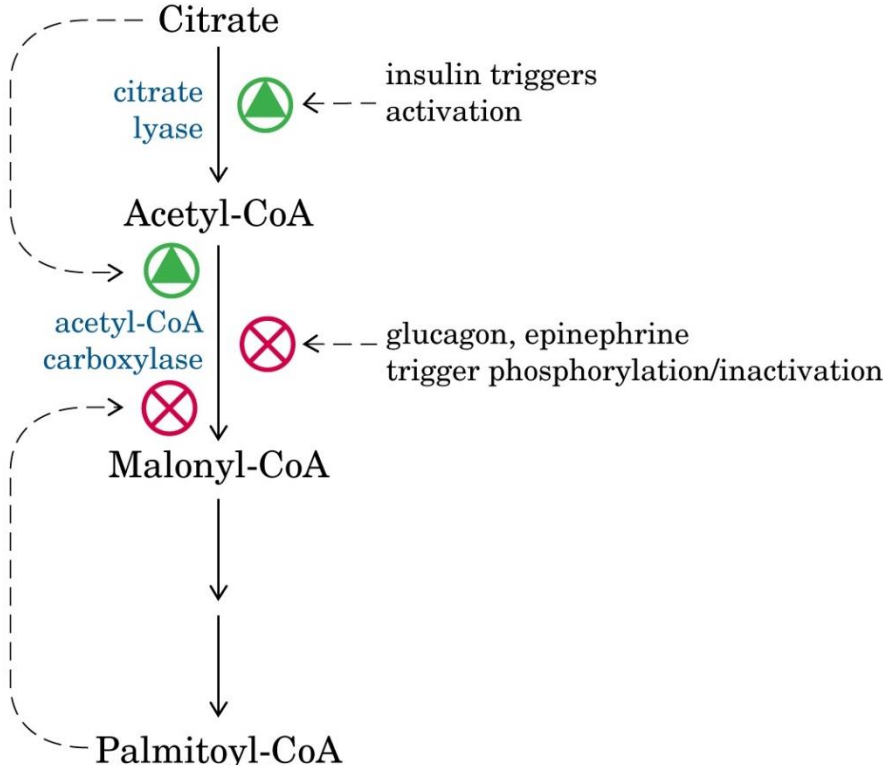
Dephospho-acetyl-CoA carboxylase
(Low [citrate] activates, high [fatty acyl-CoA] inhibits)



Phospho-acetyl-CoA carboxylase
(High [citrate] activates, low [fatty acyl-CoA] inhibits)

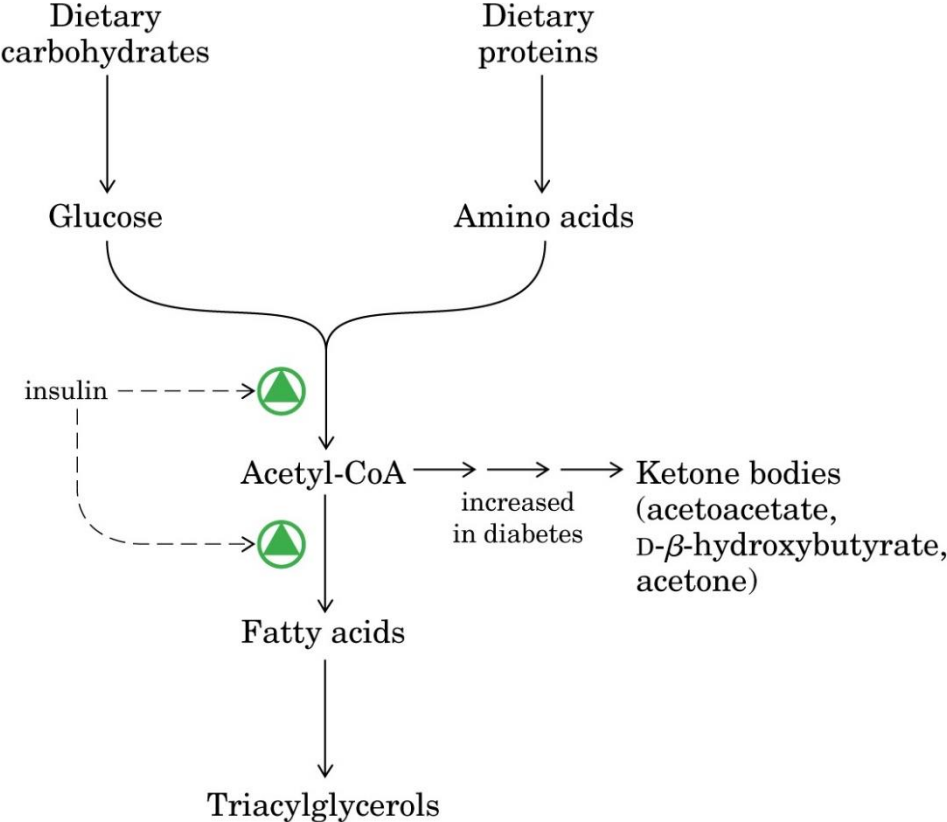


Síntesis de ácidos grasos

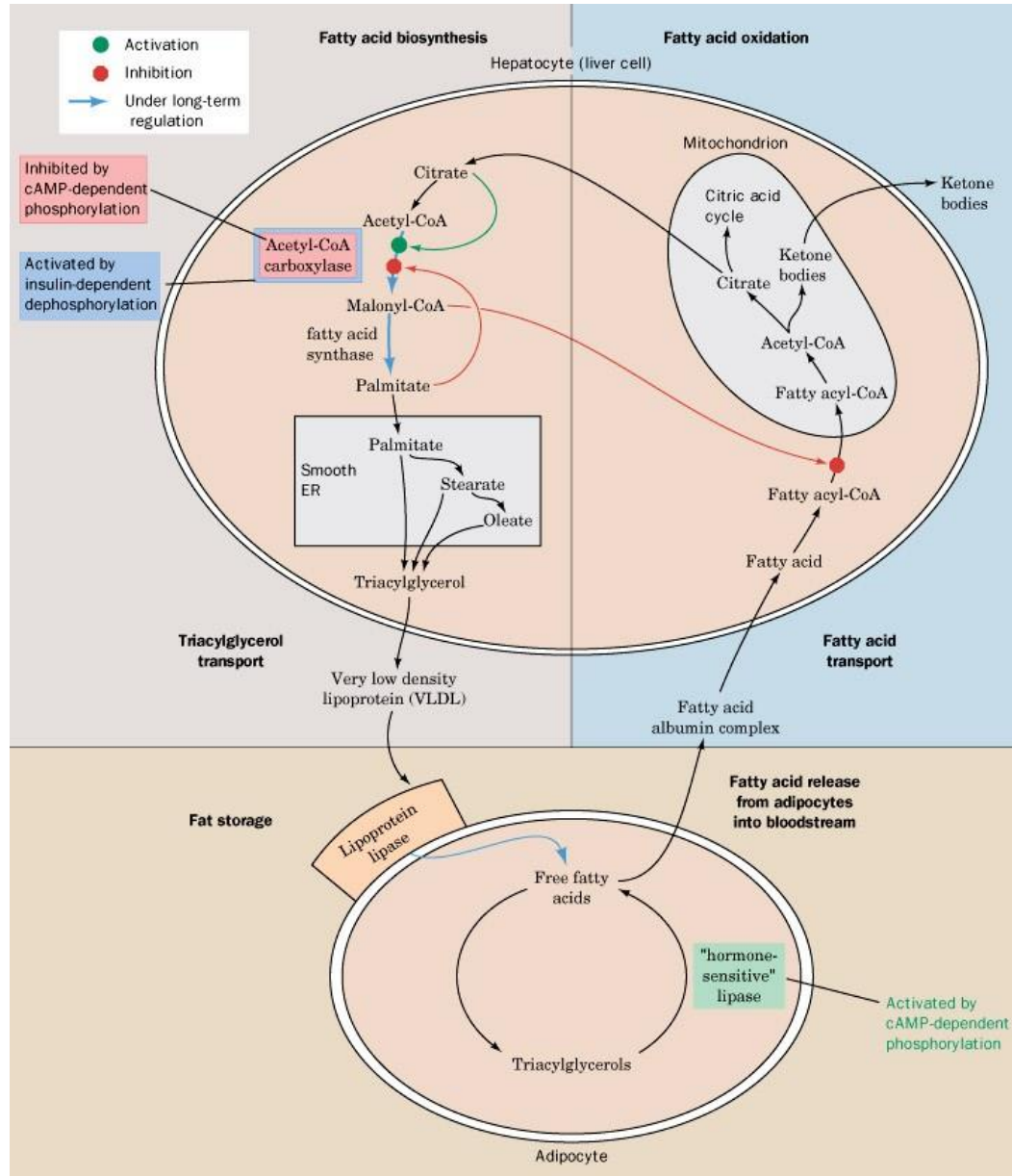


(a)

Síntesis de Triacilgliceroles



Sitios de regulación del metabolismo de ácidos grasos



Regulación de la síntesis de colesterol

Regulación de la HMG-CoA Reductasa

Etapa limitante de la velocidad, es el principal sitio de regulación en la síntesis del colesterol

Fosforilación por quinasas dependientes de AMPc inactivan a la reductasa

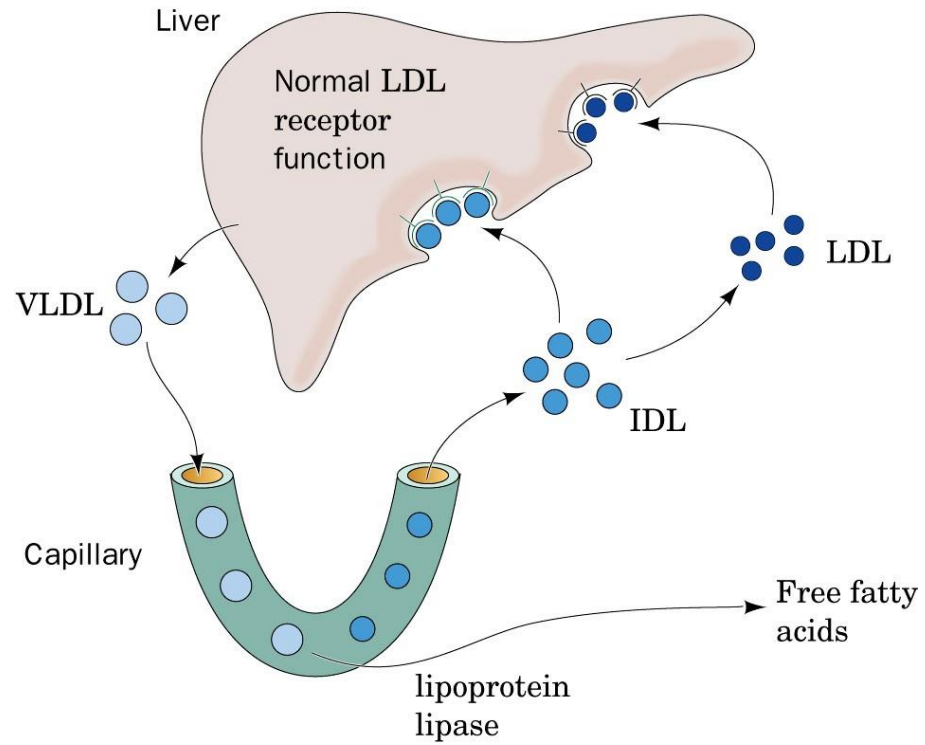
Degradación de la HMG-CoA reductasa – su vida media es de 3 horas y dependen del nivel de colesterol

Expresión génica esta controlada por los niveles de colesterol

Figure 25-59a

Control of plasma LDL production and uptake by liver LDL receptors. (a) Normal human subjects.

(a) **Normal**



(b) **Familial hypercholesterolemia**

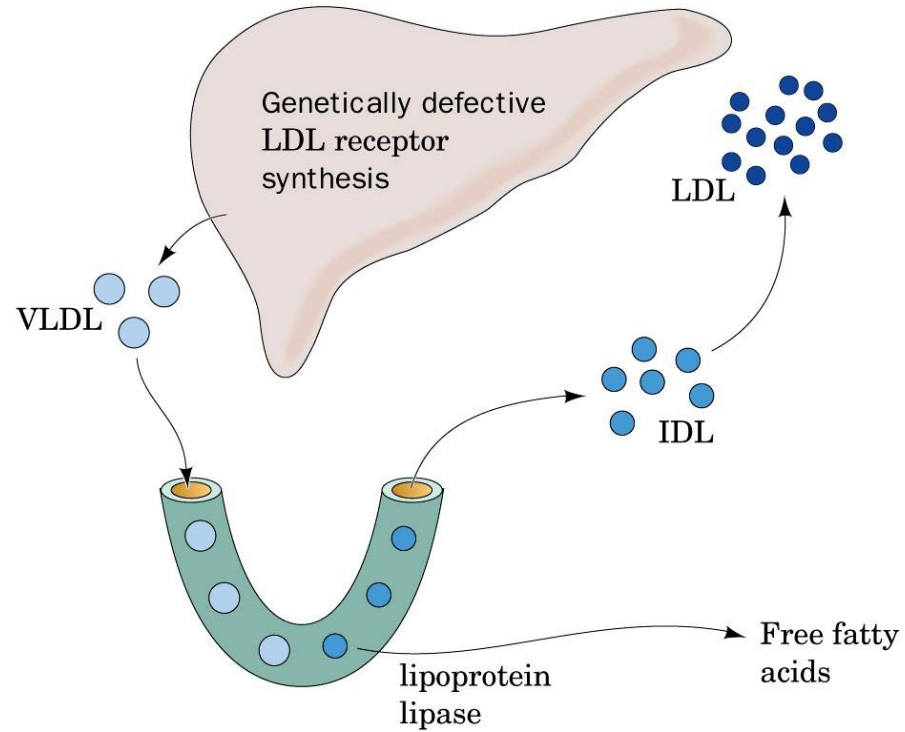


Figure 25-59b

Control of plasma LDL production and uptake by liver LDL receptors. (b) Familial hypercholesterolemia (FH).

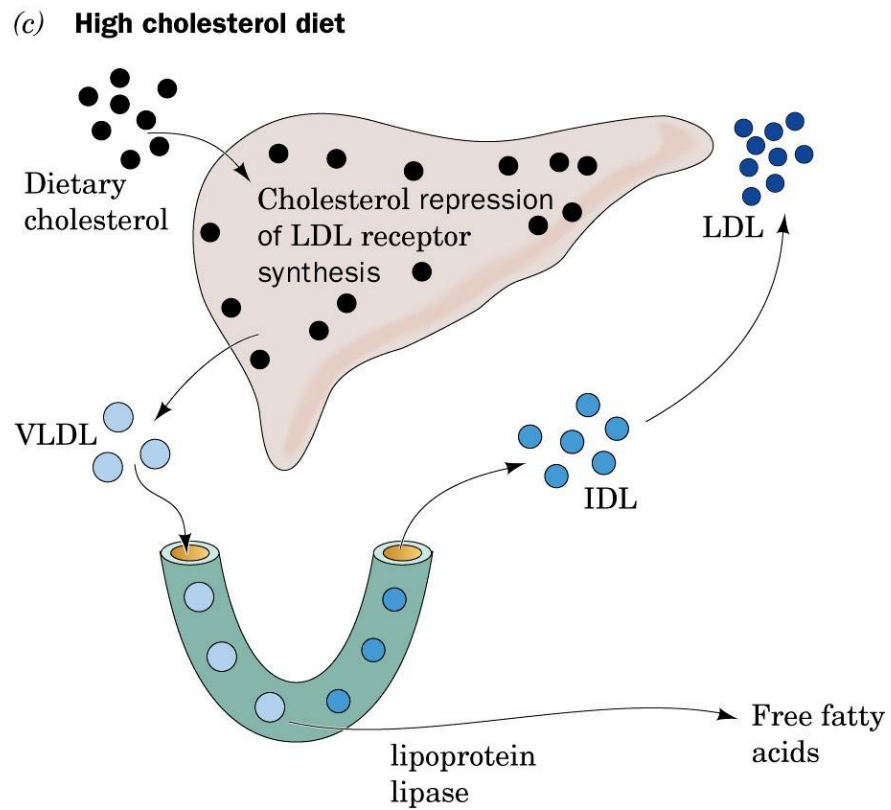


Figure 25-59c

Control of plasma LDL production and uptake by liver LDL receptors. (c) Long-term high-cholesterol diet.