

Metabolizmus mastných kyselín. Transport triacylglycerolov a cholesterolu v krvi.

8.12.2015

Stupeň 1

lipidy

↓
mastné kyseliny
a glycerol

sacharidy

↓
glukóza a iné
monosacharidy

bielkoviny

↓
aminokyseliny

Stupeň 2

β-oxidácia
mastných kyselín

glykolýza

rozklad
aminokyselín

Stupeň 3

acetyl-CoA

citrátový
cyklus

NH₄⁺

CO₂

FADH₂

NADH

Stupeň 4

ATP

ADP + P_i

dýchací reťazec

O₂

H₂O

Výhody ukladania energetických zásob do tukov

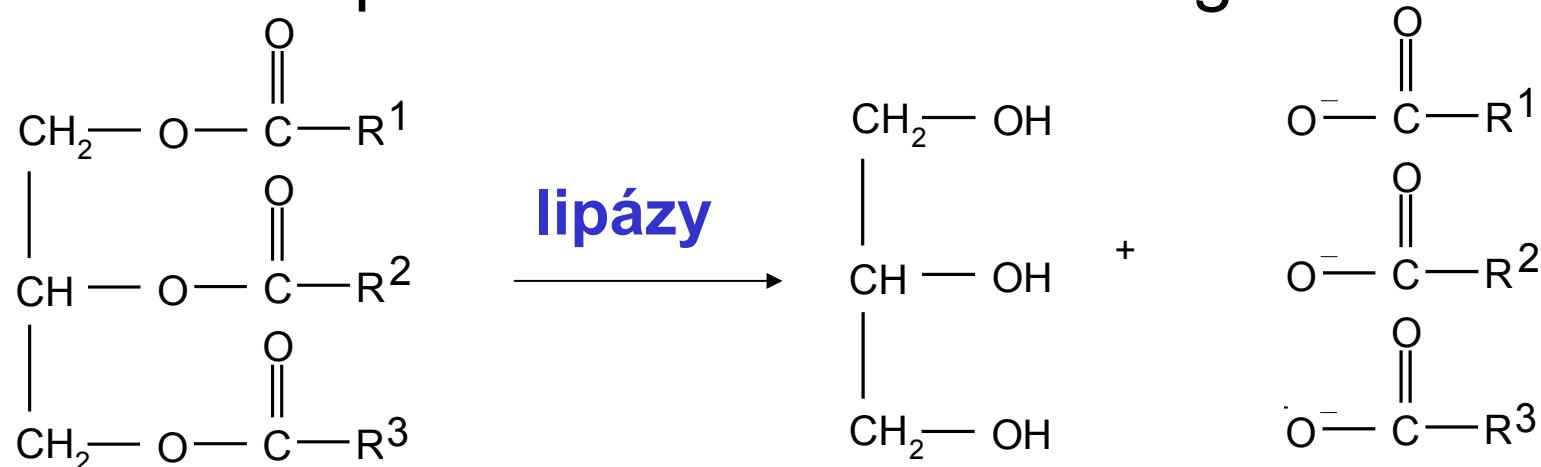
- Najredukovanejšia forma uhlíka
- Nerozpustnosť vo vode (hydrofobicita)
- Chemická inertnosť



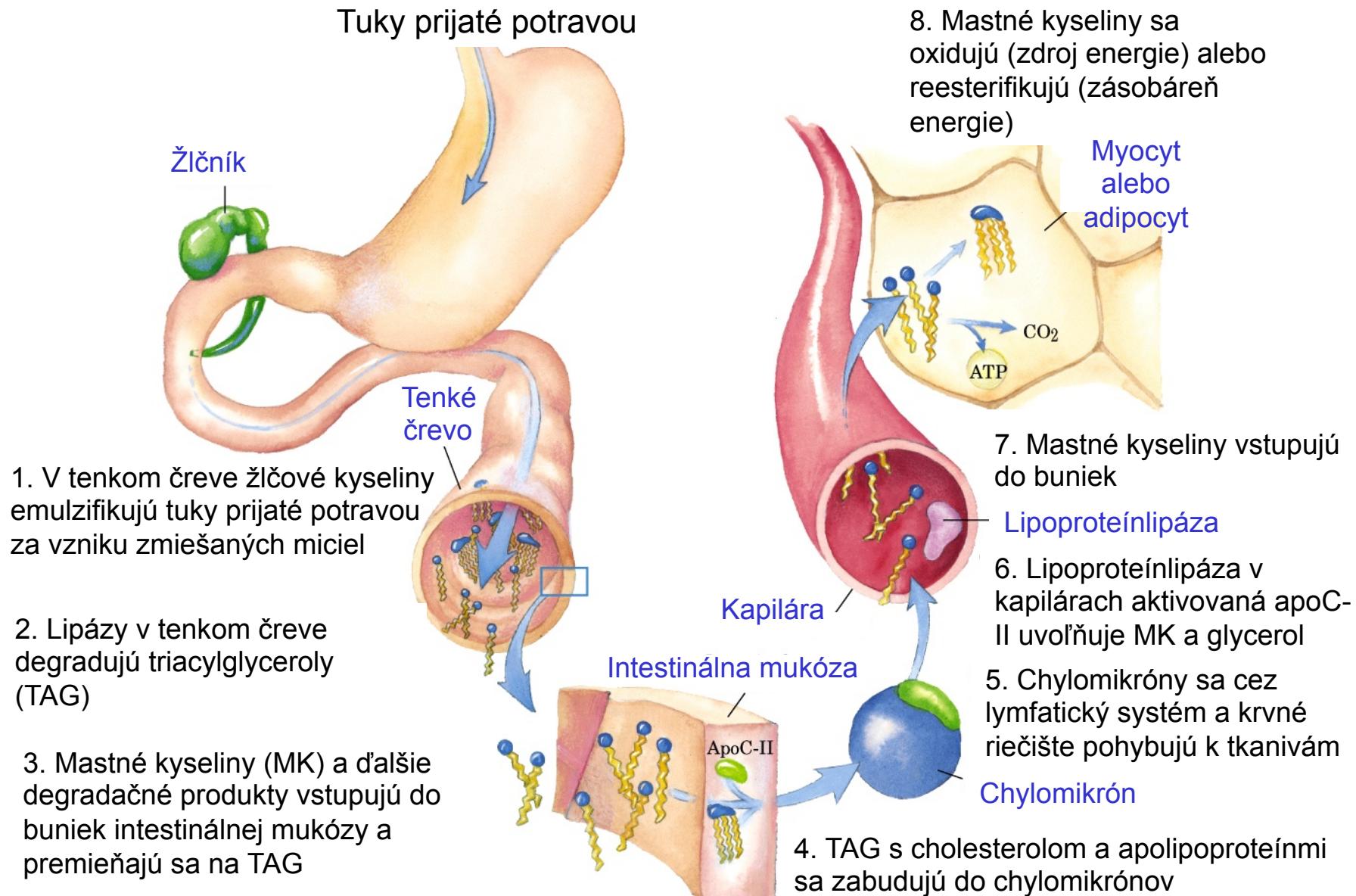
Problémy pri ich degradácii

Zdroje mastných kyselín pre bunky oxidujúce MK

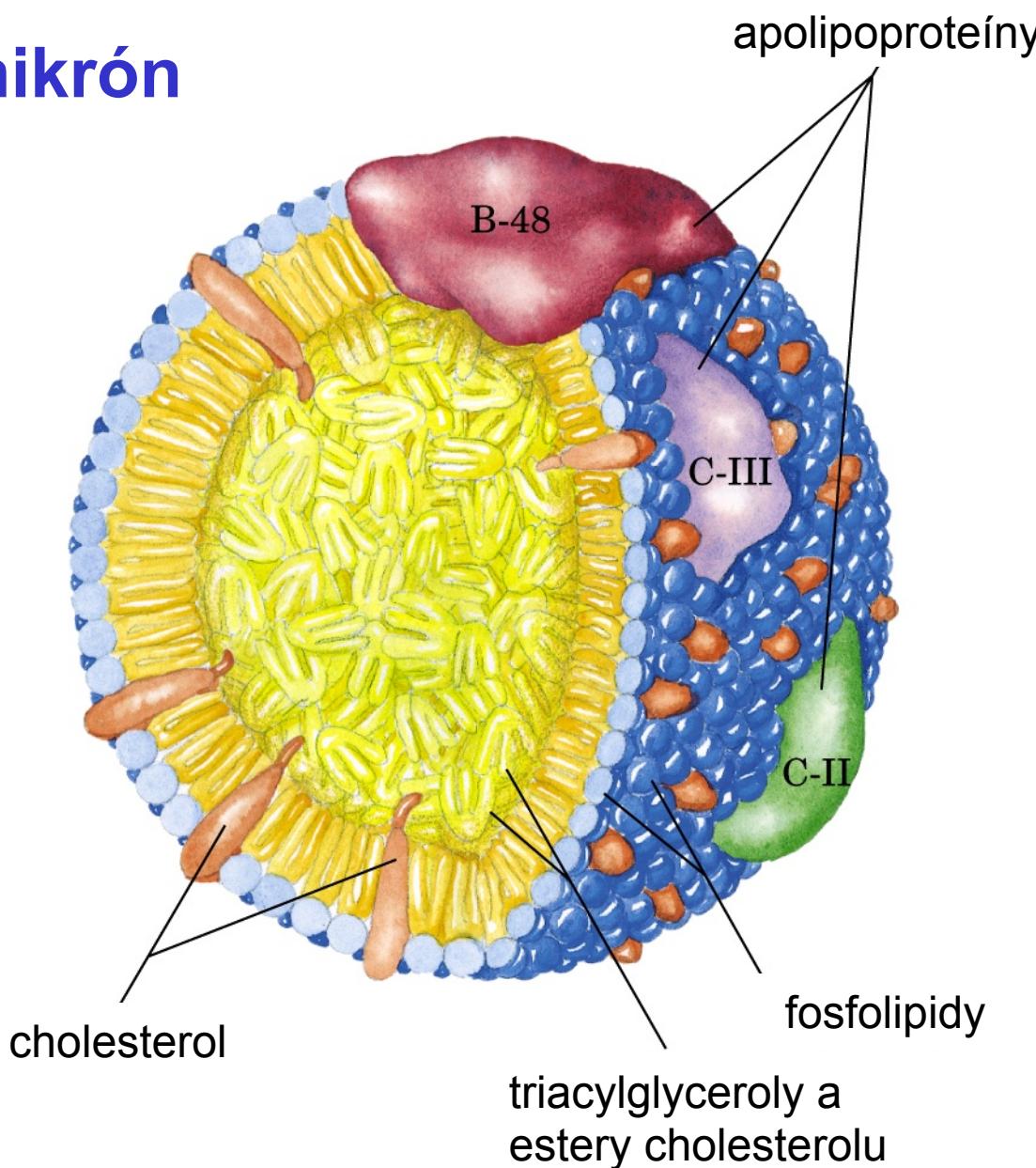
- Tuky zo stravy
- Tuky uskladnené v bunkách vo forme tukových kvapôčok
- Tuky syntetizované v jednom orgáne a následne prenesené do druhého orgánu



Trávenie tukov



Chylomikrón



Mobilizácia triacylglycerolov uskladnených v adipóznom tkanive

Nízka hladina glukózy v krvi spustí mobilizáciu TAG prostredníctvom pôsobenia hormónov **adrenálínu** alebo **glukagonu**, ktoré aktivujú adenylátcyklázu v adipocyte.

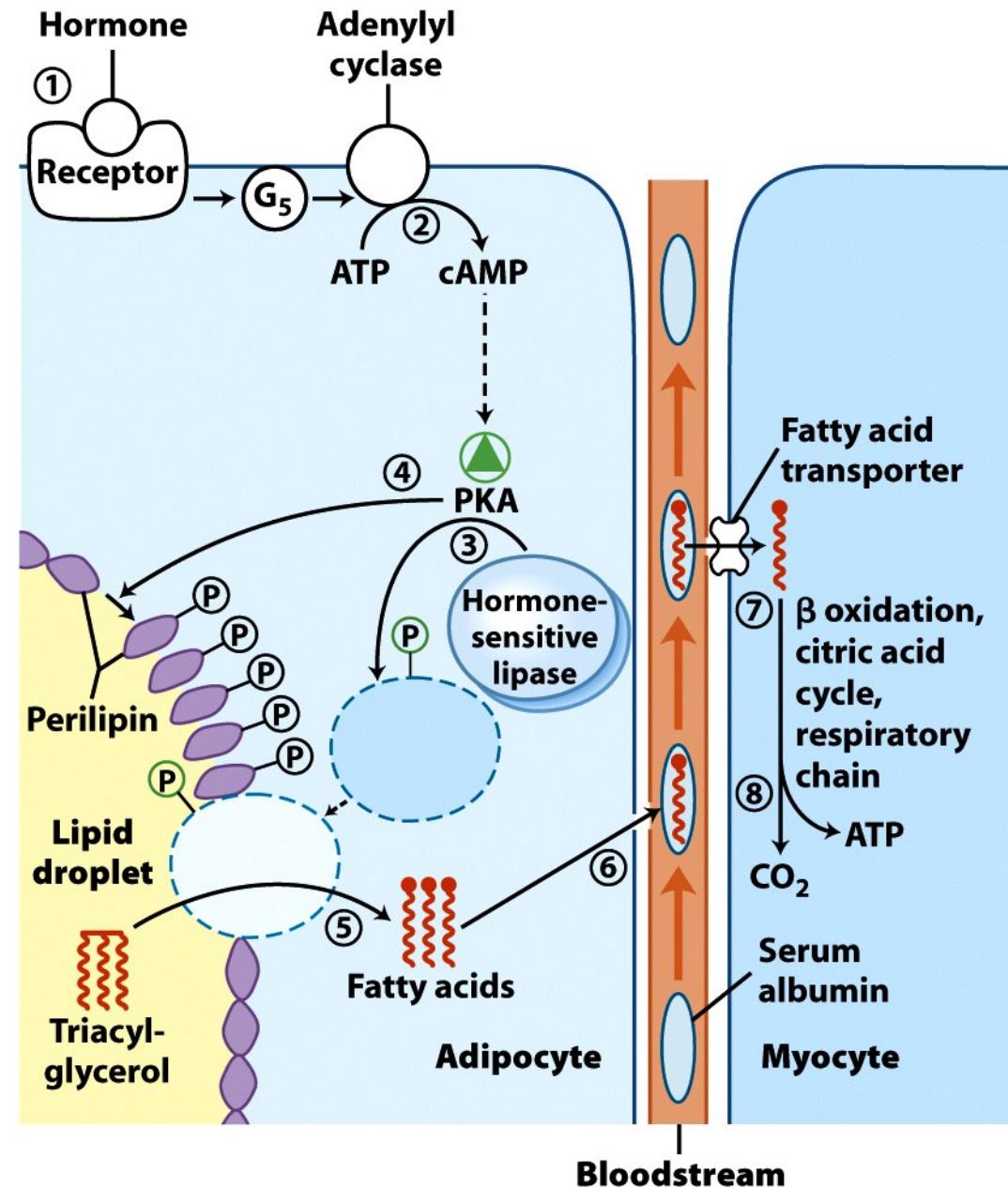


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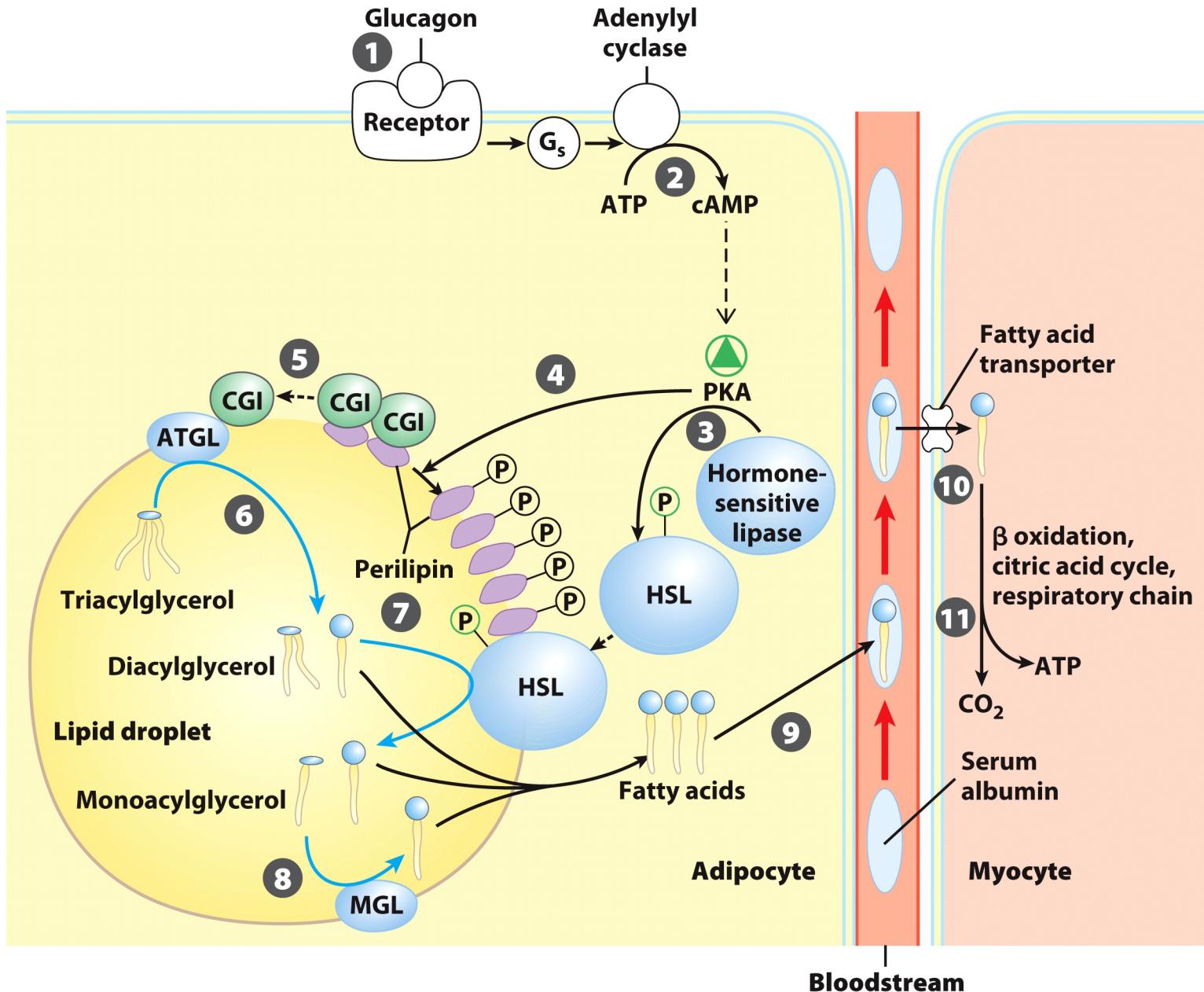


Figure 17-3

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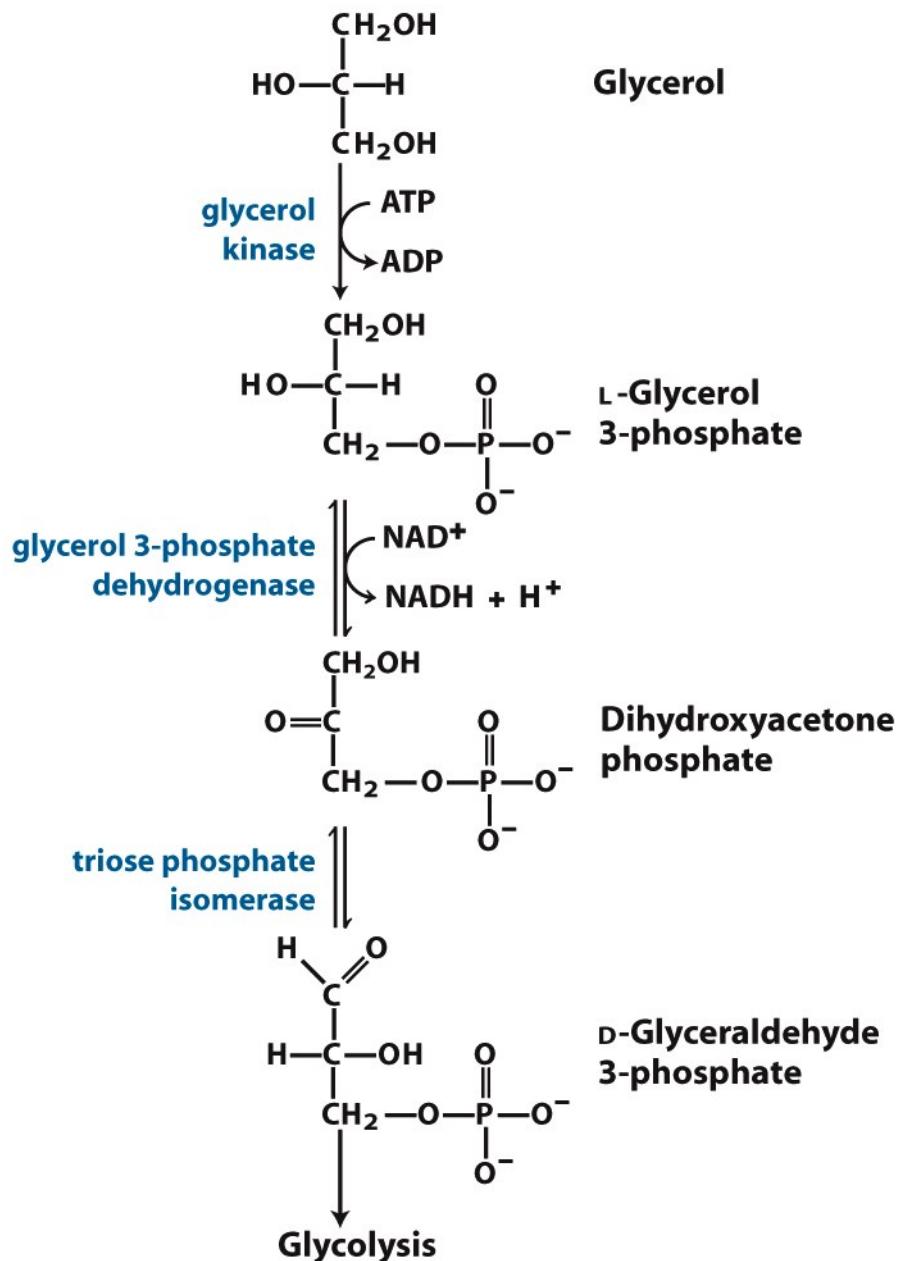


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Oxidácia mastných kyselín – β -oxidácia

- 1. Aktivácia mastnej kyseliny
- 2. Transport do mitochondrie
- 3. Reakcie β -oxidácie

1. Aktivácia mastných kyselín

AcylCoA syntetáza:



Anorganická pyrofosfátáza:

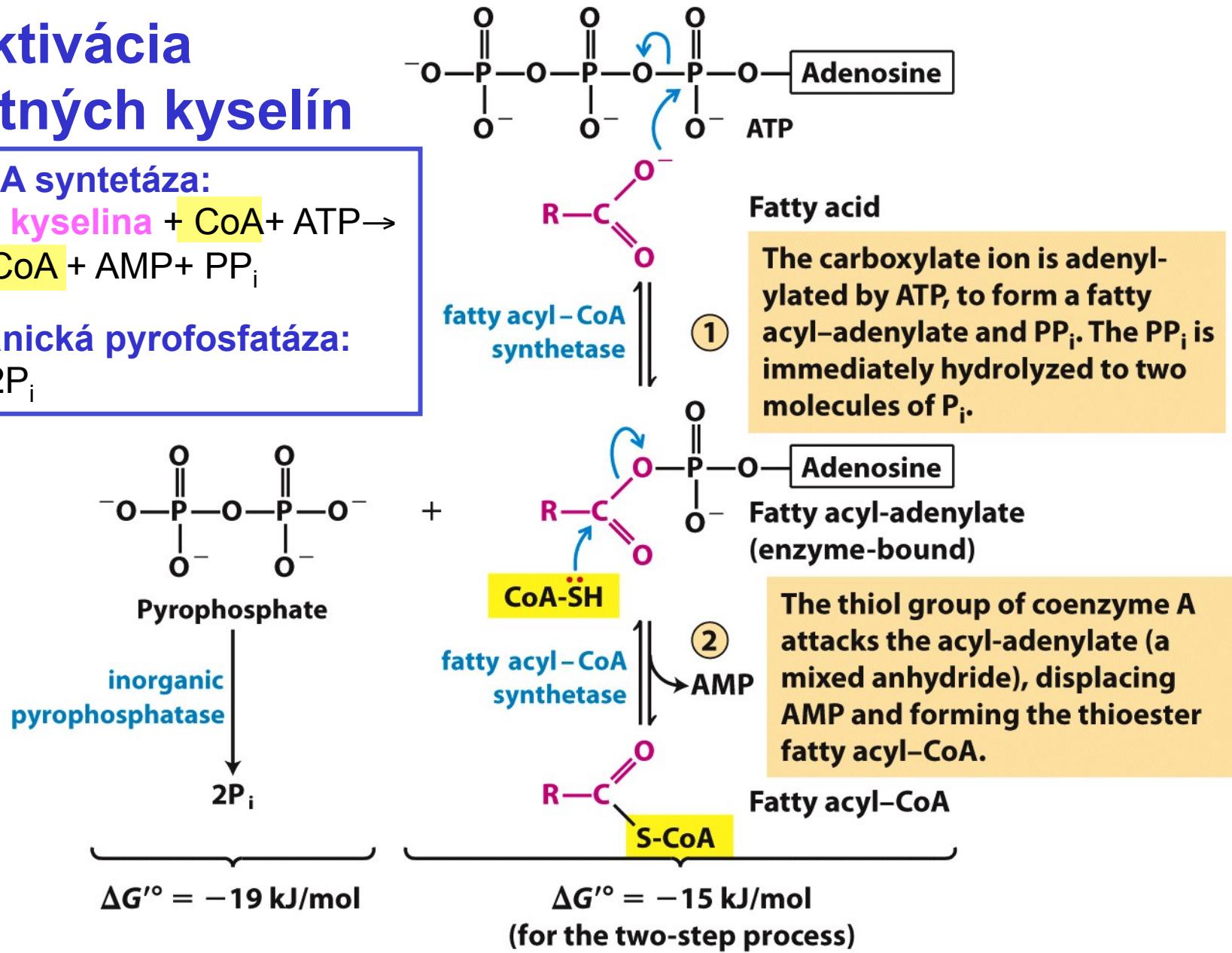
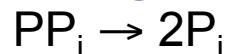


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2. Transport mastných kyselín do matrix mitochondrií cez acylkarnitín-karnitínový prenášač

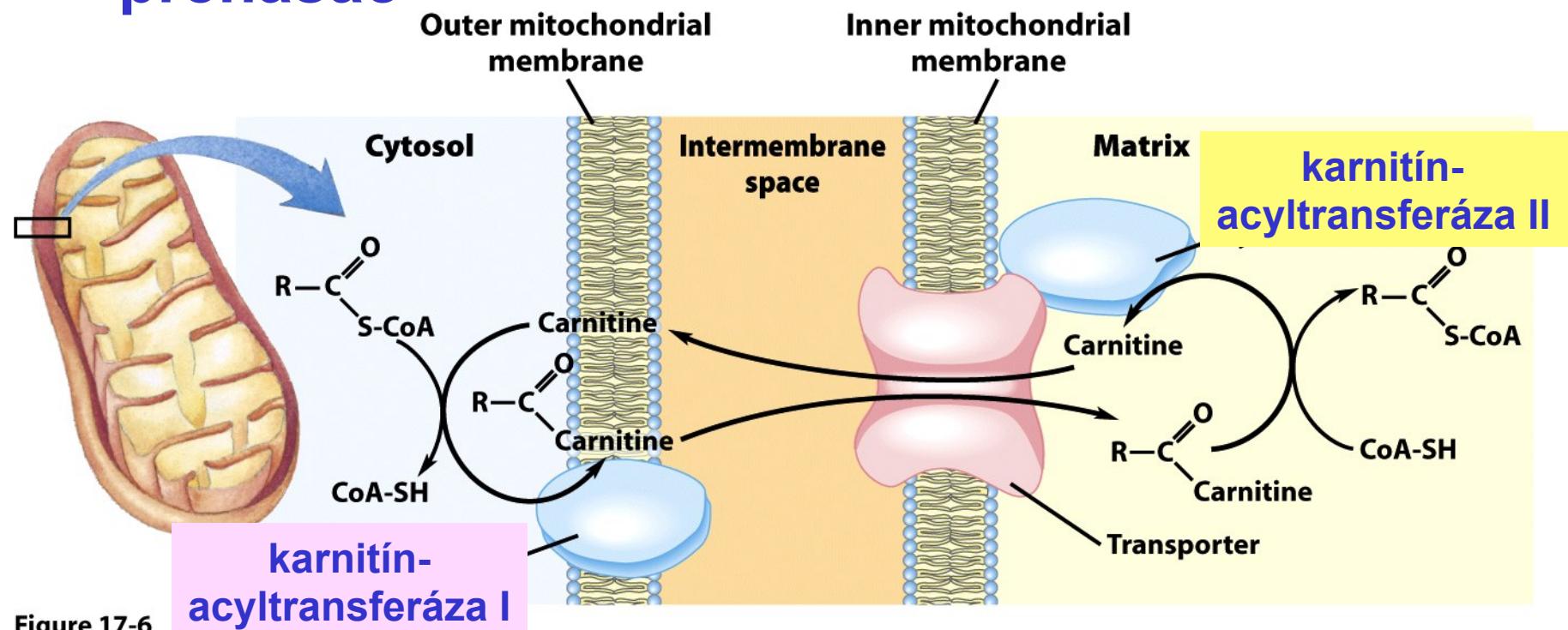
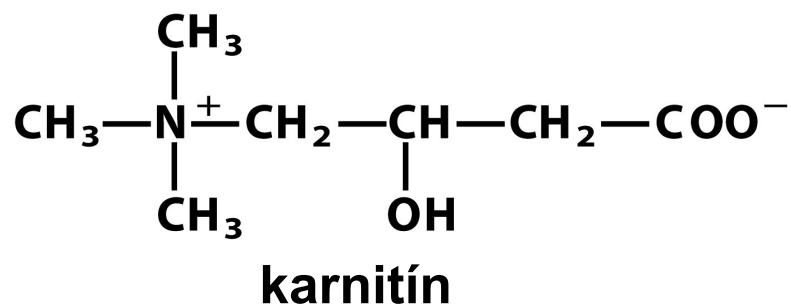


Figure 17-6

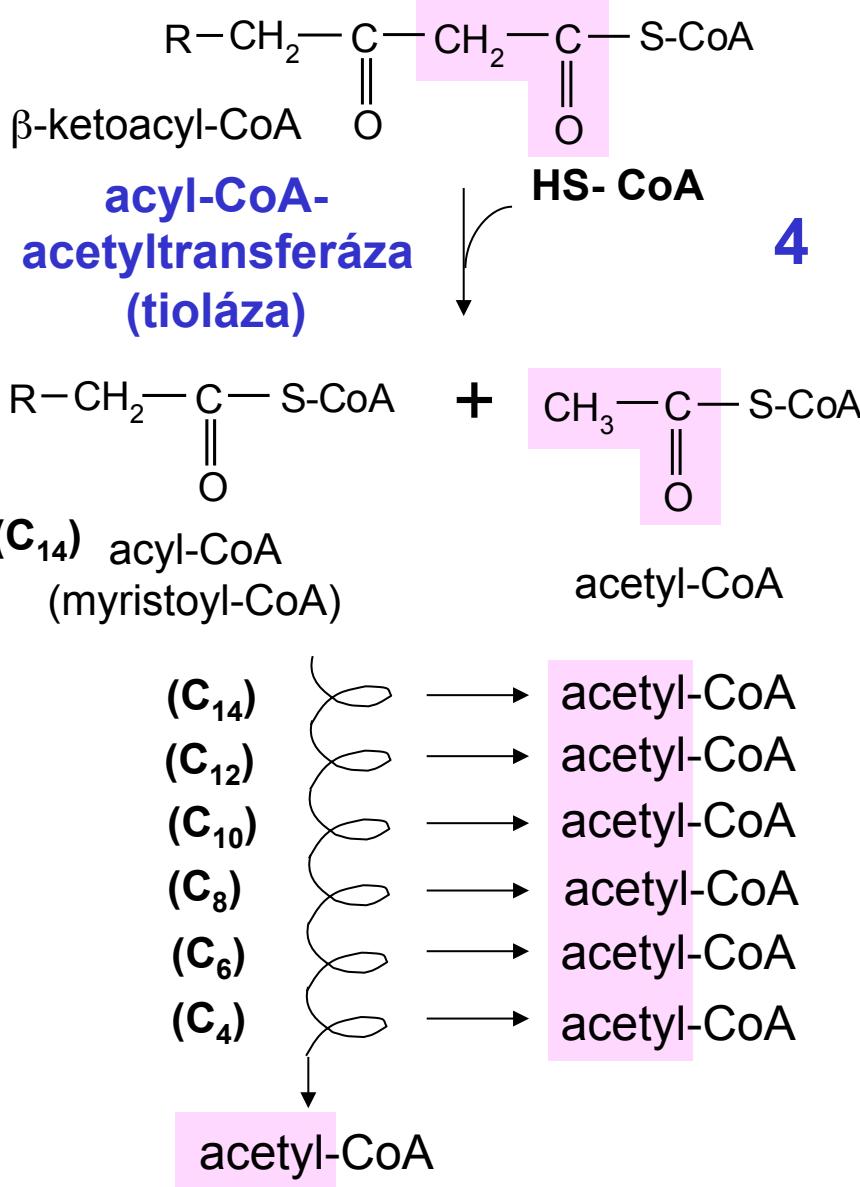
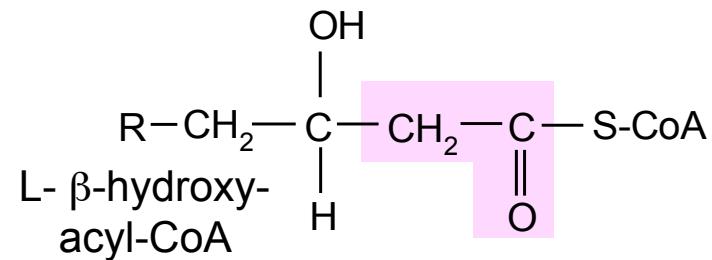
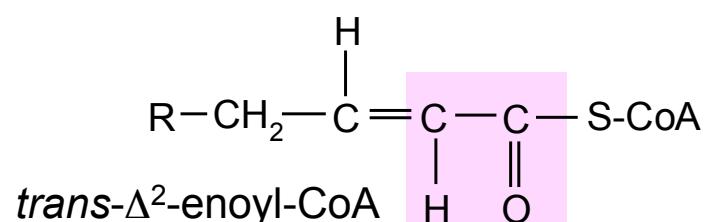
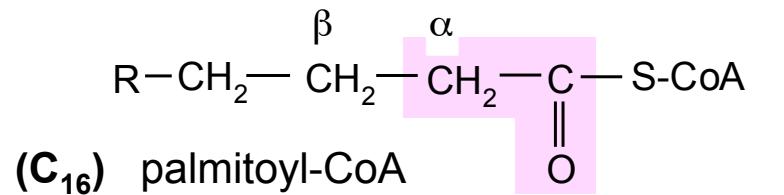
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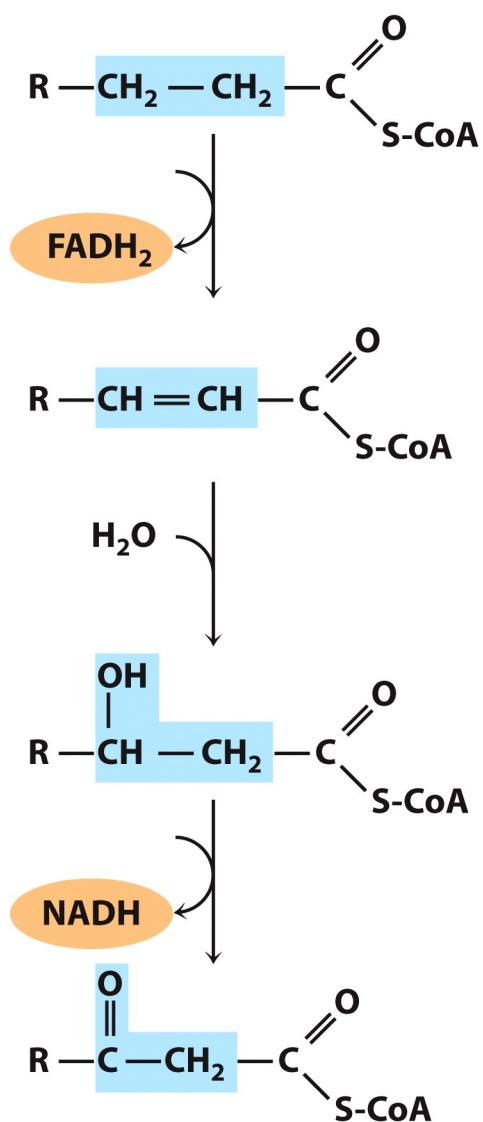
3. Reakcie β -oxidácie

- Postupnosť 4 enzymovo-katalyzovaných reakcií, ktorými sa odštepujú dva uhlíkové zvyšky (vo forme acetyl-CoA) z karboxylového konca mastnej kyseliny

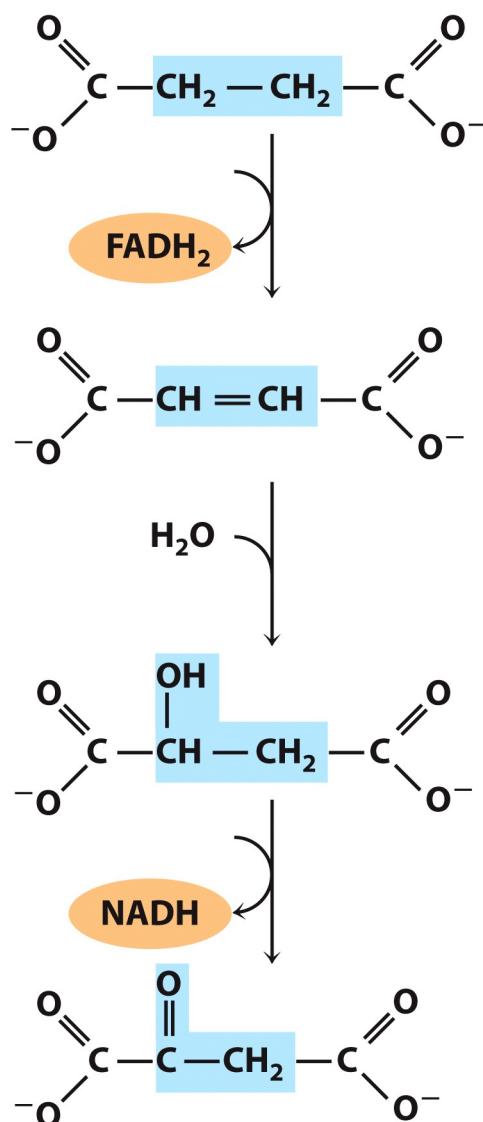


Reakcie 1,2,3 – podobnosť s reakciami KC!

β Oxidation



Citric acid cycle



Oxidation of isoleucine (leucine, valine)

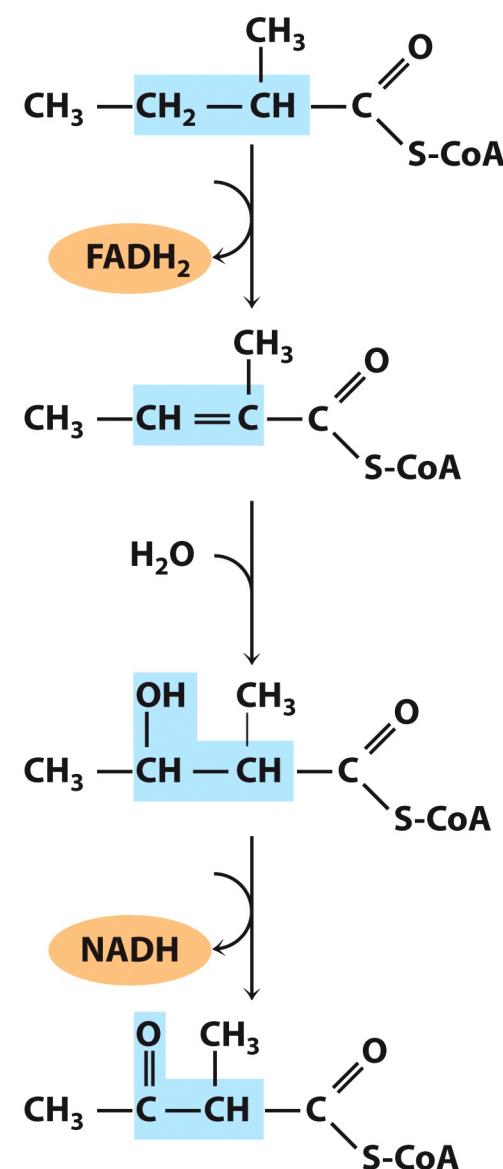


Figure 17-9

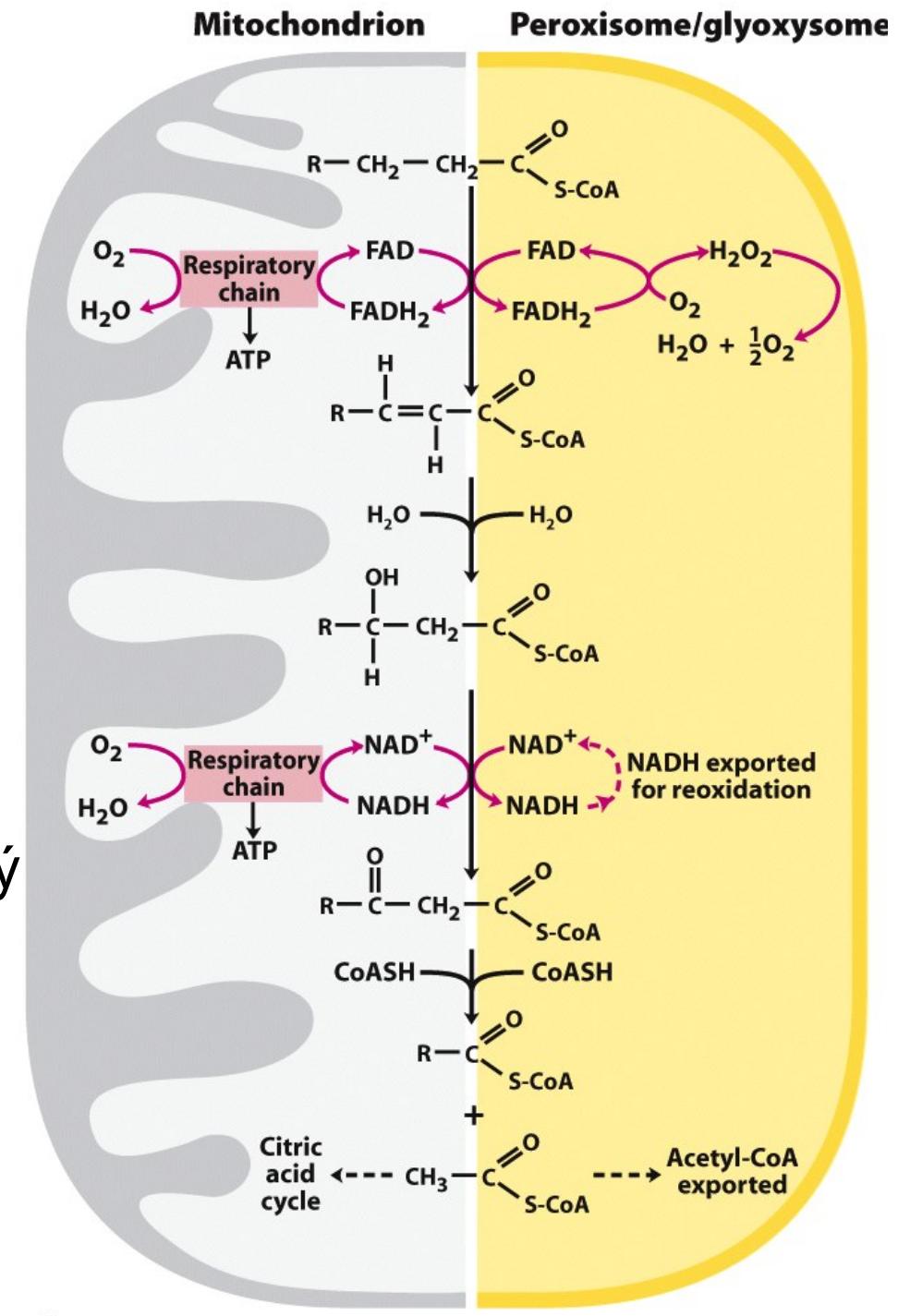
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Výťažok ATP pri oxidácii 1 molekuly palmitoyl-CoA na CO₂ a H₂O

Enzým katalyzujúci oxidačný krok	Počet NADH a FADH ₂	Počet ATP
Acyl-CoA-dehydrogenáza	7 FADH ₂	10,5
β-hydroxyacyl-CoA-dehydrogenáza	7 NADH	17,5
Izocitrátdehydrogenáza	8 NADH	20
α-ketoglutarátdehydrogenáza	8 NADH	20
(Sukcínyl-CoA syntetáza		8)
Sukcinátdehydrogenáza	8 FADH ₂	12
Malátdehydrogenáza	8 NADH	20
Spolu		108

β -oxidácia v peroxizómoch

- V živočíchoch aj rastlinách
- Rozdielny 1. krok katalyzuje:
Acyl-CoA oxidáza
- Kataláza odstraňuje vzniknutý H_2O_2
- Degraduje aj veľmi dlhé a rozvetvené masné kyseliny!



Ketolátky-

špeciálny zdroj energie pre určité tkanivá

- Niektoré Acetyl-CoA vzniknuté oxidáciou MK sa v mitochondriách pečene premieňajú na ketolátky:
acetón, acetoacetát, β -hydroxybutyrát
- Sú palivom pre mozog, srdce a svaly
- Hlavný zdroj energie pre mozog počas hladovania
- Transportovateľná forma zvyškov mastných kyselín (acetylových skupín)

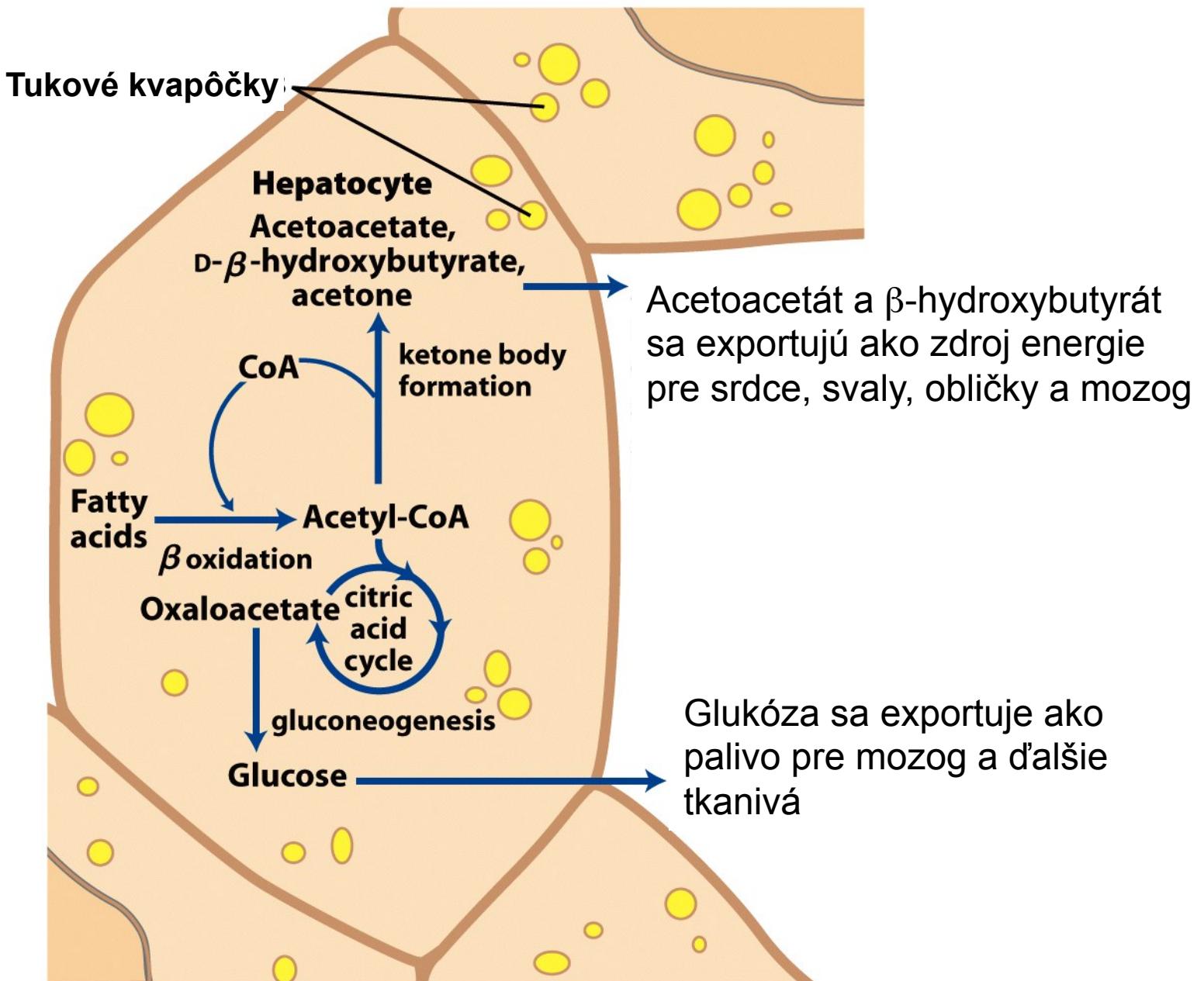
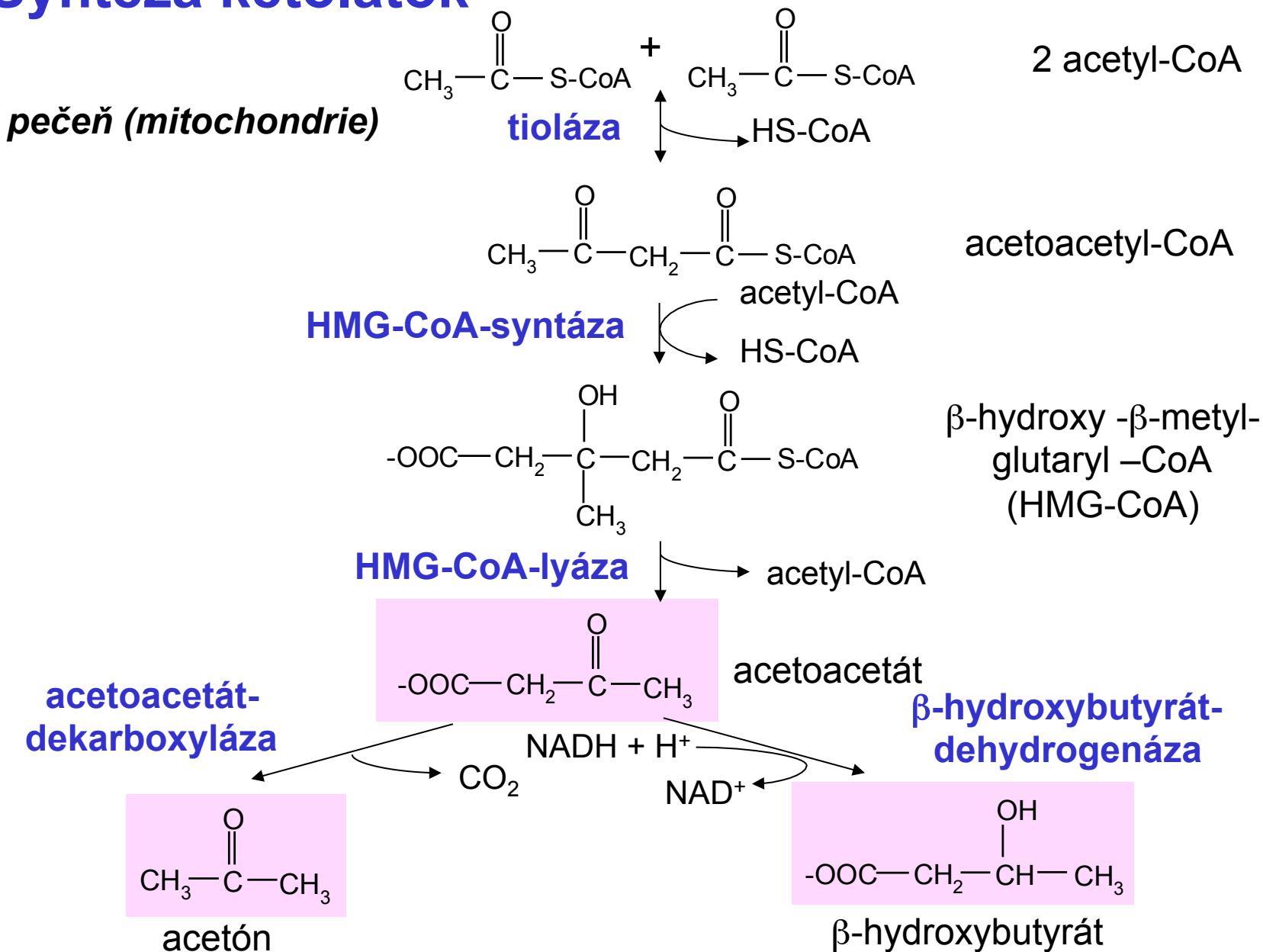


Figure 17-20

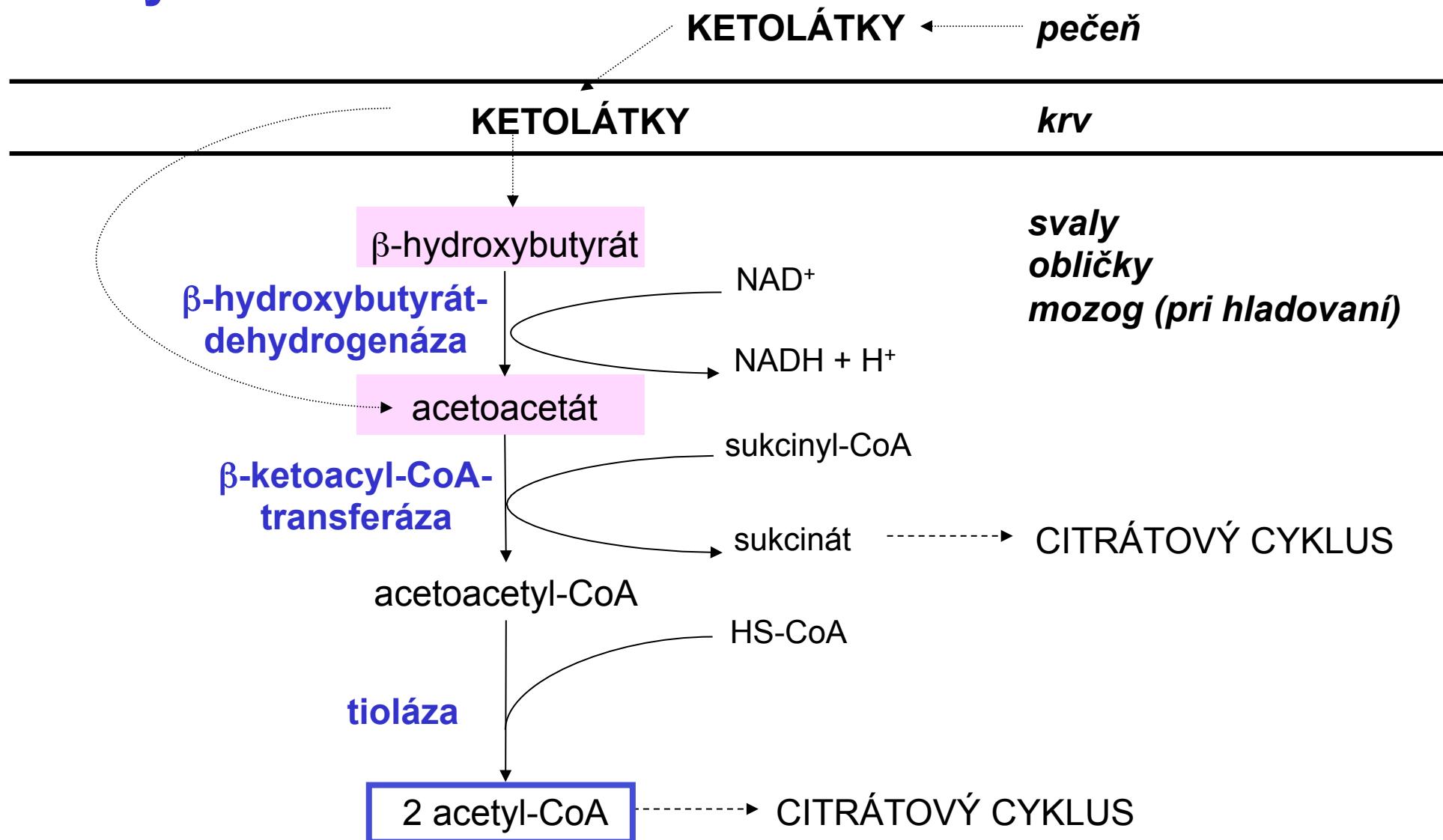
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Syntéza ketolátok



Využitie ketolátok





Triacylglyceroly ako zdroj glukózy v rastlinách

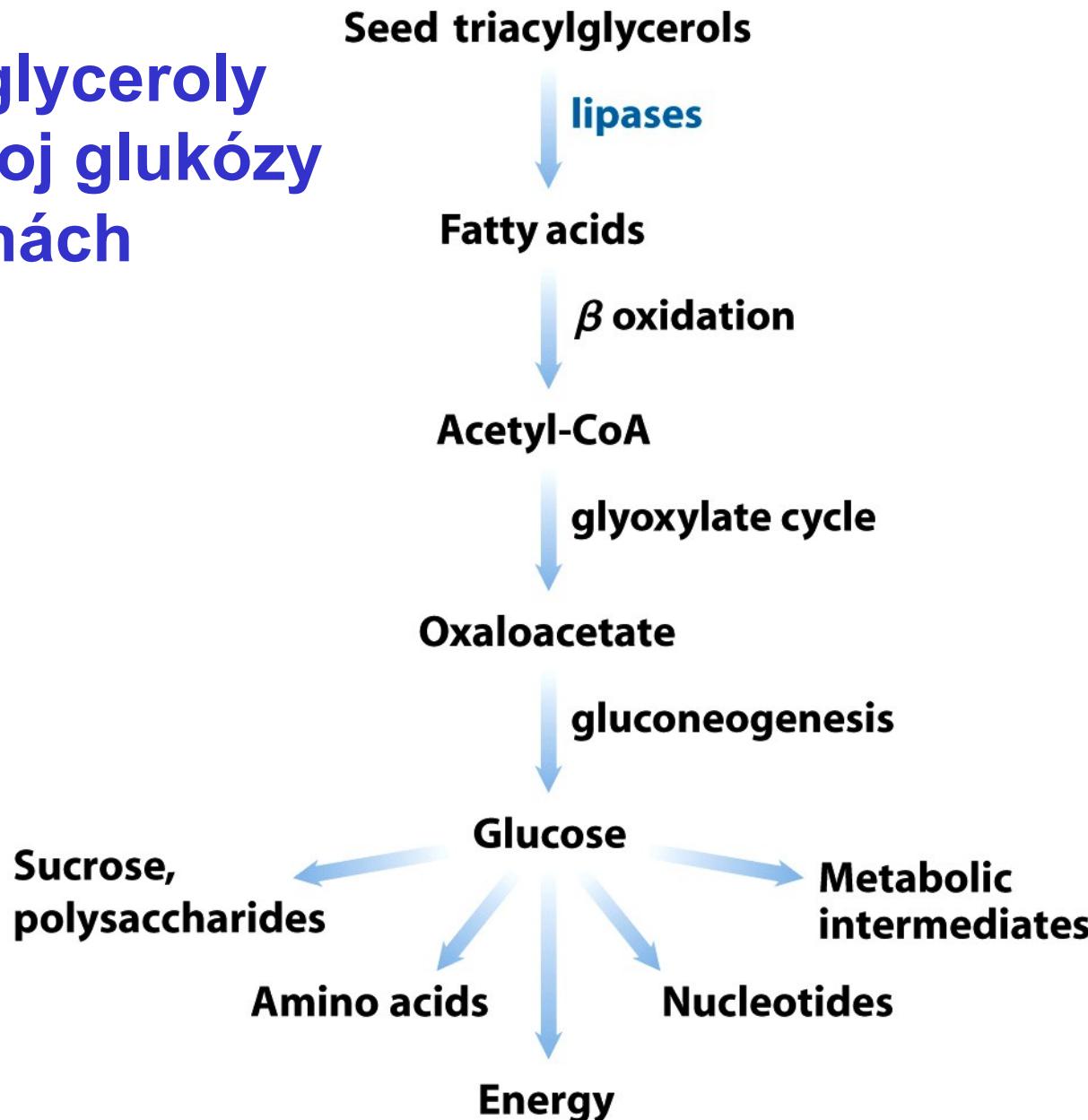


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Syntéza mastných kyselín

- β -oxidácia

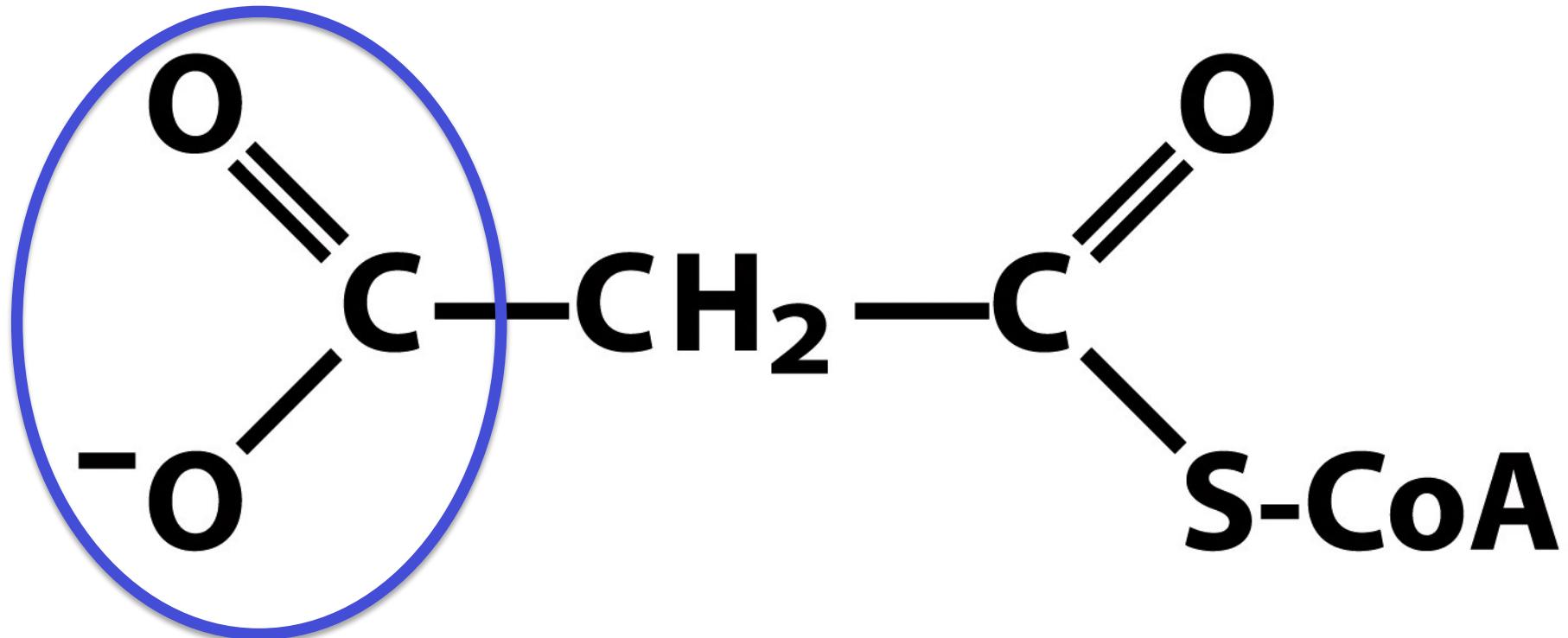
- 1. Oxidácia
- 2. Hydratácia
- 3. Oxidácia
- 4. Štiepenie



- Syntéza MK

- 4. Redukcia
- 3. Dehydratácia
- 2. Redukcia
- 1. Kondenzácia





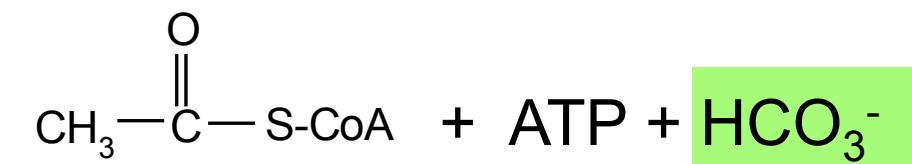
Malonyl-CoA

Unnumbered 21 p805

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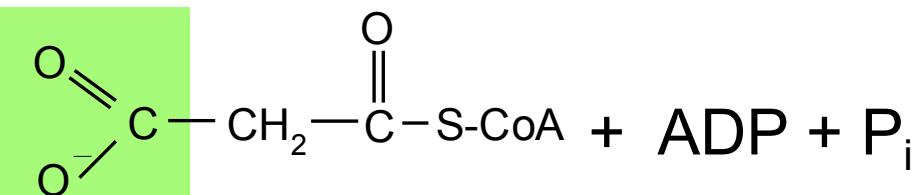
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Malonyl-CoA – donor C₂ zvyškov pre syntézu MK



acetyl-CoA

↓ **acetyl-CoA karboxyláza**



malonyl-CoA

Acetyl-CoA karboxyláza

má
3 podjednotky

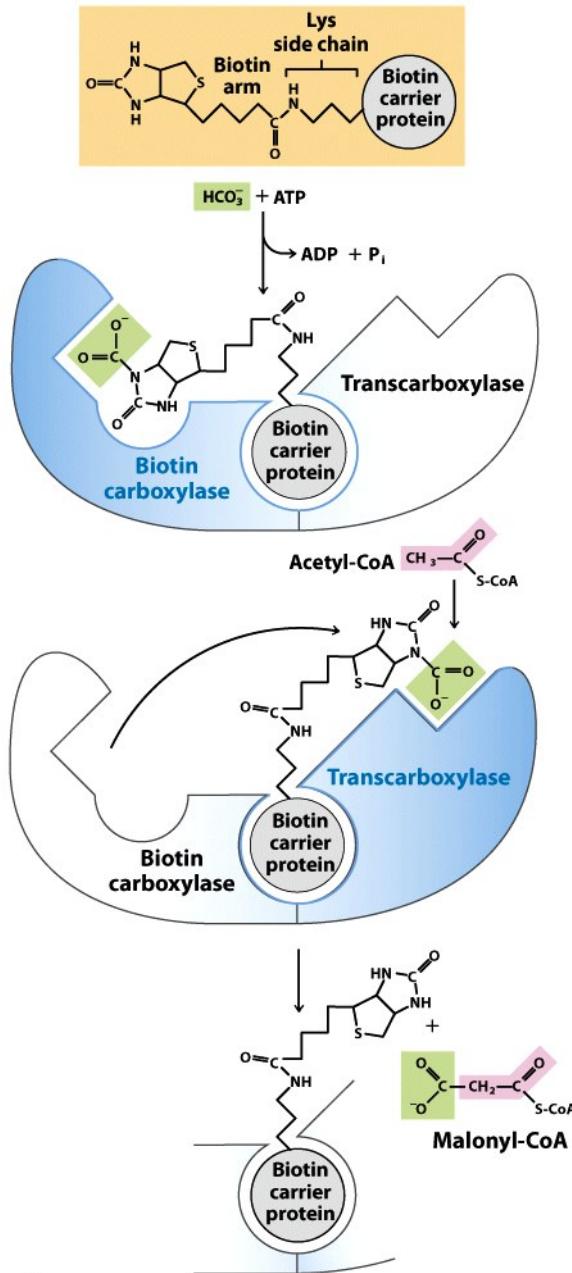


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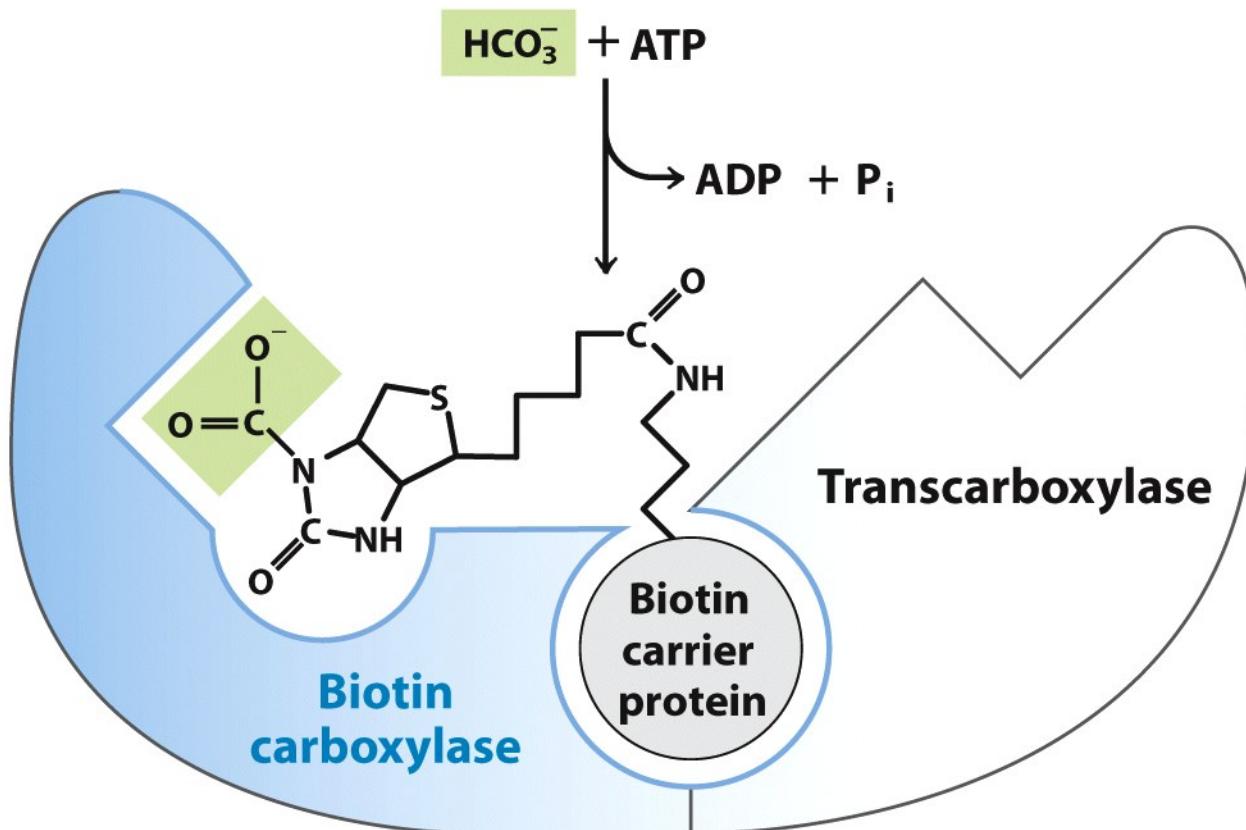
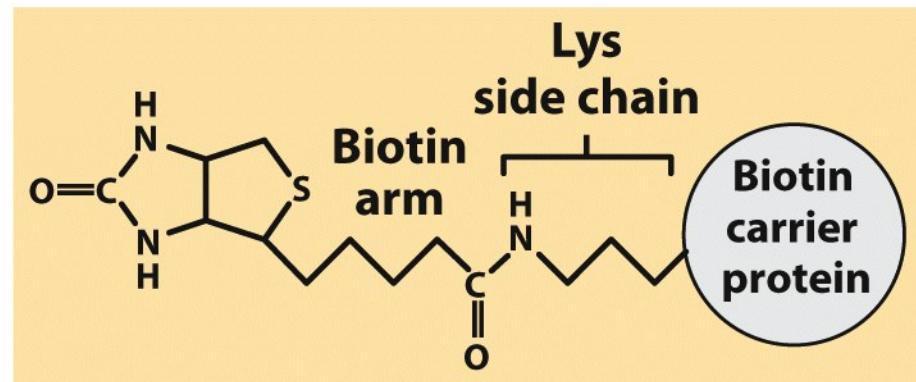


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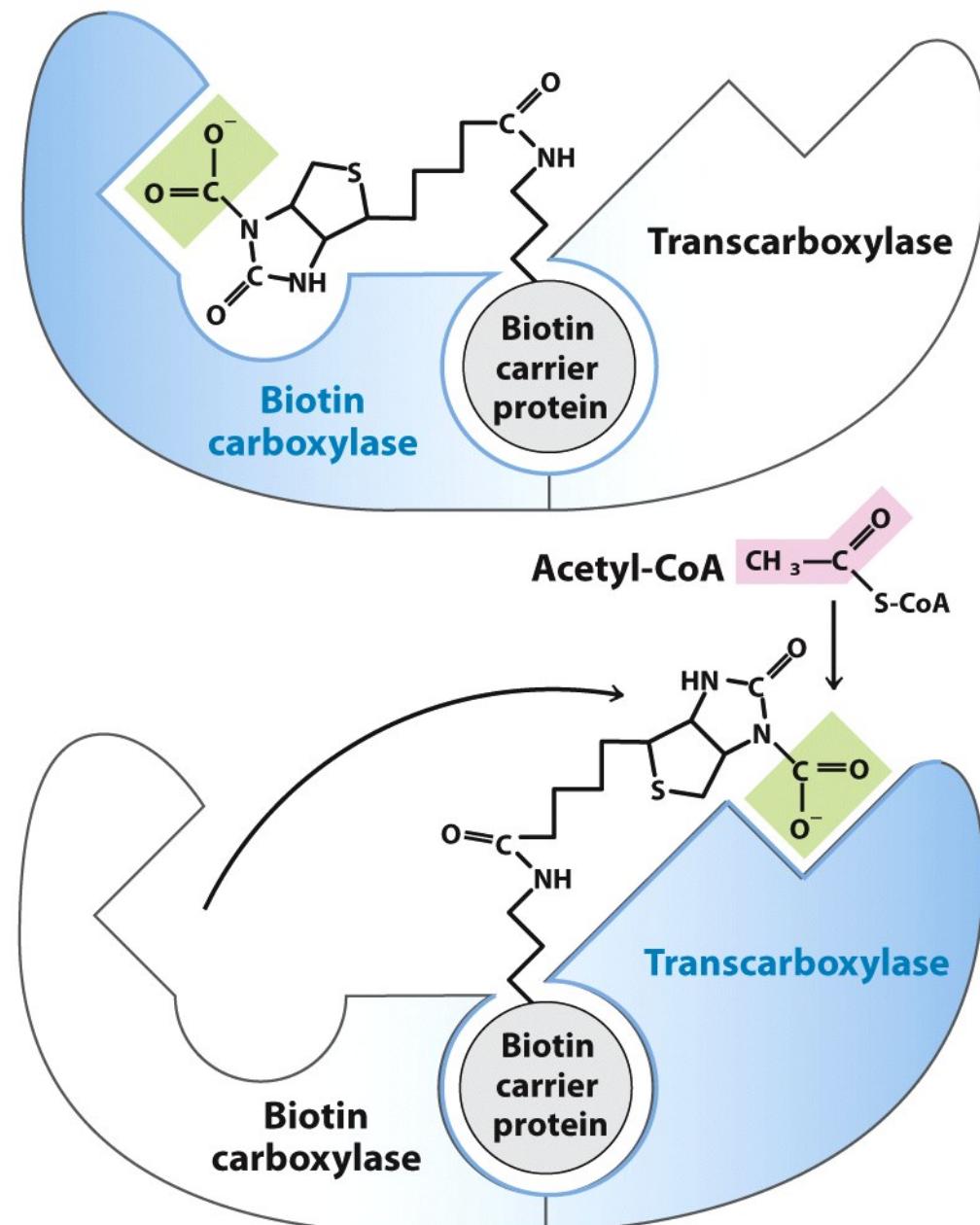


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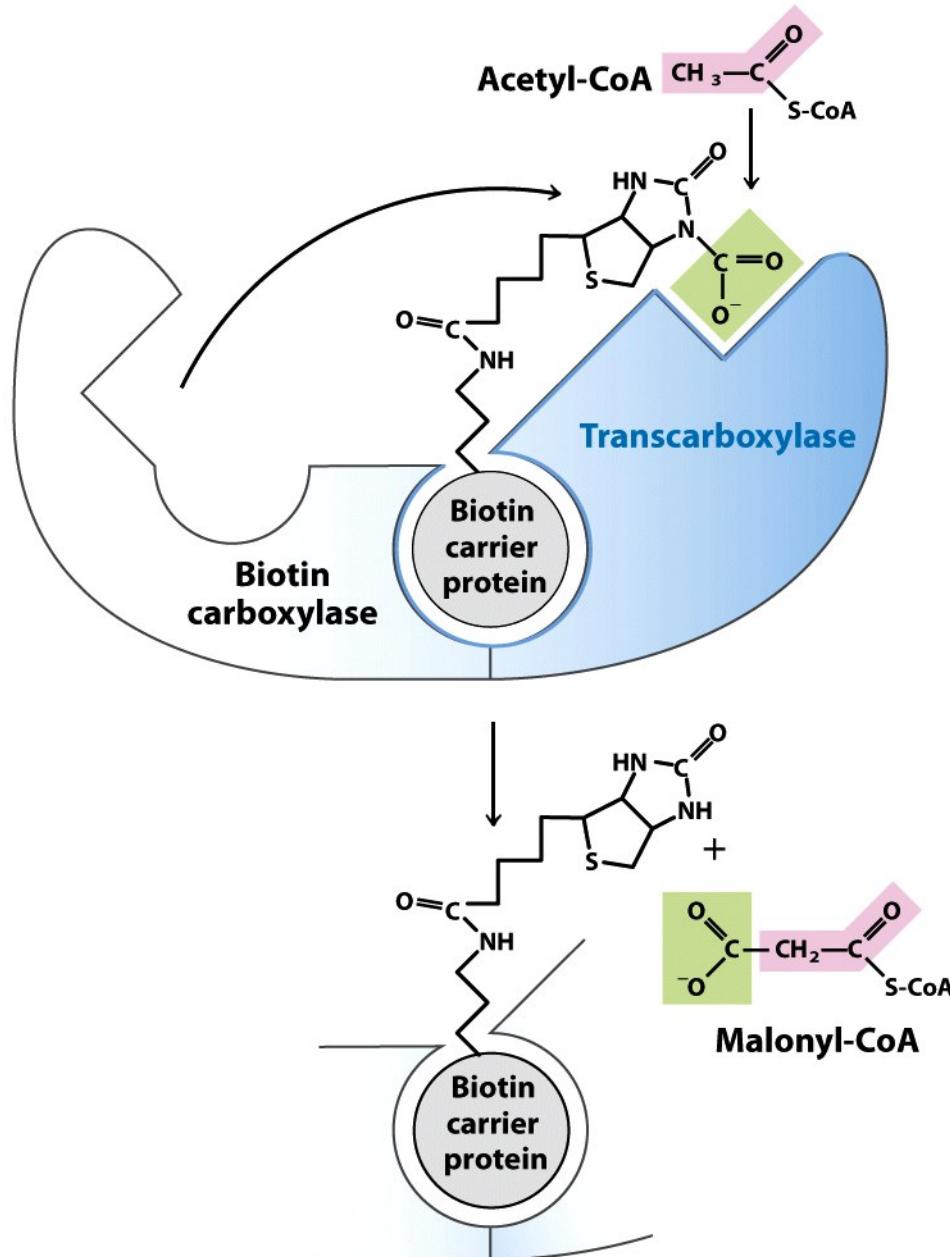
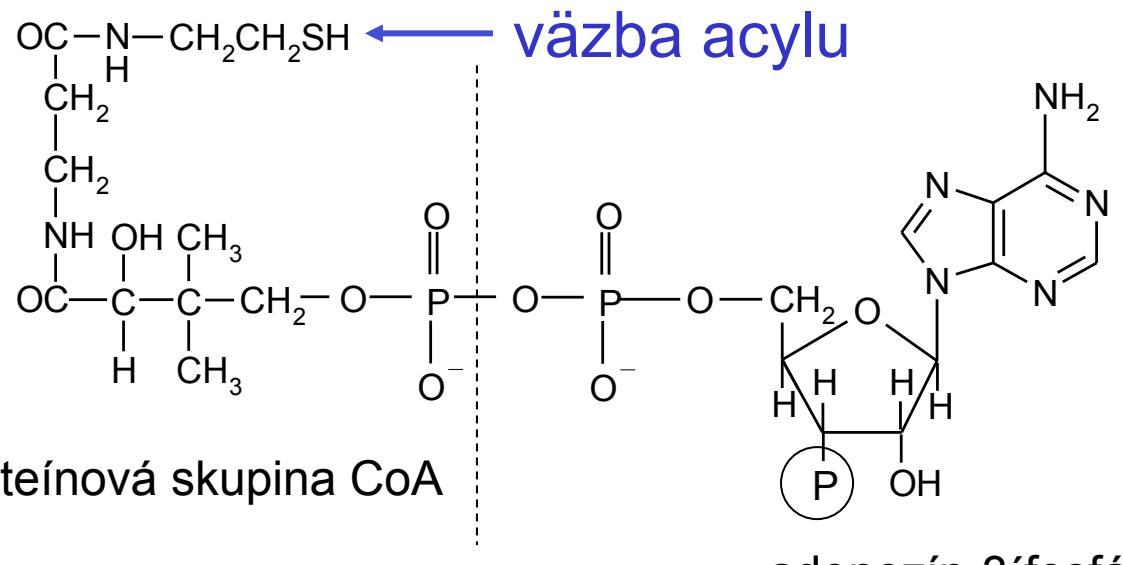
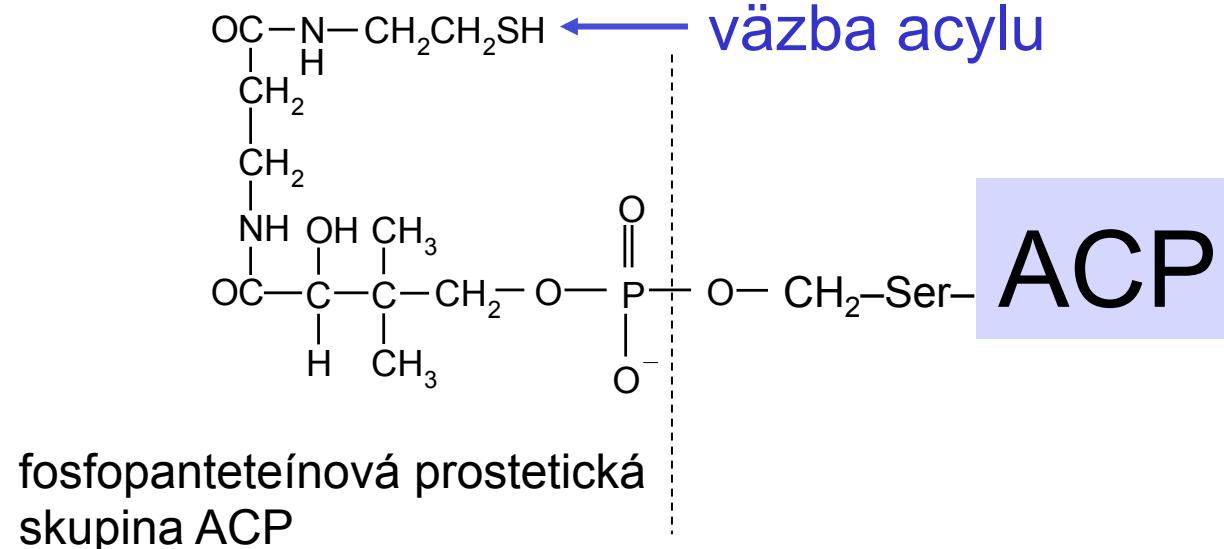


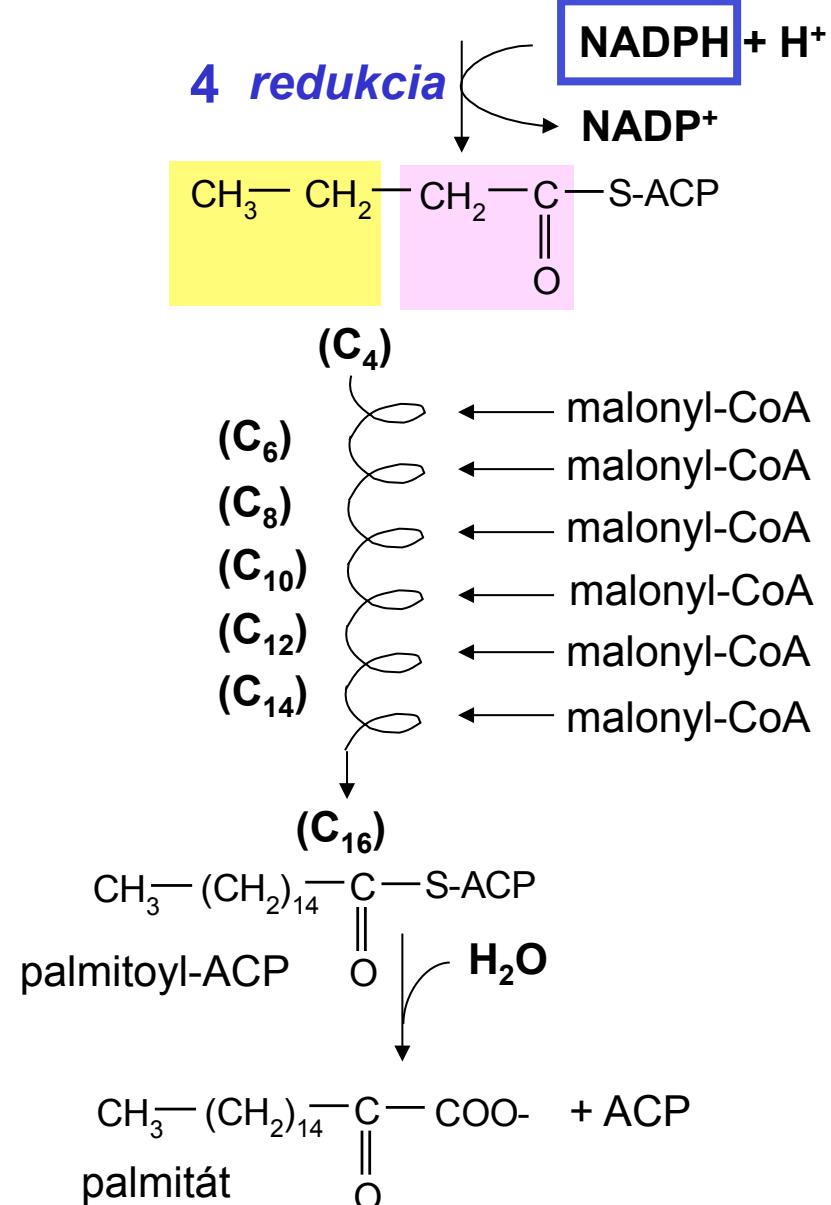
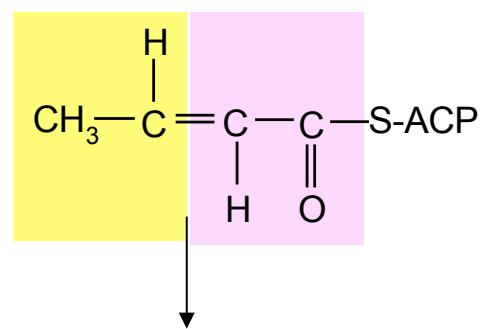
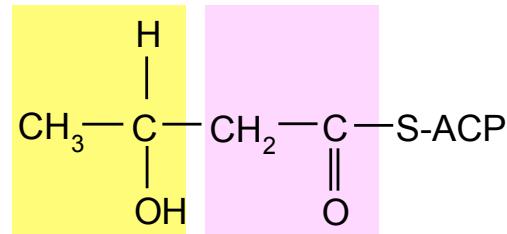
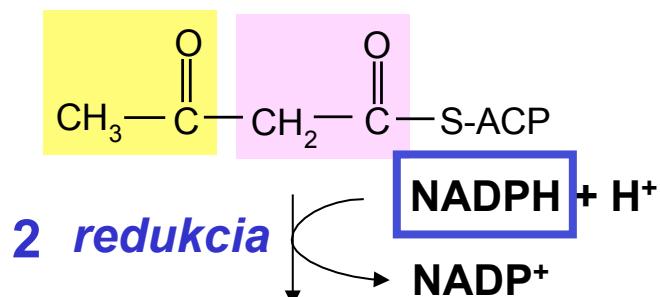
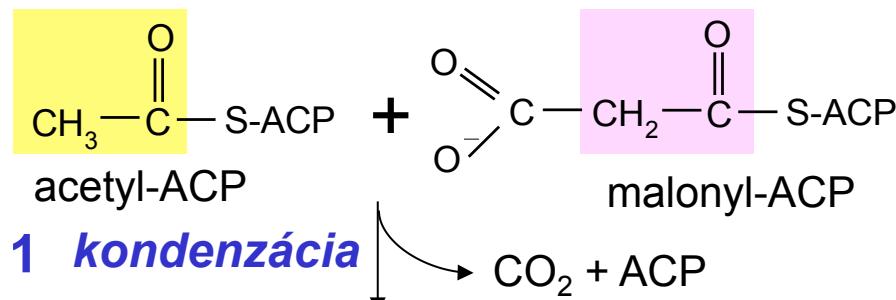
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Koenzým A (CoA)



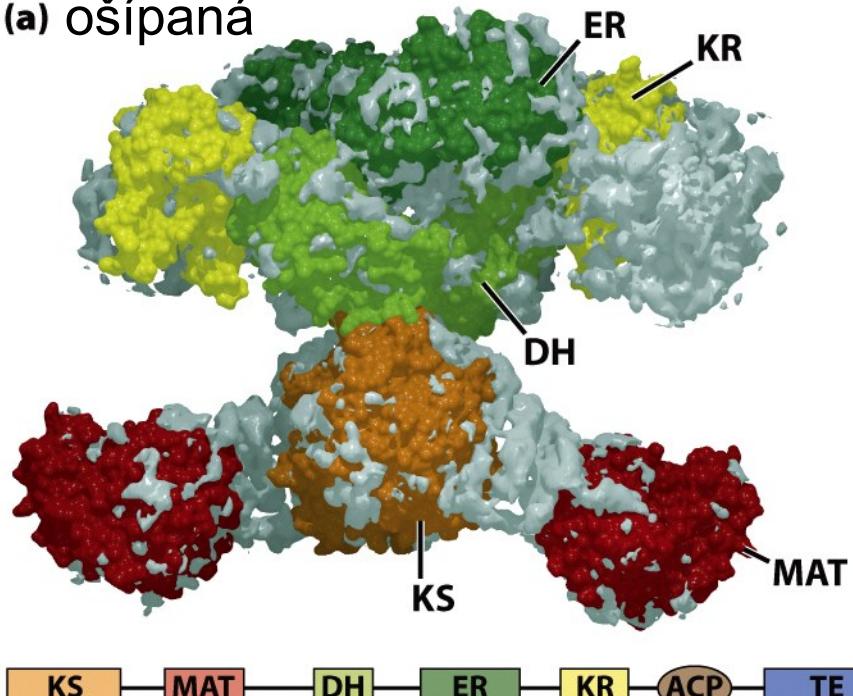
Proteín prenášajúci acyl (ACP)



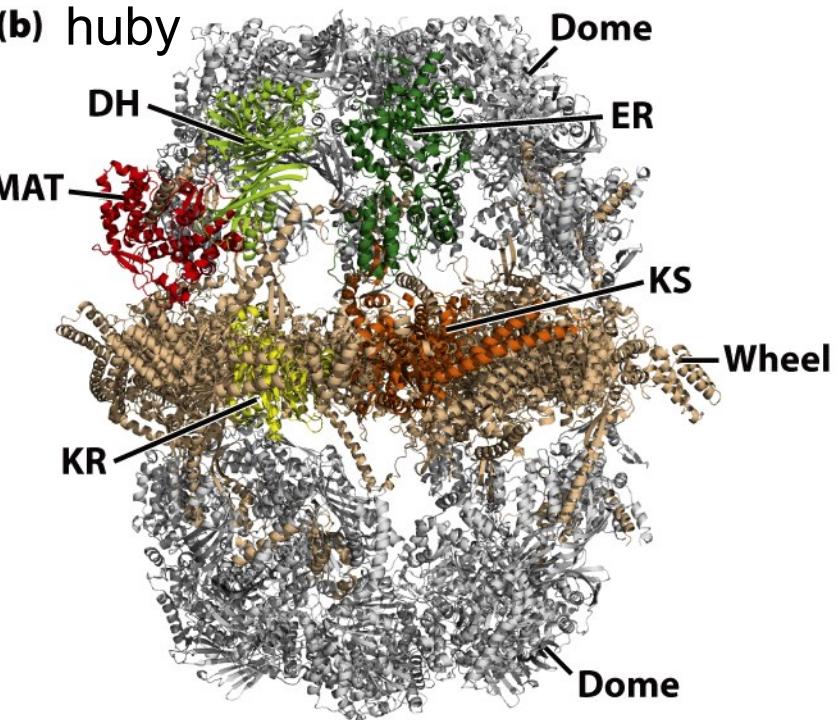


Syntáza mastných kyselín

(a) ošípaná



(b) huby



ACP- proteín prenášajúci acyl

MAT-malonyl/acetyl CoA – ACP transferáza

KS- β -ketoacyl-ACP syntáza

KR- β -ketoacyl-ACP reduktáza

DH - β -hydroxyacyl-ACP dehydratáza

ER-enoyl-ACP reduktáza

TE - tioesteráza

Baktérie, rastliny – 7 rôznych polypeptidov

Kvasinky – 2 rôzne polypeptidy

Stavovce – 1 polypeptid

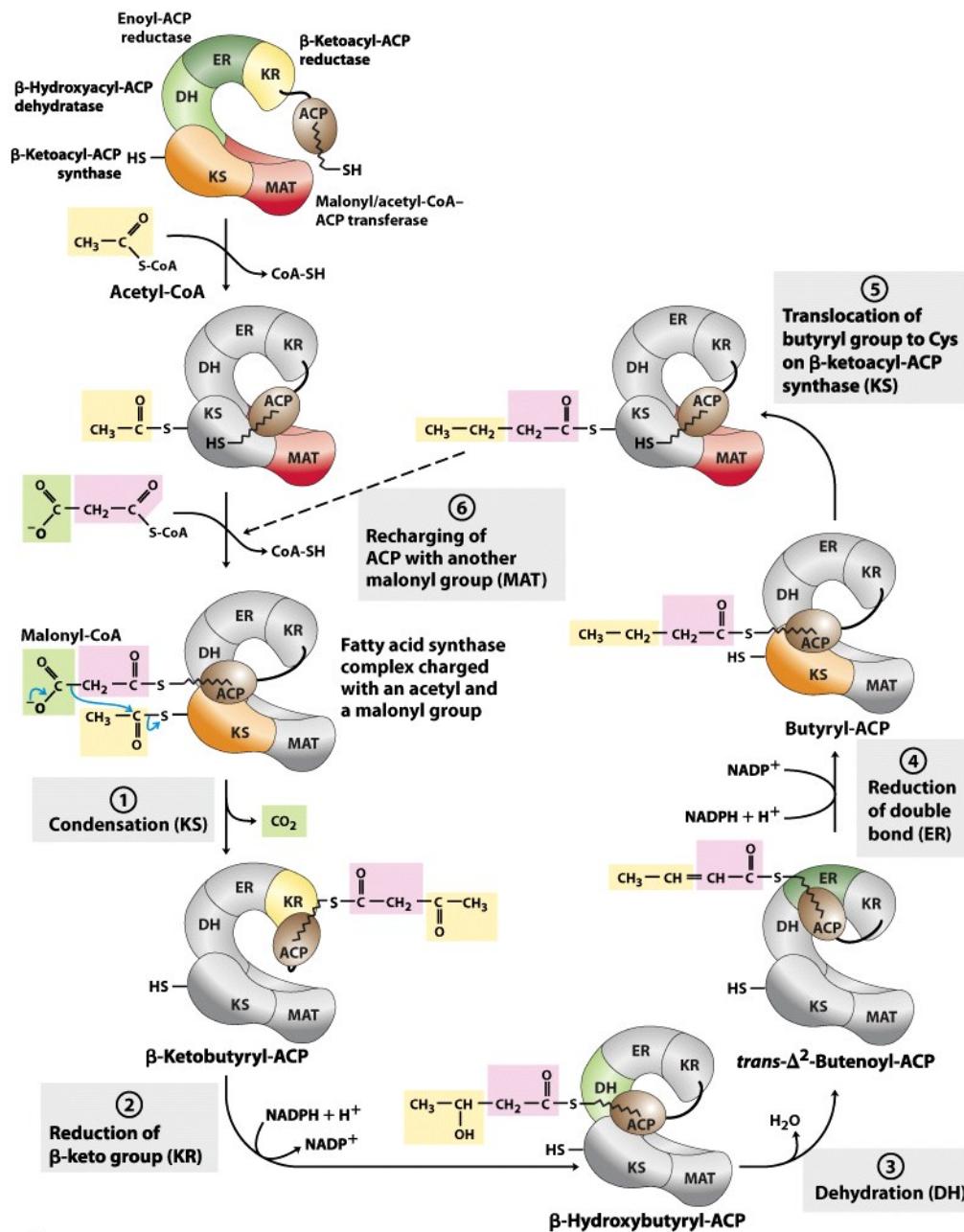


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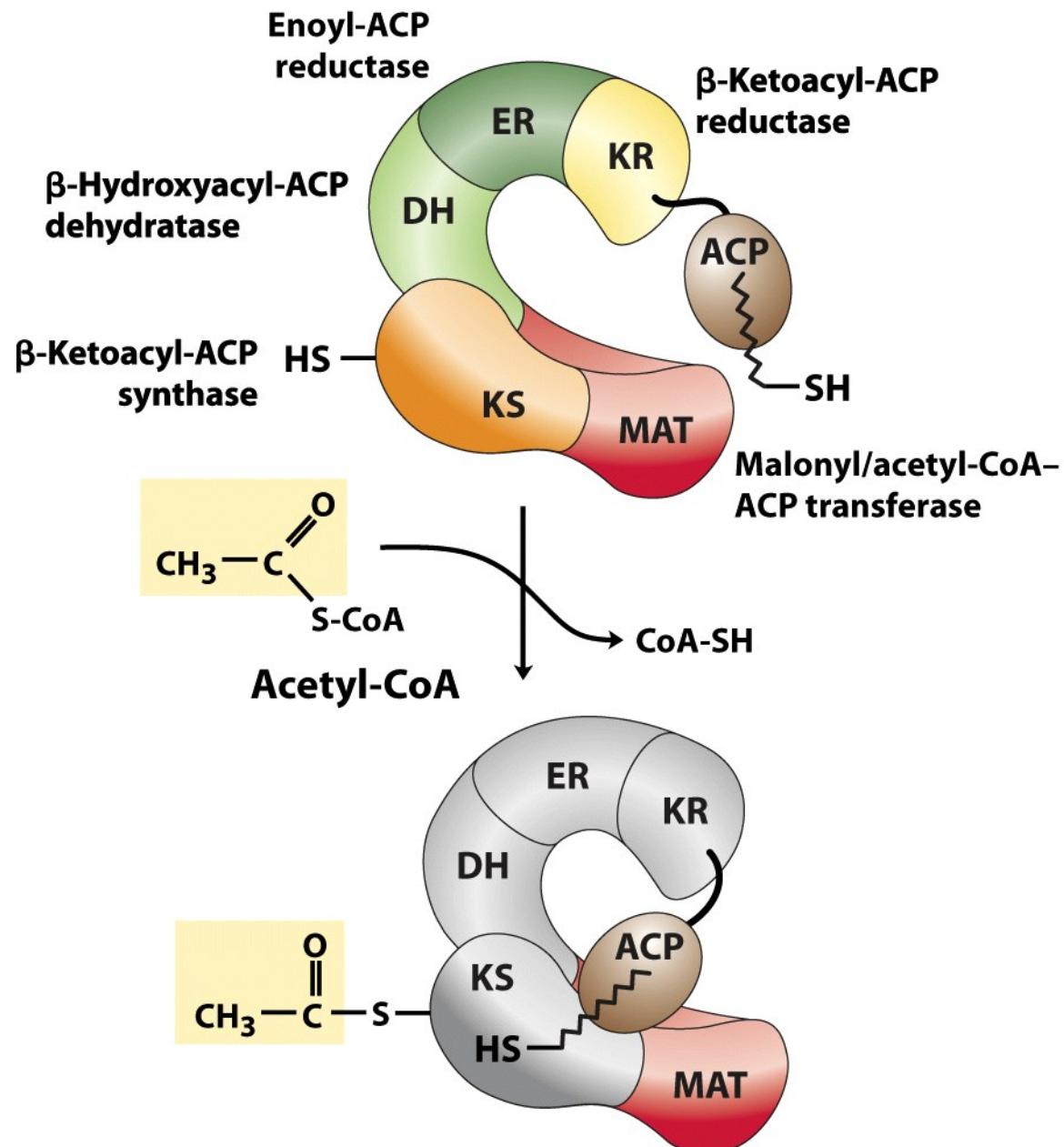


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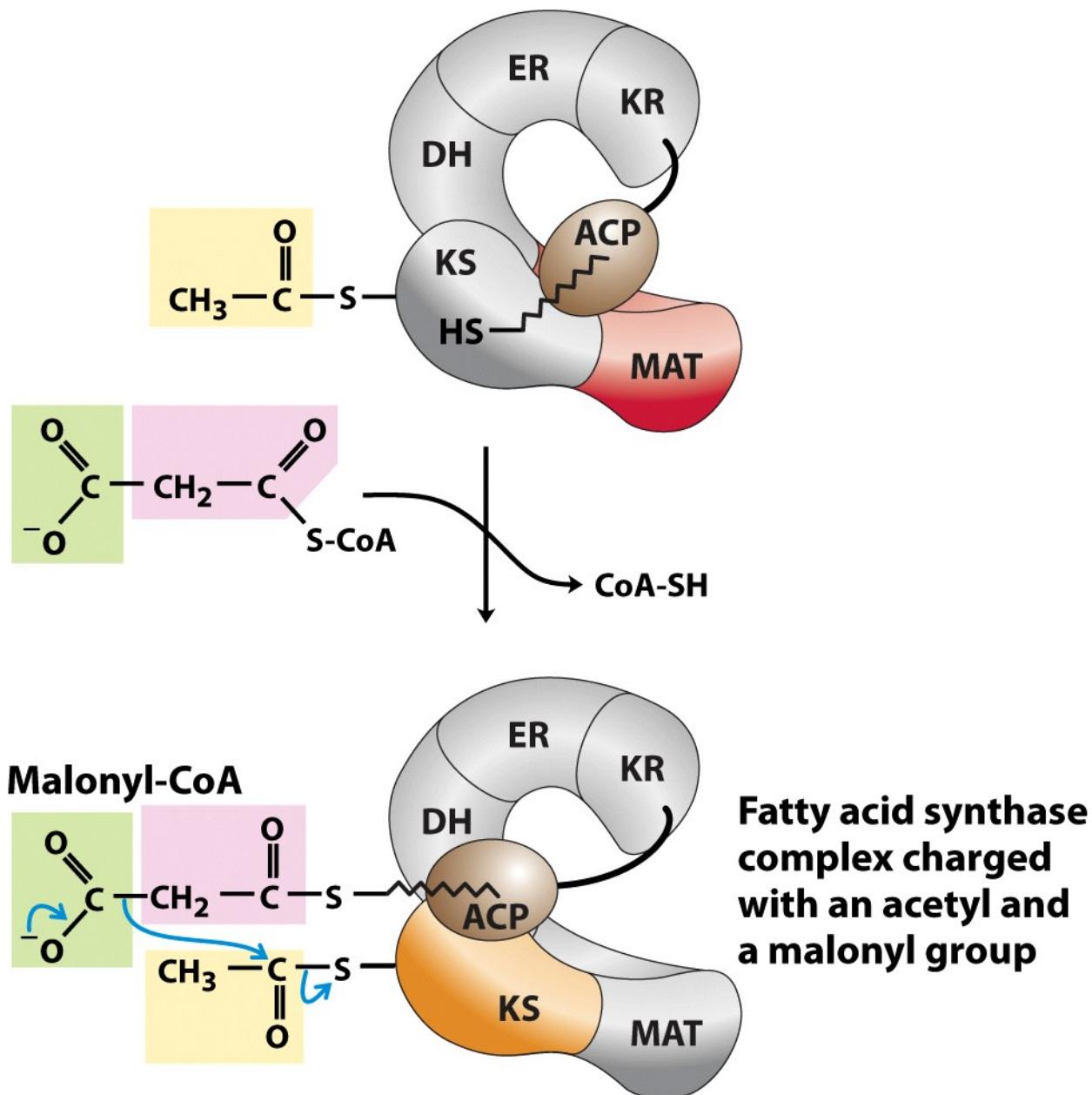


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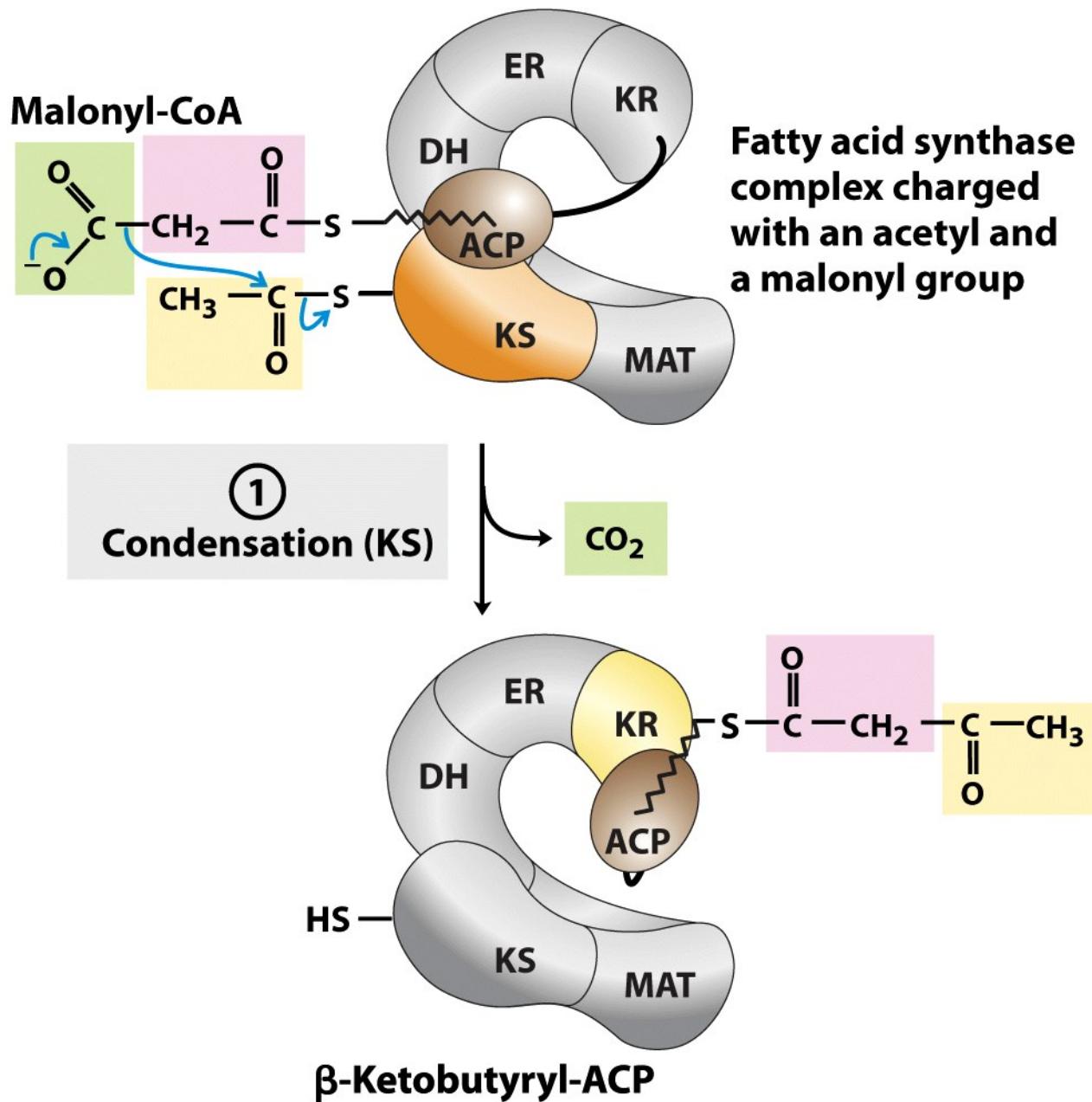


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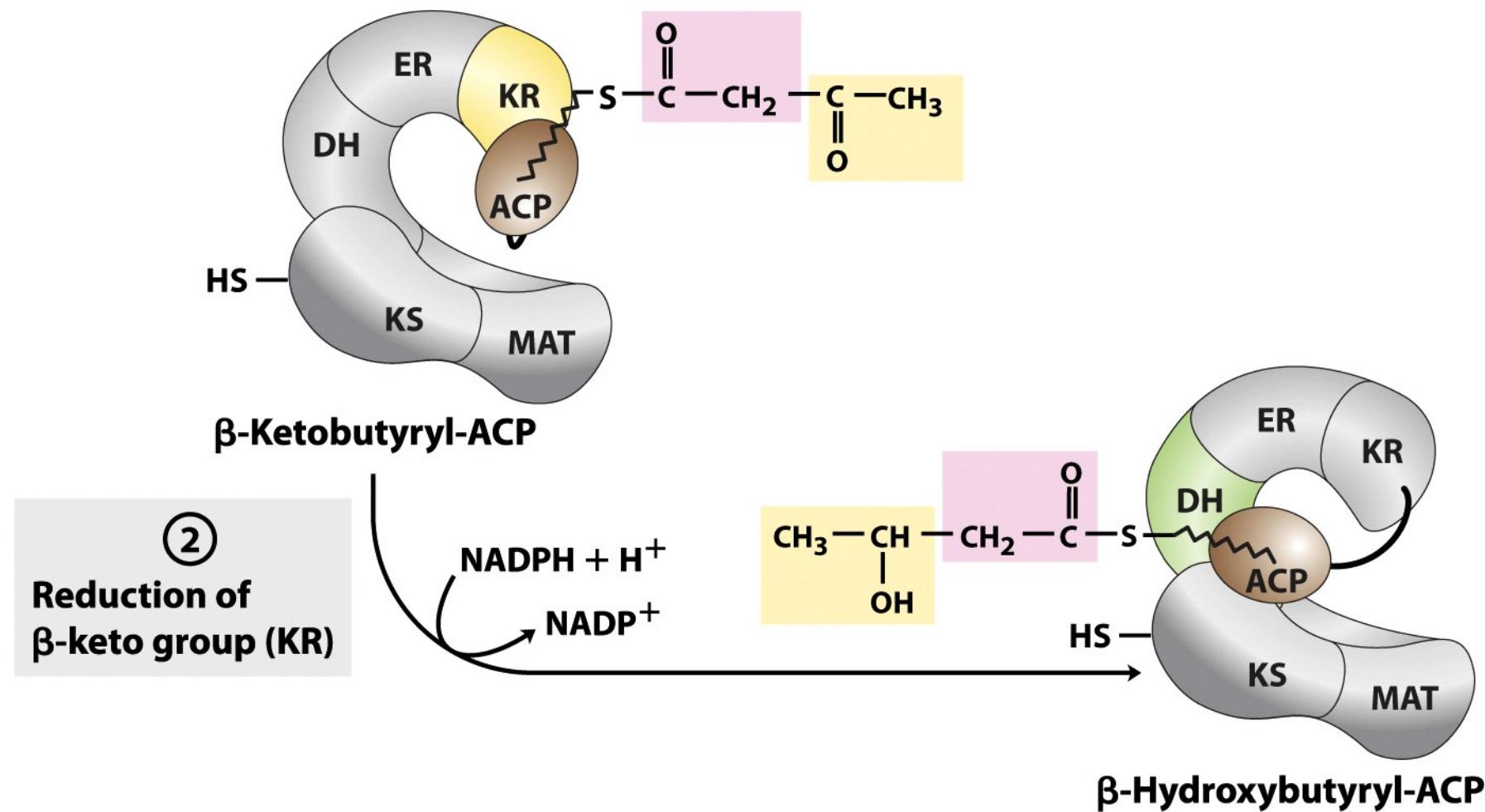


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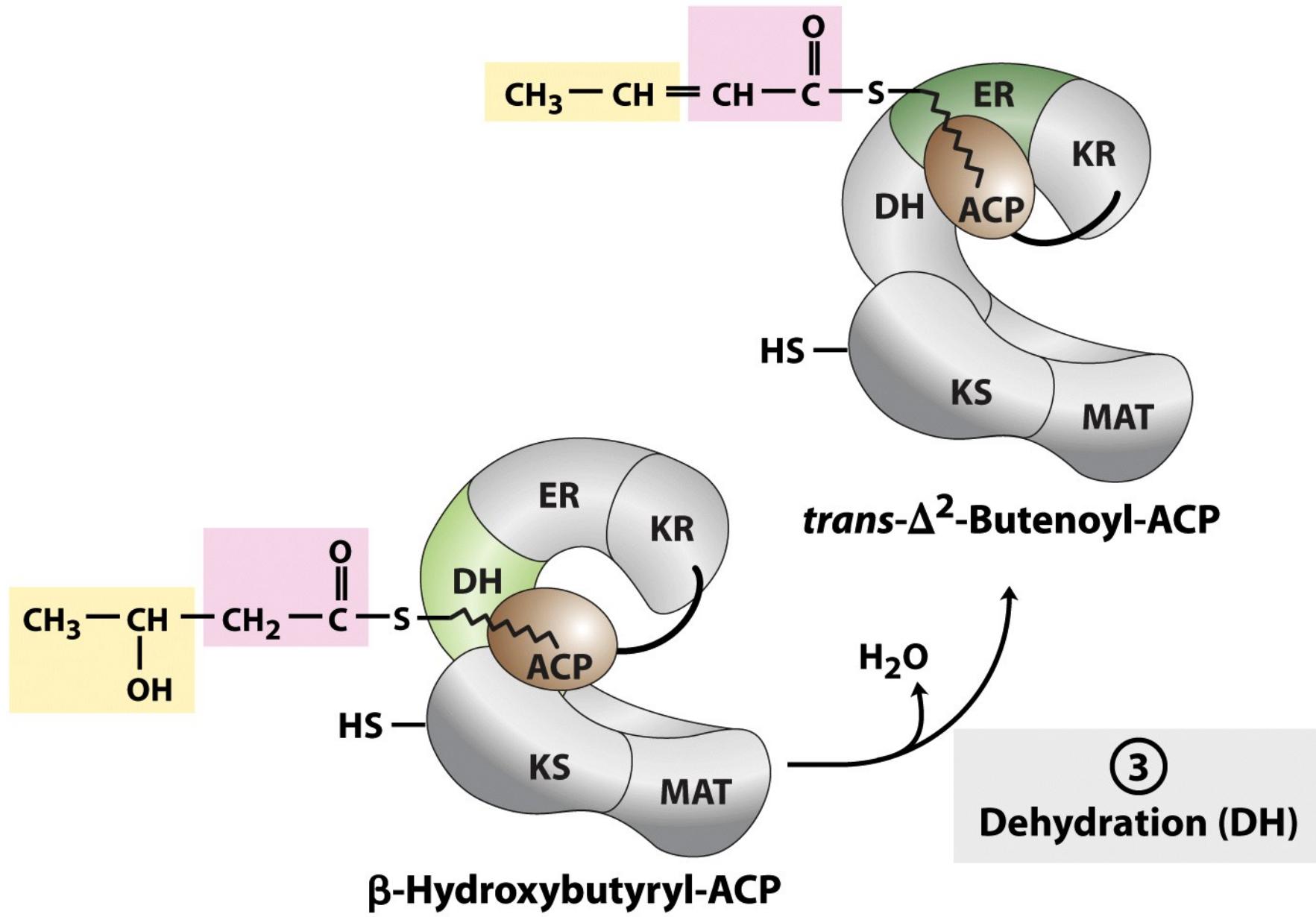


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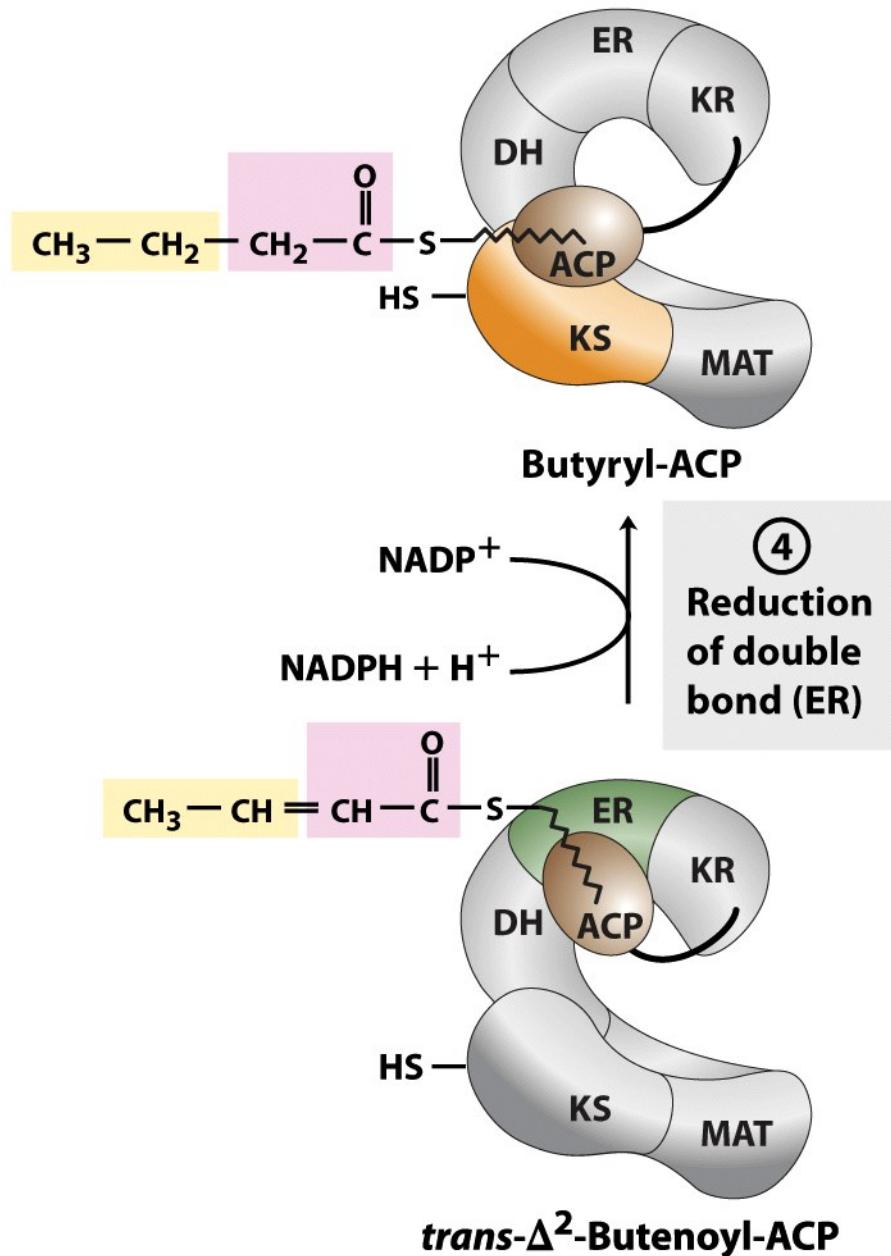


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⑤
**Translocation of
butyryl group to Cys
on β -ketoacyl-ACP
synthase (KS)**

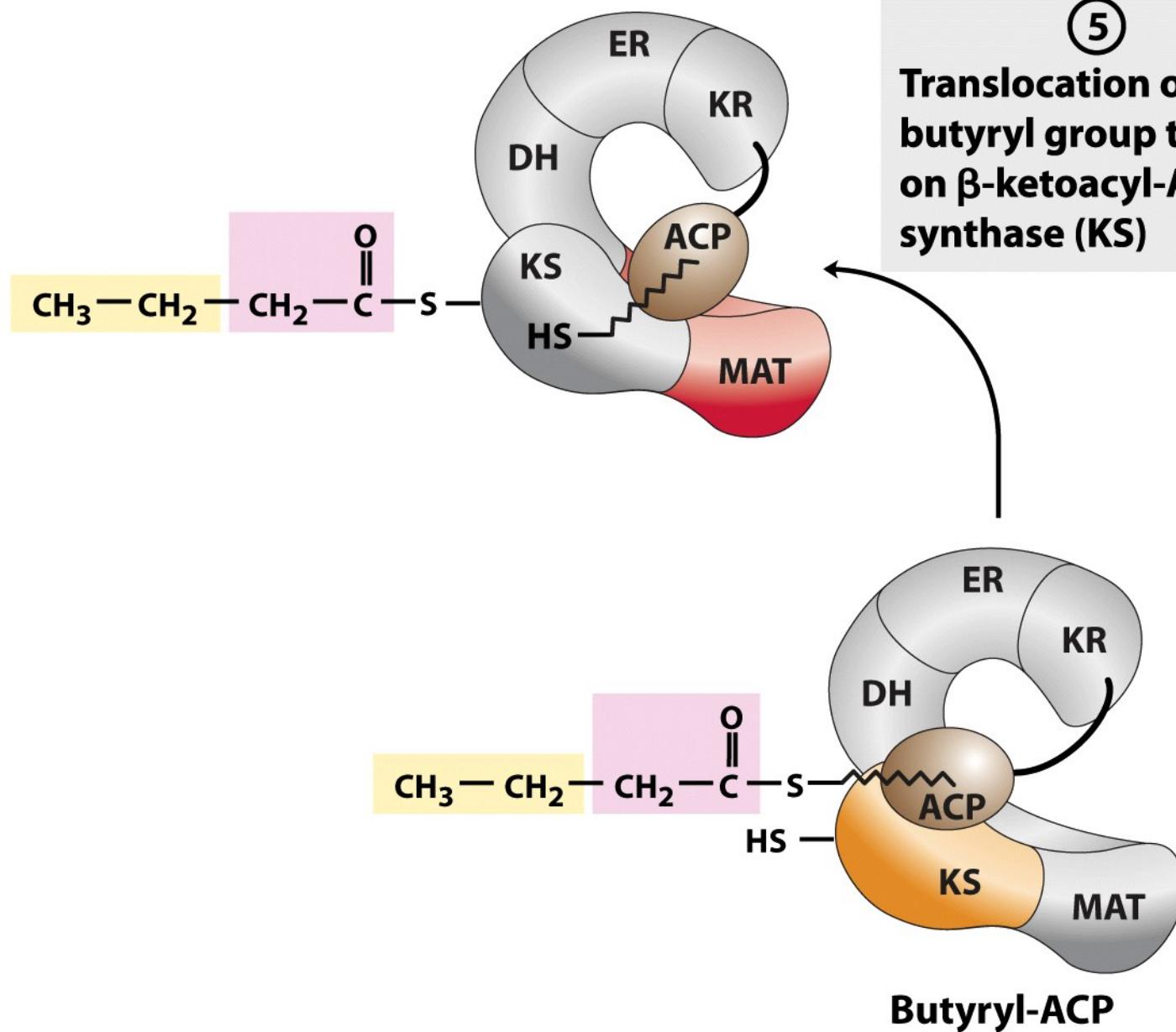


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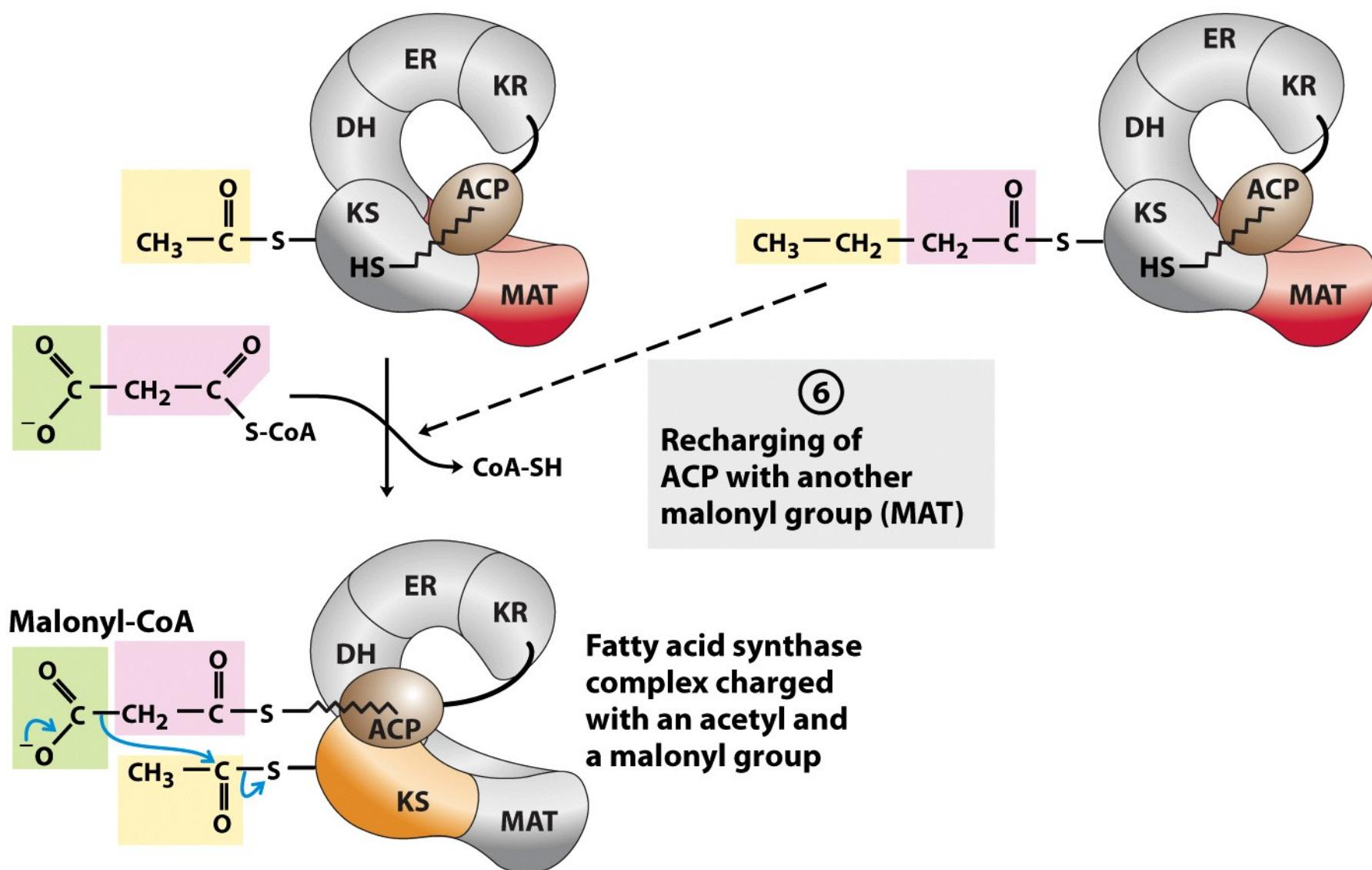


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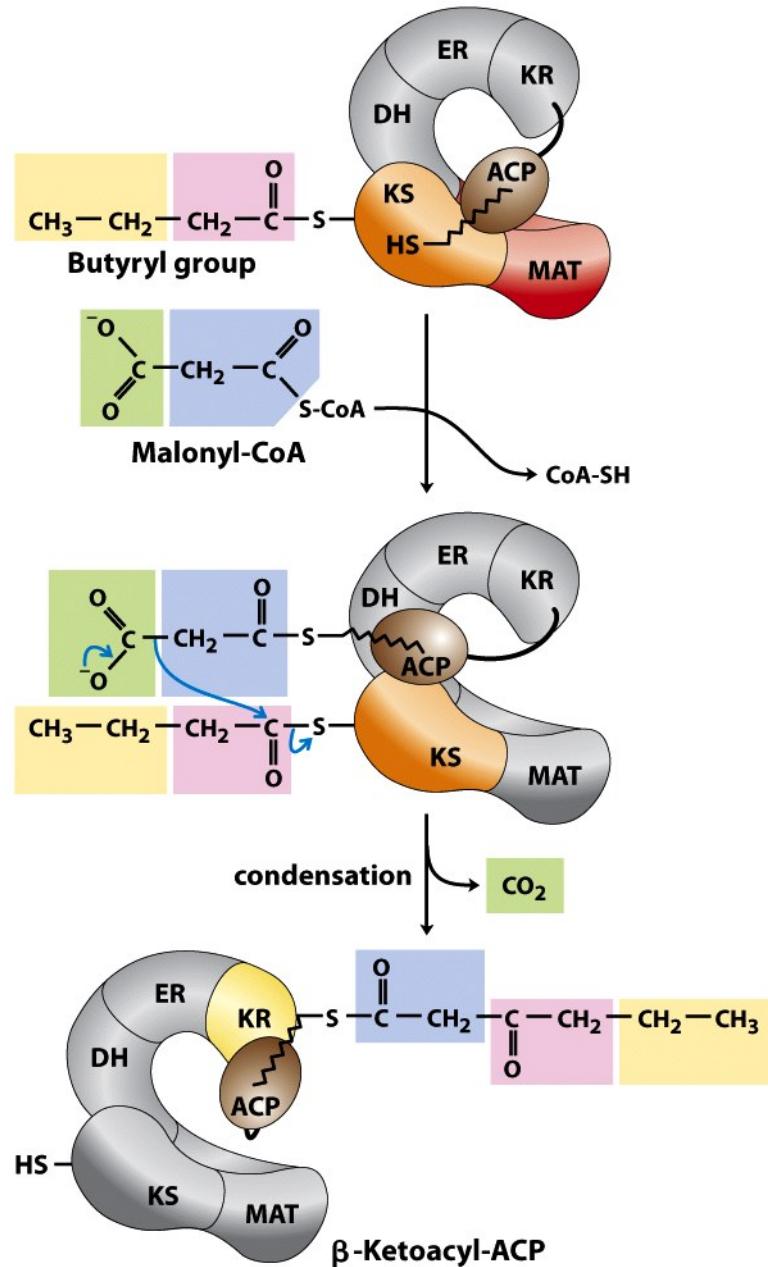


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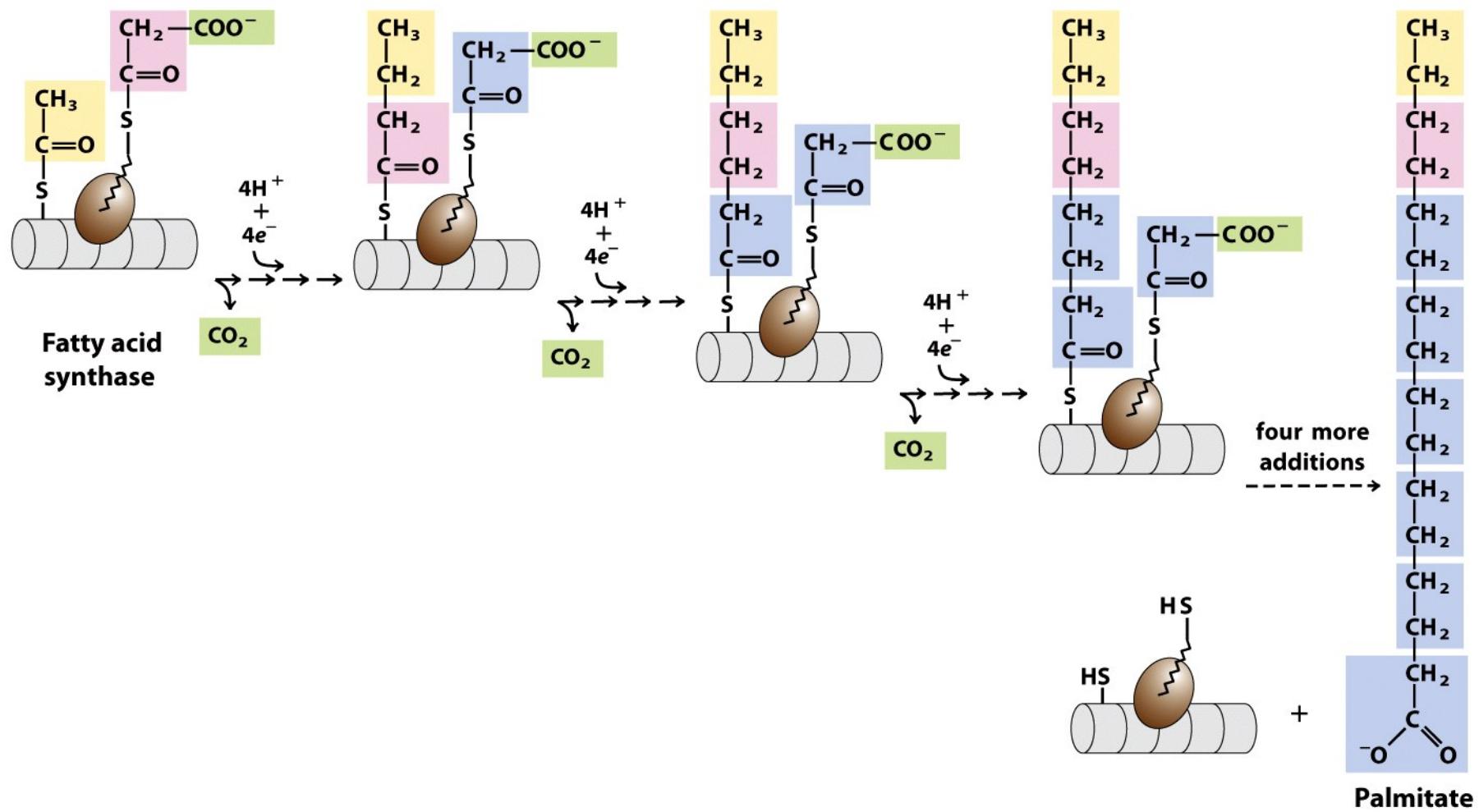


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Acetyl-CoA pre syntézu mastných kyselín musí byť lokalizovaný v cytoplazme

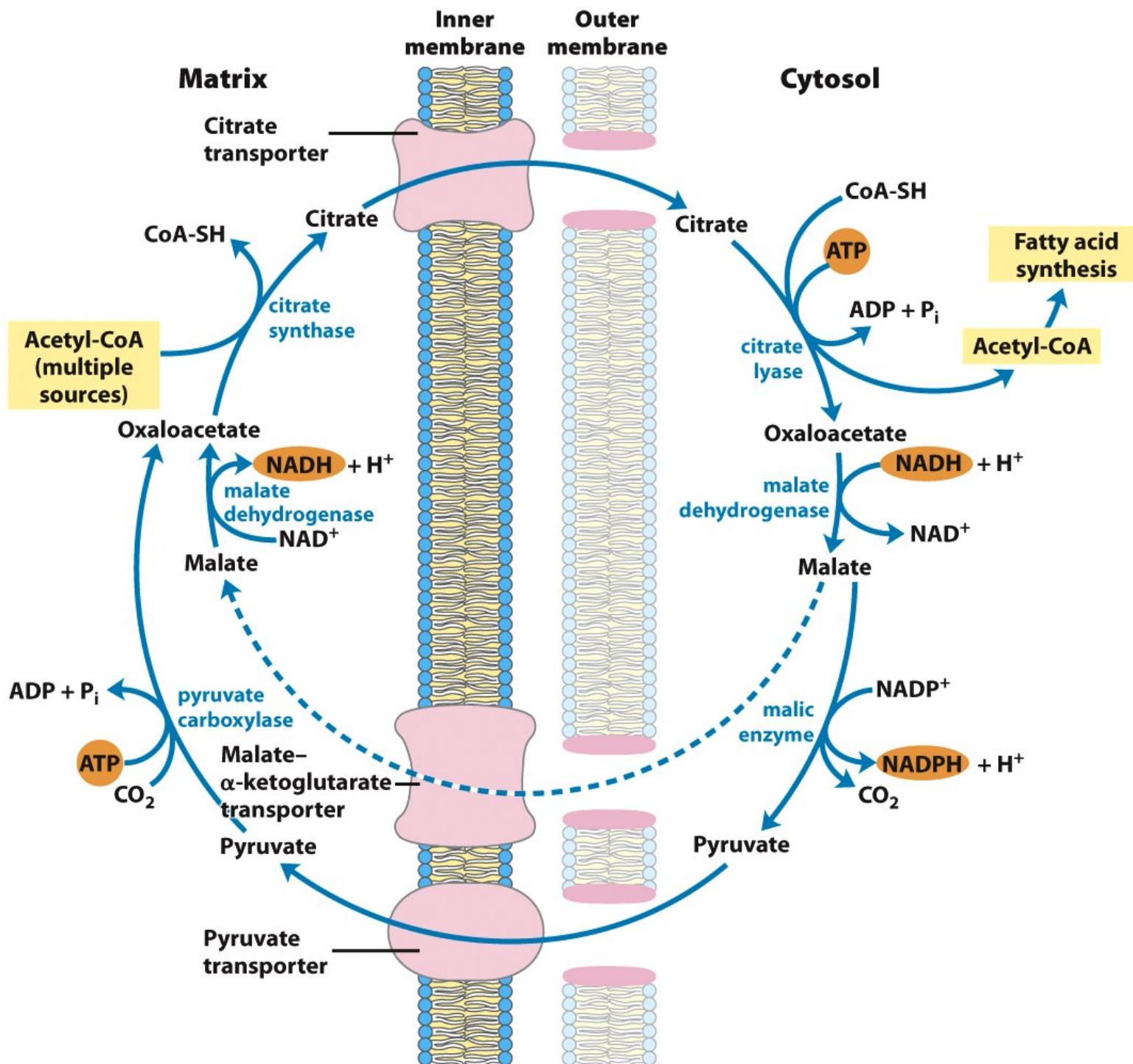
Aký je zdroj cytoplazmového Acetyl-CoA?

- Katabolizmus aminokyselín
→mitochondriálny Acetyl-CoA
- Pyruvátdehydrogenázový komplex
→mitochondriálny Acetyl-CoA

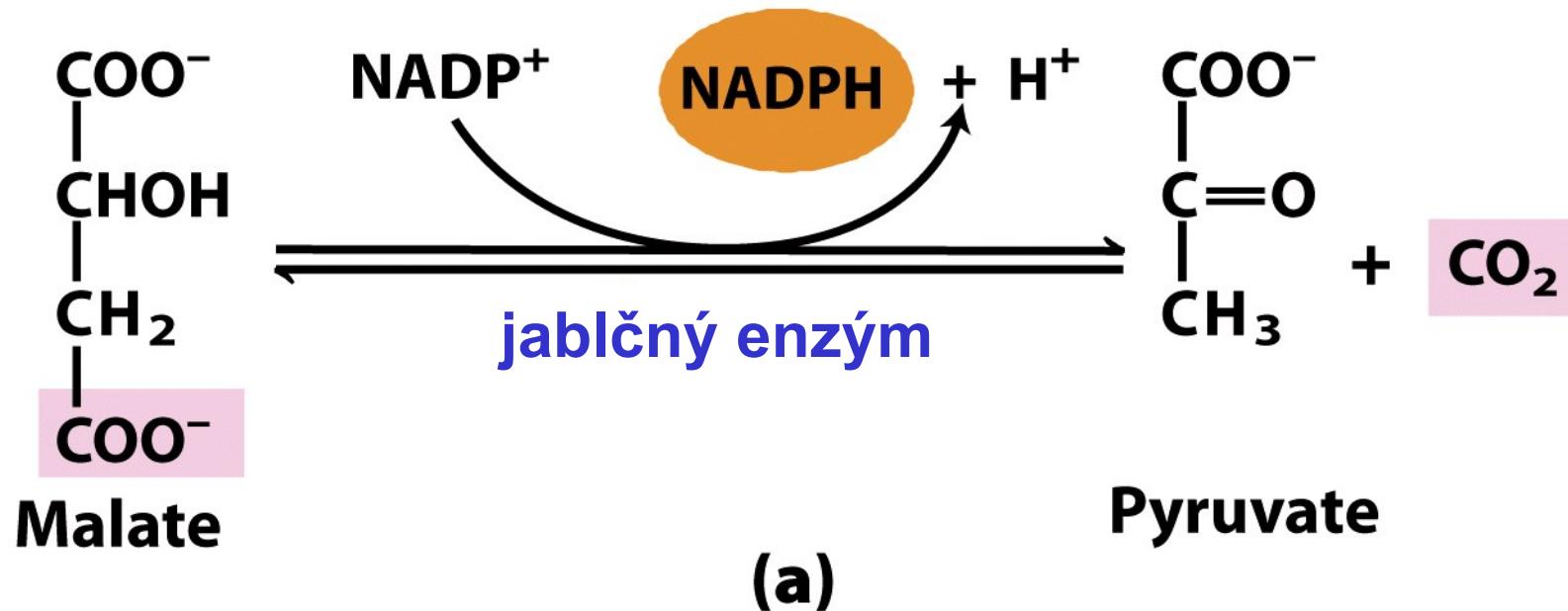
Riešenie:

CITRÁT-PYRUVÁT-MALÁTOVÝ ČLNOK,

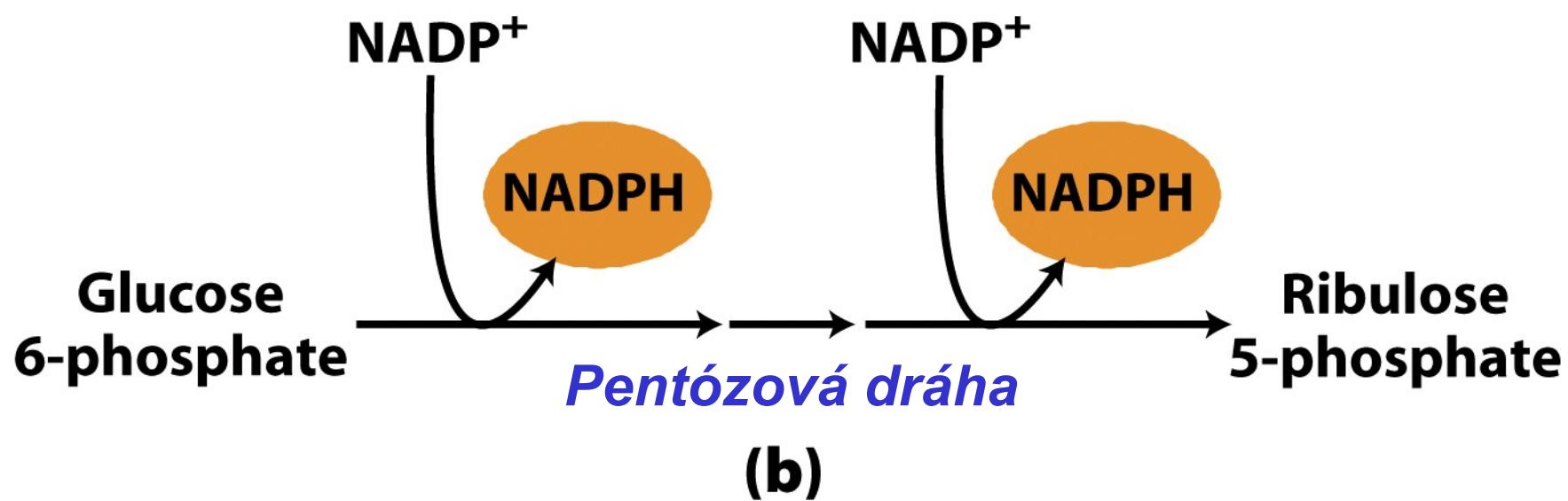
Zabezpečuje prenos acetátových zvyškov z mitochondrie do cytoplazmy a zároveň poskytuje redukčné ekvivalenty (NADPH) pre syntézu MK



Zdroje NADPH pre syntézu MK



(a)



(b)

Rozdiely

medzi syntézou a degradáciou MK

- Medziprodukty syntézy sú nавiazané na –SH skupinu proteínu prenášajúceho acyl (ACP)
- Syntéza prebieha v cytoplazme, degradácia v matrix mitochondrií
- Enzýmy syntézy sú na jednom polypeptide (u stavovcov)
- V biosyntéze sa využíva NADPH/NADP⁺, pri degradácii NADH/NAD⁺ a FADH₂/FAD

Transport cholesterolu a triacylglycerolov v krvi

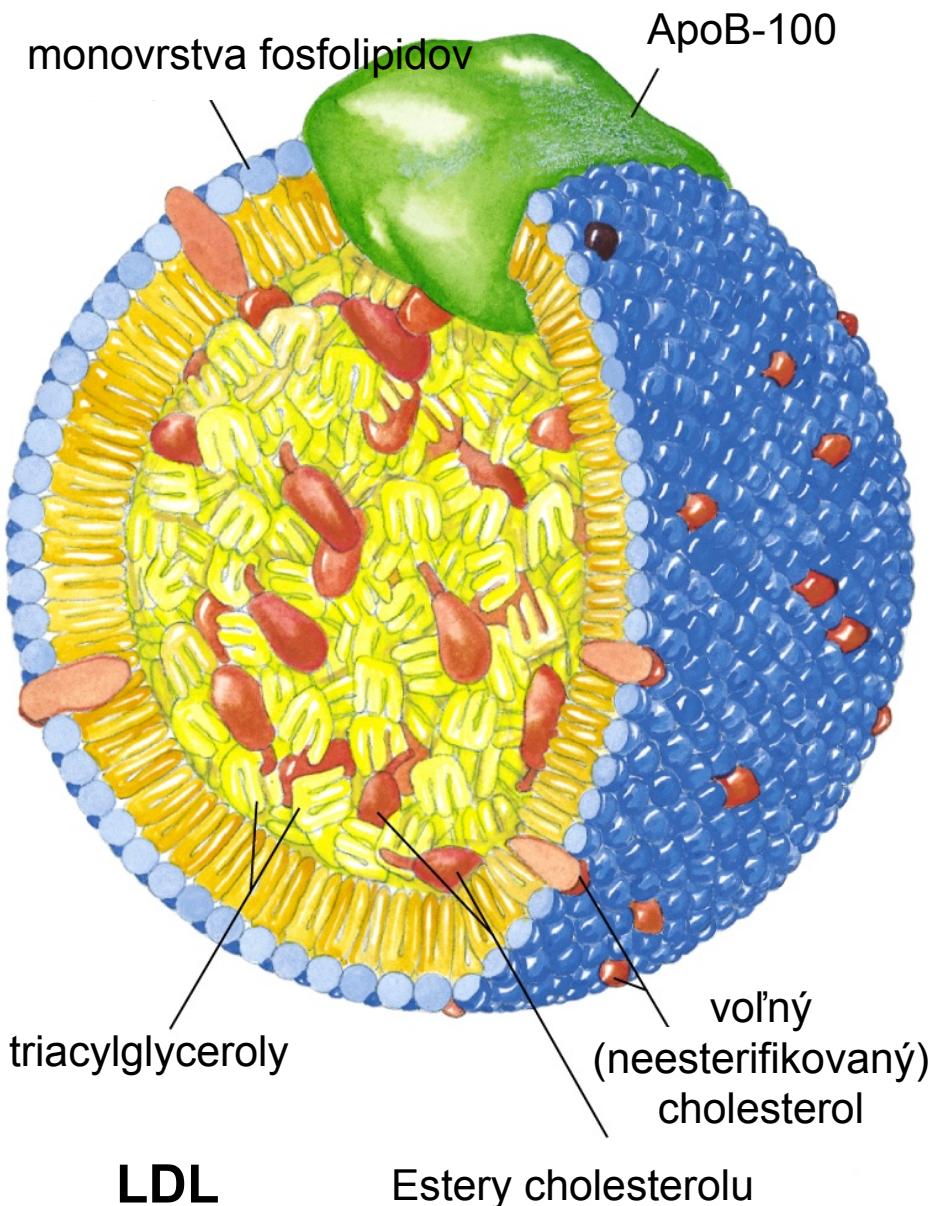
- Zabezpečujú lipoproteínové častice zložené z rôznych kombinácií:
 - apolipoproteínov
 - fosfolipidov
 - cholesterolu,
 - esterov cholesterolu
 - triacylglycerolov

Chylomikróny

VLDL-Very Low Density Lipoproteins
(lipoproteíny s veľmi nízkou hustotou)

LDL- Low Density Lipoproteins
(lipoproteíny s nízkou hustotou)

HDL-High Density Lipoproteins
(lipoproteíny s vysokou hustotou)



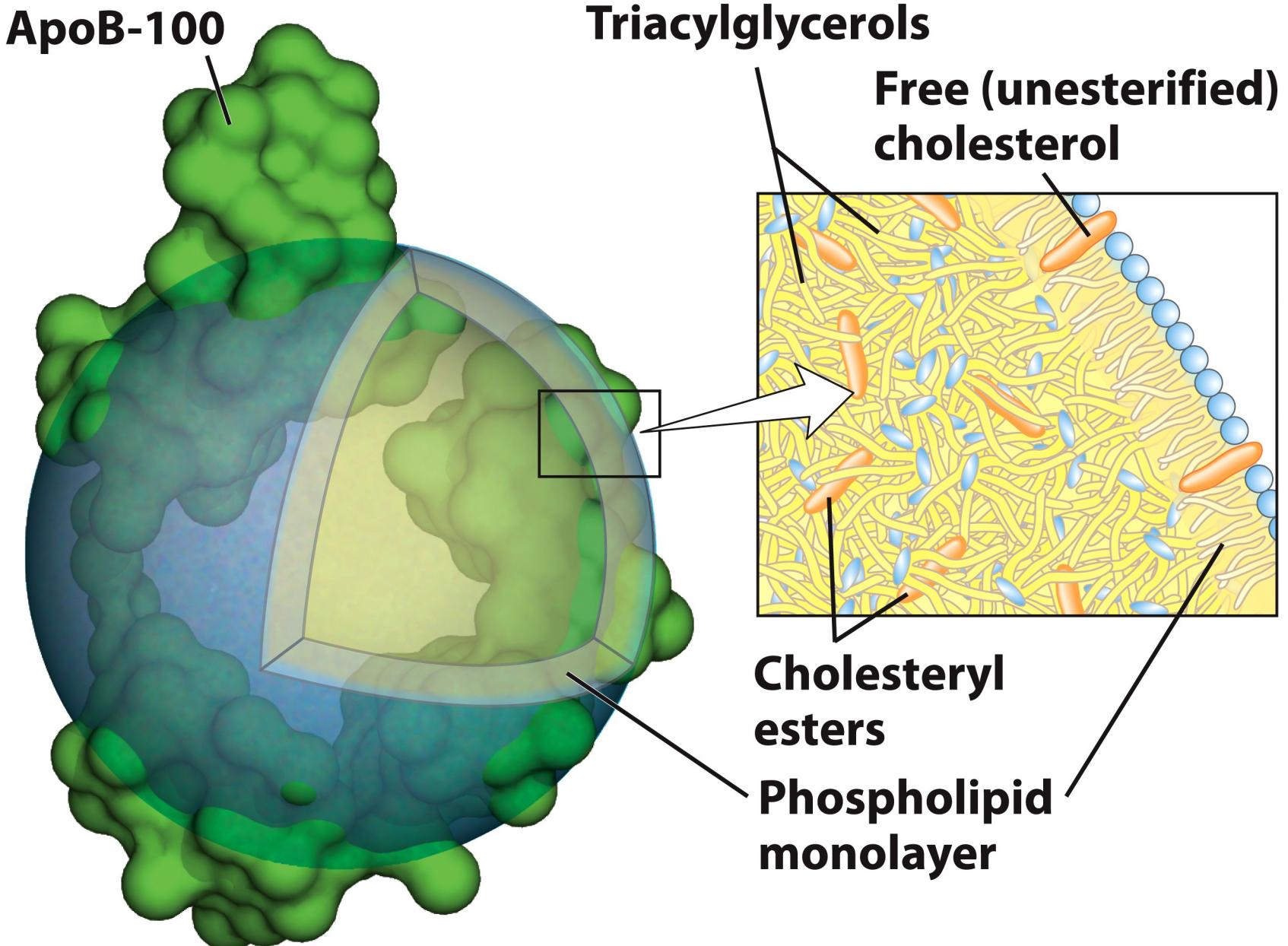
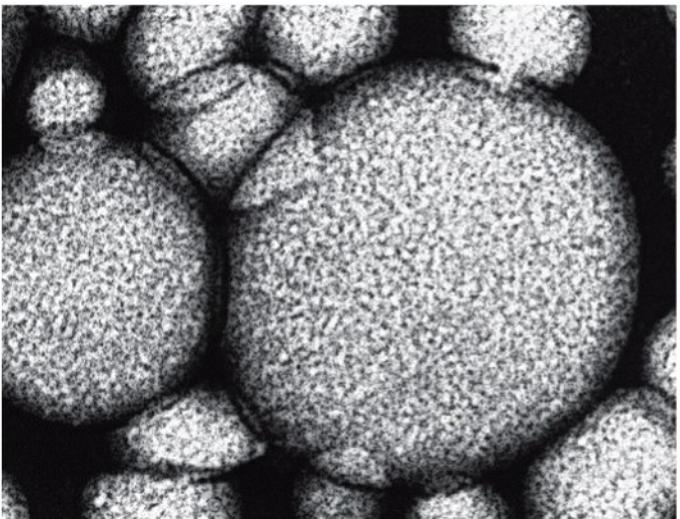
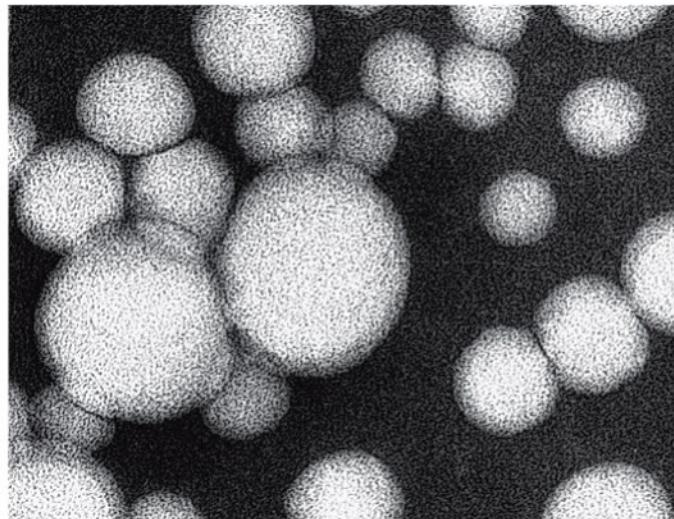


Figure 21-39a

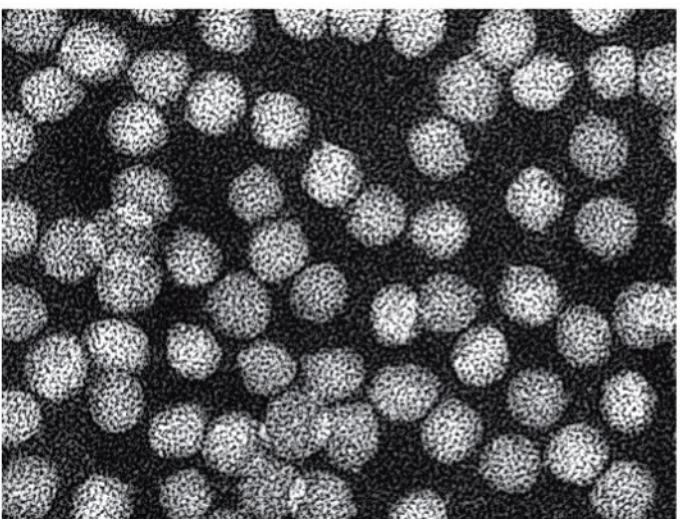
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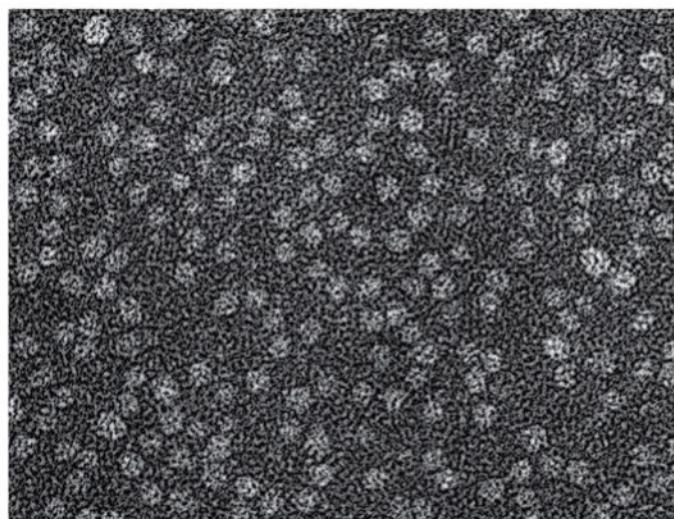
Chylomicrons ($\times 60,000$)
50-200 nm



VLDL ($\times 180,000$)
28-70 nm



LDL ($\times 180,000$)
20-25 nm



HDL ($\times 180,000$)
8-11 nm

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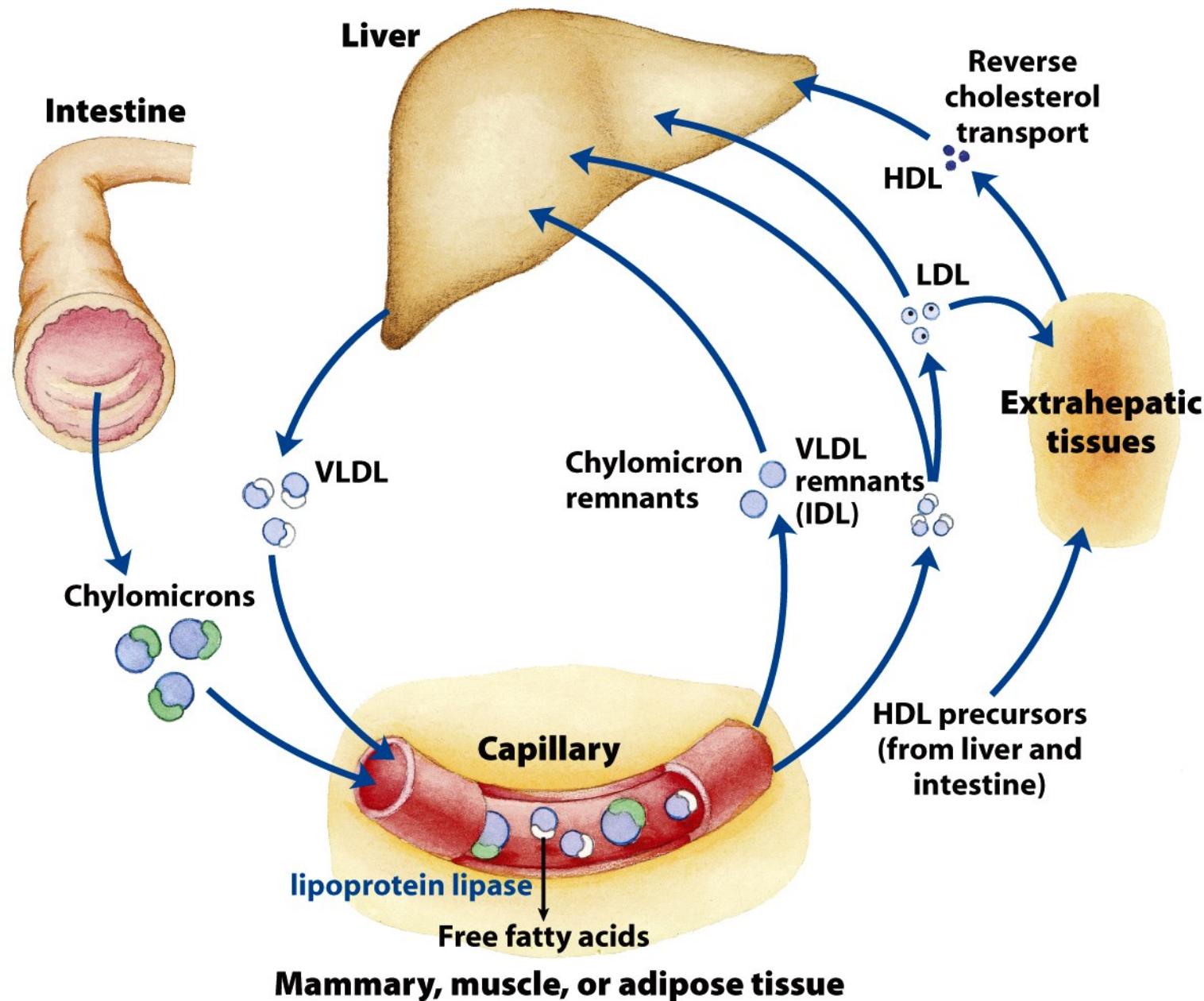


Figure 21-40a

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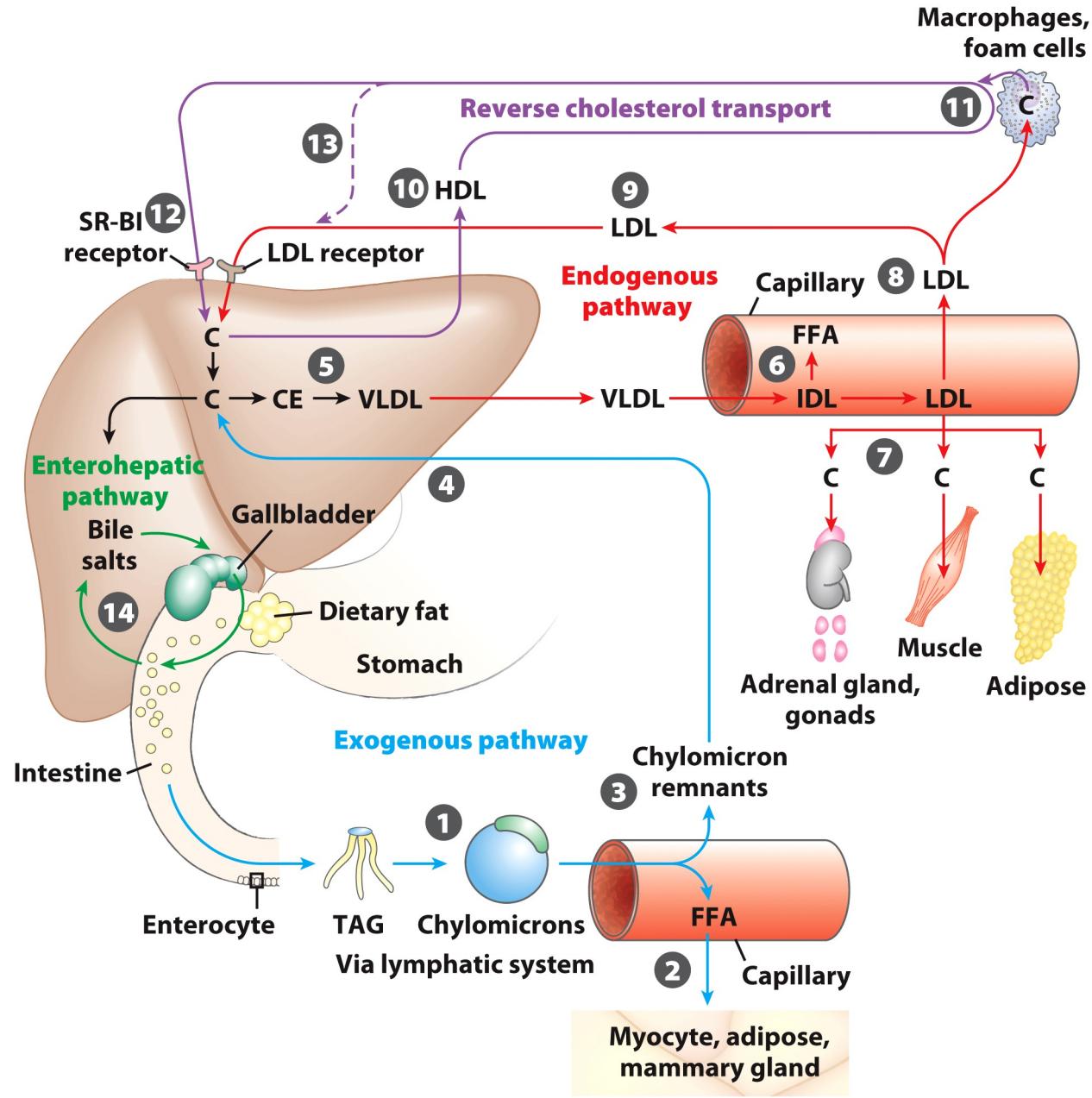


Figure 21-40

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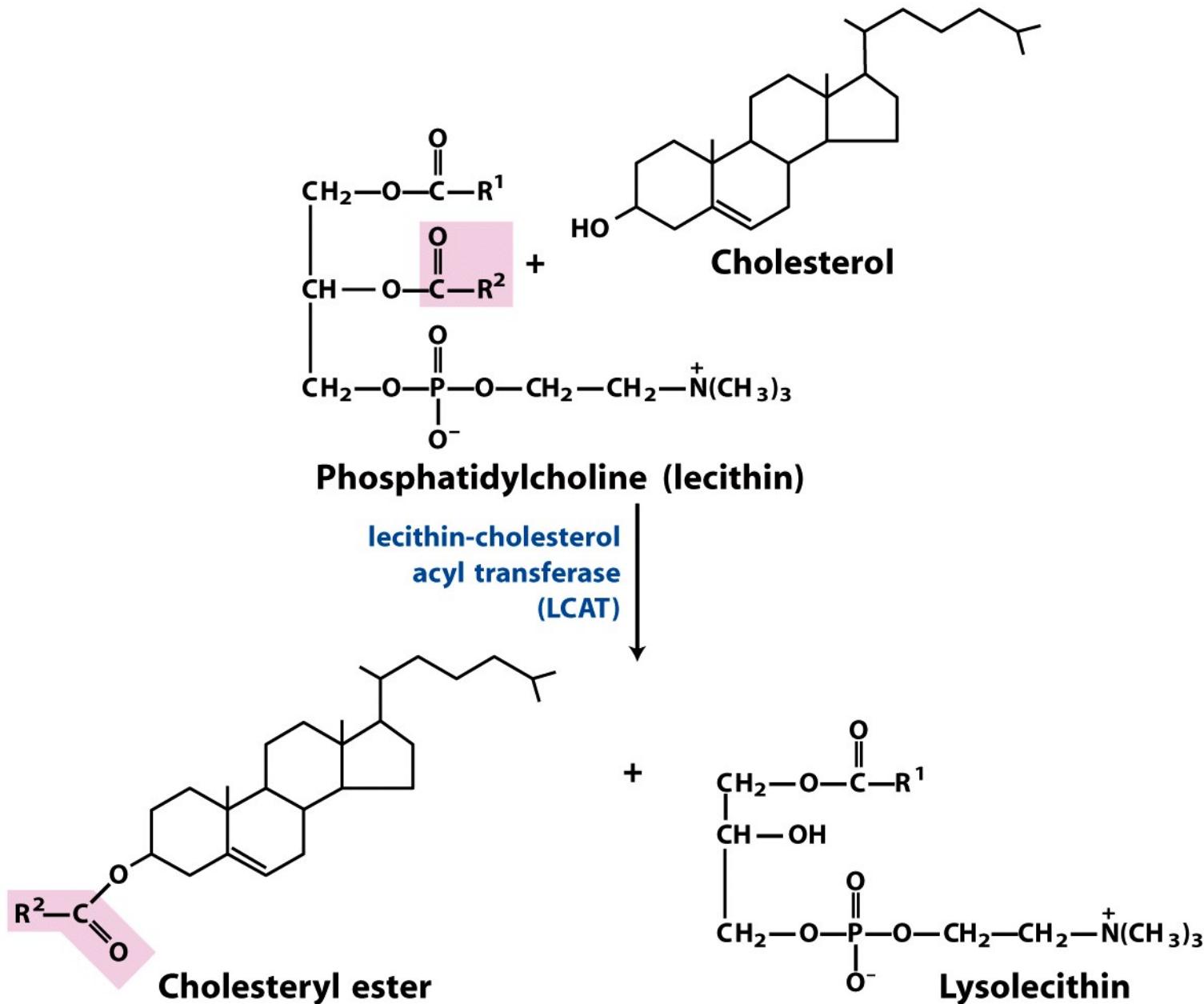


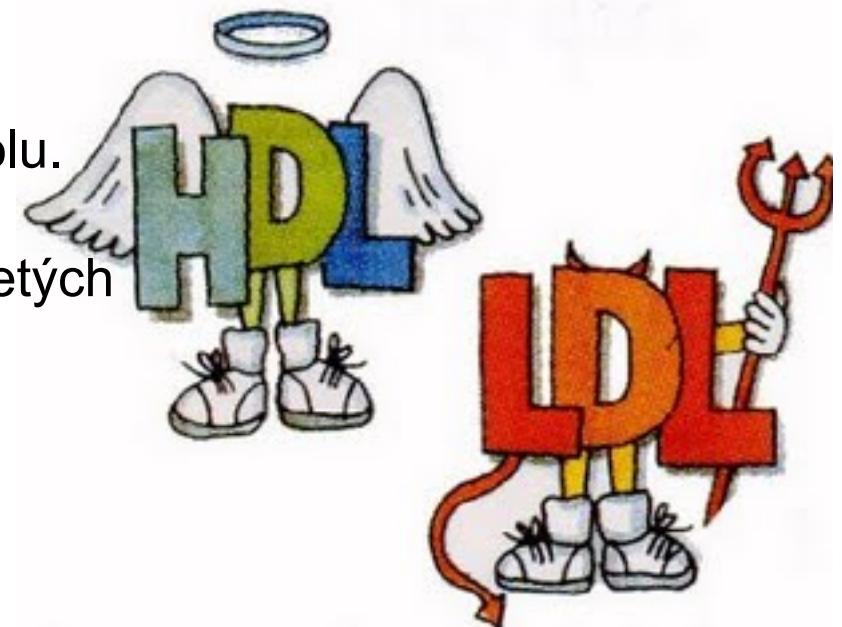
Figure 21-41

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Fyziologické úlohy lipoproteínov

- **Chylomikróny** – transport tukov, cholesterolu a ďalších lipidov z potravy
- **Zvyšky chylomikrónov** – transport esterov cholesterolu z potravy do pečene
- **VLDL** – transport endogénnych tukov a cholesterolu z pečene
- **LDL** – transport cholesterolu do periférnych tkanív
- **HDL** – reverzný transport cholesterolu.
Prenášač cholesterolu, ktorý je uvoľnený do krvnej plazmy z odumretých buniek alebo pri obnove membrán



Hlavné triedy ľudských plazmových lipoproteínov

		Zloženie (hmotnostné %)				
Lipo-proteín	Hustota (g/ml)	Proteíny	Fosfolipidy	Cholesterol	Estery cholesterolu	TAG
Chylo-mikrón	<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

Apolipo-proteín	MW	Asociácia s lipoproteínmi	Funkcia (ak je známa)
ApoA-I	28 331	HDL	Aktivuje LCAT, interaguje s ABC transportérom
ApoA-II	17 380	HDL	Inhibuje LCAT
ApoA-IV	44 000	Chylomikróny, HDL	Aktivuje LCAT; Vychytávanie/transport cholesterolu
ApoB-48	240 000	Chylomikróny	Vychytávanie/transport cholesterolu
ApoB-100	513 000	VLDL, LDL	Viaže sa k LDL receptoru
ApoC-I	7 000	VLDL, HDL	
ApoC-II	8 837	Chylomikróny, VLDL, HDL	Aktivuje lipoproteínlipázu
ApoC-III	8 751	Chylomikróny, VLDL, HDL	Inhibuje lipoproteínlipázu
ApoD	32 500	HDL	
ApoE	34 145	Chylomikróny, VLDL, HDL	Vychytávanie VLDL a zvyškov chylomikrónov

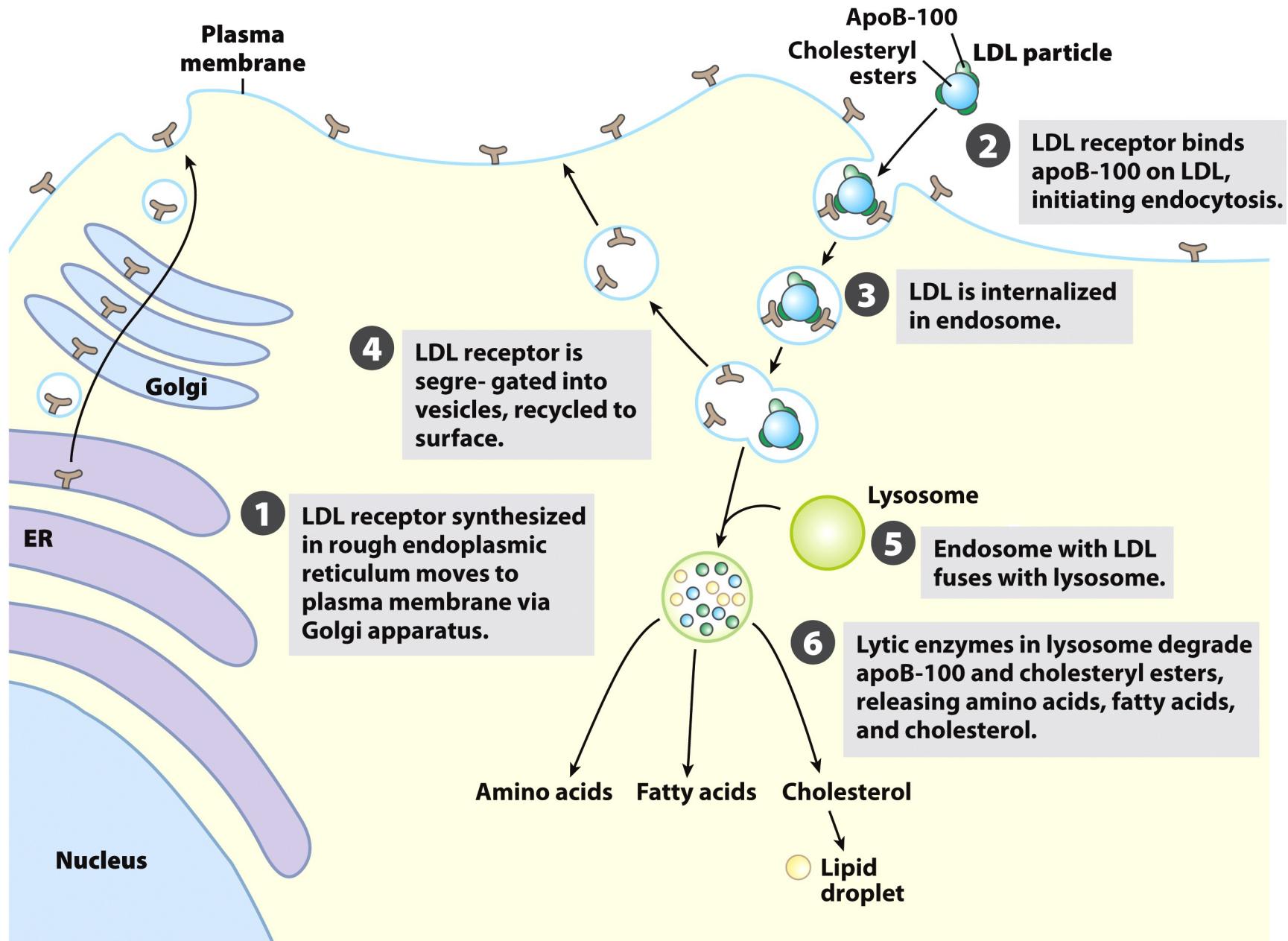


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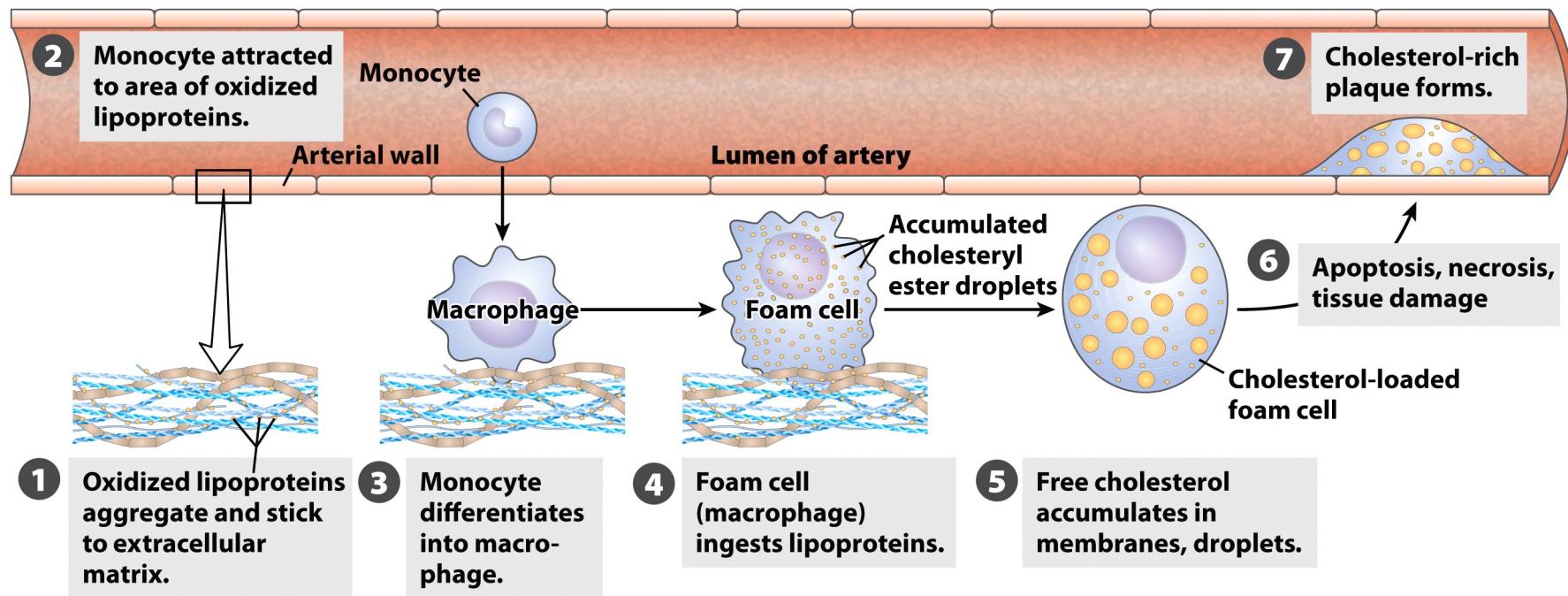


Figure 21-46

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