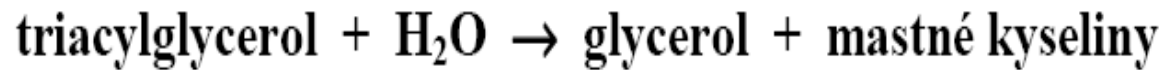


Metabolismus lipidů

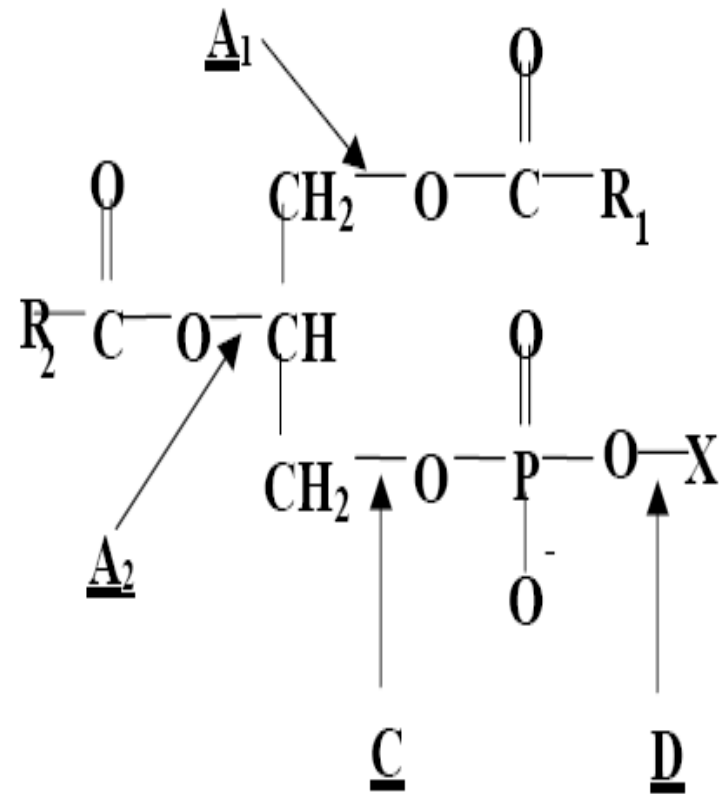
- Triacylglyceroly – 90 % potravních lipidů a zároveň hlavní zásobárnou energie – orgánový tuk
- Dvojnásobné množství energie
CH₂ - CHOH
- Jako hydrofobní látky nejsou hydratovány
- Nejsou pohotovým zdrojem energie, spíše vhodné pro skladování.

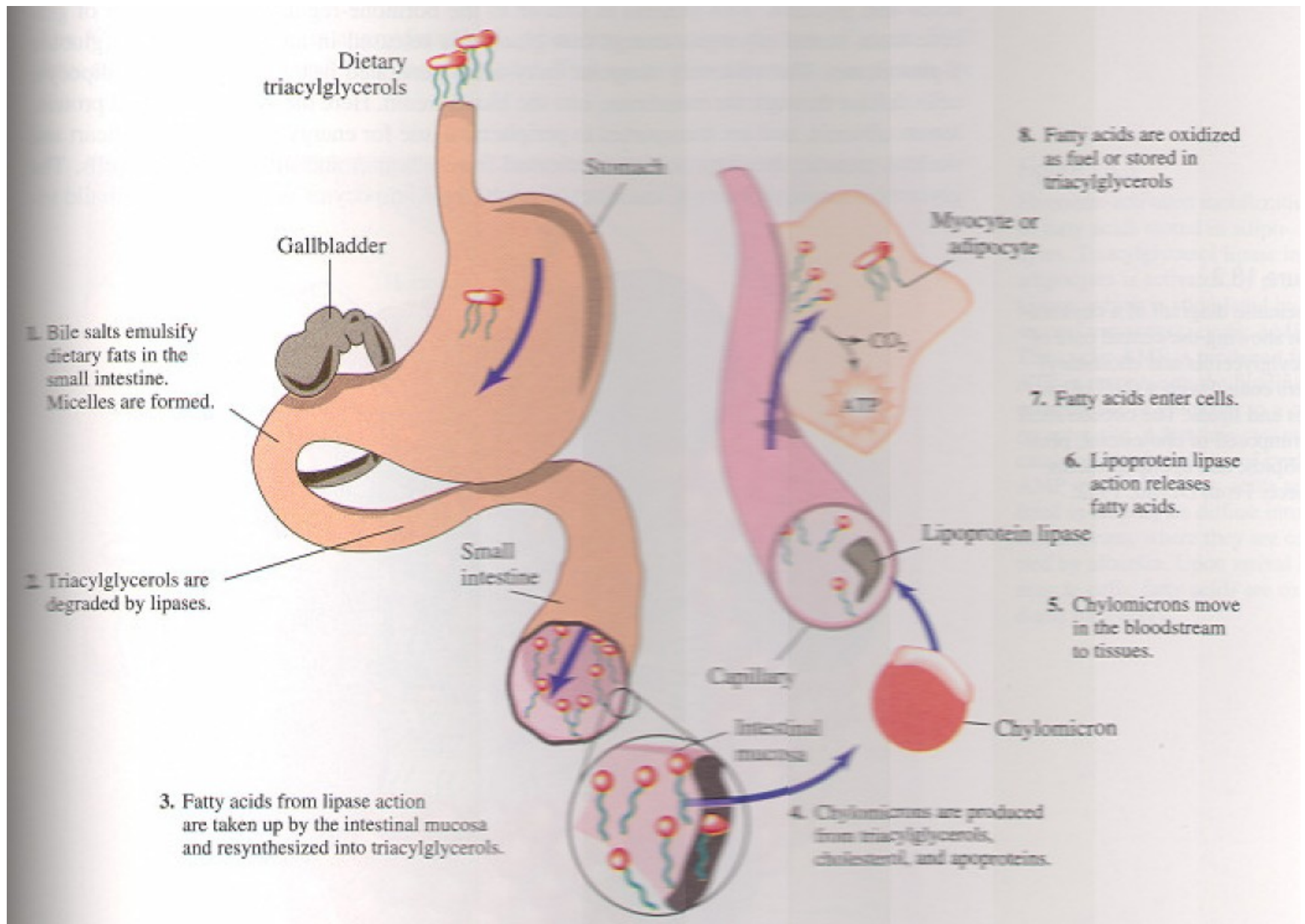
METABOLISMUS LIPIDŮ

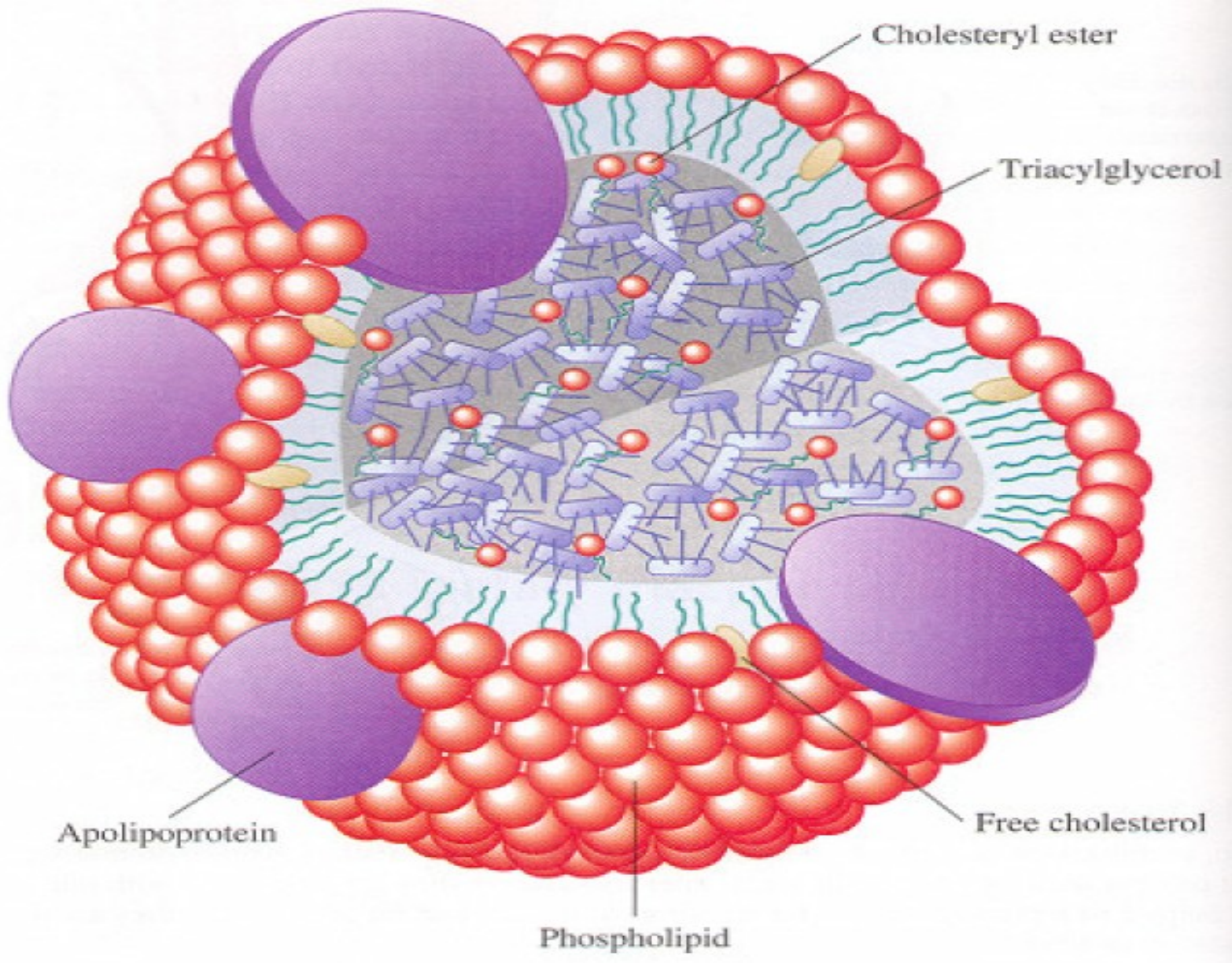
Lipasy - hydrolasy - karboxylesterasy

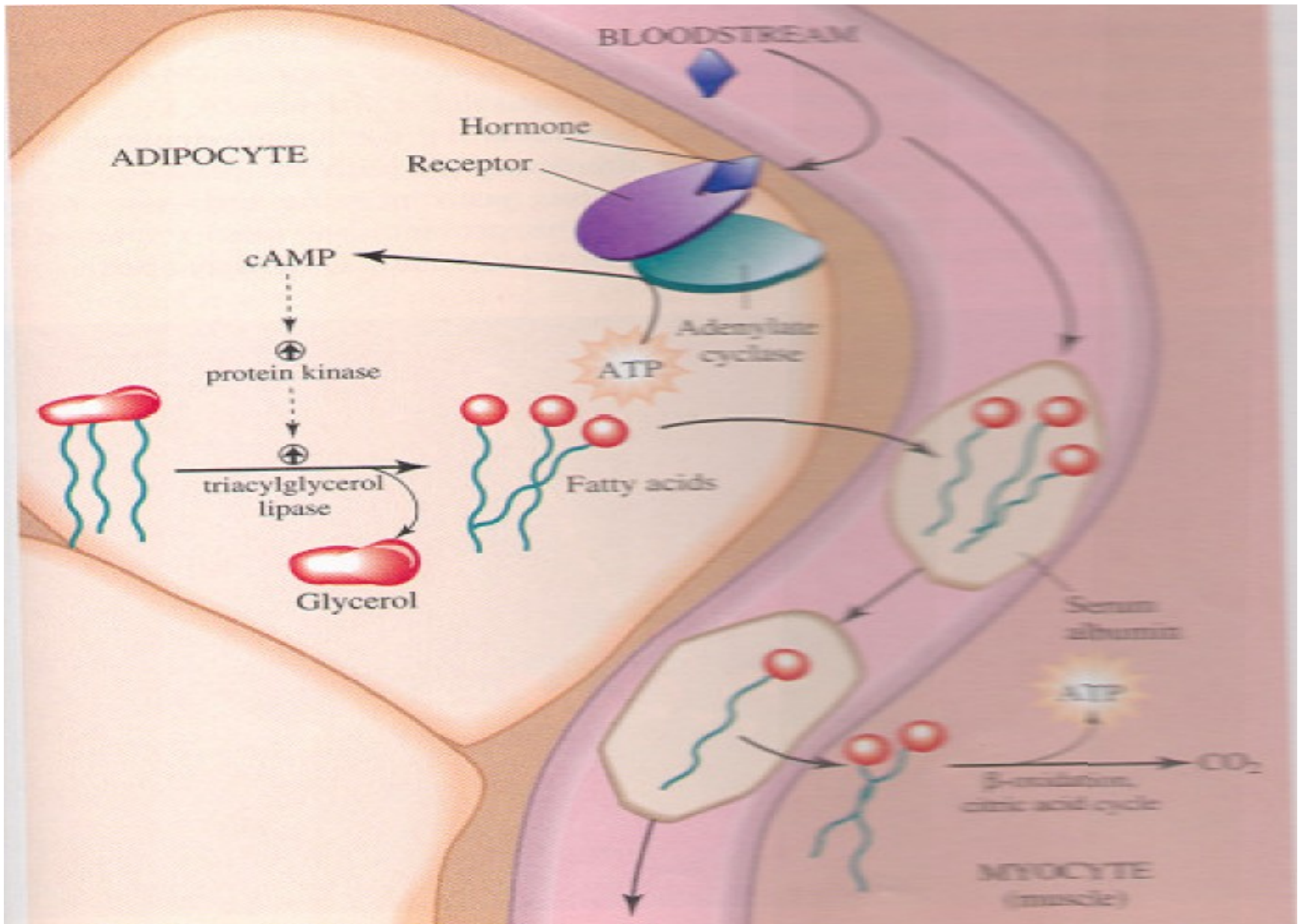


Fosfolipasy







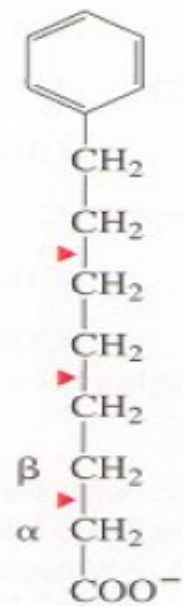


Odbourávání mastných kyselin

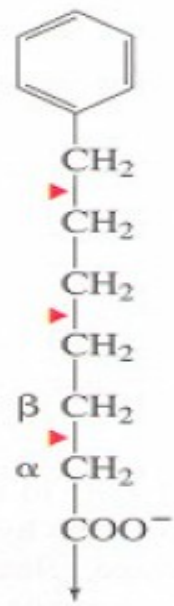
β oxidace

F.KNOOP 1909

F.LYNEN 1951

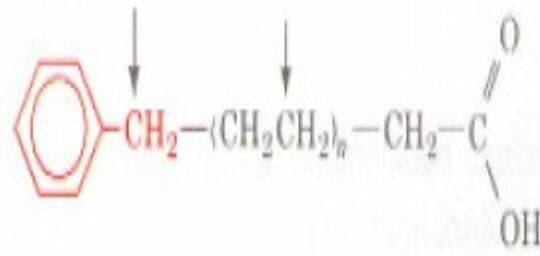


Phenylacetate
(from even-numbered
carbon chain)

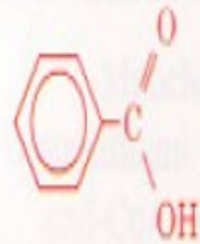


Benzoate
(from odd-numbered
carbon chain)

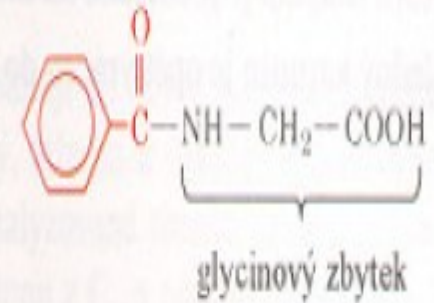
přidaná mastná kyselina



degradační produkty



exkreční produkt

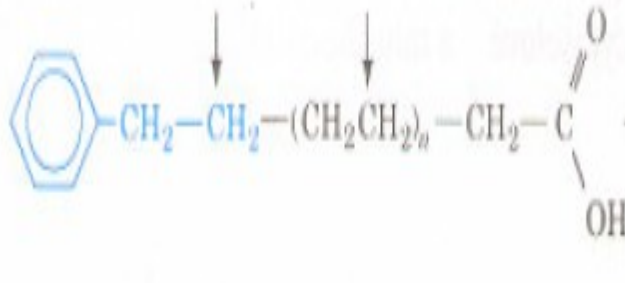


$(n+1)C_2$

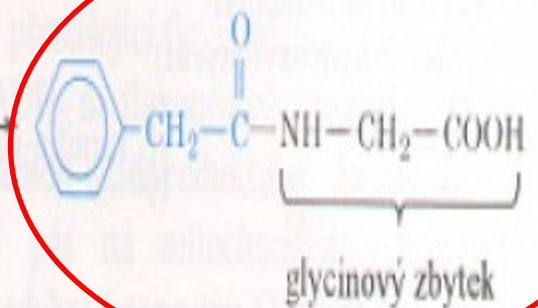
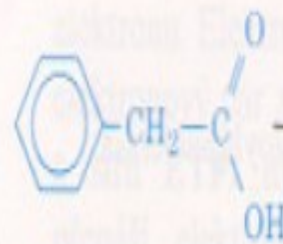
kyselina s lichým počtem C-atomů

benzoová kyselina

hippurová kyselina



$(n+1)C_2$



kyselina se sudým počtem C-atomů

fenylactová kyselina

fenylaceturová kyselina

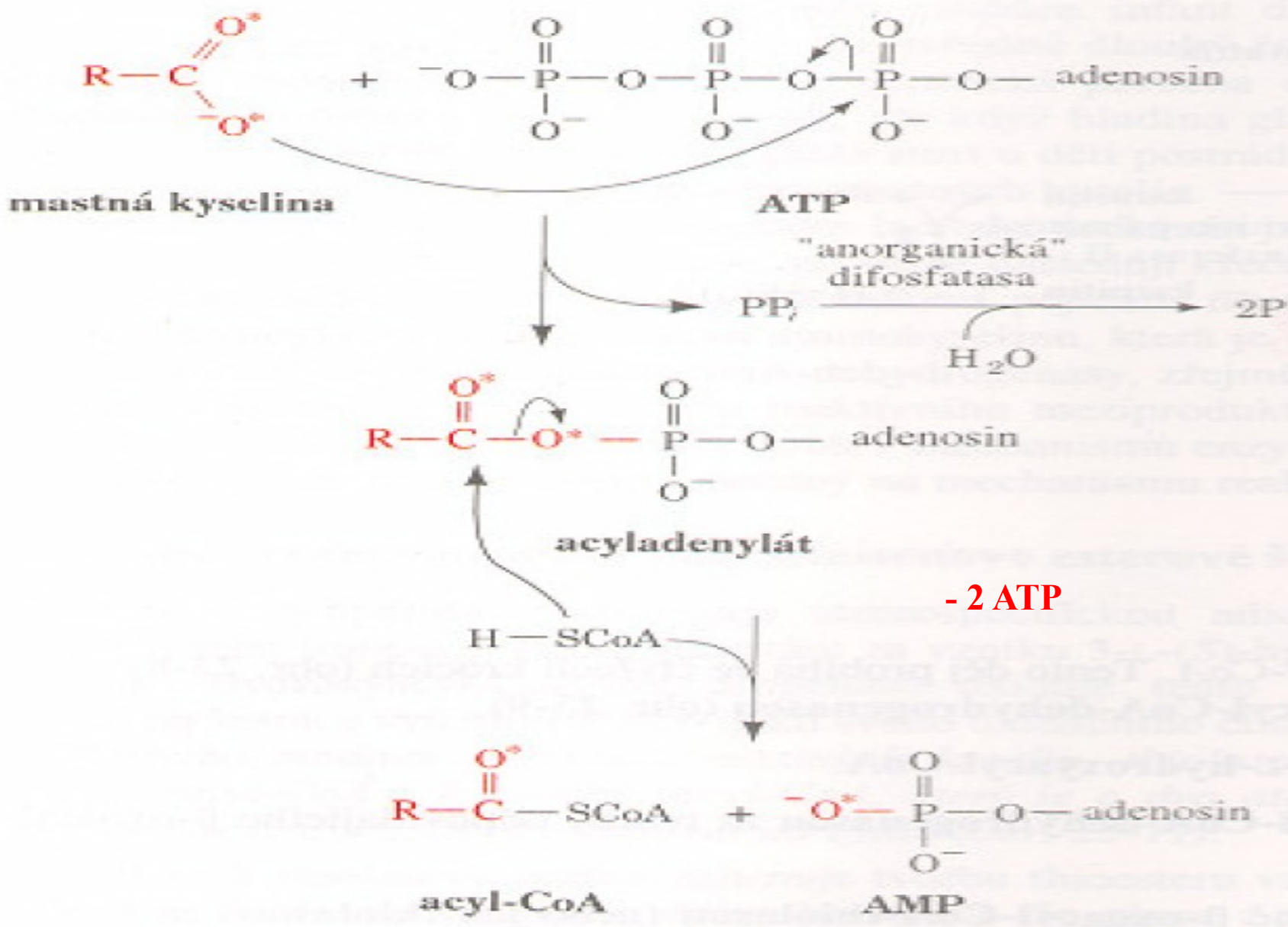
Odbourávání mastných kyselin

β oxidace

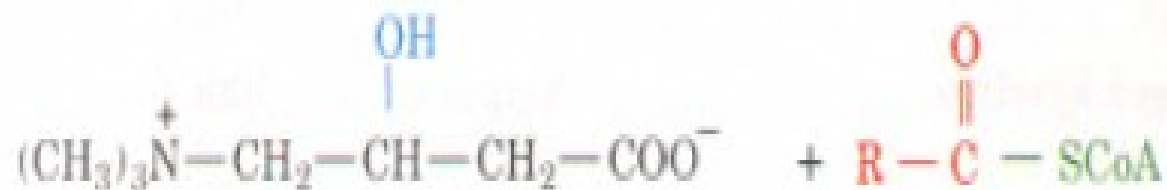
F.KNOOP 1909

F.LYNEN 1951

- Aktivace - mastné kyseliny malo reaktivní \rightarrow AcylCoA
- Lokalizace – zdroje AcylCoA v cytoplasmě \rightarrow β – oxidace mitochondrie
- Nenasycené mastné kyseliny
- Mastné kyseliny s lichým počtem C atomů

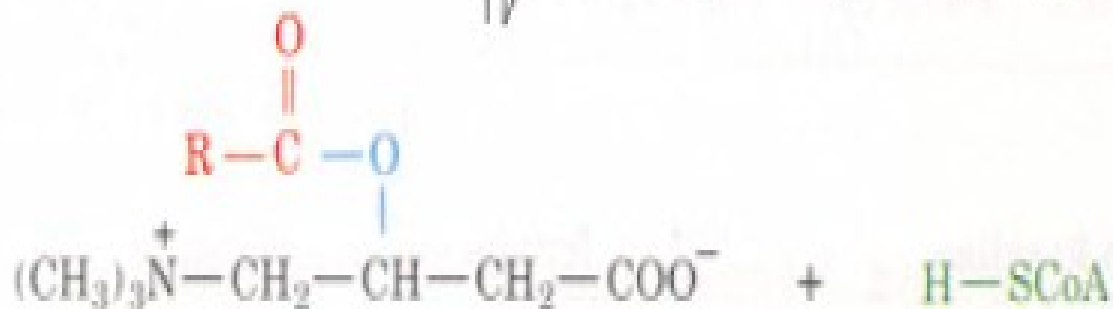


B. Transport RCOSCoA - karnitinový člunek



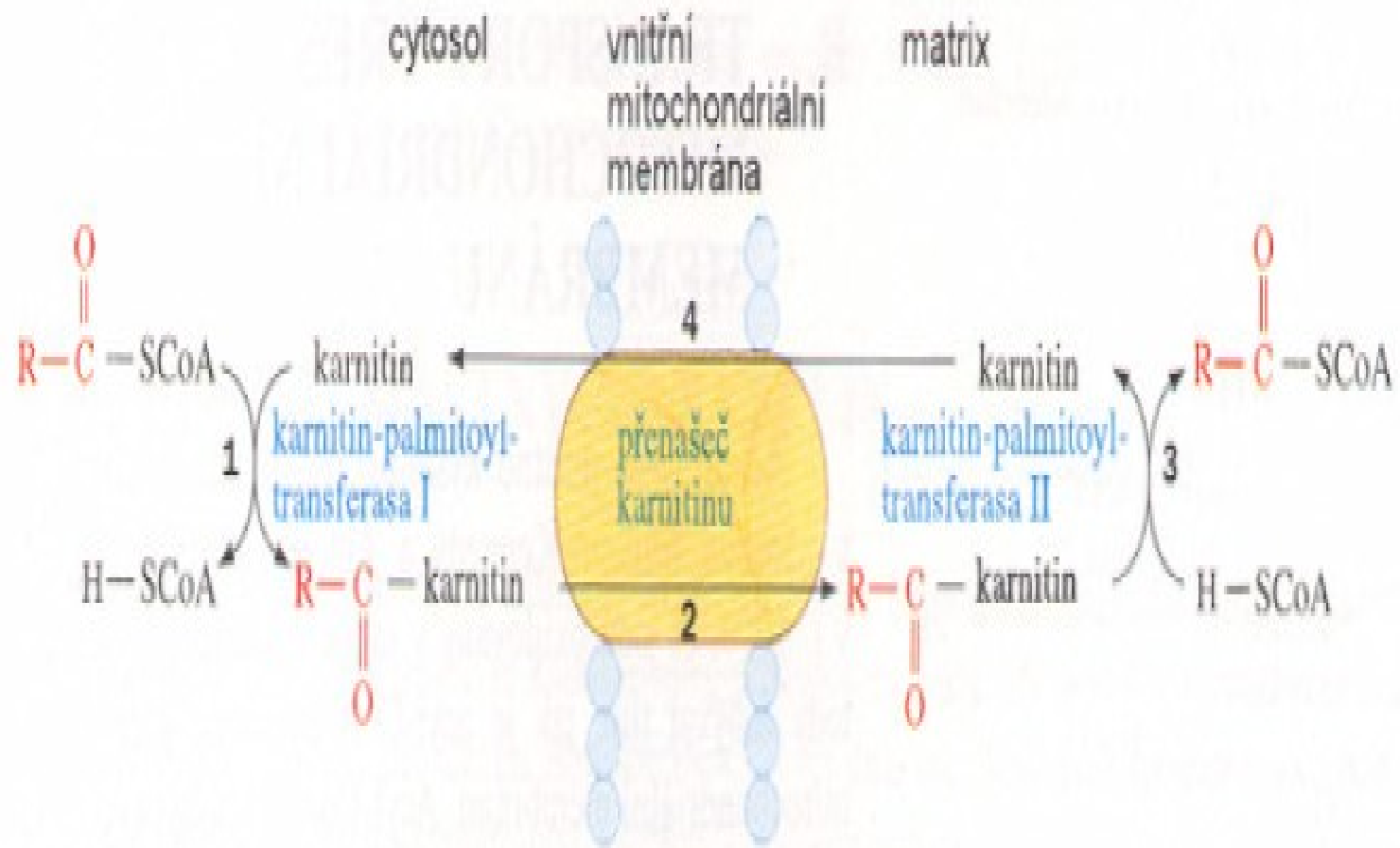
karnitin (4-trimethyl-
amino-3-hydroxybutyrát)

⇌ karnitin-palmitoyltransferasa

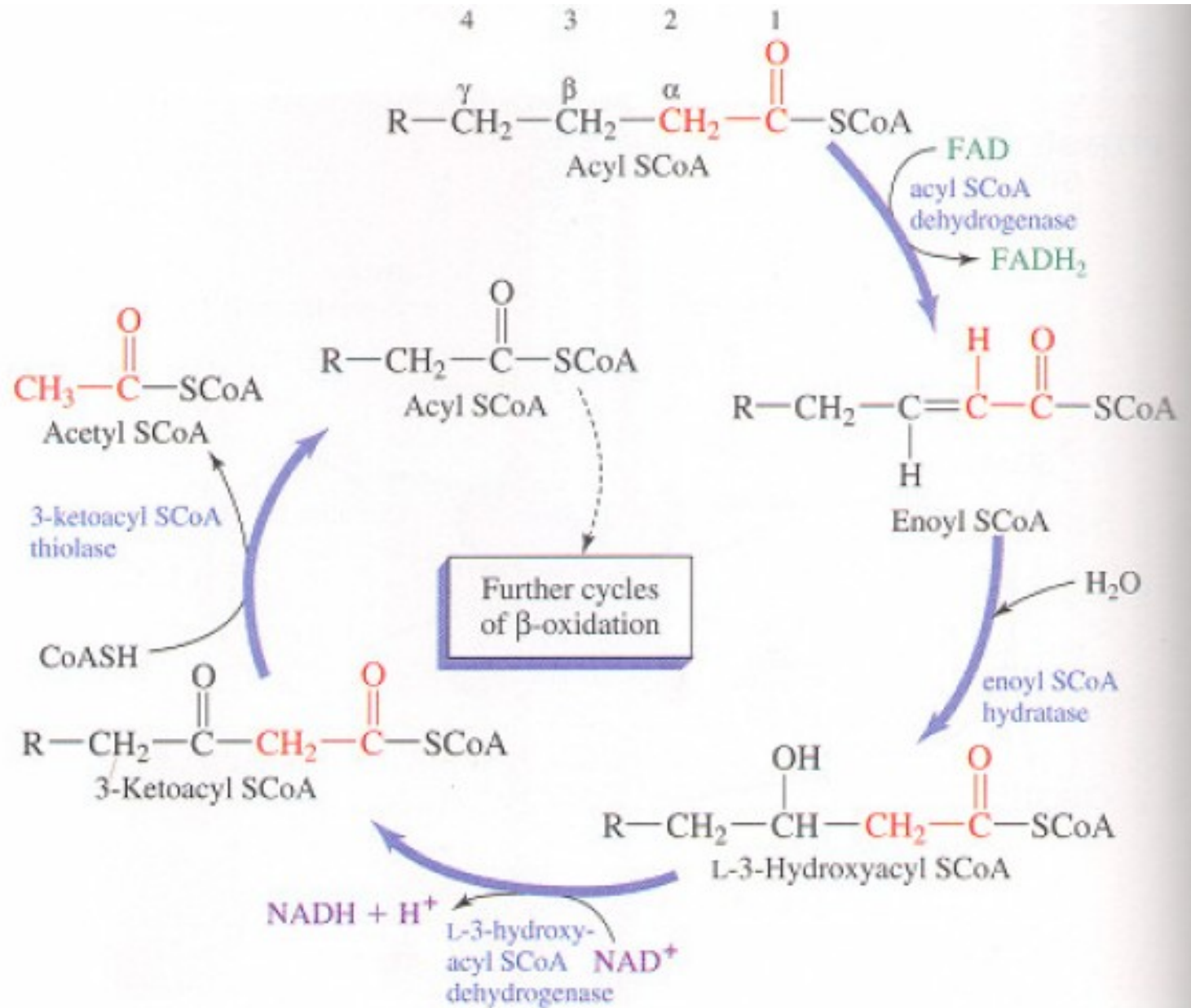


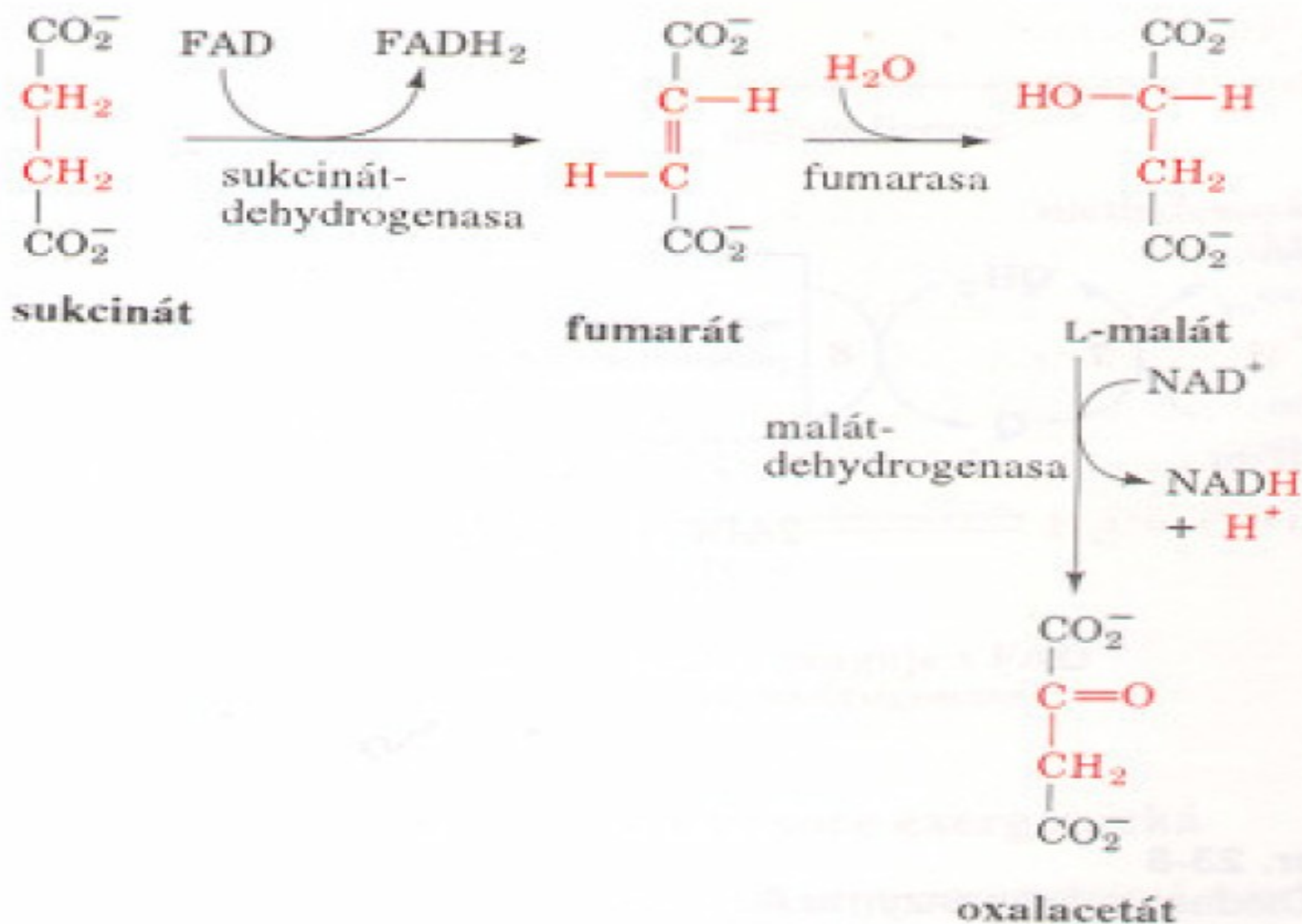
acylkarnitin

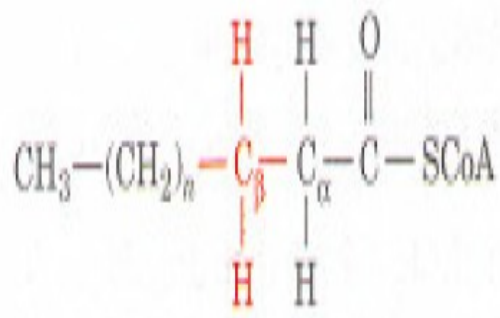
B. Transport $RCOSCoA$ - karnitinový člunek



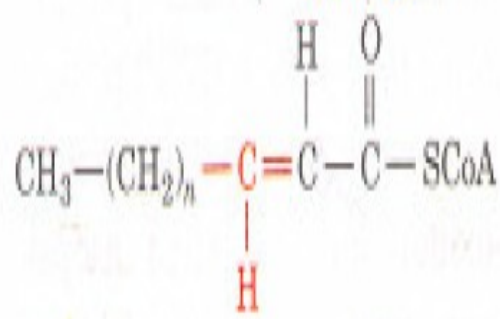
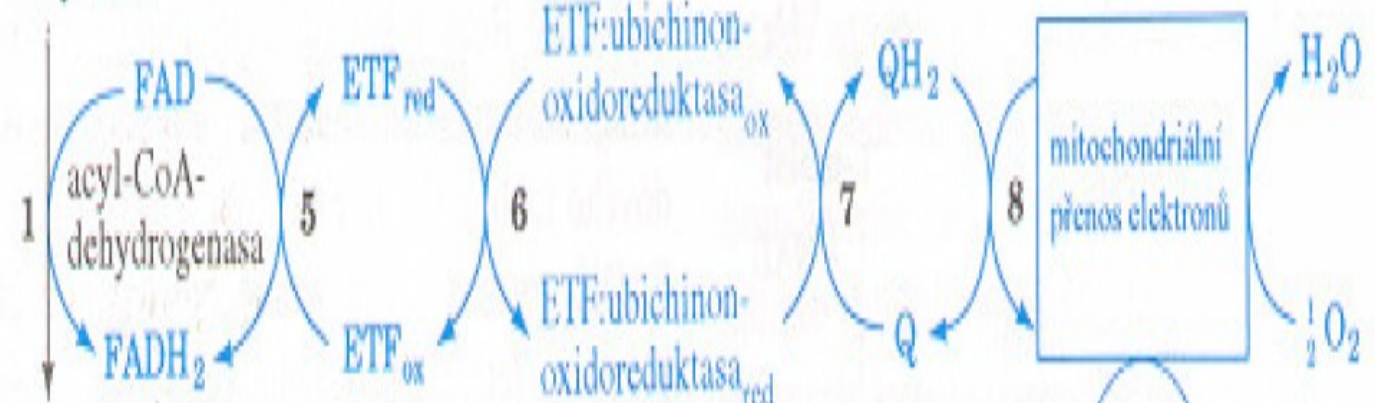
C. β oxidace







acyl-CoA

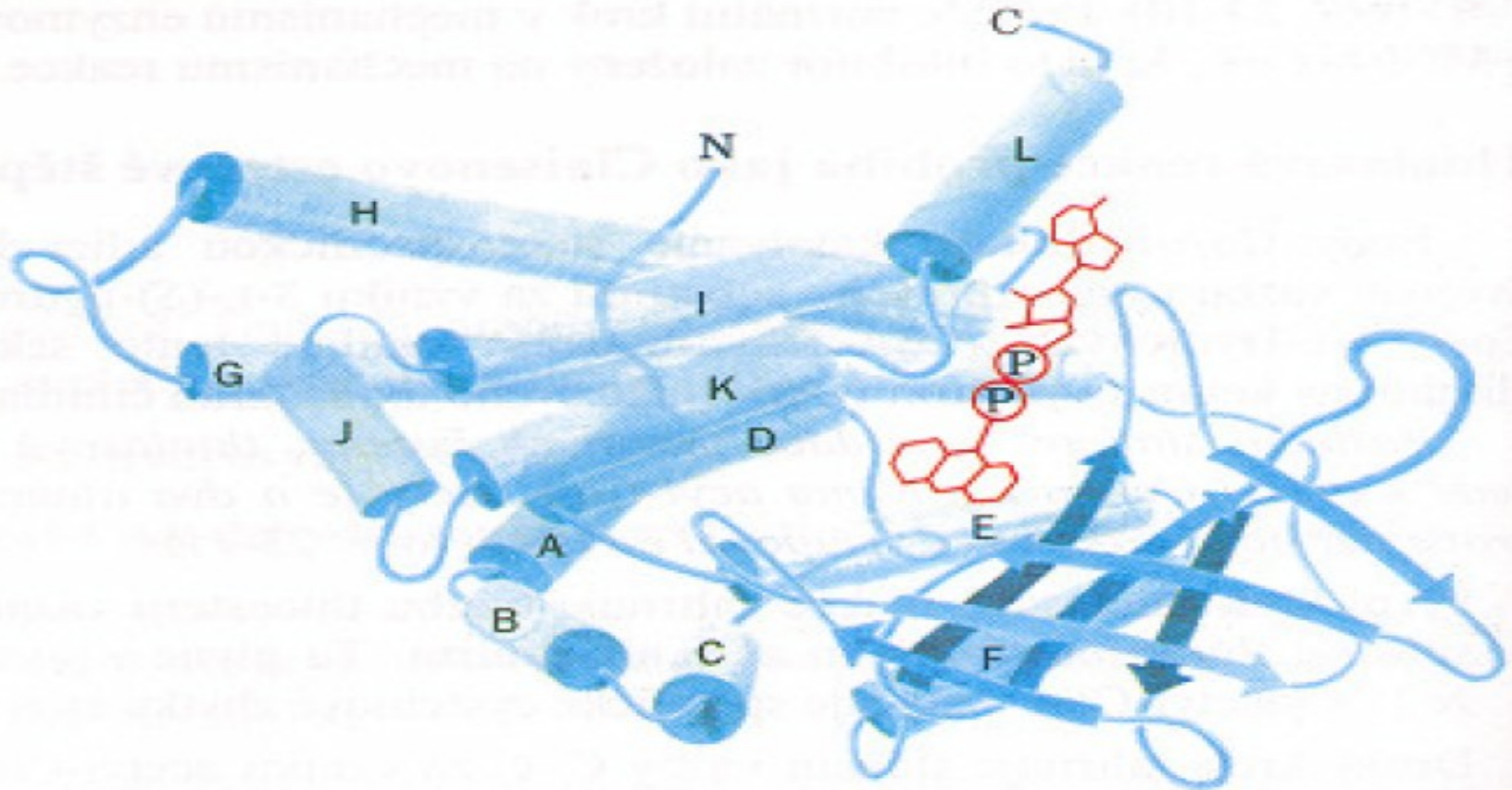


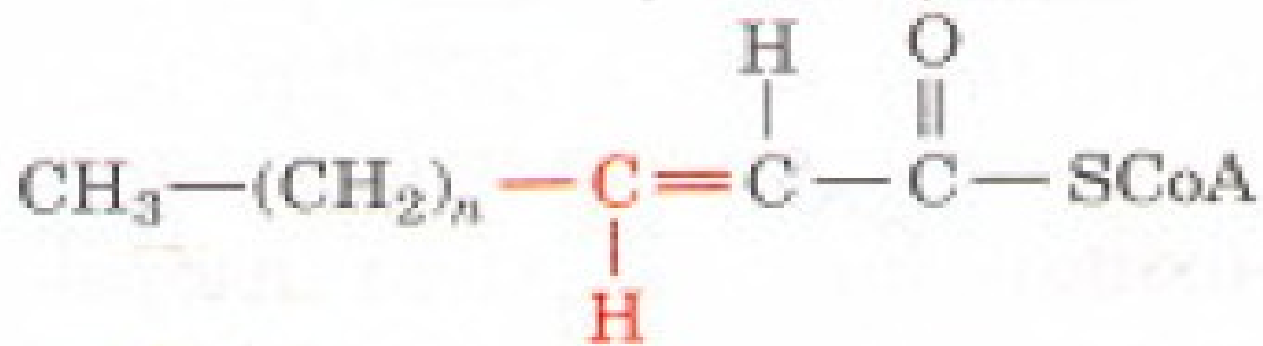
2ADP + 2P_i → 2ATP

Acyl-CoA DH

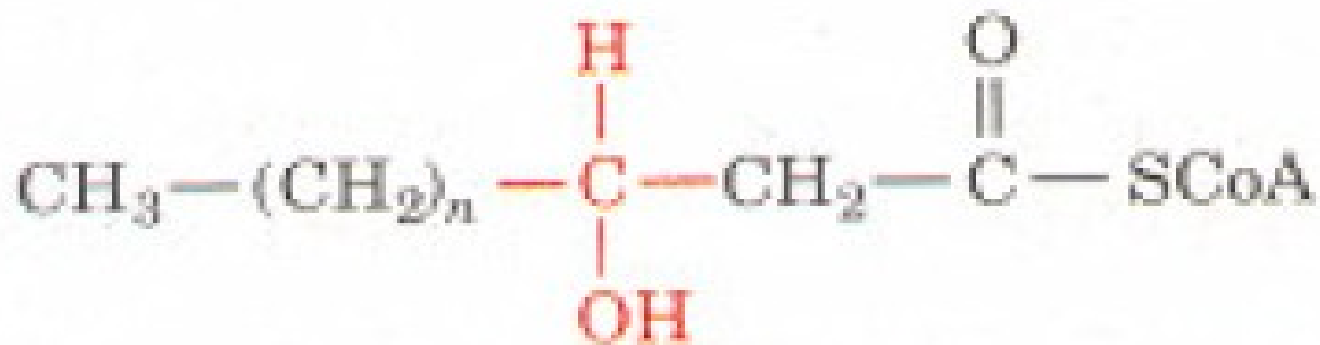
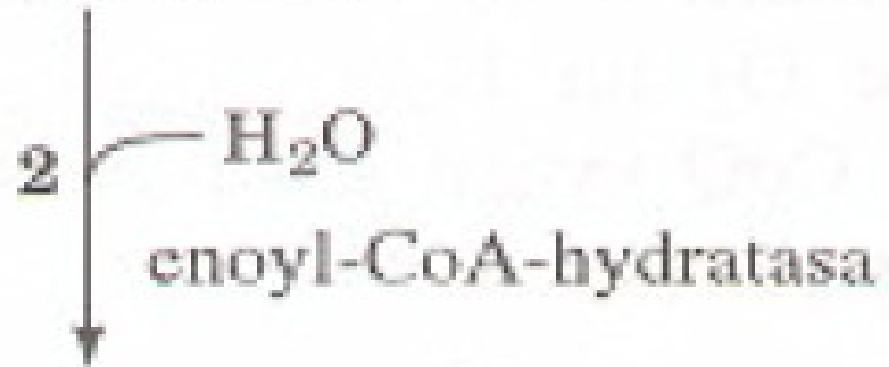
nedostatek

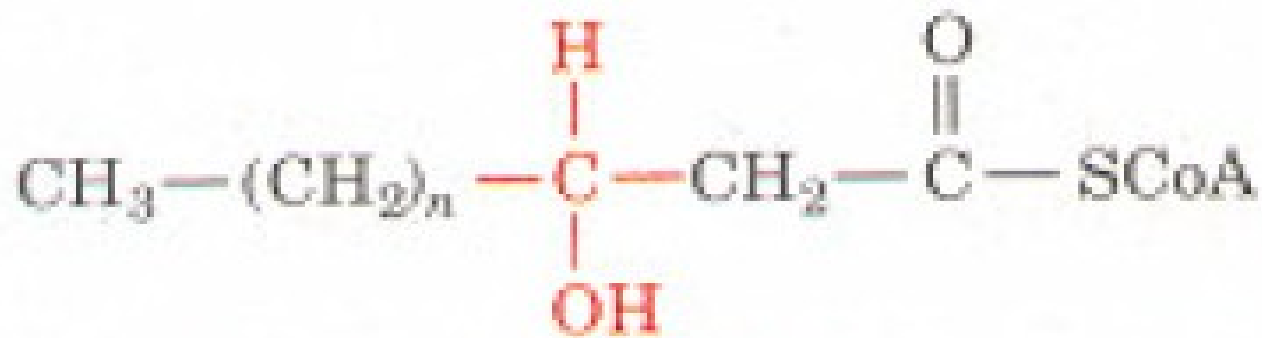
syndrom náhlého dětského úmrtí (sudden infant death syndrome, SIDS)



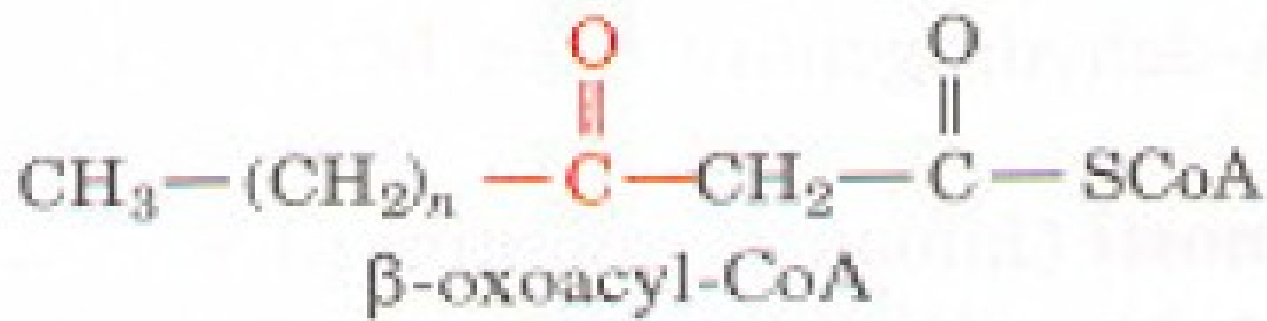
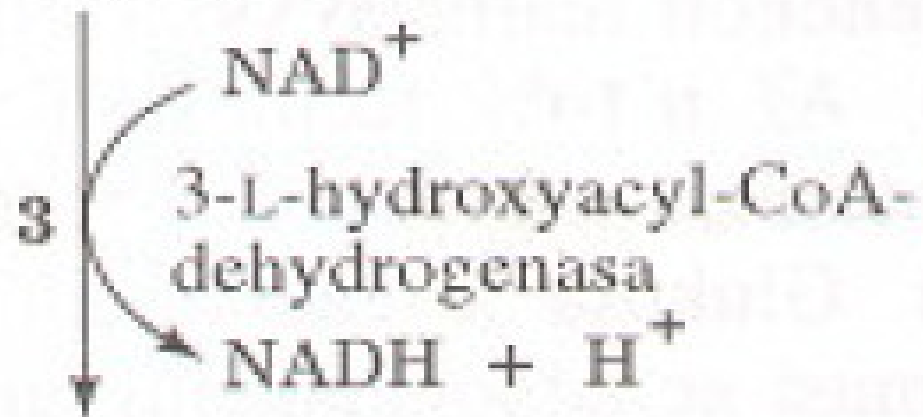


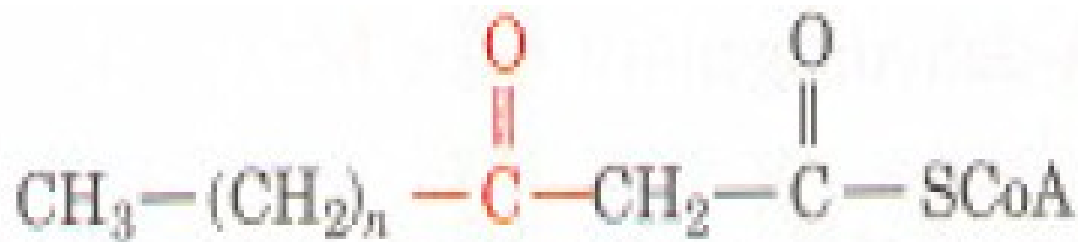
trans- Δ^2 -enoyl-CoA





3-L-hydroxyacyl-CoA



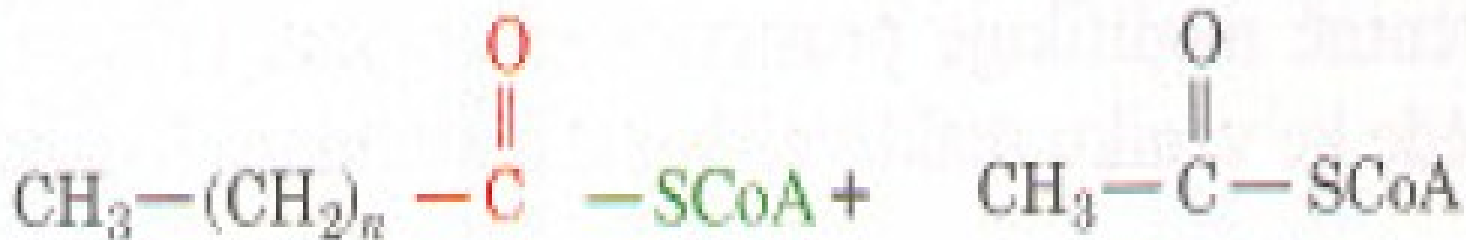


β -oxoacyl-CoA



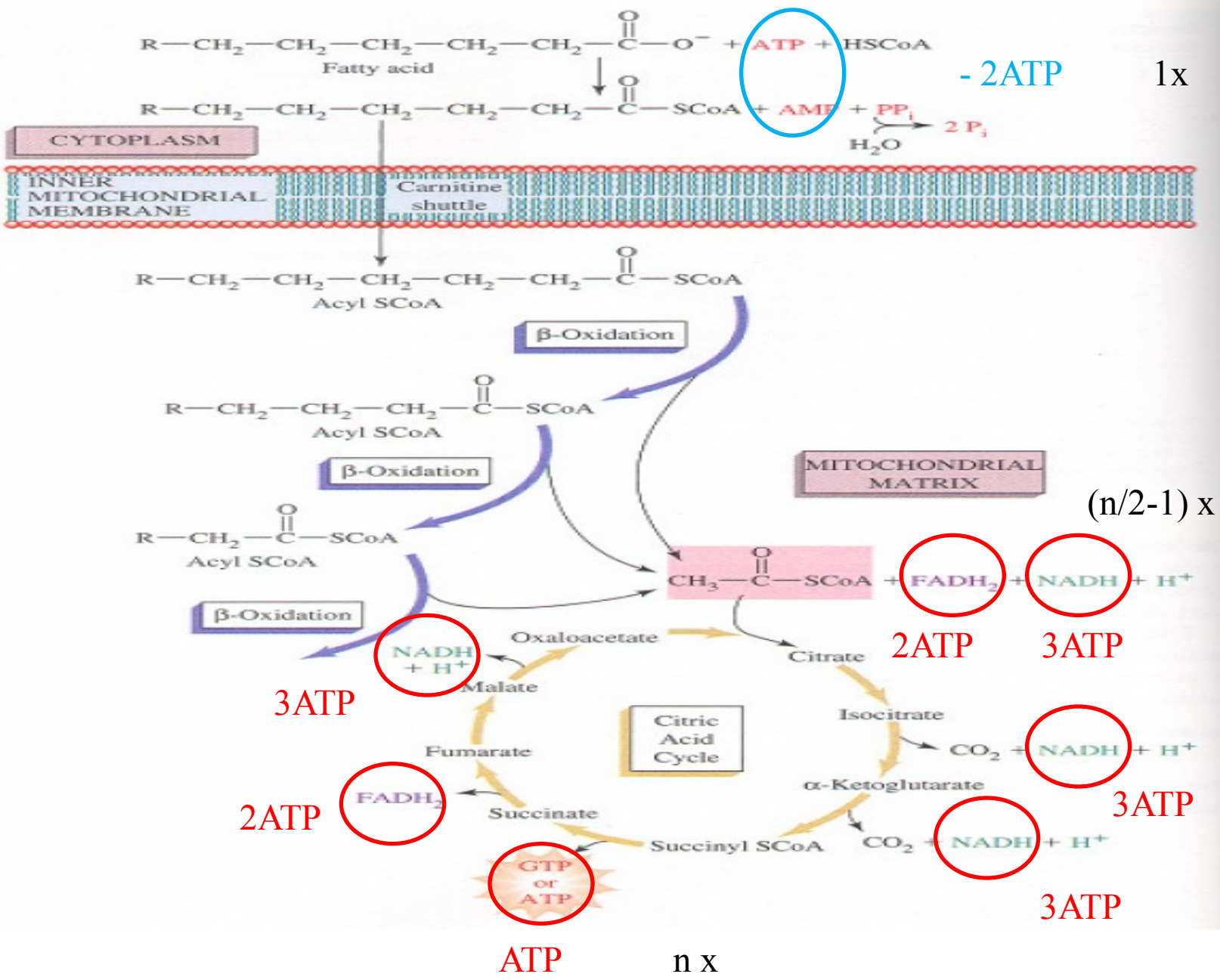
CoASH

β -oxoacyl-CoA-thiolasa



acyl-CoA
(kratší o 2C)

acetyl-CoA

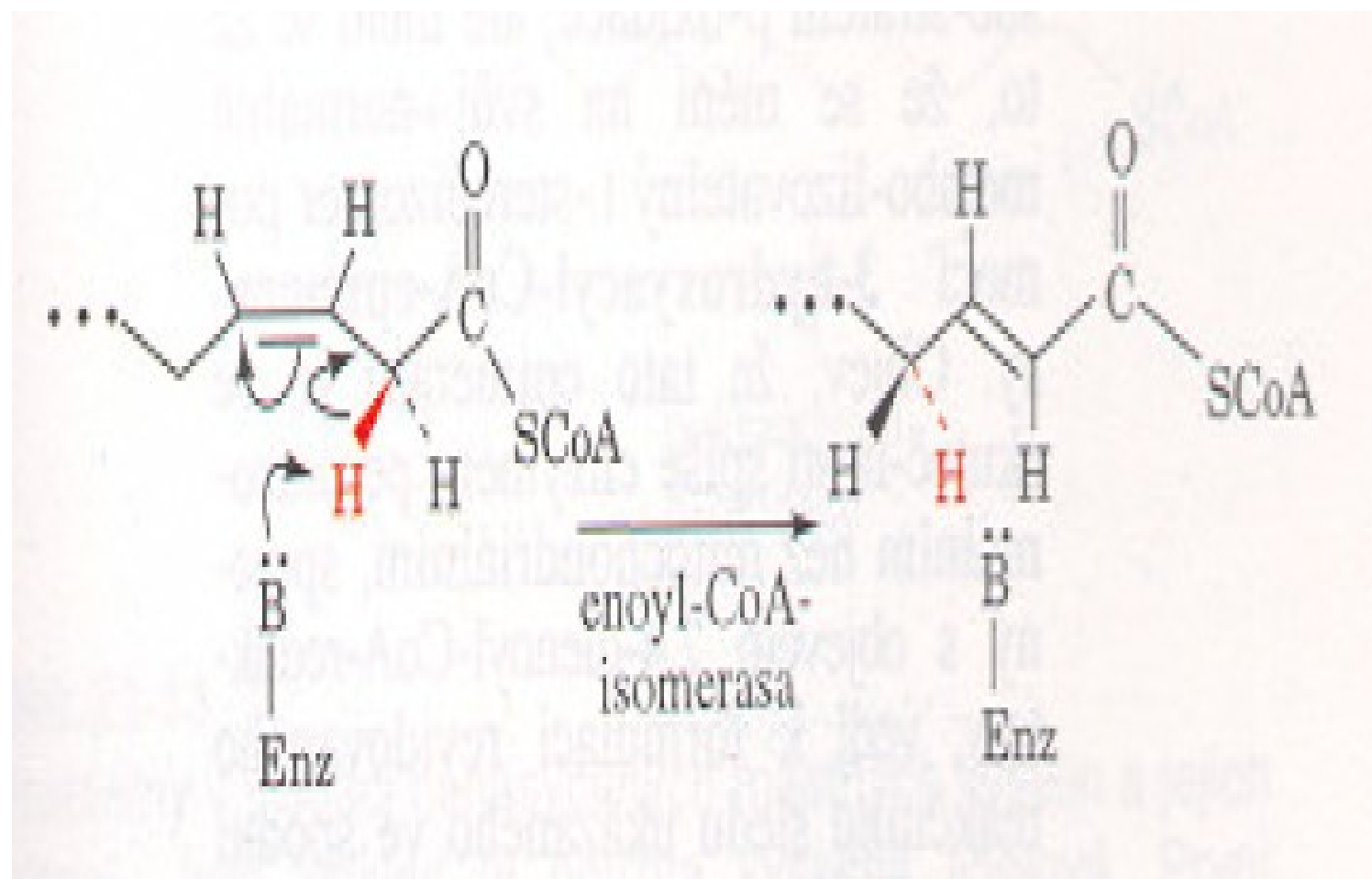


Bilance β oxidace :

1. cyklus - 1 FADH₂ (2 ATP) + 1 NADH (3 ATP) - 5 ATP
acetylCoA (citrátový cyklus) - 12 ATP

na C₁₆ - 7 x β oxidace + 8 x citrátový cyklus - aktivace
(7 x 5) + (8 x 12) - 2 ATP = 129 ATP

Odbourávání nenasycených mastných kyselin





three cycles of β -oxidation



enoyl-CoA isomerase



complete β -oxidation cycle



acyl-CoA dehydrogenase



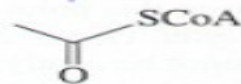
$\text{NADPH} + \text{H}^+ \rightarrow \text{NADP}^+$
2,4-dienoyl-CoA reductase

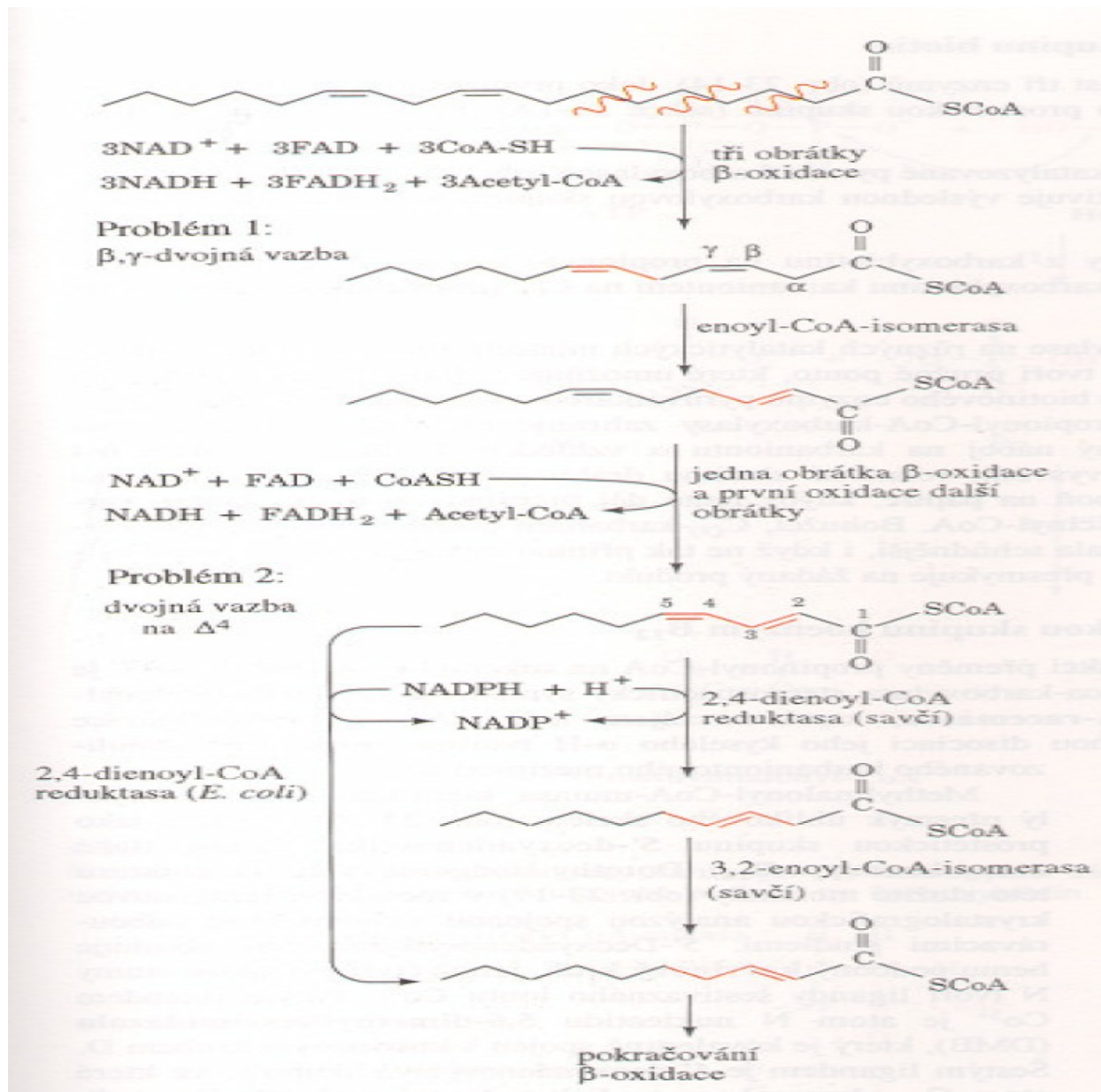


enoyl-CoA isomerase

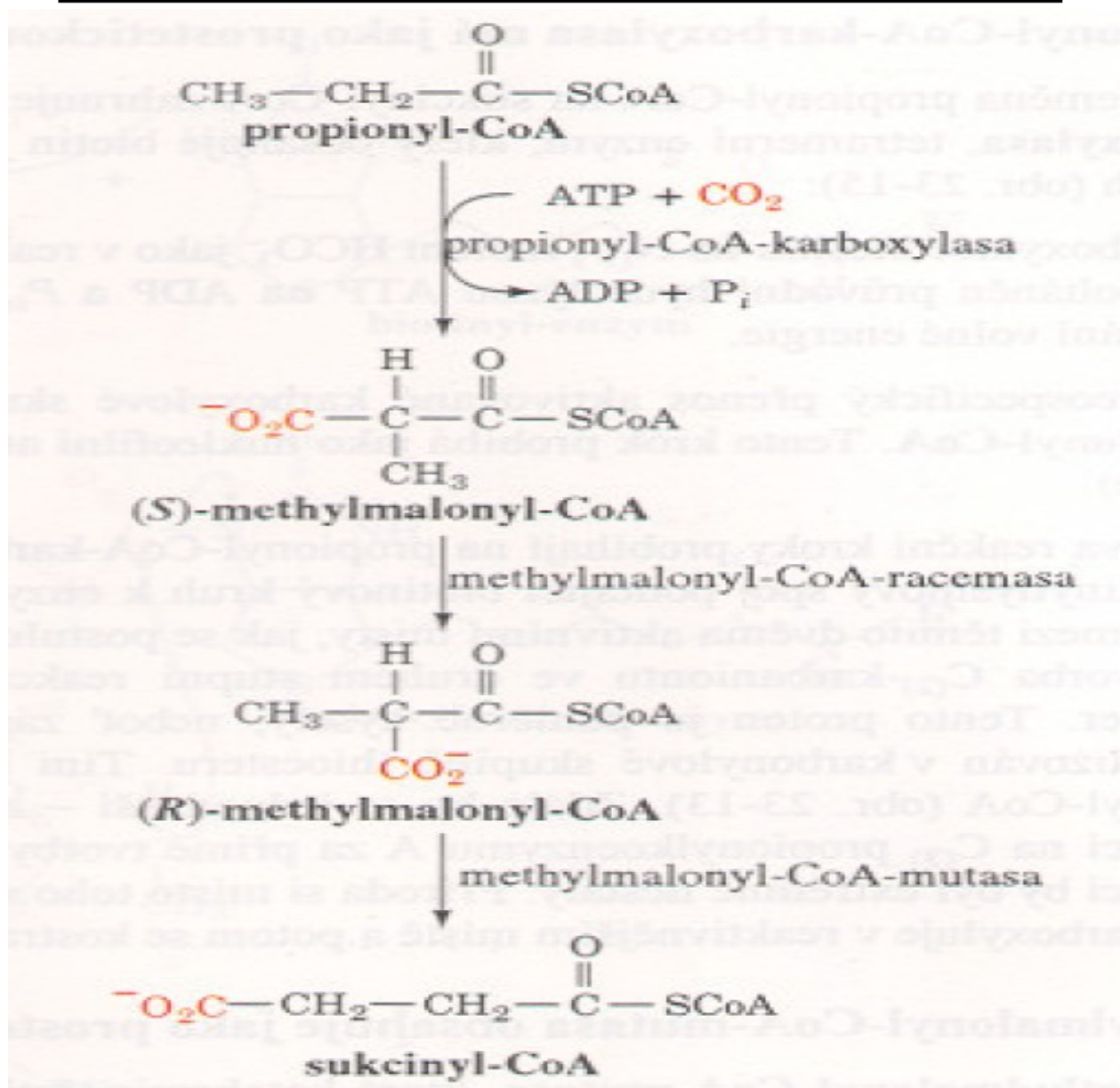


three cycles of β -oxidation

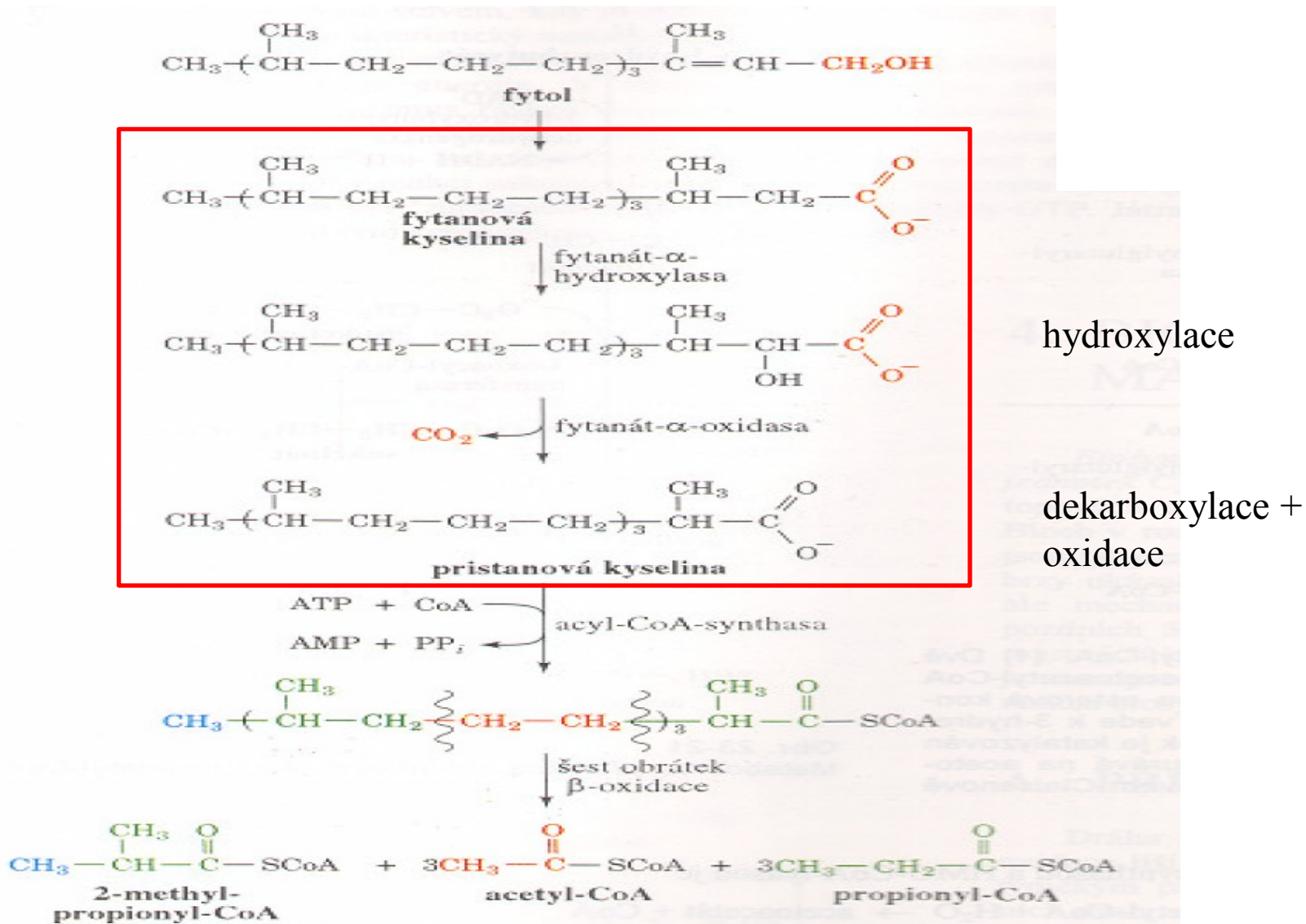


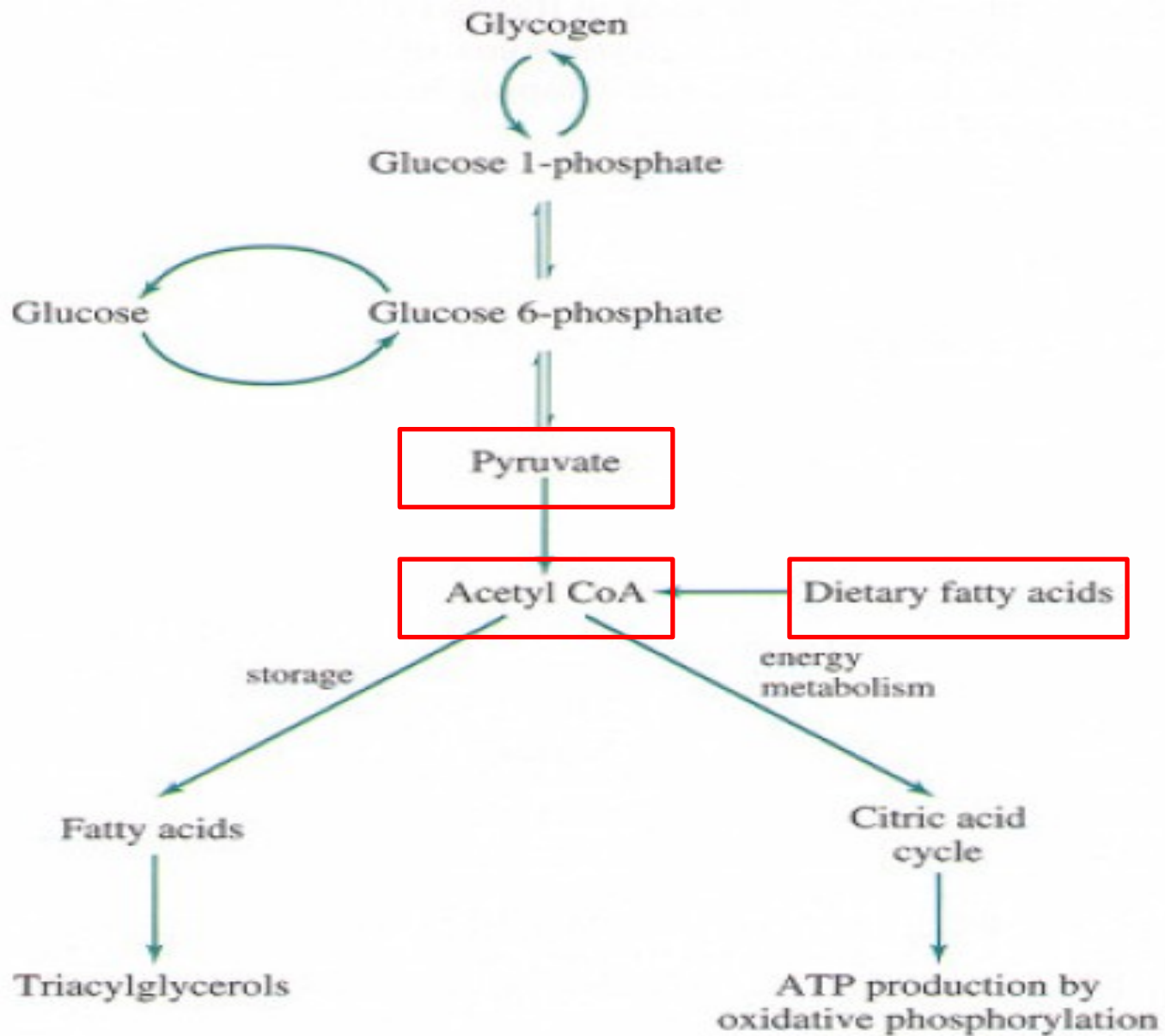


Odbourávání mastných kyselin s lichým počtem C atomů

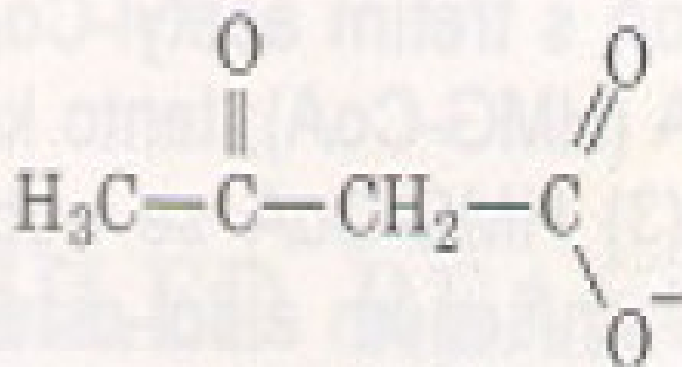


α -oxidace

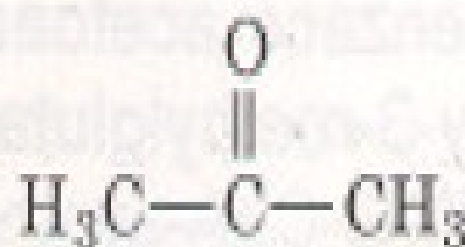




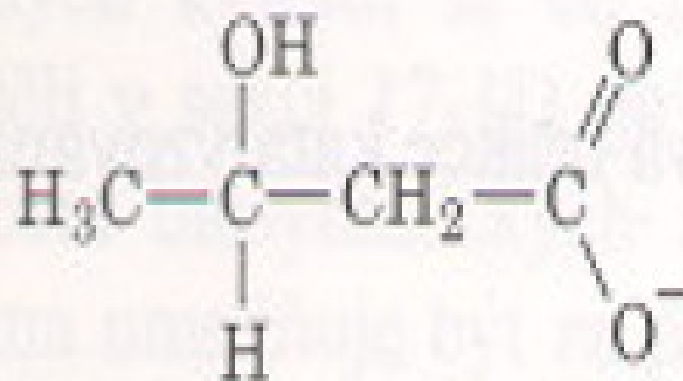
Ketonové látky



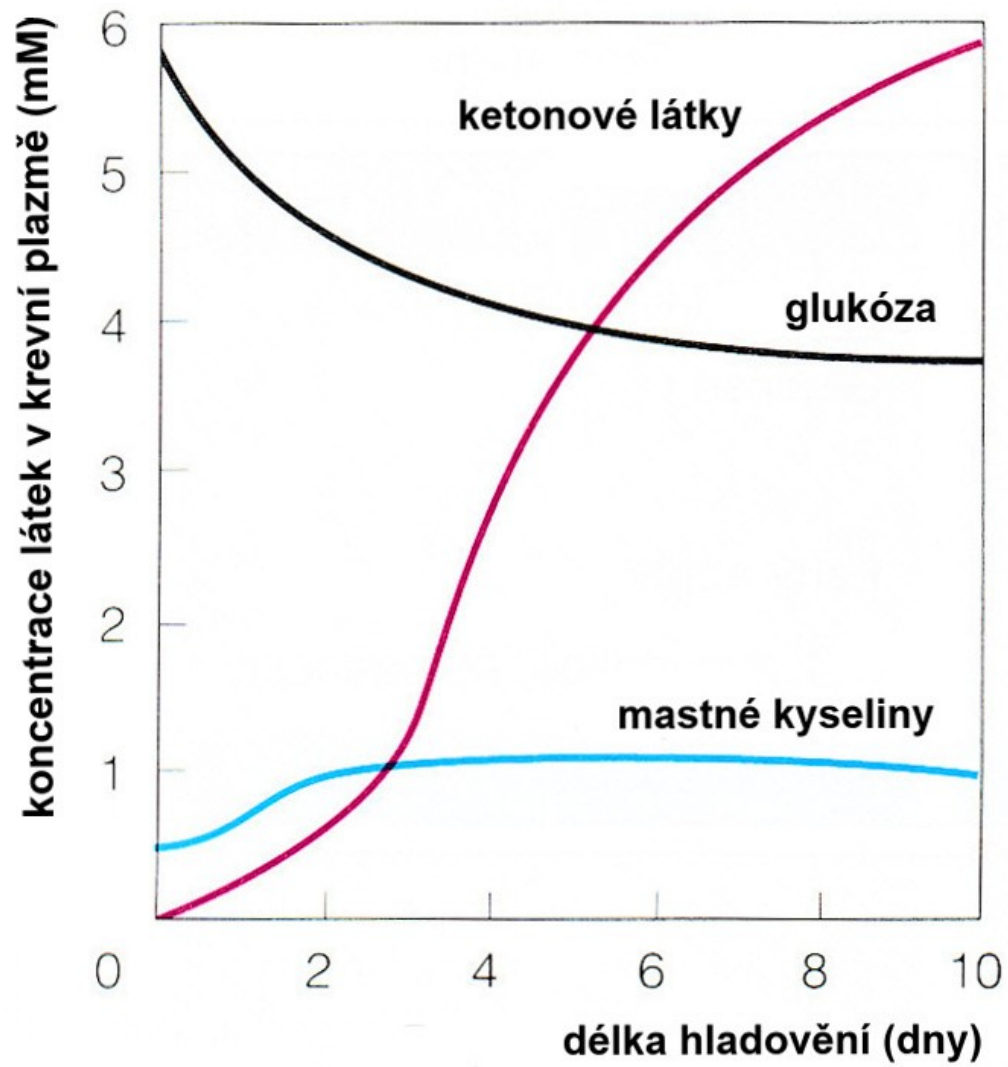
acetoacetát



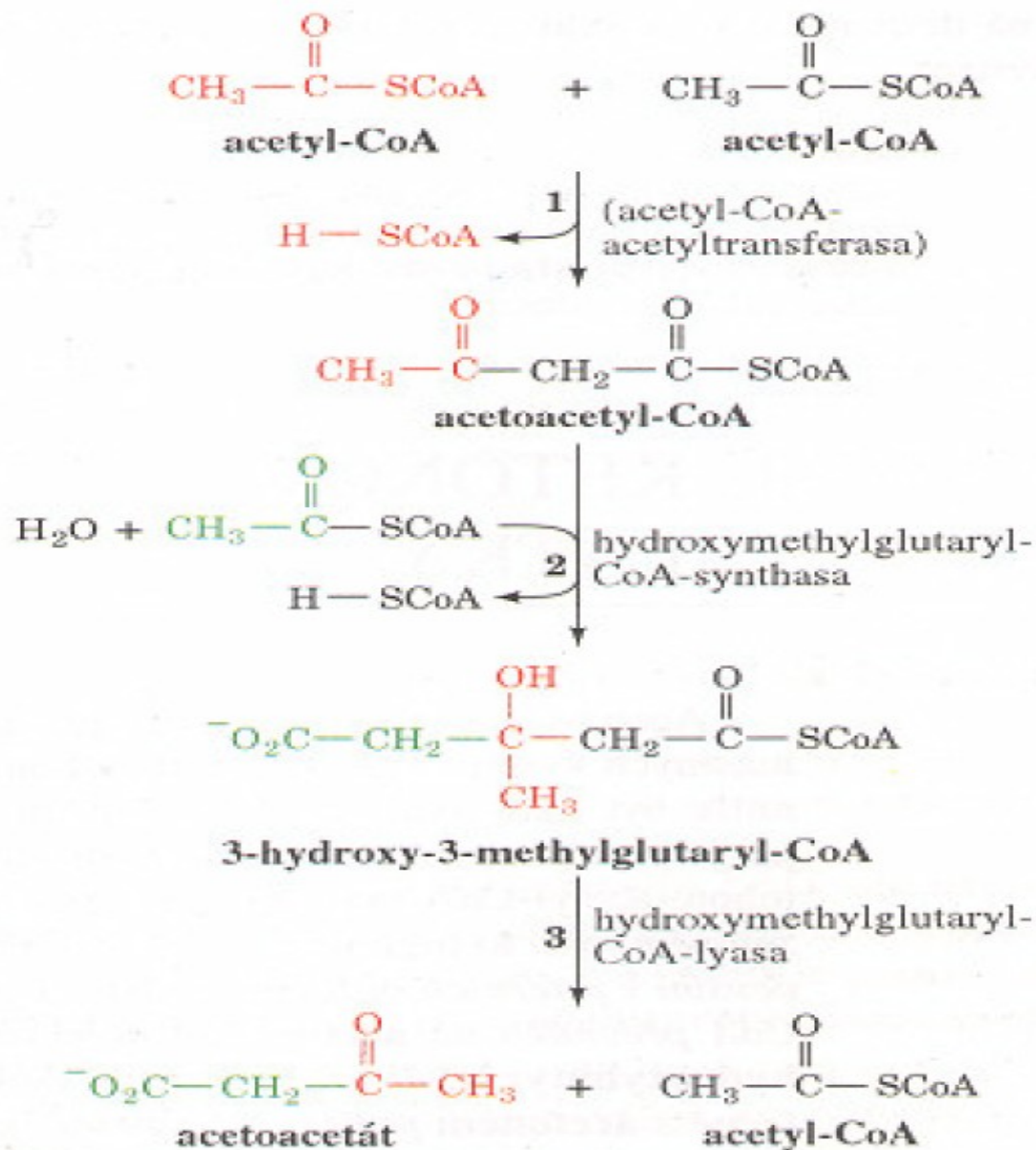
aceton



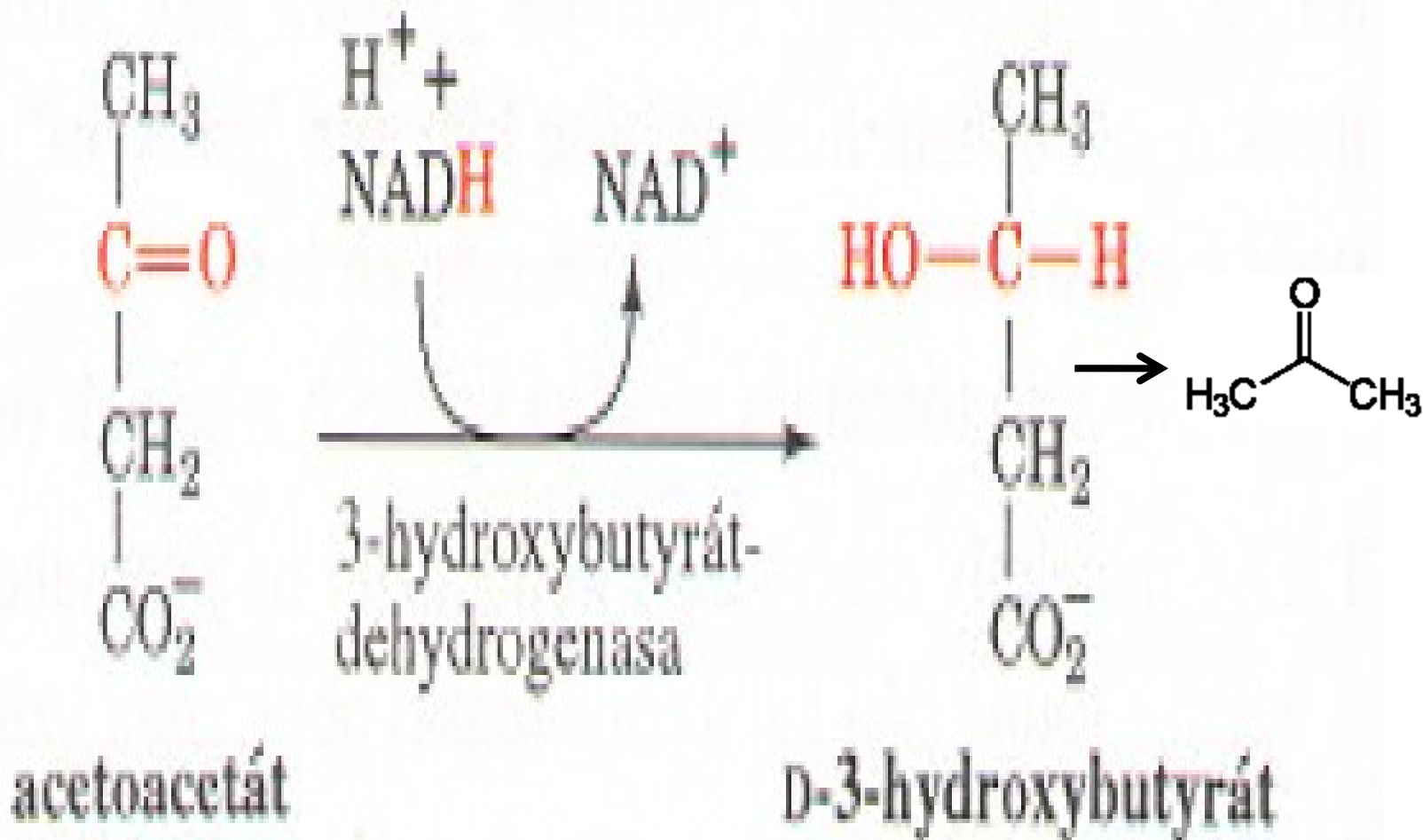
D-3-hydroxybutyrát



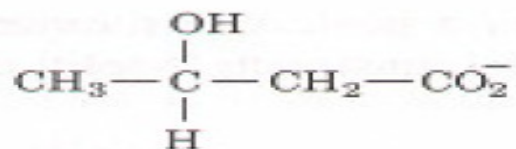
Ketonové látky



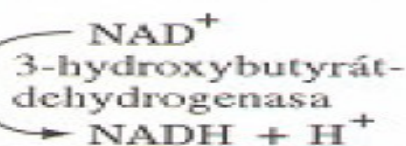
Ketonové látky



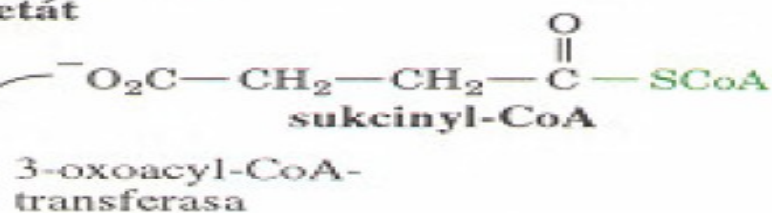
Ketonové látky



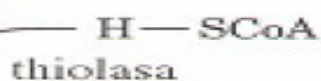
D-3-hydroxybutyrát



acetoacetát

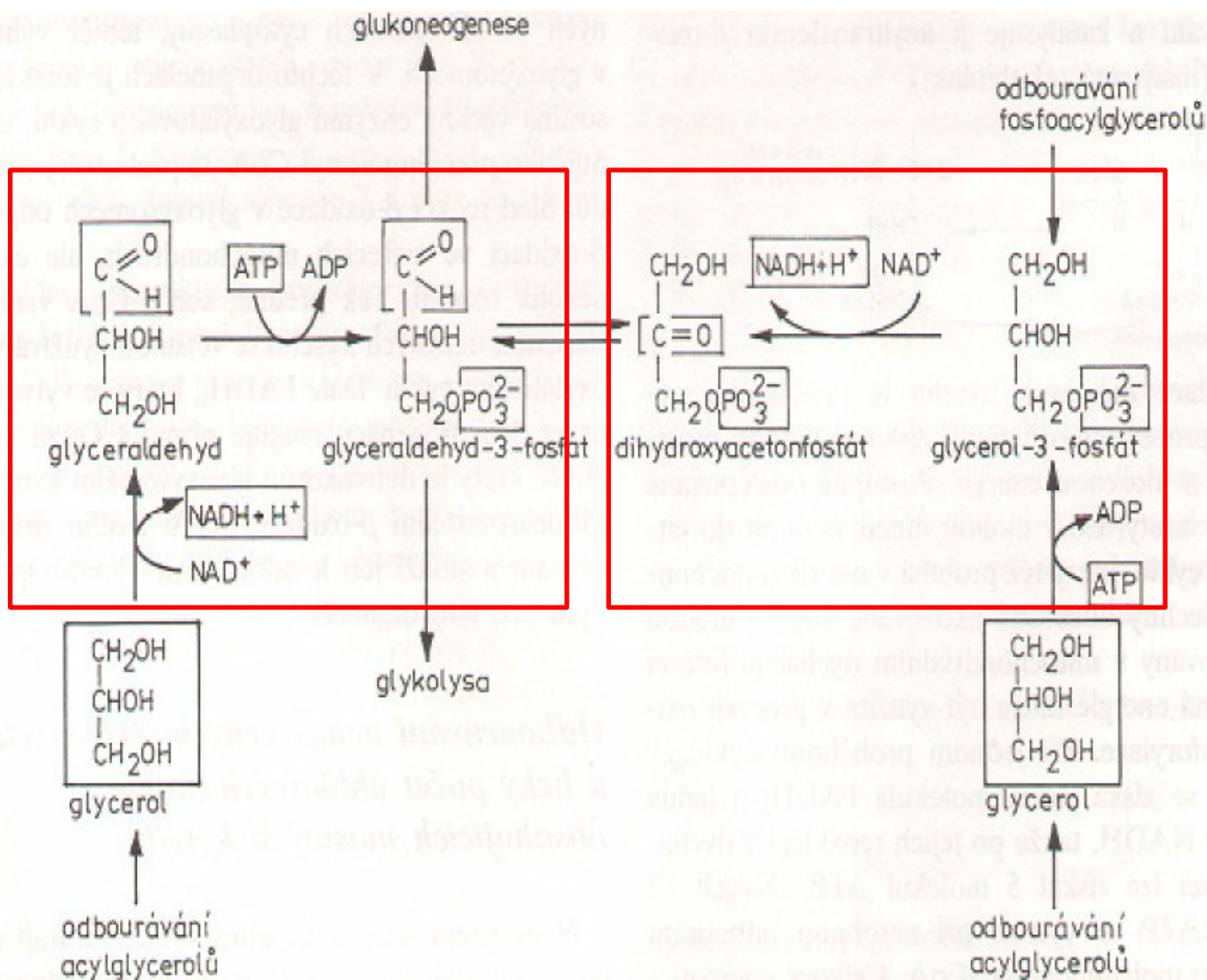


acetoacetyl-CoA

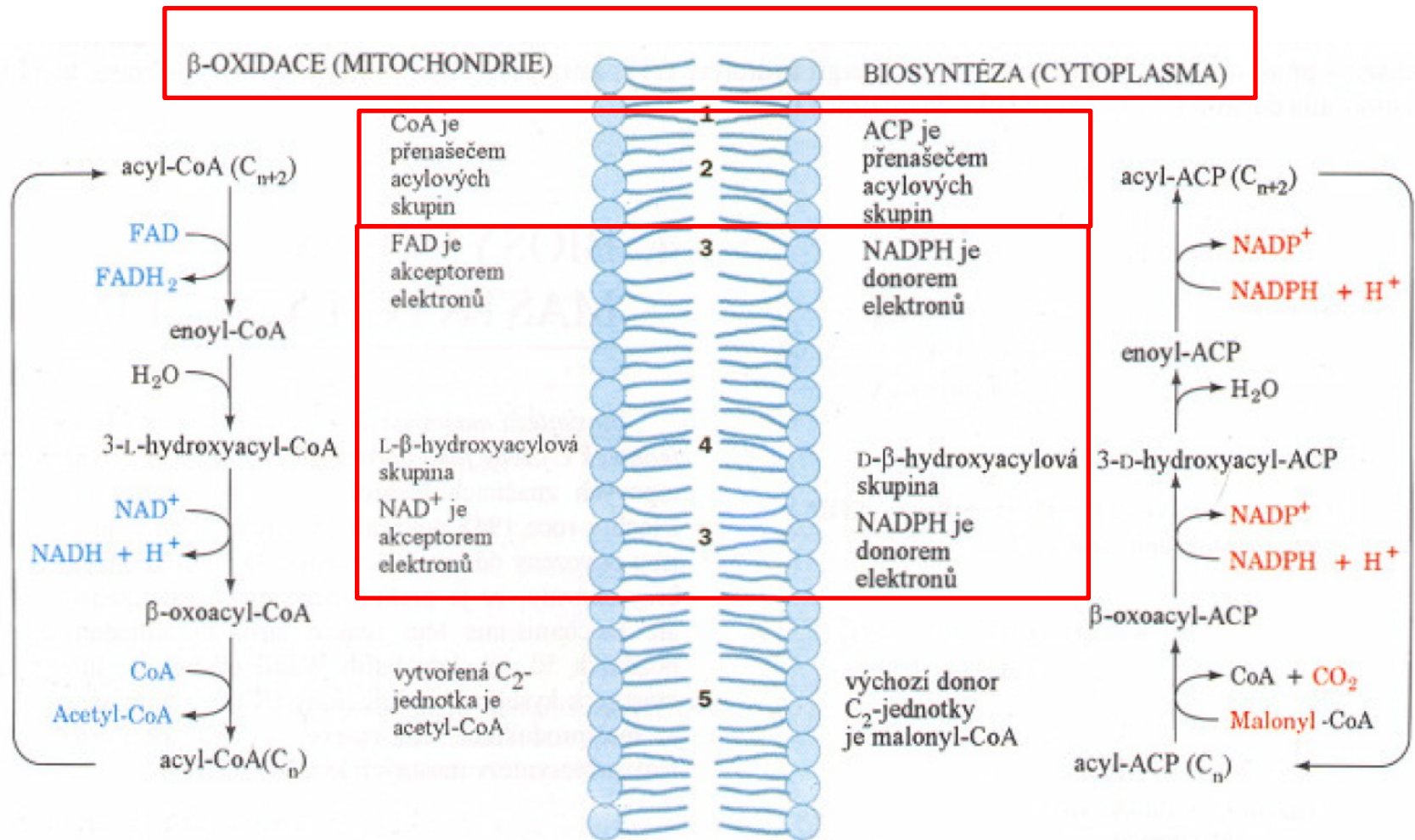


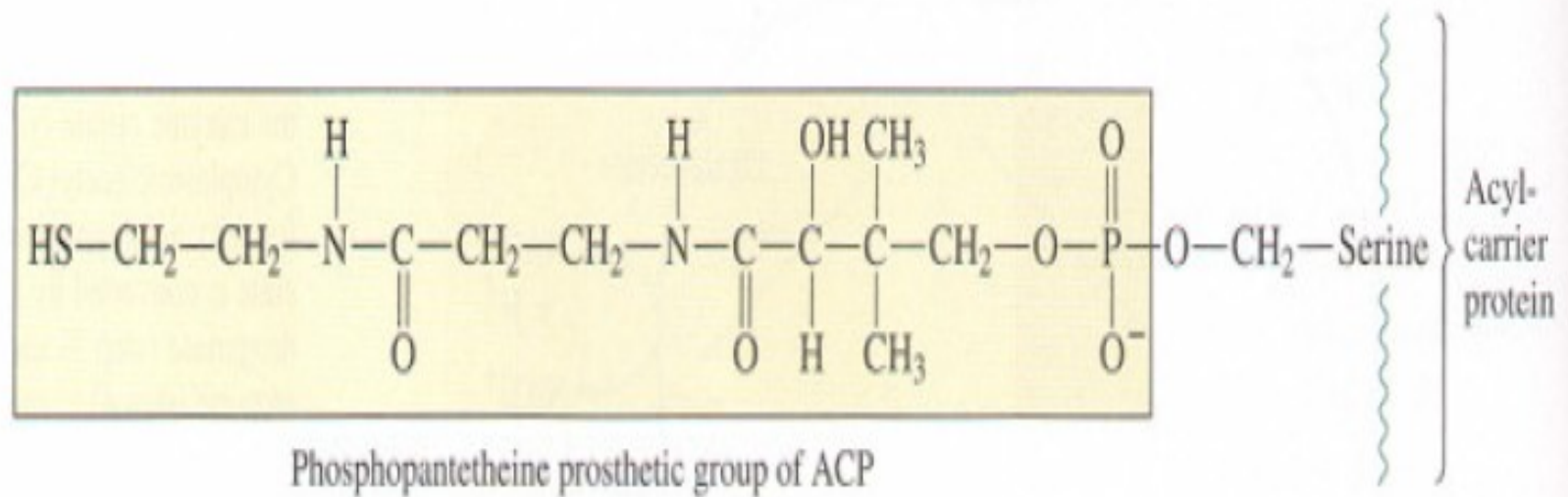
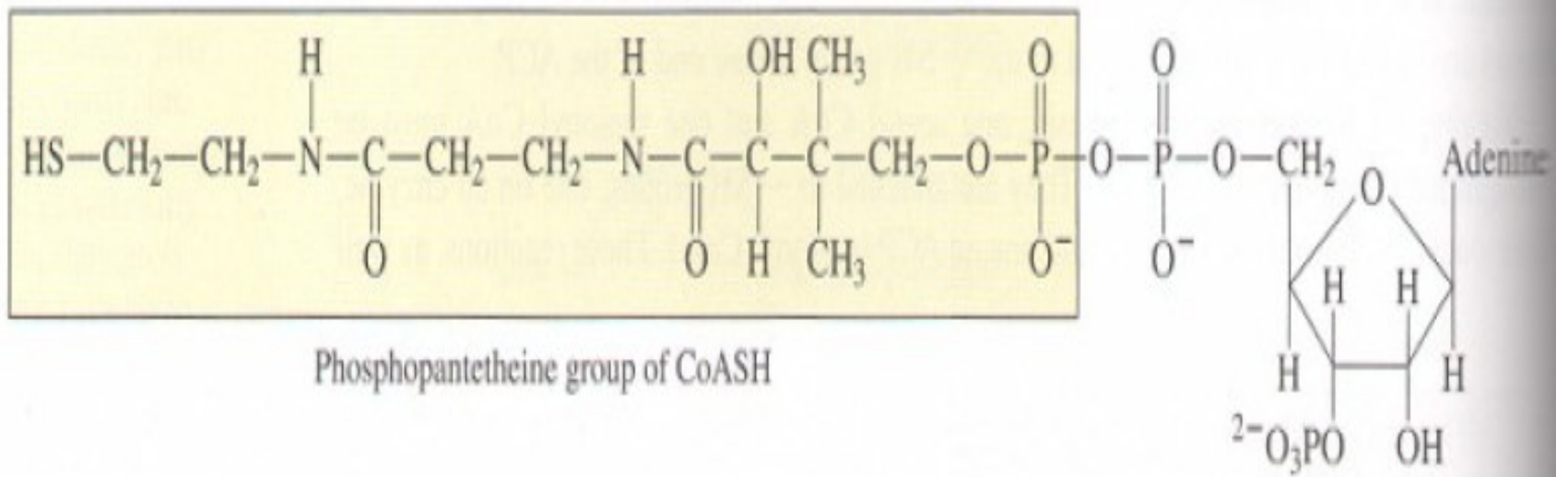
acetyl-CoA

Metabolismus glycerolu



Metabolismus versus biosyntéza MK

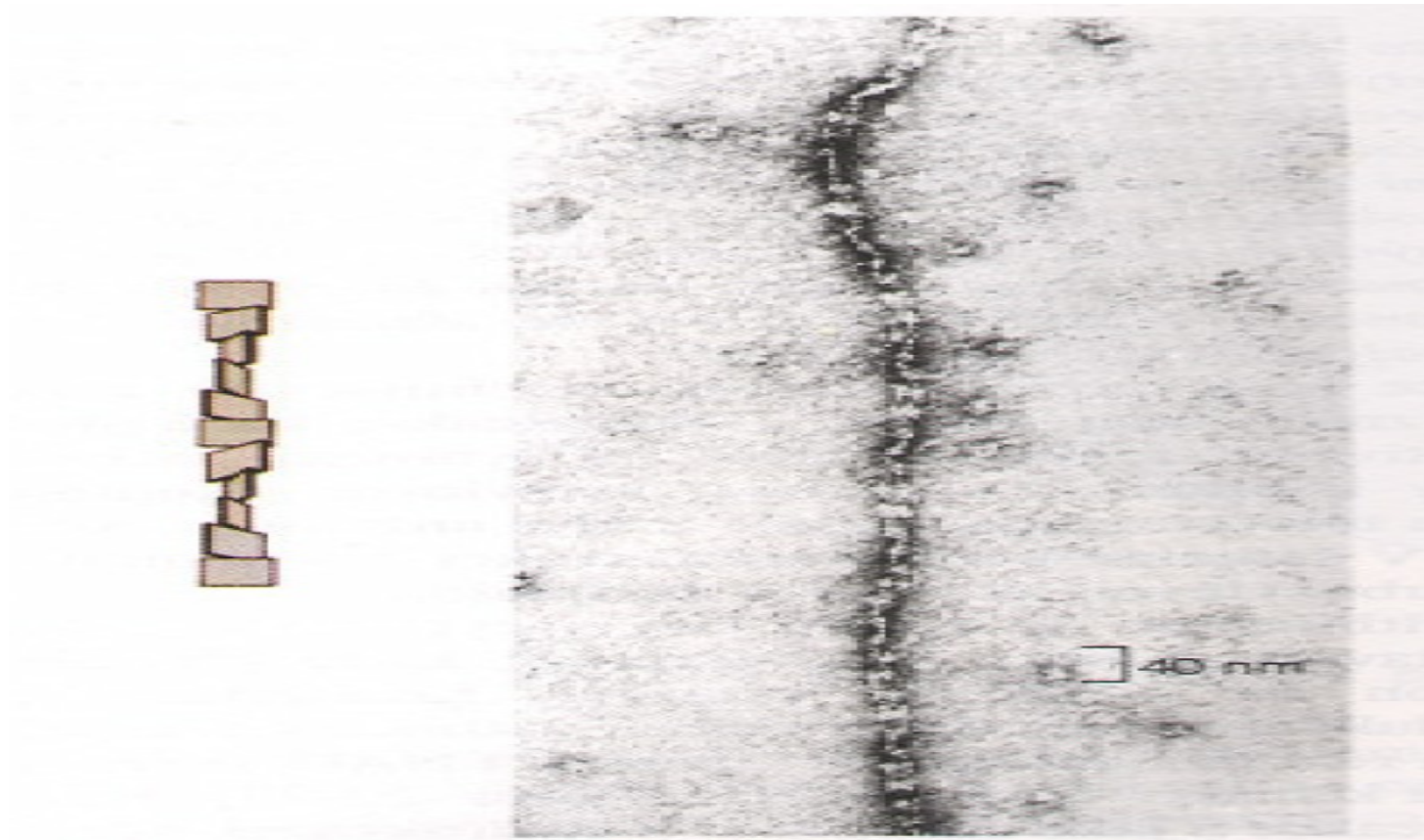




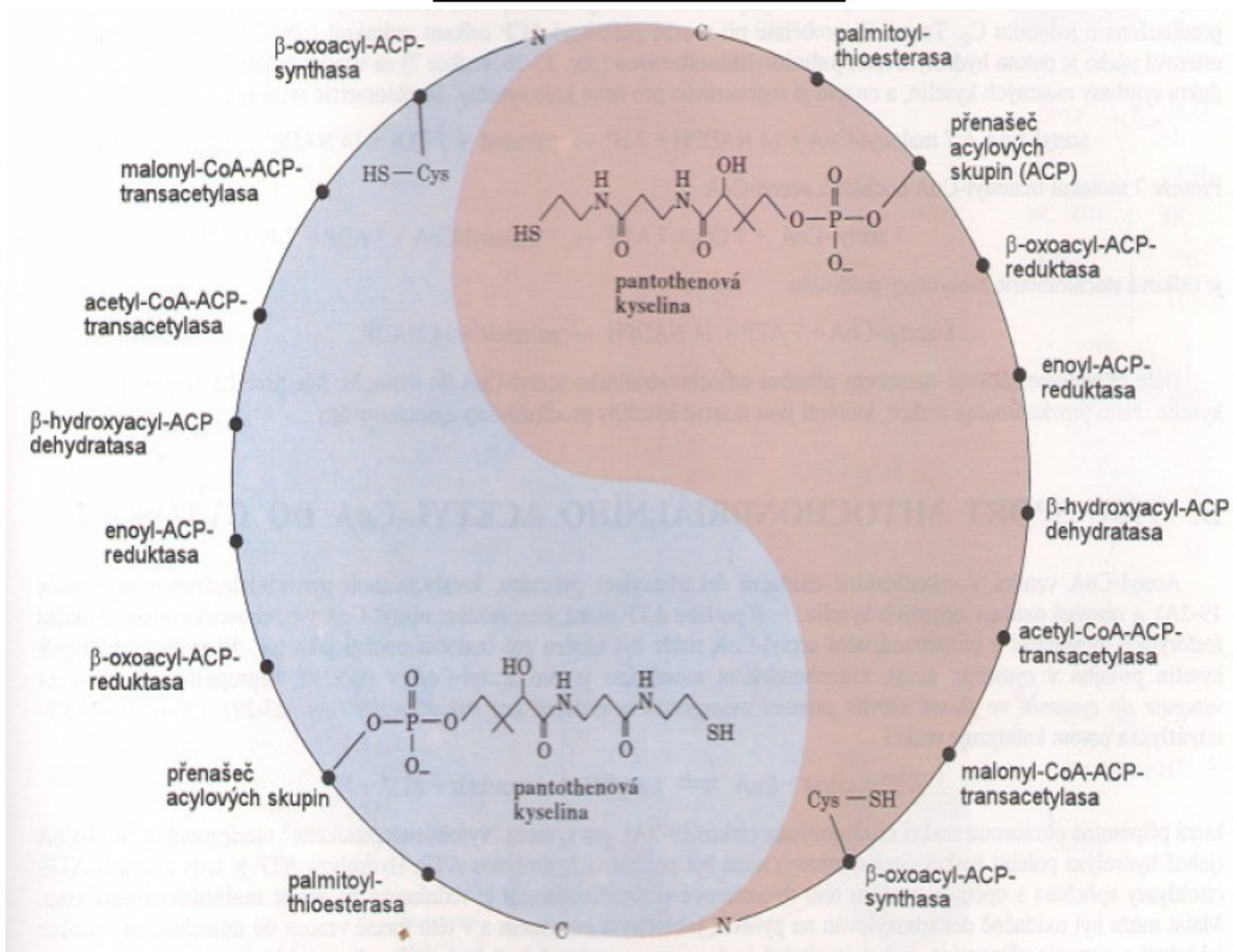
Biosyntéza mastných kyselin

- Aktivace - AcylCoA na MaCoA
- Vlastní syntéza – multienzymový komplex syntáza mastných kyselin -16 C
- Uvolnění a aktivace k.palmitové – syntéza lipidů
- Prodlužování řetězce mastné kyseliny
- Syntéza nenasycené mastné kyseliny
- Lokalizace zdrojů AcetylCoA v mitochondriích → transport do cytosolu

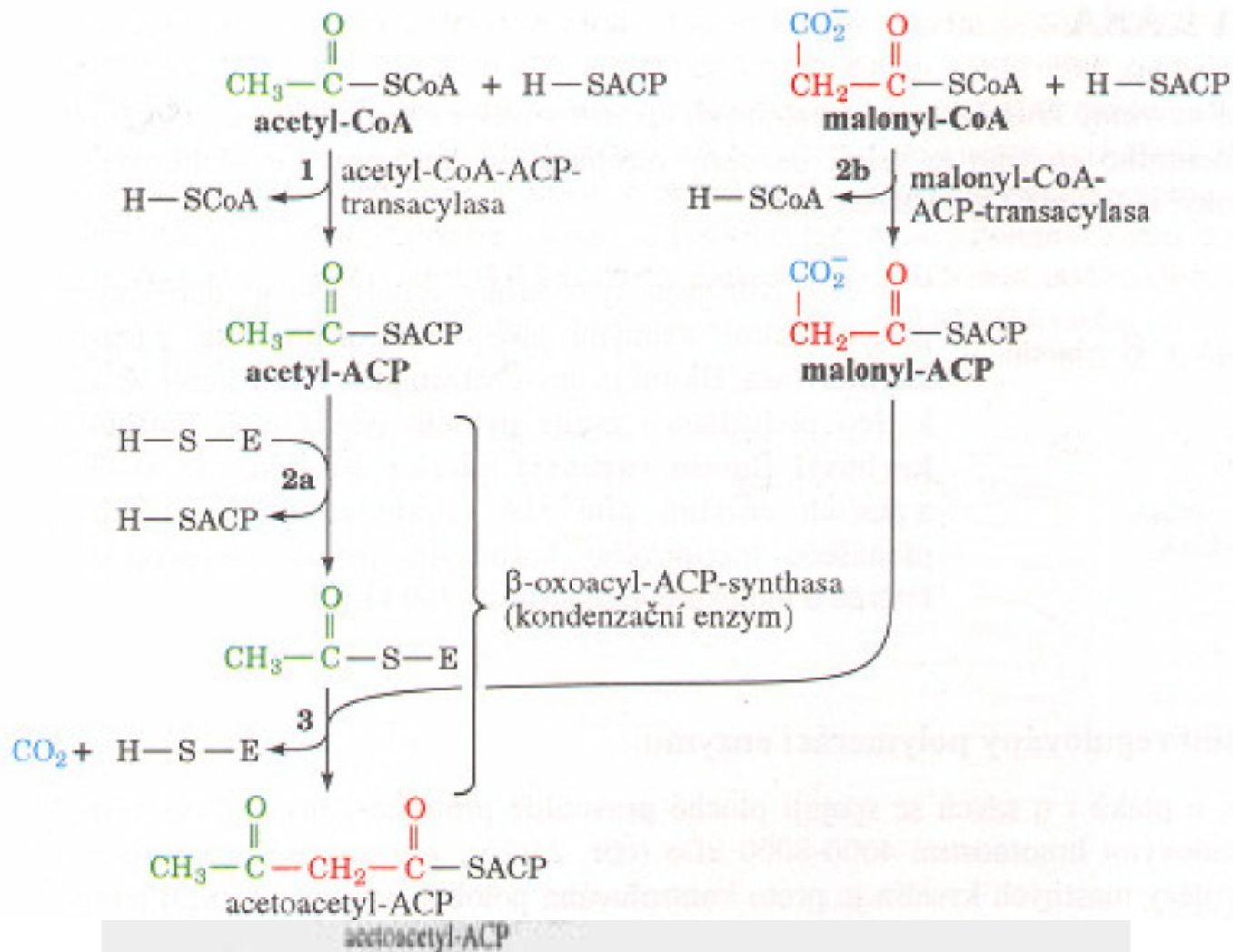
Regulace Acetyl-CoA karboxylasy

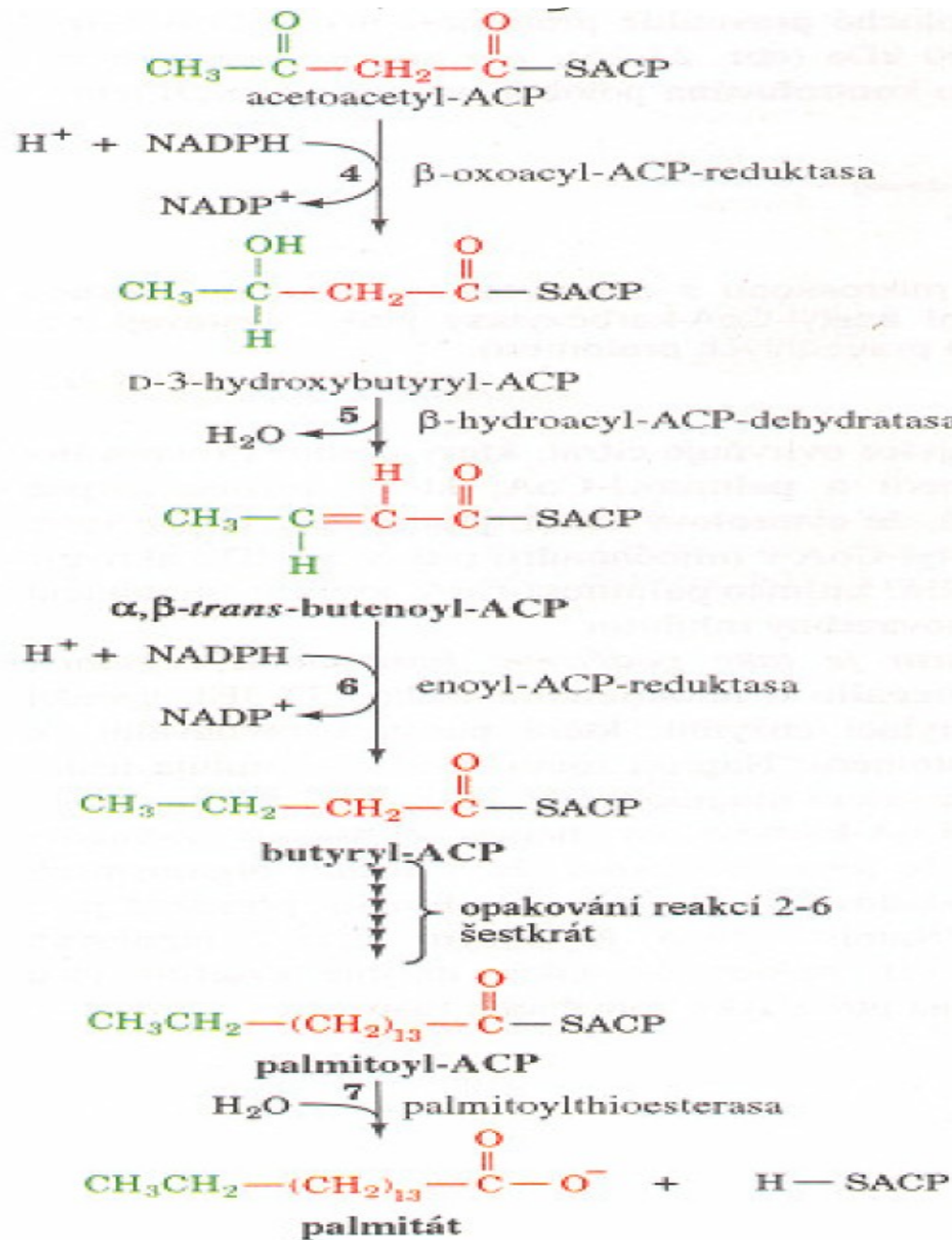


Synthasa mastných kyselin

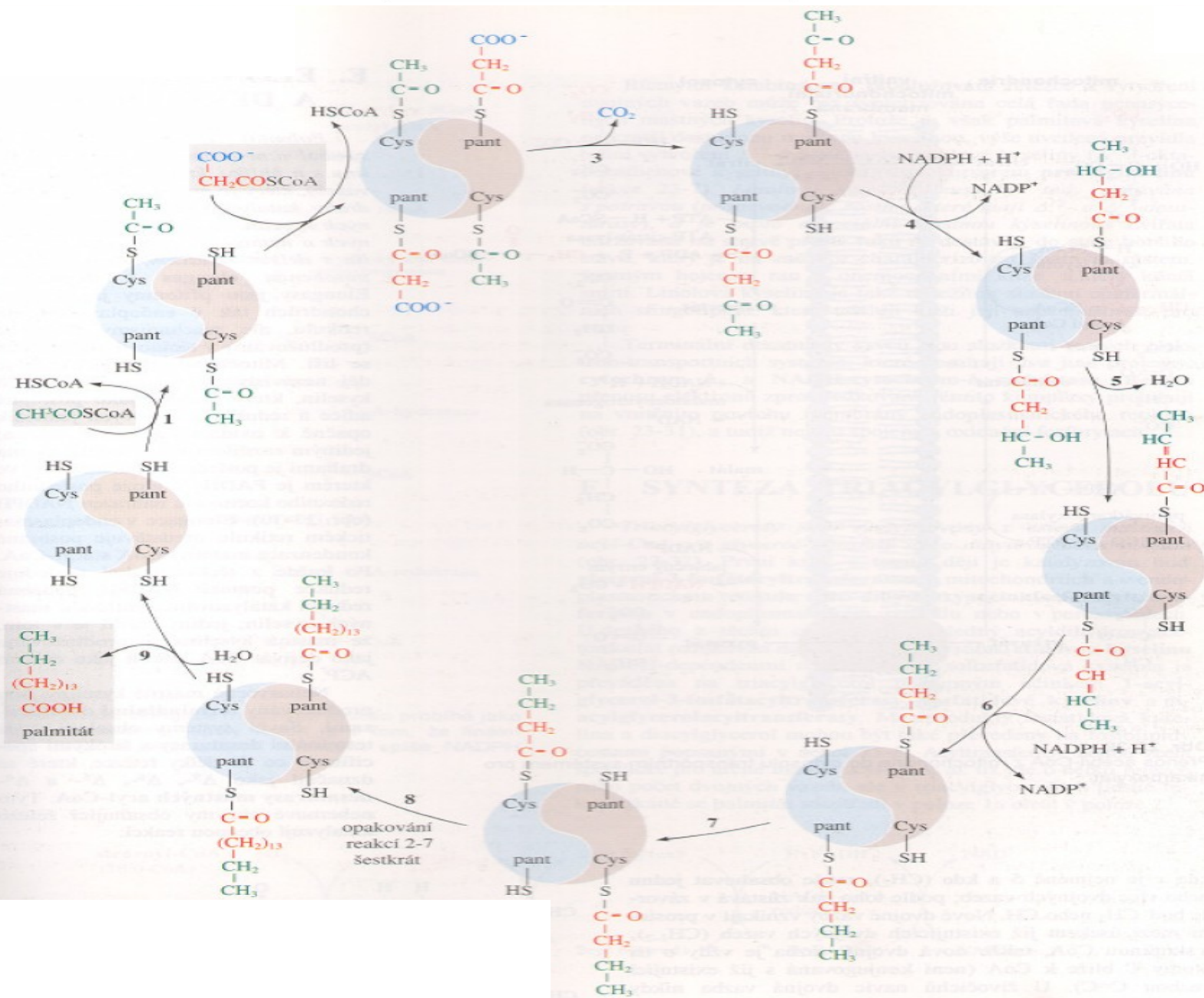


B. Syntéza palmitové kyseliny





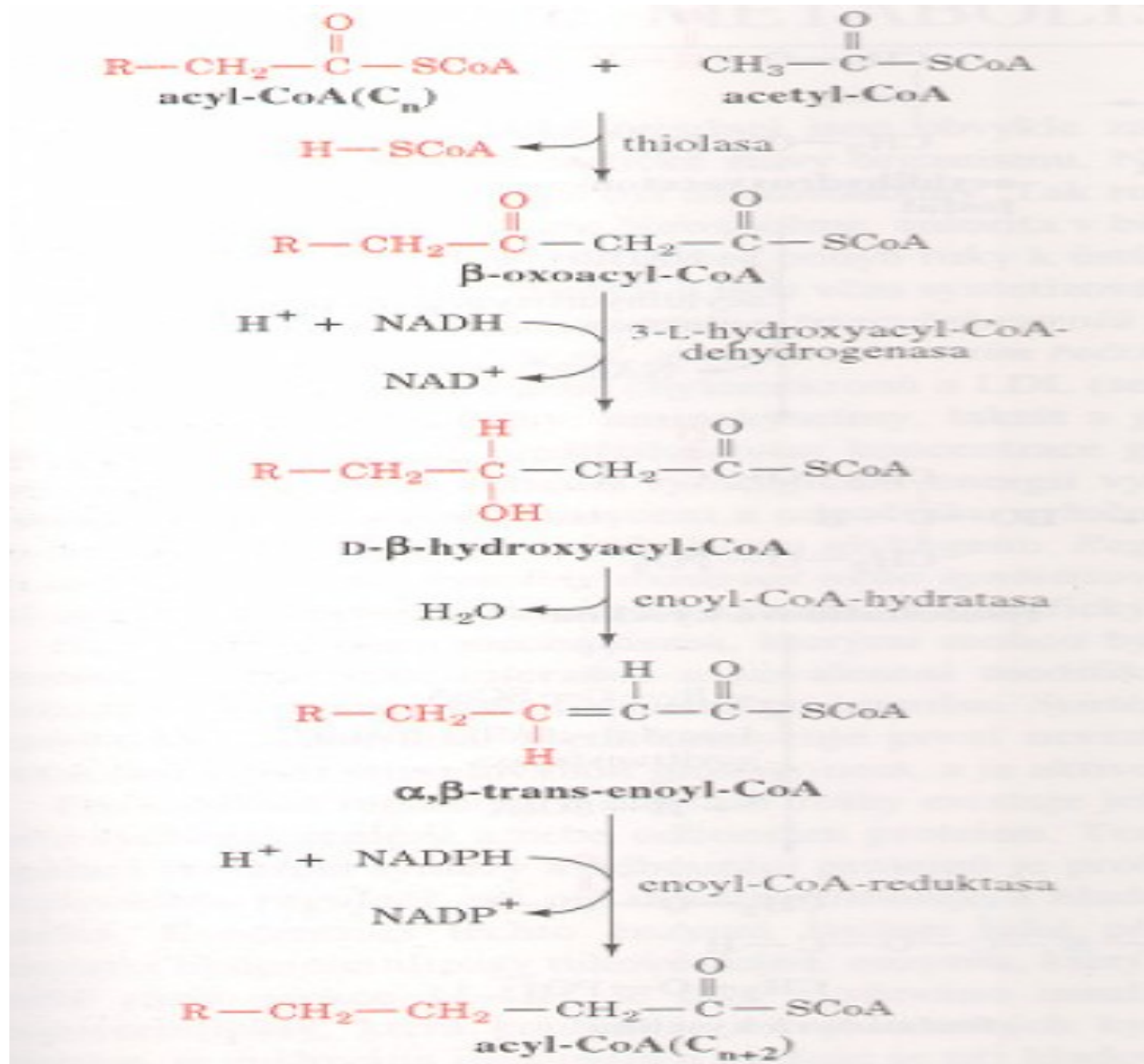
Synthesa mastných kyselin



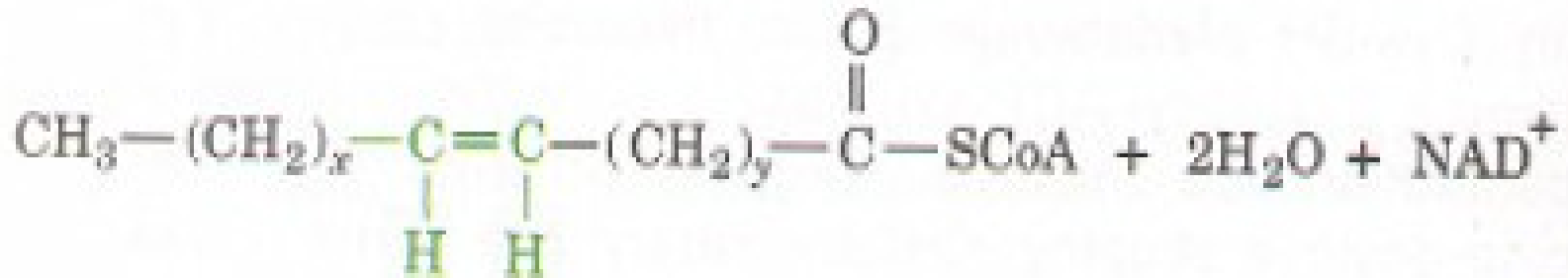
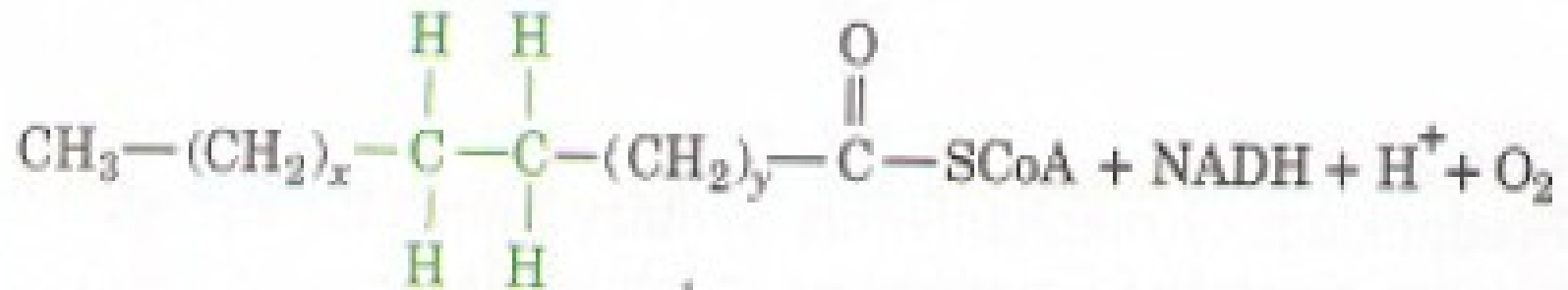
C. Další přeměny palmitové kyseliny

- **prodlužování řetězce - elongace - elongasy**
- **dehydrogenace - desaturece - desaturasy**

Elongase



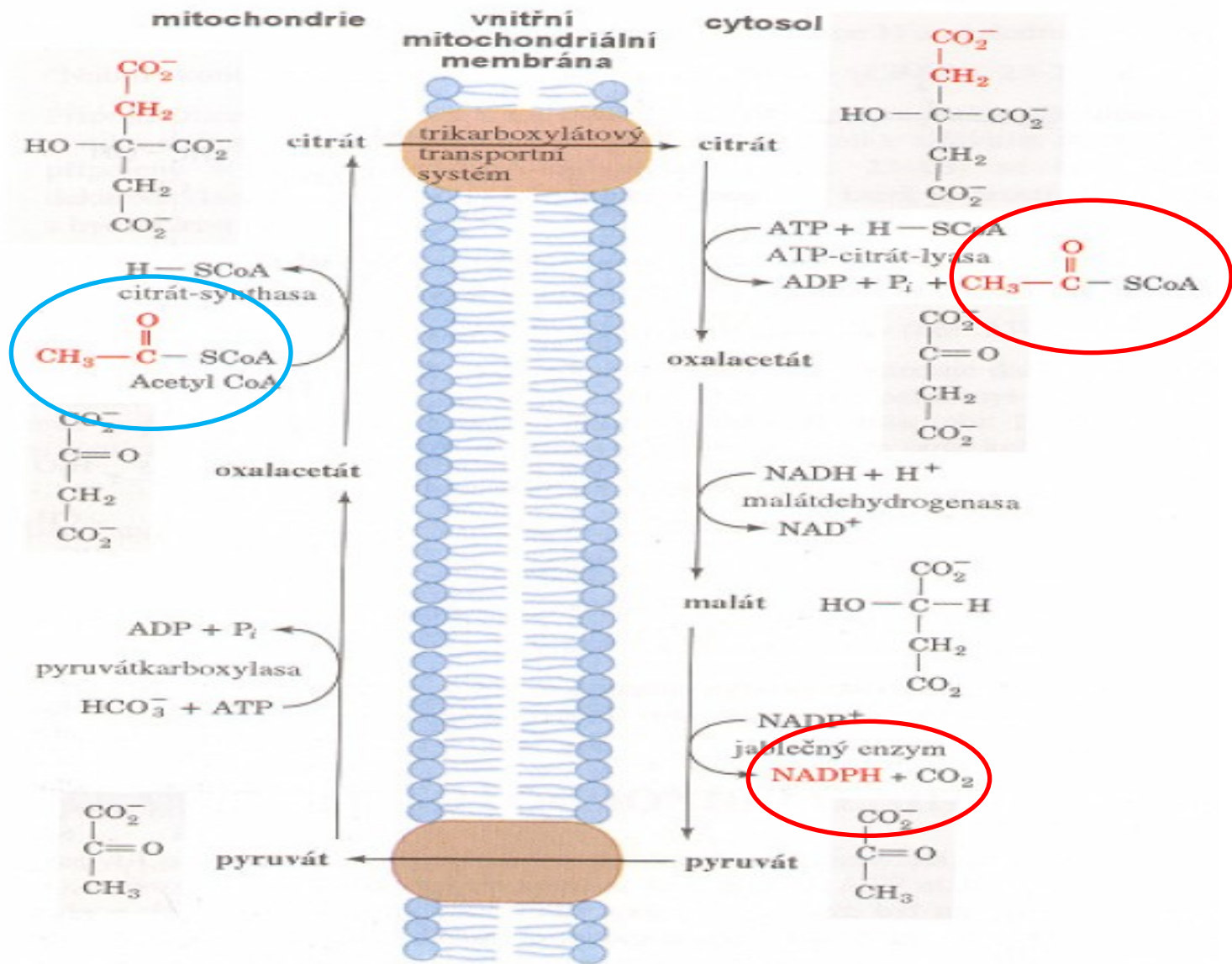
Desaturase



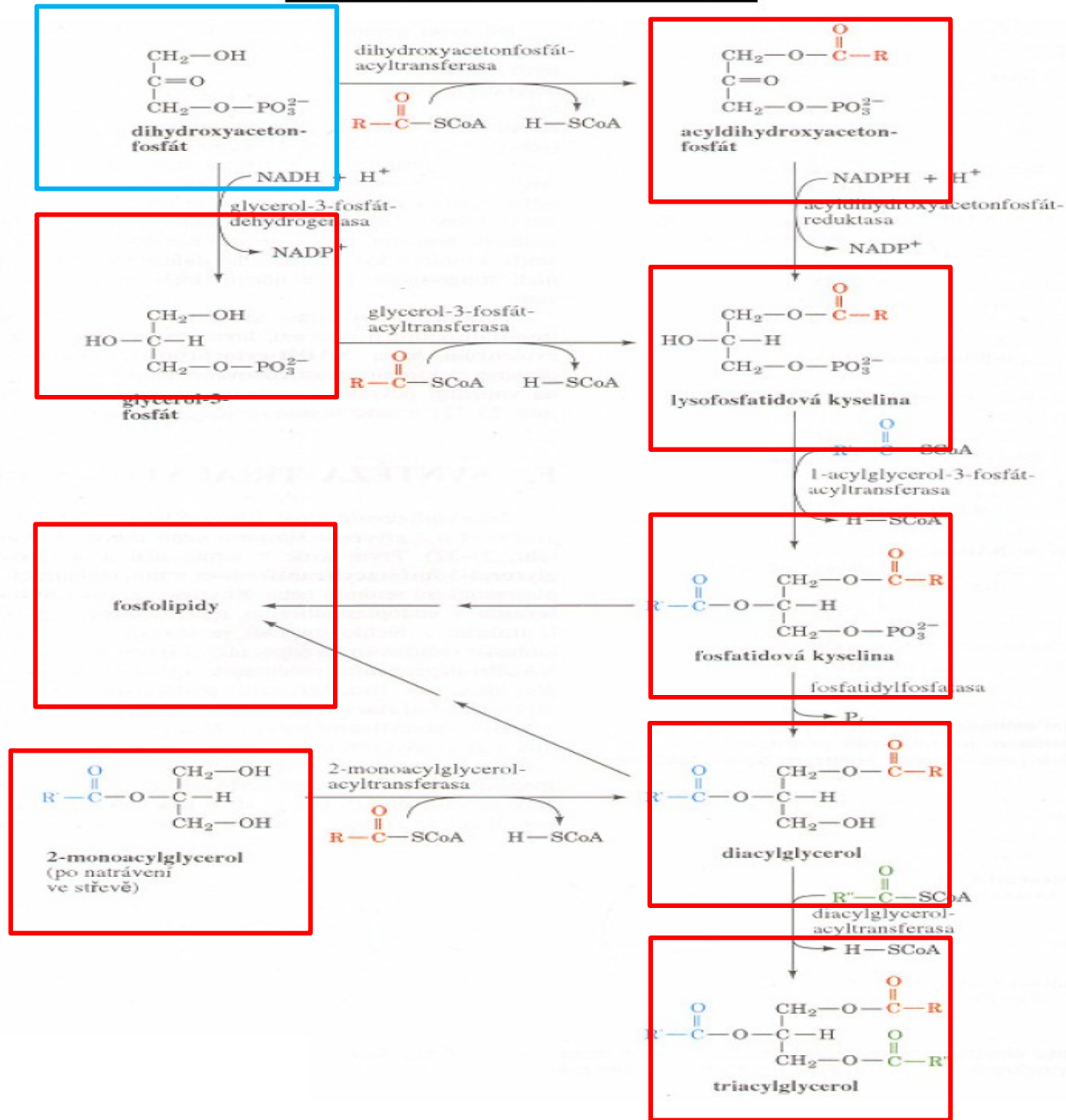
Bilance biosyntézy mastných kyselin :

1. cyklus	syntéza malonylCoA	1 ATP
	2 NADPH na redukci	6 ATP
<hr/>		
na C ₁₆	7 x ($\frac{16}{2} - 1$)	49 ATP

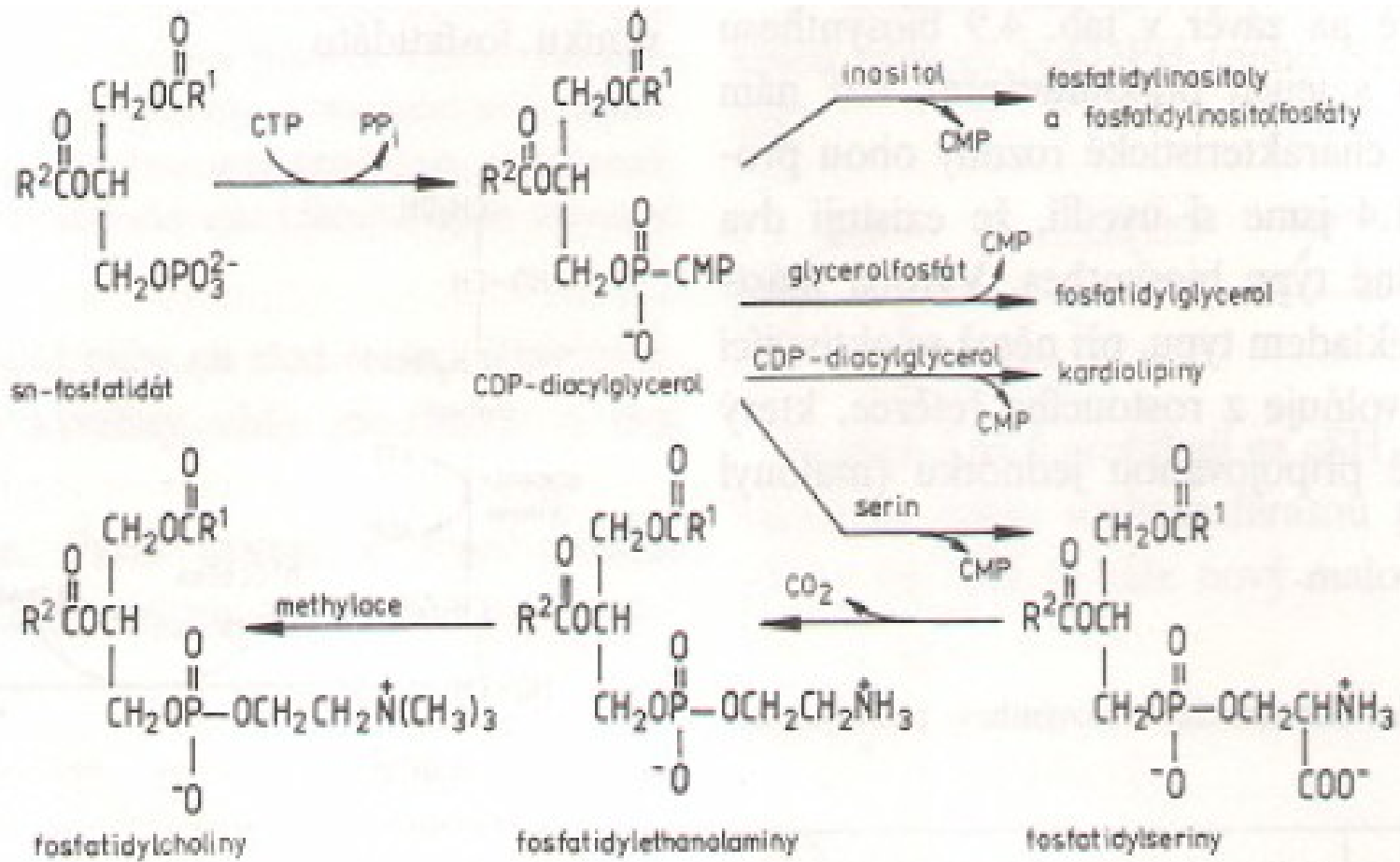
Přenos AcetCoA vně mitochondrie



Biosyntéza triacylglycerolů



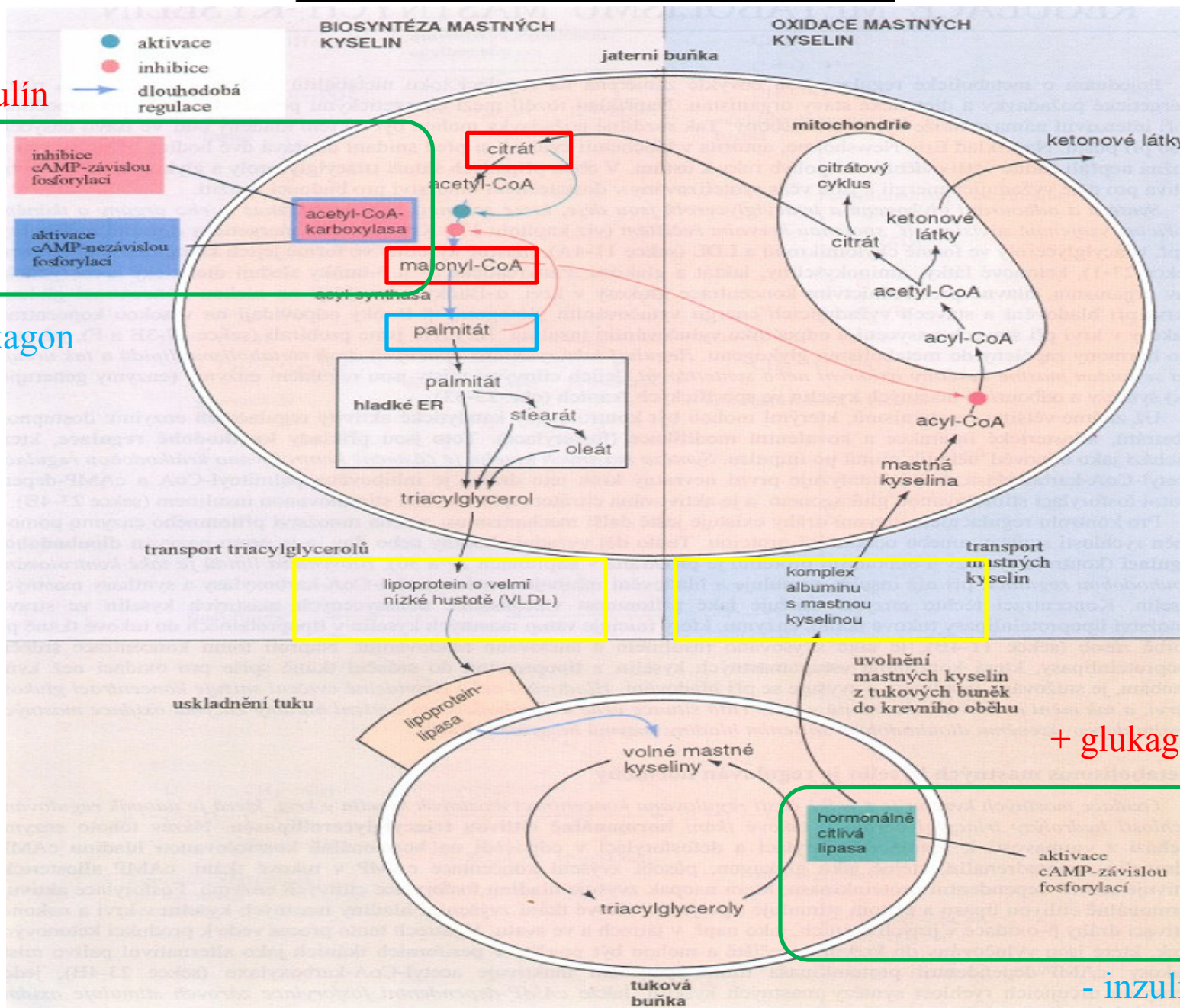
Biosyntéza fosfolipidů



Regulace metabolismu triacylglycerolů

+ inzulín

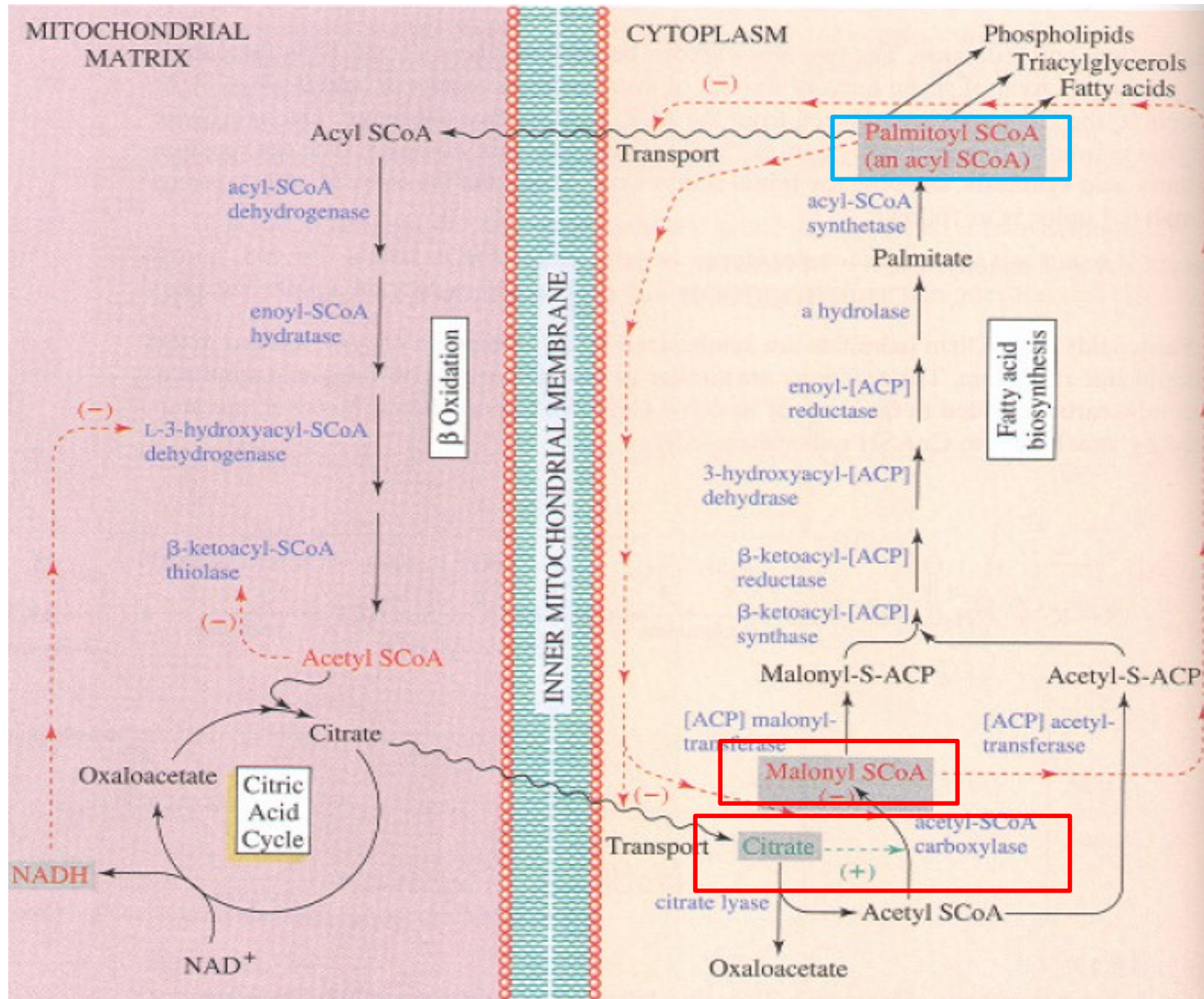
- glukagon



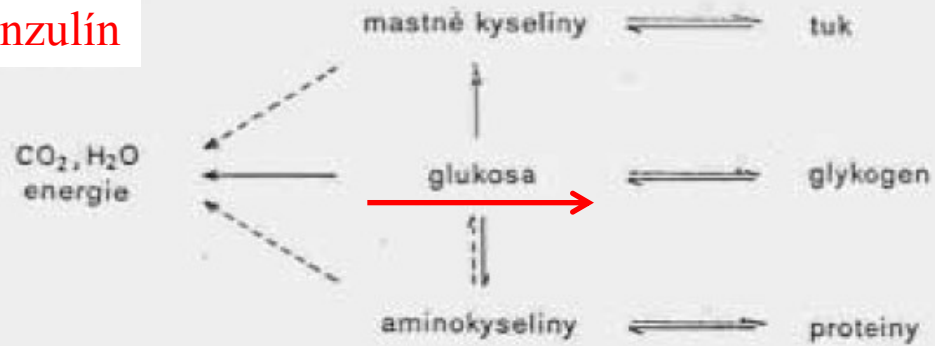
+ glukagon

- inzulín

Regulate metabolismu triacylglycerolů



inzulín



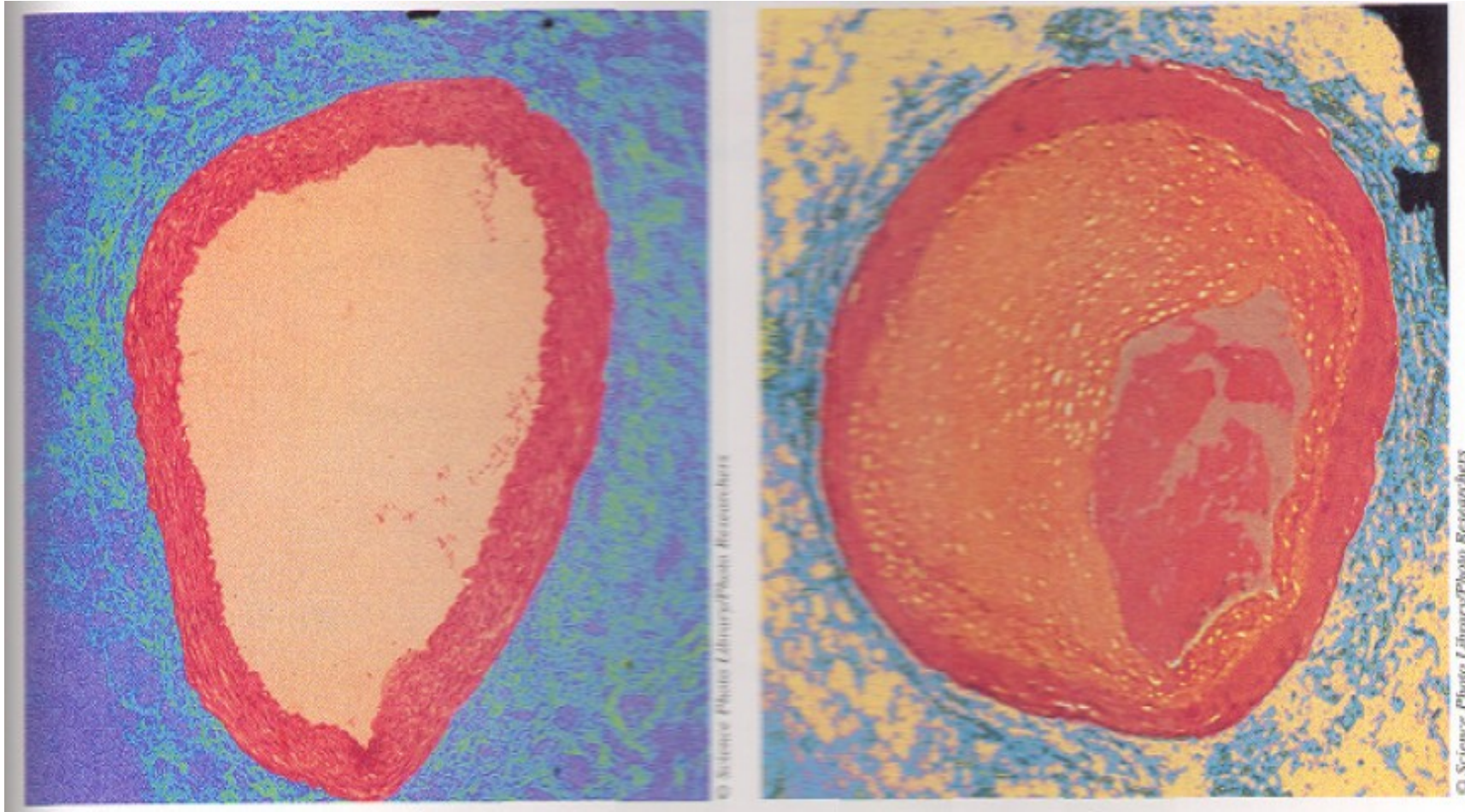
glukagon



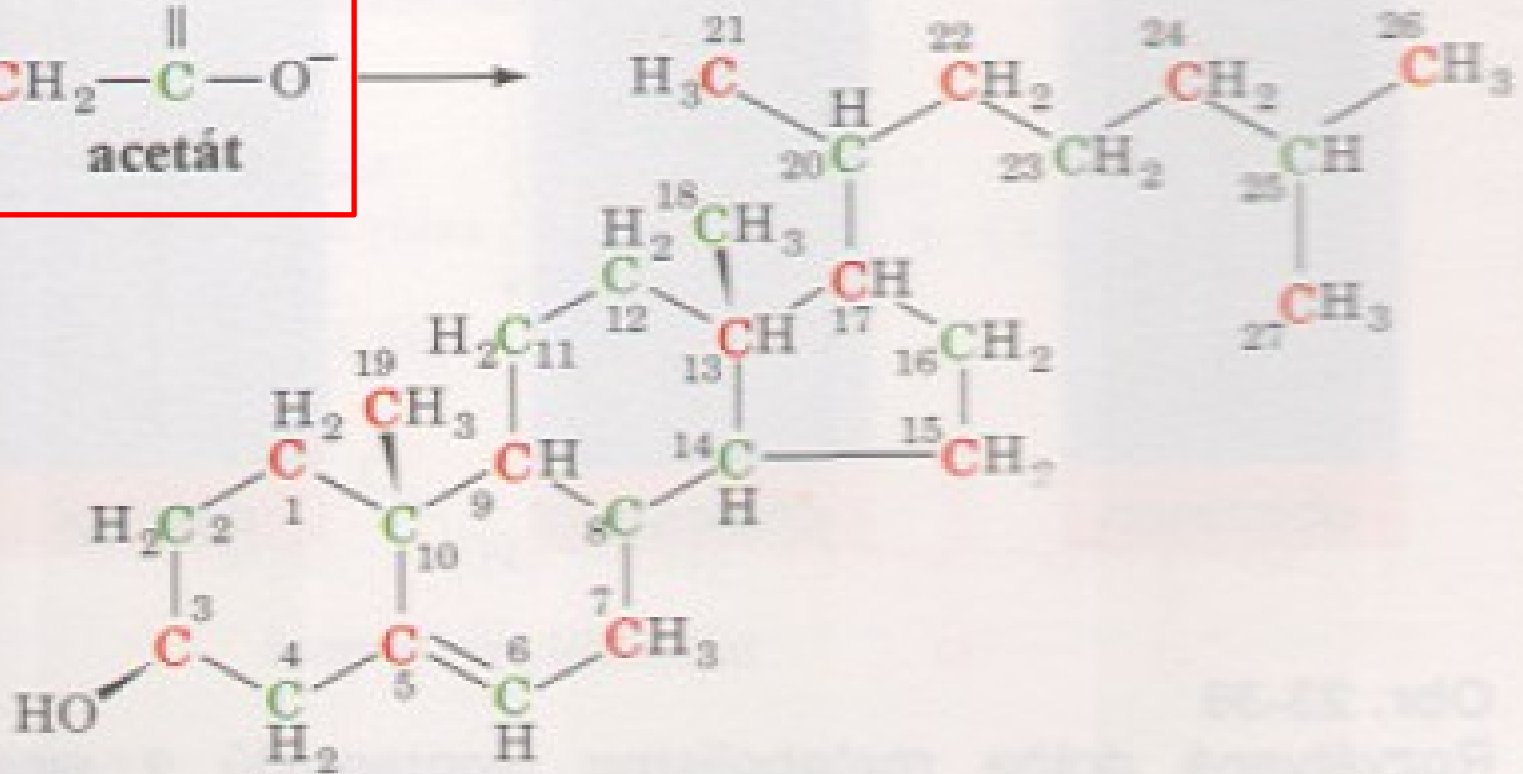
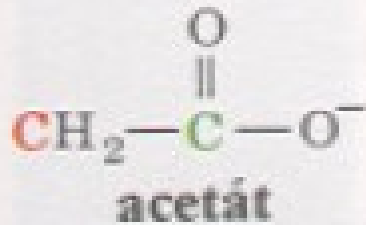
adrenalin



Cholesterol

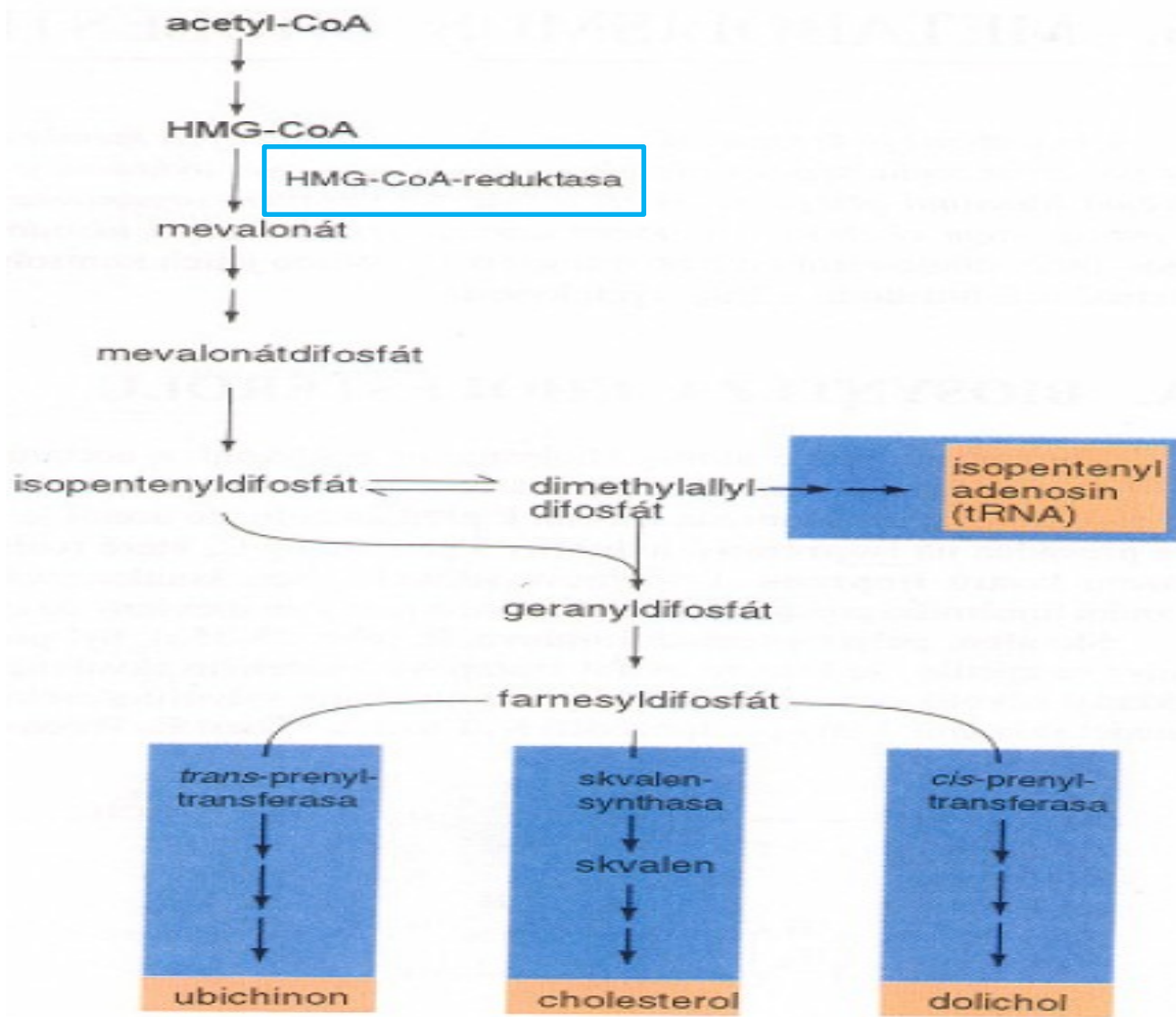


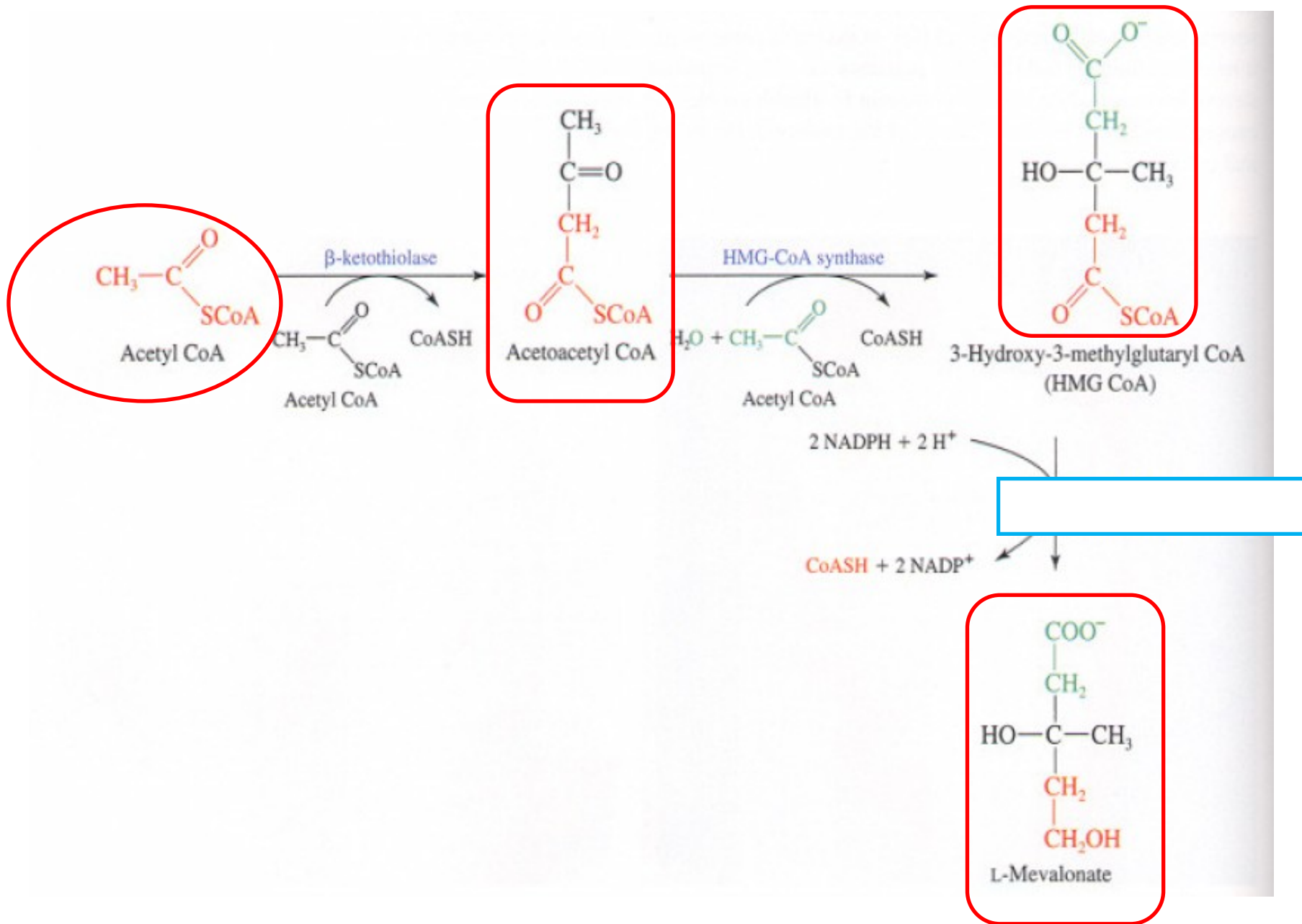
Biosyntéza cholesterolu

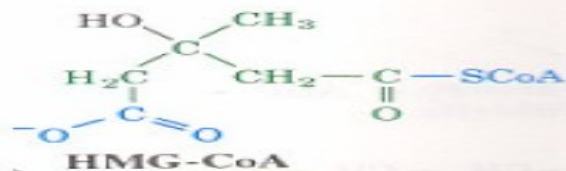


acetát → isoprenoidní intermediát → skvalen
→ produkt cyklizace → cholesterol

Biosyntéza cholesterolu





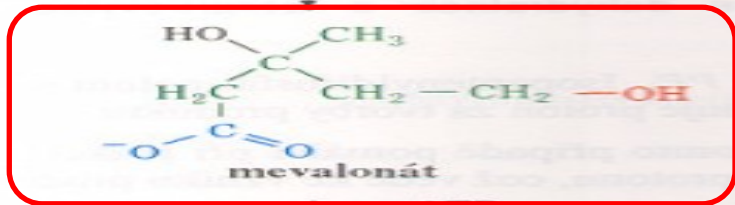


HMG-CoA-reduktasa

1

2NADPH → 2NADP⁺

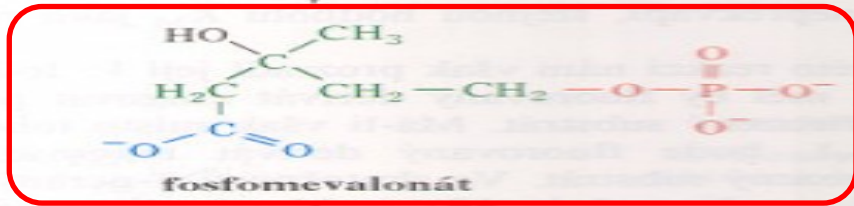
CoA



mevalonát-5-fosfo-transferasa

2

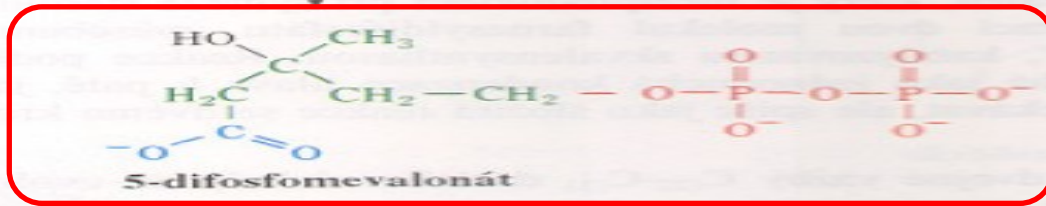
ATP → ADP



fosfomevalonát-kinasa

3

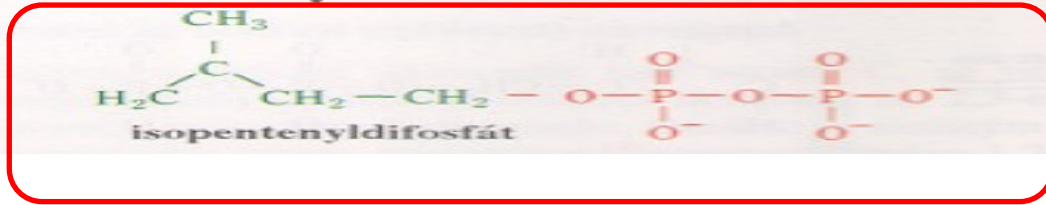
ATP → ADP

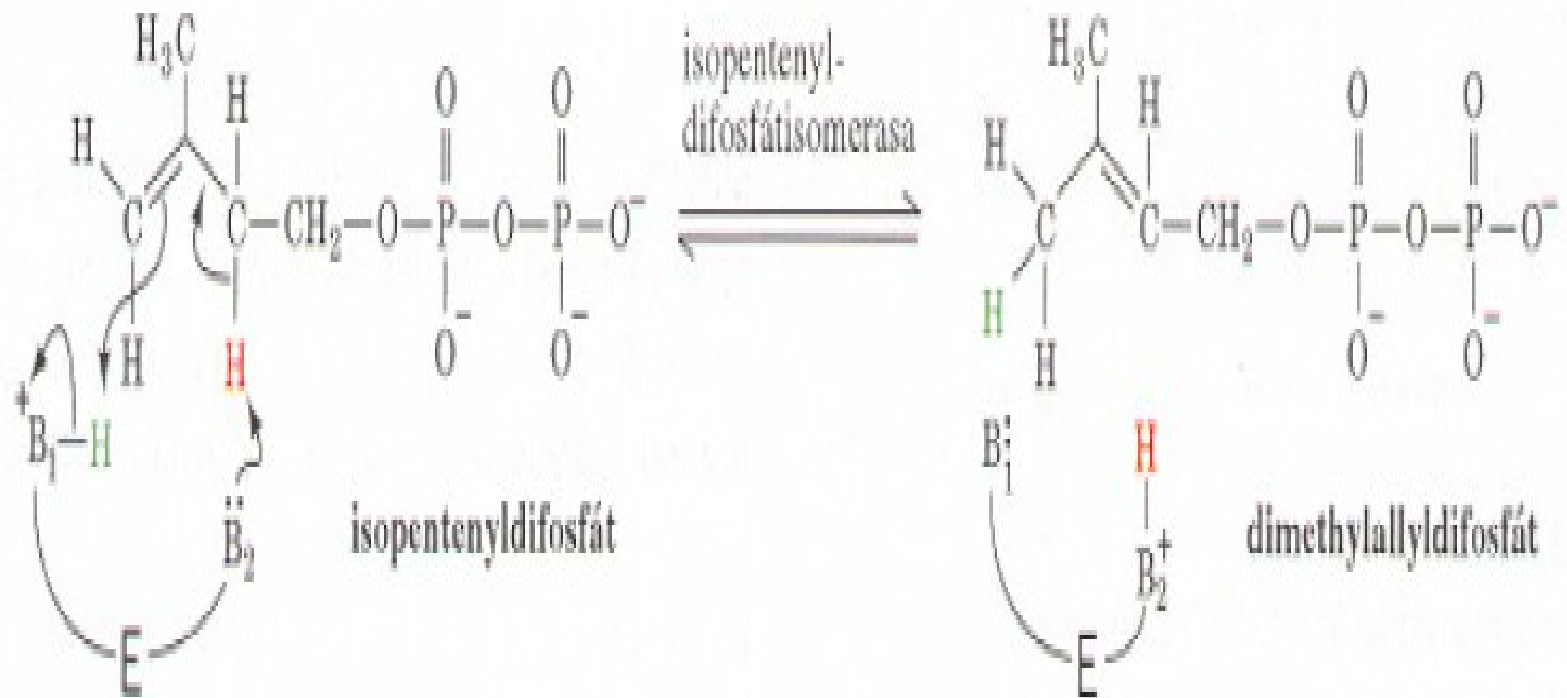


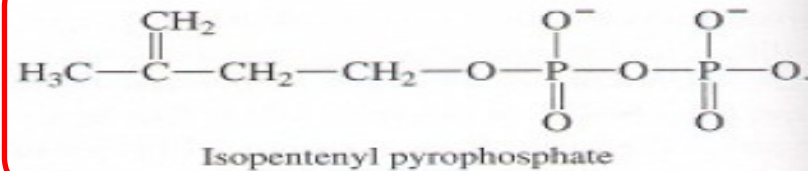
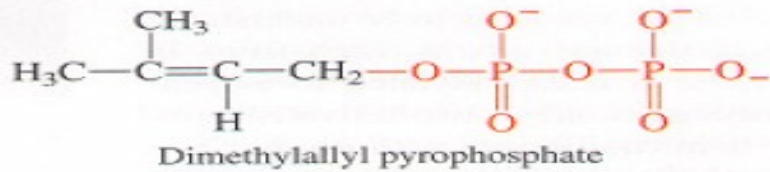
difosfomevalonát-dekarboxylasa

4

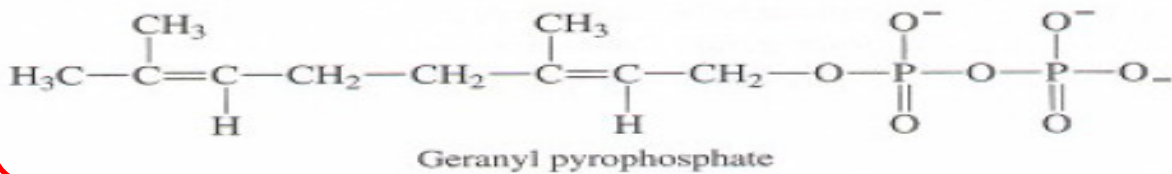
ATP → ADP + P_i + CO₂



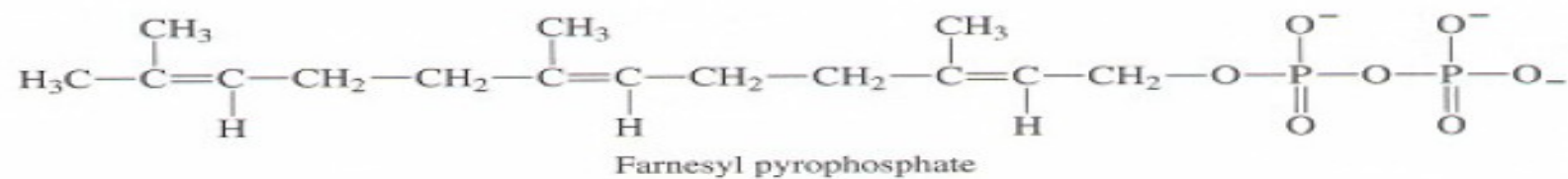
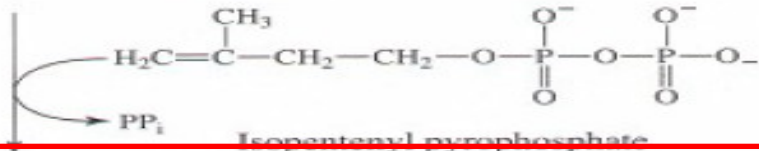




PP_i



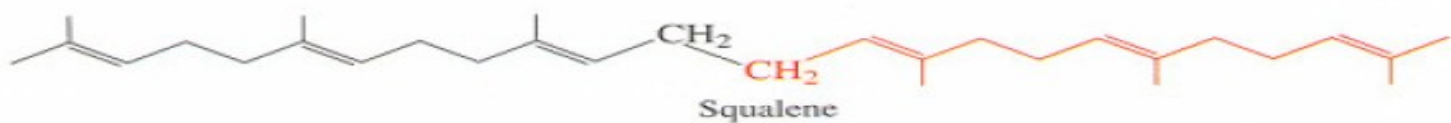
3 x

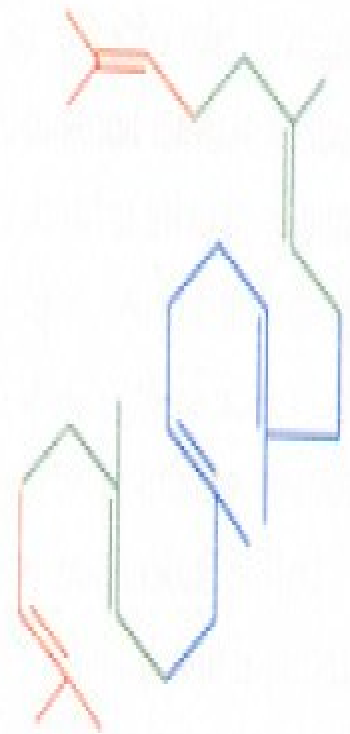
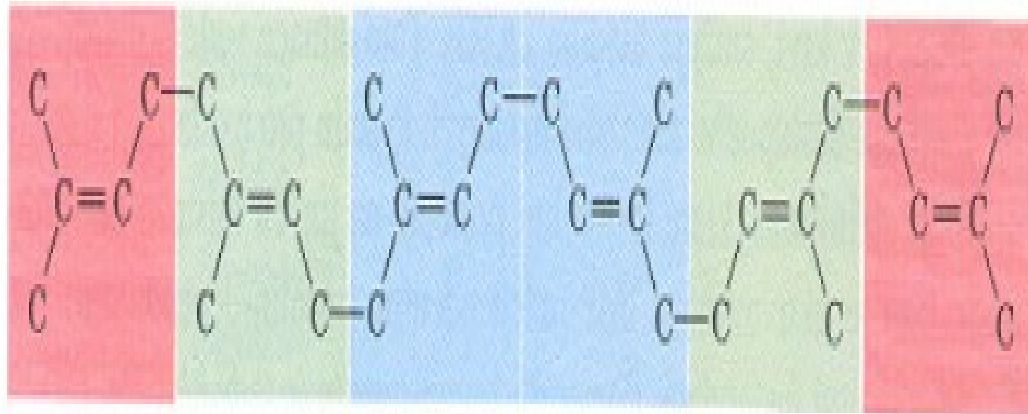


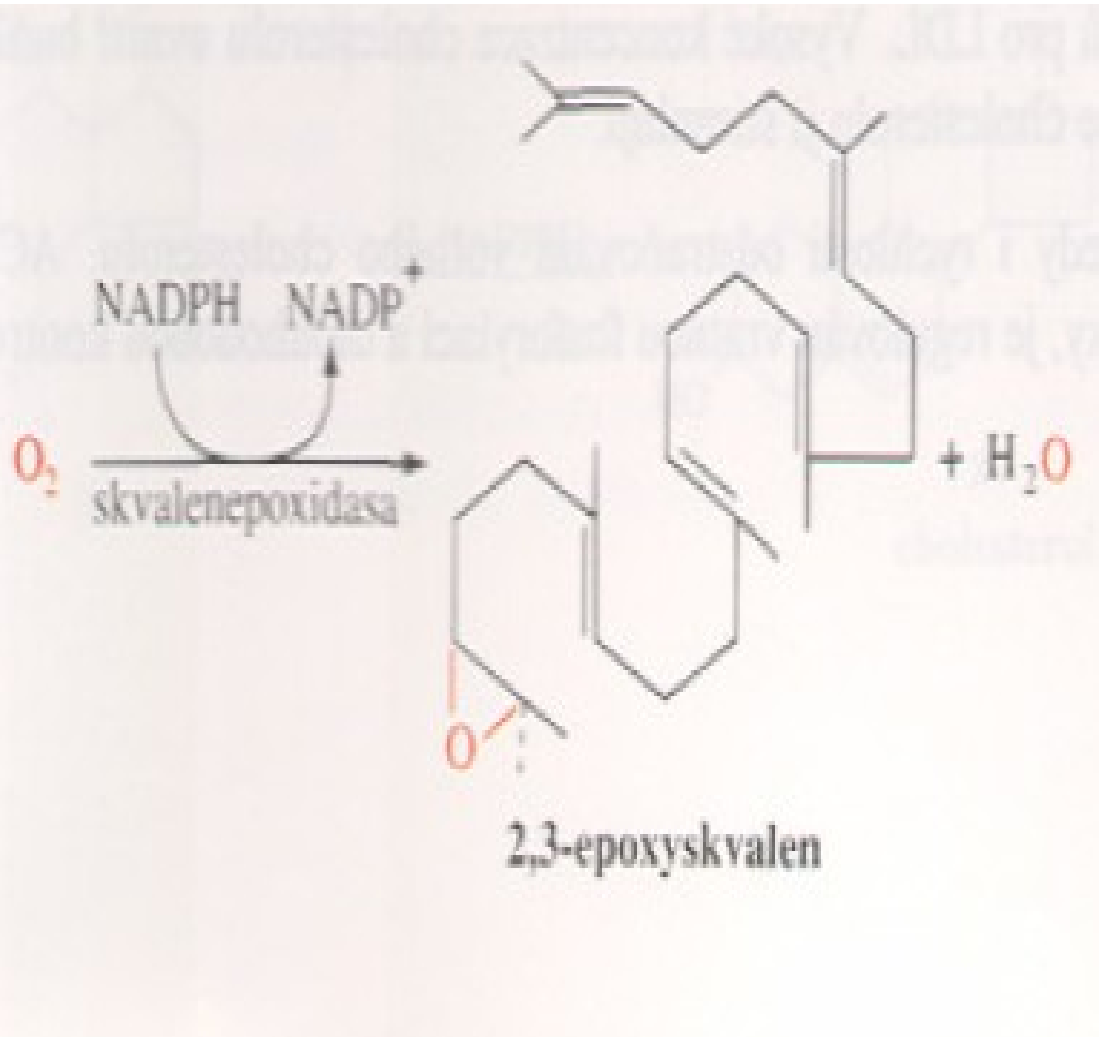
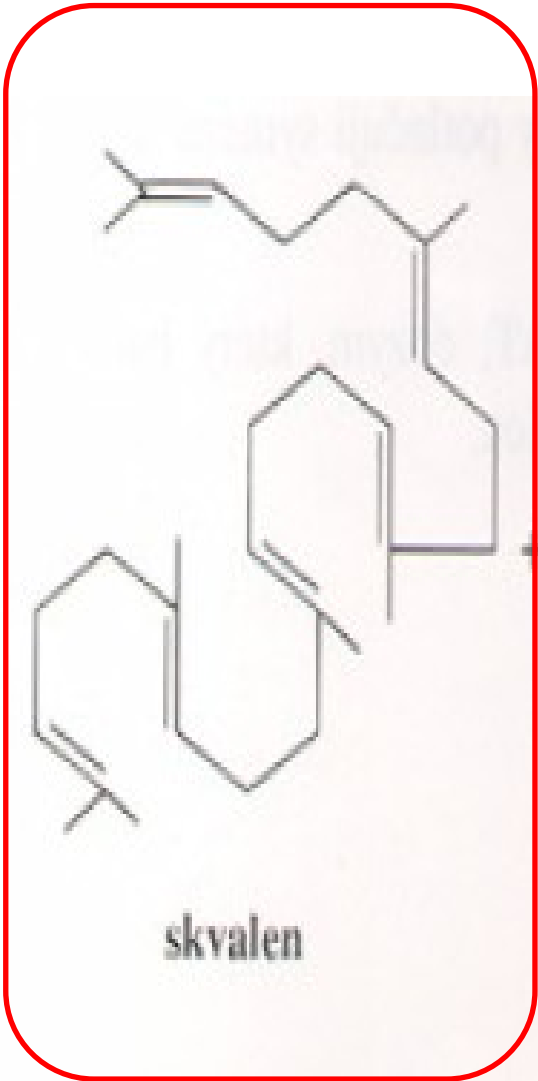
2 x

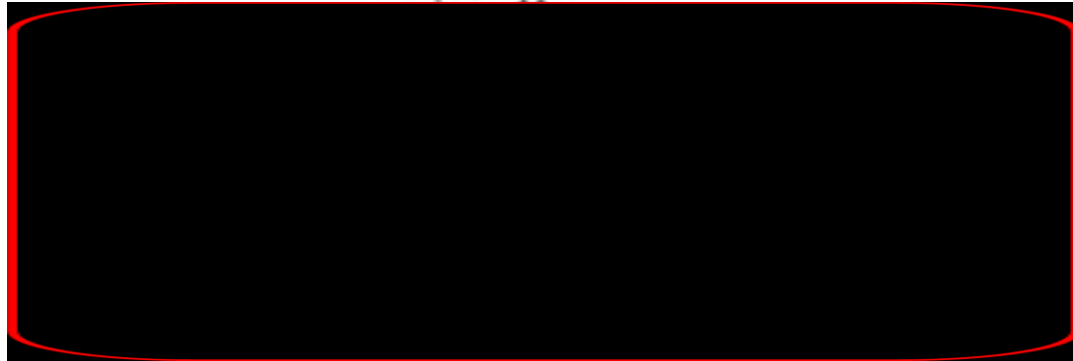
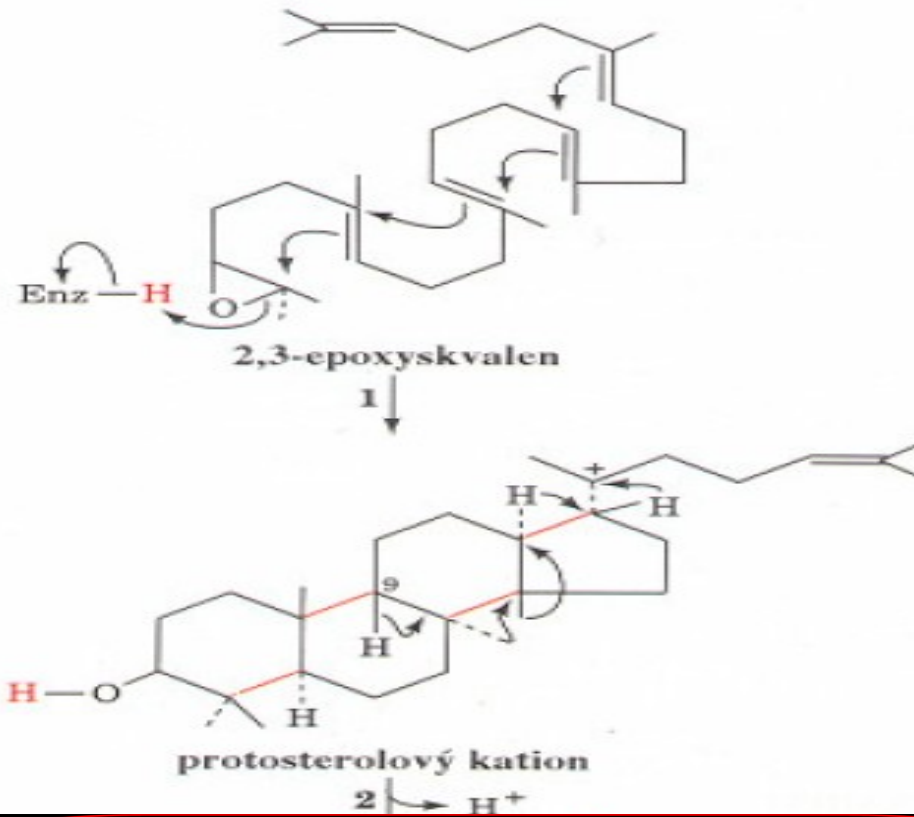
farnesyl pyrophosphate + NADPH

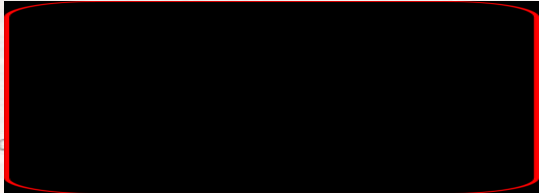
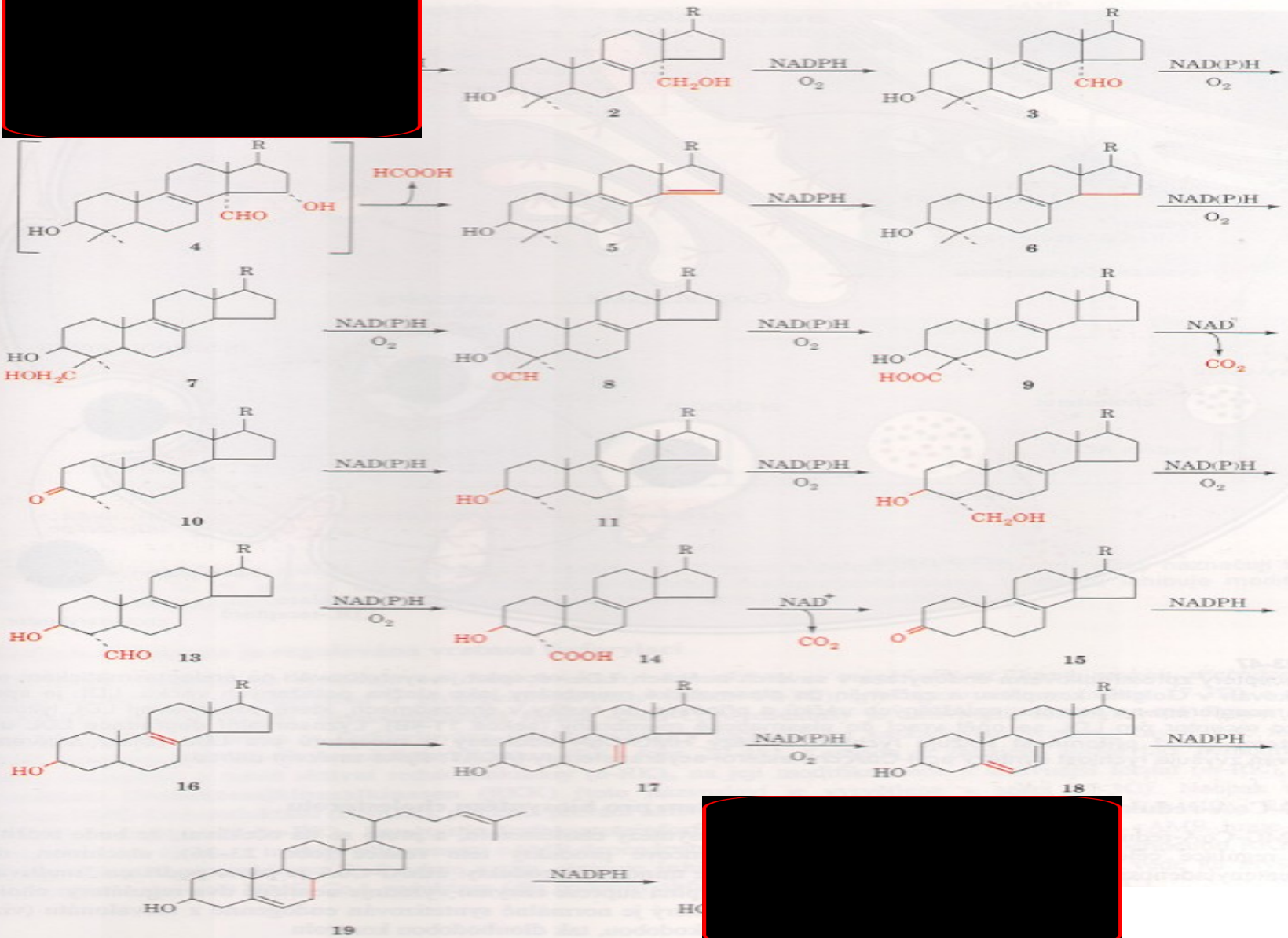
NADP⁺ + 2 PP_i











Metabolismus bílkovin

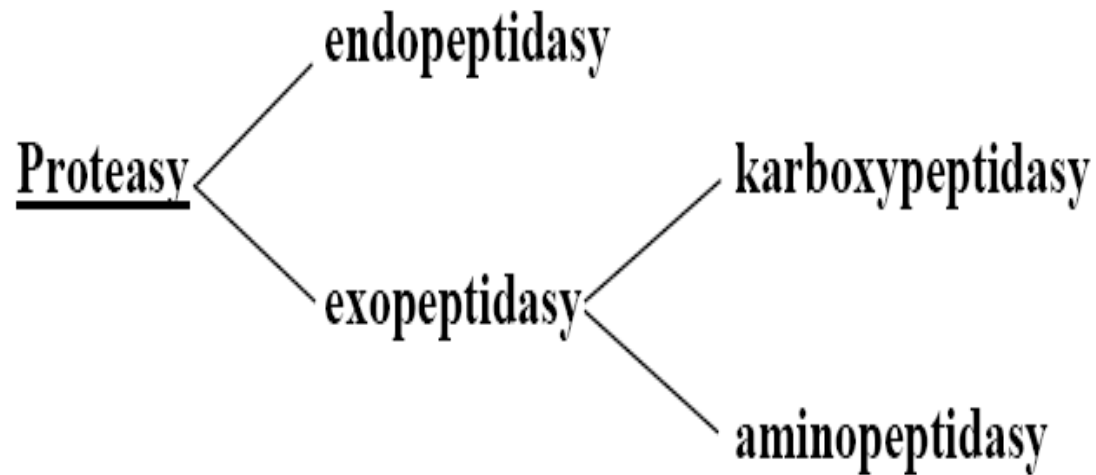
- Tuky, sacharidy – zásobárna energie, mohou se vzájemně zastupovat.
- Bílkoviny – tvorba tělních bílkovin, jsou jediným zdrojem N pro heterotrofy
- V organismu neexistuje skladiště bílkovin
- U sacharidů (glykolýza, pentozový cyklus) a lipidů (β oxidace) jednotný metabolismus, AMK individuální metabolismus

Metabolismus bílkovin

- AMK jsou prekurzory v různých metabolických drahách (puriny, pyrimidiny, protoporfiriny atd.)
- Biosyntéza bílkovin je geneticky řízena - proteosyntéza

METABOLISMUS BÍLKOVIN

Proteolýza



Proteasy - serinové

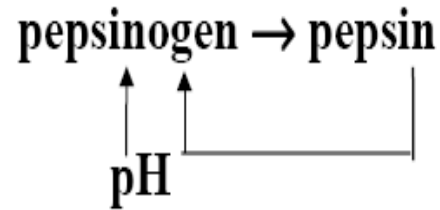
cysteinové

metaloproteasy

kyselé - aspartátové

Aktivace zymogenů

žaludek

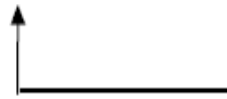


slinivka břišní

enterokinasa



trypsinogen → trypsin



chymotrypsinogen → chymotrypsin

proelastasa → elastasa

1. Žaludeční proteasy

- pepsin
- chymosin (renin, sýřidlo)

2. Pankreatické proteasy

- trypsin
- chymotrypsin
- elastasa
- karboxypeptidasa A,B

3. Proteasy střevní šťávy

- aminopeptidasy
- dipeptidasy

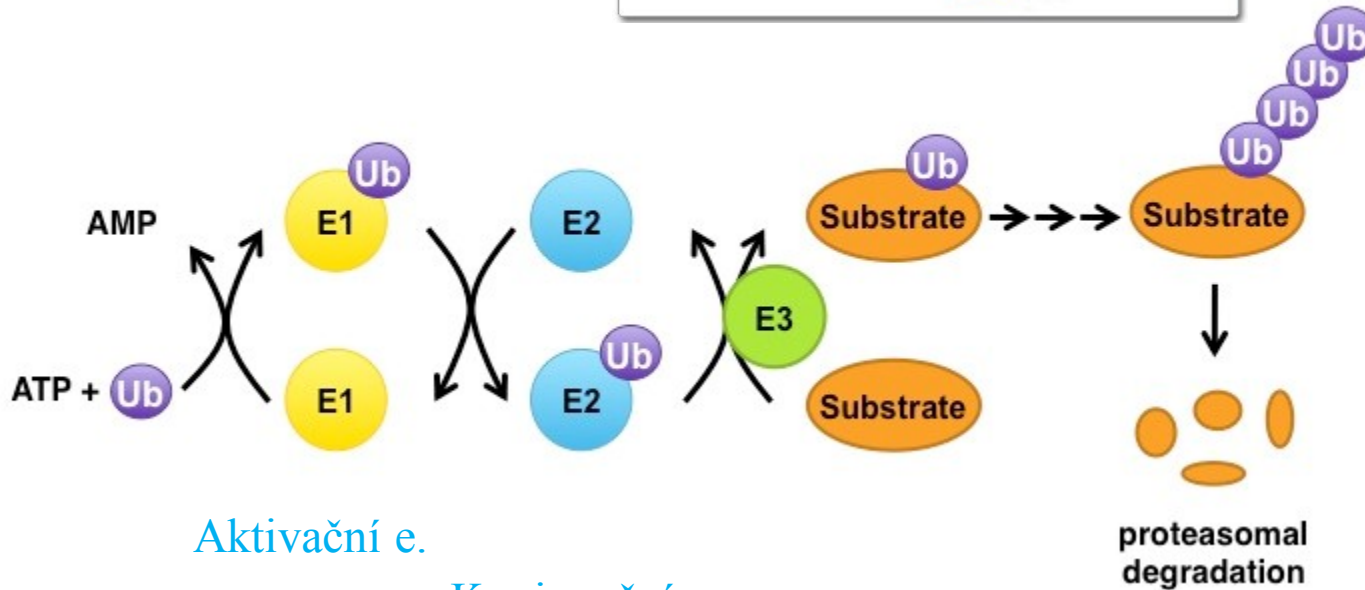
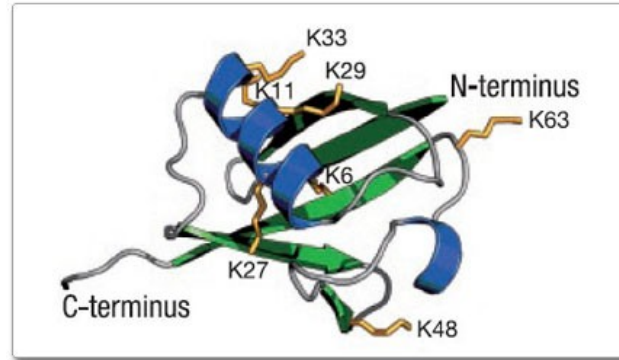
4. Buněčné proteasy

- živočichové - kathepsiny B, D, L, H, M, S a T
- rostliny - papain
- bakterie - subtilisin, pronasa

- Proteasy s jinou funkcí
- enterokinasa - aktivace zymogenů
- trombin - srážení krve

Ubikvitinace

Ubikvitin (76 AMK) NC 2004



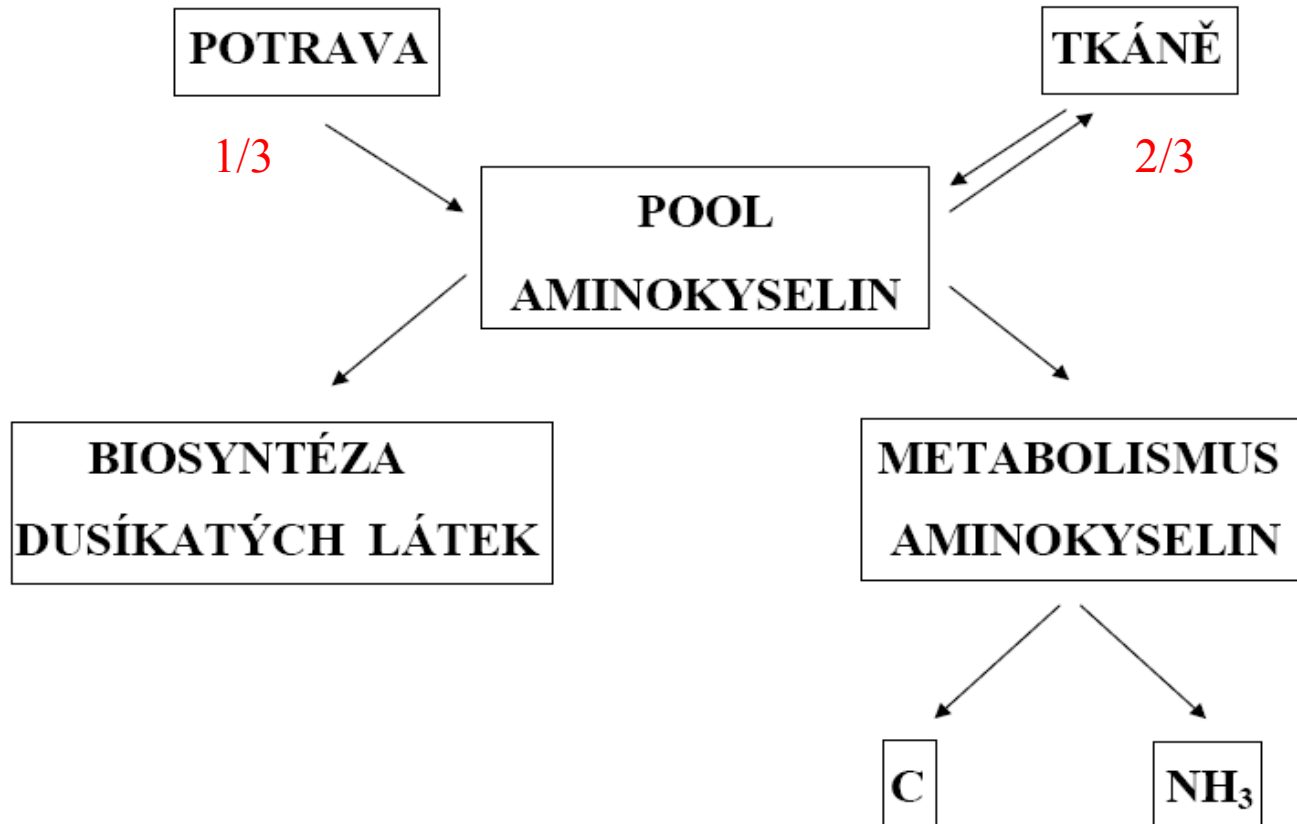
Aktivační e.

Konjugační e.

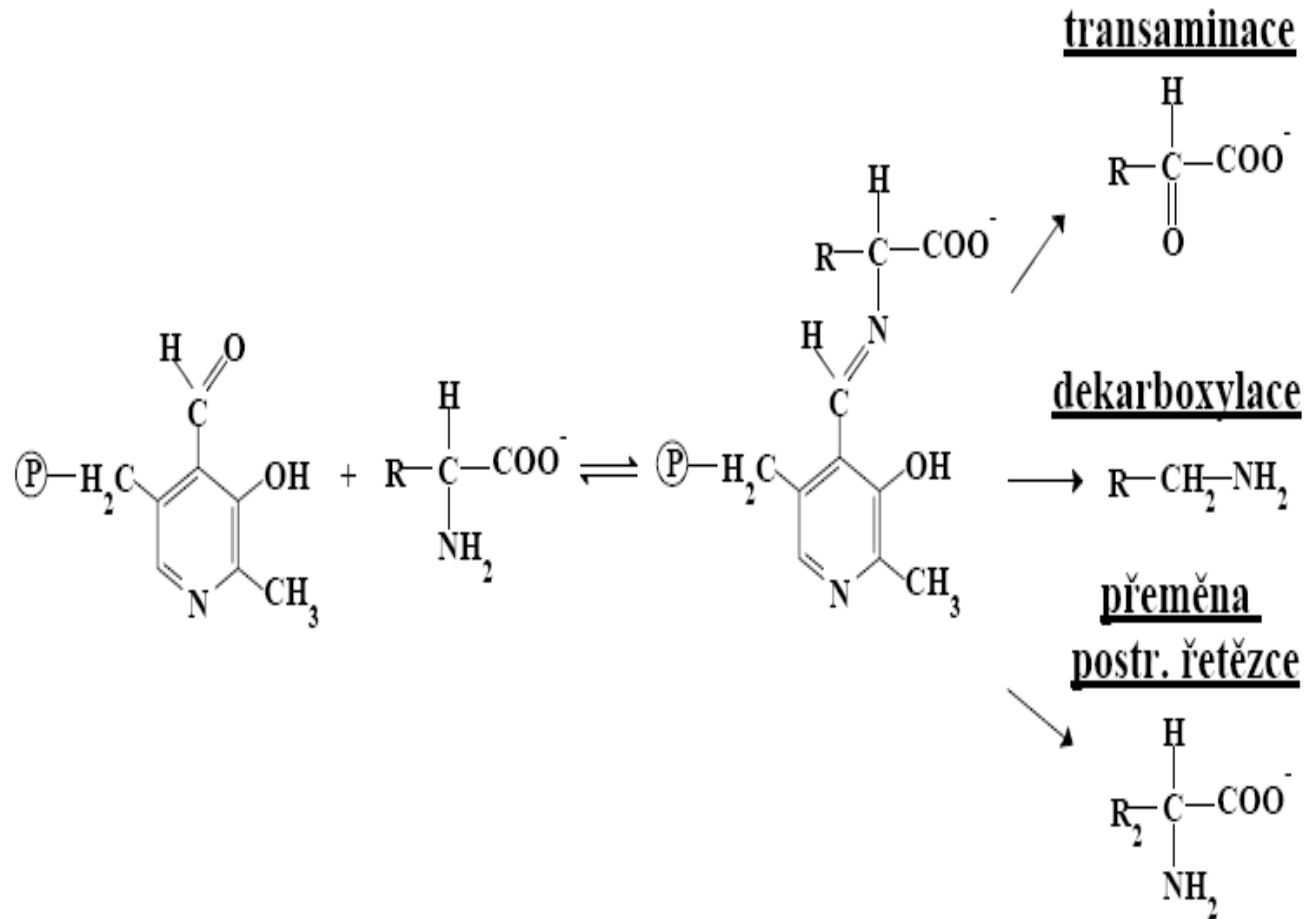
Ligační e.

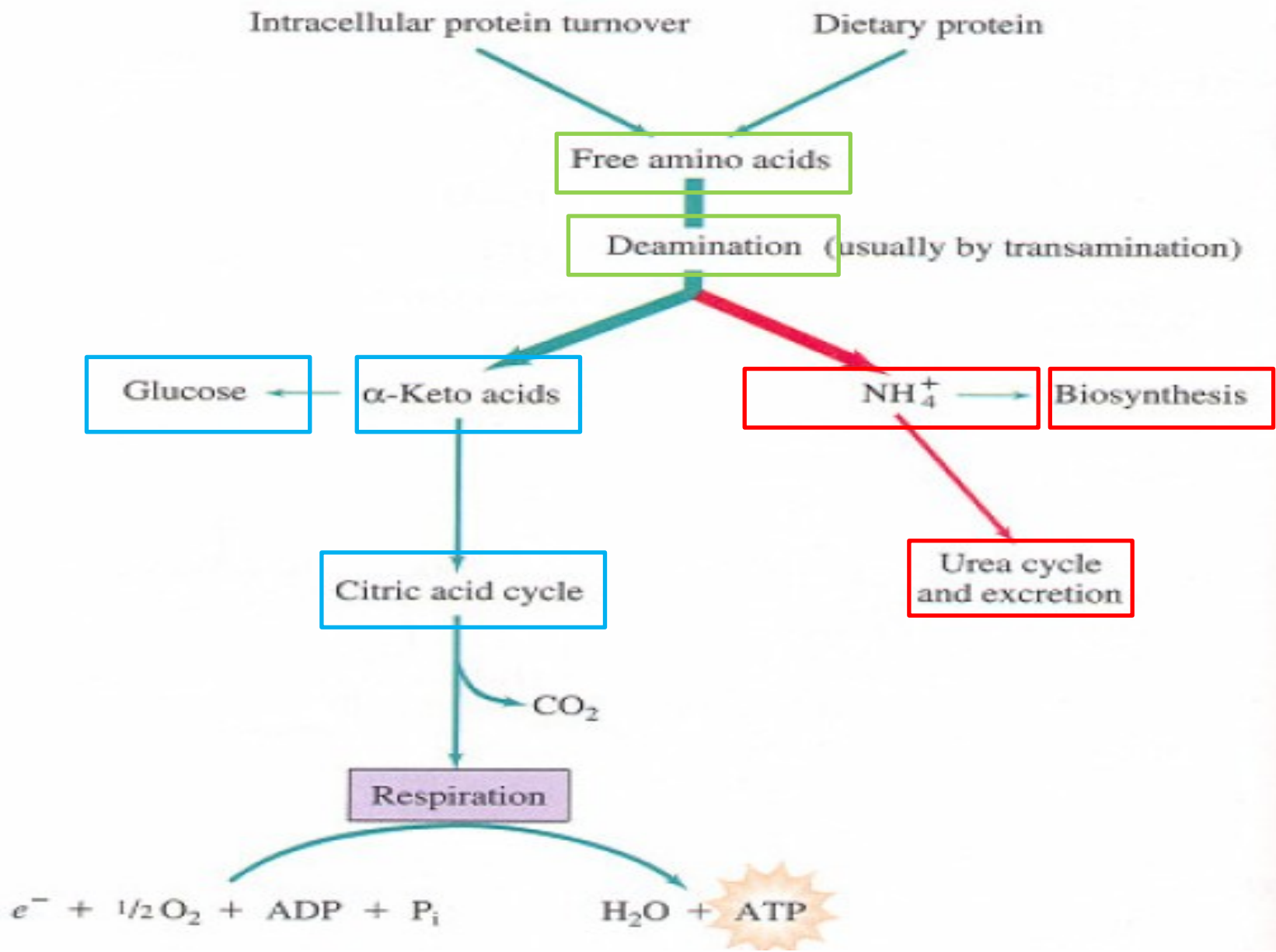
Proteasom 26S

Hotovost - pool aminokyselin

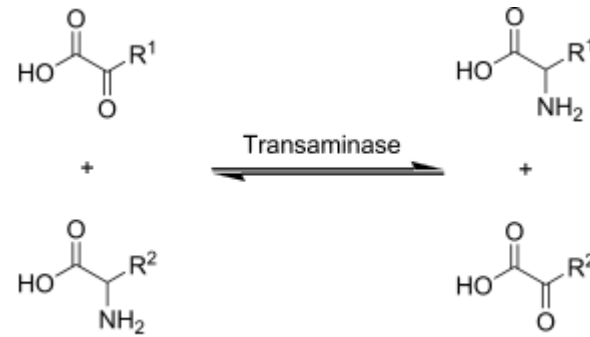
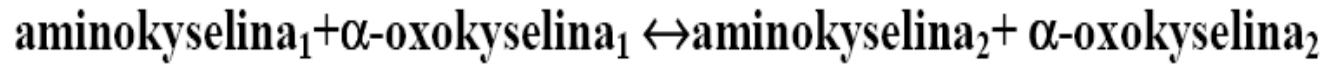


METABOLISMUS AMINOKYSELIN

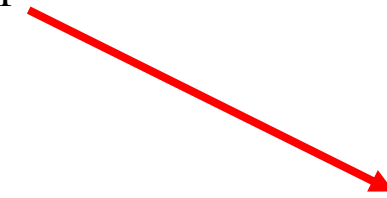




Transaminase

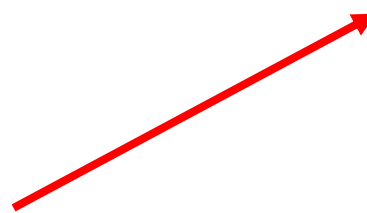


AMK1

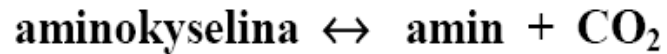


Glu

AMKn

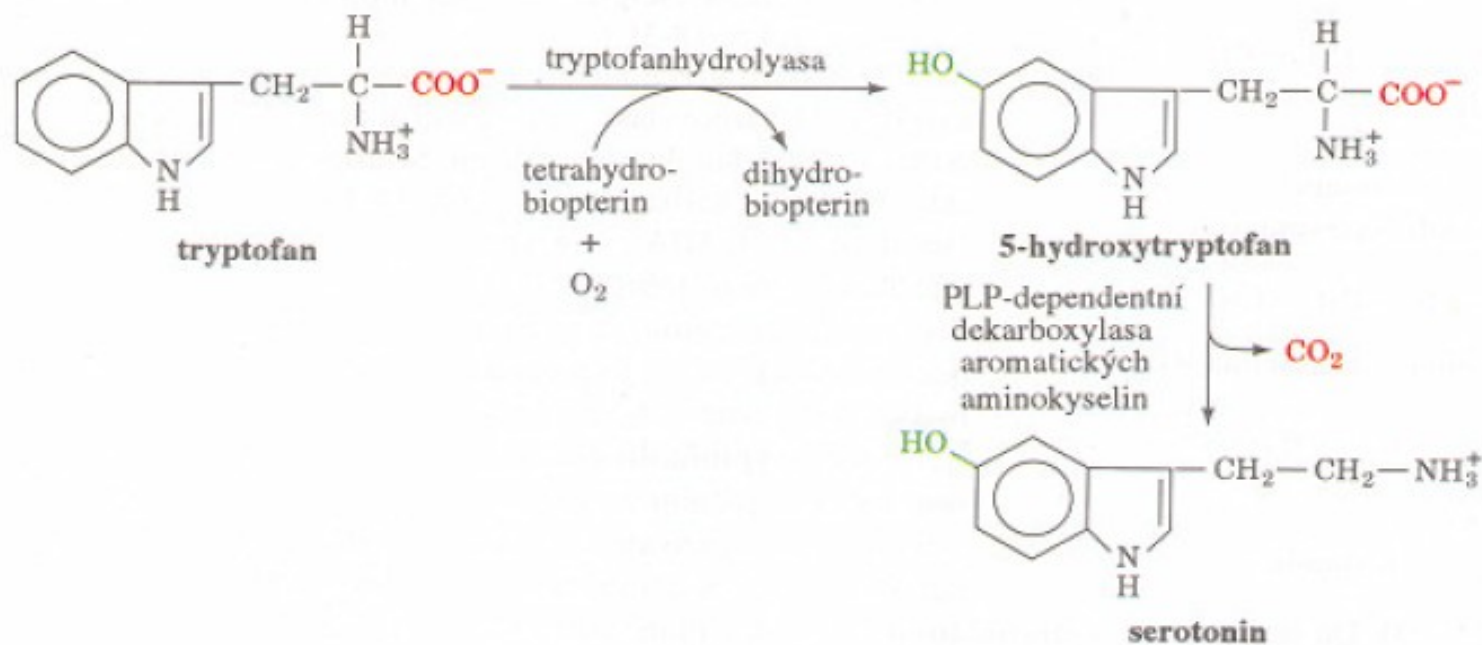
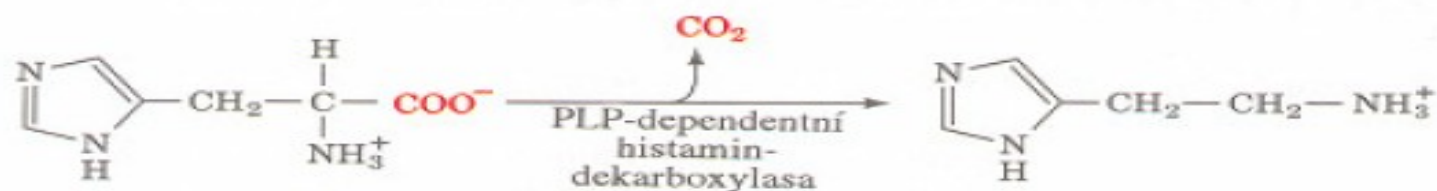
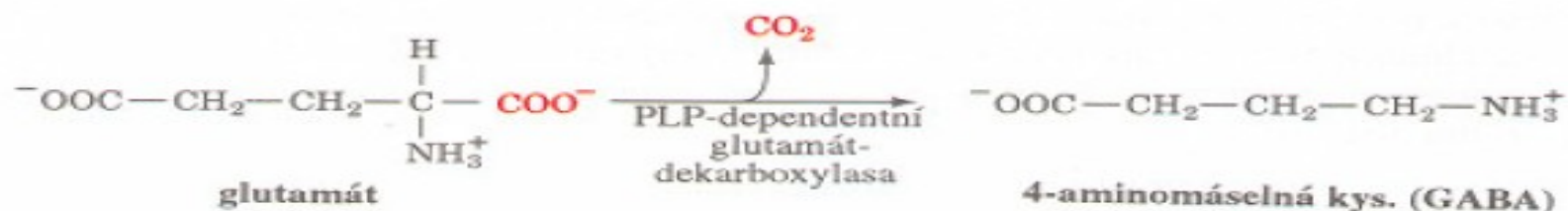


Dekarboxylace



Biogenní aminy

cystein	cystamin	CoA
k.asparagová	β alanin	„
tyrosin	tyramin	tkáňový hormon
DOPA	dopamin	„
histidin	histamin	„
hydroxytryptofan	serotonin	„
k.glutamová	k. γ -aminomáselná	neuromodulátor
serin	ethanolamin	fosfolipidy
methionin	spermin, spermidin	sperma



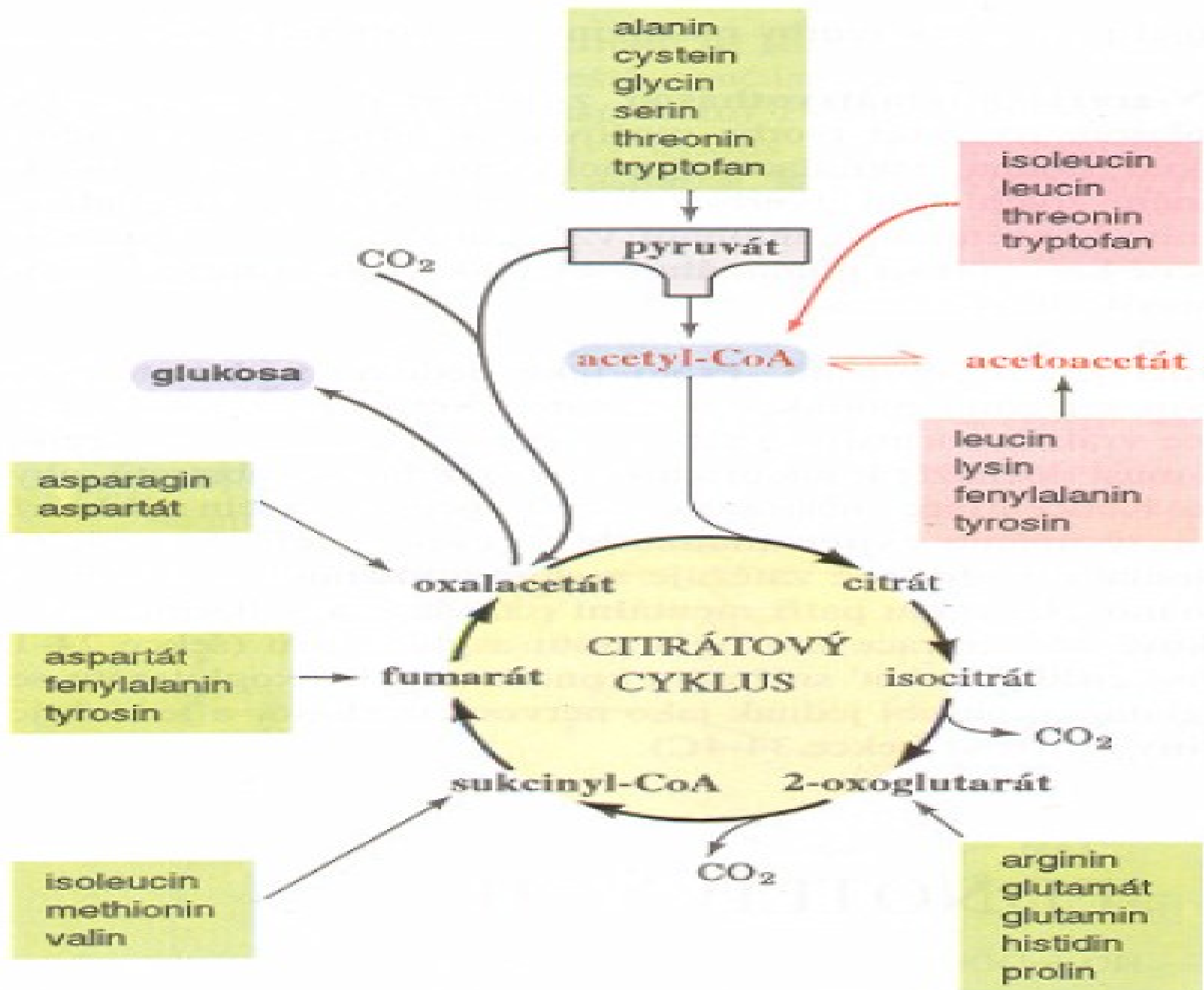
Degradace uhíkových koster aminokyselin

1. Glukogenní aminokyseliny - prekurzory sacharidů

pyruvát	-	Ser, Ala, Cys, Gly, Thr, Met, Trp
2-oxoglutarát	-	Glu, Gln, Arg, Pro, His
oxalacetát	-	Asp, Asn
fumarát	-	Phe, Tyr
sukcinyl-CoA	-	Val, Ile, Met, Thr

2. Ketogenní aminokyseliny - prekurzory mastných kyselin

acetoacetát	-	Leu, Phe, Tyr, Lys, Trp
acetyl-CoA	-	Leu, Ile, Trp

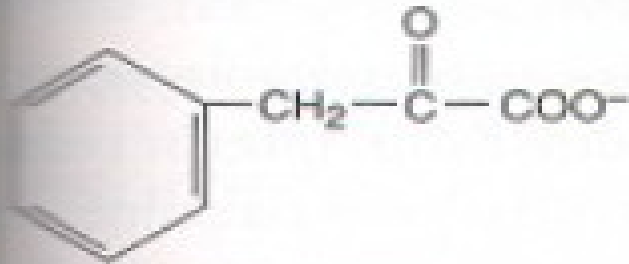
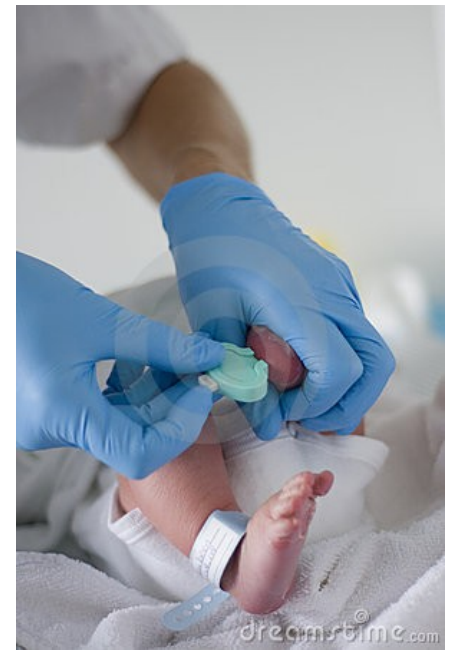


Neléčená Fenylketonurie - PKU

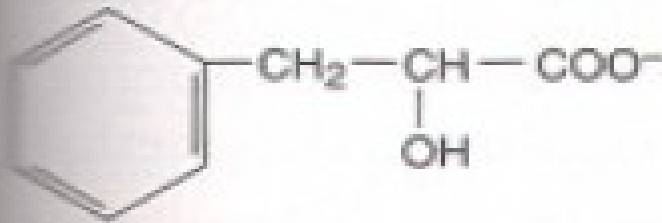
Příznaky neléčené Fenylketonurie - PKU:
mentální postižení, křeče, torpidní ekzém,
typické světlé vlasy, řasy a obočí



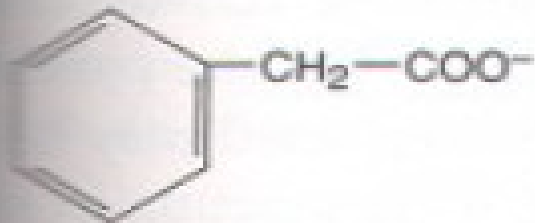
Fenylketonurie novorozenecký screening



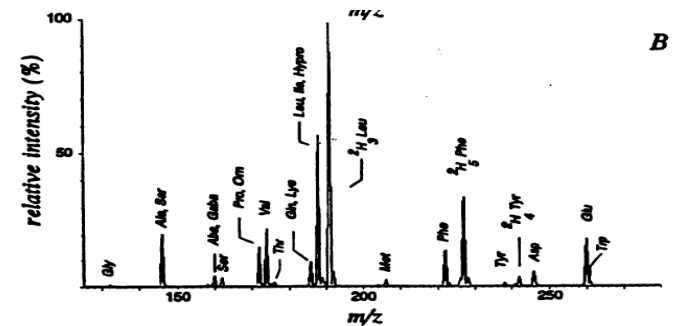
Phenylpyruvate

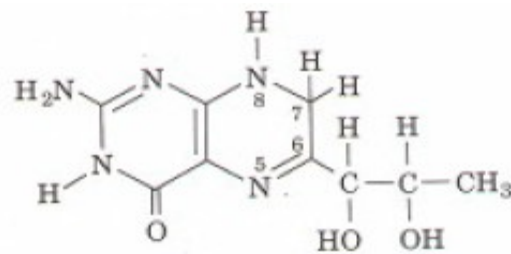


Phenyllactate

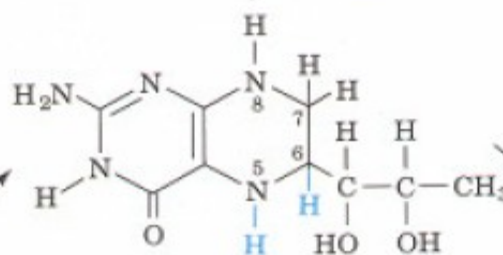


Phenylacetate

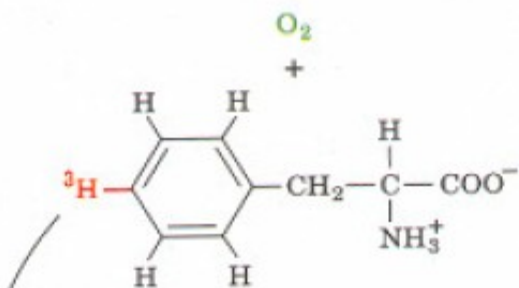




7,8-dihydrobiopterin

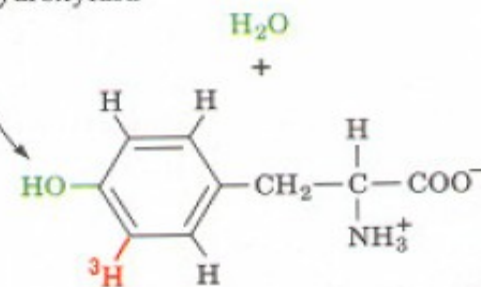


5,6,7,8,-tetrahydrobiopterin



fenylalanin

fenylalanin-hydroxylasa



tyrosin

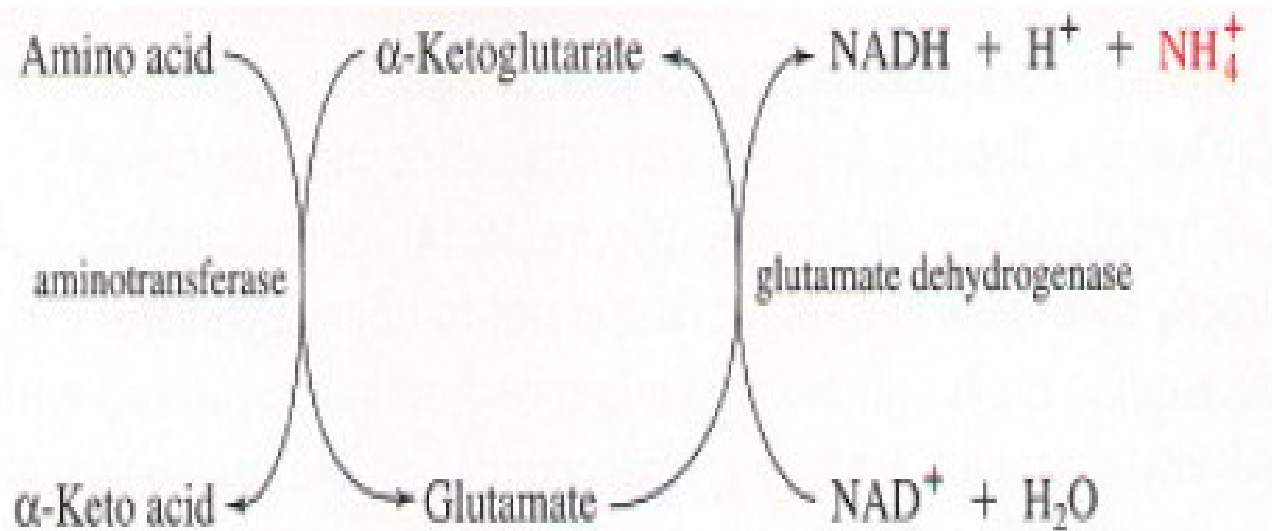
dihydropteridinreduktasa

NAD⁺

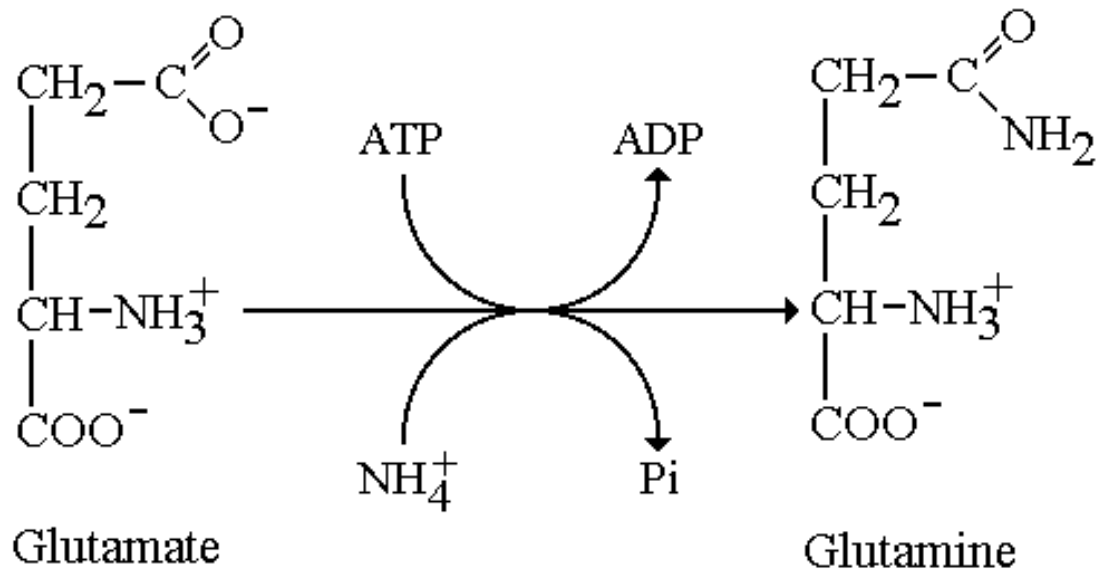
NADH

7,8-dihydrobiopterin
(chinoidní forma)

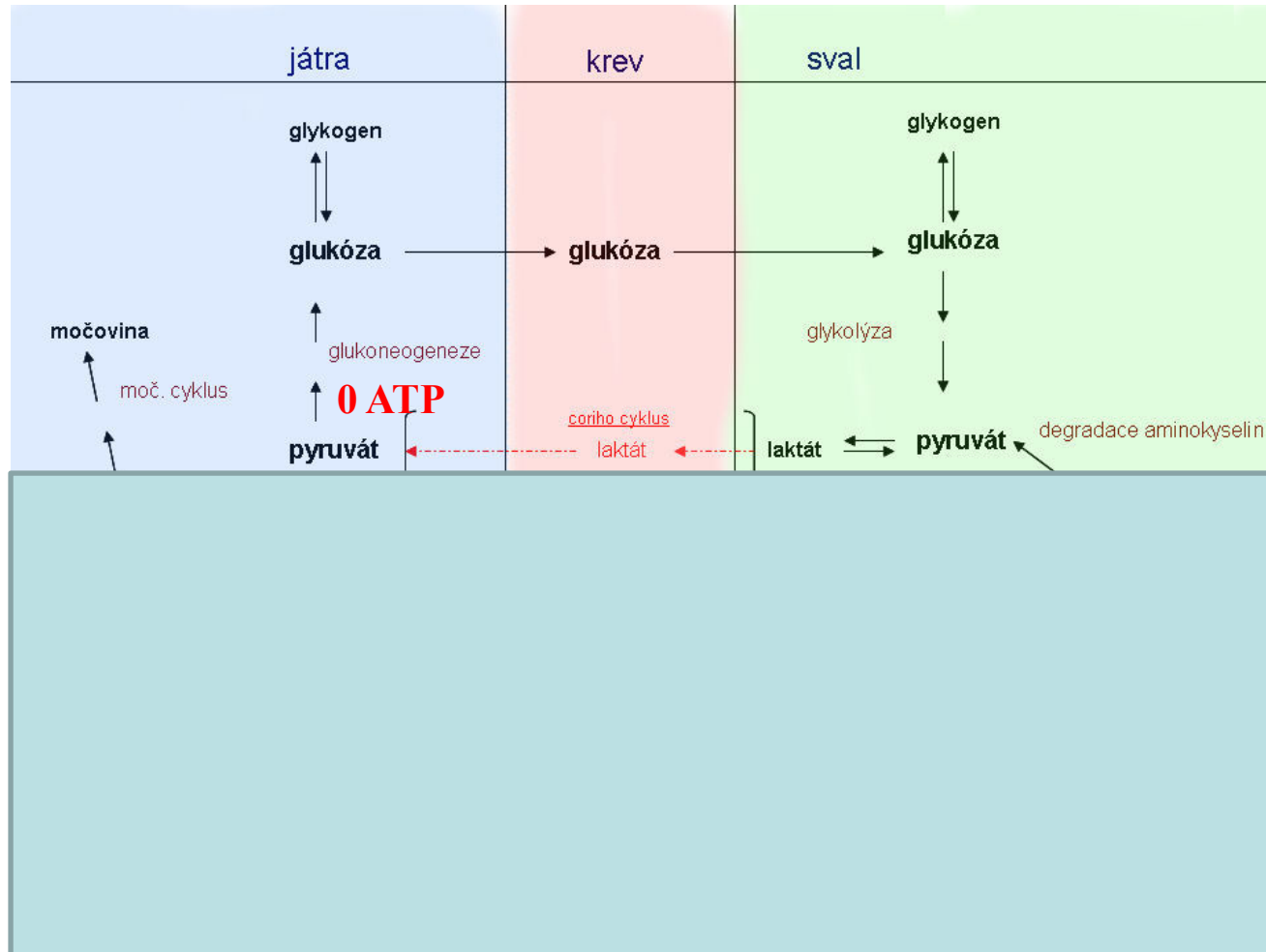
Metabolismus amoniaku



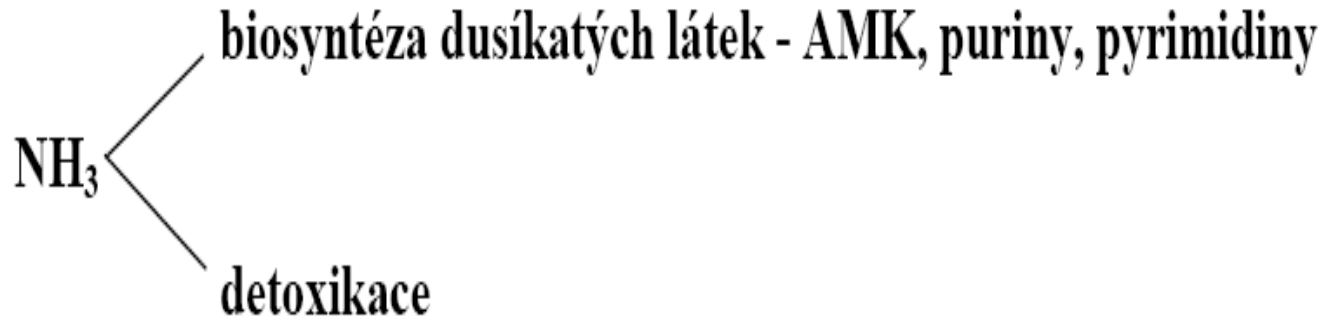
Glutamin synthethasa



Alaninový-glukosový cyklus



Metabolismus amoniaku



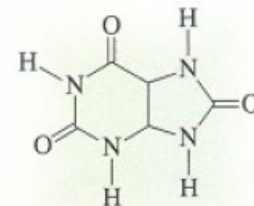
Živočichové - amonotelní - NH_3 - vodní živočichové

- urikotelní - k.močová - vejcorodí

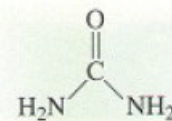
- ureotelní - močovina - placentálové

Rostliny - nevylučují NH_3

NH_4^+
(c) Ammonium ion



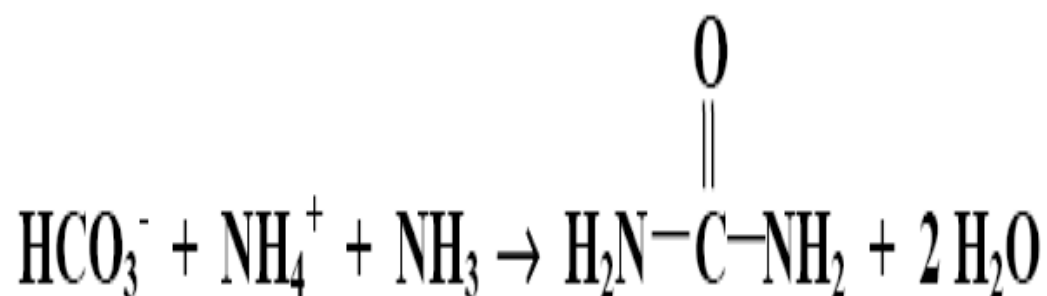
(b) Uric acid

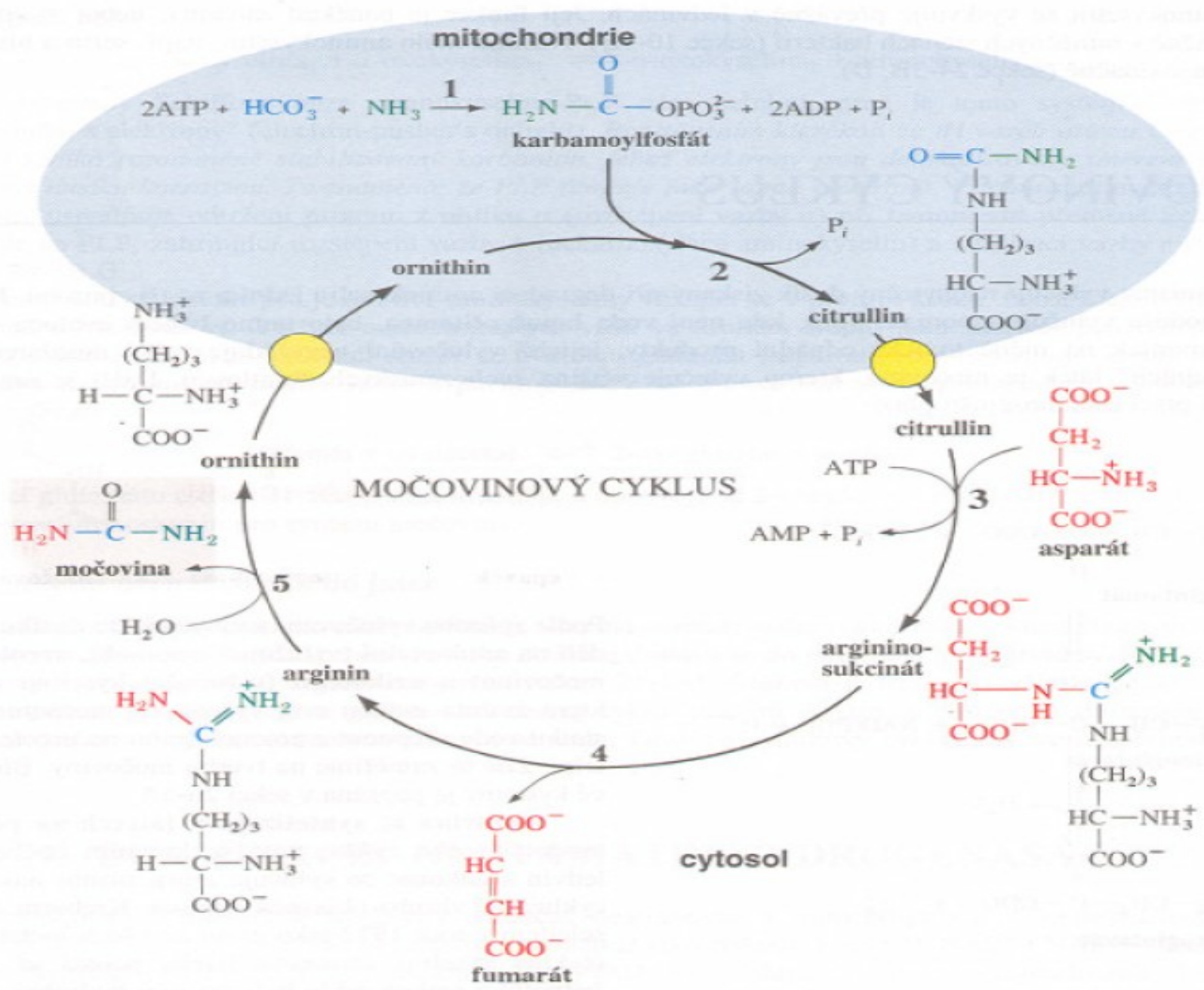


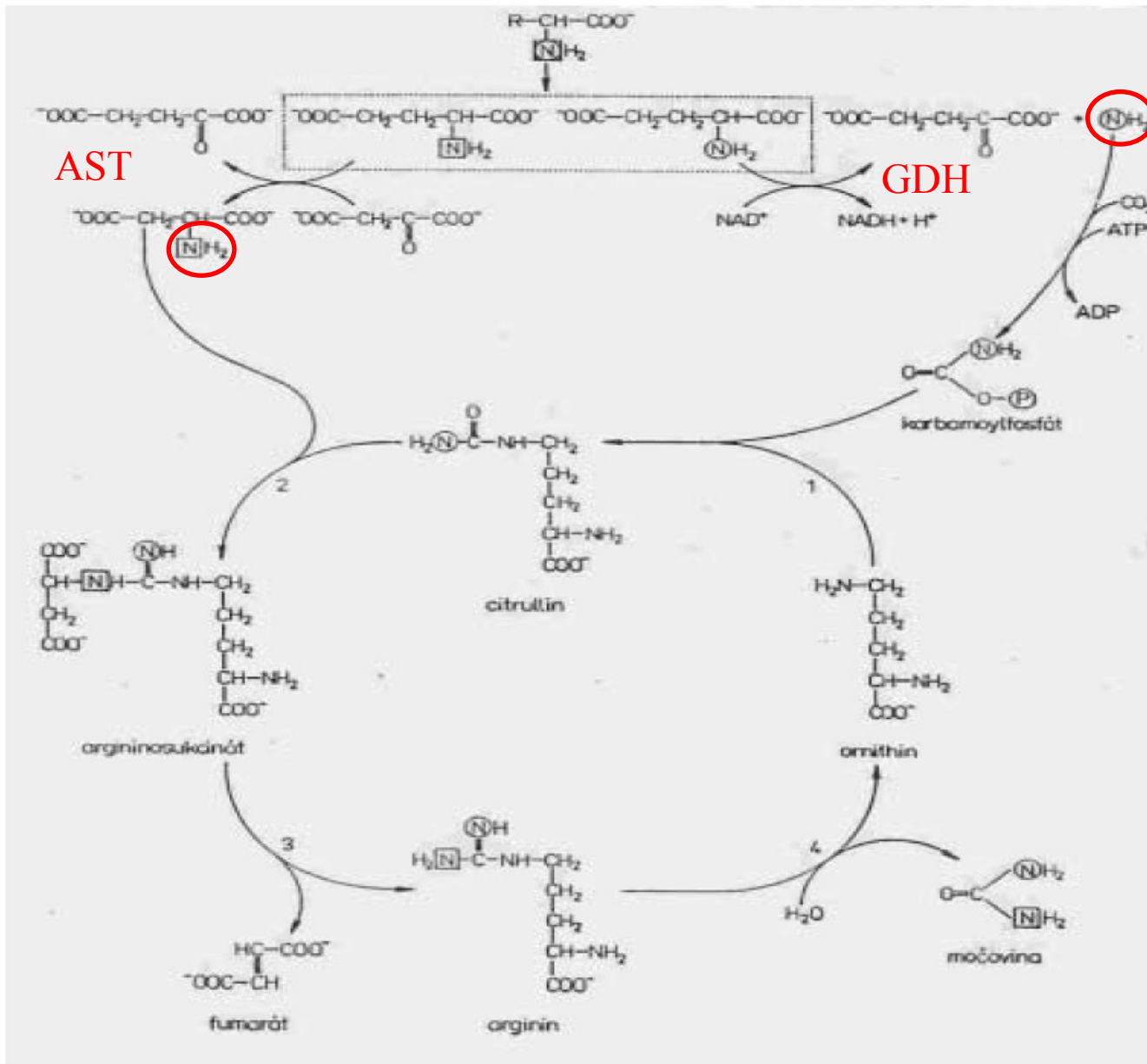
(a) Urea

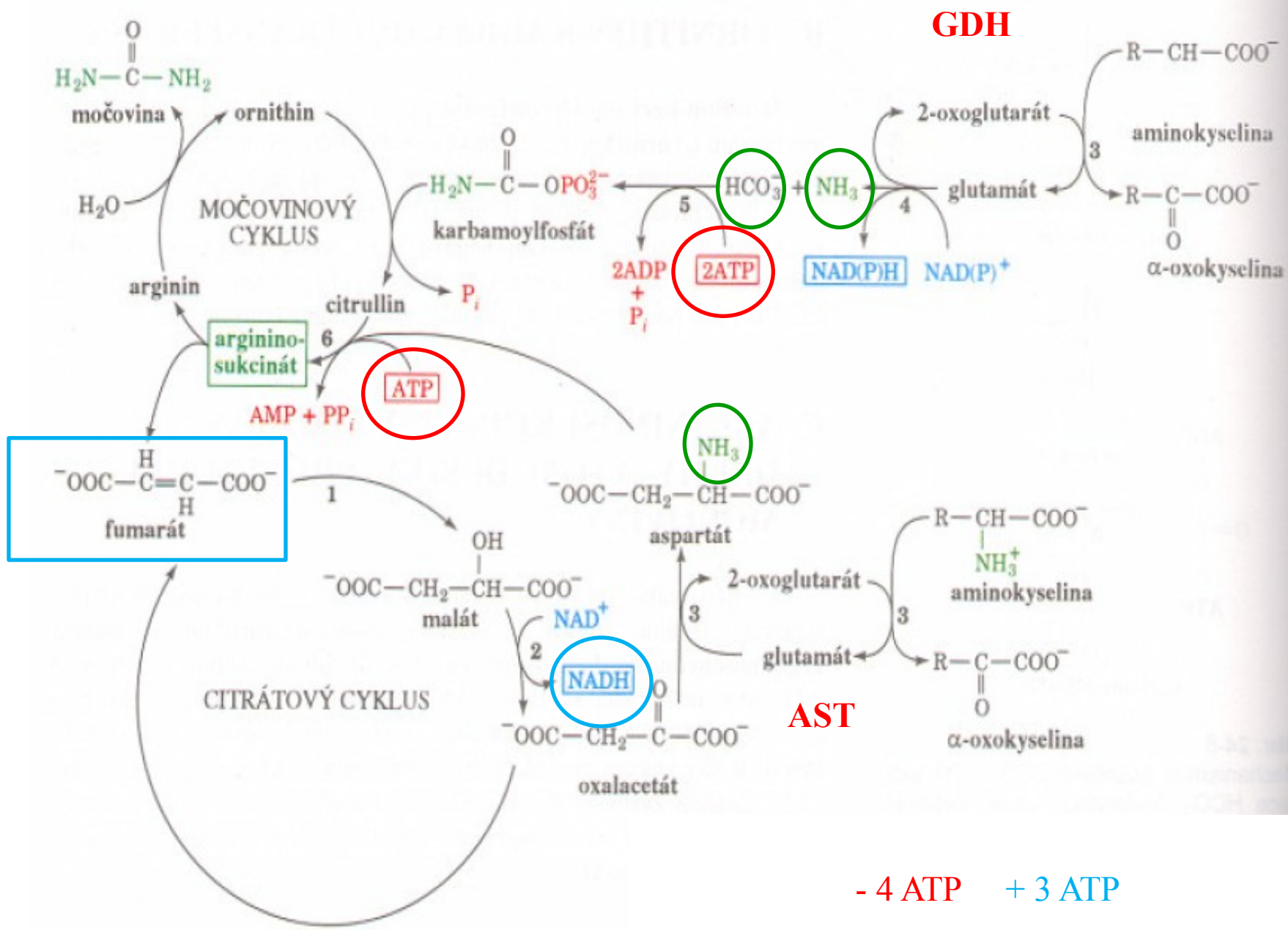
Tvorba močoviny - ornitinový cyklus

H. KREBS, K. HENSELEIT - 1932

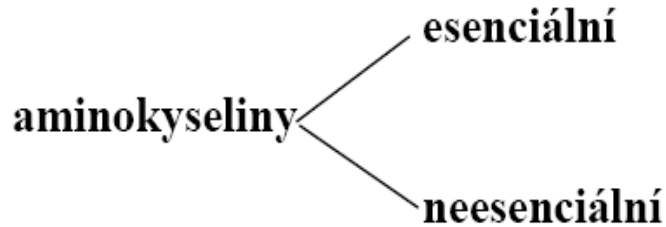






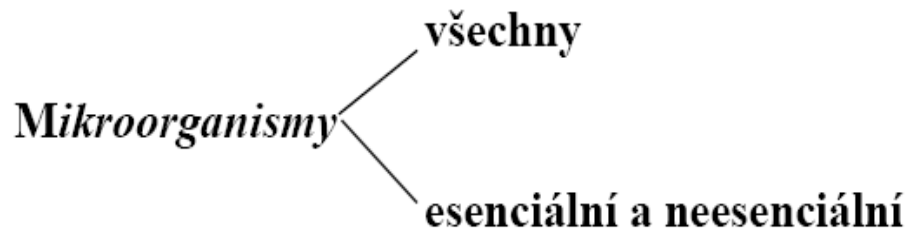


Biosyntéza aminokyselin



Rostliny - všechny

NH_2 , NH_4^+ , NO_3^- , NO_2^- , N_2



NH_2 , NH_4^+ , NO_3^- , NO_2^- , N_2

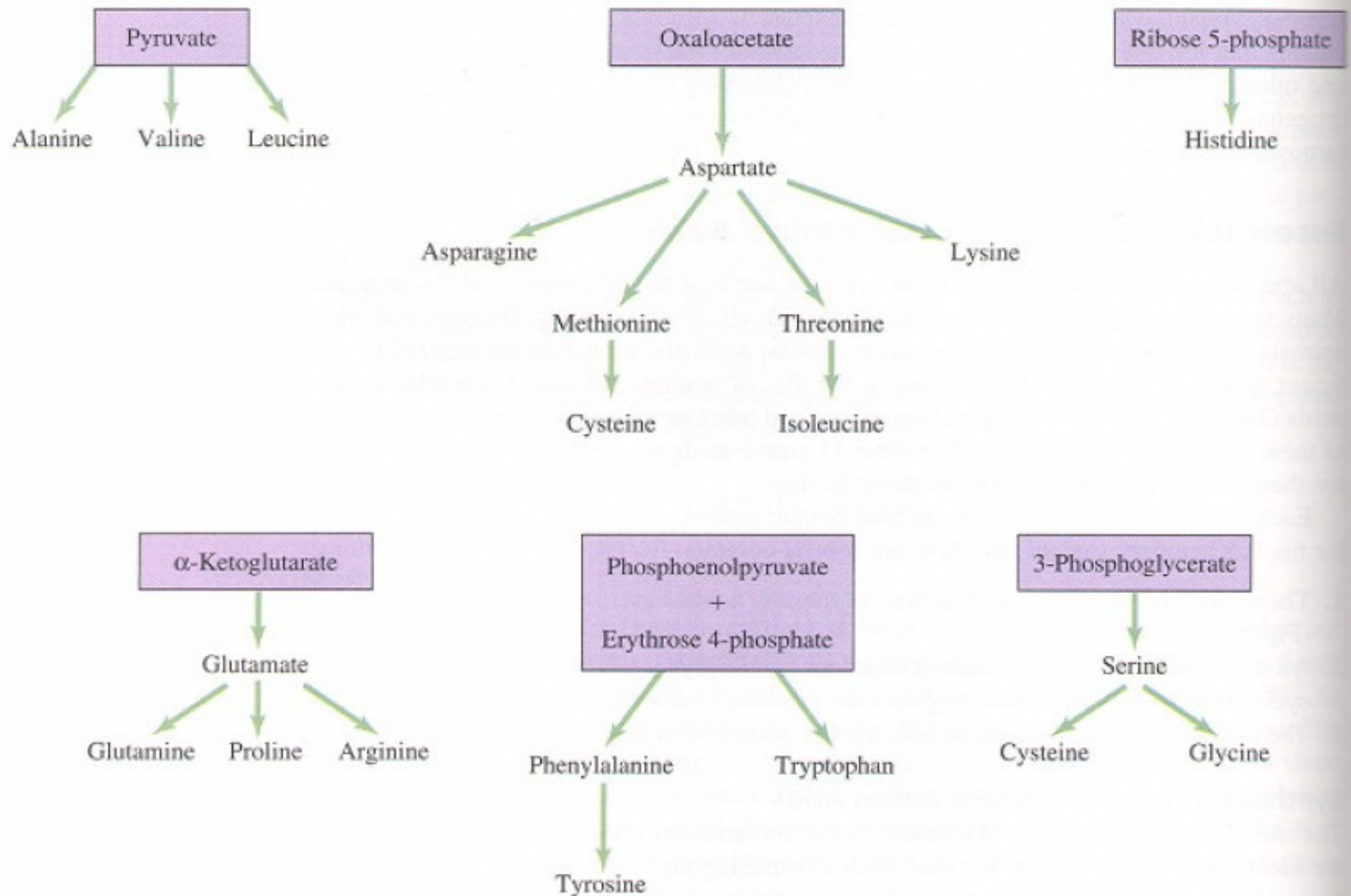
Živočichové - esenciální a neesenciální

NH_2

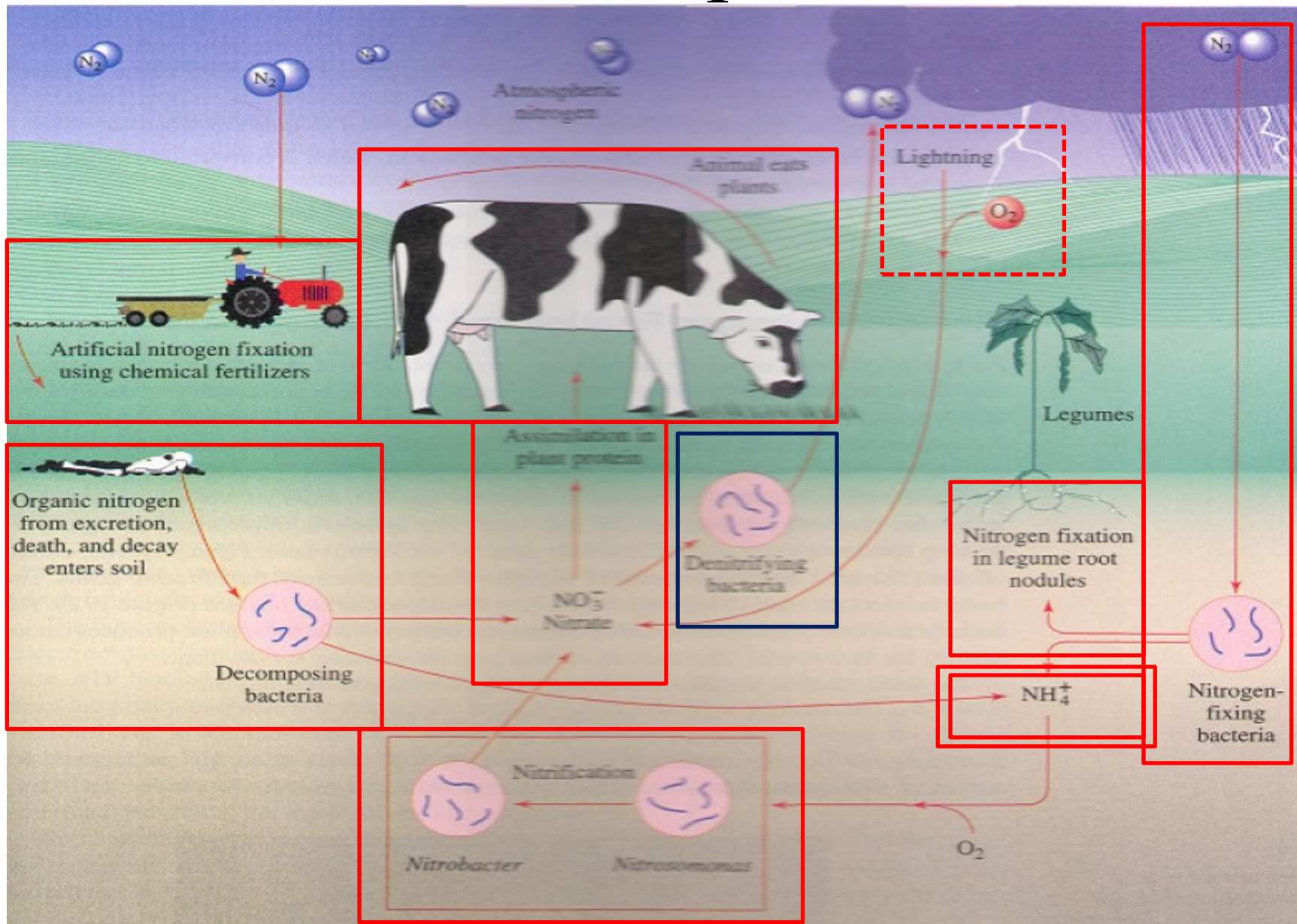
Biosyntéza aminokyselin

- **Uhlíkové kostry pocházejí z meziproduktů glykolýzy, pentózového a citrátového cyklu**
- **Biosyntéza vychází ze společných prekurzorů a probíhá přes společné meziprodukty – jen 6 drah**
- **Další AMK se tvoří přestavbou jiných AMK**
- **Neesenciální AMK jsou syntetizovány jednodušší cestou**
- **Biosyntéza esenciálních AMK je komplikovanější**

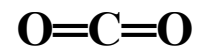
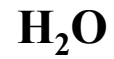
Biosyntéza aminokyselin



Osud N v přírodě



Biogenní prvky - COHN

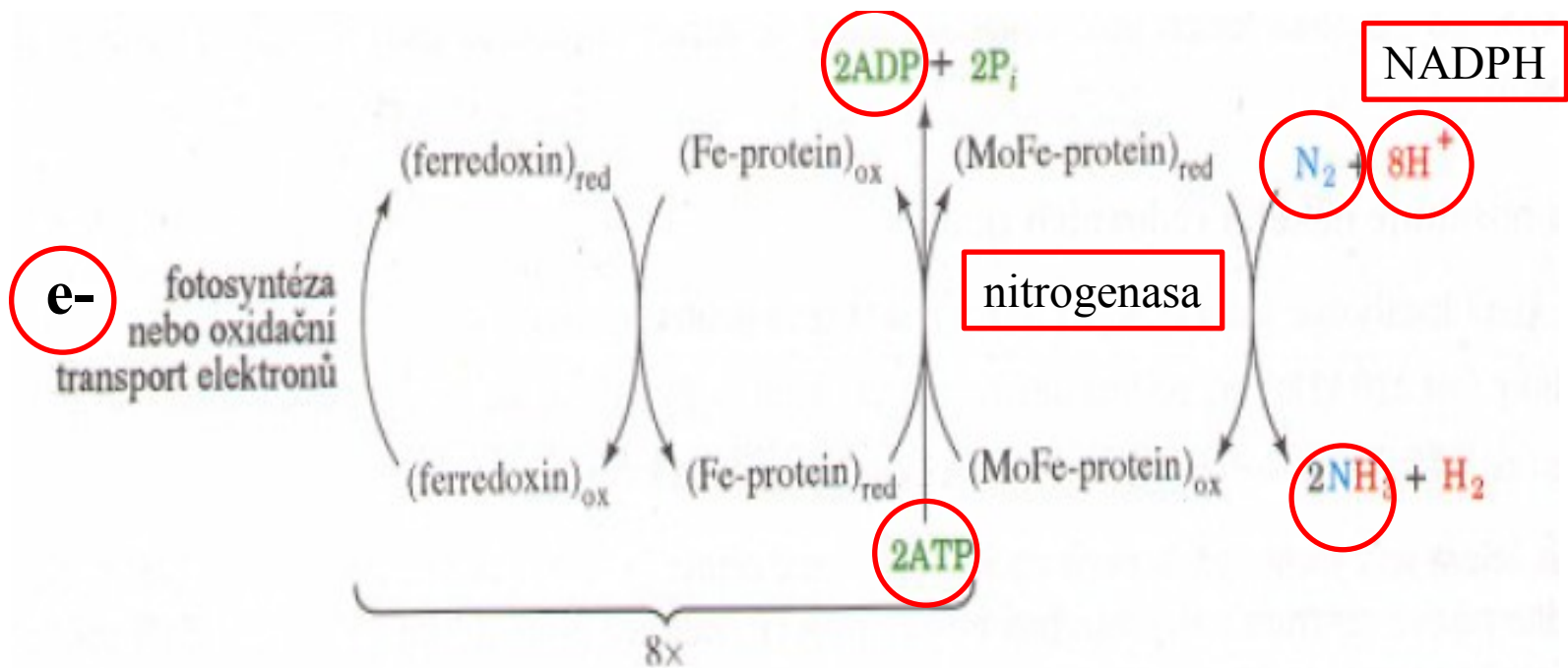


(400 kJ/mol)



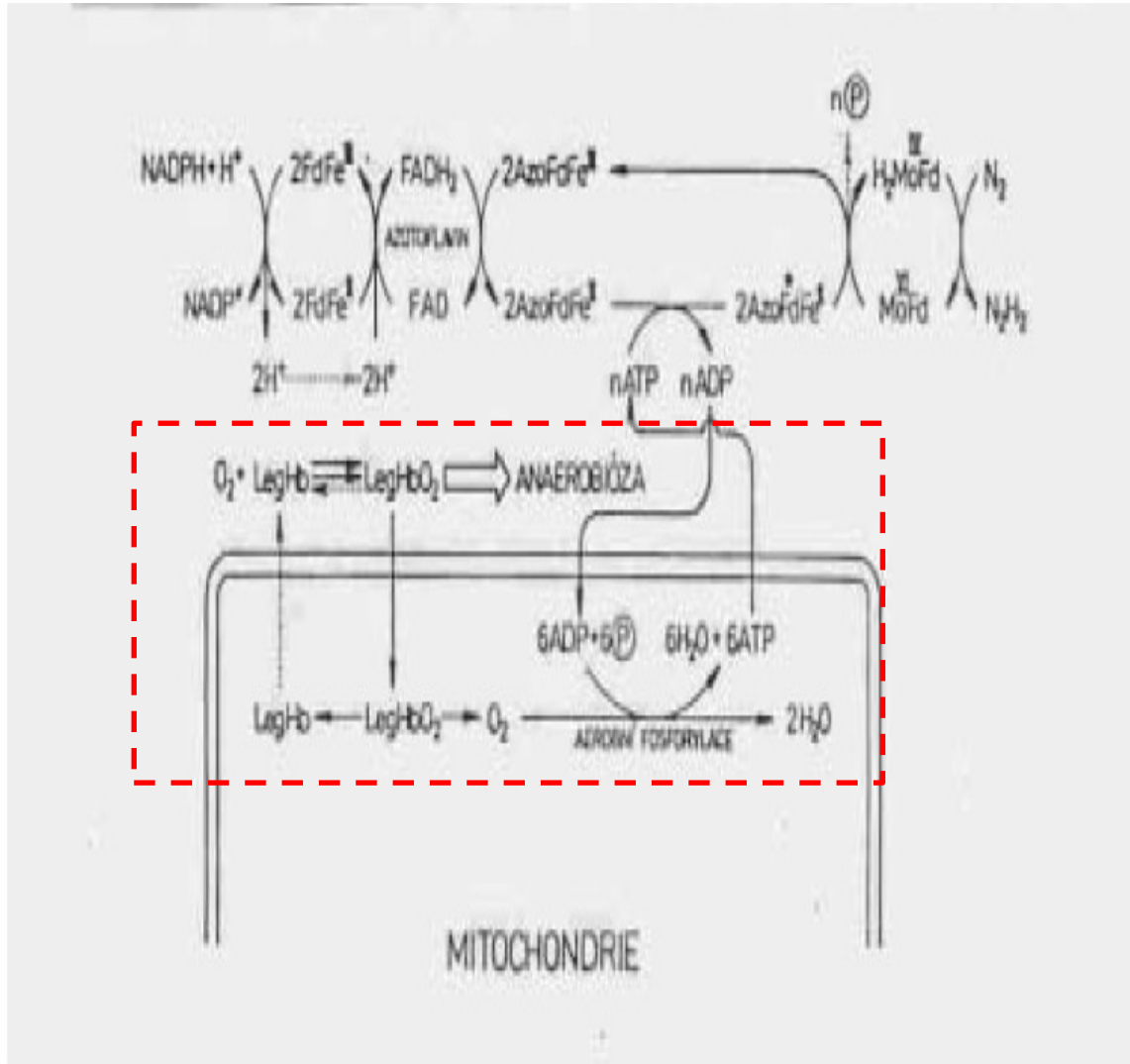
(945 kJ/mol)



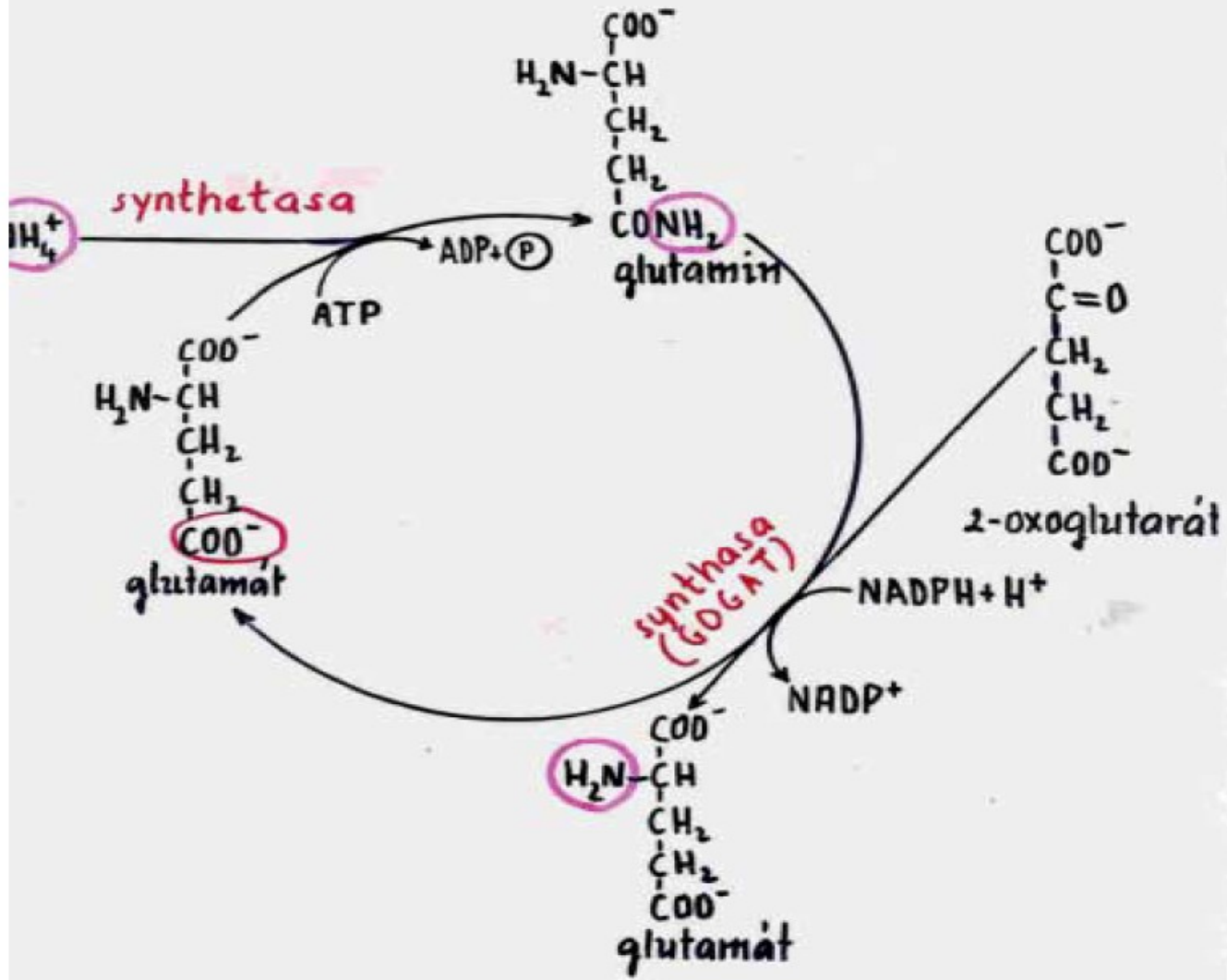


Anaerobiosa (deaktivace nitrogenasy)

- Sinice – heterocyty
- Symbiosa boboviyé rostliny a bakterie - leghemoglobin

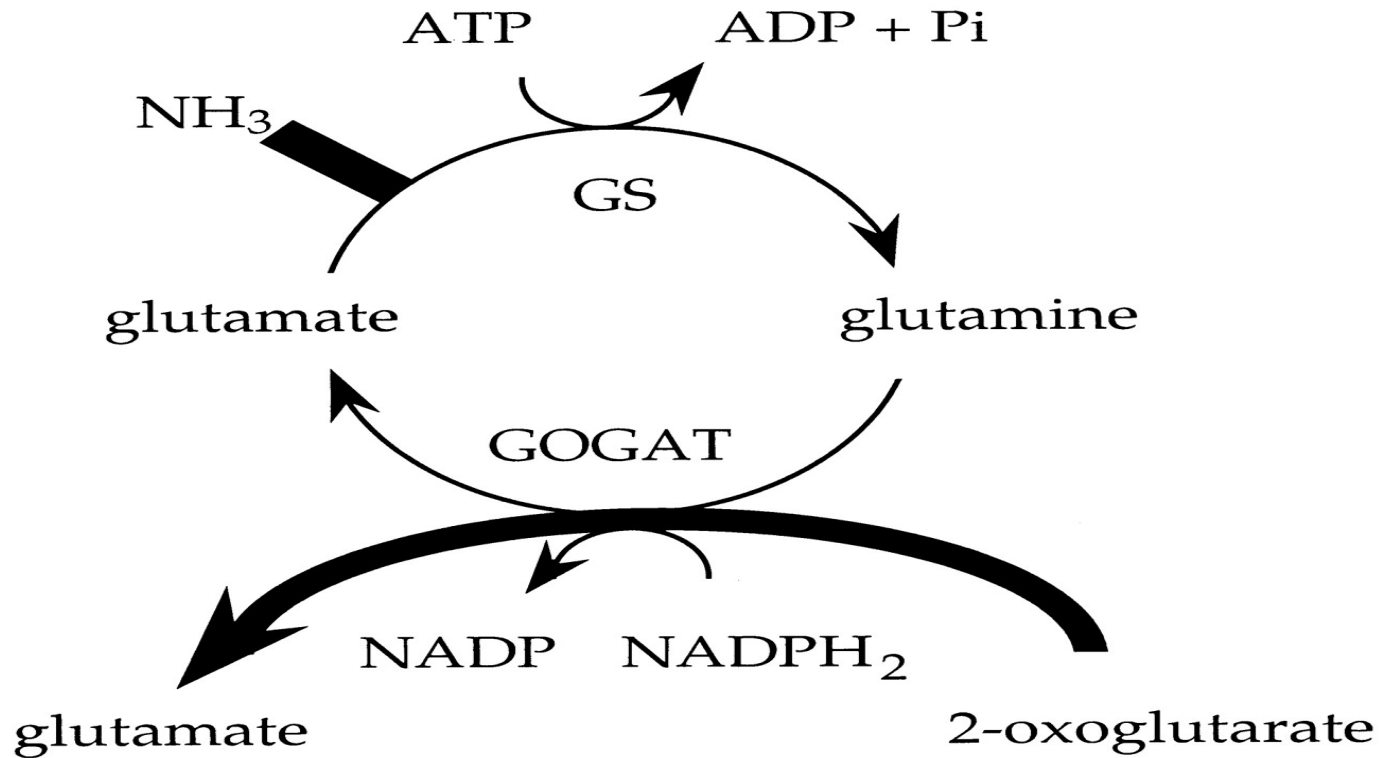


INKORPORACE NH₃ U PROKARYOT



Eukaryota - GDH

A)



B)

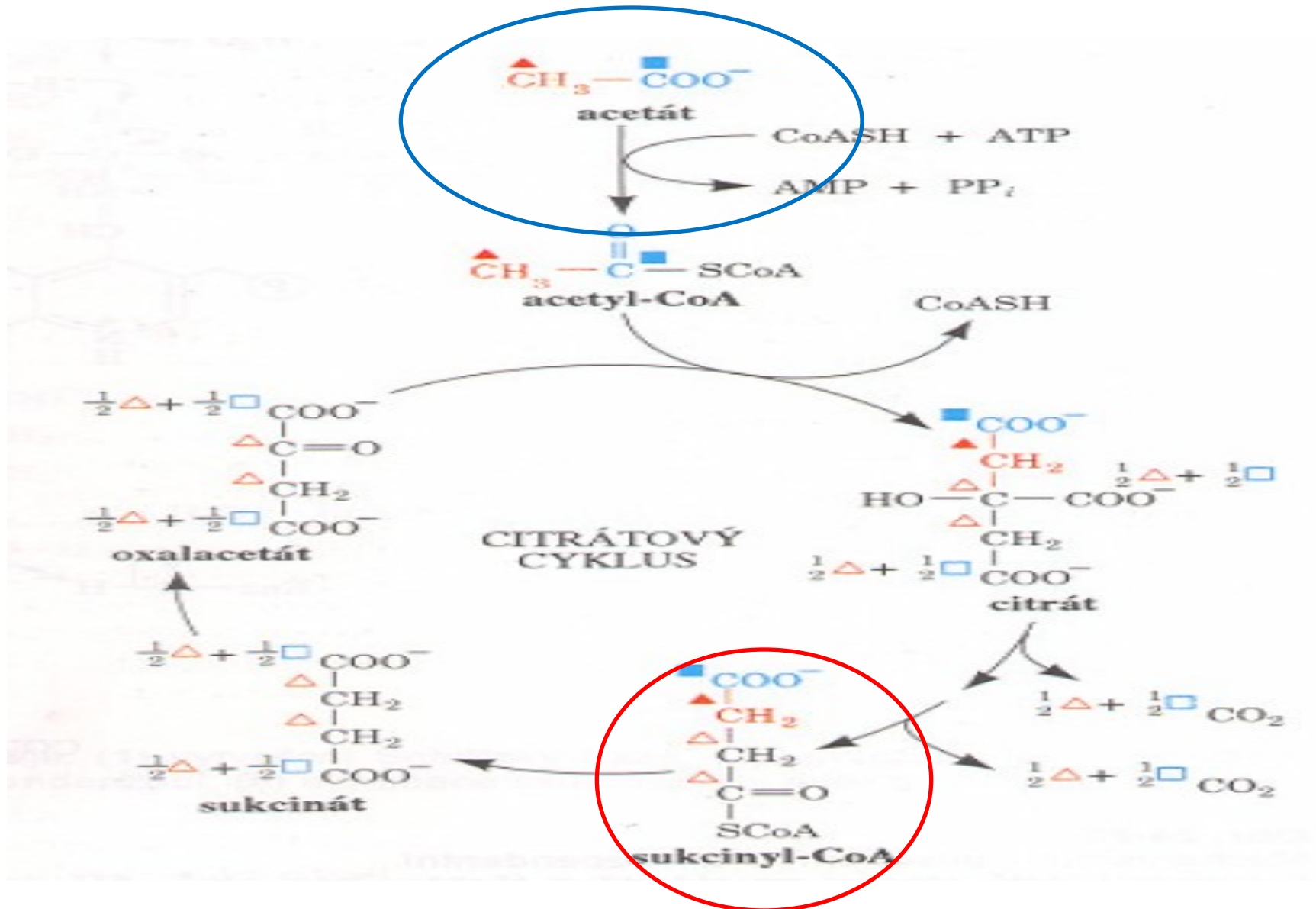


AMK jako prekurzory

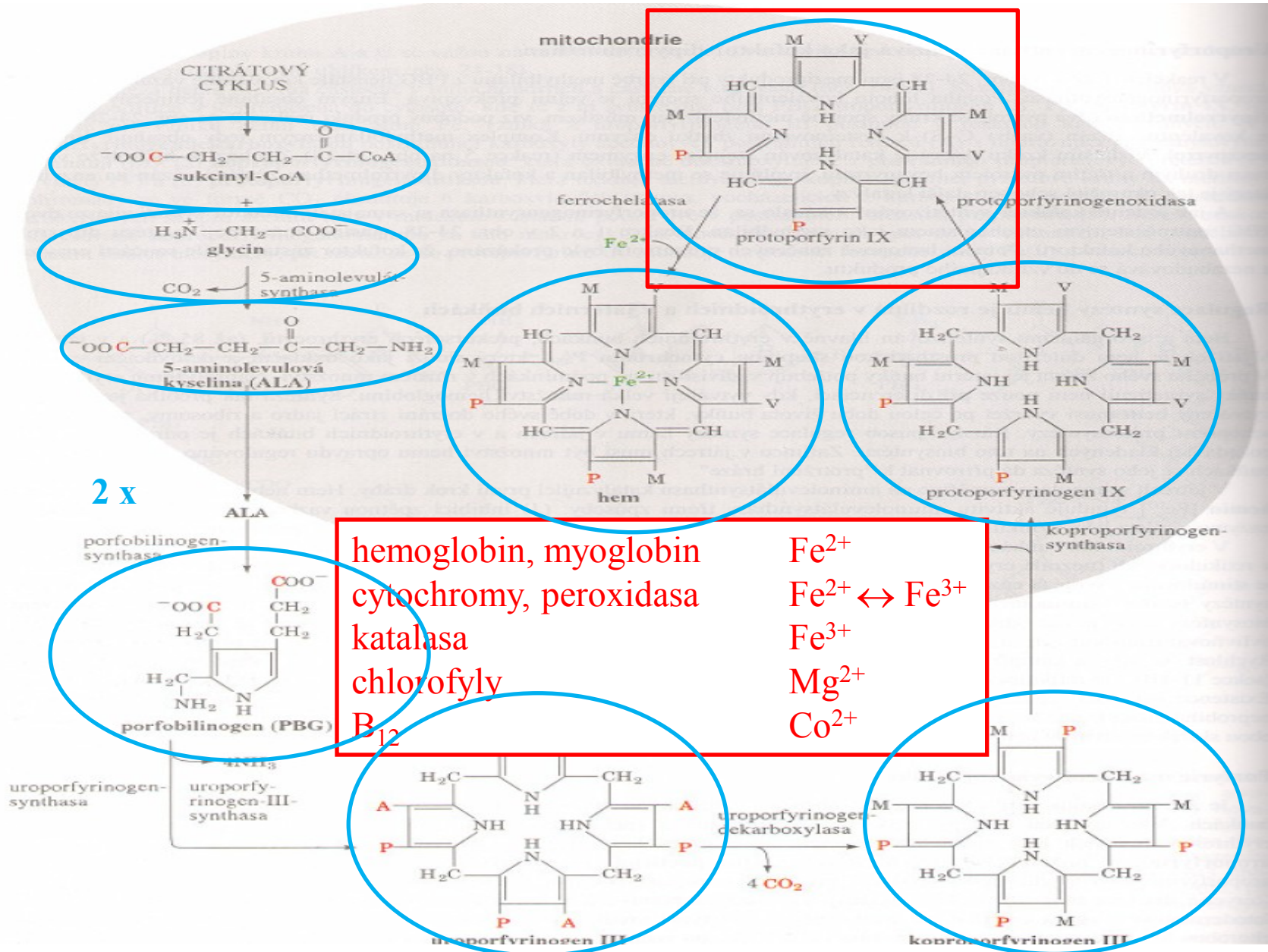
Bioactive Product	Biological Function	Amino Acid Precursor(s)
Alkaloids	Nitrogen bases in plants	Ornithine, Asp, Lys, Tyr, Trp, Phe, His
γ -Aminobutyric acid (GABA)	Inhibitory neurotransmitter	Glu
Auxin	Plant growth hormone	Trp
Catecholamines	Neurotransmitters, hormones	Tyr, Phe
Glutathione	Redox tripeptide	Gly, Glu, Cys
Histamine	Allergic response, stomach acid secretion	His
Melanin	Skin pigments	Tyr, Phe
Melatonin	Regulates sleep cycles	Trp
Nitric oxide	Cell messenger	Arg
Phosphocreatine	Energy molecule in muscle	Gly, Arg, Met
Porphyrin	Heme and chlorophyll	Gly
Purine bases	RNA, DNA, cofactors	Asp, Gly, Gln
Pyrimidine bases	RNA, DNA, cofactors	Asp
Serotonin	Neurotransmitter (hormone)	Trp
Spermine, spermidine	DNA packaging	Met, ornithine
Thyroxine	Hormone	Tyr



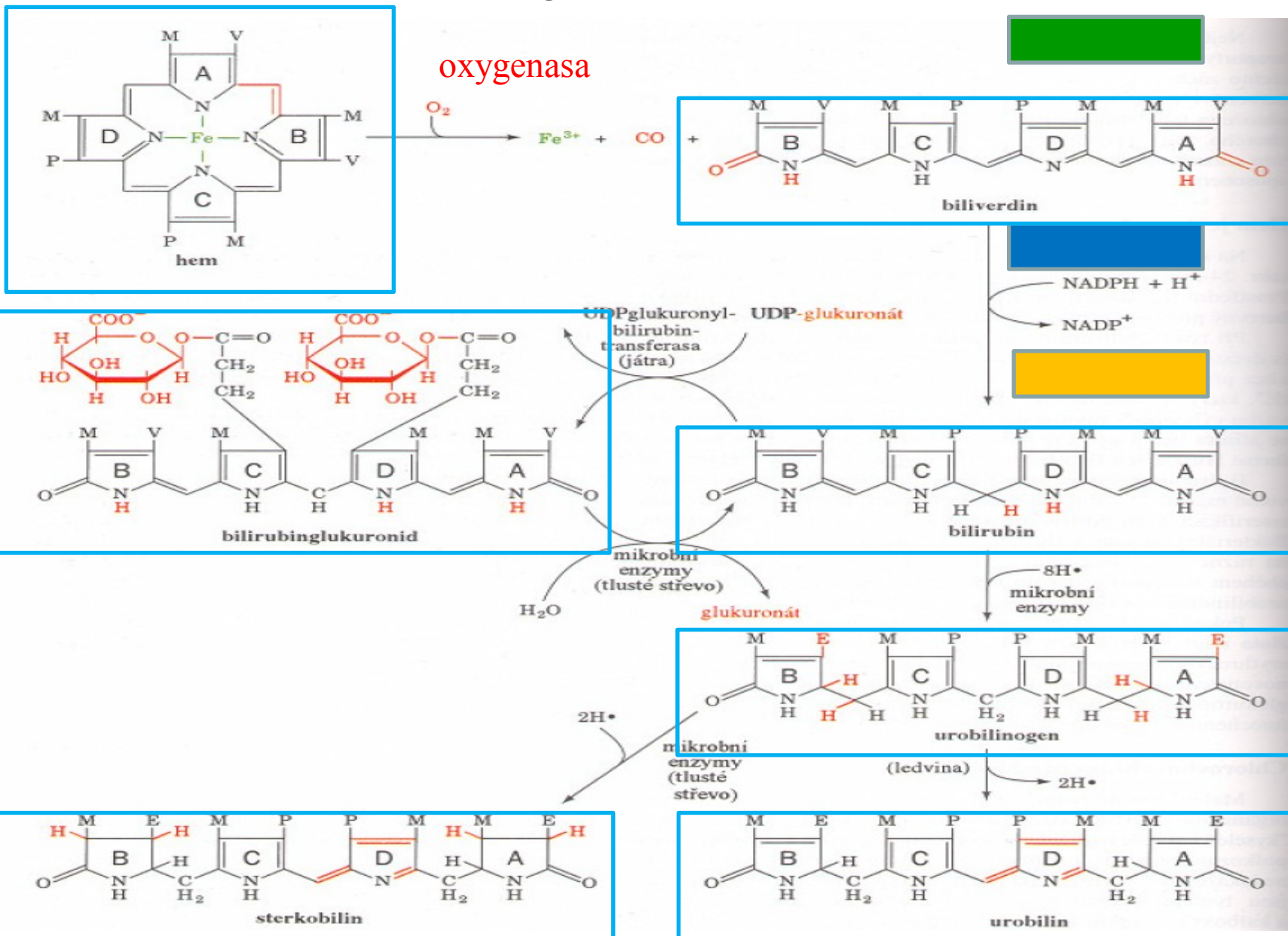
Hem



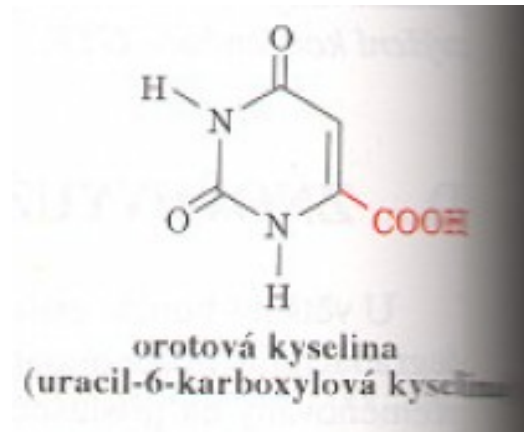
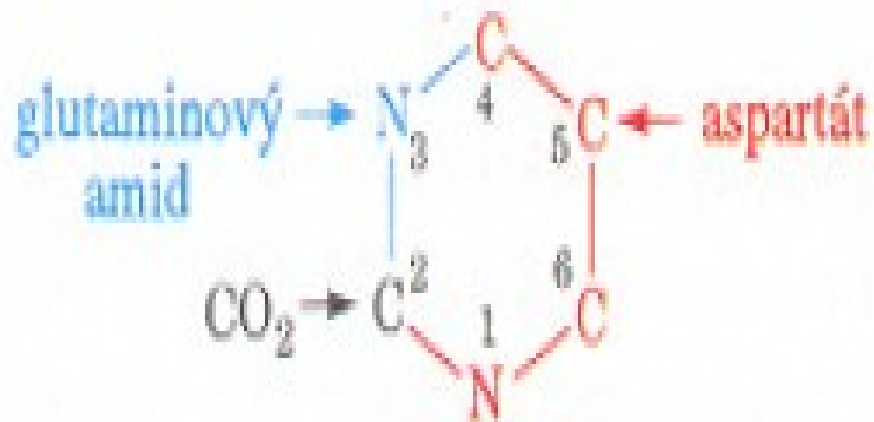
Biosyntéza hemu



Degradace hemu

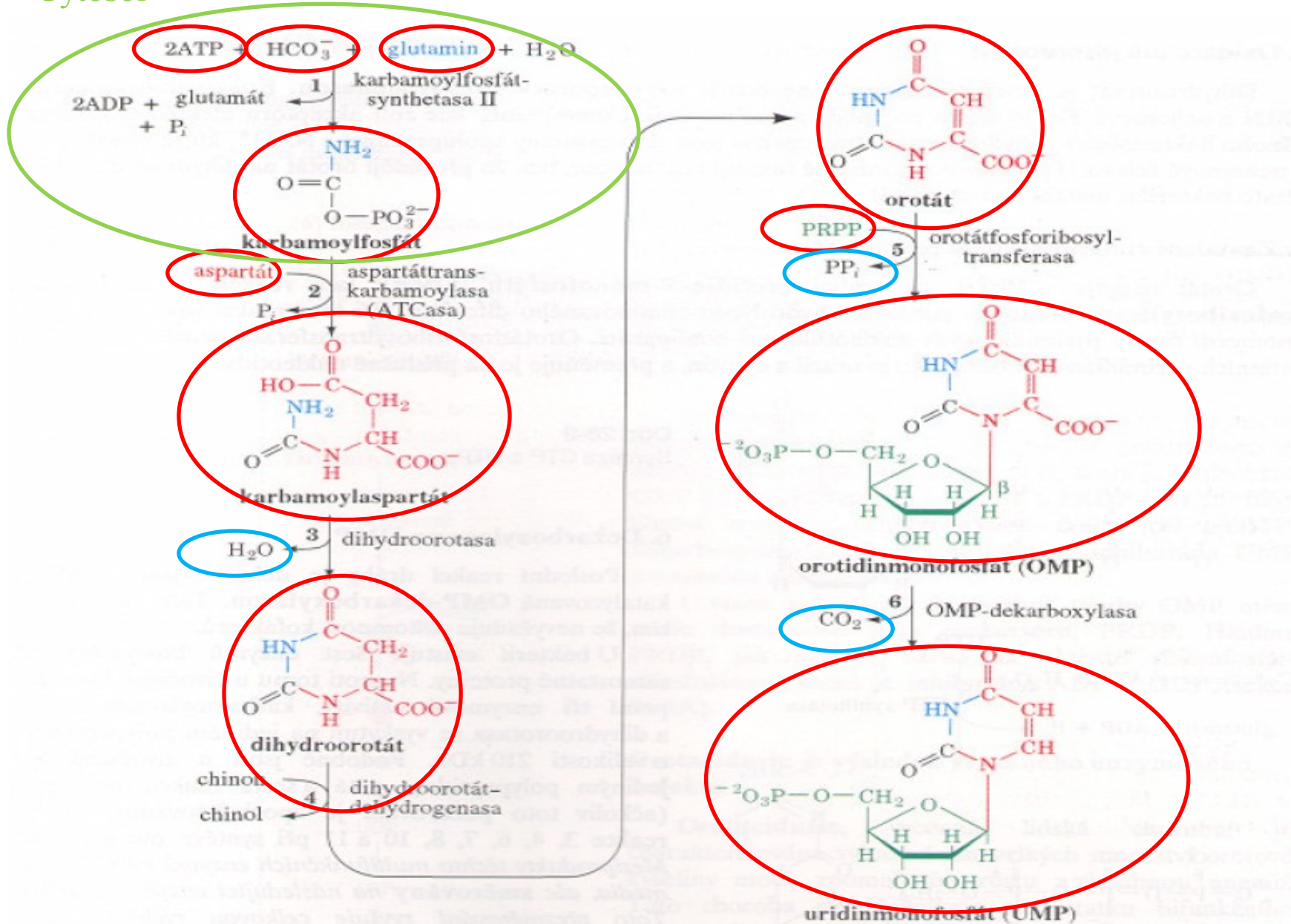


Biosyntéza pyrimidinových bází

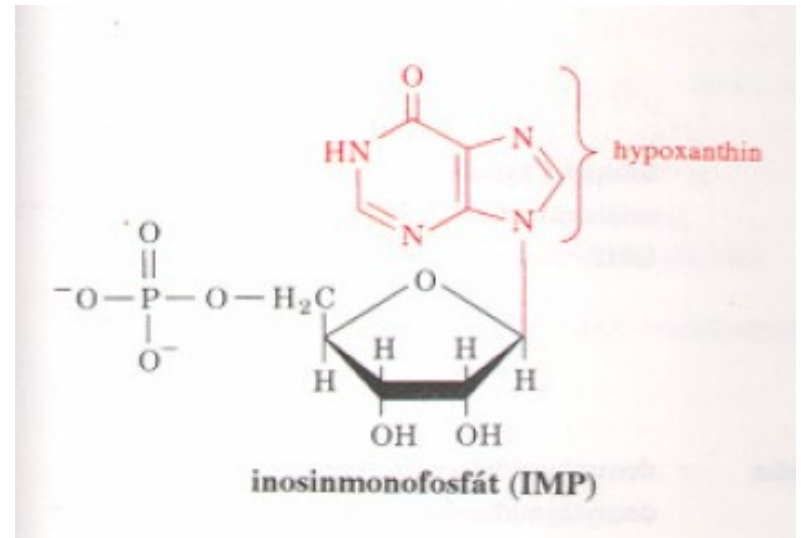
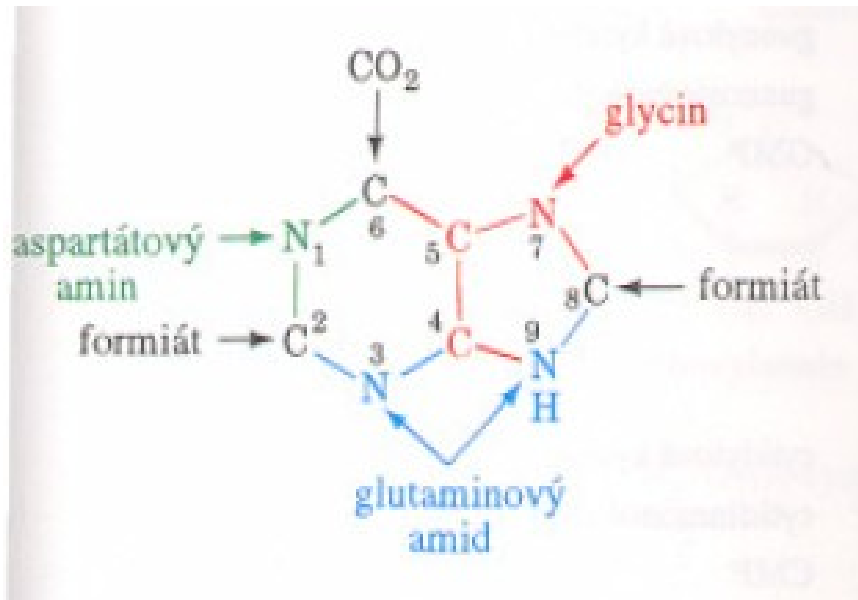


Cytosol

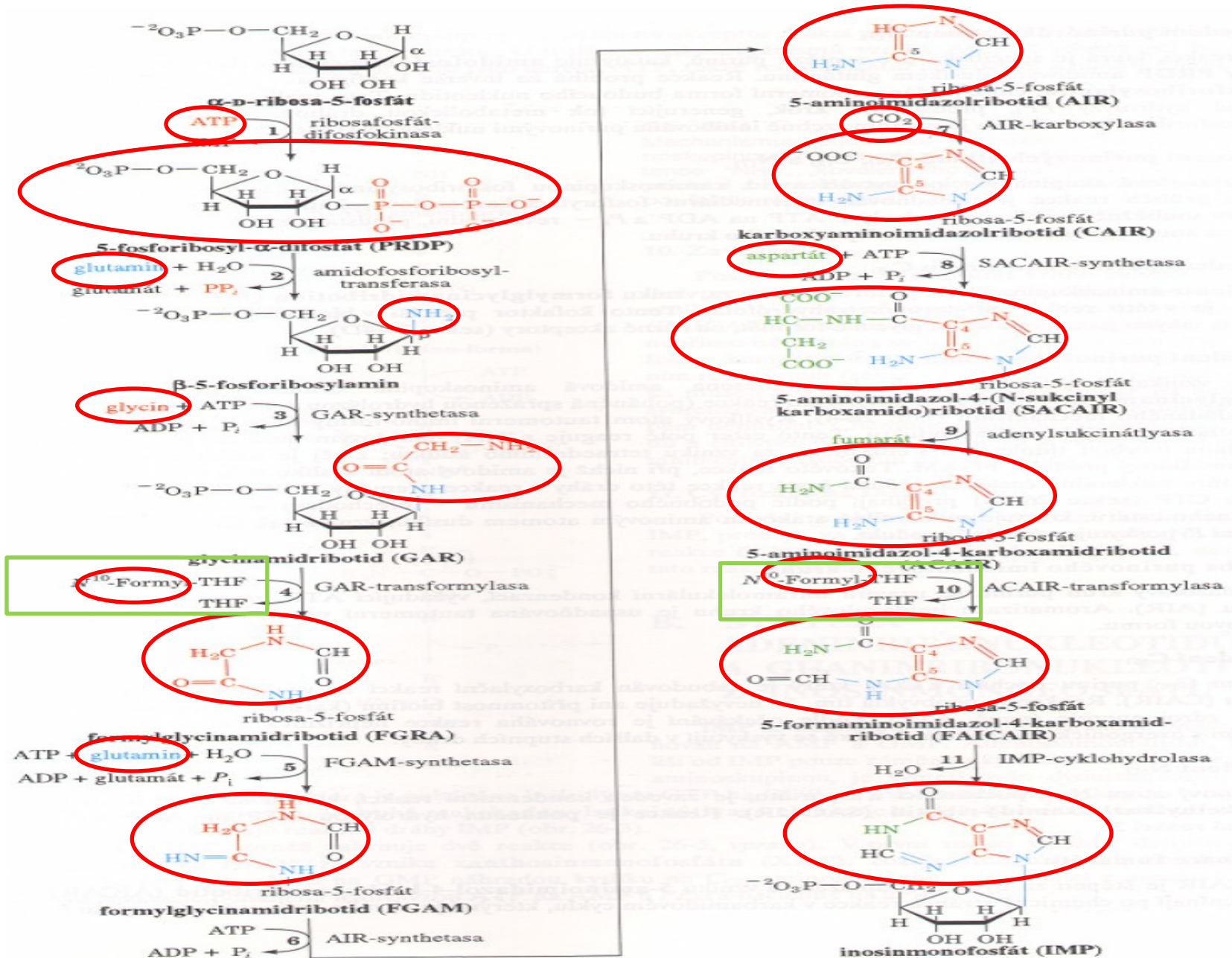
Biosyntéza pyrimidinových bází



Biosyntéza purinových bází

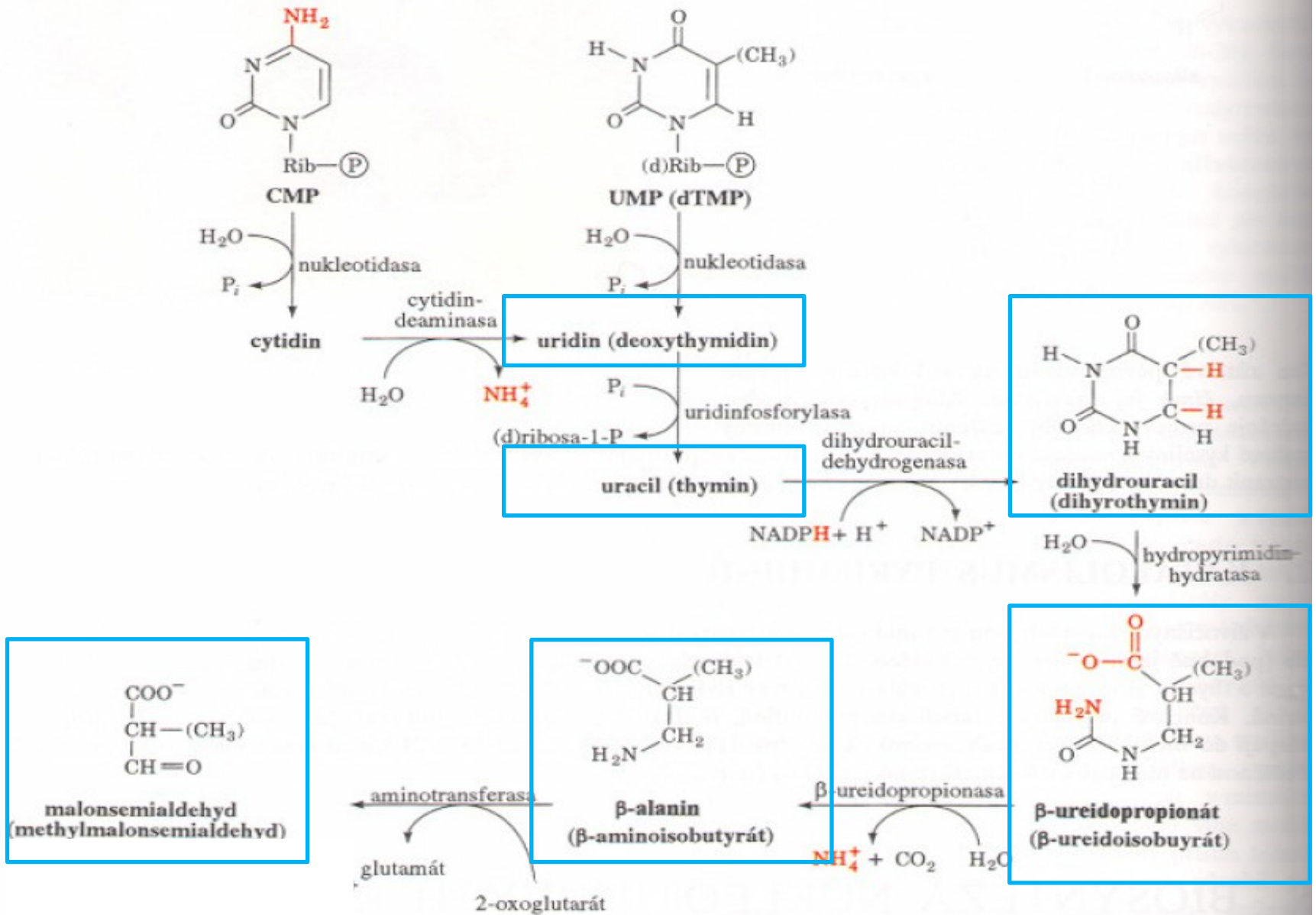


Biosyntéza purinových bází

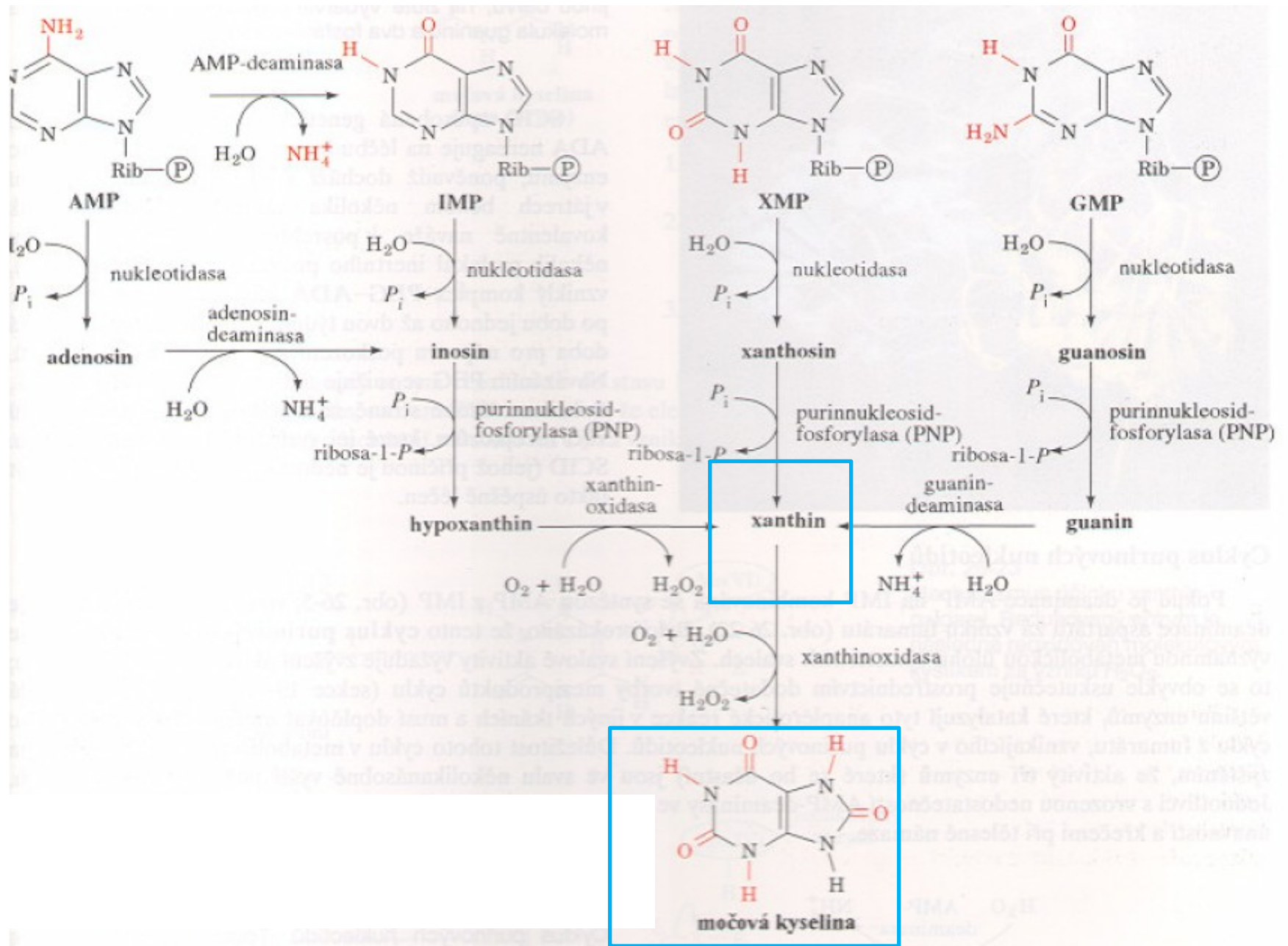


Antimetaboly - antifoláty

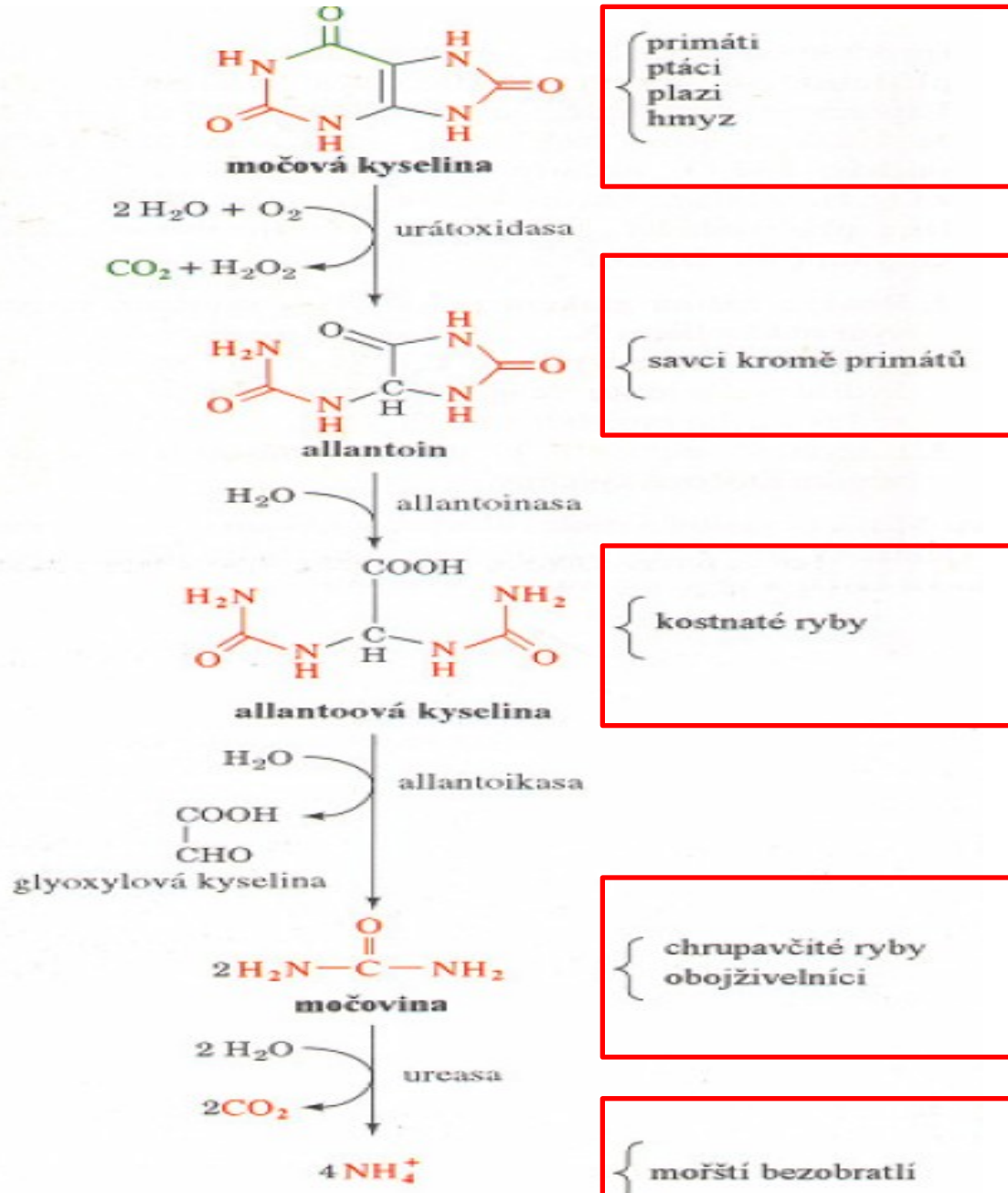
Degradace pyrimidinových bází



Degradace purinových bází



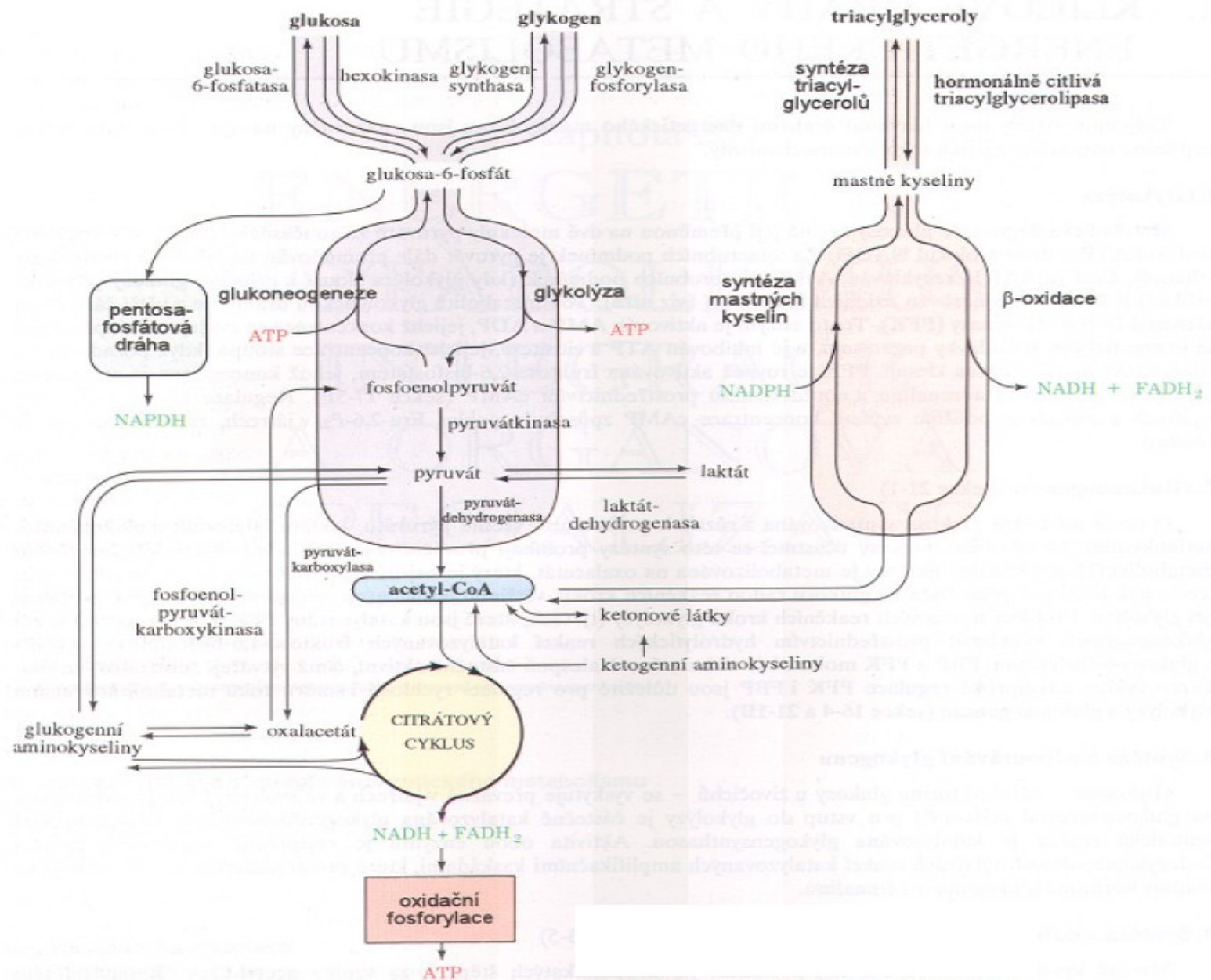
Degradace purinových bází



Metabolismus NK

- Žaludek – odštěpení proteinů pomocí HCl
- Nukleasa (fosfodiesterasa) – štěpení na oligo- a mononukletidy
- Mononukleotidasa – nukleosid + H_3PO_4
- Nukleosidasa – cukr + basa

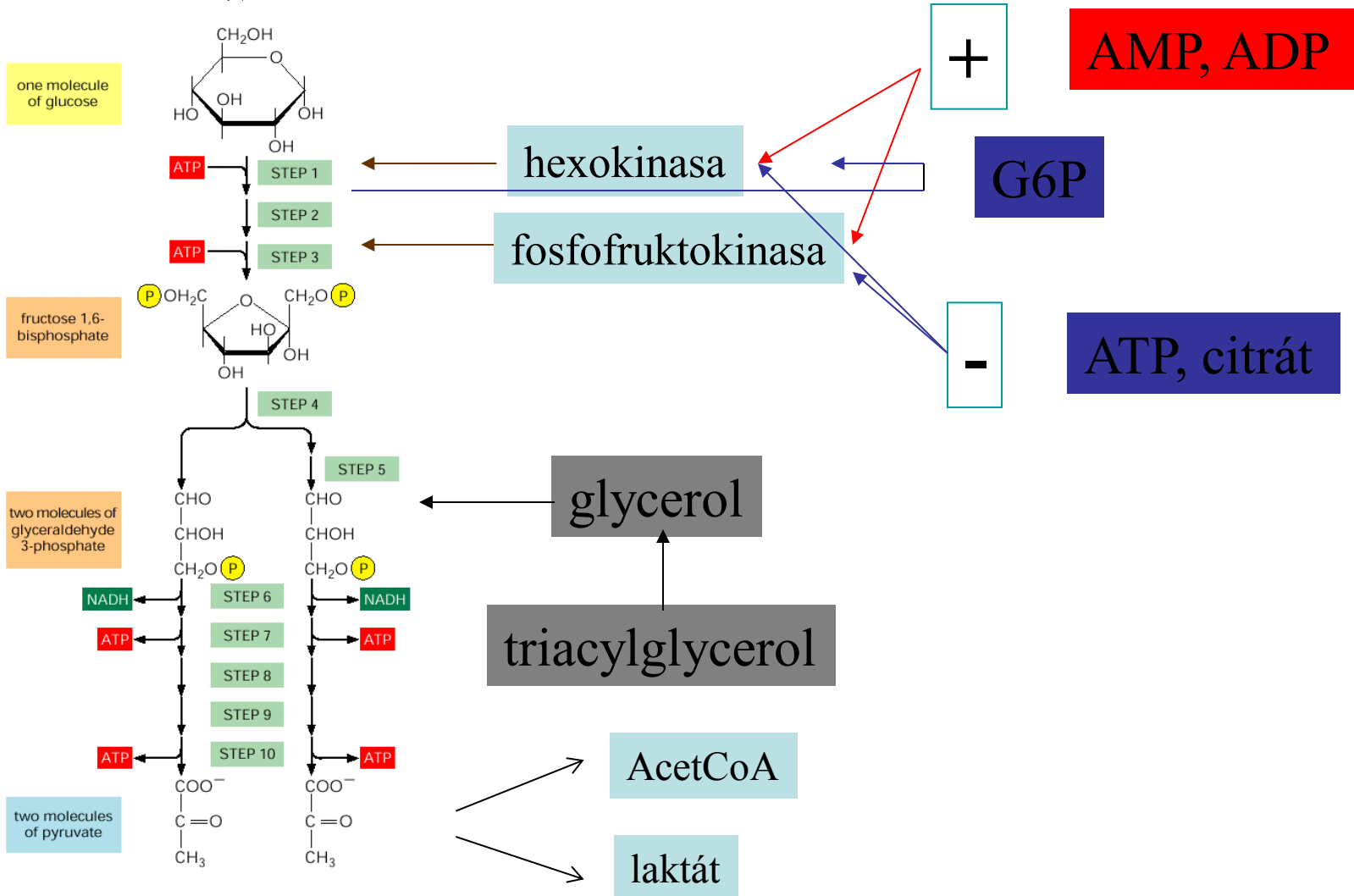
Hlavní dráhy energetického metabolismu



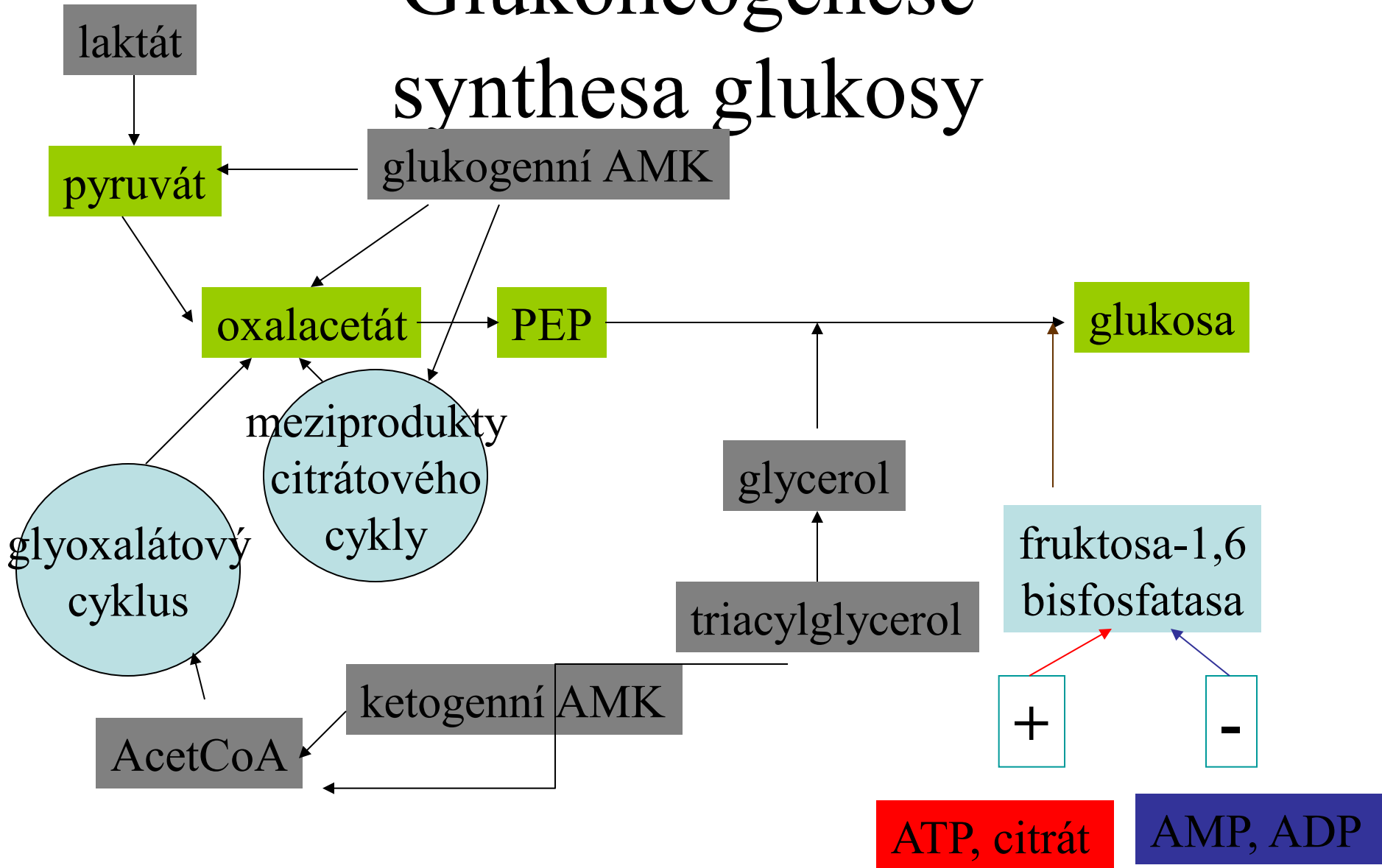
Glykolyza zisk energie

glykogen

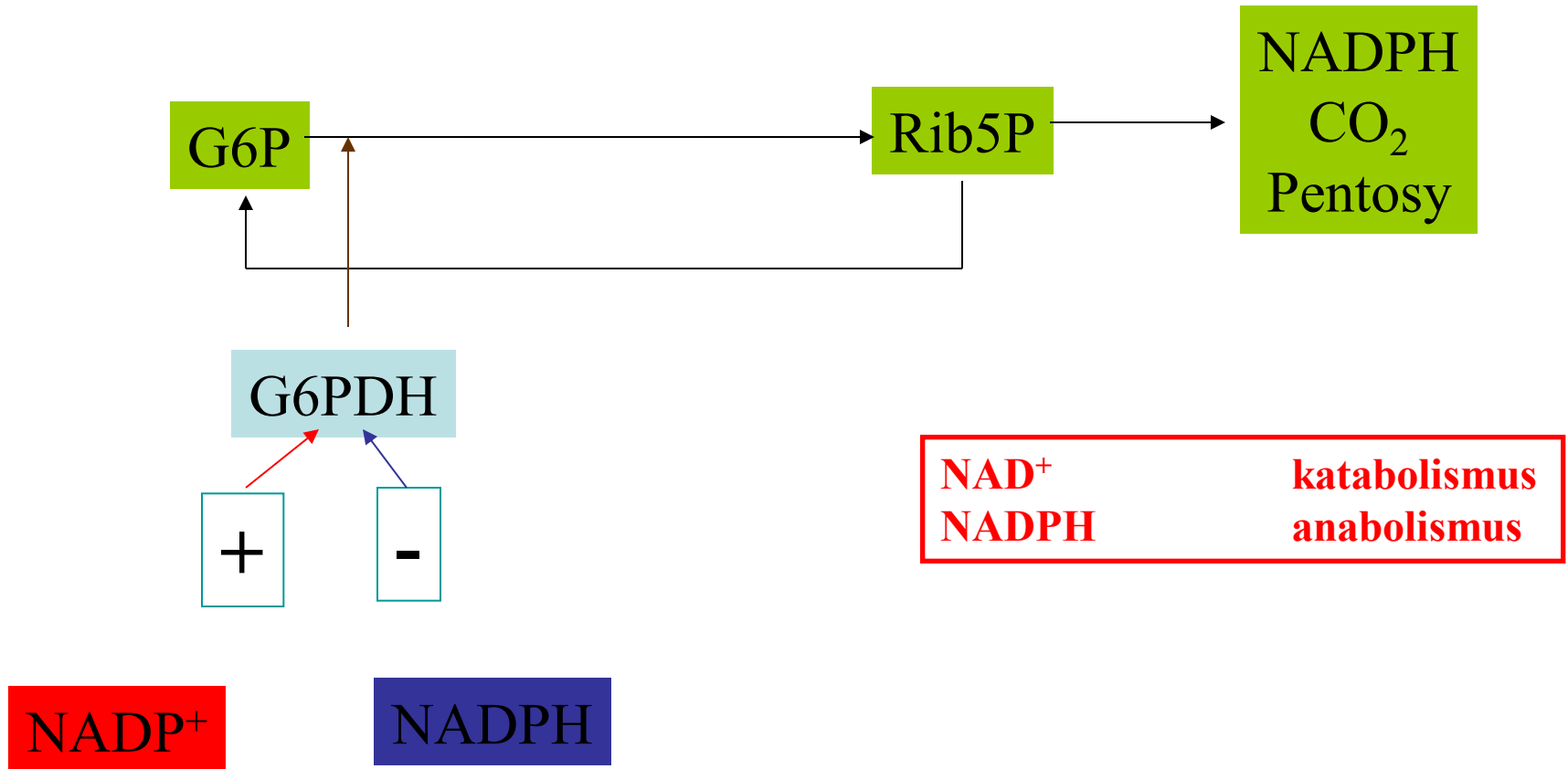
glukosa monosacharidy



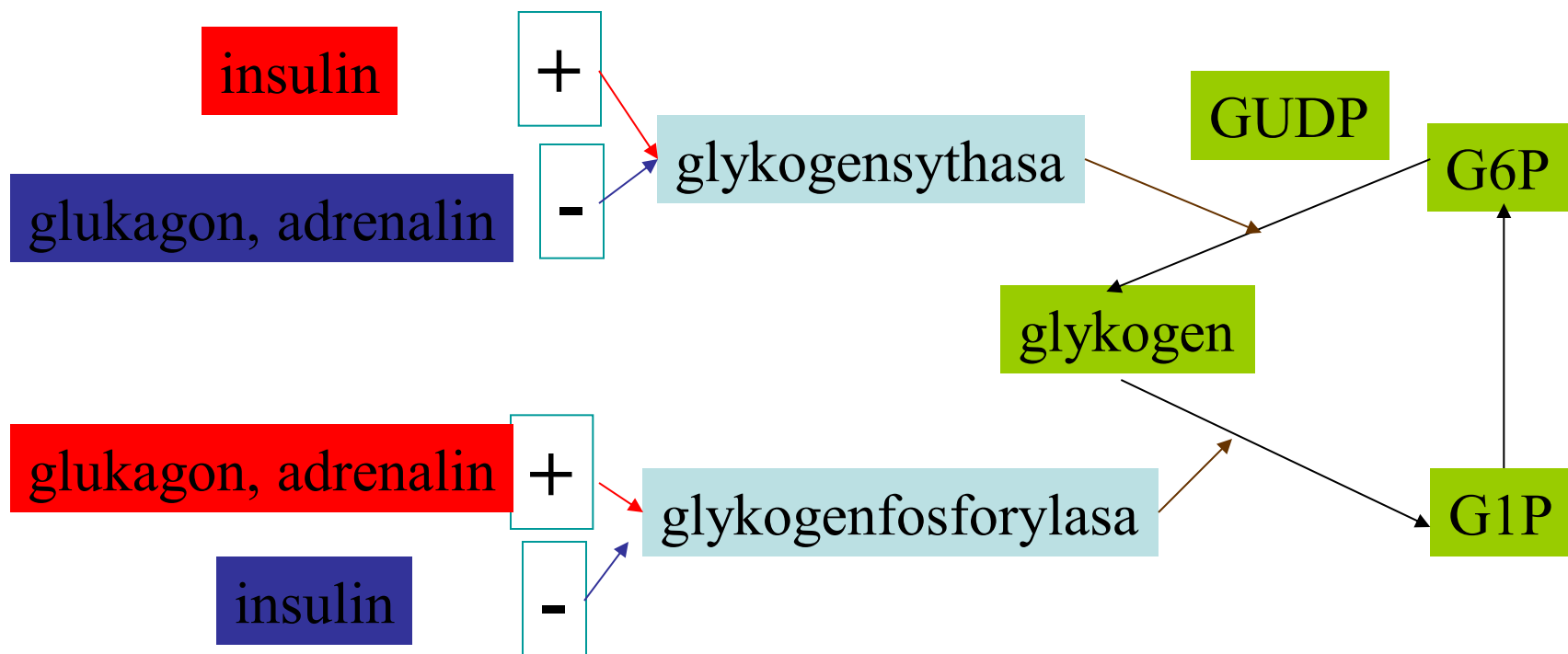
Glukoneogeneze synthesa glukosy



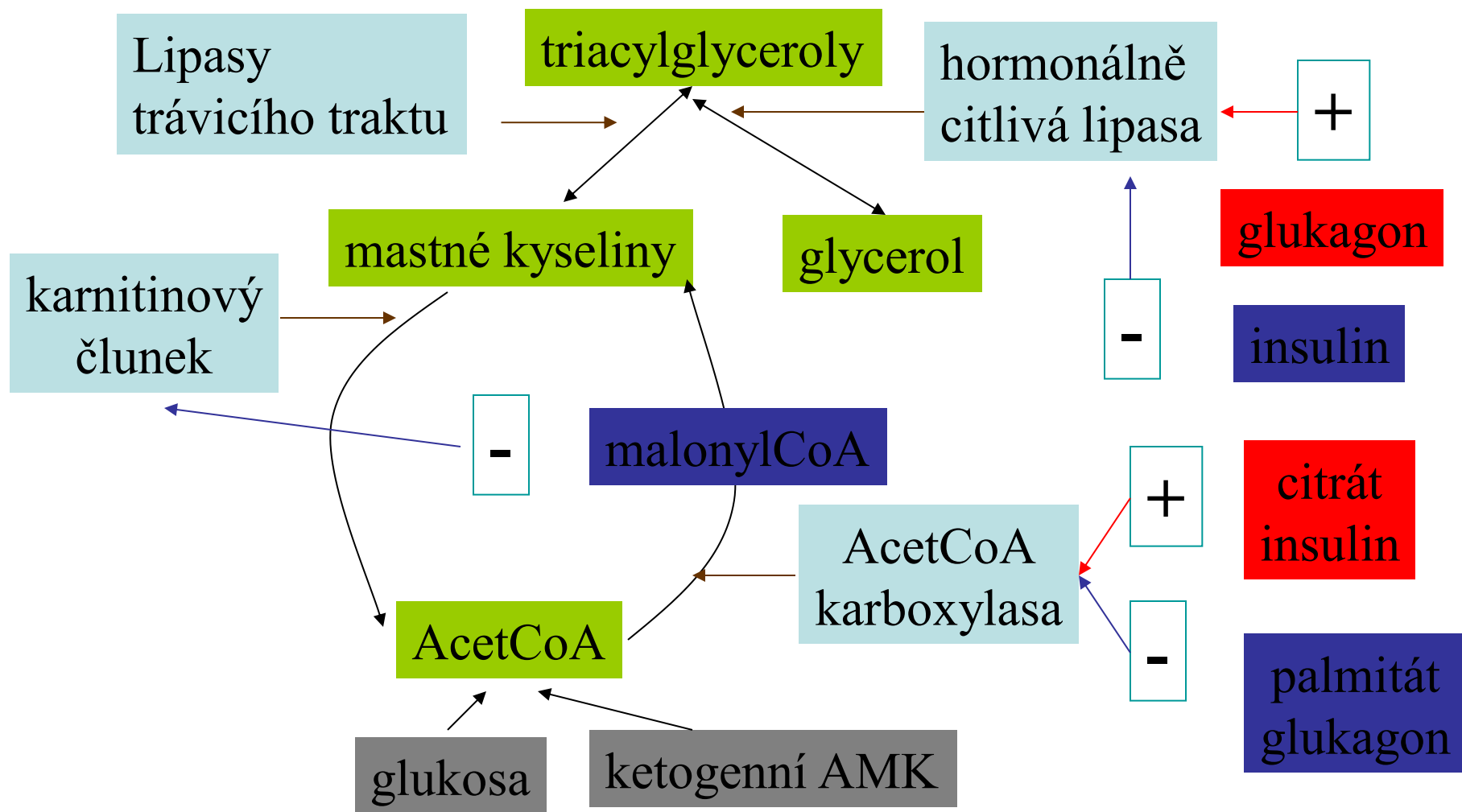
Pentosový cyklus NADPH pro biosynthesu



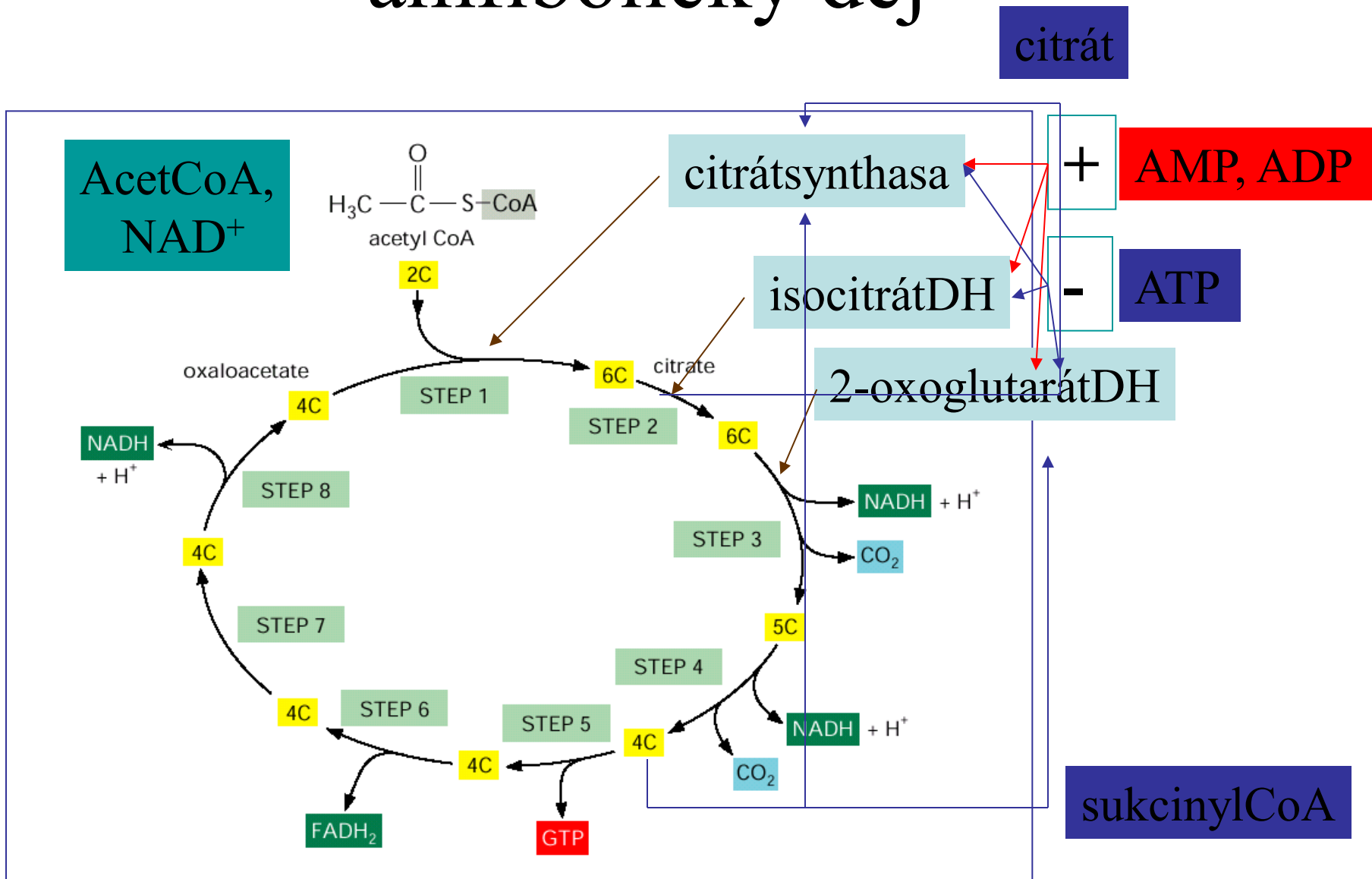
Synthesa a odbourávání glykogenu



Metabolismus triacylglycerolů

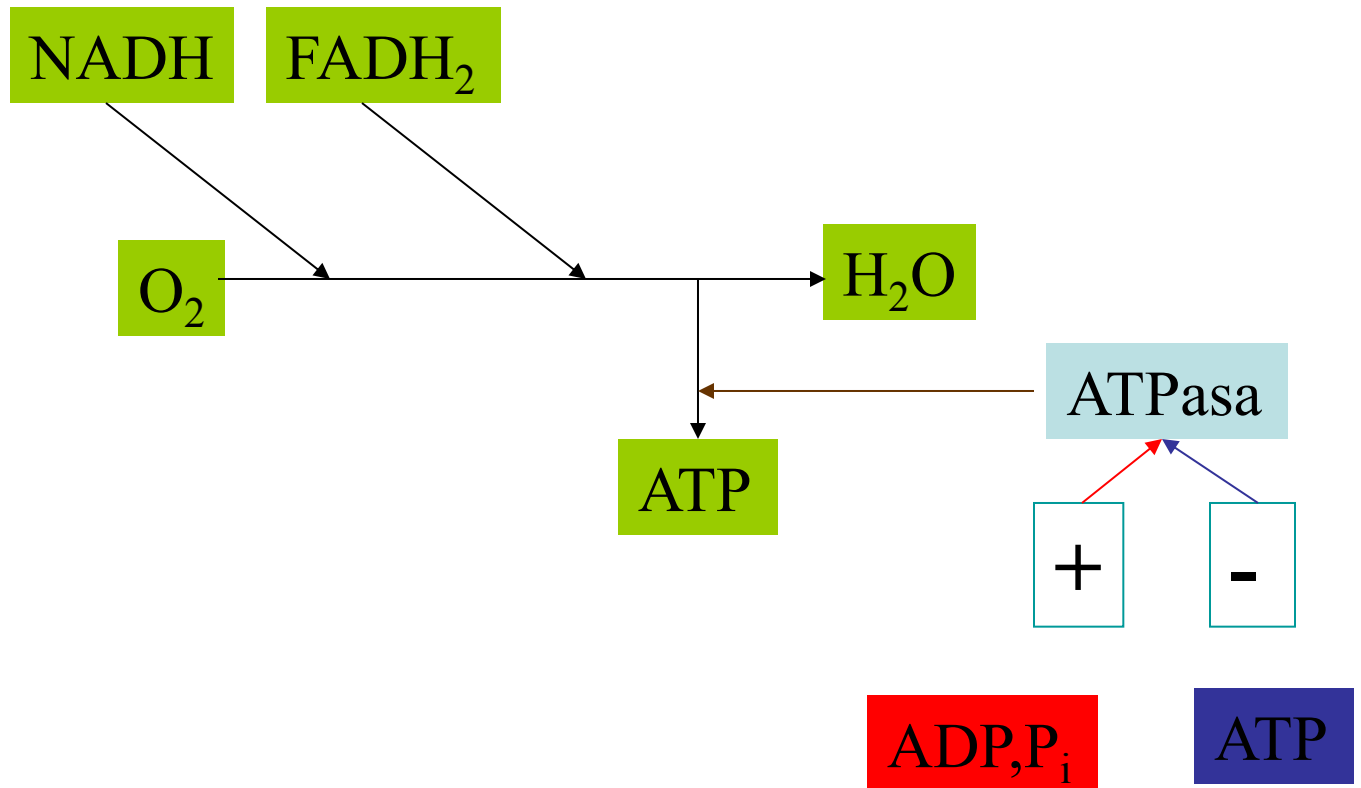


Citrátový cyklus amfibolický děj



Oxidační fosforylace

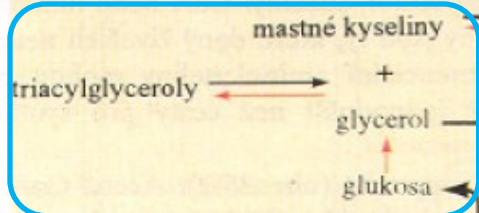
zisk ATP



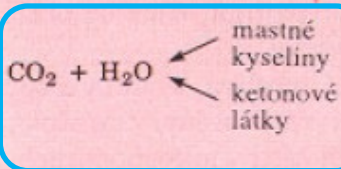
Orgánová specializace

Hnědá tuková tkáň
versus
Bílá tuková tkáň

tuková tkáň

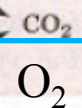


sval



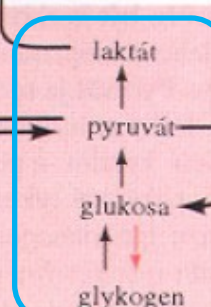
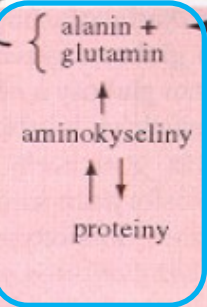
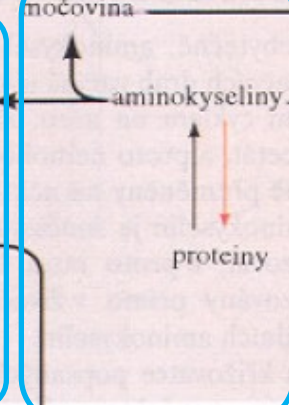
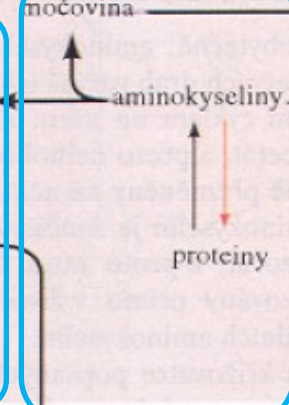
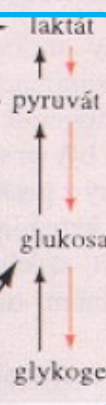
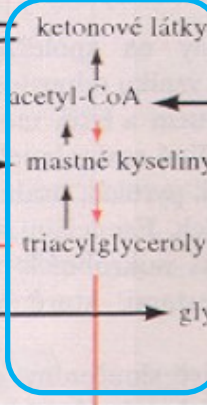
mozek

ketonové látky
glukosa



(2% hm - 20%)

játra



(30%)