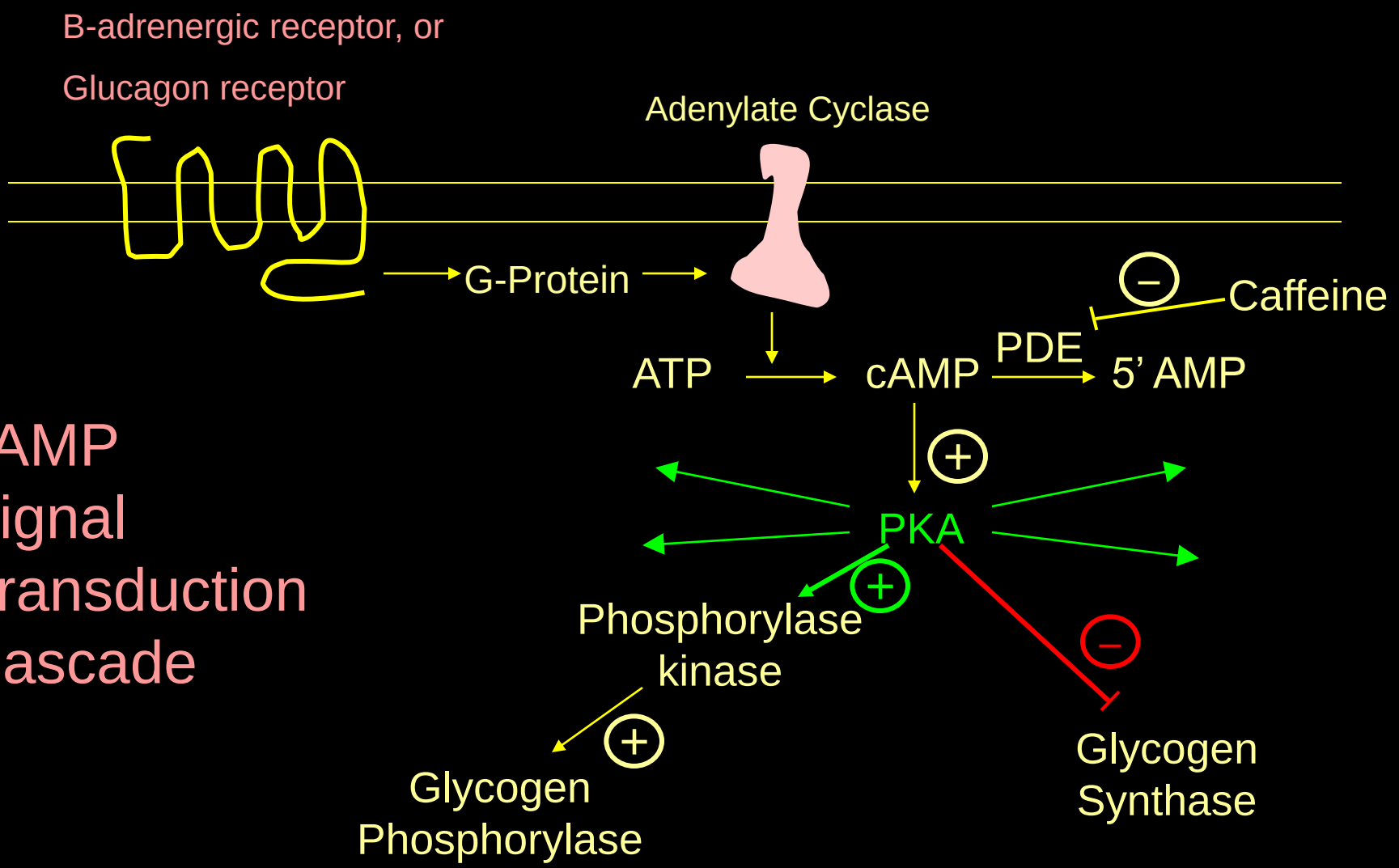
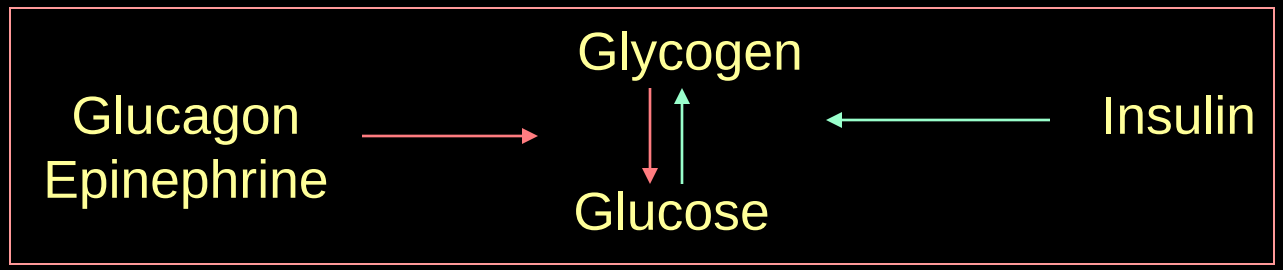
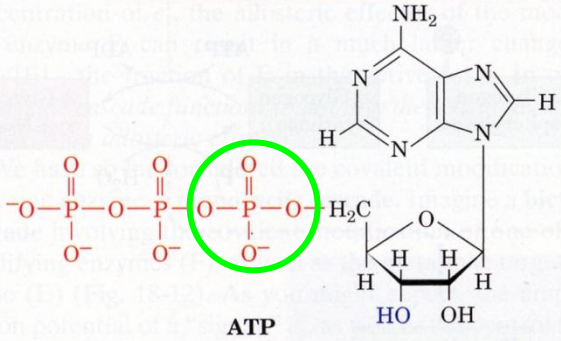
cAMP Signal Transduction Cascade

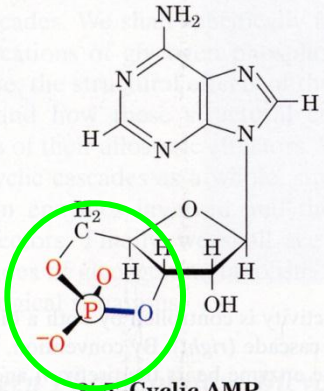






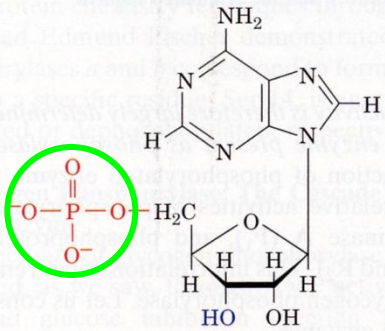
ATP

PP_i ← adenylate cyclase



3′,5′-Cyclic AMP
(cAMP)

H_2O — phosphodiesterase



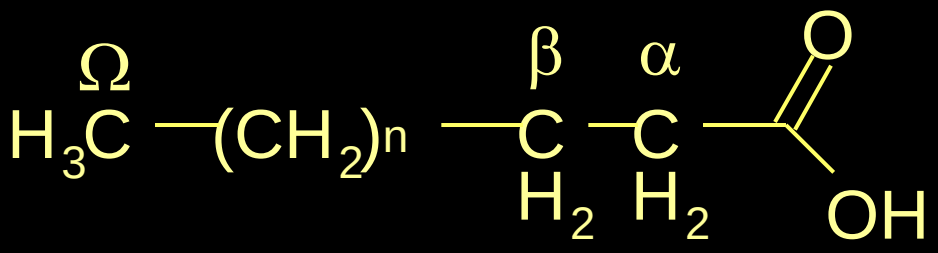
AMP

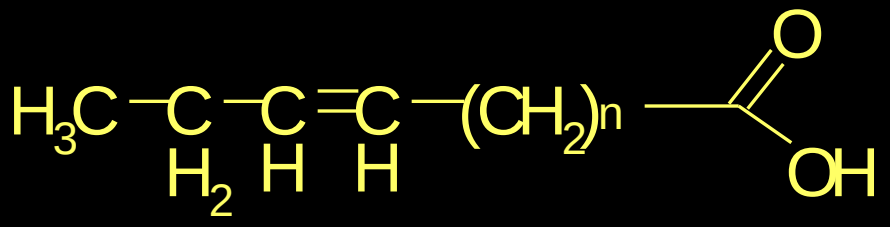
Direct targets of PKA:

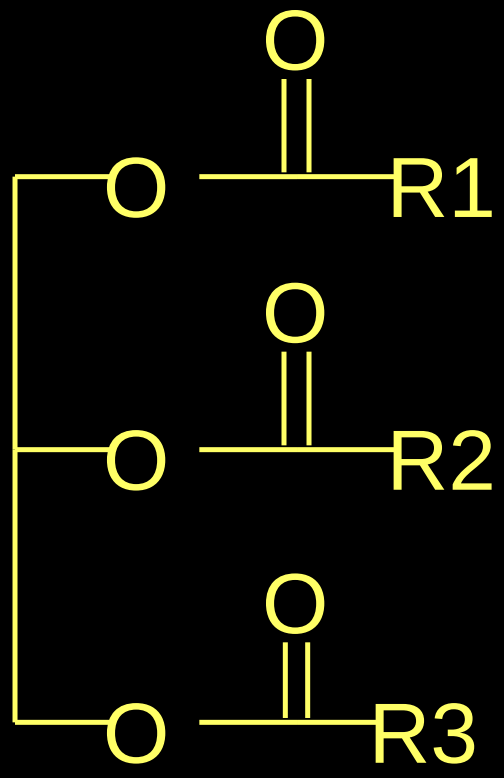
Phosphorylase kinase
Glycogen synthase
Pyruvate Kinase
PFK2 / F2,6BP
Hormone-sensitive lipase

Fatty Acid Oxidation

Structure of FA's







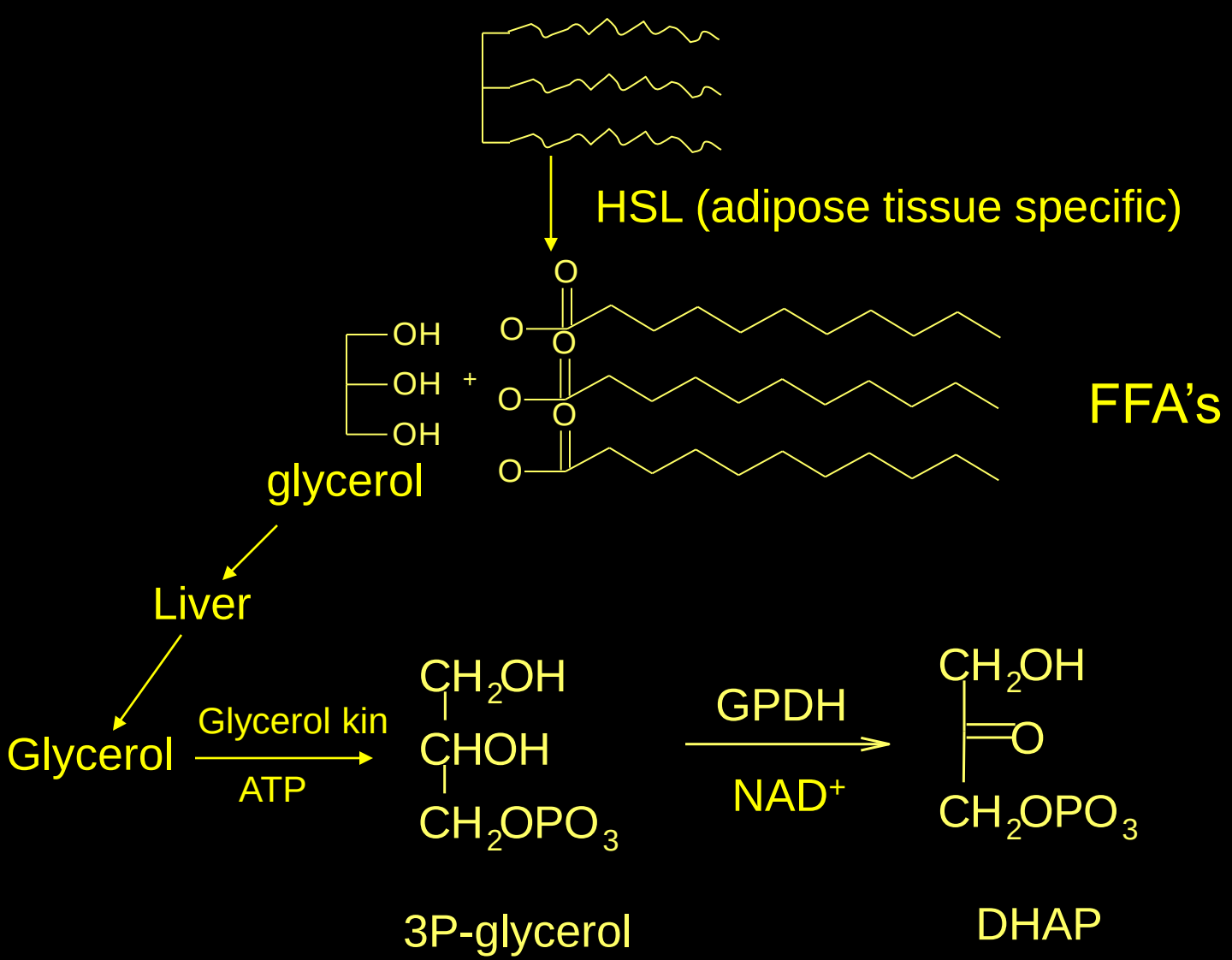

HSL (adipose tissue specific)
OH
OH
OH
+
O
O
O
O
O
O
FFA's
glycerol
Liver
Glycerol
Glycerol kin
ATP
CH2OH
CHOH
CH2OPO3
3P-glycerol
GPDH
NAD+
CH2OH
O
CH2OPO3
DHAP

Table 24-1
Some naturally occurring fatty acids in animals

Number of carbons	*Number of double bonds*	*Common name*	*Systematic name*	*Formula*
12	0	Laurate	*n*-Dodecanoate	$CH_3(CH_2)_{10}COO^-$
14	0	Myristate	*n*-Tetradecanoate	$CH_3(CH_2)_{12}COO^-$
16	0	Palmitate	*n*-Hexadecanoate	$CH_3(CH_2)_{14}COO^-$
18	0	Stearate	*n*-Octadecanoate	$CH_3(CH_2)_{16}COO^-$
20	0	Arachidate	*n*-Eicosanoate	$CH_3(CH_2)_{18}COO^-$
22	0	Behenate	*n*-Docosanoate	$CH_3(CH_2)_{20}COO^-$
24	0	Lignocerate	*n*-Tetracosanoate	$CH_3(CH_2)_{22}COO^-$
16	1	Palmitoleate	*cis*-Δ^9-Hexadecenoate	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COO^-$
18	1	Oleate	*cis*-Δ^9-Octadecenoate	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^-$
18	2	Linoleate	*cis,cis*-Δ^9, Δ^{12}-Octadecadienoate	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COO^-$
18	3	Linolenate	all-*cis*-Δ^9, Δ^{12}, Δ^{15}-Octadecatrienoate	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COO^-$
20	4	Arachidonate	all-*cis*-Δ^5, Δ^8, Δ^{11}, Δ^{14}-Eicosatetraenoate	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^-$

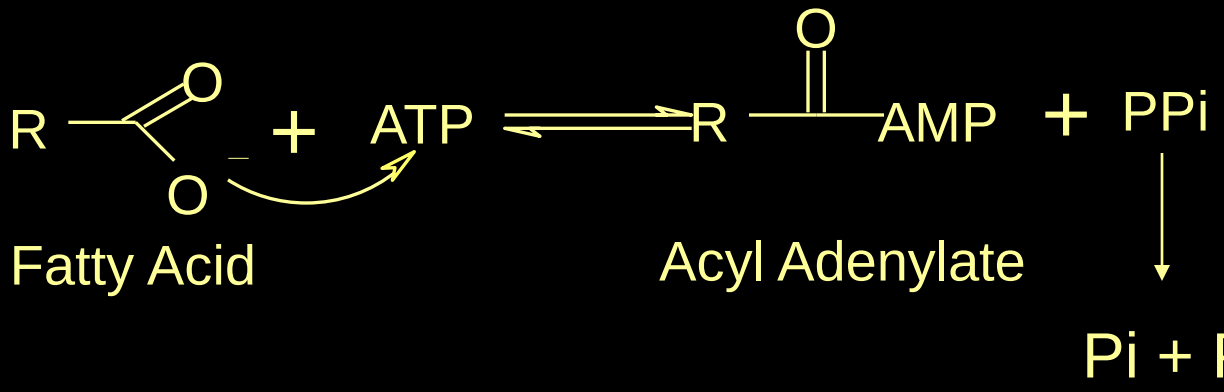
Table 6.1 Pattern of fatty acids in fats and oils (approximate percentage of total fatty acids)

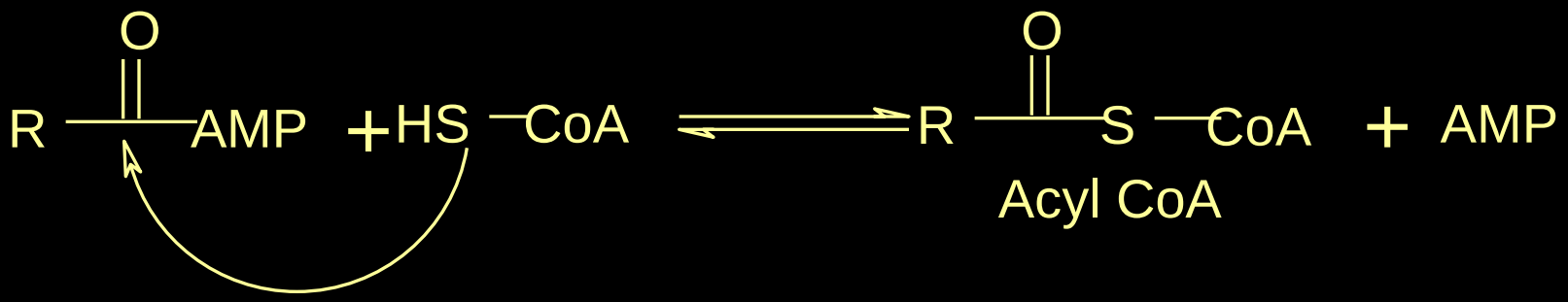
	C_{4-12} saturated	$C_{14:0}$	$C_{16:0}$	$C_{18:0}$	$C_{16:1}$ + $C_{18:1}$	$C_{18:2}$	Other PUFA	Other FAs
Butter, cream and milk	13	11	26	11	30	2	1[b]	2
Beef	—	3	29	16	48	2	1	—
Bacon and pork	—	2	26	14	50	7	1	—
Chicken	—	1	26	7	45	18	2	—
Fish oil	—	5	15	3	27	7	43[a]	—
Coconut oil	58	18	10	3	8	2	—	—
Palm oil	—	1	40	4	45	9	—	—
Cocoa butter	—	—	26	35	36	3	—	—
Rapeseed oil	—	—	3	1	24	15	10[b]	40[c]
Olive oil	—	—	12	2	73	11	1	—
Groundnut oil	—	—	12	3	53	30	1	—
Sesame oil	—	—	9	5	40	43	—	—
Cottonseed oil	—	1	24	2	20	50	1	—
Corn (maize) oil	—	—	12	2	31	53	2	—
Soya bean oil	—	—	10	4	24	53	7[b]	—
Sunflower seed oil	—	—	6	6	33	58	—	—
Safflower seed oil	—	—	7	2	13	74	—	—
Margarine	3	5	23	9	33	12	1	5
Margarine, polyunsaturated	2	1	12	8	22	52	1	—

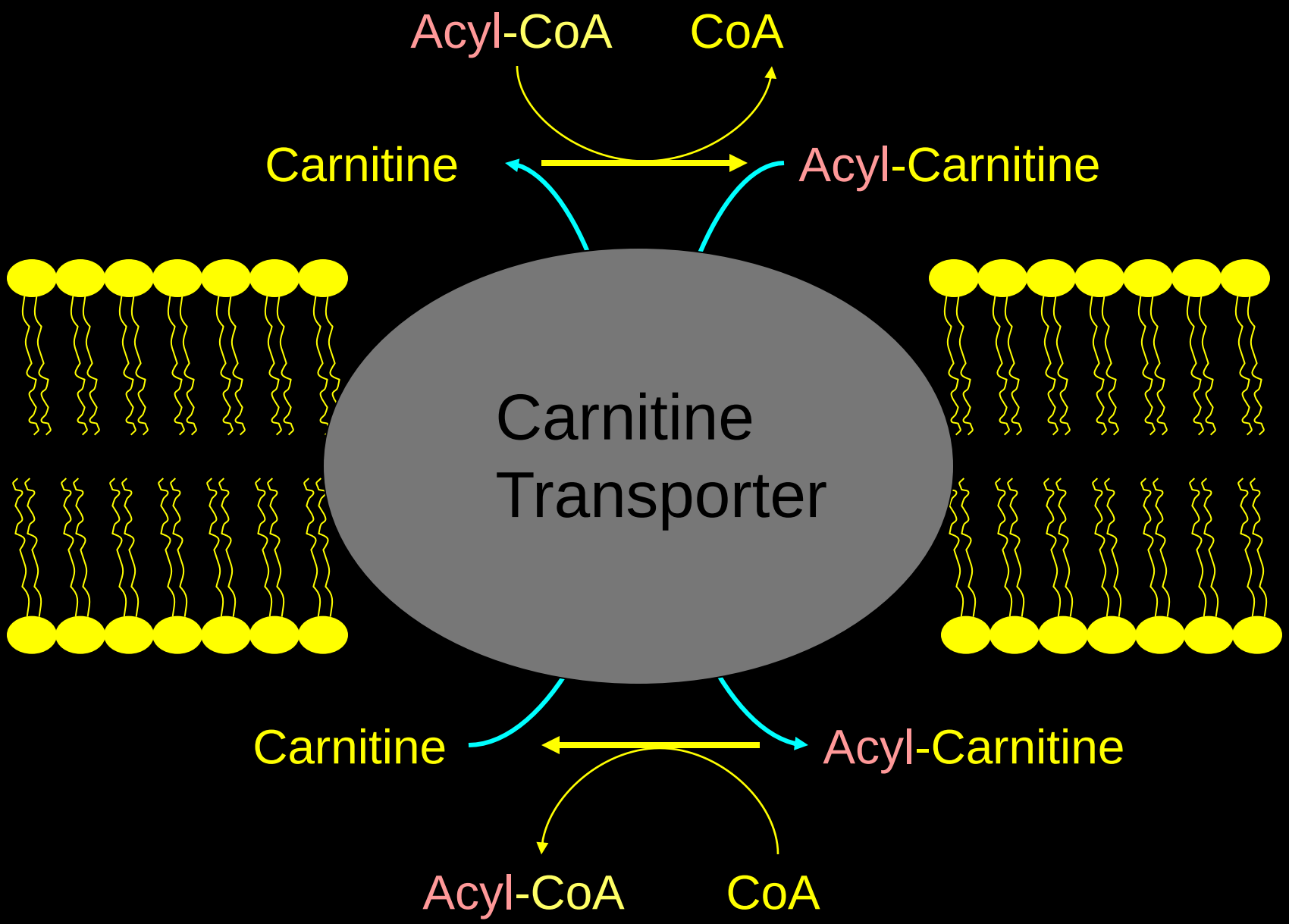
[a] Long-chain polyunsaturated fatty acids (C_{20} and C_{22}).
[b] $C_{18:3}$ (linolenic); [c] $C_{22:1}$ (erucic).
Note. The composition of all these fats and oils varies depending on methods of animal husbandry and crop production. In margarines the proportion of fats and oils for the blend are adjusted to world market prices.

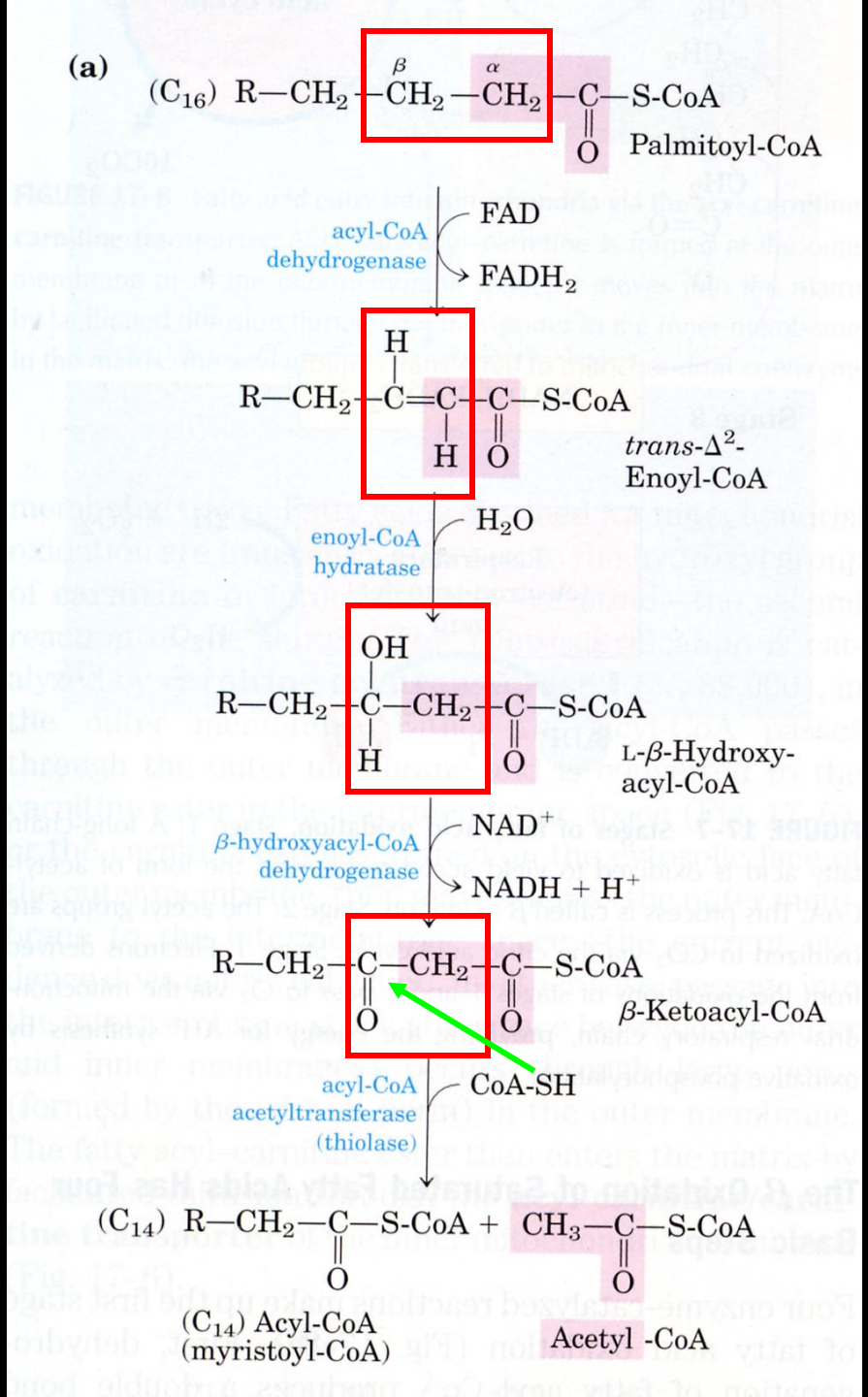
- Synthesis & Storage of FA's occurs in the cytosol
- Oxidation of FA's is carried out in the mitochondria

Activation of FFA's for oxidation (cytosolic)






Acyl-CoA
CoA
Carnitine
Acyl-Carnitine
Carnitine
Transporter
Carnitine
Acyl-Carnitine
Acyl-CoA
CoA



β-oxidation of fatty acids

Compare with reactions of TCA cycle.

Stoichiometry for the Oxidation of Palmitate (16:0)

- For each cycle of β-oxidation, the following are produced:

  1 $FADH_2$ 1.5 ATP

  1 NADH 2.5 ATP

  1 Acetyl-CoA 10 ATP

<u>For Palmitate:</u>

7 $FADH_2$ 10.5 ATP

7 NADH 17.5 ATP

8 Acetyl-CoA 80 ATP

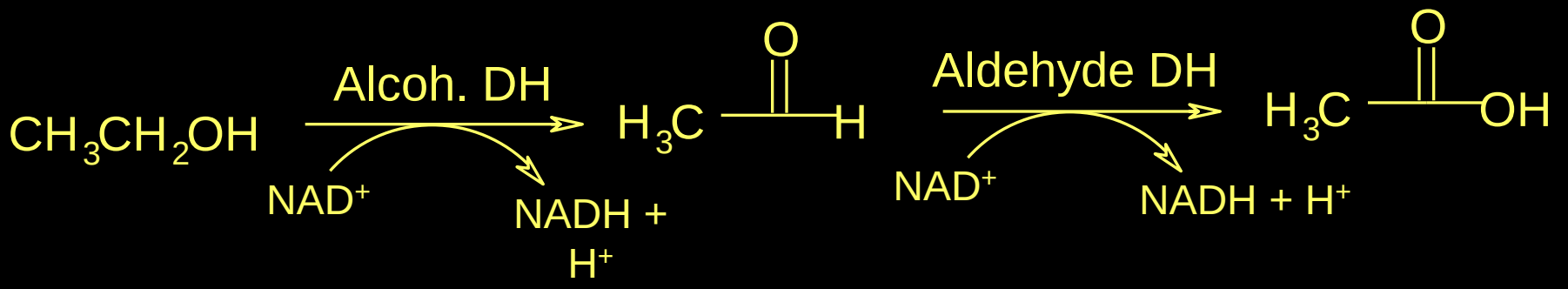
Activation of Palmitate requires energy equivalent to 2 ATP, therefore:

-2 ATP

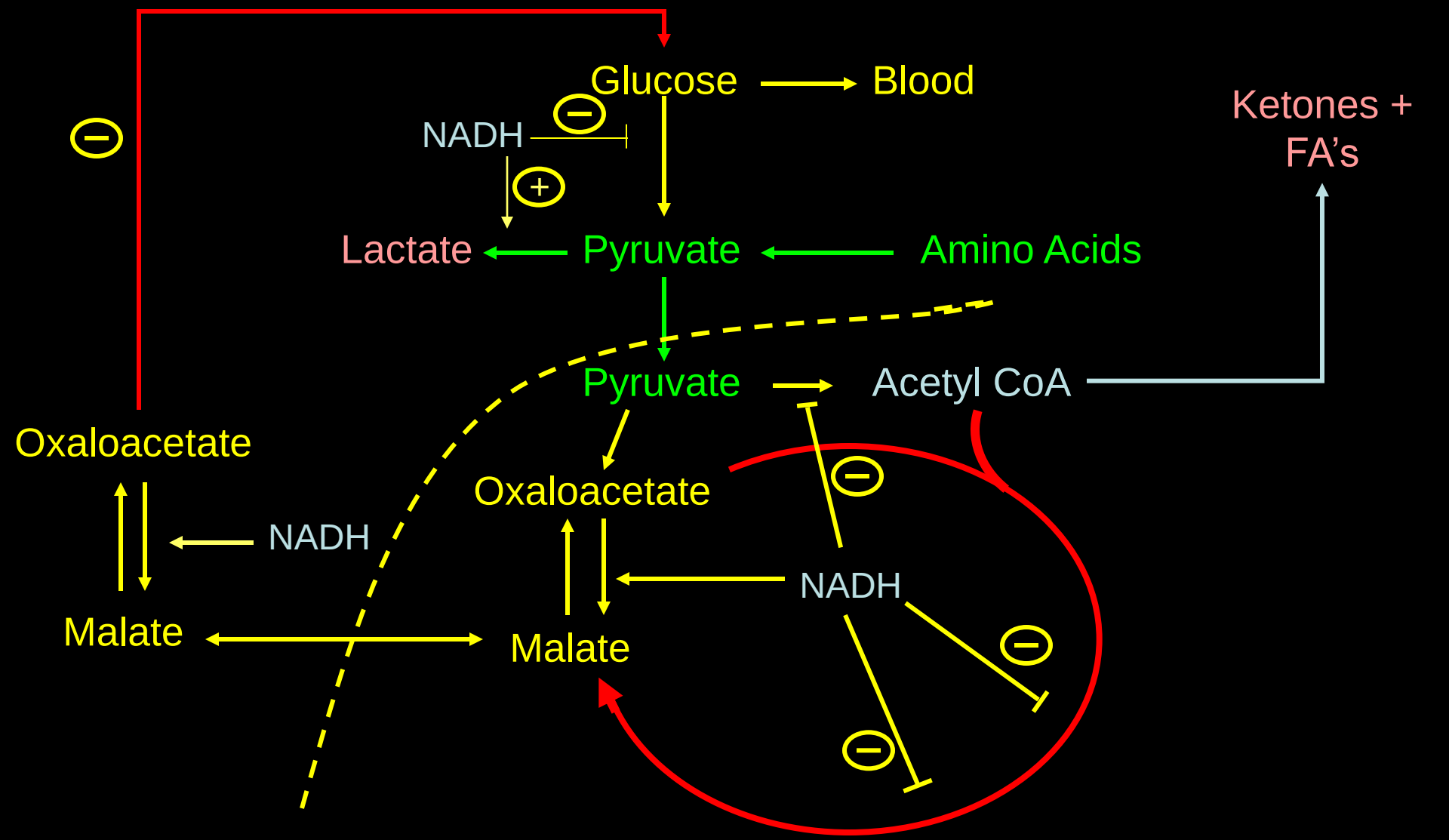
106 ATP per molecule of Palmitate

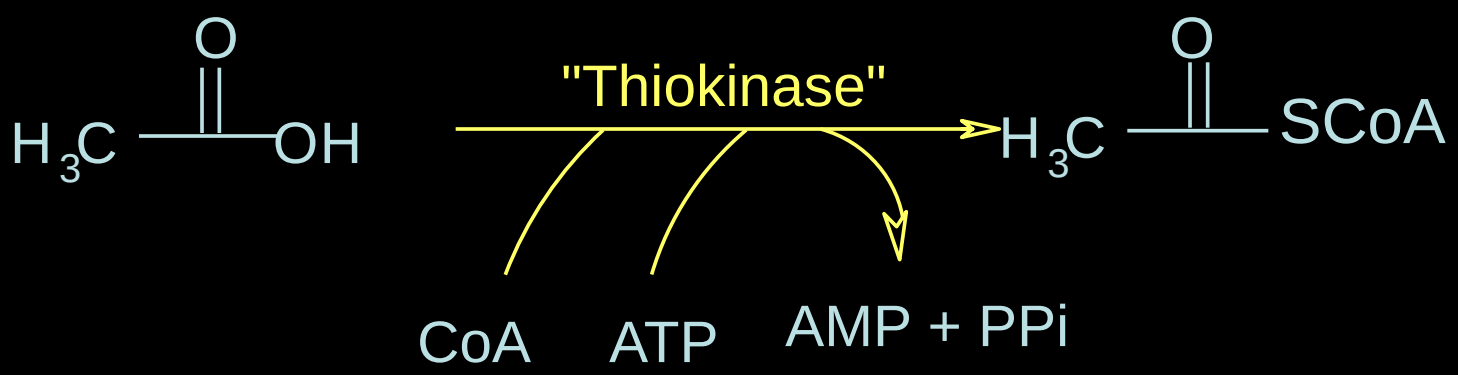
Ethanol Metabolism

Occurs only in Liver



Metabolic consequences of EtOH overload





1. Lactate accumulates
2. Acetate Accumulates leading to excess acetyl-CoA
3. Acetyl CoA → Fatty Acids (FA's).
4. Acetyl CoA → Ketone Bodies (acids).
5. Gluconeogenesis reduced – attenuated source of blood glucose.

Microsomal EtOH oxidizing system:

- Utilizes the P450 cytochrome system
- requires O_2 to generate CH_3CHO & CH_3COOH
- Therefore generates O_2 free radicals → tissue damage

Three phases of liver damage:

1. Fatty liver
2. Alcoholic hepatits – cell death, inflamation
3. Cirrhosis – fibrous scar tissue further impairs liver function