Fatty Acid Synthesis

- Requires
  - Carbon Source: Acetyl CoA
  - Reducing Power: NADPH
  - Energy Input: ATP

Why Energy ?

Fatty Acid

↓

↓

↓

↓

Acetyl CoA

ΔG^o : -ve

Acetyl CoA

↓

↓

↓

↓

Fatty Acid

ΔG^o : +ve

Why Energy ?

Fatty Acid

↓

↓

↓

↓

Acetyl CoA

ΔG^o : -ve

Acetyl CoA + n(ATP)

↓

↓

↓

↓

Fatty Acid + n(ADP)

ΔG^o : -ve

FA Degradation and Synthesis

Acyl CoA $_{(n)}$

↓ **Oxidation**

↓ **Hydration**

↓ **Oxidation**

↓ **Thyolysis**

Acyl CoA $_{(n-2)}$ + Acetyl CoA

Acyl CoA $_{(n+2)}$

↑ **reduction**

↑ **dehydration**

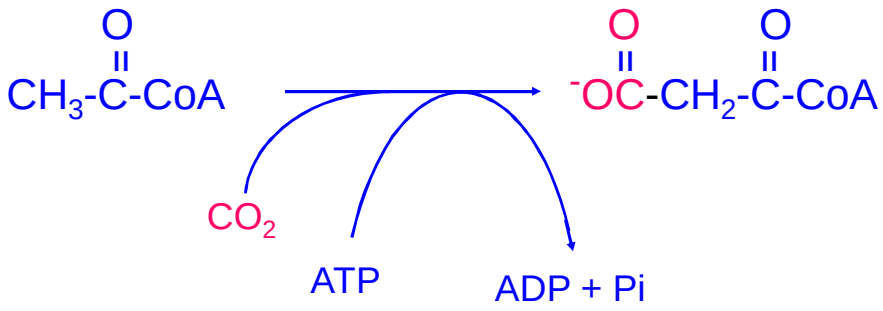
↑ **reduction**

↑ **condensation**

Acyl CoA$_{(n)}$ + Malonyl CoA

Acetyl CoA

Carboxylation of Acetyl CoA Produces Malonyl CoA

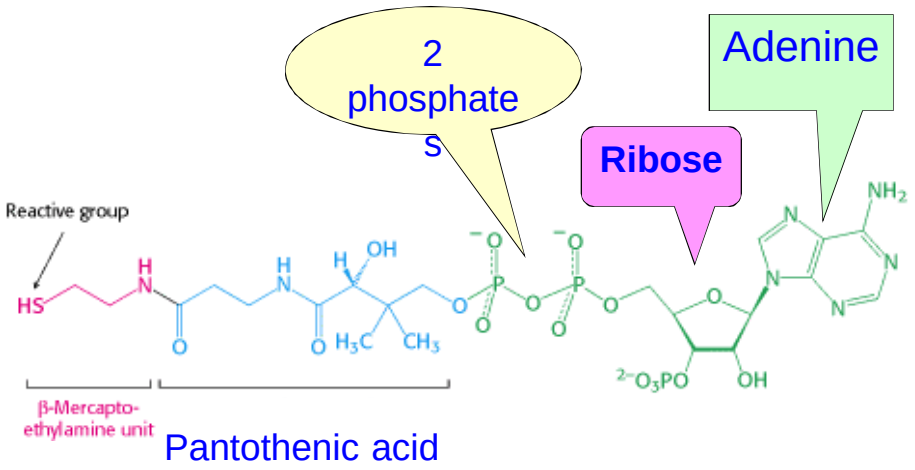


Acetyl CoA Carboxylase

Biotin-Containing Enzyme

Fatty Acid Synthase Catalyzes the remaining steps

- **Multifunctional Enzyme Complex**
- **Dimer of two Identical Chains**
- **Each has Seven Catalytic Activities**
  - One activity is Condensing Enzyme with –SH
- **One Domain is Linked to Phosphopantetheine**
  - With Reactive -SH



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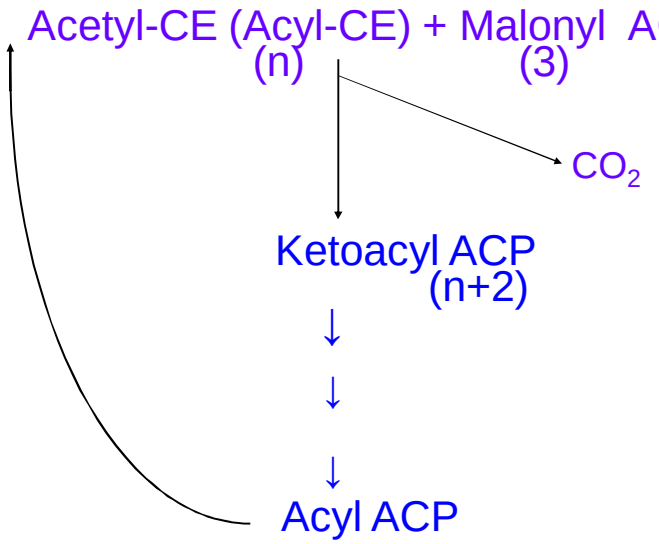
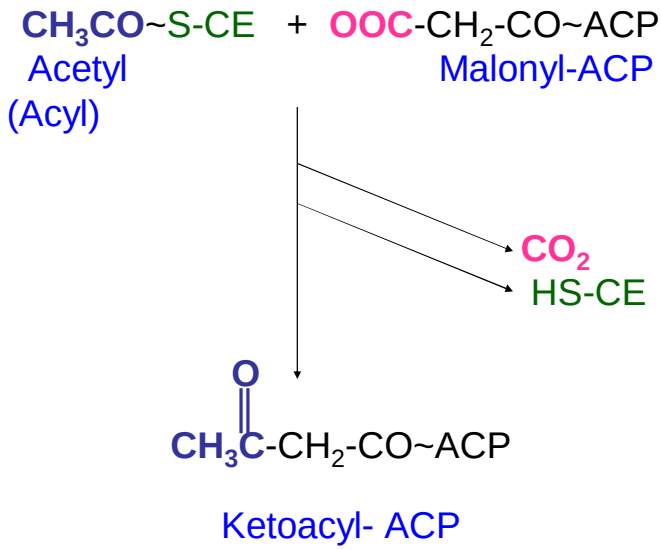
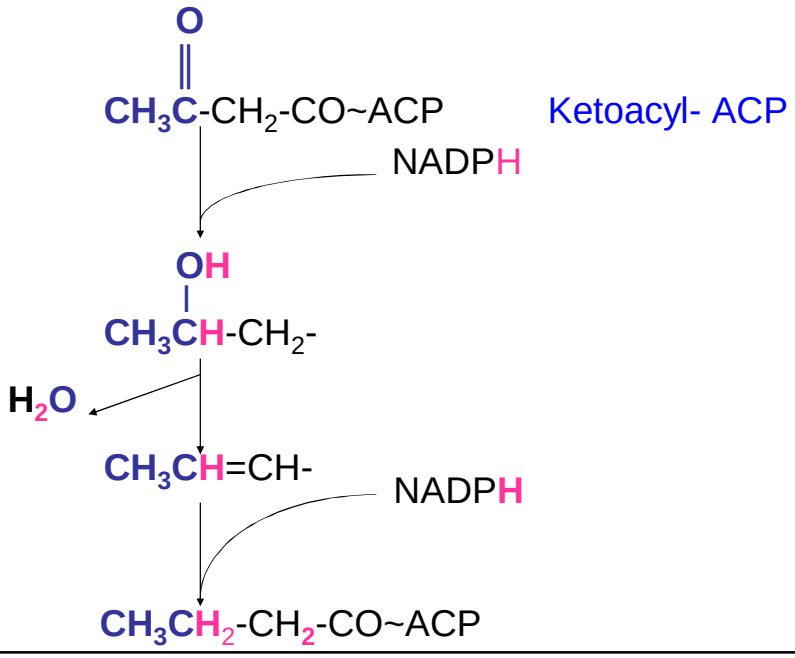
- **Each has Seven Catalytic Activities**
  - One activity is Condensing Enzyme with –SH
- **One Domain is Linked to Phosphopantetheine**
  - With Reactive -SH
  - Carries Intermediates during Catalysis
  - (Acyl, Acetyl and Malonyl Groups)
  - Known as Acyl Carrier Protein (ACP)

Fatty Acid Synthesis (Overview)

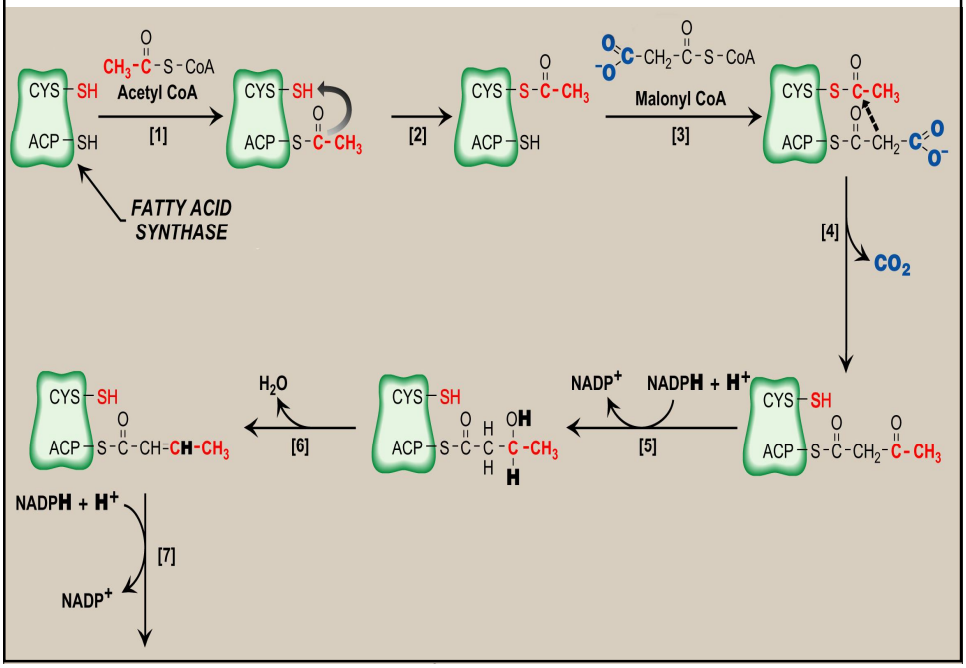




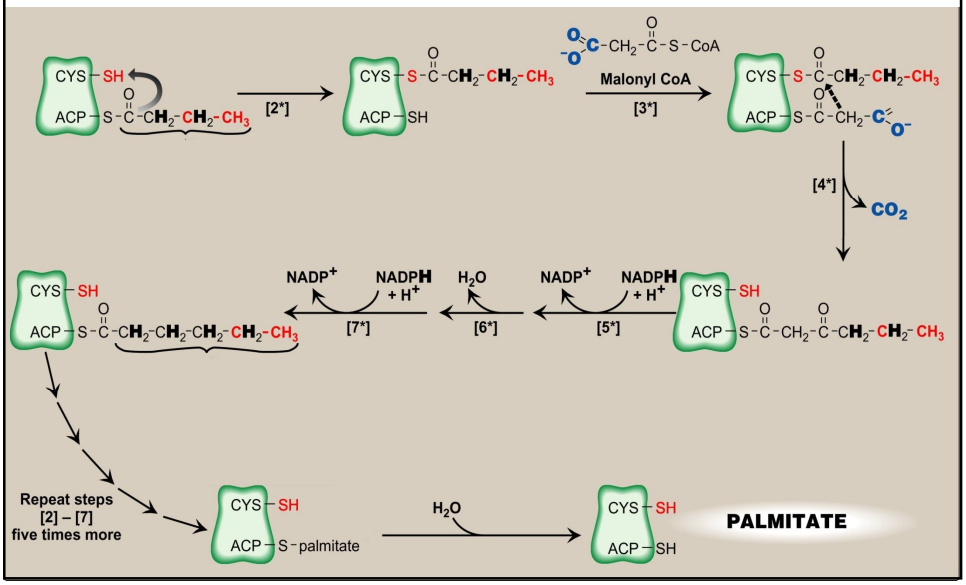
Reduction of the Ketoacyl Group



Synthesis of Palmitate by Fatty Acid Synthase



Synthesis of Palmitate by Fatty Acid Synthase (Cont.)



Synthesis of Palmitate (net reaction)

How many cycles of synthesis (Condensation)?

* 7

How many Malonyl CoA?

* 7

How many Acetyl CoA?

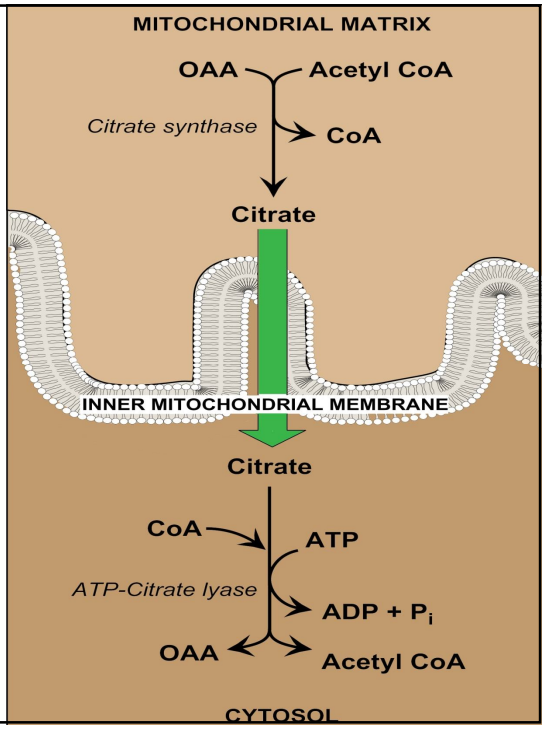
* 1

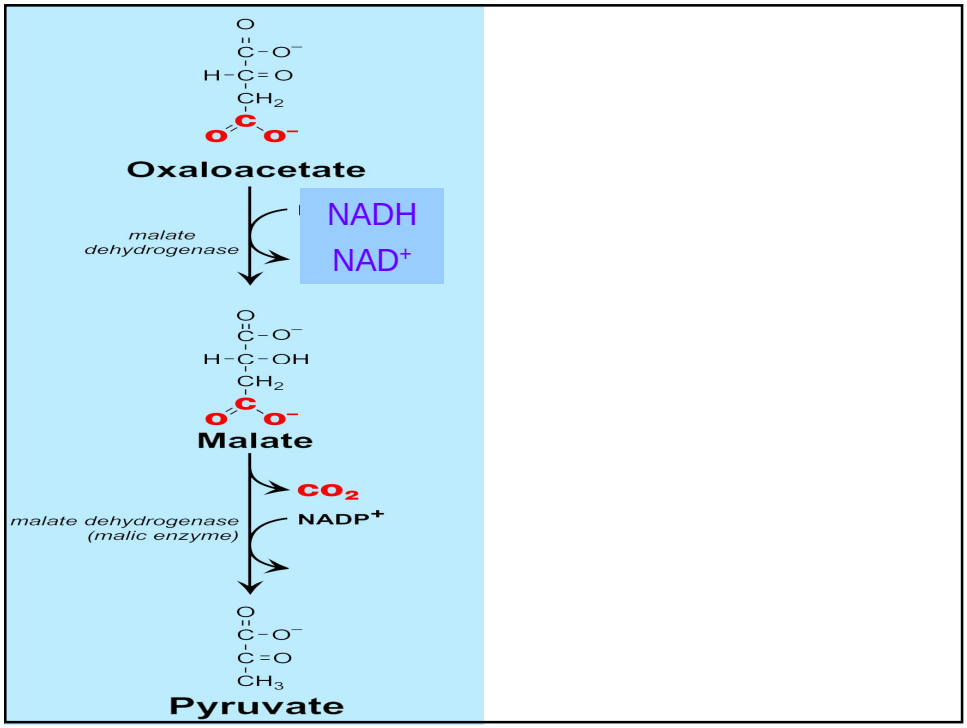
How Many NADPH?

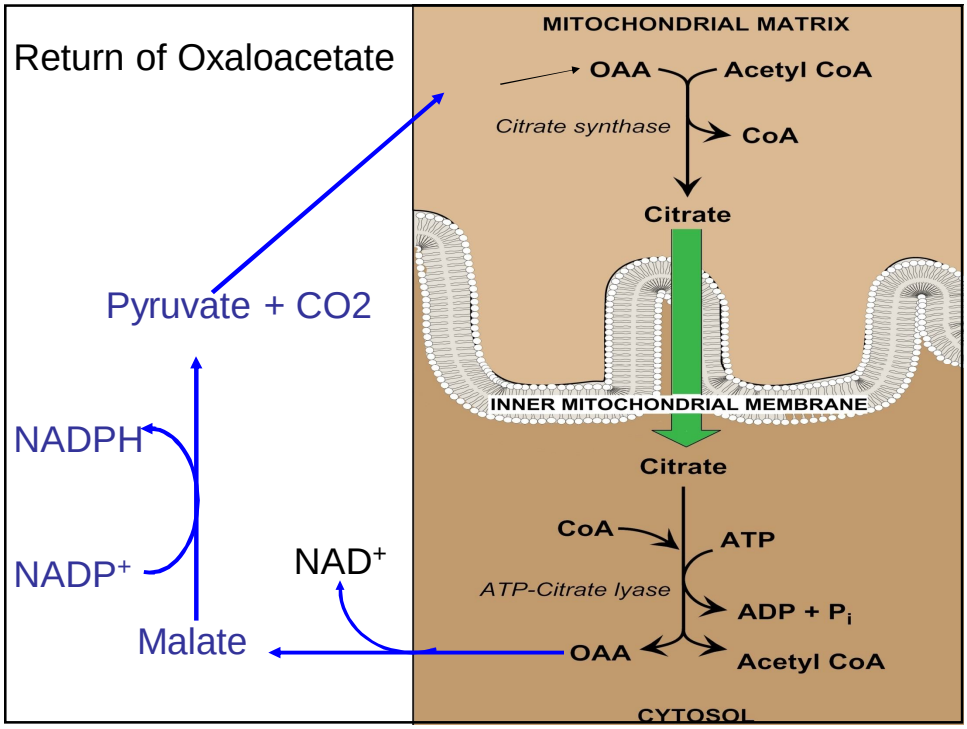
* 14

Production of Cytosolic Acetyl CoA for FA Synthesis

Inner mitochondrial membrane is immpermiable to Acetyl CoA







Regulation of FA Oxidation & Synthesis

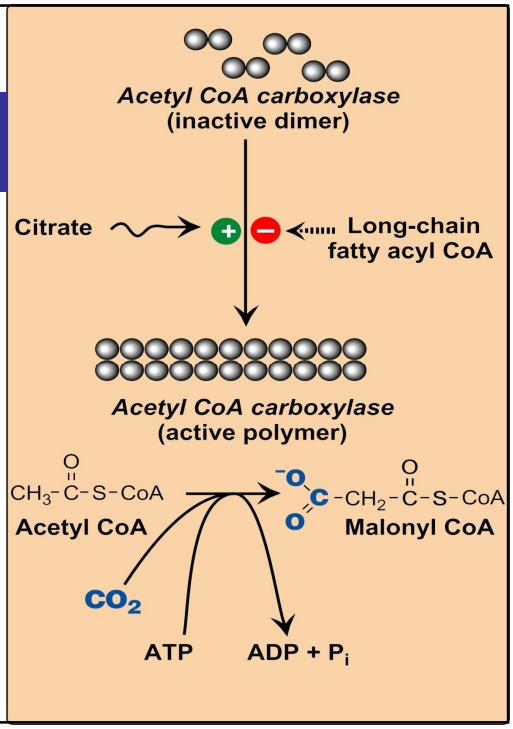
OXIDATION

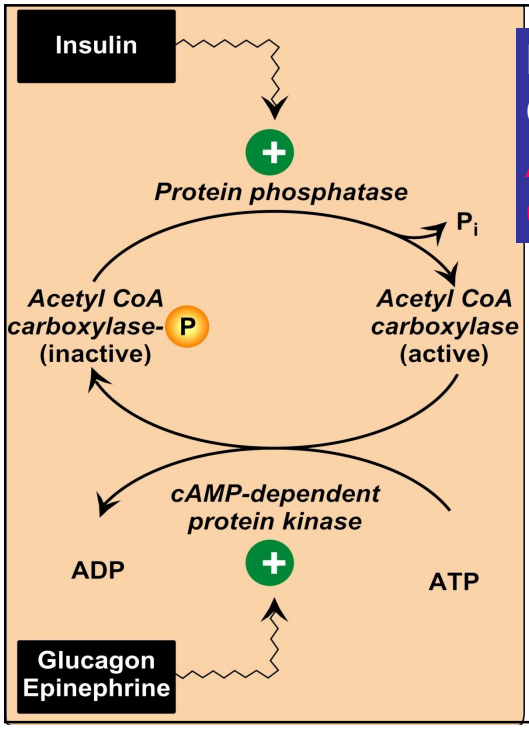
- **Supply of Fatty Acids**
  -Hormonal Control
- **Entry into Mitochondria**
- **Availability of NAD^+**

SYNTHESIS

- **Regulation of AcCoA Carboxylase**
  -Allosteric Mechanism
  - Phosphorylation
- **Amounts of Enzymes**

Allosteric Regulation of Acetyl CoA Carboxylase





Hormone-Mediated, Covalent Regulation of Acetyl CoA Carboxylase ACC

Regulation of FA Oxidation & Synthesis

OXIDATION

- **Supply of Fatty Acids**
  -Hormonal Control
- **Entry into Miochondria**
- **Availability of NAD^+**

SYNTHESIS

- **Regulation of AcCoA Carboxylase**
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  - Phosphorylation
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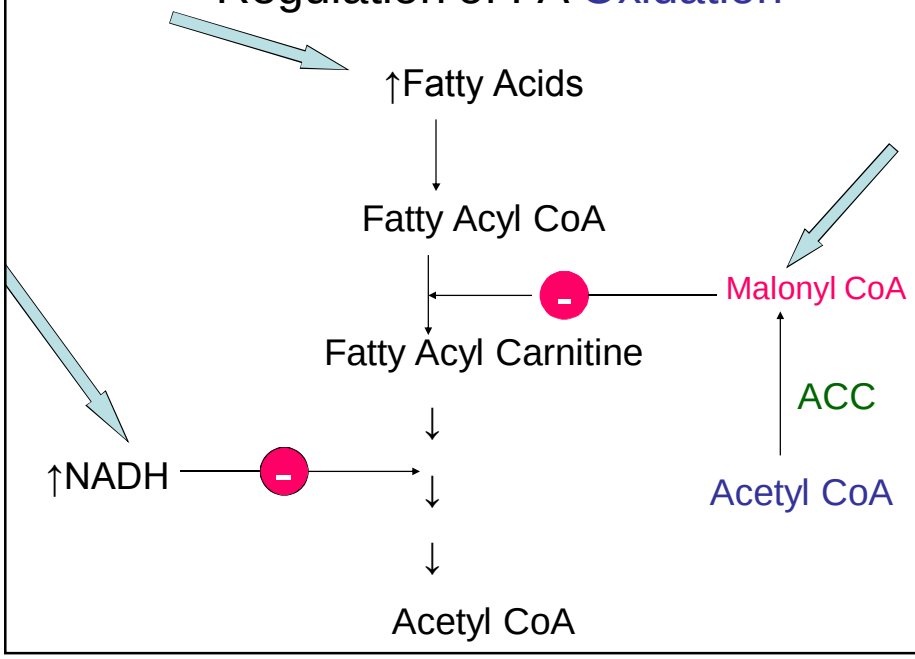
Regulation of FA Oxidation



Elongation of Fatty Acids

-in Endoplasmic Reticulum
- Similar Sequence of Reactions
- Different Enzymes

Malonyl CoA + Acyl $CoA_{(n)}$

↓

↓ 2NADPH + H^+

↓

↓ 2$NADP^+$

Acyl CoA (n+2)

n = 16 or more carbons

Elongation of Fatty Acids in Mitochondria

Acetyl CoA + Acyl CoA (n)

↓↑

↓↑ NADH + H+

↓↑ NAD+

NADPH

NADP+

Acyl CoA (n+2)

n = less than16 carbons

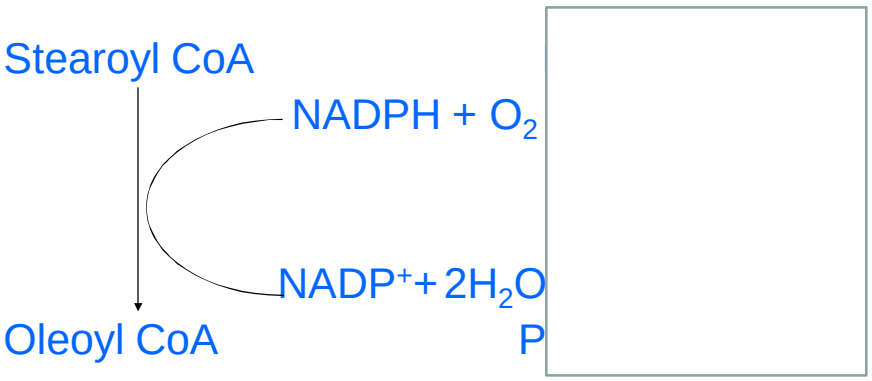
Introduction of Double Bonds

- Synthesis of Monounsaturated FA

  - Oleic Acid 18:Δ^9
  - Palmitoleic 16:Δ^9

- In endoplasmic reticulum
- No double bond can be introduced beyond carbon 9 in human

Introduction of Double Bonds (Cont.)



Δ^9 Desaturase; Cytochrome b_5

Introduction of Double Bonds (Cont.)

Formation and Modification of Polyunsaturated FA

-Elongation

- Desaturation

Additional double bonds can be introduced by:

Δ^4 Desaturase

Δ^5 Desaturase

Δ^6 Desaturase

Modification of Polyunsaturated FA

Linoleic $18:2\Delta^{9,12}$

↓ Desaturation

$18:3\Delta^{6,9,12}$ ω ?

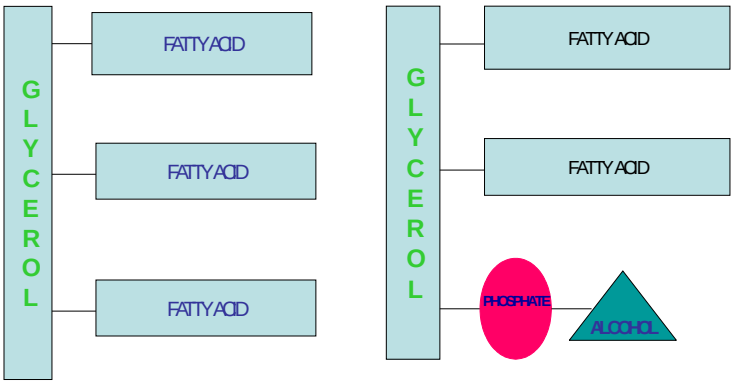
↓ Elongation

$20:3\Delta^{8,11,14}$ ω ?

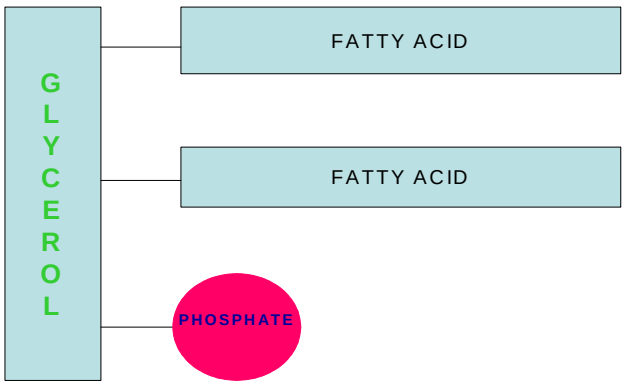
↓ Desaturation

$20:4\Delta^{5,8,11,14}$ ω ? Arachidonic

Biosynthesis of Triacylglycerol & Phosphoacylglycerol



Phosphotadic Acid is Common Intermediate



Biosynthesis of Triacylglycerol

Requires

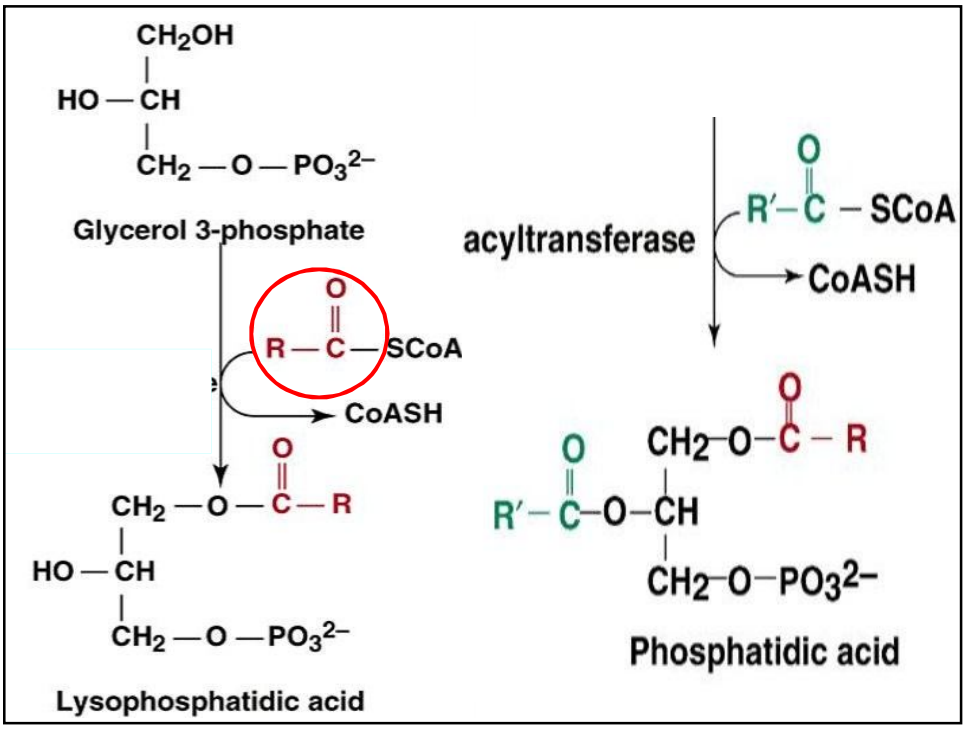
- Acyl~CoA (Active form of FA)
- Glycerol Phosphate

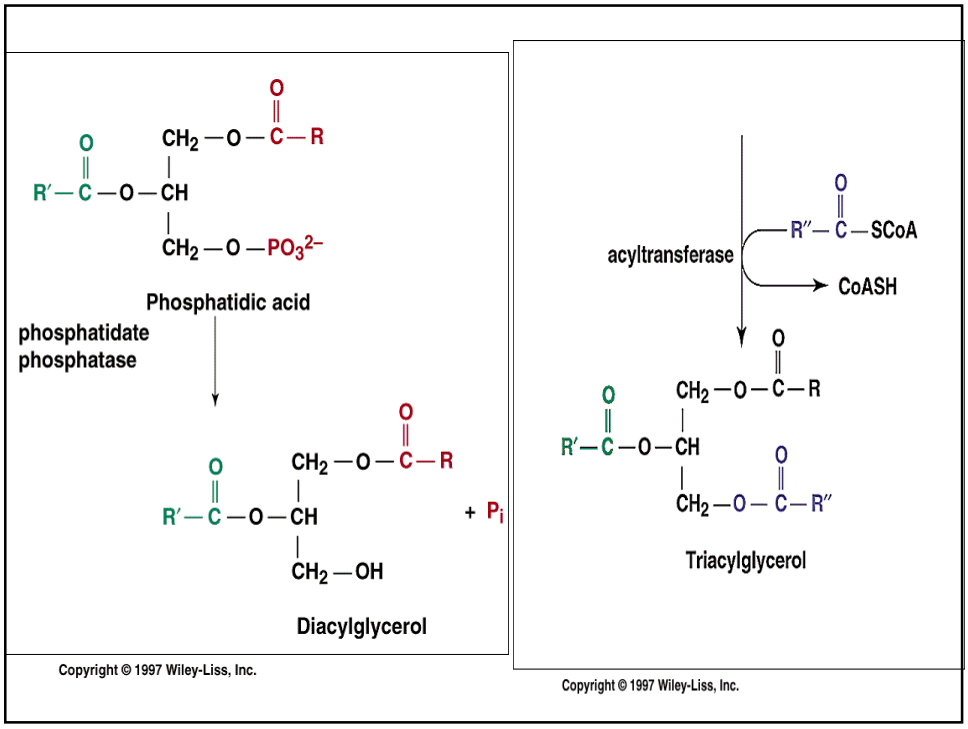
Why Active form?

$TAG + H_2O \longrightarrow DAG + FA \quad \Delta G$ –ve

$DAG + FA \longrightarrow TAG + H_2O \quad \Delta G$ +ve

$DAG + Acyl\sim CoA \longrightarrow TAG \quad \Delta G$ –ve



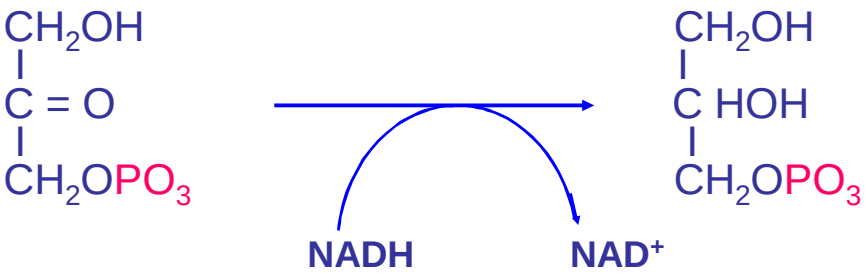


Production of Glycerol Phosphate

- Glycerol + ATP ---→ Glycerol 3 Phosphate

Enz: Glycerol Kinase

Not in Adipose tissue



Production of Glycerol Phosphate