

Chem 352 - Lecture 10  
Lipid, Amino Acid, and  
Nucleotide Metabolism  
Part I: Lipid Metabolism

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## Introduction

In Lecture 10 we will add some of the peripheral pathways in metabolism that lead to synthesis and degradation three important classes of biomolecules:

- Lipids
- Amino acids
- Nucleotides

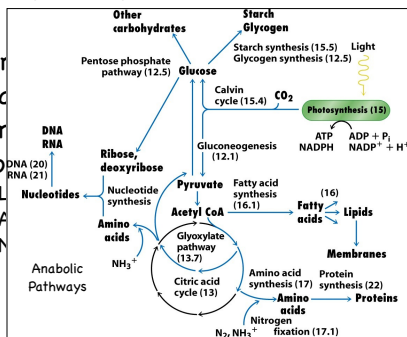
Chem 352, Lecture 10, Part I: Lipid Metabolism 2

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## Introduction

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## Introduction

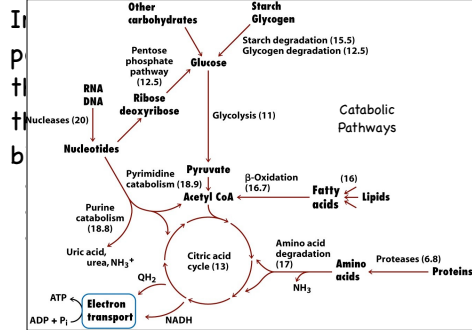
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- Lipids
- Amino acids
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2-3

## Introduction



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## Introduction

In Lecture 10 we will add some of the peripheral pathways in metabolism that lead to synthesis and degradation three important classes of biomolecules:

- Lipids
- Amino acids
- Nucleotides

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2-5

## Introduction

Lipids play many important cellular roles

- Membrane components (phospholipids, et al. and cholesterol)
- Fuels (Triacylglycerides)
  - Meet long term energy needs in mammals
- Regulators (steroids, eicosanoids)

We will focus on just a couple of key metabolic pathways.

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## Introduction

We will focus on the following sections from Chapter 16

- 16.1: Fatty Acid Synthesis
- 16.6: Synthesis of Cholesterol
- 16.7: Fatty Acid Oxidation
- 16.9: Lipid Metabolism is Regulated by Hormones in Mammals
- 16.10: Absorption and Mobilization of Fuel Lipids in Mammals
- 16.11: Ketone Bodies Are Fuel Molecules

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## Fatty Acid Synthesis

Fatty acids are synthesized by the repetitive addition of 2 carbon units to a growing chain.

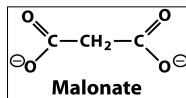
- Acetyl-CoA is the source of the 2 carbon units.
- The Acetyl groups are activated by carboxylating them to Malonyl groups

5-1

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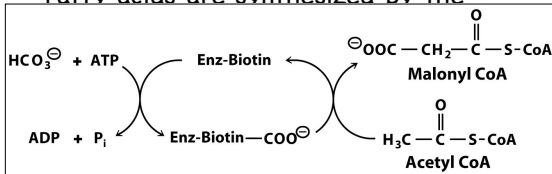
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5-2

## Fatty Acid Synthesis

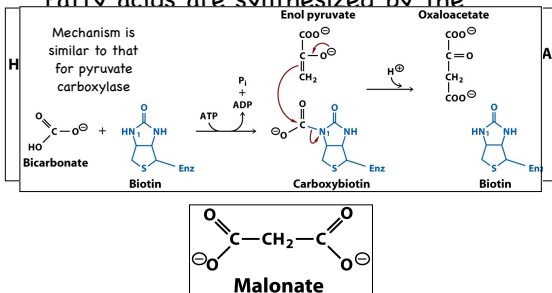
Fatty acids are synthesized by the



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## Fatty Acid Synthesis

Fatty acids are synthesized by the



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## Fatty Acid Synthesis

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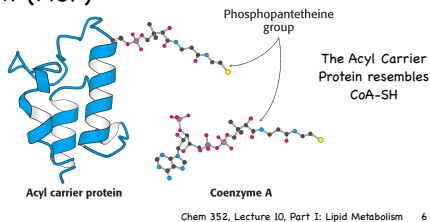
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5-5

## Fatty Acid Synthesis

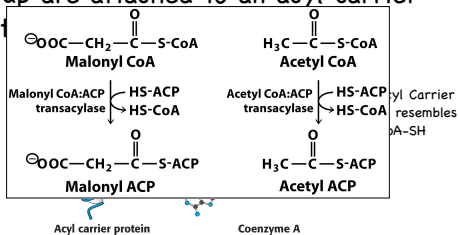
In eukaryotes, both the growing chain, the acetyl group, and the malonyl group are attached to an acyl carrier protein (ACP)



6-1

## Fatty Acid Synthesis

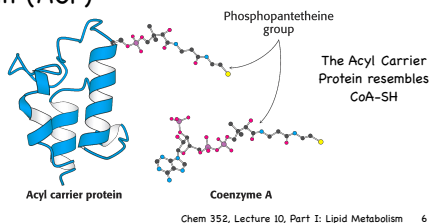
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6-2

## Fatty Acid Synthesis

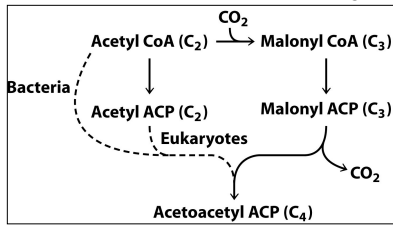
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6-3

## Fatty Acid Synthesis

The ligation of an acetyl group to the growing chain is coupled to the decarboxylation of the malonyl group.

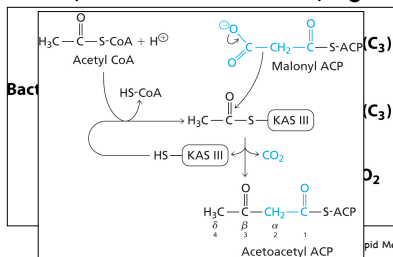


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7-1

## Fatty Acid Synthesis

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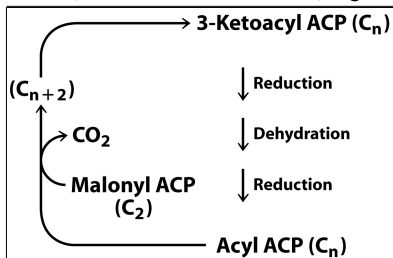


Lipid Metabolism 7

7-2

## Fatty Acid Synthesis

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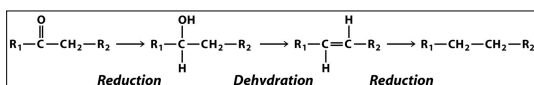


Metabolism 7

7-3

## Fatty Acid Synthesis

The reduction/dehydration/reduction steps similar to a series of reactions found in the citric acid cycle, but in reverse order.

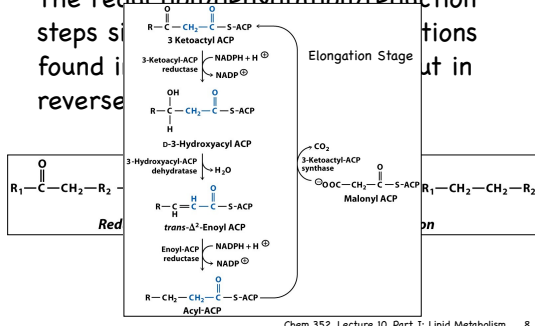


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8-1

## Fatty Acid Synthesis

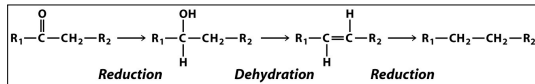
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8-2

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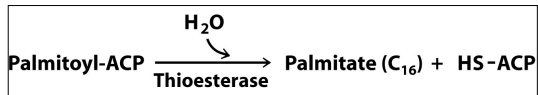


8-3

## Fatty Acid Synthesis

The elongation continues until reaching 16 carbons (palmitic acid).

- The palmitoyl group is cleaved from the ACP by a thioesterase.

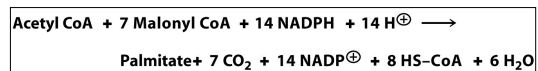
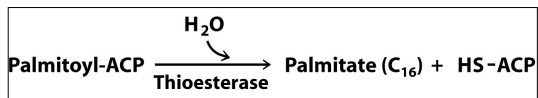


9-1

## Fatty Acid Synthesis

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9-2

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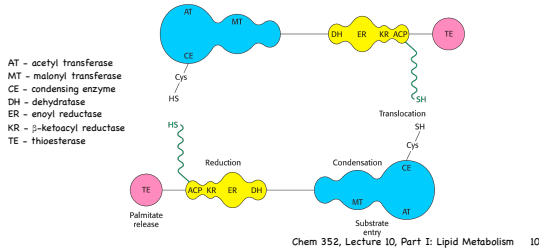


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9-3

## Fatty Acid Synthesis

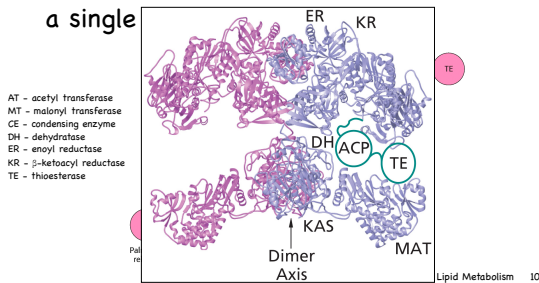
In eukaryotes, all of the active sites for fatty acid synthesis are located on a single polypeptide.



10-1

## Fatty Acid Synthesis

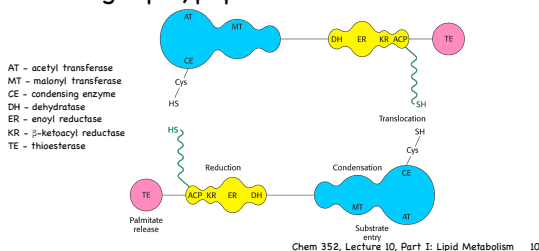
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10-2

## Fatty Acid Synthesis

In eukaryotes, all of the active sites for fatty acid synthesis are located on a single polypeptide.

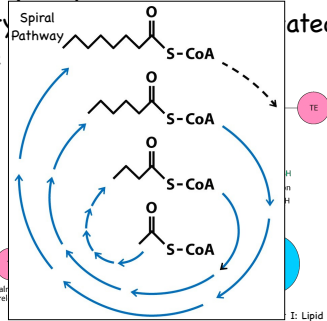


10-3

## Fatty Acid Synthesis

In eukaryotes, all of the active sites for fatty acid synthesis are located on a single

AT - acetyl transferase  
MT - malonyl transferase  
CE - condensing enzyme  
DH - dehydratase  
ER - enoyl reductase  
KR -  $\beta$ -ketoacyl reductase  
TE - thioesterase

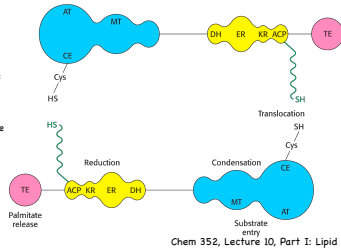


10-4

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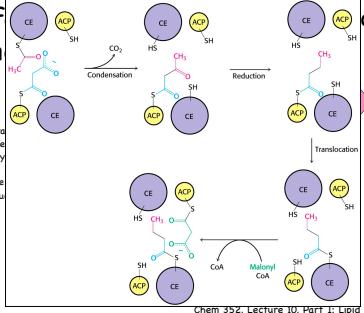


10-5

## Fatty Acid Synthesis

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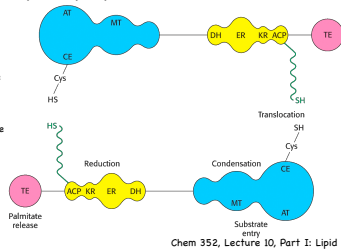


10-6

## Fatty Acid Synthesis

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TE - thioesterase



10-7



## Fatty Acid Synthesis

After palmitic acid is synthesized it is elongated and desaturated to form other fatty acids

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## Fatty Acid Synthesis

In eukaryotes, the acetyl-CoA for fatty acid synthesis in the cytosol comes from the mitochondrial matrix.

- The citrate/pyruvate shuttle is one of the systems used to move acetyl-CoA out into the cytosol.

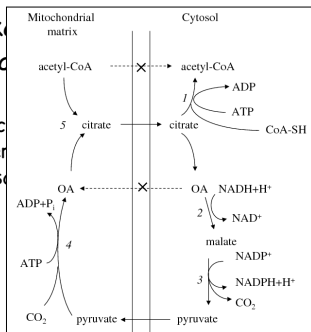
Chem 352, Lecture 10, Part I: Lipid Metabolism 12

12-1

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12-2

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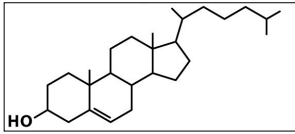
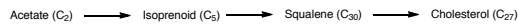
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12-3

## Cholesterol Synthesis

Cholesterol is used to modulate the physical properties of membranes in animals

- It is also the starting point for the synthesis of all other steroid molecules

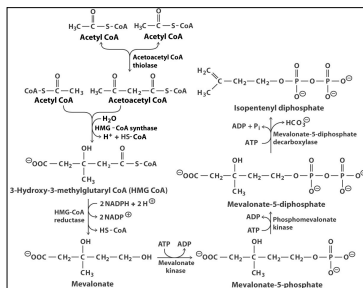


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## Cholesterol Synthesis

### Acetate to Isoprenoid

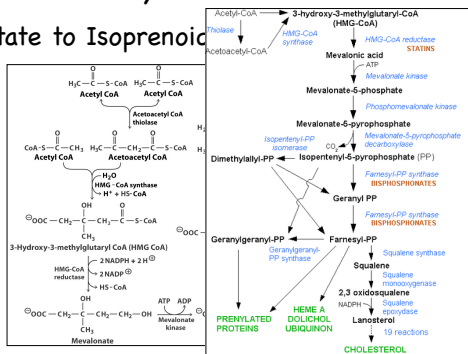


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## Cholesterol Synthesis

### Acetate to Isoprenoid

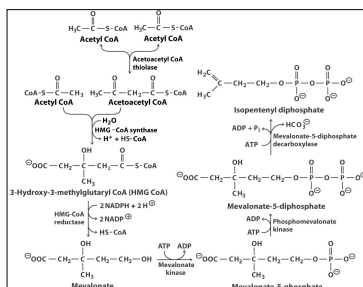


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14-2

## Cholesterol Synthesis

### Acetate to Isoprenoid

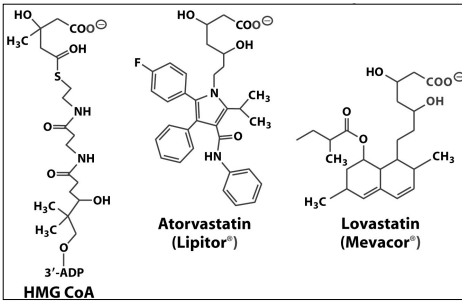


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14-3

## Cholesterol Synthesis

Statin (anticholesterol) drugs.



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## Cholesterol Synthesis

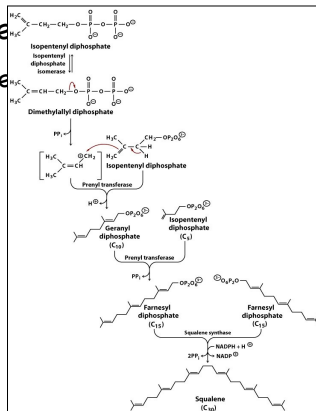
Isoprenoid to Squalene

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16-1

## Cholesterol Synthesis

Isoprenoid to Squalene

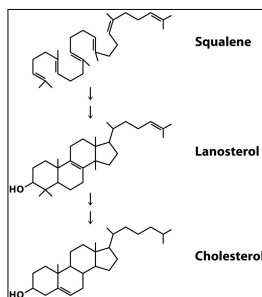


Lipid Metabolism 16

16-2

## Cholesterol Synthesis

Squalene to Cholesterol

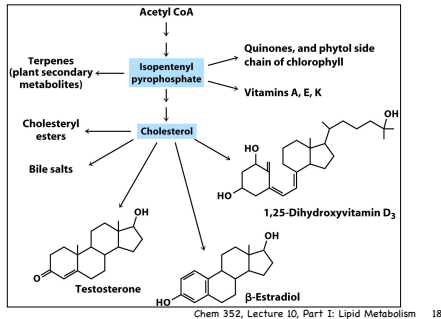


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## Cholesterol Synthesis

### Cholesterol to other steroids

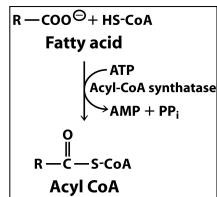


18

## Fatty acid oxidation

The catabolism of fatty acids takes place in the mitochondria

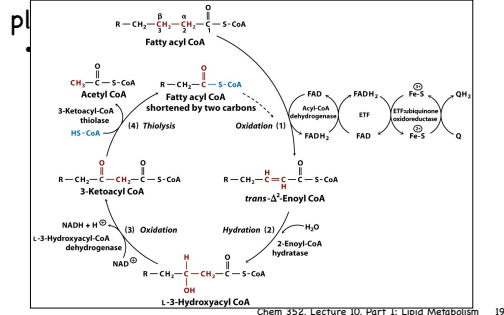
- The fatty acid must first be activated to an acyl-CoA



19-1

## Fatty acid oxidation

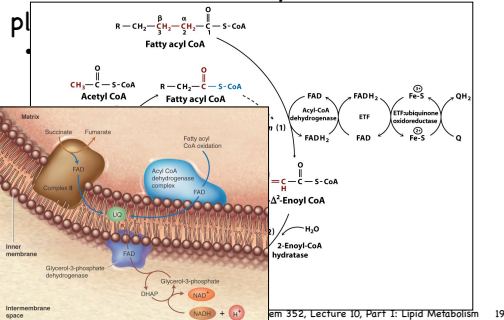
The catabolism of fatty acids takes place in the mitochondria



19-2

## Fatty acid oxidation

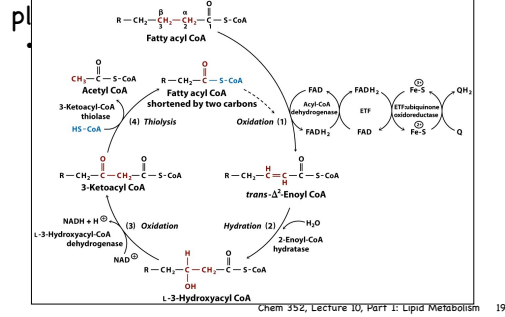
The catabolism of fatty acids takes place in the mitochondria



19-3

## Fatty acid oxidation

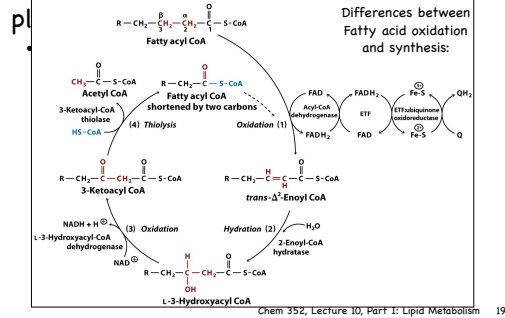
The catabolism of fatty acids takes



19-4

## Fatty acid oxidation

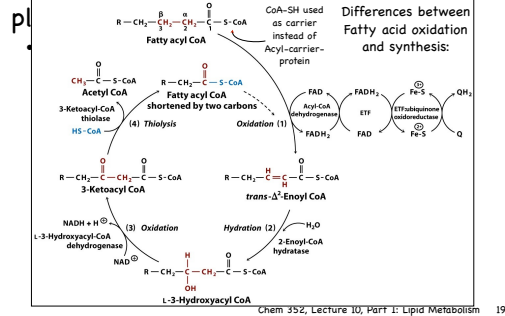
The catabolism of fatty acids takes



19-5

## Fatty acid oxidation

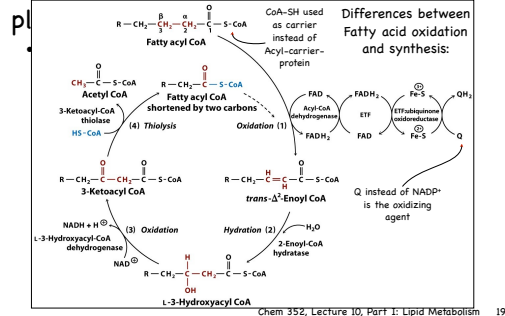
The catabolism of fatty acids takes



19-6

## Fatty acid oxidation

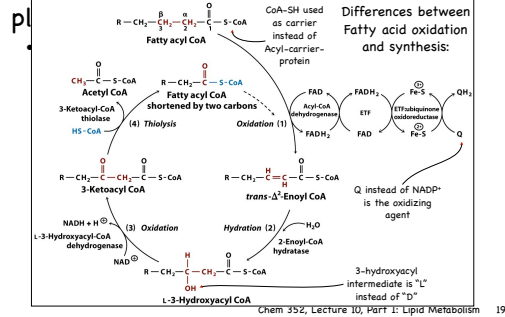
The catabolism of fatty acids takes



19-7

## Fatty acid oxidation

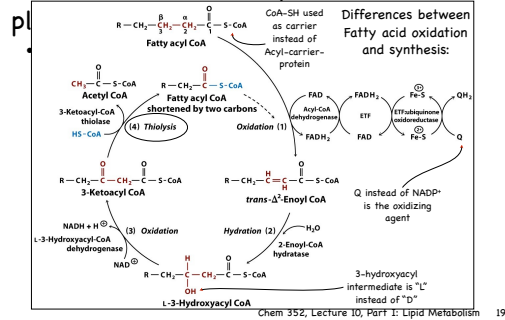
The catabolism of fatty acids takes



19-8

## Fatty acid oxidation

The catabolism of fatty acids takes

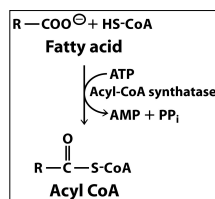


19-9

## Fatty acid oxidation

The catabolism of fatty acids takes place in the mitochondria

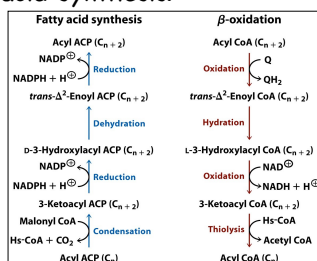
- The fatty acid must first be activated to an acyl-CoA



19-10

## Fatty acid oxidation

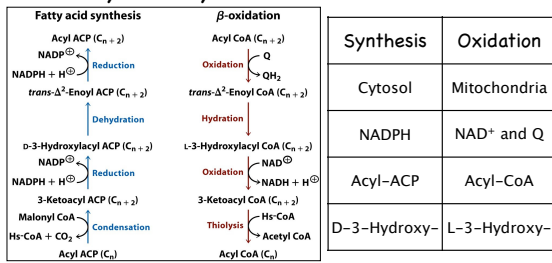
In many respects it is the reverse of fatty acid synthesis.



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## Fatty acid oxidation

In many respects it is the reverse of fatty acid synthesis.

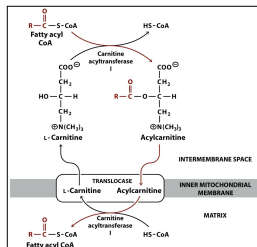


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## Fatty acid oxidation

Fatty acids enter the mitochondria by way of the carnitine shuttle.

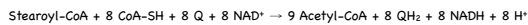


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## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)

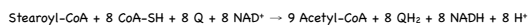


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## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)



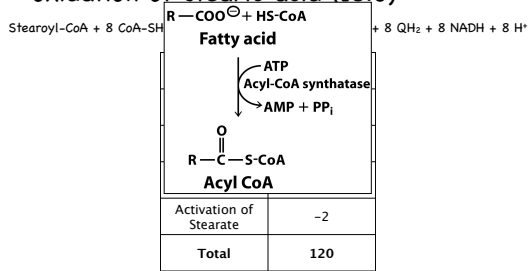
Source	ATP's
8 QH <sub>2</sub>	12
8 NADH	20
9 Acetyl-CoA	90
Activation of Stearate	-2
<b>Total</b>	<b>120</b>

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23-2

## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)

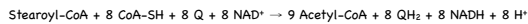


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23-3

## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)



Source	ATP's
8 QH <sub>2</sub>	12
8 NADH	20
9 Acetyl-CoA	90
Activation of Stearate	-2
<b>Total</b>	<b>120</b>

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## ATP Generation

ATP generation of the the complete oxidation of steric acid (18:0)

- Compared to Glucose (on a per C basis)

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## ATP Generation

ATP generation of the the complete oxidation of steric acid (18:0)

- Compared to Glucose (on a per C basis)

Source	ATP's
3 x Glucose	3 x 32 = 96
Stearate	120

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## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)

- Compared to Fatty Acid Synthesis

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## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)

- Compared to Fatty Acid Synthesis

Source	ATP's
8 Acetyl-CoA → 8 Malonyl-CoA	8
8 Rounds 16 NADPH	40
9 Acetyl-CoA (Calvin cycle)	$9 \times 17 = 153$
<b>Total</b>	<b>201</b>

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## ATP Generation

ATP generation of the the complete oxidation of stearic acid (18:0)

- Compared to Fatty Acid Synthesis

Source	ATP's
8 Acetyl-CoA → 8 Malonyl-CoA	8
8 Rounds 16 NADPH	40
9 Acetyl-CoA (Calvin cycle)	$9 \times 17 = 153$
<b>Total</b>	<b>201</b>

Yield =  $120/201 = 60\%$

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25-3

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## ATP Generation

### Regulation of Lipid Metabolism

- Involves same hormones as carbohydrate metabolism
  - Glucagon (fasting state)
  - Epinephrin (excited state)
  - Insulin (fed state)

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## ATP Generation

### Regulation of Lipid Metabolism

<ul style="list-style-type: none"> <li>• Involved in glucose and hormones as carbohydrate metabolism</li> <li>• Epinephrine</li> <li>• Glucagon (fasting state)</li> </ul>	<ul style="list-style-type: none"> <li>• Insulin</li> </ul>
<ul style="list-style-type: none"> <li>• Epinephrin (excited state)</li> <li>• Insulin (fed state)</li> </ul>	<ul style="list-style-type: none"> <li>• Activate formation and storage of triacylglycerides</li> </ul>
<ul style="list-style-type: none"> <li>• Inactivates acetyl-CoA carboxylase</li> <li>• Acetyl-CoA inhibits pyruvate dehydrogenase</li> </ul>	<ul style="list-style-type: none"> <li>• Activate acetyl-CoA carboxylase</li> <li>• Malonyl-CoA inhibits Carnitine acyltransferase I</li> </ul>

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## ATP Generation

### Regulation of Lipid Metabolism

<ul style="list-style-type: none"> <li>• Involved in glucose and hormones as carbohydrate metabolism</li> <li>• Glucagon</li> <li>• Epinephrine</li> <li>• Insulin</li> </ul>	<ul style="list-style-type: none"> <li>• Activate formation and storage of triacylglycerides</li> </ul>
<ul style="list-style-type: none"> <li>• Inactivates acetyl-CoA carboxylase</li> <li>• Acetyl-CoA inhibits pyruvate dehydrogenase</li> </ul>	<ul style="list-style-type: none"> <li>• Activate acetyl-CoA carboxylase</li> <li>• Malonyl-CoA inhibits Carnitine acyltransferase I</li> </ul>

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26-3

## ATP Generation

### Regulation of Lipid Metabolism

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26-4

## Transport of lipids in Blood

Lipids are transported by lipoprotein complexes

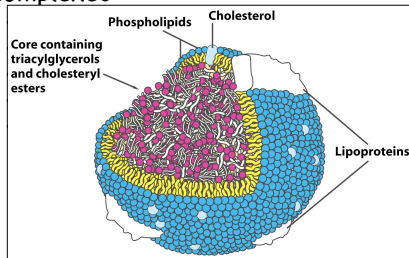
- Chylomicrons
- VLDL (Very Low Density Lipoproteins)
- IDL (Intermediate Density Lipoproteins)
- LDL (Low Density Lipoproteins)
- HDL (High Density Lipoproteins)

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27-1

## Transport of lipids in Blood

Lipids are transported by lipoprotein complexes



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27-2

## Transport of lipids in Blood

Lipids are transported by lipoprotein complexes

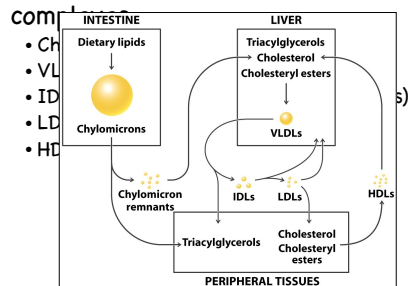
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27-3

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27-4

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## Ketone Bodies

Ketone bodies are formed from acetyl-CoA as a soluble circulating source of fat-derived energy.

- Produce under conditions of long-term fasting

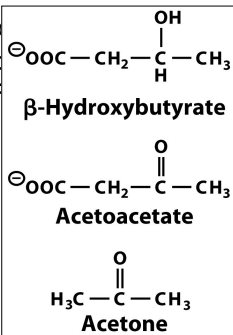
Chem 352, Lecture 10, Part I: Lipid Metabolism 28

28-1

## Ketone Bodies

Ketone bodies are formed from acetyl-CoA as a soluble circulating source of fat-derived energy.

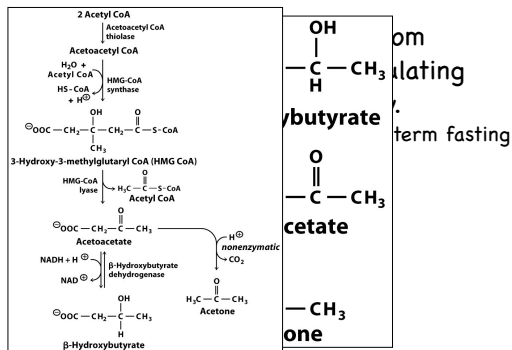
- Produce under conditions of long-term fasting



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28-2

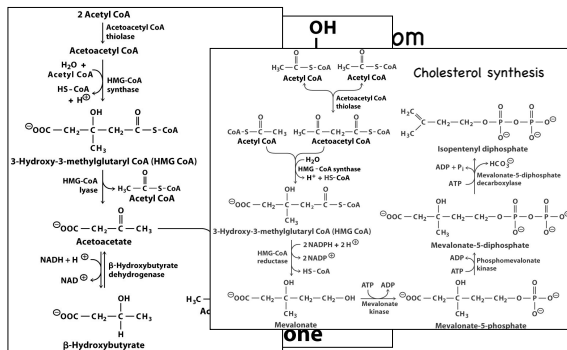
## Ketone Bodies



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28-3

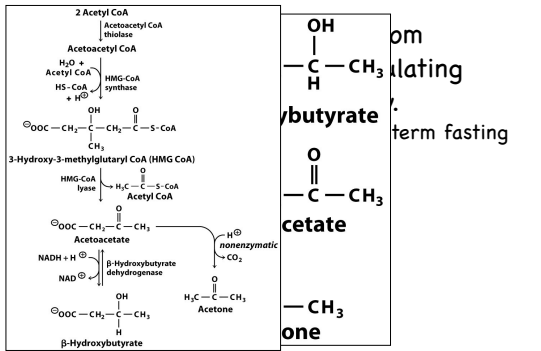
## Ketone Bodies



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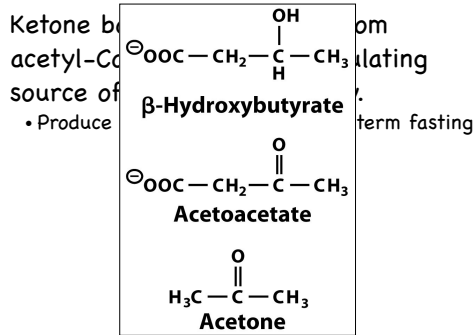
28-4

## Ketone Bodies



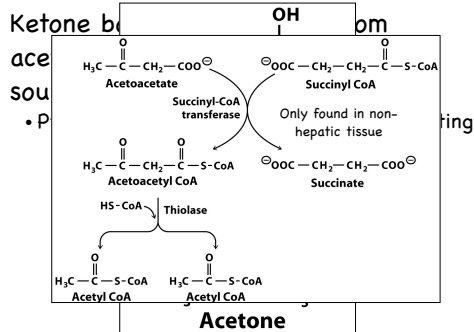
28-5

## Ketone Bodies



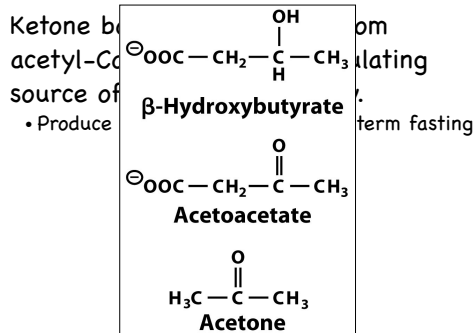
28-6

## Ketone Bodies



28-7

## Ketone Bodies



28-8

## Lipid Metabolism

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29-1

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## Lipid Metabolism

### Question:

Draw a general pathway for converting carbohydrates to fatty acids in a liver cell, and indicate which processes occur in the cytosol and which occur in mitochondria.

Chem 352, Lecture 10, Part I: Lipid Metabolism 29

29-2

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## Lipid Metabolism

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## Next Up

Lecture 10 - Part II, Amino acid metabolism (Moran et al., Chapter 17)

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