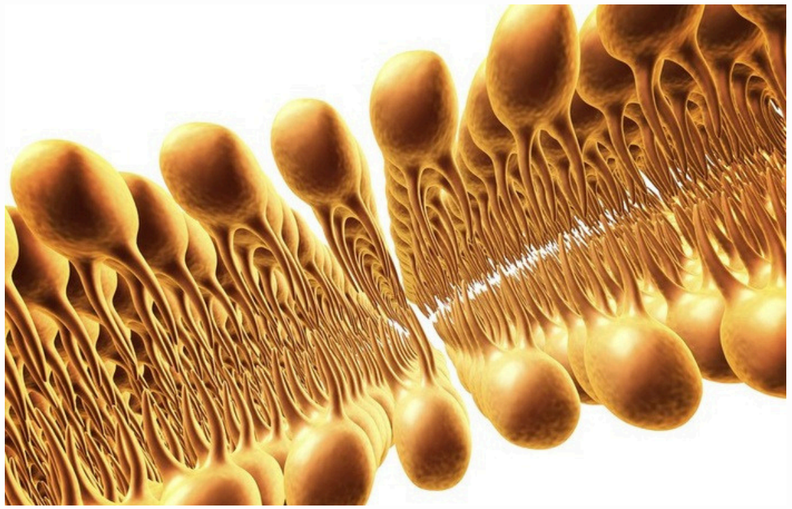
AL-FARABI KAZAKH NATIONAL UNIVERSITY
FACULTY OF BIOLOGY AND BIOTECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY



Lecture 5

# Lipids of Physiologic Significance & Oxidation of Fatty Acids

PhD, Acting Associate Professor, Doktyrbay Gulina

# Lecture Plan

1. Physiological Significance of Lipids
2. Major Types and Functions of Lipids
3. Fatty Acids and Triacylglycerols
4. Digestion, Absorption and Transport of Lipids
5. Mobilization of Fatty Acids
6. Overview of Fatty Acid Oxidation
7. β-Oxidation and the Carnitine Shuttle
8. Energy Yield and Regulation
9. Ketone Bodies and Physiological Significance
10. Clinical Significance and Student Tasks

CONTENTS

# Learning objectives

By theend of the lecture,students shouldbeable to:

- Identify the major classes of physiologically important lipids.
- Explain the major functions of lipids in the human body.
- Classify fatty acids according to chain length and degree of saturation.
- Explain how triacylglycerols are stored and mobilized.
- Describe the transport of fatty acids into mitochondria.
- Explain the mechanism of the carnitine shuttle.
- Describe the main steps of β-oxidation.
- Calculate the approximate energy yield from fatty acid oxidation.
- Explain how fatty acid oxidation is regulated.
- Describe the relationship between fatty acid and carbohydrate metabolism.
- Explain the formation and physiological role of ketone bodies.

# What are lipids?

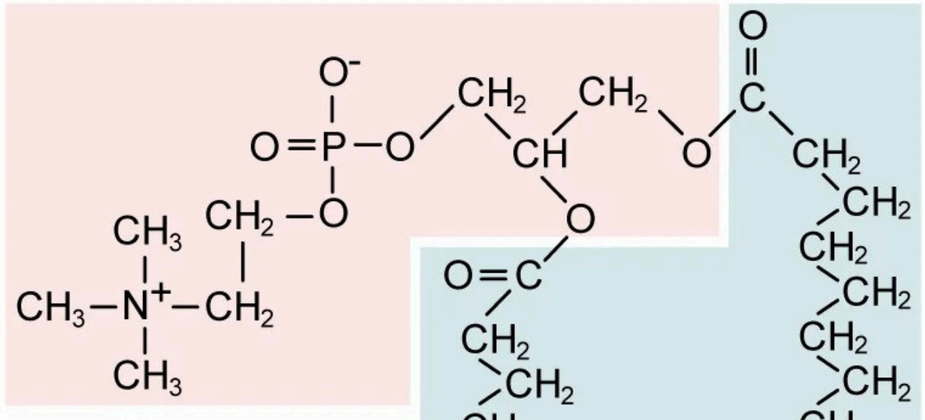
Lipids are a diverse group of biological molecules that are generally hydrophobic or amphipathic and poorly soluble in water.

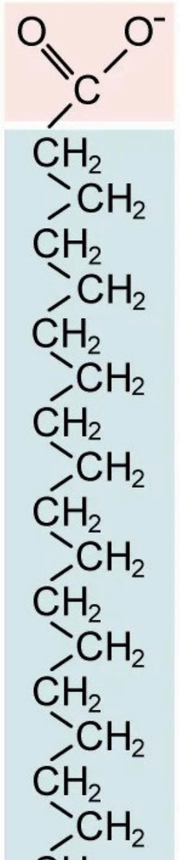
They are essential components of the human body and serve several important functions. Lipids provide a concentrated source of energy, form the structural basis of cell membranes, participate in signaling, and contribute to insulation and protection of organs.

Unlike carbohydrates, which are mainly used for rapid energy production, lipids are particularly important for long-term energy storage.

## structural formula

phospholipid (phosphatidylcholine)

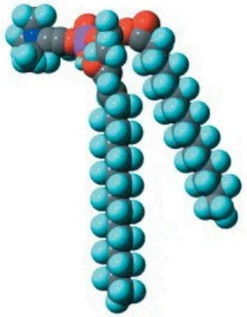




fatty acid (stearic acid)

## space-filling model

phospholipid molecule

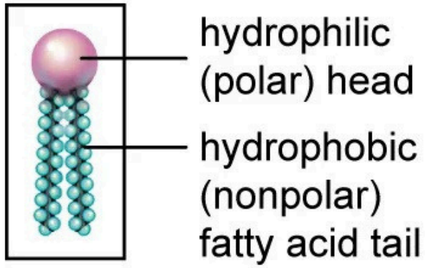


fatty acid molecule

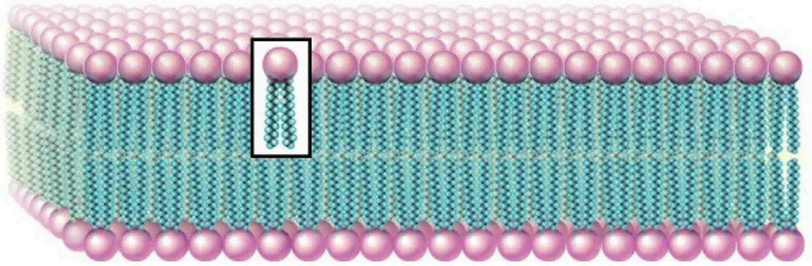


## generic simplified depiction

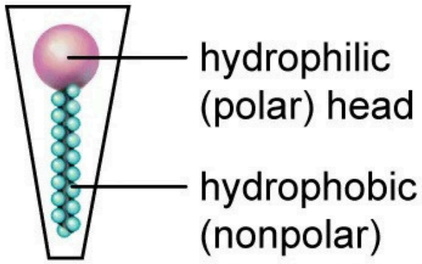
phospholipid molecule

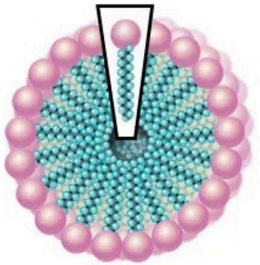



lipid bilayer



fatty acid molecule



micelle

# Major Lipids of Physiological Significance

The most important lipids in human physiology include:

| | |
|---|---|
| **Fatty acids** | Serve as energy substrates and building blocks for more complex lipids. |
| **Triacylglycerols** | The major form of stored metabolic energy. |
| **Phospholipids** | Major structural components of cell membranes. |
| **Sphingolipids** | Important components of cell membranes and nervous tissue. |
| **Cholesterol** | Important for membrane structure and is a precursor of steroid hormones, bile acids and vitamin D. |

# Main functions of lipids

Lipids performseveral majorfunctions in the body.
They provide energy, with fatty acids yielding large amounts of ATP when oxidized. Triacylglycerols are therefore an efficient form of long-term energy storage.
Lipids also have an important structural role because phospholipids, cholesterol and sphingolipids form biological membranes.
Some lipids function as signaling molecules, while others serve as precursors for hormones and other biologically active compounds.
Lipids also provide thermal insulation and mechanical protection for internal organs.

# Fatty Acids

Fatty acids consist of a hydrocarbon chain with a terminal carboxyl group.

**They can differ in:**

- chain length;
- number of double bonds;
- position of double bonds.

Fatty acids can be classified as saturated or unsaturated depending on the presence of double bonds.

**Saturated fatty acids**

Contain no carbon-carbon double bonds.

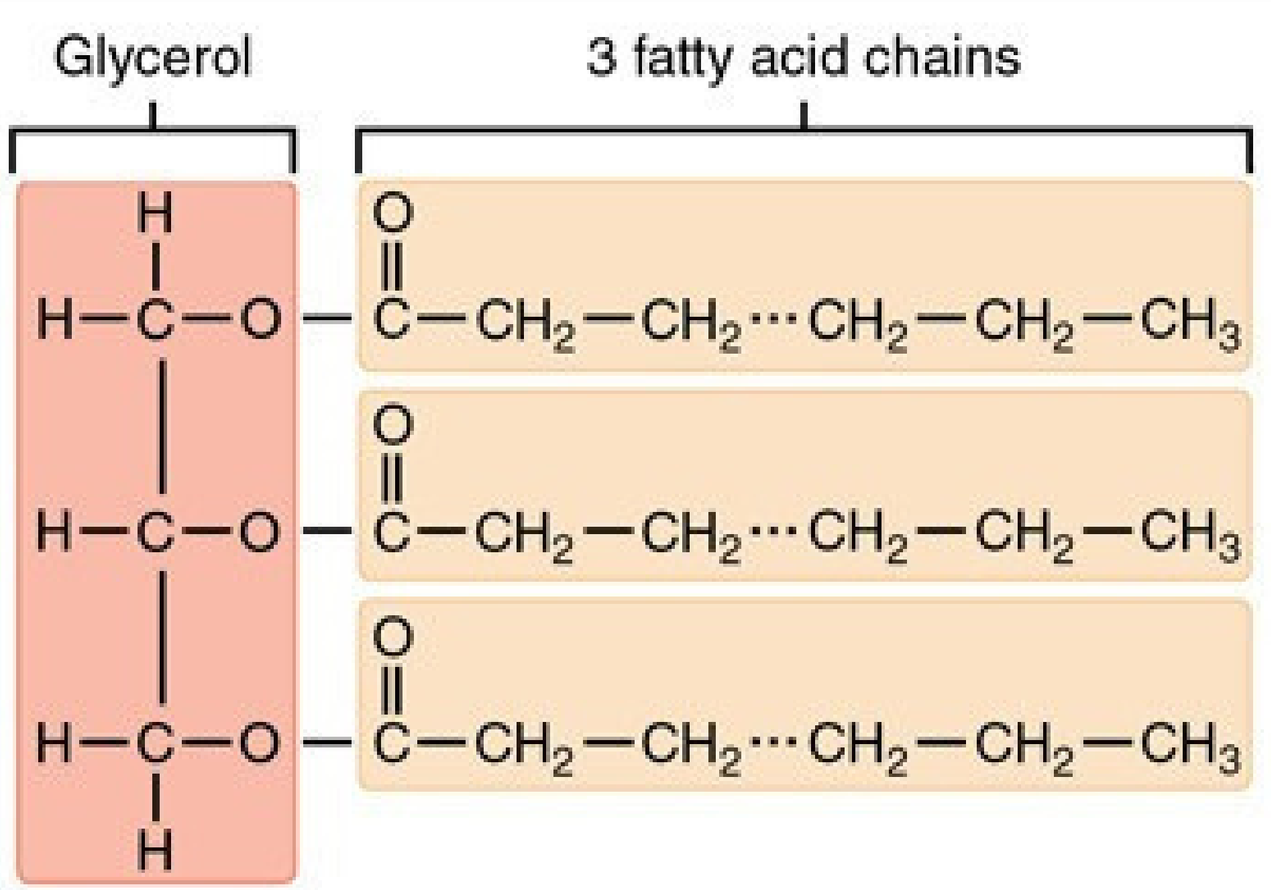
**Unsaturated fatty acids**

Contain one or more double bonds.

The structure of a fatty acid influences its physical properties and its metabolism.

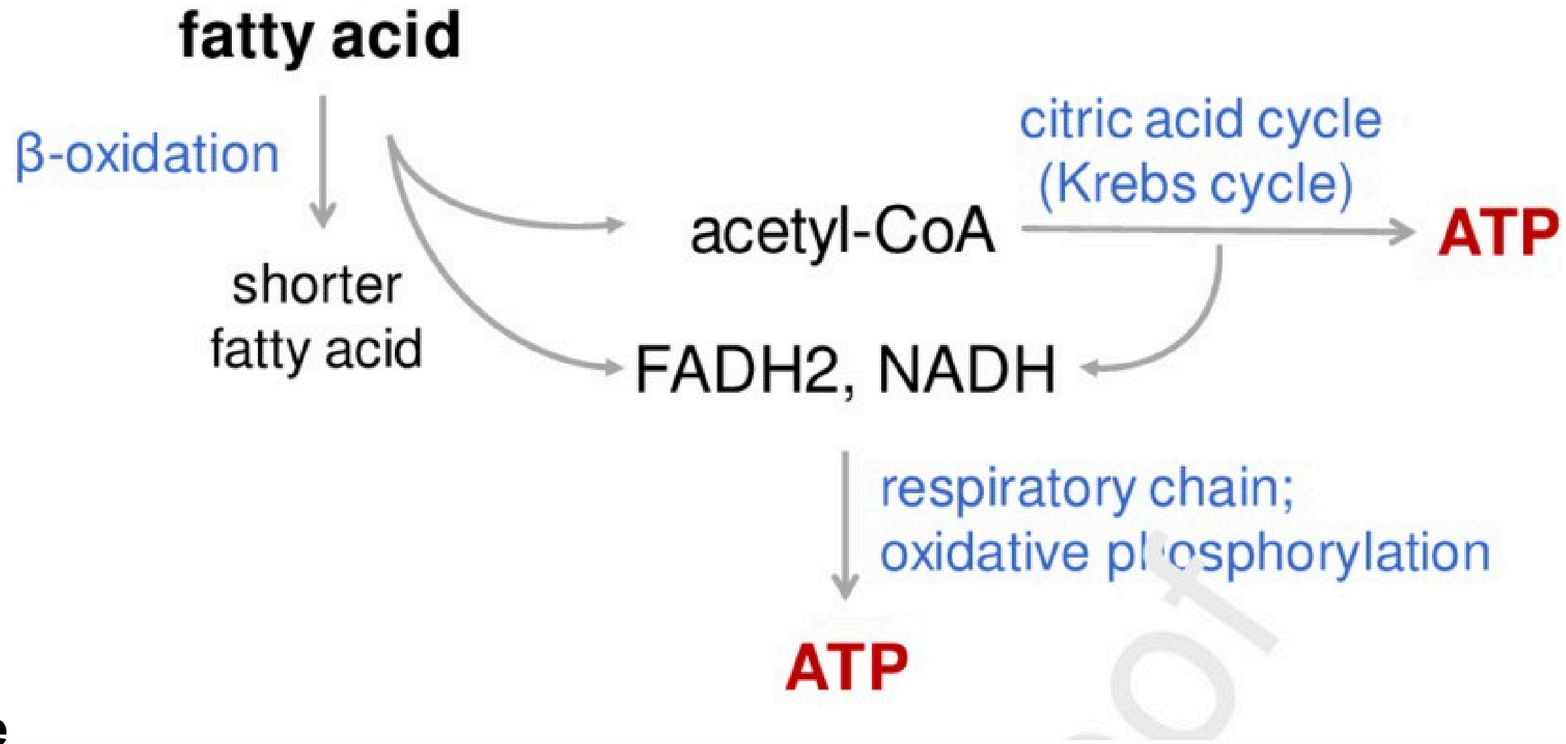
# Triacylglycerols: The Major Energy Store

Triacylglycerols (TAGs) consist of glycerol esterified with three fatty acids. They are the major form of energy storage in the human body and are mainly stored in adipose tissue. Triacylglycerols are highly energy-dense because fatty acids contain many reduced carbon-hydrogen bonds. When energy is required, stored triacylglycerols are broken down and fatty acids are released for oxidation.



# Why Are Fatty Acids an Efficient Energy Source

Fatty acids provide more energy per gram than carbohydrates.
This is because fatty acids are highly reduced molecules and contain a large number of high-energy carbon-hydrogen bonds.
When fatty acids are oxidized, their electrons are transferred to **$NAD^+$ and FAD**, producing NADH and $FADH_2$.
These electron carriers subsequently contribute to ATP production through oxidative phosphorylation.
Therefore, fatty acids are particularly suitable for **long-term energy storage and energy production.**



# Why Are Fatty Acids an Efficient Energy Source?

| Feature | Fatty acids | Carbohydrates |
|---|---|---|
| **Energy yield** | 9 kcal/g | 4 kcal/g |
| **Carbon structure** | Highly reduced | More oxidized |
| **Main storage form** | Triacylglycerols | Glycogen |
| **Water storage** | Verry little | Stored with significant water |
| **Main role** | Long-term energy storage | Rapid energy supply |

Fatty acids are highly reduced molecules, so their oxidation releases a large amount of energy.

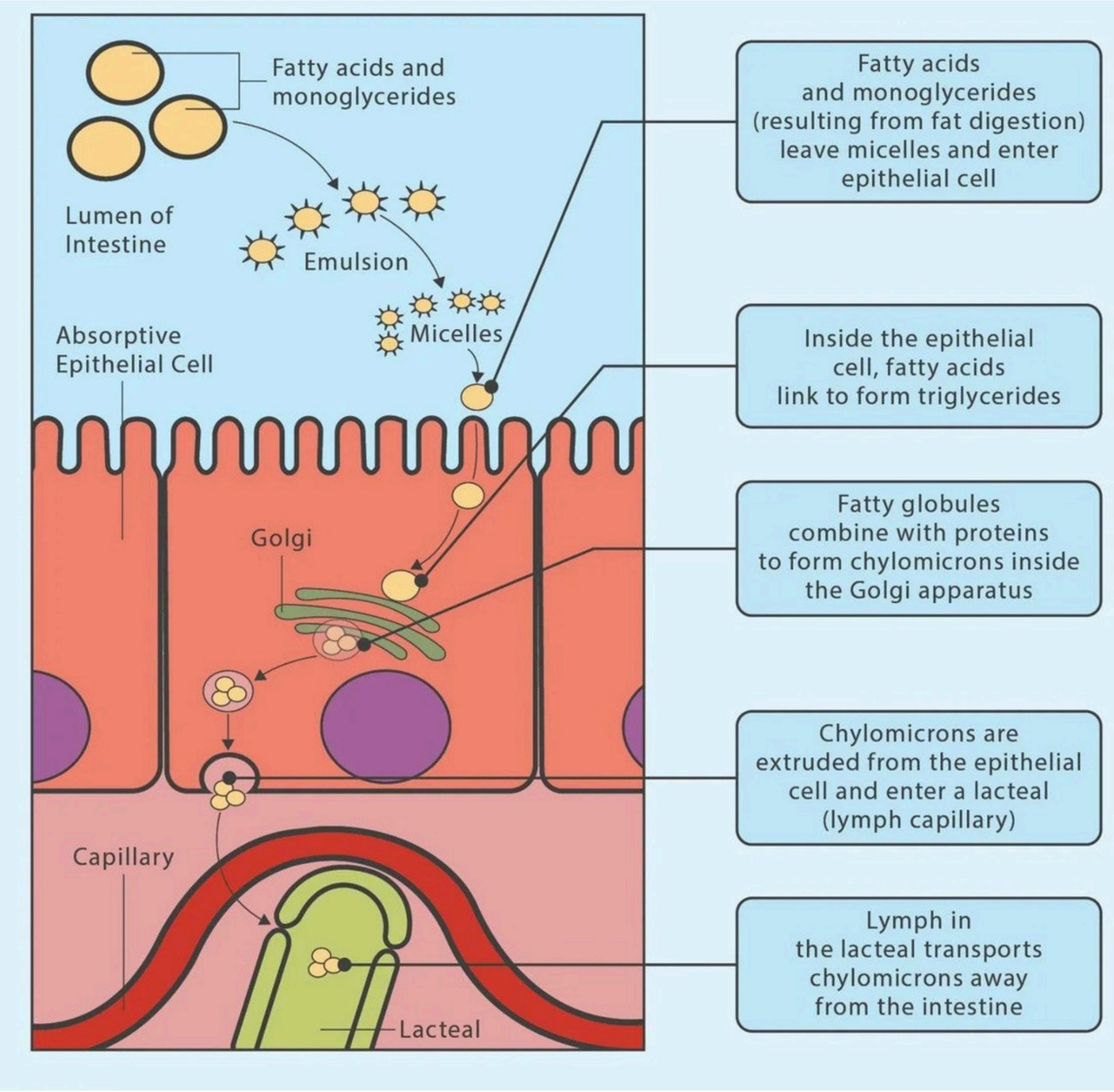
Dietary lipids are mainly present as **triacylglycerols**.

In the digestive system, they are emulsified by **bile salts**, which increase the surface area available for enzymatic digestion.

Pancreatic lipase breaks down triacylglycerols into **fatty acids and monoacylglycerols.**

These products form micelles with bile salts and are transported to intestinal cells for absorption.

Inside enterocytes, fatty acids and monoacylglycerols are reassembled into triacylglycerols and packaged into chylomicrons.



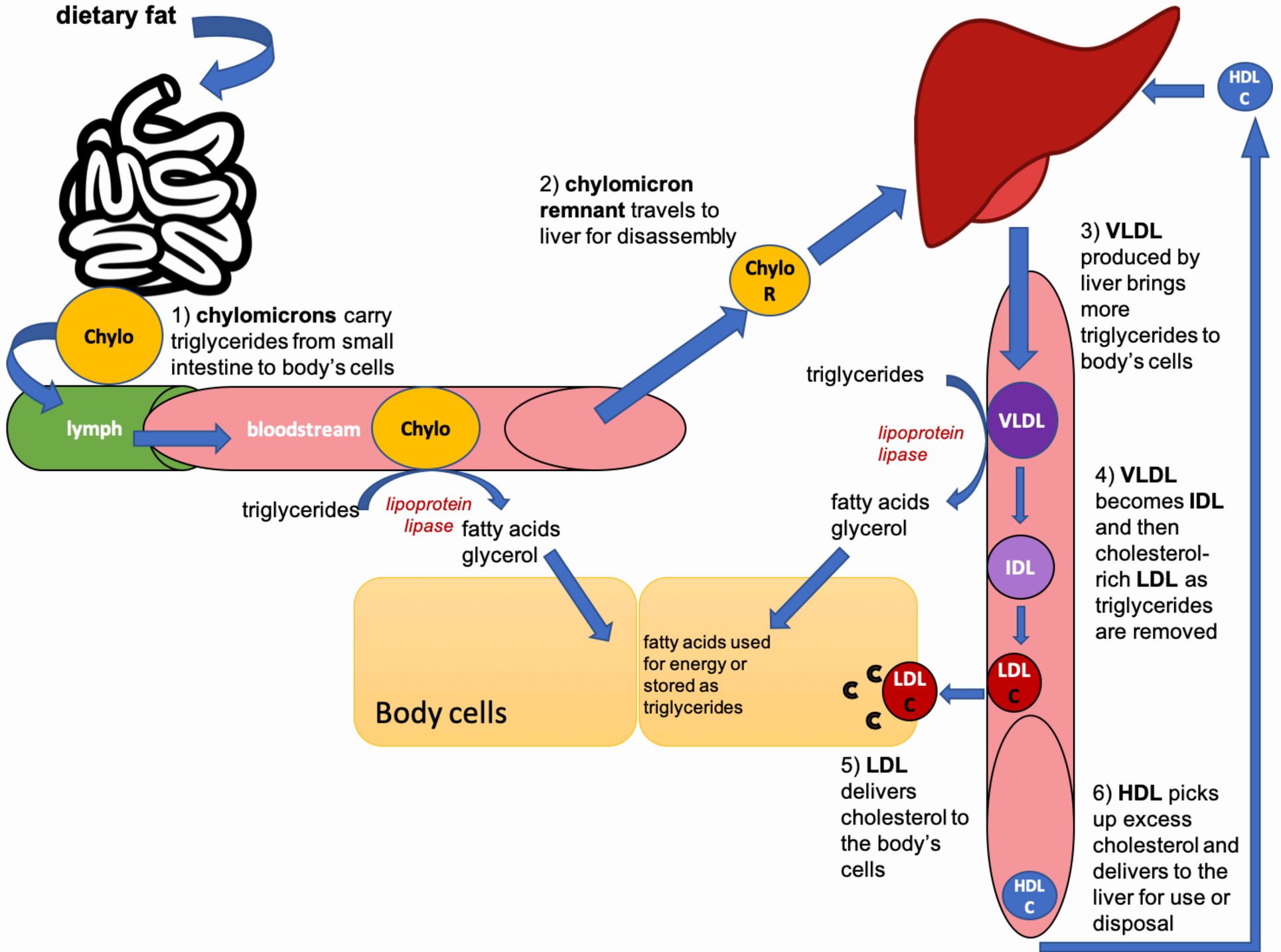
# Transport of lipids in the blood

Because most lipids are poorly soluble in water, they cannot circulate freely in the bloodstream.
They are transported in the form of lipoproteins.

Major lipoproteins include:

- **Chylomicrons** – transport dietary triacylglycerols.
- **VLDL** – transport endogenous triacylglycerols from the liver.
- **LDL** – delivers cholesterol to tissues.
- **HDL** – participates in reverse cholesterol transport.

This system allows hydrophobic lipids to be transported through the aqueous blood plasma.


dietary fat
Chylo
1) **chylomicrons** carry triglycerides from small intestine to body's cells
lymph
bloodstream
Chylo
triglycerides
*lipoprotein lipase*
fatty acids
glycerol
Body cells
2) **chylomicron remnant** travels to liver for disassembly
Chylo R
HDL C
3) **VLDL** produced by liver brings more triglycerides to body's cells
triglycerides
*lipoprotein lipase*
fatty acids
glycerol
VLDL
IDL
LDL C
4) **VLDL** becomes **IDL** and then cholesterol-rich **LDL** as triglycerides are removed
fatty acids used for energy or stored as triglycerides
C
C
C
LDL C
5) **LDL** delivers cholesterol to the body's cells
HDL C
6) **HDL** picks up excess cholesterol and delivers to the liver for use or disposal

# Mobilization of stored fat

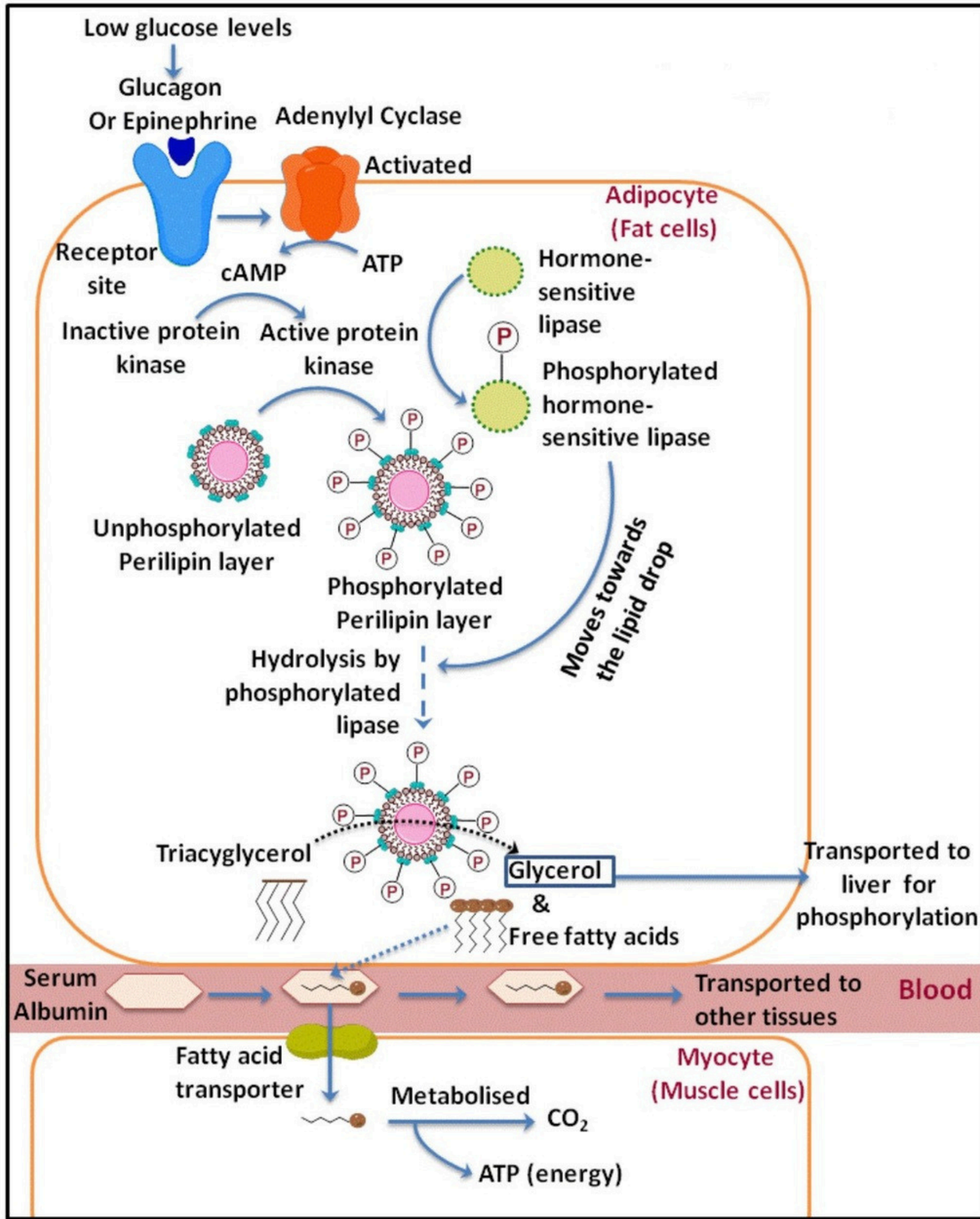
When energy demand increases, triacylglycerols stored in adipose tissue are broken down by lipolysis.

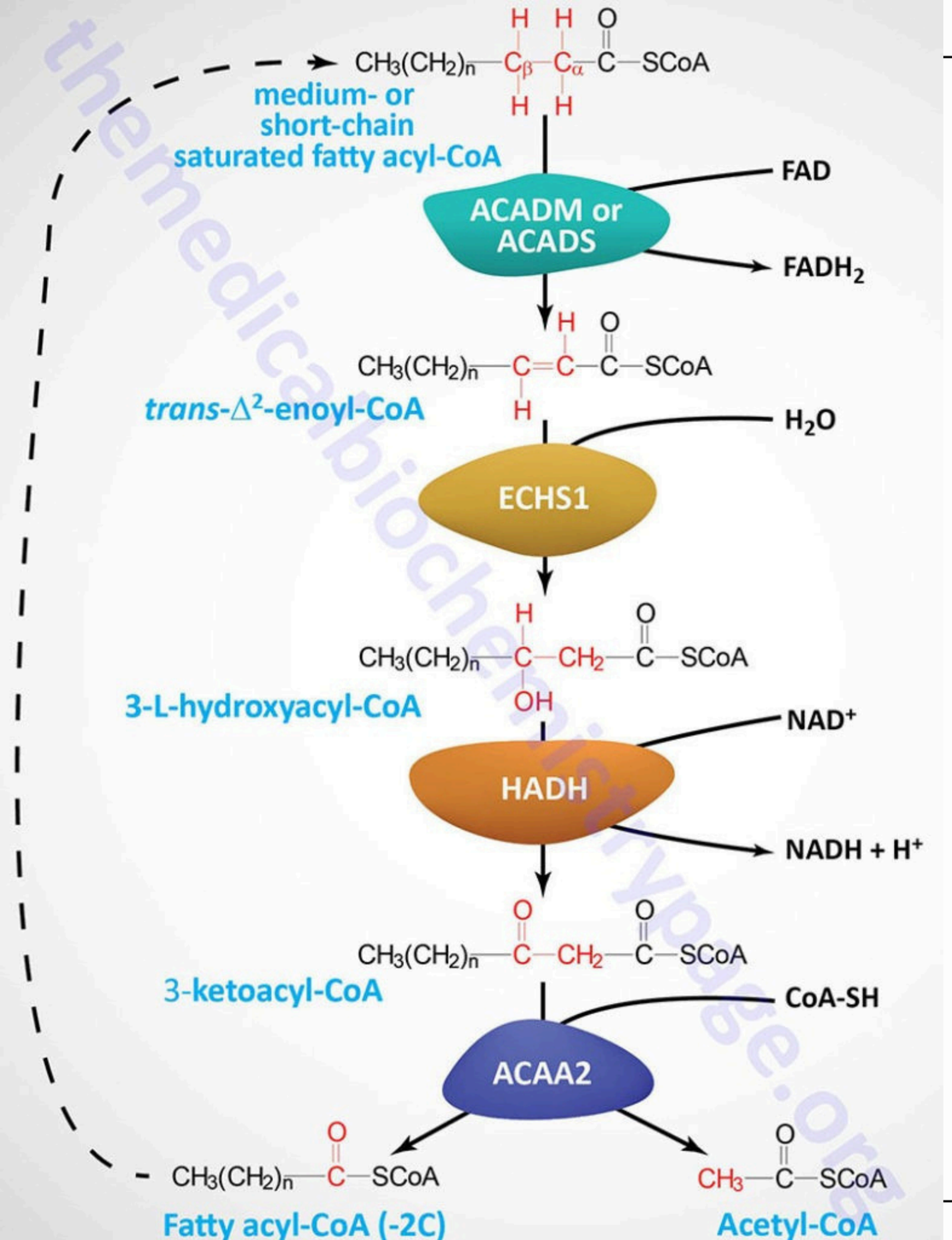
The released fatty acids enter the bloodstream and are transported to tissues that can oxidize them.

Lipolysis is stimulated during:

- fasting;
- prolonged exercise;
- low insulin levels;
- increased glucagon and epinephrine signaling.

The released fatty acids then enter cells and can be oxidized to produce ATP.






Fatty acid oxidation allows the cell to extract energy from stored fat.

During oxidation, the carbon chain of a fatty acid is gradually shortened, producing acetyl-CoA.

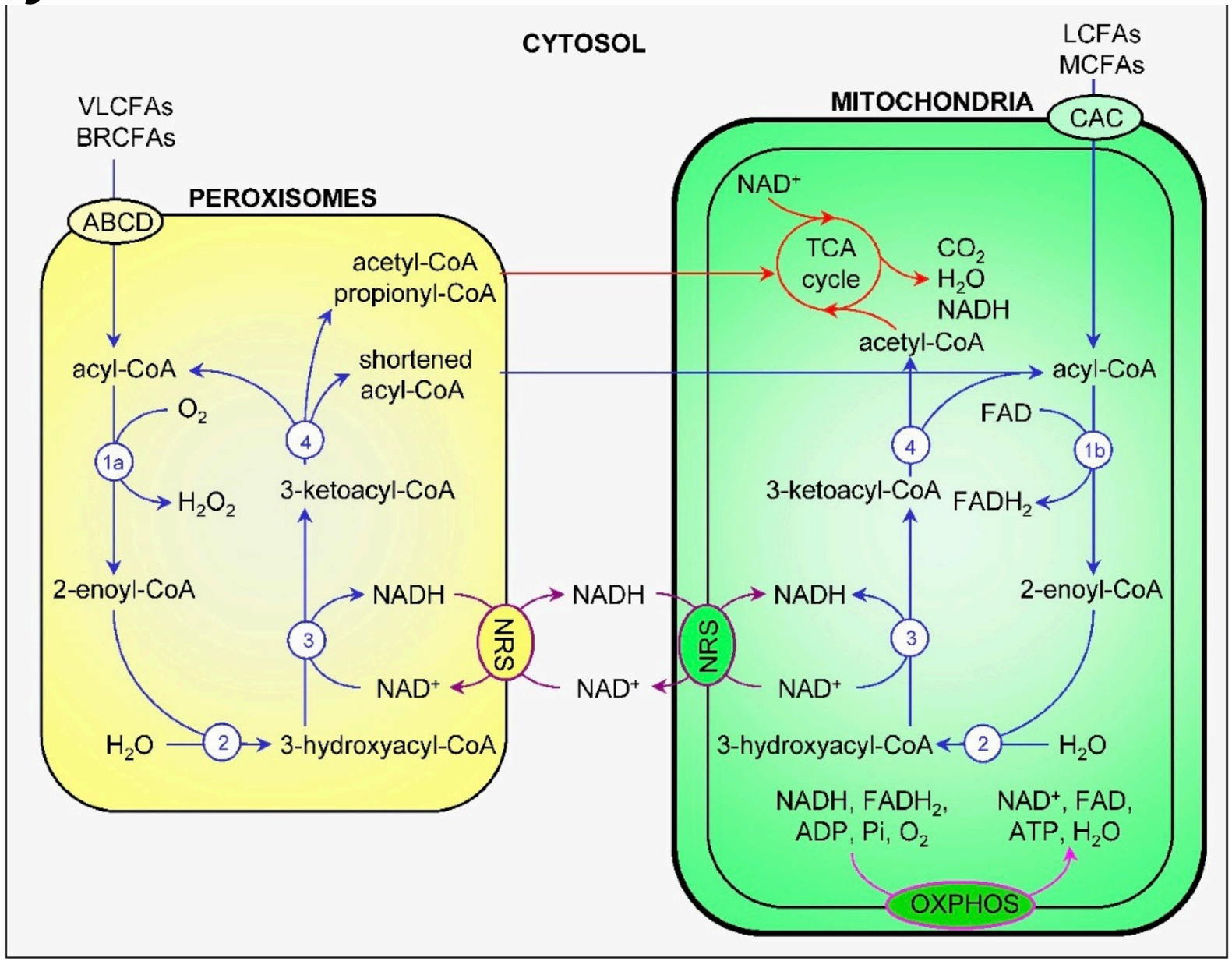
At the same time, NADH and $FADH_2$ are generated.

Acetyl-CoA enters the citric acid cycle, while NADH and $FADH_2$ transfer their electrons to the electron transport chain.

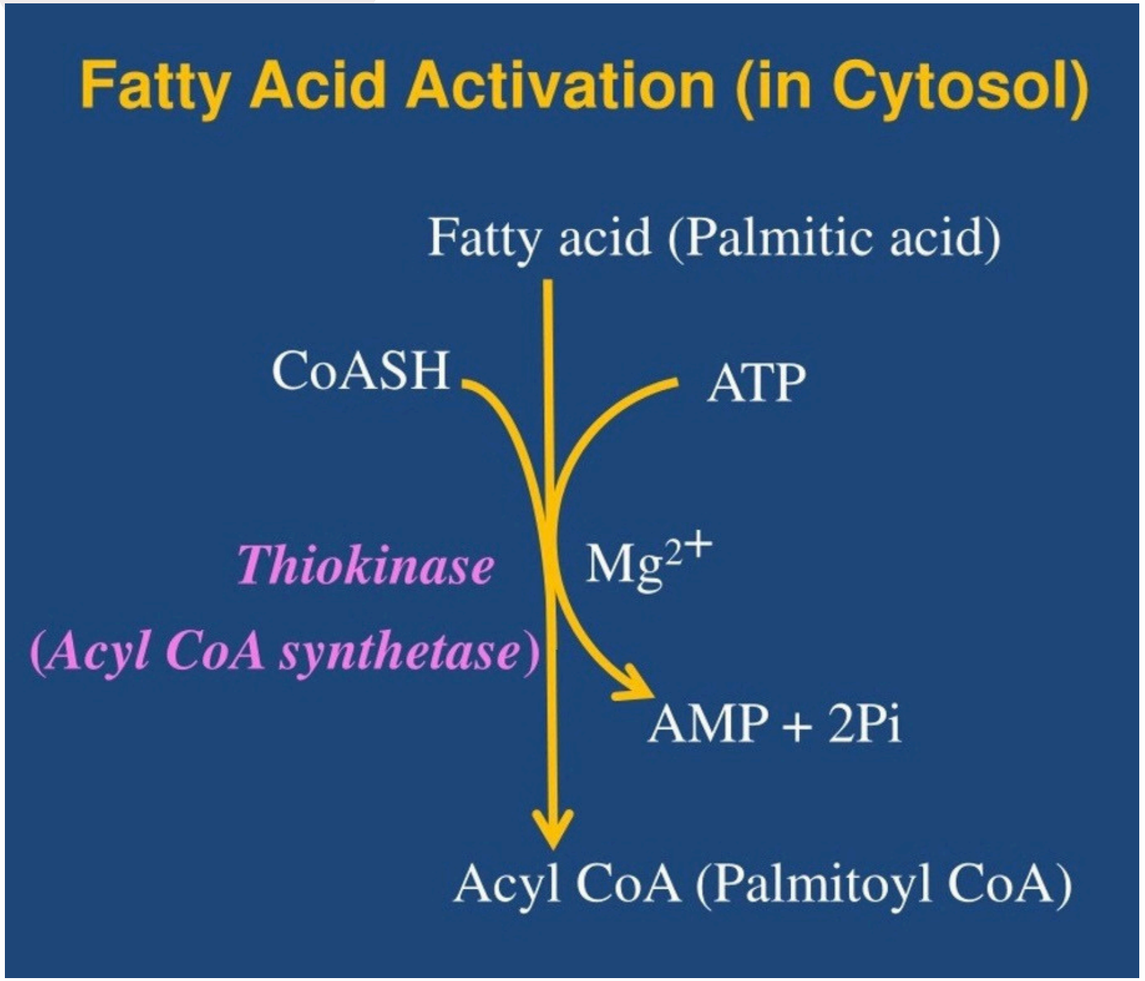
**Fatty acid oxidation → Acetyl-CoA + NADH + $FADH_2$ → ATP production**

# Where does fatty acid oxidation occur?

The main pathway for fatty acid oxidation is β-oxidation.
For most fatty acids, β-oxidation occurs in the **Mitochondrial** matrix
However, very-long-chain fatty acids can undergo initial oxidation in peroxisomes.
Before a fatty acid can undergo mitochondrial \beta-oxidation, it must first be activated and transported into the mitochondrial matrix.



# Activation of fatty acids




Before oxidation, a fatty acid must be converted into fatty acyl-CoA.

This reaction is catalyzed by acyl-CoA synt hetase.

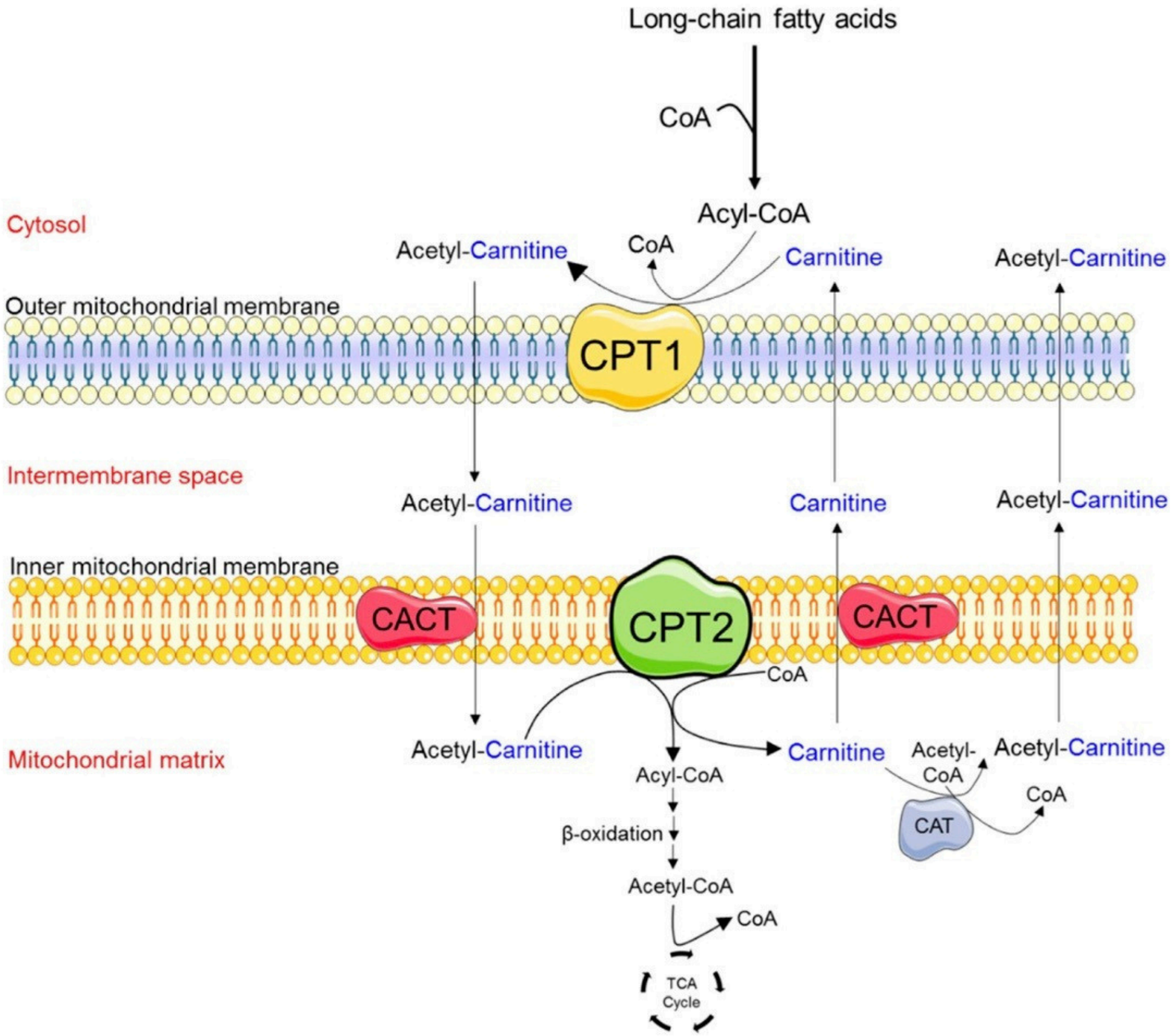
The activation reaction requires energy from ATP.

Fatty acid + CoA → Fatty acyl-CoA

Activation is necessary because the fatty acid must be attached to coenzyme A before it can enter the β-oxidation pathway.

# The carnitine shuttle

Long-chain fatty acyl-CoA molecules cannot directly cross the inner mitochondrial membrane.
They require a transport system called the carnitine shuttle.
The fatty acyl group is transferred to carnitine and transported across the inner mitochondrial membrane. Once inside the mitochondrial matrix, the fatty acyl group is transferred back to CoA.
This allows long-chain fatty acids to reach the site of β-oxidation.


Long-chain fatty acids
CoA
Acyl-CoA
Cytosol
Acetyl-Carnitine
CoA
Carnitine
Acetyl-Carnitine
Outer mitochondrial membrane
CPT1
Intermembrane space
Acetyl-Carnitine
Carnitine
Acetyl-Carnitine
Inner mitochondrial membrane
CACT
CPT2
CACT
CoA
Mitochondrial matrix
Acetyl-Carnitine
Acyl-CoA
Carnitine
Acetyl-CoA
Acetyl-Carnitine
CoA
CAT
β-oxidation
Acetyl-CoA
CoA
TCA Cycle

β-oxidation is the major pathway for the degradation of fatty acids.
During each cycle, the fatty acid chain is shortened by two carbon atoms.
These two carbons are released as acetyl-CoA.
At the same time, each cycle produces:

- 1 NADH
- 1 $FADH_2$

The acetyl-CoA enters the citric acid cycle, while NADH and $FADH_2$ contribute to ATP production.

Each cycle of β-oxidation consists of four reactions:

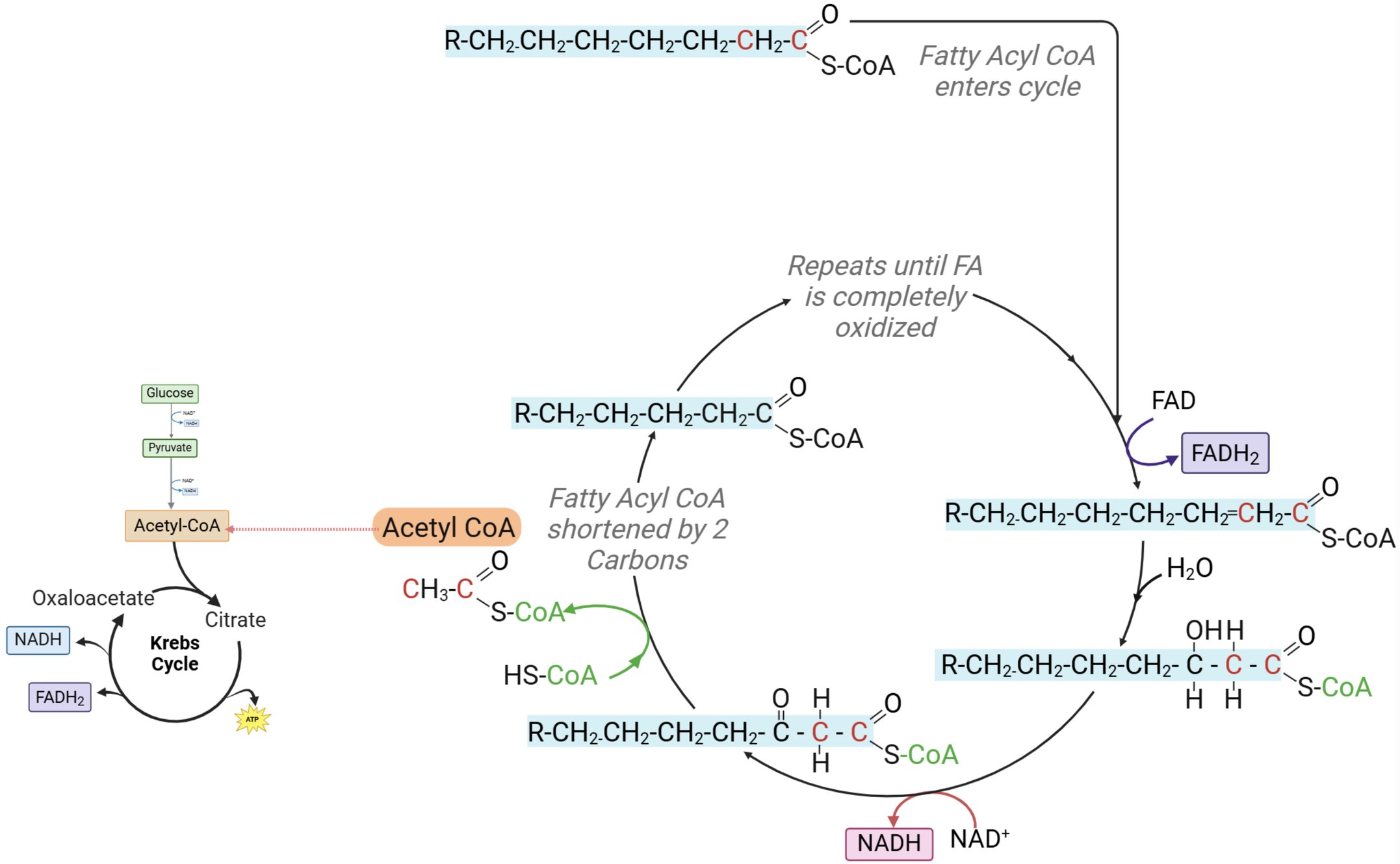
**1. Oxidation**
Produces $FADH_2$.

**2. Hydration**
Water is added to the double bond.

**3. Oxidation**
Produces NADH.

**4. Thiolysis**
The fatty acid chain is cleaved, releasing acetyl-CoA.

The shortened fatty acyl-CoA then enters another cycle.


R-CH2-CH2-CH2-CH2-CH2-CH2-C(=O)-S-CoA
Fatty Acyl CoA enters cycle
FAD
FADH2
R-CH2-CH2-CH2-CH2-CH2=CH2-C(=O)-S-CoA
H2O
R-CH2-CH2-CH2-CH2-C(OH)H-C(H)H-C(=O)-S-CoA
NAD+
NADH
R-CH2-CH2-CH2-CH2-C(=O)-C(H)=C(H)-C(=O)-S-CoA
HS-CoA
CH3-C(=O)-S-CoA
Acetyl CoA
Fatty Acyl CoA shortened by 2 Carbons
R-CH2-CH2-CH2-CH2-C(=O)-S-CoA
Repeats until FA is completely oxidized
Glucose
Pyruvate
Acetyl-CoA
Oxaloacetate
Citrate
Krebs Cycle
NADH
FADH2
ATP

# Oxidation of palmitate

Palmitateis a saturated fatty acid containing16carbon atoms.
Its complete β-oxidation requires **7 cycles**
and produces: 8 acetyl-CoA, 7 NADH, 7 $FADH_2$

The eight acetyl-CoA molecules then enter the citric acid cycle for further oxidation.
Palmitate is commonly used as an example because it clearly demonstrates the relationship between fatty acid chain length, β-oxidation cycles and ATP production.

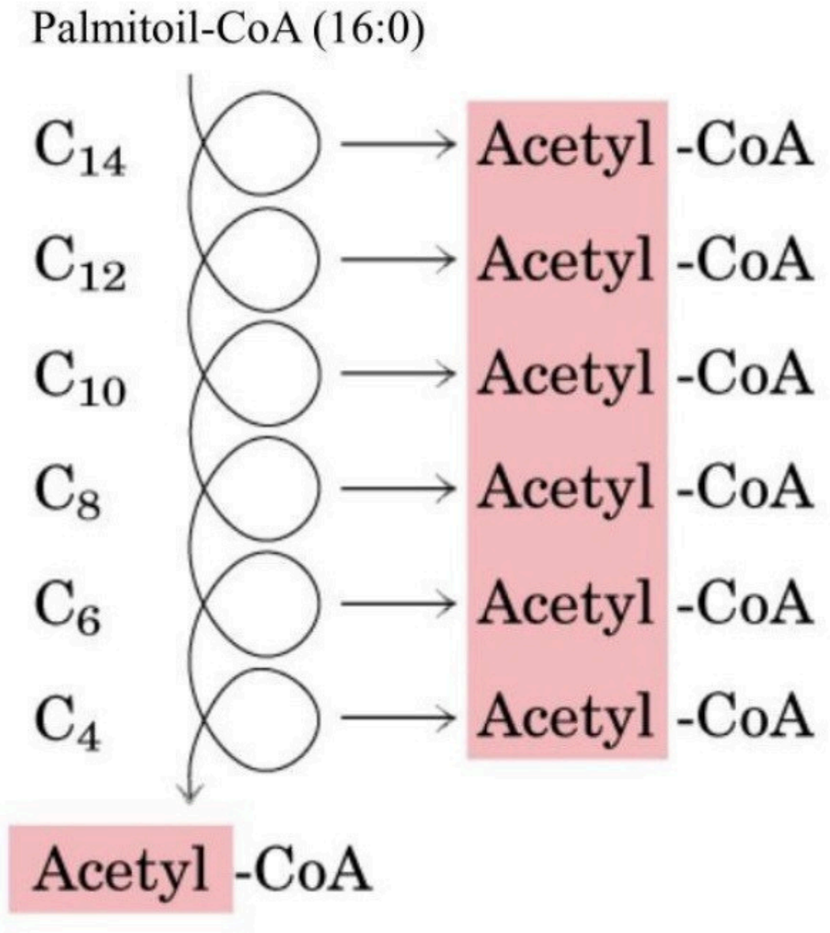
Palmitoil-CoA (16:0) + 7 CoA + 7 $NAD^+$ + 7 FAD + 7 $H_2O$

→ 8 acetil-CoA + 7 NADH + 7 $FADH_2$ + 7 $H^+$

... Logo ...

Palmitoil-CoA (16:0) + 7 CoA + 7 $O_2$ + 28 Pi + 28 ADP

→ 8 acetil-CoA + 28 ATP + 7 $H_2O$



Complete oxidation of one molecule of palmitate produces approximately:
106 ATP
This high energy yield demonstrates why fatty acids are such efficient energy-storage molecules.
The ATP is generated from:

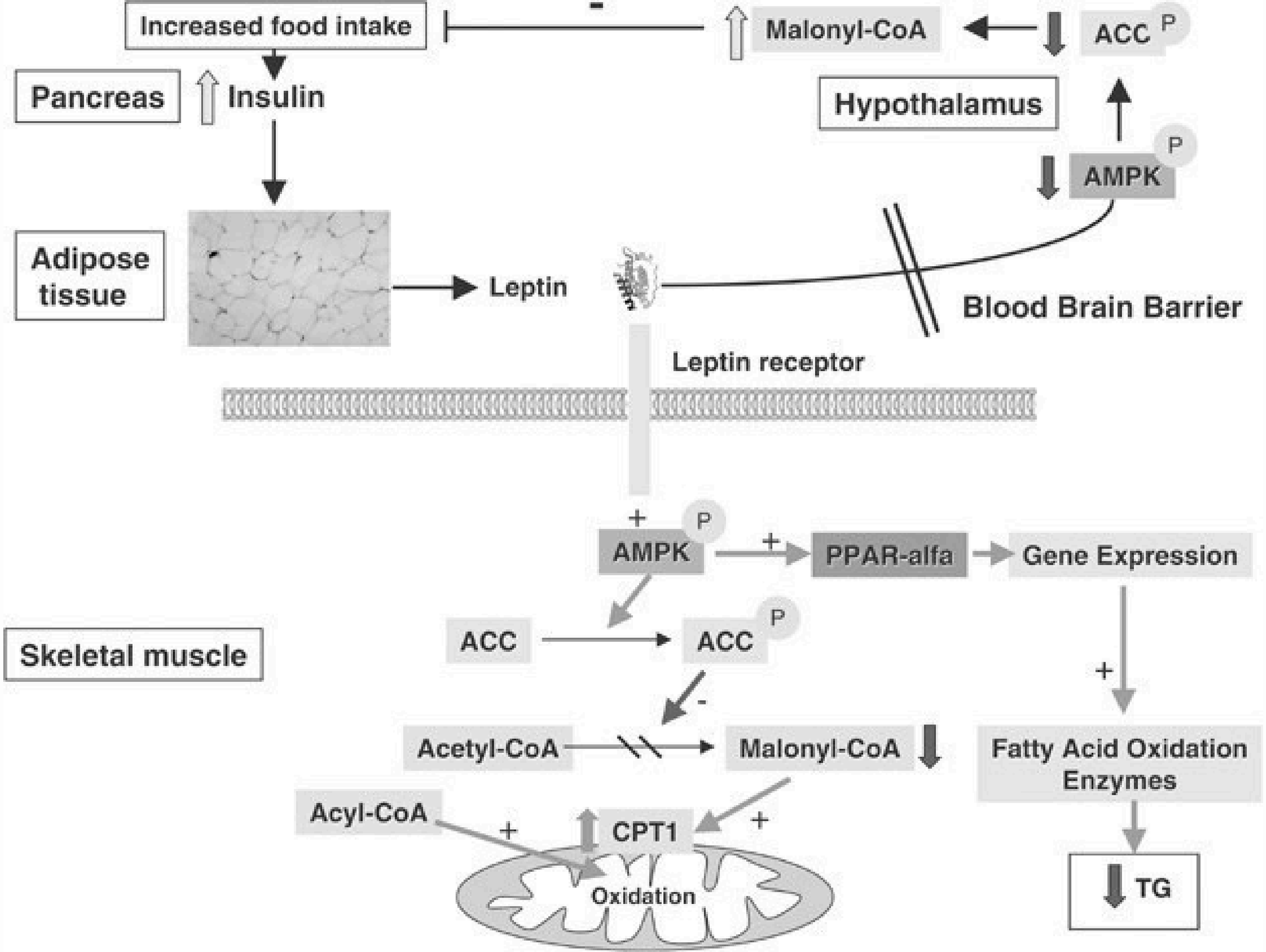
- NADH produced during β-oxidation;
- $FADH_2$ produced during β-oxidation;
- NADH and $FADH_2$ generated when acetyl-CoA enters the citric acid cycle.

**Fatty acid oxidation itself does not directly produce large amounts of ATP. It produces electron carriers and acetyl-CoA, which are subsequently used to generate ATP.**

# Hormonal regulation

Insulin promotes fat storage, whereas glucagon and epinephrine promote fat mobilization and utilization.

| Hormone | Metabolic state | Effect on lipolysis | Effect on fatty acid oxidation |
|---|---|---|---|
| Insulin | Fed state | ⬇ Inhibits | ⬇ Decreases |
| Glucagon | Fasting | ⬆ Stimulates | ⬆ Increases |
| Epinephrine | Exercise/stess | ⬆ Stimulates | ⬆ Increases |


Increased food intake
Malonyl-CoA
ACC P
Pancreas
Insulin
Hypothalamus
AMPK P
Adipose tissue
Leptin
Blood Brain Barrier
Leptin receptor
AMPK P
PPAR-alfa
Gene Expression
Skeletal muscle
ACC
ACC P
Acetyl-CoA
Malonyl-CoA
Fatty Acid Oxidation Enzymes
Acyl-CoA
CPT1
Oxidation
TG

# Fatty acid oxidation and glucose metabolism

Fatty acids and glucose are both important energy sources, but their metabolism is closely connected.

During fasting, fatty acid oxidation provides energy for many tissues and helps reduce the need for glucose.

Acetyl-CoA produced from fatty acid oxidation enters the citric acid cycle.

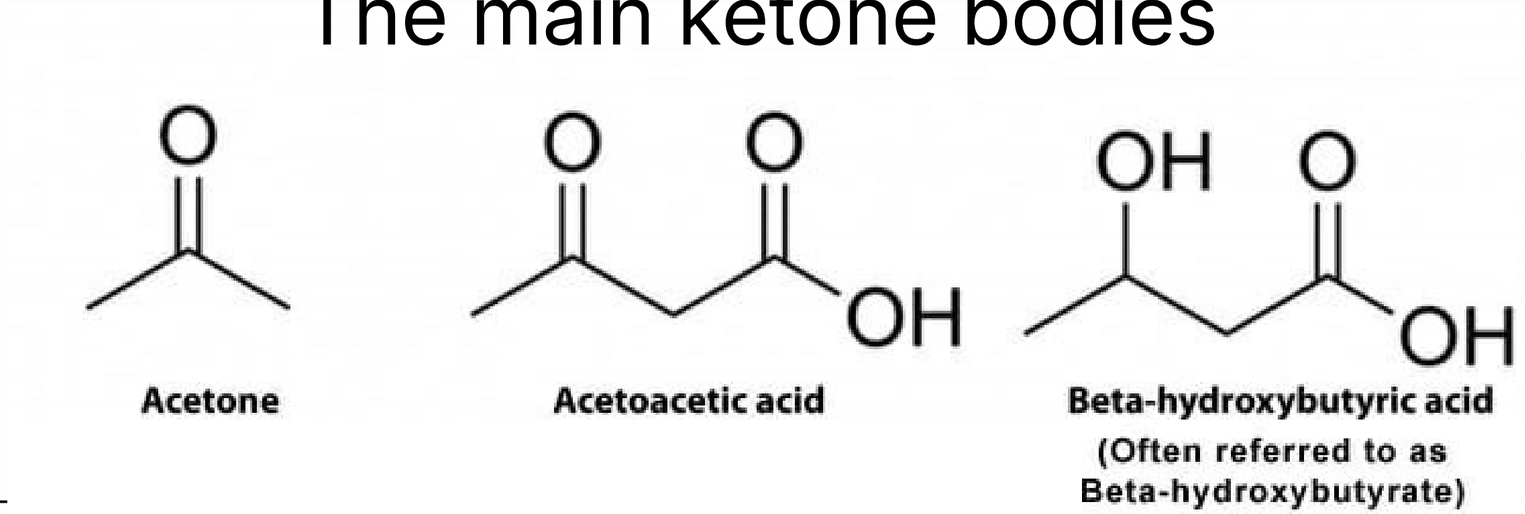
However, acetyl-CoA cannot be converted into a net amount of glucose in humans.

This is one reason why fatty acids cannot completely replace glucose under all physiological conditions.

# Ketone bodies

During prolonged fasting or carbohydrate restriction, large amounts of fatty acids are transported to the liver and oxidized.
This produces large amounts of acetyl-CoA.
When the capacity of the citric acid cycle is insufficient to process all of the acetyl-CoA, the liver converts excess acetyl-CoA into ketone bodies.
Ketone bodies can be transported to other tissues and used as an alternative energy source.

## The main ketone bodies



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Lipolysis is stimulated during:

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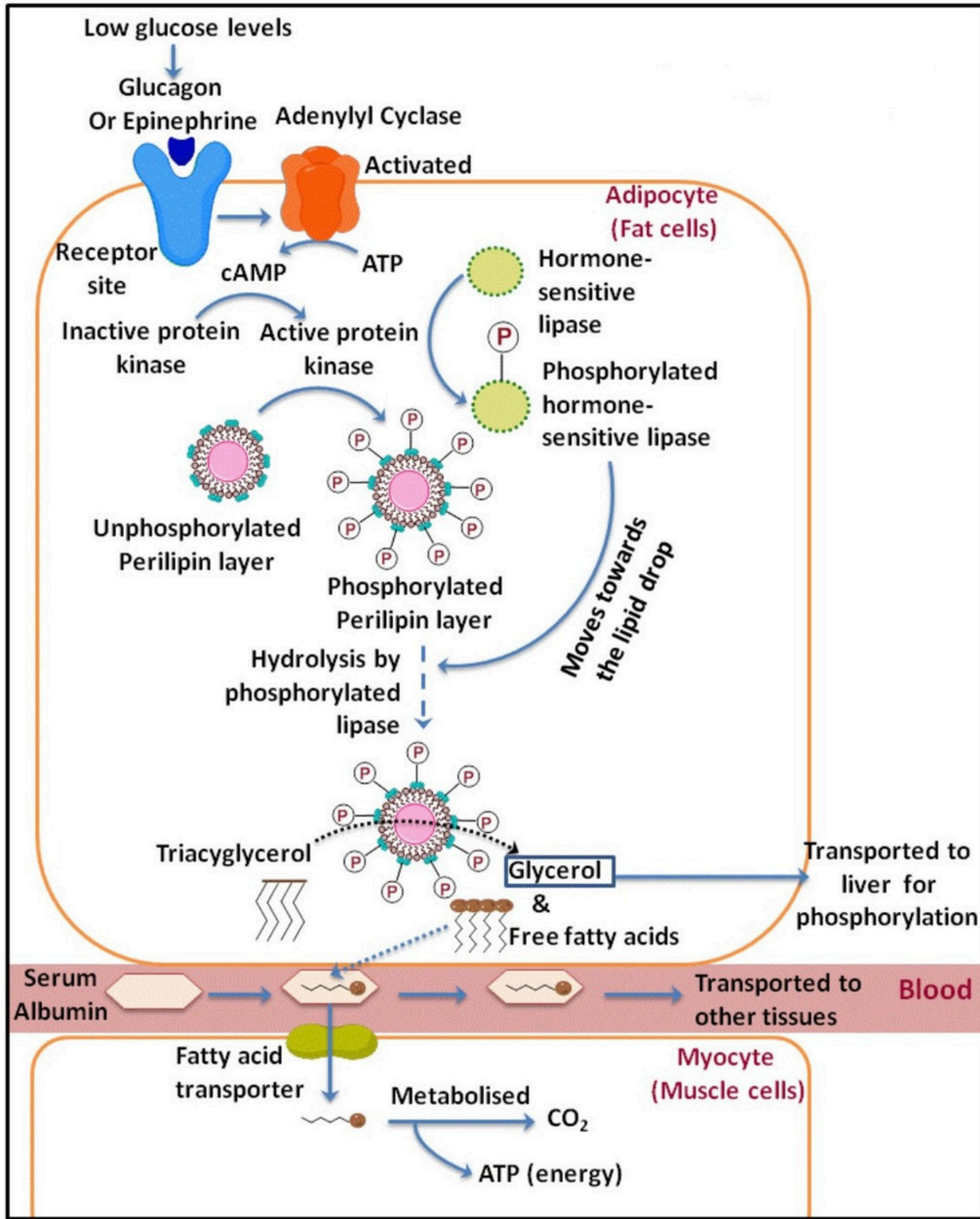

# Student task

1. What are the major classesoflipids found in the human body?
2. How are saturated and unsaturated fatty acids different?
3. What is the structure of a triacylglycerol?
4. Why are triacylglycerols considered an efficient form of energy storage?
5. What is the role of bile salts in lipid digestion?
6. Which enzyme is mainly responsible for the digestion of dietary triacylglycerols?
7. What are chylomicrons, and what do they transport?
8. What are the main differences between chylomicrons, VLDL, LDL, and HDL?
9. What is lipolysis, and when does it occur?
10. How are fatty acids activated before oxidation?
11. Why is the carnitine shuttle necessary for long-chain fatty acids?
12. Where does β-oxidation mainly take place?
13. What are the four reactions of one cycle of β-oxidation?
14. What products are generated during one cycle of β-oxidation?
15. Why does β-oxidation remove two carbon atoms at a time?

# Conclusion

Lipidssupportenergy storage, membrane structure and signaling. Triacylglycerols form the major stored energy reserve.

Lipolysisreleases fatty acidsfor fuel. Activation and the carnitine shuttle prepare long-chain fatty acids for mitochondrial oxidation.

Beta-oxidation produces acetyl-CoA, NADH and FADH2. Their further oxidation supports ATP production.

Complete oxidation of palmitate yields approximately 106 net ATP, including the energy cost of activation.

During prolonged fasting, the liver produces ketone bodies from acetyl-CoA. These provide an alternative fuel for other tissues.

# References


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