METABOLISM

بسم الله الرحمن الرحيم

FINAL – Lecture 5

Degradation Of Fatty Acids

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

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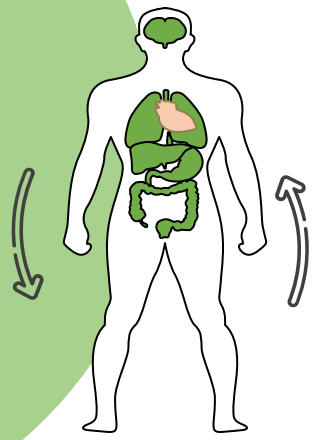


Degradation of fatty acids

Dr. Diala Abu-Hassan

Lippincott's Biochemistry, Ch. 16

المحاضرة زخمة شوي بس كتكوتة، احكوا بسم الله، جددوا النوايا ويلا بينا :)

Why FAT not carbohydrates?

Fatty acids are the main source of energy in fasting conditions or ketogenic diets. The activation and mediation of the fatty acid degradation pathway is carried out by hormonal changes. As discussed before, the storage of fats is more preferrable than carbohydrates because of the following reasons:

- More reduced:

  9 kcal per gram compared with

  4 kcal per gram of carbohydrates

- Hydrophobic:

  Can be stored without H_2O

  Carbohydrates are hydrophilic

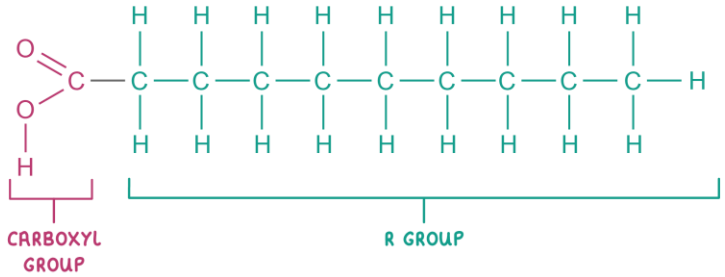
  1 gram carbohydrates : 2 grams H_2O

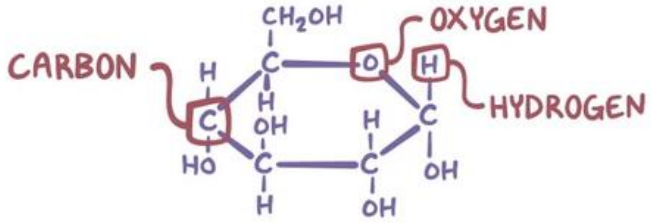
Triacylglycerol (TAG) or FAT is the major energy reserve in the body

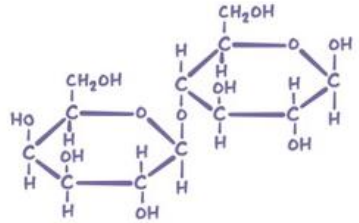
It is more efficient to store energy in the form of TAG

Ketogenic diets are diets that entail very low consumption of carbohydrates. Therefore, fatty acids are utilized as the main sources of energy.

Fatty acids are hydrophobic in nature. Despite having some polar groups in their structure, their size is rather small compared to the hydrophobic, nonpolar chain. Accordingly, fatty acid storage is more efficient because it doesn't attract water into the cell.
On the other hand, carbohydrates attract water into the cells, causing cellular swelling, a gel-like structure, and increased cell volume. This all goes to prove that the storage of fatty acids is more efficient that the storage of carbs. (Remember carbs contain hydroxyl groups that can form H-bonds with water, causing the cell to swell up. Check out the structures of these molecules)







FATTY ACID as FUELS

The major fuel used by tissues; however, **glucose** is the major *circulating* fuel.

Fuel type	**Amount used/kcal/12 hours (gram)**
Fatty acids	60 (540) 60 grams * 9 kcal/gram
Glucose	70 (280) 70 grams * 4 kcal/gram

Even though more glucose was used, the energy extracted from fatty acids was almost double that of the glucose.

سبحان الله وبحمده

The release of fatty acids from TAG

To activate the FA degradation pathway, the stored fatty acids must be obtained the TAG in adipose tissues to be oxidized and form energy.
This release is mediated via hormones, mainly glucagon (fasting state), or epinephrine (fight or flight).

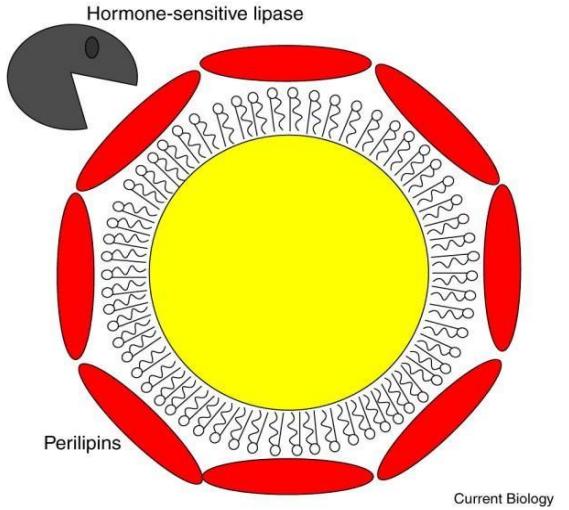
Hormonal Regulation

Both hormones (EP & glucagon) have receptors on adipocytes. They bind to GPCR and activate the receptor, then the alpha subunit, adenylyl cyclase which catalyzes the conversion of ATP to cAMP → PKA → phosphorylates many substrates. Among these substrates is **hormone-sensitive lipase (HSL),** an enzyme present in adipocytes. It hydrolyzes ester bonds in TAGs and requires hormonal activation. Phosphorylation by PKA activates this enzyme. It acts on **di**acyl glycerol only. **Adipose triglyceride lipase (ATGL)** is the enzyme that acts on **tri**acyl glycerols, it is also located in the adipocytes. ATGL removes the first fatty acid, then HSL removes the second, and MAGL (monoacylglycerol lipase) removes the third fatty acid, forming 3 free fatty acids and a glycerol molecule.

Check out the picture 2 slides over :)

Hormonal Regulation

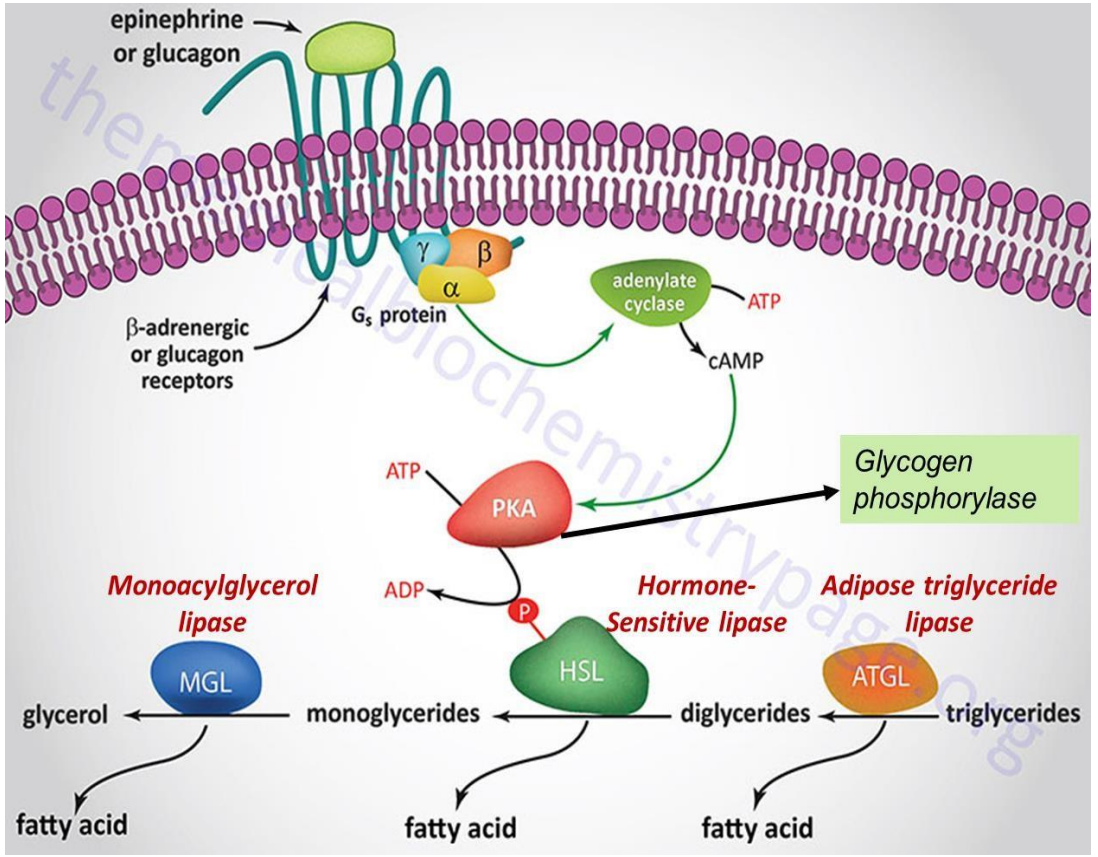
TAG in adipocytes are sequestered by a protein called **perilipin.** This protein is necessary to isolate the TAG from the cytosol and its aqueous environment. Direct contact with the aqueous environment is unstable for the TAG, can cause premature lipolysis therefore, an emulsifier is crucial for the protection of the TAG. Perilipin is phosphorylated by PKA, which induces its dissociation from the lipid droplet, allowing for HSL to easily access the TAG and initiate lipolysis. Unphosphorylated perilipin has negative charges on its surface from amino acid residues, once it is phosphorylated by PKA, the phosphate group adds additional negative charges to the perilipin. These negative charges start to repel from each other, causing the dissociation of the perilipin due to weakening of its attachment to the lipid droplet, exposing the TAG to HSL.



Perilipin (in red) coats fat droplets blocking HSL. It is phosphorylated by PKA releasing it.

Hormonal Regulation

The β-oxidation of fatty acids doesn't take place in adipocytes, but in cells that need fatty acids as a source of energy. Inhibition of fatty acid synthetic pathways is also necessary; running two contradictory pathways simultaneously wastes energy. One regulatory mechanism is the compartmentalization of the opposite pathways: β-oxidation of fatty acids occurs in the mitochondria, whereas FA synthesis occurs in the cytosol.

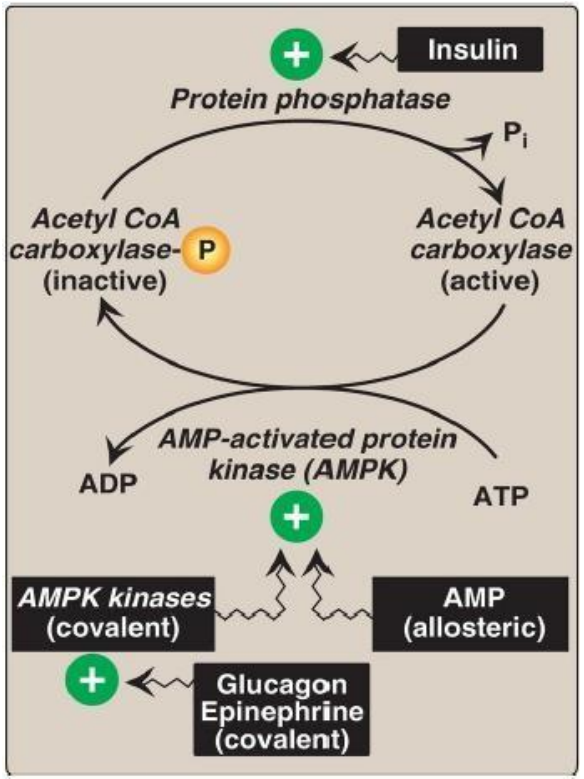


اللهم خذ بنواصينا للبر والتقوى، ولما تحب من العمل وترضى

Hormonal Regulation

EP and glucagon can also activate AMPKK (AMP activated-protein kinase kinase), the kinases that phosphorylate AMPK, activating it. Active AMPK phosphorylates acetyl CoA carboxylase-- adds a carboxyl group to acetyl CoA to form malonyl CoA (3 carbons).

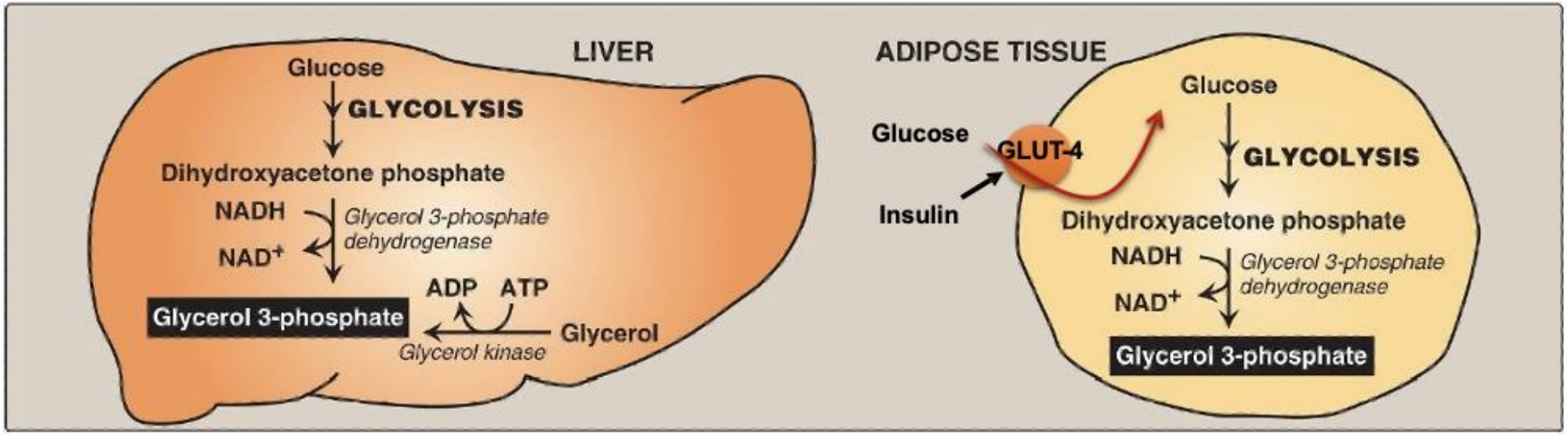
High [EP or glucagon] inhibit the synthesis of fatty acids. In turn, it is expected that the phosphorylation of acetyl CoA carboxylase inhibits its function. However, under well-fed states, insulin activates phosphatases to remove the phosphate group from acetyl CoA carboxylase. The ACC is now active and so is the fatty acid synthetic pathway.



Acetyl CoA carboxylase (important for fatty acid synthesis) is inhibited by the same signaling pathway of glucagon or epinephrine.

Glycerol in liver and adipose tissues

The products generated from the degradation of TAGs and the hydrolysis of the ester bonds between fatty acids and glycerols in the adipocytes **are free fatty acids and glycerols**. The **free fatty acids** exit adipocytes through different mechanisms depending on the length of the hydrocarbon chain. If the fatty acid chain is short or medium, they can enter the bloodstream without a carrier. On the other hand, long fatty acids, are mostly the ones that get degraded to provide energy, do require albumin as a carrier to be distributed to different cells.



Glycerol in liver and adipose tissues

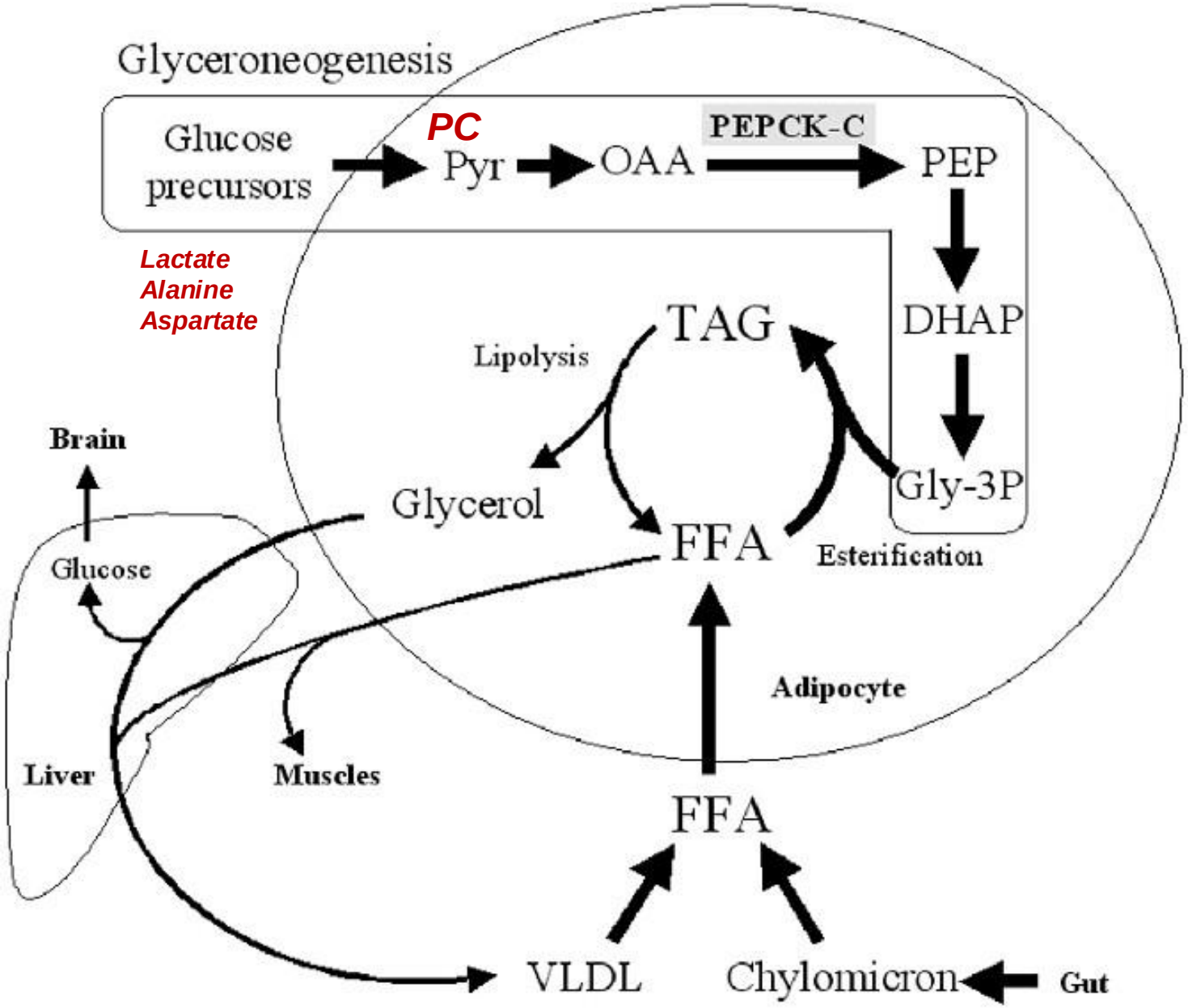
Glycerol molecules are used by cells that perform gluconeogenesis (hepatocytes and kidney cells). Glycerol is phosphorylated by glycerol kinase to glycerol-3-phosphate, then oxidized to DHAP by G3P dehydrogenase, which can be used in the gluconeogenesis pathway. In adipocytes, insulin (well-fed state) induces the expression of GLUT-4 resulting in high [glucose], activation of glycolysis, formation of DHAP. DHAP is then reduced to G3P and is used for TAG synthesis. This is why overeaters gain weight. Excessive [sugar] in our diet can promote the utilization of G3P for TAG synthesis. As TAG increase in adipocytes, body weight also increases. In young people, the number of adipocytes can increase, so more lipids can be stored. Then, this number becomes fixed, but the capacity of the adipocytes increases, allowing for more lipid storage. In overly obese people, an "overspill" of lipids can occur where stored lipids exceed the capacity of adipocytes in the body (this will be discussed later, Insha'Allah).

Glyceroneogenesis

The synthesis of glycerol molecules out of non-glucose precursors, such as lactate and amino acids (aspartate, alanine). Synthesis of glycerol takes place in adipocytes and sometimes in hepatocytes. Once they enter, they can be converted to pyruvate and then via pyruvate carboxylase it forms oxaloacetate, then PEP through PEP carboxykinase (recall gluconeogenesis). Glyceroneogenesis follows the same pathway as gluconeogenesis until the formation of DHAP. DHAP is then oxidized to form G3P which can be combined with fatty acids to from TAG. Arising issues in this pathway's regulation can cause type 2 diabetes. This is because if these precursors aren't utilized to form G3P and combine with fatty acids to be stored as TAG, consumed fatty acids linger in the bloodstream as well as glucose.

سُبْحَانَكَ اللَّهُمَّ وَبِحَمْدِكَ، أَشْهَدُ أَنْ لاَ إِلَهَ إِلاَّ أَنْتَ، أَسْتَغْفِرُكَ وَأَتُوبُ إِلَيْكَ.

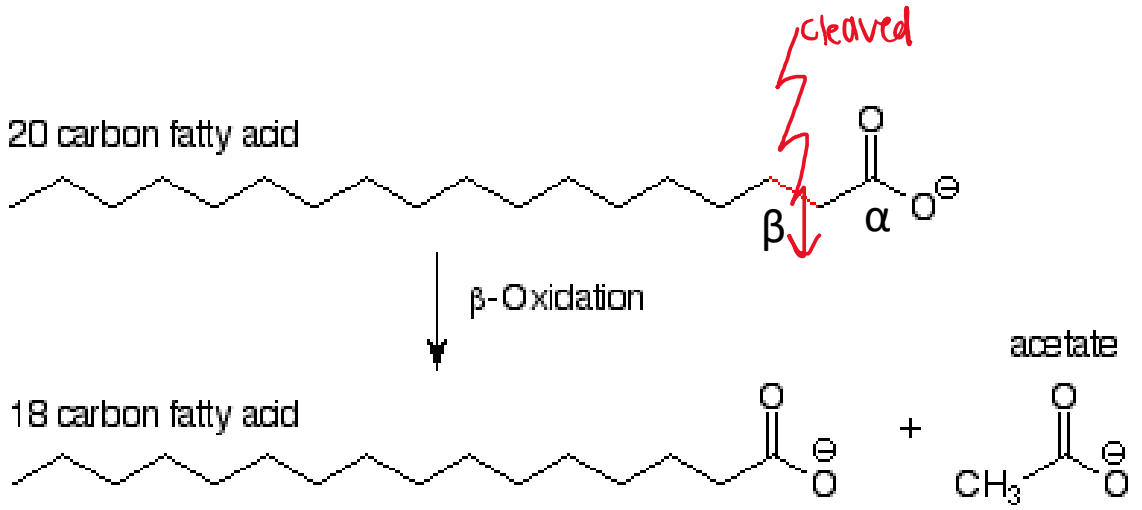
- *Purpose: regulating the levels of FAs in blood.*
- *In liver and adipose tissue*
- *Glycerol leaves the adipocytes into the liver.*
- *Failure in regulating glyceroneogenesis may lead to Type 2 diabetes due to excess fatty acids and glucose in the blood*



PC: Pyruvate carboxylase
PEPCK: **phosphoenolpyruvate** *carboxykinase*

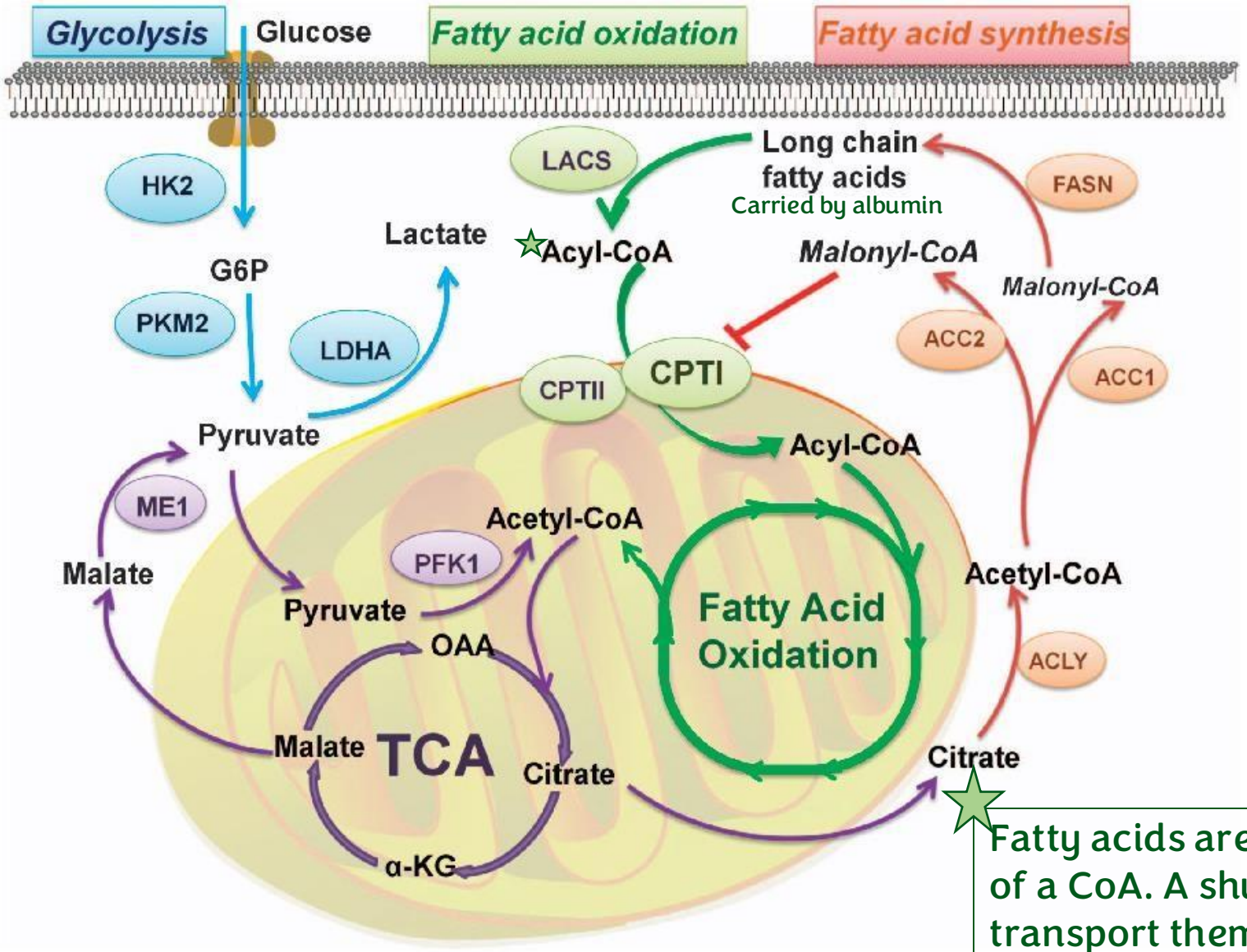
β-oxidation of Fatty acids

We mentioned earlier that short and medium length fatty acids don't require carrier to transport across the bloodstream, and that long fatty acids require albumin. Short and medium fatty acids enter the cells through the plasma membrane. Once inside the cytosol, fatty acids must be transported inside the mitochondria, where β-oxidation takes place. β-oxidation is named this because each cycle of fatty acid degradation cleaves two carbon atoms, forming acetyl CoA. *Cleaves at the second (β) carbon.*



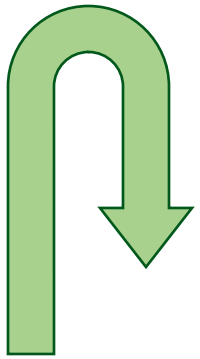
إِنِّي تَوَكَّلْتُ عَلَى اللَّهِ رَبِّي وَرَبِّكُمْ ۚ مَّا مِن دَابَّةٍ إِلَّا هُوَ آخِذٌ بِنَاصِيَتِهَا ۚ إِنَّ رَبِّي عَلَىٰ صِرَاطٍ مُّسْتَقِيمٍ. [هود 56].

β-oxidation of Fatty acids

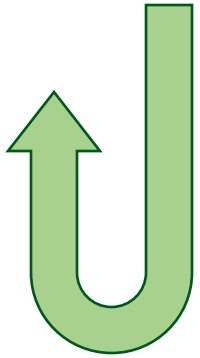


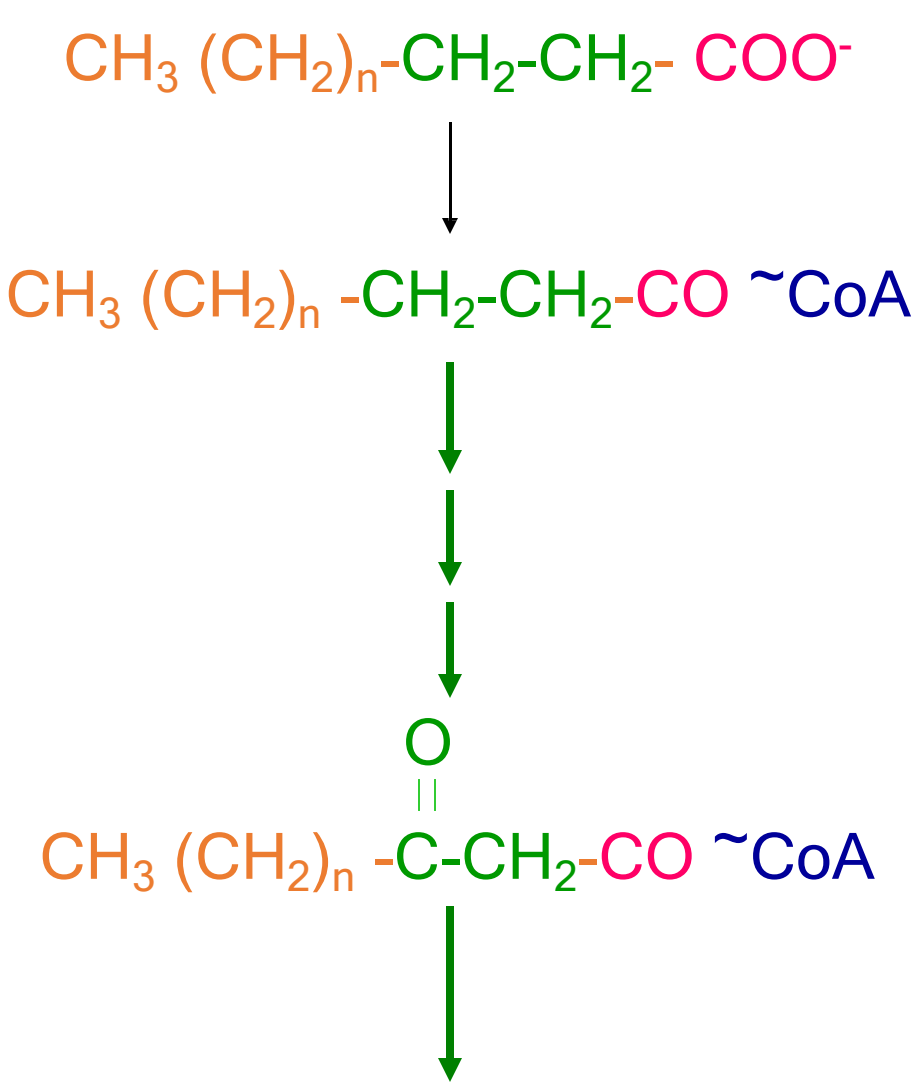
Fatty acids are activated by the addition of a CoA. A shuttle system is used to transport them to the mitochondria.

β Oxidation of Fatty Acids (overview)



This repeats again and again until we have oxidized the entirety of the fatty acid chain.





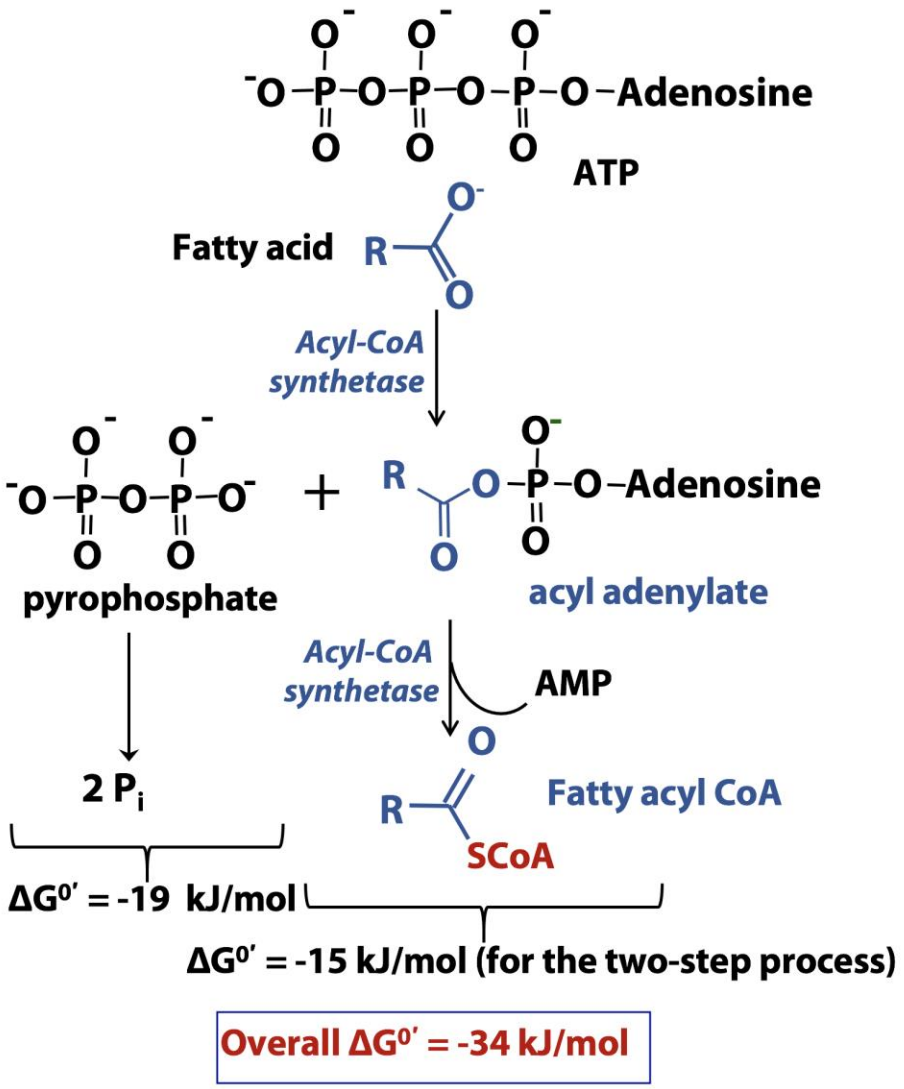
Structure of a fatty acid when it diffuses through the plasma membrane.

The fatty acid is then activated by the addition of a CoA. This activation marks the fatty acid's destination.

Before the cleavage of the β carbon, a new carbonyl group (C=O) must be formed for the CoA molecule to bind to. The fatty acid undergoes a series of reactions to produce the carbonyl group, one of which is oxidation (addition of O & removal of H). Now, we can cleave the CH3-CO~CoA, and add a CoA to the remaining fatty acid chain.

Activation of Fatty Acids

β-oxidation is enzyme-catalyzed. This pathway requires CoA, which is a high-energy group. Joining its bond with another molecule releases energy (TCA step #4). Conversely, the addition of a CoA requires energy, which cannot be supplied solely by the pathway's energy. Therefore, ATP is needed and **thiokinase** is used to catalyze. Thiokinase is also known as **acetyl CoA synthetase**, synthetases normally require energy. Fatty acids + CoA + ATP produce a fatty acyl CoA + AMP + release of pyrophosphate. Pyrophosphates are then converted to two organic phosphates. **Long chain fatty acids** cannot fully enter through the mitochondrial membrane, so their oxidation takes place on the outer mitochondrial membrane. **Short and medium fatty acids** can readily diffuse through the mitochondrial membranes via passive diffusion to the mitochondrial matrix. Once in the mitochondrial matrix, a CoA is added to the fatty acid, and thus its activation. Short and medium FAs degrade faster than long chain FAs. Their absorption and digestion from food intake is faster, reaching cells faster. They can also diffuse through both the plasma and mitochondrial membranes. Since they're relatively shorter, the duration of their degradation is also shorter.



Disregard the adenosine.

Activation of Fatty Acids

Thiokinase
(Acyl CoA Synthetase)

2 ATP equivalents are needed

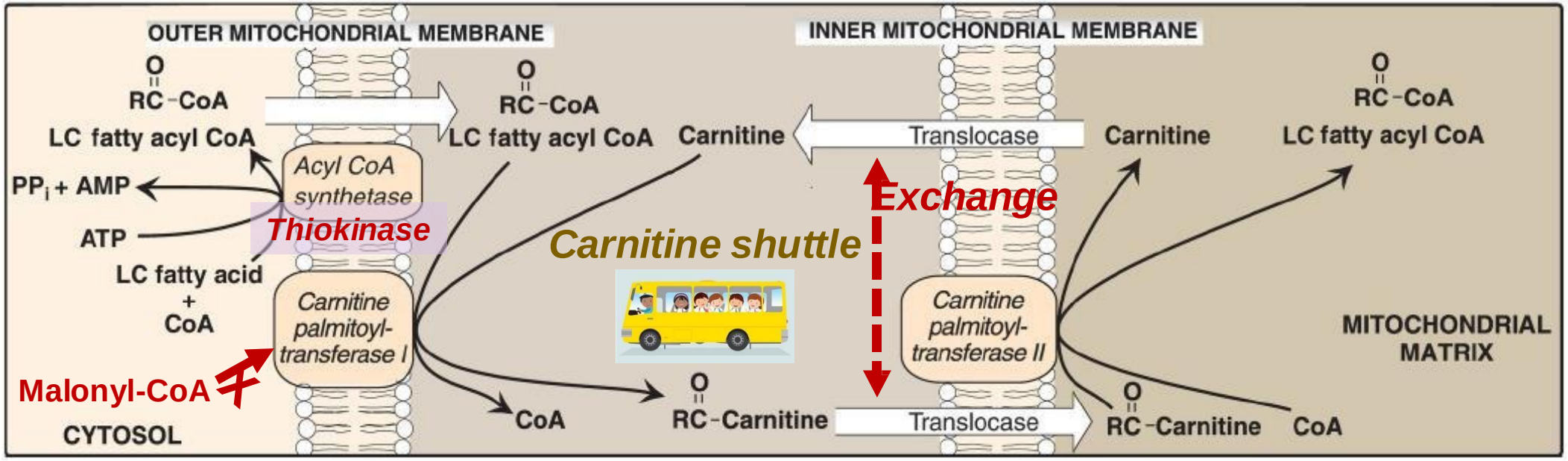
$$FA + HSCoA + ATP \rightleftharpoons FA\sim CoA + AMP + PP_i$$

$$PP_i + H_2O \longrightarrow 2\ P_i$$

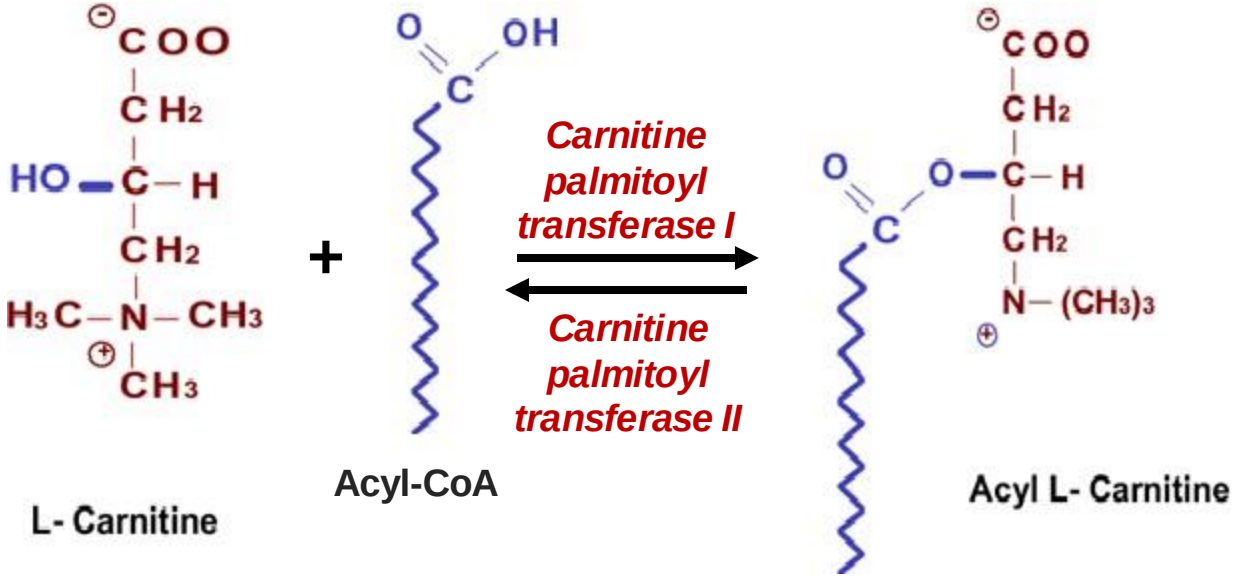
$$FA + HSCoA + ATP \longrightarrow FA\sim CoA + AMP + 2\ P_i$$

Location:
LCFA: outer mitochondrial membrane
Short and medium chain FA: mitochondrial matrix

Transport of LCFA



The transport system consists of:
1. A carrier molecule (carnitine)
2. Two enzymes
3. Membrane transport protein (translocase)

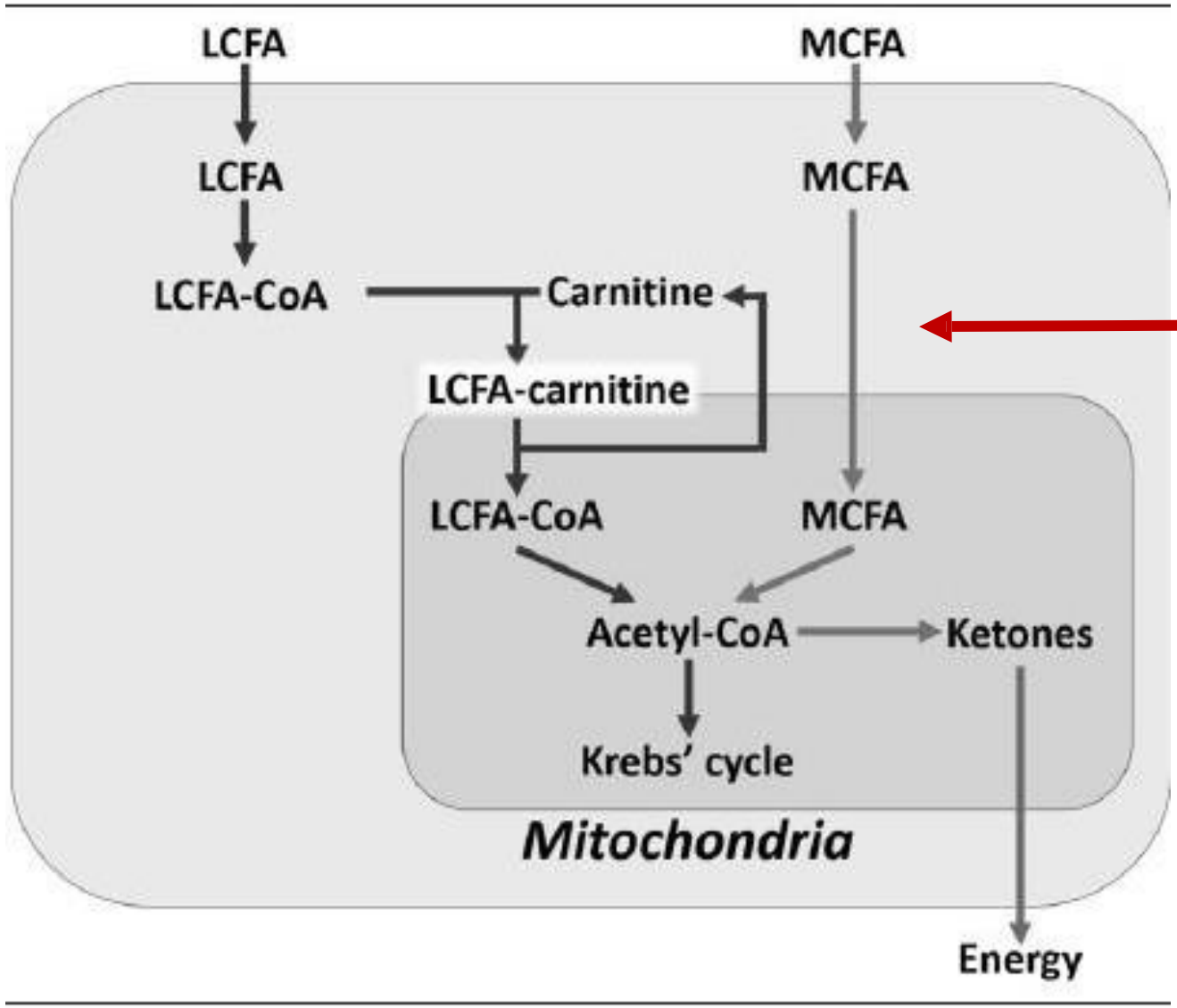


Transport of LCFA

Long-chain fatty acids are activated by CoA by thiokinase on the outer mitochondrial membrane. OMM is permeable, so the long-chain fatty acyl CoA can easily cross it. However, the IMM isn't, so the LCFA CoA stays within the intermembranous space. There are shuttling systems that function to serve this exact purpose. One of these shuttling systems is carnitine, which is present in the intermembranous space. A transferase in this shuttling system replaces the CoA with the carnitine producing a **long fatty acyl carnitine**. The LFAC can move to the mitochondrial matrix through the membrane via translocase enzymes, also a part of the shuttling system. However, LFAC must be reverted to its original form-- LCFA CoA, for oxidation. This is catalyzed by the second enzyme in the mitochondrial membrane, carnitine-palmitoyl transferase II. In conclusion, this shuttling system is composed of **carnitine, translocase, and carnitine-palmitoyl transferases I & II.** Translocase can transport LCFA carnitine into the mitochondrial matrix and also transport the carnitine back to the intermembranous space. Carnitine-palmitoyl transferase I is **inhibited by malonyl-CoA,** which is crucial for fatty acid synthesis. This is so the fatty acids that were just synthesized can't enter the mitochondria to be oxidized.

فَاطِرَ السَّمَاوَاتِ وَالْأَرْضِ أَنتَ وَلِيِّي فِي الدُّنْيَا وَالْآخِرَةِ ۖ تَوَفَّنِي مُسْلِمًا وَأَلْحِقْنِي بِالصَّالِحِينَ. [يوسف 101].

Transport of SCFAs and MCFAs

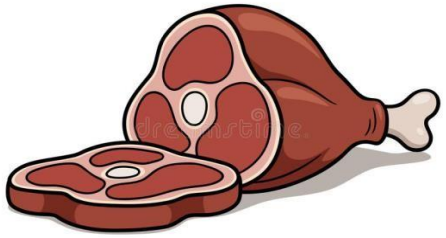


Note: No regulation of entry like that of CPTI by malonyl CoA

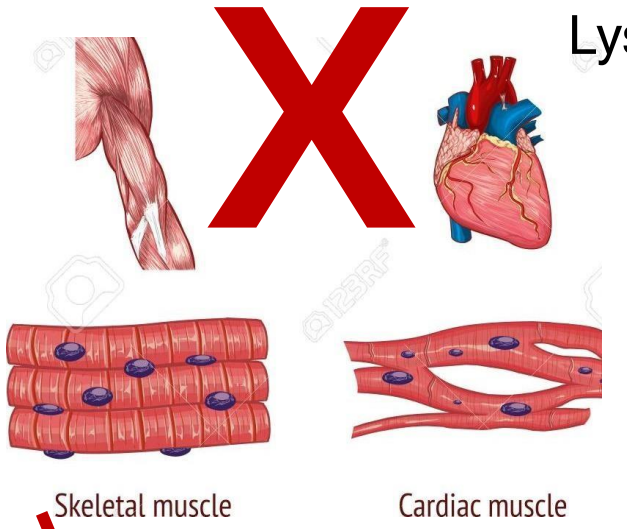
After their diffusion, MCFA will be combined with a CoA group to produce Acetyl-CoA eventually through the β-oxidization process discussed previously.

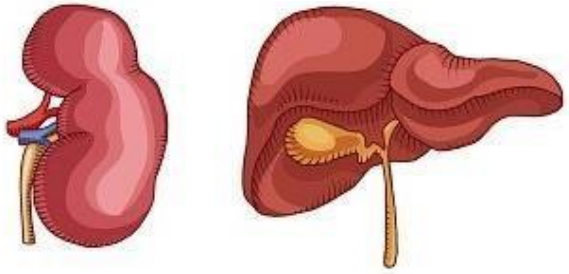
Medium chain fatty acids can diffuse through the plasma and. Mitochondrial membranes. Faster absorption and oxidation.

Application: Carnitine sources



Source: meat product and synthesis in the body from Lys and Met (liver and kidney)





contains ~97% of all carnitine in the body. No ACC1, no FA synthesis but contains a mitochondrial ACC2 to regulate fatty acid degradation.

Do not memorize this pathway

Other functions:

- Export of branched chain acyl groups from mitochondria

-Binding to acyl groups derived of AA metabolism and their execration functioning as a scavenger

Application: Carnitine sources

The primary function of carnitine in β-oxidation is to facilitate the transport of **long-chain fatty acids (LCFAs)** into the mitochondria for oxidation. The LCFAs previously discussed were either saturated or unsaturated.

Carnitine also plays a role in the **export of branched-chain fatty acids** (those with hydrocarbon branches, not other functional groups like hydroxyl groups etc) from the mitochondria.

Additionally, during the **degradation of amino acids**, various **acyl groups**, particularly **acetyl-CoA** and **acetoacetyl-CoA**, can be produced. Carnitine acts as a **scavenger**, aiding in the **excretion** of these molecules.

Although carnitine is primarily synthesized in the liver and kidneys, about 97% of the body's carnitine resides in **skeletal and cardiac muscle cells**, which are highly dependent on fatty acid oxidation for energy. These muscle cells **lack the ACC1 (Acetyl-CoA Carboxylase 1) enzyme**, which is involved in **fatty acid synthesis**, but they **express ACC2**, an isoform that regulates **fatty acid oxidation** by producing regulatory molecules (malonyl-CoA).

Application: Carnitine deficiencies

- **Primary carnitine deficiency** A direct deficiency in carnitine due to genetic mutations affecting carnitine transport or synthesis.
  - Defects in a membrane transporter: No uptake of carnitine by cardiac and skeletal muscles and the kidneys, causing carnitine to be excreted.
    - Treatment: carnitine supplementation.
- **Secondary carnitine deficiency** A deficiency caused by other underlying conditions such as metabolic disorders, certain medications, or diseases that impair carnitine absorption, increase its excretion, or disrupt its utilization.
  - Taking valproic acid (antiseizure drug) → decreased renal reabsorption
  - Defective fatty acid oxidation → acyl-carnitines accumulate → urine
  - Liver diseases → decreased carnitine synthesis
  - Transferase Deficiencies:
  - CPT-I deficiency: affects liver; no use of LCFA, no energy for glucose synthesis during fasting → severe hypoglycemia, coma, and death
  - CPT-II deficiency: affects liver, cardiac muscle, and skeletal muscle
    - Treatment: avoidance of fasting and adopting a diet high in carbohydrates and low in fat but supplemented with medium-chain TAG.

Application: Carnitine deficiencies

Primary deficiency:

- e.g. if the translocase that moves carnitine was mutated, absent, etc. It would interfere with the movement of carnitine, especially in FA oxidation-dependent cells (cardiac and skeletal muscle)
- Carnitine excretion (both diet-aquired and body-synthesized) will occur since carnitine is present but ineffective (can't move)
- Giving a carnitine supplement will overflood the area with carnitine which might result in better transport, hence improving the deficiency.

الباقيات الصَّالحات: سبحان الله، والحمد لله، ولا إله إلا الله، والله أكبر، ولا حول ولا قوة إلا بالله

Application: Carnitine deficiencies

Secondary deficiency: (indirect)

- **Valproic acid** decreases renal reabsorption of carnitine, leading to increased urinary excretion through the renal system, ultimately causing a carnitine deficiency.
- If **β-oxidation is defective**, activated fatty acids (acyl-CoA) can still enter the mitochondria due to a functional carnitine transport system. However, since fatty acids cannot undergo proper oxidation, they will accumulate inside the mitochondria.

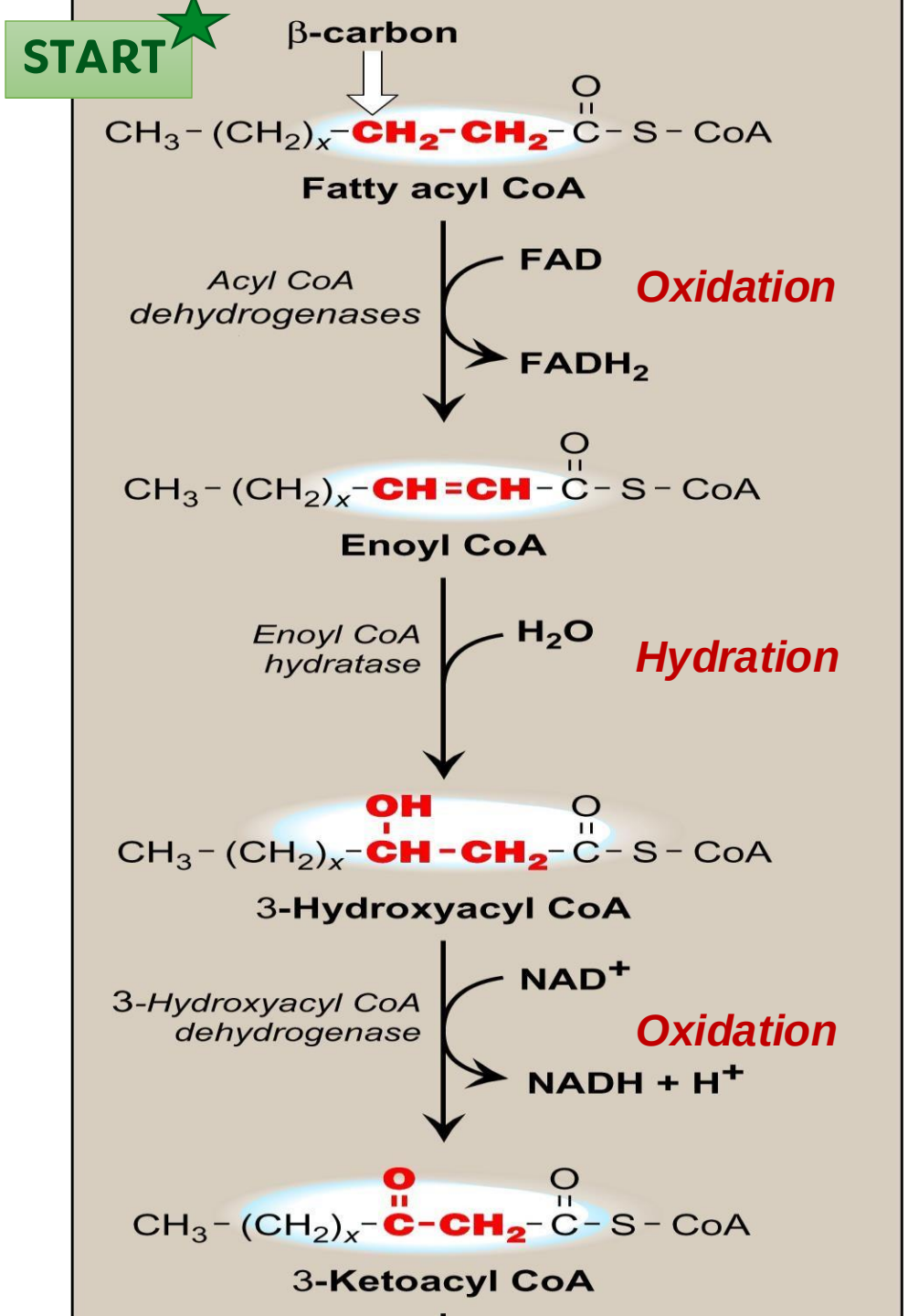
  In this case, carnitine appears deficient, not because of an actual lack of carnitine, but because its normal role in facilitating fatty acid transport becomes ineffective due to the metabolic block. Additionally, acyl-carnitine (a fatty acid-bound form of carnitine) will accumulate. This triggers increased urinary excretion of acyl-carnitine, reducing free carnitine levels and causing a secondary carnitine deficiency.
- Since the **liver** synthesizes carnitine, any liver-related issues can impair its production

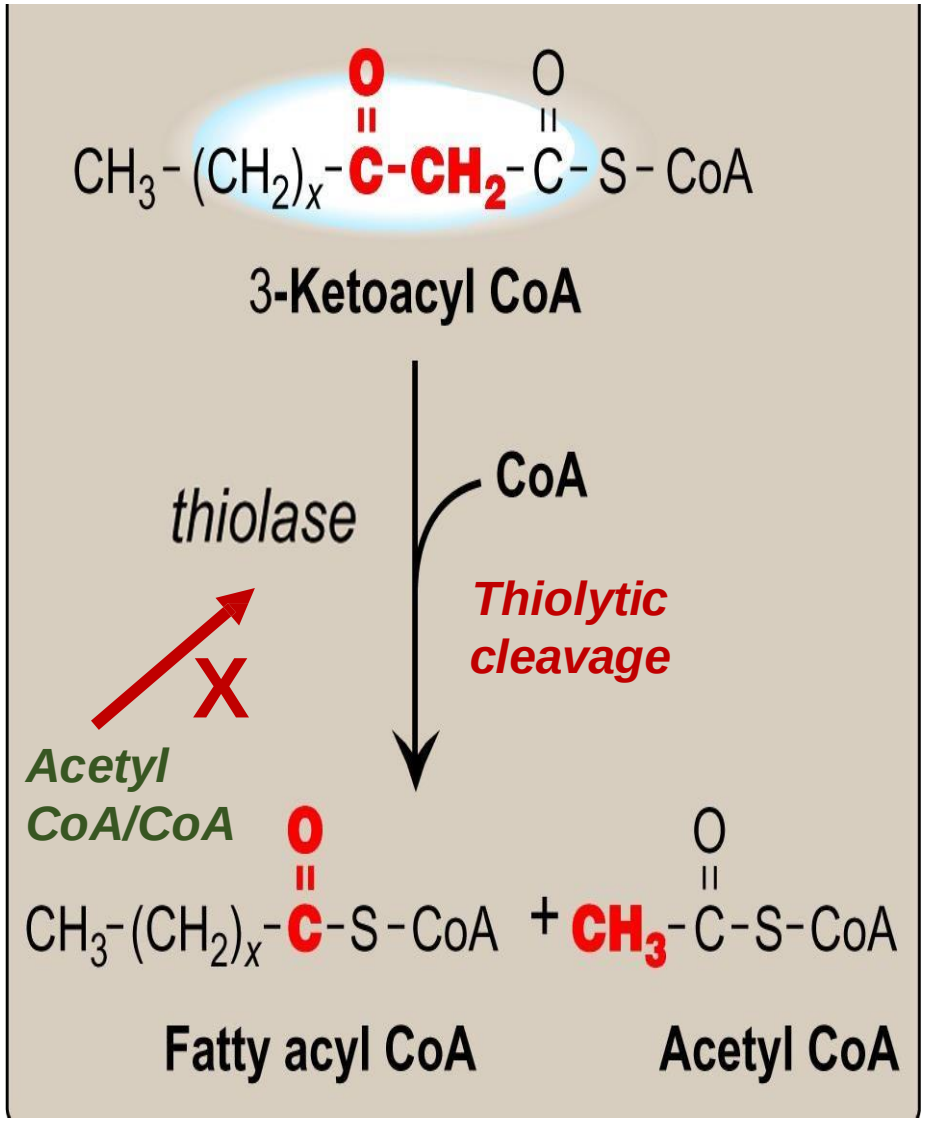
Application: Carnitine deficiencies

Secondary deficiency: (indirect)

- **Transferase Deficiencies:**
- Normally CPT-1 functions in forming Acyl-Carnitine
- If **CPT-1** (Carnitine Palmyotransferase-1 on OMM) is deficient, FA can't bind carnitine. As a result, LCFA won't be oxidized, leading to a reduced amount of energy, severe hypoglycemia because cells will resort to using glucose even during gluconeogenesis, due to the inability to degrade FA for energy. This leads to coma and death.
- Normally CPT-2 functions in forming LFAC (removing carnitine from acyl [LCFA] and adding CoA)
- If **CPT-2** (IMM) is deficient, carnitine cannot be separated from FA upon entering the mitochondrial matrix. As a result, LCFA will not bind to CoA to become LFAC, thus interfering with b-oxidation as well since FAs will not reconvert into the activated form, leading to reduction of the availability of energy under fasting conditions for dynamic cells that depend on b-oxidation like cardiac and skeletal muscles
- To reduce problems associated with these deficiencies: avoid being in fasting conditions or in ketogenic diets which obligate the body to depend on FA oxidation for energy, so they must have small-portioned high-carb low-lipid/protein frequent meals.
- These people can only benefit from SCFA and MCFA (they aren't common in diet, and aren't that effective), which could be taken as supplements to compensate.

β-Oxidation of fatty acids





Number of cycles: (n/2)-1

β-Oxidation of fatty acids

- LFACs are now ready to enter β-Oxidation reactions as they're bound to CoA.
- A carbonyl group must be made so the cleavage of the β carbon can occur.
- The first step is to create a double bond, by an oxidation reaction mediated by Acyl-CoA Dehydrogenase, it removes a hydrogen atom off the β carbon and the α carbon adjacent to it

  These hydrogens will go to FAD reducing it to FADH2 which will be oxidized again in the ETC since both processes happen in the mitochondria.
- The second step is to add an Oxygen atom, by a hydration reaction mediated by Enoyl-CoA hydratase which will add an H2O molecule and produce an alcohol group.
- Again, another Oxidation reaction to create a double bond, mediated by 3-Hydroxyacyl CoA Dehydrogenase, which will remove a hydrogen atom off the β carbon and the hydroxyl group on it, creating the carbonyl group (ketone) that's needed to drive the cleavage.

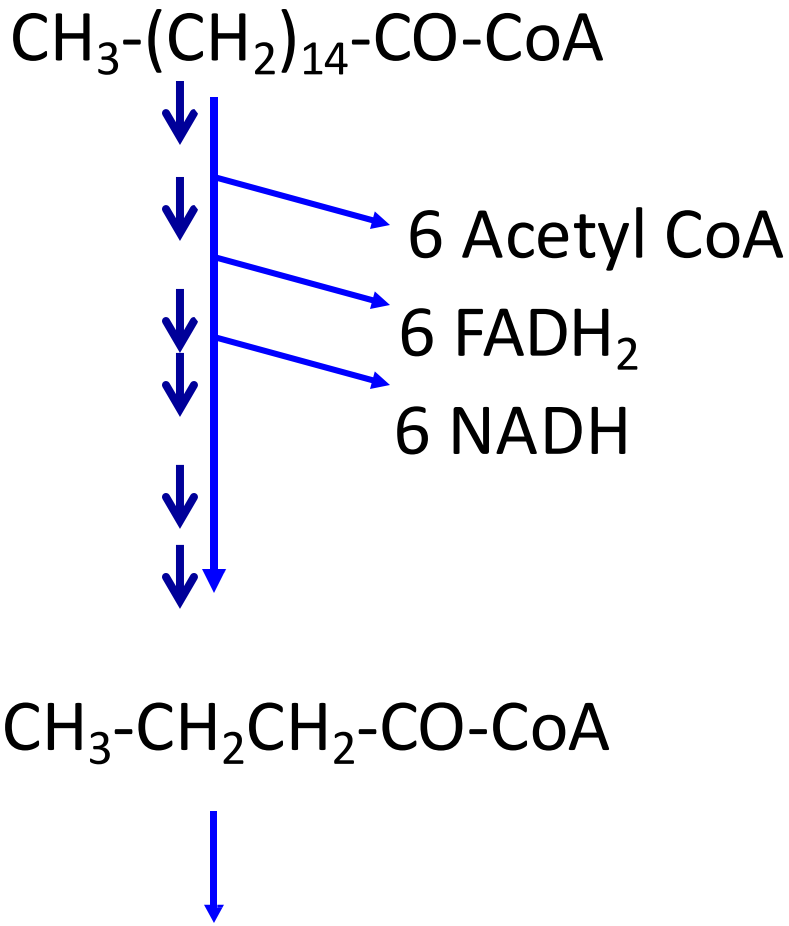
  These hydrogens will go to NAD+ reducing it to (NADH + H+) which will be oxidized again in the ETC since both processes happen in the mitochondria.

β-Oxidation of fatty acids

- Now that the carbonyl group is present, 3-ketoacyl CoA will undergo thiolytic cleavage by thiolase enzyme, since CoA will be cleaved alongside the first two carbons to produce acetyl CoA, and the lost CoA must then be replaced.
- Remember that CoA has a thiol group in it :)
- This cleavage will produce a fatty acid that is 2 carbons less in length (leftover FA)
- Thiolase is inhibited by high concentration of acetyl CoA, since the CoA levels will be depleted as they are consumed by acetyl attachement rather than being free to be used in this reaction.
- This pathway is considered a spiral pathway, as the steps will be repeated until the FA is completely oxidized.
- For even-number fatty acids, the reaction will end in the last cycle producing two acetyl-CoA molecules.
- Odd-number FA oxidation will be discussed later.

Energy Yield from FA Oxidation

This FA has n=16 carbons, divide n by 2 (bcz 2 carbons= 1ACoA released per cycle) and subtract 1 (bcz the cycle directly produces 2 ACoA in the last cycle instead of 1) So it needs 7 cycles to complete oxidation.



CH_3-CO-CoA + CH_3-CO-CoA + $FADH_2$ + NADH

This shows the last cycle directly producing: 2 ACoA, 1FADH, 1NADH2

not all ACOA will necessarily enter krebs cycle!!

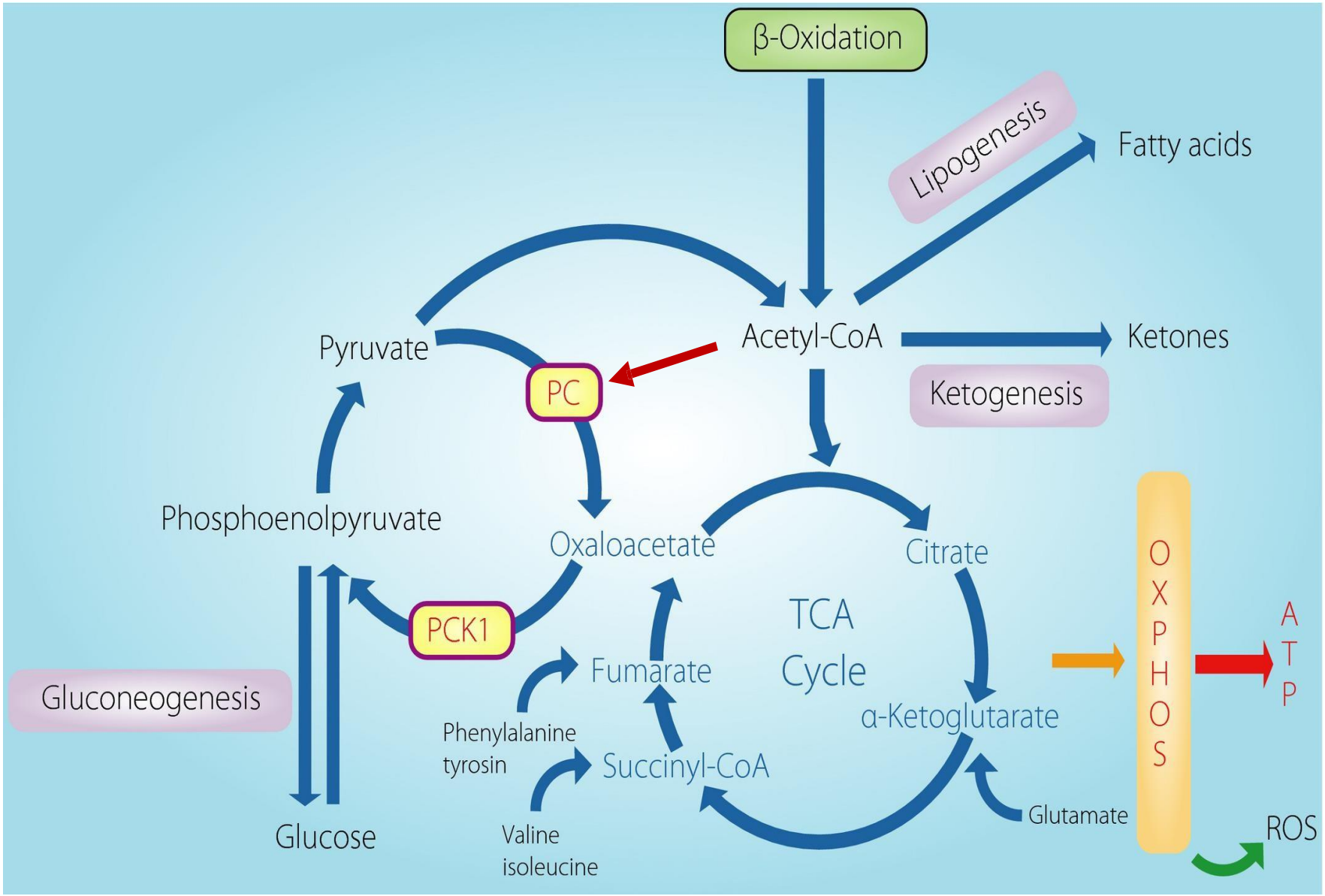
- ✓ Oxidation of C 16 FATTY ACID
  - 7 $FADH_2$ X 2 → 14 ATP
  - 7 NADH X 3 → 21 ATP
  - 8 Acetyl CoA → 96 ATP
  - 1 AcoA = 12 ATP (approx.)
- ✓ Activation of the Acid consumes 2 ATP (shown in slides 18/19)
- ✓ Net 129 ATP mole per mole of C16 Fatty Acid

Induction of gluconeogenesis and fates of acetyl CoA

Of course, the numbers presented in the previous slide are unrealistic, as not all ACoA will go into TCA cycle and produce energy.

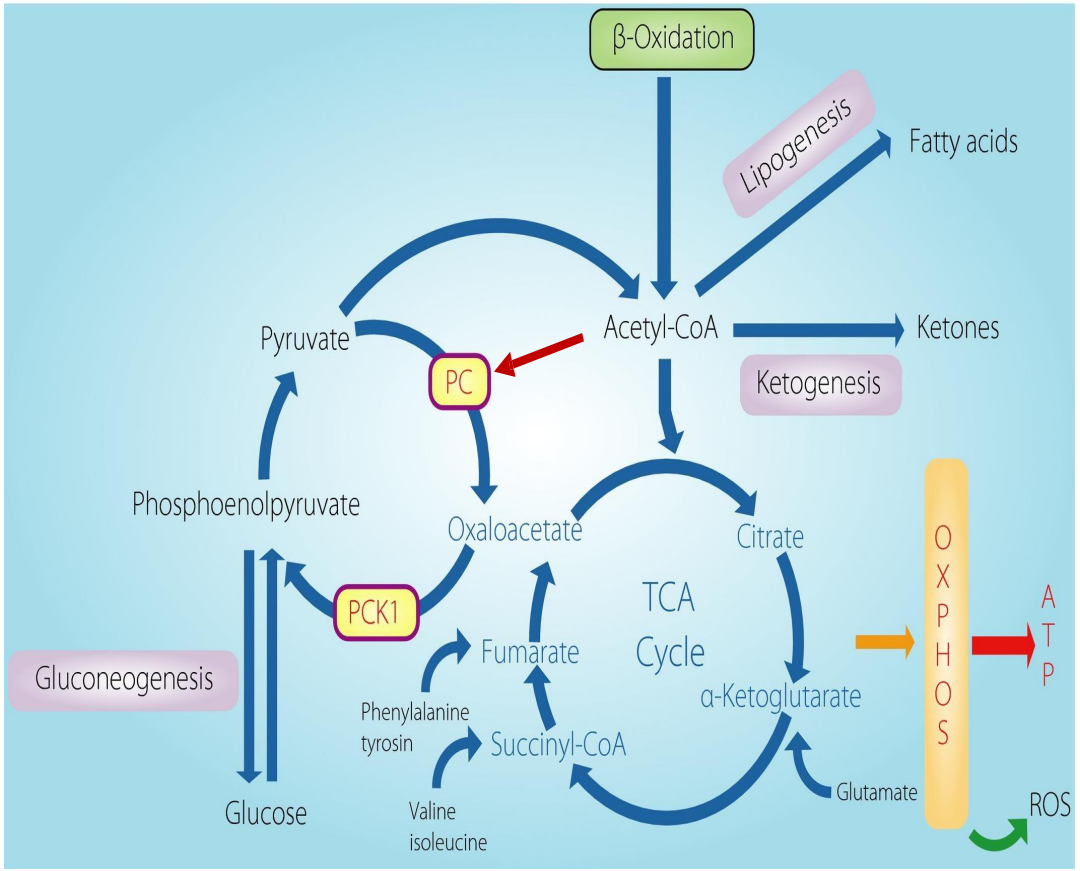
(reason explained in the next slide)

Since β-Oxidation occurs under fasting conditions, another pathway that will be active is gluconeogenesis in hepatocytes and kidney cells to provide energy for the cells that depend on glucose and to maintain glucose levels in the bloodstream.



Induction of gluconeogenesis and fates of acetyl CoA

- Gluconeogenesis consumes some of OAA (since it's a gluconeogenic intermediate).
- OAA will be distributed, a portion to TCA cycle and the other goes to gluconeogenesis.
- Therefore, **OAA's availability** is a limits the ability to use ACoA generated by β-Oxidation in TCA cycle
- This is why some of the ACoA is redirected towards another process which is **ketogenesis,** an alternative pathway.
- It produces ketone bodies, that despite their various chemical structures all contain a ketone group.
- These ketone bodies, at some point, will be used to provide energy for the brain cells, they are the only alternative to sugar in its absence.



- During prolonged fasting, the brain increasingly relies on ketone bodies for energy. Their utilization depends on their concentration in the blood—the higher the concentration, the more likely they are to cross the Blood-Brain Barrier (BBB), where they can be metabolized by brain cells to provide energy for neurons.

Prof answered a student's question:
Ketone bodies were found to be beneficial in neurodegenerative diseases, bcz the brain metabolism as a whole changes (reprogramming), to become more dependent on ketone bodies and less efficient in metabolizing sugars, so these patients are given ketone body supplements

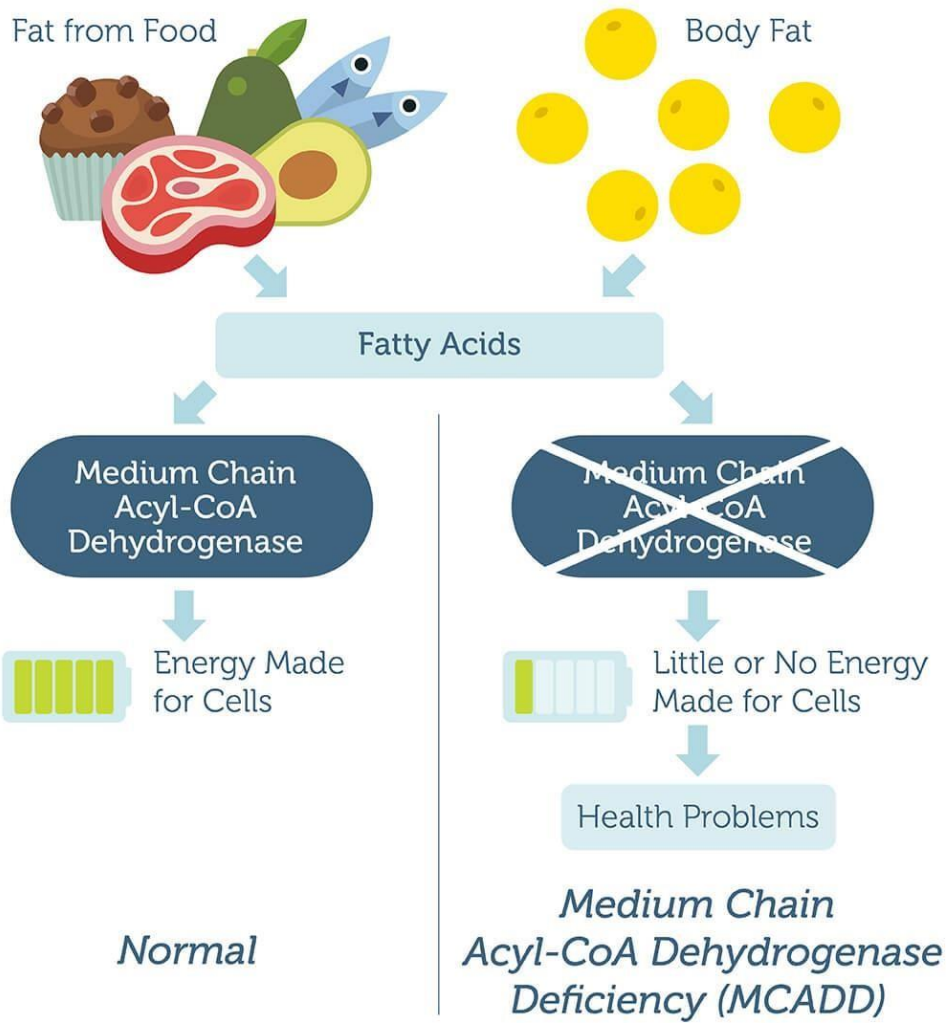
Application: MCAD deficiency

Explanation in the next slide :)

- There are 4 isozymes of fatty acyl CoA dehydrogenase (the first enzyme in β-Oxidation) for SCFA, **MCFA**, LCFA, and VLCFA (different lengths of FA).
- Medium-chain fatty acyl CoA dehydrogenase (MCAD) genetic deficiency,
  - An autosomal-recessive disorder
  - Most common inborn error of β-oxidation (1:14,000 births worldwide)
  - Higher incidence among Caucasians of Northern European descent
  - Decreased ability to oxidize MCFAs (lack of energy)
  - Severe hypoglycemia and hypoketonemia
  - Treatment: avoidance of fasting

    Regular and frequent meals and snacks

    Diet high in carbohydrates and low in fat



Application: MCAD deficiency

- In breast milk, the majority of lipids are SCFA and MCFA which are essential in the neuronal and brain development of infants after birth since they are easily diffused and oxidized, so they are considered a faster energy source than LCFA.
- MCAD is the isoform of ACD enzyme that is most affected by mutations, this is why this specific deficiency is quite common.
- As a result of this deficiency, MCFA's oxidation will be compromised, so affected individuals are more susceptible to hypoglycemia and hypoketonemia, because MCFA are considered a fast energy source & now that they can't be utilized, the body will resort to glucose, depleting its levels in the bloodstream. Also, they are normally used to produce ketone bodies, but this mechanism will be stopped as well.
- This case is not severe, just needs a few dietary adjustments.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

Reference Used:
(numbered in order as cited in the text)

1. Lippincott's Biochemistry 8th Edition (532-544)

Extra References for the Reader to Use:

1. β-Oxidation by Dirty Medicine YTV
2. β-Oxidation by MED Simplified YTV
3. β-Oxidation Article by LibreTexts
4. Carnitine Shuttle by JJ Medicine YTV
5. Carnitine Shuttle by Khan Academy
6. Other

﴿رَبَّنَا لَا تُزِغْ قُلُوبَنَا بَعْدَ إِذْ هَدَيْتَنَا وَهَبْ لَنَا مِن لَّدُنكَ رَحْمَةً ۚ إِنَّكَ أَنتَ ٱلْوَهَّابُ﴾

لا اله إلا أنت سبحانك إني كنت من الظالمين

سبحان الله وبحمده، سبحان الله العظيم