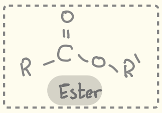
Metabolism of lipids

- Lipids :-
  - Try Acyl glycerol.
  - cholesterol estar.
  - phospholipids

  (Polymers.)

  Hydrolysis to break estar bond. (H_2O) → FAtty Acid + Mono Acyl Glycerol → Glycerol + Fatty Acid. (monomers)



- Classification of lipids
  1) fatty Acid. < essintial. / non essintial. * Free fatty acid consume as < source of energy. / synthesize keton bodies.
  2) Sterols (cholesterol)
  3) Glycerolipid
  4) sphingo lipid.
  ⋮

- Emulsifiers as bile salt bind to large fat droplets and break them down into smaller fat droplets, increasing the surface area for digestion. This creates micelles, allowing the efficient digestion of fats by enzymes like lipase , Colipase is not an emulsifier itself, but it supports the action of an emulsifier by conjunction
- High hydrophobic molecules → need emulsifiers (to make them smaller)

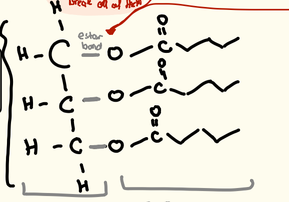
Oral Cavity → Lingual lipase (these enzyme will break estar bond, but will not break all of them)

degrade only small / medium FA

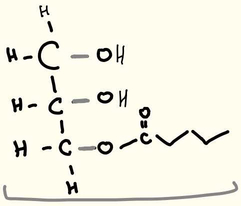
Stomach → Gastric lipase

TAG

large amount of TAG will continue to small intestine



Glycerol   3 Fatty Acids

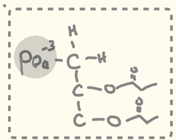


+ 2 Fatty Acids.

mono Acyl glycerol

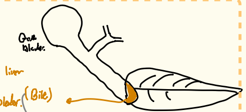
Intestine degrade Long Fatty Acid

- **Cholesterol esterase** — Hydrolyses cholesterol esters, producing cholesterol and free FATTY acid , need bile acids as emulsifier
- **Bile** — consist of phospholipid (lecithin) + Bile salts + cholesterol.
  1) (بيدخل له ويكل قطع) intestinal fluid. بحيط جزيئات الدهون عشان يقدر يدخل بال — Fat droplets (since it hydrophobic → (enter as clusters)
  2) then bile salt bind to these droplets make them smaller.
  3) colipase anchors pancreatic lipase to the micelle, ensuring effective digestion of fats
  - micelle, which is a structure that contains bile salts that surround fatty acids, Fat-soluble vitamins (A,K,E,D)are absorbed in the small intestine, but they are not water-soluble, so they need to be incorporated into micelles to be effectively transported across the intestinal , then micelle go into intestinal cells (enterocyte).
- **Pancreatic lipase** → convert TAG into 2MAG.
- **Phospho lipase A 2 (PLA2)** — Cleaves both FAs of glycerophospholipids, leaving glycerylphosphoryl basec



Hormonal control:
***CCK and secretin coordinate the digestive process in the small intestine, releasing bile and digestive enzymes, neutralizing the acidic chyme, and slowing gastric

Reformation of complex lipids
- by passive diffusion / NPC1L1 (cholesterol, FA, vitamin, MAG) (بيرجع الكبد bile salt) will go inside Entocyte specifically SER (contains specific enzymes → convert FA + cholesterol into TAG and phospholipids) then ⟹ RER add Apoprotein forming Chylomicrons
  ⇓
  Lacteals capillaries.
  ⇓
  lymphatic system
  ⇓
  muscle , tissue ..... (lipoprotein will be removed to release free FA).



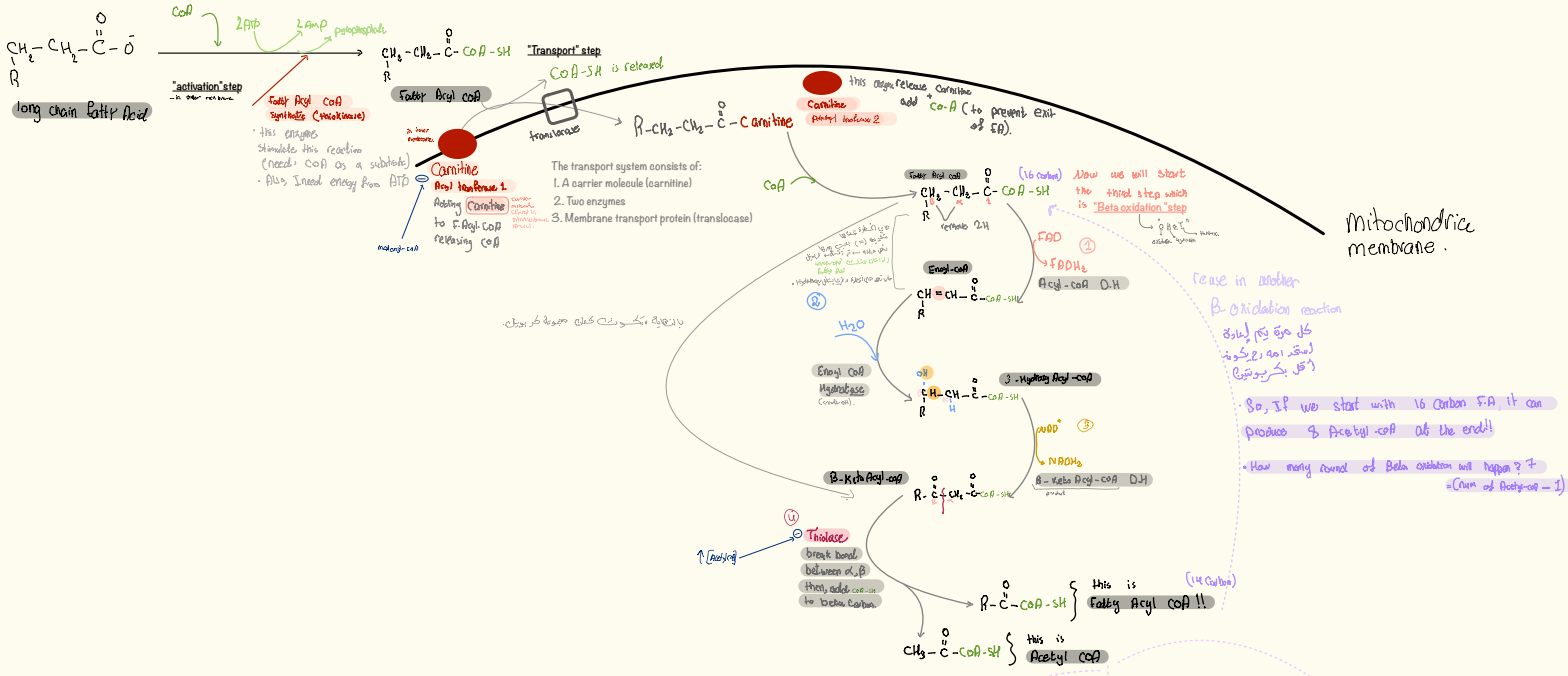
Secreted by liver and Stored in Gallbladder (Bile) → that contain lipid act as Emulsification agent. break large fat into droplet

Absorption by enterocytes ;
Micelles contain fatty acids, cholesterol, fat-soluble vitamins, and bile salts, which help transport fats to enterocytes for absorption.
Cholesterol absorption is enhanced by dietary fats, but inhibited by fiber. The process is facilitated by the NPC1L1 transporter and can be blocked by the drug ezetimibe.
Short-chain fatty acids are absorbed by passive diffusion, while long-chain fatty acids require both diffusion and protein transport.
The micelle structure, with its polar outer layer and non-polar core, helps in transporting these molecules into the enterocytes efficiently.

﴿ إِنَّ الَّذِينَ اتَّقَوْا إِذَا مَسَّهُمْ طَائِفٌ مِنَ الشَّيْطَانِ تَذَكَّرُوا فَإِذَا هُمْ مُبْصِرُونَ ﴾

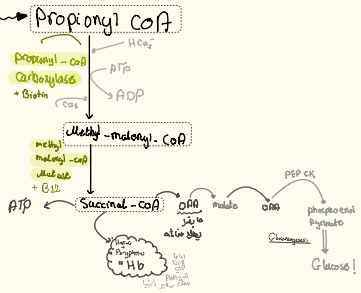
Metabolism of fatty acids

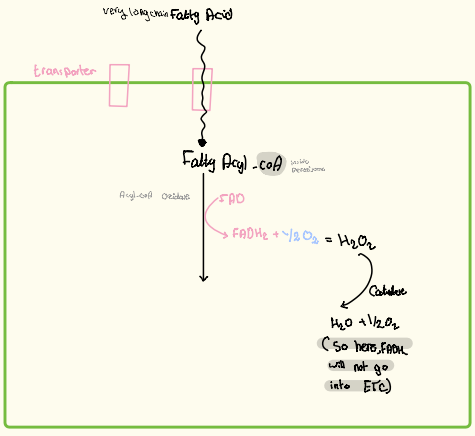
مَن كَانَ يُرِيدُ حَرْثَ الْآخِرَةِ نَزِدْ لَهُ فِي حَرْثِهِ ۖ وَمَن كَانَ يُرِيدُ حَرْثَ الدُّنْيَا نُؤْتِهِ مِنْهَا وَمَا لَهُ فِي الْآخِرَةِ مِن نَّصِيبٍ (20)



The main purpose of beta oxidation reaction is need of
Glucose since your body face low glucose level, carbs aren't available so the second source is fatty acids (to produce Acetyl-CoA)

- If it was 15 Carbon Fatty Acid, when I go through β- oxidation the products are → Acetyl CoA
  → Propionyl CoA

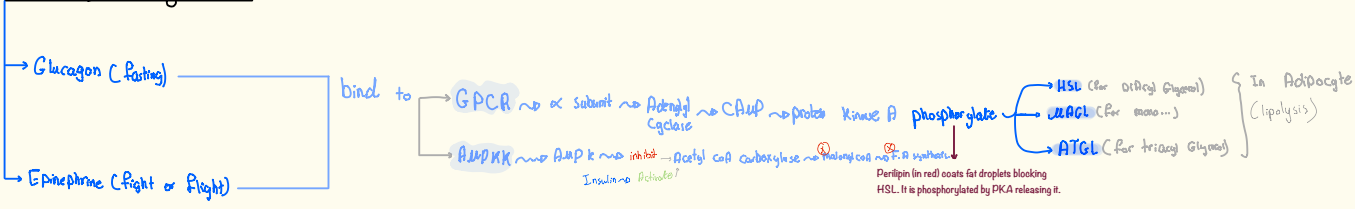




Peroxisome

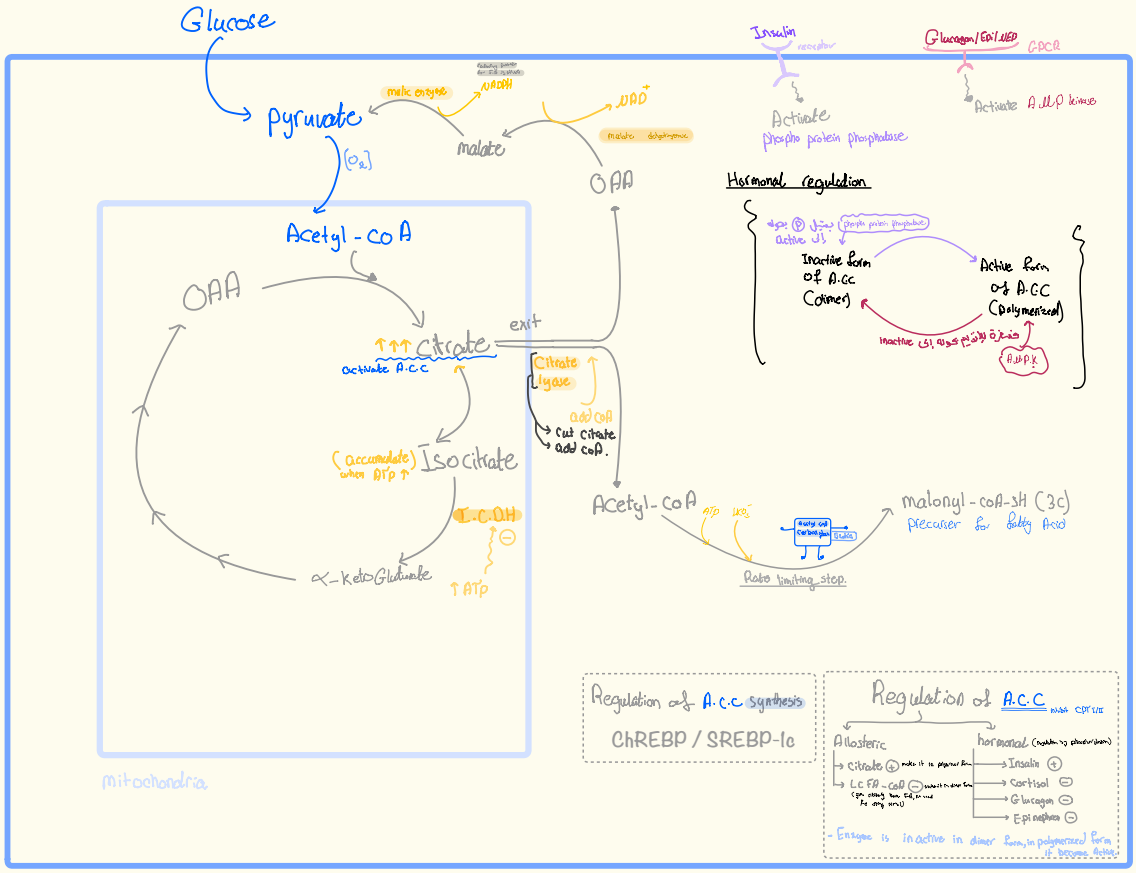
Deficincies
1- MCAD (Medium-Chain Acyl-CoA Dehydrogenase) Deficiency leads to accumulation of MFAC in liver .
2- X- linked adrenoleuko dystrophy ;deficiency in peroxisome transporter , so fatty acid can't get on which leads to accumulation of fatty acids in blood
3-Zellweger syndrome (can't form peroxisomes) .

Hormonal regulation



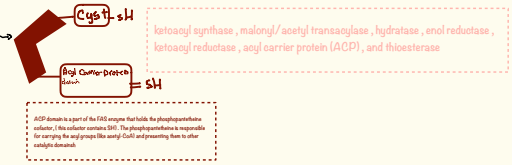
Fatty acid synthesis

- Occur in fed state , (high glucose in blood) , (high ATP level) .



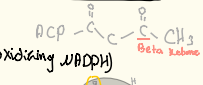
- F.A synthesis needs :-

① NADPH Reducing power
② malonyl CoA building block
③ Fatty Acid synthase I complex.
④ Acetyl - CoA
⑤ ATP



Steps :-

1) using malonyl/acetyl-CoA ACP transacylase to add Acetyl on ACP side (CoA is removed).
2) using ketoacyl ACP synthase (KS) to transfer 2 Carbon to Cystine site.
3) using malonyl/acetyl-CoA ACP transacylase, to add malonyl (3 carbon) (CoA is removed).
4) using ketoacyl ACP synthase (KS) to remove carbonyl from malonyl. then fuse them to form 4 Carbons structure on Acp side. (condesing components and Kick 1 Carbon out)
5) using 3-ketoacyl ACP reductase (Reduction → using NADPH) to reduce Beta Ketone into Hydroxyl group (oxidizing NADPH)



6) using 3-hydroxyacyl ACP dehydrate to remove H2O from β-Carbon producing Alkene!
7) using enoyl-ACP reductase to reduction (=) so become Saturated F.A.

8) using malonyl/acetyl-CoA ACP transacylase to transfer F.A to Cystine side → ACP side become free, so I can add another malonyl !!
9) At the end , Thio esterase will cleave fatty acid from ACP enzyme.

Ex: you need 16 fatty acid Carbons
How many round will happen?
16 Carbon − 4 carbon (in First round) = 12 carbon (in each round (excluding the first one) you will add 2 carbon into exist F.A. So you need 6 rounds)
As a total you need 7 rounds.

Elongation of fatty acid occurs in SER , No ACP or multifunctional enzyme is needed.so no fatty acid synthase , VLCFA produced in brain cells inside mitochondria..

synthases typically operate without the need for external energy sources like ATP, while synthetases depend on ATP (or GTP) to facilitate their reactions

اللهمَّ بعلْمِكَ الغيبَ وقُدْرَتِكَ عَلَى الخلْقِ ، أحْيِني ما علِمْتَ الحياةَ خيرًا لِي ، وتَوَفَّنِي إذا علِمْتَ الوفاةَ خيرًا لي ، اللهمَّ إنِّي أسألُكَ خشْيَتَكَ في الغيبِ والشهادةِ ، و أسألُكَ كلِمَةَ الْحَقِّ في الرِّضَا والغضَبِ ، وأسألُكَ القصدَ في الفقرِ والغِنَى ، وأسألُكَ نعيمًا لا ينفَدُ ، و أسألُكَ قرَّةَ عينٍ لا تنقَطِعُ ، وأسألُكَ الرِّضَى بعدَ القضاءِ ، وأسألُكَ بردَ العيشِ بعدَ الموْتِ ، وأسألُكَ لذَّةَ النظرِ إلى وجهِكَ ، والشوْقَ إلى لقائِكَ في غيرِ ضراءَ مُضِرَّةٍ ، ولا فتنةٍ مُضِلَّةٍ ، اللهم زيِّنَّا بزينةِ الإيمانِ ، واجعلنا هُداةً مهتدينَ