Lipids

I. Types and functions

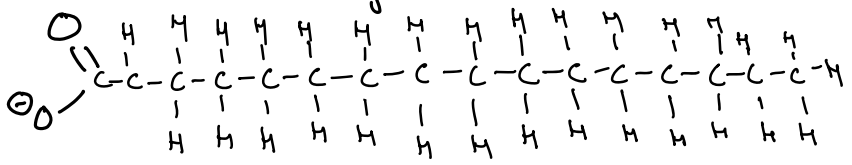
A. Fatty acid derived

16c Fatty acid saturated

16:1 Polymitic acid

acid end

methyl group



a. Structure – two aspects of FA structure

i. C-Chain length

lower mp

"Short": 2-12C

"med": 14-16C

"long": ≥18C (up to 22C)

higher fluidity - lower melting point

even C number

higher mp

ii. Saturation vs unsaturation

↓

C=C

cis or trans configuration

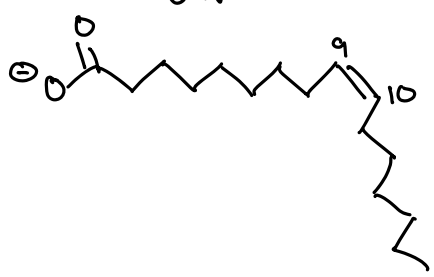
↙ lower MP

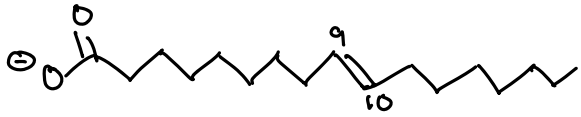
↘ Don't lower MP much

16c monounsaturated F.A. (cis-9)

trans

16:1





conformation

cis: more common overall

Trans: from microbial metabolism or chemical hydrogenation

↑ ruminents

I. A.1 Fatty acid structure + Nomenclature

b. Nomenclature

IUPAC - systematic names

Trivial names

- Omega system: count from methyl end of FA to first double bond system

ω3 or ω6

- "lipid number" system

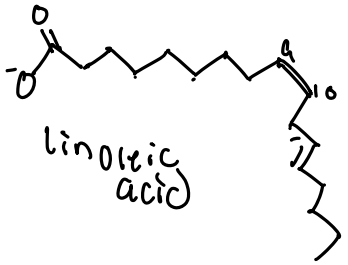
#C	:	*C=C	, (geometry + location of C=C)

16 : 0 : MA

16 : 1 : cis 9 =

I.A.2 Roles and Functions

18:2 cis 9, cis 12



IA2 Roles + Functions

a. P.2 membranes

b. Signals

b. <u>eicosanoids</u> - derived from 20:4 (arachidonic)

geometry of C=C has influence on structure + properties of resulting eicosanoid (made in animal)

I A.2.b most animals can make 20:4 from 18:2, 18:3 found in diet

18:2 18:3 must be in diet for most animals = "essential" fa

exception = Obligate carnivore - must eat 20:4

eicosanoids: Prostaglandins (anti inflammatories, inhibit)

↳ involved in inflammation, etc.

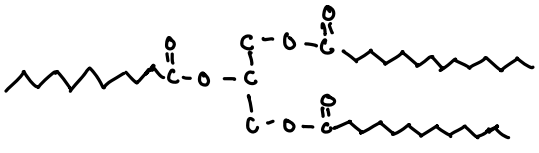
leukotrienes - immune function

thromboxanes - blood flow, etc

I A.2.C Energy storage - glycogen stores are limited by the need for water to keep in solution

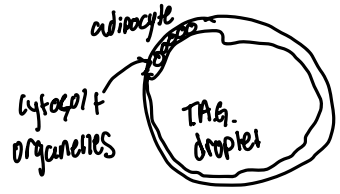
over 80% of body energy is "fat" - triacyl glycerol (coenzyme A)

triacylglycerol - totally nonpolar



Triacylglycerol (TAG) - Stored in adipose tissue

↳ constant through life



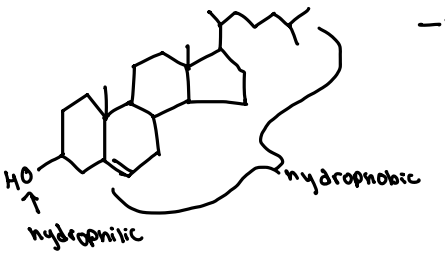
release fat or store fat

Nonpolar, no water needed

I. B. 1. Sterols / Steroids

1. Cholesterol

membrane fluidity



- bile salts - used in lipid digestion

B. 2. Steroids - derivatives of Cholesterols

mostly signaling molecules
- Estrogen
- Progesterone
- sex hormones
- corticosteroids < Mineralcorticoids / glucocorticoids
- Vit. D - calcium status, development, everything else

act through nuclear receptors to affect gene expression (long term responses)

I c. Fat soluble vitamins

A, D, E, K
- A → Development, Vision
- D → Ca^{++}
- E → antioxidant
- K → clotting

II Digestion, absorption, trafficking

A. Digestion

1. Mouth / Stomach - lingual lipase (neonatal animals)
- Gastric lipase ↑ chief cells

Both act on non-emulsified dietary fat

because the fat is not emulsified

TAG —gastric lipase (and lingual lipase)→ DAG + f.a.

A. 2. Emulsification of Fat by bile

Bile - bile salts (Cholesterol + aa, Cholesterol derivatives)
- bilirubin (heme disposal)
- some a.a and F.a.

→ Buncha amphipathic molecules

Dietary fat mostly TAG (nonpolar) forms huge lipid droplets with low surface area to volume ratio (↓ S.A.:Vol)

Bile ("baloonskin") (amphipathic molecules) emulsifies diet lipid into stable, small lipid micelles (way less intimidating)
(likesoap)
(↑SA:Vol)

A.3. Hydrolysis by pancreatic lipases.

- Pancreatic lipase
- Colipase (cofactor)
- Phospholipase A_2

TAG —(Panc. Lipase + Colipase)→ F.A. + glycerol (some) (facilitated diff.) (alcohol doesn't want to pass "OH" = OH)
+ M.A.G ← simple diff.
(monoacylglycerol)

P.L. —(Phospholipase A_2)→ F.a. + lysophospholipid
(PL missing one F.a.)

II B. Absorption

- most absorption is simple diffusion
- glycerol - facilitated diffusion
- very long F.A. get some help

C. Trafficking

1. Enterocyte re-esterifies absorbed lipids - mostly into TAG (+ some PL)

(glycerol goes directly to circulation)

2. Re-esterified (TAG + PL) lipid combines w/ huge amphipathic proteins to form a lipoprotein particle
(nonpolar lipid)

(lipids=kids)

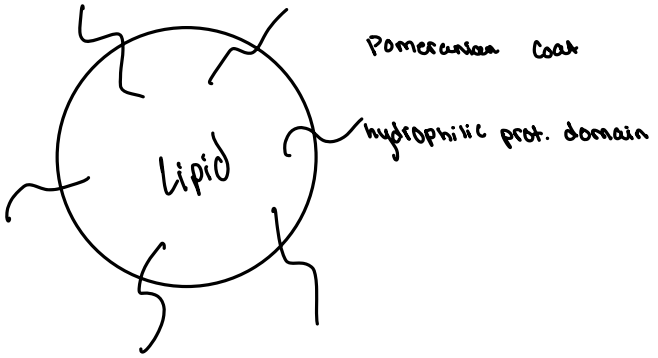
amphipathic proteins = Apolipoproteins (schoolbuss)

Safe way to get through a scary (journey)

Lipoprotein particles

Apolipoprotein: Apo A, B, C, E
- hydrophobic inside
- hydrophilic sticking out
- hydrophobic/hydrophilic

large amphipathic proteins — inside / outside



II C.3 lipoprotein types - source, role, destination, Apos, T 1/2

- time it takes for 1/2 to be removed from the pool. ↳ circulation

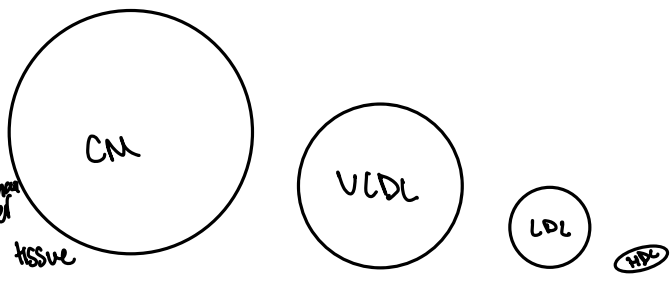
a. Chylomicron (CM) - made in enterocyte

Apo B, C, E and diet fat

- Secreted into lymph (circulation)
- delivers dietary fat to the liver (maybe some is dropped off in other tissues along the way)
- HUGE, very very low density (lots of fat : protein)
- fastest — wants to float
- T 1/2 fast (minutes) ~10-15 min

II C.3 very low density lipoprotein (VLDL)

- liver = logistics warehouse not storage
- made in liver, secreted into blood
- anything other than liver
- ensures a relatively constant supply of fat to extrahepatic tissue



- Contains Apo B, C
- Starts big, high in fat, becomes smaller and lower in fat in circulation
- Becomes (ow) density lipoprotein (LDL)

- T ½ hours

VLDL disappears to become LDL

3.C. Low density lipoprotein (LDL)

- made from VLDL in circulation
- Apo B, C
- In circulation for long time
- T ½ days
  empty school bus
- Taken up by the liver

3D. High density lipoprotein (HDL)

- Made in liver as a mix of proteins w/o any fat
- Apo A, E
- Collects "old" lipid (lots of cholesterol)

from extra hepatic tissues and other lipoprotein particles.

- Taken up by the liver "quick compared to LDL"
- T ½ = Minutes to hours

* want more HDL than LDL

4. Proteins important to lipid traffic

a. LDL receptor - clears lipoproteins from circulation by receptor-mediated endocytosis

- Expressed in the liver
- recognizes or binds Apo E, B
- affinity is highest (lots) for Apo E
- upon binding ligand (Apo B, E) initiates endocytosis of entire lipoprotein particle

II C4. LDL receptor...

Ligands: Apo B, E (Affinity for E >>> B)

- CM Both
- HDL E
- VLDL B → LDL ··· B

C426. Lipoprotein lipase (LPL)

- expressed in most extrahepatic tissues
- anchored inside the capillary (blood-oxygen) wall
- Cleaves FA from circulating lipoproteins
- Activated by Apo.C (cofactor)

C. Apolipoproteins

- Apo A: facilitates the transfer of Cholesterol from tissues and lipoproteins to HDL (*helps HDL get to Cholesterol)
- Apo B: low affinity ligand for LDL receptor - uptake of lipoproteins by liver
- Apo C: Cofactor for LPL - helps CM, VLDL drop off f.a/Cholesterol to extra hepatic tissues
- Apo E: High affinity ligand for LDL receptor

II.C.4.d. ABCA1 - expressed in most extrahepatic tissues (Make brown)

- Exports "old" Cholesterol from cells (specificaaly for Cholesterol)

e. SRB1 - expressed in the liver + steroidogenic tissues - imports cholesterol into cells (↙LPL but for Cholesterol)

Make a diagram w/ all these

CM
VLDL → LDL (Apo B) ABCA1 SRB1
HDL
LDL receptor (LDLR)
LPL

III. Lipids in body ~~ metabolism

A. Overview

- Using lipids (FA) for ℰ (ATP) —— ℰ supply is insufficient
  Supply ≠ demand "starvation / fasting"
  ℰ demand (excercise / stress)

  Lipolysis + Oxidation

- Synthesis and Storage of fat (lipogenesis)

  ℰ supply exceeds demand.

- Regulation

III.B. Using FA to generate ATP

1. When: ℰ demand exceeds supply

   Hormones? Insulin - Inhibits

   Glucagon / epinephrine

2. Where?

   Lipolysis - Adipose tissue (cytosol)

   β Oxidation - muscle + liver
   (mitochondria)

3. How?

A. lipolysis - enzymes: Adipose Triacyl Glycerol Lipase (ATGL)

Hormone Sensitive Lipase (HSL)

III B.3.a TAG —(TAGL, *regulated by hormones*)→ DAG —(*HSL, hormone-sensitive lipase)→ f.a. + glycerol

- f.a. → diffuse to blood & interact w/ albumin as noncesterified f.a. (NEFA)
- glycerol → diffuses (facilitated) to blood + taken up by liver.
  ↳ liver wants (gluconeogenesis)