
بسم الله الرحمن الرحيم

LIPID METABOLISM

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BY THE END OF THIS LESSON THE STUDENT WILL BE ABLE TO….

Inform Learner of Objectives

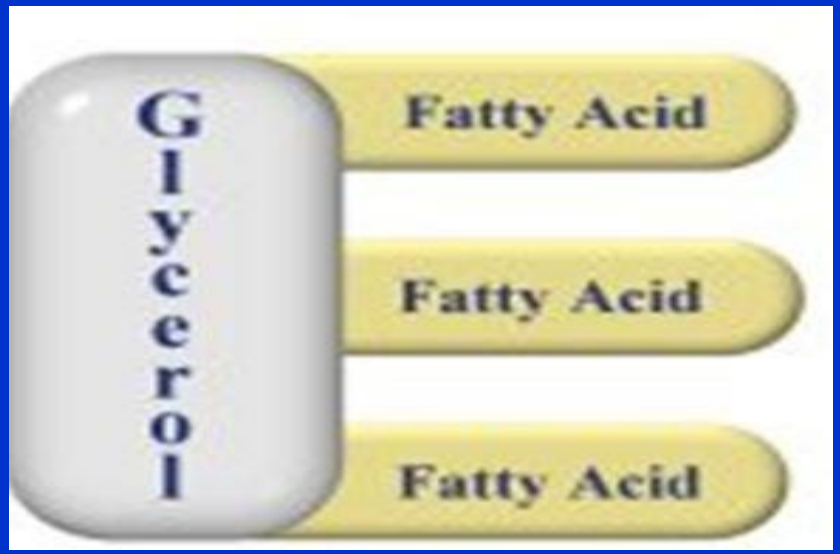
Know

- TGs chemistry
- Importance
- Adipose tissue
- TGs synthesis
- TGs degradation

What is TGs?

TRIACYLGLYCEROL

(TG)

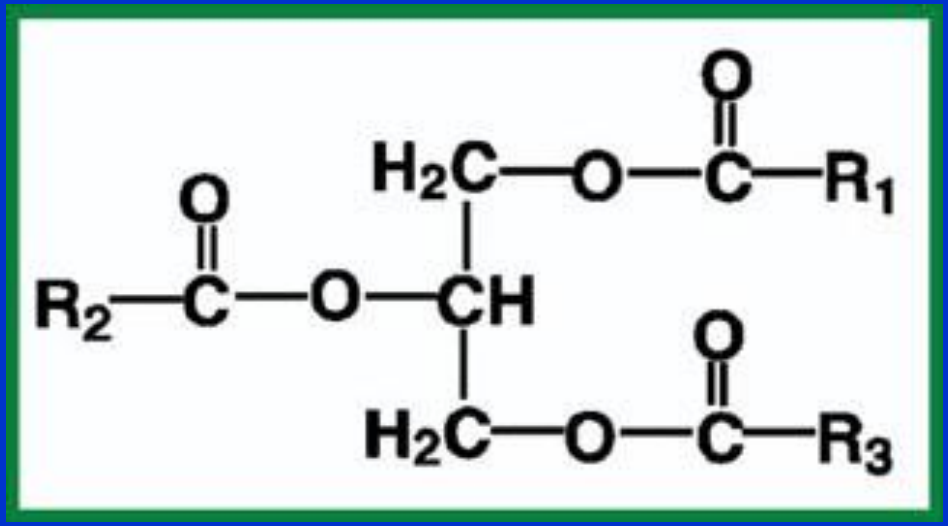


TRIACYLGLYCEROL(Neutral fats)

Triacylglycerols are esters of alcohol with three fatty acids.

Storage form of lipid which mostly occur in fat cells of Adipose tissues.

C55H98O6



IMPORTANCE

- Store of energy - released rapidly on demand
- Reserve of Essential Fatty acids
- Precursors for Eicosanoids
- Major fat of our body adeposits.
- Major portion of our food lipid.
- Removes excess potentially harmful lipids such as FFA, DAG, retinol ester, CoA ester.
- Normal serum level of TGs 75-150mg/dl.

Absorption and circulation

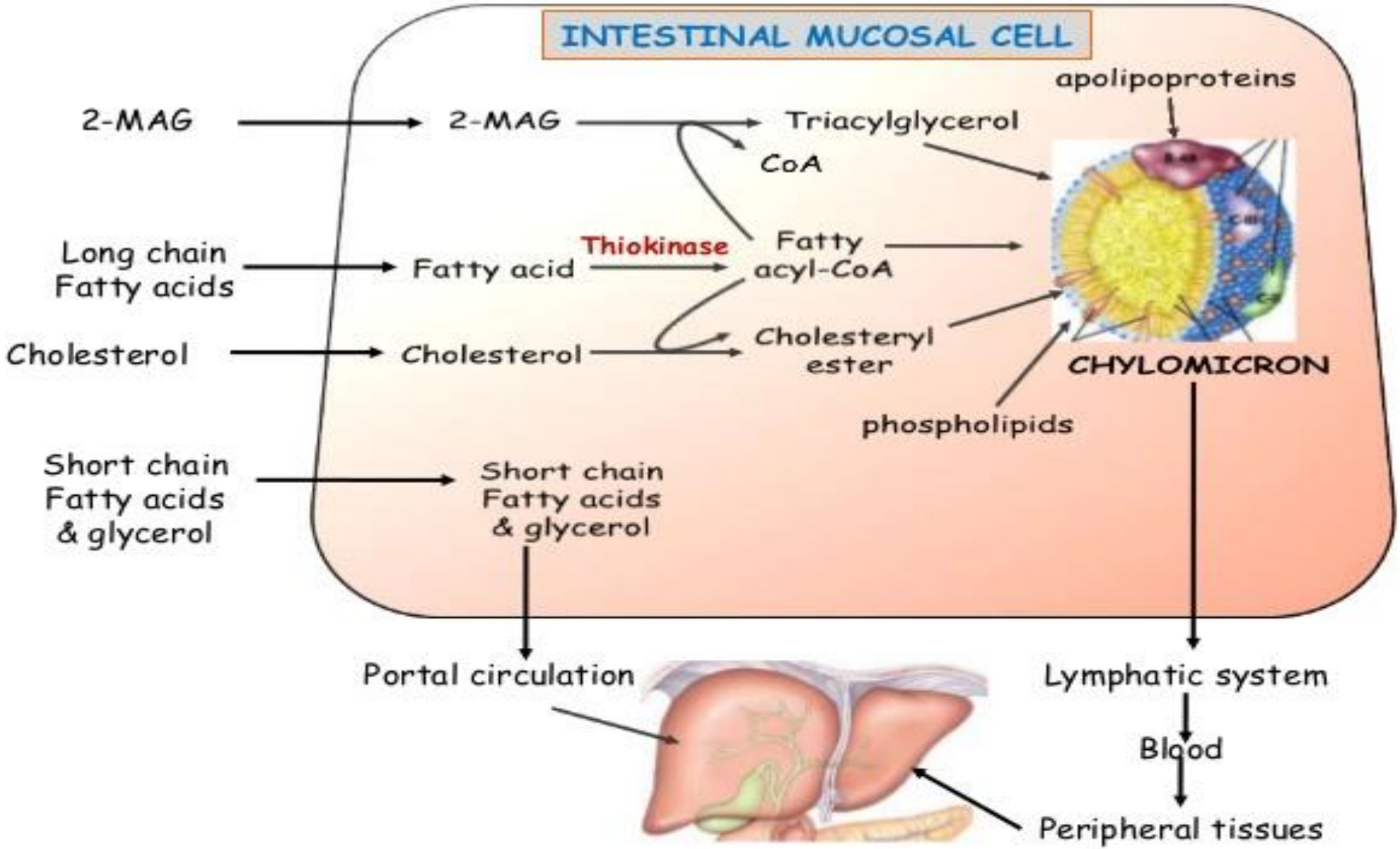
- TG (exogenous) are absorbed from the intestinal lumen and transported in the blood forming Lipoprotein complex “Chylomicrons”.
- TG(endogenous) are synthesized in the liver and transported in the blood forming Lipoprotein complex “VLDL” very low density lipoprotein.

Digestion of Dietary Triacylglycerol

- Occurs in duodenum
- Facilitated by
  - Bile salts (emulsification)
  - Alkaline medium (pancreatic juice)

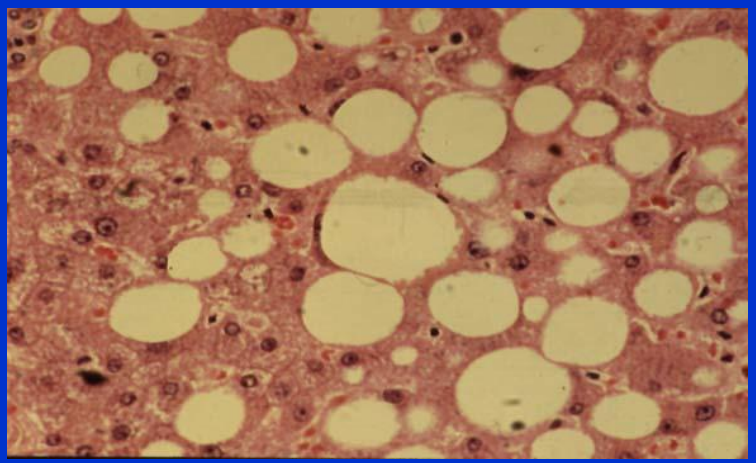
Absorption of resynthesized TG

- Synthesis of(exogenous) TG take place in the endoplasmic reticulum of mucosal cells.
- Insoluble so converted to lipo-protein complex chylomicrons.
- Chylomicrons pass through cell membrane of epithelial cells in extra cellular spaces and by lymphatic vessels enters the systemic circulation.
- TG released and hydrolyzed to produce glycerol and 3FAs.


INTESTINAL MUCOSAL CELL
2-MAG
2-MAG
Triacylglycerol
CoA
apolipoproteins
Long chain
Fatty acids
Fatty acid
Thiokinase
Fatty
acyl-CoA
Cholesterol
Cholesterol
Cholesteryl
ester
CHYLOMICRON
phospholipids
Short chain
Fatty acids
& glycerol
Short chain
Fatty acids
& glycerol
Portal circulation
Lymphatic system
Blood
Peripheral tissues

Fat Storage

- Mainly as triacylglycerols (triglycerides) in adipose cells
- Constitute 84% of stored energy as TGs
  - Protein - 15%
  - Carbohydrate (glucose or glycogen) - <1%



ADIPOSE TISSUE

- adipose tissue(body fat, or simply fat) is a loose connective tissue composed mostly of adipocytes.
- **STRUCTURE:**

Closely packed

Nucleus pushed to one side by fat droplet

- Spread in many areas throughout the body.
- Adipose tissue represents 15-20% of the body weight in men.
- In women of normal weight , 20-25% of body weight.

LOCATION

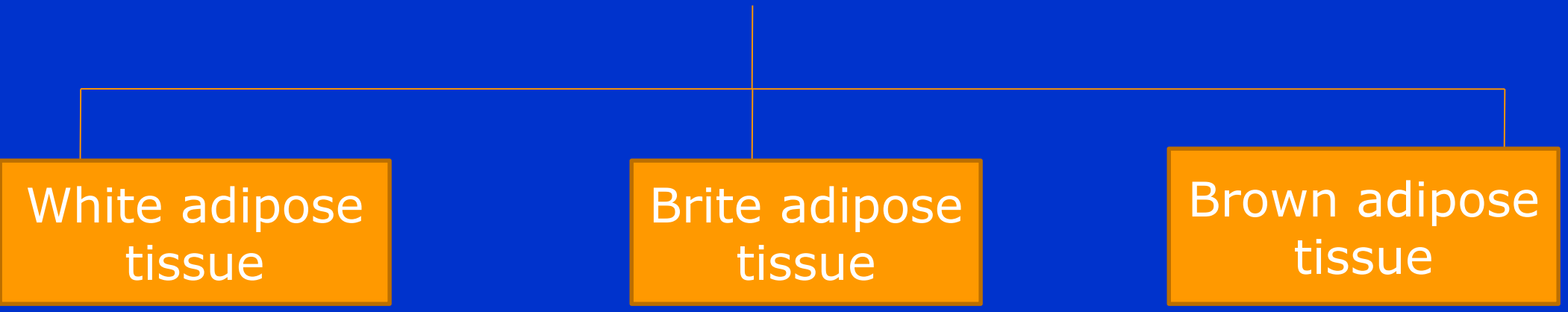
- Under skin (insulates the body and protects the organs)
- Cushions joints
- Around kidneys, between muscles , behind eye balls, within abdomen and in breasts

ADIPOSE TISSUE FUNCTIONS:

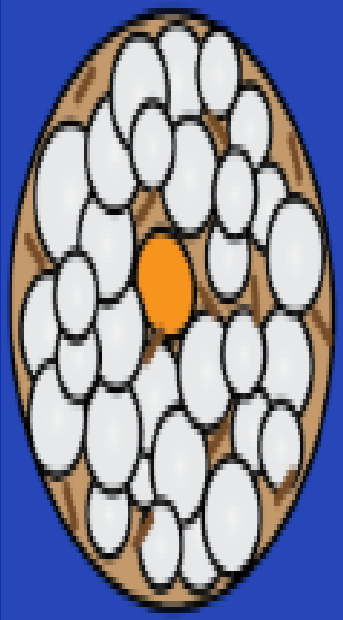
- Thermal isolation
- Techanical protection
- Reserve of energy
- Endocrine organ (leptin, estrogen, resistin, cytokine, irisin)

TYPES

- With different locations, structures, colors and pathological characteristics; they are of three types:



Brown Adipocyte



UCP1 positive

High mitochondria density

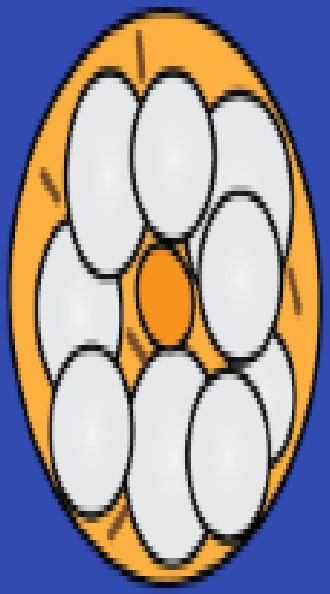
Numerous small lipid droplets

Major Functions:

Thermogenesis

Endocrine (e.g. FGF21)

Brite (or Beige) Adipocyte



UCP1 positive

Medium mitochondria density

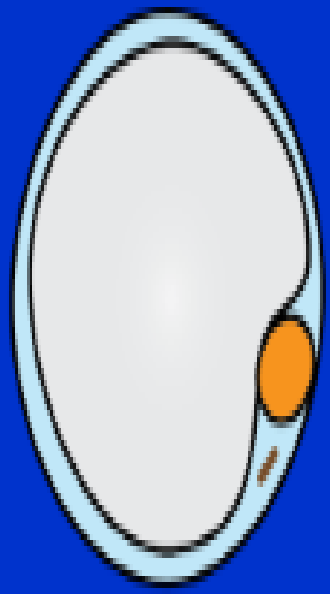
Few to many lipid droplets

Major Functions:

Thermogenesis?

Endocrine?

White Adipocyte



UCP1 negative

Low mitochondria density

One large lipid droplet

Major Functions:

Energy storage

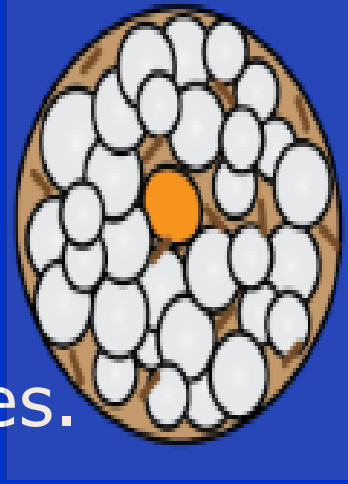
Endocrine (e.g. leptin, adiponectin)

Mitochondria

Nucleus

Lipid droplet

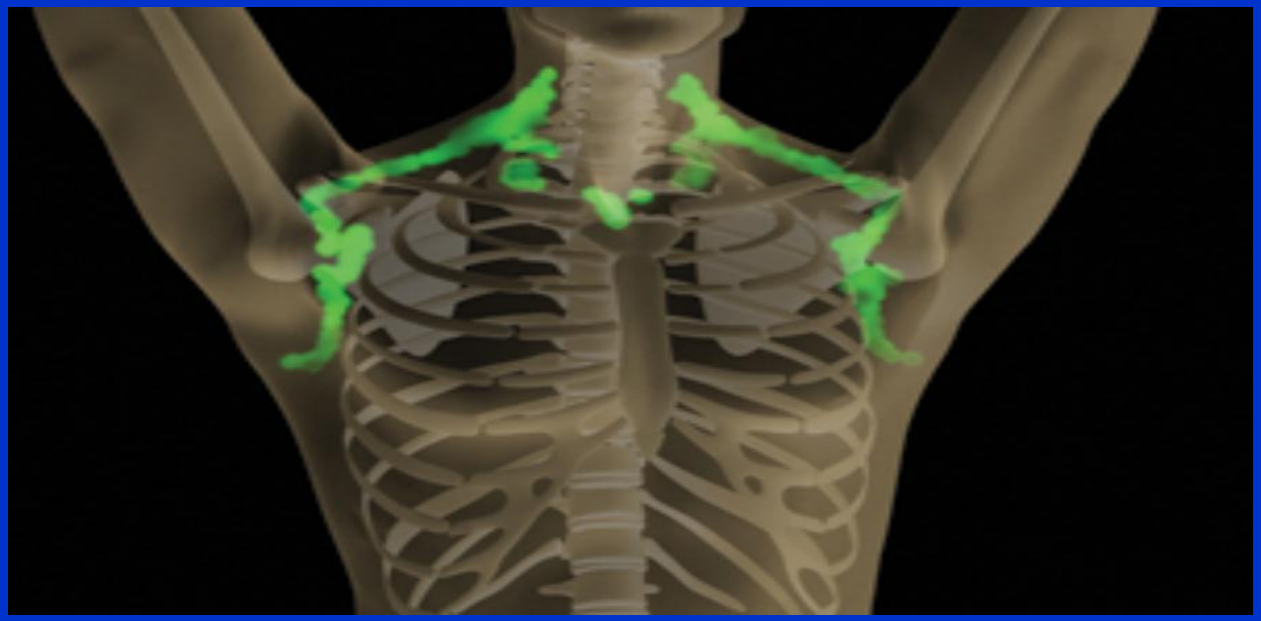
BROWN ADIPOSE TISSUE

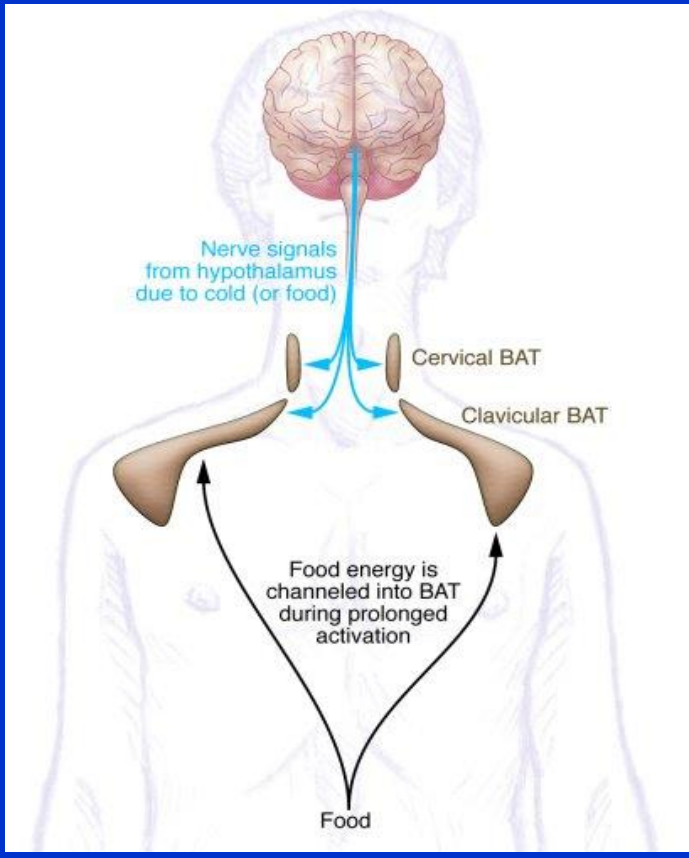


- Brown adipose tissue is darkly pigmented due to the high density of mitochondria rich in cytochromes.
- Brown adipose tissue is a specialized form of adipose tissue important for adaptive thermogenesis in humans and other mammals.
- They generate heat by "uncoupling" the respiratory chain of oxidative phosphorylation within mitochondria through tissue-specific expression of uncoupling protein 1 (UCP1).
- Rich in carnitine
- Has an enzyme glycerokinase

LOCATION

- Primarily located around the neck and large blood vessels of the thorax , where may effectively act in heat exchange.





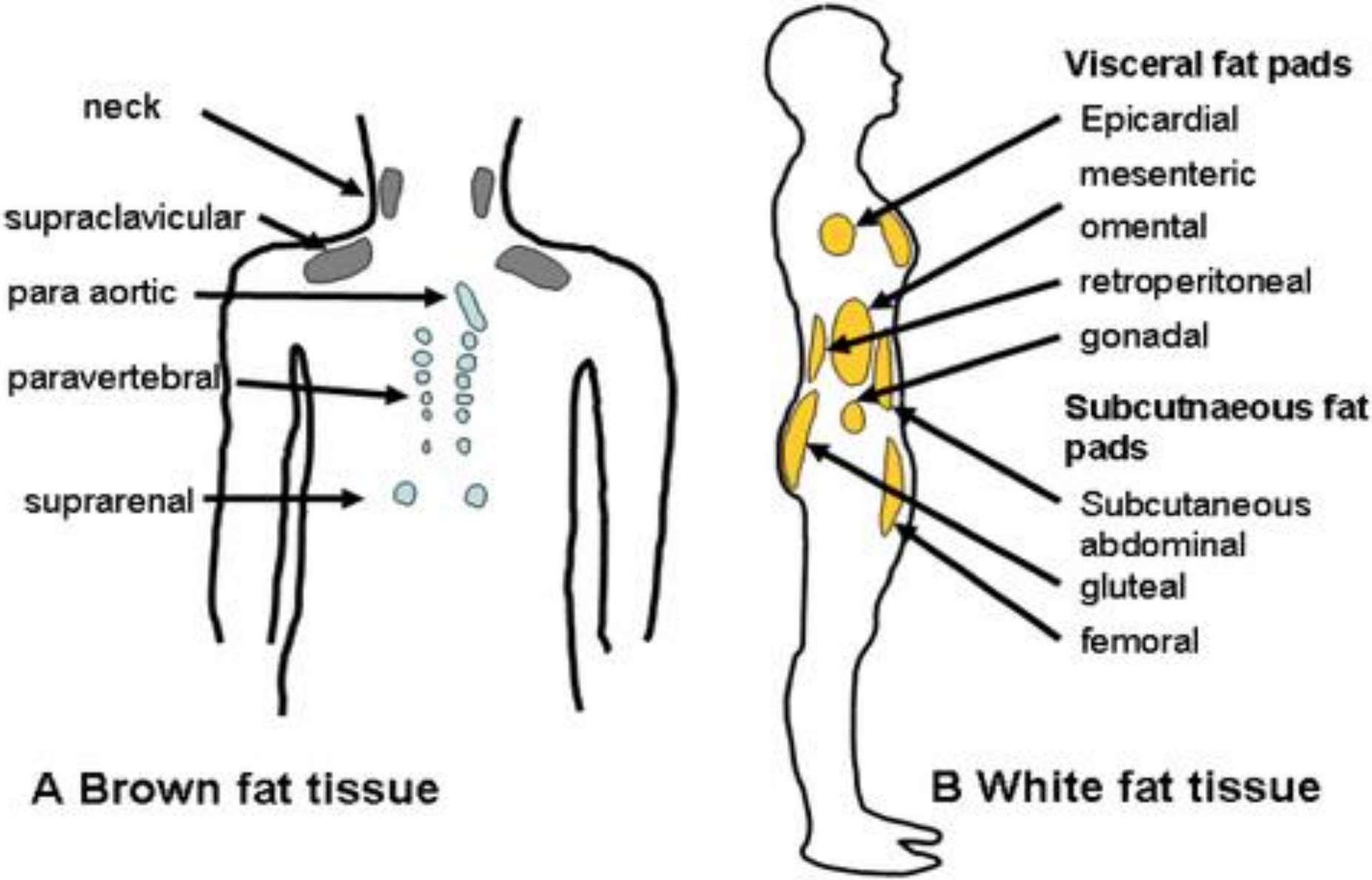


Figure 2. Brown fat (A) and white fat (B) tissue distribution in adult from [10, 11]

FUNCTION

- It promotes energy burning rather than energy storage .
- Responsible for diet-induced thermogenesis (how some persons eat more but do not get fat.
- It’s main function is to generate heat.
- Research shows that people with more brown fat are leaner and less likely to be diabetic.
- Also, exercise generates a specific hormone irisin, which convert white fat into brown fat and burn more energy during exercise.
- They make white fate cells breakdown into fatty acids

Synthesis of TRIACYLGLYCEROL

Synthesis of TAG :

- Occurs in All tissues Predominantly - Adipose tissue, Liver and intestine.
- Substrates- Fatty acid (acyl-CoA),
  Glycerol (glycerol -3-phosphate) activated prior to synthesis.
- SITE: endoplasmic reticulum and mitochondria.

Synthesis of TRIACYLGLYCEROL

- Two biosynthetic pathway

1. Glycerol-3-phosphate pathway –operates in LIVER,ADIPOSE TISSUES

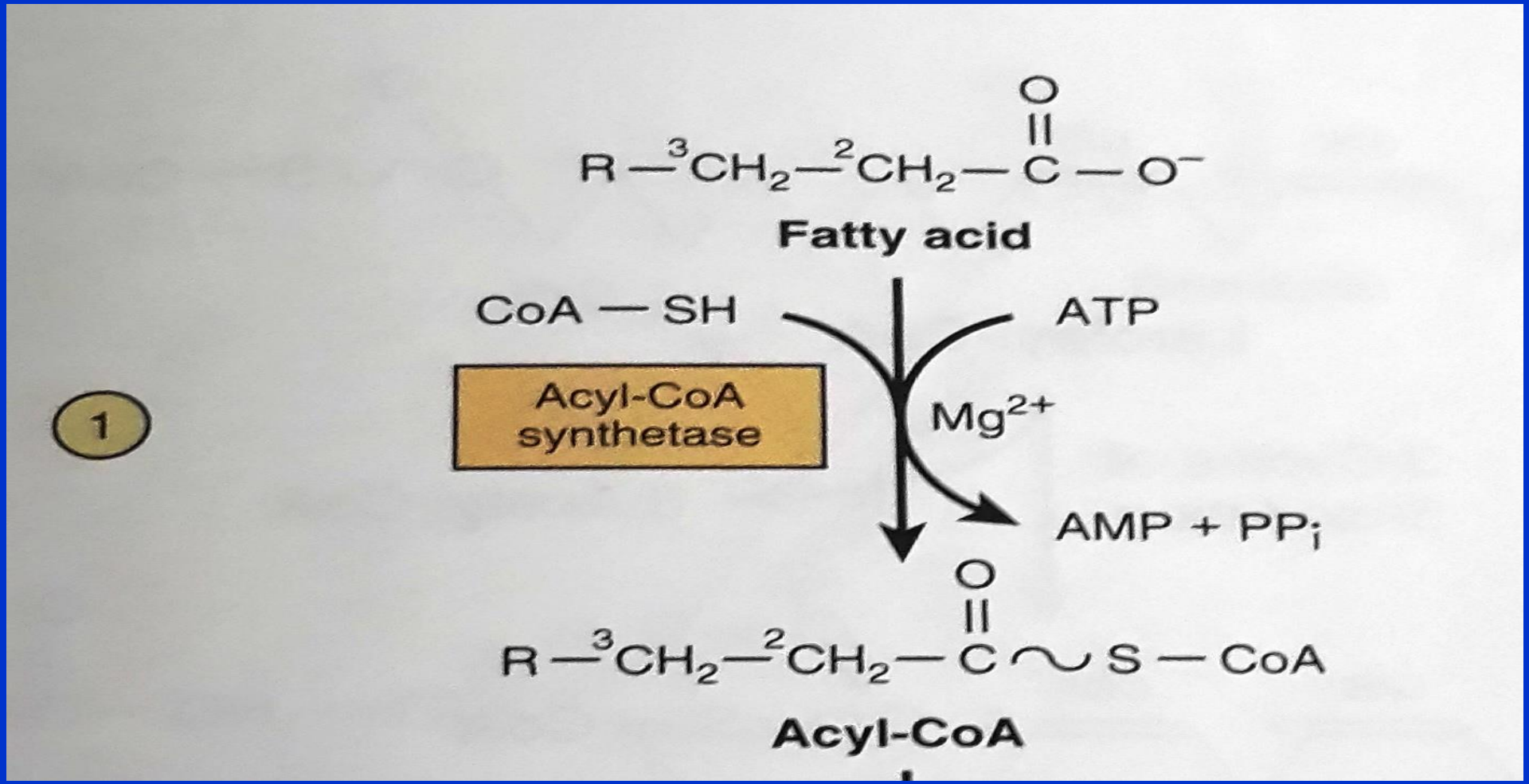
   (Only difference – source of Glycerol-3-Phosphate)

2. Monoacyl glycerol pathway – operates in INTESTINE

Synthesis of TGs in 3 phases

1.Activation of free fatty acids
2.Formation of Glycerol-3-phosphate
3.Synthesisof TGs from Glycerol-3-phosphate and Acyl CoA.

1.Activation of Fatty Acids in to Acyl CoA



2.Formation of Glycerol-3-phosphate

- 1. From dihydroxyacetone phosphate(glycolysis)

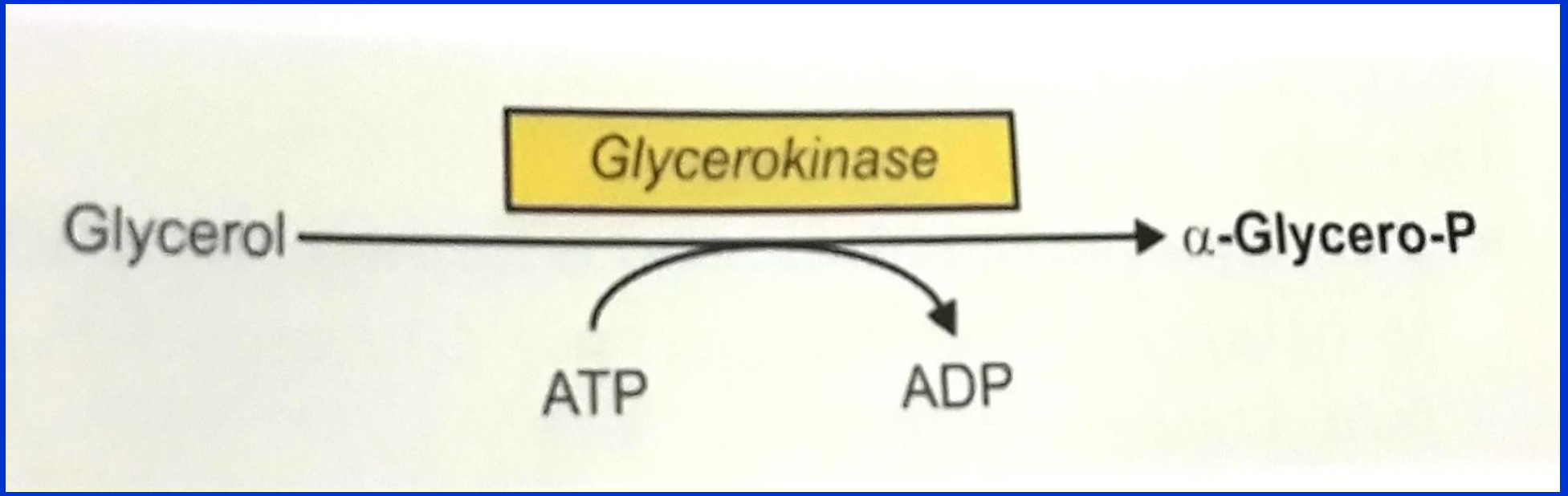
  in liver, adipose tissues.

- 2. From glycerol in liver, kidneys, intestine and lactating mammary glands.

2.Formation of Glycerol-3-phosphate

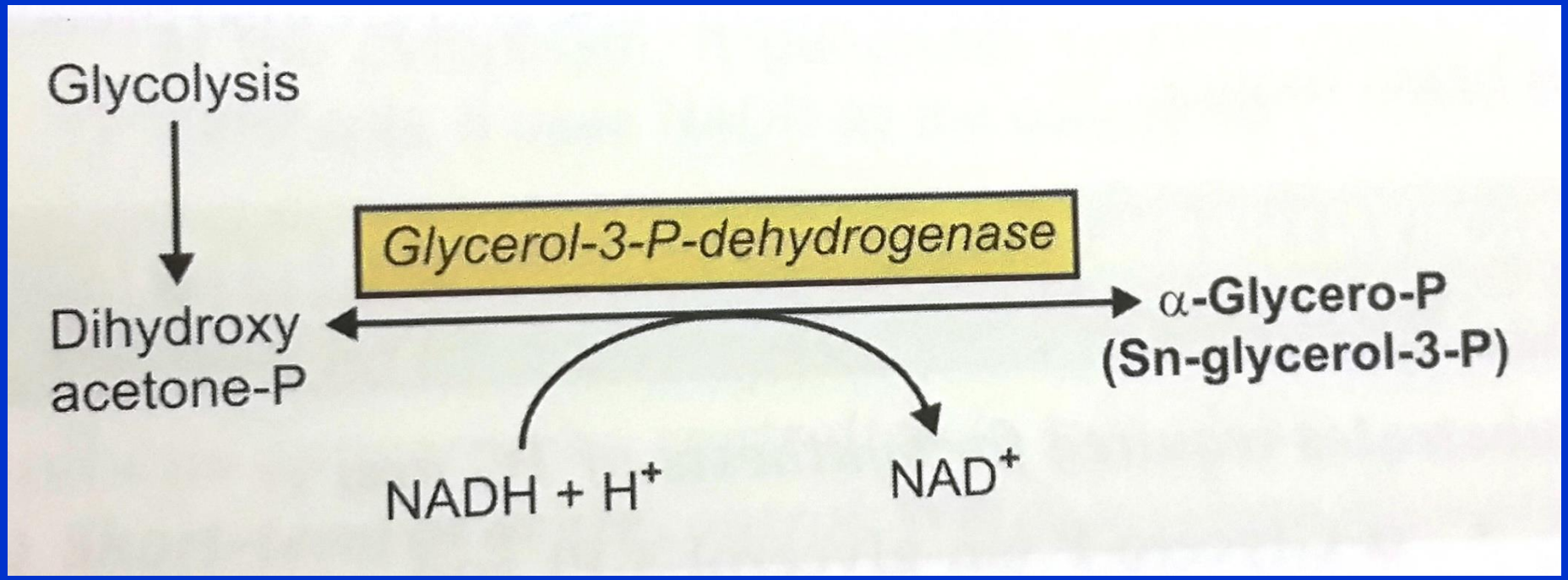
- In **liver** glycerol-3- phosphate is produced from phosphorylation of glycerol by **glycerol kinase** or from reduction of dihydroxyacetone phosphate(DHAP) derived from glycolysis.
- In **adipose tissues** glycerol kinase not present so glycerol-3- phosphate is produeced by dihydroxyacetone phosphate(DHAP)derived from glycolysis.

2.Formation of Glycerol-3-phosphate from glycerol



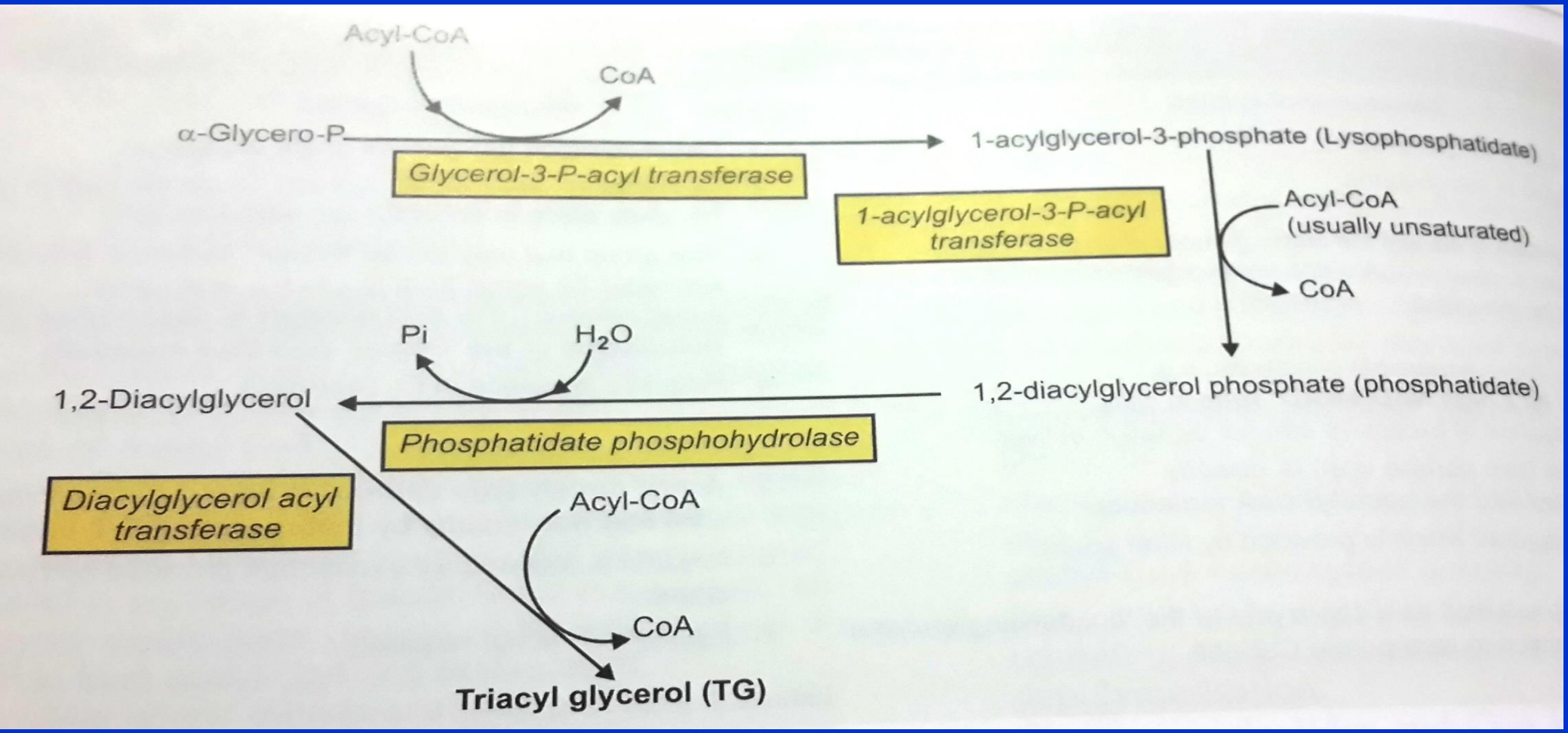
In liver cells

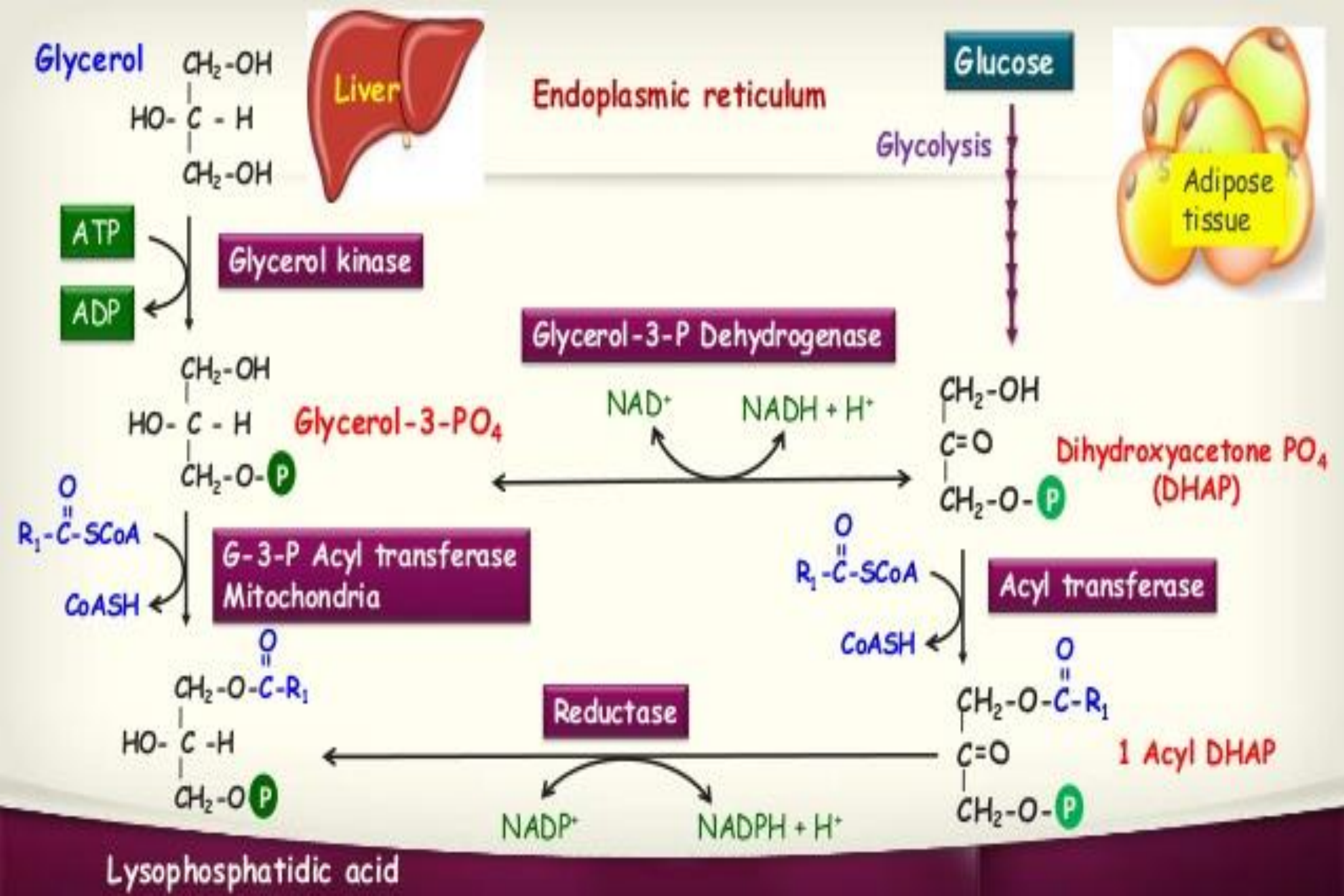
2. Formation of Glycerol-3-phosphate from dihydroxyacetone phosphate(glycolysis)

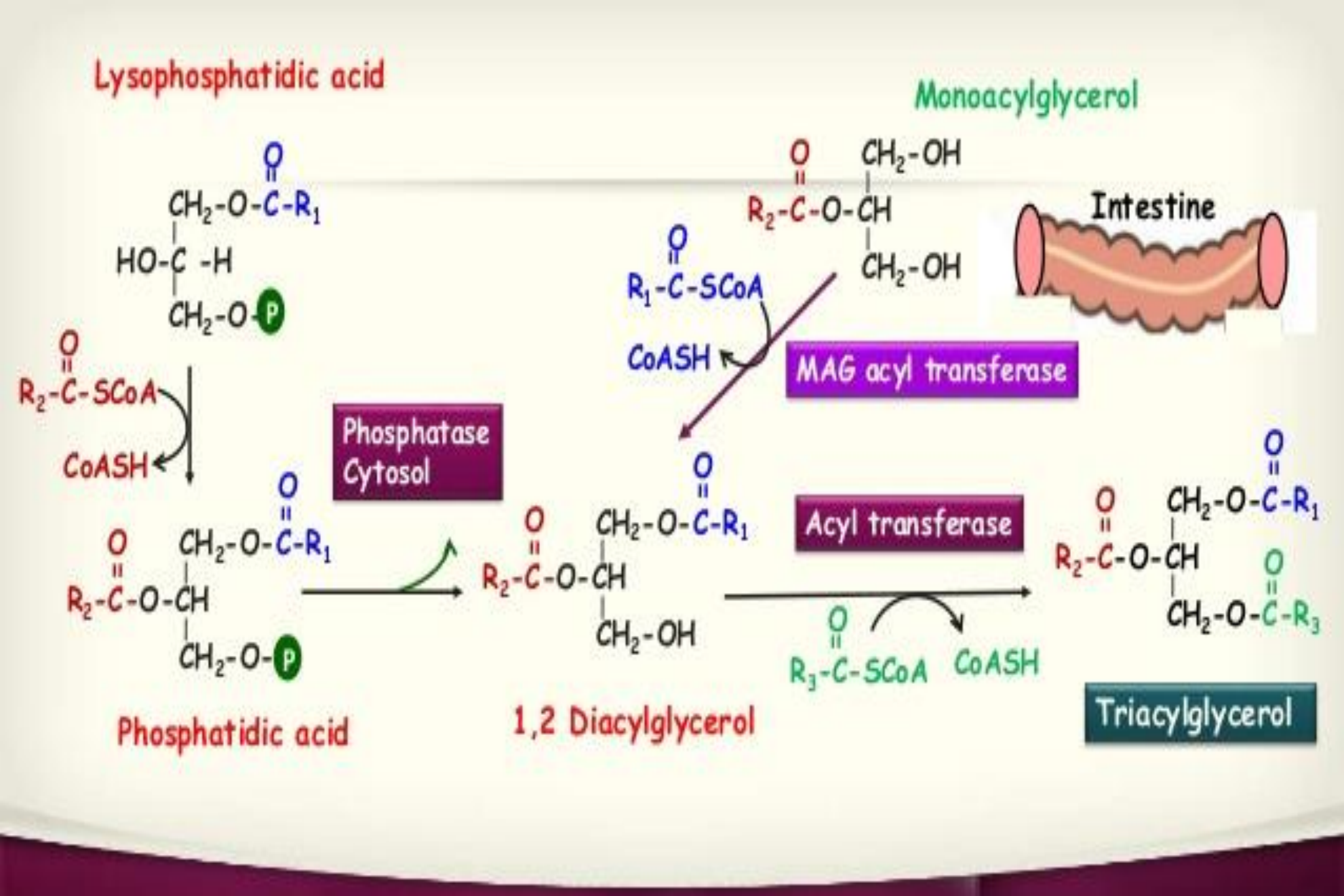


In adipose tissue

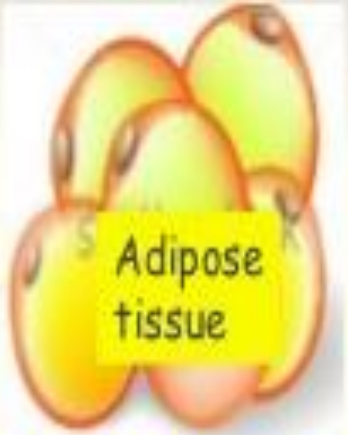
3.TG Synthesis




Glycerol
CH2-OH
HO- C - H
CH2-OH
Liver
Endoplasmic reticulum
Glucose
Glycolysis
Adipose tissue
ATP
ADP
Glycerol kinase
Glycerol-3-P Dehydrogenase
NAD+
NADH + H+
Glycerol-3-PO4
CH2-O-P
Dihydroxyacetone PO4 (DHAP)
R1-C-SCoA
CoASH
G-3-P Acyl transferase Mitochondria
Acyl transferase
CH2-O-C-R1
Reductase
1 Acyl DHAP
NADP+
NADPH + H+
Lysophosphatidic acid


Lysophosphatidic acid
Monoacylglycerol
Intestine
MAG acyl transferase
Phosphatase
Cytosol
Acyl transferase
CoASH
Phosphatidic acid
1,2 Diacylglycerol
Triacylglycerol

Glycerol



Glycerol-3-PO_4 ⟷ Dihydroxyacetone PO_4 (DHAP)

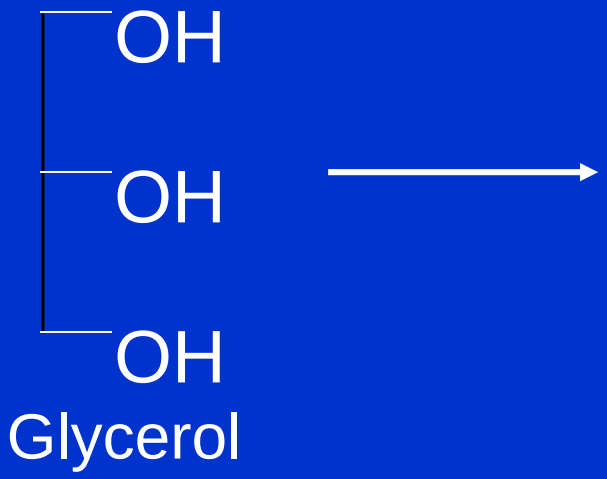
Monoacylglycerol

1,2 Diacylglycerol

Triacylglycerol

Fate of Glycerol

In Liver:



Dihydroxyacetone Phosphate

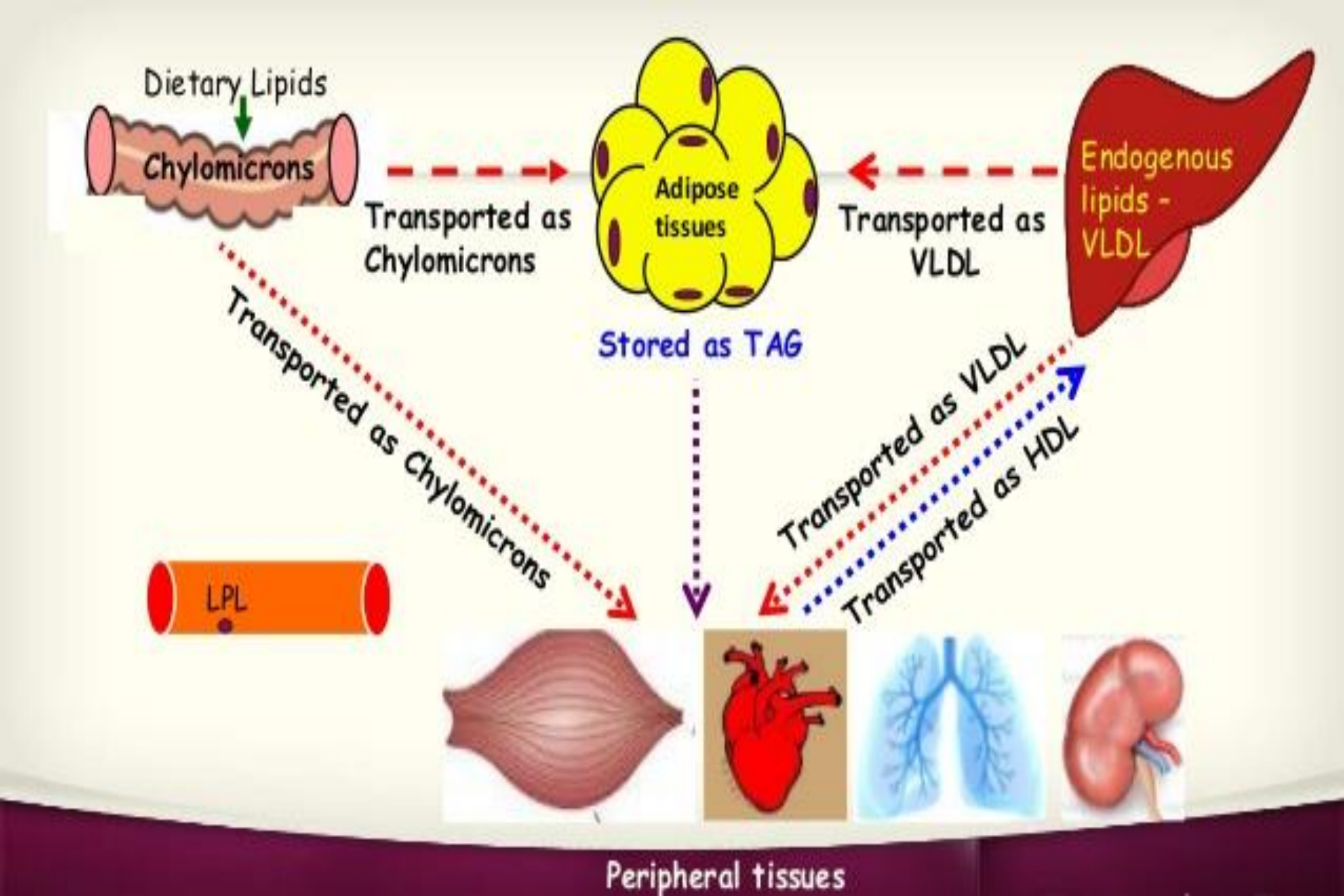
- Pyruvate — Glycolysis
- Glucose — Gluconeogenesis
- TGs

Fate Of Triacylglycerol In The Liver

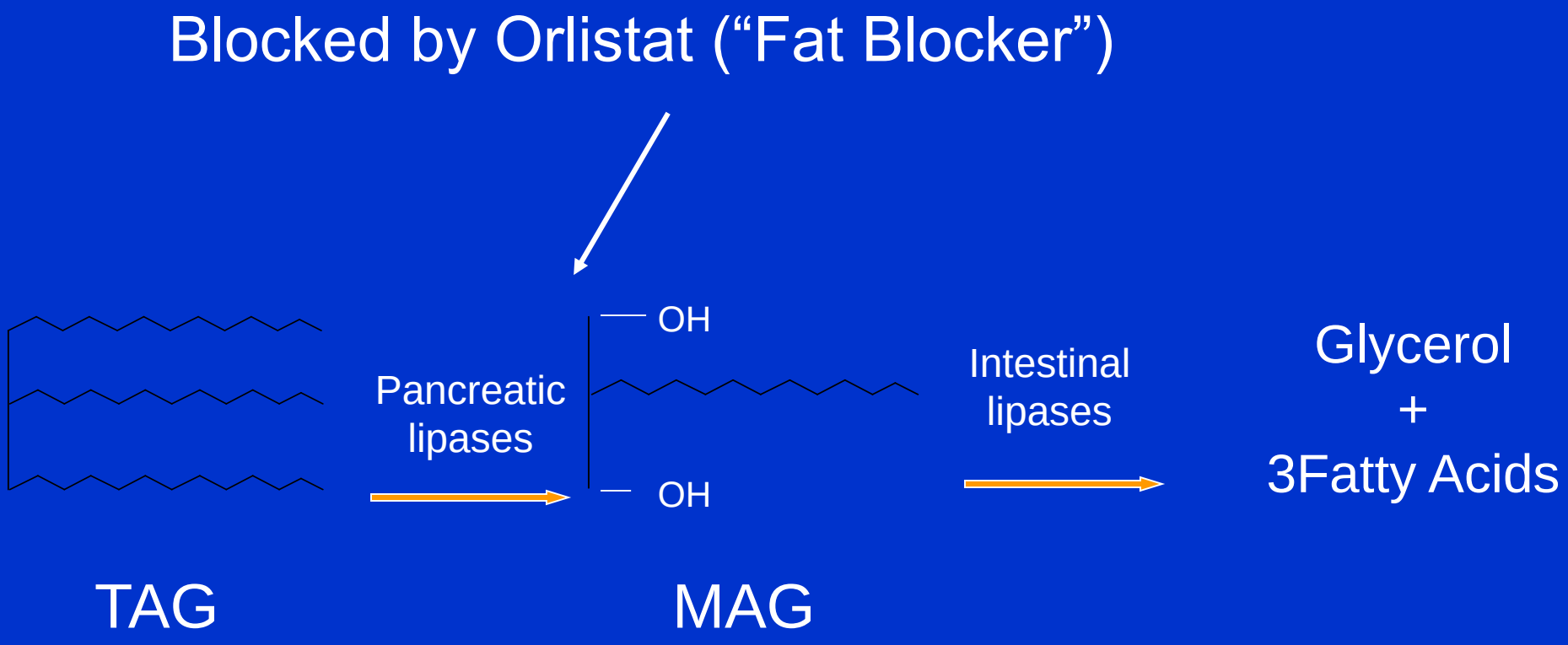
- Little TG are store in liver mostly are excreted in the form of VLDL(TGs+Cholesterol+PL+apolipoprotein+B-100) and released in the blood and delivered to peripheral tissues.
- In the blood stream TGs of VLDL is hydrolysed by lipoprotein lipase, which is located on the wall of blood capillaries. It clears the TGs in VLDL, forming FFA and Glycerol.

Fate Of Triacylglycerol In The adipose tissues

- As Depot fat ready for mobilization when require as fuel. The TGs in adipose tissues are continually undergoing lipolysis and re-estrification.
- TGs undergoes hydrolysis by hormone sensitive lipase to form FA and glycerol.
- Glycerol released in adipose tissues cannot metabolized by adipose tissue due to lack of enzyme kinase and transported by blood to liver and phosphorylate and resulting glycerol phosphate used in TGs or DHAP formation.


Dietary Lipids
Chylomicrons
Transported as Chylomicrons
Adipose tissues
Transported as VLDL
Endogenous lipids - VLDL
Stored as TAG
Transported as Chylomicrons
Transported as VLDL
Transported as HDL
LPL
Peripheral tissues

Digestion of Dietary Triacylglycerols

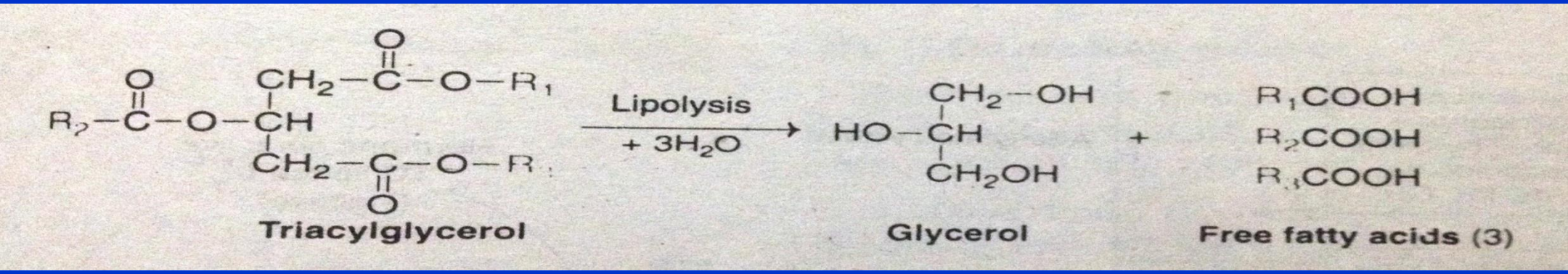


Degradation of TG

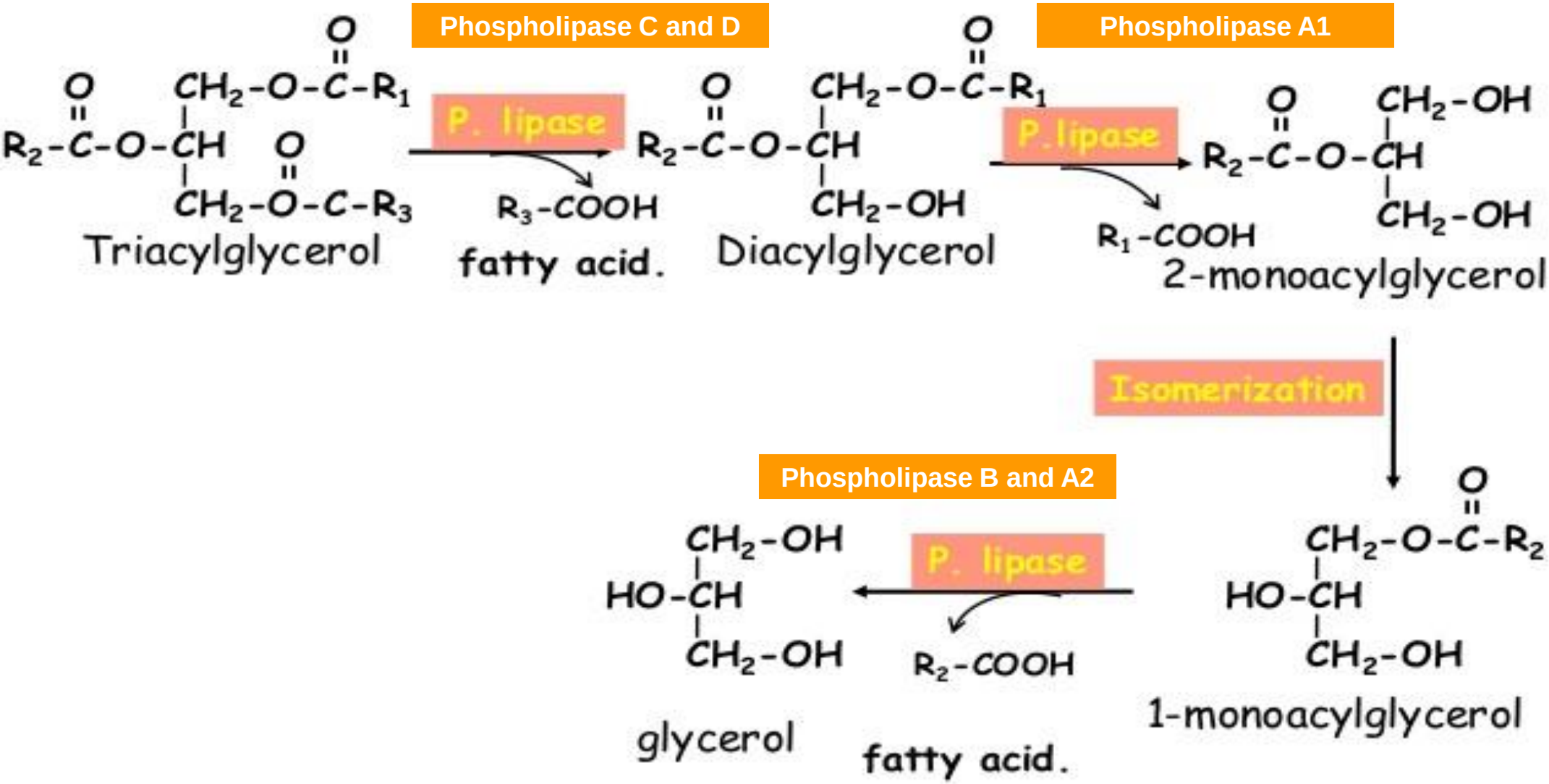
Degradation of TG

1. Phospholipase A1 enzyme hydrolyses the bond b/w C1 of glycerol and first acyl group and FA is removed.
2. Phospholipase B and A2 enzymes hydrolyses the bond b/w C2 of glycerol and second acyl group and FA is removed.
3. Phospholipase C and D enzymes hydrolyses the bond b/w C3 of glycerol and third acyl group and FA removed.

Triacylglycerol —Lipase→ 3FFA +GLYCEROL

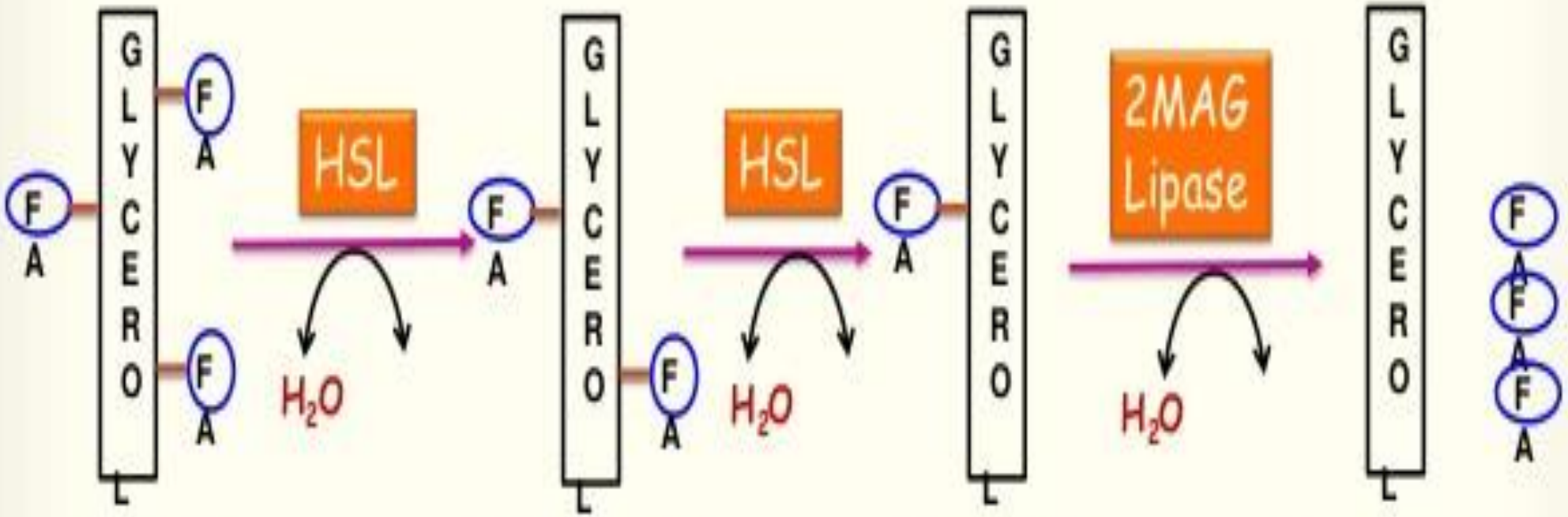


Hydrolysis of TGL by lipase



Hydrolysis of TAG / Lipolysis

Lipase catalyze sequential removal of ester bonds b/w Glycerol & FA



ANY QUESTION

- CHATTERJEA BIOCHEMISTRY
- LIPPINCOTT BIOCHEMISTRY
- HARPERS BIOCHEMISTRY
- SATYANARAYANA BIOCHEMISTRY
- INTERNET

Thank you