بسمه تعالی

گروه علوم دامی
کارشناسی ارشد
بیوشیمی تکمیلی

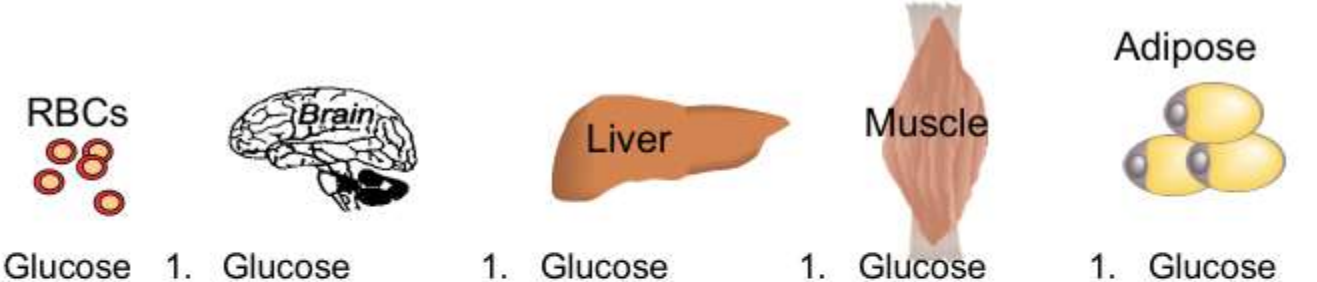
متابولیسم و تولید بیومولکول ها

ابراهیم قاسمی

تولید برخی بیومولکولها

- ترکیبات کربوهیدراتی و مشتقات آن
  - گلوکز
  - لاکتوز
  - ویتامین C
- ترکیبات لیپیدی و مشتقات آن
  - اسیدهای چرب و کلسترول
  - ایکوزانوئیدها
  - تری گلیسرید و فسفولیپیدها و لیپوپروتئین ها
  - اجسام کتونی
- اسیدهای آمینه غیرضروری و مشتقات اسیدهای آمینه

اهمیت گلوکز



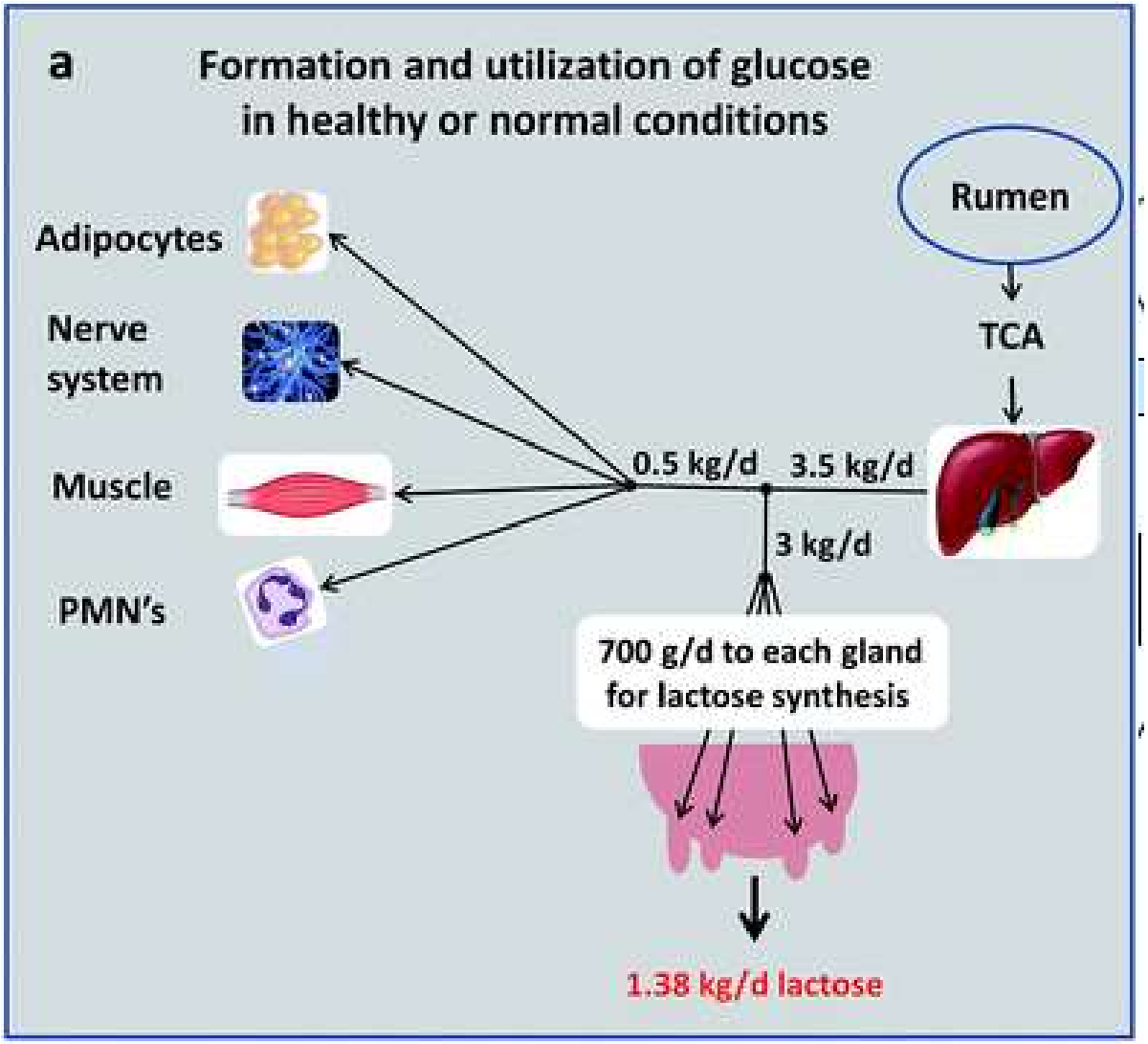
	RBCs	Brain	Liver	Muscle	Adipose
Order of preference	1. Glucose	1. Glucose 2. Ketone bodies	1. Glucose 2. Fatty acids	1. Glucose 2. Fatty acids & Ketone bodies	1. Glucose 2. Fatty acids

Glucose is first-choice fuel for ALL organs
Glucose is only fuel for RBCs → need constant supply

Importance of gluconeogenesis

- **Brain & CNS, erythrocytes, testes & kidney medulla are dependent on glucose for continuous supply for energy.**
- **Human brain alone requires about 120 g of glucose per day, out of about 160 g needed by the entire body.**
- **Glucose is the only source that supplies to the skeletal muscle, anaerobic conditions.**

سوبسترا برای لاکتوز



گلوکز خون حیوانات

Blood Glucose Levels in Domestic Animals[a]

	Glucose (Reference Range and Mean ± SD)	
Species	mmol/liter	mg/d
Horse	4.2–6.4 (5.3 ± 0.4)	75–115 (95 ± 8)
Cow	2.5–4.2 (3.2 ± 0.4)	45–75 (57 ± 7)
Sheep	2.8–4.4 (3.8 ± 0.3)	50–80 (68 ± 6)
Goat	2.8–4.2 (3.5 ± 0.4)	50–75 (63 ± 7)
Chicken	9.3	167.8

گلوکز خون در گوساله

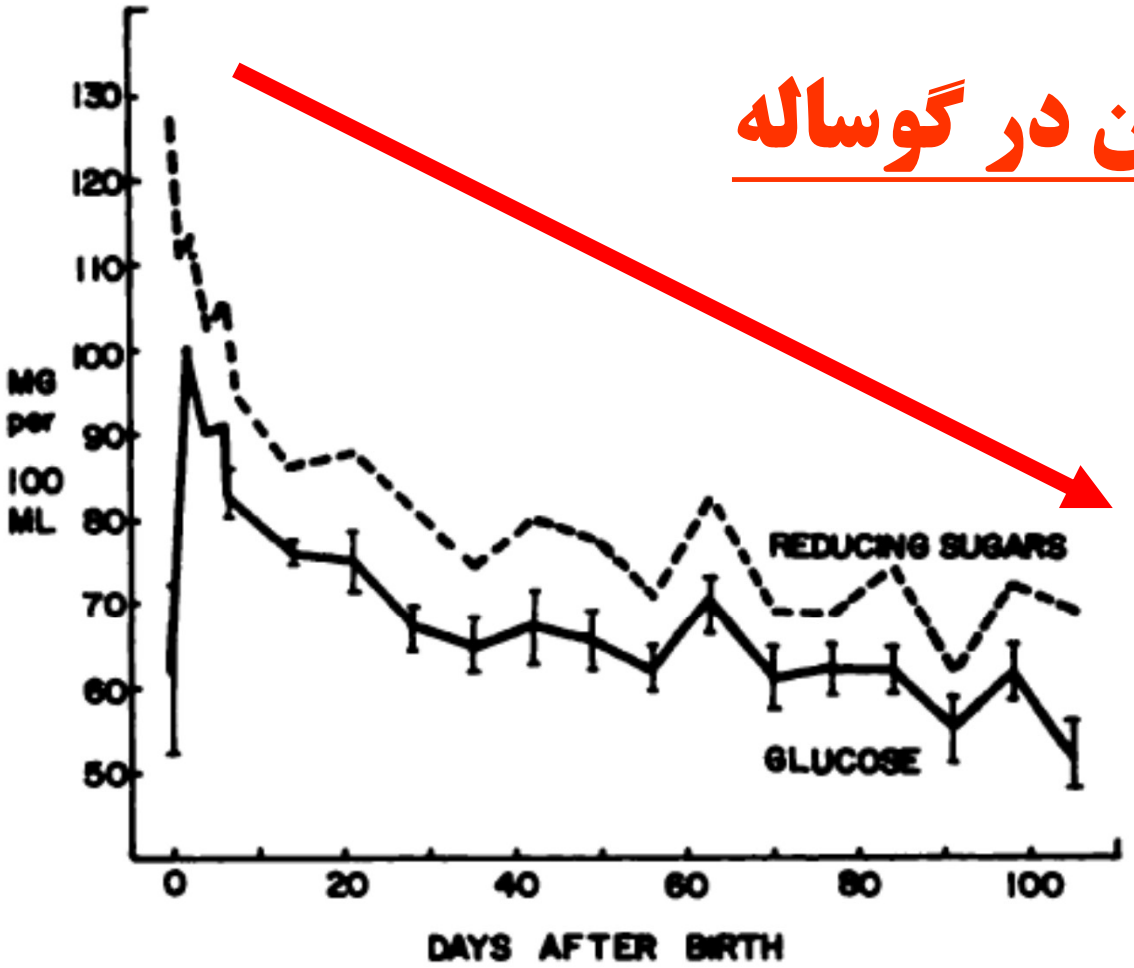


Fig. 1 Whole blood concentration of glucose and total reducing sugars in eight milk-fed calves. The SE are given for weekly glucose values only; those for reducing sugars averaged about 20% higher.

گاو پرواری

Table 3. The effect of varying concentrations of supplemental vitamin C (VC) on blood metabolites of steers consuming a common high-S (0.55% S) diet

Plasma metabolites	CON[1]	5VC[1]	10VC[1]	20VC[1]	SEM	Contrast statement *P*-values[2]		
						CON vs. VC	Linear VC	Quad. VC
Ascorbate,[3] µg/L	1,454.0	1,186.2	1,304.2	1,436.4	64.8	0.08	0.53	0.02
Insulin,[3] µg/L	1.28	1.65	1.85	1.69	0.19	0.07	0.23	0.11
Glucose,[3] mg/dL	99.27	98.43	96.08	103.64	3.31	0.98	0.35	0.23
HOMA-IR[4]	11.09	13.86	15.14	18.74	2.76	0.17	0.09	0.88
Serum NEFA,[3] µEq/L	189.69	175.18	170.82	228.58	19.6	0.93	0.12	0.11

[1]Treatments: CON: control; 5VC: 5 g vitamin C·steer^{-1}·d^{-1}; 10VC: 10 g vitamin C·steer^{-1}·d^{-1}; 20VC: 20 g vitamin C·steer^{-1}·d^{-1}.

[2]Contrast statements: CON vs. VC = no vitamin C vs. vitamin C; Linear VC = linear effect of vitamin C; Quad. VC = quadratic effect of vitamin C.

[3]Jugular blood was drawn before feeding 2 d before harvest.

[4]Homeostasis model assessment, insulin resistance.

میلی مول به میلی گرم

Table 5. Plasma metabolite concentrations of steers fed diets with 0 or 4% tallow and without or with 5 g/d abomasally infused choline[a]

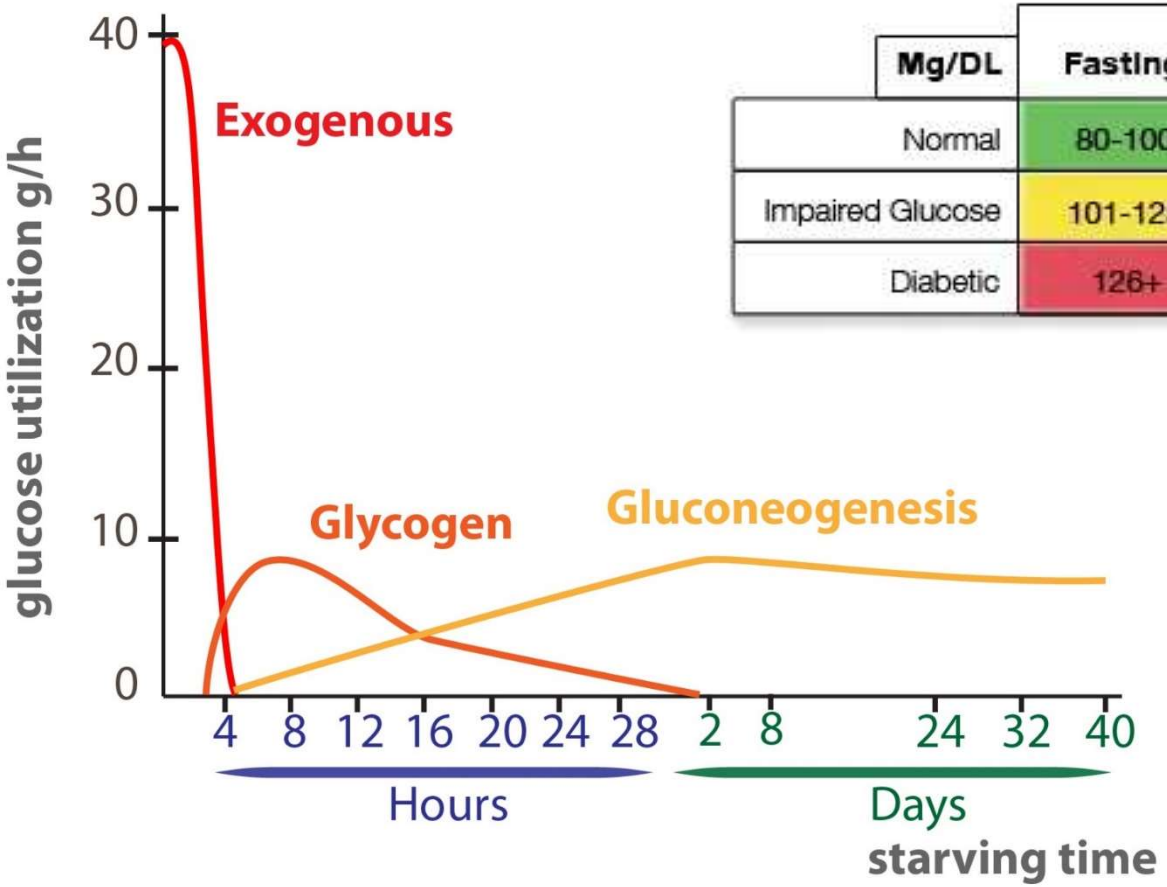
	No tallow		4% tallow		
	Abomasally infused choline, g/d				
Plasma	0	5	0	5	SEM[b]
No. of steers	6	8	8	7	
Triglycerides, mg/100 mL	9.2	7.8	14.2	12.1	2.5
Cholesterol, mg/100 mL[c,d]	85	88	125	114	13
NEFA, μM	67	54	90	102	19
Glucose, mM	5.36	5.60	5.38	5.49	0.14
Urea, mM[c]	1.90	1.52	2.09	2.10	0.15
α-amino N, mM	2.15	2.11	2.12	2.08	0.13

[a]Values are averages of concentrations before, and at 3 and 6 h after feeding on d 13.
[b]For n = 8.
[c]Effect of tallow, $P < 0.05$.
[d]Effect of implant × choline × hour, $P < 0.05$.

Table 4. Least squared means of rumen fermentation parameters, chewing activity and blood metabolites of Afshari and Lori lambs fed a high concentrate diet (% of BW)

Item	Breed		SEM[1]	P-value
	Afshari	Lori		
Rumen parameters				
pH	6.00	6.43	0.081	<0.01
Volatile fatty acids, mM	81.9	83.8	3.80	0.74
Acetate, %	43.9	41.5	2.36	0.48
Propionate, %	29.6	25.7	2.14	0.22
Butyrate, %	8.79	14.1	0.98	<0.01
Valerate, %	2.24	1.36	0.255	0.03
Isovalerate, %	1.02	1.11	0.297	0.84
Acetate: propionate	1.54	1.71	0.187	0.52
Chewing activity				
Eating time, min/d	213	180	13.0	0.13
Ruminating time, min/d	386	378	30.7	0.80
Ruminating/DMI, min/kg	281	354	8.0	0.01
Total chewing/DMI, min/kg	439	525	27.0	0.04
Plasma parameters				
Glucose, mg/dl	77.1	80.3	3.83	0.59
Cholesterol, mg/dl	64.2	57.0	3.24	0.13
Triglycerides, mg/dl	23.0	19.7	2.32	0.18
Blood urea nitrogen, mg/dl	34.0	30.5	4.21	0.57
Total protein, g/dl	6.47	6.40	0.168	0.74

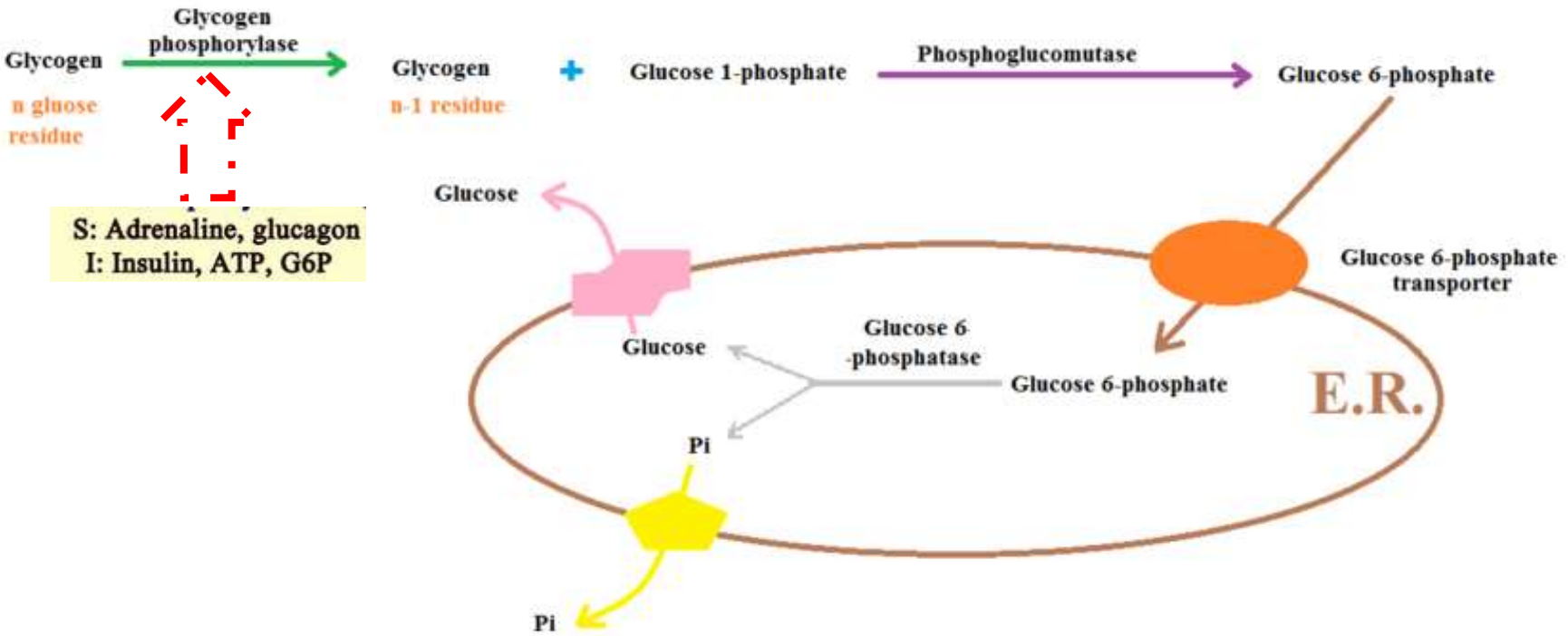
منشاء گلوکز



BLOOD GLUCOSE CHART

Mg/DL	Fasting	After Eating	2-3 hours After Eating
Normal	80-100	170-200	120-140
Impaired Glucose	101-125	190-230	140-160
Diabetic	126+	220-300	200 plus

گلیکوژنولیز



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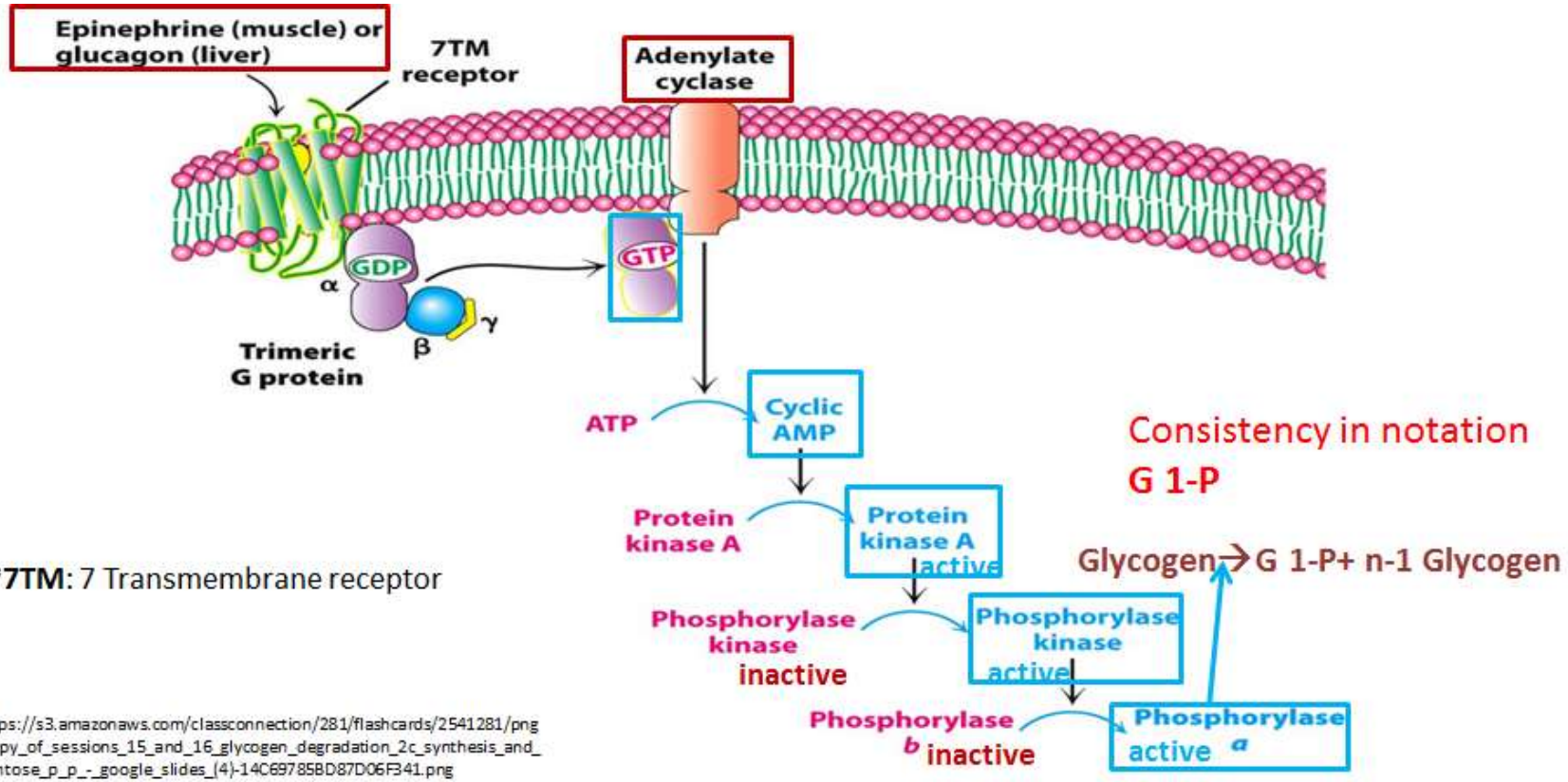

*7TM: 7 Transmembrane receptor

https://s3.amazonaws.com/classconnection/281/flashcards/2541281/png/copy_of_sessions_15_and_16_glycogen_degradation_2c_synthesis_and_pentose_p_p_-_google_slides_(4)-14C69785BD87D06F341.png

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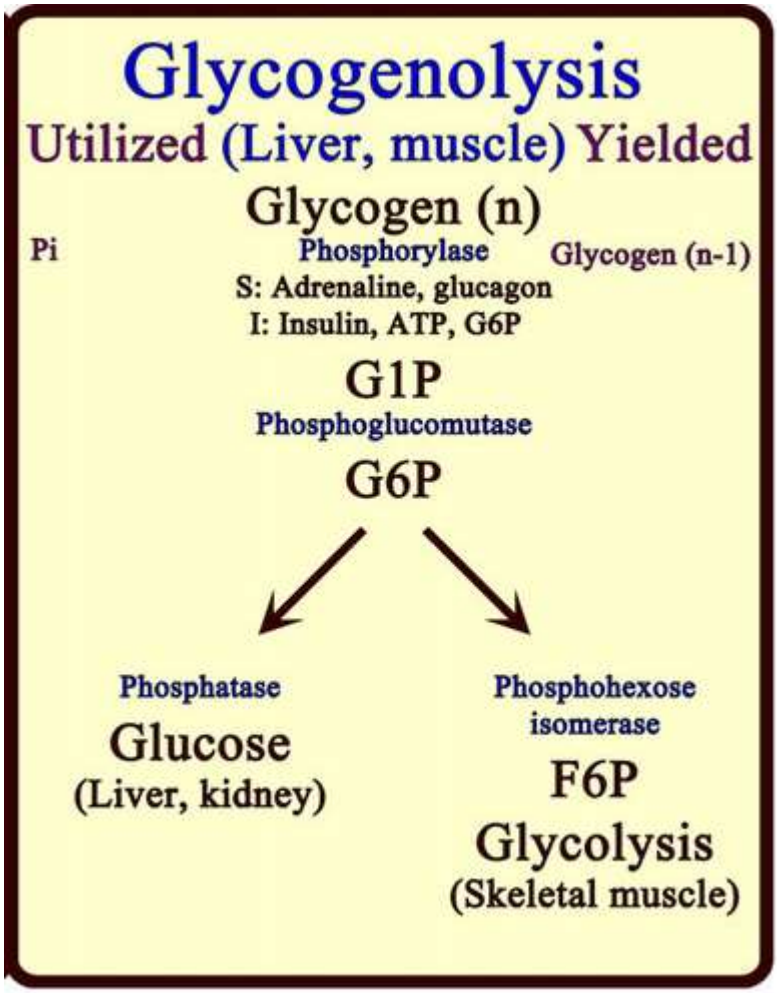
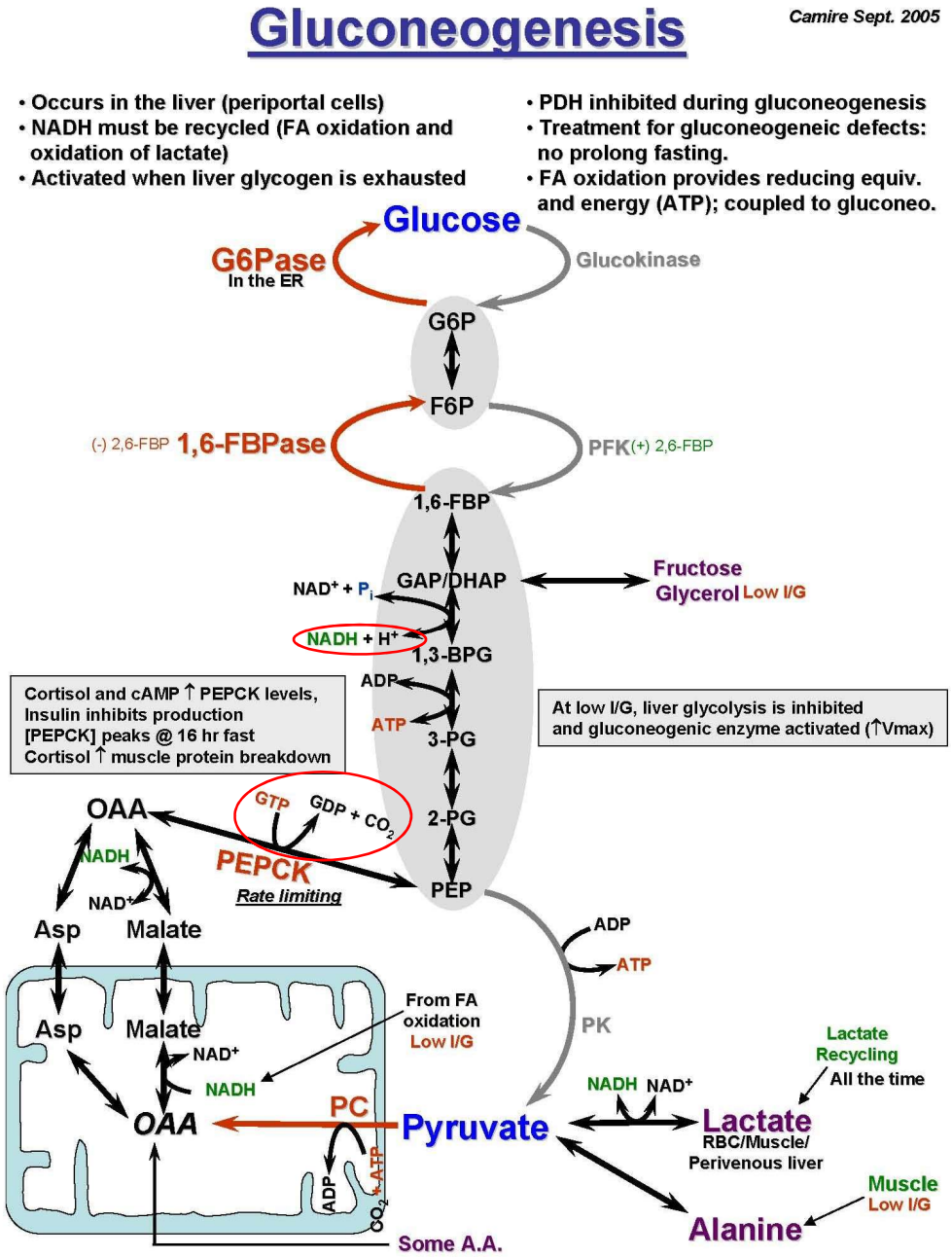


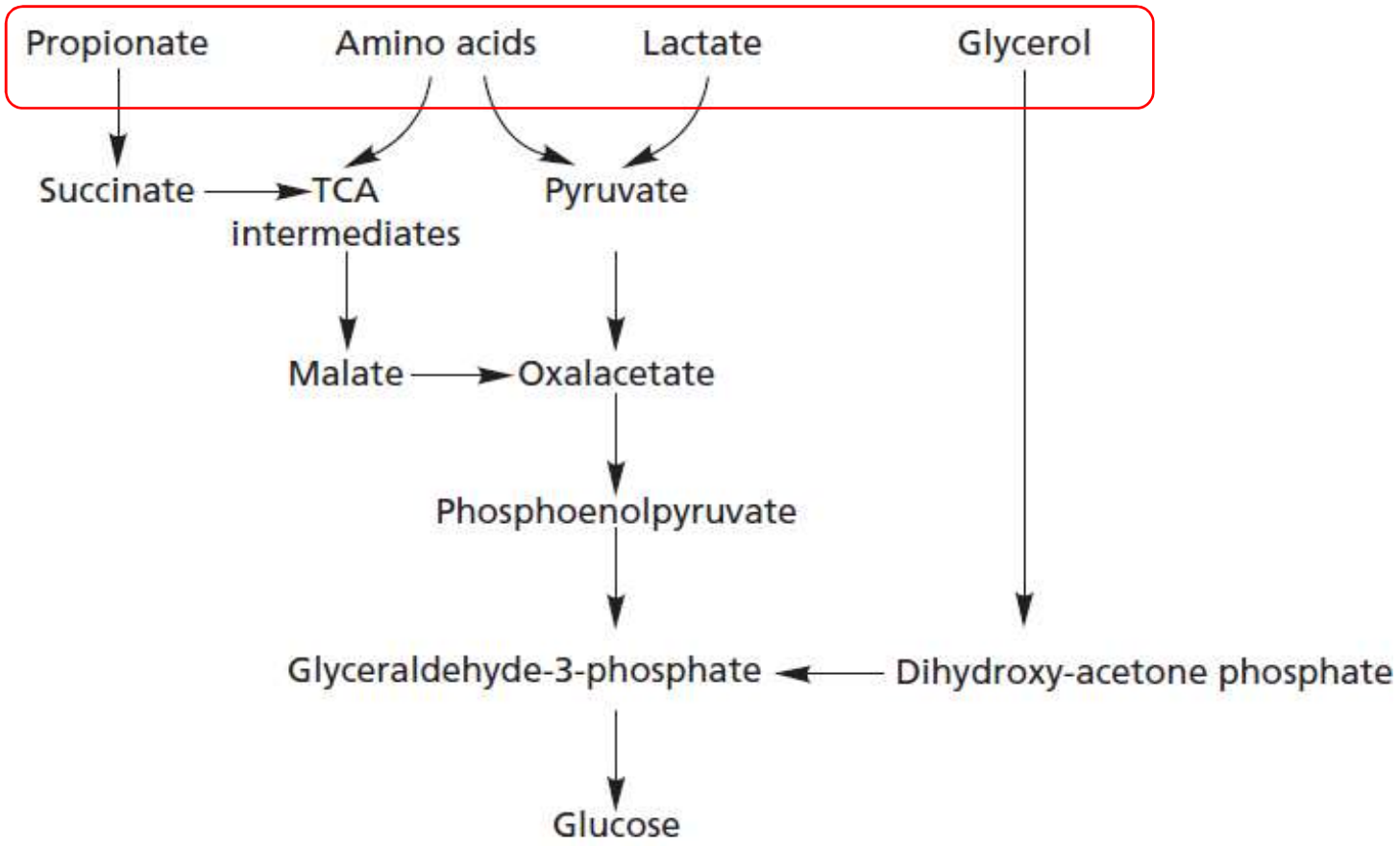


گلوکونئوژنز

- تولید گلوکز
- برداشت لاکتات و گلیسرول
- بی غذایی ۹۰ درصد کبد، کلیه و مقدار ناچیزی در روده
- در گرسنگی طولانی مدت ۶۰٪ در کلیه

گلوکونئوژنز

- گلوکونئوژنز در نشخوارکنندگان بطور مداوم
- گلوکز جذبی از روده باریک تامین کننده حدود ۱۰٪ و گلوکونئوژنز ۹۰٪



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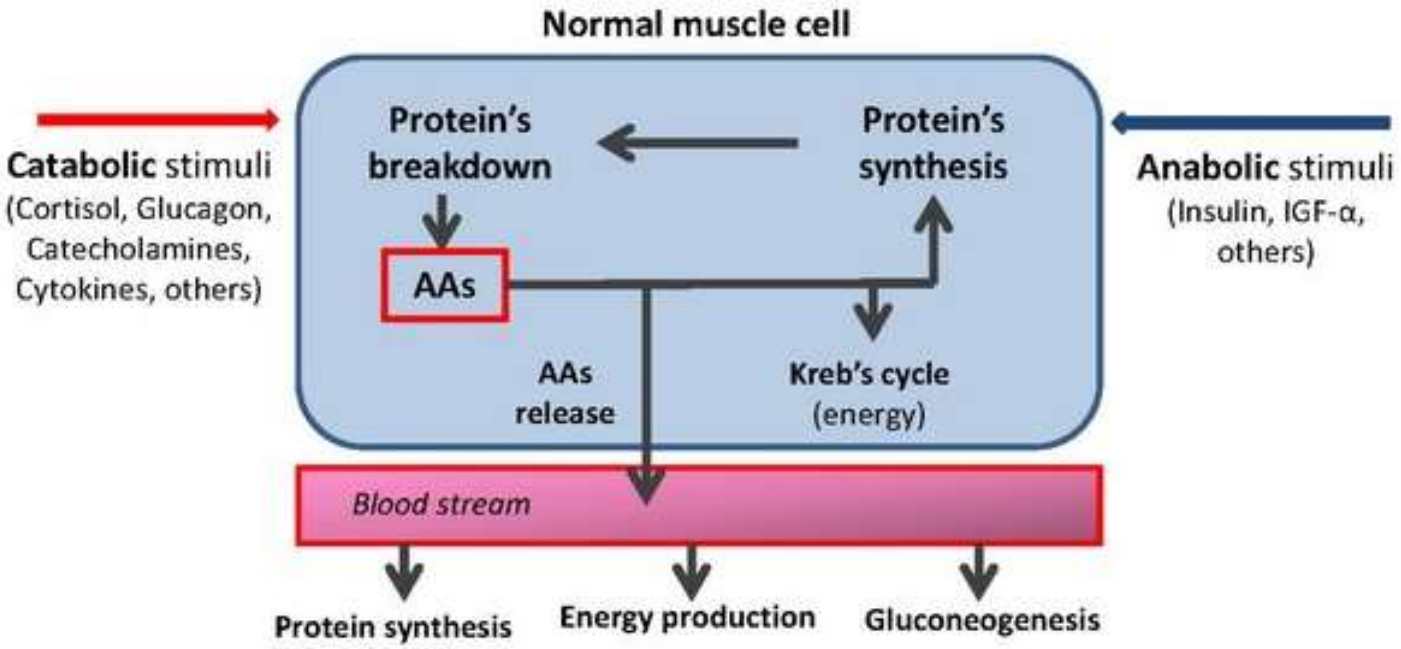
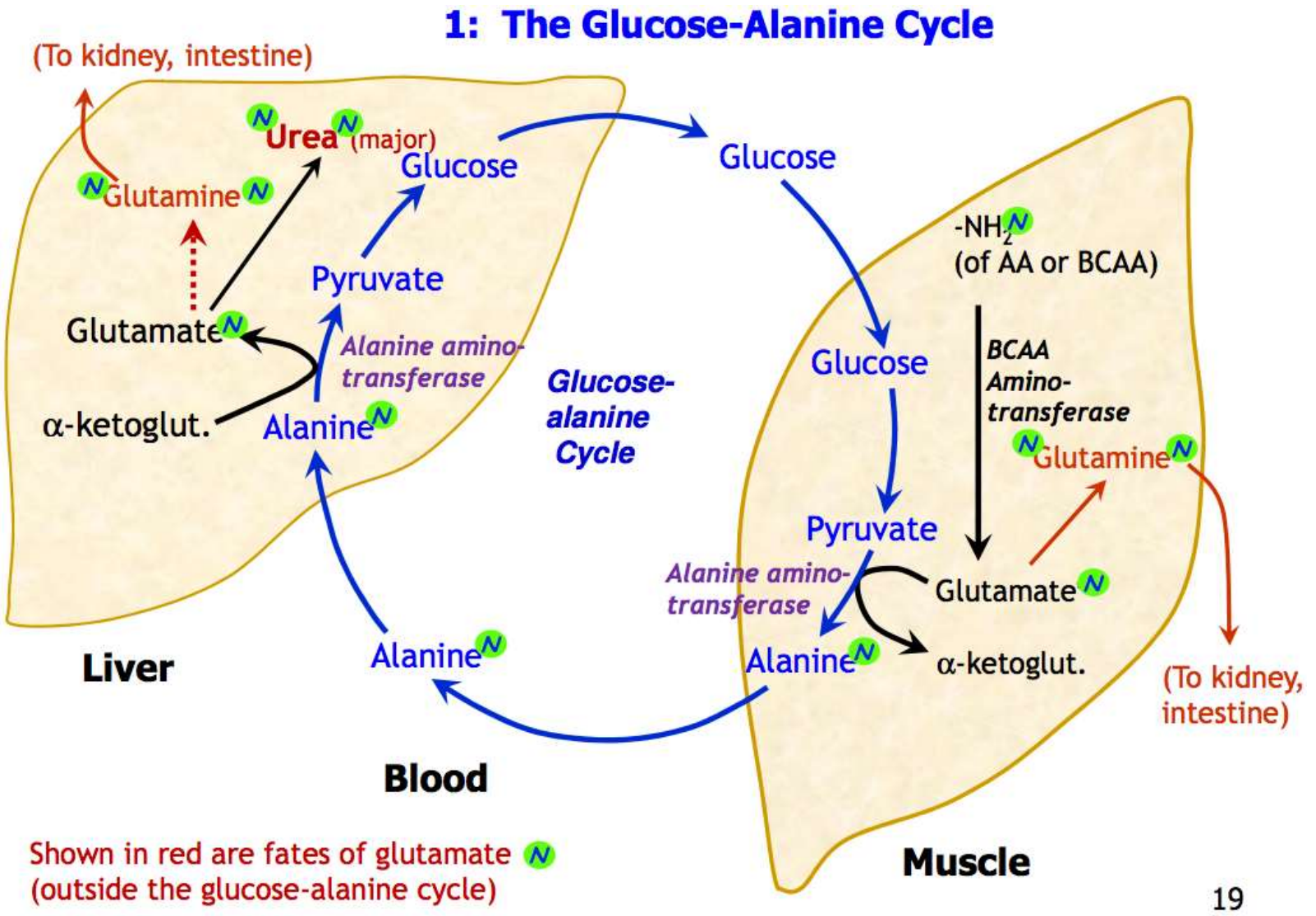
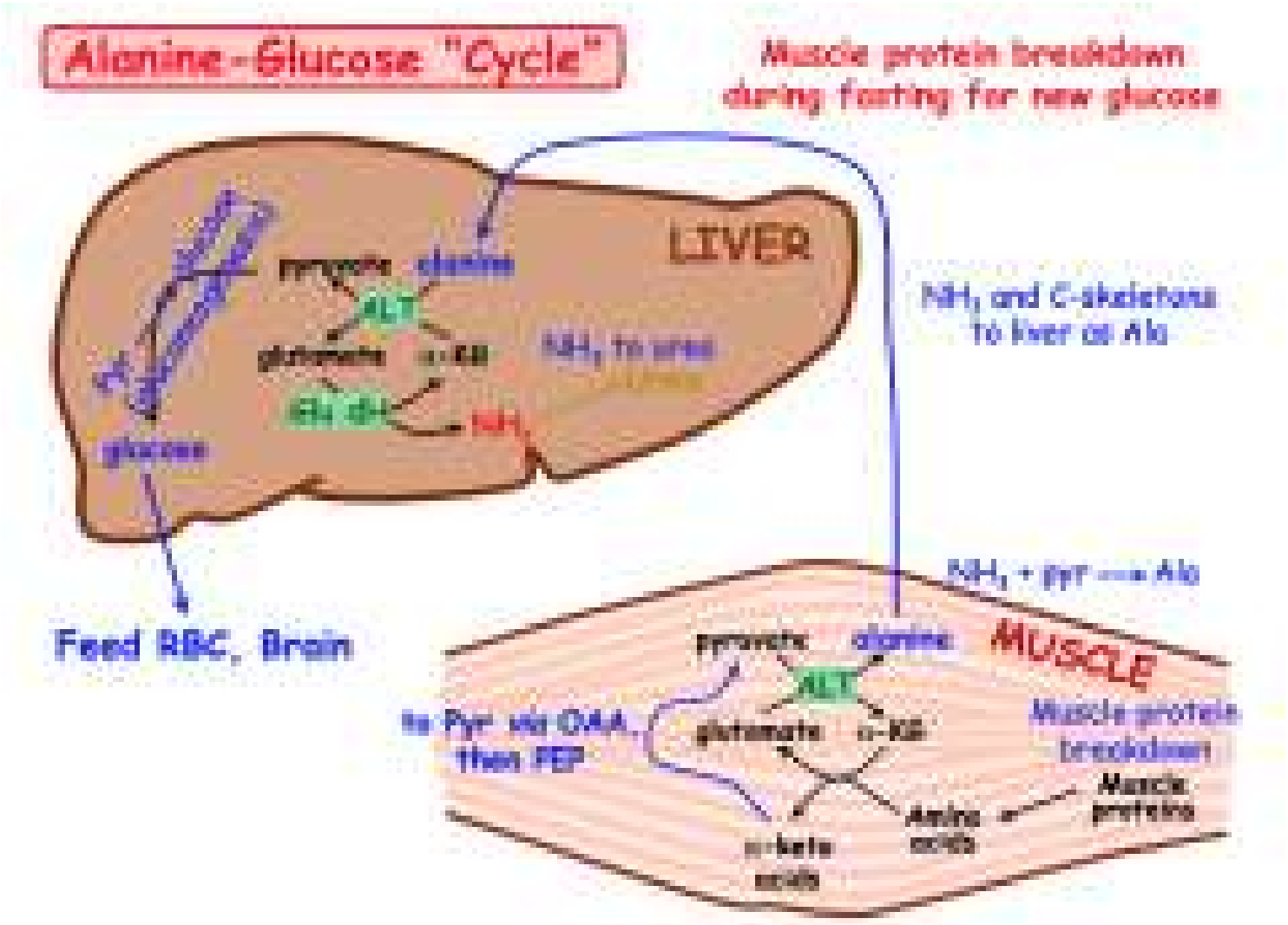
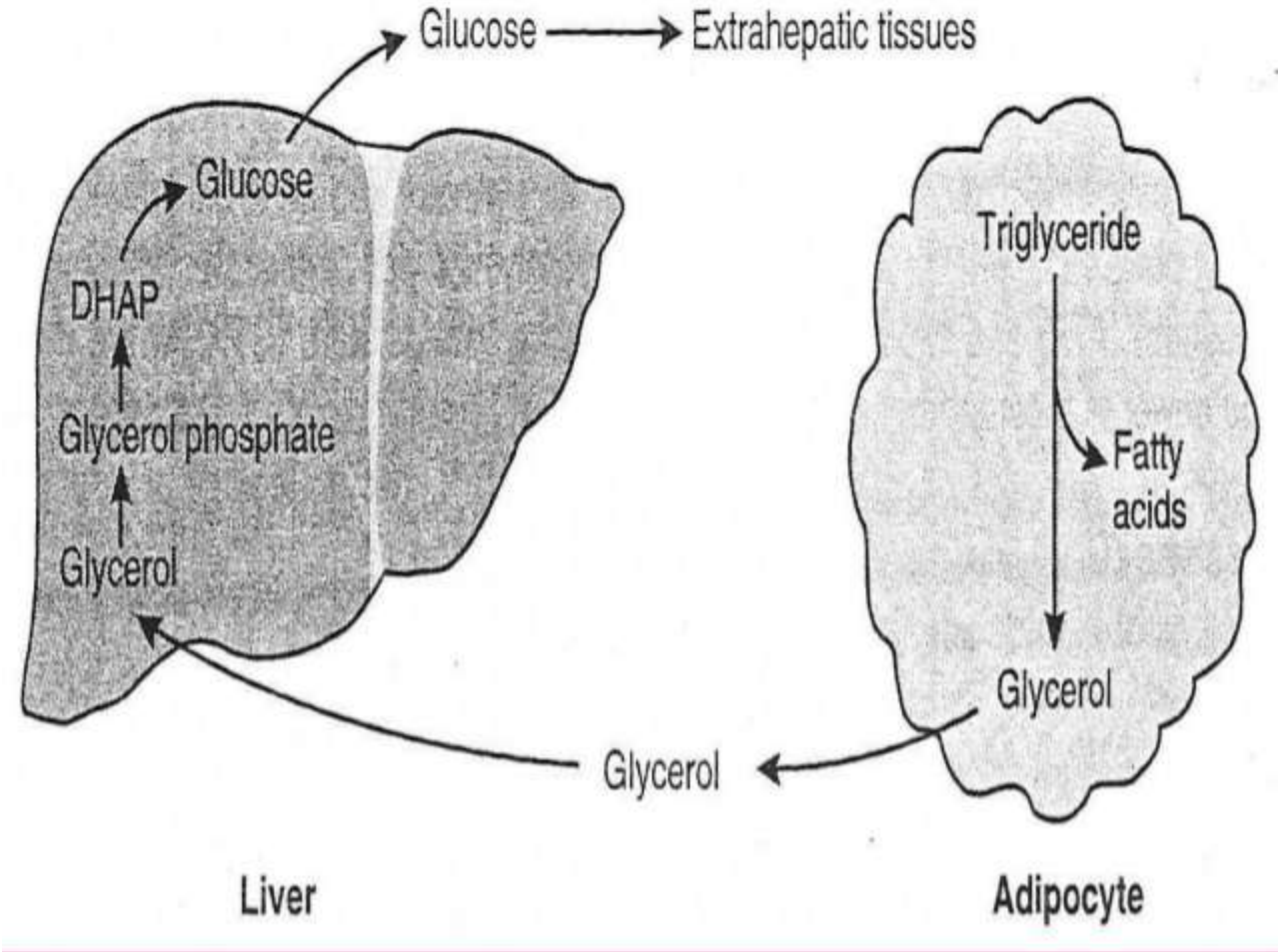

Normal muscle cell
Catabolic stimuli
(Cortisol, Glucagon, Catecholamines, Cytokines, others)
Protein's breakdown
Protein's synthesis
Anabolic stimuli
(Insulin, IGF-α, others)
AAs
AAs release
Kreb's cycle (energy)
Blood stream
Protein synthesis
Energy production
Gluconeogenesis

سوبسترا...

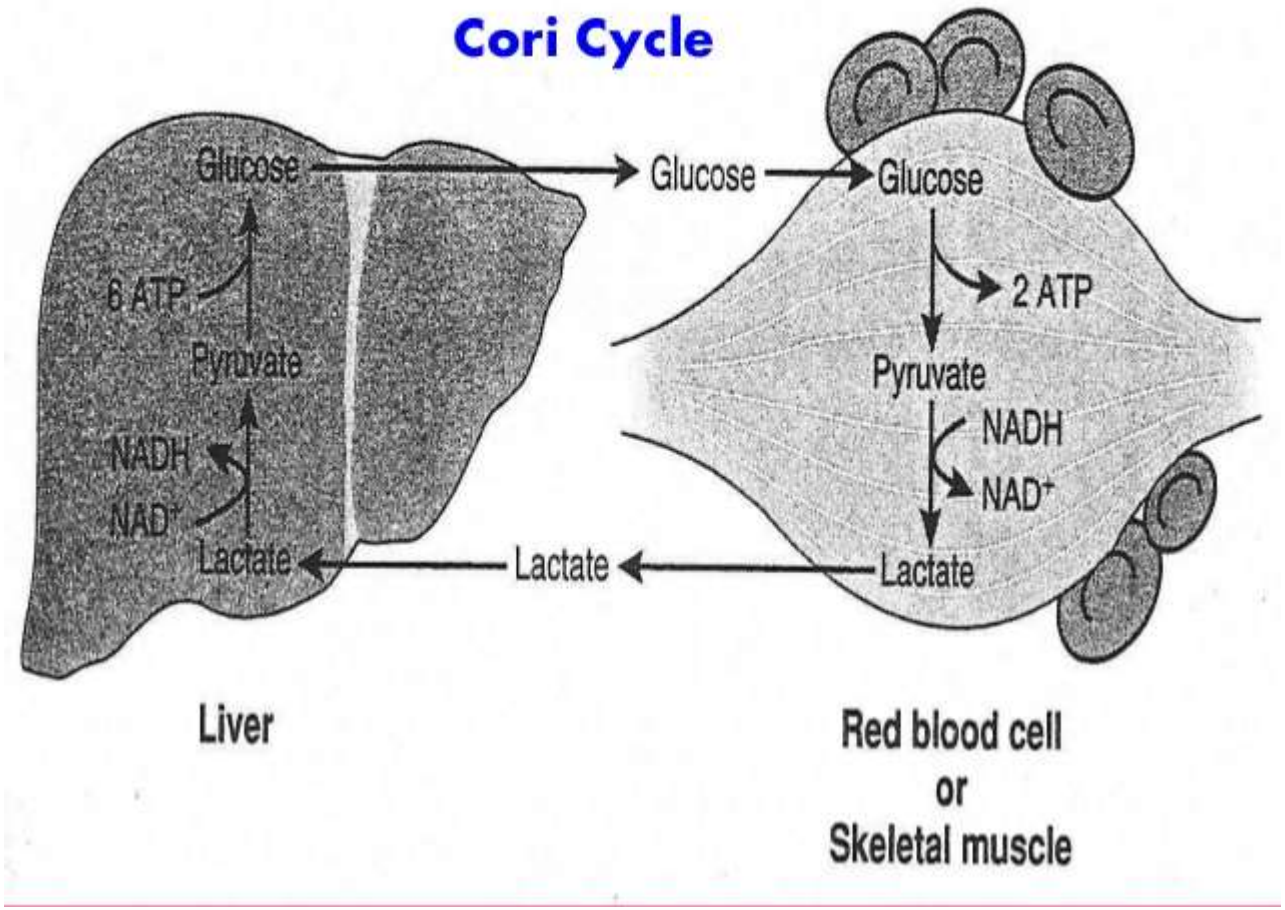

1: The Glucose-Alanine Cycle
(To kidney, intestine)
Urea (major)
Glucose
Glutamine
Pyruvate
Glutamate
Alanine amino-transferase
α-ketoglut.
Alanine
Glucose-alanine Cycle
Glucose
-NH2
(of AA or BCAA)
BCAA Amino-transferase
Glutamine
Glucose
Pyruvate
Alanine amino-transferase
Glutamate
Alanine
α-ketoglut.
(To kidney, intestine)
Liver
Blood
Muscle
Shown in red are fates of glutamate
(outside the glucose-alanine cycle)


Alanine-Glucose "Cycle"
Muscle protein breakdown during fasting for new glucose
LIVER
pyruvate
alanine
ALT
glutamate
α-KG
Glu DH
NH4
glucose
NH4 to urea
NH4 and C-skeletons to liver as Ala
Feed RBC, Brain
NH4 + pyr → Ala
MUSCLE
pyruvate
alanine
ALT
glutamate
α-KG
Muscle protein breakdown
Muscle protein
Amino acids
α-keto acids
to Pyr via OAA, then PEP

... سوبسترا


Glucose
Extrahepatic tissues
Glucose
DHAP
Glycerol phosphate
Glycerol
Triglyceride
Fatty acids
Glycerol
Glycerol
Liver
Adipocyte

... سوبسترا


Cori Cycle
Glucose
Glucose
Glucose
6 ATP
2 ATP
Pyruvate
Pyruvate
NADH
NADH
NAD+
NAD+
Lactate
Lactate
Lactate
Liver
Red blood cell
or
Skeletal muscle

... سوبسترا

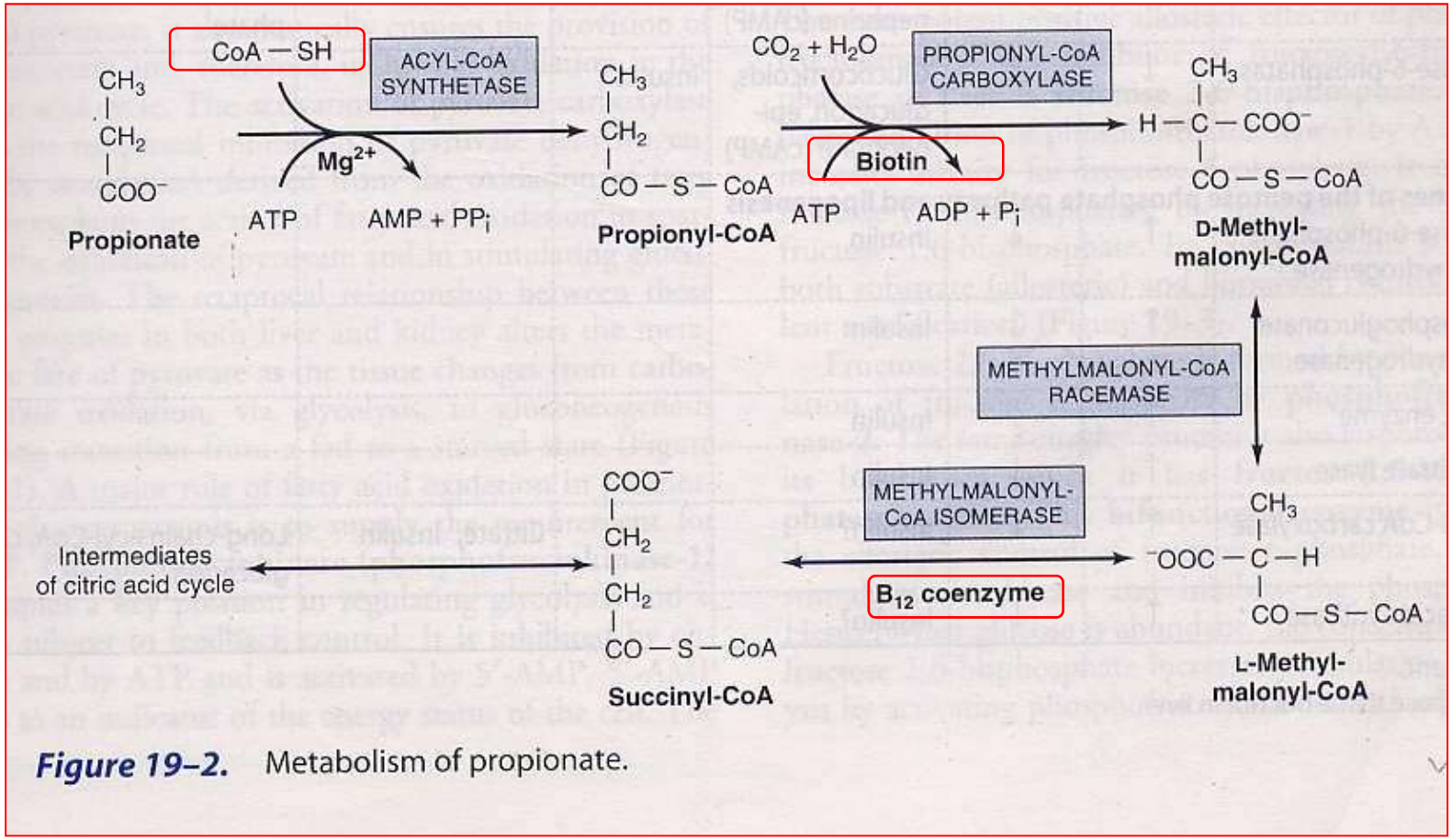


Figure 19–2. Metabolism of propionate.

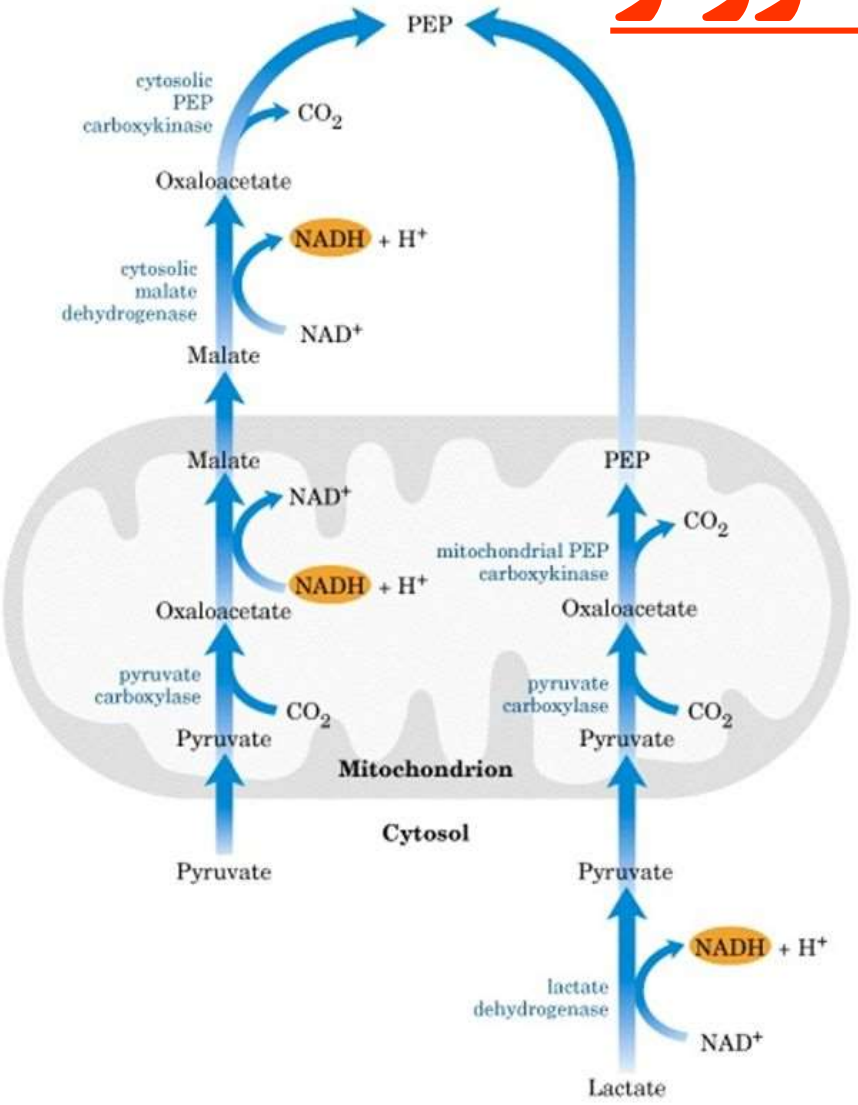
In non-ruminants, including humans, propionate arises from the Beta -oxidation of odd-chain fatty acids that occur in ruminant lipids, as well as the oxidation of isoleucine and the side-chain of cholesterol, and is a (relatively minor) substrate for gluconeogenesis.

Gluconeogenesis

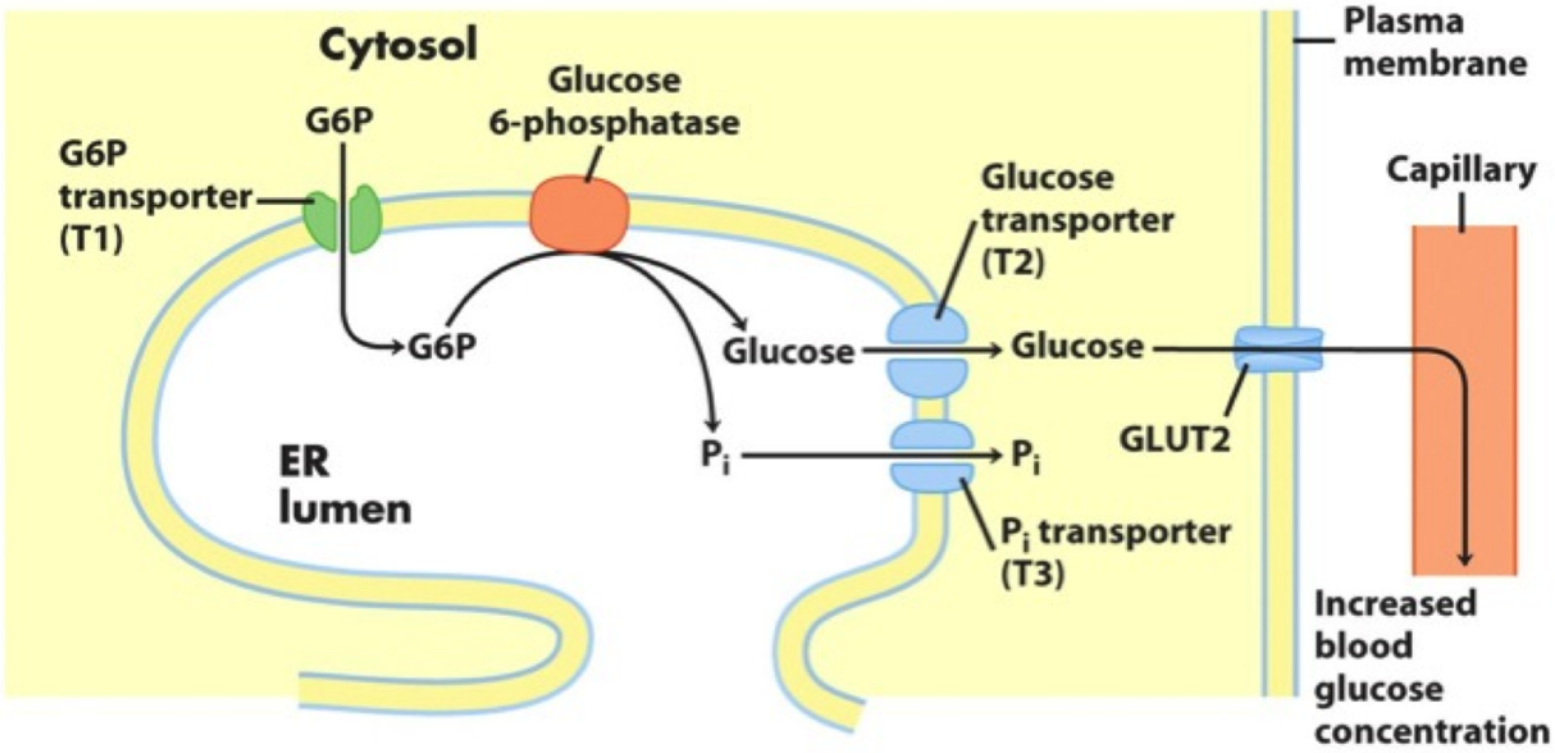
2. Enzymes

Oxaloacetate shuttled back to cytosol:

گلوکونئوژنز...



Glucose-6-Phosphatase and Release of Glucose into the Bloodstream



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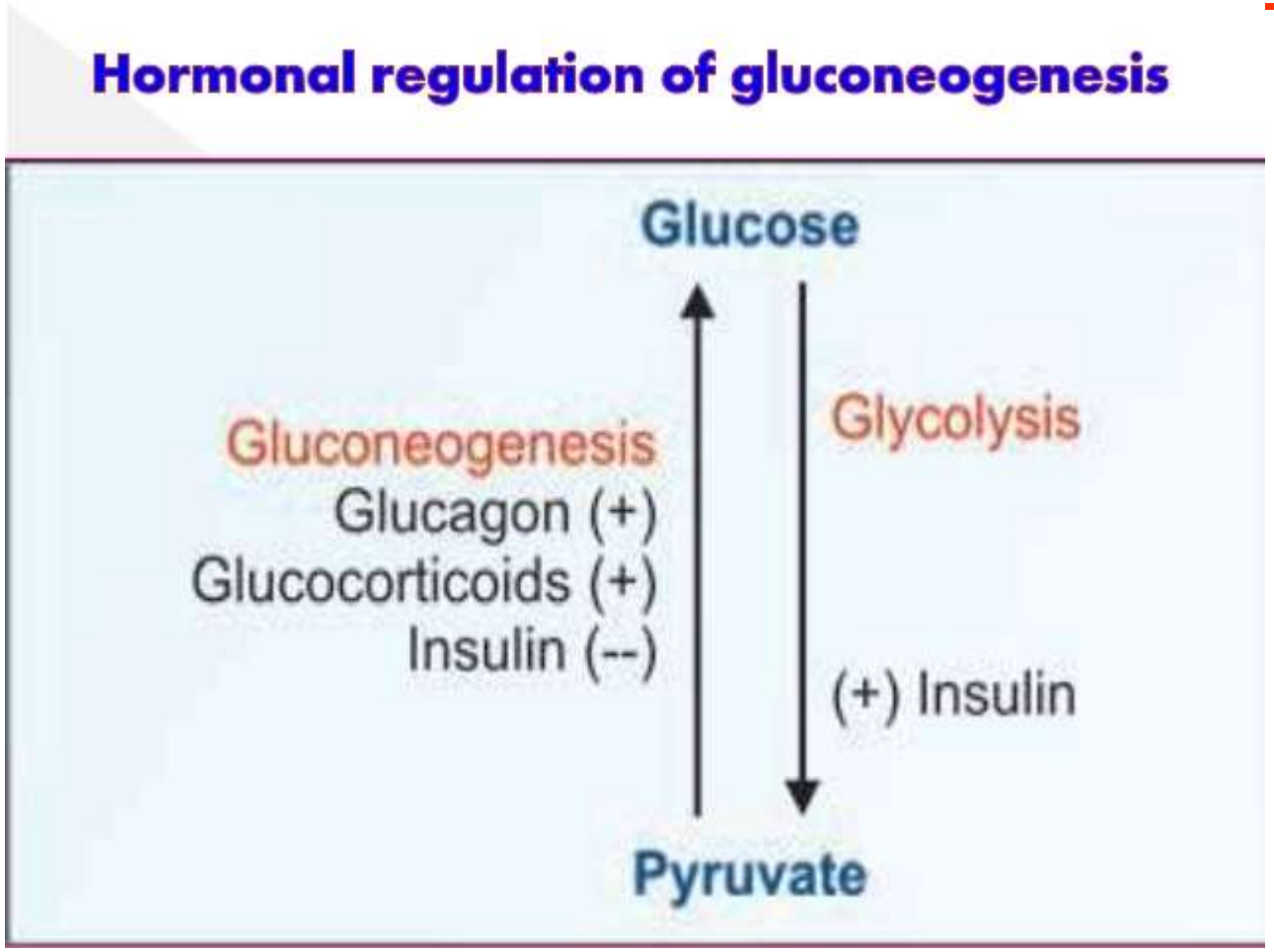
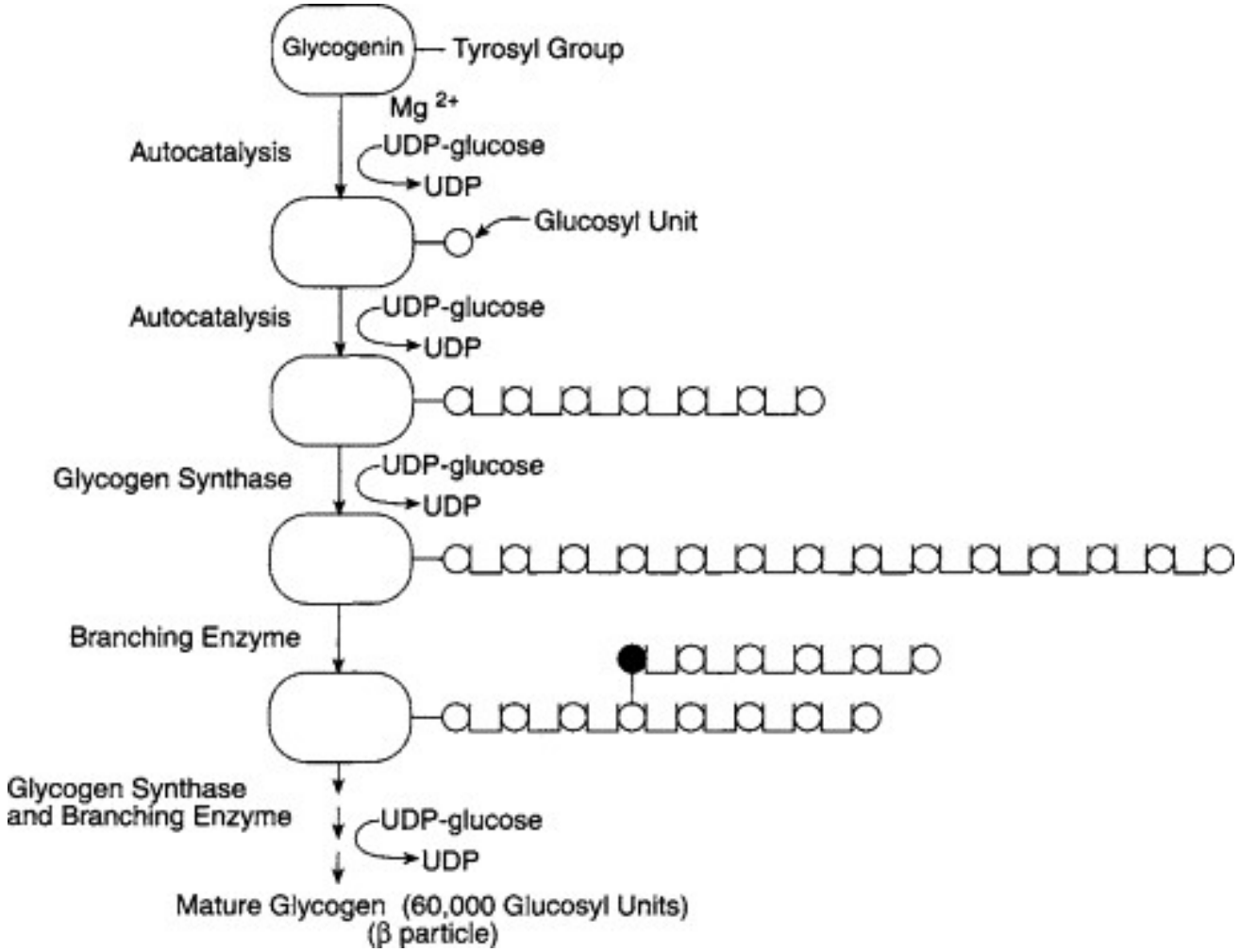

Hormonal regulation of gluconeogenesis
Glucose
Gluconeogenesis
Glucagon (+)
Glucocorticoids (+)
Insulin (--)
Glycolysis
(+) Insulin
Pyruvate

تولید گلیکوژن



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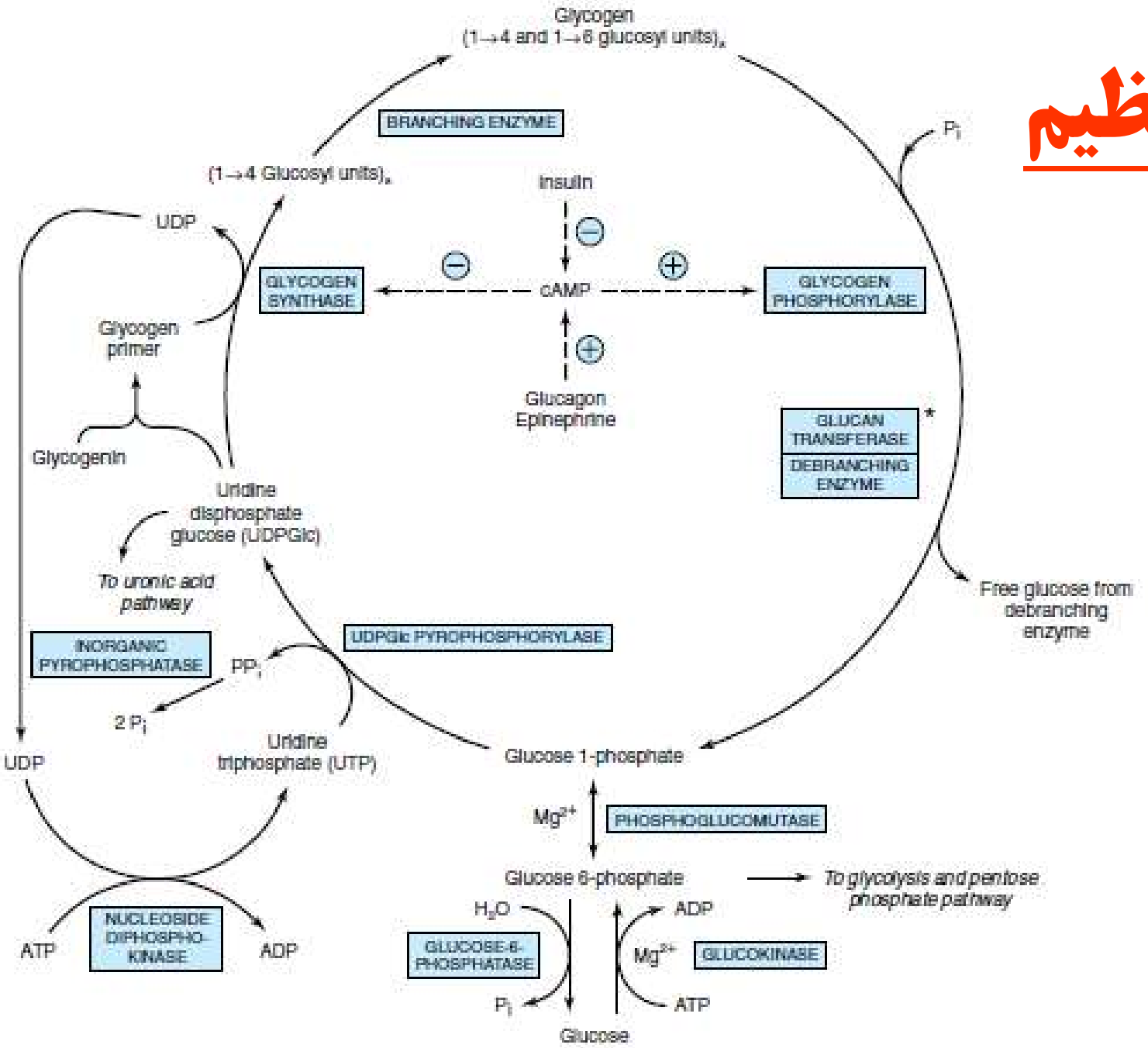
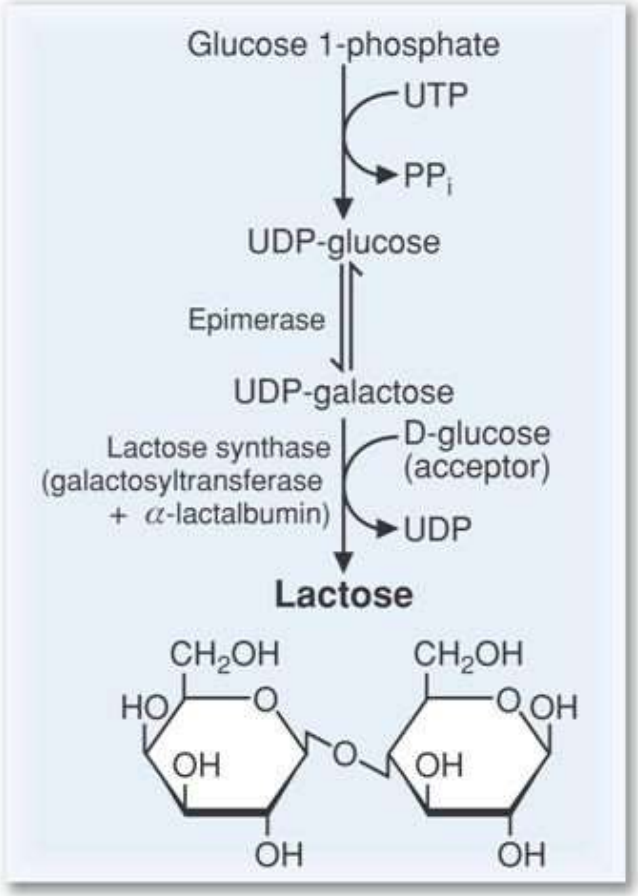

Glycogen
(1→4 and 1→6 glucosyl units)n
BRANCHING ENZYME
(1→4 Glucosyl units)n
Pi
Insulin
UDP
GLYCOGEN SYNTHASE
cAMP
GLYCOGEN PHOSPHORYLASE
Glycogen primer
Glucagon
Epinephrine
GLUCAN TRANSFERASE
DEBRANCHING ENZYME
Glycogenin
Uridine diphosphate glucose (UDPGlc)
To uronic acid pathway
Free glucose from debranching enzyme
INORGANIC PYROPHOSPHATASE
PPi
UDPGlc PYROPHOSPHORYLASE
2 Pi
UDP
Uridine triphosphate (UTP)
Glucose 1-phosphate
Mg2+
PHOSPHOGLUCOMUTASE
Glucose 6-phosphate
To glycolysis and pentose phosphate pathway
H2O
ADP
GLUCOSE-6-PHOSPHATASE
Mg2+
GLUCOKINASE
Pi
ATP
Glucose
ATP
NUCLEOSIDE DIPHOSPHO-KINASE
ADP

Synthesis of Lactose

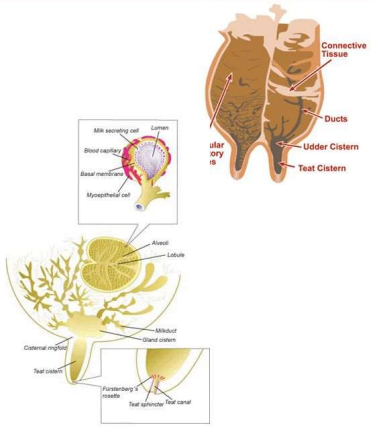


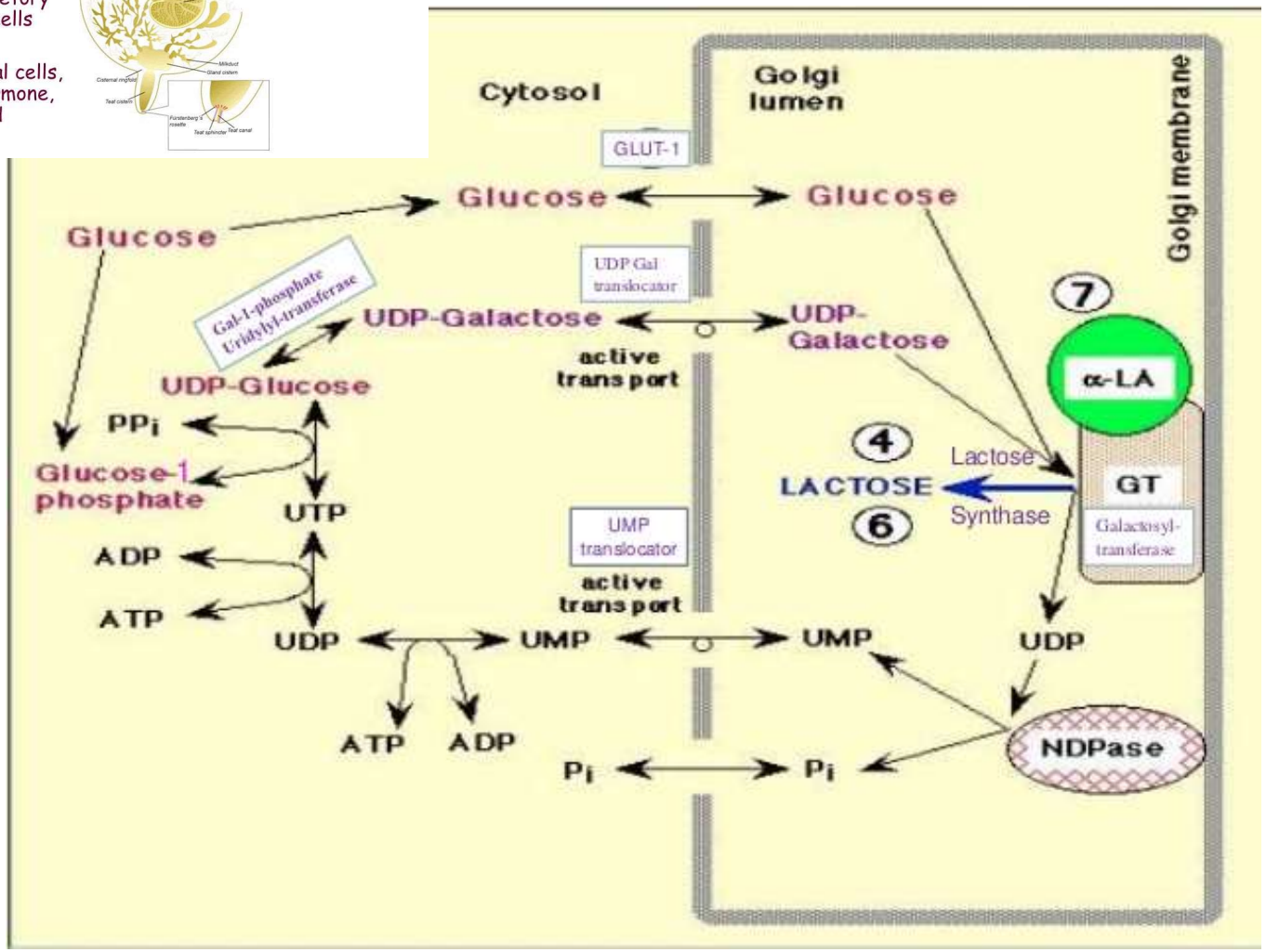
- Lactose = **glucose** + **galactose**
- Only synthesized in mammary for short periods during lactation
- **Lactose synthase** catalyzes transfer of galactose from UDP-galactose to glucose (NOT UDP-glucose) to form glycosidic bond
- Lactose synthase has 2 subunits
  1. **Galactosyltransferase** (enzyme)
  2. **α-Lactalbumin** (regulatory subunit)
     - Synthesized after childbirth in response to **prolactin**
     - Lowers K_m of galactosyltransferase for glucose (1200 mM → 1 mM) to increase rate of lactose synthesis
- Without α-lactalbumin, **Galactosyltransferase** normally transfers galactosyl units to glycoproteins
- α-Lactalbumin acts as **"specifier"** protein by altering substrate specificity

تولید لاکتوز

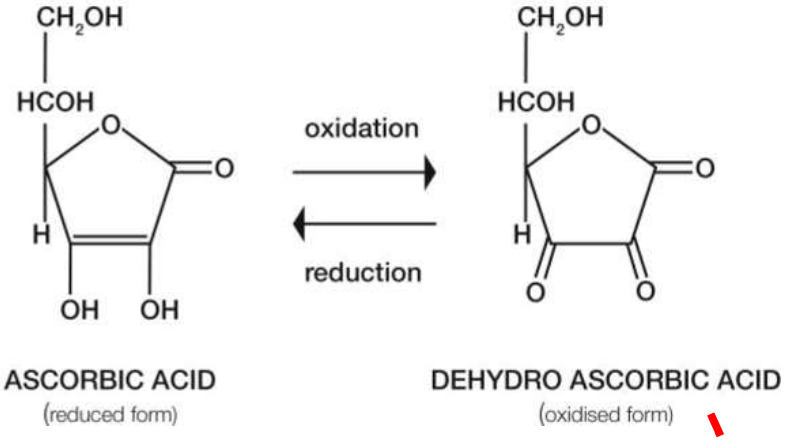
The inside of the udder has two main type of tissue:

- Connective (fibrous) tissue or collagen
- Fatty tissue (adipose cells)
- Secretory (glandular) tissue:
  - Milk ducts
  - Lobules, lobes
  - Alveoli, secretory (epithelial) cells
  - Lumen
  - Myoepithelial cells, oxytocin hormone, capillary bed



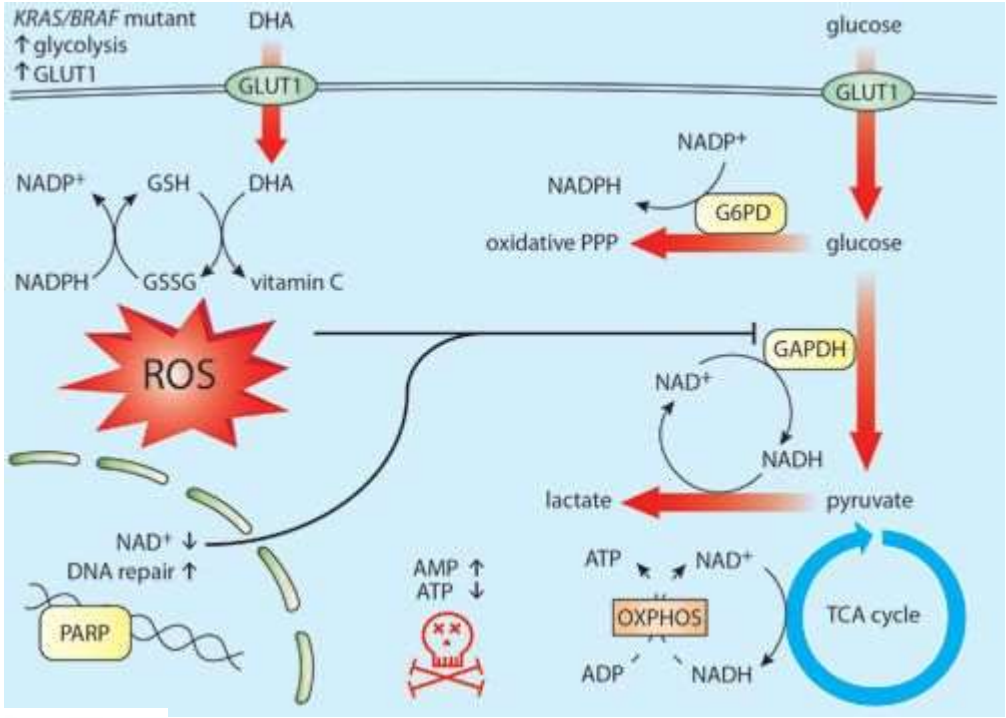


ویتامین C



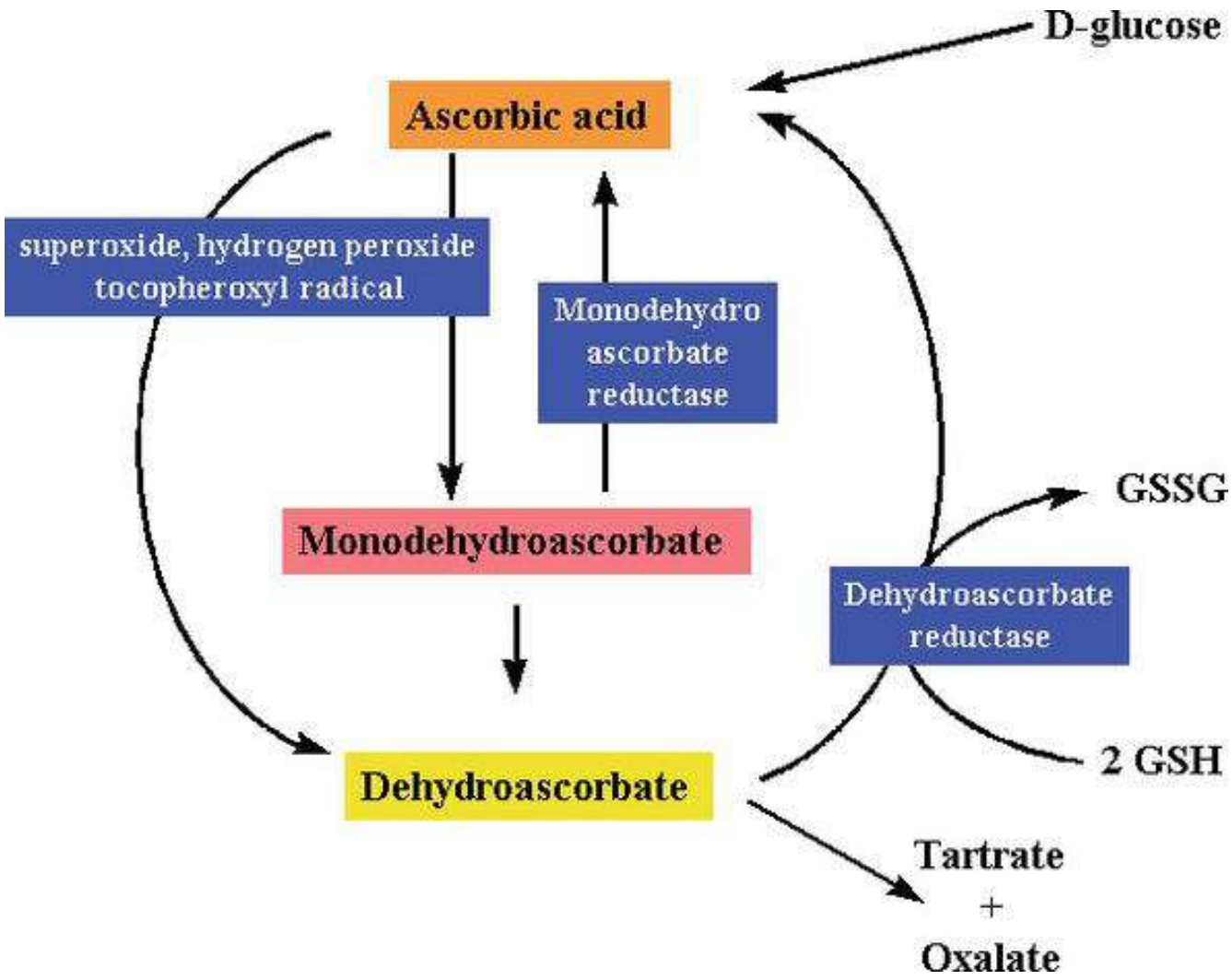
ASCORBIC ACID
(reduced form)

DEHYDRO ASCORBIC ACID
(oxidised form)



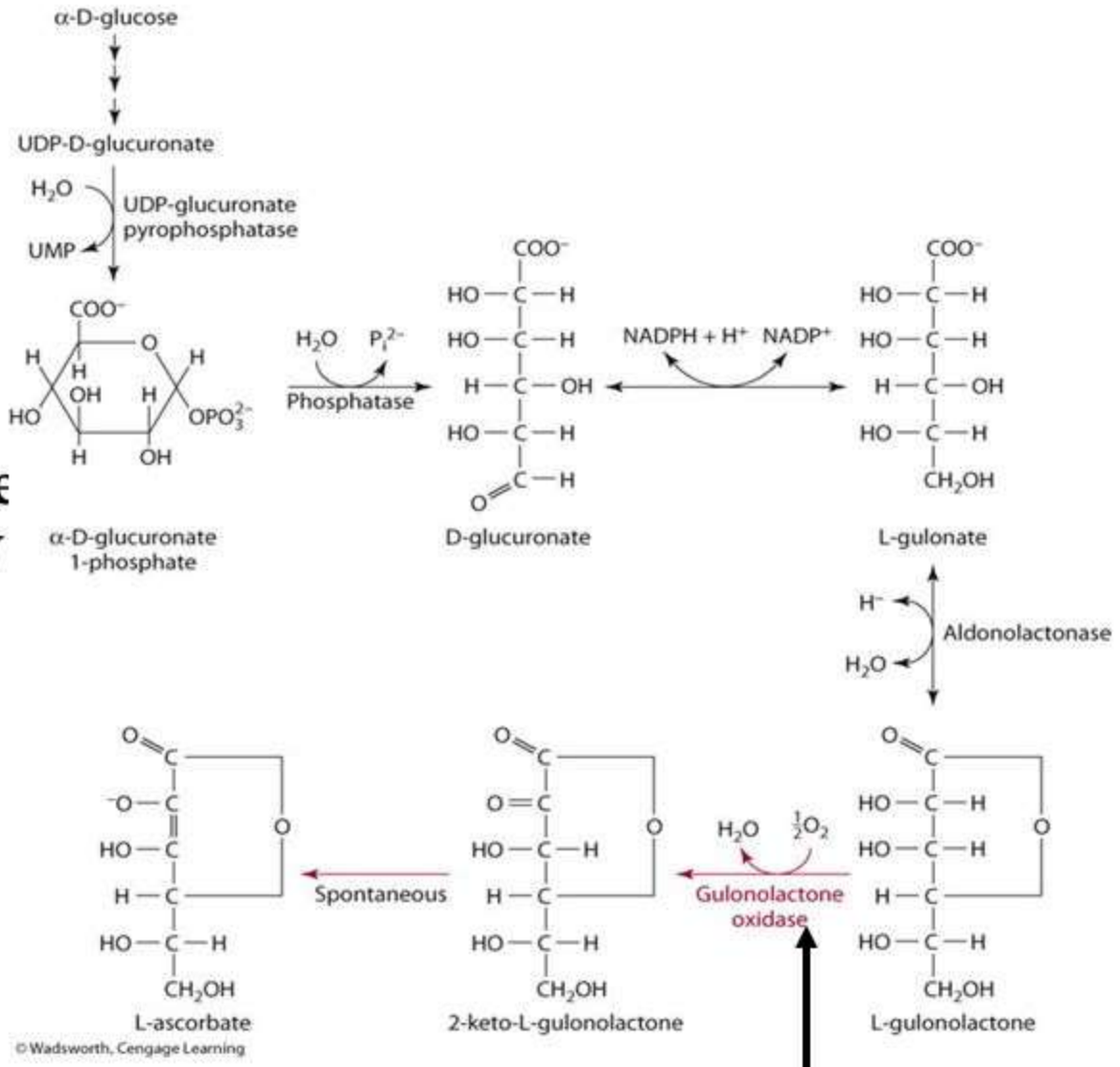
Oxidized form may be further oxidized to 2,3-diketogulonic acid.

- Diketolulonic acid is cleaved into oxalic acid and 4 or 5 carbon sugars.


D-glucose
Ascorbic acid
superoxide, hydrogen peroxide
tocopheroxyl radical
Monodehydro
ascorbate
reductase
Monodehydroascorbate
GSSG
Dehydroascorbate
reductase
2 GSH
Dehydroascorbate
Tartrate
+
Oxalate

PATHWAY OF VITAMIN C BIOSYNTHESIS:

Primates lack the enzyme marke with the ARROW



Missing enyzme

Ascorbate (Vitamin C)

- **Active form and function:**
- Active form is ascorbate
- **Functions :**

1-Important antioxidant, inactivates free oxygen radicals , and protects other antioxidant vitamins A and E.

2- Essential for iron absorption , reducing F3+ to F2+.

3 - It has mild anti-histamine effect.

4- important for the immune system (antibodies and white blood cells), strengthening resistance to infection.

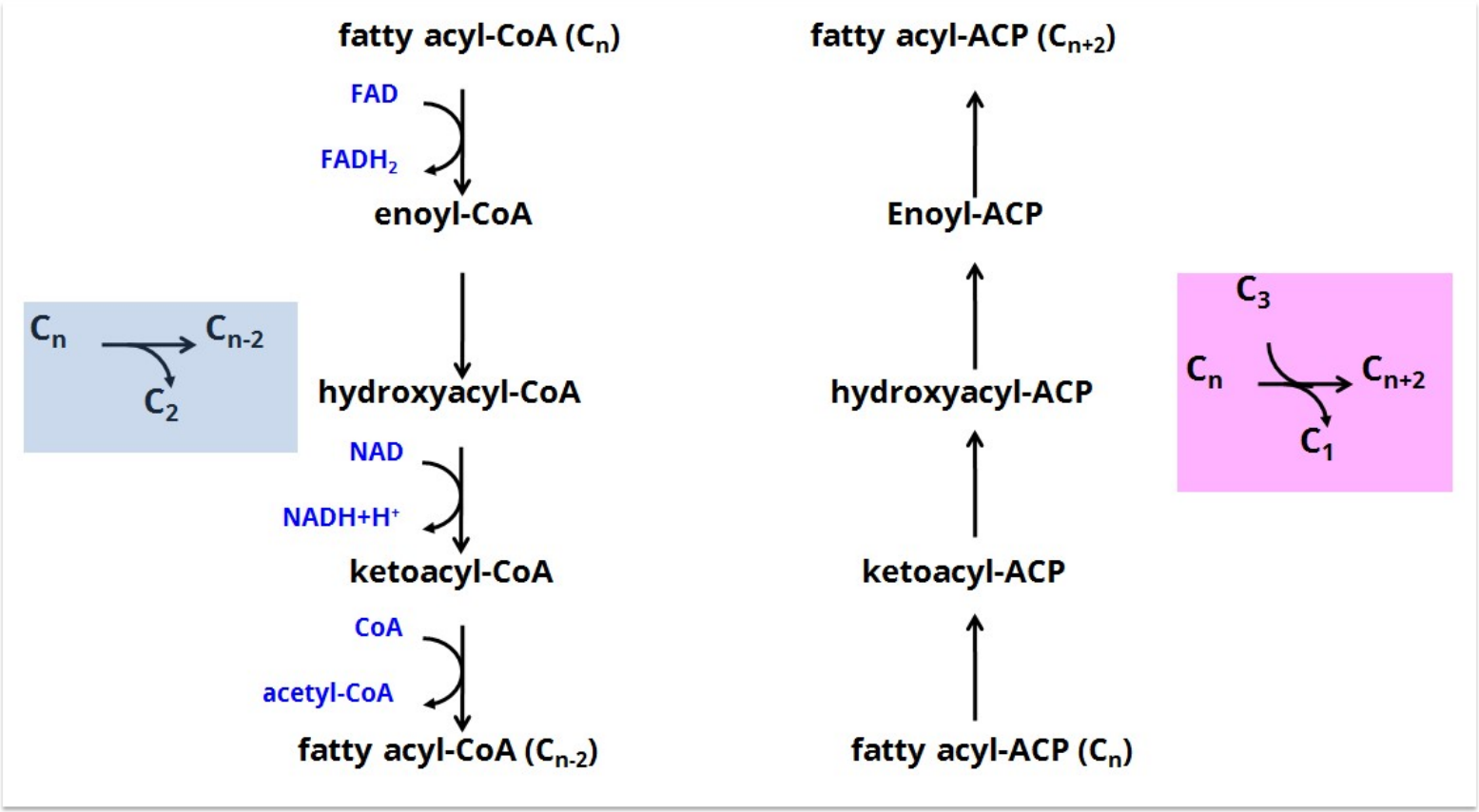
5- Coenzyme in hydroxylation reactions :

- Collagen formation (essential for formation of hydroxylysine and hydroxyproline.
- Formation of corticosteroid hormones in the adrenal gland.
- It is important for formation of adrenaline and noradrenaline.

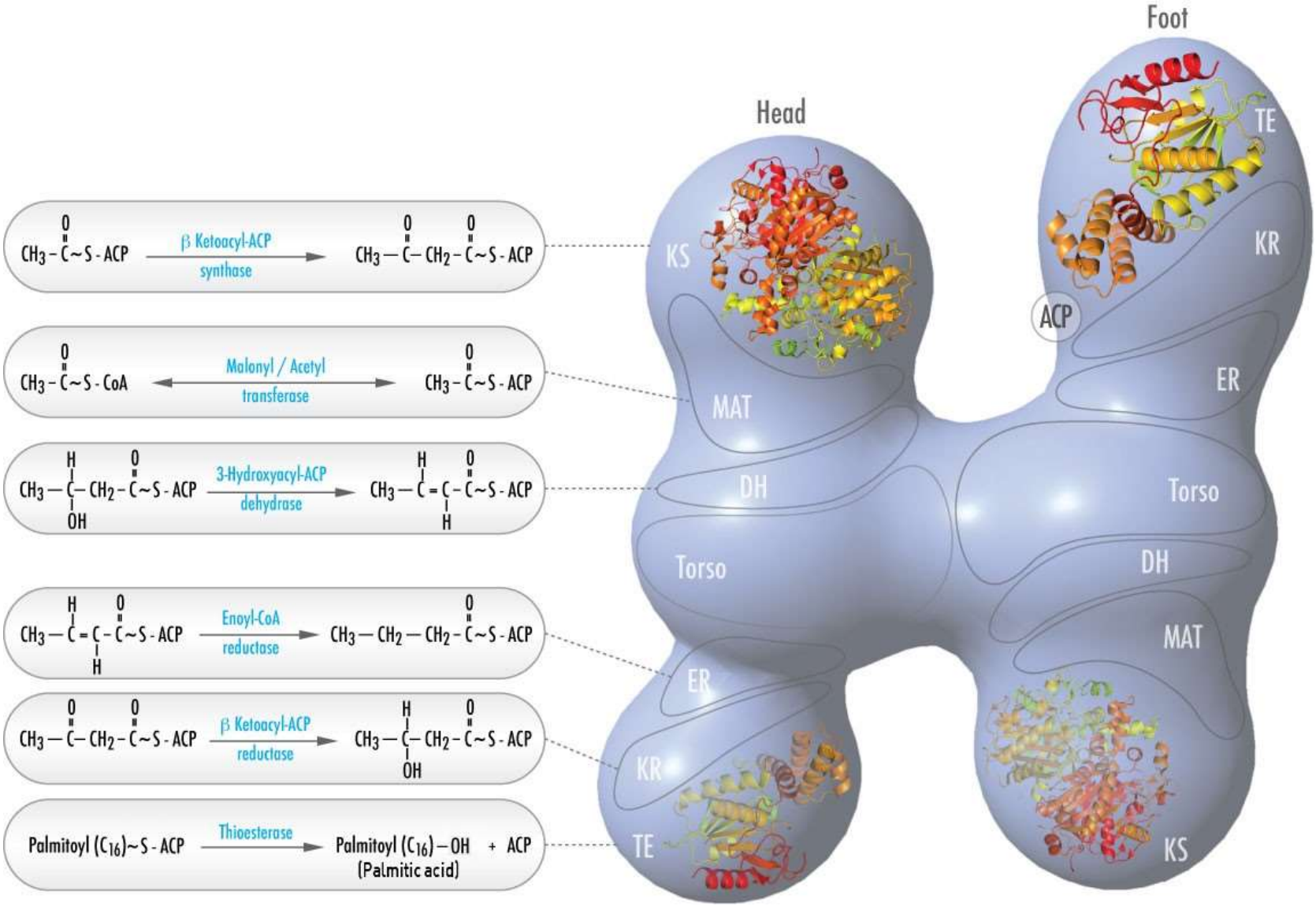
ترکیبات لیپیدی

- اسیدهای چرب
- تری گلیسرید
- کلسترول
- لیپوپروتئین ها
- ایکوزانوئیدها

ساخت اسیدهای چرب

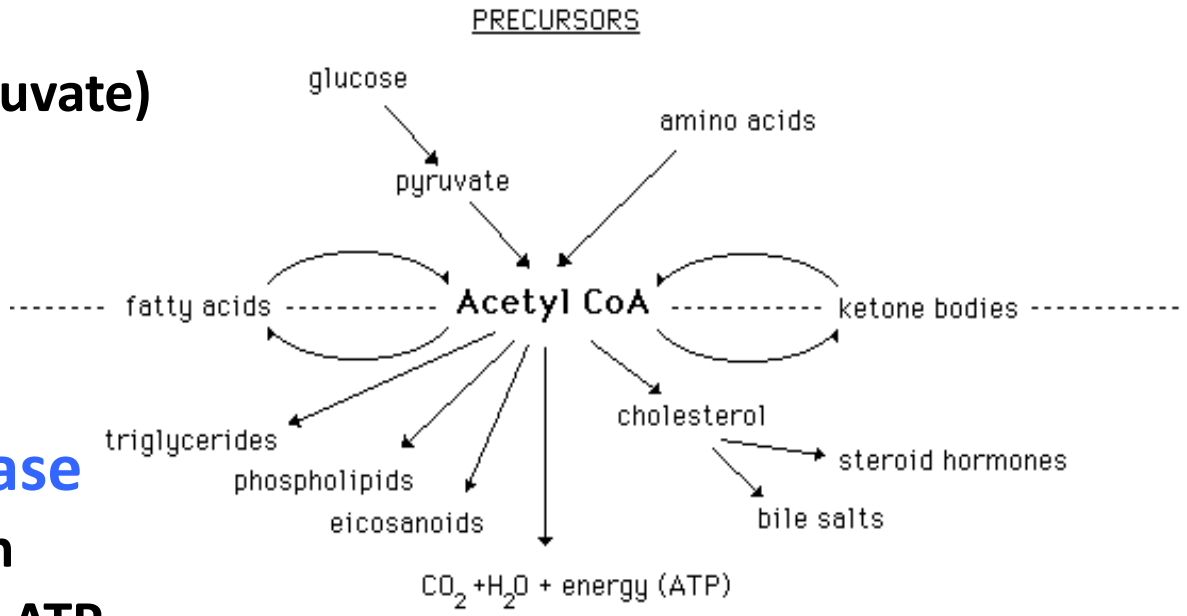


کمپلکس اسید چرب سنتاز



سوبسترا

- **Acetyl CoA**
  - **Glucose (through pyruvate) in non ruminant**
  - **Amino acids**
  - **Acetate in ruminant**
- **Acetyl CoA carboxylase**
  - **Rate-limiting reaction**
  - **Acetyl CoA + $HCO3^-$ + ATP -> malonyl CoA + ADP + Pi**
  - **Biotin**



Acetyl CoA is a central intermediate in lipid metabolism.

سوبسترا....

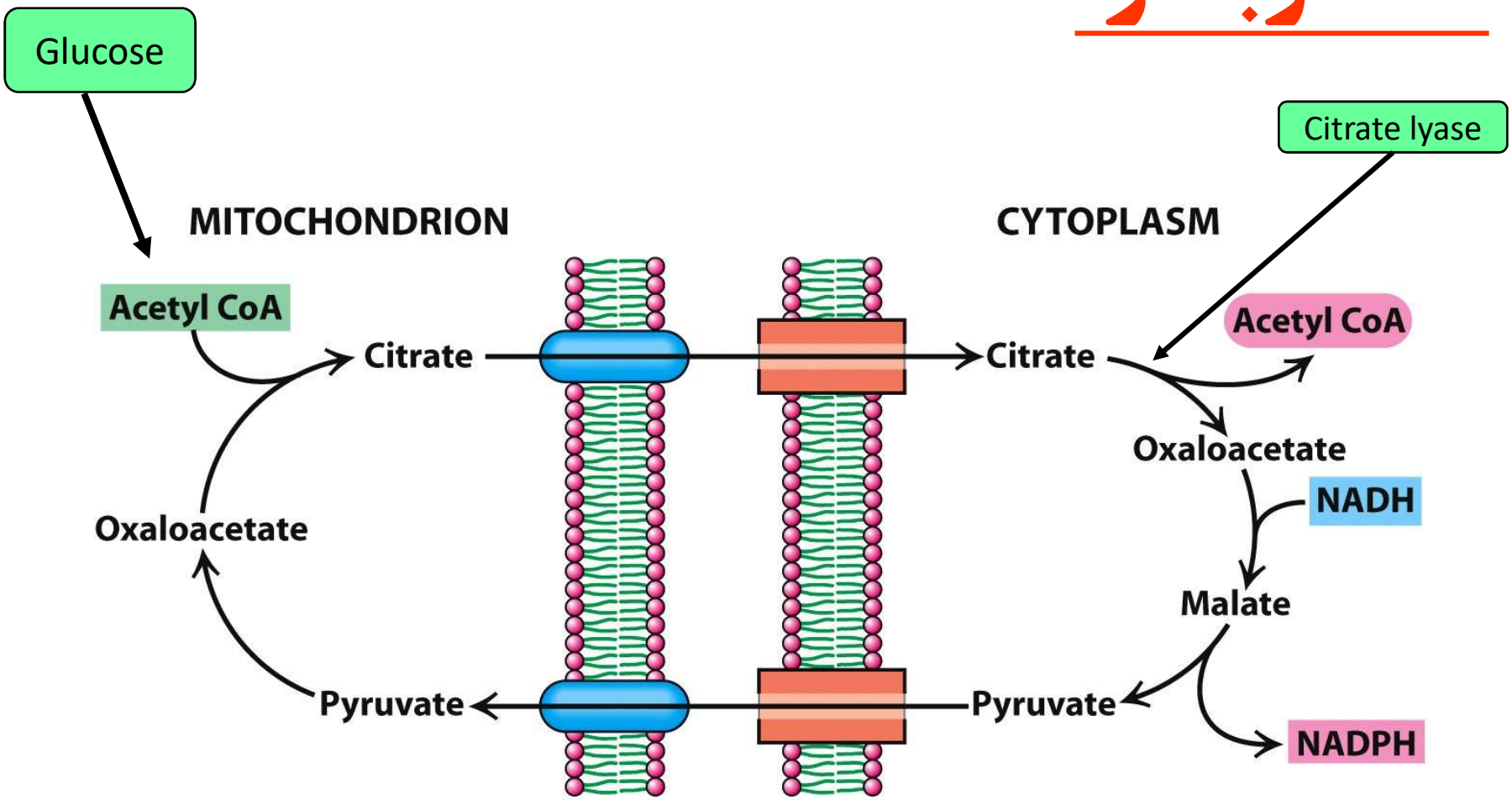
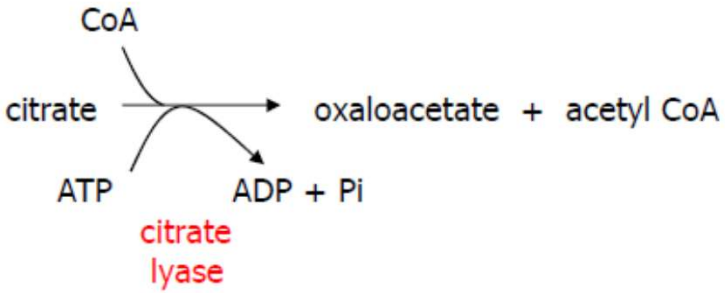


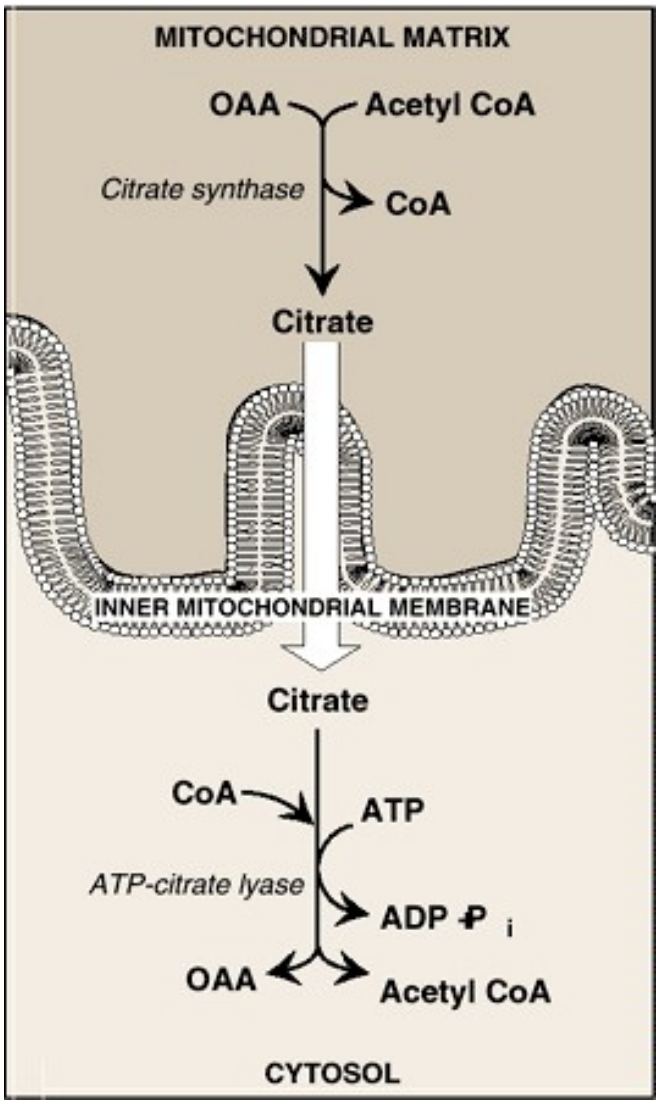
Figure 22.29
***Biochemistry*, Seventh Edition**

سیترات لیاز

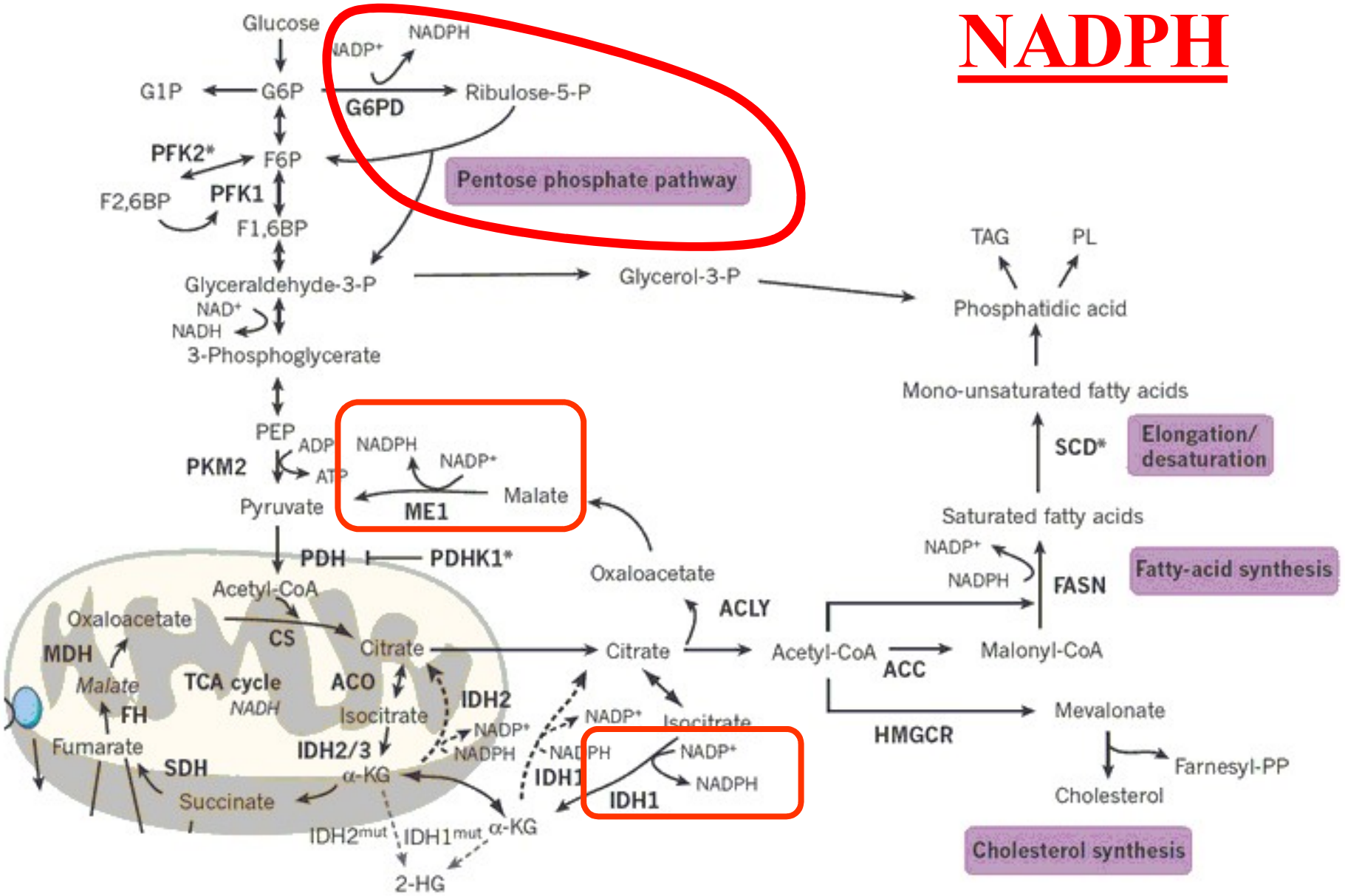


*in non-ruminants

- Absence of citrate lyase in ruminants means that little glucose carbons end up being used for FA synthesis

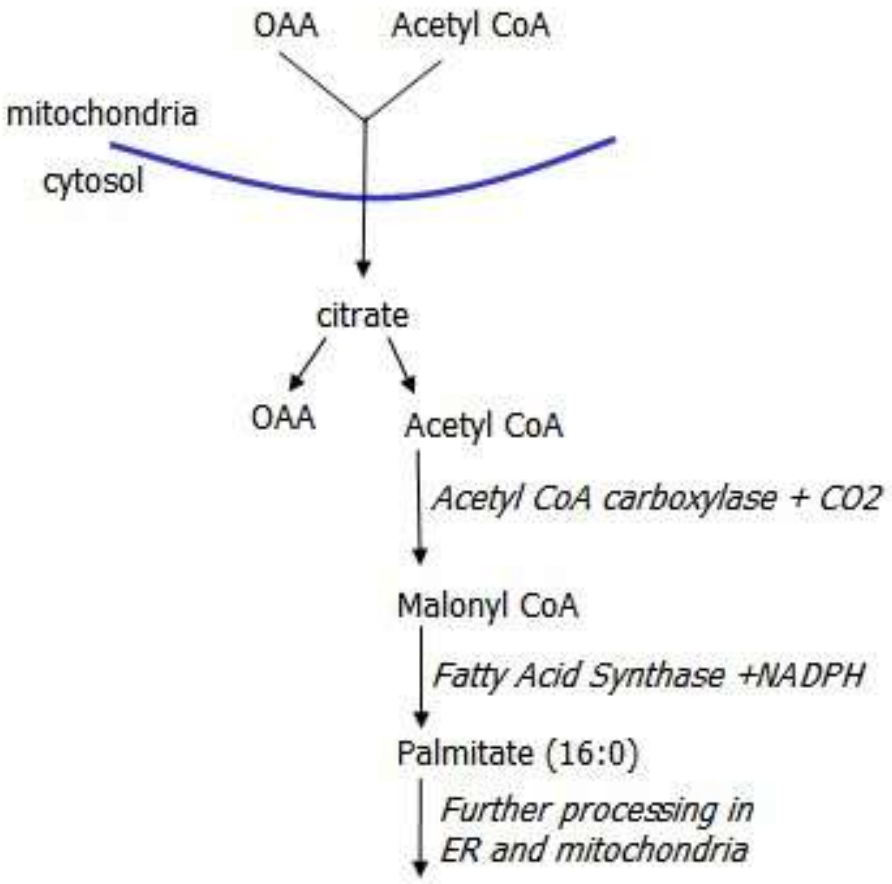


NADPH

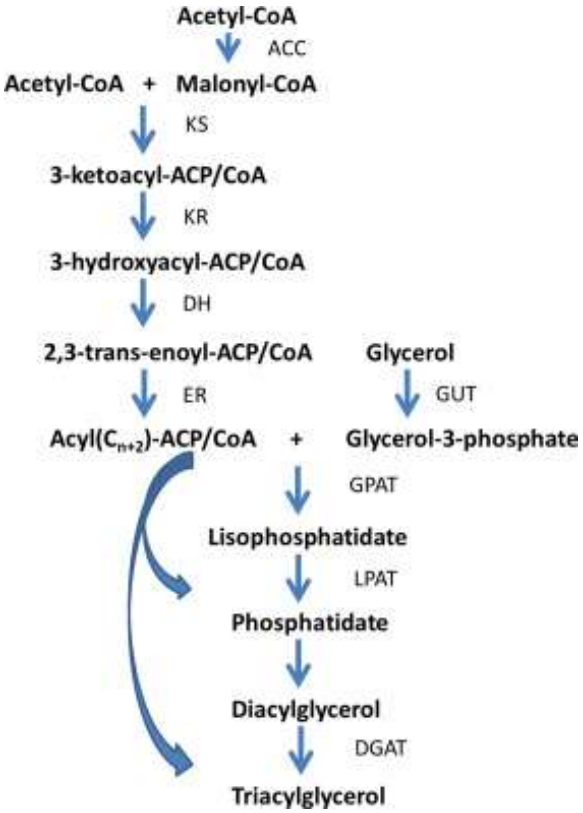

Glucose
NADP+
NADPH
G1P
G6P
G6PD
Ribulose-5-P
PFK2*
F6P
Pentose phosphate pathway
F2,6BP
PFK1
F1,6BP
Glyceraldehyde-3-P
Glycerol-3-P
TAG
PL
Phosphatidic acid
NAD+
NADH
3-Phosphoglycerate
Mono-unsaturated fatty acids
SCD*
Elongation/ desaturation
PEP
ADP
ATP
PKM2
NADPH
NADP+
Malate
ME1
Pyruvate
Saturated fatty acids
NADP+
NADPH
FASN
Fatty-acid synthesis
PDH
PDHK1*
Oxaloacetate
Acetyl-CoA
ACLY
Oxaloacetate
CS
Citrate
Citrate
Acetyl-CoA
ACC
Malonyl-CoA
MDH
Malate
TCA cycle
NADH
ACO
Isocitrate
IDH2
NADP+
NADPH
NADP+
Isocitrate
HMGCR
Mevalonate
FH
Fumarate
IDH2/3
NADPH
NADPH
NADP+
IDH1
SDH
α-KG
IDH1
NADPH
Farnesyl-PP
Succinate
Cholesterol
IDH2mut
IDH1mut
α-KG
Cholesterol synthesis
2-HG

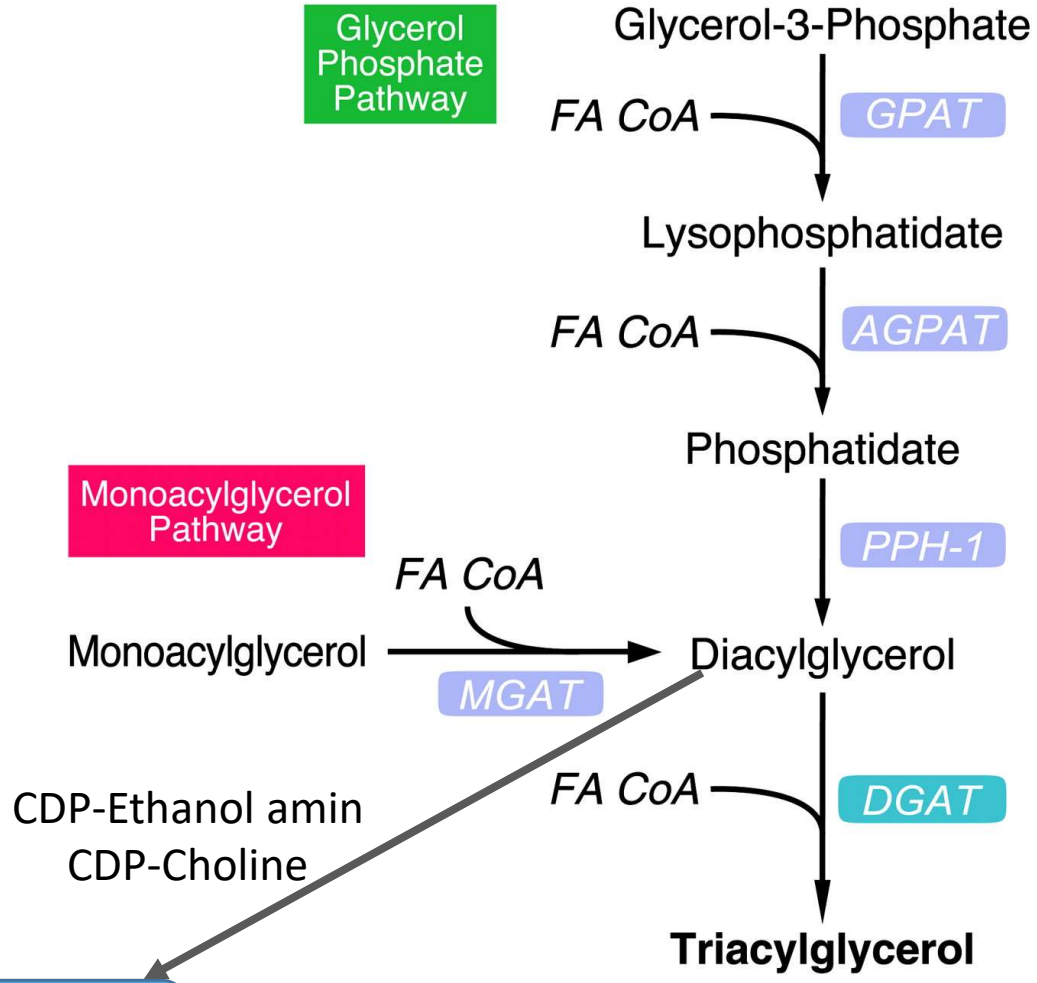
طویل سازی و غیراشباع سازی

- **Cytosolic synthesis of fatty acid synthesis**
  - **Combining 8 two-carbon fragments (acetyl groups from acetyl CoA) to form a 16-carbon saturated fatty acid, palmitate.**
- **Chain elongation**
  - **Endoplasmic reticulum uses malonyl CoA**
  - **Mitochondrial elongation uses acetyl CoA**
- **Desaturation**
  - **In endoplasmic reticulum**
  - **Desaturases for carbon 9, 6, 5 and 4.**
  - **Double bonds cannot be added from C10 to omega end of the chain**



ساخت تری گلیسرید



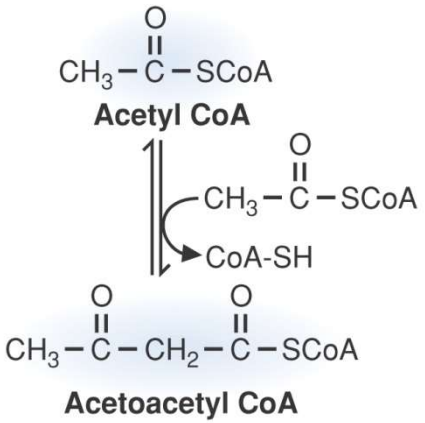


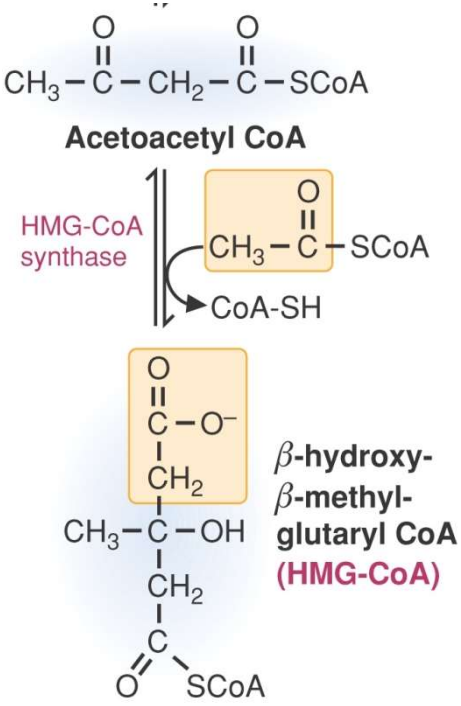
ساخت کلسترول

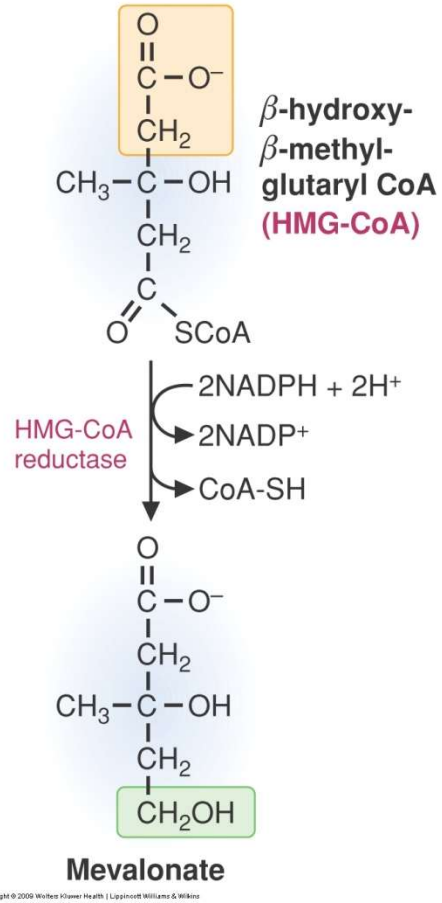
- Cholestrol is an indispensable for all cells (for plasma membranes, steroid hormones and vit. D)

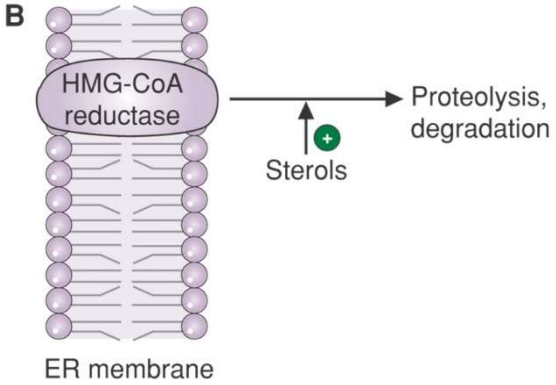
- Sources of CH
  - (1) diet
  - (2) endogenous (from acetyl-CoA)
  - (3) re-absorbed from bile (enterohepatal circulation)

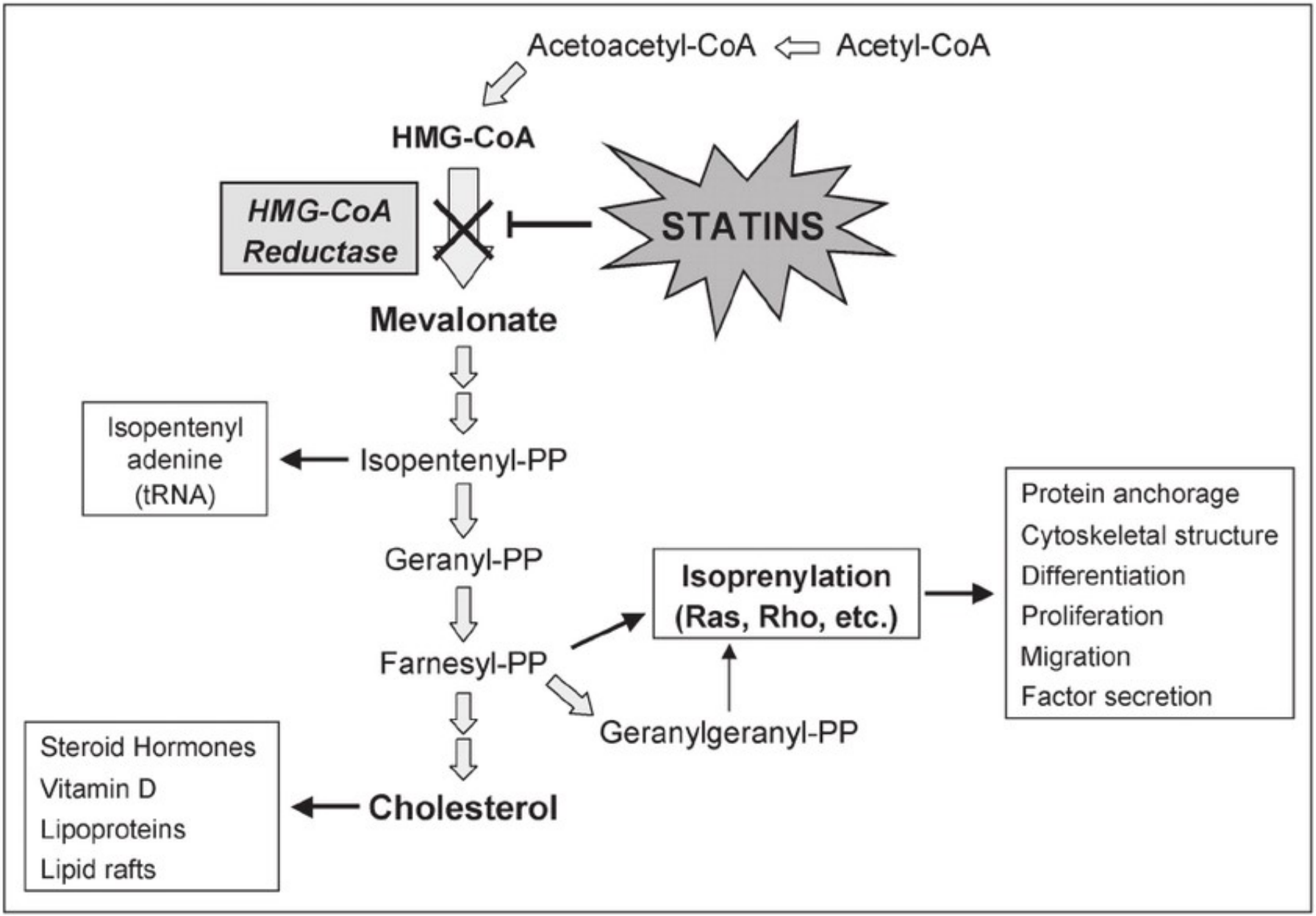
ساخت کلسترول (مسیر موالونات)





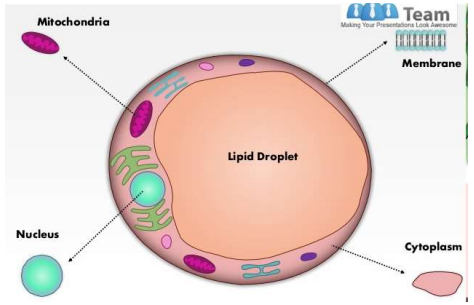


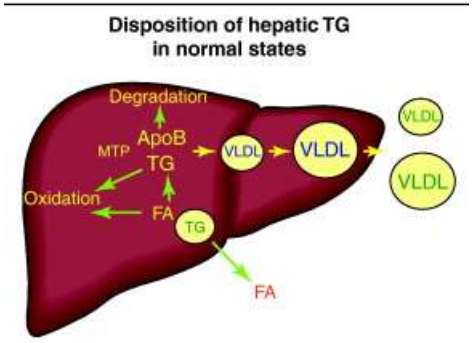


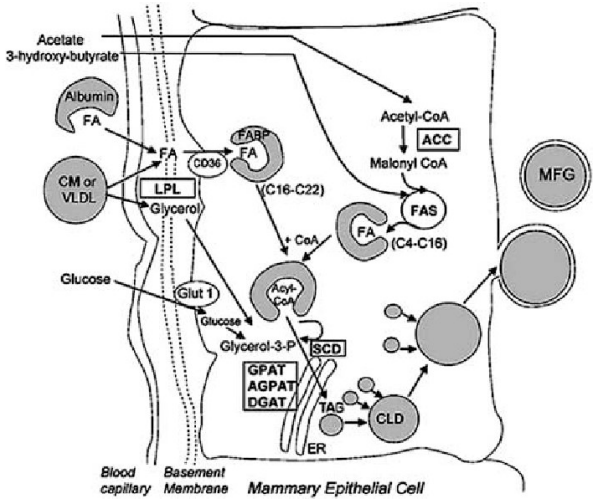

Acetoacetyl-CoA
Acetyl-CoA
HMG-CoA
HMG-CoA Reductase
STATINS
Mevalonate
Isopentenyl adenine (tRNA)
Isopentenyl-PP
Geranyl-PP
Farnesyl-PP
Isoprenylation (Ras, Rho, etc.)
Geranylgeranyl-PP
Protein anchorage
Cytoskeletal structure
Differentiation
Proliferation
Migration
Factor secretion
Steroid Hormones
Vitamin D
Lipoproteins
Lipid rafts
Cholesterol

ذخیره یا ترشح تری گلیسرید

- **Adipose tissue**
  - **TAG stored in cytosol**
- **Liver**
  - **Very little stored.**
  - **Exported out of liver in VLDL**
- **Mammary glands**
  - **Apocrine secretion**

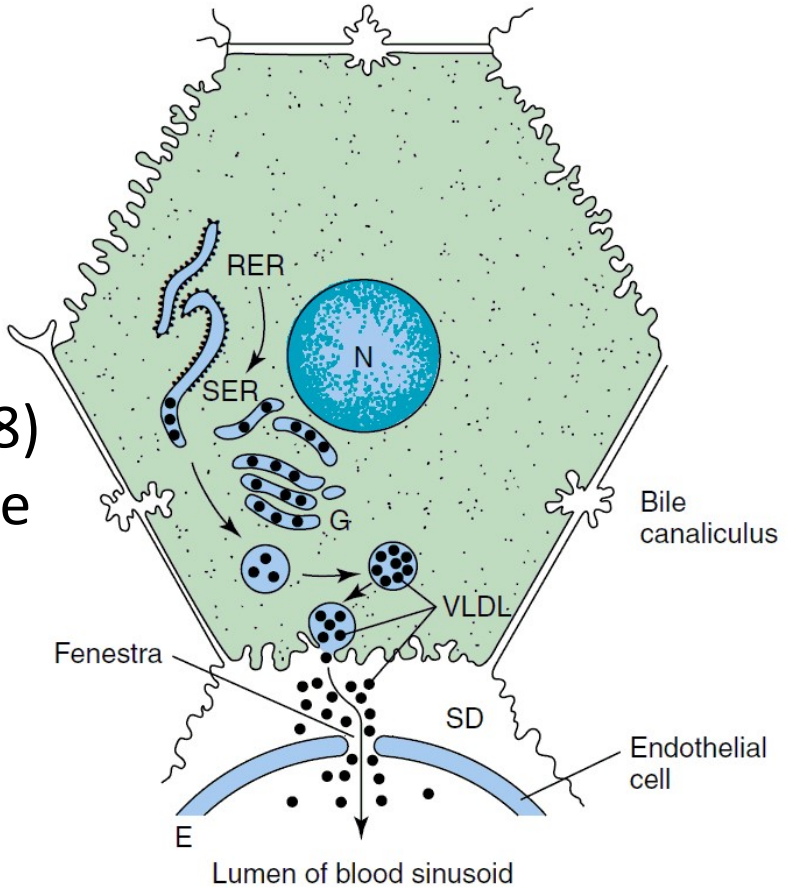






VLDL

- Liver form **VLDLs from**
  - TAG (surplus of saccharides after replenishing the liver glycogen)
  - remaining dietary TAGs CH, FFA
  - de novo synthesized CH
  - Chylomicrons contain apo B (B-48) that is synthesized in the intestine

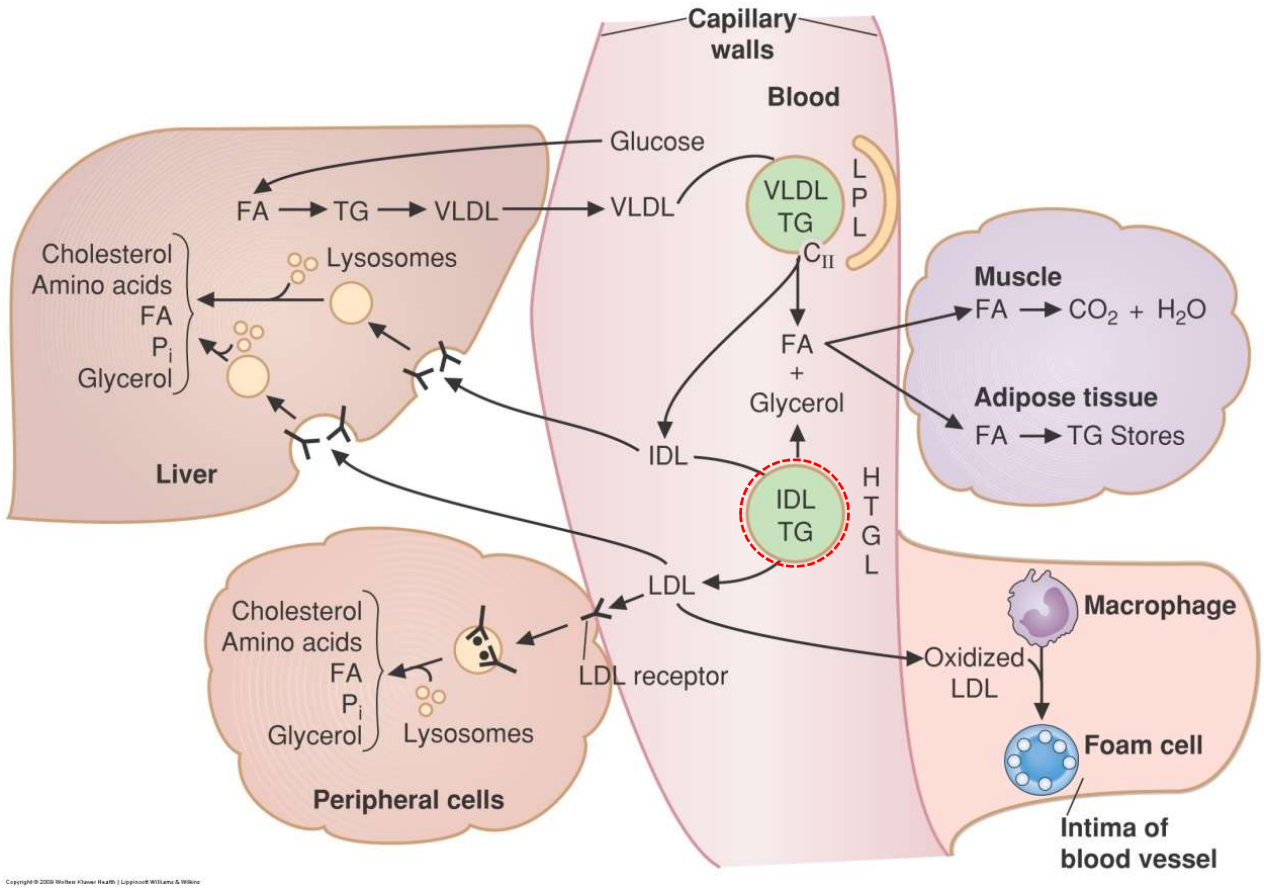


There are many types of apolipoproteins

Apoprotein	Lipoproteins	Function(s)
Apo B-100	VLDL, IDL, LDL	1) Secretion of VLDL from liver 2) Structural protein of VLDL, IDL, and HDL 3) Ligand for LDL receptor (LDLR)
Apo B-48	Chylomicrons, remnants	Secretion of chylomicrons from intestine
Apo E	Chylomicrons, VLDL, IDL, HDL	Ligand for binding of IDL & remnants to LDLR
Apo A-I	HDL, chylomicrons	1) Major structural protein of HDL 2) Activator of LCAT
Apo A-II	HDL, chylomicrons	Unknown
Apo C-I	Chylomicrons, VLDL, IDL, HDL	Activation of LCAT
Apo C-II	Chylomicrons, VLDL, IDL, HDL	Activator of LPL
Apo C-III	Chylomicrons, VLDL, IDL, HDL	Inhibitor of LPL activity

متابولیسم VLDL

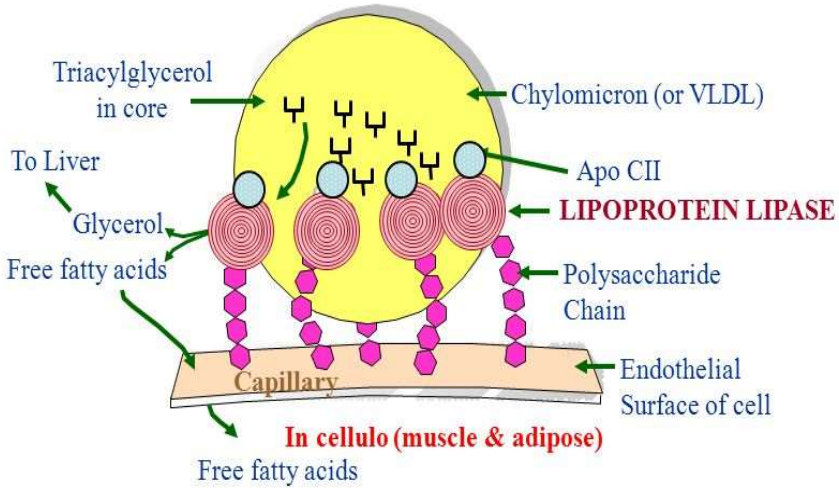
- VLDLs circulate and are - similarly to chylomicrons - source of TAG for peripheral tissues (LPL), gradually transforming into IDL and LDL



لیپوپروتئین لیپاز

- Heart lipoprotein lipase has a low Km for triacylglycerol, about one tenth of that for the enzyme in adipose tissue

- During lactation, A similar redirection to the mammary gland occurs allowing uptake of lipoprotein triacylglycerol fatty acid for milk fat synthesis



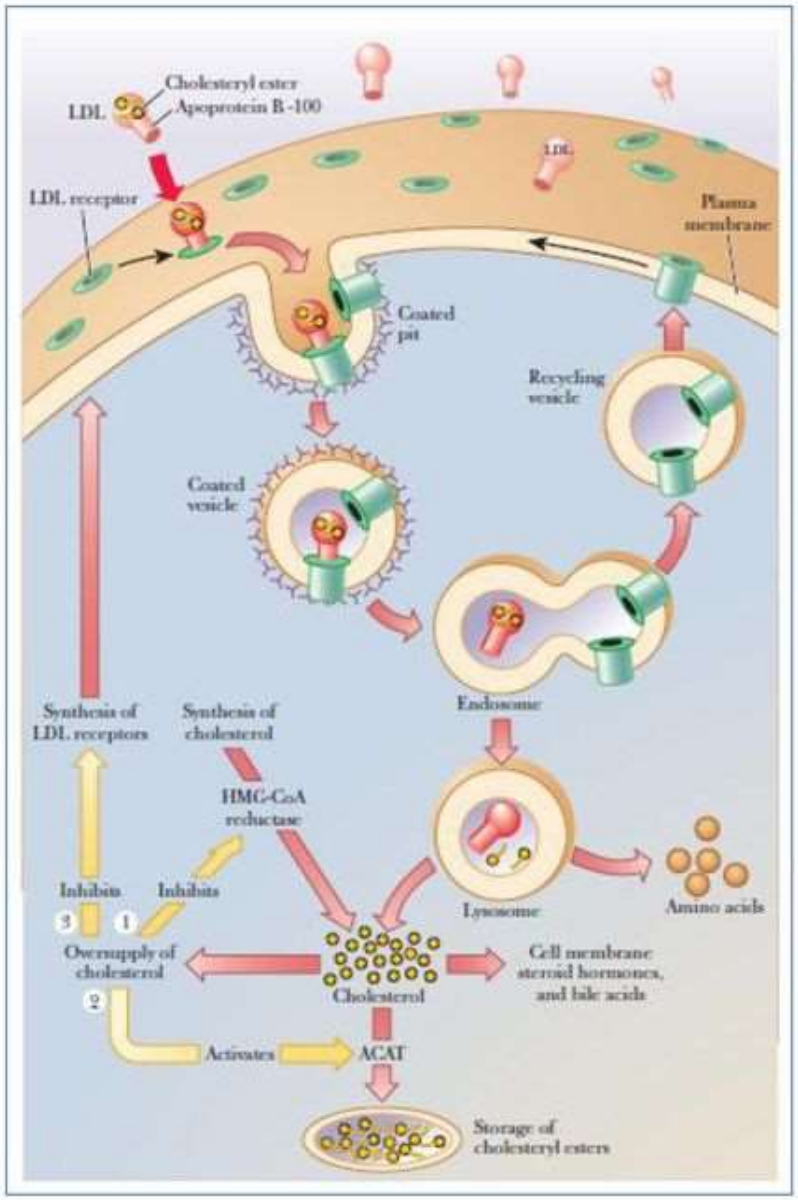
Adipose, heart, and skeletal muscle tissue, as well as in lactating mammary glands

LDL

- Representing a final stage in the catabolism of VLDL
- The main apolipoprotein of LDL (β-lipoprotein) is apolipoprotein B (B-100)
- Approximately 30% of LDL is degraded in extrahepatic tissues and 70% in the liver

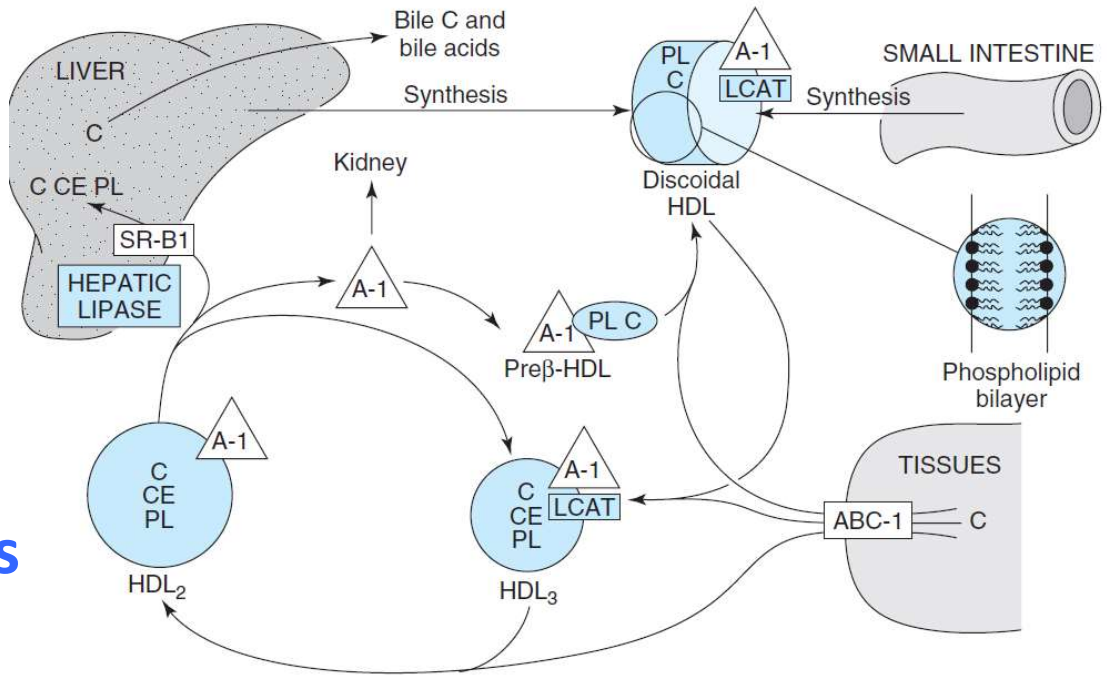
Fate of LDL

- LDL are taken into cell by endocytosis through receptor recognition
- The presence of LDL receptor on the cell surface is important for uptake of LDL
- LDL is hydrolysed to aa, cholesterol and fa
- Free cholesterol – membrane component and inhibit the production of HMG-CoA reductase- suppressed synthesis of cholesterol – and also inhibit the synthesis of receptors – reduce intake of LDL. LDL level in blood increase – deposit as plaques

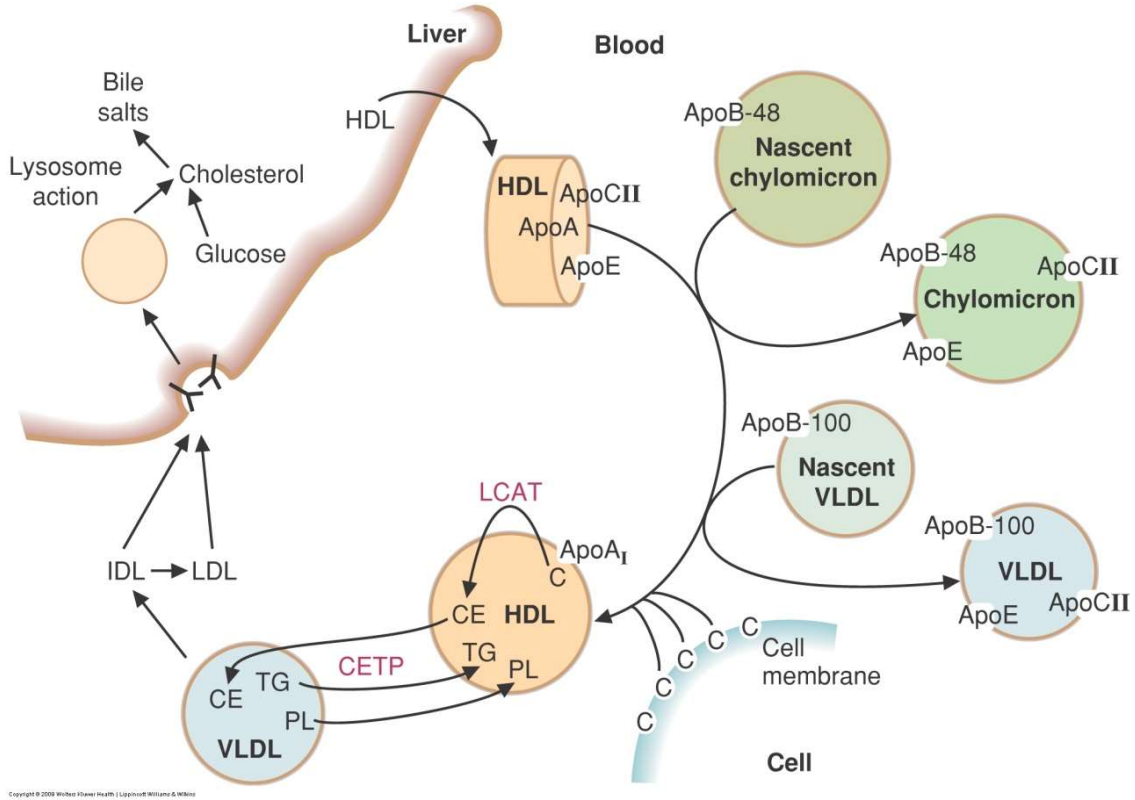


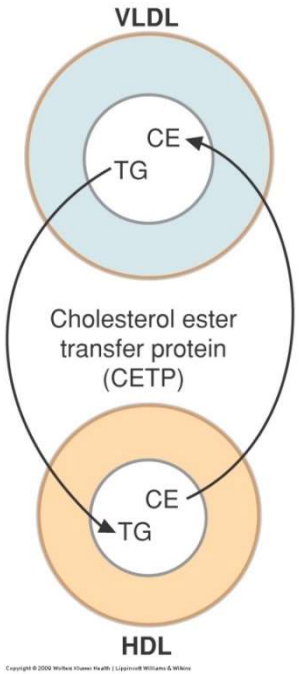
HDL

- HDL is synthesized and secreted from both liver and Intestine
- Involved in VLDL and chylomicron metabolism
- Cholesterol transport
- The major apolipoproteins of HDL (α-lipoprotein) are designated A

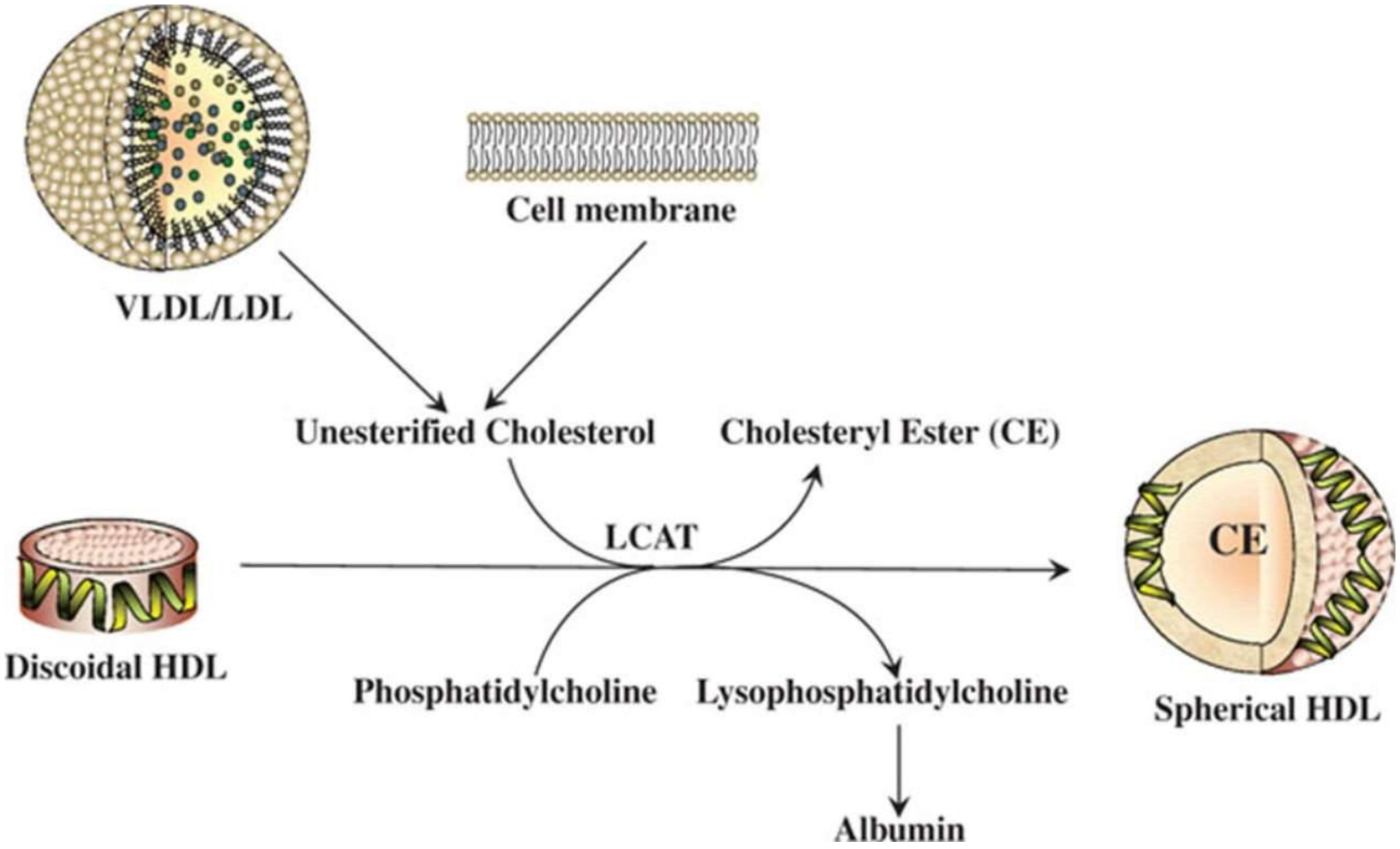


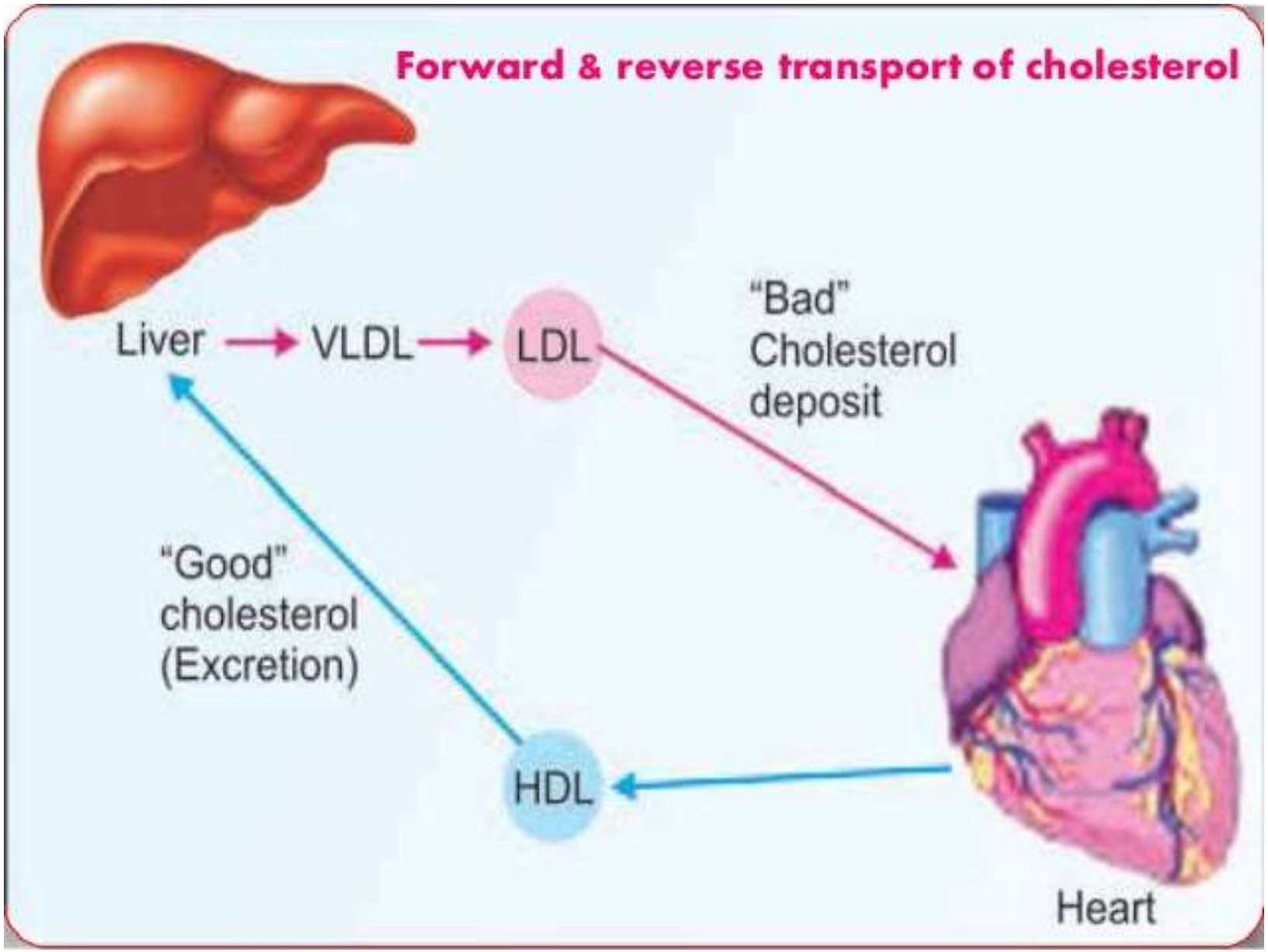
متابولیسم HDL





LCAT


VLDL/LDL
Cell membrane
Unesterified Cholesterol
Cholesteryl Ester (CE)
LCAT
Discoidal HDL
CE
Phosphatidylcholine
Lysophosphatidylcholine
Spherical HDL
Albumin


Forward & reverse transport of cholesterol
Liver
VLDL
LDL
"Bad"
Cholesterol
deposit
"Good"
cholesterol
(Excretion)
HDL
Heart

غلظت لیپوپروتئین ها

Lipid Profile Test				
	Unit	Optimal	Intermediate	High
Total Cholesterol	mg/dL	<200	200 - 239	>239
LDL Cholesterol	mg/dL	<130	130 - 159	>159
HDL Cholesterol	mg/dL	>60	40 - 60	<40
Triglycerides	mg/dL	<150	150 - 199	>199
Non-HDL-C	mg/dL	<130	130 - 159	>159
TG to HDL ratio	mg/dL	<3	3.1 – 3.8	>3.8

چربی خون حیوانات

Measure	Units	Cow	Horse	Sheep	Goat
Cholesterol	mg/dL	70-200	75-150	52–76	80–130
Acetoacetate	mg/dL	0-1.1			
B-hydroxybutyrate	mg/dL	1-9	0.67	5.73	
NEFA	mEq/L	0.03-0.52			

ساخت چربی در پستان

Milk Lipids (Fats)

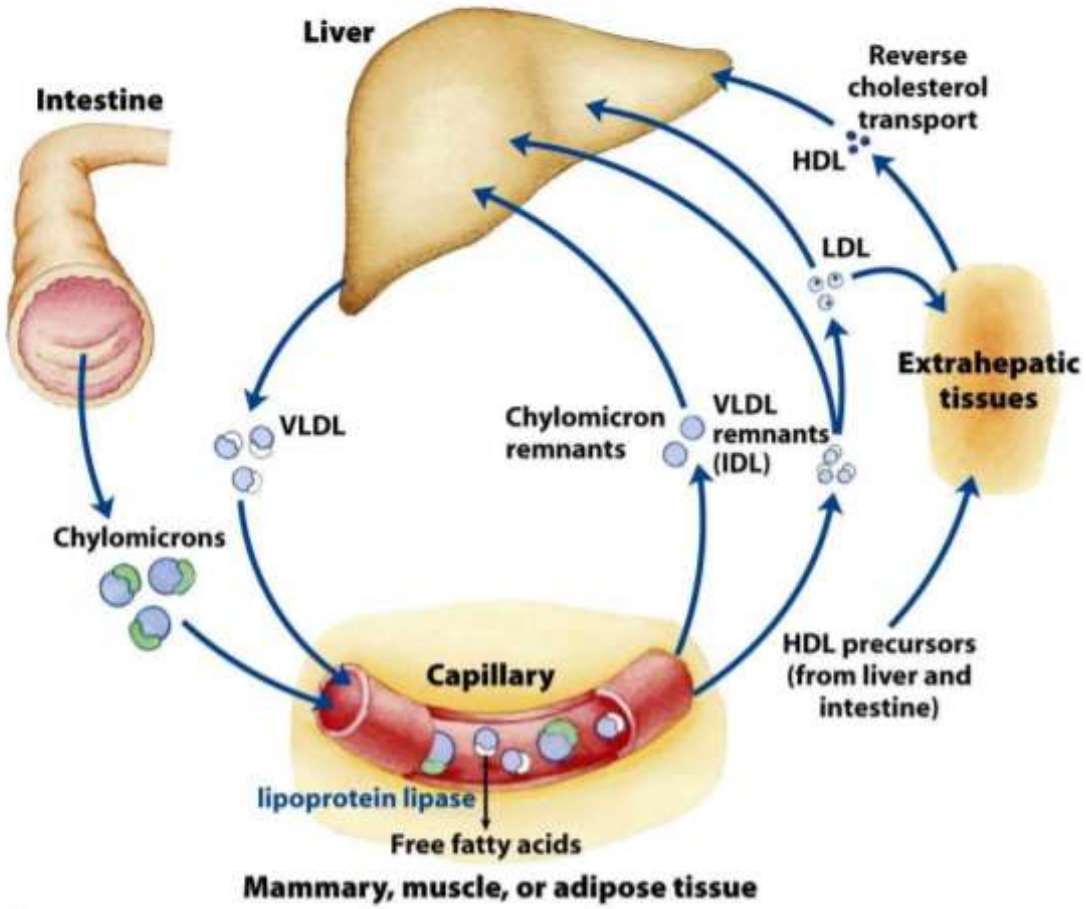
	Cow	Human	Rat
Triglycerides	97-98	98	91.3
Diacylglycerols	0.3	0.7	2.9
Monoacylglycerols	trace	trace	0.4
NEFAs	0.2	0.4	3.1
Phospholipids	1.2	0.7	0.7
Cholesterol	0.3	0.2	1.6

Milk Fatty Acid Profile

	Cow	Human	Rat	Corn Oil
6:0	1.6	trace	trace	--
8:0	1.3	trace	2.5	--
10:0	3.0	1.3	8.7	--
12:0	3.1	3.1	9.5	--
14:0	9.5	5.1	11.9	--
16:0	26.3	20.2	30.1	10.1
16:1	2.3	5.7	2.2	--
18:0	14.6	3.0	3.0	1.6
18:1	29.8	46.6	18.9	31.4
18:2	2.4	13.0	11.4	56.3
18:3	0.8	1.4	1.3	0.4
Other	5.3	?	0.5	0.2

اسیدهای چرب شیر (Preformed)

- 40 to 60% of milk fatty acids come from blood
- Mostly from very low density lipoproteins (VLDL)
- Triglycerides in the VLDL are hydrolyzed in the mammary capillaries by lipoprotein lipase (LPL)
- Synthesized on the smooth endoplasmic reticulum and form small droplets



اسیدهای چرب شیر (DE NOVO SYNTHESIS)

- Glucose is the carbon source for FA synthesis in non-ruminants
- In ruminants, the carbon sources used for FA synthesis are acetate and BHBA
- Fatty acids are built 2 carbons at a time and 16 carbon limit (short and medium chain fatty acids)

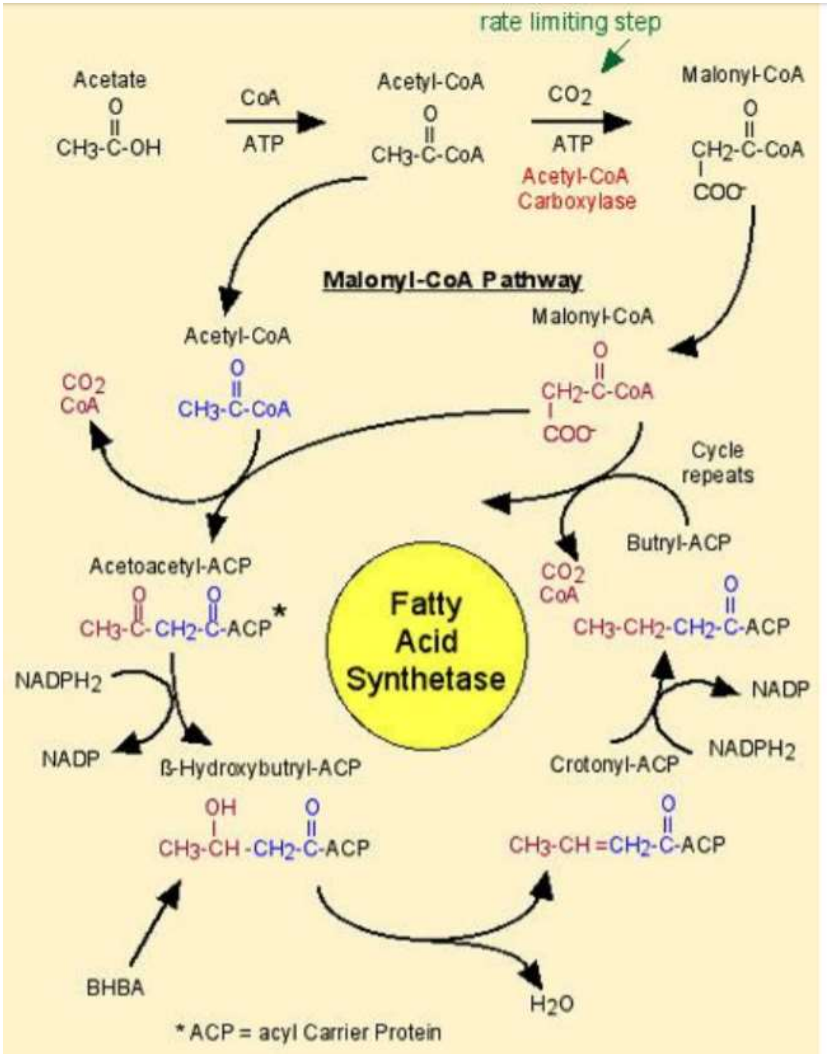
1-Acetyl CoA carboxylase

- Acetyl-CoA + HCO3- + ATP → malonyl-CoA + ADP + Pi

2-Fatty acid synthase

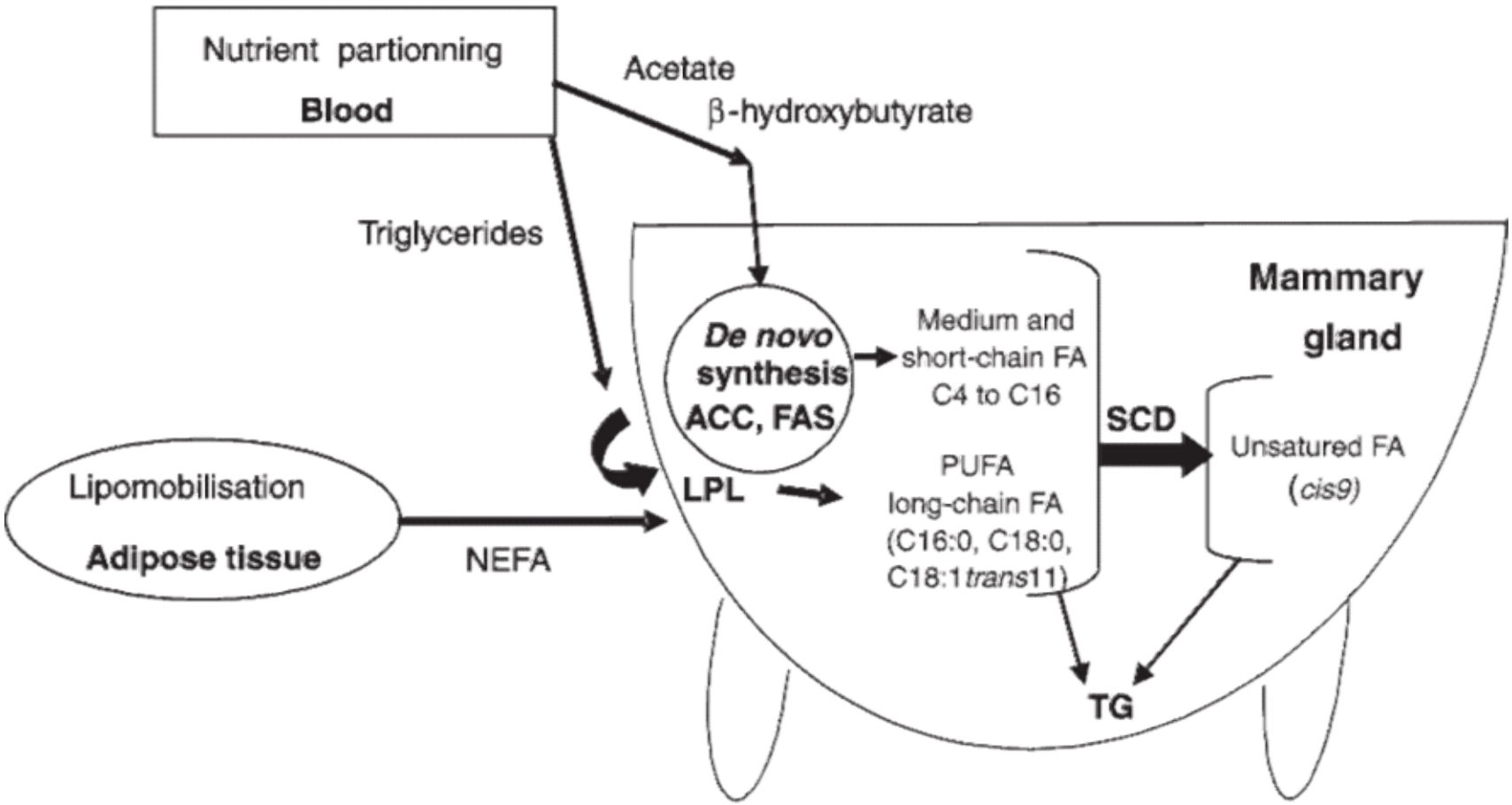
- Acetyl-CoA + 7 malonyl-CoA + 14 (NADPH + H+) → Palmitic acid (16 carbons) + 7 CO2 + 14 NADP + 8 CoA + 6 H2O

- Acylthioesterases cleave off the growing FA chain from the acyl carrier protein
- Occurs in the cytoplasm of the mammary epithelial cell



سوبسترا در پستان

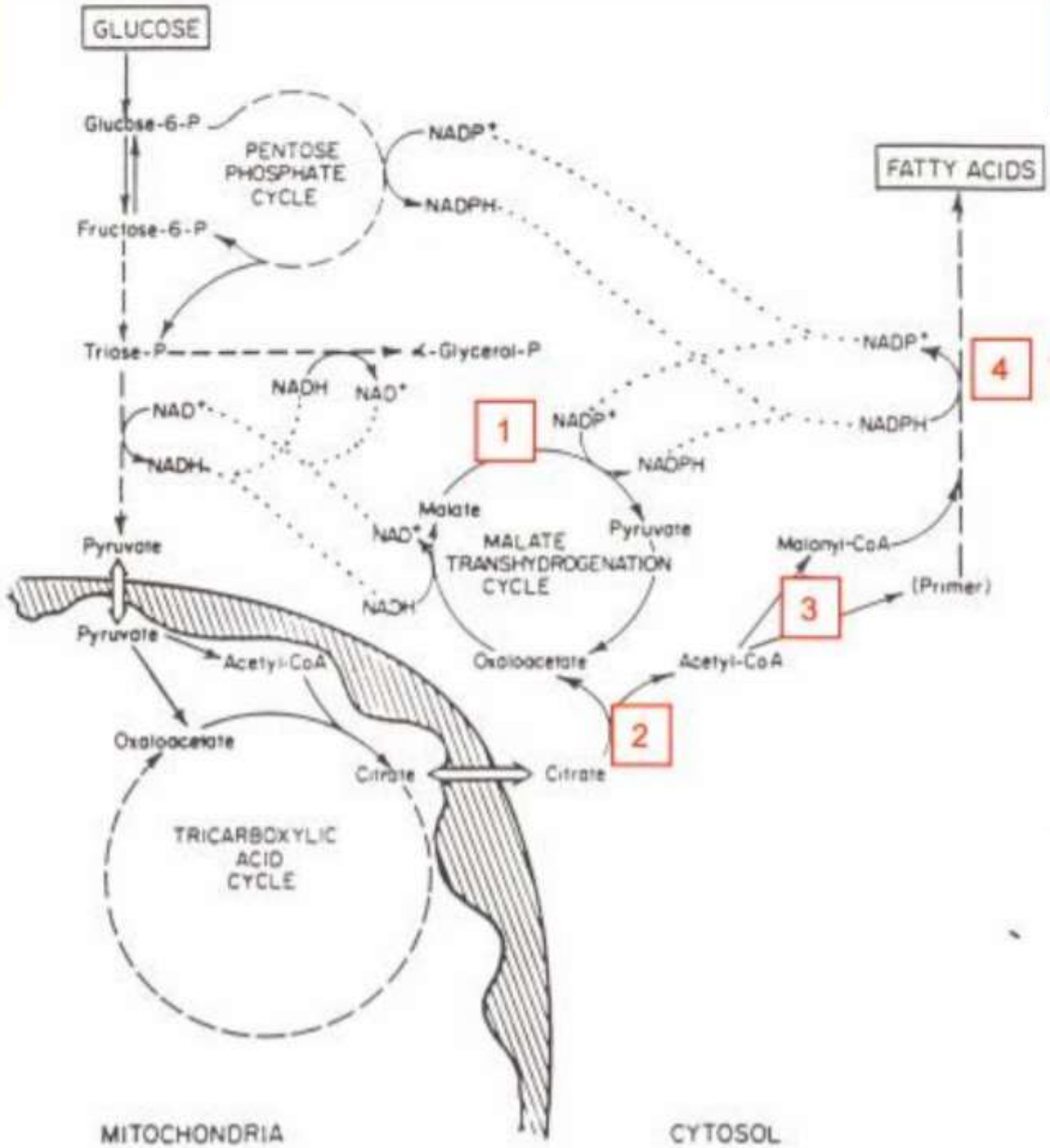
Fatty Acid	% of FA from De novo synthesis	% of FA from VLDL Fatty Acid
C4 -C10	100	0
C12	80-90	10-20
C14	30-40	60-70
C16	20-30	70-80
C18	0	100



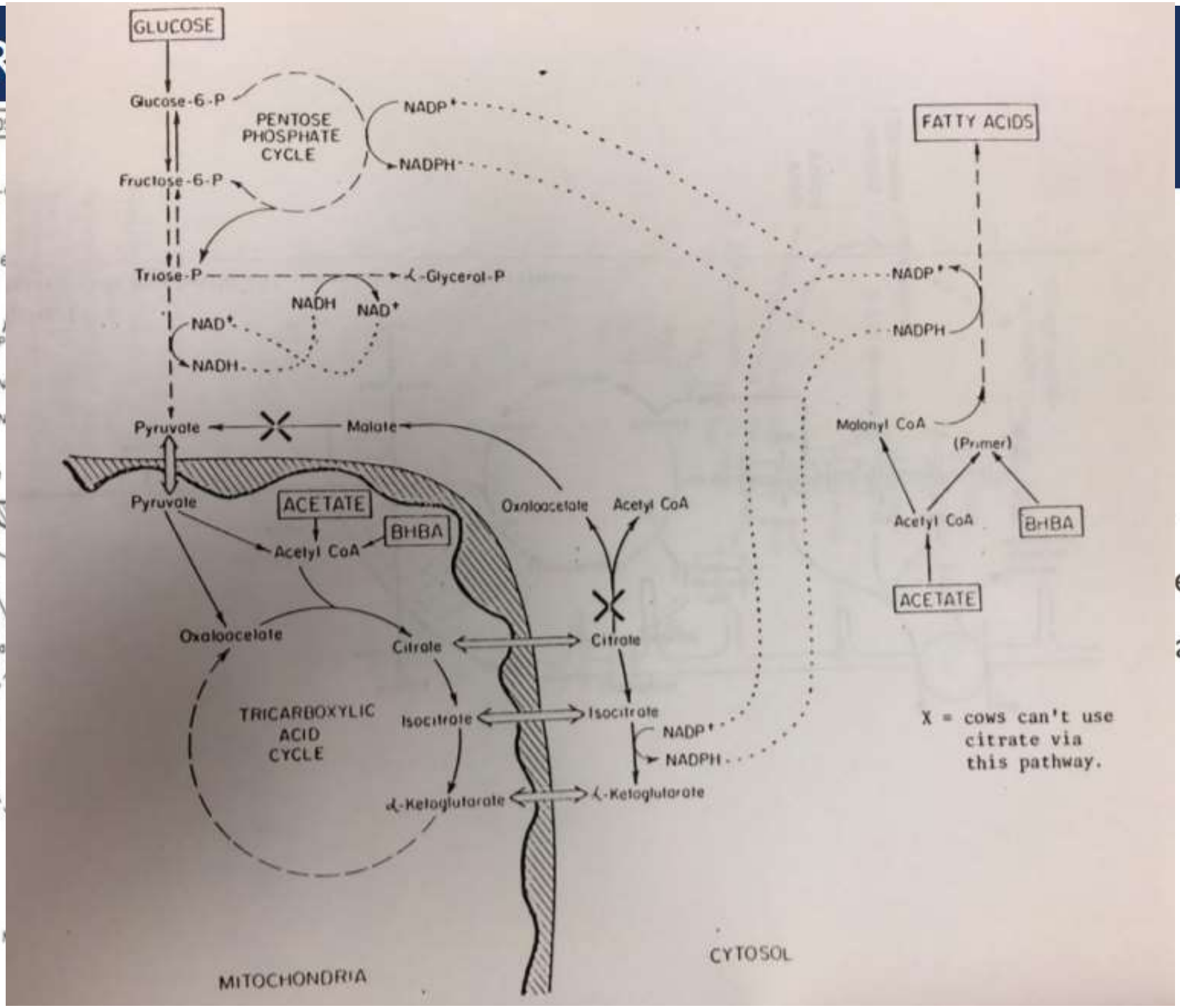
PUFA : PolyUnsaturated FA
NEFA : Non Esterified FA
TG : Triglycerides

ACC : Acetyl-CoA Carboxylase
FAS : Fatty Acid Synthase
LPL : LipoProtein Lipase
SCD : Stearoyl-CoA Desaturase

NON-RUMINANTS

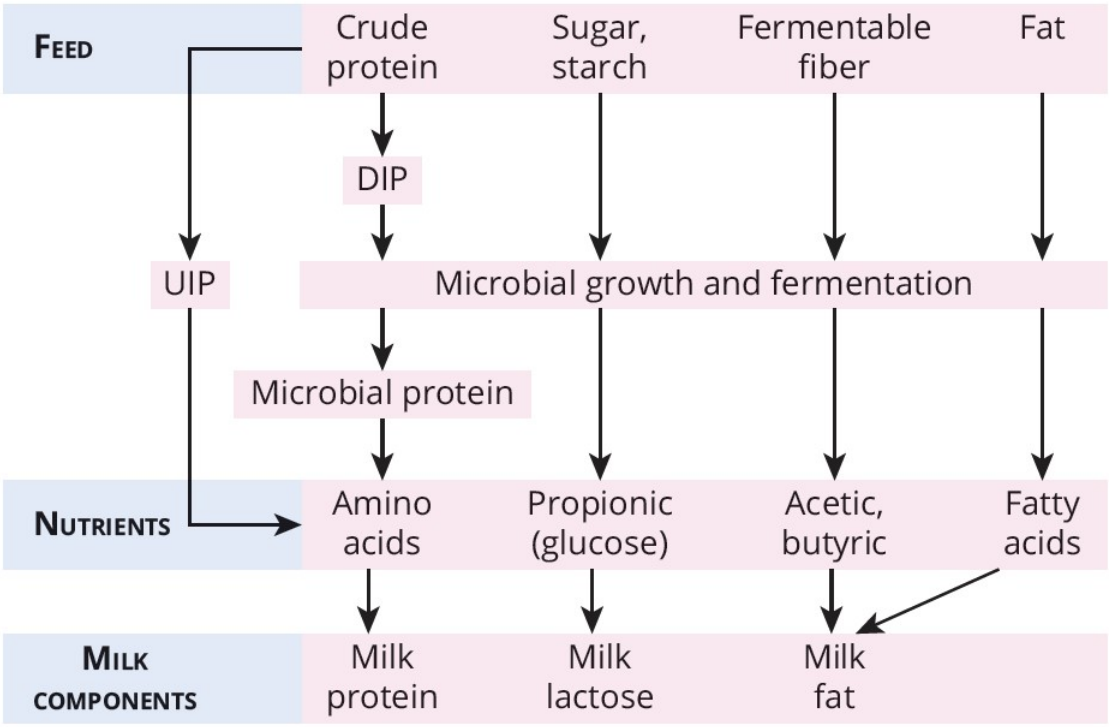


- 1. NADP malate dehydrogenase
- 2. Citrate lyase
- 3. Acetyl-CoA carboxylase
- 4. Fatty acid synthase


GLUCOSE
Glucose-6-P
PENTOSE PHOSPHATE CYCLE
NADP+
NADPH
Fructose-6-P
FATTY ACIDS
Triose-P
L-Glycerol-P
NADH
NAD+
NAD+
NADH
NADP+
NADPH
Pyruvate
Malate
Malonyl CoA
(Primer)
Pyruvate
ACETATE
BHBA
Acetyl CoA
Oxaloacetate
Acetyl CoA
Acetyl CoA
BHBA
ACETATE
Oxaloacetate
Citrate
Citrate
TRICARBOXYLIC ACID CYCLE
Isocitrate
Isocitrate
NADP+
NADPH
X = cows can't use citrate via this pathway.
α-Ketoglutarate
α-Ketoglutarate
MITOCHONDRIA
CYTOSOL

سوبسترا در نشخوارکنندگان....

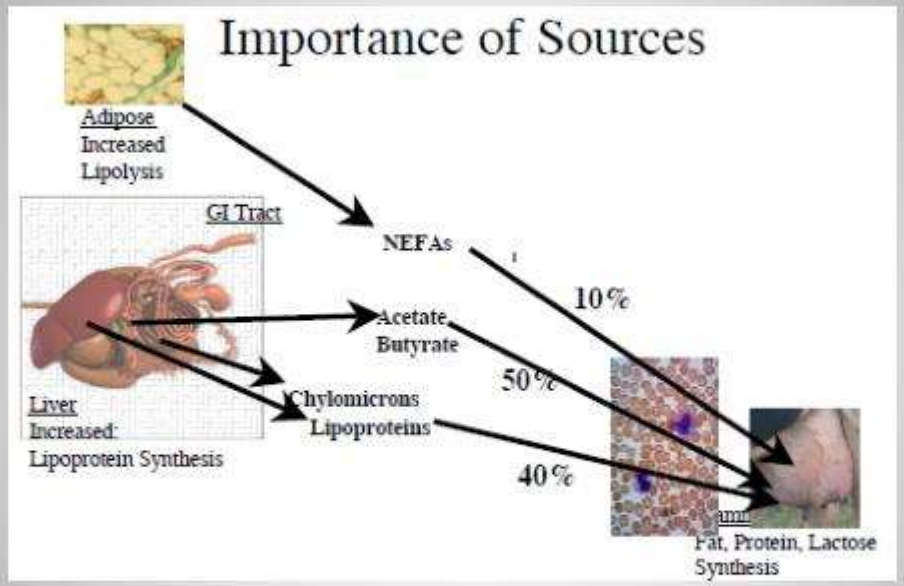
Figure 1 - Feed, nutrient flow from the rumen and milk components.



UIP = undergradable intake protein; DIP = degradable intake protein
Source: Sniffen C.J. and H.H. Herdt. The Veterinary Clinics of North America: Food Animal Practice Vol 7, No2. Philedelphia, Pa: W.B. Saunders, 1991.

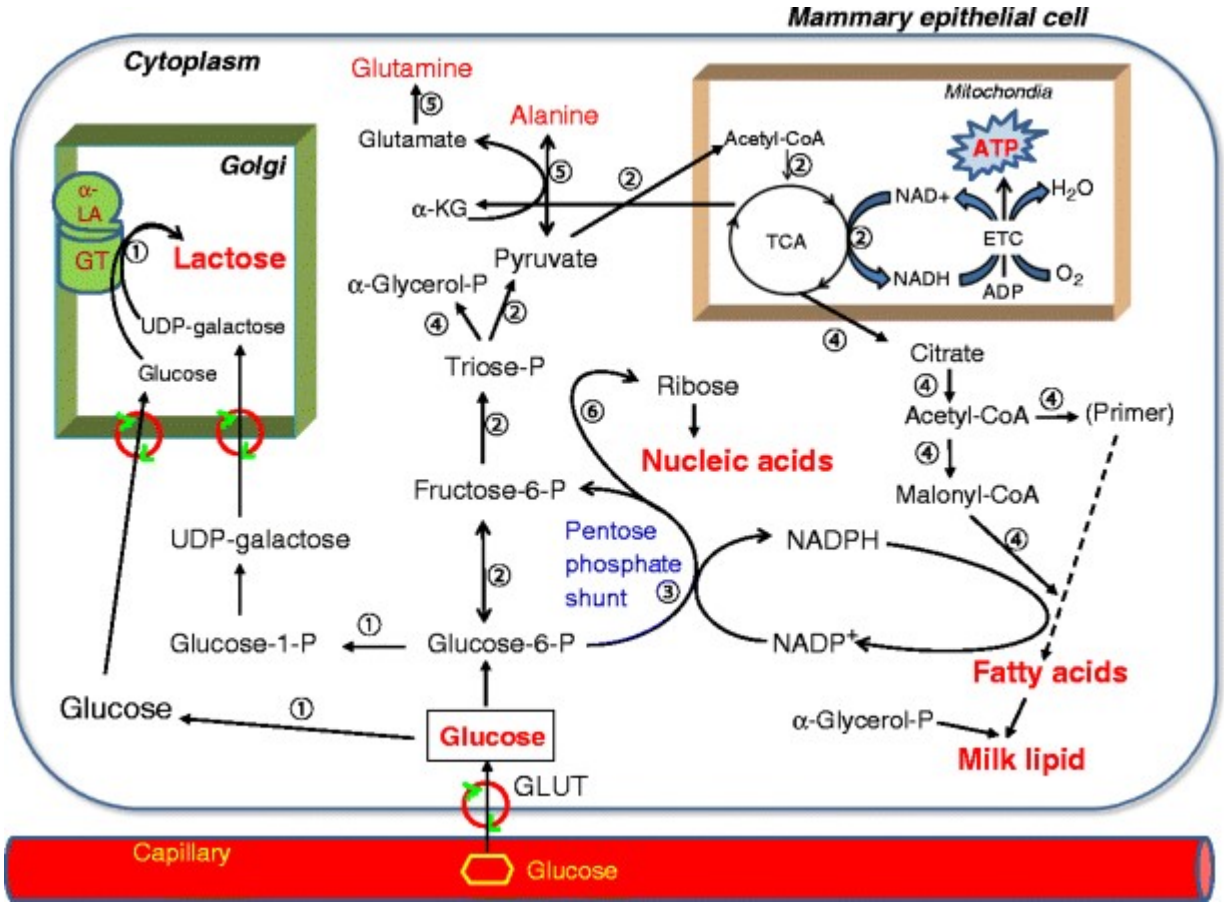
سوبسترا در نشخوارکنندگان....

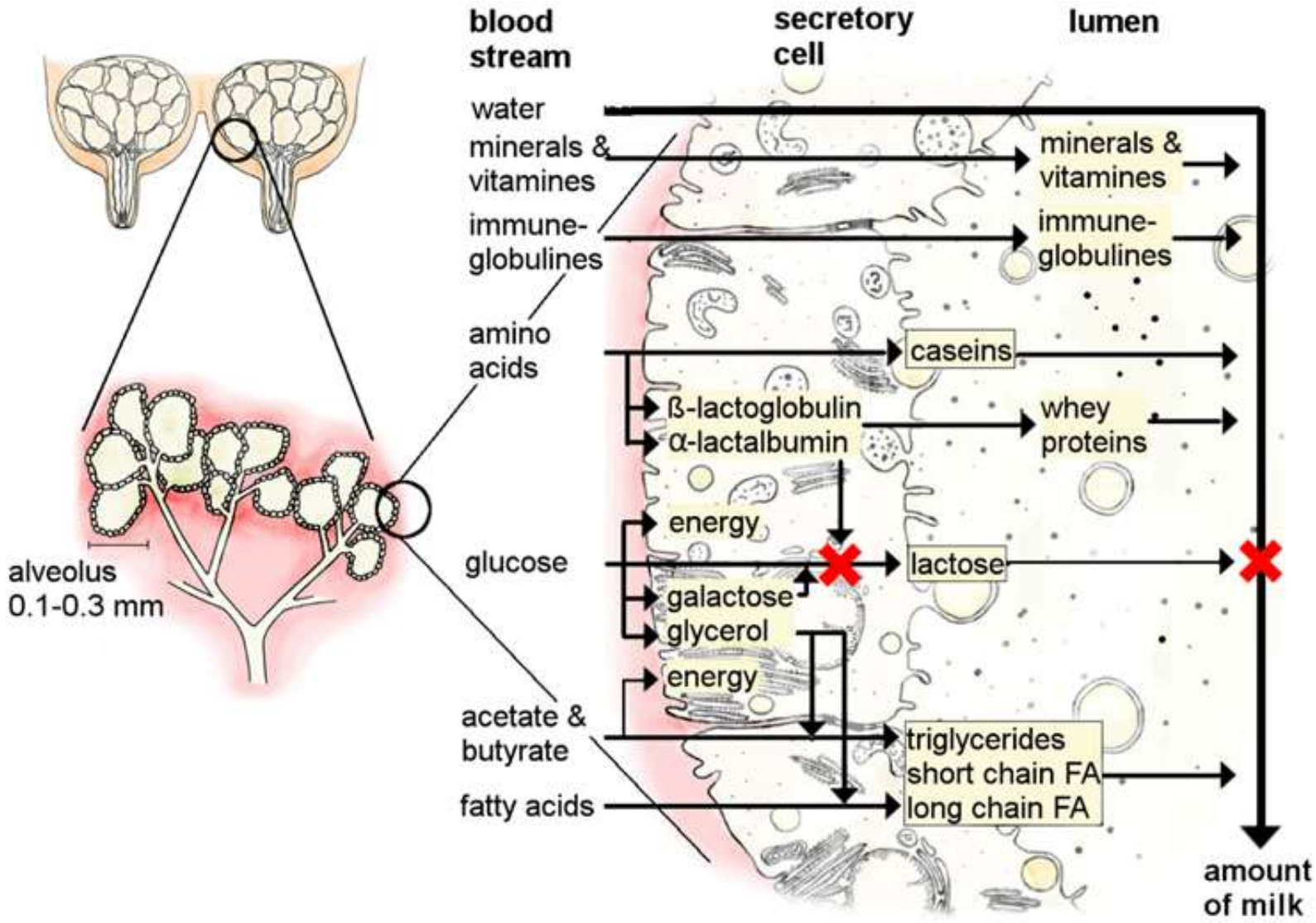
Sources of Milk Fat Precursors



Udder synthesis of fatty acids from acetate and other VFAs account for about half of the fatty acids in milk triglycerides. About 40% comes from lipoprotiens and chylomicrons, mostly as absorbed from the intestine. Only about 10% (in peak lactation and later) comes from body reserved. More may come from stored adipose tissue in early lactation, when there is a considerable energy deficit.

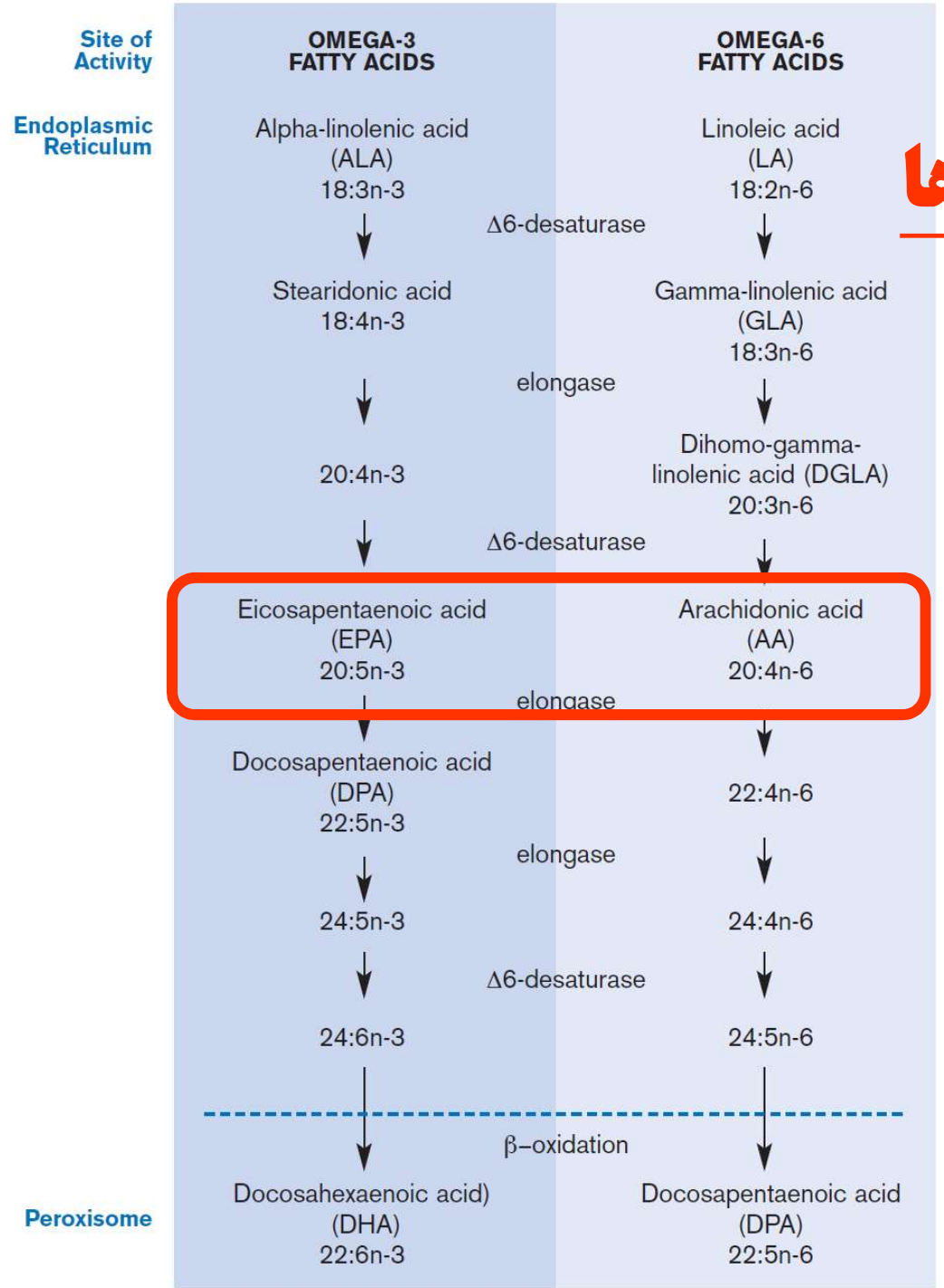
....سوبسترا در غیرنشخوارکنندگان




blood stream
secretory cell
lumen
water
minerals & vitamines
immune-globulines
amino acids
glucose
acetate & butyrate
fatty acids
alveolus
0.1-0.3 mm
minerals & vitamines
immune-globulines
caseins
ß-lactoglobulin
α-lactalbumin
whey proteins
energy
lactose
galactose
glycerol
energy
triglycerides
short chain FA
long chain FA
amount of milk

ایکوزانوئیدها

- Signaling molecules (Prostaglandins, Thromboxanes, Leukotrienes, Lipoxins) made of polyunsaturated fatty acids with 20 carbon units in length
- As local (Paracrine) hormones functioning through G-protein-linked receptors to elicit their biochemical effects
- In a variety of processes important in human health or disease
  - Reproductive function
  - Inflammation
  - Fever and pain
  - The formation of blood clots
  - The regulation of blood pressure
  - Gastric acid secretion

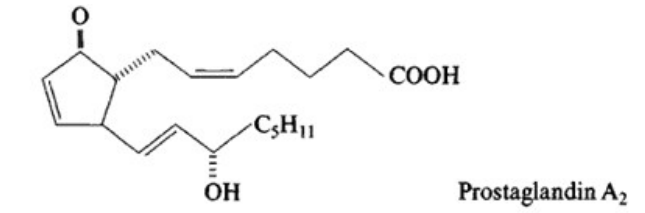


پیش ساز ایکوزانوئیدها

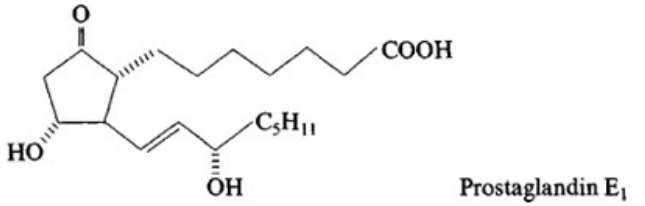
- derived from the essential fatty acids linoleate and α-linolenate
- Or directly from dietary arachidonate and eicosapentaenoate

پروستاگلاندین ها

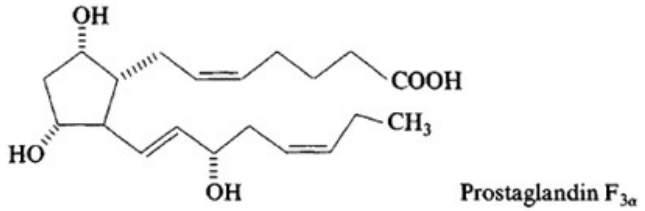
- **Prostaglandins**
  - **Five-carbon ring**
  - **PGE: ether-soluble, and PGF, for: phosphate buffer–soluble**
  - **Each group contains numerous subtypes**



Prostaglandin A_2

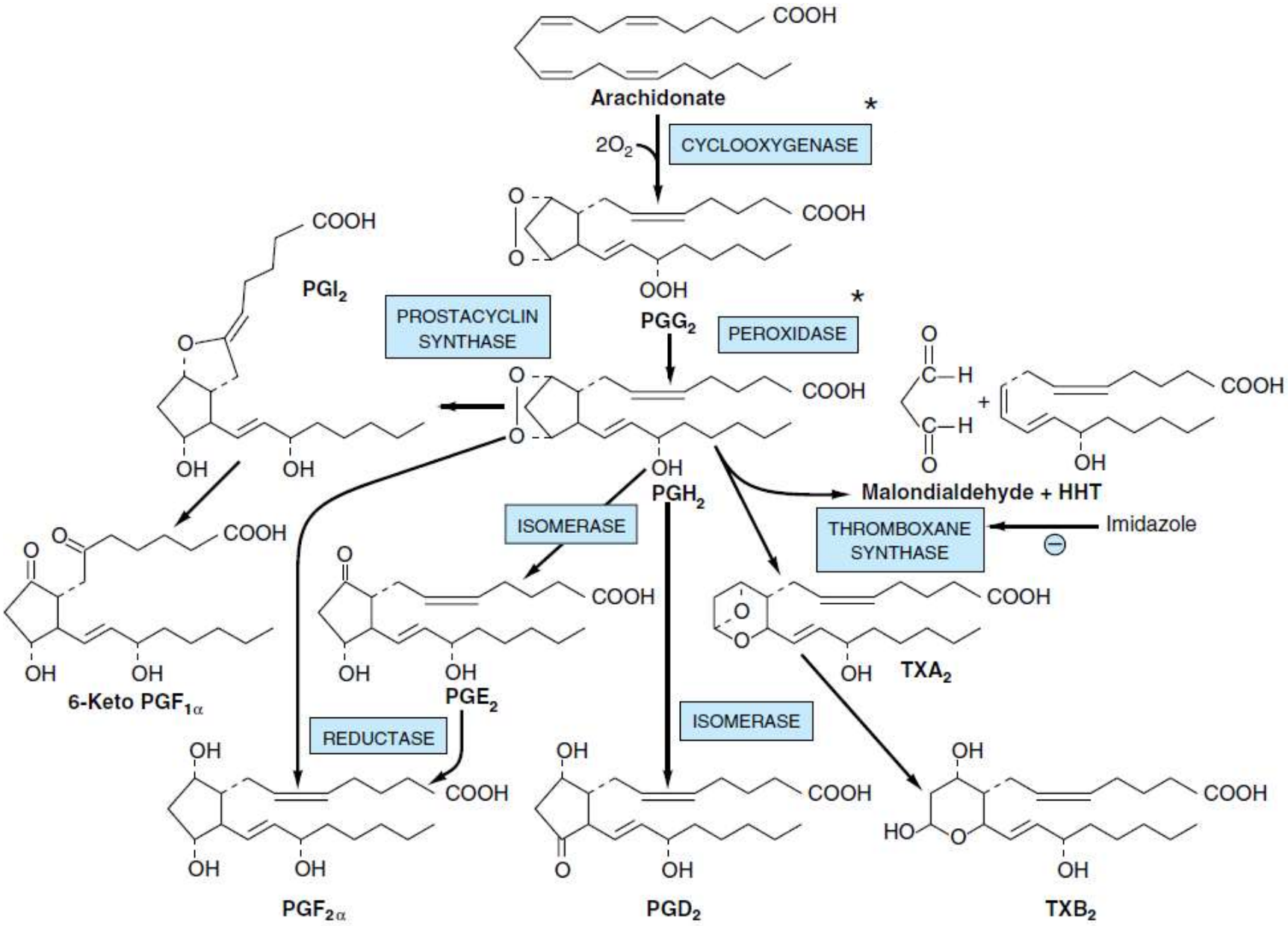


Prostaglandin E_1



Prostaglandin $F_{3\alpha}$

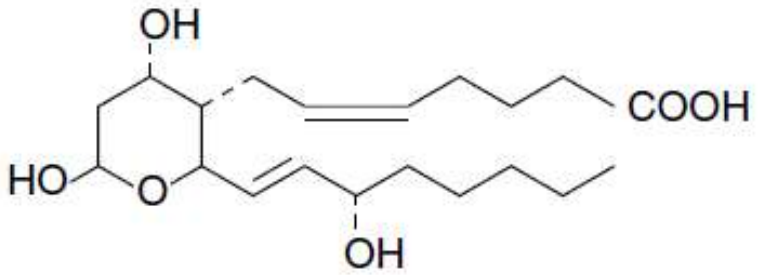
انواع PG


COOH
Arachidonate
*
$2O_2$
CYCLOOXYGENASE
COOH
OOH
PGG_2
*
PEROXIDASE
PROSTACYCLIN SYNTHASE
COOH
PGI_2
OH
OH
OH
PGH_2
Malondialdehyde + HHT
COOH
OH
ISOMERASE
THROMBOXANE SYNTHASE
Imidazole
COOH
COOH
OH
OH
6-Keto $PGF_{1\alpha}$
OH
OH
PGE_2
TXA_2
REDUCTASE
ISOMERASE
OH
COOH
OH
OH
$PGF_{2\alpha}$
OH
COOH
O
OH
PGD_2
OH
COOH
HO
O
OH
TXB_2

Type	Receptor	Receptor type	Function
PGI_2	IP	G_s	•vasodilation •inhibit platelet aggregation •bronchodilation
PGE_2	EP_1	G_q	•bronchoconstriction •GI tract smooth muscle contraction
	EP_2	G_s	•bronchodilation •GI tract smooth muscle relaxation •vasodilation
	EP_3	G_i	•↓ gastric acid secretion •↑ gastric mucus secretion •uterus contraction (when pregnant) •GI tract smooth muscle contraction •lipolysis inhibition •↑ autonomic neurotransmitters [12] •↑ platelet response to their agonists [13] and ↑ atherothrombosis in vivo [14]
	Unspecified		•hyperalgesia[12] •pyrogenic
$PGF_{2\alpha}$	FP	G_q	•uterus contraction •bronchoconstriction

ترومباکسان ها

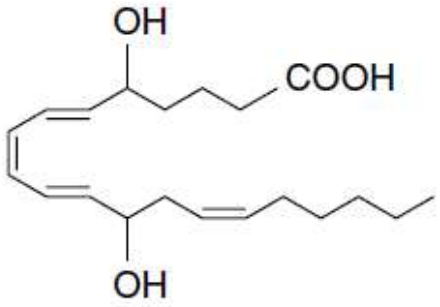
- **Thromboxanes**
  - **Six-membered ring**
  - **Thromboxanes are synthesized in platelets and upon release cause vasoconstriction and platelet aggregation**



TXB_2

لوکوترین ها

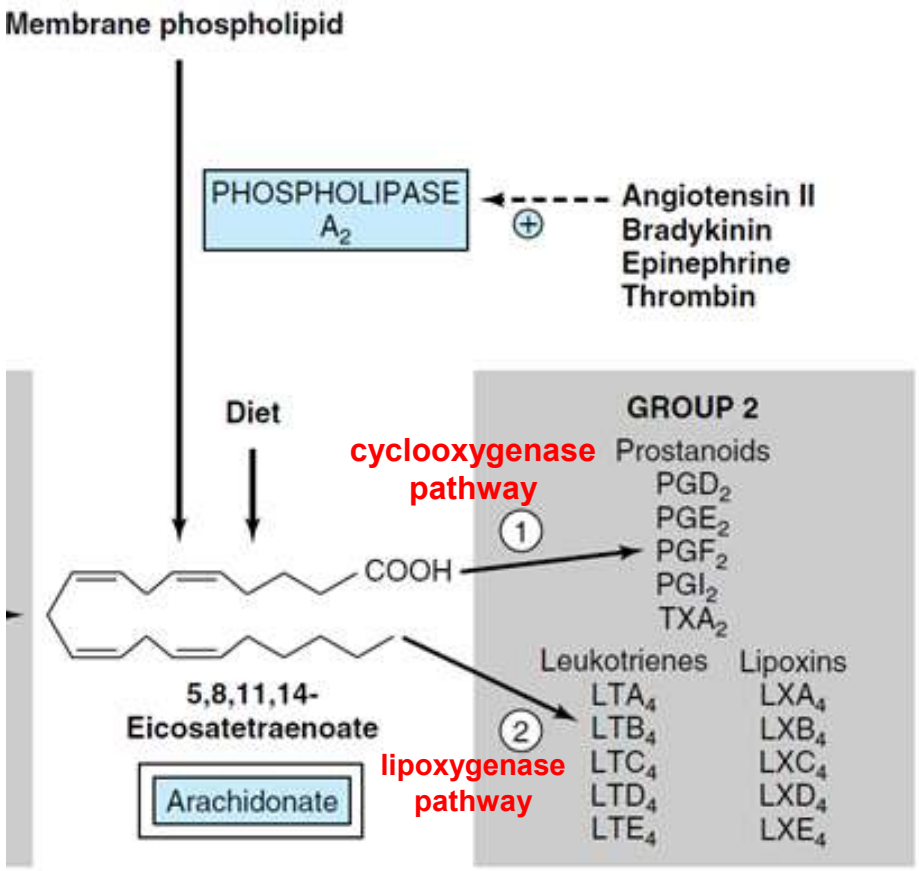
- **Leukotrienes is synthesized in leukocytes, mast cells, platelets, and macrophages by the lipoxygenase pathway in response to both immunologic and nonimmunologic stimuli**
  - **Contain three conjugated double bonds**
  - **anaphylactic shock (Overproduction of leukotrienes causes asthmatic attacks, hypersensitive to bee stings, penicillin)**



Leukotriene B_4

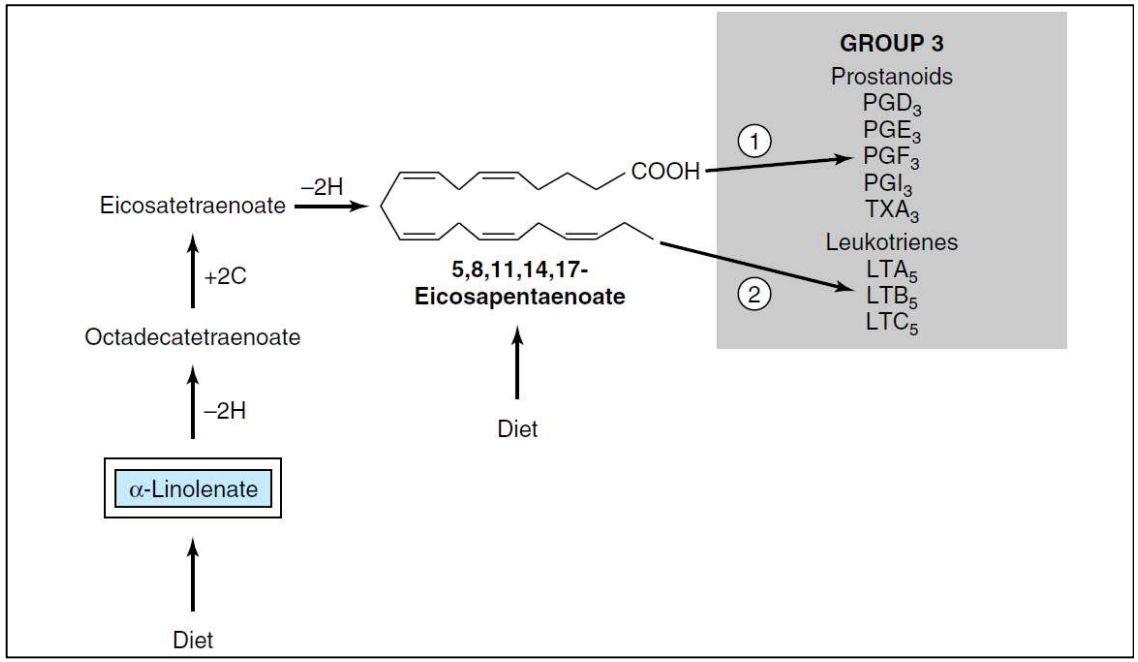
آراشیدونیک اسید پیش ساز

- PG2, TX2 series (prostanoids) by the cyclooxygenase pathway
  - Cyclooxygenase and peroxidase (prostaglandin H synthase PGHS)
  - Aspirin, a nonsteroidal anti-inflammatory drug (NSAID), inhibits cyclooxygenase
  - Transcription of PGHS is completely inhibited by anti-inflammatory corticosteroids.
- LT4 and LX4 series by the lipoxygenase pathway



ایکوزاپنتاانوئیک اسید پیش ساز

- PG3, TX3 series (prostanoids) by the cyclooxygenase pathway
  - inhibit the release of arachidonate from phospholipids and the formation of PG2 and TX2
- LT4 and LX4 series by the lipoxygenase pathway



دوکوزاهگزاانوئیک اسید

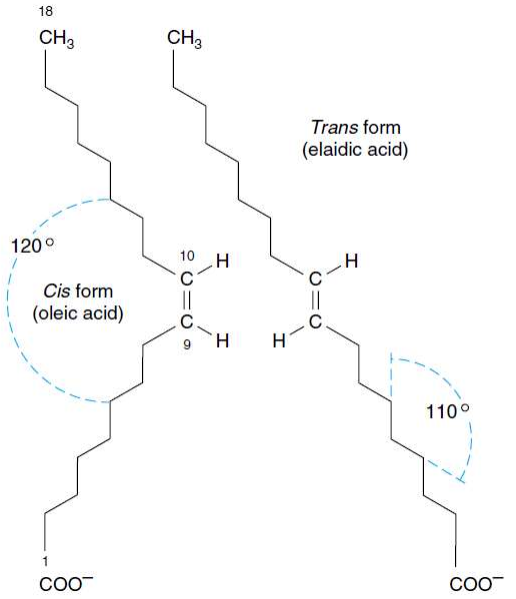
- Docosahexaenoic acid (DHA; ω3, 22:6), which is synthesized from α-linolenic acid or obtained directly from fish oils.
- Present in high concentrations in retina, cerebral cortex, testis, and sperm.
- DHA is particularly needed for development of the brain and retina
- In essential fatty acid deficiency, polyenoic acids of the ω9 family (Δ5,8,11-eicosatrienoic acid) replace or triene:tetraene ratio in plasma lipids increase

اسیدهای چرب امگا–۳

- Maintaining the nervous system
- ALA is a precursor of EPA, which is tend not to promote inflammation.
- interferes with the conversion of LA to AA and blocks the formation of cytokines and blood levels of C-reactive protein (CRP)
  - have biologic effects that make them useful in preventing and managing chronic conditions such as type 2 diabetes, kidney disease, rheumatoid arthritis, high blood pressure, coronary heart disease, stroke, Alzheimer disease, alcoholism and certain types of cancer.

اسیدهای چرب ترانس

- Increased blood levels of LDL (bad cholesterol) and decreased HDL (good cholesterol)
  - French fries, doughnuts, and cookies
  - during hydrogenation, or “hardening,” of natural oils
- Improved health
  - Dairy products and meat



کاتابولیسم تری گلیسرید (Fat Mobilization)

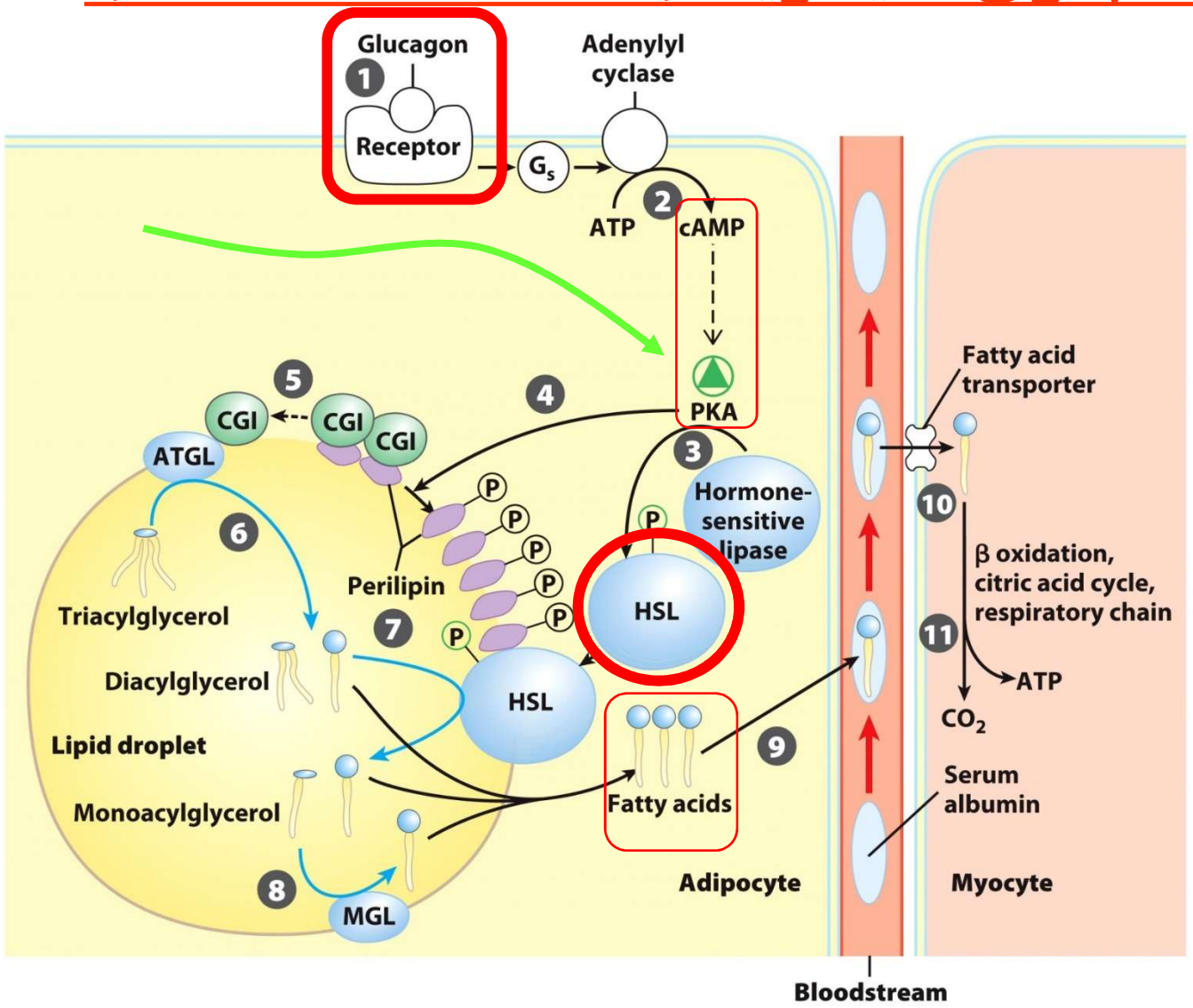
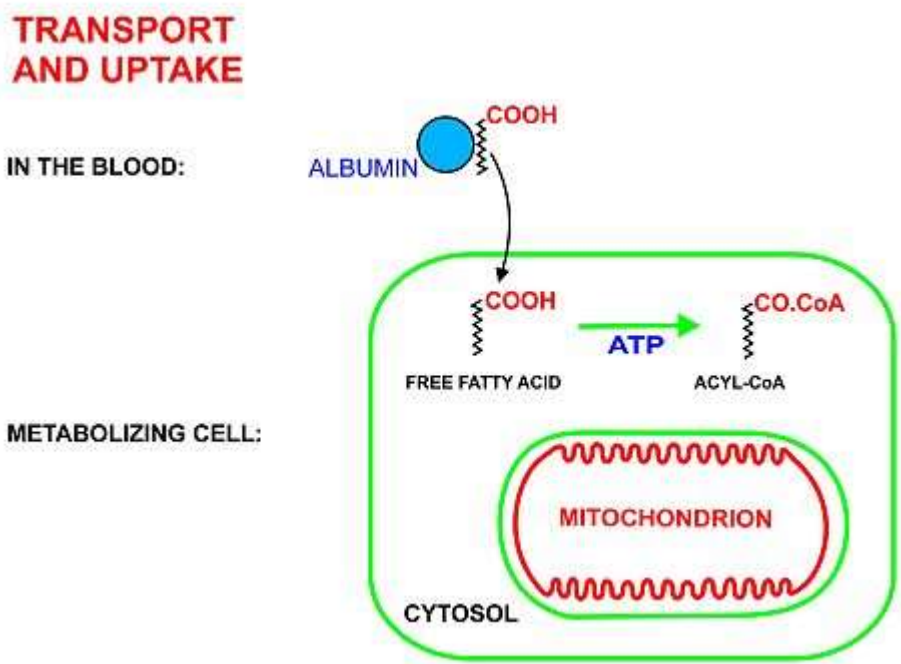
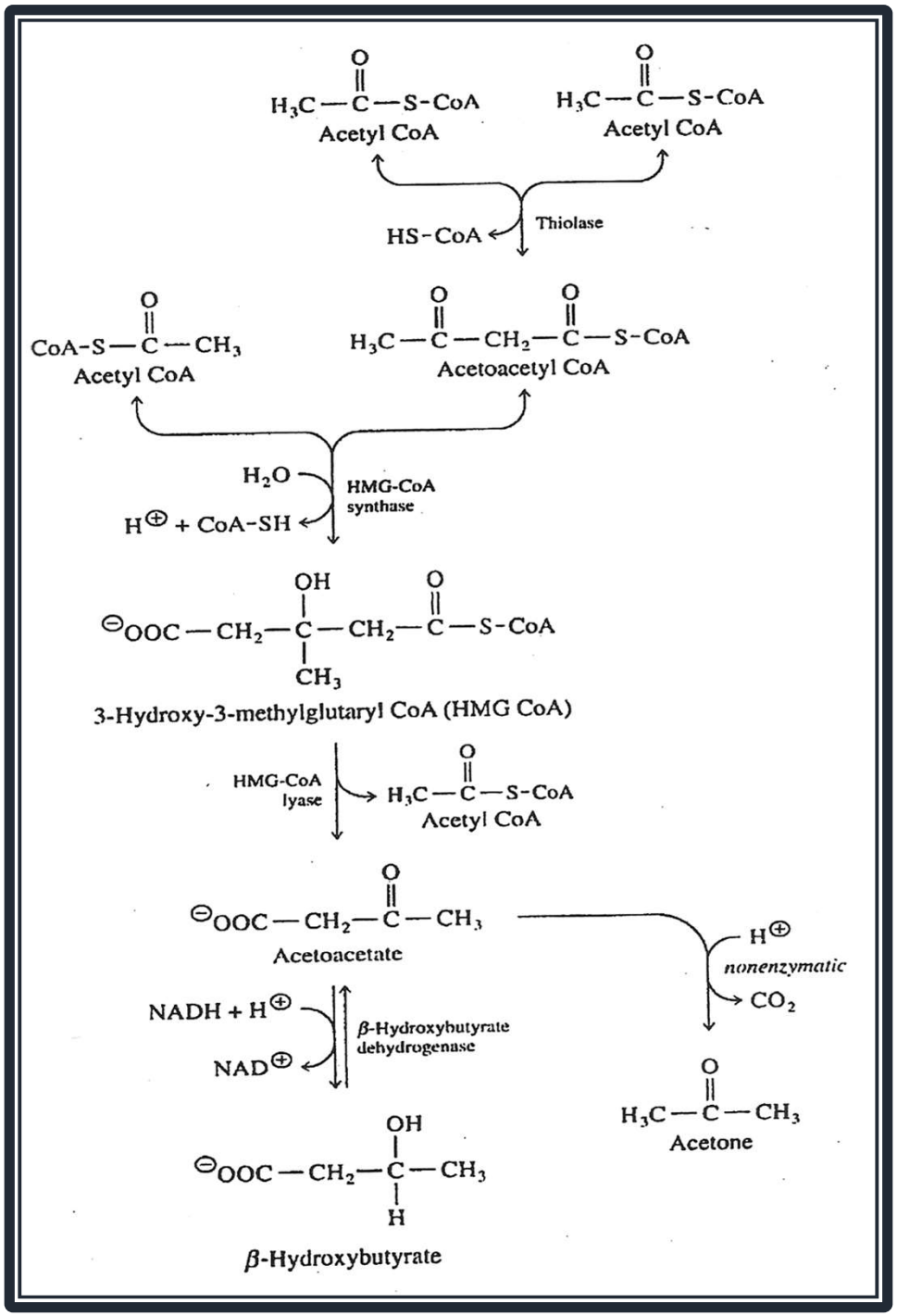


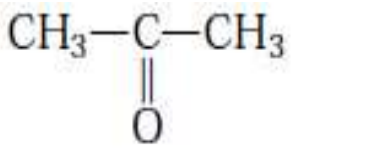
Figure 17-3
Lehninger Principles of Biochemistry, Sixth Edition

۱– انتقال توسط آلبومین

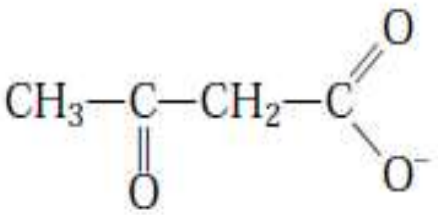


کتوژنز و اجسام کتونی

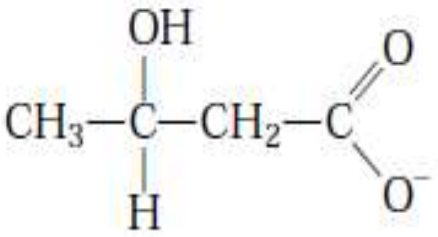




Acetone

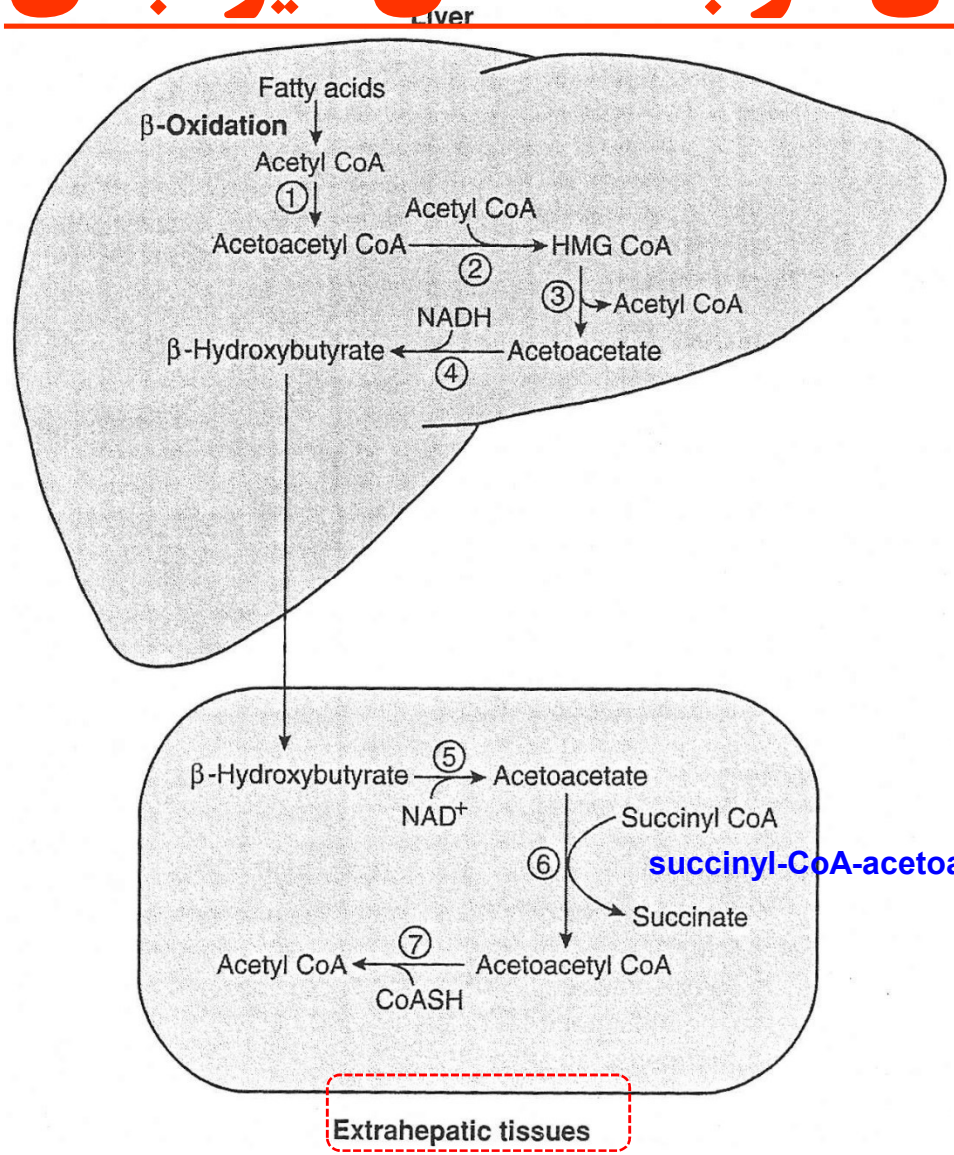


Acetoacetate



D-β-Hydroxybutyrate

مصرف اجسام کتونی در بافت های غیر کبدی



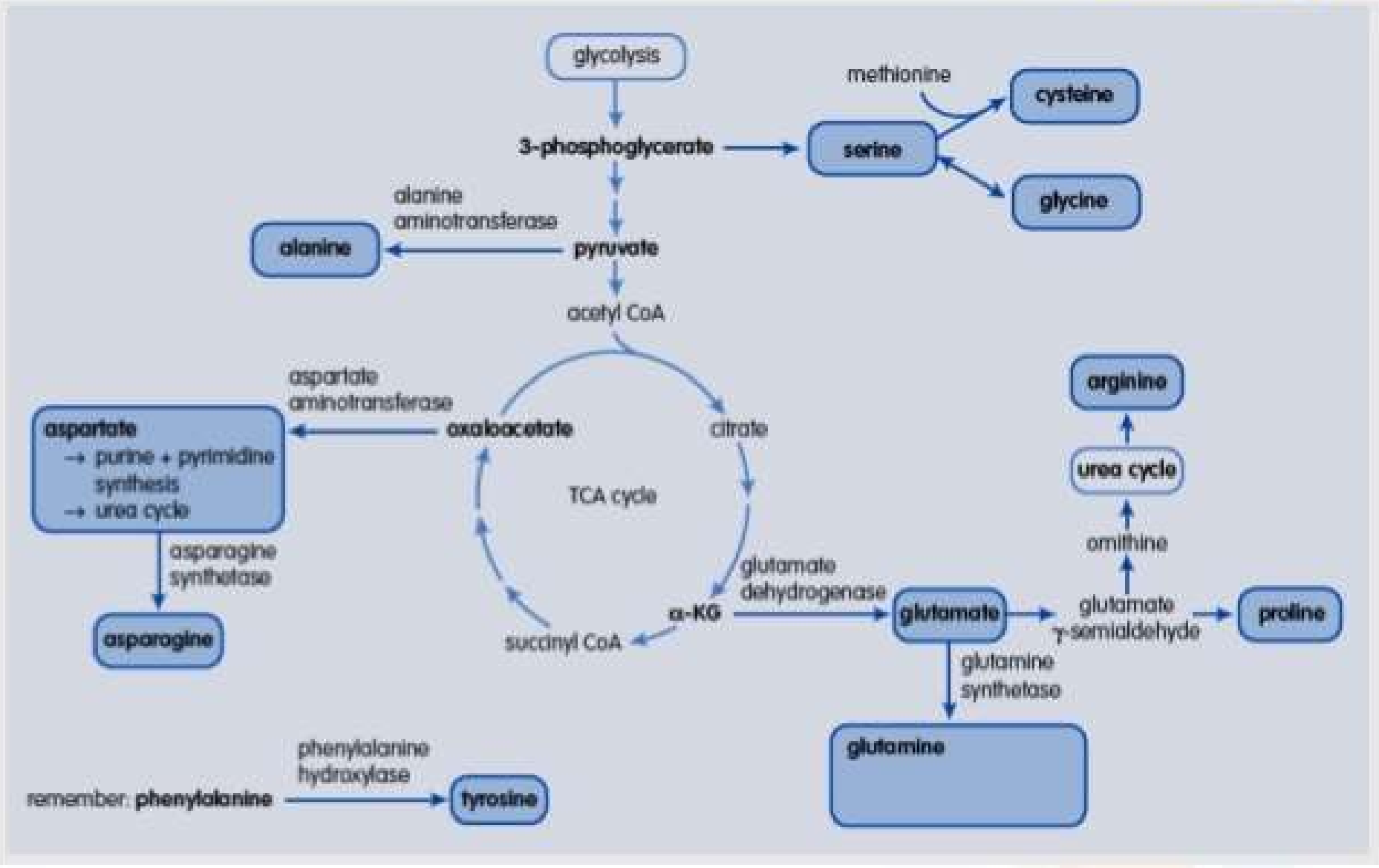
succinyl-CoA-acetoacetate CoA transferase

ساخت aa

Number of Enzymes Required to Synthesize			
Nutritionally Essential		**Nutritionally Nonessential**	
Arg[1]	7	Ala	1
His	6	Asp	1
Thr	6	Asn[2]	1
Met	5 (4 shared)	Glu	1
Lys	8	Gln[1]	1
Ile	8 (6 shared)	Hyl[3]	1
Val	6 (all shared)	Hyp[4]	1
Leu	7 (5 shared)	Pro[1]	3
Phe	10	Ser	3
Trp	5 (8 shared)	Gly[5]	1
	59	Cys[6]	2
		Tyr[7]	1
			17

[1]From Glu, [2]From Asp, [3]From Lys, [4]From Pro, [5]From Ser, [6]From Ser plus S^{2-}, [7]From Phe.

Biosynthesis of Non Essential Amino Acids

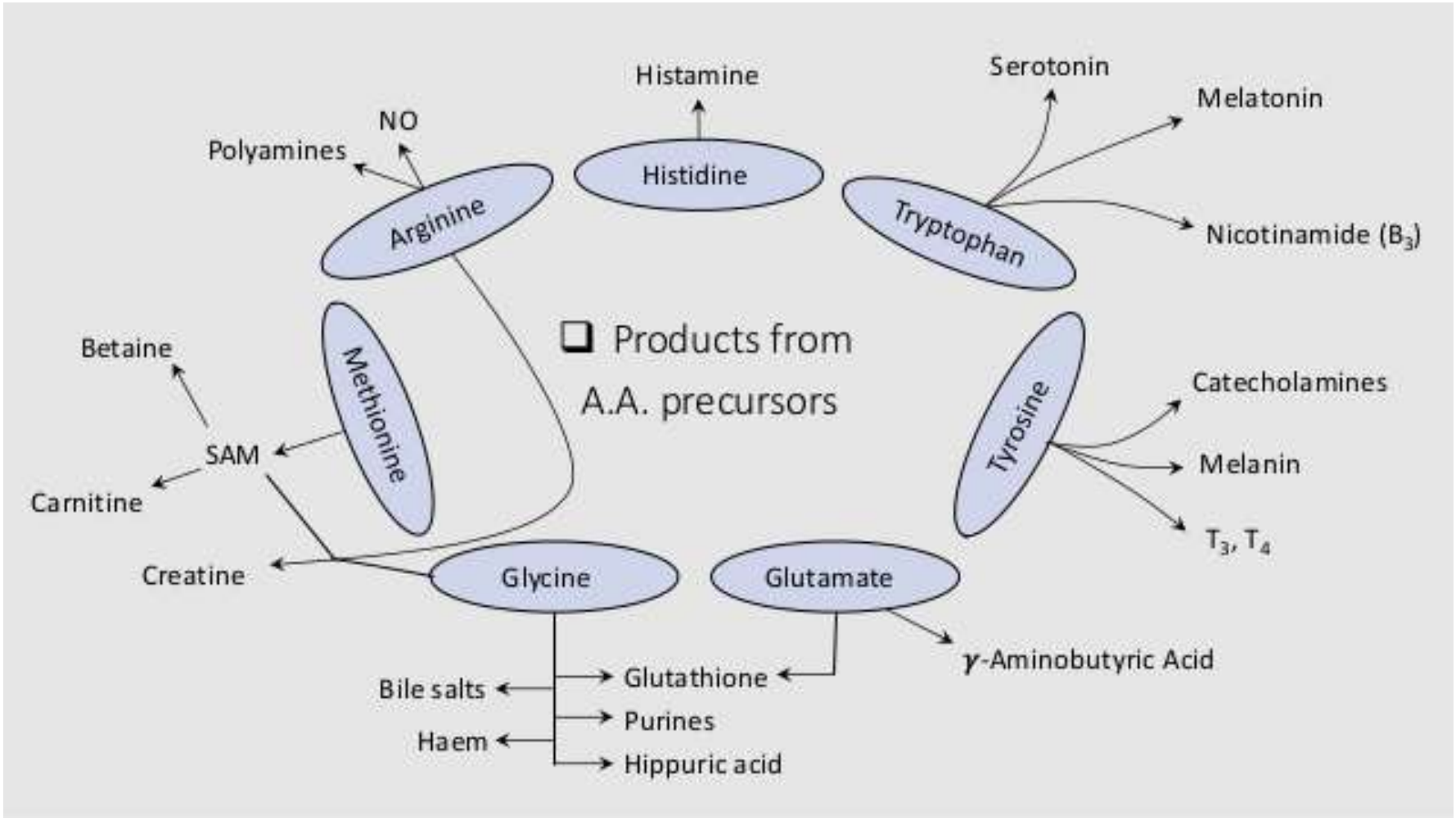


❑ Metabolism of A.A. precursors

- A.A.'s act as precursors to synthesis of physiologically important amines that show potent bioactivity. Examples: Polyamines, creatine, carnitine, neurotransmitters, melanin, betaine, bile salts, haem, purines, choline, glycosamine, purines and pyrimidines, pharmacological amines and hormones

	Amine derivative	Precursor	Physiological role
1.	**Polyamines**	Ornithine	Putrescine, spermine, and spermidine are chromatin associated
2.	**Creatine**	Gly + Arg	Phosphocreatine in muscle undergoes spontaneous dephosphorylation and is excreted as creatinine
3.	**Carnitine**	Lys (-Protein)	Shuttles fatty acids across the mitochondrial membrane
4.	**Neurotransmitters**		
4.1	γ-aminobutyrate (GABA)	Glu	Inhibits synaptic transmission
4.2	Histamine	His	Expands capillaries and constricts veins, resulting in increased local blood volume, and edema, with low b.p. during allergies
4.3	Acetylcholine	Ser + Met	Induces muscular activity

A.A. derivative	Precursor	Physiological effect
Serotonin	Try	Induces sleep (W-rich diet)
Catecholamines (L-dopa, dopamine, epinephrine, and norepinephrine)	Tyr	Increase cardiac output and cellular metabolism during stress
Melanin	Tyr	Pigmentation
Purines	Gly + Glu	Nucleic acid biosynthesis
Glutathione	Gly + Glu	Reducing environment
Nitric oxide	Arg	Signalling
Porphyrins	Gly or Glu	Nucleus of haem proteins like cytochromes and hemoglobin


Histamine
Serotonin
Melatonin
NO
Polyamines
Histidine
Arginine
Tryptophan
Nicotinamide (B_3)
Products from
A.A. precursors
Betaine
Methionine
Tyrosine
Catecholamines
SAM
Melanin
Carnitine
T_3, T_4
Creatine
Glycine
Glutamate
γ-Aminobutyric Acid
Glutathione
Bile salts
Purines
Haem
Hippuric acid