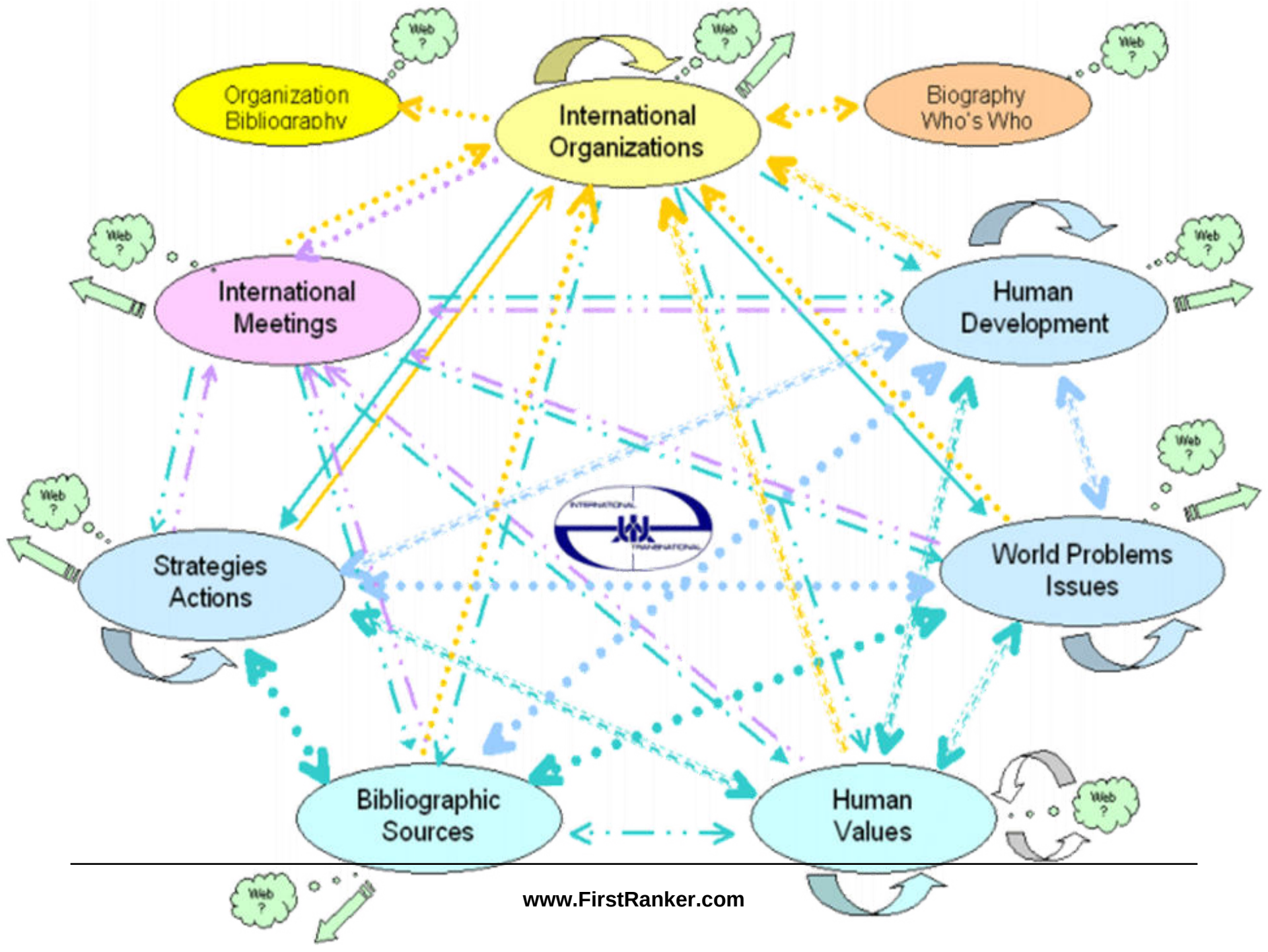
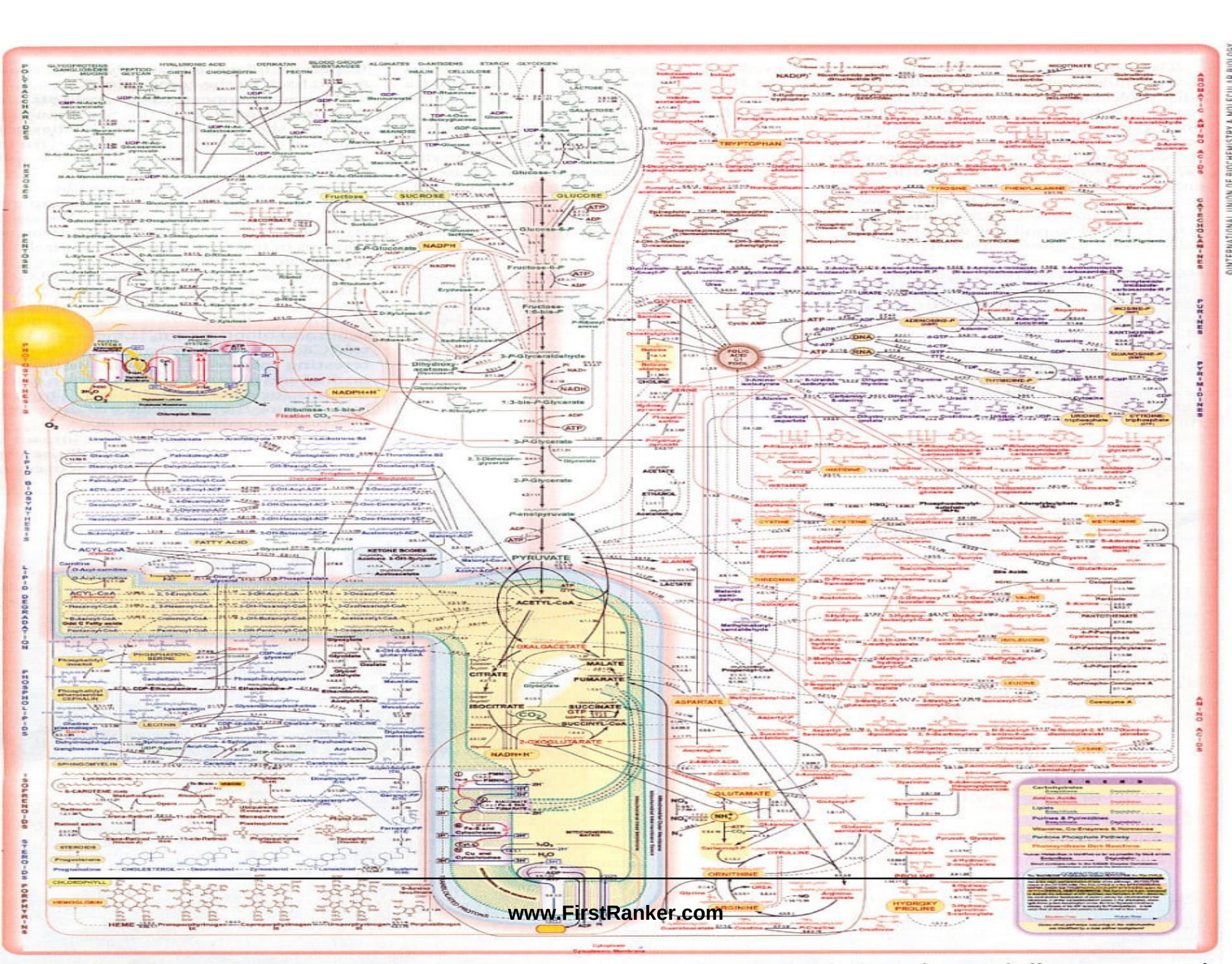
Induction To Todays Topic

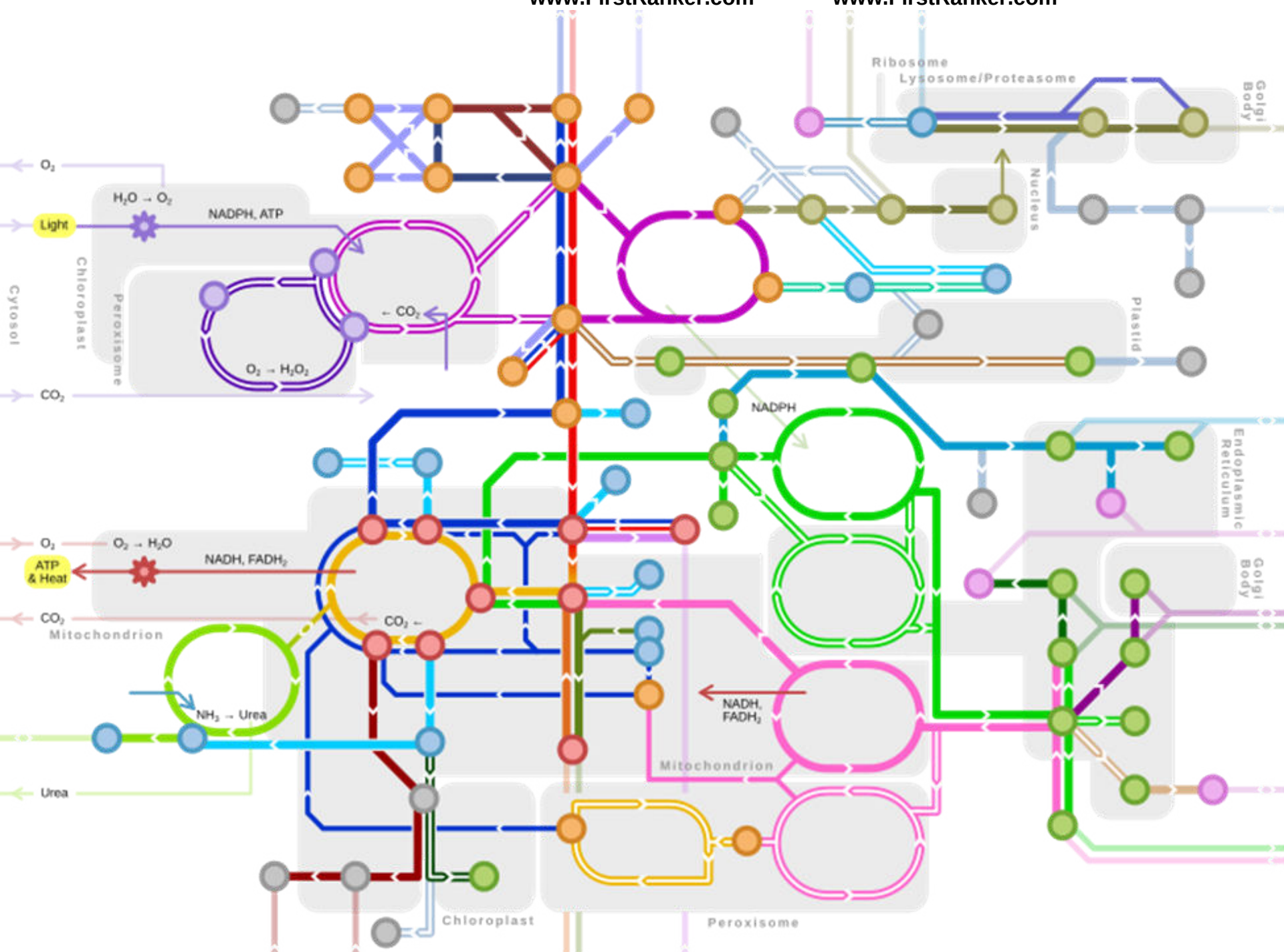
WORLD OF HUMAN BEINGS

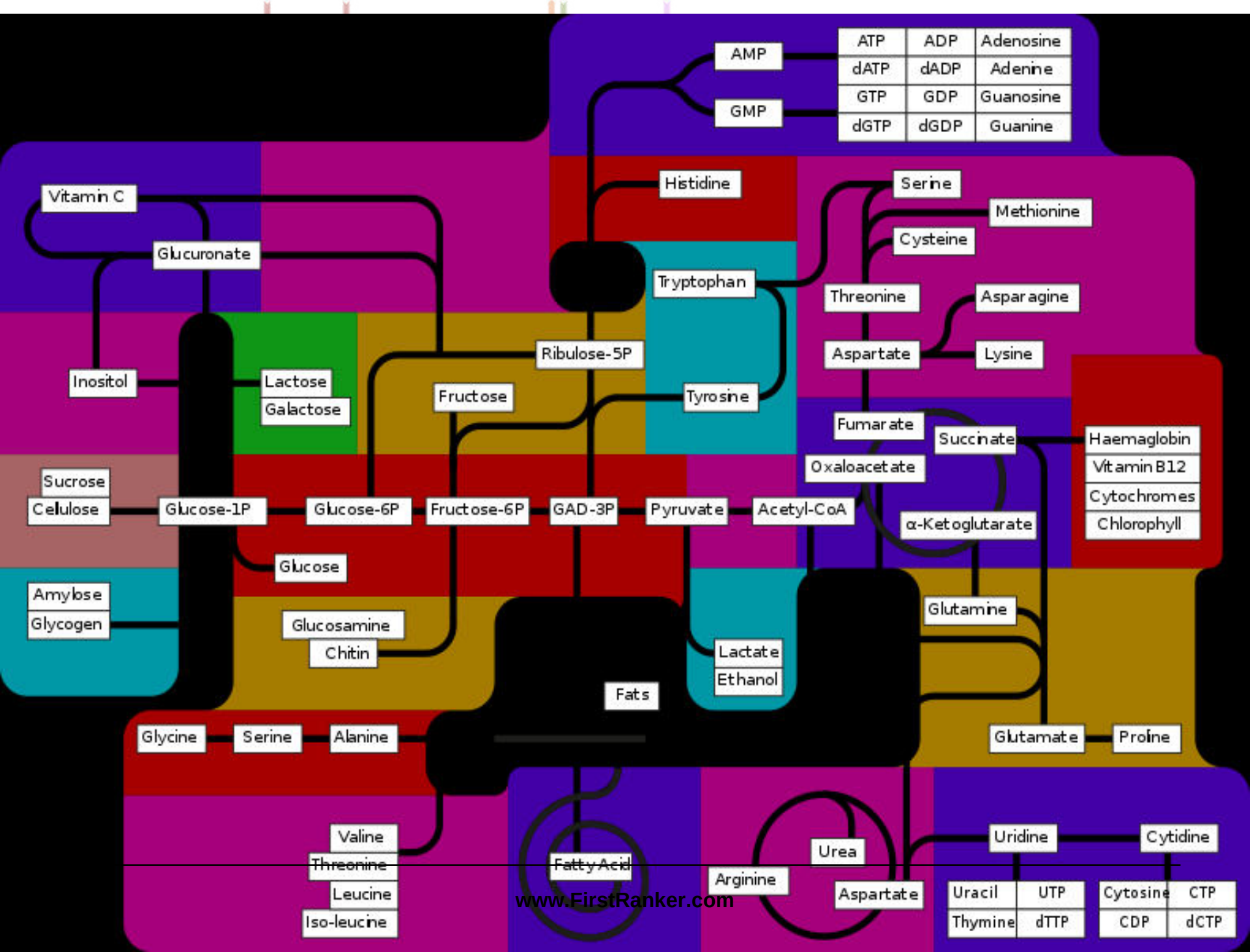
HUMAN INTER-RELATIONSHIPS



WORLD OF BIOMOLECULES
And
INTER-RELATIONSHIPS

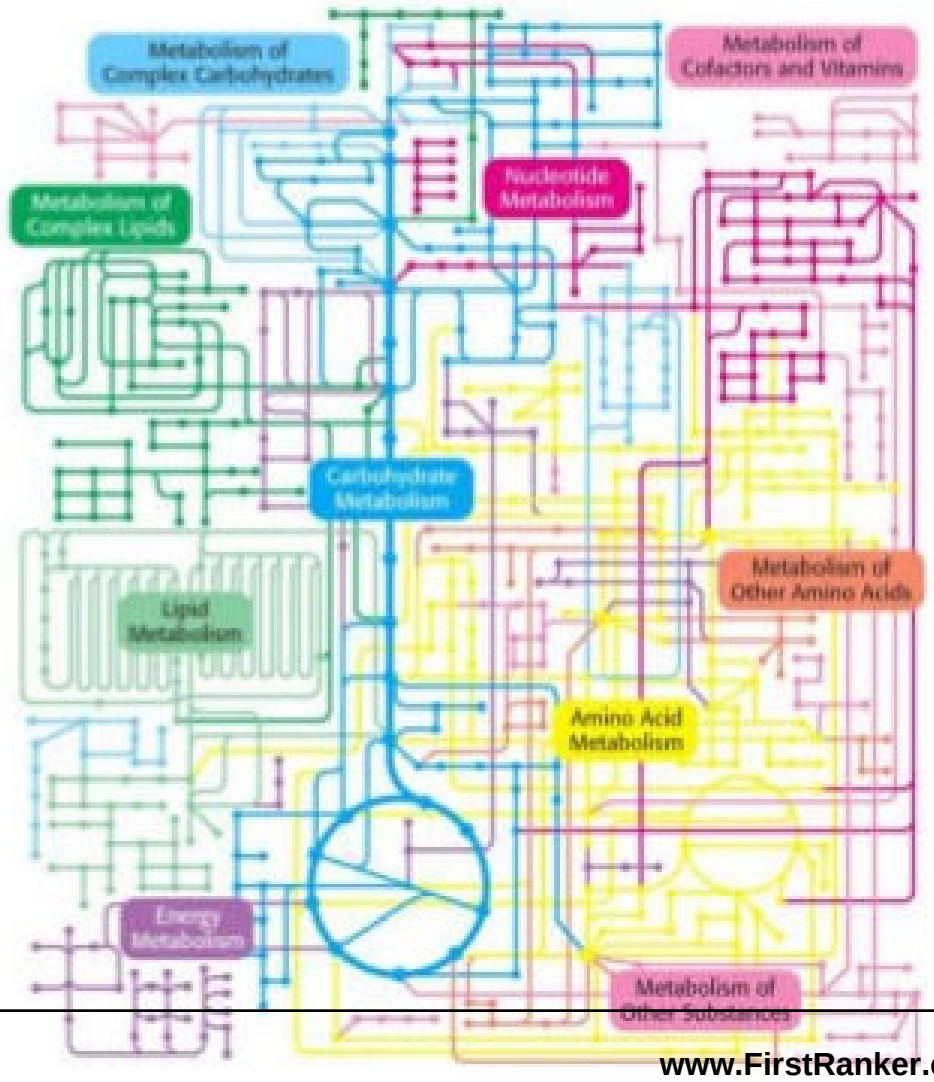






ANY GUESSES FOR TODAYS TOPIC ?

Integration of Metabolism



1. Interconnection of pathways
2. Metabolic profile of organs
3. Food intake, starvation and obesity
4. Fuel choice during exercise
5. Ethanol alters energy metabolism
6. Hormonal regulation of metabolism

Integrated Metabolism

OR

Intermediary Metabolism

OR

Interrelationship Between Various Metabolic Pathways

OR

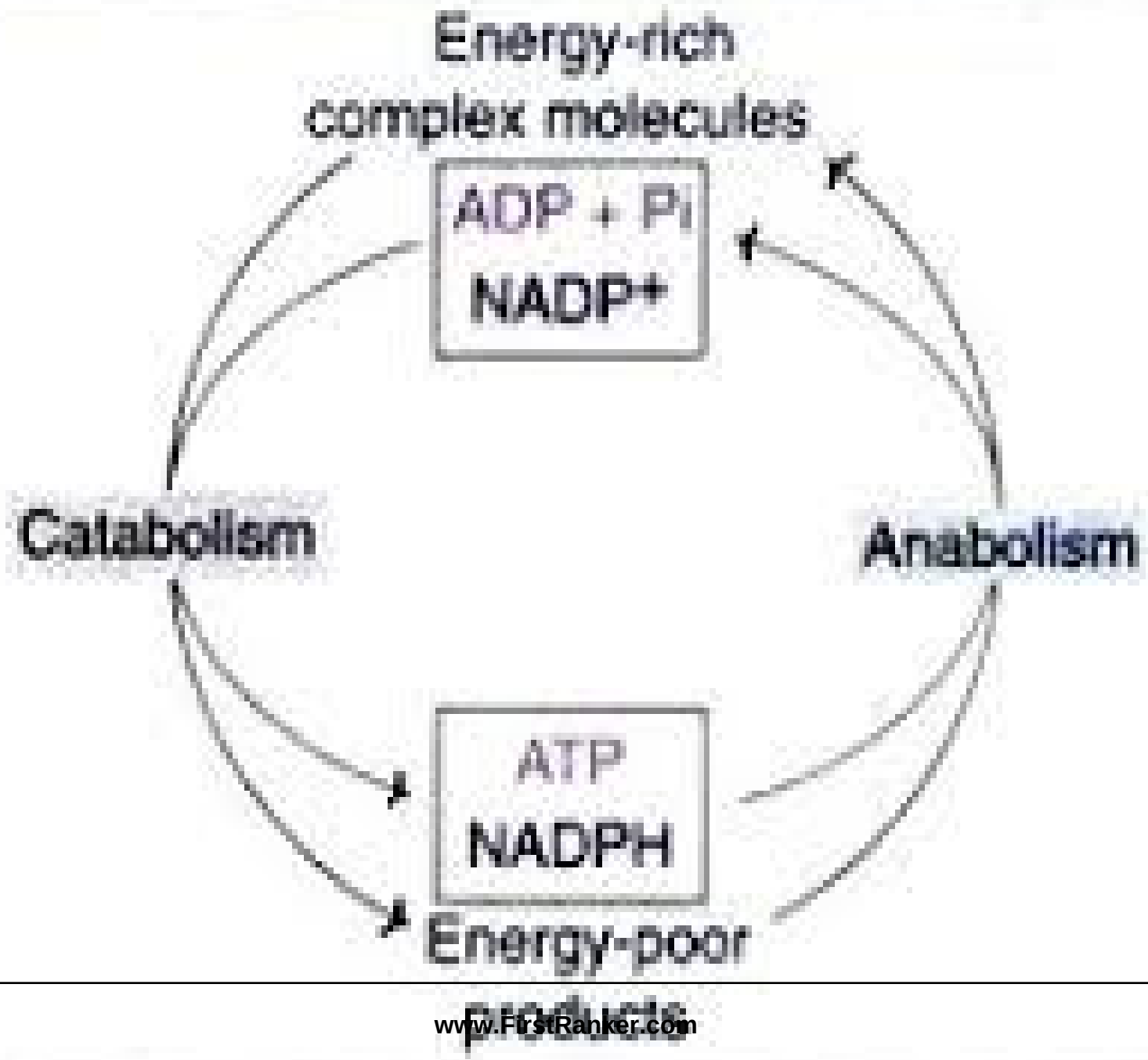
Interdependence Of Metabolic Pathways

What Is an Essence of Normal, Health, Growth and Reproduction of Human Body?

Normal Metabolism of Biomolecules

Metabolism and Types

- Metabolism is the term used to describe
  - The interconversion of chemical compounds in the body
  - The pathways taken by individual molecules,
  - Their interrelationships, and the mechanisms that regulate the flow of metabolites through the pathways
- It falls mainly in 3 categories: catabolism, anabolism and amphibolic pathways



Important Factors Of Metabolism

- Metabolites
- Hormones
- Enzymes
- Cofactors
- Coenzymes
- Water
- Oxygen

- **Various metabolic reactions, pathways and processes** of **important biomolecules** of human body viz:
  - **Carbohydrates**
  - **Lipids**
  - **Proteins**
  - **Nucleic acids**
  - **Hemoglobin**

- **Taking place in different cells and cellular compartments** of **specific tissues and organs.**

Metabolic Pathways are Compartmentalized Within Cells

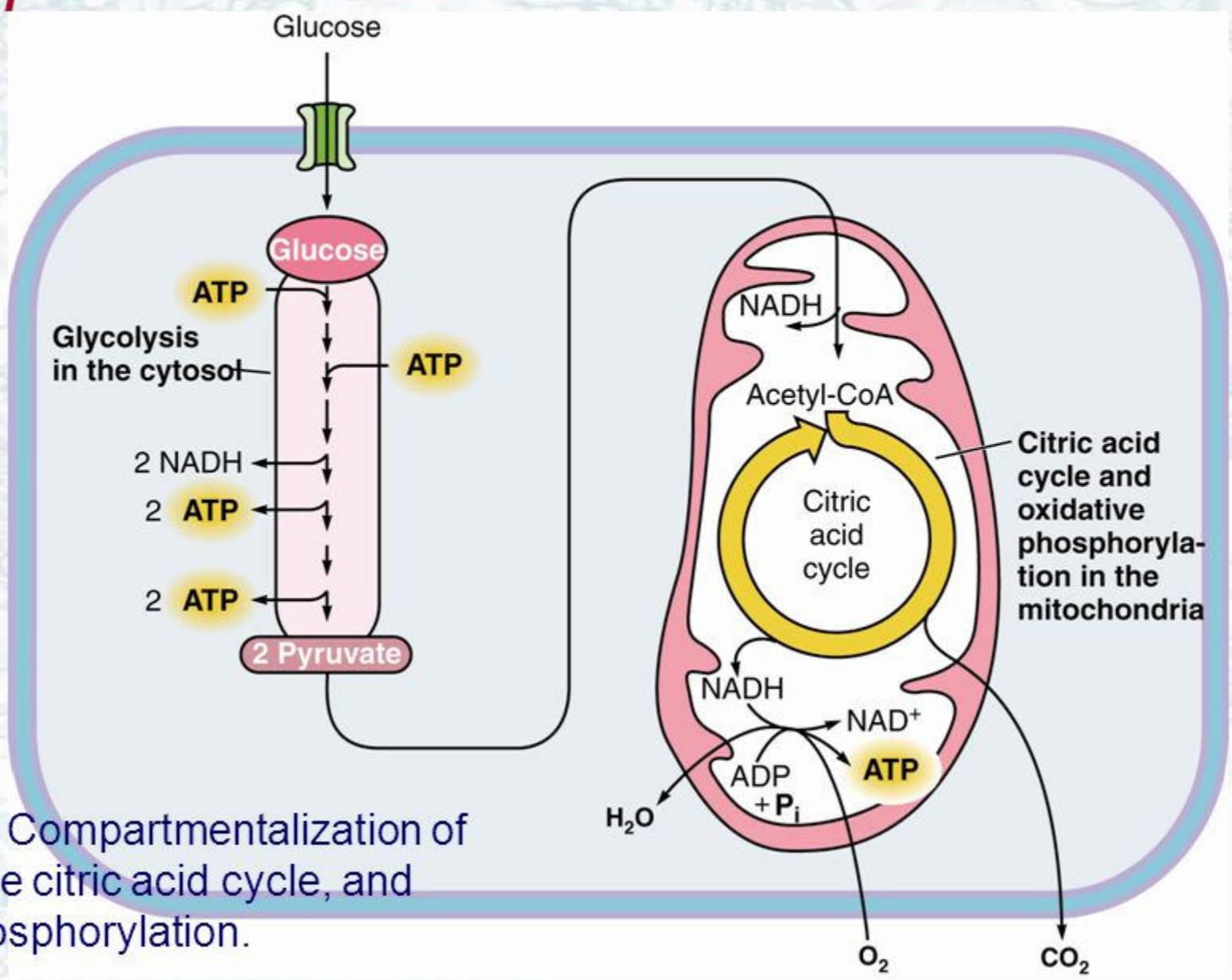


Figure 17.17 Compartmentalization of glycolysis, the citric acid cycle, and oxidative phosphorylation.

Significance To Study Individual Metabolic Pathways Of Various Biomolecules

- Metabolism of each **chief biomolecule was studied individually and separately.**

- For **convenience** and clear **understandings of metabolic reactions associated to it.**

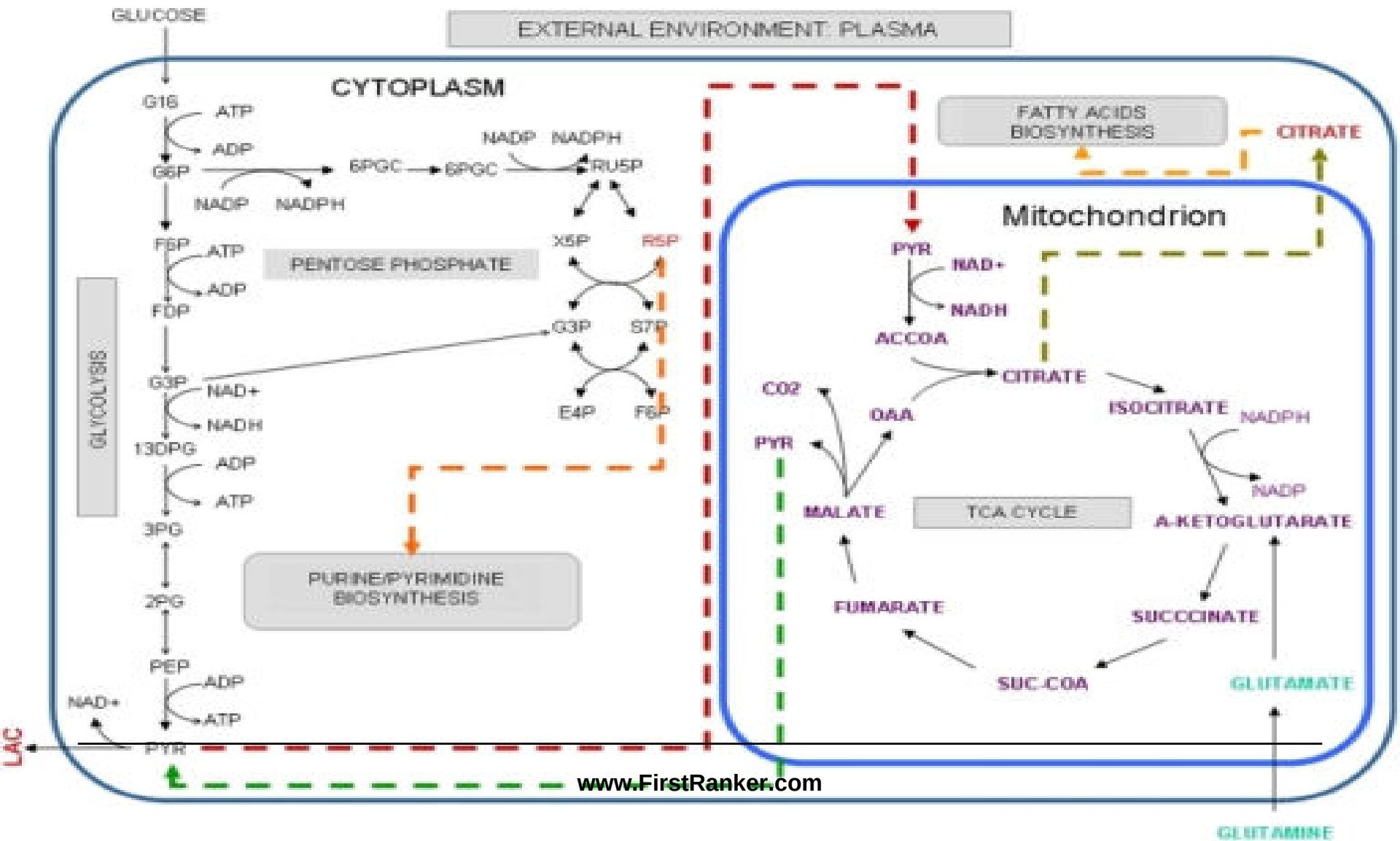
Major Metabolic Pathways

- 1. Glycolysis
- 2. Gluconeogenesis
- 3. Glycogen Metabolism
- 4. Fatty Acid Metabolism
- 5. Citric Acid Cycle
- 6. Oxidative Phosphorylation
- 7. Amino Acid Metabolism
- Only the liver can carry out all of the reaction the major pathways.

NORMAL METABOLISM

1. After a meal glucose levels rise, insulin is produced
2. Insulin suppresses glucagon secretion
3. Insulin stimulates glycogen synthase I form
4. Insulin stimulates acetyl-CoA carboxylase
5. Fat synthesis accelerated
6. Insulin stimulates glucose uptake into muscle, adipose
7. Glucose falls, glucagon secretion restored
8. cAMP activates glycogen phosphorylase, lipase
9. Liver switches to gluconeogenic mode

Features of Normal Metabolic Pathways



1. Well Planned
2. Compartmentalized
3. Well Organized/ More Systematic
4. Require Specific Conditions
5. Synergistic/Simultaneous
6. Flexible/Adapt/Change for good survival
7. Induced as per condition
8. Regular in its operation
9. Regulated/Controlled/Balanced
10. Good cooperation and coordination

Hormones Regulate Metabolism

- **Hormones** are **key regulators of Enzymes**
- **Regulatory Enzymes** are stimulated or inhibited by specific hormones
- **Enzymes are regulated by:**
  - **Allosteric Regulation**
  - **Covalent Modifications**

Metabolism Is Regulated By

- **Availability of Substrates Regulate Metabolism :**
  - **Ratio of Insulin/Glucagon**
  - **Ratio of ATP and AMP**
  - **NADH/NAD**
  - **Citrate levels**
  - **Fructose 2,6 Bisphosphate levels**

- **Low and high levels of ATP** stimulate and inhibit regulatory enzymes of Glycolysis and TCA.
- **Increased levels of Acetyl-CoA and Citrate** stimulates enzyme Acetyl CoA Carboxylase of De Novo biosynthesis of Fatty acid.
- **Increased Fructose 1,6 Bisphosphatase is**
  - **Allosteric stimulator of PFK of Glycolysis**
  - **Allosteric inhibitor of Fru1,6Bis Phosphatase of Gluconeogenesis.**

What is an Integrated Metabolism?

- **Metabolic pathways are Closely Interrelated/Integrated /Interdependent**

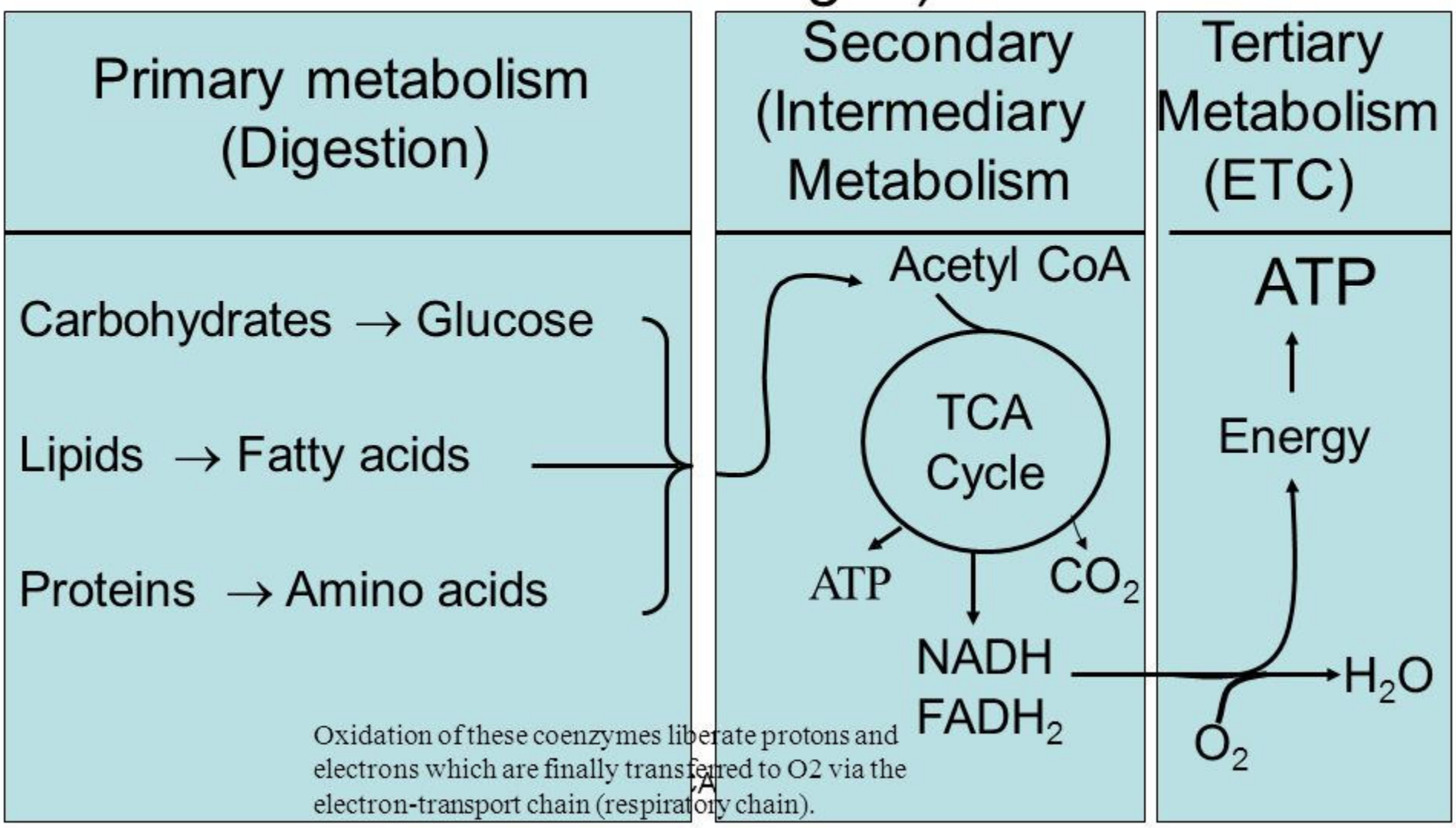
  – **Not totally dependent nor totally independent**

  OR

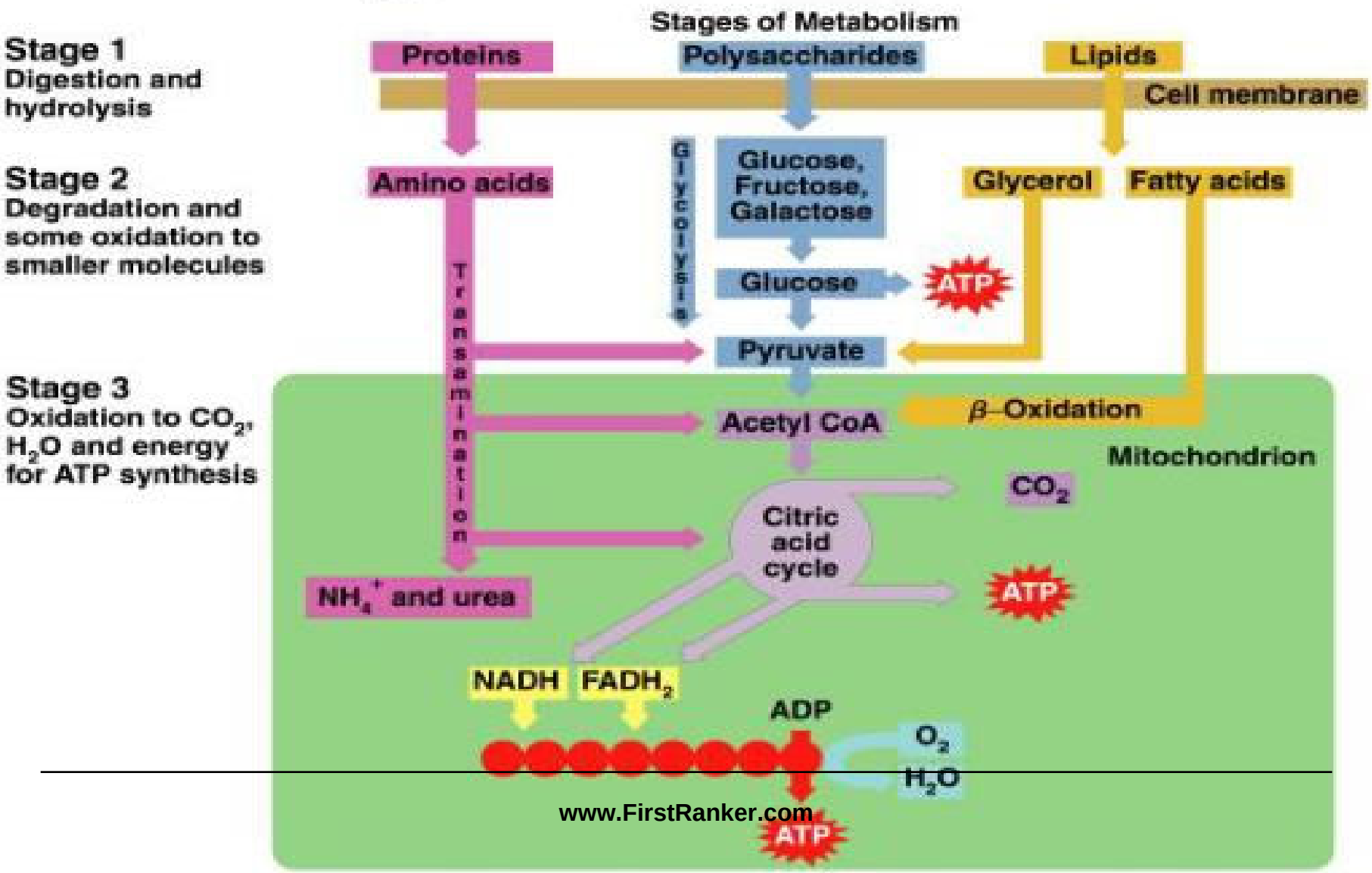
  – **But partial dependence and partial independence**

Stages Of Integrated Metabolism

Energy Production in Metabolism (Summary of Oxidation of Foodstuffs in Three Stages)



Stages of Metabolism



STAGES OF INTEGRATED METABOLISM ⑥

w.r.t CARBOHYDRATES; LIPIDS AND PROTEINS.

STARCH → MALTOSE → GLUCOSE

TRIACYLGLYCEROL → 2-MONOACYLGLYCEROL → FFA + GLYCEROL

EGG ALBUMIN → DIPEPTIDES → AMINO ACIDS

I st STAGE — PRIMARY METABOLISM — HYDROLYTIC STAGE

GLUCOSE, FFA + GLYCEROL, AMINO ACIDS → ABSORBED BY INTESTINAL MUCOSAL CELLS

BLOOD CIRCULATION

ENTERS THE CELLS OF ORGANS

GLUCOSE → Glycolysis → PYRUVATE

FFA → β-oxidation

AMINO ACIDS → catabolism / transamination → PYRUVATE

II nd STAGE — SECONDARY METABOLISM — PREPARATORY STAGE

PYRUVATE —PDH→ ACETYL-CoA ← FFA, AMINO ACIDS

ACETYL-CoA → TCA CYCLE → CO_2 ← , → H_2O

TCA CYCLE → $NADH + H^+$ & $FADH_2$ (Reduced Coenzymes)

III rd STAGE — TERTIARY METABOLISM — OXIDATIVE STAGE

ENTERS ETC / OXIDATIVE PHOSPHORYLATION

GENERATES ATP (CHEMICAL ENERGY)

In the **fed** state, nutrients are stored; In the **fasting** state, they are oxidized for energy production

Carbohydrates	Fats	Proteins

Through digestion and absorption, the food is broken down into:

Carbohydrates	Fats	Proteins
Glucose (sugar)	Fatty Acids and Glycerol	Amino Acids
Metabolic pathway of **Glycolysis**	Metabolic pathway of **Beta-Oxidation**	Metabolic pathway of **Transamination**
Stored as Glycogen or fat	Stored as triglycerides in fat cells	Stored as glycogen or fat
Synthesized into other compounds	Synthesized into cellular membranes	Made into new protein compounds
Oxidized for energy	Oxidized for energy	Oxidized for energy

Fatty Acids used to create Ketone bodies for body fuel

Glycerol used to create glucose for brain/blood cells

Starvation State

Acetyl-CoA → Kreb's Cycle (Mitochondria) → ATP created to fuel body

carbon dioxide and water are exhaled

Evidences Of Metabolic Interrelationships

Interrelationships Of Carbohydrates with Lipid Metabolism

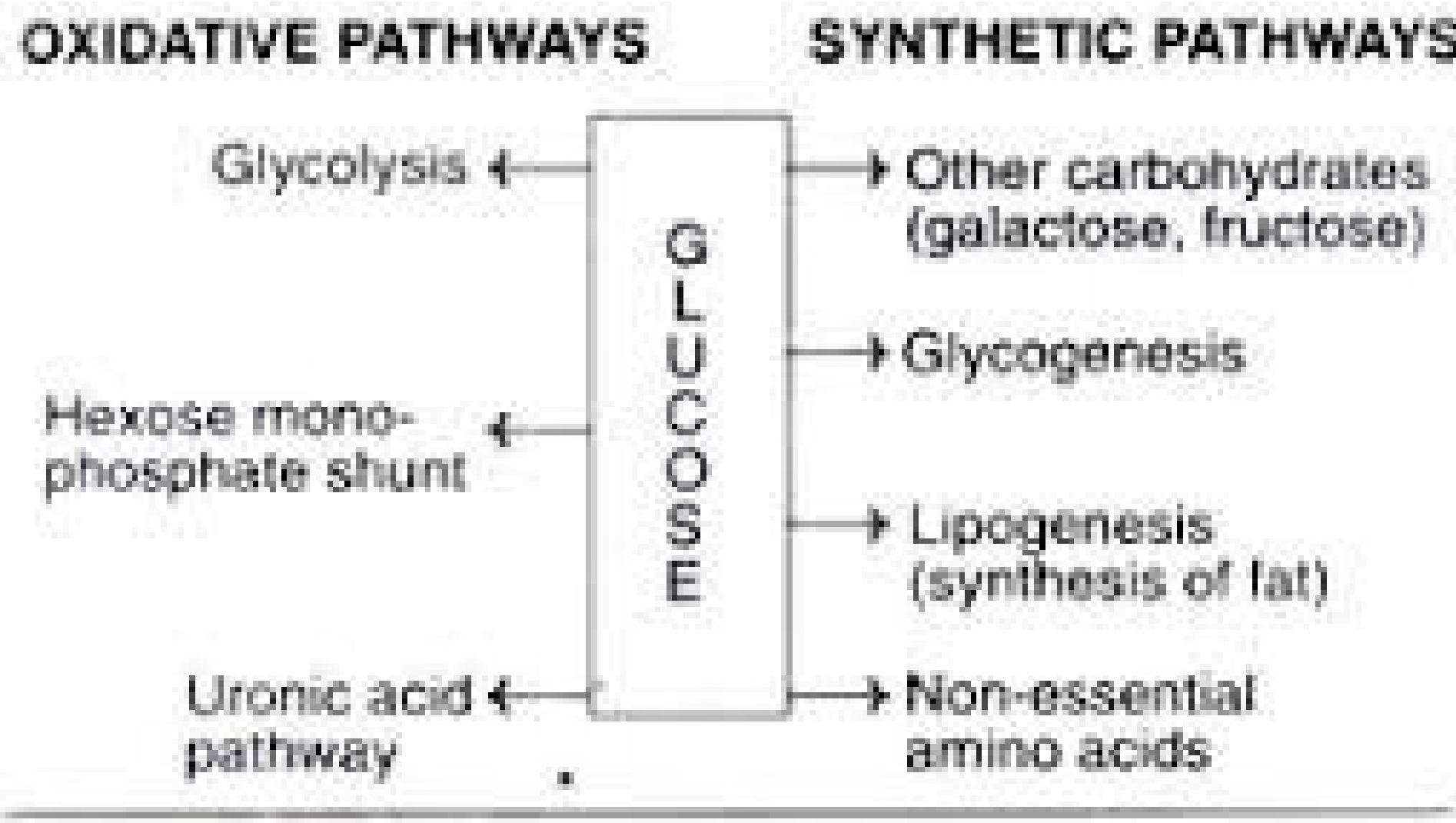


Fig. 67.3 : Overview of glucose metabolism.
*(**Note** : For majority of the pathways, glucose participates as glucose 6-phosphate).*

Free Excess of Glucose In Well Fed Condition Is a Source For Lipogenesis

Acetyl-CoA Obtained from Glucose Metabolism Is Precursor for Lipid Metabolism (Fatty acids and Cholesterol)

- **Pyruvate (3C Keto acid) an** end product **of Glycolysis** is **oxidatively decarboxylated** to **Acetyl-CoA**
- **Acetyl-CoA is then utilized** via **TCA cycle**
- **Acetyl-CoA obtained from Glucose when excess** is diverted and used for **biosynthesis** of **Fatty acids and Cholesterol.**

Glyceraldehyde Of Glycolysis Integrated as Glycerol of TAG and Glycerophospholipid

- **Glyceraldehyde-3-phosphate** an intermediate of **Glycolysis of Glucose , i**s a **source for Glycerol** production.

- **Glycerol** obtained **from Glucose** is utilized during **Lipogenesis ,for biosynthesis of Triacylglycerol and Phospholipid biosynthesis.**

- Thus when **Carbohydrates** ingested in excess **can be transformed to TAG which is**

- **Stored as reserve source** of energy in Adiposecytes

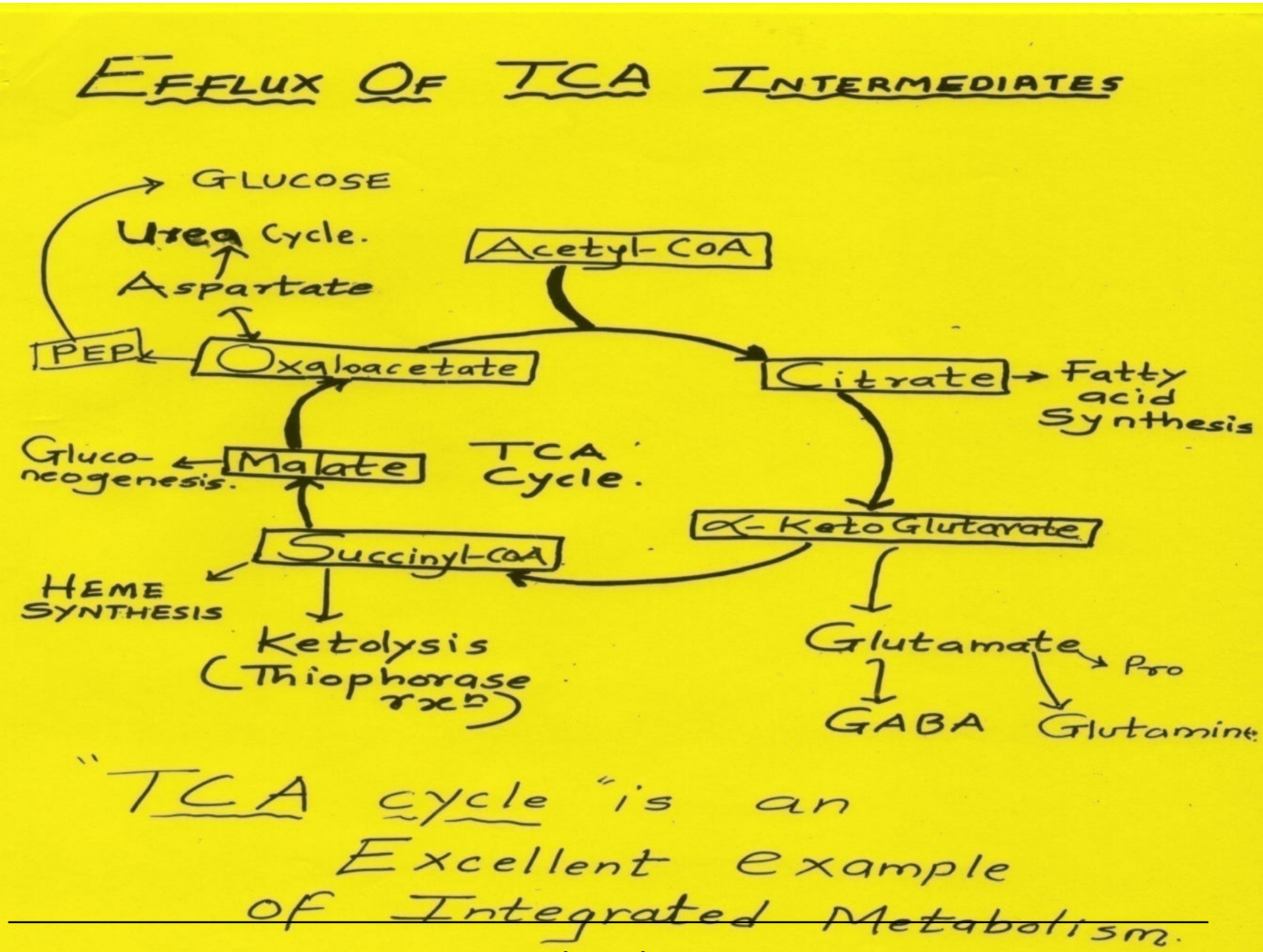
Interrelationships Of TCA Cycle

TCA Cycle Is an Excellent Example of Integrated Metabolism

- **TCA cycle intermediates** are very significant
- These intermediates are **influxed** and **effluxed** **as per the cellular need** and **maintain biochemical Homeostasis.** **(Anaplerotic Reactions)**

Efflux of TCA Intermediates

- **Citrate** – Denovo Biosynthesis of Fatty acids.
- **OAA** is reversibly transaminated to Aspartate.
- **α Ketoglutarate** reversibly transaminated to Glutamate.
- **Succinyl CoA** is effluxed for Heme biosynthesis and Ketolysis.



Influx of TCA Cycle Intermediates

- **αKetoglutarate** is added by Glutamate by it's Glutamate Dehydrogenase activity.

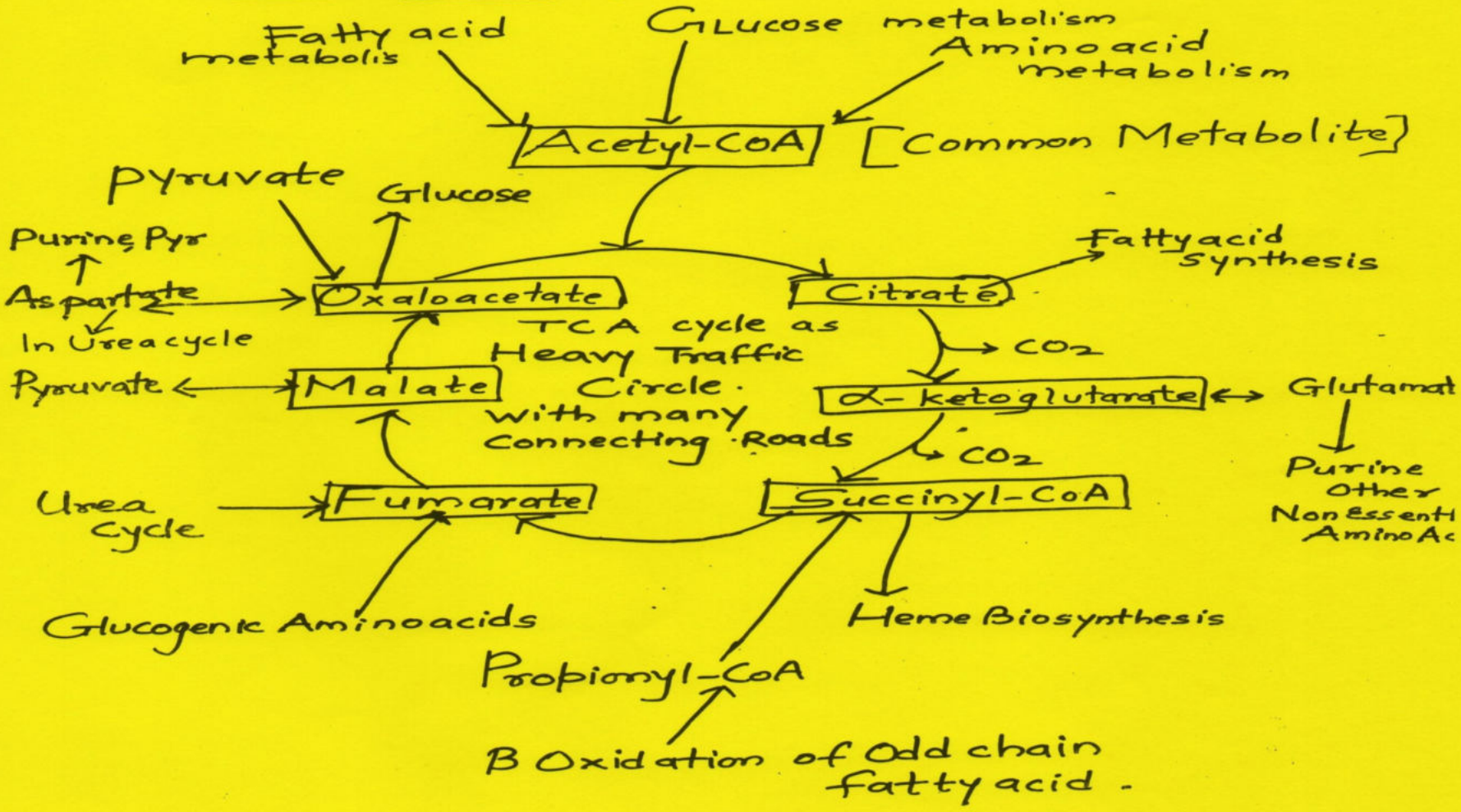
- **Succinyl -CoA** is obtained from **Propionyl-CoA** which is a source from B-oxidation of **odd chain fatty acid**

- Catabolism of **Valine, Isoleucine & Methionine** (VIM) amino acids **forms Succinyl-CoA.**

- **Fumarate** is influxed through **Phenylalanine & Tyrosine metabolism**

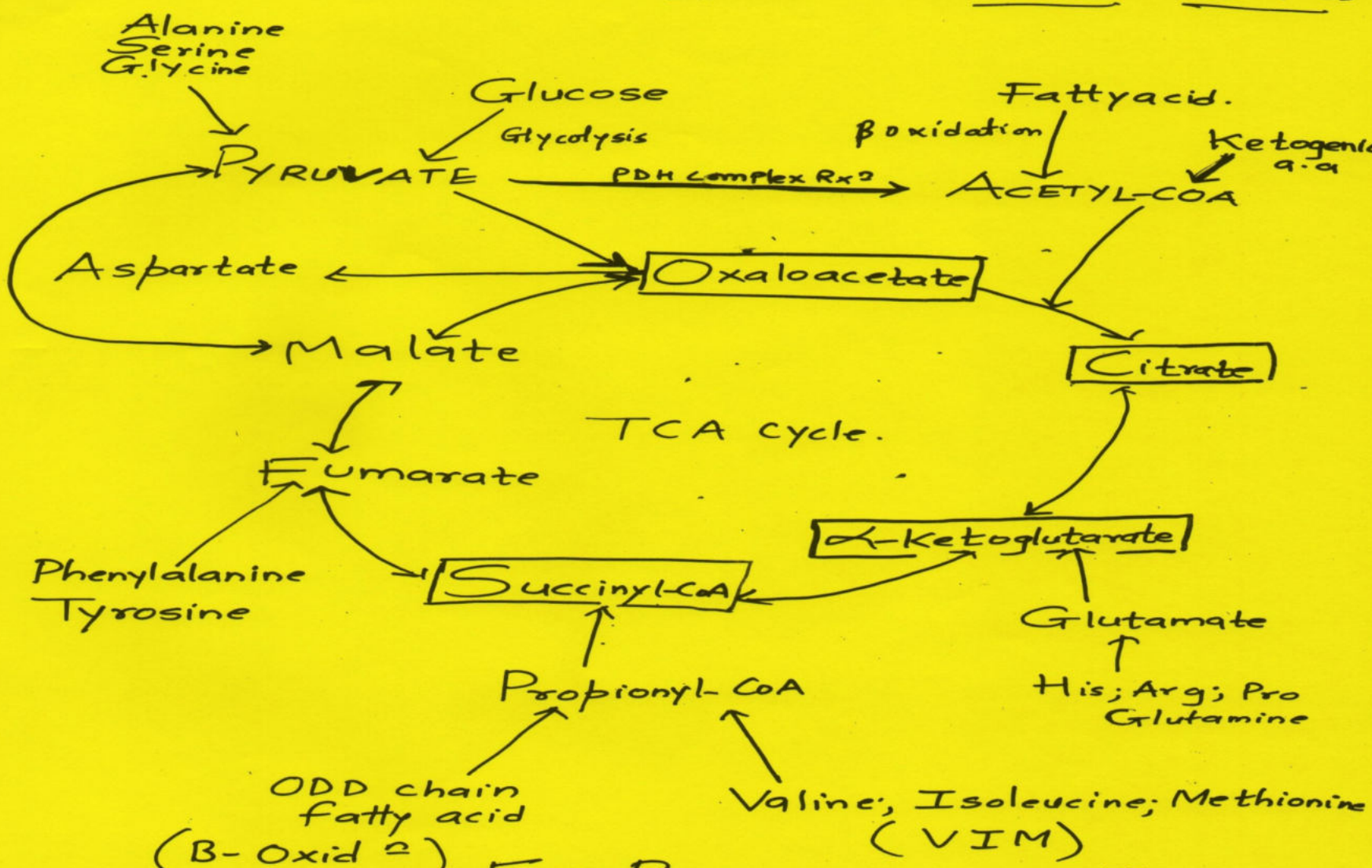
- **Fumarate** also through **Urea cycle** by Argininosuccinase activity.

INTEGRATION / INTERCONNECTIONS OF TCA CYCLE :



SIGNIFICANCE / AMPHIBOLIC NATURE OF TCA CYCLE.

INFLUX OF TCA INTERMEDIATES



" TCA INTERMEDIATES USED FOR GLUCOSE, AMINOACIDS, FATTY ACIDS, HAEM } CARBOHY BIOSYNTHESIS.

FAT BURNS UNDER THE FLAME OF CARBOHY

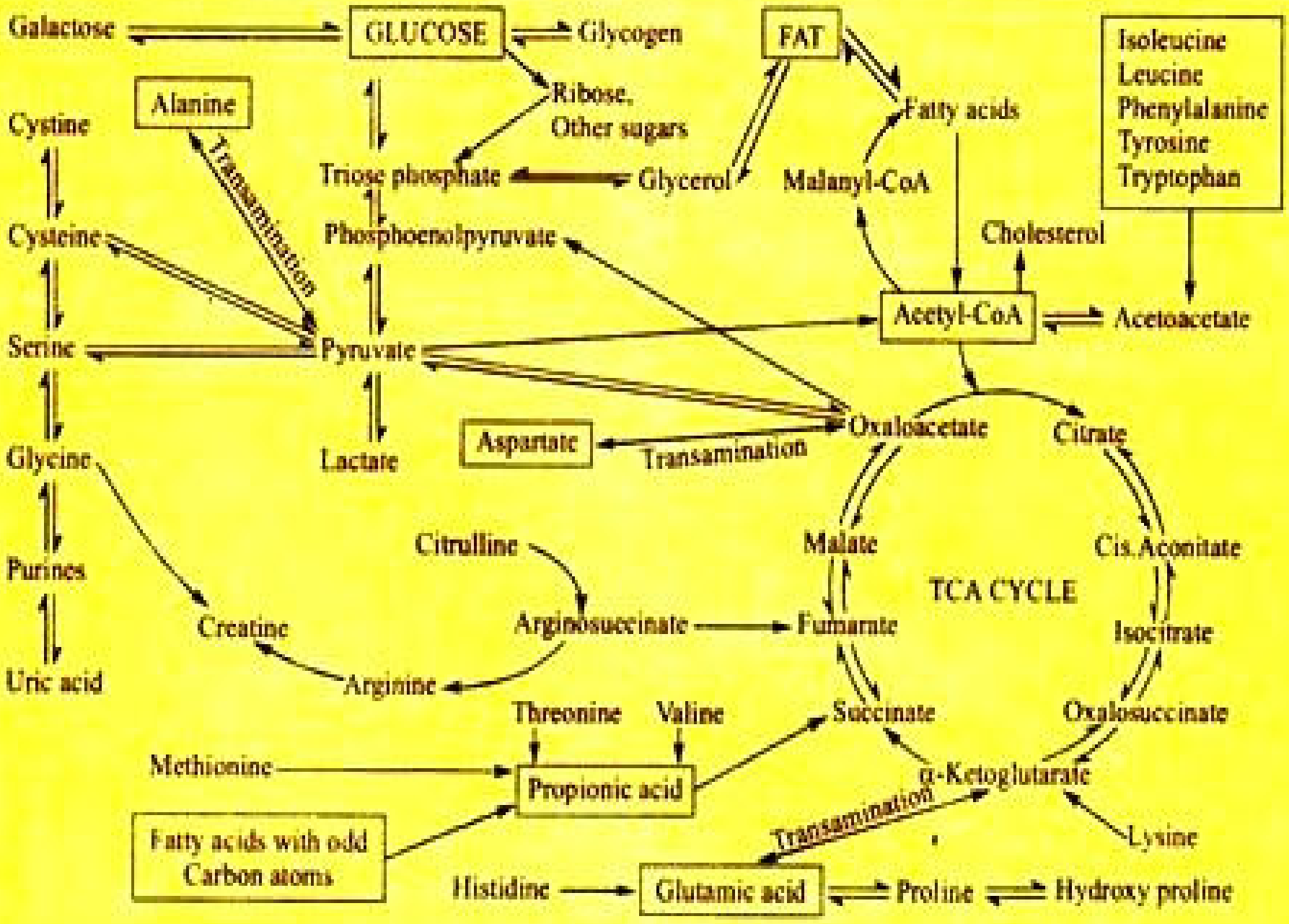
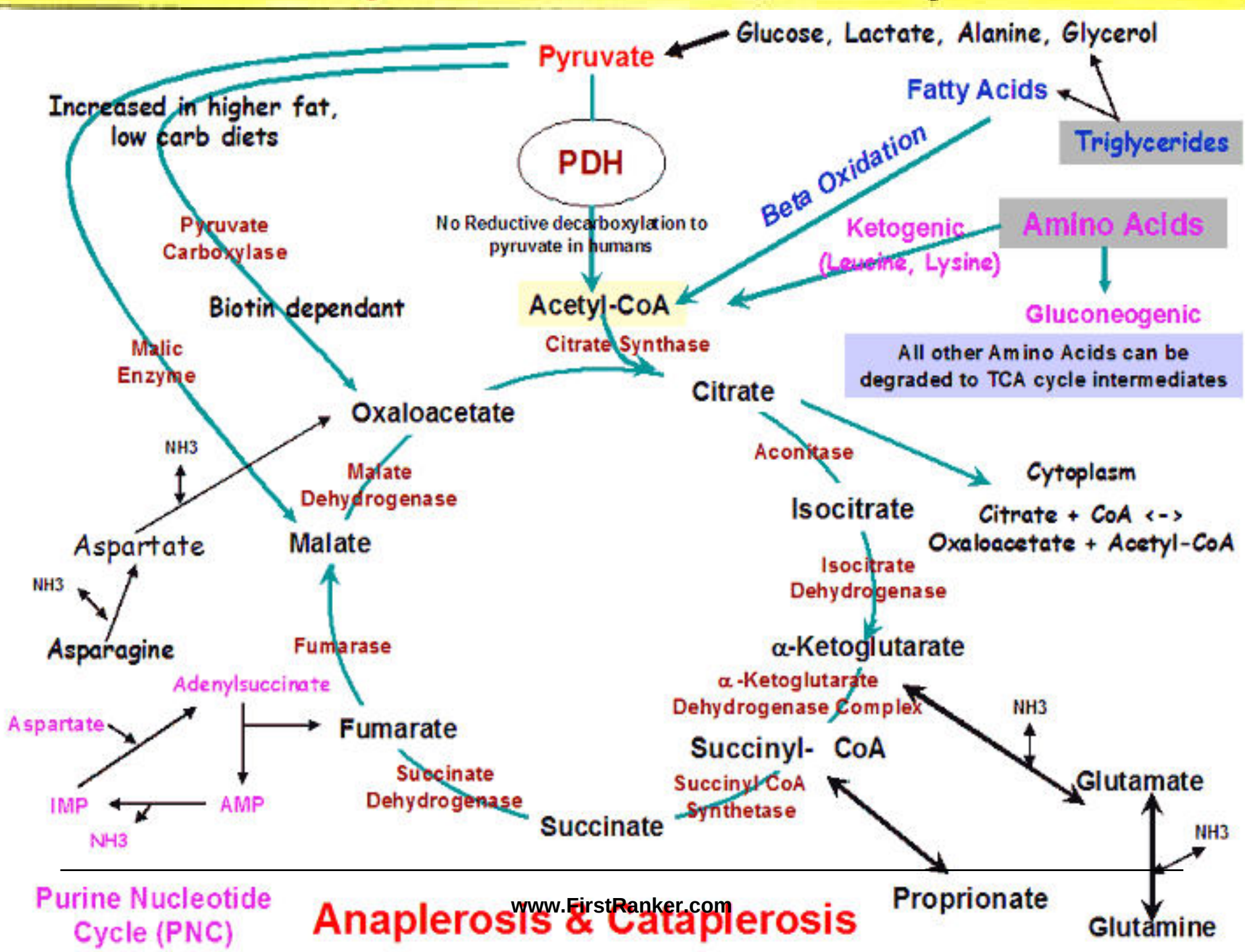
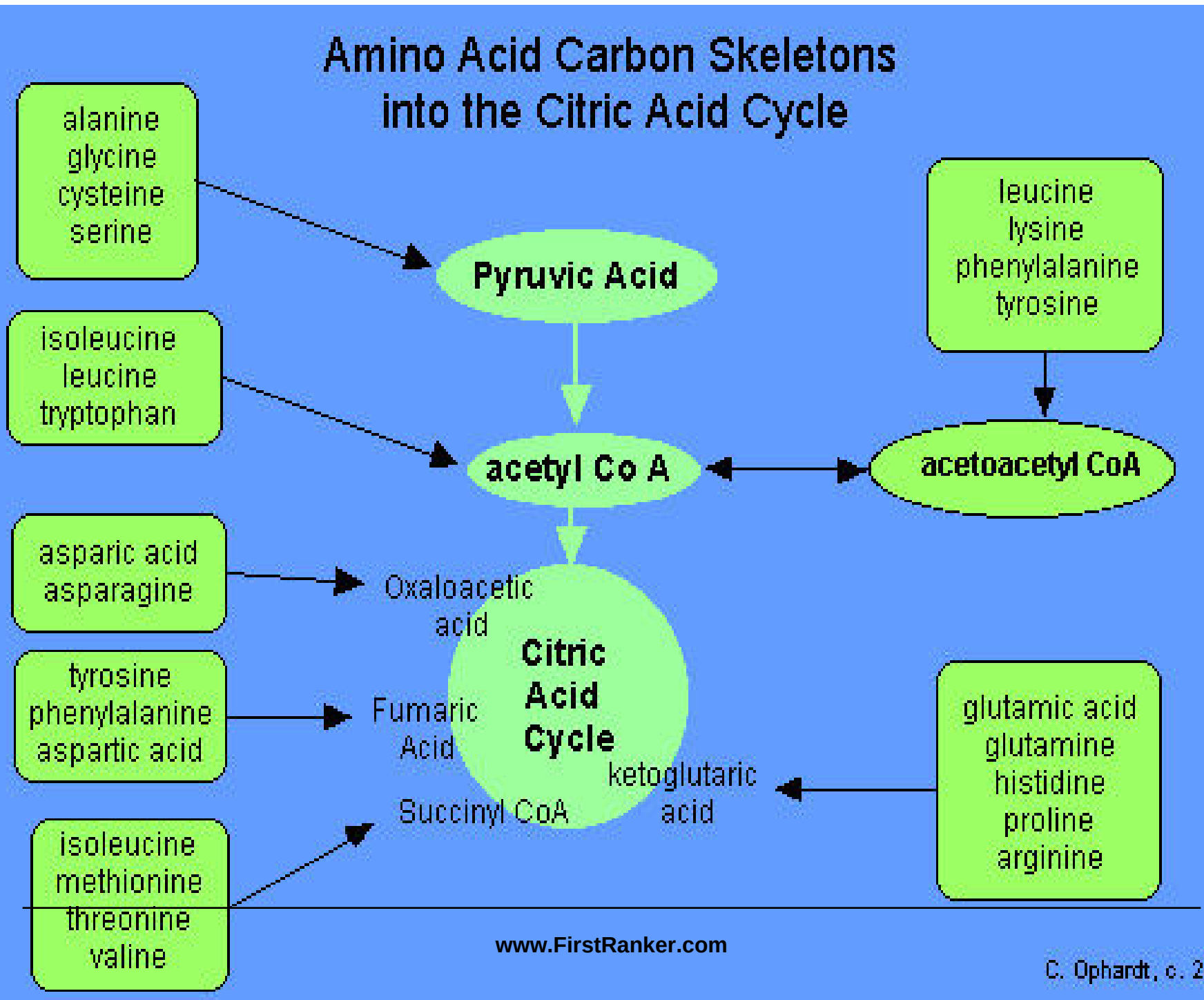


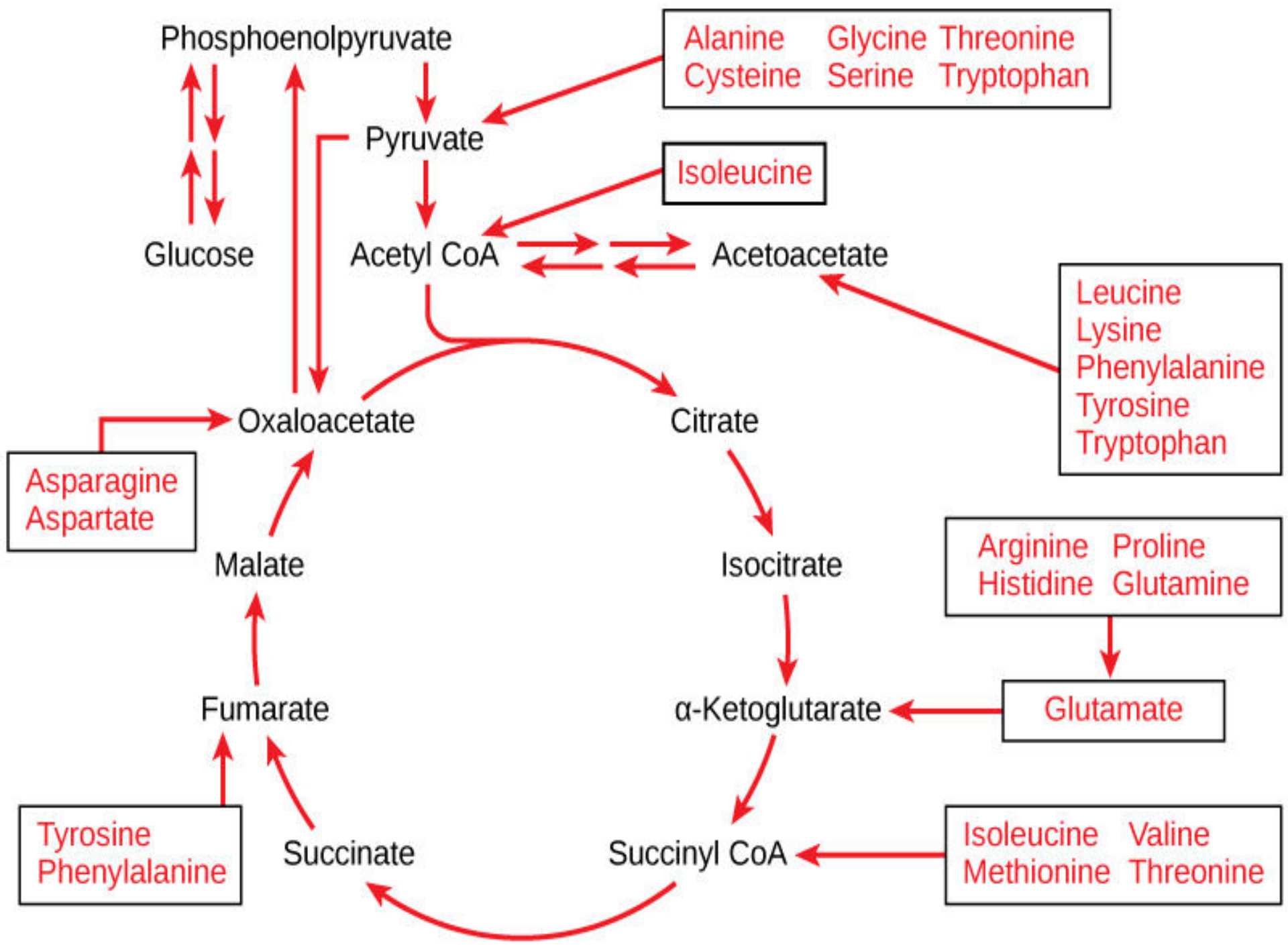
Fig. 22.1 : Inter conversion of the major foodstuffs



Points To Remember

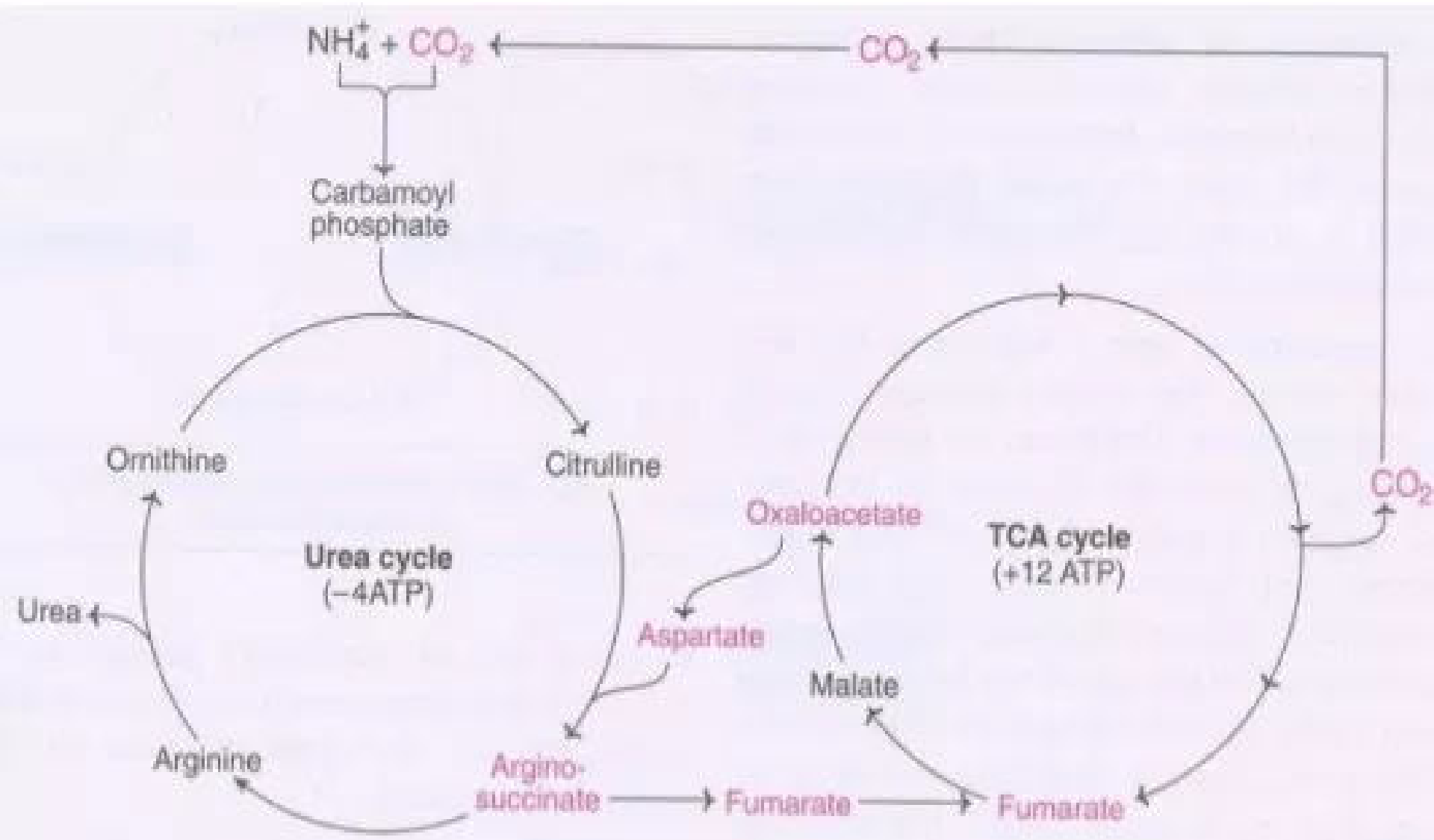
- **TCA intermediates** are involved for biosynthesis of:
  - I. Glucose
  - II. Amino acids
  - III. Fatty acids And Cholesterol
  - IV. Heme





Interrelationship Of TCA with Urea Cycle

Integration between Urea cycle and TriCarboxylic Acid (TCA) cycle



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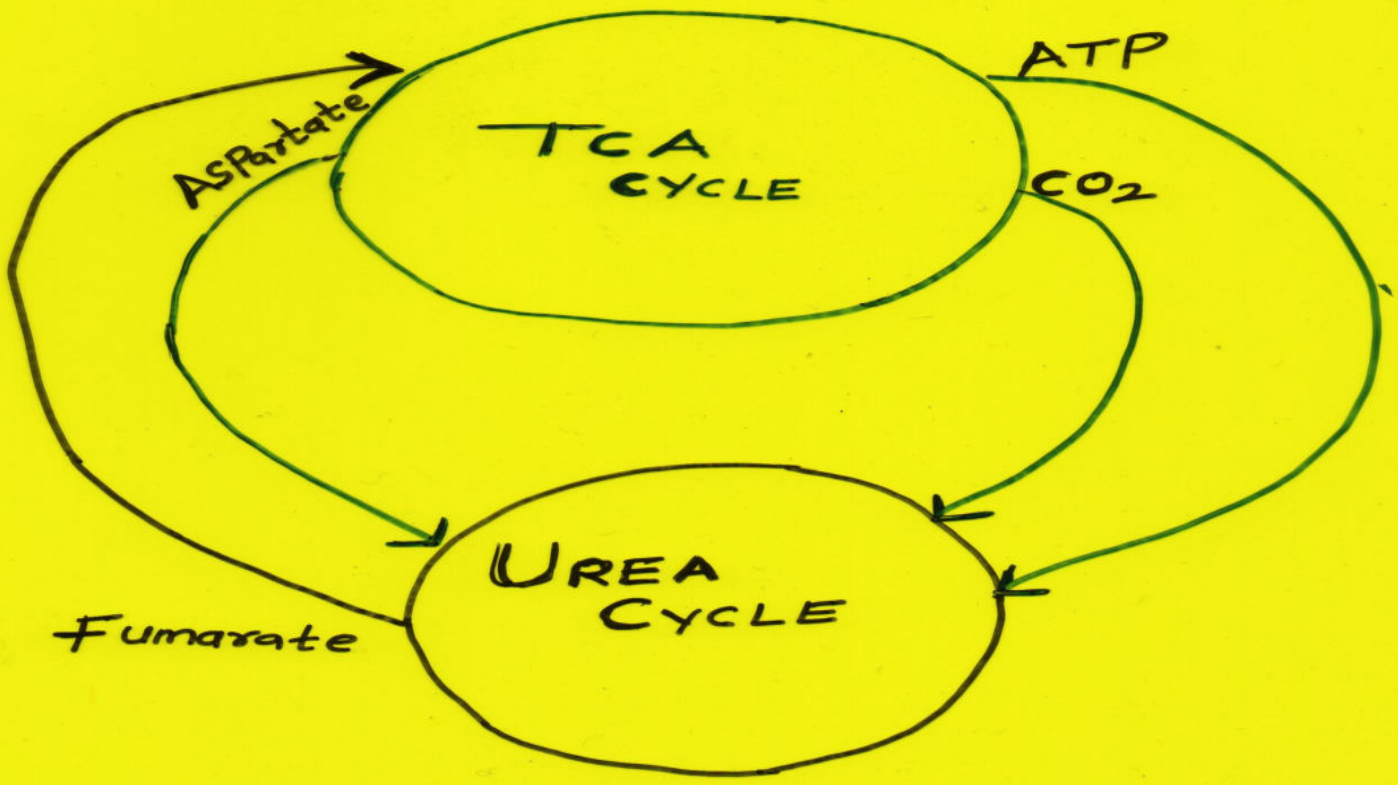
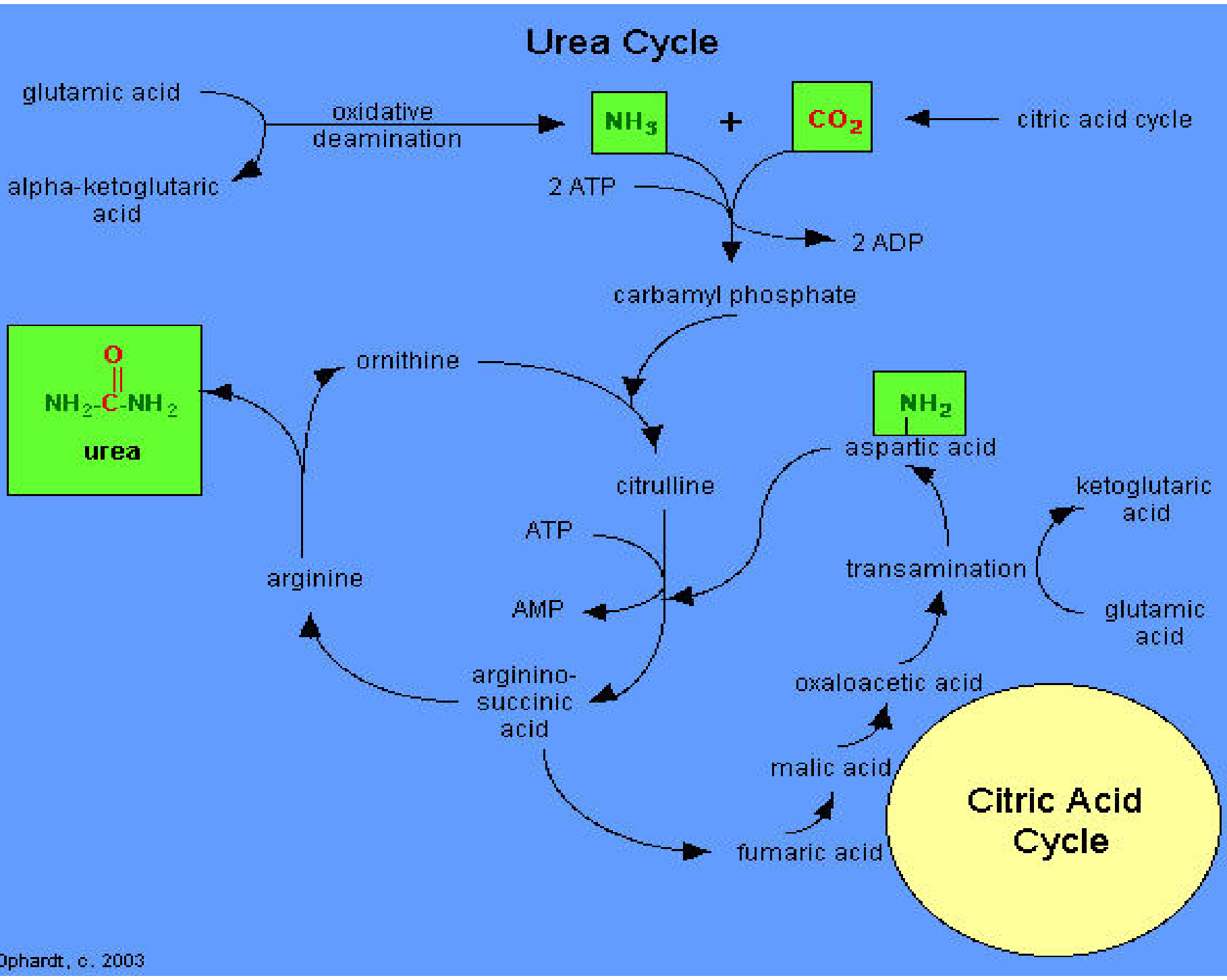
Interrelationship Between TCA And Urea Cycle



1. CO_2 From TCA cycle → Urea cycle
2. ATP FROM TCA → Urea Cycle
3. OAA ⟷ ASP → Urea cycle
4. Fumarate released in Urea cycle → TCA cycle.



Interrelationships Of Lipid With Carbohydrate Metabolism

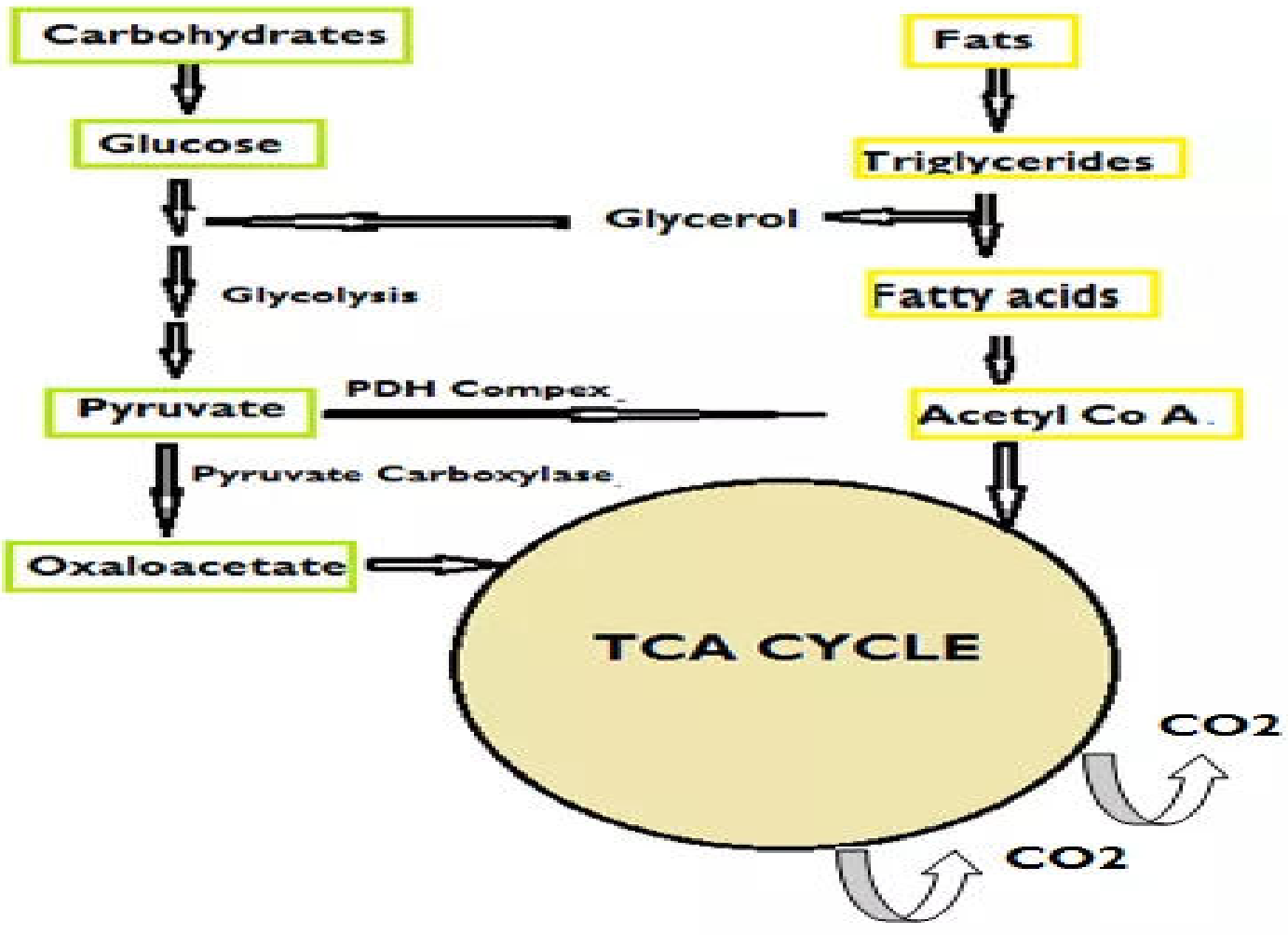
Fat Burns Under Flame of Carbohydrates

• Fat burns under the Flame of Carbohydrates

- For **complete oxidation of Fatty acids**

- Their **needs** presence of **sufficient amount of cellular Glucose**.

Oxaloacetate Serves Flame for Complete Oxidation Of Fatty acid



- **In a well fed condition**
- **Major source for OAA is Glucose**
- **By Pyruvate Carboxylase activity**

- **Oxaloacetate** is an **essential initiating metabolite for TCA cycle**

- **Oxaloacetate (OAA) serve as a flame for oxidation of Acetyl CoA via TCA cycle.**

- **Cellular deprivation of Glucose lowers OAA** leads to **incomplete oxidation of Fatty acids.**
- **Accumulates Acetyl-CoA** in Mitochondrial matrix.
- **Impermeable Acetyl-CoA is then transformed to permeable ketone bodies via ketogenesis.**

β-oxidation of Fatty acid and it's Interrelationship

- Reduced **coenzymes FADH2 & NADH+H$^+$** generated during it's pathway are

- **Integrated with ETC /oxidative phosphorylation to generate ATP.**

- **Acetyl-CoA** formed as an end product **of β oxidation of fatty acids**

- Is integrated with **TCA cycle for it's complete oxidation**.

- **Acetyl-coA** can be **a source** for **Ketone bodies** production via Ketogenesis.

- To **small extent** in **normal metabolic conditions** and **excess in emergency conditions.**

Remember

Fatty acids cannot be converted to Glucose In Human Body

- **Acetyl-CoA** obtained from Beta-oxidation of fatty acids **cannot be reversibly converted to Pyruvate**
- **Since PDH complex is irreversible in action**.
- **Thus there is no net conversion of Fatty acids (Fat) to Glucose (Carbohydrates).**

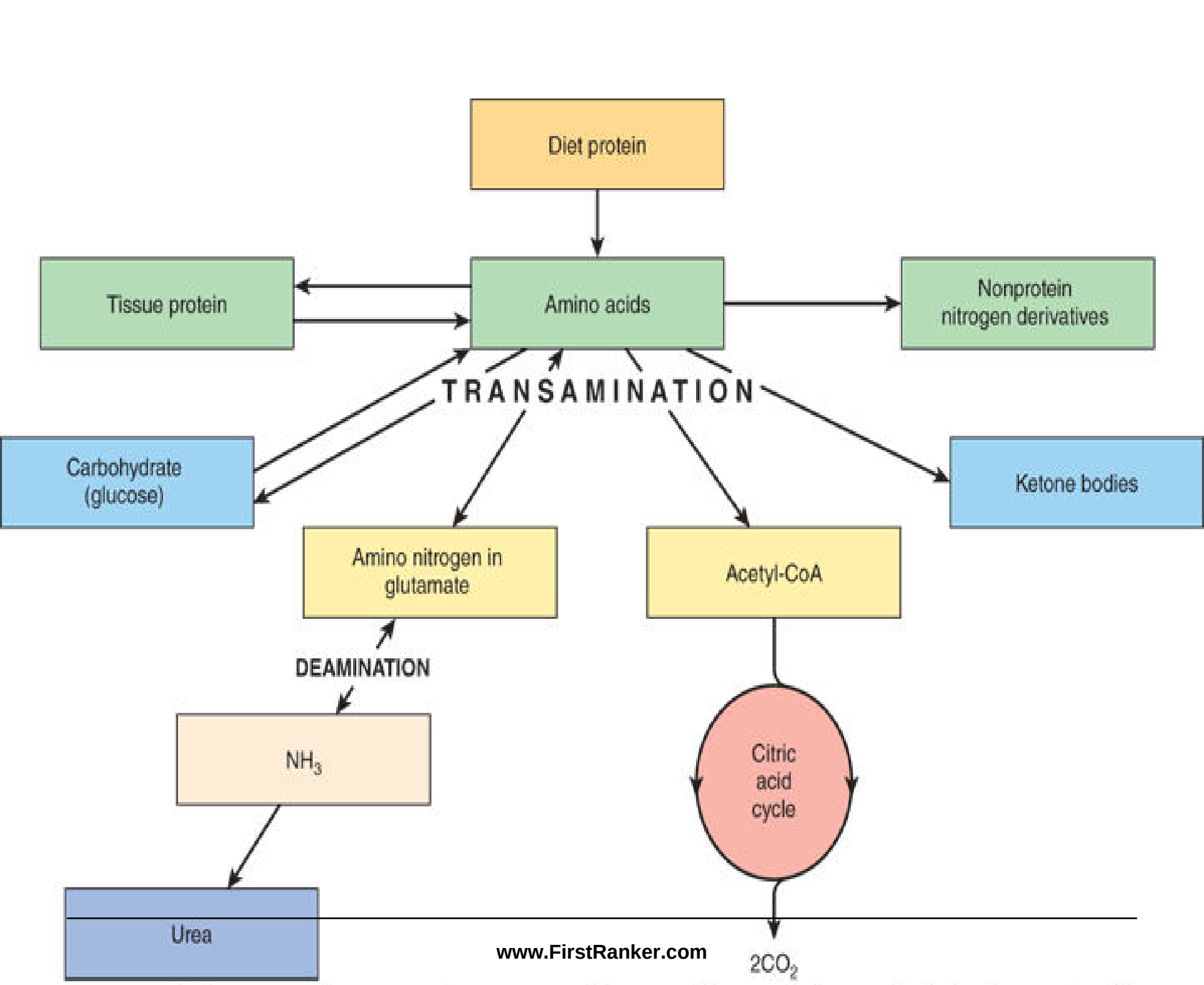
- However **Propionyl-CoA an** end product of β oxidation of **odd chain fatty acid**
- Serve as a **source for Glucose production** after conversion into **Succinyl-CoA** (intermediate of TCA cycle)
- **Succinyl-CoA in turn** can be a source for **Heme synthesis and Ketolysis**.

Interrelationship Of Carbohydrates And Protein Metabolism

- **Intermediates of Glucose** metabolism can be a **source of**

- **Carbon skeleton** for **biosynthesis of non Essential amino acids.**
  - ❖**Pyruvate to Alanine**
  - ❖**OAA to Aspartate**
  - ❖**αKetoglutarate to Glutamate**

Amino Acids And Its Interrelationships



Amino acids are interrelated for Purine and Pyrimidine biosynthesis

- **Gly , Asp, Gln** for Purine Biosynthesis
- **Asp and Gln** for Pyrimidine Synthesis

Amino acids are Source For Glucose In Human Body

- **Glucogenic amino acids** are source for production of **Glucose** via Gluconeogenesis.

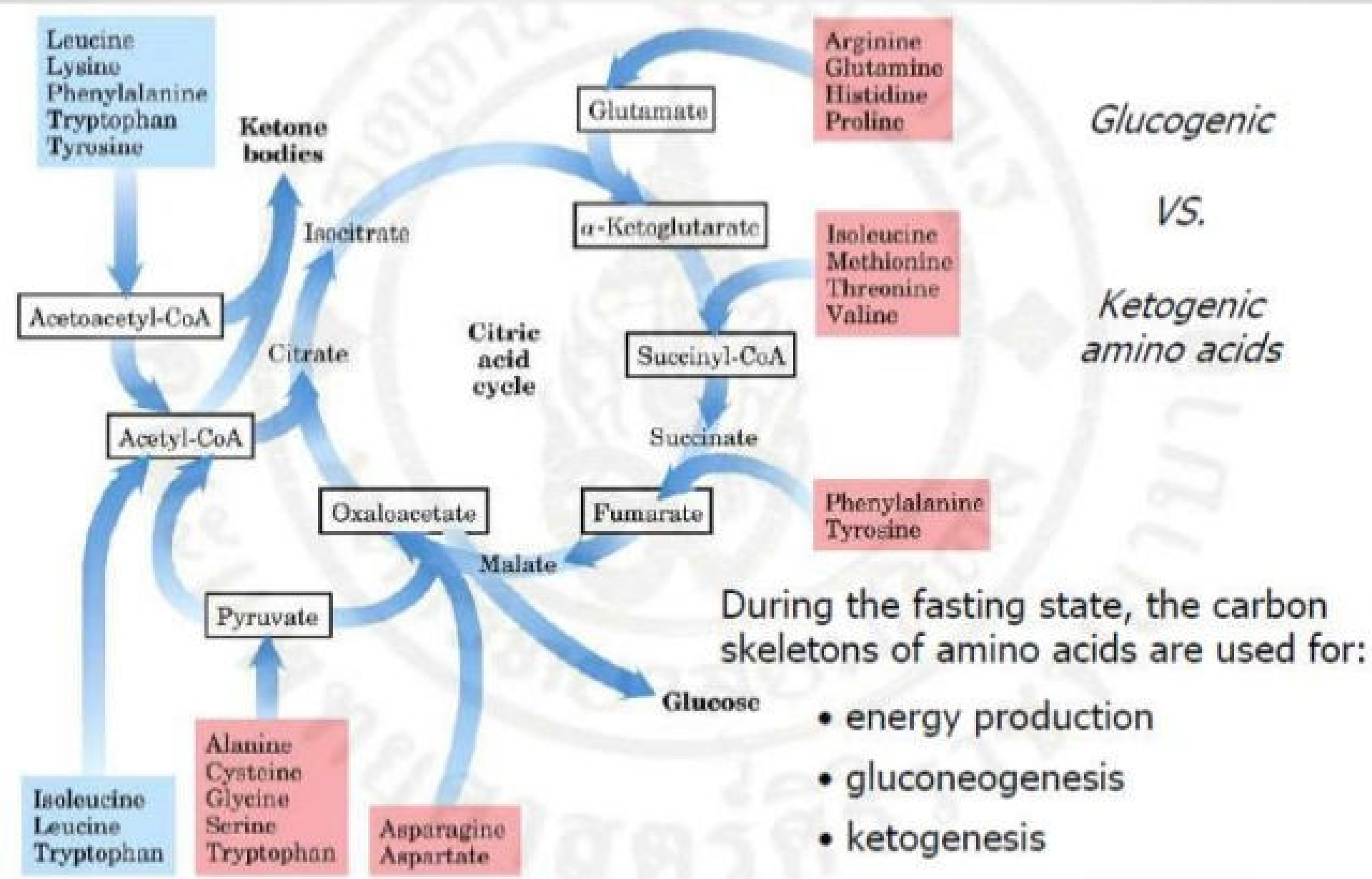
- **100 gm of Proteins can produce approx 60 gm of Glucose in human body.**

- **Amino acid Glycine** is connected to **Heme biosynthesis.**

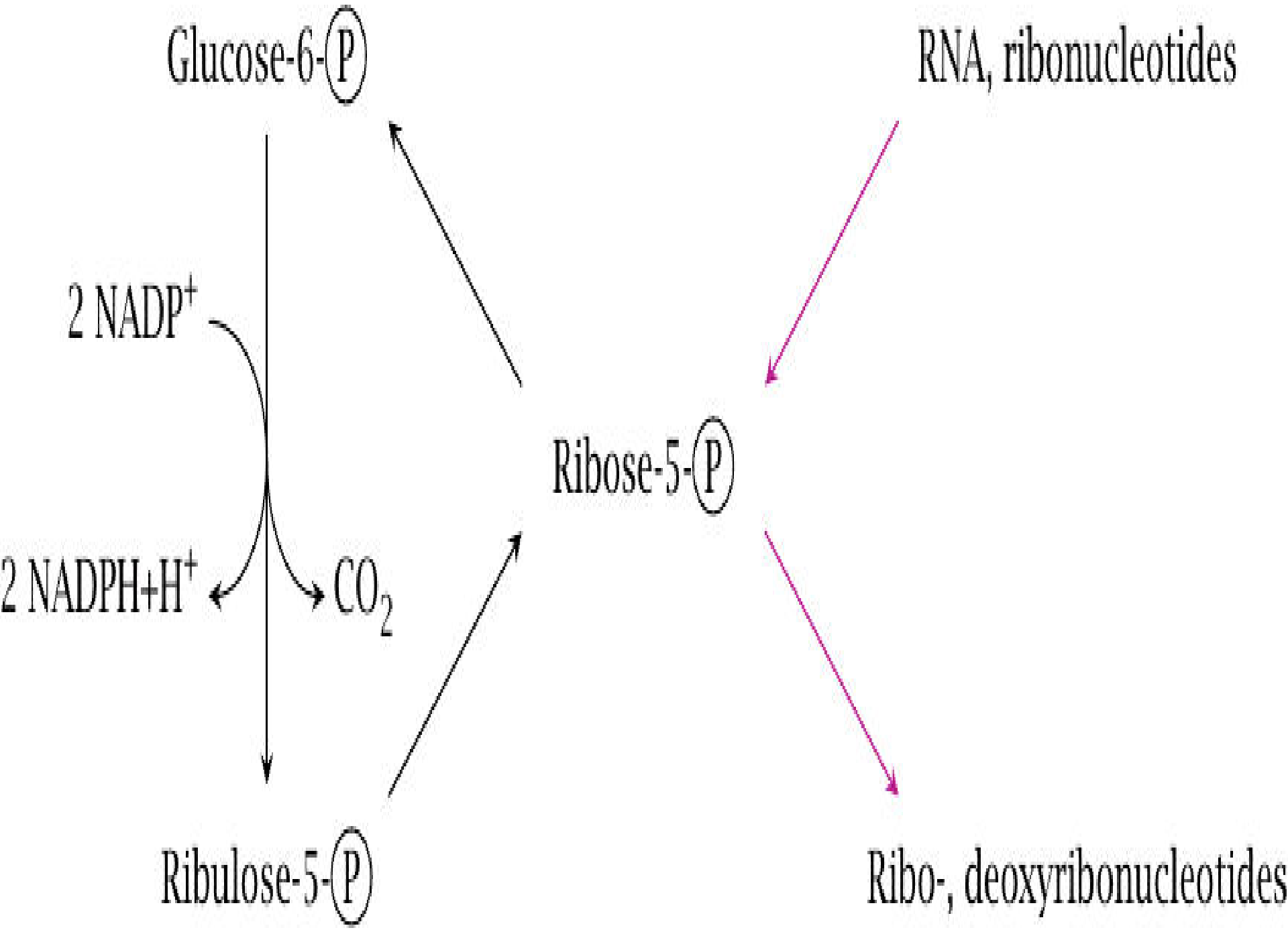
- **Glycerol** released during lipolysis of **TAG is integrated**

- **With Gluconeogenesis to produce Glucose**.

Conversion of Fats into Proteins & Proteins into Fats



HMP Shunt and It's Interrelationships

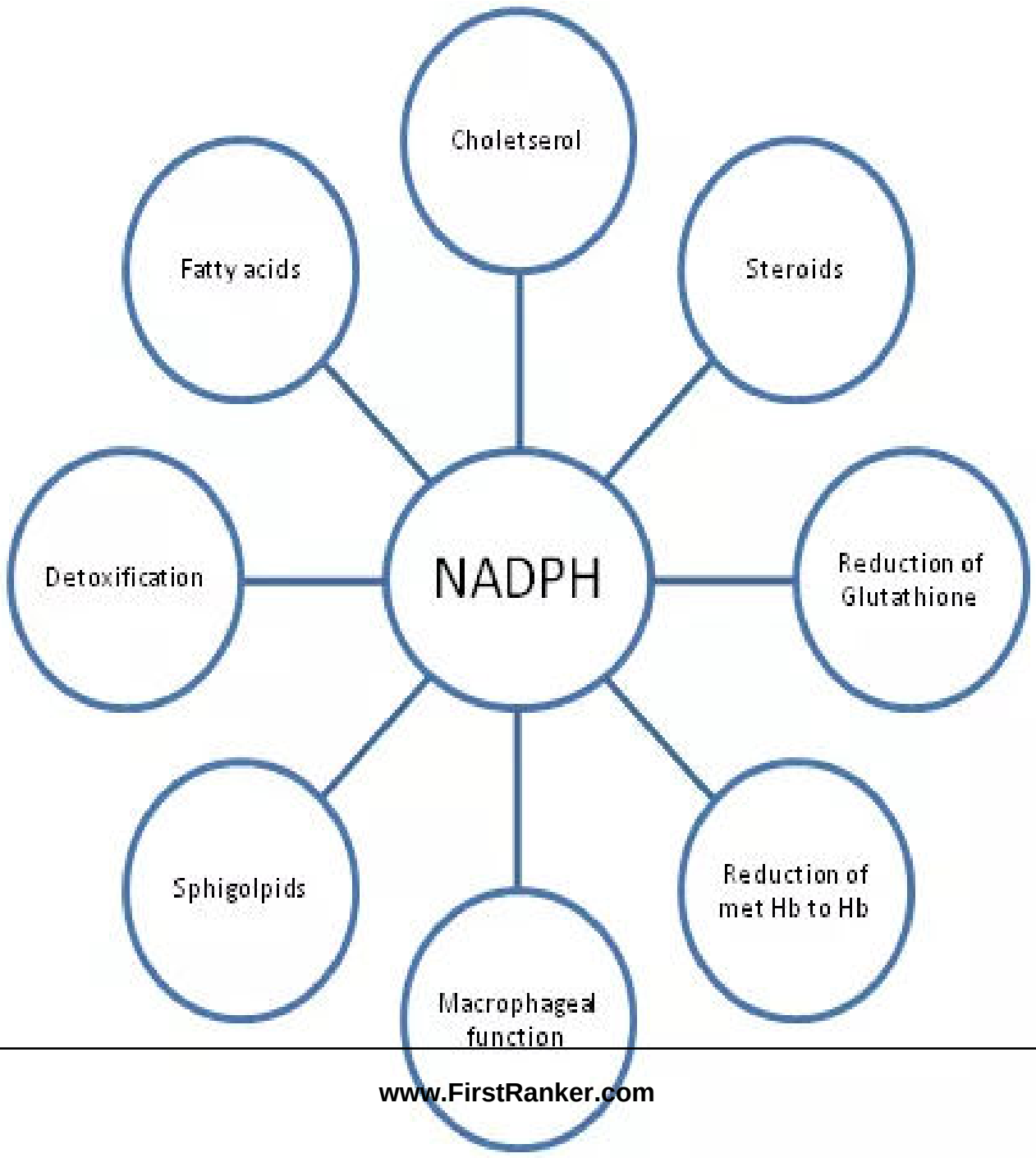


- Glucose is alternatively oxidized through HMP shunt to generate:

  - **NADPH+H$^+$** (reducing equivalents)

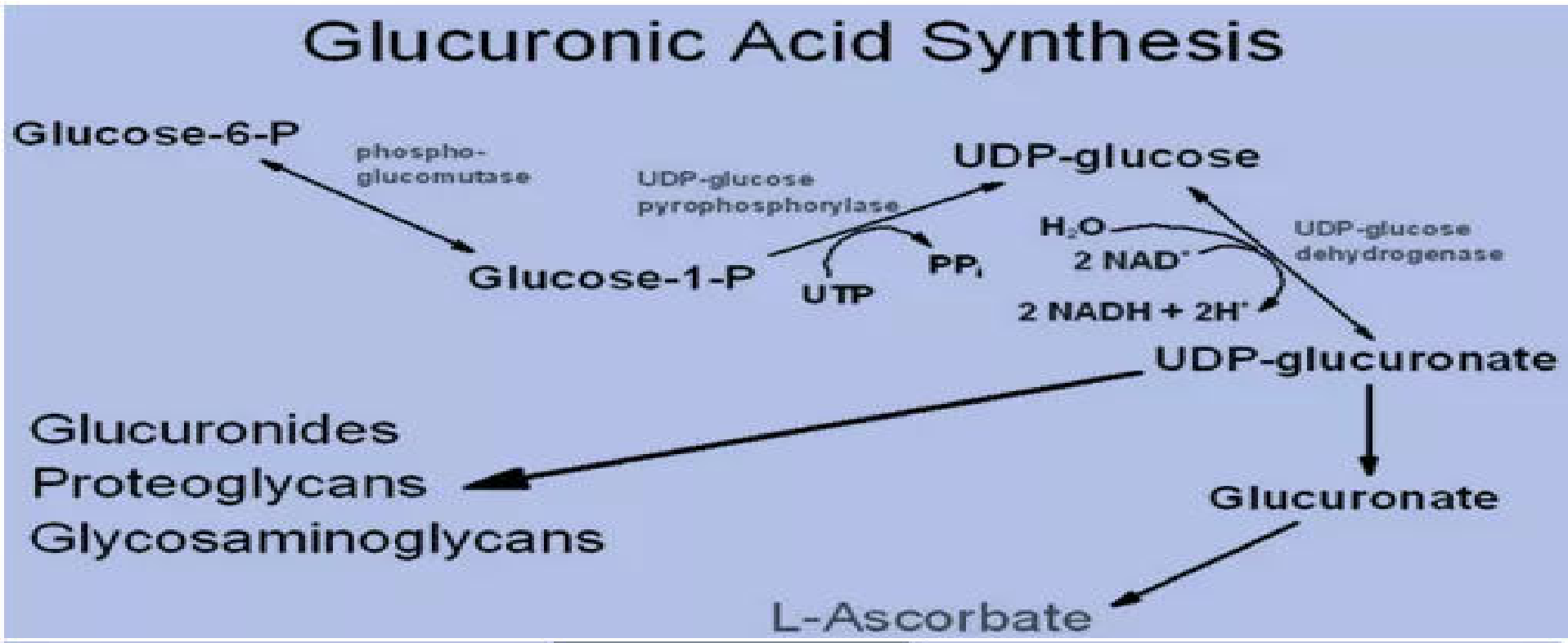
  - **Ribose-5- phosphate**

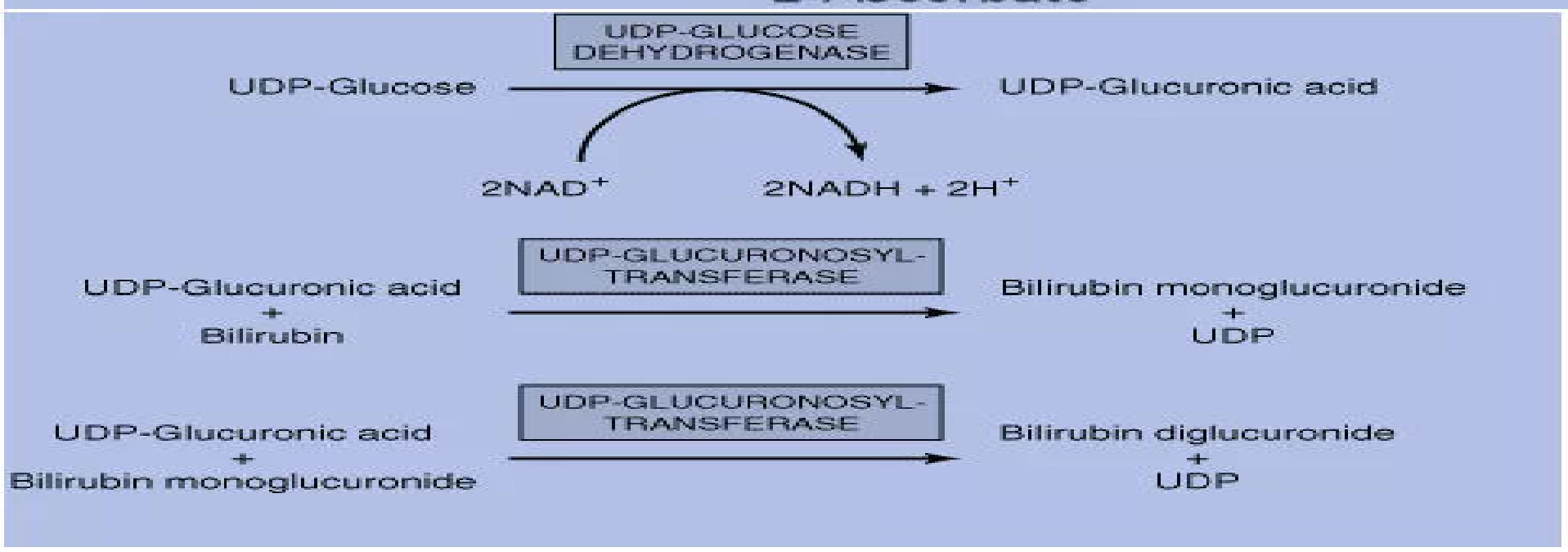
- **NADPH+H$^+$ are integrated to:**
  - ***Biosynthesis of Fatty acids**
  - ***Biosynthesis of Cholesterol**
  - ***Drug metabolism**



- **Ribose-5-phosphate** (pentose sugar) of HMP shunt is integrated for
  - **Biosynthesis** of **Purine & Pyrimidine Nucleotides**.

Interrelationships of Uronic acid pathway





- Glucuronic acid is involved in **Mucopolysaccharide biosynthesis.**

- **Glucuronic acid** of Uronic acid pathway is **integrated** with **Phase II conjugation reactions** of **detoxification process**.
  - **Glucuronic acid** is involved in:
  - **Bilirubin metabolism**
  - **Drug metabolism**

Interrelationship Of ETC

- Reduced coenzyme **NADH+H$^+$ generated** in **Glycolysis**
- By action of **Glyceraldehyde– 3 – Phosphate Dehydrogenase**
- **Enter in ETC for its reoxidation and ATP generation.**

Energy-containing nutrients

Carbohydrates
Fats
Proteins

Catabolism

Energy-depleted end products

CO_2
H_2O
NH_3

$ADP + HPO_4^{2-}$
NAD^+
$NADP^+$
FAD

ATP
NADH
NADPH
$FADH_2$

Chemical energy

Cell macromolecules

Proteins
Polysaccharides
Lipids
Nucleic acids

Anabolism

Precursor molecules

Amino acids
Sugars
Fatty acids
Nitrogenous bases

Carbo-hydrates
Some amino acids
Glycerol

Fatty acids
Some amino acids

Some amino acids

Glycolysis → Pyruvate oxidation → Citric acid cycle → Oxidative phosphorylation

ATP and Its Interrelationships

- **ATP produced during oxidative phosphorylation** are **connected to:**
  - **I. Nerve impulse conduction**
  - **II. Muscular activity**
  - **III. Active transport mechanism**
  - **IV. Biosynthetic Reactions**
  - **V. Activation Reactions**

Crossroads Of Metabolism

OR

Metabolites of Cross Roads

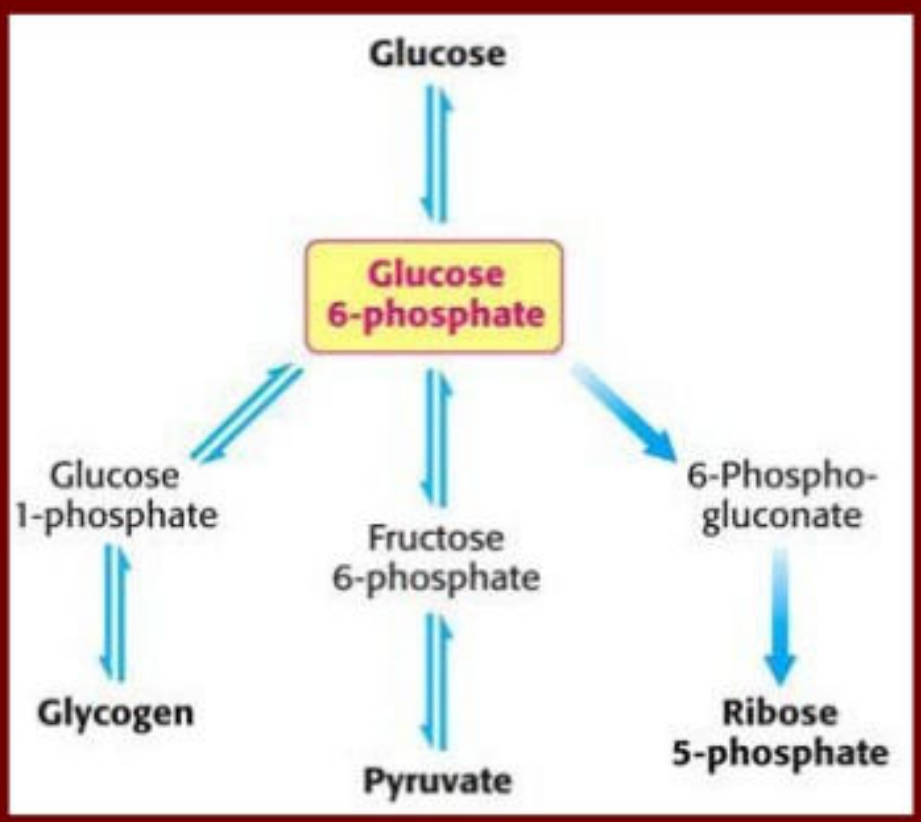
❖ **Four Important Metabolites** in human body who function as **crossroads of metabolism** :

1. **Glucose-6-Phosphate**
2. **Pyruvate**
3. **Acetyl-CoA**
4. **Oxaloacetate (OAA)**
5. **Succinyl-CoA**

The key junction points

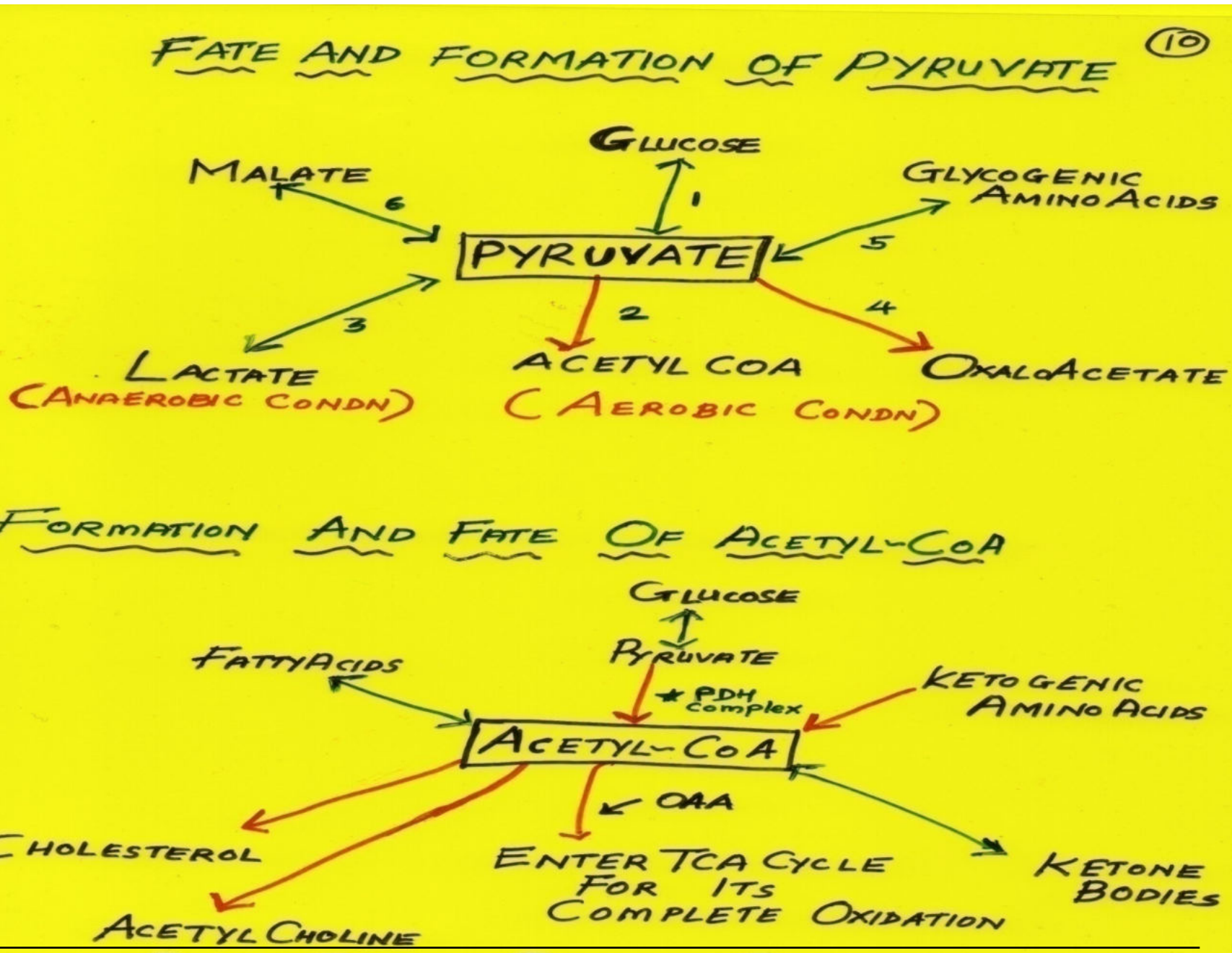
- The key junction points are:-

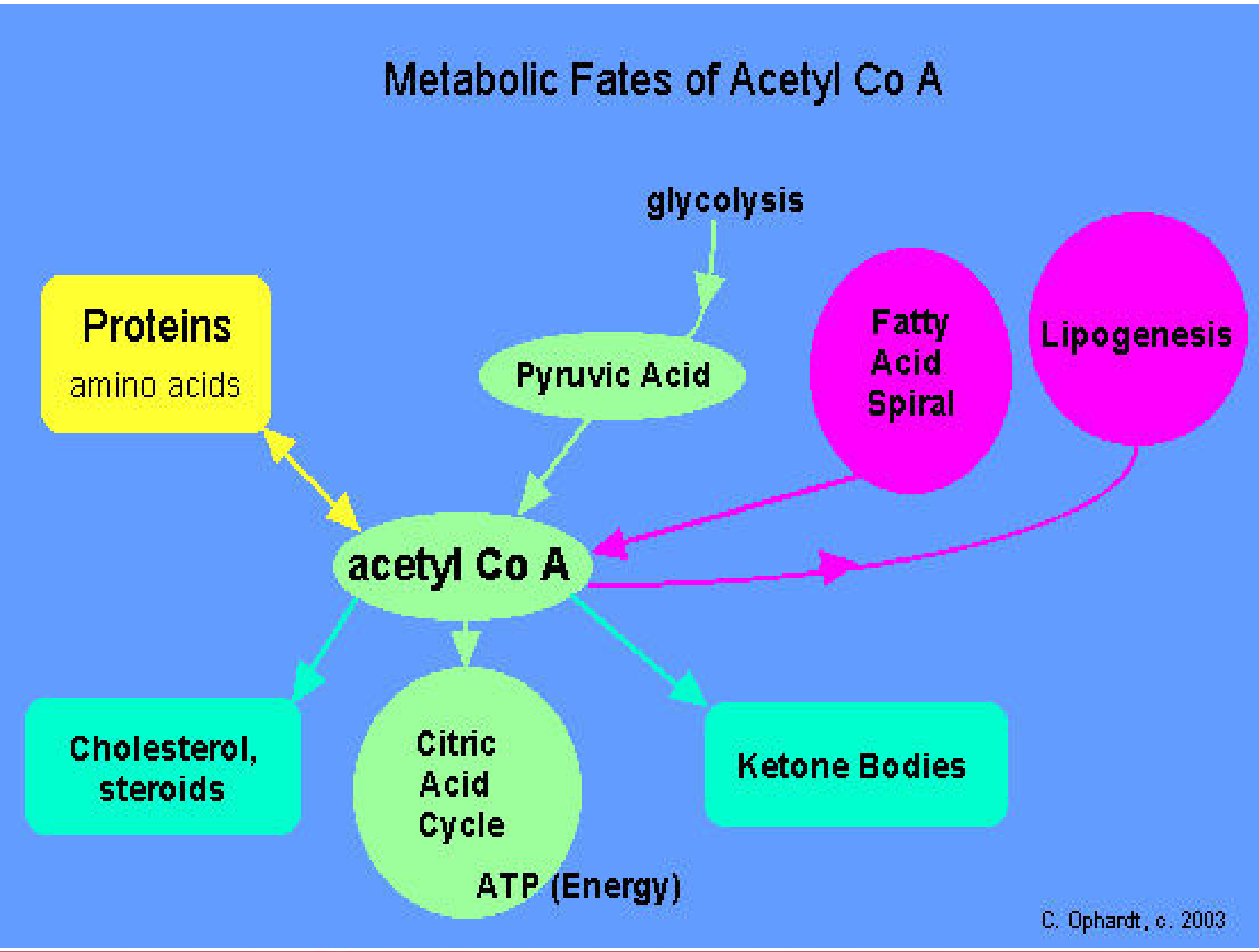
1- Glucose- 6-phosphate,
2- Pyruvate and
3- Acetyl CoA.

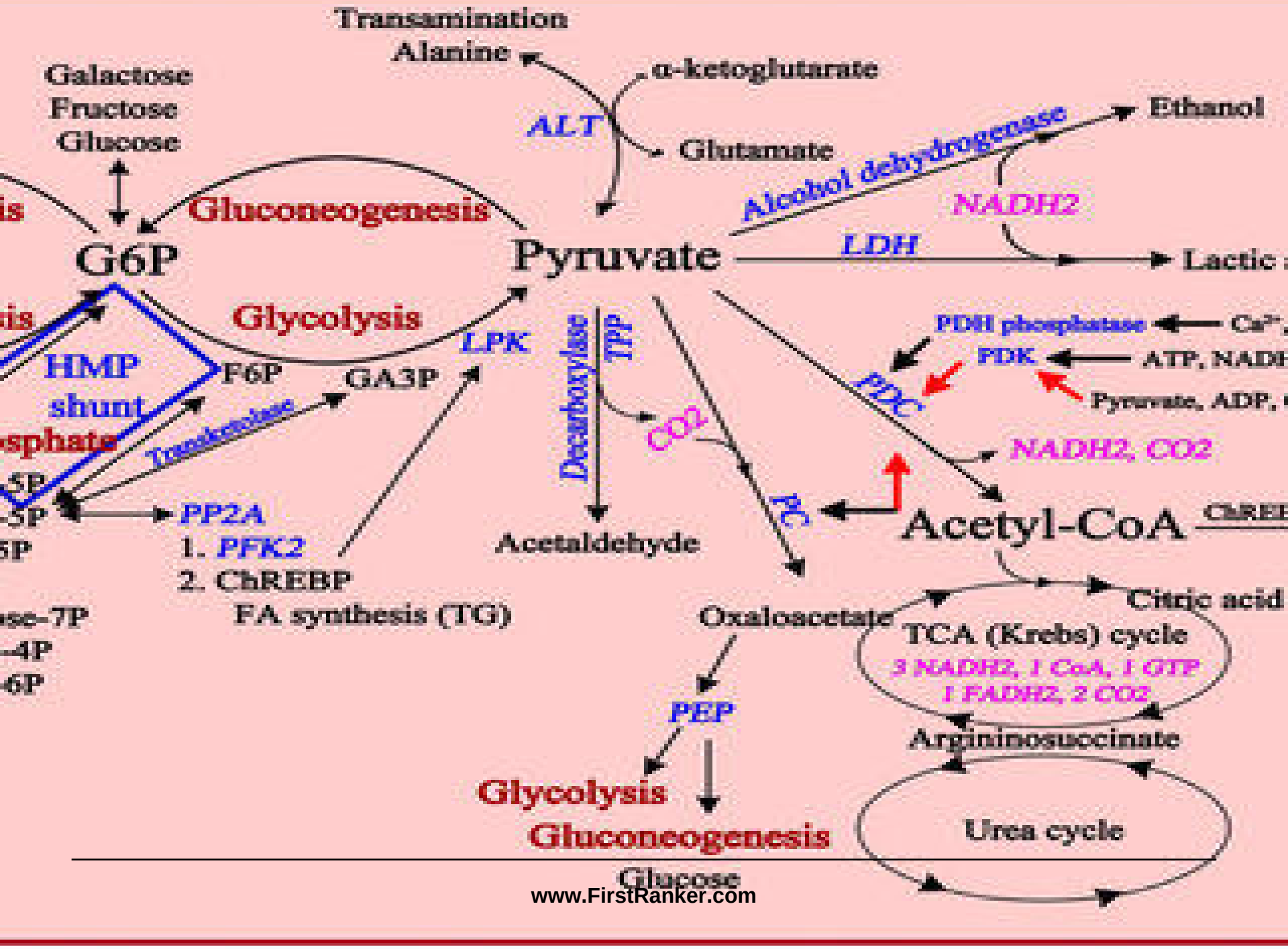


Formation And Fates Of Pyruvate

Formation And Fates Of Acetyl CoA





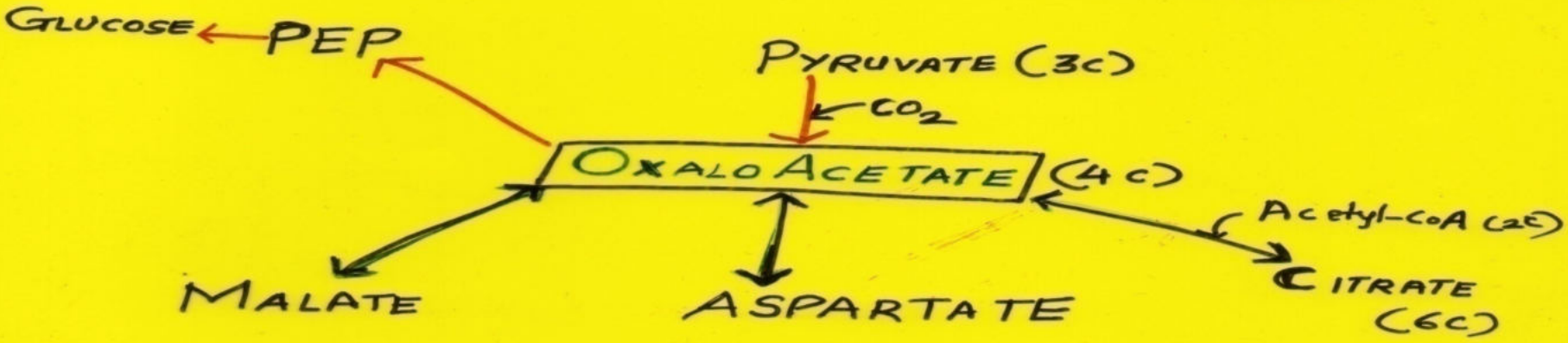


Formation And Fates Of Oxaloacetate

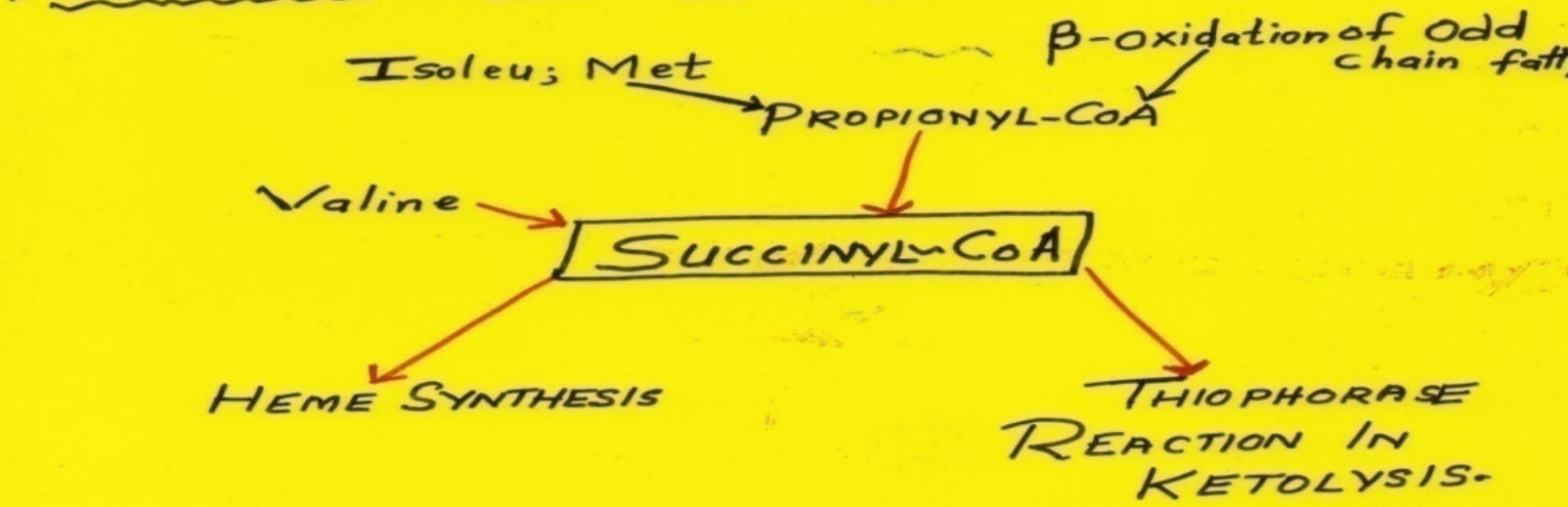
And

Formation And Fates Of Succinyl-CoA

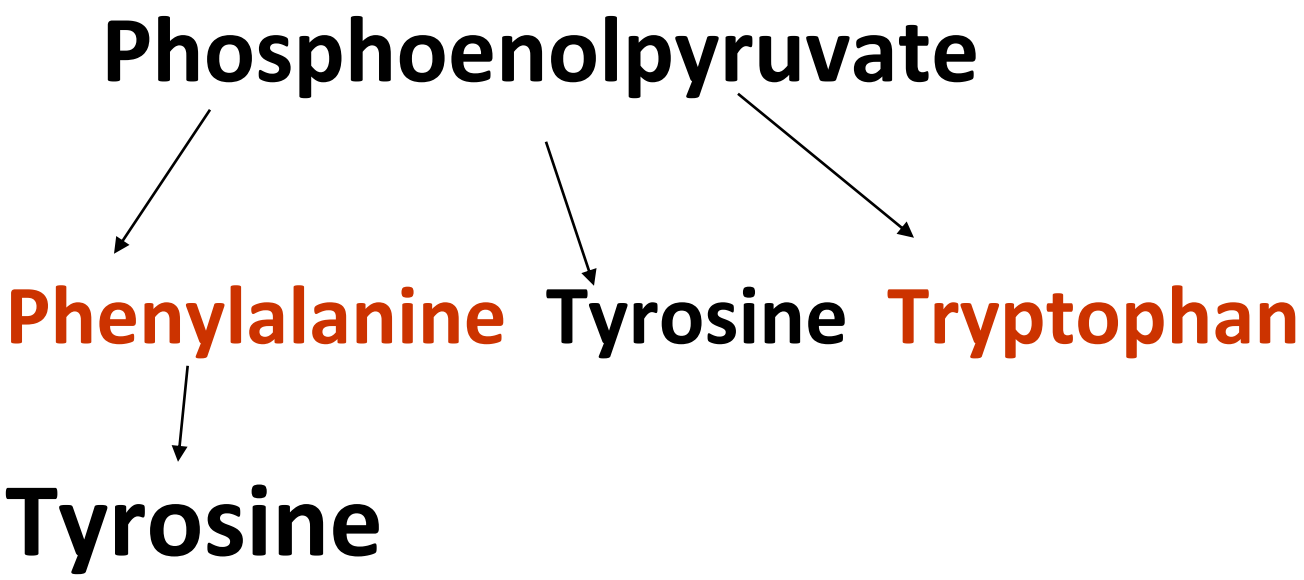
FORMATION AND FATE OF OXALOACETATE:

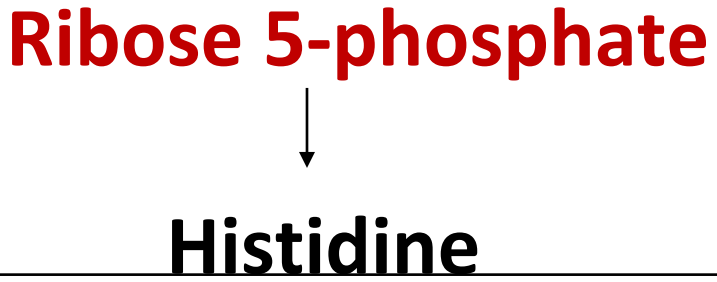


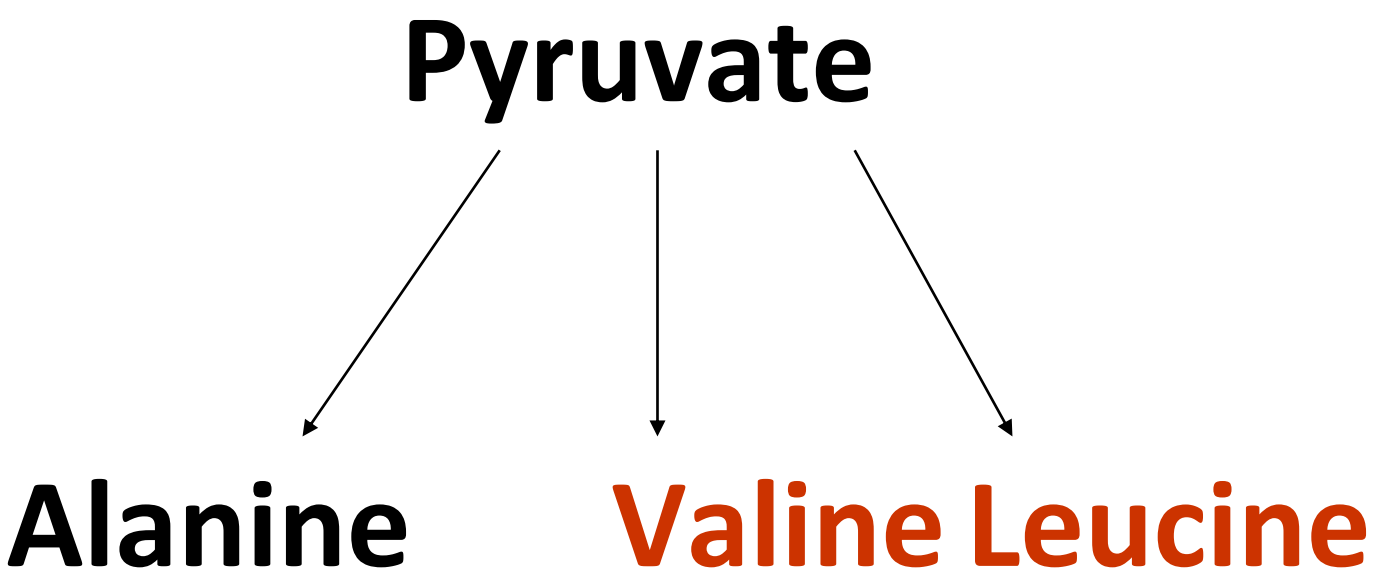
FORMATION AND FATE OF SUCCINYL-CoA

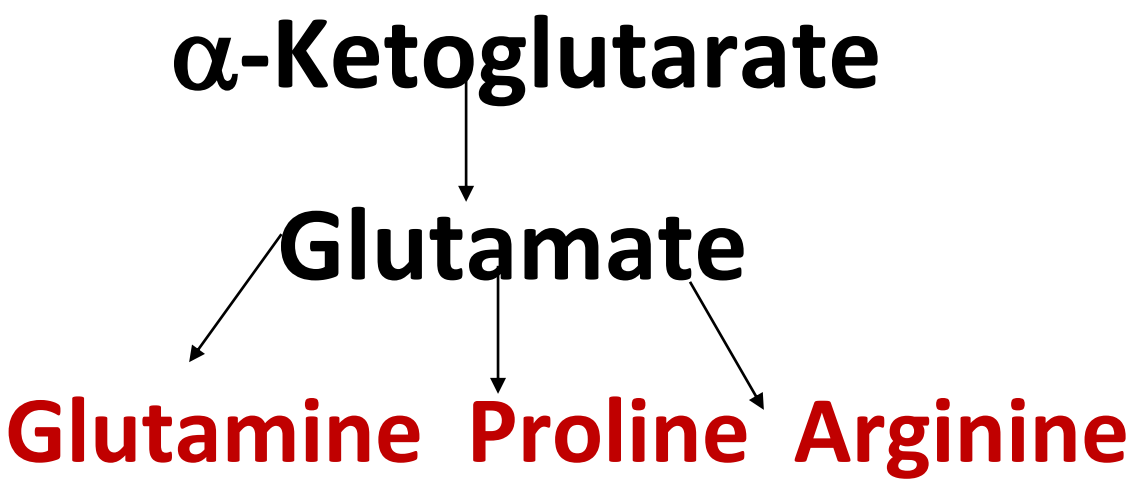


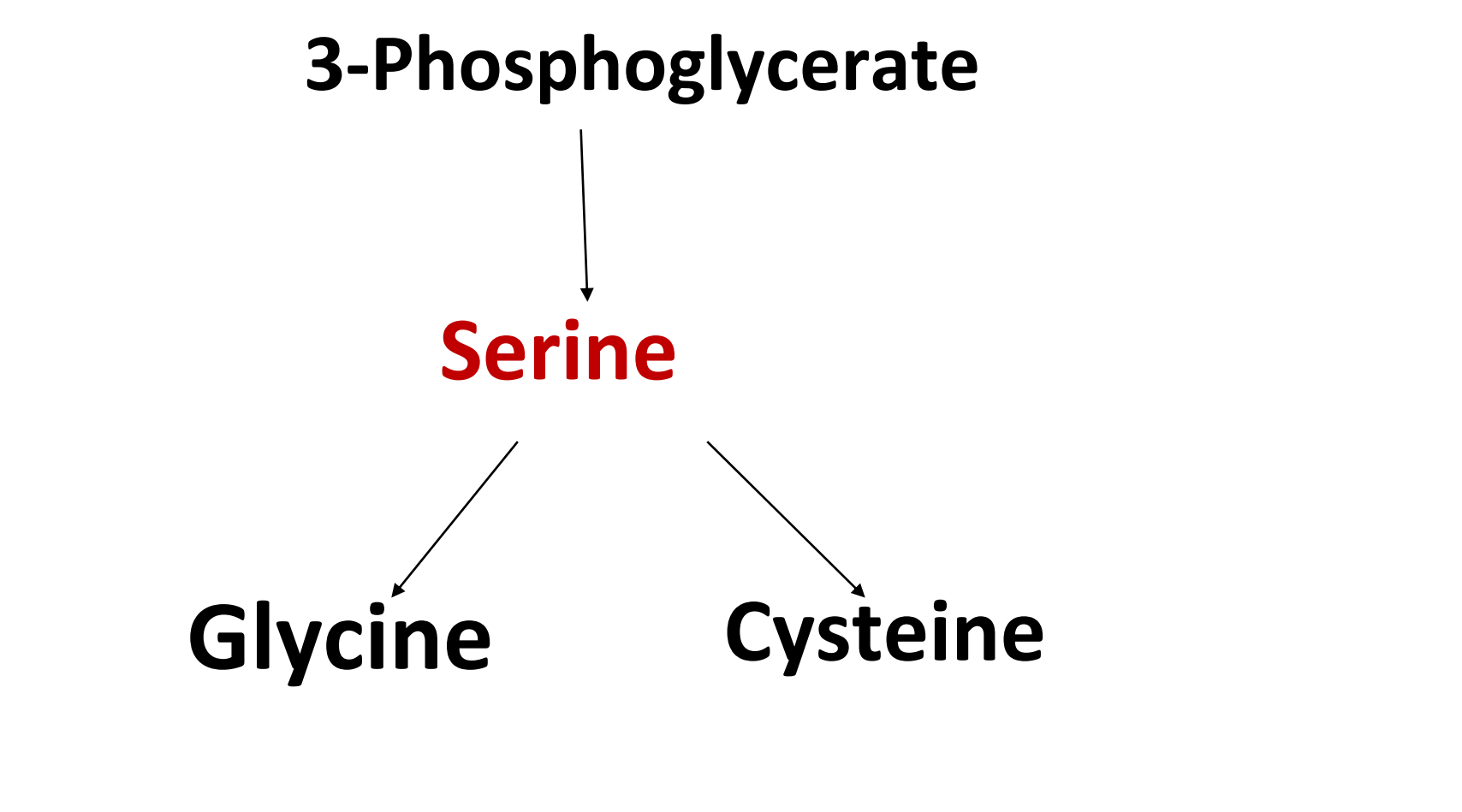
Metabolites Forming Non essential Amino acids In Human Body







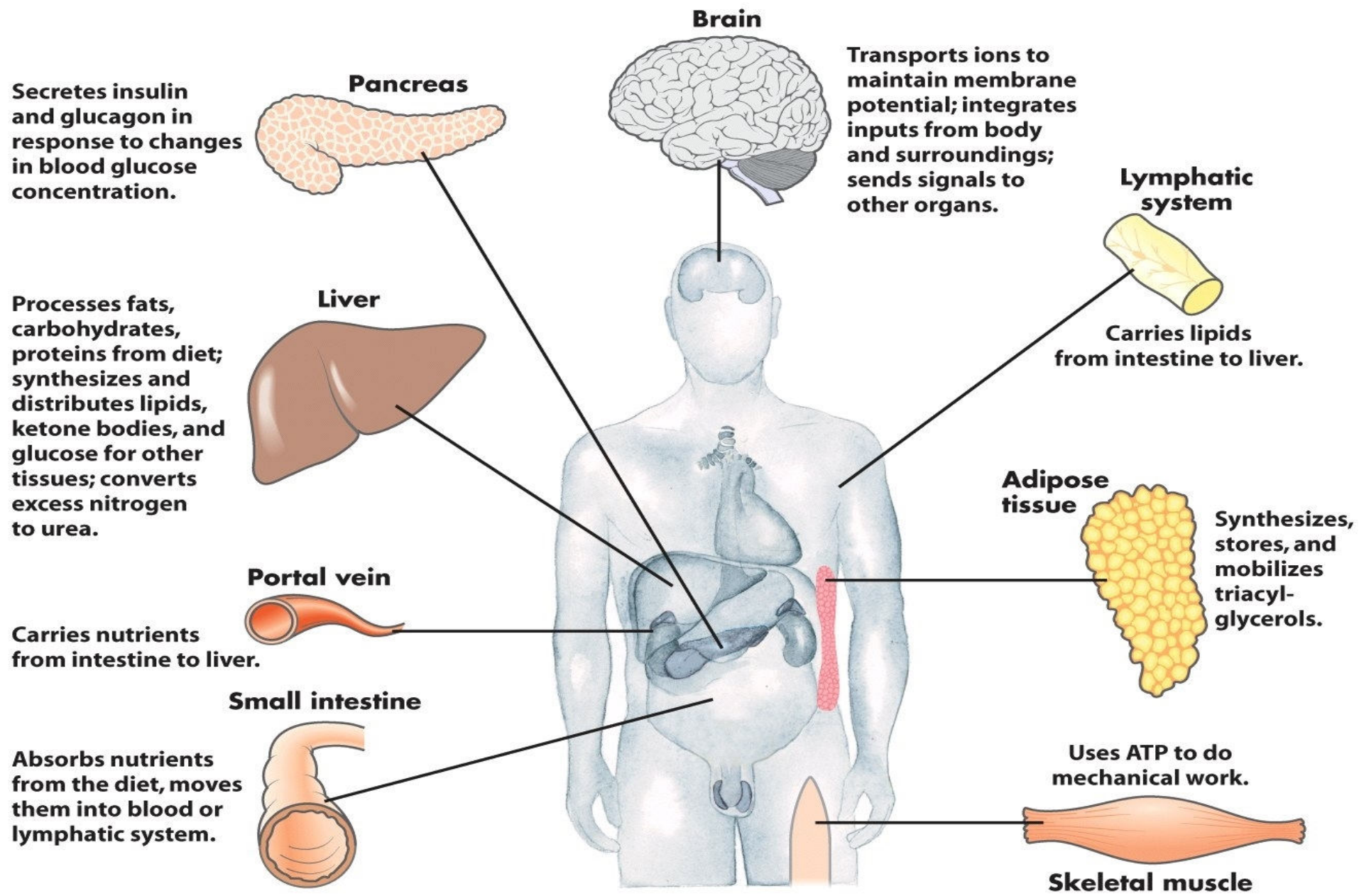




Metabolic Profile
And
Interrelationship Among Organs

Important Metabolic Organs And Their Interrelationships

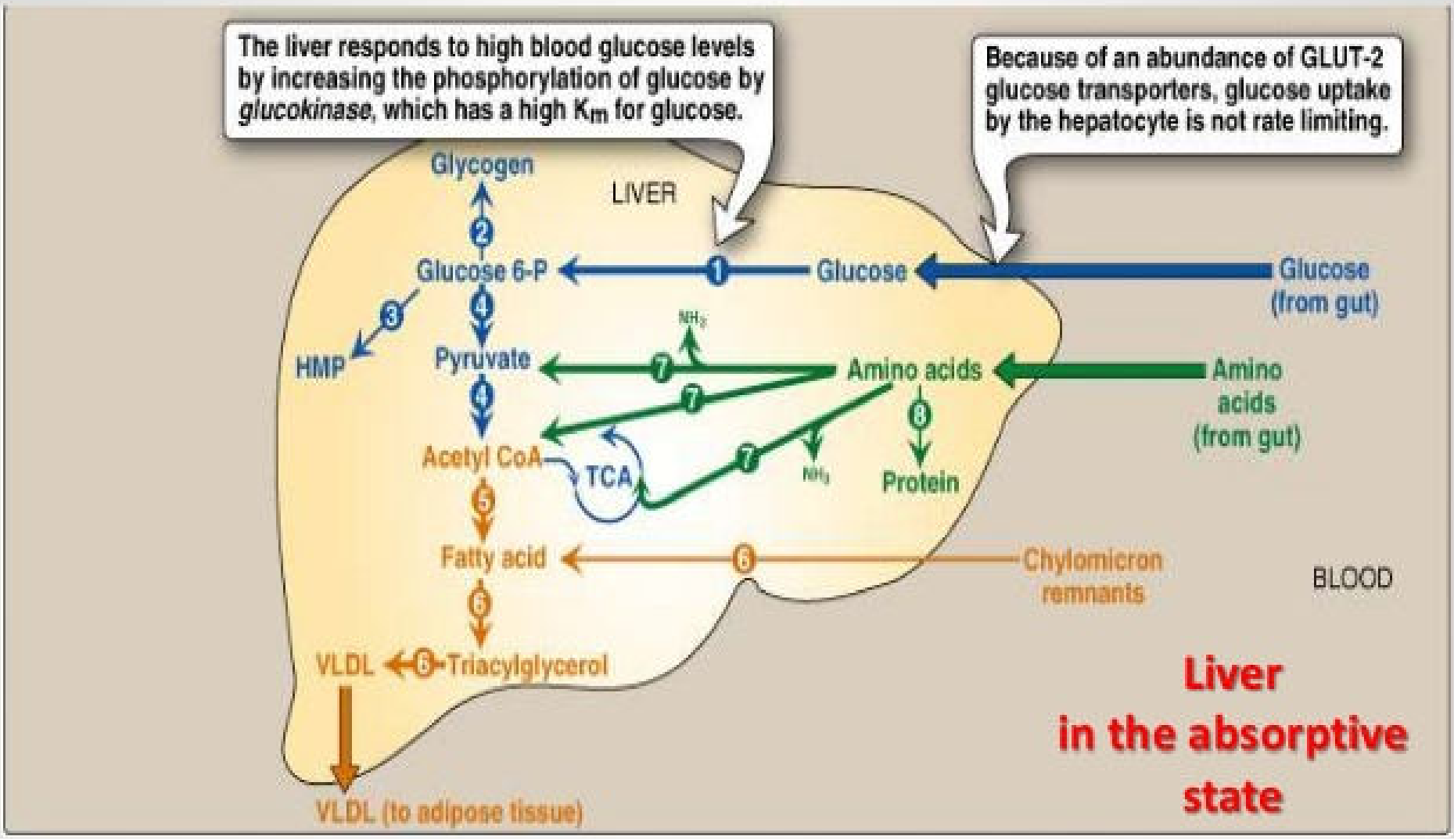
Metabolic Profile of Organs



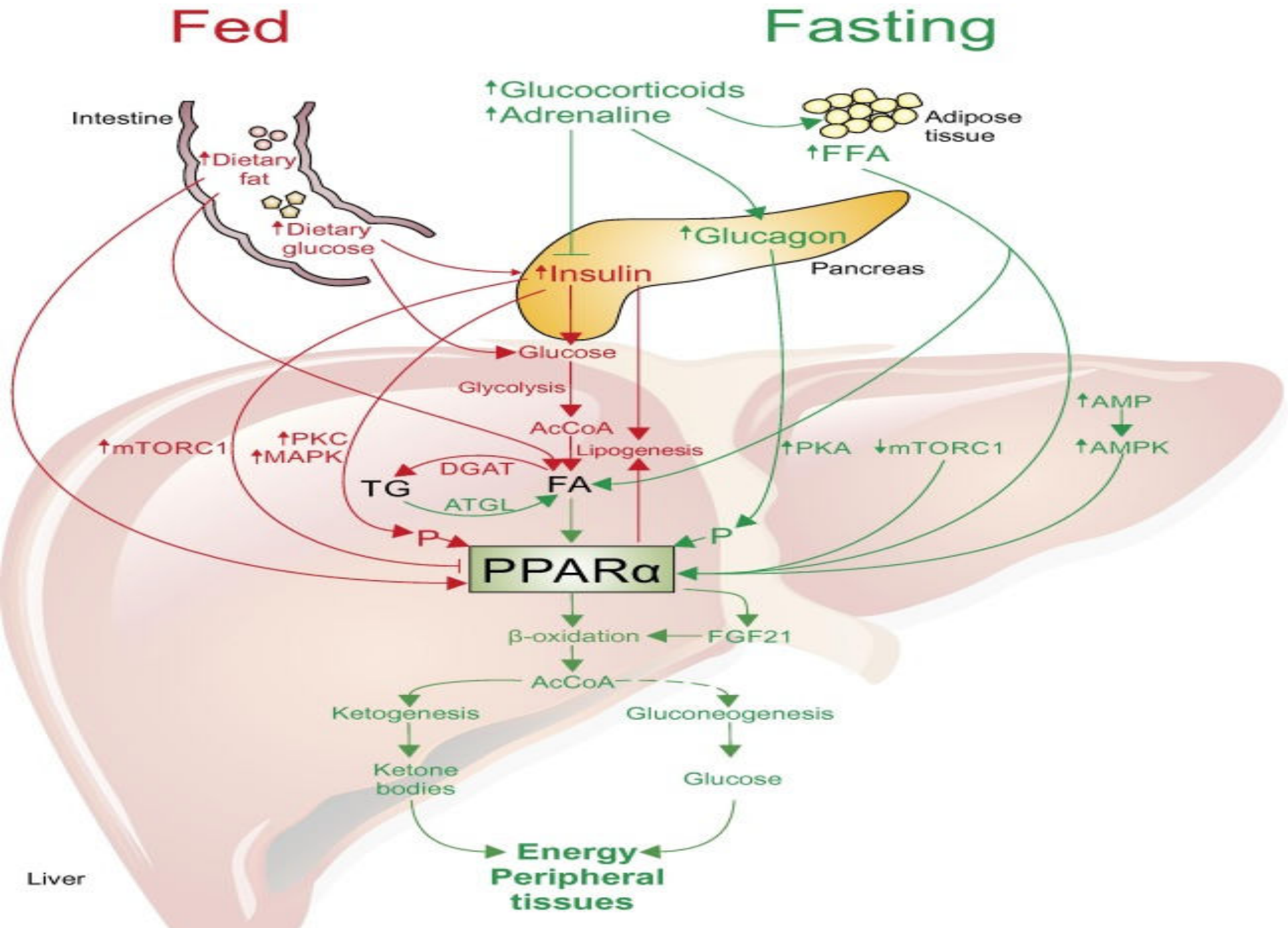
Liver

- **Biochemical Factory** of Human body
- **Metabolically very active** in all states (well fed and fasting)
- Most **Cooperative and Coordinated** organ/Understands responsibility and does its work (**Dutiful/Pious Organ)**

Liver: nutrient distribution center



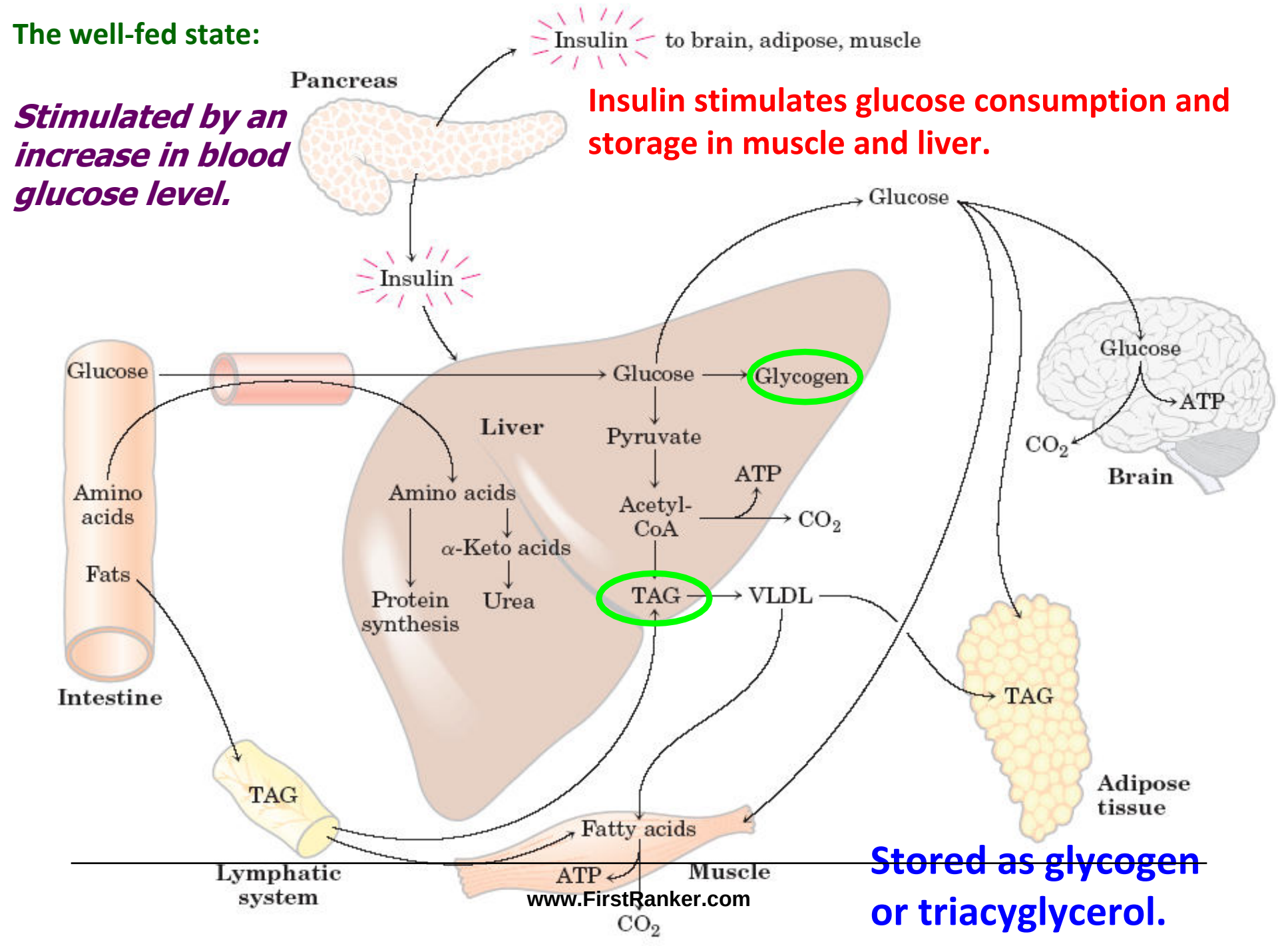
Liver is a **Glucostatic Organ**
Regulates Blood Glucose
in all conditions



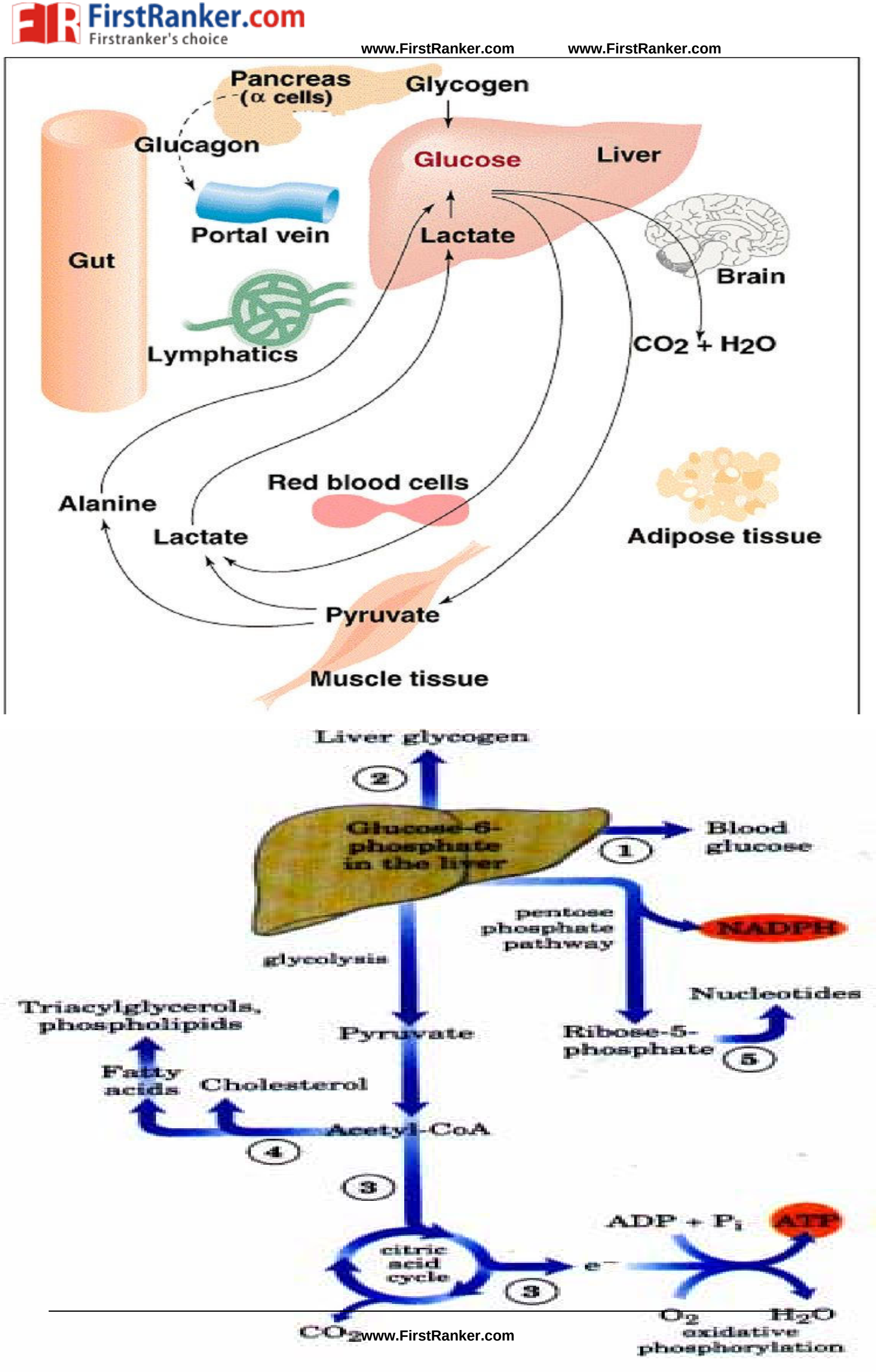
The well-fed state:

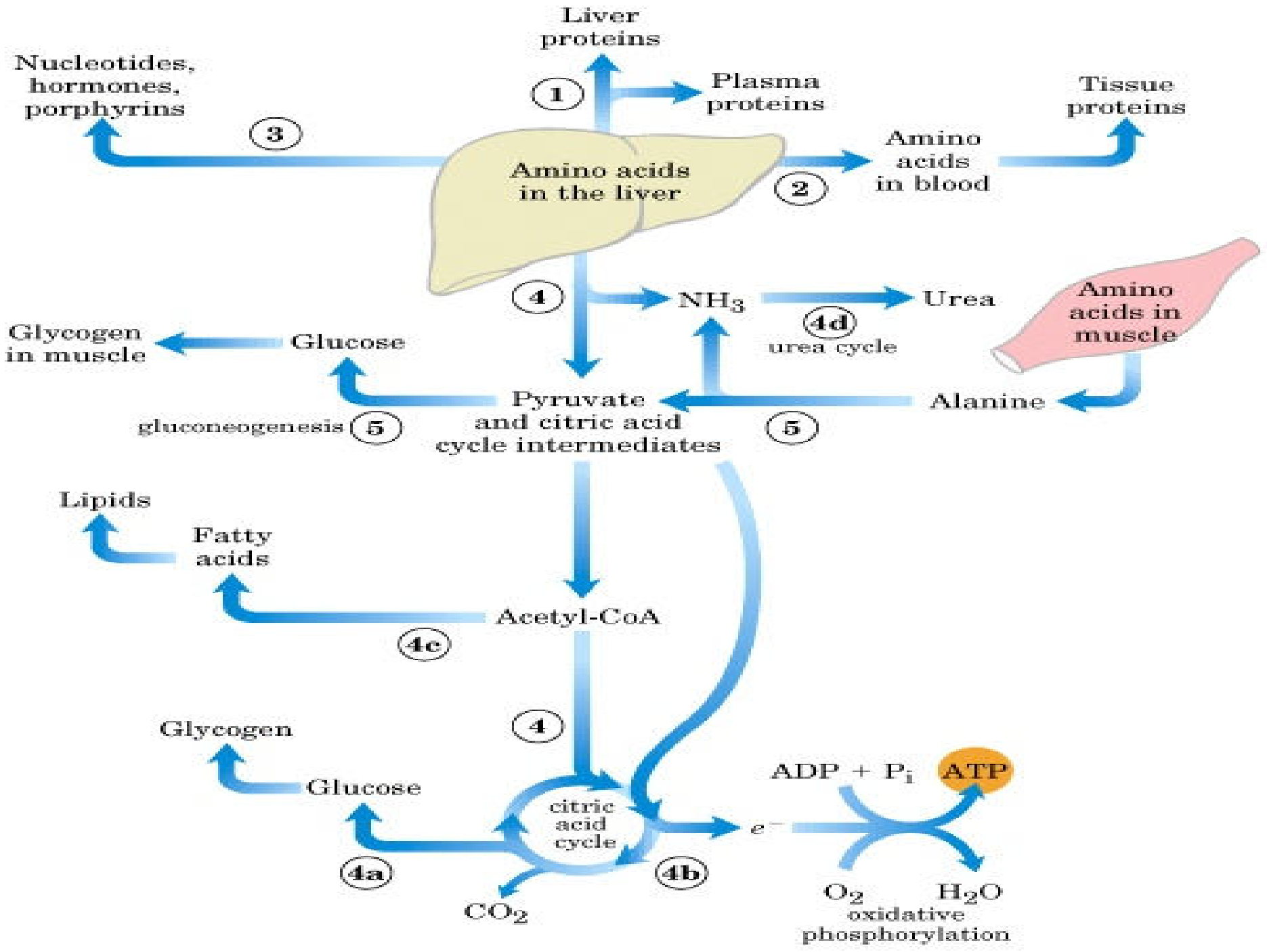
Stimulated by an increase in blood glucose level.

Insulin stimulates glucose consumption and storage in muscle and liver.



~~Stored as glycogen~~ or triacyglycerol.





–In a **well fed** condition Liver **stores excess free Glucose as Glycogen (Glycogenesis)**

–**In emergency condition In Liver Glycogen is degraded via Glycogenolysis and biosynthesizes Glucose via Gluconeogenesis.**

- Liver biosynthesizes **endogenous Lipids and mobilizes out it as VLDL** for extra hepatic use.
- Liver Centre of Ammonia Detoxification

Muscles

- In a normal metabolic state muscle uses **Glucose and Fatty acids as main sources of energy**.
- In a well fed state muscles has large **stores of Glycogen** (3/4th)

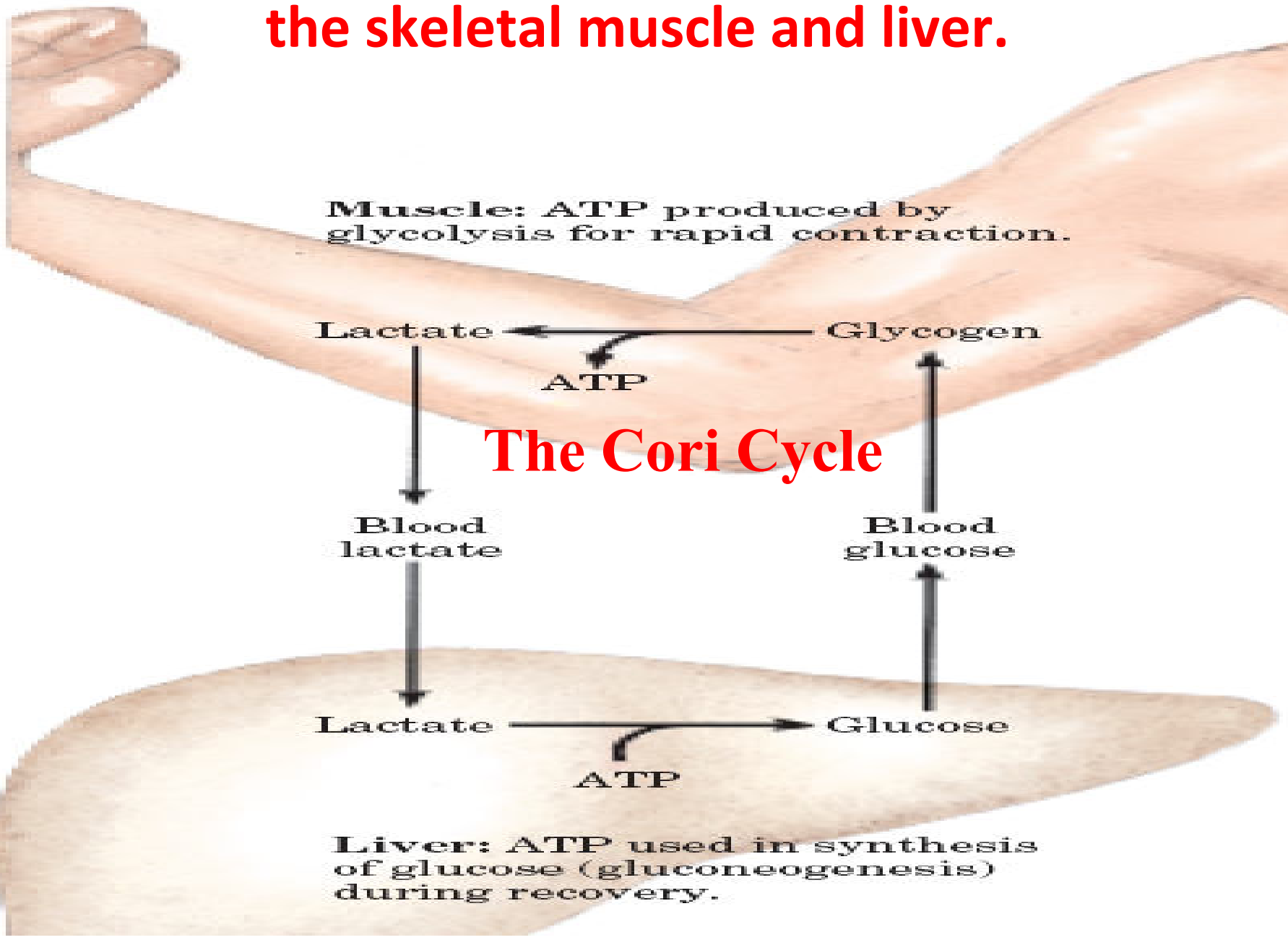
- In **contracting muscles** during **severe exercise** in **anaerobic condition** **Glycolysis ends as Lactate**.

- Later **Lactate** is metabolized by converting it **into Glucose** after carried through blood **in Liver** via **Gluconeogenesis (Cori cycle).**

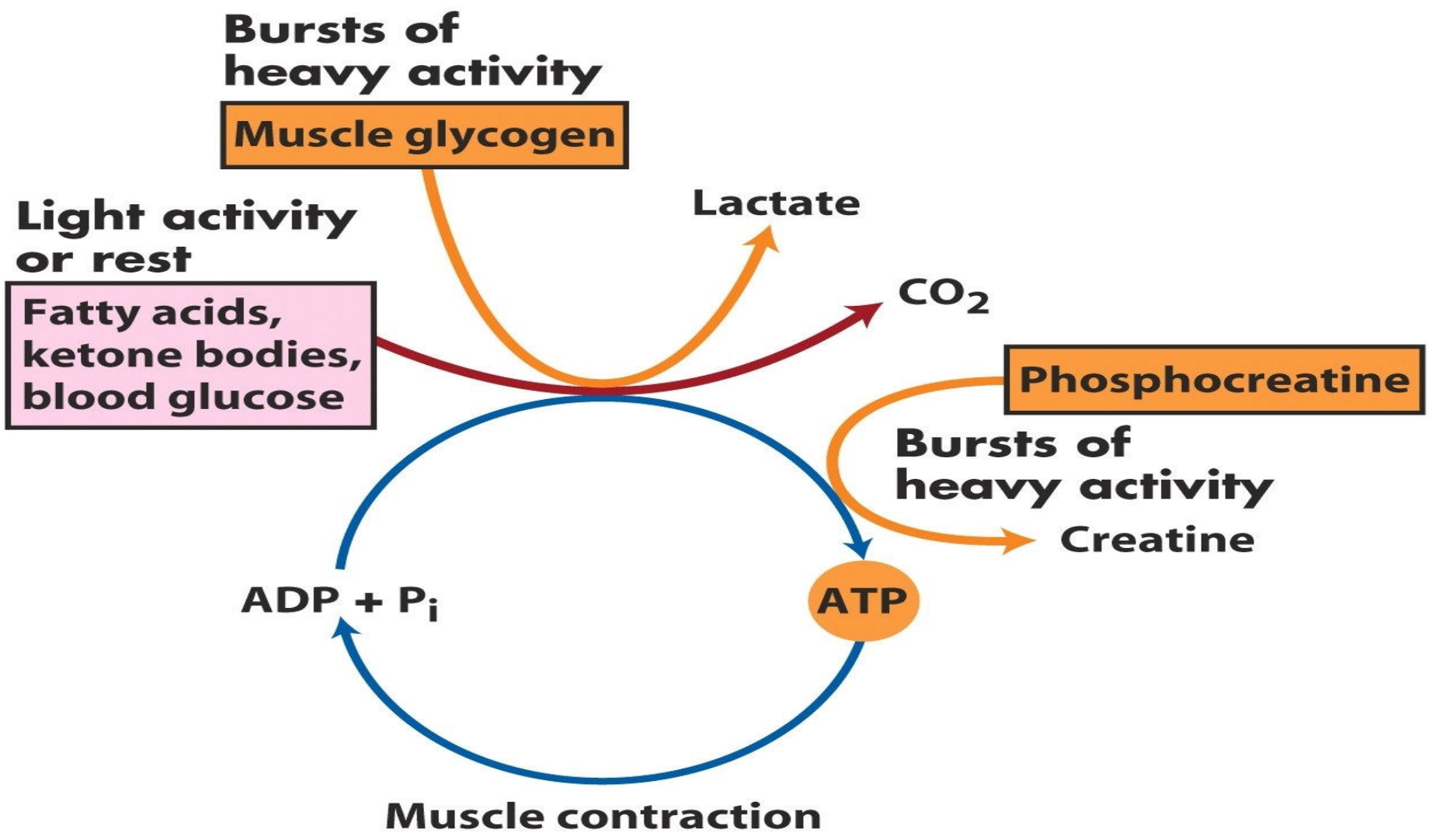
- In **resting Muscle fatty acids** are the **major source of energy**

- **This use spare Glucose to be used by Brain and Erythrocytes.**

Metabolic cooperation between the skeletal muscle and liver.



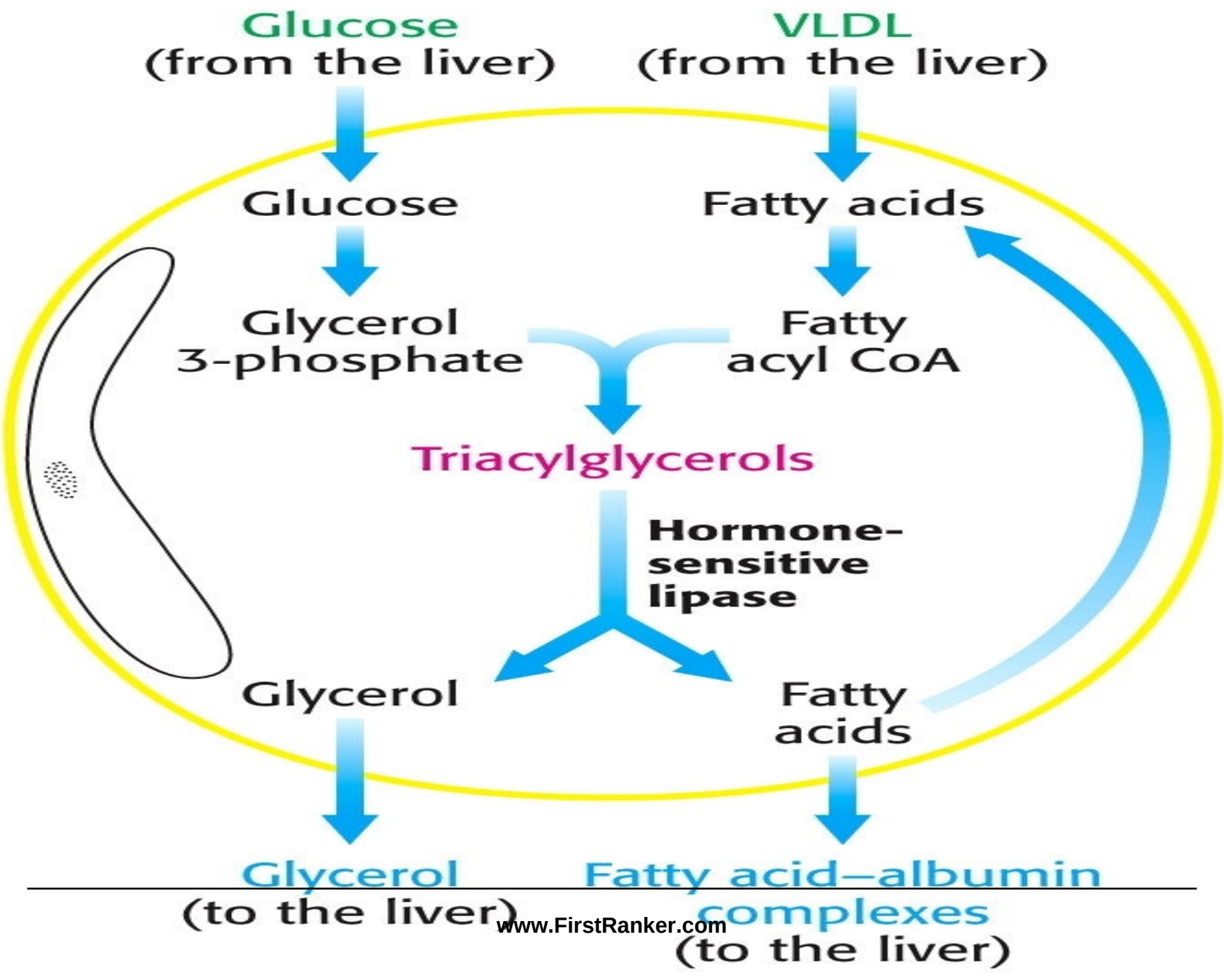
Metabolic Profile of Muscles



Adipose Tissue

- **TAG** can be abundantly and **unlimitedly stored** in adipocytes
- TAG serve as a **reserve store** of energy during well fed condition.

- TAG is the major fuel for this tissue.



Metabolic Profile of Adipose Tissue

- **Needs Glucose for biosynthesis of TAG**
- **Glucose level determines to release Fatty acids into blood**
- **Hormone sensitive Lipase is activated when Insulin/Glucagon ratio is low**

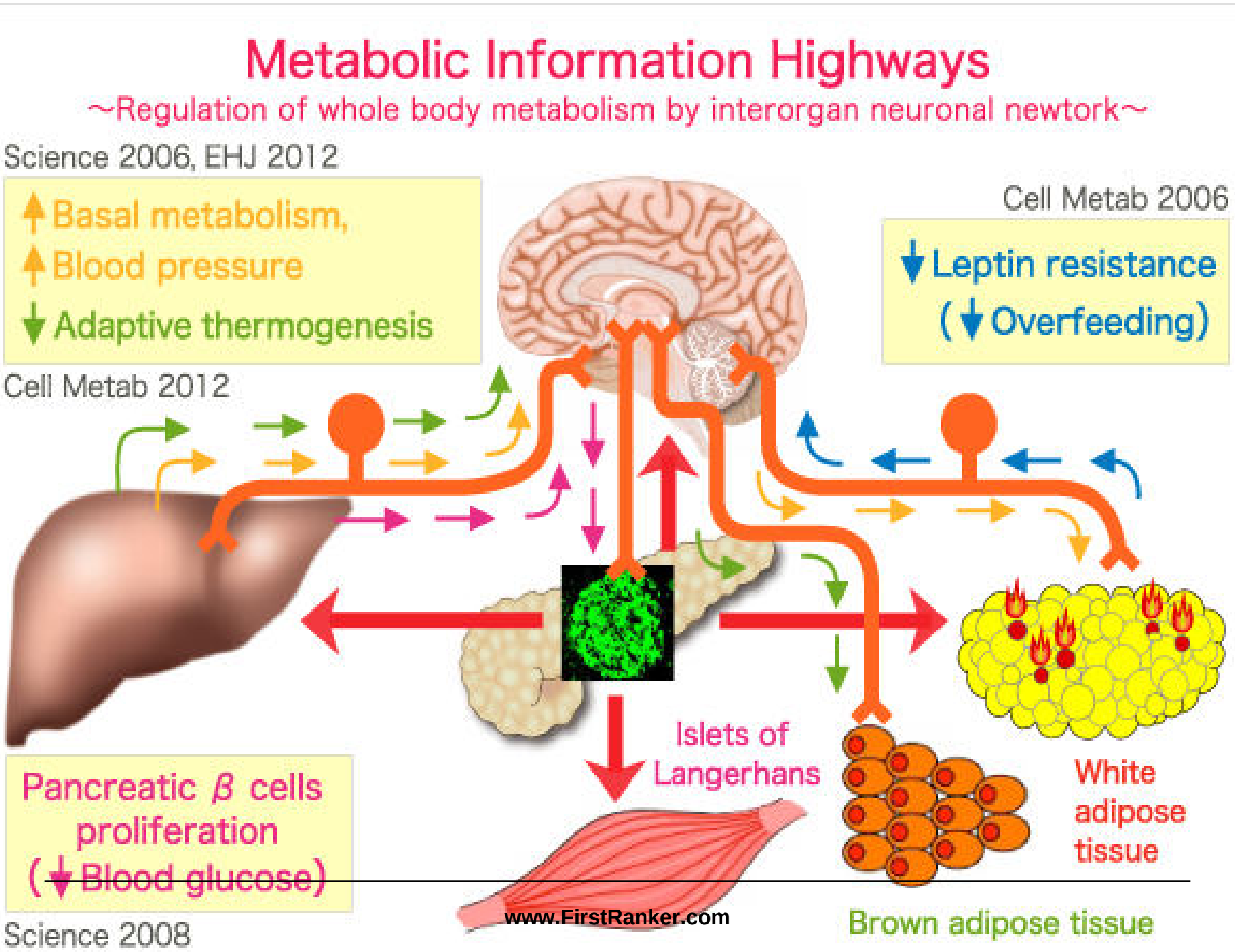
Brain

- **Glucose** is the **main fuel of Brain (120 gm/day)**
- **Fatty acids** cannot be utilized by brain as they are bound to Albumin and **cannot cross blood brain barrier.**

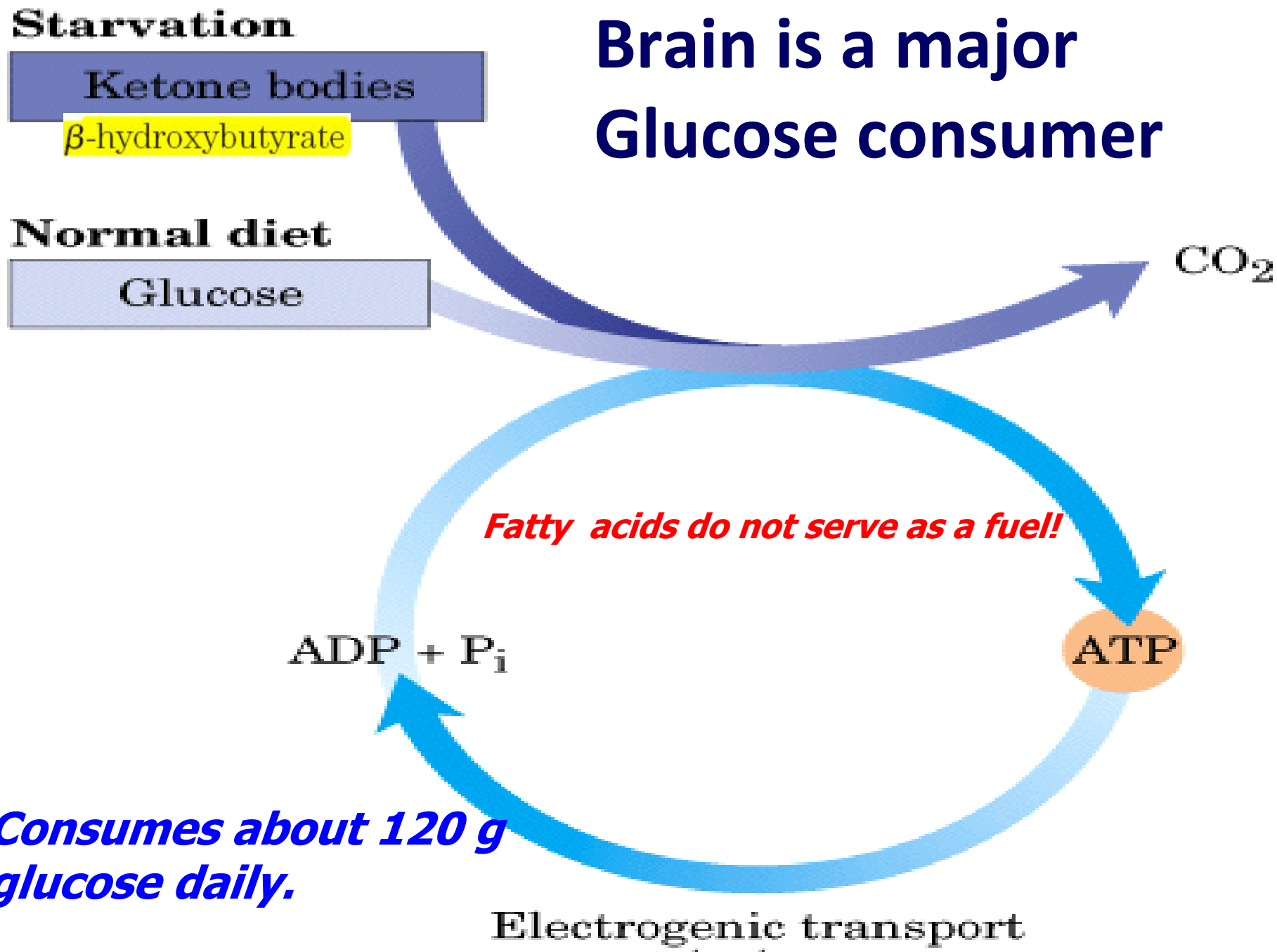
Metabolic Profile of Brain

60-70 % of bodies utilization of Glucose is by Brain.

In starvation -> Ketone bodies can replace Glucose



Brain is a major Glucose consumer



Consumes about 120 g glucose daily.

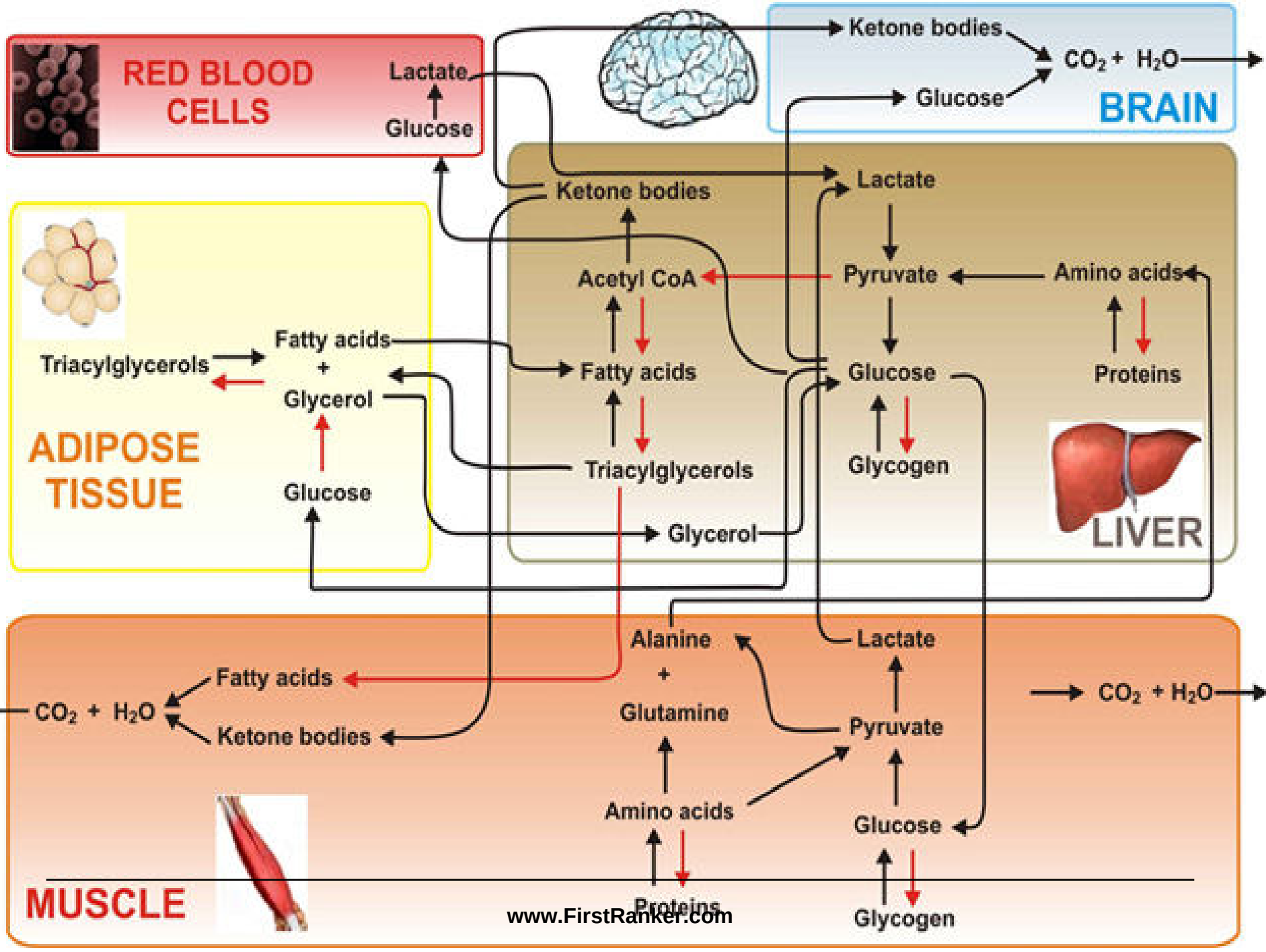
Erythrocytes

- Erythrocytes uses **obligatorily Glucose** as a source of energy for its activity.
- **Erythrocytes cannot use Fatty acids and Ketone bodies as source of energy.**
- It **lacks Mitochondria** hence the **Glycolysis ends in Lactate.**

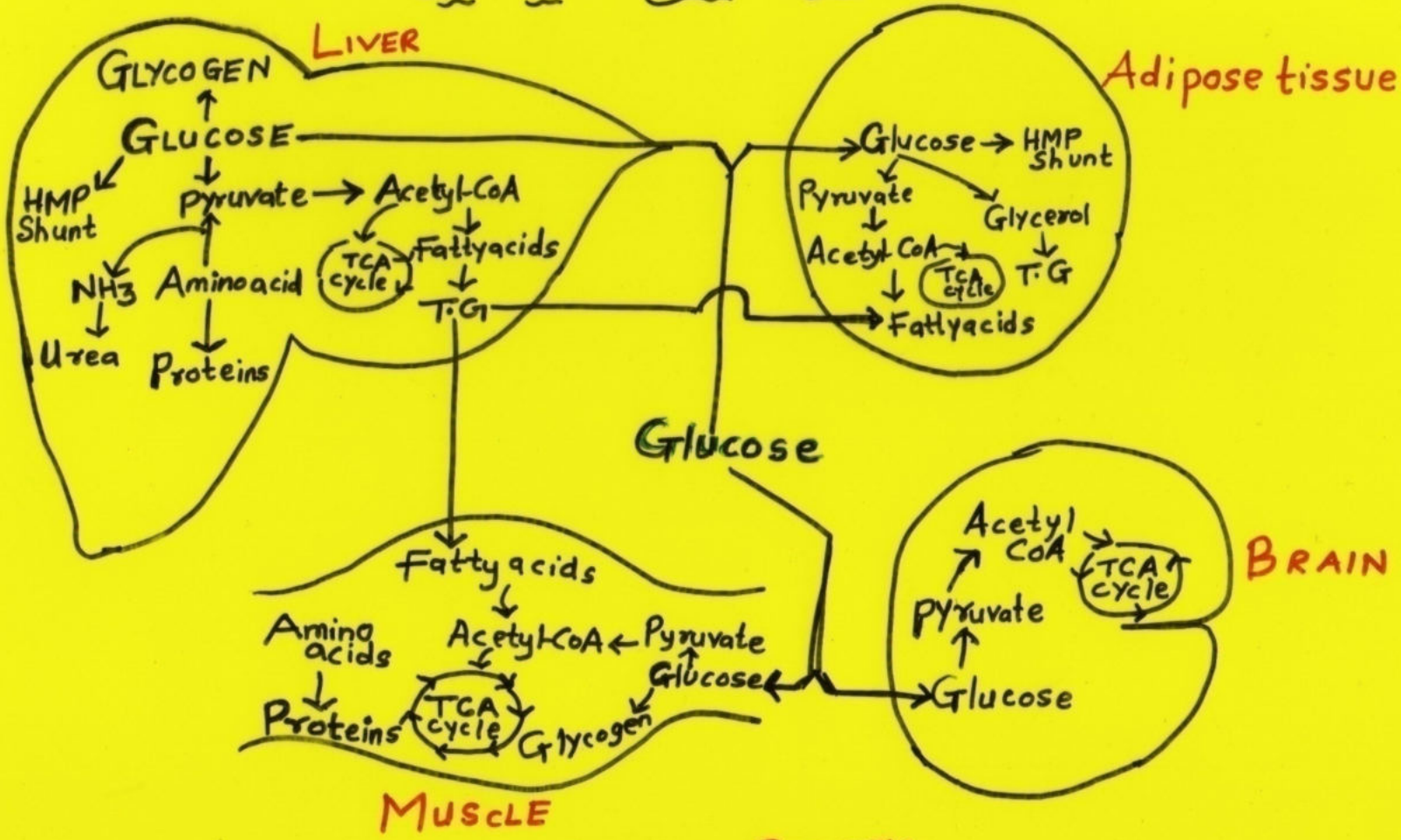
Metabolic Profile of Kidney

- **Filtration of Blood-** Plasma Ultra Filtrate
- Reabsorption ,Secretion of Substances
- From Plasma Ultra filtrate -> Water , Glucose important absorbable metabolites reabsorbed as per the threshold values.
- Production of Urine -> Secretion of waste products
- Important role in water, electrolyte ,acid base balance.

- During Starvation -> Important site of Gluconeogenesis (1/2 of blood Glucose)



METABOLIC INTERRELATIONSHIP AMONG MAJOR TISSUES IN A WELL FED STATE

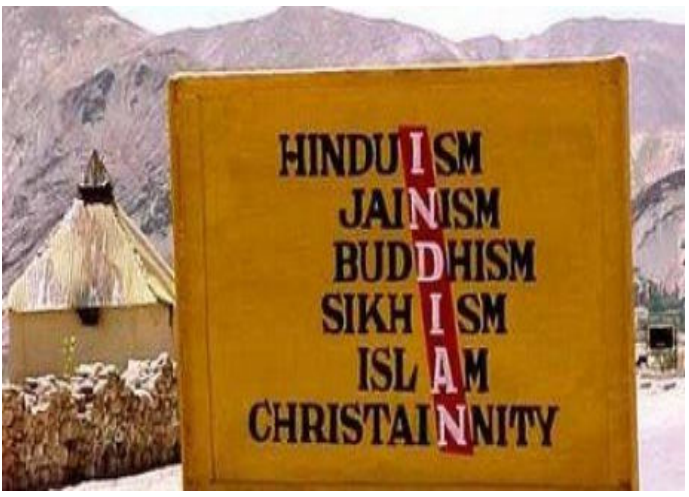


★ METABOLIC CONTROL IS ORGAN SPECIFIC

DUE TO

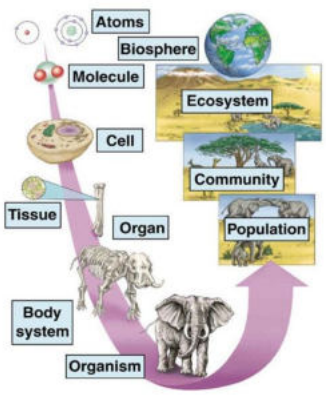
- DIFFERENT ENZYMATIC MAKE UP OF TISSUES
- DIFFERENT HORMONE RESPONSIVENESS BY TISSUES
- DIFFERENT POSSIBILITIES FOR TRANSPORT OF VARIOUS SUBSTANCES THROUGH CELL MEMBRANES.

In Human Body
There Prevails
Chemical Unity In Diversity

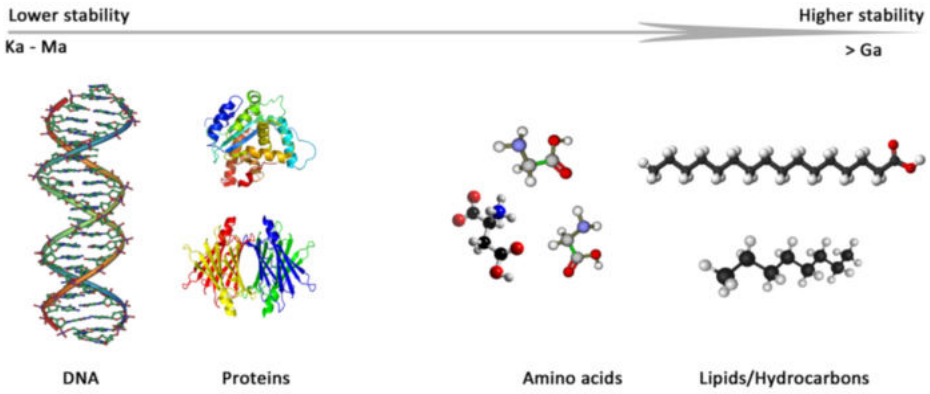


Atoms (Elements)
Needed for Life to Survive

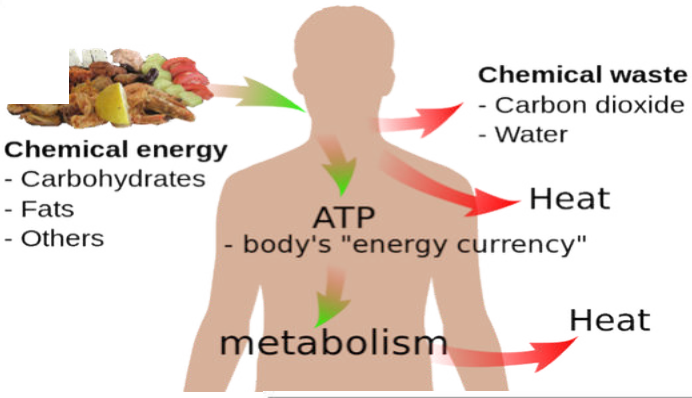
- **C** – carbon
- **H** – hydrogen
- **N** – nitrogen
- **O** – oxygen
- **P** – phosphorus
- **S** – sulfur

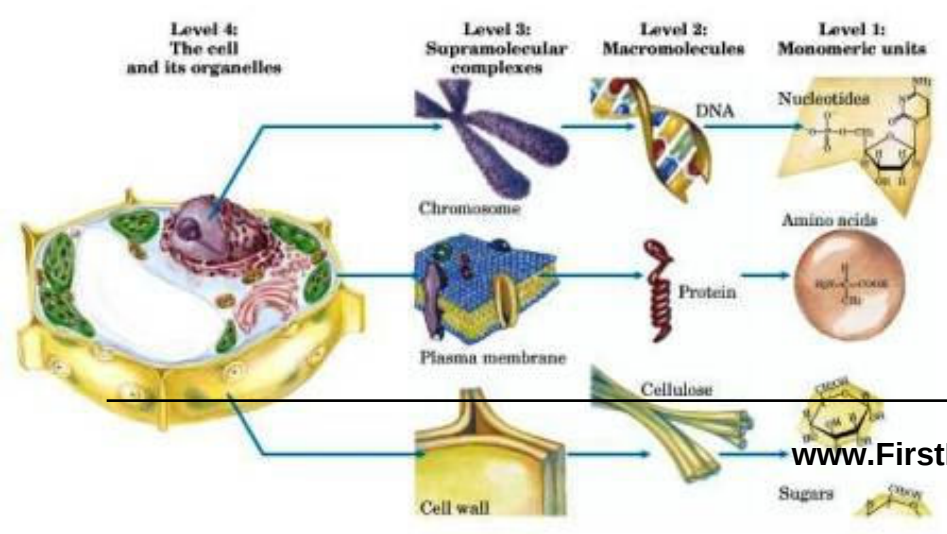


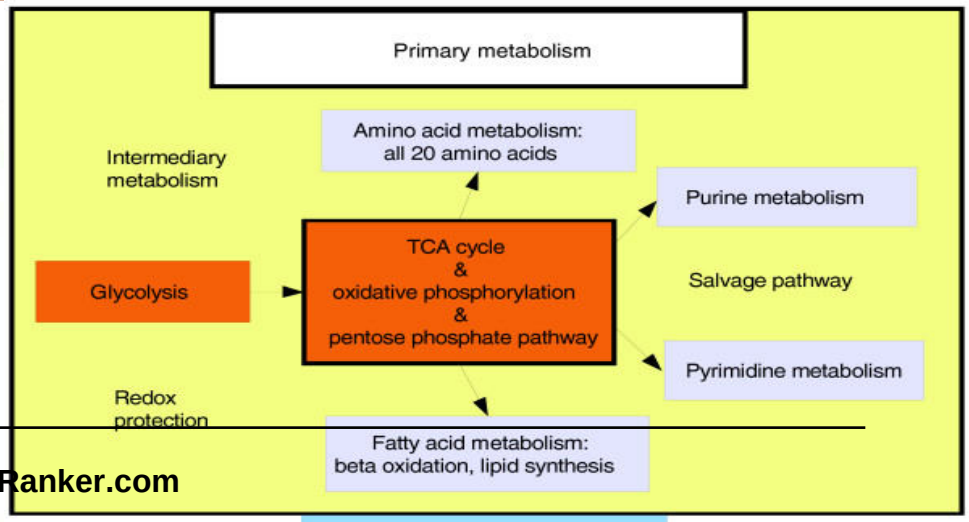
Life is built from these elements.



Energy and human life







Flow Chart Showing Overview Of Integrated Metabolism (13)

Glycogen
Glycogenolysis
Glucose
Glycogenesis
Glucose-6-PO4
Uronic acid pathway
Glucuronic acid
• Bilirubin metab
• Mucopolysacch Synth.
• Drug metabolism
Glyceraldehyde-3-PO4
PEP
Pyruvate
LDH
Lactate
Alan; Gly
Ser; Thr
GN; Asp
Gln
Asp
Glucogenic Aminoacids
Oxaloacetate
Malate
T.C.A cycle
Citrate
α-Ketoglutarate
Glutamate
Gln; Arg; His; Pro
Succinyl CoA
ketolysis
Heme
Fumarate
Phe ala; Tyr
Val
Ileu; Met
Urea cycle
Propionyl-CoA
β oxidation of Odd chain fatty acids
Ribose-5-PO4
NADPH+H+
HMP SHUNT
Lipolysis
Triglycerides
Lipogenesis
Glycerol
Fatty Acids
De novo synthesis
β Oxidation
Cholesterol
Nucleotide Synthesis
Acetyl Choline
Acetyl CoA
PDH complex
Ketogenesis
Ketone Bodies
Acetoacetate
Ileu; Try
Leu; Phe ala
Ketogenic Aminoacids
NADH+H+
FADH2
ETC
ATP

★ Coordinated & Well Regulated Integrated Metabolism protects the body against Metabolic Catastrophe

"Working Together Is Essential"

Metabolism Summary

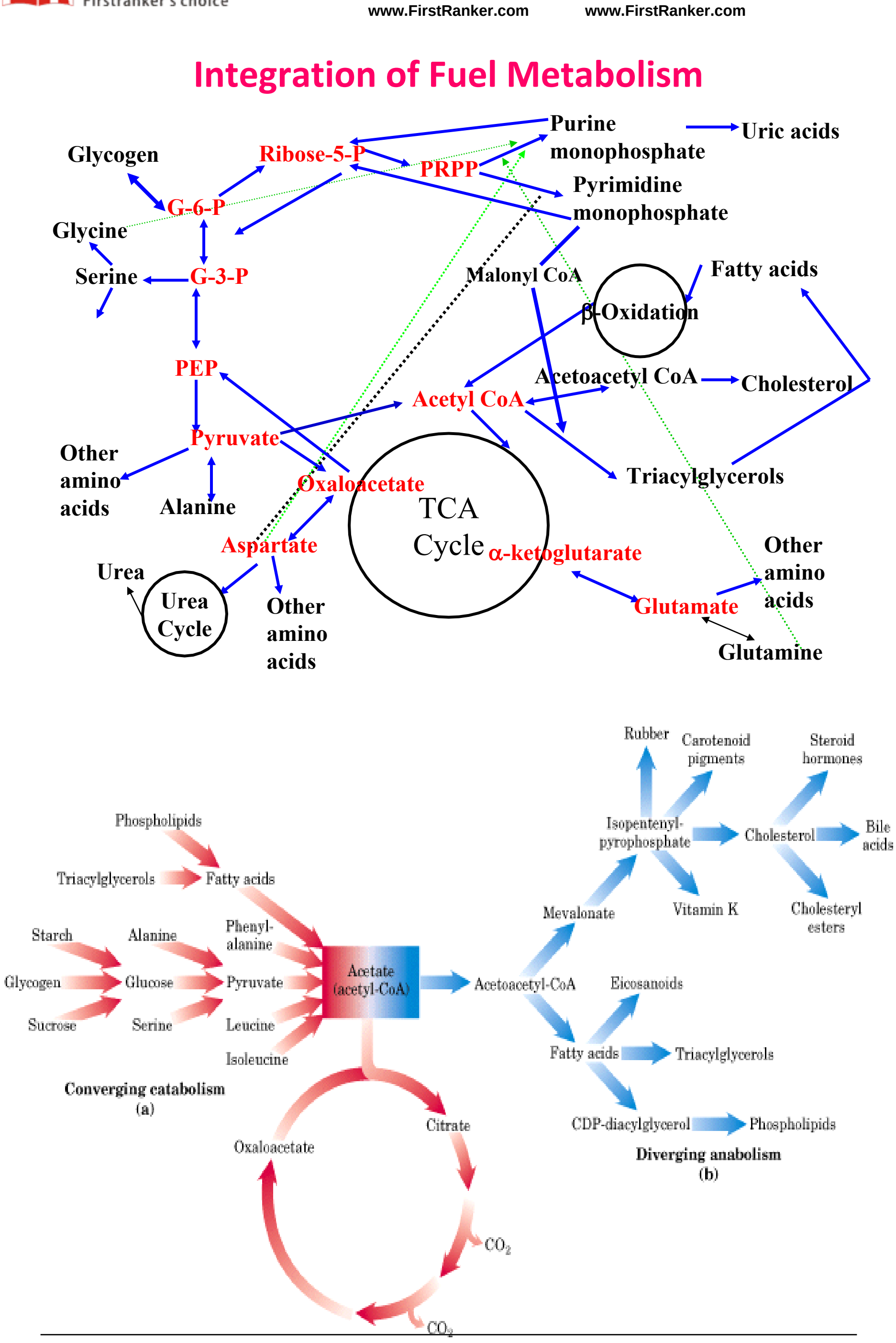
Proteins
amino acids
Carbohydrates
glucose, fructose, galactose
Fats and Lipids
fatty acid, glycerol
glycogenesis
Glycogen
Glucose-6-Phosphate
glycogenolysis
Nitrogen Pool
tissue protein
gluconeo-genesis
glycolysis
Lipogenesis
Lactic acid
Pyruvic Acid
NH_3
CO_2
Fatty Acid Spiral
acetyl Co A
Urea Cycle
Citric Acid Cycle
$2H^+$
ADP ADP ADP
O_2
Electron Transport chain
urea
CO_2
$2e^-$
ATP ATP ATP
H_2O

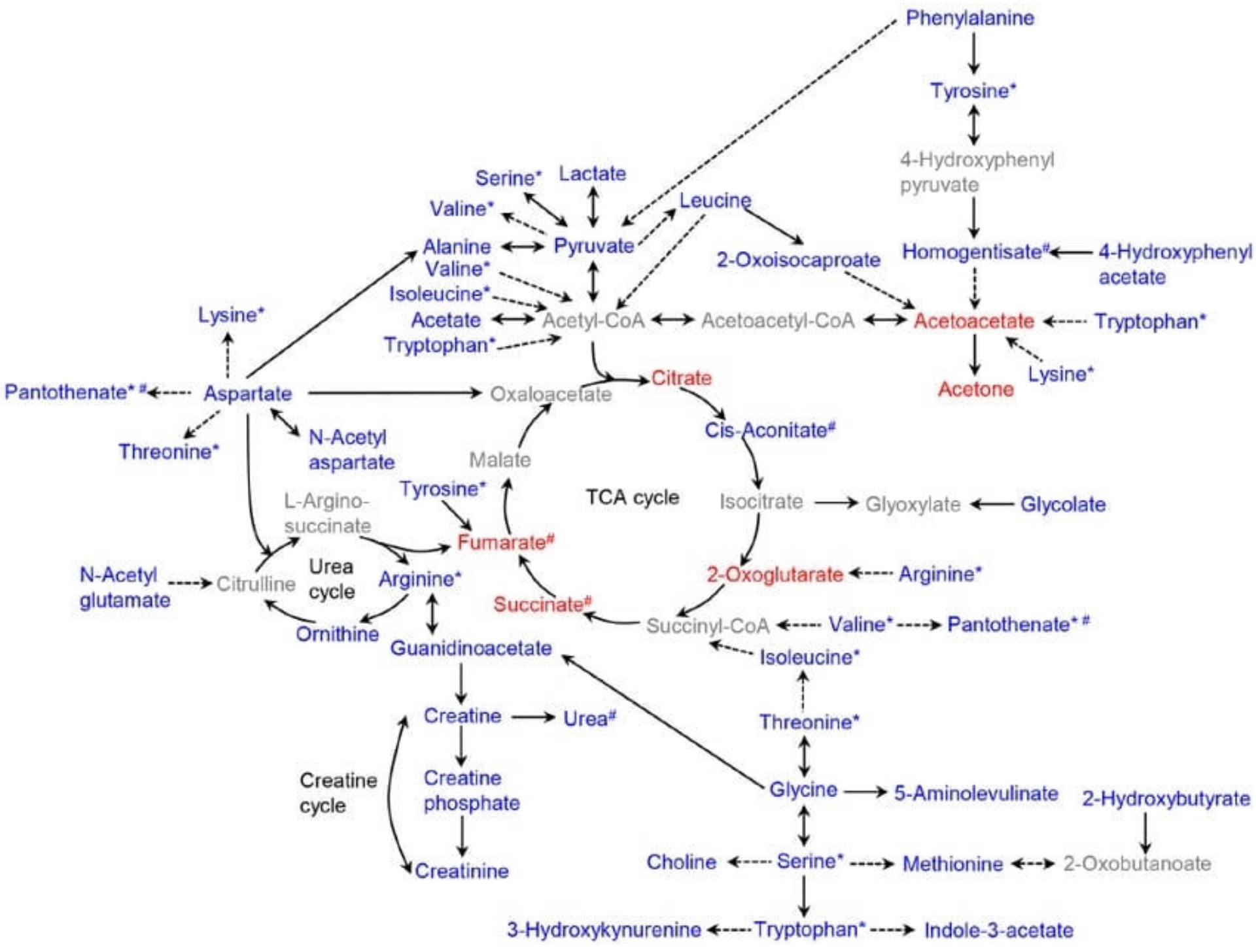
Metabolic Interrelationships

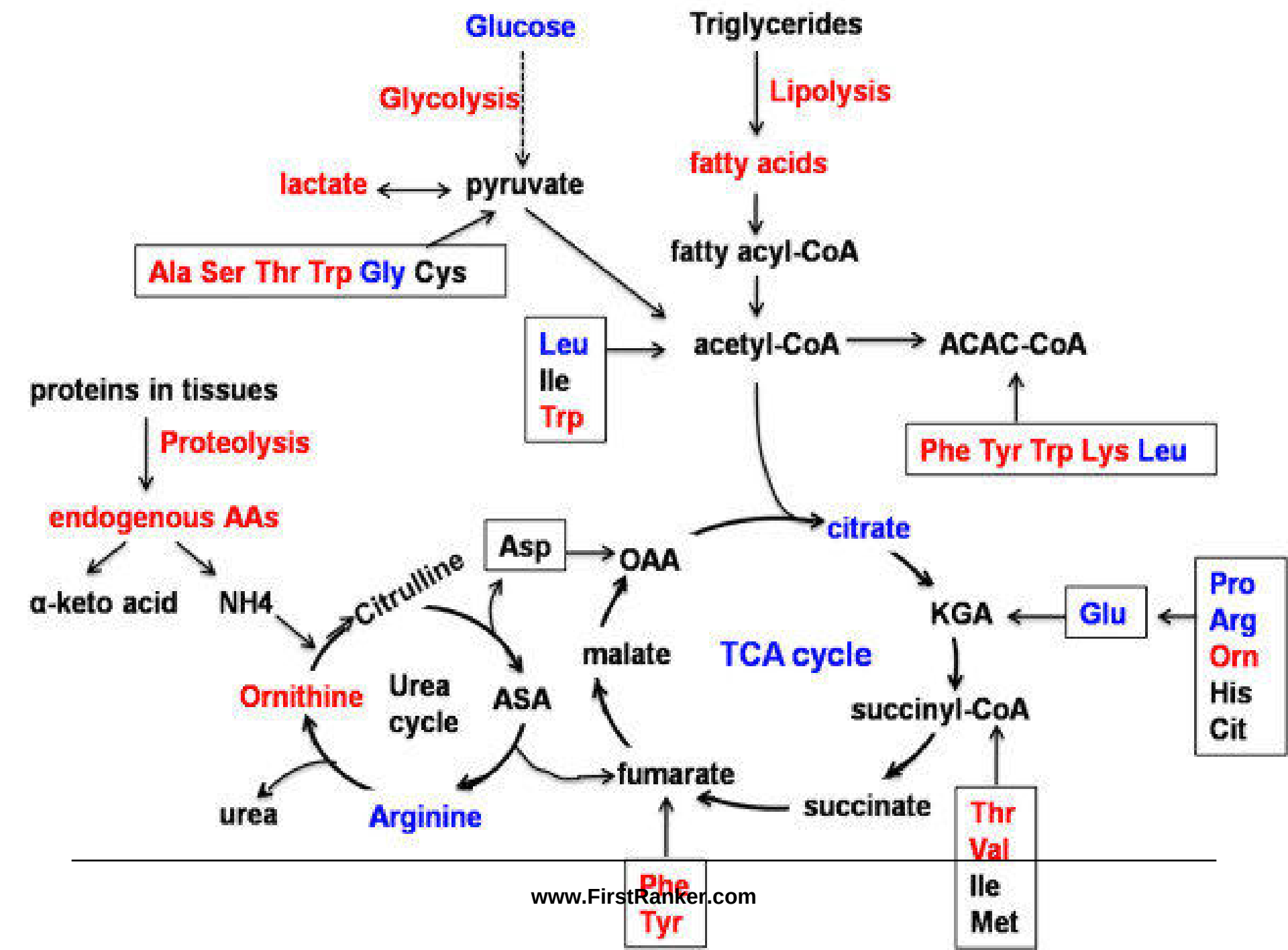
- Each chemical reaction in the body is purposeful
- All reactions are interdependent
- Fill two essential needs
  - Produce energy
  - Support growth and maintenance of healthy tissue
- Controlling agents are cell enzymes, coenzymes, and special hormones

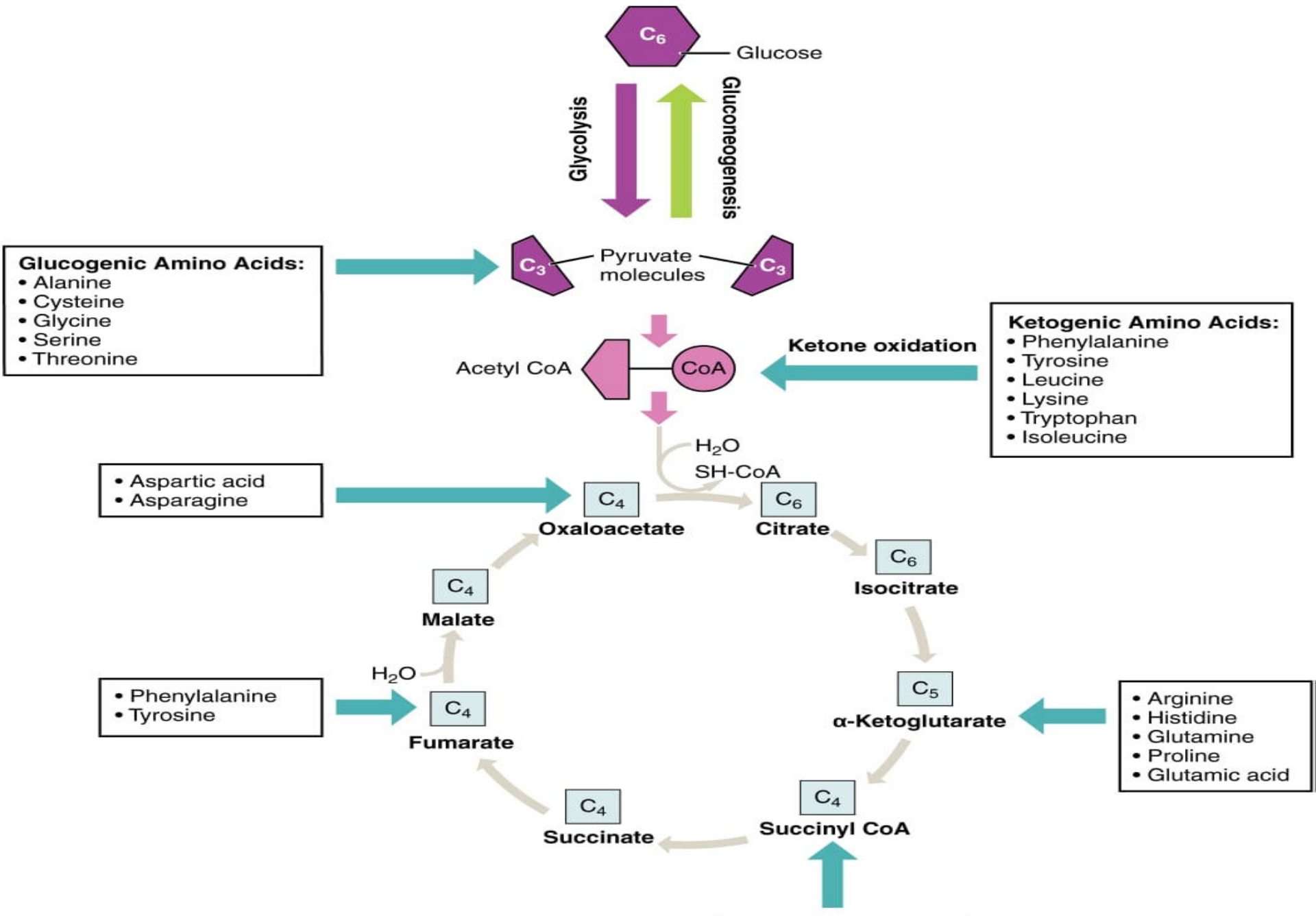
- **Intermediates/End Products** of one metabolic pathway may be connected to another metabolic pathway of **same or another.**
- An **end product** of **one metabolic pathway** of **Carbohydrate** is **connected to another metabolic pathway of Carbohydrate**.
- **Intermediate of Carbohydrate metabolic pathway** is **interrelated to a metabolic pathway of Lipid or Nucleic acid.**

Integration of Fuel Metabolism









Glucose
Enolase
β-oxidation
Triglycerides Phopholipids
Creatinine ← Creatine
Methylamine Glycine ↔ Serine ↔
PEP
Fatty acids
Ketogenesis
Acetone 3-HB
DMA
DMG
Sarcosine
Alanine
ALT
PDH
Acetate
Acetoacetate
LDH
Lactate ← Pyruvate
TMAO Methylamine metabolism
Betaine
Glycolysis
HMG-COAlyase
Acetyl-COA + Acetyl-COA → Acetoacetyl-COA
β-alamine ← Uracil ← Uridine
TMA
Choline
Oxalocetate
Citrate
Pyrimidine metabolism
Citrulline
Cis-aconitate
Malate
Cytimidine
Argininosuccinate
TCA cycle
Isocitrate
Urea cycle
Fumarate
ALT
Glutaminase
2-Ketoglutarate ← Glutamate ← Glutamine
Orinthine
Arginine
Succinate
Isoleucine
Succinyl-COA ←
Valine
Phenylalaine → Tyosine
PAH
Urea ← Allantoin ← Uric acid ← Xanthine ← GTP

Purine metabolism

ATP
Hexokinase
Glucokinase
Glycogen
Glucose 6-phosphate
D-Glucose
Glucose-6-phosphatase
Aldose reductase *
D-Sorbitol
NADPH + H+
NADP+
NAD+
NADH + H+
Sorbitol dehydrogenase
Phosphohexose isomerase
Hexokinase
Fructose 6-phosphate
ATP
D-Fructose
Diet
Fructose 1,6-bisphosphatase
ATP
Phosphofructokinase
Fructokinase
ATP
Block in essential fructosuria
Fructose 1,6-bisphosphate
Fructose 1-phosphate
Block in hereditary fructose intolerance
Aldolase B
Dihydroxyacetone-phosphate
Aldolase A
Aldolase B
Phospho-triose isomerase
Fatty acid esterification
ATP
Glyceraldehyde-3-phosphate
D-Glyceraldehyde
Triokinase
2-Phosphoglycerate
Pyruvate → Fatty acid synthesis

Synthesis and degradation of ketone bodies

Tryptophan metabolism

3-Hydroxybutyrate → Acetoacetate ⇄ Acetyl CoA ⇄ Pyruvate ← Glucose

Glycolysis/Gluconeogenesis

NADPH → NAD pathway → Quindinic acid

picolinic acid

2-Aminomuconic semialdehyde

2-Amino-3-carboxymuconic Semiadehyde

3-Hydroxykynurenine

Kynurenine hydroxylase

Kynurenic acid ← L-Kynurenine

IDO

Tryptamine ← L-Tryptophan ⇢ Tyrosine

Indole-3-acetaldehyde

5-Hydroxy-L-Tryptophan

Indoleacetate

Indole-3-ethanol

Indole → Indole-3-carboxylic acid

Serotonin

5-Methoxytryptamine

N-Acetylserotonin

melatonin

5-Methoxytryptophan

Asperate + Acetyl CoA

Glutaryl-CoA

Fumarate

TCA cycle

Hippurate acid

Succineate

Benzoate

Acetyl CoA

Oxaloactate

Valine, leucine and isoleucine biosynthesis

Valine, Leucine and Isoleucine degradation

Valine

leucine

Isoleucine

Acetolactate

L-oxobutanoate

Phenylalanine ⇄ Pyruvate ⇄ Serine ⇄ Glycine ⇄ L-Threonine

Glycine, serine and threonine metabolism

phenylacetic acid

Alanine ⇄ Aspartate ⇢ histamine

xanthine → AMP ← cyclic AMP

ATP

Glycolic acid

CO2

Formate

Ammonia

Urea Cycle

Citruline ⇄ Arginine

histidine

1-methylhistidine

Guanidinoacetate → Creatine

Creatinine

Creatine pathway

Urea → CO2

Excretion

Argininosuccinic acid

N-acetyl-citrulline

carbamoyl-p

Proline

Glutamine

NH3

Glutamate

L-Glutamine acid

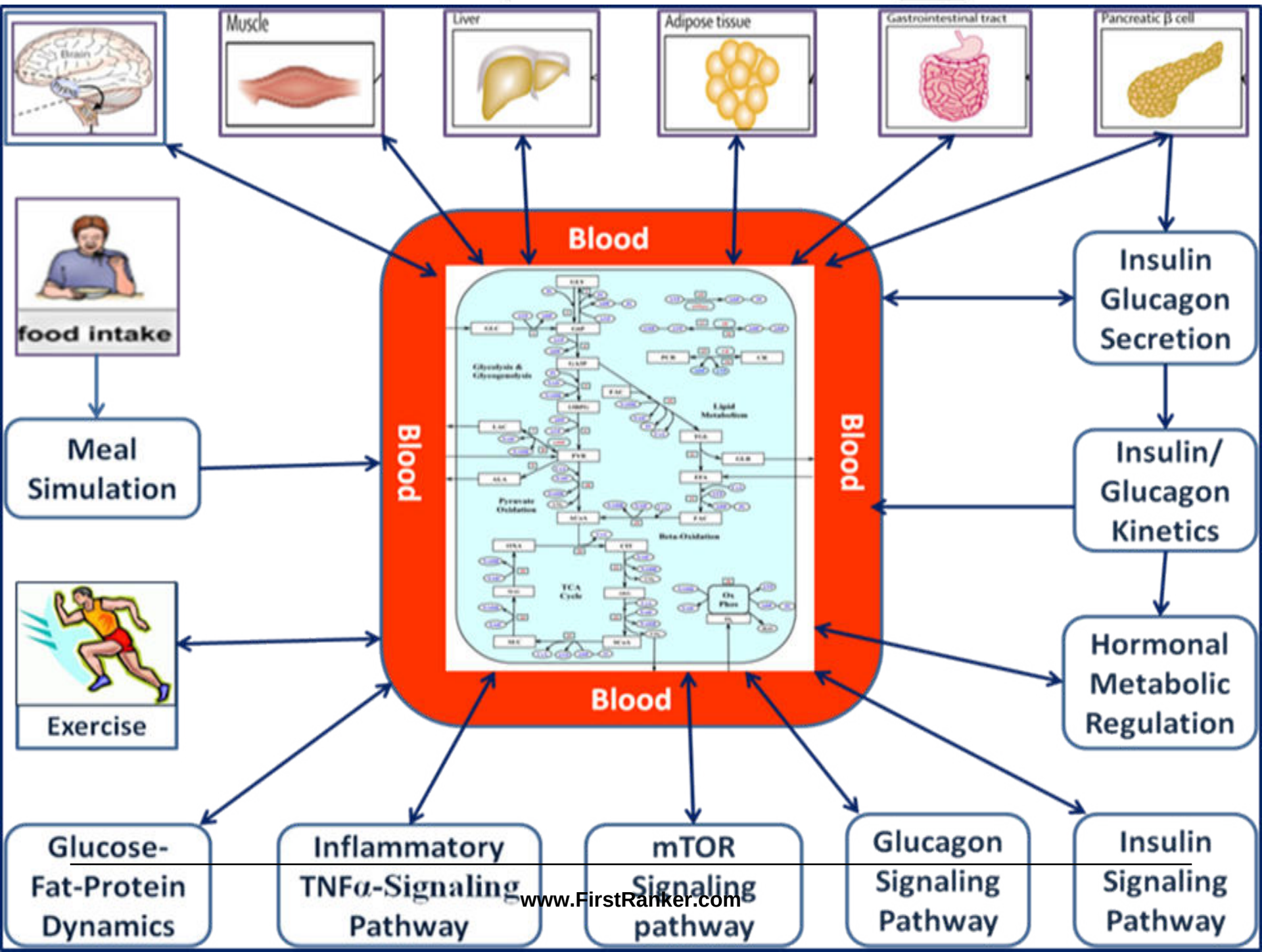
Nitrogen metabolism

N-Acetyl-L-alanine

4-Aminobutanoate ⇄ succinate → TCA Cycle

L-DOPA

dopamine



Why Metabolic Pathways are Integrated?

OR

What Is the Significance Of Integrated Metabolism To Human Body?

Integrated Metabolism Occurs To

1. To **Interconvert biochemical metabolites as per the cellular need**
2. To **meet the bodies fuel demand**
3. To **regulate levels of intermediary metabolites** and **maintain their equilibrium**
4. To **coordinate with various cells, tissues and organs for existence**
5. To **impart normal biochemical environment and maintain health**

- A well **coordinated** and **regulated integrated metabolism** of human body
- **Protects from metabolic catastrophes.**

Significance Of Knowledge Of Integrated Metabolism To Doctors

- **Prerequisite to Become A Good Doctor Is to:**
  - –Acquire **Profound Knowledge of Integrated Metabolism**
  - –With **Good Understanding Biochemical Concepts And its Interrelationships**

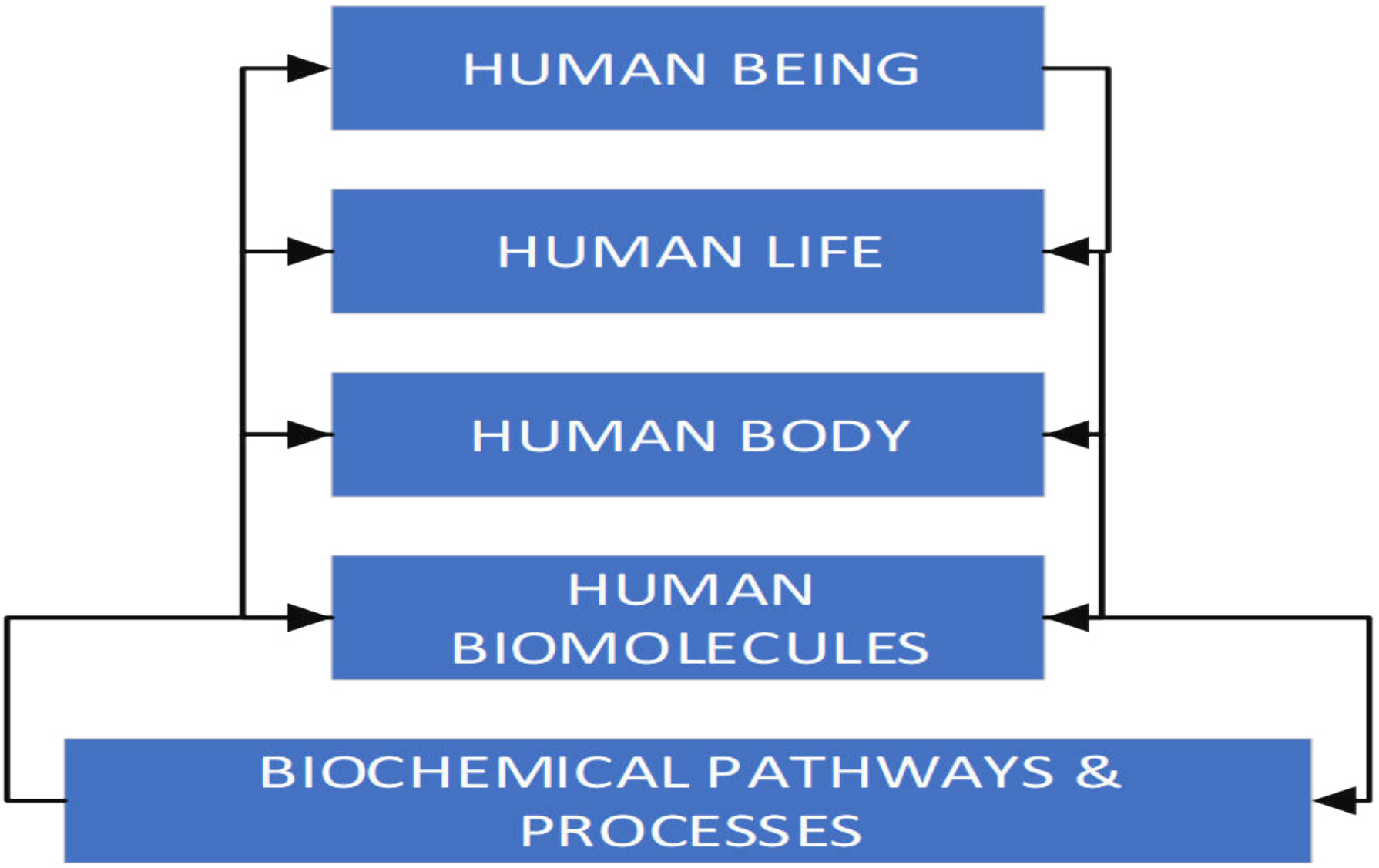
Doctors Responsibility
Health Professionalist

- **To Heal and Relieve Pain of Patients**
- **To Understand Sign Symptoms**
- **Correlate with Biochemical basis**
- **Depict Biochemical Alteration**
- **Confirm diagnosis**
- **Control, treat biochemical alterations of a disordered patients**

- **Study of integrated metabolism with their interrelationships in a normal healthy conditions helps a doctor :**
  - To **better understand** **various deranged metabolic conditions and related complexities**
  - **Rule out right biochemical underlying cause of metabolic disorders and pathogenesis**
  - **Try correct an altered metabolism in treatment**

Take Home Messages

Interrelationship Of Human Biochemical System



A good Doctor is one

Who has An

Understanding Knowledge of Intermediary Metabolism

Questions

- **Long Essays.**

- Q.1.Describe the **common metabolic pathway**.
  OR
- Why TCA cycle is called as common metabolic pathway? Explain with reactions.

- Q.2.Explain **"Fat burns under the flame of Carbohydrates"**.

- Which metabolic pathway is an excellent example of integrated metabolism? Justify it.

- Q.3.How Carbohydrate, Lipid & Protein metabolic pathways are integrated & interrelated with each other. Explain with the help of flow diagram.

- Q.4.Explain the **three stages** in the **intermediary metabolism** of Carbohydrate, Lipid & Protein.

- Influx & Efflux of TCA intermediates.

- Integration of TCA with Urea cycle.

- **Formation and Fates of**
  - Pyruvate
  - Acetyl-CoA
  - Succinyl-CoA
  - Oxaloacetate
  - α-Ketoglutarate

- **Q.5.Describe the role of following organs during wellfed condition.**
  - **–Liver**
  - **–Brain**
  - **–Muscles**
  - **–Adipose tissues**

THANK YOU

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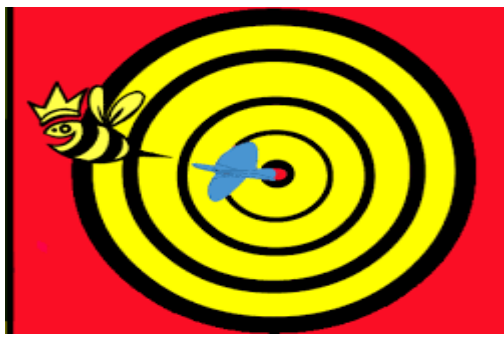
Important Tips For



Three Gifts For Human Beings
On Which Health And Success Depend Upon
How Best they are Utilized
For Significant/Good Long Term Outcome

- Body- Sense
- Time
- Energy

Factors For Quality Of Health

Normal State Of Biomolecules and Metabolism

- **Intentions and Actions**= Behavior (Sleep Cycle)
- **Nutrition** (Food Cycle)
- **Environment** (Companionship)

Health Factors	Ill Health Factors
Positive Behavior- Sensibly ,thoughtful ,rightful care of body by Controlled ,Regulated with obedient implementation's of Do's of Health and Avoid Don'ts of Health	**Negative Behavior-** Carefree ,Uncontrolled, dysregulated activities with disobedience rigid non implementations of Do's and high implementations of Don'ts
Balanced Diet- Simple and Natural Appropriate Quality and Quantity of all essential nutrients	Imbalanced Diet with more processed and refined with poor quality and improper quantity of nutrients
Proper Sleep- Time 7-8 Hrs (Early To Bed and Early To Rise)	Improper Sleep with low time in night and more time in day
Environment- Natural Unpolluted **Companionship with –** Good ,Positive, Helpers	**Environment** – Polluted with physical, chemical and biological pollutants **Companions with –** Bad,Negative,Distractors

Biomolecules And Their Processes Responsible For Health Similar Features Implemented In Practical Human Life will impart Success

1. Focused and Specific
2. Implement rules and regulations/orders of metabolism (Obedient)
3. Interdependence -Communicate and Cooperate
4. Disciplined and Dutiful-Responsible/Sensible
5. No two works at a time- For maintaining full Concentration
6. Complete one priority work and start Next priority -
7. Not much multitasking/Very few multitasking as per need
8. Do Not get overloaded at one time
9. Understand situation and work accordingly (Adapt as per condition)
10. Sparing actions, Distribute (Charity, Share and Care)
11. Work with good pace in regularity
12. Proof Read -No Chance of Mistakes/Less errors
13. Defined and Refined- Limitations
14. Homeostasize to be in limit and do not cross limits
15. Productive/Significant-Non Futile (Economical ,Reutilizes ,No wastage)

Tips To Ensure Good ,Healthy Life

- **Live Life**
  - **Thoughtfully,Righteously,Carefuly,Actively,Alertly**
- **Eat Balanced**
  - **Proportionate Quantity and Appropriate Quality**
- **Drink and Breathe**
  - **Unpolluted Water and Air**
- **Cultivate Cheerfulness**
  - **Love,Share,Care,**
  - **Thankfulness,Politeness,Selflessness**
- **Avoid Synthetic, Chemical Interactions**
  - **Chemical, Inhibitions leads to Disorders**

Live a Thoughtful, Rightful and Lawful Life

- Life is **Journey of Realization**
- Life is **path to bring changes by corrections and improvements**
- Use **Sense , Time and Energy** for **good significant long-term outcome**
- **Adopt Do's** of Health and Success
- **Quit/Sacrifice don'ts** with **steadfastness for prevention of Ill-health and Failures**

Let All of Us Realize and Clearly Differentiate

- Do’s and Don'ts of every human action
- Obedience and Disobedience
- Respect and Disrespect
- Truth and False
- Mistakes and Corrections
- Success and Failure
- Good and Bad
- Wrong and Right
- Healthy and Unhealthy
- Hygienic and Unhygienic
- Significant and Insignificant
- Helpful and Harmful
- Friend and Enemy
- Well wisher and Bad Wisher
- Patience and Impatience
- Gratitude and Thankless
- Blessings and Cursing's

Factors For Success

- **Blessings**

1. Selflessness/No Selfishness
2. Taking care equally for oneself and others
3. Obedience for truth and significant acts
4. Responsible and Dutiful
5. Being Truth and Transparent
6. Not making people wait /Lying

6. Not Cheating for our own benefits
7. Keeping and Fulfilling Promises
8. Sharing of all good you have
9. Caring for one who needs
10. Spreading/Not Hiding significant /true Knowledge
11. Not Distracting persons who are on righteous path
12. ~~Not Irritating one who is righteous~~

13. Lifting people who needs
14. Guiding for Right acts
15. Stopping from wrong acts
16. Not Hurting any soul with disrespect and disobedience
17. Obeying and implementing true words
18. Using best Sense, Energy and Time for best long term outcome

S.No	8 Rs To Implement
1	Realize
2	Recapitulate
3	Reasoning
4	Reassess
5	Respond
6	Rehearse
7	Regular and Routine
8	Rejuvenate

9 Ps Implement	9 Cs Implement
Prayers	Concentrate
Priorities	Communicate
Plan - Protocol	Cooperate
Practice	Commitment
Proof Read	Control
Perseverance	Coordinate
Positivity	Compensate
Patience	Companionship
Perfectionist	Cope up & Change

Best For Human Health

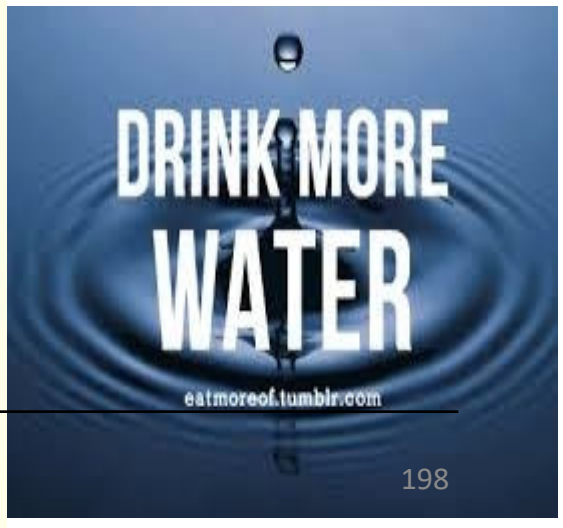
Thoughtfulness and Righteousness

Eating And Living Style

Natural-Planned ,Organized ,Regular , Disciplined

Simple , Humble, Care and Share

Yes for Good Stead Fast No For Bad



Implement
Thoughtfulness and Righteousness

- Everywhere and Anywhere
- Every work and Any work
- Every time and Anytime

Tips Of Good Success

- Good Hard work
- Good Intentions

Live An Evidenced Based Life

- **Acquire** Knowledge**-** Search/Ask **(Do's and Don'ts of priority actions)**
- **Assess**/Understand Truth
- **Accept**
- **Apply**/Implement -Truth/Dos
- **Appraise**/Evaluate its significance
- **Spread** Truth and Significance

THANKS