Abanico Veterinario. January-December 2021; 11:1-26. http://dx.doi.org/10.21929/abavet2021.47
Literature Review. Received: 03/08/2021. Accepted:15/12/2021. Published: 30/12/2021. Code: e2021-52.
https://www.youtube.com/watch?v=cFnXFVcpFMU

Biochemistry and metabolic pathways of polysaccharides, lipids, and proteins

Bioquímica y vías metabólicas de polisacáridos, lípidos y proteínas

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ABSTRACT

The eukaryotic cells are complex structures, capable of replication and performing a wide range of tasks in multicellular organisms. However, they also obey the laws of chemistry and physics that determine the metabolism of living systems. Consequently, cell biology seeks to understand metabolic processes in terms of reactions of anabolism and molecular catabolism. This review considers the chemical composition and properties of polysaccharides, lipids, and proteins as ultimately responsible for all cellular activities. The atoms and biochemical bonds of these macromolecules determine all cell dynamics, which is why the first part of each chapter reviews the nature of the functional group's hydroxyl, amino and carboxyl, responsible for the formation of monosaccharides, amino acids and fatty acids. The rest of each chapter analyzes the genesis and lysis of these molecules within each cell organelle, for the formation of acetyl-coenzyme A and the liberation of energy in the Krebs cycle. Thus, the biochemistry of cell metabolism can be understood in terms of the structures and functions of three main organic molecules polysaccharides, lipids and proteins.
Keywords: glycogenogenesis, glycolysis, lipogenesis, lipolysis, proteogenesis, proteolysis.

RESUMEN

Las células eucariotas son estructuras complejas, capaces de replicarse y realizar una amplia gama de tareas en organismos multicelulares. Sin embargo, también obedecen las leyes de la química y la física que determinan el metabolismo de los sistemas vivos. En consecuencia, la biología celular busca comprender los procesos metabólicos en términos de reacciones de anabolismo y catabolismo molecular. Esta revisión considera la composición química y las propiedades de los polisacáridos, lípidos y proteínas como responsables en última instancia de todas las actividades celulares. Los átomos y enlaces bioquímicos de estas macromoléculas determinan toda la dinámica celular, por lo que en la primera parte de cada capítulo se repasa la naturaleza de los grupos funcionales hidroxilo, amino y carboxilo, responsables de la formación de monosacáridos, aminoácidos y ácidos grasos. El resto de cada capítulo analiza la génesis y lisis de estas moléculas dentro de cada organelo celular, para la formación de acetil-Coenzima A y la liberación de su energía en el ciclo de Krebs. Así, la bioquímica del metabolismo celular, puede entenderse en términos de las estructuras y funciones de tres principales moléculas orgánicas.
Palabras clave: glucogenogénesis, glucólisis, lipogénesis, lipólisis, proteogénesis, proteólisis.

ABBREVIATIONS

aa	amino acids
Ac	acetone
AcAc	acetoacetate
DNA	deoxyribonucleic acid
NEFA	non-esterified fatty acids
Arg	arginine
mRNA	messenger ribonucleic acid
tRNA	transfer ribonucleic RNA
C	carbon
C=O	carbonyl group
C16:0	palmitic
$C_3H_3O_3$	pyruvate
Ca^{2+}	calcium ion
CO_2	carbon dioxide
$COCH_3$	acetyl group
COOH	carboxyl group
Gln	glutamine
GLU	glucose
H	hydrogen
H_2O	water
HCO_3^-	- hydrogencarbonate anion
N	nitrogen
$NADPH+H^+$	nicotinamide adenine dinucleotide phosphate
NH_2	amino group
NH_4^+	ammonium ion
O	oxygen
OH	hydroxyl Group
PO_4^{2-}	phosphate group
TAG	triacylglycerols
β-HBA	β-hydroxybutyrate

INTRODUCTION

Eukaryotic cells are composed of water, inorganic ions and thousands of organic molecules (Cooper, 2019b). They participate in systems to extract, transform and utilize energy from the environment (Tortora *et al.*, 2019b) which enables organisms to perform mechanical, chemical, osmotic and electrical work (Ameer *et al.*, 2018; Rodwell, 2018a; Melo & Cuamatzi, 2019). Most of these organic molecules belong to one of three classes of polymers: i) polysaccharides, ii) lipids and iii) proteins (Fails & Magee, 2018a). These polymers constitute 80-90% of the weight of most cells (Pavlinov *et al.*, 2019) and they are formed by the bonding (polymerization) of several low molecular weight chemical components: carbohydrates, fatty acids and amino acids, respectively (Guoyao, 2017c). The interaction between these components is dynamic; changes in one component lead to coordination or compensation changes in another (Tortora *et al.*, 2019b). It is biochemistry that describes in molecular terms, this set of interactions (Pol *et al.*, 2014). Considering two metabolic pathways primarily: i) catabolism to obtain acetyl-Coenzyme A (Tortora & Derrickson, 2018b) and ii) anabolism to acquire larger molecules (Pol *et al.*, 2014; Engelking, 2015; Menzies *et al.*, 2016). Thus contributing knowledge and practical applications in medicine (Gundu, 2020), agriculture (Milani *et al*., 2017), nutrition (Preethi & Sekar 2021) and industry (Wu *et al*., 2019) but their main concern is the cell as a living organism (Cooper, 2019a).

Therefore, this review provides an overview of the molecular dynamics at the interface of polysaccharide, lipid, and protein metabolism to ground the foundations of cell biology.

PHYSICOCHEMICAL PROPERTIES OF POLYSACCHARIDES

Polysaccharides are organic molecules consisting of more than ten monosaccharides, linked by O-glycosidic bonds (Yang *et al.*, 2015; Guoyao, 2017c). Their general formula contains carbon **(C**) atoms hydrated with water (**H_2O**) molecules (Bender & Mayes, 2018c). Therefore, they exhibit solubility in this fluid and their classification is established based on the position of their carbonyl group (**C=O**) (Chavarría & Cárabez, 2018). Formed by a **C** atom bonded to an oxygen atom (**O**) through a double bond (Cooper, 2019b). If the C=O group is located at the end of the molecule, it is an aldose. If the C=O group is

located in the middle of the molecule, it is a ketose (Mckee & Mckee, 2014a; Delbianco *et al.*, 2016).

Polysaccharides are the main biological source of energy storage and consumption (Chavarría & Cárabez, 2018) and are part of the organic structure of all living beings (Cooper, 2019b). Their entry into the organism is from food and their hydrolysis (breaking of O-glycosidic bonds) by amylases produced in the parotid glands ((Kumar & Chakravarty, 2018), and glycogen phosphorylases and glucose-6-phosphatases, produced by the acinar cells of the pancreas (Boticario & Cascales, 2012; Cárabez *et al.*, 2018a)). Subsequent to this hydrolysis, the glucose monomer (**GLU**), with the chemical formula $C_6H_{12}O_6$ (Bender & Mayes, 2018b), is released to be absorbed through the intestinal epithelium (Fails & Magee, 2018a) and distributed through the bloodstream to the different tissues (Dashty, 2013; Oosterveer & Schoonjans, 2014), where it presents five main metabolic pathways: (i) glycogenogenesis, (ii) pentose phosphate pathway (iii) glycogenolysis, (iv) glycolysis and (v) glycogenolysis (Appleton *et al.*, 2013a; Nelson & Cox, 2017b).

GLYCOGEN ANABOLISM (GLYCOGENOGENESIS)

Glycogenogenesis takes place in myocytes (Engelking, 2015) and hepatocytes (Tortora & Derrickson, 2018b), where GLU enters the cytoplasm, to be phosphorylated [addition of a phosphate group (**PO_4^{2-}**)], from adenosine triphosphate (**ATP**) (Rui, 2014) (Figure 1).

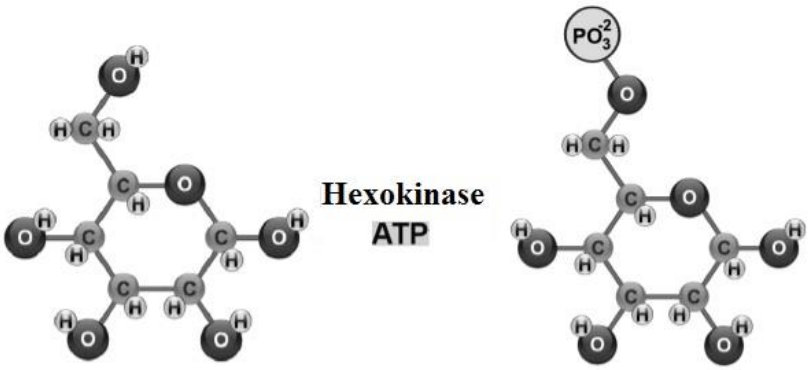

Figure 1. Glucose-6-phosphate synthesis

The resulting glucose-6-phosphate is abundant in the cytoplasm of all cells (Litwack, 2018a) and when its levels are elevated, phosphoglucomutase transfers the PO_4^{2-} group from C6 to C1 synthesizing glucose-1-phosphate (Delbianco *et al.*, 2016). Uridine triphosphate, interacts with glucose-1-phosphate, forming uridine diphosphate glucose (Fox *et al.*, 2017). Insulin activates glycogen synthase 1 expressed in myocytes and/or glycogen synthase 2 expressed in hepatocytes (Gadupudi *et al.*, 2016), so that the hydroxyl (**OH**) group of uridine diphosphate glucose binds to glycogen (creating an *O*-glycosidic bond), elongating the polysaccharide (Figure 2).

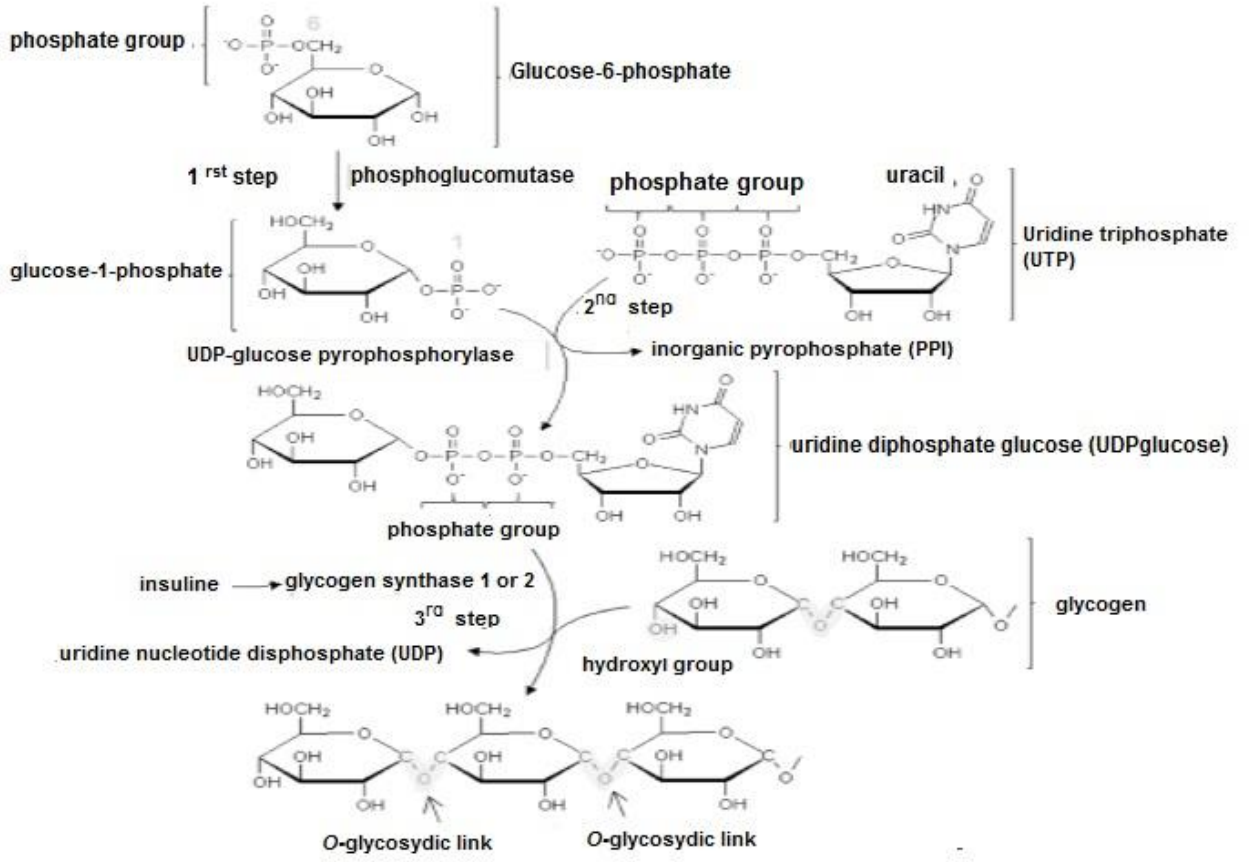

Figure 2. Glycogenogenesis. Detail of the *O*-glycosidic link

PENTOSE PHOSPHATE PATHWAY

This process takes place in the cytoplasm and is divided into two, the oxidative phase and the non-oxidative phase (Tortora & Derrickson, 2018b). The oxidative phase, presents of three reactions: i) glucose-6-phosphate is dehydrogenated [loses 2 hydrogens (**H**)] (Nelson & Cox, 2017b). As product 6-phosphogluconolactone and a nicotinamide adenine dinucleotide phosphate (**NADPH+H$^+$**) molecule are obtained, and ii) 6-phosphogluconolactone is hydrolyzed and as product 6-phosphoglucanate is obtained (Lee *et al.*, 2019) and iii) 6-phosphoglucanate is decarboxylated [removal of the carboxyl (**COOH**) group] (Mckee & Mckee, 2014b). As a product ribulose-5-phosphate (ketopentose), an NADPH+H+ molecule and carbon dioxide (**CO_2**) are obtained (Stincone *et al.*, 2015).

During the non-oxidative phase, ribulose-5-phosphate can undergo isomerization and be transformed into another molecule that has the same atoms, but arranged differently (Madigan et al., 2019a). In other words, it changes its C=O group position to become a ribose 5-phosphate (aldopentose) (Cárabez et al., 2018b). Therefore, the main functions

of the pentose phosphate pathway are (i) to synthesize 5-C monosaccharides and (ii) to generate NADPH+H+ (Nelson & Cox, 2017b).

Durante la fase no oxidativa la ribulosa-5-fosfato, puede presentar isomerización y ser transformada en otra molécula que posee los mismos átomos, pero dispuestos de forma distinta (Madigan *et al.*, 2019a). En otra palabras, cambia de posición su grupo C=O para convertirse en a ribosa 5-fosfato (aldopentosa) (Cárabez *et al.*, 2018b). Por lo tanto, las principales funciones de la ruta de las pentosas fosfato son: i) sintetizar monosacáridos de cinco C y ii) generar NADPH+H^+ (Nelson & Cox, 2017b).

GLYCOGEN CATABOLISM (GLYCOGENOLYSIS)

This process takes place in the cytoplasm of almost all cells, although particularly in muscle myocytes and liver hepatocytes (Mckee & Mckee, 2014c). When blood GLU levels are low, adrenaline or epinephrine in muscle and glucagon in liver activate protein kinases (Ahern, 2019d), and these perform phosphorylation to glycogen phosphorylase, thereby activating this enzyme (Mckee & Mckee, 2014c). Glycogen phosphorylase catalyzes the transfer of an inorganic orthophosphate at C1 of glycogen ((Fox *et al.*, 2017), and this change breaks the O-glycosidic bond and releases glucose-1-phosphate (Figure 3). Glucose-1-phosphate is transformed into glucose-6-phosphate by transferring the PO_4^{2-} group from C1 to C6 (Ahern, 2019d).

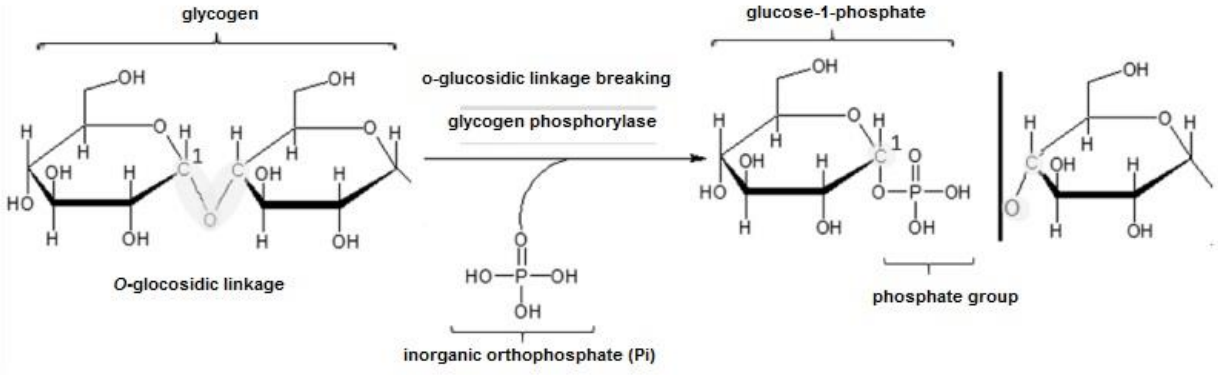

Figure 3. Glycogenolysis and glucose-1-phosphate synthesis

GLUCOSE CATABOLISM (GLYCOLYSIS)

This process consists of the degradation of glucose-6-phosphate to obtain acetyl-coenzyme A from pyruvate (**$C_3H_3O_3$**) (Ferrier, 2017b). It takes place in the cytoplasm where glucose-6-phosphate (aldohexose), shows isomerization (Mckee & Mckee, 2014c) and it is transformed into fructose-6-phosphate (ketohexose) by shifting its C=O group (Figure 4).

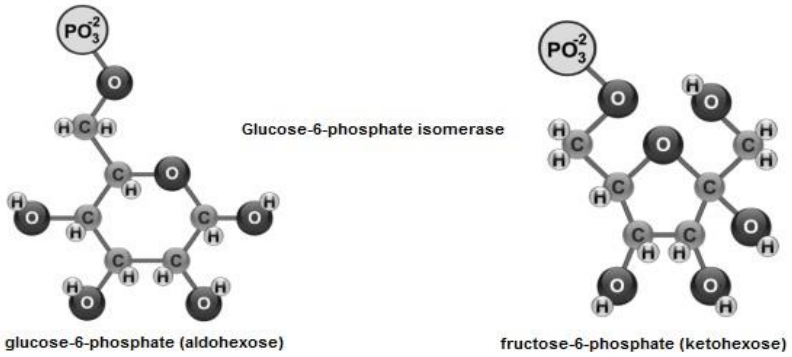

Figure 4. Isomerization of glucose-6-phosphate to fructose-6-phosphate

Fructose-6-phosphate, is phosphorylated (Figure 5), from ATP at C1 and C6 (Tortora *et al.*, 2019a), to give rise to fructose-1,6-bisphosphate (Delbianco *et al.*, 2016; Ferrier, 2017a).

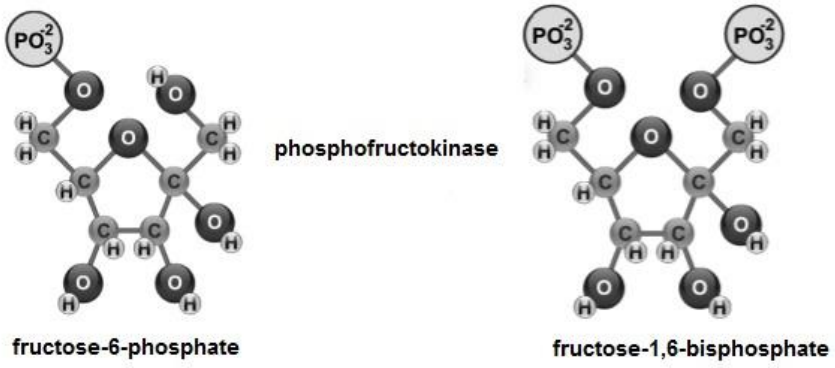

Figure 5. Synthesis of fructose-1,6-bisphosphate

Subsequently, fructose-1,6-bisphosphate (Figure 6) is cleaved into two: i) glyceraldehyde-3-phosphate and ii) dihydroxyacetone phosphate (Melo & Cuamatzi, 2019).

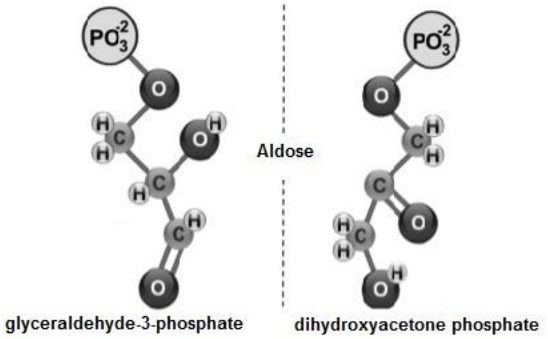

Figure 6. Fructose-1,6-bisphosphate division

El gliceraldehido-3-fosfato es oxidado y fosforilado, en los C1 y C3 formando 1,3-bifosfoglicerato () (Figura 7). Posteriormente, transfiere su grupo PO_4^{2-}, para sintetizar ATP) y se transforma en 3-fosfoglicerato.
Glyceraldehyde-3-phosphate is oxidized and phosphorylated, at C1 and C3 forming 1,3-bisphosphoglycerate (Mckee & Mckee, 2014c) (Figure 7). Subsequently, it transfers its PO42- group, to synthesize ATP (Ahern, 2019b) and is transformed into 3-phosphoglycerate (Voet *et al.*, 2016; Tortora & Derrickson, 2018b).

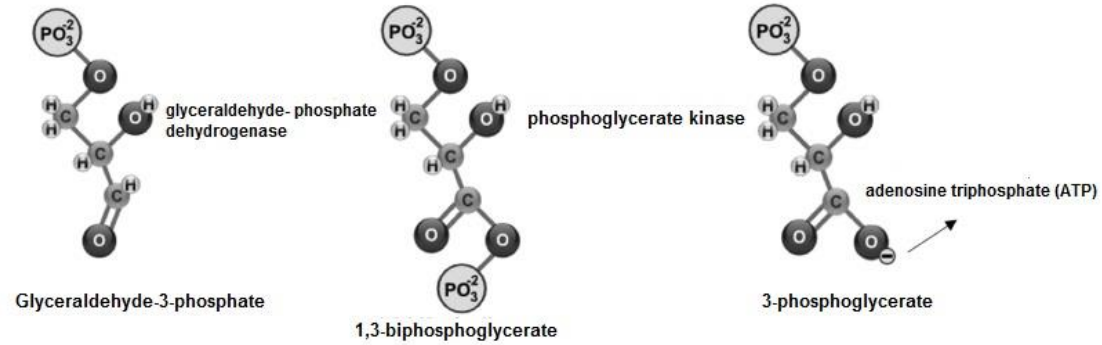

Figure 7. From glyceraldehyde-3-phosphate to 3-phosphoglycerate

The 3-phosphoglycerate shows isomerization and its PO_4^{2-} group changes from C3 to C2, transforming the molecule into 2-phosphoglycerate (Nelson & Cox, 2017b). Next, enolase promotes the formation of a double bond (Voet *et al.*, 2016), eliminating a molecule of H_2O and forming phosphoenolpyruvate (Guoyao, 2017f; Bender & Mayes, 2018a) (Figure 8).

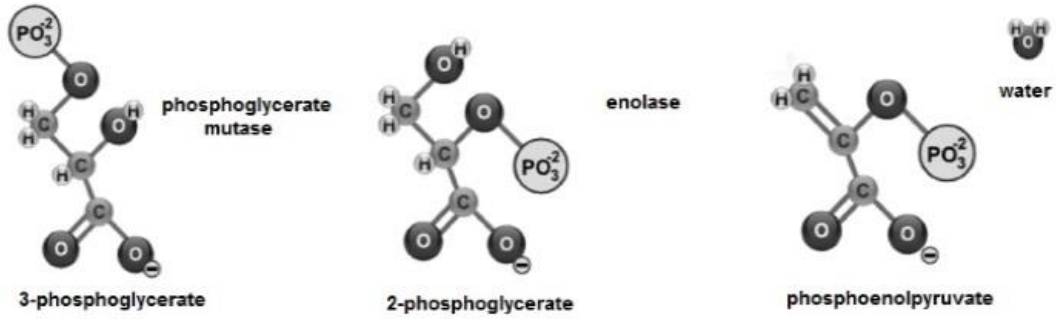

Figure 8. From 3-phosphoglycerate to phosphoenolpyruvate

Phosphoenolpyruvate transfers its PO_4^{2-} group (Cárabez *et al.*, 2018a), to synthesize ATP (Ahern, 2019b) and is transformed into $C_3H_3O_3$ (Botham & Mayes, 2018d), a molecule that is drawn into the mitochondrial matrix, using the proton-motive force generated by the respiratory chain (Fails & Magee, 2018b; Madigan *et al.*, 2019c) (Figure 9).

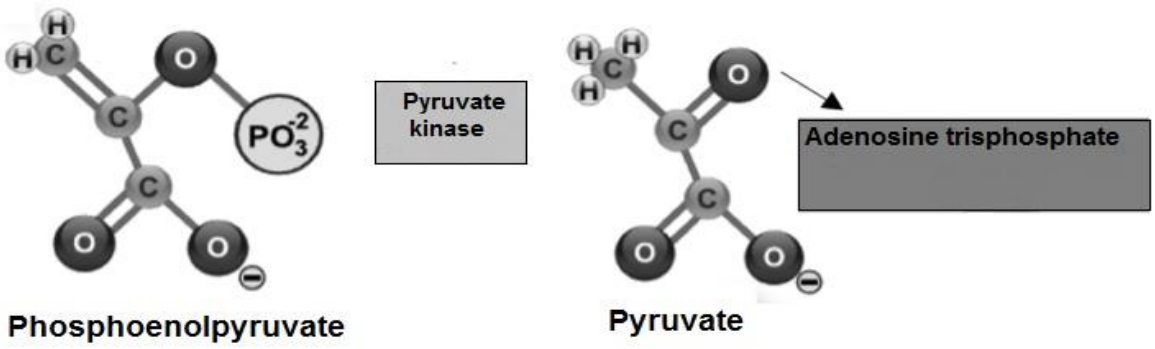

Figure 9. Phosphoenolpyruvate to pyruvate

The fate of $C_3H_3O_3$ produced in glycolysis depends on the availability of O. Under anaerobic conditions $C_3H_3O_3$ undergoes reduction by adding H atoms to form lactate (Tortora & Derrickson, 2018b). Under aerobic conditions $C_3H_3O_3$ presents decarboxylation and its COOH group is released as CO2 (Stincone *et al.*, 2015), the rest of the molecule presents oxidation, to form the acetyl group (**$COCH_3$**). Finally, Coenzyme A is transferred to the $COCH_3$ group forming acetyl-Coenzyme A (Guoyao, 2017f) (Figure 10).

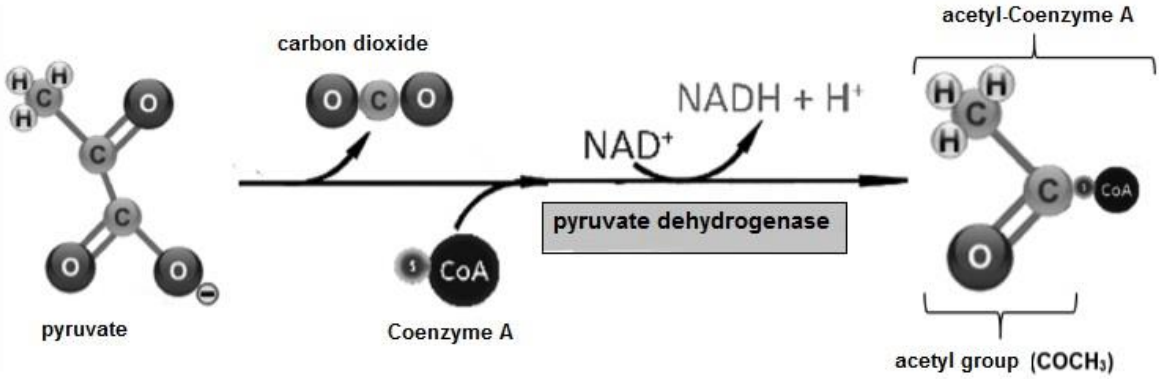

Figure 10. Oxidative decarboxylation of pyruvate

PHYSICOCHEMICAL PROPERTIES OF LIPIDS

Lipids constitute an energy storage depot in adipocytes (Guoyao, 2017a). They participate in the formation of phospholipid membranes of eukaryotic cells and their organelles (Schoeler & Caesar, 2019). In the bloodstream, they transport fat-soluble vitamins e.g. A for soft tissue and mucosal formation (Botham & Mayes, 2018c), D for calcium ion (**Ca^{2+}**) absorption (Jameson, 2017), E as an antioxidant and erythrocyte formation (Madigan *et al.*, 2019c) and K that contributes in coagulation (Guoyao, 2017a). They also act as a thermal insulator in subcutaneous tissues to retain body heat (Mas, 2018b).

Their entry into the body is from food and their hydrolysis (breaking of ester bonds) by lipases and esterases produced by the acinar cells of the pancreas (Ahern, 2019c).

Following this hydrolysis, non-esterified fatty acids (**NEFA**) and triacylglycerols (**TAG**) are released (Tortora *et al.*, 2019a), to be absorbed via the intestinal epithelium (Pol *et al.*, 2014; Guoyao, 2017d), and transported to the hepatocytes of the liver (Botham & Mayes, 2018c). Where they are packaged into very low density lipoproteins (Wadhera *et al.*, 2016), for subsequent export to peripheral tissues (Wang *et al.*, 2016). The NEFA obtained during this process are necessary to synthesize acetyl-Coenzyme A (Appleton *et al.*, 2013d).

TRIACYLGLYCEROL ANABOLISM (LIPOGENESIS)

Lipogenesis initiates in the mitochondria, with the production of acetyl-Coenzyme A (Cooper, 2019a). Because the mitochondrial membrane is impermeable to the passage of acetyl-Coenzyme A (Friedman & Nunnari, 2014), the tricarboxylate system (Figure 11) and citrate synthase are required to convert it to citrate (Nunes-Nesi *et al.*, 2013), via C-binding (Ameer *et al.*, 2018), thereby ensuring its entry into the cell cytoplasm (Botham & Mayes, 2018c). Citrate is then transformed back into acetyl-coenzyme A by ATP-citrate lyase (Nunes-Nesi *et al.*, 2013; Botham & Mayes, 2018c), yielding oxaloacetate and adenosine diphosphate (Mas, 2018a; Tortora & Derrickson, 2018a).

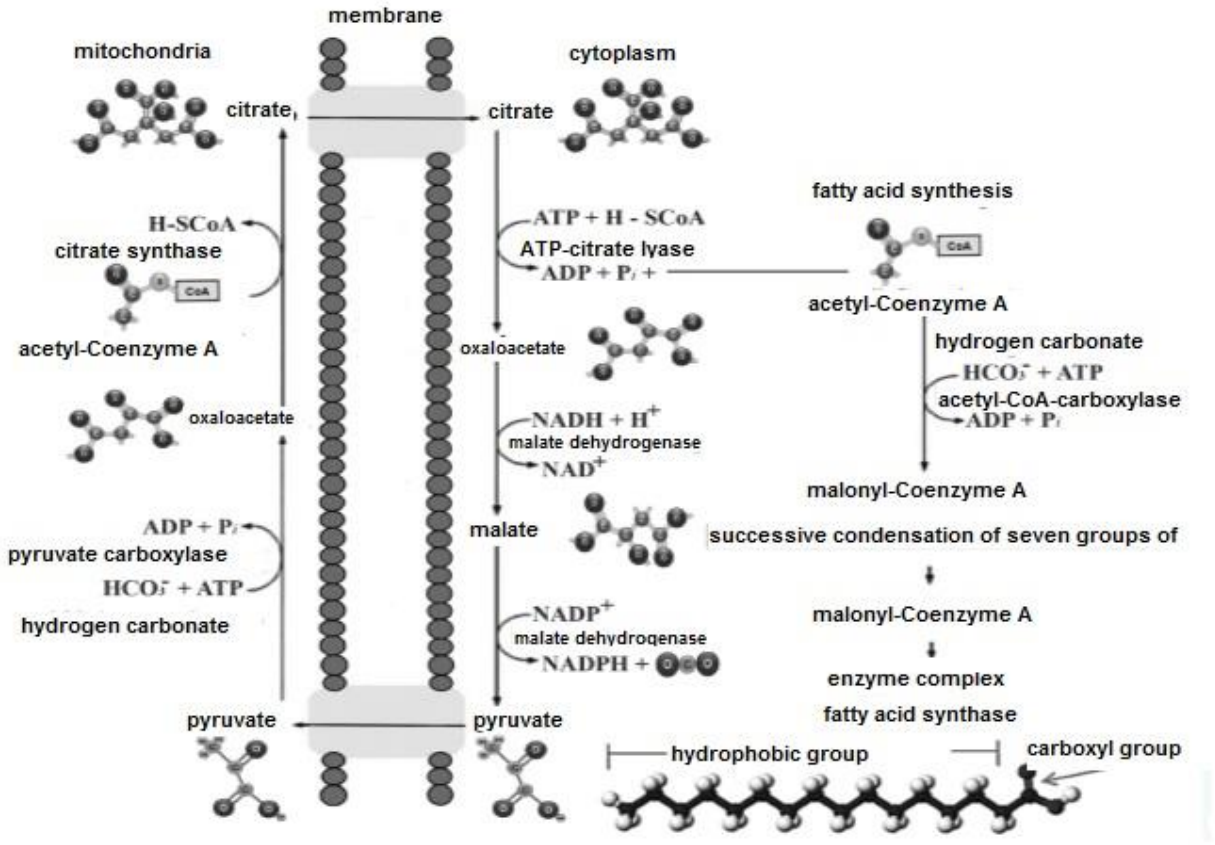

Figure 11. Tricarboxylate system and lipid anabolism

Source: (García *et al.*, 2020).

Lipogenesis is an endergonic process, therefore, acetyl-Coenzyme A must be activated by carboxylation through its binding to the hydrogencarbonate anion (HCO_3^-) in an ATP-consuming reaction (Botham & Mayes, 2018a), catalyzed by acetyl-CoA carboxylase (Cooper, 2019b). As a result, acetyl-Coenzyme A is converted to malonyl-Coenzyme A (Nelson & Cox, 2017c). In turn, oxaloacetate is reduced by malate dehydrogenase to malate, and this in turn converted to $C_3H_3O_3$ by malic enzyme, producing $NADPH+H^+$ (Appleton *et al.*, 2013e; Dashty, 2013). Subsequently, the fatty acid requires elongation, via the protein complex fatty acid synthase (Pol *et al.*, 2014). This complex performs condensation, reduction, dehydration and again reduction, coupling malonyl-Coenzyme A groups with acetyl-Coenzyme A (Nelson & Cox, 2017c). The two reductions mentioned, require $NADPH+H^+$ (Dashty, 2013), and during elongation two C groups are added to the fatty acid, always synthesizing hexadecanoic or palmitic (**C16:0**), as the final product (Guoyao, 2017d). Subsequently, C16:0 is released from the protein complex and can be elongated by introducing C into its chain, to produce other larger fatty acid molecules (Botham & Mayes, 2018c), and/or unsaturated by introducing double bonds into its chain (Cooper, 2019a). TAG synthesis, takes place in the smooth endoplasmic reticulum (Quintero, 2014).

Once different NEFAs are obtained, the lipid ester bond, is established by joining the three OH groups of glycerol (Nelson & Cox, 2017c) (Figure 12), and the COOH group (the polar part) of three fatty acids (Botham & Mayes, 2018c). This bond is a condensation or dehydration where 3 molecules of H_2O are lost (Smith, 2020b). Due to this bonding, the polar groups attached to the carbohydrate are not accessible (Pratt *et al.*, 2016). Consequently, non-polar or hydrophobic molecules, highly insoluble in water, are formed (Dowhan & Bogdanov, 2016).

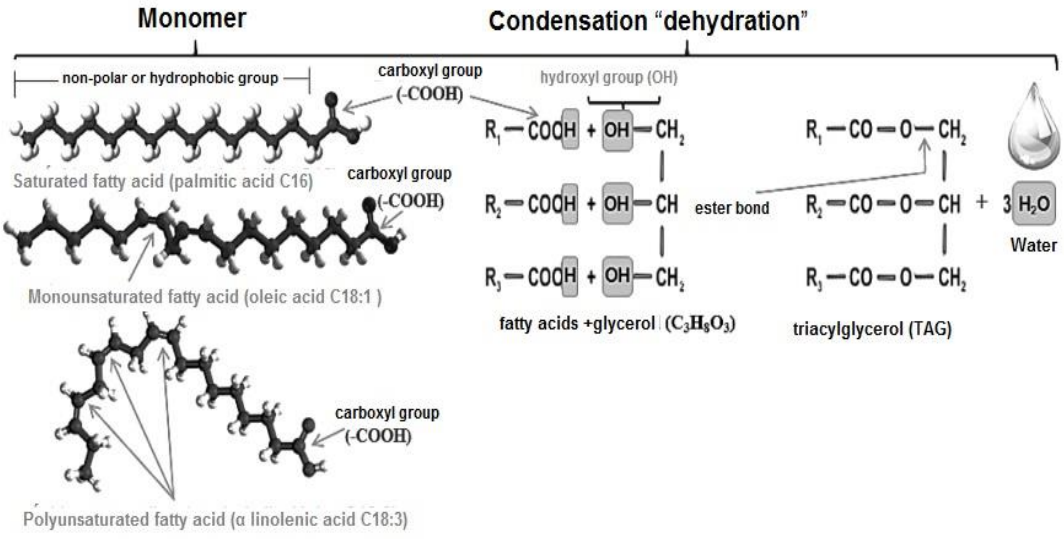

Figure 12. Formation of triacylglycerol with ester linkage

TRIACYLGLYCEROL CATABOLISM (LIPOLYSIS) AND KETOGENESIS

When glycogen stores in the cytoplasm of myocytes and hepatocytes decrease, carnitine palmitoyltransferase is activated (Longo *et al*., 2016), stimulating transport of NEFA into

the liver mitochondria (Merritt *et al*., 2020; Wang *et al*., 2020). Wang et al., 2020). Where β-oxidation, leads to a decarboxylation of the NEFA (Wanders *et al*., 2020), the COOH group is released as CO_2 and the rest of the molecule exhibits dehydrogenation, establishing the $COCH_3$ group (Botham & Mayes, 2018b). Coenzyme A, is transferred to the $COCH_3$ group and forms acetyl-Coenzyme A (Guoyao, 2017f). This molecule combines with oxaloacetate for entry into the Krebs cycle (Appleton *et al*., 2013c). If its oxidation is complete, CO_2 and pairs of H atoms will be released (Friedman & Nunnari, 2014), which will donate their electrons to perform oxidation-reduction reactions (Madigan *et al*., 2019c), H_2O formation and energy storage in the form of ATP (Jump, 2011).

However, if oxaloacetate is not sufficient, acetyl-Coenzyme A accumulates within the mitochondrion (Longo *et al*., 2016). Subsequently two molecules of acetyl-Coenzyme A react to form acetoacetyl-CoA, in a reaction catalyzed by thiolase (Merritt *et al*., 2018). Acetoacetyl-CoA condenses with another acetyl-Coenzyme A molecule to form β-hydroxy-β-methylglutaryl-CoA (Mas, 2018a). From this molecule acetoacetate (**AcAc**) is metabolized, a ketone body that leaves the mitochondria and in the cytoplasm of the hepatocyte can be reduced to β-hydroxybutyrate (**β-HBA**) (Selvaraj *et al*., 2020) or slowly and spontaneously decarboxylated to acetone (**Ac**) (Deemer *et al*., 2020).

PHYSICOCHEMICAL PROPERTIES OF PROTEINS

Of the three biomolecules discussed, proteins are the only ones that contain nitrogen (**N**) atoms (Ferrier, 2017c). They are constituted by the combination of 20 amino acids (**aa**) (Ahern, 2019a), linked by a peptide bond (Guoyao, 2017b). This covalent type bond, unites the amino group (**NH_2**) of one aa and the COOH group of another, with the formation of a H_2O molecule (Madigan *et al*., 2019b). Proteins actively participate in cellular homeostasis ((Cooper, 2019b), e.g., transporting O (Guoyao, 2017b), structuring immunoglobulins (Kenneth & Casey, 2017) and constituting enzymes (Ahern, 2019c).

They enter the body from food and are hydrolyzed (peptide bond breaking) by peptidases or proteases and aminotransferases, produced by the acinar cells of the pancreas (Ahern, 2019c). Following this hydrolysis, aa are released (Rodwell, 2018a), to be absorbed through the intestinal epithelium (Guoyao, 2017e; Piña & Flores, 2018), and transported to the hepatocytes of the liver (Appleton *et al*., 2013b)Appleton et al., 2013b), for subsequent export to peripheral tissues
(Fernández & Peimbert, 2018).

Within the cell cytoplasm, aa can lose their NH_2 group and as carbon skeletons function as: i) substrate to synthesize $C_3H_3O_3$ and subsequently acetyl-Coenzyme A (Appleton *et al*., 2013d), ii) structure purines and neurotransmitters (Rodwell, 2018b) and iii) participate in proteogenesis (Rodwell, 2018a; Madigan *et al*., 2019b) or ureogenesis (Nelson & Cox, 2017a) mainly.

PROTEIN ANABOLISM (PROTEOGENESIS)

Proteogenesis (Figure 13), begins in the cell nucleus (Noller, 2017), with the transcription of transfer ribonucleic acid (**tRNA**) (Nelson & Cox, 2017d; Madigan *et al.*, 2019d). Subsequently, the enzyme RNA polymerase performs the transcription of messenger ribonucleic (**mRNA**) from a deoxyribonucleic (**DNA**) sequence (Liu *et al.*, 2013), which serves as a template or mold for the genetic information (Litwack, 2018b). The mRNA is transported to the rough endoplasmic reticulum and its ribosomes (Weil, 2018b). During initiation, a bridge is formed between the minor and major ribosomal subunit (Weil, 2018a).

For their part, tRNA (Figure 14), have to bind with different aminoacyl-tRNA synthetases (Rodnina & Wintermeyer, 2016), to expose the NH_2 group of their nitrogenous bases (cytosine, guanine, adenine and uracil) and attach the COOH group of the different aa (Smith, 2020a).

The aa transported on the tRNA enter the ribosomal complex, which has two binding sites: i) the P or peptidyl site and ii) the A or aminoacyl site (Berk *et al.*, 2006). Translation is carried out in ribosomes, by reading triplets (three by three nucleotides) called: codon for mRNA and anticodon for tRNA (Ingolia, 2014). The first stage of translation, begins when the 5' end of the mRNA is inserted into the minor ribosomal subunit (Nelson & Cox, 2017d), exposing the initiator codon adenine-uracil-guanine or AUG for binding to the first anticodon uracil-adenine-cytosine or UAC, at the peptidyl site (Angov, 2011), originating methionine as the first aa (Madigan *et al.*, 2019d).

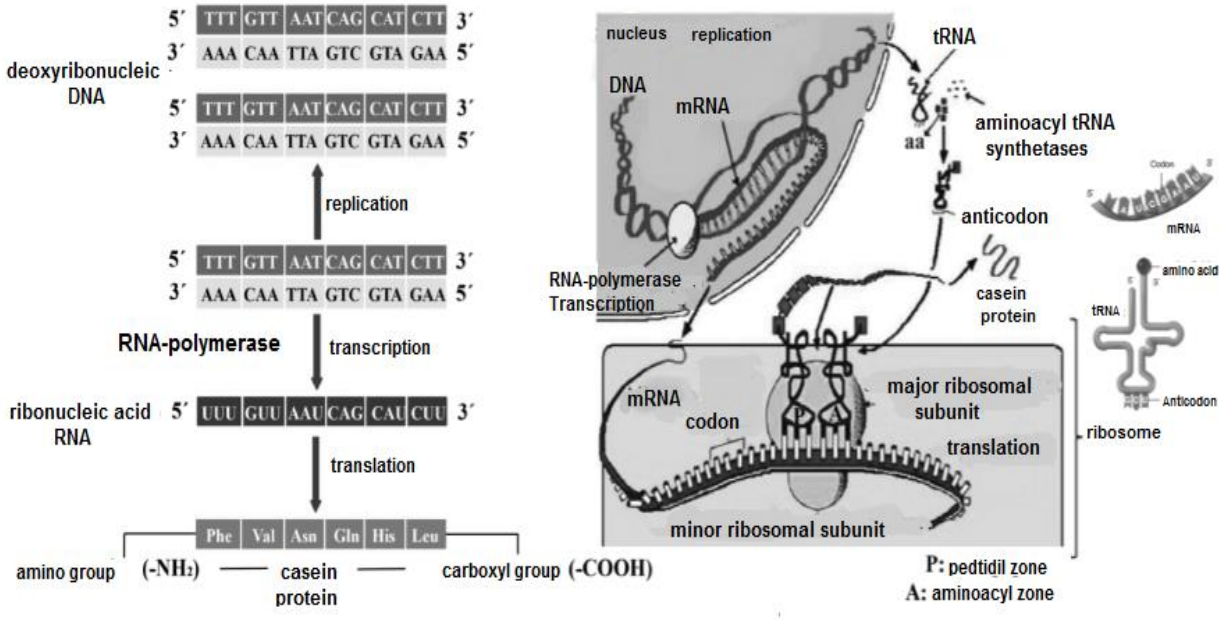

Figure 13. Proteogenesis, transcription and protein translation

Source: (García *et al.*, 2020)

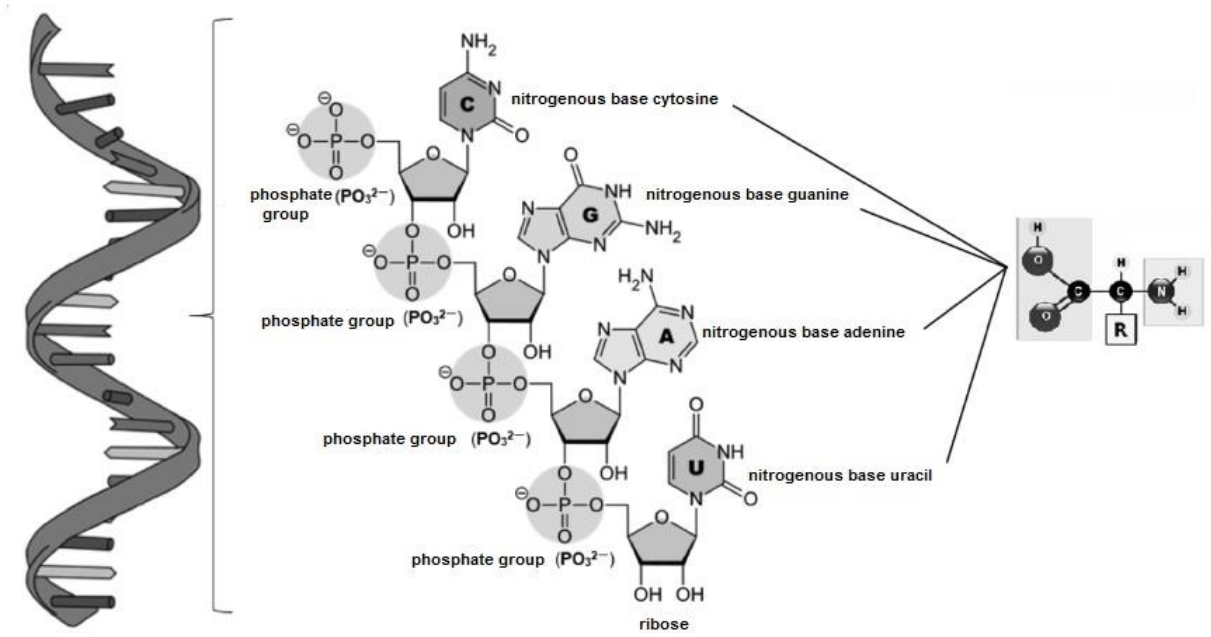

Figure 14. Transfer ribonucleic acid and its relationship to amino acids in the cytoplasm

Subsequently, when the peptidyl site and the aminoacyl site are occupied simultaneously, the peptidyl transferase enzyme establishes a peptide bond between the aa by inserting the former into the latter (Weil, 2018a). Then, in elongation codon and anticodon are precisely associated according to the complementarity of their bases (Dutta & Nandi, 2012), and this sequence of steps is repeated according to the number of aa contained in the polypeptide (Madigan *et al.*, 2019b). As a completion of this process, different proteins and enzymes mainly hydrolases are translated (Swiderek *et al.*, 2015).

PROTEIN CATABOLISM (PROTEOLYSIS) AND UREOGENESIS

After the gastric and enzymatic digestion of proteins, the breaking of their peptide bonds, and the release and absorption of aa (Piña & Flores, 2018), ammonium ion ($\mathbf{NH_4^+}$) is also obtained (Rodwell, 2018a). This molecule travels to the liver, where its first contact is with periportal hepatocytes (Guoyao, 2017e), which possess in their structure ureagenic enzymes in charge of urea synthesis (Figure 15). In the mitochondria of periportal hepatocytes, HCO_3^-, NH_4^+ and ATP (Appleton *et al.*, 2013b) are condensed to form carbamyl phosphate (Friedman & Nunnari, 2014). Ornithine enters the mitochondrion and carbamyl phosphate gives up its carbamyl group to form citrulline (Weiner *et al.*, 2015).

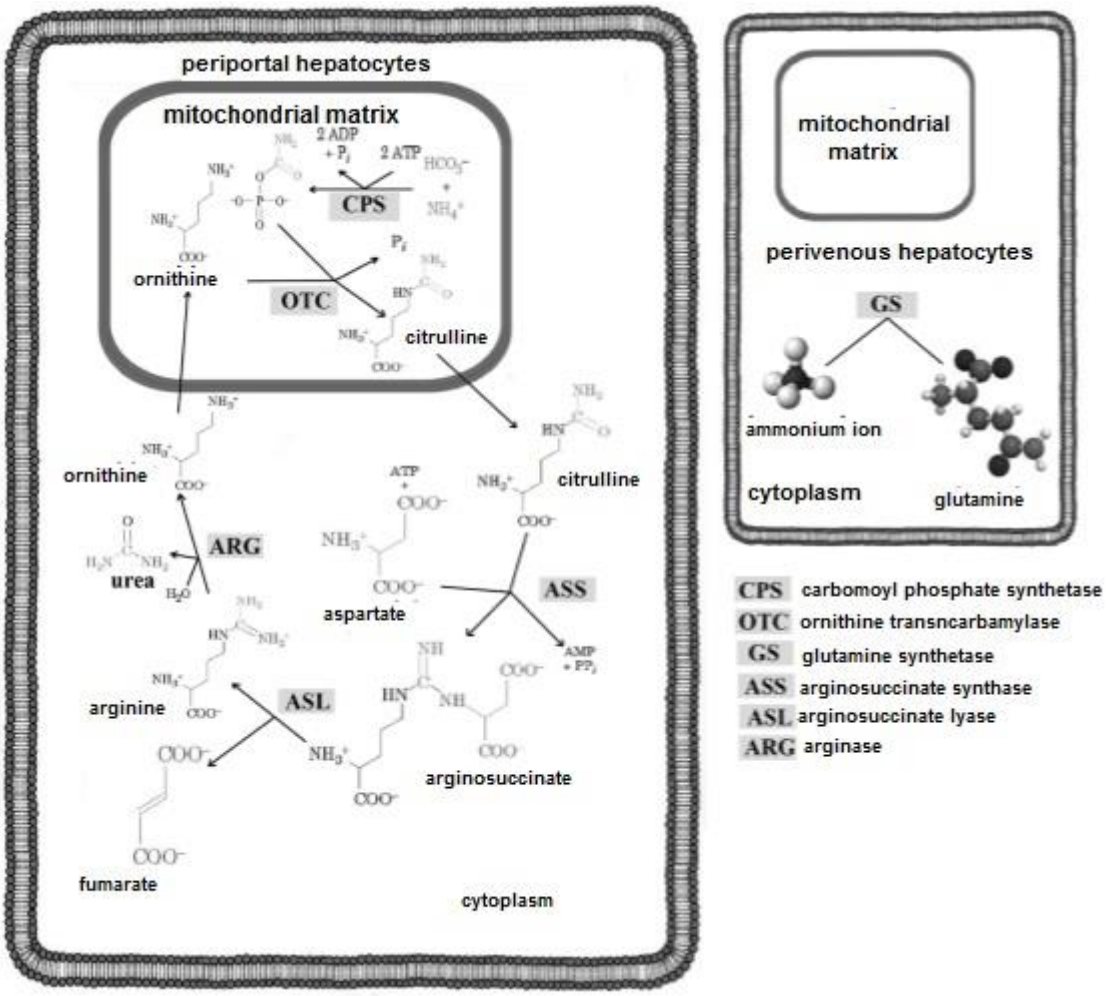

Figure 15. Ureogenesis

Source: (García *et al.*, 2020)

Citrulline exits the mitochondria into the cytoplasm, where it binds to aspartate, forming arginosuccinate (Menzies *et al.*, 2016). Arginosuccinate is cleaved into two: i) arginine (**Arg**) and ii) fumarate. Arg is hydrolyzed by arginase releasing urea and ornithine (Nelson & Cox, 2017a). The latter enters the mitochondria to initiate another turn in the cycle (Rodwell, 2018a). Urea in turn, can travel to the kidney (Guoyao, 2017b) and be excreted in urine (Marini & van Amburgh, 2003). The NH4+ ion that is not metabolized into urea, has contact with perivascular hepatocytes, which possess in their structure glutamine synthetase (Piña & Flores, 2018), which converts NH_4^+ ion into glutamine (**Gln**). This polar or hydrophilic aa, presents affinity for H_2O (Appleton *et al.*, 2013b). Therefore, it favors the transport and excretion of NH_4^+ ion in urine (Rodwell, 2018a).

ADENOSINE TRIPHOSPHATE ANABOLISM (KREBS CYCLE)

The Krebs cycle was discovered by Hans Adolf Krebs (Appleton *et al.*, 2013c). It is part of mitochondrial gas exchange (Madigan *et al.*, 2019c) and allows the release of stored energy from acetyl-Coenzyme A in the form of the nucleotide ATP (Botham & Mayes, 2018d). Acetyl-

Coenzyme A binds its $COCH_3$ group to bind with oxaloacetate to form citrate via a condensation reaction (Menzies *et al.*, 2016; Verschueren *et al.*, 2019). During a complete turn of the cycle and through hydrolysis, oxidative decarboxylation and hydration (Figure 16), citrate is converted back to oxaloacetate (Appleton *et al.*, 2013d).

The C atoms released in the process form CO_2 (Madigan *et al.*, 2019c). The Krebs cycle consumes per turn one acetyl-Coenzyme A and three NAD^+ (Nelson & Cox, 2017e). It produces for each turn two CO_2 and three $NADPH+H^+$ (Friedman & Nunnari, 2014). For each acetyl-Coenzyme A entering the Krebs cycle, 12 ATP are produced (Appleton *et al.*, 2013c), each consisting of a purine or purine nitrogenous base (adenine), linked to a ribose (aldopentose) and three PO_4^{2-} (Botham & Mayes, 2018a) (Figure 17).

For each GLU ($C_6H_{12}O_6$) entering the cycle, two $C_3H_3O_3$ are produced, which in turn produce two acetyl-Coenzyme A (Nelson & Cox, 2017e). Therefore, for each GLU ($C_6H_{12}O_6$) entering the Krebs cycle, four CO_2, six $NADPH+H^+$ and 24 ATP molecules are produced (Friedman & Nunnari, 2014).

The information presented in previous paragraphs, shows how the biomolecules that constitute living organisms, interact to maintain and perpetuate life, governed by the same physical and chemical laws that govern the inert universe. The frontier of knowledge was organized around central principles or questions of biochemistry and how cells use a relatively small set of carbon-based metabolites to create polymeric molecules, supramolecular structures and information reservoirs. The chemical structure of these components defines their cellular function, the end result of which is the transformation and self-perpetuation of that compilation of biomolecules, in short, life.

CONCLUSIONS

Eukaryotic cells are composed of water, inorganic ions and organic molecules. They contain carbon chains with hydroxyl, amino and carboxyl functional groups, responsible for the formation of cell tissue. These structures obey the laws of chemistry and physics that determine the metabolism of living systems. Animals, possessing a high chemical complexity and a robust microscopic organization, constitute in their molecular anabolism and catabolism, systems of extraction, transformation and utilization of monosaccharides, amino acids and fatty acids. For the formation of acetyl-Coenzyme A and the release of its energy in the Krebs cycle. Thus, the biochemistry of cellular metabolism can be understood in terms of the structures and functions of three main classes of organic molecules polysaccharides, lipids and proteins.

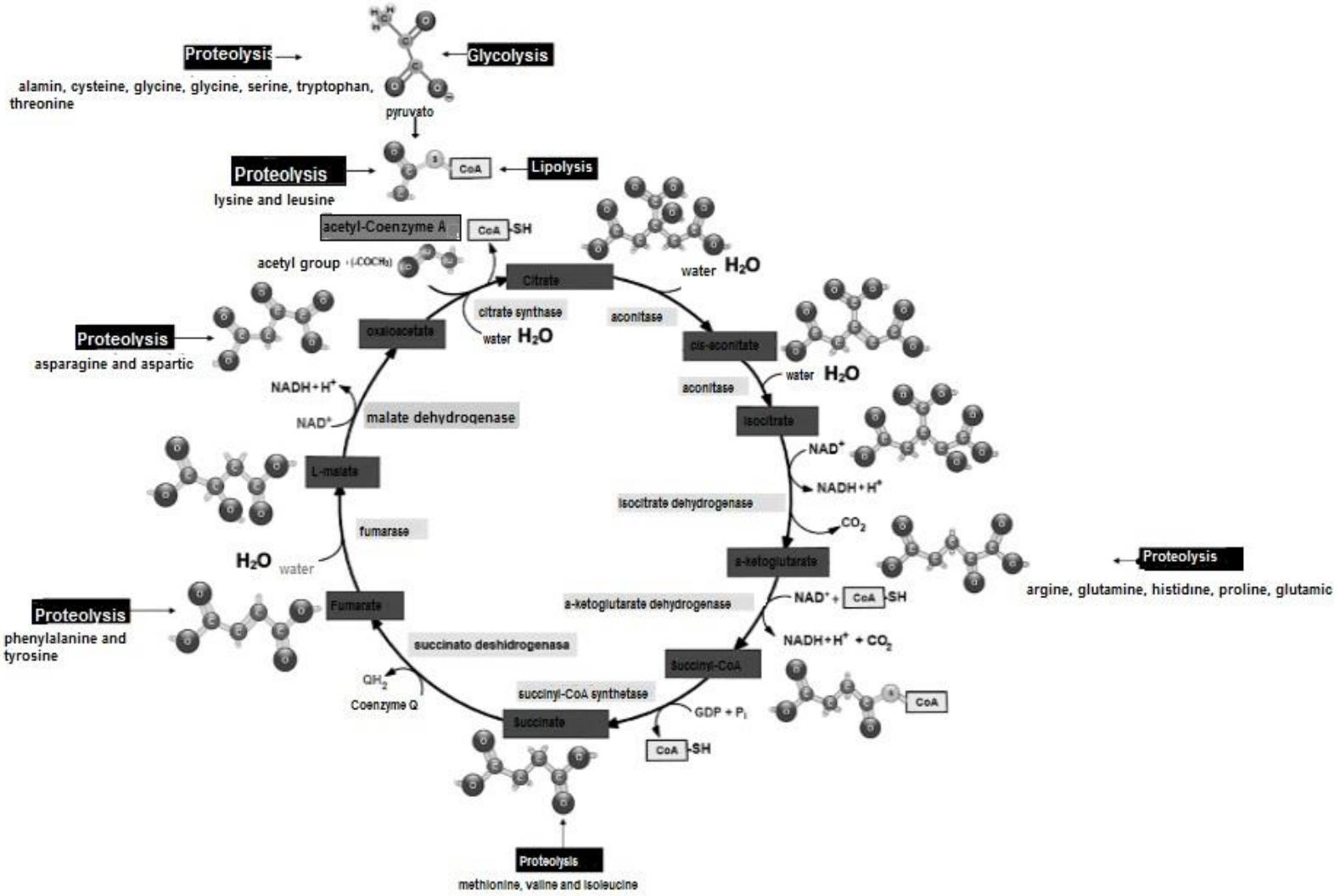

Figure 16. Krebs cycle

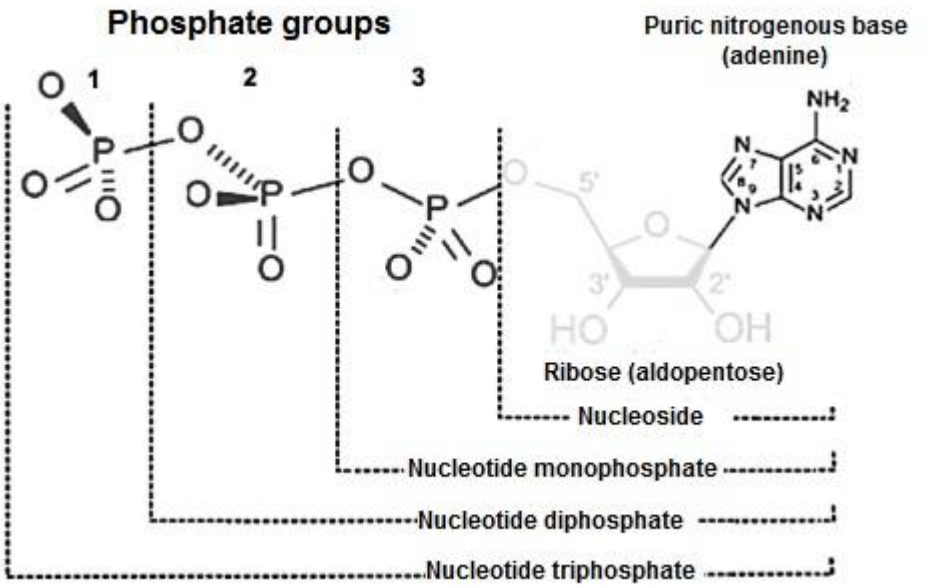

Figure 17. Adenosine triphosphate nucleotide (ATP)

ACKNOWLEDGMENTS

This work was supported by the National Council of Science and Technology (CONACyT-Mexico) (CONACyT-México) and the project: Metabolic profiles and their implications in veterinary medicine (Universidad de Colima).

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