Metabolism of a series of reactions that occur within cells of living organisms

Michael S. Dodd*

Centre for Sport, Exercise and Life Sciences, Faculty of Health and Life Sciences, Coventry University, Whitefriars Road, Coventry, U.K.

Corresponding Author*

Michael S. Dodd,

Centre for Sport, Exercise and Life Sciences, Faculty of Health and Life Sciences, Coventry University, White friars Road, Coventry, U.K

E-mail: ku.ca.yrtnevoc@ddod.ekim

Received: 06-Jul-2022, Manuscript No. jdm-22-18597; **Editor assigned:** 08-Jul-2022, PreQC No: jdm-22-18597(PQ); **Reviewed:** 22-Jul-2022, QC No. jdm-22-18597; **Revised:** 27-Jul-2022, Manuscript No. jdm-22-18597 (R); **Published:** 03-Aug-2022, DOI: 10.35248/2155-6156.1000944

Abstract

Metabolism consists of a series of reactions that occur within cells of living organisms to sustain life. The process of metabolism involves many interconnected cellular pathways to ultimately provide cells with the energy required to carry out their function. The importance and the evolutionary advantage of these pathways can be seen as many remain unchanged by animals, plants, fungi, and bacteria. In eukaryotes, the metabolic pathways occur within the cytosol and mitochondria of cells with the utilization of glucose or fatty acids providing the majority of cellular energy in animals. Metabolism is organized into distinct metabolic pathways to either maximize the capture of energy or minimize its use. Metabolism can be split into a series of chemical reactions that comprise both the synthesis and degradation of complex macromolecules known as anabolism or catabolism, respectively. The basic principles of energy consumption and production are discussed, alongside the biochemical pathways that make up fundamental metabolic processes for life.

Keywords: *iochemistry; glycolysis; metabolism*

Introduction

The basics of metabolism

When many people think about metabolism, they think of food and drink or the huge metabolic pathway diagram with thousands of connections. However, understanding metabolism is key to understanding life and this has been a subject of fascination with biochemists for more than 150 years. The great Nobel Prize-winning scientist Hans Krebs was inspired to study metabolism by his university professor Prof France Knoop (who discovered β-oxidation of fatty acids). He unpicked and described both the citric acid cycle and the urea cycle which lie as fundamental processes of metabolism. Prof Franz Knoop said: "The final goal of physiological chemistry/(metabolism)" is to "present a scheme that puts together an unbroken series of equations of all of the reactions from the food stuffs which continuously supply to the organism its energy needs, all the way to the slag that again leaves the organism as energy less final oxidation products." Prof Franz Knoop 1931 - Hans Krebs: The formation of a scientific life 1900–1933 by F.L. Holmes [1].

Whilst it can be daunting to think about every metabolic pathway that is occurring, we can break it down and understand its smaller aspects. Knoop words underpin the true meaning of metabolism and one of its central roles in biochemistry and physiological chemistry. Metabolism is derived from the Greek word, metabolic meaning 'to change' and comprises the total of all chemical reactions that take place in the cell that are essential for life [2, 3]. These chemical reactions comprise both the synthesis and degradation of complex macromolecules and can be divided into either catabolism or anabolism (Figure 1 – catabolism vs anabolism). Catabolism is the degradation of complex macromolecules into simpler molecules such as carbon dioxide, water, and ammonia. Anabolism is the biosynthetic pathways that generate complex macromolecules such as nucleic acids, proteins, polysaccharides, and lipids [4].

Anabolism utilizes energy to make macromolecules and bio molecular polymers. Catabolism releases energy when these are broken down into simpler molecules. To maintain cellular and whole-body function, living organisms require energy continuously. Energy is required for mechanical work (contraction and cellular movement), active transport of ions/substrates (i.e. K+, Mg2+, and Ca2+, for example in cardiac contraction) and the biosynthesis of complex macromolecules (such as glycogen).

This review will focus on the basics of metabolism within mammals, with mentions of other organisms too. The aim is to provide you with an understanding of the metabolic pathways that are present in animals, how energy is derived from these systems, and how they are controlled [5]. Finally, we will touch on the exciting elements of research in metabolism, including how understanding metabolism could help with treating cancer, how it can be used in biotechnology to generate bioethanol, and how metabolic diseases make up several key inherited conditions.

Why pathways?

Metabolic pathways are vital in capturing useful energy. This is in contrast with uncontrolled combustion, where energy is rapidly released into the environment, as heat and light, which would be unsustainable for life. Metabolism is organized into distinct metabolic pathways to either maximize the capture of energy or minimize its use. In catabolism, metabolic pathways are organized such that energy is released slowly in discrete quanta of energy, which is captured by the synthesis of adenosine triphosphate (ATP), guanosine triphosphate (GTP), NAD (P) H (nicotinamide adenine nucleotide (phosphate)) or by the electron transport chain (ETC). In anabolism, metabolic pathways use these discrete quanta of energy in the form of ATP and NADPH to perform work, such as the synthesis of biomolecules [6]. The action of metabolic pathways in the cell is particularly impressive with the ability to organize several hundred metabolic reactions occurring simultaneously within the cell and occurring at a relatively low temperature. Most of this is achieved by specific enzymes and compartmentalization of reactions and enzymes. Sometimes this compartmentalization is achieved by separating reactions into different organelles or by coupling reactions together, to prevent uncontrolled combustion [7]. Enzymes allow discrete reactions to occur, which when combined give the same overall effect as combustion, but in a controlled fashion. In this review, we will discuss the energy of reactions, the role of metabolic enzymes, key metabolic pathways, and then the vital organelles for energy generation [8].

Energy within the system

One of the most important biomolecules in the cell is the nucleotide; ATP. ATP has a linear triphosphate structure which provides four negative charges and therefore it exists as a highly charged molecule. Due to this negative charge, these bonds can store a large amount of energy, which can be liberated easily at the site of work. Along with ATP, NAD+ also acts as a store for energy in its reduced form, NADH + H. NAD+ acts as a universal electron carrier in the cell, transporting electrons from catabolism site to the ETC [9].

Emilie du Chatelet proposed the law of conservation, which stated that energy can be neither created nor destroyed; rather, it can only be transformed from one form into another. This is linked to the first law of thermodynamics and it helps us to explain how energy flows through biological systems. The laws of thermodynamics also help us to predict if a reaction is possible and how much energy is required or released in the process. This brings us to an important concept: the role of chemical equilibria, where a reaction can be reversible

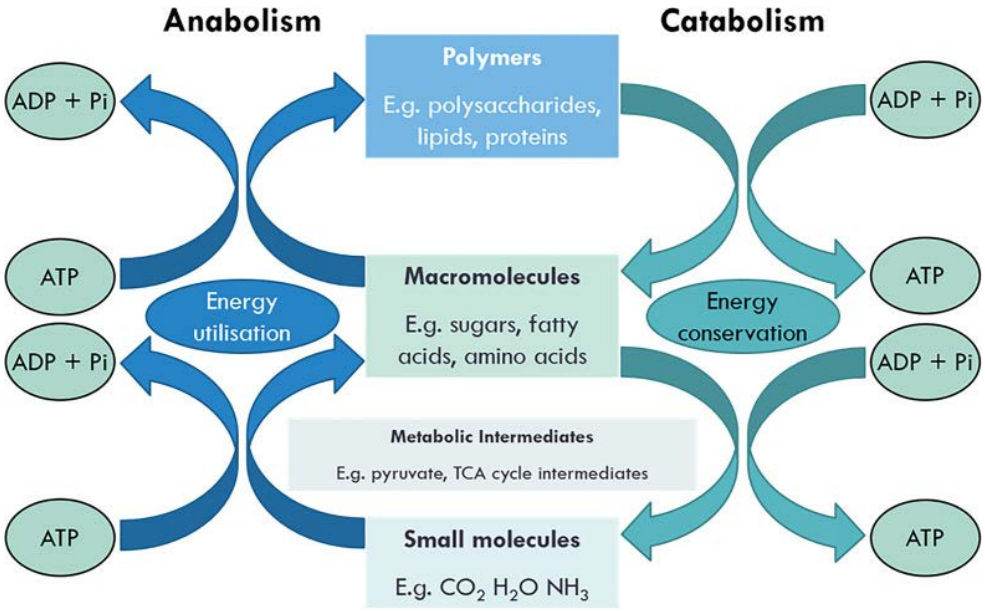

Figure 1: Coupling of anabolic and catabolic pathways.

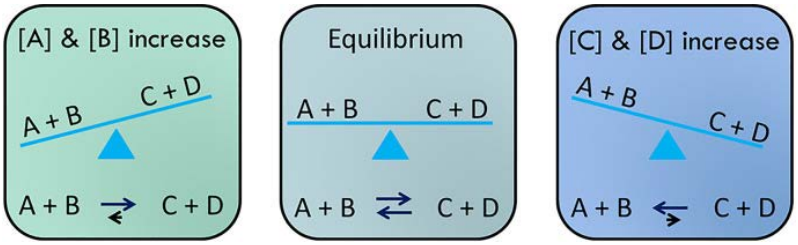

Figure 2: Reaching equilibrium.

(see Figure 2). At equilibrium, there is no net reaction as both the forward and reverse reactions are moving equally fast. The system aims to bring reactions to equilibrium [10]. However, true equilibrium is not compatible with life, as there is no longer a flow of energy. If you increase the concentration of A and B, this pushes the reaction to make more C and D. If you do the opposite and add more C and D, then the reverse reaction occurs. The aim is to bring the reaction back to equilibrium.

Glucose metabolism

Central metabolism and G6P

Glucose is transported into a cell through GLUTs and sodium glucose cotransporters (SGLTs) via facilitated diffusion. These transporters can move glucose into and out of cells. To ensure that glucose remains within the cell, it is quickly 'trapped' and phosphorylated to form G6P. This phosphorylation occurs via a kinase enzyme called hexokinase or glucokinase, which catalyses the transfer of a phosphoryl group from an ATP molecule to an acceptor molecule. In this case, G6P is a highly negative, polar molecule meaning it is unable to diffuse across the cell membrane. Furthermore, the addition of the phosphate group renders G6P too large to escape back out of the cell through GLUT transporters. By trapping glucose in cells as G6P, the gradient of glucose between the cytosol and the extracellular space increases, resulting in a net movement of glucose into cells. Glucose holds a high osmotic potential, and so by removing glucose, the movement of water out of the cell is reduced. This reaction, therefore, ensures the fate of glucose as G6P to facilitate the initiation of further metabolic processes.

G6P is the central molecule of metabolism. It is a 'crossroad' marker and holds many possible fates within a cell, dependent on its conditions and metabolic needs (Figure 2). G6P lies at the center of four metabolic pathways:

Glycolysis – The formation of pyruvate and lactate

Gluconeogenesis – G6P is converted by glucose-6-phosphatase during gluconeogenesis to form glucose. Glucose-6-phosphatase is primarily expressed in the liver but also in the kidney cortex at times of starvation. It has further been found to be expressed in the β-cells of pancreatic islets and human intestinal mucosa in starved and diabetic states [11].

Glycogenesis – Storage as glycogen. G6P is converted via glycogen synthase into glycogen for storage.

The pentose phosphate pathway (PPP) – The generation of NADPH molecules allows fatty acid synthesis. The formation of ribose-5-phosphate to synthesis nucleotides. The PPP regenerates the intermediates of glycolysis such as F6P [12].

Amino acids are the form of nitrogen found in plants. They can regulate plant growth and are precursors for defence-related metabolites. When plants are infested by herbivore insects, studies found that amino acid production increased to synthesise defensive metabolites to ensure a second attack does not occur. This increase in amino acid production occurs as genes involved in amino acid synthesis are up-regulated and sulphur assimilation, which is ultimately required for the biosynthesis of cysteine and methionine, are all up-regulated upon caterpillar feeding on Arabidopsis thaliana. Furthering this, a similar study further found that the increased expression of genes involved in amino acid biosynthesis, in particular, related to methionine and tryptophan synthesis, led to a greater accumulation of glucosinolates [13, 14]. These are defence-related molecules that are derived from methionine and tryptophan in A. thaliana. Interestingly, this was also found in tomatoes. Upon attack, tomato plants accumulate tryptophan within their stems and apex of tomatoes, to serve as a precursor for the production of defensive metabolites [15].

Plant biotechnology is a set of techniques that are used to adapt plants for survival and defence. One of the most effective ways to manage plant pathogenicity is to use genetic modification alongside genome editing. This is particularly useful in the agriculture industry to ensure increased food supply. Globally, up to 30% of food is damaged by pathogens and disease pests [16]. Therefore, the adaptation of plants to pathogens and pests is imperative for survival. Gene modification and genome editing can help manage plant pathogens to ensure plant cell survival in times of attack; these solutions currently include bacterial, viral, fungal, and oomycete pathogens.

As knowledge regarding the plant immune system has expanded, it has been shown that plants can distinguish between 'self' and 'non-self' through monitoring the extracellular and intracellular environment. However, pathogens can overcome this system by producing proteins and effectors to suppress plant host immunity and colonise it [17]. A bacterial pathogen can hijack the coronatine-insensitive protein 1 jasmonate receptor, altering the plant's defence response and activating jasmonate responses and suppressing salicylic acid defence pathways. Manipulation like these has allowed the development of biotechnology to intervene at the point of pathogen perception. These can be created by introducing receptors from other plants with novel recognition specificity, reactivation of genes disabled in NOD-like receptors, and modification of domains in NOD-like receptors that are targeted by pathogens. This knowledge reveals which components of the host can be manipulated to promote a disease state. Therefore, by removing these vulnerable points or replacing them with variants that are immune to specific effectors, the natural functionality of the plant can be retained. Bacterial pathogens, that express the transcription activate like effectors that activate susceptibility genes within the host, can be overcome by the deletion of TAL DNA-binding sites in the promoter. Another approach includes engineering resistance to bacterial pathogens by adding TAL effector binding sites to an executor gene [18].

Another way to regulate plant pathogen perception is by the intervention of the defence signalling pathways. The major hormones involved in defence signalling are salicylic acid, jasmonate, and ethylene. In tomato plants, a loss of function allele was engineered for Downy mildew resistance 6 (DMR6) to ensure resistance to bio trophic pathogens. DMR6 is widely conserved and encodes a salicylate-5-hydrozylase enzyme around infection sites.

Biotechnology advancements regarding plants and plant metabolism help ensure defence and healthy plant growth. In conclusion, biotechnology has allowed the intervention of defence signalling and regulation, pathogen recognition, effector recognition, and allowed targeting of genes associated with plant pathogenicity [19].

Conclusion

At least 25 Nobel Prizes have been awarded for work related to metabolism, with the most recent for the oxygen-sensing role of HIF1α in 2019. This review has introduced the basic metabolic pathways of life and demonstrated how a series of reactions can combine to sustain life. Over the last 150–200 years, the understanding of metabolism has moved from individual enzymes and metabolites to the complicated network we see today. This has allowed us to visualize metabolism occurring in real-time within the human body, to help us understand metabolic alterations in human disease. Manipulation of metabolic pathways in both microorganisms and plants has also led the way in the development of new biotechnological techniques.

References

1. Ameer F, Scandiuzzi L, Hasnain S, Kalbacher H, Zaidi N (2014) De novo lipogenesis in health and disease. Metabolism 63: 895-902.
2. Berg J, Tymoczko J, Stryer L (2002) The first step in amino acid degradation is the removal of nitrogen.
3. Bishop S, Campbell J (1965) Arginine and urea biosynthesis in the earthworm Lumbricus terrestris. Comp Biochem Physiol 15: 51-71.
4. Brown G, Brown W, Cohen P (1962) Comparative biochemistry of urea synthesis IV. [14C]Urea synthesis by liver slices of the metamorphosing tadpole. Biochim Biophys Acta 60: 185-186.
5. Chirala SS, Jayakumar A, Gu ZW, Wakil SJ (2001) Human fatty acid synthase: Role of interdomain in the formation of catalytically active synthase dimer. Proc Natl Acad Sci U S A 98: 3104-3108.
6. DeBerardinis R, Chandel N (2016) Fundamentals of cancer metabolism. Sci Adv 2: e1600200.
7. Esse H, Reuber T, Does D (2019) Genetic modification to improve disease resistance in crops. New Phytol 225: 70-86.
8. Frayn K, Evans R (2018) Human Metabolism: A Regulatory Perspective, 4thedn, Wiley Blackwell
9. Gartner V, McGuire P, Lee P (2015) Child Neurology: medium-chain acyl-coenzyme A dehydrogenase deficiency. Neurology 85: 37-40.
10. Gibala M, Young M, Taegtmeyer H (2000) Anaplerosis of the citric acid cycle: role in energy metabolism of heart and skeletal muscle. Acta Physiol Scand 168: 657-665.
11. Guo X, Li H, Xu H, Woo S, Dong H, et al. (2012) Glycolysis in the control of blood glucose homeostasis. Acta Pharm Sin B 2: 358-367.
12. Hanahan D, Weinberg R (2011) Hallmarks of cancer: the next generation. Cell 144: 646-674.
13. He J, Ford H, Carroll J, Douglas C, Gonzales E, et al. (2018) Assembly of the membrane domain of ATP synthase in human mitochondria. Proc Natl Acad Sci USA 115: 2988-2993.
14. Klotz M, Stein L (2008) Nitrifier genomics and evolution of the nitrogen cycle. FEMS Microbiol. Lett. 278: 146-156.
15. Koppolu V, Vasigala V (2016) Role of Escherichia coli in biofuel production. Microbiol Insights 9: 29-35.
16. Kornberg H, Beevers H (1957) A mechanism of conversion of fat to carbohydrate in castor beans. Nature 180: 35-36.
17. Krebs H (1973) The discovery of the ornithine cycle of urea synthesis. Biochem Educ 1: 19-23.
18. Leonardi R, Zhang Y, Rock C, Jackowski S (2005) Coenzyme A: back in action. Prog Lipid Res 44: 125-153.
19. Li C, Teng W, Shi Q, Zhang F (2007) Multiple signals regulate nicotine synthesis in tobacco plant. Plant Signal Behav 2: 280-281.

Cite this article: Michael S. Dodd. Metabolism of a series of reactions that occur within cells of living organisms. J Diabetes Metab, 2022, 13(7): 944.