Biosynthesis of Important Molecules

Shwetha. M[1]
I Year BDS, Amrita School of Dentistry, Kochi, India [1]

Abstract **- Biosynthesis is an enzyme catalysed process where substrates are converted into more complex products in living organisms. It consists of synthesis of carbohydrates, proteins, amino acids, fatty acids, cell wall and nucleotides. Biosynthesis of carbohydrates includes synthesis of glucose and conversion of glucose to other carbohydrates. Biosynthesis of proteins includes activation of amino acids, transfer of amino acid to tRNA, initiation of polypeptide chain, chain termination and protein translocation. Biosynthesis of amino acids includes reduction of N_2 to NH_4, transamination and synthesis of amino acid by metabolic precusors. Biosynthesis of fatty acids occurs in cytoplasm and ER of the cell similar to the beta oxidation process with a couple of differences. Synthesis of new strands in living cells is DNA replication. Synthesis of RNA from genetic information encoded by DNA is transcription, which has initiation, elongation and termination phases.**

Keywords **- carbohydrates, proteins, amino acids, fatty acids, nucleotides.**

I. INTRODUCTION

Any process which takes place in the cell requires energy in the form of Adenosine Tri Phosphate (ATP) or any other means. Biosynthetic processes in the cell also require energy in the form of ATP which is used to convert one chemical substance to another and to synthesize complex substances from simpler ones (anabolism). In short, biosynthesis can be defined as a multi-step, enzyme catalysed process where substrates are converted into more complex products in living organisms. This process often consists of various metabolic pathways which include synthesis of proteins from amino acids, biosynthesis of cell wall peptidoglycan, synthesis of DNA, synthesis of lipids etc.

II. BIOSYNTHESIS OF CARBOHYDRATES

Carbohydrates are polyhydroxy aldehydes or ketones or compounds that yield them on hydrolysis. They are the most abundant organic matter present in nature formed by the reduction of alcohols [1]. They have the general formula $(CH_2O)_n$. These are present in the food we eat, used for photosynthesis and for various purposes. Biosynthesis of carbohydrates (1) can be considered under the following two headings.

- Synthesis of glucose in animals and humans
- Conversion of glucose to other carbohydrates

Conversion of CO_2 to carbohydrates in plants-Photosynthesis

$$6H_2O + 6CO_2 \xrightarrow[\text{Chlorophyll}]{\text{Sunlight}} \underset{\text{(glucose)}}{C_6H_{12}O_6} + 6O_2 \qquad (1)$$

Gluconeogenesis:

The synthesis of glucose from non-carbohydrate sources is called gluconeogenesis. The sources are most commonly pyruvate, citric acid cycle intermediates and glucogenic amino acids. Gluconeogenesis is not the exact reversal of glycolysis; i.e. pyruvate to glucose does not occur by reversing the steps of glucose to

pyruvate [2]. The three irreversible steps of glycolysis (phosphenol pyruvate to pyruvate, fructose 6 phosphate to fructose 1,6 bisphosphate, glucose to glucose 6 phosphate) are reversed in gluconeogenesis.

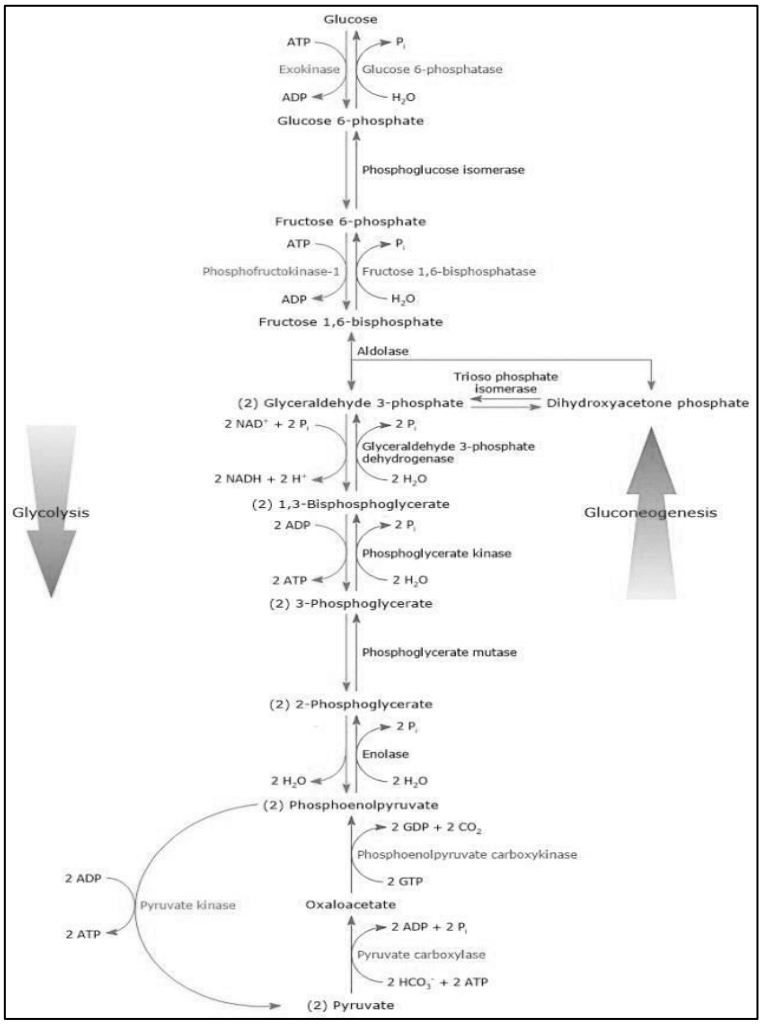

Fig. 1. Glycolysis and Gluconeogenesis

Gluconeogenesis takes place in the liver to maintain the blood glucose levels constant. This includes 3 bypass steps.

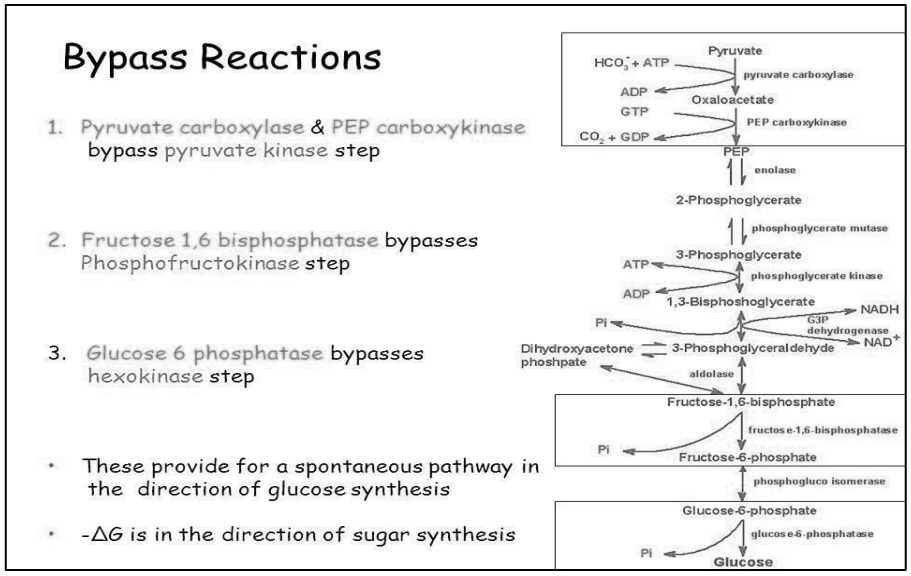

Fig. 2. Three Bypasses of Gluconeogenesis

- 1st bypass: Conversion of pyruvate to PEP: It involves 2 reactions-pyruvate converted to oxaloacettae by action of pyruvate carboxylase using ATP, oxaloacetate to PEP by action of PEP carboxykinase using GTP.
- 2nd bypass: Formation of fructose 6 phosphate from fructose 1,6 bisphosphate.
- 3rd bypass: Glucose 6 phosphate to glucose using glucose 6 phosphatase enzyme.

Other carbohydrates are generally produced from glucose where glucose is converted into hexoses and to disaccharides, oligosaccharides, polysaccharides [3]. The common step for all these being activation of glucose by Uridine Tri Phosphate (UTP) to form Uridine Di Phosphate glucose (UDP-glucose) $+P_i$ is below.

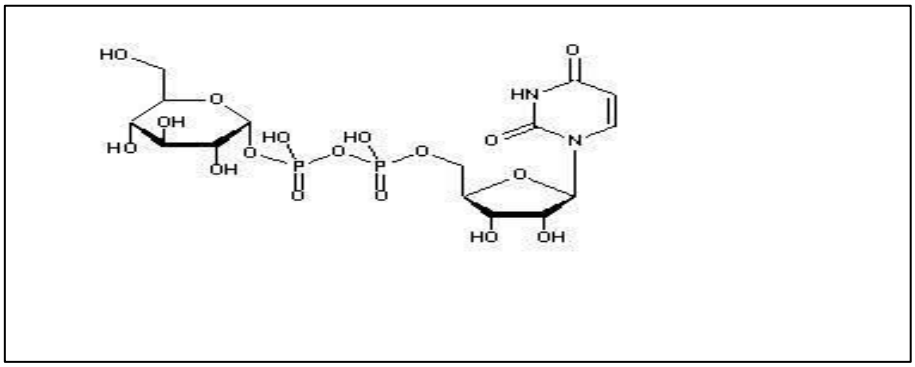

Fig. 3. Structure of Uridine Diphosphate Glucose (Udp-Glucose)+P_i

III. BIOSYNTHESIS OF PROTEINS FROM AMINO ACIDS

Amino acids are monomers which are polymerised to produce proteins. This involves a set of biochemical processes (metabolic pathways) which build the amino acids from carbon sources like glucose.

Steps in Protein Biosynthesis:

A. Activation of Amino Acids

This reaction is brought about by the binding of an amino acid with ATP. The enzyme sed here is amino acyl RNA synthetases. As a result of this reaction the amino acid and ATP combine and form a complex called amino acyl- ATP-enzyme complex [4]. It should be noticed that amino acyl RNA synthetases are specific with various amino acids.

B. Transfer of Amino Acid to tRNA

The complex formed reacts with specific tRNA. This amino acid is transferred to tRNA. As a result the enzyme and AMP are liberated.

C. Initiation of Polypeptide Chain

This charged RNA shifts to the ribosome. This is the site where protein synthesis takes place. We know that ribosomes are made up of rRNA and proteins. Ribosome also acts as a catalyst for the formation of peptide bond. The information for the sequence of amino acids is present in the sequence nitrogenous bases of mRNA. Each amino acid codes for three letter code of nucleic acid. The initiation is always brought about

by the amino acid methionine (AUG).The ribosome either binds to the acceptor site or the donor site. Each site is a composite of specific portions of SOS and 30S sub units.

The initiating methionine however can bind only to the P site. All other newly coming amino acyl t RNA bind to A site. The RNA polymerase binds to the promoter site and initiates transcription (information in a strand of DNA is copied into a new molecule of mRNA).the recognition is done by sigma factor (initiation factor) present in RNA polymerase [5]. Using nucleotide triphosphate as substrate the polymerisation occurs in a template. Thus as a result of this repetitive action for chai elongation, the polypeptide chain elongates. As a result ribosome moves from codon to codon along the mRNA towards the 3' end, the polypeptide chain of the last amino acid is inserted.

D. Chain Termination

The termination of polypeptide is signalled by one of the three terminal triplets in the mRNA. The three codons are UAG, UAA, and UGA. They are also called stop signals. At the time of termination the terminal codon follows the last amino acid codon. After this the subunits of ribosomes gets dissociated.

E. Protein Translocation

Two classes of ribosome shave been identified - **Free ribosomes** in which the termination of protein synthesis leads to the release of completed protein for cytoplasm. Some of them are translocated to mitochondria and nucleus for various purposes [6]. **Membrane bound polyribosomes** in which the polypeptide chain which grows on mRNA is inserted into the lumen of ER which become the integral part of membrane.

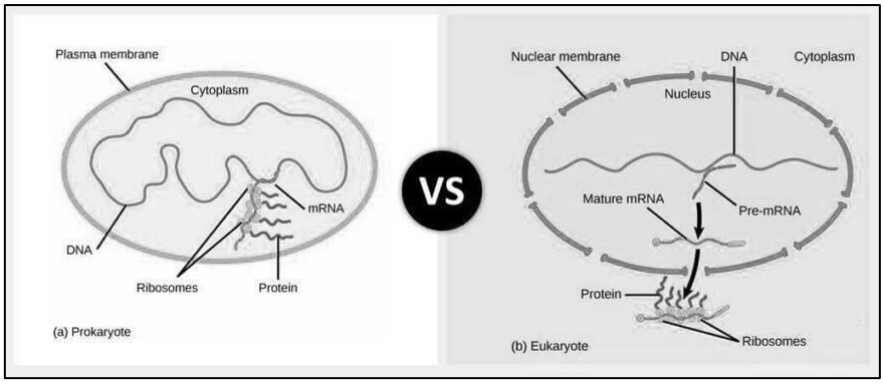

Fig. 4. Protein Synthesis in Prokaryotes and Eukaryotes

IV. BIOSYNTHESIS OF AMINO ACIDS

Amino acid synthesis is the set of biochemical processes by which the various amino acids are produced from other compounds.

Steps in Amino Acid Synthesis:

A. Reduction of N_2 to NH_4

It is the first step during synthesis of amino acids in which reduction of N_2 to NH_4 takes place. The conversion of nitrogen to ammonia is a reduction reaction which is exergonic in nature [7]. Biological fixation of nitrogen is carried out by a highly conserved complex of proteins called nitrogenase complex.

B. Transamination

It is a chemical reaction that transfers an amino group to a keto acid to form new amino acids. This is responsible for the deamination of most amino acids. This is one of the major degradation pathways which convert essential amino acid to non-essential amino acid. This accomplished by enzymes called transaminases or aminotransferase.

C. Synthesis of Amino Acid by Metabolic Precusors

All the 20 amino acids are derived from intermediates in glycolysis, citric acid cycle or pentose phosphate pathway. Nitrogen enters this pathway by the way of glutamate and glutamine.

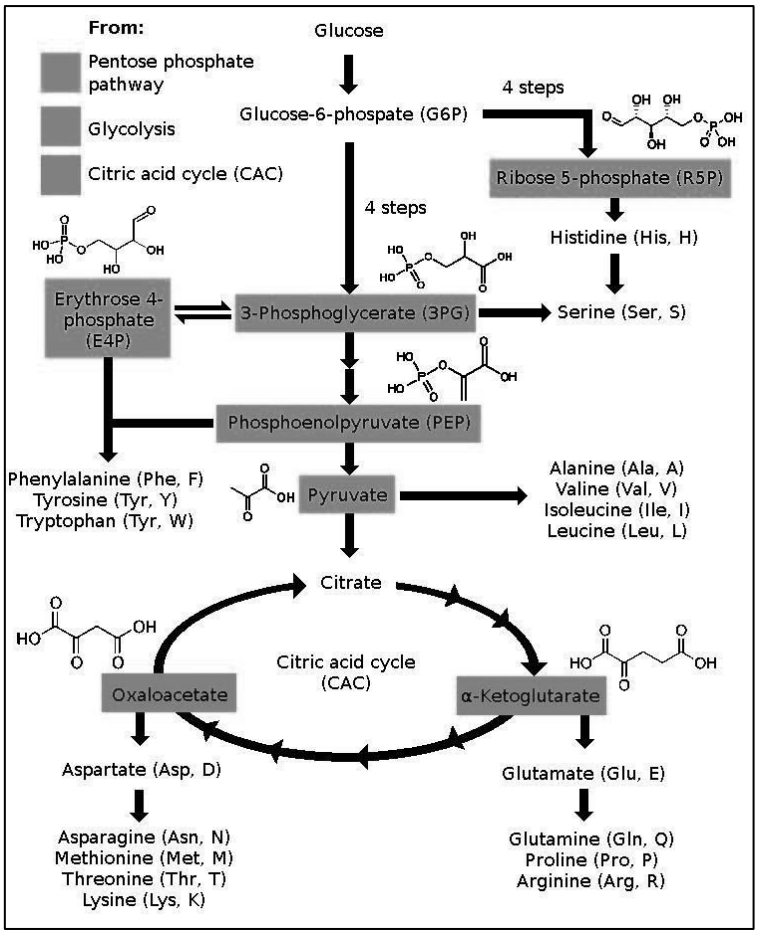

Fig. 5. Biosynthesis of Amino Acid

TABLE 1 : SYNTHESIS OF AMINO ACIDS BY MOLECULAR PRECURSORS

MOLECULAR PRECURSORS	**AMINO ACIDS**				
RIBOSE 5 PHOSPHATE	Histidine				
PYRUVATE	Alanine	Valine	Leucine		
3 PHOSPHO GLYCERATE	Serine	Cysteine	Glycine		
α KETOGLUTARATE	Glutamate	Glutamine	Proline	Arginine	
OXALOACETATE	Aspartate	Asparagine	Methionine	Isoleucine	Lysine
PHOSPHRNOL PYRUVATE & ERYTHROSE 4 PHOSPHATE	Phenylalanine	Tyrosine	Tryptophan		

V. BIOSYNTHESIS OF FATTY ACIDS

The standard way for the biosynthesis of fatty acids is through the fatty acid synthesis cycle. The synthesis occurs in the cytoplasm and ER of the cell and is chemically similar to the beta oxidation process, but with a couple of differences. The first of this occur in preparing substrates for the reactions that grow the fatty acid. Transport of acetyl CoA from mitochondria occurs when it begins to build up. Two molecules can play important role when it is moving to the cytoplasm-citrate and acetylcarcinate [8]. Joining of oxaloacetate with acetyl CoA in the mitochondria creates citrate which moves across the membrane, followed by the action of citrate lyase in the cytoplasm of the cell to release acetyl CoA and oxaloacetate.

This cycle of eight enzymes is initiated by acetic acid, CoA and ATP to make acetyl CoA using Acyl – CoA synthase as catalyst. A second step using another ATP and bicarbonate ion catalysed by Acyl –CoA carboxylase yields malonyl-CoA. With acyl transferase and keto acyl synthase catalysis malonyl CoA is added to an acyl chain, usually activated with acyl carrier protein, to make acyl chain two methylene groups longer. Further reduction, dehydration and reduction with keto acyl synthase, hydroxy acyl dehyratase, enoyl reductase catalysis respectively, leads to a saturated and dehydroxylated acyl chain activated with acyl carrier protein. If the chain is of appropriate length, it is attacked by thioesterase to release acyl carrier protein yielding the finished fatty acid.

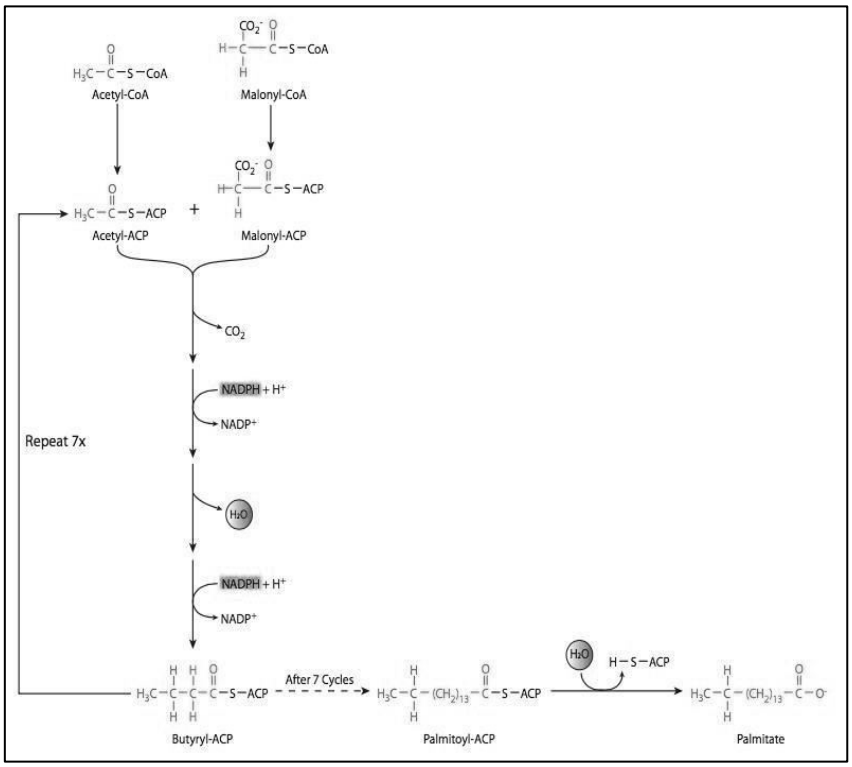

Fig.6. Synthesis of Fatty Acid

VI. BIOSYNTHESIS OF NUCLEOTIDES (DNA AND RNA)

The nucleotide is the basic unit of polynucleotide chain in both DNA and RNA. A nucleotide has three components like nitrogenous base, pentose sugar (deoxyribose in DNA or ribose in RNA) and phosphate group. Nitrogenous bases are of purines and pyrimidines. Adenine and Guanine are purines Cytosine, Thymine and Uracil are pyrimidines. Nitrogenous base is linked to the pentose sugar through N glycosidic linkage to form a nucleoside. When a phosphate group is linked to 5' OH of a nucleoside through a phosphodiester bond the resultant product is known as nucleotide. Many such nucleotides join to form a polynucleotide chain of DNA and RNA.

A. Biosynthesis of DNA

DNA or deoxyribonucleic acid is the biological molecule which contains the information needed to create a living organism. As the cell divides to become two, the DNA has to be copied so that both cells contain the necessary genetic information. The synthesis or making of new strands in living cells is referred as DNA replication.

DNA is found as a double helix where two strands of DNA are bound together into two helices. The process of DNA replication begins when the two strands of DNA separate. An enzyme called helicase unwinds and separates the bonds between the two DNA strands and both these separated strands act as template from which new strands are made [9]. DNA polymerases are a group of enzymes which make new DNA. But for this enzyme to work, it needs a primer (a short nucleotide sequence which is attached to one of the single DNA strands).

During DNA replication the primer is usually a short RNA sequence which is later degraded and replaced by DNA. The primer provides a 3' hydroxyl group onto which the DNA polymerase adds the precursors of DNA, the nucleotides. When nucleotides are added to the 3'end of the primer or the new DNA strand, a bond is formed between the 3' hydroxyl group of the primer/new DNA and the 5' phosphate group of nucleotide. There are four types of DNA nucleotides which each have different nitrogeneous bases - Adenine, Guanine Cytosine, Thymine .they are always found in pairs, A-T and C-G (Watson crick base pairing).

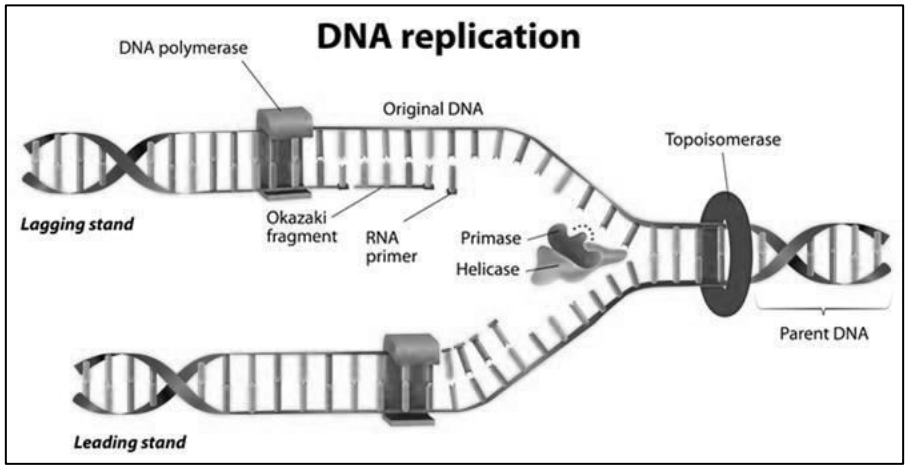

Fig. 7. DNA Synthesis

B. Biosynthesis of RNA

RNA, ribonucleic acid is a polymeric molecule essential in various biological roles in coding, decoding, regulation and expression of genes. Some RNA molecules play an active role within the cells by catalysing biological reactions, controlling gene expression or sensing and communicating responses to cellular signals. One of the active processes is protein synthesis, a universal function in which RNA molecules direct the synthesis of proteins on ribosomes. This process uses transfer RNA (tRNA) to deliver amino acids to the ribosome and rRNa then links amino acids to form encoded protein.

The process of synthesis of RNA from genetic information encoded by DNA is called transcription. The enzymes involves are RNA polymerases. Prokaryotes and eukaryotes differ from the structure of their corresponding RNA polymerases. There are three phases of transcription. It would be easier to describe about elongation first and then about initiation and termination.

1. Elongation

RNA polymerase links ribonucleotides together in a 5' to 3' direction. The polymerase induces the 3' hydroxyl group of the nucleotide at the 3'end of the growing RNA chain which attacks the phosphorous of the incoming ribonucleotide. A diphosphate is released and the 5' carbon f the incoming nucleotide is linked

through the phosphodiester bond to the 3’ carbon of the preceding nucleotide. Such incorporation is determined by base pairing with the template strand of DNA. The template is the DNA strand, also called the sense strand that is copied by the RNA polymerase into a complementary strand of RNA called the transcript [10]. The DNA strand that is not copied is known as the antisense strand. Note that while the RNA chain grows in a 5' to 3' direction the polymerase migrates along the sense strand in a 3' to 5' direction. Thus the 5' to 3' ribonucleotide sequence of the RNA transcript is identical to the 5' to 3' antisense DNA strand with uracil in place of thymidine.

2. Initiation

The initiation of transcription is directed by DNA sequences called promoters which tell the RNA polymerase where to begin transcription. The subunits that enable RNA polymerases to recognize and bind promoters are called initiation factors. The initiating nucleotide can be either a purine or pyrimidine. There are numerous eukaryotic promoters with multiple promoter sequence elements. Some of the elements specify where transcription is to be initiated; others determine the frequency with which transcription is initiated at a specific gene. The initiation of transcription in eukaryotes is complicated and involves numerous factors (proteins) that must interact with the DNA and with one another to initiate transcription.

3. Termination

Prokaryotes use two means for terminating transcription, factor-independent and factor-dependent. Certain DNA sequences function as signals that tell the RNA polymerase to terminate transcription. The DNA of a terminator sequence encoded an inverted repeat and an adjacent stretch of uracil. Factor-dependent termination involves a terminator sequence as well as a factor or protein called rho. The mechanisms by which eukaryotes terminate transcription are poorly understood [11]. Most eukaryotic genes are transcribed for up to several thousand base pairs beyond the actual end of the gene. The excess RNA is then cleaved from the transcript when the RNA is processed into its mature form.

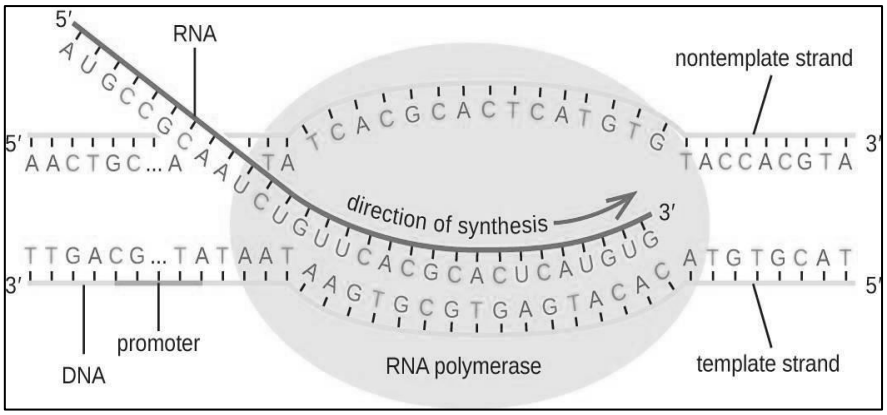

Fig. 8. RNA Synthesis

VII. CONCLUSION

Biosynthetic processes in the cell require energy, used to convert one chemical substance to another and to synthesize complex substances from simpler ones. Synthesis of carbohydrates, proteins, amino acids, fatty acids and nucleotides through various pathways with the help of various intermediates were explained. Synthesis of glucose from non-carbohydrate sources is gluconeogenesis. It takes place in liver to maintain the blood glucose levels constant. Various amino acids are produced from other compounds in amino acid synthesis. The biosynthesis of fatty acids is through the fatty acid synthesis cycle. Biosynthesis of DNA and biosynthesis of RNA constitute biosynthesis of nucleotides.

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