Nucleic Acids

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Nucleic acids

Two types of nucleic acids are present in all mammalian cells including humans. They are DNA-deoxy ribonucleic acid and RNA-ribonucleic acid. DNA is present in nucleus and mitochondria. RNA is present in nucleus and cytoplasm. Nucleic acids are also present in bacteria, viruses and plants.

Medical and biological importance

1. Nucleic acids serve as genetic material of living organisms including humans.

2. Nucleic acids are involved in the storage, transfer and expression of genetic information.

3. Nucleic acids contain all the necessary information required for the formation of individual or organism.

4. Nucleic acids determines physical fitness of an individual to life.

5. Some nucleic acids acts as enzymes and coenzymes. For example, RNA, act as catalyst and mRNA is coenzyme for telomerase which seals ends of chromosomes.

6.Some RNAs without protein products are found recently in mammals, yeast and bacteria. they are involved in cellular functions.

Chemical nature of nucleic acids

Nucleic acids are acidic substances containing nitrogenous bases, sugar and phosphorus. Both DNA and RNA are polynucleotides. They are polymers of nucleotides.

Phosphodiester linkage

In polynucleotides, nucleotides are joined together by phosphodiester linkage. Diester linkage of phosphate joins 3′ OH and 5′ OH belonging two separate sugars .

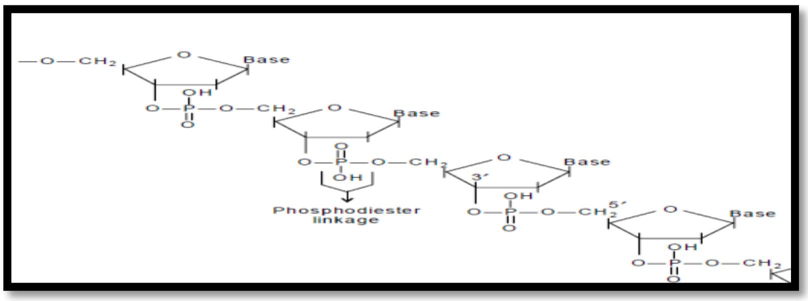

Fig.1 Structure of a polynucleotide segment

Nucleic acid structure

Primary structure of nucleic acids

Nucleotide sequence of a polynucleotide is known as primary structure of nucleic acid. Polynucleotide chain has direction. They are represented in 5′ → 3′ direction only. However, the phosphodiester linkage runs in 3′ → 5′ direction. Each poly nucleotide chain has two ends. The 5′ end carrying phosphate is shown on the left hand side and 3′ end carrying unreacted hydroxyl is shown on the right hand side (Figure. 2). Primary structures of DNA and RNA exist in single stranded DNA and RNA organisms.

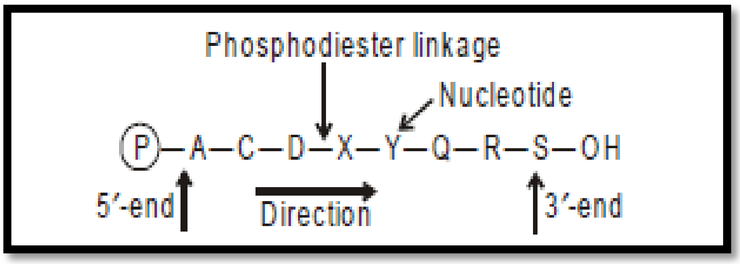

Fig. 2 Primary structure of nucleic acid. Letters A, C, D, X, Y, Q, R, S are nucleotides

Characteristics of DNA base composition

1. In DNA, number of adenine residues is equal to the number of thymine residues *i.e.*, A = T. Further number of guanine residues is equal to number of cytosine residues *i.e.*, G = C. As corollary sum of purine residues is equal to sum of pyrimidine residues A + G = C + T.
2. DNAs from different tissues of same species have same base composition.
3. Base composition of DNA varies from one species to another species.
4. DNAs from closely related species have similar base composition.
5. DNAs of widely different species have different base composition.
6. DNA base composition of a species is not affected by age, nutritional state and environment.

Salient features of double helix

1. Two polynucleotide chains are coiled around a central axis in the form of right handed double helix. It represents secondary structure of DNA. It is present in double stranded DNA containing organisms (Figure 3a).

2. Each polynucleotide chain is made up of 4 types of nucleotides.

3. Each polynucleotide chain has direction or polarity. Further each polynucleotide chain has 5′ phosphorylated and 3′ hydroxyl end.

4. The back bone of each strand consist of alternating sugar and phosphates.

5. The two strands run in opposite direction, i.e., they are anti-parallel.

6. The strands are complementary to each other. Base composition of one strand is complementary to the opposite strand. If adenine appears in one strand thymine is found in the opposite strand and vice versa. Where ever guanine is found in one strand cytosine is present in the opposite strand and vice versa (Figure 3a).

7. **Base pairing** Bases of opposite strands are involved in pairing. Pairing occurs through hydrogen bonding and it is specific. Adenine of one strand pairs with thymine of opposite strand through two hydrogen bonds. Guanine of one strand pairs with cytosine of opposite strand. Three hydrogen bonds between GC pair makes it more stronger than AT pair (Figures 3b).

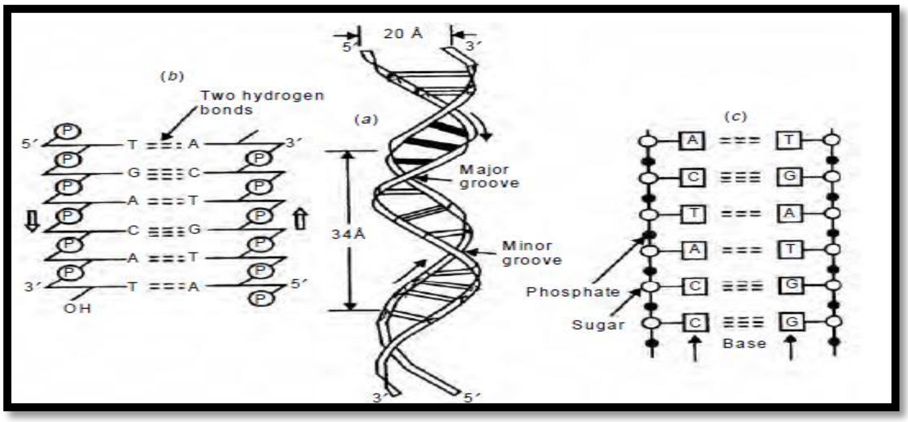

Fig. 3 (*a*) DNA double helix
(*b*) Base pairing among complementary bases of opposite strands
(*c*) Alternating sugar and phosphate form back bone of strand. Bases project inwards and perpendicular to central axis

Functions of DNA

1. DNA is the genetic material of living systems.

2. DNA contains all the information required for the formation of an individual or organism.

3. The genetic information in DNA is converted to characteristic features of living organisms like color of the skin and eye, height, intelligence, ability to metabolize particular substance, ability to with stand stress, susceptibility to disease and unable to produce or synthesize certain substances etc.

4. All the above phenotype characters of living organisms are intimately related to functions of proteins. Thus, DNA is the source of information for the synthesis of all cellular proteins. The segment of DNA that contains information for a protein is known as *gene*.

5. DNA is transmitted from parent to off spring and hence DNA flows from one generation to other in a given species. Further, DNA provides information inherited by daughter cells from parent cells.

6. The amount of DNA per cell is proportional to the complexity of the organism and hence to the amount of genetic information. The amount of DNA in mammalian cell is 1000 times more than bacteria. Likewise, bacteria contains more DNA than virus and plasmids.

7. The amount of DNA in any given species or cell is constant and is not affected by nutritional or metabolic states.

Viral DNA

Viruses are extremely small particles. They are composed of a piece of DNA, which is surrounded by protein coat called *capsid*. Viral DNA may be single stranded or double stranded. Adeno virus (cold virus), Herpes virus and Pox virus are examples for double stranded viruses. Parvo virus is a example for single strand DNA virus .

Denaturation of DNA

When DNA molecule is heated it denatures and strands separate. Thermal denaturation of DNA is known as melting of DNA. Melting point of DNA is known as *Tm*. It is a characteristic of given DNA. If the heat denatured DNA is cooled base pairing occurs between strands and reformation of double, stranded molecule takes place. This process is known as *annealing*. It is very useful in genetic engineering particularly in DNA hybridization techniques (Figure 4).

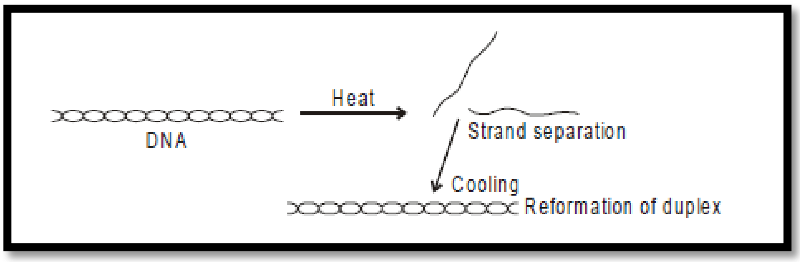

Fig. 4 DNA denaturation

Ribonucleic acids (RNAs)

Ribonucleic acids are present in nucleus and cytoplasm of eukaryotic cells. They are also present in prokaryotes. They are involved in the transfer and expression of genetic information. They act as primers for DNA formation. Some RNA act as enzymes as well as coenzymes. RNA also function as genetic material for viruses.

Chemical nature of ribonucleic acids

Like DNAs, RNAs are also poly nucleotides. In RNA polymer, purine and pyrimidine nucleotides are linked together through phosphodiester linkage. The sugar present in a RNA is ribose. There are mainly three types of RNAs in all prokaryotic and eukaryotic cells. The three types of RNA are 1. Messenger RNA or m-RNA, 2. Transfer RNA or t-RNA, 3. Ribosmal RNA or r-RNA. They differ from each other by size, function and stability.

Messenger RNA

It accounts for 1-5% of cellular RNA.

Structure

1. Majority of mRNA has primary structure. They are single-stranded linear molecules. They consist of 1000-10,000 nucleotides.
2. mRNA molecules have free or phosphorylated 3’ and 5’ end.
3. mRNA molecules have different life spans. Their life span ranges from few minutes to days.
4. Eukaryotic mRNA are more stable than prokaryotic mRNA.

5. The mRNA nucleotide sequence is complementary from which it is synthesized or copied.

Functions

1. mRNA is direct carrier of genetic information from the nucleus to the cytoplasm.
2. Usually a molecule of mRNA contains information required for the formation of one protein molecule.
3. Genetic information is present in mRNA in the form of genetic code.
4. Sometimes single mRNA may contain information for the formation of more than on protein.

Transfer RNA

t-RNA accounts for 10-15% of total cell RNA.

Structure

They are the smallest of all the RNAs. Usually they consist of 50-100 nucleotides. They are single strand molecules.

Functions

1. It is the carrier of amino acids to the site of protein synthesis.
2. There is at least one t-RNA molecule to each of 20 amino acids required for protein synthesis.
3. Eukaryotic t-RNAs are less stable where as prokaryotic RNAs are more stable.

Ribosomal RNA

Ribosomal RNA or r-RNA accounts for 80% of total cellular RNA. It is present in ribosomes. In ribosomes, r-RNA is found in combination with protein. It is known as ***ribonucleoprotein*.** The length of r-RNA ranges form 100-600 nucleotides. Both prokaryotic and eukaryotic ribosomes contain r-RNA molecules.

Structure

r-RNA molecules have secondary structure. Intra strand base pairing between complementary base generates double helical segments or loops. They are known as domains. The three-dimentional tertiary structure of r-RNA is highly complex.

Functions

1. r-RNAs are required for the formation of ribosomes.
2. RNA is involved in initiation of protein synthesis

NUCLEOTIDES

Nucleotides are present in all types of cells.

MEDICAL AND BIOLOGICAL IMPORTANCE

1. Nucleotides are high energy compounds.
2. Nucleotides are required for formation of co-enzymes of some members of vitamins B complex group.
3. Some nucleotides are called as ‘second messenger’ because many hormones exert their action through nucleotides.
4. Some nucleotides act as carrier or donor of activated sugars, sulphates and nitrogenous compounds.
5. Some nucleotides are involved in signal transduction.
6. Some nucleotides are involved in regulation of metabolic pathways.
7. Some nitrogenous bases are CNS stimulants.
8. Some bases act as anti-oxidants.
9. Some nucleotide analogs are mutagens.
10. Nucleosides also act as carriers of groups or compounds.
11. Nucleotides are building blocks of nucleic acids.
12. Purines play major role in cardiovascular biology in normal and pathological conditions. They are involved in cardiac aging, angiogenesis, hypertension etc. Purino receptors are identified in cardiovascular system.

Chemical nature of nucleotides

Hydrolysis of nucleotides produce nitrogen bases, sugars and phosphate.

Nitrogenous bases. Nucleotides contain two types of nitrogenous bases. They are purine bases and pyrimidine bases Figure 5.

- Purines: Adenine (A) and Guanine (G)
- pyrimidine: Cytosine (C), Thymine (T) and Uracil (U)

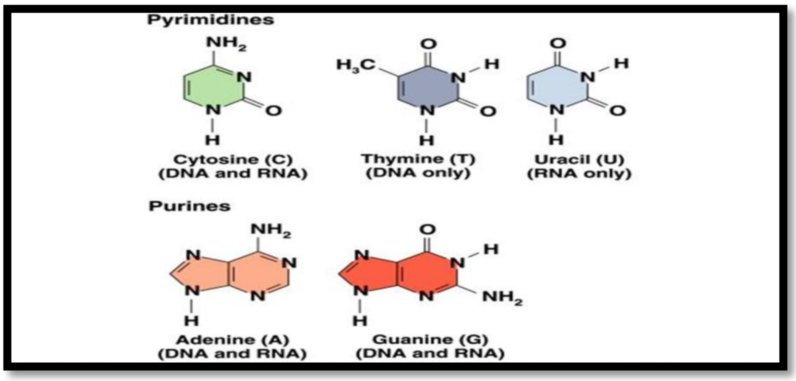

Fig. 5 Structures of pyrimidine and purine bases

Sugars

Two types of pentose sugars are found in nucleotides. They are ribose and deoxy ribose. Nucleotides are named according to the type of sugar present. If the sugar is deoxyribose then nucleotide is named as deoxyribonucleotide. Similarly, if the sugar is ribose then nucleotide is named as ribonucleotide.

Some characteristic features of sugar present in nucleotides

1. Normally it is a 5-numbered furanose ring.
2. Only D-isomer is present.
3. Configuration around first carbon atom is 'β'-form.
4. As mentioned earlier in deoxyribose, only hydrogen is present instead of OH group of 2 carbon atom of furanose ring (Fig.6).

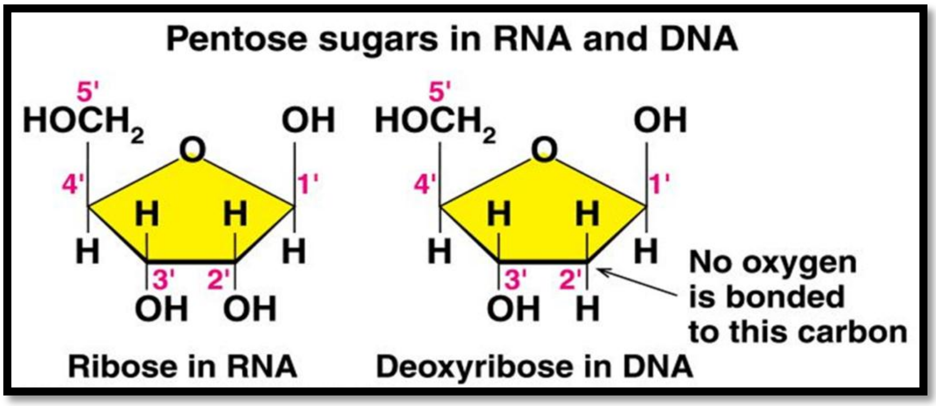

Fig. 6 Structures of ribose, deoxyribose

Nucleosides

A nucleoside is composed of purine and pyrimidine base and sugar. In the case of purine nucleosides, the sugar is attached to N-9 of purine ring where as in pyrimidine nucleosides the sugar is attached to N-1 of pyrimidine ring (Fig.7 a, b). So, the type of linkage is N glycosidic and sugar can be ribose or deoxyribose.

A nucleoside consists of a nitrogen base linked by a glycosidic bond to C1' of a ribose or deoxyribose

Nucleosides are named by changing the the nitrogen base ending to -osine for purines and –idine for pyrimidines

A nucleotide is a nucleoside that forms a phosphate ester with the C5' OH group of ribose or deoxyribose

Nucleotides are named using the name of the nucleoside followed by 5'-monophosphate

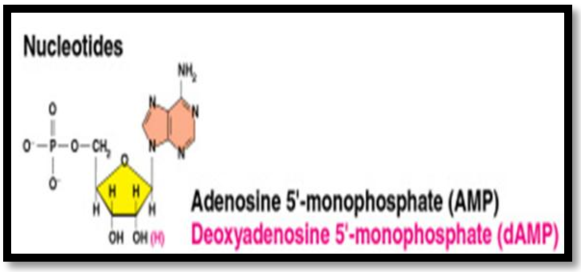

Fig. 7 a Structures of Nucleotides

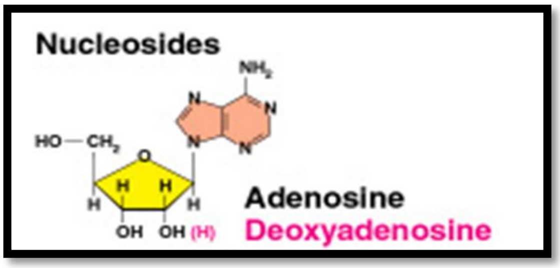

Fig. 7 b Structures of nucleoside

Nomenclature of Nucleosides and Nucleotides

Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	Deoxyadenosine 5'-monophosphate (dAMP)
Guanine (G)	Deoxyguanosine (G)	Deoxyguanosine 5'-monophosphate (dGMP)
Cytosine (C)	Deoxycytidine (C)	Deoxycytidine 5'-monophosphate (dCMP)
Thymine (T)	Deoxythymidine (T)	Deoxythymidine 5'-monophosphate (dTMP)

Factor of Denaturation

Denaturation DNA is the separation of a double strand into two single strands, which occurs when hydrogen bonds between the strands are broken .

Denaturation may result from:

- Heating above its Tm.
- High pH
- Organic solvents (dimethyl sulfoxide).
- Lowering the salt conc. of the DNA solution
- Viscosity of DNA solutions decreases on denaturation.
- Hyperchromicity (increased absorbance of UV on denaturation)