DNA: Deoxyribonucleic acid

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Nucleic acids were first isolated by Friedrich Miescher (1869) from pus cells.term was coined by Altman.Fisher (1880s) discovered the presence of purine and pyrimidine bases in nucleic acids. Watson and Crick (1953) worked out the first correct double helix model from the X-ray photographs of Wilkins and Franklin. Wilkins, Watson and Crick were awarded Nobel Prize for the same in 1962. Watson and Crick proposed that DNA consisted of a double helix with two chains having sugar phosphate on the outside and nitrogen bases on the inner side.

The nitrogen bases of the two chains formed complementary pairs with purine of one and pyrimidine of the other held together by hydrogen bonds (A-T, C-G). Complementary base pairing between the two polynucleotide chains is considered to be hall mark of their proposition. It is of course based on early finding of Chargaff that A = T and C = G Their second big proposal was that the two chains are antiparallel with 5'→ 3′ orientation of one and 3'→ 5'orientation of the other.

The two chains are twisted helically just as a rope ladder with rigid steps twisted into a spiral. Each turn of the spiral contains 10 nucleotides. This double helix or duplex model of DNA with antiparallel polynucleotide chains having complementary bases has an implicit mechanism of its replication and copying.

Here both the polynucleotide chains function as templates forming two double helices, each with one parent chain and one new but complementary strand. The phenomenon is called semi conservative replication. In vitro synthesis of DNA has been carried out by Kornberg in 1959.

Chargaff's Rules:

Chargaff (1950) made observations on the bases and other components of DNA. These observations or generalizations are called Chargaff's base equivalence rule.

(i) Purine and pyrimidine base pairs are in equal amount, that is, adenine + guanine = thymine + cytosine. [A + G] = [T + C], i.e., [A+G] / [T+C] = 1

(ii) Molar amount of adenine is always equal to the molar amount of thymine. Similarly, molar concentration of guanine is equalled by molar concentration of cytosine.

[A] = [T], i.e., [A] / [T] = 1; [G] = [C], i.e., [G] / [C] = 1

(iii) Sugar deoxyribose and phosphate occur in equimolar proportions.

(iv) A-T base pairs are rarely equal to C—G base pairs.

(v) The ratio of [A+T] / [G+C] is variable but constant for a species (Table 6.2). It can be used to identify the source of DNA. The ratio is low in primitive organisms and higher in advanced ones.

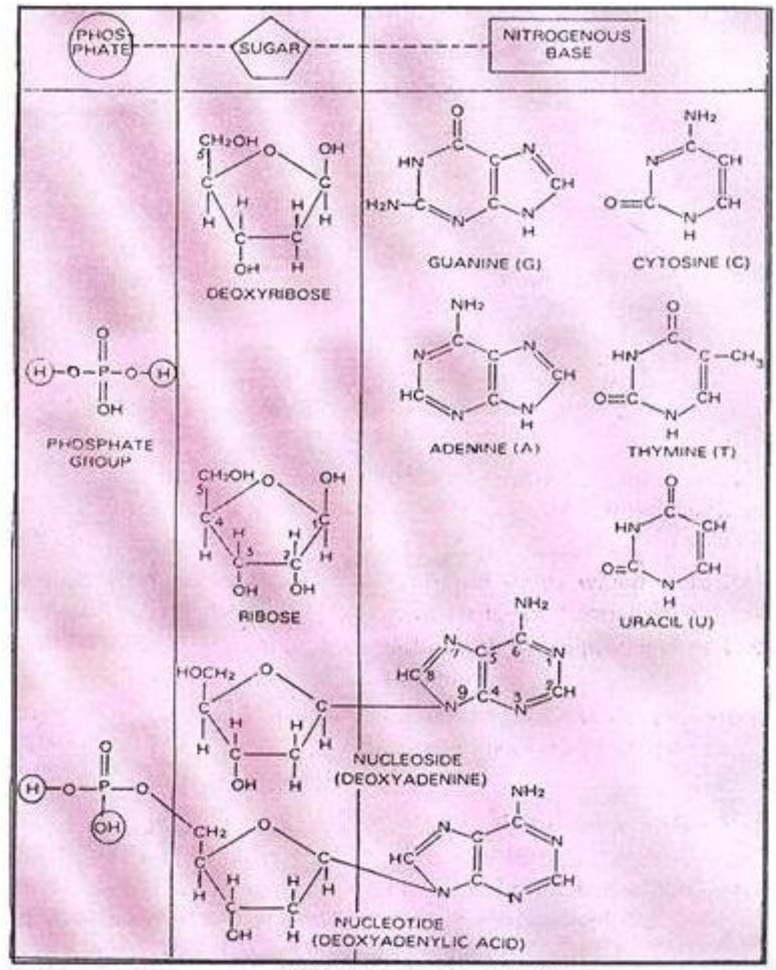
Structure of DNA:

DNA or deoxyribonucleic acid is a helically twisted double chain polydeoxyribonucleotide macromolecule which constitutes the genetic material of all organisms with the exception of rhinoviruses. In prokaryotes it occurs in nucleoid and plasmids. This DNA is usually circular. In eukaryotes, most of the DNA is found in chromatin of nucleus.

It is negatively charged due to phosphate groups. It is a long chain polymer of generally several hundred thousands of deoxyribonucleotides.

A DNA molecule has two un-branched complementary strands. They are spirally coiled. The two spiral strands of DNA are collectively called DNA duplex . Due to spiral twisting, the DNA duplex comes to have two types of alternate grooves, **major** (22 Å) and **minor** (12 Å).

In DNA, one turn of the spiral has about 10 nucleotides on each strand of DNA. It occupies a distance of about 3.4 nm (34 Å or 3.4×10^{-9} m) so that adjacent nucleotides or their bases are separated by a space of about 0.34 nm (0.34×10^{-9} m or 3.4 Å).
A deoxyribonucleotide of DNA is formed by cross-linking of three chemicals ortho- phosphoric acid (H_3PO_4), deoxyribose sugar ($C_5H_{10}O_4$) and a nitrogen base. Four types of nitrogen bases occur in DNA. They belong to two groups, purines (9-membered double rings with nitrogen at 1,3,7 and 9 positions) and pyrimidines (six membered rings with nitrogen at 1 and 3 positions). DNA has two types of purines (adenine or A and guanine or G) and two types of pyrimidines (cytosine or C and thymine or T).



Building blocks of nuclecotides

Depending upon the type of nitrogen base, DNA has four kinds of deoxyribonucleotides —

deoxy adenosine 5- monophosphate (d AMP),

deoxy guaninosine 5-monophosphate (d GMP),

deoxy thymidine 5-monophosphate (d TMP) and

deoxy cytidine 5- monophosphate (d CMP).

The back bone of a DNA chain or strand is built up of alternate deoxyribose sugar and phosphoric acid groups. The phosphate group is connected to carbon 5′ of the sugar residue of its own nucleotide and carbon У of the sugar residue of the next nucleotide by (3 '—5') phosphodiester

bonds. -H of phosphate and -OH of sugar are eliminated as H_2O during each ester formation.
Phosphate group provides acidity to the nucleic acids because at least one of its side group is free to dissociate. Nitrogen bases lie at right angles to the longitudinal axis of DNA chains. They are attached to carbon atom 1 of the sugars by N-glycosidic bonds. Pyrimidine (C or T) is attached to deoxyribose by its N-atom at 1 position while a purine (A or G) does so by N-atom at 9 position.

The two DNA chains are antiparallel that is, they run parallel but in opposite directions. In one chain the direction is 5'→ У while in the opposite one it is 3′ →5′. The two chains are held together by hydrogen bonds between their bases. Adenine (A), a purine of one chain lies exactly opposite thymine (T), a pyramidine of the other chain. Similarly, cytosine (C, a pyrimidine) lies opposite guanine (G a purine). This allows a sort of lock and key arrangement between large sized purine and small sized pyrimidine.

It is strengthened by the appearance of hydrogen bonds between the two. Three hydrogen bonds occur between cytosine and guanine (C = G) at positions 1'-1', 2′- 6′ and 6′-2′. There are two such hydrogen bonds between adenine and thymine (A=T) which are formed at positions 1'-3′ and 6′-4′. Hydrogen bonds occur between hydrogen of one base and oxygen or nitrogen of the other base. Since specific and different nitrogen bases occur on the two DNA chains, the latter are complementary.

Thus the sequence of say AAGCTCAG of one chain would have a complementary sequence of TTCGAGTC on the other chain. In other words, the two DNA chains are not identical but complementary to each other. It is because of specific base pairing with a purine lying opposite a pyrimidine. This makes the two chains 2 nm thick.

A purine- purine base pair will make it thicker while a pyrimidine- pyrimidine base pair will make it narrower than 2 nm. Further, A and C or G and T do not pair because they fail to form hydrogen bonds between them. 5′ end of each chain bears phosphate radical while the 3′ end possesses a sugar residue (3'-OH).

Sense and Antisense Strands:

Both the strands of DNA do not take part in controlling heredity and metabolism. Only one of them does so. The DNA strand which functions as template for RNA synthesis is known as template strand, minus (-) strand or antisense strand.

Its complementary strand is named nontemplate strand, plus (+) strand, sense and coding strand. The latter name is given because by convention DNA genetic code is written according to its sequence.

Functions of DNA:

1. Genetic Information (Genetic Blue Print):

DNA is the genetic material which carries all the hereditary information. The genetic information is coded in the arrangement of its nitrogen bases.

2. Replication:

DNA has unique property of replication or production of carbon copies (Autocatalytic function). This is essential for transfer of genetic information from one cell to its daughters and from one generation to the next.

3. Chromosomes:

DNA occurs inside chromosomes. This is essential for equitable distribution of DNA during cell division.

4. Recombination’s:
During meiosis, crossing over gives rise to new combination of genes called recombinations.

5. Mutations:
Changes in sequence of nitrogen bases due to addition, deletion or wrong replication give rise to mutations. Mutations are the fountain head of all variations and evolution.

6. Transcription:
DNA gives rise to RNAs through the process of transcription. It is heterocatalytic activity of DNA.

7. Cellular Metabolism:
It controls the metabolic reactions of the cells through the help of specific RNAs, synthesis of specific proteins, enzymes and hormones.

8. Differentiation:
Due to differential functioning of some specific regions of DNA or genes, different parts of the organisms get differentiated in shape, size and functions.

9. Development:
DNA controls development of an organism through working of an internal genetic clock with or without the help of extrinsic information.

10. DNA Finger Printing:
Hypervariable microsatellite DNA sequences of each individual are distinct. They are used in identification of individuals and deciphering their relationships. The mechanism is called DNA finger printing.

11. Gene Therapy:

Defective heredity can be rectified by incorporating correct genes in place of defective ones.