Revision Notes on Molecular Basis of Inheritance

DNA

(1) DNA is a long polymer of deoxyribonucleotides.

(2) The length of the DNA depends on the number of nucleotide pairs present in it.

(3) Bacteriophage lambda has 48,502 base pairs.

Central dogma of molecular biology

(1) Crick proposed the Central dogma in molecular biology

(2) It states that the genetic information flows from DNA à RNA à Protein.

(3) In some viruses like retroviruses, the flow of information is in reverse direction, which is from RNA à DNA à mRNA à Protein.

Structure of polynucleotide chain:

(1) A nucleotide has three components-

(a) A nitrogen base

(b) A pentose sugar (ribose in RNA and deoxyribose in DNA)

(c) A phosphoric acid.

(2) There are two types of nitrogen bases:

(a) Purines (Adenine and Guanine)

(b) Pyrimidines (Cytosine, Uracil and Thymine)

(3) Adenine, Guanine and Cytosine are common in RNA and DNA.

(4) Uracil is present in RNA and in DNA in place of Uracil, Thymine is present.

(5) In RNA, Pentose sugar is ribose and in DNA, it is Deoxyribose.

(6) Based on the nature of pentose sugar, two types of nucleosides are formed - ribonucleoside and deoxyribonucleotides.

(7) Two nucleotides are joined by 3'-5' Phosphodiester linkage to form dinucleotide.

(8) More than two nucleotides join to form polynucleotide chain.

(9) The two strands of DNA (called DNA duplex) are antiparallel and complementary, i.i., one in 5'->3' direction and the other in 3"->5" direction.

History of DNA

(1) DNA is an acidic substance in the nucleus.

(2) It was first identified by Friedrich Meischer in 1869. He named it as 'Nuclein"

(3) In 1953 double helix structure of DNA was given by James Watson and Francis Crick, based on X-ray diffraction data produced Maurice Wilkins and Rosalind Franklin.

Packaging of DNA Helix

(1) The basic unit into which DNA is packed in the chromatin of eukaryotes.

(2) Nucleosome is the basic repeating structural (and functional) unit of chromatin, which contains nine histone proteins.

(3) Distance between two conjugative base pairs is 0.34nm

(4) The length of the DNA in a typical mammalian cell will be 6.6 X109 bp X 0.34 X10-9 /bp, it comes about 2.2 meters.

(5) The length of DNA is more than the dimension of a typical nucleus (10-6m)

DNA Replication

(1) DNA is the only molecule capable of self duplication so it is termed as a living molecule.

(2) All living beings have the capacity to reproduce because of DNA.

(3) DNA replication takes place in S-phase of the cell cycle. At the time of cell division, it divides in equal parts in the daughter cells.

(4) **Delbruck** suggested three methods of DNA replication i.e.

(i) Dispersive

(ii) Conservative

(iii) Semi-conservative

(5) The process of DNA replication takes a few minutes in prokaryotes and a few hours in eukaryotes.

RNA

(1) RNA is the first genetic material.

(2) RNA is a non hereditary nucleic acid except in some viruses (retroviruses).

(3) RNA used to act as a genetic material as well as catalyst.

(4) It is a polymer of ribonucleotide and is made up of pentose ribose sugar, phosphoric acid and nitrogenous base (A,U,G,C).

(5) RNA may be of two types – genetic and non-genetic.

Genetic Code

(1) Term genetic code was given by **George Gamow (1954).** He was the first to propose the triplet code (one codon consists of three nitrogen bases).

(2) The relationship between the sequence of amino acids in a polypeptide chain and nucleotide sequence of DNA or mRNA is called genetic code.

(3) There occur 20 types of amino acids which participate in protein synthesis. DNA contains information for the synthesis of any types of polypeptide chain. In the process of transcription, information transfers from DNA to m-RNA in the form of complementary N_2-base sequence.

(4) A **codon** is the nucleotide sequence in m-RNA which codes for particular amino acid; whereas the **genetic code** is the sequence of nucleotides in **m-RNA** molecule, which contains information for the synthesis of polypeptide chain.

(5) 61 out of 64 codons code for only 20 amino acids.

(6) The main problem of genetic code was to determine the exact number of nucleotide in a codon which codes for one amino acid.

Characteristics of genetic code

(1) **Triplet in nature**

(a) A codon is composed of three adjacent nitrogen bases which specify one amino acid in polypeptide chain.

(b) For example- In m-RNA if there are total 90 N_2 – bases. Then this m-RNA determines 30 amino acids in polypeptide chain.

(2) **Univerality**

(a) The genetic code is applicable universally.

(b) The same genetic code is present in all kinds of living organism including viruses, bacteria, unicellular and multicellular organisms. In all these organisms, triplet code for specific amino acid.

(3) **Non-ambiguous**

(a) Genetic code is non ambiguous i.e. one codon specifies only one amino acid and not any other.

(b) In this case one codon never code two different amino acids. **Exception** GUG codon which code both valine and methionine amino acid.

(4) **Non-overlapping**

(a) A nitrogen base is a constituent of only one codon.

(4) **Comma less**

(a) There is no punctuation (comma) between the adjacent codon i.e. each codon is immediately followed by the next codon.

(b) If a nucleotide is deleted or added, the whole genetic code read differently.

(c) A polynucleotide chain having 50 amino acids shall be specialized by a linear sequence of 150 nucleotides. If a nucleotide is added in the middle of this sequence, the first 25 amino acids of polypeptide will be same but next 25 amino acids will be different.

(5) **Degeneracy of genetic code**

(a) Only two amino acids – tryptophan and methionine are specified by single codon.

UGG for tryptophan

AUG for methionine

(b) All the other amino acids are specified or coded by 2 to 6 codons.

(c) Leucine, serine and arginine are coded or specified by 6-codons.

(d) Degeneracy of genetic code is related to third position (3'-end of triplet codon) of codon. The third base is described as 'Wobble base'.

Genomics and human genome project:

(1) The term genome has been introduced by **Winkler** in 1920 and the genomics is relatively new, coined by **Thomas Rodericks** in 1986.

(2) Genomics is the subdiscipline of genetics devoted to the mapping, sequencing and functional analysis of genomes. Genomics is subdivided into following types:

(a) **Structural genomics:** It is the study of genome structure deals with the complete nucleotide sequences of the organisms.

(b) **Functional genomics:** It is the study of genome function which includes transcriptome and proteome. Transcriptome is a complete set of RNAs transcribed from a genome while proteome is a complete set of proteins encoded by a genome and aims the determination of the structure and function of all the proteins in living organisms.

(3) The human genome project, sometimes called "biology's moon shot", was launched on october 1, 1990 for sequencing the entire human genome of 2.75 billion (2.75×10^9 or 2750000 bp or 2750000 kilobase pairs or 2750 megabase pairs) nucleotide pairs.

(4) Two important scientist associated with human genome are **Francis Collins**, director of the Human Genome Project and **J. Craig Venter**, founding president of Celera genomics.

(5) The complete sequencing of the first human chromosome, small chromosome 22, was published in December 1999.

Genome of Model organisms

S. No.	Organism	No. of base pair	No. of genes
(1)	Bacteriophage	10 thousand	–
(2)	E. coli	4.7 million	4000
(3)	Saccharomyces cerevisiae	12 million	6000
(4)	Caenorhabditis elegans	97 million	18,000
(5)	Drosophila melanogaster	180 million	13,000
(6)	Human	3 billion	30,000
(7)	Lily	106 billion	–

Prospects and implications of human genome:

(1) The genome project is being compared to the discovery of antibiotics.

(2) Efforts are in progress to determine genes that will revert cancerous cells to normal.

(3) The human genome sequencing not only holds promise for a healthier living. It also holds the

prospects of vast database of knowledge about designer drugs, genetically modified diets and finally our genetic identity.

DNA finger printing

(1) **Alec Jeffreys et al** (1985) developed the procedure of genetic analysis and forensic medicine, called DNA finger printing.

(2) It is individual specific DNA identification which is made possible by the finding that no two people are likely to have the same number of copies of repetitive DNA sequences of the regions.

(3) It is also known as DNA profiling.

(4) The chromosomes of every human cell contain scattered through their DNA short, highly repeated 15 nucleotide segments called "mini-satellites" or variable-number Tandem Repeat (VNTR).

Technique for DNA fingerprinting

(1) Only a small amount of tissues like blood or semen or skin cells or the hair root follicle is needed for DNA fingerprinting.

(2) Typically DNA content of about 100,000 cells or about 1 microgram is sufficient.

(3) The procedure of DNA fingerprinting involves the following major steps:

(i) DNA is isolated from the cells in a high-speed refrigerated centrifuge.

(ii) If the sample of DNA is very small, DNA can be amplified by Polymerase Chain Reaction (PCR).

(iii) DNA is then cut up into fragments of different length using restriction enzymes.

(iv) The fragments are separated according to size using gel electrophoresis through an agarose gel. The smaller fragments move faster down the gel than the larger ones.

(v) Double stranded DNA is then split into single stranded DNA using alkaline chemicals.

(vi) These separated DNA sequences are transferred to a nylon or nitrocellulose sheet placed over the gel. This is called 'Southern Blotting' (after **Edward Southern**, who first developed this method in 1975).

(vii) The nylon sheet is then immersed in a bath and probes or makers that are radioactive synthetic DNA segments of known sequences are added. The probes target a specific nucleotide sequence which is complementary to VNTR sequences and hybridizes them.

(viii) Finally, X-ray film is exposed to the nylon sheet containing radioactive probes. Dark bands develop at the probe sites which resemble the bar codes used by grocery store scanners to identify items.

Applications of DNA fingerprinting

This technique is now used to:

(i) Identify criminals in forensic laboratories.

(ii) Settle paternity disputes.

(iii) Verify whether a hopeful immigrant is, as he or she claims, really a close relative of already an established resident.

(iv) Identify racial groups to rewrite biological evolution.