

CHAPTER 6

MOLECULAR BASIS OF INHERITANCE

POINTS TO REMEMBER

Anticodon : A sequence of three nitrogenous bases on tRNA which is complementary to the codon on mRNA.

Transformation : The phenomenon by which the DNA isolated from one type of a cell, when introduced into another type, is able to express some of the properties of the former into the latter.

Transcription : The process of copying genetic information from one strand of DNA into RNA.

Translation : The process of polymerisation of amino-acids to form a polypeptide as dictated by mRNA.

Nucleosome : The structure formed when negatively charged DNA is wrapped around positively charged histone octamer.

DNA Polymorphism : The variations at genetic level, where an inheritable mutation is observed.

Satellite DNA : The repetitive DNA sequences which form a large portion of genome and have high degree of polymorphism but do not code for any proteins.

Operon : A group of genes which control a metabolic pathway.

Exons : The regions of a gene which become part of mRNA and code for different regions of proteins.

Introns : The regions of a gene which are removed during the processing of mRNA.

Euchromatin : The region of chromatin which is loosely packed and transcriptionally active.

Heterochromatin : The chromatin that is more densely packed, stains dark and is transcriptionally inactive.

Capping : Adding of methyl guanosine triphosphate to the 5' end of hnRNA.

Splicing : The process in eukaryotic genes in which introns are removed and the exons are joined together to form mRNA.

Central Dogma :



Replication fork : The Y shaped structure formed when double stranded DNA is unwound upto a point during its replication.

VNTR : Variable Number Tandem Repeats

YAC : Yeast Artificial Chromosome

BAC : Bacterial Artificial Chromosome

SNPs : Single Nucleotide polymorphism

HGP : Human Genome Project

hnRNA : Heterogenous nuclear RNA. It is precursor of mRNA.

Chemical Structure of Polynucleotide Chain (DNA/RNA) : A nucleotide has three components—

1. **Nitrogen base**

(i) *Purines* : Adenine and Guanine

(ii) *Pyrimidines* : Cytosine, Thymine and Uracil

Thymine in DNA and Uracil in RNA.

2. **Pentose Sugar** : Ribose (in RNA) or Deoxyribose (in DNA).

3. **Phosphate Group**

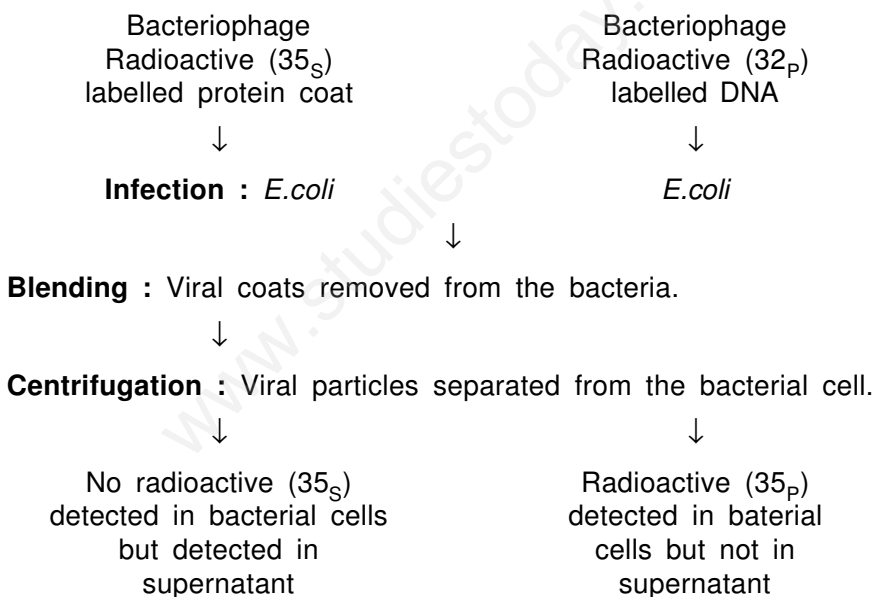
- ☐ Nitrogen base is linked to pentose sugar through N-glycosidic linkage.
- ☐ Nitrogen base + Sugar = Nucleoside
- ☐ Phosphate group is linked to 5'-OH of a nucleoside through phosphoester linkage.
- ☐ Nucleoside + Phosphate group = Nucleotide.
- ☐ Two nucleotides are linked through 3'-5' phosphodiester linkage to form a dinucleotide
- ☐ A polynucleotide chain has free phosphate group at 5'-end of ribose sugar and 3'-OH group at other end.

RNA is highly reactive than DNA : In RNA nucleotide has an addition -OH group at 2'-position in the ribose; RNA is also catalytic.

Double-helix Structure of DNA : Proposed by Watson and Crick in 1953.

- (i) DNA is made up of two polynucleotide chains.
- (ii) The backbone is made up of sugar and phosphate and the bases project inside.
- (iii) Both polynucleotide chains are antiparallel i.e. one chain has polarity 5'-3' and other chain has 3'-5'.
- (iv) These two strands of chains are held together by hydrogen bonds i.e. A=T, G=C.
- (v) Both chains are coiled in right handed fashion. The pitch of helix is 3.4 nm with 10 bp in each turn.

Hershey and Chase Experiment : In 1952, Hershey and Chase performed an experiment on bacteriophages (Viruses that infect bacteria) and proved that DNA is the genetic material.



Conclusion : DNA is the genetic material.

Meselson and Stahl's Experiment :

- ☐ Meselson and Stahl performed the experiment in 1958 on *E.coli* to prove that DNA replication is semiconservative.
- ☐ *E.coli* was grown in $^{15}\text{NH}_4\text{Cl}$ for many generations.
- ☐ ^{15}N was incorporated into newly synthesised DNA.
- ☐ This heavy DNA could be differentiated from normal DNA by centrifugation in cesium chloride (CsCl) density gradient.

- ❑ Then they transferred these *E.coli* into a medium with normal $^{14}\text{NH}_4\text{Cl}$.
- ❑ After 20 minutes, it was found that all the DNA molecules of daughter cells were hybrid—First generation.
- ❑ After 40 minutes, it was found that 50% DNA molecules were hybrid and 50% were normal—second generation.

DNA Replication :

- (i) **Origin of replication** - it is the starting point when replication of DNA begins.
- (ii) **Replication fork** - for long DNA molecules, since the two strands of DNA cannot be separated in its entire length, the replication occurs within a small opening of DNA helix, referred to as replication fork.
- (iii) **Continuous synthesis** - DNA dependent DNA polymerase catalyses polymerisation only in $5' \rightarrow 3'$ direction, one strand (the template with polarity $3' \rightarrow 5'$), the replication is continuous.
- (iv) **Discontinuous synthesis** - In the template with $5' \rightarrow 3'$ the replication is discontinuous and the fragments are joined by enzyme ligase.

Transcription in Prokaryotes : In prokaryotes the process of transcription is completed in three steps:

1. **Initiation** : RNA polymerase binds with initiation factor (sigma factor) and then binds to promoter site.
2. **Elongation** : RNA polymerase separates from sigma factor and adds nucleoside triphosphate as substrate. RNA is formed during the process following the rule of complementarity and remains bound to enzyme RNA polymerase.
3. **Termination** : On reaching terminator region RNA polymerase binds with rho factor (terminator factor). As a result nascent RNA separates.

Transcription in Eukaryotes :

- ❑ In eukaryotes three types of RNA polymerases found in the nucleus (apart from RNA polymerases are found in the organelles) are involved in transcription.

RNA Polymerase I : Transcribes rRNAs.

RNA Polymerase II : Transcribes hnRNA (which is precursor of mRNA).

RNA Polymerase III : Transcribes tRNA, 5 srRNA and snRNA.

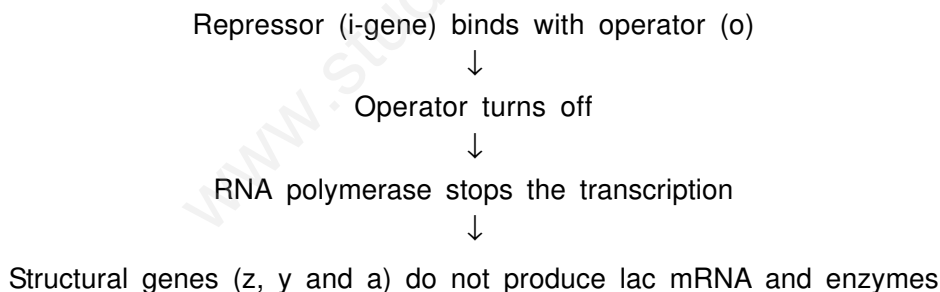
- ❑ The primary transcript has both exon and intron regions.
- ❑ Introns which are non-coding regions removed by a process called splicing.

- ❑ hnRNA undergoes two additional processes :
 - (a) **Capping** : An unusual nucleotide (methylguanosine triphosphate) is added to 5'-end of hnRNA.
 - (b) **Tailing** : Adenylate residues (200-300) are added at 3'-end.
- It is fully processed hnRNA, now called mRNA is transported out of the nucleus

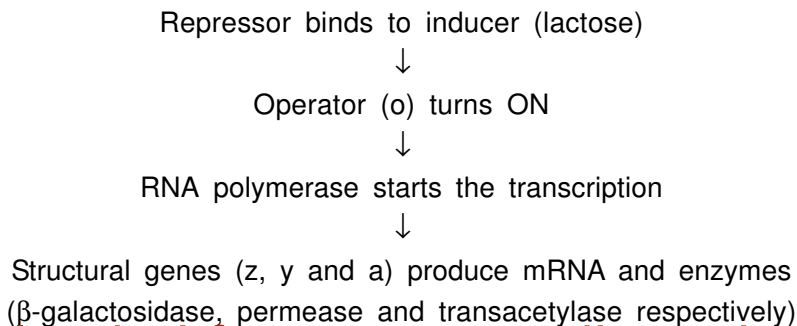
Lac Operon

- ❑ The concept of operon was proposed by Jacob Monod. Operon is a unit of prokaryotic gene expression.
- ❑ The lac operon consists of one regulatory gene (the i-gene) and three structural genes (z, y and a).
- ❑ The i-gene codes for repressor of lac operon.
- ❑ Lactose is an inducer.
- ❑ Gene Z - Codes for β -galactosidase
Gene Y - Codes for permease
Gene A - Codes for transacetylase.

In the absence of Inducer (lactose)



In the presence of Inducer (lactose)



Packaging of DNA Helix

- ❑ The average distance between the two adjacent base pairs is 0.34 nm ($0.34 \times 10^{-9} \text{m}$ or $3.4 \text{\AA}$)
- ❑ The number of base pairs in *E.coli* is 4.6×10^6 .
- ❑ **DNA Packaging in Prokaryotes** - DNA is not scattered throughout the cell. DNA (negatively charged) is held by some proteins (has positive charges) in a region termed as 'nucleoid'. The DNA in nucleoid is organised in large loops held by proteins.
- ❑ **DNA packaging in Eukaryotes** - There is a set of positively charged basic proteins called histones. Histones are rich in the basic amine and residues lysines and arginines.
- ❑ Histones are organised to form a unit of eight molecules called histone octamer.
- ❑ The negatively charged DNA is wrapped around positively charged histone octamer to form a structure called nucleosome
- ❑ Nucleosomes constitute the repeating unit of a structure in nucleus called chromatin
- ❑ The beads-on-string structure in chromatin is packaged to form chromatin fibres that are further coiled and condensed at metaphase stage of cell division to form chromosomes
- ❑ The packaging of chromatin at higher level requires additional set of protein that collectively are referred to as Non-histone chromosomal (NHC) proteins. At places chromatin is densely packed to form darkly staining heterochromatin. At other places chromatin is loosely packed to form euchromatin

Genetic Code

- (i) The codon is triplet 61 codons code for amino acids and 3 codons function as stop codons (UAG, UGA, UAA)
- (ii) One codon codes for only one amino acid, hence the codon is unambiguous and specific.
- (iii) Some amino acids are coded by more than one codon – degenerate
- (iv) The codon is read in mRNA in a contiguous fashion. There are no punctuations
- (v) The code is nearly universal
- (vi) AUG has dual functions. It codes for Methionine (met) and it also acts as initiator codon.

tRNA—the Adapter Molecule :

- ❑ tRNA has an anticodon loop that has bases complementary to the code and also has an amino acid acceptor end through which it binds to amino

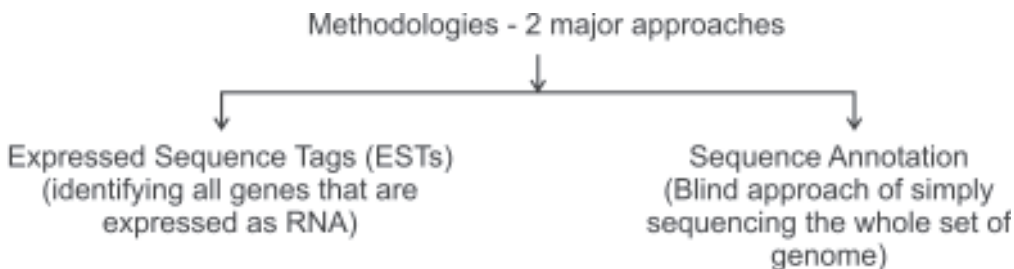
acids.

Translation :

- ❑ Translation refers to the process of polymerisation of amino acids to form a polypeptide. The order and sequence of amino acids are defined by the sequence of bases in the mRNA.
- ❑ First step is - charging of tRNA or aminoacylation of tRNA-here amino acids are activated in the presence of ATP and linked to specific tRNA.
- ❑ Initiation - Ribosome binds to mRNA at the start codon (AUG) that is recognised by the initiator tRNA.
- ❑ **Elongation phase** - Here complexes composed of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with tRNA codon. The ribosomes move from codon to codon along with the mRNA. Amino acids are added one by one, translated into polypeptide sequences.
- ❑ **Termination** - Release factors binds to the stop codon, terminating translation and releasing the complete polypeptide from the ribosome.
- ❑ **Human Genome Project** was a 13 year project coordinated by the U.S. Department of energy and National Institute of Health, It was completed in 2003.

Important goals of HGP

- (i) Identify all the apponimately 20,000-25,000 genes in human DNA.
- (ii) Determine the sequences of the 3 million chemical base pairs that make up human DNA.
- (iii) Store this information in database.
- (iv) Transfer related technologies to other sectors, such as industries.
- (v) Address the ethical, legal and social issues (ELSI) that may arise from the project.



Salient Features of Human Genome - Refer Pg - 120, NCERT Class XII)

DNA Fingerprinting - is a technique of determining nucleotide sequences of certain areas of DNA which are unique to each individual

Principle of DNA Fingerprinting - Short nucleotide repeats in the DNA are very specific in each individual and vary in number from person to person but are inherited. These are 'Variable Number Tandem Repeats' (VNTRs). Each individual inherits these repeats from his/her parents which is used as genetic markers. One half of VNTR alleles of the child resembles that of the mother and other half the father.

Steps/procedure in DNA fingerprinting –

- Extraction of DNA - using high speed refrigerated centrifuge.
- Amplification - many copies are made using PCR
- Restriction Digestion - using restriction enzymes DNA is cut into fragments.
- Separation of DNA fragments - using electrophoresis-agarose polymer gel.
- Southern Blotting : Separated DNA sequences are transferred onto nitrocellulose or nylon membrane.
- Hybridisation : The nylon memberane exposed to radio active probes.
- Autoradiography : The dark bands develop at the probe site.

Applications of DNA Fingerprinting

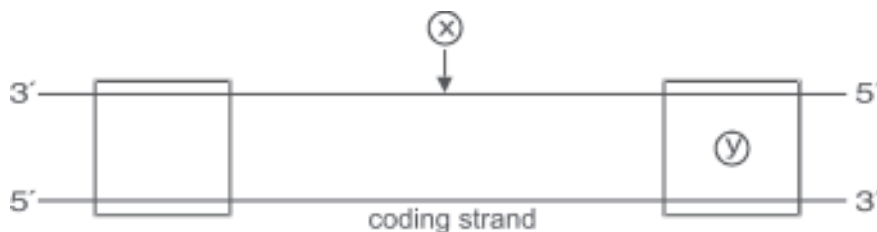
- (i) identify criminals in forensic labs.
- (ii) determine paternity
- (iii) verify whether a hopeful immigrant is really close relative of an already established resident.
- (iv) identify racial groups to rewrite biological evolution.

QUESTIONS

VSA (1 MARK)

1. Name the factors for RNA polymerase enzyme which recognises the start and termination signals on DNA for transcription process in Bacteria.
2. Mention the function of non-histone protein.
3. During translation what role is performed by tRNA
4. RNA viruses mutate and evolve faster than other viruses. Why?

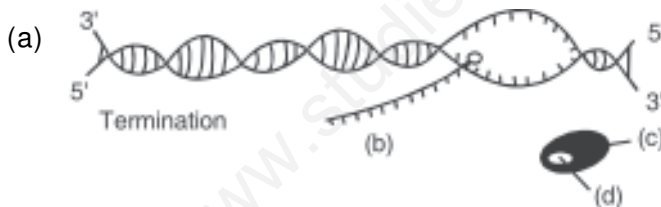
5. Name the parts 'X' and 'Y' of the transcription unit given below.



6. Mention the dual functions of AUG.
7. Write the segment of RNA transcribed from the given DNA –
 3' – A T G C A G T A C G T C G T A – 5' – Template Strand
 5' – T A C G T C A T G C A G C A T – 3' – Coding Strand.

SA-II (2 MARKS)

8. The process of termination during transcription in a prokaryotic cell is being represented here. Name the label a, b, c and d.



9. Complete the blanks a, b, c and d on the basis of Frederick Griffith Experiment.
- S Strain → inject into mice → (a)
- R strain → inject into mice → (b)
- S strain (heat killed) → inject into mice → (c)
- S strain (heat killed) + R strain (live) → inject into mice → (d)
10. Give two reasons why both the strands of DNA are not copied during transcription.
11. Mention any two applications of DNA fingerprinting.
12. State the 4 criteria which a molecule must fulfill to act as a genetic material.

SA-I (3 MARKS)

13. Give six points of difference between DNA and RNA in their structure/chemistry and function.
14. Explain how does the hnRNA becomes the mRNA.

OR

Explain the process of splicing, capping and tailing which occur during transcription in Eukaryotes.

15. Name the three major types of RNAs, specifying the function of each in the synthesis of polypeptide.
16. Enlist the goals of Human genome project.
17. A tRNA is charged with the amino acid methionine.
 - (i) Give the anti-codon of this tRNA.
 - (ii) Write the Codon for methionine.
 - (iii) Name the enzyme responsible for binding of amino acid to tRNA.
18. Illustrate schematically the process of initiation, elongation and termination during transcription of a gene in a bacterium.

LA (5 MARKS)

19. What is meant by semi conservative replication? How did Meselson and Stahl prove it experimentally?
20. What does the lac operon consist of? How is the operator switch turned on and off in the expression of genes in this operon? Explain.
21. State salient features of genetic code.
22. Describe the process of transcription of mRNA in a eukaryotic cell.
23. Describe the various steps involved in the technique of DNA fingerprinting.

ANSWERS

VSA (1 MARK)

1. Sigma (σ) factor and Rho(ρ) factor
2. Packaging of chromatin
3. (i) Structural role

(ii) Transfer of amino acid

4. –OH group is present on RNA, which is a reactive group so it is unstable and mutates faster.
5. X – Template strand, Y – Terminator.
6. (i) Acts as initiation codon for protein synthesis
(ii) It codes for methionine.
7. 5' – U A C G U C A U G C A G C A U – 3' (In RNA 'T' is replaced by 'U')

SA-II (2 MARKS)

8. (a) DNA molecule (b) mRNA transcript
(c) RNA polymers (d) Rho factor
9. (a) Mice die (b) mice live
(c) mice live (d) mice die
10. (a) If both the strands of DNA are copied, two different RNAs (complementary to each other) and hence two different polypeptides will produce; If a segment of DNA produces two polypeptides, the genetic information machinery becomes complicated.
(b) The two complementary RNA molecules (produced simultaneously) would form a doublestranded RNA rather than getting translated into polypeptides.
(c) RNA polymerase carries out polymerisation in 5' – 3' direction and hence the DNA strand with 3' – 5' polarity acts as the template strand. (Any two)
11. (i) To identify criminals in the forensic laboratory.
(ii) To determine the real or biological parents in case of disputes.
(iii) To identify racial groups to rewrite the biological evolution. (Any two)
12. (i) It should be able to generate its replica.
(ii) Should be chemically and structurally stable.
(iii) Should be able to express itself in the form of Mendelian characters.
(iv) Should provide the scope for slow changes (mutations) that are necessary for evolution.

LA (5 MARKS)

19. Meselson and Stahl, performed an experiment using *E.coli* to prove that DNA replication is semi conservative.

— Then separated heavy DNA from normal (^{14}N) by centrifugation in CsCl density gradient.

- The DNA extracted, after one generation of transfer from ^{15}N medium to ^{14}N medium, had an intermediate density.
- The DNA extracted after two generations consisted of equal amounts of light and hybrid DNA.
- They proved that DNA replicates in a semiconservative manner. (Refer figure 6.7, page 105, NCERT Biology XII).

20. Lac Operon consists of the following :

- **Structural genes** : z, y, a which transcribe a polycistronic mRNA.
- gene 'z' codes for β -galactosidase
- gene 'y' codes for permease.
- gene 'a' codes for transacetylase.
- **Promotor** : The site where RNA polymerase binds for transcription.
- **Operator** : acts as a switch for the operon
- **Repressor** : It binds to the operator and prevents the RNA Polymerase from transcribing.
- **Inducer** : Lactose is the inducer that inactivates the repressor by binding to it.
- Allows an access for the RNA polymerase to the structural gene and transcription.
- Refer figure 6.14, page 117, NCERT, Biology XII.

21. Refer notes

22. Refer notes 35 and figure 6.11, page 110, NCERT Biology XII.

23. Refer points to remember – Steps involved in DNA fingerprinting