CHAPTER **06**

Molecular Basis of Inheritance

1. Nucleic Acids

These are long polymers of nucleotides. Two types of nucleic acids are found in living systems, *i.e.* RNA and DNA.

2. Search for Genetic Material

Frederick Griffith, carried out a series of experiments with *Streptococcus pneumoniae* and discovered the genetic material as the transforming principle.

Avery, Macleod and McCarty worked to determine the biochemical nature of Griffith's transforming principle. They proved that DNA is the hereditary material. Hershey-Chase experiment with bacteriophage porved that DNA is the genetic material that is passed from one generation to the next.

(i) **DNA** acts as the genetic material in most organisms. It is a long polymer of deoxyribonucleotides. It codes for all the metabolic processes of life.

(ii) **RNA** helps in the transfer and expression of information. It functions as messenger RNA (*m*RNA) for the translation of proteins.

(iii) **Nucleoside and nucleotide** A nucleoside is formed when a nitrogenous base is linked to a pentose sugar through N-glycosidic linkage. A nucleotide is the basic unit of DNA and RNA, composed of a nitrogenous base, a pentose sugar and a phosphate group.

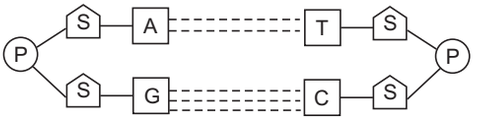
(iv) **Nitrogenous bases** are of two types, *i.e.* purines (adenine, guanine) and pyrimidines (cytosine, uracil, thymine).

RNA contains uracil in place of thymine.

Two types of sugars are present in RNA and DNA, *i.e.* ribose and deoxyribose, respectively.

- RNA functions as an adapter, structural and a catalytic molecule.
- RNA also acts as a genetic material in some viruses.
- Although both RNA and DNA can act as genetic material, but DNA being chemically and structurally more stable is a better choice.
- RNA was the first to evolve and DNA was derived from RNA.

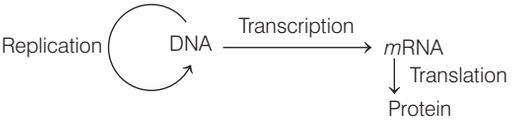
In DNA, adenine pairs with thymine through two H-bonds, while the guanine pairs with cytosine through three H-bonds. This makes one strand complementary to the other.



Polynucleotide chain

3. Central Dogma of Molecular Biology

Francis Crick proposed the 'Central dogma' in molecular biology which states that genetic information flows in the following manner.



4. Genetic Material in Prokaryotic and Eukaryotic Cells

(i) In **prokaryotic cells**, DNA (negatively charged) is held together with some proteins (positively charged) in a region known as nucleoid.

(ii) In **eukaryotic cells**, there is a set of positively charged proteins called **histones** which are organised to form a unit of eight molecules called **histone octamer**. The negatively charged DNA is wrapped around the positively charged histone octamer to form a structure called **nucleosome** which is the unit of compaction.

5. Packaging of Chromatin

The packaging of chromatin at higher level requires additional set of proteins that are collectively called as **Non-Histone Chromosomal** (NHC) proteins.

6. Euchromatin and Heterochromatin

Some regions of chromatin which are loosely packed (stain light) are called euchromatin (active chromatin). In some regions, chromatin is densely packed (stain dark), it is called heterochromatin (inactive chromatin).

7. Replication of DNA

The DNA replicates semiconservatively. According to this scheme, the two strands of double-helix would separate and act as a template for the synthesis of new complementary strands. The process is guided by complementary H-bonding. The process is catalysed by various sets of enzymes which are as follows

(i) **DNA dependent DNA polymerase**, uses DNA template to catalyse the polymerisation of deoxynucleotides.

(ii) **DNA helicase**, unwinds DNA strand for the formation of a replication fork.

(iii) **DNA ligase**, facilitates the joining of DNA strands together by catalysing the formation of phosphodiester bond.

On $3' \rightarrow 5'$ strand, replication is continuous and on $5' \rightarrow 3'$ strand, it is discontinuous. DNA replication begins at a specific and fixed position of DNA molecule known as **origin of replication**.

8. Types of RNA

There are following three types of RNA, *i.e.* **messenger RNA** (*m*RNA) which provides the template for transcription, **transfer RNA** (*t*RNA), which brings amino acids and reads the genetic code and **ribosomal RNA** (*r*RNA), which plays structural and catalytic role during translation.

Note ***t*RNA** is an adapter molecule which can read the code on one end and on the other end could bind to the specific amino acid. *t*RNA has five loops, *i.e.* anticodon loop, amino acid acceptor end, T-loop, D-loop and variable loop. It is a clover leaf-shaped molecule.

Transcription in Eukaryotes and Prokaryotes

Transcription is the process of copying genetic information from one strand of the DNA into RNA. In this only a segment of DNA or only one out of the two strands is copied into RNA.

(i) **In prokaryotes**, like bacteria, the transcribed *m*RNA is functional, so it can be directly translated.

(ii) **In eukaryotes**, the genes are split. The coding sequences, *i.e.* exons are interrupted by non-coding sequences, *i.e.* introns. Introns are removed and exons are joined together to produce functional RNA. This is called **splicing**. A transcription unit in DNA has three regions, *i.e.* a promoter, the structural gene and a terminator.

9. Post Transcriptional Modifications

Heteronuclear RNA (*hn*RNA) The *hn*RNA undergoes two additional processes

(i) **Capping,** where methyl guanosine triphosphate, is added to the $5'$ end of *hn*RNA.

(ii) **Tailing,** where adenylate residues (200-300) are added at $3'$ end in a template independent manner.

10. Genetic Code

It is the relationship between the sequence of nucleotides on *m*RNA and the sequence of amino acids in the polypeptide.

(i) **Artificial synthesis of genetic code** Dr. Har Gobind Khorana, developed a chemical method for the synthesis of RNA molecule with defined base combination to develop a genetic code.

(ii) **Important features of genetic code** It has following features

- Genetic code is unambiguous and specific, *i.e.* one codon codes for only one amino acid.
- Codon is triplet and degenerate.
- The genetic code is **universal**, *i.e.* one codon codes for the same amino acid in all organisms.
- AUG codon has dual function, *i.e.* it codes for the amino acid methionine (*met*) and also acts as an initiation codon.
- Three codons do not code for any amino acid, hence they function as **stop codon,** *e.g.* UAA, UGA, UAG.

11. Translation

The process of polymerisation of amino acids to form a polypeptide is known as translation. In this process, proteins are synthesised from *m*RNA with the help of ribosomes.

(i) **Ribosome** exists as two subunits in inactive state, *i.e.* small subunit and large subunit.

(ii) Different phases of translation are

- Initiation of polypeptide synthesis
- Elongation of polypeptide chain
- Termination of polypeptide synthesis

12. Gene Expression in Prokaryotes and Eukaryotes

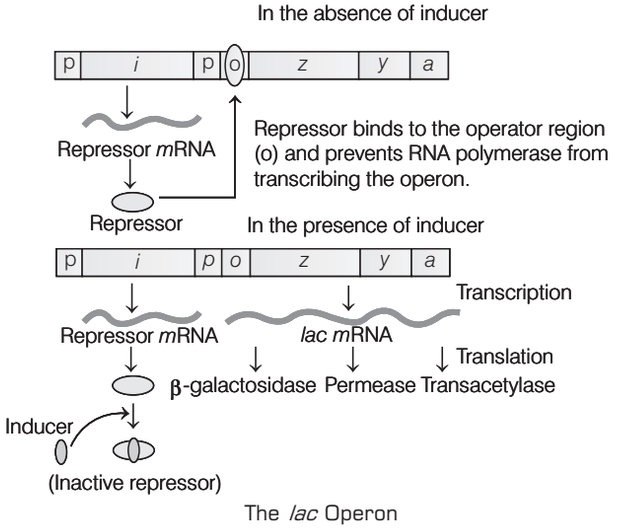
Regulation of gene expression occurs at various levels. Gene expression results in the formation of a polypeptide.

(i) In **prokaryotes**, it is regulated by the rate of initiation of transcription and in eukaryotes, regulation is achieved at the following four levels

- Transcriptional level (formation of primary transcript).
- Processing level (regulation of splicing).
- Transport of *m*RNA from nucleus to the cytoplasm.
- Translational level.

(ii) **Operon** is a transcriptionally regulated system, where a polycistronic structural gene is regulated by a common promoter and regulatory genes, *e.g. lac* (lactose) operon, *ara* (arabinose) operon, *his* (histidine) operon, *val* (valine) operon, etc.
***Lac* operon** was proposed by Francois Jacob and Jacque Monod.

(iii) ***Lac* operon** is the prototype (inducible) operon in bacteria, which codes for genes responsible for the metabolism of lactose.



The *lac* Operon

- The operon is regulated by the amount of lactose in the medium, where the bacteria are grown. Therefore, this regulation can also be viewed as regulation of enzyme synthesis by its substrate.

13. Human Genome Project

It was a mega project of 13 years. It was aimed to sequence every base in human genome. This project has yielded a lot of new information. Many new areas and avenues have opened up as a consequence of this project.

14. Rice Genome Project

Rice was the first crop whose genome was sequenced. It was a project of 10 years. It provided an excellent opportunity to illustrate the impact on plant biology and breeding. The knowledge of genetic code of rice helps breeders to develop strains of the crop with specific characteristics (*e.g.* stress tolerance, disease resistance or high yield).

15. DNA Fingerprinting

It is a technique used to find out variations in individuals of a population at DNA level. It works on the principle of polymorphism in DNA sequences. It has immense applications in the field of forensic science, genetic biodiversity, evolutionary biology and kinship relationships.

(The technique has the following steps)

(i) DNA isolation

(ii) Amplification

(iii) Separation of DNA fragments by electrophoresis

(iv) Blotting (transfer of the separated DNA fragments to synthetic membranes like nylon or nitrocellulose)

(v) Hybridisation

(vi) Autoradiography.

Practice Questions

1. The length of DNA usually depends on

(a) position of nucleotides (b) number of nucleotides
(c) Both (a) and (b) (d) None of the above

2. Find the incorrect match.

(a) A bacteriophage ($\phi \times 174$) –5386 nucleotides
(b) Bacteriophage lamda – 48502 base pairs
(c) *E. coli* – 4.6×10^6 bp
(d) Haploid content of human DNA – 3.3×10^6 bp

3. Nitrogenous bases are linked to sugar by

(a) hydrogen bond (b) phosphodiester bond
(c) N-glycosidic bond (d) O-glycosidic bond

4. When a phosphate group is linked to ...*A*... group of nucleoside through ...*B*... bond, a corresponding ...*C*... is formed.

Choose the correct option for *A, B* and *C*.

(a) A–5′ OH, B–phosphodiester bond, C–nucleotide
(b) A–3′ OH, B–phosphodiester bond, C–nucleotide
(c) A–2′ OH, B–phosphodiester bond, C–nucleotide
(d) A–5′ OH, B–phosphodiester bond, C–nucleoside

5. Choose the correct option.

(a) Pyrimidines include adenine and guanine
(b) Pyrimidines include cytosine, uracil and thymine
(c) Purines include adenine and thymine
(d) Purines include guanine and cytosine

6. A polymer or a polynucleotide chain has at one end a free .....*A*..... at 5′ end of sugar, similarly at the other end of the polymer the sugar has a free .....*B*..... of 3′ group.

(a) A – Phosphate moiety, B – OH
(b) A – OH, B – Phosphate moiety
(c) A – COOH, B – Phosphate moiety
(d) A – Phosphate moiety, B–COOH

7. Choose the incorrect option.

(a) Friedrich Miescher in 1869 identified DNA as an acidic substance and named it nuclein
(b) Erwin Chargaff said, the ratio between A and T and G and C of *ds*DNA are constant and equals one
(c) The two strands of *ds*DNA are complementary to each other
(d) None of the above

8. Which of the following is not the correct salient feature of double-helix structure of DNA?

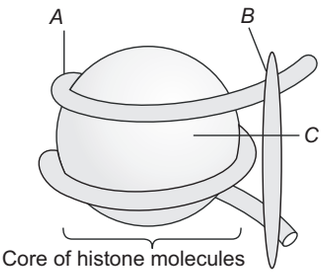
(a) Two polynucleotide chains have backbone of sugar and phosphate and bases project inside
(b) Two chains have antiparallel polarity, i.e. one is 5′ → 3′ and other is 3′ → 5′
(c) Adenine forms three hydrogen bonds with thymine and guanine forms two hydrogen bonds with cytosine
(d) The plane of one base pair stacks over the other in double helix in addition to H-bond to confer extra statbility to helical structure

9. In prokaryotes (such as *E. coli*) ...*A*... nucleus is not present, the DNA is not scattered throughout the cell. DNA is ...*B*... charged and holded by the ...*C*... charged proteins. This structure in prokaryotes is called ...*D*... .

Choose the correct option for *A, B, C* and *D*.

(a) A–undefined, B–negatively, C–positively, D–nucleoid
(b) A–undefined, B–negatively, C–positively, D–nucleus
(c) A–defined, B–negatively, C–positively, D–nucleoid
(d) A–defined, B–positively, C–negatively, D–nucleoid

10. In the given diagram, identify *A, B* and *C*.



(a) A–DNA, B–H1 histone, C–Histone octamer
(b) A–RNA, B–H1 histone, C–Histone octamer
(c) A–DNA, B–H1 histone, C–Histone tetramer
(d) A–RNA, B–H1 histone, C–Histone tetramer

11. Lightly stained part of chromatin which remains loosely packed and is transcriptionally active named as

(a) euchromatin (b) heterochromatin
(c) chromatosome (d) chromonemata

12. What was unique in Griffith's experiments?

(a) DNA was found to be the genetic material
(b) RNA was found to be the genetic material
(c) Something from dead organisms could change the living cells
(d) Viruses can live in bacteria

13. Isotopes used by Hershey and Chase were

(a) ^{32}P and ^{35}S (b) ^{35}P and ^{32}S
(c) ^{34}P and ^{31}S (d) ^{30}P and ^{32}S

14. Hershey and Chase concluded that viral infecting agent in their experiment was

(a) Protein (b) DNA
(c) RNA (d) Both (b) and (c)

15. RNA is the genetic material in

(a) All bacteria
(b) Tobacco Mosaic Viruses (TMV)
(c) QB bacteriophage
(d) Both (b) and (c)

16. Who experimentally proved the semiconservative mode of DNA replication?

(a) Mathew Meselson (b) Franklin Stahl
(c) Both (a) and (b) (d) Watson and Crick

17. In Meselson and Stahl's experiment (1958), DNA extracted from the culture one generation after the transfer from ^{15}N to ^{14}N medium had a hybrid (or intermediate) density. Why?

(a) Because the generation time of *E. coli* (culture) was about 20 minutes
(b) Because it would take 20 minutes for RNA replication
(c) Because it would take 20 minutes for replication of DNA to RNA (transcription)
(d) Because it would take 20 minutes for translation RNA to protein

18. Similar experiments like Meselson and Stahl was performed by Taylor in 1958. The experimental organism of Taylor was

(a) *Vicia faba* (b) Fungi (c) *E. coli* (d) Protista

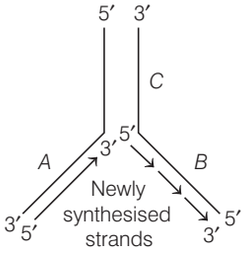
19. For long DNA molecules, the two strands of DNA cannot be separated in its entire length due to the requirement of

(a) enzymes
(b) high energy
(c) RNA
(d) phosphate and nucleotide

20. DNA-dependent DNA polymerases catalyses polymerisation in which direction?

(a) $3' \rightarrow 5'$ (b) $5' \rightarrow 2'$ (c) $5' \rightarrow 3'$ (d) $2' \rightarrow 5'$

21. Identify *A, B* and *C* strands.



(a) A–Continuous strand, B–Discontinuous strand, C–Template strand
(b) A–Leading strand, B–Lagging strand, C–Parental strand
(c) A– 5′–3′ strand, B– 3′–5′ strand, C–Parental strand
(d) All of the above

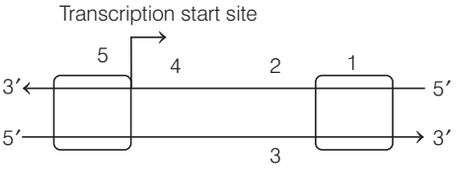
22. Deoxyribonucleoside triphosphate serve dual purposes. The purposes are

(a) act as substrate and decrease reaction rate
(b) provide energy for polymerisation and act as substrate
(c) decrease reaction rate and provide energy for polymerisation
(d) Synthesise RNA primer and decrease reaction rate

23. Why both the strands of DNA are not copied during transcription?

(a) Because RNA molecule with different sequences will be formed
(b) Because RNA molecule with same sequences will be formed
(c) Because RNA molecule with identical sequences will be formed
(d) Because DNA molecule with different sequences will be formed

24. In given diagram find out



A. Promoter site B. Structural gene
C. Terminator site D. Template strand
E. Coding strand

Codes

	A	B	C	D	E
(a)	5	1	4	2	3
(b)	5	1	4	3	2
(c)	5	4	1	2	3
(d)	5	4	1	3	2

25. In bacteria, which enzyme catalyses the transcription of all types of RNA (*m*RNA, *t*RNA and *r*RNA)?

(a) DNA-dependent RNA polymerase
(b) DNA-dependent DNA polymerase
(c) RNA-dependent RNA polymerase
(d) RNA-dependent DNA polymerase

26. Name the nucleotide added to 5′ end of *hn*RNA in capping.

(a) Ethyl cytosine triphosphate
(b) Ethyl guanosine triphosphate
(c) Methyl guanosine triphosphate
(d) Methyl cytosine triphosphate

27. Choose the correct option.

(a) Splicing represent the dominance of RNA world
(b) The presence of introns is reminiscent of antiquity
(c) Split gene arrangements represent an ancient feature of the genome
(d) All of the above

28. Codons are non-ambiguous, which means that one codon codes for

(a) more than one amino acid
(b) two amino acids
(c) Only one amino acid
(d) non-sense amino acid

29. Degeneracy refers to

(a) one amino acid has more than one code triplet
(b) one amino acid has only one code triplet
(c) codons which specify the same amino acids differ only in the third base of the triplet
(d) Both (a) and (c)

30. Choose the incorrect option for *t*RNA molecule.

(a) It has an anticodon loop that has bases complementary to the code
(b) It has an amino acid acceptor end to which it binds to amino acids
(c) *t*RNA are not specific for each amino acid
(d) *t*RNA looks like a clover leaf

31. The process of polymerisation of amino acids to form a polypeptide is

(a) transcription (b) replication
(c) translation (d) polymerisation

32. Which among the following process occur(s) during charging or aminoacylation of *t*RNA?

(a) Activation of amino acids in the presence of ATP
(b) Linking of amino acids to their cognate *t*RNA
(c) Both (a) and (b)
(d) None of the above

33. UTRs present on *m*RNA refer to

(a) Untranscribed regions at both 5′ end and 3′ end
(b) Untranslated regions at 5′ end
(c) Untranslated regions at both 5′ end and 3′ end
(d) Untranslated regions at 3′ end

34. Termination of protein synthesis or translation requires

(a) Both stop signal and starting codon
(b) Both starting codon and release factor
(c) Both release factor and stop codon
(d) GUG and AUG codon

35. In prokaryotes, control of the rate of ...*A*... is the pre-dominant site for the control of gene expression. In a transcription unit, the activity of ...*B*... at a given promoter is in turn regulated by interaction with ...*C*... proteins, which affects its ability to recognise the start sites.
Complete the statement filling the correct options in given blanks.

(a) A–RNA replication, B–DNA polymerase, C–accessory
(b) A–transcriptional initiation, B–RNA polymerase, C–accessory
(c) A–translational initiation, B–RNA polymerase, C–accessory
(d) A–DNA replication, B–RNA polymerase, C–accessory

36. Positively regulatory proteins are called

(a) activator (b) repressors
(c) necessary proteins (d) accessory proteins

37. Lactose is a substrate for

(a) galactosidase (b) α-galactosidase
(c) β-galactosidase (d) γ-galactosidase

38. Lactose is transported into cells through

(a) β-galactosidase (b) permease
(c) transacetylase (d) transferase

39. Why glucose and galactose cannot act as an inducer for *lac* operon?

(a) Because they cannot bind with the repressor
(b) Because they can bind with the repressor
(c) Because they can bind with the operator
(d) Because they can bind with the regulator

40. Which of the following option is true for Human Genome Project (HGP)?

(a) It was launched in the year 1990 and was called mega project
(b) Total estimated cost of the project would be 9 billion US dollars
(c) It aims to identify all 20000-25000 genes in human DNA
(d) All of the above

41. Identify the incorrect pair.

(a) Expressed sequence tags — Genes that are express as RNA
(b) Sequence annotation — Sequencing genome with coding sequences
(c) Automated DNA sequences — Work on the principle developed by Frederick Sanger
(d) None of the above

42. DNA fingerprinting involves identifying the differences in some specific regions in DNA sequence called

(a) non-repetitive DNA
(b) coding DNA
(c) non-coding DNA
(d) repetitive DNA

43. Alec Jeffreys used a satellite DNA as probe that shows very high degree of polymorphism. It was called as

(a) Short Number of Tandem Repeats (SNTRs)
(b) Large Number of Tandem Repeats (LNTRs)
(c) Variable Number of Tandem Repeats (VNTRs)
(d) All of the above

ANSWERS

1.	(b)	**2.**	(d)	**3.**	(c)	**4.**	(a)	**5.**	(b)	**6.**	(a)	**7.**	(d)	**8.**	(c)	**9.**	(c)	**10.**	(a)
11.	(a)	**12.**	(c)	**13.**	(a)	**14.**	(b)	**15.**	(d)	**16.**	(c)	**17.**	(a)	**18.**	(a)	**19.**	(b)	**20.**	(c)
21.	(a)	**22.**	(b)	**23.**	(a)	**24.**	(c)	**25.**	(a)	**26.**	(c)	**27.**	(d)	**28.**	(c)	**29.**	(d)	**30.**	(c)
31.	(c)	**32.**	(c)	**33.**	(c)	**34.**	(c)	**35.**	(b)	**36.**	(a)	**37.**	(c)	**38.**	(b)	**39.**	(a)	**40.**	(d)
41.	(b)	**42.**	(d)	**43.**	(c)														

Hints & Explanations

1. (***b***) Length of DNA is directly proportional to the number of nucleotides. As the number of nucleotides increases, the length of DNA also increases.

2. (***d***) Option (d) is the incorrect match and can be corrected as
Haploid content of human DNA is 3.3×10^9 bp.
Rest of the matches are correct.

8. (***c***) Option (c) is incorrect and can be corrected as
Adenine forms two hydrogen bonds with thymine of the opposite strand and *vice-versa*. On the other hand, guanine is bounded with cytosine with three H-bonds.
Rest of the options are correct.

12. (***c***) In Griffith's experiment, he found out that something from dead organism could change the living cells. From his experiment he showed that dead S-bacteria (virulent) are changing (transforming) the R-bacteria (non-virulant) into S-type, i.e. the virulent strain.

13. (***a***) Hershey and Chase grew cultures of *Escherichia coli*. One culture was supplied with radioactive sulphur (^{35}S) and the another with radioactive phosphorus (^{32}P).

17. (***a***) In Meselson and Stahl's experiment, the generation time (replication time) of *E. coli* culture is about 20 minutes. Therefore, the DNA extracted after the interval of 20 minutes in the experiment had heavy ^{15}N incorporated in its genetic material and had a hybrid density.

18. (***a***) An experiment similar to Meselson and Stahl experiment was performed on *Vicia faba* (faba beans) by Taylor and colleagues in 1958. The experiments proved that the DNA in chromosomes also replicate semiconservatively.

19. (***b***) Separation of the entire length of DNA helix needs a large amount of energy. Hence, only up to certain extent separation of DNA helix can take place.

22. (***b***) Option (b) is correct. The phosphorylated nucleotides are *de*ATP (deoxy Adenosine Triphosphate), *de*CTP (deoxy Cytidine Triphosphate), *de*TTP (deoxy Thymidine Triphosphate). These triphosphates serve dual purpose. These act as substrate as well as provide energy for polymerisation of nucleotides by releasing energy after dissociating the phosphate group.

23. (***a***) The strands in the DNA are complementary to each other, not identical. If the two RNAs are formed from both strands then RNAs with different sequences would be formed.

29. (***d***) Degeneracy refers to the fact that one amino acid has more than one code triplet and the codons which specify the same amino acids differ only in the third base of the triplet, e.g. both CAC and CAU code for the amino acid histidine.

33. (***c***) UTRs present on *m*RNA refer to Untranslated Regions present at both 5′–end (before start codon) and 3′–end (after stop codon). These are the additional sequences that are not translated. These are required for efficient translation process.

36. (***a***) Positively regulatory proteins are called activators. These activator proteins bind to regulatory sites on DNA near to the promoter regions which act as on / off switches. This binding facilitates RNA polymerase activity and transcription of nearby genes.

37. (***c***) Lactose is the substrate for the enzyme beta (β) galactosidase and it regulates the switching on and off of the *lac* operon. Hence, it is termed as inducer.

39. (***a***) An inducer binds with the repressor protein and prevents the repressor protein from binding to the operator.
Glucose and galactose cannot act as an inducer because these do not have the binding sites for attaching the repressor protein.

41. (***b***) Option (b) is the incorrect match and can be corrected as
Sequence annotation is simply sequencing the whole set of genome that contained all the coding and non-coding sequence and later assigning different regions in the sequence with functions.
Rest of the matches are correct.