Chapter 5: Molecular Basis of Inheritance

Exercises — Chapter-end Exercises

Q1 Group the following as nitrogenous bases and nucleosides: Adenine, Cytidine, Thymine, Guanosine, Uracil and Cytosine.

SOLUTION

Nitrogenous bases are the nitrogen-containing ring structures themselves (purines and pyrimidines), while nucleosides are formed when a nitrogenous base is linked to a pentose sugar via an N-glycosidic bond.

Nitrogenous bases: Adenine, Thymine, Uracil, Cytosine

Nucleosides: Cytidine (cytosine + ribose), Guanosine (guanine + ribose)

Note: Adenine, Thymine, Uracil, and Cytosine appear in the list as free bases. Cytidine and Guanosine are nucleosides (base + sugar, without a phosphate group).

Answer: Nitrogenous bases: Adenine, Thymine, Uracil, Cytosine. Nucleosides: Cytidine, Guanosine.

Q2 If a double stranded DNA has 20 per cent of cytosine, calculate the per cent of adenine in the DNA.

SOLUTION

In double-stranded DNA, base pairing follows Chargaff's rules:
— Adenine (A) pairs with Thymine (T), so %A = %T
— Guanine (G) pairs with Cytosine (C), so %G = %C
— Total: %A + %T + %G + %C = 100%

Given: %C = 20%
Therefore: %G = 20% (since G pairs with C)

%A + %T + %G + %C = 100%
%A + %T = 100% − 20% − 20% = 60%

Since %A = %T:
%A = 60% ÷ 2 = 30%

Answer: Adenine = 30%

Q3 If the sequence of one strand of DNA is written as follows:
5'-ATGCATGCATGCATGCATGCATGCATGC-3'
Write down the sequence of complementary strand in 5'→3' direction.

SOLUTION

The complementary strand is antiparallel, so it runs 3'→5' with respect to the given strand. Base pairing rules: A pairs with T, T pairs with A, G pairs with C, C pairs with G.

Given strand (5'→3'): ATGCATGCATGCATGCATGCATGCATGC

Complementary strand (3'→5'): TACGTACGTACGTACGTACGTACGTACG

Written in 5'→3' direction (reversed):
5'-GCATGCATGCATGCATGCATGCATGCAT-3'

Answer: 5'-GCATGCATGCATGCATGCATGCATGCAT-3'

Q4 If the sequence of the coding strand in a transcription unit is written as follows:
5'-ATGCATGCATGCATGCATGCATGCATGC-3'
Write down the sequence of mRNA.

SOLUTION

The coding strand has the same sequence as the mRNA, except that thymine (T) in DNA is replaced by uracil (U) in RNA.

Coding strand: 5'-ATGCATGCATGCATGCATGCATGCATGC-3'

mRNA sequence (replace T with U, same 5'→3' direction):
5'-AUGCAUGCAUGCAUGCAUGCAUGCAUGC-3'

Answer: mRNA: 5'-AUGCAUGCAUGCAUGCAUGCAUGCAUGC-3'

Q5 Which property of DNA double helix led Watson and Crick to hypothesise semi-conservative mode of DNA replication? Explain.

SOLUTION

The property of complementary base pairing between the two strands of the DNA double helix led Watson and Crick to hypothesise the semi-conservative mode of replication.

Explanation: In the double helix, adenine always pairs with thymine (via two hydrogen bonds) and guanine always pairs with cytosine (via three hydrogen bonds). The two strands are therefore complementary to each other — if the sequence of one strand is known, the sequence of the other can be predicted.

Watson and Crick reasoned that if the two strands separated, each strand could serve as a template for the synthesis of a new complementary strand. After replication, each daughter DNA molecule would consist of one original (parental) strand and one newly synthesised strand. This is termed semi-conservative replication because half of the original DNA is

conserved in each daughter molecule.

This scheme was later experimentally proven by Meselson and Stahl (1958) using $^{15}N/^{14}N$ isotope labelling and CsCl density gradient centrifugation.

Answer: The complementary base pairing property: each strand acts as a template for the new strand, so each daughter DNA retains one parental strand — semi-conservative replication.

Q6 Depending upon the chemical nature of the template (DNA or RNA) and the nature of nucleic acids synthesised from it (DNA or RNA), list the types of nucleic acid polymerases.

SOLUTION

Nucleic acid polymerases are classified based on the template used and the product synthesised:

1. DNA-dependent DNA polymerase: Template = DNA, Product = DNA. Used during replication. Example: DNA polymerase III in E. coli.

2. DNA-dependent RNA polymerase (RNA polymerase / transcriptase): Template = DNA, Product = RNA. Used during transcription. In bacteria, a single RNA polymerase transcribes all RNA types; in eukaryotes, RNA polymerases I, II, and III handle different RNA types.

3. RNA-dependent DNA polymerase (Reverse transcriptase): Template = RNA, Product = DNA. Found in retroviruses (e.g., HIV). This is the process called reverse transcription.

4. RNA-dependent RNA polymerase (RNA replicase): Template = RNA, Product = RNA. Found in RNA viruses (e.g., RNA bacteriophage Qβ, TMV) for replicating their RNA genome.

Answer: Four types: DNA-dependent DNA polymerase (replication), DNA-dependent RNA polymerase (transcription), RNA-dependent DNA polymerase (reverse transcription in retroviruses), RNA-dependent RNA polymerase (RNA virus replication).

Q7 How did Hershey and Chase differentiate between DNA and protein in their experiment while proving that DNA is the genetic material?

SOLUTION

Hershey and Chase (1952) used radioactive isotopes to differentially label DNA and protein in bacteriophages, exploiting the chemical differences between the two molecules:

— DNA contains phosphorus but not sulphur. Therefore, phages grown on ^{32}P-containing medium incorporated radioactive ^{32}P into their DNA.
— Proteins contain sulphur (in amino acids cysteine and methionine) but not phosphorus. Therefore, phages grown on ^{35}S-containing medium incorporated radioactive ^{35}S into their protein coat.

Experimental steps:
1. ^{32}P-labelled phages were allowed to infect E. coli. After infection, the bacterial cells were agitated in a blender to remove phage coats, then centrifuged. The bacterial pellet was found to

be radioactive (^{32}P), indicating that DNA had entered the bacteria.

2. ^{35}S-labelled phages were similarly used. After infection and centrifugation, radioactivity (^{35}S) was found in the supernatant (phage coats), not in the bacterial pellet, indicating that protein did NOT enter the bacteria.

Conclusion: DNA, and not protein, is the genetic material that is injected into the host cell during infection.

Answer: They labelled DNA with ^{32}P and protein with ^{35}S. After infection, ^{32}P was found in bacteria (DNA entered) while ^{35}S remained outside (protein did not enter), proving DNA is the genetic material.

Q8 Differentiate between the followings:
(a) Repetitive DNA and Satellite DNA
(b) mRNA and tRNA
(c) Template strand and Coding strand

SOLUTION

(a) Repetitive DNA vs Satellite DNA:
Repetitive DNA refers to DNA sequences that are present in multiple copies in the genome. These sequences are repeated many times (sometimes hundreds to thousands of times) and generally do not code for proteins. They include both satellite DNA and other repeated elements.
Satellite DNA is a subset of repetitive DNA. When total genomic DNA is subjected to density gradient centrifugation (CsCl), the bulk of DNA forms a main peak, but short, highly repetitive sequences with a different base composition (A:T rich or G:C rich) form separate, smaller peaks called satellite DNA. Satellite DNA includes micro-satellites and mini-satellites and is the basis of DNA fingerprinting.
In short: All satellite DNA is repetitive DNA, but not all repetitive DNA is satellite DNA.

(b) mRNA vs tRNA:
mRNA (messenger RNA) is transcribed from the template strand of DNA and carries the genetic code from the nucleus to the ribosomes. It serves as the template for translation; its codons (triplet sequences) specify the amino acid sequence of the protein.
tRNA (transfer RNA) is the adapter molecule. It has an anticodon loop that base-pairs with the mRNA codon, and an amino acid acceptor end (3'-CCA) to which a specific amino acid is attached. tRNA reads the codons on mRNA and brings the correct amino acid to the ribosome during translation. There are specific tRNAs for each amino acid.

(c) Template strand vs Coding strand:
Template strand (antisense strand) is the strand of DNA that has 3'→5' polarity and serves as the template for RNA polymerase. The RNA synthesised is complementary to this strand. It is also called the antisense or minus strand.
Coding strand (sense strand) has 5'→3' polarity and the same sequence as the mRNA (except

T in place of U). It does not directly serve as a template during transcription but is displaced. It is used as the reference strand for defining the transcription unit, and its sequence corresponds to the mRNA sequence.

Answer: (a) Satellite DNA is a subset of repetitive DNA with distinct base composition, visible as satellite bands in CsCl gradients. (b) mRNA carries genetic code as template for translation; tRNA is the adapter that brings amino acids to the ribosome. (c) Template strand (3'→5') is copied by RNA polymerase; coding strand (5'→3') has the same sequence as mRNA.

Q9 List two essential roles of ribosome during translation.

SOLUTION

Two essential roles of the ribosome during translation:

1. Provides the platform for mRNA binding and tRNA binding: The ribosome (small subunit) binds to the mRNA at the start codon (AUG). It holds the mRNA in place and provides two sites on the large subunit (A-site and P-site) for successive aminoacyl-tRNAs to bind, bringing amino acids close together for peptide bond formation.

2. Acts as a catalyst (ribozyme) for peptide bond formation: The 23S rRNA of the large subunit (in bacteria) functions as a ribozyme — it catalyses the formation of peptide bonds between adjacent amino acids. This is an example of RNA acting as an enzyme (ribozyme).

Answer: 1. Provides the structural platform for mRNA and tRNA binding (small subunit binds mRNA; large subunit has A and P sites for tRNA). 2. Catalyses peptide bond formation — the 23S rRNA acts as a ribozyme.

Q10 In the medium where E. coli was growing, lactose was added, which induced the lac operon. Then, why does lac operon shut down some time after addition of lactose in the medium?

SOLUTION

When lactose is added to the medium, it acts as an inducer. Lactose (or its isomer allolactose) binds to the lac repressor protein, inactivating it. The inactivated repressor can no longer bind to the operator, so RNA polymerase can transcribe the structural genes (z, y, a). The z gene product, β-galactosidase, hydrolyses lactose into glucose and galactose.

Over time, β-galactosidase converts all the available lactose in the medium into glucose and galactose, so the lactose concentration in the medium decreases.

When lactose is exhausted, there is no longer any inducer to inactivate the repressor. The lac repressor returns to its active form and binds again to the operator region of the lac operon. This blocks RNA polymerase from transcribing the structural genes, shutting down the operon.

In essence, the lac operon is regulated by the availability of its own substrate (lactose). Once the substrate is consumed, the regulatory system automatically turns the operon off — a classic example of regulation of enzyme synthesis by its substrate.

Answer: Once β-galactosidase hydrolyses all available lactose, there is no inducer left to inactivate the lac repressor. The active repressor re-binds the operator and shuts down transcription of the operon.

Q11 Explain (in one or two lines) the function of the followings:
(a) Promoter
(b) tRNA
(c) Exons

SOLUTION

(a) Promoter: The promoter is a DNA sequence located upstream (5'-end) of the structural gene in a transcription unit. It provides the binding site for RNA polymerase, thereby initiating transcription. It also defines which strand of the DNA will serve as the template strand.

(b) tRNA: tRNA (transfer RNA) acts as an adapter molecule during translation. It reads the genetic code on mRNA through its anticodon loop, and carries the corresponding amino acid at its 3'-acceptor end (CCA end) to the ribosome, thereby linking the nucleotide sequence of mRNA to the amino acid sequence of the protein.

(c) Exons: Exons are the coding sequences in a split (eukaryotic) gene that appear in the final, mature (processed) mRNA after splicing. They are the sequences that are ultimately translated into protein. Exons are interrupted by non-coding introns in the primary transcript (hnRNA); after introns are removed and exons are joined by splicing, the functional mRNA is produced.

Answer: (a) Promoter: binds RNA polymerase and initiates transcription. (b) tRNA: adapter molecule that reads mRNA codons (via anticodon) and carries the correct amino acid to the ribosome. (c) Exons: coding sequences retained in mature mRNA after splicing; they are translated into protein.

Q12 Why is the Human Genome project called a mega project?

SOLUTION

The Human Genome Project (HGP) is called a mega project because of the enormous scale, complexity, resources, and international collaboration involved:

1. Scale of sequencing: The human genome has approximately 3×10^9 (3 billion) base pairs to be sequenced — an unprecedented quantity of biochemical data.

2. Cost: The estimated cost at the beginning was US $3 per base pair, making the total estimated cost approximately 9 billion US dollars.

3. Data storage: If the sequence data were stored in typed books (1000 letters per page, 1000 pages per book), approximately 3300 books would be required for a single human cell's DNA sequence.

4. Computational requirements: The enormous data generated necessitated the use of high-speed computers, specialised software, and gave rise to an entirely new field —

Bioinformatics.

5. Duration and international collaboration: The project ran for 13 years (1990–2003), coordinated by the U.S. Department of Energy and the National Institute of Health, with major contributions from the Wellcome Trust (UK), Japan, France, Germany, China, and others.

6. Goals: Beyond mere sequencing, the project aimed to identify all 20,000–25,000 genes, map them to chromosomes, improve analytical tools, and address ethical, legal, and social issues.

Answer: HGP is a mega project due to its massive scale (3 billion bp to sequence), enormous cost (~$9 billion estimated), vast data storage needs (3300 books), requirement for new computational tools (Bioinformatics), 13-year duration, and global collaboration across multiple countries.

Q13 What is DNA fingerprinting? Mention its application.

SOLUTION

DNA fingerprinting is a technique used to identify individuals based on variations (polymorphisms) in specific repetitive DNA sequences in their genome. Every individual has a unique pattern of these repetitive sequences (except identical/monozygotic twins), making the technique a reliable identification tool.

The technique was initially developed by Alec Jeffreys. It exploits Variable Number of Tandem Repeats (VNTR) — a class of mini-satellite DNA — which shows a very high degree of polymorphism. The original method involved Southern blot hybridisation using a radiolabelled VNTR probe, and detection by autoradiography. The technique now uses PCR to amplify VNTR sequences, so DNA from a single cell is sufficient.

Applications of DNA fingerprinting:
1. Forensic science: Identification of suspects in criminal cases by matching DNA from crime scene samples (blood, hair, saliva, semen) with a suspect's DNA.
2. Paternity testing: Resolving disputes about parentage, since VNTR patterns are inherited from parents.
3. Determining population and genetic diversities.
4. Study of evolutionary biology and relationships between species.
5. Identification of victims in mass disasters.
6. Genetic mapping of human and other genomes (polymorphisms as markers).

Answer: DNA fingerprinting identifies individuals by their unique VNTR (satellite DNA) banding pattern. Applications: forensic identification, paternity testing, population genetics, evolutionary studies.

Q14 Briefly describe the following:
(a) Transcription
(b) Polymorphism
(c) Translation
(d) Bioinformatics

SOLUTION

(a) Transcription:

Transcription is the process of copying genetic information from one strand of DNA (the template strand) into a complementary RNA molecule. It is carried out by the enzyme DNA-dependent RNA polymerase, which reads the template strand in the 3'→5' direction and synthesises RNA in the 5'→3' direction, following complementarity (A of DNA pairs with U in RNA).

In bacteria, a single RNA polymerase transcribes all three types of RNA (mRNA, tRNA, rRNA). Transcription has three stages: initiation (RNA polymerase binds the promoter with the help of sigma factor), elongation, and termination (rho factor assists at the terminator sequence). In bacteria, transcription and translation can be coupled.

In eukaryotes, three different RNA polymerases transcribe different RNA types (Pol I for rRNA, Pol II for hnRNA/mRNA precursor, Pol III for tRNA and snRNAs). The primary transcript (hnRNA) undergoes processing — capping (methyl guanosine triphosphate added at 5'-end), tailing (200–300 adenylate residues added at 3'-end), and splicing (introns removed, exons joined) — before becoming functional mRNA that is exported for translation.

(b) Polymorphism:

Polymorphism (DNA polymorphism) refers to variation in DNA sequences at a given locus in a population where more than one variant (allele) occurs at a frequency greater than 0.01. It arises due to mutations — either in somatic cells (not inherited) or in germ cells (heritable). Mutations in non-coding DNA accumulate more freely as they do not affect reproductive fitness, making polymorphisms more likely in such regions.

Polymorphisms range from single nucleotide changes (SNPs — single nucleotide polymorphisms) to variations in the number of tandem repeats (VNTRs, microsatellites). They are the basis of DNA fingerprinting and genetic mapping of the human genome, and play an important role in evolution and speciation.

(c) Translation:

Translation is the process of polymerisation of amino acids to form a polypeptide, directed by the sequence of codons on mRNA. It occurs at the ribosome.

First, amino acids are activated by ATP and attached to their specific tRNAs (aminoacylation / charging of tRNA). The ribosome then binds to the mRNA at the start codon (AUG), which is recognised by the initiator tRNA. During elongation, successive aminoacyl-tRNAs bring amino acids to the ribosome's A-site, anticodon–codon base pairing ensures specificity, and peptide bonds are formed between adjacent amino acids (catalysed by 23S rRNA, a ribozyme). The ribosome moves along the mRNA codon by codon. Translation ends when the ribosome encounters a stop codon (UAA, UAG, or UGA); a release factor binds, causing the completed

polypeptide to be released.

(d) Bioinformatics:

Bioinformatics is an interdisciplinary field that combines biology, computer science, mathematics, and statistics to store, retrieve, organise, and analyse biological data, especially large-scale genomic and proteomic data.

The Human Genome Project generated enormous amounts of sequence data (3 billion base pairs) that could not be managed or analysed by human effort alone. This necessitated development of specialised databases (e.g., GenBank), computational algorithms, and software tools for sequence alignment, annotation, gene prediction, and comparative genomics. Bioinformatics also encompasses structural bioinformatics (protein structure prediction), systems biology, and drug discovery applications. It is fundamental to modern genomics and molecular biology research.

Answer: (a) Transcription: DNA→RNA synthesis by RNA polymerase; includes initiation, elongation, termination; eukaryotes require post-transcriptional processing. (b) Polymorphism: heritable DNA sequence variation at a locus with >1% frequency in a population; basis of DNA fingerprinting. (c) Translation: mRNA→protein at the ribosome; amino acids added codon by codon via tRNA, forming a polypeptide. (d) Bioinformatics: use of computers and algorithms to store, manage, and analyse large biological (especially genomic) datasets.