Cell Biology: Structure, Replication, and Mutation of DNA

AI-Generated Study Guide

(Based on lectures delivered by Dr. Ty C.M. Hoffman)

I. Historical Experiments Establishing DNA as Genetic Material

A. Griffith's Transformation Experiment (1928)

- **Context:** Early 20th century, scientists knew traits were heritable but not what the genetic material was. Reasonable guesses pointed to a material factor rather than a "mysterious force."
- **Experimental Design:**Used *Streptococcus pneumoniae* bacteria with two strains:
- **S strain (Smooth):** Virulent (dangerous), causes pneumonia and death in mice. Colonies appear smooth.
- **R strain (Rough):** Non-virulent (harmless), does not cause pneumonia. Colonies appear rough.

1. **Treatments and Results:Living S cells injected:** Mice died (expected).
2. **Living R cells injected:** Mice lived (expected).
3. **Heat-killed S cells injected:** Mice lived (expected, dead cells don't cause disease).
4. **Heat-killed S cells + Living R cells injected:** Mice died (surprising).

- **Conclusion:** Something from the dead S cells "transformed" the living R cells into virulent S cells. This was the first demonstration of **bacterial transformation** and the first experimental evidence of a **genetic material** – a chemical substance determining traits.
- **Mechanism of Transformation:** Bacteria can take up "naked DNA" (DNA no longer inside a cell, e.g., from exploded dead cells) from the environment. This new DNA can introduce new genes, allowing the bacterium to acquire new traits (e.g., turning a harmless R strain into a virulent S strain).

B. Hershey-Chase Experiment (1952)

- **Context:** After Griffith's experiment, the question shifted to *what* the genetic material actually was. Biologists considered macromolecules, primarily proteins and nucleic acids

(DNA/RNA). Proteins were favored due to their complexity, but DNA's function was unknown.

- **Rationale for using a Virus (Bacteriophage):** Viruses are simple, composed solely of nucleic acid (DNA or RNA) and protein. They reproduce by injecting their genetic material into a host cell, which then uses its cellular machinery to produce new viruses. Therefore, identifying what component entered the host cell would reveal the genetic material.
- **Bacteriophage:** A virus that infects bacteria. The "phage" part means "to eat," but viruses don't eat; they kill host cells.
- **Viral Replication Process:** Phage attaches to host cell, injects nucleic acid. Host cell treats viral nucleic acid as its own, replicating it and transcribing/translating its genes to produce viral proteins (capsules). New viruses assemble, lyse the host cell, and are released.
- **Experimental Design (Radio-labeling):** Used radioactive isotopes to track DNA and protein.
- **Sulfur-35 (^{35}S):** Labels **protein** (sulfur is found in some amino acids, but not in DNA).
- **Phosphorus-32 (^{32}P):** Labels **DNA** (phosphorus is a component of every nucleotide's phosphate group, but rarely in proteins).

1. **Procedure:**Grew bacteriophages in separate batches: one with ^{35}S, one with ^{32}P. This ensured that only proteins were radioactive in the ^{35}S batch, and only DNA was radioactive in the ^{32}P batch.
2. Allowed radioactive phages to infect bacteria.
3. Used a blender to separate the phage shells (outside the cell) from the infected bacteria (inside the cell). The blender provided vigorous stirring to knock off the shells without lysing the bacterial cells.
4. Centrifuged the samples: heavier bacterial cells formed a pellet at the bottom, lighter phage shells remained in the supernatant (liquid above the pellet).
5. Measured radioactivity in the pellet and supernatant for both batches.

- **Results:^{35}S (Protein-labeled) batch:** Radioactivity found predominantly in the supernatant (phage shells). Little to no radioactivity in the pellet (bacterial cells).
- **^{32}P (DNA-labeled) batch:** Radioactivity found predominantly in the pellet (bacterial cells). Little to no radioactivity in the supernatant (phage shells).
- **Conclusion:** DNA, not protein, was injected into the bacterial cells and thus carried the genetic information for viral replication. This provided strong evidence that DNA is the genetic material.

II. DNA Structure

A. Nucleotides: The Monomers of DNA

- **Nucleic Acid:** Polymer of nucleotides; also called a polynucleotide.
- "Nucleic acid" because found in the nucleus of eukaryotic cells.

- "Polynucleotide" is more descriptive, indicating it's a polymer made of nucleotide monomers.

1. **Components of a Nucleotide:Pentose sugar:** Deoxyribose in DNA.
2. **Nitrogenous Base:** Four types in DNA:

- **Purines (two-ring structure):** Adenine (A), Guanine (G).
- **Pyrimidines (one-ring structure):** Cytosine (C), Thymine (T).

1. **Phosphate group(s):** One phosphate in a DNA monomer, but raw materials are triphosphates.

B. The Sugar-Phosphate Backbone

- **Formation:** Nucleotides are strung together via covalent bonds between the sugar of one nucleotide and the phosphate of the next.
- **Structure:** Forms the "rails" or vertical parts of the DNA ladder. It's strong and stable, crucial for maintaining the integrity of the genetic sequence.
- **Nitrogenous Bases:** "Hang off" the sugar-phosphate backbone; they are not involved in forming the backbone's covalent bonds.

C. Chargaff's Rules and Complementarity

- **Chargaff's Discovery:** Erwin Chargaff analyzed DNA from various organisms and found that:

1. The amount of purines always equals the amount of pyrimidines (A+G = C+T).
2. More specifically, the amount of Adenine (A) always equals the amount of Thymine (T), and the amount of Guanine (G) always equals the amount of Cytosine (C).

- **Explanation (Double Helix and Base Pairing):Double Helix:** DNA exists as two polynucleotide strands twisted around each other.
- **Ladder Analogy:** If untwisted, DNA resembles a ladder. The sugar-phosphate backbones are the "rails," and paired nitrogenous bases form the "rungs."
- **Consistent Width:** For the ladder rungs to have a consistent width (explaining purine=pyrimidine), each rung must consist of one purine (two rings) and one pyrimidine (one ring). This results in a uniform three-ring width for each rung.
- **Strict Complementarity:** The specific pairing (A with T, G with C) is due to the number of hydrogen bonds they can form:
- **A and T:** Form two hydrogen bonds.
- **G and C:** Form three hydrogen bonds.
- This specific pairing (A-T, G-C) is called **strict complementarity**.
- **Importance:** Complementarity is fundamental to DNA's ability to store information and to accurately replicate itself. If you know the sequence of one strand, you automatically know the sequence of the complementary strand.

D. Antiparallel Strands

- **Orientation:** The two DNA strands run in opposite directions. One strand runs 5' to 3', while its complementary strand runs 3' to 5'. This is crucial for DNA replication.
- **5' End:** Refers to the phosphate group attached to the 5th carbon of the deoxyribose sugar.
- **3' End:** Refers to the hydroxyl group attached to the 3rd carbon of the deoxyribose sugar.
- **Direction of Synthesis:** New nucleotides can *only* be added to the 3' end of a growing DNA strand.

E. Rosalind Franklin's Contribution

- **X-ray Crystallography:** Franklin was an expert in this technique, which involves bombarding molecules with X-rays and analyzing the diffraction pattern to deduce their 3D structure.
- **"Photo 51":** Her famous X-ray diffraction image of DNA provided crucial evidence for its helical structure.
- **Impact:** Her data was instrumental for Watson and Crick in developing their double helix model of DNA, though she did not receive full credit during her lifetime.

III. DNA Replication

A. Semiconservative Model

- **Prediction:** DNA replication proceeds according to the semiconservative model, meaning each new DNA molecule consists of one original (parental) strand and one newly synthesized strand.
- **Alternative Models (Disproven):Conservative:** Original DNA remains intact; an entirely new DNA molecule is synthesized.
- **Dispersive:** Both original strands are broken into pieces, and new strands are a mixture of old and new segments.
- **Meselson-Stahl Experiment (1958):Method:** Used heavy nitrogen (^{15}N) and light nitrogen (^{14}N) isotopes to label DNA.

1. Grew bacteria for several generations in a medium containing only ^{15}N (heavy DNA).
2. Transferred bacteria to a medium containing only ^{14}N (light DNA).
3. Took samples after one and two generations of replication in ^{14}N medium.
4. Centrifuged DNA samples: heavier DNA settles lower in the tube, lighter DNA higher.

- **Results:Generation 0 (^{15}N only):** Single band at the bottom (heavy DNA).
- **Generation 1 (^{14}N added):** Single band at an intermediate density (hybrid DNA – half ^{15}N, half ^{14}N). This disproved the conservative model (which would predict two bands: heavy and light).

- **Generation 2 (^{14}N added):** Two bands: one intermediate and one at a lighter density (pure ^{14}N). This disproved the dispersive model (which would predict a single, progressively lighter band).
- **Conclusion:** The results strongly supported the semiconservative model.

B. Overview of Replication Process

- **Origin of Replication:** Specific sequence where DNA replication begins.
- **Prokaryotes:** Single, circular chromosome with one origin of replication.
- **Eukaryotes:** Multiple linear chromosomes, each with multiple origins of replication to speed up the process due to larger genome size.
- **Replication Bubble:** Formed when DNA strands separate at an origin of replication.
- **Replication Fork:** The Y-shaped region at each end of a replication bubble where the DNA strands are actively unwound and new strands are synthesized. Each bubble has two forks moving in opposite directions.

C. Key Enzymes and Proteins in DNA Replication

1. **Helicase:** (Green) Enzyme that unwinds and separates the two DNA strands at the replication fork, breaking hydrogen bonds.
2. **Single-Strand Binding Proteins:** (Gray) Bind to the separated single DNA strands to stabilize them and prevent them from re-annealing (reforming hydrogen bonds). Not an enzyme.
3. **Topoisomerase:** (Blue) Relieves the "overwinding" tension that builds up ahead of the replication fork as helicase unwinds the DNA. It does this by cutting, swiveling, and rejoining DNA strands.
4. **Primase:** (Pink) An RNA polymerase that synthesizes a short RNA segment called a **primer** (10-15 nucleotides long) at the origin of replication and at the beginning of each Okazaki fragment. Primers are necessary because DNA polymerase can only add nucleotides to an existing 3' end.
5. **DNA Polymerase III (Pol III):** (Orange/Red) The primary enzyme for DNA synthesis. It adds DNA nucleotides (deoxyribonucleoside triphosphates) one by one to the 3' end of the growing new strand, complementary to the template strand.

- **Energy for Synthesis:** The incoming nucleotides are triphosphates (e.g., dATP, dGTP, dCTP, dTTP). The hydrolysis of two phosphate groups (pyrophosphate, PPi) from the incoming nucleotide provides the energy for the phosphodiester bond formation.
- **Direction of Synthesis:** Always synthesizes in the 5' to 3' direction relative to the new strand.

1. **DNA Polymerase I (Pol I):** (Yellow) Removes the RNA primers and replaces them with DNA nucleotides, synthesizing in the 5' to 3' direction.
2. **DNA Ligase:** (Teal) Forms the final phosphodiester bond (covalent bond) that joins the newly synthesized DNA segments (e.g., Okazaki fragments) together after the primers have been replaced, sealing any "nicks" in the sugar-phosphate backbone.

D. Leading and Lagging Strands

Due to the antiparallel nature of DNA and the 5' to 3' synthesis rule of DNA Polymerase III:

- **Leading Strand:**Synthesized **continuously** in the same direction as the replication fork is moving.
- Requires only **one RNA primer** at the origin of replication.
- DNA Pol III continuously adds nucleotides to the 3' end.
- **Lagging Strand:**Synthesized **discontinuously** in fragments, in the direction *opposite* to the replication fork's movement.
- Each fragment requires its **own RNA primer**.
- DNA Pol III synthesizes a short segment of DNA until it reaches the primer of the previous fragment.
- These short segments are called **Okazaki fragments**.
- DNA Pol I then removes the RNA primers from the Okazaki fragments and replaces them with DNA.
- DNA Ligase then joins the Okazaki fragments together by forming phosphodiester bonds.

E. DNA Proofreading and Repair

- **High Fidelity:** DNA replication is remarkably accurate, with very few errors.
- **Proofreading:** DNA polymerases (including Pol I and Pol II, though Pol III has some proofreading) have a proofreading function, where they can "backtrack" and remove incorrectly paired nucleotides during synthesis.
- **Excision Repair:** A crucial repair mechanism that corrects errors or damage in existing DNA.
- **Nucleases:** Enzymes that cut out (excise) damaged or incorrect stretches of DNA (e.g., thymine dimers caused by UV radiation).
- **DNA Polymerase:** Fills in the gap by synthesizing new DNA, using the intact complementary strand as a template.
- **DNA Ligase:** Seals the final nick, forming a continuous strand.
- **Thymine Dimer:** A common type of DNA damage, especially due to UV radiation, where two adjacent thymines on the same strand become covalently bonded, causing a kink in the DNA.

F. Telomeres and Telomerase (Eukaryotes Only)

- **End Replication Problem:** Due to the linear nature of eukaryotic chromosomes and the inability of DNA polymerase to add nucleotides without a primer, the very ends of the lagging strands cannot be fully replicated. This leads to a shortening of DNA with each round of replication.

- **Telomeres:** Non-coding, repetitive DNA sequences at the ends of eukaryotic chromosomes ("far parts" from the middle). They act as a buffer zone, protecting the genes from being lost during replication.
- **Telomerase:** An enzyme (not present in all somatic cells) that extends the telomeres by adding more repetitive DNA sequences to the ends of the chromosomes. This prevents the loss of essential genetic information and allows for more rounds of cell division.
- **Cancer Cells:** Often exhibit high telomerase activity, contributing to their immortality.

IV. DNA Packaging: Chromatin and Chromosomes (Eukaryotes)

- **Chromatin:** The complex of DNA and proteins found in the eukaryotic nucleus. It allows for the enormous length of DNA to be compacted to fit within the tiny nucleus.
- **Histones:** The primary proteins involved in DNA packaging. They are small, positively charged proteins that DNA (negatively charged due to phosphate groups) wraps around.
- **Nucleosome:** The basic unit of chromatin packaging. It consists of a segment of DNA (approximately 147 base pairs) wrapped around a core of eight histone proteins (an octamer of histones). Often described as "beads on a string."

1. **Levels of Packaging:DNA double helix**
2. **Nucleosomes:** DNA wrapped around histones ("beads on a string"). Significantly shortens DNA.
3. **30-nm fiber:** Nucleosomes are coiled and folded into a thicker fiber.
4. **Looped domains:** The 30-nm fiber forms loops attached to a protein scaffold.
5. **Condensed chromosome:** During cell division, these looped domains further coil and compact, forming visible chromosomes (e.g., metaphase chromosomes with sister chromatids).

- **Chromosome Structure (after S-phase):** A replicated chromosome consists of two identical **sister chromatids** joined at the **centromere**. This structure ensures that each daughter cell receives a complete and identical set of genetic material.

Quiz: DNA - Molecular Basis and Replication

Instructions: Answer each question in 2-3 sentences.

1. Describe the key finding from Griffith's transformation experiment that suggested the existence of a genetic material.
2. Explain why the Hershey-Chase experiment used bacteriophages for their study.
3. How did the use of Sulfur-35 and Phosphorus-32 in the Hershey-Chase experiment help distinguish between DNA and protein as the genetic material?
4. What does "strict complementarity" mean in the context of DNA structure, and what is its significance?

5. Why is the semiconservative model of DNA replication considered accurate, and what experimental evidence supported this?
6. Briefly describe the function of helicase and single-strand binding proteins during DNA replication.
7. Explain the purpose of an RNA primer in DNA replication, considering that the final product is DNA.
8. Differentiate between the leading and lagging strands in DNA replication, focusing on their synthesis patterns.
9. What is the role of DNA ligase in DNA replication, especially concerning Okazaki fragments?
10. Why are telomeres and the enzyme telomerase necessary in eukaryotic DNA replication, but not in prokaryotic replication?

Answer Key: Quiz

1. Griffith's experiment showed that heat-killed virulent S-strain bacteria could transfer some "heritable factor" to living non-virulent R-strain bacteria, transforming them into virulent S-strain. This unexpected transformation demonstrated that a material substance, not just a force, was responsible for transmitting traits.
2. Hershey and Chase used bacteriophages because these viruses are composed only of DNA and protein. Their life cycle involves injecting genetic material into a host cell to direct replication, making them ideal tools to determine which of these two macromolecules (DNA or protein) carried the genetic information.
3. Sulfur-35 selectively labeled proteins because sulfur is present in some amino acids but absent in DNA. Phosphorus-32 selectively labeled DNA because phosphorus is a fundamental component of every nucleotide's phosphate group but is scarce in proteins. This allowed researchers to track the fate of each molecule type during infection.
4. Strict complementarity refers to the specific base pairing rules in DNA: Adenine (A) always pairs with Thymine (T), and Guanine (G) always pairs with Cytosine (C). This is crucial for maintaining a consistent DNA double helix width and enables DNA to be accurately replicated and transcribed, as one strand serves as a precise template for the other.
5. The semiconservative model posits that each new DNA molecule consists of one original strand and one newly synthesized strand. The Meselson-Stahl experiment provided evidence by showing that after one generation, DNA was of intermediate density (hybrid), and after two generations, both intermediate and light DNA bands were present, consistent with this model.
6. Helicase is an enzyme that unwinds the DNA double helix at the replication fork, breaking the hydrogen bonds between strands. Single-strand binding proteins then attach to the separated strands, preventing them from re-pairing and keeping them stable so they can serve as templates.
7. An RNA primer is a short RNA sequence laid down by primase because DNA polymerase cannot initiate new DNA synthesis from scratch. It can only add nucleotides

to an existing 3' end. The RNA primer provides this initial 3' end, which is later removed and replaced with DNA by DNA Polymerase I.

8. The leading strand is synthesized continuously in the 5' to 3' direction, moving towards the replication fork, requiring only one primer. The lagging strand is synthesized discontinuously in short segments (Okazaki fragments) in the 5' to 3' direction, moving away from the replication fork, and requires multiple primers.
9. DNA ligase is an enzyme that seals the gaps (nicks) in the sugar-phosphate backbone that remain after DNA Polymerase I removes RNA primers and replaces them with DNA. It forms the final phosphodiester bond to create a continuous DNA strand, especially important for joining Okazaki fragments on the lagging strand.
10. Telomeres are repetitive non-coding DNA sequences at the ends of eukaryotic chromosomes. Due to the end-replication problem (DNA polymerase cannot fully replicate the very ends of linear chromosomes), DNA shortens with each division. Telomerase is an enzyme that extends telomeres, preventing the loss of essential genetic information. Prokaryotes have circular chromosomes, so they don't have ends and thus don't face this problem or require telomerase.

Essay Format Questions

1. Compare and contrast the contributions of Griffith, Hershey-Chase, and Franklin in establishing DNA as the genetic material and elucidating its structure. Discuss the specific experimental techniques each utilized and how their findings built upon previous knowledge.
2. Explain the concept of DNA complementarity and its multifaceted importance in biological processes. How do hydrogen bonds contribute to both the stability and the dynamic functions of the DNA molecule?
3. Describe the semiconservative model of DNA replication and the experimental design of the Meselson-Stahl experiment that provided definitive proof for this model. Detail the expected results for the conservative, semiconservative, and dispersive models and how the observed data supported the correct one.
4. Detail the intricate process of DNA replication in a eukaryotic cell, identifying at least five key enzymes or proteins and their specific roles. Explain how the antiparallel nature of DNA leads to the existence and distinct synthesis mechanisms of the leading and lagging strands, including the formation and processing of Okazaki fragments.
5. Discuss the mechanisms that ensure the high fidelity of DNA replication and the maintenance of genomic integrity. Include in your answer an explanation of DNA proofreading, excision repair (using a thymine dimer as an example), and the role of telomeres and telomerase in eukaryotic cells.

Glossary of Key Terms

- **Adenine (A):** A purine nitrogenous base found in DNA and RNA. Pairs with Thymine (T) in DNA.

- **Amino Acid:** The monomer unit of proteins.
- **Antiparallel:** The arrangement of the two strands in a DNA double helix, where one strand runs in the 5' to 3' direction and the complementary strand runs in the 3' to 5' direction.
- **Bacterial Transformation:** The process by which bacteria take up exogenous genetic material (naked DNA) from their environment and incorporate it into their own genome, leading to a change in phenotype.
- **Bacteriophage (Phage):** A virus that infects bacteria. Used in the Hershey-Chase experiment.
- **Base Pair:** Two nitrogenous bases (e.g., A-T or G-C) held together by hydrogen bonds in a DNA double helix.
- **Centrifugation:** A technique that uses centrifugal force to separate substances of different densities, often used to separate cellular components or DNA isotopes.
- **Chargaff's Rules:** Empirical rules stating that in DNA, the amount of Adenine equals the amount of Thymine, and the amount of Guanine equals the amount of Cytosine, implying strict base pairing.
- **Chromatin:** The complex of DNA and proteins (primarily histones) that makes up eukaryotic chromosomes. It condenses to form visible chromosomes during cell division.
- **Chromosome:** A thread-like structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes. Eukaryotic chromosomes are linear, prokaryotic are circular.
- **Complementarity:** The characteristic of DNA strands where the sequence of nucleotides on one strand dictates the sequence on the other due to specific base pairing (A with T, G with C).
- **Conservative Model:** A disproven model of DNA replication where the original DNA molecule remains intact, and an entirely new DNA molecule is synthesized.
- **Covalent Bond:** A strong chemical bond formed by the sharing of electrons between atoms. Forms the sugar-phosphate backbone of DNA.
- **Cytosine (C):** A pyrimidine nitrogenous base found in DNA and RNA. Pairs with Guanine (G).
- **Deoxyribonucleoside Triphosphate:** The raw material for DNA synthesis; a nucleotide with three phosphate groups, providing energy for polymerization.
- **Deoxyribose:** The pentose sugar found in DNA nucleotides.
- **Dispersive Model:** A disproven model of DNA replication where both new DNA molecules are a mixture of old and new segments throughout each strand.
- **DNA (Deoxyribonucleic Acid):** The genetic material of most organisms, a double helix polymer of nucleotides containing deoxyribose.
- **DNA Ligase:** An enzyme that forms phosphodiester bonds to join DNA fragments (e.g., Okazaki fragments), sealing nicks in the sugar-phosphate backbone.
- **DNA Polymerase I (Pol I):** An enzyme that removes RNA primers and replaces them with DNA nucleotides during replication.
- **DNA Polymerase III (Pol III):** The primary enzyme responsible for synthesizing new DNA strands by adding nucleotides to the 3' end of a growing chain.
- **Double Helix:** The characteristic two-stranded, twisted ladder-like structure of DNA.

- **End Replication Problem:** The inability of DNA polymerase to fully replicate the 5' ends of linear eukaryotic chromosomes, leading to chromosome shortening with each replication cycle.
- **Excision Repair:** A DNA repair mechanism that removes damaged or incorrect nucleotides and synthesizes new ones to fill the gap.
- **Genetic Material:** The substance (DNA in most organisms) that carries genetic information from one generation to the next.
- **Guanine (G):** A purine nitrogenous base found in DNA and RNA. Pairs with Cytosine (C).
- **Helicase:** An enzyme that unwinds the DNA double helix at the replication forks.
- **Heritable Factor:** A historical term for the unit responsible for passing traits from parents to offspring, later identified as genes/DNA.
- **Histones:** Small, positively charged proteins around which DNA is wrapped to form nucleosomes, aiding in DNA compaction.
- **Hydrogen Bond:** A weak attraction between a hydrogen atom and an electronegative atom (like oxygen or nitrogen). Holds complementary base pairs together in DNA.
- **Lagging Strand:** The DNA strand that is synthesized discontinuously in short fragments (Okazaki fragments) in the direction opposite to the overall direction of the replication fork.
- **Leading Strand:** The DNA strand that is synthesized continuously in the same direction as the replication fork.
- **Macromolecule:** A large molecule (e.g., proteins, nucleic acids, carbohydrates, lipids) essential for life.
- **Meselson-Stahl Experiment:** A landmark experiment that used heavy and light nitrogen isotopes to prove the semiconservative model of DNA replication.
- **Naked DNA:** DNA that is not enclosed within a cell or a viral capsid, typically found in the environment after cell lysis.
- **Nitrogenous Base:** A nitrogen-containing molecule that is a component of nucleotides (A, T, C, G in DNA).
- **Nuclease:** An enzyme that cuts nucleic acid strands by breaking phosphodiester bonds.
- **Nucleic Acid:** A polymer made of nucleotide monomers (e.g., DNA, RNA).
- **Nucleoplasm:** The protoplasm within the nucleus of a eukaryotic cell.
- **Nucleoside Monophosphate:** A nucleotide containing one phosphate group; the form in which nucleotides exist within a completed DNA strand.
- **Nucleosome:** The basic structural unit of chromatin, consisting of a segment of DNA wound around a core of eight histone proteins.
- **Nucleotide:** The monomer unit of nucleic acids, consisting of a pentose sugar, a nitrogenous base, and one or more phosphate groups.
- **Okazaki Fragments:** Short, newly synthesized DNA fragments that are formed on the lagging strand during DNA replication.
- **Origin of Replication:** A specific sequence of DNA where replication begins.
- **Phosphodiester Bond:** A strong covalent bond that links nucleotides together to form the sugar-phosphate backbone of nucleic acids.

- **Primer (RNA Primer):** A short RNA sequence synthesized by primase that provides a free 3'-hydroxyl group for DNA polymerase to start synthesizing DNA.
- **Primase:** An enzyme that synthesizes short RNA primers.
- **Proofreading:** The ability of DNA polymerases to check for and correct errors (incorrectly added nucleotides) during DNA synthesis.
- **Purine:** A type of nitrogenous base with a double-ring structure (Adenine and Guanine).
- **Pyrophosphate:** Two phosphate groups linked together, cleaved from an incoming nucleotide triphosphate to release energy for DNA synthesis.
- **Pyrimidine:** A type of nitrogenous base with a single-ring structure (Cytosine and Thymine).
- **Radio-labeling:** A technique using radioactive isotopes to track molecules.
- **Replication Bubble:** An unwound and separated region of DNA that forms during replication, with two replication forks moving in opposite directions.
- **Replication Fork:** The Y-shaped region where the DNA double helix is unwound and new strands are synthesized during replication.
- **RNA (Ribonucleic Acid):** A nucleic acid polymer of nucleotides containing ribose. Functions in gene expression and sometimes as a genetic material.
- **Rosalind Franklin:** Scientist who produced crucial X-ray diffraction images of DNA, providing key evidence for its helical structure.
- **Semiconservative Model:** The accepted model of DNA replication, in which each new DNA molecule consists of one original strand and one newly synthesized strand.
- **Single-Strand Binding Proteins (SSBPs):** Proteins that bind to and stabilize single-stranded DNA during replication, preventing re-annealing.
- **Sugar-Phosphate Backbone:** The alternating sugar and phosphate groups that form the structural framework of a polynucleotide strand.
- **Telomerase:** An enzyme that extends the telomeres of eukaryotic chromosomes, preventing their shortening during DNA replication.
- **Telomere:** Repetitive non-coding nucleotide sequences at the ends of eukaryotic chromosomes that protect genes from being eroded during replication.
- **Thymine (T):** A pyrimidine nitrogenous base found in DNA. Pairs with Adenine (A).
- **Thymine Dimer:** A type of DNA damage, often caused by UV radiation, where two adjacent thymine bases on the same DNA strand become covalently bonded, causing a distortion.
- **Topoisomerase:** An enzyme that relieves overwinding strain ahead of replication forks by breaking, swiveling, and rejoining DNA strands.
- **Watson and Crick:** Scientists credited with discovering the double helix structure of DNA, using data from Franklin and Chargaff.
- **X-ray Crystallography:** A technique used to determine the three-dimensional structure of molecules by analyzing the diffraction pattern of X-rays passed through a crystal of the substance.