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Programme: M.Sc., Biomedical Science

Course Code: BM35C5

Course Title: Molecular Biology

Unit-II

Replication

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Unit II:

Replication: Principle and mechanism of replication- Conservative, Semi conservative, Uni- directional and bi-directional mode of replication- Enzymes and accessory proteins involved in replication- Prokaryotic and Eukaryotic DNA replication. DNA damage& repair (Direct repair systems, mismatch repair system, base excision repair and recombination repair)

PRESENTATION: 1

Principles and Mechanisms of DNA Replication

- DNA replication is a fundamental process that occurs in all living organisms.
- It is a process by which a cell copies its DNA before cell division, ensuring that each daughter cell inherits a complete set of genetic information.
- There are different models and modes of replication, each with distinct characteristics such as conservative, semi-conservative, unidirectional, and bidirectional modes of replication.

1. Conservative Replication

Principle: In conservative replication, the entire double-stranded DNA molecule serves as a template for the synthesis of a new double-stranded DNA molecule. After replication, one of the resulting DNA molecules consists of the **original strands**, and the **other consists entirely of new strands**.

Mechanism:

- The original DNA molecule remains intact.
- A completely new double-stranded DNA molecule is synthesized using the original molecule as a template.
- After replication, the parent molecule and the newly synthesized molecule are separate entities.

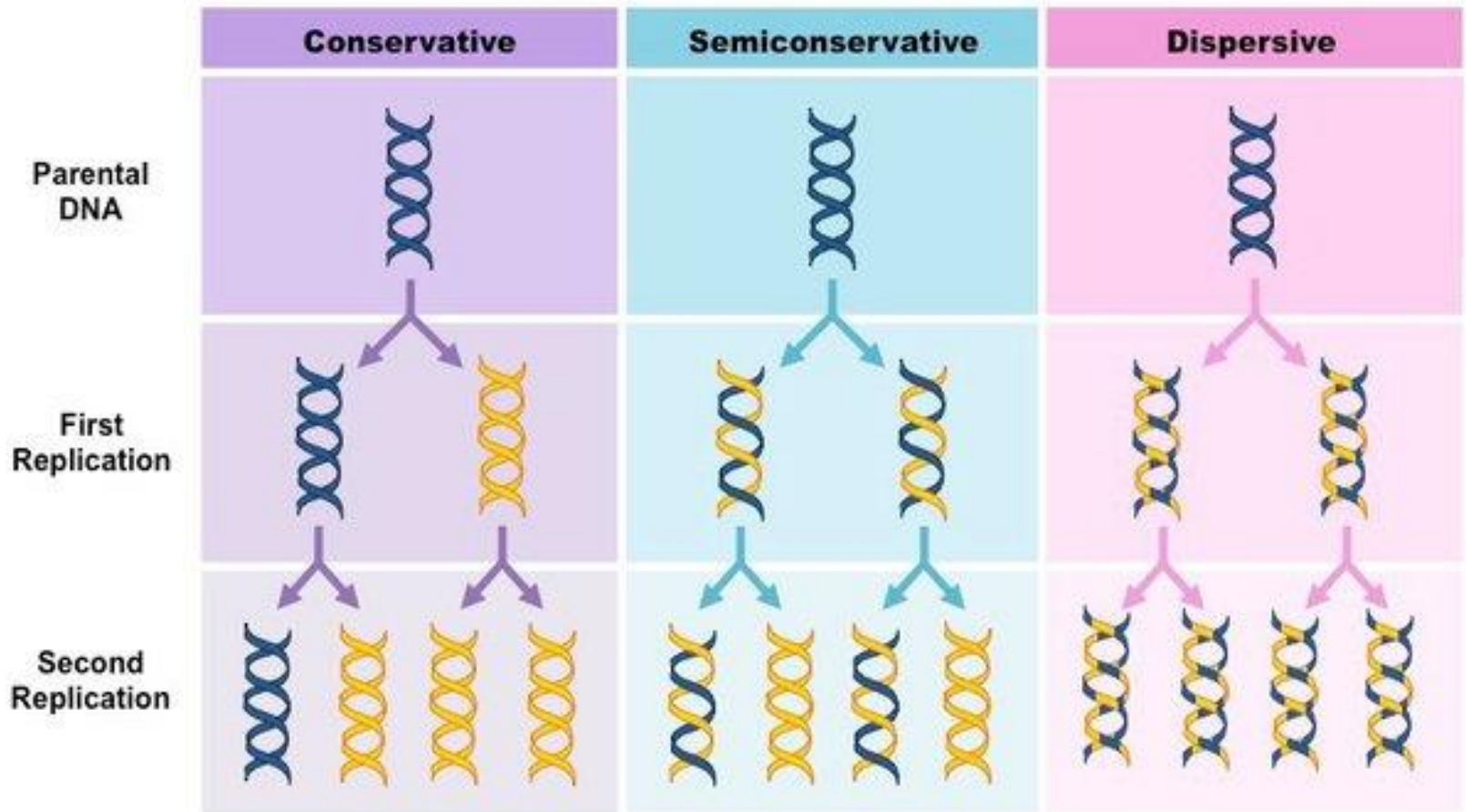
This model was proposed but not supported by experimental evidence. Instead, DNA replication in cells follows the semi-conservative model.

2. Semi-Conservative Replication

- **Principle**: In semi-conservative replication, each of the two parental DNA strands serves as a template for the synthesis of a new complementary strand. The resulting DNA molecules each contain one original (parental) strand and one newly synthesized strand.

Mechanism:

- **Initiation**: Replication begins at origins of replication.
- **Unwinding**: Helicase unwinds the DNA double helix, creating a replication fork.
- **Priming**: Primase synthesizes a short RNA primer to provide a starting point for DNA synthesis.


Conservative
Semiconservative
Dispersive
Parental DNA
First Replication
Second Replication

3. Unidirectional Replication

Principle: In unidirectional replication, the replication fork moves in one direction from a single origin of replication.

Mechanism:

- **Initiation**: Replication begins at a single origin.
- **Unidirectional Movement**: The replication fork moves in only one direction away from the origin.
- **Elongation**: DNA synthesis occurs continuously on the leading strand and discontinuously on the lagging strand as Okazaki fragments.
- **Termination**: Replication ends when the replication fork reaches a termination sequence or the end of the DNA molecule.

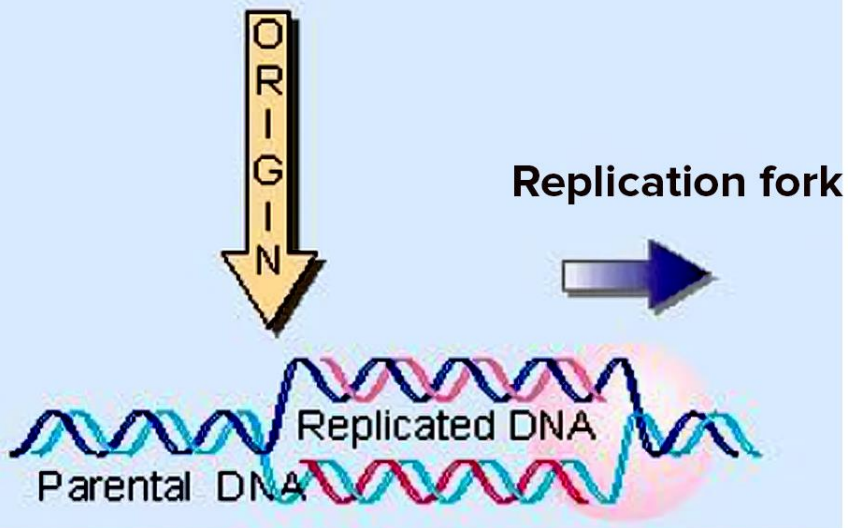
Unidirectional replication is less common and is typically observed in certain plasmids and viral genomes.

4. Bidirectional Replication

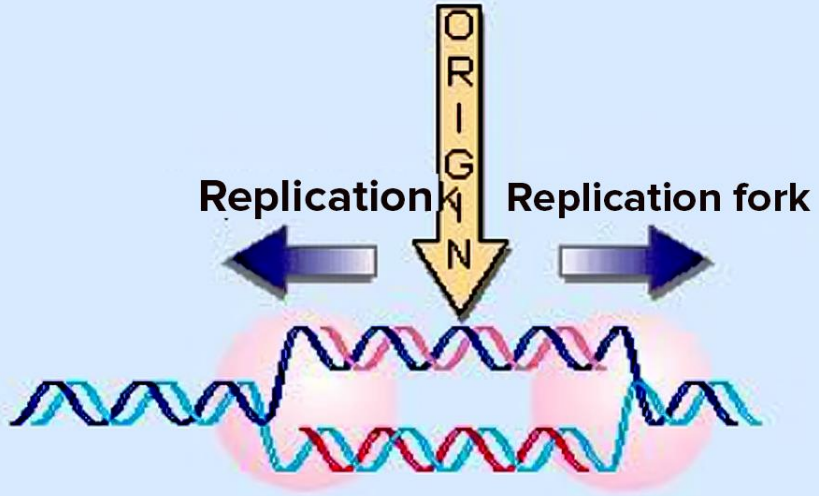
- **Principle**: In bidirectional replication, two replication forks form at the origin of replication and move in opposite directions, allowing the DNA to be copied simultaneously in both directions.
- **Mechanism**:
- **Initiation**: Replication begins at origins of replication, forming two replication forks.
- **Bidirectional Movement**: The replication forks move away from the origin in opposite directions.

- **Elongation**: DNA synthesis occurs continuously on the leading strands and discontinuously on the lagging strands at both replication forks.
  - **Leading Strands**: Synthesized continuously in the direction of each replication fork.
  - **Lagging Strands**: Synthesized as Okazaki fragments in the direction opposite to each replication fork.
- **Termination**: Replication ends when the replication forks meet, or specific termination sequences are reached.

UNIDIRECTIONAL REPLICATION



BIDIRECTIONAL REPLICATION



ENZYMES AND ACCESSORY PROTEINS IN DNA REPLICATION

1. DNA Helicase

Unwinds the DNA double helix at the replication fork, creating single-stranded DNA templates

2. Single-Strand Binding Proteins (SSBs)

Stabilize the single-stranded DNA (ssDNA) and prevent it from re-annealing or forming secondary structures.

3. RNA Primase

Synthesizes short RNA primers complementary to the template strand, providing a free 3' hydroxyl group for DNA polymerase to start synthesis.

4. DNA Polymerase

Synthesizes new DNA strands by adding nucleotides complementary to the template strand.

- DNA polymerase III (in bacteria)
- DNA polymerase α, δ, ε (in eukaryotes)
- These enzymes synthesize new DNA strands by adding nucleotides.

5. Topoisomerase

Relieves the torsional strain generated by the unwinding of the DNA helix.

Type I Topoisomerase

Type II Topoisomerase

6. Sliding Clamp (PCNA in eukaryotes, β-clamp in prokaryotes)

Increases the processivity of DNA polymerase by holding it onto the DNA.

7. Clamp Loader (RFC in eukaryotes, γ-complex in prokaryotes)

Loads the sliding clamp onto DNA.

8. DNA Ligase

Joins the discontinuous Okazaki fragments on the lagging strand by catalyzing the formation of phosphodiester bonds between adjacent fragments.

Acknowledgement

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- Thanks are due to all the original contributors and entities whose pictures were used to create this presentation.