Lecture 4
DNA Replication

DNA replication:

- DNA replication is the process of producing two identical copies from one original DNA molecule.
- This replication process is vital because it facilitates the transfer of genetic information from one generation to another
- each new cell must get a complete set of the DNA molecules
- This requires that the DNA be copied (replicated= duplicated) before cell division
- Before **cell division** DNA must be **replicated** so that every daughter cell receive a complete copy of the genome
- Happens in the **S phase** of Interphase
- Must replicate before **mitosis** or **meiosis I**
- DNA replication is the basis for the transfer of genetic information from one generation to the next one (**inheritance**).

Models for DNA replication

1) Semiconservative model:
Daughter DNA molecules contain one parental strand and one newly-replicated strand

2) Conservative model:
Parent strands transfer information to an intermediate (?), then the intermediate gets copied.
The parent helix is conserved, the daughter helix is completely new

3) Dispersive model:
Parent helix is broken into fragments, dispersed, copied then assembled into two new helices.
New and old DNA are completely dispersed

How DNA replication works:

- DNA is composed of two complementary strands.
- The two strands separate and each strand of the original DNA molecule serves as template for the production of a new complementary strand.

Semi-conservative

- The process of DNA replication is termed semiconservative.

- The term semiconservative replication means that:
  → in each of the resultant daughter DNA molecules there is one old and one new strand.

Multiple Origins of Replication:

- John Cairns (1963) showed that initial unwinding is localized to a region of the bacterial circular genome, called an "origin" or "ori" for short.
- So the process of replication begins in the DNA molecules at multiple points called "origins of replication".
- The copying progresses in both directions, forming bubble-shaped structures called "replication bubbles".
- Eventually, all the bubbles merge, yielding two double-stranded DNA molecules.

Unwinding

- The Enzyme DNA <u>Helicase</u> unwinds and separates the 2 parental DNA strands by breaking the weak hydrogen bonds producing single strand templates.
- Single-strand binding proteins (SSBs) keep strands apart.
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Replication Fork

- The separation of the two strands results in the formation of the Y-shaped structures known as **replication forks**.

Primase:

- DNA polymerase cannot start a new strand from 5`- end , but must have a ***free 3'-end*** to extend.
- ***Primase*** does not require a free 3`- end to initiate synthesis.
- ***Primase*** synthesize short RNA primers that serve as a starting points for DNA synthesis.

Elongation:

- ***DNA polymerase*** is the enzyme responsible for the synthesis of the new DNA strands.
- DNA polymerase synthesizes the new DNA strand by sequentially adding new nucleotides to the 3' end of the growing nascent chain via the creation **phosphodiester bonds**.

Leading and Lagging Strand:

- The synthesis of both DNA strands occurs in the **<u>5 ' to 3 ' direction</u>**.
- One strand, known as the **leading strand**, is synthesized as a **continuous process**.

- The other strand, known as the **lagging strand**, is synthesized in pieces called **Okazaki fragments**, which are then joined together as a continuous strand by the enzyme **DNA ligase**

Comparison:

Leading strand	Lagging strand
Synthesized continuously	Synthesized discontinuously
DNA polymerase moves toward the replication fork	DNA polymerase moves away from the replication fork
No Okazaki fragments produced	Produce Okazaki fragments

DNA Ligase:

- **Okazaki fragments**, are joined together as a continuous strand by the enzyme **DNA ligase.**