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Biology

Chapter 16

Nucleic acid & inheritance

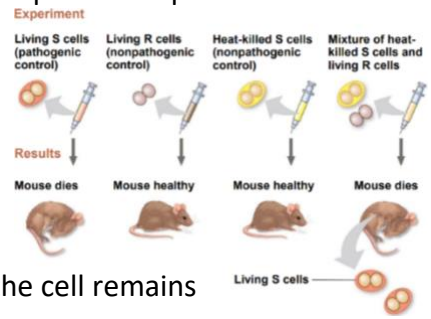
Med learn

❖ Introduction

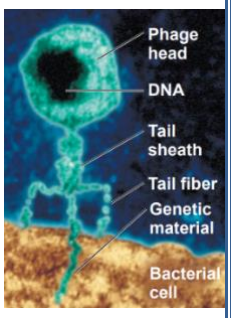
- **James Watson & Francis Crick** introduced an elegant **double-helical model** for the structure of deoxyribonucleic acid (DNA)
- **DNA** is the substance of inheritance
    1. Gregor Mendel's heritable factors and Thomas Hunt Morgan's genes on chromosomes are composed of DNA
- Nucleic acids can direct their own replication from monomers
- DNA is copied during DNA replication, and cells can repair their DNA
- Hereditary information is encoded in DNA and reproduced in all cells of the body

❖ 16.1: [DNA is the genetic material]

- **T.H. Morgan's** group showed that **genes are located on chromosomes**
- The two components of chromosomes: DNA and protein
- The discovery of the genetic role of DNA began with research by **Frederick Griffith**
    - Frederick was trying to develop a **vaccine against pneumonia**
        1. Pneumonia is a disease caused in mammals by the bacterium Streptococcus pneumonia
    - There are 2 strains (types) of the bacterium:
        2. **S (smooth) strain** → pathogenic (disease-causing) can cause pneumonia in mice; because the cells have an outer capsule that protects them from an animal's immune system
        3. **R (rough) strain** → non-pathogenic (harmless) lack a capsule

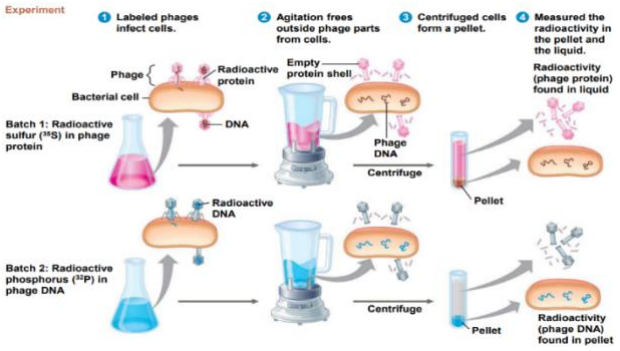


    - When he killed the pathogenic bacteria with heat and then mixed the cell remains with living bacteria of the nonpathogenic strain some of the living cells became pathogenic pathogenicity was inherited by all the descendants of the transformed bacteria, although the identity of the substance was not known
        4. Griffith called the phenomenon **transformation** ➔ change in genotype and phenotype due to the assimilation of external DNA by a cell
- Later work by **Oswald Avery, Maclyn McCarty, and Colin MacLeod** identified the **transforming substance as DNA**



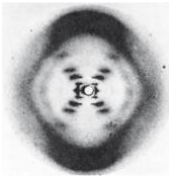
- **Bacteriophages (phages):** a type of viruses → they are much simpler than cells with a small amount of DNA enclosed by a protective coat (often a protein)
    5. To produce more viruses they must infect a cell and take over the cell's metabolic machinery
    6. Phages have been widely used as tools by researchers in molecular genetics
- **Alfred Hershey and Martha Chase** showed that DNA is the genetic material of it a phage called **T2**
    7. **T2 phage:** A phage infects Escherichia coli (E. coli) bacterium that normally lives in the intestines
- Hershey & Chase labeled the proteins & DNA of T2 by radioactive sulfur and phosphorus
    1. Radioactive **Sulfur** → for **proteins**
    2. Radioactive **Phosphorus** → for **DNA**
- The phage with labeled proteins and DNA is used to infect E.coli → after infection, only DNA has entered the bacterial cell, but protein didn't enter

- So, they concluded and **<u>provided a strong evidence that nucleic acids (DNA) is the genetic (hereditary) material</u>** which programs the cell

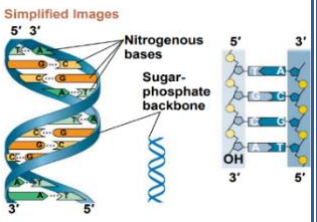


- **Remember that:** DNA is a polymer of nucleotides, each consisting of **Nitrogenous base** (A, T, C, G), **Pentose** (deoxyribose) and **Phosphate** group

- **<u>Chargaff</u>** provided a stronger evidence that DNA is the genetic matererial
- He did some experiments studying & comparing the bases of DNA molecules of different organisms
- These experiments resulted in 2 findings became known as Chargaff's rules:
    1. The base composition of **<u>DNA varies between species</u>**
    2. In any species the number of the bases **<u>A roughly equals T</u>** and the number of the bases **<u>G roughly equals C</u>**
        - ♦ The percentages are not exactly the same because of limitations in Chargaff's techniques
- Chargaff's evidence of **<u>diversity</u>** made DNA a more credible candidate for the genetic material

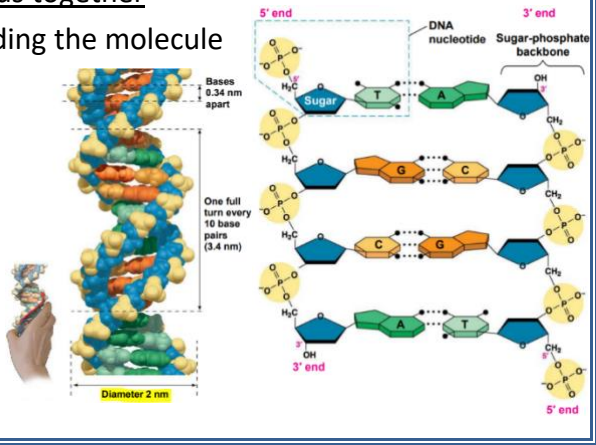


- **<u>Maurice Wilkins and Rosalind Franklin</u>** were studying the molecular structure of **<u>DNA by X-ray crystallography</u>**
- **<u>Francis Crick</u>** was studying the structure of **<u>proteins by the same technique</u>**
    3. <u>Franklin</u> produced a <u>picture of the DNA molecule</u>, when **<u>James Watson</u>** saw the photo he confirmed that <u>DNA is helical in shape</u> and made up of two strands (**Double Helix**)
    4. **Franklin's** concluded that the <u>sugar-phosphate backbones were on the outside</u> of DNA because:
        - ♦ The negatively charged **phosphate** groups facing the **aqueous** surroundings
        - ♦ The relatively hydrophobic **nitrogenous bases** were hidden in the **interior**
    5. **James Watson** concluded that the two sugar-phosphate backbones are **<u>antiparallel</u>** which mean their subunits run in opposite directions

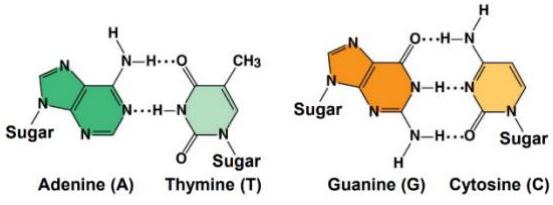


- Franklin's photo showed that:
    1. The double helix has a uniform diameter ➔ about **2 nm**
    2. The helix makes one <u>full turn every **3.4 nm**</u> along its length → with **ten base pairs** in each full turn ➔ The bases stacked just **0.34 nm** apart

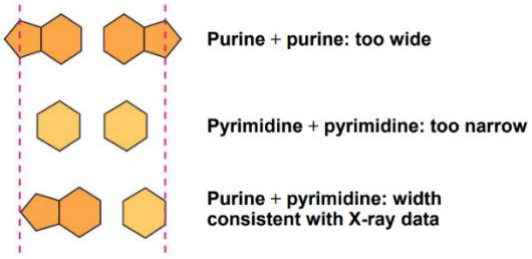
- **Phosphate** group attached to **5' carbon**, **OH** attached to **3' carbon, Nitrogenous Base** with **1' carbon**
- **Covalent** sugar-phosphate bonds link the <u>nucleotides of each strand</u>
- **Hydrogen bonds** between nitrogenous bases <u>hold the strands together</u>
- **Van der Waals** interactions between <u>stacked base pairs</u> holding the molecule



- Adenine and guanine are purines → 2 rings
- Cytosine and thymine are pyrimidines → single ring

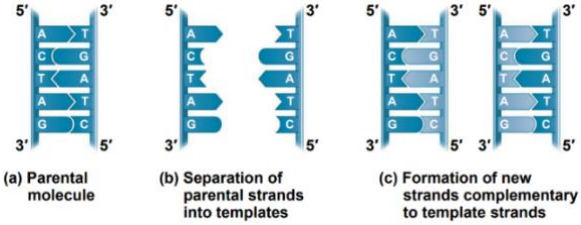


- Base pairs are hydrogen bonded in specific combinations (purine + pyrmidines):
  - Adenine (A) with thymine (T)
  - Guanine (G) with cytosine (C)
- These specific combinations are known by **Watson & Crick** with the assist of Chargaff rules



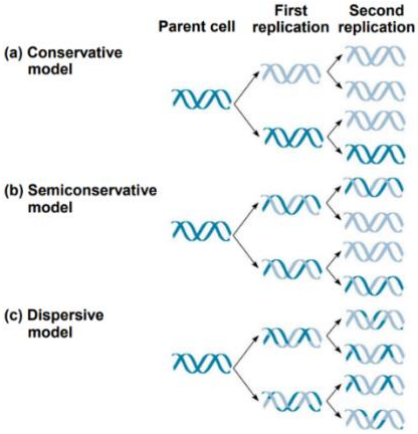
❖ 16.2: [Many proteins work together in DNA replication and repair]

- Watson and Crick noticed that the specific base pairing suggested a possible copying mechanism for genetic material
- Since the two strands of DNA are **complementary** → each strand acts as a <u>template</u> for building a new strand in replication (each stores the information necessary to reconstruct the other)

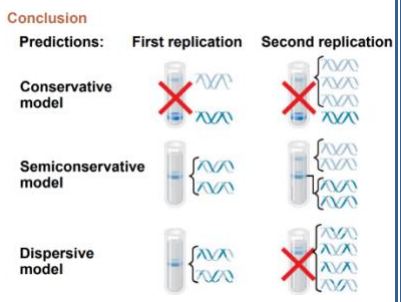


- In DNA replication, the parent molecule **unwinds**, and two new daughter strands are built based on base-pairing rules and each daughter strand is an exact replica of the parental molecule

- there 3 alternative models for replication:
  - a) **Semiconservative model (Watson and Crick's model):** predicts that when a double helix replicates, each <u>daughter molecule will have one old strand</u> derived or conserved from the parent molecule and <u>one newly made strand</u>
  - b) **Conservative model:** the <u>two parent strands rejoin</u> (the parental molecule is conserved)
  - c) **Dispersive model:** all four strands of DNA following replication have a <u>mixture of old and new DNA</u>



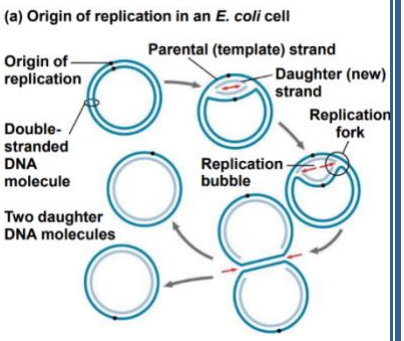
- An experiment by **<u>Matthew Meselson and Franklin Stahl</u>** supported the <u>semiconservative model</u>
  3. They cultured E.coli containing nucleotide precursors labeled with a **heavy isotope of nitrogen 15N** then transferred the bacteria to a medium with only **14N**, a lighter isotope
  4. The first replication produced a band of hybrid (15N-14N) DNA → which eliminated the conservative model
  5. The second replication produced both light and hybrid DNA → a result that refuted the dispersive model and supported the semiconservative model



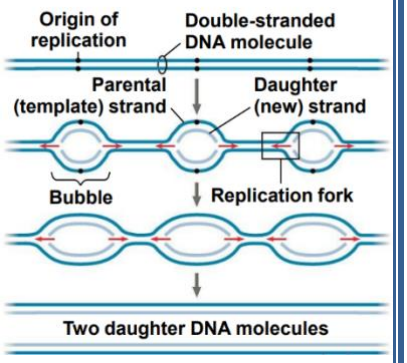
- The copying of DNA is remarkable in its <u>speed and accuracy</u> with very few errors (only about one per 10 billion nucleotides)
- Many enzymes and other proteins participate in DNA replication
- Much more is known about how the replication machine works in bacteria (such as E. coli) than in eukaryotes, however, the process is fundamentally similar between prokaryotes and eukaryotes

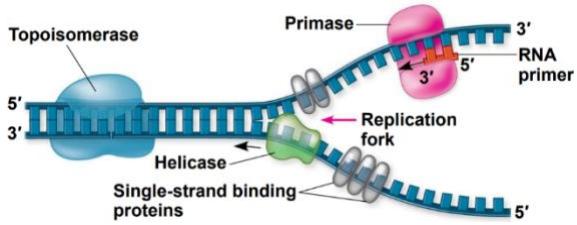
- **Origins of replication:** A particular site where the replication of chromosomal DNA <u>begins</u>
- **Replication bubble:** stretches of DNA that have a specific sequence of nucleotides where the <u>two DNA strands are separated (opened up)</u>

- A bacterial chromosomes is **circular** and has a **single origin of replication**
- A eukaryotic chromosome is **liner** and may have **hundreds or even thousands of origins of replication**

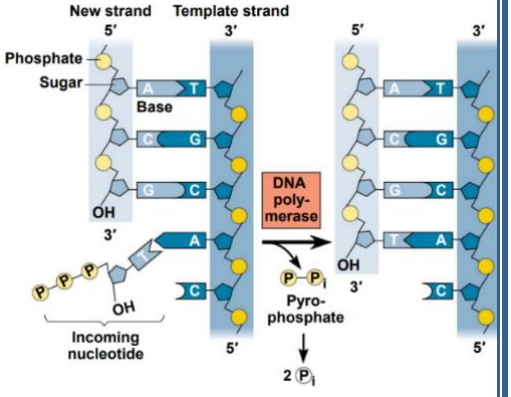


- Proteins that initiate DNA replication recognize this sequence and attach to the DNA → separating the two strands and opening up the replication bubble ➔ then the replication of DNA proceeds in **both directions** until the entire molecule is copied
- Multiple replication bubbles that are formed in eukaryotic chromosome **eventually fuse** thus speeding up the copying of the very long DNA
- **Replication fork:** a **Y-shaped** region at each end of a replication bubble where the parental strands of DNA are being unwound
- **Helicases:** Enzymes that untwist/unwinding the double helix at the replication forks, separating the two parental strands and making them available as template strands
- **Single-strand binding proteins:** Proteins that bind to the unpaired DNA strands, **keeping** them from re-pairing (**stabilizing**)
- **Topoisomerase:** Enzymes **relieving the strain** caused by unwinding, by breaking, swiveling & rejoining the parental DNA ahead of the replication fork



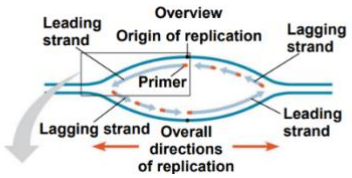


- **DNA polymerase:** An enzyme that synthesize DNA
  1. It requires a primer & a DNA template
  2. DNA polymerases catalyze the synthesis of new DNA by **adding nucleotides to the 3' end** at the replication fork of a pre-existing chain
- **Primer:** A short stretch of **RNA**, which is the initial nucleotide chain produced during DNA synthesis
  3. It is 5–10 nucleotides long and its 3' end serves as the starting point for the new DNA strand
- **Primase:** An enzyme that produce (synthesize) the primer
- **In E.coli bacterium** ➔ There are several DNA polymerases, but 2 are major (DNA polymerase III and DNA polymerase I)
- **In eukaryotes** ➔ there is at least 11 different DNA polymerases
- **DNA pol III** adds a DNA nucleotide to the RNA primer and then continues adding DNA nucleotides, complementary to the parental DNA template strand, to the growing end of the new DNA strand
- Each nucleotide that is added to a growing DNA strand is a **nucleoside triphosphate** (sugar + base + 3 phosphate groups)
  4. **dATP** supplies adenine to DNA → it is similar to the ATP of energy metabolism but the difference is in their sugars: dATP has deoxyribose while ATP has ribose
  5. As each monomer joins the DNA strand, via a **dehydration reaction**, it loses 2 phosphate groups as a molecule of **pyrophosphate** (PPi)



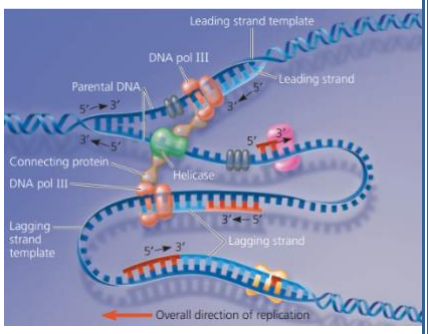
- Hydrolysis of the pyrophosphate to <u>2 molecules of inorganic phosphate (Pi)</u> is a coupled **exergonic** reaction that helps drive the polymerization reaction

- The antiparallel structure (the two strands are oriented in opposite directions) of the double helix affects replication
- DNA polymerases add nucleotides only to the **free 3' end** of a growing strand→ a **new DNA strand can elongate only in the 5' to 3' direction**



- **Leading strand:** is the stand that is synthesized **<u>continuously</u>** moving **<u>toward</u>** the replication fork
    1. **<u>Only one primer</u>** is required for the entire leading strand
- Lagging strand: The another strand which is synthesized **<u>discontinuously as a series of segments</u>** moving **<u>away</u>** from the replication fork
    1. **Okazaki fragments:** The <u>fragments</u> formed in the lagging strand
    2. Each Okazaki fragment on the lagging strand must be primed separately (<u>many primers</u>)
- After DNA pol III forms an Okazaki fragment **DNA pol I** <u>replaces the RNA nucleotides of the adjacent primer with DNA nucleotides</u>
- **DNA ligase:** It is an enzyme that <u>joins the sugar-phosphate backbones of all the Okazaki fragments</u> into a **continuous** DNA strand
- Synthesis of the leading strand and the lagging strand occur concurrently and at the same rate

- **DNA Replication Complex (Machine):** A large complex of the proteins → participate in DNA replication
    1. It facilitates interactions between these proteins → **increasing the efficiency**
    2. The DNA replication machine may be stationary (do not move along the DNA) during the replication process → the DNA may move through the complex during the replication process
    3. In eukaryotes, DNA polymerase is anchored in the **nuclear matrix**



- **Trombone model:** A model in which 2 DNA polymerase molecules (1 on each strand) reel in the parental DNA and extrude newly made daughter DNA molecules
- For each daughter strand **half of it** is made continuously as the **leading** strand, while the **other half** (on the other side of the origin) is synthesized in fragments as the **lagging** strand

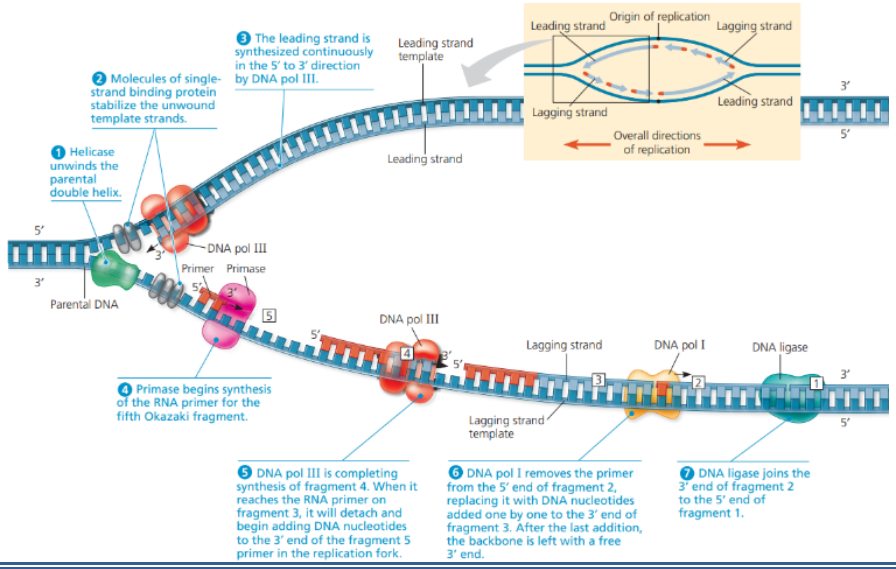
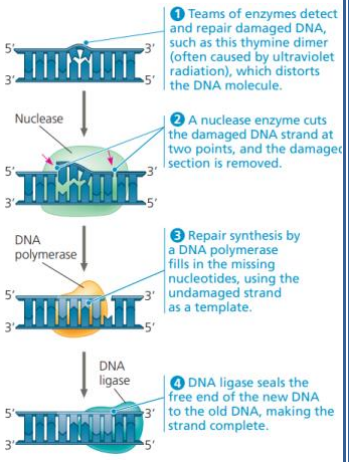


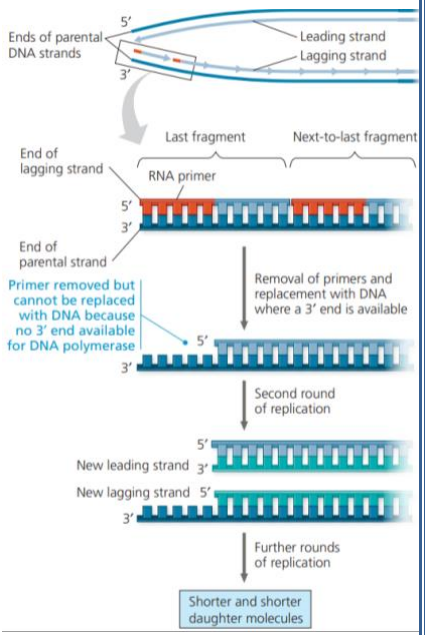
Table 16.1 Bacterial DNA Replication Proteins and Their Functions

Protein	Function
Helicase	Unwinds parental double helix at replication forks
Single-strand binding protein	Binds to and stabilizes single-stranded DNA until it is used as a template
Topoisomerase	Relieves overwinding strain ahead of replication forks by breaking, swiveling, and rejoining DNA strands
Primase	Synthesizes an RNA primer at 5′ end of leading strand and at 5′ end of each Okazaki fragment of lagging strand
DNA pol III	Using parental DNA as a template, synthesizes new DNA strand by adding nucleotides to an RNA primer or a pre-existing DNA strand
DNA pol I	Removes RNA nucleotides of primer from 5′ end and replaces them with DNA nucleotides added to 3′ end of adjacent fragment
DNA ligase	Joins Okazaki fragments of lagging strand; on leading strand, joins 3′ end of DNA that replaces primer to rest of leading strand DNA

- During DNA replication, DNA polymerases proofread each nucleotide against its template → upon finding an incorrectly paired nucleotide, the polymerase removes the nucleotide and then resumes synthesis
- In **mismatch repair** of DNA, **repair enzymes** correct errors in base pairing
    4. If these enzymes are inactive → it can cause **colon cancer**
- Changes (mistakes) in the DNA sequence can result from → **Replication errors** OR **DNA damage**
- DNA can be damaged after the replication by exposure to harmful chemical or physical agents (such as **cigarette smoke** and **X-rays**)
- These changes in DNA are usually corrected before they become **permanent changes (mutations)**
- There are many mechanisms if repairing DNA such as **nucleotide excision repair**:
    - A segment of the strand containing the damage is cut out (excised) by **nuclease enzyme** → the resulting gap is then filled in with nucleotides (by **DNA polymerase and DNA ligase**)

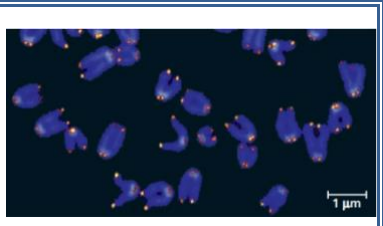


- **Thymine Dimers:** A mutation in the skin cells caused due to the exposure to the Ultraviolet rays of sunlight (UV light)
    5. In this mutation adjacent thymine bases in 1 strand are **covalently linked** to each other
    6. If this damage is not repaired → it can cause a disorder called **xeroderma pigmentosum (XP)** → mostly caused by an inherited defect in excision repair enzyme
- Individuals with XP are hypersensitive to sunlight → often resulting in skin cancer
- Mutations can rarely be beneficial → **variation** between individuals and species



- The liner DNA of eukaryotic chromosomes, in the usual replication machinery they cannot complete the 5′ ends of daughter DNA strands
- If **not completed** → repeated rounds of replication produce **shorter** DNA molecules with uneven ends
- It is not a problem for prokaryotes, most of which have **circular** chromosomes with no ends
- **The Solution for this problem in Eukaryotes:**
- **Telomeres:** special nucleotide sequences at the ends of eukaryotic chromosomal DNA → they do not contain genes
    1. They typically consists of multiple **repetitions** of one short nucleotide sequence
    2. For example: In each human telomere, the six-nucleotide sequence **TTAGGG** is repeated between 100 and 1,000 times
- **Telomeres have two protective functions:**
    - Specific proteins associated with telomeric DNA **prevent** the staggered ends of the daughter molecule from activating the cell's systems for monitoring DNA damage which leads to **cell cycle arrest or cell death**
    - Telomeric DNA acts as a kind of buffer zone that provides some **protection against the organism's genes shortening**

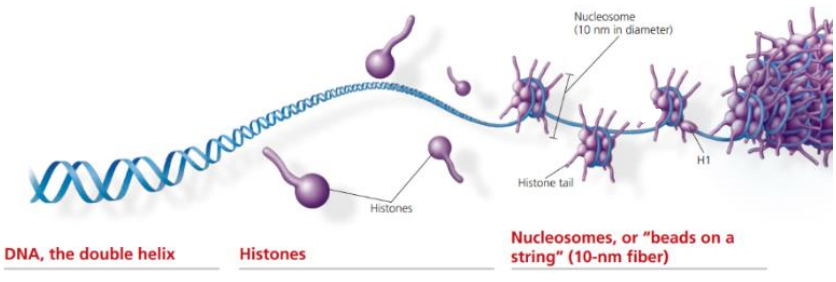
- Telomeres become shorter during every round of replication
    1. Telomeric DNA tends to be shorter in dividing somatic cells of older individuals and in cultured cells that have divided many times
    2. Shortening of telomeres is connected to **aging**



- If chromosomes of germ cells became shorter in every cell cycle, essential genes would eventually be missing from the gametes they produce
- **Telomerase:** An enzyme catalyzes the lengthening of telomeres in eukaryotic germ cells, thus restoring their original length and compensating for the shortening that occurs during DNA replication
    3. This enzyme contains its own **RNA molecule** that it uses as a template to artificially extend the leading strand, allowing the lagging strand to maintain a given length
    4. Telomerase activity varies from tissue to tissue:
        - Its activity in germ cells results in telomeres of maximum length in the zygote
        - Inactive in somatic cells
- The shortening of telomeres might **protect somatic cells from cancerous growth** by limiting the number of cell divisions (telomerase activity in cancer cells allow them to persist and divide)

❖ 16.3: [A chromosome consists of a DNA molecule packed together with proteins]

- Eukaryotic chromosomes → have linear DNA molecules associated with a large amount of protein
- Bacterial chromosome → has circular DNA molecule associated with a small amount of protein
    - In a bacterium, the DNA is supercoiled and found in a region of the cell called **nucleoid** is **not bounded** by membrane
- **Chromatin:** A complex of DNA & proteins in eukaryotic cells → allowing the DNA to fit in the nucleus
    5. Chromosomes fit into the nucleus through an elaborate multilevel system of packing
- **DNA, the double helix** → The double helix alone is **2 nm** across
- **Nucleosomes (beads on a string)**
    - Unfolded chromatin (**10-nm** fiber)
    - It is **basic unit of DNA packaging**
    - Nucleosomes consist of DNA wound twice around a protein core of **eight histones**
        6. 2 from each type of the main 4 types
    - **Linker DNA:** is the DNA segment between the 2 cores (beads)
    - The histones leave the DNA during DNA replication & transcription
    - **Histone tail:** The amino end (**N-terminus**) of each histone extending outward from the nucleosome
    - Nucleosomes (especially their histone tails) are involved in the regulation of gene expression
- **Histones**
    - They are the **proteins** responsible for the main level of DNA packing in chromatin
    - Each histone is **small** (containing only about **100 amino acids**)
    - Histone's amino acids are **positively charged** (**lysine or arginine**) and therefore bind tightly to the negatively charged DNA
    - 4 types of histones are most common in chromatin packing



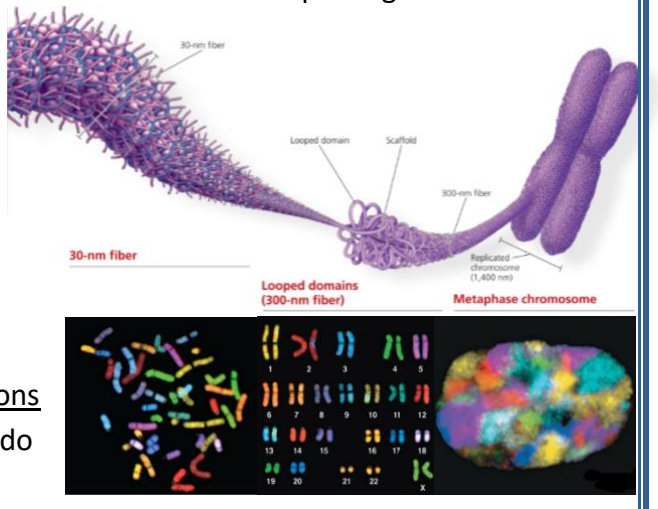
- Chromatin present in the chromosomes in 2 forms:
  1. **Euchromatin**
  - Appears as a **diffuse mass** in the nucleus with denser clumps in the centromeres and telomeres
  - It is **loosely** arranged, **less** compacted, **dispersed** interphase chromatin
  - It is **accessible** for the proteins of transcription & replication

  2. **Heterochromatin**
  - It is **densely** arranged, **more** compacted, with a **higher** level of organization
  - It isn't **accessible**

- **Notes:**
  - ✓ The basic unit of organization for both (euchromatin & heterochromatin) is the 10nm fibers (nucleosomes linked with linker DNA)
  - ✓ In the **interphase** → most chromatin is **euchromatin** (some reions are compacted into heterochromatin)
  - ✓ In the **metaphase (mitosis)** → chromatin is compacted and condensed into **heterochromatin** (short, thick metaphase chromosomes)
  - ✓ **Histones can undergo chemical modifications** that result in changes in chromatin condensation, these changes can also have multiple effects on gene expression
- In heterochromatin, the 10nm fibers are bent and folded into a higher level of organization:
- **30-nm fiber**
  - This level results from interactions between the histone tails of one nucleosome, the linker DNA and the other nucleosomes
  - These interactions cause the extended 10-nm fiber to **coil or fold** → forming a chromatin fiber roughly 30 nm in thickness (30-nm fiber)

- **Looped domains (300-nm fiber)**
  - The 30-nm fiber forms loops attached to a scaffold composed of proteins making up a 300-nm fiber
  - The scaffold is rich in one type of **topoisomerase**

- **Metaphase chromosome**
  - In a mitotic chromosome, the looped domains themselves coil and fold compacting all the chromatin to produce the metaphase chromosome
  - The width of one chromatid is **700 nm**
  - Particular genes always end up located at the same places in metaphase chromosomes



- Interphase chromosomes are **attached to nuclear lamina or matrix** → which helps organizing the chromatin when genes are active
- Interphase chromosomes occupy specific restricted regions in the nucleus, and the fibers of different chromosomes do not become entangled

- The chromosome is a dynamic structure that is condensed, loosened, modified, and remodeled as necessary for various cell processes, including mitosis, meiosis, and gene activity

Past Papers

1. **Griffith experiments on R and S types of streptococcus pneumonia emphasized the concept of:**
   A. Transformation
   B. Translation
   C. Transcription
   D. Replication
   E. Regeneration

   Answer: A

2. **The radioactive isotope P32 labels the T2 phage's:**
   A. DNA
   B. Tails
   C. Proteins
   D. Heat
   E. Base plate

   Answer: A

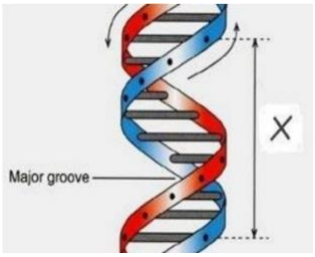
3. **Who demonstrated that DNA is genetic material in T2 phage?**
   A. Franklin
   B. Watson and crick
   C. Hershey and chase
   D. Chargaff

   Answer: C

4. **The scientists who demonstrated the double helix of DNA is:**
   A. Franklin
   B. Watson and crick
   C. Hershey and chase
   D. Chargaff

   Answer: B

5. **How many base pairs exist in the distance represented by letter (X)?**
   A. 10
   B. 5
   C. 8
   D. 12
   E. 14



   Answer: A

6. **What kind of chemical bond is found between paired bases of the DNA double helix?**
   A. Hydrogen
   B. Ionic
   C. Covalent
   D. Sulfhydryl
   E. Phosphodiester

   Answer: A

7. Multiple origins of replication on the DNA molecule of eukaryotic cell serve to:

A. Removes errors in DNA replication
B. Creates multiple copies of the DNA molecule at the same time
C. Assures the correct orientation of the two strands in the newly growing double helix
D. Shortens the time necessary for DNA replication
E. b and d are correct

Answer: D

8. Which chemical group is at the 5' end of a single polynucleotide strand?

A. Hydroxyl group
B. Phosphate group
C. Diester group
D. Nitrogen group
E. None of the above

Answer: A

9. DNA polymerase I …

A. joins Okazaki fragments
B. synthesizes primers
C. synthesizes tRNA
D. removes primers and replaces them with DNA
E. all of the above

Answer: D

10. In a nucleosome, the DNA is wrapped around:

A. polymerase molecules
B. ribosomes
C. histones
D. a thymine dimer
E. spliceosome

Answer: C

11. Which of the following true about leading strand?

A. It needs only one primer
B. It is synthesized continuously
C. It is synthesized as a series of segments called the Okazaki fragments
D. It is elongated in 3’ to 5’ direction
E. Only A and B are correct

Answer: E

12. If adenine paired with guanine and cytosine paired with thymine the shape of DNA molecule would:

A. Be longer
B. Be shorter
C. Be circular
D. Have irregular widths along its length
E. Be unwinded

Answer: D

13. Cytosine makes up 38% of the nucleotide bases in a sample of DNA, what the percentage of the thymine in this sample will be?

A. 12
B. 24
C. 31
D. 38
E. It cannot be determine

Answer: A

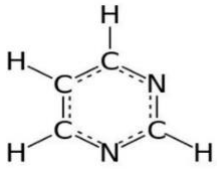
14. The enzyme that breaks, swivels, and rejoin the parental strands of DNA is:

A. Helicase
B. DNA polymerase I
C. DNA ligase
D. Primase
E. Topoisomerase

Answer: E

15. The molecule shown in the figure is:

A. Purine base
B. Pyrimidine base
C. Sugar
D. Fatty acid
E. Amino acid



Answer: B

16. A DNA strand grows only in 5' to 3' direction because:

A. DNA polymerase can only add nucleotides to the 3' end of the growing strand
B. DNA polymerase can only add nucleotides to the 5' end of the growing strand
C. The DNA molecule only unwinds in the 5' to 3' direction
D. DNA polymerase requires the addition of a starter nucleotide at the 5' end
E. mRNA can only read a DNA molecule in the 5' to 3' direction

Answer: A

17. Which of the following is true about bacterial chromosome?

A. Single linear strand of DNA
B. Double circular strand of DNA
C. Single circular strand of DNA
D. Double linear strand of DNA
E. Double linear strand of RNA

Answer: B

18. Which of the following enzymes is not involved in nucleotide excision repair:

A. Nuclease
B. Ligase
C. Primase
D. DNA polymerase
E. Both A and C

Answer: C

19. Which of the following statement is correct about DNA replication?

A. DNA replication proceeds in both directions of the origin of replication
B. DNA replication is dispersive
C. topoisomerase unwinds the double helix at the replication fork

Answer: A

20. The enzyme that involved in replacement of RNA primers with DNA is:

A. DNA poly III
B. DNA poly I
C. Ligase
D. Helicase
E. Primase

Answer: B

21. The first step of replication is catalyzed by:

A. Helicase
B. DNA Polymerase
C. Ligase
D. Primase
E. Single strand binding proteins

Answer: A

22. If % of G = 22, then the % of A =?

A. 28 %
B. 22 %
C. 44 %
D. 66 %
E. None of the above

Answer: A

23. To repair thymine dimer by nucleotide excision repair, you need:

A. Telomerase, Primase, DNA polymerase
B. Telomerase, Helicase, single strand binding proteins
C. Nuclease, DNA polymerase, DNA Ligase
D. DNA ligase, Replication fork proteins, Nuclease

Answer: C

24. The correct order of DNA packaging is:

A. Histone - Nucleosome – 30 nm fiber - 300 nm fiber (Looped domain) - metaphase chromosome
B. 30 nm fiber - 300 nm fiber (Looped domain) – Histone – Nucleosome – metaphase chromosome
C. 30 nm fiber - 300 nm fiber (Looped domain) - metaphase chromosome – Nucleosome -Histone
D. Histone - 30 nm fiber - 300 nm fiber (Looped domain) – Nucleosome – metaphase chromosome

Answer: A