Unit 3 - Transmission and Molecular Genetics

Genetics is the scientific study of inheritance and the hereditary material:
> Transmission genetics deals with how the genetic material is passed on from one cell to another during the cell cycle, and from one organism to another during the life cycle.

Module 3A – Cell Reproduction

- In this module, we will examine the cell cycle, the series of changes that a cell goes through from one generation to the next.
- We will pay particular attention to how the genetic material is passed on from parent cell to daughter cells during the cell cycle.

Objective # 1

Compare the amount and organization of genetic material in prokaryotic cells with the amount and organization of genetic material in eukaryotic cells.

Objective 1

- An average eukaryotic cell has about 1,000 times more DNA than an average prokaryotic cell.
- The DNA in a eukaryotic cell is organized into several linear chromosomes, whose organization is much more complex than the single, circular DNA molecule found in a prokaryotic cell.
Objective 1

<table>
<thead>
<tr>
<th>DNA structure</th>
<th>Prokaryotes</th>
<th>Eukaryotes</th>
</tr>
</thead>
<tbody>
<tr>
<td>single, naked, circular DNA molecule; attached to 1 point on the inner surface of plasma membrane</td>
<td>many linear chromosomes, each made of 1 DNA molecule joined with protein</td>
<td></td>
</tr>
<tr>
<td>location</td>
<td>in an area of the cytoplasm called the nucleoid</td>
<td>inside a membrane-bound nucleus</td>
</tr>
</tbody>
</table>

- If the DNA of either a prokaryotic or eukaryotic cell were completely stretched out, it would thousands of times longer than the cell itself.
- Therefore, the DNA must be folded and coiled so it will fit into the cell.
- On the next slide, you can see how this is done in a prokaryotic cell:

Objective #2

Describe the process of cell division in prokaryotic cells.

Objective 2

Prokaryotes use a type of cell division called binary fission:

1) First, the single, circular DNA molecule replicates, producing two identical copies of the original. Replication begins at a specific site called the origin of replication and proceeds bidirectionally around the circle to a specific site of termination:
Objective 2

2) As the DNA replicates, growth of the cell results in elongation. After replication is complete, the DNA molecules are actively partitioned to ¼ and ¾ of the cell length. During this process, specific DNA sequences near the origin of replication are attached to the plasma membrane.

Objective 2

3) Finally, the cytoplasm is divided in half by the growth of a new membrane and septum in the middle of the cell. This produces 2 daughter cells which are genetically identical (unless a mutation occurred) to each other and to the original cell:

Objective # 3

Describe the structure of both duplicated and unduplicated eukaryotic chromosomes; and distinguish between chromosome, chromatid, centromere, and chromatin.
Objective 3

- Eukaryotic chromosomes are made of chromatin, a complex of DNA and protein.
- Each unduplicated chromosome contains one DNA molecule, which may be several inches long.

Objective 3

- How can such long molecules fit inside a microscopic nucleus?
  - Every 200 nucleotide pairs, the DNA wraps twice around a group of 8 histone proteins to form a nucleosome.
  - Higher order coiling and supercoiling also help condense and package the chromatin inside the nucleus:

Levels of DNA Coiling in a Chromosome

- The degree of coiling can vary in different regions of the chromatin:
  - Heterochromatin refers to highly coiled regions where genes aren’t expressed.
  - Euchromatin refers to loosely coiled regions where genes can be expressed.

Objective 3

- For much of the cell cycle, most chromatin is loosely coiled.
- During this time, only the heterochromatin is visible, as dense granules inside the nucleus.
- There is also a dense area of RNA production called the nucleolus:
Objective 3

- Prior to cell division each chromosome duplicates itself.
- All the duplicated chromosomes then condense into short rod-like structures that can be seen and counted under the microscope.

Objective 3

- Because of duplication, each condensed chromosome consists of 2 identical chromatids held together by a complex of proteins called cohesins.
- Each duplicated chromosome contains 2 identical DNA molecules (unless a mistake occurred during replication), one in each chromatid.

Objective 3

- The centromere is a constricted region of the chromosome where the 2 chromatids remain connected from the middle of prophase to the start of anaphase.
- It contains repeated DNA sequences that bind specific proteins. These proteins make up a disk-like structure called the kinetochore.
Objective 3

- Kinetochores serve as points of attachment for a network of microtubules that move the chromosomes during cell division.

Objective # 4

Explain what karyotypes are and how they are useful.

Objective 4

- The particular array of chromosomes in a eukaryotic cell is called its karyotype.
- To examine a karyotype, the chromosomes are photographed when they are highly condensed, then photos of the individual chromosomes are cut out and arranged in order of decreasing size.

Objective 4

- Karyotypes are used to study the number and structure of the chromosomes present in a cell.
- They can also be used to detect chromosomal abnormalities that may be associated with specific genetic traits or defects.
**Objective # 5**

Distinguish between a haploid cell and a diploid cell. Distinguish between identical chromosomes, homologous chromosomes, and non-homologous chromosomes.

---

**Objective 5**

- In eukaryotes, every species requires a specific number of chromosomes to code for all the polypeptides produced by the organism. These chromosomes make up 1 complete set.
- Each chromosome in a set controls the production of a different group of polypeptides.

---

**Objective 5**

- Cells that contain 1 complete set of chromosomes are called haploid.
- \( n \) or \( N \) = number of chromosomes in a haploid cell.
- Cells that contain 2 complete sets of chromosomes are called diploid.
- \( 2n \) or \( 2N \) = number of chromosomes in a diploid cell.

---

**Objective 5**

- For example, 23 different chromosomes are needed to code for all the polypeptides produced by humans.
- Therefore, in humans:
  \[ N = 23 \]
  \[ 2N = 46 \]

---

**Objective 5**

- We will use different shapes to represent the different chromosomes that make up a set, and different colors to represent different sets of chromosomes.

---

**Objective 5**

- Unduplicated Chromosomes

- Haploid Cell, \( N = 3 \)
- Diploid Cell, \( 2N = 6 \)
Objective 5

Duplicated Chromosomes

Haploid Cell, $N = 3$  
Diploid Cell, $2N = 6$

In a diploid cell, the chromosomes occur in pairs. The 2 members of each pair are called homologous chromosomes or homologues.

Under the microscope, homologous chromosomes look identical.

In addition, because they code for the same polypeptides, they control the same traits.

However, homologous chromosomes are not identical because they may code for different forms of each trait. Therefore we will represent them using 2 different colors:

- Red eyes
- Short wings
- Tan body

- White eyes
- Long wings
- Tan body

Identical chromosomes:
- Look the same
- Control the same traits
- Code for the same form of each trait
- Common origin – they have both descended from the same original chromosome. (When the 2 halves of a duplicated chromosome separate, we get 2 identical chromosomes.)

Homologous chromosomes:
- Look the same
- Control the same traits
- May code for different forms of each trait
- Independent origin - each one was inherited from a different parent

Non-homologous chromosomes:
- Look different
- Control different traits
Objective # 6

Define and be able to use the following terms correctly: gene, gene locus, and allele.

Gene – a section of a DNA molecule that contains the code for making one polypeptide.

Gene locus – the location of a gene along the length of a chromosome

Alleles – genes that can occupy the same gene locus (on different chromosomes)

Objective 6

Homologous Chromosomes

Red eyes Short wings Tan body

White eyes Long wings Tan body

Objective # 7

Identify the stages of the eukaryotic cell cycle, and describe the events of each stage.

Objective 7

The cell cycle refers to the sequence of events that occur as a cell grows and divides. It is divided into 2 main stages:

- Interphase – chromosomes are not visible. Involves cell growth and duplication of the genetic material.
- Cell division – includes division of the duplicated chromosomes (mitosis) and division of the cytoplasm (cytokinesis).

- Interphase is subdivided into 3 stages:
  - $G_1$ is the primary growth phase of the cell cycle
  - $S$ is when the cell synthesizes a copy of its chromosomes (DNA duplication).
  - $G_2$ is the second growth phase, during which preparations are made for cell division.
Objective 7

- Mitosis is subdivided into 5 stages:
  - Prophase
  - Prometaphase
  - Metaphase
  - Anaphase
  - Telophase

Stages of the Cell Cycle

Objective # 8

List, describe, diagram, and identify the stages of mitosis.

Objective 8

- Mitosis:
  - some haploid and some diploid cells divide by mitosis.
  - each new cell receives one copy of every chromosome that was present in the original cell.
  - produces 2 new cells that are both genetically identical to the original cell.

Some diploid cells divide by mitosis:

DNA duplication during interphase
Some haploid cells can also divide by mitosis:

DNA duplication during interphase

Haploid Cell

Mitosis

Objective 8

Stages of Mitosis in Diploid Cell, $2N = 6$

- Prophase:
  - duplicated chromosomes condense and become visible
  - cytoskeleton is disassembled; mitotic spindle begins to form
  - Golgi and ER are dispersed
  - nuclear envelope disintegrates

- Prometaphase:
  - chromosomes attach to microtubules at the kinetochores
  - each chromosome is oriented so that the kinetochores of sister chromatids are attached to microtubules from opposite poles
  - chromosomes move toward equator of cell

- Metaphase:
  - chromosomes are aligned, in single file, along metaphase plate at the equator of cell
  - chromosomes are attached to opposite poles and are under tension
Objective 8

- **Anaphase:**
  - Centromeres split so that each duplicated chromosome becomes 2 identical, unduplicated chromosomes
  - Kinetochore microtubules shorten, pulling identical chromosomes to opposite poles
  - Polar microtubules elongate preparing cell for cytokinesis

- **Telophase:**
  - Chromosomes cluster at opposite poles of the cell and decondense
  - Kinetochores disappear
  - Polar microtubules continue to elongate, preparing cell for cytokinesis
  - Nuclear envelope reforms
  - Golgi complex, ER and cytoskeleton reform

---

**Metaphase**

**Anaphase**

**Telophase**

**Prophase**

**Stages of Mitosis in Haploid Cell, N = 3**
Objective # 9

Describe the process of cytokinesis and distinguish between mitosis and cytokinesis.
Objective 9

- Cytokinesis refers to division of the cytoplasm during cell division, while mitosis refers to division of the genetic material (chromosomes).

- Although cytokinesis generally follows mitosis, this isn’t always the case.

Objective 9

- In animal cells and other eukaryotic cells that lack a cell wall, cytokinesis is achieved by means of a constricting belt of actin filaments.

- As the filaments slide past each other, they create a cleavage furrow which deepens and eventually pinches the cell in half:

Objective 9

- Plant cells possess a cell wall which is too rigid to be squeezed in half by actin filaments.

- Instead, a new cell membrane, called a cell plate, is assembled in the middle of the cell. As this expands outward, it effectively divides the cell in two.
Objective # 10

Explain how the eukaryotic cell cycle is controlled.

Objective 10

- The eukaryotic cell cycle is controlled by a complex interaction of internal and external regulatory molecules.

- Some of these molecules act to stimulate cell division while others act to inhibit it.

The level of these regulatory molecules affects 3 principal checkpoints at which the cycle can be delayed or halted.

- The cell uses these checkpoints to both assess its internal state and evaluate external signals.

- The cell proceeds past each checkpoint only if internal and external conditions are favorable.

Objective 10

- the $G_1$/S checkpoint assesses cell growth. This is the primary point at which the cell decides whether or not to divide.
- the $G_2$/M checkpoint ensures DNA integrity. At this point the cell assesses the accuracy of DNA replication.
- the Spindle checkpoint ensures that all the chromosomes are attached to spindle fibers, with bipolar orientation, in preparation for anaphase.

Cell Cycle Control
Objective 10

- To pass each checkpoint, enzymes called Cyclin-dependent kinases (Cdks) must be activated.
- Full activation of Cdks requires binding with specific regulatory proteins called cyclins, along with the appropriate pattern of phosphorylation:

The cyclin-Cdk complex, also called MPF or mitosis promoting factor.
- MPF activates numerous proteins needed for the next stage of the cell cycle by phosphorylating them.
- When the level of MPF is high enough, the cell passes through the checkpoint and enter the next stage of the cell cycle.

Over 50 different growth factors have been identified, and each one binds to a different cell surface receptor.

In multicellular organisms, passage through cell cycle checkpoints is stimulated by external signal molecules called growth factors.

Different cyclins must bind with Cdk to pass each checkpoint.
- The cyclins needed to pass a specific checkpoint are synthesized during the stage preceding that checkpoint, and are quickly degraded during the stage following that checkpoint:

Different cyclins must bind with Cdk to pass each checkpoint.
Objective 10

- When a growth factor binds to its surface receptor, this triggers an intracellular signaling cascade that activates regulatory proteins inside the nucleus.

- The activated nuclear regulatory proteins stimulate DNA to produce proteins (e.g. Cdk or cyclins) needed to pass through cell cycle checkpoints.

- While growth factors act to stimulate cell division, other regulatory molecules may inhibit it.

- An example is a protein named p53:
  - When normal p53 detects damaged DNA, it stops cell division by preventing cyclins from joining to Cdk.
  - Abnormal p53 fails to stop division in cells with damaged DNA. If genetic damage accumulates as the cell continues to divide, the cell can turn cancerous.

Cell Division and Normal p53

1. DNA damage is caused by heat, radiation, or chemicals.
2. Cell division stops, and p53 triggers enzymes to repair damaged region.
3. p53 triggers the destruction of cells damaged beyond repair.

p53 allows cells with repaired DNA to divide.

DNA repair enzymes

Cell Division and Abnormal p53

1. DNA damage is caused by heat, radiation, or chemicals.
2. The p53 protein fails to stop cell division and repair DNA. Cell divides without repair to damaged DNA.
3. Damaged cells continue to divide. If other damage accumulates, the cell can turn cancerous.
Objective #11

Explain what cancer is, and describe how cancer can result when control of the eukaryotic cell cycle breaks down.

Objective 11

- Cancer is the uncontrolled growth and division of cells.
- Most cancers result from mutations in one of two types of growth-regulating genes:
  - proto-oncogenes
  - tumor-suppressor genes

Objective 11

- Proto-oncogenes code for proteins involved in stimulating cell division (e.g. growth factors, growth factor receptors, cyclins).
- Mutated proto-oncogenes that stimulate a cell to divide when it shouldn’t are called oncogenes (cancer-causing genes).

Objective 11

- Tumor-suppressor genes code for proteins involved in inhibiting cell division (e.g. p53).
- Mutated tumor-suppressor genes that do not inhibit cell division when they should can also cause cancer.