10 | CELL REPRODUCTION

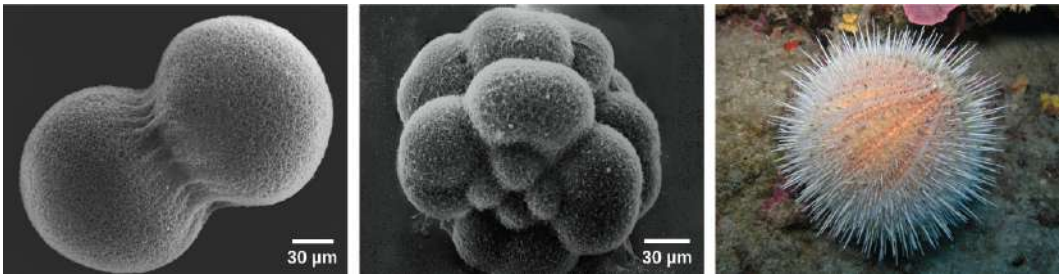

Figure 10.1 A sea urchin begins life as a single cell that (a) divides to form two cells, visible by scanning electron microscopy. After four rounds of cell division, (b) there are 16 cells, as seen in this SEM image. After many rounds of cell division, the individual develops into a complex, multicellular organism, as seen in this (c) mature sea urchin. (credit a: modification of work by Evelyn Spiegel, Louisa Howard; credit b: modification of work by Evelyn Spiegel, Louisa Howard; credit c: modification of work by Marco Busdraghi; scale-bar data from Matt Russell)

Chapter Outline

Introduction

A human, as well as every sexually reproducing organism, begins life as a fertilized egg (embryo) or zygote. Trillions of cell divisions subsequently occur in a controlled manner to produce a complex, multicellular human. In other words, that original single cell is the ancestor of every other cell in the body. Once a being is fully grown, cell reproduction is still necessary to repair or regenerate tissues. For example, new blood and skin cells are constantly being produced. All multicellular organisms use cell division for growth, maintenance, and repair of tissues. Cell division is tightly regulated, and the occasional failure of regulation can have life-threatening consequences. Single-celled organisms use cell division as their method of reproduction.

Not all cells in the body reproduce to repair tissues. Most nerve tissues, for example, are not capable of regeneration. This means people who have damaged their nerves or nervous system are often left paralyzed.

However, this may change in the future; scientists have discovered a new drug called intracellular signal peptide (ISP), which helps nerve cells regenerate in rats. It works by blocking an enzyme that causes scar tissue in damaged nerve cells allowing the nervous system a chance to repair itself. The full research study is located **here (http://openstaxcollege.org/l/32scar)** .

10.1 | Cell Division

In this section, you will explore the following question:

- What is the relationship between chromosomes, genes, and traits in prokaryotes and eukaryotes?

Connection for AP® Courses

All organisms, from bacteria to complex animals, must be able to store, retrieve, and transmit genetic information to continue life. In later chapters, we will explore how a cell's genetic information encoded in DNA, its genome, is replicated and passed to the next generation to direct the production of proteins, determining an organism's traits. Prokaryotes have single circular chromosome of DNA, whereas eukaryotes have multiple, linear chromosomes composed of chromatin (DNA wrapped around a histone protein) surrounded by a nuclear membrane. Cell division involves both mitosis, the division of the chromosomes, and cytokinesis, the division of the cytoplasm. Human somatic cells consist of 46 chromosomes—22 pairs of autosomal chromosomes and a pair of sex chromosomes. Prior to mitosis, each chromosome is duplicated to ensure that daughter cells receive the full amount of hereditary material contributed by both parents. The total number of autosomal chromosomes is referred to as the diploid ($2n$) number. (In the next chapter, we will study meiosis, the second type of cell division in sexually reproducing organisms.)

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 3 of the AP® Biology Curriculum Framework, as shown in the table. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**6.5** The student can evaluate alternative scientific explanations.
Learning Objective	**3.1** The student is able to construct scientific explanations that use the structures and mechanisms of DNA and RNA to support the claim that DNA, and in some cases, RNA are the primary sources of heritable information.

The continuity of life from one cell to another has its foundation in the reproduction of cells by way of the cell cycle. The cell cycle is an orderly sequence of events that describes the stages of a cell's life from the division of a single parent cell to the production of two new daughter cells. The mechanisms involved in the cell cycle are highly regulated.

Genomic DNA

Before discussing the steps a cell must undertake to replicate, a deeper understanding of the structure and function of a cell's genetic information is necessary. A cell's DNA, packaged as a double-stranded DNA molecule, is called its **genome**. In prokaryotes, the genome is composed of a single, double-stranded DNA molecule in the form of a loop or circle (**Figure 10.2**). The region in the cell containing this genetic material is called a nucleoid. Some prokaryotes also have smaller loops of DNA called plasmids that are not essential for normal growth. Bacteria can exchange these plasmids with other bacteria, sometimes receiving beneficial new genes that the recipient can add to their chromosomal DNA. Antibiotic resistance is one trait that often spreads through a bacterial colony through plasmid exchange.

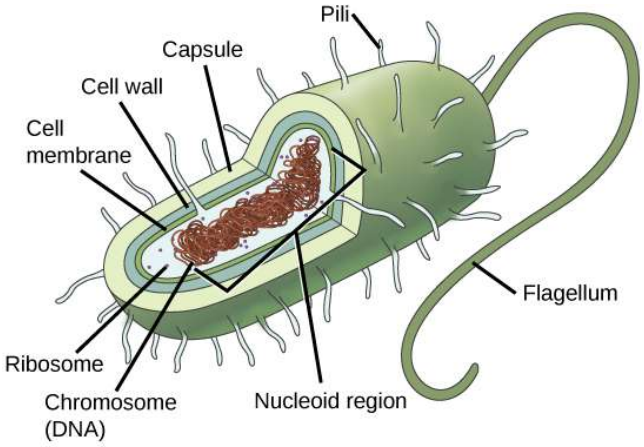

Figure 10.2 Prokaryotes, including bacteria and archaea, have a single, circular chromosome located in a central region called the nucleoid.

In eukaryotes, the genome consists of several double-stranded linear DNA molecules (**Figure 10.3**). Each species of eukaryotes has a characteristic number of chromosomes in the nuclei of its cells. Human body cells have 46 chromosomes, while human **gametes** (sperm or eggs) have 23 chromosomes each. A typical body cell, or somatic cell, contains two matched sets of chromosomes, a configuration known as **diploid**. The letter *n* is used to represent a single set of chromosomes; therefore, a diploid organism is designated 2*n*. Human cells that contain one set of chromosomes are called gametes, or sex cells; these are eggs and sperm, and are designated *1n*, or **haploid**.

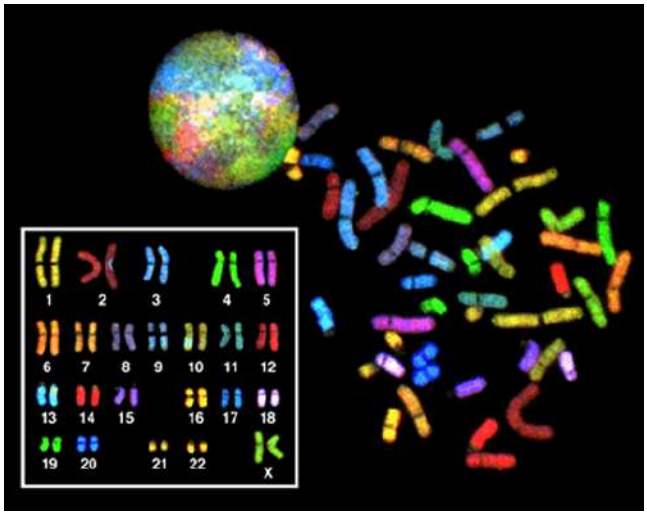

Figure 10.3 There are 23 pairs of homologous chromosomes in a female human somatic cell. The condensed chromosomes are viewed within the nucleus (top), removed from a cell in mitosis and spread out on a slide (right), and artificially arranged according to length (left); an arrangement like this is called a karyotype. In this image, the chromosomes were exposed to fluorescent stains for differentiation of the different chromosomes. A method of staining called "chromosome painting" employs fluorescent dyes that highlight chromosomes in different colors. (credit: National Human Genome Project/NIH)

Matched pairs of chromosomes in a diploid organism are called **homologous** ("same knowledge") **chromosomes**. Homologous chromosomes are the same length and have specific nucleotide segments called **genes** in exactly the same location, or **locus**. Genes, the functional units of chromosomes, determine specific characteristics by coding for specific proteins. Traits are the variations of those characteristics. For example, hair color is a characteristic with traits that are blonde, brown, or black.

Each copy of a homologous pair of chromosomes originates from a different parent; therefore, the genes themselves are not identical. The variation of individuals within a species is due to the specific combination of the genes inherited from both parents. Even a slightly altered sequence of nucleotides within a gene can result in an alternative trait. For example, there are three possible gene sequences on the human chromosome that code for blood type: sequence A, sequence B, and sequence O. Because all diploid human cells have two copies of the chromosome that determines blood type, the blood type

(the trait) is determined by which two versions of the marker gene are inherited. It is possible to have two copies of the same gene sequence on both homologous chromosomes, with one on each (for example, AA, BB, or OO), or two different sequences, such as AB.

Minor variations of traits, such as blood type, eye color, and handedness, contribute to the natural variation found within a species. However, if the entire DNA sequence from any pair of human homologous chromosomes is compared, the difference is less than one percent. The sex chromosomes, X and Y, are the single exception to the rule of homologous chromosome uniformity: Other than a small amount of homology that is necessary to accurately produce gametes, the genes found on the X and Y chromosomes are different.

Eukaryotic Chromosomal Structure and Compaction

If the DNA from all 46 chromosomes in a human cell nucleus was laid out end to end, it would measure approximately two meters; however, its diameter would be only 2 nm. Considering that the size of a typical human cell is about 10 µm (100,000 cells lined up to equal one meter), DNA must be tightly packaged to fit in the cell's nucleus. At the same time, it must also be readily accessible for the genes to be expressed. During some stages of the cell cycle, the long strands of DNA are condensed into compact chromosomes. There are a number of ways that chromosomes are compacted.

In the first level of compaction, short stretches of the DNA double helix wrap around a core of eight **histone proteins** at regular intervals along the entire length of the chromosome (**Figure 10.4**). The DNA-histone complex is part of the chromatin. Each beadlike histone-DNA complex is called a **nucleosome**, and DNA connecting the nucleosomes is called linker DNA. A DNA molecule in this form is about seven times shorter than the double helix without the histones, and the beads are about 10 nm in diameter, in contrast with the 2-nm diameter of a DNA double helix. The next level of compaction occurs as the nucleosomes and the linker DNA between them are coiled into a 30-nm chromatin fiber. This coiling further shortens the chromosome so that it is now about 50 times shorter than the extended form. In the third level of packing, a variety of fibrous proteins is used to pack the chromatin. These fibrous proteins also ensure that each chromosome in a non-dividing cell occupies a particular area of the nucleus that does not overlap with that of any other chromosome (see the top image in **Figure 10.3**).

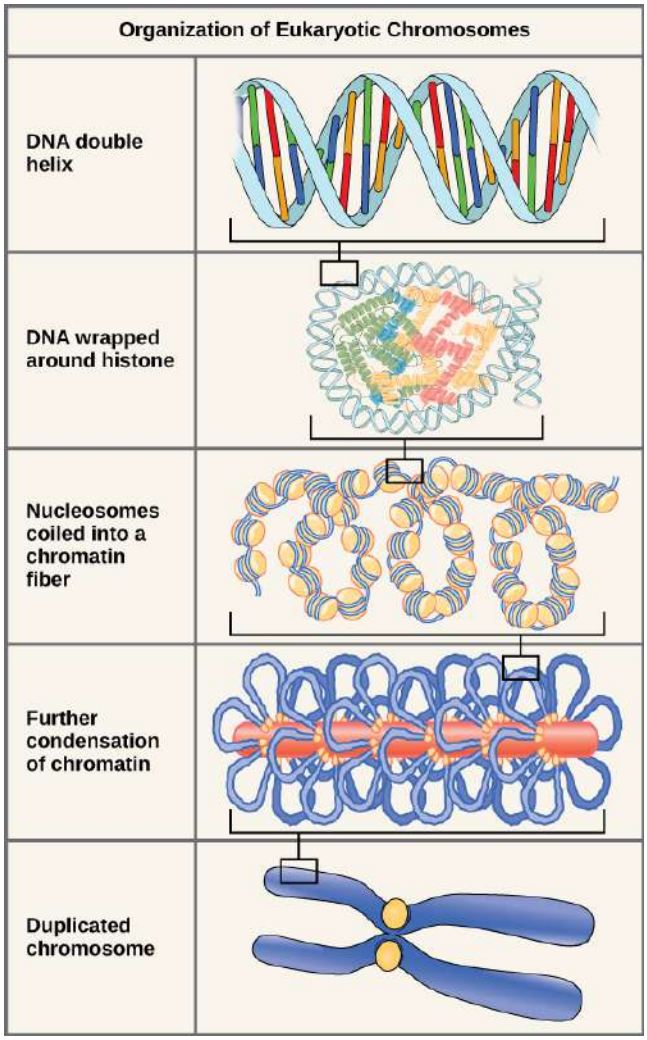

Figure 10.4 Double-stranded DNA wraps around histone proteins to form nucleosomes that have the appearance of "beads on a string." The nucleosomes are coiled into a 30-nm chromatin fiber. When a cell undergoes mitosis, the chromosomes condense even further.

DNA replicates in the S phase of interphase. After replication, the chromosomes are composed of two linked sister **chromatids**. When fully compact, the pairs of identically packed chromosomes are bound to each other by cohesin proteins. The connection between the sister chromatids is closest in a region called the **centromere**. The conjoined sister chromatids, with a diameter of about 1 µm, are visible under a light microscope. The centromeric region is highly condensed and thus will appear as a constricted area.

This animation (http://openstaxcollege.org/l/Packaged_DNA) illustrates the different levels of chromosome packing.

Why is nucleosome formation required for the packaging of DNA?

a. Nucleosome formation results in compaction of the DNA to form chromatin.

b. Nucleosome formation results in DNA synthesis.

c. Nucleosome formation decreases the number of introns in DNA.

d. Nucleosome formation increases the number of introns in the DNA.

Think About It

What is the relationship between a genome and chromosomes?

10.2 | The Cell Cycle

In this section, you will explore the following questions:

- What processes occur during the three stages of interphase?
- How do the chromosomes behave during the mitotic phase?

Connection for AP® Courses

The cell cycle describes an orderly sequence of events that are highly regulated. In eukaryotes, the cell cycle consists of a long preparatory period (interphase) followed by mitosis and cytokinesis. Interphase is divided into three phases: Gap 1 (G_1), DNA synthesis (S), and Gap 2 (G_2). Interphase represents the portion of the cell cycle between nuclear divisions. During this phase, preparations are made for division that include growth, duplication of most cellular contents, and replication of DNA. The cell's DNA is replicated during the S stage. (We will study the details of DNA replication in the chapter on DNA structure and function.) Following the G_2 stage of interphase, the cell begins mitosis, the process of active division by which duplicated chromosomes (chromatids) attach to spindle fibers, align themselves along the equator of the cell, and then separate from each other.

Following mitosis, the cell undergoes cytokinesis, the splitting of the parent cell into two daughter cells, complete with a full complement of genetic material. In animal cells, daughter cells are separated by an actin ring, whereas plant cells are separated by the cell plate, which will grow into a new cell wall. Sometimes cells enter a Gap zero (G_0) phase, during which they do not actively prepare to divide; the G_0 phase can be temporary until triggered by an external signal to enter G_1, or permanent, such as mature cardiac muscle cells and nerve cells.

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 3 of the AP® Biology Curriculum Framework, as shown in the tables. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory

experience, instructional activities, and AP® exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**6.4** The student can make claims and predictions about natural phenomena based on scientific theories and models.
Learning Objective	**3.7** The student can make predictions about natural phenomena occurring during the cell cycle.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**1.2** The student can describe representations and models of natural or man-made phenomena and systems in the domain.
Learning Objective	**3.8** The student can describe the events that occur in the cell cycle.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**5.3** The student can evaluate the evidence provided by data sets in relation to a particular scientific question.
Learning Objective	**3.11** The student is able to evaluate evidence provided by data sets to support the claim that heritable information is passed from one generation to another generation through mitosis.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.35][APLO 2.15][APLO 2.19][APLO 3.11][APLO 2.33][APLO 2.36][APLO 2.37][APLO 2.31]

The **cell cycle** is an ordered series of events involving cell growth and cell division that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produces two identical (clone) cells. The cell cycle has two major phases: interphase and the mitotic phase (**Figure 10.5**). During **interphase**, the cell grows and DNA is replicated. During the **mitotic phase**, the replicated DNA and cytoplasmic contents are separated, and the cell divides.

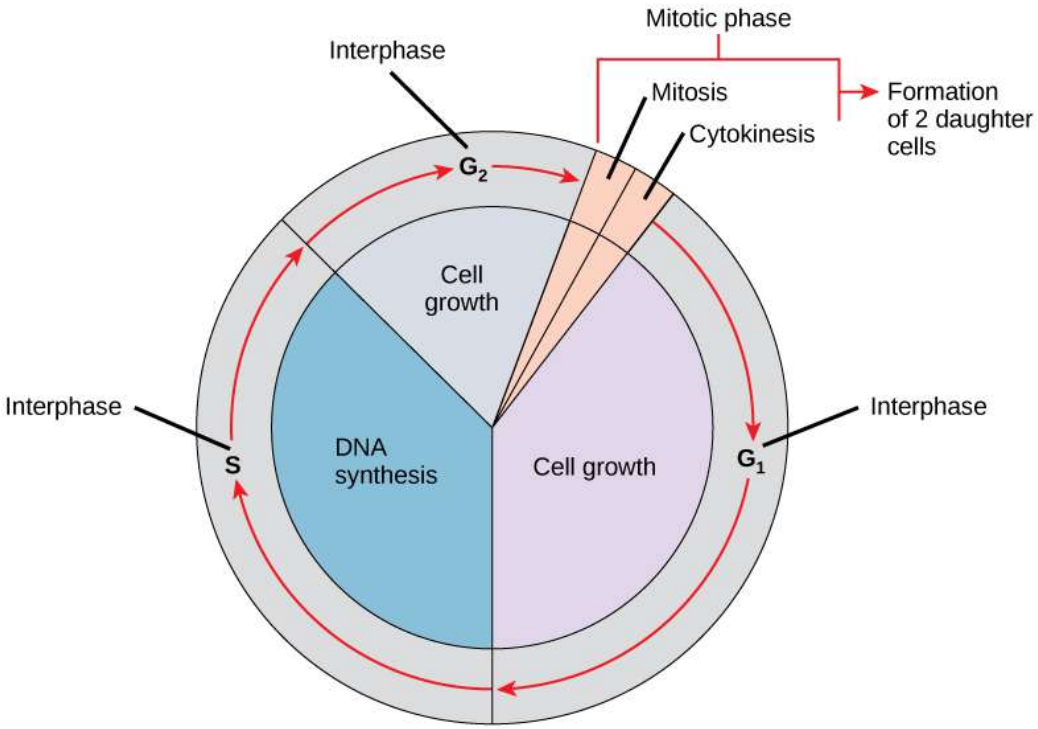

Figure 10.5 The cell cycle consists of interphase and the mitotic phase. During interphase, the cell grows and the nuclear DNA is duplicated. Interphase is followed by the mitotic phase. During the mitotic phase, the duplicated chromosomes are segregated and distributed into daughter nuclei. The cytoplasm is usually divided as well, resulting in two daughter cells.

Interphase

During interphase, the cell undergoes normal growth processes while also preparing for cell division. In order for a cell to move from interphase into the mitotic phase, many internal and external conditions must be met. The three stages of interphase are called G_1, S, and G_2.

G_1 Phase (First Gap)

The first stage of interphase is called the **G_1 phase** (first gap) because, from a microscopic aspect, little change is visible. However, during the G_1 stage, the cell is quite active at the biochemical level. The cell is accumulating the building blocks of chromosomal DNA and the associated proteins as well as accumulating sufficient energy reserves to complete the task of replicating each chromosome in the nucleus.

S Phase (Synthesis of DNA)

Throughout interphase, nuclear DNA remains in a semi-condensed chromatin configuration. In the **S phase**, DNA replication can proceed through the mechanisms that result in the formation of identical pairs of DNA molecules—sister chromatids—that are firmly attached to the centromeric region. The centrosome is duplicated during the S phase. The two centrosomes will give rise to the **mitotic spindle**, the apparatus that orchestrates the movement of chromosomes during mitosis. At the center of each animal cell, the centrosomes of animal cells are associated with a pair of rod-like objects, the **centrioles**, which are at right angles to each other. Centrioles help organize cell division. Centrioles are not present in the centrosomes of other eukaryotic species, such as plants and most fungi.

G_2 Phase (Second Gap)

In the **G_2 phase**, the cell replenishes its energy stores and synthesizes proteins necessary for chromosome manipulation. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic phase. There may be additional cell growth during G_2. The final preparations for the mitotic phase must be completed before the cell is able to enter the first stage of mitosis.

The Mitotic Phase

The mitotic phase is a multistep process during which the duplicated chromosomes are aligned, separated, and move into two new, identical daughter cells. The first portion of the mitotic phase is called **karyokinesis**, or nuclear division. The

second portion of the mitotic phase, called cytokinesis, is the physical separation of the cytoplasmic components into the two daughter cells.

Revisit the stages of mitosis at this **site (http://openstaxcollege.org/l/Cell_cycle_mito)** .

Gout is a form of arthritis that causes a painful inflammation of joints. One treatment for gout is colchicine, a medication that inhibits mitosis. Explain why this medication is beneficial for people with gout and why it can cause undesirable side effects, such as low white blood cell counts.

a. Colchicine increases inflammation by inhibiting mitosis. Inhibition of mitosis results in decreased white blood count.

b. Colchicine decreases inflammation by inhibiting mitosis. Inhibition of mitosis results in decreased white blood count.

c. Colchicine increases inflammation by inhibiting mitosis. Inhibition of mitosis results in increased white blood count.

d. Colchicine decreases inflammation by inhibiting mitosis. Inhibition of mitosis results in increased white blood count.

Karyokinesis (Mitosis)

Karyokinesis, also known as **mitosis**, is divided into a series of phases—prophase, prometaphase, metaphase, anaphase, and telophase—that result in the division of the cell nucleus (**Figure 10.7**).

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These budding plants demonstrate asexual reproduction, one of the main purposes of mitosis. The other two purposes are growth and repair.

Figure 10.6

Which of the following statements best describes the relationship between mitosis and asexual reproduction?

a. Mitosis is a process that can result in asexual reproduction.

b. Mitosis is a process that always results in asexual reproduction.

c. Asexual reproduction is a process that always results in mitosis.

d. Asexual reproduction is a process that can result in mitosis.

visual CONNECTION

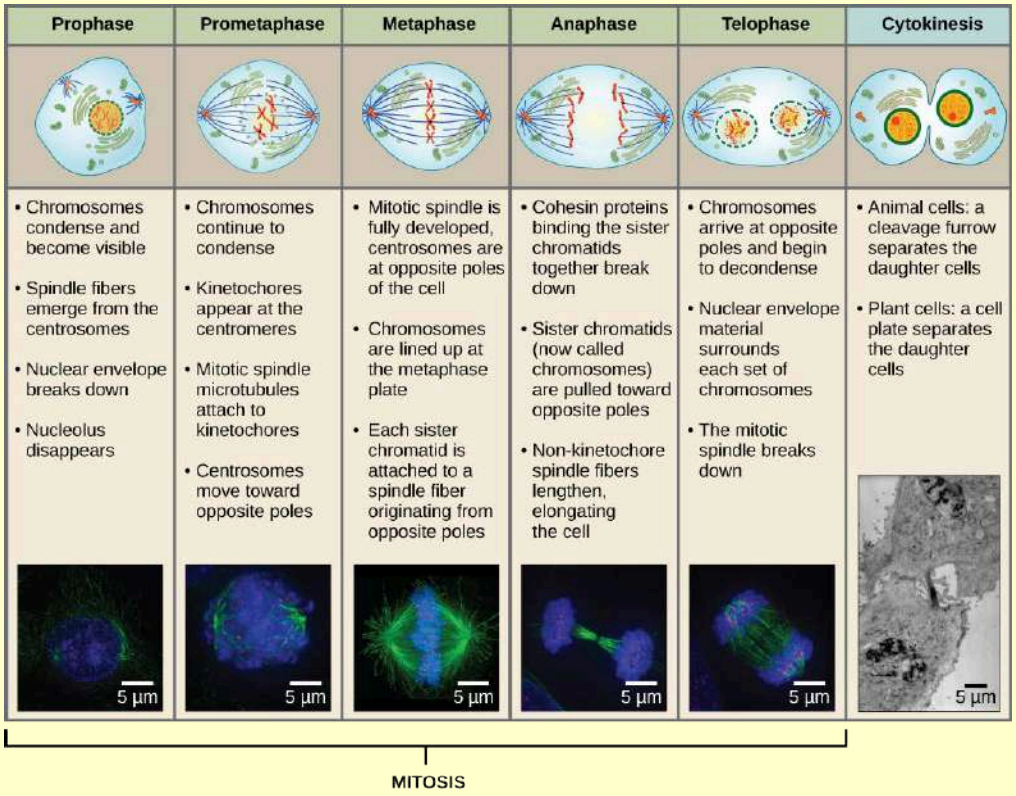

Figure 10.7 Karyokinesis (or mitosis) is divided into five stages—prophase, prometaphase, metaphase, anaphase, and telophase. The pictures at the bottom were taken by fluorescence microscopy (hence, the black background) of cells artificially stained by fluorescent dyes: blue fluorescence indicates DNA (chromosomes) and green fluorescence indicates microtubules (spindle apparatus). (credit “mitosis drawings”: modification of work by Mariana Ruiz Villareal; credit “micrographs”: modification of work by Roy van Heesbeen; credit “cytokinesis micrograph”: Wadsworth Center/New York State Department of Health; scale-bar data from Matt Russell)

Which of the following is the correct order of events in mitosis?

a. Sister chromatids line up at the metaphase plate. The kinetochore becomes attached to the mitotic spindle. The nucleus reforms and the cell divide. Cohesin proteins break down and the sister chromatids separate.

b. The kinetochore becomes attached to the mitotic spindle. Cohesin proteins break down and the sister chromatids separate. Sister chromatids line up at the metaphase plate. The nucleus reforms and the cell divides.

c. The kinetochore becomes attached to the cohesin proteins. Sister chromatids line up at the metaphase plate. The kinetochore breaks down and the sister chromatids separate. The nucleus reforms and the cell divides.

d. The kinetochore becomes attached to the mitotic spindle. Sister chromatids line up at the metaphase plate. Cohesin proteins break down and the sister chromatids separate. The nucleus reforms and the cell divide.

During **prophase**, the "first phase," the nuclear envelope starts to dissociate into small vesicles, and the membranous organelles (such as the Golgi complex or Golgi apparatus, and endoplasmic reticulum), fragment and disperse toward the periphery of the cell. The nucleolus disappears (disperses). The centrosomes begin to move to opposite poles of the cell. Microtubules that will form the mitotic spindle extend between the centrosomes, pushing them farther apart as the microtubule fibers lengthen. The sister chromatids begin to coil more tightly with the aid of **condensin** proteins and become visible under a light microscope.

During **prometaphase**, the "first change phase," many processes that were begun in prophase continue to advance. The remnants of the nuclear envelope fragment. The mitotic spindle continues to develop as more microtubules assemble and stretch across the length of the former nuclear area. Chromosomes become more condensed and discrete. Each sister chromatid develops a protein structure called a **kinetochore** in the centromeric region (**Figure 10.8**). The proteins of the kinetochore attract and bind mitotic spindle microtubules. As the spindle microtubules extend from the centrosomes, some of these microtubules come into contact with and firmly bind to the kinetochores. Once a mitotic fiber attaches to a chromosome, the chromosome will be oriented until the kinetochores of sister chromatids face the opposite poles. Eventually, all the sister chromatids will be attached via their kinetochores to microtubules from opposing poles. Spindle microtubules that do not engage the chromosomes are called polar microtubules. These microtubules overlap each other midway between the two poles and contribute to cell elongation. Astral microtubules are located near the poles, aid in spindle orientation, and are required for the regulation of mitosis.

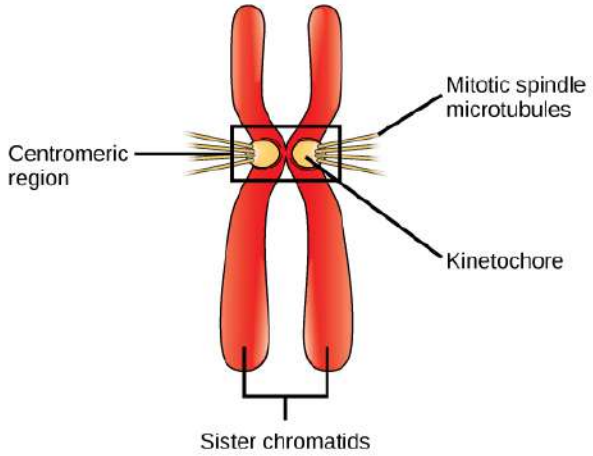

Figure 10.8 During prometaphase, mitotic spindle microtubules from opposite poles attach to each sister chromatid at the kinetochore. In anaphase, the connection between the sister chromatids breaks down, and the microtubules pull the chromosomes toward opposite poles.

During **metaphase**, the "change phase," all the chromosomes are aligned in a plane called the **metaphase plate**, or the equatorial plane, midway between the two poles of the cell. The sister chromatids are still tightly attached to each other by cohesin proteins. At this time, the chromosomes are maximally condensed.

During **anaphase**, the "upward phase," the cohesin proteins degrade, and the sister chromatids separate at the centromere. Each chromatid, now called a chromosome, is pulled rapidly toward the centrosome to which its microtubule is attached. The cell becomes visibly elongated (oval shaped) as the polar microtubules slide against each other at the metaphase plate where they overlap.

During **telophase**, the "distance phase," the chromosomes reach the opposite poles and begin to decondense (unravel), relaxing into a chromatin configuration. The mitotic spindles are depolymerized into tubulin monomers that will be used to assemble cytoskeletal components for each daughter cell. Nuclear envelopes form around the chromosomes, and nucleosomes appear within the nuclear area.

Cytokinesis

Cytokinesis, or "cell motion," is the second main stage of the mitotic phase, during which cell division is completed via the physical separation of the cytoplasmic components into two daughter cells. Division is not complete until the cell components have been apportioned and completely separated into the two daughter cells. Although the stages of mitosis are similar for most eukaryotes, the process of cytokinesis is quite different for eukaryotes that have cell walls, such as plant cells.

In cells such as animal cells that lack cell walls, cytokinesis starts during late anaphase. A contractile ring composed of actin filaments forms just inside the plasma membrane at the former metaphase plate. The actin filaments pull the equator of the

cell inward, forming a fissure. This fissure, or “crack,” is called the **cleavage furrow**. The furrow deepens as the actin ring contracts, and eventually the membrane is cleaved in two (**Figure 10.9**).

In plant cells, a new cell wall must form between the daughter cells. During interphase, the Golgi apparatus accumulates enzymes, structural proteins, and glucose molecules prior to breaking into vesicles and dispersing throughout the dividing cell. During telophase, these Golgi vesicles are transported on microtubules to form a phragmoplast (a vesicular structure) at the metaphase plate. There, the vesicles fuse and coalesce from the center toward the cell walls; this structure is called a **cell plate**. As more vesicles fuse, the cell plate enlarges until it merges with the cell walls at the periphery of the cell. Enzymes use the glucose that has accumulated between the membrane layers to build a new cell wall. The Golgi membranes become parts of the plasma membrane on either side of the new cell wall (**Figure 10.9**).

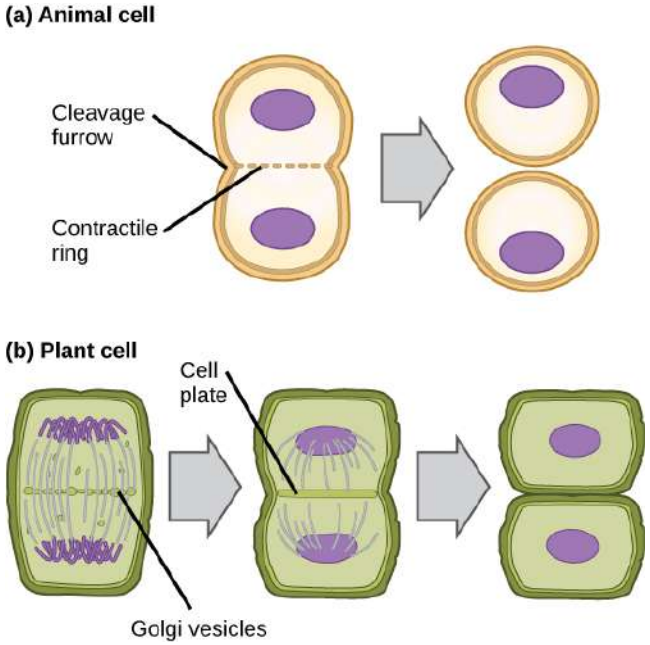

Figure 10.9 During cytokinesis in animal cells, a ring of actin filaments forms at the metaphase plate. The ring contracts, forming a cleavage furrow, which divides the cell in two. In plant cells, Golgi vesicles coalesce at the former metaphase plate, forming a phragmoplast. A cell plate formed by the fusion of the vesicles of the phragmoplast grows from the center toward the cell walls, and the membranes of the vesicles fuse to form a plasma membrane that divides the cell in two.

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Activity

- Use a set of pipe cleaners (or other materials as directed by your teacher) that you can use to model chromosomes during mitosis and meiosis:
  1. Each of the pipe cleaners represents a single, unreplicated chromosome. Each chromosome should differ in size, as they do in most organisms. Assume that your dividing cell contains 3 chromosomes: numbered chromosome 1, 2, and 3.
  2. Using both members of each homologous pair for chromosomes 1–3, model how the chromosomes would appear in a cell that had just finished the S phase of the cell cycle. Once your teacher has approved your model, have one member of your group document the model by photographing or drawing it.
  3. Now, repeat step 2 but show the cell at metaphase during mitosis.
  4. Finally, model the two daughter cells that will result from mitosis. Again, have one member of your group document the model.
  5. Repeat steps 2–5 for both meiosis I and meiosis II. Remember that you should have four daughter cells at the end of meiosis II. Also remember to ask your teacher for approval and document your model before moving on to the next phase of meiosis.
  6. Exchange/ copy all of the drawings or photographs that your group took of your models. As a group or individually (as directed by your teacher) create a report to turn in that labels and explain each picture of your model.
- An organism's ploidy count is the total number of chromosome sets contained in each body cell. Most organisms have a ploidy level of 2, meaning that they have two sets of chromosomes due to presence of homologous pairs. However, some plants are multiploid, meaning they can have ploidy levels greater than 2. The table shows possible multiploid levels of some common crop plants.

Common name	Multiploid chromosome count	Normal chromosome count
Bananas	33	11
Potatoes	48	12
Wheat	42	7
Sugar cane	80	10

Analyze the data with a partner of in a group as directed by your teacher. On a separate sheet of paper, answer the following questions.

a. How does the multiploid count of the crop plants relate to their normal chromosome count?

b. Explain the basis for the relationship you described in part a, in terms of what occurs to chromosomes during replication and meiosis.

c. Give one additional example of a possible multiploid chromosome count for each species in the table above.

Exercise 10.1

A. A comparison of the relative time intervals of mitotic stages can be made by completing the task described. In evaluating each time interval, the problem suggests that you assume that the length of time to complete one cell cycle is 24 hours. How can that assumption be tested?

Suppose that you have a growth chamber in which roots of a newly germinated plant can be examined visually with a lens that provides a magnification from which lengths can be determined with a precision of ± 0.05 mm. The field of view can be rotated so that measurements can be made of both the length and diameter of the growing tip. A large number of growing roots can be studied. Tips can be sampled, sectioned, and examined microscopically with a 25× magnification so that estimates of the diameter and length of cells can be made.

Cells in the growing tip of the root rapidly undergo mitosis, just as the whitefish blastula described in **Figure 10.10**. With increasing distance from the growing tip, the rate at which mitosis occurs slows until tissue is reached in which the initiation of the cell cycle is delayed.

A. **Describe** a sequence of measurements that could be used to test the assumption that the cell cycle, once started, has a total time interval of 24 hours. Hint: Rather than counting cells, it might be useful to measure the length of the root tip and the average length of a cell.

B. Using the data obtained from your measurements described in part A, how can the rate of cell division be calculated?

An experiment that is perhaps similar to one you have proposed was conducted previously (Beemster and Baxter, 1998), and the results are shown in the table.

Distance (mm)	Per hour
0	0.035 ± 0.01
0.1	0.047 ± 0.005
0.2	0.044 ± 0.01
0.3	0.039 ± 0.01
0.4	0.042 ± 0.01
0.5	0.031 ± 0.005

Table 10.1

C. Using these data, **estimate** the length of time of the cell cycle, including an estimate of precision by calculating the standard deviation.

Growth factors are signals that initiate cell division in eukaryotes. (The data in the table above show that cells in the plant root less than a mm from the root tip are showing a reduction of growth rate.) The interaction of two plant hormones, auxin and brassinosteroids, have been shown [Chaiwanon and Wang, *Cell*, 164(6), 1257, 2016] to regulate cell division in root tips. Auxin concentrations are higher near the root tip and decrease with distance from the tip. Brassinosteroids decrease in concentration near the root tip. Auxin is actively transported between cells, whereas brassinosteroids have limited transport between cells.

D. Based on these data and the observed distribution of brassinosteroids and auxin in the growing root, **predict** a mechanism for their interaction and **justify the claim** that brassinosteroid synthesis is negatively regulated by auxin transported to the cell, and that auxin is positively regulated and amplified.

Think About It

Chemotherapy drugs such as vincristine and colchicines disrupt mitosis by binding to tubulin (the subunit of microtubules) and interfering with microtubule assembly and disassembly. What mitotic structure is targeted by these drugs, and what effect would this have on cell division?

G_0 Phase

Not all cells adhere to the classic cell cycle pattern in which a newly formed daughter cell immediately enters the preparatory phases of interphase, closely followed by the mitotic phase. Cells in **G_0 phase** are not actively preparing to divide. The cell is in a **quiescent** (inactive) stage that occurs when cells exit the cell cycle. Some cells enter G_0 temporarily until an external signal triggers the onset of G_1. Other cells that never or rarely divide, such as mature cardiac muscle and nerve cells, remain in G_0 permanently.

Determine the Time Spent in Cell Cycle Stages

Problem: How long does a cell spend in interphase compared to each stage of mitosis?

Background: A prepared microscope slide of blastula cross-sections will show cells arrested in various stages of the cell cycle. It is not visually possible to separate the stages of interphase from each other, but the mitotic stages are readily identifiable. If 100 cells are examined, the number of cells in each identifiable cell cycle stage will give an estimate of the time it takes for the cell to complete that stage.

Problem Statement: Given the events included in all of interphase and those that take place in each stage of mitosis, estimate the length of each stage based on a 24-hour cell cycle. Before proceeding, state your hypothesis.

Test your hypothesis: Test your hypothesis by doing the following:

1. Place a fixed and stained microscope slide of whitefish blastula cross-sections under the scanning objective of a light microscope.
2. Locate and focus on one of the sections using the scanning objective of your microscope. Notice that the section is a circle composed of dozens of closely packed individual cells.
3. Switch to the low-power objective and refocus. With this objective, individual cells are visible.
4. Switch to the high-power objective and slowly move the slide left to right, and up and down to view all the cells in the section (**Figure 10.10**). As you scan, you will notice that most of the cells are not undergoing mitosis but are in the interphase period of the cell cycle.

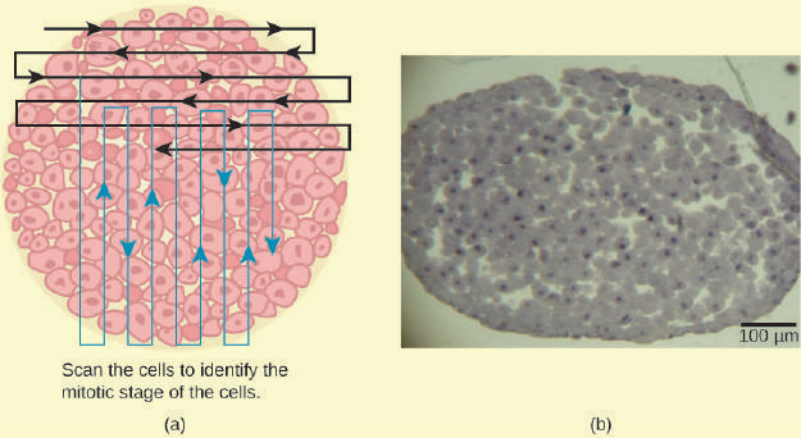

Figure 10.10 Slowly scan whitefish blastula cells with the high-power objective as illustrated in image (a) to identify their mitotic stage. (b) A microscopic image of the scanned cells is shown. (credit “micrograph”: modification of work by Linda Flora; scale-bar data from Matt Russell)

5. Practice identifying the various stages of the cell cycle, using the drawings of the stages as a guide (**Figure 10.7**).
6. Once you are confident about your identification, begin to record the stage of each cell you encounter as you scan left to right, and top to bottom across the blastula section.
7. Keep a tally of your observations and stop when you reach 100 cells identified.
8. The larger the sample size (total number of cells counted), the more accurate the results. If possible, gather and record group data prior to calculating percentages and making estimates.

Record your observations: Make a table similar to **Table 10.2** in which you record your observations.

Results of Cell Stage Identification

Phase or Stage	Individual Totals	Group Totals	Percent
Interphase			
Prophase			

Results of Cell Stage Identification

Phase or Stage	Individual Totals	Group Totals	Percent
Metaphase			
Anaphase			
Telophase			
Cytokinesis			
Totals	100	100	100 percent

Table 10.2

Analyze your data/report your results: To find the length of time whitefish blastula cells spend in each stage, multiply the percent (recorded as a decimal) by 24 hours. Make a table similar to **Table 10.3** to illustrate your data.

Estimate of Cell Stage Length

Phase or Stage	Percent (as Decimal)	Time in Hours
Interphase		
Prophase		
Metaphase		
Anaphase		
Telophase		
Cytokinesis		

Table 10.3

10.3 | Control of the Cell Cycle

In this section, you will explore the following questions:

- What are examples of internal and external mechanisms that control the cell cycle?
- What molecules are involved in controlling the cell cycle through positive and negative regulation?

Connection for AP® Courses

Each step of the cell cycle is closely monitored by external signals and internal controls called checkpoints. There are three major checkpoints in the cell cycle: one near the end of G_1, a second at the G_2/M transition, and the third during metaphase. Growth factor proteins arriving at the dividing cell's plasma membrane can trigger the cell to begin dividing. Cyclins and cyclin-dependent kinases (Cdks) are internal molecular signals that regulate cell transitions through the various checkpoints. Passage through the G_1 checkpoint makes sure that the cell is ready for DNA replication in the S stage of interphase; passage through the G_2 checkpoint triggers the separation of chromatids during mitosis. Positive regulator molecules like the cyclins and Cdks allow the cell cycle to advance to the next stage; negative regulator molecules, such as tumor suppressor proteins, monitor cellular conditions and can halt the cycle until specific requirements are met. Errors in the regulation of the cell cycle can cause cancer, which is characterized by uncontrolled cell division.

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined

in Big Idea 3 of the AP® Biology Curriculum Framework, as shown in the tables. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**6.4** The student can make claims and predictions about natural phenomena based on scientific theories and models.
Learning Objective	**3.7** The student can make predictions about natural phenomena occurring during the cell cycle.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**1.2** The student can describe representations and models of natural or man-made phenomena and systems in the domain.
Learning Objective	**3.8** The student can describe the events that occur in the cell cycle.

The length of the cell cycle is highly variable, even within the cells of a single organism. In humans, the frequency of cell turnover ranges from a few hours in early embryonic development, to an average of two to five days for epithelial cells, and to an entire human lifetime spent in G_0 by specialized cells, such as cortical neurons or cardiac muscle cells. There is also variation in the time that a cell spends in each phase of the cell cycle. When fast-dividing mammalian cells are grown in culture (outside the body under optimal growing conditions), the length of the cycle is about 24 hours. In rapidly dividing human cells with a 24-hour cell cycle, the G_1 phase lasts approximately nine hours, the S phase lasts 10 hours, the G_2 phase lasts about four and one-half hours, and the M phase lasts approximately one-half hour. In early embryos of fruit flies, the cell cycle is completed in about eight minutes. The timing of events in the cell cycle is controlled by mechanisms that are both internal and external to the cell.

Regulation of the Cell Cycle by External Events

Both the initiation and inhibition of cell division are triggered by events external to the cell when it is about to begin the replication process. An event may be as simple as the death of a nearby cell or as sweeping as the release of growth-promoting hormones, such as human growth hormone (HGH). A lack of HGH can inhibit cell division, resulting in dwarfism, whereas too much HGH can result in gigantism. Crowding of cells can also inhibit cell division. Another factor that can initiate cell division is the size of the cell; as a cell grows, it becomes inefficient due to its decreasing surface-to-volume ratio. The solution to this problem is to divide.

Whatever the source of the message, the cell receives the signal, and a series of events within the cell allows it to proceed into interphase. Moving forward from this initiation point, every parameter required during each cell cycle phase must be met or the cycle cannot progress.

Regulation at Internal Checkpoints

It is essential that the daughter cells produced be exact duplicates of the parent cell. Mistakes in the duplication or distribution of the chromosomes lead to mutations that may be passed forward to every new cell produced from an abnormal cell. To prevent a compromised cell from continuing to divide, there are internal control mechanisms that operate at three main **cell cycle checkpoints**. A checkpoint is one of several points in the eukaryotic cell cycle at which the progression of a cell to the next stage in the cycle can be halted until conditions are favorable. These checkpoints occur near the end of G_1, at the G_2/M transition, and during metaphase (**Figure 10.11**).

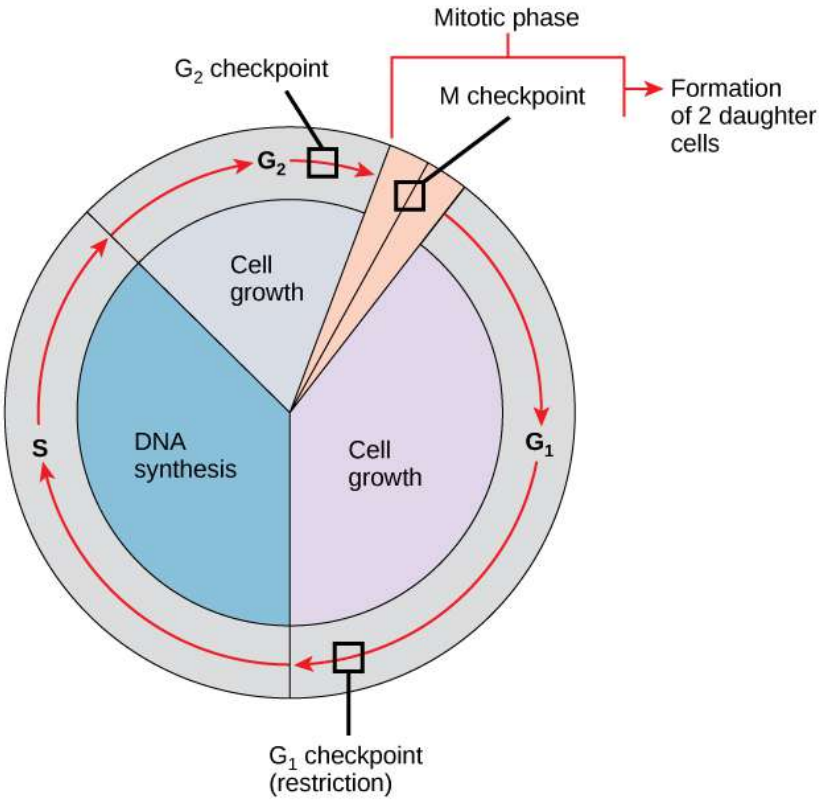

Figure 10.11 The cell cycle is controlled at three checkpoints. The integrity of the DNA is assessed at the G_1 checkpoint. Proper chromosome duplication is assessed at the G_2 checkpoint. Attachment of each kinetochore to a spindle fiber is assessed at the M checkpoint.

The G_1 Checkpoint

The G_1 checkpoint determines whether all conditions are favorable for cell division to proceed. The G_1 checkpoint, also called the restriction point (in yeast), is a point at which the cell commits to the cell division process. External influences, such as growth factors, play a large role in carrying the cell past the G_1 checkpoint. In addition to adequate reserves and cell size, there is a check for genomic DNA damage at the G_1 checkpoint. A cell that does not meet all the requirements will not be allowed to progress into the S phase. The cell can halt the cycle and attempt to remedy the problematic condition, or the cell can advance into G_0 and await further signals when conditions improve.

The G_2 Checkpoint

The G_2 checkpoint bars entry into the mitotic phase if certain conditions are not met. As at the G_1 checkpoint, cell size and protein reserves are assessed. However, the most important role of the G_2 checkpoint is to ensure that all of the chromosomes have been replicated and that the replicated DNA is not damaged. If the checkpoint mechanisms detect problems with the DNA, the cell cycle is halted, and the cell attempts to either complete DNA replication or repair the damaged DNA.

The M Checkpoint

The M checkpoint occurs near the end of the metaphase stage of karyokinesis. The M checkpoint is also known as the spindle checkpoint, because it determines whether all the sister chromatids are correctly attached to the spindle microtubules. Because the separation of the sister chromatids during anaphase is an irreversible step, the cycle will not proceed until the kinetochores of each pair of sister chromatids are firmly anchored to at least two spindle fibers arising from opposite poles of the cell.

Watch what occurs at the G_1, G_2, and M checkpoints by visiting this **website (http://openstaxcollege.org/l/cell_checkpnts)** to see an animation of the cell cycle.

Down Syndrome is a genetic, developmental condition caused by nondisjunction of chromosome 21 during meiosis. Explain how a problem with the spindle checkpoint can cause this to occur in the cell.

a. Failure in spindle checkpoint results in the formation of one gamete cell with two extra chromosomes and another gamete cell lacking chromosomes.

b. Failure in spindle checkpoint yields the same number of chromosomes in each gamete cell.

c. Failure in spindle checkpoint will form two gamete cells without any chromosomes.

d. Failure in spindle checkpoint results in the formation of one gamete cell with an extra chromosome and another gamete cell lacking a chromosome.

Regulator Molecules of the Cell Cycle

In addition to the internally controlled checkpoints, there are two groups of intracellular molecules that regulate the cell cycle. These regulatory molecules either promote progress of the cell to the next phase (positive regulation) or halt the cycle (negative regulation). Regulator molecules may act individually, or they can influence the activity or production of other regulatory proteins. Therefore, the failure of a single regulator may have almost no effect on the cell cycle, especially if more than one mechanism controls the same event. Conversely, the effect of a deficient or non-functioning regulator can be wide-ranging and possibly fatal to the cell if multiple processes are affected.

Positive Regulation of the Cell Cycle

Two groups of proteins, called **cyclins** and **cyclin-dependent kinases** (Cdks), are responsible for the progress of the cell through the various checkpoints. The levels of the four cyclin proteins fluctuate throughout the cell cycle in a predictable pattern (**Figure 10.12**). Increases in the concentration of cyclin proteins are triggered by both external and internal signals. After the cell moves to the next stage of the cell cycle, the cyclins that were active in the previous stage are degraded.

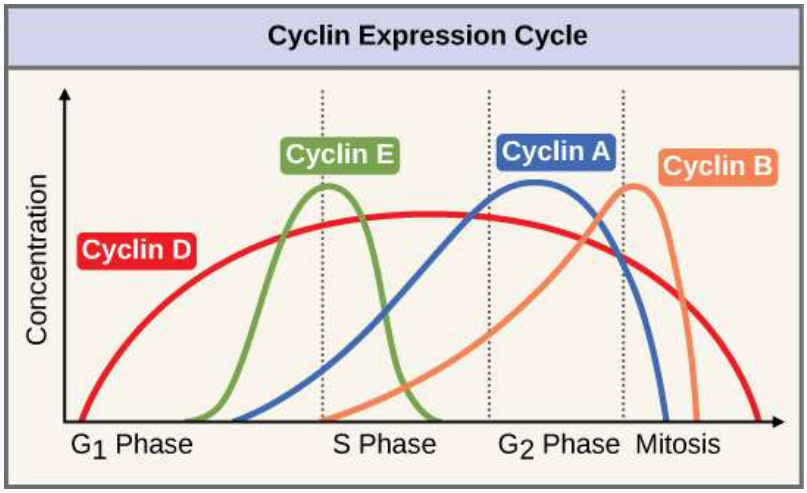

Figure 10.12 The concentrations of cyclin proteins change throughout the cell cycle. There is a direct correlation between cyclin accumulation and the three major cell cycle checkpoints. Also note the sharp decline of cyclin levels following each checkpoint (the transition between phases of the cell cycle), as cyclin is degraded by cytoplasmic enzymes. (credit: modification of work by "WikiMiMa"/Wikimedia Commons)

Cyclins regulate the cell cycle only when they are tightly bound to Cdks. To be fully active, the Cdk/cyclin complex must also be phosphorylated in specific locations. Like all kinases, Cdks are enzymes (kinases) that phosphorylate other proteins. Phosphorylation activates the protein by changing its shape. The proteins phosphorylated by Cdks are involved in advancing the cell to the next phase. (**Figure 10.13**). The levels of Cdk proteins are relatively stable throughout the cell cycle; however, the concentrations of cyclin fluctuate and determine when Cdk/cyclin complexes form. The different cyclins and Cdks bind at specific points in the cell cycle and thus regulate different checkpoints.

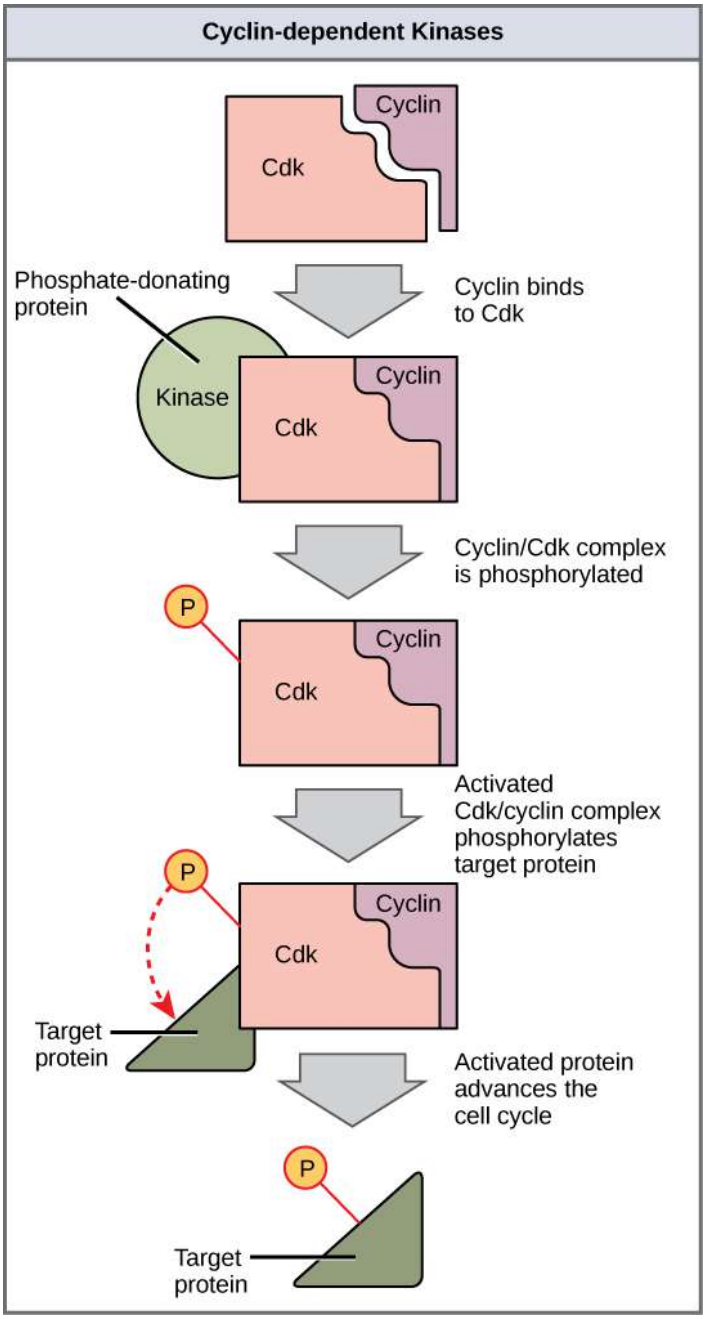

Figure 10.13 Cyclin-dependent kinases (Cdks) are protein kinases that, when fully activated, can phosphorylate and thus activate other proteins that advance the cell cycle past a checkpoint. To become fully activated, a Cdk must bind to a cyclin protein and then be phosphorylated by another kinase.

Since the cyclic fluctuations of cyclin levels are based on the timing of the cell cycle and not on specific events, regulation of the cell cycle usually occurs by either the Cdk molecules alone or the Cdk/cyclin complexes. Without a specific concentration of fully activated cyclin/Cdk complexes, the cell cycle cannot proceed through the checkpoints.

Although the cyclins are the main regulatory molecules that determine the forward momentum of the cell cycle, there are several other mechanisms that fine-tune the progress of the cycle with negative, rather than positive, effects. These mechanisms essentially block the progression of the cell cycle until problematic conditions are resolved. Molecules that prevent the full activation of Cdks are called Cdk inhibitors. Many of these inhibitor molecules directly or indirectly monitor a particular cell cycle event. The block placed on Cdks by inhibitor molecules will not be removed until the specific event that the inhibitor monitors is completed.

Negative Regulation of the Cell Cycle

The second group of cell cycle regulatory molecules are negative regulators. Negative regulators halt the cell cycle. Remember that in positive regulation, active molecules cause the cycle to progress.

The best understood negative regulatory molecules are **retinoblastoma protein (Rb)**, **p53**, and **p21**. Retinoblastoma proteins are a group of tumor-suppressor proteins common in many cells. The 53 and 21 designations refer to the functional molecular masses of the proteins (p) in kilodaltons. Much of what is known about cell cycle regulation comes from research conducted with cells that have lost regulatory control. All three of these regulatory proteins were discovered to be damaged or non-functional in cells that had begun to replicate uncontrollably (became cancerous). In each case, the main cause of the unchecked progress through the cell cycle was a faulty copy of the regulatory protein.

Rb, p53, and p21 act primarily at the G_1 checkpoint. p53 is a multi-functional protein that has a major impact on the commitment of a cell to division because it acts when there is damaged DNA in cells that are undergoing the preparatory processes during G_1. If damaged DNA is detected, p53 halts the cell cycle and recruits enzymes to repair the DNA. If the DNA cannot be repaired, p53 can trigger apoptosis, or cell death, to prevent the duplication of damaged chromosomes. As p53 levels rise, the production of p21 is triggered. p21 enforces the halt in the cycle dictated by p53 by binding to and inhibiting the activity of the Cdk/cyclin complexes. As a cell is exposed to more stress, higher levels of p53 and p21 accumulate, making it less likely that the cell will move into the S phase.

Rb exerts its regulatory influence on other positive regulator proteins. Chiefly, Rb monitors cell size. In the active, dephosphorylated state, Rb binds to proteins called transcription factors, most commonly, E2F (**Figure 10.14**). Transcription factors “turn on” specific genes, allowing the production of proteins encoded by that gene. When Rb is bound to E2F, production of proteins necessary for the G_1/S transition is blocked. As the cell increases in size, Rb is slowly phosphorylated until it becomes inactivated. Rb releases E2F, which can now turn on the gene that produces the transition protein, and this particular block is removed. For the cell to move past each of the checkpoints, all positive regulators must be “turned on,” and all negative regulators must be “turned off.”

visual CONNECTION

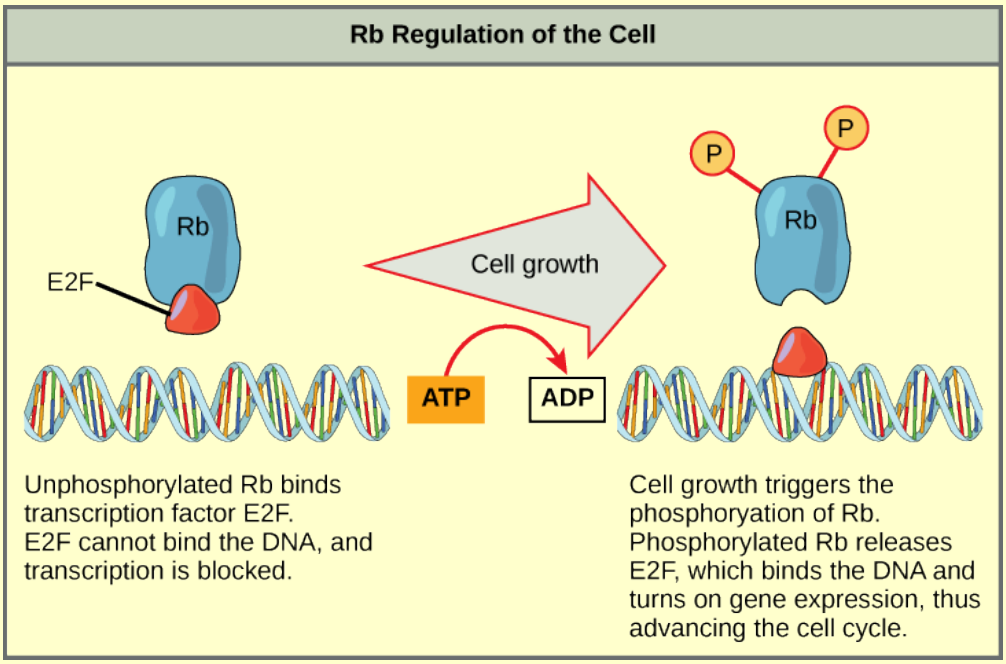

Figure 10.14 Rb halts the cell cycle and releases its hold in response to cell growth.

Rb and other proteins that negatively regulate the cell cycle are sometimes called tumor supressors. Why do you think the name tumor suppressor might be appropriate for these proteins?

a. They inhibit cell division.
b. They enhance the rate of cell division.
c. They start the cell cycle, thereby suppressing tumor formation.
d. These proteins, when phosphorylated, allow the cell cycle to proceed.

science practices CONNECTION for AP® Courses

- Rb is a negative regulator that blocks the cell cycle at the G_1 checkpoint until the cell achieves a requisite size. What is the most likely mechanism that Rb employs to halt the cell cycle?
- A cell has a mutation that results in the production of an abnormal cyclin-dependent kinase at the G_2/M checkpoint. What is a likely consequence of the mutation on the cell cycle?

10.4 | Cancer and the Cell Cycle

In this section, you will explore the following question:

- What causes uncontrolled cell growth, and why does it often cause cancer?

Connection for AP® Courses

Cancer results from unchecked cell division caused by a breakdown of the mechanisms that regulate the cell cycle. The loss of control begins with a change in the DNA sequence of a gene that codes for one of the regulatory molecules. Faulty instructions lead to a protein that does not function as it should. One culprit that has been identified is the p53 protein (coded for by the *p53* gene), a major regulator at the G_1 checkpoint. Normally, p53 proteins monitor DNA. If they find cells with damaged DNA, p53 will trigger repair mechanisms or destroy the cells, thus suppressing the formation of a tumor. However, mutations in *p53* can result in abnormal p53 proteins that fail to stop cell division if the cell's DNA is damaged. This results in an increased number of mutations, leading to abnormal daughter cells. Eventually, all checkpoints in the cell become nonfunctional, and the abnormal cells can crowd out normal cells.

Information presented and the examples highlighted in the section support concepts and Learning Objectives outlined in Big Idea 3 of the AP® Biology Curriculum Framework, as shown in the table. The Learning Objectives listed in the Curriculum Framework provide a transparent foundation for the AP® Biology course, an inquiry-based laboratory experience, instructional activities, and AP® exam questions. A Learning Objective merges required content with one or more of the seven Science Practices.

Big Idea 3	Living systems store, retrieve, transmit and respond to information essential to life processes.
Enduring Understanding 3.A	Heritable information provides for continuity of life.
Essential Knowledge	**3.A.2** In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
Science Practice	**6.4** The student can make claims and predictions about natural phenomena based on scientific theories and models.
Learning Objective	**3.7** The student can make predictions about natural phenomena occurring during the cell cycle.

The Science Practice Challenge Questions contain additional test questions for this section that will help you prepare for the AP exam. These questions address the following standards:
[APLO 2.32][APLO 2.34][APLO 3.6][APLO 3.7][APLO 3.8][APLO 4.6][APLO 4.14][APLO 4.22]

Cancer comprises many different diseases caused by a common mechanism: uncontrolled cell growth. Despite the redundancy and overlapping levels of cell cycle control, errors do occur. One of the critical processes monitored by the cell cycle checkpoint surveillance mechanism is the proper replication of DNA during the S phase. Even when all of the cell cycle controls are fully functional, a small percentage of replication errors (mutations) will be passed on to the daughter cells. If changes to the DNA nucleotide sequence occur within a coding portion of a gene and are not corrected, a gene mutation results. All cancers start when a gene mutation gives rise to a faulty protein that plays a key role in cell reproduction. The change in the cell that results from the malformed protein may be minor: perhaps a slight delay in the binding of Cdk to cyclin or an Rb protein that detaches from its target DNA while still phosphorylated. Even minor mistakes, however, may allow subsequent mistakes to occur more readily. Over and over, small uncorrected errors are passed from the parent cell to the daughter cells and amplified as each generation produces more non-functional proteins from uncorrected DNA damage. Eventually, the pace of the cell cycle speeds up as the effectiveness of the control and repair mechanisms decreases. Uncontrolled growth of the mutated cells outpaces the growth of normal cells in the area, and a tumor ("-oma") can result.

Proto-oncogenes

The genes that code for the positive cell cycle regulators are called **proto-oncogenes**. Proto-oncogenes are normal genes that, when mutated in certain ways, become **oncogenes**, genes that cause a cell to become cancerous. Consider what might happen to the cell cycle in a cell with a recently acquired oncogene. In most instances, the alteration of the DNA sequence will result in a less functional (or non-functional) protein. The result is detrimental to the cell and will likely prevent the cell from completing the cell cycle; however, the organism is not harmed because the mutation will not be carried forward. If a cell cannot reproduce, the mutation is not propagated and the damage is minimal. Occasionally, however, a gene mutation causes a change that increases the activity of a positive regulator. For example, a mutation that allows Cdk to be activated

without being partnered with cyclin could push the cell cycle past a checkpoint before all of the required conditions are met. If the resulting daughter cells are too damaged to undergo further cell divisions, the mutation would not be propagated and no harm would come to the organism. However, if the atypical daughter cells are able to undergo further cell divisions, subsequent generations of cells will probably accumulate even more mutations, some possibly in additional genes that regulate the cell cycle.

The Cdk gene in the above example is only one of many genes that are considered proto-oncogenes. In addition to the cell cycle regulatory proteins, any protein that influences the cycle can be altered in such a way as to override cell cycle checkpoints. An oncogene is any gene that, when altered, leads to an increase in the rate of cell cycle progression.

Tumor Suppressor Genes

Like proto-oncogenes, many of the negative cell cycle regulatory proteins were discovered in cells that had become cancerous. **Tumor suppressor genes** are segments of DNA that code for negative regulator proteins, the type of regulators that, when activated, can prevent the cell from undergoing uncontrolled division. The collective function of the best-understood tumor suppressor gene proteins, Rb, p53, and p21, is to put up a roadblock to cell cycle progression until certain events are completed. A cell that carries a mutated form of a negative regulator might not be able to halt the cell cycle if there is a problem. Tumor suppressors are similar to brakes in a vehicle: Malfunctioning brakes can contribute to a car crash.

Mutated p53 genes have been identified in more than one-half of all human tumor cells. This discovery is not surprising in light of the multiple roles that the p53 protein plays at the G_1 checkpoint. A cell with a faulty p53 may fail to detect errors present in the genomic DNA (**Figure 10.15**). Even if a partially functional p53 does identify the mutations, it may no longer be able to signal the necessary DNA repair enzymes. Either way, damaged DNA will remain uncorrected. At this point, a functional p53 will deem the cell unsalvageable and trigger programmed cell death (apoptosis). The damaged version of p53 found in cancer cells, however, cannot trigger apoptosis.

visual CONNECTION

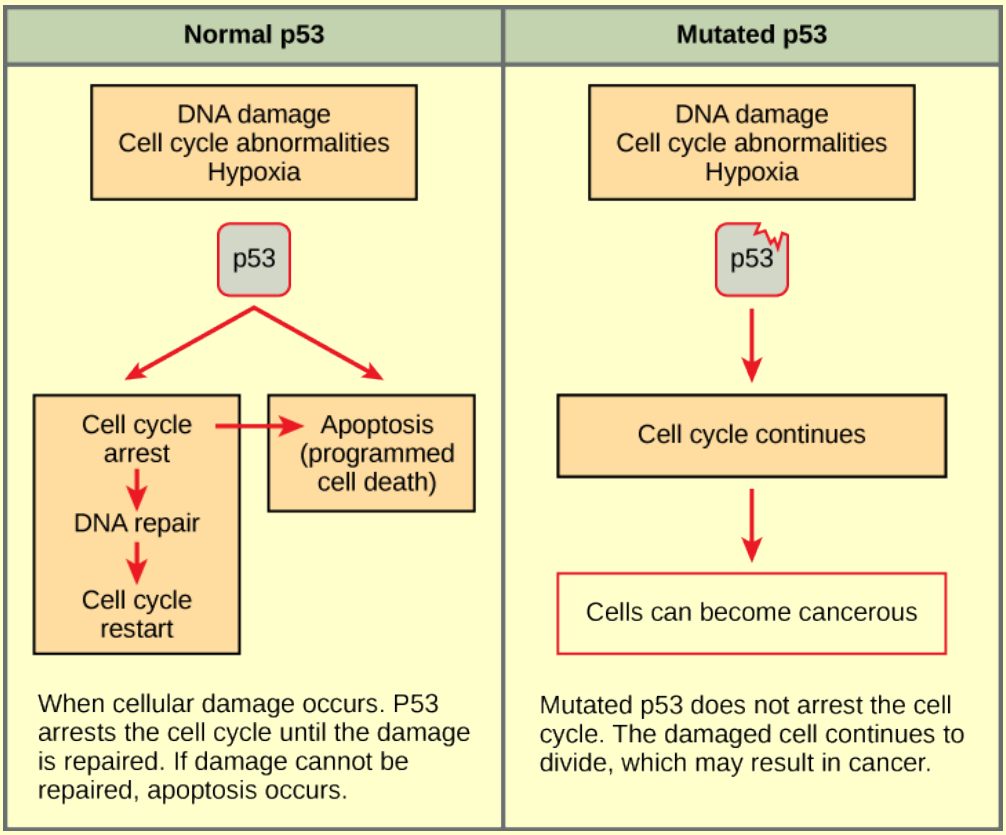

Figure 10.15 The role of normal p53 is to monitor DNA and the supply of oxygen (hypoxia is a condition of reduced oxygen supply). If damage is detected, p53 triggers repair mechanisms. If repairs are unsuccessful, p53 signals apoptosis. A cell with an abnormal p53 protein cannot repair damaged DNA and thus cannot signal apoptosis. Cells with abnormal p53 can become cancerous. (credit: modification of work by Thierry Soussi)

Human papillomavirus can cause cervical cancer. The virus encodes E6, a protein that binds p53. Based on this fact and what you know about p53, what effect do you think E6 binding has on p53 activity?

a. E6 activates p53
b. E6 inactivates p53
c. E6 mutates p53
d. E6 binding marks p53 for degradation

The loss of p53 function has other repercussions for the cell cycle. Mutated p53 might lose its ability to trigger p21 production. Without adequate levels of p21, there is no effective block on Cdk activation. Essentially, without a fully functional p53, the G_1 checkpoint is severely compromised and the cell proceeds directly from G_1 to S regardless of internal and external conditions. At the completion of this shortened cell cycle, two daughter cells are produced that have inherited the mutated p53 gene. Given the non-optimal conditions under which the parent cell reproduced, it is likely that the daughter cells will have acquired other mutations in addition to the faulty tumor suppressor gene. Cells such as these daughter cells quickly accumulate both oncogenes and non-functional tumor suppressor genes. Again, the result is tumor growth.

Go to this **website (http://openstaxcollege.org/l/cancer)** to watch an animation of how cancer results from errors in the cell cycle.

Treating cancer can be described as a fight against natural biologic processes. Explain what this means in terms of tumor formation.

a. Cancer forms when natural defenses are inhibited and cells divide uncontrollably.

b. Mutated cells undergo apoptosis, causing cells to divide uncontrollably.

c. Cancer treatment would require inhibiting apoptosis which is a natural defense.

d. In cancerous cells, apoptosis occurs.

Think About It

Human papillomavirus (HPV) can cause cervical cancer. The virus encodes E6, a protein that binds p53. Predict the most likely effect of E6 binding on p53 activity, and explain the basis for your prediction.

10.5 | Prokaryotic Cell Division

In this section, you will explore the following question:

- How does the process of binary fission in prokaryotes differ from cell division in eukaryotes?

Prokaryotes, such as bacteria, propagate by binary fission. For unicellular organisms, cell division is the only method to produce new individuals. In both prokaryotic and eukaryotic cells, the outcome of cell reproduction is a pair of daughter cells that are genetically identical to the parent cell. In unicellular organisms, daughter cells are individuals.

To achieve the outcome of cloned offspring, certain steps are essential. The genomic DNA must be replicated and then allocated into the daughter cells; the cytoplasmic contents must also be divided to give both new cells the machinery to sustain life. In bacterial cells, the genome consists of a single, circular DNA chromosome; therefore, the process of cell division is simplified. Karyokinesis is unnecessary because there is no nucleus and thus no need to direct one copy of the multiple chromosomes into each daughter cell. This type of cell division is called **binary (prokaryotic) fission**.

Binary Fission

Due to the relative simplicity of the prokaryotes, the cell division process, called binary fission, is a less complicated and much more rapid process than cell division in eukaryotes. The single, circular DNA chromosome of bacteria is not enclosed in a nucleus, but instead occupies a specific location, the nucleoid, within the cell (**Figure 10.2**). Although the DNA of the nucleoid is associated with proteins that aid in packaging the molecule into a compact size, there are no histone proteins and thus no nucleosomes in prokaryotes. The packing proteins of bacteria are, however, related to the cohesin and condensin proteins involved in the chromosome compaction of eukaryotes.

The bacterial chromosome is attached to the plasma membrane at about the midpoint of the cell. The starting point of replication, the **origin**, is close to the binding site of the chromosome to the plasma membrane (Figure 10.16). Replication of the DNA is bidirectional, moving away from the origin on both strands of the loop simultaneously. As the new double strands are formed, each origin point moves away from the cell wall attachment toward the opposite ends of the cell. As the cell elongates, the growing membrane aids in the transport of the chromosomes. After the chromosomes have cleared the midpoint of the elongated cell, cytoplasmic separation begins. The formation of a ring composed of repeating units of a protein called **FtsZ** directs the partition between the nucleoids. Formation of the FtsZ ring triggers the accumulation of other proteins that work together to recruit new membrane and cell wall materials to the site. A **septum** is formed between the nucleoids, extending gradually from the periphery toward the center of the cell. When the new cell walls are in place, the daughter cells separate.

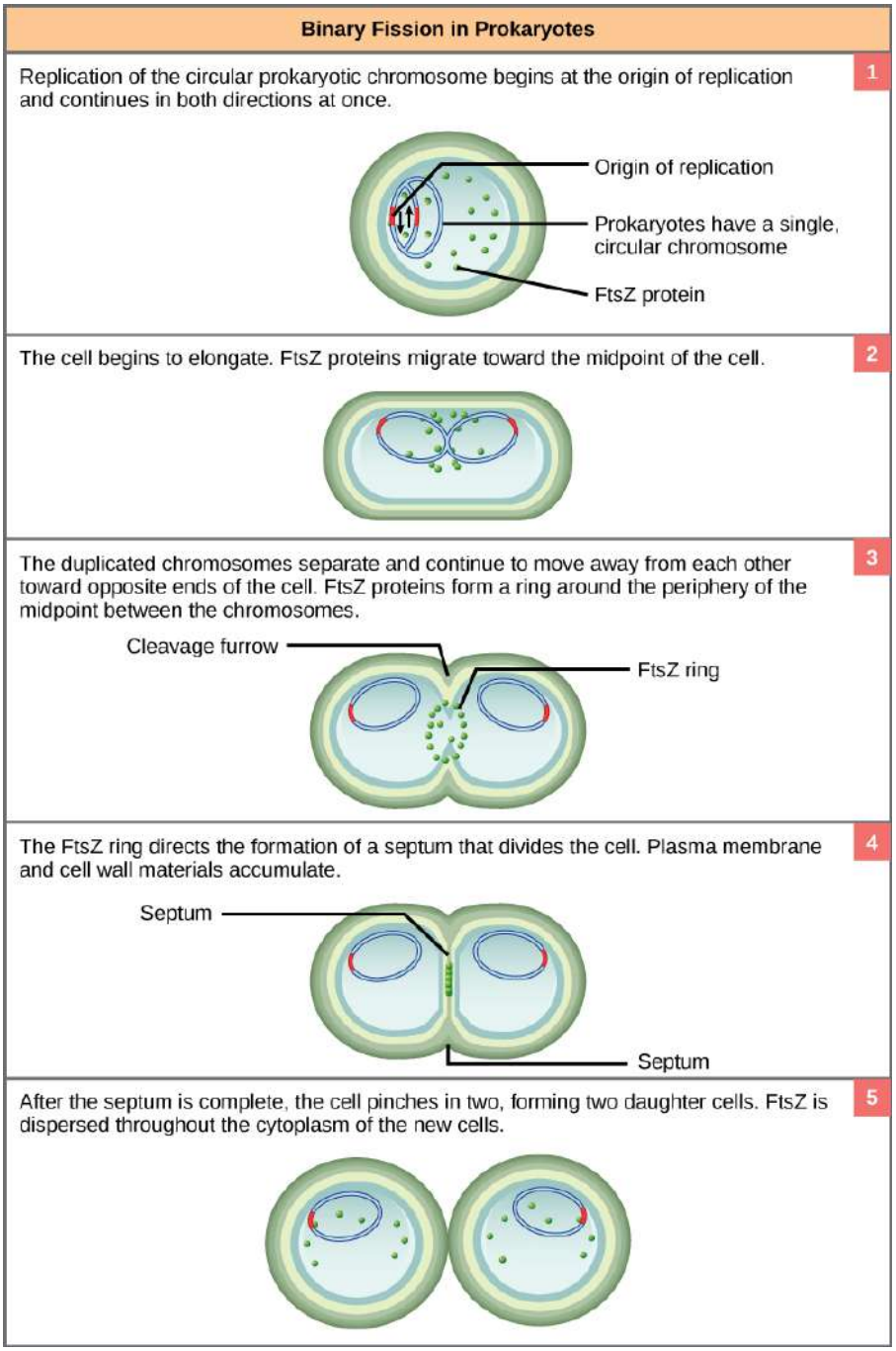

Figure 10.16 These images show the steps of binary fission in prokaryotes. (credit: modification of work by "Mcstrother"/Wikimedia Commons)

evolution CONNECTION

The precise timing and formation of the mitotic spindle is critical to the success of eukaryotic cell division. Prokaryotic cells, on the other hand, do not undergo karyokinesis and therefore have no need for a mitotic spindle. However, the FtsZ protein that plays such a vital role in prokaryotic cytokinesis is structurally and functionally very similar to tubulin, the building block of the microtubules that make up the mitotic spindle fibers that are necessary for eukaryotes. FtsZ proteins can form filaments, rings, and other three-dimensional structures that resemble the way tubulin forms microtubules, centrioles, and various cytoskeletal components. In addition, both FtsZ and tubulin employ the same energy source, GTP (guanosine triphosphate), to rapidly assemble and disassemble complex structures.

FtsZ and tubulin are homologous structures derived from common evolutionary origins. In this example, FtsZ is the ancestor protein to tubulin (a modern protein). While both proteins are found in extant organisms, tubulin function has evolved and diversified tremendously since evolving from its FtsZ prokaryotic origin. A survey of mitotic assembly components found in present-day unicellular eukaryotes reveals crucial intermediary steps to the complex membrane-enclosed genomes of multicellular eukaryotes (Table 10.4).

Cell Division Apparatus among Various Organisms

	Structure of genetic material	Division of nuclear material	Separation of daughter cells
Prokaryotes	There is no nucleus. The single, circular chromosome exists in a region of cytoplasm called the nucleoid.	Occurs through binary fission. As the chromosome is replicated, the two copies move to opposite ends of the cell by an unknown mechanism.	FtsZ proteins assemble into a ring that pinches the cell in two.
Some protists	Linear chromosomes exist in the nucleus.	Chromosomes attach to the nuclear envelope, which remains intact. The mitotic spindle passes through the envelope and elongates the cell. No centrioles exist.	Microfilaments form a cleavage furrow that pinches the cell in two.
Other protists	Linear chromosomes exist in the nucleus.	A mitotic spindle forms from the centrioles and passes through the nuclear membrane, which remains intact. Chromosomes attach to the mitotic spindle, which separates the chromosomes and elongates the cell.	Microfilaments form a cleavage furrow that pinches the cell in two.
Animal cells	Linear chromosomes exist in the nucleus.	A mitotic spindle forms from the centrosomes. The nuclear envelope dissolves. Chromosomes attach to the mitotic spindle, which separates the chromosomes and elongates the cell.	Microfilaments form a cleavage furrow that pinches the cell in two.

Table 10.4

FtsZ is a prokaryotic protein and tubulin is a eukaryotic protein. These two proteins share many structural and functional similarities and are believed to have evolved from the same ancestral protein. However, there are also some important differences between these proteins. In what way are these proteins different?

a. Tubulin proteins can rapidly disassemble, but FtsZ proteins cannot.

b. Tubulin proteins can form long filaments, but FtsZ proteins cannot.
c. Tubulin uses GTP as an energy source, but FtsZ does not.
d. Tubulin pulls chromosomes apart, but FtsZ does not.

KEY TERMS

anaphase stage of mitosis during which sister chromatids are separated from each other

binary fission prokaryotic cell division process

cell cycle ordered series of events involving cell growth and cell division that produces two new daughter cells

cell cycle checkpoint mechanism that monitors the preparedness of a eukaryotic cell to advance through the various cell cycle stages

cell plate structure formed during plant cell cytokinesis by Golgi vesicles, forming a temporary structure (phragmoplast) and fusing at the metaphase plate; ultimately leads to the formation of cell walls that separate the two daughter cells

centriole rod-like structure constructed of microtubules at the center of each animal cell centrosome

centromere region at which sister chromatids are bound together; a constricted area in condensed chromosomes

chromatid single DNA molecule of two strands of duplicated DNA and associated proteins held together at the centromere

cleavage furrow constriction formed by an actin ring during cytokinesis in animal cells that leads to cytoplasmic division

condensin proteins that help sister chromatids coil during prophase

cyclin one of a group of proteins that act in conjunction with cyclin-dependent kinases to help regulate the cell cycle by phosphorylating key proteins; the concentrations of cyclins fluctuate throughout the cell cycle

cyclin-dependent kinase one of a group of protein kinases that helps to regulate the cell cycle when bound to cyclin; it functions to phosphorylate other proteins that are either activated or inactivated by phosphorylation

cytokinesis division of the cytoplasm following mitosis that forms two daughter cells.

diploid cell, nucleus, or organism containing two sets of chromosomes ($2n$)

FtsZ tubulin-like protein component of the prokaryotic cytoskeleton that is important in prokaryotic cytokinesis (name origin: **F**ilamenting **t**emperature-**s**ensitive mutant **Z**)

G_0 phase distinct from the G_1 phase of interphase; a cell in G_0 is not preparing to divide

G_1 phase (also, first gap) first phase of interphase centered on cell growth during mitosis

G_2 phase (also, second gap) third phase of interphase during which the cell undergoes final preparations for mitosis

gamete haploid reproductive cell or sex cell (sperm, pollen grain, or egg)

gene physical and functional unit of heredity, a sequence of DNA that codes for a protein.

genome total genetic information of a cell or organism

haploid cell, nucleus, or organism containing one set of chromosomes (n)

histone one of several similar, highly conserved, low molecular weight, basic proteins found in the chromatin of all eukaryotic cells; associates with DNA to form nucleosomes

homologous chromosomes chromosomes of the same morphology with genes in the same location; diploid organisms have pairs of homologous chromosomes (homologs), with each homolog derived from a different parent

interphase period of the cell cycle leading up to mitosis; includes G_1, S, and G_2 phases (the interim period between two consecutive cell divisions

karyokinesis mitotic nuclear division

kinetochore protein structure associated with the centromere of each sister chromatid that attracts and binds spindle microtubules during prometaphase

locus position of a gene on a chromosome

metaphase stage of mitosis during which chromosomes are aligned at the metaphase plate

metaphase plate equatorial plane midway between the two poles of a cell where the chromosomes align during metaphase

mitosis (also, karyokinesis) period of the cell cycle during which the duplicated chromosomes are separated into identical nuclei; includes prophase, prometaphase, metaphase, anaphase, and telophase

mitotic phase period of the cell cycle during which duplicated chromosomes are distributed into two nuclei and cytoplasmic contents are divided; includes karyokinesis (mitosis) and cytokinesis

mitotic spindle apparatus composed of microtubules that orchestrates the movement of chromosomes during mitosis

nucleosome subunit of chromatin composed of a short length of DNA wrapped around a core of histone proteins

oncogene mutated version of a normal gene involved in the positive regulation of the cell cycle

origin (also, ORI) region of the prokaryotic chromosome where replication begins (origin of replication)

p21 cell cycle regulatory protein that inhibits the cell cycle; its levels are controlled by p53

p53 cell cycle regulatory protein that regulates cell growth and monitors DNA damage; it halts the progression of the cell cycle in cases of DNA damage and may induce apoptosis

prometaphase stage of mitosis during which the nuclear membrane breaks down and mitotic spindle fibers attach to kinetochores

prophase stage of mitosis during which chromosomes condense and the mitotic spindle begins to form

proto-oncogene normal gene that when mutated becomes an oncogene

quiescent refers to a cell that is performing normal cell functions and has not initiated preparations for cell division

retinoblastoma protein (Rb) regulatory molecule that exhibits negative effects on the cell cycle by interacting with a transcription factor (E2F)

S phase second, or synthesis, stage of interphase during which DNA replication occurs

septum structure formed in a bacterial cell as a precursor to the separation of the cell into two daughter cells

telophase stage of mitosis during which chromosomes arrive at opposite poles, decondense, and are surrounded by a new nuclear envelope

tumor suppressor gene segment of DNA that codes for regulator proteins that prevent the cell from undergoing uncontrolled division

CHAPTER SUMMARY

10.1 Cell Division

Prokaryotes have a single circular chromosome composed of double-stranded DNA, whereas eukaryotes have multiple, linear chromosomes composed of chromatin, all surrounded by a nuclear membrane. The 46 chromosomes of human somatic cells are composed of 22 pairs of autosomes (matched pairs) and a pair of sex chromosomes, which may or may not be matched. This is the 2*n* or diploid state. Human gametes have 23 chromosomes representing one complete set of chromosomes; a set of chromosomes is complete with either one of the sex chromosomes. This is the *n* or haploid state. Genes are segments of DNA that code for a specific protein. An organism's traits are determined by the genes inherited from each parent. Duplicated chromosomes are composed of two sister chromatids. Chromosomes are compacted using a

variety of mechanisms during certain stages of the cell cycle. Several classes of protein are involved in the organization and packing of the chromosomal DNA into a highly condensed structure. The condensing complex compacts chromosomes, and the resulting condensed structure is necessary for chromosomal segregation during mitosis.

10.2 The Cell Cycle

The cell cycle is an orderly sequence of events. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages. In eukaryotes, the cell cycle consists of a long preparatory period, called interphase. Interphase is divided into G_1, S, and G_2 phases. The mitotic phase begins with karyokinesis (mitosis), which consists of five stages: prophase, prometaphase, metaphase, anaphase, and telophase. The final stage of the mitotic phase is cytokinesis, during which the cytoplasmic components of the daughter cells are separated either by an actin ring (animal cells) or by cell plate formation (plant cells).

10.3 Control of the Cell Cycle

Each step of the cell cycle is monitored by internal controls called checkpoints. There are three major checkpoints in the cell cycle: one near the end of G_1, a second at the G_2/M transition, and the third during metaphase. Positive regulator molecules allow the cell cycle to advance to the next stage. Negative regulator molecules monitor cellular conditions and can halt the cycle until specific requirements are met.

10.4 Cancer and the Cell Cycle

Cancer is the result of unchecked cell division caused by a breakdown of the mechanisms that regulate the cell cycle. The loss of control begins with a change in the DNA sequence of a gene that codes for one of the regulatory molecules. Faulty instructions lead to a protein that does not function as it should. Any disruption of the monitoring system can allow other mistakes to be passed on to the daughter cells. Each successive cell division will give rise to daughter cells with even more accumulated damage. Eventually, all checkpoints become nonfunctional, and rapidly reproducing cells crowd out normal cells, resulting in a tumor or leukemia (blood cancer).

10.5 Prokaryotic Cell Division

In both prokaryotic and eukaryotic cell division, the genomic DNA is replicated and then each copy is allocated into a daughter cell. In addition, the cytoplasmic contents are divided evenly and distributed to the new cells. However, there are many differences between prokaryotic and eukaryotic cell division. Bacteria have a single, circular DNA chromosome but no nucleus. Therefore, mitosis is not necessary in bacterial cell division. Bacterial cytokinesis is directed by a ring composed of a protein called FtsZ. Ingrowth of membrane and cell wall material from the periphery of the cells results in the formation of a septum that eventually constructs the separate cell walls of the daughter cells.

REVIEW QUESTIONS

1. A diploid cell has how many times the number of chromosomes as a haploid cell?

a. four times
b. half
c. one-fourth
d. twice

2. The first level of DNA organization in a eukaryotic cell is maintained by which molecule?

a. cohesion
b. condensin
c. chromatin
d. histone

3. What inherited feature, in specific combinations, determines an organism's traits?

a. cell membranes
b. genes
c. proteins
d. RNA

4. What are identical copies of chromatin held together by cohesin at the centromere called?

a. histones
b. nucleosomes
c. chromatin
d. sister chromatids

5. Chromosomes are duplicated during what stage of the cell cycle?

a. G_1 phase

b. prophase

c. pro-metaphase

d. S-phase

6. Which of the following events does not occur during some stages of interphase?

a. DNA duplication

b. increase in cell size

c. organelle duplication

d. separation of sister chromatids

7. Attachment of the mitotic spindle fibers to the kinetochores is a characteristic of which stage of mitosis?

a. anaphase

b. prophase

c. prometaphase

d. metaphase

8. The fusing of Golgi vesicles at the metaphase plate of dividing plant cells forms what structure?

a. actin ring

b. cell plate

c. cleavage furrow

d. mitotic spindle

9. What would be the outcome of blocking S-phase of interphase?

a. The cell would enter karyokinesis.

b. DNA replication would not occur.

c. Centrosomes would be duplicated.

d. The cytoskeleton would be dismantled.

10. At which of the cell cycle checkpoints do external forces have the greatest influence?

a. G_1 checkpoint

b. G_2 checkpoint

c. M checkpoint

d. G_0 checkpoint

11. If the M checkpoint is not cleared, what stage of mitosis will be blocked?

a. prophase

b. prometaphase

c. metaphase

d. anaphase

12. Which protein is a positive regulator that phosphorylates other proteins when activated?

a. p53

b. Retinoblastoma protein (Rb)

c. cyclin

d. Cyclin-dependent kinase (Cdk)

13. Which negative regulatory molecule can trigger apoptosis if vital cell cycle events do not occur?

a. p53

b. p21

c. Retinoblastoma protein (Rb)

d. Cyclin-dependent kinase (Cdk)

14. What is the main prerequisite for clearance at the G_2 checkpoint?

a. The cell has a reached a sufficient size.

b. The cell has an adequate stockpile of nucleotides.

c. An accurate and complete DNA replication has occurred.

d. Proper attachment of mitotic spindle fibers to kinetochores has occurred.

15. What do you call changes to the order of nucleotides in a segment of DNA that codes for a protein?

a. proto-oncogenes

b. tumor suppressor genes

c. gene mutations

d. negative regulators

16. Human papillomavirus can cause cervical cancer. The virus encodes E6, a protein that binds p53. Based on this fact and what you know about p53, what effect do you think E6 binding has on p53 activity?

a. E6 activates p53.

b. E6 protects p53 from degradation.

c. E6 mutates p53.

d. E6 binding marks p53 for degradation.

17. What is a gene that codes for a positive cell cycle regulator called?

a. kinase inhibitor

b. oncogenes

c. proto-oncogenes

d. tumor suppressor genes

18. Which molecule is a Cdk inhibitor or is controlled by p53?

a. anti-kinase

b. cyclin

c. p21

d. Rb

19. Which eukaryotic cell cycle events are missing in binary fission?

a. cell growth
b. DNA duplication
c. karyokinesis
d. cytokinesis

20. Which of the following statements about binary fission is false?

a. In both prokaryotic and eukaryotic cells, the outcome of cell reproduction is a pair of daughter cells, which are genetically identical to the parent cell.
b. Karyokinesis is unnecessary in prokaryotes because there is no nucleus.
c. Replication of the prokaryotic chromosome begins at the origin of replication and continues in both directions at once.
d. The mitotic spindle draws the duplicated chromosomes to the opposite ends of the cell followed by formation of a septum and two daughter cells.

21. The formation of what structure, that will eventually form the new cell walls of the daughter cells, is directed by FtsZ?

a. contractile ring
b. cell plate
c. cytoskeleton
d. septum

CRITICAL THINKING QUESTIONS

22. Compare and contrast a human somatic cell to a human gamete.

a. Somatic cells have 46 chromosomes and are diploid, whereas gametes have half as many chromosomes as found in somatic cells.
b. Somatic cells have 23 chromosomes and are diploid, whereas gametes have half as many chromosomes are are present in somatic cells.
c. Somatic cells have 46 chromosomes and are haploid, whereas gametes have 23 chromosomes and are diploid.
d. Somatic cells have 46 chromosomes with one sex chromosome. In gametes, 23 chromosomes are present with two sex chromosomes.

23. Eukaryotic chromosomes are thousands of times longer than a typical cell. Explain how chromosomes can fit inside a eukaryotic nucleus.

a. The genetic material remains distributed in the nucleus, mitochondria, and chloroplast.
b. The genome is present in a looped structure, thus it fits the size of the nucleus.
c. The DNA remains coiled around proteins to form nucleosomes.
d. The genetic material remains bound to the nuclear envelope, forming invaginations.

24. Briefly describe the events that occur in each phase of interphase.

a. G_1 - assessment for DNA damage, S - duplication of genetic material, G_2 - duplication and dismantling organelles
b. G_1 - duplication of organelles, S - duplication of DNA, G_2 - assessment of DNA damage
c. G_1 - synthesis of DNA, S - synthesis of organelle genetic material, G_2 - assessment of DNA damage
d. G_1 - preparation for DNA synthesis, S - assessment of DNA damage, M - Division of cell

25. Chemotherapy drugs such as vincristine and colchicines disrupt mitosis by binding to tubulin (the subunit of microtubules) and interfering with microtubule assembly and disassembly. Exactly what mitotic structure do these drugs target, and what effect would that have on cell division?

a. The drugs bind tubulin and inhibit the binding of spindle to the chromosome. This can arrest the cell cycle.

b. The drugs bind the tubulin, which leads to an error in the chromosome separation. This could lead to apoptosis.

c. The drugs bind the tubulin, thereby inhibiting their division in S-phase. This inhibits cell division.

d. The drugs bind the spindle fiber and hinder the separation of chromatins. This promotes the division spontaneously.

26. List some reasons why a cell that has just completed cytokinesis might enter the G_0 phase instead of the G_1 phase.

a. Some cells are physiologically inhibited from undergoing any division and remain in the G_0 phase to provide assistance to their neighboring cells.

b. Some cells reproduce only under certain conditions and, until then, they remain in the G_0 phase.

c. Suspected DNA damage can lead the cell to undergo the G_0 phase.

d. The lack of important components of cell division makes cells stay in the G_0 phase.

27. Describe the general conditions that must be met at each of the three main cell cycle checkpoints.

a. G_1 checkpoint - assessment of DNA damage, G_2 - assessment of new DNA, M checkpoint - segregation of sister chromatids in anaphase.

b. G_1 checkpoint - Energy reserves for s phase, G_2 checkpoint - assessment of new DNA, M checkpoint- attachment of spindle to kinetochore.

c. G_1 checkpoint - assessment of DNA damage, G_2 checkpoint - energy reserves for duplication, M checkpoint - attachment of spindle to kinetochore

d. G_1 checkpoint - Energy reserves for S-phase, S checkpoint - synthesis of DNA, G_2 checkpoint - assessment of new DNA

28. Explain the roles of the positive cell cycle regulators compared to the negative regulators.

a. Positive regulators promote the cell cycle but negative regulators block the cell cycle.

b. Positive regulators block the cell division in cancerous cells but negative regulators promote in such cells.

c. Positive regulators promote the cell cycle but negative regulators arrest the cell cycle until certain events have occurred.

d. Positive regulators show positive feedback mechanisms but negative regulators show negative feedback in the cell cycle.

29. Describe what occurs at the M checkpoint and predict what would happen if the M checkpoint failed.

a. The M checkpoint checks for proper separation of sister chromatids and if it fails, then cells may undergo nondisjunction of chromosomes.

b. The M checkpoint checks if the DNA is damaged and promotes its repair. If it fails, then the daughters end up with damaged DNA.

c. The M checkpoint ensures the proper duplication of DNA and if it fails, the cells may undergo nondisjunction of chromosomes.

d. The M checkpoint ensures that all the components required for cell division are available and if it fails, the cell cycle will be inhibited.

30. List the regulatory mechanisms that might be lost in a cell producing faulty p53.

a. assessment of damaged DNA, recruiting repair enzymes, and binding of spindle to kinetochore

b. quality of DNA, triggering apoptosis, and recruiting repair enzymes

c. quality of DNA, binding of spindle to kinetochore, and assessment of DNA repair

d. triggering apoptosis, recruiting repair enzymes, and proper binding of spindle to kinetochore

31. p53 can trigger apoptosis if certain cell cycle events fail. How does this regulatory outcome benefit a multicellular organism?

a. The apoptosis helps in controlling the consumption of energy by the extra cells.

b. The apoptosis inhibits the production of faulty proteins, which could be produced due to the DNA damage.

c. The process of apoptosis stops the invasion of viruses in the other cells.

d. The cells are killed due to the production of reactive oxygen species produced, which could harm the organism.

32. Name the processes that eukaryotic cell division and binary fission have in common.

a. DNA duplication, division of cell organelles, division of the cytoplasmic contents

b. DNA duplication, segregation of duplicated chromosomes, and division of the cytoplasmic contents

c. formation of a septum, DNA duplication, division of the cytoplasmic contents

d. segregation of duplicated chromosomes, formation of a septum, division of cell organelles

33. The formation of what structure, that will eventually form the new cell walls of the daughter cells, is directed by FtsZ?

a. contractile ring

b. cell plate

c. cytoskeleton

d. septum

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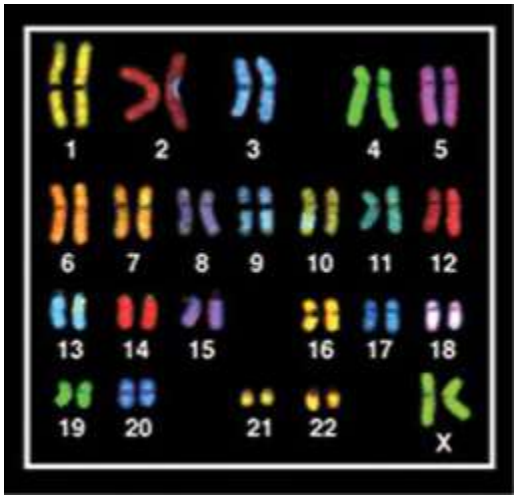
34.



Which of the following statements cannot be inferred from the karyotype shown?

a. The cell contains DNA.

b. The cell contains 46 chromosomes.

c. The cell is diploid.

d. The cell is prokaryotic.

35. Explain how DNA, which in humans measures approximately two meters, can fit inside a human cell that is about $10\,\mu m$. Discuss how the organization of the genetic material in eukaryotes differs from prokaryotes.

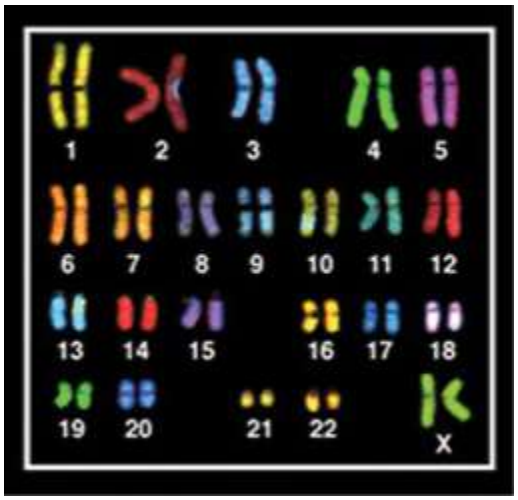
a. The DNA is found wrapped around histones to form nucleosomes, which further compact and ultimately form linear chromosomes. The prokaryotic genome is found as a loop and in eukaryotes as a double-stranded linear structure.

b. The DNA is wrapped around the nucleosomes to show a compact structure. The eukaryotes show a loop structure and prokaryotes show a double-stranded linear genome.

c. The genetic material shows ringed heterochromatin structure. The prokaryotes show multiple loops, and eukaryotes show a condensed chromatin.

d. The genetic material is wrapped around histones. The prokaryotes have a condensed structure in nucleoids, but eukaryotes have double-stranded linear structure.

36.



Which of the following statements about structure 1 on the karyotype is not true?

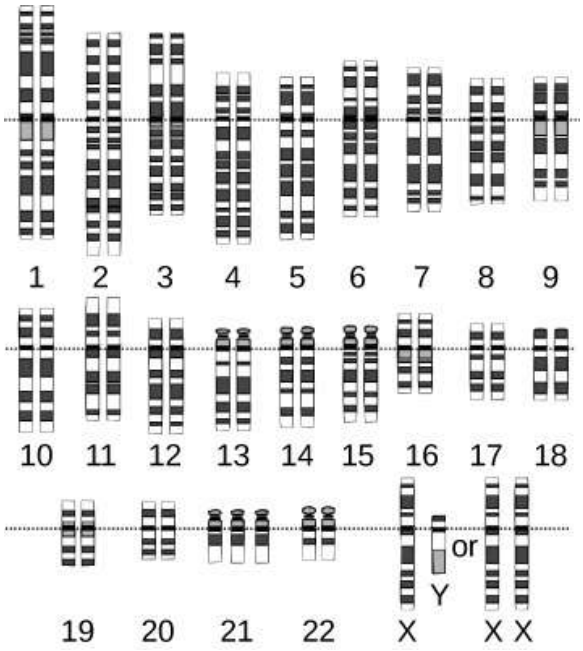
a. Structure 1 consists of homologous chromosomes.

b. The two parts of structure 1 will have genes in different loci.

c. The two parts of structure 1 originate from different parents.

d. The two parts of structure 1 will have slightly different sequences of nucleotides.

37.



Based on the karyotype provided, the nondisjuction of which chromosome causes Down Syndrome?

a. chromosome 21

b. chromosome 22

c. X chromosome

d. Y chromosome

38. Describe the sequence of mitotic cell cycle for one pair of chromosome that is undergoing normal mitotic division.

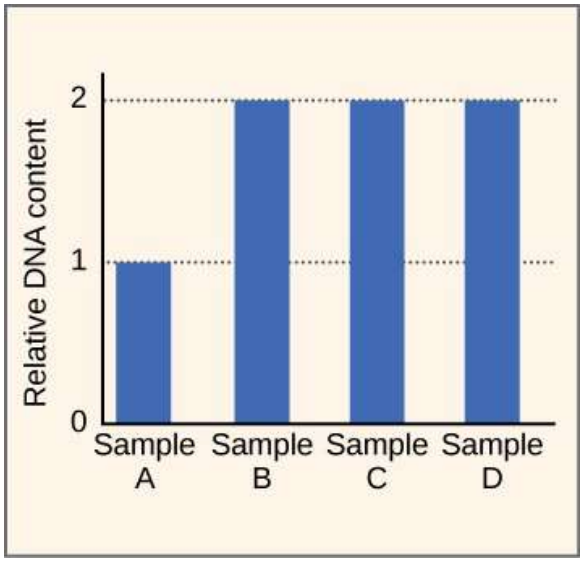
a. anaphase - metaphase - prophase - cytokinesis

b. anaphase - prophase - metaphase - cytokinesis

c. prophase - anaphase - metaphase - cytokinesis

d. prophase - metaphase - anaphase - cytokinesis

39.



In a study on cell division, researchers culture synchronously dividing human cells with thymidine. This causes the cells to arrest at the G_1 boundary. The cells are then placed in medium lacking thymidine, which releases the block, and the cells begin to divide again. Starting with Sample A and ending with Sample D, the DNA content of the cells is measured at different times after thymidine is removed. Results for four samples (A-D) are shown in the graph. Which sample presents the expected results for cells in S-phase?

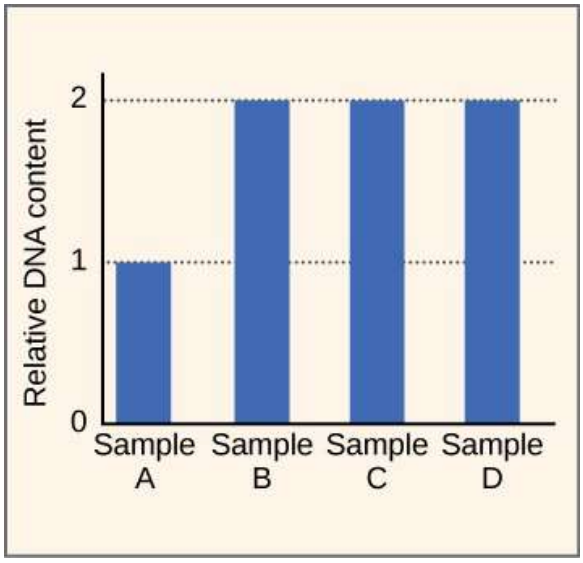
a. sample A

b. sample B

c. sample C

d. sample D

40.



In a study on cell division, researchers culture synchronously dividing human cells with thymidine. This

causes the cells to arrest at the G_1 boundary. The cells are then placed in medium lacking thymidine, which releases the block, and the cells begin to divide again. Starting with Sample A and ending with Sample D, the DNA content of the cells is measured at different times after thymidine is removed. Results for four samples (A-D) are shown in the graph. Explain what is happening in terms of the cell cycle and DNA content in sample B.

a. All the contents of the cell have been doubled.

b. The DNA content of the cell has doubled.

c. Two cells have been fused.

d. The cells are showing the semiconservative mechanism of cell division.

41. Li-Fraumeni syndrome (LFS1) is a rare hereditary disorder that leads to a predisposition to cancer. This hereditary disorder is linked to mutations in the tumor suppressor gene encoding the transcription factor p53. p53 acts at the G_1 checkpoint. If damaged DNA is detected, p53 halts the cell cycle. As p53 levels rise, the production of p21 is triggered. p21 enforces the halt in the cell cycle. A variant of Li-Fraumeni, called LFS2, is thought to occur due to a mutation of the CHK2 gene, which is also a tumor suppressor gene. CHK2 regulates the action of p53. Which of the following cascades is most likely to occur in a normal cell that does not contain the LFS mutation?

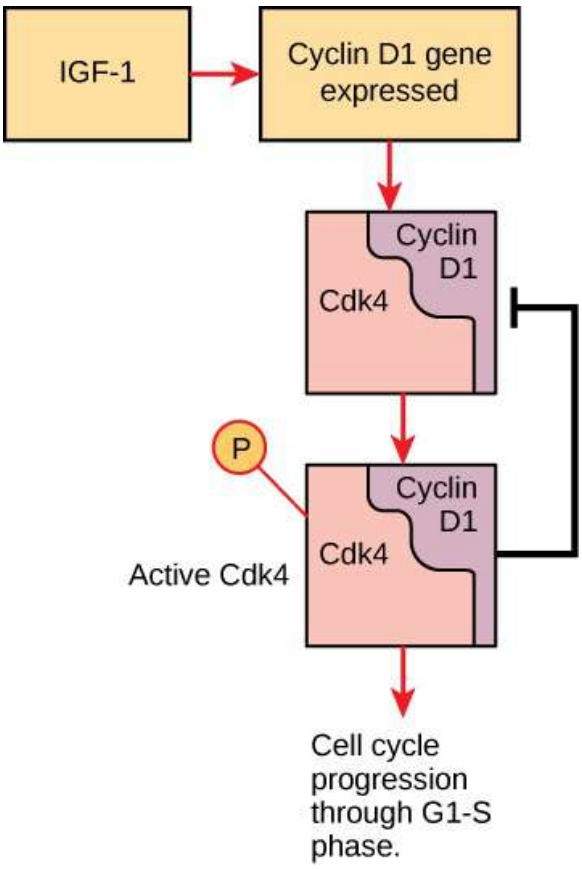
a. 1. cell cycle progression
   2. p53
   3. p21
   4. CHK2

b. 1. p53
   2. p21
   3. CHK2
   4. cell cycle progression

c. 1. p21
   2. p53
   3. CHK2
   4. cell cycle progression

d. 1. CHK2
   2. p53
   3. p21
   4. cell cycle progression

42.



The insulin growth factor (IGF-1) promotes cell proliferation as shown in the diagram. The expression of which protein in the diagram is controlled through negative feedback?

a. active Cdk4

b. Cyclin D1

c. Cyclin D1/Cdk4 complex

d. IGF-1

43. Explain why p53, p21, and CHK2 are considered tumor suppressor genes, not proto-oncogenes. Give an example of a proto-oncogene.

a. p53, p21, and CHK2 suppress the proteins that regulate the cell cycle, whereas proto-oncogenes, like phosphorylated Rb, help in cell cycle progression.

b. p53, p21, and CHK2 are negative cell cycle regulators, whereas Cdks are proto-oncogenes, which could cause cancer when mutated.

c. p53, p21, and CHK2 suppress the proteins that regulate the cell cycle, whereas Rb is considered a proto-oncogene, as it is the most primitive

d. The three proteins help stop the formation of tumors, whereas Cdk's are called proto-oncogenes because they are the most primitive of all.

SCIENCE PRACTICE CHALLENGE QUESTIONS

44. Many biological processes are synchronized with the 24-hour rotational period of Earth. Circadian (24-hour) periodicity is common across phyla. One of these processes is the cell cycle. The currently accepted explanation is that the low-oxygen atmosphere of early Earth had no ozone layer to filter out the solar ultraviolet radiation that damages DNA. Completing the S phase of the cell cycle at night provided a selective advantage. The internal clock controlling the cell cycle and the circadian clock became synchronized. Research has demonstrated that changes in one clock, either the circadian clock or the cell cycle clock, disrupt timing in the other. The question was, which clock controls the other?

Researchers have found that the circadian clock, which can be observed by fluorescent markers on proteins that carry the circadian signal, can be disrupted by changes in light, nutrition, or exposure to the steroid dexamethasone. Nutrition can also disrupt the cell cycle clock. Rat fibroblasts (cells constantly undergoing mitosis) were cultured on medium containing different levels of fetal bovine serum (FBS) with and without the addition of dexamethasone. Confluence is a phenomenon that occurs in tissue culture when the surface of the growth medium becomes covered with cells, and the cells stop dividing. The circadian and cell cycle periods were measured.

	FBS	Dexa-meth-asone	Con-flu-ence	Circa-dian Period (hr)	Cell Cycle Period (hr)
a	0%	no	no	24± 0.5	24± 0.5
b	10%	no	no	21.9± 1.1	21.3± 1.3
c	15%	no	no	19.4± 0.5	18.6± 0.6
d	10%	yes	no	24.2± 0.5	20.1± 0.94
e	*20%	yes	no	21.25± 0.36	19.5± 0.42
f	20%	yes	no	29± 1.05	16.05± 0.48
g	10%	yes	yes	24± 0.5	na

Table 10.5 * Subsets of samples with 20% FBS and dexamethasone were clustered around two means for each measured period.

A. Based on these data, **describe** the connections between the circadian period and the cell cycle period for each of the experimental conditions.

B. Based on these data, **justify the claim** that in cells that are actively dividing, the circadian period is set by the cell cycle period rather than the reverse.

45. Cells in different tissues of a fully developed human show significant variations in the length of time that they remain in the G0 phase of the cell cycle: muscle (lifetime), nerve (lifetime), adipose (years), liver (year), erythrocyte (months), bone osteoclasts (weeks), leukocyte (days), and epidermal (hours). For each of these types of tissues, **propose a reason** based on internal and external factors and function that might account for the differences among their longevities.

46. Describe the essential components and results of mitosis and the activities that occur during interphase to prepare the cell for mitosis.

47. Cancer comprises many different diseases with a common cause: uncontrolled cell growth. Cancer is a complex response to a host of environmental mutagens as well as the accumulation of random mutations. Since the “war on cancer” began in 1971, the death rate due to cancer has changed very little despite the discovery of several tumor suppressor genes, including p53.

A. Briefly **describe** the multiple functions of p53, including the role of p53 in apoptosis.

B. A principle of biology is that "form follows function." The protein p53, which has multiple functions, is named for its molecular mass—approximately 53 kDa. This is not a large polymer by comparison with other proteins; for example, ATP synthase, which has only one function, has a molecular mass of approximately 550 kDa. Based on analogies to processes involved in cellular signaling, **create a model(s) to explain** how so many functions can be supported by a single, relatively simple structure.

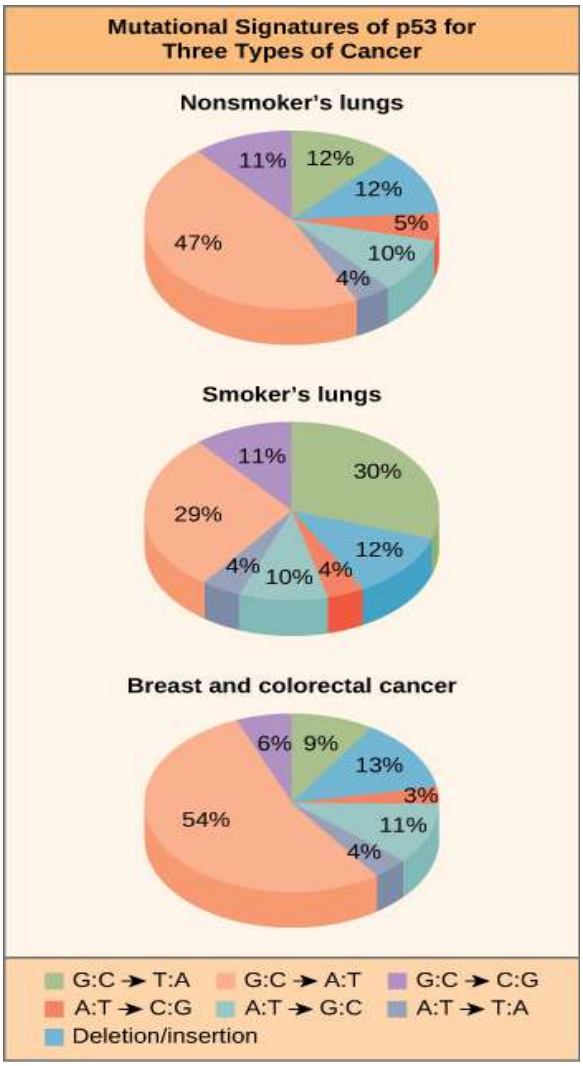


Figure 10.17

C. Mutational signatures of p53 are shown in the figure above [G.P. Pfeifer et al., Nature, 21(48), 2002] for the three types of cancer with the highest death rates in the U.S.: lung (~225,000 deaths in 2016), breast (246,000), and colorectal (381,000). These data can be obtained by sequencing the gene that encodes p53. Approximately 85% of lung cancers occur in smokers. Based on these data, **calculate** how many deaths due to lung cancer among nonsmokers were reported in 2016. How much does smoking increase the likelihood of death due to lung cancer?

D. As shown under each graph, particular transversions (replacement of a pyrimidine by a purine of vice versa) or transitions (replacement of a purine or pyrimidine by the alternative purine or pyrimidine) are features of specific mutational signatures. Based on these data, **identify** the transversion or transition that seems to be induced by cigarette smoke.

E. Using your answer to B above, **predict** possible mechanisms, that is, transversion or transition, for the different mutational signatures among lung cancers of smokers and those of other cancers, and for the very similar mutational signatures of lung cancers of nonsmokers and of breast and colorectal cancers. The partitioning of function along the length of the protein can lead to functional and nonfunctional segments. It is believed that the transversions due to smoking are caused by polyaromatic hydrocarbons. The hotspots for these mutations lie in the segment that binds to DNA. The transition hotspots are in segments that regulate apoptosis.