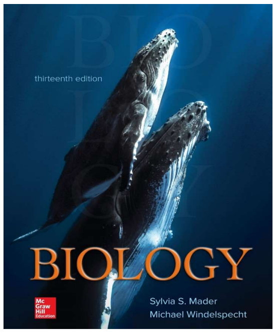
The Cell Cycle



Biology

Sylvia S. Mader
Michael Windelspecht

Chapter 9
The Cell Cycle and Cellular Reproduction
Lecture Outline

See separate FlexArt PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.

9-1

Outline

9-2

9.1 The Cell Cycle

The **cell cycle** is an orderly set of stages from the first division of a eukaryotic cell to the time the resulting daughter cells divide.

Just prior to the next division:

- Cell grows larger
- Number of organelles doubles
- DNA is replicated

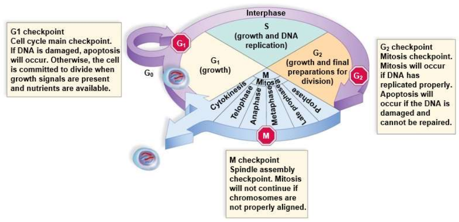
The two major stages of the cell cycle:

- **Interphase** (includes several stages)
- Mitotic stage (includes **mitosis** and **cytokinesis**)

9-3

The Cell Cycle

The Cell Cycle (1)



9-4

The Cell Cycle (2)

Interphase

- Most of the cell cycle is spent in interphase.
- Cell performs its usual functions.
- Time spent in interphase varies by cell type.
- Nerve and muscle cells do not complete the cell cycle (remain in the $\mathbf{G_0}$ stage).

9-5

The Cell Cycle (3)

Interphase consists of G_1, S, and G_2 phases.

- It takes up 90% of the cell cycle.
- G_1 Phase:
  - Cell is in recovery from previous division.
  - Cell doubles its organelles.
  - Cell grows in size.
  - Cell accumulates raw materials for DNA synthesis.
- S Phase:
  - DNA replication takes place.
  - Proteins associated with DNA are synthesized.
  - Chromosomes enter S phase with 1 **chromatid** each.
  - Chromosomes leave S phase with 2 identical chromatids (**sister chromatids**) each.
  - Sister chromatids remain attached until they are separated during mitosis.
- G_2 Phase:
  - G_2 phase is located between DNA replication and onset of mitosis.
  - Cell synthesizes proteins, including microtubules, necessary for division.

9-6

The Cell Cycle

The Cell Cycle (4)

M (Mitotic) Stage

- Includes:
  - **Mitosis**
    - Nuclear division
    - Daughter chromosomes are distributed by the **mitotic spindle** to two daughter nuclei.
  - **Cytokinesis**
    - Division of the cytoplasm
- Results in two genetically identical daughter cells

9-7

The Cell Cycle (5)

Apoptosis is programmed cell death.

It involves a sequence of cellular events that bring about the destruction of the cell.

- Fragmenting of the nucleus
- Blistering of the plasma membrane
- Engulfing of cell fragments by white blood cells or other cells

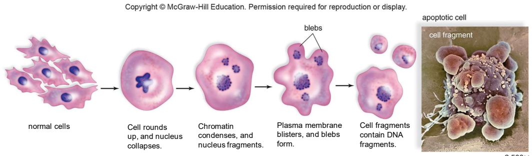
Apoptosis is caused by enzymes called caspases.

Mitosis and apoptosis are opposing forces.

- Mitosis increases cell numbers.
- Apoptosis decreases cell numbers.

9-8

Apoptosis



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Jump to Apoptosis Long Description

9-9

The Cell Cycle

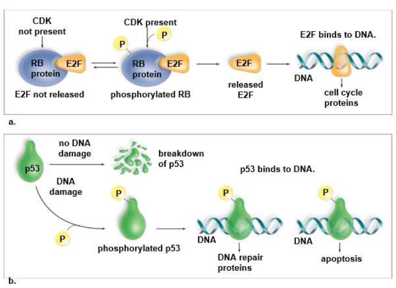
Apoptosis and Cell Division

Apoptosis

- Cell division and apoptosis occur throughout our lifetimes to maintain the body's homeostasis.
- An abnormal cell that could become cancerous or a virus-infected cell are cells that die through apoptosis.
- Cells harbor caspase enzymes that are normally kept in check by inhibitors.
  - Can be unleashed by internal or external signals
- Signaling protein **p53**
  - Stops the cell cycle at G_1 when the cell's DNA is damaged
  - Initiates an attempt at DNA repair
    - If successful, the cycle continues to mitosis.
    - If not, apoptosis is initiated.

9-10

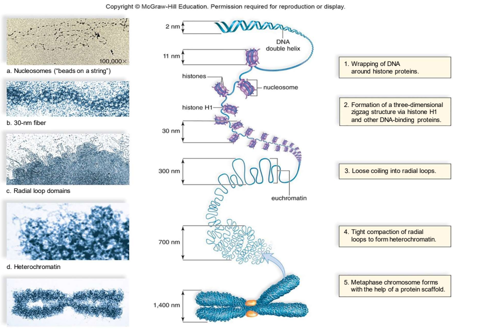
Regulation at the G_1 Checkpoint



Jump to Regulation at the G_1 Checkpoint Long Description

9-11

Structure of the Eukaryotic Chromosome



Jump to Structure of the Eukaryotic Chromosome Long Description

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The Cell Cycle

9.2 The Eukaryotic Chromosome

Contains a single DNA molecule (double helix)

- DNA is associated with **histones** (proteins).
- DNA and histone proteins are collectively called **chromatin**.
  - Histones
    - Play a structural role
    - Have essential survival functions
    - Primarily 5 types
    - Responsible for DNA packing into nucleus
- DNA wound around an 8-histone core is called a nucleosome, which appears as a bead.
  - Nucleosomes joined together by "linker" DNA appear as beads on a string.
  - The string "folds" into a compact zigzag structure.
  - Then it loops into radial loops.
  - It is loosely coiled.
  - Euchromatin represents the active chromatin that can be transcribed by RNA polymerase and transcription factors.

9-13

The Eukaryotic Chromosome

A more highly compacted form of the chromosome is heterochromatin.

- Inactive chromatin
- Genes hardly ever transcribed
- Compact chromosomes are more easily moved than extended chromatin.
- Most chromosomes have both compaction levels.

9-14

9.3 Mitosis and Cytokinesis

Eukaryotic cell division involves mitosis (nuclear division) and cytokinesis (division of cytoplasm).

During mitosis, sister chromatids are separated and distributed to daughter cells.

Before mitosis begins:

- Chromatin condenses (coils) into distinctly visible chromosomes.
- Each species has a characteristic chromosome number.

9-15

The Cell Cycle

Diploid Chromosome Numbers of Some Eukaryotes

Table 9.1 Diploid Chromosome Numbers of Some Eukaryotes

Type of Organism	Name of Chromosome	Chromosome Number
Fungi	*Saccharomyces cerevisiae* (yeast)	32
Plants	*Pisum sativum* (garden pea)	14
	Solanum tuberosum (potato)	48
	Ophioglossum vulgatum (Southern adder's tongue fern)	1,320
Animals	*Drosophila melanogaster* (fruit fly)	8
	Homo sapiens (human)	46
	Carassius auratus (goldfish)	94

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Mitosis and Cytokinesis (1)

The **diploid (2n)** number includes two sets of chromosomes of each type.

- Humans have 23 different types of chromosomes.
  - Each type is represented twice in each body cell (diploid).
  - Only sperm and eggs have one of each type.
    - Termed **haploid (n)**
- The haploid (n) number for humans is 23.
  - Has two representatives of each chromosome type
  - Makes a total of $2n = 46$ in each nucleus
    - One set of 23 from individual's father (paternal)
    - Other set of 23 from individual's mother (maternal)

9-17

Mitosis and Cytokinesis (2)

During interphase, a cell prepares for cell division.

Organelles are duplicated including centrosome.

At the end of S phase:

- Each chromosome internally duplicated
- Consists of two identical double-helical DNA molecules
  - Sister chromatids (two strands of genetically identical chromosomes)
  - Attached together at a single point (called **centromere**)

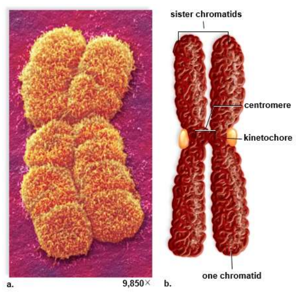
During mitosis:

- Centromeres holding sister chromatids together separate
- Sister chromatids separate
- Each becomes a daughter chromosome
- Daughter chromosomes of each type are distributed to the opposite daughter nuclei.

9-18

The Cell Cycle

Duplicated Chromosomes



Jump to Duplicated Chromosomes Long Description

9-19

Mitosis and Cytokinesis (3)

Just outside the nucleus is the **centrosome**.

- This is the microtubule-organizing center in animal cells.
- The centrosome was also replicated in S-phase of interphase, so there are two centrosomes before mitosis begins.
  - In animals, the centrosome contains two barrel-shaped **centrioles**.
    - Oriented at right angles to each other within the centrosome
- Centrosome organizes the mitotic spindle.
  - The spindle contains many fibers.
  - Each fiber is composed of a cylindrical bundle of microtubules.
  - Microtubules assemble when tubulin subunits join, and when the subunits disassemble, they form mitotic spindle fibers or allow the cell to change shape for cell division.

9-20

Mitosis and Cytokinesis (4)

Phases of Mitosis:

- **Prophase**
- Nuclear division is about to occur.
  - Chromatin condensed
    - Chromosomes are distinguishable with microscope.
    - Each chromosome has two sister chromatids held together at the centromere.
  - Nucleolus disappears
  - Nuclear envelope fragments
  - Spindle begins to assemble
  - Two centrosomes move away from each other.
  - In animal cells, microtubules form star-like arrays termed **asters**.

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The Cell Cycle

Mitosis and Cytokinesis (5)

Phases of Mitosis

- **Prometaphase**
  - Preparations for sister chromatid separation are evident.
  - The centromere of each chromosome develops two kinetochores.
    - Specialized protein complex
    - One attached to each sister chromatid
      - Physically connect sister chromatids with specialized microtubules (**kinetochores**)
      - These connect sister chromatids to opposite poles of the mother cell.

Mitosis and Cytokinesis (6)

Stages of Mitosis

- **Metaphase**
  - Chromosomes pulled around by kinetochore fibers
  - Forced to align across the equatorial plane of the cell
    - **Metaphase plate** – Represents plane through which mother cell will be divided
    - Nonattached, polar spindle fibers overlap
    - M checkpoint delays the start of anaphase until kinetochores are attached properly.
- **Anaphase**
  - Centromere dissolves, releasing sister chromatids
  - Sister chromatids separate at the centromere.
    - Now called daughter chromosomes
    - Pulled to opposite poles along kinetochore fibers
    - The poles move farther apart.

Mitosis and Cytokinesis (7)

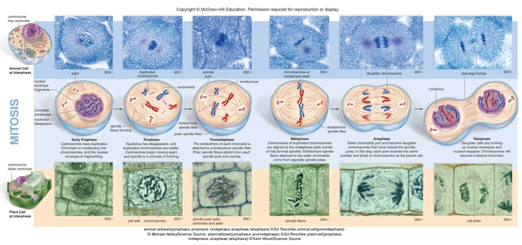
Stages of Mitosis

- **Telophase**
  - The spindle disappears.
  - New nuclear envelopes form around daughter chromosomes.
  - There are now two clusters of daughter chromosomes.
    - Still, there are two of each type with all types represented.
    - Clusters are incipient daughter nuclei.
    - Nuclear envelopes form around the two incipient daughter nuclei.
    - Each daughter nucleus receives one chromosome of each type.
  - Division of the cytoplasm requires cytokinesis.

Chromosomes become diffused chromatin once again.

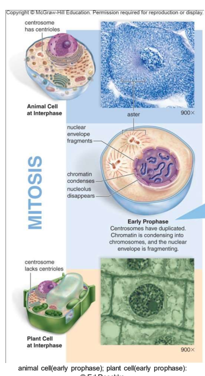
The Cell Cycle

Phases of Mitosis in Animal and Plant Cells (1)



Jump to Phases of Mitosis in Animal and Plant Cells (1) Long Description

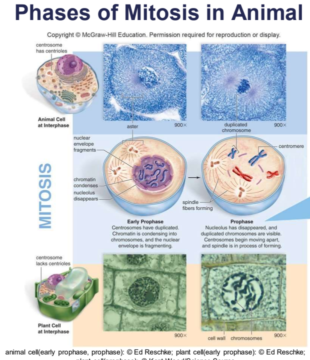
Phases of Mitosis in Animal and Plant Cells (2)



Early Prophase
Centrosomes have duplicated. Chromatin is condensing into chromosomes, and the nuclear envelope is fragmenting.

animal cell(early prophase); plant cell(early prophase): © Ed Reschke

Phases of Mitosis in Animal and Plant Cells (3)

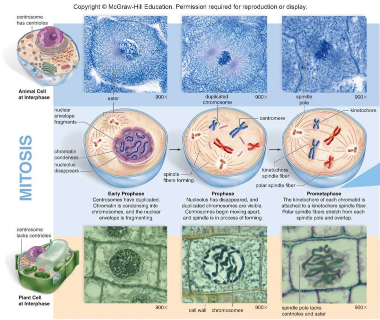


Prophase
Nucleolus has disappeared, and duplicated chromosomes are visible. Centrosomes begin moving apart, and spindle is in process of forming.

animal cell(early prophase, prophase): © Ed Reschke; plant cell(early prophase): © Ed Reschke; plant cell(prophase): © Kent Wood/Science Source

The Cell Cycle

Phases of Mitosis in Animal and Plant Cells (4)



Prometaphase
The kinetochore of each chromatid is attached to a kinetochore spindle fiber. Polar spindle fibers stretch from each spindle pole and overlap.

animal cell(early prophase, prophase): © Ed Reschke; animal cell(prometaphase): © Michael Abbey/Science Source; plant cell(early prophase, prometaphase): © Ed Reschke; plant cell(prophase): © Kent Wood/Science Source

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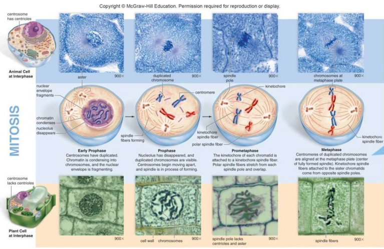
Phases of Mitosis in Animal and Plant Cells (5)



Metaphase
Centromeres of duplicated chromosomes are aligned at the metaphase plate (center of fully formed spindle). Kinetochore spindle fibers attached to the sister chromatids come from opposite spindle poles.

animal cell(early prophase, prophase, metaphase): © Ed Reschke; animal cell(prometaphase): © Michael Abbey/Science Source; plant cell(early prophase, prometaphase): © Ed Reschke; plant cell(prophase, metaphase): © Kent Wood/Science Source

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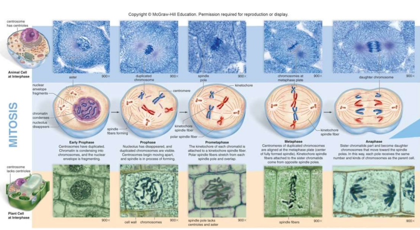
Phases of Mitosis in Animal and Plant Cells (6)



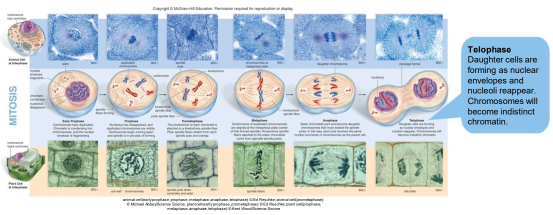
Anaphase
Sister chromatids part and become daughter chromosomes that move toward the spindle poles. In this way, each pole receives the same number and kinds of chromosomes as the parent cell.

animal cell(early prophase, prophase, metaphase, anaphase): © Ed Reschke; animal cell(prometaphase): © Michael Abbey/Science Source; plant cell(early prophase, prometaphase): © Ed Reschke; plant cell(prophase, metaphase, anaphase): © Kent Wood/Science Source

9-30

The Cell Cycle

Phases of Mitosis in Animal and Plant Cells (7)



Cytokinesis in Plant and Animal Cells (1)

Cytokinesis = division of cytoplasm

Allocates the mother cell's cytoplasm equally to daughter nucleus

Encloses each daughter cell in its own plasma membrane

Often begins in anaphase

Proceeds differently in plant and animal cells

Animal cytokinesis:

- **Cleavage furrow** appears between daughter nuclei.
- Formed by a contractile ring of actin filaments
- Like pulling on a drawstring
- Eventually pinches the mother cell in two

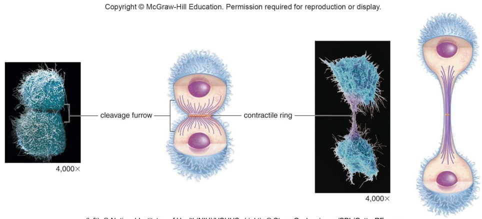
Cytokinesis in Plant and Animal Cells (2)

Cytokinesis in plant cells begins with the formation of a **cell plate**.

- Rigid cell walls outside plasma membrane do not permit furrowing.
- Many small membrane-bounded vesicles are made by Golgi.
- They eventually fuse into one thin vesicle extending across the mother cell.
- The membranes of the cell plate become the plasma membrane between the daughter cells.
- The space between the daughter cells becomes filled with the middle lamella.
- Daughter cells later secrete primary cell walls on opposite sides of the middle lamella, which cements the primary cell walls together.

The Cell Cycle

Cytokinesis in Animal Cells



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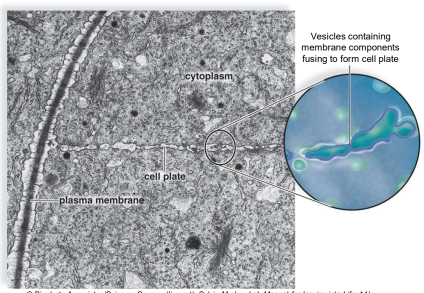
Jump to Cytokinesis in Animal Cells Long Description

9-34

Cytokinesis in Plant Cells



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Jump to Cytokinesis in Plant Cells Long Description 9-35

Functions of Mitosis in Animal and Plant Cells

Functions of Mitosis:

- It permits growth and repair.
- In flowering plants, meristematic tissue retains the ability to divide throughout the life of the plant.
- Trees increase their girth (width) each growing season.
- In mammals, mitosis is necessary when:
  - A fertilized egg becomes an embryo.
  - An embryo becomes a fetus.
  - After birth, a child becomes an adult.
  - A cut heals or a broken bone mends.

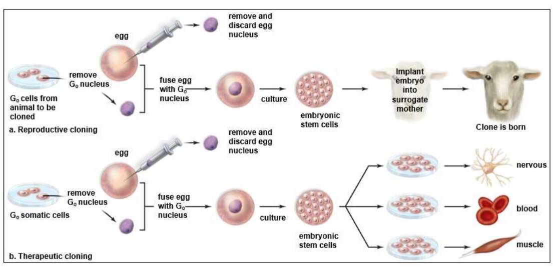
9-36

Functions of Mitosis in Animal Cells

Stem Cells

- Many mammalian organs contain stem cells.
  - They retain the ability to divide.
  - Red bone marrow stem cells divide to produce various types of blood cells.
- **Therapeutic cloning** to produce human tissues can begin with either adult stem cells or embryonic stem cells.
- Embryonic stem cells can be used for **reproductive cloning**, the production of a new individual.

Two Types of Cloning – Reproductive and Therapeutic



Jump to Two Types of Cloning – Reproductive and Therapeutic Long Description

9.4 The Cell Cycle and Cancer

Abnormal growth of cells is called a **tumor**.

- **Benign** tumors are not cancerous.
  - Encapsulated
  - Do not invade neighboring tissue or spread
- **Malignant** tumors are cancerous.
  - Not encapsulated
  - Readily invade neighboring tissues
  - May also detach and lodge in distant places (metastasis)
  - Results from mutation of genes regulating the cell cycle

Development of **cancer**

- Tends to be gradual and multistep
- May take years before cell is obviously cancerous

The Cell Cycle

The Cell Cycle and Cancer (1)

Characteristics of Cancer Cells

- Lack differentiation
  - Cells are non-specialized.
  - Cells are immortal (can enter cell cycle repeatedly).
- Have abnormal nuclei
  - Cells may be enlarged.
  - Cells may have abnormal number of chromosomes.
  - Cells often have extra copies of genes.
- Do not undergo apoptosis
  - Normally, cells with damaged DNA undergo apoptosis.
  - The immune system can also recognize abnormal cells and trigger apoptosis.
  - Cancer cells are abnormal but fail to undergo apoptosis.

9-40

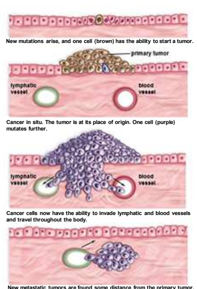
The Cell Cycle and Cancer (2)

Characteristics of Cancer Cells

- Form tumors
  - Mitosis is normally controlled by contact with neighboring cells: contact inhibition.
    - Cancer cells have lost contact inhibition.
- Undergo metastasis
  - The original tumor easily fragments.
  - New tumors appear in other organs.
- Undergo **angiogenesis**
  - They form new blood vessels.
    - They bring nutrients and oxygen to the tumor.

9-41

Progression of Cancer



Jump to Progression of Cancer Long Description

9-42

The Cell Cycle

Cancer Cells versus Normal Cells

Table 9.2 Cancer Cells Versus Normal Cells

Cancer Cells	Normal Cells
Nondifferentiated cells	Differentiated cells
Abnormal nuclei	Normal nuclei
Do not undergo apoptosis	Undergo apoptosis
No contact inhibition	Contact inhibition
Disorganized, multilayered	One organized layer
Undergo metastasis	Remain in original tissue

9-43

The Origin of Cancer

Normal growth and tissue maintenance depends on a balance between signals that promote and inhibit cell division.

Two types of genes may be mutated when the balance is upset, which may cause cancer.

- **Oncogenes**
  - **Proto-oncogenes** code for proteins which promote the cell cycle in various ways.
  - If a proto-oncogene is mutated, it may become an oncogene.
- **Tumor suppressor genes code for proteins** which inhibit the cell cycle and promote apoptosis in various ways.
  - If a tumor suppressor gene becomes inactive, it may promote cancer development.
- Both proto-oncogenes and tumor suppressor genes are normally regulated in coordination with organism's growth plan.

9-44

Tumor Suppressor Genes Become Inactive

These directly inhibit the cell cycle and prevent cells from dividing uncontrollably.

- Some tumor suppressors promote apoptosis.
- A mutation in a tumor suppressor causes the cell cycle to accelerate.
  - Examples are the *RB* and *p53* genes which code for proteins with the same names.
    - Retinoblastoma is an inherited condition that results from a mutation in the *RB* gene.
    - The *p53* gene turns on the expression of other cell cycle inhibitory genes.
    - Half of human cancers involve an abnormal or deleted *p53* gene.

9-45

The Cell Cycle

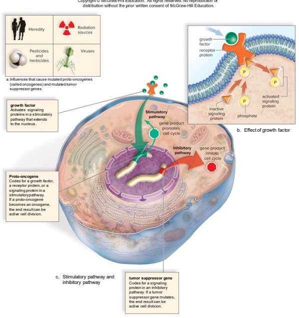
Proto-oncogenes Become Oncogenes

Proto-oncogenes are normal genes which are part of a stimulatory pathway.

- They promote progression through the cell cycle.
- They include receptors and signaling molecules.
- Mutations in proto-oncogenes cause them to become oncogenes.
  - These can specify an abnormal protein product or produce abnormally high levels of a normal product.
  - Uncontrolled cell division results.
  - There are 100 oncogenes which can lead to tumors.
    - Example is *BRCA1*, mutations of which can cause breast and ovarian cancer.

9-46

Causes of Cancer



Jump to Causes of Cancer Long Description

9-47

Other Causes of Cancer – Telomeres

Chromosomes normally have special material at each end called **telomeres**.

These get shorter each cell division.

When they get very short, the cell will no longer divide.

Telomerase is an enzyme that maintains the length of telomeres.

Mutations in telomerase gene:

- Cause telomeres to continue to lengthen, which
- Allows cancer cells to continually divide

9-48

The Cell Cycle

9.5 Prokaryotic Cell Division

The prokaryotic (bacteria and archaea) chromosome is a ring of DNA and a few associated proteins.

- Folded up in an area called the **nucleoid**
- 1,000X the length of cell
- Replicated into two rings prior to cell division
- Replicated rings attach to the plasma membrane

Binary fission

- Splitting in two
- Two replicate chromosomes are distributed to two daughter cells.
- Produces two daughter cells identical to original cell—**asexual reproduction**
- *Escherichia coli*, an intestinal microbe, has a generation time of about 20 minutes

9-49

Comparing Prokaryotes and Eukaryotes

Binary fission and mitosis both ensure that the daughter cell is genetically identical to the parent.

Prokaryotes, protists (many algae and protozoans), and some fungi (yeasts) are single-celled.

- Cell division of single-celled organisms produces two new individuals.

In multicellular fungi, plants, and animals, cell division is important for growth, renewal, and repair.

During binary fission, the chromosome duplicates and each daughter receives one copy as the parent cell elongates and a new cell wall and membrane form between daughter cells.

No spindle is involved in binary fission.

9-50