

Genetics and Information Transfer

INVESTIGATION 7

CELL DIVISION: MITOSIS AND MEIOSIS

How do eukaryotic cells divide to produce genetically identical cells or to produce gametes with half the normal DNA?

■ BACKGROUND

One of the characteristics of living things is the ability to replicate and pass on genetic information to the next generation. Cell division in individual bacteria and archaea usually occurs by binary fission. Mitochondria and chloroplasts also replicate by binary fission, which is evidence of the evolutionary relationship between these organelles and prokaryotes.

Cell division in eukaryotes is more complex. It requires the cell to manage a complicated process of duplicating the nucleus, other organelles, and multiple chromosomes. This process, called the cell cycle, is divided into three parts: interphase, mitosis, and cytokinesis (see Student Manual, page S83, Figure 1). In the first growth phase (G_1), the cell grows and prepares to duplicate its DNA. In the synthesis phase (S), the chromosomes are replicated. In the second growth phase (G_2), the cell prepares to divide. In mitosis, the duplicated chromosomes are separated into two nuclei. In most cases, mitosis is followed by cytokinesis, when the cytoplasm divides and organelles separate into daughter cells. This type of cell division is asexual and is important for growth, renewal, and repair of multicellular organisms.

Cell division is tightly controlled by complexes made of several specific proteins. These complexes contain enzymes called cyclin-dependent kinases (CDKs), which turn on or off the various processes that take place in cell division. CDK partners with a family of proteins called cyclins. One such complex is mitosis-promoting factor (MPF), sometimes called maturation-promoting factor, which contains cyclin A or B and cyclin-dependent kinase (CDK). (See Figure 1a.) CDK is activated when it is bound to cyclin, interacting with various other proteins that, in this case, allow the cell to proceed from G_2 into mitosis. The levels of cyclin change during the cell cycle (Figure 1b). In most cases, cytokinesis follows mitosis.

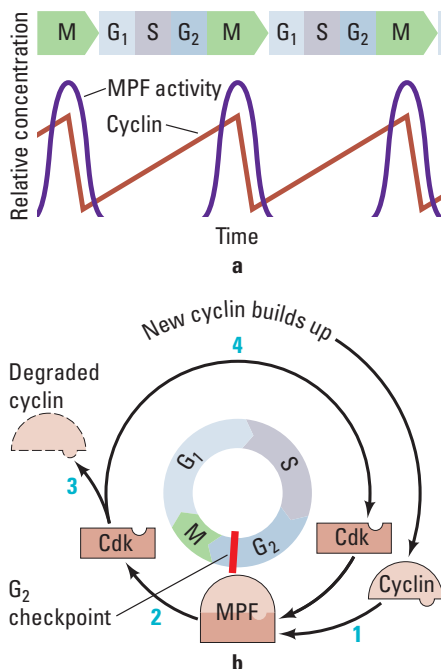


Figure 1a-b. MPF Production During the Cell Cycle

As shown in Figure 2, different CDKs are produced during the phases. The cyclins determine which processes in cell division are turned on or off and in what order by CDK. As each cyclin is turned on or off, CDK causes the cell to progress through the stages in the cell cycle.

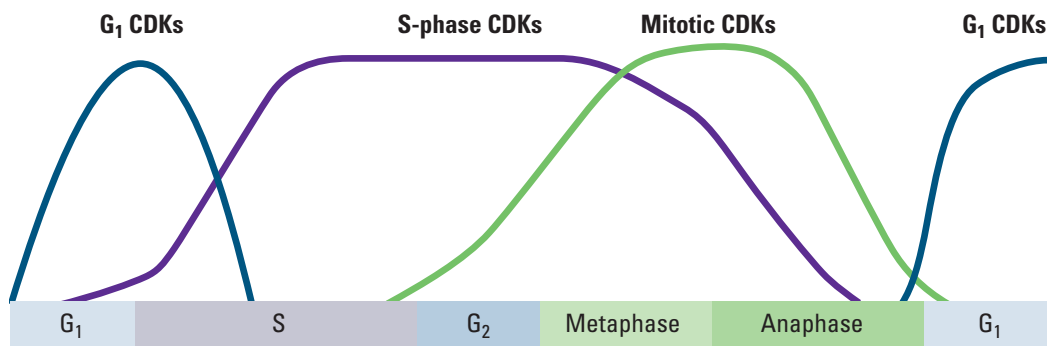


Figure 2. Levels of CDKs During the Cell Cycle

Cyclins and CDKs do not allow the cell to progress through its cycle automatically. There are three checkpoints a cell must pass through: the G_1 checkpoint, G_2 checkpoint, and the M-spindle checkpoint (see Student Manual, page S85, Figure 4). At each of the checkpoints, the cell checks that it has completed all of the tasks needed and is ready to proceed to the next step in its cycle. Cells pass the G_1 checkpoint when they are stimulated by appropriate external growth factors; for example, platelet-derived growth factor (PDGF) stimulates cells near a wound to divide so that they can repair the injury. The G_2 checkpoint checks for damage after DNA is replicated, and if there is damage, it

prevents the cell from going into mitosis. The M-spindle (metaphase) checkpoint assures that the mitotic spindles or microtubules are properly attached to the kinetochores (anchor sites on the chromosomes). If the spindles are not anchored properly, the cell does not continue on through mitosis. The cell cycle is regulated very precisely. Mutations in cell cycle genes that interfere with proper cell cycle control are found very often in cancer cells.

Figure 3 illustrates how the chromosomes move during mitosis. It is important for your students to model how the duplicated chromosomes align, separate, and move into new cells.

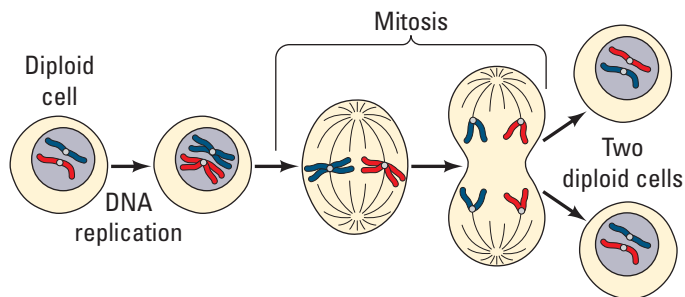


Figure 3. Mitotic Cell Division Emphasizing Chromosome Movement

■ PREPARATION

Materials and Equipment

■ Parts 1 and 4: Modeling Mitosis and Meiosis

Following are suggested chromosome models and useful websites.

Sockosomes: 3 pairs of sockosomes per group (4 students per group)

- Small or medium children's crew socks (various colors, but not black or blue)
- Fiberfill
- Self-stick squares or circles of Velcro
- Needle and thread
- Masking tape
- Permanent marker pens
- http://serendip.brynmawr.edu/sci_edu/waldron/pdf/MitosisMeiosisTeachPrep.pdf

Clay chromosomes

- Modeling clay (several colors)
- Twist ties
- www.nclark.net/CrossingOver.doc

Pipe cleaners

- Pink and blue pipe cleaners, cut into pieces about 3 cm long (one set has 11 pieces of each color; one set per group)
- 6 beads per set; two pipe cleaners fit through one bead snugly
- Small plastic petri dishes or small plastic bags
- <http://www.indiana.edu/~ensiweb/lessons/gen.mm.html>

Pop-It Beads

■ Part 2: Effects of Environment on Mitosis

- Onion sets or scallions; each scallion will produce about 10 root tips, enough for three students
- Jars with lids; 2 jars (one per treatment) for 6 students
- Sand
- Ethanol
- Glacial acetic acid (17.4 M)
- Hydrochloric acid
- Carbol-fuschin (Ziehl-Neelson) stain
- Lectin (phytohemagglutinin PHA-M from *Phaseolus vulgaris*)
- Razor blades (one per student)
- Forceps (one per student)
- Dissection scissors
- Dissection probes or needles
- Slides, cover slips
- Scientific cleaning wipes, such as Kimwipes
- Coplin jars (one per group of 4 students)
- Petri dish
- Disposable gloves
- Compound microscopes

■ Part 3: Cell Cycle Control

- Karyotype pictures of normal and HeLa cells

■ Timing and Length of Lab

This investigation requires a minimum of four lab periods of about 45 minutes each, plus time for a discussion on cell cycle control (Part 3). In addition, time is needed for students to discuss their results from Parts 2 and 5. Students can work in pairs or small groups for Parts 1 and 4.

Teacher preparation is needed to make the model chromosomes from socks or pipe cleaners. Onion bulb preparation will take one hour for the treatment and two hours (plus the 4–18 hour fixation time) for the root tips. This must be done a week ahead of

the lab time. The root tips can be stored in 70% ethanol for several weeks. There is little preparation time for the *Sordaria* crosses if plates are purchased from a biological supply company.

■ Safety and Housekeeping

This laboratory investigation, especially Parts 1, 3, and 4, has a few safety concerns. Remind students to wear gloves and safety goggles or glasses when handling the chemicals and razor blades in Parts 2 and 5. To avoid injuries, students should use a pencil eraser rather than their thumbs to press down on the cover slips.

■ ALIGNMENT TO THE AP BIOLOGY CURRICULUM FRAMEWORK

This investigation pertains to the storage and transmission of genetic information (big idea 3). As always, it is important to make connections between big ideas and enduring understandings, regardless of where in the curriculum the lab is taught. The concepts align with the enduring understandings and learning objectives from the AP Biology Curriculum Framework, as indicated below.

■ Enduring Understandings

- 3A1: DNA, and in some cases RNA, is the primary source of heritable information.
- 3A2: In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.
- 3A3: The chromosomal basis of inheritance provides an understanding of the pattern of passage (transmission) of genes from parent to offspring.
- 3C2: Biological systems have multiple processes that increase genetic variation.

■ Learning Objectives

- The student can make predictions about natural phenomena occurring during the cell cycle (3A2 & SP 6.4).
- The student can describe the events that occur in the cell cycle (3A2 & SP 1.2).
- The student is able to construct an explanation, using visual representations or narratives, as to how DNA in chromosomes is transmitted to the next generation via mitosis, or meiosis followed by fertilization (3A2 & SP 6.2).
- The student is able to represent the connection between meiosis and increased genetic diversity necessary for evolution (3A2 & SP 7.1).
- 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, or meiosis followed by fertilization (3A2 & SP 5.3).
- The student is able to construct a representation that connects the process of meiosis to the passage of traits from parent to offspring (3A3 & SP 1.1, SP 7.2).
- The student is able to construct an explanation of the multiple processes that increase variation within a population (3C2 & SP 6.2).



■ ARE STUDENTS READY TO COMPLETE A SUCCESSFUL INQUIRY-BASED, STUDENT-DIRECTED INVESTIGATION?

Before students begin these investigations, they should be able to demonstrate understanding of the following concepts. The concepts may be scaffolded according to level of skills and conceptual understanding.

- Cellular structure and organelles
- The purposes for cell division
- The outcomes for mitosis and meiosis

In addition, this lab reinforces the following skills:

- Use of a microscope to observe cell structure
- Data collection

■ Skills Development

Students will develop the following skills:

- Preparation of specimens for microscopic analyses
- Data analysis and use of a statistical test
- Calculation of crossover frequencies

■ Potential Challenges

Many students have memorized the stages of mitosis and meiosis without understanding the processes. These exercises emphasize the processes and results of cell division. You should have your students discuss the relationship between meiosis and evolution.

The equipment costs, besides the microscopes, are minimal. Model chromosomes and karyotype pictures can be reused. Safety issues are minimized by treating and fixing the onion root tips before having the students stain them.

■ THE INVESTIGATIONS

■ Getting Started: Prelab Assessment

The replication of cells and organisms is a central concept in biology. Organisms must pass on their genetic material to their offspring. You can ask students how multicellular organisms grow during development and how they repair themselves and replace cells. A good example is what happens to epidermal (skin) cells to heal a cut.

Chromosome movement during mitosis and meiosis is not easily understood. Ask students to think about this scenario: You have a plate filled with cooked spaghetti, all tangled together. Next to it is a plate of cooked macaroni. Which will you be able to pull apart into individual pieces more easily? Which is more likely to be tangled? Which is more likely to be broken as you separate the pieces? The point is that condensed chromosomes like the more compact macaroni are much more easily and safely moved than are elongated chromosomes.

Another difficulty that students have is understanding terms such as sister chromatids, tetrads, and chromosomes. Most diagrams of cells show duplicated chromosomes, meaning they are showing cells in G_2 rather than in G_1 . You should explain that while the cells might have twice as much DNA in G_2 , they do not contain any more information, since the sister chromatids are copies.

Ask your students to consider whether they resemble any family member and describe how their parents' genetic information was passed onto them through gametes. Crossing over during meiosis is a difficult concept to grasp and is best illustrated using simple models and *Sordaria* asci formation.

You may assign the following for homework; as a think, pair/group, share activity, in which pairs or small groups of students brainstorm ideas and then share them with other groups; or as a whole-class discussion to assess students' understanding of key concepts pertaining to mitosis and meiosis:

- How many cells are in your body? How were those cells produced from a single cell called a zygote? How does the genetic information in one of your body cells compare to that found in other body cells?
- What are some advantages of asexual reproduction in plants?
- What is the importance of the fact that DNA is replicated prior to cell division?
- How do chromosomes move inside a cell during cell division?
- How is the cell cycle controlled? What would happen if the control were defective?

■ Part 1: Modeling Mitosis

The mitosis lab begins with a discussion section during which you ask your students to think about how they developed from a single-celled zygote to a 300-trillion-celled organism. How does the genetic information in a cell from your toe compare to the genetic information in a cell from your arm?

After the students have had a sufficient time to discuss this question, ask the following questions: What other purposes besides growth would require cell division? How do cells divide? What must happen to ensure successful cell division?

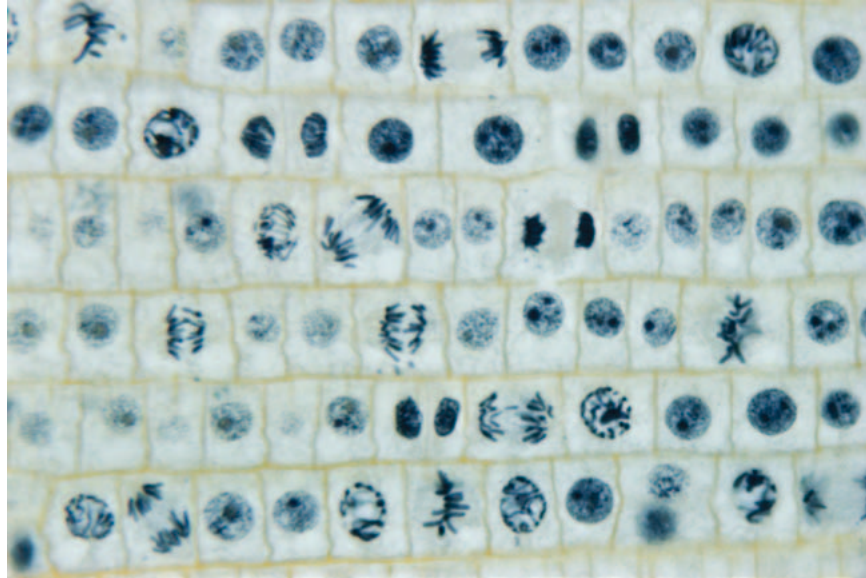
Write down the students' answers on the whiteboard, but do not elaborate on their answers. The students will be expected to investigate these questions further throughout the lab.

Students can use sockosomes, Pop-It Beads, clay, or pipe cleaners to review chromosome duplication and movement.

■ Part 2: Effects of Environment on Mitosis

Students will set up and analyze an experiment using onion bulbs based upon “A Scenario-Based Study of Root Tip Mitosis”¹. The exercise is supported by the premise that lectins increase the rate of mitosis in the roots. Lectins are proteins that bind to specific carbohydrate groups. Help students to identify the different cell phases before doing their onion root tips squashes (Figure 4).

1 Bonner, J.M., “A Scenario-Based Study of Root Tip Mitosis.” *Association for Biology Laboratory Education*. (2010): Proceedings, 31:36–49. <http://www.ableweb.org/proceedings/SPT-FullRecord.php?ResourceId=764>.



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Figure 4. Onion Root Tip

Scientists reported that a fungal pathogen may affect the growth of soybeans (*Glycine max*). The soybean growth was decreased during three years of high rainfall. The soybean roots were poorly developed. Close relatives of *R. anaerobis* are plant pathogens and grow in the soil. A lectin-like protein, which may be secreted by the fungus, was found in soil surrounding the soybean roots. Lectins accelerate mitosis in some root apical meristems; however, in many instances, rapid cell division weakens plant tissues. We are using onions instead of soybeans since onion root tips are more easily grown and studied.

■ Prelab Questions

These questions will help your students learn to design an experiment based upon an observation. Students can answer these questions for homework or as a group activity.

- What is your experimental hypothesis? Your null hypothesis? Are these the same?
- How would you design an experiment with onion bulbs to test whether lectins increase the number of cells in mitosis?
- What would you measure, and how would you measure it?
- What would be an appropriate control for your experiment?

Notes about the lectin: Phytohemagglutinin (PHA-M) is a lectin; a lectin is a protein that binds to specific carbohydrates. PHA-M induces mitosis (acts as a mitogen) in cultured T-lymphocytes by binding to the T-cell receptor for antigen (part of the T_1 - C_3 complex). This causes an intracellular signal involving Ca^{2+} release from the endoplasmic reticulum, ultimately causing cell replication.

Materials

- Onion sets; scallions work well
- Jars with lids; 8–10 cm in diameter
- Sand
- Ethanol
- Glacial acetic acid (17.4 M)
- Hydrochloric acid (12 M)
- Carbol-fuschin (Ziehl-Neelson) stain
- Lectin (phytohemagglutinin PHA-M from *Phaseolus vulgaris*)
- Razor blades
- Forceps
- Dissection scissors
- Slides, cover slips
- Scientific cleaning wipes
- Coplin jars
- Petri dish
- Disposable gloves
- Compound microscopes

Lectin: Dissolve 10 mg lectin in 200 mL H₂O. Exposure to the lectin may cause irritation; wear gloves and weigh the lectin in a fume hood.

Carnoy's fixative: 125 mL glacial acetic acid mixed with 375 mL 95% ethanol

You may treat the bulbs ahead of time and have your students prepare the chromosome squash slides. In this manner, they will not know which bulbs are treated with lectin and which ones are the controls. Treat the slides (Coplin jar) and the cover slips (dish) with 70% ethanol.

Preparing the Onion Root Tips

1. Fill two jars with 1.5 cm of fine sand. Label one jar “control” and the other “lectin.”
2. Wet the sand in the control jar with H₂O.
3. Wet the sand in the lectin jar with lectin solution (50–75 mL).
4. Prepare the bulblets by peeling of the dried outer skin.
5. Cut off the green leaves.
6. Cut off dried roots back to the bulb base with a razor blade.
7. Insert the bulblets into the sand until they touch the bottom of the jar.
8. Store the jars in the dark for one and a half to two days.

Harvesting the Onion Root Tips

1. Wearing gloves, remove the bulblets from the sand and rinse off the sand, with H₂O.
2. Cut off the roots from each bulblet using fine dissection scissors.
3. Place cut root tips into Carnoy's fixative for 4–18 hours.
4. Decant off fixative and rinse tips with 25 mL 70% ethanol.
5. Place tips in 70% ethanol and store covered at 4°C.

Preparing Chromosome Squashes

You can demonstrate the proper technique for the students.

1. Place the onion root tip in 1 M HCl for 4 minutes.
2. Transfer the tip to Carnoy's fixative for 4 minutes.
3. Remove the slide from the Coplin jar containing 70% ethanol, dry with a scientific cleaning wipe, and label it.
4. Place the onion tip on the slide, and cut off the distal 2 mm portion of the tip; discard the remainder of the tip.
5. Cover the root tip piece with carbol-fuchsin stain for 2 minutes.
6. Blot off excess stain and cover tip with 1–2 drops of H₂O.
7. Gently tease the root tip apart with dissecting probes or needles. Place the cover slip over the root tip and cover the cover slip with a scientific cleaning wipe.
8. Firmly press down on the cover slip with your thumb or with the eraser end of a pencil. Do not twist the slide.

Counting Cells and Analyzing Data

1. Observe the cells at high magnification (400–500 X).
2. Look for well-stained, distinct cells.
3. Within the field of view, count the cells in each phase. Repeat the counts in two other root tips. Identification of these stages is prerequisite knowledge.
4. Collect the class data for each group, and calculate the mean and standard deviation for each group.
5. Compare the number of cells from each group in interphase and in mitosis.
6. Use a chi-square distribution test to statistically analyze the data.

Alternative Procedure

You can mask root tips on prepared slides with masking tape and have the students count cells. Students can compare cells close to the end of the root tip to those farther from the end.

Table 1. Onion Root Tip Cell Phase Data; Treatment Group _____

Tip	Number of Cells		
	Interphase	Mitotic	Total
1			
2			
3			
Total			

Table 2. Table of Observed Values (o)

	Interphase	Mitosis	Total
Control	A	B	A + B
Treated	C	D	C + D
Total	A + C	B + D	A + B + C + D = N

1. Collect the class data and enter the values into Table 1; these are the observed values for the four groups.
2. Use the data from Table 1 to calculate the totals using the formulas found in Table 2. (For example, A equals the number of interphase cells in the control group.)
3. Use the totals from Table 2 to calculate the expected values (e) using the formulas from Table 3.
4. Enter the observed values (o) from Table 2 and expected values (e) from Table 3 for each group into Table 4. Calculate the chi-square (χ^2) value for the data by adding together the numbers in the right column.
5. Compare this value to the critical value in Table 5.

Table 3. Table of Expected Values (e)

	Interphase	Mitosis
Control	$\frac{(A + B)(A + C)}{N}$	$\frac{(A + B)(B + D)}{N}$
Treated	$\frac{(C + D)(A + C)}{N}$	$\frac{(C + D)(B + D)}{N}$

Table 4. Calculation of Chi-Square Value

Group	Observed (o)	Expected (e)	(o - e)	(o - e) ²	(o - e) ² /e
Control Interphase					
Control Mitosis					
Treated Interphase					
Treated Mitosis					

Total of (o - e)²/e = chi-square (χ^2) =

Table 5. Critical Values of the Chi-Square Distribution

Probability	Degrees of Freedom (DF)				
	1	2	3	4	5
0.05	3.84	5.99	7.82	9.49	11.1
0.01	6.64	9.21	11.3	13.2	15.1
0.001	10.8	13.8	16.3	18.5	20.5

1. The degrees of freedom (df) equals the number of treatment groups minus one multiplied by the number of phase groups minus one. In this case, there are two treatment groups (control, treated) and two phase groups (interphase, mitosis); therefore $df = (2 - 1)(2 - 1) = 1$.
2. The p value is 0.05, and the critical value is 3.84. If the calculated chi-square value is greater than or equal to this critical value, then the null hypothesis is rejected. If the calculated chi-square value is less than this critical value, the null hypothesis is not rejected.

SAMPLE DATA

Sample Table 2: Table of Observed Values (o)

	Interphase	Mitosis	Total
Control	148	25	173
Treated	161	88	249
Total	309	113	422

Sample Table 3: Table of Expected Values (e)

	Interphase	Mitosis
Control	127	46
Treated	179	67

Sample Table 4: Calculation of Chi-Square Value

Group	Observed (o)	Expected (e)	(o - e)	(o - e) ²	(o - e) ² /e
Control Interphase	148	127	21	441	3.47
Control Mitosis	25	46	-21	441	9.59
Treated Interphase	161	182	-21	441	2.42
Treated Mitosis	88	67	21	441	6.58

Total of $(o - e)^2/e = \text{chi-square } (\chi^2) = 22.06$

Since the calculated χ^2 is greater than the table value, the null hypothesis (treatment has no effect) is rejected.

■ Postlab Review

These questions can be answered in a report, as a group activity, or as homework.

- What was the importance of collecting the class data?
- Was there a significant difference between the groups?
- Did the fungal pathogen lectin increase the number of cells in mitosis?
- What other experiments should you perform to verify your findings?
- Does an increased number of cells in mitosis mean that these cells are dividing faster than the cells in the roots with a lower number of cells in mitosis?
- What other way could you determine how fast the rate of mitosis is occurring in root tips?

■ DESIGNING AND CONDUCTING INDEPENDENT INVESTIGATIONS

Students can design and conduct an investigation to determine what substances in the environment might increase or decrease the rate of mitosis. Consider, for example, abiotic soil factors such as salinity, temperature, and pH, or biotic factors, including roundworms, which might alter root growth.


■ Part 3: Loss of Cell Cycle Control in Cancer

Materials

- Karyotype pictures of normal and HeLa cells (Students can search for these on the Internet.)

■ Prelab Questions

- Many of us have family members who have or have had cancer. Cancer occurs when cells divide abnormally. There are many questions students should consider before beginning their investigation.
- How are normal cells and cancer cells different from each other?
- What are the main causes of cancer?
- How can we explain the fact that there so many different cancers, even in the same types of cells or tissues?
- How is the cell cycle controlled in normal cells?
- What are cyclins and cyclin-dependent kinases? What do these proteins do in a cell?
- What goes wrong during the cell cycle in cancer cells?
- What makes some genes related to increased cancer risk?
- Do you think that the chromosomes might be different between normal and cancer cells?



Have your students form groups and ask each group to form a hypothesis as to how the chromosomes of a cancer cell might appear in comparison to a normal cell and how those differences are related to the behavior of the cancer cell.

Show your students a picture of cancer cells and ask them what they know about cancer. After your students are given time to share their knowledge, ask them to think about ways the cancer cells might be different from normal, healthy cells.

Inform your students that, in cancer cells, division is fundamentally different from that in normal cells, but do not inform the students as to why. Ask each group to form a hypothesis as to how the chromosomes of a normal cell might appear in comparison to a cancer cell.

Give each group pictures of chromosomes from normal and HeLa cells. The students should count the number of chromosomes found in each type of cell and discuss their appearance. Did the results match their hypothesis? If not, ask your students what type of information they might need to know in order to understand their results. If their results matched their hypothesis, ask them to identify what type of information they could find that would validate their conclusions.

Explain to your students that in normal cells mitosis is blocked if there is DNA damage. Ask them to consider what would happen if cells with mutated DNA replicated. More than 50% of human cancers have loss of p53 function; this protein blocks mitosis if there is DNA damage. P53 acts at the G₁-S checkpoint and initiates DNA repair or apoptosis.

“But I’m Too Young!” is a case from The National Center for Case Study Teaching in Science. The case discusses cell cycle control as it relates to ovarian cancer and has additional references.

(See http://sciencecases.lib.buffalo.edu/cs/collection/detail.asp?case_id=481&id=481.)

■ Postlab Questions

You may pick some of these questions to help your students understand the underlying causes of cancer.

- What happens in a normal cell if the DNA has mutations?
- What would happen if cells with mutated DNA replicate?
- How do cells monitor DNA integrity?
- What went wrong in Henrietta Lacks’s cells?
- How does infection with human papillomavirus virus increase the risk of cervical cancer?

As an extension activity, you may assign *The Immortal Life of Henrietta Lacks* by Rebecca Skloot for reading. Ask students to complete some of the following questions and activities:

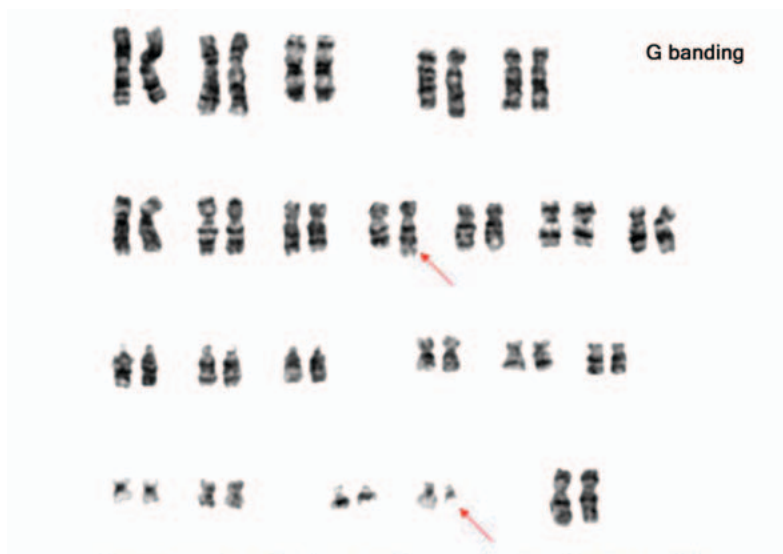
- Should tissue be removed from a patient without his or her consent for research?
- How was the HeLa cell line cultured?
- What virus infected Henrietta Lacks and may have caused her cervical cancer? What cellular process is affected by this virus?

- Was there bias in the way Henrietta Lacks was treated at Johns Hopkins?
- Put the use of HeLa cells on trial. Debate what is more important: an individual's rights to his/her own body tissues or the medical knowledge gained by studying a patient's tissues?
- Should Henrietta Lacks's family be compensated the discoveries made using her cells?
- Do companies or universities have the right to patent discoveries made using a patient's tissues or genes without consulting the patient?
- What other legal and ethical questions raised in this book?
- Write an article about someone who has benefited from research on HeLa cells.
- Research the number of laboratories worldwide that have used or are using HeLa cells.

Case 2: Philadelphia Chromosomes

In normal cells, mitosis usually is blocked if there is DNA damage. Sometimes, though, DNA damage makes cells divide more often. Certain forms of leukemia have a unique feature called a Philadelphia chromosome. Look at the photos of the karyotype of leukemia cells in Figure 5.

- What happens in a normal cell if the DNA has mutations?
- What would happen if cells with mutated DNA replicated?
- How do cells monitor DNA integrity?
- How are the chromosomes different in the cancer cells compared to normal cells?
- How could these differences lead to cancer?



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Figure 5. Karyotype of a Patient with Chronic Myelogenous Leukemia Indicating Chromosomal Deformity

Part 4: Modeling Meiosis

Meiosis is a cell division resulting in the halving, or reduction, of chromosome number in each cell. A diploid organism has two sets of chromosomes ($2n$), while a haploid cell or organism has one set ($1n$). Meiosis produces gametes (ova and sperm) in animals and spores in fungi, plants, and protists. Three other important characteristics of meiosis are the exchange of genetic material (“crossing over”) between homologous chromosomes, the independent assortment of the chromosomes, and the separation of alleles of the same gene (Figure 6). These characteristics, along with random fertilization, increase the genetic variability in the offspring. These mechanisms are essential to our understanding of genetics and evolution in sexually reproducing organisms.

The hallmark of sexual reproduction is the great diversity seen in the gametes and in the offspring. Meiosis is integral to sexual reproduction. Ask your students the following questions before they begin the exercise:

- How is meiosis important to a sexually reproducing organism?
- What would happen if eggs and sperm were produced by mitosis instead of meiosis?
- How can crossing over between homologous chromosomes be detected?
- How do meiosis and fertilization affect genetic diversity and evolution?
- How do sexually reproducing organisms produce gametes from diploid cells?
- How does the process increase gamete diversity?
- What are the outcomes from independent assortment and crossing over?
- How does the distance between two genes or a gene and a centromere affect cross-over frequencies?

Use socks, clay, or pipe cleaners to model meiosis and crossing-over events and mimic nondisjunction and the relationship to genetic disorders. See Parts 1 and 4: Modeling Mitosis and Meiosis under Materials and Equipment.

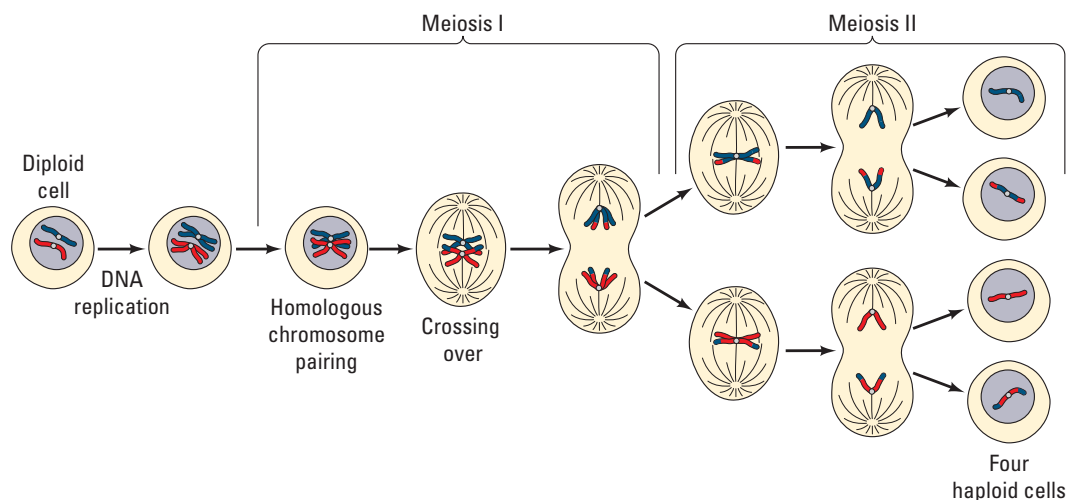


Figure 6. Meiotic Cell Division Emphasizing Chromosome Movement

Part 5: Meiosis and Crossing Over in *Sordaria*

In this experiment, students will measure crossover frequencies and genetic outcomes in a fungus. Your students will examine *Sordaria fimicola* asci produced by crossing wild type (black) with tan parents. Each ascus contains eight spores. Parental type asci have four black and four tan spores in a row (4:4 pattern), as shown in Figure 7. Recombinant asci will not have this pattern (Figure 8).

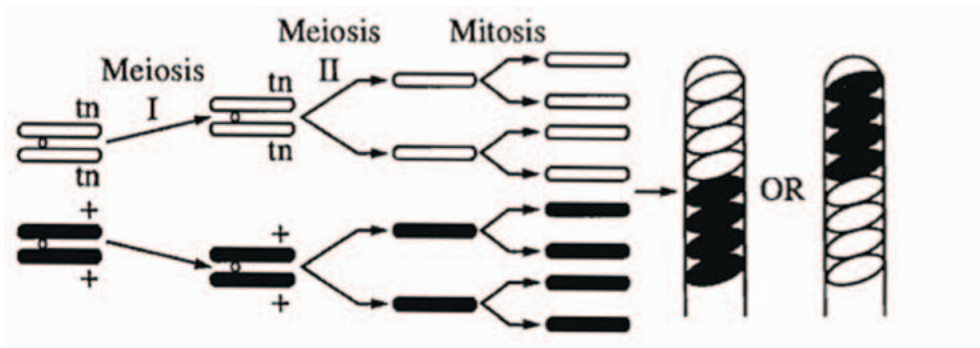


Figure 7. Meiosis with No Crossing Over

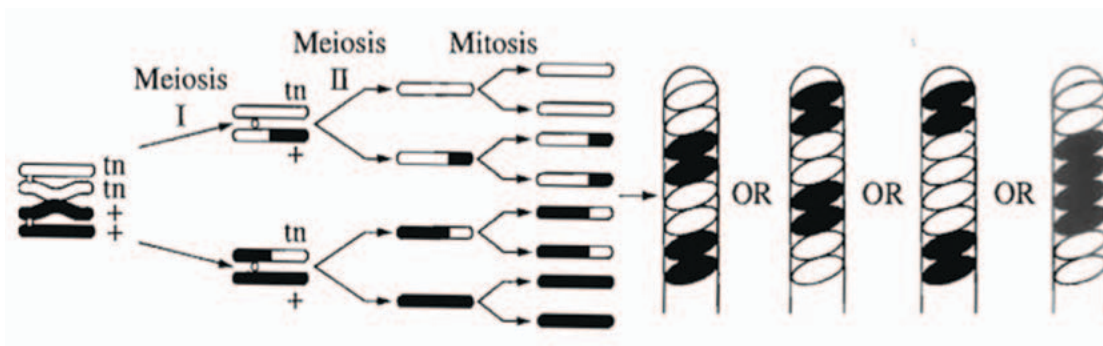


Figure 8. Meiosis with Crossing Over

Prelab Questions

Assign the following questions as homework or as group discussion questions.

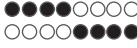
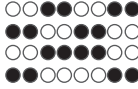
- How do you explain the differences between the recombinant asci and the parental types?
- What meiotic event can account for this difference?
- Using the model chromosomes from Part 4, predict the possible meiotic outcomes.

Materials

- Culture plate containing *Sordaria perithecia*, wild type X tan cross (one plate per 4–6 students)
- Slides and cover slips
- Scientific cleaning wipes
- Toothpicks or scalpels
- Compound microscopes

1. Place a drop of water onto the microscope slide.
2. Gently scrape some perithecia from the agar plate near where the two strains meet.
3. Place a cover slip over the perithecia and put a scientific cleaning wipe over the cover slip.
4. Gently press down on the cover slip using the eraser end of a pencil.
5. Count at least 50 asci, and score them as either parental or recombinant (crossing over).
6. Record your results in Table 6.

Table 6. Analysis of Results

Number of 4:4 	Number of Asci Showing Crossover 	Total	% Asci Showing Crossover Divided by 2	Gene to Centromere Distance (map units)

The published map distance between the gene and the centromere is 26 map units. How did the class data compare with this distance? What can account for disparities between the class data and the published data?

Summative Assessment

The following are suggested as guidelines to assess students' understanding of the concepts presented in the investigation, but you are encouraged to develop your own methods of postlab assessment. Some of the tasks can be assigned for homework following completion of the investigation.

1. Revisit the learning objectives. Do you think your students have met these, based upon their answers to the analysis questions?
2. Did the students demonstrate evidence of what they knew, and can they apply their knowledge within the context of the learning objectives?
3. Students should record their experiments, including the design, methods, data, results, and conclusions in a laboratory notebook.

Where Can Students Go from Here?

1. Have students act out the process of chromosome movement or prepare a video.
2. Students can research cancer and how carcinogens affect the cell cycle. A great study is the human papillomavirus (HPV), which probably caused Henrietta Lacks's cancer. HPV blocks the tumor suppressor protein called retinoblastoma (Rb); Rb acts at the G₁-S checkpoint to stop DNA synthesis. Rb binds to transcription factor

E2F. E2F binds to the promoters of other transcription factors that allow the cell to proceed through mitosis. If the conditions are right, Rb is phosphorylated and dissociated from E2F.

Other tumor suppressors included BRCA1 and BRCA2, which are associated with breast cancer. These genes can increase cancer risk if they are mutated (recessive mutations). Other cancer-related genes are called proto-oncogenes. These are associated with growth factor receptors. For example, *c-sis* is the β -chain of platelet-derived growth factor. When *c-sis* is mutated (dominant mutation), PDGF is overexpressed by cells. The simian sarcoma virus (SSV) carries the gene, so infection by SSV increases cancer risk.

3. Ask students to consider how much genetic variation there would be without crossing over.
4. Ask students what mechanisms of genetic change they have learned about in the investigation, and have them explain how each affects genetic diversity. These mechanisms include crossing over, independent assortment, segregation, nondisjunction, and random fertilization.
5. Do your students know what the basis is for genetic variability? The answer is in DNA sequence differences caused by mutations. These mutations can be caused either by damage to the DNA (usually from radiation or chemicals) or by a cell's making a mistake as it copies its DNA. Most of the time, these "copy errors" are repaired.

■ SUPPLEMENTAL RESOURCES

■ Prelab Activities

<http://bioweb.wku.edu/courses/biol121/Genetics/genetics.asp>

This resource provides excellent pictures and videos to acquaint students with mitosis and meiosis. In addition, there is a link to a survey from the American Academy of Dermatology about sun exposure and skin cancer.

http://www.phschool.com/science/biology_place/labbench/lab3/intro.html

This resource gives a review of mitosis and meiosis as well as quizzes.

http://www.pbs.org/wgbh/nova/baby/divi_flash.html

This NOVA-linked site compares the chromosome movements and outcomes of mitosis and meiosis.

http://www.biology.arizona.edu/cell_bio/cell_bio.html

The Cell Project provides diagrams and quizzes for mitosis and meiosis review.

http://iknow.net/cell_div_education.html

iknow.net has movies on the cell cycle and plant cell mitosis. A bonus is the video of living amphibian lung cell mitosis.



■ Onion Root Tip

http://www.biology.arizona.edu/cell_bio/activities/cell_cycle/cell_cycle.html

The Cell Project has onion cell pictures to help students classify the stages.

http://biologyjunction.com/mitosis_activity.htm

The lab page provides pictures of onion cells undergoing mitosis.

■ Control of Cell Cycle

<http://nobelprize.org/educational/medicine/2001/>

The Nobel Prize website discusses the discovery of cyclins and CDKs. There is an interactive game about cell cycle control.

<http://outreach.mcb.harvard.edu/animations/checkpoints.swf>

<http://science.education.nih.gov/supplements/nih1/cancer/default.htm>

Both of these websites have good cell cycle animations. The NIH resource, Cell Biology and Cancer, has a section on cancer, the cell cycle, tumor suppressor genes, and oncogenes.

■ Other Resources

http://www.cellsalive.com/toc_cellbio.htm

Cells Alive! has animations on mitosis, meiosis, the cell cycle, and apoptosis.

<http://www.nclark.net/MitosisMeiosis>

This webpage displays an extensive list of online resources for mitosis and meiosis.

http://www.biology.arizona.edu/human_bio/activities/karyotyping/karyotyping.html

This online activity from The Biology Project covers karyotype analyses in normal cells and in cells carrying a genetic defect.

Genetics and Information Transfer

INVESTIGATION 7

**CELL DIVISION:
MITOSIS AND MEIOSIS**

How do eukaryotic cells divide to produce genetically identical cells or to produce gametes with half the normal DNA?

BACKGROUND

One of the characteristics of living things is the ability to replicate and pass on genetic information to the next generation. Cell division in individual bacteria and archaea usually occurs by binary fission. Mitochondria and chloroplasts also replicate by binary fission, which is evidence of the evolutionary relationship between these organelles and prokaryotes.

Cell division in eukaryotes is more complex. It requires the cell to manage a complicated process of duplicating the nucleus, other organelles, and multiple chromosomes. This process, called the cell cycle, is divided into three parts: interphase, mitosis, and cytokinesis (Figure 1). Interphase is separated into three functionally distinct stages. In the first growth phase (G_1), the cell grows and prepares to duplicate its DNA. In synthesis (S), the chromosomes are replicated; this stage is between G_1 and the second growth phase (G_2). In G_2 , the cell prepares to divide. In mitosis, the duplicated chromosomes are separated into two nuclei. In most cases, mitosis is followed by cytokinesis, when the cytoplasm divides and organelles separate into daughter cells. This type of cell division is asexual and important for growth, renewal, and repair of multicellular organisms.

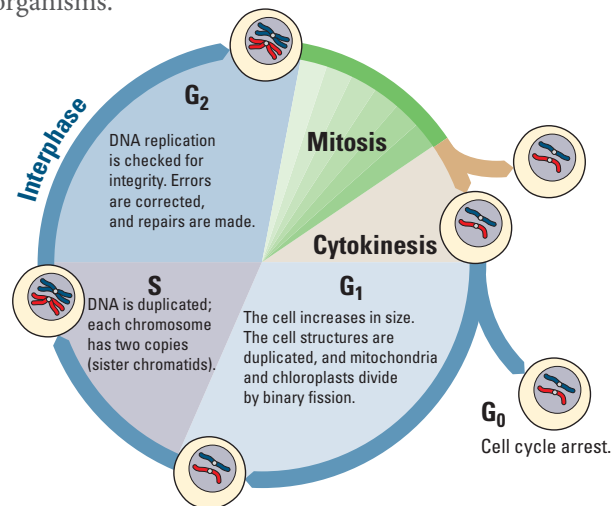


Figure 1. The Cell Cycle Showing G_1 , S, and G_2 Phases, Mitosis, and Cytokinesis

Cell division is tightly controlled by complexes made of several specific proteins. These complexes contain enzymes called cyclin-dependent kinases (CDKs), which turn on or off the various processes that take place in cell division. CDK partners with a family of proteins called cyclins. One such complex is mitosis-promoting factor (MPF), sometimes called maturation-promoting factor, which contains cyclin A or B and cyclin-dependent kinase (CDK). (See Figure 2a.) CDK is activated when it is bound to cyclin, interacting with various other proteins that, in this case, allow the cell to proceed from G_2 into mitosis. The levels of cyclin change during the cell cycle (Figure 2b). In most cases, cytokinesis follows mitosis.

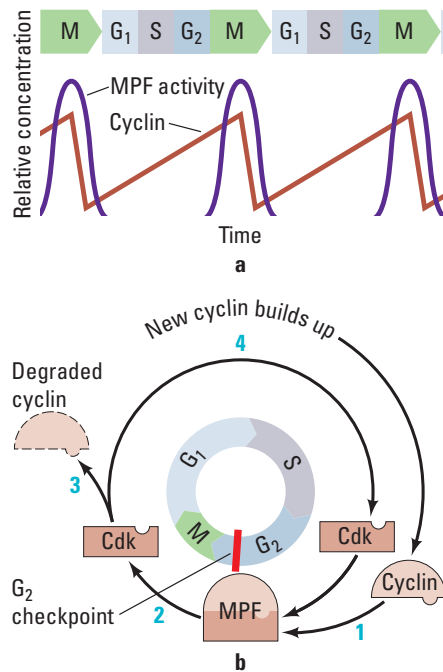


Figure 2. MPF Production During the Cell Cycle

As shown in Figure 3, different CDKs are produced during the phases. The cyclins determine which processes in cell division are turned on or off and in what order by CDK. As each cyclin is turned on or off, CDK causes the cell to move through the stages in the cell cycle.

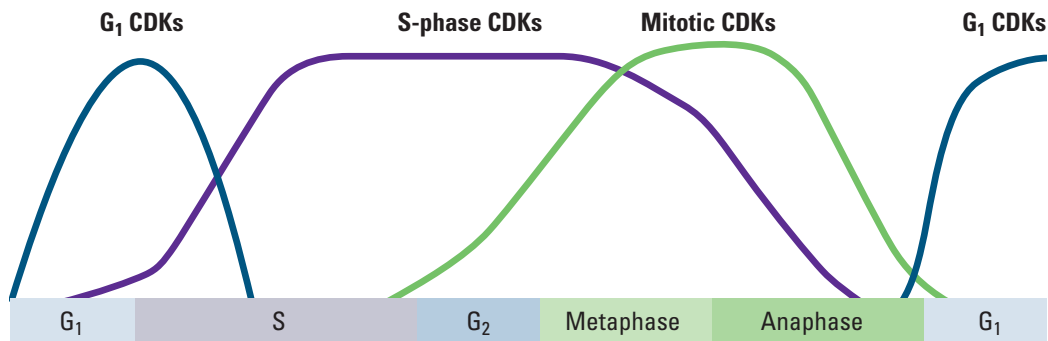


Figure 3. Levels of CDKs During the Cell Cycle

Cyclins and CDKs do not allow the cell to progress through its cycle automatically. There are three checkpoints a cell must pass through: the G_1 checkpoint, G_2 checkpoint, and the M-spindle checkpoint (Figure 4). At each of the checkpoints, the cell checks that it has completed all of the tasks needed and is ready to proceed to the next step in its cycle. Cells pass the G_1 checkpoint when they are stimulated by appropriate external growth factors; for example, platelet-derived growth factor (PDGF) stimulates cells near a wound to divide so that they can repair the injury. The G_2 checkpoint checks for damage after DNA is replicated, and if there is damage, it prevents the cell from going into mitosis. The M-spindle (metaphase) checkpoint assures that the mitotic spindles or microtubules are properly attached to the kinetochores (anchor sites on the chromosomes). If the spindles are not anchored properly, the cell does not continue on through mitosis. The cell cycle is regulated very precisely. Mutations in cell cycle genes that interfere with proper cell cycle control are found very often in cancer cells.

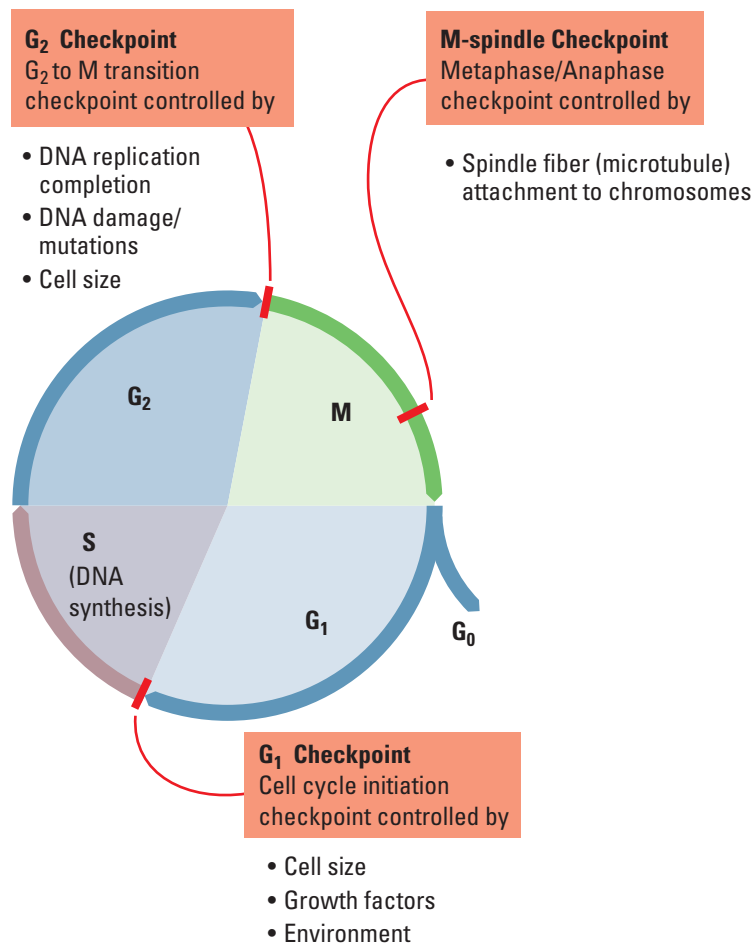


Figure 4. Diagram of the Cell Cycle Indicating the Checkpoints



■ Learning Objectives

- To describe the events in the cell cycle and how these events are controlled
- To explain how DNA is transmitted to the next generation via mitosis
- To explain how DNA is transmitted to the next generation via meiosis followed by fertilization
- To understand how meiosis and crossing over leads to increased genetic diversity, which is necessary for evolution

■ General Safety Precautions

You must be careful when preparing specimens for viewing under the compound microscope. Always cover the cover slip with a scientific cleaning wipe, such as a Kimwipe, and press down using a pencil eraser.

You should wear safety goggles or glasses and disposable gloves when handling the chemicals and razor blades in Parts 2 and 5. All materials should be disposed of properly as per your teacher's instructions.

■ THE INVESTIGATIONS

■ Getting Started

These questions are designed to see how well you understand and can explain the key concepts related to cell division before you begin your investigations.

1. How did you develop from a single-celled zygote to an organism with trillions of cells? How many mitotic cell divisions would it take for one zygote to grow into an organism with 100 trillion cells?
2. How is cell division important to a single-celled organism?
3. What must happen to ensure successful cell division?
4. How does the genetic information in one of your body cells compare to that found in other body cells?
5. What are some advantages of asexual reproduction in plants?
6. Why is it important for DNA to be replicated prior to cell division?
7. How do chromosomes move inside a cell during cell division?
8. How is the cell cycle controlled? What would happen if the control were defective?

■ Procedures

■ Part 1: Modeling Mitosis

You will investigate mitosis using models. Your teacher will give you sockosomes, Pop-It Beads, clay chromosomes, or pipe-cleaner chromosomes.

Review chromosome duplication and movement using these model chromosomes. Think about these questions as you review the cell cycle and mitosis.

- If a cell contains a set of duplicated chromosomes, does it contain any more genetic information than the cell before the chromosomes were duplicated?
- What is the significance of the fact that chromosomes condense before they are moved?
- How are the chromosome copies, called sister chromatids, separated from each other?
- What would happen if the sister chromatids failed to separate?

■ Part 2: Effects of Environment on Mitosis

Scientists reported that a fungal pathogen, may negatively affect the growth of soybeans (*Glycine max*). Soybean growth decreased during three years of high rainfall, and the soybean roots were poorly developed. Close relatives of *R. anaerobis* are plant pathogens and grow in the soil. A lectin-like protein was found in the soil around the soybean roots. This protein may have been secreted by the fungus. Lectins induce mitosis in some root apical meristem tissues. In many instances, rapid cell divisions weaken plant tissues.

You have been asked to investigate whether the fungal pathogen lectin affects the number of cells undergoing mitosis in a different plant, using root tips.

- What is your experimental hypothesis? Your null hypothesis? Are these the same?
- How would you design an experiment with onion bulbs to test whether lectins increase the number of cells in mitosis?
- What would you measure, and how would you measure it?
- What would be an appropriate control for your experiment?

Your teacher will provide you with untreated and lectin-exposed roots. You should be comfortable identifying cells in mitosis or in interphase before you begin examining the chromosome squashes.

Preparing Chromosome Squashes

1. Place the onion root tip in 1 M HCl for 4 minutes.
2. Transfer the tip to Carnoy's fixative for 4 minutes.
3. Remove the slide from Coplin jar containing 70% ethanol, dry with a scientific cleaning wipe, and label it.
4. Place the tip on the slide and cut off the distal 2 mm portion of the tip; discard the remainder of the tip.
5. Cover the root tip piece with carbol-fuchsin stain for 2 minutes.
6. Blot off excess stain and cover the tip with 1–2 drops of H₂O.
7. Gently tease the root tip apart with dissecting probes or needles. Place the cover slip over the root tip and cover the cover slip with a scientific cleaning wipe.
8. Firmly press down on the cover slip with the eraser end of a pencil. Do not twist the slide, and be careful not to break the cover slip.

Counting Cells and Analyzing Data

1. Observe the cells at high magnification (400–500 X).
2. Look for well-stained, distinct cells.
3. Within the field of view, count the cells in each phase. Repeat the counts in two other root tips.
4. Collect the class data for each group, and calculate the mean and standard deviation for each group. You must make a table in your notebook for the class data.
5. Compare the number of cells from each group in interphase and in mitosis.

Table 1. Onion Root Tip Cell Phase Data; Treatment Group _____

Tip	Number of Cells		
	Interphase	Mitotic	Total
1			
2			
3			
Total			

Table 2. Table of Observed Values (o)

	Interphase	Mitosis	Total
Control	A	B	A + B
Treated	C	D	C + D
Total	A + C	B + D	A + B + C + D = N

1. Collect the class data and enter the values into Table 1; these are the observed values for the four groups.
2. Use the data from Table 1 to calculate the totals using the formulas found in Table 2. (For example, A equals the number of interphase cells in the control group.)
3. Use the totals from Table 2 to calculate the expected values (e) using the formulas from Table 3.
4. Enter the observed values (o) from Table 2 and expected values (e) from Table 3 for each group into Table 4. Calculate the chi-square (χ^2) value for the data by adding together the numbers in the right column.
5. Compare this value to the critical value in Table 5.

Table 3. Table of Expected Values (e)

	Interphase	Mitosis
Control	$\frac{(A + B)(A + C)}{N}$	$\frac{(A + B)(B + D)}{N}$
Treated	$\frac{(C + D)(A + C)}{N}$	$\frac{(C + D)(B + D)}{N}$

Table 4. Calculation of Chi-Square Value

Group	Observed (o)	Expected (e)	(o - e)	(o - e) ²	(o - e) ² /e
Control Interphase					
Control Mitosis					
Treated Interphase					
Treated Mitosis					

Total of (o - e)²/e = chi-square (χ^2) =

Table 5. Critical Values of the Chi-Square Distribution

Probability	Degrees of Freedom (DF)				
	1	2	3	4	5
0.05	3.84	5.99	7.82	9.49	11.1
0.01	6.64	9.21	11.3	13.2	15.1
0.001	10.8	13.8	16.3	18.5	20.5

1. The degrees of freedom (df) equals the number of treatment groups minus one multiplied by the number of phase groups minus one. In this case, there are two treatment groups (control, treated) and two phase groups (interphase, mitosis); therefore $df = (2 - 1)(2 - 1) = 1$.
2. The p value is 0.05, and the critical value is 3.84. If the calculated chi-square value is greater than or equal to this critical value, then the null hypothesis is rejected. If the calculated chi-square value is less than this critical value, the null hypothesis is not rejected.

■ Postlab Review

- What was the importance of collecting the class data?
- Was there a significant difference between the groups?
- Did the fungal pathogen lectin increase the number of root tip cells in mitosis?
- What other experiments should you perform to verify your findings?
- Does an increased number of cells in mitosis mean that these cells are dividing faster than the cells in the roots with a lower number of cells in mitosis?
- What other way could you determine how fast the rate of mitosis is occurring in root tips?

■ DESIGNING AND CONDUCTING YOUR INVESTIGATION

Now that you have worked with the root tip model system, design and conduct an investigation to determine what biotic or abiotic factors or substances in the environment might increase or decrease the rate of mitosis in roots. For instance, what factors in the soil might affect the rate of root growth and development? Consider, for example, abiotic soil factors such as salinity and pH or biotic factors, including roundworms, that might alter root growth.

■ Part 3: Loss of Cell Cycle Control in Cancer

Many of us have family members who have or have had cancer. Cancer can occur when cells lose control of their cell cycle and divide abnormally. This happens when tumor-suppressor genes, such as p53 or Rb (retinoblastoma), are mutated. There are many questions you should consider before beginning your investigation.

Review from Part 1

- How is the cell cycle controlled in normal cells?
- What are cyclins and cyclin-dependent kinases? What do these proteins do in a cell?

Prelab Questions for Part 3

- How are normal cells and cancer cells different from each other?
- What are the main causes of cancer?
- What goes wrong during the cell cycle in cancer cells?
- What makes some genes responsible for an increased risk of certain cancers?
- Do you think that the chromosomes might be different between normal and cancer cells?

The last question is the focus of this part of the lab. With your group, form a hypothesis as to how the chromosomes of a cancer cell might appear in comparison to a normal cell and how those differences are related to the behavior of the cancer cell.

For each of the following cases, look at pictures of the chromosomes (karyotype) from normal human cells. Compare them to pictures of the chromosomes from cancer cells. For each case, count the number of chromosomes in each type of cell, and discuss their appearance. Then answer the following questions.

- Do your observations support your hypothesis?
- If not, what type of information might you need to know in order to understand your observations?
- If yes, what type of information can you find that would validate your conclusions?

Case 1: HeLa cells

HeLa cells are cervical cancer cells isolated from a woman named Henrietta Lacks. Her cells have been cultured since 1951 and used in numerous scientific experiments. Henrietta Lacks died from her cancer not long after her cells were isolated. Lacks's cancer cells contain remnants of human papillomavirus (HPV), which we now know increases the risk of cervical cancer.

- From your observations, what went wrong in Henrietta Lacks's cervical cells that made them cancerous?
- How does infection with human papillomavirus virus (HPV) increase the risk of cervical cancer?

Your teacher may ask you to read *The Immortal Life of Henrietta Lacks* by Rebecca Skloot. As you read it, think about the following questions:

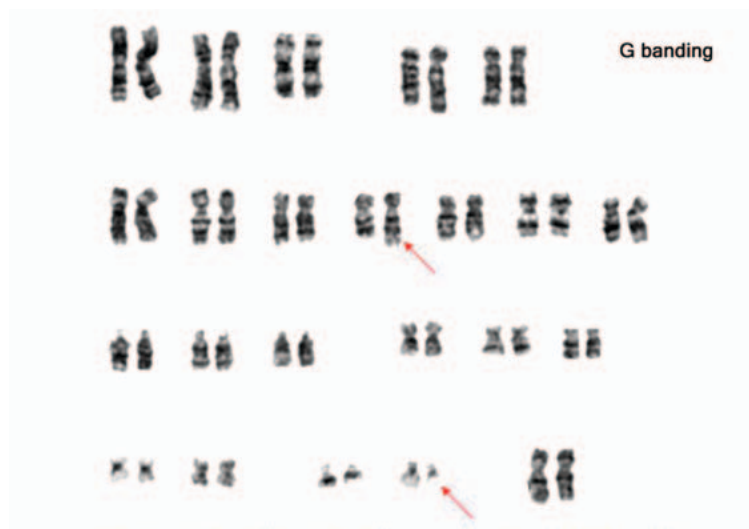
- Should tissue be removed from a patient without his or her consent for research?
- How was the HeLa cell line cultured?
- What virus infected Henrietta Lacks and may have caused her cervical cancer? What cellular process is affected by this virus?

- Was there bias in the way Henrietta Lacks was treated at Johns Hopkins?
- Put the use of HeLa cells on trial. Debate what is more important: an individual's rights to his/her own body tissues or the medical knowledge gained by studying a patient's tissues?
- Should Henrietta Lacks's family be compensated for the discoveries made using her cells?
- Do companies or universities have the right to patent discoveries made using a patient's tissues or genes without consulting the patient?
- What other legal and ethical questions are raised in this book?

■ Case 2: Philadelphia Chromosomes

In normal cells, mitosis usually is blocked if there is DNA damage. Sometimes, though, DNA damage makes cells divide more often. Certain forms of leukemia have a unique feature called a Philadelphia chromosome. Look at the karyotype of leukemia cells in Figure 5, and answer the following questions:

- What happens in a normal cell if the DNA has mutations?
- What would happen if cells with mutated DNA replicated?
- How do cells monitor DNA integrity?
- How are the chromosomes different in the cancer cells compared to normal cells?
- How could these differences lead to cancer?



©Prof. Philippe Vago/ISM/Phototake

Figure 5. Karyotype of a Patient with Chronic Myelogenous Leukemia Indicating Chromosomal Deformity

Part 4: Modeling Meiosis

Meiosis resembles mitosis but serves a very different purpose. Meiosis is a cell division resulting in the halving, or reduction, of chromosome number in each cell. A diploid organism has two sets of chromosomes ($2n$), while a haploid cell or organism has one set ($1n$). Meiosis produces gametes (ova and sperm) in animals and spores in fungi, plants, and protists. Three other important characteristics of meiosis are the exchange of genetic material (“crossing over”) between homologous chromosomes, the independent assortment of the chromosomes, and the separation of alleles of the same gene (Figure 6). These characteristics, along with random fertilization, increase the genetic variability in the offspring. These mechanisms are essential to our understanding of genetics and evolution in sexually reproducing organisms.

The hallmark of sexual reproduction is the great diversity seen in the gametes and in the resulting offspring produced by fertilization. Meiosis is integral to this process because this type of cell division produces the sex cells, gametes. Before you begin the modeling exercise, your teacher will ask you to discuss these questions.

- How do sexually reproducing organisms produce gametes from diploid progenitors?
- How does the process increase gamete diversity?
- What are the outcomes from independent assortment and crossing over?
- How does the distance between two genes or a gene and a centromere affect crossover frequencies?

Use the model chromosomes from Part 1 to explain meiosis and crossing-over events. During your investigation, answer the following questions:

- When is the DNA replicated during meiosis?
- Are homologous pairs of chromosomes exact copies of each other?
- What is crossing over?
- What physical constraints control crossover frequencies?
- What is meant by independent assortment?
- How can you calculate the possible number of different kinds of gametes?
- What happens if a homologous pair of chromosomes fails to separate, and how might this contribute to genetic disorders such as Down syndrome and cri du chat syndrome?
- How are mitosis and meiosis fundamentally different?

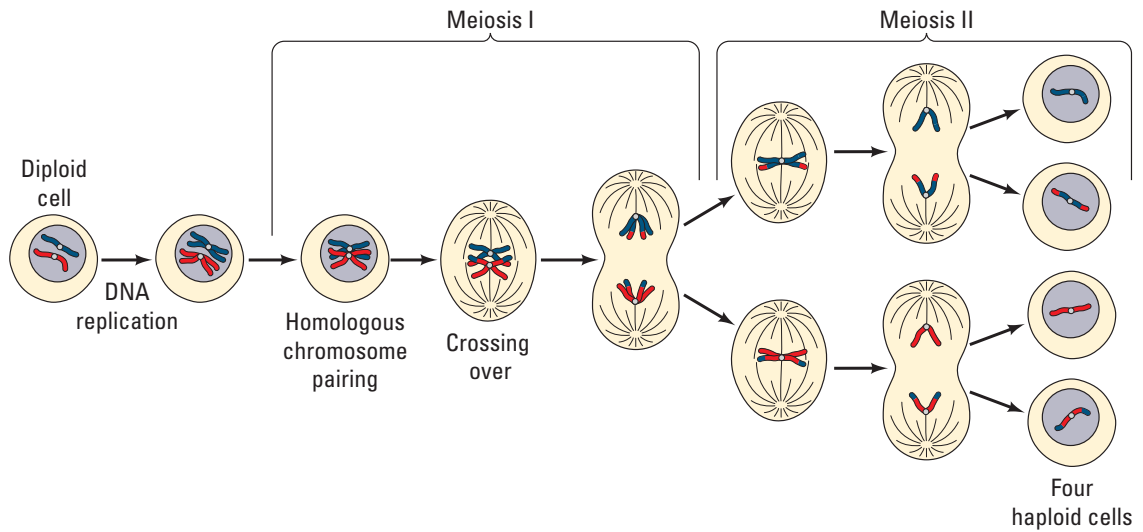


Figure 6. Meiotic Cell Division Emphasizing Chromosome Movement

■ Part 5: Meiosis and Crossing Over in *Sordaria*

The fungus *Sordaria fimicola* exchanges genetic material when two mycelia meet and fuse. The resulting zygote undergoes meiosis to produce asci; each ascus contains eight haploid spores. A single gene determines the spore color. (See Figures 7 and 8.)

A cross was made between wild type (+; black) and tan (tn) strains. The resulting zygote produces either parental type asci, which have four black and four tan spores in a row (4:4 pattern), or recombinant asci, which do not have this pattern.

- How do you explain the differences between the recombinant asci and the parental types?
 - What meiotic event can account for this difference?
 - Using the model chromosomes from Part 4, predict the possible meiotic outcomes.
1. Place a drop of water onto the microscope slide.
 2. Gently scrape some perithecia from the agar plate near where the two strains meet.
 3. Place a cover slip over the perithecia and put a scientific cleaning wipe over the cover slip.
 4. Gently press down on the cover slip using the eraser end of a pencil.
 5. Count at least 50 asci, and score them as either parental or recombinant (crossing over).
 6. Enter the data in Table 3 and make the calculations. One map unit equals one percent recombination. The percent of asci showing recombination divided by 2 equals the map units separating the spore-color gene from the centromere. The percent of asci showing recombination is divided by 2 because only half of the spores in each ascus are the result of a crossing-over event.

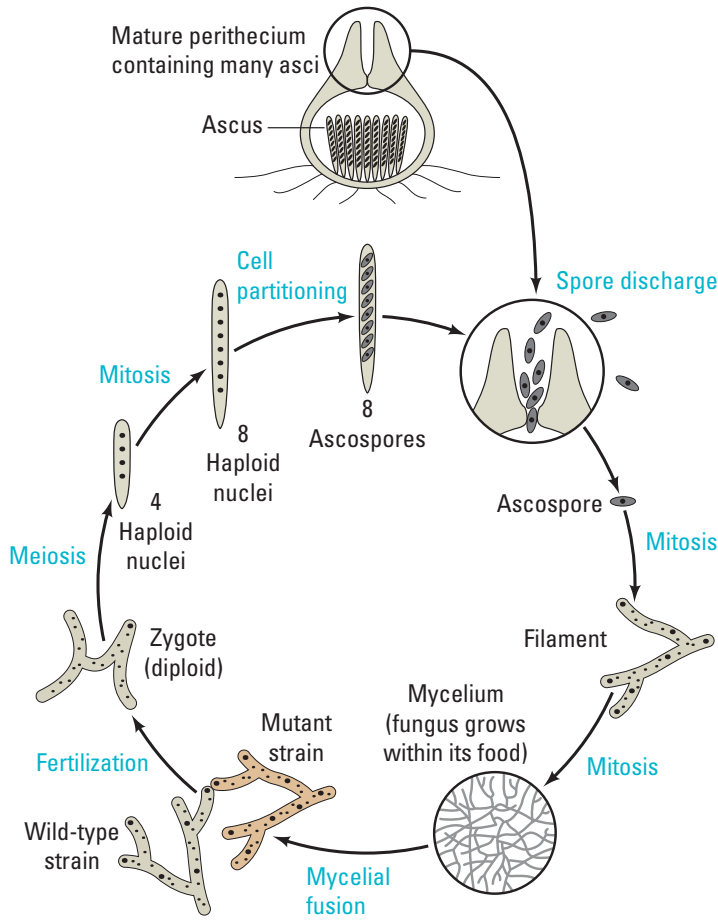


Figure 7. *Sordaria* Life Cycle

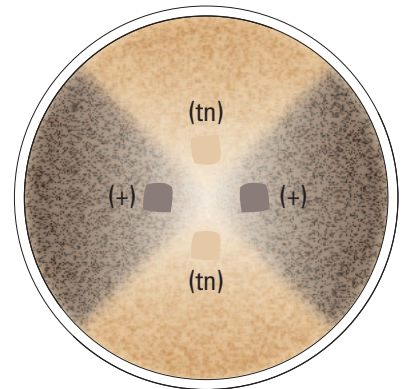


Figure 8: *Sordaria* Cross Plate

Table 3. Analysis of Results

Number of Asci Showing 4:4 Pattern	Number of Asci Showing Crossover	Total # of Asci	% Asci Showing Crossover Divided by 2	Gene to Centromere Distance (Map Units)



■ Evaluating Results

1. Why did you divide the percentage of asci showing crossover (recombinant) by 2?
2. The published map distance between the spore color gene and the centromere is 26 map units. How did the class data compare with this distance?
3. How can you account for any disparities between the class data and the published data?
4. Illustrate what happened during meiosis to produce the results you found.
5. Do you think the Philadelphia chromosome is a result of crossing over as seen in this part of the investigation or some other chromosomal abnormality? Explain your answer.
6. Do you think the cell cycle described for mitosis could be applied to meiosis as well? Explain your answer.

■ Where Can You Go from Here?

1. Can the same (or any) environmental factors you tested above affect the amount of crossing over that occurs in *Sordaria*? How would you set up an experiment to test this? For example, how does humidity or pH affect the crossover frequency?
2. Revisit the learning objectives stated earlier. Do you better understand mitosis and meiosis? Could you teach this to another class?
3. How do the mechanisms of cell replication affect genetic diversity and evolution? Consider the mechanisms such as crossing over, independent assortment, segregation, nondisjunction, and random fertilization.
4. Prepare a video or write and produce a play about the process of chromosome movement.
5. Investigate how growth factors affect the cell cycle. This will help you review cell communication.
6. Research what tumor suppressors do in the cell cycle and which types of cancers may be caused by mutations in tumor suppressor genes. Specific examples include human papillomavirus (HPV), retinoblastoma protein (Rb), BRCA1 and BRCA2, and p53.