Teacher Preparation Notes for “Mitosis and the Cell Cycle”
– How a Single Cell Develops into the Trillions of Cells in a Human Body”¹

In this hands-on, minds-on activity, students use model chromosomes and answer analysis and discussion questions to learn how the cell cycle produces genetically identical daughter cells. Students learn how DNA replication and mitosis ensure that each new cell gets a complete set of chromosomes with a complete set of genes. Students learn why each cell needs a complete set of genes and how genes influence phenotypic characteristics. To understand how a single cell (the fertilized egg) develops into the trillions of cells in a human body, students analyze an exponential growth model of increase in number of cells. In our follow-up meiosis and fertilization activity (http://serendipstudio.org/sci_edu/waldron/#meiosis) students learn how the movement of gene-carrying chromosomes during meiosis and fertilization results in the inheritance of genes.²

This activity can be used as an introduction to mitosis or to reinforce understanding of mitosis. We estimate that this mitosis activity will require 2-4 50-minute periods.

Before beginning this activity, students should know what a cell is and have a basic understanding of the functions of DNA and proteins (e.g. using "Understanding the Functions of Proteins and DNA"; http://serendipstudio.org/exchange/bioactivities/proteins).

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¹ By Drs. Ingrid Waldron, Jennifer Doherty, Scott Poethig and Lori Spindler, Department of Biology, University of Pennsylvania, 2020. These Teacher Preparation Notes and the Student Handout are available at https://serendipstudio.org/sci_edu/waldron/#mitosis. We are grateful to K. Harding for her helpful suggestion to use hair roller curlers for the model chromosomes and to local high school and middle school teachers who have contributed helpful suggestions for revision of this activity.

² Analysis and discussion versions of these activities (which can be used for remote instruction) are available at https://serendipstudio.org/exchange/bioactivities/MitosisRR and https://serendipstudio.org/exchange/bioactivities/meiosisRR. These activities are part of an integrated sequence of learning activities for teaching genetics, presented in "Genetics – Major Concepts and Learning Activities" (available at http://serendipstudio.org/exchange/bioactivities/GeneticsConcepts).
Learning Goals
In accord with the Next Generation Science Standards:\(^3\):

- Students will gain understanding of several Disciplinary Core Ideas:
  - LS1.A: Structure and Function – "All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins."
  - LS1.B: Growth and Development of Organisms – "In multicellular organisms individual cells grow and then divide by a process called mitosis, thereby allowing the organism to grow. The organism begins as a single cell (fertilized egg) that divides successively to produce many cells, with each parent cell passing identical genetic material (two variants of each chromosome pair) to both daughter cells. Cellular division and differentiation produce and maintain a complex organism, composed of systems of tissues and organs that work together to meet the needs of the whole organism."\(^4\)
  - LS3.A: Inheritance of Traits – "Each chromosome consists of a single very long DNA molecule, and each gene on the chromosome is a particular segment of that DNA. The instructions for forming species' characteristics are carried in DNA. All cells in an organism have the same genetic content …"

- Students will engage in the Scientific Practices:
  - “Developing and Using Models – Develop, revise, and/or use a model (including mathematical and computational) to generate data to support explanations, predict phenomena, analyze systems, and/or solve problems."
  - “Constructing Explanations – Apply scientific ideas, principles and/or evidence to provide an explanation of phenomena…".

- This activity provides the opportunity to discuss the Crosscutting Concepts
  - "Systems and system models – … Models can be valuable in predicting a system’s behaviors…"
  - “Cause and Effect: Mechanism and Explanation – … A major activity of science is to uncover such causal connections, often with the hope that understanding the mechanisms will enable predictions… [Students] suggest cause and effect relationships to explain and predict behaviors in complex natural and designed systems. They also propose causal relationships by examining what is known about small-scale mechanisms within the system."

- This activity helps to prepare students for the Performance Expectations:
  - HS-LS1-4, "Use a model to illustrate the role of cellular division (mitosis) and differentiation in producing and maintaining complex organisms."
  - HS-LS3-1, "Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring."

More Detailed Content Learning Goals

- Each cell contains chromosomes and each chromosome contains a long DNA molecule. Each DNA molecule has many genes. A gene provides the instructions for making a protein. Different versions of a gene are called alleles, and different alleles give the instructions for making different versions of a protein. These different versions of a protein can result in different phenotypic characteristics.

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\(^3\) Quotations from http://www.nextgenscience.org/sites/default/files/HS%20LS%20topics%20combined%206.13.13.pdf

\(^4\) To help students understand this Disciplinary Core Idea and meet Performance Expectation HS-LS1-4, we recommend combining this activity with "Cell Differentiation and Epigenetics" (http://serendipstudio.org/exchange/bioactivities/epigenetics).
• Chromosomes come in pairs of homologous chromosomes. In each pair of homologous chromosomes, both chromosomes have the same genes at the same locations, but a gene may have different alleles in the two chromosomes of a homologous pair.

• The cell cycle includes two growth phases, DNA replication, mitosis and cytokinesis. DNA replication and mitosis ensure that each daughter cell receives a complete copy of the DNA in the parent cell. The cell cycle produces new cells for growth and repair.

• At the beginning of mitosis, the two copies of the DNA in each chromosome are condensed into compact sister chromatids which are attached at a centromere. During mitosis, spindle fibers line up the chromosomes in the middle of the cell and then separate the sister chromatids of each chromosome, resulting in two complete sets of chromosomes at opposite ends of the cell.

• At the end of mitosis, cytokinesis separates the two halves of the cell to form two genetically identical daughter cells.

• An exponential growth model illustrates how the number of cells can increase from a single-cell zygote to roughly a trillion cells in a newborn baby. If each cell divided each day, the number of cells would double each day; after 40 days, this would produce a trillion cells.

Making the Model Chromosomes
We recommend two students per group for this activity. If you have more students in a group, a third student can be in charge of arranging and rearranging the string cell membrane for the modeling activity on page 6 of the Student Handout, and the third and fourth students can use their arms as spindle fibers to separate the sister chromatids for the second pair of homologous chromosomes for the modeling activity on page 7.

For the more complete Student Handout, each student group will need two pairs of homologous model chromosomes. For the follow-up activity "Meiosis and Fertilization – Understanding How Genes Are Inherited" (http://serendipstudio.org/sci_edu/waldron/#meiosis), you will need the two pairs of homologous model chromosomes to be different colors.

<table>
<thead>
<tr>
<th>First Pair of Homologous Model Chromosomes</th>
<th>Second Pair of Homologous Model Chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Model Chromosome" /></td>
<td><img src="image2" alt="Model Chromosome" /></td>
</tr>
</tbody>
</table>

Each model chromosome consists of two sister chromatids which are attached with hook and loop fasteners (Velcro) in the centromere region (approximately the location where the two chromatids touch in the above figures). For each pair of homologous chromosomes, one of the chromosomes has a stripe on each chromatid to represent the multiple differences in alleles between the two chromosomes in a homologous pair.

You can use rolosomes (made from hair roller curlers) or sockosomes (made from socks). The rolosomes provide model chromosomes that are engaging and easy to make. Sockosomes are more time-consuming to make, but they may be sturdier for long-term use in multiple classes. The figures in the above chart show the approximate shape of sockosome model chromosomes;

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5 You may prefer to use H and h as the symbols for the normal and sickle cell hemoglobin, since these are more easily distinguished in student answers than S and s (or α).
the shape of rolosomes is shown in the photo below.\(^6\)

**Rolosomes**

**Supplies**

For each group of 2-4 students in your largest class:

- 8 hair roller curlers, 4 in one color and 4 in another color (Hereafter, these hair roller curlers will be referred to as rollers. Rollers are readily available online. You may need to order from two different manufacturers in order to get rollers that have similar diameter but different colors.)
- 4 pairs of self-stick hook-and-loop dots (Velcro). (The hook and loop dots should have a slightly smaller diameter than the rollers. In our experience, the dots do not stick well if the diameter of the dots is larger than the diameter of the rollers.)

You will also need a permanent marker to make the rolosomes.

![Photo of rolosomes](image-url)

The rolosomes in this photo represent two pairs of homologous chromosomes. Each rolosome has sister chromatids attached by Velcro fasteners in the centromere region.

The first rolosome has the alleles a and s. The second rolosome is homologous to the first rolosome and has the alleles A and S.

The two rolosomes on the right represent a pair of homologous chromosomes with the alleles l and L, respectively. (Both chromatids of the L chromosome have a stripe, although this is not clearly visible in this photo.)

**Making the Rolosomes**

To make the four rolosomes for each group of 2-4 students you will need four rollers of one color and four rollers of a different color.

1. For two rollers of the same color, stick a Velcro hook-and-loop dot with hooks on one roller and a matching fuzzy dot with loops on the other roller, so the two rollers can be attached as sister chromatids.
   
   Note: The pair of rollers attached by hook-and-loop dots is a rolosome. In the rolosome, each roller represents a chromatid. After mitosis is completed, each roller represents a chromosome in a daughter cell.

2. Repeat step 1 to make four rolosomes, each with two sister chromatids.

3. Use the chart on page 3 and the figure on this page to label the alleles on each pair of

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\(^6\) Another option is to use pipe cleaners with different color beads to represent the different alleles of the various genes. Two pipe cleaners can be twisted together when representing sister chromatids and untwisted when mitosis separates the sister chromatids.
homologous model chromosomes. To avoid possible confusion, make the s allele particularly small and the S allele particularly large. Make a long stripe down both chromatids of one of each pair of homologous chromosomes, as shown.

**Sockosomes** (You do not need these if you make rolosomes. These instructions are provided in case you prefer to make sockosomes.)

**Supplies**
- Small or medium children’s crew socks (no more than half of any one color; even number of pairs of each color sock; four pairs of socks for each group of 2-4 students in your largest class; avoid black and dark blue socks typically found in packs of boys socks).
- Fiber fill
- Self-stick circles of hook-and-loop fasteners (Velcro; if you are making more than 36 sockosomes it may be more cost effective to purchase a roll of self-stick hook-and-loop tape and cut it into 1/2” pieces.)
- Needle and thread
- 1” wide masking tape and permanent marker

**Making the Sockosomes**
1. Attach one part of a self-stick hook-and-loop fastener (the fuzzy part) to the heel of one sock, and attach the other part (the part with hooks) to the heel of the other sock; secure with staples or by sewing.
2. Fill each sock with fiber fill, and sew the end of each sock closed.
3. Stick the socks together at the heels. You now have a model chromosome with two chromatids, where each sock represents a chromatid. Note that a sockosome refers to the pair of socks attached by hook-and-loop fasteners, not the individual socks. After mitosis is completed, each individual sock represents a chromosome in a daughter cell.
4. Pairs of homologous chromosomes will be represented by two sockosomes of the same color, one with a stripe marked along the length of each sock with a permanent marker (see chart on page 3). In the location of each allele, put a ring of tape around each sock in each sockosome; the tape stays on best if it goes completely around the sock, overlapping at the ends. Use the chart on page 3 and the instructions in step 3 on page 4 to guide you in labeling the alleles on each chromatid in your sockosomes.

**Additional Supplies and Requirements for the Modeling Activity**
Students sometimes have difficulty recognizing that the two sets of chromosomes are in two different daughter cells at the end of mitosis. Therefore, we recommend that you provide pieces of string or yarn for students to use as cell membranes. For example, for the modeling activity on page 6 of the Student Handout, each student group will need a piece of string approximately 6 feet long to represent the membrane around the original cell and then the membranes around the daughter cells. Alternatively, you can have your students use chalk or dry erase markers to draw the cell membranes on their lab tables.

Students should carry out the modeling activities on a lab table or similar large flat surface, so they can more easily see the processes and outcomes.

**Instructional Suggestions and Background Biology**
In the Student Handout, numbers in bold indicate questions for the students to answer and ➢ indicates a step in the modeling procedures for the students to do.

If you are using the Word version of the Student Handout, please check the PDF version to make sure that all figures and formatting are displayed properly in the Word version on your computer.
To maximize student learning and participation, we recommend that you have students work in pairs to answer each group of related questions. Student learning is increased when students discuss scientific concepts to develop answers to challenging questions; furthermore, students who actively contribute to the development of conceptual understanding and answers to questions gain the most. After pairs of students have worked together to answer a group of related questions, we recommend that you have a class discussion to probe student thinking and help students develop a sound understanding of the concepts and information covered.

If you would like to have a key with the answers to the questions in the Student Handout, please send a message to iwaldron@upenn.edu. The following paragraphs provide additional instructional suggestions and background information.

In the Student Handout for this activity, we have introduced multiple technical terms (shown in bold). We have omitted the technical terms for some of the concepts introduced in the Student Handout in order to allow students to focus on learning the basic concepts without becoming overwhelmed by memorizing vocabulary. If you want your students to learn the names of the phases of mitosis, these terms can easily be incorporated in questions 7 and 9 of the Student Handout.

Cells, Chromosomes and Genes

Question 1 will stimulate students to begin thinking about the driving question, “How does a single cell (the fertilized egg) develop into the trillions of cells in a human body?” Scientists have estimated that a newborn baby has 1-4 trillion cells and an adult has 20-40 trillion cells (not counting bacteria; http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002533). You may want to show your students this one-minute time-lapse video of zygotes developing in vitro (https://www.youtube.com/watch?v=4TGiIW7-9eQ).

Many students have difficulty distinguishing the concepts of DNA, genes and chromosomes, so you will probably want to reinforce student understanding that a gene is part of a DNA molecule contained in a chromosome. You could use either or both of the following questions for this purpose.

2. Fill in the blanks in the following sentences.

A chromosome contains one long ______ molecule. Each gene in this ______ molecule gives the instructions for making a ____________________.

3a. Each cell has
   a. more chromosomes than genes.
   b. more genes than chromosomes.
   c. the same number of genes and chromosomes.

3b. Explain how you know.

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8 One reason that we have included both the albinism and sickle cell genes on one pair of model chromosomes is to counteract the tendency for some students to assume that each chromosome has only a single gene. A chromosome contains not only a DNA molecule, but also proteins (e.g. histones; see figure on page 8 of these Teacher Preparation Notes).
In the Student Handout a gene is defined as a segment of DNA that gives the instructions for making a protein. You should be aware that the definition of a gene has changed as scientific understanding has progressed. Initially, a gene was conceived as a unit of heredity that determines a phenotypic characteristic. A more sophisticated contemporary definition of a gene is a segment of DNA that codes for an RNA molecule, which may be pre-mRNA (which is modified to be messenger RNA that codes for the sequence of amino acids in one or more proteins), ribosomal RNA, transfer RNA or regulatory RNA. There is no single universally agreed-upon definition of a gene at this time. The changing definition of a gene illustrates the constantly evolving nature of science as scientists develop progressively more sophisticated understanding of concepts such as the gene. For additional information about the challenges and complexities of defining a gene, see http://www.biologyreference.com/Fo-Gr/Gene.html.

The Student Handout includes the statement, "each cell needs to have a complete set of chromosomes". As you no doubt know, there are exceptions to this generalization, e.g. mammalian red blood cells (which do not have any chromosomes) and gametes (which have only one from each pair of homologous chromosomes). To avoid undue complexities, we have omitted discussion of the special case of red blood cells and we have postponed discussion of gametes to “Meiosis and Fertilization – Understanding How Genes Are Inherited” (http://serendipstudio.org/sci_edu/waldron/#meiosis).

The Cell Cycle – How One Cell Becomes Two Cells
The S phase is named for DNA synthesis. The G₁ and G₂ phases were named for the gaps between the S phase and mitosis, but the gap terminology is not introduced in the Student Handout. Not all daughter cells produced by the cell cycle continue to divide; for example, differentiated nerve cells do not divide.

After question 6, if you have already discussed the reasons why cell size is limited, you may want to refer back to that discussion by asking your students why our bodies aren’t made up of just one or a few large cells. You should be aware that mitosis can occur without cytokinesis; for example, this is how multinucleate skeletal muscle fibers are formed. Also, some cells lose their nucleus as they differentiate (e.g. red blood cells).

For additional information on the cell cycle, see https://courses.lumenlearning.com/biology1/chapter/the-cell-cycle/. If you would like your students to know more about DNA replication, you can use pages 3-4 of the Student Handout for “DNA Structure, Function and Replication” (https://serendipstudio.org/exchange/bioactivities/DNA).

Mitosis – How Each Daughter Cell Gets a Complete Set of Chromosomes
The figure below provides additional information about how DNA is structured in chromatin during interphase vs. in chromatids during mitosis. For human cells, the total extended length of the DNA would be nearly 2 meters (2 million micrometers). This DNA must fit into a nucleus

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9 Mammalian red blood cells have no nucleus or mitochondria which maximizes the amount of hemoglobin and thus oxygen that each red blood cell transports. In consequence, red blood cells only survive about four months and red blood cells cannot undergo mitosis; new red blood cells are produced by mitosis and differentiation of stem cells in the red bone marrow.
with a diameter of 5-10 micrometers. During interphase, most of the DNA is wound around histone proteins, so a typical human chromosome is about 1000 micrometers in length. Each chromosome is folded in loops within the nucleus. Chromatin’s more extended, thin form allows proteins such as RNA polymerase or DNA polymerase to contact the DNA to carry out important cellular functions such as producing RNA or replicating the DNA.

At the beginning of mitosis, several types of protein guide the folding of chromatin into sister chromatids. The shorter, fatter structure of the chromatids protects the relatively fragile DNA molecules from being broken as they are moved during mitosis. Also, the shorter chromatids help to prevent entanglement of sister chromatids or of different chromosomes during mitosis.

Students often have difficulty understanding the difference between chromosomes and chromatids, so we have made a special effort to clarify this distinction (in questions 7 and 9 in the Student Handout). It may help your students if you mention that there is no such thing as a single chromatid without a sister chromatid; once the chromatids have separated they have become independent chromosomes.

If you want your students to learn the names of the stages of mitosis, these terms can easily be incorporated in questions 7 and 9 of the Student Handout. The figures in these questions show mitosis in hypothetical cells with either one or two pairs of homologous chromosomes. Many students know that human cells have 23 pairs of homologous chromosomes, so you may want to explain that the same process is observed for all 46 chromosomes in a human cell, but these figures show simplified cases for clarity.

After question 7, we recommend that you show one or more of the following videos:

- A Great Mitosis Video (https://www.youtube.com/watch?v=AhgRhXI7w_g or https://www.youtube.com/watch?v=VIv97K1-9QB0; 1.5 minutes)
- Actual Footage of Cell Division (Kidney Cells) (https://www.youtube.com/watch?v=N97cgUqV0Cg; 1 minute)
- Mitosis (https://www.youtube.com/watch?v=C6hm3sA0ip0; ~6 minutes).

The last video will be particularly appropriate if you want your students to learn the stages of mitosis. If you want your students to learn the names of the phases of mitosis, these terms can easily be incorporated in questions 7 and 9.

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*Chromatin structure changes as the molecular activity in the cell changes. For example, when a gene becomes active, the chromatin typically unwinds.*
The Student Handout shows cytokinesis in animal cells. Cytokinesis in plant cells is illustrated in this figure.

Genes and Human Characteristics
In our experience, our emphasis on understanding genes and how they move during mitosis, meiosis and fertilization contributes to student interest and understanding, especially in our follow-up activity on meiosis and fertilization where the use of model chromosomes with labeled alleles leads naturally to understanding inheritance and provides an excellent introduction to Punnett squares.

In answering question 10, your students should recognize that enzymes and hemoglobin are proteins, but they may not know that melanin is not a protein. This figure shows part of the structural formula of the most common type of melanin (eumelanin); the arrow shows where the polymer continues.

We do not introduce the terms homozygous, heterozygous, dominant or recessive in the Student Handout for this activity, but instead introduce them in our Genetics activity (http://serendipstudio.org/sci_edu/waldron/#genetics). If you prefer, these terms can easily be introduced when you discuss page 5 of the Student Handout. For this purpose, you may want to include the following prose and questions after question 13.

If both copies of a gene have the same allele, the person is homozygous for that gene. If the two copies of a gene have different alleles, the person is heterozygous.

14. Match each item in the list on the left with the best match from the list on the right.

Aa genotype ___ a. heterozygous
SS genotype ___ b. homozygous

Often, in a heterozygous individual a dominant allele determines the observable characteristic and the other recessive allele does not affect the phenotype. Thus, a heterozygous person has the same phenotype as a person who is homozygous for the

11 In a heterozygous individual, typically each allele is transcribed and both versions of the protein are produced. For many genes, the allele that codes for a functional protein results in the production of enough normal protein to produce a normal phenotype. In these cases, the allele that codes for a functional protein is dominant and the allele that codes for a nonfunctional protein is recessive. The example of albinism is shown on page 5 of the Student Handout.

The sickle cell allele could best be described as co-dominant, since both alleles affect the phenotype of a heterozygous person; a heterozygous person does not have sickle cell anemia (due to the allele for normal hemoglobin) and also has increased resistance to malaria (due to the sickle cell allele).

An exception, where the allele for the nonfunctional protein is dominant, is the gene for the enzyme that disposes of a harmful molecule produced by alcohol metabolism (see page 7 of the Student Handout). The functional enzyme consists of four normal polypeptides bound together; even one nonfunctional polypeptide in this tetramer may inactivate the enzyme. This helps to explain why the allele for the nonfunctional protein is dominant.

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dominant allele. In our example, the A allele is dominant because it codes for normal, functional enzyme and, even in a heterozygous individual, there is enough of this normal, functional enzyme to produce enough melanin to result in normal skin and hair color. The a allele is recessive because it codes for a non-functional enzyme which does not affect skin or hair color in a heterozygous individual.

**15a.** What are two different genotypes for the albinism gene that result in the same phenotype?

**15b.** Explain how two people with different genotypes can have the same phenotype.

For more information on each of the genes discussed in the Student Handout and their phenotypic effects, see pages 12-14 of these Teacher Preparation Notes.

**Modeling Mitosis with One Pair of Homologous Chromosomes and Multiple Pairs of Homologous Chromosomes**

Before beginning the modeling of mitosis, you may want to review mitosis by showing one of the videos listed on page 8 of these Teacher Preparation Notes.

To prevent student confusion during the modeling activities:

- It is crucial to circulate among student groups continuously and provide considerable input.
- As the students model mitosis, remind them to check the figures on pages 3 and 4 in the Student Handout. They should notice that the spindle fibers line up all the chromosomes in the middle of the cell and then simultaneously separate the sister chromatids of each of the chromosomes.
- You will probably want to reinforce student understanding that the modeling activity begins with chromosomes that have replicated DNA in sister chromatids (represented by complete rolosomes) and ends with chromosomes that do not have replicated DNA (represented by a single roller in each daughter cell).
- For questions which require students to label the s allele in diagrams, you may want to have your students use a lowercase s with a line above it or a cursive a, in order to avoid confusion with the S allele.

To ensure accurate modeling and reinforce understanding of sister chromatids, you may want to add the following question to the middle of page 6 of the Student Handout.

**14.** Suppose that your partner has put the model chromosomes back together as shown in the diagram. What is wrong? Explain how you know.

The Student Handout emphasizes that mitosis produces genetically identical daughter cells. Recent research indicates that in some cases the daughter cells are not entirely genetically identical so human bodies typically have some minor mosaicism (https://www.nytimes.com/2018/05/21/science/mosaicism-dna-genome-cancer.html).
How Repeated Cell Division Can Make Trillions of Cells

Questions 18 and 19 help students to understand how a process that adds only one cell each time a cell divides can produce a newborn baby’s 1-4 trillion cells in just nine months. The model implied in these questions is relatively realistic for the first four days, but after that it is only representative of the potential for exponential growth in the number of cells. Although the model presented in questions 18 and 19 is not a realistic description of embryonic and fetal development, it does demonstrate how mitosis can produce trillions of cells from a single cell in just nine months.

To answer question 19a, your students should recognize that they need to multiply 1000×1000. To answer question 19b, they should calculate:

\[10^3 \times 10^3 \times 10^3 = 10^6 = 10^{12} = 1,000,000,000,000 = 1 \text{ trillion cells}\]

This is an example of exponential growth, which explains how cell division could produce a trillion cells in 40 days. You may want to introduce the term, exponential growth, and explain the relevance of exponential growth for other topics such as population growth (see “Understanding and Predicting Changes in Population Size – Exponential and Logistic Population Growth Models vs. Complex Reality”, available at https://serendipstudio.org/exchange/bioactivities/pop).

Question 20 in the Student Handout engages students in synthesizing and summarizing what they have learned about the cell cycle, mitosis, and how a single cell develops into the trillions of genetically identical cells in a human body. This question can be used for formative assessment. If this question is challenging for your students, you can provide scaffolding as follows.

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12 The exponential growth model also ignores the important roles of cell differentiation, cell death, and morphogenesis in development. A brief introduction to cell differentiation and morphogenesis in the development of embryos is available at http://www.biology-pages.info/E/EmbryonicDevelopment.html. If you want your students to learn about cell differentiation, you can use “Cell Differentiation and Epigenetics” (https://serendipstudio.org/exchange/bioactivities/epigenetics).
• If your students have trouble learning vocabulary, you may want to precede question 20 with a question that asks for definitions of the terms listed (or perhaps a matching question in which you provide your preferred definitions for these terms).

• You may want to provide your students with the handout that is shown on the last page of these Teacher Preparation Notes; students can label and explain the figures as part of their answer to this synthesis/review question.

• Students may benefit from a preliminary small group discussion of this question. However, each student should prepare a written answer in his or her own words.

To consolidate student learning and correct any misunderstandings your students may have, we recommend a whole-class discussion of student answers to question 20. To facilitate this discussion, you may want to require your students to use diagrams in their answers to question 20 and have pairs or small groups of students prepare their answers on whiteboards. For information about how to make inexpensive whiteboards and use them in your teaching, see "The $2 interactive whiteboard" and "Resources for whiteboarding" in https://fnoschese.wordpress.com/2010/08/06/the-2-interactive-whiteboard/.

Question 21 engages students in thinking about the need for cell division even in a fully grown adult. The rate of cell replacement by mitosis varies for different types of cells and in different circumstances. The rate is greater when an injury has occurred. Cells that are routinely exposed to injury (e.g. skin cells or the epithelial cells that line the lumen of the stomach) are replaced within days or a couple of weeks. In contrast, nerve cells and muscle cells can last a lifetime.

You may want to conclude with a class discussion of the Crosscutting Concept, Systems and System Models. It may be helpful for students to think about how the hands-on modeling activity and the second figure on page 3 of the Student Handout helped them to understand mitosis. You may also want to include a discussion of how the quantitative modeling in questions 18-19 helped them to understand how a process that adds only one cell on day 1 can produce trillions of cells in nine months.

Background Information on Albinism, Sickle Cell Anemia and Alcohol Sensitivity

Albinism
In the most common form of albinism, the defective enzyme for producing melanin not only results in albino skin and hair color, but also affects the appearance and function of the eyes. The defective enzyme is tyrosinase which is needed for the first two steps in converting tyrosine

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13 Some additional tips for using whiteboards are:
– Coat the white boards with Endust (or similar product) before using. Every once in a while, wipe them clean and reapply Endust.
– Do not use markers that are old or almost empty. The ink from these are more difficult to erase.
– Black markers erase easiest.
– Best if boards are erased immediately after use.
– Teacher and/or students can take a picture of the information on the whiteboard if they want to save it.

14 The role of mitosis in asexual reproduction is discussed in the Student Handout and the Teacher Preparation Notes for our meiosis and fertilization activity (http://serendipstudio.org/sci_edu/waldron/#meiosis).

15 A model is a simplified representation of reality that highlights certain key aspects of a phenomenon and thus helps us to better understand and visualize the phenomenon. Many students tend to think of a model as a physical object and may not understand how a figure or quantitative model can be considered a model. It may be helpful to introduce the idea of a conceptual model and give examples of conceptual models that students may have used, e.g. a map, a diagram of a football play, a concept map, and an outline for an essay a student is writing.
to melanin. In a heterozygous individual, the normal allele is dominant because it codes for the functioning enzyme and even when there is only one copy of the normal allele there is enough of this functioning enzyme to produce enough melanin to prevent albinism. For additional information about the various forms of albinism see https://medlineplus.gov/ency/article/001479.htm and https://omim.org/entry/203100.16

Sickle cell anemia
A person who is homozygous for the sickle cell allele and produces only sickle cell hemoglobin has sickle cell anemia. Sickle cell hemoglobin is less soluble in the watery cytosol of the red blood cells than normal hemoglobin, particularly when oxygen concentrations are low. Consequently, sickle cell hemoglobin tends to form long stacks or rods of hemoglobin molecules. These stacks of sickle cell hemoglobin molecules result in the sickled shape of some red blood cells in a person who is homozygous for the sickle cell allele.

<table>
<thead>
<tr>
<th>Genotype (genes)</th>
<th>→</th>
<th>Protein</th>
<th>→</th>
<th>Phenotype (characteristics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 copies of the allele that codes for normal hemoglobin (SS)</td>
<td>→</td>
<td>Normal hemoglobin dissolves in the cytosol of red blood cells.</td>
<td>→</td>
<td>Disk-shaped red blood cells can squeeze through the small blood vessels → normal health</td>
</tr>
<tr>
<td>2 copies of the allele that codes for sickle cell hemoglobin (ss)</td>
<td>→</td>
<td>Sickle cell hemoglobin can clump in long rods in red blood cells.</td>
<td>→</td>
<td>When sickle cell hemoglobin clumps in long rods → sickle-shaped red blood cells → clogged small blood vessels + fragile red blood cells → pain, damage to body organs + anemia = sickle cell anemia</td>
</tr>
</tbody>
</table>

The sickled red blood cells tend to clog the tiny capillaries, blocking the circulation in different parts of the body. Also, the sickled red blood cells do not survive as long as normal red blood cells, contributing to a tendency to anemia. Resulting symptoms include pain, physical weakness, impaired mental functioning, and damage to organs such as the heart and kidneys.

In a person who is heterozygous for the sickle cell and normal hemoglobin alleles, each red blood cell has both sickle cell and normal hemoglobin. The amount of normal hemoglobin is

16 Students may ask about the distinction between inherited albinism and vitiligo. Albinism is the inability of the body's cells to produce melanin and affects the whole body. Vitiligo is a patterned loss of melanin pigment resulting from the destruction of melanocytes; the hypopigmented areas appear on the skin of a person with normal pigmentation. (Additional information is available at http://www.mayoclinic.org/diseases-conditions/vitiligo/symptoms-causes/syc-20355912.)
sufficient to prevent the symptoms of sickle cell anemia in almost all cases. The sickle cell hemoglobin in each red blood cell decreases the severity of malaria in heterozygous individuals because the malaria parasite doesn't grow as well in red blood cells containing sickle cell hemoglobin.

Additional information can be found at:
- https://omim.org/entry/603903

**Alcohol Intolerance**
The enzyme, acetaldehyde dehydrogenase, plays a major role in alcohol metabolism.

\[
\text{alcohol} \xrightarrow{\text{dehydrogenase}} \text{acetate} \xrightarrow{\text{dehydrogenase}} \text{acetaldehyde} \xrightarrow{\text{dehydrogenase}} \text{acetic acid}
\]

An inactive form of acetaldehyde dehydrogenase results in the accumulation of high levels of acetaldehyde after drinking alcohol. The accumulation of acetaldehyde results in unpleasant symptoms including increased heart rate and stroke volume and associated heart palpitations, increased blood flow to the skin and flushing, and a general "terrible feeling overall". This condition is called alcohol intolerance or alcohol sensitivity.

Heterozygous individuals accumulate acetaldehyde and have substantial symptoms; the functional enzyme is a tetramer and apparently even one abnormal protein in the tetramer may inactivate the enzyme. Although heterozygous individuals are sensitive to alcohol, alcohol intolerance is more severe in homozygous individuals who experience very unpleasant symptoms whenever they drink alcohol; consequently, homozygous individuals almost never develop alcoholism.

The drug Antabuse (disulfiram), which is given to treat alcohol abuse, works by blocking the enzyme acetaldehyde dehydrogenase. If a person who has taken Antabuse drinks alcohol, concentrations of acetaldehyde will become elevated, which results in highly unpleasant symptoms.

The allele that codes for a relatively inactive version of acetaldehyde dehydrogenase and causes alcohol intolerance is relatively common in people of East Asian descent, but extremely rare in people of European descent.


**Follow-up and Related Activities**
We recommend that you follow this mitosis activity with "Meiosis and Fertilization – Understanding How Genes Are Inherited" (http://serendipstudio.org/sci_edu/waldron/#meiosis). In this hands-on, minds-on activity, students use model chromosomes and answer analysis and discussion questions to learn about the processes of meiosis and fertilization. Students first analyze how the processes of meiosis and fertilization result in the alternation between diploid and haploid cells in the human lifecycle. To learn how meiosis produces genetically diverse
gametes, students analyze the results of crossing over and independent assortment. As they model meiosis and fertilization, students follow the alleles of a human gene from the parents' body cells through gametes to zygotes; thus, students learn how a person inherits one copy of each gene from each of his/her parents. A final brief section contrasts sexual reproduction with asexual reproduction.

Another recommended follow-up activity is “Cell Differentiation and Epigenetics” (http://serendipstudio.org/exchange/bioactivities/epigenetics). In this analysis and discussion activity, students answer minds-on questions as they learn about the differentiation of specialized cell types, including the role of changes in epigenetic control of gene expression during cell differentiation. Students also learn about environmental influences on epigenetic control of gene expression and the need for cell division and differentiation even in a fully grown adult.

These activities are part of an integrated sequence of learning activities for teaching genetics (“Genetics – Major Concepts and Learning Activities”; available at http://serendipstudio.org/exchange/bioactivities/GeneticsConcepts)

"Chromonoodles: Jump into the Gene Pool" by Farrar and Barnhart, The Science Teacher, Summer 2011, 78:34-39 presents an informative series of activities using chromonoodles (made from swim noodles) to demonstrate fertilization, the cell cycle, meiosis, karyotyping and genetics concepts, including Punnett squares. These activities are whole class demonstrations, in contrast to the more structured modeling activities for small groups of students presented in the Student Handouts for our activities. Additional suggestions for the use of chromonoodles are provided in “Using Pool Noodles to Teach Mitosis and Meiosis”, Genetics 2005, 170(1): 5-6.

Additional resources that you may find helpful are provided in the podcasts available at http://www.bozemanscience.com/028-cell-cycle-mitosis-and-meiosis/ .

Sources for Figures in the Student Handout
- First figure on page 1 modified from http://media1.britannica.com/eb-media/16/166816-004-5EA0F269.jpg
- Second figure on page 1 constructed using cell image from https://cdn.thinglink.me/api/image/620015517125574658/1240/10/scaletowidth
- Figure on page 2 modified from https://www2.le.ac.uk/projects/vgec/diagrams/22-Cell-cycle.gif
- First figure on page 3 modified from https://www.researchgate.net/profile/Kevin_Verstrepen/publication/51196608/figure/fig1/AS:276923784679429@1443035183356/Chromatin-structure-DNA-is-wrapped-around-a-histone-octamer-to-form-nucleosomes.png
- Second Figure on page 3 modified from https://dr282zn36sxsg.cloudfront.net/datastreams/f-d%3A878df64c63462553305d51d5deccdec3c0cb0ae48fa51aeb9297f1b%2BIMAGE_THUMB_POSTCARD_TINY%2BIMAGE_THUMB_POSTCARD_TINY_1
- Figure on page 4 adapted from Krogh, Biology – A Guide to the Natural World

All the other figures were prepared by the authors.
Possible Handout to Provide Scaffolding to Help Students Answer Question 20