Teacher Notes for
"Introduction to Genetics – Similarities and Differences between Family Members"[1]

To begin this activity, students propose a hypothesis about how genes contribute to the similarities and differences in appearance of family members. Students refine their hypothesis as they learn more. Students learn that different versions of a gene give the instructions for making different versions of a protein which can result in different characteristics. Next, students review how genes are transmitted from parents to offspring through the processes of meiosis and fertilization. Then, students analyze several examples that illustrate how inheritance of genes can result in family resemblance and/or differences. Concepts covered include Punnett squares, dominant and recessive alleles, incomplete dominance, and polygenic inheritance.

Before beginning this activity, your students should have a basic understanding of meiosis and fertilization. For this purpose, I recommend:
– the analysis and discussion activity, "Understanding How Genes Are Inherited via Meiosis and Fertilization" (https://serendipstudio.org/exchange/bioactivities/meiosisRR%20)
– *or* the hands-on activity, "Meiosis and Fertilization – Understanding How Genes Are Inherited" (http://serendipstudio.org/sci_edu/waldron/#meiosis).
It will also be helpful if your students have a basic understanding of DNA and proteins. If your students need a refresher, you may want to show them the 5-minute video, "What Is DNA and How Does It Work?" (https://www.youtube.com/watch?v=zwibgNGe4aY).

Unless your students already have a good basic knowledge of genetics, I recommend that you plan two 50-minute class periods for this activity.

Learning Goals
In accord with the Next Generation Science Standards:[2]

- This activity helps to prepare students for two Performance Expectations:
  - 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."
  - HS-LS3-2, "Make and defend a claim based on evidence that inheritable genetic variations may result from: (1) new genetic combinations through meiosis…."
- Students will gain understanding of two 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."
  - 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."
- Students will engage in two Scientific Practices:
  - Developing and Using Models: "Develop and/or use a model… to predict phenomena, analyze systems, and/or solve problems."

[1] By Dr. Ingrid Waldron, Dept Biology, Univ Pennsylvania, 2021. These Teacher Preparation Notes and the related Student Handout are available at https://serendipstudio.org/exchange/bioactivities/geneticsFR.

[2] http://www.nextgenscience.org/sites/default/files/HS%20LS%20topics%20combined%206.13.13.pdf and http://www.nextgenscience.org/sites/default/files/Appendix%20G%20-%20Crosscutting%20Concepts%20FINAL%20edited%204.10.13.pdf

- Constructing Explanations: "Apply scientific ideas, principles, and/or evidence to provide an explanation of phenomena…, taking into account possible unanticipated effects."
- This activity provides the opportunity to discuss the Crosscutting Concept:
  - Cause and Effect: "Cause and effect relationships can be suggested and predicted for complex natural… systems by examining what is known about smaller scale mechanisms within the system."

Additional Content Learning Goals

Genes in DNA → Proteins → Characteristics

- Genes in DNA provide the information necessary to make proteins, and proteins carry out many biological functions and thus influence our characteristics.
- Different alleles (different versions of the same gene) code for different versions of a protein which can result in differences in a person's appearance or other characteristics.
- A person is homozygous for a gene if both alleles for that gene are the same. A person is heterozygous if they have two different alleles for the gene.
- For some pairs of alleles, the characteristics of a heterozygous individual are the same as the characteristics of one of the two types of homozygous individual. The allele that results in the same characteristics for both the homozygous and heterozygous individuals is dominant. The other allele is recessive.
- In other cases, neither allele is completely dominant or completely recessive. For example, in incomplete dominance, the characteristic of a heterozygous individual is halfway between the characteristics of the two homozygous individuals.
- Many characteristics are influenced by more than one gene. A person's characteristics are also influenced by the environment.

Meiosis and Fertilization → Inheritance

- The behavior of chromosomes during meiosis and fertilization provides the basis for understanding the inheritance of genes.
- As a result of meiosis, each egg receives one copy of each gene from the mother and each sperm receives one copy of each gene from the father. When the gametes unite in fertilization, the zygote that develops into the child receives one copy of each gene from the mother and another copy of each gene from the father. Repeated mitosis ensures that each cell in a child's body has the same genes as the zygote.
- Because children get their genes from their parents, they tend to resemble their parents and their siblings.
- However, meiosis results in genetically diverse sperm and eggs which, together with random fertilization, results in genetic diversity of the zygotes/children produced by the same mother and father. This can result in phenotypic diversity.

Punnett Squares → Probabilistic Predictions of Inheritance

- The processes of meiosis and fertilization can be summarized in Punnett squares.
- A Punnett square can be used to predict the probability of each possible offspring genotype.
- Each fertilization event is independent of other fertilization events, so the genotype of each child is independent of the genotype of any siblings. Therefore, the probability of a given genotype or characteristic is the same for each of a couple's offspring.

This activity will help to counteract the following common **misconceptions**.[3]

[3] These misconceptions are taken primarily from http://knowgenetics.org/common_misconceptions/ and https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2278104/ (especially tables 5 and 6).

- Each trait is influenced by a single gene (not recognizing how common polygenic traits are).
- A person who doesn't have a characteristic lacks the gene for this characteristic (not recognizing that the person has other alleles for this gene).
- Genes are the sole determinants of traits (not recognizing environmental influences).
- Students often fail to recognize the probabilistic nature of Punnett square predictions and inheritance.

Instructional Suggestions and Background Biology

If your students are learning online, we recommend that they use the Google Doc version of the Student Handout available at https://serendipstudio.org/exchange/bioactivities/geneticsFR. To answer questions 4 and 6-8, students can either print the relevant pages, draw on them and send pictures to you, or they will need to know how to modify a drawing online. To answer online, they can double-click on the relevant drawing in the Google Doc to open a drawing window. Then, they can use the editing tools to answer the questions.[4] You may want to use the GoogleDoc or Word document to prepare a version of the Student Handout that will be more suitable for your students; if you do this, please check the format by viewing the PDF.

To maximize student learning, I recommend that you have your students complete groups of related questions in the Student Handout individually or in pairs and then have a class discussion of these questions. In each discussion, you can probe student thinking and help them to develop a sound understanding of the concepts and information covered before moving on to the next part of the activity.

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.

Question 1a asks students to summarize what they have observed about the similarities and differences in appearance of family members; this is the anchoring phenomenon for this activity. Question 1b introduces the driving question, "How do genes contribute to the similarities and differences in family members' characteristics?" You may want to omit the second sentence in question 1b and use class discussion to elicit questions about these specific issues from your students.

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[4]To draw a line

1. At the top of the page, find Select line and pick the type of line you want.
2. Place the line on your drawing:
    - Line, Elbow Connector, Curved Connector or Arrow: Click to start, then drag across the canvas.
    - Curve or Polyline: Click to start, then click at each point you want the line to bend. Double-click or complete the shape to finish.
    - Scribble: Click to start, then drag across the canvas.

To draw a shape

1. At the top of the page, find and click Shape.
2. Choose the shape you want to use.
3. Click and drag on the canvas to draw your shape.

To insert text

1. At the top of the page, click Insert.
    - To place text inside a box or confined area, click Text Box and drag it to where you want it.
2. Type your text.
3. You can select, resize and format the word art or text box, or apply styles like bold or italics to the text.

When you are done, click Save and Close.

I recommend that you have a class discussion of question 1 before proceeding to the next section. This introductory discussion will stimulate students to begin thinking about the driving question for this activity and will inform you about your students' current knowledge and any misconceptions they may have.[5] You may want to display a list of your students' questions and a consensus hypothesis or several hypotheses to be evaluated as students learn more during this activity. You can refer to the students' questions at appropriate times as you progress through the activity, and your students will revise the hypothesis or hypotheses in questions 10, 13, 18c, 18d and 20c.

How do genes influence our characteristics?

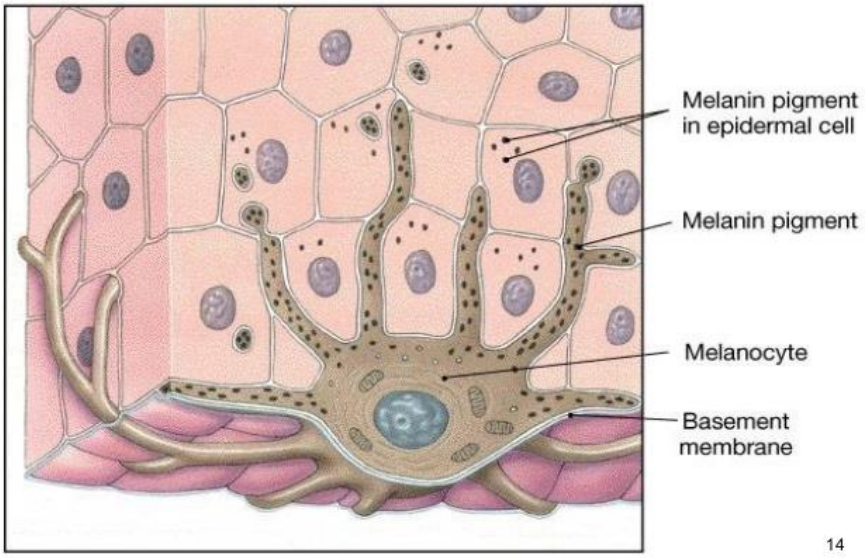
This section of the Student Handout begins with the definition of a gene as "a segment of DNA that gives the instructions for making a protein". The definition of a gene has changed as scientific understanding has progressed. Initially, a gene was conceived as a unit of heredity that determines a phenotypic characteristic. A more sophisticated contemporary definition of a gene is a segment of DNA that codes for an RNA molecule, which may be 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.

This section introduces multiple useful vocabulary words and concepts (genotype, homozygous, heterozygous, dominant and recessive). The chart on page 1 of the Student Handout provides the opportunity to counteract the common misconception that characteristics are due to the presence or absence of a gene.

A major theme of this section is that genotype determines which version or versions of a protein are made, and the protein in turn influences our characteristics. For the albinism example, the specific protein is tyrosinase, an enzyme that plays a crucial role in the synthesis of melanin, the primary pigment in skin and hair. The normal allele codes for functional tyrosinase; the allele for albinism codes for a defective, non-functional version of this enzyme. The allele for albinism is recessive because, even when there is only one copy of the normal allele, the normal allele codes for enough functional enzyme to produce enough melanin to result in normal skin and hair color. Often, a dominant allele codes for a functional protein and recessive alleles code for non-functional protein. For this type of albinism, the lack of the pigment melanin affects not only skin and hair color, but also the appearance and function of the eyes. Certain alleles of other genes can also result in albinism. For additional information about albinism see http://www.nlm.nih.gov/medlineplus/ency/article/001479.htm and http://omim.org/entry/203100.

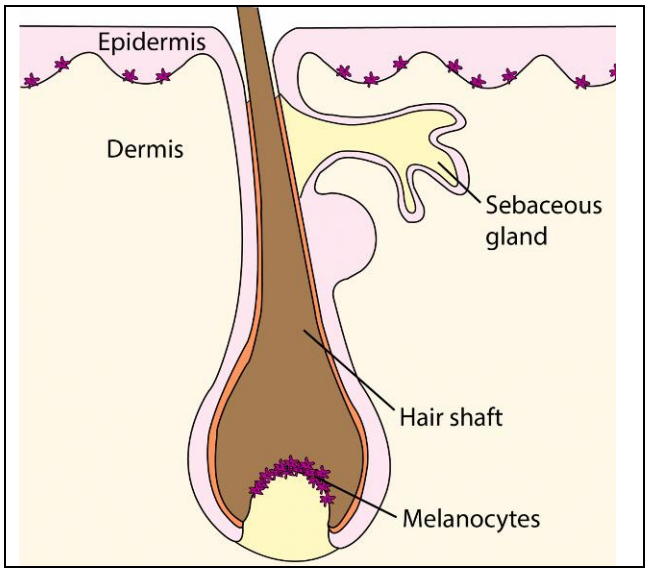
[5] During this discussion you may want to mention that for genetics analyses, we are concerned with biological parents even when they are not living with their children.

Melanin is produced in melanosomes inside melanocytes and transported into the epidermal cells in the outer layer of the skin. A good explanation is provided in the short video, "How We Get Our Skin Color".[6]



(https://image.slidesharecdn.com/smartscreen-skin-150715094615-lva1-app6891/95/skin-14-638.jpg?cb=1436953811)

This figure shows a hair follicle. The cells of the hair follicle produce the acellular hair Melanin is produced by hair follicle melanocytes and transferred to the growing hair (https://genetics.thetech.org/ask-a-geneticist/hair-color-can-change).



Additional examples you can use to reinforce student understanding that genes provide the instructions for making proteins which influence phenotypic characteristics include:

- normal vs. sickle cell hemoglobin, which can result in sickle cell anemia or sickle cell trait (see "The Genetics of Sickle Cell Anemia and Sickle Cell Trait", https://serendipstudio.org/exchange/bioactivities/geneticsSCA)
- normal vs. defective clotting proteins, which can result in hemophilia (see "Understanding the Functions of Proteins and DNA", http://serendipstudio.org/exchange/bioactivities/proteins).

Additional examples (cystic fibrosis and phenylketonuria) are discussed on pages 6-7 of these Teacher Notes.

How does a child inherit genes from his or her mother and father?

This section of the Student Handout provides an overview of human reproduction which provides a useful context for the more detailed analyses which follow. Due to meiosis and fertilization, a zygote has one copy of each gene from the mother and one copy from the father.

[6]Available at http://www.hhmi.org/biointeractive/how-we-get-our-skin-color.

The zygote undergoes many rounds of mitosis to produce the cells in a child's body. Mitosis produces daughter cells with the same genetic makeup as the original cell, so each cell in a child's body has the same genetic makeup as the zygote.

How Inheritance of Genes can Result in Family Similarities and Differences
Questions 6-9 guide students to understand that:

- Punnett squares summarize the possible outcomes of meiosis and fertilization.
- If you know the genotypes of the parents, Punnett squares can be used to predict the possible genotypes of their offspring.

Questions 10-13 engage students in analyzing examples that illustrate:

- how inheritance via meiosis and fertilization contributes to the tendency of children to resemble their parents
- how meiosis and fertilization can result in an offspring who has a genotype that results in a characteristic that is not observed in either parent.

Questions 10 and 13 revisit the driving question introduced in question 1b. You may want to have your students compare their answers with the hypothesis they developed in response to question 1b.

Students should realize that parents who have the characteristic associated with a recessive allele must be homozygous for the recessive allele and therefore won't have a child with the dominant allele (unless there is a new mutation).[7] In contrast, two parents who have the characteristic associated with the dominant allele may both be heterozygous so they could have a child who has inherited two copies of the recessive allele and has the associated characteristic. The latter point will prepare students to interpret the pedigree shown in question 15.

The prevalence of albinism is only 1 in 20,000 individuals worldwide. Therefore, your students should realize that most parents are not heterozygous for the albinism allele. As you discuss student answers to question 14, we recommend that you introduce the important point that Punnett squares predict outcomes for a particular pair of parental genotypes, and not for the general population. To make predictions for the general population, we would need to know the prevalence of genotypes in the population and whether there is assortative mating.

Other conditions that are caused by a recessive allele of a single gene, and inherited in the same manner as albinism, include:

- cystic fibrosis, which is caused by a faulty membrane protein which indirectly results in difficulty in breathing and shortened life expectancy (https://medlineplus.gov/genetics/condition/cystic-fibrosis/);
- phenylketonuria (PKU) which is due to defective versions of the enzyme that converts phenylalanine to tyrosine, which is an important step in disposing of excess phenylalanine. Excessive levels of phenylalanine result in mental retardation unless phenylketonuria is detected at birth and treated with a special diet. In an individual who is homozygous for the PKU allele, mental retardation can be prevented by minimizing phenylalanine in the diet by avoiding the artificial sweetener aspartame and high-protein

[7] There are rare exceptions to the generalization that two albino parents cannot have a child with normal skin and hair color. For example, the parents may be homozygous for recessive albinism alleles in different genes, so their child could inherit one dominant allele for normal skin and hair color for each of these genes. This child would be heterozygous for both genes and would have normal skin and hair color.

foods (e.g. meat, fish, milk, cheese, eggs, nuts, beans, tofu, and even foods with flour) and substituting special low-phenylalanine foods. Minimizing intake of phenylalanine is especially important for babies and young children when the brain is developing rapidly and for pregnant women (to protect the rapidly developing brain of her fetus). For additional information on PKU and how to treat PKU, see http://www.mayoclinic.com/health/phenylketonuria/DS00514/DSECTION=treatments-and-drugs and http://www.genome.gov/25020037).

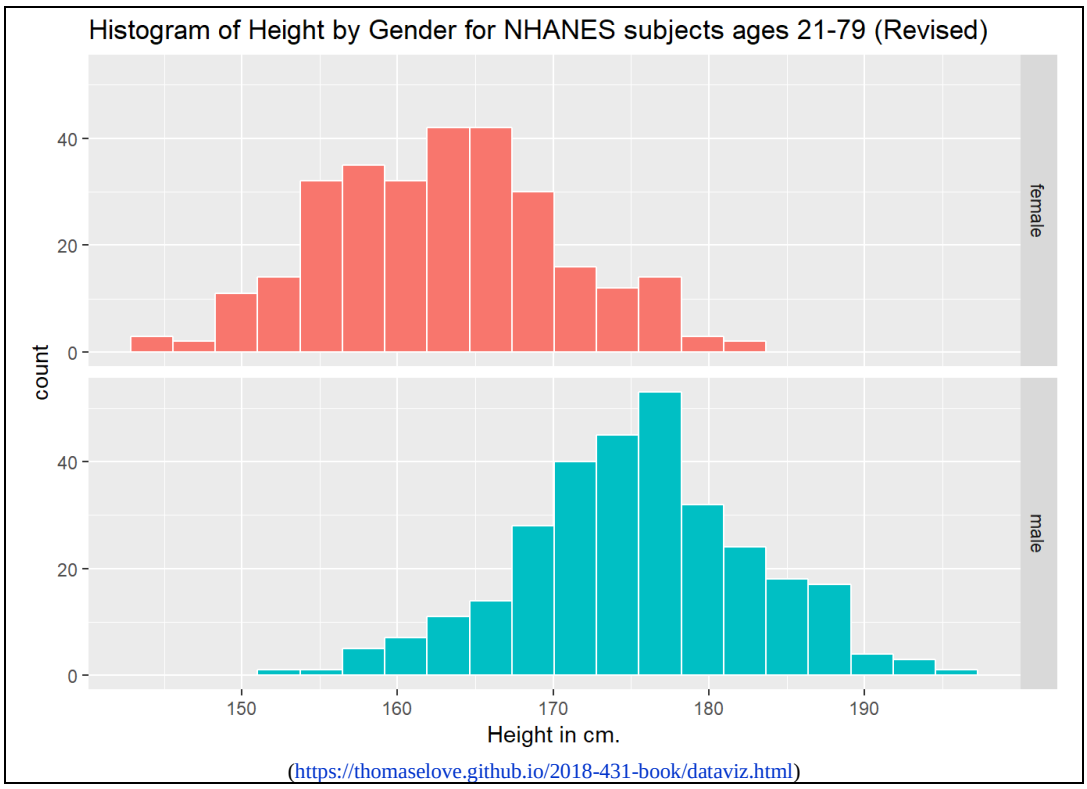
After your students have completed question 15, you may want to use the first episode in "Soap Opera Genetics" (http://serendipstudio.org/exchange/bioactivities/SoapOperaGenetics) for review and assessment. You can enhance student learning and retention of important concepts and vocabulary by having your students complete this activity using active recall (without referring to previous notes or materials), and then providing prompt feedback to clarify any points of confusion and correct any misconceptions (e.g. by having a class discussion of student answers).

Question 16 should prompt students to recognize that the two alleles of the one gene that they have considered thus far could not possibly be responsible for the whole range of skin colors that humans have. This question provides a transition to considering the polygenic inheritance of height in the next section. If you want your students to learn about polygenic inheritance of skin color, you can use "Were the babies switched? – The Genetics of Blood Types" (https://serendipstudio.org/sci_edu/waldron/#blood) or the second episode of "Soap Opera Genetics" (http://serendipstudio.org/exchange/bioactivities/SoapOperaGenetics).

Family Similarities and Differences for Characteristics that are Influenced by Multiple Genes

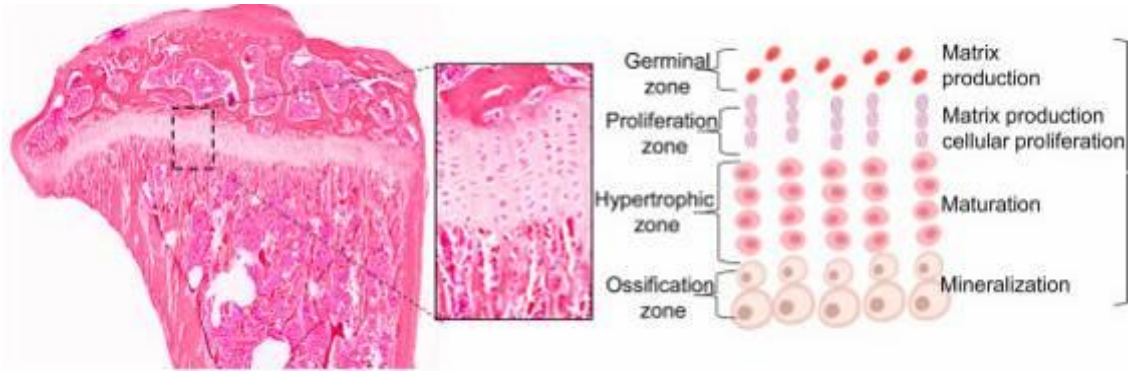
This section presents the important concept that a phenotypic characteristic is often influenced by multiple genes, as well as environmental factors. When a phenotypic characteristic is influenced by multiple genes, this is called polygenic inheritance. Height, like many polygenic traits, is a quantitative, continuous variable. This contrasts with a categorical variable like albino vs. not albino. Categorical variables are easier to analyze in Punnett squares and are often the focus of introductory genetics learning activities. However, it is important to introduce polygenic inheritance, since so many human characteristics are polygenic. For example, height, weight, skin color, blood pressure, and risk of diabetes are each influenced by multiple genes and the environment.

The figure below shows the distribution of adult heights in the US. Most of the research evidence is for adult height, so the Student Handout discusses the genetics of adult height.



(https://thomaselove.github.io/2018-431-book/dataviz.html)

The activity of cells in the growth plate determines how much the leg bones grow during childhood and adolescence, which is a major determinant of adult height. The figure below provides additional information about the structure and function of a growth plate.



(https://www.sciencedirect.com/science/article/pii/S0303720720303543)

The **G** gene described on page 5 of the Student Handout is the gene for the Growth Hormone Releasing Hormone Receptor (GHRHR); this protein determines how effectively Growth Hormone Releasing Hormone stimulates the release of Growth Hormone. Growth Hormone stimulates the proliferation and differentiation of cells in the growth plate to produce cartilage which is subsequently mineralized to become bone (https://www.nature.com/articles/nature01657). The effect of the **G** gene on adult height is estimated to be between 1 and 4 cm (https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0004464). Most of the genes that influence height have smaller estimated effects, with the exception of very rare deleterious

alleles (https://academic.oup.com/jes/article/4/4/bvaa025/5781121; https://academic.oup.com/jcem/article/103/9/3155/5047296).[8]

The table in the middle of page 5 of the Student Handout summarizes the effects of the $\mathbf{G^0}$ and $\mathbf{G^1}$ alleles, *if* everything else is held constant. For example, $\mathbf{G^1G^1}$ males will be shorter than other males who have the same alleles for the other genes that influence height; however, $\mathbf{G^1G^1}$ males will be taller than females who have the same alleles for all the other genes that influence height except the **SRY** gene (see flowchart on the top of page 6 of the Student Handout and graph on page 7 of these Teacher Notes). To reinforce the importance of other genes, you may want to ask this question after question 18b.

Give a reason why these parents might not be the shortest.

Discussion of this question could help your students understand that differences in the alleles for the other genes that influence height could result in greater heights for the parents with the $\mathbf{G^1G^1}$ genotype.

The $\mathbf{G^0}$ and $\mathbf{G^1}$ alleles are described as showing incomplete dominance.[9] I couldn't find any actual evidence for incomplete dominance of these alleles, but incomplete dominance is assumed in Genome-Wide Association Studies, which have provided much of the evidence that dozens or perhaps hundreds of different genes influence height (https://academic.oup.com/jcem/article/103/9/3155/5047296). The table below summarizes the key points about different types of dominance.

Type of Dominance	Phenotype of Heterozygous Individual
Dominant-recessive pair of alleles	Same as phenotype of individual who is homozygous for the dominant allele
Incomplete dominance	Intermediate between phenotypes of the two types of homozygous individual (typically observed for quantitative traits); phenotype different from either homozygous individual
Codominance[10]	Shows different observable phenotypic effects of both alleles

Questions 18c and 18d revisit the concepts in questions 10 and 13, but for a gene that shows incomplete dominance rather than dominant and recessive alleles.

The **SRY** gene described in the flowchart on the top of page 6 of the Student Handout initiates the development of testes which play a key role in male development. In contrast, the absence of an **SRY** gene in **XX** females results in the development of ovaries and female anatomy. One aspect of sex differences in development is that female leg bone growth stops earlier during the teen years, because the growth plates are converted to bone earlier for females than for males. This is a major reason why females are shorter than males.

[8] An example of a rare allele that has a large effect on height is analyzed in "A mistake in copying DNA can result in dwarfism" (https://serendipstudio.org/exchange/bioactivities/geneticsdwarf).

[9] Incomplete dominance can occur when each allele results in the production of a set dose of protein product and the phenotype is proportionate to the amount of protein. Thus, incomplete dominance is sometimes called a dosage effect.

[10] This activity does not discuss the concept of codominance. Blood types are a good example of codominance; this example is discussed in "Were the babies switched? – The Genetics of Blood Types" (https://serendipstudio.org/sci_edu/waldron/#blood) and in the second episode of "Soap Opera Genetics" (http://serendipstudio.org/exchange/bioactivities/SoapOperaGenetics). Most genes show codominance at the molecular level of protein production within the cell, as illustrated in the chart on page 1 of the Student Handout.

In addition to the many genes that influence height, several environmental factors also influence height. Important environmental factors include nutrition of the mother during pregnancy, nutrition during childhood and adolescence, and infectious diseases (especially those that cause diarrhea) or intestinal parasites (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4892290/). Trends in these environmental factors are the probable cause of trends toward increased adult height in many countries during the twentieth century. Researchers have estimated that 53-84% of variation in height within a population is due to genetic factors, with environmental factors playing a less important role.

You may want to explicitly compare the information in the Punnett squares vs. the flowchart on pages 5-6 of the Student Handout. The Punnett squares provide specific information about the inheritance and effects of two specific alleles of one gene. In contrast, the flowchart provides an overview that includes the contributions of multiple genes and the environment, as well as a partial explanation of how these factors influence adult height. This overview is crucial for understanding the genetic and environmental reasons why height is a quantitative, continuous variable (question 19).[11]

Information from both the Punnett squares and the flowchart will help students to answer question 20c, in which students will develop their final model of how genes contribute to family similarities and differences in appearance. In your class discussion of student answers to question 20c, you may want to refer back to earlier versions of their models.

Obviously, the genes discussed in this activity are only a tiny sample of the 20,000-25,000 human genes. To help your students understand why family members do not look exactly the same (unless they are monozygotic twins), you may want to mention the very large number of human genes, remind them of independent assortment and crossing over during meiosis, and perhaps also mention mutation.

Possible Additional Section on Probabilistic Interpretations of Punnett Squares
To introduce probabilistic interpretations of Punnett squares and the effects of random variation on the genotypes of children in a real family, you may want to insert the following question between questions 13 and 14.

14a. In a Punnett square, each offspring genotype shown is equally likely. What is the probability that the first child of two heterozygous **Aa** parents will be albino?

a. 0% b. 25% c. 50% d. 75% e. 100%

14b. What is the probability that the second child of these parents will be albino?

a. 0% b. 25% c. 50% d. 75% e. 100%

f. can't decide without knowing whether their first child was albino

14c. Explain your reasoning.

14d. If two heterozygous parents have four children, how many of the children will be albino?

a. 0 b. 1 c. 2 d. could be any of these (or possibly even more)

14e. Explain your reasoning.

[11] If you want your students to learn about the genetics of blood types (mentioned in question 19), you can use "Were the babies switched? – The Genetics of Blood Types" (https://serendipstudio.org/sci_edu/waldron/#blood) or the second episode of "Soap Opera Genetics – Genetics to Resolve Family Arguments" (https://serendipstudio.org/exchange/bioactivities/SoapOperaGenetics).

You may want to refer back to the figure in question 7 to help your students understand the following points.

- Since gametes with either type of allele are equally likely and fertilization is random, each genotype in a Punnett square is equally likely.
- A heterozygous offspring can result from an **A** sperm fertilizing an **a** egg or an **a** sperm fertilizing an **A** egg; this explains why the probability of an **Aa** offspring is 50%.

In discussing the proposed additional question, you may want to include the following points.

- A Punnett square can only predict the probability of various genotypes and not the actual genotype of the next birth.
- Each fertilization event is independent of any previous fertilization events.

Alternatively, you may want to use one of the following activities to develop student understanding of the probabilistic interpretations of Punnett squares and the effects of random variation on the genotypes of the children in real families.

- "Coin Flip Genetics" (pages 3-5 in the Student Handout for "Genetics", https://serendipstudio.org/sci_edu/waldron/#genetics).
- "Genetics and Probability – Sex Ratios of Births" (https://serendipstudio.org/exchange/bioactivities/geneticsSRB).

An Integrated Sequence of Learning Activities for Teaching Genetics

This genetics activity is part of an integrated sequence of learning activities which is presented in Genetics – Major Concepts and Learning Activities (http://serendipstudio.org/exchange/bioactivities/GeneticsConcepts). Part I of this overview summarizes key concepts in genetics. Part II presents common misconceptions. Part III recommends an integrated sequence of learning activities on the biological basis of genetics, plus seven human genetics learning activities. These learning activities develop student understanding of key concepts and counteract common misconceptions. Each of these recommended learning activities supports the Next Generation Science Standards (NGSS; https://www.nextgenscience.org/).