Teacher Preparation Notes for Genetics and Genetics Supplement

These activities help students to understand basic principles of genetics, including:
– how genotype influences phenotype via the effects of genes on protein structure and function
– how genes are transmitted from parents to offspring through the processes of meiosis and fertilization.

The Genetics Student Handout includes three modules:
– an introductory module with an analysis of albinism that teaches both the relationship of genotype to phenotype (including the concepts of dominant and recessive alleles) and how genes are inherited by meiosis and fertilization (including understanding Punnett squares); this module uses model chromosomes and is designed for use after "Meiosis and Fertilization – Understanding How Genes Are Inherited" (available at http://serendip.brynmawr.edu/sci_edu/waldron/#meiosis);
– a Coin Toss Genetics activity that helps students understand the probabilistic nature of inheritance and Punnett square predictions; this module helps students to understand why there are discrepancies between Punnett square predictions and many real families;
– an analysis of the inheritance of sickle cell anemia that introduces the important points that a single gene often has multiple phenotypic effects and alleles are often neither completely dominant nor completely recessive.

The Genetics Supplement Student Handout includes three modules:
– an alternative version of the introductory module with an analysis of albinism that does not use model chromosomes;
– a module that analyzes the genetics of sex determination and helps students understand the probabilistic nature of inheritance and the limitations of Punnett square predictions; this module can be used after the Coin Toss Genetics activity;
– pedigree analyses for recessive and dominant alleles, including challenge questions that introduce the role of new mutations and engage students in evaluating the advantages and disadvantages of Punnett squares and pedigrees as models of inheritance.

We recommend that you start with either version of the introductory module, followed by the Coin Toss Genetics module. Depending on your learning goals, you could follow this pair of modules with the genetics of sex determination module, the sickle cell anemia module and/or the pedigree module.

Before beginning this activity, your students should have a basic understanding of meiosis and fertilization. For this purpose, we recommend the hands-on activity "Meiosis and Fertilization – Understanding How Genes Are Inherited" (available at http://serendip.brynmawr.edu/sci_edu/waldron/#meiosis).

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1 By Drs. Ingrid Waldron and Jennifer Doherty, Dept Biology, Univ Pennsylvania, 2017. These Teacher Preparation Notes and the related Student Handout and Genetics Supplement are available at http://serendip.brynmawr.edu/sci_edu/waldron/#genetics.
Learning Goals

Learning Goals Related to National Standards

- 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."
  - 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."
  - LS3.B: Variation of Traits – In sexual reproduction, meiosis can create new genetic combinations and thus more genetic variation.

- Students will engage in several Scientific Practices:
  - developing and using models
  - analyzing and interpreting data
  - constructing explanations
  - engaging in argument from evidence.

- This activity provides the opportunity to discuss two Crosscutting Concepts:
  - Systems and System Models: Models can be used “to predict the behavior of a system, [but] these predictions have limited precision and reliability due to the assumptions and approximations inherent in the models”.
  - 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”.

- This activity helps to prepare students for the 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…"
  - HS-LS3-3, "Apply concepts of statistics and probability to explain the variation and distribution of expressed traits in a population."

The sickle cell anemia module will also help students meet Common Core English Language Arts Standards for Science and Technical Subjects, including "cite specific textual evidence to support analysis of science and technical texts" and "write arguments focused on discipline-specific content".

Specific Learning Goals

How Genotype Influences Phenotype

- A gene provides the instructions for making a protein. Different versions of a gene are called alleles; different alleles give the instructions for making different versions of a protein. The different versions of a protein can result in different phenotypic characteristics.

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3 http://www.corestandards.org/
Each cell has two copies of each gene. If both copies of the gene have the same allele, the individual is homozygous for that gene. If a person is heterozygous (has two different alleles for a gene), often one (dominant) allele affects the phenotype and the other (recessive) allele does not. In other cases, neither allele is completely dominant or completely recessive.

- Recessive alleles often code for non-functional proteins; the dominant allele codes for enough functional protein to ensure the normal phenotype.
- A single gene may influence more than one phenotypic characteristic.

**Meiosis and Fertilization → Inheritance**

- The behavior of chromosomes during meiosis and fertilization provides the basis for understanding the inheritance of genes.
- The combination of meiosis and fertilization results in each offspring having one copy of each gene from his or her mother and another copy of each gene from his or her father. Consequently, children tend to resemble their parents and their siblings.
- However, meiosis results in genetically diverse sperm and eggs which, together with random fertilization, result in genetic diversity of the zygotes and children produced by the same mother and father.

**Punnett Squares → Probabilistic Predictions of Inheritance**

- The processes of meiosis and fertilization can be summarized in Punnett squares to make predictions about the genotypes and phenotypes of offspring.
- These predictions are accurate for large samples, but random variation in the genetic makeup of the sperm and egg that unite to form each zygote often results in substantial discrepancies between the Punnett square predictions and the outcomes observed in small samples such as individual families.
- Each fertilization event is independent of other fertilization events, so the genetic makeup of each child is independent of the genetic makeup of any siblings.
- Punnett squares are a useful model for understanding how meiosis and fertilization result in the various possible genotypes and phenotypes of offspring. Pedigrees are a useful model for analyzing inheritance in individual families.

Specific Learning Goals for each module are presented in the later sections on Instructional Suggestions and Background Biology for Genetics and for the Genetics Supplement.

**Supplies**

For "Inheritance of Albinism" in the introductory module in "Genetics"
- Model chromosomes (This module is designed for use after "Meiosis and Fertilization – Understanding How Genes Are Inherited" (available at http://serendip.brynmawr.edu/sci_edu/waldron/#meiosis). Instructions for making the model chromosomes are provided on pages 3-4 in the Teacher Preparation Notes for that activity; you will need the modified model chromosomes described in the paragraph that begins on page 3 and ends on the top of page 4.)
- Chalk or tape to outline rectangles (See page 2 of the Genetics Student Handout.)

For "Coin Toss Genetics" module in “Genetics”:
- Pennies (or checkers) (1 per student)
- Paper cup (optional, 1 per student; having each student shake a coin in a paper cup may result in more random tossing and less chance of coins on the floor)
General Instructional Suggestions
In both Student Handouts, numbers in bold indicate questions for the students to answer and in the Genetics Student Handout
➢ indicates a step in the modeling or coin-tossing procedures for the students to do.

If you use the Word version of the Student Handout to make changes, please check the PDF version to make sure that all formatting and figures are displayed properly in the Word version on your computer.

To maximize student learning, we 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 Handouts, please send a message to iwaldron@sas.upenn.edu. The following paragraphs provide additional background information.

Instructional Suggestions and Background Biology for Genetics
A. The introductory module on pages 1-3 of the Genetics Student Handout introduces students to both basic aspects of genetics:
   – how genotype influences phenotype via the effects of genes in DNA on protein structure and function
   – how genes are transmitted from parents to offspring through the processes of meiosis and fertilization.

We recommend that, before you begin the activity, you have a class discussion of the introductory question on the top of page 1. This discussion will help to get students thinking about what they already know about genetics, and you will have a chance to become familiar with their current understanding of genetics, including any misconceptions they may have.

Page 1 of the Student Handout includes a definition of a gene as a segment of DNA that gives the instructions for making a protein. 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 (https://en.wikipedia.org/wiki/Gene; http://www.biologyreference.com/Fo-Gr/Gene.html). As you probably know, 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. 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.

In discussing question 2, you will probably want to emphasize how the table shows the effects of genotype on proteins which in turn influence phenotype. In albinism, the lack of the pigment melanin affects not only skin and hair color, but also the appearance and function of the eyes. (For additional information about albinism see http://www.nlm.nih.gov/medlineplus/ency/article/001479.htm and http://omim.org/entry/203100). Students may ask questions concerning 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.mynvfi.org/about_vitiligo.)

Questions 2 and 5 provide the opportunity to discuss the Cause and Effect Crosscutting Concept: 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”. The allele for albinism is recessive because it codes for a defective enzyme for producing melanin, while the normal allele codes for the functional enzyme and, even when there is only one copy of the normal allele, there is enough of the functional enzyme to produce enough melanin to prevent albinism. As discussed in question 5, recessive alleles often code for a non-functional protein, while dominant alleles often code for a functional protein.

The second page of the Student Handout is designed to foster student understanding of how meiosis and fertilization result in inheritance of genes (one copy of each gene from the mother and one copy of each gene from the father). Students are instructed to draw the rectangles from this chart on their lab table with chalk. You may prefer to provide them with tape instead of chalk.

As students model meiosis and fertilization for two heterozygous parents, they should notice that a heterozygous zygote can arise in two different ways (dominant allele from mother or from father). This observation should help students understand why the heterozygous genotype is twice as likely as either homozygous genotype.

In interpreting Punnett squares, it is important for students to realize that the genotype of a person who develops from a zygote is the same as the genetic makeup of the zygote (as discussed in question 9). The zygote undergoes many rounds of mitosis to produce the cells in the person's body, and mitosis produces daughter cells with the same genetic makeup as the original cell.

Questions 10-12 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 phenotype that is different from the phenotype either parent

Question 13 should stimulate students to realize that parents with the phenotype of 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). In contrast, two parents with the phenotype of 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 phenotype. These insights are crucial for pedigree analysis.

Questions 10-13 illustrate how the Punnett square model is useful for predicting various features of the inheritance of albinism. Question 14 illustrates one limitation of Punnett squares as models
of inheritance. Since Punnett squares do not include information about the population prevalence of different genotypes among the parents, they do not predict the population prevalence of different genotypes among children in the general population. This illustrates the Crosscutting Concept that models can be useful "to predict the behavior of a system, [but] these predictions have limited precision and reliability due to the assumptions and approximations inherent in models".

Many students tend to think of a model as a physical object and may not understand that a Punnett square is a model, so you may want to introduce the idea of a conceptual model. As noted in A Framework for K-12 Science Education, "Conceptual models allow scientists… to better visualize and understand a phenomenon under investigation… Although they do not correspond exactly to the more complicated entity being modeled, they do bring certain features into focus while minimizing or obscuring others. Because all models contain approximations and assumptions that limit the range of validity of their application and the precision of their predictive power, it is important to recognize their limitations." 4

After your students have completed the introductory module, we recommend that you use the first episode in "Soap Opera Genetics" (http://serendip.brynmawr.edu/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 episode 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).

B. The Coin Toss Genetics module helps students understand the importance of random variation, particularly in small samples. Discussion of random variation will help your students to reconcile their experience of variation in outcomes in real world families with the predictions of Punnett squares in the classroom. This module also introduces students to the independence of each fertilization event, so the genotype of each child is independent of the genotypes of any older siblings.

Students will observe that results for an individual family of 4 coin toss children often deviate substantially from the results predicted by the Punnett square. The table below illustrates the high probability that the genotypes of 4 children born to two heterozygous parents will differ from the predictions of the Punnett square.

<table>
<thead>
<tr>
<th>Observed Outcome for 4 Coin Tosses</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 aa</td>
<td>32%</td>
</tr>
<tr>
<td>1 aa</td>
<td>42%</td>
</tr>
<tr>
<td>2 or more aa</td>
<td>26%</td>
</tr>
<tr>
<td>1 AA + 2 Aa + 1 aa</td>
<td>19%</td>
</tr>
</tbody>
</table>

(Calculated using the multinomial calculator available at http://stattrek.com/Tables/Multinomial.aspx)

When your students carry out the coin tosses to create 4 families of 4 children each, there is a 78% probability that they will get at least one family with no albino (aa) children and a 70% probability that they will get at least one family with 2 or more albino children.

The results for larger samples are generally closer to the predicted distribution and less likely to show extreme deviations. For example, for two heterozygous parents a finding of no albino

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children is expected in 32% of families of 4 children, but in only 1% of samples of 16 children, and less than one in a million samples of 100 children (which should be roughly the size of your sample for the total class data for the "coin toss children").

The analyses in this module illustrate another limitation of the Punnett square model of inheritance. The Punnett square model does not take account of random variation, which has a strong effect on the genotypes of the children in a real family. Therefore, the Punnett square does not reliably predict the composition of individual families. This illustrates the Systems and System Models Crosscutting Concept: Models can be used “to predict the behavior of a system, [but] these predictions have limited precision and reliability due to the assumptions and approximations inherent in the models.”

C. The Genetics of Sickle Cell Anemia module:

- introduces a basic understanding of the biology of sickle cell anemia (additional information given below)
- reinforces some basic concepts of inheritance (question 2) and
- uses student analysis of the boxed reading on page 6 to extend their understanding of genetics by introducing two complexities that are common in genetics:
  - multiple phenotypic effects of a single gene (question 3)
  - many alleles are neither completely dominant nor completely recessive, as illustrated by the fact that the phenotype of an individual who is heterozygous for the sickle cell and normal hemoglobin alleles is not the same as the phenotype of an individual who is homozygous for either of these alleles (question 4).

Sickle cell hemoglobin is less soluble in the watery cytosol of the red blood cells than normal hemoglobin, particularly when oxygen concentrations are low. Thus, sickle cell hemoglobin tends to clump into long stacks or rods of hemoglobin molecules; this results in the sickled and other abnormal shapes of some of the red blood cells in a person who is homozygous for the sickle cell allele. The abnormally shaped red blood cells tend to clog the capillaries, thus blocking the circulation in various parts of the body. Also, these red blood cells do not survive as long as normal red blood cells, contributing to a tendency to anemia. Together, these effects result in the multiple symptoms of sickle cell anemia, including pain, physical weakness, impaired mental functioning, and damage to organs such as the heart and kidneys.

Even in a person who has severe sickle cell anemia, most red blood cells are not sickled. The degree of clumping of sickle cell hemoglobin, sickling of red blood cells, and consequent symptoms are influenced by multiple factors, including oxygen levels in the blood, dehydration, and other genes. A sickling crisis with pain and organ damage can be triggered by an infection that induces vomiting and diarrhea, resulting in dehydration; dehydration increases the hemoglobin concentration in red blood cells and thus increases the tendency of sickle cell hemoglobin to clump into long rods and produce sickled red blood cells which block the circulation in the small blood vessels. These observations illustrate how environment and genotype interact to influence phenotype. A useful summary of the medical aspects of sickle cell anemia, including symptoms, diagnosis and treatment is available at http://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/home/ovc-20303267. For additional information, see http://omim.org/entry/603903.

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 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. (The heterozygous individual is said to have sickle cell trait.)

Malaria infections are common in many tropical countries where there are lots of the type of mosquitoes that transmit the malaria parasite. In areas where malaria is widespread, people who are heterozygous for the sickle cell allele are less likely to become seriously ill and die. Because the sickle cell allele contributes to increased survival of heterozygous individuals, this allele became relatively common in regions like West Africa where malaria is common. Since African-Americans are descended from populations in which the sickle cell allele was relatively common, African-Americans have relatively high rates of the sickle cell allele (approximately 8% are heterozygous for this allele and 0.16% are homozygous).

**Instructional Suggestions and Background Biology for Genetics Supplement**

A. The first four pages of the Genetics Supplement provide an alternative version of the introductory module in the Genetics Student Handout. This alternative version will be appropriate if your students have not completed "Meiosis and Fertilization – Understanding How Genes Are Inherited" (available at [http://serendip.brynmawr.edu/sci_edu/waldron/#meiosis](http://serendip.brynmawr.edu/sci_edu/waldron/#meiosis)) and/or you do not want to use model chromosomes.

The background information and suggestions for discussion on pages 4-6 of these Teacher Preparation Notes are relevant for this alternative module, although the specific questions and page numbers differ in the two modules. For example, as students complete question 8 in this alternative module, they should realize that a heterozygous zygote can arise in two different ways (dominant allele from mother or from father). This should help your students understand why the heterozygous genotype is twice as likely as either homozygous genotype.

B. The Genetics of Sex Determination module can be used after the Coin Toss Genetics module in the Genetics Student Handout. Both modules foster student understanding of the probabilistic nature of inheritance and the limitations of Punnett square predictions.

The Y chromosome contains the **SRY gene**, which stands for Sex-determining Region of the Y chromosome. If a zygote has a Y chromosome with the SRY gene, the embryo will develop testes and male anatomy. If a zygote does not have a Y chromosome with the SRY gene, the embryo will develop ovaries and female anatomy. The SRY gene codes for a protein that binds to regulatory DNA and activates multiple genes that stimulate the gonads to develop into testes instead of ovaries. The testes secrete testosterone and other chemical messengers that stimulate the genitalia to develop into penis, scrotum, vas deferens, etc. In the absence of the SRY gene, the gonads develop into ovaries, and in the absence of testosterone the genitalia develop into clitoris, labia, uterus, etc.; this happens both in XX females and in rare XY individuals whose Y chromosome lacks the SRY gene.

Additional genes on multiple chromosomes contribute to the normal development of male and female reproductive organs. Defects in these genes can lead to **anomalies** in the development of male or female reproductive organs, e.g. due to defective hormone receptors or defective enzymes to produce hormones. Examples are:

- Androgen Insensitivity Syndrome results from lack of functional molecular receptors for testosterone and dihydrotestosterone. Due to the lack of these molecular receptors, testosterone and dihydrotestosterone do not affect the cells in the fetal genitalia of an XY fetus with Androgen Insensitivity Syndrome, so female external genitalia develop. These individuals are raised and live as females, but they have testes instead of ovaries. They
are infertile. This syndrome is typically detected when a teenage female fails to menstruate.

- Congenital Adrenal Hyperplasia (also called Adrenogenital Syndrome) develops when an enzyme needed to produce cortisol is defective or missing, resulting in abnormal hormonal feedback which leads to excessive production of androgens by the adrenal cortex. The elevated androgen levels in a XX fetus result in varying degrees of masculinization of the external genitalia. As a result, the baby's sex may appear ambiguous or even be mistaken for male.

Other anomalies in sexual development are due to too many or too few copies of the sex chromosomes in each cell, e.g. Kleinfelter and Turner Syndromes (see [http://ghr.nlm.nih.gov/condition/turner-syndrome](http://ghr.nlm.nih.gov/condition/turner-syndrome) and Teacher Notes for "How Mistakes in Cell Division Can Result in Down Syndrome and Miscarriages", available at [http://serendip.brynmawr.edu/exchange/bioactivities/mmfmistakes](http://serendip.brynmawr.edu/exchange/bioactivities/mmfmistakes)). It should be noted that a zygote must have at least one X chromosome to survive and develop into an embryo.

**Question 5.** is intended to consolidate student understanding of what Punnett squares can accurately predict and what they cannot. The data in question 6a will demonstrate that a Punnett square cannot accurately predict the percent male in specific families. Random variation usually averages out in large samples, so the predictions of the Punnett square model are more accurate for larger samples. This table shows the expected ranges of results for different sample sizes. Even with relatively large samples, rather substantial variation from one sample to the next will be relatively common.

<table>
<thead>
<tr>
<th>Number of Children in the Sample</th>
<th>If data were collected for a large number of samples, 68% of results expected to be in this range:</th>
<th>95% of results expected to be in this range:</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>39%-61% males</td>
<td>28%-72% males</td>
</tr>
<tr>
<td>40</td>
<td>42%-58% males</td>
<td>34%-66% males</td>
</tr>
<tr>
<td>60</td>
<td>43.5%-56.5% males</td>
<td>37%-63% males</td>
</tr>
<tr>
<td>80</td>
<td>44.4%-55.6% males</td>
<td>39%-61% males</td>
</tr>
</tbody>
</table>

With regard to the prediction of the outcome for very large samples, slightly more males than females are born (51.2% males in the US in 2000, slightly lower for African-Americans and slightly higher for Asian-Americans). Thus, there is a slight deviation from the Punnett square model, possibly due to higher mortality for female fetuses.

In general, we cannot extrapolate from Punnett squares to population prevalence unless we know the percent of each genotype in the population (as discussed for the albinism example). We can extrapolate from the Punnett square for inheritance of sex chromosomes to the population prevalence of male and female sex, because we do know the percent of each genotype in the population – every mother has two X chromosomes and every father has an X and a Y chromosome.

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5 Ranges were calculated based on the normal approximation to the binomial distribution. It should be mentioned that the ranges in this table have been calculated based on several simplifications. Specifically, we have not taken into account the fact that slightly more males than females are born. Also, there appears to be some biological tendency for some couples to produce more female or more male offspring, and this would increase expected variation in results.
The data in question 6a are actual results for a real extended family with a total of 33 children in three generations. These data illustrate that a Punnett square does not predict the outcome for any individual family. Based on a 50-50 chance for each child to be either a boy or a girl and the independence of outcomes for each child in the family, one quarter of two-child families would be expected to have two girls, one quarter of two-child families would be expected to have two boys, and only half of two-child families would be expected to have one child of each sex (with half of these families having a girl first and half having a boy first).

These analyses illustrate both:

- the usefulness of the Punnett square model of inheritance (predicting the percent male in large samples of children and the probability that a child will be male) and
- the limitations of the Punnett square model (not accurately predicting the makeup of individual families or the sex of a specific child, both of which vary due to random variation in which sperm fertilizes which egg).

This provides the opportunity to reinforce the Crosscutting Concept that models can be used “to predict the behavior of the system, [but] these predictions have limited precision and reliability due to the assumptions and approximations inherent in models”.

C. The Pedigree Analysis module:

- introduces analysis of pedigrees
- reinforces understanding of basic principles of inheritance
- helps students to understand that some dominant alleles are rare
- introduces the concept that some genetic conditions are not inherited, but rather are due to new mutations
- engages students in thinking about the advantages and limitations of Punnett squares and pedigrees as models of inheritance.

This module can be used as an extension activity after completing the Genetics Student Handout or this module could be carried out immediately after the Inheritance of Albinism.

The analysis of the first pedigree assumes that students know that the allele for albinism is recessive. The conclusion that the allele for albinism is recessive is also indicated by the pedigree, since two unaffected parents have an affected offspring. (This could be the result of a new mutation for a dominant allele, but this is unlikely since an affected offspring of unaffected parents occurs twice within three generations of this family.) This pedigree also indicates that the allele for albinism is autosomal recessive and not X-linked recessive, since the affected son (6) inherited an allele for albinism from his father (3), but he did not inherit an X chromosome from his father.

Other conditions with this mode of inheritance are mentioned, including phenylketonuria (PKU). PKU is due to recessive alleles that code for defective versions of the enzyme that converts phenylalanine to tyrosine (an important step in disposing of excess phenylalanine). As noted in the Genetics Supplement, PKU "results in mental retardation unless phenylketonuria is detected at birth and treated with a special diet". This provides the opportunity to discuss the important point that phenotype is determined by the effects of both genes and environment. To enhance student understanding of this important point, you can:

- discuss how mental retardation can be prevented in an individual with phenylketonuria by minimizing phenylalanine in the diet by avoiding the artificial sweetener aspartame and high-protein foods (e.g. meat, fish, milk, cheese, eggs, nuts, beans, tofu, and even foods with flour) and substituting special low-phenylalanine foods; minimum intake of
phenylalanine is especially important for babies and young children when the brain is developing rapidly; for additional information, see http://www.genome.gov/25020037 and http://www.mayoclinic.com/health/phenylketonuria/DS00514/DSECTION=treatments-and-drugs

- mention the influence of environmental factors on symptoms of sickle cell anemia (see page 6 in these Teacher Preparation Notes)
- mention the effect of sun exposure/tanning on skin color (see "II. Were the babies switched?" in "Soap Opera Genetics", http://serendip.brynmaur.edu/exchange/bioactivities/SoapOperaGenetics)

The second pedigree in this module indicates that the allele for achondroplasia is dominant, since two affected parents have normal children. (Furthermore, this allele must be autosomal dominant and not X-linked dominant, since an affected father (1) has an unaffected daughter.) The allele for achondroplasia is considered dominant because an individual who is heterozygous for this allele and the normal allele has the dwarf phenotype. However, there are important differences between a heterozygous individual (~7% risk of infant death) and an individual who is homozygous for the achondroplasia allele (~100% early mortality, due to difficulty breathing as a result of a small rib cage plus brain problems resulting from abnormalities of the skull). The specific mutation responsible for achondroplasia results in a protein that is overactive in inhibiting bone growth. Additional information about achondroplasia is available at http://ghr.nlm.nih.gov/condition/achondroplasia.

Question 3 stimulates students to notice that achondroplasia is an example of a condition caused by an allele which is dominant, but rare in the population. 99.99% of the population is homozygous for the normal recessive allele for this gene. Achondroplasia is rare because there is substantial selection against inheritance of the achondroplasia allele and the mutation rate is low (estimated ~1/10,000).

Question 4 raises the important point that achondroplasia is an example of a condition which is genetic, but usually not inherited. In more than 80% of cases, neither parent has the allele for achondroplasia and the person has achondroplasia due to a new mutation which occurred during production of one of the gametes (see "This Genetic Condition Was Not Inherited", available at http://serendip.brynmaur.edu/exchange/bioactivities/GeneticsInherited).

Question 5 stimulates students to think about and evaluate Punnett squares and pedigrees as models of inheritance. One advantage of Punnett squares as a model of inheritance is that a Punnett square summarizes how the processes of meiosis and fertilization contribute to inheritance of different alleles of a gene. For parents with specified genotypes, Punnett squares can identify the possible combinations of alleles in offspring and the resulting possible phenotypes, and Punnett squares can make quantitative predictions concerning the frequency of these genotypes and phenotypes in large samples of the children of this type of couple. Limitations of Punnett squares as models of inheritance include the lack of information about likely variation in small samples such as individual families and the lack of information about population prevalence of parental genotypes (so no predictions can be made about population prevalence of offspring genotypes and phenotypes). Also, the predictions of a Punnett square model may be inaccurate if important complexities are omitted (e.g. the effects of multiple genes
or the possibility of mutation). The failure to take account of all the complexities is, of course, a general limitation of models, which are simplified representations of complex processes.

Pedigrees can be useful for figuring out the mode of inheritance for a phenotypic condition observed in multiple members of a family, and pedigrees can provide a useful basis for genetic counseling. Pedigrees can be quite complex to interpret, e.g. if a mutation has occurred, if environment influences the phenotype, and/or if more than one gene influences the phenotype. Also, pedigrees do not directly represent the underlying biological processes of meiosis and fertilization.

**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://serendip.brynmawr.edu/exchange/bioactivities/GeneticsConcepts).

This overview summarizes important genetic concepts and proposes an integrated sequence of learning activities to develop student understanding of these key concepts. Part I provides an outline of key concepts needed to understand how genes influence phenotypic characteristics and how genes are transmitted from parents to offspring. Part II recommends an integrated sequence of learning activities that are aligned with the Next Generation Science Standards and provides links for additional resources for helping students to understand genetics.

A useful activity to reinforce and expand concepts learned in this genetics activity is Soap Opera Genetics – Genetics to Resolve Family Arguments (http://serendip.brynmawr.edu/exchange/bioactivities/SoapOperaGenetics). This analysis and discussion activity contains three "soap opera" episodes that contribute to student understanding of the principles of inheritance and the relevance of genetics to everyday life. In the first episode, students explain the biology summarized in a Punnett square to answer the probing questions of a skeptical father who wants to know how his baby could be albino when neither he nor his wife is albino. This can be very useful to reinforce and assess student understanding of concepts introduced in the first two modules in the Student Handout of Genetics or Genetics Supplement. Concepts covered in the second episode include co-dominance, incomplete dominance, polygenic inheritance, and the combined effects of genes and the environment on phenotypic characteristics. In the third episode, students analyze sex-linked inheritance. Each episode can be used separately or with other episodes, depending on your teaching goals. This activity is aligned with the Next Generation Science Standards.  

We recommend that you use the first episode of the "Soap Opera Genetics" activity to engage your students in active recall of key concepts presented in this "Genetics" activity. You can enhance student learning and retention of important concepts and vocabulary by having your students complete the first episode of "Soap Opera Genetics" without referring to their notes, 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).

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6 For example, two blue-eyed parents generally do not have brown-eyed children because the most common allele responsible for blue eyes is recessive. However, exceptions can occur due to mutation (reversing the point mutation generally responsible for blue eyes) or complex interactions between the multiple genes that influence eye color. For an introductory explanation and video, see http://genetics.thetech.org/ask/ask29; for a more complete discussion, see http://sciencecases.lib.buffalo.edu/cs/collection/detail.asp?case_id=562&id=562.

7 Next Generation Science Standards (http://www.nextgenscience.org/next-generation-science-standards)