Teacher Preparation Notes for Genetics

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Teaching Points:
Meiosis and Fertilization → Inheritance
- The <u>behavior of chromosomes during meiosis and fertilization provides the basis for understanding the inheritance of genes</u>.
- 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 <u>resemble</u> their parents and their siblings.
- However, meiosis results in genetically diverse sperm and eggs which, together with random fertilization, results in <u>genetic diversity</u> 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 <u>Punnett squares</u> to make predictions about the genotypes and phenotypes of offspring.
- These predictions are accurate for large samples, but <u>random variation</u> 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 <u>independent</u> of the genetic makeup of any siblings.

Additional Teaching Points
- Meaning of genetics <u>vocabulary</u>, including allele, homozygous, heterozygous, dominant, recessive, genotype, phenotype
- Genetics of sex determination
- Adaptive advantage for sickle-cell heterozygous individuals where malaria is prevalent
- How to carry out basic <u>pedigree</u> analysis and interpret pedigrees

Supplies:
For "Inheritance of Albinism" which introduces Punnett Squares (pp. 1-3 of the Student Handout) (1) Model chromosomes (optional);[2] you can use any of the following:
- sockosomes from the Mitosis, Meiosis, and Fertilization hands-on activity available at http://serendip.brynmawr.edu/sci_edu/waldron/ <u>or</u>
- posterboard sockosomes prepared using the templates in the Teacher Preparation Notes for the Mitosis, Meiosis and Fertilization activity <u>or</u>
- pipe cleaner model chromosomes, each one made by twisting together two pipe cleaners and using masking tape to label the **A** or **a** alleles on each chromatid of the model chromosome.

Ideally, you will have one blue and one red model chromosome with the **A** allele and one blue and one red model chromosome wth the **a** allele for each student group. Blue and red pipe cleaners can be ordered at low cost from http://www.discountschoolsupply.com/.
 (2) Blue and red pens, pencils or markers (optional; one of each color per student group or per student; see Suggestions for Implementation section)

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[1] These teacher preparation notes and the related student handout are available at http://serendip.brynmawr.edu/sci_edu/waldron/.

[2] If you prefer not to use model chromosomes, you can use an alternative version of pages 1-3 of the Student Handout; the substitute version is shown on pages 6-9 of these Teacher preparation Notes.

(1) Pennies (1 per student)
(2) Calculator for converting fractions to percents (optional)

Suggestions for Implementation
Ideally, this hands-on activity should immediately follow the Mitosis, Meiosis and Fertilization hands-on activity available at http://serendip.brynmawr.edu/sci_edu/waldron/. You can use the instructions on pages 7 and 9-10 of the Student Handout for the Mitosis, Meiosis and Fertilization activity to guide students in using the model chromosomes for pages 1-2 of the Student Handout for this Genetics activity. If you are doing both of these activities, you may want to omit pages 9-10 of the Student Handout for the Mitosis, Meiosis and fertilization activity.

If you do not have enough class time to complete all the Genetics activities, you can use page 1 through the top of page 5 as an introduction to the first seven teaching points on page 1. If you do not want to use model chromosomes, you can use the alternate version of pages 1-4 of the Student Handout provided at the end of these Teacher Preparation Notes.

Each of the subsequent sections can be used independently or added to the introductory sections, according to your teaching needs. Additional suggestions for teaching approaches are provided in "Genetics -- Major Concepts and Learning Activities", available at http://serendip.brynmawr.edu/exchange/waldron/GeneticConcepts.

If you have blue and red model chromosomes, have the student who is modeling the father use the blue model chromosomes and the student who is modeling meiosis in the mother use the red model chromosomes. If you have blue and red pens, pencils or markers available, have students use blue for the father's alleles and red for the mother's alleles in questions 1 and 2 on page 2 of the Student Handout. This will help students see how each zygote receives one copy of the gene from the father and one from the mother.

For the coin toss activity, results for an individual "family of numeral for children" often deviates substantially from the results predicted by the Punnett square (see next section on statistical information). Results for larger samples generally are closer to predictions, so we suggest that you prepare a table that compiles the outcomes of the coin tosses for the entire class and calculate the total number of "children" and the percent of each genotype for the class data. Discussion of random variation will help your students to reconcile the precise predictions of Punnett squares in their classroom learning with their experience of variation in outcomes in real world families. For this activity, some teachers prefer having each student shake a checker in a paper cup (may result in more random tossing and less chance of coins on the floor).

For the genetics of sex determination part of this activity, we post a chart on the board with columns for number of males and total number of children, so students can enter the data for their family or group in order to compile the data needed to answer question 5 on page 6. If your class is sex-biased, you should modify the instructions to prevent biased results due to whatever factors have resulted in a preponderance of males or females in your class. Specifically, the students should exclude themselves when answering questions 5-6 on page 6 and just count all of their siblings (and step-siblings), each of whom represents an independent fertilization event and thus should be unaffected by whatever bias has affected enrollment in your class.

Statistical Information for Interpreting Results

For the Coin Toss Genetics activity, one of the teaching points is that the results for small samples often deviate substantially from the predictions of the Punnett Square but the results for larger samples usually are fairly close to the predicted distribution. The table below gives some information about the expected variation in outcomes for families of 4 children.

Observed Outcome for 4 Coin Tosses	Probability
0 **aa**	32%
1 **aa**	42%
2 or more **aa**	26%
1 **AA** + 2 **Aa** + 1 **aa**	19%

(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 from larger samples are more likely to be close to the predicted distribution and less likely to show extreme deviations. For example, for two heterozygous parents a finding of no albino 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.

For the Genetics of Sex Determination activity, the following table shows the expected ranges of results for different sample sizes. Even with relatively large samples, rather substantial variation from one class to the next will be relatively common.

Number of Children For All the Mothers in a Class	If data were collected for a large number of classes,	
	68% of results expected to be in this range:	95% of results expected to be in this range:
20	39%-61% males	28%-72% males
40	42%-58% males	34%-66% males
60	43.5%-56.5% males	37%-63% males
80	44.4%-55.6% males	39%-61% males

(Calculated based on normal approximation to binomial distribution)

It should be mentioned that these ranges have been calculated based on several simplifications. Specifically, we have not taken into account the fact that slightly more males than females are born (51% males in US, slightly lower for African-Americans and slightly higher for Asian-Americans). Also, there appears to be some biological tendency for some couples to produce more female or more male offspring; this would increase expected variation in results. As discussed in Suggestions for Implementation, if you have a preponderance of males or females in your class, you should use only the siblings and omit the students in your class in order to avoid biased results.

Background Biology
The allele for <u>albinism</u> is recessive because it codes for a defective enzyme for producing melanin, while the normal allele codes for the functioning enzyme; 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. Recessive alleles often code for a non-functional protein, while dominant alleles often code for a functional protein.

In the most common form of albinism, the lack of the pigment melanin affects not only skin and hair color, but also the appearance and function of the eyes. Further information about the various forms of albinism, as well as additional information concerning many of the conditions discussed below and a great deal of information on other aspects of human genetics, is available from OMIM, Online Mendelian Inheritance in Man (www.ncbi.nlm.nih.gov/omim/).

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 from the National Vitiligo Foundation is available at www.nvfi.org.)

The Y chromosome contains the SRY gene which codes for a protein that binds to regulatory DNA and activates multiple genes that stimulate the gonad 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. Multiple additional genes contribute to the normal development of male and female reproductive organs.

Students often ask questions concerning the various sex determination anomalies. Some of these are due to too many or too few copies of the sex chromosomes in each cell, e.g. Kleinfelter and Turner Syndromes which are described in many biology textbooks. In addition, several syndromes result from defective hormone receptors or defective enzymes to produce hormones, as discussed in the next two paragraphs.

Androgen Insensitivity Syndrome results from lack of functional molecular receptors for testosterone and dihydrotestosterone, so these hormones have no effect on the body. Consequently, a 46XY fetus develops female external genitalia. These individuals are raised and live as females, but they are infertile due to the lack of ovaries and a uterus. 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 46XX 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.

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 form long stacks or rods of hemoglobin molecules, which results in the sickled shape of some red blood cells in a person who is homozygous for the sickle cell allele and consequently has sickle cell anemia. The sickled red blood cells tend to clog the 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 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 <u>malaria</u> in heterozygous individuals because the malaria parasite doesn't grow as well in red blood cells containing sickle cell hemoglobin.

The pedigree on page 8 of the Student Handout indicates that the allele for <u>albinism</u> is recessive, since two unaffected parents have an affected offspring. (This pedigree also indicates that the allele for albinism is autosomal recessive and not X-linked recessive, since the affected daughter (5) presumably inherited one allele for albinism from her unaffected father (2).)

The pedigree on page 9 of the student handout indicates that the allele for this particular condition is dominant, since two affected parents have normal children. (This allele must be autosomal dominant and not X-linked dominant, since an affected father (A) has an unaffected daughter.) The allele for <u>achondroplasia</u> 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 any heterozygous individual (~7% risk of infant death) and someone who is homozygous for the achondroplasia allele (~100% early mortality, due to difficulty breathing as a result of a small rib cage and 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.

Achondroplasia provides the opportunity to discuss two additional interesting points. 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. Also, achondroplasia is a good example of a condition which is genetic, but generally not hereditary; in more than 80% of cases neither parent has the allele for achondroplasia and the child has achondroplasia due to a new mutation which occurred during production of the sperm. These ideas are developed in the activity "This Genetic Condition Was Not Inherited", available at http://serendip.brynmawr.edu/exchange/bioactivities/GeneticsInherited.

Additional Activities for teaching/learning genetics include:
-- Soap Opera Genetics (You can use one or more of the four episodes to reinforce understanding of genetic principles, Punnett squares, and the relevance of genetics to everyday life.)
 http://serendip.brynmawr.edu/exchange/waldron/SoapOperaGenetics
-- Genetics -- Major Concepts and Learning Activities
 http://serendip.brynmawr.edu/exchange/bioactivities/GeneticsConcepts
-- Genetics Vocabulary Taboo Game
 http://serendip.brynmawr.edu/exchange/bioactivities/GeneticsVocabGame
-- Genetics Jeopardy Review Game
 http://serendip.brynmawr.edu/exchange/bioactivities/GeneticsJeopardy
-- Two versions of Dragon Genetics
 http://serendip.brynmawr.edu/sci/waldron/
-- Genetics Practice Problems
 http://biology.clc.uc.edu/courses/bio105/geneprob.htm
-- Learning Mendelian Genetics through a Simple Coin Toss Game
 http://www.wsu.edu/~omoto/papers/cointoss.html
-- Learning Genetics with Paper Pets
 Science Scope, March, 2006, pp. 18-23 or
 http://www.nsta.org/main/news/stories/science_scope.php?news_story_ID=51647

The next four pages provide an alternative version of pages 1-4 of the Student Handout that does not use model chromosomes.

Genetics

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We all know that children tend to resemble their parents in appearance. Parents and children generally have similar eye color, skin color, hair texture, height and other characteristics because children inherit **genes** that control these characteristics from their parents.

Where are genes found in our bodies?
Researchers have shown that genes are parts of DNA molecules, and DNA molecules are contained in chromosomes in the nucleus of each cell in our body.

How do genes influence our characteristics?
Each gene is a segment of the DNA molecule that gives the instructions for making a protein. For example, one gene gives the instructions for making a protein enzyme which helps to make melanin, the pigment which contributes to the color of skin, eyes and hair. Different versions of the gene (called **alleles**) code for different versions of the protein. One allele of this gene codes for an enzyme that produces melanin, resulting in normally pigmented skin and hair; it is symbolized by **A**. Another allele of this gene codes for an enzyme that cannot produce melanin, resulting in very pale skin and hair, which is called albinism; this allele is symbolized by **a**.

(Russell 1994)

How does a baby inherit genes from his or her mother and father?
When we talk about genes being inherited from one generation to the next, we are really talking about how the gene-carrying chromosomes behave during meiosis and fertilization.   As you will see in the next section, if you understand how the mother's and father's chromosomes behave during meiosis and fertilization, you can understand why the zygote that becomes a baby has two copies of each gene, one copy from the mother and one copy from the father.

Inheritance of Albinism
To learn more about how genetic traits are inherited, you will analyze a specific question: If each parent has one **A** allele and one **a** allele (i.e. both parents are **Aa**), what different combinations of **A** and/or **a** alleles would you expect to observe in the children of these parents?

1. To answer this question, first draw a diagram showing how each parent's alleles are separated into the gametes produced by meiosis. Then diagram fertilization to show how the alleles from the egg and sperm are combined in the zygote which becomes the child.

Meiosis → Gametes	Fertilization → Zygotes

Biologists use a **Punnett Square** to analyze inheritance and answer questions such as "What genetic makeup would be expected for the children of two parents who are **Aa**?" The figure below shows more details than a typical Punnett Square. It shows that, as a result of meiosis in a mother who is **Aa**, half of her eggs will have a chromosome which carries the **A** allele, and the other half will have a chromosome with the **a** allele. Similarly, half of the father's sperm will have an **A** allele, and half will have the **a** allele.

The four smaller squares within the larger Punnett Square show the possible genetic combinations in the zygotes resulting from fertilization of the two different types of eggs by the two different types of sperm. Each zygote undergoes repeated mitosis to become a child, so the child will have the same genetic makeup as the zygote.
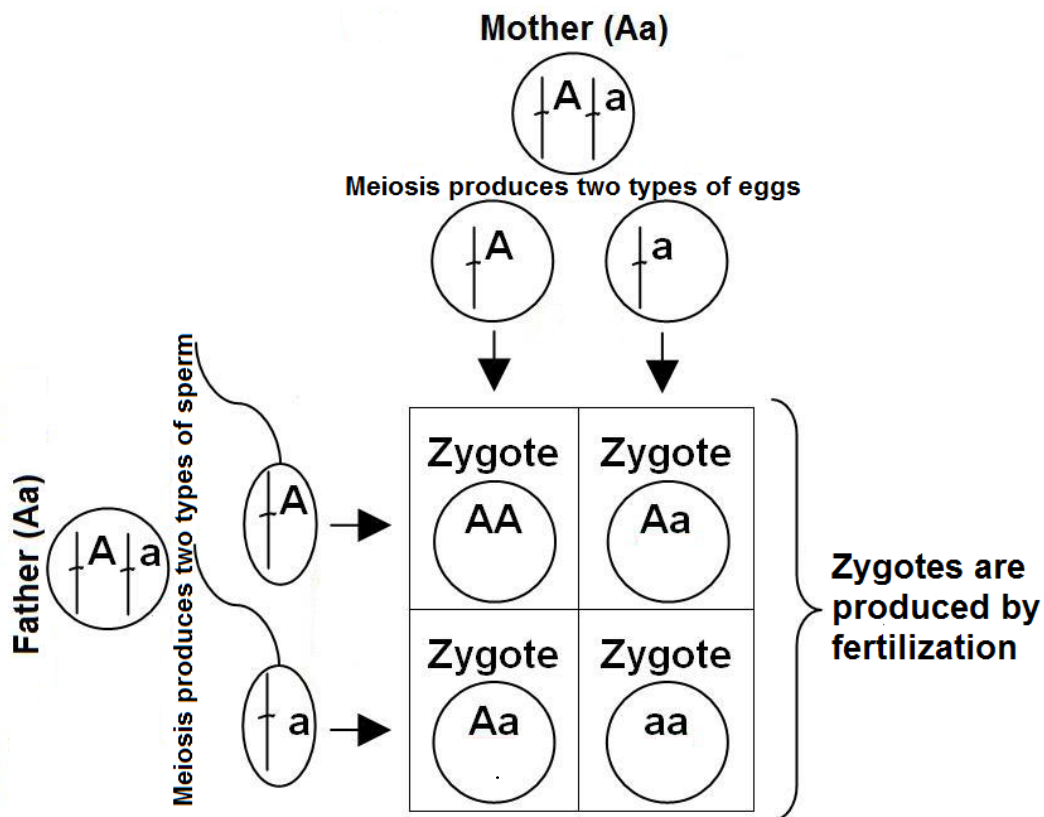
Typically, Punnett squares exclude much of the explanatory material we have included in the above Punnett square. The simplified version of this Punnett square shown below illustrates the usual format of a Punnett square.

	A	a
A	AA	Aa
a	Aa	aa

2. What fraction of this couple's children would you expect to be **AA**? _____

3. What fraction of this couple's children would you expect to be **Aa**? _____

4. What fraction of this couple's children would you expect to be **aa**? _____

The children who have **AA** alleles will have normal pigmentation, and the children who have **aa** alleles will have albinism. These children are homozygous for the **A** allele or the **a** allele. **Homozygous** means that both copies of the gene have the same allele.

2

The next question is: Will children who have **Aa** alleles have normal pigmentation or be albino? This type of combination of two different alleles is called **heterozygous**. Often, one allele in a heterozygous pair of alleles is **dominant** and the other allele is **recessive**; this means that the dominant allele determines the observable characteristic of the heterozygous individual. Typically, the dominant allele is symbolized by a capital letter, in this case **A** for the allele for normal pigmentation. Thus, heterozygous (**Aa**) individuals will have normal pigmentation.

5. What fraction of the couple's children would you expect to have normal pigmentation? _____

6. What fraction of the couple's children would you expect to have albinism? _____

The **genotype** refers to the genetic makeup of an individual. The **phenotype** refers to the observable physical and physiological characteristics of an individual.

7. Give an example of two individuals who have the same phenotype, but different genotypes for the albinism gene. Explain how two individuals with the same phenotype can have different genotypes.

Biologists frequently express the fractions of different genotypes or phenotypes as <u>ratios</u>. For example, for the mating between two heterozygous parents, the genotype fractions are 1/4 **AA**, 2/4 **Aa**, 1/4 **aa**, which can also be expressed as a 1:2:1 ratio.

8. For the corresponding phenotypes, the fraction with normal pigmentation is _____ and the

   fraction with albinism is _____, so the corresponding ratio is _____.

9. Suppose a father has **aa** alleles and a mother has **Aa** alleles. Complete the Punnett Square to describe this mating and determine what fraction of this couple's children would be expected to have albinism.

Coin Toss Genetics

The way genes behave can easily be simulated using two-sided coins, where tails represent the recessive allele that controls pigment production (**a**), and heads represent the dominant allele (**A**). Suppose a parent is heterozygous (**Aa**). Then, tossing a coin and checking for tails up vs. heads up represents the 50-50 chance that an egg or sperm produced by the parent will include an **a** allele or an **A** allele. To simulate a mating between two heterozygous (**Aa**) parents, two students will each toss a coin and the result of the pair of coin tosses will indicate the pair of alleles contributed by an egg and a sperm to the baby that results from that mating.

1. Find someone to "mate" with.

2. Each of you will toss your coin, and this pair of coin tosses will indicate the pair of alleles in the first child produced by a mating of two heterozygous (**Aa**) parents. Make three more pairs of coin tosses to determine the genetic makeup for the second, third and fourth children in this family. Record how many of these 4 children had each of the 3 possible combinations (**AA**, **Aa**, or **aa**) in the row labeled "first family of 4 children" in the table below.

3. Now make 4 more pairs of coin tosses to indicate the alleles in a second family of 4 children. Record these genotypes in the second row in the table below.

4. Do this two more times and record the results in the third and fourth rows of the table below.

	Genetic makeup of "children" produced by two heterozygous (**Aa**) parents		
	AA	**Aa**	**aa**
First family of 4 children			
Next family of 4 children			
Next family of 4 children			
Next family of 4 children			
Total			
Predictions based on Punnett Square (page 2)	1/4 = 25%	2/4 = 50%	1/4 = 25%
Class data -- Percents (Total # children = _____)			

5. Add up your results to determine the total number of children from your coin tosses who had **AA**, **Aa**, and **aa**. Add your numbers to the table of class data.

6. For each family of 4 children produced by your coin toss matings, compare the results with the predictions from the Punnett Square. Are the numbers of **AA**, **Aa**, and **aa** genotypes in your families of 4 children similar to the predicted?

Did you get different results in different families?

Did any family have no albino (**aa**) children?

Did any family have 2 or more albino children?