

Dragon Genetics

-- Independent Assortment and Genetic Linkage

This activity, by Dr. Ingrid Waldron and Jennifer Doherty, Department of Biology, University of Pennsylvania, © 2008, incorporates ideas from Dragon Genetics Lab, 2002, Bob Farber, Central High School, Philadelphia, PA and Dragon Genetics by Dr. Pamela Esprivalo Harrell, in the January 1997 issue of Science Scope, 20:4, 33-37.¹

In this activity you will study the patterns of inheritance of multiple genes in (imaginary) dragons. These dragons have two pairs of homologous chromosomes in each cell. You will see that, since genes are carried on chromosomes, the patterns of inheritance are determined by the behavior of chromosomes during meiosis and fertilization.

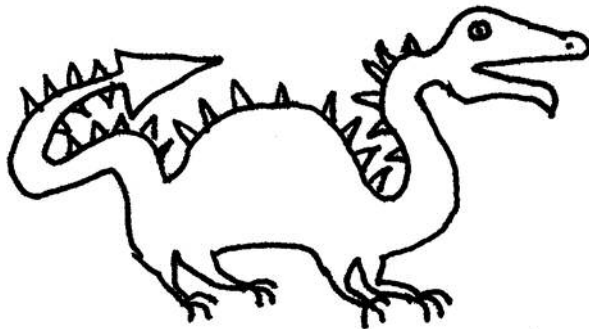
The Law of Independent Assortment -- Inheritance of Genes on Different Chromosomes

For this activity, we will only consider one gene on each chromosome. These genes are described in the following table.

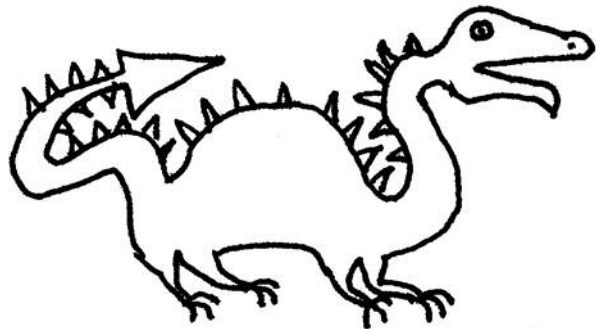
| | <u>Dominant Alleles</u> | <u>Recessive Alleles</u> |
|--------------|-------------------------|--------------------------|
| Chromosome 1 | W = has wings | w = no wings |
| Chromosome 2 | H = big horns | h = small horns |

The mother dragon is heterozygous for the wing gene (**Ww**) and the horn gene (**Hh**). The father is homozygous recessive for the wing gene (**ww**) and the horn gene (**hh**). What phenotypic traits will each parent have? (Phenotypic traits are the observable bodily characteristics.) Draw the appropriate characteristics for each parent.

Mother



Father



Review of Inheritance of Single Genes

Draw a Punnett Square to show the inheritance of the horn alleles for a mating between this mother and father.

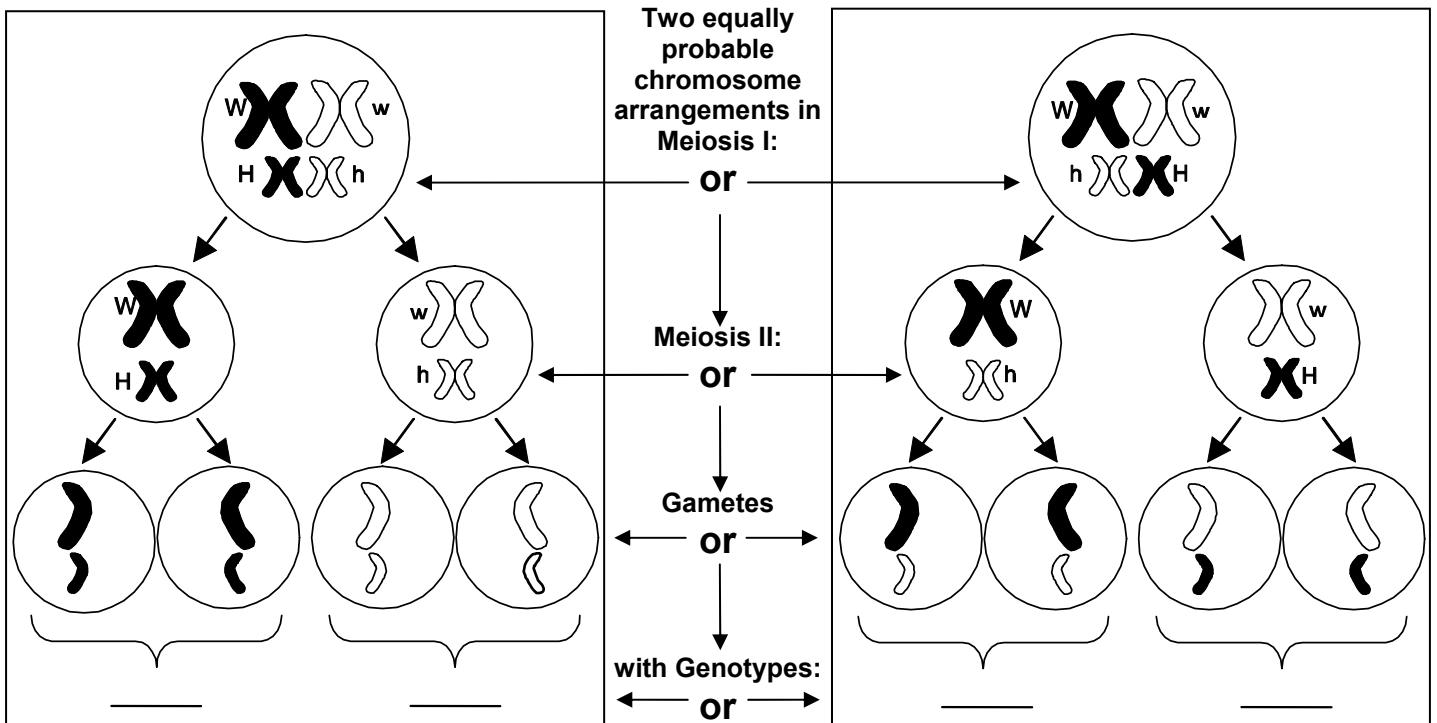
On average, what fraction of the baby dragons will have big horns?

¹ Teachers are encouraged to copy this student handout for classroom use. A Word file (which can be used to prepare a modified version if desired), Teacher Preparation Notes, comments, and the complete list of our hands-on activities are available at http://serendip.brynmawr.edu/sci_edu/waldron/.

Predictions of Inheritance of Two Genes on Different Chromosomes

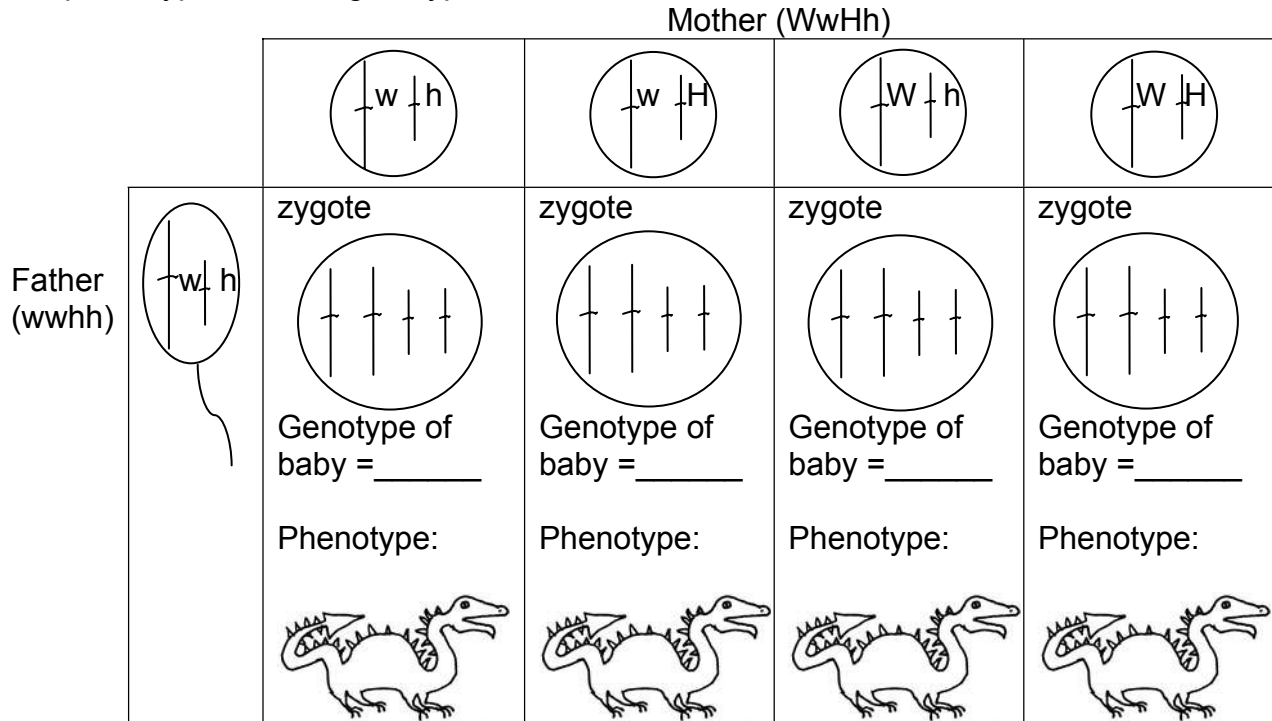
To predict the inheritance of the wing and horn genes, you first need to determine the genotypes of the eggs produced by the heterozygous (**WwHh**) mother dragon and the sperm produced by the homozygous (**wwhh**) father dragon. Considering both the wing and horn genes, what different genotypes of eggs could the heterozygous mother dragon produce? Use the figure below to answer this question.

Notice that, in a cell that is prepared for meiosis 1, the homologous chromosomes are always paired with each other, but the specific arrangement of the chromosomes can differ. Describe this difference and the effect that this has on the genotypes of the eggs produced.



What genotypes or genotype of sperm can the homozygous (**wwhh**) father dragon produce? Draw a diagram to show how meiosis would occur in the father, starting with a diploid cell ready to undergo meiosis 1 and ending with four haploid sperm.

The next step in predicting the inheritance of the wing and horn genes is to predict the outcome of fertilization between these eggs and sperm. In the following chart, label the gene on each chromosome in each type of zygote that could be produced by a mating between this mother and father. Then, fill in the genotypes of the baby dragons that result from each zygote and sketch in the characteristics of each baby dragon to show the phenotype for each genotype.



This type of mating involving two different genes is more typically shown as a Punnett square with four rows and four columns (see below). Notice that, because the father is homozygous for both genes, all his sperm have the same genotype, so all four rows are identical.

| | | Mother (WwHh) | | | |
|---------------|----|---------------|------|------|------|
| | | wh | wH | Wh | WH |
| Father (wwhh) | wh | wwhh | wwHh | Wwhh | WwHh |
| | wh | wwhh | wwHh | Wwhh | WwHh |
| | wh | wwhh | wwHh | Wwhh | WwHh |
| | wh | wwhh | wwHh | Wwhh | WwHh |

Considering only the baby dragons *with* wings, what fraction do you expect to have big horns? (To answer this question, it may be helpful to begin by shading in the two columns of the above Punnett square that include all the baby dragons with wings.)

Considering only the baby dragons *without* wings, what fraction do you expect to have big horns?

Do you expect that baby dragons with wings and without wings will be equally likely to have big horns?

Procedure to Test Inheritance of Two Genes on Different Chromosomes

To test whether baby dragons with wings and baby dragons without wings will be equally likely to have big horns, you will carry out a simulation of the simultaneous inheritance of the genes for wings and horns. Since the father is homozygous (**wwhh**), you know that all of the father's sperm will be **wh**. Therefore, to determine the genetic makeup of each baby dragon produced in your simulation, you will only need to determine the genetic makeup of the egg which is fertilized to become the zygote that develops into the baby dragon. During meiosis, each egg randomly receives one from each pair of homologous chromosomes. Your simulation will mimic this process.

For this simulation, each of the mother's pairs of homologous chromosomes will be represented by a popsicle stick with the genes of one chromosome shown on one side and the genes of the other homologous chromosome shown on the other side.² Since the mother dragon is heterozygous for both genes (**WwHh**), you will have one Popsicle stick representing a pair of homologous chromosomes which are heterozygous for the wing gene (**Ww**) and another Popsicle stick representing a pair of homologous chromosomes which are heterozygous for the horn gene (**Hh**).

1. Hold one Popsicle stick in each hand about 6 inches above the desk. Hold each Popsicle stick horizontally with one side facing toward you and the other facing away (with one edge of the Popsicle stick on the bottom and the other edge on the top). The two Popsicle sticks should be lined up end-to-end, simulating the way pairs of homologous chromosomes line up in the center of the cell during the first meiotic division. Simultaneously drop both Popsicle sticks on the desk. The side of each Popsicle stick that is up represents the chromosome that is contained in the egg. This indicates which alleles are passed on to the baby dragon. Put a **I** in the appropriate box in the chart below to record the genotype of the resulting baby dragon.

| | | Mother (WwHh) | | | |
|---------------------------|-----------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| | | wh | wH | Wh | WH |
| Father (wwhh) | wh | Genotype of baby = wwhh | Genotype of baby = wwHh | Genotype of baby = Wwhh | Genotype of baby = WwHh |
| | | Number of babies with this genotype = _____ | Number of babies with this genotype = _____ | Number of babies with this genotype = _____ | Number of babies with this genotype = _____ |

2. Repeat step 1 three times to make and record three more baby dragons.

² For the purposes of this activity, we will ignore the sister chromatids of each chromosome, since they are not relevant for understanding the genetics discussed in this activity. Also, we assume that both of the chromosomes under investigation are autosomes.

Summary and Interpretation of Data

1. Compile the data for all the baby dragons produced by all the students in the following chart.

| | | Mother (WwHh) | | | |
|---------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
| | | wh | wH | Wh | WH |
| Father (wwhh) | wh | Genotype of baby = _____ | Genotype of baby = _____ | Genotype of baby = _____ | Genotype of baby = _____ |
| | Number of babies with this genotype = ____ | Number of babies with this genotype = ____ | Number of babies with this genotype = ____ | Number of babies with this genotype = ____ | Number of babies with this genotype = ____ |
| | Phenotype: Wings ____ or no wings ____ | Phenotype: Wings ____ or no wings ____ | Phenotype: Wings ____ or no wings ____ | Phenotype: Wings ____ or no wings ____ | Phenotype: Wings ____ or no wings ____ |
| | Horns big ____ or small ____ | Horns big ____ or small ____ | Horns big ____ or small ____ | Horns big ____ or small ____ | Horns big ____ or small ____ |

2. Do any of the baby dragons with wings have small horns?

Does either parent have the combination of wings and small horns? (See page 1.)

How did this new combination of characteristics (wings and small horns) arise in some of the baby dragons? (Your answer will include events during meiosis and fertilization, so you may find it helpful to review the diagram of meiosis on page 2 and the chart of fertilization on page 3.)

3. On page 3 you used your understanding of meiosis and fertilization to predict whether baby dragons with wings and without wings would be equally likely to have big horns. What was your prediction?

Use the class results shown above to complete the following table.

| | Fraction that have big horns | |
|---------|------------------------------|----------------------------|
| | Baby dragons with wings | Baby dragons without wings |
| Results | | |

Do your results match your prediction?

This example illustrates the **Law of Independent Assortment**, which states that, if two genes are on different chromosomes, then the alleles for these genes separate independently of each other during the formation of eggs or sperm. Therefore, the traits determined by these two genes are inherited independently. For example, the wing gene and the horn gene are located on different chromosomes so they are inherited independently.

Genes on different chromosomes are inherited independently of each other because each pair of homologous chromosomes lines up independently of the others when the chromosomes line up in the center of the cell near the beginning of the first meiotic division. Consequently, when the pairs of homologous chromosomes separate during the first meiotic division, the chromosome that has an **H** allele is equally likely to end up in the same egg with the chromosome that has the **W** allele or with the chromosome that has the **w** allele. (This is illustrated in the figure on page 2.) In this activity, when you dropped the two chromosome Popsicle sticks, each stick independently landed with one particular side up, and this corresponds to the independent assortment of chromosomes and their alleles during meiosis.

4. To illustrate how the Law of Independent Assortment applies to humans, consider the inheritance of the recessive allele for sickle cell anemia (**s**, located on chromosome 11) and the **SRY** gene. The SRY gene is located on the Y chromosome and the SRY gene results in male development. This explains why a person who has both an X chromosome and a Y chromosome in each cell is a male, and a person who has two X chromosomes and no Y chromosome is a female.

Suppose that a father and mother are both heterozygous for the allele for sickle cell anemia (**Ss**). The following Punnett square shows the inheritance of the sickle cell and **SRY** genes, with **X** representing the X chromosome with no **SRY** gene and **Y** representing the Y chromosome which does have an **SRY** gene. Complete the Punnett square.

| | | Mother (SsXX) | | | |
|---------------|----|---------------|----|----|----|
| | | SX | sX | SX | sX |
| Father (SsXY) | SX | | | | |
| | sX | | | | |
| | SY | | | | |
| | sY | | | | |

Based on this Punnett square, what fraction of the sons will have sickle cell anemia?

What fraction of the daughters will have sickle cell anemia?

Is there any sex difference in the risk of inheriting sickle cell anemia?

The Law of Independent Assortment applies to genes which are located on different chromosomes, but it does not apply to genes which are located near each other on the same chromosome, as you will see in the next activity.

Genetic Linkage

-- Inheritance of Genes which are Close Together on the Same Chromosome

Obviously, real chromosomes have more than one gene each. In this activity, you will analyze the inheritance of multiple genes which are close together on the same chromosome. We will consider three genes on Chromosome 1 and one gene on Chromosome 2, as indicated in the following table.

| | <u>Dominant Alleles</u> | <u>Recessive Alleles</u> |
|---------------------|-------------------------------------------------------|----------------------------------------------------------|
| <u>Chromosome 1</u> | W = has wings F = fire-breathing N = long fangs | w = no wings f = no fire-breathing n = short fangs |
| <u>Chromosome 2</u> | H = big horns | h = small horns |

For this activity, the father is heterozygous for each of these genes (**WwFfNnHh**), and the mother is homozygous for the recessive alleles (**wwffnnhh**). For the three genes on chromosome 1 for the father, the dominant alleles are all located on one chromosome and the recessive alleles are all located on the other homologous chromosome.

The Chromosome 1 pairs for the father and mother look like this.

Father

(W F N)

(w f n)

Mother

(w f n)

(w f n)

Draw the genes for the Chromosome 2 pairs for the father and mother.

Father

()

()

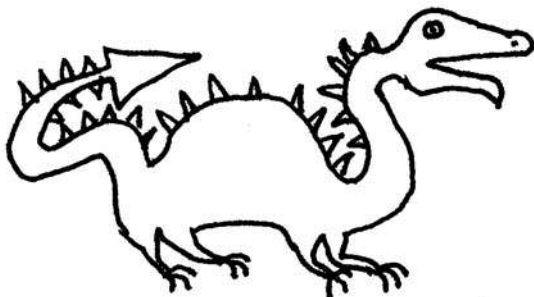
Mother

()

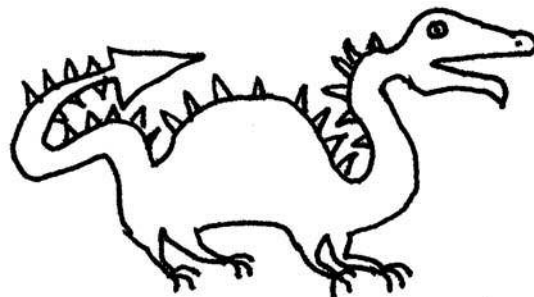
()

1. In the figures below, draw the phenotypes of the heterozygous father and the homozygous mother.

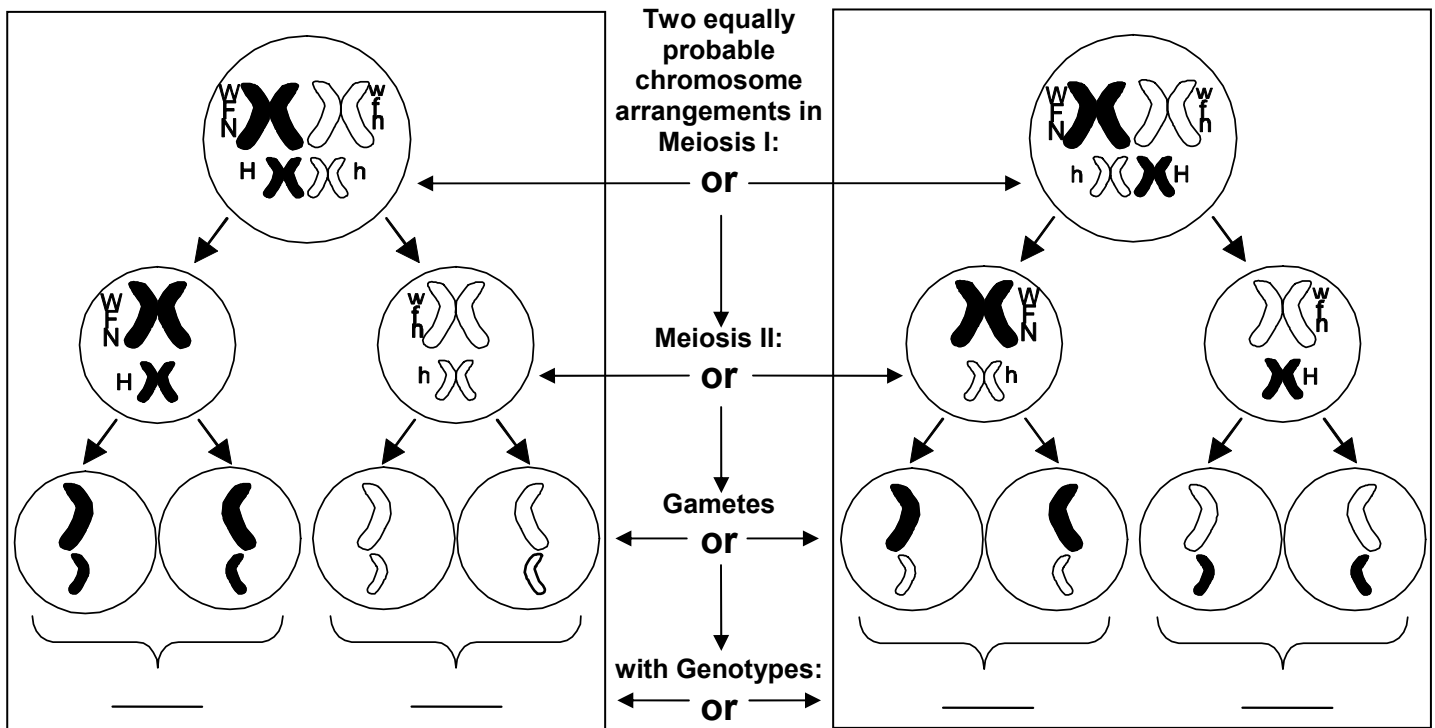
Father



Mother



2. What different combinations of alleles can be found in the different types of sperm that the heterozygous (**WwFfNnHh**) dragon father can produce?³ To answer this question, complete the genotypes in the figure below. (It may help to note that the alleles on the large white chromosomes are w, f, and n.)



How many different combinations of alleles can be found in the eggs produced by the homozygous (**wwffnnhh**) mother dragon? Show the genotype(s) of the mother's eggs.

3. Draw a Punnett square to show the genotypes of the baby dragons that could be produced by this father and mother. You may want to use the popsicle sticks representing the father's and mother's chromosomes to help you visualize the different combinations of alleles.

Based on this Punnett square, will any of the baby dragons have the dominant allele **W** for wings, but not the dominant allele **F** for fire-breathing?

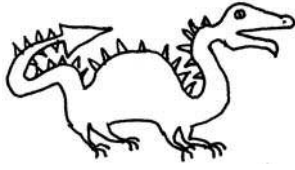
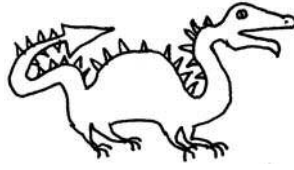
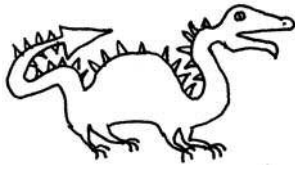
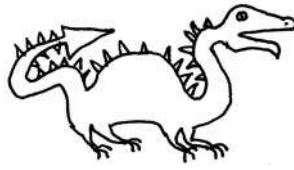
Will any of the baby dragons have the dominant allele **W** for wings, but not the dominant allele **H** for big horns?

Explain the difference in results for the inheritance of the wing and fire-breathing genes vs. the inheritance of the wing and horn genes.

³ Assume that the wing, fire-breathing and fang genes are so close together on Chromosome 1 that there is no crossing over within this region of the chromosome.

Genes that are located near each other on the same chromosome will move together during meiosis and fertilization. Therefore, the inheritance of these genes is linked. This is referred to as **genetic linkage**. As discussed previously, genes on different chromosomes are inherited independently, in accordance with the Law of Independent Assortment.

4. In the chart below, indicate the four possible genotypes of the baby dragons produced by this father and mother, and draw the phenotype for each genotype.

| Genotype | Phenotype | Genotype | Phenotype |
|----------|-----------------------------------------------------------------------------------|----------|-------------------------------------------------------------------------------------|
| _____ |  | _____ |  |
| _____ |  | _____ |  |

5. Will any of the baby dragons with wings have short fangs?

Will any of the fire-breathing baby dragons have short fangs?

Will any of the fire-breathing baby dragons have no wings?

Explain how genetic linkage accounts for these results.

6. Based on your drawings in the above chart and the Punnett square on the previous page, answer the following two questions.

On average, what fraction of the baby dragons with big horns will be fire-breathers?

On average, what fraction of the baby dragons with small horns will be fire-breathers?

Use the principles of genetics, including the Law of Independent Assortment, to explain these observations.

Discussion

The principles of inheritance in these dragons also apply to inheritance in humans, other animals, and plants. However, inheritance in humans, other animals, and plants is much more complex than inheritance in these dragons.

First, list the two principles of inheritance illustrated by this Dragon Genetics activity.

What are some additional complexities of inheritance in humans, other animals, and plants? Discuss the following questions.

- Genetic linkage is very strong for genes which are located close to each other on the same chromosome. What happens in the case of two genes which are far apart on the same chromosome?
- Are all alleles either completely dominant or completely recessive?
- Do any genes have more than two alleles?
- Does each gene influence only one phenotypic trait?
- Is each phenotypic trait influenced by only one gene (i.e. one pair of alleles on a pair of homologous chromosomes)?
- For the genes that are on the X chromosome in humans and other mammals, what are the differences in inheritance for males vs. females?

Teacher Preparation Notes for Dragon Genetics Lab -- Principles of Mendelian Genetics

Materials

- colored paper (2 each of orange, green, red, and yellow, and 1 each of blue and pink or purple)
- print out the page of genes for each type of autosome and sex chromosome (given at the end of these instructions)
- rubber cement or Elmer's glue
- popsicle sticks (5 for each student in the class)

Instructions for Preparing Chromosomes

Each popsicle stick should be prepared to represent a pair of homologous chromosomes. You will want to have a complete set of five popsicle sticks for each student in your class. Xerox or print two copies of each page of autosome genes on the appropriate color paper and one copy of each page of sex chromosome genes on the appropriate color paper. This will provide enough popsicle sticks for 36 students (18 dragon mothers and 18 dragon fathers). Each page of autosome genes (given at the end of these instructions) intentionally includes some gene deletions and inversions.

For each page of genetic traits, cut out the strips, each with a vertical column of letters representing the genes in one chromosome. (There are 12 strips in each section of the page, for a total of 36 strips per page.) Apply rubber cement or Elmer's glue to both sides of a popsicle stick, and glue strips on both sides of the popsicle stick, continuing this until all the strips have been used to make popsicle stick chromosomes. For the autosomes and for the sex chromosomes for females, you can use any two strips from the same page. For the sex chromosomes for males, be sure to include an X-chromosome on one side and a Y chromosome on the other side of each popsicle stick.

Comments for Discussion with Students

For codominant traits (Ee and Ss), there are the same number of both alleles, so that the teacher can show a class ratio of 1:2:1. Other traits such as fangs/no fangs (N = no fangs, n = fangs) are set up to show that a recessive trait can be the predominant trait in the population. This can be discussed in terms of the need for fangs for survival, but the possible advantage of no fangs if meat is not available and plants begin to play a larger part in the diet.

The sex-linked traits also can stimulate the students to come up with some interesting theories. Males tend to fight more and therefore need protection of the chest plate (W = no chest plate, w = chest plate), and the same may be said of tail spikes (X/x). Short arms may be more powerful, while females may benefit from longer arms to hold/care for babies (Z/z).

The sex-influenced traits also lead to some theories. Female tend to have wings (M/m) which allows them to get away from those pesky males or to flee danger with their babies. Elbow spikes (T/t) are found in males and may relate to fighting.

The most confusing trait for students is the comb (R/r). Only males have a comb, although females have the genes for the comb. This usually leads to a discussion that you can inherit secondary sexual traits from either parent.

Dragon Genes

GREEN AUTOSOMES

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A | A | a | a | a | a | a | A | A | A | A | A |
| B | b | B | B | B | b | b | b | b | | b | B |
| C | c | c | C | C | C | C | c | c | C | c | C |
| D | d | d | D | d | d | | D | D | d | d | D |
| E | e | E | E | e | e | e | e | E | e | e | E |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A | A | A | A | A | A | a | a | a | a | a | a |
| B | B | B | b | b | b | b | b | b | B | B | B |
| C | C | c | c | c | C | C | C | c | c | c | c |
| D | d | D | d | D | d | D | | d | D | d | d |
| E | e | e | E | E | e | | E | e | | e | E |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| a | a | a | a | a | a | | A | A | A | A | A |
| b | b | b | b | B | D | B | b | b | c | b | b |
| c | c | c | C | C | c | C | c | C | b | C | C |
| d | d | D | D | d | B | d | D | d | d | D | d |
| e | E | E | E | | E | e | e | e | e | e | e |

RED AUTOSOMES

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F | F | F | F | F | H | f | f | f | f | h | F |
| G | G | g | g | g | G | G | G | G | g | G | g |
| H | | h | H | F | h | h | H | H | F | | h |
| I | I | i | i | I | i | i | | I | I | I | i |
| J | j | j | j | j | j | j | j | j | J | J | J |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| f | f | f | f | f | g | f | | f | F | F | F |
| G | g | g | g | G | G | G | G | g | g | g | g |
| H | h | h | h | h | h | j | H | H | h | h | H |
| I | I | I | I | I | I | H | i | i | i | i | i |
| J | j | J | J | J | j | i | j | J | J | J | j |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| F | f | f | | F | F | F | | f | f | F | F |
| G | g | g | g | g | G | G | G | g | g | g | G |
| H | h | H | H | H | H | h | h | h | h | H | H |
| I | I | I | i | i | i | i | | I | I | I | I |
| J | J | J | j | j | j | j | J | j | J | J | j |

Orange Autosomes

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| K | K | K | K | K | k | k | k | k | k | k | k |
| L | l | l | L | L | L | L | l | l | l | L | L |
| M | m | m | m | M | p | m | m | M | M | M | M |
| N | n | N | n | n | O | n | n | n | n | n | n |
| O | o | o | O | o | n | O | O | O | | o | O |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| K | k | k | k | k | k | K | K | K | K | K | K |
| L | l | L | l | L | l | l | l | L | L | l | l |
| M | m | m | | m | M | m | m | M | | M | M |
| N | n | n | n | o | N | n | n | n | n | n | n |
| O | O | o | o | n | O | O | o | o | O | O | O |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| K | k | K | k | k | K | K | k | K | k | K | k |
| L | l | l | L | L | l | L | l | L | l | L | l |
| M | m | m | M | M | m | m | M | m | M | M | m |
| N | n | n | n | n | n | N | n | n | n | N | N |
| O | o | o | | O | O | O | O | o | O | o | O |

Yellow Autosomes

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| P | p | p | P | P | P | p | p | p | P | P | p |
| Q | q | q | q | q | q | r | Q | q | q | q | Q |
| R | r | R | R | r | r | Q | r | R | r | r | R |
| S | s | S | s | S | s | S | s | S | s | S | s |
| T | T | t | T | t | t | T | t | T | t | t | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| P | p | p | P | p | P | p | P | P | p | P | p |
| Q | q | q | q | q | Q | Q | Q | Q | Q | q | q |
| R | R | r | r | r | R | R | R | r | r | r | R |
| S | s | t | s | s | S | S | s | S | s | s | S |
| T | t | s | T | t | t | T | T | T | T | t | t |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| P | p | p | p | p | | P | P | P | P | P | P |
| Q | Q | Q | Q | Q | s | q | q | q | q | q | q |
| R | r | r | r | | r | R | R | r | t | r | R |
| S | S | s | s | S | q | s | S | S | S | s | s |
| T | t | t | t | T | t | T | T | T | r | t | t |

SEX CHROMOSOMES—X/X chromosomes [pink or purple]

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| U | U | U | U | U | U | u | u | u | u | u | u |
| V | v | v | v | V | V | V | v | v | v | v | V |
| W | w | w | w | W | w | w | w | w | w | w | W |
| X | x | x | x | X | X | X | x | x | x | x | X |
| Z | z | z | Z | z | z | z | Z | Z | Z | z | z |
| - | - | - | - | + | + | + | + | + | - | - | - |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| U | U | u | u | u | u | U | U | U | u | u | U |
| V | v | v | v | v | v | V | V | V | V | V | V |
| W | W | w | w | w | w | w | w | w | w | w | w |
| X | x | x | X | X | X | X | x | x | x | x | x |
| Z | z | z | z | z | Z | Z | Z | Z | z | z | z |
| + | - | + | - | + | - | + | - | - | - | + | + |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| U | u | u | u | u | u | U | U | U | U | U | U |
| V | v | v | v | V | V | V | v | v | v | v | v |
| W | w | w | w | w | w | w | w | w | W | W | w |
| X | X | X | x | x | x | x | x | X | X | X | x |
| Z | z | z | z | z | z | z | Z | Z | Z | Z | z |
| + | + | + | - | - | - | - | + | + | - | + | - |

SEX CHROMOSOMES --X/Y chromosomes [blue]

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| U | u | u | u | u | u | u | u | u | u | u | u |
| V | v | v | V | V | V | V | V | V | V | V | v |
| W | W | W | W | W | W | Y | Y | Y | Y | Y | Y |
| X | x | x | X | X | X | | | | | | |
| Z | z | z | Z | Z | Z | | | | | | |
| + | - | + | - | + | - | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| u | u | u | u | u | u | u | u | u | u | u | u |
| v | v | v | v | v | v | v | v | v | V | V | V |
| w | W | W | W | w | w | Y | Y | Y | Y | Y | Y |
| X | X | x | x | x | x | | | | | | |
| Z | z | z | y | Z | Z | | | | | | |
| - | - | - | - | + | + | | | | | | |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| U | U | U | U | U | u | u | u | u | u | u | u |
| V | v | v | v | v | v | v | V | V | V | V | V |
| W | W | w | w | w | w | Y | Y | Y | Y | Y | Y |
| X | x | X | X | X | x | | | | | | |
| Z | z | Z | Z | z | z | | | | | | |
| + | + | + | + | - | - | | | | | | |

Genetics¹

by Drs. Scott Poethig, Ingrid Waldron, and Jennifer Doherty, Department of Biology, University of Pennsylvania, Copyright, 2011

We all know that children tend to resemble their parents in appearance. Parents and children generally have similar eye color, hair texture, height and other characteristics because children inherit **genes** that control specific 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 (symbolized by **a**) codes for an enzyme that cannot produce melanin; this results in very pale skin and hair, which is called albinism.



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. In the next section, you will demonstrate this, using model chromosomes.

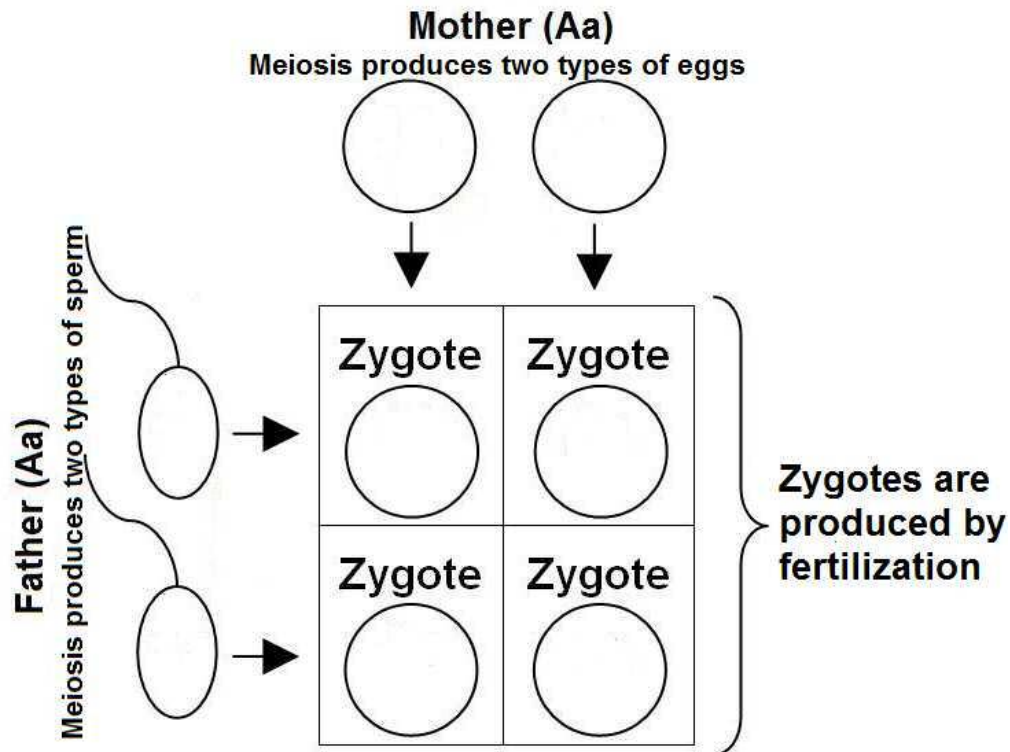
Inheritance of Albinism

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?

To answer this question your group will use four model chromosomes. The pair of homologous chromosomes for each parent will include one model chromosome with an **A** allele and a second model chromosome with an **a** allele.

¹ Teachers are encouraged to copy this student handout for classroom use. A Word file (which can be used to prepare a modified version if desired), Teacher Preparation Notes, comments, and the complete list of our hands-on activities are available at http://serendip.brynmawr.edu/sci_edu/waldron/. An alternative version of this activity that does not use model chromosomes is available in the Teacher Preparation Notes for this activity. Additional genetics activities are available at <http://serendip.brynmawr.edu/exchange/bioactivities>.

1. One of you should be the mother and use your model chromosomes to demonstrate how meiosis produces different types of eggs, and another should be the father and demonstrate how meiosis produces different types of sperm. In the chart below, write in the genetic makeup of the two types of eggs and the two types of sperm produced by meiosis.



2. Next, model fertilization, using the model chromosome for each type of sperm to fertilize each type of egg. Write the genetic makeup of the resulting zygotes in the chart.

To answer the following questions, remember that each zygote undergoes repeated mitosis to become a child, so the child will have the same genetic makeup as the zygote.

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**? _____
5. 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.

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.

6. What fraction of this couple's children would you expect to have normal pigmentation? _____
7. What fraction of this 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.

8. 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 ratios. 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.

9. For the corresponding phenotypes, the fraction with normal pigmentation is _____ and the fraction with albinism is _____, so the corresponding ratio is _____.

Notice that the chart you completed on page 2 has been very useful in helping you to answer important questions about the inheritance of albinism. Biologists frequently use a simplified version of this chart, called a **Punnett Square**, to analyze inheritance. The chart below shows a Punnett Square for the example you have been analyzing.

| | | |
|----------|-----------|-----------|
| | A | a |
| A | AA | Aa |
| a | Aa | aa |

10. For this Punnett Square, use arrows to indicate the genetic makeup of each sperm and egg and circle the genetic makeup of each type of zygote.

11. Sally and Harry fall in love. They introduce Sally's identical twin, Emily, to Harry's identical twin, Ken. Soon there is a double wedding where Sally marries Harry and Emily marries Ken. Both Sally and Emily get pregnant. They wonder "Will their babies look exactly alike?" Answer their question, and explain your reasoning. (To answer this question, think about the children that could be produced if both pairs of identical twins are heterozygous **Aa**.)

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.

Find someone to “mate” with.

1. 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.
2. 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.
3. 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 3) | 1/4 = 25% | 2/4 = 50% | 1/4 = 25% |
| Class data -- Percents (Total # children = _____) | | | |

4. 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?

7. Enter the results for the class data in the table on page 4. Are the percents of each genotype in the class data similar to the predictions of the Punnett Square?

If there is a difference between the results for the class data and the predictions, is this difference relatively small or large?

In many cases, the results for a family of four children will not match the predictions of the Punnett Square. Random variation in which particular sperm fertilizes which particular egg explains why the children in the individual families may differ considerably from the predictions based on the Punnett Square. The random variation observed in small samples usually averages out in large samples. Therefore, the results for a large number of children from multiple pairs of parents with the same genetic makeup are usually close to the predictions of the Punnett Square.

Genetics of Sex Determination

As you probably know, human males have an X and a Y chromosome (**XY**), whereas females have two X chromosomes (**XX**). A zygote must have at least one **X** chromosome to survive. The gene that causes the development of male anatomy is located on the Y chromosome. This gene is called **SRY**, 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.

Your understanding of meiosis and fertilization provides the basis for understanding the inheritance of X and Y chromosomes. During meiosis in a female, the two X-chromosomes separate, so each egg has a single X-chromosome. In males, even though the X and the Y-chromosomes are very different, they can nevertheless pair with each other and separate from each other during meiosis. This means that males produce two kinds of sperm; half have an X chromosome and half have a Y chromosome.

1. What will be the sex of a child produced when an egg is fertilized by a sperm that has a Y chromosome?

What type of sperm must fertilize an egg to result in a female child?

2. Draw a Punnett Square which shows the inheritance of the sex chromosomes. Use X to indicate an egg or sperm with an X chromosome and Y to indicate a sperm with a Y chromosome.

| | |
|--|--|
| | |
| | |

3. Based on this Punnett Square, what percent of children would you expect to be male?

4. To test this prediction, begin by writing down the initials of all the children your mother has had. Arrange these initials in order from the oldest to the youngest, indicating whether each was male or female.

5. Complete the following table.

| | Total number of children | Number of males | % males |
|-----------------------------------------------------------|---------------------------------|------------------------|----------------|
| Your mother's children | | | |
| Children of the mothers of all the students in your class | | | |
| Predicted percent from Punnett square, page 5 | | | |

6. Next, compare the predicted percent male with the observed percent male for your mother's children, for the children of the mothers of the other members of your group, and for all the children in the class sample. How similar to the prediction are the observed results for individual families and for all the families combined?

Notice that the percent male children varies in different families and the percent male children in some families is very different from the predicted. To understand why, remember that each time a sperm fertilizes an egg to form a new zygote, there is random variation in whether the sperm has an X or Y chromosome. Random variation tends to average out in large samples, so the overall percent male children for all the mothers will usually be fairly close to the predicted 1/2.

7. To answer the following questions, look at your group's lists in question 4 above.

If a mother's first child is a son, is the next child necessarily a daughter?

If a mother's first child is a daughter, is the next child necessarily a son?

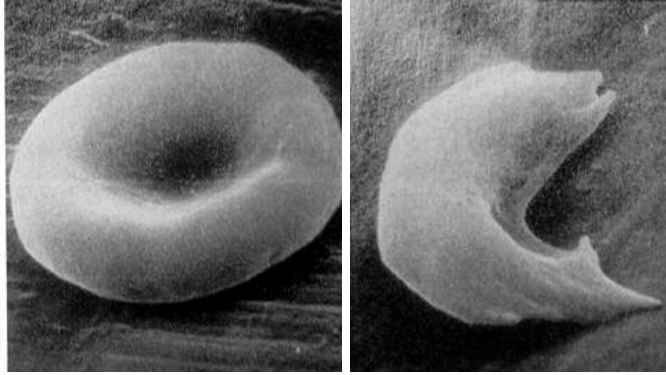
If a mother's first two children are sons, is the next child necessarily a daughter?

If a mother's first two children are daughters, is the next child necessarily a son?

These observations illustrate that you cannot predict the sex of the next child based on the sex of a previous child or children. Each time a sperm fertilizes an egg, the results are independent of any previous fertilizations that resulted in older brothers or sisters.

Genetics of Sickle Cell Anemia

Some alleles of certain genes can cause disease. An example is the gene for hemoglobin, the protein that carries oxygen in red blood cells. One allele codes for normal hemoglobin, while another allele codes for altered hemoglobin, called sickle cell hemoglobin. When a person is homozygous for the sickle cell allele, this causes a serious disease called sickle cell anemia. The sickle cell hemoglobin tends to clump into long rods that cause the red blood cells to assume a sickle shape, in contrast to the normal disk-shaped red blood cell shown on the left in the figure below.



1. What problems might be caused by the sickle-shaped red blood cells?

A person who is heterozygous for the sickle cell and normal hemoglobin alleles usually does not have symptoms of sickle cell anemia, so in this respect they are like a person who is homozygous for the normal hemoglobin allele. This is why textbooks usually describe the sickle cell allele as recessive. However, people who are heterozygous for the sickle cell allele are not exactly like people who are homozygous for the normal hemoglobin allele.

People who are heterozygous for the sickle cell allele are less likely to develop severe malaria, an infection of the red blood cells which is transmitted by mosquitoes in many tropical countries. Thus, 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 of this advantage, the sickle cell 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).

2. Suppose that a person who is heterozygous for the sickle cell allele (**Ss**) marries a person who is also heterozygous for this allele (**Ss**). Draw a Punnett Square to show the expected genetic makeup of their children.

3. On average, what fraction of their children will suffer from sickle cell anemia?

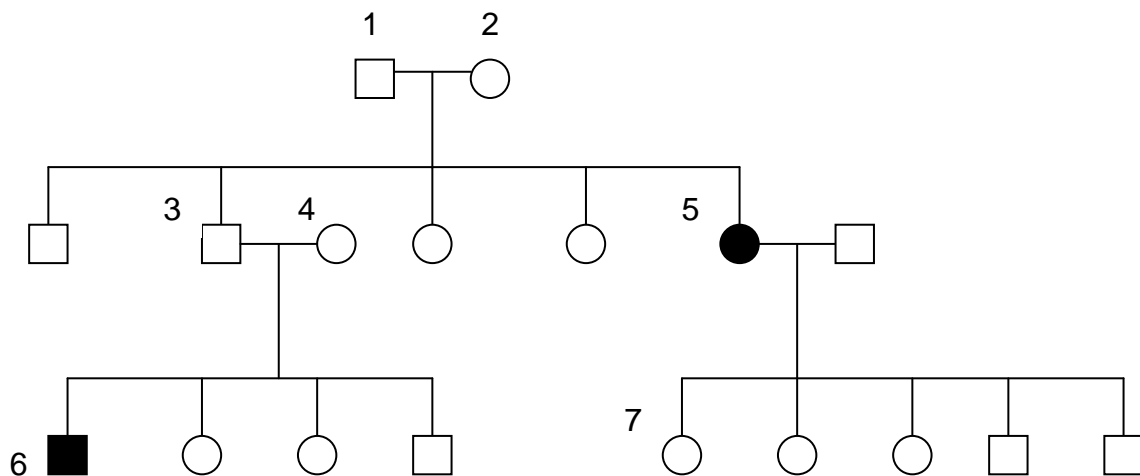
4. On average, what fraction of their children will be heterozygous for the sickle cell allele? (These children will not have sickle cell anemia and will be less likely to develop severe malaria.)

Pedigree Analysis

Human geneticists illustrate the inheritance of a gene within a family by using a pedigree chart. On such a chart, males are symbolized by a square (\square) and females are symbolized by a circle (\circ). People who are affected by a disease are symbolized by a dark square or circle.

The pedigree chart below shows inheritance of albinism. 1 and 2 represent a couple who had five children, including a son who is labeled 3 and a daughter who is labeled 5. Only one of the children, 5, was albino. The son who is labeled 3 and his wife who is labeled 4 had four children, including a son who is labeled 6.

1. In the pedigree below write the genotypes of the individuals who are labeled with numbers, using (**A**) to represent the dominant allele and (**a**) to represent the recessive allele. Start by indicating the genotypes of 5 and 6. Next, draw a Punnett Square for parents 3 and 4 and their offspring to figure out what the genotypes for 3 and 4 must be.



Next, determine the genotypes of 1 and 2. Finally, determine the genotype of 7.

Many other genes have a recessive allele which is inherited in the same manner as the recessive allele for albinism. These include the recessive alleles that cause some genetic diseases, such as sickle cell anemia, cystic fibrosis (a genetic disease that results in difficulty in breathing and serious illness), and phenylketonuria (a genetic disease that results in mental retardation unless detected at birth and treated with a special diet, etc.).

Challenge Question

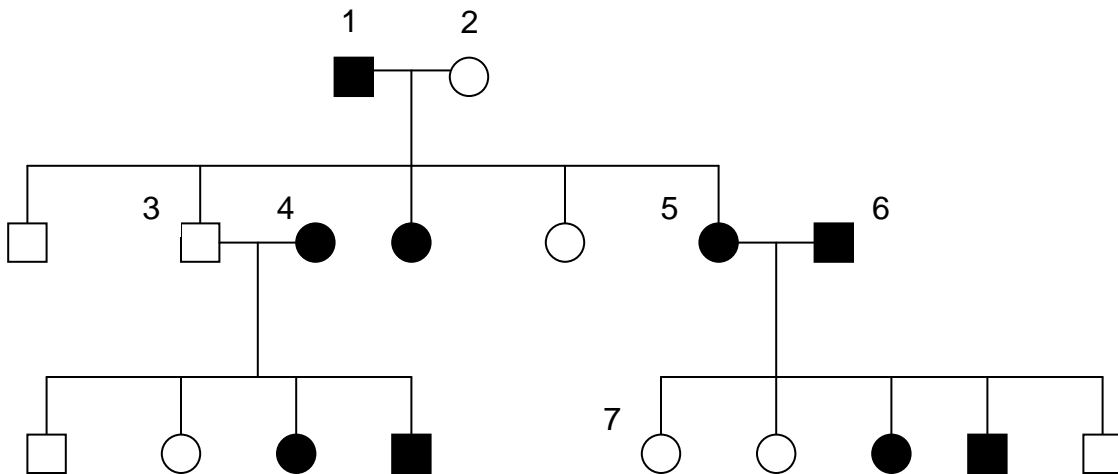
Shown below is a pedigree chart for the inheritance of achondroplasia (ay-kon-druh-**play**-zhuh), a form of dwarfism. Dark circles or squares indicate individuals with achondroplasia. Examine the pedigree chart, and answer the following questions.

1. Is the allele that causes this form of dwarfism recessive or dominant?

How do you know?

2. Using **D** to represent the dominant allele and **d** to represent the recessive allele, write the genotypes of the indicated individuals. Start by indicating the genotypes of 2, 3 and 7. Next, draw a Punnett Square for parents 5 and 6 and their offspring to figure out what the genotypes for 5 and 6 must be.

Next, determine the genotypes of 1 and 4.



3. Based on the frequency of dwarfs among the people you have seen in your lifetime, do you think that the allele for achondroplasia is common or rare in the population?

Teacher Preparation Notes for Genetics

by Dr. Ingrid Waldron and Dr. Jennifer Doherty, Department of Biology, University of Pennsylvania, 2011¹

Teaching Points:

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, results 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.

Additional Teaching Points

Meaning of genetics vocabulary, 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 pedigree 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/ or

posterboard sockosomes prepared using the templates in the Teacher Preparation Notes for the Mitosis, Meiosis and Fertilization activity or

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 with 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)

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.

For "Coin Toss Genetics" and "Genetics of Sex Determination" (pp. 3-6 of Student Handout)

(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 albinism 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. Klinefelter 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 malaria 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 albinism 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 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 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/bioactivities/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_edu/waldron/#dragon1
- 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

by Drs. Scott Poethig, Ingrid Waldron, and Jennifer Doherty, Department of Biology, University of Pennsylvania, copyright 2011

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**.



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

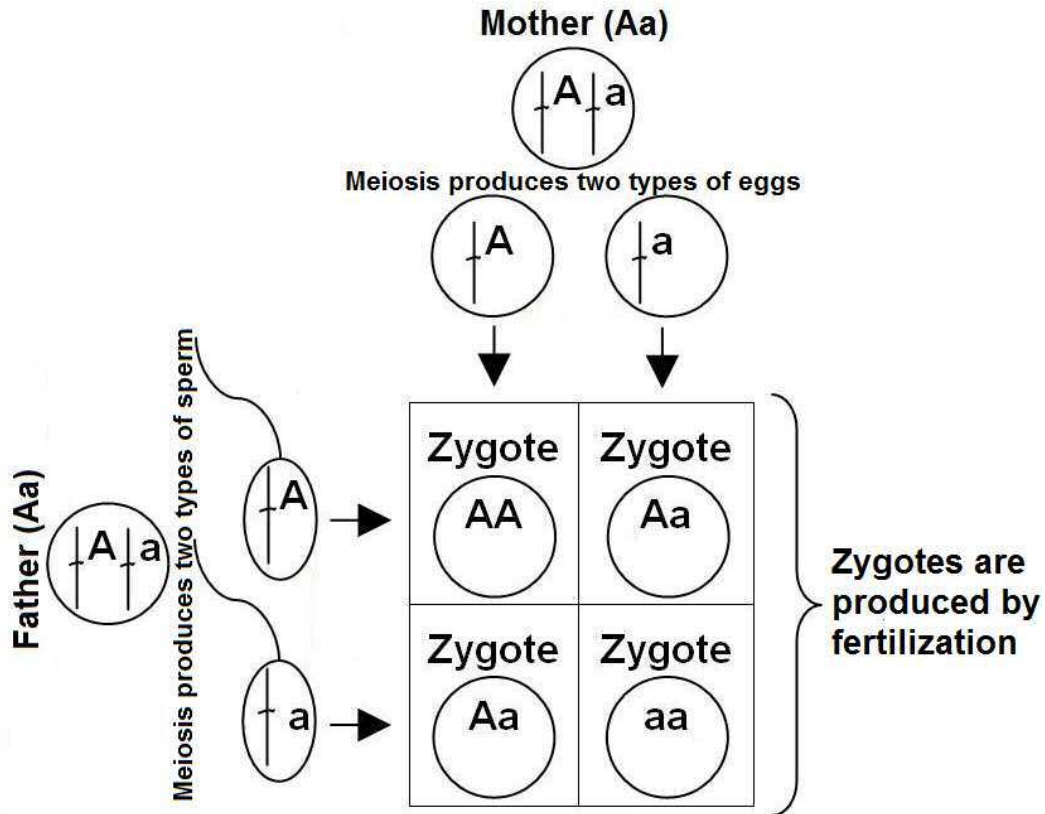
To learn more about how genetic traits are inherited, you will analyze a specific question: If each parent has one **A** allele and one **a** allele (i.e. both parents are **Aa**), what different combinations of **A** and/or **a** alleles would you expect to observe in the children of these parents?

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.

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 ratios. 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?