

## Teacher Guide: Finding a Gene on the Chromosome Map

### ACTIVITY OVERVIEW

**Abstract:**

In this activity students use a pedigree and jigsaw puzzles to explore how scientists use genetic information from a family to identify a gene associated with a genetic disorder.

**Module:**

Genetic Disorder Corner

**Prior Knowledge Needed:**

DNA, chromosome, gene, protein, patterns of inheritance (dominant vs. recessive, autosomal vs. sex-linked)

**Key Concepts:**

All humans have the same genes, arranged in the same order on the chromosomes. Each person is unique because the information carried in genes differs slightly from person to person. An alteration in the DNA sequence of

a gene(s) may cause a genetic disorder. Scientists use pedigrees as a tool to identify a gene associated with a genetic disorder, and to map that gene to a specific location on the chromosomes.

**Materials:**

Copies of student handouts

**Appropriate For:**

Ages: 12 - 18  
USA grades: 7 - 12

**Prep Time:**

15 minutes

**Class Time:**

20 minutes

**Activity Overview Web Address:**

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=121>

Other activities in the *Genetic Disorder Corner* module can be found at:  
<http://gslc.genetics.utah.edu/teachers/tindex/>

## Teacher Guide: Finding a Gene on the Chromosome Map

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### I. PEDAGOGY

#### A. Learning Objectives

- Students will learn that all humans have the same genes, arranged in the same order along the twenty-three pairs of chromosomes.
- Students will understand that every person is unique because the information carried in genes differs slightly from person to person, i.e. an individual inherits one form (or allele) of every gene from each of his or her parents, resulting in a unique combination.
- Students will be able to explain how a mutation (or permanent change in the DNA sequence) may cause a gene to be defective, possibly causing a medical condition known as a genetic disorder.
- Students will gain experience using a pedigree to determine the inheritance pattern of a genetic disorder.
- Students will understand that scientists use pedigrees as a tool to identify a gene associated with a particular genetic disorder.

#### B. Background Information

Genetic disorders are medical conditions caused by permanent changes (or mutations) in the DNA sequence. When we hear about the discovery of a gene responsible for a genetic disorder, what exactly does this mean? It means that scientists have identified a gene that causes a genetic disorder—but only when it is mutated. It is important to understand that all humans have the same basic set of genes, arranged in the same order along our twenty-three pairs of chromosomes; a medical condition only arises when the DNA sequence of a gene is mutated.

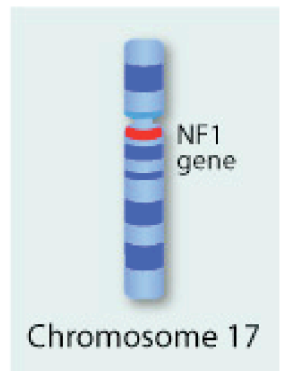
Although all humans have the same set of genes, this does not mean that every person's DNA sequence is exactly the same. In fact, it is the small variations within our genes that make each of us unique. Different variations or forms of a gene are referred to as "alleles". One can inherit different alleles of a gene and not develop a genetic disorder. However, when a gene is mutated in a way that causes its protein product to malfunction, the effects can be deleterious to the cell and the organism.

The genetic disorder Type I Neurofibromatosis (NF1) is an example of what can happen when a protein malfunctions. It is one of the most common autosomal dominant disorders, affecting approximately 1 in 3,000 individuals. NF1 is a disorder of the nervous system characterized by tumor growth on or around different types of nerve cells. The gene responsible for NF1 is a gene of the same name, *NF1*. In 1990, independent research teams at the University of Utah and the University of Michigan discovered the gene's location on human chromosome seventeen. The *NF1* gene encodes a protein called Neurofibromin

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(NEU-ro-fi-BRO-min). This protein interacts with and regulates another protein called Ras, which promotes cell division. Mutations in the *NF1* gene can produce a Neurofibromin protein that is unable to properly interact with Ras and regulate its function. As a result, the Ras protein is more active than usual causing the cell to divide more often. When cell division is not controlled, excess cells begin to accumulate and form a tumor.

The genetic disorder NF1 runs in families and exhibits an autosomal dominant pattern of inheritance. What does this mean? An autosome is any of the twenty-two chromosomes that are not sex chromosomes. The *NF1* gene is located on chromosome seventeen, an autosome. It exhibits a dominant pattern of inheritance, meaning that symptoms of the disorder will arise even when an individual inherits just one mutated copy of the gene. This is in contrast to a recessive pattern in which an individual must inherit two mutated copies of a gene—one from each parent—in order to develop symptoms of the disorder. (If they only inherit one mutated copy, usually the other copy can provide enough normal protein product for the cell to function; these people are called “carriers”.)



So, how do scientists find the gene responsible for a genetic disorder like NF1? The first step is to study large families that include individuals who have been affected by the disorder. This is done by constructing a pedigree for each family. A pedigree is a diagram that describes family relationships and depicts which individuals have been diagnosed with the disorder. Next, scientists look for variations in the DNA sequence that are always present in individuals that have the disorder, yet are never present in unaffected individuals. (Scientists use a variety of biochemical and molecular techniques, such as PCR, gel electrophoresis, and DNA sequencing, to detect this genetic variation.) The evaluation and measurement of variation within affected families allows scientists to “map” a gene to a specific location on the chromosomes, and thereby identify the gene associated with the disorder. Once a gene has been identified, it can be studied. Scientists study the gene to determine the normal function of its protein product in the cell, and the mechanism by which gene malfunction causes disease. When a disease gene has been identified or mapped and its function determined, the diagnosis and treatment of the genetic disorder can be improved.

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### C. Teaching Strategies

#### 1. Classroom Implementation

- Begin class by reviewing how the terms DNA molecule, chromosome, and gene are interrelated. Remind students that each gene contains instructions for building a particular protein; protein molecules are important because they do the majority of the work in our cells.
- Discuss the similarities and differences observed in human beings at the molecular level. Explain that all humans have the same set of genes (approximately 20,000 of them); this identifies us as a single species. Yet, each person is unique because the information carried in genes differs slightly from person to person. For example, we may inherit slightly different forms (or alleles) of each gene, resulting in a unique combination of traits.
- Define what a mutation is and discuss the consequences mutations might have on a gene's protein product and the function of a cell. Include the following in your discussion:
  - Mutations are permanent changes in the DNA sequence.
  - Changes in the DNA sequence may cause a gene's protein product to malfunction and result in a medical condition called a genetic disorder.
  - Type I Neurofibromatosis (NF1) is an example of a genetic disorder caused by a mutation in a single gene. Describe the symptoms of this disorder (see Additional Resources).
- Explain that scientists identified the gene responsible for NF1 when they determined its location on chromosome seventeen. Discuss what it means when it is reported that scientists have identified a gene that causes a genetic disorder. Emphasize that we all have the newly discovered gene but will not develop the symptoms of the disease unless that gene is faulty due to mutation.
- Invite students to imagine they are scientists studying a hypothetical disorder called Whirling disorder. Describe the symptoms of this disorder. Explain that you would like them to identify the gene responsible for Whirling disorder, as this is the first and key step in determining gene function and, thereby, the nature of the disease. If they can accomplish this, they will be able to more accurately diagnosis and treat this disorder, improving the quality of life for hundreds of affected families.
- Pass out the student pages, or project the color overhead masters or PowerPoint slides, then allow students to complete the activity either alone or in pairs.
  - Ask students to read the background information on page S-1.

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- Explain to students that they will be analyzing jigsaw puzzles rather than human DNA to identify the Whirling disorder gene, but the logic and strategy they will use is similar to that of scientists. Scientists obtain DNA samples from large families with a history of the disorder, then compare their DNA to look for unique sequence that is present in all who have the disorder and absent from those who do NOT have the disorder.
- Introduce pedigrees as a tool used by doctors and scientists to 1) illustrate relationships among family members, and 2) identify which individuals are affected or unaffected by the genetic disorder.
- Ask students to use the information in the pedigree to identify the color and number of the puzzle piece (or gene) responsible for Whirling disorder. You may need to give them the following hint: find the colored puzzle piece that is consistently present in individuals who have the disorder, and absent in individuals that do NOT have the disorder.
- Once students have completed the activity, ask one of the students to explain the logic he or she used to come to this conclusion.
- Explain that pedigrees are also useful in determining the pattern of inheritance for a particular disorder. This helps a family to know the probability a disorder might be passed on to their children. Conclude class with a discussion of the different patterns of inheritance: autosomal vs. sex-linked, recessive vs. dominant.
- Assess students' understanding of inheritance by asking them to answer the questions found on page S-3.

### 2. Extensions

- Ask students to find information in the media about the discovery and identification of a gene responsible for a particular genetic disorder.
- Once a disorder gene has been identified, screening the population for the disease-causing mutation becomes possible. This activity could be followed with the activity *Colorful Electrophoresis* in which students use gel electrophoresis to simulate the genetic test for the disorder sickle cell anemia (see Additional Resources). You can build your own electrophoresis chambers using the step-by-step instructions in the activity *Build a Gel Electrophoresis Chamber* (see Additional Resources).
- Once a disorder gene is identified and a genetic test becomes available, many ethical and social concerns arise. To explore these issues with your students, use the activity *Newborn Genetic Screening: What Should We Test and Why?* in which students serve on a task force to develop a public health policy on

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screening infants for genetic disorders (see Additional Resources).

### 3. Common Misconceptions

- Students often think that every person is unique because each has different genes. This is not true. Emphasize that all humans have the same genes. In fact, our genes are even in the same order along our chromosomes. We are each unique because we inherit different combinations of alleles, resulting in a unique combination of traits.
- Students may interpret disease gene discovery to mean that only those who have the disease have the gene. This is not true. Emphasize that each of us has the newly discovered gene, but none of us will develop the symptoms of that disease unless we inherit a form of the gene that is faulty due to mutation.

## II. ADDITIONAL RESOURCES

### Activity Resources linked from the online Activity Overview at:

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=121>

- Overheads: Generate your own color overheads showing enlarged versions of the pedigree and puzzles used in the activity.
- PowerPoint: Color slides showing enlarged versions of the pedigree and puzzles used in the activity.
- Website: *What is NF1?* Illustrated description of the various symptoms of NF1, the criteria doctors use to diagnose it, and more.
- Activity: *Colorful Electrophoresis* A basic how-to guide for gel electrophoresis in the classroom using easily obtainable and inexpensive materials. Colored dyes are used instead of DNA or protein samples, and a variety of easy to find agar sources are listed. Scenarios provide examples of applications in forensics and genetic testing.
- Activity: *Build a Gel Electrophoresis Chamber* Step-by-step, illustrated instructions on how to build a gel electrophoresis chamber for use in the classroom. Uses inexpensive and easily obtainable materials.
- Activity: *Newborn Genetic Screening: What Should We Test and Why?* Students form task forces to research genetic disorders, then develop a public health policy on screening newborn infants for those disorders.

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### III. MATERIALS

#### Detailed Materials List

- Color copies of the student pages (S-1 to S-2), and/or color overheads or PowerPoint slides containing enlarged versions of the pedigree and puzzles
- Copies of student questions (S-3)
- Sheet protectors for the color copies (optional)

### IV. STANDARDS

#### A. U.S. National Science Education Standards

##### Grades 5-8:

- Content Standard C: Life Science - Reproduction and Heredity; in many species, including humans, an individual receives genetic information from its mother and its father; hereditary information is contained in genes, located in the chromosomes of each cell; each gene carries a single unit of information; a human cell contains many thousands of different genes.

##### Grades 9-12:

- Content Standard C: Life Science - Molecular Basis of Heredity; each DNA molecule in a cell forms a single chromosome; most of the cells in a human contain two copies of each chromosome and, therefore, two copies of each gene; this explains many features of human heredity, such as how variations that are hidden in one generation can be expressed in the next; transmission of genetic information to offspring occurs through egg and sperm (germ cells) that contain only one representative from each chromosome pair; an egg and a sperm unite to form a new individual; mutations in germ cells can create variations that change an organism's offspring.

#### B. AAAS Benchmarks for Science Literacy

##### Grades 5-8:

- The Living Environment: Heredity - in some kinds of organisms, all the genes come from a single parent, whereas in organisms that have sexes, typically half of the genes come from each parent.
- Human Organism: Human Development - the developing embryo and later the newborn infant encounter many risks from faults in its genes.

##### Grades 9-12:

- The Living Environment: Heredity - some new gene combinations make little difference, some can produce organisms with new and perhaps enhanced capabilities, and some can be deleterious.
- The Human Organism: Human Identity - the similarity of human DNA



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sequences and the resulting similarity in cell chemistry and anatomy identify human beings as a single species.

- The Human Organism: Physical Health - faulty genes can cause body parts or systems to work poorly; a fuller understanding of the nature of disease gives today's human beings a better chance of staying healthy than their forebears.

### C. Utah Secondary Science Core Curriculum

#### 7th Grade

Standard 4: Students will understand that offspring inherit traits that make them more or less suitable to survive in the environment.

Objective 1: Compare how sexual and asexual reproduction passes genetic information from parent to offspring.

- Compare inherited traits of offspring and their parents.

Objective 3: Analyze issues related to genetics.

- Cite advantages and disadvantages of genetic technologies.

#### Biology (9-12)

Standard 4: Students will understand that genetic information coded in DNA is passed from parents to offspring by sexual and asexual reproduction; changes in DNA may alter genetic expression.

Objective 2: Predict and interpret patterns of inheritance in sexually reproducing organisms.

- Explain Mendel's laws of segregation and independent assortment and their role in genetic inheritance; demonstrate possible results of recombination in sexually reproducing organisms using one or two pairs of contrasting traits in the following crosses: dominance/recessive, incomplete dominance, codominance, and sex-linked traits.

Objective 3: Explain how the structure and replication of DNA are essential to heredity and protein synthesis.

- Describe how mutations may affect genetic expression; research, report, and debate genetic technologies that may improve the quality of life.

## V. CREDITS

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### Funding:

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## Teacher References:

### Answer Key

#### 1. Which puzzle piece is responsible for Whirling disorder? Explain.

Piece #36 is responsible for Whirling disorder. The puzzle piece (gene) must be the same color in every affected individual, and some other color in every unaffected individual. Piece #36 is the only one that fits these criteria. All of the affected individuals (1, 3, 6, 8, 10, 11 and 12) share the same red puzzle piece (#36), whereas none of the unaffected individuals (2, 4, 5, 7 and 9) has a red #36 puzzle piece.

One way to solve this problem is: Individual #1 on the pedigree has the disorder and all red puzzle pieces. Therefore, you know that the puzzle piece responsible for the disorder must be red as well. Search through the puzzles of individuals who have the disorder (1, 3, 6, 8, 10, 11 and 12) to find the puzzles with the fewest red pieces. Puzzles 6 and 12 have three red pieces; puzzles 5 and 11 have four. Piece #36 is the only red piece shared by all four puzzles. Check to make sure that none of the unaffected individuals (2, 4, 5, 7 and 9) has a red #36 puzzle piece. This confirms that puzzle piece #36 does indeed carry the disorder gene.

#### 2. Is the inheritance pattern for Whirling disorder dominant or recessive? autosomal or sex-linked?

Whirling disorder would likely be inherited in an autosomal dominant manner.

Dominant inheritance is characterized by a lack of skipped generations. That is, approximately half of all the children born to a parent with Whirling disorder also show the effects of the mutation.

Sex-linked genes are those genes that are found either on the X or Y chromosome. Since the Y chromosome contains very few genes, this means that sex-linked genes are found on the X chromosome. The fact that approximately equal numbers of males and females are affected by Whirling disorder indicates that the Whirling disorder gene is not sex-linked. If the gene were sex-linked, then fathers with the disorder would contribute the Whirling disorder gene to all of their daughters (to whom they contribute an X chromosome), but never to their sons (to whom they contribute a Y chromosome). This is not what the pedigree shows.

#### 3. For person "A", the colors of the puzzle pieces should be: 1/2 dark blue, 1/2 red.

Individual A's father has all red puzzle pieces, so half of A's pieces are red. We cannot know what color(s) A's mother had without looking at A's daughter. Individual A's daughter has approximately 1/2 light green puzzle pieces from her mother (individual 7), as well as approximately 1/4 red pieces and 1/4 dark blue pieces. Since her mother

## Teacher References:

has all light green puzzle pieces, the dark blue must have come from her father. Therefore, her paternal grandmother must have had all dark blue puzzle pieces. Individual A would have received half of his puzzle pieces from each parent and must have  $\frac{1}{2}$  red (from his father) and  $\frac{1}{2}$  dark blue (from his mother).

**4. For person “B”, the colors of the puzzle pieces should be:** all pink.

To discover what color pieces individual B has, we can look at his granddaughter, individual 11. She has light blue puzzle pieces from her mother, individual 9. Her father would have passed on her light green, red and dark blue puzzle pieces from his mother, individual B’s wife (individual 8). Therefore the remaining pink puzzle pieces must have come from her paternal grandfather, individual B. It is very unlikely that individual B had more than one color of puzzle piece and only passed on the pink ones. Therefore we can assume that individual B had all pink puzzle pieces.

**5. For person “C”, the colors of the puzzle pieces should be:** all yellow.

To discover what color pieces individual C has, we can look at her son, individual 4. Her son has yellow, red, dark blue and dark green puzzle pieces. The dark green pieces came from his paternal grandfather, individual 2. The red and dark blue pieces came from his paternal grandmother, individual 3. Therefore, the yellow puzzle pieces must have come from his mother, individual C. Since approximately  $\frac{1}{2}$  of his pieces are yellow, we can assume that she had all yellow puzzle pieces.

**6. For person “D”, the colors of the puzzle pieces should be:**  $\frac{1}{2}$  dark green,  $\frac{1}{4}$  red, and  $\frac{1}{4}$  dark blue.

Individual D’s father had all dark green puzzle pieces, therefore individual D has  $\frac{1}{2}$  dark green pieces. Individual D’s mother had  $\frac{1}{2}$  red and  $\frac{1}{2}$  dark blue puzzle pieces. Since individual D received  $\frac{1}{2}$  of his puzzle pieces from his mother, he has  $\frac{1}{2} \times \frac{1}{2}$  or  $\frac{1}{4}$  red and  $\frac{1}{4}$  dark blue pieces.

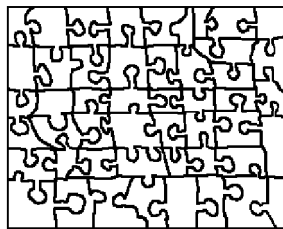
# Finding a Gene on the Chromosome Map



As a scientist, you've noticed that a genetic disorder runs in families, and you want to find the gene responsible for it. First, you identify a large family, in which some individuals have the disorder, and others don't. After enlisting the family's support and collecting DNA samples from all family members, you're ready to begin looking for the gene. Where do you go from here?

### Here's one way to think about genes:

Say the genetic information in each family member were like a jigsaw puzzle. Each puzzle piece would represent a gene organized in a specific



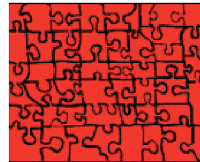
location on the chromosome puzzle. Because all humans have the same set of genes, arranged in the same order, every family member would have the same basic set of puzzle pieces for each chromosome. A generic human jigsaw puzzle for one of our chromosomes might look like this.

But the information carried in genes differs slightly from person to person. This is what makes each of us unique. As a result, the colors of the puzzle pieces would be different between family members.

### What might a family's puzzles look like?

While some relatives might share puzzle pieces of a certain color, other pieces would be different. Only identical twins share the exact same combination of colors.

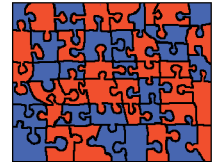
Look at the family of jigsaw puzzles below.



Mother's genes



Father's genes



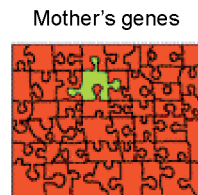
Child's genes

Can you see how some of the child's genes are derived from one parent and some from the other parent?

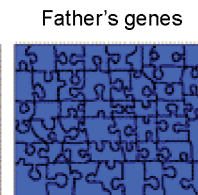
The child receives half of its genetic information from the mother and half from the father.

### What can our genes tell us about our chances of inheriting a genetic disorder?

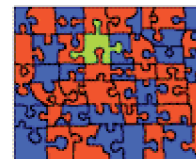
When a mutation (or change in the DNA sequence) occurs in a gene, a medical condition called a genetic disorder may result. Type I neurofibromatosis (NF1) is an example of a genetic disorder. If one parent has the *NF1* disorder gene, indicated by the green puzzle piece, then the child has a 50% chance of inheriting the gene.



Mother's genes



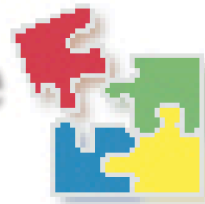
Father's genes



Child's genes

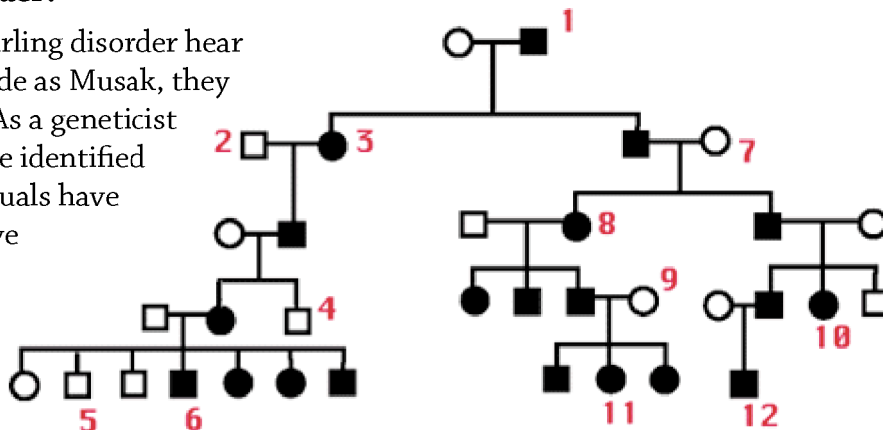
This child has inherited the *NF1* gene from his mother; the child will have the disorder since the inheritance pattern for NF1 is dominant.

# Finding a Gene on the Chromosome Map



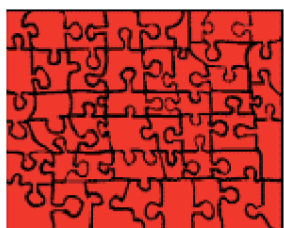
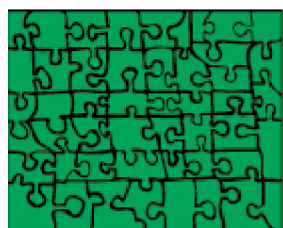
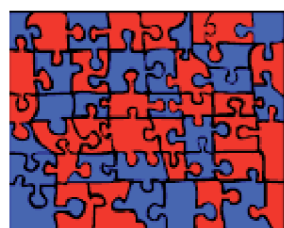
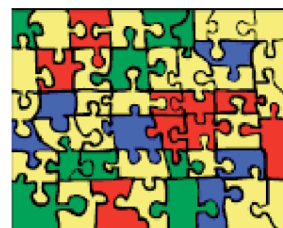
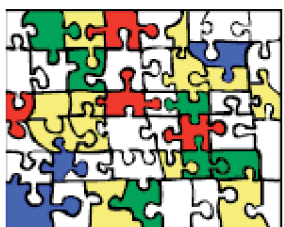
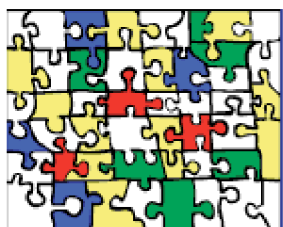
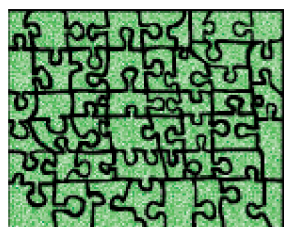
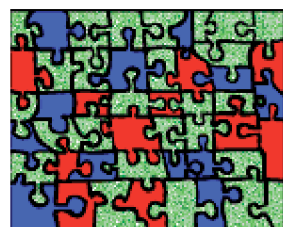
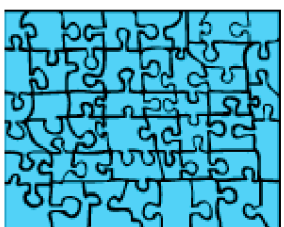
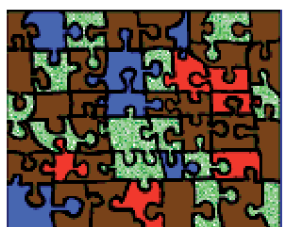
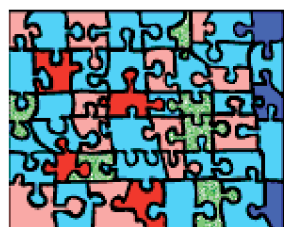

## Find the gene for Whirling disorder!

When individuals afflicted with Whirling disorder hear old Rolling Stones tunes, even remade as Musak, they let loose and dance uncontrollably. As a geneticist studying Whirling disorder, you have identified a large family in which some individuals have the disorder, and others don't. You've drawn a pedigree for this family. A pedigree is a diagram that shows (1) how family members are related, and (2) which individuals have Whirling disorder, indicated by black circles (females) and black squares (males).

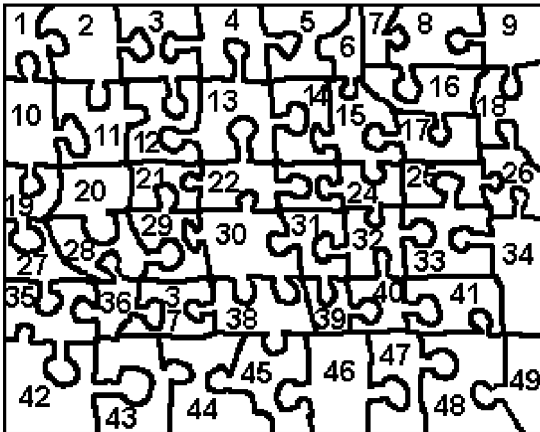
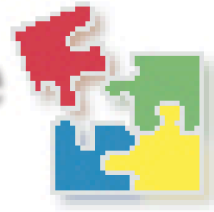


## Here's your challenge:

Below are genetic jigsaw puzzles for 12 members of your Whirling disorder family. Each puzzle has a number that corresponds to an individual in the pedigree above. Your job is to find the puzzle piece (or gene) that is responsible for Whirling disorder.

			
1	2	3	4
			
5	6	7	8
			
9	10	11	12

# Finding a Gene on the Chromosome Map



1. Which puzzle piece is responsible for Whirling disorder? Explain your answer.

2. Is the inheritance pattern for Whirling disorder dominant or recessive? autosomal or sex-linked? Explain your answer.

The jigsaw puzzles for individuals A, B, C, and D in the pedigree below were not given. Imagine what their puzzles would look like, and determine what color(s) the puzzle pieces should be. Explain your answers on the back.

3. For person "A", the colors of the puzzle pieces should be:  
 a. dark blue  
 b. 1/2 dark blue, 1/2 red  
 c. 1/2 light green, 1/2 dark blue

4. For person "B", the colors of the puzzle pieces should be:  
 a. red  
 b. dark blue  
 c. pink  
 d. light blue

5. For person "C", the colors of the puzzle pieces should be:  
 a. red  
 b. 1/2 dark green, 1/2 yellow  
 c. dark green  
 d. yellow

6. For person "D", the colors of the puzzle pieces should be:  
 a. 1/2 dark green, 1/4 red, 1/4 dark blue  
 b. 1/2 dark green, 1/2 red  
 c. 1/4 yellow, 1/4 dark green, 1/4 red, 1/4 dark blue  
 d. 1/2 red, 1/2 dark blue

