Finding a Gene on the Chromosome Map

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.

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.

Estimated time

- Class time 20 minutes
- Prep time 15 minutes

Materials

Copies of student handouts

- Color copies of pages 1-2

  (or you may want to project enlarged versions of pedigree and puzzles for the whole class)

- Copies of page 3 for each student

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 (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.

Instructions

1. 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.

2. 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.

3. 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.

4. 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.

5. 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.

6. 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.

a. Ask students to read the background information on student sheet

b. 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.

c. 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.

d. 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.

7. Once students have completed the activity, ask one of the students to explain the logic he or she

used to come to this conclusion.

8. 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.

9. Assess students' understanding of inheritance by asking them to answer the questions found on pages 2-3 of the student sheet.

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.
- 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 screening infants for genetic disorders.

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.

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