

Are the Voices in the Genes — Schizophrenia

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 – 12

Teaching materials developed by VCU Life Sciences.

V i r g i n i a C o m m o n w e a l t h U n i v e r s i t y

Classroom Tested Lesson

Video Description

“Secrets of the Sequence,” Show 147, Episode 3

“Are The Voices in the Genes: Schizophrenia ” – approximately 9 minutes viewing time.

Schizophrenia is a mysterious, tragic brain disease that affects 24 million adults worldwide with hallucinations, delusions and other symptoms. Keafer understands the disease first hand – he has it. Like most victims of the disease he was diagnosed when he was in his late teens and has often wondered, “why me?” Is it genetic or environmental? Researchers are closing in on the cause.

Ward Television

Producer: Kip Prestholdt

Associate Producer: Luke Cline

Featuring: Dr. Anand Pandurangi, Psychiatrist, Virginia Commonwealth University, Dr. Kenneth Kendler, Psychiatry, Virginia Commonwealth University, Dr. Richard Straub, National Institute of Mental Health, Dr. Kari Stefansson, Founder and CEO, deCODE genetics.

Lesson Author; Reviewers: Beth Richert; Catherine Dahl and Dick Rezba, Kieron Torres

Trial Testing Teachers: Regina Ahmann, Amanda Stewart, Judy McOsker

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry

As a result of their activities in grades 9-12, all students should develop:

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science

As a result of their activities in grades 9-12, all students should develop understanding of the cell

- Molecular basis of heredity
- Behavior of organisms

Content Standard F: Science in Personal and Social Perspectives

As a result of their activities in grades 9-12, all students should develop understanding of

- Personal and community health

Selected State Science Standards Connections

Use <http://www.eduhound.com> (click on "Standards by State") or a search engine to access additional state science standards.

Illinois

STATE GOAL 11: Understand the processes of scientific inquiry and technological design to investigate questions, conduct experiments and solve problems.

- 11.A.5a Formulate hypotheses referencing prior research and knowledge.
- 11.A.5b Design procedures to test the selected hypotheses.
- 11.A.5c Conduct systematic controlled experiments to test the selected hypotheses.
- STATE GOAL 12: Understand the fundamental concepts, principles and interconnections of the life, physical and earth/space sciences
- 12.A.5b Analyze the transmission of genetic traits, diseases and defects.
- STATE GOAL 13: Understand the relationships among science, technology and society in historical and contemporary contexts
- 13.A.5b Explain criteria that scientists use to evaluate the validity of scientific claims and theories.

Oklahoma

Priority Academic Student Skills Oklahoma State Department of Education 4 Science-High School

Process Standard 4: Interpret and Communicate

- Select appropriate predictions based on previously observed patterns of evidence.

BIOLOGY I Standard 2: The Molecular Basis of Heredity

- Cells function according to the information contained in the master code of DNA (i.e., cell cycle, DNA to DNA, and DNA to RNA). Transfer RNA and protein synthesis will be taught in life science courses with rigor greater than Biology I.
- A sorting and recombination of genes in reproduction results in a great variety of possible gene combinations from the offspring of any two parents (i.e., Punnett squares and pedigrees). Students will understand the following concepts in a single trait cross: alleles, dominant trait, recessive trait, phenotype, genotype, homozygous, and heterozygous.

Overview

People used to think mental illness was caused by external factors, but researchers are now recognizing that there is a genetic basis for schizophrenia. Schizophrenia is a mental disorder characterized by separation between thought and emotions, and by delusions, hallucinations, and bizarre behavior. It is a little understood chronic brain disease with a long-term diagnosis. It afflicts the young, usually ages 15-25 and affects them all their life. Typically the victim has led a perfectly normal life up to onset of the illness when symptoms suddenly appear.

Testing: A sample related multiple choice item from State Standardized Exams

Dr. F. Agnes Stroud-Lee determines the origins of birth defects by studying chromosome abnormalities. Dr. Stroud-Lee's research could involve all of these topics **EXCEPT** —

- A. chemicals that alter the DNA arrangement
- B. plants that show variable rates of photosynthesis *
- C. radiation that can pass through cytoplasm
- D. mitosis that produces multiple copies of genetic material

Source: Texas Education Agency, 2000

Video Preparation

Preview the video and make note of the locations at which you will later pause the video for discussion.

Before Viewing

1. Ask the students if they have seen the movie, "A Beautiful Mind", which is about John Nash, a Princeton Mathematician, who has schizophrenia. Discuss the movie and their reactions to it. The movie trailer from "A Beautiful Mind" can be found at <http://videodetective.com/home.asp?PublishedID=912182>.
Note: There is a commercial while the video is downloading, so you might want to download it beforehand.
2. Ask: What does the word lunatic mean and where does it come from?
A person who is insane . Luna is Latin for moon; ancient lore suggested that the full moon could make a person crazy.
3. Ask: What kinds of mental illness have you heard about?
 - *Multiple disorders*
 - *Depression*
 - *Schizophrenia*
 - *Chronic paranoia*
 - *Psychosis*
 - *Phobia*
4. Have a student look up the word schizophrenia to determine its derivation and meaning and share it with the class (*from the Greek, schizein = cleave, and phren = mind; a mental disorder characterized by separation between thought and emotion*).
5. Ask: What do you know about schizophrenia and what are some of the symptoms you would expect for someone suffering from this disease? List their responses on the board and then ask students to watch the video carefully to check that you have them all.
 - *Depression*
 - *Hearing multiple voices*
 - *Disturbances in thinking*
 - *Delusions*
6. Ask: Are all hallucinations unpleasant? If not, is there still a potential for pleasant hallucinations to be dangerous?
7. A trial test teacher suggested bringing in a news clipping of a specific case (such as Andrea Yates) to discuss a "real" condition.

During Viewing

1. **START** the video.
2. **PAUSE** the video (5:38 minutes into the video) after the scientist says, "... we can develop more efficient and quicker ways of getting at these genes."
Tell the students: You have just viewed a section of the video describing how researchers have found a gene on Chromosome 6 called Dyspyndin concentrated in an area of the brain previously associated with schizophrenia.

Ask: What is the term used to describe the process of linking a gene with a particular disease and what is the significance of this identification?

Linkage analysis- once a specific gene can be linked to a disease such as this disease of the brain, there is hope that a drug could be designed to more effectively treat that particular area of the brain where the gene is expressed.

NOTE: Because this section of the video on linkage analysis comes right after a good description of how an international research team studied 1000 families in Ireland, you may also want to have a discussion on scientific research methodology.

3. **OPTIONAL PAUSE** suggested by trial test teacher (6.53 minutes into the video) after Dr. Kenneth Kendler says, "... and that the chances of being able to develop treatments that we can't even dream of now is what is really exciting; that's the eventual payoff."

Ask: Do you think research institutions work with or against each other?

They work together because they publish information that adds to the body of knowledge we call science; however, they also work against each other for funding and recognition of new breakthroughs.

4. **RESUME** the video and play to the end.

After Viewing

1. Stigmas were mentioned at the end of the video. Discuss with the students what a stigma means to them and then ask the following questions.
 - Did you have any preconceived notions or possible misconceptions of patients with schizophrenia?
 - How did the video help to change your views of those patients?
 - Who are some other individuals in our society that are stigmatized?
 - Are the stigmas always correct?
2. Have students look at some chromosome maps (Go to <http://k-12.pisd.edu/currInst/science/Genetic/Chromosome-Maps.htm> or <http://www.ncbi.nlm.nih.gov/mapview/maps.cgi?ORG=hum&MAPS=ideogr,est,loc&LINKS=ON&VERBOSE=ON&CHR=21#summary>) in order to see the sheer number and complexity of genes on each individual chromosome. This will help make the genes "real" to the student. For example, you could even direct students to the second website and click on a map of chromosome 21 and point to where Downs syndrome is associated with a particular gene on that chromosome.
3. Have students do additional research on schizophrenia in the library and on the Internet.
4. Consider reading a story about someone who suffers from schizophrenia firsthand. These are available on the Internet, as is the story of John Nash, the mathematician in "A Beautiful Mind."

Teacher Notes for the Student Activity: Finding a Gene on the Chromosome map

This activity uses the analogy of a puzzle to assist learners in understanding how scientists use genetic information from individuals in a family to locate genes that cause genetic disorders. In the case of schizophrenia, locating the gene on a particular chromosome would allow for better treatment and diagnosis for the disease. The first part of the activity can be used to provide beginning learners with experience reading and interpreting a pedigree. The remainder of the activity teaches students how locating genes is similar to finding a piece of a jigsaw puzzle. Additional questions provide a challenge for more advanced learners.

Equipment and Materials

A. For use as an Internet-based activity: Access to computers with Internet connections and the following URL:

<http://gslc.genetics.utah.edu/units/disorders/pedigree/>

B. For use as a paper-based activity:

The following paper version activity is adapted from the Internet activities at the Genetic Science Learning Center at the Eccles Institute of Human Genetics, University of Utah.

<http://gslc.genetics.utah.edu/units/disorders/pedigree/>

Make reusable color copies of the student handout for each student. Color copies are needed; otherwise this activity cannot be done by students because they will be unable to identify specific pieces of the puzzles. You may want to put these handouts in plastic sleeves or laminate them for reuse. As a separate handout, copy the Answer Sheet for students to complete and submit.

Procedure

1. Tell the students that this activity will give them an idea about how scientists map chromosomes and predict inheritance. Scientists trace phenotypes to certain chromosomes and then more specifically to genes on that chromosome.
2. Beginning-level students can complete the first part of the activity; while more advanced students will be challenged by the additional questions. Warn students that everyone sees things differently and that they are all different in terms of problem-solving skills. Some will get it immediately – they need to keep the answer quiet! Others need to keep working and not give up.
3. Have students work individually or in pairs to decide which puzzle piece contains the gene responsible for *whirling disorder*, a fictional genetic disease that is inherited similarly to schizophrenia.
4. For those students using the Internet, have them read the page entitled *Finding a Gene on the Chromosome Map* and then instruct them to click on the activity in the box on the right side of the Web page – *Find the gene for Whirling Disorder*.
5. Some students may need additional help. Ask them to begin and circulate among them to determine their success or frustration. Use the hints below as needed to insure student success.

NOTE: Most of this lesson refers to looking at a specific gene on a chromosome. Students may question the fact that each gene has 2 alleles and whether they are at the same position on the chromosome, which they would be.

Answer Key to the questions on the Student Handout

Which puzzle piece is responsible for Whirling Disorder? Number 36

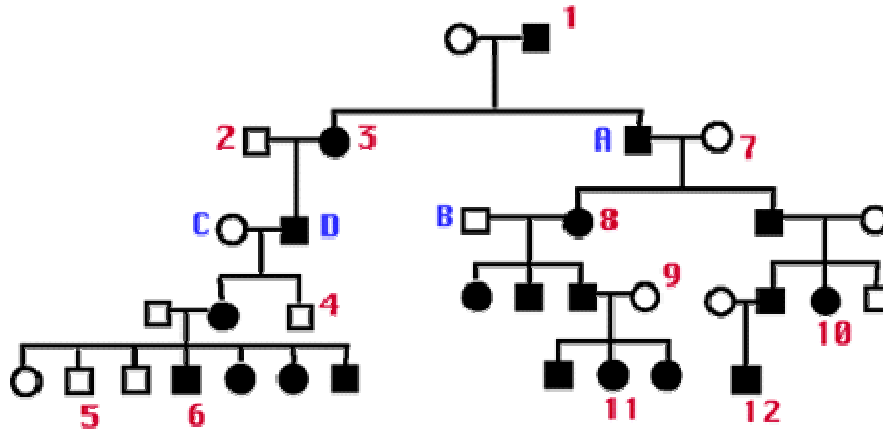
Hints for students: *The key to this problem is the puzzle piece containing the gene must be the same color in every affected individual and a different color in every unaffected individual. There is only one puzzle piece that fits those criteria: #36. All of the affected individuals (1, 3, 6, 8, 10, 11 and 12) share a red #36 puzzle piece.*

One way to solve this problem: *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; puzzle 11 has four. Piece #36 is the only red piece shared by all three of these puzzles. Confirm that it is also found in the other infected individuals 3, 8, 10.*

Additional Questions

1. Is whirling disorder dominant or recessive?

*It is very likely inherited in a dominant manner. Approximately half of all the children born to a parent with whirling disorder also show the effects of the mutation. However, it is possible that whirling disorder is recessively inherited. If the disorder were recessive, every unaffected individual who married into this family would have to be a carrier of the mutant whirling gene, **which is highly unlikely**. Because we do not know which individuals are carriers of the whirling allele from the data in this pedigree, we cannot be 100% certain. All we know is which individuals show the whirling phenotype.*



2. Is this disorder sex-linked?

The fact that approximately equal numbers of males and females are affected by whirling disorder indicates that the whirling gene is not sex-linked. If the whirling gene were sex-linked on the X chromosome, then fathers with the disorder would contribute the whirling gene to all of their daughters (to whom they contribute a X chromosome,) but never to their sons (to whom they contribute a Y chromosome). This is not what the pedigree shows. Also if the whirling gene were sex-linked, then mothers with the disorder would contribute the whirling gene equally to their sons and daughters (to whom they contribute an X chromosome), which is also not what the pedigree shows. Therefore because the gene is not sex-linked, it must be found on an autosome (any chromosome other than X or Y).

3. For person "A", the colors of the puzzle pieces are:

b. $\frac{1}{2}$ dark blue, $\frac{1}{2}$ red

Individual A's father has all red puzzle pieces, so half of A's pieces are red. We do not know what color(s) A's mother had without looking at A's daughter. Individual A's daughter has approximately $\frac{1}{2}$ light green puzzle pieces from her mother (Individual 7) as well as approximately $\frac{1}{4}$ red pieces and $\frac{1}{4}$ dark blue pieces. Because her mother 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) puzzle pieces.

4. For person "B", the colors of the puzzle pieces are:

c. **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. 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 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 are:

d. **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. Because approximately half 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 are:

a) **$\frac{1}{2}$ dark green, $\frac{1}{4}$ red, $\frac{1}{4}$ dark blue**

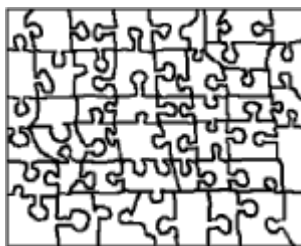
Individual D's father had all dark green puzzle pieces, therefore individual D has $\frac{1}{2}$ dark green pieces. Individual D's mother had $\frac{1}{2}$ red and $\frac{1}{2}$ dark blue puzzle pieces. Because individual D received $\frac{1}{2}$ of his puzzle pieces from his mother, he has $\frac{1}{4}$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

Student Handout: Find the Gene for Whirling Disorder

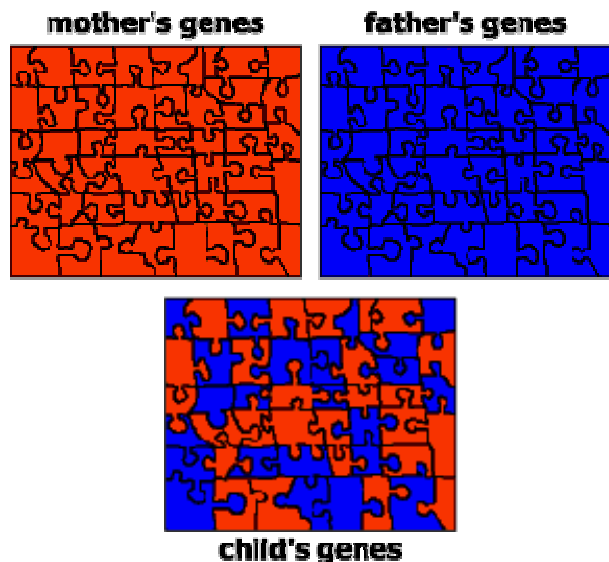
Introduction

You are a scientist who has noticed that a particular genetic disorder runs in families. You want to find the gene responsible for it. First, you identify a large family, in which some individuals have the disorder, and others do not. 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: If the genetic information in each family member were like a jigsaw puzzle, then each puzzle piece would represent a set of genes organized in a specific way, similar to a chromosome. 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. A generic human jigsaw puzzle might look like this (see picture below).



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 among family members. 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. What might a family's puzzles look like? Look at the family of jigsaw puzzles below.

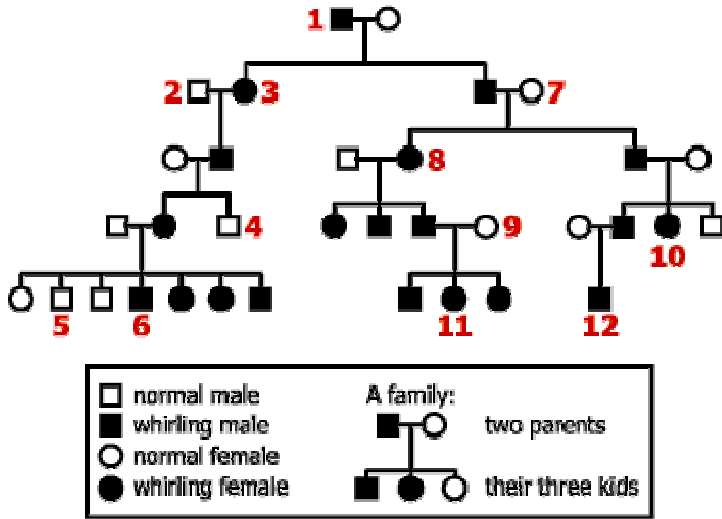


Can you see how some of the child's genes come from one parent and some from the other parent? The child receives exactly half of its genetic information from the mother and exactly half from the father. The genes the child receives from each parent are random, based on the principle of independent assortment. Looking at things this way, can you see how you might identify a genetic link in paternity suits, where a genetic connection is sought between a child and a possible father? Half of the child's puzzle pieces must be the same as the father's.

Procedure

When individuals afflicted with Whirling Disorder hear old Rolling Stones songs, they let loose and dance uncontrollably.

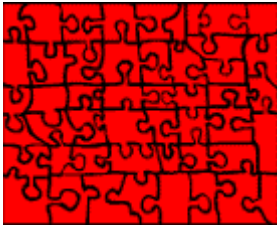
As a geneticist studying "Whirling Disorder", you have identified a large family in which some individuals have the disorder, and others do not. For this family, you have already drawn a pedigree. A pedigree is a diagram that shows how family members are related and which individuals have Whirling Disorder:



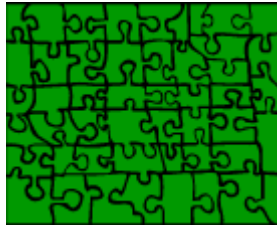
Here's your challenge

Below, you'll find genetic jigsaw puzzles for 12 members of the 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 that is responsible for Whirling Disorder.

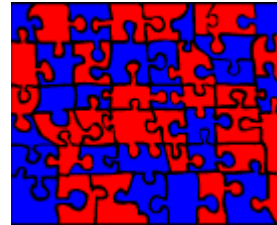
1



2



3



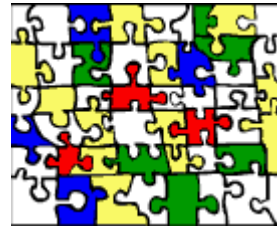
4



5



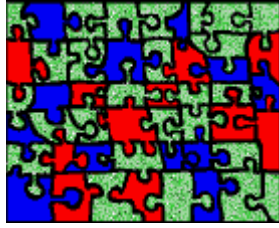
6



7



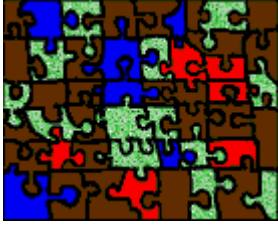
8



9



10



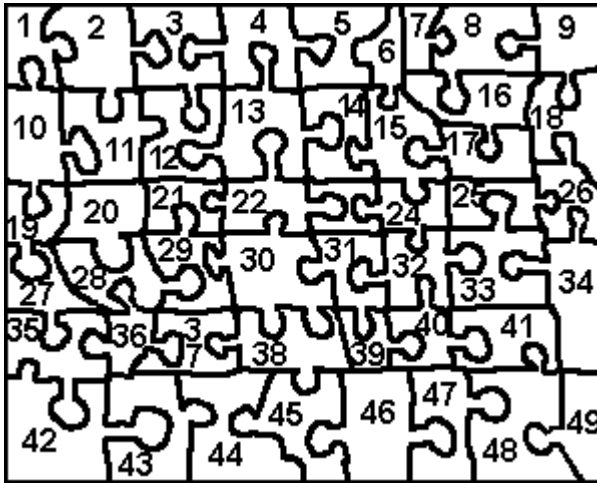
11



12



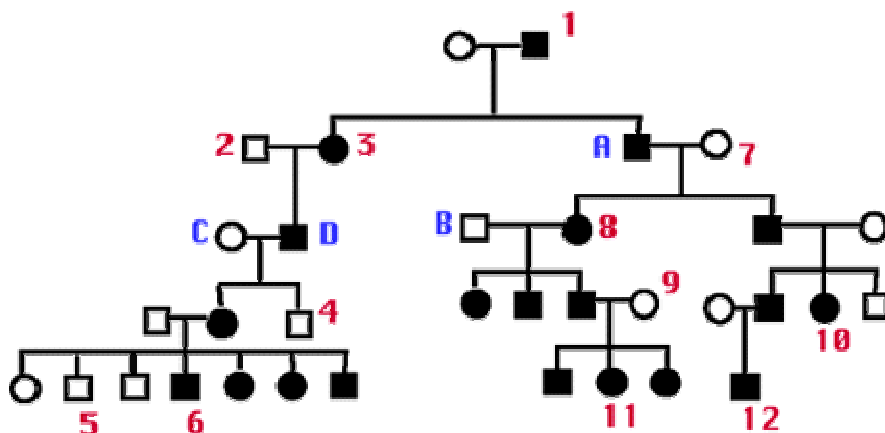
Which puzzle piece is responsible for Whirling Disorder? (Record on Answer sheet)



Name _____

Student Handout: Answer Sheet

Which puzzle piece was responsible for whirling disorder? _____ On the back of this paper, describe how you came up with that conclusion.



1. Is whirling disorder dominant or recessive? _____
2. Is this disorder sex-linked? _____
3. For person "A", what are the colors of the puzzle pieces? Circle your answer.
 - a) dark blue
 - b) $\frac{1}{2}$ dark blue, $\frac{1}{2}$ red
 - c) $\frac{1}{2}$ light green, $\frac{1}{2}$ dark blue
4. For person "B", what are the colors of the puzzle pieces? Circle your answer.
 - a) red
 - b) dark blue
 - c) pink
5. For person "C", what are the colors of the puzzle pieces? Circle your answer.
 - a) red
 - b) $\frac{1}{2}$ dark green, $\frac{1}{2}$ yellow
 - c) dark green
 - d) yellow
6. For person "D", what are the colors of the puzzle pieces? Circle your answer.
 - a) $\frac{1}{2}$ dark green, $\frac{1}{4}$ red, $\frac{1}{4}$ dark blue
 - b) $\frac{1}{2}$ dark green, $\frac{1}{2}$ red
 - c) $\frac{1}{4}$ yellow, $\frac{1}{4}$ dark green, $\frac{1}{4}$ red, $\frac{1}{4}$ dark blue
 - d) $\frac{1}{2}$ red, $\frac{1}{2}$ dark blue

Source: Internet activities at the Genetic Science Learning Center at the Eccles Institute of Human Genetics, University of Utah. <http://gslc.genetics.utah.edu/units/disorders/pedigree/>

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to generate new Web sites.

The activity in this lesson is adapted from the activities at the Genetic Science Learning Center at the Eccles Institute of Human Genetics, University of Utah. <http://gslc.genetics.utah.edu/units/disorders/pedigree/>

For additional activities please click on the following URL:

<http://gslc.genetics.utah.edu/>

Fact about Schizophrenia

<http://www.mayoclinic.com/invoke.cfm?objectid=5D4E015A-B256-4F25-B5AFBC00F1B4E886&si=2525&WT.srch=1>

Official Website (includes success stories)

<http://www.schizophrenia.com/>

Gene Testing

http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetest.shtml

Other Genetic Nervous System Disorders

http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetest.shtml

Firsthand stories about schizophrenia:

<http://www.psychlaws.org/GeneralResources/article35.htm>

<http://mentalhealth.about.com/gi/dynamic/offsite.htm?zi=1/XJ&sdn=mentalhealth&zu=http%3A%2F%2Fwww.mentalhealth.com%2Fstory%2Fp52-sc03.html>

Genomic Revolution The Web site to the government-funded Human Genome Project with links about genomics, the history of the project, and more.

http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtml

Secrets of the Sequence Videos and Lessons

This video and 49 others with their accompanying lessons are available *at no charge* from

www.vcu.edu/lifesci/sosq