



Lesson 3: Genetics: Cancer Genetics

Lesson Summary:

In this lesson, students revisit the story of Steve and Nikki, who are learning more about the role genetics can play in cancer risk. Students engage with a brief history of advances in cancer research since the 1950s. They are introduced to the BRCA1 and BRCA2 genes and how substitutions, additions, and deletions in their underlying genetic code lead to mutated genes with changed function. Students practice transcribing and translating the DNA strand into amino acid sequences for both normal and mutated genes and compare them.

Next, students learn about genetic counseling and how family history of cancer influences cancer risk. They role-play a genetic counseling session and chart a family history to analyze the cancer risk of Steve and Nikki's parents. As their homework, students look at their own family history as an example.

Finally, students learn about genetic testing, including an exploration of two methods: gel electrophoresis and Sanger sequencing.

Lesson Duration: One or two 45-60-minute class periods

How to Use This Guide

This lesson plan was created to aid instructors in planning their lesson. It provides slide-by-slide details so educators will be prepared to engage, explain, discuss, and analyze every part of the lesson. The lesson is designed to be two 45-60-minute class periods, but it is flexible, depending on the students' needs and time available. Note there are several activities that are optional and can be deleted or modified for specific classroom needs. All handouts are included in this guide, as well as additional resources for more learning activity ideas.

Objectives:

- Upon completion of this lesson, students will be able to:
- Describe the history of cancer research and related technological advances
- Summarize the relationships among DNA, genes, and chromosomes
- Examine the effects of different mutations on gene sequences and resulting proteins
- Transcribe and translate genetic sequences
- Explain the role of family history in determining cancer risk
- Describe genetic counseling
- Discuss genetic testing
- Describe and analyze gel electrophoresis
- Interpret a family tree and discuss inherited traits





Materials:

- Handout: Genetics Review Worksheet (optional prep assignment)
- Handout: Cancer Innovations and Pop Culture Events cards
- Handout: BRCA1 Protein
- Handout: BRCA2 Protein
- Handout: Genetic Mutations Worksheet
- Handout: Codon Chart
- Handout: Williams Family Pedigree
- Handout: Williams Family Pedigree Analysis
- Handout: Genetic Counseling Script
- Handout: Sample Patient Letter
- Handout: Gel Electrophoresis Simulation Worksheet
- Handout: Genetic Test Results
- <u>Activity Instructions: Gel Electrophoresis Activity</u>
- Homework assignment: My Family Health Portrait website:
 - https://familyhistory.hhs.gov/FHH/html/index.html
- Virtual Lab: Gel Electrophoresis
 - o http://learn.genetics.utah.edu/content/labs/gel/
 - Video: Sanger Sequencing Presentation
 - o http://www.yourgenome.org/teachers/sequencing.shtml
- Lesson 3 Quiz
- Answer Keys
- Interactive white board (optional)
- Computer with Internet access/LCD projector

Subjects:

- Health
- Language Arts and Literacy
- Science

Vocabulary:

allele, amino acid, BRCA1, BRCA2, carrier, codon, deletion, DNA, DNA sequencing, dominant, family health history, founder mutation, frameshift mutation, gel electrophoresis, gene, gene expression, genetic counselor, genetic testing, genetics, genotype, heredity, heterozygous, homozygous, insertion, mRNA mutagen, mutation, nucleic acid, nucleotide, peptide bond, phenotype, point mutation, Polymerase Chain Reaction (PCR), protein, recessive, ribosome, RNA transcription, trait, translation





Advance Preparation:

Day 1

Real-World Scenario-Steve and Nikki

• Review Steve and Nikki's real-world scenarios in all of the lessons so that you can effectively use their story in the classroom.

Genetics Review Worksheet (optional pre-work)

• Make one copy per student of the Genetics Review Worksheet. This can be assigned in advance as a homework assignment as a refresher or introduction to genetics terminology. If used, this should be reviewed at the start of Day 1.

Timeline of Cancer Research Innovations

• Make several copies of the Cancer Innovations Cards and Pop Culture Events Cards, one copy per group of students (3–5 students per group). The correct answers for class review are on the Cancer Innovations Handout.

Translation and Transcription Activity

- Make 1 copy per student (or alternatively, one per group of 3–5 students) of the blank Genetic Mutations Worksheet and the Codon Chart handout for the genetic mutations activity. The codon chart can also be projected for the whole class, if this activity is done during class time.
- Make several copies of the BRCA1 and BRCA 2 Sequence Handouts to distribute to groups during the founder mutations activity.

Create and Analyze a Family History

• Make 1 copy per group of the blank (partially filled out) Williams Family Pedigree and Williams Family Pedigree Analysis Handout for students to complete in class or as homework.

Day 2

Role Play a Genetic Counseling Session

- Make one copy per three students of the Genetic Counseling Script.
- Optional: Make only one copy for the trio of students who role-play the script for the entire class.

Homework: Write a Letter to Mr. and Mrs. Williams

• Print one copy per student of the Sample Patient Letter for students to use for their homework.

Gel Electrophoresis Lab

- Review the Gel Electrophoresis Virtual Lab
 (http://document.org/laba/gel/
 - (http://learn.genetics.utah.edu/content/labs/gel/) to ensure it will work in the classroom.
- Make one copy per student of the Gel Electrophoresis Simulation Worksheet for students to complete as they go through the Lab.
- Life-Size Gel Electrophoresis Activity (Optional)
- Print and review the Gel Electrophoresis Activity supplement for this optional classroom activity simulating gel electrophoresis.

Sanger Sequencing Presentation

 Review the presentation video; ensure LCD projector works properly http://www.yourgenome.org/teachers/sequencing.shtml

Analyze Genetic Test Results

• Print one copy per student of the Genetic Test Results for Mr. and Mrs. Williams for students.





Career Connection

- Physician
- Genetic Counselor
- Researcher

A Note for the Teacher about Cancer

Cancer is a disease that unfortunately touches many people. You may have students with a parent, guardian, or loved one affected by cancer. Adolescents affected by cancer cope in their own ways. Some students may want to share their personal experiences, while others may not. Reassure students that you want them to be comfortable in the classroom and will not require them to share any personal or private experiences.

You may learn a student is personally affected prior to or while implementing the curriculum. If you discover a student is affected by cancer, speak with them privately and make sure they are comfortable with participating in the learning activities, discussions, and explorations.

If you know a student is affected by cancer prior to starting the curriculum:

• Give the student a brief summary of the lessons, and ask how they feel about it. Tell the student it may not bother them now, but they should let you know if it does.

If you learn a student is affected by cancer while implementing the curriculum:

• Ask whom they have spoken with about the cancer. If the answer is no one, ask if they would like to talk to someone, such as a guidance counselor or other trusted adult.

Connect students with support. Possible sources include the following:

- Guidance counselors
- Family friends
- Family doctors or pediatricians
- Faith-based counselors

Look for warning signs. Keep an eye out for signs of distress, such as

- Changes in academic performance
- Changes in behavior with other students
- Evidence of alcohol or drug use
- Evidence of anxiety or depression





Lesson 3 Plan – Day 1: Cancer Genetics

Optional Pre-Lesson Prep: Genetics Review Worksheet

• [Slides 1–2] Distribute the optional pre-lesson prep assignment, the Genetics Review Worksheet. If you have covered genetics in class already, students may be able to do this entirely on their own; if not, it can be paired with a relevant reading from a biology text or web resource to help them complete the two-page fill-in-the-blank worksheet.

ENGAGE

Scenario: Steve and Nikki

- [Slide 5] Reintroduce Steve and Nikki. They know about their mother's diagnosis and have been learning about the role of genetic factors in her breast cancer.
- [Slide 6] Learning Activity: Small Group Brainstorm. Review the connection between Steve's message and what the class knows so far about genetics and cancer.
 - Divide the class into small groups and have students brainstorm their thoughts about Steve's questions. Ask each group to organize their thoughts and decide how to respond to Steve's questions below. Assign roles, such as a recorder, if needed.
 - What does a gene have to do with cancer?
 - How do they even know it exists?
 - Did my mom get it from her mom?
 - Can Nikki get it?
 - Do not be too concerned with what students write at this point. This is meant to be an open-ended activity to assess what students know about genetics and cancer.

EXPLORE

Advances in Cancer Activity

- [Slides 7–8] To introduce the timeline activity and elicit students' prior knowledge, take about 5 minutes to ask students what they think have been some of the major discoveries in cancer research.
 - Tell the class they will be doing an activity to create a timeline of cancer innovations.
 - o For any discoveries they propose, ask if they know the approximate time period (e.g., double helix structure discovered → 1950s). Write students' ideas on the board.
 - Divide the class into small groups. Give each group one set of <u>Cancer</u> <u>Innovations Cards and Pop Culture Events Cards</u>. Tell the groups to match each innovation card with a pop culture event card and put them in order from oldest to most recent. Students should use their knowledge of genetics to order the innovations, but the pop culture events can provide hints.
 - After groups have finished, review the correct sequence and highlight what year the innovations and pop culture events occurred.





• **Note:** The correct sequence is in a separate handout with the cards.

EXPLAIN

Breast Cancer Genetics: BRCA1 and BRCA2

- [Slides 9–10] Introduce BRCA1 and BRCA2, which were discovered in 1990 and 1994 respectively. BRCA1 is on chromosome 17 and BRCA2 is on chromosome 13.
- [Slides 11–14] Each slide has a blank for which you can call on students to fill in:
 - Slide 11: BRCA1 and BRCA2 are <u>tumor suppressor genes</u>, normally expressed in cells of breast and other tissue.
 - Slide 12: Both genes play an important role in repair of <u>DNA double strand</u> <u>breaks</u>.
 - Slide 13: These genes themselves are normal. <u>Mutations</u> of these genes are abnormal.
 - Slide 14: There are approximately <u>2.000 known mutations</u> of BRCA1 and BRCA2.
- [Slides 15–19] Introduce the key metaphor that a body's DNA is like a complex recipe in a cookbook.
 - The DNA is the instructions.
 - The bases are the ingredients.
 - Proteins are the end result, like a cake.
 - There can be substitutions, deletions, and additions to the recipe ingredients, all of which will change the resultant protein in some way.
 - Some of the changes will not make a big difference; others will have a significant difference in effect (such as substituting applesauce versus broccoli for oil).
 - $\circ~$ Since the BRCA genes are tumor suppressor genes, mutations can increase risk for tumors and cancer.

Genetic Mutations Activity

- [Slide 20] Explain the process by which DNA code leads to the creation of a protein:
 - The code is **transcribed** into RNA code.
 - The code is then **translated** at the ribosome into an amino acid code.
 - The amino acid is created based on this code.
- [Slide 21] Distribute copies of the <u>BRCA1 and BRCA2 protein sequences</u>, several copies of the <u>Genetics Mutations worksheet</u>, and the <u>Codon Chart</u>. (You can also project these using the overhead projector.)
 - Review the blank <u>Genetic Mutations worksheet</u> with the class. You can complete the worksheets as a class, or divide students into groups to complete it together.
 - Explain how the BRCA1 mutation 187delAG is notated and what each symbol means.





- Walk through the process of finding the normal (non-mutated) sequence for part of the BRCA1 gene.
 - [Slide 22] Locate the 187th nucleotide to begin the sequence. This is the coding strand DNA or **sense strand**.
 - [Slide 23] Explain that the **anti-sense strand** is a mirror image of the sense strand, completing the base pair.
 - \circ $\,$ Use the table to replicate the sense strand into the anti-sense strand.
 - [Slide 24] Use table to **transcribe** the anti-sense strand into an **mRNA** sequence.
 - [Slide 25] Use the <u>codon chart</u> to translate each codon in the mRNA sequence into an amino acid. For example, GGU \rightarrow glycine.
 - [Slide 26] Make a note of the final amino acid sequence; this is the sequence for the non-mutated BRCA1 gene.
- Now repeat this process for the mutated gene, using 187delAG. Ask the class for answers to portions of the process this second time through.
 - [Slide 27] Begin the process again using the mutated sequence. Find the sense strand.
 - [Slide 28] Replicate the mutated coding strand to find the anti-sense strand. Then transcribe the anti-sense strand into mRNA.
 - [Slide 29] Use the codon chart to translate the mutated mRNA codons into the amino acid sequence.
 - Note: This is a good place to remind students the difference between **transcription** and **translation**:
 - **Transcription** is the process by which the anti-sense strand is converted to an mRNA sequence.
 - **Translation** is the process by which mRNA codons are converted into an amino acid sequence.
 - [Slide 30] Once you have completed translating the mutated sequence, compare the normal and mutated amino acid sequences.
 - Ask the class what effects they observe as a result of the mutation.
 - Note that compared to the normal BRCA1 protein, the mutated amino acid sequence has been changed and shortened. The resulting protein will also be shortened (truncated) and may not function properly.

Group Activity: Explore Founder Mutations

- [Slide 31] Explain what founder mutations are and present them in the table of example founder mutations identified in BRCA1 and BRCA2.
 - Distribute the <u>BRCA1 and BRCA2 DNA Sequence handouts</u> if you have not already. Note that the sequences in the handouts are abbreviated from the complete nucleotide sequence.
 - Assign each group 2–3 mutations from the table to investigate, not including 187delAG, which you have already translated. You may also allow groups to choose their mutation to analyze.





- Some mutations may not list deleted bases; for example, in BRCA2 mutation 1536del4, four bases are deleted, beginning at position 1536.
- Some mutations are insertions: for example, in the BRCA1 mutation 1136insA, an A is inserted at the 1136th position.
- Note: If class time is running short, you may want to assign this activity as homework. Have each student choose 1–2 mutations to investigate and compare with the normal version of the gene. Tell them to come prepared to show the differences between the normal and mutated genes and discuss the possible effects of these differences.

ELABORATE

Introduction to Genetic Counseling

- [Slide 32] Learning Activity: Class Discussion. Ask students if they have ever heard of genetic counselors, using the questions on the slide as a guide. Record students' preconceptions on a whiteboard or overhead.
 - What do you know about genetic counseling?
 - What is its purpose?
 - What information do genetic counselors use to make recommendations?
- [Slide 33] Explain what genetic counselors do, starting with genetic counselors in general (left column) and continuing to cancer genetic counselors (right column), who are more specialized in cancer-specific counseling.
- [Slides 34–35] Reintroduce the scenario of Steve and Nikki. Their parents visited a genetic counselor for advice regarding genetic tests associated with cancer. Steve writes an e-mail to the counselor to ask some questions:
 - If mom's cancer may have been genetic, does that mean I have this mutated BRCA gene?
 - How does a family tree work?
 - \circ $\;$ What information do I have to gather to fill out the tree?
- [Slide 35] Learning Activity: Think-Pair-Share Activity. Divide the class into small groups (2–3 students) and have them brainstorm responses to Steve's e-mail for 1-2 minutes.
 - $\circ\;$ Ask each group to organize their thoughts and decide how they would respond to Steve.
 - Assign roles, such as recorder, if needed.
 - Debrief the activity by asking groups what information they came up with. Record the information on a whiteboard or projector.
 - Do not be too concerned about what students write at this point; this is meant to be an open-ended activity to assess students' preconceptions about cancer.





Family History Discussion

- [Slide 36] Ask students to compare their responses to Steve's questions with those of the genetic counselor, Ms. Smith. Go over the important information in a family pedigree needed in order to begin an analysis of a family's cancer risk:
 - History of cancer in the family and number of generations affected (If cancer is found in every generation, there is a greater possibility that a genetic mutation is present.)
 - Types of cancer present (Certain genetic mutations are associated with more than one type of cancer. For example, BRCA2 mutations cause increased risk of breast and ovarian cancer in women and breast and prostate cancer in males. Therefore, if these types of cancer are present in one family, there may be a BRCA mutation present.)
 - Age of cancer diagnosis (Since the main risk factor for cancer is age, a diagnosis of cancer before age 50 strongly suggests there may be an inherited genetic mutation present.)
 - Multiple cancers in one generation
 - Other causes of death
 - Current age or age of death
- Note to students that not all cases of breast cancer are caused by an inherited mutation; only 5–10 percent of breast cancer is inherited. Most cancer may be the result of environmental exposures, or a combination of both genetic and environmental factors.

Group Discussion and Activity: Williams Family Pedigree

- [Slides 37–38] Explain to students that they will use the family history information that Nikki found to complete a pedigree of the Williams family.
- [Slide 39] Learning Activity: Discussion. Distribute copies of the <u>Incomplete Williams</u> <u>Family Pedigree</u> and ask students to fill in the missing information in small groups or as a class. As a class, discuss relevant information from the incomplete Williams Family Pedigree worksheet, including the following:
 - History of cancer in the family and number of generations affected (If cancer is found in every generation, there is a greater possibility that a genetic mutation is present.)
 - Types of cancer present (Certain genetic mutations are associated with more than one type of cancer. For example, BRCA2 mutations cause increased risk of breast and ovarian cancer in women and breast and prostate cancer in males. Therefore, if these types of cancer are present in one family, there may be a BRCA mutation present.)
 - Age of cancer diagnosis (Since the main risk factor for cancer is age, a diagnosis of cancer before age 50 strongly suggests there may be an inherited genetic mutation present.)
 - \circ Multiple cancers in one generation
 - Other causes of death
 - Current age or age of death





- [Slides 40-41] Learning Activity: Group Activity. Divide students into groups of 3-4 students each. Distribute copies of the <u>Williams Family Pedigree Analysis</u> handout. Allow 5-7 minutes for students to work together to answer the questions on the handout:
 - How many generations are shown in the pedigree?
 - What does the pedigree reveal about the family's history of breast cancer?
 - If someone has a mutated BRCA gene, does that mean they have or will have breast cancer? Why?
 - BRCA mutations are dominant. Who could potentially have an inherited BRCA mutation? Why?
- Have students share their responses to the questions and clarify any misunderstandings.

EVALUATE

Homework Assignment: Create Your Own Family Pedigree

- [Slide 42] Tell students they will use information from their family to create a family pedigree, or family health history, using a site like *My Family Health Portrait* (Located at <u>https://familyhistory.hhs.gov/FHH/html/index.html</u>).
 - Explain to students that this exercise is to help them build understanding of the kinds of information that can be important for family members to know, but they will NOT be required or asked to submit their pedigrees for review.
 - Explain that their family pedigree may help them make decisions about their health now and in the future, but they are private.
 - Note: Some students may not have access to their own family history—for example, if they are adopted. In this case, they can research their adoptive family history for practice, but should be aware that it does not affect their health.

Lesson 3 Plan – Day 2: Cancer Genetics

ENGAGE

Review of Homework/Discussion

- [Slide 44] Begin a discussion of the homework assignment—using the family health history tool to create and explore students' own family history. Use the reflection and discussion questions below to begin this conversation.
- NOTE: Be careful not to ask students to share personal or family health information. The purpose of the activity is exploration of the tool, not the specific results of any one student's search.
 - What kind of information is important to know before building a family pedigree or health history?
 - Did anything surprise you about this process?
 - How many generations were you able to find information about? What was challenging about this?





EXPLORE

Role Play a Genetic Counseling Session

- [Slide 46 Share the following additional detail with students about what happens in a typical genetic counseling session:
- Collect a detailed personal medical and family history
- Perform a cancer risk assessment
- Discuss the implications of genetic testing for the individual and the family
- Identify the most appropriate person to test in the family
- Discuss potential medical management options
- For the patient and the family
- Discuss genetic testing process
- Ordering the test
- Insurance Preauthorization
- Informed Consent
- [Slide 47] Learning Activity: Role Play. Explain to students that they will experience a genetic counseling session to learn more about the risks and genetics of breast cancer and to see what a genetic counseling session is like.
 - Divide students into pairs and distribute the <u>Genetic Counseling Script</u> to each student. Once students have chosen their roles and are familiar with the script, allow time for each pair to role-play the genetic counseling session.
 - Debrief the role-play by asking students to share their thoughts about the role of genetic counselors in cancer diagnosis and treatment. Assess whether any of their preconceptions about genetic counseling have changed.
 - Advise students that they will be doing a homework assignment related to genetic counseling.

Homework Assignment: Letter to Mr. and Mrs. Williams

- [Slide 48] Distribute the <u>Sample Patient Letter</u> and the <u>Genetic Counseling Script</u> to students for their homework assignment. Review the template and answer any student questions about the assignment.
- Homework Assignment. Tell students that after a genetic counseling session, the counselor writes a letter to the patient.
 - The purpose of the letter is to summarize the session so the patient has a written record of what was discussed.
 - Tell students they will assume the role of a genetic counselor and write a letter to Mr. and Mrs. Williams regarding whether or not they should be tested based on the Williams' pedigree.
 - Students should include their recommendation for both parents and provide at least two to three reasons for their choice in the letter.
 - Students should also address the pros and cons of getting tested.
 - A <u>Sample Patient Letter</u> is provided.





EXPLAIN

Genetic Testing Introduction

- [Slide 49] Learning Activity: Small Group Brainstorm. Divide the class into small groups and have students brainstorm their thoughts about Nikki's question: How do they look at the genes in a genetic test?
 - Ask each group to organize their thoughts and decide how they will answer Nikki's questions. Assign roles, such as recorder, if needed.
 - Debrief the activity by recording groups' preconceptions about genetic testing on a whiteboard or overhead projector.
 - Do not be too concerned about what students write at this point. This is meant to be an open-ended activity to assess what students know about genetics and cancer.
- [Slide 50] Tell students that a genetic test is the analysis of human DNA, RNA, chromosomes, proteins, or certain metabolites in order to detect alterations in genes.
 - With advances in technology, BRCA1 and BRCA2 are now analyzed with modern automated DNA sequencing instruments. However, historically, genes were analyzed through various methods, including **gel electrophoresis**.
 - Gel electrophoresis allows for separation of DNA fragments based on their size and charge.

Virtual Lab and Research Activity: Gel Electrophoresis

- [Slide 51] Distribute the *Gel Electrophoresis Simulation Worksheet*, which students can complete as they go through the activity.
- Tell students they will conduct an interactive simulation gel electrophoresis activity online. Direct students to the Gel Electrophoresis Virtual Lab at <u>http://learn.genetics.utah.edu/content/labs/gel/</u>. The simulation takes approximately 10 minutes to complete.
- Debrief the activity by going through the sheet with the class and discussing students' findings.

Optional Activity: Life-Size Gel Electrophoresis

- [Slide 52] This activity requires a large space, such as an open room, gym, or outside area to represent the "gel." The area should accommodate 4 rows or "lanes" that students will navigate through.
 - If you plan to conduct the activity in a classroom, use desks or chairs to create lanes.
 - If you plan to conduct the activity outside, mark off lanes with chalk, yarn, or other natural markers, such as trees or rocks.
- Tell students they will be doing an activity to explore gel electrophoresis. Review the <u>Gel</u> <u>Electrophoresis Activity</u> supplement for full instructions on this activity.





Video Presentation: Sanger Sequencing

- [Slide 53] This video presents another method of genetic testing without gel electrophoresis: Sanger sequencing.
 - Direct students to the video at: <u>http://www.yourgenome.org/teachers/sequencing.shtml</u>
 - Alternatively, present the video for the class using a projector.

ELABORATE

Analyze Genetic Test Results

- [Slides 54–55] Distribute the <u>Genetic Test Results</u> handout (2 pages—one each for John and Sarah's results).
- Distribute the genetic test results (2 pages —1 each for John and Sarah). Lead a class discussion of what the results mean and how this affects the cancer risk of the family members in the family tree (John, Sarah, Steve, Nikki, and Jen).
 - Ask the class what their answer to Steve's question would be—Should Nikki or I get tested, or one of our cousins?
 - Remind the class that Steve, Nikki, and their cousins should **not** be tested. According to the genetic counselor in the role-play activity, it is not recommended to get BRCA gene mutation testing until at least age 25. Steve and Nikki are not at increased risk for cancer while they are still young. If they do decide to pursue genetic testing as adults, they should have the same pre-test counseling process that Sarah and John went through so they understand the implications.

EVALUATE

- Homework Assignment. Tell students that after a genetic counseling session, the counselor writes a letter to the patient.
 - The purpose of the letter is to summarize the session so the patient has a written record of what was discussed.
 - Tell students they will assume the role of a genetic counselor and write a letter to Mr. and Mrs. Williams regarding whether or not they should be tested based on the Williams' pedigree.
 - Students should include their recommendation for both parents and provide at least two to three reasons for their choice in the letter.
 - Students should also address the pros and cons of getting tested.
 - A <u>Sample Patient Letter</u> is provided.
- Lesson 3 Quiz





Additional Resources

- American Cancer Society, The History of Cancer. Use "History of Cancer" as a search term or visit <u>http://www.cancer.org/docroot/CRI/content/CRI_2_6x_the_history_of_cancer_72.as</u> p?sitearea=&level
- Dolan DNA Learning Center. (2002). DNA From the Beginning. <u>http://www.dnaftb.org/</u>
- Dolan DNA Learning Center. (2002). Your Genes, Your Health. http://www.ygyh.org/
- Genetic Science Learning Center, University of Utah, http://learn.genetics.utah.edu
- Nature. Milestones in Cancer. <u>http://www.nature.com/milestones/milecancer/index.html</u>
- National Human Genome Research Institute. <u>http://www.genome.gov/Education/</u>
- National Human Genome Research Institute. Life in the Lab. <u>http://www.genome.gov/19016848</u>
- NOVA Online. Cracking the Code of Life. <u>http://www.pbs.org/wgbh/nova/genome/</u>
- The Protein Data Bank. (2000). <u>http://www.rcsb.org/pdb/home/home.do</u>
- U.S. National Library of Medicine. (1993). Genetics Home Reference. <u>http://ghr.nlm.nih.gov/</u>
- <u>http://highschoolbioethics.georgetown.edu/</u>
- Cancer Institute (2002). Genetic Testing for BRCA1 and BRCA2: It's Your Choice. http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA
- National Human Genome Research Institute. Genomics: Towards a Healthier You. Podcast available at <u>http://www.genome.gov/19016848</u>
- National Human Genome Research Institute. What is Genetic Counseling?
 <u>http://www.genome.gov/Pages/Education/DNADay/TeachingTools/GeneticCounselingProfession.pdf</u>
- Paideia. <u>http://www.paideia.org</u>
- US Dept. of Health and Human Services (2005). My Family Health Portrait. http://familyhistory.hhs.gov/
- Dept. of Health and Human Services and the Centers for Disease Control and Prevention. Genetics in the Workplace: Implications for Occupational Safety and Health. Chapters 4 and 7. <u>http://www.cdc.gov/niosh/docs/2010-101/</u>
- Baker, C. (1999). Your Genes, Your Choices: Exploring the Issues Raised by Genetic Research. The American Association for the Advancement of Science. <u>http://www.ornl.gov/sci/techresources/Human_Genome/publicat/genechoice/index_.html</u>
- Lab Tests Online. <u>http://labtestsonline.org/</u>
- The University of Utah. (2008). PCR Virtual Lab. <u>http://learn.genetics.utah.edu/content/labs/pcr/</u>
- Welcome Trust Sanger Institute. yourgenome.org. DNA Sequencing <u>http://www.yourgenome.org/teachers/sequencing.shtml</u>





Next Generation Science Standards

Performance Indicators

HS-LS3 Heredity: Inheritance and Variation of Traits

- HS-LS3-1. Ask questions to clarify relationships about the role of DNA and chromosomes in coding the instructions for characteristic traits passed from parents to offspring
- HS-LS3-2. Make and defend a claim based on evidence that inheritable genetic variations may result from: (1) new genetic combinations through meiosis, (2) viable errors occurring during replication, and/or (3) mutations caused by environmental factors.

Science and Engineering Practices

Asking Questions and Defining Problems

Ask questions that arise from examining models or a theory to clarify relationships. (HS-LS3-1)

Engaging in Argument from Evidence

• Make and defend a claim based on evidence about the natural world that reflects scientific knowledge, and student-generated evidence. (HS-LS3-2)

Disciplinary Core I deas

LS1.A: Structure and Function

 All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins. (secondary to HS-LS3-1) (Note: This Disciplinary Core Idea is also addressed by HS-LS1-1.)

LS3.A: Inheritance of Traits

• Each chromosome consists of a single very long DNA molecule, and each gene on the chromosome is a particular segment of that DNA. The instructions for forming species' characteristics are carried in DNA. All cells in an organism have the same genetic content, but the genes used (expressed) by the cell may be regulated in different ways. Not all DNA codes for a protein; some segments of DNA are involved in regulatory or structural functions, and some have no as-yet known function. (HS-LS3-1)

LS3.B: Variation of Traits

In sexual reproduction, chromosomes can sometimes swap sections during the process
of meiosis (cell division), thereby creating new genetic combinations and thus more
genetic variation. Although DNA replication is tightly regulated and remarkably
accurate, errors do occur and result in mutations, which are also a source of genetic
variation. Environmental factors can also cause mutations in genes, and viable
mutations are inherited. (HS-LS3-2)





Crosscutting Concepts

Cause and Effect

• Empirical evidence is required to differentiate between cause and correlation and make claims about specific causes and effects. (HS-LS3-1),(HS-LS3-2)





Appendix I: Supplemental Materials

		Pa	age 1 of 2				
Name:				Date:			
		Answer the f	following questions:				
		W	/ord Bank				
	Activities	Guanine	Nucleus	Transcribed			
	Adenine	Meiosis	Protein	Translated			
	Cytosine	Mitosis	RNA				
	Function	Mutation	Thymine				
1.	The four nitrogen ba	ases are:					
2. Adenine always bonds with and Cytosine always bonds with							
3.	In eukaryotic cells, D	NA is found in the orga	anelle called the				
4.	DNA contains a code	ed message which cont	trols all cell				
5.	This code is replicated during the S phase of the cell cycle and passed on to daughter cells during						
6.	This code is		into a	code which is			
	thenat		into a code which is the ribosome into an amino acid code which makes up				
_							
7.	 Any change to the DNA code is called a and may affect the amir acid sequence in the coded protein. 						
8.	A defective amino acid sequence may affect the 3-dimensional structure andof the protein.						
9.	Transcribe the follow	ving DNA sequence int	o mRNA:				
	5'TAC CAT GAT ACA	ATC3'					

10. Translate the mRNA sequence into an amino acid sequence:





Genetics Review Worksheet

Page 2 of 2

Answer the following questions:

Word Bank

Dominant	Genotype	Phenotype
Exons	Introns	Recessive
Forty-six (46)	Many	Traits
Gene	One (1)	Twenty-three (23)

11. Normal human somatic (body) cells contain ______ chromosomes.

- 12. A section of a chromosome that codes for one particular protein is called a _____
- 13. Proteins determine ______ (whether you have brown or blue eyes).

14. Each chromosome contains ______ genes.

- 15. As a result of sexual reproduction, offspring receive ______ copy of each gene from each parent.
- 16. The combination of genes received from your parents is called your ______ and determines what you look like (your ______).
- 17. A gene is ______ when only one copy of the gene is needed in order to see that trait in your phenotype.
- 18. Traits that require two of the same gene be present for expression of the trait are called
- 19. When DNA is transcribed, some intervening pieces are not incorporated into the resulting mRNA. These sections are called ______.
- 20. The remaining sections of the gene that are transcribed (expressed) and that code for the gene protein are called ______.





Genetics Review Worksheet Answers

Page 1 of 2

Answer the following questions:

Word Bank

Activities	Guanine	Nucleus	Transcribed
Adenine	Meiosis	Protein	Translated
Cytosine	Mitosis	RNA	
Function	Mutation	Thymine	

- 1. The four nitrogen bases are: Adenine, Thymine, Guanine and Cytosine.
- 2. Adenine always bonds with *thymine* and Cytosine always bonds with *guanine*.
- 3. In eukaryotic cells, DNA is found in the organelle called the *nucleus*.
- 4. DNA contains a coded message which controls all cell *activities*.
- 5. This code is replicated during the S phase of the cell cycle and passed on to daughter cells during mitosis.
- 6. This code is transcribed into a RNA code which is then translated at the ribosome into an amino acid code which makes up a protein.
- 7. Any change to the DNA code is called a *mutation* and may affect the amino acid sequence in the coded protein.
- 8. A defective amino acid sequence may affect the 3-dimensional structure and *function* of the protein.
- 9. Transcribe the following DNA sequence into mRNA:

SENSE STRAND 5'TAC CA	r gat aca atc3'
-----------------------	-----------------

ANTISENSE STRAND 3'ATG GTA CTA TGT TAG5'

mRNA UAC CAU GAU ACA AUC

10. Translate the mRNA sequence into an amino acid sequence:

mRNA

UAC CAU GAU ACA AUC

Tyrosine Leucine Aspartine Threoninie Isoleucine





Genetics Review Worksheet Answers

Page 2 of 2

Answer the following questions:

Word Bank

Dominant	Genotype	Phenotype
Exons	Introns	Recessive
Forty-six (46)	Many	Traits
Gene	One (1)	Twenty-three (23)

- 11. Normal human somatic (body) cells contain *forty-six (46)* chromosomes.
- 12. A section of a chromosome that codes for one particular protein is called a *gene*.
- 13. Proteins determine *traits* (whether you have brown or blue eyes).
- 14. Each chromosome contains many genes.
- 15. As a result of sexual reproduction, offspring receive one (1) copy of each gene from each parent.
- 16. The combination of genes received from your parents is called your *genotype* and determines what you look like (your <u>phenotype</u>).
- 17. A gene is *dominant* when only one copy of the gene is needed in order to see that trait in your phenotype.
- 18. Traits that require two of the same gene be present for expression of the trait are called *recessive*.
- 19. When DNA is transcribed, some intervening pieces are not incorporated into the resulting mRNA. These sections are called *introns*.
- 20. The remaining sections of the gene that are transcribed (expressed) and that code for the gene protein are called *exons*.



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Cancer Innovations

James Watson, Francis Crick and Rosalind Franklin determined that the structure of the DNA molecule is a double helix.
The number of chromosomes in humans was determined to be 46, instead of the widely believed 48.
The genetic code was cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids.
First human tumor-suppressor genes were discovered.
Gel electrophoresis was developed to sequence DNA using an electric current.
A technique for making many copies of a specific DNA sequence, the polymerase chain reaction (PCR), was developed.





Cancer Innovations

Cancer was linked to damage at cell cycle checkpoints.

A mutation on a single gene in 5-10% of women with breast cancer was determined to be linked to breast cancer.

The gene on chromosome 17 is named the Breast Cancer 1 gene.

The BRCA1 gene was cloned. People could now be screened for BRCA1 mutations.

The entire sequence of DNA composing human chromosomes was completed.

FDA approved three-dimensional mammography for routine screening as diagnostic tool for breast cancer.

Two vaccines (called Gardasil and Cervarix)have the market to protect against two types of HPV (HPV-16 & HPV-18) cancer causing viruses





Pop Culture Events

First Academy Awards (Oscars) televised.
First McDonald's opened in Des Plaines, Illinois.
Color TV became popular.
Disney World opened in Orlando, Florida.
Motorola obtained patent for first portable (cell) mobile phone.
Micheal Jackson's "Beat It" topped charts.





Pop Culture Events

First episode of <i>The Simpsons</i> aired.
Pretty Woman and Home Alone premiered.
Justin Bieber was born.
Facebook was founded.
The final Harry Potter movie, <i>Harry Potter and the Deathly Hallows: Part 2</i> was released.
The ALS Association raised \$115 M from the ALS Ice Bucket Challenge.





Cancer Innovations and Pop Culture Events

Allsweis								
Date	Innovation	Pop Culture Event						
1953	James Watson, Francis Crick and Rosalind Franklin determined that the structure of the DNA molecule is a double helix .	First Academy Awards (Oscars) televised.						
1955	The number of chromosomes in humans was determined to be 46, instead of the widely believed 48.	First McDonald's opened in Des Plaines, Illinois.						
1966	The genetic code was cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids.	Color TV became popular.						
1971	First human tumor-suppressor genes were discovered.	Disney World in Orlando, Florida opened.						
1975	Gel electrophoresis was developed to sequence DNA using an electric current.	Motorola obtained patent for first portable mobile (cell) phone.						
1983	A technique for making many copies of a specific DNA sequence, the polymerase chain reaction (PCR), was developed.	Michael Jackson's "Beat It" topped charts.						
1989	Cancer was linked to damage at cell cycle checkpoints.	First episode of The Simpsons aired.						
1990	A mutation on a single gene in 5-10% of women with breast cancer was determined to be linked to breast cancer. The gene on chromosome 17 is named the Breast Cancer 1 gene.	Pretty Woman and Home Alone premiered.						
1994	The BRCA1 gene was cloned. People could now be screened for BRCA1 mutations.	Justin Bieber was born.						
2003	The entire sequence of DNA composing human chromosomes was completed.	Facebook was founded.						
2011	FDA approved three-dimensional mammography for routine screening as diagnostic tool for breast cancer.	The final Harry Potter movie was released.						
2014	Two vaccines (called Gardasil and Cervarix) have the market to protect against two types of HPV (HPV-16 & HPV-18) cancer causing viruses	The ALS Association raised \$115 Million from the ALS Ice Bucket Challenge.						

Answers





Sense Stand 5'--3'

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1 ctt agc ggt agc ccc ttg gtt tcc gtg gca acg gaa aag cgc ggg aat tac aga taa att 61 aaa act gcg act gcg cgg cgt gag ctc gct gag act tcc tgg acg ggg gac agg ctg tgg 121 ggt ttc tca gat aac tgg gcc cct gcg ctc agg agg cct tca ccc tct gct ctg ggt aaa 181 ggt agt aga gtc ccg gga aag gga cag ggg gcc caa gtg atg ctc tgg ggt act ggc gtg 241 gga gag tgg att tcc gaa gct gac aga tgg gta ttc ttt gac ggg ggg tag ggg cgg aac 301 ctg aga ggc gta agg cgt tgt gaa ccc tgg gga ggg ggg cag ttt gta ggt cgc gag gga 361 agc gct gag gat cag gaa ggg ggc act gag tgt ccg tgg ggg aat cct cgt gat agg aac 421 tgg aat atg cct tga ggg gga cac tat gtc ttt aaa aac gtc ggc tgg tca tga ggt cag 481 gag ttc cag acc agc ctg acc aac gtg gtg aaa ctc cgt ctc tac taa aaa tac aaa aat 541 tag ccg ggc gtg gtg ccg ctc cag cta ctc agg agg ctg agg cag gag aat cgc tag aac 601 ccg gga ggc gga ggt tgc agt gag ccg aga tcg cgc cat tgc act cca gcc tgg gcg aca 661 gag cga gac tgt ctc aaa aca aaa caa aac aaa aca aaa caa aaa aca ccg gct ggt atg 721 tat gag agg atg gga cct tgt gga aga aga ggt gcc agg aat atg tct ggg aag ggg agg 781 aga cag gat ttt gtg gga ggg aga act taa gaa ctg gat cca ttt gcg cca ttg aga aag 841 cgc aag agg gaa gta gag gag cgt cag tag taa cag atg ctg ccg gca ggg atg tgc ttg 901 agg agg atc cag aga tga gag cag gtc act ggg aaa ggt tag ggg cgg gga ggc ctt gat 961 tgg tgt tgg ttt ggt cgt tgt tga ttt tgg ttt tat gca aga aaa aga aaa caa cca gaa 1021 aca ttg gag aaa gct aag gct acc acc acc tac ccg gtc agt cac tcc tct gta gct ttc **1081** tct ttc ttg gag aaa gga aaa gac cca agg ggt tgg cag caa tat gtg aaa aaa ttc aga 1141 att tat gtt gtc taa tta caa aaa gca act tct aga atc ttt aaa aat aaa gga cgt tgt 1201 cat tag ttc ttt ggt ttg tat tat tct aaa acc ttc caa atc tta aat tta ctt tat ttt **1261** aaa atg ata aaa tga agt tgt cat ttt ata aac ctt tta aaa aga tat ata tat atg ttt 1321 ttc taa tgt gtt aaa gtt cat tgg aac aga aag aaa tgg att tat ctg ctc ttc gcg ttg





Sense Stand 5'--3'

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1381 aag aag tac aaa atg tca tta atg cta tgc aga aaa tct tag agt gtc cca tct ggt aag 1441 tca gca caa gag tgt att aat ttg gga ttc cta tga tta tct cct atg caa atg aac aga 1501 att gac ctt aca tac tag gga aga aaa gac atg tct agt aag att agg cta ttg taa ttg 1561 ctg att ttc tta act gaa gaa ctt taa aaa tat aga aaa tga ttc ctt gtt ctc cat cca 1621 ctc tgc ctc tcc cac tcc tct cct ttt caa cac aaa tcc tgt ggt ccg gga aag aca ggg **1681** act ctg tct tga ttg gtt ctg cac tgg ggc agg aat cta gtt tag att aac tgg cat ttt 1741 ggc ttt tct tcc agc tct aaa aca agc tcc atc act tga aat ggc aaa ata aaa tca tgg **1801** atg agg ccg agg gcg gtg gct tat gcc tgt aat ccc agc act ttg gga ggc caa ggt ggt 1861 agg atc acg agg tca gga gat cga gac cat cct ggc caa cat ggt gaa acc ccc tct cca **1921** cta aaa ata caa aaa tta gct ggg cgt agt ggc atg tgc ctg taa tcc cag cta ctc agg **1981** agg ctg agg cag gag aat cac ttg aac cag gag gca gat gtt gct gtg agc caa tat ggc 2101 aac atg gat gat cgg tgt cgt tga gag gat agg tat ttg gaa gaa cct ttg ttt gaa act 2161 ggc tct gta cat aca atg aaa tta cat act tat tta cat aca atg aaa tgc aga ggt ttt 2221 ttt ttt ata tag gat ctc tgt cga gag gct gga gtg cag tgg tgc tat cac agc tca ctg 2281 cag cct caa cct cgt cag gct caa gca atc ctc cca cct cag cct cca gag tag cag gga 2341 cga tag gtg tgc acc acc atg ccc agc taa ttt ttg tat ttt ttt ttt ttt ttga gat **2401** gga gtc ttg ctc tgt tgc cca ggc tgg agt gca gtg gcg cga tct cag ctc act gca aac 2461 tct gcc tcc cgg gtt cat gcc att ctt ctg cct gag cct cct gaa tag ctg gga cta caa 2521 gca ccc act acc acg ccc ggc taa ttt ttt gta ttt ttt ttt ctt ttt tag tag agg cgg 2581 gat ttc acc gtg tta gcc agg ata gtc ttg atc tcc tga cct tgt gat cca ccc gcc tgg **2641** gcc tcc caa agt gct agg att aca ggc ata agc cac tgc gtc cag cca ttc ttg tat ttt 2701 tct gtt gta gag ata ggg ttt tgc tat gtt ggc cat gct ggt ctc aaa ctc ctg acc tca **2761** agt gat cta ccc tcc ctt ggc ctc tca agg tgc tgg gat tac agg cct gag cca ttg cac





Sense Stand 5'--3'

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2821 cca gcc atg gtc taa aaa tct tga ttg aaa tac cac ctt ttc att tcc aga cac ccc tat 2881 tta aaa tta cca cac ccc cag cac aca ctt tat ctt cta ttc ctg ctg ctt ctc cat aac 2941 act gat tac tag ctg aca ttc tat gta atg tat cca ttt ttt atc tct agt ccc aca gaa **3001** tgt aaa ctc cag gat ggg att ttt gtt ttg ttt aca tac atc tgt atg ttc agt agt tag 3061 aac ggt act tgg gac cta gtt gcc act caa taa aca ttt gtc aaa taa ata ata aac taa 3181 aaa ata agt tga aaa gtt gta cca ttg cct ctt acc cac aat aaa aaa ggg taa att ctt **3241** ttc tgc ttt atg aaa gtt gtt ttt cat att tga agt caa gtt aat cag att aag gaa aat **3301** gta tgt tgt gtt ttc aga gcg ata caa gat tta taa ata acc atc ctc tcc ctt gcc ctt 3361 caa cat tat agc taa aca aaa ata aga gga aaa cag gat tca caa ttt atc aat tta ttg **3421** aaa atc aga gcc aga gaa gca gga aat gac att gta gga aaa aac tgc ttt tga aaa agc 3481 aca aaa ctt act cat gac aat cag tga tca gga aaa tcc tca ata gtg tgg cat ttg gat **3541** aca ttt atg ttt cat ttc cat ggg aga gag tca taa aaa tag gat gtt ctt tct cat tct 3601 ggc aaa tta aac cat caa tta aaa act cag ata cat aaa aat taa aga tgt aag aat gaa 3661 aat gct aaa ttg tta ttt tca atc aac tat tat gtt ttc tag ctt ttc att gct ttt ttc **3781** ggc tct tgt tgc cca ggc tgg agt gca gtg gca caa tct cgg ctc act aca acc tcc acc **3841** tcc cgg gtt caa gca att ctg ctg cct cag cct ccg gag tac ctg gga ttg cag gca tgt 3901 gcc atc aca cca gct aat ttt gta ttt tta gta gag aca ggg ttt ctc cat att ggt cag **3961** gtt ggt ctc gaa ctc ctg acc tca ggt gat cct cct gcc ttg gcc tcc gaa agt gct ggg 4021 att aca ggc gtg agc cac cgc tcc cag act ttt tgt ttt gtt ttg ttt tgt ttt tgt ttt tgt ttt tgt ttt tgt ttt gag **4081** aca cgg tct cgc tct gct gcc tag gct gga gtg cag tgg cac gat ctt ggc tca ctg cca





Sense Stand 5'--3'

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4141 gct ccg cct ccc ggg ttc agg cca ttc tcc tgc ctc agc ctc ccg agt agc tgg gac tac **4201** agg cgc cca cca cta tgc ccg gct aat ttt ttg tat ttt tag tag aga cgg ggt ttc acc 4261 atg tta gcc aag atg gtc tcg atc tcc tga cct tgt gat cca ccc gcc tca gcc ttc caa 4321 agt gct ggg att aca gtc ctg agc cac tgc gcc cgg cct gga cct ttt ttt ttc ggg gtg **4381** ggg ggt tgg agt ctg gct ctg tcg ccc agg ctg gag tgc agt ggc gcc atc ttg gct cac 4441 tgc aac ctc cgc ctg cca ggt tca agt tca agc gct tct cct gcc tca gcc tcc tga gta 4501 gct ggg att ata ggc gca cgc cac cgt ggc cgg cta att ttg tat ttt tag tag aga tag **4561** ggt ttc atc acg ttg gtc agg ctg gtc ttg aag tcc tga tct cgt gat cca ccc gcc tcg 4621 gcc ttc caa agt gct ggc gtg agc cac tgc gcc tgg ctt aag att aat ttt tgt ttg ttt 4681 tgt ttt tga gac gga gtc tcg ctc ttt cac cca ggc cgg agt gca gtg gcg cca tct cgg 4741 ctc act gca agc tcc gcc tcc cgg gtt cac gcc att ctc ctg cct cgg ccc ccc aag tag 4801 ctg gga cta cag gcg tcc acc acg ccc ggc taa ttt ttt gta ttt tta gta gag acg **4861** ggg ttt cac cgt gtt agc cag gat ggt ctc cac ttc ctg acc tcg tga tcc gcc cac ctc 4921 ggc ctc cca aag tgc tgg gat tac agg cgt gag cca ccg cgc ccg gcc tta aga tta att **4981** ttt atg gtg ttt tac att cat ttg tat gga aag ttc tag gat agg gat cat att tca ctt 5041 cct ttt aat ata gta cag tat agc aca att tgc agt tat gtc tta ata tgt gat cag gaa 5101 tga tca tga ctg gaa aca gtg tta ttt gtg gta gct ata ggg tag gta agg ttt tca gcc 5161 tgt ttt agg ttt ctt gaa cta aaa ttc ctt ctg ctg tct tct aag tca ata ttg gca gct 5221 att tct gac aat tgg tag ttc ttt gta act ttt tac cta tga cta taa cat ttt tga ctt 5281 tca gaa gaa ttt gct aaa atg tgt tcc ccg gtg ggt tgt tgt ttt tca acc taa acc tag 5341 ctg ctt ttt cca gtc act tat ccg tat tgg aag ctc aaa atg caa ata tac agt agg cct 5401 aaa ata ttg cct ggt ttg aaa agt gtt taa aat att tga atc att ttt ata gta aac att 5461 tac tct cat cag gac cta gaa ggg gaa cat ttt aat ttt ttt tct ttt ccc ttt tca cag 5521 tct tcc ttc aac att cat tac ctt ttt aca tat cgg agt ttt cat ctg ttc aaa gtt tgt





Sense Stand 5'--3'

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1 gtg gcg cga gct tct gaa act agg cgg cag agg cgg agc cgc tgt ggc act gct gcg cct **121** cag att tgt gac cgg cgc ggt ttt tgt cag ctt act ccg gcc aaa aaa gaa ctg cac ctc **181** tgg agc ggg tta gtg gtg gtg gta gtg ggt tgg gac gag cgc gtc ttc cgc agt ccc agt 241 cca gcg tgg cgg ggg agc gcc tca cgc ccc ggg tcg ctg ccg cgg ctt ctt gcc ctt ttg 301 tct ctg cca acc ccc acc cat gcc tga gag aaa ggt cct tgc ccg aag gca gat ttt cgc **361** caa gca aat tcg agc ccc gcc cct tcc ctg ggt ctc cat ttc ccg cct ccg gcc cgg cct 421 ttg ggc tcc gcc ttc agc tca aga ctt aac ttc cct ccc agc tgt ccc aga tga cgc cat **481** ctg aaa ttt ctt gga aac acg atc act tta acg gaa tat tgc tgt ttt ggg gaa gtg ttt 541 tac age tgc tgg gca cgc tgt att tgc ctt act taa gcc cct ggt aat tgc tgt att ccg 601 aag aca tgc tga tgg gaa tta cca ggc ggc gtt ggt ctc taa ctg gag ccc tct gtc ccc 661 act agc cac gcg tca ctg gtt agc gtg att gaa act aaa tcg tat gaa aat cct ctt ctc 721 tag tcg cac tag cca cgt ttc gag tgc tta atg tgg cta gtg gca ccg gtt tgg aca gca 781 cag ctg taa aat gtt ccc atc ctc aca gta agc tgt tac cgt tcc agg aga tgg gac tga 841 att aga att caa aca aat ttt cca gcg ctt ctg agt ttt acc tca gtc aca taa taa gga **901** atg cat ccc tgt gta agt gca ttt tgg tct tct gtt ttg cag act tat tta cca agc att 961 gga gga ata tcg tag gta aaa atg cct att gga tcc aaa gag agg cca aca ttt ttt gaa 1021 att ttt aag aca cgc tgc aac aaa gca ggt att gac aaa ttt tat ata act tta taa att **1081** aca ccg aga aag tgt ttt cta aaa aat gct tgc taa aaa ccc agt acg tca cag tgt tgc 1141 tta gaa cca taa act gtt cct tat gtg tgt ata aat cca gtt aac aac ata atc atc gtt 1201 tgc agg tta acc aca tga taa ata tag aac gtc tag tgg ata aag agg aaa ctg gcc cct 1261 tga cta gca gta gga aca att act aac aaa tca gaa gca tta atg tta ctt tat ggc aga





Sense Stand 5'--3'

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1321 agt tgt cca act ttt tgg ttt cag tac tcc tta tac tct taa aaa tga tct agg acc ccc **1381** gga gtg ctt ttg ttt atg tag ctt acc ata tta gaa att taa aac taa gaa ttt aag gct 1441 ggg cgt ggt ggc tca cgc ctg taa tcc cag cac ttt ggg agg ccg agg tgg gcg gat cac 1501 ttg agg cca gaa gtt tga gac cag cct ggc caa cat ggt gaa acc cta tct cta cta aaa 1561 ata caa aaa atg tgc tgc gtg tgg tgg tgc gtg cct gta atc cca gct aca cgg gag gtg 1621 gag gca gga gaa tcg ctt gaa ccc tgg agg cag agg ttg cag tga gcc aag atc atg cca 1681 ctg cac tct agc ctg ggc cac ata gca tga ctc tgt ctc aaa aca aac aaa caa aca aaa 1741 aac taa gaa ttt aaa gtt aat tta ctt aaa aat aat gaa agc taa ccc att gca tat tat 1801 cac aac att ctt agg aaa aat aac ttt ttg aaa aca agt gag tgg aat agt ttt tac att 1861 ttt gca gtt ctc ttt aat gtc tgg cta aat aga gat agc tgg att cac tta tct gtg tct 1981 att tta ata gtt ttc agt tac ttt ttg gta ttt ttc ctt gta ctt tgc ata gat ttt tca 2041 aag atc taa tag ata tac cat agg tct ttc cca tgt cgc aac atc atg cag tga tta ttt 2101 gga aga tag tgg tgt tct gaa tta tac aaa gtt tcc aaa tat tga taa att gca tta aac 2221 ggt aga aat gag cca ctg gaa att cta att ttc att tga aag ttc aca ttt tgt cat tga 2281 caa caa act gtt ttc ctt gca gca aca aga tca ctt cat tga ttt gtg aga aaa tgt cta 2341 cca aat tat tta agt tga aat aac ttt gtc agc tgt tct ttc aag taa aaa tga ctt ttc 2401 att gaa aaa att gct tgt tca gat cac agc tca aca tga gtgctt ttc tag gca gta ttg 2461 tac ttc agt atg cag aag tgc ttt atg tat gct tcc tat ttt gtc aga gat tat taa aag 2521 aag tgc taa agc att gag ctt cga aat taa ttt tta ctg ctt cat tag gac att ctt aca 2581 tta aac tgg cat tat tat tac tat tat ttt taa caa gga cac tca gtg gta agg aat ata 2641 atg gct act agt att agt ttg gtg cca ctg cca taa ctc atg caa atg tgc cag cag ttt





Sense Stand 5'--3'

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2701 tac cca gca tca tct ttg cac tgt tga tac aaa tgt caa cat cat gaa aaa ggg aaa tga 2761 ttc cat agc gtt att atg aaa gta gtt ttg aac tgt aat ggt aga gga tga ata gct cac 2821 aat aca aat ttg tca ttt ccc ttt aag aga gaa ttc cca ttt tat gtg aga gtc cac atg 2881 ttc ctc ata ccc ata gtt tgc cac atc ttg agt act ctt cag aat tat ttg aat ttt ttg **3001** tgc cca ggc tgg aat gca gtg gcg tga tct cgg ctc act gca acc acc gcc tcc tgg gtt **3061** caa gtg att ctc ctg tgg cag cct ccg gag tag ctg gga cta cag gcg tgt gcc acc atg 3121 ctt ggc taa ttt ttt gtg ttt tta gta aag atg ggg ttt caa cgt gtt agc aag gtt ggt 3181 ctc gatctga cctcgtgatc tgctcgcctc agcctcccaa agtgttggga ttacaggcgt 3241 gag ccc ccg cac ctg gcc gaa ttt tat cgt gga atg tat tct taa tgt gaa tag ttt ttg **3301** att ccg aac cat gaa taa taa gaa aat aaa taa aat tta aat gaa aat aaa agc taa tat 3361 ata cag ctt tta ata ata tag tta aat gcc atc ttg taa ctt ttg tga act ctt gtt aca 3421 cct ttc tat aga ttc gca aga gaa tgg att aat gat ctt gtt taa tta ata tgc ctt aac 3481 aaa agt aat cca tag tca aga tct taa gca ttt ttt tcc tta tga tct tta act gtt ctg 3541 ggt cac aaa ttt gtc tgt cac tgg tta aaa cta agg tgg gat ttt ttt ttt aaa tag att 3601 tag gac caa taa gtc tta att ggt ttg aag aac ttt ctt cag aag ctc cac cct ata att 3661 ctg aac ctg cag aag aat ctg aac ata aaa aca aca att acg aac caa acc tat tta aaa 3721 ctc cac aaa gga aac cat ctt ata atc agc tgg ctt caa ctc caa taa tat tca aag agc 3781 aag ggc tga ctc tgc cgc tgt acc aat ctc ctg taa aag aat tag ata aat tca aat tag 3841 act tag gta agt aat gca ata tgg tag act ggg gag aac tac aaa cta gga att tag gca **3901** aac ctg tgt taa aat ctt agc tca ttc att aat tgt gtc atg ctg ggc aaa tca gtc tct 3961 ctg gcc tct ttt tcc tca ctc gaa aaa tgg aga cga tga aaa taa tgt ctc ata ggt ttg





Sense Stand 5'--3'

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4021 gat taa att aaa taa tgt agg tac tta gta aat gtt ctc ttt cat ccc tcc ttt gat aaa 4081 ttt gcc aac tga gat ttg ctg aat tac gtc ttt ctt atg cca aaa aaa cct agg act tgt 4141 ttt gat gtt aat taa act aaa cta tat ttc tgc aag cta tca cag agg aca gag att att 4201 tta ccg ata tac tat aag tat cat gat ttg gaa gga gtt tcc ctg gcg tag gtg ccg cat 4261 gtt tct aag caa tta tgt aat aag att ata tat tca gtc att caa ata att att acc tac 4321 ttg aca taa gta atg aac ttt ccc ttt tct tca gag tgt taa tct cta gta agg gga ata 4441 taa aaa agt ata atg aga gtt gag aag aaa gag caa ata gta ttg ggc aaa gtt agg caa 4501 tta ttc ctt tga gct aaa cct tga agg ata ggt gag aga tta aga aat ttg aag atg tgg 4561 tag agt gat aat gtt cta ggc aga ggg aac aac atg agg aag aat atg tag tgt gtt cag 4621 gaa ata gca agt aat tca ggt tgg ctt tgg ttg ttt tgt gtc tga aag gga cca ata gac 4681 aag gca aaa agg cag act aaa ggc agg cat tga atg cca agc taa aga aat tga att tgt 4741 ttg gtt ggt tgg tga gca gag aaa tca cat gca aat ttc atc atg cta ctt att gtg tca 4801 aac ctt aga tca cct ccc ttt gtc ctt ata gca aaa tct aaa ctt gat atg gct ttc aag **4861** ttc ctt tgt gat cag gcc cct gat tta cac tct tgg ctc agc ttg cca tat tca tcc tct **4921** cac cta tct tca ttt gcc att cat tcc tac tga att tct ttt cgt tac caa aac cac aat 4981 gct ctc tgg ctc ttt att aaa cat att gtt acc tct acc cac aac cta ctt ttt ccc tac 5041 ttt ttg tct agc taa ttt gcg tgc tcg tct ttc aga tct tgg ctt att tct gct tct gag 5101 aaa tac ttc ctg tct gcc ctc gtt gag ctt cta gtg aag gag aca tac ata agc aat tat 5161 agt gtg ata cat gct ttg aaa gaa att cat ggc tat agg gag tgc ata tac aaa ggg aat 5221 ata ggt aat ggg caa ata ttt aca tgt atg tta ttg gat acc aaa tgg tat aca tag gat 5341 aca gca gtc ttt gga gat aac gtt ttt caa aat gtc atg tct gtg cca tta gaa tct tct 5401 aga ctg ctc att gaa agg aca gat tcc agg ccc cac tct gaa tct ctt aat tta taa ttt





Sense Stand 5'--3'

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5461 ttg gaa atg atg ccc atg agt cta cat ttt aaa cta cct gaa tga tcc cta tag aaa gag 5521 aaa act gga ggt agg aag atc agt tag ggg atg tgt aat ggt cta ggt gat aga gac aag 5581 tgc ctg aat tac agt aat aac agt gaa agt aaa tat gga aca taa aac tat agg acc ttg 5641 cag tag tct aga tat gga gga ttc aaa aaa agg aac aaa tga cag ggc aaa gca tat gca 5701 gaa cac agt agt aac agt cat aga aat gga taa ggg agt cat cca ttc tgc aaa tac tta 5761 gtg ctt act tgt gtc tgg caa cct gct cgg cat taa gga tac aaa tat gaa taa gat gtc 5821 ctt tga cct cta agt act cag tct cgt aag cac gtc ttg taa gca cat ctt ggt tgc ttc 5881 cat aaa aat aaa tac act agt gtg ata tgt tat aag agc atg tac caa gtg cat gaa aag 5941 tga gca gcc atc tct ggt tgg tca gaa aaa gct cca taa agc agt ttt tgc tga atc ttg 6001 aaa gat ata cct aag gtc aaa tgg tta att ctt taa tca taa cct gct aga att gat cta 6061 taa cca agg aag gat agt aag gaa tta ata agg cca ctc tca act cac tgc aaa gga gtt 6121 aac ttt ttg aag gct gta ata cat aaa tct gct gac tag tct ctt gag acc ttt tgc ttt 6181 tac gtt tac ttt aga ttc agt att gaa aag taa gag taa tgg act taa gct gtg ttt ttc 6241 aac ctg ttt tgt tca gtt cta aca tgt aat att ttt taa aaa att att cct aaa gtt cta 6301 tga gga att gtg ctg ttt ctg cct ctc agc agt cct tcc ttt tgc att aaa tca tag gca 6361 ttt ctg tta cca ttc ttc agc tta tta atg aga tcc tca ggt tat ttg gga aat gtt tat 6421 ttg gta att aac tct ttt tca cct agt tca ttt ttt taa ctt ttt tta aat agc cga 6481 gtt tct ttt cat tgc tga act aaa atg gat gtg tta tta tta gct gaa ctc ctt agt tta 6541 ctt tag agt tca ccc ttt gta tgg ttc tat gga ttt tga caa att gta taa tgt cgt ata





Sense Stand 5'--3'

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6601 tct gcc att atg gca tta tac aga ata att ttg ctg ccc taa aaa tct ccc gag ttc cac 6661 ctg ctc acc cat ccc tcc tga gcc cct ggc agc cac tga tct ttt tac tgt ctg tat 6721 agt ttt gcc ttt tcc aga atg tca tgt agt tgg aat cat aca gaa tat agc att ttc aga 6781 ctg gct tct ttc act tag caa tat gcc gag acc agc tcg att gta gag acc cta acc cag 6841 cgg cac tag agg aat taa agg cac aca gaa ata tag cgg tgt gga gtg gga aat cag ggg 6901 tct cac agc ctt ttg aca gca agc cag tga taa gca ttg ttt cta tag att ata gat taa 6961 ctg aaa gta ttc ctt agg gga aat aaa ggg ctg ggc cga agt aaa ggg atg ggt ctg gct 7021 agt tat ctg cag cag gag aat gtc ctt aag gca cag gtc gct cat gat agt ttg tgg ttt 7081 aag aac gcc ttt aag cgg ttt tct gcc ccg ggt ggg cca ggt gtt cct tgc cct cat tcc 7141 ggt aaa ccc aca agc ttc cag cgt ggg tgt cat ggc cat cac gaa cat gtc aca gtg ctg 7201 cag aga ttt tgt tta tgg cca gtt ttg ggg cca gtt ccc aac agc aat atg tgt tta agg 7261 ttc ttc cat gtc ttt taa tga ttt cat gct gaa taa tat tcc atc gta ttg atg tac cac 7321 agc ttg ttt atc cat tca tct att gaa gga cat ctt gat tgc ttc caa att ttg gca att 7381 atg aat aaa gct ggt ata aat att cac ata cag gtt tgt gtg tga ata tat ttt caa ctc 7441 att ttg gtt cac acc aaa gag cac gat tgt ggg atc ata tag taa gag tat gtt tag ttt 7501 tat gag aaa cta caa gct ttc ttc caa agt agc tgt tgc att ttg tat tcc cac cag cag 7561 tga atg aga gtt ctt gtt gct cac atc ctc acc agc att tgg tgt gtc agt gtt ttg aat 7621 tct agc cat tct aac aag tgt gta gtg gta cct cat tgt ttg ttt tat tta att ttt ttt 7681 ttt ttt ttt tgg aga tga aat ctc gct ttg tcg ccc agg ctg gag tgc agt ggc gtg atc 7741 ttg gct cac tgc aag ctc cgc ctc cca ggt tca cgc cat tct cct gcc tta gcc tcc tga **7801** gta gct ggg act aca ggc acc cgc cac cac acc tgg ctg att ttt ttg tat ttt tag tag 7861 aga cgg ggt ttc act gtg tta gcc agg atg gtc ttg atc tcc tga cct cgt gat ccg ctc 7921 gcc tcg gcc tcc caa agt gct ggg att aca ggc gtg agc cat cat gcc cgg cct gtt tta 7981 ttt ttt aaa gtc aat ttt ctt tca aga att agc tac ttt tta gta tct tta att aaa aat





Genetic Mutations

Name:			Date:							
			Locat	Location of sequence:						
Normal Sequence										
Template Strand DNA	3′									5′
(Anti-Sense Strand):	Ξ,									2/
Coding Strand DNA: (Sense Strand):	5									3′
mRNA:	S'									
Amino Acid:	<u> </u>									
Mutation Sequence										
Template Strand DNA (Anti-Sense Strand):	3′					<u></u>				5
Coding Strand DNA: (Sense Strand):	5′									3
mRNA:	5'									
Amino Acid:	5									

1. What type of mutation is this?

2. What result does the mutation have on the protein?





Answers

Name of Population: Bristish Location of sequence: BRCA 1 Start with 4174 End With 4197

Normal Sequence Coding Strand DNA (Sense Strand): 5'CTC AGC CTC CCG AGT AGC TGG GAC 3' Template Strand DNA (Anti-Sense Strand): 3'GAG TCG GAG GGC TCA TCG ACC CTG 5' mRNA: CUC AGC CUC CCG AGU AGC UGG GAC Amino Acid: Leu Ser Leu Pro Ser Ser Trp Asp Mutation Sequence 4184 Del 4 Coding Strand DNA (Sense Strand): 5'<u>CTC AGC CTC CGA GCT GGG AC 3</u>' Template Strand DNA (Anti-Sense Strand): 3'GAG TCG GAG GCT CGA CCC TG 5' mRNA: CUC AGC CUC CGA GCU GGG AC Amino Acid: Leu Ser Leu Arg Ala Gly 1. What type of mutation is this? Deletion What result does the mutation have on the protein? 2. Codes for different amino acids and results in a shorter (truncated) protein. Name of Population: Italians Location of sequence: BRCA 1 Start with 5080 End With 5130

Normal Sequence

Coding Strand DNA	5' <u>GTC TTA ATA <i>TGT GAT CAG GAA TGA TCA T</i>GA CTG GAA ACA GTG TTA TTT GTG</u> 3'
(Sense Strand):	
Template Strand DNA	3' <u>CAG AAT TAT ACA CTA GTC CTT ACT AGT ACT</u> GAC CTT TGT CAC AAT AAA CAC 5'
(Anti-Sense Strand):	
mRNA:	<u>GUC UUA AUA UGU GAU CAG GAA UGA UCA UGA CUG GAA ACA GUG UUA UUU GUG</u>
Amino Acid:	Val Leu lle Cys Val Gln Glu Ser Ser Stop Leu Glu Thr Val Leu Phe Val

Mutation Sequence 5083 Del 19

Coding Strand DNA (Sense Strand):		5′ <u>GTC GAT CAT GAC TGG AAA CAG TGT TAT TTG TGG TA</u> 3′		
Template Strand DNA (Anti-Sense Strand):		3' <u>CAG CTA GTA CTG ACC TTT GTC ACA ATA AAC ACC AT</u> 5'		
mRNA:		<u>GUC GAU CAU GAC UGG AAA CAG UGU UAU UUG UGG UA</u>		
Amino Acid:		Val Asp His Asp Trp Lys GIn Cys Try Leu Trp		
1.	What type of mutation is this? Deletion			

2. What result does the mutation have on the protein? Codes for different amino acids and results in a shorter (truncated) protein.





Answers

Name of Population: Norwegians Location of sequence: BRCA 1 Start with 1132 End With 1152

Normal Sequence Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand): mRNA: Amino Acid:

Mutation Sequence 1136 Ins A

Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand): mRNA:

Amino Acid:

- 1. What type of mutation is this? *Insertion*
- 2. What result does the mutation have on the protein? Codes for different amino acids.

5'AAA TTC AGA ATT TAT GTT GTC 3' 3'TTT AAG TCT TAA ATA CAA CAG 5' AAA UUC AGA AUU UAU GUU GUC Lys Phe Arg lle Tyr Val Val

5'<u>AAA TTA CAG AAT TTA TGT TGT C</u> 3' 3'<u>TTT AAT GTC TTA AAT ACA ACA G</u> 5' <u>AAA UUA CAG AAU UUA UGU UGU C</u> Lys Leu Gln Asn Leu Cys Cys

Name of Population: <u>Norwegians</u> Location of sequence: <u>BRCA 1</u> Start with <u>1672</u> End With <u>1689</u> Normal Sequence

Coding Strand DNA (Sense Strand):	5 <u>′AAG ACA GGG ACT CTG TCT</u> 3′
Template Strand DNA (Anti-Sense Strand):	3′ <u>TTC TGT CCC TGA</u> <u>GAC AGA</u> 5′
mRNA:	<u>AAG ACA GGG ACU CUG UCU</u>
Amino Acid:	Lys Thr Gly Thr Leu Ser
Mutation Sequence <u>1675 Del A</u>	
Coding Strand DNA (Sense Strand):	5′ <u>AAG CAG GGA CTC TGT CT</u> 3′
Template Strand DNA (Anti-Sense Strand):	3′ <u>TTC GTC CCT GAG ACA GA</u> 5′
mRNA:	<u>AAG CAG GGA CUC UGU CU</u>
Amino Acid:	Lys Gln Gly Leu Cys

1. What type of mutation is this? *Deletion.*

2. What result does the mutation have on the protein? Codes for different amino acids.





Answers

Name of Population: Icelanders Location of sequence: BRCA 2 Start with 6169 End With 6192

Normal Sequence Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand): mRNA: Amino Acid:

Mutation Sequence <u>6174 Del T</u> Coding Strand DNA (Sense Strand):

mRNA:

Amino Acid:

Template Strand DNA (Anti-Sense Strand):

5'ACC TTT TGC TTT TAC GTT TAC TTT 3' 3'TGG AAA ACG AAA ATG CAA ATG AAA 5' ACC UUU UGC UUU UAC GUU UAC UUU Thr Phe Cys Phe Tyr Val Tyr Phe

5'ACC TTT GCT TTT ACG TTT ACT TT 3' 3'TGG AAA CGA AAA TGC AAA TGA AA5' ACC UUU GCU UUU ACG UUU ACU UU Thr Phe Ala Phe Thr Phe Thr

1. What type of mutation is this? Deletion

What result does the mutation have on the protein?
 Codes for different amino acids and results in a shorter (truncated) protein.

Name of Population: Filipinos Location of sequence: BRCA 2 Start with 4855 End With 4875

Normal Sequence			
Coding Strand DNA (Sense Strand):	5′ <u>TTC AAG TTC CTT TGT GAT CAG</u> 3′		
Template Strand DNA (Anti-Sense Strand):	3' <u>AAG TTC AAG GAA ACA CTA GTC</u> 5'		
mRNA:	<u>UUC AAG UUC CUU UGU GAU CAG</u>		
Amino Acid:	Phe Lys Phe Leu Cys Asp Gln		
Mutation Sequence <u>4859 Del A</u>			
Coding Strand DNA (Sense Strand):	5' <u>TTC AGT TCC TTT GTG ATC AG</u> 3'		
Template Strand DNA (Anti-Sense Strand):	3 <u>′AAG TCA AGG AAA CAC TAG TC</u> 5′		
mRNA:	<u>UUC AGU UCC UUU GUG AUC AG</u>		
Amino Acid:	Phe Ser Ser Phe Val lle		
1. What type of mutation is this?			

What type of mutation is this?
 Deletion
 What result does the mutation have on the protein?

Codes for different amino acids and shortens the protein.





Answers

Name of Population: *Filipinos* Location of sequence: <u>BRCA 2</u> Start with <u>4261</u> End With <u>4278</u> Normal Sequence Coding Strand DNA (Sense Strand): 5'GTT TCT AAG CAA TTA TGT 3' Template Strand DNA (Anti-Sense Strand): 3'CAA AGA TTC GTT AAT ACA 5' mRNA: GUU UCU AAG CAA UUA UGU Amino Acid: Val Ser Lys Gln Leu Cys Mutation Sequence 4265 Del CT Coding Strand DNA (Sense Strand): 5'<u>GTT TAA GCA ATT ATG T</u> 3' Template Strand DNA (Anti-Sense Strand): 3'CAA ATT AAT CGT TAA TAC A 5' mRNA: GUU UAA GCA AUU AUG U Amino Acid: Val stop Ala lle Met 1. What type of mutation is this? Deletion. What result does the mutation have on the protein? 2. Codes for different amino acids and results in a shorter (truncated) protein. Name of Population: Dutch Location of sequence: BRCA 2 Start with 5572 End With 5595 Normal Sequence Coding Strand DNA (Sense Strand): 5'AGA GAC AAG TGC CTG AAT TAC AGT3' Template Strand DNA (Anti-Sense Strand): 3'TCT CTG TTC ACG GAC TTA ATG TCA 5' mRNA: AGA GAC AAG UGC CUG AAU UAC AGU Amino Acid: Arg Asp Lys Cys Leu Asn Tyr Ser Mutation Sequence 5579 Ins A Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand):

mRNA: Amino Acid: 5'AGA GAC AAA GTG CCT GAA TTA CAG T 3' 3'TCT CTG TTT CAC GGA CTT AAT GTC A 5' AGA GAC AAA GUG CCU GAA UUA CAG T Arg Asp Lys Val Pro Glu Leu Gln

1. What type of mutation is this? Insertion.

What result does the mutation have on the protein? 2. Codes for different amino acids.





Answers

Name of Population: <u>African Americans</u> Location of sequence: <u>BRCA 2</u> Start with <u>1531</u> End With <u>1554</u> Normal Sequence

Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand): mRNA: Amino Acid:

5'<u>CAA CAT GGT GAA ACC CTA TCT CTA</u>3' 3'<u>GTT GTA CCA CTT TGG GAT AGA GAT</u> 5' <u>CAA CAU GGU GAA ACC CUA UCU CUA</u> Gln His Gly Glu Thr Leu Ser Leu

Mutation Sequence 1536 Del 4

Coding Strand DNA (Sense Strand): Template Strand DNA (Anti-Sense Strand): mRNA: Amino Acid:

5'<u>CAA CAG AAA CCC TAT CTC TA3</u>' 3'<u>GTT GTC TTT GGG ATA GAG AT</u> 5' <u>CAA CAG AAA CCC UAU CUC UA</u> Gln Gln Lys Pro Try Leu

- 1. What type of mutation is this? *Deletion.*
- What result does the mutation have on the protein?
 Codes for different amino acids and results in a shorter (truncated) protein.



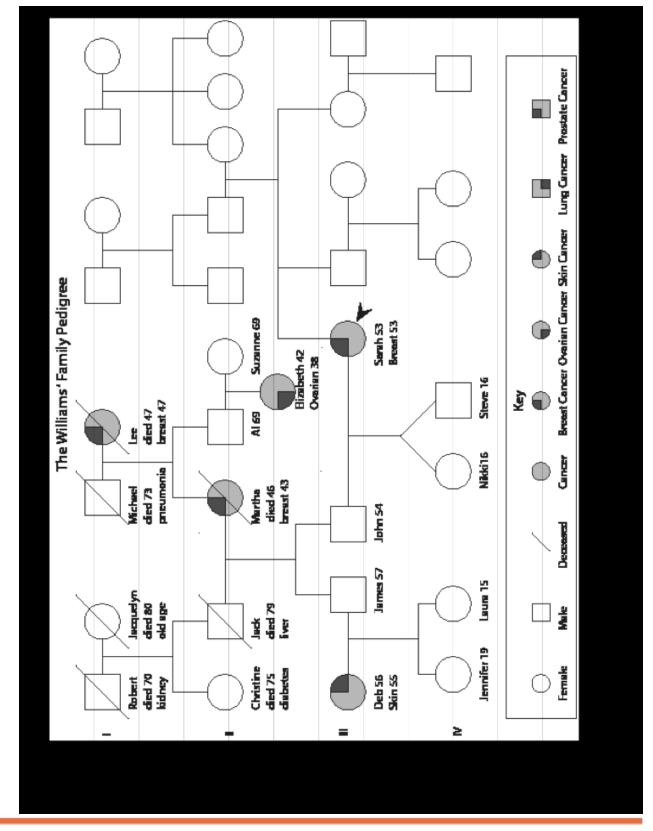


Codon Chart

	S E C O N D										
		ι ι	J		_	/	4		Ĵ		
		υυυ	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U	
		υυς	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	С	
	U	UUA	Leu	UCA	Ser	UAA	Stop	UGA	Stop	А	
		UUG	Leu	UCG	Ser	UAG	Stop	UGG	Trp	G	
		CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U	
F	C	CUC	Leu	ССС	Pro	CAC	His	CGC	Arg	С	Т
I	C	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	А	н
R		CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G	
s		AUU	lle	ACU	Thr	AAU	Asn	AGU	Ser	U	R
Т	^	AUC	lle	ACC	Thr	AAC	Asn	AGC	Ser	С	D
	A	AUA	lle	ACA	Thr		Lys	AGA	Arg	А	
		AUG	Met	ACG	Thr	AAG	Lys	AGG	Arg	G	
		GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U	
	C	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	С	
	G	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	А	
		GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G	



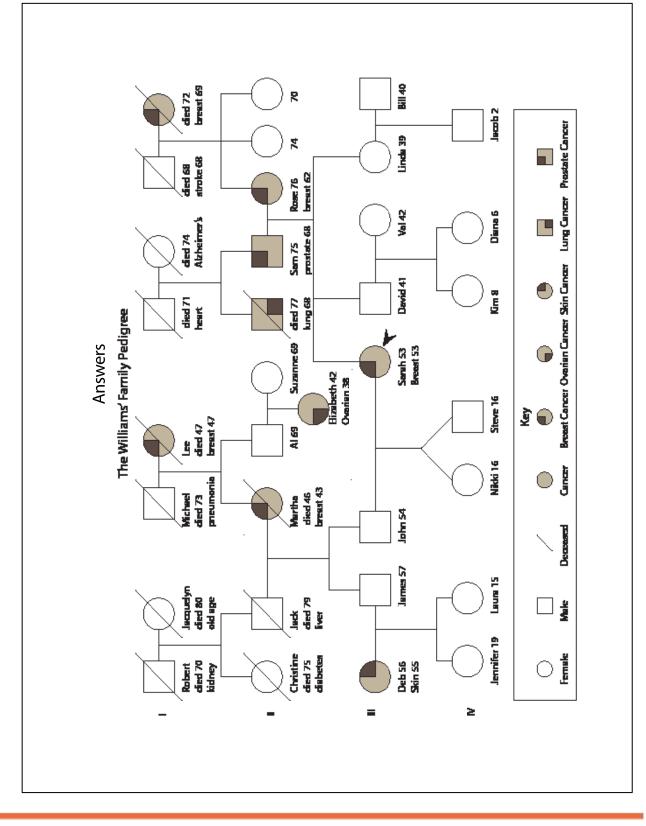




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Williams' Family Pedigree Analysis

Name:	Date:
Complete the Williams' Family Pedigree and then answer t	he following questions.
1. How many generations are shown in the pedigree?	

2. Describe what the pedigree reveals about the family's history of breast cancer.

3. If someone has a mutated BRCA gene, does that mean they have or will have breast cancer? Why?

4. BRCA mutations are dominant. Who could potentially have an inherited BRCA mutation? Why?





Williams' Family Pedigree Analysis Answers

Complete the Williams' Family Pedigree and then answer the following questions.

1. How many generations are shown in the pedigree?

Four.

2. Describe what the pedigree reveals about the family's history of breast cancer.

Both sides of the family have a history of breast cancer. Cancer is multigenerational.

3. If someone has a mutated BRCA gene, does that mean they have or will have breast cancer? Why?

No. Every person has two copies of each BRCA gene. Even if one gene is mutated, the other may still function properly.

4. BRCA mutations are dominant. Who could potentially have an inherited BRCA mutation? Why?

Mrs. Williams and her siblings because their mother had breast cancer. Mr. Williams and his cousin because women in his family have a history of breast and ovarian cancer at a young age.





Genetic Counseling Script

Page 1 of 3

GC: Hi, I'm the genetic counselor here. How are you the both of you?

Sarah: I'm fine thank you.

GC: I understand that you have some concerns about your personal and family history of cancer.

Sarah: Yes, our son, Steve, recently brought up our family history because he had been learning about genetics for one of his classes. My doctor also asked me to be seen for genetic counseling because I was just diagnosed with breast cancer at 53 years old and have a family history of breast cancer.

GC: Let's draw out your family pedigree. Who has a history of cancer in your family?

Patient: My mother had breast cancer at 62 and is currently 76. My maternal grandmother had breast cancer at 69 and died at 72. My father had prostate cancer at 68 and is currently 75. My paternal uncle was diagnosed with lung cancer at 68 and died at 77.

GC: Since your husband is here with you today and you are concerned about your children, let's get his family history as well. John, who in your family has had cancer?

John: My mom was diagnosed with breast cancer at 43 and died at 46. My maternal cousin (maternal uncle's daughter) had ovarian cancer at 38 and died at 42. My maternal grandmother was diagnosed and died of breast cancer at 47.

GC: Sarah, based on the multiple generations of breast cancer in your family, it is possible that these cancers are all related and due to mutations in hereditary breast cancer genes, such as BRCA1/2. John, based on your family history of early onset breast cancer as well as ovarian cancer, your side of the family is also suggestive of a BRCA1/2 mutation.

Sarah: Can you tell me how a mutation in the BRCA1/2 genes causes cancer?

GC: BRCA1 and BRCA2 are tumor suppressor genes. Every person is born with two copies of each gene. When these genes are working properly, their job is to stop a cell from forming cancer. But when there is a mutation in one of these genes, they do not work, the cell divides uncontrollably, and it forms cancer. Genetic testing can look for mutations in the BRCA genes.

Sarah: Okay, so as I understand it we all have these genes in working form, but when these genes do not work, we are at increased risk for developing cancer?





Genetic Counseling Script Page 2 of 3

GC: Yes, that's correct. Mutations in the BRCA1/2 genes lead to an increased risk for cancer. However, it is important to remember that even if you have a mutation in the BRCA1 or BRCA2 gene, you may or may not develop cancer depending on other factors.

Sarah: By how much is the risk for cancers increased if you have a mutation in the BRCA1 or BRCA2 genes?

GC: For breast cancer, the risk is significantly increased compared to the average woman. Also, women who carry a BRCA mutation, and who have had breast cancer in the past, are at increased risk for a second breast cancer. The risk for ovarian cancer is also significantly increased compared to the average woman. Cancer risk for males with a mutation is also higher (but not as high as the risk for females) and includes male breast cancer and prostate cancer. The risk for pancreatic cancer may be increased in both men and women.

Sarah: What happens if I test positive for a BRCA mutation?

GC: If you test positive, there are medical options ranging from screening to medications to riskreducing surgery. We will work with you and your physicians to determine which of these options are right for you. These decisions are personal, because everyone handles risk differently. If you choose to have genetic testing, we will discuss your options in detail based on your test result.

Sarah: Well, all this information may explain why I got breast cancer as well as explaining the other cancers in the family. What could this mean for my children?

GC: If you test positive for a BRCA mutation, then we have identified the cause for your cancer and the cancer in the family. Each of your children would have a 50% risk for inheriting the same mutation found in you. But it is important to remember that genetic testing is <u>not</u> recommended for children. We don't recommend that people have genetic testing before the age of 25, and your children would not be at increased risk for cancer while they are still young. If they decide to pursue genetic testing as adults, we recommend that they have the same pre-test counseling process that you have gone through so they understand the implications. We have learned a great deal about how these genes cause breast and ovarian cancer, but we continue to learn more about them every day. Therefore, as science advances, medical recommendations for people with BRCA mutations may improve in the future.

Sarah: So if I test positive for a mutation, my children will have the opportunity to be proactive and to be followed more closely.

GC: Exactly. Hopefully, they won't have to face cancer the way your generation and your parents' generation did. They may be able to detect cancer early or even prevent it.

Sarah: Can you tell me more about the genetic testing process itself?





Genetic Counseling Script Page 3 of 3

GC: Sure. Ideally, the first person in a family tested for a BRCA1 or BRCA2 mutation should be someone who has already had breast or ovarian cancer. Starting with this family member gives us better information because a family member with breast cancer is most likely to have the mutation. So in your family, you are the best person for genetic testing. John, in your family, you are the best person to test since there are no family members with cancer still living.

Sarah: Are the test results always accurate?

GC: Yes, this testing is highly accurate. However, it is possible that testing may not detect a mutation that is present in these genes. Also, there may be other genes that the testing may not identify, and these genes may also be responsible for the cancers in the family. There is new technology that can test for many breast cancer genes at the same time, in addition to BRCA1/2. However, both of your families are most suggestive of a BRCA1/2 mutation. Therefore, we will start testing there. Should that testing be negative, we may consider multi-gene testing for hereditary breast cancer.

Sarah: What is the cost of the test?

GC: About \$2,000, but most insurance companies cover some or all of the cost.

Sarah: Will my health insurance coverage be affected if I test positive for a mutation?

GC: Some people are worried about health insurance discrimination. However, there are federal and state laws that protect genetic information and prevent health insurance discrimination. These laws also keep employers from discriminating based on genetic test results.

Sarah: Thanks very much for the information. I think I will go forward with genetic testing.

John: I didn't think I would need to get tested, but for my future risk of cancer and more importantly, for my children's sake, I will also like to go ahead with testing.





Sample Patient Letter

Instructions: Write a letter to the William's family from the point of view of a genetic counselor. Suggest whether or not you believe they should proceed with genetic testing. Make sure to address all topics listed below.

Dear Mr. & Mrs. Williams,

Introduction

- State the purpose of the letter. Recommend the William's family share this letter with their family.
- Describe breast cancer and the factors that may cause it (environment, diet, risk factors).
- Explain the importance of family history and breast cancer susceptibility genes (BRCA1 & 2).
- State what percentage of all cancer is due to cancer susceptibility gene.
- Describe what factors suggest a breast cancer mutation in a family (age, types of cancer, men with breast cancer).

Patient's Medical and Family History

- Describe patient's medical history.
- Review pedigree and discuss family history of breast cancer.
- Summarize if patient's family history suggests a gene mutation and explain your reasoning.

Genetic Testing Recommendations

- Explain how the patient can get a genetic test and the costs.
- Explain the implications of test results (what a positive/negative test can mean).
- Discuss genetic discrimination and federal/state laws that protect against it.

Conclusion

- Determine if you believe/do not believe the William's should get tested.
- Summarize why the patient should/should not get tested.

Sincerely,

(Your name)





Sample Patient Letter

Dear Mr. & Mrs. Williams,

Introduction

This letter summarizes our genetic counseling session. We suggest you save this letter as a part of your medical records. We also encourage you to share this letter with your family and doctors.

Breast cancer is a common disease. Many factors, such as age, family history, hormones, and other factors such as diet and environmental exposures affect risk. Researchers do not know exactly how these factors interact to cause cancer. Typically, cancer is caused by a buildup of genetic mutations that interact with the environment over a lifetime.

Family history is a risk factor for breast cancer. Approximately 5–10% of all cancers are due to a cancer susceptibility gene, such as BRCA1 and BRCA2, which may increase the risk for breast and ovarian cancer. A family may have a mutated BRCA1 or BRCA2 gene if many people in different generations have breast and ovarian cancer, cancer is diagnosed at younger ages and men have breast cancer.

Medical and Family History

Based on your personal and family history, you may/may not be a good candidate for genetic testing because...

Genetic Testing Recommendations

As we discussed, the test is simple. A nurse will take a small amount of blood from your arm using a needle. The blood sample will then go to a lab to be analyzed. The test costs about \$2,000. Most insurance companies will cover some or all of the cost.

A positive result does not mean you will get cancer. A negative result does not mean there is no genetic basis for your cancer. There may be other mutations that have not been discovered yet.

We also talked about genetic discrimination. There are federal and state laws that protect genetic information and prevent discrimination.

Conclusion

After consideration, you indicated you are/are not interested in genetic testing.

Sincerely,

(Your name)





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Name:		Date:	

Instructions: Go to: http://learn.genetics.utah.edu/content/labs/gel/ and complete the Gel Electrophoresis Virtual Lab Activity. Answer the questions below.

- 1. Molecules of DNA can be separated based on their ______ with electrophoresis.
- 2. Besides DNA, what other molecule can be separated with electrophoresis?
- 3. Describe the structure of the gel used in electrophoresis.
- 4. Why does DNA move through the gel?
- 5. What size strands move furthest from the wells at the top of the gel?
- 6. List the SIX things you need to make an electrophoresis gel.
 - 1)
 - 2)
 - 3)
 - 4)
 - 5)
 - 6)
- 7. What is agarose made from?





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- 8. What is the buffer solution made from?
- 9. Why do researchers use buffer solution?
- 10. What must be done with the agarose/buffer mixture?
- 11. What do you do with the comb?
- 12. Explain the purpose of the comb.
- 13. What two things do you need to set up the electrophoresis box?
- 14. Besides conducting electricity, what is another job of the buffer solution?
- 15. To load the samples, in addition to the box with the gel, what 4 things do you need?
 - 1)
 - 2)
 - 3)
 - 4)





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16.	What are two characteristics of the loading buffer that are helpful (and why are they helpful)?
	Characteristic Why helpful
	1)
	2)
17.	Explain the purpose of the DNA standard.
18.	The red end of the power supply generates a charge and the black end generates a charge.
19.	DNA has a (<u>positive /negative</u>) charge so it will move to the <u>(red positive /black</u> <u>negative)</u> electrode which must be plugged in at the end <u>(closest to /furthest from)</u> the wells.
20.	When looking in the electrophoresis box, how will you know that the current is actually running?
21.	Explain the purpose of ethidium bromide.
22.	What type of light do you need?
23.	Where does ethidium bromide attach to DNA molecules?
24.	Why must you wear gloves when working with ethidium bromide?
25.	How long were each of the DNA fragments in your experiment?
	abp
	bbp

c. _____bp





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Instructions: Go to: http://learn.genetics.utah.edu/content/labs/gel/ and complete the Gel Electrophoresis Virtual Lab Activity. Answer the questions below.

- 1. Molecules of DNA can be separated based on their *size* with electrophoresis.
- 2. Besides DNA, what other molecule can be separated with electrophoresis? *Proteins*
- 3. Describe the structure of the gel used in electrophoresis.

Spongy, with many tiny holes. Similar to gelatin.

4. Why does DNA move through the gel?

DNA moves through the gel because of an electric current. The negatively charged DNA moves toward the positive end of the gel.

5. What size strands move furthest from the wells at the top of the gel?

Small

- 6. List the SIX things you need to make an electrophoresis gel.
 - 1) Agar
 - 2) Buffer solution
 - 3) Flask
 - 4) Gel comb
 - 5) Gel mold
 - 6) Microwave
- 7. What is agarose made from?

Seaweed





Page 2 of 3

- What is the buffer solution made from? Salt water mixture.
- Why do researchers use buffer solution? To conduct electricity.
- 10. What must be done with the agarose/buffer mixture? It is heated and poured in the gel mold.
- What do you do with the comb? Place it into the gel.
- Explain the purpose of the comb.
 To create wells so samples can be entered.
- What two things do you need to set up the electrophoresis box? Gel and Buffer solution.
- Besides conducting electricity, what is another job of the buffer solution? To keep the gel from drying out.
- 15. To load the samples, in addition to the box with the gel, what 4 things do you need?
 - 1) Loading buffer
 - 2) DNA sample
 - DNA size standard
 - Pipette





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16. What are two characteristics of the loading buffer that are helpful (and why are they helpful)?

Characteristic	Why helpful
1) Contains dye	Makes the sample easy to see when loading
2) Goopy (thick)	Thickens DNA so it stay in wells

17. Explain the purpose of the DNA standard.

To serve as a size reference.

- The red end of the power supply generates a <u>positive</u> charge and the black end generates a <u>negative</u> charge.
- DNA has a <u>negative</u> charge so it will move to the <u>red positive</u> electrode which must be plugged in at the end <u>furthest from</u> the wells.
- 20. When looking in the electrophoresis box, how will you know that the current is actually running?

You can see tiny air bubbles coming out of the electrodes.

21. Explain the purpose of ethidium bromide.

It stains DNA by binding to it.

22. What type of light do you need?

Florescent.

- Where does ethidium bromide attach to DNA molecules?
 Between the rungs on the DNA ladder.
- Why must you wear gloves when working with ethidium bromide? It can damage your DNA.
- 25. How long were each of the DNA fragments in your experiment?
 - a. <u>6,000</u>bp
 - b. <u>3,500</u>bp
 - с. <u>1,500</u> bp





CONFIDENTIAL

BRCA1-BRCA2 Gene Sequence Analysis Result

Patient				
Name:	Williams, John			
Date of Birth:	August 14, 1954			
Patient ID: B1010JK				
Gender:	Male			
Specimen:	Blood			

Specific Gene Variant
943ins10
None Detected

Interpretation	
POSITIVE FOR A DELETERIOUS MUTATIC	N

The results of this analysis are consistent with the germline BRCA1 frameshift mutation 943ins10, resulting in a stop codon at amino acid position 289 of the BRCA1 protein. Although the exact risk of breast and ovarian cancer conferred by this specific mutation has not been determined, studies of this type of mutation in high-risk families indicate that deleterious mutations in BRCA1 may confer as much as an >80% risk of breast cancer by age 70 in women (Am. J. Hum. Genet. 62: 676-689, 1998). Mutations in BRCA1 have been reported to confer up to a 1.2% risk of male breast cancer by age 70 (J Natl Cancer Insi 99: 1811-4, 2007), as well as increased (albeit low) risks of some other cancers, such as prostate cancer. The implications of BRCA1 mutations for the medical management of men, however, have not yet been established. Each first degree relative of this individual has a one-in-two chance of having this mutation. Family members can be tested for this specific mutation with a single site analysis.





CONFIDENTIAL

BRCA1-BRCA2 Gene Sequence Analysis Result

Patient				
Name: Williams, Sarah				
Date of Birth:	October 29, 1955			
Patient ID:	A1136KB			
Gender:	Female			
Specimen:	Blood			

Test Result				
Gene Analyzed	Specific Gene Variant			
BRCA1	None Detected			
BRCA2	None Detected			

Interpretation	
NEGATIVE FOR A DELETERIOUS MUTATION	

No deleterious mutation was found in BRCA1 or BRCA2 in this individual. This test is designed to identify mutations in 22 exons and approximately 750 adjacent intronic base pairs of BRCA1 as well as 26 exons and approximately 950 adjacent intronic base pairs of BRCA2 (a total of over 17,600 base pairs analyzed. There are other, uncommon genetic abnormalities in BRCA1 and BRCA2 that this test will not detect. This result, however, rules out the majority of abnormalities believed to be responsible for hereditary susceptibility to breast and ovarian cancer (Ford D et al., Am J Human Genetics 62: 676-689, 1998). If this individual has never had breast or ovarian cancer, it is recommended that testing an affected relative be considered to help clarify the clinical significance of this individual's negative test result.





Life-Size Gel Electrophoresis Activity Instructions

Note: The activity requires a large space, such as an open room, gym or outside area to represent the "gel." The area should accommodate 4 rows or "lanes" that students will navigate through. If you plan to conduct the activity in a classroom, use desks or chairs to create lanes. If you plan to conduct the activity outside, mark off lanes with chalk, yarn or other natural markers, such as trees or rocks.

1. Tell students they will be doing an activity to explore gel electrophoresis. Select ten students to conduct the activity. Other students should observe. Depending on the size of your class, you can have different groups of ten students rotate so all students can participate in the activity. Assign or have the ten students select the nitrogenous base (ATGC) they will be (the actual bases selected do not matter). Use nametags or different colored stickers to represent the different bases. Place students into groups or "fragments" of DNA.

2. Divide the ten students into the following groups:

Fragment 1: 1 student Fragment 2: 2 students Fragment 3: 3 students Fragment 4: 4 students

The students within Fragments 2–4 should be connected (all students in Fragment 2 connected, etc.). Students can hold hands or hold pieces of yarn to be connected.

Fragment 1	Fragment 2	Fragment 3	Fragment 4
Student 1	Student 2 Student 3	Student 4 Student 5 Student 6	Student 7 Student 8 Student 9 Student 10

3. Designate one end of the room as the Negative end of the gel and the other as the Positive end. Have each Fragment line up in a lane at the Negative end; only one group per lane (Fragments do not have to be in any particular order). Tell the class the DNA is now loaded into the gel.

Ask students what will happen in gel electrophoresis when the electrical current is turned on. Students should note that the DNA fragments will move across the gel toward the Positive end of the gel.

4. Tell students you will call, "Go!" or "Start!" to represent the electrical current being switched on. Each fragment should quickly navigate through their lane. Tell students you will call "Stop!" to represent the electrical current being switched off. Groups must freeze when you call stop.

5. Call "Stop" when the first Fragment reaches the end of their lane. All groups should stop moving and remain where they are. Ask the class to look at every Fragment's position and describe what they see. Students should note that due to the structure of the gel, smaller fragments are able to travel further and faster than the larger fragments.

6. Students can summarize what they learned via writing or drawing for homework. Students can also write how they would conduct the activity to relate it to the William's family test results.





Lesson 3 Quiz

1. Transcription and translation of a gene composed of 30 nucleotides would form a protein containing no more than ____ amino acids.

- а. З
- b. 10
- c. 60
- d. 90
- 2. Describe transcription and translation.

3. Where does the mutation 187delAG start in the BRCA1 DNA sequence and what effect does it have on the reading frame?

4. Explain the roles of a genetic counselor.

5. Emily has tested positive for a BRCA mutation. Explain how that affects her risk of developing breast cancer.

6. Explain how gel electrophoresis separates DNA fragments.

7. During gel electrophoresis, what size strands of DNA move furthest from the wells at the top of the gel?

8. When running a gel to analyze DNA, why is it important to run DNA standards in addition to the samples?





Lesson 3 Quiz Answers

1. Transcription and translation of a gene composed of 30 nucleotides would form a protein containing no more than ___ amino acids.

- a. 3
- b. 10
- c. 60
- d. 90

Correct Answer: b. 10

2. Describe transcription and translation.

Model Answer: Transcription is the process of converting DNA nucleotide sequence information into RNA sequence information. Both nucleic acid sequences use similar language, and the information is simply transcribed, or copied, from one molecule to the other. Translation is the production of proteins by decoding mRNA produced in transcription. In translation, messenger RNA (mRNA) is decoded to produce a specific polypeptide according to the rules specified by the genetic code.

3. Where does the mutation 187delAG start in the BRCA1 DNA sequence and what effect does it have on the reading frame?

Model Answer: 187 delAG is a BRCA1 mutation that starts at nucleotide 187 and deletes nucleotides A and G. This is a deletion mutation that shifts the reading frame of the DNA sequence.

4. Explain the roles of a genetic counselor.

Model Answer: Genetic counselors are health professionals trained in areas of medical genetics and counseling. They discuss genetic testing with patients and help patients make decisions that are right for them. If a patient decides to get a genetic test, the genetic counselor explains the test results with the patient and their family, as well as offers support.

5. Emily has tested positive for a BRCA mutation. Explain how that affects her risk of developing breast cancer.

Correct Answer: BRCA1 and BRCA2 are tumor suppressor genes. That means that when they are working properly, they help prevent cancer by controlling cellular division. However, in an individual with a mutation, one of the copies of the gene is not functioning properly. This increases the risk of uncontrolled cell growth. Therefore, Emily has a higher risk of developing breast cancer than a person who does not have a BRCA mutation.





6. Explain how gel electrophoresis separates DNA fragments.

Model Answer: Gel electrophoresis is a technique used for the separation of DNA, RNA, or protein molecules using an electric current applied to a gel matrix. Gel electrophoresis works because DNA is negatively charged, it moves toward the positive electrode. The DNA fragments that are shortest will travel farthest, while the longer fragments will remain closest to the origin.

7. During gel electrophoresis, what size strands of DNA move furthest from the wells at the top of the gel?

Correct Answer: The smallest strands move the furthest.

8. When running a gel to analyze DNA, why is it important to run DNA standards in addition to the samples?

Model Answer: DNA standards are used to ensure that the gel electrophoresis was performed properly and the results are accurate. If the DNA standard does not produce the expected bands, the results of the gel electrophoresis may not be correct. DNA standards are also used to determine the lengths or identities of sample fragments based on similar migration distances.