BRAND NAME GENES

How and Why We Investigate
Genes Associated with Cancer and Other Diseases

UNC
MOREHEAD

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The DESTINY Traveling Science Learning Program is a science education outreach initiative of Morehead Planetarium and Science Center (moreheadplanetarium.org) at UNC-Chapel Hill that serves pre-college teachers and schools across North Carolina. DESTINY develops and delivers a standards-based, hands-on curriculum and teacher professional development with a team of educators and a fleet of vehicles that travel throughout the state.

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KEY TERMS

amplicon. The product of a DNA amplification reaction. Also see **PCR**.

amplification. To increase the number of copies of a DNA sequence, either in vivo by inserting into a cloning vector that replicates within a host cell, or in vitro by polymerase chain reaction.

annealing. Binding of oligonucleotide primers to complementary sequences on the template DNA strands.

benign. Not malignant, or not disease-causing. Benign tumors may grow larger but do not spread to other parts of the body.

billion. 1,000,000,000 (one million times one thousand).

bioprospecting. The search for useful organic compounds in microorganisms, plants, and fungi. Often, these organisms grow in extreme environments, such as rainforests, deserts, and hot springs.

biopsy. The removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue.

biotechnology. The use of living cells and their molecules to solve problems and make useful products.

BRCA1 and **BRCA2.** These terms are shorthand for "Breast Cancer 1" and "Breast Cancer 2," the first breast cancer genes to be identified. Mutated forms of these genes are believed to be responsible for about half the cases of inherited breast cancer, especially those that occur in younger women. Both are tumor suppressor genes.

cancer. Diseases in which abnormal cells divide and grow unchecked. Cancer can spread from its original site to other parts of the body and can also be fatal if not treated adequately.

carcinogen. Any substance that causes cancer.

carcinogenesis. The process by which normal cells are transformed into cancer cells.

carcinoma. Any of the various types of cancerous tumors that form in the epithelial tissue, the tissue forming the outer layer of the body surface and lining the digestive tract and other hollow structures. Examples of this kind of cancer include breast, lung, and prostate cancer.

DCIS. Ductal carcinoma *in situ* is a common type of non-invasive cancer that starts in the milk ducts and stays in the same place (*in situ*).

deletion. A particular kind of mutation: loss of a piece of DNA from a chromosome. Deletion of a gene or part of a gene can lead to a disease or abnormality.

denature. The process of melting apart two complementary DNA strands. In vivo, denaturation is accomplished by enzymes. In PCR, denaturation is accomplished by heat and sets the stage for each strand of DNA to be doubled (i.e., replicated twice).

deoxynucleoside triphosphates. See **dNTPs**.

dNTPs. Common abbreviation for all four deoxynucleotide triphosphates (dATP, dTTP, dGTP, dCTP) used in synthesizing DNA.

ELSI. This acronym stands for Ethical, Legal, and Social Issues. The ELSI Research Program was established in 1990 as an integral part of the Human Genome Project to foster understanding of the wide-ranging implications of genetic and genomic research for individuals, families, and communities.

enzyme. A protein that encourages a biochemical reaction, usually speeding it up. Organisms could not function if they had no enzymes. Enzymes are produced by live organisms, and they can be artificially manufactured in large quantities through biotechnology.

extension. This refers to the process of Taq polymerase adding dNTPs (deoxynucleotide triphosphates—dATP, dTTP, dCTP, or dGTP) onto the ends of oligonucleotide primers. Extension follows the base pairing rule and proceeds in the 5' to 3' direction. Extension is catalyzed by the Taq polymerase enzyme.

family history. A record of the relationships among family members along with their medical histories. This includes current and past illnesses. A family history may show a pattern of certain diseases in a family. Also called family medical history.

genetic counseling. A short-term educational counseling process for individuals and families who have a genetic disease or are at risk for such a disease. Genetic counseling provides them with information about their condition and helps them make informed decisions.

genome. A person's complete nuclear genetic make-up. The blueprint to make exactly one particular person, tree, dog, or anything else that relies on DNA.

genomic DNA. The sum total of the DNA that is found within the nucleus.

GINA. In May 2008, President Bush signed into law the Genetic Information Nondiscrimination Act (GINA), which prohibits U.S. insurance companies and employers from discriminating on the basis of information derived from genetic tests.

inherited. Transmitted through genes from parents to offspring.

locus. A genetic marker. A locus refers to a position on a chromosome, and may or may not be linked to a gene. The plural is "loci" (not "locuses").

mammogram. An x-ray of the breast.

mastectomy. Surgery to remove the breast (or as much of the breast tissue as possible).

master mix. The main solution of a PCR reaction which contains all of the necessary components (dNTPs, primer, buffer, salts, polymerase, magnesium) of the reaction except the template DNA.

mutation. A permanent structural alteration in DNA. In most cases, DNA changes either have no effect or cause harm, but occasionally a mutation can improve an organism's chance of surviving and passing the beneficial change on to its descendants.

nucleotide. The fundamental unit of DNA or RNA. Each consists of a sugar (deoxyribose or ribose), phosphate, and nitrogenous base (adenine, thymine, cytosine, or guanine and uracil in place of thymine in RNA).

oligonucleotide. A DNA or RNA molecule usually composed of a small number of nucleotides. Also see **primer**.

oncogene. A gene that is capable of causing the transformation of normal cells into cancer cells.

oncology. The study of cancer.

pathobiology. Also called pathology, this is the study of tissues and organs in connection with disease.

pathologist. A doctor who identifies diseases by studying cells and tissues under a microscope.

pathology report. The description of cells and tissues made by a pathologist based on microscopic evidence, and sometimes used to make a diagnosis of a disease.

PCR. The commonly used abbreviation for polymerase chain reaction, the process of amplifying or synthesizing DNA within a test tube.

pedigree. A simplified diagram of a family's genealogy that shows family members' relationships to each other and how a particular trait or disease has been inherited.

phenotype. The observable traits or characteristics of an organism, for example hair color, weight, or the presence or absence of a disease. Phenotypic traits are not necessarily genetic.

polymerase chain reaction. See **PCR**.

polymorphism. Among individuals, a polymorphism is a common variation in their DNA. A single locus may be polymorphic in different individuals, having several different alleles. Literally translates as "many forms."

primer. A short, single-stranded piece of DNA (usually 3-30 bases in length) that binds to one side of a specific region of another single-stranded piece of DNA and initiates (or primes) the process of adding more nucleotides along that strand. Primers for PCR are usually synthesized in a laboratory. Also see **oligonucleotide**.

Taq DNA polymerase. Heat-stable DNA polymerase that was isolated from the heat-tolerant bacterium *Thermus aquaticus*. This DNA polymerase is commonly used in PCR reactions. In 1989, *Science* magazine named *Taq polymerase* "The Molecule of the Year."

template. The strand of DNA that contains the target sequences of the oligonucleotide primers and that will be copied into its complementary strand.

thermocycler. A device with an incubation well whose temperature can be programmed to change very rapidly, accurately, and in repetitive cycles. An incubation well is a metal block into which special sample tubes fit perfectly.

thermophile. An organism which is adapted to high temperatures, such as in hot springs and geysers, smoker vents on the sea floor, and domestic hot water pipes. A wide range of bacteria, fungi, and simple plants and animals can grow at temperatures up to 50^0C; thermophiles grow and reproduce at above 50^0C.

thermostable. A molecule which retains its biological activity at some specified higher temperature.

tissue. A group or layer of cells that work together to perform a specific function.

tumor. An abnormal mass of tissue, also called a neoplasm, that results when cells divide more than they should or do not die when they should. Tumors may be benign (not cancer) or malignant (cancer).

tumor suppressor gene. A protective gene that normally limits the growth of tumors. When a tumor suppressor is mutated, it may fail to keep a cancer from growing. BRCA1 and *p53* are well-known tumor suppressor genes.

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THE KEY COMPONENTS OF THE 5E MODEL

PHASE	WHAT THE TEACHER DOES THAT IS	
	Consistent with the 5E Model	Inconsistent with the 5E Model
ENGAGE 	• Creates interest • Generates curiosity • Raises questions • Elicits responses that uncover what students know or think about the concept/subject	• Explains concepts • Provides definitions and answers • States conclusions • Provides premature answers to students' questions • Lectures
EXPLORE 	• Encourages students to work together without direct instruction from teacher • Observes and listens to students as they interact • Asks probing questions to redirect students' investigations when necessary • Provides time for students to puzzle through problems • Acts as a consultant for students	• Provides answers • Tells or explains how to work through the problem • Tells students they are wrong • Gives information or facts that solve the problem • Leads students step-by-step to a solution
EXPLAIN 	• Encourages students to explain concepts and definitions in their own words • Asks for justification (evidence) and clarification from students • Formally provides definitions, explanations, and new labels • Uses students' previous experiences as the basis for explaining concepts	• Accepts explanations that have no justification • Neglects to solicit students' explanations • Introduces unrelated concepts or skills
ELABORATE 	• Expects students to use formal labels, definitions and explanations provided previously • Encourages students to apply or extend concepts and skills in new situations • Reminds students of alternative explanations • Refers students to existing data and evidence and asks "What do you already know?""Why do you think . . . ?"	• Provides definitive answers • Tells students they are wrong • Lectures • Leads students step-by-step to a solution • Explains how to work through the problem
EVALUATE 	• Observes students as they apply new concepts and skills • Assesses students' knowledge and/or skills • Looks for evidence that students have changed their thinking or behaviors • Allows students to assess their own learning and group process skills • Asks open-ended questions, such as "Why do you think . . . ?""What evidence do you have?""What do you know about x?""How would you explain x?"	• Tests vocabulary words, terms, and isolated facts • Introduces new ideas or concepts • Creates ambiguity • Promotes open-ended discussion unrelated to concept or skill

(Trowbridge & Bybee, 1990), adapted by Biological Sciences Curriculum Study
Available online at http://science.education.nih.gov/supplements/nih1/diseases/guide/module3.htm

North Carolina Standard Course of Study for Biology — Grades 9-12	
Highlighted sections are objectives addressed in the Brand Name Genes module	
Strands: Nature of Science, Science as Inquiry, Science and Technology, Science in Personal and Social Perspectives. The strands provide the context for teaching of the content Goals and Objectives.	
Competency Goal 1: **The learner will develop abilities necessary to do and understand scientific inquiry.**	
Objectives 1.01 Identify biological questions and problems that can be answered through scientific investigations.	• Students consider how science can be used to discover and understand the genetic predisposition for breast cancer and related cancers.
1.02 Design and conduct scientific investigations to answer biological questions. • Create testable hypotheses • Identify variables. • Use a control or comparison group when appropriate. • Select and use appropriate measurement tools. • Collect and record data. • Organize data into charts and graphs. • Analyze and interpret data. • Communicate findings.	• Students conduct a PCR experiment and analyze the results in order to understand how science investigators can determine a genetic predisposition for breast cancer and related cancers.
1.03 Formulate and revise scientific explanations and models of biological phenomena using logic and evidence to: • Explain observations • Make inferences and predictions • Explain the relationship between evidence and explanation	• Students use research data for comparison as they investigate under microscope which tissue samples are cancerous or normal.
1.04 Apply safety procedures in the laboratory and in field studies: • Recognize and avoid potential hazards •Safely manipulate materials and equipment needed for scientific investigations	• While conducting an experiment using PCR and gel electrophoresis techniques, students wear appropriate safety glasses and gloves; operate equipment, which involves electricity, in a safe manner; and dispose of experimental materials in appropriate containers.
1.05 Analyze reports of scientific investigations from an informed, scientifically literate viewpoint including considerations of: • Appropriate sample • Adequacy of experimental controls • Replication of findings •Alternative interpretations of the data	

Competency Goal 2: The learner will develop an understanding of the physical, chemical and cellular basis of life.	
Objectives 2.01 Compare and contrast the structure and functions of the following organic molecules: • Carbohydrates • Proteins • Lipids • Nucleic acids	• Students review their understanding of the structure of deoxyribonucleic acid (DNA). • Students learn that enzymes are proteins and serve a number of catalyzing functions that are harnessed in biotechnology.
2.02 Investigate and describe the structure and functions of cells including: • Cell organelles • Cell specialization • Communication among cells within an organism.	• Students learn about the differences between the structure of normal and cancerous cells.
2.03 Investigate and analyze the cell as a living system including: • Maintenance of homeostasis • Movement of materials into and out of cells • Energy use and release in biochemical reactions	
2.04 Investigate and describe the structure and function of enzymes and explain their importance in biological systems.	• Students learn about the discovery, biological sources, and catalyzing functions of various enzymes used in biotechnology, including Taq DNA polymerase in the process of PCR.
2.05 Investigate and analyze the bioenergetic reactions: • Aerobic respiration • Anaerobic respiration • Photosynthesis	
Competency Goal 3: **The learner will develop an understanding of the continuity of life and the changes of organisms over time.**	
Objectives 3.01 Analyze the molecular basis of heredity including: • DNA replication • Protein synthesis (transcription, translation) • Gene regulation	• Students review their understanding of the replication of DNA as they learn the three main steps of PCR.
3.02 Compare and contrast the characteristics of asexual and sexual reproduction.	

3.03 Interpret and predict patterns of inheritance. • Dominant, recessive and intermediate traits • Multiple alleles • Polygenic inheritance • Sex-linked traits • Independent assortment • Test cross • Pedigrees • Punnett squares	• Students learn about inherited traits, particularly as they relate to genetic mutations potentially leading to cancer. • Students construct a pedigree using materials related to a family history.
3.04 Assess the impact of advances in genomics on individuals and society. • Human genome project • Applications of biotechnology	• Students learn about and assess the implications of society's increasing access to genetic information. • Students learn about biotechnology applications in medicine and industry.
3.05 Examine the development of the theory of evolution by natural selection, including: • Development of the theory • The origin and history of life • Fossil and biochemical evidence • Mechanisms of evolution • Applications (pesticide and antibiotic resistance)	
Competency Goal 4: **The learner will develop an understanding of the unity and diversity of life.**	
Objectives 4.01 Analyze the classification of organisms according to their evolutionary relationships. • The historical development and changing nature of classification systems • Similarities and differences between eukaryotic and prokaryotic organisms • Similarities and differences among the eukaryotic kingdoms: protists, fungi, plants, animals • Classify organisms using keys	
4.02 Analyze the processes by which organisms representative of the following groups accomplish essential life functions including: • Unicellular protists, annelid worms, insects, amphibians, mammals, non vascular plants, gymnosperms and angiosperms • Transport, excretion, respiration, regulation, nutrition, synthesis, reproduction, and growth and development	• Students learn about cell regulation in connection with tumor suppressor genes, mutations on these genes, and cancer.

4.03 Assess, describe and explain adaptations affecting survival and reproductive success. • Structural adaptations in plants and animals (form to function) • Disease-causing viruses and microorganisms • Co-evolution	
4.04 Analyze and explain the interactive role of internal and external factors in health and disease: • Genetics • Immune response • Nutrition • Parasites • Toxins	• Students learn about genetics related to individuals' or groups' inherited predispositions for diseases such as cancer. • Students learn about nutritional choices that individuals can make to lower their risks of cancer. • Students learn about toxins that have the potential to cause cancer.
4.05 Analyze the broad patterns of animal behavior as adaptations to the environment. • Innate behavior • Learned behavior • Social behavior	
Competency Goal 5: **The learner will develop an understanding of the ecological relationships among organisms.**	
Objectives 5.01 Investigate and analyze the interrelationships among organisms, populations, communities, and ecosystems. • Techniques of field ecology • Abiotic and biotic factors • Carrying capacity	
5.02 Analyze the flow of energy and the cycling of matter in the ecosystem. • Relationship of the carbon cycle to photosynthesis and respiration • Trophic levels — direction and efficiency of energy transfer	
5.03 Assess human population and its impact on local ecosystems and global environments. • Historic and potential changes in population • Factors associated with those changes • Climate change • Resource use • Sustainable practices/stewardship	

CORRELATION TO THE NATIONAL SCIENCE EDUCATION STANDARDS

The Teaching Standards	
Brand Name Genes Correlation	
Each activity in the module provides short-term objectives for students. There is a conceptual flow of activities that help teachers plan a timeline for teaching the module. Use of this module helps teachers to update their curriculum in response to student interest in the topic. The module's focus is active, collaborative, and inquiry-based learning.	Standard A: Teachers of science plan an inquiry-based science program for their students. In doing this, teachers • develop a framework of yearlong and short-term goals for students. • select science content and adapt and design curriculum to meet the interests, knowledge, understanding, abilities, and experiences of students. • select teaching and assessment strategies that support the development of student understanding and nurture a community of science learners.
Student inquiry is encouraged by all activities in the module. The module promotes discourse among students, and challenges students to accept responsibility for their learning. The use of the 5E instructional model with collaborative learning is an effective way of responding to diversity in student backgrounds and learning styles.	Standard B: Teachers of science guide and facilitate learning. In doing this, teachers • focus and support inquiries while interacting with students. • orchestrate discourse among students about scientific ideas. • challenge students to accept and share responsibility for their own learning. • recognize and respond to student diversity and encourage all students to participate fully in science learning. • encourage and model the skills of scientific inquiry, as well as the curiosity, openness to new ideas and data, and skepticism that characterize science.
There are a variety of assessment components provided in module. Answers are provided to help teachers analyze student feedback.	Standard C: Teachers of science engage in ongoing assessment of their teaching and of student learning. In doing this, teachers • use multiple methods and systematically gather data about student understanding and ability. • analyze assessment data to guide teaching.
The answers provided for teachers model respect for the diverse ideas, skills, and experiences of all students. Students work collaboratively in teams to complete activities in the module. Discussion activities in this module model the rules of scientific discourse.	Standard E: Teachers of science develop communities of science learners that reflect the intellectual rigor of scientific inquiry and the attitudes and social values conducive to science learning. In doing this, teachers • display and demand respect for the diverse ideas, skills, and experiences of all students. • structure and facilitate ongoing formal and informal discussion based on a shared understanding of rules of scientific discourse. • model and emphasize the skills, attitudes, and values of scientific inquiry.

CORRELATION TO THE NATIONAL SCIENCE EDUCATION STANDARDS

The Content Standards in Grades 9-12	
Brand Name Genes Activities	Specific Understandings and Abilities within the Standards
• The pre-lab, wet-lab, and post-lab activities emphasize the role and conduct of scientific inquiry in to further understanding and treatment of cancer and related health concerns.	Standard A (Science as Inquiry) : All students should develop • abilities necessary to do scientific inquiry. • understanding about scientific inquiry.
• A pre-lab role-play activity reinforces understanding of the structure and replication of DNA molecules. • Pre-lab and wet-lab activities focus on chemical reactions in living systems that are catalyzed by protein molecules called enzymes.	Standard B (Physical Science) : All students should develop understanding of • structure and properties of matter. • chemical reactions.
• A pre-lab station focuses on normal and cancerous cells; two additional stations focus on inherited genetic traits. • A pre-lab role-play activity reinforces understanding of the structure and replication of DNA molecules.	Standard C (Life Science): All students should develop understanding of • the cell. • molecular basis of heredity.
• Pre-lab activities, including a video or skit introduction and stations focusing on bioprospecting and genetic testing, help students understand the discovery and development of biotechnology products and services. • The wet-lab activity involves students in hands-on experience with two important laboratory techniques: polymerase chain reaction (PCR) and analysis of PCR products through gel electrophoresis. • Post-lab activities lead students to understand the role of surgery and other medical techniques in the evaluation and treatment of cancer.	Standard E (Science and Technology): All students should develop • understanding about science and technology.
• Pre- and post-lab activities let students explore choices that communities and individuals can make to impact health, particularly on the risk and treatment of cancers. • Pre- and post-lab activities focus students' attention on the ability of science and technology to address personal and community health challenges.	Standard F (Science in Personal and Social Perspectives): All students should develop understanding of • personal and community health. • natural resources. • environmental quality. • natural and human-induced hazards. • science and technology in local, national, and global challenges.
• Pre-lab activities lead students to understand the role of individuals in the discovery and development of scientific materials and techniques. • Post-lab activities highlight for students the roles of individuals as providers and consumers of modern health care resources.	Standard G (History and Nature of Science): All students should develop understanding of • science as a human endeavor. • nature of scientific knowledge. • historical perspectives.

INTRODUCTION

In *Brand Name Genes: How and Why We Investigate Genes Associated with Cancer and Other Diseases*, students take on the roles of employees at D.N.Aces, Inc., a fictional global biotech company. Visiting divisions within the company, students acquire knowledge that enables them to carry out a polymerase chain reaction (PCR) experiment to determine the presence of a simulated BRCA2 mutation among four siblings. The module's culminating activity focuses on diagnosis and treatment of breast cancer.

Activities in the *Brand Name Genes* module enable students to fulfill the following objectives:

- observe and describe the differences between normal and cancerous cells observed under a microscope;
- understand connections between BRCA genes and breast cancer;
- develop a medical pedigree for a family with a history of cancer;
- learn about the discovery of Taq DNA polymerase and its catalyzing role in PCR;
- learn about global bioprospecting for enzymes and their connection to the development of research techniques and consumer products;
- know the main ingredients and steps of polymerase chain reaction (PCR);
- calculate the effect of exponents in the PCR process;
- prepare a simulated PCR using correct technique and equipment to avoid contamination and produce accurate results;
- perform gel electrophoresis of actual PCR products to determine the presence of a simulated BRCA2 mutation;
- consider ethical, legal, and social issues (ELSI) related to genetic testing and other real-world applications of scientific breakthroughs;
- observe the scientific approach to diagnosis and treatment of a breast cancer patient;
- explore careers in medicine and biotechnology.

Brand Name Genes has been developed for Biology, Advanced Placement Biology, Medical Technology, and Allied Health courses at the high school level.

DISCOVERING PCR

Much of the PCR process was developed in the 1980s by biochemist Kary Mullis (a North Carolinian by birth) in a series of thoughts he had while driving one night in California. In his Nobel Prize lecture, given in exuberant style in 1993, Mullis described his process of discovery, including his realization of the role exponential growth could play in this new scientific technique:

> But what if the **oligonucleotides** in the original extension reaction had been extended so far they could now hybridize to unextended oligonucleotides of the opposite polarity in this second round. The sequence which they had been extended into would permit that. What would happen?
>
> EUREKA!!!! The result would be exactly the same only the signal strength would be doubled.
>
> EUREKA again!!!! I could do it intentionally, adding my own **deoxynucleoside triphosphates**, which were quite soluble in water and legal in California.
>
> And again, EUREKA!!!! I could do it over and over again. Every time I did it I would double the signal. For those of you who got lost, we're back! I stopped the car at mile marker 46,7 on Highway 128. In the glove compartment I found some paper and a pen. I confirmed that two to the tenth power was about a thousand and that two to the twentieth power was about a million, and that two to the thirtieth power was around a **billion**, close to the number of base pairs in the human genome. Once I had cycled this reaction thirty times I would be able to [obtain] the sequence of a sample with an immense signal and almost no background.

Brand Name Genes activities and materials lead students to an understanding of the components of the type of experiment Mullis envisioned and the place that this experiment now has on a routine basis in laboratories around the world. The D.N.Aces, Inc., Employee Welcome video introduces students to C.E.O. A. Neal Stage (the "**annealing** stage" of PCR), enzymologist Polly Merase (polymerase), and the concept of exponential growth. At the Human Resources Station, students assess the value of a retirement plan by calculating the exponential growth of their initial investment.

An additional pre-lab activity, "Paper Chain Reaction," enables students to simulate the PCR process with paper models of the DNA **template**, **primers**, nucleotides, and Taq polymerase. "Paper Chain Reaction" emphasizes the three main steps of the PCR process and the temperature change at each step. The second video in the *Brand Name Genes* collection demonstrates the process of PCR, providing background, explaining the ingredients, and demonstrating the steps and equipment.

Brand Name Genes highlights not only the "eureka moment" of PCR's discovery, but also the process of discovery that occurs at many times, in many spheres of science. In the 1960s, microbiologist Thomas D. Strock and his undergraduate assistant Hudson Freeze discovered *Thermus aquaticus* (now more commonly known by the abbreviation "Taq") in the hot springs of Yellowstone National Park. Years later, a sample of this bacterium, which Strock had made available to other researchers, would be invaluable to the development of the PCR process. The heat-loving *T. aquaticus* yields a DNA polymerase that can withstand the high temperature the PCR technique requires as it denatures (separates the strands of) DNA.

The search for organisms that will yield commercially useful genetic materials—a practice called **bioprospecting**—plays an important role in the manufacture of many familiar products, from contact-lens cleaners to stonewashed jeans. Bioprospecting discoveries are also responsible for a significant number of cancer drugs—over 62 percent, according to a United Nations report. This aspect of biotechnology research and development is explored in *Tiq Taq Go!*, a boardgame at the Bioprospecting Station.

The *Brand Name Genes* video collection includes the Employee Welcome video as an introduction to D.N.Aces, Inc. During the pre-lab and wet-lab activities, students role-play new employees of this company. This provides them an opportunity to explore different dimensions of scientific practice in the real world.

UNDERSTANDING CANCER

When we see cells in textbooks, we are usually looking at normal, or healthy, tissue. But, as we know, cells can become abnormal or unhealthy. One example is a condition that occurs when something—an **inherited** or acquired factor—causes cells to change and divide uncontrollably. Sometimes doctors and pathologists say that cancer cells look "messy." This is because, as well as growing rapidly, the cells are misshapen and clumped together. The mass, or **tumor**, which the cells form can, in turn, become malignant. Malignancy means, basically, that the tumor is becoming destructive to the body. There are about a 100 diseases that we include in the category of **cancer**.

In *Brand Name Genes*, students learn about cancer from multiple perspectives. Visiting the **Pathobiology** Station during the pre-lab, students view normal and cancerous breast tissue samples under microscopes and compare them to illustrated and photographic figures. They must hypothesize which of the samples is normal and which is not. Among the data they are provided is a photo array, "Development of Breast **Carcinoma**," prepared by Drs. David DeNardo and Lisa Coussens, which gives the students an opportunity to view and use the work of current cancer researchers. The materials at this station also provide vocabulary the students draw upon as they write about their decisions on their worksheets.

While helping students understand cancer at the cellular level, *Brand Name Genes* also takes care to show the human face of this disease. Students are able to engage with some of the opportunities and issues that arise when breakthroughs in scientific research make their way into our everyday lives. The D.N.Aces, Inc., Employee Welcome video introduces students to Elsie D. Bates ("ELSI debates") a genetic counselor whose family has been touched by cancer. As they consider the D.N.Aces employees' insurance plans at the Human Resources Station, students explore some of the ethical, legal, and social issues surrounding genetic testing, with a focus on testing for mutations on the BRCA1 and BRCA2 genes associated with breast cancer. At the Medical History Station, they construct the medical pedigree of a family to determine whether testing for the BRCA mutations is appropriate for the four youngest family members. When they perform the wet-lab, students will "meet" these four siblings again.

As a culminating activity, students watch and write about *Breast Cancer Surgery: Mastectomy*, the third

video in the *Brand Name Genes* collection. Dr. Keith Amos, a surgeon in the University of North Carolina's Medical School, leads students through the process of diagnosing a patient and performing surgery, after which he describes follow-up care.

Like all the activities in *Brand Name Genes*, this video has been specifically designed to meet North Carolina and national science education standards. Dr. Amos emphasizes the scientific approach he and his colleagues take in their decision-making, including gathering data that will help him evaluate his hypothesis about the patient's condition. *Breast Cancer Surgery* provides a reality check—demonstrating the result and power of scientific discovery, helping students follow the arc that reaches from research carried out in the field and in the laboratory to its practical application in a health care setting.

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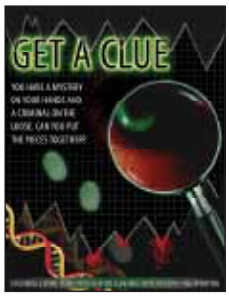
CONNECTION TO OTHER DESTINY MODULES

BRAND NAME GENES

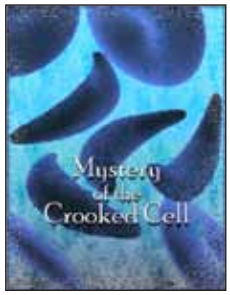
Students play the roles of employees in a global biotech company to understand connections between BRCA genes and breast cancer. Students learn about cancerous cells, medical pedigrees, ethics of genetic testing, enzyme technology, and the steps of polymerase chain reaction (PCR). In the two-part wet-lab, students prepare a simulated PCR and perform gel electrophoresis of actual PCR products to determine the presence of a simulated BRCA2 mutation among four siblings. Follow-up activities focus on diagnosis and treatment of breast cancer. For Biology, AP Biology, Medical Technology, and Allied Health courses.



GET A CLUE

In *Get a Clue*, students use agarose gels and horizontal gel chambers to separate DNA that has been cut with a restriction enzyme. *Brand Name Genes* provides an opportunity for students to analyze actual PCR product by gel electrophoresis.

MYSTERY OF THE CROOKED CELL



The *Brand Name Genes* module examines the connections between genetics and health through examination of PCR products using gel electrophoresis techniques. As either preparation for or an extension of *Brand Name Genes*, we recommend *Mystery of the Crooked Cell*, a module developed by Boston University School of Medicine's CityLab. In *Mystery of the Crooked Cell*, students examine the genetic basis for sickle cell anemia. Students observe functional differences in the normal hemoglobin and sickle cell hemoglobin which result from a point mutation that changes the DNA. In both modules students perform an electrophoresis of proteins and examine the changes that result in the protein as a result of changes in the DNA.

BIOBUSINESS

Brand Name Genes includes a focus on biotechnology, with an emphasis on bioprospecting and its applications in product development and medical research. In *BioBusiness*, students discover how businesses use recombinant DNA technology to tailor products to meet customers' needs. Students perform a procedure known as genetic transformation, which occurs when a cell takes up and expresses a new piece of genetic material. The result is a genetically modified organism that can be used in industry. In medicine, gene therapies that use similar methods are a focus for treating some cancers and other diseases caused by defective genes.

SEQUENCE OF MODULES

This suggested sequence relates these four modules:

1. GET A CLUE
2. MYSTERY OF THE CROOKED CELL
3. BRAND NAME GENES
4. BIOBUSINESS

BRAND NAME GENES IMPLEMENTATION PLAN — PRE-LAB			
Activity	Estimated Time	Summary	Purpose/Objectives
Engagement: D.N.Aces, Inc., employee welcome video.	10 mins.	Students are introduced to their new "workplace"—D.N.Aces, Incorporated—a global biotechnology company.	To provide a real-world context for the pre- and wet-lab activities.
Exploration Stations: • Bioprospecting • Human Resources • Family History Research • Pathobiology	50-60 mins.	During their first day as D.N.Aces employees, students rotate through four important divisions in the company.	To introduce information that will aid students' understanding of the technique and use of PCR, including— • the role of enzymes, including *Taq polymerase*, in biotechnology; • the power of exponents; • genetic testing for predisposition to breast cancer and other diseases.
Explanation: Paper Chain: PCR Paper Models	20 mins.	Students simulate the process of PCR through the use of paper models.	To familiarize students with the steps, ingredients, and technology associated with polymerase chain reaction (PCR).

ENGAGEMENT ACTIVITY

WELCOME TO D.N.ACES, INC.

BACKGROUND

This engagement activity sets the scene for the main pre-lab activities and the wet-lab in the *Brand Name Genes* module. Students become new employees of D.N.Aces, Incorporated, a global biotechnology company. During their first day (a class period!) as employees, the students rotate through four important divisions in the company.

The short welcome video introduces several of the D.N.Aces divisions (bioprospecting, human resources, medical history). These divisions reappear as stations for group work during the pre-lab phase of *Brand Name Genes*. Some of the personnel (a C.E.O./researcher, an international patent lawyer, and an enzymologist) who speak in the video also reappear in the bioprospecting station during the pre-lab.

In describing the purpose and activities of the company, the video highlights biotechnology-related jobs (from product development to genetic counseling), that a range of needs can be met by products emerging through gene-based research, and the concept that science is relevant to business, law, health, and other important sectors of our society.

MATERIALS

- DNAces, Inc., Employee Welcome video (included in the *Brand Names Genes* video collection)
- DVD player

Alternatively, students can be called upon to play characters in a skit based on the video script. The script is included in this guide.

INSTRUCTIONS

Explain to the class that they have recently been employed by D.N.Aces, Incorporated. Ask them, as they watch the company's employee welcome message, to be attuned to details such as these:

- the jobs people perform
- the names of the people who speak
- the company's key divisions
- how large the company has grown
- how quickly the company has grown

These are all details that will become important as they visit some of the company's divisions later in the class period and as they learn more about PCR.

D.N.Aces, Inc.

EMPLOYEE WELCOME VIDEO SCRIPT

Voice-over

This film is designed to introduce you to the history, core values, and main divisions of D.N.Aces, Incorporated. You will meet some of your fellow employees and learn about the exciting work to which you will be contributing as part of the D.N.Aces team. . . . The Founder and C.E.O. of D.N.Aces, Dr. A. Neal Stage—

A. Neal Stage, Ph.D.
D.N.Aces, Inc., Founder and CEO

I was inspired to start D.N.Aces because I wanted to use my knowledge of biology to transform every area of consumers' lives. I hope that you will share my commitment to providing the most innovative, the most effective, and the most trusted gene-based products in the world!

Voice-over

With annual revenues topping the 20 billion dollar mark—and a logo that has worldwide recognition—D.N.Aces is a leader in gene-based consumer products —from detergents and cosmetics to biofuels and reagents.

Polly Merase, Ph.D., Enzymologist

Sometimes I feel like a gold prospector in the Old West. Except that I am on D.N.Aces' team of bioprospectors. We search the world for organisms whose genes code for enzymes we can use in our products.

Voice-over

The newest division of D.N.Aces is its Medical History Division. Corporate, government, and private customers trust D.N.Aces to develop reliable medical histories of single families and large populations.

Elsie D. Bates, MS, CGC.
Genetic Cancer Risk Counselor

I come from a family that has been touched by cancer. This is why I am so passionate about working with the D.N.Aces team that focuses on the BRCA2 gene. We help men and women understand and possibly even change their genetic destinies.

Voice-over

Wealth magazine recently named D.N.Aces one of the world's 10 best biotechnology companies to work for. As a D.N.Aces employee, you will receive a competitive salary, excellent insurance and retirement benefits, and opportunities to advance within your division.

Peyton Lawe, J.D.
International Patent Lawyer

D.N.Aces started with just one employee—Dr. A. Neal Stage. Since then, our workforce has grown exponentially, literally doubling every year for 15 years. You are joining a global company that now has over 30,000 employees. We are glad to you have on board!

EXPLORATION ACTIVITY

FIRST DAY AT D.N.ACES, INC.

INTRODUCTION FOR THE TEACHER

Following the Employee Welcome video, students now embark on their first day as D.N.Aces employees. As the students rotate through four important divisions in the company (set up in four locations around the classroom), they acquire information to aid their understanding of the technique and real-world use of polymerase chain reaction (PCR). Each of the stations can also be used separately within other types of lesson plans—to reinforce knowledge about cell structure, genetic pedigrees, enzymes, and so forth.

HUMAN RESOURCES STATION

This station includes two activities that draw upon an experience that is typical for most new employees in a large company: learning about options for retirement and insurance plans. In one activity, students decide which retirement choice would be more beneficial to them: a penny doubled every year for 30 years or a payment of $10,000,000 at the end of the same period of time. This math problem highlights the power of exponents at work in the PCR process. In the second activity, students use information gathered at the station to discuss the company's insurance plans and then craft a letter stating their opinions about the company's approach to genetic testing. This writing prompt helps them engage some of the ethical, social, and legal implications (ELSI) involved when scientific breakthroughs have real-world applications.

MEDICAL HISTORY STATION

This station helps students better understand the role and pattern of inheritance in the genetic predisposition of groups and individuals for certain diseases and other traits. Students learn about some of the types of evidence that researchers have used to construct family histories of genetic traits. They also learn how researchers record these traits by completing a family's pedigree chart based on information they are given. The scenario for the *Brand Name Genes* wet-lab involves students in testing the DNA of four siblings from this family to determine the presence of a simulated BRCA2 mutation.

BIOPROSPECTING STATION

This station enables students to learn about the role that enzymes play in biotechnology. Students learn that enzymes are found in diverse organisms and locations around the world. They also learn about some of the wide range of careers that are available in fields related to the discovery and manufacture of gene-based products (e.g., microbiologist, enzymologist, business development manager, lawyer, CEO).

One of the enzymes students learn about is Taq DNA polymerase, an important catalyst in PCR. Taq polymerase is derived from the bacterium *Thermus aquaticus*, a thermophile discovered in a hot spring in Yellowstone National Park. Taq polymerase can withstand the high temperatures that the PCR technique requires as it denatures (separates the strands of) DNA.

PATHOBIOLOGY STATION

At this station, students learn about characteristics that differentiate cancerous cells from normal cells. They also have the opportunity to compare normal tissue to cancerous tissue, which they view on slides under microscopes. Photographs and instructions at the station guide students' inquiry as they observe the samples, compare them to each other and to the photographs, describe their observations, and determine which sample shows breast cancer.

D.N.Aces, Inc.

DEPARTMENT REPORT

Employee/s completing this report:

DEPARTMENT: PATHOBIOLOGY

The following differences between normal and cancer cells were noted:

The following differences between the slides were noted:

Slide _____ may show cancer for the following reasons:

DEPARTMENT: BIOPROSPECTING

PRODUCT	ENZYME	ORGANISM	LOCATION	EMPLOYEE

DEPARTMENT: HUMAN RESOURCES

Retirement Plan: I/We have decided to take Choice _____ for the following reasons:

Insurance Plan: I/We have decided to take Choice _____ for the following reasons:

DEPARTMENT: MEDICAL HISTORY

_____ I/We recommend that this client's children be tested.

_____ I/We do not recommend that this client's children be tested.

Reasons:

BRAND NAME GENES EXPLORATION ACTIVITY

BIOPROSPECTING STATION

OVERVIEW

This station enables students to learn about the role that enzymes play in biotechnology. Students learn that enzymes are found in diverse organisms and locations around the world. They also learn about some of the wide range of careers that are available in fields related to the discovery and manufacture of gene-based products: biochemist, lawyer, CEO. (Three of the employees in the *Tiq Taq Go!* game cards actually appear in the D.N.Aces, Inc., welcome video.)

One of the enzymes students learn about is Taq polymerase, an important catalyst in polymerase chain reaction (PCR). Taq polymerase is derived from the bacterium *Thermus aquaticus*. ("Taq" is a commonly used nickname for *Thermus aquaticus*.)

MATERIALS

- Station Instruction Sheet
- Bioprospecting Table Sign
- D.N.Aces Department Report (worksheet)
- *Tiq Taq Go!* game board
- *Tiq Taq Go!* game cards

INSTRUCTIONS

D.N.Aces is developing **four new product**s that require industrial enzymes. At this station, the students are responsible for determining which **enzyme**, **organism**, and **location** to focus on for each product and which **employee** to send to each location.

The *Tic Taq Go!* game board and game cards help students organize their choices before recording them on the worksheet. Clues are provided on the back of each game piece. The choices for where to send the employees may vary, depending upon students' rationales for their decisions. However, the other matches are indeed dictated by the clues.

Typically, there are clues that pinpoint the matches (and exclude other possibilities. For instance, the clues for pepsin indicate the following: "Speeds protein breakdown. Found in stomachs!" Since the Antarctic rock cod is the only organism on the board that has a stomach, this fish is the source of the organism needed

OPTIONAL FOLLOW-UP ACTIVITY

Blank game cards are provided in this guide so that teachers can assign students to create new *Tiq Taq Go!* game pieces based on their own research into enzymes that can be used to manufacture imagined new products. Students can even create marketing plans replete with ad copy and illustrations for their products.

KEY

KEY TO TIQ TAQ GO!				
PRODUCT	ENZYME	ORGANISM	LOCATION	EMPLOYEE (Answers can vary.)
Youth Fruit Skin Cream	Papain	Papaya	Ethiopia	Product Manager
Fungas Biofuel	Cellulase	*Trichoderma reesi*	Solomon Islands	Enzymologist
Scram! Detergent	Pepsin	Antarctic Rock Cod	Antarctica	Patent Lawyer
Neotaq DNA Polymerase	DNA Polymerase	*Thermus aquaticus*	Yellowstone National Park	Microbiologist

D.N.Aces, Inc.

BIOPROSPECTING

D.N.Aces, Inc.

BIOPROSPECTING

D.N.Aces, Inc.

DEPARTMENT: BIOPROSPECTING

YOUR JOB TODAY

D.N.Aces, Inc., is developing **four new product**s that require industrial enzymes. Your group is responsible for determining which **enzyme**, **organism**, and **location** to focus on for each product and which **employee** to send to each location.

INSTRUCTIONS

Read the clues on each of the game cards to find out where on the *Tic Taq Go!* board the cards must go.

First, look for the **products** that D.N.Aces is planning to develop and place each product card in a matching space on the board.

Look for the **enzyme** that each product needs.

Look for the **organism** that can be the source of each enzyme.

Look for the **location** of the organism.

Decide which **employee** should go to that location

When all of the cards have been placed on the *Tic Taq Go!* board, record your decisions on your worksheet.

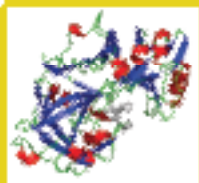
Please replace the cards in the bag before you move to the next station.

TIQ TAQ GO! BIOPROSPECTING GAME BOARD: Upper Left Corner (1 of 4)

TIQ TAQ GO! BIOPROSPECTING GAME BOARD: Upper Right Corner (2 of 4)

TIQ TAQ GO! BIOPROSPECTING GAME BOARD: Lower Left Corner (3 of 4)

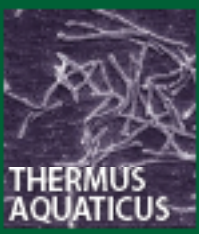
TIQ TAQ GO! BIOPROSPECTING GAME BOARD: Lower Right Corner (4 of 4)

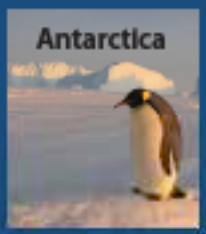

PEPSIN

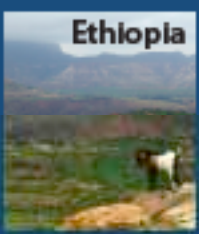

PAPAIN

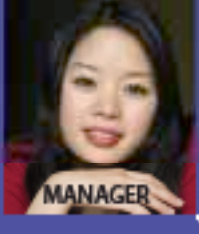

CELLULASE


DNA Polymerase









PRODUCT

This reagent speeds copying of DNA.

Can survive the high temperatures of PCR, a lab technique that copies DNA strands.

PRODUCT

Get cleaner clothes at a lower cost.

Laundry detergent for use in cold water.

PRODUCT

Whisk away tired skin cells with this cosmetic treatment inspired by nature.

PRODUCT

This biofuel is made from corn husks in a process catalyzed by a fungal enzyme.

ENZYME

Increases the speed of copying DNA.

Found in bacteria, for example.

ENZYME

Cellulase breaks down plant fibers into sugars.

Found in fungi, for example.

ENZYME

Papain digests protein.

Found in papaya.

ENZYME

Pepsin speeds protein breakdown.

Found in stomachs!

ORGANISM

A bacterium nicknamed "Taq."

Discovered in a very hot spring.

ORGANISM

A fish that can live in icy cold waters.

ORGANISM

A fungus.

Produces cellulose enzymes that turn plant fiber into sugars it can eat!

ORGANISM

A fruit tree.

Found in warm climates.

LOCATION

East African country.

An important producer of papaya fruit.

LOCATION

Famous hot springs here can reach temperature higher than 400°F.

LOCATION

The U.S. Army camped here in WWII.

Canvas tents were damaged by "jungle rot" caused by fungus.

LOCATION

Earth's coldest continent.

Surrounded by the chilly Southern Ocean.

EMPLOYEE

Mary-Claire is a business development manager who identifies opportunities for successful personal care and household cleaning products.

EMPLOYEE

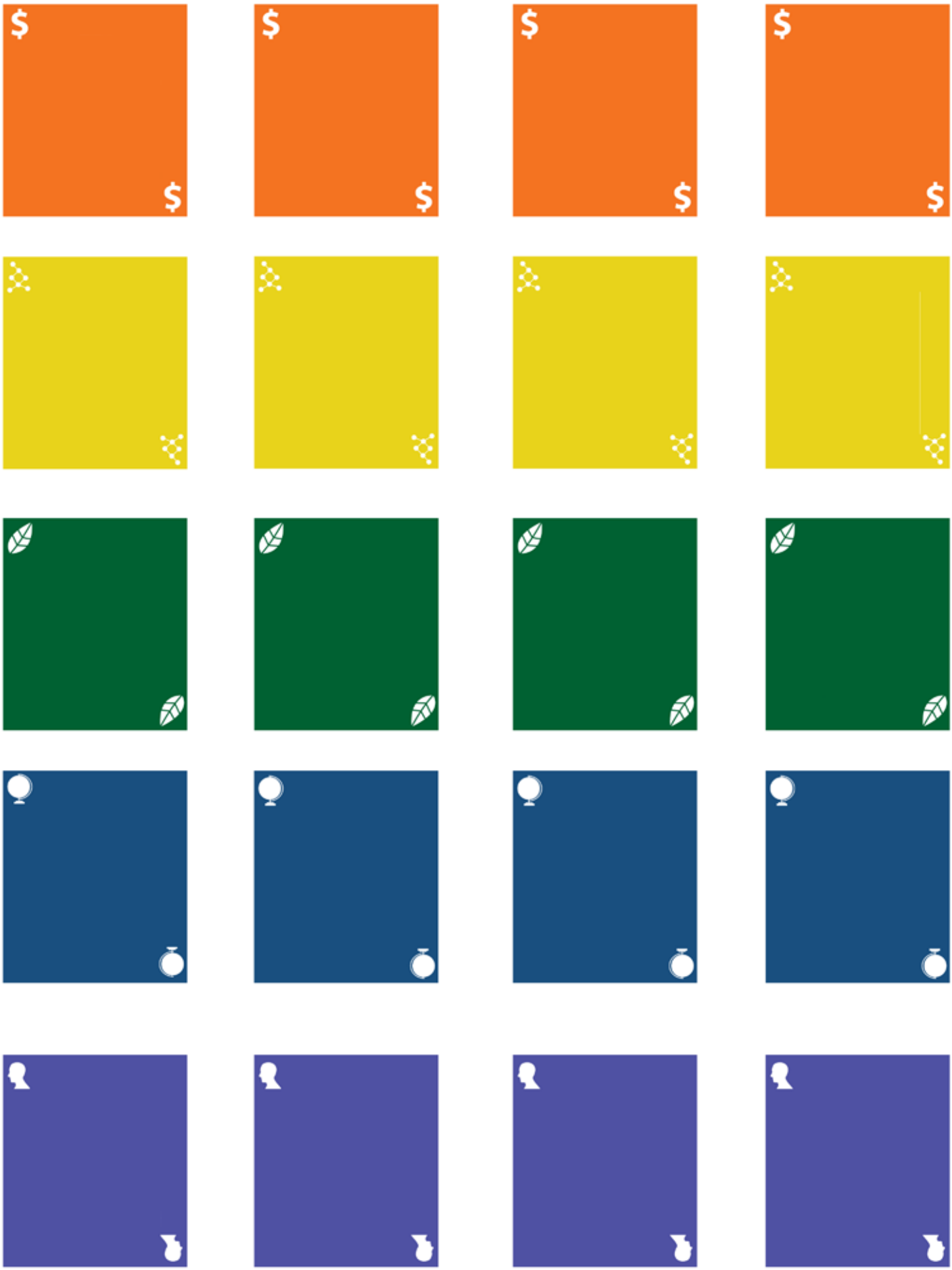
Peyton is an international patent lawyer focusing on ownership of genes and enzymes used in industry.

EMPLOYEE

Polly is an enzymologist searching for organisms whose genes code for enzymes that can be used in new products.

EMPLOYEE

Neal is C.E.O. of a biotech company and a scientist whose research focuses on inherited diseases, including some types of cancer.



PRODUCT

PRODUCT

PRODUCT

PRODUCT

ENZYME

ENZYME

ENZYME

ENZYME

ORGANISM

ORGANISM

ORGANISM

ORGANISM

LOCATION

LOCATION

LOCATION

LOCATION

EMPLOYEE

EMPLOYEE

EMPLOYEE

EMPLOYEE

BRAND NAME GENES EXPLORATION

HUMAN RESOURCES STATION

OVERVIEW

During their first weeks at almost any company, new employees may visit the personnel or human resources office. There they are likely to be given information to help them make some key decisions about their retirement and health insurance plans. With this real-life situation as a backdrop, the scene is set for learning about mathematics that are fundamental to PCR and about ethical issues raised by the availability of genetic testing.

MATERIALS

- Station Instruction Sheet
- Human Resources Table Sign
- D.N.Aces Department Report (worksheet)
- D.N.Aces scientific calculator
- Informational materials (e.g., genetic testing kit, pamphlets about breast cancer and insurance, news stories (e.g., about cancer research, genetic privacy legislation)
- Paper (one piece for each group) on which to compose letters to the HR director

INSTRUCTIONS

Step 1: The first activity at this station asks students to determine which retirement choice would be more beneficial to them: a penny doubled every year for 30 years; or a payment of $10,000,000. The number of years to retirement reflects the number of cycles that are often involved in PCR experiments.

This activity recalls the calculation that biochemist Kary Mullis made when he was developing the PCR process, as he explained in his Nobel Prize acceptance speech:

> I stopped the car at mile marker 46,7 on Highway 128. In the glove compartment I found some paper and a pen. I confirmed that two to the tenth power was about a thousand and that two to the twentieth power was about a million, and that *two to the thirtieth power was around a billion*, close to the number of base pairs in the human genome. Once I had cycled this reaction thirty times I would be able to [obtain] the sequence of a sample with an immense signal and almost no background.

Students who recall what they learned about exponents in their math classes will be able to lead the way in quickly calculating the value of the penny doubled 30 times. In this calculation, your students will have a base of 2 (to represent doubling) and an exponent of 30 (the number of years): 2^{30}.

On the D.N.Aces calculator, they will press [2] [y^x] [30]. The result—1073741824, which is over a billion pennies—translates into a total investment of $10,737,418.24.

You may choose to provide a hint to any group that asks for help, possibly by discussing exponents with them. You can remind them that the lawyer who appears at the end of the Employee Welcome video mentioned that D.N.Aces, Inc., had grown exponentially. Peyton Lawe mentioned that the company had doubled each year, going from one employee to over 30,000 in 15 years.

Alternatively, you may prefer not to provide hints, but rather encourage students to think through the problem and make their best estimate before moving on to Step 2 at this station. Let your students know that the class will discuss the calculation together after all the stations are completed.

Step 2: In the second activity, students discuss D.N.Aces' insurance plans, make choices about the plan they want, and then craft a letter stating their opinions about the company's approach to genetic testing. While honing writing and collaboration skills, this prompt helps students engage with ethical, social, and legal implications (ELSI) of breakthroughs in genetic science.

A range of informational materials can be provided at the station: a genetic testing kit, pamphlets about breast cancer and health insurance, relevant news stories, and more. The materials be updated to reflect current issues (e.g., research breakthroughs, new legislation) and answer questions students may have asked (e.g., can men get breast cancer? Are there local organizations involved in issues related to cancer?)

D.N.Aces,Inc.

HUMAN RESOURCES

D.N.Aces,Inc.

HUMAN RESOURCES

D.N.Aces, Inc.

DEPARTMENT: HUMAN RESOURCES

YOUR JOB TODAY

As a D.N.Aces employee, you will receive a competitive salary and excellent insurance and retirement benefits. Today you will make some decisions about your retirement and insurance plans.

INSTRUCTIONS

Step 1: Your Retirement Plan

Choice A
D.N.Aces, Inc., will invest a penny on your behalf today. The value of this penny will double each year until your retirement in 30 years.

Choice B
D.N.Aces will pay you a lump sum of $10,000,000 upon your retirement in 30 years.

Record and explain your decision on your worksheet.

Step 2: Your Insurance Plan

D.N.Aces, Inc., provides genetic testing and counseling to all employees who desire it. Employees use this information to determine which types of insurance plans they prefer for themselves and their families.

Please note that the Genetic Information Nondiscrimination Act of 2008 (GINA) strictly prohibits employers from discriminating against an employee because of genetic information.

Step 2, Continued: Your Insurance Plan

Genetic tests for a wide range of traits—from earwax type to predisposition for heart attack—are available to the health-care consumer.

Beginning this year, D.N.Aces, Inc., is making available to all employees testing for BRCA1 and BRCA2 mutations. These mutations increase the risk for breast, ovarian, and prostate cancers.

Two options are available to employees:

Option 1: Employees will undergo, at no cost, testing to detect mutations on their BRCA1/BRCA2 genes. Included in this option are free genetic counseling, mammograms, preventative therapies, and treatments for employees who have mutations on the BRCA1/BRCA2 genes and diseases that may be related to these mutations.*

Option 2: Employees will not undergo testing on their BRCA1/BRCA2 genes. Genetic counseling, mammograms, follow-up tests, preventative drug therapies, and related treatments for these employees are available through the company insurance plan at 50% cost.

Please indicate your choice on your Department Report.

*Employees choosing this plan give D.N.Aces, Inc., permission to use the anonymous test data to project future health insurance costs, medical services, and sick and personal leave company-wide.

Step 3: Your Proposal for the Company's Insurance Plan

As a group, discuss the choices you have made and compose a memorandum to D.N.Aces' Director of Human Resources. Please address the following points:

- The most positive aspect of the company's insurance plan.
- The most negative aspect of the company's insurance plan.
- Two suggestions that your group has for improving the plan.

Your memo must refer to information from an article or brochure available in this department.

BRAND NAME GENES EXPLORATION

PATHOBIOLOGY STATION

OVERVIEW

At this station, your students will have the opportunity to compare normal tissue to cancerous tissue, which they will view on slides under microscopes.

Photographs and instructions at the station will guide your students' inquiries as they observe the samples, compare them to each other and to the illustrations and photographs, describe their observations, and determine which sample shows breast cancer and which tissue sample is normal.

MATERIALS

- Station Instruction Sheet
- Pathobiology Table Sign
- D.N.Aces Department Report (worksheet)
- Microscope
- Slide with cancerous breast tissue
- Slide with normal breast tissue
- "Normal and Cancer Cells Structure" diagram
- "Development of Breast Carcinoma" photo array

The cancerous slide included in the *Brand Name Genes* teacher's kit is Carolina Biological's "Human Adenocarcinoma of Breast sec. 31-8766," and the normal breast tissue slide is Carolina Biological's "Human Resting Mammary Gland sec. 31-4638."

Hide the label on each slide by placing a sticker like these on it:

INSTRUCTIONS

The main activity at this station involves students in deciding which slide shows cancerous breast tissue and which shows normal breast tissue.

Instruct students to look carefully at the "Normal and Cancer Cells Structure" diagram and the "Development of Breast Carcinoma" photo array. They will need the vocabulary and visual references contained in these documents in order to complete their pathobiology tasks on the department report.

After the students tour all the stations, lead the class in a discussion of how they came to their decisions about the slides they viewed.

D.N.Aces, Inc.

PATHOBIOLOGY

D.N.Aces, Inc.

PATHOBIOLOGY

D.N.Aces, Inc.

DEPARTMENT: PATHOBIOLOGY

YOUR JOB TODAY

D.N.Aces researchers study the links between genes and certain diseases, including cancer. Today you will do one of our most difficult jobs: analyzing cancer and normal tissue samples.

Pathobiology, also called pathology, is the study of tissues and organs in connection with disease.

INSTRUCTIONS

Step 1: Read Background Information

Cancer results from mistakes (mutations) in the DNA that cause a particular gene (an oncogene or tumor suppressor gene) in a cell to be switched on or off.

The mutations may be inherited or acquired, and they can occur in just one cell or in a group of cells. The result is uncontrolled cell division – *mitosis in overdrive*.

The BRCA1 and BRCA2 genes are associated with breast, ovarian, and prostate cancers.

Note that BRCA1 and BRCA2 are tumor suppressor genes. Normally, they would help regulate functions within the cell. When one or more mutations occur, these genes' normal functions are impaired.

Step 2: Compare Normal and Cancer Cells

As a group, review and discuss the "Normal and Cancer Cells Structure" figure.

Also review photographs from a recent scientific paper. These show normal, DCIS, and invasive cancer tissue.

Using knowledge that you have acquired about cell structure, note at least 5 (and no more than 10) significant differences that you find between normal and cancer cells, and record these on your worksheet.

DCIS ("ductal carcinoma in situ") is a common type of non-invasive cancer that starts in the milk ducts and stays in the same place ("in situ").

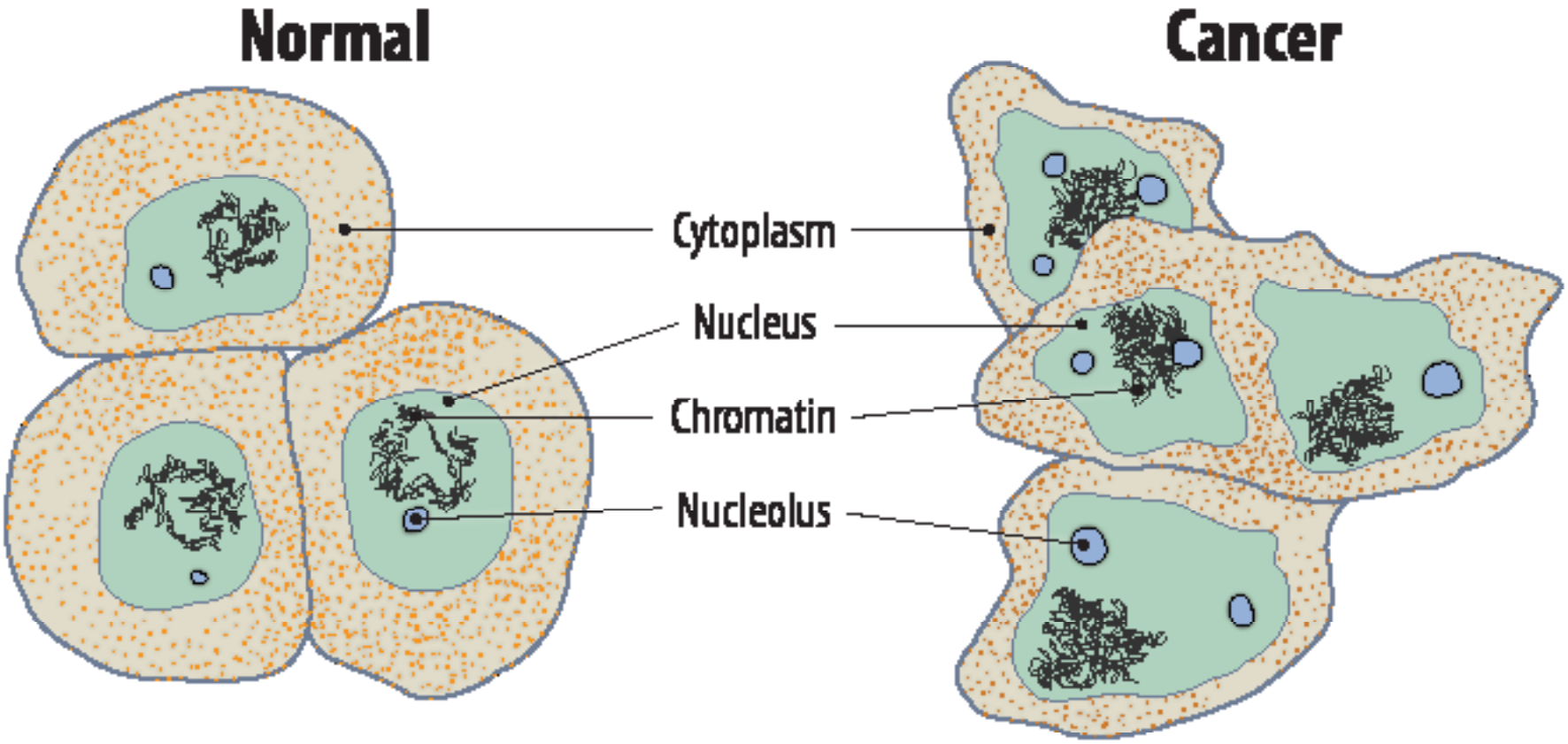
The tissue samples in the photographs have been stained so that they may be viewed more easily.

Step 3: Examine Slides

Using a microscope, study each of the slides provided. One shows normal (healthy) breast tissue. One shows breast cancer.

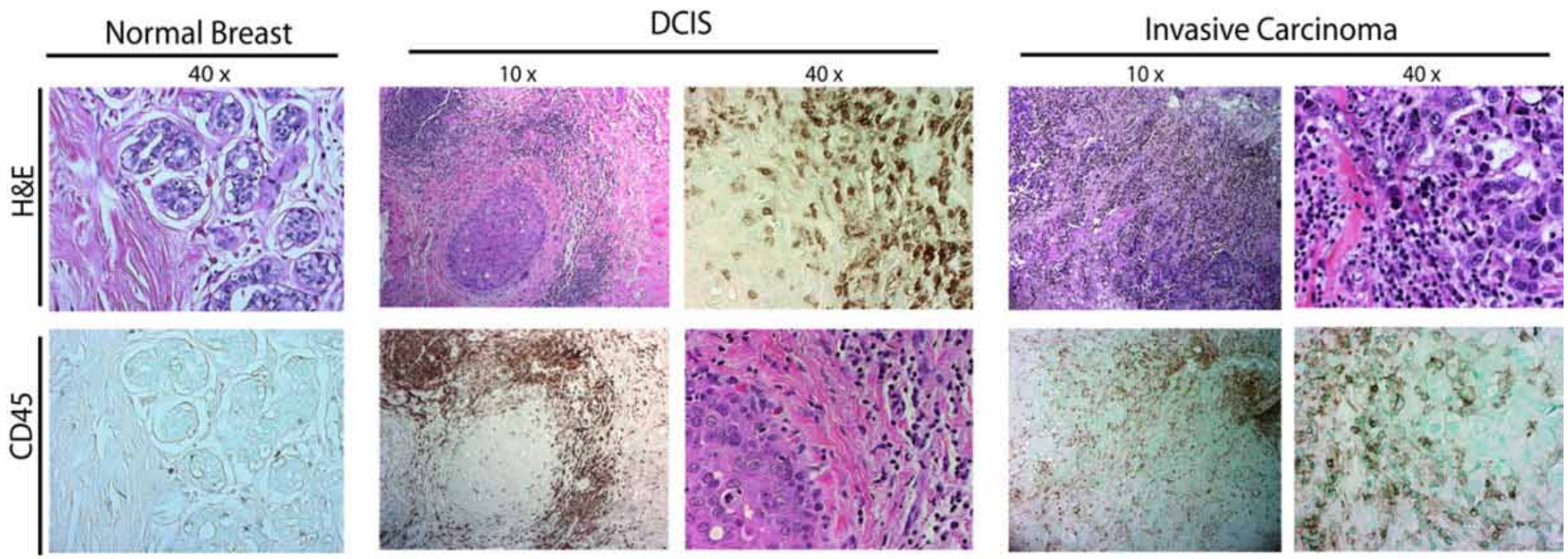
On your worksheet, record (in words or drawings) any differences you find. Speculate as to which slide (A or B) shows cancer, and provide your group's reasoning.

Normal and Cancer Cells
Structure



- Large cytoplasm
- Single nucleus
- Single nucleolus
- Finely textured chromatin

- Small cytoplasm
- Multiple nuclei
- Multiple and large nucleoli
- Coarsely textured chromatin



Development of human breast carcinoma is characterized by abundant infiltration of immune cells. Representative sections of normal, premalignant, and malignant human breast tissue stained with hematoxylin and eosin (H&E) (upper panels), and following immunodetection of CD45 (leukocyte common antigen, brown staining). DCIS, ductal carcinoma in situ.

DeNardo and Coussens Breast Cancer Research 2007 9:212 doi:10.1186/bcr1746

BRAND NAME GENES EXPLORATION ACTIVITY

MEDICAL HISTORY STATION

BACKGROUND

This activity helps students better understand the role and pattern of inheritance in the genetic predisposition of groups and individuals for certain diseases and other traits.

Students learn about some of the types of evidence that researchers have used to construct family histories of genetic traits. They also learn how researchers record these traits by completing a family's pedigree chart based on clues they are given.

MATERIALS

- Station Instruction Sheet
- Medical History Table Sign
- D.N.Aces Department Report (worksheet)
- "Examples of Medical Pedigrees" diagram
- Markers or crayons
- Small circles and squares of colored construction paper (or similar)
- Glue
- Large sheet of poster paper or flip chart paper (or similar) for each group

INSTRUCTIONS

The pedigree that the students will create at this station focuses on a history of cancer, including breast cancer, through several generations of a family.

Instruct students to look carefully at the "Examples of Medical Pedigrees" diagram. The visual representation of genders, generations, and states of health will provide the basis for the pedigrees the students create.

Students will apply paper circles and squares, glue, and markers or crayons to the poster or flip chart paper as they construct a pedigree based on the information provided at the station.

This activity at this station can be carried out by individual students. However, it is an ideal group activity, with some students taking the lead on gluing and drawing, while others keep track of all the data that must be included. Using a large sheet of poster paper or flip chart paper ensures that all members of the group can see—and participate in developing—the pedigree. Also, when it is time to share and compare results after all stations are completed, the entire class can more easily observe the pedigrees as they are shown.

D.N.Aces, Inc.

MEDICAL HISTORY

D.N.Aces, Inc.

MEDICAL HISTORY

DEPARTMENT: MEDICAL HISTORY

YOUR JOB TODAY

Customers trust D.N.Aces, Inc., to develop reliable medical histories (also called "pedigrees"). Today you will create a medical pedigree for a woman who has recently had surgery to remove a cancerous tumor in her breast.

Medical history research draws upon personal memories, historical records, genetic tests, and other information to trace the occurrence of diseases, such as cancer, within families and large populations. This research can be used to assess the probability that people within these groups may be predisposed to these diseases.

INSTRUCTIONS

Step 1: Study the examples of medical pedigrees.

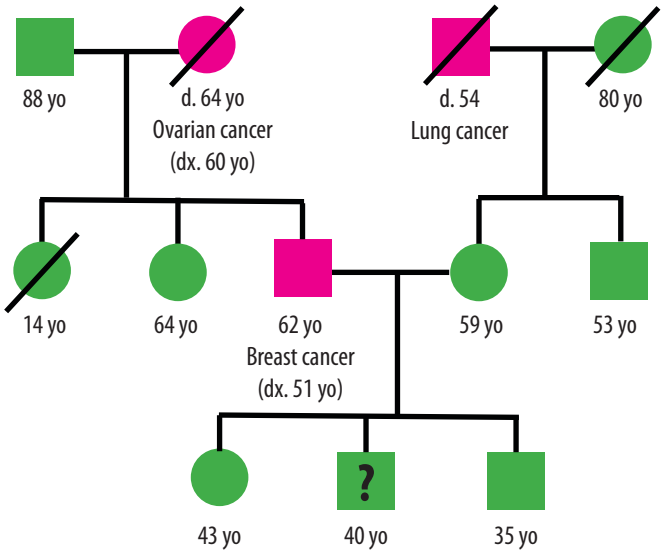
- Note how male and female individuals are symbolized.
- Note how deceased individuals are symbolized.
- Note how individuals affected with diseases are symbolized.
- Note how relationships between individuals and different generations are shown.

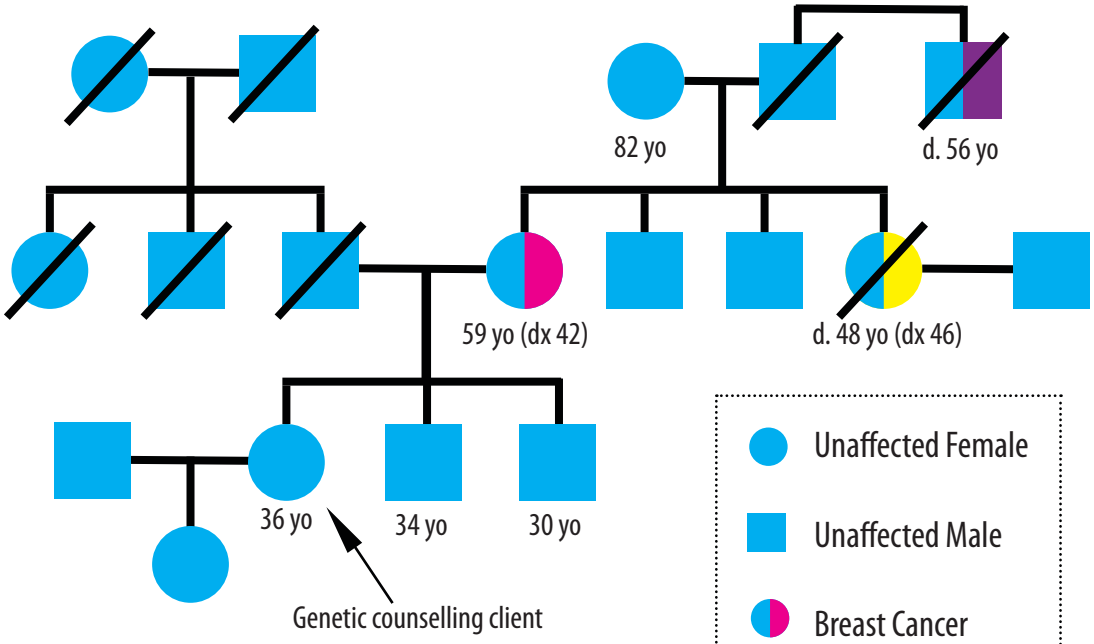
Step 2: Using the materials provided, create and label a pedigree based on the patient's family medical history. Include the following information:

- The patient's mother was diagnosed with breast cancer when she was 48.
- The patient's maternal grandmother died of ovarian cancer when she was 62.
- The patient's aunt (her mother's sister) is in good health.
- The patient's husband and father are in good health.
- The patient's paternal grandfather, a smoker, died of lung cancer at age 70.
- The patient has four healthy children: two daughters and two sons.

Step 3: Would your group recommend that this patient's children be tested for mutations on the BRCA2 gene, which is associated with breast cancer in women and men? Record your group's answer on your worksheet.

EXAMPLES OF MEDICAL PEDIGREES





- Unaffected Female
- Unaffected Male
- Breast Cancer
- Ovarian Cancer
- Prostate Cancer
- Deceased
- dx Diagnosed

BRAND NAME GENES EXPLANATION ACTIVITY

PAPER CHAIN REACTION

LEARNING THE STEPS OF POLYMERASE CHAIN REACTION

BACKGROUND

This low-budget, paper-based activity enables students to learn the basic principles of polymerase chain reaction. They learn about the three main steps, the ingredients, and the power of exponential growth as each cycle doubles the amount of DNA sample that will be available to the researcher carrying out the process.

In preparation for conducting this activity, teachers may wish to review "The Three Main Steps of PCR" in the Wet-Lab section of this guide.

MATERIALS

- DNA Template paper models (1 set)
- Free nucleotide paper models (Use the DNA Template for these—making one copy of the template for each cycle. Cut apart the models to make free nucleotides.)
- Primer paper models (Copy additional primers—doubling the amount of primers with each cycle.)
- 94°C, 52°C, 72°C, and Taq polymerase signs

The quantity of the materials needed will depend upon the number of cycles that will be simulated in the classroom. One set of these materials can be used for a small class, with all the students gathering round in a central area to take part. For much larger classes, several sets of materials may be created, so that the students can participate in smaller groups.

INSTRUCTIONS

1. Four students can be given the 94°C, 52°C, 72°C, and Taq polymerase signs and made responsible for coming forward when those stages are signalled by the teacher. Alternatively, the teacher can hold up these signs as needed. Other students can be made responsible for adding primers to each cycle.

2. The original DNA strands (template) should be placed on the classroom floor (or table) and should be bonded together (both pieces placed so they fit together).

3.. Remind students of the structure of DNA (double helix), the bases (ATCG), and how they are bonded.

4. Explain to students that right now we are beginning with a single piece of DNA. However, this is not enough DNA for a scientist to study. We need to increase the amount of the DNA we have and focus on a particular part of the DNA strand (look at the target DNA). In order for scientists to increase a particular part of DNA, they use a technique known as polymerase chain reaction (PCR). This method doubles the amount of DNA with every cycle that is run.

5. The teacher or designated student reads the bolded parts of the PCR Process below and the other students act out their parts.

PCR Process

a. The DNA template, two primers, Taq polymerase, and nucleotides are placed into a PCR chamber. Have students assigned to these roles take their symbols and go to the middle of the room. Students can act as if they are floating around in solution (which also contains buffer).

b. The solution is heated to 94°C. Have the person representing this temperature walk through the center.

c. The heat separates the strands of the DNA template. Have the students representing the two strands separate the pieces from each other.

d. Reduce the temperature to 52°C. Have the person representing the lower temperature walk through the center.

e. Primers bind to the target sites. Have the primers bind to the sites at the 3' and 5' ends. Make sure they bind to their appropriate counterparts. If needed, remind students A binds with T and G binds with C.

f. Heat the solution to 72°C. Have the person representing the warmer temperature walk through the middle of the room.

g. Taq polymerase extends the primers to replicate the rest of the DNA strands. Have the

student representing the Taq go through and read the partial DNA strands and call out their counterpart (do this for about the first six bases). Have the students representing free nucleotides bind to their complementary sites. Each free nucleotide should be added in order along the strand, with the nucleotides being added in the appropriate direction.

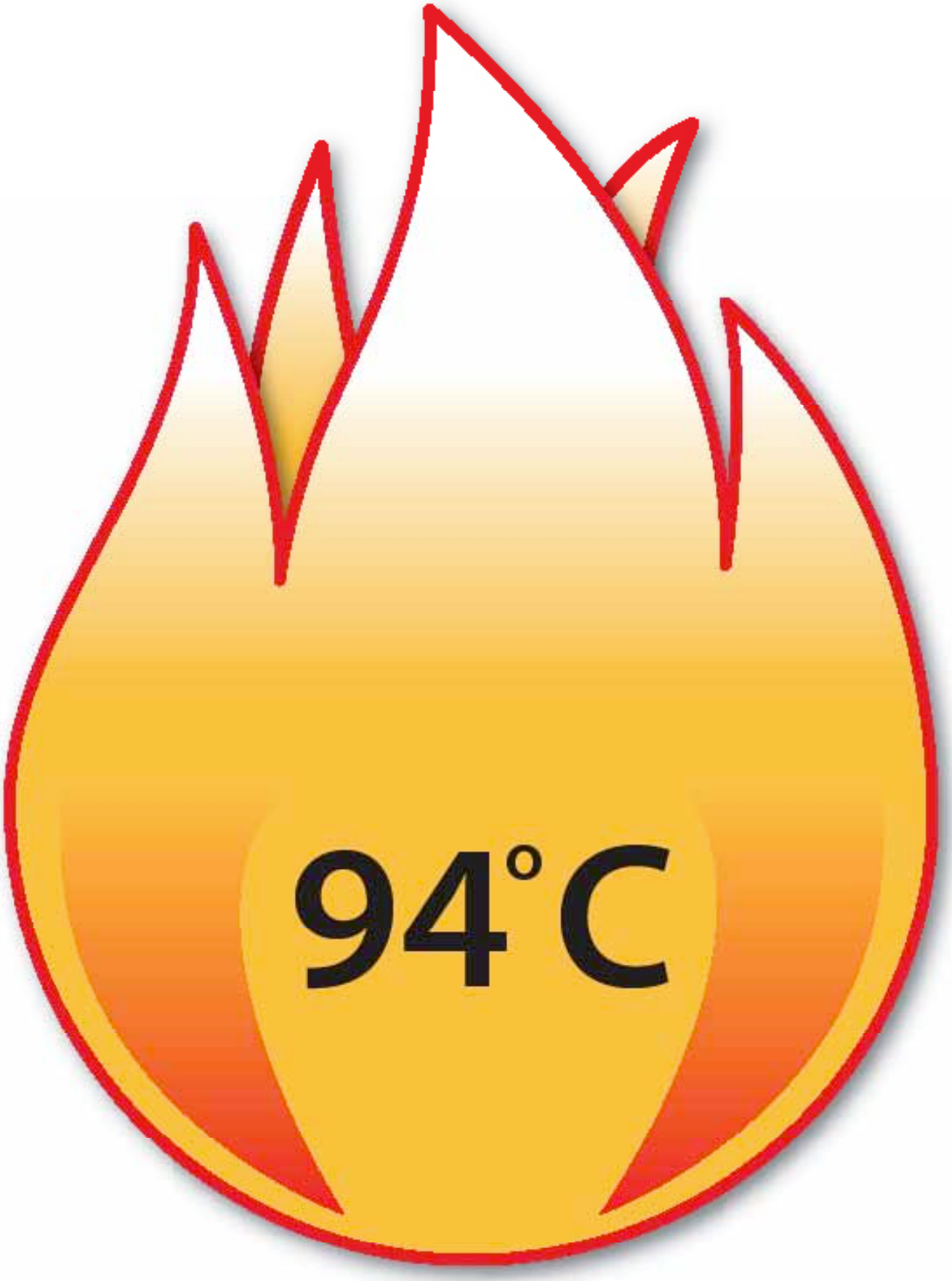
h. Ask the students how many pieces of DNA were originally together in the solution and how many are there now. There was originally one complete (two-stranded) piece of DNA and now there should be two.

i. Tell the students that this was only one cycle of PCR. Remind students that each cycle doubles the amount of DNA in the solution.

j. Ask the students to complete another cycle. Repeat steps b through h above.

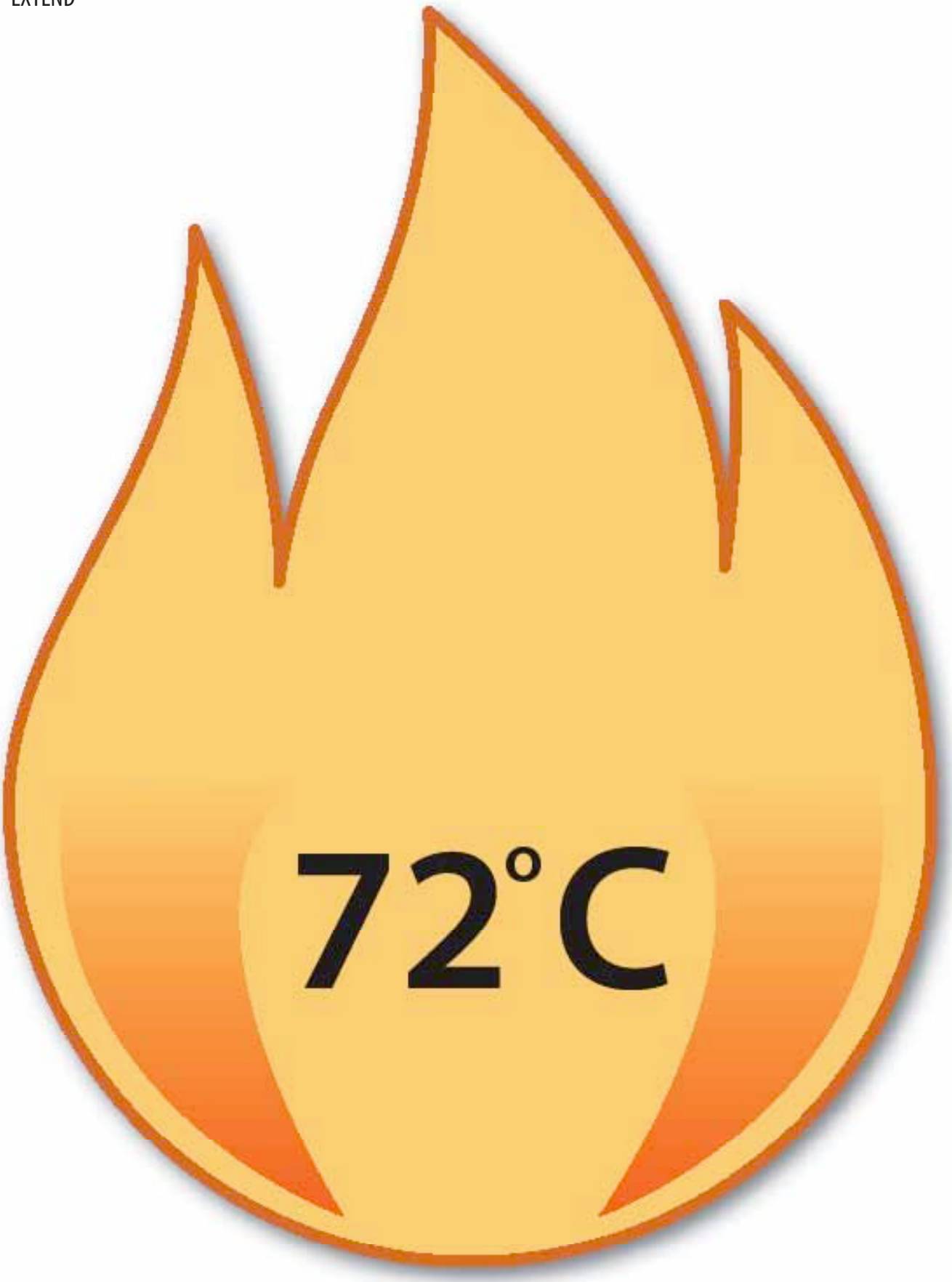
These steps can be repeated as often as the teacher would like.

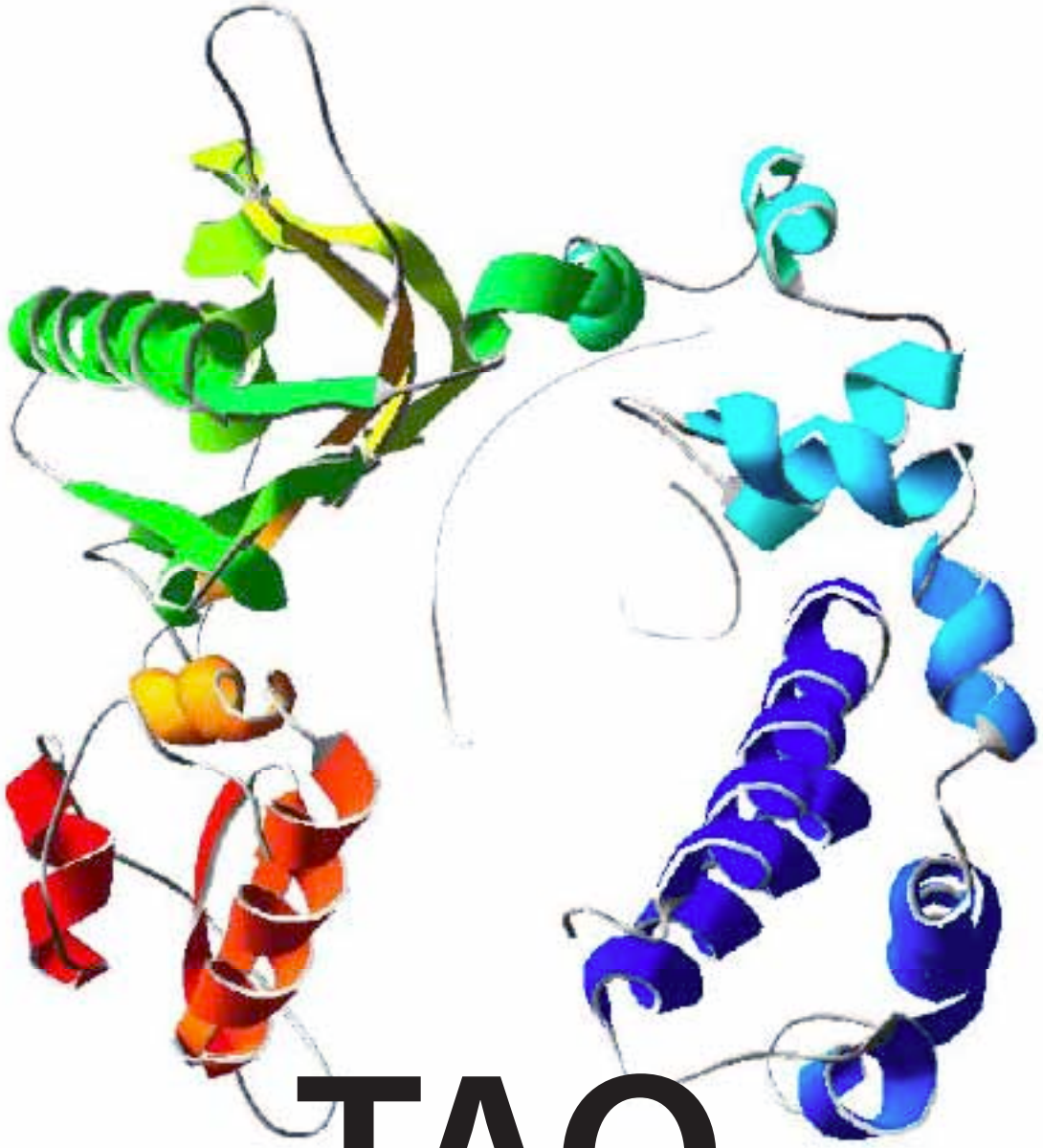
DENATURE



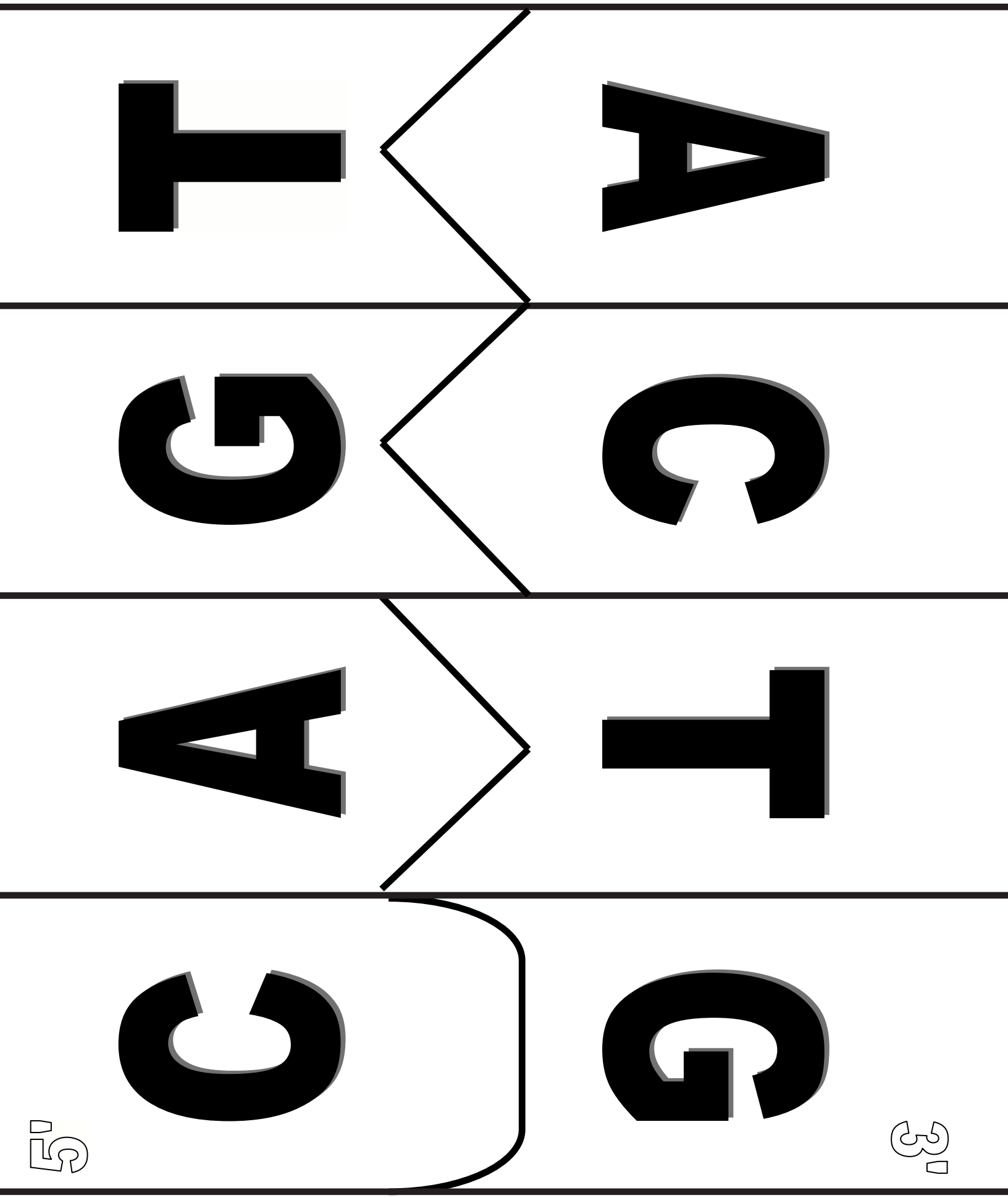
ANNEAL

EXTEND





TAQ POLYMERASE


A
T
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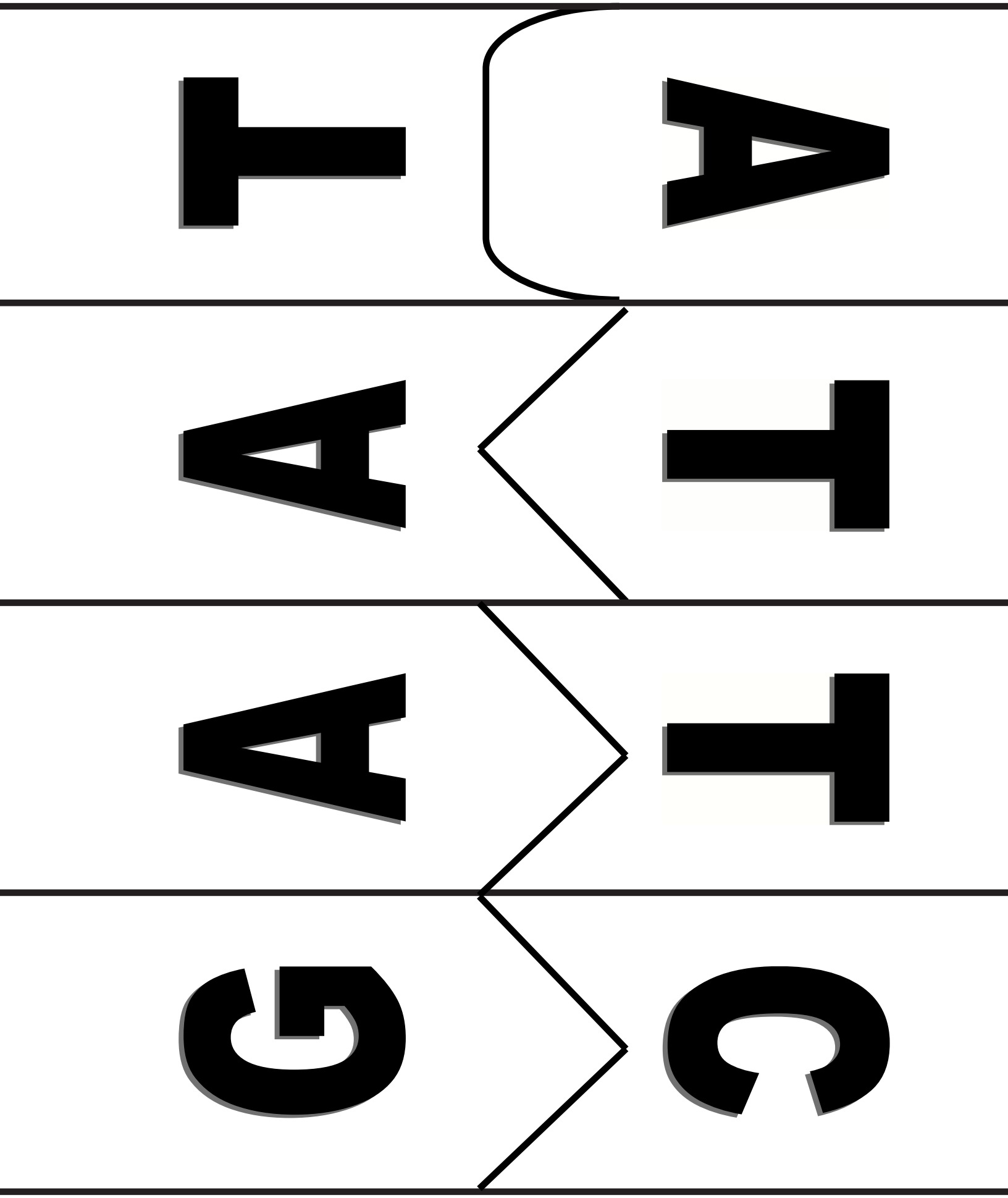
G
G
C
T
A
3'
5'


A
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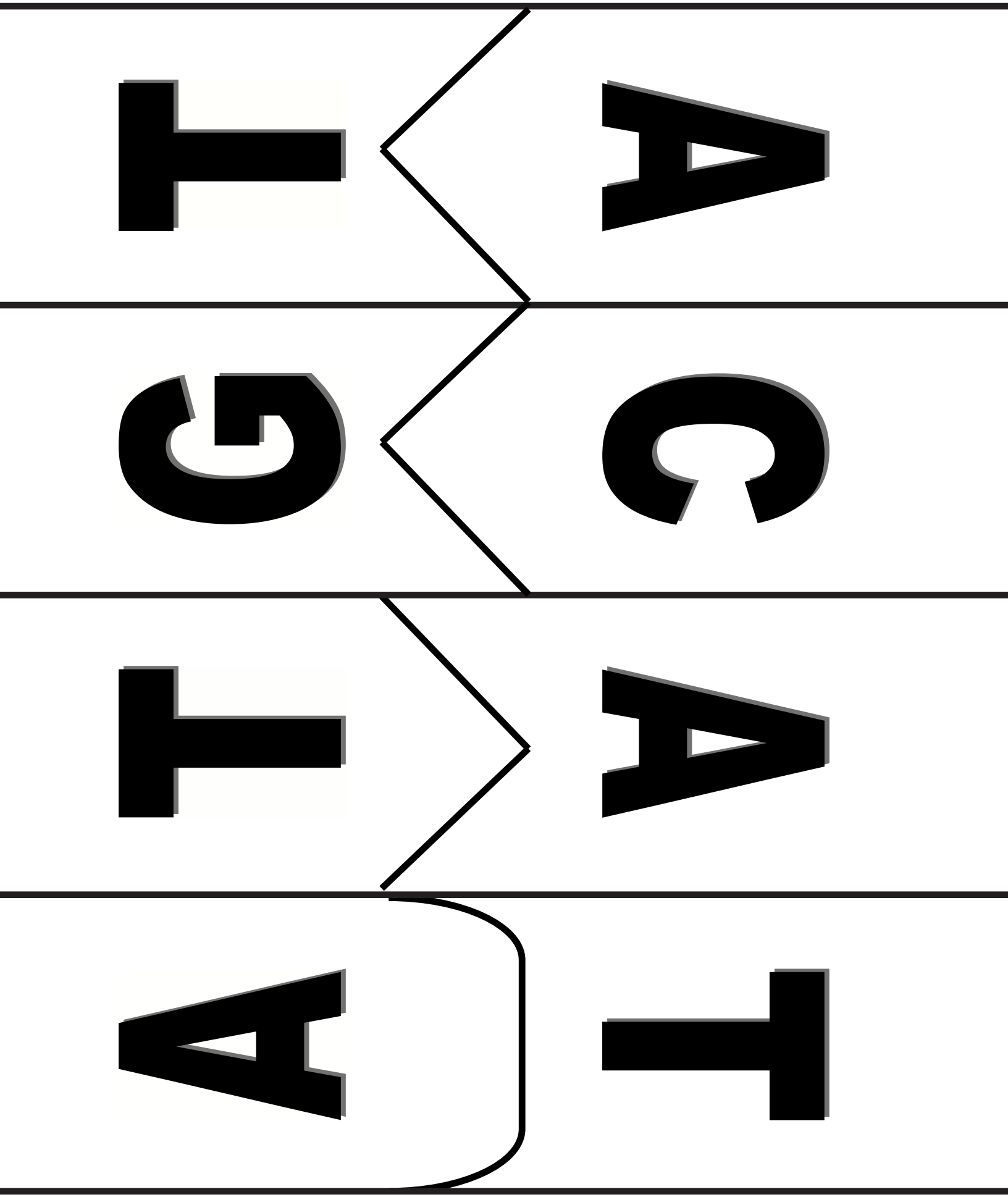
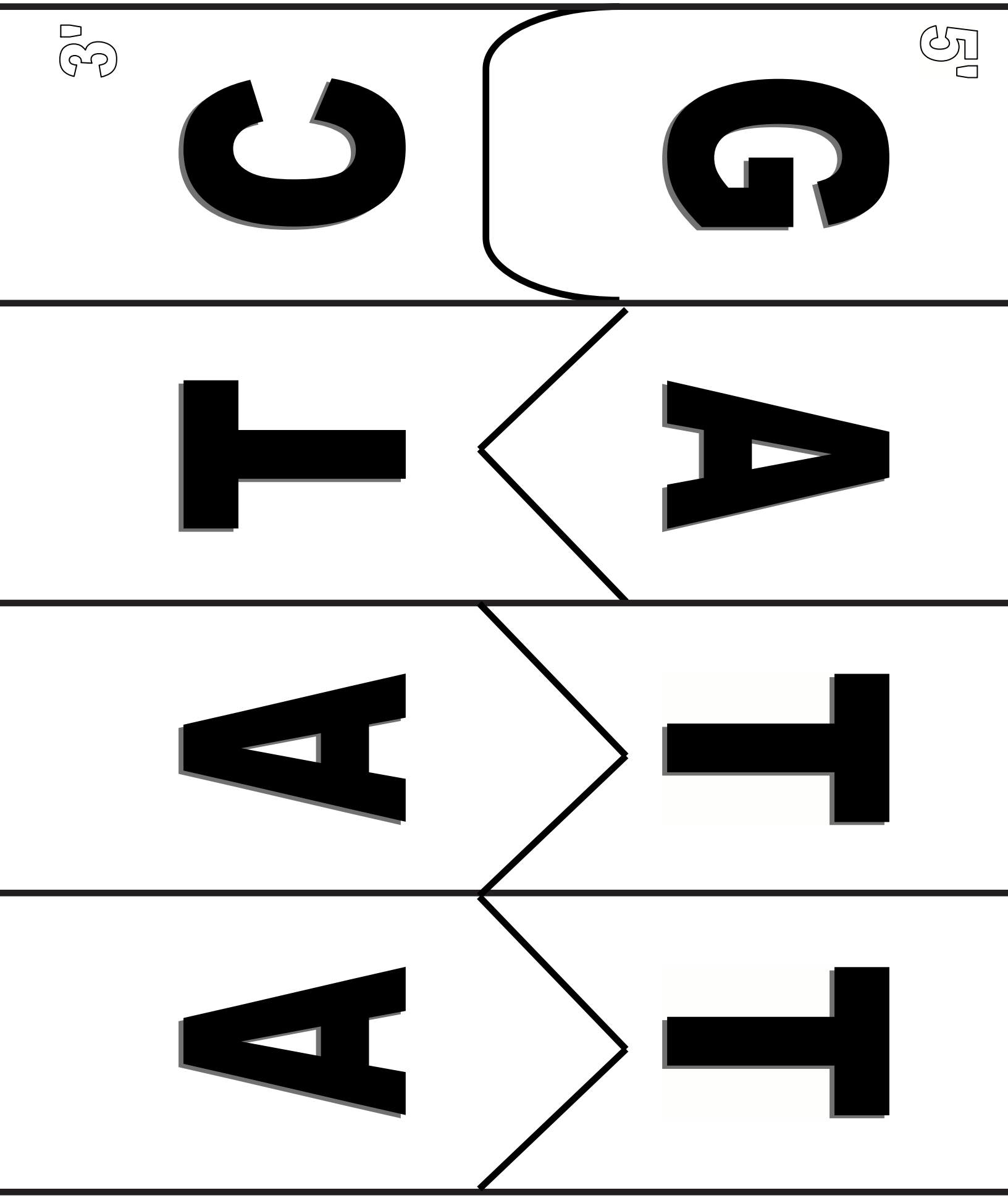
A
T
A
C
G


A
T
C
G
A
T
T
A


5'
G
A
T
C
3'
T
A
A
T

PRIMER 1

PRIMER 2

BRAND NAME GENES IMPLEMENTATION PLAN — WET-LAB			
Activity	Estimated Time	Summary	Purpose/Objectives
Exploration: Polymerase Chain Reaction Experiment	2 Class Periods	In this two-part lesson, students (still in the role of D.N.Aces employees) prepare a simulated PCR and perform gel electrophoresis of actual PCR products to determine the presence of a simulated BRCA2 mutation among 4 siblings.	To provide students with a hands-on laboratory experience involving both the execution and analysis of an experiment involving PCR.
Alternative Exploration: Simulated Polymerase Chain Reaction Experiment (located in "Additional Activities" section)	1 Class Period	In this two-part lesson, students (still in the role of D.N.Aces employees), prepare a simulated PCR experiment using whichever pipette type is available in the classroom, followed by a simulated, paper-based analysis of their product.	To provide students with a hands-on laboratory experience involving both the execution and analysis of an experiment involving PCR.

THE THREE MAIN STEPS OF PCR

BACKGROUND INFORMATION FOR THE TEACHER

To begin the process of polymerase chain reaction (PCR), a DNA sample along with two oligonucleotide primers, thermostable DNA polymerase (Taq), a quantity of the four deoxynucleotides (A, T, G, C), and a reaction buffer are mixed in a single micro test tube. The tube is placed into a thermal cycler, which contains an aluminum block that holds the sample and can be rapidly heated and cooled across extreme temperature differences.

From this point, PCR involves a repetitive series of thermal, or temperature, cycles. The three steps involved in each cycle are described below.

1. DENATURING STAGE

The first step of the PCR temperature cycling procedure involves heating the sample to 94°C. At this high temperature, the strands of the DNA sample separate. The process of separation is called denaturing.

To better understand the denaturing step, students must remember what they know about the structure of DNA.

The DNA molecule is a long polymer consisting of nucleotides. Each nucleotide is comprised of a nitrogen base, a deoxyribose sugar, and a phosphate group. The same ribose sugar and phosphate group are in each nucleotide. What makes a nucleotide different is its nitrogen base: adenine (A), thymine (T), guanine (G), or cytosine (C).

A DNA nucleotide chain is created by the connection of the phosphate group of one nucleotide to the ribose sugar of the next nucleotide. The sugar contains 5 carbons. The phosphate group (PO_4) of a given nucleotide is connected to the 5' carbon of the sugar. A hydroxyl group (-OH) is attached to the 3' carbon of the sugar, and this 3' OH group connects to the phosphate group of the next nucleotide in the chain.

Thus, the end of a single-strand DNA molecule that has a free phosphate group (i.e., not attached to another nucleotide) is called the 5' (pronounced "five prime") end, and the end of the DNA molecule with a free hydroxyl group is called the 3' ("three prime") end.

It has become standard that a single-stranded DNA molecule is written with the 5' end on the left and the 3' end on the right. Therefore, a single-stranded DNA chain's sequence is represented from left to right, starting on the left with the 5' nucleotide and moving to the right until the 3' nucleotide is last. Most DNA sequences are read 5' to 3'.

New strands of DNA are always synthesized in the 5' to 3' direction. The single strand of DNA that will be used to synthesize its complementary strand is called the template strand.

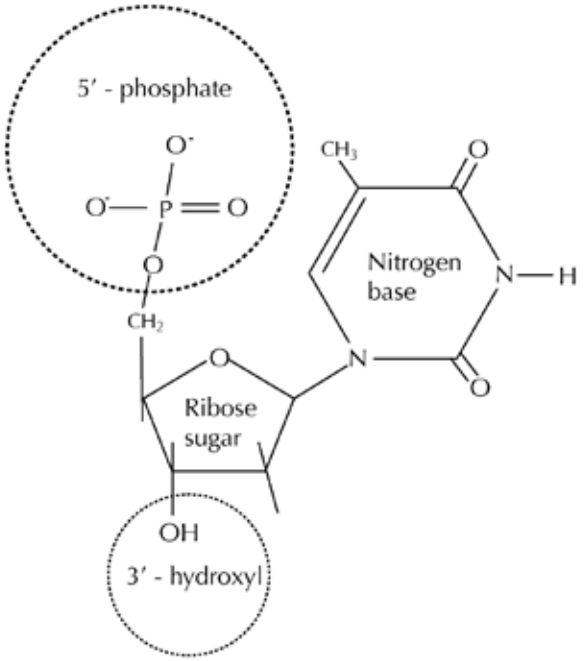


FIGURE 1. STRUCTURE OF ONE NUCLEOTIDE OF DEOXYRIBONUCLEIC ACID

"The Three Main Steps of PCR" adapts and condenses material provided in Bio-Rad's Crime Scene Investigator PCR Basics™ Kit.

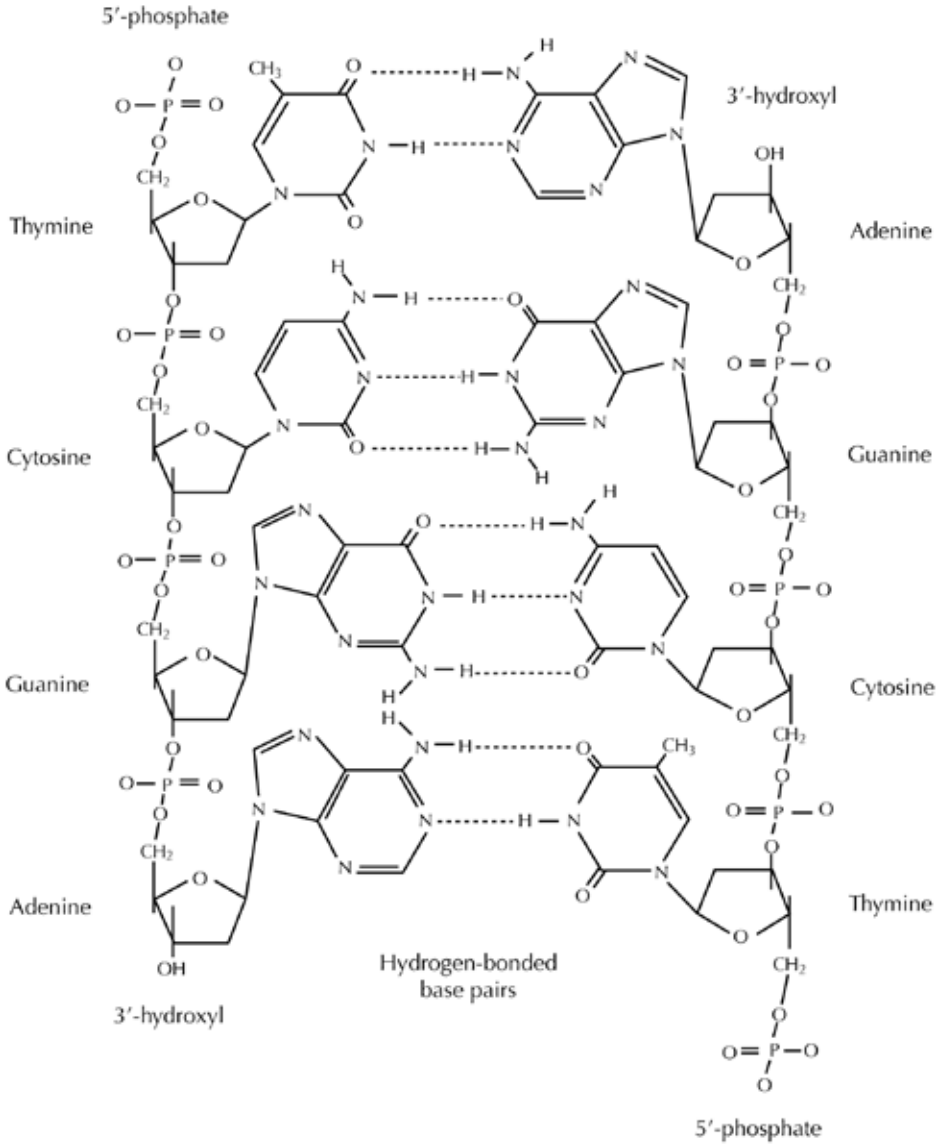


FIGURE 2. STRUCTURE OF A PORTION OF A DOUBLE-STRANDED DNA MOLECULE

2. ANNEALING STAGE

The thermal cycler rapidly cools to 52°C to allow the primers to anneal, or stick, to the separated template strands.

Primers (also called oligonucleotides) are short stretches of DNA, usually 3 to 30 nucleotides long. The two primers are designed and synthesized in the laboratory with a specific sequence of nucleotides such that they can anneal at the opposite ends and on the opposite strands of the stretch of double-stranded DNA (template strand) to be amplified.

Before a region of DNA can be amplified, one must identify and determine the sequence of a piece of DNA upstream and downstream of the region of interest. These areas are then used to determine the sequence of oligonucleotide primers that will be synthesized and used as starting points for DNA replication. Primers are complementary to the up- and downstream regions of the targeted sequence to be amplified, so they anneal to those regions on the template DNA.

Primers are needed because DNA polymerase cannot create a new DNA chain on its own. Instead, it requires

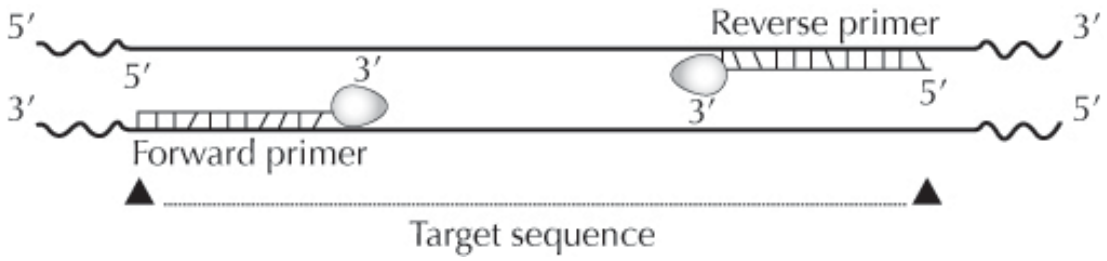


FIGURE 3. PRIMERS ANNEALED TO A TARGET DNA SEQUENCE DURING PCR

a pre-existing chain of nucleotides (the primers) to add more nucleotides onto. In other words, these short stretches of DNA "prime" the DNA synthesis reaction.

During PCR and DNA replication, DNA polymerase recognizes a complex of single-stranded template DNA plus a primer. The primer must have a free 3' hydroxyl group (-OH) for DNA polymerase to attach the 5' phosphate group of the next nucleotide.

The two original template strands may re-anneal to each other or compete with the primers for the primers' complementary binding sites. However, the primers are added in excess, so they actually out-compete the original DNA strands for the complementary binding sites.

3. EXTENDING STAGE

The thermal cycler heats the sample to 72°C so that the Taq DNA polymerase can extend the primers and make complete copies of each template DNA strand. Taq polymerase works most efficiently at this temperature. The DNA polymerase grabs free (single) nucleotides from the surrounding environment and joins the 5' phosphate of the new nucleotide to the 3' hydroxyl group (-OH) of the new complementary strand. This creates the backbone of the new DNA strand.
The newly synthesized strand maintains its complementarity with the template strand because the DNA polymerase only joins two nucleotides during new strand synthesis if the new nucleotide has its complement on the template strand. For example, the DNA polymerase will only join a G to the 3' end of the newly synthesized strand if there is the C counterpart on the template strand. Guanine will not be joined to the new strand if A, T, or G is the opposite nucleotide on the template strand.

There are now two sets of double-stranded DNA (dsDNA), which can be used as templates for another thermal cycle and subsequent strand synthesis. At this stage, a complete temperature cycle (thermal cycle) has been completed.

Each complete cycle of the strand synthesis reaction causes exponential growth of the number of template molecules (i.e., the number of DNA strands doubles at each cycle). Therefore, after 35 cycles there will be 3.4 x 10^{10}, or over 30 billion times more copies than at the beginning. Once the DNA sample has been sufficiently amplified, it can be visualized by researchers.

BRAND NAME GENES EXPLORATION ACTIVITY

POLYMERASE CHAIN REACTION EXPERIMENTAL PROTOCOL

OVERVIEW

Depending on availability of supplies and the educational needs of your students, there are several alternatives for using the *Brand Name Genes* wet-lab in your classroom.

Teachers with all of the necessary equipment might choose to set up the PCR during one class period, running the samples in the thermocycler overnight, and analyzing the product during the next class period.

The protocol described here enables students to conduct a PCR experiment over the course of two class periods. To prepare your students for this experiment, teachers may wish to show the *PCR Demonstration* video included in the *Brand Name Genes* video collection.

MATERIALS (included in the Bio-Rad kit)

This experiment uses BioRad's Crime Scene Investigator PCR Basics Kit. The kit contains enough materials for eight lab stations:

- Crime scene DNA
- DNA samples from suspects A, B, C, and D
- PCR master mix
- Crime Scene Investigator primers
- Allele ladder
- Orange G loading dye
- PCR tubes
- Capless PCR tube adaptors
- Colored microtubes
- Foam microtube holders

MATERIALS (not included in the Bio-Rad kit)

- Clear micro tubes
- Distilled water
- Cooler with ice
- Styrofoam cups
- Agarose
- TE buffer

LABORATORY PREPARATION: DAY 1

This prep can be done one day ahead of the laboratory activity. (Ideally, prep is done one hour ahead.)

1. Thaw PCR reagents at room temperature. This should take about 10 minutes. Labeling tubes can be done while waiting.

2. Label the colored microtubes as follows:

- 9 Yellow = "MMP" (master mix and primers) [1 of these is for preparing the stock solution]
- 8 Pink = + (positive control)
- 8 Purple = #1
- 8 Green = #2
- 8 Blue = #3
- 8 Orange = #4
- 8 Clear = – (negative control) *Note that clear tubes are not included in the Bio-Rad PCR kit and must be purchased separately.*

3. Pulse-spin all supply tubes in centrifuge.

4. Keep tubes on ice to keep cold.

5. Pipet 1000 µL master mix into a YELLOW tube labeled "MMP." Add 20 µL Crime Scene Investigator Primers to this tube. Mix well and pulse-spin to bring contents to bottom of tube. This solution should be notably blue. Store on ice.

6. Aliquot 125 µL master mix primer solution to each of the remaining YELLOW student tubes labeled "MMP." Store tubes on ice.

7. Aliquot 25 µL template DNA into student tubes as listed below. *Please note: the color of the label on each of the Bio-Rad vials should match the color of the tube. Check the labels as this may change.*

- Suspect D to the PINK tubes labeled "+"
- Crime scene DNA to the PURPLE tubes labeled "1"
- Suspect A to the GREEN tubes labeled "2"
- Suspect B to the BLUE tubes labeled "3"

- Suspect C to the ORANGE tubes labeled "4"
- Aliquot 25 µL of distilled water into the clear tube labeled "–."
- The thermocycler should also be set up as indicated in the "Thermocycler Settings" chart provided.

STUDENT STATIONS: DAY 1

Materials for Each Station

- 1 foam block
- 6 capless tube adapters
- 6 PCR tubes
- P-20 pipettes
- P-20 tips
- Cup filled with ice
- Master mix and DNA samples (should be stored in the ice)
- Waste containers
- Permanent marking pen

Student Steps

1. Insert capless tube adapters into the foam block on ice.

2. Label each PCR tube (+,1,2,3,4, or –).

3. Place each labeled PCR tube into the capless tube adapter.

4. Pipette 20 µL of MMP into each PCR tube. The same tip can be used.

5. Pipette 20 µL of DNA sample from each colored tube to its corresponding PCR tube. Mix each sample well. Be sure to use a new tip for each sample.

6. Cap all the tubes and place in thermocycler.

7. Start thermocycler.

TEACHER'S INTRODUCTORY SCRIPT: DAY 1

Today we are going to test four children in a family with a history of breast cancer to determine if any of them have a genetic predisposition to the disease.

Because the actual PCR process takes a couple of hours, you are going to prepare a set of reactions that will run overnight. During our next class, we will be able to analyze the product.

PCR = Polymerase Chain Reaction. This is a powerful means of amplifying DNA.

It is really important not to contaminate samples with your own DNA, or to cross contaminate your samples.

Today, we are using this technique to amplify a specific gene out of the genome. DNA was extracted from epithelial cells obtained by swabbing the inside of each patient's mouth.

For this process we need to be able to measure very small volumes, fractions of milliliters called microliters

THERMOCYCLER SETTINGS

STEP	FUNCTION	TEMP	DURATION	NUMBER OF CYCLES
Initial denaturing	Denature	94^{0}C	2 minutes	X1
Thermal cycling	Denature	94^{0}C	30 seconds	X35
	Anneal	52^{0}C	30 seconds	
	Extend	72^{0}C	1 minute	
Final Extension	Extend	72^{0}C	10 minutes	X1
Holding	Hold	4^{0}C	Forever	X1

and abbreviated µL. The tool we use (as molecular biologists) to measure these volumes is called a "micropipette." *(Give a pipette lesson specific to the model you have in your classroom and practice using pipette.)*

You have several different types of tubes at your station. The larger ones are microcentrifuge tubes. The smaller ones are PCR tubes. Notice how the PCR tubes have a thinner wall. This thin wall allows heat to pass through the tube more easily, which is required for PCR.

You will also find master mix at your stations. Scientists use this to both ensure that the same material is in each reaction and avoid measuring volumes below the effective ranges of these pipettes. Master mix contains all reagents that will be the same in each reaction. The components of master mix are:

- dNTPs (nucleotides, the building blocks of DNA)
- Taq polymerase (*Thermus aquaticus*, the heat stable form of DNA polymerase)
- Mg^{2+} (an ion the polymerase needs in order to function properly)
- Buffer (to control the pH of the reaction)

We will also add primers for our gene of interest. "Primers" are short pieces of single-stranded DNA that will bind to the ends of the gene to help begin synthesis of DNA.

Student Steps

1. Label each of your PCR tubes "+, 1, 2, 3, 4, or –."

2. Pipette 20 µL of master mix into each PCR tube.

3. Change tip and pipette 20 µL of sample into corresponding tube (+, 1, 2, 3, 4, or –).

4. Place your tubes in the PCR machine. Make sure you know which are yours.

5. When all the tubes are in the machine, begin the run.

LABORATORY PREPARATION: DAY 2

Gels can be prepared several days in advance if stored in an airtight container with moist paper towels.

Preparation of 1X TE Buffer

Concentrated TE buffer should be diluted to 1X using distilled water. Aerosol barrier tips are not necessary for this portion of the experiment. Standard pipette tips can be used.

Preparation of 3% Agarose Gels

Due to the size of the fragments generated in this PCR, a 3% agarose gel works best for these samples. This will be sufficient to make four small gels. Adjust the recipe to fit your equipment and class sizes.

- 3g agarose
- 100 mL of 1X TE buffer
- 2 drops Carolina Blu gel and buffer stain (optional)

1. Mix agarose and 1X TE in Erlenmeyer flask.

2. Microwave on high until agarose is dissolved, stirring each minute.

3. Let agarose cool until flask is cool enough to touch with your hand.

4. Add Carolina Blu.

5. Pour into gel trays so that the bottom of the combs are covered with gel.

6. Let cool until solidified.

Preparation of Samples

1. Thaw Orange G loading dye and allele ladder. Pulse spin in centrifuge to bring contents to bottom of tubes if necessary.

2. Add 50 µL Orange G loading dye to the allele ladder.

3. Label 8 tubes "LD" for loading dye and 8 tubes "Ladder" for allele ladder.

4. Aliquot 65 µL of Orange G loading dye into the tubes marked "LD." Store at 4°C.

5. Aliquot 45 µL of Orange G allele ladder to the tubes labeled "Ladder." Store at 4°C.

STUDENT STATIONS: DAY 2

Materials for Each Station

- Power supply
- Electrophoresis chamber
- Agarose gel
- 1X TE buffer covering gel in chamber
- PCR products on ice
- Loading dye aliquots labeled "LD"
- DNA ladder aliquots labeled "Ladder"
- DNA stain

Student Steps

1. Set up electrophoresis equipment according to the manufacturer's instructions.

2. Place gels into gel electrophoresis chambers with wells at the negative pole (black) end.

3. Fill chamber with 1X TE buffer so that the buffer covers the gel.

4. Create a gel map to indicate where each sample and ladder will be loaded in the gel.

5. Add 10 µL of Orange G loading dye to each PCR product. Please note: be sure to mix well and change tips between each sample.

6. Load 20 µL of ladder from the tube labeled "Ladder" into outside lanes.

7. Load 20 uL of PCR product containing loading dye into gel according to gel map.

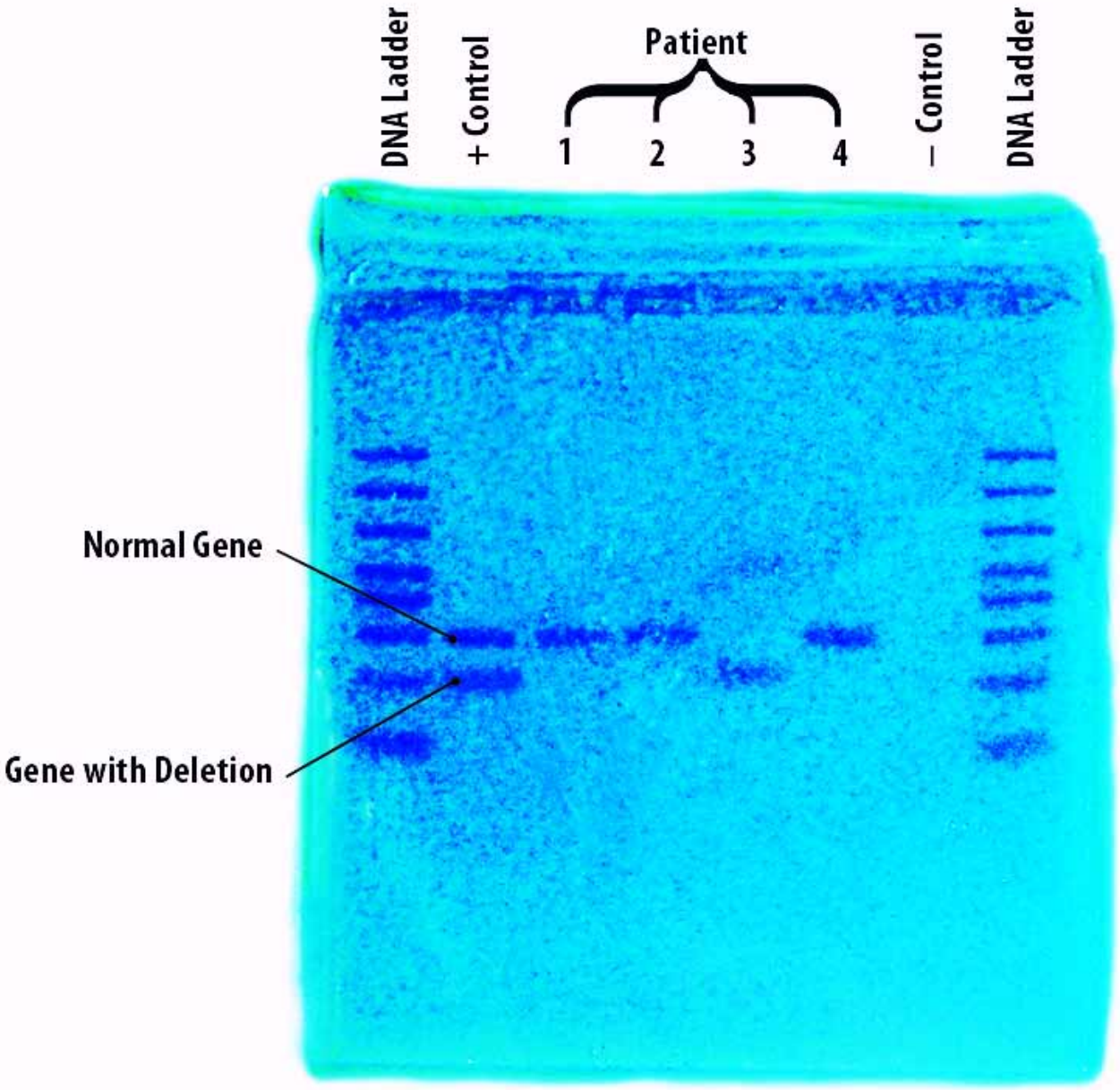
8. Run gels at 100V for 30 minutes. Do not let the orange dye front migrate off the gel.

9. Turn off power and remove gels from the electrophoresis chambers.

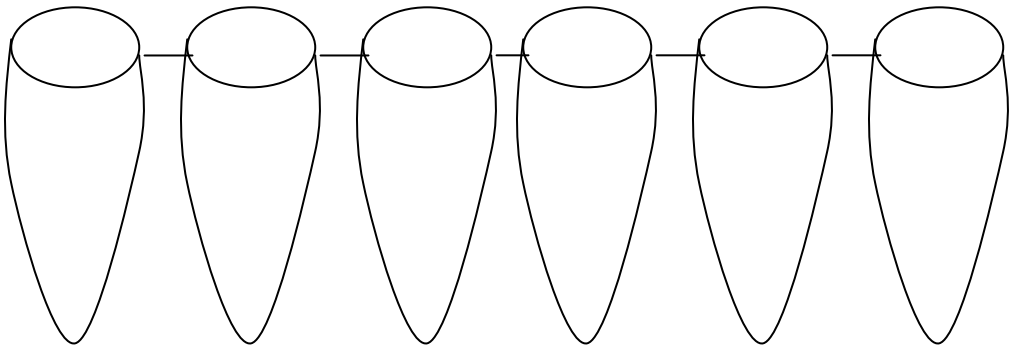
10. Stain with DNA stain according to the instructions provided by the manufacturer until bands are visible.

11. Gels can be stored in an airtight container with a wet paper towel until you are ready to analyze them.

GEL ELECTROPHORESIS OF PCR PRODUCT



Name _____ Weigh Boat Number _____



	+ Con	1	2	3	4	- Con
MM	_____	_____	_____	_____	_____	_____
DNA	_____	_____	_____	_____	_____	_____

1. What is the purpose of the negative control?

2. Why do we use DNA polymerase from *Thermus aquaticus*? Why can't we use DNA polymerase from just any organism?

3. Why is it important to change tips when adding each sample of DNA, but not when adding the master mix?

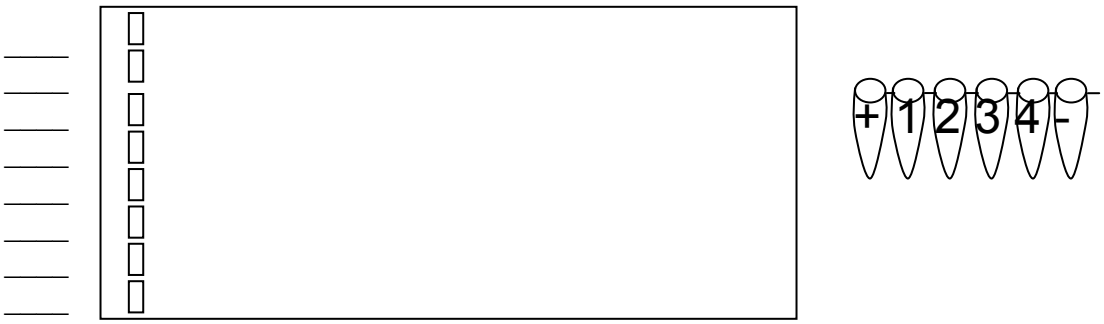
4. What steps make up the PCR cycle? What happens at each step?

THE POWER OF PCR MATH PRACTICE: Complete the chart below.

Number of Cycles	Exponents	Number of Copies
0	2^0	1
1		2
2		4
3		
4		
5		
6		
7		
8		

Name _____ Weigh Boat Number _____

USE THIS GEL MAP TO: record where you load each sample.
record the electrophoresis result.



1. Why are larger DNA fragments closer to the wells while the smaller pieces are at the other end? Would a gene with a deletion migrate farther or stay closer to the wells?

2. What is the purpose of the ladder?

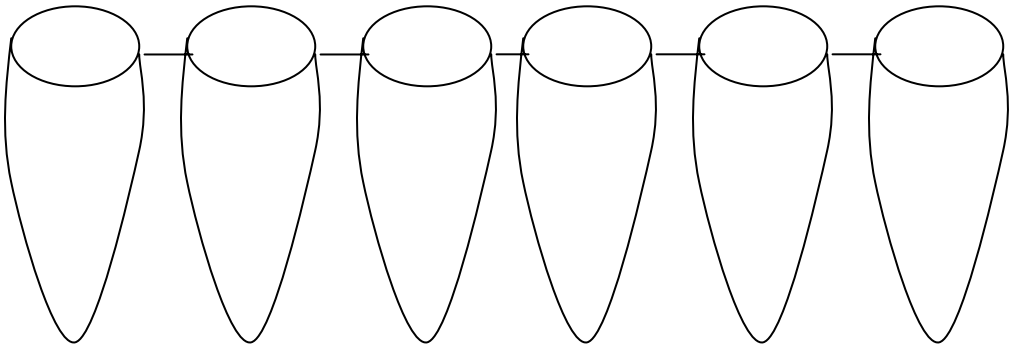
MASTER MIX MICROLITER MANIA

Your assignment is to prepare materials for a PCR reaction. Calculate the volumes required to create 10 PCR reactions. Use the **Reagent** and the **Volume** from the chart below and enter your answers in the **Reagent Volume Required** column.

Reagent	Volume	X 10	Reagent Volume Required
Magnesium-containing buffer	2 uL	X 10	
dNTPs	2 uL	X 10	
Forward primer	0.5 uL	X 10	
Reverse primer	0.5 uL	X 10	
Taq polymerase	0.25 uL	X 10	
Water	4.75 uL	X 10	
Total	10 uL		

Name _____ Weigh Boat Number _____

KEY



	+ Con	1	2	3	4	- Con
MM	_____	_____	_____	_____	_____	_____
DNA	_____	_____	_____	_____	_____	_____

1. What is the purpose of the negative control?
   To check if the master mix is contaminated with DNA. Contamination would cause false results.

2. Why do we use DNA polymerase from *Thermus aquaticus*? Why can't we use DNA polymerase from just any organism?
   Since the Thermus aquaticus *bacteria lives in hot springs, it is not destroyed in the hot temperatures required for the denaturing phase of PCR.*

3. Why is it important to change tips when adding each sample of DNA, but not when adding the master mix?
   The master mix is the same for all of the tubes in the reaction. The DNA is different; therefore, it is important to not get the wrong DNA in the wrong tube.

4. What steps make up the PCR cycle? What happens at each step?
   Denature: DNA strands separate.
   Anneal: Primers bond to their complementary sequence.
   Extension: Taq polymerase adds bases according to base pairing rules.

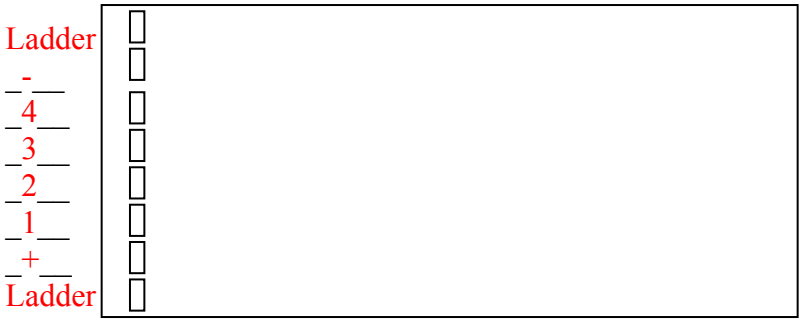
THE POWER OF PCR MATH PRACTICE: Complete the chart below.

Number of Cycles	Exponents	Number of Copies
0	2^0	1
1	2^1	2
2	2^2	4
3	2^3	8
4	2^4	16
5	2^5	32
6	2^6	64
7	2^7	128
8	2^8	256

Name _____ Weigh Boat Number _____

KEY

USE THIS GEL MAP TO: record where you load each sample.
record the electrophoresis result.



1. Why are larger DNA fragments closer to the wells while the smaller pieces are at the other end? Would a gene with a deletion migrate farther or stay closer to the wells?
   The larger fragments are slowed more by the agarose than the smaller fragments. Since a deletion would result in a smaller piece of DNA, it would move further than its non-mutated counterpart.

2. What is the purpose of the ladder?
   The ladder is pieces of DNA of known size. These serve as a reference for determining the size of the DNA fragments in our samples.

MASTER MIX MICROLITER MANIA

Your assignment is to prepare materials for a PCR reaction. Calculate the volumes required to create 10 PCR reactions. Use the **Reagent** and the **Volume** from the chart below and enter your answers in the **Reagent Volume Required** column.

Reagent	Volume	X 10	Reagent Volume Required
Magnesium-containing buffer	2 uL	X 10	20 uL
dNTPs	2 uL	X 10	20 uL
Forward primer	0.5 uL	X 10	5 uL
Reverse primer	0.5 uL	X 10	5 uL
Taq polymerase	0.25 uL	X 10	2.5 uL
Water	4.75 uL	X 10	47.5 uL
Total	10 uL		100 uL

Equipment Needed for Brand Name Genes Wet-lab				
Vendor	Catalog Number	Item	Unit	Minimum Purchase
REQUIRED EQUIPMENT				
For Students' Workstations				
Bio-Rad	166-4000EDU	Horizontal Gel Electrophoresis Chamber	1	4-8
Bio-Rad	166-0506EDU	Adjustable Micropipet 2-20 µl	1	1-8 (recommend at least 4)
Bio-Rad	166-0507EDU	Adjustable Micropipet 20-20 µl	1	1
Bio-Rad	166-0508EDU	Adjustable Micropipet 100-1000 µl	1	1
Bio-Rad	211-2006EDU	Aerosol Barrier 2-20 µl Pipet Tips	1 box*	1
Bio-Rad	211-2016EDU	Aerosol Barrier 20-200 µl Pipet Tips	1 box**	1
Bio-Rad	211-2021EDU	Aerosol Barrier 100-1000 µl Pipet Tips	1 box	1
Bio-Rad	170-9701EDU	MyCycler™ Thermocycler	1	1
Bio-Rad	164-5050EDU	Power Pac™ Basic Power Supply	1	2-4
CONSUMABLES				
Bio-Rad	166-2600EDU	Crime Scene Investigator PCR Basics Kit***	1	1
The following consumables are not included in the Bio-Rad kit: clear micro tubes, distilled water, cooler with ice, styrofoam cups, agarose, and TE buffer.				
* Fixed volume pipettes of 10 µl (166-0512EDU) and 20 µl (166-0513EDU) can also be used at a considerable savings. ** Aerosol barrier pipette tipes are necessary for preparation of the PCR to minimize contamination prior to amplification. *** Contains enough materials for 8 lab stations.				

BRAND NAME GENES IMPLEMENTATION PLAN — POST-LAB			
Activity	Estimated Time	Summary	Purpose/Objectives
Evaluation: "Breast Cancer Surgery: Mastectomy" Video with Writing Prompts and Examination Questions	Varies	Viewing of the "Breast Cancer Surgery: Mastectomy" DVD included in the Brand Name Genes video collection leads to a choice of discussion topics, writing assignments, and examination questions.	To extend and evaluate students' understanding of a range of scientific content presented in a real-world context—the discovery and treatment of breast cancer in a North Carolina patient. Among the topics that can be covered: • the careful gathering and analysis of scientific data to make informed decisions about personal health • the use of PCR to screen for genetic traits related to cancer • careers in the medical field
"Breast Cancer Surgery: Mastectomy" DVD	6 mins.	DVD presentation—from the surgeon's perspective—of the discovery and treatment of breast cancer in a North Carolina patient.	To provide students with a realistic perspective on the diagnosis and treatment of breast cancer. The video invites students to use knowledge gained in Brand Name Genes to discuss and write about a range of scientific content they are learning about in class.

BRAND NAME GENES EVALUATION ACTIVITY

"BREAST CANCER SURGERY: MASTECTOMY"

INTRODUCTION FOR THE TEACHER

This evaluation activity has as its focus a short video showing a surgeon discussing and performing breast cancer surgery. Provided as part of the *Brand Name Genes* video collection, *Breast Cancer Surgery: Mastectomy* enables students to view cancer from a surgeon's perspective and share with him the data-gathering process that informs his and his patient's decisions.

Dr. Keith Amos, a surgeon at the University of Chapel Hill's School of Medicine, discusses medical evidence he considered in preparation for the mastectomy he performs. He then takes viewers into the operating room with him to explain elements of the surgery.

The video presents several kinds of visual information about cancer: a digital X-ray showing a tumor within the body, a pathology report on a tissue sample, and a naked-eye view of the exterior of a tumor when removed from the body.

In addition, the video introduces students to several kinds of careers in the medical field and some of the data that doctors consider when the possibility of cancer is involved. This information is potentially useful to students as they consider job opportunities and also as they make decisions about their own or their families' health in the future.

Particularly valuable to visual and auditory learners, the video enables students to:

- Learn that surgeons use logic and evidence (e.g., X-rays, tissue samples) to develop diagnoses and treatment plans.
- Observe medical professionals using surgical equipment appropriately and taking safety precautions (e.g., to resist infection).
- Listen to a surgeon explaining medical findings that contribute to the decision to perform surgery in a case of breast cancer.
- See what happens when cell division is uncontrolled in the human body and a cancerous tumor forms.

The discussion questions and writing prompts provided below connect the video to additional learning goals in the North Carolina Standard Course of Study. They also serve as evaluation tools. Spoken and written responses to the questions and prompts selected by the teacher will indicate the extent to which students have grasped concepts and content presented throughout the *Brand Name Genes* module.

ABOUT KEITH D. AMOS, M.D.

Dr. Amos is an assistant professor of surgery in the University of North Carolina's Medical School. His specialties are general surgical oncology, breast diseases, breast surgery, and melanoma.

After his undergraduate education at Xavier University of Louisiana, Dr. Amos earned an M.D. at Harvard Medical School. He then completed a three-year residency at Washington University's Barnes-Jewish Hospital in St. Louis and a three-year fellowship at Houston's M.D. Anderson Cancer Center.

Dr. Amos has received many awards for teaching and research. He was even honored as a member of the *USA Today* All-USA College Academic Team in 1992.

KEY

BRAND NAME GENES EVALUATION ACTIVITY

"BREAST CANCER SURGERY: MASTECTOMY"

VIDEO VIEWING GUIDE

BEFORE VIEWING

Ask students to think of the following questions as they watch the video:

- What is the patient's motivation for participating in the making of the DVD?
- What is the surgeon's hypothesis?
- What information does the surgeon gather?
- What is the diagnosis?
- Who helps the surgeon?
- What safety precautions are taken?
- What medical tools and equipment are used?
- How long does the surgery last?
- What happens next?

AFTER VIEWING

Short Discussion Questions with Answer Key

1. Why did Dr. Amos's patient allow a video of her surgery to be made?

   She wanted students to learn from her experience.

2. Dr. Amos gathered information (data) before he made the decision to perform surgery. What kinds of data were mentioned in the video?

   He examined x-rays. He performed a biopsy and studied a pathology report. He talked to his colleagues. He talked to his patient.

3. What hypothesis was Dr. Amos testing when he performed the biopsy on the unusual mass detected in the x-ray?

   He tested the hypothesis that the mass might be cancerous.

4. What disease did Dr. Amos's patient have?

   She had breast cancer.

5. Did Dr. Amos work alone? What were the job titles of hospital personnel mentioned or seen in the video?

   No, he worked with others. His colleagues included an x-ray technologist, pathologist, anesthesiologist, anesthesia nurse, operating room circulating nurse, and operating room scrub technician.

6. List the medical instruments and equipment shown or mentioned in the video.

   X-ray machine, scalpel, needle driver, retractors/rakes.

7. Describe the tumor that Dr. Amos removed. How large was it? What shape was it? What color was it? Did it look as you expected it would look?

   Answers may vary.

8. What actions did you see Dr. Amos and his colleagues taking to ensure that the surgery would be carried out in a safe manner?

   In addition to gathering information about the presence of the tumor, they made sure to operate in a sterile manner (washing hands thoroughly, wearing sterile gowns and gloves, putting on masks and goggles).

9. How long did the surgery last?

   It lasted four hours.

10. What follow-up treatment did Dr. Amos mention at the end of the video?

    He mentions that the evaluation showed that the tumor was completely removed. Follow-up treatment included receiving chemotherapy.

BRAND NAME GENES EVALUATION ACTIVITY

"BREAST CANCER SURGERY: MASTECTOMY"

WRITING PROMPTS AND EXAMINATION QUESTIONS

The following prompts and questions draw upon knowledge gained from activities included in the *Brand Name Gene*s module. You may wish to select one prompt or question that best suits your particular class's needs and interests, or you may prefer to give your students a choice of several to work on. The length of each writing assignment can be determined based on the time available.

Prompts 1-3 can be used as examination questions or as in-class writing assignments. Prompts 4-7 can be given as project assignments to be completed in a week or two by students working alone or in groups. Prompt 8 can be given as a homework assignment or used during a class period spent in the computer lab or media center.

1. **Explain how PCR could be used in this case.** Using your knowledge of polymerase chain reaction (PCR), describe how and why you would perform PCR to provide information to this patient's three children (one daughter and two sons). Be sure to explain:

    - Which of the children you would test and why.
    - What sort of biological sample or samples you would need.
    - How you would process this material in the lab.
    - What you would be looking for.
    - How the information you generated could be used to help this family.

2. **Discuss how breast cancer develops.** The cancerous tumor shown in the video was the result of a process of change within the patient's body. Using your knowledge of human-cell structure and the cell cycle, discuss the changes involved in the formation of this tumor. Begin by discussing the difference between inherited and acquired genetic mutations that may be responsible for breast cancer. Be sure to discuss the different characteristics of normal and cancerous cells that can be seen under a microscope.

3. **Create a medical pedigree.** Using appropriate symbols and lines, draw and label a chart based on the patient's family medical history. Include the following information:

    - The patient's younger sister was diagnosed with breast cancer when she was 34.
    - The patient's elder sister is in good health.
    - The patient's maternal grandmother is in good health; her maternal grandfather is no longer living.
    - The patient's aunt (her father's sister) died of ovarian cancer when she was 65.
    - The patient's husband and father are in good health.
    - The patient's paternal grandfather died of prostate cancer at age 70; her paternal grandmother is in good health.
    - The patient has two healthy children: a daughter and a son.

    Discuss whether the medical pedigree you have drawn supports a hypothesis that this patient's children may have a genetic predisposition for breast cancer.

4. **Talk to the patient.** Imagine that you are a journalist preparing to interview the patient in the video. The focus of your article is "21st Century Approaches to Breast Cancer." Based on what you have learned about cells, breast cancer, genetics, and ELSI, write down 10 topics you want to cover with the patient. List the topics in the order of their importance and include sample questions for each one. In addition, write a paragraph summarizing how you will introduce yourself and your planned article to the patient before the interview begins. In your introduction, be sure to explain why you think the article will be interesting and valuable to readers.

5. **Write a review.** Imagine that you are reviewing this video for a publication that is distributed to science teachers. Do the following three things: (1) provide a synopsis of the video, (2) describe what students can learn from viewing the video, and (3) argue for or against showing the video to students. Give your review an attention-getting title.

6. **Design a DVD cover.** Imagine you work on a marketing team that has been hired to create a DVD cover for this video. Design an illustration or other graphic for the front (be sure to include the title) and write information on the back that will let potential buyers know what is in the video and entice them to purchase it. In addition to preparing the cover, write a half-page memo to your supervisor indicating why you think your cover will be appealing to the buyers you have in mind for the video.

7. **Develop a sequel.** Imagine that you are part of a team that is developing a sequel to this video. Write a memorandum to an investor you are approaching for funds. In making a persuasive request for funds, your memorandum should provide the following information: (1) a brief synopsis of the video you are proposing, (2) an explanation of how the new video is like and unlike the first video, (3) an explanation of who the audience for the new video will be, (4) an explanation of what the audience will learn from the video, and (5) an argument for why your video will be a worthwhile investment. Give your sequel an attention-getting title.

8. **Explore a career.** Choose one of these professions represented in the video: anesthesiologist, operating room nurse, pathologist, surgeon, X-ray technologist. Using the Internet, find five current job openings related to your choice. Record the following information for each job:

   - Where you found the job listing, including the URL.
   - Which hospital, university, or other organization is offering the job.
   - Where the job is located geographically.
   - What the minimum degree, training, and other requirements are.
   - What the salary range is.
   - What the procedures for applying are.
   - What the deadline for applying is.

BRAND NAME GENES IMPLEMENTATION PLAN — ADDITIONAL ACTIVITIES			
Activity	Estimated Time	Summary	Purpose/Objectives
Alternative Exploration: Simulated Polymerase Chain Reaction Experiment (located in "Additional Activities" section)	1 Class Period	In this two-part lesson, students (still in the role of D.N.Aces employees), prepare a simulated PCR experiment using whichever pipette type is available in the classroom, followed by a simulated, paper-based analysis of their product.	To provide students with a hands-on laboratory experience involving both the execution and analysis of an experiment involving PCR.

SIMULATED POLYMERASE CHAIN REACTION EXPERIMENTAL PROTOCOL

BACKGROUND

Depending on the availability of supplies and the educational needs of your students, there are several alternatives to using the *Brand Name Genes* wet-lab in your classroom.

Teachers without equipment can have their students prepare a simulated PCR experiment using whichever pipette type they have at their disposal (adjustable volume, fixed volume, or even disposable pipettes), followed by a simulated, paper-based analysis of their product.

MATERIALS

- Food coloring (red, blue, yellow, green)
- Water
- PCR tubes (micro tubes or even test tubes can be used in their place for this simulation)
- Microcentrifuge tubes (pink, orange, yellow, green, blue, purple, and clear) one of each color for each lab group. Alternatively clear tubes can be used.
- Pipettes (adjustable or fixed volume - one per lab group) (disposable—7 per lab group, plus a few more for preparation)
- Pipette tips (if necessary)
- Larger tubes, such as conical tubes or test tubes (7 total)
- Tube racks or foam floats (enough for each lab group to hold 13 tubes)
- Capless PCR tube adapters if using PCR tubes (6 per lab group)

Colored Water Solutions

Colors can be adjusted to suit personal preference. The recipes listed below have proven to work well for 8mL volumes:

- Orange = 8 mL water + 2 drops yellow food coloring
- Yellow = 8 mL water + 5 drops of orange (from above) ** you will need to make about 3 tubes of yellow.
- Blue = 8 mL water + 1 drop Blue food coloring
- Pink = 8 mL water + 1 drop red
- Green = 8 mL water + 1 drop green
- Purple = 8 mL water + 2 drops red, 1drop purple -> 15 drops of this mixture into fresh tube with additional 8mL water (serial dilution)

Aliquot the following solutions to their respective colored micro tubes:

- Yellow = about 750 µL (20 drops with disposable pipette)
- All other colors approximately 250 µL (7 drops with disposable pipette)
- Clear tubes should have 250 µL of plain water added

Label colored micro centrifuge tubes:

- Yellow = "MMP" (master mix & Primers)
- Pink = + (positive control)
- Purple = #1
- Green = #2
- Blue = #3
- Orange = #4
- Clear = - (negative control)

STUDENT LAB STATION

- One of each color tube (7 total)
- 6 PCR tubes & capless tube adapters (or micro centrifuge tubes)
- 1 micro pipette (or 7 disposable pipettes)
- Sufficient tube racks (or foam floats) to hold all tubes

STUDENT PROCEDURE:

1. Students should arrange PCR tubes, and map out which tube is in which location in their rack.

2. Label PCR tubes (+, 1, 2, 3, 4, -). *This can be challenging and difficult to read. Mapping the location of the tube is important. (Alternatively, micro centrifuge tubes can be used, and the labeling is much easier.)*

3. Add 20uL (1 drop if using disposable pipettes) of simulated MMP from the YELLOW stock tube to each of the PCR tubes.

4. Add 20 uL of simulated DNA sample from the colored stock tube to the corresponding PCR tube. *Be sure to change tips to prevent contaminating samples!* If using micropipettes, the contents of each PCR tube can be mixed by pipetting up and down a few times.

5. If contamination occurred it should be visible based on the altered color of the solutions.

Name _____

POLYMERASE CHAIN REACTION (PCR)

In the sequences below, locate the forward and reverse primer sequences. Next, highlight or underline the segment of the gene that would be amplified with PCR using those primers. Record the length of the amplicon (amplified sequence).

Forward primer: 5' CGAT 3' Reverse primer: 3' TAAG 5'

Positive Control

5' T G A G C G A T G G T A A T G C C G A T C T T A T C A A A T T C C G C G **3'**
3' A C T C G C T A C C A T T A C G G C T A G A A T A G T T T A A G G C G C **5'**

Number of base pairs in amplicon =

Patient 1

5' T G A G C G A T G G T A A T G C C T G G A T C T T A T C A A A T T C C G **3'**
3' A C T C G C T A C C A T T A C G G A C C T A G A A T A G T T T A A G G C **5'**

Number of base pairs in amplicon =

Patient 2

5' T G A G C G A T G G T A A T G C C G A T C T T A T C A A A T T C C G C G **3'**
3' A C T C G C T A C C A T T A C G G C T A G A A T A G T T T A A G G C G C **5'**

Number of base pairs in amplicon =

DNA ELECTROPHORESIS

In DNA electrophoresis, fragments of DNA migrate at different speeds based on their length. Shorter fragments migrate farther. Longer fragments are unable to pass through the gel as quickly and, therefore, do not migrate as far. Fill in the location of the DNA bands in the gel below based on the sizes of the sequences amplified in the above PCR.

Number of Base Pairs	Positive Control	Patient 1	Patient 2
34			
33			
32			
31			
30			
29			
28			
27			
26			
25			
24			
23			
22			
21			
20			

Name _____

KEY

POLYMERASE CHAIN REACTION (PCR)

In the sequences below, locate the forward and reverse primer sequences. Next, highlight or underline the segment of the gene that would be amplified with PCR using those primers. Record the length of the amplicon (amplified sequence).

Forward primer: 5' CGAT 3' Reverse primer: 3' TAAG 5'

Positive Control

5' T G A G C G A T G G T A A T G C C G A T C T T A T C A A A T T C C G C G **3'**
3' A C T C G C T A C C A T T A C G G C T A G A A T A G T T T A A G G C G C **5'**

Number of base pairs in amplicon = 28bp

Patient 1

5' T G A G C G A T G G T A A T G C C T G G A T C T T A T C A A A T T C C G **3'**
3' A C T C G C T A C C A T T A C G G A C C T A G A A T A G T T T A A G G C **5'**

Number of base pairs in amplicon = 30bp

Patient 2

5' T G A G C G A T G G T A A T G C C G A T C T T A T C A A A T T C C G C G **3'**
3' A C T C G C T A C C A T T A C G G C T A G A A T A G T T T A A G G C G C **5'**

Number of base pairs in amplicon = 28bp

DNA ELECTROPHORESIS

In DNA electrophoresis, fragments of DNA migrate at different speeds based on their length. Shorter fragments migrate farther. Longer fragments are unable to pass through the gel as quickly and, therefore, do not migrate as far. Fill in the location of the DNA bands in the gel below based on the sizes of the sequences amplified in the above PCR.

Number of Base Pairs	Positive Control	Patient 1	Patient 2
34			
33			
32			
31			
30		■	
29			
28	■		■
27			
26			
25			
24			
23			
22			
21			
20			

BRAND NAME GENES IMPLEMENTATION PLAN — INTERDISCIPLINARY BRIDGES			
Activity	Estimated Time	Summary	Purpose/Objectives
Learning from Patients: Journalistic Writing Assignment about Cancer Research.	Varies.	Students act as journalists on assignment to cover a noted cancer researcher's lecture.	To provide students an opportunity to draw upon and develop their language-arts skills as they research and write about science's current understanding of cancer.

BRAND NAME GENES INTERDISCIPLINARY ACTIVITY

LEARNING FROM PATIENTS

JOURNALISTIC WRITING ASSIGNMENT ABOUT CANCER RESEARCH

BACKGROUND

This writing assignment asks students to take on the role of journalists as they view—and then write about—a lecture from HHMI's *Learning from Patients* DVD (2003).

Disc 1 of *Learning from Patients* includes four lectures: two by Dr. Bert Vogelstein about cancer and two more lectures by Dr. Huda Zoghbi about neurodegenerative diseases. All four lectures include valuable information for biology students; however, the first half of Dr. Vogelstein's lecture is of particular relevance to the *Brand Name Genes* module.

MATERIALS

Lecture 1in HHMI's *Learning from Patients: The Science of Medicine* DVD

HHMI has provided these DVDs for the *Brand Name Genes* teachers kits. The DVD is also available without charge at http://www.hhmi.org/biointeractive/cancer/index.html.

Information about the lecturer, Dr. Vogelstein, is available at http://www.hhmi.org/biointeractive/cancer/vogelstein.html and at other websites, including his home institution, Johns Hopkins University.

TOPICS COVERED IN THE LECTURE

- History of cancer research
- Tumor types (benign, malignant, metastatic)
- Blood vessel recruitment of tumors (diffusion limitation of tumor size)
- Cell division and cell death (apoptosis)
- Gene mutations
- Carcinogens
- Role of environment vs. genes in disease
- Genes, including *p53*, that control cell growth and proliferation

INSTRUCTIONS

Show "Research Mechanics: Putting the Brakes on Cancer," which is Lecture 1 in HHMI's *Learning from Patients: The Science of Medicine* DVD. This lecture lasts 53 minutes without the introduction. It last 57 minutes with the introduction.

While students watch the video they should pretend they are newspaper reporters assigned to cover Dr. Bert Vogelstein's lecture about cancer.

Their articles should include background information on Dr. Vogelstein, including his education and past and present research. The students' articles should also cover the main points of the lecture, including the types of tumors and the types of genes involved in cancer.

Encourage students to write articles that are each a full page, typed and made to look like a newspaper article. Tell them to include catchy headlines as well as their names in the bylines. Each article can also include a picture with a caption.