BIOBUSINESS

How Businesses Use Recombinant DNA Technology to Tailor Products to Meet Customers' Needs

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KEY TERMS

Agar plate — a Petri dish containing an extract of certain species of red seaweeds that is used as a gelling agent in microbial culture media. Nutrient agar consists of a broth made from beef extract or blood that is gelled with agar and used for the cultivation of bacteria, fungi, and some algae.

Ampicillin — an antibiotic which inhibits the growth of bacteria.

Arabinose — a sugar normally used as a source of food by bacteria which induces the over expression of the Green Fluorescent Protein in cloned cells.

Bacterial chromosome — the chromosome found in the bacterial cell.

Biotechnology — any process that uses cells, organelles, macromolecules, biochemicals, or biochemical pathways to create a product. Fermentation is an ancient biotechnology; gene therapy is a more recent one.

Blunt ends — even ends of DNA after it is cut by restriction enzyme; they attach to the ends of other DNA fragments.

Cloning — the production of exact copies of a particular gene or group of genes using genetic engineering techniques. The DNA containing the target DNA is split into fragments using restriction enzymes. The fragments are then inserted into cloning vectors, such as bacterial plasmids or bacteriophages, which transfer the recombinant DNA to suitable host cells, such as bacterium E. coli. Inside the host cell the recombinant DNA undergoes replication; thus, a bacterial cell will give rise to a colony of cells containing the cloned target gene. Gene cloning enables large quantities of a desired protein product to be produced. Human insulin is now produced by bacteria containing the cloned gene.

DNA ligase — an enzyme that rejoins cut pieces of DNA.

Endonucleases — naturally occurring restriction enzymes that protect DNA from the effects of foreign DNA; they cut the DNA at specific points between its ends.

Exonucleases — an enzyme that catalyses the cleavage of nucleotides from the end of a nucleic acid molecule.

Five prime (5') — the phosphate ends of a DNA fragment; the number 5 refers to the fifth carbon in the sugar.

Gel electrophoresis — procedure used to separate and analyze DNA fragments by placing a mixture of DNA fragments at one end of a porous gel and applying an electric current to the gel.

Gene — combined sections that carry a code for building a single protein.

Gene Therapy — the application of genetic engineering techniques to alter or replace defective genes which may be able to cure or prevent genetic diseases such as cystic fibrosis

Gene transfer — the process of taking a gene from one organism and inserting the gene into the germ line of another organism so that it is replicated as part of the genome and present in all of the recipient's cells

Genetic engineering — process of making changes in the DNA code of living organisms; genetic engineering is an umbrella term for any process or procedure that adds, alters, replaces, augments or silences a gene or its expression in an organism.

Genetic marker — gene that makes it possible to distinguish bacteria that carry a plasmid with foreign DNA from those that do not

Genetic modification — any change in the genetic makeup of an organism.

Genetically modified organism (GMO) — organism whose genomes incorporate and express genes from another species

Green Fluorescent Protein (GFP) — a protein originally isolated from the bioluminescent jellyfish which has been cloned, and when exposed to ultraviolet light, gives off energy in the form of visible green light

Golden rice — genetically engineered rice using the genes from a petunia and a bacterium to produce provitamin A (beta carotene)

Hybridization — breeding technique that involves crossing dissimilar individuals to bring together the best traits of both organisms.

Inbreeding — continued breeding of individuals with similar characteristics.

Mutagen — an agent that causes a change in the DNA and results in an increase in the number of mutants in a population.

pAMP — plasmid with an ampicillin-resistant gene

pGLO™ — plasmid containing the Green Fluorescent Protein (GFP) sequence and ampicillin resistance gene.

pKAN — a plasmid with a kanamycin-resistant gene.

Plasmid — circular DNA molecule found in bacteria.

Polymerase chain reaction (PCR) — technique that allows molecular biologists to make many copies of a particular gene.

Recombinant DNA — DNA produced by combining DNA from different sources.

Restriction enzymes — enzyme that cuts DNA at specific sequence of nucleotides; widely used in the techniques of genetic engineering.

Selective breeding — method of improving a species by allowing only those individual organisms with desired characteristics to produce the next generation.

Sticky ends — uneven ends of DNA after it is cut by restriction enzyme; they attach to the ends of other DNA fragments.

Three prime ends (3') — the sugar ends opposite the 5' ends of DNA molecules.

Transformation — Transfer of DNA from one organism to another, often using a carrier called a vector (such as a plasmid, virus, or other form of mobile DNA); transformation can also be accomplished by physical means, including electroplating the plasma membrane or physically shooting DNA into the cells.

Transgene — any gene that is transferred to an organism using molecular tools.

Transgenic — term used for any organism whose genome incorporates and expresses genes from the same or a different species; the gene is introduced into the somatic cells, gametes, fertilized ova or embryos, so that the change is perpetuated and present in all cells of the mature organism and its progeny.

Vector — a vehicle used in gene cloning to insert a foreign DNA fragment into the genome of host cell For bacterial hosts three different types of vectors are used: bacteriophages, plasmids, and their hybrid derivatives, cosmids. The foreign DNA is spliced into the vector DNA using specific restriction enzymes and ligases to cleave the vector DNA and join the foreign DNA to the two ends created.

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

2005-06 North Carolina Standard Course of Study for Biology — Grades 9-12

*** Highlighted sections are objectives addressed in the BioBusiness 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.
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

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

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

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

2.02 Investigate and describe the structure and functions of cells including:
- Cell organelles
- Cell specialization
- Communication among cells within an organism.

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.
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

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

3.04 Assess the impact of advances in genomics on individuals and society.
- Human genome project
- Applications of biotechnology

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

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

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.

BioBusiness
Correlation to the National Science Education Standards

The Teaching Standards	
BioBusiness Correlation	
Each activity in the module provides short –term objectives for students. There is a conceptual flow of activities and a timeline for teaching the module and helping teachers plan. 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.	**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 interest, 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 own learning by using hands-on, inquiry-based activities. 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 the module, such as group discussion, data collection, and student writing activity. 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 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.

BioBusiness
Correlation to the National Science Education Standards

The Content Standards	
BioBusiness activity	
Pre-lab Activities **Wet-lab Activities** **Additional Activities: Bioethical Issues**	**Standard A (Science as Inquiry) : As a result of activities in grades 9-12, all students should develop** **1. abilities necessary to do scientific inquiry.** • identify questions and concepts that guide scientific investigations • Use technology and mathematics to improve investigations and communications • Formulate and revise scientific explanations and models using logic and evidence • Recognize and analyze alternative explanations and models • Communicate and defend a scientific argument **2. understanding about scientific inquiry.**
Pre-lab Activities **Additional Activities Bioethical Issues**	**Standard C (Life Science): As a result of their activities in grades 9-12, all students should develop understanding of** **1. the cell.** • Cells store and use information to guide their functions • Cells can differentiate, and complex multicellular organisms are formed as a highly organized arrangement of differentiated cells
Pre-lab Activities **Wet-lab Activities** **Additional Activities Bioethical Issues**	**2. molecular basis of heredity.** • In all organisms, DNA carries the instructions for specifying organism characteristics. • Changes in DNA occur spontaneously at low rates.
Wet-lab Activities **Additional Activities**	**Standard E (Science and Technology): As a result of activities in grades 9-12, all students should develop understanding of** **1. abilities of technological design.** **2. understandings about science and technology.** • Scientist in different disciplines ask questions, use different methods of investigation, and accept different types of evidence to support these explanations • Science often advances with the introduction of new technologies • Creativity, imagination, and good knowledge base are all required in the work of science and engineering • Science and technology are pursued for different purposes
Additional Activities **Interdisciplinary Activities**	**Standard F (Science in Personal and Social Perspectives): As a result of activities in grades 9-12, all students should develop understanding of** **1. personal and community health.** **5. human-induced hazards.** **6. science and technology in local, national, and global challenges.**
Pre-lab Activities **Wet-lab Activities** **Post-lab Activities** **Additional Activities** **Interdisciplinary Activities**	**Standard G: As a result of activities in grades 9-12, all students should develop understanding of** **1. science as a human endeavor.** **2. nature of scientific knowledge.** **3. historical perspectives.**

INTRODUCTION

This module illustrates the breadth of current, real-world applications of genetic engineering while fulfilling the following objectives:

1. To define biotechnology and provide examples of its current societal uses;
2. To recognize the benefits of using E. coli bacteria as a model organism;
3. To identify and explain the multi-step process of bacterial transformation;
4. To analyze the growth of bacteria on various media, and to interpret results within the context of gene expression; and
5. To recognize the roles that external and internal factors play in gene expression.

BACKGROUND

What does each of the following scenarios have in common? A diabetic and a child with vitamin A deficiency are losing their eyesight. An accidental spill pours oil into a patch of ocean, leaving years of environmental clean-up in its wake. An uncontrollable number of insects decimates fields of corn and potatoes, and devastates farmers' agricultural pocketbooks. Each of these scenarios, though extremely unfortunate, shares an unexpected potential solution: the use of genetic engineering.

KEY CONCEPT

Biotechnology involves the use of biological and engineering techniques on living organisms or associated living processes.

Genetic Engineering is the process of manipulating the DNA, or genetic material, of an organism, often to include DNA from a foreign organism. The advent of genetic engineering has led to a phenomenal explosion of new possibilities for health treatments, agricultural applications, environmental solutions, and much more. The development of intricate molecular techniques, including those related to genetic engineering, has contributed substantially to the booming field of **biotechnology**. Biotechnology involves the use of biological and engineering techniques on living organisms or associated living processes.

Biotechnology is one of the most exciting new sciences of the century. Biotech companies are enthusiastic about its many possibilities for making products more quickly and efficiently. Ultimately, consumers will decide for themselves whether these new products make sense for providing improvements in the quality of our nutrition, health and environment.

Modern-day applications and controversies of biotechnology are as varied as the organisms and biochemical processes used in the field. The booming field of **genetically modified organisms**, or GMOs, has spurred a fiery debate about the pros versus the cons of introducing such organisms into our research and our food supply.

On one hand, GMOs could pose a problem in terms of interfering with genetic diversity. Many people who do not support GMOs fear that the manipulated genes of GMOs will contaminate "natural" foods, leading to a mix of regular and genetically engineered DNA within organisms. Fears such as these have led to international concern, and varying degrees of support (or lack thereof) for genetically modified foods exist within countries and continents as far apart as Africa, Europe, and North America. Ultimately, scientists, politicians, and many other key players need to strike a knowledgeable balance between the nutrition needs of mass populations, and issues of safety and environmental awareness. Other examples illustrate the controversy surrounding genetically modified plants. A Cornell study done in 1999 on the relationship between Bt corn (a crop genetically engineered for pesticide resistance) and monarch butterflies indicated potential harm done to the butterflies that fed on milkweed pollinated by Bt corn growing nearby. Related studies, however, have produced different results.

Positive outcomes of biotechnology include developments in medicine, agriculture, and even the environment. Once unimaginable quantities of insulin are now produced by bacteria to treat diabetes. For hemophiliacs, scientists can currently manufacture a protein called Factor VIII to help blood clot properly. For heart attack and stroke patients, another protein, called Tissue Plasminogen Activator

(or tPA for short), does just the opposite: it unclogs blood clots associated with heart disease. Various crops with altered genes have created new products with an array of potential benefits, such as "golden rice" rich in vitamin A, pest-resistant crops, and potatoes with a molecularly built-in vaccine to prevent disease. In each of these cases, geneticists employ the power of molecular techniques to treat disease and enhance quality of life.

BACTERIA'S VERSATILITY

Biotechnology's applications not only sustain human life, but they also extend to the environment at large. For instance, genetically altered bacteria break down toxic chemical compounds, such as those in an oil spill, to reduce the amount of harmful substances in soil or water, in a process known as **bioremediation**.

KEY CONCEPT

Why use bacteria:
- fast reproduction
- safety
- size

Why use bacteria? Bacteria's versatility can be summed up in three words: size, reproduction, and safety. First, size: bacteria are unicellular, making them easy to work with because of their simplicity. Multicellular organisms would pose a more complex problem, since every single cell would need to contain the desired genetic alteration. A second benefit to using bacteria is reproduction: the faster a model organism reproduces, the more generations of offspring can be quickly produced. Numerous generations of organisms provide a wealth of information ripe for simultaneous analysis. Geneticists often value organisms such as fruit flies (*Drosophila melanogaster*) or bacteria for this reason. Third, safety: organisms should be chosen carefully to ensure they do not pose a danger to the people who are studying them.

When safety, fast reproduction, and size are taken into consideration, bacteria arise as ideal candidates for genetic manipulation. As a particular example of a model organism, the unicellular bacterium *Escherichia coli (E. coli)* reproduces quickly. Furthermore, although certain strains of E. coli have infamously been attributed to food scares and toxicity, many other strains remain innocuous, or even helpful (such as those naturally found in the human digestive system).

BACTERIAL ANATOMY

Bacteria contain several important features, many of which distinguish them from other organisms. Scientists classify bacteria as **prokaryotes**, as opposed to eukaryotes (the category to which other unicellular organisms, such as yeast, and multicellular organisms belong). As a prokaryote, a bacterium contains no nucleus, which normally serves as the control center and houses the DNA of a typical eukaryote. Furthermore, prokaryotes have no membrane-bound organelles (such as lysosomes to function in intracellular digestion) that are typically found in eukaryotes.

A bacterial cell [see Figure 1 below] typically contains a cell wall on the outside surface, which provides structure and protection to the cell. Cell walls encase the cells of bacteria and plants, but not animals. Inside of the cell wall is a cell membrane, similar to the cell membranes found in all living cells. The genetic material of a bacterium floats, uncontained by any membrane, inside of the cell's cytoplasm. **Plasmids**, which are small, circular pieces of DNA, can also be found in bacteria. Bacteria, like all cells, must produce protein, so they contain a fair share of ribosomes for this purpose. Finally, some bacteria move by way of whip-like structures known as flagella.

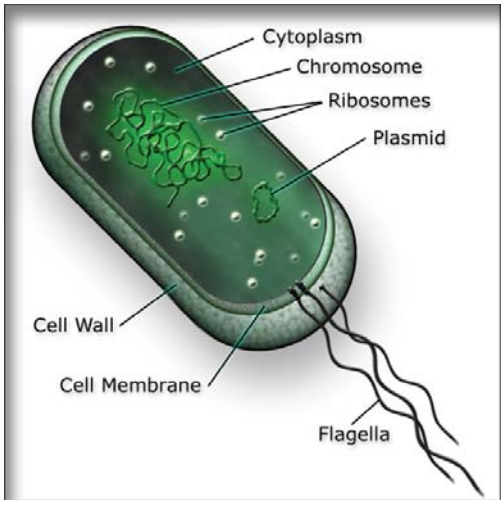


Figure 1: A Bacteria Cell

FROM ONE FORM TO ANOTHER:

The process by which bacteria acquire altered genetic characteristics from a different source is known as **bacterial transformation**. Transformation takes place in many different ways. Sometimes, a vector serves as the vehicle for DNA transport; examples of **vectors** include viruses and plasmids. The wet-lab portion of this introduction more closely investigates the process of bacterial transformation. As an example of how scientists use transformation in the context of genetic engineering, one can look at the production of insulin as a specific case. The following steps are necessary to produce insulin:

1. Isolating the DNA. Plasmids are taken out of bacterial cells and isolated. Also, DNA must be taken out of a normal human cell (from a non-diabetic person) and isolated. This human DNA contains the gene for insulin, a hormone necessary for diabetics. The Polymerase Chain Reaction, or PCR, is then used to make many copies of the gene that code for insulin.
2. Making molecular cuts. Restriction enzymes act as genetic scissors and cut open each plasmid, leaving a space within which to insert a desired gene—in this case, the gene that codes for insulin. Restriction enzymes also act on human DNA, and cut out the gene for insulin.
3. Forming Recombinant DNA. Each plasmid and human insulin gene combine to form a plasmid with the new piece of human DNA. This is known as recombinant DNA. DNA ligase, an enzyme, seals the ends of the plasmid with those of the gene for insulin. DNA ligase helps form covalent bonds between plasmid and gene.
4. Re-introducing the plasmid. The plasmid, containing both new and old genetic material, is introduced to a culture of bacteria. Through the process of transformation (described in the wet-lab section of this introduction), bacteria take in the plasmid with the new insulin gene.
5. Reproducing genetic material. The bacterial cells, many now containing one or more copies of the plasmid with the gene that codes for insulin, are allowed to reproduce, making many copies of the insulin gene and the gene product insulin.
6. Selecting for transformed cells. Some cells undergo successful transformation, while others do not. Only transformed cells with the new gene for insulin are desired, so these cells must be distinguished from the rest.
7. Utilizing the protein and/or genes. The multiple bacterial cells churn out mass quantities of the protein insulin, which can be used to treat diabetes. In some cases other than those of insulin production, the genes themselves can be placed into other organisms, such as plants, to enhance pesticide resistance or to address environmental issues.

PRE-LAB

The pre-lab of this module is designed to introduce students to the processes of genetic engineering and transformation. Students will first be introduced to some common products which are genetically engineered and will be asked to work in groups to create marketing campaigns that will successfully sell their assigned products. Students will have the opportunity to closely examine characteristics of their genetically engineered products, and will be faced with the ethical issue of whether or not to advertise the products as being genetically engineered.

In subsequent pre-lab activities, students will learn the process of transformation by learning how insulin is mass-produced for medical purposes. Students will first use linkable "Tangle® Toys" to learn how the gene for insulin production is removed from human DNA and inserted into a bacterial plasmid, which is then inserted into a bacterium for cloning and insulin production. Students then will receive a graphic of the process of genetic transformation, and will use their own words to describe what is going on in each step of the process. After being introduced to the correct terminology, students will receive more Tangle® Toys and build models of each step in the process, using correct terminology. To evaluate students' understanding, each student will put a scrambled list of steps used in mass-producing insulin for medical purposes in the correct order. By introducing students to genetic engineering and transformation in a way that illustrates the real-world applica-

tions of these techniques, students will be more engaged and will better see the applicability of the lessons taught in this module to their own lives.

WET-LAB

Biotechnologists use genetic engineering and transformation techniques for a variety of applications. The agricultural industry utilizes genetically modified plants that have been engineered to resist harsh natural conditions that might stunt or prohibit plant growth. The medical industry uses genetically transformed bacteria to manufacture human insulin which is given to patients with diabetes, and is experimenting with using gene therapy to give people with nonfunctional or mutated genes the functional genes to treat a genetic disease such as cystic fibrosis. Even environmental assets of genetic transformation are possible; transformed bacteria can aid in the chemical break down of oil spills.

Genetic engineering is the process of making changes in the DNA code of living organisms. Genetic engineering is an umbrella term for any process or procedure that adds, alters, replaces, augments or silences a gene or its expression in an organism. E. coli is an ideal candidate for transformation because: 1) It's unicellular, ideal since the new gene must be inserted into every cell of an organism; 2) It reproduces every 20 minutes, allowing scientists to quickly determine if the new gene was passed on to offspring; 3) The modified *E. coli* doesn't make people sick; and 4) *E. coli* can't survive outside the lab.

In this lab students will perform the process of genetic transformation on E. coli, and will investigate the effects of antibiotic resistance on E. coli growth. Students will work with Bio-Rad's pGLO™ plasmid, which contains two important genes of interest:

1) A jellyfish gene that codes for Green Fluorescent Protein (GFP) in the presence of the sugar arabinose; and 2) a gene that confers resistance to the antibiotic ampicillin.

E. coli normally have what is known as an arabinose operon, a set of genes that will code

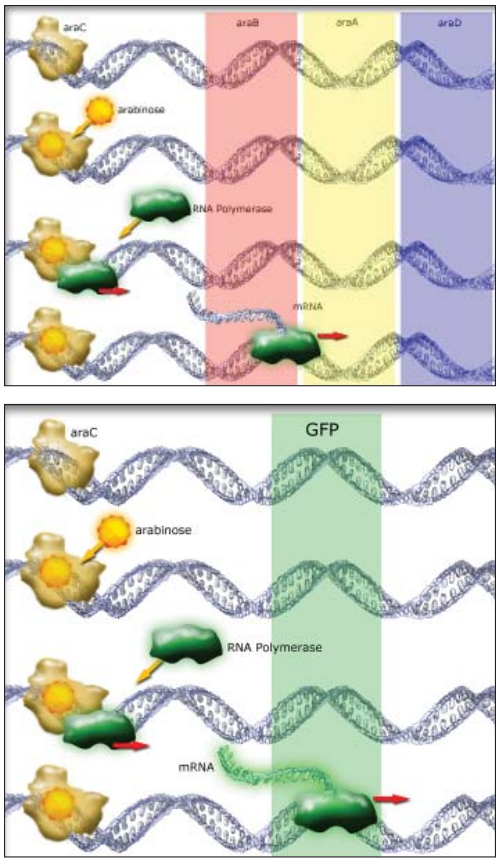


Figure 3: Both the promoter (PBAD) and the araC gene are present. However, the genes which code for arabinose catabolism, araB, A and D, have been replaced by the single gene which codes for GFP.

for enzymes that sequentially break down the sugar arabinose. These genes are only active when arabinose is present. Arabinose attaches to a part of the operon known as the promoter, which activates subsequent genes farther down the DNA strand ("downstream" of the promoter) [see Figure 2].

In the pGLO™ plasmid, the promoter still binds to arabinose, but the genes that normally produce enzymes to break it apart (ara A, ara B, and ara D in Figure 2) are replaced with a gene that codes for Green Fluorescent Protein (GFP). Therefore, when arabinose binds to the new promoter, Green Fluorescent Protein is produced, and the bacterial colonies will glow in the presence of ultraviolet light.

In order to select for successfully transformed cells, students will analyze the effects of pGLO™ on bacterial growth by growing transformed cells on four different media:

1. pGLO™ + LB/amp: This plate has luria broth (LB), which provides nutrients to the bacteria, and the antibiotic ampicillin (amp). Result: Only transformed cells will grow in ampicillin because the pGLO™ plasmid has a gene that confers resistance to ampicillin. These transformed cells will not glow, however, because arabinose is necessary for the production of GFP.

2. pGLO™ + LB/amp/arabinose: Now, arabinose sugar is also present. Result: Only transformed cells will grow. They will also glow in the presence of UV light since arabinose is present. Arabinose attaches to the promoter, which turns on GFP production, so that the bacteria can fluoresce.

3. LB/amp: same as 1) without the pGLO™ transformed cells. Result: No growth. The ampicillin kills the bacteria, since they have not been transformed with the ampicillin-resistant gene.

4. LB only. Result: Bacterial growth. Given the proper nutrients supplied by luria broth, bacteria grow very well.

In order to show students the importance of having both experimental and control groups, two of the plates above (1 and 2) involve the transformation of bacteria with pGLO™; two of the plates (3 and 4) do not.

TRANSFORMATION

KEY CONCEPT

Four steps of transformation:
1. Pre-incubation
2. Incubation
3. Heat shock
4. Recovery

The process of bacterial transformation, when bacteria acquire the pGLO™ plasmid, can be explained in four steps:

1. Pre-incubation: Calcium chloride, a transformation solution, is added to the bacteria. The ionic character of $CaCl_2$ (calcium's positive ions) allows it to interact with the biochemistry of the cell membrane and the bacterial DNA to allow external DNA to more easily enter the cell.

2. Incubation: The pGLO™ plasmid is added to the cell culture.

3. Heat shock: Bacteria are subjected to extreme differences in temperature, a process which allows the cell wall to expand, contract, and more easily take in the new pGLO™ plasmid.

4. Recovery: The bacteria are grown in luria broth and are briefly incubated to foster growth.

These four steps enable gene expression of pGLO™ in the presence of arabinose sugar and ultraviolet light.

POST-LAB AND ADDITIONAL ACTIVITIES

The post-lab activities are designed to help reinforce the concepts taught in the BioBusiness wet-lab. In addition to using transformation grids to analyze the results from the wet-lab, students will calculate the transformation efficiency to determine the extent to which E. coli cells were genetically transformed. Students will also be given review and analysis questions to answer that will allow them to demonstrate their understanding of the subject. Students can further demonstrate their understanding by participating in the DESTINY Quiz Game, a fun evaluation tool that allows students to demonstrate their knowledge in the style of the popular TV game show Jeopardy! Teachers are provided a computer program which can project the game board onto a screen to allow interactive play, or they can use printed versions of the questions and answers in class.

In another post-lab activity, students will watch the 60 Minutes II video titled Growth Industry. The 20-minute video is a look at the use of Human Growth Hormone in the life of a boy. Accompanying the video is a bioethical analysis model that relates to the film.

The additional activities included in the module were designed to augment the activities of the pre-, wet-, and post-labs. Students can explore careers and fields in biotechnology through researching and creating an informational brochure about one biotech career. Teachers can choose to have students construct a timeline of innovations in biotechnology from prehistory to the present using the information provided in the teacher's notebook. An additional lab activity

using soybeans provides students an excellent way of observing and graphing differences between genetically modified organisms and unmodified organisms.

Teachers who wish to incorporate a writing lesson into their classrooms can ask students to write a paper explaining how genetic engineering has affected them personally. In another activity, students can use the Internet, magazines, and other article sources to investigate the ethical issues surrounding genetic engineering. A final activity taps into students' creative expression by allowing them to make a persuasive advertisement to announce their position on a bioethical issue. The use of any or all of these post-lab and additional activities will provide teachers with a way to evaluate student understanding of concepts covered in the module, as well as give students a way to link what they did in the wet-lab with real world applications.

SOURCES

Bio-Rad's pGLO™ Bacterial Tranformation Kit Instructor Booklet

Bio-Rad's Biotechnology Explorer™ Catalogue

Cambell, Neil A., et al. *Biology: Concepts & Connections*. San Francisco: Benjamin Cummings, 2003. pp. 230-253.

Arabinose Operon:
http://www.mun.ca/biochem/courses/3107/Topics/Ara_operon.html

Bacteria:
http://www.emc.maricopa.edu/faculty/farabee/BIOBK/BioBookDiversity_2.html
http://www.cellsalive.com/cells/bactcell.htm

Bacterial Transformation:
http://www.rlc.dcccd.edu/mathsci/reynolds/micro/lab_manual/transformation.html

Bioremediation:
http://water.usgs.gov/wid/html/bioremed.html
http://programs.weber.edu/bioremediation/

Bt Corn and Monach Butterflies:
http://www.ipm.iastate.edu/ipm/icm/1999/6-14-1999/monarchbt.html
http://www.ars.usda.gov/is/br/btcorn/index.html#bt1
http://www.uky.edu/Agriculture/Entomology/entfacts/fldcrops/ef118.htm

DNA:
http://faculty.clintoncc.suny.edu/faculty/Michael.Gregory/files/Bio%20100/Bio%20100%20Lectures/DNA/dna.htm

E. coli:
http://people.ku.edu/%7Ejbrown/ecoli.html

Hemophilia:
http://www.hemophilia.ca/en/index.html
http://www.hemophilia.org/resources/wwwresources.htm#hemovon

Heart Disease and blood clots:
http://www.intstudy.com/articles/ec192a05.htm
http://www.intstudy.com/articles/ec192a05.htm

Prokaryotes v. Eukaryotes:
http://web.mit.edu/esgbio/www/cb/prok_euk.html

Recombinant DNA:
http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/R/RecombinantDNA.html

"BIOBUSINESS" IMPLEMENTATION PLAN—PRE-LAB			
Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Engagement What do these products have in common? Marketing Plan	25 minutes	Copies of "What Do These Products Have in Common?" handout for each student Copies of instructions for developing a marketing plan and description of assigned product for each group, 1 large sheet of paper for each group, markers	**Purpose:** To introduce students to the concept and process of bacterial transformation **Objectives:** • To develop a definition of biotechnology • To identify the steps involved in the process of transformation • To describe and demonstrate the process of transformation **Essential Question:** What is bacterial transformation?
Exploration Model the process of genetic engineering	15 minutes	Tangle® Toys	
Explanation Steps in making recombinant DNA	20 minutes	Copies of unlabeled graphic for each student; color overhead with labels Tangle® Toys, labels, and blank cell diagrams for each group	
Elaboration Board meeting agenda	25 minutes	Board Meeting Agenda handout for each student, list of products from Engagement activity	
Evaluation	5 minutes	Envelope with strips for steps of transformation	

Alignment with NC Competency Goals	
Biology	
Goal 1 Objectives 1.01, 1.02, 1.03, 1.04, 1.05 Goal 2 Objectives 2.02	Goal 3 3.01, 3.04 Goal 4 Objectives 4.01, 4.04

BIOBUSINESS PRE-LAB ACTIVITIES

Purpose

• To introduce students to the process of genetic engineering
• To explain how scientists manipulate DNA

Objectives

• To define genetic engineering
• To demonstrate the process of bacterial transformation
• To introduce students to the advantages and challenges of genetic engineering
• To understand what techniques can be used to make multiple copies of a gene
• To understand what features make plasmids beneficial in transformation

Engagement

Split class into groups; give each student one "What do these three products have in common?" handout. Ask students to brainstorm 4-5 similarities among the given products. Class discussion follows, leading to a working definition of "biotechnology."

Split class into groups with one marketing handout per group and assign each group one product for which to develop a marketing plan. (Six product overviews are provided, including the three products used in the previous engagement activity.) Give each group a large sheet of paper and markers to record their marketing ideas.

Exploration

Using contrasting colors of Tangle® Toys, have groups of students model the process of cloning a gene into a bacterial plasmid. Show what happens to the genetically engineered plasmid when the bacteria cell divides.

Explanation

Have students fill in the steps of creating recombinant DNA in their own words, using the handouts provided. Use color overhead to discuss.

Split class into groups; provide each group a set of Tangle® Toys and 5 images of cells. Have each group model the steps of creating recombinant DNA (their results should resemble the graphic used in the first step of the Explanation.)

Elaboration

Provide each student a handout of the Board Meeting Agenda. Explain the premise—the students are board members of a company that

specializes in genetically modified products (the same list of products used in the Engagement activity). The board needs to prepare for an important meeting with Acme Corporation, who is thinking about acquiring the classroom's company for an enormous sum of money. But before they will vote, the shareholders of Acme Corporation have some questions about genetic modification that require clarification. As chair of the board, engage the board members in an informed discussion to answer Acme's questions.

Evaluation

Have students arrange the steps of bacterial transformation in the correct sequence.

BIOBUSINESS ENGAGEMENT ACTIVITY — INTRODUCTION

NOTE FOR TEACHERS

The 2000 edition of the Oxford English Dictionary gives this definition for **biotechnology**:

The branch of technology concerned with modern forms of industrial production utilizing living organisms, esp. micro-organisms and their biological processes.

bio- = life

techno- = art, craft

-ology = study or science of something (e.g., biology, psychology, philology)

1. Divide the class into small groups.

2. Distribute the handout "What do these three products have in common?" (These three products, along with the three products on the following page in the teacher's notebook, will be the products assigned to student groups for the marketing plan activity.)

3. Ask each group to read the handout and jot down four or five things the products have in common. (Point out the leading questions at the top of the handout.)

4. After 2-3 minutes, ask the groups to report on their discussions. Jot their comments on the board, noting where they overlap.

5. Lead the class discussion toward the following outcomes:

- The three products all involve the application of organisms and their products for human use.

- The three products all involve the understanding and manipulation of genetic information.

6. Point out that these two characteristics define the term biotechnology.

WHAT DO THESE THREE PRODUCTS HAVE IN COMMON?

Things to Consider: How are they manufactured? Why are they manufactured?
What do the manufacturers need to know in order to make these products?

Product: Human insulin	
The science behind it	In the laboratory, the gene for human insulin (a protein found in the pancreas) is inserted into yeast or bacteria, from which large quantities of the human insulin molecule are then manufactured.
Characteristics	Insulin regulates the use and storage of nutrients (food), particularly carbohydrates. Human insulin results in fewer immune rejections and side effects than does porcine (pig) insulin modified for use in humans.
Uses	To treat diabetes.

Product: Recombinant Bovine Growth Hormone (rBGH)	
The science behind it	rBGH is a genetically engineered version of a hormone (bovine somatotropin, or bST), which is found in the pituitary gland of cows and controls milk production.
Characteristics	rBGH can increase cows' milk production by as much as 20-30%.
Uses	To farm and to make dairy products.

Product: Spider silk	
The science behind it	One method involves inserting a gene from an orb-weaving spider into a fertilized goat egg. The resultant "spider-goats" produces milk that can be manufactured into strong fibers.
Characteristics	Elastic, lightweight fiber five times stronger than steel.
Uses	To make flak jackets, rope, textiles, sutures, artificial tendons, bandages for burn victims.

WHAT DO THESE THREE PRODUCTS HAVE IN COMMON?

Things to Consider: How are they manufactured? Why are they manufactured?
What do the manufacturers need to know in order to make these products?

Product: Golden rice	
The science behind it	Genes for making beta-carotene are taken from daffodils and inserted into the genome of a strain of rice.
Characteristics	Contains beta-carotene, which forms vitamin A.
Uses	To protect undernourished people from blindness caused by a lack of vitamin A.

Product: Edible vaccine	
The science behind it	Specific antigen genes are inserted into cells taken from plants such as tomatoes and potatoes; the genetically enhanced cells are then grown into new plants that express the antigen genes and can be used as vaccines.
Characteristics	Can be administered without needles; do not need refrigeration for storage or transportation; can be grown in countries without manufacturing facilities.
Uses	To treat Norwalk virus (which causes severe diarrhea); potential uses include treatment of measles, Hepatitis B and malaria.

Product: Bt crops	
The science behind it	*Bacillus thuringiensis* (Bt) is a bacterium that is toxic to some insects. In the laboratory, the gene that produces Bt's toxic effect is inserted into the DNA of plants such as corn, cotton, and potatoes.
Characteristics	Bt crops produce an insecticide protein thousands of times more powerful than the chemical insecticides normally sprayed on crops.
Uses	Prevention of crop destruction by harmful insects.

BIOBUSINESS ENGAGEMENT ACTIVITY:
Designing a Marketing Plan

Biotechnology is one of the most exciting new sciences of the century. Biotech companies are enthusiastic about its many possibilities for making products more quickly and efficiently. Ultimately, consumers will decide for themselves whether these new products make sense for providing improvements in the quality of our nutrition, health and environment.

You are employed by a marketing/public relations company and your customer is a multi-national biotechnology company. Your firm is asked to develop a marketing campaign for one of its new products.

Each team will be assigned one product to market.

Use a sheet of poster paper and markers to develop marking strategies for the product your team is assigned.

Take into account:

• What name will you give your product?

• Which specific target group(s) do you want to address?

• What are 3 main selling points/benefits?

• What is your call to action? (What are you asking people to do?)

• What kinds of marketing and PR will you use to get people to do the desired action (advertisement, direct selling, special event, TV or radio commercial, print, jingle, rap or other)?

• Your goal is to sell your product but you must be accurate in describing it. (Make it sound as exciting as possible without making false claims.)

• Do you plan to tell the public it is a genetically engineered product? If so how do you plan to tell them?

BIOBUSINESS EXPLORATION ACTIVITY:
Modeling the Process of Genetic Engineering

In this activity, students are given Tangle® Toys and are asked to manipulate them in a way to simulate the process of making recombinant DNA.

EXPLORE

Teacher Preparation:
For each set of Tangle® Toys, do the following:
Designate one color strand to be the eukaryotic DNA. Remove any extra links to the strand so that it has 15 links total. Using a Sharpie permanent marker, write an "I" on one link. This strand represents a double strand of DNA containing the gene of interest (insulin production).

Use the strand of contrasting color to create a circle of 4 links. This will represent a bacterial plasmid.

You will have 3 links of the first color Tangle® Toy and 14 links of the second color Tangle® Toy left over. Include these in the bag as well; they will be used in the Explanation activity.

Instructions:
Give each group of student a set of the two Tangle® Toys strands — the strand you have prepared as the eukaryotic DNA and the strand of a contrasting color from which you have created a bacterial plasmid.

Explain to the students what each of the Tangle® Toys represents and point out that one of the eukaryotic chromosomes contains a gene for insulin production (the link marked with an "I").

Tell the students that you want the bacterial plasmid to be able to produce insulin, and that they need to use their Tangle® Toys to figure out how to simulate the process. They may not use the extra links in the bag for this step. Allow students a few minutes to figure out how this can be accomplished.

Results:
Students should examine the Tangle® Toy models and note that the single strand contains a gene that codes for insulin production, but the contrasting colored strand does not. Students should remove the insulin gene from the single strand, and insert it into the bacterial plasmid. The product should be a round plasmid, with one link of one color and the remaining links being of the contrasting color. The single link should be the gene that codes for insulin, and it should be easy to see that the gene coding for insulin production came from an organism different from the bacteria plasmid, as it is the only link in the plasmid which is a different color.

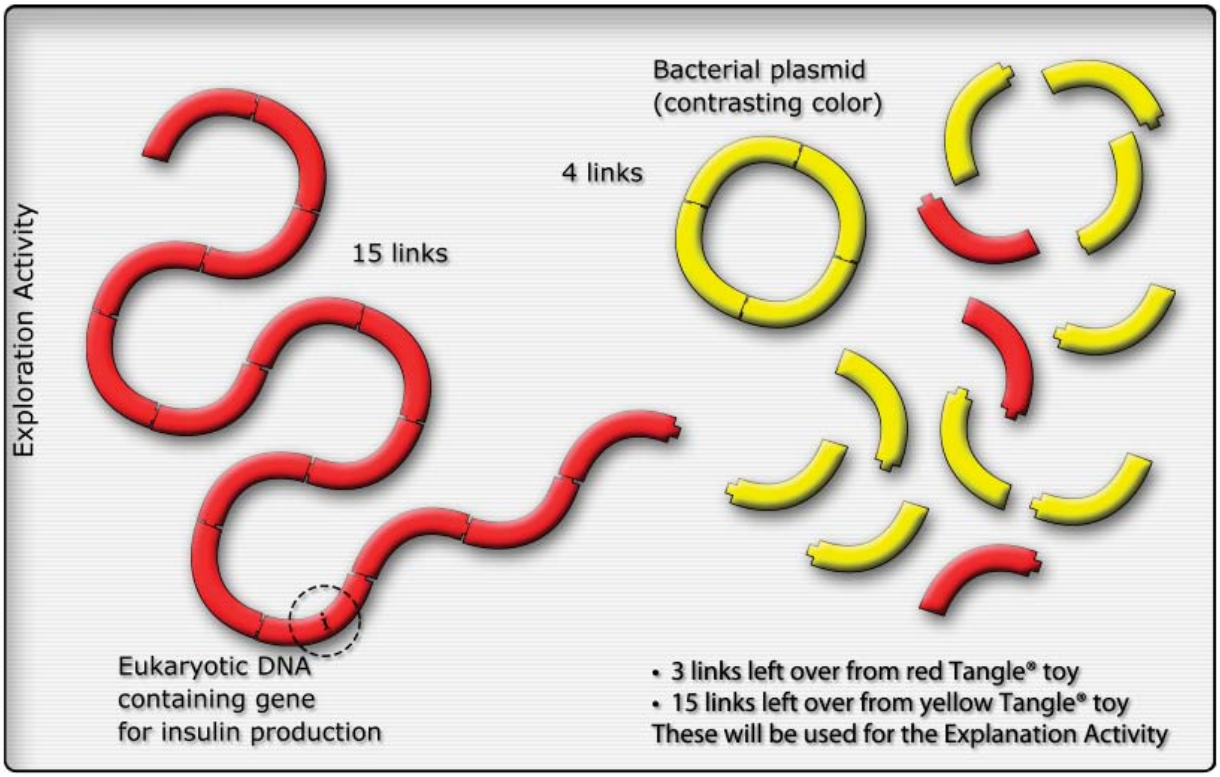
Ask students to explain in their own words how the plasmid was changed to contain the insulin gene.

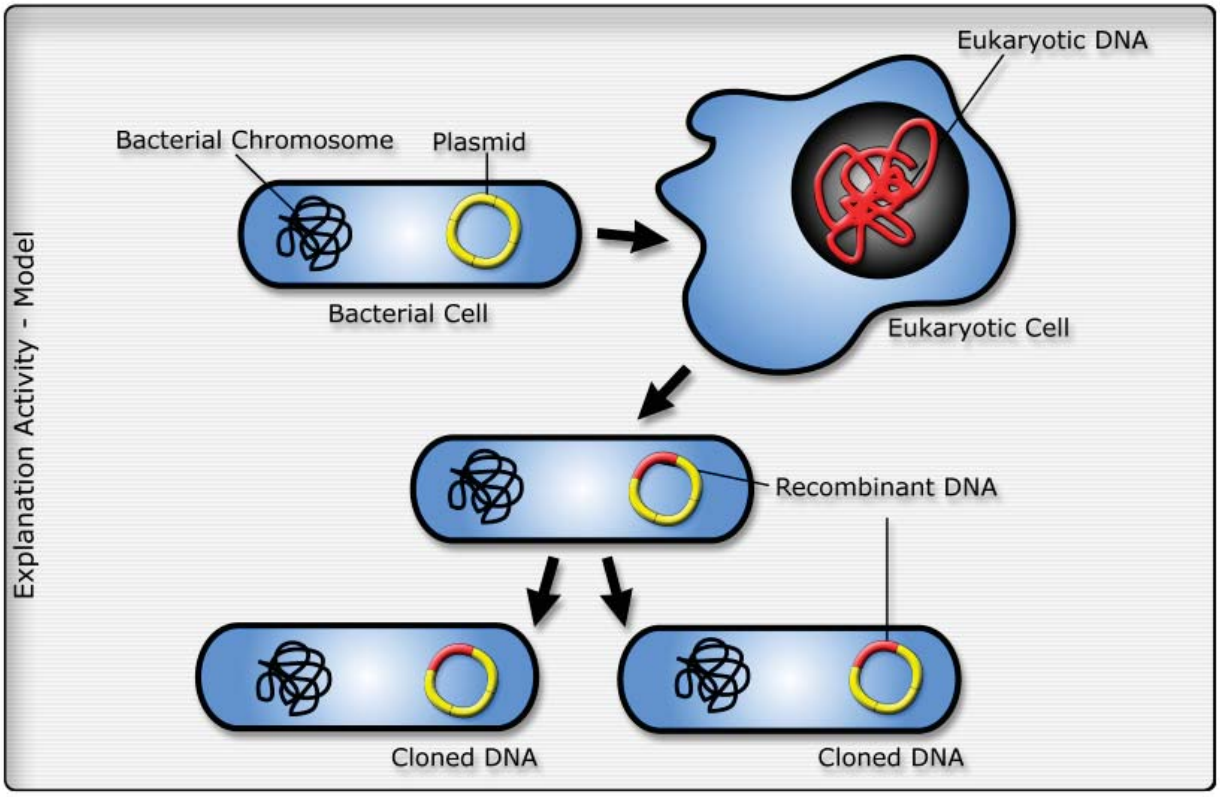
Explain to students that they have created what is called recombinant DNA.

Explain that in the next step scientists would place that plasmid back into a bacterium, so that the bacterium would clone itself, thereby cloning the genetically engineered plasmid.

Explain that this is actually done to manufacture insulin, which is useful to diabetics.

Each group's set should contain:





BIOBUSINESS EXPLANATION ACTIVITY

Modeling the Process of Genetic Engineering

EXPLAIN

Step One

In this step, students are given a figure showing the process of creating recombinant DNA and have the opportunity to describe what is happening in their own words. They will then be given the appropriate vocabulary and will be asked once again to describe what is happening.

Instructions

Give each student a copy of the graphic showing the steps in making recombinant DNA without labels of each step, along with a sheet to write down what is happening in each step. Ask students to take a few minutes to study the steps in bacterial transformation, and then write in their own words what is happening in each step of the process.

After students have completed this activity, show an overhead with all of the correct terminology and phrases explaining the steps.

Introduce students to the new terminology. Discuss the following concepts as they relate to genetic engineering.

Key Concepts

Explain the difference between a plasmid and a bacterial chromosome.
Point out that the bacterium is a prokaryote, and the cell containing the gene of interest is eukaryotic.
Explain the difference between bacterial chromosome and a plasmid.
Explain the role of restriction enzymes in the process of removing the gene of interest, and in opening the bacterial plasmid.
Explain how the recombinant DNA is placed back into a bacterial cell.
Explain the roles of genetic markers in identifying the location of the gene of interest.

Step Two

In this step, students are once again given Tangle® Toys, and are asked to use them and cut outs of cells to create models representing each step of the process of creating recombinant DNA.

Instructions

Give each group of students a set of Tangle® Toys as prepared for the Exploration activity including extra links and cut-outs of 5 cells, with one cell being eukaryotic showing a nucleus and the other 4 being prokaryotic.

Ask students to create a model representing each step of creating recombinant DNA, beginning with a bacterial cell containing a plasmid and a eukaryotic cell containing the gene of interest (insulin production). Tell the students to use the labels included in the plastic bag to label specific structures (use Labels for Explanation Activity provided).

Results

Students should create a model that looks similar to the graphic used in the explanation activity using the correct terminology. An example of their finished model is provided for reference on the following page.

Key Points

After students complete their models some of the following topics can be covered:
• Explain the usefulness of this technique in gene therapy and hybridization of organisms.
• Compare and contrast selective breeding and genetic engineering
• How does DNA get into cells? (Gene Transfer)
• Genetic Markers
• Vectors
• Cloning and transgenic organisms
• Genetically Modified Organisms
• Benefits of genetically engineered products

STEPS IN THE TRANSFORMATION PROCESS

Describe in your own words what is happening in each step of bacteria transformation.

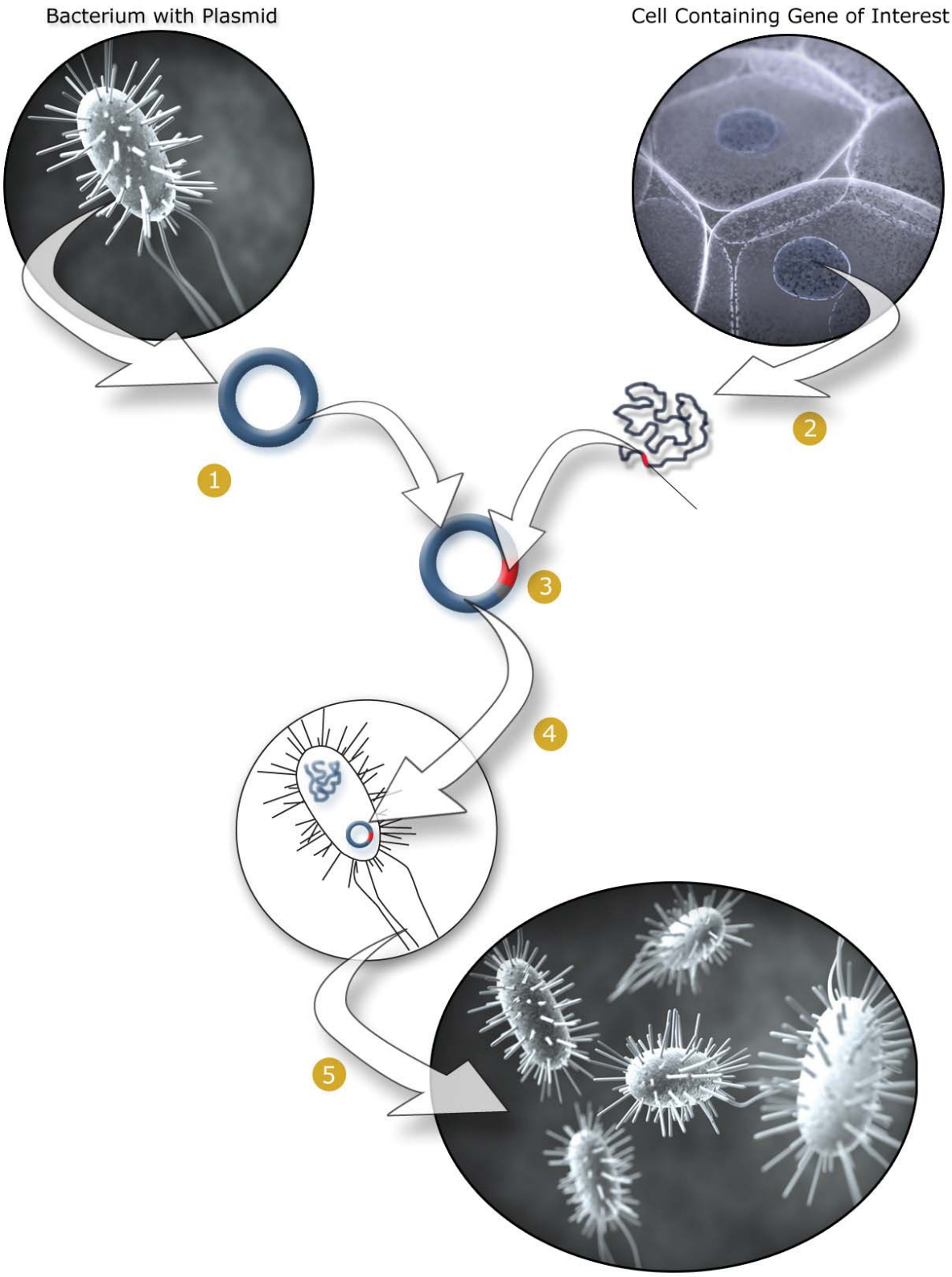
1._____

2. _____

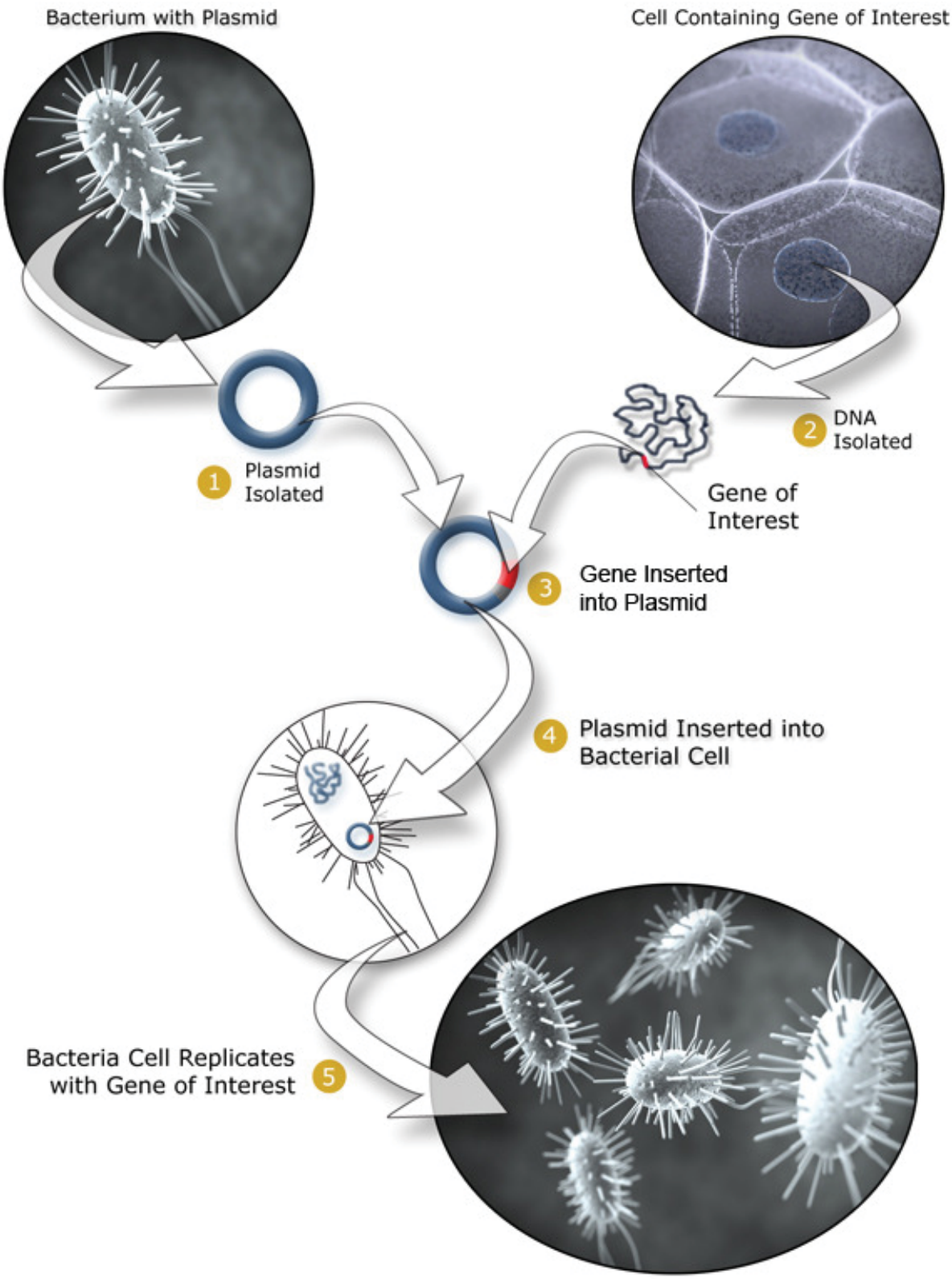
3. _____

4. _____

5. _____


Bacterium with Plasmid
Cell Containing Gene of Interest
1
2
3
4
5

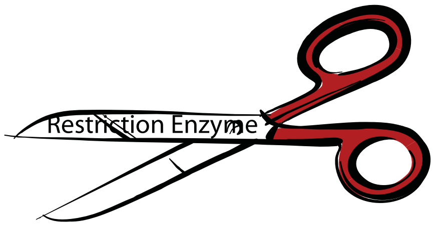
KEY

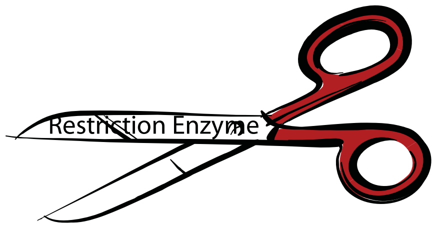


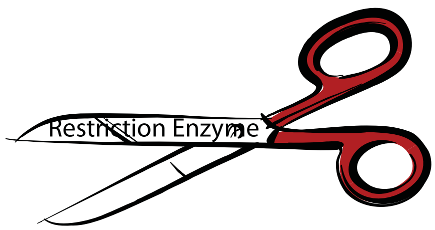
LABELS FOR THE EXPLANATION ACTIVITY

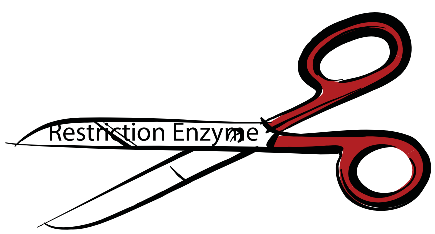
Each group needs one set of labels and two pairs of scissors from the following pages.

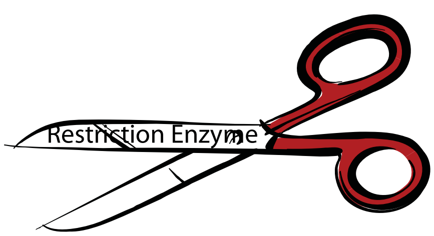
Bacterial Cell	Bacterial Cell	Bacterial Cell
Plasmid	Plasmid	Plasmid
Eukaryotic Cell	Eukaryotic Cell	Eukaryotic Cell
Eukaryotic DNA	Eukaryotic DNA	Eukaryotic DNA
Cloned DNA	Cloned DNA	Cloned DNA
Recombinant DNA	Recombinant DNA	Recombinant DNA
Bacterial Chromosome	Bacterial Chromosome	Bacterial Chromosome
Bacterial Cell	Bacterial Cell	Bacterial Cell
Plasmid	Plasmid	Plasmid
Eukaryotic Cell	Eukaryotic Cell	Eukaryotic Cell
Eukaryotic DNA	Eukaryotic DNA	Eukaryotic DNA
Cloned DNA	Cloned DNA	Cloned DNA
Recombinant DNA	Recombinant DNA	Recombinant DNA
Bacterial Chromosome	Bacterial Chromosome	Bacterial Chromosome

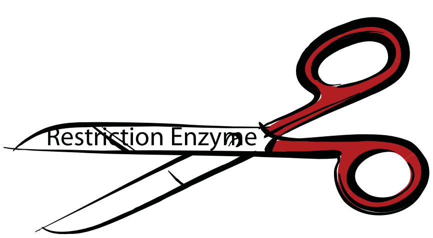


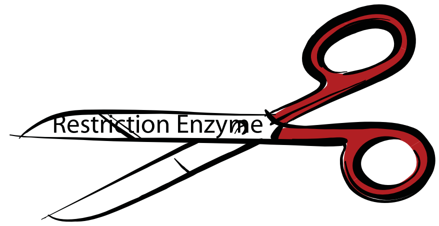


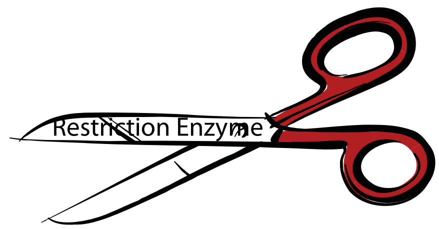


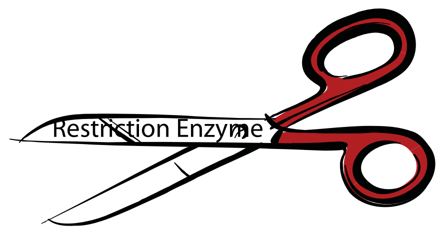


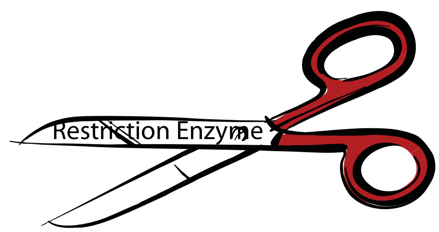


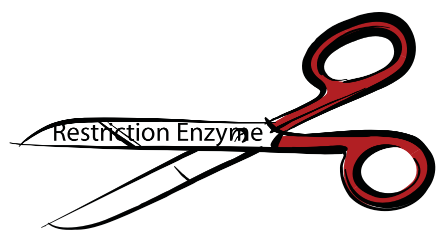


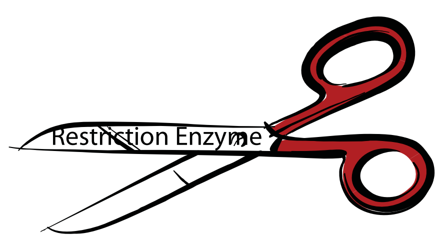












BOARD MEETING AGENDA

Items for discussion at today's meeting: Preparing for Acme Corporation acquisition
Acme Corporation is considering purchasing our company for an enormous sum of money, enough that we can all retire immediately! But before they will vote, the shareholders of Acme Corporation have some questions about genetic modification that require clarification. We will consider each question as an agenda item.

1. Our company produces products by genetic engineering. How does genetic engineering differ from selective breeding, which has been used for centuries to produce organisms with certain desirable traits?

2. Do we use inbreeding and hybridization to genetically engineer our products? Are the organisms we produce considered to be transgenic organisms?

3. Are the products our company produces considered to be genetically enhanced or genetically modified?

4. How are the following used in the production of our products?

Recombinant DNA

Plasmid

Vector

Restriction enzyme

Genetic markers

Polymerase Chain Reaction (PCR)

Cloning

5. Our company produces several genetically modified organisms (GMOs). What are the benefits and risks of such products?

Benefits

Risks

KEY

BIOBUSINESS ELABORATION ACTIVITY

Students are provided a Board Meeting Agenda containing questions that need clarification before the upcoming stockholders' meeting. Discussing these questions related to genetic engineering will allow students an opportunity to use formal labels, definitions, and explanations.

BOARD MEETING AGENDA

ELABORATE

Items for discussion at today's meeting: Preparing for Acme Corporation acquisition
Acme Corporation is considering purchasing our company for an enormous sum of money, enough that we can all retire immediately! But before they will vote, the shareholders of Acme Corporation have some questions about genetic modification that require clarification. We will consider each question as an agenda item.

1. Our company produces products by genetic engineering. How does genetic engineering differ from selective breeding, which has been used for centuries to produce organisms with certain desirable traits?

Selective breeding consists of selecting desired traits and crossing organisms that have those traits, or selecting undesired traits and breeding to eliminate them. Genetic engineering, on the other hand, refers to the direct manipulation of an organism's genetic material (DNA) by introducing or eliminating specific genes. Selective breeding's disadvantages are that generations of breeding are required to effect significant change, and closely related organisms have to be bred, resulting in inbreeding.

2. Do we use inbreeding and hybridization to genetically engineer our products? Are the organisms we produce considered to be transgenic organisms?

No. Inbreeding means crossing two closely related organisms—in animals, mating can be done between siblings; in plants, inbreeding is done by self-pollination. After many generations, inbreeding can decrease health or fertility of each succeeding generation. Hybridization is combining germ cells and culturing them in a laboratory. Scientists broke the pollination barrier by combining germ cells and nurturing them in a tissue culture. All of our products are genetically engineered through manipulation of DNA. Our products are, however, considered to be transgenic, because they result in organisms with an added gene through genetic engineering that will pass that gene on to future generations.

3. Are the products our company produces considered to be genetically enhanced or genetically modified?

Both. Genetically enhancing or modifying an organism literally refers to a change in the genetic makeup of an organism. This can be accomplished by genetic engineering or traditional breeding schemes such as those used in agriculture.

4. How are the following used in the production of our products?

Recombinant DNA
genetically engineered DNA is prepared by transplanting or splicing cut segments of DNA. DNA enters cells by transformation process (electroporation, injection with needles, firing with gun)

Plasmid
circular piece of DNA from a bacterial cell

Vector
transports DNA; can be a virus or bacterial plasmid

Restriction enzyme
proteins produced by bacteria that cut DNA

Genetic markers
a known DNA sequence that lies close to the faulty gene or the gene or interest

Polymerase Chain Reaction PCR
invented by Cary Mullis; makes copies of a specific DNA sequence

Cloning
creates potentially endless copies of a single organism or parts of an organism

5. Our company produces several genetically modified organisms (GMOs). What are the benefits and risks of such products?

Benefits
increase crop yield, improve nutritional value, reduce pesticide use; potential uses include edible vaccines

Risks
potential allergic reactions; potential danger of eating foreign DNA; reduction in genetic diversity of crops; spread of antibiotic resistance markers; potential threat to non-targeted species; possible creation of "super weeds" if crops pollinate weeds and pass on GM herbicide resistance; Bt crops carry a gene that kills harmful insects but also may kill the Monarch butterfly

BIOBUSINESS EVALUATION ACTIVITY

In this activity, students will create a kind of "organizational chart" showing the steps of creating recombinant DNA.

EVALUATE

Instructions

Cut out the steps to creating recombinant DNA that are found on the following page (one set of steps for each student group).

Pass out an envelope containing the cut-up slips to each student group. Tell the students that it is their job to create massive amounts of insulin for medical purposes. The students are to put the steps in the order necessary to create massive amounts of insulin for medical use.

Results

Use the order of steps on the following page as a guide. However, the steps are not fixed; for example, step 3 can come before either step 2 or step 1, and step 7 occurs after both step 5 and 6. Use the discussion time to point out that more than one way of viewing the process can be correct.

Key Points:

- Have the students explain the steps and the following terms:
    - o Restriction enzyme (function)
    - o Plasmid (difference between plasmid and chromosomal DNA).

EVALUATION ACTIVITY

Cut out the following steps for use in the evaluation activity.
***Note, do not cut out the step numbers.*

1	A plasmid is isolated from a bacterial cell.
2	The plasmid is cut with a restriction enzyme.
3	The gene for making insulin is isolated from a human cell using a restriction enzyme.
4	The gene for making insulin is inserted into the plasmid.
5	The plasmid is inserted into a bacterial cell.
6	The bacterial cell clones itself, producing multiple copies of the recombinant plasmid.
7	The bacteria produce insulin.

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"BIOBUSINESS" IMPLEMENTATION PLAN — WET-LAB

Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Lab Preparation 4-5 days before lab (store in the refrigerator)	60 minutes	Prepare LB Agar plates LB Agar Hot water bath (hot plate and large 1000ml beaker) Ampicillin	**Purpose:** To introduce students to the concept of transformation as a method of genetic engineering and provide them with the opportunity to apply the methods in the laboratory **Objectives:** • To prepare agar plates for culturing bacteria • To apply the concept of a control • To carry out the appropriate procedure to transform *E. coli* using a plasmid • To record and analyze the results of the investigation **Essential Question:** How can we apply the process of genetic engineering in the laboratory?
Streak Starter Plates 1 day before the lab **Student Lab Briefing** Transformation Process: 1. Pre-incubation 2. Incubation 3. Heat Shock 4. Post-incubation/Recovery	15 minutes 20 minutes	Streak 6 Starter Plates 6 LB plates *E. coli* culture 6 Inoculating loops Incubator to incubate plates at 37 degrees C for 12-24 hours	
Actual Lab Day Colony Transformation Experiment	55 minutes	Set up for each workstation: 2 sterile 15 mL transformation tubes Vial of calcium chloride (on ice) 6 sterile 1 mL transfer pipettes 3 sterile inoculating loops 1 vial of sterile Luria broth Sterile cell spreader Beaker with 50 mL 95% ethanol, which should be kept covered Beaker of cracked ice Laboratory marker, masking tape Student instructions, data sheet 2 LB Plates and 2 LB+amp Plates Box of Tip for P200 and P20 P20 and P200 Pipettmen Clock or stopwatch Shared Workstation Plasmid DNA (on ice) Water bath at 42 degrees C Incubator set at 37 degrees C	

Alignment with NC Competency Goals

Biology

Goal 1 Objectives 1.01, 1.02, 1.03, 1.04, 1.05 Goal 2 Objectives 2.02	Goal 3 Objectives 3.01, 3.04 Goal 4 Objectives 4.01, 4.04

LAB BACKGROUND INFORMATION

Genetic transformation is used in many areas of biotechnology:

Agriculture: genes coding for traits such as frost-, pest-, or drought-resistance can be genetically transformed into plants

Bio-remediation: bacteria can be genetically transformed with genes enabling them to digest oil spills

Medicine: diseases caused by defective genes are beginning to be treated by gene therapy; gene therapy is genetically transforming a sick person's cells with healthy copies of the gene involved in their disease.

pGLO™ System

GFP (Green Fluorescent Protein) – real-life source of this gene is the bioluminescent jellyfish Aequorea Victoria.

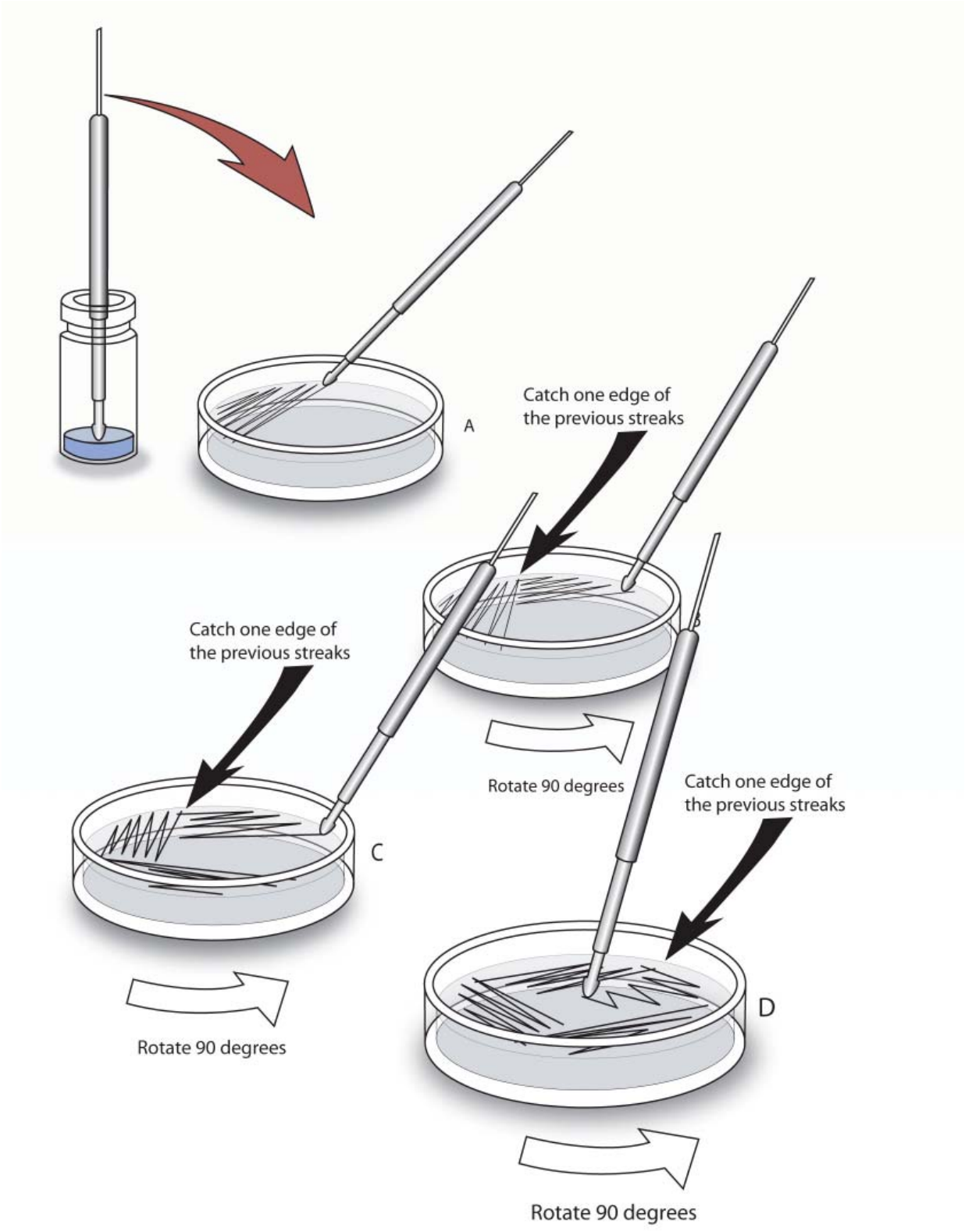
The pGLO™ plasmid encodes for the gene for GFP and a gene for resistance to the antibiotic ampicillin.

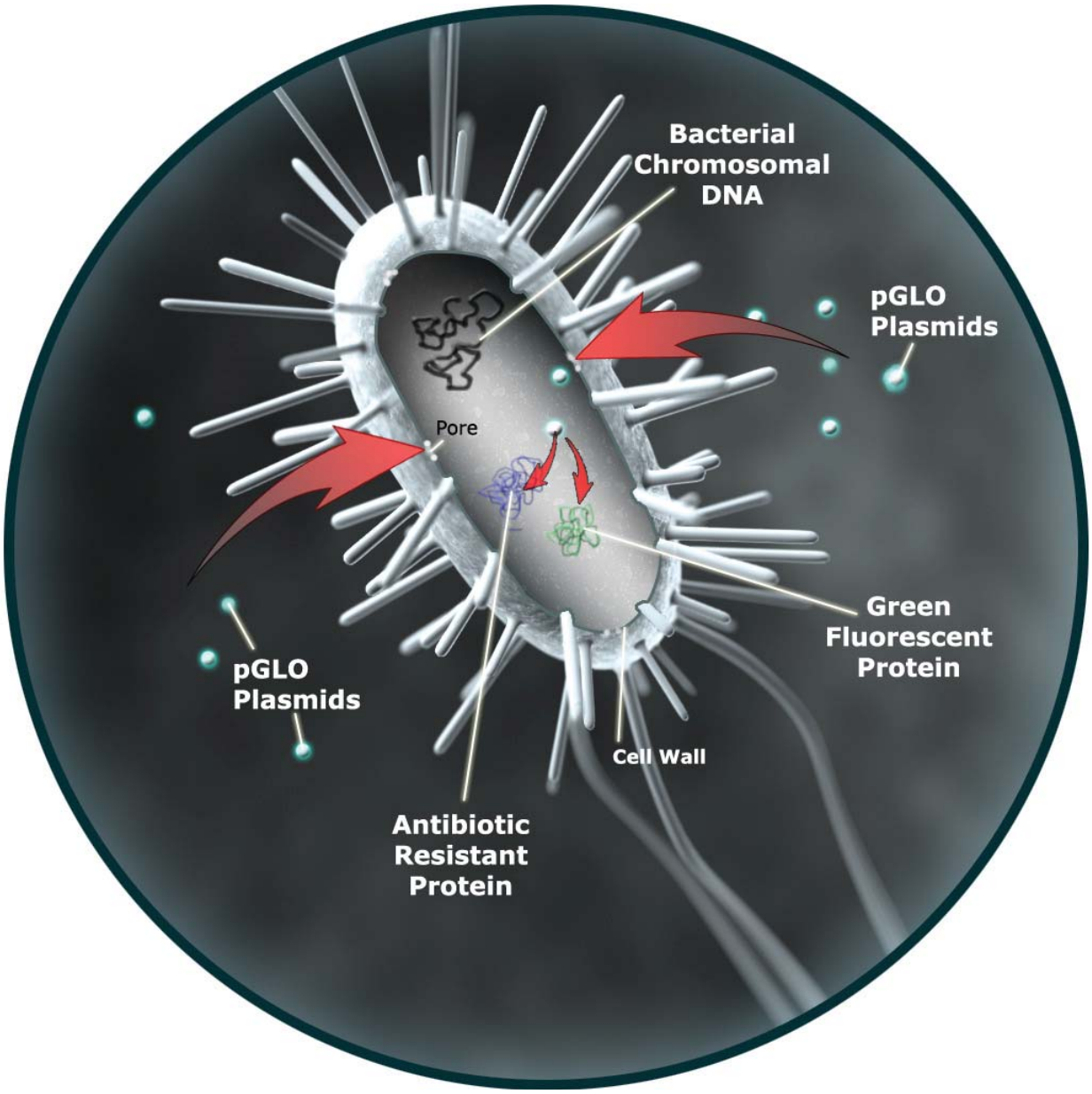
pGLO™ also incorporates a special gene regulation system that can be used to control expression of the fluorescent protein in transformed cells.

- The GFP can be switched on in transformed cells simply by adding the sugar arabinose to the cells' nutrient medium.

- Selection for cells that have been transformed with pGLO™ DNA is accomplished by growth on antibiotic plates. Transformed cells will appear white on plates not containing arabinose, and fluorescent green when arabinose is included in the nutrient agar.

STREAK STARTER PLATES TO PRODUCE SINGLE BACTERIAL COLONIES





Bacteria cell with pGLO plasmid

TRANSFORMATION KIT QUICK GUIDE

From Bio-Rad's pGLO Bacterial Transformation Kit Manual

1. Label one closed micro test tube +DNA and another -DNA. Label both tubes with your group's name. Place them in the foam tube rack.

2. Open the tubes and using a sterile transfer pipette, transfer 250 µl of Transformation Solution (CaCl2).

3. Place the tubes on ice.

4. Use a sterile loop to pick up one single colony of bacteria from your starter plate. Pick up the + DNA tube and immerse the loop into the Transformation Solution at the bottom of the tube. Spin the loop between your index finger and thumb until the entire colony is dispersed in the Transformation Solution (no floating chunks). Place the tube back in the tube rack in the ice. Using a new sterile loop, repeat for the -DNA tube.

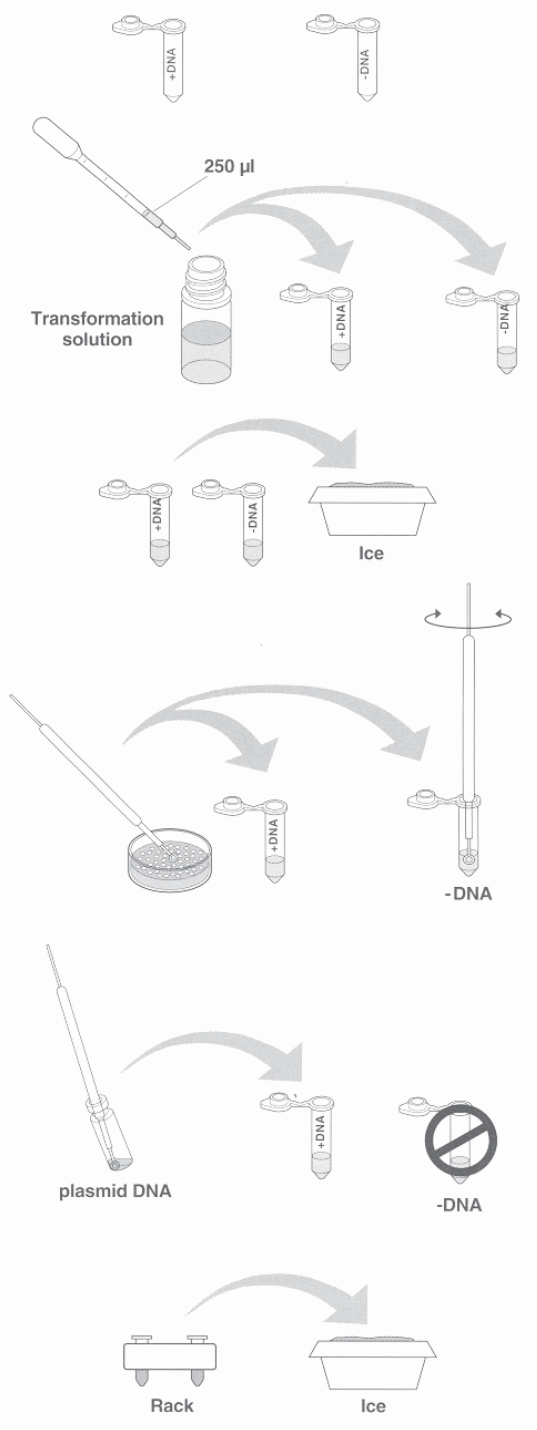
5. Examine the pGLO DNA solution with the UV lamp. Note your observations. Immerse a new sterile loop into the plasmid DNA stock tube. Withdraw a loop full. There should be a film of plasmid solution across the ring. This is similar to seeing a soapy film across a ring for blowing soap bubbles. Mix the loop full into the cell suspension of the + DNA tube. Close the tube and return it to the rack on ice. Also close the -DNA tube. Do not add plasmid DNA to the -DNA tube. Why not?

6. Incubate the tubes on ice for 10 minutes. Make sure to push the tubes all the way down in the rack so the bottom of the tubes stick out and make contact with the ice.

7. While the tubes are sitting on ice, label your four agar plates on the bottom (not the lid) as follows: Label one LB/amp plate: +DNA; Label the LB/amp/ara plate: +DNA. Label the other LB/amp plate: -DNA; Label the LB plate: -DNA.

8. Heat shock. Using the foam rack as a holder, transfer both the (+) and (-) tubes into the water bath set at 42 °C for exactly 50 seconds. Make sure to push the tubes all the way down in the rack so the bottom of the tubes stick out and make contact with the warm water. When the 50 seconds are done, place both tubes back on ice. For the best transformation results, the change from the ice (0 °C) to 42°C and then back to the ice must be rapid. Incubate tubes on ice for 2 minutes.

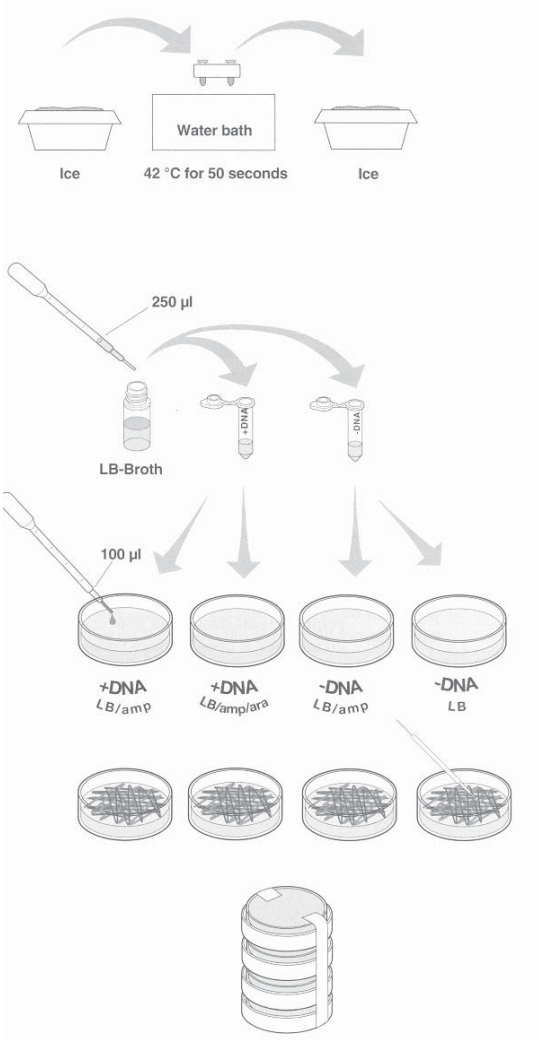
9. Remove the rack containing the tubes from the ice and place on the bench top. Open a tube and, using a new sterile pipette, add 250 µl of LB broth to the tube and re-close it. Repeat with a new sterile pipette for the other tube. Incubate the tubes for 10 minutes at room temperature.



10. Tap the closed tubes with your finger to mix. Using a new sterile pipette for each tube, pipette 100 µl of the transformation and control suspensions onto the appropriate plates.

11. Use a new sterile loop for each plate. Spread the suspensions evenly around the surface of the agar by quickly skating the flat surface of a new sterile loop back and forth across the plate surface.

12. Stack up your plates and tape them together. Put your group name and class period on bottom of the stack and place it upside down in the 37 °C incubator until the next day.



Steps in Bacterial Transformation

1. Pre-incubation

Cells are suspended in Ca+ and incubated at 0 degrees Celsius

2. Incubation

DNA is added to the cells and the mixture is incubated at 0 degrees Celsius

3. Heat Shock

The cells /DNA mixture is briefly incubated at 42 degrees Celsius, then returned to 0 degrees Celsius

4. Recovery

LB both is added to the DNA /cell suspension prior to plating on selective media

Name _____

BioBusiness Data Observation Sheet

1. Why did you label one tube "+" and the other "-"? What do the "+" and "-" indicate?

2. Why did we add the bacteria to the cold calcium chloride solution?

3. Why did we put bacteria in both tubes?

4. Why did we heat shock the bacteria and place them on ice?

5. Why did we add Luria broth (LB) to the tubes? Why did we change pipette tips before adding LB to the second tube?

Data Collection

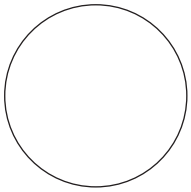
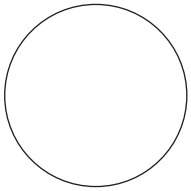
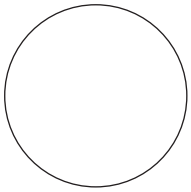
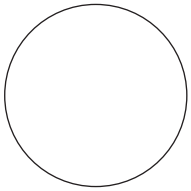
Observe the results you obtained from the transformation lab under normal room lighting. Then turn out the light and hold the UV lights over the plates.

1. Observe and draw what you see on each of the four plates carefully. Put your drawings in the data table in the column on the right. Record your data to allow you to compare observations of the "+ DNA" cells with those you record for the non-transformed E. coli Write down the following observations for each plate.

2. How much bacterial growth do you see on each, relatively speaking?

3. What color are the bacteria?

4. Count how many bacterial colonies there are on each plate (the spots you see).

		OBSERVATIONS
TRANSFORMATION PLATES	+pGLO LB/amp	
	+pGLO LB/amp/ara	
		OBSERVATIONS
CONTROL PLATES	-pGLO LB/amp	
	-pGLO LB	

Name _____

KEY

BioBusiness Data Observation Sheet

1. Why did you label one tube "+" and the other "-"? What do the "+" and "-" indicate?
   The "+" tube will receive the plasmid DNA; the "-" tube does not get the plasmid.

2. Why did we add the bacteria to the cold calcium chloride solution?
   Ca^{2+} cations of the transformation solution, pH 6.1, neutralize the repulsive negative charges of the phosphate backbone of the DNA and the phospholipid of the cell membrane, allowing DNA to enter the cell.

3. Why did we put bacteria in both tubes?
   The plus tube serves as the experiment and the minus tube serves as a control.

4. Why did we heat shock the bacteria and place them on ice?
   The rapid temperature change and the duration of the heat shock increase the bacterial uptake of the foreign DNA.

5. Why did we add Luria broth (LB) to the tubes? Why did we change pipette tips before adding LB to the second tube?
   The LB solution allows the cells to grow and express the foreign DNA if present.

Data Collection

KEY

Observe the results you obtained from the transformation lab under normal room lighting. Then turn out the light and hold the UV lights over the plates.

1. Observe and draw what you see on each of the four plates carefully. Put your drawings in the data table in the column on the right. Record your data to allow you to compare observations of the "+ DNA" cells with those you record for the non-transformed E. coli Write down the following observations for each plate.

2. How much bacterial growth do you see on each, relatively speaking?

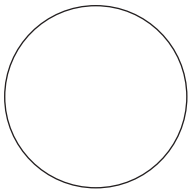
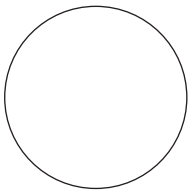
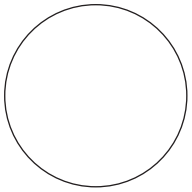
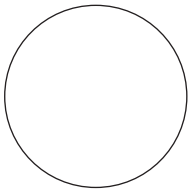
There should be multiple colonies on both the LB/amp and LB/amp/ara plates which received the pGLO™ plasmid (~ 75-300 colonies). There should be no growth on the LB/amp (-) DNA plate. There should be a lawn of bacteria on the LB (-) DNA plate.

3. What color are the bacteria?

The bacteria on the (+) DNA LB/amp plate and the (-) DNA LB plates should be whitish in color. The bacteria on the (+) DNA LB/amp/ara plate should appear whitish when exposed to normal, room lighting, but fluoresce green upon exposure to the UV light.

4. Count how many bacterial colonies there are on each plate (the spots you see).

There should be ~75-300 bacterial colonies on the two (+) DNA plates. The lawn of bacteria on the LB plate contains an even spread of bacteria and individual colonies can't be counted.

		OBSERVATIONS
TRANSFORMATION PLATES	+pGLO LB/amp	 Many transformed colonies of bacteria (~75-300). Colonies appear white.
	+pGLO LB/amp/ara	 Many transformed colonies of bacteria (~75-300). Colonies appear white when exposed to room light but fluoresce bright green when exposed to UV light.
		OBSERVATIONS
CONTROL PLATES	-pGLO LB/amp	 No bacterial growth present on this plate.
	-pGLO LB	 An even lawn of bacteria is present on this plate. The lawn appears an off-white color.

BioBusiness Equipment Needed						
Vendor	**Catalog Number**	**Item**	**Unit**	**Price**	**Minimum Purchase**	**TOTAL**
Bio-Rad	166-0500EDU	Long Wave UV Lamp	1	$28.00	4	$112.00
Bio-Rad	166-0603EDU	Mini Centrifuge	1	$260.00	1	$260.00
					EQUIPMENT TOTAL	**$372.00**
REQUIRED CONSUMABLES						
Bio-Rad	166-0003EDU	pGLO™ Bacterial transformation Kit	1	$65.00		$65.00
					CONSUMABLES TOTAL PER CLASS OF 24 STUDENTS/8 STUDENT GROUPS	**$65.00**
OPTIONAL EQUIPMENT						
Bio-Rad	166-0501EDU	Mini Incubation Oven	1	$295.00		
Bio-Rad	166-0504EDU	Water Bath	1	$505.00		
Carolina Biological	21-5570	Micro-Test tube Rack, Polypro-pylene	1	$4.00		
Bio-Rad	166-0709EDU	Rocking Platform	1	$575.00		
		Microwave Oven				

"BIOBUSINESS" IMPLEMENTATION PLAN — POST-LAB			
Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Use the transformation grids included in the Data Collection and Analysis section, to encourage students to analyze and discuss the results of their transformation experiment.	30 minutes	Copies of the Transformation Grids and questions Post-lab section of the teacher's notebook UV lamps, goggles Overhead transparencies: Transformation Grids	**Purpose:** To introduce students to the concepts of transformation as a method of genetic engineering and provide them with the opportunity to apply the method in the laboratory **Objectives:** • To apply the concepts of a control to an experiment • To record and analyze the results of the investigation **Essential Question:** What evidence indicates whether your attempt at performing a genetic transformation was successful or not successful?
Lesson 1 Focus Questions (from Bio-Rad's pGLO™ Bacterial Transformation Kit Manual)	10 minutes	Copies of focus questions	
Analysis of Wet-lab Results (From Bio-Rad's pGLO™ Bacterial Transformation Kit Manual)	10 minutes	Copies of student handout	
Video – Growth Industry and Activity – Bioethical Analysis Model	20 minutes 30 minutes	Video: 60 Minutes II Growth Industry and copies of the activity from the Post-lab section of the teacher's notebook	
BioBusiness Quiz Game	20 minutes	Quiz questions and answers from notebook, CD-ROM, or DESTINY web site: www.destiny.unc.edu	
Calculate Your Transformation Efficiency	30 minutes	Instructions for Calculating Transformation Efficiency found in Post-lab section of teacher's notebook	
You may also choose to select an activity from the "Additional Activities" or "Interdisciplinary Bridges" sections of your teacher's notebook. A variety of activities are included to meet the varying needs and learning styles of your students.			

Alignment with NC Competency Goals	
Biology	
Goal 1 Objectives 1.01, 1.02, 1.03, 1.04, 1.05 Goal 2 Objectives 2.02	Goal 3 Objectives 3.01, 3.04 Goal 4 Objectives 4.01, 4.04

Name _____

BioBusiness Data Observation Sheet

1. Why did you label one tube "+" and the other "-"? What do the "+" and "-" indicate?

2. Why did we add the bacteria to the cold calcium chloride solution?

3. Why did we put bacteria in both tubes?

4. Why did we heat shock the bacteria and place them on ice?

5. Why did we add Luria broth (LB) to the tubes? Why did we change pipette tips before adding LB to the second tube?

Data Collection

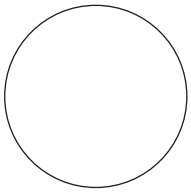
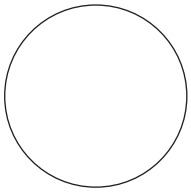
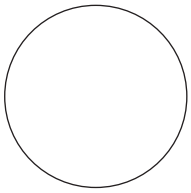
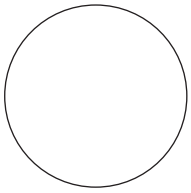
Observe the results you obtained from the transformation lab under normal room lighting. Then turn out the light and hold the UV lights over the plates.

1. Observe and draw what you see on each of the four plates carefully. Put your drawings in the data table in the column on the right. Record your data to allow you to compare observations of the "+ DNA" cells with those you record for the non-transformed E. coli Write down the following observations for each plate.

2. How much bacterial growth do you see on each, relatively speaking?

3. What color are the bacteria?

4. Count how many bacterial colonies there are on each plate (the spots you see).

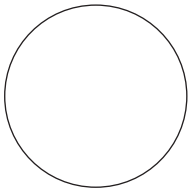
		OBSERVATIONS
TRANSFORMATION PLATES	+pGLO LB/amp	
	+pGLO LB/amp/ara	
		OBSERVATIONS
CONTROL PLATES	-pGLO LB/amp	
	-pGLO LB	

Transformation Grids

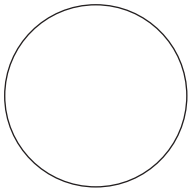
TRANSFORMATION PLATES

OBSERVATIONS

+pGLO
LB/amp



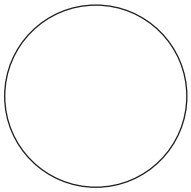
+pGLO
LB/amp/ara



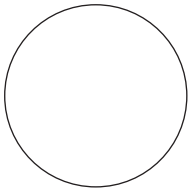
CONTROL PLATES

OBSERVATIONS

-pGLO
LB/amp



-pGLO
LB



Lesson 1 Focus Questions

From Bio-Rad's pGLO™ Bacterial Transformation Kit Manual

There are many considerations that need to be thought through in the process of planning a scientific laboratory investigation. Below are a few for you to ponder as you take on the challenge of doing a genetic transformation.

Since scientific laboratory investigations are designed to get information about a question, our first step might be to formulate a question for this investigation.

Consideration 1
Can I genetically transform an organism? Which organism?

1. To genetically transform an entire organism, you must insert the new gene(s) into every cell in the organism. Which organism is better suited for total genetic transformation—one composed of many cells, or one composed of a single cell?

2. Scientists often want to know if the genetically transformed organism can pass its new traits on to its offspring and future generations. To get this information, which would be a better candidate for your investigation, an organism in which each new generation develops and reproduces quickly, or one which does this more slowly?

3. Safety is another important consideration in choosing an experimental organism. What traits or characteristics should the organism have (or not have) to be sure it won't harm you or the environment?

4. Based on the above considerations, which would be the best choice for a genetic transformation: bacteria, earthworm, fish, or mouse? Describe your reasoning.

Teacher Answer Guide
Lesson 1 Focus Questions
From Bio-Rad's pGLO™ Bacterial Transformation Kit Manual

KEY

1. To genetically transform an entire organism, you must insert the new gene(s) into every cell in the organism. Which organism is better suited for total genetic transformation—one composed of many cells, or one composed of a single cell?

A single-celled organism would be the best recipient for a genetic transformation, because it contains only one cell which needs to take up the new gene.

2. Scientists often want to know if the genetically transformed organism can pass its new traits on to its offspring and future generations. To get this information, which would be a better candidate for your investigation, an organism in which each new generation develops and reproduces quickly, or one which does this more slowly?

An organism which reproduces quickly. Fast production of offspring or new progeny will allow you to quickly assess if the new trait has been passed on.

3. Safety is another important consideration in choosing an experimental organism. What traits or characteristics should the organism have (or not have) to be sure it won't harm you or the environment?

The organism should not produce any toxins or compounds which could make people sick. The organism should grow vigorously in the lab environment, but should not be able to survive outside the laboratory. The organism should not be able to infect plants or animals.

4. Based on the above considerations, which would be the best choice for a genetic transformation: bacteria, earthworm, fish, or mouse? Describe your reasoning.

Bacteria would be the best host organism. Bacteria are small, single-celled organisms which reproduce quickly and easily.

Note: The bacteria Escherichia coli (E. coli), strain HBIOl;K-12, best fits the requirements described above: it is made of only one cell, it reproduces every 20 minutes, it doesn't make people sick, and it can't survive outside the laboratory.

Analysis of the Results

1. Which of the traits that you originally observed for E. coli did not seem to become altered? In the space below list these non-transformed traits and how you arrived at this analysis for each trait listed.

2. Of the E. coli traits you originally noted, which seem now to be significantly different after performing the transformation procedure? List those traits below and describe the changes that you observed.

3. If the genetically transformed cells have acquired the ability to live in the presence of the antibiotic ampicillin, then what can be inferred about the other genes on the plasmid that were involved in your transformation procedure?

4. From the results that you obtained, how could you prove that these changes that occurred were due to the procedure that you performed?

Teacher Answer Guide

KEY

Analysis of the Results

1. Which of the traits that you originally observed for E. coli did not seem to become altered? In the space below list these non-transformed traits and how you arrived at this analysis for each trait listed.

Original trait	Analysis of observations
Color	Bacteria are a whitish color
Colony size	Colony size is similar both before and after transformation

2. Of the E. coli traits you originally noted, which seem now to be significantly different after performing the transformation procedure? List those traits below and describe the changes that you observed.

New trait	Observed change
Color	The colonies on the LB/amp/ara plate fluoresce green under UV light
Ampicillin resistance	The transformed colonies can grow on ampicillin

3. If the genetically transformed cells have acquired the ability to live in the presence of the antibiotic ampicillin, then what can be inferred about the other genes on the plasmid that were involved in your transformation procedure?

The plasmid must express a gene for ampicillin resistance (the protein product of the bla gene codes for beta-lactamase, the protein that breaks down ampicillin).

4. From the results that you obtained, how could you prove that these changes that occurred were due to the procedure that you performed?

The best way is to compare the control to the experimental plates. Cells that were not treated with the plasmid ((-) DNA and LB/amp plate) could not grow on ampicillin, whereas cells that were treated with the plasmid ((+) DNA) can grow on the LB/amp plate. Thus, the plasmid must confer resistance to ampicillin.

Name _____

60 MINUTES II VIDEO: *GROWTH INDUSTRY*

Bioethical Analysis Model

Using the model below analyze the video Growth Industry as a bioethical issue. Determine the goals, rights, and responsibilities of each individual or group of individuals listed.

	Goals	Rights	Responsibilities
Michael Finley			
Eli Lilly Drug Company Distributors of GH Humatrop			
Michael's Coach			
Michael & Lee Finley			
Dr. Dana Harden			
Michael's classmates			
Insurance Company			

1. Where do major conflicts exist in the goals, rights and responsibilities for Michael, the Finley's, the drug company, Michael's coach, classmates and Dr. Harden.?

2. Should Michael be given the growth hormone? What is the justification for your position?

3. Is Michael handicapped?

Teacher Answer Guide

KEY

60 Minutes II Video: Growth Industry

Bioethical Analysis Model

There are no right and wrong answers for the goals, rights, and responsibilities of the main stakeholders in the video. Students may have varying responses; the point is for them to think of the events in the video analytically within a bioethical framework.

There is no "correct" answer to Michael's dilemma. It is important that students understand that they will be faced with many such issues as progress continues to be made in science and technology.

For question 3, "Is Michael handicapped?", students should respond negatively. Michael is not handicapped; he is in the normal height range.

BioBusiness Quiz Game Questions

	Genetic Code	DNA and Such	Bio-Business	Genetic Transformation	Key Terms	Hodge Podge
200	Fact or fiction? 99.9% of a person's DNA is identical to everyone else's DNA.	Fact or fiction? No two people have identical DNA.	When placing bacteria colonies into pink and blue microtubes, why was one tube labeled + and one labeled - ?	Fact or fiction? Genetic Transformation is a brand new technique, and it does not have any "real world" applications yet.	What is Golden Rice?	What is the name of the circular bacterial DNA that is used to transfer a gene into a bacterium?
400	Fact or fiction? A person's muscle cell and a person's nerve cell are genetically identical.	How many chromosomes do humans have?	What was the purpose of adding bacteria to the cold calcium chloride solution?	Define Transformation.	What is the term for a sequence of DNA that codes for a protein and determines a trait?	What piece of equipment was used in the wet-lab to measure out very small quantities of liquid?
600	What are the four nucleotides that make up DNA, and which nucleotides pair up?	What is a restriction enzyme used for?	What purpose did heat shock and ice treatment serve in the wet-lab?	Explain one way genetic transformation might be used in agriculture.	Define recombinant DNA.	When a restriction enzyme cuts DNA it leaves one of two types of end where the cut took place. Name these two types of ends, and define them.
800	Give the nucleotide sequence that would complement this strand of DNA: CTTGACTTGGACC.	What is meant when someone refers to the "Blueprint of Life"?	What effect did adding the recombinant plasmid with pGLO™ have on the bacteria?	Explain the process of using bacteria to produce insulin.	What is a genetic marker?	In the wet-lab, what effect does adding arabinose to agar plates have on the bacteria?
1000	What does DNA stand for, and why is it important?	Explain how DNA codes for a trait.	Explain whether or not bacteria colonies appeared and if they glowed under UV light in each of the following agar plates: +DNA/LB/amp; +DNA/LB/amp/ara; -DNA/LB/amp/; -DNA/LB.	In the wet-lab, E. coli bacteria was transformed. Give 3 reasons why E. coli is an ideal candidate for transformation.	Define genetic engineering.	In the wet-lab, some bacteria were placed on agar plates containing ampicillin. What is ampicillin and what does it do?

BioBusiness Quiz Game Answers

KEY

	Genetic Code	DNA and Such	Bio-Business	Transformation	Key Terms	Hodge Podge
200	Fact. It is the 0.1% of our DNA that makes us genetically unique.	Fiction. Identical twins have identical DNA.	The tube labeled + would eventually get the plasmid with pGLO™, and the tube labeled – would not.	Fiction: Transformation has been widely used in medicine, biotechnology, and agriculture (for example, to make drought, frost, or pest resistant crops); to produce insulin for diabetics; etc.	Golden rice is genetically engineered rice containing the genes from a petunia and a bacterium which produce provitamin A (beta carotene).	plasmid
400	Fact. The cells are genetically identical, but what makes them unique are the particular genes that are expressed in each.	Humans have 46 chromosomes (23 pairs).	The calcium chloride solution neutralized the plasmid DNA, allowing it to penetrate the cell.	Transfer of DNA from one organism to another, often using a carrier called a vector (such as a plasmid, virus, or other form of mobile DNA)	Gene	Digital micropipette (micropipette is also acceptable)
600	Adenine, Guanine, Cytosine, Thymine; Adenine pairs with Thymine; Guanine pairs with Cytosine.	Restriction enzymes cut the DNA strands at very specific sites.	Heat shock and ice treatment made the cell membrane more permeable to the plasmid DNA.	Answers will vary. Example: A gene for disease resistance may be transferred to corn or another crop to yield a healthier plant.	Recombinant DNA is DNA produced by combining DNA from multiple sources.	1) Blunt ends- The 2 strands of DNA are even; 2) Sticky ends- The 2 strands of DNA are uneven
800	The nucleotide sequence of the complement strand would read: GAACTGAACCTGG	"The blueprint of life" refers to the set of genes encoded by an individual's DNA. DNA serves as a blueprint because it contains a set of instructions used to make proteins, just as blueprints are a set of instructions used to build a house.	It made the bacteria resistant to ampicillin and made it glow in the presence of arabinose.	A plasmid is isolated from a bacterial cell and cut with a restriction enzyme; the gene for making insulin is cut from a human cell with the same restriction enzyme; the gene for making insulin is inserted into the plasmid; the plasmid is inserted into a bacterial cell; the bacteria clones itself; and original and cloned bacteria produce insulin.	A Genetic Marker is a gene that makes it possible to distinguish bacteria that carry a plasmid with foreign DNA from those that do not.	The arabinose was metabolized by bacteria, and in the presence of arabinose, the pGLO™ gene was activated, causing colonies to glow under UV light.
1000	Deoxyribonucleic Acid. DNA is important because it acts as the blueprint for all living organisms. In humans, DNA codes for everything that we are genetically – how tall we will be, what color hair and eyes we will have, etc.	When a gene is activated, DNA is read and a complement strand of mRNA is created. That mRNA strand is then read, and amino acids are produced. Those amino acids form chains that form proteins. One or multiple proteins are what give people traits.	+DNA/LB/amp produced colonies that did not glow; +DNA/LB/amp/ara produced colonies that glowed; -DNA/LB/amp produced no colonies; -DNA/LB produced colonies that did not glow.	E. coli is an ideal candidate for transformation because: 1) It's unicellular, ideal since the new gene must be inserted into every cell of an organism; 2) It reproduces every 20 minutes, allowing us to see if the new gene was passed on to offspring; 3) It doesn't make people sick and can't survive outside the lab.	Genetic Engineering is the process of making changes in the DNA code of living organisms; genetic engineering is an umbrella term for any process or procedure that adds, alters, replaces, augments or silences a gene or its expression in an organism.	Ampicillin is an antibiotic, which kills bacteria.

Calculate Transformation Efficiency

From Bio-Rad's pGLO™ Bacterial Transformation Kit Manual

Your next task in this investigation will be to learn how to determine the extent to which you genetically transformed E. coli cells. This quantitative number is referred to as the transformation efficiency.

In many experiments, it is important to genetically transform as many cells as possible. For example, in some types of gene therapy, cells are collected from the patient, transformed in the lab, and then put back into the patient. The more cells that are transformed to produce the needed protein, the more likely it is that the therapy will work. A number called transformation efficiency is calculated to help scientists determine how well the transformation is working.

The Task

You are about to engage in calculating the transformation efficiency from the information you collected in the laboratory procedure. Transformation efficiency gives you an indication of how effective you were in getting DNA molecules into a colony of bacterial cells. Transformation efficiency is a number. It represents the total number of bacterial cells that express the green protein divided by the amount of DNA used in the experiment. (It tells us the total number of bacterial cells transformed by one microgram of DNA.) In formula terms this can be symbolized as:

$$\text{Transformation efficiency} = \frac{\text{Total number of cells growing on the agar plate}}{\text{Amount of DNA spread on the agar plate}}$$

Therefore, before you can calculate the efficiency of your transformation, you will need two pieces of information:

(1) The total number of green fluorescent colonies growing on your LB/amp/ara plate.

(2) The total amount of DNA (pGLO™) in the bacterial cells spread on the LB/amp/ara plate.

1. Determining the Total Number of Green Fluorescent Cells

Place your LB/amp/ara plate near a UV light source. Each colony on the plate can be assumed to be derived from a single cell. As individual cells reproduce, more and more cells are formed and develop into what is termed a colony. The most direct way to determine the total number of green fluorescent cells is to count the colonies on the plate.

Enter that number here → | Total number of cells = _____

2. Determining the Amount of DNA (pGLO™) in the Bacterial Cells Spread on the LB/amp/ara Plate

We need two pieces of information to find out the amount of DNA (pGLO™) in the bacterial cells spread on the LB/amp/ara plate in this experiment. (a) What was the total amount of DNA we began the experiment with, and (b) What fraction of DNA (in the bacteria) actually got spread onto the LB/amp/ara plates.

Once you calculate this data, you will need to multiply the total amount of DNA used in this experiment by the **fraction of DNA** you spread on the LB/amp/ara plate. The answer to this multiplication will tell you the amount of DNA (pGLO™) in the bacterial cells that was spread on the LB/amp/ara plate.

a. Determining the total amount of DNA

The total amount of DNA we began with is equal to the product of the concentration and the total volume used, or

DNA(µg) = (concentration of DNA) x (volume of DNA µl)

In this experiment you used 10 µl of pGLO™ at concentration of 0.03 µg/µl. This means that each microliter of solution contained 0.03 µg of pGLO™ DNA. Calculate the total amount of DNA used in this experiment.

Enter that number here → | Total amount of DNA (µg) used in this experiment = _____

• How will you use this piece of information?

b. Determining the fraction of DNA (in the bacteria) that actually got spread onto the LB/amp/ara plate

Since not all the DNA you added to the bacterial cells will be transferred to the agar plate, you need to find out what fraction of the DNA was actually spread onto the LB/amp/ara plate. To do this, divide the volume of DNA you spread on the LB/amp/ara plate by the total volume of liquid in the test tube containing the DNA. A formula for this statement is

$$\text{Fraction of DNA used} = \frac{\text{Volume spread on LB/amp plate}}{\text{Total sample volume in test tube}}$$

You spread 100 µl of cells containing DNA from a test tube containing a total volume of 510 µl of solution. Do you remember why there is 510 µl total solution? Look in the laboratory procedure and locate all the steps where you added liquid to the reaction tube. Add the volumes.

Use the above formula to calculate the **fraction of DNA** you spread on the LB/amp/ara plate.

Enter that number here →

Fraction of DNA =   _____

• How will you use this piece of information?

So, how many micrograms of DNA did you spread on the LB/amp/ara plates?

To answer this question, you will need to multiply the **total amount of DNA** used in this experiment by the **fraction of DNA** you spread on the LB/amp/ara plate.

pGLO™ DNA spread (µg) = Total amount of DNA used (µg) x fraction of DNA

Enter that number here →

pGLO™ DNA spread (µg) =   _____

• What will this number tell you?

Look at all your calculations above. Decide which of the numbers you calculated belong in the table below. Fill in the following table.

Number of colonies on LB/amp/ara plate =	
Micrograms of pGLO DNA spread on the plates	

Now use the data in the table to calculate the efficiency of the pGLO transformation efficiency

$$\text{Transformation efficiency} = \frac{\text{Total number of cells growing on the agar plate}}{\text{Amount of DNA spread on the agar plate}}$$

Enter that number here →

Transformation efficiency =   _____ transformants/µg

Analysis

Transformation efficiency calculations result in very large numbers. Scientists often use a mathematical shorthand referred to as scientific notation. For example, if the calculated transformation efficiency is 1,000 bacteria/µg of DNA, they often report this number as:

10^3 transformants/µg (10^3 is another way of saying 10 x 10 x 10 or 1,000)

• How would scientists report 10,000 transformants/µg in scientific notation?

Carrying this idea a little farther, suppose scientists calculated an efficiency of 5,000 bacteria/µg of DNA. This would be reported as:

5.0 x 10^3 transformants/µg (1,000 times 5)

• How would scientists report 40,000 transformants/µg in scientific notation?

One final example: If 2,600 transformants/µg were calculated, then the scientific notation for this number would be:

2.6 x 10^3 transformants/µg (1,000 times 2.6)

Similarly:

5,600 = 5.6 x 10^3 271,000 = 2.71 x 10^5 2,420,000 2.42 x 10^6

- How would scientists report 960,000 transformants/µg in scientific notation?
- Report your calculated transformation efficiency in scientific notation.
- Use a sentence or two to explain what your calculation of transformation efficiency means.

Biotechnologists are in general agreement that the transformation protocol that you have just completed generally has a transformation efficiency of between 8.01 x 102 and 7.0 x 103 transformants per microgram of DNA.

- How does your transformation efficiency compare with the above?
- In the table below, report the transformation efficiency of several of the teams in the class.

Team	Efficiency

• How does your transformation efficiency compare with theirs?

• Calculate the transformation efficiency of the following experiment using the information and the results listed below.

0.08 µg/µl DNA plasmid concentration

250 µl $CaCl_2$ transformation buffer

10 µl plasmid solution

250 µl LB broth

100 µl cells spread on agar

227 colonies of transformants counted

Fill in the following chart and show your calculations to your teacher:

Number of colonies on LB/amp/ara plate =	
Micrograms of pGLO DNA spread on the plates	
Transformation efficiency =	

• Extra Credit Challenge:

If a particular experiment was known to have a transformation efficiency of 3×10^3 bacteria/µg of DNA, how many transformant colonies would be expected to grow on the LB/amp/ara plate? You can assume that the concentration of DNA and fraction of cells spread on the LB agar are the same as for the pGLO lab.

Teacher Answer Key
Calculating Transformation Efficiency

KEY

1. Determining the Total Number of Green Fluorescent Cells

Place your LB/amp/ara plate near a UV light source. Each colony on the plate can be assumed to be derived from a single cell. As individual cells reproduce, more and more cells are formed and develop into what is termed a colony. The most direct way to determine the total number of green fluorescent cells is to count the colonies on the plate.

Enter that number here → Total number of cells = 190

2. Determining the Amount of DNA (pGLO) in the Bacterial Cells Spread on the LB/amp/ara Plate

We need two pieces of information to find out the amount of DNA (pGLO) in the bacterial cells spread on the LB/amp/ara plate in this experiment. (a) What was the total amount of DNA we began the experiment with, and (b) What fraction of DNA (in the bacteria) actually got spread onto the LB/amp/ara plates.

Once you calculate this data, you will need to multiply the total amount of DNA used in this experiment by the **fraction of DNA** you spread on the LB/amp/ara plate. The answer to this multiplication will tell you the amount of DNA (pGLO) in the bacterial cells that was spread on the LB/amp/ara plate.

a. Determining the total amount of DNA

The total amount of DNA we began with is equal to the product of the concentration and the total volume used, or

DNA(µg) = (concentration of DNA) x (volume of DNA µl)

In this experiment you used 10 µl of pGLO at concentration of 0.03 µg/µl. This means that each microliter of solution contained 0.03 µg of pGLO DNA. Calculate the total amount of DNA used in this experiment.

Enter that number here → Total amount of DNA (µg) used in this experiment = 0.3

• How will you use this piece of information?
This number will be multiplied by the fraction of DNA used to determine the total amount of DNA spread on the agar plate.

b. Determining the fraction of DNA (in the bacteria) that actually got spread onto the LB/amp/ara plate

Since not all the DNA you added to the bacterial cells will be transferred to the agar plate, you need to find out what fraction of the DNA was actually spread onto the LB/amp/ara plate. To do this, divide the volume of DNA you spread on the LB/amp/ara plate by the total volume of liquid in the test tube containing the DNA. A formula for this statement is

$$\text{Fraction of DNA used} = \frac{\text{Volume spread on LB/amp plate}}{\text{Total sample volume in test tube}}$$

You spread 100 µl of cells containing DNA from a test tube containing a total volume of 510 µl of solution. Do you remember why there is 510 µl total solution? Look in the laboratory procedure and locate all the steps where you added liquid to the reaction tube. Add the volumes.

Use the above formula to calculate the **fraction of DNA** you spread on the LB/amp/ara plate.

Enter that number here →

Fraction of DNA =

0.2

• How will you use this piece of information?

This number will be multiplied by the amount of DNA used to calculate the amount of DNA spread on an agar plate.

So, how many micrograms of DNA did you spread on the LB/amp/ara plates?

To answer this question, you will need to multiply the **total amount of DNA** used in this experiment by the **fraction of DNA** you spread on the LB/amp/ara plate.

pGLO DNA spread (µg) = Total amount of DNA used (µg) x fraction of DNA

Enter that number here →

pGLO DNA spread (µg) =

0.06

• What will this number tell you?

This number tells you how much DNA was spread on the agar plate.

Look at all your calculations above. Decide which of the numbers you calculated belong in the table below. Fill in the following table.

Number of colonies on LB/amp/ara plate =	190
Micrograms of pGLO DNA spread on the plates	0.06µg

Now use the data in the table to calculate the efficiency of the pGLO transformation efficiency

Transformation efficiency = $\frac{\text{Total number of cells growing on the agar plate}}{\text{Amount of DNA spread on the agar plate}}$

Enter that number here →

Transformation efficiency =

3.166 transformants/µg

Analysis

Transformation efficiency calculations result in very large numbers. Scientists often use a mathematical shorthand referred to as scientific notation. For example, if the calculated transformation efficiency is 1,000 bacteria/µg of DNA, they often report this number as:

10^3 transformants/µg (10^3 is another way of saying 10 x 10 x 10 or 1,000)

- How would scientists report 10,000 transformants/µg in scientific notation?
  104

Carrying this idea a little farther, suppose scientists calculated an efficiency of 5,000 bacteria/µg of DNA. This would be reported as:

5.0 x 10^3 transformants/µg (1,000 times 5)

- How would scientists report 40,000 transformants/µg in scientific notation?
  4.0 x 104

One final example: If 2,600 transformants/µg were calculated, then the scientific notation for this number would be:

2.6 x 10^3 transformants/µg (1,000 times 2.6)

Similarly:

5,600 = 5.6 x 10^3 271,000 = 2.71 x 10^5 2,420,000 2.42 x 10^6

- How would scientists report 960,000 transformants/µg in scientific notation?
  9.6 x 105

- Report your calculated transformation efficiency in scientific notation.
  3.2 x 103

- Use a sentence or two to explain what your calculation of transformation efficiency means.
  Transformation efficiency is a quantitative number which describes how effective you were at getting a plasmid into bacteria. The number represents the number of transformed colonies produced per microgram of DNA added.

Biotechnologists are in general agreement that the transformation protocol that you have just completed generally has a transformation efficiency of between 8.01 x 102 and 7.0 x 103 transformants per microgram of DNA.

- How does your transformation efficiency compare with the above?
  The calculated efficiency (3.2 x 103) is within the predicted limits of efficiency for this protocol.

- In the table below, report the transformation efficiency of several of the teams in the class.

Team	**Efficiency**
Answers will vary.	

• How does your transformation efficiency compare with theirs?
Answers will vary.

• Calculate the transformation efficiency of the following experiment using the information and the results listed below.

0.08 µg/µl DNA plasmid concentration

250 µl $CaCl_2$ transformation buffer

10 µl plasmid solution

250 µl LB broth

100 µl cells spread on agar

227 colonies of transformants counted

Fill in the following chart and show your calculations to your teacher:

Number of colonies on LB/amp/ara plate =	227
Micrograms of pGLO DNA spread on the plates	0.06
Transformation efficiency =	3.8×10^3

• Extra Credit Challenge:

If a particular experiment was known to have a transformation efficiency of 3×10^3 bacteria/µg of DNA, how many transformant colonies would be expected to grow on the LB/amp/ara plate? You can assume that the concentration of DNA and fraction of cells spread on the LB agar are the same as for the pGLO lab.

Transformation efficiency = # colonies/DNA spread on plate (µg)

3.0 x 103 = X/0.06

(3.0 x 103)(0.06) = X

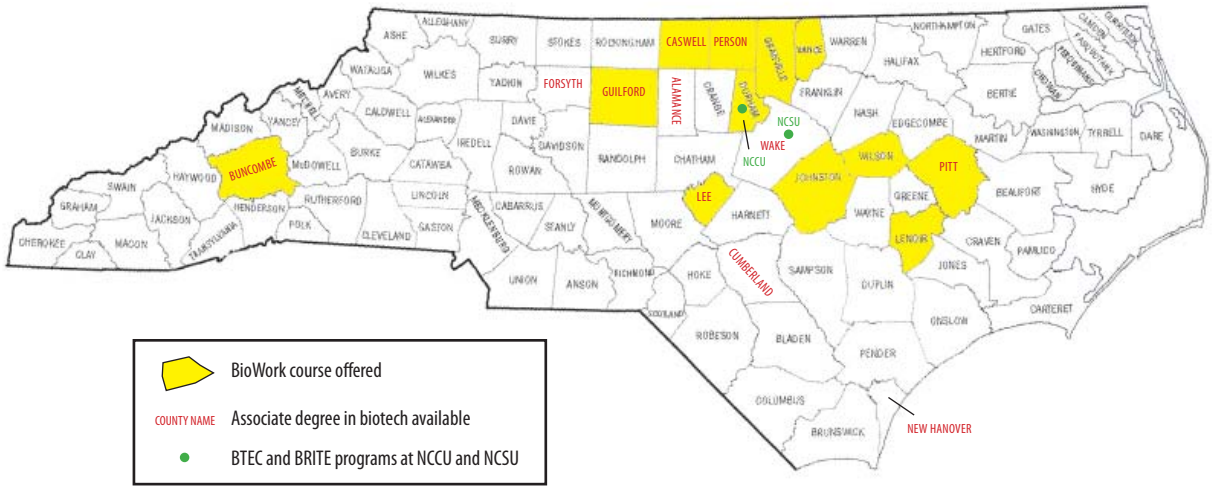
180 = X

180 transformant colonies

"BIOBUSINESS" IMPLEMENTATION PLAN — ADDITIONAL ACTIVITIES				
Activity	Estimated Time	Materials/Equipment	Other Subjects Covered	Suggestions
Biotechnology Careers Brochure on a Biotech Career and Additional Career Resources	1 hour	Instructions and scoring rubric; BPTC handout, paper and materials for brochure construction	Writing	Compile finished brochures in a biotech "career center"
Critical Analysis of a Bioethical Issue: Human Growth Hormone	30 minutes	Copies of activity	Social studies, English	
Biotechnology Stock Activity	Intermittent over a 9 week period	Internet access, newspapers, copies of activity	Math, Social Studies, Technology	
Lab: Genetically Modified Soybeans vs. Traditional Soybeans	30 minutes + 10 minutes every other day for 22 days	Soybeans, planters, soil, herbicide, weed or mustard seeds (or kit from Carolina Biological), copies of activity	Technology	
Bioprocessing: Using Yeast Fermentation to Make Root Beer	25 minutes prep; 2 weeks fermentation (60 minute optional activity)	2-liter bottles, baker's yeast, spring water, root beer extract, large bowls, funnels, mixing spoons, granulated sugar, measuring cups, measuring spoons, masking tape	Food science, Chemistry, Math	
Timeline Activity for Biotechnology	45-60 minutes (plus additional research time)	Copies of activity	Social studies, English, Math, Technology	Have students conduct research as homework assignment
Write a paper on how genetic engineering has affected you personally now and what impact genetic engineering may have on you by your fifteenth class reunion.	1 hour	Internet access	English, Writing	Possible homework/ Enrichment
Make a poster or some other "advertisement" which convincingly announces your position on a bioethical issue.	1 hour	Internet access, Poster board, markers	Creative expression	Possible homework/ Enrichment

Additional Resources:
Links on Biotech Topics, in Additional Activities section of teacher's notebook
www.nhgri.nih.gov/educationkit/
http://vector.cshl.org/dnaftb/
http://www.pbs.org/wgbh/harvest/ -- "Harvest of Fear: Exploring the Growing Fight over Genetically Modified Foods" – includes teacher guide, online video and activities
Your World Biotechnology & You (A magazine of biotechnology applications in healthcare, agriculture, the environment, and industry)

BIOTECHNOLOGY TRAINING OPPORTUNITIES IN NORTH CAROLINA: THE BIOMANUFACTURING AND PHARMACEUTICAL TRAINING CONSORTIUM



Once your students are excited about biotechnology after researching and preparing a brochure on a career in the field, you can provide them with more career information by helping them find opportunities for training and education in biotechnology across North Carolina.

The Biomanufacturing and Pharmaceutical Training Consortium (BPTC) is a collaboration among the University of North Carolina system, the North Carolina Community College system, the North Carolina Bioscience Organization (representing industry), and the North Carolina Biotechnology Center. North Carolina's Golden LEAF Foundation has provided $60 million in initial costs for the BPTC, and industry has donated over $5 million in equipment and services to support the venture. Members of the consortium are collaborating to create targeted programs that will provide education and training at all levels in biotechnology, life sciences, chemistry, engineering, and applied science degree programs.

North Carolina State University's Biomanufacturing Training and Education Center (BTEC)

The BTEC will be a bioprocessing pilot plant located on NCSU's Centennial Campus that will offer hands-on training in cell-culture, fermentation, purification, quality control, and much more. It will have components for community college, university, and graduate students as well as industry employees and college faculty. Its distance-learning component will enable a broad outreach. (Scheduled to open in 2006)

North Carolina Central University's Biomanufacturing Research Institute and Technology Enterprise (BRITE)

BRITE will offer both undergraduate and graduate degrees in programs related to biomanufacturing and process development. A new building will provide laboratories and classrooms for biotechnology and biomanufacturing research. (Scheduled to open in 2007)

BioNetwork

Through a statewide initiative, working in conjunction with the North Carolina Community College System, the state has developed six centers for specialty training in biotechnology, including concentrations such as BioBusiness, BioEd, and BioAg. Additionally, the BioNetwork has developed a specialized course called BioWork and features a dozen community colleges offering associate degrees in biotechnology-related subjects.

BioWork Course

This 128-hour course provides an introduction to manufacturing technology and science fundamentals, preparing students for entry-level positions in pharmaceutical and chemical manufacturing as well as biotechnology. Students learn about quality systems, safety management, and team problem-solving. For more details, refer students to the NCCCS BioNetwork site at http://www.ncbionetwork.org.

This course is currently offered at the following North Carolina community colleges:

Asheville-Buncombe Technical Community College
Central CaCommunity College
Durham Technical Community College
Guilford Technical Community College
Johnston Community College
Lenoir Community College
Piedmont Community College
Pitt Community College
Vance-Granville Community College
Wilson Technical Community College

Associate in Applied Science Degree

Programs leading to a degree in Applied Science include specializations in biotechnology, bioprocess technology, chemical process technology, industrial pharmaceutical technology, and nanotechnology. These programs vary by county; for detailed information, refer students to the NCCCS BioNetwork site at http://www.ncbionetwork.org.

Degrees are currently offered at the following North Carolina community colleges:

Alamance Community College
Asheville-Buncombe Technical Community College
Cape Fear Community College
Central Carolina Community College
Fayetteville Technical Community College
Forsyth Technical Community College
Guilford Technical Community College
Piedmont Community College
Pitt Community College
Wake Technical Community College

BROCHURE ON A BIOTECH CAREER

Assignment:

Construct a brochure describing a specific career in the biotechnology industry. The following items should be addressed in your brochure: education needed to perform the job, salary, job description/daily responsibilities, working conditions, chances for advancement, classes offered at your high school that would be beneficial to students wishing to pursue this career, and type of biotechnology company hiring for the job.

SCORING RUBRIC

1 - Criterion: Quality of Research				
1	2	3	4	5
1 source		3 sources		5 sources
2 - Criterion: Question and Answer				
1	2	3	4	5
Many factual errors		Some factual errors		No factual errors
3 - Criterion: Graphics				
1	2	3	4	5
No Graphics		Graphics that describe the career		Graphics that instruct as well as dazzle!
4 - Criterion: Organization				
1	2	3	4	5
Little evidence of design and planning		Some evidence of design and planning		Strong evidence of design and planning
5 - Criterion: Oral Presentation				
1	2	3	4	5
Did little to describe career		Explained career adequately		Grabbed everyone's attention

Consider these career fields:

Biotechnology's impact on human health careers (detecting and treating hereditary diseases), biotechnology in veterinary medicine, applications to agriculture and plant science, animal science and livestock production, biotechnology in law enforcement, producing products, waste management, energy production, mining, and oil production.

Examples of job positions in these and other biotechnology fields:

Research and development (Research Scientist, Research Associate, Biochemist, Enzymologist, Molecular Biologist, Immunologist, Technician)

Production and quality control (Research Assistant, Chemical Engineer, Technician, Botanist)

Management, Sales and Marketing, Regulatory affairs, Legal affairs, Support functions (Program Manager, Public Relations, Marketing Specialist, Accountant, Salesperson, Graphic Designer, Communications, Patent Lawyer, Contract Lawyer, Financial Analyst, Secretaries, Accountants, Computer Technicians)

CRITICAL ANALYSIS OF BIOETHICAL ISSUES

Human Growth Hormone

Teacher Note: These are suggested activities that can be implemented after students watch the 60 MINUTES II video, Growth Industry.

Overview

New technology, medical procedures, and advances in biotechnology raise many social and ethical issues. Camera cell phones may violate individual privacy, and the internet offers access to an individual's financial records. Advances in plastic surgery have allowed many people to design their own faces and bodies.

The video, Growth Industry, talks about a biomedical advance. Human growth hormone was developed and is being prescribed to children who fall into a particularly short height percentile. However, the video points out there are several other children and parents who are using this human growth hormone to "assist" children who are in the other height percentiles. Using the suggested activities below, your class will learn to think critically about the ethics involved in choosing medical treatments.

Activities

Ask students to read the "case study" provided at the end of this lesson. There are several ways to analyze this "case study" within your classroom. Choose from any of the suggestions below:

• Students debate the pros and cons of human growth hormone. One team of students argue for the use of growth hormone to promote the athletic potential of a high school basketball player while the other team argues against the use of the human growth hormone where it is not deemed medically necessary.

• Students take on the role of a physician writing to the insurance company arguing for coverage of the human growth hormone while other students take on the role of the insurance company writing to deny coverage. Make sure students playing both roles use facts to back their decision.

• Students create a PRO vs. CON chart on the uses of human growth hormone.

• Divide the class into groups of three. One group is responsible for "Goals," one for "Rights," and one for "Duties." Provide each with large poster board or sheets of paper divided into columns. One column will be "Brian," one is "doctor," "parents," and "coaches." The "goal" team would list the goals of each person involved; the "rights" team the rights of each person, etc. The posters would be placed at the front of the class, and then the groups could be rearranged as jigsaw groups or the class could discuss the scenario together. In the end, they could vote, write a position paper, etc.

• Students answer the guiding questions (following the case study) for homework.

Case Study

Brian has just completed ninth grade and is attending Destiny High School. The varsity basketball team at Destiny High School has won the state championship for the last four years. Brian has attended basketball camps at the university and is one of the best basketball players in the state. He is the leading scorer as a forward, and the high school coach and the coach at the university basketball camp recognize Brian's potential as a high school and college player.

The only concern for both coaches is Brian's height. He is five feet ten inches. Brian and his parents have consulted an endocrinologist to discuss this concern and have asked that the endocrinologist provide biosynthetic human growth hormone. Thus far, the endocrinologist has refused saying that human growth hormone is used to treat only children who fail to achieve a particular height percentile. The endocrinologist also states that Brian does not have a legitimate medical need for the human growth hormone. Brian is warned about the potential side effects, which are irreversible. They include diabetes, heart enlargement and enlargement of the kidneys, high blood pressure, and elongation of the facial bones, hands, and feet.

Brian has made the endocrinologist aware that he can get human growth hormone on the black market if he cannot get it prescribed. Brian would prefer to use the hormone prescribed and administered by the endocrinologist because the hormone would be pure, and his progress would be medically monitored.

Guiding questions:

1. What should the endocrinologist do?

2. What would you do?

3. Who should decide whether Brian has access to a treatment?

4. Dr. Vance, a human growth hormone specialist at the University of Virginia, has stated, "Basically, you're saying these otherwise healthy children are not adequate because they are short. It's just a desire to have designer children. And because of the cost involved, it's one that could be achieved only by the very wealthy." Do you agree or disagree with this statement? Why?

5. Should a patient's psychological needs outweigh their physical needs when doctors treat patients?

6. What are the goals of Brian, Brian's coaches, Brian's parents, and Brian's endocrinologist?

7. Companies now produce human growth hormone for distribution through medical prescription and under a physician's supervision. What responsibilities do these companies have to their customers?

When answering these questions consider three areas: a) Goals, b) Rights, and c) Responsibilities. Each area should be considered from every individual's perspective. For example, the high school coach may have a different perspective than that of Brian as to whether Brian receives human growth hormone.

a) Goals: When examining any ethical issue, one must consider what the goal or end result one intends to accomplish. If a dying patient wants to maintain a quality of life, they may choose to be disconnected from a machine that keeps them alive but immobile in the hospital. The physician's goal may be different in that they would want to take any and all measures to keep the patient alive.

b) Rights: Most of us are familiar with our rights especially the ones guaranteed by the Constitution. What right does a terminally ill patient have to refuse a treatment that will prolong their life? What right does a physician have to a terminally ill patient when that patient wants to refuse a treatment?

c) Duties: Everyone has duties or obligations to others. We all have been compelled to help a friend, keep a promise, or tell the truth. We often justify our duty based on whether we are achieving a worthy goal or on the basis of an individual's rights. In our example of the terminally ill patient, does the physician have a duty to prolong the life of the patient when it agrees with his own goal of preserving the life of a patient? Or does the physician recognize and respect the patient's goal of a right to die even if it goes against his goal of preserving the life of his patients?

All students must be allowed to express very diverse opinions. During the discussion, remind the class that with an ethical dilemma, there is often no right or wrong answer, and everyone is equally entitled to their opinion. If the discussion does not appear to be progressing, step back and approach the issue from the framework of goals, rights and duties. The key to an effective class discussion is for the teacher to remain neutral.

After students discuss their responses, present their positions, and compare these with those of other students, they should have a sound platform on which to reach a responsible position. This process will expose your students to the first steps toward becoming critical thinkers.

BIOTECH STOCKS ARE HOT!!!! BUY NOW!!!

To complete this activity, students will need some background knowledge of stock markets. They may have covered this information in their Civics and Economics coursework. General information about stock markets may also be found at http://www.wsjclassroomedition.com/pdfs/stock_guide.pdf

In this lesson students will be given $5000.00 of (IMAGINARY) funds to invest in the biotechnology companies of their choice. Based on their research, they will select the stock(s) that they predict will be most successful over a nine week period of time.

- Follow several biotechnology companies' stocks over a one week period. Be sure to note their highs and lows, as well as their current selling prices.

- Take a few minutes over the next week to research the companies on the internet, finding out what products they make, services they provide, and how they might influence different populations. A few sample websites:

    - Pfizer: www.pfizer.com
    - Monsanto: www.monsanto.com
    - Enzon Pharmaceuticals: www.enzon.com
    - Human Genome Sciences: www.hgsi.com

- With the knowledge gained over the first week, select one to three biotech stocks to invest the $5000.00 in. Money is limited so they must choose among stocks trying to weigh potential costs and benefits, hoping to maximize benefits. Some things to consider may be price per share, fast growth vs. slow growth, stock history, growth potential, etc.

- The next page lists a small sample of biotechnology companies. Students may use these to begin their research.

Here is a small sample of biotechnology stocks for your students to research.

Abiomed (NASDAQ: ABMD)

Amgen (NASDAQ: AMGN)

Advanced Tissue Repair Sciences (NASDAQ: ATIS)

Amgen (NASDAQ: AMGN)

Bio-Rad Laboratories (AMEX: BIO)

Biomatrix (NYSE: BMX)

Cell Genesys (NASDAQ: CEGE)

Cephalon (NASDAQ: CEPH)

Chiron (NASDAQ: CHIR)

ENZON Pharmaceuticals (NASDAQ: ENZN)

Gene Logic (NASDAQ: GLGC)

Genzyme (NASDAQ: GENZ)

Human Genome Sciences (NASDAQ: HGSI)

MedImmune, Inc. (NASDAQ: MEDI)

Medtronic (NYSE: MDT)

Merck (NYSE: MRK)

Monsanto (NYSE: MON)

Myriad Genetics (NASDAQ: MYGN)

Novavax (NASDAQ: NVAX)

OSI Pharmaceuticals (NASDAQ: OSIP)

Onyx Pharmaceuticals (NASDAQ: ONXX)

Phizer (NYSE: PFE)

Pharmacopeia (NASDAQ: PCOP)

Qiagen (NASDAQ: QGEN)

Repligen (NASDAQ: RGEN)

SciClone Pharmaceuticals (NASDAQ: SCLN)

Sonus Pharmaceuticals (NASDAQ: SNUS)

Name _____

BIOTECH STOCKS ARE HOT!!!! BUY NOW!!!

1. What are the characteristics of a perfect stock? What do you consider when making a purchase (products, business practices, ethics, etc)?

2. What is your selected biotech stock/s? How much did each share cost? How many shares did you purchase?

3. Why did you choose your selected stock/s? What do you anticipate happening with them over the next eight weeks?

4. What products/services does your company provide?

- Will a large percentage of the population want these products/services?

- What are your personal feelings about the company you invested in? Do you support their services/products? Are they revolutionary?

5. What current events in the United States or other nations will affect growth of businesses in your branch of the biotech industry?

6. Is the overall economy of the United States booming or slowing down? How can you tell?

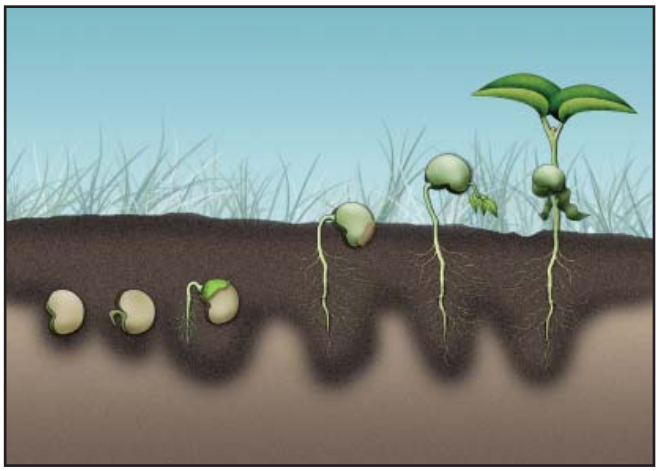
GENETICALLY MODIFIED SOYBEANS VERSUS TRADITIONAL SOYBEANS — HOW DO THEY COMPARE?

Do genetically modified soybeans look different form traditional ones? Can we detect a difference in how they grow and respond to environmental stimuli?

Equipment and Supplies Needed*
Traditional Soybeans and Roundup Ready Soybeans purchased at your local seed store.
40 plastic circular planters filled with soil
Herbicide Roundup
Weed Seeds (mustard seeds)
***Note: A kit with all necessary materials is available from Carolina Biological: 1-800-334-5551**.

PROCEDURE

Day 0
Plant 1 GM soybean in each of 20 planters and mark those planters "GM" to indicate that they contain genetically modified seeds. Place 1 traditional soybean in each of 20 different planters and mark the planters "T" to indicate that they contain traditional seeds. Continuously provide plenty of light and water. On even numbered days, count the number of seeds that have germinated and record the color of the plants. In addition, measure the heights of the plants that have germinated, and calculate the average height. Record all measurements and observations in the table below.



Day 5
Add the same amount of weed seeds to each planter. Continue to observe and water the seedlings.

Day 15
Apply the Roundup herbicide to soybeans in each pot.

Day 22
Final day to take measurements and record observations.

DATA ANALYSIS

Use Microsoft Excel or graph paper to graph the mean height of plants over time for both the genetically modified and traditional soybeans. A single line graph will probably be most effective for this activity. Instructions for how to make a line graph in Excel are below.

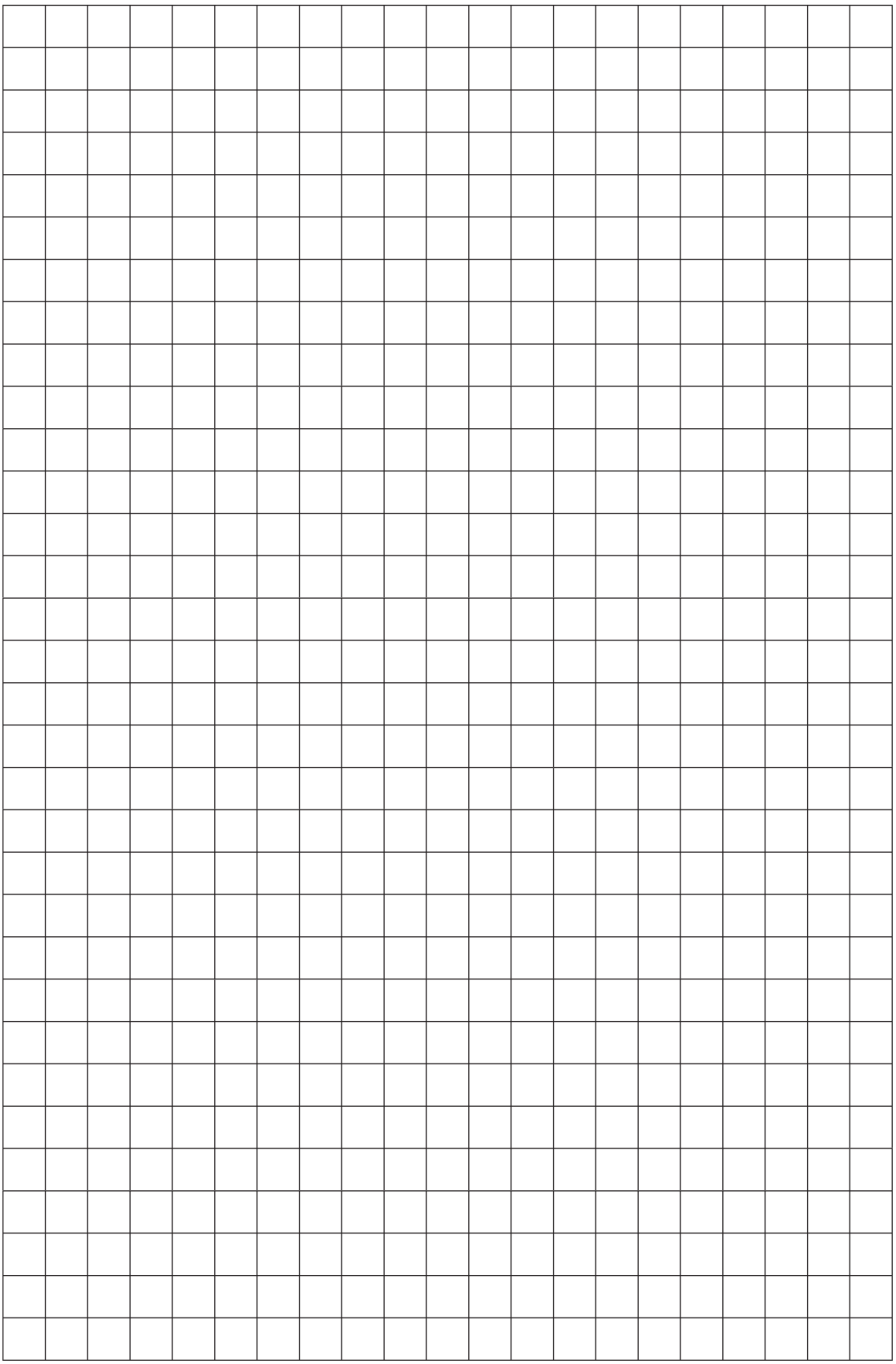
Have students prepare a lab report outlining the procedures used, the results, and the significance of their findings. Students can use the graph that they prepared in the results section of the lab report.

TABLE 1

Record the mean height, color, the number of seeds germinated, and any observations on even numbered days from day 2 through day 22. On day 5, plant weeds, on day 15, plant weeds and record any observations.

Day	Genetically Modified Soybeans				Traditional Soybeans			
	Mean Height	Color	# seeds germinated	Observations	Mean Height	Color	# seeds germinated	Observations
0	**Seeds Are Planted**				**Seeds Are Planted**			
2								
4								
5	**Plant Weeds**				**Plant Weeds**			
6								
8								
10								
12								
14								
15	**Apply Herbicide**				**Apply Herbicide**			
16								
18								
20								
22								

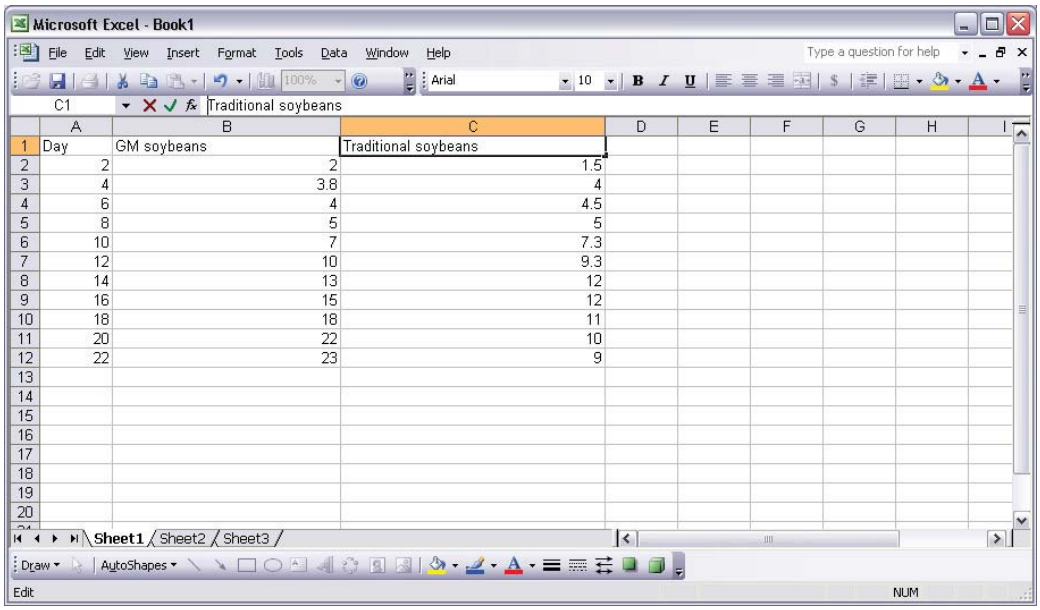
Graph paper



INSTRUCTIONS FOR USING EXCEL TO GRAPH YOUR DATA

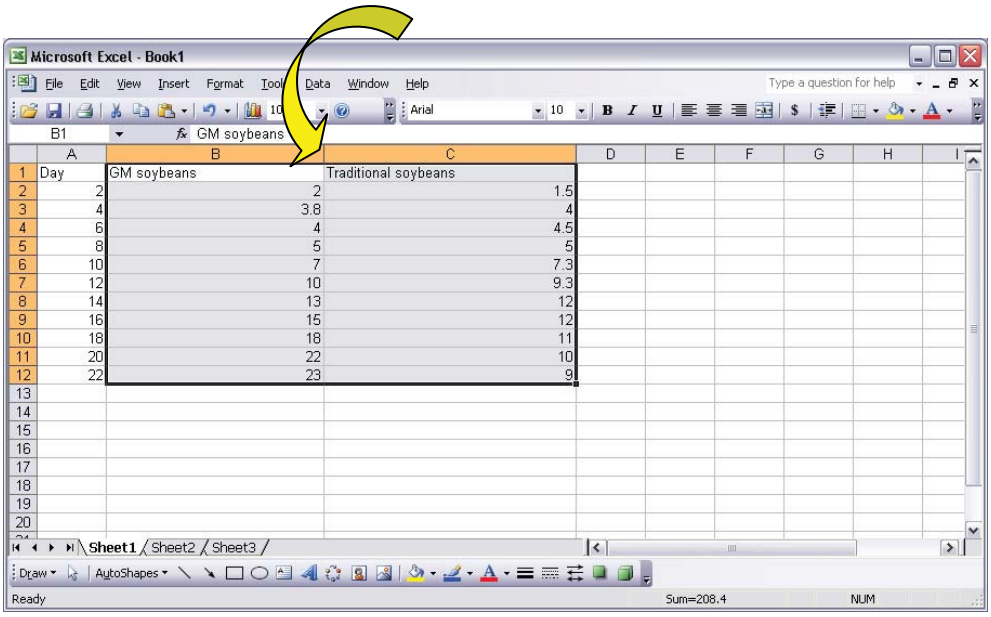
1. Go to the Programs Menu and open Microsoft Excel.
    a. A spreadsheet will appear on the screen.

2. In cells A1, B1 and C1; type in your labels (Day, GM soybeans, and Traditional soybeans)
    a. In cells A2- A12, type in day numbers.
    b. In cells B2-B12, type in the mean height of the GM soybeans for the corresponding day.
    c. In cells C2- C12, type in the mean height of the Traditional soybeans for the corresponding day.



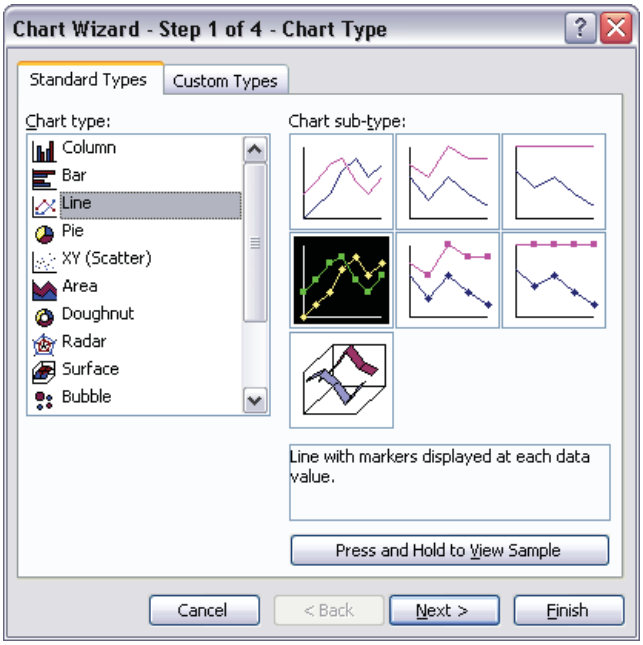
	A	B	C
1	Day	GM soybeans	Traditional soybeans
2	2	2	1.5
3	4	3.8	4
4	6	4	4.5
5	8	5	5
6	10	7	7.3
7	12	10	9.3
8	14	13	12
9	16	15	12
10	18	18	11
11	20	22	10
12	22	23	9

3. Highlight columns B and C including the labels in cells B1 and C1.
    a. Click the Chart Wizard tool button on the right side of the Formatting Toolbar, or choose Chart under the Insert menu option.

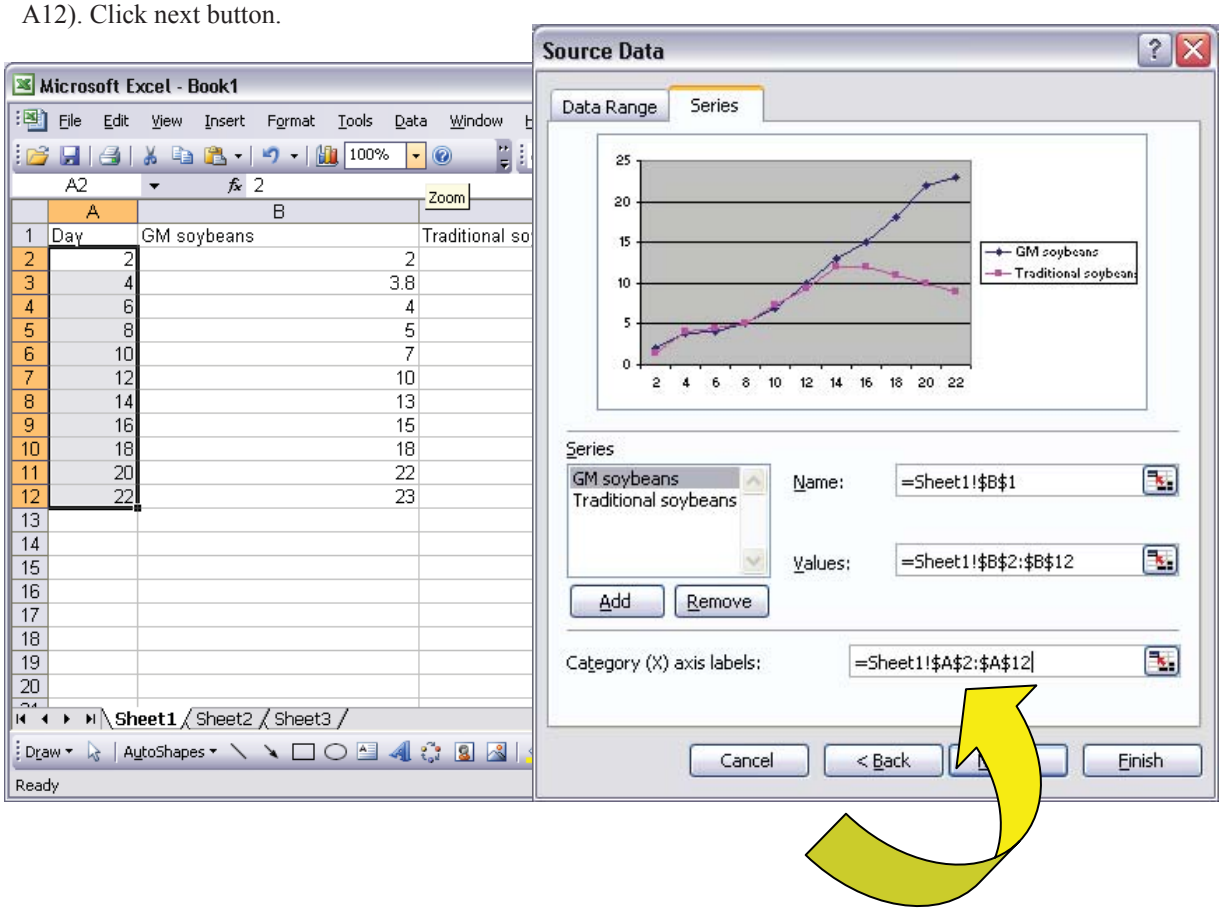


	A	B	C
1	Day	GM soybeans	Traditional soybeans
2	2	2	1.5
3	4	3.8	4
4	6	4	4.5
5	8	5	5
6	10	7	7.3
7	12	10	9.3
8	14	13	12
9	16	15	12
10	18	18	11
11	20	22	10
12	22	23	9

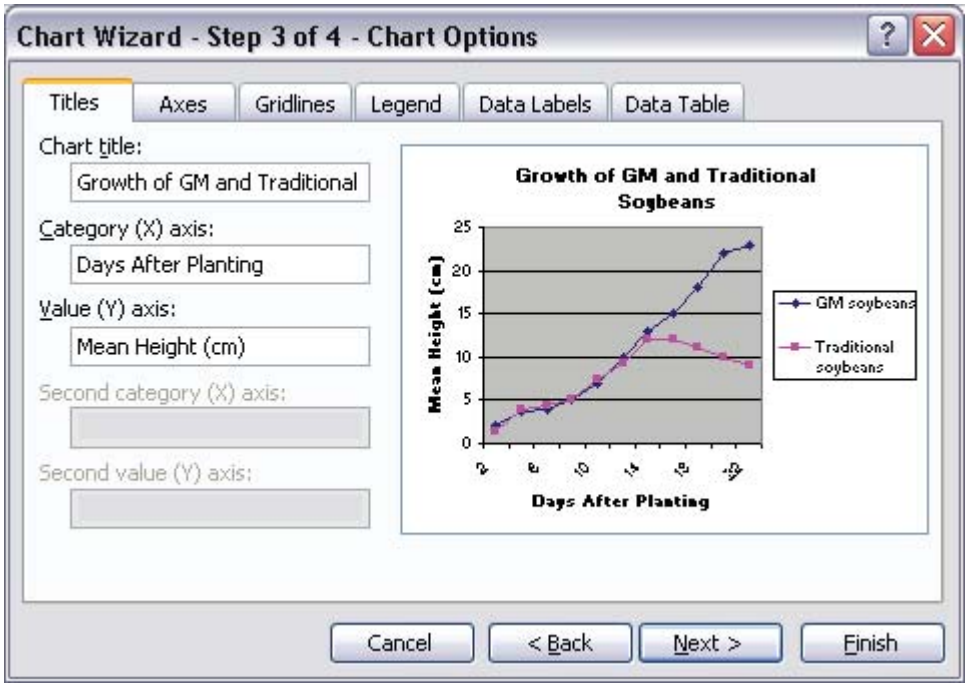
4. In Step 1 of 4: Select chart type (Line). Select the sub type you would like, and then click the "Next" button



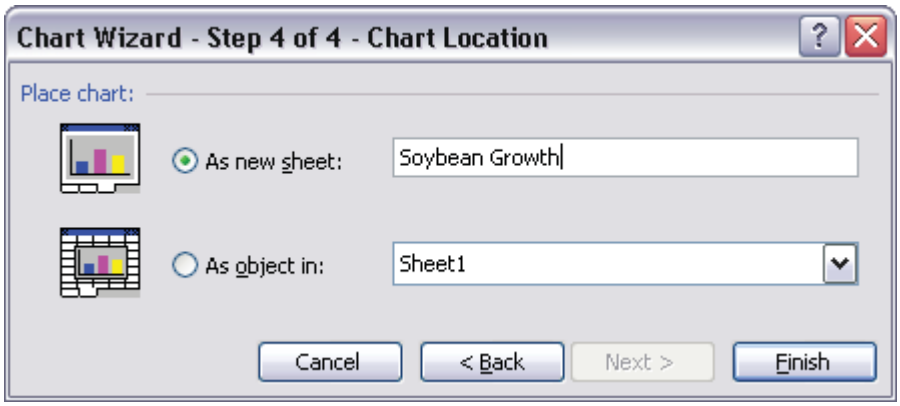
5. In step 2 of 4: Select column in the series in choice. Then choose the series tab. Mouse click one time in the Category (X) axis label blank, and when the cursor is in the blank, highlight the day numbers (cells A2 through A12). Click next button.



6) In step 3 of 4, fill in the chart title, as well as labels for X and Y axes. Click "Next."



7) Choose the "As new sheet:" option and give the chart a title. Click "Finish."



BIOPROCESSING: USING YEAST FERMENTATION TO MAKE ROOT BEER

INTRODUCTION

Bioprocessing is a technique in which microorganisms, living cells, or their components are used to produce a desired end product. A common bioprocessing technique is the use of yeast, tiny unicellular fungi, in the making of food and beverages. Yeast cells use an anaerobic (without oxygen) process called fermentation to obtain energy from glucose. During this process, ethanol (a kind of alcohol) and CO2 are given off. As a result, people use yeast to make wine, beer and other alcoholic drinks. In addition, the CO2 that is produced is useful in making bread and baked goods light and airy. In this laboratory investigation, we will use fermentation to make root beer.

Equipment and Supplies Needed*
6 Plastic 2-liter bottles
1 Tablespoon dry bakers yeast
4 Gallons of warm spring water
12 Tablespoons root beer extract
6 Large bowls
6 Funnels
6 Mixing spoons
7 Cups of granulated sugar
Measuring cups
Measuring spoons
Masking tape

PROCEDURE

Divide students into 6 groups, each group will perform the following set of steps:

1) Dissolve 1/8 teaspoon of dry yeast in ½ cup of very warm water. Let stand for 5 minutes.

2) In a bowl, combine 1½-2 tablespoons root beer extract with 1 1/8 cups sugar in enough warm water to dissolve the sugar (probably about 1 ½ cups of warm water).

3) Use the funnel to add the yeast mixture and the sugar mixture to the 2-liter bottle.

4) Add more warm water to fill the bottle to 2 inches from the top. Place lid on tightly and hold the bottle upside down momentarily to assure that there is no leaking. Use tape to label the bottle with your initials.

5) Store root beer in a warm dark place for 3-4 days, then store in a cool, dark place for 2-12 more days. Root beer should be aged a total of 7 days, but will taste best after aging 14. Check bottles caps every day for tightness; if bottles get too pressurized they will explode.

6) Chill root beer overnight and taste. Refrigeration will stop the fermentation process and kill the yeast.

Note: Though alcohol is a product of fermentation, negligible amounts of alcohol in this particular procedure. Also inform students that in commercial root beers, carbon dioxide is forced into the root beer, and yeast fermentation is not used.

FOLLOW-UP QUESTIONS

1) Explain the purpose of using yeast fermentation in making root beer.

2) What are the by-products of anaerobic yeast fermentation that are useful in making food and beverages?

3) Why were yeast and sugar necessary in this recipe?

4) How do you think yeast fermentation is used in bread making?

5) Why was it important to soak the yeast in warm water for 5 minutes prior to mixing it with sugar mixture?

ANSWERS TO FOLLOW-UP QUESTIONS

KEY

1) Explain the purpose of using yeast fermentation in making root beer.

Yeast fermentation is used as a way to add carbonation to root beer. Yeast cells metabolize glucose and produce CO_2, which will add carbonation to the soda.

2) What are the by-products of anaerobic yeast fermentation that are useful in making food and beverages?

Fermentation produces ethanol and CO_2. The production of ethanol is useful in making wine, beer, and other alcoholic drinks. The production of CO_2 is useful in making bread and other baked goods.

3) Why were yeast and sugar necessary in this recipe?

Yeast is needed to carry out the fermentation process, which produces CO_2 and adds carbonation to the root beer. The sugar is necessary to feed the yeast in order for fermentation to occur.

4) How do you think yeast fermentation is used in bread making?

When yeast produces CO_2 through fermentation, the small air bubbles of CO_2 are trapped within the bread dough, making the baked bread light and airy.

5) Why was it important to soak the yeast in warm water for 5 minutes prior to mixing it with sugar mixture?

Soaking the yeast in warm water activates it, or "wakes it up" from its dry state and prepares it to metabolize the sugar for fermentation.

FOR FURTHER INVESTIGATION

To further investigate the process of yeast fermentation, you can carry out the following experiment to answer the question "How much carbon dioxide is produced during yeast fermentation"?

Equipment and Supplies Needed
6 empty 1 pint water bottles
6 packets of dry yeast
6 cups of very warm water
12 Tablespoons sugar
6 large rubber balloons
6 lengths of string
6 meter sticks

PROCEDURE

Divide students into 6 groups; each group will perform the following set of steps:

1. Blow up the balloon several times to stretch it out; set aside.

2. Add 1 packet of yeast and 2 Tablespoons of sugar to 1 cup of warm water and stir.

3. Once the yeast and sugar have dissolved, pour into the bottle.

4. Attach the balloon to the mouth of the bottle; wait several minutes for the balloon to fill with carbon dioxide and expand.

5. Once the balloon has stopped inflating, wrap the length of string around the equator of the balloon, marking with your finger the length at which the string touches itself again.

6. Use the meter stick to measure the length of string needed to completely circle the balloon. This length is the circumference.

7. Have students use resources available to them – internet and math books – to determine the volume of the carbon dioxide that was produced.

Timeline Activity for Biotechnology

Introduction

Do your students feel that they are affected by biotechnology? Some people think biotechnology only deals with DNA or genetic engineering. But the simple truth is that biotechnology has been around since the brewing of beer by the Sumerians around 1750 B.C.E. Ask your students if they have ever eaten cheese or enjoyed bread. Biotechnology affects several areas of our lives such as food production and food processing, medicines such as vaccinations, and the use of bacteria to produce hormones like insulin and human growth hormone.

In this activity, student will research advances in biotechnology and use their findings to construct a class timeline.

Materials

Adding machine paper divided into time segments labeled as follows:

BC time period

0-1500 AD, and then each century that follows up to the current 21st century. If you prefer, the 21st century can be subdivided into decades.

Colored construction paper cut into strips; these can be color coded as to the topic areas. An example would be scientists = red, biotech advances = blue, technology = green, etc...

One copy of the student handout "Biotechnology Advances" for each student or group

Student Activity

Assign student teams or individual students an achievement in biotechnology to research from the list provided on the student handout. Each student or team will prepare a strip of colored construction paper by labeling the strip with the biotechnology achievement, the year of the biotechnology discovery, and the researchers associated with it. In an oral presentation to the class, students must tell how previous discoveries affected this advancement. After reporting to the class, students or teams will attach the strip of colored paper onto the timeline at the correct time period. Teachers may use the scoring rubric located at the end of this lesson to grade the presentations. (NOTE: Many scientific discoveries occur over a period of time; students' dates may vary slightly from those given.)

Graphing activity

Have students create a bar graph showing the number of biotechnology achievements for each time period. Students answer the following questions according to their graph.

Which time period has the most achievements in biotechnology? What other factors contribute to the number of achievements in each time period? Examples may include technology, such as the microscope.

Extension Activity Ideas

1) During the year students may research other topics such as scientists, cell discoveries, genetic research advances, etc. and add them to the timeline.

2) The timeline activity can serve as an ongoing current events lesson. Have students clip articles from newspapers or magazines on biotechnology achievements. After they report these achievements to the class, they can add the colored strip to the timeline representing the achievement.

3) Students can create parallel timelines on one or more of the following topics:

- Transportation methods
- Technology and inventions
- Clothing
- World leaders
- Sports events and athletes

4) The website, http://www3.iptv.org/exploremore/ge/Teacher_Resources/webquests.cfm, has several related WebQuests for students to complete.

SCORING RUBRIC

1 - Criterion: Quality of Research				
1	2	3	4	5
1 source		3 sources		5 sources
2 - Criterion: Question and Answer				
1	2	3	4	5
Many factual errors		Some factual errors		No factual errors
3 - Criterion: Graphics				
1	2	3	4	5
No Graphics		Some Graphics		Graphics that instruct as well as dazzle!
4 - Criterion: Organization				
1	2	3	4	5
Little evidence of design and planning		Some evidence of design and planning		Strong evidence of design and planning
5 - Criterion: Oral Presentation				
1	2	3	4	5
Did little to describe career		Explained career adequately		Grabbed everyone's attention

TIMELINE: ADVANCES IN BIOTECHNOLOGY

Research an achievement in biotechnology from the list provided.

1. A four-year-old girl suffering from an immune disorder is treated with the first federally approved gene therapy treatment.
2. An enzyme involved in the synthesis of a nucleic acid is isolated for the first time.
3. Arabidopsis thaliana is the first plant to have the complete genome sequence decoded.
4. Artificial “silk” first commercially produced in U.S.
5. Bacteria are discovered.
6. Bacteria are used to treat sewage for the first time.
7. Biogen builds a $50 million plant in the Research Triangle Park, NC, to manufacture recombinant interferon drugs for the treatment of multiple sclerosis.
8. Boom of rayon industry.
9. Brewing beer and making cheese.
10. First cells are discovered.
11. Classification of the plasmids.
12. Coined the term “gene”. Proposed that chromosomes carry genes (factors which Mendel said that could be passed from generation to generation).
13. Crop rotation for soil fertility/grafting techniques are developed.
14. Uses the same restriction enzyme to cut sections of viral DNA and bacterial DNA.
15. Sickle cell anemia identified as a molecular disease.
16. A sequence of three nucleotide bases discovered to determine each of 20 amino acids.
17. Determined that there is always a ratio of 1:1 adenine to thymine in DNA of many different organisms.
18. The double helix structure of DNA is discovered.
19. Developed the technique for staining and identifying bacteria.
20. Discovered antibiotic properties of certain molds; penicillin as an antibiotic.
21. DNA polymerase I is discovered.
22. Discoverers of restriction enzymes receive Nobel Prize in medicine.
23. First restriction enzymes are discovered.
24. DNA fingerprinting technique is developed.
25. DNA is identified as the genetic material of all living organisms.
26. Plants and livestock are now domesticated by early man.

27. Electron Microscope used to identify and characterize a bacteriophage.
28. The bacterium, Escherichia coli, is discovered.
29. Explained how DNA functions to make protein.
30. Fermentation process is patented.
31. First artificial chromosome is synthetically made.
32. First baboon-to-human bone marrow transplant is performed on an AIDS patient.
33. First biotech-driven interferon drugs for the treatment of cancer are approved by the FDA.
34. First breast cancer gene is discovered.
35. First cancer-causing virus is discovered.
36. Rice becomes the first crop to have its entire genome decoded.
37. First enzymes are isolated.
38. First field trials of DNA recombinant plants resistant to insects, viruses, bacteria are performed.
39. First genetic markers for specific inherited diseases are discovered.
40. First practical application of genetic engineering, human growth hormone, is produced by bacterial cells.
41. First rabies vaccine is administered.
42. First successful transplantation of a mammalian gene.
43. First transfer of foreign gene in plants is successful.
44. Flavr Savr tomatoes, engineered to resist rotting, are sold to the public.
45. First time genetic engineering techniques used to produce human insulin in E. coli.
46. Golden rice is modified to make Vitamin A.
47. Human Genome Project (rough draft) is completed by Celera Genomics.
48. Human Genome Project is funded by the US Congress.
49. Human growth hormone is discovered.
50. Humatrope, the drug for treating Human Growth Hormone deficiency, is developed.
51. Humulin is the first biotech drug to be approved by the FDA.
52. Mutation rate in fruit flies is increased by exposing them to x-rays.
53. Invention of the microscope.
54. Investigated how traits are passed from generation to generation, calling them factors. Discovers the laws of heredity
55. Isolated DNA from the nuclei of white blood cells using trout sperm.

56. Isolation of m-RNA; Hybrid DNA-RNA molecules are created.
57. The process of reverse transcriptase is isolated.
58. Licensed Eli Lily to make insulin.
59. Activated sludge for sewage treatment process is developed.
60. Moldy soybean curds are used as an antibiotic to treat boils.
61. The guidelines for the study of recombinant DNA are developed by The National Institute of Health.
62. Noted that a rough kind of bacterium changed to a smooth type when unknown "transforming principle" from smooth type was present.
63. First organized a course to study a type of bacterial virus that consists of a protein coat containing DNA.
64. PCR, Polymerase Chain Reaction technique is developed.
65. Penicillin is first mass-produced.
66. Performed transformation experiment with Griffith's bacterium.
67. Phages, or bacterial viruses, are discovered.
68. Plant hybridization technique is developed and used.
69. Powdered chrysanthemums first used as an insecticide.
70. Produced first recombinant DNA organism.
71. Proposed "one gene, one enzyme" hypothesis.
72. Proteins and DNA studied by x-ray crystallography.
73. First proteins are discovered.
74. Proved existence of microorganisms. He showed that all living things are produced by other living things and developed the Theory of Biogenesis.
75. Proved that genes are carried on chromosomes.
76. "Biotechnology" term is first used.
77. Science and Nature publishes the sequence of the Human Genome.
78. Scientists in Scotland clone a sheep using DNA from an adult sheep.
79. Scientists clone three generations of mice at the University of Hawaii.
80. Developed the process where viral DNA is spliced to the bacterial DNA.
81. "Molecular biology" term is coined.
82. The entire sequence of the HIV virus is cloned and sequenced.
83. The first genetically engineered blood clotting factor is approved in the U.S.
84. The gene responsible for Cystic Fibrosis is discovered.

85. The genetic code of the fruit fly, *Drosophila melanogaster*, is published.
86. The North Carolina Biotechnology Center is the nation's first state-sponsored program to support biotechnology. It is created and funded by the NC State Legislature.
87. Transposable elements, "or jumping genes," are discovered.
88. U.S. Supreme Court decided that man-made microbes could be patented.
89. Used acetone, produced by plants, to make bombs.
90. Used living microorganisms to protect people from disease.
91. Used radioactive labeling to determine that it is the DNA, not protein, which carries the instructions for assembling new phages.
92. Developed the Cell Theory – all organisms are composed of cells, every cell arises from a pre-existing cell.
93. Hypothesized that animal and plant populations adapt over time to best fit the environment. On the Origin of Species is published.
94. Cultivation and breeding of potato varieties first begun.
95. Made preservation of blood possible by separating plasma.

TEACHER GUIDELINES: ADVANCES IN BIOTECHNOLOGY

8000 BC	Humans	Plants and livestock are now domesticated by early man.
3000 BC	Incas	Begin cultivating and breeding potato varieties.
1750 BC	Sumerians	Brewing beer and making cheese.
500 BC	Chinese	Moldy soybean curds used as an antibiotic to treat boils.
250 BC	Greeks	Crop rotation for soil fertility/grafting techniques are developed.
100 AD	Chinese	Powdered chrysanthemums first used as an insecticide.
1590	Janssen	Invention of the microscope.
1663	Hooke	First cells are discovered.
1675	Leeuwenhoek	Bacteria are discovered.
1797	Jenner	Used living microorganisms to protect people from disease.
1830	Mulder	Proteins are discovered.
1833	Payen, Persoz	First enzymes are isolated.
1835	Schleiden, Schwann, Virchow	Developed the Cell Theory — all organisms are composed of cells, every cell arises from a pre-existing cell.
1859	Charles Darwin	Hypothesized that animal and plant populations adapt over time to best fit the environment. On the Origin of Species is published.
1864	Louis Pasteur	Proved existence of microorganisms. He showed that all living things are produced by other living things and developed the Theory of Biogenesis.
1865	Gregor Mendel	Investigated how traits are passed from generation to generation, calling them factors. Discovers the laws of heredity.
1869	Johann Meischer	Isolated DNA from the nuclei of white blood cells using trout sperm.
1870	Burbank	Developed new strains of fruits, vegetables, and flowers, including a potato which was blight-resistant.
1877	Koch	Developed the technique for staining and identifying bacteria.
1885	Pasteur	First rabies vaccine is administered.
	Escherich	The bacterium, Escherichia coli, is discovered.
1893	Koch, Pasteur	Fermentation process is patented.
1902	Walter Sutton	Coined the term “gene.” Proposed that chromosomes carry genes (factors which Mendel said that could be passed from generation to generation).
1910	Avtek Fibers, Inc.	Artificial “silk” (rayon) first commercially produced in U.S.

1910	Thomas H., Morgan	Proved that genes are carried on chromosomes.
1911	Rous	First cancer-causing virus is discovered.
1914		Bacteria are used to treat sewage for the first time.
1915		Phages, or bacterial viruses, are discovered.
1918	Germans	Used acetone, produced by plants, to make bombs.
		Activated sludge for sewage treatment process is developed.
1919		"Biotechnology" term is first used.
1920	Evans and Long	Human growth hormone is discovered.
		Boom of rayon industry.
1927	Herman Mueller	Mutation rate in fruit flies is increased by exposing them to x-rays.
1928	Frederick Griffiths	Noticed that a rough kind of bacterium changed to a smooth type when unknown "transforming principle" from smooth type was present.
	Alexander Fleming	Discovered antibiotic properties of certain molds; penicillin as an antibiotic.
1920-30		Plant hybridization.
1938		Proteins and DNA studied by x-ray crystallography.
		Term "molecular biology" is coined.
1939-40	Charles Drew	Made preservation of blood possible by separating plasma.
1941	Beadle/Tatum	Proposed "one gene, one enzyme" hypothesis.
1942		Electron Microscope used to identify and characterize a bacteriophage.
		Penicillin is first mass-produced.
1943-53	Linus Pauling	Sickle cell anemia identified as a molecular disease. DNA is identified as the genetic material of all living organisms.
1944	Oswald Avery	Performed transformation experiment with Griffith's bacterium.
1945	Max Delbruck	First organized a course to study a type of bacterial virus that consists of a protein coat containing DNA.
1950	Erwin Chargaff	Determined that there is always a ratio of 1:1 adenine to thymine in DNA of many different organisms.
1951	McClintock	Transposable elements, or "jumping genes", are discovered.
1952	Hershey/ Chase	Used radioactive labeling to determine that it is the DNA, not protein, which carries the instructions for assembling new phages.

1953	Watson/Crick	The double helix structure of DNA is discovered.
1955		An enzyme involved in the synthesis of a nucleic acid is isolated for the first time.
1957	Francis Crick	Explained how DNA functions to make protein.
1958	Kornberg	DNA polymerase I is discovered.
1960		Isolation of mRNA; Hybrid DNA-RNA molecules are created.
1965		Classification of the plasmids.
1966	Nirenberg/ Ochoa	A sequence of three nucleotide bases discovered to determine each of 20 amino acids.
1970		The process of reverse transcriptase is isolated.
1971		First complete synthesis of a gene; Discovery of restriction enzymes.
1972	Paul Berg	Uses the same restriction enzyme to cut sections of viral DNA and bacterial DNA.
		Spliced viral DNA to the bacterial DNA.
1973	Cohen/Boyer	Produced first recombinant DNA organism.
1976		National Institute of Health guidelines developed for study of recombinant DNA.
1977		First practical application of genetic engineering, human growth hormone, is produced by bacterial cells.
1978	Genentech, Inc.	Genetic engineering techniques used to produce human insulin in *E. coli*.
	Stanford University	First successful transplantation of mammalian gene.
		Discoverers of restriction enzymes receive Nobel Prize in medicine.
1979	Genentech, Inc.	Produced human growth hormone and two kinds of interferon; DNA from malignant cells transformed a strain of cultured mouse cells, producing a new tool for analyzing cancer genes.
1980		U.S. Supreme Court decided that man-made microbes could be patented.
1981		The North Carolina Biotechnology Center is the nation's first state-sponsored program to support biotechnology. It is created and funded by the N.C. State Legislature.
1982		Humulin is the first biotech drug to be approved by the FDA.
1983	Genetech, Inc.	Licensed Eli Lily to make insulin.
		PCR, Polymerase Chain Reaction technique is developed.
		First artificial chromosome is synthetically made.
		First genetic markers for specific inherited diseases are discovered.
		First transfer of foreign gene in plants.

1984		DNA fingerprinting technique is developed.
	Chiron	The entire sequence of the HIV virus is cloned and sequenced.
1985		Plants can be patented.
1986		First field trials of DNA recombinant plants resistant to insects, viruses, bacteria.
		First biotech-driven interferon drugs for the treatment of cancer are approved by the FDA.
1987		Humatrope, the drug for treating HGH deficiency, is developed.
1988		Human Genome Project is funded by the US Congress.
		First living mammal was patented.
1989		The gene responsible for Cystic Fibrosis is discovered.
1990		A four-year-old girl suffering from an immune disorder is treated with the first federally approved gene therapy treatment.
1992		The first genetically engineered blood clotting factor is approved in the U.S.
1993		Flavr savr tomatoes, engineered to resist rotting, are sold to public.
1994		First breast cancer gene is discovered.
1995		First baboon-to-human bone marrow transplant is performed on an AIDS patient.
1996		Biogen builds a $50 million plant in the Research Triangle Park, NC, to manufacture recombinant interferon drugs for the treatment of multiple sclerosis.
1997		Scientists in Scotland clone a sheep using DNA from an adult sheep.
1998		Scientists clone three generations of mice at the University of Hawaii.
2000		Human Genome Project (rough draft) is completed by Celera Genomics.
		Golden rice is modified to make Vitamin A.
		The genetic code of the fruit fly, *Drosophila melanogaster*, is published.
		Arabidopsis thaliana is the first plant to have the complete genome sequence decoded.
2001		*Science* and *Nature* publishes the sequence of the Human Genome.
2002		Rice becomes the first crop to have its genome decoded.

"BIOBUSINESS" IMPLEMENTATION PLAN — INTERDISCIPLINARY BRIDGES							
Activity	Arts	English	Health	Math	Science	Social Studies	Provided materials
Online Lesson Plans and Resources		X	X		X	X	Links and descriptions of online lesson plans dealing with biotechnology
Battling Bioterrorism: Understanding the Science and Politics			X		X	X	Lesson plans and activities
A Discovery-Based Approach to Understanding Clinical Trials		X	X		X	X	Lesson plan, with handouts based on a current clinical trial testing human growth hormone
Technology and Global Connections: The Green Revolution and World Hunger		X			X	X	Lesson plan, suggested activities, articles from International Food Policy Research Institute (www.ifpri.org)

Online Lesson Plans and Resources

Lesson Plans

Altered Genes: Exploring the Economic Implications of Consumer's Worries about Genetically Engineered Foods
http://www.nytimes.com/learning/teachers/lessons/19990830monday.html?searchpv=learning_lessons

Subjects: Economics, English, Science, Social Studies

Overview: Students investigate the controversy surrounding the use of gene-altered crops in food products sold in the US and overseas. Students will explore the economic implications of the use of such crops as well as of the refusal of some countries and companies to buy gene-altered crops. After reading and discussing the NY Times article, "New Trade Threat for US Farmers," students participate in an 'international trade meeting,' taking the perspective of one of the parties represented in the article. They then write a personal essay expressing their views of the issues raised.

Reaching New Heights: Debating the Use of Growth Hormones for Short Children
http://www.nytimes.com/learning/teachers/lessons/20030902tuesday.html?searchpv=learning_lessons

Subjects: English, Health, Science

Overview: In this lesson, students read about the use of Humatrope, a biosynthesized human growth hormone, to increase the heights of short children. They take on the role of members of the Food and Drug Administration and debate the practical and ethical concerns of approving this drug. Then, students write position papers either in favor or against the use of Humatrope.

Harvesting the Seeds of Technology: Exploring Our Responsibilities as Stewards of the Earth in a Technological Era
http://www.nytimes.com/learning/teachers/lessons/19990422thursday.html?searchpv=learning_lessons

Subjects: English, Science, Social Studies

Overview: Students examine the roles of all people as 'stewards of the earth' and evaluate whether or not technology and science are at odds with our stewardship of the earth.

All Rights Reserved? Global Economic and Scientific Impacts of Genetic Ownership of Biological Products
http://www.nytimes.com/learning/teachers/lessons/19991202thursday.html?searchpv=learning_lessons

Subjects: Science, Social Studies

Overview: In this multi-day lesson plan, students explore, through discussion, research, dramatic skits, and writing, the debate over genetic ownership of biological products and evaluate the economic viewpoints of the countries and companies involved.

Resources

Pew Initiative on Food and Biotechnology
http://pewagbiotech.org/
The Pew Initiative on Food and Biotechnology was established in 2001 to be an independent and objective source of credible information on agricultural biotechnology for the public, media, and policymakers. Funded through a grant from The Pew Charitable Trusts to the University of Richmond, the Initiative advocates neither for, nor against, agricultural biotechnology. Instead, the Initiative is committed to providing information and encouraging debate and dialogue so that consumers and policymakers can make their own informed decisions.

Science and Development Network: Biotechnology opportunities for developing countries
http://www.scidev.net/ms/naturebiotech/
Online version of a special supplement to the December 2004 issue of *Nature Biotechnology*, presenting case studies of progress in health biotechnology in seven countries in the developing world.

Battling Bioterrorism: Understanding the Science and Politics

Developed by Susan Hirsch, East Wake High School, and Brian Wood, Enloe High School

OVERVIEW

The fear of an attack of bioterrorism has increased tremendously since September 11, 2001, and the US government has budgeted an unprecedented amount of money to be used for research on this topic. In the following activities, students assume the role of research scientists from different government agencies who do research and other studies in order to prepare and prevent an attack where chemical or biological agents are used.

Learning about bioterrorism brings the study of science into your classroom while following the Social Studies standard course of study. It allows the students to research a very timely topic and discover how many agencies are involved in the defense of our country against a bioterrorist attack. The four activities described below can be used with a unit on the Legislative Branch and Congress or while teaching economics and the government's budgets.

OBJECTIVES

- Explore an aspect of the United States' anti-terrorism preparations
- Learn about the role of scientific research in governmental activities
- Discuss the roles of the US Legislative Branch and Congress
- Learn about the national budget
- Develop public speaking skill

I. CONGRESSIONAL COMMITTEE HEARING SIMULATION ON BIOTERRORISM

Students work in pairs or alone to research a government agency that has been assigned by the US government to research, prepare, and prevent a biological or chemical attack. Let each student/group draw numbers and whoever draws # 1 gets to pick which agency they want. Continue this practice until all students have chosen. Before the students choose their agency, briefly explain what each agency is doing.

Government Agencies

- Center for Disease Control (CDC)
  www.cdc.gov
- Food and Drug Administration (FDA)
  www.fda.gov
- Health and Human Services (HHS)
  www.hhs.gov
- Homeland Security
  www.dhs.gov
- Center for Civilian Biodefense Strategies
  Johns Hopkins — www.hopkins-biodefense.org
- USDA
  www.usda.gov
- Environmental Protection Agency (EPA)
  www.epa.gov
- Federal Trade Commission (FTC)
  www.ftc.gov
- Department of Justice
  www.usdoj.gov
- Department of Labor (OSHA)
  www.osha.gov
- US Army Medical Research
  www.usamriid.army.mil/education
- FBI
  www.fbi.gov
- CIA
  www.cia.gov
- National Institute of Allergy and Infections (NIAID)
  www.niaid.nih.gov
- Project Bio Shield
  www.whitehouse.gov/bioshield

After students have completed their research, each student or group of students will prepare a 2- to 4-minute oral presentation, including some type of visual—it may be poster/s, a PowerPoint, or individual sheets for each of the other students. Students make their presentations before a congressional committee (class and teacher). The job of each agency (student or group of students) is to convince the congressional committee

that their agency deserves be the lead in all research on bioterrorism. The committee will decide which agency will take the lead and receive funding for bioterrorism research.

Each presentation should address the following questions:

• What is the main emphasis of the current research being conducted? (diseases, data reporting, storage, biodefense, vaccines, preparation, prevention)
• What are the plans for future research?
• How much money has been budgeted for your agency to spend?

II. BIOTERRORISM "HYPE OR THREAT" ACTIVITY

Each of the following possible biological warfare agents should be placed on a sign. Make a masking tape line on the floor. One end of the line represents a low threat and the other end a high threat based on a scale from 1 to 10. Threat will be defined as likelihood that the agent would make a practical biological terrorist agent. The signs should be distributed to students, and the students will rank each agent in terms of the perceived list. Make a digital camera picture of the rankings.

Possible Biological Warfare Agents

Anthrax
Plague
Tularemia
Brucellosis
Q fever
Smallpox
Equine encephalitis viruses
Foot and Mouth Disease
Ebola virus
Hemorrhagic fevers (other than Ebola)
Influenza virus
Staph enterotoxin B
Ricin
Botulism toxins
Trichothecene mycotoxins

Students work in pairs or alone to research specific diseases or biological agents and develop a five- to ten-minute poster or PowerPoint presentation on their assigned biological warfare agent. Let each student/group draw numbers and whoever draws # 1 gets to pick which disease or agent they want to research. Continue this practice until all students have chosen.

The presentations should include the following information:

• History of the bacteria, virus, or toxin
• Any use as a biological weapon in the past
• Structure (what does it look like)
• Changes such as mutations to make it a more efficient biological weapon
• Mode of transmission including host species
• Symptoms and diagnosis
• Treatment
• Containment options if an outbreak should occur
• Social implications including the economic and political impact of an outbreak

A good starting point for research is the Center for Disease Control website: www.cdc.gov. Emphasize that students should cite their sources.

During the presentation the teacher should give students participation forms with a section for notes on each disease. Students take notes during the presentations and turn them in for evaluation.

After all of the presentations, the students will repeat the first exercise to see if their perceptions of the risk of each agent have changed and determine if their previous concerns were based on science or media hype.

III. SUPPLEMENTARY BIOTERRORISM LESSON PLANS

• Write a handbook on how to clean up a community after a biological or chemical attack.

• Discuss the Hippocratic Oath and the responsibility of the physician to the infected if there was a biological attack. If you were in the medical profession, would you knowingly treat someone who had been infected with a contagious disease?

• Write a grant application to a Biotech company where you are a researcher wanting to sequence a recently discovered virus. Give past, present and future uses of this process and convince your supporter that this research is important. (Persuasive letter)

• Discuss the economic importance of a biological attack on the U. S. economy. What about on the world economy?

- Create a mock drill on how a region would react to a smallpox outbreak.
- Write a report on how the government should prioritize those who should get vaccinated if there is an outbreak of a contagious disease.
- Keep a two-week journal as if you were being quarantined because of an outbreak of a contagious disease.
- Research the history of a disease such as smallpox and present to the class.
- Go to the Center for Disease Control (CDC) website and create 10-15 thought-provoking questions about bioterrorism and/or plagues that could be used as a lesson for the rest of the class.
- Research different companies and corporations as to how they handle their mail since the anthrax and ricin-laced letters were mailed in 2001 and 2004 respectively.
- Imagine that you work for the post office. Write a list of procedures that should be in place to safely handle mail.

IV. PAIDEIA SEMINARS: "EFFECTS OF BIOTERRORISM" AND *THE SPECKLED MONSTER*

Paideia comes from "pediatrician" and "encyclopedia", an ancient Greek belief of education that all children should have a general knowledge base. *Paideia* is the general learning that should be the possession al all children.

The Paideia seminar is a formal discussion based on text, in which the leader of the discussion asks open-ended questions designed to precipitate spirited and thoughtful dialogue. As a result, the participants are asked to articulate, justify, and clarify their own ideas as well as their responses to the ideas of others. The ultimate goal of a seminar is that all participants develop a more sophisticated understanding of the text through thoughtful interaction with the ideas of others. Neither consensus nor closure should signal the end of a seminar; rather continued inquiry and reflection should flow directly out of the experience.

There are four components of a successful seminar activity:

- Pre-seminar activity — Once the text is given to the participants, questions or an assignment that focused on content should be assigned so that before the seminar, the participants will have read and understood the text.
- Coaching activity — In this component, students develop in-depth understanding of the topic by problem solving and application.
- Seminar — The teacher becomes the facilitator and leads the students in a discussion of the assigned texts. The participation of the students consists of thinking, listening, speaking, referring to the text, and respecting all participants.
- Post-seminar activity — An assignment such as a writing assignment is made to assess and apply both content and process.

SEMINAR ON "EFFECTS OF BIOTERRORISM"

This seminar activity consists of three readings and can be used in its entirety or in small parts as class discussions, outside or in-class readings, cooperative learning activities or as seminars. The readings are "Prologue" from The Anthrax Letters by Leonard Cole and "The Horror of Halabja" and "What Leaders and Citizens Can Do," from Avoiding Armageddon, with quotes from former President Mikhail Gorbachev of the Soviet Union and former President Jimmy Carter of the U. S.

Pre-Seminar Activity: After reading the three selections, complete all activities on this page on your own paper in ink and answer any questions in complete sentences.

The Anthrax Letters

1. Write five questions as if you were an investigator that you would ask people who lived on and around Nassau Street in Princeton, New Jersey.
2. Describe how anthrax was used in the Bible according to the author.
3. Why is anthrax the preferred instrument of terror?
4. List the steps that anthrax spores go through once it get in the body.
5. Describe how you would react if you had been Pat Hallengren on August 10, 2002.

"Horror of Halabja"

Write a one-day journal entry as if you were the Iraqi Air Force pilot who flew over Halabja on March 16, 1988.

"What Leaders Can Do"

Summarize what both Gorbachev and Carter said was right and wrong with the world. Next, explain who you agree with the most and why.

Coaching Activity: Divide the class into cooperative learning groups with four students per group and give each student a copy of the readings "Definition of Bioterrorism" and "History of Biowarfare and Bioterrorism" (www.hs.state.az.us/phs/edc/edrp/es/bioterror.htm) and a large piece of poster board or construction paper. Divide the reading into four parts and assign each student in the group one section to read. Then have them divide their poster board in four by drawing a line down and across. Let them use colored pencils or magic markers and illustrate what they had read on the poster. Once everyone is finished, have each group present it to the class.

Opening seminar question: What scares you the most about bioterrorism?

Core seminar questions:

1. Pat Hallengren's first thought was of her mailman, Mario. What would be your first reaction if you had been in her situation?
2. You are the postal inspector in 2001. What are some rules you would make to keep the mail safe?
3. The person who sent anthrax has not been found as of yet. If you were an investigator and in the process of trying to solve the crime, what are some questions that you would ask the public to try to arrive at the truth?
4. What punishment would you recommend for the person who committed this crime, if they are found?
5. The secret code for the dropping of nerve gas in Halabja was "Rain, Rain, Rain." Think of another secret code that you may have used.
6. Describe how you would react if you were told to drop a chemical gas and kill innocent people or die.
7. Explain what punishment you would inflict on the pilot if you were an American soldier and you arrested him.
8. Analyze one way that what Gorbachev said is different from what Carter said.

Closing Question: The President of the United States is in the room. What is one thing you would say to him about bioterrorism?

Post-Seminar Activity: Write entries in a journal for 14 days as if you had been exposed to a biological or chemical agent but had no symptoms. Each entry must be dated and be at least one half of a page. Create a cover for this journal.

Seminar on *The Speckled Monster: A Historical Tale of Battling Smallpox*

This book by Jennifer Lee Carrell tells the dramatic story–both historical and timely–of two parents who dared to fight back against smallpox. This unit concentrates on the introduction (www.speckledmonster.com/intro.html) to the book, and the chapter "Rosebuds in Lily Skin" (www.speckledmonster.com/partone.html), which tells how Lady Mary Wortley Montagu saved her daughter and helped save the city of London from the deadliest disease mankind had known. We suggest reading the introduction of the book to the students so that they have a frame of reference as what and how this chapter fits into the entire story.

Pre-Seminar Activity: Answer all questions in ink on your own paper and in complete sentences.

1. How did Lady Mary react to John Dryden's quote: Blisters with pride swelled, which through's flesh did sprout / Like rosebuds stuck i' th' lily skin about."
2. What do you think about the above quote?
3. Explain the line "the smallpox had been slashing its way through her friends and family."
4. Why did Lady Mary not take Princess Anne's death personally?
5. How did Lady Mary protect her daughter, Mary?
6. How did King George I react when his son, Prince of Wales, challenged his power in Parliament?
7. What brought the father and son back together?
8. How did the people of London react to the outbreak of smallpox?
9. What could have prevented the nurse from contacting smallpox?
10. What was Lady Mary's request of Mr. Maitland?
11. What were Mr. Maitland's demands and why did they change?
12. What preparations did Lady Mary want to avoid?
13. How did little Mary react to the doctor's procedure?
14. Who is the hero in this story and why?

Coaching Activity: Divide the class into cooperative learning groups with four students per group and give each student a copy of the reading the "Definition of Bioterrorism" and the "History of Biowarfare and Bioterrorism" (www.hs.state.az.us/phs/edc/edrp/es/bioterror.htm) and a large piece of poster board or construction paper. Divide the reading into four parts and assign each student in the group one section to read. Then have them divide their poster board in four by drawing a line down and across. Let them use colored pencils or magic markers and illustrate what they had read on the poster. Once everyone is finished, have each group present it to the class.

Opening Seminar Question: All vaccinations risk killing or harming some percentage of otherwise healthy people, in order to protect the majority. What criteria should be used to decide when to begin vaccinating the majority of the population? Also, who should decide and who, if anyone is to blame, when things go wrong?

Core Seminar Questions:

1. Explain what made Lady Mary and others like her willing to risk inoculation in 1721 for themselves and their family members? Consider the following arguments:
   - Emotional and personal
   - Scientific
   - Religious
   - Political
   - Economic
2. How do the above issues relate to modern concerns about vaccination?
3. Compare the fears in London of the spread of smallpox to our fear of a bioterrorist attack today. How are they alike and how are they different?
4. In 1721 the British government tested smallpox inoculation on prisoners under sentence of death; it did so with the prisoners' consent, and in exchange for pardons. In researching cures and vaccines for various diseases, the U. S. government has in the past run tests on human subjects both with and without their informed consent. What would have to happen to make you volunteer to be a part of medical testing for a cure for a deadly disease?
5. If no one consents to be tested, how should scientists test the safety of new vaccines and medicines?
6. If you were Lady Mary, how would you have reacted if your child or you may be exposed to a deadly disease?
7. If you were Princess Caroline, what would you have done in her situation—pick your spouse or your children?

Closing Seminar Question: Who was the medical hero in our story?

Post-Seminar Activity: Write a one- to two-page report to be presented to the Department of Homeland Security on how the government should prioritize those who should get vaccinated if there is an outbreak of a contagious disease. Include a list of people who should be charged, if you feel there should be any. Think about citizens and non-citizens, young and old, healthy and sick, rich and poor, etc.

Online Resources

- www.globallink.org.uk/Esc2Saf/Rebwar.htm — Story and artwork by survivor of chemical attack on the Kurdish in Halabja, Iraq
- www.pbs.org/wgbh/nova/bioterror/linksandbooks.html — NOVA online information on bioterrorism
- www.pbs.org/newshour/health/bioterrorism/threat_m.html — Online "News Hour with Jim Lehrer" about bioterrorism
- www.pbs.org/newshour/extra/features/july-dec02/bio.html — Jim Lehrer's Web page for students concerning bioterrorism
- academic.udayton.edu/health/syllabi/Bioterrorism/00intro02.htm — On the early biological war on Native Americans

A Discovery-Based Approach to Understanding Clinical Trials

Subjects: English, Health, Science, Social Studies

Overview: In modern society, the drugs we take and the medical procedures we undergo are the result of extensive research. Most people have seen the ads for clinical trials, recruiting people with heart disease or high blood pressure or some other possible mental or physical ailment. Yet, many don't fully understand the procedures involved in clinical research. According to the US National Institute of Health website, ClinicalTrials.gov, clinical research is the "fastest and safest way to find treatments that work in people and ways to improve health." This lesson plan, designed to be covered in one 90 minute class (or at the end and beginning of two successive classes), will help students to learn about the make-up of clinical research and the provisions in place to ensure the safety of the human participants.

The lesson will also be useful in teaching critical reading and informational writing skills. Social Studies teachers may wish to expand on the content provided here by focusing on the history, ethics, and regulations of clinical trials. General information may be found at "The history of clinical testing and its regulation" (http://www.roche.com/pages/facets/18/histclinte.htm). Objectives: Students think critically about the ways in which scientific researchers approach health problems, while also learning to analyze texts and write informational, science-based compositions.

RESOURCES

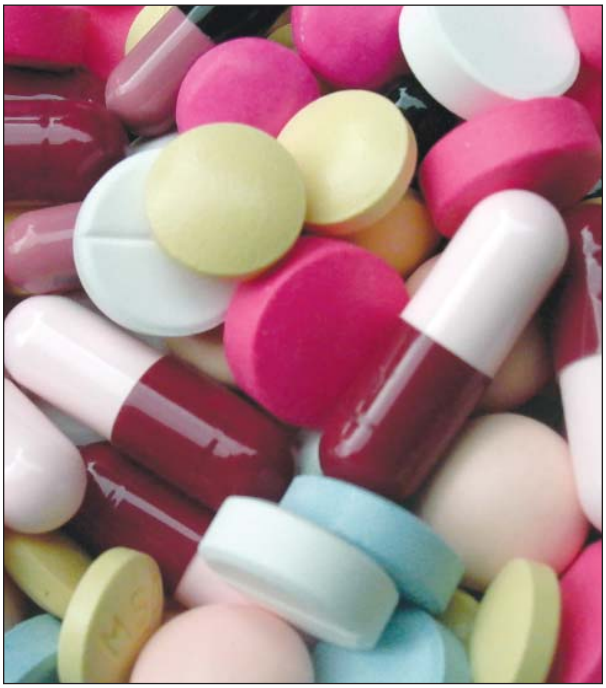
• 3 Handouts (attached): Engagement Activity, FAQ and Glossary (Understanding Clinical Trials), Exploration Activity ("Childhood-onset Growth Hormone Deficiency").
• Students and teachers may also wish to consult the website ClinicalTrials.gov.

ACTIVITIES/PROCEDURES

I. Engagement Activity (15 minutes)

a. At the beginning of class, provide each student with a copy of the attached "Engagement Activity" handout, which lists four different clinical trials. (Alternatively, place the handout on an overhead projector.)

b. Ask the students to look over the handout and jot down answers to the following questions:



i. What is the purpose of each of these trials?
ii. Would you consider participating in one of these trials, if you met the requirements? Why?
iii. Would you do it if you got paid?
iv. What questions would you want to ask the researchers before you agreed to participate?
v. Would you be interested in the results of any of these trials? Why?

II. Explore (this activity may also be assigned as individual or group homework) (45 minutes)

a. Divide students into small groups and provide each group with copies of the attached "Exploration Activity" handout — "Childhood-onset Growth Hormone Deficiency" and the attached "FAQ and Glossary" handout — "Understanding Clinical Trials" (or direct them to the ClinicalTrials.gov website).

b. Ask students to complete the "Student Activities" section of the "Exploration Activity" handout.

III. Explain (15 minutes)

a. Students share the answers to the "Student Activities" section of the "Exploration Activity" handout with the entire class.

IV. Elaborate (homework) – choose a or b
   a. Students may locate 2 additional clinical trial descriptions from either the unchealthcare.org website (clinical trials are listed under "Health & Patient Care") or the ClinicalTrials.gov website, and use the descriptions to answer questions 2, 3, and 4 from the "Student Activities" section of the "Exploration Activity" handout.
   b. Using the "Childhood-onset Growth Hormone Deficiency" as a model, students devise their own proposed clinical trial. They, of course, will not conduct this trial but will outline the protocol, exclusion/inclusion criteria, time-line and include a description of the proposed trial. Suggestions for possible trials:
      i. The effect of video games on violence in teenagers
      ii. The effect of fast food advertising on teenage food purchases
      iii. The correlations between wearing sandals and blistered and calloused feet

V. Evaluate
   a. Teachers may choose to evaluate students based on class participation and completion of the homework assignment(s)

ENGAGEMENT ACTIVITY

Think You Might Have Gum Disease?

RESEARCH PATIENTS NEEDED

UNC Center for Inflammatory Disorders
-and-
UNC Center for Oral and Systemic Diseases

Male and female subjects with periodontal (gum) disease are needed for a clinical research study. This study will assess the effect of gum treatments on general health. Eligible subjects will receive certain treatments at reduced fees or no charge.

For information please call or e-mail the
UNC School of Dentistry GO Health Center.

Lung study

Do you currently smoke cigarettes?

Have you quit smoking, but smoked for at least 10 years?

The Center of Environmental Medicine at UNC is looking for individuals for a research study. This study involves 1 visit and a total of 1½ hours of your time.

You will be reimbursed for completion of the study. If you participate, you will have a breathing test and learn more about your lungs. Participants that are interested in quitting smoking will be given information and guidance to help them quit.

Genetic Study of Anorexia Nervosa in Families

We are seeking families with at least two members who have or had anorexia nervosa, and who would be willing to participate. Experts from around the world are working to help identify the genes that might predispose individuals to develop anorexia nervosa.

UNC Eating Disorders Program

African American Couples Needed for a Research Study

If you have been living with your partner for at least 9 months, are not taking anti-hypertensive or anti-depressant medications, are between the ages of 18 and 50, and are willing to have blood samples and blood pressure taken, then you may qualify for a study about the benefits of partner relationships.

Receive up to $200 per couple for completion of 2 lab visits.

If interested, please call the UNC
Stress and Health Research Program.

All advertisements on this page were retrieved on April 27, 2005, from unchealthcare.org

UNDERSTANDING CLINICAL TRIALS

FREQUENTLY ASKED QUESTIONS

What is a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

A clinical trial is an experimental research study that evaluates the effect of a new drug or medical device on human beings. Clinical research is a process of discovery that is intended to improve medical care. Researchers attempt to answer questions such as "Which medication works better?" or "What is the best way to treat a medical problem?"

Who can participate in a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

All participants in a clinical trial are volunteers who have agreed to participate in a particular study. Some volunteers seek out clinical trials, and some are referred to clinical trial opportunities by their physicians. There are research opportunities in clinical trials for persons with specific diseases and conditions and for persons in generally good health. Volunteers participating in a study are referred to as "subjects" or "participants." Volunteers can leave a study at any time for any reason.

What are the benefits and risks of participating in a clinical trial? (*from* ClinicalTrials.gov)

Benefits

• Play an active role in personal health care.
• Gain access to new research treatments before they are widely available.
• Obtain expert medical care at leading health care facilities during the trial.
• Help others by contributing to medical research.

Risks

• There may be unpleasant, serious or even life-threatening side effects to experimental treatment.
• The experimental treatment may not work for the participant.
• The trial may require more time and attention than standard treatment, including trips to the study site, more treatments, hospital stays or complex requirements.
• The participant may be placed in the "placebo" group

How is the safety of the participant protected? (*from* ClinicalTrials.gov)

The ethical and legal codes that govern medical practice also apply to clinical trials. In addition, most clinical research is federally regulated with built in safeguards to protect the participants. The trial follows a carefully controlled protocol, a study plan which details what researchers will do in the study. As a clinical trial progresses, researchers report the results of the trial at scientific meetings, to medical journals, and to various government agencies. Individual participants' names remain secret and are not mentioned in these reports.

Every clinical trial in the U.S. must be approved and monitored by an Institutional Review Board (IRB) to make sure the risks are as low as possible and are worth any potential benefits. An IRB is an independent committee of physicians, statisticians, community advocates, and others that ensures that a clinical trial is ethical and the rights of study participants are protected.

What should people consider before participating in a trial? (*from* ClinicalTrials.gov)

People should know as much as possible about the clinical trial and feel comfortable asking the members of the health care team questions about it, the care expected while in a trial, and the cost of the trial. The following questions might be helpful for the participant to discuss with the health care team.

• What is the purpose of the study?
• Who is going to be in the study?
• Why do researchers believe the experimental treatment being tested may be effective? Has it been tested before?
• What kinds of tests and experimental treatments are involved?
• How do the possible risks, side effects, and benefits in the study compare with my current treatment?
• How might this trial affect my daily life?
• How long will the trial last?
• Will hospitalization be required?
• Who will pay for the experimental treatment?
• Will I be reimbursed for other expenses?
• What type of long-term follow up care is part of this study?
• How will I know that the experimental treatment is working?
• Will results of the trials be provided to me?
• Who will be in charge of my care?
• What happens if I'm injured because of the study?

GLOSSARY

Blind — A clinical trial is "Blind" if participants are unaware on whether they are in the experimental or control arm of the study; also called masked.

Control group — In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo (See Placebo).

Double-blind study — A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study.

Efficacy — The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.

Expanded access — Refers to any of the FDA procedures that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

Food and Drug Administration (FDA) — The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices. The FDA also works with the blood banking industry to safeguard the nation's blood supply.

Inclusion/exclusion Criteria — The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are often based on age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

Informed consent — The process of learning the key facts about a clinical trial before deciding whether or not to participate. It is also a continuing process throughout the study to provide information for participants.

Peer review — Review of a clinical trial by experts chosen by the study sponsor. These experts review the trials for scientific merit, participant safety, and ethical considerations.

Phase I trials — Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients.

Phase II trials — Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.

Phase III trials — Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labeling.

Phase IV trials — Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

Placebo — An inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment. No sick participant receives a placebo if there is a known beneficial treatment.

Protocol — A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Randomized trial — A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial.

Single-blind study — A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study.

Information on this page was retrieved on April 28, 2005, from the National Library of Medicine's website, ***ClinicalTrials.gov.***

EXPLORATION ACTIVITY: COOL.CLICK™ ADOLESCENT TRANSITION STUDY: STUDY OF SAIZEN® IN SUBJECTS WITH CHILDHOOD-ONSET GROWTH HORMONE DEFICIENCY

This study is currently recruiting patients.

Sponsored by:	Serono
Information provided by:	Serono

PURPOSE

The primary objective is to evaluate the efficacy and safety of two different dose regimens of r-hGH (Saizen®) in subjects with childhood-onset growth hormone deficiency (COGHD) during the transition phase from childhood to adulthood.

Condition	Treatment or Intervention	Phase
Childhood-onset growth hormone deficiency Pituitary Dwarfism	Drug: Saizen®	Phase III

- Study type: Interventional
- Study design: , Randomized, Open Label, Dose Comparison, Single Group Assignment, Efficacy Study
- Official title: A Phase IIIb, Prospective, Multi-center, Randomized, Open-label Study to Determine the Safety and Efficacy of Two Different Dosing Regimens of Saizen® (recombinant human growth hormone (r-hGH), using cool.click™ in Subjects with Childhood-onset Growth Hormone Deficiency during the Adolescent Transition Phase (CATS)

Further Study Details:

- Primary outcomes: Increase in percent of trunk fat in COGHD
- Secondary outcomes: Changes in lean body mass and body composition parameters
- Expected total enrollment: 60
- Study start: August 2004; Expected completion: August 2006
- Last follow-up: July 2006; Data entry closure: July 2006

This is a phase IIIb, prospective, multi-center, randomized, open label study to determine the safety and efficacy of two different dose regimens of r-hGH with a dose escalation scheme. Screening assessments must be completed 30 days prior to SD1 (Study Day 1). Eligible subjects ages 13 to 21 years will be randomized in equal allocation in a 1:1 ratio to one of two treatment groups (30 subjects/group). Daily subcutaneous injections will be self-administered or received from a designated individual using cool.click™, the needle-free growth hormone (GH) delivery device. The study consists of three periods: screening (up to 30 days prior to Study Day 1), active treatment (up to 24 weeks), and follow-up (4 week safety evaluation after the last dose of study medication).

Each subject will be required to complete a daily treatment diary to assess dosing compliance, adverse events, and concomitant medications. Each subject will receive one treatment diary at SD1, weeks 8, 12, and 24. Subjects will be required to record daily diary entries that will capture dosing compliance, adverse events, and concomitant medications. Depending upon treatment allocation and subject tolerability, dose titration will be increased as follows:

- Group A: 0.005 mg/kg/day for 30 days then increasing, with the Investigator's approval, to 0.010 mg/kg/day from day 31 to week 24.
- Group B: 0.010 mg/kg/day for 14 days with the opportunity to dose escalate, with the Investigator's approval, on day 15 to 0.02 mg/kg/day and day 30 to 0.03 mg/kg/day.

Scheduled study visits include screening, baseline, and weeks 8, 12, and 24. Dosage adjustments will be based on subject tolerability and telephone assessments from study drug initiation through week 6. Trunk fat will be measured at SD1, weeks 12 and 24 (or early termination visit). Routine clinical laboratory assessments (hematology, blood chemistries, and urinalysis) will be performed pre-treatment (-30 to -1 SD1) and post-treatment on week 24 (or early termination visit). Special laboratory assessments include the central analysis of lipid panel, fasting insulin, fasting glucose, IGF-I, IGFBP-3, free T4 , total T4, CRP. Physical exams will be performed at screening, weeks 12 and 24. Safety evaluations will occur during scheduled study visits, through telephone assessments, and by the review of adverse events and concomitant events on the subject treatment diary.

ELIGIBILITY

Ages Eligible for Study: 3 Years-21 Years

Genders Eligible for Study: Both

Inclusion Criteria:

The day of entry or Study Day 1 is defined as the first day of study treatment. To be eligible for inclusion into this study, the subjects must fulfill all of the following criteria within 30 days prior to Study Day 1.

- Male or female from 13 to 21 years of age, inclusive
- Diagnosis of childhood onset GH deficiency and prior completed GH treatment as evidenced by bone age greater than 14 years for girls and 16 years for boys or no height increase > 0.5 cm in the 6 months prior to SD1.
- Have documented GH deficiency (acquired or idiopathic), established by a standard provocative test, such as insulin (<5 ng/mL) or growth hormone releasing hormone plus arginine (<9 ng/mL) within the past 6 months.
- If hypopituitary, must have been on adequate replacement therapy (if required) of glucocorticosteroids, thyroid and sex hormones (hormone levels on replacement being in normal/mildly elevated range) for at least 6 months prior to study entry.
- Be willing and able to comply with the protocol for the duration of the study.
- Have given written informed consent before any study-related procedure not part of the subject's normal medical care, with the understanding that the subject may withdraw consent at any time without prejudice to future medical care.
- Female subjects of childbearing potential must use a hormonal contraceptive, intra-uterine device, diaphragm with spermicide or condom with spermicide for the duration of the study. Confirmation that a female patient is not pregnant must be established by a negative hCG pregnancy test (urine or serum) within 7 days of study enrolment (SD1).

Exclusion Criteria:

To be eligible for inclusion in this study the subjects must not meet any of the following criteria:

- Known allergy or hypersensitivity to growth hormone or diluent.
- Previous treatment with GH within six months prior to study entry.
- Severe illness during the previous six months.
- Active malignancy (except non-melanomatous skin malignancies).
- Diabetes mellitus (type I or II).
- Seropositivity for human immunodeficiency virus (HIV), Hepatitis B surface antigen (HbsAg) and/or Hepatitis C Virus (HCV) serology.
- Pregnancy or lactation.
- History of drug and/or alcohol abuse or use of drugs for non-therapeutic purposes.
- Any medical condition that, in the opinion of the Investigator, would jeopardize the patient's safety following exposure to study drug.
- Clinically significant abnormal hematology, chemistry or urinalysis results at screening in the judgment of the Investigator.
- Have taken another investigational drug or had any experimental procedure in the six months preceding study entry.

ClinicalTrials.gov processed this record on 2005-06-07

STUDENT ACTIVITIES

1. Visit the "Resources" page of ClinicalTrials.gov, and click on "Glossary of Clinical Trial Terms" (or, use the handout provided by your teacher). Using this glossary, write down definitions for the three words underlined on page 1 of this handout.

2. Additionally, write down definitions for each of the following words
   a. Inclusion/Exclusion Criteria

   b. Protocol

3. Answer the following questions:
   a. What are the inclusion criteria for this study?

   b. What are the exclusion criteria?

   c. Who is sponsoring this trial?

   d. What is the trial's protocol?

   e. Why is protocol important?

4. On the front of the "Understanding Clinical Trials" handout, there is a list of questions that people should consider before participating in a clinical trial. Read over this list. (On the website, this list is under the question "What should people consider before participating in a trial?")
   a. Using the information provided in the description of the "Childhood-onset Growth Hormone Deficiency" clinical trial, answer the list of questions that people should consider before participating in a clinical trial.

   b. What questions can you not answer?

   c. What could you do to find the answers?

5. What are the possible benefits of conducting this trial, both to the participants and to the general public?

Technology and Global Connections: The Green Revolution and World Hunger

I. Class Discussion: As a class, discuss the two attached articles from the International Food Policy Research Institute: "Green Revolution: Curse or Blessing?" and "Biotechnology, Trade, and Hunger."

II. Class Assignment: Divide students into a "pro" and "con" group to research and debate the potential benefits and risks of genetically modified (GM) crops. Provide a list of benefits and risks for students to elaborate upon.

a. Potential Benefits
   i. Pest Resistant Plants
   ii. Hardier Plants
   iii. Better Nutrition (golden rice)
   iv. Handling – delayed ripening and post-harvest pest resistance
   v. Safety – less pesticides, reduced allergens and toxins

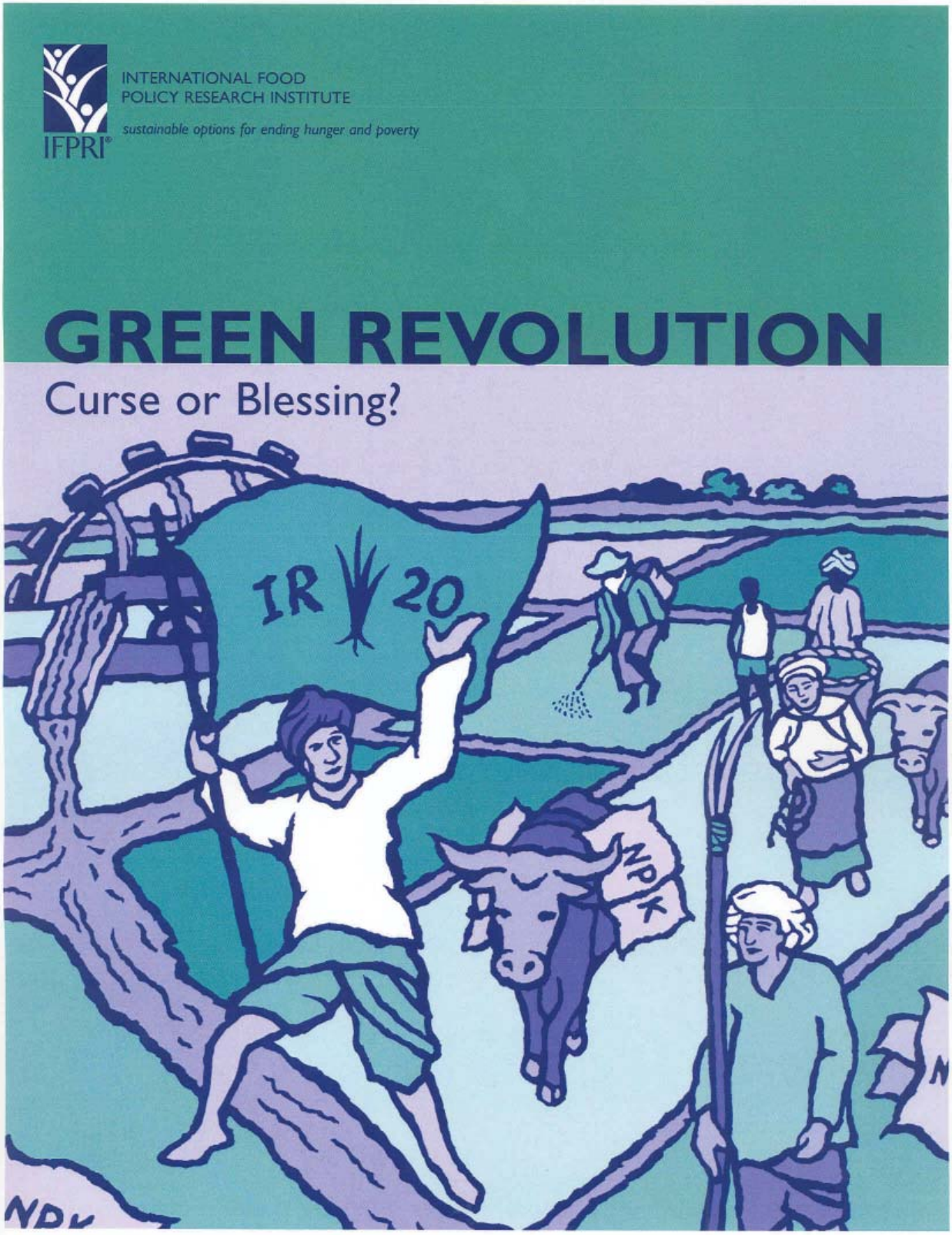
b. Potential Risks
   i. Environmental Risks
   ii. Human Health Risks
   iii. Loss of Biodiversity
   iv. Land Degradation
   v. Fossil Fuel Dependence

c. Sources for Research
   i. Pan American Health Organization: Battling over Biotechnology (pro-GM foods) – http://www.paho.org/English/DD/PIN/Number18_article3.htm
   ii. Pew Initiative on Food and Biotechnology (neutral) – http://pewagbiotech.org
   iii. Biotechnology Industry Organization (pro-GM foods) – http://www.bio.org/foodag/
   iv. Food First: Lessons from the Green Revolution (anti-GM foods) – http://www.foodfirst.org/media/opeds/2000/4-greenrev.html
   v. Slow Food: Manifesto on Biotechnologies (anti-GM foods) – http://www.foodfirst.org/media/opeds/2000/4-greenrev.html

III. Classroom Debate (approximately 1 hour)
   i. One team member will present a short introduction to the topic.
   ii. Each member of the team will present 2-3 minutes.
   iii. One team member will then present a summary of the position's key points.
   iv. After the team has presented, members of the opposing team will ask questions based on the positions presented.
   v. The team will then respond to questions presented by opposing team.
   vi. Items 1-5 will be repeated for the opposing team.

IV. Final Reflection
   i. Discuss the final sentence from "Biotechnology, Trade, and Hunger" as a class: "To achieve food security for the entire world population, countries must work to reduce poverty and achieve a more equitable distribution of income – tasks that technology alone can only support, not achieve."
   ii. Ask students to address this sentence by writing a research paper on a particular country (India, China, country in South America or Africa) or by writing a reflective essay.

J. Shelton Murphy



Food problems have haunted mankind since time immemorial. With few technological breakthroughs to increase yields, the food needs of growing populations were historically met by expanding the cultivated area. As the most fertile land became scarce, further expansion meant bringing poorer and lower-yielding land into cultivation. By the 19th century, there was growing pessimism about the possibility of feeding ever-growing populations, as exemplified in the writings of Thomas Malthus (1766–1834). The task seemed even more daunting as advances in medicine and public health led to longer life expectancies and more children born.

In the 20th century, massive public investments in modern scientific research for agriculture led to dramatic yield breakthroughs in the industrial countries. The story of English wheat is typical. It took nearly 1,000 years for wheat yields to increase from 0.5 to 2 metric tons per hectare, but only 40 years to climb from 2 to 6 metric tons per hectare. Modern plant breeding, improved agronomy, and the development of inorganic fertilizers and modern pesticides fueled these advances. Most industrial countries achieved sustained food surpluses by the second half of the 20th century, and eliminated the threat of starvation.

These advances were much slower in reaching developing countries. The colonial powers invested little in the food production systems of these countries, and by independence, their populations were growing at historically high rates. By the mid-1960s, hunger and malnutrition were widespread, especially in Asia, which increasingly depended on food aid from rich countries. Back-to-back droughts in India during the mid-1960s made the already precarious situation worse, and a 1967 report of the U.S. President's Science Advisory Committee concluded that "the scale, severity and duration of the world food problem are so great that a massive, long-range, innovative effort unprecedented in human history will be required to master it."

In response, the Rockefeller and Ford foundations took the lead in establishing an international agricultural research system to help transfer and adapt scientific advances to the conditions in developing countries. The first investments were in research on rice and wheat, two of the most important food crops for developing countries. The breeding of improved varieties, combined with the expanded use of fertilizers, other chemical inputs, and irrigation, led to dramatic yield increases in Asia and Latin America, beginning in the late 1960s. In 1968, U.S. Agency for International Development (USAID) Administrator William S. Gaud coined the term "Green Revolution" to describe this phenomenal growth in agriculture.

To achieve higher yields for rice and wheat, scientists needed to develop plants that were more responsive to plant nutrients and that had shorter, stiffer straw to support the weight of heavier heads of grain. They also needed to develop varieties that could mature quicker and grow at any time of the year, thereby permitting farmers to grow more crops each year on the same land. New varieties also needed to be resistant to major pests and diseases, which flourish under intensive farming conditions, and to retain desirable cooking and consumption traits.

Borrowing from rice-breeding work undertaken in China, Japan, and Taiwan, the International Rice Research Institute (IRRI) in the Philippines developed semi-dwarf varieties that met most of these requirements. Similar achievements were made for wheat after Norman Borlaug (later awarded the Nobel Peace Prize for his work) crossed Japanese semi-dwarf varieties with Mexican wheats at what is now known as the International Center for Maize and Wheat Improvement (CIMMYT) in Mexico.

Although the term Green Revolution originally described developments for rice and wheat, high-yielding varieties (HYVs) have since been developed for other major food crops important to developing countries, including sorghum, millet, maize, cassava, and beans. Moreover, a full-fledged system of international agricultural research centers now works on many aspects of developing-country agriculture (the Future Harvest Centers that make up the Consultative Group on International Agricultural Research).

IMPACTS ON AGRICULTURAL PRODUCTION

The adoption of HYVs occurred quickly. By 1970, about 20 percent of the wheat area and 30 percent of the rice area in developing countries were planted to HYVs, and by 1990, the share had increased to about 70 percent for both crops. Yields of rice and wheat virtually doubled. Higher yields and profitability also led farmers to increase the area of rice and wheat they grew at the expense of other crops. And with faster-growing varieties and irrigation, they grew more crops on their land each year. These changes more than doubled cereal production in Asia between 1970 and 1995, while population

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increased by 60 percent. Instead of widespread famine, cereal and calorie availability per person increased by nearly 30 percent, and wheat and rice became cheaper.

Latin America experienced significant gains as well, but the impact in Sub-Saharan Africa was much more modest. Poor infrastructure, high transport costs, limited investment in irrigation, and pricing and marketing policies that penalized farmers made the Green Revolution technologies too expensive or inappropriate for much of Africa.

SOCIAL IMPACTS

The Green Revolution led to sizable increases in returns to land, and hence raised farmers' incomes. Moreover, with greater income to spend, new needs for farm inputs, and milling and marketing services, farm families led a general increase in demand for goods and services. This stimulated the rural nonfarm economy, which in turn grew and generated significant new income and employment of its own. Real per capita incomes almost doubled in Asia between 1970 and 1995, and poverty declined from nearly three out of every five Asians in 1975 to less than one in three by 1995. The absolute number of poor people fell from 1.15 billion in 1975 to 825 million in 1995 despite a 60 percent increase in population. In India, the percentage of the rural population living below the poverty line fluctuated between 50 and 65 percent before the mid-1960s but then declined steadily to about one-third of the rural population by 1993. Research studies show that much of this steady decline in poverty is attributable to agricultural growth and associated declines in food prices.

The Green Revolution also contributed to better nutrition by raising incomes and reducing prices, which permitted people to consume more calories and a more diversified diet. Big increases occurred in per capita consumption of vegetable oils, fruits, vegetables, and livestock products in Asia.

PROBLEMS WITH THE GREEN REVOLUTION

A revolution of this magnitude was bound to create some problems of its own. Critics charged that the Green Revolution resulted in environmental degradation and increased income inequality, inequitable asset distribution, and worsened absolute poverty. Some of these criticisms are valid and have been or still need to be addressed. But there is a tendency today to overstate the problems and to ignore the appropriate counterfactual situation: what would have been the magnitude of hunger and poverty without the yield increases of the Green Revolution and with the same population growth?

The Green Revolution in Asia stimulated a large body of empirical literature on how agricultural technological change affects poor farmers. Critics of the Green Revolution argued that owners of large farms were the main adopters of the new technologies because of their better access to irrigation water, fertilizers, seeds, and credit. Small farmers were either unaffected or harmed because the Green Revolution resulted in lower product prices, higher input prices, and efforts by landlords to increase rents or force tenants off the land. Critics also argued that the Green Revolution encouraged unnecessary mechanization, thereby pushing down rural wages and employment. Although a number of village and household studies conducted soon after the release of Green Revolution technologies lent some support to early critics, more recent evidence shows mixed outcomes. Small farmers did lag behind large farmers in adopting Green Revolution technologies, yet many of them eventually did so. Many of these small-farm adopters benefited from increased production, greater employment opportunities, and higher wages in the agricultural and nonfarm sectors. Moreover, most smallholders were able to keep their land and experienced significant increases in total production. In some cases, small farmers and landless laborers actually ended up gaining proportionally more income than larger farmers, resulting in a net improvement in the distribution of village income.

Development practitioners now have a better understanding of the conditions under which the Green Revolution and similar yield-enhancing technologies are likely to have equitable benefits among farmers. These conditions include: (1) a scale-neutral technology package that can be profitably adopted on farms of all sizes; (2) an equitable distribution of land with secure ownership or tenancy rights; (3) efficient input, credit, and product markets so that farms of all sizes have access to modern farm inputs and information and are able to receive similar prices for their products; and (4) policies that do not discriminate against small farms and landless laborers (for instance, no subsidies on mechanization and no scale biases in agricultural research and extension). These conditions are not easy to meet. Typically, governments must make a concerted effort to ensure that small farmers have fair access to land, knowledge, and modern inputs.

Another shortcoming of the Green Revolution was that it spread only in irrigated and high-potential rainfed areas, and many villages or regions without access to sufficient water were left out. Although evidence suggests that even in these cases villagers obtained important indirect benefits through increased employment and migration opportunities and cheaper food, the benefits were rarely sufficient to prevent further widening of income gaps. In India, for example, poverty in many low-potential rainfed areas has improved little even while irrigated and high-potential rainfed areas have progressed. Regional inequalities have worsened in China as well.

The Green Revolution has also been widely criticized for causing environmental damage. Excessive and inappropriate use of fertilizers and pesticides has polluted waterways, poisoned agricultural workers, and killed beneficial insects and other wildlife. Irrigation practices have led to salt build-up and eventual abandonment of some of the best farming lands. Groundwater levels are retreating in areas where more water is being pumped for irrigation than can be replenished by the rains. And heavy dependence on a few major cereal varieties has led to loss of biodiversity on farms. Some of these outcomes were inevitable as millions of largely illiterate farmers began to use modern inputs for the first time, but inadequate extension and training, an absence of effective regulation of water quality, and input pricing and subsidy policies that made modern inputs too cheap and encouraged excessive use also created negative environmental impacts. These problems are slowly being rectified without yield loss, and sometimes with yield increases, thanks to policy reforms and improved technologies and management practices, such as pest-resistant varieties, biological pest control, precision farming, and crop diversification.

Often ignored, however, is the positive impact of higher yields in saving huge areas of forest and other environmentally fragile lands that would otherwise have been needed for farming. In Asia cereal production doubled between 1970 and 1975, yet the total land area cultivated with cereals increased by only 4 percent.

Conclusions

Overall, the Green Revolution was a major achievement for many developing countries and gave them an unprecedented level of national food security. It represented the successful adaptation and transfer of the same scientific revolution in agriculture that the industrial countries had already appropriated for themselves. The Green Revolution also lifted large numbers of poor people out of poverty and helped many nonpoor people avoid the poverty and hunger they would have experienced had the Green Revolution not occurred. The largest benefits to the poor were mostly indirect, in the form of lower food prices, increased migration opportunities, and greater employment in the rural nonfarm economy. The direct benefits to the poor through their own on-farm adoption, greater agricultural employment, and empowerment have been more mixed and depend heavily on local socioeconomic conditions. In many cases inequalities between regions and communities that adopted Green Revolution technologies and those that did not also worsened. At the same time, the Green Revolution had many negative environmental impacts that have still to be adequately redressed.

Agricultural research remains a potent force for good in the developing world and is the key to increasing yields further to meet the continuing growth of food needs in developing countries. This need is especially urgent in Sub-Saharan Africa, which has yet to experience an agricultural revolution of its own. But simply adding to the pile of food will not be enough. The indirect benefits for the poor are likely to be weaker in the future as globalization and trade make food prices less responsive to local production and as agriculture becomes less important to the livelihoods of the poor. Policymakers will need to target the poor more precisely to ensure that poor people receive greater direct benefits from new technologies. New technologies will also need to be more environmentally sustainable. By building on the strengths of the Green Revolution while seeking to avoid its weaknesses, scientists and policymakers can take significant steps toward achieving sustainable food security for all the world's people.

Further Reading

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This brief is a slightly altered version of an article by Peter B.R. Hazell that will appear in J. Mokyr, ed., *The Oxford Encyclopedia of Economic History* (Oxford University Press, forthcoming in 2003).

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Biotechnology and Genetic Resource Policies

Brief 2, January 2003

BIOTECHNOLOGY, TRADE, AND HUNGER

Eugenio Díaz-Bonilla and Sherman Robinson

About the Authors

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Demographers predict that the world population will stabilize some time in the second half of the 21st century. Projections by IFPRI and others show that agricultural productivity can grow fast enough to sustain the world's population, if new technologies are pursued. But there is more to feeding the world than making sure agricultural productivity stays ahead of population growth. International trade will also play a large role. Projections reveal that regions such as Africa will import a larger share of their food requirements in the future. At the same time, regions with a strong comparative advantage in agriculture will produce the additional food needed by the world.

But the new genetic modification (GM) technologies that many expect will help the world meet its food needs—not only through quantity, but nutritional quality as well—raise critical issues for international trade, including this key question: What will happen if pressure from consumers and environmentalists in the developed world leads to a new generation of trade restrictions, or to the segmentation of GM-food product markets, as appears to be happening in Europe and Japan? An answer to this question requires a brief look at agricultural trade and involves both legal and economic analysis.

Agriculture and International Trade

Currently, a large share of agricultural production is consumed in the producing countries. This is true despite major grain and oilseed exports from countries such as Argentina, Australia, Canada, and the United States, and even after accounting for major export crops such as coffee, tea, cocoa, and sugar. IFPRI and others, however, forecast a growing role for international agricultural trade in the 21st century.

There is likely to be increasing specialization in agricultural production, with more exports from countries that specialize in particular types of agriculture. Many developing countries may well hold a comparative advantage in producing high-value, labor-intensive specialty crops and horticulture, while land-abundant countries may be better at producing bulk goods such as wheat, maize, and soybeans. Research indicates that it is neither efficient nor environmentally sound for developing countries to seek food security by becoming self-sufficient in the production of food crops, particularly when such production involves inefficient, unsustainable methods on fragile lands.

GM technologies may facilitate increased specialization, while also boosting local food production and improving food security through the development of plant varieties specifically tailored to particular agroecological environments. Although the technologies have the potential to affect both traded and nontraded products, most applications to date have involved highly traded agricultural commodities.

To benefit from increases in agricultural productivity, developing countries have an enormous interest in being able to market their goods in developed countries. The world agricultural trading system is still dominated by developed countries with protected markets and domestic subsidy programs that ultimately distort international markets and potentially increase price volatility, to the detriment of developing countries.

Major goals of developing countries in the new round of World Trade Organization (WTO) trade talks should include opening markets in developed countries for their agricultural exports, including high-value, labor-intensive commodities, and reducing or preferably eliminating trade-distorting domestic policies in developed countries—especially export subsidies and price supports.

While these goals appear desirable, the picture is complicated by the possible impact of consumer and environmental concerns, particularly within developed countries, on the development of biotechnology. To consumers in high-income countries, the price-reduction benefits from biotechnology seem minor, while the unknown dangers are magnified by lack of information and mistrust in the ability of their governments to regulate the safety of the food supply.

A ban on GM products in developed countries, based on domestic consumer and environmental concerns, not only would affect market access but could also make it more difficult for developing countries to gain financial support from industrialized nations to conduct research and build human capital for biotechnology activities. Another possibility is that consumer and environmental concerns could spill over into developing countries and block or slow the development of biotechnology in those countries.

International Legal Issues

Any attempt to limit trade in GM products must be compatible with existing international legal agreements. There are only a few agreements (including environmental treaties) setting out the WTO legal framework regarding trade in GM products. These include the Sanitary and Phytosanitary (SPS) Agreement and the Agreement on Technical Barriers to Trade (TBT) of the WTO as well as a multilateral environmental agreement, the Convention on Biological Diversity, and particularly its Cartagena Protocol on Biosafety.

The question is what role these legal agreements may play in either keeping open or closing the opportunities offered by GM products. The international system is clearly under stress in this area, with growing tensions between the need for fairness in international trade and the need to respond to domestic concerns about food and environmental safety.

The Sanitary and Phytosanitary Agreement, which concerns food safety and animal and plant health, says that WTO members have "the right to take sanitary and phytosanitary measures necessary for the protection of human, animal or plant life or health." But those measures must be applied "only to the extent necessary to protect human, animal or plant life or health" and must be "based on scientific principles." The agreement also states that WTO members must "ensure that their SPS measures do not arbitrarily or unjustifiably discriminate between Members where identical or similar conditions prevail, including between their own territory and that of other Members" and, furthermore, that those measures "shall not be applied in a manner which would constitute a disguised restriction on international trade." In addition, the agreement suggests the use of international standards when possible.

The goal of all these regulations phrased in legal language is to allow countries to maintain standards of food safety but to prevent them from doing so in a way that unfairly discriminates against foreign suppliers.

The difficulty with GM products is that there are as yet no international food safety standards that really apply to them. The Codex Alimentarius defines international standards of food safety, but it does not yet specifically address GM products. Although the countries participating in the Codex are currently discussing adequate standards for GM products, a possible agreement is still some years away.

In the absence of agreed-upon international standards, some countries invoke the "precautionary principle" that allows them to set standards provisionally where relevant scientific evidence is lacking, although they are supposed to do the necessary research within a reasonable period of time. Other countries argue that the precautionary principle is being abused in order to protect less-efficient domestic producers from foreign competition. Again, the challenge lies in adequately addressing both safety concerns and fairness in trade. Currently, a review of available scientific evidence indicates that GM foods have not been found

to be unsafe—a double negative that highlights the difficulties of balancing consumer concerns, science, and international law. Proponents of GM products correctly argue that research has shown no health risks, while opponents argue that such research is not enough to prove that there are no such risks.

The basic issue continues to be market uncertainty about how consumers, mostly in developed countries, will react to GM foods. Regardless of the science, if consumers decide they do not want to consume GM goods, markets will adjust to satisfy their demands. If these negative reactions persist, markets will adjust to different scenarios of prohibition, market segmentation, and product differentiation. These market adjustments in developed countries will have an impact on developing countries.

The Economics of GM Trade

What will happen if consumers in developed countries refuse to consume GM commodities? Can world markets adjust to a complete segmentation of the markets for GM and non-GM commodities? Will developing countries still benefit from these new technologies if world markets are completely segmented and if, in addition, some developed countries refuse to adopt the new technologies at all? To provide tentative answers to these questions, IFPRI has undertaken research jointly with the Danish Institute of Agriculture, Forestry, and Fisheries Economics. Using multicountry models of world trade focused on agriculture, the research analyzes the price, production, and trade consequences of changing consumer preferences regarding the use of GM organisms in food production.

In the world model, the two primary GM crops, soybeans and maize, are specified as either GM or non-GM. This GM and non-GM split is maintained throughout the entire processing chain: GM livestock and GM food processing industries use only GM intermediate inputs; likewise, non-GM livestock and non-GM food-processing industries use only non-GM intermediate inputs. The underlying assumptions in the model are that developing countries will adopt the new technologies, to varying degrees, and that countries such as the United States will continue to use them, while Europe and Japan will not adopt them and will restrict their demand for such goods. The issue is which countries, if any, would benefit from the new technologies, to varying degrees, given the growing segmentation of the markets.

The empirical results show that global markets are able to adjust to this segregation in the sense that non-GM exports are diverted to the GM-intolerant regions, while GM exports are diverted to the indifferent regions. Price differentials are significant but tempered by commodity arbitrage. In particular, in certain GM-favorable regions, the prices of the non-GM varieties also decline because of the high degree of substitutability between the GM and non-GM varieties in domestic use and increased production of non-GM varieties to supply GM-intolerant consumers. The market results are analogous to what one would expect from increased consumer preferences in developed countries for organic foods. Such foods are more expensive to produce and command higher prices in the market. There is a gap between prices for organic and other foods, which ultimately reflects cost differences in their production and distribution. Similarly, price differentials between GM and non-GM commodities will reflect their different costs of production and distribution, with consumers who are indifferent benefiting from access to cheaper goods they find to be equivalent to non-GM goods and producers benefiting from the higher productivity of GM crops.

An important finding of this empirical analysis is that the developing countries are also responsive to GM preference changes and redirect their trade flows among partners accordingly. Furthermore, given the existing bilateral trade patterns for these particular crops, the price wedges that arise in the developing countries mainly reflect productivity differences, not preference changes in the developed world. Overall, the regions most receptive to the productivity-enhancing technology gain most, including developing countries that adopt the new technologies.

Appropriate Technology Is a First Step in Feeding the Hungry

The development of GM technology appears to hold great promise, with the potential to complement other, more traditional research methods as the new driving force for sustained agricultural productivity growth in the 21st century. Such agricultural productivity growth is crucial if the world is to produce

enough food to provide for what is likely to be a stable but large world population in this century. At this point, the many problems and concerns surrounding the new GM technologies do not seem insurmountable, just very difficult.

A world with an adequate supply of food is clearly more desirable than a Malthusian world in which food is scarce, food prices are high and rising, and people are in conflict over scarcity. Providing an adequate aggregate food supply will not eliminate malnutrition and hunger, however, now or in the future. To do that requires much more. To achieve food security for the entire world population, countries must work to reduce poverty and achieve a more equitable distribution of income—tasks that technology alone can only support, not achieve.

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