Subject Area(s)
Biology

Associated Unit
None

Lesson Title
Genetic Decoding for Gene Therapy

Header

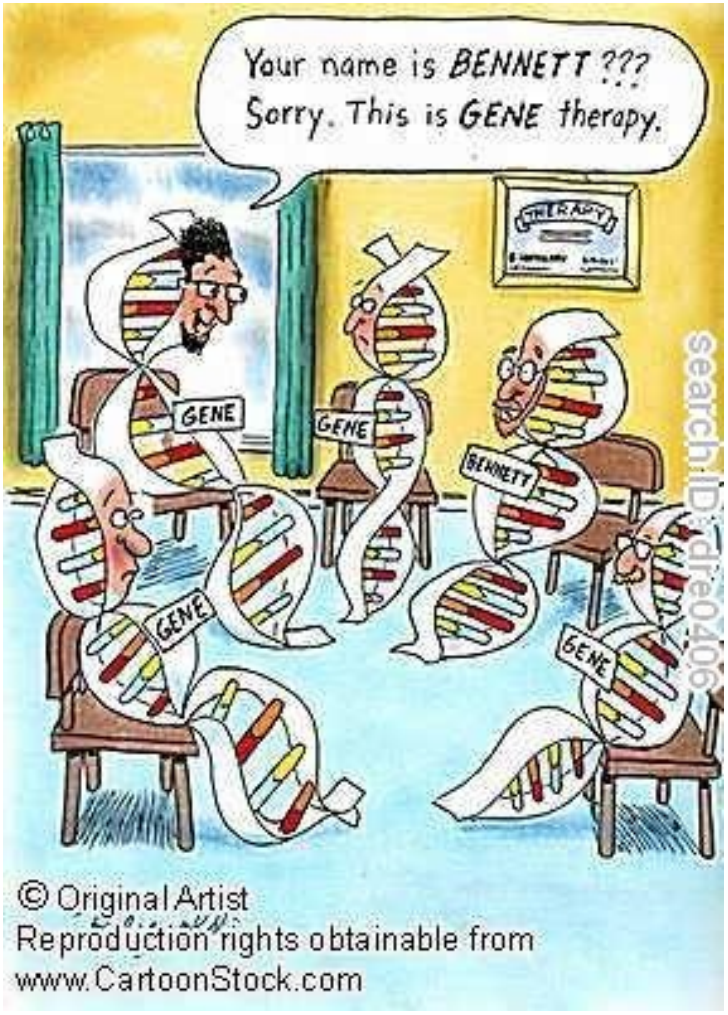

Image 1

ADA Description: Comic cartoon showing a doctor's waiting room with six people, five of which named Gene and one named Bennett.

Caption: Gene therapy

Image file: therapy_cartoon.jpg

Source/Rights: Copyright © CartoonStock.com (http://www.cartoonstock.com/directory/g/gene_therapy.asp)

Grade Level 10 (9-12)

Lesson # __ of __

Lesson Dependency
None

Time Required
50 minutes

Summary
The study of genes and their functions has the potential to reveal the initiation mechanism of a wide variety of diseases that are associated with defective genes. As genes are made up of tens of thousands of nucleotide bases (adenine (A), thymine (T), cytosine (C), guanine(G)) arranged in a particular order, decoding the entire sequence that defines a particular gene can be daunting task that requires a large amount of time. New techniques such as the DNA microarray allow for the rapid sequencing of genes and are based on recent advancements in nanotechnology fabrication. This lesson introduces students to the concept of rapid DNA sequencing using the DNA microarray and DNA hybridization. The activity associated with this lesson is based on an online interactive demonstration showing the steps involved in the DNA microarray analysis.

Engineering Connection
Chemical engineers and biologists use genetic manipulation to study the role of genetic diseases and the predisposition of certain individuals to certain disease. Also, genetic manipulation is increasingly used to design plants that are immune to certain bacteria or pests and that grow faster and produce more, one of the most notorious examples being corn. Complex experiments are used to study the role of the genes in the functioning of cells and tissues. Nanotechnology and the manufacturing of nano-sized devices play a critical role in the genetic sequencing and analysis.

Engineering Category = #1
Choose the category that best describes this lesson's amount/depth of engineering content:
1. Relating science and/or math concept(s) to engineering
2. Engineering analysis or partial design
3. Engineering design process

Keywords
DNA hybridization, DNA microarray, gene decoding, gene sequencing

Educational Standards
Biology: Texas Essential Knowledge and Skills (112.34. Biology, Beginning with School Year 2010--2011)

(6) Science concepts. The student knows the mechanisms of genetics, including the role of nucleic acids and the principles of Mendelian Genetics. The student is expected to:
(A) identify components of DNA, and describe how information for specifying the traits of an organism is carried in the DNA;

(B) recognize that components that make up the genetic code are common to all organisms;

(E) identify and illustrate changes in DNA and evaluate the significance of these changes;

(H) describe how techniques such as DNA fingerprinting, genetic modifications, and chromosomal analysis are used to study the genomes of organisms.

Pre-Requisite Knowledge

Basic knowledge of DNA and gene expression: students must know that genes are segments along the DNA, DNA is a double stranded (helix) molecule made of nucleotide bases (A, T, C, G), base pairing rules (A-T, C-G), gene expression (from DNA to messenger RNA (mRNA) to translation in the ribosome to protein).

Learning Objectives

After this lesson, students should be able to:

- think of DNA or genes as genetic information that is encoded in a unique sequence of As, Ts, Cs, Gs on a tape (the DNA strands)
- know that many diseases result from proteins that don't function properly (misfolded, denatured proteins)
- know that protein defects are likely a result of genetic mutations in the genes that produced that protein
- know that genetic mutations are changes in the sequence of the nucleotide bases

Introduction / Motivation

Genetic mutations happen naturally or as a consequence of environmental factors such as radiation or chemical intoxication. Although some mutations are harmless as they involve DNA sequences that are not critical for the functioning of cells, most of the mutations have deleterious effects on the cells and the organism. As gene expression results in the manufacturing of proteins which are essential the functioning of cells, a mutation in the gene sequence (e.g., point mutation: A is replaced by C) can result in a modified protein. If this modified protein is involved in important cell processes such as division, it can have an important impact on the cell behavior. Most diseases are a result of defective proteins and many of these defects are a direct result of genetic mutations.

New strategies to eradicate or treat diseases include the identification of the genes responsible for the diseases and the replacement of the mutated genes with healthy ones. This relatively new idea is known as gene therapy, and, although its prospects are promising, there are still many obstacles to overtake until safe clinical implementation can be achieved.

One important part of gene therapy involves gene sequencing, or decoding. Comparing the sequences of a mutated and a healthy gene can pinpoint the genetic mutations that are responsible for a particular disease. Because genes are very long strands of nucleotide bases, it takes a long time to decode their sequence. The DNA microarray was introduced as a relatively cheap and fast method to decode, in parallel, segments of a gene.

The idea behind the DNA microarray is very simple as it is based on the nucleotide base pairing. An unknown genetic sample is poured over an array of hundreds of wells, each of which containing genetic code with a known sequence. If there is a match between the unknown sequence and the sequence inside one of the array's wells, then the unknown sequence or part of it can be decoded. The fabrication of the microarray is a complicated process based on nanotechnology advancements that would not have been possible a few decades ago. This lesson shows students how advancements in nanotechnology can improve the understanding of life and can help find answers and cures for diseases such as cancer, diabetes and genetic disorders.

Lesson Background & Concepts for Teachers

The genetic information stored in the DNA is used to manufacture proteins, which, in turn are used by cells. The DNA molecule can be thought of as a long tape made from nucleotide bases (A, T, C, G). Genes are segments of DNA of different lengths that undergo transcription into messenger RNA (mRNA) which is then used by the ribosome to produce proteins. A point mutation in the gene sequence (let's say adenine is replaced by cytosine) that is used for protein synthesis will result in a change in the amino acid chain that makes up the protein and can result in a defective or inactive protein and/or enzyme. As

scientists have gained better knowledge of how cells function, they have come to the conclusion that most of the diseases are a direct result of defective or inactive proteins and enzymes. One strategy to fix bad proteins and enzymes is to fix the bad or mutated genes that are responsible for their synthesis. To achieve this, scientists must know the exact sequence (the unique order of A, T, C, and G) that define the healthy gene and the mutated gene to identify the locations of gene mutation.

The DNA microarray analysis is a fast and efficient method to decode segments of genes. This device consist of a table (array) of very small wells and each well is filled with a particular strand (single strands) of complementary DNA (cDNA) whose genetic sequence is known (Figure 1). Single strands cDNA extracted from cells with bad genes and cells with healthy genes are inserted into the array and distributed in each well. If the samples of cDNA find their complementary sequences in one the wells then they will attach to them. Using biotin molecules and biomarkers such as fluorescence proteins that glow when the two cDNA strands are bounded, the base sequence of the sample cDNA can be found by taking the complement of the known cDNA sequence from that particular well. Because a typical DNA array contains thousands of such wells, a large number of cDNA sequences can be analyzed at the same time.

Image 1 [note position: left justified, centered or right justified]

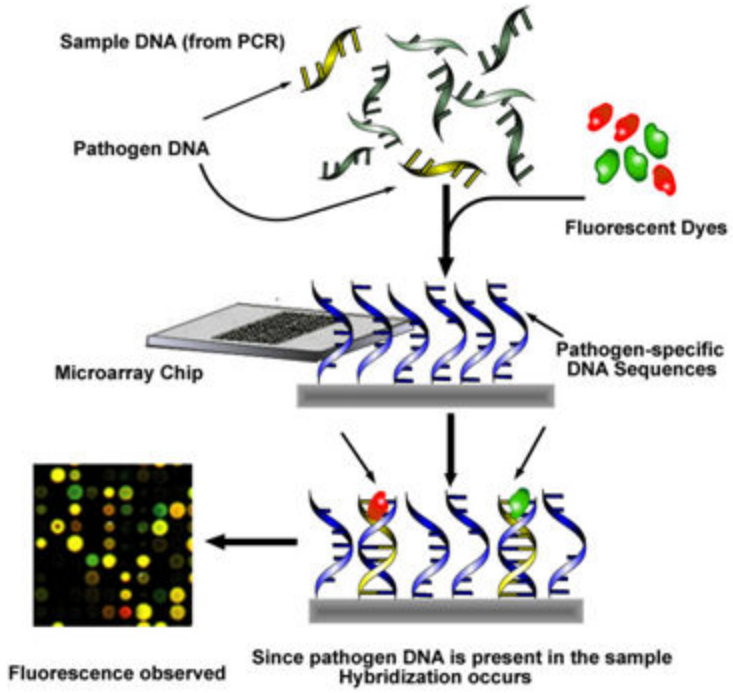

Figure 1

ADA Description: Diagram showing the principles behind the microarray.

Caption: Figure 1. DNA microarray principle

Image file: microarray.jpg

Source/Rights: Copyright © ISAAA (http://www.isaaa.org/resources/publications/pocketk/22/default.asp)

Vocabulary / Definitions

Word	Definition
Base pairing	the linking between two nucleotide bases on opposite complementary DNA strands that are connected by hydrogen bonds
Complementary DNA	single strand of DNA that is synthesized from messenger RNA (MRNA)
DNA	deoxyribonucleic acid contains genetic information for the development and functioning of living organisms
Enzyme	proteins that catalyze certain chemical reactions
Gene	segment along the DNA that encodes a certain function for the organism
Microarray	a 2D array that assays biological material, usually DNA
Messenger RNA	single stand of nucleotide bases transcribed from DNA and from which proteins are synthesized

Associated Activities

Decoding the tape

Lesson Closure

Assessment

Gene Decoding Worksheet (worksheet.doc)

Lesson Extension Activities

Additional Multimedia Support

References

Attachments

Other

Redirect URL

Contributors

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Supporting Program

University of Houston GK12 Program under the National Science Foundation Grant (DGE--0840889).

Version: September 2010

Subject Area(s)
Biology

Associated Unit
None

Associated Lesson
Genetic Decoding for Gene Therapy

Activity Title
Decoding the Tape

Header

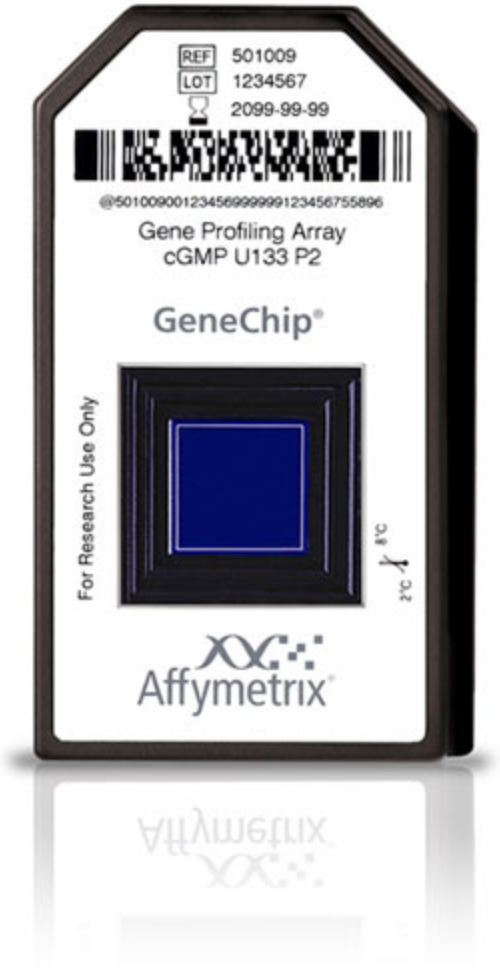

Image 1

ADA Description: Rectangular shaped plate with a blue square in the middle that represents the microarray chip

Caption: Microarray for genetic decoding

Image file: gene_array.jpg

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Grade Level 10 (9-12)

Activity Dependency

Time Required
45 minutes

Group Size

3 to 4 students

Expendable Cost per Group US$___

Summary
This activity introduces the method of fast genetic sequencing by DNA microarray to the class and the concept behind it. The activity consists of two parts: a short, interactive talk about genes, DNA, nucleotide bases and pairing rules (i.e. each base only binds to their complementary one, e.g., A-T and C-G), single strand messenger RNA (ribonucleic acid) and complementary DNA (cDNA); an interactive demonstration of a typical DNA microarray analysis using the online demonstration from the University of Utah Genetics Lab.

Engineering Connection
Chemical engineers and biologists use genetic manipulation to study the role of genetic diseases and the predisposition of certain individuals to certain disease. Also, genetic manipulation is increasingly used to design plants that are immune to certain bacteria or pests and that grow faster and produce more, one of the most notorious examples being corn. Complex experiments are used to study the role of the genes in the functioning of cells and tissues. Nanotechnology and the manufacturing of nano-sized devices play a critical role in the genetic sequencing and analysis.

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3. Engineering design process

Keywords
Cancer, cDNA, DNA hybridization, DNA microarray, gene decoding, gene sequencing, genetic diseases, genetic mutation,

Educational Standards
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(6) Science concepts. The student knows the mechanisms of genetics, including the role of nucleic acids and the principles of Mendelian Genetics. The student is expected to:
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(H) describe how techniques such as DNA fingerprinting, genetic modifications, and chromosomal analysis are used to study the genomes of organisms.

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Learning Objectives

After this activity, students should be able to:

- know that many diseases result from proteins that don't function properly (misfolded, denatured proteins)
- know that protein defects are likely a result of genetic mutations in the genes that produced that protein
- know that genetic mutations are changes in the sequence of the nucleotide bases
- know the basic steps involved in gene sequencing: collecting samples of diseased (bad) tissue and healthy tissue to compare the genes in both samples, translation of DNA into mRNA and then into cDNA, attaching labeling protein to the sample of cDNA, DNA hybridization, microarray analysis to find the genetic sequence of the healthy gene and of the mutated gene

Materials List

Each group needs:

- pen or pencil and the worksheet
- computer with internet connection and Java and Flash Player enabled web browser

To share with the entire class:

- Projector for the short introductory lecture

Introduction / Motivation

A relatively new field of research, gene therapy, promises to deliver highly effective treatments for genetic diseases by identifying the bad genes or the bad (mutated) sequence of nucleotide bases in a gene and replace them with normal ones. The first step involved in this complex process is the comparison of the mutated genes with the normal ones and identifying all the locations in the base sequence that have undergone mutations. The tremendous amount of genes and their sequences that need to be studied is overwhelming but a fast method has been developed in the late 1990s that allows for such genetic analysis to be done in a much shorter amount of time by using a DNA (deoxyribonucleic acid) microarray. This device consists of a table (array) of very small wells and each well is filled with a particular strand (single strands) of complementary DNA (cDNA) whose genetic sequence is known. Single strand DNA extracted from cells with bad genes is inserted into the array and distributed in each well. If it finds a complementary sequence in one the wells then it will attach to it. Using biotin molecules and biomarkers such as fluorescence proteins that glow when the two DNA strands are bounded, the microarray wells that contain complementary sequences that have bound to each other can be identified using a laser scanner and a computer for data analysis. Thus, the base sequence of the sample DNA can be found by taking the complement of the known cDNA sequence residing in the microarray well. Because a typical DNA array contains thousands of such wells, a large number of DNA sequences can be analyzed at the same time.

The DNA microarray helps scientists to find genetic mutations by comparing DNA from healthy and diseases cells such as cancer cells. The ultimate goal is to find the genes and the exact genetic mutations that are responsible for generating diseases such as cancer, diabetes, Alzheimer's and inherited genetic disorders. To motivate students about the importance of genetic decoding, a short presentation on cancer and how genetic mutations usually result in cancer should be given. An excellent resource about

this can be found at the National Institutes of Health website (http://ghr.nlm.nih.gov/handbook). Also, students should be reminded about DNA, mRNA, cDNA, and the rules of base pairing.

Vocabulary / Definitions

Word	Definition
Base pairing	the linking between two nucleotide bases on opposite complementary DNA strands that are connected by hydrogen bonds
Complementary DNA	single strand of DNA that is synthesized from messenger RNA (MRNA)
DNA	deoxyribonucleic acid contains genetic information for the development and functioning of living organisms
Enzyme	proteins that catalyze certain chemical reactions
Gene	segment along the DNA that encodes a certain function for the organism
Microarray	a 2D array that assays biological material, usually DNA
Messenger RNA	single stand of nucleotide bases transcribed from DNA and from which proteins are synthesized

Procedure

Background

The activity is based on the interactive online demonstration from the University of Utah Genetics Lab (http://learn.genetics.utah.edu/content/labs/microarray/) and provides very useful information on the importance of gene decoding and how can this be accomplished by fast genetic decoding. The students will need to access website by using the link above and perform Part 3: The experiment. The step by step demonstration contains explanations and descriptions of the biological and chemical phenomena involved and provides students with brief reviews about DNA, mRNA, cDNA, and base paring.

Before the Activity

- Start a short conversation with the pupils about genetic diseases and the role of genes and the mutations that take place in the base sequence of genes. Guide the discussion toward the concept of gene therapy, i.e., what if one knows that a particular genetic mutation in a certain gene is responsible for a disease or for predisposition toward a disease and what if one can design a method to replace this faulty or bad gene with a healthy. The following link provides some useful information on gene therapy: http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetherapy.shtml

With the Students

1. Have the students form groups of three or four people and have them sit in front of a computer
2. Students should go to the following webpage: http://learn.genetics.utah.edu/content/labs/microarray/
3. Click on the microarray icon and choose Chapter 3: The Experiment
4. Students should follow the instructions and pay attention to the text bubbles describing each step of the demonstration.
5. Perform the post-activity assessment

Attachments

Worksheet.doc

Safety Issues

-

Troubleshooting Tips

Investigating Questions

Assessment

Post-Activity Assessment
Descriptive Title: Decoding Genes

Activity Extensions

Activity Scaling

- For lower grades, ___?
- For upper grades, ___?

Additional Multimedia Support

References

Other

Redirect URL

Contributors

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Supporting Program

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