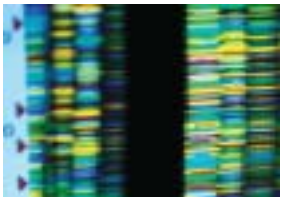

Roche *Genetics*

Education Program

Teacher Manual

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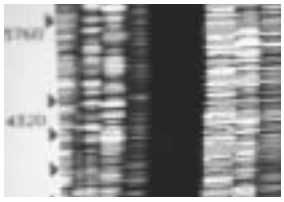

Roche *Genetics*

Education Program

Teacher Manual

Contents

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A Teaching Resource To Accompany the Roche Genetics Education Program

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Acknowledgements

During the summer of 2002, approximately 25 teachers had an opportunity to view a newly developed CD-ROM , Roche Genetics Education Program. While this CD provides a rich resource for classroom use, it did not include a teacher guide and appropriate lesson plans. To effectively build upon the Roche Genetics Education Program CD-ROM and ensure ease of access for a wide audience, a project to develop ancillary materials was proposed for funding.

This project was undertaken as a joint venture between Roche and New Jersey Science Education Leadership Association (NJSELA). Individuals from several Roche site communities were identified to form a team of 6 educators (5 teachers and a science supervisor) to create a teacher guide with suggested lesson plans as an accompaniment to the Genetics CD-ROM. This group represents Roche facilities in the San Francisco Bay area, Indianapolis, and New Jersey. Choice of such a diversified group ensured several important design features. These people provided different perspectives on the appropriate teacher materials necessary for the successful implementation of the CD-ROM within a science classroom.

Overview of CD Contents

Unit 1 — Introduction to Genetics: A Journey Through the Cell

This module covers the basic principles of molecular genetics such as:

- How genes function and how they are studied;
- The different types and effects of mutations;
- The principles of inheritance and recombination; and
- How these concepts can be applied to genetic linkage studies.

Section Overview	Frames
Genes Concepts addressed include structure and function of DNA, concept of a gene, transcription and translation, gene expression	1-18
Identifying Genes and their functions Concepts addressed include how the function of a gene is identified, gene cloning, expression studies, pharmacogenomics and toxicogenomics, use of model organisms for genetic studies	1-11
Mutations Concepts addressed include different types of mutations, difference between somatic and germ-line mutations, how mutations in a gene can affect the product in terms of gene expressions and protein structure, the effect of mutations in evolution	1-13
Mendelian Inheritance Concepts addressed include Mendelian Inheritance of autosomal dominant and recessive patterns, X-linked dominant and recessive patterns, variance from the expected Mendelian Inheritance patterns (penetrance, phenoscopy, genetic heterogenicity, and allelic heterogeneity)	1-14
Recombination Concepts addressed include meiosis and mitosis, recombination frequency, genetic and physical distance, linkage analysis, lod scores, genetic maps, polymorphic markers, linkage disequilibrium	1-16

Unit 2 — Finding Genes Associated with Diseases: In the Genetics Jungle

This module reviews two positional cloning strategies used by scientists to help identify new genes relevant to disease. These approaches are helpful for identifying new potential drug targets relevant to the disease when there is little understanding of the disease mechanism. Positional cloning was a successful strategy for identifying the CFTR and Leptin genes.

Section Overview	Frames
Positional cloning and the Cystic Fibrosis Gene Positional Cloning is a strategy used to identify genes based on localizing their position on the genome. Positional cloning does not require knowledge of gene function. The CFTR gene was identified by the use of linkage and linkage disequilibrium analyses. Identifying the CFTR gene was an important step towards understanding CF.	1-27
Leptin and Obesity The leptin gene identification strategy took advantage of the several known concepts related to mice populations. First, larger number meioses can be analyzed on mice; second, mice strains are genetically homogeneous; third, mice can be bred in a controlled environment; and finally, there is a strong homology between mouse and human genes.	1-18

Unit 3 — Genetics of Common Complex Disorders: The Gene Pool

The challenge of identifying susceptibility genes is a major area for research because:

- Genetic studies allow better predicting of relative risk for disease;
- Different susceptibility genes and different environments can contribute to the same disease;
- There are many risk factors for each of us;
- We can reduce some environmental risks;
- Drugs may be able to prevent some of these diseases.

The current model for disease treatment involves treatment because the patient seeks treatment, diagnosis therapy, and therapy monitoring. Predisposition screening, targeted monitoring, and prevention or early recognition of the disease will precede these steps in the future model for disease treatment.

Section Overview	Frames
What are they? This section describes common complex disorders; gives several examples of common complex disorders; discusses roles of genes and environment on the phenotype of an individual; and addresses the roles of genetic and environmental risk and protective factors upon the disease.	1-13
Genetic Component Population and migration studies help us understand that: • There may be greater disease prevalence due to more susceptibility genes in the gene pool of a particular ethnic group; • There is an interaction of genetic and environmental factors; • Disease resistance can be due to absence of susceptibility gene variants (or presence of protective gene variants) in a population group's gene pool.	1-13
What is the Phenotype? Common complex disorders are often genetically heterogeneous because one disease may originate from different susceptibility genes. Subdivision by clinical disease phenotypes is one approach to identifying the genes involved. Examples include age of onset, disease severity, degree of familial aggregation (or apparent inheritance patterns) and plasma protein markers.	1-4
Susceptibility Genes This section addresses an explanation of susceptibility genes, the relationship of inheritance patterns for susceptibility genes, and the importance in studies for identifying the disease and potential drug targets. Investigations using linkage analyses and association studies with respect to autoimmune diseases are discussed as well as the use of relative risk and odds ratios.	1-18

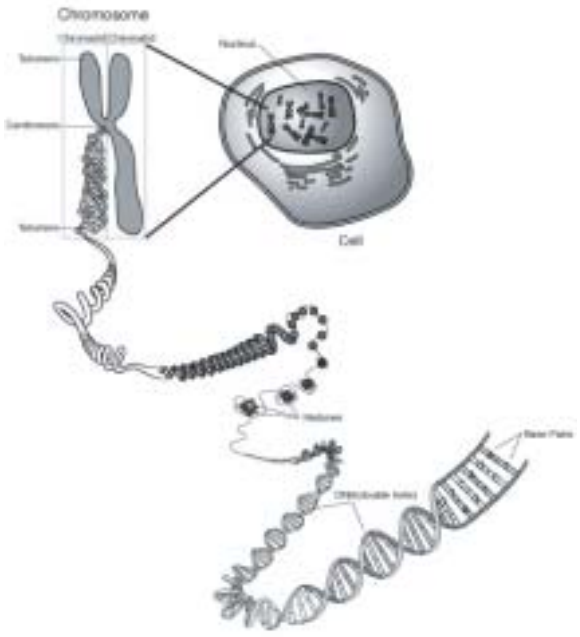
Unit 4 — Pharmacogenetics: The Gene Scene

Pharmacogenetics concerns the effects of genes on the efficacy of drugs. People have different responses to the same drug for several reasons. Individual responses could be caused by differences in the rate that the drug is metabolized (enzyme control), differences in the affinity of receptor molecules for a particular drug (target variation), or the disease may be a collection of different subtypes with different biochemical pathways. The goal of pharmacogenetics is to approach a more targeted, more individualized, and therefore more successful delivery of health care.

Section Overview	Frames
Pharmacogenetics This section explores the principles of pharmacogenetics through a simulated case study.	1-34

Unit 5 — Ethical, Legal, and Social Issues: Genetics and Medicine

This section addresses the Ethical, Legal, and Social Issues (ELSI) arising from recent and continuing human genetic studies and their personal, societal, and legal applications. The concepts addressed are in a verbal format and provide a beginning background for examining and improving understanding of case studies involving conflicting goals and values.



Introduction to Genetics:
A Journey through the Cell

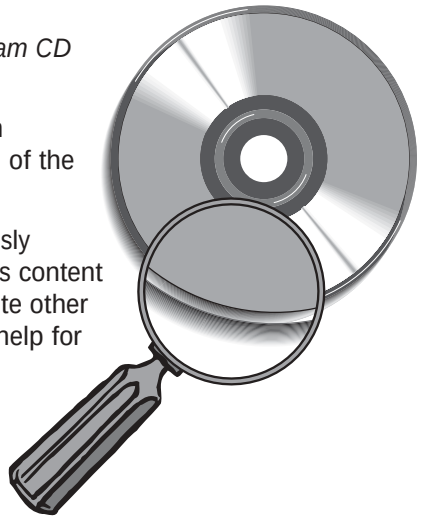
Activity 1:

Disc Quest

Topic: Genetics Revisited – A Basic Review

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
Ability to navigate the *Roche Genetics Education Program CD*



Teacher Directions:
This activity is not meant to replace a traditional unit in genetics. Rather it correlates to information in unit one of the Roche Genetics Education Program CD.

The purpose is to review and reinforce content previously presented by the teacher. A basic understanding of this content will help students understand and successfully complete other activities in the manual. Other uses may include extra help for students requiring home tutoring, make up work, or additional support.

Student Activity 1:

Genetics Revisited – A Basic Review

Name _____

Genes (Frames 1-18):

1. What are the nucleotides found in DNA? Which nucleotides pair with each other?

_____

_____

2. The order of nucleotides in DNA is the _____. What is the significance of the order of the base pairs?

_____

_____

3. Describe how a DNA molecule replicates.

_____

_____

4. Distinguish between autosomal chromosomes and sex chromosomes.

_____

_____

_____

_____

5. Define the following:

a. haploid: _____

b. diploid: _____

c. exons: _____

d. introns: _____

6. Describe the following processes including the terms DNA, mRNA, tRNA, amino acids and proteins:

a. transcription _____

b. translation _____

7. What is the genetic code and how is it used?

_____

_____

Mutations (Frames 1-13):

1. Define genetic mutation.

_____

2. List and define the four types of single base (point) mutations that occur in coding regions.

_____

_____

_____

_____

3. Discuss three causes of mutations in DNA.

4. Explain the mechanism used by eukaryotic cells to repair DNA.

5. What is a somatic mutation? Can these mutations be passed on to offspring?

6. How is a germ-line mutation different from a somatic mutation?

7. Define the following:

   a. locus:

   b. allele:

   c. genotype:

   d. homozygous:

   e. heterozygous:

Mendelian Inheritance (Frames 1-13):

1. What is a haplotype?

2. Define phenotype.

3. What is the difference between an autosomal dominant inheritance pattern and an autosomal recessive inheritance pattern?

4. What is an X-linked trait?

Recombination (Frames 1-5):

1. Mitosis is the division of _____ cells.
2. Are the daughter cells produced during mitosis haploid or diploid? _____
3. Does recombination occur during mitosis? _____
4. Meiosis is the process that creates _____.
5. Are the cells produced during meiosis haploid or diploid? _____
6. Does recombination occur during meiosis? _____
7. What is recombination? What is the significance of recombination in genetics?

Answer Key — Student Activity 1:

Genetics Revisited – A Basic Review

Genes (Frames 1-18):

1. What are the nucleotides found in DNA? Which nucleotides pair with each other?

   Adenine (A), Thymine (T), Guanine (G), Cytosine (C). Adenine pairs with Thymine and Guanine pairs with Cytosine.

2. The order of nucleotides in DNA is the ***sequence***. What is the significance of the order of the base pairs?

   Genetic information is determined by the order of the base pairs.

3. Describe how a DNA molecule replicates.

   The DNA strands separate and new complementary strands are built to create 2 identical DNA molecules.

4. Distinguish between autosomal chromosomes and sex chromosomes.

   a. ***Autosomal chromosomes are homologous and are the same in both males and females. They are labeled 1 through 22.***

   b. ***Sex chromosomes are non-homologous and are found in the X form and Y form. Males have XY and females have XX.***

5. Define the following:

   a. haploid: ***When a cell has a single copy of each chromosome.***

   b. diploid: ***When a cell has 2 copies of each chromosome.***

   c. exons: ***Coding sequence of a gene.***

   d. introns: ***Non-coding sequence of a gene found between two exons.***

6. Describe the following processes including the terms DNA, mRNA, tRNA, amino acids and proteins:

   a. transcription ***In the nucleus, the DNA sequence is copied into an mRNA sequence. However "T" is replaced with "U" in RNA.***

   b. translation ***In the cytoplasm, the mRNA is read in groups of three bases (codons) by the tRNA. The tRNA places amino acids in the correct order based on these codons to create a protein.***

7. What is the genetic code and how is it used?

   Information in the DNA sequence that determines the amino acid sequence in protein synthesis.

Mutations (Frames 1-13):

1. Define genetic mutation.

   Changes in the DNA sequence.

2. List and define the four types of single base (point) mutations that occur in coding regions.

   Missense: ***one or more nucleotides in a codon are altered to create an amino acid substitution.***

   Silent: ***a nucleotide substitution occurs but there is no change in the amino acid sequence.***

   Nonsense: ***a stop codon is introduced and causes an early termination of protein synthesis.***

   Frameshift: ***a single base deletion or insertion causes the entire codon sequence to be read differently.***

3. Discuss three causes of mutations in DNA.

   An incorrect base is used during DNA replication.

   Exposure to mutagens, for example, UV light or X-rays.

   Chemicals react or bind to the DNA.

4. Explain the mechanism used by eukaryotic cells to repair DNA.

Proofreading polymerases correct errors in the base sequence made during replication and/or from mutagens.

5. What is a somatic mutation? Can these mutations be passed on to offspring?

Changes in the DNA of body cells may cause these affected cells to divide uncontrollably. These mutations are not passed to offspring.

6. How is a germ-line mutation different from a somatic mutation?

These mutations are in the gametes and can be inherited by offspring.

7. Define the following:

a. locus: ***Location of a gene in the genome.***

b. allele: ***Alternative form of a gene.***

c. genotype: ***The observed alleles for an individual at a genetic locus.***

d. homozygous: ***2 identical alleles at a locus.***

e. heterozygous: ***2 different alleles at a locus.***

Mendelian Inheritance (Frames 1-13):

1. What is a haplotype?

The series of alleles on a single chromosome.

2. Define phenotype.

Description of observable characteristics of an individual.

3. What is the difference between an autosomal dominant inheritance pattern and an autosomal recessive inheritance pattern?

Dominant: mutation in a single copy of a gene is sufficient to cause the phenotype. Recessive: mutation causes genes to be non-functioning. Two copies of these non-functioning genes are necessary to cause the phenotype.

4. What is an X-linked trait?

A mutation in a gene on the X chromosome or a phenotype caused by mutated gene on the X chromosome.

Recombination (Frames 1-5):

1. Mitosis is the division of ***Somatic*** cells.

2. Are the daughter cells produced during mitosis haploid or diploid? ***Diploid***

3. Does recombination occur during mitosis? ***No***

4. Meiosis is the process that creates ***Gametes***.

5. Are the cells produced during meiosis haploid or diploid? ***Haploid***

6. Does recombination occur during meiosis? ***Yes***

7. What is recombination? What is the significance of recombination in genetics?

Recombination is the exchange of genetic material between homologous chromosomes. This creates shuffling of genetic material.

Activity 2:

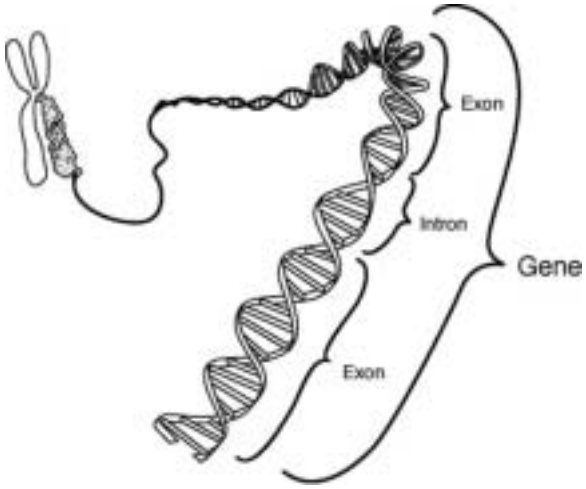
Phenotype to Genotype and Back Again, Learning Genetic Principles Through Cystic Fibrosis

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
Students should understand the concept of a gene as well as types of mutations. Students should also understand the principles of transcription and translation. **Completion of Unit 1 — Activity 1: Genetics Revisited** will prepare students for this exercise.

Teacher Directions:
This activity will require students to perform outside research to gain an understanding of Cystic Fibrosis disease processes. Students will make use of their understanding of basic genetic principles to construct mRNA and protein sequences from DNA sequences. Students' understanding of the structure of our genetic material will be reinforced.

This activity will take approximately two 50-minute periods to complete. The first section, **Part I,** requires some outside research, which can be done in the classroom if access to the internet is available there, or might be assigned as preparative homework for **Part II.** This second section requires access to the ***Roche Genetics CD-ROM*** as a reference. Answers for Part I are readily available on the websites provided. Answers for Part II are provided.



Part I:

Gathering Information on Cystic Fibrosis

Name _____

What is Cystic Fibrosis (CF)? To improve your knowledge, answer the questions below.

Some websites you might find useful:

- The Cystic Fibrosis Foundation: www.cff.org
- National Library of Medicine and National Institutes of Health Cystic Fibrosis information page: www.nlm.nih.gov/medlineplus/cysticfibrosis.html
- National Center for Biotechnology Information GeneMap '99: www.ncbi.nlm.nih.gov/genemap99

1. What is the phenotype of CF patients?

2. What is the mode of inheritance of the disease? What is the frequency of affected individuals in the US population as a whole? What is the carrier frequency?

3. What is the biochemical defect that produces the disease? Where in the genome is that gene located?

Part II:

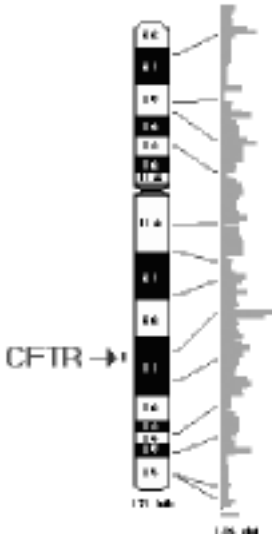
DNA to Protein

Name _____

Below are partial DNA sequences of four CFTR alleles. Answer the questions below based on these sequences.

Chromosome 7

http://www.ncbi.mln.nih.gov/science96/



1. Below each sequence, write the mRNA sequence that would be produced during transcription.

GGG TTC TTT GTG GTG TTT TTA TCT GTG CTT CCC TAT GCA

GGG TTC TTG TGG TGT TTT TAT CTG TGC TTC CCT ATG CAC

GGG TTC TTT GTG GTG TTT GTA TCT GTG CTT CCC TAT GCA

GGG TTC TTT GTG GTG TTT TAA TCT GTG CTT CCC TAT GCA

2. Assuming the top allele is from an unaffected individual and the others are from affected individuals, what type of mutation is found in each of the lower three alleles? What major type of point mutation is **NOT** found in these sequences?

3. Under the mRNA sequence, write the protein produced during translation. Refer to the translation table in ***Unit1: Introduction to Genetics, Genes*** **(Frame 15).**

4. For each of the lower three alleles, describe how the protein produced is different from that of the unaffected individual.

5. Do you think the differences in these protein sequences will affect the function of each of the proteins? Why or why not?

Answer Key — Activity 2:

Part II — DNA to Protein

1. Below each sequence, write the mRNA sequence that would be produced during transcription.

GGG	**TTC**	**TTT**	**GTG**	**GTG**	**TTT**	**TTA**	**TCT**	**GTG**	**CTT**	**CCC**	**TAT**	**GCA**
CCC	AAG	AAA	CAC	CAC	AAA	AAU	AGA	CAC	GAA	GGG	AUA	CGU
GGG	**TTC**	**TTG**	**TGG**	**TGT**	**TTT**	**TAT**	**CTG**	**TGC**	**TTC**	**CCT**	**ATG**	**CAC**
CCC	AAG	AAC	ACC	ACA	AAA	AUA	GAC	ACG	AAG	GGA	UAC	GUG
GGG	**TTC**	**TTT**	**GTG**	**GTG**	**TTT**	**GTA**	**TCT**	**GTG**	**CTT**	**CCC**	**TAT**	**GCA**
CCC	AAG	AAA	CAC	CAC	AAA	CAU	AGA	CAC	GAA	GGG	AUA	CGU
GGG	**TTC**	**TTT**	**GTG**	**GTG**	**TTT**	**TAA**	**TCT**	**GTG**	**CTT**	**CCC**	**TAT**	**GCA**
CCC	AAG	AAA	CAC	CAC	AAA	AUU	AGA	CAC	GAA	GGG	AUA	CGU

2. Assuming the top allele is from an unaffected individual and the others are from affected individuals, what type of mutation is found in each of the lower three alleles? What major type of point mutation is **NOT** found in these sequences?

   Sequence #1: Normal

   Sequence #2: Deletion

   Sequence #3: Substitution

   Sequence #4: Substitution

   Not found: Inversion

3. Under the mRNA sequence, write the protein produced during translation. Refer to the translation table in ***Unit 1: Introduction to Genetics, Genes*** **(Frame 15).**

   Answers are readily accessible from the disc (Unit 1: Introduction to Genetics, Genes) (Frame 15).

4. For each of the lower three alleles, describe how the protein produced is different from that of the unaffected individual.

   Have students compare and contrast the resulting amino acid sequences and identify the differences and similarities.

5. Do you think the differences in these protein sequences will affect the function of each of the proteins? Why or why not?

   The properties of proteins are determined by the order in which different amino acids are joined together to produce polypeptides. A change in the amino acid sequence changes the polypeptide structure and the resulting protein. Mutations or changes may alter the protein so it is unable to perform its normal function.

Activity 3:

Learning Genetics Principles Through Karyotypes and Subsequent Activities

Level: Grades 9-12

Previous Knowledge or Prerequisite Required:
Students can begin this activity with little background in that their first task is simply to cut and locate human chromosomes. With this beginning organizational structure, many concepts can be addressed. Disc material in the **Unit I: Introduction to Genetics** section on **Genes** frames 6/18 through 9/18 will supplement this activity. In addition the section on **Mendelian Inheritance,** frames 1/14 through 4/14 will add important connections between the behavior of chromosomes and Mendelian laws.

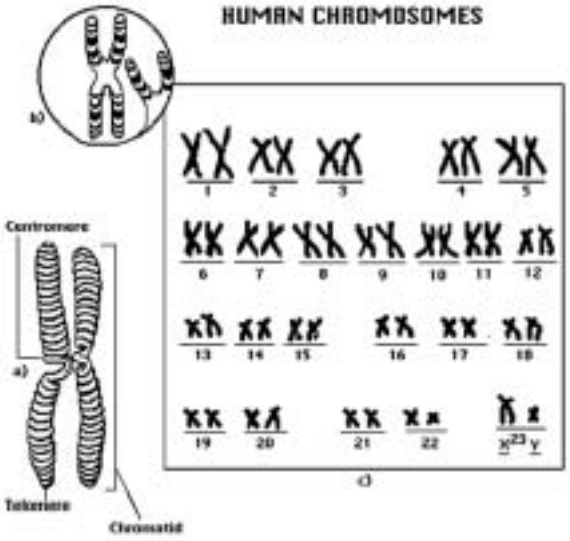
Objectives:
Students often hold a common misconception is that genes are inherited separately (See teacher resource materials). This exercise will visually present the mode of inheritance of chromosomes through three generations, demonstrating the percent of chromosome inheritance from a grandparent as being a matter of chance.
After completing this activity, students should be able to:

- Visually demonstrate the concept that chromosomes (linkage groups) are inherited and not individual genes;
- Understand the procedure of locating gene loci;
- Understand the concept of homologous chromosomes and crossing-over;
- Better understand the use of karyotypes and their analysis;
- Demonstrate the following genetic concepts: dominant, recessive, homozygous, heterozygous, genotype, phenotype, complete and incomplete dominance, polygenic inheritance, sex-linkage, probability, gene loci, karyotyping, and Mendel's Laws of Segregation and Independent Assortment;
- Understand the relationship between genes on a chromosome and the resulting phenotypes.

Time Allotment: 2 to 3 class periods. Some activities may be completed at home.

Materials:

- Scissors;
- Scotch tape/paste/glue;
- Colored pencils;
- Pens-2 colors (dark/light blue for males and dark/light red for females) per student;
- 1 coin per student;
- Blank Karyotype Sheet — 1 per 2 students;
- Carolina Biological Supply Company, Burlington North Carolina (Bioreview sheet 17-4850) and Chromosome sheet, Human Chromosomes (Male and female) 1 per student (Bioreview sheet 17-4801/4802);
- **Human Genome Sheet,** the sheet with human traits and genotypes listed — 1 per student.



Teacher Information:
This hands-on activity is highly adaptable. It can be used as an introduction to many genetic concepts, or as reinforcement to concepts already introduced in class. It is recommended that the terms and concepts be introduced during the activity when the concept is clearly visible to the student. For example, only after a student has located two number two chromosomes and visually paired them on a karyotype, should the term "homologous" be introduced. Concepts such as dominant, recessive, homozygous, heterozygous, genotype, phenotype, complete and incomplete dominance, sex linkage, linkage groups, crossing-over, polygenic inheritance, homologous chromosomes, Punnett squares, karyotypes, and Mendel's Laws of Segregation and Independent Assortment can be introduced and explained in the context of the activities.

The reference numbers from McKusick's Mendelian Inheritance in Man have been included. These will be helpful if further studies include research of the etiology of each condition. For introductory classes, students may reference the chart for those alleles associated with conditions such as color blindness, Rh factor, or Huntington's and mark the appropriate chromosome. More advanced classes may use the chart to establish location of alleles.

(*Suggestion:* The teacher can add alleles to coordinate with the case study found later in the pharmacogenetics unit on the disc.)

Student Activity 3:

Inheritance of Chromosomes

Student Directions

1. Each student in your group should have a blank karyotype sheet and a copy of a metaphase spread of human chromosomes (gender accurate for them). Locate and match the 23 pairs of human chromosomes from your sample and then pair them on the appropriate places on the karyotype sheet. Make sure the patterns of light and dark and the size are the same. Tape or glue each pair onto the karyotype sheet. You will discover they are in order from the largest pair to the smallest pair excluding the sex chromosomes.
2. Color your karyotype. You should use one pencil color for assigning that chromosome to be from your mother and the other color to indicate the chromosome came from your father. For example, if you are male, assign a dark blue for the paternal chromosome and light blue for the maternal. If you are female, assign a dark red for paternal chromosomes and light red for the maternal. This will help keep these designations clear later in the activity. **Outline** each chromosome in the correct color. (**Remember:** males have an X chromosome from their mother and a Y chromosome from their father. Females have two X chromosomes, one from each parent).
3. Using the **Human Genome Sheet,** determine the gene carried on each of your parent's chromosomes. For example, chromosome # 4 carries the gene associated with Huntington's Disease. The alleles are **"H"** = Huntington's and **"h"** = inactive (No disease). You may have these genotypes assigned by the teacher or you may choose which alleles are present in your karyotype. Write the allele(s) at the top of each of your parents' chromosomes. At this point you should have a karyotype which displays your unique genotype, probably unlike anybody else in class. Determine the locus of each gene listed on the **Human Genome Sheet.** Indicate its position by coloring in the locus using the correct color previously assigned each parent. Some genes are hypothetical to illustrate a concept, so you may place them anywhere on the chromosome.
4. Find a partner to marry. Be sure this person has used two different colors for the parents. You will have one child with this person, sharing your chromosomes to create the next generation. Each of you will have to toss a coin to determine which of your parental chromosomes will be passed down in your gamete (e.g., heads will be the chromosome you obtained from mother and tails will be your father's chromosome). You may only pass on one chromosome to your offspring. Toss your coin 23 times, making a mark by the chromosome that was determined by the toss. Cut out these chromosomes, keeping the colored dot at the bottom and the genotype at the top. Paste or tape the chromosome pairs together on the karyotype sheet, starting with the first chromosome pair and ending with two X's or the X and Y.
5. Determine the entire genotype of your child using the **Human Genome Sheet.** List these in order starting with the first chromosome set.
6. Based the genotype assigned by your teacher or selected by you for your karyotype and your partner's, determine the entire phenotype of your child, describing all traits starting from the first set of chromosomes.
7. Count the number of chromosome in your child. Which chromosomes were inherited from the maternal grandmother, the maternal grandfather, the paternal grandmother, and the paternal grandfather? Determine the total percentage of chromosomes inherited from each grandparent.

Baby Karyotype Sheet

Name _____

_____	_____	_____	_____	_____	_____
1	2	3	4	5	6
_____	_____	_____	_____	_____	_____
7	8	9	10	11	12
_____	_____	_____	_____	_____	_____
13	14	15	16	17	18
_____	_____	_____	_____	_____	
19	20	21	22	23	

To be used with karyotype sheet from Carolina (Male and Female Chromosomes #4801/4802).

Application Questions

Name _____

1. What is the significance of using a coin in this exercise?

2. Give one example to illustrate the difference between genotype and phenotype. What other factor(s) will affect phenotypic expression?

3. Give an example to illustrate the difference in phenotype between complete and incomplete dominance.

4. What is the difference in inheritance when two genes are on different chromosomes versus when they are on the same chromosome?

5. Explain how it might be possible that a person could be genetically unrelated to one of his/her biological grandparents. What assumption is being made here?

6. What is the difference between crossing-over in sister chromatids and crossing-over in homologous chromosomes?

7. If two genes linked on the same chromosome have a 50% crossover rate, what could you summarize about their inheritance? What would you infer about their positions on the chromosome?

8. What are your assumption of the probability of inheritance between the two genes for colorblindness and hemophilia versus the genes for **Marfans Syndrome** and **Familial Hypercholesterolemia?**

9. Which example illustrates polygenic inheritance?

10. Develop a model using chromosome numbers 13, 14, 16 and 18, that could illustrate how a male could grow to a height of five feet ten inches.

Application Questions and Answers

1. What is the significance of using a coin in this exercise?

   It represents a 50% chance, which is the same chance that a particular chromosome is in position at meiosis to become part of that gamete.

2. Give one example to illustrate the difference between genotype and phenotype. What other factor(s) will affect phenotypic expression? ***Answers will vary.***

3. Give an example to illustrate the difference in phenotype between complete and incomplete dominance. ***Answers will vary.***

4. What is the difference in inheritance when two genes are on different chromosomes versus when they are on the same chromosome?

   They will be inherited together if they are on the same chromosome, unless crossing over occurs. Consult the disc discussion of haplotypes.

5. Explain how it might be possible that a person could be genetically unrelated to one of his/her biological grandparents. What assumption is being made here?

   Through random chance, none of the grandparent's chromosomes ended in one of the gametes producing the person. The assumption here is that no crossing-over occurs on any of the chromosomes.

6. What is the difference between crossing-over in sister chromatids and crossing-over in homologous chromosomes?

   There would be no difference in sister chromatids as they are identical. There would be no new genetic recombination.

7. If two genes linked on the same chromosome have a 50% crossover rate, what could you summarize about their inheritance? What would you infer about their positions on the chromosome?

   It would be the same as their being on separate chromosomes. They probably have loci that are far apart.

8. What are your assumption of the probability of inheritance between the two genes for colorblindness and hemophilia versus the genes for **Marfans Syndrome** and **Familial Hypercholesterolemia?**

   The genes for colorblindness and hemophilia would be inherited together more frequently due to being linked on the same chromosome.

9. Which example illustrates polygenic inheritance? **Answers will vary.**

10. Develop a model using chromosomes numbers 13, 14, 16 and 18, that could illustrate how a male could grow to a height of five feet ten inches.

    Example could be: AaBbCcDd- 5'4", each active gene adds 3", therefore AABbCcDD.

Human Genome Sheet

CHROMOSOME	GENE	LOCATION	COMMENT
1 (11700)	Rh blood type Rh+, Rh-	1p36 Rh- (AR)	85% Rh+phenotype
2 (120180)	Ehler-Danlos E=affected e=not affected	2q31 (AD)	Fragile, hyperflex skin 1/150,000
3** (with 6)	Acne (2Locus model) N=active allele for acne n=inactive	Anywhere (MF)	NNNN = severe NNNn = moderate NNnn = mild Nnnn = very mild Nnnn = none
4 (143100)	Huntington's disease H=Huntington's h= inactive	4p16 (AD)	mid-life neurologic decline 1/20,000
6**(with 3)	Acne N'=active n'=inactive		
6 (222100)	Diabetes mellitus, insulin dependent D=normal d=afflicted	6p21 (AR)	
7 (219700)	Cystic Fibrosis C=normal c=cystic fibrosis	7q31 (AR)	1/20 Caucasian carriers
9	ABO blood group IA, IB, i	9q34 (AD)m CoD)	
9 (230400)	Galactosemia G=normal g=galactosemia	9p13 (AR)	Missing enzyme
10**	Short/long index finger S=short S'=long Male-dominant S'S'=long SS'=short SS=short Female-recessive S'S=long SS'=long SS=short	Anywhere (Sex-influenced)	Short Long
11(141900)	Sickle Cell hemoglobin HbA=normal	11p15 (AR)	HbAHbS=sickle cell Trait HbSHbS=sickle cell anemia
12 (261600)	Phenylketonuria P=normal p=PKU		Newborn Screening
13** (see 14,16,18)	Tallness A=active a=inactive	12p24 (AR)	
14**	Tallness B=active b=inactive		
15 (162200)	Tay Sachs T=normal t=Tay Sachs		Death usually within 2 years
16**	Tallness C=active c= inactive	15q23 (AR)	
17 (162200)	Marfans M=Marfans m=normal		20,000 affected in USA, 15% new mutation
17 (162200)	Neurofibromatosis N=normal n=Neurofibromatosis	17q21 (AD)	Elephant Man
18**	Tallness D=active d=inactive	17q11 (AR)	
18 (137589)	Tourette Syndrome T=Normal t=Tourette		
19 (143890)	Familial Hypercholesterolemia F=affected f=normal	18q22 (AR)	300-500 Cholesterol levels
X (303700)	Xcb, XN=Colorblindness/Normal	19p16 (AD)	8% Caucasian males
X (306700)	Xh XN=Hemophilia/ Normal	Xq28 (XLR)	
X (310200)	Xdmd,XN= Duchene Muscular Dystrophy/Normal	Xq28 (XLR)	
Y	Testis determining factor (Tdf)	Xp21 (XLR)	maleness

**Hypothetical

Reference:

McKusick, V.A. *Mendelian Inheritance in Man.* (9th ed.). Baltimore: The Johns Hopkins University Press, 1990.

Activity 4:

Cloning Part of the Cystic Fibrosis Gene

Level: Advanced

Prerequisite or Previous Knowledge Required:
A basic understanding of several techniques is necessary. Concepts include:

- PCR
- Subcloning
  - – Plasmid vectors and restriction maps
  - – Restriction digests
  - – Ligation
- Use of bacteria to amplify plasmid DNA
  - – Transformation
  - – Bacterial culture including use of antibiotic selection
  - – Plasmid purification from bacteria
- Techniques for gene expression analysis, such as
  - – cDNA, RT-PCR
  - – Northern Blotting
  - – Western Blotting
  - – Microarrays

Teacher Directions: This activity models a process in which scientists select a gene segment that is thought to be involved in Cystic Fibrosis, isolate that segment and test it for the ability to affect CF disease symptoms. By necessity some of the more complex steps are simplified, to focus on the techniques that students are likely to find on the CD and in other classroom references. Teachers are encouraged to support student research to clarify particular procedures or go into more detail in other areas.

This activity is designed to draw out advanced students' knowledge of the cloning techniques and functional assays described in the ***Main and Deeper*** levels of the ***Roche Genetics Genetics CD-ROM.*** The activity might be used as a prelude or follow-up to a hands-on experience with subcloning of DNA, or as a "dry lab" if access to necessary equipment or supplies is not possible.

The focus of the activity is on the *purpose* of each of the steps in cloning a segment of DNA, not on the specific tasks that might be found in a detailed protocol. Many of the questions could easily be extended to include greater detail, if appropriate resources are available.

The activity lends itself well to completion in pairs or small groups, as students sometimes stumble and might benefit from sharing knowledge. A brief question-by-question key is included following the student version.

One approach to beginning this activity is to assign students to review and/or research the above topics. If research is required, students could work individually or in pairs on a single topic and share with the class. Then students can be challenged to place the techniques in a logical order (such as that above) to accomplish the goal of isolating, amplifying and testing the gene segment of interest. Students could then proceed to completing the activity questions below.

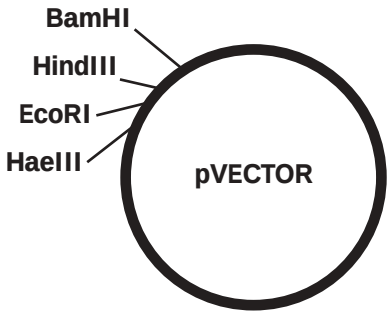
Student Activity 4:

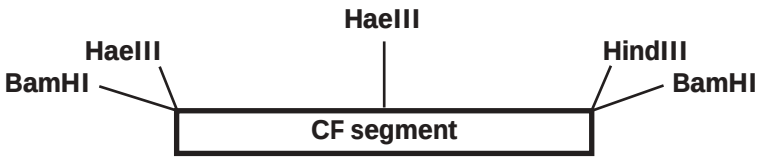
Cloning a Segment of the Cystic Fibrosis Gene

Name _____

1. You are a scientist at an up-and-coming pharmaceutical company and have identified a region of the Cystic Fibrosis (CF) gene that you would like to target for gene therapy. First, though, you must amplify that region and test its behavior in vitro (outside of an organism). In the space below, describe a procedure that would allow you to amplify a specific 476 base pair region of your gene of interest. Include a discussion of how the principle of hybridization makes this process possible, and of the key enzyme that is involved.

2. Now you would like to insert the amplified fragment into a vector, so that you will be able to manipulate the fragment and test its expression in cells. In the diagrams below are restriction maps, used to identify the positions of cut sites for restriction enzymes in DNA. On the left is the vector, and on the right is the amplified segment of the CF gene. In the space below the diagrams, describe what a restriction enzyme does, and suggest which restriction enzyme(s) you would use in a procedure to insert the amplified fragment into the vector.

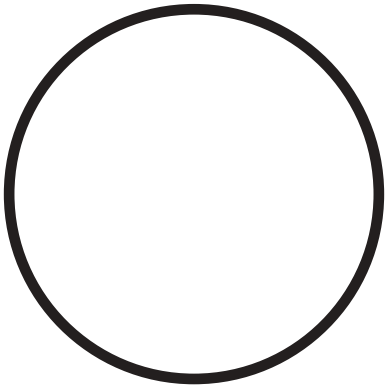




3. Which restriction enzyme(s) would you definitely not use in the above procedure? Why?

4. What type of enzyme would be needed to join the fragment to the vector?

5. On the blank map below, draw an approximate restriction map for the new plasmid, containing the CF gene segment as an insert. Mark the area that contains the insert, and don't forget to give your new plasmid a name!



Name _____

6. Now that you have created your plasmid of interest, you need to purify large amounts of that plasmid. Describe the first step in this process, in which the plasmid is inserted into bacteria and those bacteria are grown on plates.

7. Describe a process used to determine which of the colonies on your plate contain your plasmid of interest.

8. In order to create a drug using the gene segment you have cloned, you must understand the effects of that segment on cells. There are several techniques that could be used to determine the effect of transcribing RNA or expressing protein from the gene segment you have cloned into your plasmid. Describe ONE such technique below, and include a discussion of what you would learn from using that technique.

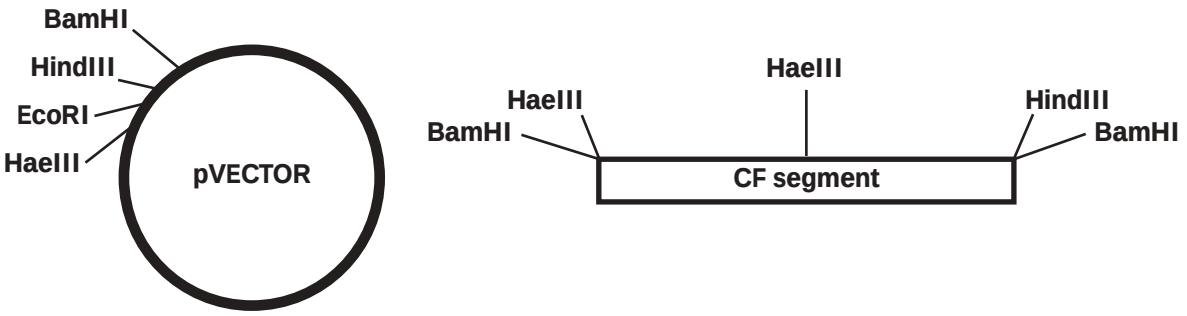
9. Congratulations! Your collaborators in the Research and Development Department have shown that the segment you cloned has beneficial effects on cells from a CF patient, and they plan to test the plasmid as a gene therapy in an animal model. The scientists have asked you for your opinion on which animal model they should use. What would you choose, and why?

Cloning a Segment of the Cystic Fibrosis Gene

1. You are a scientist at an up-and-coming pharmaceutical company and have identified a region of the Cystic Fibrosis (CF) gene that you would like to target for gene therapy. First, though, you must amplify that region and test its behavior in vitro (outside of an organism). In the space below, describe a procedure that would allow you to amplify a specific 476 base pair region of your gene of interest. Include a discussion of how the principle of hybridization makes this process possible, and of the key enzyme that is involved.

   The best procedure for the required process is Polymerase Chain Reaction, or PCR. Students should be able to describe the base-pairing between the primer and the template that allows for amplification, and know that at least some of the region's sequence must be available for PCR primers to be made. Students should also understand that the discovery of Taq DNA Polymerase made PCR possible. Teachers should address the need for repeated heating and cooling cycles in the procedure, and discuss the effects of such cycles on DNA and on proteins, thereby making the connection to the need for a heat-stable enzyme.

2. Now you would like to insert the amplified fragment into a vector, so that you will be able to manipulate the fragment and test its expression in cells. In the diagrams below are restriction maps, used to identify the positions of cut sites for restriction enzymes in DNA. On the left is the vector, and on the right is the amplified segment of the CF gene. In the space below the diagrams, describe what a restriction enzyme does, and suggest which restriction enzyme(s) you would use in a procedure to insert the amplified fragment into the vector.



   Students should understand the concept of a vector (plasmid backbone containing an origin of replication, and additions such as antibiotic resistance genes) and should know that a restriction enzyme cuts both strands of a double-stranded DNA molecule at a specific sequence.
   Good choices for enzymes for this procedure would be BamHI, or a BamHI/HindIII double digest. Students should understand that the vector and the insert must be cut with the same enzyme or combination of enzymes.

   Teachers may want to address the following additional concepts: sticky vs. blunt-ended restriction digests, expression vectors (those which contain promoters for expression of the inserted segment), and advantages or disadvantages of single- and double-enzyme digests.

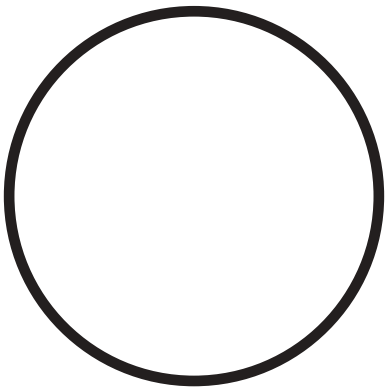
3. Which restriction enzyme(s) would you definitely not use in the above procedure? Why?

   HaeIII would be a bad choice because it cuts the insert in two pieces. Students should understand that in a complete restriction digest, all of the recognition sites are cut. In situations where technique is a major emphasis, teachers might address the concept of partial restriction digests and the techniques needed to identify and isolate the segments of interest from such a digest.

4. What type of enzyme would be needed to join the fragment to the vector?

   Students should understand that DNA ligase would be used to join the fragments. The concept of compatibly-cut ends may be reinforced here.

5. On the blank map below, draw an approximate restriction map for the new plasmid, containing the CF gene segment as an insert. Mark the area that contains the insert, and don't forget to give your new plasmid a name!



Name _____

Students should be able to visualize how the insert and vector would come together to form the new molecule. They should also understand that molecules cut with the same restriction enzyme and rejoined with ligase recreate the original restriction site. If any portions of either of the original molecules are not included in the final plasmid, students should understand that any restriction sites in those regions would not be present in the resulting plasmid. Teachers may also want to address the concept of a double digest, in regards to the directionality of the insert in the final plasmid.

6. Now that you have created your plasmid of interest, you need to purify large amounts of that plasmid. Describe the first step in this process, in which the plasmid is inserted into bacteria and those bacteria are grown on plates.

Students should be able to describe a transformation and understand that the process involves the uptake of naked DNA by bacteria. Students should also be able to visualize a bacterial plate with colonies on it (visual aids will help significantly) and understand that each colony should have arisen from an individual bacteria, thereby representing a single transformation event with each colony therefore containing many copies of a single plasmid.

Teachers may wish to address the concept of antibiotic selection at this step.

7. Describe a process used to determine which of the colonies on your plate contain your plasmid of interest.

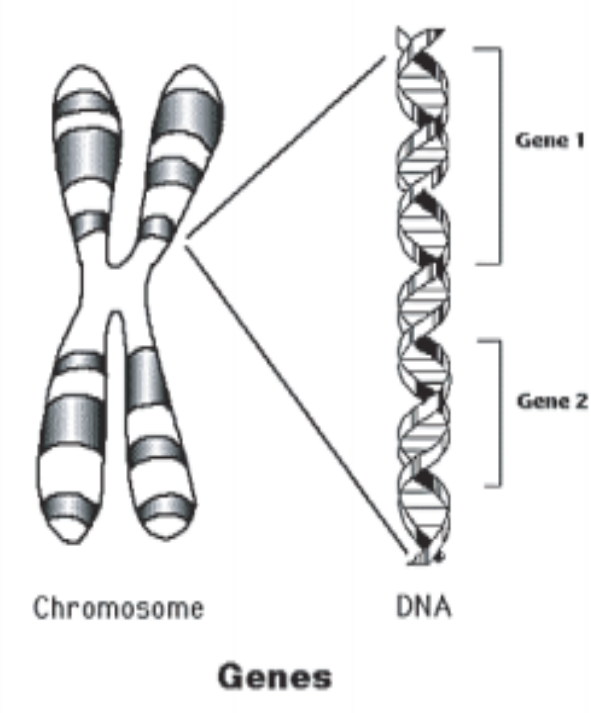
Specific procedures for isolating DNA from bacteria will vary but students should be able to refer to a "miniprep" or related technique. Students should understand that all such techniques involve growth of a colony of bacteria that contains a single plasmid of interest, lysis of the bacteria, and separation of nucleic acid components from other cellular elements. Additionally, the use of restriction digests for verifying the plasmid of interest should be discussed. Teachers may also want to address troubleshooting of cloning procedures at this step.

8. In order to create a drug using the gene segment you have cloned, you must understand the effects of that segment on cells. There are several techniques that could be used to determine the effect of transcribing RNA or expressing protein from the gene segment you have cloned into your plasmid. Describe ONE such technique below, and include a discussion of what you would learn from using that technique.

Several applicable techniques are discussed on the CD. A pitfall of examining such advanced techniques is that students tend to focus on the mechanics of the technique and not on the knowledge that may or may not be gained from a specific technique. Teachers should therefore help students to distinguish between techniques that allow measurement of RNA levels as opposed to protein levels, and between techniques that focus only on a few genes of interest as compared to processes that allow the examination of hundreds or thousands of different molecules at once. A general discussion of gene regulation may be necessary, so that students understand that RNA production and stability as well as protein production, stability and post-translational regulation all contribute to the functional outcome for the cell.

9. Congratulations! Your collaborators in the Research and Development Department have shown that the segment you cloned has beneficial effects on cells from a CF patient, and they plan to test the plasmid as a gene therapy in an animal model. The scientists have asked you for your opinion on which animal model they should use. What would you choose, and why?

Students should understand that an animal model must mirror the human condition as closely as possible. Some common animal models such as C. elegans nematodes or D. melanogaster flies are not useful in this context because the circulatory and respiratory systems in those organisms are not very similar to that of humans. Mice would likely be the best choice, and students should justify using criteria such as similarity to humans, ease of handling, etc.



Finding Genes Associated with Diseases: In the Genetic Jungle

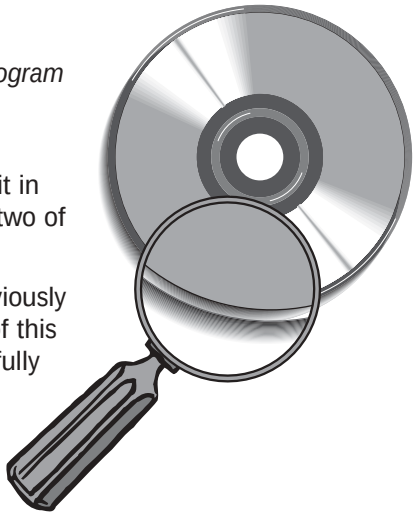
Activity 1:

Disc Quest

Topic: Navigating the Genetics Jungle

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
Ability to navigate the *Roche Genetics Education Program CD*



Teacher Directions:
This activity is not meant to replace a traditional unit in genetics. Rather it correlates to information in unit two of the *Roche Genetics Education Program CD.*

The purpose is to review and reinforce content previously presented by the teacher. A basic comprehension of this content will help students understand and successfully complete other activities in the manual. Other uses may include extra help for students requiring home tutoring, make up work, or additional support.

Student Activity 1:

Navigating the Genetics Jungle

Name _____

1. What are some benefits of identifying genes involved in genetic diseases?

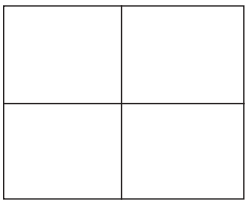
2. Why are the words “positional cloning” appropriate to describe the technique used to identify the genes involved in causing genetic diseases?

3. What types of diseases have positional cloning been most successful in identifying? List three specific examples of disease genes identified by positional cloning.

4. Which organs in the human body are affected by Cystic Fibrosis? What are the symptoms of Cystic Fibrosis in an affected individual?

5. Cystic Fibrosis is an autosomal _____ single gene disease.

6. Solve the following genetic cross using a Punnett square. What is the probability that these parents will have a child with Cystic Fibrosis? A child who is a carrier for Cystic Fibrosis? A child who carries no alleles for Cystic Fibrosis?



N=Normal **n**=Cystic Fibrosis genetic cross: **Nn** x **Nn**

7. What percentage of the Caucasian population are carriers for Cystic Fibrosis? How many Caucasians are affected by Cystic Fibrosis?

8. Describe the basic strategy used to identify the Cystic Fibrosis gene.

Leptin and Obesity (Frames 1-18):

1. What is an animal model? List the advantages of using animal models in scientific research. Can you think of any disadvantages?

2. Scientists often use mice as animal models. Why are mice a good model to use? (Hint: how similar are human and mouse genes?)

3. Obesity is caused by both _____ and _____ factors.

4. Briefly explain how scientist conducted the cross circulation experiment between lean and obese mice.

5. What do the results of the cross circulation experiment show us about obesity?

6. Is the inheritance of the obesity trait autosomal dominant or autosomal recessive? Explain your answers, using data from the results of genetic crosses in mice?

7. Discuss where the ob gene mutation occurs in the DNA sequence. Why does this mutation cause obesity in mice?

8. What is leptin and how can it help to reduce fat tissue in obese mice?

9. How can the knowledge of the leptin gene discovered in mice help to treat obesity in humans?

Answer Key — Student Activity 1:

Navigating the Genetics Jungle

1. What are some benefits of identifying genes involved in genetic diseases?

   Improve the understanding of the disease etiology and mechanism, early disease risk assessment, discover new drug targets, disease prevention, and provide a molecular definition of disease.

2. Why are the words "positional cloning" appropriate to describe the technique used to identify the genes involved in causing genetic diseases?

   Strategy that identifies a gene of interest by its relative position in the genome with respect to other genes or markers.

3. What types of diseases have positional cloning been most successful in identifying? List three specific examples of disease genes identified by positional cloning.

   A single gene disease — example: Cystic Fibrosis, Huntington disease, myotonic dystrophy, and familial forms of breast cancer and Alzheimer's disease.

4. Which organs in the human body are affected by Cystic Fibrosis? What are the symptoms of Cystic Fibrosis in an affected individual?

   Lungs, pancreas, and sweat glands
   Symptoms — Mucus accumulates in the lungs and creates severe respiratory complications and infections.

5. Cystic Fibrosis is an autosomal ***recessive*** single gene disease.

6. Solve the following genetic cross using a Punnett square. What is the probability that these parents will have a child with Cystic Fibrosis? A child who is a carrier for Cystic Fibrosis? A child who carries no alleles for Cystic Fibrosis?

NN	***Nn***
Nn	***nn***

N=Normal **n**=Cystic Fibrosis genetic cross: **Nn** x **Nn**

25% chance of having Cystic Fibrosis

50% chance of being a carrier

25% chance of having no CF alleles

7. What percentage of the Caucasian population are carriers for Cystic Fibrosis? How many Caucasians are affected by Cystic Fibrosis?

   2% are carriers and 1 in 2,500 Caucasians are affected.

8. Describe the basic strategy used to identify the Cystic Fibrosis gene.

   To find the gene, they searched the genome using genetic markers of known location (linkage analysis in families that have Cystic Fibrosis in their lineage). Once they had narrowed down the region of interest, the region was screened for genes, and the genes were screened for differences among diseased and non-diseased individuals.

Leptin and Obesity (Frames 1-18):

1. What is an animal model? List the advantages of using animal models in scientific research. Can you think of any disadvantages?

   Animal models are used to first identify a gene of interest in an animal and then the homolog is identified in humans.

   Advantages to animal models — large numbers of subjects for observation, bred to be genetically homogeneous, relatively controlled environment, faster reproduction rate.

   Disadvantages to animal models — answers will vary.

2. Scientists often use mice as animal models. Why are mice a good model to use?
   (Hint: how similar are human and mouse genes?)

   Human and mice genes are 80-95% similar.

3. Obesity is caused by both ***environmental*** and ***genetic*** factors

4. Briefly explain how scientist conducted the cross circulation experiment between lean and obese mice.

   Obese and lean mice were surgically joined and were able to interchange blood. The obese mice reduced food intake and lost weight while the lean mice remained constant.

5. What do the results of the cross circulation experiment show us about obesity?

   Obese mice are deficient in a circulating satiety factor that is involved in weight control.

6. Is the inheritance of the obesity trait autosomal dominant or autosomal recessive? Explain your answers, using data from the results of genetic crosses in mice?

   Autosomal recessive because, if it were dominant, obesity would have been expressed in all animals in the F1 generation (remember, the obese strain is inbred, which means that it is homozygous for all genes and loci).

7. Discuss where the ob gene mutation occurs in the DNA sequence. Why does this mutation cause obesity in mice?

   The mutation occurs in chromosome 6. The gene mutation has a premature stop codon, which creates a truncated (abnormally short and therefore non-functional) from of a protein that is involved in the control of food intake.

8. What is leptin and how can it help to reduce fat tissue in obese mice?

   Leptin is a protein that acts as a signal to the brain to limit food intake.

9. How can the knowledge of the leptin gene discovered in mice help to treat obesity in humans?

   It allows us to screen individuals for possible mutations of the leptin gene, and if found, it may be possible to treat them by administering synthetic leptin protein as a medicine to help them reduce food intake.

Activity 2:

Developing a Genetic Disease Brochure

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
Knowledge of Mendelian Genetics, Protein Synthesis, and Pedigrees

Teacher Directions:
This activity is to be completed after students have been instructed in the areas listed in prerequisites. Teachers should allow access time to a library and the Internet. Students should be allowed time to conduct a peer review of the completed brochure. Resources for this activity can be found in **Frames 1-27 of the Genetics CD-ROM.**

Student Activity 2:

Genetic Disease Brochure Project

You have been selected by a local doctor to design a genetic disease brochure for her office. She has asked that you select a genetic disease that would present information for patient education. The brochure should be designed so that it can be folded into thirds and displayed in her waiting room. Please be sure to include the following information:

1. The inheritance pattern of the genetic disease. How is the disease inherited from one generation to another? If a parent either has the disease or is a carrier, how does the child get the disease? Has the gene been identified with a chromosome? Include a pedigree of at least three generations to demonstrate the inheritance pattern. Be sure to label the pedigree chart accurately.
2. Characteristics of the genetic disease. How does one know that he/she has the genetic disease? Is there any prenatal testing and testing for heterozygotes? If it is known, what biochemical pathway is being affected? Has the protein been identified, if so, what is its function? What tests are available that can help determine if one has the genetic disease?
3. Special interest groups for the genetic disease. In some, but not all cases, one particular ethnic group, age, group, sex, etc. is more affected by disease than others. Who is at risk and why is the genetic disease more prevalent for that group? What is the frequency of having the disease or being a carrier in a population?
4. Cures or treatments for the genetic disease. After a person has been diagnosed with the genetic disease, what treatments are available and what is the cost for treatment? If there is a cure, how available is it? What is the prognosis for a person who has the genetic disease?
5. Other information concerning the genetic disease. Include answers for other questions a person might ask about this genetic disease. Will genetic engineering or medicines developed from biotechnology aid a person who has the genetic disease? Are there support groups available for those who have the genetic disease? Include how a person could contact these groups.
6. Bibliography. Include references on the back of the brochure to support your information. Be sure to use correct formatting as supported by your school.
7. Creativity. Design a cover for the front of the brochure. Include diagrams and pictures where appropriate. Do not let the brochure include only text.

You may choose any genetic disease that you like. Refer to the following websites to aid you in your decision. Be sure that there is published evidence that supports the method of inheritance. It is important that you get approval from the doctor (the teacher) on the genetic disease that you have selected.

Resources:

Human Gene Project: On Line Mendelian Inheritance in Man: http://www.ncbi.nlm.nih.gov/Omim/
Heredity Disease Foundation: http://www.hdfoundation.org/
Genetic Support Groups: http://www.kumc.edu/gec/support/
Gene Cards: Human Genes, Proteins, & Diseases: http://bioinformatics.weizmann.ac.il/cards/

Genetic Pamphlet Scoring Rubric

Disease Name _____

Points Possible

Inheritance Pattern **1** **2** **3** **4** **5**

Is the disease identified correctly as autosomal dominant, etc.?
Is the probability of inheritance given?
Do the parents have the disease?

Pedigree **1** **2** **3** **4** **5**

Does the pedigree match the inheritance pattern?
Are the labels correct on the pedigree?

Characteristics **1** **2** **3** **4** **5**

Is the biochemical pathway identified?

Signs of the disease

Group Affected **1** **2** **3** **4** **5**

Who is at risk?
Can the disease be found anywhere?

Cure/Treatment **1** **2** **3** **4** **5**

Is there a cure?
Are treatments available?
Is genetic therapy available?

Miscellaneous Information **1** **2** **3** **4** **5**

What current research is taking place?
Is genetic engineering having an effect on this disease?
What support groups are available?

Bibliography **1** **2** **3** **4** **5**

References for further contact

Creativity **1** **2** **3** **4** **5**

Cover Design relates to genetic disease
Pictures and diagrams included
Spelling correct

Total **40**

Activity 3:

Cystic Fibrosis — Impact and Implications

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
An understanding of the disease phenotype of Cystic Fibrosis (CF)

Teacher Directions:
Before beginning this activity, it advisable for the teacher to determine how the topic of CF would affect students on a personal level. For example, if a student has CF or has siblings with CF, it is advisable to first talk to the student to see how s/he would react to having this activity in the classroom. Some students may prefer not to have this activity addressed in class, some may prefer to remain anonymous, while others may welcome the opportunity for fellow students to learn more about this condition.

For more advanced classes, students can look at all aspects of the psychosocial effects of CF. For general biology students, another option is to assign a specific area to each group to present and discuss as a class.

Contact the local Cystic Fibrosis foundation to investigate the possibility of a guest speaker visiting the class.

Reference: www.cff.org

Student Activity 3:

Cystic Fibrosis — Impact and Implications

Name _____

Introduction
Depending upon the condition, genetic disease can have variable effects upon the affected individual. However, other members of the immediate and extended family can also be dramatically affected when one member has a genetic condition requiring specialized care. On a larger scale, society is also affected. In each arena, there are new needs, responsibilities, and choices. In this project you will investigate the psychosocial effects of Cystic Fibrosis upon the affected individual, family members, and society.

Cystic Fibrosis and the Affected Individual
Cystic Fibrosis affects the respiratory, digestive, and reproductive systems. Therefore, how is the lifestyle of a person with CF affected? Consider daily routines, school, after school activities, and other relevant areas. What kinds of changes would you predict in these activities? How might these changes be addressed?

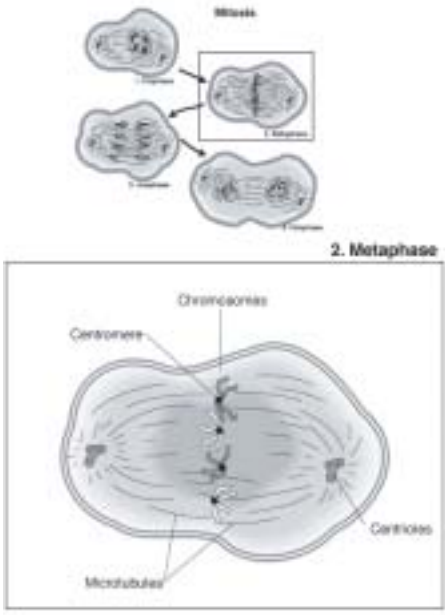
Cystic Fibrosis and the Family
How are the daily activities of family members affected if one member of the family has CF? How would the interpersonal relationships change within the family? How might these changes be addressed? Which community resources exist to help support families with CF members? How could these resources be accessed and shared?

Cystic Fibrosis and Society
CF is a major area of study among geneticists and medical professionals. What is the frequency of CF in the American population? What is the frequency of CF carriers? What is the impact of this condition upon society? Consider the effects upon health providers, school and work absenteeism, and national policy for research on CF.

Cystic Fibrosis and You
Consider how you might learn about and support a person affected with CF. What specific things could you do?

Summary
What are some options for sharing the information you have gathered? Options could include a poster presentation, computer presentation, or leading a class discussion.

Reference: www.cff.org



Genetics of Common Complex Disorders: The Gene Pool

Activity 1:

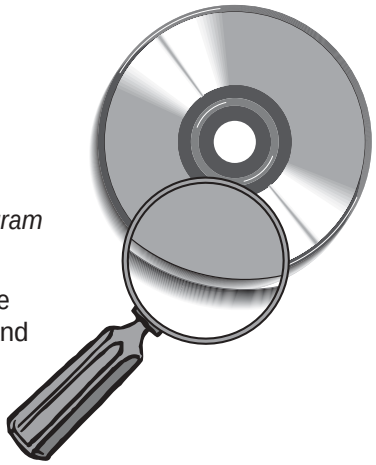
Disc Quest

While this unit focuses on genes increasing one's risk of getting a disease, genes can also confer resistance to getting some aliments. For example, it is commonly recognized that the environmental effects of smoking and drinking can negatively affect health and cause disease. Some individuals, however, will live long lives despite the use of tobacco and alcohol due to their genetic background. For this reason, it is important to remember that genes can be "good guys" as well as "bad guys."

Topic: Wading in the Gene Pool and Do You Know the Facts?

Level: Grades 9-12 (advanced)

Prerequisite or Previous Knowledge Required:
Ability to navigate the *Roche Genetics Education Program CD*



Teacher Directions:
This activity is not meant to replace a traditional unit in genetics. Rather it correlates to information in unit one of the *Roche Genetics Education Program CD.*

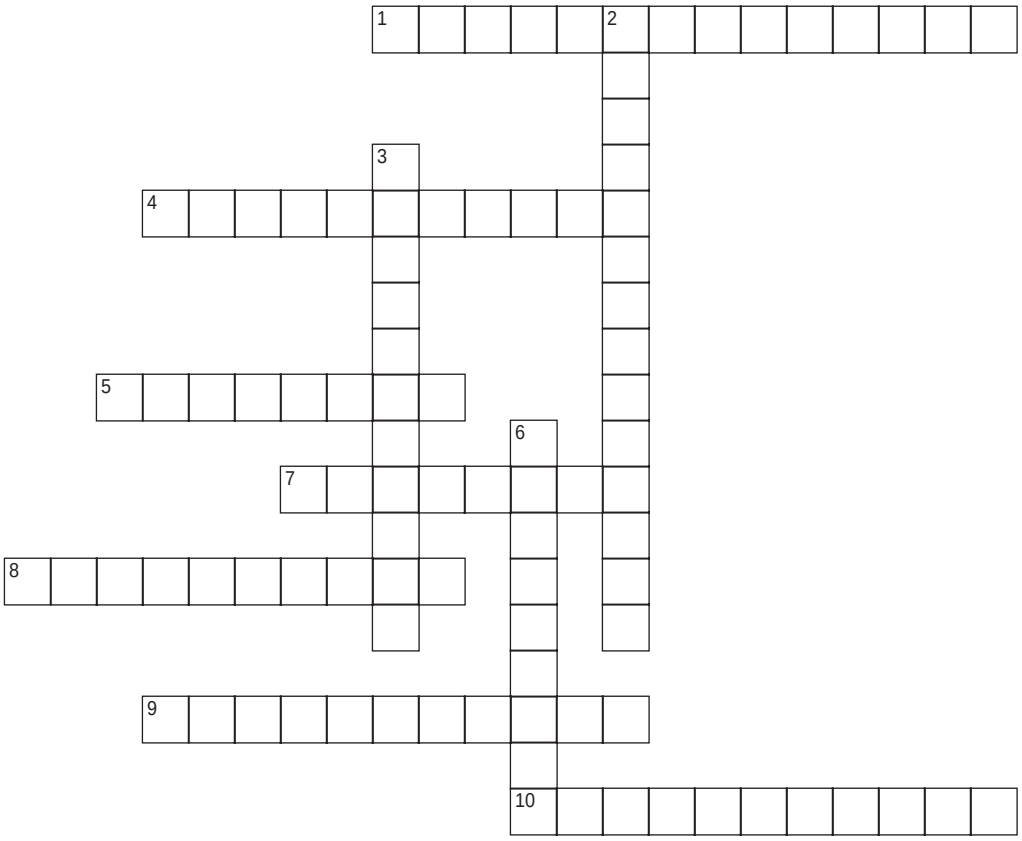
The purpose is to review and reinforce content previously presented by the teacher. A basic understanding of this content will help students understand and successfully complete other activities in the manual. Other uses may include extra help for students requiring home tutoring; make up work, or additional support.

This unit also contains sophisticated concepts that may be appropriate for more advanced courses. Activity 1 focuses on vocabulary and basic information presented throughout this section. Some of the questions are interactive questions asked directly within various frames of the unit. Activities 2 and 3 require an advanced level of analysis and more teacher direction.

Student Activity 1:

Wading in the Gene Pool

Name _____



Across

1. Genetic background making you more susceptible to a disease
4. Transmission of genetic information from parents to offspring
5. Definition of a trait that is either present or absent
7. Disorder that tends to be shared by family members
8. Definition of a trait that has a range of values
9. Genetically identical twins
10. Sharing of a phenotype between individuals

Down

2. Increased likelihood (often based on genetic make-up) to suffer from a disease
3. Trait with 2 discrete categories
6. Non-identical twins

Do You Know the Facts?

Name _____

Directions: Answer the following questions after completing **Unit 3** from the *Roche Genetics Education Program CD.*

(Hint: Do not forget to read the "Did You Know?" segments on designated frames).

Part I: Common Complex Disorders: What are They? (Frames 1-10):

1. Which of the disease shown on frame 3 are common complex disorders? Why can these diseases be classified this way?

_____

_____

_____

2. How was the blood cholesterol of the 88-year-old man affected by eating 25 eggs per day? How can this individual's genetic make up explain how this occurred?

_____

_____

_____

3. Why is the sickle-cell mutation so prevalent in the African population?

_____

_____

_____

Part II: Common Complex Disorders: Genetic Component (Frames 1-13):

1. How do monozygotic twins differ from each other?

_____

2. Are concordance rates for a disease influenced by genes higher in monozygotic twins than dizygotic twins?

_____

3. Are concordance rates for a disease influenced by environment different in monozygotic versus dizygotic twins?

_____

4. What kind of studies separates environmental and genetic factors that contribute to complex traits?

_____

Part III: Common Complex Disorders: Susceptibility Genes (Frames 1-17):

1. To date very few genes involved in common complex diseases have been identified. Why do you think this is so?

_____

Answer Key — Student Activity 1:

Wading in the Gene Pool

Across

1. Predisposition
4. Inheritance
5. Discrete
7. Familial
8. Continuous
9. Monozygotic
10. Concordance

Down

2. Susceptibility
3. Dichotomous
6. Dizygotic

Do You Know the Facts?

Part I: Common Complex Disorders: What are They? (Frames 1-10):

1. Which of the disease shown on frame 3 are common complex disorders? Why can these diseases be classified this way?

   Cancer, cardiovascular disease, schizophrenia, diabetes, hypertension, obesity, Alzheimer disease, and stroke.

   These disorders are not caused by a single identified gene and involve several causes.

2. How was the blood cholesterol of the 88-year-old man affected by eating 25 eggs per day? How can this individual's genetic make up explain how this occurred?

   His genetic make-up apparently has made him unusually resistant to the effects of diet on plasma cholesterol (protective alleles).

3. Why is the sickle-cell mutation so prevalent in the African population?

   Sickle cell mutation is common in Africans and individuals from Mediterranean countries as it also creates some degree of resistance against malaria (a prominent disease in Africa and Mediterranean countries), and therefore provided a certain advantage.

Part II: Common Complex Disorders: Genetic Component (Frames 1-13):

1. How do monozygotic twins differ from each other?

   Genetically they are identical. Environmental exposures may vary.

2. Are concordance rates for a disease influenced by genes higher in monozygotic twins than dizygotic twins?

   Yes

3. Are concordance rates for a disease influenced by environment different in monozygotic versus dizygotic twins?

   Yes, they may or may not be, depending on the degree of shared vs. non-shared environmental influences.

4. What kind of studies are used to separate environmental and genetic factors that contribute to complex traits?

   Adoption studies

Part III: Common Complex Disorders: Susceptibility Genes (Frames 1-17):

1. To date very few genes involved in common complex diseases have been identified. Why do you think this is so?

   Several genes interacting with non-genetic factors are involved, and this complex situation is difficult to do research on.

Activity 2:

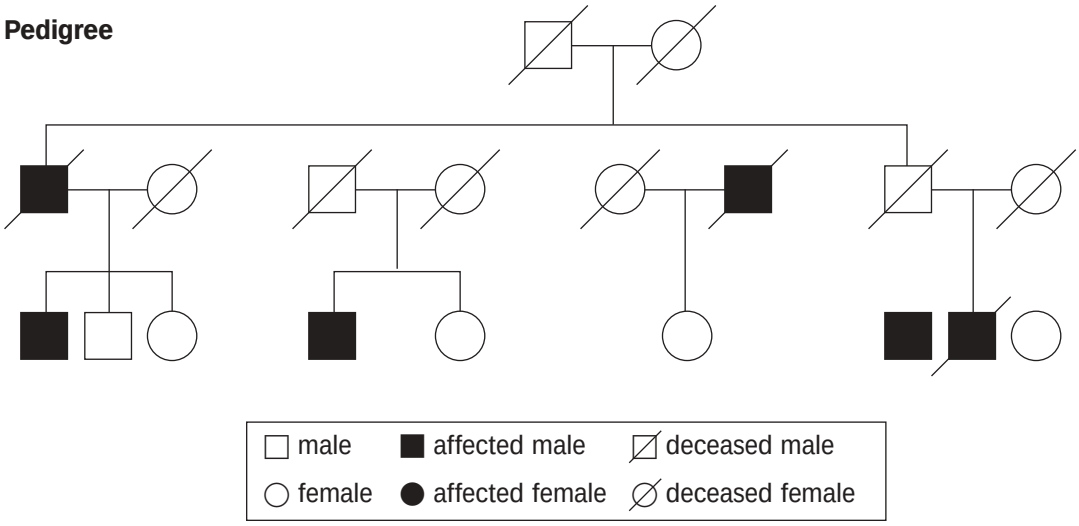
Creating a Family Health History — Pedigrees and Probability

Level: Advanced

Previous Knowledge or Prerequisite Required:
Students who have done the first activity of this program will have the needed prerequisite knowledge.

Teacher directions:
This activity easily takes the form of a student project in which the student will research his/her own family history. The highly personal aspect of this research is both an advantage and disadvantage. The amount of personal investment and the consequent beneficial application of this project can make it one of the most meaningful and useful activities of a student's education. At the same time, it may be a project that requires variable lengths of time and assessments that will require flexibility. An additional burden for the teacher is the responsibility to communicate carefully to students the value of confidentiality and the necessity to be careful with information. Students should carefully weigh what they choose to reveal about their family structure and history. Again, the personal nature of this investigation can create significant growth in teacher/student relationships or it can create difficult dilemmas for the teacher with respect to confidentiality and obligatory reporting.

Pedigree



Student Activity 2:

Back to the Future Creating a Useful Family Health History

Introduction

The genetics story that you have been studying is one of information; about cells, genes, and chromosomes, about new ways of manipulating and decoding DNA, and about how new medicines might be developed using these technologies. With all of these traditional and new ways of using genetic information, we must not forget the most informative source of all, our parents and other relatives. These related individuals give us some insight into how their genes express over time; the very same genes we might have inherited from them. Now this is a bit tricky, in general, because not everyone has access to their biological parents and a lot of the genetic information our relatives possess and have passed to you is not visibly expressed. There are a lot of biochemical reactions, tissue types, and structural aspects your parents have, and may have passed on to you, that are not easily determined. As our ability to decode DNA increases and our knowledge of how to create drugs that are more individually targeted increases, knowledge of our family health history becomes an increasingly important part of our personal medical portfolio. The reasons for generating a working family history include the assessment of risk, probability of detection if necessary, and the increased prevention based on new knowledge.

First, knowing, or at least having the opportunity to know, about you is better than not knowing when it comes to family health history. In addition, our own right to decide what we do with the information should be protected. The bioethics section on this disc (Unit 5) explains the ethical principle called autonomy. This is the right to have sufficient information to make self-directed decisions about those matters that affect you. Issues regarding confidentiality and the right to know are difficult and the bioethics sections will explore the ethical analysis of these conflicts.

Genetic conditions can have their origin in different ways. Some conditions are chromosomal in that whole chromosomes are partially of fully missing or extra, or parts of chromosomes can be rearranged. Single gene traits may follow a family inheritance pattern from which you can determine the mode of inheritance. Review the introduction area of the disc to understand the various modes of inheritance. Last, multifactorial traits often called complex traits can follow a familial pattern but are explained by a different polygenic model. In your early activity making the **Karyotype Baby,** height was an example of a trait for which alleles from more than one locus contribute equal and additive amounts toward the phenotype. These are genes that work exactly as you have studied in the introduction material. They individually follow Mendel's laws, but the outcome is a combination of the expression of several alleles and also influenced in various ways by the environment. Many conditions, such as hypertension in the pharmacogenetics section, are explained genetically by this model.

Creating a Family History

Let's go on a web quest to create a family history. First we shall make a pedigree, a symbolized chart that represents the relationships of family members to each other. This informational tool is the "symbolic language of clinical genetic services and of human genetic research." Later we can extend the genetic relationship of the family to include useful health information about family members. Review the section of the disc about complex traits to get further insight into the meaning of these relationships and how to interpret your risk.

1. Go to the following site. http://www.kumc.edu/gec/gcsim.html
2. Explore these links and use the information to create a family pedigree. Using the Family History form and other reference guides to taking family histories, try to generate a "genetic" family history.
3. Summarize this information into a one-page document that includes a pedigree. This information should be presented to your family doctor to be included in your health history. The importance of this practice is summarized by Robin Bennett:

   "The construction of an accurate family pedigree is a fundamental component of a clinical genetic evaluation and of human genetic research…and to the provision of clinical genetic services.… Review of a family pedigree aids the clinician in diagnosis, helps establish the pattern of inheritance, and assists in identifying persons at risk."

The information you generate about your family may cause your health care provider to suggest further information and counseling would be appropriate. Some conditions that would cause you to consider genetic counseling might include:

1. Multiple family members with the same or related conditions
2. Diagnosis of a known inherited condition
3. Early onset of a common disease
4. Mental retardation
5. Multiple pregnancy loss, or birth defects
6. Consanguinity (mating between close relatives)

Ethical questions can arise as you gather family information and new questions emerge related to what is done with the new information. The ethical principles discussed on this disc can be applied to these questions. For example:

- What if you find information about yourself based on genetic testing which would inform your siblings of a greater risk? Are you obligated to tell them of your personal results? In this situation, your autonomy, or right to act independently on your own information, may be in conflict with beneficence or the "greater good" for other people.
- Would you seek out a genetic test for an allele that would express later in your life? Should this test be mandatory for those individuals at risk? Who owns the test results, and consequently should control their distribution? Should insurance companies or potential employers know the results of the test, especially if they have paid for them?
- Should a university student, age 35, aspiring to be a teacher, reveal that he/she has the allele for Huntington Disease? Would a school system superintendent discriminate against a person who might be able to teach only a few years and then require expensive disability support for the rest of his/her life?
- Knowledge is powerful like a sword; however both edges can cut with equal sharpness. Generating knowledge with out careful consideration regarding its use may expand harm instead of reducing it. The Website, the links under ethical decision-making, and the associated materials of this lesson guide are provided to encourage you to always connect information with responsibility. Knowledge creates power and power creates choice. Choices demand responsibility. Choose well.

Reference:

Bennett, Robin. *Recommendations for Standardized human Pedigree Nomenclature.* American Journal of Human Genetics. 56:745-752. 1995

Activity 3:

Interpreting Probability and Pedigrees

Level: Advanced

Prerequisite or Previous Knowledge Required:
Students who have done the first two activities of this program will have the needed prerequisite knowledge.

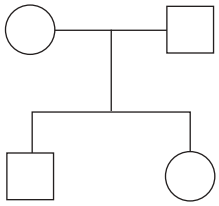
Teacher Directions:
In the following activity, students will read about a family history and chart the occurence of “Disease X” in various family members. Based on information from three separate pedigrees, students will calculate the probability of one of the members, Betty, having carrier status. This activity works well in a co-operative group setting followed by a class discussion of probability and genetic risk.

Student Activity 3:

Interpreting Probability and Pedigrees

Name _____

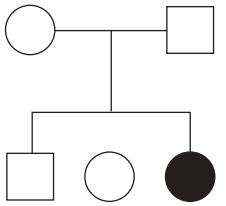
This scenario is about a family and how the knowledge about that family contributes to our computation of risk. Betty and her family are visited on three occasions over a period of 15 years. On each visit, we will explore Betty's risk of being a carrier of Disease X. The frequency of this disease is 1 in 1600 in the general population of which Betty is a member. Disease X is an autosomal recessive condition. In 1985, Betty is an unaffected child in a family with no known members with Disease X. What is the chance of Betty being a carrier?



1985 Pedigree

Answer:

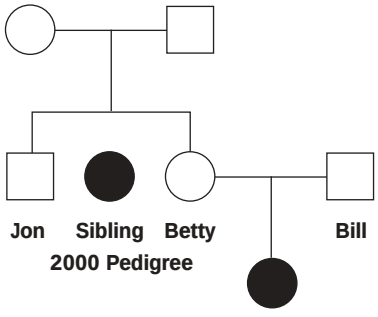
In 1995, Betty's parents have a third child who has Disease X. Now, Betty has an increased probability of carrying the recessive allele. Since both Betty's parents are now known to be carriers, and we know that Betty is not homozygous recessive (affected with Disease X), we can calculate her carrier status based on the new evidence. What is her probability of being a carrier with this new information?



1995 Pedigree

Answer:

In 2000, Betty decides to marry Bill. They later have a child with Disease X. This new information again changes the probability we can assign to Betty with respect to carrier status. Since both parents, Betty and Bill, would need to contribute a recessive disease allele for their child to be affected, both can be considered carriers. That is a 100% chance of being a carrier. Our scenario demonstrates how information in our families can provide insight into our own probabilities of both carrier status and the chance of having an affected child



2000 Pedigree

Answer:

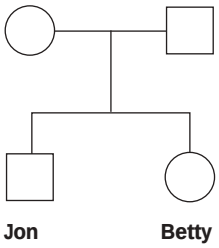
One last question: If Jon married, and he and his wife wanted to have a child, what would be the chance that this child would have disease X?

Answer Key — Activity 3:

Interpreting Probability and Pedigrees

This scenario is about a family and how the knowledge about that family contributes our computation of risk. Betty and her family are visited on three occasions over a period of 15 years. On each visit, we will explore Betty's risk of being a carrier of Disease X. The frequency of this disease is 1 in 1600 in the general population of which Betty is a member. Disease X is an autosomal recessive condition. In 1985, Betty is an unaffected child in a family with no known members with Disease X. What is the chance of Betty being a carrier?

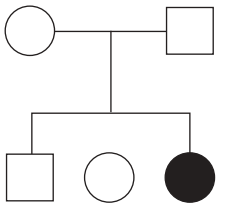
Betty's chance of being a carrier is calculated from the population frequency cited above, 1 in 1600. Betty's probability of being a carrier is 1 in 20. This is computed using population genetics calculations where q2 is 1/1600 making q = 1/40. Carrier frequency is essentially 2pq which would be 1/20.



1985 Pedigree

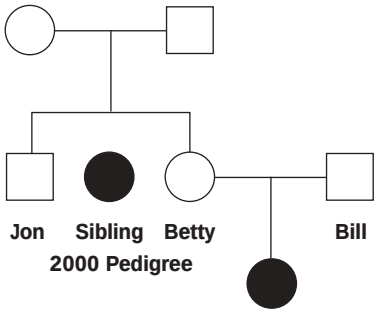
In 1995, Betty's parents have a third child who has Disease X. Now, Betty has an increased probability of carrying the recessive allele. Since both Betty's parents are now known to be carriers, and we know that Betty is not homozygous recessive (affected with Disease X), we can calculate her carrier status based on the new evidence. What is her probability of being a carrier with this new information?

Betty has 2/3 probability of being a carrier and a 1/3 chance of being normal. The presence of her siblings condition has changed Betty's probability of being a carrier even though Betty has done nothing to change her inherited DNA.



1995 Pedigree

In 2000, Betty decides to marry Bill. They later have a child with Disease X. This new information again changes the probability we can assign to Betty with respect to carrier status. Since both parents, Betty and Bill, would need to contribute a recessive disease allele for their child to be affected, both can be considered carriers. That is a 100% chance of being a carrier. Our scenario demonstrates how information in our families can provide insight into our own probabilities of both carrier status and the chance of having an affected child.



2000 Pedigree

One last question: If Jon married, and he and his wife wanted to have a child, what would be the chance that this child would have disease X?

Answer:

First we assume Jon's wife, Jan, has no family history of Disease X and so she is at 1/20 population risk of being a carrier. Jon has a 2/3 chance of being a carrier since he has an affected sibling. Our calculation is the following. Jon's chance of being a carrier is 2/3 and his wife is 1/20. Two carriers have a 25% chance of both passing on the recessive allele to the offspring. Therefore, 2/3 X 1/20 X 1/4 = 2/240 or 1/120. The product of Jon and Jan's child being born with Disease X is the product the three independent probabilities needed for this result to occur.

Pharmacogenetics:
The Gene Scene

Activity 1:

Disc Quest

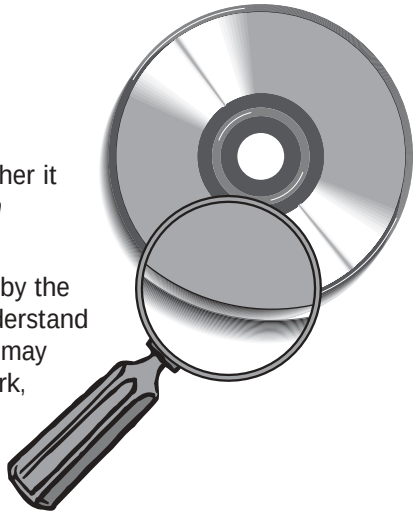
Topic: Investigating the Gene Scene, How Do We Test New Drugs?

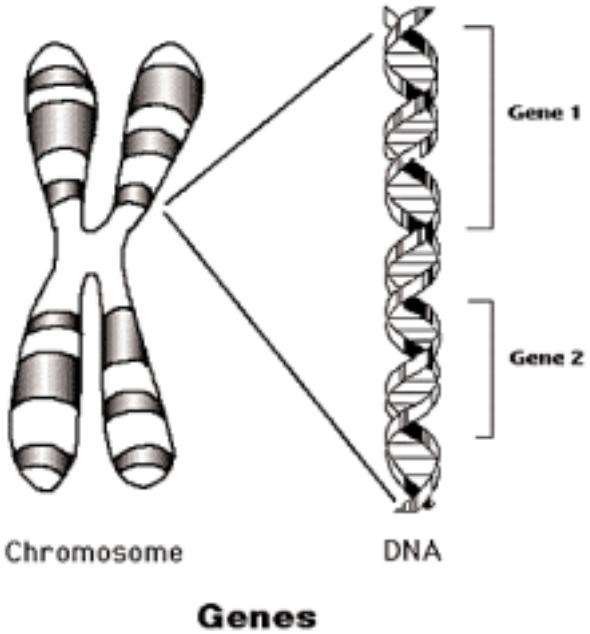
Level: Grades 9-12

Prerequisite:
Ability to navigate the *Roche Genetics Education Program CD*

Teacher Directions:
This activity is not meant to replace a traditional unit in genetics. Rather it correlates to information in unit one of the *Roche Genetics Education Program CD.*

The purpose is to review and reinforce content previously presented by the teacher. A basic understanding of this content will help students understand and successfully complete other activities in the manual. Other uses may include extra help for students requiring home tutoring, make up work, or additional support.





Genes

Student Activity 1:

Investigating the Gene Scene — How Do We Test New Drugs?

Name _____

Unit 4 (Frames 1-12):

1. What is pharmacogenetics?

2. Why do reported mean responses to drugs sometimes not tell the whole story of how a drug really works in different individuals?

3. What are the possible reasons for different responses to a drug in different individuals? Use the information in frames 1-12 to provide specific examples for each reason stated.

4. What do pharmacogenetic studies require?

5. Why are informed consent forms necessary?

Answer Key — Student Activity 1:

Investigating the Gene Scene — How Do We Test New Drugs?

Unit 4 (Frames 1-12):

1. What is pharmacogenetics?

   The study of genetic variation underlying differential response to drugs.

2. Why do reported mean responses to drugs sometimes not tell the whole story of how a drug really works in different individuals?

   Mean responses mask the fact that some individuals respond very well to a drug while others do not respond at all. This is because mean responses show the overall "average" response of all individuals involved in the study.

3. What are the possible reasons for different responses to a drug in different individuals? Use the information in frames 1-12 to provide specific examples for each reason stated.
   - ***Metabolism of the drug – example: if a drug is metabolized too fast, it is eliminated before it can work;***
   - ***Ability of a drug to bind to a target – example: if the shape of the target doesn't let the target bind to it, the drug cannot perform its function;***
   - ***The amount of drug target produced by different individuals – example: individuals with less of the target have less opportunity for the drug to bind and therefore function;***
   - ***Different pathways causing the same disease – example: a drug may only target certain chemical pathways.***

4. What do pharmacogenetic studies require?
   - ***A blood sample for DNA extraction;***
   - ***Analysis of DNA for the identification of specific genetic variants;***
   - ***Actual clinical response data;***
   - ***Of course, like all other studies, an informed consent is necessary.***

5. Why are informed consent forms necessary?

   Pharmacogenomic research, like all other clinical research, needs to be carefully explained to the potential participant so that they can make a fully informed decision about whether or not to volunteer.

Activity 2:

How Are Drugs Developed?

Level: Grades 9-12

Prerequisite or Previous Knowledge:
Completion of activity one in the pharmacogenetic unit.

Teacher Directions:
The purpose of this activity is for students to investigate how new drugs are developed. The students will learn about how clinical trials are conducted and what type of information can be gathered from them. Therefore, in this activity, it is suggested to use information found on the Food and Drug Administration's (FDA) website preliminarily and then use the *Roche Genetics Education Program* disc.

The activity will direct students to the Center for Drug Evaluation and Research (CDER) handbook in order to investigate the components drug development. The web site (http://www.fda.gov.cder/handbook/) serves as an excellent resource for teachers who are introducing the concept of how new drugs are tested using animal models and clinical trials. The site provides interactive charts/diagrams that explain the components of drug development and drug review in detail.

Student Activity 2:

How Are Drugs Developed?

Introduction:
The Food and Drug Administration (FDA) has a division titled the Center for Drug Evaluation and Research (CDER). There is now a CDER Handbook available online through the following web address:

http://www.fda.gov/cder/handbook/

This site provides detailed information regarding the drug development and review processes.

Procedure:
1. Type in the web address above.
2. Click on the icon titled "New Drug Development and Review"
3. Click on the bullet titled "New Drug Development Process"
4. You will now have access to an interactive chart that displays all the components of the new drug development process. You can find an explanation of each component by clicking on the boxes or words on the chart. Answer the following questions on a separate sheet of paper, *in your own words,* using the interactive chart:
   - What is the difference between short-term and long-term animal testing? Why are these tests needed in the drug development process?
   - Explain the difference between phase 1, phase 2, and phase 3 clinical trials. Make sure you include when each phase is conducted throughout the study, what type of subjects are involved in each phase, and how the results of each phase impacts the success of marketing the new drug.
   - What is an Institutional Review Board? What role do these boards play in the development of a new drug? Why are they necessary?
5. Once you have completed your investigation of the new drug development process, we will discuss your findings as a class.

Going Further:
6. On the Roche Genetics Education Program CD click on **Unit 4: Pharmacogenetics** in the main menu.
7. Complete **Frames 13-33** and review the clinical trial results of a particular drug named **"Blockal."** Make sure to complete all interactive components on these frames.

Extension:
Another way to incorporate the FDA's website mentioned in this activity into your class is to use a lesson plan provided by **PBS/NOVA.** This lesson plan also has students investigate the steps involved in the new drug development process. However, it does so in a different manner. It also incorporates case studies where students use the FDA New Drug Development Process to determine if a drug should be put on the drug development fast track.

If you are interested in reviewing this lesson as well, the website is:

http://www.pbs.org/wgbh/nova/teachers/activities/2909_menigit.html

Activity 3:

Would You Participate in a Clinical Trial?

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
Completion of disc quest for Pharmacogenetics.

Teacher Directions:
This activity can be used as a small group or individual assignment. Students should be encouraged to share drafts with each other before constructing the final copy. Class discussions can evolve from student updates or questions arising from their work. As an option, teachers may elect to send a response either accepting or denying a student's request to "participate" in a clinical trial. Students can then discuss their reactions to the response and any next steps they would like to take. For example: Applying for a Compassionate Use request.

References:

Clinical Trials:

http://www.centerwatch.com/patient/backgrnd.html

http://www.clinicaltrials.gov/ct/info/resources

http://www.hivclinicaltrials.northwestern.edu/participate.asp

http://www.canceractionnow.org/index.html

Informed Consent:

http://www.umn.edu/consent

Student Activity 3:

Would You Participate in a Clinical Trial?

Background Reading:

http://www.centerwatch.com/patient/backgrnd.html

http://www.clinicaltrials.gov/ct/info/resources

Introduction:
An important part of the drug development process is a multi-step clinical trial procedure. During a clinical trial, a new potential drug is tested in very controlled ways, upon volunteer patients. If successful in treating or controlling a targeted disease condition, the drug moves on to the next steps to become available for general patient use, usually through a physician's prescription.

Activity:
Imagine that you have a disease condition for which a clinical trial is now recruiting volunteers. The new drug has the potential for being more effective than your current medication. Therefore, it could improve your quality of life.

1. In making your decision to participate in the trial you need to determine the benefits and risks of such a decision. Where would you go to find out more information about the trial? Determine three benefits and three risks that would apply to your decision?
2. After evaluating your benefits and risks, would you agree to sign an informed consent to participate in this trial? Remember informed consent means that you:
   - Understand that the trial is a scientific experiment and there may be risks and dangers to your health;
   - Have been told about the reasons for doing the trial, the drugs you might be given, the number of visits and the kinds of lab tests required;
   - Have been given the information you need to decide whether to take part in the trial.

Follow-up:
Write a letter to the drug company indicating your decision to participate in the clinical trial. Provide reasons for your decision. Be sure to include any concerns or questions that you have about this trial.

Activity 4:

Comparative Study of *Blockal* and *Enzex* Hypertension Drugs

Level: AP Biology, Genetics, Physiology (Advanced Biology)

Prerequisite or Previous Knowledge:
Completion of Unit 4: Activity 2.

Teacher Directions:
Opening Activity

Here they will learn that Tom and Pierre have decided to participate in the ***Blockal*** clinical trials for different hypertension drugs. Before proceeding with the activity, students should view frame 12 and respond to the questions. Students will then view ***Frames 15-33.*** Using these frames, students will add information about the neural hormone to the pedigrees previously constructed in Activity 2. Based on the information and evidence they gather, students are asked to predict whether Tom or Pierre will benefit from the drug ***Blockal.***

Student Activity 4:

A Study of Two Hypertension Drugs, *Blockal* and *Enzex*

Name _____

You have just learned that Tom and Pierre have agreed to participate in the clinical trials for a new drug, ***Blockal.*** Please refer to ***Frame 12*** and the deeper meaning button to answer the following questions.

1. Pharmacogenetic studies need approval by the Institutional Review Board (IRB) an ethical review committee. Why is this necessary? Give one reason for each step. How does a pharmacogenetic study compare to clinical trials for other drugs?

2. **Refer to frames 15-21.** Answer the following questions:

- How does ***Blockal*** work?

- How does ***Enzex*** work?

- What regulates blood pressure? How does this chemical work to regulate blood pressure?

- How does the neurohormone receptor vary in the population?

- What is the effect of the neurohormone receptor differences on blood vessel control?

- **Refer to Frame 22.** Examine the graph and describe the differences in patient response to ***Blockal.*** What is the genotypic make-up of each phenotype? Predict which genotype will be associated with Tom and Pierre.

- Consider the common variant type. Why can some individuals with this variant type have a good response and others with the same type have a poor response?

- What other factors affect the way that Blockal is metabolized?

Refer to Frames 23-30.

- How does an enzyme **(CyP2D6)** affect drug metabolism?

- How do competing drugs and diet affect the rate of drug metabolism?

- Use the information in **Frames 26-30** to compare and contrast *prodrugs* and active drugs. Why are *prodrugs* important?

Your Prediction:

- Based on all of the new information, predict how Tom and Pierre will react to the drug treatments. Support your prediction. (**Frame 32** provides information on their responses to the drug).

Extension:

- **Refer to frame 33.** This is a new scenario that focuses on a drug called Cural and its affects the blood sugar levels. Use the information provided to summarize individual patient responses to the drug.

- Use the summary frame **(1/1)** to list the causes of different responses to the same drug.

Answer Sheet — Student Activity 4:

A Study of Two Hypertension Drugs, *Blockal* and *Enzex*

1. Pharmacogenetic studies need approval by the Institutional Review Board (IRB) an ethical review committee. Why is this necessary? Give one reason for each step. How does a pharmacogenetic study compare to clinical trials for other drugs?

   Answers are based on information obtained by reading Frame 15 and accessing more information from the deeper level button.

2. **Refer to frames 15-21.** Answer the following questions:

- How does ***Blockal*** work?

  See Frame 15

- How does ***Enzex*** work?

  See Frame 15

- What regulates blood pressure? How does this chemical work to regulate blood pressure?

  Vasoactive neurohormone NH regulates blood pressure. This neurohormone binds to its receptors in cells that form blood vessel walls. NH triggers a signal that results in blood vessel narrowing.

- How does the neurohormone receptor vary in the population?

  See Frame 15

- What is the effect of the neurohormone receptor differences on blood vessel control?

  See Frame 15

- **Refer to Frame 22.** Examine the graph and describe the differences in patient response to ***Blockal.*** What is the genotypic make-up of each phenotype? Predict which genotype will be associated with Tom and Pierre.

  Have students read and analyze Frame 22

- Consider the common variant type. Why can some individuals with this variant type have a good response and others with the same type have a poor response?

  Other factors may affect patient response. For example, the way the drug is metabolized may affect efficacy.

- What other factors affect the way that Blockal is metabolized?

  Mutation of the gene, CYP2D6 may cause metabolism to increase or decrease.

Refer to Frames 23-30.

- How does an enzyme **(CyP2D6)** affect drug metabolism?

  High expression of CYP2D6 causes more enzyme formation and faster metabolic rate.

- How do competing drugs and diet affect the rate of drug metabolism?

  See Frame 15

- Use the information in **Frames 26-30** to compare and contrast *prodrugs* and active drugs. Why are *prodrugs* important?

  Have students record information from the comparison table on Frame 26

Your Prediction:

- Based on all of the new information, predict how Tom and Pierre will react to the drug treatments. Support your prediction. (**Frame 32** provides information on their responses to the drug).

  Answers will vary.

Extension:

- **Refer to frame 33.** This is a new scenario that focuses on a drug called Cural and its affects the blood sugar levels. Use the information provided to summarize individual patient responses to the drug.

  Frame 33 has a short interactive sequence. Have students click on the question and follow the discussion.

- Use the summary frame **(1/1)** to list the causes of different responses to the same drug.

  See Frame 1/1

Activity 5:

Part I: Informed Consent
Part II: Connections Between Clinical Trials and Advertising

Level: Advanced

Previous Knowledge or Prerequisite:
Ability to navigate the *Roche Genetics Education Program CD.* Completion of Disc Quest for **Unit 4: Pharmacogenetics.** *This activity is designed in two parts and concludes with a summary activity.*

Part I: Informed Consent

- **Part I** involves helping students understand the significance of a clinical trial and to think about reasons for why they would or would not choose to participate in a clinical trial;
- Questions D and E include some basics of experimental design through the concepts of a control and large numbers of people necessary for an appropriately designed clinical trial;
- For question F, consider using sample prompts for questions given in the resource from *Centerwatch.*

This activity provides a good opportunity to address the issue of privacy of medical and genetic records. Students might consider the value of privacy as weighed against the need for professionals to have data to move drug development forward. Perhaps students can suggest ways to meet both goals.

Student groups can work to answer questions, and then report out to the class for further discussion. Another method would be to assign one question to each student group and then report out or jig saw further groups to share the information. A third alternative would be to have students take notes on their own thoughts first and then share with other students in pairs or small groups.

This lesson could also be an independent assignment.

Additional Resources:
While selected questions are given to help students think about the significance of clinical trials, the following resources are some examples of those useful for more details.

http://www.fda.gov/cder/handbook/develop.htm
The New Drug Development Process: Steps from Test Tube to New Drug application Review
- This resource includes a schematic diagramming the drug approval process, information about animal and toxicological studies, and explanations about clinical trials (Phases 1, 2 and 3).

http://www.centerwatch.com/patient/backgrnd.html
- This resource from Center Watch/Clinical Trials Listing Service offers an introduction and explanations for how experimental drugs are tested in humans, who pays for clinical research, guidelines for questions to ask before participating in clinical research, information sources for clinical research, and a glossary of clinical research terms.

http://centerwatch.com/patient/backgrnd.html
- Part of the previous reference, this page lists specific questions one would ask to determine whether or not to participate in a clinical trial.

These questions could be used as prompts for students generating their own question list:
- How long will the trial last?
- Where is the trial being conducted?
- What treatments will be used and how?
- What is the main purpose of the trial?
- How will patient safety be monitored?
- Are there any risks involved?
- What are the possible benefits?
- What are the alternative treatments besides the one being tested in the trial?
- Who is sponsoring the trial?
- Do I have to pay for any part of the trial?
- What happens if I am harmed by the trial?
- Can I opt to remain on this treatment, even after termination of the trial?

Helpful Web sites:
For information on orphan drug programs from the US food and Drug Administration
http://www.fda.gov/orphan/progovw.htm

For information on Fast track, Priority Review, and Accelerated Approval
http://www.accessdata.fda.gov/scripts/cder/onctools/accel.cfm

Part II: Connections between Clinical Trials and Advertising

Part II provides a connection for linking the value of clinical trials and **recruitment of subjects** with new drug options for treating diseases more effectively. Discussion questions could also include:

- What is the value of advertising to clinical trials and patients?
- What is the value of clinical trials to patients and why would they participate?
- Do you know anyone who has participated in a clinical trial?
- If so, what led them to participate in clinical trial (MD recommendation, saw ad, read about trial in newspaper, saw 800 number on TV, radio, etc.)?
- Do you think individual responses to medications vary because of ethnic **and/or gender** differences? For reference on ethnic differences, see:
  - CD **Frame 17,** Deeper Level button, for a cited reference, and
  - CD **Frame 26** for a table of Ethnic variations of Drug metabolizing enzymes
- How do we measure the success of clinical trial recruitment?

This could also be a good time to schedule a guest speaker addressing topics such as clinical trials, informed consent, **and/or recruitment of subjects for such research.** Your school Parent association, a local pharmaceutical industry, or a university could be a possible resource for identifying such a speaker.

The following Web sites can be provided to the students for their research on advertisements for clinical trial participation:

Web sites:
www. NIH.gov
www.centerwatch.com/patient/backgrnd.html
http://www.cnahealthpro.com/amt/rmissues.html

Guidelines for Advertising for Clinical Trials
http://www.neirb.com/AD_Guidelines11.02.pdf

ClinicalTrials.gov
http://clinicaltrials.gov/ct

Center for Drug Evaluation and Research
http://www.fda.gov/cder/guidance/4155fnl.htm

Assessment:
Writing a brief summary and sharing it in a home conference are the goals of this activity. Allow class time for students to share their adult feedback.

As an Alternative Summary Activity, students could do the following:
Imagine that you see an ad for a clinical trial relating to a disease condition that you have. Imagine also that, if the drug under study is successful, it could treat your disease condition more effectively than your current medication and improve your quality of life.

Use what you have learned in this activity to write a letter to the Clinical Trials Department in which you:

- State your situation;
- Indicate your interest in finding out more about the trial, and;
- Include specific questions asking for more information about the trial.

Student Activity 5:

Informed Consent

Name _____

Part I:

Introduction

An important part of the drug development process involves clinical trials. During a clinical trial, new potentially helpful drugs are tested using carefully regulated procedures upon human volunteers. If successful in treating or controlling a targeted disease condition, the drug progresses through further testing and potentially could become available for patient use. Advertising is often necessary to recruit volunteers for clinical trials. Today, advertising to tell the public about new drugs is becoming increasingly more common.

In these activities, you will:

- Think about why a person would or would not choose to participate in a clinical trial;
- Examine and analyze advertising examples for drugs currently offered to the public;
- Evaluate connections between clinical trials and advertising as related to the process of bringing new drugs to the public.

Part I: Informed Consent

Review **Unit 4: Pharmacogenetics** frames 11-12 on the *Roche Genetics Education Program CD.* Click the "deeper" button on frame 12 to read about "Genetic Sample Banking." Now think about the following questions. Be prepared to share your answers with the class.

1. Where does "informed consent" fit into the pathway for pharmacogenetics studies?

_____

_____

2. Why is informed consent an important part of these studies?

_____

_____

3. Why is a control group an important part of a clinical trial?

_____

_____

4. Why is it important to have a large number of participants in a clinical trial?

_____

_____

5. Which questions would you want to ask before making a decision to participate/not to participate in a clinical trial?

_____

_____

6. Under which circumstances would you participate in a clinical trial? Give reasons for your answer. (For example, how sick would you be before choosing to do so? Which risks would you be willing to take?)

_____

_____

7. Assuming you were participating in a clinical trial, at which point would you change your mind? Why?

_____

_____

Connections Between Clinical Trials and Advertising

Name _____

Part II:

Now that you have thought about the purpose of informed consent and clinical trials, you can begin to explore some connections between clinical trials and the recruitment of volunteers as related to the process of bringing new drugs to the public.

Some topics for discussion follow:

1. What is the connection between clinical trials and informed consent?

2. How does the public become aware of a clinical trial? How must the advertisement be objective and make no unfair promises for the product being investigated? What expectations, if any, can the potential participant be offered?

3. Which ethical guidelines should be followed in research that involves human subjects?

4. Who do you think should make these decisions?

5. What other questions do you have about clinical trials and the recruitment of subjects?

6. Where could you go to find answers to your questions?

Activity Summary:

Summarize briefly what you have learned about

- Informed consent and participation in clinical trials;
- Recruitment of subjects for clinical trials, and the;
- Connection between these two topics.

Share this written summary with an adult at home. Invite the adult to give you feedback and add his/her signature. Record the amount of time you spent in this discussion.

Activity 6:

Drugs Work Better for Some People Than for Others

Level: Advanced

Prerequisite or Previous Knowledge:
Completion of Activity I in Unit 4. Understanding of Unit 1: Introduction of Genetics, Unit 3: Genetics of Complex Disorders, and Protein Synthesis.

Teacher Directions:
This activity provides an opportunity for students to predict outcomes based on evidence. At the conclusion of the activity the students should be able to apply what they have learned to a new situation.

Opening Activity:
Have students view **Frame 2 of Unit 4.** In this frame, Tom and Pierre share their experiences with the hypertension drug ***Enzex.*** Students are to construct pedigrees on Tom and Pierre based on their conversations. Using these pedigrees, students are asked to discuss reasons why each man has a different reaction.

Possible answers/reasons:
- Diet differences
- Genetic differences
- Dosage of drug
- Drug interference

(Hint: Refer to ***Summary 1 for Unit 4*** to help provide reasons for the differences between the two men).

Student Activity 6:

Drugs Work Better for Some People Than for Others

Name _____

Opening Activity

Unit 4 (Frame 2):

1. Based on the conversation between Tom and Pierre, construct a family pedigree of hypertension for each of them.

Tom **Pierre**

2 List some reasons for the differences in their response to the drug ***Enzex.***

_____

_____

_____

_____

_____

_____

3. Use the glossary to find the meaning of pharmacogenomics and pharmacogenetics. Which term best describes the differences between Tom and Pierre?

Group Activity: When is a drug ready for the market?

You are the Chief Research Officer (CRO) of the local pharmaceutical company. The research team working on the anti-asthma drug has recently brought to you the results of their first clinical trial (*refer to* ***Frame 6***).
You and the team must decide, based on the evidence, whether this drug is ready to be put on the market.
If is not ready, give your reasons. Please discuss any further evidence that needs to be collected to aid you in your decision. If necessary, provide suggestions for further research to understand the differential responses.
Write your response as a memo to the research team.

Consider the following:

- What is the action of the drug (pharmacodynamics/binding action)?
- How is the drug metabolized in the patient (pharmacokinetics)?
- What are possible sources of interaction with the drug? (Environmental, other drug interactions, etc.)
- How does the configuration of the target site affect the binding of the drug?
- How do we express drug efficacy? (Hint: Refer to **Frame 5**)

Before writing the memo, consult Frames 7-10 on the CD. List your findings and evidence below. Use this information to support your decision.

Notes

Frame 7:
What reasons are given for differences in drug response?

Frame 8:
Study the graphs on the left-hand side of the slide. Using the evidence provided, explain how metabolic rate (too fast or too slow) affects drug action.

Frame 9:
Examine the diagram. Identify the active site. What occurs at this position? Predict what would happen if the target protein site is altered? Would the drug, in this case ***Enzex,*** be effective?

Frame 10:
There may be more than one biochemical pathway involved in a disease. Examine the diagram on the slide. List the differences and similarities seen in the biochemical pathways A (Tom) and B (Pierre) for hypertension.

DIFFERENCES	SIMILARITIES

Would ***Enzex*** work in each situation? Explain your response.

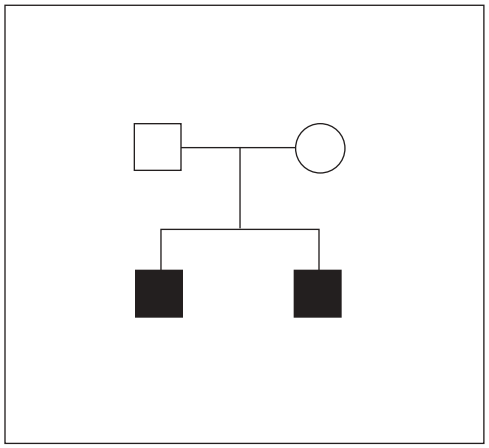
Answer Sheet — Student Activity 6:

Drugs Work Better for Some People Than for Others

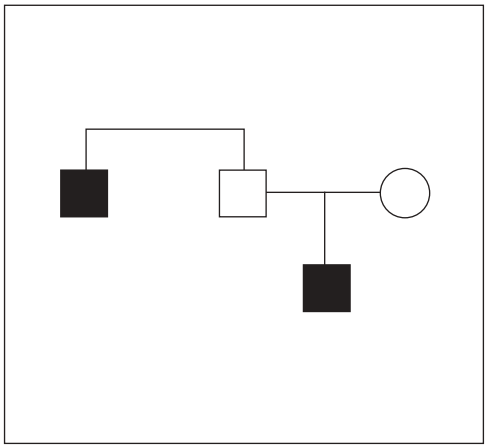
Opening Activity

Unit 4 (Frame 2):

1. Based on the conversation between Tom and Pierre, construct a family pedigree of hypertension for each of them.



Tom



Pierre

Key: Filled square = high blood pressure

2 List some reasons for the differences in their response to the drug ***Enzex.***

Tom:

Enzex works but causes headaches
Shows normal expression of NH receptor
Fast metabolizer
Healthy diet low in salt
Exercises

Pierre:

Enzex does not work
Shows over expression of NH receptor
Increased vessel contraction
Healthy diet low in salt
Exercises

3. Use the glossary to find the meaning of pharmacogenomics and pharmacogenetics. Which term best describes the differences between Tom and Pierre?

The remaining answers are obtained from the Genetics CD-ROM as part of student research .

Activity 7:

Analysis of a Drug Product Advertisement

Level: Advanced

Previous Knowledge or Prerequisite:
Ability to navigate the *Roche Genetics Education Program CD.* Completion of Disc Quest for **Unit 4: Pharmacogenetics**

This activity invites students to investigate and analyze public advertisements for drugs regarding their purpose, target audience, and methods of appealing to various groups of people. Before starting this activity, it would be wise to set appropriate guidelines for the types of drug products you would like students to research. For example, you may wish to include only drug advertisements for certain types of diseases. Or you may wish to distinguish over the counter medications from prescription drugs.

This activity is designed to work best with small group interactions. As discussion is a major part of the activity, be sure students understand the class guidelines for participating in discussions in which differing opinions need to be presented and heard politely and objectively.

This activity could lend itself well to interdisciplinary teaching with areas such as English, Social Studies, Psychology, or Art. Consider working with a colleague to brainstorm how to help students use this study of drug advertising in multiple disciplines.

For extensions, students could create a collage of drug advertisement cutouts with an appropriate title. They could also design an effective drug ad for an imaginary product.

Again, this activity could also be an independent activity.

Student Activity 7:

Analysis of a Drug Product Advertisement

Name _____

Have you seen advertisements for drug products in magazines, newspapers, or on TV? What kinds of drugs are advertised? Which people represent the target audiences for these ads? What is the effect of these ads? Discover why such ads must be objective and fair in promises made for the product.

In this part of the activity, you will:
- Collect sample advertisements for drug products;
- Think about the goals of these ads and who they are intended to reach (target audience);
- Discuss the effectiveness of these ads as they inform the public about potential new drug products;
- Differentiate between product and corporate (i.e. Pfizer is a corporate image vs. Claritan is a product).

1. Look in magazines, newspapers, or on TV and identify one advertisement for a drug product. If possible, bring a copy of the advertisement (or a videotape of the TV ad) to school for use in class.

2. Work with your group to determine the following:
   - Give the name of the drug and its manufacturer
   - What is the drug intended to do?
   - Who is the target audience?
   - What are the side effects?
   - How is the drug distributed? (Prescription? over the counter?)
   - Why would someone choose to take this drug?
   - Why would someone not choose to take this drug?
   - What else does the ad tell you about the drug?
   - Do you think this ad is effective or not effective? Give reasons for your answer.
   - What questions do you have that are not answered by the information in the ad?
   - On the basis of this ad, would you take this drug or recommend it to others? Why or why not?
   - Again based on the ad, how would you recommend effectiveness of this drug?

3. Share this information with your class.

4. Do you think it is appropriate to present drug advertisements to the public? Why or why not?

Ethical Legal, and Social Issues:
Genetics and Medicine

Ethical, Legal, and Social Issues: Genetics and Medicine:

Overview

Ethics education is similar to science education in that it involves structuring information and tracing the chain of consequences that follow a given action. Recognizing a decision as a moral issue is to see that it incorporates the elements of human freedom, choice, and responsibility. Ethical issues pose ethical "dilemmas" that are not easily answered.

Bioethics is a field that has emerged as a result of new technology, new discoveries, new choices, and new dilemmas. Within a science curriculum, it can provide an exciting avenue for bridging scientific facts with current and real life events. There are several other considerations worthy of note, if such a unit is undertaken. First, a topic such as bioethics can provide an alternative activity within a traditional science course. Second, if a non-threatening environment is maintained, then students have the freedom to express ideas on ethical questions that others are willing to listen to and take seriously. Finally, an ethics discussion should be open to various perspectives, even possible disagreements, which can lead to constructive problem solving.

Decision-Making Strategy

In an effort to provide structure to an ethics discussion, a strategy can be used to guide the discussion process. This method was developed and is published in the manual **New Choices, New Responsibilities: Ethical Issues in the Life Sciences. A Teaching Resource on Bioethics for High School Biology Courses, (1990) The Hastings Center.**

This strategy for analyzing ethical issues consists of the following six steps:

Identify the ethical problem(s) present

- The first step in ethical analysis is to emphasize that that identification of the problem should be as clear as possible in order to reduce uncertainty. The problem should be phrased as a question to encourage further analysis since the question must be answered. This question usually begins with "should".
- What has to be decided, who should decide, and what ethical problems does the decision pose?

Assess the factual information available to the decision-makers

- What facts are presented within the case study? Of those facts, which ones are relevant to the ethical problem? Are there other facts that must be known before a decision is made? How can we separate fact from hearsay or opinion?

Identify the "stakeholders" involved

- List all those affected directly or indirectly by a decision in this case. In what way will they be affected? Will they be directly harmed by the decision and is this harm intentional by the decision maker? Are the "stakeholders" voluntary participants or are they "innocent bystanders" of the decision? If they are harmed, is this justified by greater benefit to others?

Identify the values at stake in the decision

- Values that have importance or worth relative to situations such as, human well being, care and treatment of animals, ecological protection, or genetic research. Values indicate what is "good," employ preference, are supported by rational justification, incorporate strong feelings, and specify a course of action (Kieffer). Some examples of values include justice, altruism, respect for others, truth telling, doing good, doing no harm, pursuit of scientific knowledge, and humane treatment of animals.

Identify the options available to the decision-maker

- While initially ethical cases may appear to present only hard moral choices even tragic choices, ethical decision making is creative problem solving. Would more information help one see more options? Can the decision wait until such information is available? Is there a situation of compromise that will provide support for more stakeholders' interests?

Consider the process for making the decision and the values that pertain to the process.

- Several ways of evaluating the rightness of an ethical decision exist. One can compare the consequences of the action with one's value set. Can I live with this decision? If I had to personally experience the consequences, is the action acceptable. Does the decision and the resulting action bother me and why? Another way is to consider what would be the consequences (long term and short term) if everyone did this (universalization)? Or to evaluate if the action or decision offers the greatest good and is therefore ethically valid (consequentialist ethics)?

Activity I (Parts I, II, II) allows students to explore various decision-making models with their teacher. It should be used as a preview to the activities that follow.

Kieffer, G.H. (1979). Can Bioethics Be Taught? *The American Biology Teacher* 41(3):176.

Activity 1:

Developing a Decision-making Model

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
The teacher should review Unit 5 of the CD-ROM for a background material. The teacher should also discuss the decision-making model with the students prior to performing these activities.

Teacher Directions:
The teaching strategy begins by asking students to identify important considerations they have when confronting an important decision. Students proceed to translate that thinking into a chronological list of steps and eventually into an individual working model for decision making. This process is often accompanied by many revisions as students begin to think more deeply and become exposed to the thinking of other students. An alternate decision making model (Adapted from the Jon R. Hendrix/Pat Somers Model, Ball State University) is introduced to students for comparison. Students individually and collectively, compare and contrast these working models. Students must ultimately generate their list of essential components of an effective decision making mode. Last, students explore more personal decision making situation in which they might benefit from effective decision making. Student learning and performance can be assessed informally at the various steps of this lesson and by the student's final product, an authentic decision making model. Effective rubrics for this assessment are not included but could be produced by students and/or the teacher.

This teaching strategy illustrates application of guiding principles of constructivism including: (a) posing essential problems of relevance to students; (b) focusing on primary concepts; (c) seeking and valuing students' points of view; (d) responding to students' suppositions, and (e) assessing student learning within the context of teaching. Students who achieve the skill of ethical reasoning and decision making have an essential tool for building desirable and valuable lifelong skills.

Student Activity 1:

Constructing a Decision-Making Model

Name _____

Part I:

1. When you have an important decision to make, what are some of the things you take into consideration before making that decision?

2. What are some things you could do to improve the likelihood that your decision would be the correct one for you?

3. How would you assess whether or not your decision was one with which you could be satisfied?

4. What do you think is the relationship between the number of solutions and consequences generated and the quality of your decision?

Constructing a Pattern for Making Decisions

Part II:

Share your answers to these questions with the members of your group. As you become aware of new ideas, add them to your answer sheet. List as many responses as possible. Can you organize these ideas in some way? Is there a natural or most reasonable sequence of steps in decision making? Working together, try to find agreement on a logical set of directions for decision making. This pattern might be the basis for a more detailed "decision making model." Be prepared to justify each step and why that step is present and in a particular place in your sequence.

STEPS in making decisions:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____

Constructing a Working Decision Making Model

Part III:

Using your list of steps for making important decision, create a working document that would lead a person through the decision making process. Provide written directions, places for written responses, and any other information to clarify the task. After your group is satisfied with the decision making model, make a copy for each group member.

1. Take a few moments to reflect on your thinking. Is there anything about this activity that is particularly difficult?

_____

_____

_____

_____

_____

2. List the distinguishing characteristics (critical attributes) of an effective decision making model.

_____

_____

_____

_____

_____

Comparing and Contrasting Two Decision Making Models

Use the Alternative Bioethical Decision Making model designed by Jon R. Hendrix/Pat Somers from Ball State University. It is probably similar to the one you have just constructed. With further instructions from your teacher, compare and contrast the two models.

1. How are these two models similar?

2. How are these two models different?

3. Discuss the strengths and weaknesses of each mode.

4. Which model would you choose as a decision making tool? Why?

5. Describe five situations (real or hypothetical) where you might choose to use a decision making model as a thinking tool.

A. _____

B. _____

C. _____

D. _____

E. _____

(Written by Dr. Gordon Mendenhall based on the question set written by Dr. Jon Hendrix).

Alternative Bioethical Decision-making Model

(Adapted from the Jon R. Hendrix/ Pat Somers Model, Ball State University)

1. State the bioethical problem. State problem as an ought to do question (e.g., "What ought I do when…")

_____

_____

_____

_____

2. List possible alternative actions or solutions to the problem, even if you don't agree with some. (five is the minimum)

Ranking	Solutions
1. _____	_____
2. _____	_____
3. _____	_____
4. _____	_____
5. _____	_____
6. _____	_____
7. _____	_____
8. _____	_____

3. Rank these alternatives in order of preference by placing numbers beside them. For example, place #1 beside the first choice, #2 beside the second, etc. (Rank them from the one (#1) your values agree with most to the one (#?) your values agree with least.

4. Take your #1 solution and list at least 5 values you hold that cause you to rank it #1.

"I" Value	Personal Meaning of Value Word
1. _____	_____
2. _____	_____
3. _____	_____
4. _____	_____
5. _____	_____
6. _____	_____
7. _____	_____
8. _____	_____

5. Now take your solution and describe the CONSEQUENCES you think it would have. Do any 5 of the long-term and short-term consequences.

How would this solution
Affect my: (_____) Short Term Long Term

Money _____

Time _____

Personal relationships _____

Family _____

Friends _____

Psychological self _____

Community _____

Country _____

6. Place a (+) beside each consequence you hold as "good" and a (–) beside each consequence you hold as "bad."

7. Are there any real "bad" consequences that you couldn't live with? If so, try another solution or modify your solution.

8. List 3 reasons why others might not agree with your solution to the problem.

1. _____

2. _____

3. _____

9. Restate your solution and then place a confidence or conviction measure on it by X-ing the number on the confidence scale below.

My solution: _____

_____

_____

_____

HIGH CONFIDENCE			LOW CONFIDENCE
1	2	3	4
Very Sure			Not Very Sure

Introduction:

Using a Bioethical Case Study in the Classroom

New technological advances have presented us with difficult choices and decisions. The media emphasizes the need and urgency for us and our students to form opinions. Recent developments have raised questions such as, "Should we screen for genetic defects?" "How should we responsibly use genetic information?" "Should cloning of a human be allowed?" "How can we decide who receives a needed transplant?" Answers to these questions present society with ethical "dilemmas" that have no clear cut answers. As such, ethical issues the resulting implications offer a different landscape for teachers and students to explore.

Ethics/Bioethics/Values

Terms like "ethics," "bioethics," "values," and "morals," are used frequently in this unit. A basic understanding of each would be helpful for both teacher and students. Students will relate to terms such as morals and values and can provide their understanding of each. We can define **morals** as the standards that guide people in a particular society. Therefore, morality is what people do and believe. **Values** are those things that have worth and are judged to be important. It is something we act upon. **Ethics** is the systematic study of morality that is the standards of good and bad, right and wrong. In a simple analogy, ethics is the theory and study of what people believe; and morality can be considered the practice of that belief system. **Bioethics** then can be defined as ethics applied to decision making in the area of biology, medicine, and health care.

Teaching Strategy for Using Bioethics in the Classroom

As teachers, we are presented with ethical questions by our students, the material we teach, and the media. If we are to deal with such issues in the classroom, we need new teaching strategies. Case study methodology has been shown to be one of the more effective ways to engage students in a bioethical decision-making process. A case study is a story including background about an ethical or bioethical issue. Those individuals involved, either directly or indirectly, are defined as stakeholders. The assignment of "stakeholder roles" to students is meant to create an understanding of different perspectives. Associating values with a stakeholder's position helps students analyze a person's viewpoint and actions. Teachers who use ethical/bioethical/moral issues in the classroom have found that students appear more engaged in the activity. It has been the experience of many teachers that a bioethics unit is very successful in achieving the following goals:

- **Stimulating the Moral Imagination:** Students should gain some sense of the emotions and the feelings provoked by difficult ethical choices. They will also gain insight into how different moral viewpoints influence how individuals lead their lives;
- **Recognizing Ethical Issues:** Students will learn to perceive a certain state of affairs as a moral issue. Moral issues will be shown to involve considerations of human value, questions of human freedom and choice, and implications for harms or benefits to society;
- **Developing Analytical Skills:** Students will acquire an ability to use certain evaluative categories such as rights, duties, virtue, justice, responsibility, freedom, respect, dignity, and well-being in constructing arguments that are logical, consistent, and defensible;
- **Eliciting a Sense of Moral Responsibility:** This goal is to help students to make better and more thoughtful choices. It is to encourage them to take action in accordance with ethical commitments and to have them assume a sense of responsibility for their own conduct and its affect on others;
- **Coping with Moral Ambiguity:** Students will learn to tolerate disagreements and ambiguity, to locate and clarify the sources of disagreement, to resolve ambiguities as much as possible, and to search for resolution of differences of moral viewpoint. Students will come to understand that some ethical issues have no final clear answer.

The following activities will provide two separate ethical case studies dealing with cloning and HIV. The case studies were selected from **New Choices, New Responsibilities: Ethical Issues In Life Sciences: A Teaching Resource On Bioethics For High School Biology Courses.** Suggested lesson plans for how to use these case studies in the classroom are also included. These types of activities usually take several class periods depending on how in depth you wish to pursue the topic. Following these activities, you will find an extension section that provides many other resources for bringing ethical issues and the decision making model into the classroom.

References:

Kieffer, G.H. (1979). Can Bioethics Be Taught? *The American Biology Teacher* 41(3):176.
Bruce Jennings, Kathleen Nolan, Courtney S. Campbell, and Strachan Donnelley. **New Choices, New Responsibilities: Ethical Issues In Life Sciences: A Teaching Resource On Bioethics For High School Biology Courses,** Second Edition, Revised 1997.

Activity 2:

Privacy and Genetic Screening

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
The teacher should review **Unit 5** of the CD-ROM for a background material. Discuss the decision-making model with the students prior to performing this activity.

Objective:
Using a hypothetical scenario, students can explore the ethical issues surrounding genetic testing. The results of the "genetic tests" are not meant to represent the actual proportion of individuals who would actually have such genotypes. Rather, the "results" are used for classroom purposes so that students might have the opportunity to wrestle with the problems they pose. As a follow up activity, students can research one of the genetic diseases disclosed in the hypothetical testing.

Teacher Directions:
Cut the "genetic" information template into individual squares. Place one square in an envelope for each student in the class and seal it (Use opaque envelopes so that students can not see their results). Certain squares can be eliminated for smaller classes. The represented "genotypes" are not meant to represent actual distribution in a population. Rather they represent possibilities and opportunities for researching genetic diseases.

Begin the activity by asking the class to imagine that they have the opportunity to learn specific genetic information about themselves. This information will be made available to them through a blood test that will screen them for certain genetic conditions. Since they have all had a recent blood test as part of their physical, the results are now ready. Review with them that some of them will have normal results (no significant disorders), some will have a pre-disposition to a condition that may or may not develop (BRCA 1 & BRCA 2), some may have a high disposition to a treatable condition (diabetes), and others may be disposed to a certain and untreatable condition (i.e. Huntington's Disease).

At this point, randomly hand out the sealed envelopes to each student. Ask them to keep the envelopes sealed for a few minutes. Begin the discussion with the following questions:

- Do you want open your envelope? What advantages or disadvantages might there be to your decision?
- If this information became public, what are the consequences?
- If this information was available as part of pre-natal screening, what might be some of the consequences?
- How does this information change your behavior? For example, if you inherit an allele(s) pre-disposing you to lung cancer, how can life style choice affect your chances of actually getting the disease?

For each question, have students consider the case of an individual who sought the genetic test. Also consider those individuals who are tested without their consent — children, fetuses, etc. After students have struggled with these questions for a time, have them respond to the questions individually on paper. Now ask them if they would like to open their envelopes. Have students respond by moving to one side of the room if their answer is "yes" and the opposite side if "no". Do not open the envelopes.

Continue the discussion and encourage the class to think about access to genetic information:

- Who should have access to the information inside the envelope? Who should not? Why?
- If you do not open your envelope, how can others gain information to the contents?
- Why might parents, doctors, health insurers, school systems, and employers want access to genetic information?

The discussion should engage students in a dialogue about issues such as privacy, fairness (Justice), individual rights (Autonomy), doing good (Beneficence), not causing harm (Non-maleficence), and informed consent. Review the Unit 5 on the CD-ROM for definitions and background information.

End the discussion by allowing students who wish to open their envelopes. Some students may not want to open their test results and that should be respected.

Genetics Results Template

Huntington's Disease (HD) — Dominant mid-life onset; early dementia and degeneration of nervous system; no treatment, no cure	Duchenne Muscular — Dominant in males/recessive in females; no cure	Cystic Fibrosis — Recessive; causes problems with mucous producing glands; interferes with breathing and digestion; treatment extends life	Thalassemia — Recessive; causes a type of anemia; treatment possible	BRCA2 defective mutation — Early onset breast cancer; 85-90% chance of expression
CONGRATULATIONS BRCA 1 & BRCA 2 — Healthy genes	Two copies of allele e4 — increases chance of developing Alzheimer's to 5-30 times the average	Color Blindness — Sex-linked; gene carried on the X chromosome	XYY — "Supermale" syndrome; has been linked erroneously to aggressive behavior in the past.	Multiple sclerosis — gene present; will activate in twenties
Gene for "addictive" behavior present	Growth hormone deficiency — treatment with GH necessary to achieve normal adult height	Lung Cancer — predisposition present; will be expressed if exposed to cigarette smoke	Hemophilia — sex-linked; recessive in females	Polyposis coli — tumors of the colon which may become malignant
Predisposed to bipolar depression — strong family history	Schizophrenia — predisposition present	Predisposed to early heart disease — prevention needed	Limb Girdle Muscular Dystrophy — Dominant in males; mid-life onset	***CONGRATULATIONS*** *NO SIGNIFICANT DISORDER*
Lung Cancer — predisposition present; will be expressed if exposed to cigarette smoke	***CONGRATULATIONS*** *NO SIGNIFICANT DISORDER*	BRCA2 defective mutation — Early onset breast cancer; 85 – 90% chance of expression	***CONGRATULATIONS*** *NO SIGNIFICANT DISORDER*	Lung Cancer — predisposition present; will be expressed if exposed to cigarette smoke
Hypercholesterolemia — early onset coronary artery disease; treatable	Tay-Sachs — recessive trait; result of missing enzyme necessary for lipid breakdown; neurological damage results in early death	Polycystic disease — Leads to progressive kidney failure	***CONGRATULATIONS*** *NO SIGNIFICANT DISORDER*	ADHD — Attention deficit hyperactive disorder; treatable

Activity 3:

Introduction to Ethics/Bioethics and Values

Level: Grades 9-12

Prerequisite or Previous Knowledge Required:
The teacher should review **Unit 5** of the CD-ROM for a background material. Discuss the decision-making model with the students prior to performing these activities.

Teacher Directions:
Day One: Introduction to Ethics/Bioethics and Values

Objective:
Students will gain an understanding of the study of ethics and bioethics within our society. They will recognize a need for informed decision-making in view of the expanding technology. The term *values* will be defined. The role of values in decision-making will be explored.

Activity:

- **Ask students to define the term value. List their responses on the board.** Suggestions from the students may include a value is what is important, worthwhile, and/or good. A value is chosen freely by an individual. A value is something we use to guide our behavior and decision-making. A value is something we act on repeatedly;
- **Ask the class where values come from.** Students may answer parents, church, religion, friends, and individual, the media, society;
- **Brainstorm with the class to give names to values.** List these responses on the board. Answers may include: honesty, fairness, loyalty, being trustworthy, kindness, not harming others, money, happiness, physical appearance, love, prestige, pursuit of knowledge, personal freedom, quality of life, power, achievement, family, compassion, emotional well-being, sincerity, courage, material satisfaction, religion;
- **Place the students into groups of four or five and ask them to categorize the values listed as individual, religious, and societal. This list will be used in the next class activity.**

Day Two: Bioethics/Decision Making

Overview:
The following materials may be used with case study **"The Cloning of a Human Organism"** in the genetics section of the manual listed below. For the purposes of this unit, the case study has been included in a modified form.

Text:
New Choices, New Responsibilities: Ethical Issues In Life Sciences: A Teaching Resource On Bioethics For High School Biology Courses, Second Edition, Revised 1997.

Objective: To enable students to consider the need for continuing genetic research in the light of uncharted territory. This case study asks the student to consider the benefits and/or burdens of pursuing human cloning. Some of the questions addressed include:

- Are there other means by which this couple can have a child other than cloning?
- Are the rights of the injured child and the cloned child being considered?
- Should insurers be compelled to provide coverage for cloning procedures if they become standard medical practice?

Method: One of the best ways to stimulate the moral imagination is to role-play a situation. This is best accomplished in small group format in order to encourage individual participation and reduce discomfort. Students are placed in groups of 5-6 members. It is most important that all members clearly understand their role as a stakeholder in this process. Therefore, roles with accompanying descriptions are distributed.

Materials: Roles (included) are printed on index cards and placed in an envelope with I.D. labels (self-stick tags with titles). Each group receives a folder with an envelope, task sheet (included), case study (included), and any other information selected. Clipped to the outside of the folder is a *Group Leader* card which describes the procedure (group leader can be randomly assigned). It is also helpful if each group receives a sheet of large newsprint paper and felt markers. Finished work will be displayed and discussed by each group.

Planning: While this lesson can be accomplished in a variety of time sequences, the following is an agenda for 2-3 class periods. Suggested times are listed:

- 45 minutes: Distribute folders to a selected group leader. Allow all members to familiarize themselves with the case and their personal roles. Remind each of them to identify with their role and respond as that stakeholder. Students should have the task sheet (see sample) completed and information listed on the large sheet of paper within the allotted time limit. Each group will select a spokes person to report to the class;
- 35 minutes: Each group spokesperson should present their group's finished product to the class;
- 35 minutes: This time can be used to briefly compare each group's work. Comparisons are made on the basis of similarities and differences in each group's final product. The following items are highlighted: the ethical problem identified by each group; stakeholders listed; possible solutions for this problem; values considered. Additionally, each group presents its best solution and defends it.

Day Three: Review of Previous Day's Work and Construction of a Survey

Overview: As a follow-up exercise, students will generate a qualitative survey that will investigate the public opinion regarding cloning. They will then collect data from a designated population (age specific and gender balanced). This data will be evaluated and reviewed. (**Note:** It is advisable to check school policy regarding distribution of surveys.)

Objective: The purpose of this final activity is to familiarize students with population sampling, qualitative versus quantitative data, age group bias, and the use of statistics for research and for public information. Students will also spend time reviewing the decision making process.

Method: Students will assemble in groups and list at least five possible questions to be used on the general survey. Each groups' list of questions will be presented to the class and ten questions will be selected from those presented. A sample population will be selected and students will collect data from ten individuals as an outside activity.

Student Evaluation: In order to provide students with a measurable goal and individual accountability, students will be evaluated on the basis of the following suggested guidelines:

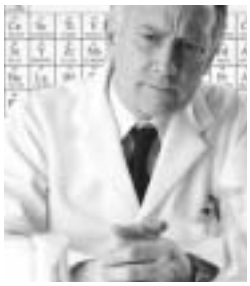
1. **Group work:** This may include role-playing, a debate format, or a co-operative design situation. Students are judged on individual preparation as well as group dynamics. It is particularly helpful if assignments are given to each group member. **40 points**

2. **Survey sheets:** Survey sheets may either be distributed by the instructor or compiled by the class. These sheets are used to increase public awareness of a particular issue. Each student is to assess 10-20 members of the selected population. Data will be compiled and simple statistics will be generated and discussed. **30 points**

3. **Assessment: Each student will submit personal answers to the following questions.**
   - Please summarize in five sentences your personal feelings about this case;
   - List two things you learned through research;
   - List one difficulty you encountered in doing this case study. **30 points**

Stakeholders: (Role Assignments)

Role: Child Advocate
You have been selected to represent the bronson child and the potential "cloned" child. Consider the cloned child will have a stake in the process, since she may be raised with expectations. The parents may expect her to be a certain type of child. They may expect her to fulfill their dreams for their first child. If the injured child survives, the clone will have to learn to live with a genetically "identical" sibling.



Role: Doctors and Researchers
You are concerned that opportunities for research in this field might improve or decline depending upon the decision made by the committee. This group includes members of the hospital staff, and researchers. It is your job to decide if this research procedure serves the "greater" good. How will this impact other research such as stem cell cloning which has therapeutic advantage? If this type of research is restricted, opportunities for research in this field including stem cell cloning may be compromised.

Role: Regulatory Officials
As regulatory officials, you will have to balance competing values and norms in this particular case. This decision will definitely impact others. You realize that the general citizenry has a stake in whether cloning will be allowed. If you approve of cloning as a component of standard medical care, then insurers may be compelled to provide coverage for this practice. Of course, you are an elected official and you are up for re-election in six months

Role: Citizen and Community Representative
If cloning becomes a component of standard medical practice, insurers may be compelled to provide coverage for this practice. You are concerned how this will impact the cost of insurance to the average citizen. You also empathize for the parents and feel that their right to be parents should be upheld. However, if they are allowed to clone a cell of their child, they will have to address the challenges of living with a child identical to their first child. You wonder if this is a problem. You also have questions about the difference between cloning and stem cell research. How will the decision made impact further research?

Group leader: please distribute cards and matching stick on labels to each group member. Each person should wear their identity label. Select one member of your group for the additional role as group spokesperson and give them their assignment card. Your group will also need a recorder so please select one.

CASE: The Cloning of a Human Organism

The child of a young couple is badly injured when she is hit by a car while bicycling home. Upon learning that the child is unlikely to survive, the parents ask the hospital administrator for permission to take genetic material from their daughter so that they can clone a new child. It took several years and numerous visits to a fertility clinic for them to have this child, and they think it unlikely that they will be able to conceive another. Their daughter is an only child, and cloning her genetic material would provide them with another child with a genetic contribution from both of them. This is very important to both parents. They take their concerns to a private fertility clinic and research center where research into human and non-human cloning is relatively unregulated. While the researches inform the parents that there is a high rate of failure in efforts to clone mammals, they are prepared to assist the couple. A clinic staff member leaks this information to the media, and a State Congressman recommends an immediate ban upon all human cloning within both public and private facilities. A State task force is established to review the request of the parents and you are appointed to the committee.

Adapted from: New Choices, New Responsibilities: Ethical Issues In Life Sciences: A Teaching Resource On Bioethics For High School Biology Courses, Second Edition, Revised 1997.

STATE TASK FORCE

You are members of the Governor's State Task Force. All members of the group are expected to participate in the discussion. ONE member will act as the SPOKESPERSON for the group; however, each member should be prepared to report.

Task Force Directions:

1. Identify your stakeholder role to the group.
2. As a group, read the Case Study. Begin your discussion and record comments on the task sheet. If you have further questions, ask the instructor.
3. When you have completed the group work, a recorder should list the results on the newsprint. One member of the group will act as spokesperson; however, everyone should be prepared to answer any questions from the class.

Reminder: Each of you has a different role assignment. As you complete this see the problem as that person would see it.

Points to Ponder:

- What are the benefits or burdens of pursuing human cloning?
- Are there other means by which this couple can have a child other than cloning?
- Are the rights of the injured child being considered?
- Should insurers be compelled to provide coverage for cloning procedures if they become standard medical practice?
- Should researches have the right to offer this option of "cloned" babies to couples and single individuals?
- Should everyone regardless of economic status have the right to such a procedure?

Task Sheet

Name _____

Stakeholder Role _____

1. What are the facts presented in this case study?

2. Identify one problem of major importance presented in this case study. Remember to phrase this as a question to receive full credit ("Should…").

3. List any stakeholders (those affected by this problem either directly or indirectly) involved in this issue in any capacity. Also list those values important to each stakeholder.

Stakeholder	Value
1. _____	1. _____
2. _____	2. _____
3. _____	3. _____
4. _____	4. _____
5. _____	5. _____
6. _____	6. _____
7. _____	7. _____
8. _____	8. _____
9. _____	9. _____
10. _____	10. _____

4. Outline several possible options. Consider the following: what action will be performed, by whom, how will the needs of each couple be considered, why will it solve the problem, where will the action take place, and when? List these options. Considering all options, select the best possible solution from your list and "star" it.

5. Consider what values you used in choosing a solution. For example: scientific autonomy; benefits versus harms; beneficence; non-maleficence; risk perception; non-interference with nature; right to procreate; ethical significance of this type of medical intervention; fairness; patient autonomy; advancement of science. List the values that support your decision.

Final Review:

Once the group has completed discussing the case and recording their notes, group consensus must be reached. Remember to list all results on the newsprint sheet provided. The group will be presenting these results to the class. Be prepared to explain and support your decision. Your teacher will direct you in the class discussion. Follow the rules for open discussions established by the teacher.

Activity 4:

Case Study – HIV and Wrestling

Level: Grades 9-12

Prerequisite:
The teacher should have read through activity one for this unit, which explains how to use an ethical decision-making model in the classroom. The teacher should also discuss this model with the students prior to performing these activities.

Teacher Directions:
The following activity provides an ethical case study and suggested lesson plan dealing with HIV. After students read the case study, they should be organized into stakeholder groups to prepare their presentations. Once each group has completed this task, several students should be selected to represent the Board of Education. Each of the stakeholder groups will present their argument to this group who will then make a decision regarding the status of the student wrestler. This activity will take at least two 45 minute class periods.

This activity is followed by an extension section that provides many other resources for bringing ethical issues and the decision making model into the classroom.

Student Activity 4:

HIV and Wrestling Case Study

Objective:
The objective of this activity is to evaluate a problem from the viewpoint of its ethical impact, and determine the effect of various solutions on those affected by the problem.

Background Information:
Refer to the handouts provided by your teacher for the current update on the HIV/AIDS epidemic. The Centers for Disease Control also have the latest statistical information regarding HIV and AIDS available at http://www.cdc.gov.

Case Study: HIV in Wrestling

James is a 12 year-old who has always been small for his age, but strong and wiry. He lives with his aunt, Rachel, and his older sister, Christina. James wants to try out for the wrestling team, and he believes that Aunt Rachel will be supportive, although she knows that he is HIV-positive.

Although James has never had any illness associated with HIV infection, the principal at his school is aware of his status. James, Aunt Rachel, and the principal have arranged a meeting with the wrestling coach, Mr. Binder. They explain to Mr. Binder that James has bee infected with HIV since birth but has never had any health problems that were felt to be due to HIV infection. He is physically capable of wrestling with others his own size and he feels that wrestling is a sport at which he may excel. Mr. Binder has been trained in the use of universal precautions for any episodes of bleeding that occur during wrestling practices and matches. Nonetheless, he hesitates as he hears James' request, wondering what are his obligations to the other wrestlers, their parents, and others who may at some point learn that an HIV-infected student has been allowed to join the team. What should Mr. Binder do?

From: New Choices, New Responsibilities: Ethical Issues In Life Sciences: A Teaching Resource On Bioethics For High School Biology Courses, Second Edition, Revised 1997.

Procedure for this activity:

1. As a class, read the case study HIV and Wrestling out loud (included).
2. Brainstorm and identify the ethical question(s) associated with this case study.
3. Brainstorm and identify the stakeholders involved in this ethical issue. The class will vote to determine the stakeholders that will be represented during this class discussion.
4. Groups will be randomly selected to discuss one stakeholder each and determine what values are driving that stakeholder's thoughts and behaviors regarding the ethical issue. The groups will then develop an argument to bring in front of the Board of Education. Students from this class or students/teachers from another class will be selected to represent the Board members.
5. Each group will be allowed to present their argument to the Board one at a time. After each group has presented, any group that wishes to present a rebuttal to comments from other groups may do so in an organized fashion according to the Board members' direction.
6. The Board of Education will leave the room and come to a decision based on the arguments presented.
7. As a class we will discuss how the Board's decision impacts each stakeholder.
8. Each student is responsible for completing the follow-up assignment outlined below.

Follow-up Assignment:

Find out if there is an existing policy in your school district that deals with students and/or staff who have an infectious disease. You may want to ask an administrator and/or the school nurse where you can locate this information. Please be courteous and do not wait until the last minute to ask these individuals for help with your assignment. It is expected that you will approach them in a professional manner and will provide them with adequate time to help you.

Write down what the policy is. Discuss if you agree or disagree with this policy. Explain WHY you feel this way. Make sure you use factual information that you have received in class or from other reliable sources to support your opinion. If you do not agree with the policy, rewrite it to create a version that you would feel comfortable with. If a policy is currently not in place, create one that you feel would be appropriate to present to the Board of Education. Explain WHY you feel your policy is fair. Once again, use factual information to support your statements.

Activity 5:

Culture and the Perception of Genetic Disease

Level: Grades 9-12

Previous Knowledge Required:
This activity could be done in conjunction with others or independently. No specific knowledge of genetic diseases is needed, although a basic understanding of different possible modes of inheritance is recommended.

Teacher Instructions:
To extend the concepts addressed in activity 3, students could undertake an examination of the ways in which cultures construct and maintain particular concepts of genetic diseases that are endemic in the area. There are numerous examples of otherwise rare conditions that become quite common in particular communities due to genetic drift events. For instance, the rate of congenital deafness on the island of Martha's Vineyard was over 300 times the national average in the 1700's; the condition was accepted in the community and sign language became a common method of communication. Another example is albinism, which is common in some Central and South American indigenous populations as well as some South Pacific groups, and many societies have developed mythologies about the condition. Other ideas for further study include polydactyly and thalassemia. Students could research these or other similar situations and write a paper or give an oral presentation about the condition and the ways in which the individuals who have the trait are perceived in the community. This project fosters research and writing skills in students and exposes them to cultures that may be very different from the students' own. This activity might satisfy requirements for writing across the disciplines as well as integration of multicultural elements into the curriculum.

Some websites that might be useful for getting started:

On the deaf community in Martha's Vineyard
http://www.marthasdirect.com/deafness/community.html

On albinism and the Cuna, a Panamanian indigenous population
http://www.nhbvi.com/internet/Eye/albinism.html
http://thorup.com/cuna.html

Teacher Resources

The following is a list of resources that will help you further explore how to use ethical case studies in the classroom:
http://www.bio.org/bioethics/
http://www.georgetown.edu/research/kie/
http://www.georgetown.edu/research/nrcbl/nbac/

The National Committee on Vital and Health Statistics, The Public Advisory Body to the Secretary of Health and Human Services
http://www.ncvhs.hhs.gov/

University of Minnesota
http://www.bioethics.umn.edu/

University of Pennsylvania Bioethics Center
http://www.med.upenn.edu/bioethic/

The **Coalition for the Advancement of Medical Research (CAMR)** is comprised of nationally-recognized patient organizations, universities, scientific societies, foundations, and individuals with life-threatening illnesses and disorders, advocating for the advancement of breakthrough research and technologies in regenerative medicine — including stem cell research and somatic cell nuclear transfer — in order to cure disease and alleviate suffering.
http://www.camradvocacy.org/fastaction/default.asp

President's Council on Bioethics
http://www.bioethics.gov/

"Ethics Matters" is a biweekly feature from the University of Minnesota's Center for Bioethics and CNN Interactive. "Ethics Matters" is written by Jeffrey P. Kahn, Ph.D., M.P.H.
http://www.cnn.com/HEALTH/bioethics/archive.index.html

Genetic Science Learning Center at the Eccles Institute of Human Genetics University of Utah
http://gslc.genetics.utah.edu/

For a variety of case studies appropriate to life and physical science classes:
http://onlineethics.org/edu/precol/classroom/index.html

The Northwest Association for Biomedical Research Webpage includes useful links to resources and teacher lesson plans:
http://www.nwabr.org/education/bioethresc.html

Yahoo Bioethics Search
http://dir.yahoo.com/Science/Biology/Biomedical_Ethics/
http://www.dnaftb.org/dnaftb/
http://www.eugenicsarchive.org/eugenics/
http://www.nih.gov/sigs/bioethics/
http://www.hopkinsmedicine.org/bioethics/
http://www.shef.ac.uk/bioethics-today/

This site is sponsored by the **Eubios Ethics Institute,** which promotes bioethics on an international scale. This site is titled **Bioethics for the People by the People.** It provides a good overview of international bioethics and the idea of how genetic disease can be perceived differently in various cultures. It also includes an international bioethics survey.
http://www.biol.tsukuba.ac.jp/~macer/BFP.html

This site is sponsored by the **McGraw Hill Companies** and provides case studies dealing with a multitude of topics. Each case study has accompanying analysis questions.
http://www.mhhe.com/biosci/genbio/casestudies/

Case Studies in Bioethics by Ronnee Yashon
This is a book that provides an introduction to using bioethics in the classroom, as well as several case studies dealing with various topics. Each case study has accompanying analysis questions.

Extension Activities:
Career Explorations

Activity 1:

Exploring Careers in Genetics Using an Informational Interview

Level: Grades 9-12

Teacher Directions:
The purpose of this activity is to explore careers in genetics, biotechnology, and pharmaceutical areas. Additionally, students will have opportunity to begin thinking about how to communicate, dress, and behave in a manner suitable for professional interactions.

This activity lends itself well to interdisciplinary collaboration. You could work collaboratively with teachers from the business and/or English departments in your school to develop student communication skills for business phone calls and emails, interviewing, and writing thank you notes.

This activity can be used as a team or small group assignment, or an individual assignment. If it is the student's first interview experience, a team approach could work well, with students alternating asking questions. Class discussions can evolve from student updates, questions arising from their work, and results of the interviews.

Contacting the Employee

Depending on your students, you may want to prearrange some contacts for students. It may be that your school parent group could help gather names of willing candidates. Prearranging candidates would also provide opportunity to decide how students will conduct the interviews. If students themselves contact the employees, some coaching may be necessary to help students follow through successfully with professional business phone calls or email.

Interview Questions

It is recommended that students create their own list of interview questions. However, students may need suggestions for sample questions, in order to begin generating their own questions. Possible questions might include:

- What is the title of your position?
- What do you do?
- Which parts of your job do you like most? Like least? Why?
- How long have you been in this position?
- What is the academic preparation for your position?
- What kind of experience did you have before beginning this position?
- Do you usually work alone or with others?
- Does your position require you to travel? If so, why, where, and how often?
- Do you have to keep learning to keep up with your position? If so, how and where?
- Is this the job that you thought you were going to have when you were my age?
- What are your future career goals?

Once questions have been determined, a question template for note taking can be designed either by students or by the teacher. This question template should have a header where students can enter the employee name, position, company name, contact information, and date of the interview.

Beginning and Concluding the Interview

Students may need some coaching before the interview regarding appropriate dress and behavior. Time permitting; students could practice self-introductions with each other, giving a handshake, their name and their school. Students could also practice posing their questions and concluding the interview.

Class Follow-up

As basis for a class discussion, students can share verbally the results from their interview experiences. They could also create a class notebook to collect all the interview templates and notes for future reference. Students could discuss how to write a thank you note or email and follow through with this communication. As a formative assessment for your own future use, you might have students write a brief summary for you telling what they learned from this experience, how it was useful to them, and how they would like to do it differently next time.

Any future job shadowing arrangements can be completed on an individual or group basis, in compliance with the company's procedural and insurance guidelines and those of the school.

Student Activity 1:

Exploring Careers in Genetics Using an Informational Interview

Introduction:
What kinds of careers are available in the fields of genetics, biotechnology, and the pharmaceutical industry? Why do people working in these areas like their jobs? What is the background of people who work in these positions? To help increase your understanding of possible career options, it is often helpful to talk to someone in the field. An informational interview is a good way to begin a conversation and learn more about specific careers in genetics, biotechnology, and the pharmaceutical industry.

Informational Interview:
An informational interview can be conducted in person, on the telephone, or online. It can be done individually, or as a team. What would be the best way for you to conduct an informational interview?

Contacting the Employee:
Perhaps you, your family, or a friend knows someone you would like to interview. If so, the first step can be simply to ask the person if he or she would mind meeting with you, speaking with you on the phone, or communicating with you by email.

If you need to make a new contact for the interview, look for a company or work site near you so you can call or email the community outreach representative for a reference. If necessary, make an appointment for a personal or phone conversation at a time of mutual convenience.

Interview Questions:
Before the interview, think of what you would like to know about the person's job. Make a list of these questions. If you work on email, the questions can be emailed to the employee. If the interview will be conducted on the phone or in person, make a question template so you can take notes during the interview. Be sure you include a header for the name of the employee, his or her position, the company, contact information, and date of the interview.

Beginning the Interview:
If your interview is in person, it is important to arrive on time for the interview and dress in a professional manner. You might greet the employee with a handshake while giving your name and school. During the interview, you may want to take some notes on your question template.

Concluding the Interview:
At the end of the interview, remember to thank the employee for his/her time in talking with you. In addition, it is professionally courteous to send a thank you note after you have talked with the employee.

If you have discovered after the interview that you are interested in learning more about this person's job, you might ask if is possible to visit the employee again.

Sometimes companies permit students to job shadow employees for a few hours. If you would like to do this, ask your teacher about specifics for the company in which you have interest.

Activity 2:

Exploring the Profile of a Biotechnology or Pharmaceutical Company

Level: Grades 9-12

Teacher Directions:
This assignment offers students an opportunity to investigate a biotechnology or pharmaceutical company to learn about many areas such as what the company does, the structure and some of the current activities of the company.

Roche is used as a model for this investigation because Roche is an example of a large company having international sites and many areas of research and product development. However, if you have other biotechnology and pharmaceutical companies located in your area, you may want students to investigate these companies also. Students might enjoy looking at small companies as well as some of the larger, more established firms and making comparisons among them.

The activity lends itself well to teamwork using student teams of two to prepare a one-page summary of the company being researched. It can be used as a homework assignment, if students have access to online computer searches. It also works well as a class assignment if students have online access as a class or through a school computer lab.

To summarize this activity and share information with the class, there are several options.
Some suggestions follow:

1. Student teams can present their findings orally to the class. Class discussion could include addressing questions such as:
   - Advantages/disadvantages of working for this company?
   - What other questions do you have about this company?
   - Where could you go to find answers to these questions?
2. Compile a class notebook of each team's submissions. Alphabetize the entries and use the notebook for further reference by all students in the class or for use in contacting the companies for further information.
3. Share the class notebook with other classes as a resource for their own class research.
4. Item #4, the last search and question, can be used as an extra assignment or as a separate assignment.

Student Activity 2:

Exploring the Profile of a Biotechnology or Pharmaceutical Company

Name _____

Introduction

What does a biotechnology or pharmaceutical company do? What are the goals of the company? How is the company organized to reach the desired goals? How could you learn more about a biotechnology or pharmaceutical company? Where could you find answers to questions such as these? One method is to do an online research investigation. Then you could share your information with the class and others.

There are many biotechnology and pharmaceutical companies of differing sizes and types located in the US and throughout the world. This investigation offers you opportunity to investigate Roche as an example of a large company having international sites and many areas of research and product development.

Directions

1. Use a search engine to enter a search for "Roche.com."

2. Explore this web site to investigate the following areas:

   • Name of the company

   _____

   • Contact information (web address, address of main office, phone number if available)

   _____

   _____

   _____

   • Size of company

   _____

   • Company history

   _____

   _____

   _____

   _____

   _____

   • Company goals

   _____

   _____

   _____

   _____

   _____

   • Areas of focus

   _____

   _____

   _____

   _____

- Job opportunities

- Other information you find interesting

3. Summarize your findings onto one page, suitable for sharing with others.
4. Time permitting, use the Roche web site and click on "Roche as Healthcare Provider." Look at each of the following categories: Healthcare, Predisposition, Targeted Screening, Self-medication (over the counter drugs), Prevention, Diagnosis, Therapy, Monitoring, Integrated Programmes and Experiencing health. Use this information to answer the following question:

   - How do these areas of emphasis combine to create a sequence of modern healthcare based upon our new knowledge of human genetics?

Teacher Resources:

- *Glossary Activity*
- *Misconceptions about Genetics*
- *Questions used with Decision Making Models*

Glossary Activity

Topic: Glossary of Terms

Level: Grades 9-12

Prerequisite of Previous Knowledge Required: Varied

Teacher Directions:
Students learning about genetics will no doubt benefit from a ready reference to biotechnology and genetics terms. Classroom text glossaries vary widely regarding the inclusion of up to date terms. Therefore, students may need to explore other sources for contemporary glossaries. The following web references include a variety of glossary options incorporating understandable, usable terms describing content and concepts related to current genetic issues and practices.

1. Use a search engine to investigate "Biotechnology glossary of terms." Several glossary options are displayed, requiring a wide variation in reading level as well as level of understanding. A search of this site could be interesting and challenging for advanced level students. For students of a beginning level, the following two options may be more suitable.
2. Under the web site http://filebox.vt.edu/cals/cses/chagedor/glossary.html is a 64K glossary titled "An Agricultural and Environmental Biotechnology Annotated Dictionary" by Susan Allender-Hagedorn and Charles Hagedorn, with "occasional updates." Terms are listed alphabetically and are concise enough for use by many high school biology students.
3. Again, under the web site http://www.kumc.edu/gec/glossary.html is an extensive web site from the University of Kansas titled "Glossaries of Genome/Human Genetics Terms." There are many interesting choices under this web site. The initial "Glossary of Genetic Terms" could be suitable for high school use and is somewhat less extensive than the Hagedorn reference.
4. The second option, "Glossary of Genetics," is a talking dictionary from the National Human Genome Research Institute. The web site for this resource is: http://www.genome.gov.glossary.cfm

Misconceptions about Human Genetics

Introduction

Introductory genetics is a complex science and its early learning can be difficult. In order for students to attain deep understanding of genetics concepts, they must explore their prior understanding and overcome misconceptions, become capable of using genetics terms that represent key concepts correctly, and employ models of inheritance at several levels of organization such as persons, families, and populations.

Misconceptions can originate from many places and have the capability of becoming resistant to new understanding. Students will often revert to prior misconception even wen new information and experiences should guide them to construct new meaningful learning. Since the causes of genetic inheritance are basically invisible and are demonstrated across time and with varied organisms, the core concepts are difficult to distill.

In this section, ten prevalent misconceptions will be identified and strategies to overcome them will be explained. Reference to the Roche disc will be included in the teaching suggestions.

Misconception # 1: Sperms (eggs) carry genes for half the features found in the offspring. (Relevant disc sections: Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

Students may assume that the information that controls half of the discreet features of the offspring are completely determined by the gamete from one parent and that the other parent contributes genetic material for the other half of the features. Phrases such as, “this baby has your mother’s eyes and your father’s chin” contribute to this misconception.

An initial strategy to correct this misconception is to introduce students to a human karyotype (lesson?) so they can visualize the paired nature of chromosomes. Use the frames in Mendelian genetics to explain the paired bits of information called alleles that appear in linear fashion along the chromosomes. Explain that these alleles can be different forms of the same gene and that this genetic information (DNA, understood from the first discs explanation) is paired on these matching chromosomes. These alleles control the same trait; therefore, each parent contributes one of each pair of chromosomes (carrying the allele) to the offspring. The reasoning follows that each parent then contributes information about every trait in the offspring. Later study will clarify how modes of inheritance, sex linkage and other phenomena contribute to actual phenotypes. Students will better understand the details of meiosis, the process by which one chromosome of each homologous pair gets sorted into a gamete. From activity 3 in Unit 1, students will have manipulated these chromosomes to understand how the offspring gets one of each kind of chromosome from each parent. This early understanding is essential for student to build more complex understanding of gene function, complex (multifactorial) conditions, and the source of human genetic variation.

Misconception # 2: Males inherit their traits from father and females get their traits from mother. (Relevant disc sections: Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

The karyotype activity 3 in Unit 1will help the student visualize the transmission of chromosomes to the offspring. When gene loci are identified on the chromosomes and the transmission is understood, the student can recognize that information for every trait arrives from both parents. As modes of inheritance are identified, the various combinations of alleles and phenotypes become clear. Clear examples of unaffected mothers carrying an allele for colorblindness and passing it to half their sons will help dispel this misconception. Refer to the Roche disc sections on pedigree analysis and gene expression – Unit I: Mutations frames 1-14 and Mendelian inheritance 1-4/14.

Misconception # 3: Normal, healthy parents cannot pass a genetic disease to their offspring. (Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

The section on modes of inheritance will clarify that individual parents can each carry a recessive allele, and each can contribute that allele to the offspring. All individuals carry at least a few such recessive disease producing alleles that when paired can produce a disease phenotype. For example, recessive disease producing alleles can be carried by normal females and then passed to sons whose phenotype is affected. In addition, situations of incomplete penetrance and new mutation can create this phenomenon of healthy parents contributing information to the offspring that causes their condition.

Misconception # 4: If a couple has a child with a recessive condition, their next three children will NOT have the condition.
Or
If a couple has had three children born with a recessive disorder, the chance that the fourth child will also be affected is very small.
(Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

Students often misunderstand the meaning of independent and dependent events. They believe that recent events will always have an influence on the outcome of future events. Students must come to recognize that the assortment of each pair of chromosomes at each separate pregnancy is an independent event. More clearly, the outcome of one event, in this situation, does not affect the outcome of the next event. In activity 3 Unit 1, you may have had student flip a coin to determine which chromosome of each pair is sent to the offspring. If so, you can ask students if heir flip for chromosome pair # 1 influenced their flip for chromosome pair # 2. When they deduce that there is no causative connection between those events, they may transfer this understanding to the same independent determination of allele combinations in an offspring. The probability of successive independent events considered together will be the product of the independent probabilities. However, the probability of each separate event remains constant.

Genetic misconception # 5: If a genetic trait is dominantly inherited, all children of a person with that trait will also have the trait.
Or
If all children of normal parents have a genetic trait, this proves dominant inheritance.
(Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

Further investigation in the section about modes of inheritance will reiterate the independence of each pregnancy and the possible combinations of offspring to parents with a given genotype. Dominantly inherited conditions in one or both of the parents are not necessarily inherited because the parental genotype can be heterozygous. Only half the time, on the average, will a parent pass on the allele that expresses the dominant phenotype.

Dominant inheritance is vertical in transmission in that the allele must be present in order to be passed on. Exceptions such as incomplete penetrance in a parent and other exceptions can be explored with order students.

Misconception # 6: A trait that occurs in several brothers and sisters who have normal parents is not hereditary.
(Unit I: Intro to Genetics, Mendelian inheritance 1-4/14)

Some modes of inheritance including autosomal recessive and X-inked recessive are consistent with unaffected parents and affected offspring. With independent events, if an offspring genotype can occur once, it can occur multiple times. With complex polygenic traits several of the offspring could have enough active alleles to have the phenotype even if the parents are not affected. Consider the following example. Several brothers and sisters could be in an environmental setting different from their parents. Their genetic predisposition could bring them to a disorder that was not present in the parents. In this scenario, the genetic component would be genetic (polygenic and familial) but not necessarily identified with a single gene.

Misconception # 7: Traits can be classified as either genetic or environmental.

Genes never work in a vacuum. There is always an environment in which genes express their information. Each gene works in concert with the other 30,000 or so others genes in a human. In addition, this gene expression occurs in an outside environment consisting of all we breathe, eat, ingest, and contact. There is virtually unlimited variety in human genotypes and so the range of responses to outside agents including pharmaceutical medicine is in turn virtually unlimited. Therefore, no genetic condition is beyond some modification by the individual's environment. The complex instructions of the human genome as expressed in the living organism are in constant interaction with an environment. Each domain modifies the other. In short genes determine the powers of adaptation; they specify the complex mechanisms of homeostasis and individuality. That is they set the limits within which each individual can respond to his/her environment. They determine, not what we are, but what we can and what we cannot be."

In conclusion, genes and environment always combine in varying proportion to produce the phenotype of the moment.

Misconception # 8: Hereditary traits are passed through blood.

Our language perpetrates this misconception as we use terms such as “bloodlines”, “blood brothers”, or “it runs in the blood”. The blood contains nucleated white cells that are grown and examined to create metaphase pictures of human chromosomes. But these are not the cells or gametes which do the work of genetic transmission. Some individual would be concerned that a blood transfusion would transmit human traits from the person who donated. Transmission of human traits occurs through eggs and sperm and the chromosomes they contain. Basic genetic lessons in these materials will reinforce this reality.

Misconception # 9: Body cells are different types because they contain different genes.

The wide variety of cell types in humans would seemingly reflect the wide variation in genetic expression. The misconception that each cell is different because the genes are different probably exists because it is close to being accurate. The genes of each cell are the same since each cell is produced by the accurate replication of the genetic material of the previous cell. The wide variety of phenotypes that exist in this collection of “cloned” cells is because selective expression of those genes. Each exerts control over which genes are active and which are not expressed. The variety is variable expression, not variable numbers or kinds of genes. Environment can play a part in inducing expression of genes too. When a person’s individual variation is determined, medicines can be designed that will have the best effect on that genotype.

Misconception # 10: Incompletely dominant and polygenic traits result from a “mixing” of genes. (Mendelian basic experiments and relevant disc sections)

When a resulting phenotype is intermediate with respect to two contrasting parental traits, or when a trait has continuous variation, a student may assume the “blend” is at the gene level. When clear instruction has preceded the introduction of these observations, models that explain these patterns are clearly understood. Often the intermediate phenotype is a result of expression of both alleles with the blend consisting of the visual mix of the expression. An example is roan cattle. In polygenic inheritance, chromosomes are segregating independently, genes are working normally, and the resulting continuously distributed range of phenotypes is actually because of the variation produced by individual chromosomes independently assorting. The unknown aspect of this polygenic model is how each gene contributes in an equal and additive way to the phenotype. The key misconception is that the DNA at the molecular level is involved in some “mix” to create this expression.

Misconception # 11: Dominance is associated with males and/or dominant genes are more powerful than recessive genes.
(Relevant disc sections)

The misconception that there is dominance associated with gender is confronted with our initial view of the karyotype. Point out to students that gender is controlled by the presence of the Y chromosome and that the 23rd pair of chromosomes independently segregates at meiosis just like the other 22 pairs. The patterns or modes of inheritance reviewed in the disc include those that are considered autosomal. Gender is entirely independent of the distribution of these genes. In contrast to the misconception, X-linked dominant traits do exist where the allele responsible for the trait only occurs on the X chromosome. In this mode of inheritance, all the daughters of an affected male will be affected with the condition. In contrast however, an affected heterozygous female, in this mode of transmission, will transmit the condition on the average, to only half of her sons.

At the molecular level, dominance is simply the ability to create a phenotype with only one allele. This process has nothing to do with strength, however you might define the term, but simply the presence or absence of some particular protein in a pathway. Recessive traits result when two alleles combine to produce the phenotype.

Questions to Accompany an Ethical Decision-making Model Used with a Case Study

1. State the Ethical Problem

a. Do you think or feel this is a hard question to answer? Why?
b. What are some things you would consider in making this decision?
c. What are the key points of this conflict for you?
d. What elements of this situation do you see as irrelevant?
e. Using the concept of rights, goals, or duties, categorize this conflict.
f. What issues in this dilemma are hard to talk about? What makes it difficult?
g. Can you see yourself facing the possibility of making a decision around a problem such as this? Why or why not?
h. Have you read or heard about a similar situation recently?
i. What important missing information would you want in this case?

2. List Alternatives or Possible Solutions

a. List solutions that you would never choose.
b. List some solutions your parents might choose.
c. Think of the most non-conforming students in school. What might they choose?
d. What would a spiritual leader of your faith do in this situation?
e. List some solutions that reflect a "conservative" point of view.
f. List some alternatives that the adults around you would expect.
g. List some alternatives that seem the best for you.

3. Place a (+) beside each "good" consequence and a (-) beside each "bad" one.

a. How would you define "good" and "bad" as you classify these consequences?
b. Are there any ethical principles or rules of conduct you consider as you make your classification?
c. What are the things you consider when deciding if a consequence is "good" or "bad"?

4. Consequences which Make a Solution Totally Unacceptable

a. Is simply adding and subtracting the pluses and minuses an adequate way of assessing all of the consequences?
b. Are there other considerations in addition to consequences that influence your classification?
c. Did you identify a single consequence that makes this solution unacceptable?
d. Do you know anyone else for whom your decision would be unacceptable? Why?
e. What new knowledge would change your decision?

5. List Three Reasons Why Others Might Disagree With Your Solution

a. How can people with equal knowledge of the facts still disagree?
b. Identify a value held by someone who would disagree with you.
c. Using the concepts of rights, goals, and duties, discuss why someone else might disagree with you.
d. How do institutions like school, government, and industry deal with disagreement?

6. Restate Your Solution and Give a Confidence Measure on the Scale

a. Why do you think that your confidence measure is at that point on the scale?
b. What are reasons a person would NOT have high confidence?
c. What suggestions would you give a friend who never seemed to be satisfied with their important decisions?
d. What would be your response if important information relevant to the problem became available AFTER your decision was made?