Module Guide: Gene Therapy: Molecular Bandage?

Module Overview

Abstract:
This guide for teaching the *Gene Therapy: Molecular Bandage?* module includes: (1) a summary of the module content, (2) Essential Questions and Enduring Understandings, (3) example lesson plans for 2-8 days, (4) suggested uses for each activity, and (5) science education standards.

Appropriate For:
Ages: 12 - 20
USA grades: 7 - 14

Class Time:
1-8 class periods, as suggested in this guide

Module Overview Web Address:
http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=gtmod

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Module Content Summary

To assist you in learning about this topic and in planning lessons for your students, we begin this Module Guide with a summary of essential information about gene therapy. Additional details and more advanced topics are provided in the module materials.

Gene therapy is a way to treat disorders caused by mutated genes. It involves adding a normally functioning copy of the gene(s) to enough affected cells to restore normal function.

Disorders that are candidates for gene therapy have the following characteristics:

- They are due to mutations in one or more genes; single-gene disorders are more easily treated.
- The responsible gene is known and has been cloned in the laboratory.
- The affected tissues are known.
- The role of the protein encoded by the gene is known.
- Adding a normal copy of the gene will fix the problem.
- It is feasible to deliver the gene to the affected cells.

To design and carry out a gene therapy treatment, a researcher must: 1. Identify the gene(s) responsible for the disorder. 2. Make copies of the normal gene. 3. Insert the copies into vectors. 4. “Infect” the affected cells with the vectors. 5. Activate the gene so that transcription and translation take place.

Viruses, liposomes, and naked DNA have all been used as vectors. To create viral vectors, the genome (DNA or RNA) is removed from a virus and replaced by the gene therapy genetic material. Also, the surface proteins on some viruses can be genetically engineered so that they will bind to particular cell types, providing specificity for delivery.

There are several critical factors to consider when choosing a vector for gene therapy. These include:

- Gene size - Most vectors have an upper limit on the number of base pairs they can hold.
- Target tissue – Some vectors only infect a particular type of cell while others can be engineered to this specificity.
- Integration into the genome – Vectors that lead to integration of DNA into the genome, or copying of DNA along with the genome, have a long-lasting effect. Vectors that do not function in these ways have a short-lived effect. Vectors that lead to random integration in the genome may disrupt other genes, causing negative side-effects.
- Cell cycle stage – Some vectors only infect dividing cells, others infect non-dividing cells, and some can infect both types.

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Both *in vivo* and *ex vivo* techniques have been used for gene therapy. *In vivo* techniques involve injecting the vector directly into the patient's body, using a vector designed to target the affected cells. For *ex vivo* techniques, the affected cells (such as bone marrow cells) are removed from the patient's body, cultured in a Petri dish, "infected" with the normal gene, and returned to the patient's body.

Once inside the target cells, the normal DNA may be carried to the nucleus, where it may integrate into a chromosome. In order for the therapy to be successful, the normal gene must be activated and transcription and translation must take place, leading to the production of the normal protein.

Although research on gene therapy has been ongoing for several decades, there have been few successes to date. Challenges to developing successful treatments include:

- Immune system responses to vectors, which can lead to serious illness or death (as in the Jesse Gelsinger case)
- Controlling integration of the new gene into the genome so that it does not disrupt other genes (as happened with treatment of several cases of SCID)
- Appropriate gene activation
- Delivering the gene to cells in the target tissue, but not to germline (reproductive cells), where it would be passed on to offspring
- Delivering enough copies of the gene to target tissues to serve as an effective treatment.

As with many new technologies, gene therapy raises ethical and social issues. One of the greatest concerns is that the techniques developed for gene therapy could be used for genetic enhancement; i.e., to alter any genetically-based physical or behavioral trait without a medical need. However, this possibility may not be realistic since (1) most traits are controlled by multiple genes whose interactions are, for the most part, not currently known, and (2) an individual's traits are determined by an interaction of genes with environmental factors, making the outcome difficult to predict.

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Essential Questions and Enduring Understandings

This module was developed utilizing a set of Essential Questions (EQ) and Enduring Understandings (EU)[1]. The Essential Questions are designed to guide student's inquiry as they explore the topic of gene therapy. The associated Enduring Understandings represent the fundamental concepts students should gain from their study of this topic, and which, it is hoped, they will remember long after the course has ended. The concepts listed under "More specialized knowledge" represent information you may wish to emphasize in instruction and assessment.

***EQ:** What is gene therapy?*
EU: Gene therapy is a treatment or cure for diseases caused by defective genes.

***EQ**: How is gene therapy done?*
EU: Normal genes are added to the cells affected by defective genes.
More specialized knowledge:
- A carrier (vector) is used to move normal genetic material into cells receiving gene therapy treatment.
- Viruses, liposomes, or naked DNA are modified and used as vectors to deliver genes into cells.
- Vectors are either introduced using an *in vivo* (in the body) or *ex vivo* (outside the body) approach.

***EQ:** Is gene therapy effective?*
EU: Gene therapy is still in the experimental phases and is not yet perfected.
More specialized knowledge:
- Immune response, interruption of other genes, and integration into the wrong cells are all risks associated with gene therapy.

***EQ:** Are there ethical, legal and social implications of gene therapy?*
EU: Gene therapy, like all new genetic technologies, raises ethical and social issues about how it should be used.
More specialized knowledge:
- The risks and benefits to participants in gene therapy trials carry with them ethical, legal and social issues that must be considered before gene therapy trials are widely used. The more informed we are, the better decisions we can make.
- With successful gene therapy comes the potential to use the technology to enhance genetic traits where no disorder exists. This has ethical and social implications.

[1]Wiggins, G and McTighe J (1998) *Understanding by Design*. Association for Supervision and Curriculum Development, Alexandria, VA.

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Activity Type Table

We assume that each teacher using this module will select and order activities in a way that reflects their teaching style and that is appropriate for their students. Many of the activities in this module can be used in multiple ways, such as a "hook" to engage student interest, content delivery, or assessment. To assist you in planning your lesson or unit, the Activity Type Table lists the module activities, their mode of delivery (online and/or paper), and suggested uses.

Interactive Web activity, estimated time = 10 mins., longer if noted with an "*"

Print-and-Go™ activity, see Activity Overview for estimated time

Activity	Engage	Content Delivery	Reinforcement	Alternative to Online	Extension	Assessment
What is Gene Therapy?	X	X				
Exploring Gene Therapy	X	X				
Choosing Targets for Gene Therapy		X				
Gene Delivery: The Key to Gene Therapy		X				
How Do Viruses Recognize a Target Cell?	X		X		X	
Tools of the Trade *	X	X				
Vector Selector			X			X
From Research to Trials	X	X			X	

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Activity	Engage	Content Delivery	Reinforcement	Alternative to Online	Extension	Assessment
Challenges in Gene Therapy		X			X	
Space Doctor *	X		X			X
New Approaches to Gene Therapy		X			X	
Enhancement: Gene Therapy and Science Fiction	X				X	
Treatment, Enhancement or Both?	X				X	
What Are Some Issues in Gene Therapy?		X	X			
Positions, Beliefs and Values	X		X		X	
The Bioethics of Gene Therapy	X		X		X	
Patient Education			X			X
Mapping Gene Therapy Concepts			X			X
Additional Resources		X				

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Sample Lesson Plans

To assist you in planning your lesson or unit we provide sample timelines for 2, 4, and 5-8 days of instruction. A brief summary of each activity is included to assist you in "visualizing" the flow of instruction.The timelines below are suggested for a 50 minute class period. If you teach in a block, adjust as necessary. Activity overviews and print materials (where applicable) for activities listed below can be found in the online Classroom Activities Index for this module (http://gslc.genetics.utah.edu/teachers/)

A.

TIMELINE 1 : 2 days		
Day 1: 50 minutes	What is Gene Therapy?	A brief online introduction and definition of gene therapy. Use this to engage student interest in the topic.
	Exploring Gene Therapy	A webquest that takes students through the entire Gene Therapy: Molecular Bandage? module, hitting all key aspects of gene therapy.
Day 1: (alternate) 50 Minutes	Gene Therapy: Molecular Bandage? PowerPoint presentation and Vector Selector	A downloadable PowerPoint presentation that covers the key areas of gene therapy. Students also enage in an brief version of the Vector Selector activity chosing the best vector for treating a genetic disorder.
Day 2: 50 minutes	Space Doctor *	Students must apply what they have learned about gene therapy to create a treatment for a fictious patient. Targeting the correct tissue and choosing the right vector are emphasized. Help is available within the activity.
	Choose one: •Positions, Beliefs and Values	Students explore and state their beliefs about the appropriate use of gene therapy.
	•Bioethics of Gene Therapy	Students explore the ethical, legal and social implications of actual gene therapy trials.
	•Treatment, Enhancement or Both?	Students ponder potential applications of gene therapy and classify them as treatments, enhancements or both.

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B.

TIMELINE 2 : 4 days		
Day 1: 50 minutes	What is Gene Therapy?	A brief online introduction and definition of gene therapy. Use this to engage student interest in the topic.
	Choosing Targets for Gene Therapy	Online content delivery
	Gene Delivery: The Key to Gene Therapy	Online content delivery
	Treatment, Enhancement or Both?	Students are required to consider applications of gene therapy and categorize them as treatments, enhancements, or both. Use this to explore the possible implications of widely successful gene therapy techniques.
Day 2: 50 minutes	How Do Viruses Recognize a Target Cell?	An engaging activity that demonstrates viral specificity for target cell types. Use this to introduce the mechanism by which gene therapy vectors delver genes.
	Tools of the Trade *	Interactive online content delivery about vectors used in gene therapy.
	Space Doctor *	Students apply what they have learned about gene therapy vectors to design a treatment for a patient. Outcomes are random to reflect the actual success rate of gene therapy trials.
Day 3: 50 minutes	Challenges in Gene Therapy	Online content delivery
	Mapping Gene Therapy Concepts	Students create concpets maps outlining all they have learned about gene therapy. Use as a review or an assessment.
Day 4: 50 minutes	*Choose one:* • Vector Selector	Vector Selector: Mini-project. Students must apply what they have learned to develop and market a gene therapy vector for a specific disease.
	• Bioethics of Gene Therapy	Bioethics: Students explore the ethical, legal, and social implications of actual gene therapy trials, both successful and not.

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C. TIMELINE 3 : 5 or more days

Day 1: 50 minutes	What is Gene Therapy? 	A brief online introduction and definition of gene therapy. Use this to engage student interest in the topic.
	Choosing Targets for Gene Therapy 	Online content delivery
	Gene Delivery: The Key to Gene Therapy 	Online content delivery
	Tools of the Trade  * 	Interactive online content delivery about vectors used in gene therapy.
Day 2: 50 minutes	How Do Viruses Recognize a Target Cell? 	An engaging activity that demonstrates viral specificity for target cell types. Use this to review the mechanism by which gene therapy vectors deliver genes.
	Space Doctor  *	Students apply what they have learned about gene therapy vectors to design a treatment for a patient. Outcomes are random to reflect the actual success rate of gene therapy trials. Use this to help students tie it all together and practice for the next assignment.
	Vector Selector 	Mini-project. Students must apply what they have learned to develop and market a gene therapy vector for a specific disease. This reinforces what they practiced in Space Doctor.
Day 3: 50 minutes	Vector Selector Continued 	See above
Day 4: 50 minutes	Enhancement: Gene Therapy and Science Fiction 	Online content delivery that addresses concerns about the potential misuse of gene therapy.
	Treatment, Enhancement or Both? 	Students are required to consider applications of gene therapy and categorize them as treatments, enhancements, or both. Use this activity to explore the possible implications of successful gene therapy techniques.

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TIMELINE 3 : 5 or more days - continued		
Day 5: 50 minutes	Challenges in Gene Therapy 	Online content delivery
	What are Some Issues in Gene Therapy 	Online content delivery
	Bioethics of Gene Therapy 	Students explore the ethical, legal, and social implications of actual gene therapy trials, both successful and not.
Day 6: 50 minutes	From Research to Trials 	A comprehensive look at the steps necessary to begin a gene therapy trial for Adenosine Deaminase defficiency (ADA).
	New Approaches to Gene Therapy 	Online content delivery about proposed approaches to gene therapy designed to off-set some of the negative side effects of previously trials.
	Patient Education 	A project that requires students to tie all they have learned about gene therapy together to create educational material about gene therapy for the public. Use this as an assessment.
Day 7: 50 minutes	Patient Education Continued 	See above
Day 8: 50 minutes	Mapping Gene Therapy Concepts 	Students create concept maps of all they have learned about gene therapy. Use this as a review, wrap-up or assessment.
	Positions, Beliefs and Values 	Wrap-up. Students use what they have learned to state their opinion about various aspects of gene therapy.

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STANDARDS

A. U.S. National Science Education Standards

Grades 5-8:

- Content Standard C: Life Science - Structure and Function of Living Systems; each type of cell, tissue and organ has a distinct structure and set of functions that serve the organism as a whole.
- Content Standard C: Life Science - Reproduction and Heredity; hereditary information is contained in genes, located in the chromosomes of each cell; an inherited trait of an individual can be determined by one or by many genes; a single gene can influence more than one trait.
- Content Standard E: Science and Technology - Abilities of Technological Design; Identify Appropriate Problems for Technological Design; students should develop their abilities by identifying a specific need, considering its various aspects, and talking to different potential users or beneficiaries.

Grades 9-12:

- Content Standard C: Life Science - The Cell; cells store and use information to guide their functions; the genetic information stored in DNA is used to direct synthesis of thousands of proteins that each cell requires.
- Content Standard C: Life Science - The Molecular Basis of Heredity; in all organisms, the instructions for specifying the characteristics of the organism are carried in DNA.
- Content Standard E: Science and Technology - Abilities of Technological Design; students should demonstrate thoughtful planning for a piece of technology or technique.
- Content Standard F: Science in Personal and Social Perspectives - Science and Technology in Local, National and Global Challenges ; progress in science and technology can be affected by social issues and challenges. Funding priorities for specific health problems serve as examples of ways that social issues influence science and technology.
- Content Standard F: Science in Personal and Social Perspectives - Science and Technology in Local, National and Global Challenges; individuals and society must decide on proposals involving new research and the introduction of new technologies into society.

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B. AAAS Benchmarks for Science Literacy

Grades 6-8:

- The Living Environment: Cells - different body tissues and organs are made up of different kinds of cells.

Grades 9-12:

- The Living Environment: Heredity - some new gene combinations make little difference, some can produce organisms with new and perhaps enhanced capabilities, and some can be deleterious.
- The Living Environment: Heredity - genes are segments of DNA molecules; inserting, deleting, or substituting DNA segments can alter genes; an altered gene may be passed on to every cell that develops from it; the resulting features may help, harm, or have little or no effect on the offspring's success in its environment.
- The Living Environment: Cells - every cell is covered by a membrane that controls what can enter and leave the cell.
- The Living Environment: Cells - cell behavior can also be affected by molecules from other parts of the organism or even other organisms.
- The Human Organism: Physical Health - faulty genes can cause body parts or systems to work poorly.
- The Designed World: Health Technology - knowledge of genetics is opening whole new fields of health care; in diagnosis, mapping of genetic instructions in cells makes it possible to detect defective genes that may lead to poor health.

C. Utah Secondary Science Core Curriculum

Intended Learning Outcomes for Seventh and Eighth Grade Integrated Science
Students will be able to:

1. Use Science Process and Thinking Skills
   c. Develop and use categories to classify subjects studied.
4. Communicate Effectively Using Science Language and Reasoning
   a. Provide relevant data to support their inferences and conclusions.

Intended Learning Outcomes for Biology
Students will:

1. Use Science Process and Thinking Skills
   b. Use comparisons to help understand observations and phenomena.
   h. Construct models, simulations and metaphors to describe and explain natural phenomena.
2. Manifest Scientific Attitudes and Interests
   c. Maintain an open and questioning mind toward ideas and alternative points of view.
   d. Accept responsibility for actively helping to resolve social, ethical and ecological prob-

lems related to science and technology.

4. Communicate Effectively Using Science Language and Reasoning
   a. Provide relevant data to support their inferences and conclusions.
5. Demonstrate Awareness of Social and Historical Aspects of Science
   a. Cite examples of how science affects human life.
6. Demonstrate Understanding of the Nature of Science
   i. Understand that science and technology may raise ethical issues for which science, by itself, does not provide solutions.

Biology (9-12)
Standard IV: Students will understand that genetic information coded in DNA is passed from parents to offspring by sexual and asexual reproduction. The basic structure of DNA is the same in all living things. Changes in DNA may alter genetic expression.
Objective 3: Explain how the structure and replication of DNA are essential to heredity and protein synthesis.

- Research, report, and debate genetic technologies that may improve the quality of life (e.g., genetic engineering, cloning, gene splicing).

Credits and Funding:

Credits:

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