# Teacher Guide: Exploring Gene Therapy

## ACTIVITY OVERVIEW

<table>
<thead>
<tr>
<th>Abstract:</th>
<th>Students navigate the <em>Gene Therapy: Molecular Bandage?</em> module to learn about gene therapy while completing a webquest.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Materials:</td>
<td>Computers with Internet access, student handouts</td>
</tr>
<tr>
<td>Module:</td>
<td>Gene Therapy: Molecular Bandage?</td>
</tr>
<tr>
<td>Prior Knowledge Needed:</td>
<td>None</td>
</tr>
<tr>
<td>Key Concepts:</td>
<td>Gene therapy; vectors; risks and challenges associated with gene therapy</td>
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<tr>
<td>Appropriate For:</td>
<td>Ages: 12 - 18 USA grades: 7 - 12</td>
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<tr>
<td>Prep Time:</td>
<td>15 minutes</td>
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<tr>
<td>Class Time:</td>
<td>45 minutes</td>
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</tbody>
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**Activity Overview Web Address:**
http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=gtquest

Other activities in the *Gene Therapy: Molecular Bandage?* module can be found at:
http://gslc.genetics.utah.edu/teachers/tindex/
I. PEDAGOGY

A. Learning Objectives
   • Students will learn about gene therapy and its associated risks and challenges.
   • Students will compare and contrast vectors used in gene therapy.
   • Students will practice reading for information.

B. Teaching Strategies
   1. Timeline
      • 2-3 weeks before activity:
         - reserve a computer lab with Internet access
      • 1 day before activity:
         - make copies of the student pages (S-1 – S-4), one for each student
      • Day of activity:
         - take students to the computer lab and pass out student handouts for them to complete

   2. Classroom Implementation
      • Hand out the Exploring Gene Therapy webquest (student pages S-1 – S-4)
      • Bring your class to the computer lab and have them log on to:
      • Instruct your students to use this module to answer the questions on the Exploring Gene Therapy webquest.

   3. Assessment Suggestions
      • Use the completed Exploring Gene Therapy webquest as an assessment.

   4. Extensions
      • Please see Additional Resources for more gene therapy activities.

   5. Common Misconceptions
      • Students sometimes think that gene therapy replaces a faulty gene with a functional copy. It is important that they understand this is not the case. Gene therapy endeavors to add a functional copy of the gene of interest in the hope that its function will counteract the effect of the faulty gene.
II. ADDITIONAL RESOURCES

A. Activity Resources linked from the online Activity Overview at:
   http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=gtquest

   • Website: Classroom Activities Index: *Gene Therapy: Molecular Bandage?* -
     Online and Print-and-Go™ activities covering topics in gene therapy.

III. MATERIALS

A. Detailed Materials List

   • Computers with Internet access
   • Student handouts (pages S-1 – S-4)

IV. STANDARDS

A. U.S. National Science Education Standards

   Grades 5-8:
   • 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.

   Grades 9-12:
   • 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.

B. AAAS Benchmarks for Science Literacy

   Grades 9-12:
   • 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 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.
Teacher Guide: Exploring Gene Therapy

C. Utah Secondary Science Core Curriculum

*Intended Learning Outcomes for for Ninth to Twelfth Grade Science*

Students will:

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 4: Students will understand that genetic information coded in DNA is  
  passed from parents to offspring by sexual and asexual reproduction. The ba-  
  sic 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).

V. CREDITS

Activity created by:  
Molly Malone, Genetic Science Learning Center  
Pete Anderson, Genetic Science Learning Center (illustrations)

Funding:  
Funding for this module was provided by a Science Education Partnership Award  
(No. 1 R25 RR16291) from the National Center for Research Resources, a  
component of the National Institutes of Health.
Exploring Gene Therapy - Answer Key

Log on to: http://gslc.genetics.utah.edu/units/genetherapy and explore this module to find the answers to the questions below.

Hint: the Search feature on this website may or may not help you find what you are looking for; it is best to go through the module to find the answers.

Questions:

1. What is gene therapy?

   Adding a normally functioning copy of a mutated gene to help affected cells, tissues and organs work properly.

2. What are the five criteria for a gene therapy candidate disease?

   1. The condition must result from mutations in one or more genes.
   2. You must know which gene is involved and have an available DNA copy of that gene.
   3. You must know the biology of the disorder - which tissue is affected, the role of the protein encoded by the gene, and how mutations in the gene affect the protein product.
   4. Adding a normal copy of the gene must fix the problem.
   5. It must be possible to deliver the gene to cells of the affected tissue.

3. Case Study: Is cystic fibrosis a good candidate for gene therapy? Why or why not?

   Yes, cystic fibrosis meets all of the criteria above.

4. What are the hallmarks of successful gene delivery in gene therapy trials?

   Targeting the right cells, activating the gene, integrating the gene into the cells, avoiding harmful side effects.

5. Explain the in vivo technique of delivering genes to a patient’s cells.

   The vector carrying the gene is injected directly into the body. The in vivo approach happens inside the body.

6. Explain the ex vivo technique of delivering genes to a patient’s cells.

   Cells from the affected tissue are isolated and cultured in a Petri dish. The vector carrying the gene is introduced to the cells in the Petri dish. The ex vivo approach happens outside the body.
7. What are vectors? What are the six different types of vectors contained in the Vector Toolbox?

A vector is:

A “vehicle” used to deliver genes.

The six different types of vectors are:

- Retrovirus
- Adenovirus
- Adeno-Associated Virus
- Herpes Simplex Virus
- Liposome
- Naked DNA

8. Go through the Vector Toolbox. Fill out the attached Vector Types Table.

9. Which vector would be the best choice for a cystic fibrosis gene therapy? Why?

The Adeno-Associated Virus would be the best choice for a cystic fibrosis gene therapy because it is large enough to hold the gene, it infects cells that divide irregularly (as is the case with cells you want to target to treat cystic fibrosis), it infects the right type of tissue, and it typically will not cause an immune response.

10. Become the Space Doctor and design a gene therapy for one of the three given patients. Fill out the following:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Answers will vary</th>
<th>Disease</th>
<th>Answers will vary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue targeted</td>
<td>Answers will vary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vector chosen (consult the toolbox if you need a refresher)</td>
<td>Answers will vary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was your therapy in vivo or ex vivo?</td>
<td>Answers will vary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was your therapy successful?</td>
<td>Answers will vary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Why or why not?</td>
<td>Answers will vary</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

List all of the vectors that worked for this gene therapy

Answers will vary

Answers will vary

Answers will vary

Answers will vary
11. What are the challenges of gene therapy? List and briefly describe each one:

a. Introducing changes into the germline

You must make sure not to introduce the new gene into the patient’s reproductive cells or they may pass the new gene on to their offspring. This could have varying consequences.

b. Immune response

Vectors used in gene therapy can trigger the body’s natural immune response.

c. Disrupting important genes in target cells

When incorporating itself into the host cell’s DNA, the new gene may incorporate itself into the middle of a functioning gene, disrupting that gene’s function.

12. What are some issues involved in gene therapy?

Answers will vary but might include:

When should it be used?
What effect would gene therapy have on future generations if germline (reproductive) cells were genetically altered?
Who should decide what are “good” or “bad” uses of genetic modifications?
What if we can alter traits not associated with human disease?
Who will have access to gene therapy, treatments, and long-term follow-up?
### Vector Types

<table>
<thead>
<tr>
<th>RETROVIRUS</th>
<th>ADENOVIRUS</th>
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<th>LIPOSOME</th>
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<tr>
<td><strong>How the vector carries genetic material</strong></td>
<td>In the form of RNA rather than DNA. The most famous is Human Immunodeficiency Virus (HIV), which causes AIDS.</td>
<td>Double-stranded DNA The common cold virus.</td>
<td>Single-stranded DNA</td>
<td>Single-stranded DNA Plasmid DNA packaged into miniature lipid –based pockets that can fuse to the cell's own membranes, The DNA is released and transported into the nucleus</td>
<td>Plasmid DNA molecule all by itself that can be taken up by some cells, and transported into the nucleus</td>
</tr>
<tr>
<td><strong>Maximum length of DNA that can be inserted into vector</strong></td>
<td>8,000 base pairs</td>
<td>7,500 base pairs</td>
<td>5,000 base pairs</td>
<td>20,000 base pairs</td>
<td></td>
</tr>
<tr>
<td><strong>ADVANTAGES</strong></td>
<td>+ Infects only dividing cells</td>
<td>+ Infects both dividing and non-dividing cells very effectively</td>
<td>+ Does not cause illness in humans + Infects a wide range of dividing and non-dividing cell types very effectively + Need the assistance of a “helper” virus to replicate themselves inside cells + Possible to target specific cell types by engineering proteins on the virus surface to recognize special proteins on the target cell's surface + Integrates into the host cell's genome; 95% of the time, it will integrate into a specific region on Chromosome 19, greatly reducing the chance that integration will disrupt the function of other genes in the cell + Typically will not cause an immune response</td>
<td>+ Infects cells of the nervous system + Will not integrate into the host cell's genome, but is a circular piece of DNA that replicates when the cell divides; will stay in the cell's nucleus for a long time + Will not disrupt the function of other genes in the host cell</td>
<td>+ Will not generate an immune response + Better suited for ex vivo gene therapy approaches</td>
</tr>
<tr>
<td><strong>DISADVANTAGES</strong></td>
<td>- Integrates into the host cell's genome in random locations; might integrate into a place where it disrupts another gene - Can cause an immune response</td>
<td>- Will not integrate into the host cell's genome; the cell will discard the virus and gene activation will be lost - Can cause an immune response</td>
<td>- 5% chance of integrating and disrupting the function of other genes in the cell</td>
<td>- Can cause an immune response in the patient</td>
<td>- Not specific for any cell type - Enter, cells far less effectively than viruses - Will not integrate into the host cell's genome</td>
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Was your therapy in vivo or ex vivo? ______________

Was your therapy successful? ______

Why or why not? ____________________________________________

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________________________

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a.

b.

c.

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