Tissue Engineering — Building Body Parts

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 — 12
Teaching materials developed by **VCU** Life Sciences

Virginia Commonwealth University

Classroom Tested Lesson

Video Description

"Secrets of the Sequence," Show 112, Episode 2

"Tissue Engineering: Building Body Parts" – approximately 7:44 minutes viewing time

Scientific research is investigating the possibility of replacing damaged organs or tissues with lab-created, tissue-engineered kidneys, livers, and hearts. Does it sound like science fiction? Not any more – scientists are already successfully growing many kinds of organs and tissues in the lab.

Ward Television
Producer: Paul Gasek
Featuring: Linda Griffith, Chemical and Biological Engineering at Massachusetts Institute of Technology, Dr. Julie Fuchs, Harvard Medical School, Dr Joseph Vacant, Massachusetts General Hospital & Harvard Medical School, Dr. Anthony Atala, Children's Hospital Boston & Harvard Medical School
Lesson Author; Reviewers: Catherine Dahl; Dick Rezba, Selvi Sriranganathan
Trial Testing Teachers: Amy Benton, Suzannah Pokorski, Kate Donovan

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard A: Science as Inquiry

As a result of activities in grades 9-12, all students should develop:

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard C: Life Science

As a result of their activities in grades 9-12, all students should develop understanding of

- The cell

Content Standard E: Science and Technology

As a result of their activities in grades 9-12, all students should develop

- Abilities of technological design
- Understandings about science and technology

Content Standard F: Science in Personal and Social Perspectives

As a result of their activities in grades 9-12, all students should develop understanding of

- Personal and community health
- Science and technology in local, national and global challenges

Selected State Science Standards Connections

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Virginia
BIO.6 The student will investigate and understand common mechanisms of inheritance and protein synthesis. Key concepts include

a) cell growth and division;
c) cell specialization;
e) genetic variation (mutation, recombination, deletions, additions to DNA);
i) exploration of the impact of DNA technologies.

Florida
9-12 Science - Biology
Processes of Life

Standard 1
The student describes patterns of structure and function in living things. (SC.F.1.4)
2. knows that body structures are uniquely designed and adapted for their function.

Standard 2
The student understands the process and importance of genetic diversity. (SC.F.2.4)
2. knows that every cell contains a "blueprint" coded in DNA molecules that specify how proteins are assembled to regulate cells.

The Nature of Science

Standard 3
The student understands that science, technology, and society are interwoven and interdependent. (SC.H.3.4)
2. knows that technological problems often create a demand for new scientific knowledge and that new technologies make it possible for scientists to extend their research in a way that advances science.
6. knows that scientific knowledge is used by those who engage in design and technology to solve practical problems, taking human values and limitations into account.

Overview

The supply of donor organs cannot possibly keep up with today's demand for these precious supplies. Therefore, researchers are working hard to develop new ways to replace organs – this is the science of tissue engineering. This video describes how tissue engineering is conducted to restore skin, muscle, or bone tissue, or even a whole organ. In order to grow tissues from individual cells, it is necessary to first create a biodegradable structure on which these cells can grow. Without a base structure to grow on, cells would not be able to connect or communicate with each other even if they have some 'memory' of their function. A specific example of tissue engineering is illustrated using a "liver chip". The video also explains the difference between tissue engineering and genetic engineering.

Testing: A sample related multiple choice item from State Standardized Exams

Cells are the functional units that make up tissues. Tissues then become the functional units that make up –

A) enzymes
B) organs *
C) other cells
D) DNA

Source: Virginia Spring 2002 End of Course Biology.

Video Preparation

Preview the video and make note of the locations at which you will later pause the video for discussion.

Before Viewing

1. As student watch the video, ask them to look for and record the 4 steps that are used to engineer new tissues as they watch the video.
   - *Extract the cells from either a donor or the patient*
   - *Build a scaffold for the cells to grow on*
   - *Supply nutrients and oxygen to the cells*
   - *Grow cells on the scaffold until the scaffold dissolves at the point where there is enough tissue structure for the cells to continue to grow and attach to themselves.*

During Viewing

1. START the video.

2. PAUSE the video (4:39 minutes into the video) on the close-up of the liver chip immediately after Linda Griffith of MIT laboratory says, "Fluid is consumed, oxygen and so forth, and then comes out here."

   Using this close-up view, ask students to:
   - draw a diagram of the liver chip,
   - label the incoming and outgoing flows,
   - describe the function of each.

   The incoming flow acts as an artery bringing in a culture medium to supply the liver chip with oxygen and nutrients. The outgoing flow acts as a vein removing the depleted supply of fluid (blood) from the organ.

3. RESUME the video and play to the end.

After Viewing

1. Ask: "What is the goal of tissue engineering?"
   Tissue Engineering is about restoring, repairing, and maintaining organs.

2. Ask: "What is the difference between tissue engineering and genetic engineering? What is their major similarity?"

Tissue engineering and genetic engineering are not the same. The ultimate goal of tissue engineering is organ replacement in humans by stimulating cells to form specific tissues. The goal of genetic engineering, however, is the manipulation of the genetic code. Despite the difference in their goals, both can involve the use of embryonic stem cells. Genetic engineers manipulate the DNA in embryonic stem cells, while tissue engineers use embryonic cells to grow tissues because stem cells have some "memory" and know what to do once they are correctly cued to grow into a certain tissue type.

3. Ask: "What is the tissue that researchers believe is the easiest to grow and why?"
   The easiest tissue to engineer is cartilage because;
   a) cartilage cells do not need a great deal of oxygen
   b) cartilage cells receive nutrients by diffusion
   c) therefore cartilage cells do not require extensive networks of blood vessels to survive

Teacher Notes for the Student Activity: Engineering Bones

In Part I students will construct a bone model and test its resistance to bending and collapse. In Part II, they will modify the bone model in some way and compare its load resistance to that of the original model.

Note: Your students may have general questions about bone formation and physiology. You may want to do a quick review of these topics with your class before you begin the activity. More information can be found at http://en.wikipedia.org/wiki/Bone.

Materials

- Sheets of standard office quality white paper (8.5" x 11")
- Transparent tape
- Scales
- Foam or paper cups (in some trial tests, foam cups ripped)
- *Large* paperclips
- "Weights" - gram masses or a uniform material such as large nuts or bolts
- Optional: calculators for each student/group

Additional materials needed by some groups for Part II:

- Assorted papers – 8.5 x 11 sheets of newspaper, notebook, thin cardboard
- Scissors
- Rulers

Procedure

Part I

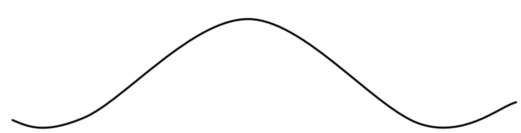
1. Before students begin have them read Appendix A for background information.

2. In Part I of this activity every group will begin by constructing and testing the same artificial bone made of a single sheet of office quality paper. Students will tightly roll the paper along it longest dimension leaving a hollow center of about 2 cm in diameter. Have them tape the length of the long edge to create a tube.

3. Instruct students to suspend their 'paper bone' between two stacks of books or other supports so that 2 cm of each side of the bone model rests on the supports.

4. Although students can make their own 'buckets', it will save time if you have pre-constructed the cup that they will hang from the middle of their bone model and into which they will place increasing amounts of load. *See picture on the Student Handout.*

5. Make a handle for the 'bucket' by straightening a large paper clip into a shape similar to a bell-shaped curve. The height of the curve should be 3 to 4 cm to allow the bone model to pass under the handle.



6. Insert one end of the 'paperclip handle' through the cup about 1 cm below the lip and push across and then out through the opposite side of the cup. You should now have a cup with a handle similar to a bucket.

7. Make sure the handle is bent enough so that the bone model can be inserted under the handle.

8. Before you conduct this activity with students, try it yourself because the amount of mass it takes to collapse the bone model may be surprising. After making a bone model, pass it under the cup handle and then support the two ends. See the picture on the student handout.

9. Add a series of 'weights' until the bone model collapses. Because the model is much stronger than it appears, it generally takes far more load to collapse it than most students think. Be sure to ask students to predict how much mass it will take to bend the bone model. Because it generally takes from 200-250 pennies to cause this collapse, it is better to use standard gram masses if available or other heavy items such as large nuts or bolts. You could also have students add sand or gravel and then mass the amount it took to collapse the bone model. To avoid a mess, be sure there is a container below to catch the material when collapse occurs.

10. After the groups have collected their data,
    - Create a class data table on the board (or on an overhead) to summarize the groups' results. (see example below)

Model	A = Mass of Model	B = Mass of maximum load	B ÷ A = Strength
Group 1			
Group 2			
Group 3			
Group 4			
Group 5			
Group 6			

- Find the mean and range (Note: You may need to define these terms and write the appropriate equations on the board)
- Discuss the possible causes for differences in the results

Note: Depending on your classroom equipment, students may need to convert between U.S. customary units and their metric equivalents. You may need to write the following conversions on the board: 1 kg = 2.2046 lb and 1 lb = 0.4536 kg.

Part II

1. In Part II students will modify the original design to see the effects on "load resistance". There are a number of ways that student can affect the resistance to bending in designing their new bone model. Have students select one of the following:
    - Change the length
    - Change the material (i.e., try different papers)
    - Change the construction (i.e., instead of rolling, crease and fold into a triangle or square while retaining a hollow interior)
    - Change the number of points of stress (i.e., use two equally distance hanging cups instead of one)
    - Some other variable suggested by students and approved by you.

    Note: Allowing the students to select their own variable allows for more autonomy and encourages curiosity, but it may result in narrow results. That is, some variables may be favored as more likely to increase strength, leaving less obvious solutions unexplored. You may wish to encourage your students to select a variety of variables, including those of their own design.

2. Only one variable should be changed; all others should remain the same. For example, if students change the material, the length and diameter of the tube must remain the same.

3. Be sure you have students predict the effects of the changes they will make.

4. Have each group add their results to a summary table that you can put up on the board (or on an overhead) and discuss their findings. (see example below)

Model	A = Mass of Model	B = Mass of maximum load	B ÷ A = Strength
Original model			
Different length model			
Different paper model			
Different construction			
Different # of stress points			
Other variable:			

Part III (Optional)

If time allows, an interesting variation of this exercise can provide students with insights regarding implanted scaffolds (artificial matrices). In orthopedic medicine, critical defects remain a major challenge for the physician. These defects, usually due to the amount of bone lost, cannot heal by themselves. This type of bone defect is thus a prime candidate for tissue engineering.

Researchers are implanting biodegradable and bio-reabsorbable scaffolds into these defects to regenerate bone tissue. The scaffolds are seeded with cells capable of differentiating into osteoblast (bone-forming) cells. Although the site of these implants would normally be immobilized, it would be interesting to test the mechanical properties of the implanted scaffold.

1. To simulate this type of test, the students should construct a bone model as before.

2. A critical defect could be cut from the *middle* of the model, followed by the implantation of a ‘scaffold’ into the defect site. The implant should be secured by tape or glue.

3. Similar to the original activity, the strength of the scaffold implant should be tested by hanging the cup over the defect site. A strength comparison of the original, undamaged model and the implant-containing model might prove interesting.

Student Handout: Engineering Bones

In Part I of this engineering exercise you will construct a bone model and test its resistance to bending and collapse. After completing Part I, you will modify the bone model in some way and compare its load resistance to that of the original model.

Materials Needed per Group

- 1 sheet of standard office quality white paper (8.5” x 11”)
- Transparent tape
- Scale
- A cup with a handle
- “Weights” - gram masses or a uniform material such as large nuts or bolts
- Optional: calculator

Additional materials need by some groups for Part II:

- Assorted papers – 8.5 x 11 sheets of newspaper, notebook, thin cardboard
- Scissors
- Rulers

Procedure

Part I

1. Before beginning this activity read the attached handout *on Background Information for Engineering Bones*.
2. Using a single sheet of office quality white paper, construct a paper bone model by tightly rolling the paper along it longest dimension leaving a hollow center of about 2 cm in diameter. Tape the length of the paper edge to create a tube that is 11.5 inches long.
3. Record the mass of your bone model. ______________
4. Slide the bone model under the cup handle and suspend the bone model between two stacks of books or other supports so that 2 cm of each side of the bone model rests on the supports.

5. Adjust the location of the cup so that it is at the center of the bone model
6. Predict and record how much mass you think it will take to cause the bone model to bend and collapse. ______________
7. Slowly add mass until the bone model bends and collapses.
8. To avoid a mess, be sure there is a container below to catch the material when collapse occurs.
9. Using a scale, determine the mass it took to collapse the bone model. This is your *maximum load*. ______________
10. Calculate the strength of your bone model by dividing the mass of the maximum load by the mass of the bone model itself. ______________

11. After you have collected your data,
    - Enter your data into a class data table that your teacher has created on the board (or on an overhead transparency)
    - Find the *mean* (the sum of all strengths divided by the number of models) _________ and *range* (the difference between the greatest strength and the smallest strength) _________
    - Discuss the possible causes for differences in the results.

Part II

1. In Part II you will modify the original design to see how the change you make affects load resistance. Chose one of the following:
    - Change the length
    - Change the material (i.e., try different papers)
    - Change the construction (i.e., instead of rolling, fold into a triangle or square while retaining a hollow interior)
    - Change the number of points of stress (i.e., use two equally distance hanging cups instead of one)
    - Some other variable approved by your teacher

2. Follow the procedure in Part I keeping everything the same except the one variable you are changing.
3. After you have collected your data,
    - Calculate the strength of your bone model by dividing the mass of the maximum load (i.e., the total mass it took to collapse your model) by the mass of the bone model itself.
    - Enter your data in a class data table that your teacher will have created on the board (or on an overhead transparency)

Questions

1. How did your modification to the original model affect the mass necessary to cause collapse?

2. Which of the modifications made by the class had the greatest effect on the mass necessary to cause collapse?

3. Which modification made the original design weaker? Which made it stronger?

Source: Adapted from PTEI's "Bone Strength Activity," available at http://www.ptei.org/tepmanual.asp

APPENDIX A

Background Information for "Engineering Bones"

The tissues of your body possess cells and an extra cellular component called a matrix.
The cells of a tissue are analogous (similar) to the compartments of a beehive. Bees devote part of their time to building and maintaining a structure in which they will reside. The physical and chemical properties of this structure - the hive - are critical to the proper functioning of the colony. Tissue engineers are very aware of the importance of the extra cellular matrix in which cells reside.

Although bone is a living, dynamic tissue with varying biological and inorganic components, it is often viewed as only a structural material within the body. In fact, most people give little attention to bone tissue until bones fail to adequately provide the expected supportive or protective function. Support and protection are important roles to consider when attempting to duplicate and preserve function, and tissue engineers often draw upon mechanical engineering analyses to evaluate their models.

Bone engineers realize that a successfully engineered bone must be able to withstand the same types of mechanical stresses as healthy bone. Bridges are also subjected to stress resistance tests during their design and construction. Civil engineers and biomedical engineers clearly encounter similar problems in design and construction, leading to the common overlap of these fields.

The goal of biomedical engineers is to regenerate mineralized bone tissue in a bone defect. To accomplish this, they often implant an artificial matrix, called a scaffold, into the defect site. The scaffold is seeded with cells and the proper signals (growth factors) that will stimulate the cells to manufacture a new matrix. These cells can then maintain the structure and function of the new matrix. The implanted scaffold is not necessarily as strong as normal bone, although it is hoped that the scaffold will lead to the regeneration of strong bone. Generally, the area of implantation is immobilized until sufficient new bone has been generated, greatly reducing the need for initial mechanical strength of the artificial scaffold.

Bone engineers need to evaluate the strength of normal bone, diseased bone, engineered scaffolds, bone with scaffold implants, and regenerated bone to be successful.

Source: Adapted from www.ptei.org/stuff/bone_strenth_activity.doc

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to locate new Web sites

http://www.tissue-engineering.net/

http://en.wikipedia.org/wiki/Tissue_engineering

http://www.med.ic.ac.uk/divisions/8/

http://www.ukcte.org/

http://www.tissue-engineering.net/index.php?seite=News_detail&action=show&nr=125

http://tissue.rice.edu/index.cfm?doc_id=3983

http://tissue.medicalengineer.co.uk

www.ptei.org/stuff/bone_strenth_activity.doc

http://www.brown.edu/Administration/George_Street_Journal/vol29/29GSJ06e.html
For more information on biohybrid limbs

Genomic Revolution
http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtmL
This Web site of the government-funded Human Genome Project has links about genomics, the history of the project, and more.

Secrets of the Sequence Videos and Lessons
This video and 49 others with their accompanying lessons are available *at no charge* from www.vcu.edu/lifesci/sosq