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Teacher's Guide • The Tissue Issue • Volume 7, Issue 1

This issue of *Your World/Our World* deals with the emerging field of tissue engineering. Although still in its infancy, this field is making rapid strides towards learning how to replace and repair tissues that can be accepted by and integrated into the human body. The student magazine presents an overview of the field, two articles on science concepts essential to the field, several articles on how these concepts are being applied, an article on different fields and careers within tissue engineering, and a hands-on classroom activity. To help you use this issue in your classroom, we are including in this Teacher's Guide an overview of the articles with comprehension questions, additional explanatory information, guidelines for activities, and a crossword puzzle/glossary for students.

Tissues Under Repair: From Ancient Greece to Tomorrow (Page 3)

Key concepts
Regeneration, Cells, Tissues, Organs

Goal
Students will reflect on: 1) why some tissues repair and rebuild themselves and others can't; and 2) why it is important to develop better ways to repair damaged tissue

Have the class brainstorm about how tissues get damaged (birth defects, accidents, cancer and other disease, aging); the ways doctors have traditionally repaired tissues (setting broken bones, taking skin grafts from one part of the body to another, organ transplants); and the drawbacks of these methods (they can be painful and require disfiguring surgery; the body can reject replacement organs). If tissue engineers succeed in developing new ways to repair and replace tissues, their techniques may one day make these traditional methods seem crude and old fashioned.

To understand the difficulty of generating tissues and organs, students need to appreciate the intricacy of organs and systems, as well as the relationship of structure to function within the body. Review the building block scheme by which cells organize to form tissues, tissues form organs, and organs form systems (circulatory, respiratory, digestive, nervous, etc.). You may also want to have students develop a table of different organs and their functions, similar to the one on the back page of the student magazine.

Question
1) What are tissues made of and what do they do? *Specialized cells that work together to perform a specific function.*

Tissue Construction Sites (Pages 4-5)

Key Concepts
Scaffold (extra-cellular matrix), Biomaterial. (Your class can explore the concept of a scaffold in the activity on page 15.)

Goal
Students will understand that: 1) the structure of a tissue helps defines its function in an organ; and 2) this structure is made possible by an extra cellular matrix that provides the spaces for cells to grow in. We refer to this matrix as a "scaffold" in this magazine.

As a tissue develops, cells are present first and they secrete proteins that serve as a scaffold (an extra-cellular matrix). In cartilage, the cells produce collagen, which collects outside the cells to form the scaffold. In bones, the cells also produce collagen for their scaffold, but additional activity of the bone cells cause mineralization of the scaffold with calcium. When tissue engineers use a biomaterial scaffold, they bypass these initial steps (cells first, then proteins), since they create the scaffold in the laboratory. The tissue engineer's bioscaffold provides the spatial home for the cells that are "seeded." These seed cells then go on to produce the matrix proteins and to deposit minerals. As the cells produce their own matrix (scaffold), they also absorb the biomaterial, thus continuing the process of tissue/organ genesis.

(continued on inside)

(continued from cover)

About the Graphic from the Visible Human Project

Have students identify the different kinds of organs in this "slice of life." Then have them examine each organ to find different tissues (connective tissues, cartilage, bone marrow, membranes, muscle fibers of different texture, etc.). For more views of the human body and a "fly through" video simulation, see the websites listed on the back of the student magazine.

Questions

1) Give an example of how the function of a tissue or organ depends on the structure (form or shape) of the tissue. *Answers will vary.*
2) What roles does a scaffold play in a tissue? *It provides the three-dimensional shape that determines the structure of the tissue. It also provides the spaces for cells to grow in as they reproduce during the tissue's development.*
3) What is a biomaterial and how do tissue engineers use it? *A biomaterial is an artificial substance that mimics the structure and function of natural, biological material. Tissue engineers use biomaterials to make a scaffold similar to the kind a tissue's cells would make in the body in order to grow that kind of tissue.*

Differentiation: How Does a Cell Know What Cell to Be? (Pages 6-7)

Key Concepts

Differentiation, Stem Cells (and Tissue-Specific Stem Cells)

Goal

Students will understand the role of cell differentiation in creating the huge variety of tissues in the body, and they will learn how tissue engineers can use undifferentiated stem cells to grow tissue in a biomaterial.

Questions

1) What is differentiation? *Differentiation is the process through which cells that start out the same reproduce to create daughter cells that are different from the original cells. As they become more different from each other, they also become more specialized. That is, they perform different jobs.*
2) How does differentiation affect the development of tissues? *As cells become differentiated to perform different functions, they begin to form different tissues. The cells in one tissue cannot perform the job of cells in another kind of tissue.*
3) What is a stem cell and how is it important to tissue engineering? *A stem cell is an immature cell that is not very differentiated, so it does not perform a specific function in the cells. Its function is to reproduce and produce one or more types of other functional cells when and where they are needed in the tissue. Tissue engineers can use these immature cells to "seed" the biomaterial scaffold; these stem cells then orchestrate the growth of new cells in the tissue according to the right pattern.*

Bone Marrow Stem Cells

Bone marrow has at least two types of stem cells. The *hematopoietic* cells are involved in blood production to meet the body's needs. The *mesenchymal* cells can produce cells for fat, bone, muscle, tendon, etc.

New Products: Skin, Bones, and More (Pages 8-9)

Goal

Students will learn about three areas in which the scientific concepts covered in the last two articles are being applied clinically. The creation of new skin, bones, and cartilage represent the early successes of tissue engineering, and they may soon become more widely available clinically.

Questions

1) What kind of biomaterial do scientists need to engineer skin, bones, and cartilage tissues? *For all three, they start with a biomaterial made of collagen.*
2) What structure would these biomaterials have? *The shape and texture of the collagen-based biomaterial will vary according to the tissue they need to grow: skin needs a thin, flexible sheet; bones, a rigid stick-like shape; and joints, a knobby rounded shape. Adding minerals and proteins to the biomaterial (such as calcium for bones) can fine-tune the structure of the biomaterials.*
3) How would different tissues develop from these biomaterials? *The type of tissue that develops depends on the type of cells that are placed in the biomaterial scaffold.*

Under Design: Complex Organs (Pages 10-11)

Goal

Students will understand that: 1) engineering an organ such as a heart or liver is a very difficult task, since these organs have several types of tissues that must be integrated by blood vessels, nerves, and connective tissues and membranes; and 2) the structure of each component in the organ is critical to the function of the entire organ.

It will be many years before tissue engineers can perfect such organs, yet they may soon be able to repair parts of organs (such as the heart muscle as described in the Profile on page 14) or perform part of the function of the organ (such as one of the liver's task of cleaning blood).

Sidebar on "Spare Parts"

This section raises difficult ethical and social issues that can lead to an open-ended class discussion or lively debate. Try to establish rules of fair discussion and debate:

- Students must respect each others right to disagree;
- There are no right or wrong answers or points of view, but positions should be backed by logical reasoning;
- These issues are not unique to tissue engineering; they are also issues in organ transplants, experimental surgery and treatment, as well as gene therapy, transgenic animals, etc. (Some of these topics have been explored in other *Your World/Our World* Issues: Gene Therapy, Transgenic Animals, Exploring the Human Genome);
- Experts disagree on these issues, and society as a whole has not reached consensus by passing uniform laws or regulations.

A Note About Organ Transplants

Students probably know that many organs and tissues (such as hearts, livers, lungs, kidneys, retinas, heart valves) can be successfully transplanted from one person to another, or even from animals to humans. However, there is a drastic shortage of many of these organs, and many people die waiting for a transplant. Furthermore, the body can reject a transplanted organ because the immune system recognizes it as foreign. These are some of the problems that tissue engineering hopes to be able to overcome. If successful, tissue engineering could eventually produce a sufficient supply of organs so people would no longer die while waiting for a donor. In addition, since tissues can be engineered from the person's own cells, they would not be rejected by the immune system.) Still, we are a long way away from these potential benefits. In the meantime, we must all take care for the organs we have!

A Note About Cloning Animals

The idea of cloning animals for replacement organs (and for the production of pharmaceuticals) has received a lot of attention. Tissue engineering has quite a different goal: producing specialized parts, rather than reproducing an entire animal.

Questions

1) Why is it harder to engineer a complex organ like a heart than to engineer new skin or bones? *See discussion above.*

Mini Activity

Have student write a short story that illustrates both advantages and disadvantages for creating a ready supply of tissues. Send the stories to the Pittsburgh Tissue Engineering website (see address on the back of the student booklet) for publication.

Parallel Technologies//Careers (Pages 12-13)

Goal

Students will be encouraged to explore the many varied fields that must work in tandem to accomplish tissue engineering, which entails understanding tissues on the gross anatomy, the cellular, and the genetic level.

Profile: Doris Taylor, Assistant Research Professor (Page 14)

Question

1) How does Doris Taylor apply the concept of tissue-specific stem cells to her quest to repair heart muscles that are damaged after a heart attack? *She takes tissue-specific stem cells called myoblasts from skeletal muscles and places them in the damaged heart muscle. These skeletal muscle stem cells are immature, and they divide to produce more muscle cells. In contrast, in the mature heart, the muscle cells do not divide and they have no stem cells. By growing large numbers of myoblasts in the laboratory, Doris can create enough muscle cells to repair the damaged heart muscle.*

"Reverse" Tissue Engineering (Page 15)

Tissue engineering requires too many sophisticated techniques to pursue in an average classroom. (If you think of one, though, please let us know!) In this activity, your students will "reverse" the process in which a tissue is built upon its scaffold.

Bones are complex structures that are nevertheless easy to study as an example of tissue development and organ structure. The bone develops from a soft, flexible scaffold to one that is strong and rigid so that it can perform its structural function in the body. In the same way, other organs grow and adapt according to the demands the body places on them. Tissue engineers need to understand how organs develop as a system of interactive tissues in order to construct viable replacement tissues and organs.

Objectives for Activity

Students will be able to:

- Identify different tissues that make up a bone
- Explain the role of calcium in bones
- Understand what happens when bones are demineralized
- Understand the nature of a bone's scaffold
- Realize how important it is for them to keep their bones "calcium rich" throughout their lives.

About the Materials

Vinegar: Students will realize at the end of the activity that vinegar is an acid that leaches the calcium out of the bone.

Distilled water: Tap and bottled water differ in their acidity. Distilled water has a neutral pH, so it provides the best "control" for the bone soaked in vinegar.

About the Procedure

You may conduct this activity as a classroom activity, with just one set of bones. Alternatively, you may have students do the activity in small groups, giving each group a set of bones and beakers. *Note: This activity is adapted from: Seeley/Stephens/Tate, Anatomy and Physiology, 1989, Mosby College Publishing.*

Conclusions

1) Did either of the two liquids affect the flexibility and strength of the bone? *Yes, vinegar made the bone soft and flexible, the way it would have been before it became mineralized with calcium deposits. The bone soaked in water serves the function of a control, so students will not conclude that simply soaking the bone in any liquid would make the bone flexible.*

2) Which of the two liquids do you think is acidic? *Vinegar is a mild acid capable of leaching minerals from the bones. If your class has studied pH, you may conduct pH tests on the substances used. If your class has studied chemistry, you may explore these concepts:*

- Bones contain calcium ions: Ca^{++}
- Vinegar is an acetic acid: CH_3COO^-
- The calcium ion complexes with two acetyl groups to form calcium acetate: $(CH_3COO^-)_2 + Ca^{++} = (CH_3COO)_2Ca$

3) Which of the soaked bones shows what the bone's scaffold is like before it becomes mineralized? *The bone soaked in vinegar reveals the original nature of the bone scaffold.*

Extensions

1) Describe how the bones of a newborn baby, a teenager, and an elderly person differ. *Babies bones are still quite soft and flexible because they do not yet contain much calcium. Their bones still have a lost of "give" and do not break as easily a teenager's. A teenager's bones are much more rigid because they have been more mineralized during their development. Elderly people may have lost a great deal of their bones' calcium. If so, their bones are weak, thin, and brittle. These bones are easy to break and can actually collapse under the weight of the person.*

2) The loss of bone mass in older adults is called *osteoporosis*, and it is a major health issue for the elderly. Find out more about why people lose their bone mass, what you can do to prevent it happening to you, and why you should start now! *Calcium intake is critical in teenagers, whose bones are still developing. They need to build up a store of calcium now, and continue replenishing it as they age. Life-long weight-bearing exercise also keeps the body depositing minerals in the bones.*

If you were a tissue engineer, how would this activity help you understand what kind of scaffold you would need to design to engineer a bone? *This activity shows how a bone would appear if the scaffold were not mineralized. (See discussion on pages 1 and 2 of this guide.)*

What kind of cells would you "plant" in the scaffold? *Tissue engineers would plant osteoblasts (bone builders, p. 8) in the scaffold to begin building new bone tissue.*

Extensions

<u>Dissecting a Chicken Thigh</u>

1) Start with a whole, unskinned chicken thigh.

2) Dissect the thigh, examining the different kinds of tissues (skin, fat, cartilage, tendons, muscle, bone, blood vessels).

3) Cut the bone in half and examine the bone marrow.

<u>Examining Bones Under the Microscope</u>

1) Prepare slides of a cross section of an intact bone.

2) Adjust the focus on the microscope

until you see several concentric circles.

3) Switch the focus to high power and look for the light central core of these circles. This core is the *Haversian canal*, and the concentric circles around the canal are the *lamellae*.

4) Find the long dark spots between the *lamellae*. These openings are the *lacunae* which contain the bone cells called *osteocytes*.

5) Find the dark lines that look like spokes of a wheel extending from the central Haversian canals. These lines, called *canalicules*, carry fluids from one part of the bone to another.

6) Move the slide around so you can see the edge of the bone. Look for a thin layer of tissue, called the *periosteum*, covering the bone.

7) Draw a cross section of the bone, labeling the Haversian canal, the lamellae, lacunae, osteocytes, canalicules, and periosteum.

7) Discuss as a class how a bone is like other living tissues.

8) Repeat this activity with a decalcified bone. What differences do you see?

Further References

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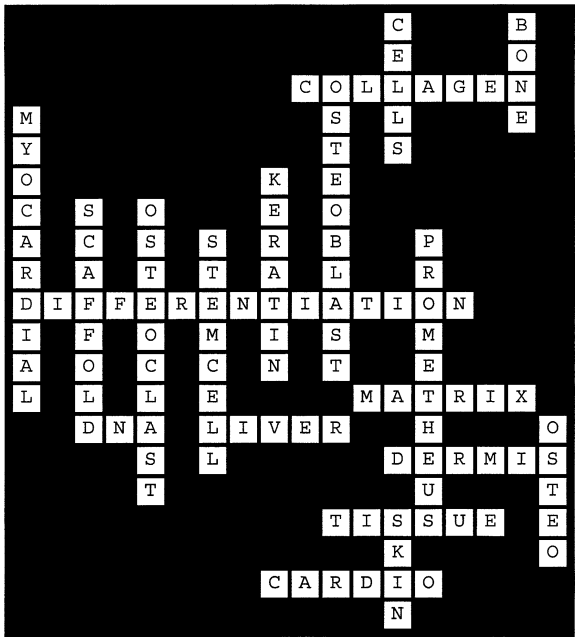
Key to Crossword puzzle on page 7.



TISSUE ENGINEERING

ACROSS

3 A protein that gives a tissue an elastic quality.

11 The process in which cells start out the same, but produce offspring with specialized functions.

12 A 3-D structure with spaces to be filled by cells.

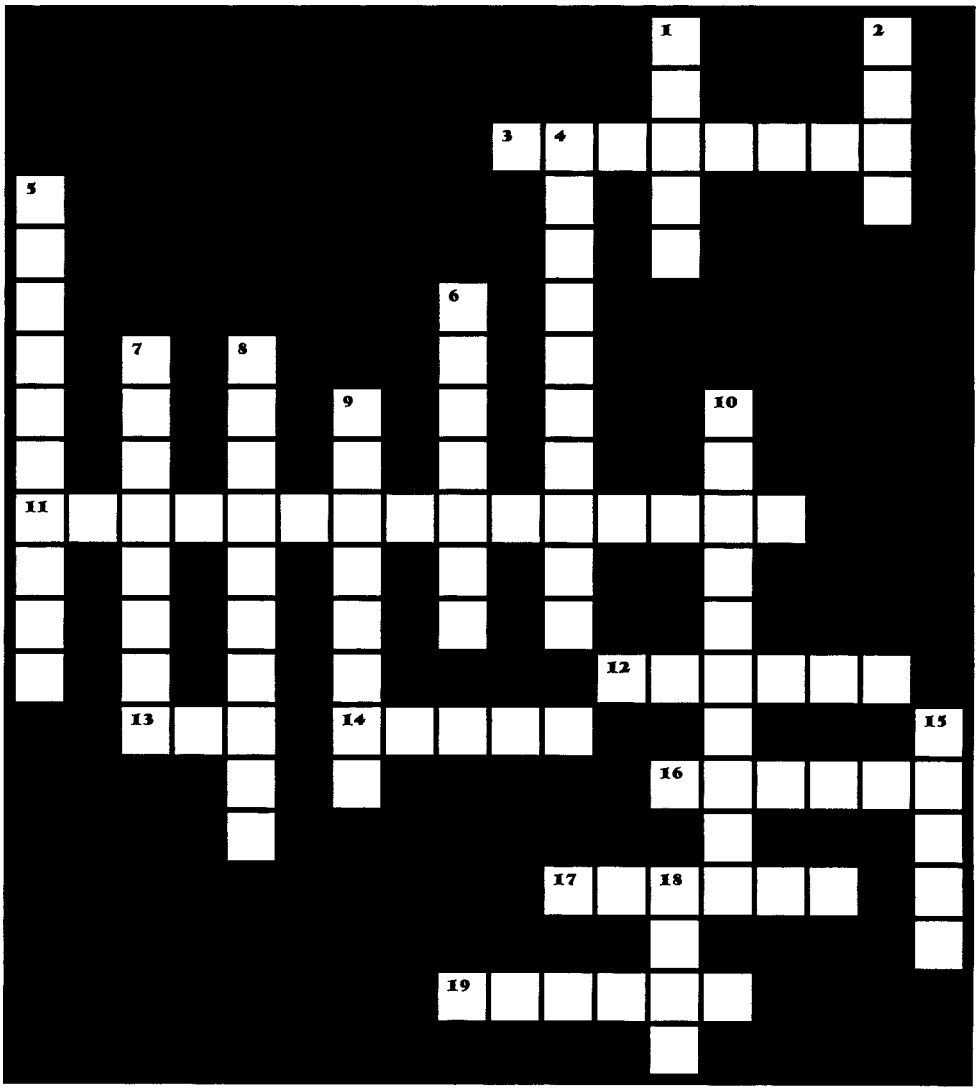
13 The genetic material in cells.

14 The ____ creates proteins, protects against infection, removes toxins from the blood and helps digest food.

16 The deep layer of skin is called the ____.

17 A group of specialized cells that do a unique job.

19 Referring to the heart.



DOWN

1 Small structural units of an organ (hint: tissues are composed of these).

2 A "pillar" of the body.

4 Cells that build bone material.

5 Word that combines the Greek words for muscle and heart.

6 The substance scientists use to engineer the epidermal layer of skin.

7 The ____ determines the three-dimensional shape of a tissue.

8 Cells that remodel bone.

9 A ____ can divide to produce a specialized cell and a undifferentiated cell.

10 The character from Greek mythology who suffered a wounded liver.

15 The Greek word for "Bone."

18 ____ protects you from invading organisms, controls your body temperature, and contains touch and pressure sensors.

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