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**Unit IV-Chapter 4**



# Regenerative Medicine

## Introduction

### Contents

The goal of **regenerative medicine** is to grow replacement tissues or organs and to develop healing cell therapies for patients who have sustained an injury or have had a disease that permanently damaged their tissue. Researchers are figuring out how to grow some of these replacement tissues from patients' own cells, reducing the need for donor organs and long-term use of immunosuppressant drugs. North Carolina is the home of several institutions that are leaders in this exciting, growing field. One of the most prominent of these organizations is the Wake Forest Institute for Regenerative Medicine (WFIRM). WFIRM researchers are studying techniques for growing replacement tissues and organs for more than 40 parts of the body, including skin, bladders, livers, kidneys and ears. They are developing new healing technologies and are doing the necessary work to translate basic research findings into practical clinical applications. In partnership with more than 500 institutions, including North Carolina Agricultural and Technical State University, Winston-Salem State University, and Forsyth Technical Community College, WFIRM scientists are working to accelerate the transition of new regenerative medicine technologies into commercial products available to doctors and their patients. Similarly, other researchers in North Carolina and around the world are working to understand the basic mechanisms that regulate cell growth and differentiation, and they are developing healing therapies for many different ailments and are translating these discoveries into clinical care for patients. Veterinary researchers also are studying regenerative medicine for animals.

The goals of this chapter are to help students understand scientific concepts underlying regenerative medicine, learn about current research topics in regenerative medicine, and explore some of the many career possibilities in this exciting new field.

### Key Vocabulary

A list of terms used in the reference sections of this chapter.

### Reference *Healing Promise*

The reference provides an introduction to regenerative medicine using the story of Luke Massella who received a new bladder grown outside his body from his own cells.

### Lesson Plan and Handout *Regenerative Medicine: Changing Life*

This lesson plan and handout ask students to explore the definition of regenerative medicine. Students will use online resources to research current advances in regenerative medicine. Students also will create and present an infographic highlighting current advances in regenerative medicine.

# Regenerative Medicine (continued)

**Reference**  
*Background  
Science*

The reference discusses topics that are foundational to regenerative medicine. From cells and extracellular matrix, to body-on-a-chip, this reference provides definitions of terms in the setting of regenerative medicine.

**Reference**  
*Ethical and  
Societal Issues  
in Regenerative  
Medicine*

The reference discusses the four basic principles of ethical decision making and the seven requirements for ethical clinical research.

**Lesson Plan and  
Handout**  
*May I Conduct  
This Research?*

In this lesson, students explore principles and guidelines for clinical research and apply these principles and guidelines to historic and current research with human research subjects.

**Lesson Plan and  
Handout**  
*Discover the  
Scaffolding of  
Tissue*

This lesson plan and handout explore scaffolding and the decellularization of animal and plant tissues and explain how the extracellular matrix can be used for the scaffolding of engineered tissue.

**Lesson Plan and  
Handout**  
*Building Better  
Tissue*

This lesson plan and handout ask students to define scaffolding and create simple structures such as a sphere or a worm with sodium alginate and a calcium water bath. Students also are asked to demonstrate the connection between scaffolding and the sodium alginate experiment by creating a poster to explain tissue and organ engineering.

**Lesson Plan and  
Handout**  
*Stem Cells Are All  
the Same... Aren't  
They?*

This lesson plan and handout ask students to describe stem cells. Students will use web resources to learn about different types of stem cells, such as multipotent and pluripotent stem cells. Next, students will create and present a public service announcement for a designated type of stem cell. Students also will analyze the advantages and disadvantages of different types of stem cells for therapeutic uses.

# Regenerative Medicine (continued)

**Lesson Plan and Handout**  
*What Makes an Organoid an Organoid?*

This lesson plan and handout ask students to explore the relationships between cells, tissues, organs and systems. Students will learn about organoids and how they are useful for medical research.

**Lesson Plan and Handout**  
*BOC for a Disease*

In this lesson, students explore the major systems of the human body. Students will learn about organ-on-a-chip (OOC) and body-on-a-chip (BOC) technologies. Students will design an OOC or BOC to analyze a specific disease.

**Reference**  
*Regenerative Medicine in Space*

The reference defines space and low Earth orbit and discusses how low Earth orbit offers many benefits for regenerative medicine research and manufacturing.

**Lesson Plan and Handout**  
*Look Up*

This lesson plan and handout ask students to learn about microgravity and low Earth orbit. Students will compare and contrast research/manufacturing on Earth and in low Earth orbit. Students will design an experiment to fit in a module that could theoretically go to the International Space Station.

**Reference**  
*AI in Regenerative Medicine*

This reference defines artificial intelligence and discusses how AI may be used to improve regenerative medicine research, manufacturing and clinical medicine.

**Lesson Plan and Handout**  
*ABCs of AI for RM*

This lesson plan and handout ask students to learn the basics of artificial intelligence. Students will identify ways AI is being used to aid regenerative medicine, and they will create an ABC chart for AI and regenerative medicine. An extension provides the outline for analyzing a dataset manually with statistical software such as Excel and with AI.

**Lesson Plan and Handout**  
*Regenerative Medicine: Buy My Treatment*

This lesson plan and handout ask students to review bioethics and the four principles of bioethics. Students will create a set of advertising guidelines using the four principles of bioethics.

# Regenerative Medicine (continued)

**Reference**  
*Careers in  
Regenerative  
Medicine*

The reference highlights three scientists who discuss their jobs and education.

**Key Vocabulary**

- **Artificial intelligence** is the ability of a computer to perform tasks that require human intelligence, including reasoning and problem solving.
- **Autonomy** is the capacity to make informed decisions for oneself. The principle of autonomy states that doctors and researchers should respect the right of competent patients to make decisions about their own care. For this reason, researchers must fully inform patients of potential risks and benefits, and patients must give consent to treatment and research.
- **Beneficence** – The principle of beneficence states that doctors and researchers must act in the best interests of patients.
- **Biomaterials** are synthetic or natural biocompatible materials used to replace part of a living system or function in intimate contact with living tissue.
- A **biopsy** is a small sample of cells taken from a patient.
- **Bioprinting** is a type of tissue engineering that involves the use of 3D printing techniques and biological materials to build tissues and organs.
- A **bioreactor** is a specialized device designed to create a controlled environment to grow and mature cells, tissues or even organs for living organisms.
- A **body-on-a-chip (BOC)** is two or more organoids linked to each other on a microfluidic chip.
- **Cells** are the smallest unit of life.
- **Confidentiality** – The principle of confidentiality states that data collected from study participants should be kept private.
- **Decellularization** is the process of removing cells from the extracellular matrix.
- **Deep learning** is a type of machine learning that involves the analysis and classification of large amounts of data.
- **Epigenetics** is the study of heritable changes in gene expression that are not caused by changes in the DNA sequence.
- **Epithelial tissue** covers body surfaces such as organs and glands.

# Regenerative Medicine (continued)

- **Ethics** is the study of what is right and wrong and the principles by which decisions should be made.
  - **Bioethics** or **biomedical ethics** is the study of ethical, social and legal issues that arise in biomedicine and biomedical research
- To **excrete** something means to get rid of it.
- The **extracellular matrix** surrounds and supports the cells that form tissues and organs in the body. It is created and maintained by cells.
- An object is in **freefall** if gravity is the only force acting upon it.
- **Informed consent** – The principle of informed consent states that a research participant must be given complete, understandable information about a study and must consent to participate before being enrolled.
- **Justice** – The principle of justice states that doctors and researchers should treat all patients fairly and equitably. This principle is often needed and becomes more complex when deciding how to allocate scarce resources.
- **Low Earth orbit (LEO)** is an orbit around the Earth at an altitude between 100 and 2,000 kilometers.
- **Machine learning** involves allowing computers to learn from data without being explicitly programmed to do so.
- **Media** is a surface that contains the nutrients cells need to grow.
- **Microfluidic chips** are small devices that contain tiny chambers collected by microchannels and are used to precisely control the flow of fluids when studying an organ-on-a-chip or body-on-a-chip.
- **Microgravity** is a state in which people and objects appear to be weightless.
- **Non-maleficence** – doctors and researchers should not harm patients, should not cause pain, and should not give offense.
- **An organ**, such as the heart, skin, kidney or stomach, combines two or more tissues that function together.
- An **organoid** is a small section of tissue that mimics the structure and function of a human organ.
- An **organ-on-a-chip (OOC)** is an organoid grown on a microfluidic chip.
- The **perivascular area** is the fluid-filled space that surrounds blood vessels.
- A **scaffold** is a support structure. In regenerative medicine, scaffolds are support structures for cells to grow and orient themselves when building replacement tissues and organs.
- **Regenerative medicine** is a field focused on repairing damaged tissues through techniques such as tissue engineering and stem cell therapies.

# Regenerative Medicine (continued)

- **Space** is the expanse that exists outside of the Earth's atmosphere.
- **Stem cells** are undifferentiated cells that give rise to other cells.
  - **Hematopoietic stem cells** are stem cells found in bone marrow that can differentiate into blood cells.
  - **Embryonic stem cells** are pluripotent stem cells found in embryos that differentiate to form specialized cells needed by adults.
  - **Induced pluripotent stem cells** are adult cells that have been engineered to behave like human embryonic stem cells.
  - **Mesenchymal stem cells** are found mainly in bone marrow and can differentiate into mesenchymal cells (bone, cartilage, fat and muscle).
  - **Multipotent stem cells** can give rise to the cell types needed in the tissue from which they are derived but not to other types of cells found in the body.
  - **Neural stem cells (NSCs)** are found in the brain and can differentiate into neurons, astrocytes and oligodendrocytes.
  - **Pluripotent stem cells**, such as human embryonic stem cells (hESCs), can give rise to all the other types of body cells.
  - **Totipotent stem cells** can give rise to all the other tissues needed by the body as well as the extra embryonic tissues (e.g., the placenta).
- A **stem cell-based intervention** involves the use of stem cells to treat a disease or repair damaged tissues, whether that use has been proven effective or not.
- **Systems** are groups of organs with the same function.
- A **tissue** is a group of similar cells from the same organ performing a specific function (e.g., smooth muscle tissue or connective tissue).
- **Tissue engineering** is a field that uses biomaterials to create substitutes for damaged tissues.
- **Virtual reality** is a simulation that allows users to interact with a computer-generated world as though it were real.
- A **zygote** is a single cell formed by the joining of an egg and sperm.

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# Regenerative Medicine (continued)

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# Healing Promise

Luke Massella was born with spina bifida, a birth defect involving the spinal column. In 2001, he was seriously ill. He could not run around or play outside with his friends. He could barely go to school. In Luke's case, the defect in his spinal column led to a paralyzed bladder. When the bladder does not function properly, urine can back up and cause damage to the kidneys, which are responsible for filtering waste from the blood. When the kidneys don't work, toxins build up. Kidney damage is often life-threatening. Even after 16 surgeries, Luke's kidneys were in danger. He was losing weight and unable to live a normal life. Then, Luke received a new bladder grown from his own cells outside his body using techniques from the new and experimental field of regenerative medicine. This preserved his kidneys and restored his health. He even became captain of his high school wrestling team and went on to graduate from college. Now, he is a healthy, active adult. Luke's doctor for this groundbreaking treatment was Dr. Anthony Atala, Director of the Wake Forest Institute for Regenerative Medicine (WFIRM) in Winston-Salem, N.C. (*See the Resources section later in this chapter for links to TED Talk videos of Dr. Atala explaining his techniques and meeting with Luke 10 years after Luke received a new bladder.*)

However, regenerative medicine is still in its infancy. Damaged and diseased organs present huge medical challenges. Human organ transplants from living or dead donors are a way to treat severely damaged organs, but these types of organ transplants pose many issues and are not a cure-all. In 2024, there were 48,150 organ transplants in the United States, 1,544 of which were done in North Carolina.<sup>1</sup> Sadly, this does not begin to meet the need for such transplants. More than 100,000 people in the United States are waiting for an organ transplant — the majority for a kidney. An average of 13 people die each day while waiting.<sup>2</sup> Furthermore, even a successful transplant leads to a lifetime of special drugs to keep the body from rejecting the donated organ. Unfortunately, these immune suppressant drugs also weaken the body's response to disease. Sometimes doctors can repair or replace damaged organs with artificial parts, but these parts (such as a titanium hip or an artificial heart valve) can deteriorate over time and may cause infection or inflammation. Artificial replacement parts are a particular problem for children because they don't grow with the child, so these replacement parts must be replaced again as the child grows.

The fantastic promise of regenerative medicine is that someday doctors will be able to heal patients with cell and gene therapies and grow tissues and organs from the patient's own cells to replace a diseased or damaged part.

# Healing Promise (continued)

This might occur by stimulating the patient's cells to grow replacement tissues within the body, or the replacement tissues might be grown in the lab and then transplanted into the patient. If replacement tissues are grown from the patient's own cells, the patient's immune system will accept the transplant without powerful immune suppressant drugs, and the patient will be able to live a much healthier life. Luke's miraculous story was part of a clinical trial. While his treatment was successful, this type of treatment involves many challenges that must be overcome before organ replacement can become routine — and other approaches may turn out to be more successful or more replicable. Research being done today in North Carolina and around the world is solving these problems and others and will lead to new treatments for patients. While much remains to be studied and developed, the promise of regenerative medicine is beginning to be kept. A few regenerative medicine therapies have effectively helped patients and are approved for clinical use in the U.S. In the next section, we will look in more depth at the science underlying regenerative medicine and the challenges involved in bringing it to the patients who need it.

## Resources:

- Atala, A. (2011, March). *Printing a Human Kidney* [Video]. Ted Conferences. 16.5 minutes. [https://www.ted.com/talks/anthony\\_atala\\_printing\\_a\\_human\\_kidney](https://www.ted.com/talks/anthony_atala_printing_a_human_kidney)
  - Dr. Anthony Atala provides an engaging overview of regenerative medicine with an emphasis on the need for organs and the potential of 3D printers for creating human organs to replace damaged or diseased organs. He discusses the history of regenerative medicine and then the state of the field in 2011, showcasing some experimental technologies and key areas of research. He introduces Luke, the recipient of a lab grown replacement bladder. The video is a good introduction to the field of regenerative medicine and would be accessible to middle and high school students.
  - Critical moments in the video: Overview of regenerative medicine at 0:44, history at 1:17, three main challenges at 1:48, advances in biomaterials at 2:41, use of cells at 3:44, engineered heart valve 5:04, bladder at 5:23, liver at 6:06, 3D printing with cells 7:15, printing a kidney on stage at 10:30, introduces Luke Massella at 12:21 first with a 30-second clip, and then Luke comes on the TED stage at 14:02.

# Healing Promise (continued)

- Atala, A. (2009, October). *Growing New Organs* [Video]. TEDMED. 17:35 minutes. [https://www.ted.com/talks/anthony\\_atala\\_growing\\_new\\_organs](https://www.ted.com/talks/anthony_atala_growing_new_organs)
  - Dr. Anthony Atala provides an overview of regenerative medicine, including a discussion of salamander limb regeneration and the more limited regeneration that humans can do. He discusses and shows various types of tissues and organs being engineered in the lab. He explains and shows the decellularization of tissues to provide a scaffold for building a new organ using the patient's own cells. He ends with a discussion of the challenges of going from lab to clinical trial to standard treatment. While somewhat dated, the overall video is a good introduction to the field of regenerative medicine and would be accessible to middle and high school students.
  - Critical moments in the video: Salamander regeneration at 1:51, regenerating muscle 5:58, blood vessel at 6:33, detailed steps involved in engineering a new bladder at 8:09, printing an experimental heart at 10:48, decellularization at 11:27, discussion of challenges at 14:59, ends with a patient successfully treated at 16:35.
- Wake Forest University School of Medicine. (n.d.). *Innovative Treatment Advances Medical Treatments*. <https://school.wakehealth.edu/features/research/innovative-teamwork-advances-medical-treatments>
  - This website defines regenerative medicine and describes the Wake Forest Institute for Regenerative Medicine and some of its current research. There is a short (1:26 minutes) embedded video that emphasizes the importance of teamwork in regenerative medicine research. The first section of the website that defines regenerative medicine and the video are accessible for high school students.
- Millan, M. (2020, January). *The First Step into a New Era: Regenerative Medicine* [Video]. TEDxGunnHighSchool. 18:45 minutes. [https://www.ted.com/talks/maria\\_millan\\_the\\_first\\_step\\_into\\_a\\_new\\_era\\_regenerative\\_medicine](https://www.ted.com/talks/maria_millan_the_first_step_into_a_new_era_regenerative_medicine)
  - Dr. Maria Millan introduces gene and cell therapies, including CRISPR for sickle cell disease and CAR-T cell therapy for some cancers. Her discussion of sickle cell disease starts with the patients' perspective and then talks about the first patient to be cured with CRISPR therapy. The video is a good introduction to cell and gene therapies and would be accessible to middle and high school students.
  - Critical moments in the video: story of a child with no immune system at 6:07, sickle cell disease at 9:17; CAR-T cell therapy for cancer at 13:43.

# Healing Promise (continued)

## Footnotes

<sup>1</sup> Organ Procurement and Transplantation Network (August 2025). *National Data: Transplants in the U.S. by State*. <https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#>

<sup>2</sup> Health Resources & Services Administration. (August 2025). *Organ Donation Statistics*. <https://www.organdonor.gov/learn/organ-donation-statistics>

# Regenerative Medicine: Changing Life

## Learning Outcomes

- Students will define regenerative medicine.
- Students will use online resources to research current advancements in regenerative medicine.
- Students will create and present an infographic highlighting current advancements in regenerative medicine.

## Key Vocabulary

- Regenerative medicine

## Time Required

- Approximately 90 minutes to research regenerative medicine (may be done outside of class)
- Approximately 60 minutes to create regenerative medicine infographic (may be done outside of class)
- Approximately 90 minutes to present regenerative medicine infographics (for class of 30 students)

## Materials

- Computers with internet access and print materials for research
- Rubric

## Background Information

Regenerative medicine holds the possibility of using stem cells to engineer and grow tissues and organs. In the past, if someone had a diseased bladder, he or she most likely would develop kidney disease and possibly would die. But in 2001, a young boy was given a new bladder that had been grown for him in a lab. Today, doctors are able to print 3D skin grafts for burn patients. This field of medicine continues to evolve; thus, students must keep up with new advances by reading current research.

## Teaching Notes

This activity allows students to work in groups to learn about regenerative medicine and the advances in this field. Depending on student access to the Internet, you may choose to have students do this research in or out of class. After gathering and synthesizing information, students will create a magazine cover highlighting their favorite advances in regenerative medicine. This activity may be adapted into an individual project.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing.

# Regenerative Medicine: Changing Life (continued)

## Procedure

Begin by watching a video on regenerative medicine. Consider using one of the videos below or find a video on a part of regenerative medicine that would be more impactful for your context.

- Science Channel. (2022, August 30). *How It's Made: Regenerative Medicine* [Video]. YouTube. <https://youtu.be/HngRdfTzOeQ>
  - This video provides a description of regenerative medicine and how researchers are working to grow tissues such as blood vessels and heart valves (5:24 watch time).
- Discovery Channel Southeast Asia. (2024, November 25). *Medical Elite: Regenerative Medicine* [Video]. YouTube. <https://youtu.be/q95hYGI7Htk>
  - This video provides a description of regenerative medicine and how researchers are using stem cells to repair and grow tissues. This video also highlights how stem cell treatment is seeking to treat and cure chronic diseases (5:31 watch time).

After watching the video, the students will have many questions. Write these questions on the board. Explain that they will be able to answer many of these questions and others after completing this project.

Explain that regenerative medicine is a constantly changing field, and they will be using online resources to discover current advances. The student will work in pairs to complete the following *Regenerative Medicine: Changing Life* handout. The students will use two or three resources to answer the questions.

In order to move to the next section, the teacher may use the student sheet as a formative assessment.

After the students have completed the research, the students will create an infographic highlighting a key use of regenerative medicine and details of this use.

## Assessment

The infographic may be evaluated using the rubric at the end of this lesson plan. Rubrics help students understand what is expected of them. They should be shared with students in advance and may be developed with students.

Teachers may adjust this rubric to fit their grading system and to emphasize different aspects of the project as appropriate for their curriculum.

# Regenerative Medicine: Changing Life (continued)

## Extension

This activity may be extended by asking students to research and create a projected timeline for the research and clinical trial process for the new applications of regenerative medicine.

## Resources

There is a plethora of regenerative medicine information online. Because this research area is evolving rapidly, online information is more likely to be up to date than information in print.

Some options include:

- National Institutes of Health. (n.d.). *Regenerative medicine*. <https://www.nih.gov/about-nih/nih-turning-discovery-into-health/transformational-technologies/regenerative-medicine>
  - This website provides an introduction to regenerative medicine and links to transformational technologies.
- Sung, Y. H., Lee, S.-H., & Chang, J. (2022). Regenerative medicine applications: An overview of clinical trials. *Frontiers in Bioengineering and Biotechnology*, 10, Article 942750. <https://doi.org/10.3389/fbioe.2022.942750>
  - This article provides an introduction to regenerative medicine and a list of cellular and tissue engineered products that are FDA approved (2022).
- RegenMed Development Organization. (n.d.). *RegenMed engine*. <https://regenmedengine.com/>
  - This website provides information about the Regenerative Medicine Engine in North Carolina. It provides links to partners and technologies in North Carolina.
- McGowan Institute for Regenerative Medicine. (n.d.). *What is regenerative medicine?* <https://mirm-pitt.net/about-us/what-is-regenerative-medicine/>
  - This article focuses on three areas of regenerative medicine: tissue engineering and biomaterials, cellular therapies, and medical devices and artificial organs. Each area also has links to current research.

# Regenerative Medicine: Changing Life (continued)

- Wake Forest Institute for Regenerative Medicine. (n.d.). *Awards, honors, and media coverage*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/awards-honors-and-media-coverage>
  - This website lists and provides links for current regenerative medicine research and honors at WFIRM.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *A record of firsts*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/a-record-of-firsts>
  - This website lists the “firsts” of regenerative medicine research at WFIRM.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Cell and gene therapy research*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/cell-and-gene-therapy-research>
  - This website lists and provides links for current regenerative medicine research focusing on cell and gene therapy at WFIRM.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Military applications*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/military-applications>
  - This website lists and provides links for current regenerative medicine research that has military applications at WFIRM.
- PBS North Carolina. (n.d.). *Dr. Tony Atala, surgeon & researcher – Side by Side with Nido Qubein* [Video]. PBS. <https://www.pbs.org/video/dr-tony-atala-surgeon-researcher-su0k24/>
  - This video features cell and tissue regeneration (26:46 interview watch time).
- California Institute for Regenerative Medicine. (n.d.). *Home page*. <http://www.cirm.ca.gov>
  - This website lists and provides links for current regenerative medicine research at the California Institute for Regenerative Medicine.

# Regenerative Medicine: Changing Life (continued)

- Mayo Clinic. (2018, April 21). *What is regenerative medicine?: Mayo Clinic Radio* [Video]. YouTube. <https://www.youtube.com/watch?v=yXk3vYxr4>
  - This video focuses on regenerative immunotherapy (10:27 watch time).
- The Stem Cell Podcast. (2019, July 15). *Episode 198: Printing human tissues featuring Dr. Anthony Atala* [Audio podcast episode]. <https://stemcellpodcast.com/ep-198-printing-human-tissues-featuring-dr-anthony-atala>
  - This video features tissue engineering research (interview starts at the 30:03 timestamp, 35:03 interview watch time).

# Regenerative Medicine: Changing Life (continued)

## Rubric for Regenerative Medicine: Changing Life Assignment

Category/ Points	4	3	2	1
Notes and sources	Student took notes for each section and shows sources of all information.	Student took notes for most sections (six or more) and shows sources of most.	Student took notes for at least three sections and shows sources for some information.	Student found little information or does not show any sources. Cites none of the pictures used.
Content from the webquest	Shows a complete understanding of an advance in regenerative medicine. Cites all pictures used.	Shows a good understanding of an advance in regenerative medicine. Cites some pictures used.	Shows partial understanding of an advance in regenerative medicine. Cites one of the pictures used.	Does not seem to understand an advance in regenerative medicine. Cites none of the pictures used.
Current nature of sources	All material taken from current sources.	Presents current material 90% to 95% of the time.	Presents current material 75% to 89% of the time.	Presents little to no current material.
Infographic quality	Creates an infographic about regenerative medicine with an appropriate title that highlights a current advance.	Creates an infographic about regenerative medicine that highlights a current advance.	Creates an infographic about regenerative medicine.	Creates a basic infographic about science.
Presentation/ infographic pitch	Speaks clearly with correct pronunciation of terms. Maintains eye contact. Presents the information in a logical and interesting process.	Speaks clearly with mostly correct pronunciation of terms. Maintains eye contact most of the time. Presents the information in a logical process.	Occasionally speaks clearly with some correct pronunciation of terms. Maintains eye contact at times but reads most of the presentation. Difficult to follow presentation.	Does not speak clearly or pronounce terms. Lack of eye contact because the presentation is read. Unable to follow presentation.

# Regenerative Medicine: Changing Life — Student Worksheet

Thanks for accepting this assignment. You will be researching regenerative medicine and the current advancements in this field. You have a list of questions to answer. As you research, you also should add a couple questions of your own to the list. Keep track of your notes and sources in the chart below. (A list of suggested sources is provided on the next page.) After you have completed the research, create an infographic cover explaining a current advance in regenerative medicine. At the end of this process, you will have the opportunity to share your infographic with the class.

Question	Notes	Resource/Website/Publication Date
What is a current advance in regenerative medicine?		
Where is this current advance being studied/implemented?		
How will this advance impact life?		

# Regenerative Medicine: Changing Life — Student Worksheet (continued)

## Suggested Sources

- Sung, Y. H., Lee, S.-H., & Chang, J. (2022). Regenerative medicine applications: An overview of clinical trials. *Frontiers in Bioengineering and Biotechnology*, 10, Article 942750. <https://doi.org/10.3389/fbioe.2022.942750>
  - This article introduces regenerative medicine and provides a list of cellular and tissue engineered products that are FDA approved (2022).
- McGowan Institute for Regenerative Medicine. (n.d.). *What is regenerative medicine?* <https://mirm-pitt.net/about-us/what-is-regenerative-medicine/>
  - This article focuses on three areas of regenerative medicine: tissue engineering and biomaterials, cellular therapies, and medical devices and artificial organs. Each area also has links to current research.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Awards, honors, and media coverage*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/awards-honors-and-media-coverage>
  - This website lists and provides links for current regenerative medicine research and honors at WFIRM.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *A record of firsts*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/a-record-of-firsts>
  - This website lists the “firsts” of regenerative medicine research at WFIRM.

# Background Science

## Tissues and Organs

**Tissues** are groups of similar **cells** performing a similar function. **Organs** are made up of multiple tissues working together to perform a function, while **systems** consist of organs and tissues working together to perform a function. Scientists are researching ways to regenerate more than 40 different tissues and organs, including skin, bone, blood vessels, bladders, kidneys, lungs and livers. Organs range in form and complexity from flat organs (such as skin) to tubes (such as blood vessels or ureters), to hollow, bag-like organs (such as the bladder or stomach) to complex, solid organs (such as the kidneys or brain). More complex organs include more different tissues and have more complicated architecture. For example, the bladder is a hollow, bag-shaped organ made up of several layers of tissue, including a lining of smooth **epithelial tissue** (a type of tissue that forms glands and covers body and organ surfaces) on the inside that protects the bladder from urine and a layer of smooth muscle tissue on the outside that contracts to allow a person to urinate. Solid organs, such as kidneys, are more complex. Kidneys have multiple specialized parts to filter waste from the blood and **excrete** (get rid of) it as urine while maintaining a constant water and mineral balance and retaining important nutrients. As of 2025, regenerative medicine techniques have been approved to treat blood disorders in the U.S. and replace damaged corneal tissue in Europe.<sup>1</sup> They also have been used to repair or replace damaged skin, cartilage, heart muscle tissues, the urethra, the bladder and the trachea in human patients. However, many of these treatments remain experimental. Many questions about materials, safety and procedures still must be answered before regenerative treatments to repair or replace these organs become standard medical practice. It will be even longer before a complex, solid organ such as the kidney can be regenerated successfully and placed in a human patient.

## The Extracellular Matrix: A Scaffold for Building New Organs

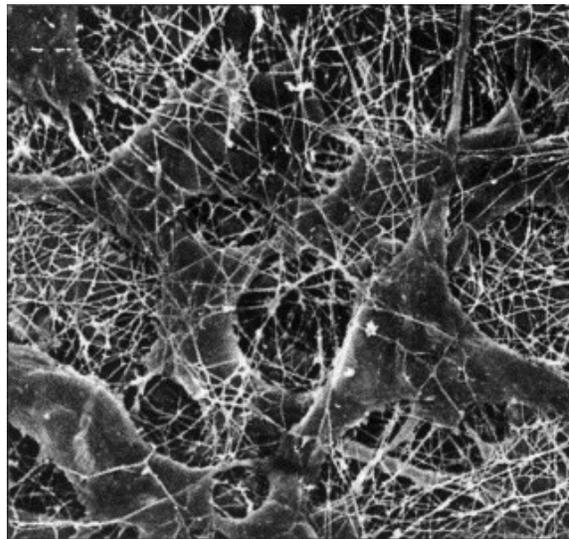
The first step of generating replacement organs is to build a supporting framework called a **scaffold**. Simple tissues and complicated organs are similar in that they grow and reside in a supportive **extracellular matrix**. This extracellular matrix is outside the cells and consists of proteins and polysaccharides. The polysaccharides are linked to proteins to form a gel-like substance in which other fibrous proteins are embedded. This gel allows nutrients, waste and other chemicals to diffuse to and from the cells. The fibrous proteins form a strong, resilient scaffold and help organize the cells. Amazingly, tissues and organs can be decellularized. In other words, all the cells can be removed, leaving only the extracellular matrix. The matrix forms a scaffold

## Background Science (continued)

for the cells but is not made of living tissue. This matrix then can be used as a scaffold to build a new organ.

To build a new tissue or organ, researchers place new cells of the desired types in the correct locations on the scaffold. Then they grow the cells on the scaffold in a growth medium for several weeks. The scaffold is important not only because it provides support, but also because it influences where and how the cells grow. This helps orient the cells correctly for their function. Scaffolds can come from deceased human donors, animal organs or synthetic biomaterials. All of these are much more readily available than human organs suitable for transplant.

*Image 1: Scanning Electron Micrograph of Extracellular Matrix*



A scanning electron micrograph of native extracellular matrix in connective tissue. It is largely composed of collagen fibrils. The hydrogel, composed of proteoglycans and glycosaminoglycans, that normally fills the interstices of this fibrous network has been removed by the processing treatment.

**Image Credit:** Reprinted from *Trends in Biotechnology*, Vol 16, edition 5, Byung-Soo Kim and David J. Mooney, "Development of biocompatible synthetic extracellular matrices for tissue engineering," Copyright 1998, with permission from Elsevier.

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Researchers studying these scaffolds deal with several challenges. One important challenge is developing biomaterials to build artificial scaffolds. These biomaterials must not react with the human immune system, and they need to have the right texture to signal cells to grow and orient themselves correctly. They also need to be strong enough to last until the new organ creates its own extracellular matrix, then dissolve away like surgical sutures. Researchers also are investigating the effects of embedding various growth factors or anti-inflammatory medications in the scaffolds.

The decellularization of animal tissues presents a different challenge: removing all the cells without damaging the function of the scaffold. This is difficult

# Background Science (continued)

because the scaffold not only needs to have the right structure, it also must have the right texture and chemical properties. Different tissues require different techniques, and these techniques may affect the structure and composition of the scaffold in different ways. Researchers are experimenting with a variety of detergents and enzymes as well as with different protocols to perfuse (add liquid into) the tissue and remove the cells.

## Stem Cells

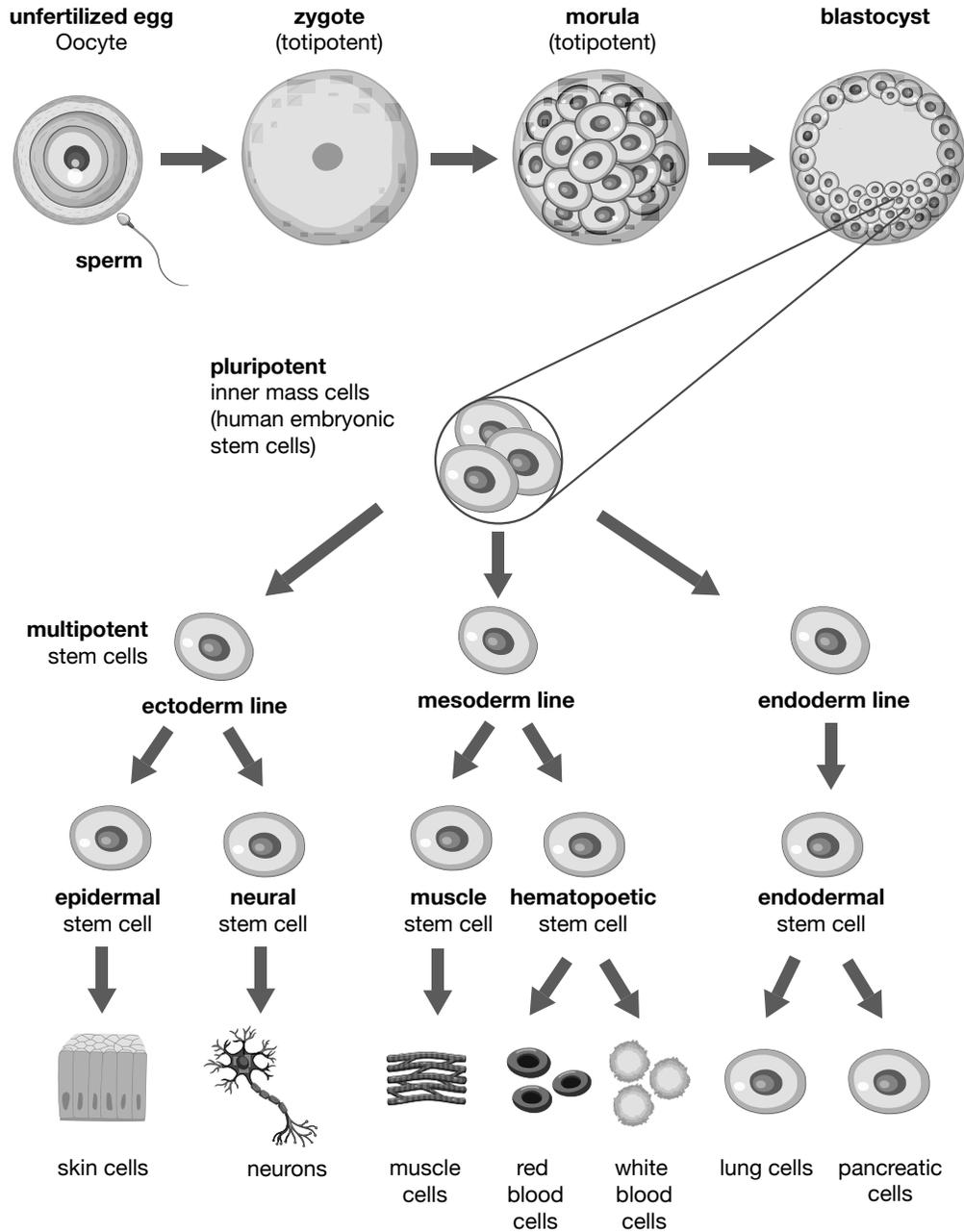
A variety of regenerative therapies, including production of cells to populate the extracellular matrix, depend on stem cells. Stem cells are widely discussed in the news and promoted by health influencers, yet many people do not understand what they really are or why they may lead to exciting advances in medicine. This section explains some of the different types of stem cells, how they are currently used to save lives, and how researchers are investigating new potential stem cell treatments.

Think about your body. It is composed of many different types of cells. You already may be familiar with neurons, red blood cells and muscle cells. All these different cells must be generated from a **zygote**, a single cell formed by the joining of an egg and a sperm. As multicellular organisms develop from zygotes to adults, they must produce differentiated cells capable of forming all the organism's different tissues and organs. The undifferentiated cells that give rise to other types of cells are called **stem cells**. There are many different types of stem cells found at different stages of development and in different parts of the body. The hope is that these cells can be used to repair tissues and grow new organs, but to do this, we must understand how these cells work. Researchers are beginning to learn how development and differentiation are controlled at the molecular level.

When a zygote first begins to divide, it is **totipotent**. This one cell can give rise to all the tissues needed for the body as well as the cell types needed for the extra embryonic tissues, such as the placenta. As the zygote divides and goes through the various stages of development, the cells begin to differentiate. The differentiation is controlled by chemical signals that cause changes in cell **epigenetics**. In an epigenetic change, the sequence of the nucleotides (ACGT) is unchanged, but chemical changes in the chromosome turn on or off particular genes. *(See the Resources section later in this chapter for a link to more about epigenetics.)*

# Background Science (continued)

Image 2: Human Embryonic Stem Cells Differentiation into Specialized Cell Types



In this image, you will notice the human embryonic stem cells are found in the inner cell mass of a blastocyst, and are pluripotent stem cells that can differentiate into a variety of specialized cell types.

## Background Science (continued)

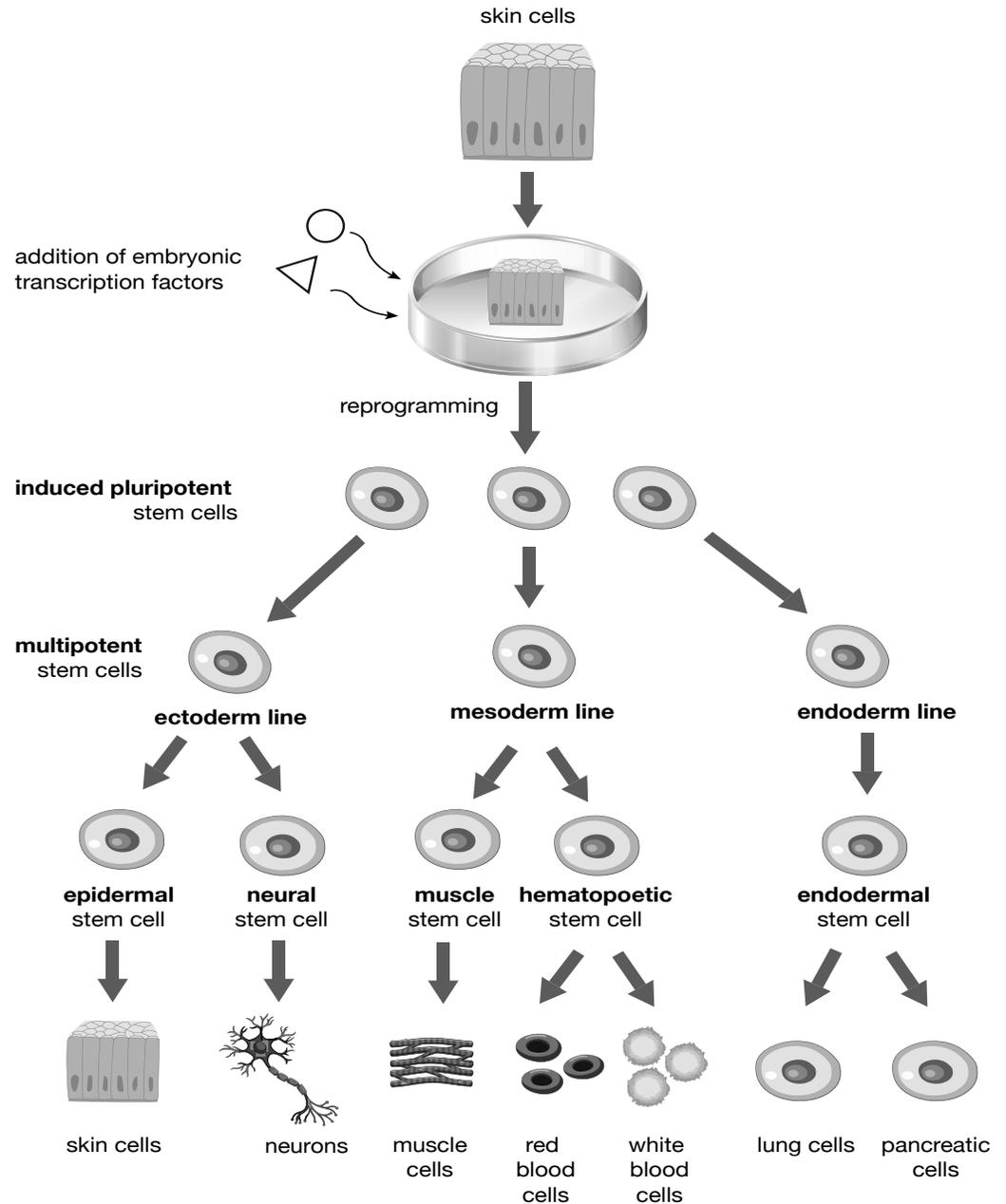
These genes then stay turned on or off even as the cell divides so that the changes are passed on to the daughter cells. This means that normally once a cell has differentiated into one type of cell (a nerve cell, for example) it cannot differentiate backward into another type of cell. Therefore, even though each cell in an organism has all the information for all the types of cells found in that organism, only some of this information is available to the cell.

Embryonic stem cells are **pluripotent**. Pluripotent cells can give rise to all the other types of body cells but not the extra embryonic tissues. Previously, researchers used human embryonic stem (hES) cells derived from human embryos created as a part of the in vitro fertilization process at fertility clinics. The embryonic stem cell lines came from extra embryos donated for research purposes. Because this has the potential to save lives but also destroys these embryos, the creation of new embryonic stem cells has been the subject of extensive ethical and legal debate, as well as state and federal laws and guidelines.

Currently, almost all research using hES depends on pre-established cell lines. In addition, the need for hES has sharply decreased since the discovery of **induced pluripotent stem cells (iPSCs)**. Induced pluripotent stem cells are adult cells engineered to behave like hES cells. In 2006, Japanese researchers published the first report of iPSCs in mice.<sup>2</sup> In 2007, that group and two others published results indicating they had created pluripotent stem cells from adult human cells.<sup>3</sup> They did this by adding transcription factors, specific proteins that regulate how often a gene is or is not transcribed. This seemed to reprogram the cells back to an undifferentiated state. The resulting cells then could be cultured and induced to differentiate into adult cells of various types — even beating heart muscle. These induced pluripotent stem cells are exciting because researchers can use them to create cultures of tissues from organisms with various diseases, which allows for in vitro studies of disease processes and potential drug treatments. They also increase the potential for growing replacement tissues or even organs from a patient's own cells, which reduces the likelihood of the patient's immune system rejecting the replacement tissues as foreign. iPSCs already have been successful in treating blood disorders in mice. Unfortunately, the reprogrammed cells do not always behave in the same way as embryonic stem cells. They have different epigenetic markers, and they sometimes lead to tumors in experimental animals. More research is needed to understand how to control the programming of these cells.

# Background Science (continued)

Image 3: Adult Stem Cells Differentiation into Induced Pluripotent Stem Cells



In this image, you will notice the induced pluripotent stem cells can be derived from adult skin cells and can differentiate into the same cell types as hESCs.

## Background Science (continued)

Adult stem cells (also called somatic stem cells) are undifferentiated cells found in differentiated tissues of children and adults. These stem cells are **multipotent**. They can give rise to the multiple cell types needed in the tissue they come from, but due to epigenetic control they are no longer pluripotent. **Hematopoietic** (blood) **stem cells** have been used successfully for years to treat various blood disorders such as leukemia and lymphoma. In these cases, stem cells from the patient's or donor's bone marrow replace diseased bone marrow cells. However, until the mid-2000s, most other types of adult stem cells were difficult to find and work with, and little was known about them. Now treatments involving many different types of stem cells are in clinical trials and have the potential to treat a whole range of disorders. For example, stem cells may help replace diseased tissue either by integrating with the tissue and producing new cells or by producing growth factors that cause the patient's cells to regenerate and repair themselves.

Researchers are experimenting with various approaches to using stem cells to treat burn patients. First, skin stem cells are isolated from an unburned area on the patient's own skin. Then, the printer or spray gun is used to place the skin stem cells and other skin cells directly on the burn. Special stem cells provide growth factors to the damaged skin so it can regrow faster rather than integrating with it and becoming part of the new skin. This technique was piloted in humans in a 2005 study, where researchers in Russia transplanted multipotent stem cells from the bone marrow of a patient onto severe thermal burns on her skin.<sup>4</sup> The patient healed faster than was typical for the severity of the burn she had experienced, and the researchers were able to perform a skin graft only four days after the stem cell treatment. A 2015 review of the use of stem cells in treatment of burns found that many techniques were being tested on animals, but few had been applied to human patients.<sup>5</sup> Though "spray-on skin" treatments have been approved by the FDA, these treatments use keratinocytes and fibroblasts from a patient rather than stem cells. Treatments are being studied that use **mesenchymal stem cells** to treat burns. These cells are multipotent, and typically can differentiate into bone, cartilage, fat or muscle. However, in the lab, mesenchymal stem cells can be induced to differentiate into various types of skin cells. Stem-cell based burn treatments from several different sources are currently undergoing clinical trials.<sup>6</sup>

Other researchers are working to develop new treatments using stem cells, including therapies for heart disease, diabetes and many other diseases. Treatments using neural stem cells (stem cells that can differentiate into various

## Background Science (continued)

neural cell types) are being tested in clinical trials as treatments for Parkinson's disease, epilepsy and spinal cord injuries.

Another source of stem cells is human amniotic fluid. Amniotic fluid is the fluid that surrounds the developing baby in the womb. Amniotic fluid-derived stem cells come from the amniotic fluid taken in an amniocentesis or are naturally produced at birth. Thus, they do not involve destroying an embryo. They are multipotent and can form all sorts of tissues. Unlike embryonic stem cells, they do not form tumors when grown in animals. Scientists are continuing to study the effects of various growth factors on the growth and differentiation of amniotic fluid stem cells when placed into various types of tissues and scaffolds. *(See the Resources section later in this chapter for a link to a paper discussing regulation of stem cell research, including a timeline of stem cell research and discoveries.)*

### Curing Hemophilia Before Birth

Dr. Graça Almeida-Porada and her research team at WFIRM are studying how stem cells could be used to cure devastating diseases before birth.<sup>7</sup> One of these diseases is hemophilia A, the most common X-linked bleeding disorder present in 1 in 5,000 male babies born in the U.S. Individuals with hemophilia A have very low levels of Factor VIII, a protein responsible for blood clotting. Unless they receive expensive infusions of Factor VIII several times a week, patients with hemophilia A are constantly in danger of succumbing to spontaneous bleeds. Even with treatment, micro-bleeding around the joints leads to debilitating injuries, and many people with this disease cannot walk unassisted by the age of 20.

The WFIRM team is studying the use of stem cells to try to halt the progression of hemophilia A before the effects of the disease are felt. They took stem cells from a human placenta, which already produced some Factor VIII, and used genetic engineering to modify them so that they produced extra Factor VIII. Next, they injected those engineered cells into sheep fetuses at the human equivalent of 18 to 22 weeks of pregnancy. After the sheep were born, they monitored the levels of Factor VIII present in their blood and looked for where the placental multipotent stem cells were functioning. They found that the injected cells were lodged in **perivascular areas** (the fluid filled space that surrounds blood vessels), and they also found that the sheep did not demonstrate any immune reaction to the human stem cells. The levels of Factor VIII were significantly elevated in sheep that had been injected with the cells.

## Background Science (continued)

Because pregnant women and fetuses are both protected classes of research subjects under FDA regulations, the treatment developed by Dr. Almeida-Porada and her team has not yet been tested on human subjects. For now, her lab is working on refining the Factor VIII treatment in sheep, carrying out and publishing more studies to show the potential efficacy of this work. Eventually, this research could lead to prenatal treatment for hemophilia A.

### Bioprinting

Though regenerative medicine has led to exciting innovations, such as the transplanting of lab-grown bladders into human patients, the field is still very much in its infancy. Only a few treatments involving lab-grown organs (e.g. skin grafts) have been FDA approved, and scientists are working to find alternate ways that regenerative medicine techniques can be used to support research and help patients. Technological advances have led to researchers developing 3D printing as a potential way to build organs. The printing process starts with a **biopsy** (a small sample of cells) that is taken from a patient and mixed with a liquid containing the nutrients cells need to grow called **media**. Once the cells grow, they are mixed in with a gel that mimics the extracellular matrix – a nonliving material made of proteins and carbohydrates that is found between cells in the human body. This “organ ink” is then loaded into a bioprinter. In ink printers, different colors of ink are kept in separate cartridges and printed together to form the exact desired color. Similarly, bioprinters can keep cells and different substances separate until placing them exactly where needed in the new tissue. The printing process typically takes several hours. Use of a printer means that the cells can be loaded onto a scaffold shaped like the new organ with more precision than if the cells were placed on the scaffold by hand. 3D bioprinters also are being developed to build scaffolds. Dr. Atala and the research team at the WFIRM have demonstrated how printing replacement tissues and organs might work by printing functional models of kidneys, heart valves and other tissues for use in research. However, due to the size and complexity of human organs, printed internal organs have not yet been transplanted into humans.

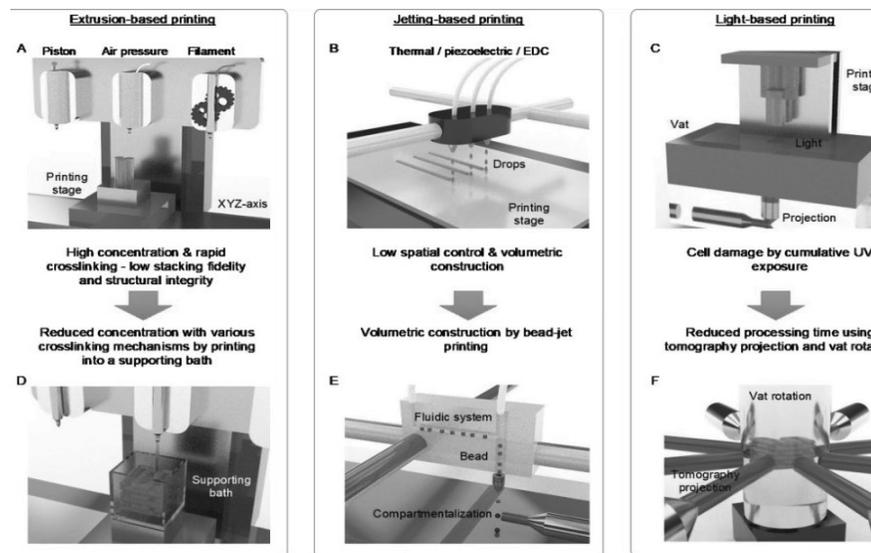
Growing new cells on a scaffold and preparing a tissue or organ for its role within the body also is challenging, but researchers are making progress. Researchers are finding that many tissues have some undifferentiated cells that will reproduce and grow in the right environment and with the right nutrients in the culture media. Experimentation with growth factors is leading to improved control of cell proliferation and differentiation. Researchers also are designing

# Background Science (continued)

equipment to simulate the normal environment of the body with hydrostatic pressure, pulsing fluid flow and stretching and compressing tissues. This exercises and conditions the tissues to their environment and helps signal the growing cells to organize themselves correctly. For example, researchers grow a regenerated heart valve in a tube and pump the growth medium through the tube to simulate the rate and pressure of blood flow. Such laboratory devices are referred to as **bioreactors**. They play a key role in growing replacement tissues and organs.

## Image 4: Different 3D Printing Methods for Cell-Based Bioprinting

Image Credit Reprinted from Lee, S. J., Jeong, W., & Atala, A. (2024). 3D Bioprinting for Engineered Tissue Constructs and Patient-Specific Models: Current Progress and Prospects in Clinical Applications. *Advanced Materials*, 36(49), 2408032. <https://doi.org/10.1002/adma.202408032> with permission from WFIRM.



In this image, you see conventional 3D printing: (A) Extrusion, (B) jetting, and (C) light-based printing methods. Advanced 3D printing methods; (D) Emedded printing using supporting bath, (E) bead-jetting printing, and (F) volumetric printing by vat rotation and tomography-projection.

## Organoids

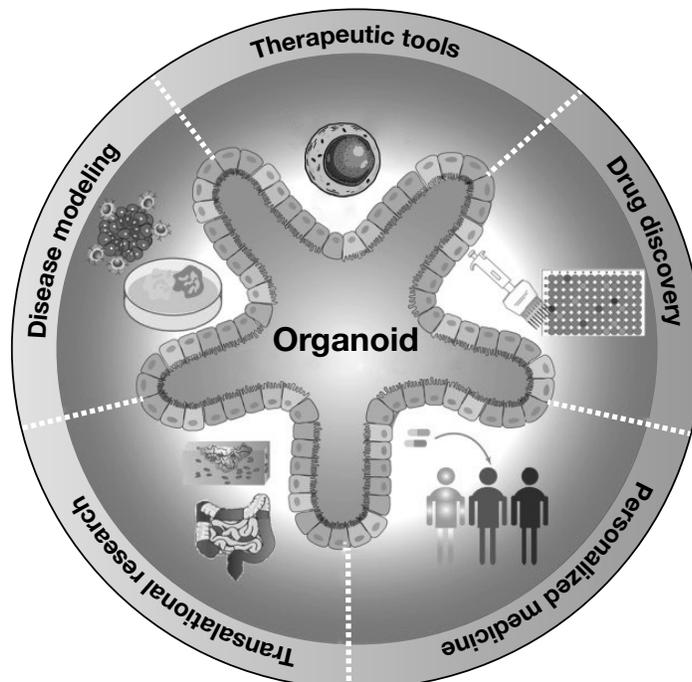
Though bioprinting technology is not yet being used to print replacement organs for clinical use, researchers are using bioprinters to create **organoids**. These are tiny tissue cultures grown from stem cells that, while smaller and less complex, are similar in structure and function to organs and provide realistic models for regenerative medicine research. Currently, medications intended for human use

## Background Science (continued)

are first tested for initial indications of safety and efficacy on human cells in the lab. If the medication passes these tests, it is then tested on animals before being tested in clinical trials in human subjects. However, this system leads to major losses of time and money because problems with the treatment often do not show up until they are tested in humans — in fact, nearly 90% of drugs developed by pharmaceutical companies fail either before or when they are tested in humans, and efforts to develop these drugs add up to around \$2 billion annually.<sup>8</sup> In addition, unforeseen adverse effects may appear during clinical trials or even after the approval of a drug. One of the major limitations of 3D printed organs is providing nutrition to the printed cells. Because 3D printed organoids are much smaller than their corresponding organs (from the width of a hair to five millimeters), they are easier both to print correctly and to keep alive once they are printed. Importantly, organoids are not the same thing as organs. However, they mimic in miniature the function of organs and can be used to assess the potential effects of different substances on the function of human cells, tissues and organs providing a safer, faster and less expensive way to test new medications.

### *Image 5: Uses of Organoids*

Image Credit: Modified from Tian, Cm., Yang, Mf., Xu, Hm. et al. Stem cell-derived intestinal organoids: a novel modality for IBD. *Cell Death Discov.* 9, 255 (2023). <https://doi.org/10.1038/s41420-023-01556-1> with permission from Creative Commons.



# Background Science (continued)

## Organ-on-a-chip

Seeing the need for improved simulations of human reactions to drugs that can be used before human testing, researchers at WFIRM are working on a project funded by the Defense Threat Reduction Agency of the U.S. Department of Defense.<sup>9</sup> The “**organ-on-a-chip**” project involves 3D printing organoids and growing them in **microfluidic chips**, which then can be exposed to various stimuli to see their potential effects on humans. These stimuli could be drugs, diseases or even known toxins like chemical warfare agents. The microfluidic chips have tiny chambers connected by microchannels with valves and sensors. The microchannels allow the introduction of nutrients and test materials, while the valves allow scientists to control the flow of materials within the chip, and the sensors allow assessment of the results.

## Body-on-a-chip

Because chemical agents and stimuli often affect multiple body systems, researchers connect the organoids with fluid channels that carry artificial blood. WFIRM researchers have developed a three-organoid “**body-on-a-chip**” system,<sup>10</sup> with a miniature heart, liver and lung linked on a chip that is only two inches long — that’s less than the width of a credit card! Sensors on the chip measure the temperature, oxygen levels and pH of the blood substitute. The three organs can be linked together so that the “blood” flows through them in different orders, forming a plug-and-play system that responds to a variety of interventions. The liver and heart were chosen because toxicity to these organs is both the first and second most common reason that drugs fail in clinical trials, respectively. After these organoids were constructed, a lung organoid was added because the lungs are the first organ exposed to airborne particles.

The WFIRM researchers validated the responses of each of the organoids to different stimuli to ensure that they reacted like human organs. For example, they introduced acetaminophen (known to cause liver damage at high doses) to the liver organoid. Some liver organoids got no acetaminophen, some received a low dose, some received a high dose, and some received a high dose along with a countermeasure to mitigate the toxic effects of acetaminophen on liver cells. The percentage of dead cells in organoids from each treatment was recorded. The lowest percentage of dead cells was found in the control (no acetaminophen added), but the organoid with a high dose of acetaminophen along with a countermeasure also did not have many dead cells compared to the two treatments that received acetaminophen without a countermeasure. This indicates that the organoid responded to the treatment like a human liver.

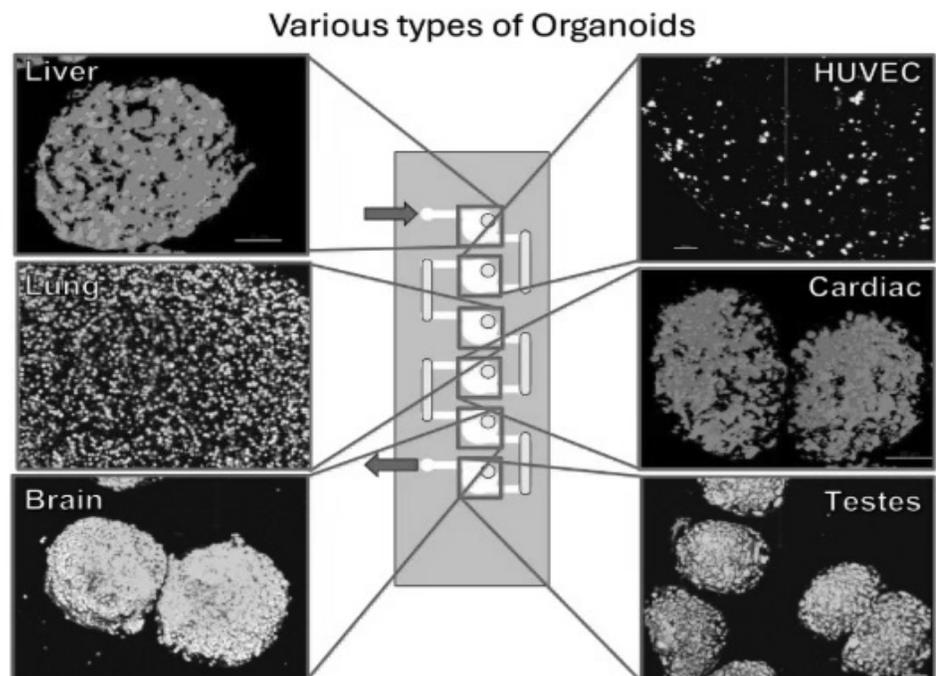
## Background Science (continued)

Similar validations were carried out on the heart and lung organoids.

After testing the functionality of the organoids individually, the WFIRM researchers used the three-organoid system to observe the effects of bleomycin, a drug used to treat some cancers that is known to cause lung inflammation and scarring. They expected to see that the heart and liver organoids were unaffected by the drug, but what happened surprised them. After exposure to bleomycin, the heart organoid tissue appeared less structured and eventually stopped beating. The researchers next exposed an isolated heart organoid to bleomycin and found it was undamaged. What was going on? Upon further investigation, the researchers discovered that exposure to bleomycin caused the lung organoid to release specific inflammatory factors that then affected the heart organoid. This result points to the importance of including multiple-organoid models in early testing of medications, as interactions between organs occur in human patients leading to unexpected toxicities.

### *Image 6: Example of a Body-on-a-Chip*

Image Credit: Reprinted from Skardal A, Shupe T, Atala A. Organoid-on-a-chip and body-on-a-chip systems for drug screening and disease modeling. *Drug Discov Today*. 2016 Sep;21(9):1399-1411. doi:10.1016/j.drudis.2016.07.003. Epub 2016 Jul 12. PMID: 27422270; PMCID: PMC9039871 with permission from WFIRM.



# Background Science (continued)

## Resources

- Because stem cells, organoids and bioprinting are rapidly developing areas of research, online information is likely to provide the most up-to-date information. Some resources include:  
Mayo Clinic Staff. (2024, March 23). *Stem cells: What they are and what they do*. Mayo Clinic. <https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/in%20depth/stem-cells/art-20048117>
  - This article covers what stem cells are, where they come from, ethical debates around stem cells, and how stem cells relate to cloning (10 min. read time).
- TED-Ed. (2013, September 15). *What are stem cells?* (Craig A. Kohn) [Video]. ed.ted.com. <https://ed.ted.com/lessons/what-are-stem-cells-craig-a-kohn>
  - This animated video briefly introduces stem cells, their potential in regenerative medicine, and different types of stem cells. Note that the narrator calls multipotent stem cells “tissue-specific stem cell” or “adult stem cells,” but they’re the same thing (4:11 watch time).
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Cell and gene therapy research*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/cell-and-gene-therapy-research>
  - This webpage gives an overview of major research projects being done at WFIRM, including those that are testing stem cell therapies as treatments for hemophilia, cystic fibrosis, diabetes and inflammatory bowel disease.
- International Society for Stem Cell Research. (2025, August 6). *Stem cell glossary: About stem cells*. ISSCR. <https://www.aboutstemcells.org/info/glossary>
  - A collection of important vocabulary words related to stem cells.
- Corró, C., Novellademunt, L., & Li, V. S. W. (2020). A brief history of organoids. *American Journal of Physiology. Cell Physiology*, 319(1), C151–C165. <https://doi.org/10.1152/ajpcell.00120.2020>
  - This article provides a summary of major events in the history of in vitro cell culture and a timeline for when specific organoids were first successfully grown (36 min. read time).

## Background Science (continued)

- HSCI. (2017, November 7). *Organoids: A new window into disease, development and discovery*. Harvard Stem Cell Institute; Harvard University. <https://www.hsci.harvard.edu/organoids>
  - This article describes the research projects being done using organoids at the Harvard Stem Cell Institute (9 min. read time).
- Jensen, K. B., & Little, M. H. (2023). Organoids are not organs: Sources of variation and misinformation in organoid biology. *Stem Cell Reports*, 18(6), 1255–1270. <https://doi.org/10.1016/j.stemcr.2023.05.009>
  - This article clarifies the difference between organoids derived from multipotent stem cells as well as those derived from pluripotent stem cells. The authors discuss challenges common to organoid research and the need for standardization in use of organoids (36 min. read time).
- BioTechniques. (2023, June 23). *What is organ-on-a-chip technology?* YouTube; YouTube. <https://www.youtube.com/watch?v=8tIHd5pYHOY>
  - This animated video briefly explains the fundamentals of organ-on-a-chip technology and multi-organoid systems and why they are important (3:08 watch time).
- ITN. (2021, February 11). *Organ-on-Chip and the 3R: A virtual lab tour*. YouTube; YouTube. <https://www.youtube.com/watch?v=5I0QVeFbS0c>
  - The video explains methods for making microfluidic chips, how cells are added, and how the organoids are monitored. It features several Ph.D. students discussing which organ system they are studying with this technology (6:14 watch time).
- UCTV. (2019, July 31). *Making Brain Organoids: A Primer*. YouTube; YouTube. <https://www.youtube.com/watch?si=YkGk0XF35Am25Hy1&v=lwReDWWMU0E&feature=youtu.be>
  - This video explains how brain organoids are grown and what they are used for in research (2:29 watch time).
- HSCI. (2017, November 7). *Organoids: A new window into disease, development and discovery*. Harvard Stem Cell Institute; Harvard University. <https://www.hsci.harvard.edu/organoids>
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  - This video explains how brain organoids are grown and what they are used for in research (2:29 watch time).
- Farhang Doost, N., & Srivastava, S. K. (2024). A comprehensive review of organ-on-a-chip technology and its applications. *Biosensors*, 14(5), 225. <https://doi.org/10.3390/bios14050225>
  - This review provides information on the design of the microfluidic chips used in organ-on-a-chip and body-on-a-chip systems, as well as considerations taken when designing chips for organoids mimicking specific organs (49 min. read time).
- StarTalk. (2025, May 10). *Groundbreaking Studies Recreate Human Brain Circuits in a Dish.* YouTube; YouTube. <https://www.youtube.com/watch?si=3I6R1kWmfbLRxf8J&v=HEBjpYCEiBo&feature=youtu.be>
  - This episode of Neil deGrasse Tyson’s science podcast *StarTalk* interviews neuroscientist Sergiu Pașca about his lab’s work researching assembloids — two or more organoids combined to mimic more complex tissues — in relation to the human brain and neurological disorders. (1:04:52 watch time).
- Skardal, A., Murphy, S. V., Devarasetty, M., Mead, I., Kang, H.-W., Seol, Y.-J., Shrike Zhang, Y., Shin, S.-R., Zhao, L., Aleman, J., Hall, A. R., Shupe, T. D., Kleensang, A., Dokmeci, M. R., Jin Lee, S., Jackson, J. D., Yoo,

## Background Science (continued)

J. J., Hartung, T., Khademhosseini, A., ... Atala, A. (2017). Multi-tissue interactions in an integrated three-tissue organ-on-a-chip platform. *Scientific Reports*, 7(1), 8837. <https://doi.org/10.1038/s41598-017-08879-x>

- This research paper covers the three-organoid body-on-a-chip interaction experiments that have been done at WFIRM thus far. It introduces the development of each of the three organoids and how they were validated before discussing the unexpected results from testing bleomycin on the system (50 min. read time).
- *Building a better body on a chip*. (n.d.). Wake Forest University School of Medicine. Retrieved November 22, 2025, from <https://school.wakehealth.edu/features/research/bodyonachip>
  - This article summarizes some of the results of the body-on-a-chip project at WFIRM (3 min. read time).
- Brandauer, K., Schweinitzer, S., Lorenz, A., Krauß, J., Schobesberger, S., Frauenlob, M., & Ertl, P. (2025). Advances of dual-organ and multi-organ systems for gut, lung, skin and liver models in absorption and metabolism studies. *Lab on a Chip*, 25(6), 1384–1403. <https://doi.org/10.1039/D4LC01011F>
  - This review discusses the variety of body-on-a-chip experiments that have been carried out in relation to drug testing (42 min. read time).
- Rogers, K. (2022, June 10). *When we'll be able to 3D-print organs and who will be able to afford them*. CNN. <https://www.cnn.com/2022/06/10/health/3d-printed-organs-bioprinting-life-itself-wellness-scen>
  - This article provides an overview of why bioprinting is exciting, how tissues are printed, and what progress needs to be made before printed organs become available (9 min. read time)
- TEDEd. (2019, October 17). *How to 3D print human tissue – Taneka Jones* [Video]. YouTube. [https://www.youtube.com/watch?v=uHbn7wLN\\_3k](https://www.youtube.com/watch?v=uHbn7wLN_3k)
  - This video provides a description of bioprinting and the associated challenges (5:11 watch time).

# Background Science (continued)

## Footnotes

- <sup>1</sup> *Eye disease: How could gene and cell therapy help?* | EuroGCT. (n.d.). Retrieved November 21, 2025, from <https://www.eurogct.org/eye-disease-how-could-gene-and-cell-therapy-help>
- <sup>2</sup> Takahashi, K., & Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell*, 126(4), 663–676. <https://doi.org/10.1016/j.cell.2006.07.024>
- <sup>3</sup> Takahashi, K., Tanabe, K., Ohnuki, M., Narita, M., Ichisaka, T., Tomoda, K., & Yamanaka, S. (2007). Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell*, 131(5), 861–872. <https://doi.org/10.1016/j.cell.2007.11.019>
- <sup>4</sup> Rasulov, M. F., Vasil'chenkov, A. V., Onishchenko, N. A., Krashennnikov, M. E., Kravchenko, V. I., Gorshenin, T. L., Pidtsan, R. E., & Potapov, I. V. (2005). First experience in the use of bone marrow mesenchymal stem cells for the treatment of a patient with deep skin burns. *Bulletin of Experimental Biology and Medicine*, 139(1), 141–144. <https://doi.org/10.1007/s10517-005-0232-3>
- <sup>5</sup> Ghieh, F., Jurjus, R., Ibrahim, A., Geagea, A. G., Daouk, H., El Baba, B., Chams, S., Matar, M., Zein, W., & Jurjus, A. (2015). The use of stem cells in burn wound healing: A review. *BioMed Research International*, 2015, 1–9. <https://doi.org/10.1155/2015/684084>
- <sup>6</sup> Abdul Kareem, N., Aijaz, A., & Jeschke, M. G. (2021). Stem cell therapy for burns: Story so far. *Biologics: Targets & Therapy*, 15, 379–397. <https://doi.org/10.2147/BTT.S259124>
- <sup>7</sup> Rodriguez, M., Trevisan, B., Ramamurthy, R. M., George, S. K., Diaz, J., Alexander, J., Meares, D., Schwahn, D. J., Quilici, D. R., Figueroa, J., Gautreaux, M., Farland, A., Atala, A., Doering, C. B., Spencer, H. T., Porada, C. D., & Almeida-Porada, G. (2023). Transplanting FVIII/ET3-secreting cells in fetal sheep increases FVIII levels long-term without inducing immunity or toxicity. *Nature Communications*, 14(1), 4206. <https://doi.org/10.1038/s41467-023-39986-1>
- <sup>8</sup> Davis, J. (2024, October 25). *Triad researchers developing chemical treatments with simulated organs*. WXII. <https://www.wxii12.com/article/wake-forest-researchers-using-technology-to-simulate-the-human-body/62709622>
- <sup>9</sup> *Wake Forest Institute for Regenerative Medicine (WFIRM) awarded up to \$48 million to utilize body-on-a-chip technologies to study fibrosis-inducing chemical injuries*. (2024, October 24). Atrium Health Wake Forest Baptist. <https://newsroom.wakehealth.edu/news-releases/2024/10/wfirm-awarded-millions-to-utilize-body-on-a-chip-technologies>
- <sup>10</sup> Skardal, A., Murphy, S. V., Devarasetty, M., Mead, I., Kang, H.-W., Seol, Y.-J., Shrike Zhang, Y., Shin, S.-R., Zhao, L., Aleman, J., Hall, A. R., Shupe, T. D., Kleensang, A., Dokmeci, M. R., Jin Lee, S., Jackson, J. D., Yoo, J. J., Hartung, T., Khademhosseini, A., ... Atala, A. (2017). Multi-tissue interactions in an integrated three-tissue organ-on-a-chip platform. *Scientific Reports*, 7(1), 8837. <https://doi.org/10.1038/s41598-017-08879-x>

# Ethical and Societal Issues in Regenerative Medicine

Regenerative medicine, like any other form of medicine and medical research, presents ethical and societal questions:

- Are the subjects of medical research, human research participants, patients or both?
- When is it ok to test a new, unproven treatment on a human research participant/patient?
- How should medical privacy be safeguarded?
- Does research on organoids created from human cells pose ethical concerns?
- Who should pay for expensive individualized treatments?

New technologies — from the act of writing and the use of the crossbow, to more recent innovations, including social media, genetic engineering and artificial intelligence — often raise societal and ethical concerns. In ancient Greece, Socrates worried that writing might weaken people’s ability to remember and that reading might weaken learning because students might read without instruction. In early medieval Europe, the Christian church worried that because the crossbow allowed peasants to strike knights from a distance, the social order would be upended by its use. Mechanical clocks, the printing press, the telescope, the cultivation of potatoes in Europe, and telephones all raised ethical and societal concerns when they were first developed,<sup>1</sup> yet are widely accepted technologies today. Other recent technologies, from social media to genetically modified food crops, are still contentious today. **Ethics** is the study of what is right and wrong and the principles by which decisions should be made. **Bioethics** or **biomedical ethics** is the study of ethical, social and legal issues that arise in biomedicine and biomedical research.<sup>2</sup> The study of bioethics can help health professionals and researchers make good decisions as they develop new medical treatments, techniques and technologies.

At first glance, medical research may seem to be an uncontroversial good for society; the benefits of developing new treatments and cures are widely thought to outweigh potential harm. However, medical research is complex and often involves unknown risks and competing interests. An experimental treatment may not only fail to work but may also be painful or make a patient’s condition worse. Collecting patients’ medical data creates risks to privacy. Moreover, the costs of research and treatment create ethical issues, as resources are never enough to meet everyone’s needs. In response to cruel, unethical and

# Ethical and Societal Issues in Regenerative Medicine (continued)

morally unacceptable research in the past, the U.S. and many other countries have developed institutions, laws, regulations and guidelines to guide medical research. These protections in turn are based on four basic principles and seven requirements of ethical decision making in the context of clinical research. The four basic principles are:

- **Beneficence** – doctors and researchers must act in the best interests of patients and research participants.
- **Non-maleficence** – doctors and researchers should not harm patients or research participants, should not cause pain, and should not give offense.
- **Autonomy** – doctors and researchers should respect the right of competent patients and research participants to make decisions about their own care. For this reason, researchers must fully inform research participants of potential harms and benefits, and patients and research participants must give consent to treatment and research.
- **Justice** – doctors and researchers should treat all patients and research participants fairly and equitably. This principle is often needed and becomes more complex when deciding how to allocate scarce resources.

On the basis of these four underlying principles, an influential paper, titled *What Makes Clinical Research Ethical?*, lays out the following seven requirements for ethical clinical research:<sup>3</sup>

1. The research must lead to improved health or enhanced knowledge.
2. The research must be scientifically valid and conducted in a methodologically rigorous manner.
3. Study sites and participants must be chosen fairly.
4. The benefits of the study should outweigh the risks.
5. The research should be reviewed by people independent of the project.
6. Research participants should be informed about the research and provide their voluntary consent.
7. Research participants and potential research participants should be respected. Respect includes protecting participants' privacy, allowing them to withdraw at any time, providing them with any new information learned during or from the study, and monitoring their well-being.

# Ethical and Societal Issues in Regenerative Medicine (continued)

These principles and requirements serve as the foundation for thinking about research ethics. They inform the design of research studies, including those in regenerative medicine, and the concerns of those reviewing studies for ethical issues. Consider the following questions — how do the ethical principles and guidelines for clinical research apply?

- Researchers are required to obtain research participants' informed consent to enroll them in clinical trials. How much information do researchers need to give to research participants about the potential harms and benefits of a clinical trial before enrollment? What information should they share with research participants as the trial progresses?
- In some cases, clinical trials are stopped before the planned endpoint. This may happen when the data indicates that the treatment being tested is clearly unsafe or not helping. But in some cases, the trial is ended early because the treatment being tested is helping more than expected such that it is unethical to withhold it from the control group. However, when a trial is ended early, fewer data are collected, the results are more likely to be due to chance, and important long-term outcomes may be missed. How should the parameters for stopping early be set?
- How should research participants' medical privacy and data be safeguarded? To what extent is it ethical to collect data for use in multiple future studies that have not yet been developed and so cannot yet be described in the consent form used at the time of data collection? How can the researcher respect the research participant's autonomy in this case?
- Is it ethical to do research on brain organoids? What about assembloids (more complex organoids) that scientists may create in the future? These miniature sections of organs, grown from human stem cells, may in the future have a type of nervous system and might be able to feel pain or have a form of consciousness but be unable to communicate that to researchers. Do researchers need to consider harm to human tissue functioning outside a human?
- What obligations do researchers have to continue making an unproven treatment available to research participants if a clinical trial is stopped before completion? Regardless of the trial's outcome, there must be a plan for all research participants who are patients to be helped to return to standard treatment, or to transition to the new treatment if it is proven safe and effective in the trial, after their participation is completed.

# Ethical and Societal Issues in Regenerative Medicine (continued)

- When should patients be allowed to try experimental treatments? Should companies be allowed to advertise and sell these treatments? Sometimes seriously ill patients have conditions for which there is no known safe and effective treatment. In these cases, they may want to try an investigational treatment but are not eligible to participate in the clinical trial for that unproven treatment. Right-to-try and expanded access laws at the federal and state level govern these decisions.
- How should we decide who gets a particular treatment if there are not enough resources to ensure that everyone who could benefit from the treatment gets it? Some treatments currently being developed must be individualized to the patient, making the treatments extremely expensive (millions of dollars per patient) — far beyond the resources available. Should our society invest in the development of these treatments?

In many cases, more than one principle may apply, and the most ethical course of action may not be evident. For example, beneficence and autonomy may come into conflict with justice when scarce or extremely expensive resources cannot be provided to all in need.

## Resources

- Emanuel, E. J., Wendler, D., & Grady, C. (2017). What makes clinical research ethical? In *Research Ethics* (pp. 229-239). Routledge. [https://www.nwabr.org/sites/default/files/pagefiles/What\\_Makes\\_Clinical\\_Research\\_Ethical.pdf](https://www.nwabr.org/sites/default/files/pagefiles/What_Makes_Clinical_Research_Ethical.pdf)
  - This article will be accessible to advanced high school students and provides an in-depth discussion of ethical guidelines for clinical research.
- Maynard, A. (2025). *Technology-driven moral panics*. [Website] <https://techlashed.org/>
  - This fun website explores how new ideas and technologies have been looked at with suspicion throughout time.
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (1979). *The Belmont report: Ethical principles and guidelines for the protection of human subjects of research*. U.S. Department of Health and Human Services. <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html>

# Ethical and Societal Issues in Regenerative Medicine (continued)

- This report was produced by a national commission responsible for developing guidelines for ethical research in the U.S.
- National Institute of Environmental Health Sciences. (2024). Bioethics. <https://www.niehs.nih.gov/research/resources/bioethics>
  - This website provides numerous resources and links for further understanding research ethics and integrity.

## Footnotes

<sup>1</sup>Maynard, A. (2025). Technology-driven moral panics. [Website]. <https://techlashed.org/>

<sup>2</sup>National Institute of Environmental Health Sciences. (2024). Bioethics. <https://www.niehs.nih.gov/research/resources/bioethics>

<sup>3</sup>Emanuel, E. J., Wendler, D., & Grady, C. (2017). What makes clinical research ethical?. In *Research Ethics* (pp. 229-239). Routledge.

# May I Conduct This Research?

**Learning  
Outcomes**

- Students will define bioethics.
- Students will discuss the four principles of bioethics (autonomy, beneficence, non-maleficence and justice).
- Student will be introduced to the seven requirements of clinical research.
- Students will discuss how to apply the four principles of bioethics to historical or current research scenarios.

**Key Vocabulary**

- Bioethics
- Autonomy
- Beneficence
- Non-maleficence
- Justice
- Informed consent
- Confidentiality

**Time Required**

- Approximately 15 minutes of preparation time
- Approximately 90 minutes of class time for activity and discussion over two days
- Approximately 45 minutes of class time for small group presentations (for approximately eight groups)

**Materials**

- Internet resources
- Student worksheet

# May I Conduct This Research?

(continued)

## **Background Information**

Regenerative medicine holds the possibility of replacing or regenerating cells, tissues and organs. But the process of deciding what research should or should not occur and how research should include and safeguard human subjects is an important focus of bioethics. Ethics is the study of moral principles and how to make decisions about what is right and wrong. Bioethics examines ethical issues related to biology, medicine and the environment. It includes the study of ethical questions related to medicine and medical research, including regenerative medicine. Bioethics, like science, has developed over time. Bioethics considers questions such as how genetic information should be used, how research participants' consent for research and treatment should be obtained, and how we design systems for allocating scarce medical resources. Four core principles: autonomy, beneficence, non-maleficence and justice are used to inform analysis of bioethical decisions. Teachers will choose between students looking at historical events or current research and determine how the four principles of bioethics were/were not or should be applied. A curated list of resources that teachers and students may use is provided in the lesson.

## **Teaching Notes**

This activity introduces students to bioethics through examination of historical events or current research. The teacher will introduce bioethics and associated principles. Students will define each of the bioethical principles and develop a visual to explain them. Students will work in small groups to review a specific case and discuss how the four principles were applied or should have been applied to the case. Students will be evaluated based on the group's discussion of application of the four principles to the chosen case.

## **Safety**

Students should follow school/district internet access guidelines to ensure safe browsing. Establish rules for discussion to ensure all students have an opportunity to participate and share their opinions and ideas in productive manner.

## **Procedure**

Ask students to define autonomy, beneficence, non-maleficence and justice based on their current understanding.

Depending on the maturity and experience of the students discussing controversial topics, the teacher may lead a whole class discuss of the following resources or allow small groups of students to review the resources together.

# May I Conduct This Research?

(continued)

Use these resources for students to refine their definitions of the four principles:

- Print resource: Varkey, B. (2020). *Principles of clinical ethics and their application to practice. Medical Principles and Practice, 30(1)*, 17–28. <https://doi.org/10.1159/000509119>
  - This article provides definitions for each of the four bioethical principles and discusses when these principles conflict with each other. This introduction is followed by six case studies that each concern one or more bioethical principles. Students could read the definitions of the four principles and then discuss one or more of the case studies in small groups. (approximately 35 min. read time)
- Video resource: Columbia SPS. (2018, October 31). *CUHK Ethical Principles* [Video]. YouTube.
  - This narrated video defines the four bioethical principles and provides examples of relevant potential questions that researchers and medical professionals would ask with regards to bioethics. The video emphasizes that while the principles themselves are simple, following all of them at the same time can be complicated, and the principles can sometimes seem to conflict with one another. (3:12 watch time)

Lead a whole class discussion on how informed consent and confidentiality relate to the principle of autonomy, the right of an individual to make their own decisions and control their own lives. Informed consent requires that a researcher explain to the individual the purpose, process, risks and benefits of the research, while confidentiality is the principle that an individual has the right for their decision and information to be kept private. The teacher may also choose to introduce the seven requirements of clinical research to students using the following resource: Emanuel, E. J., Wendler, D., & Grady, C. (2000). What makes clinical research ethical?. *JAMA, 283(20)*, 2701–2711. <https://doi.org/10.1001/jama.283.20.2701>.

After discussing the four principles as a large group and agreeing to definitions, allow each student to create a visual to explain the four principles of bioethics (see the student worksheet).

# May I Conduct This Research?

(continued)

Divide the students into small groups and ask them to serve as an ethics review board. Each group will research a specific historical/current case (see *Resources* for suggested ideas) and determine how each bioethical principle was applied in the case or how it should have been applied. Students then will present their findings to the whole class.

## Assessment

Students should complete the *May I Conduct This Research?* handout. The student work should be evaluated individually and as a small group. (A suggested rubric is provided at the end of this lesson plan.) Rubrics help students understand what is expected of them. They should be shared with students in advance and may be developed with students. Teachers may adjust this rubric to fit their grading system and to emphasize different aspects of the project as appropriate for their curriculum.

## Extension

This activity may be extended by asking students to review current regenerative medicine research articles. Students may identify how researchers followed the four principles of bioethics in their research. The podcast *playing god?* by the Johns Hopkins Berman Institute of Bioethics (<https://podcasts.apple.com/us/podcast/playing-god/id1706337131>) provides some examples of current bioethically relevant cases in medicine

## Resources

Because regenerative science is an ever-evolving area of research, online information concerning the case studies and application of bioethics is likely to provide the most up-to-date information. Some resources include:

- Presidential Commission for the Study of Bioethical Issues. (n.d.). *Deliberative scenarios*. U.S. Department of Health & Human Services. <https://bioethicsarchive.georgetown.edu/pcsbi/node/5707.html>
  - This webpage is a collection of bioethical scenarios designed for the high school classroom and provides five detailed scenarios for students to deliberate and role-play as different stakeholders. A teacher's guide is included for each scenario.

If a teacher would like students to choose from a curated list of historical events, use the Bioethics Timeline:

# May I Conduct This Research?

(continued)

The Hastings Center Bioethics Timeline Committee. (n.d.). *Bioethics Timeline*. The Hastings Center. <https://www.thehastingscenter.org/bioethics-timeline/>

If a teacher would like students to choose from a smaller selection of historical events with curated resources, use the cases below:

Public Health Service’s Tuskegee Study:

- Centers for Disease Control and Prevention. (2024, September 4). *About the Untreated Syphilis Study at Tuskegee*. CDC. <https://www.cdc.gov/tuskegee/about/index.html>
  - This website provides an overview of the Public Health Service’s Tuskegee Study (4 min. read time). It also includes two embedded videos: reflections of family members of study participants (51:25 watch time) and 50<sup>th</sup> anniversary remembrance ceremony (2:36:49 watch time).
- Black History in Two Minutes or So. (2020, February 7). *The Tuskegee Study: Black History in Two Minutes* [Video]. YouTube.
  - This video focuses on the reasons the Tuskegee study was unethical. (3:02 watch time)
- CrashCourse. (2018, April 18). *Henrietta Lacks, the Tuskegee Experiment, and ethical data collection: Crash Course Statistics #12* [Video]. YouTube.
  - This video provides brief information on the Tuskegee Study and several other instances of unethical data collection. (11:24 watch time; 3:14-4:05: Tuskegee Study introduced)

“God Committee”: the story of a group of citizens tasked with deciding which patients could receive dialysis treatments in Seattle, Washington, during the early 1960s.

- Alexander, S. (1962, November 9). *They decide who lives, who dies: Medical miracle puts a moral burden on a small committee*. *LIFE Magazine*, 53(19), pages 102–125.
  - This is the Google Book archive of Life Magazine November 9, 1962. The text of the article is reposted without images on the Nephrology Journal Club website. (Alexander, S. (1962, November 9). *They decide who lives, who dies* [Repost]. *Nephrology Journal Club*. <https://www.nephjc.com/news/godpanel>)

# May I Conduct This Research?

(continued)

- Lu, S. (2020, May 27). *God panels, then and now*. *Proto Magazine*. Massachusetts General Hospital. <https://protomag.com/policy/god-panels-then-and-now/>
  - This website gives an overview of the Seattle “God Committee” and ties it into modern bioethical dilemmas of medical device shortages (7 min. read time) <https://protomag.com/policy/god-panels-then-and-now/>

Gene Therapy for SMA patients:

- NBC 5 DallasFort Worth. (2022, May 15). *Texas family fights to access a \$2.1 million treatment for baby* [News story]. NBC 5 Responds. <https://www.nbcdfw.com/news/nbc-5-responds/texas-family-fights-to-access-2-1-million-treatment-for-baby/2966684/>
  - This website introduces a family and their successful attempt to gain insurance coverage for their baby to receive Zolgensma, an extremely expensive gene therapy drug that halts the progression of SMA. (6 min. read time). It also includes a video summarizing the story (6:29 watch time)
- Schneider, L. (2023, April 13). *Providing hope for infants with spinal muscular atrophy*. UT Health Austin. <https://uthealthaustin.org/blog/providing-hope-for-infants-with-spinal-muscular-atrophy>
  - The video provides a brief summary by UT Health Austin, one of the first clinics to offer Zolgensma, of what SMA is, how it is diagnosed, and how Zolgensma works. (5 min. read time)

If a teacher would like students to choose from a current research or medical events, search news websites such as the following:

- LiveScience. (n.d.). *LiveScience*. <https://www.livescience.com/>
- RegMedNet. (n.d.). *RegMedNet*. <https://www.regmednet.com/>

# May I Conduct This Research?

(continued)

## Rubric for May I Conduct This Research? Assignment

Category/ Points	4	3	2	1
Notes and sources	Student took notes for each section and correctly cites sources of all information.	Student took notes for most sections (four or more) and shows sources of most information	Student took notes for at least two sections and shows sources for some information.	Student found little information or does not show any sources.
Group Discussion Content	Shows a full understanding of the four principles.	Shows a good understanding of the four principles.	Shows partial understanding of the four principles.	Does not seem to understand the four principles very well.
Accuracy (of both written notes and oral presentation)	Student uses appropriate sources. Material accurate based on available sources.	Presents accurate material 90% to 95% of the time.	Presents accurate material 75% to 89% of the time.	Hard to tell if the student knew the material.
Comprehension	Student is able to accurately articulate how ethical principles apply to a scenario.	Student is mostly able to accurately articulate how ethical principles apply to a scenario.	Student is partly able to accurately articulate how ethical principles apply to a scenario.	Student is mostly unable to articulate how ethical principles apply to a scenario.

# May I Conduct This Research? — Student Worksheet

## Bioethics and the Four Principles

Before looking at how bioethics have developed over time, define bioethics and the four principles. Create a visual to explain how the four principles work together to protect research participants and patients. Use the resources below to assist your research.

- Varkey B. (2021). Principles of Clinical Ethics and Their Application to Practice. *Medical principles and practice: international journal of the Kuwait University, Health Science Centre*, 30(1), 17–28. <https://doi.org/10.1159/000509119> <https://pubmed.ncbi.nlm.nih.gov/articles/PMC7923912/>
- CUHK-Ethical Principles: <https://www.youtube.com/watch?v=xL-3VXs22hA>

Define the following terms:

Bioethics	
Autonomy	
Beneficence	
Non-maleficence	
Justice	

Visual to Explain Bioethical Principles:

# May I Conduct This Research? — Student Worksheet (continued)

## Apply the Four Principles

The job of your research team is to apply the four principles to your chosen case. Research your case and find the answers to the following questions. On another sheet of paper make a chart similar to this one but with enough space to record all your findings. Be sure to record the sources of your information

**Case:** \_\_\_\_\_

Questions	Notes	Information Source
Background (What, when, where, who, why, how) of event		
Was autonomy observed? How or how should it have been used?		
Was beneficence observed? How or how should it have been used?		
Was non-maleficence observed? How or how should it have been used?		
Was justice observed? How or how should it have been used?		

# Discover the Scaffolding of Tissue

*Plant tissue decellularization procedure adapted from Adamski, M., Fontana, G., Gershlak, J.R., Gaudette, G.R., Le, H.D., Murphy, W.L. Two Methods for Decellularization of Plant Tissues for Tissue Engineering Applications. J. Vis. Exp. (135), e57586, doi:10.3791/57586 (2018).*

*Animal tissue decellularization procedure adapted with permission from Evaluation of Decellularization Procedures for Porcine Arteries by Aubrey Smith of California Polytechnic State University.*

## Learning Outcomes

- Students will investigate scaffolding and decellularization of plant or animal tissues.
- Students will explain how an extracellular matrix can be used for scaffolding of engineered tissue.

## Key Vocabulary

- Scaffold
- Decellularization
- Extracellular matrix (ECM)
- Tissue engineering

# Discover the Scaffolding of Tissue (continued)

## Materials

Plant Protocol	Animal Protocol
<ul style="list-style-type: none"> <li>• Personal protective equipment: goggles, gloves, etc.</li> <li>• Magnetic stirrer/hot plate</li> <li>• Fume hood</li> <li>• Parsley or chive leaves</li> <li>• 5% (v/v) Bleach (NaClO) (Check the SDS Sheet for your bleach to make sure it is the proper strength).</li> <li>• Baking soda (NaHCO<sub>3</sub>)</li> <li>• Deionized water</li> <li>• Glass beakers</li> </ul>	<ul style="list-style-type: none"> <li>• Personal protective equipment: goggles, gloves, etc.</li> <li>• Magnetic stirrer</li> <li>• Fume hood</li> <li>• Animal tissue</li> <li>• 10% liquid SDS (sodium dodecyl sulfate solution)</li> <li>• Scissors</li> <li>• Sterile PBS (phosphate buffered saline solution)</li> <li>• Glass beakers</li> </ul>

## Time Required

Plant Protocol:	Animal Protocol
<ul style="list-style-type: none"> <li>• Approximately 60 minutes of preparation time</li> <li>• Approximately 90 minutes of class time for activity and discussion over two days</li> </ul>	<ul style="list-style-type: none"> <li>• Approximately 60 minutes of preparation time</li> <li>• Approximately 3 days of tissue washing</li> <li>• Approximately 90 minutes of class time for activity and discussion over two days</li> </ul>

## Background Information

The body is composed of organs, which are composed of tissues. Tissues are composed of living cells and an extracellular matrix. The extracellular matrix is made by the cells. It is found outside of and between the cells and provides support and structure. It consists of proteins, such as elastins and collagens, and proteoglycans, which are proteins attached to polysaccharides. The living cells can be washed away with detergent, leaving the extracellular matrix. The matrix then can be used as a scaffold for growing new tissues and organs. In this activity, students will remove the living cellular material from plant or animal tissue to reveal the scaffolding of the tissue.

# Discover the Scaffolding of Tissue (continued)

## Teaching Notes

Any organic tissue may be decellularized. Solid organs may take weeks to decellularize and require more specialized equipment to perfuse the tissues. For a classroom exercise, a thinner material such as a plant leaf or an animal vein will work better. For the plant procedure, consider using parsley leaves or hollow chive leaves. For the animal procedure, ask a butcher to prepare a vein from animal tissue. The animal tissue may be frozen or fresh.

The teacher may speed up the process by preparing the tissue samples for each student group. Provide time for each student group to observe the tissue before and after decellularization. These observations may be completed with a magnifying glass or microscope.

Tissues may be decellularized through a detergent-free or detergent approach. For this activity, a detergent-free approach is used for plant tissue and a detergent approach for animal tissue. Teachers are encouraged to review the original research articles explaining plant and animal tissue decellularization procedures, which are referenced at the beginning of this lesson. A video demonstrating both detergent-free and detergent approaches to the decellularization may be accessed via the National Library of Medicine version of the plant tissue decellularization article: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6101437/>.

**Detergent-free Approach:** For the plant tissue, the tissue must be washed with a bleach (sodium hypochlorite) solution and baking soda (sodium bicarbonate) solution. Household bleach and baking soda can be used to make the appropriate dilution. A 5.0% bleach solution, which is appropriate for decellularization, can be made from household bleach. Before the bleach solution is diluted, please refer to the manufacturer's Safety Data Sheet (SDS) for the initial concentration of the household bleach.

# Discover the Scaffolding of Tissue (continued)

The following equations may be used to calculate the desired volume of 5.0% bleach solution:

Example calculation for 5% (v/v) bleach solution:

Use the dilution formula:  $C_1V_1=C_2V_2$

$C_1$  = Initial bleach concentration (from SDS sheet) — Information from the sample SDS sheet notes 6%.

$V_1$  = Volume of initial bleach needed — This is what you need to find to create your dilution.

$C_2$  = 5% bleach concentration — This is the concentration that you need to make.

$V_2$  = Desired volume of 5% bleach solution

For the example calculation, the desired volume is 100mL.

$$C_1V_1=C_2V_2$$

$$V_1=(C_2V_2)/C_1$$

$$V_1=(5\%)(100\text{mL})/(6\%)$$

$$V_1=83\text{mL of the 6\% (v/v) bleach solution.}$$

Example calculation for 3% (w/v) sodium carbonate solution:

Use the equation for percent weight of solute by volume of solution equation:

$$\% \text{ (w/v) solution} = \text{weight of solute} / \text{volume of solution}$$

3% (w/v) sodium carbonate solution = 3 g of sodium carbonate per 100 mL of solution.

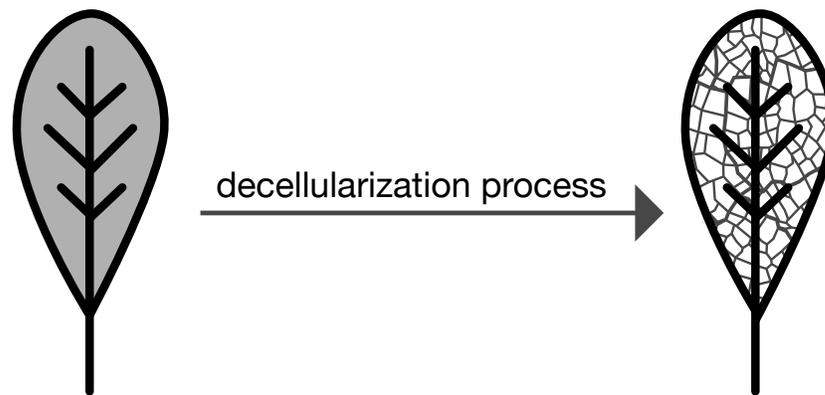
Suggestion for creating 100mL of bleach/baking soda solution:

1. Add approximately 80mL of water to beaker.
2. Add 3 g of baking soda. Stir and dissolve the baking soda in the solution.
3. Add 5 mL of bleach to the beaker. Stir the solution.
4. Add enough water (approximately 15 mL) to reach the final volume (100mL of solution.)

# Discover the Scaffolding of Tissue (continued)

The plant tissue must be stirred for at least 15-20 minutes in the bleach and sodium bicarbonate solution before washing. Plan ahead before implementing the activity to ensure the lab can be completed during the class period. After the plant tissue has been decellularized, the extracellular matrix should be washed multiple times with deionized water.

*Image 7: Illustration of Leaf Before and After Decellularization*



**Detergent Approach:** The tissue must be washed with a detergent solution made from SDS (sodium dodecyl sulfate). SDS can be purchased from a chemical supply company. A 0.075% SDS solution, which is appropriate for decellularization, can be made from 10% liquid SDS stock solution. SDS also can be found in several shampoos and toothpastes.

The following equations may be used to calculate the desired volume of 0.075% SDS solution:

Example calculation for 0.075% SDS solution from pure SDS solution:

Use the equation for percent volume of solute by volume of solution equation:

$$\% \text{ v/v solution} = \text{volume of solute} / \text{volume of solution}$$

$$\text{Solve for volume of solute need: volume of solute} = \text{volume of solution} * \% \text{ (v/v) solution (decimal form)}$$

$$\text{Volume of pure SDS solution needed} = 100\text{mL total volume of solution} * 0.00075$$

For 100mL of 0.075% (v/v) SDS solution, 0.075mL of pure SDS solution in 99.925mL of PBS water

# Discover the Scaffolding of Tissue (continued)

SDS Stock solution is often 10% (w/v) solution. Example calculation for 0.075% SDS solution from 10% SDS solution:

Use the dilution formula:  $C_1V_1=C_2V_2$

$C_1 = 10\%$  (w/v) SDS concentration — Concentration of SDS standard stock solution.

$V_1 =$  Volume of 10% (w/v) SDS solution — This is what you need to find to create your dilution.

$C_2 = 0.075\%$  (w/v) SDS solution — This is the concentration that you need to make.

$V_2 =$  Desired volume of 0.075% SDS solution

For the example calculation, the desired volume is 100mL.

$$C_1V_1=C_2V_2$$

$$V_1=(C_2V_2)/C_1$$

$$V_1=(0.075\%)(100\text{mL})/(10\%)$$

$$V_1=0.75\text{mL of the } 0.075\% \text{ (w/v) SDS solution.}$$

The animal tissue must be stirred for at least 20 hours in the SDS solution before washing. Plan ahead before implementing the activity to ensure the lab can be completed in back-to-back days. After the animal tissue has been decellularized, the extracellular matrix should be washed with PBS (phosphate buffered saline) solution. PBS solution may be purchased from a chemical supply company.

## Safety

Students should use proper laboratory techniques as required by the local school district. Students should wear personal protective equipment, including chemical splash goggles, gloves, closed-toe shoes and long pants/skirt. The decellularization process should take place in a fume hood. Proper care should be taken when handling raw animal tissue, and tissue and solutions should be properly disposed of.

# Discover the Scaffolding of Tissue (continued)

## Procedure- Introduction

Begin the discussion by asking students what the body is composed of. Allow the students to discuss the cells and ask to see if they think there is any structure supporting the cells. Explain that in this activity they will investigate the supportive materials that surround cells. Step-by-step instructions for each protocol are provided in the student worksheet. Below you will find the instructions for the animal tissue protocol.

## Plant Protocol

- Use appropriate personal protective equipment throughout the lab.
- Cut the leaves into small sections using scissors.
- Observe the tissue and use a magnifying glass to make careful observations.
- Describe the look and feel of the tissue.
- Under the fume hood, have students place their tissue pieces in a labeled beaker of 5% (v/v) bleach solution and 3% (w/v) sodium bicarbonate solution. All tissue pieces may be placed in the same beaker.
- Place the beaker on the mixer or stir for 10-15 minutes.
- Pour the solution down the drain.

Teachers: Give each group a piece of decellularized tissue and allow the students to rinse the material five times for a total of 10 minutes with deionized water.

- Using goggles and gloves, describe the look and feel of the material. Use a magnifying glass to make careful observations. Observe the remaining material. All that should remain is the extracellular matrix.

## Animal Protocol

- Use appropriate personal protective equipment throughout the lab.
- Remove animal tissue from the freezer and defrost the tissue in a warm water bath. (If fresh tissue is used, skip this step.)
- Cut the tissue into 4 cm to 5 cm sections using scissors or a razor blade.
- Using goggles and gloves, describe the look and feel of the material. Use a magnifying glass to make careful observations. Describe the look and feel of the tissue.

Teachers: Have students place under the fume hood their animal tissue pieces in a labeled beaker of 0.075% SDS solution. All tissue pieces may be placed in the same beaker.

- Place the beaker on the mixer and stir for at least 20 hours.
- Pour the SDS solution down the drain.

# Discover the Scaffolding of Tissue (continued)

Teachers: Give each group a piece of decellularized tissue and allow the students to rinse the material five times for 10 minutes with sterile PBS.

- Using goggles and gloves, describe the look and feel of the material. Use a magnifying glass to make careful observations. All that should remain is the extracellular matrix.

## **Assessment**

Students should complete the *Discover the Scaffolding of Tissue* handout. Students should work together to create a poster explaining how scaffolding is the basis for tissue and organ engineering.

## ***Extension***

The activity may be extended by allowing students to figure out the most effective protocol. Students may try different types of detergent or compare forms of tissue, such as frozen, defrosted or fresh. Students also may test the plant procedure using other tissue, such as chives and green onion leaves.

# Discover the Scaffolding of Tissue — Student Protocol

Engineered tissues and organs need material on which to grow. The base structure for animal tissues and organs is called the extracellular matrix. It functions as a supportive structure, or scaffold, for tissue growth and repair. It normally is created by an organism's own cells. However, doctors have learned to use extracellular matrix from pig intestines to help repair human injuries and scientists are experimenting with creating artificial scaffolds in the laboratory. New cells may be placed on the scaffold to grow replacement tissues. In this activity, you will investigate the scaffolding of tissue.

<b>Plant Tissue (Detergent-free Approach)</b>	<b>Animal Tissue (Detergent Approach)</b>
<ol style="list-style-type: none"> <li>1. Use appropriate personal protective equipment throughout the lab.</li> <li>2. Cut parsley leaf and add to the beaker.</li> <li>3. Observe the tissue. Using goggles and gloves, describe the look and feel of the tissue. Use a magnifying glass to make careful observations.</li> <li>4. In a fume hood, cover the cut parsley leaf with the warm (60-70° C) NaClO/NaHCO<sub>3</sub> solution provided by your instructor. (If available, place the beaker on the mixer and stir for 10-15 minutes.)</li> <li>5. Observe the leaf and describe changes in the leaf during step four.</li> <li>6. Rinse the decellularized material in deionized water five times for 10 minutes.</li> <li>7. Observe the decellularized material. Using goggles and gloves, describe the look and feel of the material. Use a magnifying glass to make careful observations.</li> </ol>	<ol style="list-style-type: none"> <li>1. Use appropriate personal protective equipment throughout the lab.</li> <li>2. Remove tissue from the freezer and defrost the tissue in a warm water bath. (If fresh tissue is used, skip to step 3.)</li> <li>3. Cut the tissue into 4 cm to 5 cm sections using scissors.</li> <li>4. Observe the tissue. Using goggles and gloves, describe the look and feel of the tissue. Use a magnifying glass to make careful observations.</li> <li>5. Under a fume hood, place the tissue in a beaker of 0.75% SDS solution (detergent). Place the beaker on the mixer and stir for at least 20 hours.</li> <li>6. Observe the tissue. Using goggles and gloves, describe the look and feel of the tissue. Use a magnifying glass to make careful observations.</li> <li>7. Pour the SDS solution down the drain.</li> <li>8. Rinse the decellularized material five times for 10 minutes with sterile PBS.</li> <li>9. Observe the decellularized material. Using goggles and gloves, describe the look and feel of the material. Use a magnifying glass to make careful observations.</li> </ol>

# Discover the Scaffolding of Tissue — Student Protocol (continued)

## Observations

Original Tissue	Decellularized Material

## Discussion Questions

1. What is decellularization?

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2. What is the extracellular matrix? What is it composed of?

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3. What features of the original tissue can be seen in the matrix? How can this matrix be used for regenerative medicine?

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# Discover the Scaffolding of Tissue — Student Protocol (continued)

4. What other types of materials could be used as scaffolding for tissue engineering? What characteristics of the material would allow it to be used as scaffolding?

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# Building Better Tissue

*Procedure adapted with permission from:*

Harper, A., & Nickels, K. (2008). *Alginate worms: Teacher worksheet*. Queensland University of Technology. [https://cms.qut.edu.au/\\_\\_data/assets/pdf\\_file/0010/23995/Alginate\\_worms\\_teacher.pdf](https://cms.qut.edu.au/__data/assets/pdf_file/0010/23995/Alginate_worms_teacher.pdf)

## Learning Outcomes

- Students will define scaffolding.
- Students will create simple structures, such as a sphere or a worm, with sodium alginate and a calcium water bath.
- Students will demonstrate the connection between scaffolding and the sodium alginate experiment by creating a poster to explain tissue and organ engineering.

## Key Vocabulary

- Scaffold
- Bioprinting

## Time Required

- Approximately 15 minutes of teacher prep time
- Approximately 90 minutes of class time for lab and discussion

## Materials

For Demonstration	For 15 Lab Sets
25mL Gaviscon® (over-the-counter heartburn medication)	375mL Gaviscon® (over-the-counter heartburn medication)
100mL 1% w/v calcium chloride solution	1.5L 1% w/v calcium chloride solution
75mL saturated sodium chloride solution	1.125L saturated sodium chloride solution
2 containers or beakers	15 containers or beakers
1 plastic syringe	15 plastic syringes

## Background Information

Perhaps you have seen scaffolding surrounding a building. This kind of scaffolding is a temporary support for people and supplies to build and remodel the building. Once the building is complete, the scaffolding is removed. In regenerative medicine, tissue and organs can be engineered and built, then placed in the body. However, the tissue and organs need support to grow. In animals this support is provided naturally by the extracellular matrix, which is made by the cells themselves. Scientists at the Wake Forest Institute for Regenerative Medicine are experimenting with various ways to provide this supportive structure for replacement tissues and organs. One way is to use decellularized animal tissues. Another way is to create a scaffold with synthetic, biocompatible materials that will support new cell growth then gradually break down and be replaced by the extracellular matrix created by the patient's own cells.

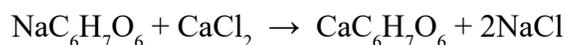
# Building Better Tissue (continued)

These scaffolds are being engineered to create a support structure for the cells. Scientists are experimenting to see which materials and textures work best. They also are working on adding beneficial chemicals such as growth factors and anti-inflammatory agents. In this activity, students will create a chemically engineered support to hold another chemical together in a threadlike structure.

This activity is a great way to introduce students to materials engineering. Scientists must investigate which materials have the right characteristics to support and direct the growth of the engineered tissue. The materials must be put through numerous trials. In this activity, the students will be materials engineers and will try to discover the best way to create structures to hold a given liquid.

## Teaching Notes

Alginates are used in medicine and as a thickener for foods. In the past, sodium alginate ( $\text{NaC}_6\text{H}_7\text{O}_6$ ) has been cross-linked with calcium ions to form spheres and threads in which food has been presented in unique ways, such as the fruit caviar you might find as a topping in a frozen yogurt shop. In this experiment, students will cross-link alginate with the calcium ions to form threads and spheres.



Gaviscon<sup>®</sup> is an over-the-counter antacid medicine found in many drug stores. One of its components is alginate. Calcium chloride may be purchased from a chemical supply company. It also is the main component of the moisture absorber DampRid<sup>®</sup>, which is available at building supply and drug stores. The calcium chloride solution can be created by making 100mL of 1% w/v (weight of solute/volume of solution) solution by adding 1 gram of calcium chloride (or DampRid<sup>®</sup>) to 100mL of water. Calcium ions will be formed by dissolving the calcium chloride in water.

In medicine, alginate is used in making scaffolds for tissue engineering and cell culture as well as in creating bandages. Alginate dressings aid in wound healing because they can slowly release medications and eventually be absorbed by the body.

## Safety

Students should use proper laboratory techniques. Even though this process is used in food manufacturing, the materials used in this lab should not be ingested. Students should wear safety goggles. Do not swallow these products.

# Building Better Tissue (continued)

*Image 8: Construction Scaffolding Provides Similar Support as Extracellular Matrix*

Image Credit: Image in the Public Domain from

<https://en.wiktionary.org/wiki/andaimc#/media/File:Cincinnati-scaffolding.jpg>.



## Procedure

Begin the discussion by showing the picture of scaffolding above. Ask students to name what is in front of the building and explain how it is used. Encourage the students to see that scaffolding provides support for building and for supplies.

- Explain that the activity will show how chemicals can be manipulated to create support like this scaffolding.
- Pour 100mL of calcium chloride solution into a labeled container.
- Pour 20mL Gaviscon® into different labeled container.
- Squirt a small amount of Gaviscon® into the calcium chloride solution. Do not to allow the calcium chloride solution to be sucked back into the sodium alginate pipette. If the calcium chloride goes into the pipette, it will become clogged with cross-linked ions.
- Encourage the students to add more Gaviscon® into the calcium chloride solution and explore the shapes that can be created. Allow the students to take their creations out of the calcium chloride solution and onto a paper plate for observation.

# **Building Better Tissue** (continued)

**Assessment**

Students may complete the *Building Better Tissue* student handout. Students should work together to create a poster explaining how scaffolding is the basis for tissue and organ engineering.

**Extension**

The activity may be extended by researching the types of materials used to create scaffolds and the advantages and disadvantages of each type. Students may use the resources found on selected websites, such as the Regenerative Medicine Foundation (<http://www.regenerativemedicinefoundation.org>).

# Building Better Tissue — Student Worksheet

Engineered tissues and organs need materials on which to grow. The base structure for tissues and organs is called a scaffold. In this activity, chemicals will be used to create a support for other materials.

## Procedure

1. Pour 100mL of calcium chloride solution into a labeled container.
2. Pour Gaviscon<sup>®</sup> into a different labeled container.
3. Squirt Gaviscon<sup>®</sup> into the calcium chloride solution. Be careful — do not allow the calcium chloride to be sucked into the pipette. Observe.
4. Record and draw what happened.

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# Building Better Tissue — Student Worksheet (continued)

5. Create as many different shapes as you can. What other shapes can you create?

6. Take the shapes out of the calcium chloride solution. How do the shapes act outside the solution?

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# Building Better Tissue — Student Worksheet (continued)

## Discussion Questions

1. What is scaffolding?

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2. How could the different shapes created in this activity help in organ engineering?

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3. What characteristics should scaffolding used in regenerative medicine have?

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# Stem Cells Are All the Same ... Aren't They?

## Learning Outcomes

- Students will define a stem cell.
- Students will research information on different types of stem cells, such as multipotent stem cells and pluripotent stem cells.
- Students will create and present a commercial for the assigned type of stem cell.
- Students will analyze the advantages and disadvantages of the different types of stem cells.

## Key Vocabulary

### For All Classes:

- Stem cell
- Embryonic stem cell
- Totipotent stem cell
- Pluripotent stem cell
- Multipotent stem cell
- Hematopoietic stem cell

### For AP Classes:

- Induced pluripotent stem cell
- Mesenchymal stem cell
- Neural stem cell (NSC)

## Time Required

- Approximately 90 minutes to research stem cells (may be done outside of class)
- Approximately 60 minutes to create stem cell public service announcement (may be done outside of class)
- Approximately 90 minutes to present public service announcements and conduct gallery walk (for class of 30 students)

## Materials

- Computers with Internet access and print materials for research
- Rubric

## Background Information

Regenerative medicine holds the possibility of using stem cells to engineer and grow tissues and organs. Stem cells have been politically controversial, and the media often neglect to discuss what stem cells really are, how they are being used in research and treatments, the many different kinds of stem cells, and recent advances in stem cell research that may reduce or eliminate the need for controversial human embryonic stem cells (hESCs).

# Stem Cells Are All the Same ... Aren't They? (continued)

Stem cells can be used as unique building blocks in bioengineering and in growing tissues and organs. This activity will provide students opportunities to define stem cells and research their characteristics.

## Teaching Notes

This activity asks students to use the internet to research what stem cells are and the different types of stem cells. The vocabulary list has suggestions for all classes to research and additional terms for AP classes. The students will research the characteristics, and the advantages and disadvantages of different stem cells. To make the most effective use of student research time, suggested resources have been provided. Depending on student access to the internet, you may choose whether to have students do this research in or out of class. After gathering and synthesizing information, the students will create a public service announcement to share their findings with other students. The public service announcements may be presented as skits for the class or as video files. The discussion of stem cells will culminate with a gallery walk that synthesizes the information learned about stem cells.

Sharing the rubric at the end of this lesson plan helps students meet expectations.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing.

## Procedure

- Begin with warm-up questions: What is a stem cell? Where have you heard this phrase?
- Discuss answers and list them on the board.
- Explain to students that they will have the opportunity to define this term and research how different types of stem cells are used in different therapies.
- Explain that stem cells are the worker cells of regenerative medicine.
- The students will use the *Stem Cells Are All The Same...Aren't They?* handout to answer the question: What is a stem cell? They will use two or three resources to research this basic question and to find out what is different between adult and embryonic stem cells. (Sample resources are included in the student handout.)
- In order to move to the next section of this activity, each student will write a paragraph explaining what a stem cell is, which may be used as a formative assessment. Teacher may refer to the stem cell section, page Unit IV-4.22.

# Stem Cells Are All the Same ... Aren't They? (continued)

- After the students have completed their paragraph satisfactorily, place students in small groups and allow them to choose to research pluripotent or multipotent stem cells. (The teacher will need to make sure students are evenly divided between these topics. Sample resources are included in the student handout.) Their research will be presented to the rest of the class in a one- to two-minute public service announcement. The students will be required to explain how the specific stem cell is used and the advantages and disadvantages of its use.

## Discussion

### Helping Students Build Understanding and Make Connections

After students share their public service announcements, they will synthesize the information by completing a gallery walk. Place four (or more) posters on the wall with the following labels: *Pluripotent Advantages*, *Pluripotent Disadvantages*, *Multipotent Advantages*, *Multipotent Disadvantages*.

1. Divide the class into groups of no more than four students each. Students in each group will write down as many facts on the sheet as they can remember in three minutes.
2. After three minutes, the posters will be passed to the next group and the process repeated until all groups have written on each of the posters.
3. Place the posters on the wall and allow students to walk around the room silently and place two checks on each paper for the strongest point.
4. These posters will provide a visual representation of the research that can be posted in the class and referred to throughout this course.
5. To conclude the discussion, allow students to create a concept map showing the connections between the types of stem cells, such as the diagram on the next page.

## Assessment

Students should complete the *Stem Cells Are All The Same...Aren't They?* handout. Students should create a public service announcement. The public service announcement should be evaluated using a rubric. (A suggested version is provided at the end of this lesson plan.) Rubrics help students understand what is expected of them. They should be shared with students in advance and may be developed with students. Teachers may adjust this rubric to fit their grading system and to emphasize different aspects of the project as appropriate for their curriculum.

# Stem Cells Are All the Same ... Aren't They? (continued)

## Extension

This activity may be extended by asking students to research how stem cells may be used to combat chronic disease such as cancer.

## Resources

Current stem cell research:

- Wake Forest Institute for Regenerative Medicine. (n.d.). *Cell and gene therapy research*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/cell-and-gene-therapy-research>
  - This webpage gives an overview of major research projects being done at WFIRM, including those that are testing stem cell therapies as treatments for hemophilia, cystic fibrosis, diabetes and inflammatory bowel disease.
- National Institutes of Health. (n.d.). *Current research*. Stem Cell Information. <https://stemcells.nih.gov/NIH-Stem-Cell-Research>
  - Includes links to several different NIH-funded stem cell research labs and projects.
- Harvard Stem Cell Institute. (2025). *StemBook*. <http://www.stembook.org>
  - A database of studies, articles and protocols related to stem cell science.
- International Society for Stem Cell Research & Harvard Medical School. (2025). *Stem cell medicine: From scientific research to patient care* [Free online course]. Harvard Medical School. <https://learn.hms.harvard.edu/programs/stem-cell-medicine#Course-Fees>
  - This online course provides an overview of stem cell biology, clinical trials, unproven stem cell treatments and ethical debates around stem

Stem cell video resources:

- PBS. (2023, June 28). *Hope for healing – The power of stem cells* [Video]. PBS. <https://www.pbs.org/video/hope-for-healing-the-power-of-stem-cells-vozcrb/>
  - This video from PBS discusses the use of stem cells in medicine and introduces some of the patients whose lives are being positively impacted by clinical trial stem cell treatments (26:56 watch time).
    - Key moments: 3:17-regenerative medicine introduced, 4:07-introduction of Hunter with Duchenne muscular dystrophy, 9:12-stem cell treatment for DMD, 13:37-introduction of Bill Souza with a tongue injury, 14:55-stem cell treatment for tongue injury, 17:30-prenatal stem cell treatment for spina bifida,

# Stem Cells Are All the Same ... Aren't They? (continued)

20:53-introduction of Emily and Robbie, first patients for spina bifida surgery.

- EuroStemCell. (n.d.). *Video resources*. EuroStemCell. <https://www.eurostemcell.org/resource-type/video?page=0>
  - A collection of videos covering different topics in stem cell research (2-12 min. watch time).
- TED-Ed. (2013, September 15). *What are stem cells?* (Craig A. Kohn) [Video]. ed.ted.com. <https://ed.ted.com/lessons/what-are-stem-cells-craig-a-kohn>
  - This animated video briefly introduces stem cells, their potential in regenerative medicine, and different types of stem cells. Note that the narrator calls multipotent stem cells “tissue-specific stem cell” or “adult stem cells,” but they’re the same thing (4:11 watch time).

Stem cell teaching resources:

- University of Utah, Genetic Science Learning Center. (n.d.). *Stem cells*. Learn.Genetics. <https://learn.genetics.utah.edu/content/stemcells/>
  - A collection of videos and articles covering basic information about stem cells, how they are used, and the ethical debate around use of hESCs.
- American Museum of Natural History. (n.d.). *Differentiate! The stem cell card game*. AMNH. <https://www.amnh.org/explore/ology/genetics/differentiate-the-stem-cell-card-game>
  - Instructions and printable cards for a game where players race to grow three different types of cells while learning about totipotent, pluripotent and multipotent stem cells.

# Stem Cells Are All the Same ... Aren't They? (continued)

## Rubric for Stem Cells Are All the Same...Aren't They? Assignment

Category/ Points	4	3	2	1
Notes and sources	Student took notes for each section and shows sources of all information.	Student took notes for most sections (four or more) and shows sources of most.	Student took notes for at least two sections and shows sources for some information.	Student found little information or does not show any sources.
Public service announcement content	Shows a full understanding of the stem cell.	Shows a good understanding of the stem cell.	Shows partial understanding of the stem cell.	Does not seem to understand the stem cell very well.
Accuracy (of both written notes and oral presentation)	Student uses appropriate sources. Material accurate based on available sources.	Presents accurate material 90% to 95% of the time.	Presents accurate material 75% to 89% of the time.	Hard to tell if the student knew the material.
Comprehension	Student is able to accurately articulate the topic.	Student is able to accurately articulate most of the topic.	Student is able to accurately articulate part of the topic.	Student is unable to accurately articulate the topic.

# Stem Cells Are All the Same ... Aren't They? — Student Worksheet

## What is a Stem Cell?

Stem cells. This phrase is heard on the news. Politicians talk about them. But what are they?

Before delving deeper into the uses of different types of stem cells, define the phrase “stem cell.” Write a paragraph definition and provide an explanation of adult and embryonic stem cells. Use the resources below to assist your research.

- PBS. (2023, June 28). *Hope for healing – The power of stem cells* [Video]. PBS. <https://www.pbs.org/video/hope-for-healing-the-power-of-stem-cells-vozcrb/>
  - This video from PBS discusses the use of stem cells in medicine and introduces some of the patients whose lives are being positively impacted by clinical trial stem cell treatments (26:56 watch time).
  - Key moments: 3:17-regenerative medicine introduced, 4:07-introduction of Hunter with Duchenne muscular dystrophy, 9:12-stem cell treatment for DMD, 13:37-introduction of Bill Souza with a tongue injury, 14:55-stem cell treatment for tongue injury, 17:30-prenatal stem cell treatment for spina bifida, 20:53-introduction of Emily and Robbie, first patients for spina bifida surgery.
- National Institutes of Health. (n.d.). *Stem cell basics*. Stem Cell Information. <https://stemcells.nih.gov/info/basics/stc-basics>
  - This article covers why stem cells are important, how they are cultured in the lab, and how they are used in medicine (9 min. read time).
- Mayo Clinic Staff. (2024, March 23). *Stem cells: What they are and what they do*. Mayo Clinic. <https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/indepth/stem-cells/art-20048117>
  - This article covers what stem cells are, where they come from, ethical debates around stem cells, and how stem cells relate to cloning (10 min. read time).

## Create a Public Service Announcement

Your team has just been asked to produce a public service announcement explaining what a stem cell is and how a specific type of stem cell (pluripotent or multipotent) is used. Your job is to research the specific type of stem cell assigned. Find the answers to the following questions. On another sheet of

# Stem Cells Are All the Same ... Aren't They? — Student Worksheet (continued)

paper, make a chart similar to this one but with enough space to record all your findings. Be sure to record the sources of your information. Use the resources below to assist your research.

- MedlinePlus. (2025). *Stem cell summary*. U.S. National Library of Medicine. <https://medlineplus.gov/stemcells.html>
  - This webpage includes links to articles and videos about stem cells.
- EuroStemCell. (n.d.). *Video resources*. EuroStemCell. <https://www.eurostemcell.org/resource-type/video?page=0>
  - A collection of videos covering different topics in stem cell research (2-12 min. watch time).
- TED-Ed. (2013, September 15). *What are stem cells?* (Craig A. Kohn) [Video]. ed.ted.com. <https://ed.ted.com/lessons/what-are-stem-cells-craig-a-kohn>
  - This animated video briefly introduces stem cells, their potential in regenerative medicine, and different types of stem cells. Note that the narrator calls multipotent stem cells “tissue-specific stem cells” or “adult stem cells,” but they’re the same thing (4:11 watch time).
- Harvard Stem Cell Institute. (2025). *StemBook*. <http://www.stembook.org>
  - A database of studies, articles and protocols related to stem cell science.
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Cell and gene therapy research*. Wake Forest University School of Medicine. <https://school.wakehealth.edu/research/institutes-and-centers/wake-forest-institute-for-regenerative-medicine/research/cell-and-gene-therapy-research>
  - This webpage gives an overview of major research projects underway at WFIRM, including those that are testing stem cell therapies as treatments for hemophilia, cystic fibrosis, diabetes and inflammatory bowel disease.

# Stem Cells Are All the Same ... Aren't They? — Student Worksheet (continued)

## Stem cell classification:

	Notes	Source of Information
Definition		
Source		
Use		
Advantages		
Disadvantages		

# What Makes an Organoid an Organoid?

## Learning Outcomes

- Students will define tissue.
- Students will define organ.
- Students will define organoid.
- Students will compare and contrast organoids, tissues and organs.
- Students will investigate the production and uses of organoids in medical research.

## Key Vocabulary

- Tissue
- Organ
- Body system
- Organoid

## Time Required

- Approximately 15 minutes of preparation time
- Approximately 90 minutes of class time for activity

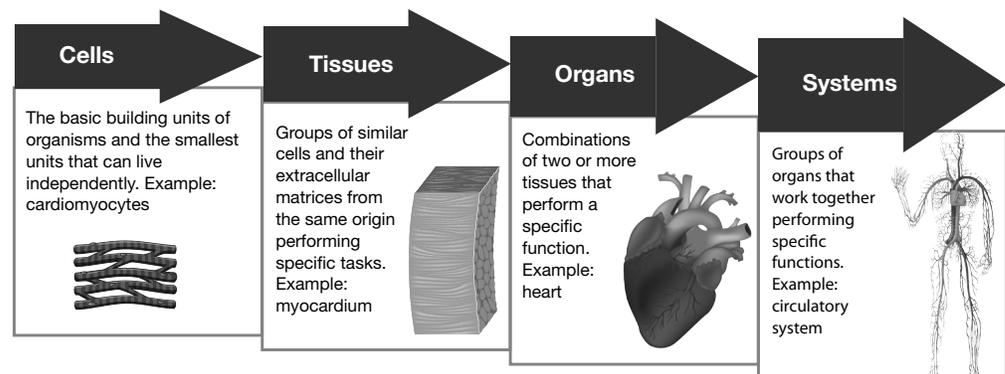
## Materials

- Internet resources
- Student worksheet

## Background Information

The human body is composed of a hierarchy of structures. The body is composed of systems. Systems are composed of organs and organs are composed of tissues. Tissues are composed of cells and their extracellular matrix. Historically, scientists have used animal models or human patients to study disease. Animal models, however, are imperfect and using patients as research subjects poses ethical challenges in terms of informed consent and risk-benefit.

*Image 9: Composition of the Body*



# What Makes an Organoid an Organoid? (continued)

With the discovery of induced pluripotent stem cells in 2006, scientists developed improved ways to produce small clusters of cells that resemble organs in terms of structure and function. These clusters of cells are called mini-organs or organoids. These lab grown 3D structures provide scientists the opportunity to model diseases, test drugs and possibly grow tissues that could be transplanted to repair damaged or diseased tissues in human patients. Organoids also have the potential to be used for personalized medicine. For instance, scientists may take cells from a diseased organ and grow organoids. The organoids can be used to test the effectiveness of drugs on the diseased organ.

## Teaching Notes

This activity introduces students to organoids by comparing organoids with tissues and organs. The teacher will review the definition of tissue and organ. Students will create a visual showing the connecting tissue, organ and body system's anatomical parts as tissues or organs. The teacher will then introduce the concept of organoids and discuss how they are grown. Using the student handout, students will work with a partner to review the resources in the *But What is an Organoid?* section. Students will be evaluated based on the group's *Organ or Organoid — What is the Difference* Venn diagram.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing. Establish rules for discussion to ensure all students have an opportunity to participate and share their opinions and ideas in a productive manner.

## Procedure

Ask students to work in pairs to complete the Tissue, Organ and System section of the student handout. Students will define the terms tissue, organ and system.

Lead a discussion of the definitions and solicit examples of each term from the students. For definitions and examples, refer to the image in the *Background Information* section of the lesson. Encourage students to refine their definitions based on class discussion.

Have students create a visual showing the connections between the three terms and provide two different examples for each term.

Provide an opportunity for students to share their visuals and identify the key parts of each term's definition.

# What Makes an Organoid an Organoid? (continued)

Explain how induced pluripotent stem cells have led to the development of organoids. Because pluripotent stem cells can differentiate into any cell type, researchers can direct them towards a specific differentiated cell type by applying a specific cocktail of growth factors and inhibitors. While organoids can be grown from multipotent stem cells, they are limited to whatever types of cell that multipotent stem cell can differentiate into. Because there is an ethical debate around the use of human embryonic stem cells, and because experiments using hESCs have been restricted in some jurisdictions, induced pluripotent stem cells provide an attractive option for researchers to grow any type of organoid they want starting with one cell type.

Allow the students to use student worksheet resources in *But What is an Organoid?* (Unit IV-4.85) to complete the provided worksheet.

Conduct a class discussion to clarify any misconceptions about organoids, their production and uses. Teacher may refer to the organoid section, page Unit IV-4.29.

After discussing organoids, assign students to create a Venn diagram showing the similarities and differences between organs and organoids.

## Assessment

Students should complete the handout: *What Makes an Organoid an Organoid?* Formative assessment may be conducted during the class discussion about tissues, organs and systems. Summative assessment may be conducted by reviewing the *Tissue, Organ and System* visual and the *Organ or Organoid — What is the Difference?* Venn diagram created by each pair of students.

# What Makes an Organoid an Organoid? (continued)

## Extension

This activity may be extended by asking students to learn about methods (e.g. bioprinting, a 3D culture environment) used in the production of organoids. Students may identify different ways researchers print tissue and organs. Students may research how organoids have been used in pre-clinical trials.

- TEDEd. (2019, October 17). *How to 3D print human tissue – Taneka Jones* [Video]. YouTube. [https://www.youtube.com/watch?v=uHbn7wLN\\_3k](https://www.youtube.com/watch?v=uHbn7wLN_3k)
  - This video provides a description of bioprinting and the associated challenges (5:11 watch time).
- CNET. (2023, April 30). *3Dprinting heart tissue with human stem cells* [Video]. YouTube. <https://www.youtube.com/watch?v=mMeOjwH4NVU>
  - This video provides a description of bioprinting process of heart tissue (3:59 watch time).

# What Makes an Organoid an Organoid? (continued)

## Resources

Because organoids are a new and developing methodology, online information is likely to provide the most up-to-date information. Some resources include:

- *Organoid technologies in research* [Video]. (2019, April 19). YouTube. <https://www.youtube.com/watch?v=2SG5ivm6jkw>
  - This video explains why organoids are useful in research and the challenges of using organoids in research (3:16 watch time).
- Tang, X.-Y., Wu, S., Wang, D., Chu, C., Hong, Y., Tao, M., Hu, H., Xu, M., Guo, X., & Liu, Y. (2022). Human organoids in basic research and clinical applications. *Signal Transduction and Targeted Therapy*, 7(1), 168. <https://doi.org/10.1038/s41392-022-01024-9>
  - This article summarizes the difference between organoids derived from multipotent and pluripotent stem cells, discusses how organoids are being used in research, and lays out challenges in this field (50 min. read time).
- *Making brain organoids: A primer* [Video]. (2019, July 31). UCTV / YouTube. <https://youtu.be/lwReDWWMU0E>
  - This video explains how brain organoids are grown and what they are used for in research (2:29 watch time).

## Resources for AP Biology and AP Anatomy and Physiology Classes:

- Jang, J., & Yang, S.-R. (2025). Bioprinted 3dimensional lung organoids for respiratory disease modeling and therapeutic applications. *Organoid*, 5, e8. <https://j-organoid.org/journal/view.php?number=80>
  - This review summarizes work done with lung organoids and specific challenges in doing research on them (21 min. read time).
- Park, J.-C., et al. (2024). Advancements in brain organoid models for neurodegenerative disease research. *Organoid*, 4, e12. <https://doi.org/10.51335/organoid.2024.4.e12>
  - This review discusses the use of brain organoids in studying neurodegeneration and ways their production could be improved (12 min. read time).

# What Makes an Organoid an Organoid? — Student Worksheet

## Tissue, Organ and System

*Define the following terms:*

Tissue:

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Organ:

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Body system:

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*Create a visual connecting tissues, organs and systems.* Choose a specific body system and provide two or more specific examples (each) of tissues and organs for this system. Create a visual showing how the tissues and organs are connected to form a system.

# What Makes an Organoid an Organoid? — Student Worksheet (continued)

## But What is an Organoid?

Use the resources below to research the answers to the questions below:

- *Organoid technologies in research* [Video]. (2019, April 19). YouTube. <https://www.youtube.com/watch?v=2SG5ivm6jkw>
  - This video explains why organoids are useful in research and the challenges in using organoids in research (3:16 watch time).
- BioTechniques. (2022, October 25). *An introduction to organoids* [Video]. YouTube. <https://www.youtube.com/watch?v=cED5yuc3UwY>
  - This video explains what organoids are and how they are grown (1:56 watch time).
- Barbuzano, J. (n.d.). *Organoids: A new window into disease, development and discovery*. Harvard Stem Cell Institute. <https://www.hsci.harvard.edu/organoids-a%20new%20window%20into%20disease%20development%20and%20discovery>
  - This article contains summaries of research projects at the Harvard Stem Cell Institute being done on organoids along with video interviews with the researchers leading these projects.
- Jensen, K. B., & Little, M. H. (2023). Organoids are not organs: Sources of variation and misinformation in organoid biology. *Stem Cell Reports*, 18(6), 1255–1270. <https://doi.org/10.1016/j.stemcr.2023.05.009>
  - This article clarifies the difference between organoids derived from multipotent stem cells as well as those derived from pluripotent stem cells. The authors discuss challenges common to organoid research and the need for standardization in use of organoids (36 min. read time). There also is an associated podcast *Organoids: Multi-Dimensional Standards for Three Dimensional Models* from The Stem Cell Report with Janet Rossant: <https://www.buzzsprout.com/1661578/episodes/13364832> .

# What Makes an Organoid an Organoid? — Student Worksheet (continued)

What is an organoid?

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How are organoids produced?

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How may organoids be used?

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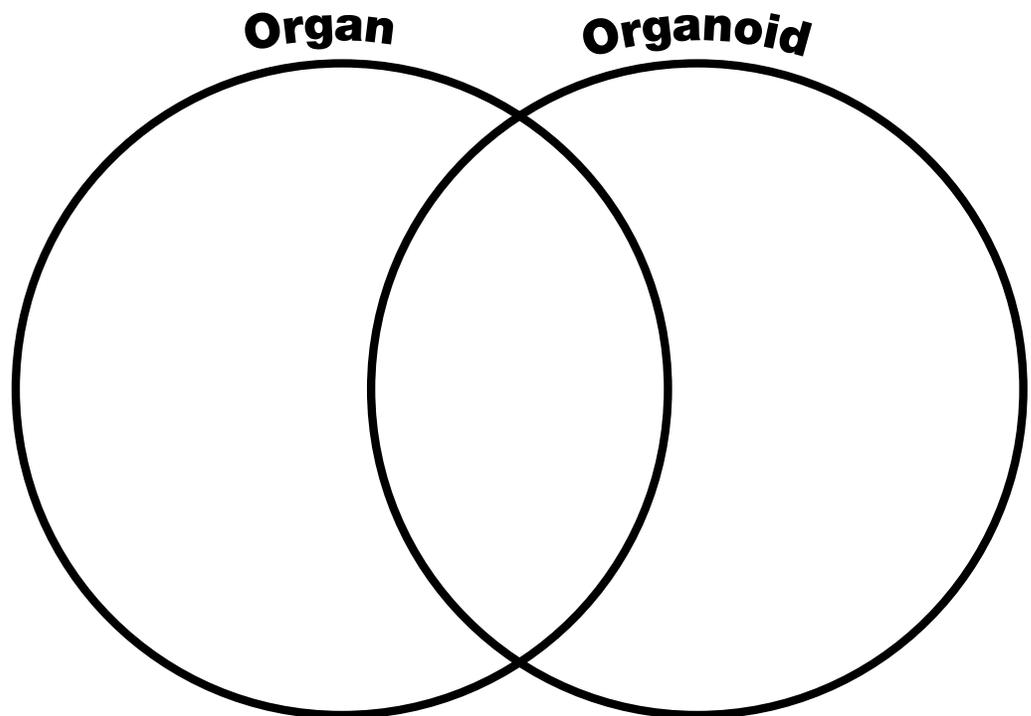
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# What Makes an Organoid an Organoid? — Student Worksheet (continued)

## Organ or Organoid — What is the difference?

Using a Venn diagram, provide three ideas that explain differences and similarities for organs and organoids.



# BOC for a Disease

## **Learning Outcomes**

- Students will identify the organs associated with the major systems of the human body.
- Students will define organ-on-a-chip (OOC) and body-on-a-chip (BOC).
- Students will hypothesize how to construct an organ-on-a-chip (OOC) or body-on-a-chip (BOC) to analyze a specific disease.

## **Key Vocabulary**

- Organoid
- Organ
- Body system
- Organ-on-a-chip (OOC)
- Body-on-a-chip (BOC)

## **Time Required**

- Approximately 15 minutes of preparation time
- Approximately 90 minutes of class time for activity and discussion over two days

## **Materials Background Information**

- Internet resources
- Student worksheet
- Optional: body system and organ cards (Cards need to be enlarged for printing)

When a scientist considers whether a medicine will work for a specific disease, they must also consider how the medicine will impact the rest of the body. Using organoids, scientists can test medicines using organ-on-a-chip (OOC) technology. OOC involves 3D printing of organoids and then exposing them to various medicine or stimuli to see their potential effect on human cells. Because the body is a complex group of systems composed of organs, scientists also have developed body-on-a-chip (BOC) technology to test how medicine or stimuli affect multiple organs and systems. BOCs connect organoids with fluid channels that carry artificial blood. Medicines can be entered into the BOC to see how the other organoids are impacted by the medicine or stimuli. On a small chip the size of a credit card, scientists have conducted research with organoid combinations such as heart, lung and liver to look at cardiopulmonary models or toxicity. (For more examples, see the research article *Advances of dual-organ and multi-organ systems for gut, lung, skin and liver models in absorption and metabolism studies* <https://pubs.rsc.org/en/content/articlehtml/2025/lc/d4lc01011f?utmom>).

# BOC for a Disease (continued)

## Teaching Notes

This activity directs students to review body systems with organ and system cards. Students will research and define organ-on-a-chip and body-on-a-chip. Working in small groups, students will research a disease, identify which organs should be included in a BOC for the disease and defend their choices. Students will create a poster/visual presentation to use in their presentation for the class. This activity may be adapted into an individual project.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing.

## Procedure

Divide the students into pairs and provide each pair with a set of organ and system cards (located at the end of the lesson). You may need to print the cards as a larger image size.

Using the body systems as header, ask the students to assign each organ to the proper system. Have pairs team up and defend their systems.

Check the systems by allowing groups to share their systems with the class.

**Table: Body Systems and Organs**

<b>Circulatory</b>	<b>Digestive</b>	<b>Endocrine</b>	<b>Integumentary</b>	<b>Lymphatic</b>
Heart Blood vessels	Mouth Pharynx Esophagus Stomach Small intestines Large intestines Anus Liver Gallbladder Pancreas	Pituitary gland Pineal gland Thyroid gland Parathyroid gland Adrenal gland Pancreas Ovaries Testes Thymus	Skin Hair Nails Sweat glands Sebaceous glands	Lymph nodes Spleen Thymus Tonsils Appendix Lymphatic vessels

## BOC for a Disease (continued)

Muscular/ Skeletal	Nervous	Reproductive	Respiratory	Urinary
Skeletal muscle Smooth muscle Cardiac muscle Bones	Brain Spinal cord Nerves	Ovaries Uterus Vagina Cervix Vulva Uterine tubes (Fallopian tubes) Testes Epididymis Vas deferens Seminal vesicles Prostate gland Bulbourethral glands (Cowper's glands) Penis Scrotum	Mouth Nose Pharynx Larynx Trachea Bronchi Lungs	Kidney Bladder Urethra Ureters

Review what an organoid is. (Organoids are explained in detail in the activity *What Makes an Organoid an Organoid?* Additional background material is available on page Unit IV-4.29.)

Introduce organ-on-a-chip and body-on-a-chip by watching as a class or in small groups one or more of the following videos:

- BioTechniques. (2023, June 23). *What is organ-on-a-chip technology?* [Video]. YouTube.
  - This animated video briefly explains the fundamentals of organ-on-a-chip technology and multi-organoid systems and why they are important (3:08 watch time).
- LLNL. (2015, May 19). *Creating a tiny human body on a chip* [Video]. YouTube.
  - This video introduces the iCHIP, a multiple-organoid system project at the Lawrence Livermore National Laboratory (3:40 watch time).
- After watching the video, explain that OOC/BOC interventions are constantly developing and that student groups will serve as research teams.

# **BOC for a Disease** (continued)

- Assign each group a disease to research. Scientists have conducted research on the following diseases using OOC and BOC at the time of printing this resource: Alzheimer's disease, Parkinson's disease, multiple sclerosis, stroke, epilepsy, heart failure, asthma, cystic fibrosis, chronic obstructive pulmonary disease, breast cancer, colorectal cancer, pancreatic cancer, diabetes, hepatitis B/C, inflammatory bowel disease, rheumatoid arthritis, Duchenne muscular dystrophy and polycystic kidney disease.
- Using the student handout as a guide, students should research their assigned disease, identify the associated organs and develop a defense of which organs should be included in a BOC.
- Small groups should design a final material or electronic presentation such as a poster. The presentation should include the disease, BOC and reason for organoid inclusion.
- Student groups should present their BOC to the class.

## **Assessment**

The BOC poster/visual guidelines may be evaluated using the rubric at the end of this lesson plan. Rubrics help students understand what is expected of them. They should be shared with students in advance and may be developed with students. Teachers may adjust this rubric to fit their grading system and to emphasize different aspects of the project as appropriate for their curriculum. Teachers should explain the citation style they expect students to use to cite sources.

## **Extension**

This activity may be extended by asking students to research if an OOC or BOC has been developed for a disease using research articles that may be found in PubMed, a database of the National Library of Medicine at the National Institutes of Health, or in Google Scholar.

**Resources**

## **BOC for a Disease** (continued)

- Organ-on-a-chip and Body-on-a-chip research is constantly advancing; therefore, it is essential for teachers to update their resources by reviewing the current research. Some options include:
- StarTalk. (2025, May 10). *Groundbreaking studies recreate human brain circuits in a dish* [Video]. YouTube.
  - This episode of Neil deGrasse Tyson’s science podcast *StarTalk* interviews neuroscientist Sergiu Pașca about his lab’s work researching assembloids — two or more organoids combined to mimic more complex tissues — in relation to the human brain and neurological disorders. (1:04:52 watch time).
- EUROoC International Training Network. (2021, February 11). *Organ-on-Chip and the 3R: A virtual lab tour* [Video]. YouTube.
  - The video explains methods for making microfluidic chips, how cells are added and how the organoids are monitored. It features several Ph.D. students discussing which organ system they are studying with this technology (6:14 watch time).
- Miller, J. (2013, September 23). ‘Body on a chip’ uses 3D printed organs to test vaccines. *BBC News*. <https://www.bbc.com/news/technology-24125678>
  - This article discusses how the body-on-a-chip project is being used to test responses to bioterrorism agents and medications (3 min. read time).
- Wake Forest Institute for Regenerative Medicine. (n.d.). *Building a better body on a chip*. Wake Health. <https://school.wakehealth.edu/features/research/bodyonachip>
  - This article summarizes some of the results of the body-on-a-chip project at WFIRM (3 min. read time).
- Brandauer, K., Schweinitzer, S., Lorenz, A., Krauß, J., Schobesberger, S., Frauenlob, M., & Ertl, P. (2025). *Advances of dual-organ and multi-organ systems for gut, lung, skin and liver models in absorption and metabolism studies*. *Lab on a Chip*, 25, 1384–1403. <https://doi.org/10.1039/D4LC01011F>
  - This review discusses the variety of body-on-a-chip experiments that have been carried out in relation to drug testing (42 min. read time).

# **BOC for a Disease** (continued)

## **System and Organ Cards –**

<b>Body Systems</b>			
Circulatory	Digestive	Endocrine	Integumentary
Lymphatic	Muscular	Nervous	Reproductive
Respiratory	Skeletal	Urinary	

# BOC for a Disease (continued)

Organs			
Heart	Blood vessels	Mouth	Pharynx
Esophagus	Stomach	Small intestines	Large intestines
Anus	Liver	Gallbladder	Pancreas
Pituitary gland	Pineal gland	Thyroid gland	Parathyroid gland
Adrenal gland	Pancreas	Ovaries	Testes
Testes	Thymus	Skin	Hair
Nails	Sweat glands	Sebaceous glands	Lymph nodes
Spleen	Thymus	Tonsils	Appendix
Lymphatic vessels	Skeletal muscle	Smooth muscle	Cardiac muscle
Brain	Spinal cord	Nerves	Ovaries
Uterus	Vagina	Cervix	Vulva
Uterine tubes (Fallopian tubes)	Testes	Epididymis	Vas deferens
Seminal vesicles	Prostate gland	Bulbourethral glands (Cowper's glands)	Penis
Scrotum	Nose	Pharynx	Larynx
Trachea	Bronchi	Lungs	Mouth
Ureters	Kidney	Bladder	Urethra
Bones			

# BOC for a Disease (continued)

## Rubric for BOC for a Disease Assignment

Category/ Points	4	3	2	1
Notes and sources	Student took notes for each section and shows sources of all information. Sources are cited correctly.	Student took notes for most sections (six or more) and provides citations for most information.	Student took notes for at least three sections and provides sources for some information.	Student found little information or does not show any sources. Cites none of the pictures used.
Disease research	Shows an advanced understanding of the disease including its causes and how it impacts different body organs and systems.	Shows a good understanding of the disease and how it impacts a body system.	Shows partial understanding of the disease and how it impacts various body parts.	Does not seem to understand what the disease is.
Poster/Visual	Creates a poster/visual presentation that explains the disease and provides a BOC diagram with explanations for why the organoids (organs) should be included in the BOC.	Creates a poster/visual presentation that explains the disease and provides a BOC diagram but does not explain why the organoids (organs) should be included in the BOC.	Creates a poster/visual presentation that explains the disease and lists the organoids (organs) that should be included in the BOC diagram.	Creates a poster/visual presentation that discusses disease and does not create a BOC to study the disease.
Presentation	Speaks clearly with correct pronunciation of terms. Maintains eye contact. Presents the information in a logical and interesting manner.	Speaks clearly with mostly correct pronunciation of terms. Maintains eye contact most of the time. Presents the information in a logical manner.	Occasionally speaks clearly with some correct pronunciation of terms. Maintains eye contact sometimes but reads most of the presentation. Difficult to follow presentation.	Does not speak clearly or pronounce terms. Lack of eye contact because the presentation is read. Unable to follow presentation.

# BOC for a Disease — Student Worksheet

As a research team, it is your responsibility to create a body-on-a chip for your assigned disease and share your results with other research teams at your institution. You will be researching the disease and the impact of the disease on human organs/systems. (Don't forget to list your sources.) After you have completed your background research, design the ideal BOC for research on your assigned disease and create a poster/visual presentation of your BOC. The visual should show and explain your design choices.

Question	Term	Description	Source
What disease are you studying?			
What system(s) or organs are impacted by the disease?			
Which organs would you include on a BOC? (Include at least two organs in your BOC.)	Organ 1:	Reason for inclusion:	
	Organ 2:	Reason for inclusion:	
	Organ 3:	Reason for inclusion:	

# Regenerative Medicine in Space

## Space, The Final Frontier ... For Stem Cells?

How could changing the gravitational force acting on objects contribute to research in regenerative medicine? As it turns out, doing regenerative medicine research in space isn't an idea straight out of science fiction — it's happening right now. Space provides a unique place for scientists to conduct experiments and manufacture products, which may provide new opportunities for regenerative medicine and economic development. Cells in general, and stem cells in particular, behave differently in space — helping scientists understand fundamental mechanisms and potentially providing an environment for developing cell therapies. While working in space has advantages, there also are many challenges that need to be considered to work in this unique environment.

The International Space Station (ISS) orbits the Earth at an altitude of roughly 400 kilometers, which falls into the zone known as **Low Earth Orbit (LEO)**.<sup>1</sup> LEO is typically defined as a flight path below 2,000 kilometers. However, there also is a lower boundary for LEO, called the Kármán Line. This imaginary line, 100 kilometers above Earth's surface, is approximately where Earth's atmosphere becomes too thin to support traditional aircraft. **Microgravity** is what an object experiences when the gravitational pull on it is significantly smaller than what we experience on Earth, and LEO provides this kind of environment. However, microgravity is not the same as zero-gravity. In fact, objects in LEO are still subject to about 90% of the force of gravity that we experience on Earth. Astronauts and objects onboard the ISS float around and appear to be weightless because they are all orbiting the Earth at such high speeds that everything is falling together in a state of constant **freefall** around the Earth. The microgravity environment that allows astronauts to float around the ISS isn't just for fun — it provides vital opportunities to conduct research that cannot be done in other environments. The weightless state changes the forces on materials and organisms causing changes in properties and affecting growth and behavior. Discoveries made in space are leading to new understanding and new techniques for the fields of bioengineering and medicine here on Earth.

A major goal of current stem cell research is to grow as many high-quality stem cells as possible without them differentiating. This allows the cells to be induced to differentiate into whatever cell type is needed once they are returned to Earth. Experiments with neural stem cells grown on the ISS found that they proliferated at a normal rate and did not differentiate after 39 days of growing without manipulation. When the cells were sent back to Earth, they were

# Regenerative Medicine in Space (continued)

cultured in a specific media designed to encourage them to differentiate into neurons. The cells became neurons, indicating that the microgravity environment did not affect the stem cells' viability or their potential to differentiate.<sup>2</sup> A project from Cedars-Sinai Medical Center studying whether induced pluripotent stem cells divide faster in space was launched to the ISS in August 2025.<sup>3</sup>

To take advantage of the microgravity environment, the ISS introduced the BioFabrication Facility in 2019. This unique micro-laboratory was designed with the goal of bioprinting in microgravity. Tissues printed in the BioFabrication Facility have maintained their architecture and cells have stayed viable.

Other projects are being developed in North Carolina. For example, WFIRM is currently collaborating with NASA on a project to grow functional liver tissue in space<sup>4</sup> as a bridge to transplantation. This work resulted from NASA's Vascular Tissue Challenge, issued in 2016. Successful submissions required that a piece of solid organ tissue remain metabolically active and survive outside the body for at least 30 days. WFIRM submitted two entries into the challenge, taking both first and second prize. Their liver tissue contained vascular channels — an impressive feat considering that a major limitation in growing functional internal organs is keeping the cells alive by providing them with nutrients. One of WFIRM's prize-winning tissue constructs (engineered tissue made by growing cells on an extracellular matrix) was launched to the ISS in May 2023 on the second private astronaut mission conducted by Axiom Space (Ax-2).<sup>5</sup> A follow-up mission was launched in August 2025.

When it returns to Earth, WFIRM researchers will study the effects of microgravity on cell characteristics, such as whether vascular cells correctly arrange themselves to line the blood vessels within the tissue. WFIRM also has partnered with Axiom Space to develop regenerative medicine technologies for use in microgravity.<sup>6</sup> These technologies will be used aboard Axiom Station, the first commercial space station and a successor to the ISS.

Microgravity offers a unique environment for biomanufacturing, which could lead to breakthroughs in bioengineered organs. The space environment allows cells to proliferate and self-organize in three dimensions, mimicking the growth

# Regenerative Medicine in Space (continued)

environment of the human body, potentially improving vascularization of bioengineered thick tissues. It also removes the need for a scaffold and prevents issues common to bioprinting on Earth, including weight-induced distortion, soft bioinks collapsing under their own weight, and cells sedimenting, or sinking to the bottom of the scaffold.<sup>7</sup> Promising work has already been done in this direction and WFIRM, in collaboration with Auxilium Biotechnologies (which already has successfully printed the first medical devices in space<sup>8</sup>), plans to evaluate 3D bioprinting of their tissue constructs in orbit in 2026.

Researchers at the company LambdaVision have launched several projects to the ISS investigating whether the advantages of layer-by-layer deposition in Low Earth orbit can be leveraged to manufacture protein-based artificial retinas.<sup>9</sup> Retinal implants are being considered as a treatment for retinitis pigmentosa, a genetic disorder that causes vision loss and currently has no cure. In microgravity, surface tension becomes the dominant force, which allows proteins and polymers to layer more uniformly and create defect-free implants to restore sight. Eventually, these implants may be used for other retinal diseases and conditions including macular degeneration, a frequent cause of blindness in elderly people.

However, there also are issues requiring further study associated with biomanufacturing in space. In microgravity, cells adopt a spherical, rather than flattened shape, their cytoskeletons can become disordered, and they experience an increase in oxidative stress.<sup>10</sup> While these are important considerations when printing tissues in space, microgravity also can reveal biological phenomena that are normally masked by gravitational forces. More study in this fascinating research area may help us reap the benefits of regenerative medicine in microgravity while avoiding the downsides.

## Resources

Because regenerative medicine in space is ever changing, online information is likely to provide the most up-to-date information. Some resources include:

- *Types of orbits*. (2020, March 30). ESA; The European Space Agency. [https://www.esa.int/Enabling\\_Support/Space\\_Transportation/Types\\_of\\_orbits](https://www.esa.int/Enabling_Support/Space_Transportation/Types_of_orbits)

# Regenerative Medicine in Space (continued)

- This article explains different types of orbits, including low Earth orbit (18 min. read time).
- Tagle, D. (2025). *Tissue chips in space*. NCATS; NIH. <https://ncats.nih.gov/research/research-activities/tissue-chip/projects/space>
  - This webpage briefly discusses the history of tissue chip technology that has been sent to the ISS National Lab (5 min. read time).
- Rainey, K. (2025, July 21). Results From ISS National Lab-Sponsored Research Published in Peer-Reviewed Journals. *ISS National Lab*. <https://issnationallab.org/space-news/sponsored-research-published-journals/>
  - This article discusses several recent ISSNL projects, including one where a skeletal-muscle-on-a-chip was developed to study the effects of microgravity on muscle tissue (4 min. read time).
- ISSNL. (2024, July 30). Cancer research in space for life on Earth: Five projects selected through ISS National Lab solicitation in partnership with NASA. *ISS National Lab*. <https://issnationallab.org/press-releases/release-issrdc2024-igniting-innovation-project-selection/>
  - This article discusses five research projects that were sent to the ISS lab, including three that used organoids (cardiac, tumor and colon) to study cancer (8 min. read time).
- ISS National Lab. (2025, August 20). *NASA's SpaceX CRS-33 Overview Video-Tissue Engineering in Space*. YouTube; YouTube. <https://www.youtube.com/watch?si=UzzyxPQDuX5nmFbt&v=2qFMA53PhYw&feature=youtu.be> (press release NASA's SpaceX CRS-33 to Advance Tissue Engineering, Stem Cell Research, and Space Computing: <https://issnationallab.org/press-releases/nasas-spacex-crs-33-to-advance-tissue-engineering-stem-cell-research-and-space-computing/>)
  - This video discusses WFIRM's successful response to NASA's Vascular Tissue Challenge and the reason why sending their vascularized liver organoid project to space is important (2:56 watch time).
- Thompson, A. (2024, February 1). *Orbital Insights: Heart Cells in Microgravity*. ISS National Lab; ISS National Lab. <https://issnationallab.org/iss360/iss360-kate-rubins-q-and-a-heartcells/>
  - Astronaut Kate Rubins answers questions about a pioneering study she conducted aboard the ISS in 2016 using iPSCs to observe the function of heart cells in microgravity (7 min. read time).

# Regenerative Medicine in Space (continued)

- RegenMed Engine. (2024, September 5). Cancer research in space for life on earth. *NSF Regenerative Medicine Engine*. <https://regenmedengine.com/news/cancer-research-in-space-for-life-on-earth-wake-forest-institute-for-regenerative-medicine-selected-through-international-space-station-national-lab-solicitation-in-partnership-with-nasa/>
  - This article discusses a project by WFIRM studying organoids grown from the cells of cancer patients that are being flown to the ISS to study the effects of different chemotherapies on the organoids (4 min. read time). Includes a video interviewing Dr. Shay Soker, project lead, about how this research can help cancer patients (3:32 watch time).
- Ghani, F., & Zubair, A. C. (2024). Discoveries from human stem cell research in space that are relevant to advancing cellular therapies on Earth. *NPJ Microgravity*, 10(1), 88. <https://doi.org/10.1038/s41526-024-00425-0>. Focus on the Introduction and Stem Cell Studies in Space and Their Potential Application.
  - This article discusses microgravity experiments on hemopoietic stem cells, mesenchymal stem cells and neural stem cells. It lays out how each of these studies could impact medical research on Earth (25 min. read time).
- UCTV. (2024, June 3). *A Closer Look at...Stem Cells in Space*. YouTube; YouTube. [https://www.youtube.com/watch?v=h2flwNtb\\_rs](https://www.youtube.com/watch?v=h2flwNtb_rs)
  - This video includes three different presentations on how stem cell research in microgravity relates to cancer research, brain organoids and patient advocacy (58:57 watch time).

# Regenerative Medicine in Space (continued)

## Footnotes

- <sup>1</sup> NASA. (2020, January 29). NASA Explorers S4 E1: Orbiting Laboratory. YouTube; YouTube. <https://www.youtube.com/watch?v=yqHiShYGkZQ>
- <sup>2</sup> Ghani, F., & Zubair, A. C. (2024). Discoveries from human stem cell research in space that are relevant to advancing cellular therapies on Earth. *NPJ Microgravity*, 10(1), 88. <https://doi.org/10.1038/s41526-024-00425-0>
- <sup>3</sup> Elkavich, A. (2025, August 21). NASA's SpaceX CRS-33 to Advance Tissue Engineering, Stem Cell Research, and Space Computing. ISS National Lab. <https://issnationallab.org/press-releases/nasas-spacex-crs-33-to-advance-tissue-engineering-stem-cell-research-and-space-computing/>
- <sup>4</sup> Elkavich, A. (2025, August 20). ISS National Lab-Sponsored Experiment Tests 3D Bioprinted Tissue for Growing Artificial Livers. ISS National Lab. <https://issnationallab.org/press-releases/iss-national-lab-sponsored-experiment-tests-3d-bioprinted-tissue-for-growing-artificial-livers/>
- <sup>5</sup> Axiom Space. (2023, April 24). Ax-2 Mission to Expand Microgravity Research to Combat Human Disease. Axiom Space; Axiom Space, Inc. <https://www.axiomspace.com/mission-blog/ax2-lifesciences2>
- <sup>6</sup> Axiom Space. (2024, March 6). Axiom Space partners with Wake Forest Institute for Regenerative Medicine on National Science Foundation Regional Innovation Engines. Axiom Space; Axiom Space, Inc. <https://www.axiomspace.com/release/nsfgrant>
- <sup>7</sup> Mozneb, M., Arzt, M., Moses, J., Escopete, S., Wiegand, L., & Sharma, A. (2025). Stem cell research in space: Advancing regenerative medicine beyond Earth. *Cell Stem Cell*, 32(10), 1491–1508. [https://www.cell.com/cell-stem-cell/fulltext/S1934-5909\(25\)00332-7](https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(25)00332-7)
- <sup>8</sup> BioSpace. (2025, February 5). *Auxilium Biotechnologies Successfully Prints Medical Devices for the First Time on the International Space Station*. <https://www.biospace.com/press-releases/auxilium-biotechnologies-successfully-prints-medical-devices-for-the-first-time-on-the-international-space-station>
- <sup>9</sup> ISSNL. (2024, January 23). LambdaVision sends sight-saving research to the ISS. *ISS National Lab*. <https://issnationallab.org/press-releases/release-ng20-lambdavisision-retinal-implant/>
- <sup>10</sup> Marotta, D., Ward, N., Bauer, S. R., Hunsberger, J., Stoudemire, J., Savin, K., Giulianotti, M., Jamieson, C. H. M., Roberts, D., & Roberts, M. (2025). Biomanufacturing in low Earth orbit: A paradigm shift. *Stem Cell Reports*, 20(7), 102536. <https://doi.org/10.1016/j.stemcr.2025.102536>

# Look Up

## **Learning Outcomes**

- Students will define Low Earth orbit.
- Students will be able to list characteristics of working in microgravity.
- Students will compare and contrast research/manufacturing on the surface of the earth and in Low Earth orbit.
- Students will design an experiment to fit in a module that could theoretically go to the International Space Station.

## **Key Vocabulary**

- Space
- Low Earth orbit
- Microgravity

## **Time Required**

- Approximately 15 minutes of preparation time
- Approximately 90 minutes of class time for activity

## **Materials**

- Internet resources
- Student worksheet

## **Background Information**

Outer space, or simply **space**, is the expanse that exists beyond the atmosphere of the Earth. It often is defined as the area above which planes cannot fly, typically around 100 kilometers above the Earth's surface. **Low Earth orbit (LEO)** is an orbit around the Earth with an altitude of 2,000 kilometers or less. It provides a unique place for scientists to conduct experiments and produce products that can't be produced on Earth. Low Earth orbit stands to change the paradigm of healthcare and technology. The **microgravity** in Low Earth orbit provides the opportunity for material purity, production of drugs/biologics, enhanced cell growth, as well as tissue/organoid growth with 3D structure and improved organization. While working in space has advantages, there also are challenges, including logistics, radiation, equipment/material transport, cost, accessibility, standardization, ethics and integration/reintegration of materials/products. These challenges need to be addressed as the new sectors of the space economy emerge.

# Look Up (continued)

## Teaching Notes

This activity provides structure for students to develop an understanding of Low Earth orbit and why it is useful for regenerative medicine. The teacher will review the definition of Low Earth orbit and microgravity. Students will complete a chart comparing gravity on Earth with microgravity in Low Earth orbit. Students will work in small groups to develop a module for the Axiom space station, which is set to replace the International Space Station (ISS), or for free-flyer commercial space stations such as Vast Haven-1 and Voyager Starlab that are being developed as part of the transition from the ISS by 2030. Students will be evaluated based on the module's design and integration of regenerative medicine.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing. Establish rules for discussion to ensure all students have an opportunity to participate and share their opinions and ideas in a productive manner.

## Procedure

- Teacher should drop a ball and ask students why it fell.
- Conduct a short discussion on gravity and what this force does.
- Ask students to work in pairs to use the microgravity resources provided to define Low Earth orbit and microgravity. Consider having the class watch a video: NASA. (2020, January 29). *NASA Explorers S4 E1: Orbiting Laboratory* [Video]. YouTube. <https://youtu.be/yqHiShYGkZQ>
  - This video features interviews with astronauts aboard the ISS describing the advantages of doing research in microgravity (6:16 watch time).
- Have each pair share their definitions. Encourage students to help other groups sharpen their definitions.
- Using the microgravity resources on the student handout as a guide, create a list of advantages and challenges for conducting research in Low Earth orbit.
- Allow two or three small groups to gather and share their advantages/challenges lists.
- Move from group to group and check for understanding.
- To review the information as a whole class, ask each group to share one advantage or challenge.

# Look Up (continued)

- Explain to the class that North Carolina researchers are partnering with space agencies and businesses to conduct experiments in space. Consider having the class watch the following video about partnerships: *America's Future: Commercial Space Destinations*. YouTube. <https://www.youtube.com/watch?v=v7sS4vVtHpI>
- Working in small groups, students should design a flight box focusing on regenerative medicine research for a space station/voyage such as the Axiom space station, Vast Haven-1 or Voyager Starlab.
- Encourage students to choose a specific purpose/experiment for the flight box and include four specific items/parts with an explanation of how each part is needed for the proposed regenerative medicine research.

## **Assessment**

Students should complete the *Look Up* handout. Each small group should develop a module with a specific purpose related to regenerative medicine. The module should have four specific items/parts with explanation of how each part is needed for regenerative medicine in space. Consider using a group work assessment rubric to evaluate both the product and process of each small group as well as individual student contributions.

## **Extension**

This activity may be extended by asking students to investigate current regenerative medicine research in space. Students may write a short synopsis of a current regenerative medicine project in space. Students may find information on the experiments being conducted on the International Space Station on NASA websites, such the Space Station Research Results page, <https://www.nasa.gov/international-space-station/space-station-research-and-technology/space-station-research-results/>.

# Look Up (continued)

## Resources

Because regenerative medicine in space is ever changing, online sources are likely to provide the most up-to-date information. Some resources include:

- NASA. (2024). *NASA's Low Earth Orbit Microgravity Strategy*. NASA. <https://www.nasa.gov/wp-content/uploads/2024/12/2024-12-lms-final-goals-and-objectives.pdf?emrc=b262e6> (Focus on page 8-13).
  - The selected pages of this document discuss NASA's goals for human presence in LEO, as well as why a LEO environment is essential both for scientific discoveries and prepping for future space exploration (12 min. read time).
- Tagle, D. (2025). *Tissue chips in space*. NCATS; NIH. <https://ncats.nih.gov/research/research-activities/tissue-chip/projects/space>
  - This webpage briefly discusses the history of tissue chip technology that has been sent to the ISS National Lab (5 min. read time).
- UCTV. (2024, June 3). *A Closer Look at...Stem Cells in Space*. YouTube; YouTube. [https://www.youtube.com/watch?v=h2fIwNtb\\_rs](https://www.youtube.com/watch?v=h2fIwNtb_rs)
  - This video includes three different presentations on how stem cell research in microgravity relates to cancer research, brain organoids and patient advocacy (58:57 watch time).
- Progress, Potential, and Possibilities. (2022, January 10). *Dr Anthony Atala, MD - Director, Wake Forest Inst for Regenerative Medicine—Printing Human Tissues*. YouTube; YouTube. <https://www.youtube.com/watch?v=rhYRUMnyofo>
  - This video focuses on the importance of vascularization and NASA Vascular Tissue Challenge (relevant portion: 5:37-13:45)

# Look Up — Student Worksheet

## Low Earth Orbit and Microgravity:

1. Define the following terms using the microgravity resources.
  - Low Earth orbit:
  - Microgravity:
2. Using the microgravity resources provided, create a list of advantages and challenges for conducting research/manufacturing in Low Earth orbit versus on Earth.

Advantages and Challenges for Conducting Research/Manufacturing in Low Earth Orbit	
Advantage	Challenge

## Low Earth Orbit/Microgravity Resources:

- *What is microgravity?* - NASA. (2009, February 13). <https://www.nasa.gov/centers-and-facilities/glenn/what-is-microgravity/>
  - This article describes what microgravity is and how it is different from zero-gravity (4 min. read time).
- *Types of orbits.* (2020, March 30). ESA; The European Space Agency. [https://www.esa.int/Enabling\\_Support/Space\\_Transportation/Types\\_of\\_orbits](https://www.esa.int/Enabling_Support/Space_Transportation/Types_of_orbits)
  - This article explains different types of orbits, including Low Earth orbit (18 min. read time).
- NASA. (2020, January 29). *NASA Explorers S4 E1: Orbiting Laboratory* [Video]. YouTube. <https://youtu.be/yqHiShYGkZQ>
  - This video features interviews with astronauts aboard the ISS describing the advantages of doing research in microgravity (6:16 watch time).
- NASA. (2024, August 26). *Envisioning the Next Generation of Human Presence in Low Earth Orbit.* YouTube; YouTube. [https://www.youtube.com/watch?v=UDiNFG9\\_EWE](https://www.youtube.com/watch?v=UDiNFG9_EWE)
  - This brief video summarizes the ISS's legacy of continuous human presence in space (1:01 watch time).

# Look Up — Student Worksheet (continued)

- NASA. (2024). *NASA's Low Earth Orbit Microgravity Strategy*. NASA. <https://www.nasa.gov/wp-content/uploads/2024/12/2024-12-lms-final-goals-and-objectives.pdf?emrc=b262e6> (Focus on page 8-13).
  - The selected pages of this document discuss NASA's goals for human presence in LEO, as well as why a LEO environment is essential both for scientific discoveries and prepping for future space exploration (12 min. read time).
- Tissue engineering and regenerative medicine. (n.d.). *ISS National Lab*. Retrieved November 24, 2025, from <https://issnationallab.org/research-and-science/space-research-overview/research-areas/in-space-production-applications/tissue-engineering-and-regenerative-medicine/>
  - The webpage for the ISSNL includes a discussion of why it is important to conduct research in space.

Regenerative medicine scientists want to take advantage of the benefits of Low Earth orbit for research and biomanufacturing. Scientists across the globe are developing experiments to be sent on short term space flights or long-term flights on the International Space Station. North Carolina researchers at Wake Forest University have developed partnerships to take their research to the next level.

## North Carolina Regenerative Medicine Research in Space

Use the following resources to research the answers to the questions below:

- ISS National Lab. (2025, August 20). *NASA's SpaceX CRS-33 Overview Video-Tissue Engineering in Space*. YouTube; YouTube. <https://www.youtube.com/watch?si=UzzyxPQDuX5nmFbt&v=2qFMA53PhYw&feature=youtu.be> (press release NASA's SpaceX CRS-33 to Advance Tissue Engineering, Stem Cell Research, and Space Computing: <https://issnationallab.org/press-releases/nasas-spacex-crs-33-to-advance-tissue-engineering-stem-cell-research-and-space-computing/>)
  - This video discusses WFIRM's successful response to NASA's Vascular Tissue Challenge and the reason why sending their vascularized liver organoid project to space is important (2:56 watch time).
- RegenMed Engine. (2024, September 5). Cancer research in space for life on earth. *NSF Regenerative Medicine Engine*. <https://regenmedengine.com/news/cancer-research-in-space-for-life-on-earth-wake-forest-institute-for-regenerative-medicine-selected-through-international-space-station-national-lab-solicitation-in-partnership-with-nasa/>

# Look Up — Student Worksheet (continued)

- This article discusses a project by WFIRM studying organoids grown from the cells of cancer patients that are being flown to the ISS to study the effects of different chemotherapies on the organoids (4 min. read time). Includes a video interviewing Dr. Shay Soker, project lead, about how this research can help cancer patients (3:32 watch time).
- Axiom Space. (2024, March 6). *Axiom Space partners with Wake Forest Institute for Regenerative Medicine on National Science Foundation Regional Innovation Engines*. Axiom Space; Axiom Space, Inc. <https://www.axiomspace.com/release/nsfgrant>
  - This press release discusses the partnership between Axiom Space and WFIRM in providing access to regenerative medicine laboratory facilities aboard Axiom Station, one of the successors to the ISS (4 min. read time).

1. What two types of tissue did WFIRM enter in the Vascular Tissue Challenge?

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2. What regenerative medicine products and tissue chip/organoid models that resulted from the Vascular Tissue Challenge are WFIRM working on?

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3. Which organizations has WFIRM partnered with to take additional experiments beyond the ISS?

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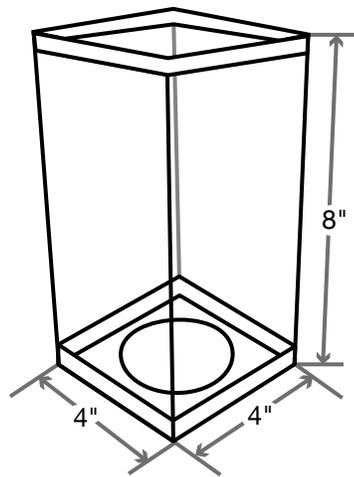
# Look Up — Student Worksheet (continued)

## Design Your Flight Box

*Note this activity has been modified from the NASA Techrise 2025 competition:  
<https://www.futureengineers.org/nasatechrise>*

NASA often holds student competitions where students propose experiments to be carried out in various conditions including microgravity. Your group will design a flight box to carry out an experiment or manufacturing project in Low Earth orbit related to regenerative medicine. With your group, determine a research or manufacturing objective for your flight box. Then write a short description of what research/manufacturing will occur in your module and why this is important. Design a flight box with components that will fit in a 4 in x 4 in x 8 in box and weigh less than 1 kg. Identify four key features of the flight box and explain why each is needed to carry out your plan in Low Earth orbit. Then create a poster with a diagram explaining your ideas.

### Flight Box



Regenerative medicine research/manufacturing flight box name:

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Objective:

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Description/Significance:

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# Look Up — Student Worksheet (continued)

Benefits to life on Earth:

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Feature 1:

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Feature 2:

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Feature 3:

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Feature 4:

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# AI in Regenerative Medicine

## What is AI?

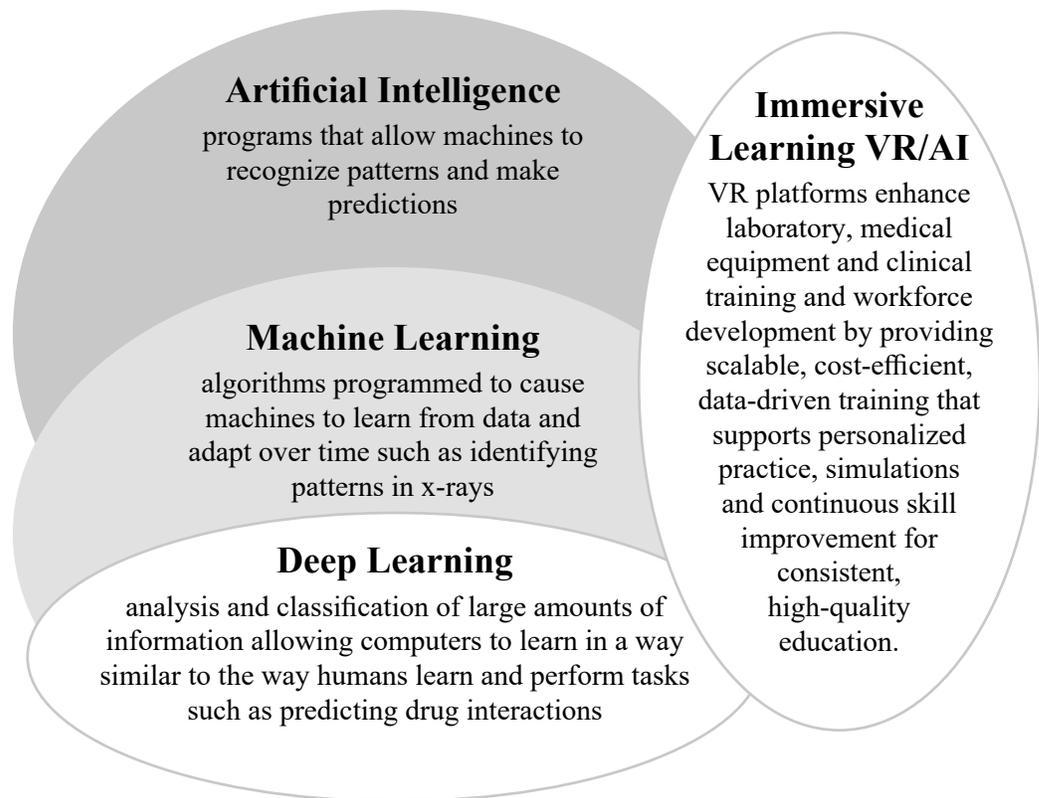
**Artificial intelligence (AI)** has been a topic in pop culture and science alike for many years. Movies such as *The Terminator* and *The Matrix* depict dystopian worlds where humanity is attacked by rogue AI programs. As early as 1950, Alan Turing, a pioneering computer scientist, stated that if a person questioning a machine and a human cannot reliably distinguish which is which, then that machine can be said to think.<sup>1</sup> This criterion became known as the Turing test and was one of the founding ideas of the then-nascent field of AI. Compared to a classical computer program that follows programmed rules, AI can learn from and make decisions based on provided data without all rules being explicitly programmed. With the development of chatbots such as ChatGPT and Google Gemini, discussion of AI has exploded. In this section, we'll discuss how a few types of AI are playing a role in regenerative medicine currently, ethical concerns that arise from the use of AI in these settings, and where these technologies may lead in the future.

One subset of AI is **machine learning (ML)**, which uses algorithms programmed to cause machines to learn from data and adapt over time.<sup>2</sup> **Deep learning** is a type of machine learning where computers analyze and classify large amounts of information, allowing computers to learn in a way similar to the way humans learn. This type of learning depends on a neural network, which uses interconnected nodes to mimic the interconnected neurons in the human brain. Large language models (LLMs) are a result of deep learning and are trained on large amounts of text to mimic human responses. Two broad varieties of AI are traditional and generative AI. While traditional AI takes in selected data and uses algorithms to make predictions from that data, generative AI creates something new from a prompt input by a user. Traditional AI is designed to do specific tasks reliably and efficiently and includes diagnostic tools, fraud detection systems, autocorrect and text suggestions in word processors, and autonomous vehicle navigation systems. Generative AI can do more general and creative tasks than traditional AI, and it can create text, art and software code. Examples include LLMs like ChatGPT and image generators like Midjourney. However, generative AI uses vast amounts of data and may not distinguish between accurate and inaccurate sources. It may then produce flawed results and false information with made up sources.

# AI in Regenerative Medicine

(continued)

Image 10: Illustration of AI Usage in Regenerative Medicine



## Current Uses of AI in Regenerative Medicine

Artificial intelligence has been used in several different ways to aid either directly, or indirectly, in the field of regenerative medicine. AI is being used in training, diagnostics, drug development and tissue engineering. The RegeneratOR Test Bed at WFIRM is a laboratory designed to give companies developing new biomedical products access to state-of-the-art biomanufacturing equipment, industry expertise and talent to support prototyping and commercial product development. AI is being used to provide immersive training for researchers using the RegeneratOR Test Bed as well as to improve the workflow and solve manufacturing challenges. Scientific equipment is very expensive, but with an AI virtual reality simulation these tools are available for training and planning research at a fraction of the cost. In addition, these simulations can be done remotely — enabling collaboration between teams in different locations and reducing travel costs.

Pharmaceutical companies are using traditional AI models to analyze millions

# AI in Regenerative Medicine

(continued)

of chemical compounds. Using machine learning, AI can help predict the efficacy of a given drug or therapy for a specific illness. This is useful because AI can analyze vastly more data in a smaller time frame than a human can and therefore detect patterns that may otherwise go unseen. At least forty regenerative medicine therapies are being developed with the help of AI, three of which are currently in Phase II human clinical trials, including a therapy for Parkinson's disease that uses patient-derived induced pluripotent stem cells.<sup>3</sup>

AI also is being studied as a possible mechanism for diagnosing diseases. A recent Johns Hopkins study used a special type of ML algorithm called a support vector machine to classify electrical signals produced by brain organoids.<sup>4</sup> Researchers used iPSCs derived from bipolar, schizophrenic and healthy patients to grow brain organoids and classify their neural firing patterns. Their AI algorithm differentiated between organoids from schizophrenic and healthy patients 95% of the time, and between those from bipolar and healthy patients 83% of the time. This study included only twelve patients, and its results need further research and validation.

AI is also being used to help solve a major problem: there is currently no way to reliably manufacture healthy induced pluripotent stem cells at scale. Instead, batches of cells must be processed by hand, with trained researchers scraping away cells that they deem to be less fit for use. A research team led by Wei Xie at Northeastern University is working to change that, and her lab has recently published two papers proposing AI models to predict the behavior and mechanisms within both a single iPSC and a cluster of them.<sup>5</sup> If iPSCs can be produced in bulk, this will make them more available both for researchers and patients and could help lower the cost of personalized treatments.

Finally, AI can be integrated into **virtual reality** (VR) environments to serve as a training ground for medical professionals and technicians. This can provide hands-on experience that overcomes traditional barriers such as geographic limitations, physical resources and safety concerns. A virtual environment can be accessed by individuals and teams around the world, enabling international and interdisciplinary collaboration. In addition, VR provides medical professionals in less affluent areas with the opportunity to train on state-of-the-art equipment in a virtual environment. Because VR platforms are more cost-efficient than physical equipment, they can be deployed to many individuals at once, accommodating widespread training needs across multiple locations.

# AI in Regenerative Medicine

(continued)

AI algorithms analyze user interactions, skill progression, and outcomes to identify strengths and areas for improvement, enabling adaptive feedback and personalized content delivery. This data-driven approach not only streamlines the learning process but also ensures that each user receives the most effective and relevant training experience.

## **Ethics of AI in Healthcare**

Although AI is a potential boon to the field of regenerative medicine, ethical issues emerge when it is used in research and healthcare. One of these issues is potential algorithmic bias. AI can only make predictions or generate content based on the information given to it. Machine learning requires the input of data from another source, so algorithms that are trained on inadequate datasets can perpetuate or exacerbate existing biases.<sup>6</sup> For example, if a program were trained to recognize malignant melanomas but the input dataset only included photos of white individuals, the program may not detect occurrences of melanomas in nonwhite individuals. To avoid this issue, it is vital to train AI on diverse, representative datasets and regularly test AI systems for bias.

When data that is put into AI models includes sensitive research participant or patient information, this raises privacy concerns.<sup>6</sup> Worries about data breaches are not unique to AI. However, for many AI programs, there are additional concerns about a lack of transparency regarding how submitted information is both processed and stored. AI can be a “black box,” with little information available about how it makes decisions or how data is protected. For AI to be used in medical research as well as patient care, the way that it makes decisions and stores information must be clear.

An additional question involves autonomy: research participants may not understand the ways that AI is being used in a research project, and patients may not understand how it is being used in their diagnosis and treatment.<sup>6</sup> Research participants and patients need complete and comprehensible information to give informed consent. Researchers and providers need an understanding of AI to understand the strengths and limitations of this rapidly developing technology and to be able to educate research participants and patients.

## **The Future of AI in Regenerative Medicine**

Though some forms of AI are already being used in healthcare in general and regenerative medicine in particular, there are other possibilities for how AI

# AI in Regenerative Medicine

(continued)

could be used. For example, AI could be used to anticipate the risk of a disease years before it may become reality.<sup>7</sup> AI trained on a large enough dataset may recognize patterns and precursors to a particular medical issue that humans may not be aware of. For the same reason, AI is being considered to match research participants with the most promising clinical trials for them. Of course, as AI advances towards these and other goals, it is important to keep potential ethical issues (discussed above) in mind.

## Resources

- *What is Artificial Intelligence (AI)?* (n.d.). Michigan Technological University. Retrieved November 21, 2025, from <https://www.mtu.edu/computing/ai/>
  - This resource summarizes what AI is, where it is used, the components and functions of AI, the history and future of AI technology, and possible careers in AI. There also is a vocabulary section summarizing key terms and tips for students interested in working in AI (14 min. read time).
- Monahan, J. (2023, July). *Artificial Intelligence, explained*. Carnegie Mellon University's Heinz College; Carnegie Mellon University. <https://www.heinz.cmu.edu/media/2023/July/artificial-intelligence-explained>
  - This article provides a brief timeline of developments in AI, a glossary of important terms, and a summary of how generative AI works (10 min. read time).
- TEDx Talks. (2021, November 18). *Artificial intelligence in healthcare: Opportunities and challenges*. YouTube; YouTube. <https://www.youtube.com/watch?v=uvqDTbusdUU>
  - This video features a discussion of how AI models can help in diagnosing and treating patients, as well as how they can help hospitals run more efficiently (8:37 watch time).
- AI for Good. (2022, March 9). *AI and Regenerative Medicine: AI-Enabled Manufacturing of Stem-cell Based Therapies*. YouTube; YouTube. <https://www.youtube.com/watch?v=CmnCHDoyfX8&t=224s>
  - Nabiha Saklayen, co-founder of Cellino Bio, presents on how AI is helping manufacture new stem cell treatments, with a Q&A included at the end (1:00:38 watch time). Key moments: 7:07 — what iPSCs are and why they matter, 24:04 — how AI relates to reprogramming of cells, 36:05 — image-based analysis and AI.

# AI in Regenerative Medicine

(continued)

- Mayo Clinic (2023, September 8). *Can Mayo Clinic Use AI to Diagnose Heart Disease?* YouTube; YouTube. [https://www.youtube.com/watch?v=45plAwwIN\\_k](https://www.youtube.com/watch?v=45plAwwIN_k)
  - This video discusses a Mayo Clinic project to design an algorithm to help diagnose heart disease (1:29 watch time).
- GEN. (2025, September 22). *AI detects schizophrenia and bipolar disorder neural signatures in organoids*. GEN - Genetic Engineering and Biotechnology News. <https://www.genengnews.com/topics/artificial-intelligence/ai-detects-schizophrenia-and-bipolar-disorder-neural-signatures-in-organoids/>
  - This resource reports on a Johns Hopkins University study where researchers trained AI to recognize disease-specific signals from brain organoids derived from the cells of schizophrenia and bipolar disorder patients. There is a very brief overview of the study design and some quotes from the study PI (5 min. read time).
- Forsyth Tech. (2025, January 24). *SciTech Lecture Series | Discussion w/ Josh Tan & Dr. Joshua Hunsberger*. YouTube; YouTube. <https://www.youtube.com/watch?v=4HIv8IM3UHo>
  - Interview with Josh Tan (assistant manager of the radiology department at Wake Forest Baptist Health) and Joshua Hunsberger (CTO at RegenMed Development Organization) on how AI and VR are being used to advance medicine (32:13 watch time). Key moments: 5:28 — technology increasing international collaboration, 16:55 — the future of AR and VR in biomanufacturing, 24:10 — career opportunities and skill levels needed for increased technology in regenerative medicine.
- Garmany, A., & Terzic, A. (2024). Artificial intelligence powers regenerative medicine into predictive realm. *Regenerative Medicine*, 19(12), 611–616. <https://doi.org/10.1080/17460751.2024.2437281>
  - This article explains potential ways AI can be used in regenerative medicine, including helping ensure quality control through automated monitoring of manufacturing, and helping guide clinical trial design (12 min. read time).
- Gharibshahian, M., Torkashvand, M., Bavisi, M., Aldaghi, N., & Alizadeh, A. (2024). Recent advances in artificial intelligent strategies for tissue engineering and regenerative medicine. *Skin Research and Technology*, 30(9), e70016. <https://doi.org/10.1111/srt.70016>
  -

# AI in Regenerative Medicine

(continued)

- This article discusses the use of AI in designing and building scaffolds and tissues. It discusses advantages of using AI in these capacities (34 min. read time).
- Vo, Q. D., Saito, Y., Ida, T., Nakamura, K., & Yuasa, S. (2024). The use of artificial intelligence in induced pluripotent stem cell-based technology over a 10-year period: A systematic scoping review. *PLOS ONE*, 19(5), e0302537. <https://doi.org/10.1371/journal.pone.0302537>
  - This review paper discusses the use of AI in processing iPSCs, with a focus on its ability to conduct genetic analyses and monitor cell functionality (26 min. read time).

## Footnotes

- <sup>1</sup> Oppy, G., & Dowe, D. (2021). The Turing Test. In E. N. Zalta (Ed.), *The Stanford Encyclopedia of Philosophy* (Winter 2021). Metaphysics Research Lab, Stanford University. <https://plato.stanford.edu/entries/turing-test/>
- <sup>2</sup> Monahan, J. (2023, July). *Artificial Intelligence, explained*. Carnegie Mellon University's Heinz College; Carnegie Mellon University. <https://www.heinz.cmu.edu/media/2023/July/artificial-intelligence-explained>
- <sup>3</sup> GlobalData Healthcare. (2025, March 3). Using artificial intelligence to enhance regenerative medicine. *Pharmaceutical Technology*. <https://www.pharmaceutical-technology.com/analyst-comment/artificial-intelligence-enhance-regenerative-medicine/>
- <sup>4</sup> GEN. (2025, September 22). *AI detects schizophrenia and bipolar disorder neural signatures in organoids*. GEN - Genetic Engineering and Biotechnology News. <https://www.genengnews.com/topics/artificial-intelligence/ai-detects-schizophrenia-and-bipolar-disorder-neural-signatures-in-organoids/>
- <sup>5</sup> Kuzub, A. (2024, April 3). Northeastern scientists propose AI framework for mass-manufacturing of stem cells for regenerative medicine. *Northeastern Global News*. <https://news.northeastern.edu/2024/04/03/regenerative-medicine-stem-cell-manufacturing/>
- <sup>6</sup> Yu, S., Lee, S.-S., & Hwang, H. (2024). The ethics of using artificial intelligence in medical research. *Kosin Medical Journal*, 39(4), 229–237. <https://doi.org/10.7180/kmj.24.140>
- <sup>7</sup> Mayo Clinic Press Editors. (2024, March 27). *AI in healthcare: The future of patient care and health management*. Mayo Clinic Press; Mayo Clinic Press. <https://mcpres.mayoclinic.org/healthy-aging/ai-in-healthcare-the-future-of-patient-care-and-health-management/>

# ABCs of AI in RM

**Learning  
Outcomes**

- Students will define artificial intelligence.
- Students will list ways artificial intelligence can be used to assist regenerative medicine.
- Students will analyze a dataset to look for trends using traditional methods and artificial intelligence.

**Key Vocabulary**

- Artificial intelligence
- Machine learning
- Deep learning

**Time Required**

- Approximately 15 minutes of preparation time
- Approximately 90 minutes of class time for activity

**Materials**

- Internet resources
- Student worksheet

**Background  
Information**

**Artificial intelligence** is widely discussed in many arenas, but what exactly is it? In its simplest form, AI is the ability of a program or computer system to perform tasks normally associated with human intelligence such as reasoning, learning or problem-solving. A major subfield of artificial intelligence is **machine learning**, which focuses on enabling computer systems to learn from data without being explicitly programmed to do so. One type of machine learning is **deep learning**, where computers are trained in analysis and classification using extremely large datasets. This type of learning is thought to resemble the way that humans learn, and depends on a neural network, with multiple connected nodes that mimic the function of a human brain. Because of the flexibility of AI technology, it has many applications in the field of regenerative medicine. AI is being used to develop new biomedical products, predict the usefulness of drugs and diagnose diseases. In this activity, students will learn about the uses of AI in regenerative medicine and some of the benefits and challenges of this work.

**Teaching Notes**

This activity introduces students to the following terms: artificial intelligence, machine learning and deep learning. The teacher will review the terms using the text on page Unit IV-4.112 and the lesson resources. The teacher will share video/print resources to demonstrate how AI can be used to assist regenerative medicine. Students will work in a small group to create an alphabet chart of AI and regenerative medicine.

# **ABCs of AI in RM** (continued)

## **Safety**

Students should follow school/district Internet access and AI guidelines to ensure safe browsing. Establish a safe environment for all students to share their opinions and ideas in productive manner.

## **Procedure**

- Ask students to create a definition for the following terms: artificial intelligence, machine learning and deep learning.
- Lead a discussion of the definitions and solicit examples of each term from the students. For definitions and examples, refer to the text and image found on page Unit IV-4.113. Encourage students to refine their definitions based on class discussion.
- Provide video/print resources to help students understand the concepts.
- Allow the students to share ways they think AI could be used in regenerative medicine.
- Conduct a class discussion to discuss the pros and cons of using AI in regenerative medicine.
- After the class discussion, have students work in small groups and develop an alphabet chart for regenerative medicine. The alphabet chart should include ways AI is used in regenerative medicine. For example, R is for regenerative medicine.

## **Assessment**

Students should complete the *ABCs of AI in RM* handout. The student work should be evaluated individually and as a small group. Students will create an ABC chart for regenerative medicine.

## **Extension**

This activity may be extended by asking students to identify current regenerative medicine research that uses AI by searching PubMed, a database of the National Library of Medicine at the National Institutes of Health, or in Google Scholar.

For another extension, students may be asked to analyze a dataset using non-AI methods (Excel, Google Sheets) and AI methods, then compare whether or how their analysis differs depending on the analysis method and tools. Students can find open-access datasets in repositories such as Data.gov and Kaggle. Students may also compare the results from two different AI tools using the same prompt.

# ABCs of AI in RM (continued)

## Resources

Because regenerative medicine in AI is ever changing, online information is likely to provide the most up-to-date information. Some resources include:

- *What is Artificial Intelligence (AI)?* (n.d.). Michigan Technological University. Retrieved November 21, 2025, from <https://www.mtu.edu/computing/ai/>
  - This resource summarizes what AI is, where it is used, the components and functions of AI, the history and future of AI technology, and possible careers in AI. There also is a vocabulary section summarizing key terms and tips for students interested in working in AI (14 min. read time).
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- TEDx Talks. (2021, November 18). *Artificial intelligence in healthcare: Opportunities and challenges*. YouTube; YouTube. <https://www.youtube.com/watch?v=uvqDTbusUU>
  - This video features a discussion of how AI models can help in diagnosing and treating patients, as well as how they can help hospitals run more efficiently (8:37 watch time).
- AI for Good. (2022, March 9). *AI and Regenerative Medicine: AI-Enabled Manufacturing of Stem-cell Based Therapies*. YouTube; YouTube. <https://www.youtube.com/watch?v=CmnCHDoyfX8&t=224s>
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  - This video discusses a Mayo Clinic project to design an algorithm to help diagnose heart disease (1:29 watch time).

## ABCs of AI in RM (continued)

- GEN. (2025, September 22). *AI detects schizophrenia and bipolar disorder neural signatures in organoids*. GEN — Genetic Engineering and Biotechnology News. <https://www.genengnews.com/topics/artificial-intelligence/ai-detects-schizophrenia-and-bipolar-disorder-neural-signatures-in-organoids/>
  - This resource reports on a Johns Hopkins University study where researchers trained AI to recognize disease-specific signals from brain organoids derived from the cells of schizophrenia and bipolar disorder patients. There is a very brief overview of the study design and some quotes from the study PI (5 min. read time).
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  - Interview with Josh Tan (assistant manager of radiology department at Wake Forest Baptist) and Joshua Hunsberger (CTO at RegenMed Development Organization) on how AI and VR are being used to advance medicine (32:13 watch time). Key moments: 5:28-technology increasing international collaboration, 16:55-the future of AR and VR in biomanufacturing, 24:10-career opportunities and skill levels needed for increased technology in regenerative medicine.
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  - This article explains potential ways AI can be used in regenerative medicine, including helping ensure quality control through automated monitoring of manufacturing, and helping guide clinical trial design (12 min. read time).
- Gharibshahian, M., Torkashvand, M., Bavisi, M., Aldaghi, N., & Alizadeh, A. (2024). Recent advances in artificial intelligent strategies for tissue engineering and regenerative medicine. *Skin Research and Technology*, 30(9), e70016. <https://doi.org/10.1111/srt.70016>
  - This article discusses the use of AI in designing and building scaffolds and tissues. It discusses advantages of using AI in these capacities (34 min. read time).

# ABCs of AI in RM (continued)

- Vo, Q. D., Saito, Y., Ida, T., Nakamura, K., & Yuasa, S. (2024). The use of artificial intelligence in induced pluripotent stem cell-based technology over 10-year period: A systematic scoping review. *PLOS ONE*, 19(5), e0302537. <https://doi.org/10.1371/journal.pone.0302537>
  - This review paper discusses the use of AI in processing iPSCs with a focus on its ability to conduct genetic analyses and monitor cell functionality (26 min. read time).

# ABCs of AI for RM

Using the provided resources, create an alphabet chart for AI and Regenerative Medicine.

A is for...	B is for...	C is for...	D is for...
E is for...	F is for...	G is for...	H is for...
I is for...	J is for...	K is for...	L is for...
M is for...	N is for...	O is for...	P is for...
Q is for...	R is for...	S is for...	T is for...
U is for...	V is for...	W is for...	X is for...
Y is for...	Z is for...		

# Regenerative Medicine: Buy My Treatment

## Learning Outcomes

- Students will review bioethics and the four principles.
- Students will research and analyze a current regenerative medical research study.
- Students will evaluate the research study considering the four bioethical principles.
- Students will create a set of advertising guidelines using the four bioethical principals.

## Key Vocabulary

- Regenerative medicine
- Autonomy
- Beneficence
- Non-maleficence
- Justice
- Stem cell-based interventions

## Time Required

- Approximately 45 minutes to review bioethics and introduce the stem-cell based interventions.
- Approximately 45 minutes to investigate current stem cell-based interventions and the associated research (may be done outside of class)
- Approximately 45 minutes to develop guidelines for stem cell-based intervention advertisement in small groups (may be done outside of class)
- Approximately 45 minutes to present advertising guidelines (for eight small groups)

## Materials

- Computers with Internet access and print materials for research
- White Paper Rubric

# Regenerative Medicine: Buy My Treatment (continued)

## Background Information

In 2024, the N.C. General Assembly passed an extension of the 2015 “Right To Try” Act. The original version of this law allowed patients with life-threatening illnesses to be prescribed drugs or therapies that were not fully approved by the FDA, provided they have exhausted all FDA-approved treatments. A 2019 law added that terminally ill patients could access unapproved treatments derived from adult stem cells, while the 2024 expansion allows patients to also be prescribed individualized treatments based on their unique genetic makeup. By their nature, individualized treatments do not lend themselves well to the FDA approval process, which involves large-scale clinical trials. There are worries that this newest version of right-to-try will result in a proliferation of advertisements for expensive and possibly dangerous therapies that may have little or no evidence of effectiveness. In this activity, students will apply the four bioethical principles (autonomy, beneficence, non-maleficence and justice) to current events, as they research advertisements for stem cell therapies.

## Teaching Notes

This activity allows students to work in groups to research stem cell-based interventions and review associated advertisements. Depending on student access to the Internet, you may choose to have students do this research in or out of class. After gathering and synthesizing information, small groups of students will create a set of advertising guidelines that incorporate the four bioethical principles. This activity may be adapted into an individual project.

## Safety

Students should follow school/district Internet access guidelines to ensure safe browsing.

## Procedure

Begin by watching a video on stem cell-based interventions that appear to be fraudulent, such as Stem Cell Fraud: A 60 Minutes Investigation (<https://www.youtube.com/watch?v=ovPZkQYee8Y>) and Doctors Sell False Hope with Unproven Stem Cell Treatments (<https://www.youtube.com/watch?v=KAfSFvEKTZg>). After watching the video, students will have many questions. Write these questions on the board. Show students sample stem cell therapy advertisements using the sample advertisements listed in the resource section. Alternatively, students may research and find examples of stem cell research advertisements. Explain that they will be reviewing stem cell research/advertisements and creating guidelines for advertisements that adhere to the four bioethical principals.

# Regenerative Medicine: Buy My Treatment (continued)

Explain that stem cell-based interventions are ever evolving. Discuss how stem cell-based interventions are sometime brought to market reporting results that may or may not have been proven. The students will work in groups of three or four to complete the following *Regenerative Medicine: Buy My Treatment* handout. The students will review stem cell-based therapies and advertisements.

After the students have completed the research, each student group will create a set of advertising guidelines that incorporates the four bioethical principles. Student groups will defend their guidelines to the whole class.

## Assessment

The advertising guidelines may be evaluated using the rubric at the end of this lesson plan. Rubrics help students understand what is expected of them. They should be shared with students in advance and may be developed with students. Teachers may adjust this rubric to fit their grading system and to emphasize different aspects of the project as appropriate for their curriculum.

## Extension

This activity may be extended by asking students to evaluate if the original research associated with the stem cell-based intervention used the four bioethical principles. Additionally, students may read and discuss *Regenerative Medicine: Case Study for Understanding and Anticipating Emerging Science and Technology* (<https://nam.edu/perspectives/regenerative-medicine-case-study-for-understanding-and-anticipating-emerging-science-and-technology/>) produced by the National Academy of Medicine.

## Resources

Stem cell research is constantly changing; therefore, it is essential for teachers to update their resources by reviewing the current research. Some options include:

- UCSF Orthopaedic Surgery. (November 2, 2022). *The ethics behind unproven stem cell therapies with Zubin Master, PhD* [Video]. YouTube. <https://www.youtube.com/watch?v=seqF7akUfOU>
  - This podcast interviews bioethicist Zubin Master about what unproven stem cell treatments are and how to talk to physicians and patients about them. He discusses the importance of educating patients to reduce the demand for these treatments rather than simply regulating providers (22:59 watch time).

# Regenerative Medicine: Buy My Treatment (continued)

- Sipp, D., Caulfield, T., Kaye, J., Barfoot, J., Blackburn, C., Chan, S., De Luca, M., Kent, A., McCabe, C., Munsie, M., Sleeboom-Faulkner, M., Sugarman, J., van Zimmeren, E., Zarzeczny, A., & Rasko, J. E. J. (2017). *Marketing of unproven stem cell-based interventions: A call to action. Science Translational Medicine*, 9(397), eaag0426. <https://doi.org/10.1126/scitranslmed.aag0426>
  - This article summarizes the difficulty in regulating unproven stem cell treatments and suggests some options for moving forward in this field, including the importance of international cooperation (15 min. read time).
- Master, Z., Matthews, K. R. W., & Abou-el-Enein, M. (2021). *Unproven stem cell interventions: A global public health problem requiring global deliberation. Stem Cell Reports*, 16(6), 1435–1445. <https://doi.org/10.1016/j.stemcr.2021.05.004>
  - This article, co-written by Zubin Master, highlights the attempts to regulate unproven stem cell treatments in the U.S. and limitations in doing this (28 min. read time).
- CBS News. (2012, January 9). *Stem Cell Fraud: A 60 Minutes investigation* [Video]. YouTube. <https://www.youtube.com/watch?v=ovPZkQYee8Y>
  - This video introduces a family who took their child with cerebral palsy to receive an unproven stem cell treatment and their later participation in an investigation to expose a fraudulent stem cell clinic (16:10 watch time).
- CBS Chicago. (2018, November 15). *Doctors Sell False Hope With Unproven Stem Cell Treatments* [Video]. YouTube. <https://www.youtube.com/watch?v=KAfSFvEKTZg>
  - This video reports on fraudulent stem cell treatments, how they are advertised, and how they have affected several patients (6:42 watch time).
- Rice University’s Baker Institute for Public Policy. (n.d.). *Making stem cell interventions and advertisements safer and more effective: Recommendations for Texas*. Baker Institute. Retrieved from <https://www.bakerinstitute.org/research/making-stem-cell-interventions-and-advertisements-safer-and-more-effective-texas>
  - This article discusses ways that stem cell clinics advertise to customers, as well as recommendations about this advertising to help patients be more informed (12 min. read time).

# Regenerative Medicine: Buy My Treatment (continued)

The following three resources provide summaries of legal complaints against three different stem cell companies involving questionable advertisements.

- Federal Trade Commission. (2025, January 8). *Stem Cell Institute co-founders and companies banned from marketing stem cell treatments and ordered to pay more than \$5.1 million for refunds and civil penalties* [Press release]. FTC. <https://www.ftc.gov/news-events/news/press-releases/2025/01/stem-cell-institute-co-founders-companies-banned-marketing-stem-cell-treatments-ordered-pay-more-51>
  - This article discusses the legal judgement against the Stem Cell Institute of America clinic for fraudulent advertising (2 min. read time).
- New York Attorney General Letitia James. (2019, April 4). *Attorney General James announces lawsuit against New York City stem cell clinic for scamming vulnerable patients out of thousands* [Press release]. New York State Office of the Attorney General. <https://ag.ny.gov/press-release/2019/attorney-general-james-announces-lawsuit-against-new-york-city-stem-cell-clinic>
  - This article discusses a complaint against Park Avenue Stem Cell for fraudulent advertising (3 min. read time).
- Associated Press. (2024, June 15). *Some hawking stem cells say they can treat almost anything. They can't.* AP News. <https://apnews.com/article/23789b100f28a9abda6e287773369790>
  - This article describes complaints against Summit Health Centers as well as how the center advertised to patients (6 min. read time).

## Sample advertisements:

- Advertisements from Stem Cell Institute of America (also linked on FTC webpage, ads on pages 13-29): [https://www.ftc.gov/system/files/documents/cases/1.\\_complaint.pdf](https://www.ftc.gov/system/files/documents/cases/1._complaint.pdf)
- Advertisements from Park Avenue Stem Cell (also listed on New York AG's webpage, ads on pages 6-21): [https://ag.ny.gov/sites/default/files/park\\_ave\\_stem\\_cell\\_clinic\\_complaint.pdf](https://ag.ny.gov/sites/default/files/park_ave_stem_cell_clinic_complaint.pdf)
- Advertisements from Summit Health Centers (also linked in AP News article, ads on pages 13-23): [https://www.iowaattorneygeneral.gov/media/cms/05771\\_EQCE089356\\_PFLD\\_12442054\\_2FF7FDC6D0BFC.PDF](https://www.iowaattorneygeneral.gov/media/cms/05771_EQCE089356_PFLD_12442054_2FF7FDC6D0BFC.PDF)

# Regenerative Medicine: Buy My Treatment (continued)

## Rubric for Regenerative Medicine: Buy My Treatment Assignment

Category/ Points	4	3	2	1
Notes and sources	Student took notes for each section and correctly cites sources of all information.	Student took notes for most sections (six or more) and shows sources of most information.	Student took notes for at least three sections and shows sources for some information.	Student found little information or does not show any sources. Cites none of the pictures used.
Content of stem cell-based intervention research	Shows an understanding of multiple ways stem cell-based interventions are advertised.	Shows a good understanding of how stem cell-based interventions are advertised.	Shows partial understanding of how stem cell-based interventions are advertised.	Does not seem to understand how stem cell-based interventions are advertised.
Current nature of sources	All material taken from current sources.	Presents current material 90% to 95% of the time.	Presents current material 75% to 89% of the time.	Presents little to no current material.
Advertising guidelines	Creates a set of advertising guidelines that address each of the four bioethical principles.	Creates a set of advertising guidelines that address two to three of the four bioethical principles.	Creates a set of advertising guidelines that address at least one bioethical principle.	Discusses advertising issues and/or does not create a set of advertising guidelines that address the bioethical principles.
Presentation	Speaks clearly with correct pronunciation of terms. Maintains eye contact. Presents the information in a logical and interesting process.	Speaks clearly with mostly correct pronunciation of terms. Maintains eye contact most of the time. Presents the information in a logical process.	Occasionally speaks clearly with some correct pronunciation of terms. Maintains eye contact sometimes but reads most of the presentation. Difficult to follow presentation.	Does not speak clearly or pronounce terms. Lack of eye contact because the presentation is read. Unable to follow presentation.

# Regenerative Medicine: Buy My Treatment — Student Worksheet

As a legislative advisory committee, it is your responsibility to create advertisement guidelines for stem cell-based interventions. You will be researching stem cell-based interventions and associated advertisements. After you have completed the research, create a set of advertising guidelines that integrate bioethical principles. At the end of this process, you will have the opportunity to pitch your guidelines to the legislative advisory committee (your classmates).

<b>Ethical Principle</b>	<b>Advertising Guideline</b>	<b>Reasoning</b>
Autonomy		
Beneficence		
Non-maleficence		
Justice		

# Careers in Regenerative Medicine

Regenerative medicine depends on bringing together fundamental research from many areas of medicine. It also depends on moving research from basic science to animal trials to clinical trials in humans, and eventually to patient care. This can be done more efficiently with a large, coordinated team approach than with the more traditional academic departments in which each senior scientist leads an independent research team. At WFIRM, for example, teams of scientists working together include molecular biologists, cell biologists, physiologists, pharmacologists, biomedical engineers, surgeons, veterinarians and others.

## **Focus on Technicians: Katie Benson**

Katie Benson is a Core Technician at the RegeneratOR Test Bed lab. A collaboration of WFIRM and RegenMed Development Organization, the Test Bed provides free space to companies working to develop regenerative medicine technologies. Scientists from these companies work side by side in the Test Bed with WFIRM researchers and lab techs like Katie. The lab contains specialized, state-of-the-art biotechnology. One example of this is the Biospheric Xvivo X2, a closed system that keeps cells in a consistent, optimal environment for a tenth of the cost of a traditional lab clean room. The hope of researchers at WFIRM is that the Test Bed can help companies create regenerative medicine treatments that can be scaled up more easily and precisely, and that the free lab space and equipment will translate into companies being able to develop more of these treatments. This matches what Katie sees as the overall goal of regenerative medicine: getting treatments into patients.

Katie wasn't always interested in regenerative medicine. She received her Bachelor of Arts in Music from Wake Forest University and worked in animal rescue and welfare for 11 years. She loved the job, but after more than a decade of working seven days a week, she was burned out and wanted to change careers. One day, she saw a video about Dr. Anthony Atala's work at WFIRM implanting lab-grown bladders into children. From then on, she decided she wanted to work in regenerative medicine, so she enrolled at Forsyth Technical Community College to earn her associate degree in applied science in biotechnology. While there, she completed an internship at WFIRM, which led to a job there as a Core Technician after graduation. Katie says that she uses things she learned in school every day in her job at WFIRM. For high schoolers interested in a career in regenerative medicine, Katie says that organizations are looking for skills beyond micropipetting or other lab techniques. In the Test Bed, she works elbow-to-elbow with other lab techs and researchers, so having

# Careers in Regenerative Medicine (continued)

solid people skills is important when applying for lab jobs.

## **Focus on Student Scientists: Caleb Heathershaw**

Caleb Heathershaw is a Ph.D. student at WFIRM. He works in the lab of Dr. Joshua Maxwell studying in vitro models of heart attacks in humans using iPSC-derived cardiomyocytes (muscle cells responsible for the force behind pumping blood). Because these iPSC-derived cells behave like pacemaker cells (cells that generate electrical impulses that cause the heart to pump), clumps of them together will begin to contract, forming a cardiac organoid that can be studied in a similar way to the contractions of a full-sized human heart.

The process of working in a lab comes in seasons for Caleb. The first season is cell culturing — making sure the cardiac organoids are healthy and functioning. Next comes an experimental period, where the cardiac organoids are exposed to an anaerobic environment. Hypoxia (lack of oxygen) is a primary cause of heart attacks. Different drugs are added to the organoids to see how they react. They are visualized under a microscope, and their contractility is measured. Third, Caleb and the research team gather and analyze the data, and finally the team puts together a poster presentation, or academic paper to communicate their findings. For Caleb, the most challenging parts of his job are doing paperwork and statistical analysis. His favorite parts of his job are talking about science, doing cell culture work, running experiments and watching his cardiac organoids contract under the microscope.

Caleb's interest in science began at a young age. As a middle schooler living in Wilkesboro, N.C., Caleb was interested in herpetology, the study of reptile and amphibian biology. When his family moved to Florida, he began taking dual enrollment classes and became interested in regenerative medicine through a TedTalk by Dr. Anthony Atala. Dr. Atala raised a simple question, "If a salamander can regrow its arm, why can't we?" Caleb pursued a bachelor's degree in biomedical engineering at the University of Miami, doing research in a lab working with cardiac iPSCs. After that, he moved back to North Carolina, 45 minutes from where he grew up, to study at WFIRM. He emphasized that experiences that weren't STEM-related have helped him in his research — his time playing piano improved his hand-eye coordination, which gives him an advantage in pipetting tiny organoids between wells in a plate, while his past speech and debate experience helps him accomplish his goal of making science accessible to multiple audiences. Caleb's advice to students is to look closely,

# Careers in Regenerative Medicine (continued)

stay curious, and listen to your heart. Or, at least study it.

## **Focus on Scientists: Graça Almeida-Porada**

Dr. Graça Almeida-Porada is a professor at WFIRM, and the director of the Fetal Research and Therapy Program. She obtained her M.D. in 1985 from the University of Porto, Portugal, and her Ph.D. from the same school in 1995. She worked as a physician in Portugal and in the U.S. and was a faculty member at several universities before joining WFIRM. She has been the principal investigator (PI) of grants funded by NIH and the USDA, served as the co-editor-in-chief of *Current Stem Cell Reports*, and co-founded the International Fetal Transplant and Immunology Society.

Dr. Almeida-Porada studies ways to use stem cells to treat and cure genetic disorders in the womb. Because of improvements in technology, severe genetic disorders are being diagnosed earlier than ever before, giving a wider window in which patients can be treated. Fetuses do not have a fully developed immune system, so they are less likely to have an adverse reaction to the introduction of stem cells as part of a treatment. In addition, fetuses have more capacity to regenerate cells and tissues, so treatments may be more effective in fetuses than in adults. Dr. Almeida-Porada and her team focus on prenatal treatments of sickle cell disease and hemophilia A using multipotent stem cells (*for more information, see “Curing Hemophilia Before Birth” on page Unit IV-4.27*).

Dr. Almeida-Porada was encouraged in her childhood interests in science and math by her family. Her father exposed her to engineering and built electronic devices and Morse code keys with her and her siblings. Her mother and teachers promoted women studying science and taught her that there were no limits to what one should aspire. She firmly believes that children should be introduced to science early in school, and that experiential learning should always be a part of the curriculum. In high school, she was inspired to pursue science, in part because of the opportunity for hands-on experimentation not present in other subjects. She has combined her interests in research and medical knowledge to become a pioneer in a field that has the potential to change how we treat genetic disorders.