Summary:
Students read about adult and embryonic stem cells. They sequence pictures of the steps used to create an embryonic stem cell line. They use simulated stem cells and growth factors from differentiated cells that could be used to treat diseases.

Core concepts:
- Stem cells are unspecialized cells that have the potential to form new stem cells or to differentiate into more specialized types of cells.
- Embryonic stem cell lines can be created from donated embryos.
- Growth factors can be used to make stem cells differentiate into specialized cell types.

Class time required:
Two 40-minute class periods

Additional Resources (optional):
Visit the Life Sciences Learning Center website to explore extension activities, videos, and slide shows that can be used to accompany this lab activity.
http://lifesciences.envmed.rochester.edu/downloads.html

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Preparing lab materials:

1. For each student lab group, label 8 microtubes (or small test tubes) and 8 droppers with the following labels: Adult Stem Cells - ASC, Embryonic Stem Cells - ESC, GFA, GFB, GFC, GF1, GF2, and GF3.

2. Prepare the solutions indicated in the chart below and fill the labeled tubes.

<table>
<thead>
<tr>
<th>Label on tubes and droppers</th>
<th>Solution</th>
<th>Amount of solution needed per lab team</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryonic Stem Cells - ESC</td>
<td>0.1% bromothymol blue</td>
<td>2 ml</td>
</tr>
<tr>
<td>Adult Stem Cells - ASC</td>
<td>100 ml water + 1 drop india ink + 1 drop yellow food color</td>
<td>2 ml</td>
</tr>
<tr>
<td>GF A</td>
<td>0.05% methyl red</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>GF B</td>
<td>0.05% methyl red</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>GF C</td>
<td>0.05% methyl red</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>GF 1</td>
<td>100 ml pH 3 buffer + 2 drops yellow food color</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>GF 2</td>
<td>100 ml pH 7 buffer + 2 drops yellow food color</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>GF 3</td>
<td>100 ml pH 10 buffer + 2 drops yellow food color</td>
<td>0.5 ml</td>
</tr>
</tbody>
</table>

3. Each student lab group gets the following materials (see the Quick Guide graphic):
   - 8 labeled droppers: Adult Stem Cells - ASC, Embryonic Stem Cells - ESC, GFA, GFB, GFC, GF1, GF2, and GF3
   - 8 labeled, filled tubes: Adult Stem Cells - ASC, Embryonic Stem Cells - ESC, GFA, GFB, GFC, GF1, GF2, and GF3
   - 1 microtube rack (optional)
   - 6 “Culture Cups” – use small (1 oz.) condiment cups or a spot plate with at least 6 depressions
   - 1 Growth Factors (GF) Involved in Stem Cell Differentiation diagram
   - Scissors

4. Each student gets the following materials:
   - 1 copy of Stem Cells student instructions
   - 1 copy of Development Diagram Sheet
   - Goggles
   - Gloves (optional)
A. Zygote
B. 4 cell stage embryo
C. Egg
D. Egg
E. Blastocyst
F. Many cell stage embryo
G. 2 cell stage embryo
H. Continued mitosis
I. Blastocyst
J. Transfer cell to culture dish

Development Diagram Sheet
Growth Factors (GF) and Stem Cell Differentiation Flow Chart

Heart Muscle Cell (Red)

GF-1

GF-A

Embryonic Stem Cells

GF-B

GF-2

Nerve Cells (Green)

GF-C

Pancreas Cells (Blue)

GF-3
Quick Guide:

Embryonic Stem Cells (ESC)

Adult Stem Cells (ASC)

GF 1

GF 2

GF 3

GF A

GF B

GF C

Culture Cups

Microtube Rack
Stem Cells: **Teacher Answer Key**

**Part 1: What is a Stem Cell?**

Stem cells differ from other kinds of cells in the body. When a stem cell divides by mitosis, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function. All stem cells—regardless of their source—have three special properties:

1. **Stem cells are unspecialized.** A stem cell does not have any tissue-specific structures that allow it to perform specialized functions. For example, a stem cell cannot work with its neighbors to pump blood through the body (like a heart muscle cell), cannot carry oxygen molecules through the bloodstream (like a red blood cell) or carry impulses (like nerve cells).

2. **Stem cells are capable of dividing and self-renewing continually.** Specialized cells like muscle cells, blood cells, or nerve cells normally do not divide. Stem cells can self-renew by dividing many times to produce millions of stem cells.

3. **Stem cells differentiate into specialized cells.** When unspecialized stem cells give rise to specialized cells, the process is called differentiation. The specialized cells that form from stem cells can be very different from one another, even though they have the same genetic instructions. This is because different genes in stem cells are used (turned on) in different types of cells and are influenced by the cell’s environment.

1. Stem cells are **unspecialized.** What does this mean?

   *A stem cell does not have any tissue-specific structures that allow it to perform specialized functions.*

2. Stem cells can **self-renew.** What does this mean?

   *Stem cells may divide many times to produce millions of stem cells.*

3. Stem cells can **differentiate.** What does this mean?

   *Stem cells can give rise to specialized cells that can be very different from one another.*
Stem Cells in the Lab

Scientists are already using stem cells in the laboratory. For example, stem cells are being used to study normal tissue development and to identify the causes of birth defects. Scientists are looking for ways to use stem cells to treat diseases such as diabetes, and heart disease. However, much work remains to be done in the laboratory and the clinic to understand how to use stem cells to treat disease.

The stem cells that scientists use for laboratory research come from two different sources.

Adult Stem Cells

Some fetal or adult tissues (such as umbilical cord blood, bone marrow, muscle, and brain) contain adult stem cells that produce cells to replace ones that are lost through normal wear and tear, injury, or disease. Adult stem cells can be isolated and grown in special conditions in the laboratory. Under proper conditions, adult stem cells can divide but they can only differentiate into a limited number of tissue types.

Embryonic Stem Cells

Embryos contain stem cells that have the remarkable potential to develop into the different cell types in the body. Embryonic stem cells can be isolated and grown in special conditions in a laboratory. Under proper conditions, embryonic stem cells can divide and differentiate to form all tissue types in the adult body. However, embryonic stem cells cannot develop into an entire fetus or adult because they cannot form tissues such as the placenta and umbilical cord that provide nourishment to a developing embryo.
4. What are the two types of stem cells?

   *Embryonic and adult stem cells*

5. Which type of stem cell is capable of dividing and differentiating into any cell type?

   *Embryonic stem cells*

6. Explain why embryonic stem cells cannot be used to make a baby.

   *Embryonic stem cells cannot develop into an entire fetal or adult organism because they cannot form tissues such as the placenta that provide nourishment to a developing embryo.*

7. Why do scientists think it is important to do research using stem cells?

   *Scientists are already using stem cells in the laboratory to study normal tissue development and identify the causes of birth defects. Stem cells offer new potentials for treating diseases such as diabetes, and heart disease.*
Part 2: Creating Embryonic Stem Cell Lines

Scientists are currently doing research using embryonic stem cell lines. A cell line is a group of cells grown under special conditions in a laboratory. All cells in a specific cell line are genetically identical. In this activity, you will use diagrams to help you understand how an embryonic stem cell line is produced.

1. Your kit contains a Development Diagram Sheet with cards that illustrate the steps for making an embryonic stem cell line. Cut along the dotted lines on this sheet to make a set of diagram cards (A-J).

2. Read the information in the brief article below.

In Vitro Fertilization (IVF) to make embryonic stem cells

In vitro fertilization (IVF) offers infertile couples a chance to have a child who is biologically related to them. With IVF, a method of assisted reproduction, a man’s sperm and a woman's eggs are combined in a laboratory dish (“in vitro”), where fertilization occurs to form a zygote (fertilized egg). Then the zygote begins to divide by mitosis.

After many mitotic divisions in a laboratory dish, a blastocyst is formed. A blastocyst is a four to five day old embryo made of about 100 cells that each contain DNA from both of the parents. For assisted reproduction, between two and four of the blastocysts may be transferred to the woman’s uterus (womb) to implant and hopefully develop into a baby. Extra (“left-over”) embryos may be stored for future use or may be donated for use in embryonic stem cell research.

Scientists can use donated blastocysts to create embryonic stem cell lines. To do this, they remove cells from the inner cell mass of a blastocyst and transfer these cells into another laboratory culture dish. The transferred cells then divide by mitosis to form many identical stem cells that can be used for research.

3. Use the information in the reading passage to arrange the diagram cards in the correct sequence to illustrate how in vitro fertilization is used to create an embryonic stem cell line.

4. Once you have arranged the cards in the correct sequence, record the order of the cards by writing the letters of the cards in the correct sequence on the lines below.

   C  D  A  G  B  F  E  I  J  H

5. Using the cards as a source of information, explain (in your own words) how in vitro fertilization is used to produce an embryonic stem cell line.

   Cells are removed from a blastocyst and transferred to a culture dish where they grow and divide.
Part 3: Could Stem Cells Be Used to Treat Disease?

If scientists can make stem cells differentiate into specialized cells, these differentiated cells could then be transplanted into patients to replace cells lost or damaged by disease. In the future, stem cells may be used to treat diseases such as spinal cord injury, diabetes, and heart disease.

To make stem cells differentiate into specialized types of cells, scientists place them in environments that contain signal molecules called growth factors. These growth factors include proteins and other molecules that turn on, or turn off, the expression of specific genes that lead to specific cell structures and functions.

In this simulation you will begin with “cultures” of embryonic and adult stem cells and tubes of growth factors (signal molecules). By selecting a certain sequences of growth factors you may be able to create differentiated cells that could be used to treat different diseases.

A. Using EMBRYONIC stem cells to treat diseases

Imagine you are a scientist who would like to use the embryonic stem cells to produce three types of differentiated cells that could be used to treat three different diseases:

- Muscle cells used to treat heart damage
- Nerve cells used to treat spinal damage
- Pancreas cells used to treat diabetes

Your kit contains a tube of embryonic stem cells and 6 different types of growth factors (GF-A, GF-B, GF-C, GF-1, GF-2 and GF-3). Your job is to decide which growth factors to use to turn the embryonic stem cells into specific types of differentiated cells.

1. Use the information on the Growth Factors and Stem Cell Differentiation Flow Chart in your lab kit to complete Column 1, Column 2, and Column 3 of Data Table 1 below. You will complete Column 4 in later steps.

Data Table 1: Using Embryonic Stem Cells to Treat Disease

<table>
<thead>
<tr>
<th>Type of differentiated cell you are trying to produce from embryonic stem cells</th>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
<th>Column 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle cells used to treat heart damage</td>
<td>GF-A</td>
<td>GF-1</td>
<td>red</td>
<td>Yes</td>
</tr>
<tr>
<td>Nerve cells used to treat spinal cord damage</td>
<td>GF-B</td>
<td>GF-2</td>
<td>green</td>
<td>Yes</td>
</tr>
<tr>
<td>Pancreas cells used to treat diabetes</td>
<td>GF-C</td>
<td>GF-3</td>
<td>blue</td>
<td>Yes</td>
</tr>
</tbody>
</table>
You will now use the information from your data table to see if you can get embryonic stem cells to differentiate into each of the cell types: muscle cells, nerve cells, and pancreas cells.

2. Use the information from your data table to see if you can get embryonic stem cells to differentiate into **muscle cells** that could be used to treat heart disease.
   - Use the “ESC” dropper to add 10 drops of embryonic stem cell culture to a clean small cup.
   - Add one drop of the *first* growth factor you selected (GF-A, GF-B, or GF-C) then add one drop of the *second* growth factor (GF-1, GF-2, or GF-3). *Hint: It is easier to see the resulting colors if you put the small cup on a white background.*
   - If you succeeded in turning embryonic stem cells into muscle cells that could be used to treat heart damage, write “Yes” in Column 4 of the appropriate row on Data Table 1. If not, write “No.”

3. Use the information from your data table to see if you can get embryonic stem cells to differentiate into **nerve cells** that could be used to treat heart damage.
   - Use the “ESC” dropper to add 10 drops of embryonic stem cell culture to a clean small cup.
   - Add one drop of the first growth factor you selected then add one drop of the second growth factor.
   - If you succeeded in turning embryonic stem cells into nerve cells that could be used to treat spinal cord injuries, write “Yes” in Column 4 of the appropriate row on Data Table 1. If not, write “No.”

4. Use the information from your data table to see if you can get embryonic stem cells to differentiate into **pancreas cells** that could be used to treat diabetes.
   - Use the “ESC” dropper to add 10 drops of embryonic stem cell culture to a clean small cup.
   - Add one drop of the first growth factor you selected then add one drop of the second growth factor.
   - If you succeeded in turning embryonic stem cells into pancreas cells that could be used to treat diabetes, write “Yes” in Column 4 of the appropriate row on Data Table 1. If not, write “No.”

5. In this part of the lab (Part 3 A), you treated **embryonic** stem cells with growth factors. Summarize the results of your experiment by listing the types of specialized cells that you produced and the types of conditions that these cells could be used to treat.

   *Treatment with growth factors can change embryonic stem cells into muscle, nerve, and pancreas cells. These cells could be used to treat heart damage, spinal cord damage, and diabetes.*
B. Using ADULT stem cells to treat disease

Bone marrow stem cells usually divide and differentiate to only form red blood cells, white blood cells, or platelets. You wonder if you could use adult stem cells isolated from bone marrow, instead of embryonic stem cells, to treat heart damage, spinal cord injuries, or diabetes.

You want to see if you can add specific growth factors to adult bone marrow stem cells so that the adult bone marrow cells will differentiate into muscle cells, nerve cells, or pancreas cells.

1. Do you think that the information on the Growth Factors and Stem Cell Differentiation Flow Chart could be used to make bone marrow stem cells differentiate into muscle cells, nerve cells, and pancreas cells? Explain why or why not.

   Student answers will vary. Accept any reasonable answer that is supported by an explanation. Students may say “NO, because this chart is only for embryonic stem cells. Students may say “Yes, because embryonic and adult stem cells are similar.

2. Use the information on the Growth Factors and Stem Cell Differentiation flow chart in your kit to complete the Columns 1, 2 and 3 on Data Table 2 below.

Data Table 2: Using Adult Stem Cells to Treat Disease

<table>
<thead>
<tr>
<th>Type of differentiated cell you are trying to produce from adult stem cells</th>
<th>Column 1</th>
<th>Column 2</th>
<th>Column 3</th>
<th>Column 4</th>
</tr>
</thead>
<tbody>
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<td>No</td>
</tr>
<tr>
<td>Pancreas cells used to treat diabetes</td>
<td>GF-C</td>
<td>GF-3</td>
<td>blue</td>
<td>No</td>
</tr>
</tbody>
</table>

3. You will now use the tube of adult stem cells (ASC) in your kit, the growth factors, and the information from your data table to see if you can get adult stem cells to differentiate into each of the cell types: muscle cells, nerve cells, and pancreas cells.

   For each cell type, remember to:
   - Use the “ASC” dropper to add 10 drops of adult stem cell culture (ASC) to a clean small cup.
   - Add one drop of the first growth factor you selected then add one drop of the second growth factor.
   - If you succeeded in turning adult stem cells into each of the cell types, write “Yes” in Column 4 of the appropriate row on Data Table 1. If not, write “No.”
4. In this part of the lab (Part 3 B), you treated adult stem cells with growth factors. Summarize the results of your experiment by listing the types of specialized cells that you produced and the types of health conditions that these cells could be used to treat.

*Treatment with growth factors can change adult stem cells into muscle cells. That could be used to treat heart damage.*

5. Based on the results of your experiments with embryonic and adult stem cells, why do you think scientists feel it is important to be able to do research using embryonic stem cells?

*Embryonic stem cells can differentiate into more cell types than adult stem cells or can be used to treat more types of disease.*

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Human embryonic stem cell research is controversial because the current technology requires destruction of embryos. Opponents of embryonic stem cell research argue that a human embryo is a human life that should not be destroyed. Supporters of embryonic stem cell research argue that this research should be pursued because embryonic stem cells are more likely to result in treatments for a variety of diseases. They also note that excess embryos created for in vitro fertilization could be donated with consent and used for the research.

6. Explain why opponents of stem cell research think that scientists SHOULD NOT be allowed to do research using embryonic stem cells.

*They think that it is not ethical to destroy embryos for research*

7. Explain why supporters of stem cell research think that scientists SHOULD be allowed to do research using embryonic stem cells.

*They think that this research is more likely to result in treatments for different diseases OR they think that it is acceptable to use excess embryos donated for research.*