14 Stem Cell Differentiation

INVESTIGATION • 1 CLASS SESSION

OVERVIEW

To investigate how embryonic stem cells become specialized cells, students draw from a set of colored chips that represent specific molecular factors that determine the next step of specialization. They discuss the paths stem cells take as they differentiate into specialized cells.

KEY CONTENT

1. Stem cells can produce a variety of specialized cells.
2. The process by which stem cells produce specialized descendent cells is called differentiation.

MATERIALS AND ADVANCE PREPARATION

For the teacher

Transparency 14.1, "The Organization of Multicellular Organisms"

For each pair of students

cup containing 9 chips (3 green, 3 blue, 3 orange)

3 colored pencils

For each student

Student Sheet 14.1, "Stem Cell Differentiation"

TEACHING SUMMARY

Getting Started

- Discuss the process of differentiation in producing the many types of specialized cells in a multicellular organism, such as a human.

Doing the Activity

- Students complete the investigation.

Follow-up

- The class discusses the importance of stem cell differentiation.

BACKGROUND INFORMATION

Stem cells and precursors cells

A stem call produces daughter cells that might remain as stem cells or begin a pathway of differentiation into one of a variety of specialized cell types. Stem cells are classified into three groups, depending on where they are on the pathway toward differentiation. Totipotent stem cells can produce any kind of cell in the body, and have an unlimited ability to self-renew. The embryonic cells that form during the first few divisions after an egg is fertilized are totipotent. Pluripotent stem cells can become almost any type of cell in the body, except the cells of the placenta and certain other uterine tissues. Totipotent stem cells become pluripotent after three or four divisions. Multipotent stem cells produce only certain types of cells. For example, one line of multipotent stem cells gives rise to all the blood cells, including red and white blood cells. Adult stem cells are multipotent.

Precursor (or progenitor) cells are immature cells that are precursors to a fully differentiated cell of the same tissue type. They are in a stage between a stem cell and a fully differentiated cell. Precursor cells are usually unipotent (capable of developing into only one type of cell). They multiply quickly and regenerate tissue, but are limited in the type(s) of cell they produce. For example, a lymphoid precursor cell might be able to make only T lymphocytes.

In this activity students focus on the differentiation of embryonic stem cells. Embryonic stem cells come from five-day-old pre-implantation embryos created at fertility clinics. They develop into the cells and tissues of the three primary germ layers—endoderm, mesoderm, and ectoderm.

GETTING STARTED

1 Project Transparency 14.1, "The Organization of Multicellular Organisms." Ask students to name some organs in the human body. Likely suggestions are the heart, liver, and kidney. Explain that all of these organs are made of specialized tissues and cells. As students have learned, specialized cells have specialized arrangements of structures and organelles that allow them to perform their specific function. Ask, *How do you think all of the specialized cells that make up your body develop?*

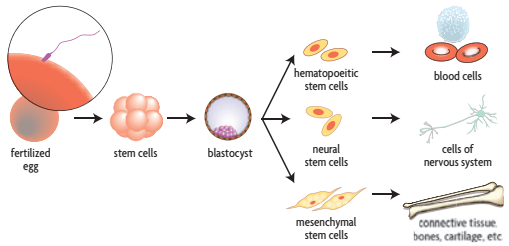
Accept students' ideas. They will likely state that something happens during development of the embryo. Explain that all cells start as identical stem cells in a developing embryo, and that these embryonic stem cells are capable of producing all cell types. The process in which stem cells become specialized cells is called **differentiation.** Emphasize that a stem cell itself does not become a differentiated cell, but one or both of its daughter cells may change in some way. These cells, in turn, produce daughter cells that are different from the parent cell, until a fully specialized cell results. Explain to students that they will investigate a simplified model of stem cell differentiation in this activity. Instruct them to read the introduction.

14 Stem Cell Differentiation

1 THE HUMAN BODY is made of many kinds of specialized cells. Red blood cells, white blood cells, muscle cells, nerve cells, and skin cells are just some examples. Each specialized cell performs a function in the body. You have learned about several conditions that result when cells don't function normally. Diabetes damages the cells in the pancreas that make insulin. Sickle cell disease is a genetic condition that alters the functioning of the hemoglobin protein in red blood cells. And many kinds of cells may become cancerous when they lose their normal cell cycle controls.

Every cell in your body is the offspring of another cell and has the same genetic material as the fertilized egg from which it developed. It is amazing that the many different types of cells all arise from a single fertilized egg cell. Yet that is what happens during embryo development. Initially, all the cells in the embryo are alike. But as they divide, they become more specialized and produce their own characteristic proteins. Cells that have the ability to produce a variety of types of specialized cells are called **stem cells.** The process by which stem cells produce specialized cells is called **differentiation.** As differentiation progresses, segments of the genetic material are either activated or suppressed.

You have probably heard about stem cell research in the news. This is an important area of cutting-edge research. Once we understand exactly how a human develops from a single cell to a multicellular organism we might learn how certain conditions, such as some birth defects, and diseases, such as cancer, develop. Researchers around the world are trying to figure out how stem cells might be used to replace diseased or damaged tissues in any number of diseases.



The development of specialized cells from stem cells.

236

DOING THE ACTIVITY

2 Distribute Student Sheet 14.1, "Stem Cell Differentiation." Explain to students that the chart is a representation of some of the types of stem cells in the body and some of the types of cells that differentiate from the stem cells. It does not include every type of stem cell or differentiated cell in the body. Circulate around the room to monitor students' progress through the Procedure, and answer questions when necessary. You may want to tell students that many of the molecular differentiation factors represented by the chips are proteins, and are classified as signaling proteins.

In this activity, you will learn about the differentiation of human stem cells. In the next activity you will have a chance to apply what you learn about stem cells to stem cells' potential for curing diseases.

Challenge

How do stem cells produce specialized cells?

MATERIALS

FOR EACH PAIR OF STUDENTS

cup containing 9 chips (3 blue, 3 green, 3 orange)
3 colored pencils

FOR EACH STUDENT

Student Sheet 14.1, "Stem Cell Differentiation"

2 Procedure

1. The colors of the chips in the cup represent the specific protein or chemical factor that directs the differentiation of an embryonic stem cell. You and your partner will share the cup of chips, but you will each draw your own chips and follow your own cell on Student Sheet 14.1, "Stem Cell Differentiation." With your partner, decide who will begin. Take turns drawing one chip from the cup. When drawing a chip, look away to make sure your selection is random. Use the key below to find out how your stem cell differentiates. Put the chip back in the cup before your partner draws a chip. Select a colored pencil. On Student Sheet 14.1, draw a line from the embryonic stem cell to the type of stem cell it produced.

   Note: Differentiation cannot be reversed from this point forward.

Differentiation Key 1

DIFFERENTIATION PROTEIN (CHIP COLOR)	STEM CELL TYPE PRODUCED
Blue	Endoderm—the innermost layer of cells in an embryo These cells develop into the linings of the digestive tract and most of the respiratory system.
Green	Mesoderm—the middle layer of cells in an embryo These cells develop into muscles and most of the circulatory, reproductive, and excretory organ systems.
Orange	Ectoderm—the outermost layer of cells in an embryo These cells develop into sense organs, nerves, and the outer layer of skin.

2. Have the second person draw one chip and repeat Step 1.

3. Take turns drawing a second chip from the cup to represent the next step in the pathway of differentiation from the same stem cell. Use the key below to find out how your differentiated cell differentiates further. Sometimes, a protein will have no effect on a certain stem cell. If the factor has no effect, take a chip of another color. Put all of the chips back in the cup before your partner draws again.

Differentiation Key 2

DIFFERENTIATION FACTOR (CHIP COLOR)	ENDODERM	MESODERM	ECTODERM
Blue	no effect	hematopoietic (blood-forming) stem cell	skin precursor cell
Green	pancreas precursor cell	no effect	no effect
Orange	intestinal epithelial stem cell	muscle stem cell	neural stem cell

On your Student Sheet 14.1, "Stem Cell Differentiation," using the colored pencil you used before, draw a line to show the next step in your cell's differentiation.

4. Take turns drawing a third chip. Using the colored pencil you used before, draw a line from your cell from Step 3 to the next type of cell on Student Sheet 14.1, based on the color key below. If the factor has no effect, draw another chip. Put all of the chips back in the cup before your partner draws chips.

Differentiation Key 3

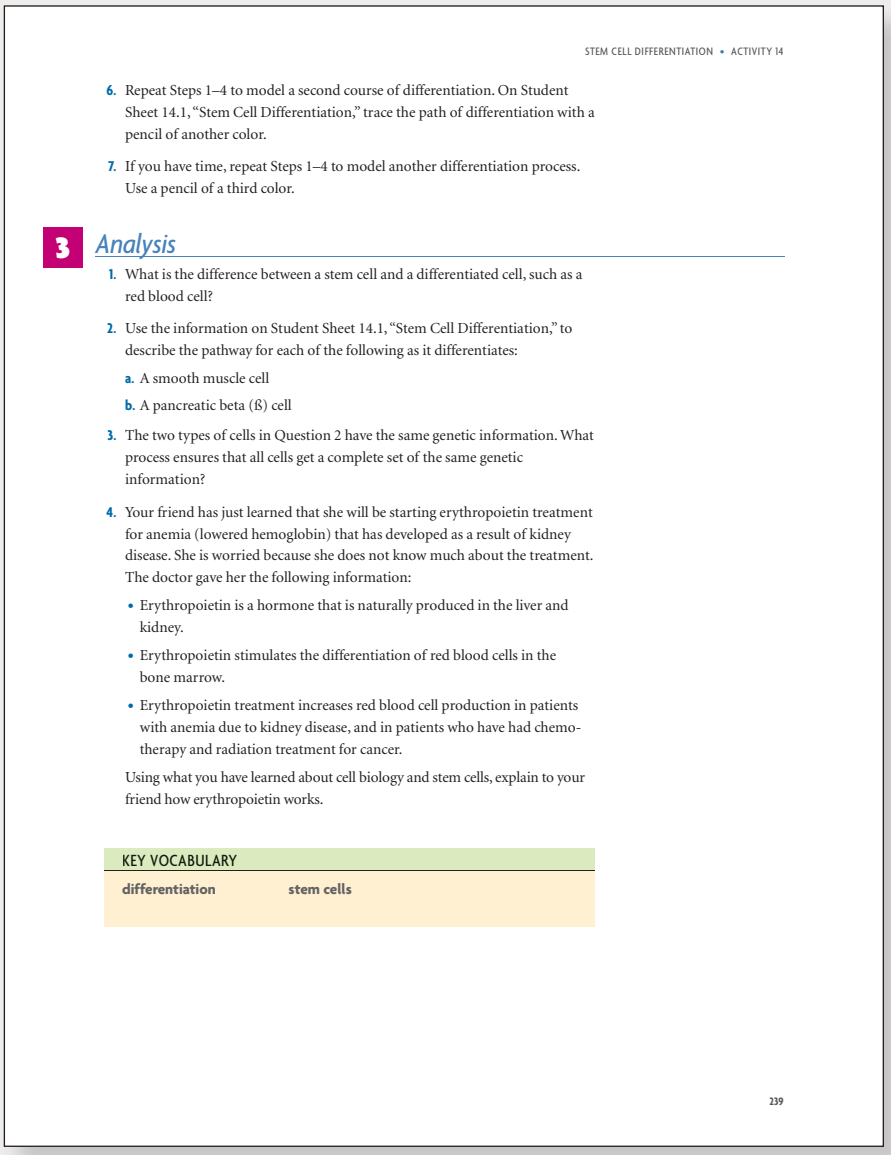
	PANCREAS PRECURSOR CELL	INTESTINAL STEM CELL	MUSCLE STEM CELL	HEMATOPOIETIC (BLOOD-FORMING) STEM CELL	SKIN PRECURSOR CELL	NEURAL STEM CELL
Blue	no effect	no effect	heart muscle cell (differentiation complete)	macrophage (differentiation complete)	hair follicle cells (differentiation complete)	motor neuron (differentiation complete)
Green	alpha (α) cell producing glucagon (differentiation complete)	intestinal epithelial cell (differentiation complete)	no effect	no effect	no effect	no effect
Orange	beta (β) cell producing insulin (differentiation complete)	no effect	smooth muscle cell (differentiation complete)	**red blood cell (differentiation complete)**	**cheek lining cell (differentiation complete)**	**photoreceptor (differentiation complete)**

5. Show the path of differentiation of your embryonic stem cells to your group. Discuss the various paths of differentiation that occurred for each person in the group.

FOLLOW-UP

3 Emphasize that specialized cells each produce specific proteins that they need for performing their specialized functions. In the *Science and Global Issues* "Genetics: Feeding the World" unit, students will learn about the processes that regulate gene expression and determine the proteins a cell produces. Instruct students to go back to the introduction of the activity and re-read the third paragraph. Ask, *Now that you know more about stem cells and differentiation, why do you think scientists think stem cells are the key to replacing diseased or damaged tissues in patients with heart disease, cancer, or diabetes?*

Since stem cells are capable of becoming a variety of specialized cells, if these cells can be put into humans who have diseased cells of a given type, they could develop into healthy cells and perhaps treat or prevent a disease.



STEM CELL DIFFERENTIATION • ACTIVITY 14

6. Repeat Steps 1–4 to model a second course of differentiation. On Student Sheet 14.1, "Stem Cell Differentiation," trace the path of differentiation with a pencil of another color.
7. If you have time, repeat Steps 1–4 to model another differentiation process. Use a pencil of a third color.

3 *Analysis*

1. What is the difference between a stem cell and a differentiated cell, such as a red blood cell?
2. Use the information on Student Sheet 14.1, "Stem Cell Differentiation," to describe the pathway for each of the following as it differentiates:
   a. A smooth muscle cell
   b. A pancreatic beta (ß) cell
3. The two types of cells in Question 2 have the same genetic information. What process ensures that all cells get a complete set of the same genetic information?
4. Your friend has just learned that she will be starting erythropoietin treatment for anemia (lowered hemoglobin) that has developed as a result of kidney disease. She is worried because she does not know much about the treatment. The doctor gave her the following information:
   - Erythropoietin is a hormone that is naturally produced in the liver and kidney.
   - Erythropoietin stimulates the differentiation of red blood cells in the bone marrow.
   - Erythropoietin treatment increases red blood cell production in patients with anemia due to kidney disease, and in patients who have had chemotherapy and radiation treatment for cancer.

   Using what you have learned about cell biology and stem cells, explain to your friend how erythropoietin works.

KEY VOCABULARY

differentiation **stem cells**

239

SAMPLE RESPONSES

1. Stem cells can become a variety of types of cells, while differentiated cells like red blood cells are fully specialized cell types.
2. a. A stem cell produces a mesoderm cell, which can then further differentiate to form a muscle stem cell. From there it differentiates into a smooth muscle cell.
   b. An embryonic stem cell divides and gives rise to an endoderm cell, which divides and produces a pancreas precursor cell. From there the precursor differentiates into a specialized beta (ß) cell in the pancreas.
3. The replication of DNA in the S phase of the cell cycle and equal division of the chromosomes during mitosis ensure that each cell contains a complete copy of all of the DNA for that individual.
4. Because of kidney disease, your body is not producing erythropoietin, which normally stimulates the production of red blood cells by stem cells in your bone marrow. Without erythropoietin, your body is not producing enough red blood cells, and so you are anemic. Your doctor wants to treat you with additional erythropoietin. This will stimulate stem cells in your bone marrow to produce red blood cells.

REVISIT THE CHALLENGE

Stem cells produce specialized cells in a developing embryo through a number of cell divisions. Differentiation factors stimulate stem cells to give rise to more differentiated stem cells in a process that ends when a cell has become fully specialized.