Stem Cells

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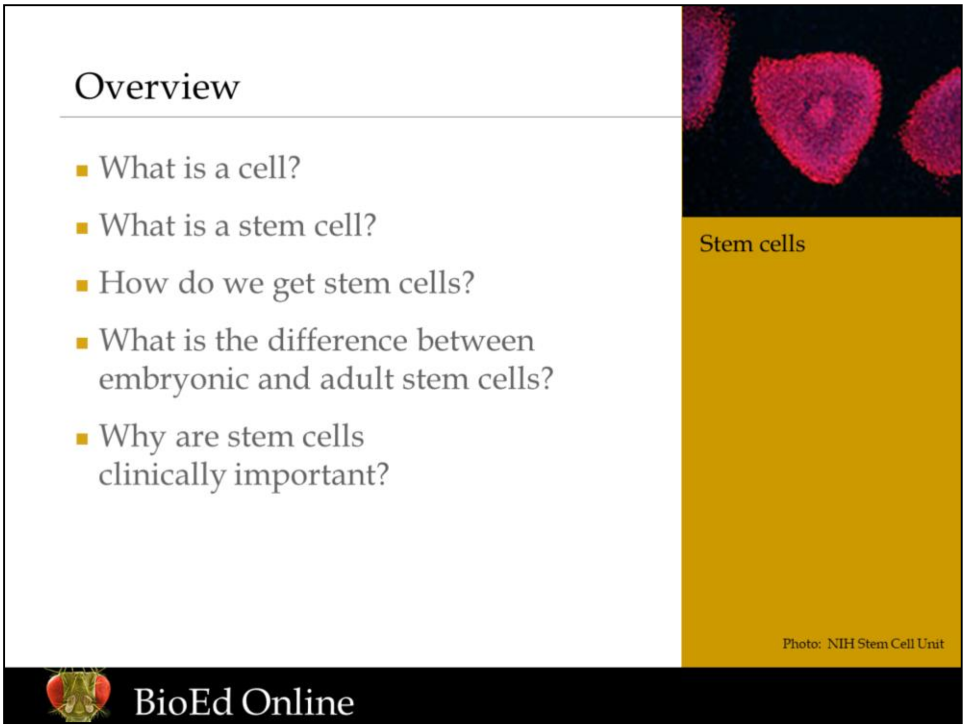
BioEd Online



Overview

Stem cell research seeks to understand how an organism develops from a single cell and how damaged or malfunctioning cells and tissues are replaced in the adult organism. Recent research indicates that stem cells could be used to alleviate a number of life threatening diseases and injuries among humans. A majority of scientists agree there is great promise for treatments involving stem cells, and the therapeutic potential of this technology is enormous. However, stem cell research remains a very controversial issue. This presentation will attempt to answer the following basic questions related to stem cell research.

1) What is a cell?
2) What is a stem cell?
3) How do we get stem cells?
4) What is the difference between embryonic and adult stem cells?
5) Why are stem cells clinically important?

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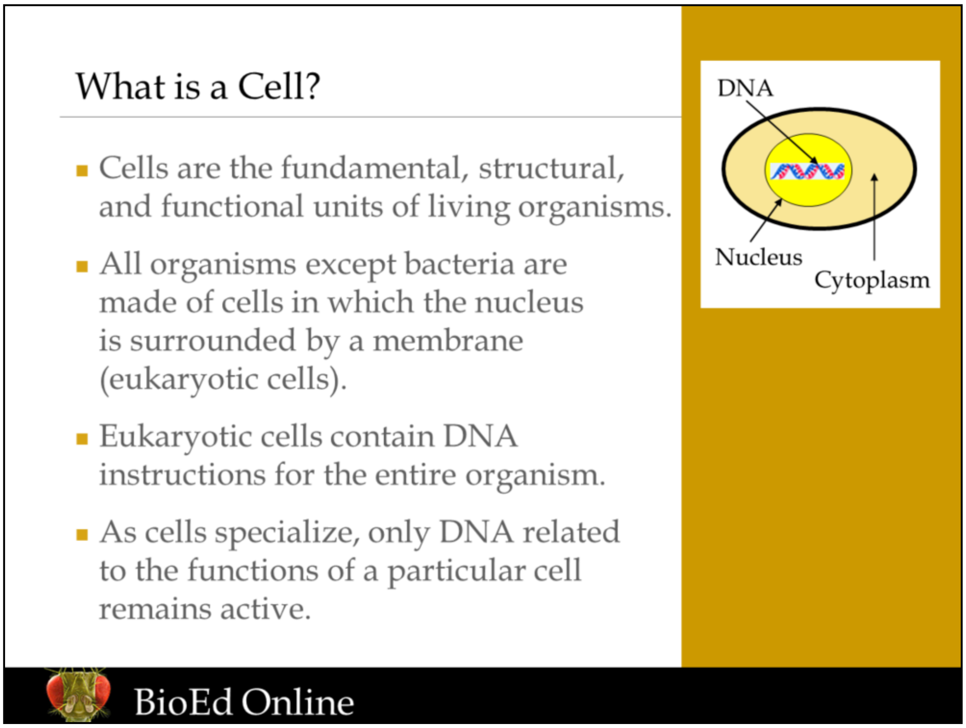

What is a Cell?

Cells are the fundamental, structural, and functional units within living organisms. All living organisms consist of one or more cells. With the exception of bacteria, organisms are made of eukaryotic cells, which have a membrane enclosed nucleus and organelles (mitochondria, endoplasmic reticulum, and ribosomes). The nucleus within each cell contains the hereditary information for the entire organism, encoded within DNA.

In multi-cellular organisms, cells differentiate and specialize. Specialized cells organize into tissues (muscle, blood, bone, fat, nerve), which make up organs (kidneys, heart, stomach, lung), which, in turn, make up organ systems (respiratory, digestive, excretory). Genes that do not pertain to the functioning of each individual cell "turn off." For example, a kidney cell uses only the DNA needed to be a kidney cell. The remaining information is "turned off," but it is still present. There are more than 200 different types of cells (nerve cells, muscle cells, epithelial cells, blood cells, bone cells, etc.) among the human body's estimated <u>100,000,000,000,000</u> total cells.

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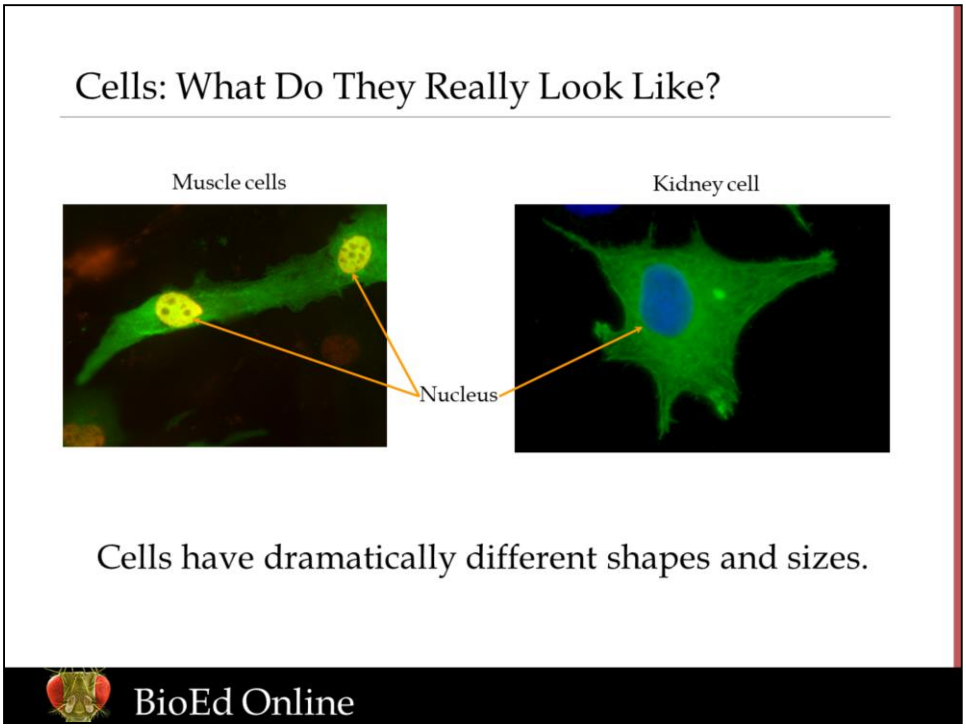

Cells: What Do They Really Look Like?

Different cells have dramatically distinct shapes and sizes. For example, muscle cells (also called myoblasts), which are required for movement, are long and thin, and contain contractile elements. Meanwhile, bone cells (osteoblasts), which are responsible for bone maintenance, are very small and round, and must live embedded in hard calcified bone. Epithelial cells, which make up the nephron in the kidney, filter waste products. These epithelial cells must be able to retain nutrients and materials needed by the body and return them to circulation, while leaving wastes, toxins, and excess water to be excreted. These cells are thin and dense.

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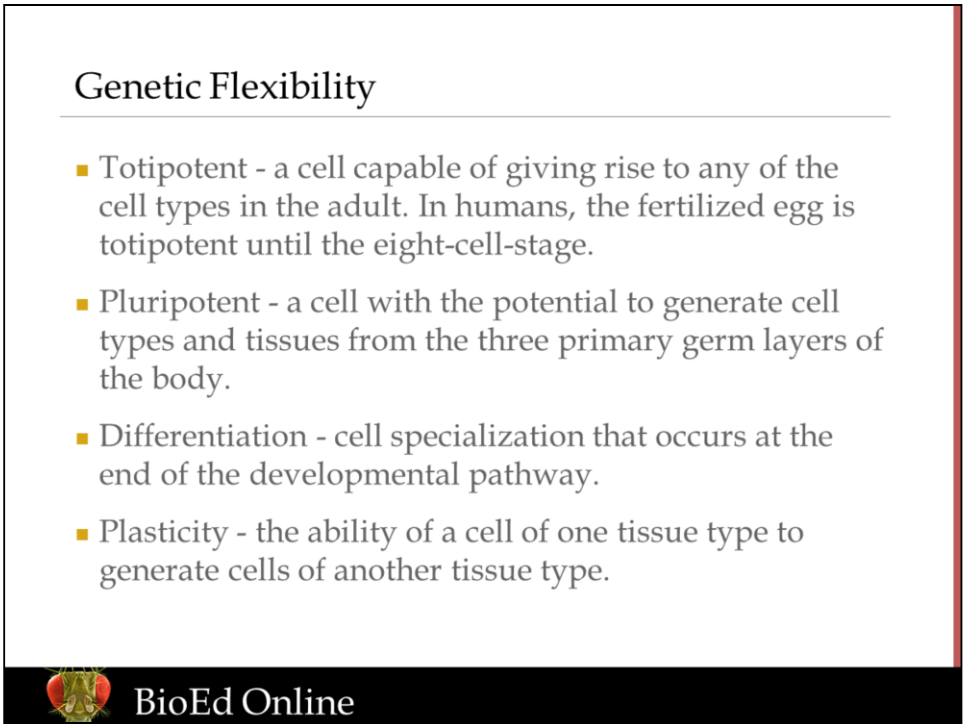

Genetic Flexibility

The mechanism a single fertilized, undifferentiated cell undergoes to generate the diverse range of tissues that make up a multicellular organism is a fascinating process. During development, many types of cells arise from the fertilized egg. As cells differentiate, only portions of the total genetic information contained within the nucleus are expressed within each cell type. For example, even though all cells contain the DNA sequence coding for insulin, only cells of the islets of Langerhans in the pancreas activate this sequence to manufacture and secrete insulin. With that said, it is important to clarify the terminology used in describing the genetic flexibility of cells during the developmental pathway.

Stem cell – a cell from an embryo, fetus, or adult that can reproduce itself for long periods of time and can give rise to specialized cells and tissues.

Totipotent – a cell capable of expressing all the genes of the genome (can give rise to any part of the later embryo or adult). In humans, the fertilized egg is totipotent until the eight-cell-stage. Most plant cells retain totipotency even after becoming specialized.

Pluripotent – a cell with the potential to generate cell types and tissues from all three primary germ layers of the body

Differentiation – cell specialization that occurs at the end of the developmental pathway. Only certain genes are activated.

Plasticity - the ability of a stem cell of one tissue type to generate cells from another tissue type.

Progenitor or precursor cell – occurs when a stem cell divides into two partially differentiated cells, neither of which can replicate itself.

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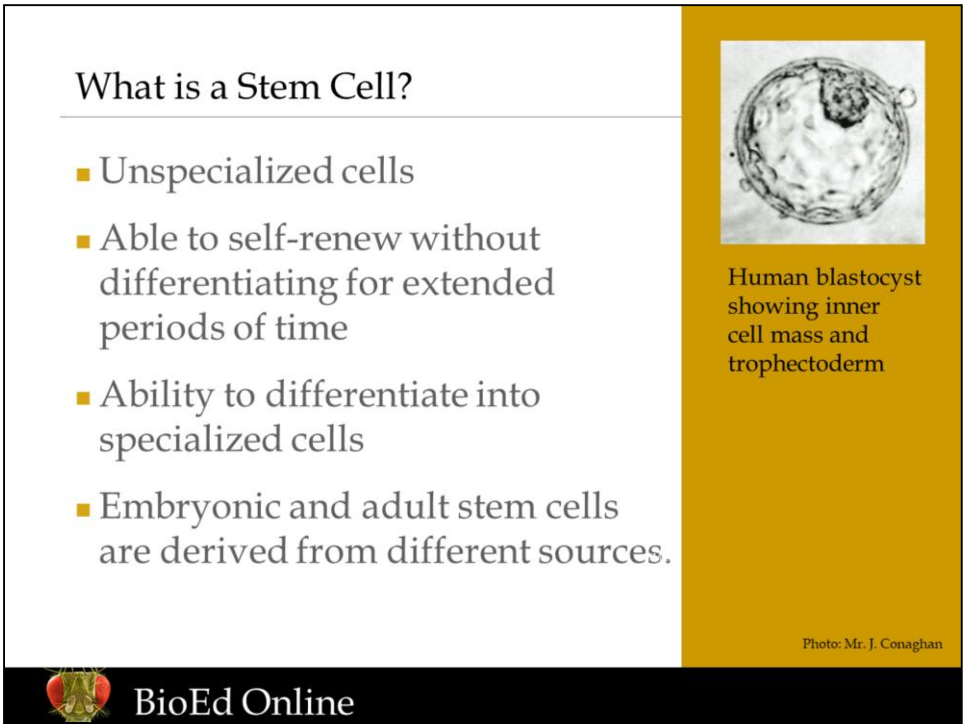

What Is a Stem Cell?

Stem cells are unspecialized cells that can self-renew (or "proliferate") for extended periods of time without differentiating. They exhibit a stable, normal chromosome complement. Stem cells cannot perform any specialized functions but have the potential to give rise to cells with specialized functions (a process known as "differentiation"), such as pulsating heart muscle cells or defensive immune cells.

A fertilized egg is said to be "totipotent" because it has the potential to generate all cell types and tissues that make up an organism. Embryonic stem cells, derived from the inner cell mass of the blastocyst stage of development (pre-implantation, ~5-6 days old) have the potential to generate cell types and tissues from all three primary germ layers of the body (pluripotent). Adult stem cells (somatic stem cells) are found in tissues such as brain, bone marrow, skin, liver, skeletal muscle and peripheral blood vessels. It is suggested that some of these cells may be able to differentiate into multiple cell types (called "plasticity" or "trans-differentiation"). For example, brain stem cells may be able to generate blood and skeletal muscle cells. However, stem cells in adult tissues do not appear to have the same capacity or potential to differentiate as embryonic stem cells do. It may be that adult stem cells in many differentiated tissues are typically unipotent (capable of only one lineage).

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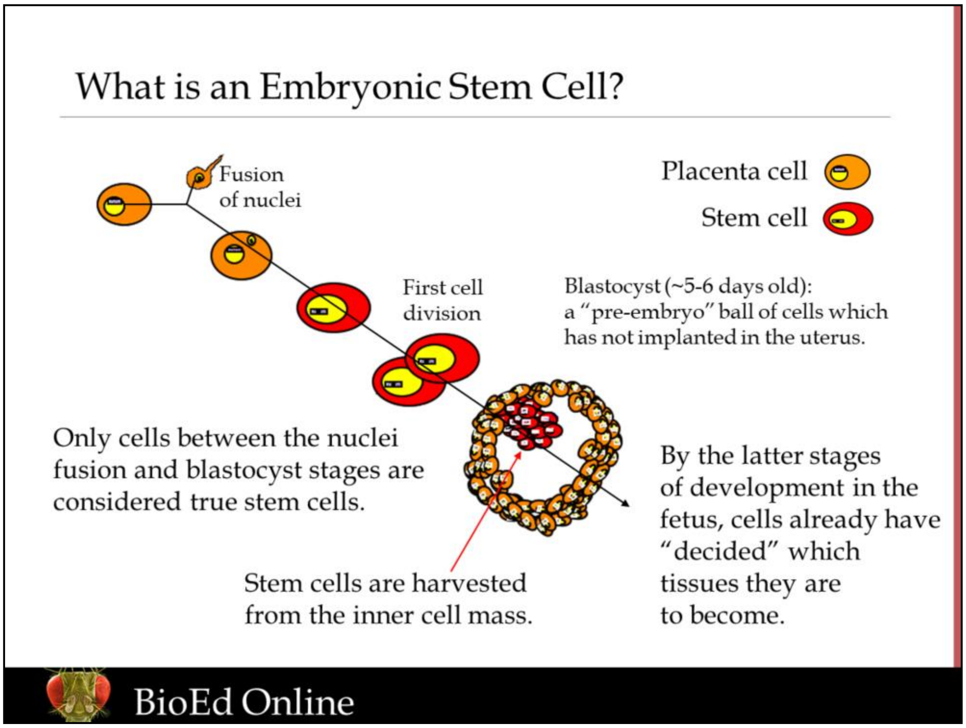

What is An Embryonic Stem Cell?

Embryogenesis is the process by which a single cell, formed from the union of the nucleus from a sperm and an egg, produces a complete organism. The fertilized egg is said to be totipotent, meaning that it has the potential to generate all the specialized cells and tissues of the body, as well as the tissues for its development in the uterus.

The DNA within the fertilized egg instructs the cell to divide (usually 24 – 36 hours after fertilization). The cell divides into two cells, and then each cell divides again, producing four cells. This process continues for about five to six days. At that point, the single cell has become a hollow ball of cells, called a blastocyst, that has not formed an attachment within the uterus. All mammals produce a hollow ball of cells during embryogenesis. The blastocyst is composed of two distinct cell types: 1) cells that will become the placenta; and 2) the inner cell mass. The inner mass of cells (in red) are stem cells. These cells are unique and described as pluripotent, since they retain the ability to read all information contained in the DNA within their nuclei and the capacity to generate cells from all three primary germ layers (mesoderm, ectoderm, and endoderm).

A very specific event occurs after about 5-6 days: the blastocyst changes very subtly and the cells in the inner cell mass lose their ability to read all of their DNA. In other words, cells are no longer pluripotent after this point in development.

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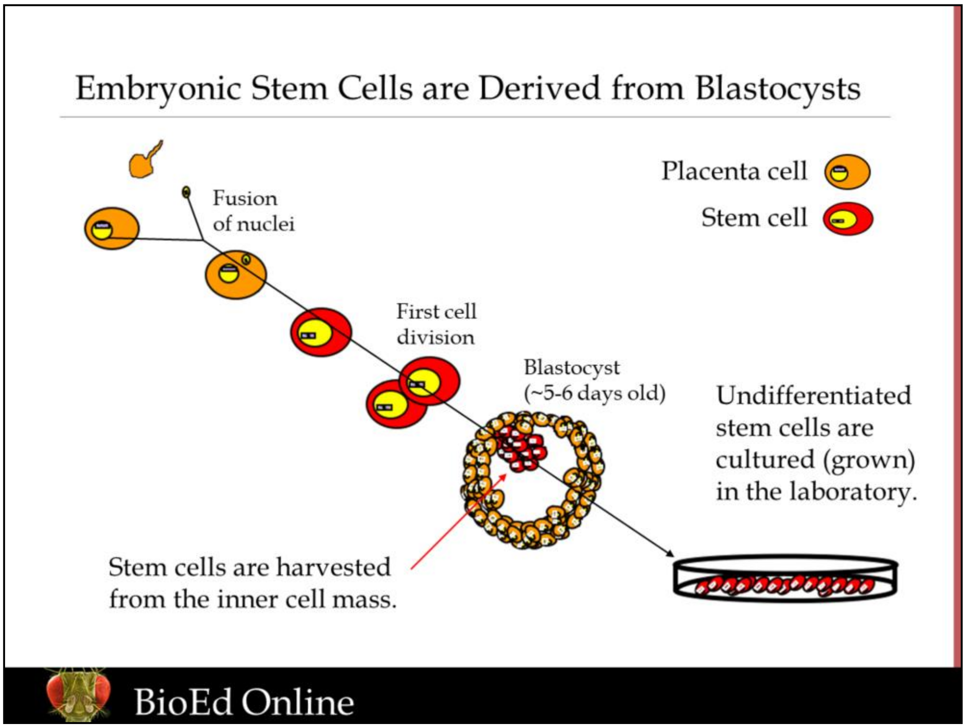

Stem Cells Are Derived from Blastocysts

Scientists can remove the inner cell mass of a blastocyst by microsurgery or immunosurgery (use of antibodies). The harvested cells are transferred to a petri dish containing a specialized nutrient broth known as a culture medium. After 9 -15 days, when clumps of cells have formed, cells from the periphery are separated and plated in the same type of culture medium. Not all the cells of the inner cell mass will survive. Some will differentiate pre-maturely. Cells that do not differentiate and retain the ability to generate any cell type become stem cell lines. As the cells grow and crowd the dish, individual cells are removed and placed in a new dish to continue the cell culture. Cells that grow and do not differentiate for at least six months are called a stem cell line. These cells are described as being pluripotent, which means they are able to a give rise to cells of all three embryonic germ layers.

Since 1998, scientists have created about 30-40 stem cell lines for research. These stem cell lines can be maintained for a very long time in the laboratory, and even frozen to be used at a later date.

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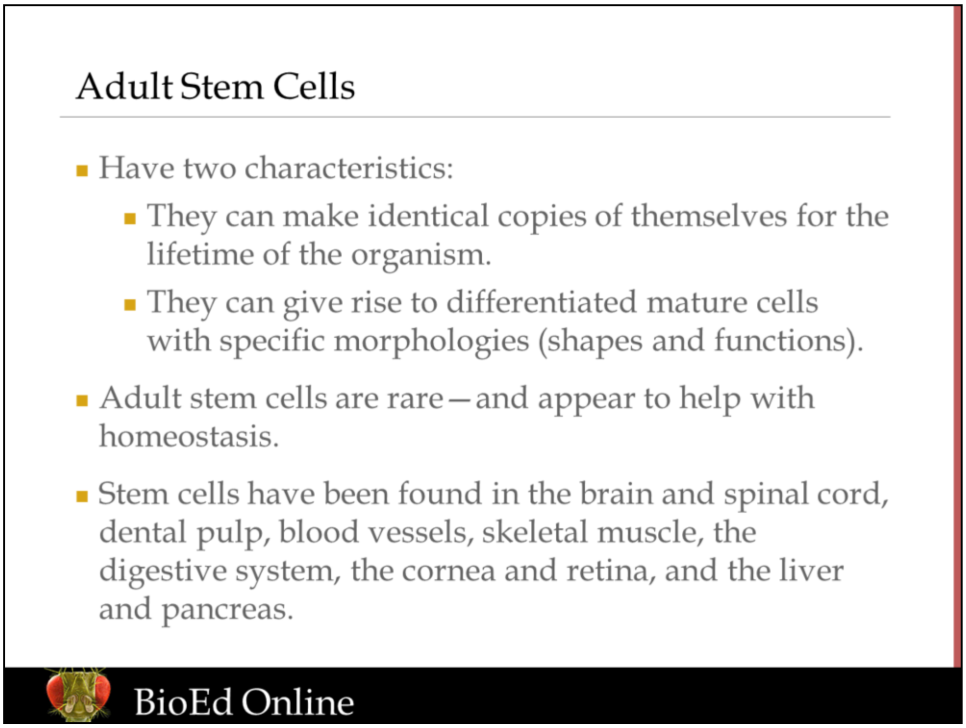

Adult Stem Cells

Recently, scientists have discovered cells in various parts of the human body (skeletal muscle, brain, liver, retina, etc.) that seem to exhibit many properties of blastocyst-derived stem cells. These cells are called “adult stem cells” or “somatic stem cells.” Adult stem cells are rare and dispersed throughout the body. Like all stem cells, they have the long-term ability to make identical copies of themselves and to produce differentiated mature cells.

While much is being learned, important questions remain about adult stem cells. Where are they found in the body and how many kinds exist? Can they be manipulated to grow, and do they normally exhibit the ability to generate cells of all tissue types? Can they access all of the DNA within their nuclei?

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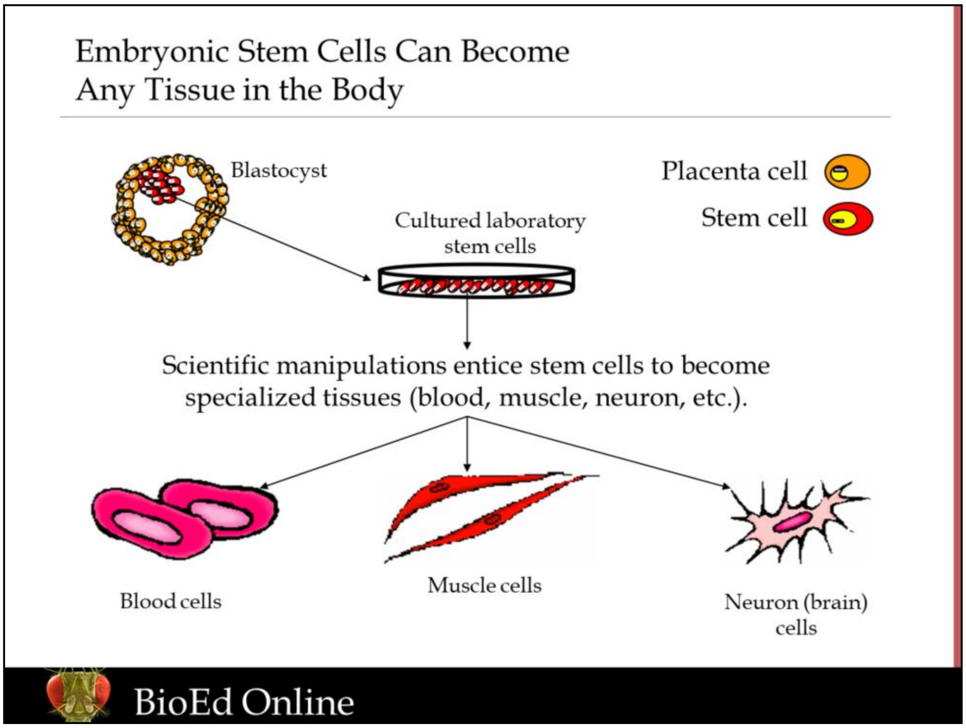

Embryonic Stem Cells Can Become Any Tissue In The Body

Stem cell cultures grown in the laboratory may be used to generate specialized, differentiated cells. The most common method to induce embryonic stem cells to differentiate is to introduce growth factors or change the chemical composition of the surface on which they grow. For example, if the growth surface medium is treated in such a way that the cells cannot adhere to it, the cells float and begin to interact with each other. This cell-to-cell interaction, when combined with the introduction of specific growth factors (*in vitro*), can induce cells to differentiate along a specific pathway.

In 1998, James Thompson at the University of Wisconsin-Madison was the first scientist to keep human embryonic stem cells alive in the laboratory. Before this, scientists could harvest the inner cell mass of the blastocyst, but were able to keep them alive only for a very short time.

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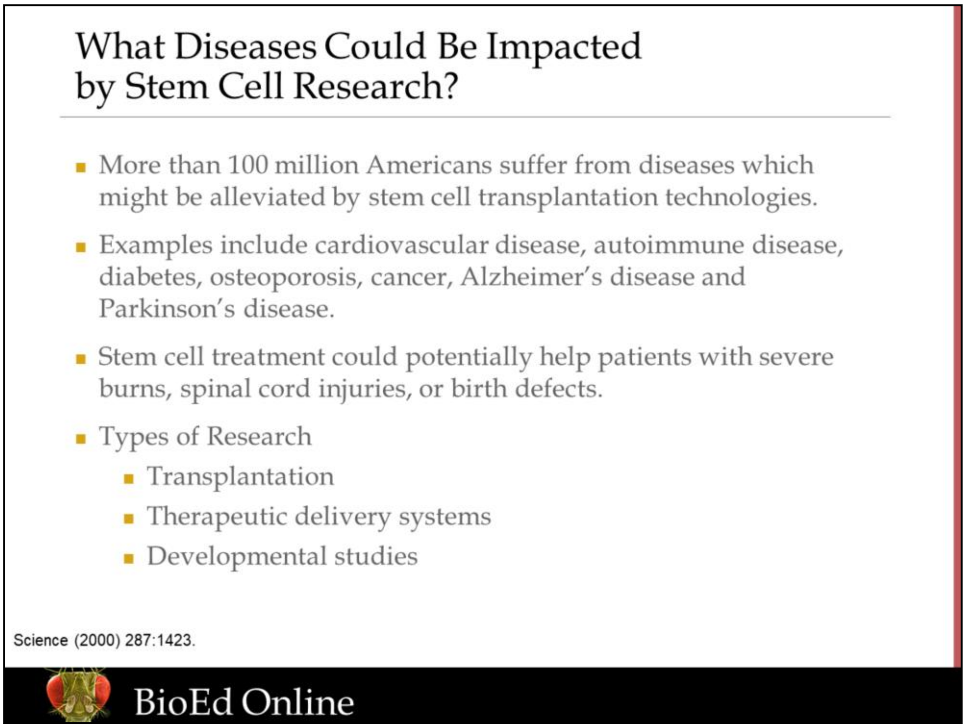

What Diseases Could Be Impacted by Stem Cell Research?

Research has shown that stem cell investigations may offer promising advances in medical treatment for a number of diseases and injuries. The use of stem cells to generate replacement tissues to treat neurological diseases, pancreatic disease, liver failure, chronic heart disease, cancer, and kidney failure is a major focus of scientists. The challenge is to take undifferentiated cells and direct their development into a purified specialized cell population. So far, only hematopoietic (blood producing) stem cells have been demonstrated safe for clinical application.

Current studies focus on the use of stem cells to generate transplantable and replacement tissues within the body. Scientists are working to apply stem cell research to the treatment of cancer by finding ways to deliver stem cell treatments that will either destroy or modify cancer cells. Stem cell research also is an important tool in our understanding of embryological development problems.

What lies ahead? According to the United States National Institutes of Health:

> Predicting the future of stem cell applications is impossible, particularly given the very early stage of the science of stem cell biology. To date, it is impossible to predict which stem cells—those derived from the embryo, the fetus, or the adult—or which methods for manipulating the cells, will best meet the needs of basic research and clinical applications. The answers clearly lie in conducting more research.

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