ABSTRACT

Stem cells are biological cells found in all multicellular organisms, that can divide through mitosis and differentiate into diverse specialized cell types and can self renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells that are isolated from the inner cell mass of blastocysts, and adult stem cells that are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues. Medical researchers believe that stem cell therapy has the potential to dramatically change the treatment of human disease. A number of adult stem cell therapies already exist, particularly bone marrow transplants that are used to treat leukemia. In the future, medical researchers anticipate being able to use technologies derived from stem cell research to treat a wide variety of diseases including cancer, Parkinson’s disease, spinal cord injuries, Amyotrophic lateral sclerosis, multiple sclerosis, and muscle damage, amongst a number of other impairments and conditions.
INTRODUCTION

Stem cells are biological cells found in all multicellular organisms, that can divide through mitosis and differentiate into diverse specialized cell types and can self renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells that are isolated from the inner cell mass of blastocysts, and adult stem cells that are found in various tissues. In adult organisms, stem cells and progenitor cells act as repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

IMPORTANCE OF STEM CELLS:
Stem cells have the remarkable potential to develop into many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell. Stem cells are distinguished from other cell types by two important characteristics. First, they are unspecialized cells capable of renewing themselves through cell division, sometimes after long periods of inactivity. Second, under certain physiologic or experimental conditions, they can be induced to become tissue- or organ-specific cells with special functions. In some organs, such as the gut and bone marrow, stem cells regularly divide to repair and replace worn out or damaged tissues. In other organs, however, such as the pancreas and the heart, stem cells only divide under special conditions.

SOURCE FOR STEM CELLS:
Stem cells are a class of undifferentiated cells that are able to differentiate into specialized cell types. Commonly, stem cells come from two main sources:
1. Embryos formed during the blastocyst phase of embryological development (embryonic stem cells) and
2. Adult tissue (adult stem cells).
Both types are generally characterized by their potency, or potential to differentiate into different cell types (such as skin, muscle, bone, etc.).

ADULT STEM CELLS
Adult or somatic stem cells exist throughout the body after embryonic development and are found inside of different types of tissue. These stem cells have been found in tissues such as the brain, bone marrow, blood, blood vessels, skeletal muscles, skin, and the liver. They remain in a quiescent or non-dividing state for years until activated by disease or tissue injury. Adult stem cells can divide or self-renew indefinitely, enabling them to generate a range of cell types from the originating organ or even regenerate the entire original organ. It is generally thought that adult stem cells are limited in their ability to differentiate based on their tissue of origin, but there is some evidence to suggest that they can differentiate to become other cell types.

EMBRYONIC STEM CELLS
Embryonic stem cells are derived from a four- or five-day-old human embryo that is in the blastocyst phase of development. The embryos are usually extras that
have been created in IVF (in vitro fertilization) clinics where several eggs are fertilized in a test tube, but only one is implanted into a woman. Sexual reproduction begins when a male's sperm fertilizes a female's ovum (egg) to form a single cell called a zygote. The single zygote cell then begins a series of divisions, forming 2, 4, 8, 16 cells, etc. After four to six days - before implantation in the uterus - this mass of cells is called a blastocyst. The blastocyst consists of an inner cell mass (embryoblast) and an outer cell mass (trophoblast). The outer cell mass becomes part of the placenta, and the inner cell mass is the group of cells that will differentiate to become all the structures of an adult organism. This latter mass is the source of embryonic stem cells - totipotent cells (cells with total potential to develop into any cell in the body).

In a normal pregnancy, the blastocyst stage continues until implantation of the embryo in the uterus, at which point the embryo is referred to as a fetus. This usually occurs by the end of the 10th week of gestation after all major organs of the body have been created. However, when extracting embryonic stem cells, the blastocyst stage signals when to isolate stem cells by placing the "inner cell mass" of the blastocyst into a culture dish containing a nutrient-rich broth. Lacking the necessary stimulation to differentiate, they begin to divide and replicate while maintaining their ability to become any cell type in the human body. Eventually, these undifferentiated cells can be stimulated to create specialized cells.

**COMPARISON BETWEEN EMBRYONIC & ADULT STEM CELLS:**

<table>
<thead>
<tr>
<th>Differences</th>
<th>EMBRYONIC</th>
<th>ADULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>How Obtained</td>
<td>By killing a 5 day old human embryo</td>
<td>From you own body cells</td>
</tr>
<tr>
<td>Tissue compatibility</td>
<td>Different DNA-can be rejected as foreign tissue</td>
<td>These are your own cells and will not be rejected</td>
</tr>
<tr>
<td>Infection</td>
<td>If donor has infection it will be transmitted</td>
<td>You cannot infect yourself</td>
</tr>
<tr>
<td>Tumors</td>
<td>These can and do form multicellular tumors</td>
<td>These do not form tumors</td>
</tr>
<tr>
<td>Feasibility</td>
<td>-More expensive</td>
<td>Cheaper</td>
</tr>
<tr>
<td></td>
<td>-More complicated</td>
<td>Easier to do</td>
</tr>
<tr>
<td>Morality</td>
<td>Immoral – it kills a human</td>
<td>Completely ethical</td>
</tr>
<tr>
<td>Success</td>
<td>Not one human cure to date and future ones are questionable</td>
<td>Over 80 human diseases and conditions have been cured</td>
</tr>
</tbody>
</table>

**STEM CELL CULTURES**

![Figure 1](image)

**Human embryonic stem cell colony**

Stem cells are either extracted from adult tissue or from a dividing zygote in a culture dish. Once extracted, scientists place the cells in a controlled culture that prohibits them from further specializing or differentiating but usually allows them to divide and replicate. The process of growing large numbers of embryonic stem cells has been easier than growing large numbers of adult stem cells, but progress is being made for both cell types.
STEM CELL LINES

Once stem cells have been allowed to divide and propagate in a controlled culture, the collection of healthy, dividing, and undifferentiated cells is called a stem cell line. These stem cell lines are subsequently managed and shared among researchers. Once under control, the stem cells can be stimulated to specialize as directed by a researcher - a process known as directed differentiation. Embryonic stem cells are able to differentiate into more cell types than adult stem cells.

PROPERTIES

SELF-RENEWAL

The classical definition of a stem cell requires that it possess two properties:

- **Self-renewal** - the ability to go through numerous cycles of cell division while maintaining the undifferentiated state. (Fig. 2).
- **Potency** - the capacity to differentiate into specialized cell types. In the strictest sense, this requires stem cells to be either totipotent or pluripotent - to be able to give rise to any mature cell type, although multipotent or unipotent progenitor cells are sometimes referred to as stem cells.

![Figure 2](image)

**Two mechanisms exist to ensure that the stem cell population is maintained:**

1. **Obligatory asymmetric replication** - a stem cell divides into one father cell that is identical to the original stem cell, and another daughter cell that is differentiated.
2. **Stochastic differentiation** - when one stem cell develops into two differentiated daughter cells, another stem cell undergoes mitosis and produces two stem cells identical to the original.

POTENCY

Stem cells are categorized by their potential to differentiate into other types of cells. Embryonic stem cells are the most potent since they must become every type of cell in the body. The full classification includes:

**POTENCY DEFINITIONS:**

![Figure 3](image)

*Pluriototent, embryonic stem cells originate as inner mass cells within a blastocyst. The stem cells can become any tissue in the body, excluding a placenta. Only the morula’s cells are totipotent, able to become all tissues and a placenta.*
Potency specifies the differentiation potential (the potential to differentiate into different cell types) of the stem cell.\[^4\]

- Totipotent (a.k.a omnipotent) stem cells can differentiate into embryonic and extraembryonic cell types. Such cells can construct a complete, viable organism.\[^4\]
These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent.\[^5\]

- Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells,\[^4\] i.e. cells derived from any of the three germ layers.\[^6\] The ability to differentiate into almost all cell types. Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation

- Multipotent stem cells can differentiate into a number of cells, but only those of a closely related family of cells.\[^4\] Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets.

- Oligopotent stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.\[^4\]

- Unipotent cells can produce only one cell type, their own,\[^4\] but have the property of self-renewal which distinguishes them from non-stem cells (e.g. muscle stem cells).

**IDENTIFICATION OF STEM CELLS**

The practical definition of a stem cell is the functional definition - a cell that has the potential to regenerate tissue over a lifetime. For example, the defining test for a bone marrow or hematopoietic stem cell (HSC) is the ability to transplant one cell and save an individual without HSCs. In this case, a stem cell must be able to
produce new blood cells and immune cells over a long term, demonstrating potency. It should also be possible to isolate stem cells from the transplanted individual, which can themselves be transplanted into another individual without HSCs, demonstrating that the stem cell was able to self-renew.

Properties of stem cells can be illustrated in vitro, using methods such as clonogenic assays, in which single cells are assessed for their ability to differentiate and self-renew.\[7\][8] Stem cells can also be isolated by their possession of a distinctive set of cell surface markers. However, in vitro culture conditions can alter the behavior of cells, making it unclear whether the cells will behave in a similar manner in vivo. There is considerable debate as to whether some proposed adult cell populations are truly stem.

**DISEASES TREATABLE WITH STEM CELLS**

Scientists and researchers are interested in stem cells for several reasons. Although stem cells do not serve any one function, many have the capacity to serve any function after they are instructed to specialize. Every cell in the body, for example, is derived from first few stem cells formed in the early stages of embryological development. Therefore, stem cells extracted from embryos can be induced to become any desired cell type. This property makes stem cells powerful enough to regenerate damaged tissue under the right conditions. (fig5)

Diseases and conditions in which stem cell treatment is promising or emerging.\[9\] Bone marrow transplantation is, as of 2009, the only established use of stem cells. Medical researchers believe that stem cell therapy has the potential to dramatically change the treatment of human disease. A number of adult stem cell therapies already exist, particularly bone marrow transplants that are used to treat leukemia.\[10\] In the future, medical researchers anticipate being able to use technologies derived from stem cell research to treat a wider variety of diseases including cancer, Parkinson’s disease, spinal cord injuries, Amyotrophic lateral sclerosis, multiple sclerosis, and muscle damage, amongst a number of other impairments and conditions.\[11][12\] However, there still exists a great deal of social and scientific uncertainty surrounding stem cell research, which could possibly be overcome through public debate and future research, and further education of the public.

One concern of treatment is the risk that transplanted stem cells could form tumors and...
become cancerous if cell division continues uncontrollably.\textsuperscript{13} 
Stem cells are widely studied, for their potential therapeutic use and for their inherent interest.\textsuperscript{14} 
Supporters of embryonic stem cell research argue that such research should be pursued because the resultant treatments could have significant medical potential. It has been proposed that surplus embryos created for in vitro fertilization could be donated with consent and used for the research.

**ORGAN AND TISSUE REGENERATION**
Tissue regeneration is probably the most important possible application of stem cell research. Currently, organs must be donated and transplanted, but the demand for organs far exceeds supply. Stem cells could potentially be used to grow a particular type of tissue or organ if directed to differentiate in a certain way. Stem cells that lie just beneath the skin, for example, have been used to engineer new skin tissue that can be grafted on to burn victims.

**BRAIN DISEASE TREATMENT**
Additionally, replacement cells and tissues may be used to treat brain disease such as Parkinson's and Alzheimer's by replenishing damaged tissue, bringing back the specialized brain cells that keep unneeded muscles from moving. Embryonic stem cells have recently been directed to differentiate into these types of cells, and so treatments are promising cells attempting to sustain cardiac output, leading to heart failure, and eventual death. Restoring damaged heart muscle tissue, through repair or regeneration, is therefore a potentially new strategy to treat heart failure.

The use of embryonic and adult-derived stem cells for cardiac repair is an active area of research. A number of stem cell types, including embryonic stem (ES) cells, cardiac stem cells that naturally reside within the heart, myoblasts (muscle stem cells), adult bone marrow-derived cells including mesenchymal cells (bone marrow-derived cells that give rise to tissues such as muscle, bone, tendons, ligaments, and adipose tissue), endothelial progenitor cells (cells that give rise to the endothelium, the interior lining of blood vessels), and umbilical cord blood cells, have been investigated as possible sources for regenerating damaged heart tissue. All have been explored in mouse or rat models, and some have been tested in larger animal models, such as pigs.
CELL DEFICIENCY THERAPY
Healthy heart cells developed in a laboratory may one day be transplanted into patients with heart disease, repopulating the heart with healthy tissue. Similarly, people with type I diabetes may receive pancreatic cells to replace the insulin-producing cells that have been lost or destroyed by the patient's own immune system.

The only current therapy is a pancreatic transplant, and it is unlikely to occur due to a small supply of pancreases available for transplant.

BLOOD DISEASE TREATMENT
Adult hematopoietic stem cells found in blood and bone marrow have been used for years to treat diseases such as leukemia, sickle cell anemia, and other immunodeficiencies. These cells are capable of producing all blood cell types, such as red blood cells that carry oxygen to white blood cells that fight disease. Difficulties arise in the extraction of these cells through the use of invasive bone marrow transplants. However hematopoietic stem cells have also been found in the umbilical cord and placenta. This has led some scientists to call for an umbilical cord blood bank to make these powerful cells more easily obtainable and to decrease the chances of a body's rejecting therapy.

CONCLUSION
Medical researchers believe that stem cell therapy has the potential to dramatically change the treatment of human disease. A number of adult stem cell therapies already exist, particularly bone marrow transplants that are used to treat leukemia.10 In the future, medical researchers anticipate being able to use technologies derived from stem cell research to treat a wider variety of diseases including cancer, Parkinson's disease, spinal cord injuries, Amyotrophic lateral sclerosis, multiple sclerosis, and muscle damage, amongst a number of other impairments and conditions.11,12 However, there still exists a great deal of social and scientific uncertainty surrounding stem cell research, which could possibly be overcome through public debate and future research, and further education of the public.
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Wound healing:

