

# Stem Cell: Basics, Classification and Applications

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## ABSTRACT

Stem cells are unspecialized cells that develop into the specialized cells that make up the different types of tissue in the human body. They are characterized by the ability to renew themselves through mitotic cell division and differentiating into a diverse range of specialized cell types. They are vital to the development, growth, maintenance, and repair of our brains, bones, muscles, nerves, blood, skin, and other organs. Stem cells are found in all of us, from the early stages of human development to the end of life. Stem cell research holds tremendous promise for the development of novel therapies for many serious diseases and injuries. While stem cell-based treatments have been established as a clinical standard of care for some conditions, such as hematopoietic stem cell transplants for leukemia and epithelial stem cell-based treatments for burns and corneal disorders, the scope of potential stem cell-based therapies has expanded in recent years due to advances in stem cell research. It has been only recently that scientists have understood stem cells well enough to consider the possibilities of growing them outside the body for long periods of time. With that advance, rigorous experiments can be conducted, and the possibility of manipulating these cells in such a way that specific tissues can be grown is real.

**Keywords:** Stem cell, Treatment, Therapy, Research.

## INTRODUCTION

Stem cells are defined as cells that have clonogenic and self-renewing capabilities and differentiate into multiple cell lineages. Stem cells are found in all of us, from the early stages of human development to the end of life. Stem cells are basic cells of all multicellular organisms

having the potency to differentiate into wide range of adult cells<sup>1</sup>. Self renewal and totipotency are characteristic of stem cell. Though totipotency is shown by very early embryonic stem cells, the adult stem cells possess multipotency and differential plasticity which can be exploited for future

generation of therapeutic options<sup>2</sup>. All stem cells may prove useful for medical research, but each of the different types has both promise and limitations<sup>3</sup>.

For decades, researchers have been studying the biology of stem cells to figure out how development works and to find new ways of treating health problems<sup>4</sup>. The scientific researchers and medical doctors of today hope to make the legendary concept of regeneration into reality by developing therapies to restore lost, damaged, or aging cells and tissues in the human body<sup>5</sup>. This research has opened new horizons for stem cell research.

Stem cell research holds tremendous promise for the development of novel therapies for many serious diseases and injuries. While stem cell-based treatments have been established as a clinical standard of care for some conditions, such as hematopoietic stem cell transplants for leukemia and epithelial stem cell-based treatments for burns and corneal disorders, the scope of potential stem cell-based therapies has expanded in recent years due to advances in stem cell research<sup>6</sup>. It is impossible to project when actual treatments or cures might emerge from such research, but the paths this research might take and potential applications have been much discussed<sup>7</sup>. Stem cells can now be grown and transformed into specialized cells with characteristics consistent with cells of various tissues such as muscles or nerves through cell culture. Highly plastic adult stem cells from a variety of sources, including umbilical cord blood and bone marrow, are routinely used in medical therapies. This review focuses on types of stem cells, their sources, stem cell research and future aspects<sup>7</sup>.

### Historical perspectives

The history of stem cell research had a benign, embryonic beginning in the mid

1800's with the discovery that some cells could generate other cells. In the early 1900's the first real stem cells were discovered when it was found that some cells generate blood cells. The term "stem cell" was proposed for scientific use by the Russian histologist Alexander Maksimov in 1908. Bone marrow transplant between two siblings successfully treated SCID in 1968. Haemopoietic stem cells were discovered in human cord blood in 1978<sup>8</sup>.

James Thomson and coworkers derived the first human embryonic stem cell line at the University of Wisconsin–Madison in 1998<sup>8</sup>. More recently, in 2005, scientists at Kingston University in England were purported to have found another category of stem cells. These were named cord blood embryonic-like stem cells, which originate in umbilical cord blood. Korean researcher Hwang Woo-Suk (2004–2005) claimed to have created several human embryonic stem cell lines from unfertilised human oocytes<sup>9</sup>.

Scientists at Newcastle University in England create the first ever artificial liver cells using umbilical cord blood stem cells in October 2006<sup>10,11</sup>. It is suggested that these stem cells have the ability to differentiate into more cell types than adult stem cells, opening up greater possibilities for cell-based therapies. Then, in early 2007, researchers led by Dr. Anthony Atala claimed that a new type of stem cell had been isolated in amniotic fluid<sup>12</sup>. This finding is particularly important because these stem cells could prove to be a viable alternative to the controversial use of embryonic stem cells<sup>13</sup>. Mario Capecchi, Martin Evans, and Oliver Smithies won the 2007 Nobel Prize for Physiology or Medicine for their work on embryonic stem cells from mice using gene targeting strategies producing genetically engineered mice (known as knockout mice) for gene research<sup>14</sup>.

The first published study of successful cartilage regeneration in the human knee using autologous adult mesenchymal stem cells is published by clinicians from Regenerative Sciences in 2008<sup>15</sup>. Embryonic stem cell isolated from a single human hair was reported in 2008<sup>16</sup>. Australian scientists (2009) found a way to improve chemotherapy of mouse muscle stem cells<sup>17</sup>. Kim *et al.* 2009<sup>18</sup>. Announced that they had devised a way to manipulate skin cells to create patient specific "induced pluripotent stem cells" (iPS), claiming it to be the 'ultimate stem cell solution'. For the first time, human embryonic stem cells have been cultured under chemically controlled conditions without the use of animal substances, which is essential for future clinical uses in 2010<sup>19</sup>.

Over the last few years, national policies and debate amongst the public as well as religious groups, government officials and scientists have led to various laws and procedures regarding stem cell harvesting, development and treatment for research or disease purposes. The goals of such policies are to safeguard the public from unethical stem cell research and use while still supporting new advancements in the field.

### Stem cell

A stem cell is a non-specialized, generic cell which can make exact copies of itself indefinitely and can differentiate and produce specialized cells for the various tissues of the body<sup>2</sup>. Stem cells are cells found in most, if not all, multi-cellular organisms. They are characterized by self-renewal and potency i.e. - the ability to renew themselves through mitotic cell division and differentiating into a diverse range of specialized cell types<sup>2</sup> (Fig. 1). They are vital to the development, growth, maintenance, and repair of our brains,

bones, muscles, nerves, blood, skin, and other organs<sup>3</sup>.

Laboratory studies of stem cells enable scientists to learn about the cells' essential properties and what makes them different from specialized cell types. Scientists are already using stem cells in the laboratory to screen new drugs and to develop model systems to study normal growth and identify the causes of birth defects<sup>20</sup>. Research on stem cells continues to advance knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. Stem cell research is one of the most fascinating areas of contemporary biology, but, as with many expanding fields of scientific inquiry, research on stem cells raises scientific questions as rapidly as it generates new discoveries<sup>21</sup>. Over the past year, adult stem cells have been used either exclusively or in combination with other treatments to achieve significant "healthcare benefits" for sufferers of the every tissue of human body (Fig.-2)<sup>22,23</sup>.

### Classification of stem cells on the basis of potency

Stem cells can be classified by the extent to which they can differentiate into different cell types. These four main classifications are totipotent, pluripotent, multipotent, or unipotent.

#### Totipotent

The ability to differentiate into all possible cell types (Fig-3). Examples are the zygote formed at egg fertilization and the first few cells that result from the division of the zygote.

#### Pluripotent

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

The ability to differentiate into a closely related family of cells. Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets.

### Oligopotential

The ability to differentiate into a few cells. Examples include (adult) lymphoid or myeloid stem cells.

### Unipotent

The ability to only produce cells of their own type, but have the property of self-renewal required to be labeled a stem cell. Examples include (adult) muscle stem cells<sup>24</sup>.

### Classification of stem cells on the basis of their sources

The easiest way to categorize stem cells is by dividing them into two types: Early or embryonic and mature or adult. Early stem cells, often called embryonic stem cells, are found in the inner cell mass of a blastocyst after approximately five days of development. Mature stem cells are found in specific mature body tissues as well as the umbilical cord and placenta after birth<sup>25</sup>.

### Embryonic stem cells

Embryonic stem cells are self-replicating pluripotent cells that are potentially immortal<sup>26</sup>. They are derived from embryos at a developmental stage before the time of implantation would normally occur in the uterus<sup>2</sup>. The embryos from which human embryonic stem cells are derived are typically four or five days old and are a hollow microscopic ball of cells called the blastocyst<sup>27</sup>.

### Adult stem cells

Adult stem cells are undifferentiated totipotent or multipotent cells, found throughout the body after embryonic development, that multiply by cell division to replenish dying cells and regenerate damaged tissues. (Fig.-4). The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. Unlike embryonic stem cells, which are defined by their origin (the inner cell mass of the blastocyst), the origin of adult stem cells in some mature tissues is still under investigation<sup>28</sup>.

### Pluripotent stem cells<sup>1</sup>

Recently, a third type of stem cell, with properties similar to embryonic stem cells, has emerged. Scientists have engineered these induced pluripotent stem cells<sup>1</sup> (iPS cells) by manipulating the expression of certain genes - 'reprogramming' somatic cells back to a pluripotent state<sup>29-31</sup>.

### Stem cell culture

Growing cells in the laboratory is known as cell culture. Human embryonic stem cells (hESCs) are generated by transferring cells from a preimplantation-stage embryo into a plastic laboratory culture dish that contains a nutrient broth known as culture medium. The cells divide and spread over the surface of the dish. However, if the plated cells survive, divide and multiply enough to crowd the dish, they are removed gently and plated into several fresh culture dishes. The process of replating or sub culturing the cells is repeated many times and for many months. Each cycle of subculturing the cells is referred to as a passage. Once the cell line is established, the original cells yield millions of embryonic stem cells (Fig. 5). Embryonic stem cells that have proliferated in cell culture for six or more months without

differentiating, are pluripotent, and appear genetically normal are referred to as an embryonic stem cell line. At any stage in the process, batches of cells can be frozen and shipped to other laboratories for further culture and experimentation<sup>32</sup>.

### Stem cell lines

A stem cell line is a family of constantly dividing cells, the product of a single parent group of stem cells. They are obtained from human or animal tissues and can replicate for long periods of time *in vitro* ("within glass"; or, commonly, "in the lab", in an artificial environment). They are frequently used for research relating to embryonic stem cells or cloning entire organism (Fig. 5). 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<sup>33</sup>.

### Applications of stem cells

The goal of any stem cell therapy is to repair a damaged tissue that can't heal itself. Ongoing research on stem cell therapies gives hope to patients who would normally not receive treatment to cure their disease but just to alleviate the symptoms of their chronic illness. Stem cell therapies involve more than simply transplanting cells into the body and directing them to grow new, healthy tissue. It may also be possible to coax stem cells already in the body to work overtime and produce new tissue.

### Possible treatments by stem cells

A number of stem cell therapeutics exist, but most are at experimental stages and/or costly, with the notable exception of bone marrow transplantation (Fig. 6). Medical researchers anticipate that adult and embryonic stem cells will soon be able to treat cancer, Type 1 diabetes mellitus, Parkinson's disease, Huntington's disease,

Celiac Disease, cardiac failure, muscle damage and neurological disorders, and many others<sup>34</sup>. They have suggested that before stem cell therapeutics can be applied in the clinical setting, more research is necessary to understand stem cell behavior upon transplantation as well as the mechanisms of stem cell interaction with the diseased/injured microenvironment.

Bone marrow transplants (BMT) are a well known clinical application of stem cell transplantation. BMT can repopulate the marrow and restore all the different cell types of the blood after high doses of chemotherapy and/or radiotherapy, our main defense used to eliminate endogenous cancer cells. The isolation of additional stem and progenitors cells is now being developed for many other clinical applications. Several are described below.

### Skin replacement

The knowledge of stem cells has made it possible for scientists to grow skin from a patient's plucked hair. Skin (keratinocyte) stem cells reside in the hair follicle and can be removed when a hair is plucked<sup>35</sup>. These cells can be cultured to form an epidermal equivalent of the patients own skin and provides tissue for an autologous graft, bypassing the problem of rejection.

### Brain cell transplantation

Stem cells can provide dopamine - a chemical lacking in victims of Parkinson's disease. It involves the loss of cells which produce the neurotransmitter dopamine. The first double-blind study of fetal cell transplants for Parkinson's disease reported survival and release of dopamine from the transplanted cells and a functional improvement of clinical symptoms<sup>36</sup>. However, some patients developed side effects, which suggested that there was an over sensitization to or too much dopamine.

Although the unwanted side effects were not anticipated, the success of the experiment at the cellular level is significant.

#### Treatment for diabetes

Diabetes affects millions of people in the world and is caused by the abnormal metabolism of insulin. Normally, insulin is produced and secreted by the cellular structures called the islets of langerhans in the pancreas. Recently, insulin expressing cells from mouse stem cells have been generated<sup>37</sup>. In addition, the cells self assemble to form structures, which closely resemble normal pancreatic islets and produce insulin. Future research will need to investigate how to optimize conditions for insulin production with the aim of providing a stem cell-based therapy to treat diabetes to replace the constant need for insulin injections.

#### Scientists and stem cell research

Scientists believe that stem-cell research could lead to cures for a myriad of diseases afflicting humans. Anti-abortion groups, some religious groups, and conservative citizens say that using cells from embryos is immoral because it destroys life. However, recent news has shown that support stem cell research by a 2-1 margin and say that it should be funded by the federal government, despite controversy over the use of human embryos<sup>38</sup>.

#### CONCLUSION

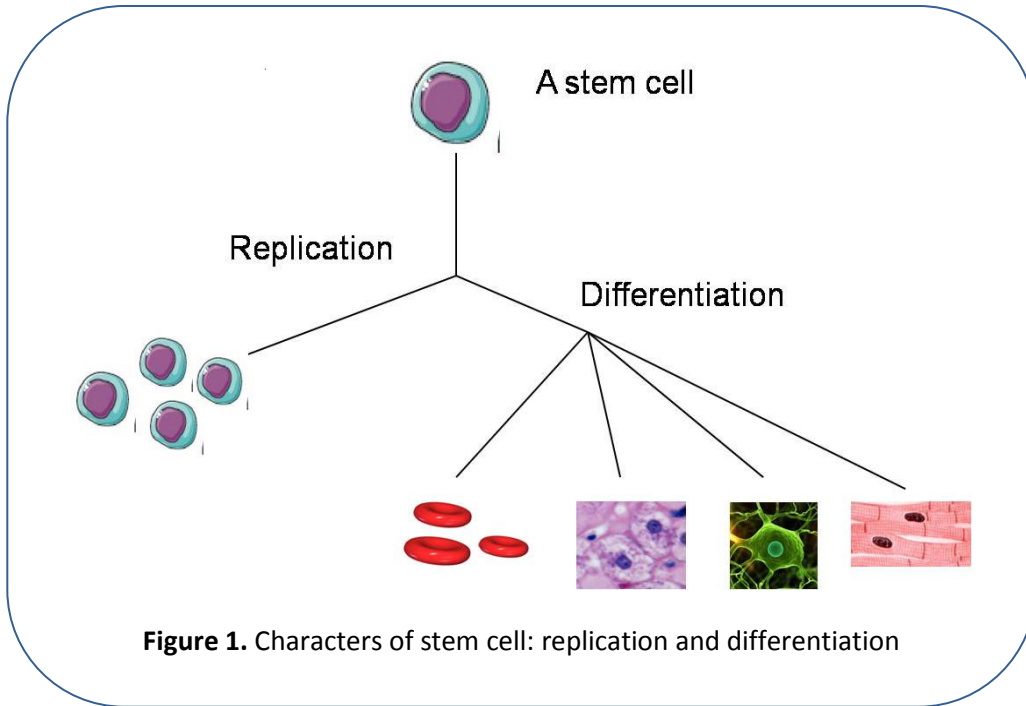
We conclude that ongoing research on stem cell therapies gives hope to patients who would normally not receive treatment to cure their disease. Stem cells have a bright future for the therapeutic world by promising stem cell therapy. We hope to see new horizon of therapeutics in the form of bone marrow transplant, skin replacement, organ development, and replacement of lost

tissue such as hairs, tooth, retina and cochlear cells.

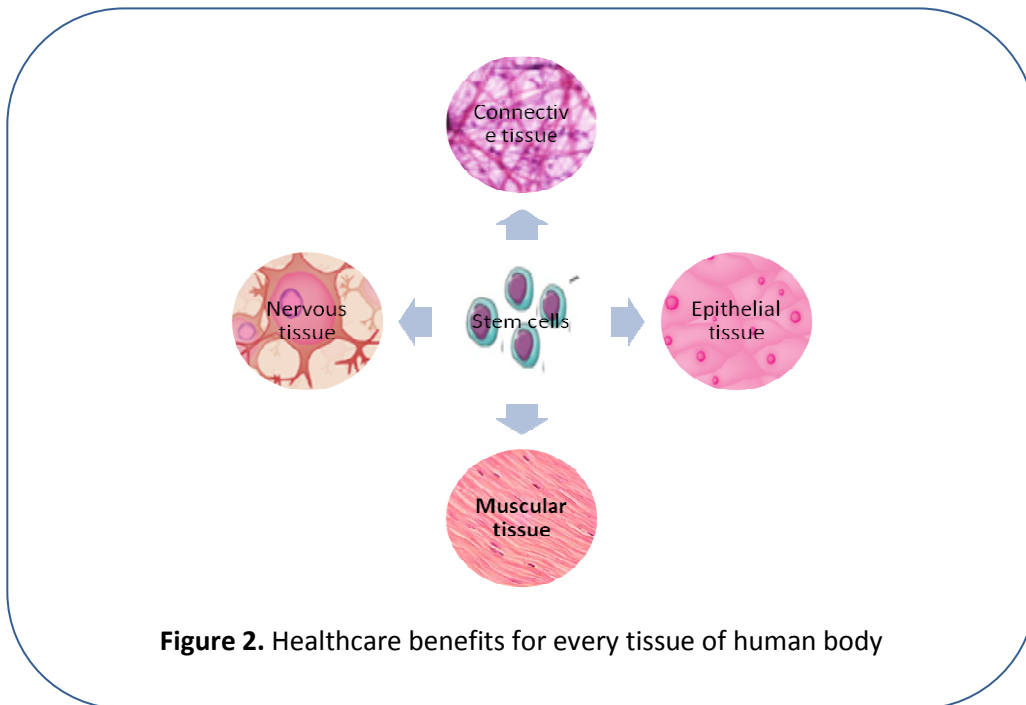
#### REFERENCES

1. C.S. Potten, *Stem Cells*. 1997 London: Academic Press.
2. S. Avasthi, R. N. Srivastava, A. Singh and M. Srivastava "Stem cells: Past, Present, Future – a review article", *Internaet J. Med. Update*, 2008, 3(1):22-30.
3. *Understanding Stem Cells, An overview of the Science and Issues from the National Academics*, The National Academics, Advisers to the Nation on Sciences, Engineering and Medicine. ([www.national-academics.org](http://www.national-academics.org)).
4. (<http://learn.genetics.utah.edu/content/tech/stemcells/scresearch/>).
5. A. Charles and Jr. Goldthwaite *Regenerative Medicine*. Department of Health and Human Services. Report, August 2006.
6. ISSCR, International Society for stem cell research, *Guidelines for the Clinical Translation of Stem Cells*. 2008.
7. A. R. Chapman, S. Mark, Frankel, and M. Garfinkel, "Stem Cell Research and Applications: Monitoring the Frontiers of Biomedical Research", American Association for the Advancement of Science, 1999.
8. J.A Thomson, E.J. Eldor , S.S Shapiro, M.A Waknitz , J.J Swiergiel, V.S Marshall ,J.M Jones , "Embryonic stem cell lines derived from human blastocysts". *Science*, 1998, 282 (5391): 1145–7.
9. K. Takahashi, S. Yamanaka, "Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors". *Cell*, 2006, 126 (4): 663–76.
10. "Good news for alcoholics". *Discover Magazine*. March 2007. <http://discover-magazine.com/2007/mar/good-news-for-alcoholics>.
11. The Scotsman. Archived from the original on 2007-02-03. <http://web.archive.org/web/20070203010452/http://news.scotsman.com/health.cfm?id=1608072006>.
12. P. De Coppi, G. Bartsch ,M.M Siddiqui *et al.* , "Isolation of amniotic stem cell lines with

- potential for therapy". *Nat Biotechnol.*, 2007, 25 (1): 100–6.
13. <http://www.explorestemcells.co.uk/HistoryStemCellResearch.html>
  14. "The Nobel prize in physiology or medicine 2007". Nobelprize.org. [http://nobelprize.org/nobel\\_prizes/medicine/laureates/2007/index.html](http://nobelprize.org/nobel_prizes/medicine/laureates/2007/index.html). Retrieved 8 October 2007.
  15. C.J Centeno, D. Busse, J. Kisiday, C. Keohan, M. Freeman and D. Karli, "Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells". *Pain Physician*. 2008, 11 (3): 343–53.
  16. M. Baker, "Embryonic-like stem cells from a single human hair". *Nature Reports Stem Cells*. October 2008. <http://www.nature.com/stemcells/2008/0810/081030/full/stemcells.2008.142.html>.
  17. <http://www.gummy-stuff.org/stem-cells.htm>.
  18. D. Kim ,C.H. Kim , J.I Moon , Y.G Chung ,M.Y. Chang , B.S.Han , S. Ko ,E. Yang , K. Y. Cha, R. Lanza and K.S. Kim, "Generation of human induced pluripotent stem cells by direct delivery of reprogramming proteins". *Cell Stem Cell* May 2009, 4 (6): 472–6.
  19. *Biotech Daily International staff writers* Breakthrough in Stem Cell Culturing without the Use of Animal Substances. 2010. <http://www.biotechdaily.com/biochemistry/articles>.
  20. Nucleus Catalog Medical Reference Library <http://catalog.nucleusinc.com/displaymonograph.php>.
  21. "Stem Cell Basics: Introduction" In *Stem Cell Information* [World Wide Web site]. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services, 2009 [cited Wednesday, June 30, 2010 Available at <<http://stemcells.nih.gov/info/basics/basics1>.
  22. The successful treatment of Severe Combined Immunodeficiency Disease (SCID).using adult stem cells (<http://www.globalchange.com/stemcells.htm>).
  23. <https://www.msu.edu/~fellrath/atl/diagram2.jpg>.
  24. [http://www.medicalnewstoday.com/info/stem\\_cell/](http://www.medicalnewstoday.com/info/stem_cell/).
  25. [www.findingtruthmatters.org/articles/stem-cell](http://www.findingtruthmatters.org/articles/stem-cell).
  26. M. K. Jeffrey, M. Ponzetti and S. A. David., stem cells An Interactive Qualifying Project Report, Submitted to the Faculty of worcester polytechnic institute In partial fulfillment of the requirements for the Degree of Bachelor of Science, 2006.
  27. [juanv.files.wordpress.com/.../stemcells2-gif.gif](http://juanv.files.wordpress.com/.../stemcells2-gif.gif), <http://juanv.wordpress.com>.
  28. [www.nature.com/.../images/nature06800-f2.2.jpg](http://www.nature.com/.../images/nature06800-f2.2.jpg)
  29. H. R. Schöler, "The Potential of Stem Cells: An Inventory". In Nikolaus Knoepffler, Dagmar Schipanski, and Stefan Lorenz Sorgner. *Humanbiotechnology as Social Challenge*. Ashgate Publishing, Ltd. 2007, p. 28. ISBN 0754657558.
  30. F. Ulloa-Montoya, C.M Verfaillie and W.S Hu, "Culture systems for pluripotent stem cells". *J Biosci Bioeng.*, 100 (1), 2005, 12–27.
  31. [schools-wikipedia.org](http://schools-wikipedia.org).
  32. <http://www.kumc.edu/stemcell/images/stemcellscomefrom.jpg>.
  33. <http://gslc.genetics.utah.edu/units/stemcells/create>.
  34. I. Singec, R. Jandial, A. Crain, G. Nikkhah and E.Y. Snyder, "The leading edge of stem cell therapeutics". *Annu. Rev. Med.* 58, 2007, 313–328.
  35. C. Jahoda. And A. Reynolds, "Skin stem cells — a hairy issue." *Nature Medicine*, 6, 2000, 1095-1097.
  36. C.R. Freed, P.E. Greene, R.E Breeze, W-Y Tsai, W. DuMoucel, R. Kao, S. Dillon, H. Winfield, S. Culver, J.Q. Trojanowski, D. Eidelberg and S. Fahn, "Transplantation of embryonic dopamine neurons for severe parkinson's disease" *New England J. of Med.*, 344, 2000, 710-719.
  37. N. Lumelsky, O. Blondel, P. Laeng, I. Velasco,, R. Ravin and R. McKay, "Differentiation of embryonic stem cells to insulin-secreting structures similar to pancreatic islets" *Science*, 292, 2001, 1389-1394.
  38. "Public backs stem cell research." An analysis by Gary Langer for ABCnews.com on June 16, 2001, using results from their survey conducted by TNS Inter search between June, 20-24, 2001. Accessed 6/01. <http://www.abcnews.go.com/sections/politics/DailyNews/poll010626.html>.

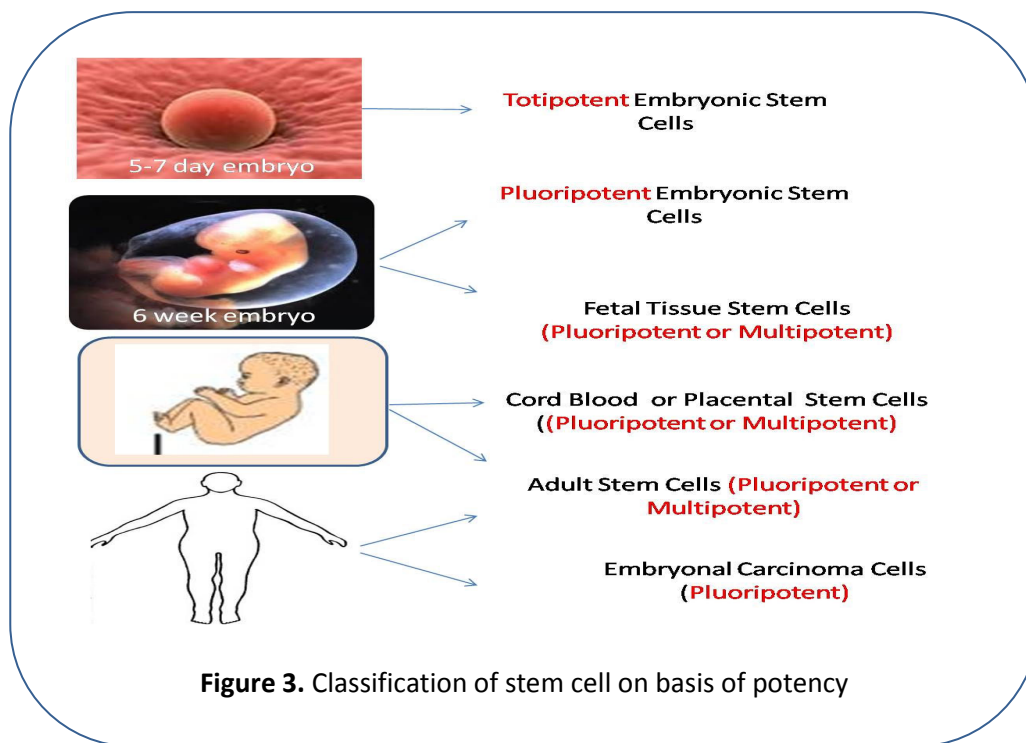


**Figure 1.** Characters of stem cell: replication and differentiation



**Figure 2.** Healthcare benefits for every tissue of human body





Source	Type of Cell	Mechanism of action	Effect
<b>Blastula</b>	Embryonic stem cells (ESC)	Differentiation into cardiomyocytes	Direct contribution to contractility
<b>Skin Fibroblasts</b>	ESC		Remodeling of electrical properties
<b>Heart</b>	Cardiac stem cells	Differentiation into endothelial cells	Remodeling of infarcts
<b>Blood</b>	Endothelial progenitor cells (EPC)	Differentiation into smooth muscle cells	Angiogenesis
<b>Bone marrow</b>	EPC & Mesenchymal stem cell (MSC)		Remodeling of the extracellular matrix
<b>Fat cells</b>	MSC	Paracrine effects	Activation of endogenous stem cells

**Figure 4. Sources of adult stem cells**

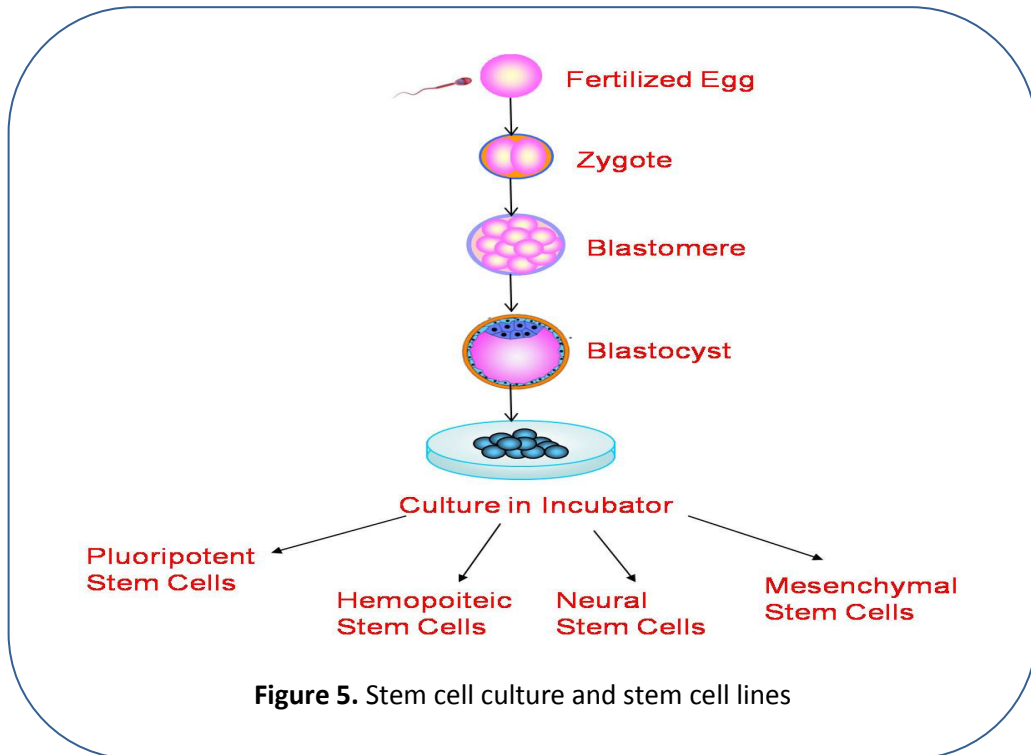


Figure 5. Stem cell culture and stem cell lines

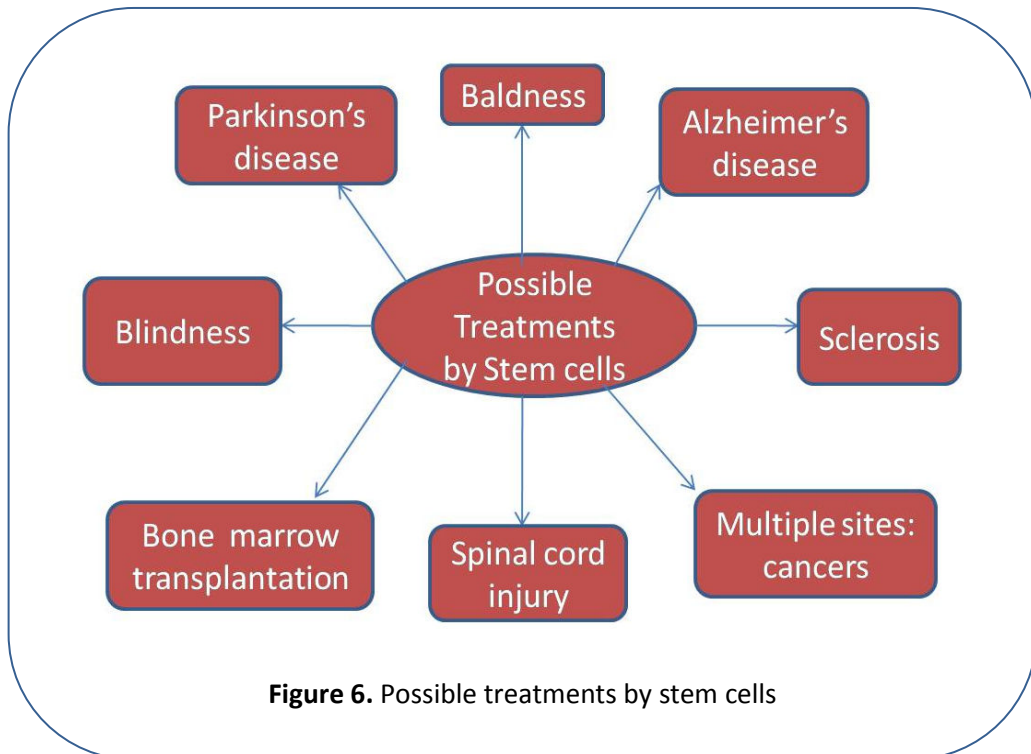


Figure 6. Possible treatments by stem cells