Review Article

Indian Journal of Genetics and Molecular Research
Volume 8 Number 1, January - June 2019
DOI: http://dx.doi.org/10.21088/ijgmr.2319.4782.8119.4

Comparative Study of Human Embryonic and Adult Stem Cells: A Review

Dhanesh Kumar Sharma

How to cite this article:

Dhanesh Kumar Sharma. Comparative Study of Human Embryonic and Adult Stem Cells: A Review. Indian J Genet Mol Res. 2019;8(1):27-34.

Abstract

The Stem Cells are natural as well as organic cells which have ability to be differentiated into other types of cells of body and can multiply to produce similar stem cells. As per the standard definition, a stem cell possesses two properties; firstly the *Self-renewal* means ability to undergo numerous cycles of cell division by sustaining its undifferentiated status and secondly the *Potency* that is the ability to be differentiated into particular cell types. In human being, two broad types of stem cells have been described, the Embryonic Stem Cells (ESCs) which are derived from the inner cell mass of blastocyst and the Adult Stem Cells (ASCs) which are present in the various tissues of body. The aim of this review study is to bring actual facts between the ESCs and the ASCs in human. Related literatures on the subject reviewed through electronic database like PubMed, NCBI, Google Scholar, Web of science etc. The final conclusion was achieved by comparing their structural and functional similarities, dissimilarity, potency, advantages, disadvantages and related recent clinical advancement as regenerative medicine. A number of diseases are being claimed to be treated by the pleuripotent ESCs including blood & immune-system related genetic & malignant disorders, Juvenile diabetes, Parkinson's, Blindness and Spinal cord injuries. On the one side, the uses of the ESCs in research & therapy is controversial as they are derived from 5 days old embryos generated by IVF clinics designated for scientific research and on the other side the ASCs treatments are being employed successfully in many illnesses in last many years especially for treating leukemia & related bone cancers through bone marrow implants. The utilizing ASCs in research and therapy are not as divisive and controversial as that of the ESCs, because the construction of the ASCs does not require the damage of an embryo.

Keywords: Pleuripotent; Multipotent; Self-renewal; Potency; Induced.

Introduction

The Stem Cells are associated with their two great characteristics having the ability to divide or self-renew indefinitely and the potency to be differentiated into particular cell types. The four main types of stem cells have been categorized by the researchers working with them. These are the Embryonic Stem Cells (ESCs), the Adult Stem Cells (ASCs), the fetal stem cells and more recently the

Author's Affiliation: Additional Professor and Head, Department of Anatomy, All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh 492099, India.

Corresponding Author: Dhanesh Kumar Sharma, Additional Professor and Head, Department of Anatomy, All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh 492099, India.

E-mail: dhyanesh.sharma@gmail.com

Received on 19.05.2019; **Accepted on** 28.06.2019

induced stem cells. According to some scientists, apart from the two main types the ESCs and ASCs, there are three other types of stem cells named the cord blood stem cells (can be taken from the umbilical cord blood just after birth), the amniotic fluid stem cells (can be taken from the amniotic fluid before birth) and the induced pleuripotent stem cells (can be produced from the stem cells in various parts of body).

In a developing embryo, the stem cells make a distinction into all the specialized cells of ectoderm, endoderm and mesoderm and also uphold the regular turnover of regenerative organs like blood, skin, intestinal and all other body tissues. After embryonic life, the stem cells act as a repair/ restore system for the body by replenishing the damaged and the dead tissues. The stem cells differ from other kinds of cells in the body by their two characteristic features of self-renewal and potency to be differentiated in to particular cell types. In other words, all the stem cells regardless of their source have three general properties as they are capable of dividing and renewing themselves for long periods, they are unspecialized and they can give rise to specialized cell types. The characteristics of the stem cells may be demonstrated by using techniques like clonogenic assesses, where single cells are assessed for having their capability to self-renew and differentiate. The stem cells may be secluded also by their possessing an individual deposit of cell surface signs. There are significant and important disputes about some projected adult cell populations that whether they are strictly stem cells are not [1].

The *totipotent* cells can form all the cell types in a body including the extraembryonic and placental cells. The only embryonic cells within the first one or two couples of cell divisions after fertilization, that is an earlier stage of morula, are totipotent, able to become all tissues in the body and the extraembryonic tissues and placenta too. The *pleuripotent* cells can give rise to all of the cell types that make up the body but the extraembryonic & placental cells which develop from the trophoblast cells. The ESCs derived from inner cell mass within a blastocyst, are considered as the pleuripotent. The *multipotent* cells can develop into more than one cell type and are little limited than the pleuripotent cells. The ASCs and the cord blood stem cells are considered as multipotent. The *oligopotent* stem cells can differentiate into only a few cell types, such as lymphoid or myeloid stem cells. The *unipotent* cells can produce only one cell type of their own, but have the property of self-renewal, which distinguishes them from non-stem cells like progenitor cells which cannot self-renew [2].

A line of investigations and research studies on stem cells rose out from the findings by

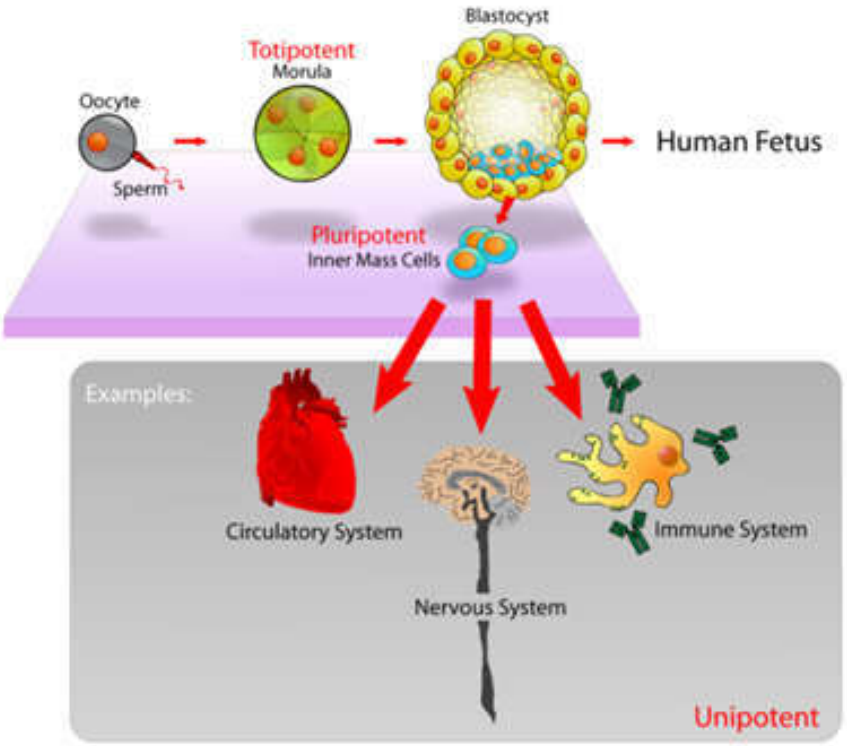

Fig. 1: Totipotent and Pleuripotent cells

McCULLOCH EA and Till JE in the University of Toronto in 1960s [3,4]. The ASCs are commonly being used at present in a variety of medical therapies such as bone marrow transplantation. The stem cells can be artificially grown and transformed into the precise cell types with characteristics steady with cells of a variety of tissues like muscles, nerves etc. The ESCs and autologous ESCs produced by somatic cell nuclear reassign and conversion have also been anticipated as promising candidates for upcoming therapies [5]. Finally, the ASCs may contain more DNA abnormalities due to sunlight, toxins and errors in making more DNA copies during the path of a lifetime. The ESCs are derived from embryos that develop from eggs and have been fertilized in vitro in an in vitro fertilization clinic and then donated for research purposes with informed consent of the donors.

Embryonic Stem Cells

The ESCs are the cells of the inner cell mass of a blastocyst, an early-stage embryo developed before implantation [6]. Blastocyst is 4-5 days post fertilization stage, at this time it consists of about 50–150 cells. The ESCs are pleuripotent and give rise to all the derivatives of the three primary germ layers, ectoderm, endoderm and mesoderm to develop more than 200 cell types of the adult body under appropriate necessary stimulation. The ESCs do not contribute to the extra-embryonic membranes or the placenta and they have ability to propagate self partition to regenerate damaged cells and to form organs & tissues by plasticity and potentially unlimited competence for self-renewal. Their properties also include a normal karyotype, sustained high telomerase activity and a remarkable long-term proliferative potential. Due to combined abilities of unconstrained expansion and pleuripotency, the ESCs should be a theoretically potential and prospective resource for regenerative medication and remedy for the tissue replacement after injury or the disease [7], but there are no approved and accepted standard treatments using the ESCs at present.

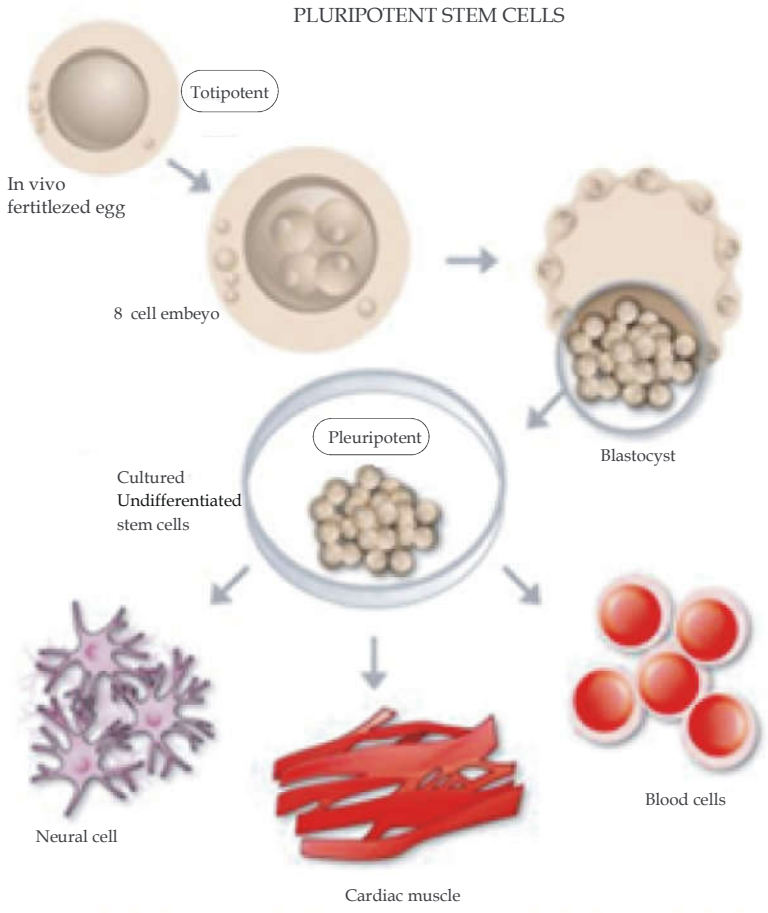

Fig. 2: ESCs (Pleuripotent)

Although the first human experiment was accepted by the US Food and Drug Administration in January 2009 [8] however the human being investigation on stem cells had not commenced until October 13, 2010 in Atlanta for spinal cord injury. Avoiding transplant rejection are just a few of the hurdles that the ESCs researchers still face at the time of distinguishing the ESCs into usable cells [9]. Due to pleuripotency, the ESCs require unambiguous signs for correct discrimination and when injected into another body, they will differentiate into different types of cells, leading to a teratoma. The ethical consideration to use unborn human tissue is another reason lacking approved treatments by using ESCs. On the other hand many nations currently have suspension or limitations on the human ESCs production and research. Over all at present there are no approved and agreed treatments using the ESCs. A number of diseases are being claimed to be treated by the pleuripotent ESCs including blood and immune-system related genetic and malignant disorders; juvenile diabetes; Parkinson's; blindness and spinal cord injuries. The use of human ESCs in research and therapy is controversial as they are derived from human 5 days old embryos generated by IVF clinics designated for scientific research.

Adult stem cells

The ASCs also called somatic stem cells or tissue-specific stem cells and they exist throughout the body after embryonic development and are found inside of different types of tissues in the human body. They are found in children, as well as adults [10]. They maintain and repair the tissue in which they are found. The pleuripotent ASCs are rare and generally small in number, but they can be found in umbilical cord blood and other tissues [11]. The autologous ASCs are derived from the organism of the selfsame individual from its three well-known accessible sources, the bone marrow, the adipose tissue and the blood. They are also found in tissues such as the brain, the blood vessels, the skeletal muscles, the skin and the liver. The stem cells by autologous harvesting involve the least risk in all the stem cell therapy types. The bone marrow is a loaded resource of the ASCs [12] which are being utilized in managing numerous conditions like liver cirrhosis [13], chronic limb ischemic conditions [14] and ending stage of heart failure [15]. The number of bone marrow stem cells turns down with the advancing age and is larger in males than in females in their reproductive periods [16].

Most of the ASCs researches at present are intended to exemplify their potency and self-renewal aptitudes. The damage of DNA mounts up with the age in the stem cells and in the cells surrounding them and this damage is responsible, at least in part for increasing dysfunction of stem cells [17]. Mostly the ASCs are multipotent and referred by their tissue of origin like the

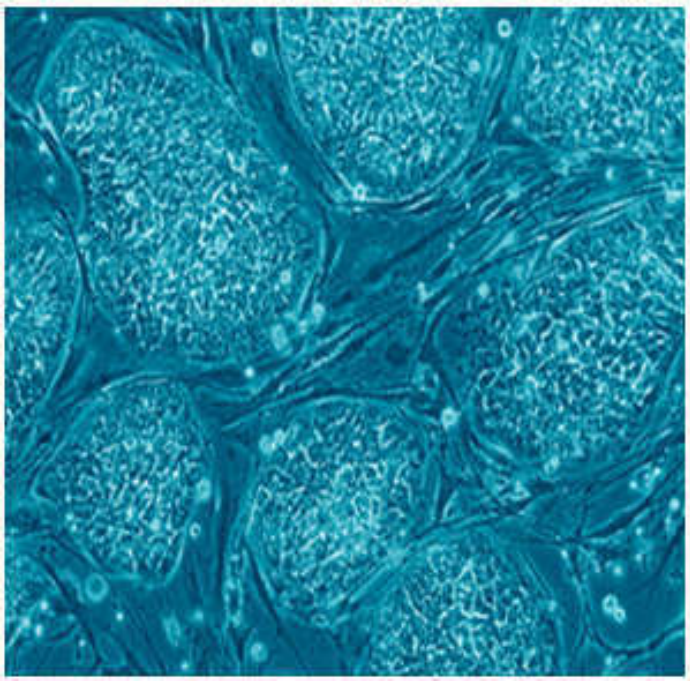

Fig. 3: Human ESCs colonies undifferentiated

mesenchymal stem cell, the adipose stem cell, the endothelial stem cell, the dental-pulp stem cell etc [18]. A recently discovered multi-lineage stress enduring (MUSE) pleuripotent stem cell type is found in the multiple adult tissues like the adipose, the dermal fibroblasts, the bone marrow etc. and is called MUSE stem cell. The ASCs treatments are being employed successfully in last many years for treating the leukemia and the related bone cancers through the bone marrow implants. It is now clear that utilizing the ASCs in research & therapy are not as divisive & controversial as that of the ESCs, because the construction of the ASCs does not require the damage of an embryo. The ASCs are known to have a restricted natural life in vitro and to enter the replicative senescence or the organic process of growing older and showing the effects of increasing age almost undetectably upon starting in vitro culturing [19]. With rising requirement of the ASCs for the research & therapy, there is a need to fulfill the gap between the expansion of the cells in vitro and the capability to tie together the issues towards replicative senescence.

Key Differences

The ESCs and the ASCs both provide the required differentiated cells in the body. Both are capable of the self renewing and the differentiating into specialized different particular cells in the body. The inner cell mass of the blastocyst gives rise to the ESCs and are derived from the three germ layers whereas the ASCs are localized in various parts of the human body after birth and with diversity. The main characteristic difference has been proved that the ESCs are pleuripotent while the ASCs are multipotent.

The ESCs develop in the inner cell mass of the *blastocyst,* a primarily hollow ball of cells formed during three to five days after fertilization of an ovum by a sperm. A blastocyst in a human is about the size of the dot. Normally in the development, the cells of the inner cell mass give rise to the more specialized differentiated cells which form the tissues and organs of our entire body. It is observed by the scientists that on extracting the inner cell mass and growing its cells in special laboratory conditions, these cells retain the properties of the ESCs. The ESCs are *pleuripotent,* meaning they can give rise to every cell type in the fully formed body, excepting the cells in the placenta and the umbilical cord. These cells are extremely important as they provide a renewable resource for studying normal development & diseases; and also for testing drugs & other therapies in diagnostic and

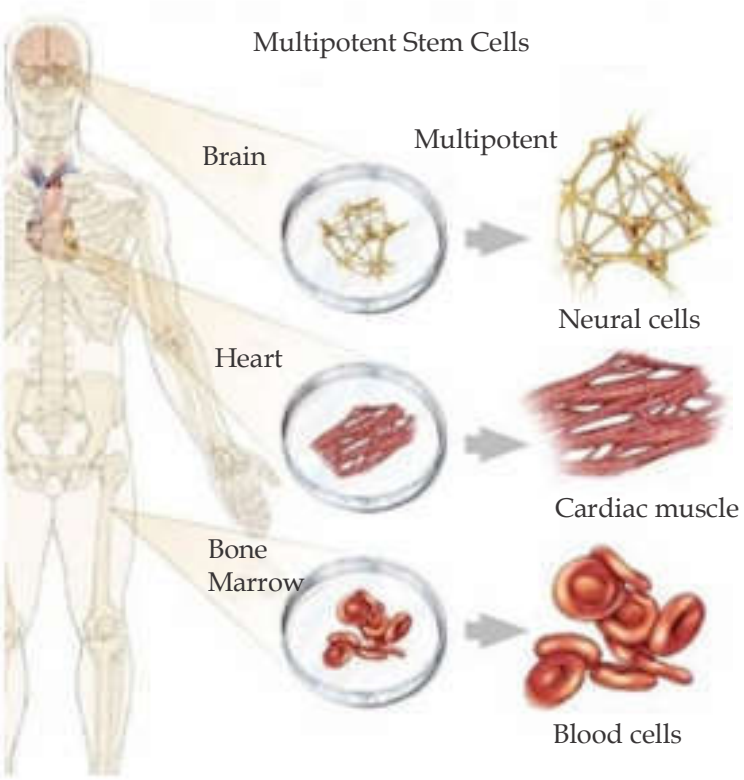

Fig. 4: ASCs (Multipotent)

therapeutic purposes.

The ASCs are more specialized and specific than the ESCs. They can generate different cell types for the specific tissue, organ and system in which they are situated. For instance, the blood-forming or *hematopoietic* ASCs in the bone marrow can give rise to the red blood cells, the white blood cells and the platelets. It means the blood-forming ASCs can't produce the liver, the lung or the brain cells and similarly the ASCs in other tissues and organs can't generate the blood cells and the platelets. It is important to know that some tissues and organs in the body contain small caches of tissue-specific ASCs with job to replace the cells in that tissue which are lost in normal day-to-day activities or in injuries like in the skin, the blood, the lining of gut etc. These tissue-specific ASCs are difficult to find and self-renew in culture as easily as the ESCs do.

The ESCs are the stem cells derived from the inner cell mass of a blastocyst that is an early-stage of the embryo, approximately during 4-5 days after fertilization. On the other hand, the ASCs are derived from the tissues after birth and have the ability to regenerate into all the cell types of the organ from which they originate. The embryo with the stage of inner cell mass has about 50–150 cells. The embryos can be generated in in-vitro fertility (IVF) clinics, so that the researchers could study the stem cells and their insinuation & implication. The ESCs are also known as pleuripotent stem cells as they have the ability to differentiate into any cell type, which means that they have a possibility of infinite applications within the human body. Like the ASCs, the ESCs also have the ability to regenerate indefinitely, as practically the entire human body grows from the single embryo. However the ESCs research has been the subject of much controversy among scientists due to the fact that the ESCs are taken from an embryo which is inhumane as embryos have life and should have the same rights. Many people also look down upon, condemn and pass judgments on the fact that these embryos are generated by IVF, which they consider unnatural and to be against nature.

The ASCs are the reserve cells that each creature has in the various parts of its body and they have the ability to grow and multiply into the cell type that is required by that body part, so that they can replace any dead or damaged cells. Many systems in our body have a supply of the ASCs that help them to heal and replace any dead or damaged parts like the integumentary system, the digestive system etc. however in contrary, there are some other organ & systems in our body like the heart, pancreas and nervous system, which do not have a supply of stem cells. The ASCs are undifferentiated cells, means they have not become specialized stem cells with a particular function. These cells have the ability to divide or self-renew indefinitely. They also have ability to generate all the cell types of the organ from which they originate. The ASCs are derived from the various tissues in the body after birth and depending on those tissues they have the ability to regenerate into all the cell types of the organ from which they originate. Researchers are currently working to develop stem cells that may help to heal and/or replace the damaged and dead parts of the body.

The ESCs originate in the inner cell mass which form three germ layers of the embryo while the ASCs originate in the differentiated tissues but they remain undifferentiated. The ESCs cells are in a wide-ranging and common sense more powerful than the ASCs and happily turn into many different kinds of differentiated tissues, while the ASCs simply cannot do that to the same extent and have some restrictions. The ESCs based therapies are not as safe as the ASCs based therapies as the ESCs are more prone to develop into the malignant cells, so the ASCs based therapies are safer and they have more advantages than the ESCs based therapies [20]. The ESCs have the potential of differentiation into the various cell types thus they are pleuripotent while the ASCs cannot be differentiated into any kind of the specialised cell and have some restrictions thus they are multipotent. The ESCs are relatively new and less known whereas the ASCs are well known. They could be produced only about a dozen years ago, that is many decades after the ASCs, so it is difficult and unreasonable to compare the ESCs and the ASCs in terms of our knowledge base or the extent of their use at the present time. The ESCs in large number can be harvested or grown in culture from embryos by relatively easy methods than the ASCs. The ASCs are rare in mature full grown tissues and so separating these cells from them is challenging & difficult; and methods to increase their numbers in cell culture have yet been worked out to a very little extent. This is an important dissimilarity of the ASCs from the ESCs, as large numbers the ASCs are needed for stem cell replacement and regenerative therapies.

The scientists believe that tissues derived from the ESCs and the ASCs may differ in the probability of being rejected and discarded after transplantation. The ASCs and the tissues derived from them are at present believed less likely to commence rejection after transplantation. This is because the patient's own cells are expanded

in culture and then reintroduced into the same patient. The use of the ASCs and tissues derived from the patient's own ASCs is in favour that in transplantation and regenerative therapy the cells are less likely to be rejected by the immune system. This represents a significant advantage, as immune rejection can be circumvented only by continuous use of immunosuppressive drugs, and the drugs themselves may cause deleterious toxic side effects. The ASCs have definitively been established to have relatively lower tumorigenic (malignancy producing) potential than the ESCs. It means in a general sense, the ASCs are safer than the ESCs, but this does not mean that all the ASCs based therapies are inherently safe and it does not mean that the ESCs based therapies are unsafe, but would be accurate to say that in a general sense the ASCs have a better advantage than the ESCs.

Conclusion

A systematic review aims to provide a complete, exhaustive summary of current literature relevant to a research question. In accordance, this review study concluded by comparing the ESCs and the ASCs as follows:

- The ESCs originate in the inner cell mass which form three germ layers of the embryo while the ASCs originate in the differentiated tissues of the body in post natal life and remain undifferentiated.
- The ESCs cells are in a wide-ranging and common sense more powerful than the ASCs and happily turn into many different kinds of differentiated tissues, while the ASCs simply cannot do that to the same extent due to little restrictions. The ESCs have the potential of differentiation into any kind of cell types thus they are pleuripotent while the ASCs cannot be differentiated into any kind of the specialised cell and have some limitations thus they are multipotent.
- The ESCs cells are comparatively rather new and less well known than the ASCs. They could be produced only about a dozen years ago, that is many decades after the ASCs, so it is difficult and unreasonable to compare the ESCs and the ASCs in terms of our knowledge base or the extent of their use at the present time.
- The ESCs in large number can be harvested or grown in culture from embryos by relatively easy methods than the ASCs. The ASCs are rare or paucity in number in mature full grown tissues of the body and so separating these cells from them is challenging & difficult.
- The ASCs have definitively been established to have relatively lower tumorigenic (malignancy producing) potential than the ESCs. The use of the ASCs and tissues derived from the patient's own ASCs is in favour that in transplantation and regenerative therapy the cells are less likely to be rejected by the immune system. It means in a general sense, the ASCs are safer than the ESCs, but this does not mean that all the ASCs based therapies are inherently safe and the ESCs based therapies are unsafe, but would be accurate to say that the ASCs have a better advantage than the ESCs.

References

1. Sekhar L, Bisht N. Stem Cell Therapy. Apollo Medicine. 2006-09-01;3(3):271-6.
2. Scholer HR. The Potential of Stem Cells: An Inventory. In Nikolaus Knoepffler, Dagmar Schipanski, Stefan Lorenz Sorgner (eds.). Human biotechnology as Social Challenge. Ashgate Publishing. 2007.p.28.
3. Becker AJ, Mcculloch EA, Till JE. Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells. Nature. February 1963;197(4866):452-4.
4. Siminovitch L, Mcculloch EA, Till JE. The distribution of colony-forming cells among spleen colonies. Journal of Cellular and Comparative Physiology. 1963 Dec;62(3):327-36.
5. Tuch BE. Stem cells: A clinical update. Australian Family Physician. 2006;35(9):719-21.
6. Thomson JA, Itskovitz EJ, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, Jones JM. Embryonic stem cell lines derived from human blastocysts. Science. 1998 Nov;282(5391):1145-7.
7. Mahla RS. Stem Cells Applications in Regenerative Medicine and Disease Therapeutics. International Journal of Cell Biology. 2016;7:1-24.
8. Ron W & Alicia M. First Embryonic Stem-Cell Trial Gets Approval from the FDA. The Wall Street Journal. 23 January 2009.
9. Wu DC, Boyd AS, Wood KJ. Embryonic stem cell transplantation: potential applicability in cell replacement therapy and regenerative medicine. Frontiers in Bioscience. 2007 May;12(8-12):4525-35.
10. Jiang Y, Jahagirdar BN, Reinhardt RL, Schwartz RE, Keene CD, Ortiz-Gonzalez XR, Reyes M, Lenvik T, Lund T, Blackstad M, Du J, Aldrich S, Lisberg

A, Low WC, Largaespada DA, Verfaillie CM. Pluripotency of mesenchymal stem cells derived from adult marrow. Nature. 2002 Jul;418(6893):41-9.

11. Ratajczak MZ, Machalinski B, Wojakowski W, Ratajczak J, Kucia M. A hypothesis for an embryonic origin of pluripotent Oct-4(+) stem cells in adult bone marrow and other tissues. Leukemia. 2007 May;21(5):860–7.
12. Narasipura SD, Wojciechowski JC, Charles N, Liesveld JL, King MR. P-Selectin coated microtube for enrichment of CD34+ hematopoietic stem and progenitor cells from human bone marrow. Clinical Chemistry. 2008 Jan;54(1):77-85.
13. Terai S, Ishikawa T, Omori K, Aoyama K, Marumoto Y, Urata Y, Yokoyama Y, Uchida K, Yamasaki T, Fujii Y, Okita K, Sakaida I. Improved liver function in patients with liver cirrhosis after autologous bone marrow cell infusion therapy. Stem Cells. 2006 Oct;24(10):2292–8.
14. Subrammaniyan R, Amalorpavanathan J, Shankar R, Rajkumar M, Baskar S, Manjunath SR, Senthilkumar R, Murugan P, Srinivasan VR, Abraham S. Application of autologous bone marrow mononuclear cells in six patients with advanced chronic critical limb ischemia as a result of diabetes: our experience. Cytotherapy. 2011 Sep;13(8):993-9.
15. Madhusankar N. Use of Bone Marrow derived Stem Cells in Patients with Cardiovascular Disorders. Journal of Stem Cells and Regenerative Medicine. 2007;3(1):006.
16. Dedeepiya VD, Rao YY, Jayakrishnan GA, Parthiban JK, Baskar S, Manjunath SR, Senthilkumar R, Abraham SJ. Index of CD34+ Cells and Mononuclear Cells in the Bone Marrow of Spinal Cord Injury Patients of Different Age Groups: A Comparative Analysis. Bone Marrow Research. 2012;2012:787414:1–8.
17. Behrens A, van Deursen JM, Rudolph KL, Schumacher B. Impact of genomic damage and ageing on stem cell function. Nature Cell Biology. 2014 Mar;16(3):201-7.
18. Gimble JM, Katz AJ, Bunnell BA. Adipose-derived stem cells for regenerative medicine. Circulation Research. 2007 May;100(9):1249-60.
19. Oliveira PH, da Silva CL, Cabral JM. Genomic Instability in Human Stem Cells: Current Status and Future Challenges. Stem Cells. 2014;32(11):2824-32.
20. National Research Council (US) and Institute of Medicine (US) Committee on the Biological and Biomedical Applications of Stem Cell Research. Project Overview and Definitions. Stem Cells and the Future of Regenerative Medicine. U.S. National Library of Medicine, 01 Jan. 1970. Web. 28 Mar. 2017.