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REVIEW ARTICLE

STEM CELLS RESEARCH: A BOON FOR SCIENCE AND SOCIETY

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ABSTRACT

Stem cell research has emerged as an innovative scientific tool in the field of science such as biology, drug discovery, regenerative medicine and toxicological studies which allow us to develop novel techniques for restoration and replacement of damaged tissue. Stem cells are unspecialized cells which show the capacity to develop various cell types in the body. These are derived from a variety of sources (embryos, umbilical cord, blood and placentas) and are classified on the basis of their sources, origin and development and plasticity of differentiation. These also aid to the mechanism of disease evolution and thereby assists in the development of safer and effective drugs. Stem cells are known to treat various diseases such as Alzheimer's, Parkinson's, cancer, Type I diabetes, cardiovascular, gastrointestinal, urogenital, ocular and neurodegenerative diseases. Though stem cell has proved its effectiveness for various chronic illnesses, the hurdles lie in the fact that, research involves the destruction of an embryo or foetus which therefore raises sharp ethical and political controversies. These issues need to be discussed along with scientific challenges to ensure that stem cell research is carried out in an ethical manner. This review article provides a new insight in stem cell research which offers great promises for the benefit of science and society.

INTRODUCTION

Stem cell research is one of the major powerful tools that has recently attracted tremendous clinical, scientific and public interest due to its potential applications in the field of biology, drug discovery, medicine regenerative and toxicological studies (Sidhu *et al.,* 2012). Stem cells are valuable tools for gene targeting, cloning, chimera production and transgenic animals which brought much excitement in the field of medicine (Zwaka and Thomson, 2003; Gade *et al.,* 2012). Stem cells have the capability to evolve into different cell types in the body during early stage of cell growth and development. The term "stem cell" was first originated from botanical monographs where the word "stem" was used for cells localised in the apical meristem which is responsible for the continous growth of plants (Kaufman and Thomson, 2000). The definition says a cell with has the ability to divide indefinitely in culture with the potential to give rise to mature specialized cells (Alison *et al.,* 2002). These cells are "unspecialized" cells derived from various sources including embryos, umbilical cord, blood, placenta, bone marrow and other non-embryonic tissues. These cells are skilled but are not fully differentiated and can divide to produce either cells like themselves (self-renewal), or cells of one or several specific differentiated types. They have the ability to split up or replicate many times and renew themselves for longer period of time unlike muscle, blood, or nerve cells. (Blau *et al.*, 2001; Pazhanisamy and Jyothi, 2009; Duran and George, 2011; Minguell *et al.*, 2011; Kumar *et al.*, 2011; Shevde, 2012). There are three important characteristic properties which differentiate stem cells from other cell types (Mimeault and Batra, 2006; NIH, 2009a). Firstly, they are unspecialized (non-differentiated) cells and do not have any tissue-specific structures which perform specialized functions i.e. a stem cell cannot function like its neighbours to pump blood through the body which is a function of heart muscle cell and also it cannot carry oxygen molecules through the bloodstream (like a red blood cell). Secondly, they are capable of renewing themselves through cell division, even after a long period of inactivity. Lastly, under certain physiological or experimental conditions, they can give rise to more specialized differentiated cells such as nerve cells, muscle cells or insulin producing cells etc. (Weissman, 2000; Gardner, 2002; Bongso and Richards, 2004; Pazhanisamy and Jyothi, 2009).

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Discovery and History

The table given below summarizes the various chronological events in the discovery of stem cell.

Table 1. Major events in the history of stem cells

Year	Discovery
1908	Alexander Maksimov, was the first one to propose the term "Stem Cell" and first to hypothesise the existence of haematopoietic stem cells
1924	Alexander Maximow identified a cell within the mesenchyme that develop into different types of blood cells and later named as mesenchymal stem cells.
1963	James Edgar Till and Ernest McCulloch, illustrates the existence of self-renewing cells in mouse bone marrow.
1968	First bone marrow transplant was done for the treatment of severe combined immunodeficiency (SCID).
1978	Haematopoietic stem cells were discovered in human cord blood.
1981	Martin Evans and Matthew Kaufman extracted and cultured mice embryonic stem cells from mice blastocysts. Gail R. Martin first coined the term "embryonic stem cell".
1989	Sally Temple, described the existence of multipotent stem cells in the subventricular zone (SVZ) of mouse brain.
1992	Brent A. Reynolds and Samuel Weiss isolated neural stem cells from the adult mice brain. In the same year Cepko and Evan Y. Snyder isolated multipotent cells from the mouse cerebellum and transfected them with the oncogene v-myc.
1997	John E. Dick suggested the existence of cancer stem cells.
1998	James Thomson, first derived human embryonic stem cells and John Gearhart extracted germ cells from fetal gonadal tissue.
2001	Early staged human embryos were clone (at 4 to 6 cells stage) in an Biotech oriented company name as Advanced Cell Technology.
2003	A new source for extracting adult stem cells was discovered from the primary teeth of children by Songtao Shi.
2005	Researchers at UC Irvine's Reeve-Irvine research centre, restore partial mobility in paralysed rats, with induced spine damage by using neural stem cells. Cord blood-derived multipotent stem cells with pluripotent capacities were identified at. the University of Illinois, Chicago.
2006	Shinya Yamanaka was first to derive induced pluripotent stem cells from mice. England was the first to differentiate umbilical cord blood cells into liver cells. Anthony Atala *et al.* discover amniotic fluid stem cells (AFS cells), a new type of pluripotent stem cell. Mario Capecchi, Martin Evans and Oliver Smithies received the Nobel prize for their work on mouse embryonic stem cells.
2007	Shinya Yamanaka was the first to create human induced pluripotent stem cells. Robert Lanza at Advanced Cell Technology, Santa Monica, created first HES cellss without destructing embryo. Successful regeneration of human knee cartilage by the use of autologous mesenchymal adult stem cells was reported. Human pluripotent stem cells were created from spermatogonial cells of adult testis by Sabine Conrad *et al*. In the same month scientists created induced pluripotent stem cells from a single human hair.
2008	Paolo Macchiarini transplanted the trachea fully grown from stem cells on a Colombian female who had her own collapsed due to tuberculosis.
2010	The first human clinical trial involving embryonic stem cells commences and was later cancelled.
2011	Stem cell from an endangered species *Mandrillus leucophaeus* and the nearly extinct northern white rhinoceros, *Ceratotherium simum cottoni* was produced by Inbar Friedrich Ben-Nun.
2012	Advance Cell Technology announces human stem cell clinical trial.

*Source: http://www.stemcellsfreak.com/p/stem-cell-history.html)

CLASSIFICATION OF STEM CELLS

Stem cells can be classified on the basis of their sources, origin and development and plasticity of differentiation.

(i) Source

Stem cells can be obtained from a variety of sources; research is currently undergoing to explore the role of stem cells derived from all the sources. Depending upon the source they are classified as embryonic stem cells and adult stem cells (Boiani and Scholer, 2005; Gade *et al.*, 2012).

a) Embryonic stem cells

Embryonic stem (ESCs) cells are extracted from embryos and are believed to hold the most potential ability as they are pluripotent. They are obtained from the inner cell mass (ICM) of the blastocyst (early mammalian embryo) and possesses the ability to become any tissue in the body, except placenta (Spiegel and Fischbach, 2000; Fong *et al.*, 2004). The ESCs are capable of unlimited, undifferentiated proliferation *in vitro* (Thomson *et al.*, 1998; Kumar *et al.*, 2011). ESCs have the capability to self-renew and give rise to any specialized cell types, such as liver and brain cells. ES cells are sensitive to pH, overcrowding, oxygen and temperature changes, making it imperative to care for these cells daily. The research is still going on to understand the signals inside and outside the cells that trigger the differentiation of these stem cells. These internal signals in a cell are controlled by various genes which are interspersed across DNA that carries coded instructions for all the structures and functioning of a cell. There are certain external signals which include several chemicals secreted by other adult stem cells. (Ying *et al.*, 2003; Mitjavila-Garcia *et al.*, 2005; Evans, *et al.*, 2006; Alp Can, 2008; Kumar *et al.*, 2009).

Adult stem cells

Adult stem cells (ASCs) have the ability to differentiate into cells within a specific lineage and regenerative tissues. These stem cells can be derived from different parts of the body and depending on where they are from have different properties. (Serafini and Verfaillie, 2006; Holden, 2007; Michaud, 2009; Pei *et al.*, 2010). They have been identified in various organs and tissues, but are limited in number in each tissue. They require the presence of a tightly regulated environmental niche comprising other cell types, stroma and growth factors for survival called a "stem cell niche" (Rizo *et al.*, 2006; Scadden, 2006). In this specific area of tissue they may remain inactive for many years until they are activated by tissue injury or disease (Kumar *et al.*, 2009). The primary function of adult stem cells in living organisms is to repair and maintain homeostasis in the tissues in which they are located. Adult stem cells share two major characteristic properties firstly, they can make their identical copies for long periods of time and secondly, they demonstrate the ability to proliferate (long-term self renewal) (Marcus and Woodbury, 2008). ASCs can be obtained from a large number of tissues and organs such as adipose tissue, brain, blood, bone marrow, intestine, pancreas, umbilical cord and liver (Kumar *et al.*, 2011). Blood-forming adult stem cells in bone marrow (called hematopoietic stem cells, or HSCs), are currently the only type of stem cell commonly used to treat human diseases. These adult stem cells are mainly multipotent or unipotent in nature. The term somatic

stem cell at times is also referred instead of adult stem cell as these are the tissues derived from somatic cell and are believed less likely to initiate rejection after transplantation. This is because a patient's own cells could be cultured, differentiated and then can be reintroduced into the patient body (Krause *et al.,* 2001; Körbling and Estrov, 2003). Due to such defined characteristic properties, ASCs have been extensively studied for their potential neuroregenerative therapy such as Huntington's disease. Huntington's disease is a fatal disorder characterised by chorea (excessive spontaneous movements) and progressive dementia that it is caused by the death of particular brain cells (Ryu *et al.,* 2004; McBride *et al.,* 2004).

(ii) Origin and Development

On the basis of origin and method of derivation, stem cells can be classified as (a) Human embryonic stem cells (HES cells), which can be derived from a pre-implantation embryo at the blastocyst stage. (b) Human embryonic germ cells (HEG cells), which can be isolated from the primordial germ cells of the foetus and (c) Human somatic stem cells (HSS cells), which can be isolated from adult or foetal tissues, organs, blood and umbilical cord.

(a) Human embryonic stem cells

HES/ES cells are derived from an epiblast, the inner mass of a blastocyst, stage of roughly 100 cells which is totipotent in nature i.e. they can give rise to fully functional organisms as well as every cell type in the body (Edwards, 2004). In the human, the blastocyst stage lasts for five or six days before implanting in the uterine wall. If during the blastocyst stage embryo does not implant in the uterine wall, it will not undergo further development. Embryonic stem cells can give rise to cells from all three embryonic germ layers which include ectoderm, mesoderm and endoderm. Ectoderm gives rise to brain, spinal cord, nerve cells, hair, skin, teeth, sensory cells of eyes, ears, nose, mouth and pigment cells. Mesoderm gives rise to muscles, blood, blood vessels, connective tissues and the heart. Endoderm gives rise to gut (pancreas, stomach and liver), lungs, bladder and germ cells (eggs or sperm). These are called tissue-specific stem cells, or lineage-restricted stem cells. It is these cells that are used for transplantation purposes. HES cells serve as a potential infinite bank from which these more specific cells can be created as and when needed. Human ES stem cells are unique in one aspect that they lack the G_1 phase of cell cycle and predominately reside in the S phase during which they synthesize DNA. These cells show large number of applications in transplantation therapy, pharmaceutical screening, gamete and embryo production, congenital anomalies and infant cancers (Bongso and Richards, 2004).

(b) Human embryonic germ cells

Human embryonic germ cells (HEG cells) are derived from primordial germ cells occurring in the gonadal ridge of an embryo and are pluripotent in nature. They are isolated when the fertilized egg is a foetus between 4 and 5 weeks of development. These early cells derived from foetal tissue during initial development can become sperm and eggs. After several days, the cells in an embryo begin to differentiate and develop specific functions. As the cells specialize and begin to create particular tissues and body parts, they lose their plasticity and ability to generate into other cell types. Nevertheless, the foetus retains a "reserve" of embryonic germ cells that remain pluripotent. Thus, in terms of the ability to make other cell types, embryonic germ cells are very similar if not identical to ES cells. Despite their potential, there exist significant obstacles to the use of embryonic germ cells for research and therapy. An early embryo starts with only about 50 of these rare cells, making them very difficult for isolation and studies. The source of these cells is foetal tissue where the large-scale manufacturing of products is questionable and the procurement of these cells raises obvious ethical issues (Shamblott *et al.,* 1998).

(c) Human somatic stem cells

These are unique post embryonic cells that have the ability to divide extensively and generate the cell types of a particular tissue. This is an intermediate stage between the ES cells and the other cell types of body. Tissue-specific stem cells are isolated from specific sites of the developing or adult tissue. The most widely discussed potential use of stem cells and progenitor cells is in tissue repair. There are well documented evidences for restoration of normal physiological function in animal models of liver failure, diabetes and a variety of neurological disorders. The human somatic stem cells or tissue-specific (adult) stem cells are further classified into various subtypes such as hemopoietic, mesenchymal, liver, epidermal (skin, hair), neuronal, eye, gut and pancreas stem cells (Bongso and Richards, 2004).

(iii) Plasticity of stem cells

The plasticity is the ability of stem cells to differentiate and to produce other cells in the body which may form one cell type or multiple cells types. Stem cells can be divided into various categories depending upon their plasticity i.e. totipotent, pluripotent, multipotent and unipotent stem cells (Boiani and Scholer, 2005). Cell differentiation takes place in several stages starting from a totipotent state, differentiation proceeds through a pluripotent stage and ends in a lineage committed state. The degree of stemness determines whether stem cells are totipotent, pluripotent, multipotent or unipotent. Totipotent is the least and multipotent the most restricted stem cells (Sidhu *et al.,* 2012). Totipotent cells show the ability to differentiate into all three germ layers including placenta, similarly pluripotent stem cells can form all three germ layers except the placenta, whereas multipotent stem cells can differentiate into multiple cell types of particular tissue type and unipotent can form only one cell type (Tokuzawa *et al.,* 2003; Boiani and Scholer, 2005; Alp, 2008).

(a) Totipotent stem cells

Considered to be one of the most significant types of stem cell, they have the potential to grow and differentiate into any type of cell found in the human body, including the placenta. In the process of human development, the egg and the sperm fuse together to form a single celled zygote (Boiani and Scholer, 2005. The zygote then divides several times and form cells that are the precursors to the trillions of cells which constitute the

human body. These formed cells are known as totipotent, as their potential is 'total'. It is during the early cell divisions that more totipotent cells are produced which further divide to produce more number of totipotent cells and after four days the cells begin to specialise into pluripotent cells. Basically, the pluripotent stem cell can do everything as the totipotent cells, except for creating an entire organism (Sidhu *et al.,* 2012).

(b) Pluripotent stem cells

Pluripotent embryonic stem cells (PSCs) were first isolated in the year 1981 from the inner cell mass of mouse blastocysts (Evans and Kaufman, 1981; Martin, 1981)**.** PSCs can be derived from diverse somatic cells and share many characteristic properties of embryonic stem cells (ESCs). Pluripotent stem cells were initially isolated by two different research groups: Dr. James Thomson *et al.* and Dr. John Gearhart *et al*. in 1998 (NIH, 2006). Pluripotent stem cells are often termed 'true' stem cells as they can give rise to cell lines which are capable of maintaining themselves *in vitro* for an unlimited period a similar property as of cancer cells (Takahashi and Yamanaka, 2006; Li *et al.,* 2010). This means that under the right circumstances a stem cell isolated from an embryo can produce almost all the cells of the body. PSCs descend from totipotent stem cells and after several days they can differentiate into any type of cell except totipotent stem cells. Approximately four days after fertilization the totipotent cells begin to differentiate and form a cluster of cells known as a blastocyst. The blastocyst has yet another smaller group of cells known as the inner cell mass and it is these pluripotent stem cells that will go on to produce most of the cells and tissues of the human body (Palmer *et al.,* 2001; Smith, 2001; Hansis *et al.,* 2002). PSCs show large rate of multiplication in culture, maintain a normal karyotype and shows the potential to generate into any cell type of the body. They also present an incredible resource for the repair of diseased or damaged tissues in our bodies and open a new window for embryonic development of our species (Donovan and Gearhart, 2001).

Advantages of pluripotent stem cells

Pluripotent stem cells provide an opportunity to obtain a renewable source of healthy cells and tissues to treat a broad array of diseases such as heart disease and diabetes. Burn victims and those suffering from autoimmune diseases such as Parkinson's can all be potentially benefited by use of PSCs. Another potential application of PSCs is in the transplantation of cells and tissues and their ultimately transformation to replace diseased cells and tissues. The use of pluripotent stem cells in drug research is another important area that has to be worked out. To assess the safety and use of drugs instead of testing drugs on animals, pluripotent stem cells can be used for drug testing. Afterwards, those drugs that appear to be tolerated and safe can then be tested on animals and humans. In the year 2006, another category of PSCs known as induced pluripotent stem cells was derived from any adult tissue. Induced pluripotent stem cells (iPSCs) have now been generated from multiple terminally differentiated somatic cells and adult stem cells from mouse (Lowry *et al.*, 2008) as well as from human (Takahashi and Yamanaka, 2006; Aasen *et al.,* 2008; Nishikawa *et al.,* 2008; Josipa and Izpisua-Belmonte, 2012).

(c) Multipotent cells

Multipotent stem cells hold the same characteristic properties as of all stem cells and are unspecialized cells that have the ability to self-renew for long periods of time and differentiate into specialized cells with specific functions. These descend from pluripotent stem cells and can differentiate into many cell lines within a specific type of tissue. A multipotent stem cell can give rise to other types of cells but it is restricted in its ability to differentiate for example, cells in the brain that give rise to different neural cells and glia or haematopoietic cells, which can give rise to different blood cell types, but they can't create brain cells (Kirschstein and Skirboll, 2001; Kumar *et al.,* 2011; Porrata *et al.,* 2011; Sidhu *et al.,* 2012). A multipotent stem cell is also known as a mesenchymal stem cell that has the ability to give rise to a narrow range of cells, suitable to a particular location such as blood stem cells give rise to red blood cells, white blood cells and platelets, whereas skin stem cells give rise to the various types of skin cells (Bongso and Richards, 2004; Spencer et al., 2011). Adult stem cells are considered multipotent because their specialization potential is limited to one or more cell lines (Pazhanisamy and Jyothi, 2010). Multipotent stem cells are found in the tissues of adult mammals. It is believed that they are in most organs of the body, where they replace diseased or aged cells. Thus, they function to replenish the body's cells throughout an individual's lifetime. Multipotent adult stem cells are useful in transplants as they can be isolated, albeit often with difficulty, from a person's tissues and then directed to evolve into a certain type of cell, before being transferred back into the same patient. This avoids the immunological challenges of pluripotent foetal stem cell usage, where a patient's immune system could potentially reject a 'foreign' tissue. Another advantage is the controversies regarding the ethical issues in extracting foetal stem cells can be prevented, as in this case neither foetal tissues nor an aborted embryo is used for the treatments (NIH, 2009b).

(d) Unipotent Stem Cells

Unipotent stem cell refers to a cell that has the lowest differentiation potential in comparison with other types of stem cells i.e. they are specialized to differentiate along only a single lineage and develop only into cell types of their own tissue. Unipotent stem cells are descendant of a multipotent stem cell and can give rise to an individual cell type and can be localized in adult tissues (Sidhu *et al.,* 2012). Due to immense importance of totipotent and pluripotent stem cells, unipotent are being neglected. However, the unipotent adult stem cells in the body's tissues showed the important property of self-renewal that is shared by all stem cells. Despite their differentiation potential being low, they are still able to generate healthy and viable cells for transplant purposes which have huge therapeutic potential to treat injuries and diseases. For example, skin cells, are one of the most abundant types of unipotent stem cells. The patient suffering from burn can be treated by removing a part of a patient's own undamaged skin stem cells and transplanting that as sheets of skin over burned areas of the patient's body. A major limitation of this technology, is that, it is extremely time consuming. It can take several weeks to obtain a sufficiently sized piece of skin (Boiani and Scholer, 2005; Alp, 2008). Using the stem cell

technique, the skin cells of a burnt person can be treated using stem cells.

APPLICATIONS OF STEM CELLS

Stem cell research has created much excitement and thrill since their discovery at the University of Wisconsin-Madison ten years ago. It is believed that stem cells will soon revolutionize the field of medical sciences as it has led to the emergence of a new field of regenerative medicine which will allow physicians to replace damaged or lost cells, with stem cells (Chapman *et al.,* 1999; Gardner, 2007). Stem cell is a beneficial laboratory tool for better understanding of origin and causes for many chronic and acute diseases. This could lead to unprecedented cures and palliative treatments. Stem cells are capable of eluding detection by the host's immune system and acts as a promising source for therapeutic applications (Lin *et al.,* 2006; Priddle *et al.,* 2006). For a person suffering from Parkinson's disease scientist take stem cells and introduce them into the nervous system. Since these cells have the ability to become cells of different types, there is possibility that they would repair the diseased Parkinson's brain by becoming new, dopamine producing nerve cells, thus replacing the specialized nerve cells that had been lost. The same would hold true for treating heart attacks replacing the heart cells that were killed during the heart attack. Stem cells also have the power to replace glial cells which help in insulating nerves and cause them to conduct electrical impulses quickly as in multiple sclerosis.

Stem cells are currently used to treat various diseases and disorders, cancers such as leukaemia, bone marrow transplants which have been used for decades now to provide a healthy source of cells in the body. Development of cell specific gene therapeutic approaches are now underway to cure various diseases including premature aging diseases, Alzheimer's disease, cancer, Parkinson's disease, Type I diabetes, spinal cord injuries, atherosclerosis, hematopoietic, cardiovascular, primary immunodeficiency diseases, nervous system diseases, gastrointestinal, pulmonary, urogenital, ocular, etinal diseases, neurodegenerative, stroke, skin disorders and myocardial infarction (Atkinson and Eisenbarth, 2001; Street *et al.,* 2004; Lindvall and Kokaia, 2006; Mimeault and Batra, 2009; Tam and Khouri, 2009; Ribitsch *et al.,* 2010; Abdel-Salam, 2011; White *et al.,* 2011).

ETHICAL ISSUES CONCERNING STEM CELL RESEARCH

Various chronic illnesses can be cured by stem cell research however hurdles lie in the fact that it involves destruction of an embryo. Destruction of the potential human (in the form of embryos) conflicts with religious and moral values of our society, but for the people suffering from chronic illnesses where there is no treatment, this religious and emotional concern is of no value. It is always recommended to consider all the options and opinions available to make a balance between the advantages and disadvantages of the research which are beneficial for people suffering from debilitating diseases. For avoiding any ethical issues, the embryonic stem and germ cells can be obtained either from donated embryos or from pregnancies that were terminated due to some medical or social reasons (Robertson, 1999; McLaren, 2001; Ruiz-Can, 2002). It is reported that there are about 400,000 human embryos lying stored in infertility clinics in the United States. These embryos were created, using *in vitro* fertilization (IVF) for couples trying to have a child. Many of these artificially created embryos are no longer needed by their parents and are destined for destruction. Scientist supporting stem cell research are of opinion that these spare embryos should be made available for research, as they are ultimately be discarded (Hoffman *et al.,* 2003). The other major ethical issue lies with the fact that the combination of embryonic stem cell with the cloning technologies may led to the generation of an embryo which is considered to be the genetic clone of donor nucleus. This type of embryo generation can raise the eyebrows of those working against human cloning. A major obstacle to the development of new medical therapies based on stem cells is opposition to embryonic stem cell research on ethical, moral, or religious grounds (Lo and Parham, 2009). In countries like Australia, legislation states that no embryo can be created for the purpose of stem cell research.

CONTROVERSIES FOR STEM CELL RESEARCH

Several sources are available to obtain pluripotent stem cells without destroying human embryos. Out of these, four major proposals are being mentioned below **(**Nicanor, 2010). According to first proposal human pluripotent stem cells can be obtained from early IVF dead embryos. These embryos at times may contain cells that are still alive which could be used to obtain PSCs. This option is equivalent to organ donation where the dead embryo can be used by science for the benefit of others. However, this proposal has generated much debate as it is difficult to know whether the embryo is truly dead or the death is natural or artificial i.e. killed just for the purpose of obtaining cells for stem cell research (Ruiz-Can, 2002). The second proposal states that, human pluripotent stem cells could be obtained by biopsy of an early stage human embryo but using human embryos for purposes of no benefit to them, and without their knowing consent, would be an act of injustice to them. This is again a matter of debate amongst scientists and ethicists as it can never be justified to expose human embryo by doing experimental manipulation. According to the third proposal, pluripotent human stem cells could be obtained from non-embryonic biological artifacts created using genetic tricks to manipulate eggs and cells. This approach will lead to the creation of disabled embryos at the same time it will lead to the commercialization of human reproductive tissue and exploitation of women, especially in the developing world (Thomas, 2007). The fourth proposal states that pluripotent stem cells could be obtained by reprogramming of differentiated cells taken from adult human beings. This proposal has attained most scientific success. Two research teams of Japan and United States, independently reported that they had successfully reprogrammed adult human cells into pluripotent stem cells called induced pluripotent stem (iPS) cells, which were indistinguishable from pluripotent stem cells taken from human embryos (Hanna *et al.,* 2007; Takahashi *et al.,* 2007).

CONCLUSION

Despite the fact there has been tremendous progress in our understanding of stem cells in the past few years, stem cell therapeutics is still considered to be a young field as many aspects are still need to be elucidated to fully understand its

therapeutic potential. Recent insights into differentiation and development of embryonic, adult and induced pluripotent stem cells provide great benefits to the society, but also raise several fundamental questions about their clinical applications. It is evident that major challenges still remain in deriving potential human embryonic stem cells by exploiting the iPSc technology. The long term application and the end result of successful stem cell transplantation are still to be explored. As we don't know how long these stem cell will be useful while replacing the old and damaged tissues. It is also fascinating to know how an organism drives stem cell mobilization and their reestablishment at distal tissue organs in response to a variety of stress signals. Given that complex degenerative disorders persist despite the conventional therapies further propagates our immense interest in the development of novel strategies based on stem cell therapeutics. There is a need for deeper insights of the stem cells to develop most-promising targeted therapies for various chronic degenerative disorders.

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