*Journal of Studies in Dynamics and Change (JSDC), ISSN:2348-7038*
*Vol. 2, No. 1, January-March 2015*
JSDC
*Suggested Citation*
Chaudhary,J.K.(2015). Harnessing Stem Cell Potential for Regenerative Medicine and Cell-Based Therapy. *Journal of Studies in Dynamics and Change (JSDC), 2*(1), Pages. 18-22

# Harnessing Stem Cell Potential for Regenerative Medicine and Cell-Based Therapy

**Jitendra Kumar Chaudhary**
Ph.D. Molecular Biology Laboratory, School of Life Sciences, JNU

ABSTRACT

Stem cell-based therapies are thought of as among the most promising new combative strategies against various developmental, traumatic, oncogenic and degenerative, including neurodegenerative, diseases. The progress, in the field of stem cell research was made on the basis of multiple research initiative, such as finding out the location of resident stem cell in the animal body, their isolation, *in vitro* culture and propagation, lineage and trans-lineage differentiation, multi-pronged experimentation both *in vitro* as well as in a dazzling array of animal models. While the hope for stem cell-based regenerative medicine grows by leaps and bounds, it is becoming explicitly clear from multiple pre-clinical and clinical trials that we still need a greater insight and understanding of the fundamentals of stem cell biology as well as the underlying mechanism of disease in order to devise an efficient, efficacious, safe, reliable, scalable, pragmatic, cost-effective, accessible and affordable cell based therapy.

**Keywords**; *Stem cells, induced-pluripotent stem cells, embryonic stem cells, cell-based therapy.*

**JEL Classification:** L65, C99

***Author Details and Affiliations***

Dr. Jitendra Kumar Chaudhary, Ph.D. Molecular Biology Laboratory, School of Life Sciences, Jawaharlal Nehru University, New Delhi-110067, India and can be contacted at jnujitendra@gmail.com; dujitendra2013@gmail.com

## Introduction

Stem cells have an interesting history, hugely replete with varied discourse, debate and controversy. Researchers, in mid 1800s, discovered that cells were basically the building blocks of life, and that some cells had the ability to produce other cells. Later on, owing to several years of relentless thinking and efforts, mammalian eggs could be fertilised outside of the human body. In the early 1900s, cells with remarkable ability to generate blood cells were identified. After a gap of 8-9 decades, researchers discovered blood producing stem cells, called as hematopoietic stem cells, followed by another resident of bone marrow stem cells, named as mesenchymal stem cells. Furthermore, during the first decade of 21st century, scientists successfully programmed differentiated somatic cells into stem cell-like cell that was called as induced pluripotent stem cells (iPSCs). The greatest advantages of the iPSCs, apart from being a potential prospective candidate for cell therapy, is the lack of any ethical concerns like other category of stem cells, such as embryonic stem cells (ESCs). Besides, stem cells are also being used to generate multiple functional organs *in vitro* to study, and explicitly decipher the structural organisation and concerted working of these vital organs in the human body, which will further help in deepening the insight, understanding and designing new therapeutic strategy to ameliorate and cure the multiple diseases. Recent findings have proved that the stem cells may offer shining rays of hope, and be explored for treatment of deadly degenerative and incurable diseases in years to come.

## Brief historical perspective

The trajectory of the discovery of stem cells/related cells has been quite interesting over the century. Some landmark events in the field of stem cell research include:

1978: Stem cells were discovered in human cord blood

1981: First in vitro stem cell line developed from mice

1988: Embryonic stem cell lines created

1995: First embryonic stem cell line derived from a primate

1997: Cloned lamb from stem cells

2006: Discovery of induced-pluripotent stem cells (iPSCs)

In the following year i.e., 1998, Thompson, isolated cells from the inner cell mass of early embryos, and successfully developed the first embryonic stem cell lines. In the same year, Gearhart et al. derived germ cells from cells in foetal gonad tissue; pluripotent stem cell lines were developed from both sources. Then, in 1999 and 2000, scientists discovered that manipulating adult mouse tissues, by coaxing and tweaking their residential environment, could produce different cell types. This meant that cells from bone marrow could produce nerve or liver cells and cells in the brain could also yield other neuronal and non-neuronal cell types. Furthermore, Shiyana Yamanaka, in 2006, came up with defined set of genetic factors (also called as pluripotency-associated transcription factors, such as Sox2, Oct4, Nanog, Klf4, Myc), and showed that somatic cells could be induced to become stem cells with acquisition of stem cell-specific biological characteristics (*1*), and these newly formed stem cells are called as induced pluripotent stem cells (iPSCs). This study proved very significant and has paved way for various interesting discoveries made in the following years. Aforementioned discoveries were exciting for stem cell research, with the promise of greater scientific control over stem cell differentiation and proliferation and offers fresh hope for cell based therapy in years to come.

## What is a stem cell?

Over the period, growing body of research has explicitly revealed that human body consists of three types of cells; germ cells, somatic cells and stem cells. Cells are smallest unit of unicellular and multicellular organisms, and their number and the particular way of arrangement make the organism what they eventually look like at the different stages of development as well as for the rest of their life. All the three important categories of cells are derived from the inner cell mass (ICM) of embryo through the synchronized and precisely regulated process of development, which is accompanied by the differentiation, dedifferentiation and specialization of cells eventually forming the complete individual. Somatic cells contribute the bulk proportion of cells in the body, while germ cells give rise to gametes i.e., sperm and egg. Stem cells are rationally believed to be present in least number in almost every post natal organs and parts of the body (*2*).

Stem cells are defined as "cells having tremendous but controlled proliferation, self-renewal and differentiation potential and possess immense capability of giving rise to various specialized cells *in vitro*. Stem cells are sort of potentially dynamic reservoir of unspecialized cells and can make any type of cells following intrinsic and extrinsic molecular/ or milieu/ niche driven-instructions/signalling. They are capable of doing so because they have almost all genes/ cellular machinery in either "on" or they can make them in "on-off" positions as per the need unlike the somatic and differentiated cells. Stem cells, upon division, give rise to two types of daughter cells; specialized/differentiated daughter cells and undifferentiated daughter stem cells, thereby maintaining constant repertoire of organ specific stem cells (called as stem cell self-renewal) along with the new differentiated cells which can replace the damaged, lost or diseased cells. Stem cell plasticity is another attribute of stem cells which refers to the ability to differentiate and form cell types of non-residing tissues/organs. Stem cells are highly clonogenic and slow-cycling and generally represent very small percentage of total cellular make-up of an organ.

## Nomenclature of Stem Cells

Broadly stem cells are divided into two main categories; pluripotent embryonic stem cells (ESCs) and multipotent/unipotent adult stem cells (ASCs) or also called as somatic stem cells (SCCs). The most recent entrant category of stem cells is induced pluripotent stem cells (iPSCs). The name of stem cells is given on the basis of organ they are derived or isolated from. For example, bone marrow-derived stem cell, adipose tissue-derived stem cells, dental pulp-derived stem cells, skin-derived stem cells, mammary gland-derived stem cells, muscle-derived stem cells, and brain-derived stem cells and so on and so forth. This nomenclature list of stem cells is still expanding with the rapid discovery of new members.

Embryonic stem cells are the most sought after among the stem cells as they are supposed to be mother of all kind of stem cells and are isolated from inner mass of 3-5 days embryo called blastocyst. ESCs come first in the life and in fact, new life begins from these cells. During the development they can make various specialized and functional cells, tissues and organs while renewing themselves, and thereafter provide guidance and supports till the end stage of embryonic development. Now a day, despite so much significance and immense clinical importance, working on embryonic stem cells has become difficult as it is surrounded and hindered by lots of ethical controversies and misconceptions.

Adult stem cells are also unspecialized and reside in virtually all types of tissues and organ of an adult individual. In contrast to embryonic stem cells, they are believed to possess limited therapeutic potential. Bone marrow-derived stem cells (Haematopoietic, mesenchymal and multipotent adult progenitor stem cells), adipose tissue-derived stem cells, dental pulp-derived stem cells; brain- and skin-derived stem cells and several others come under the category of adult stem cells. These stem cells are comparably easy to isolate without going to the extent of destroying individual they are isolated from and there are not so much ethical and medical controversy surrounding adult stem cells.

In the recent years, placenta and associated extra-embryonic tissues, which are medically discarded following delivery, are being considered as one of the richest sources of stem cells. They are multipotent and easy to work with as its source of origin i.e., human placenta is easily available at the hospitals across the globe. One advantage with this cell type is that they reflect the overlapping biological properties of both i.e., adult and embryonic stem cells. Cord blood obtained from umbilical cord also acts as source of stem cells. It is collected from the fetal end of cord and cryopreserved at $-196^0$ C, and then stored in cord blood bank for future transplantation. Cord blood stem cells are currently being used in the treatment of more than 75 life threatening diseases, including neurodegenerative disorders.

**Therapeutic applications of stem cells**

Human beings have long been fascinated by the differential rejuvenating and regenerating abilities of certain animals, wherein the remaining tissues remarkably recalibrate and reorganize to form a missing body part partly and/or completely depending on the extent of damage/ loss. Over the humongous period of evolution, the animals belonging to different phyla have evolved differential regeneration abilities both at the cell and tissue levels. For instance, planarian flatworms and Hydra possess the intrinsic ability to regenerate the entire organ of their body with high precision and accuracy. On the contrary, higher invertebrates have lost this amazing whole-organ regeneration ability and are limited to very few parts of organs and tissue, such as hepatic tissue.

Our body continuously undergo various internal and external assault-induced wear and tear processes, and as a result, cells/tissues start dying or they become non-functional incapacitated and defunct. Now the role of stem cells becomes important here. What do stem cells do in these circumstances? Here, stem cells can ameliorate the diseases/assault by following methods (1); they themselves can take over the functions of lost cells/ or organs. (2) Can help recover damaged cells by providing support by secreting various growth factors and cytokines or they can help recover the damage by the integrating themselves at the damaged site or by combination of both functions.

Besides, the applications of stem cells are manifold and likely to go beyond medical imagination. Stem cells from different sources have promised to revolutionize the very prospect of regenerative medicine through the provision of cell-based therapy to treat the potentially debilitating diseases. For example, stem cells are being looked at with great hope and immense potential to address hitherto incurable diseases such as Parkinson's, Alzheimer's, Diabetes, Cancer, heart disorders, debilitating spinal cord injuries, bone marrow disorders and so on. Their potential applications also lie in development of *in vitro* assay system for drug screening and development, drug discovery, toxicity measurement and disease modelling for understanding the basic processes underlying developmental process as well as the etiology. As a proof of concept, researchers have been able to develop an *in vitro* model of the 'brain' using human multipotent stem cells, called as cerebral organoids (*3*), which could possibly provide deeper insights into brain development, several brain-related functions and pathologies, including the neurodegenerative diseases in future. Based on the above findings, it may be prudently concluded that stem cells could be used for cell based therapy for treatment of neurodegenerative diseases in days to come.

**Why Stem Cells?**

A common man wonders why stem cells have become such a hotly debated topic with respect to cell/tissue based regenerative medicine. The reasons are as follows; 1) In case a person suffers from cancers and immunological disorders and no currently available medicine work, stem cell-based therapy and stem cell transplantation may come to patient's rescue. 2) The second point is that with respect to stem cell transplantation there are fewer problems of immunological rejections as the stem cells to be transplanted come from healthy part of patient's own body. 3) Side effects are minimal unlike allopathic and other conventional medicines. 4) Entire cellular machinery is transplanted hence it has wider spectrum of benefits. 5) Stem cells have mobile capability unlike the fixed and differentiated cells, thereby offering promises as drugs delivery vehicles to the desired part of body. Till now, stem cells have been transplanted in various metabolic and genetic disorders, such as leukemia, skin diseases, bone marrow, diabetes, thalassemia, retinal problems, and various neurodegenerative diseases like Parkinson's, Alzheimer's and others with differential degree of clinical success. However, there are lots of unexplored aspects of stem cells which have to be fully mastered and understood by clinicians and researchers before it become reality for treatment of untreatable and incurable diseases like cancer and neurodegeneration.

**Types of stem cell transplantation**

Broadly transplantation refers to the "moving of live and functional cells, organs or part of tissues from one body to another or from donor sites of patient's own body in order to compensate tissue , organ or cell losses". Now- a-day in most cases of stem cell transplantation, doctor takes the normal stem cells from patient's own body, grow them under appropriate *in vitro* conditions, and eventually put them back to the desired body's location. Transplantation can be of different types depending on the origin of the cells and tissues to be used as therapeutic transplant.

*Autotransplantation or autograft*: the origin of transplant and transplantation site belongs to same person.

*Allotransplantation or allograft*: donor and recipient are genetically non-identical but belong to the same family.

*Isotransplantation or isograft*: transplantation between identical twins.

*Xenotransplantation or xenograft:* donor and recipient belong to different species.
*Split transplantation:* Sometimes a deceased's live organ (e.g., liver) is divided into two and given to two different patients.

**Stem cell transplantation centres in India**

In Indian, there are several transplantation centres in different major cities and its number is increasing with the advancement and dissipation of knowledge in field of stem cell biology and transplantation (*4*). Few major centres are mentioned below;

1. Christian Medical College Hospital, Vellore
2. Tata Memorial Hospital, Mumbai
3. All India Institute of Medical Sciences, New Delhi
4. Apollo Hospital, Chennai
5. Jaslok Hospital, Mumbai
6. Research and Referral Hospital of the Armed Forces, New Delhi
7. Sahayadri Hospital, Pune
8. Gujarat Cancer Research Center, Ahmedabad
9. Sanjay Gandhi Post Graduate Institute, Lucknow
10. Kidwai Memorial Hospital, Bangalore

**Future prospect of stem cell-based therapy**

Stem cell-based therapies are thought of as among the most promising new combative strategies against various developmental, traumatic, oncogenic and degenerative, including neurodegenerative, diseases. The progress, in the field of stem cell research was made on the basis of multiple research initiative, such as finding out the location of resident stem cell in the animal body, their isolation, *in vitro* culture and propagation, lineage and trans-lineage differentiation, multi-pronged experimentation both *in vitro* as well as in a dazzling array of animal models. While the hope for stem cell-based regenerative medicine grows by leaps and bounds, it is becoming explicitly clear from multiple pre-clinical and clinical trials that we still need a greater insight and understanding of the fundamentals of stem cell biology as well as the underlying mechanism of disease in order to devise an efficient, efficacious, safe, reliable, scalable, pragmatic, cost-effective, accessible and affordable cell based therapy.

## Works Cited

Takahashi, K., and Yamanaka, S. (2006) Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors, *Cell 126*, 663-676.

Da Silva Meirelles, L., Chagastelles, P. C., and Nardi, N. B. (2006) Mesenchymal stem cells reside in virtually all post-natal organs and tissues, *J Cell Sci 119*, 2204-2213.

Lancaster, M. A., Renner, M., Martin, C. A., Wenzel, D., Bicknell, L. S., Hurles, M. E., Homfray, T., Penninger, J. M., Jackson, A. P., and Knoblich, J. A. (2013) Cerebral organoids model human brain development and microcephaly, *Nature 501*, 373-379.

Chandy, M. (2008) Stem cell transplantation in India, *Bone Marrow Transplant 42 Suppl 1*, S81-S84.