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RESEARCH ARTICLE

# STEM CELL AND REGENERATIVE MEDICINE: THERAPEUTIC APPROACHES AND CHALLENGES – A REVIEW

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**ABSTRACT**

**Aim:** To emphasize the recent updates on stem cell and regenerative medicine - therapeutic approaches and challenges.
**Objective:** To study and review the various available literatures on stem cell and regenerative medicine both their therapeutic approaches and challenges in the field of medicine and dentistry
**Background:** Stem cells have been defined as clone cells that undergo both self-renewal and differentiation to more committed progenitors and functionally specialized mature cells. In the recent times, stem cells have been identified in a variety of tissues of an adult body. Depending on the source, they have the ability to form one or more, or even all cell types of an organism. Stem cell research has shed light on our understanding of developmental biology and offered much hope for cell replacement therapies overcoming a variety of diseases.
**Reason:** The literature survey inoculates the various approaches for the application of stem cell in modern world for the benefit of mankind.



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## INTRODUCTION

Stem cells are unique type of cells that have specialized capacity for self-renewal and potency, can give rise to one and sometimes many different cell types. "They are found in almost many of the multi cellular organisms and are characterized by the ability to renew through mitotic cell division while maintaining the undifferentiated state".( Sunil *et al.*, 2012) Regenerative medicine and emerging biotechnologies stand to revolutionize the practice of medicine. Advancements in stem cell biology, including embryonic and postnatal somatic stem cells, have made the prospect of tissue regeneration a potential clinical reality (Sylvester, 2004). Stem cell biology is currently one of the most exciting areas of biomedical research, as enthusiasm for the application of this technology toward regenerative medicine continues to expand. The application of cells in a therapeutic fashion may become a natural extension of the presumed potential of these unique cell populations with wide-ranging capabilities. As with many new and exciting technologies, much remains to be tested, proved, and delivered to separate the hope from the hype (Manipal *et al.*, 2014). This review highlights the use of these tiny but yet powerful cells in relation to its therapeutic use and the challenges to be faced.

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## DISSCUSION

### Stem cell

Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. They are found in multicellular organisms. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues (Kumar *et al.*, 2014). In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues (Saraswathi *et al.*, 2010).

There are three known accessible sources of autologous adult stem cells in humans:

- Bone marrow, which requires extraction by *harvesting*, that is, drilling into bone
- Adipose tissue
- Blood, which requires extraction through apheresis, wherein blood is drawn from the donor , and passed through a machine that extracts the stem cells and returns other portions of the blood to the donor (Shabeenataj *et al.*, 2014)

## Types of stem cells

### Adult stem cell

### Bone marrow derivedmesenchymal stem cell

The bone marrow is a complex tissue containing stem cells with hematopoietic properties. These bone-marrow mesenchymal stem cells have been identified as the source of multipotent stem cells. Bone-marrow-derived mesenchymal stem cells (BM-MSCs) are also referred to as stromal progenitor cells which are self-renewing and expandable stem cells used for regenerative studies (Kern *et al*., 2016). Pittenger *et al*. (1999) reported that MSCs are only a very small fraction of the total population of nucleated cells in the marrow. Bone-marrow derived mesenchymal stem cells (BM-MSCs) are also know as stromal progenitor cells, and they are self-renewing and expandable. MSCs constitute approximately 0.01-0.001% of the whole bone-marrow cells (Koc *et al*., 1999). . Nowadays BM-MSCs represent an ideal stem cell source for cell therapies and regeneration studies due to their multi-potent property (Bartold, 2004)

### Adipose tissue derived stem cell

Compared with bone marrow-derived mesenchymal stem cells, adipose tissue-derived stromal cells (ADSC) do have an equal potential to differentiate into cells and tissues of mesodermal origin, such as adipocytes, cartilage, bone, and skeletal muscle. However, the easy and repeatable access to subcutaneous adipose tissue and the simple isolation procedures provide a clear advantage (Schäffler *et al*., 2007). The adipose tissue is a highly complex tissue and consists of mature adipocytes, preadipocytes, fibroblasts, vascular smooth muscle cells, endothelial cells, resident monocytes/macrophages (Weisberg *et al*., 2003). The stromal-vascular cell fraction (SVF) of the adipose tissue has come more and more into the focus of stem cell research since this tissue compartment provides a rich source of pluripotent adipose tissue-derived stromal cells.( Zuk, 2002)

### Embryonic stem cells

Multipotent stem cells are also found in amniotic fluid. These stem cells are very active, expand extensively without feeders and are not tumorigenic. Amniotic stem cells are multipotent and can differentiate in cells of adipogenic, osteogenic, myogenic, endothelial, hepatic and also neuronal lines (Abdulrazzak *et al*., 2010). It is possible to collect amniotic stem cells for donors or for autologuous use (Takahashi, 2006)

Also,Umbilical cord blood is the blood that remains in the blood vessels of the placenta and the portion of umbilical cord attached to it. Cord blood is often used nowadays on an experimental basis as a source of stem cells similar to those found in bone marrow. Umbilical cord blood is source of rare but precious haematopoetic stem cells and progenitor cells. Cord blood has an enhanced capacity to proliferate the progenitor cells and self renewal in vitro. Cord blood is easier to collect than bone marrow and can be stored frozen until it is needed. A major limitation of cord blood transfusion is that the blood obtained from a single umbilical cord does not contain as many haematopoeitic stem cells as a bone marrow donation. Banking cord blood is a way of preserving potentially lifesaving cells that is usually thrown away after birth. Newer techniques involving the stored cord blood may be developed to treat many diseases in the future (Moise, 2005).

### Induced pluripotent stem cell

Induced pluripotent stem cells(IPS) is an evolving concept in which 3-4 genes found in the stem cells are transfected into the donor cells using appropriate vectors. The stem cells thus derived by culturing will have properties almost like embryonic stem cells. This path breaking discovery may have a major role in future stem cell therapy (Gronthos *et al*., 2000).

## Therapeutic uses of stem cells

The concept of producing 'spare parts' of the body for replacement of damaged or lost organs lies at the core of the varied biotechnological practices referred to generally as tissue engineering. Use of postnatal stem cells has the potential to significantly alter the perspective of tissue engineering. Successful long-term restoration of continuously self-renewing tissues such as skin, for example, depends on the use of extensively self-renewing stem cells. The identification and isolation of stem cells from a number of tissues provides appropriate targets for prospective gene therapies (Bianco, 2001).

Stem cell transplantation seems to be a promising strategy for treatment of several central nervous system degenerative diseases like Alzheimer's disease, Parkinson's disease (Wu *et al*., 2010). Bone marrow mesenchymal stem cells (BMSCs) are an example of self-renewing multipotential cells with the developmental capacity to give rise to certain cell types (McKay, 1997; Cameron and McKay, 1998). These cells seem to be able to differentiate into hepatocytes, osteocytes, cardiomyocytes, and neural cells *in vitro* (Brazelton *et al*., 2000; Mezey *et al*., 2000). Dental pulp tissue has the regenerative potential to form dentin in response to any injury.Tubular dentin formation was observed when human pulp stem cells with scaffold (hydroxyapatite/tricalcium phosphate) were implanted in immunocompromised mice. Reparative dentin formation on amputed pulp was found when stem cells were combined with recombinant human bone morphogenetic protein 2 (BMP 2) in experimental studies on animal models (Iohara *et al*., 2004). Regeneration of the pulp inside the damaged tooth can be the basic clinical application of stem therapy in dentistry. Root canal treatment in a young permanent molar will stop the tooth's continuous maturation process there by leaving thin egg shell like weak tooth that is susceptible to fracture. Regeneration of pulp with stem cell therapy will be a better option. Stem cells harvested from the pulp of unwanted teeth like third molar can be utilized to regenerate the pulp of severely injured tooth there by preventing the need for endodontic treatment in adults (Huang, 2009)

## Challenges faced in stem cell therapy and regenerative medicine

Stem cell treatments may require immunosuppression because of a requirement for radiation before the transplant to remove the person's previous cells, or because the patient's immune system may target the stem cells. One approach to avoid the second possibility is to use stem cells from the same patient who is being treated (Moore *et al*., 2015). Pluripotency in certain stem cells could also make it difficult to obtain a specific cell type. It is also difficult to obtain the exact cell type needed, because not all cells in a population differentiate uniformly. Undifferentiated cells can create tissues other than desired types. Some stem cells form tumors after transplantation pluripotency is linked to tumor formation especially in embryonic stem cells, fetal proper stem cells, induced pluripotent stem cells. Fetal proper stem cells form tumors despite multipotency (Snyder, 2010)

**Conclusion**

As the debate about stem cell research continues, the scientific discoveries of earlier claims should proceed. Obvious potential clinical benefits may result from much of this work, but in a larger sense the rethinking of long-held biological patterns may prove to be ultimately as valuable. Although stem cell transplantation strategies have not yet been clinically approved, they are currently the most effective and efficient way to improve the medical standard of the human population. Studying the role of chemokine receptors and adhesion molecules on MSCs may allow the development of therapeutic strategies to fix damaged or diseased tissues. This could lead to various therapeutic possibilities such as supporting tissue regeneration, correcting inherited disorders (e.g., of bone), dampening chronic inflammation, and using these cells as vehicles for the delivery of biological agents. A great deal of basic research is needed to further explore the current candidate cell populations before potential clinical benefits of stem cell research can begin to be realized.

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