

## Stem cell plasticity (Systematic review)

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**Abstract: Objective:** To study stem cell plasticity and its role in the treatment of different diseases. **Data sources:** MEDLINE, EMBASE and PUBMED databases were searched. The search was performed on 1 October 2014 and included articles published ahead of print with no language restrictions. **Study selection:** The initial search presented 500 articles, papers and journals about stem cells, stem cell therapy and Stem cell plasticity. **Data extraction:** Data from each eligible study were independently abstracted in duplicate using a data collection form to capture information on study characteristics, interventions, quantitative results reported for each outcome of interest. **Data synthesis:** Because of heterogeneity of stem cells, stem cell therapy and stem cell plasticity and outcome measures reported, it was not possible to pool the data and carry out a meta-analysis. Significant data were collected. Thus, a structured review was performed. **Conclusion:** Excellent outcomes have been achieved in the field of stem cell plasticity and Stem cell therapy of several diseases such as diabetes mellitus, stroke, cardiovascular Diseases, hepatic diseases and neurodegenerative diseases.

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**Keywords:** Stem Cell, Renewal, Plasticity, Tissues, Therapy, Disease

### 1. Introduction:

Stem cells are characterized by their ability to transform into different lineages and the capacity for self-renewal. These cells have two main types: embryonic stem cells (ESC) and adult stem cells [1].

#### Figure (1).

Stem cells are populated in most adult mammalian tissues to keep the tissue homeostasis and take part in tissue repair and regeneration when exposed to damage [2].

Stem cells can be divided into two types, non-definitive and definitive stem cells. Definitive stem cells can be divided into two types; those that maintain continuously proliferating cell systems and those that maintain partially proliferating cell systems. [3].

Self-renewal refers to the ability of a cell to preserve its identity after division. pluripotent stem cells must undergo uniform self-renewal divisions in which each daughter cell maintains pluripotency. [4].

Potency refers to the potential of differentiation (the potential to differentiate into different cell types) of the stem cell. [5].

Stem cell plasticity is usually not demonstrated spontaneously, but is rather something inherent in the cells that can only be induced artificially. [42].

In a slowly proliferating tissue such as the liver, cellular plasticity may allow differentiated cell types to de-differentiate into stem/progenitor-like cells upon tissue damage. [47].

### 2. Material and Method

The guideline for conducting this review according to guidance developed by the center for review and dissemination. It was used to assess the methodology and outcome of the studies.

#### Search strategy

Search was performed in several database. It included Medline, articles in Medscape, AAFP and PubMed. The search was performed on 1st November 2014, and included all articles published. No restriction according to language.

#### Study selection:

All researches were assessed to include in the review by three researchers. They were included if they fulfilled.

- 1- Definition of stem cells.
- 2- Different types of stem cells.
- 3- Role of stem cell therapy.
- 4- Stem cell plasticity.

Participants: Persons suffering from neurodegenerative diseases and some chronic disease s such as diabetes.

Intervention: Early investigation and management.

Comparative: neurodegenerative diseases and some chronic disease s such as diabetes.

Outcome: proper health.

Articles in no English language were translated. The article title and abstract were initially screened. Then the selected articles were read in full and further assessed for eligibility. All references from the eligible articles were reviewed in order to identify additional studies.

**Data extraction:**

Data from each eligible study were independently abstracted in duplicate using a data collection form to capture information on study characteristics, interventions, quantitative results reported for each outcome of interest. Conclusion and comments on each study made.

There was heterogeneity in the collected data. It was not possible to perform meta-analysis. Significant data were collected. Thus, a structured review was performed with the result tabulated.

**Data synthesis:****3. Result:**

The selected studies were six studies. The studies were deemed eligible by fulfilling the inclusion criteria. There was a high degree of heterogeneity regarding evidence of presence of stem cell plasticity and its roles in health and diseases.

**4. Discussion:**

According to **Bianco, et al., 2013(6)** Adult stem cells are found all over the body, where they play a role in the maintenance of the different organs or tissues. Under physiological circumstances, every type of tissue stem cell only gives cells of its original site, the blood (hematopoietic) stem cell generates blood and so on. According to **Kondo et al., 2003(7)** Hematopoietic stem cells are the most distinguished adult stem cell subtypes. According to **Elkhafif, et al., 2011(8)** Blood stem cells are stem cells that have the capability of self-renewal and the ability to differentiate into blood cells that perform some biological activities. Blood stem cells plasticity can give many types of adult cells such as hepatocyte. According to **Ding, et al., 2011(9)** Mesenchymal stem cells (MSCs) were primarily found in the bone marrow, but after that they were found in other systems such as adipose tissue and menstrual blood. According to **Dimarino, et al., 2013(10)** MSCs have a hopeful option for cell therapy owing to their accessible isolation, great expansion potential, and the ability to form new blood vessels.

According to **Gieseck, et al., 2015 (11)** Recent treatments for many degenerative diseases such as Alzheimer and Parkinson disease, multiple sclerosis, diabetes, and heart diseases, as well as for many types of cancer, are mainly symptomatic, and for certain diseases, total recovery requires whole organ transplantation. According to **Wagers and Weissman, 2004(12)** Plasticity is characterized by the reciprocal replacement ability from one type of stem cells into different types. In tissue specific stem cell produces differentiated elements distinctive to a particular tissue. Under some circumstances, these cells may be forced to produce elements not found in the original

tissue. According to **Tetteh et al., 2015(13)** Plasticity is defined as the ability of a cell to have new features in a tissue-specific, controlled manner, in response to particular context-dependent intracellular or extracellular environments. Of note, unlike transdifferentiation, where cell fate can change between different lineages, cellular plasticity occurs within a specific tissue lineage.

According to **Chan, et al. 2014(14)** Mesenchymal stem cells obtained from the Umbilical cord showed favorable plasticity. Adult stem cells mesenchymal stem cells enhanced the recovery of functions in animal models of stroke even when administered after a delayed time. According to **Liu and Rando, 2011(15)** Stem cells are rare and are able to self-renew to give rise to many types of mature cells. In each tissue or organ with high cell turnover, stem cells should be long lived to constantly refill cells lost and to keep homeostasis. Therefore, stem cells are exposed to the damaging effects of both intrinsic and extrinsic effectors of damage during organismal aging. According to **Folmes, et al., (2012) (16)** In line with stem cells' intrinsic self-renewal ability, specific endogenous small molecules obtained from stem cells (e. g., metabolites of essential nutrients and other building blocks) regulate cell type-specific signaling, metabolic, transcriptional and epigenetic mechanisms by taking part in protein modifications, or serving as endogenous receptor ligands or enzyme cofactors. According to **Copley, et al., 2012(17)** Several outstanding reviews also concentrated on self-renewal in adult stem cells, including those of the intestine and blood stem cells. According to **Nakada, et al, 2009(18)** the ability to self-renew is not restricted to stem cells, as some progenitor cells can also do. According to **Schöler and Hans, 2007(19)** Potency refers to the differentiation potential (the potential to transform into different cell types) of the stem cell. According to **Ilic and Polak, 2011(20)** Multipotency refers to the ability of cells to transform only into a closely related family of cells.

According to **Birbrair, et al., 2016(21)** Stem-cell niche refers to a microenvironment, inside the specific anatomic location where stem cells are found, which interacts with stem cells to regulate cell fate. According to **Morrison and Scadden, 2014(22)** Stem cells are stored in niches, which are situated deeply in the tissue to protect it from damaging stimuli. According to **Morrison and Spradling, 2008(23)** A niche is composed of cells including the stem cells whose state (quiescence, self-renewal, amplification or differentiation) is set by a collection of cell specific properties (intrinsic determinants) and of signals residing and spreading in the micro-environment hosting the stem cells (extrinsic determinants). **Figure (2).**

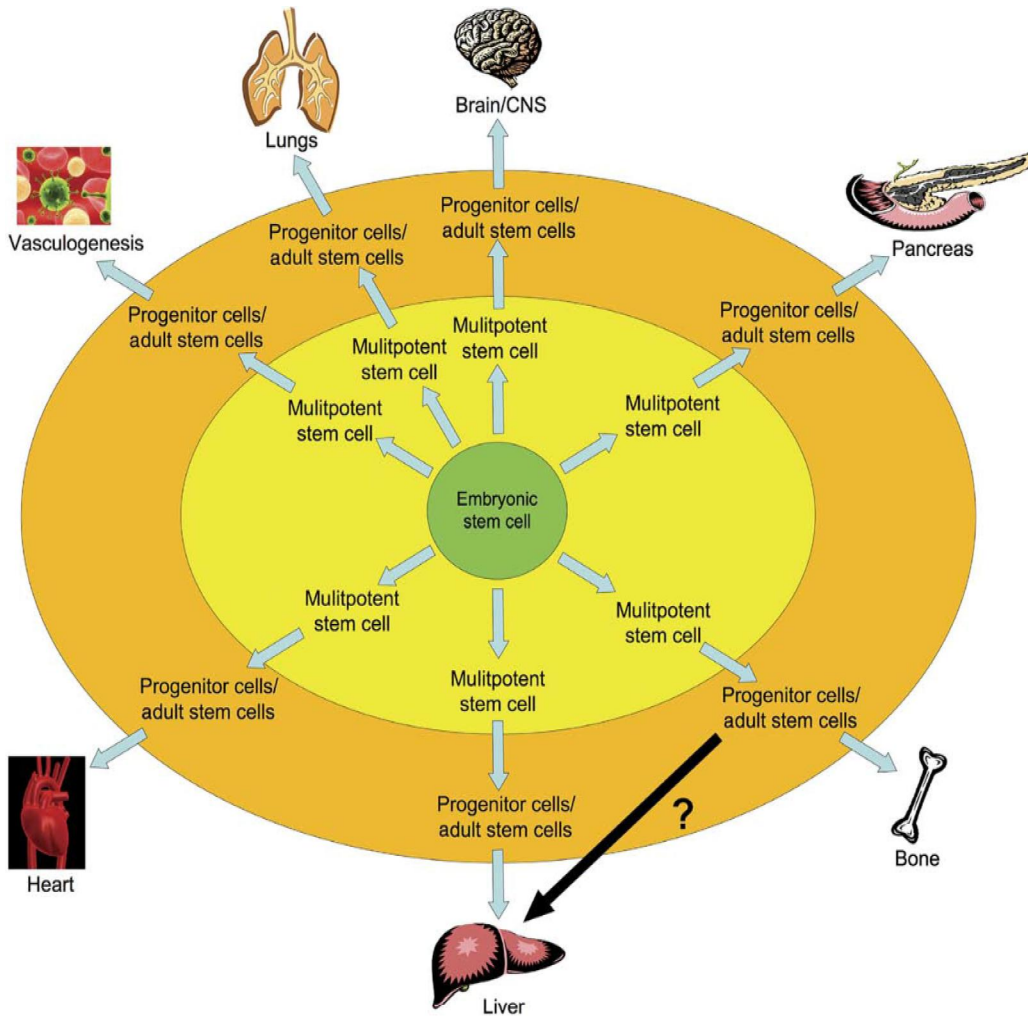
According to **Kai and Spradling, 2003(24)** Markers of gene expression have been sought that would distinguish stem cells based on a unique underlying process. Markers truly specify for one or multiple stem cells. According to **Mannelli and Gallo, 2012(25)** The main markers used for isolation, identification and purification of cancer stem cells (CSCs) include surface cell-adhesion molecules (e. g., CD133, CD24, receptor CD44), cyto-protective enzymes (such as aldehyde dehydrogenase, ALDH), transcription factors (e. g., OCT-4, SOX-2), and drug-efflux pumps (e. g., ATP binding cassette (ABC) drug transporters and multidrug resistance transporter1, MDR1). According to **Mandal, 2013(26)** Embryonic stem cells can be obtained from the inner cell mass of blastocysts 5-10 days after *in vitro* fertilization. According to **Chong, et al., 2014(27)** Human embryonic stem cells (h ESC) are useful for the perfect cell replacement therapies and regenerative medicine.

According to **Zheng, et al., 2008(28)** Fetal stem cells have great value for research for some relevant reasons, they could be obtained by minimally invasive techniques during pregnancy, for prenatal diagnosis. According to **Bianco, et al, 2013(29)** Adult stem cells are found all over the body, where they maintain the organ or tissue in which they are found during the lifespan. Most rapidly renewing tissues are maintained by stem cells. According to **Strauer, et al., 2009(30)** Adult stem cells can be used in stem cell therapy. According to **Ema, et al., 2014(31)** Blood stem cells are the first described adult stem cells. According to **Passweg, et al., 2014(32)** Hematopoietic stem cell transplantation (HSCT) is a proven procedure of therapy. Several congenital and acquired diseases are treated with HSCT, and the frequency of transplants is increasing worldwide every year. **Figure (3)** According to **Takahashi, et al., 2007(33)** The discovery in 2007 that human induced pluripotent stem cells could be generated opened the door to unprecedented opportunities to supply multiple functional human cells in huge quantities. According to **Ding, et al., 2011(34)** Mesenchymal stem cells (MSCs) were originally identified in the bone marrow, but after that they can be isolated from other systems such as menstrual blood, umbilical cord and adipose tissue. According to **Daley, 2012(35)** A central strategy in regenerative medicine is to treat patients by

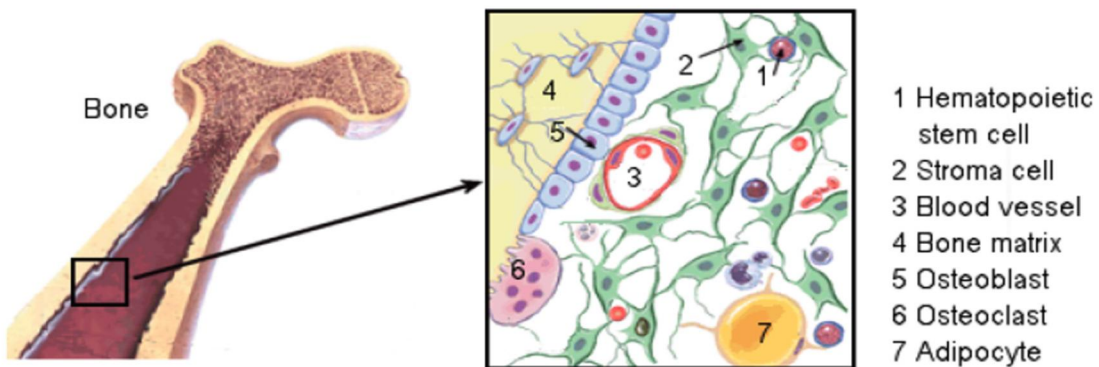
transplanting stem cells or their differentiated derivatives. **Figure (4)** According to **Watt and Driskell, 2010(36)** Stem cells play an important role in regenerative medicine because they can extensively self-renew and generate differentiated progeny. According to **Yu, et al., 2013(37)** Preconditioning strategies in stem cell therapy improve cell survival rate and differentiation ability and improve effects in reducing inflammatory factors and fibrosis; these effects enhance organ and tissue regeneration and functional recovery after cell implantation. According to **Rebeiro and Moore, 2016(38)** Stem cells can be used to treat neurodegenerative conditions, such as in Parkinson's, Amyotrophic lateral sclerosis, and Alzheimer's disease. **Figure (5)** According to **Theise, 2010(39)** Stem cell plasticity was given a very broad definition. Four different cell development pathways were described standard lineage differentiation, Cell dedifferentiation, changing gene expression and cell fusion. According to **Graf and Enver, 2009 (40)** Transdifferentiation includes the irreversible change of cells from one differentiated cell type to another. According to **Pournasr, et al., 2011(41)** stem cell plasticity can be used in gene therapy and regenerative medicine. According to **Takahashi, and Yamanaka, 2006(42)** Stem cell plasticity cannot present spontaneously, but can only be produced artificially.

According to **Cobaleda and Sanchez-Garcia, 2009(43)** Stem cell plasticity can give rise to the origin of diseases. According to **Font-Burgada, et al., 2015(44)** Studies have also recently supported a role for stem/progenitor compartments in liver homeostasis.

According to **Takebe, et al., 2013(45)** In a 2013 study, scientists showed that induced pluripotent stem cells can be used to create liver cells. According to **Sanchez Alvarado and Yamanaka, 2014(46)** Throughout adult life, tissues maintain cellular function and constant cell number through robust homeostatic mechanisms that maintain the fragile equilibrium between proliferation and differentiation. The rate of cellular proliferation depends on the turnover requirement of the tissue. According to **Blanpain and Fuchs, 2014(47)** In a slowly proliferating tissue such as the liver, cellular plasticity may allow differentiated cell types to de-differentiate into stem/progenitor-like cells upon tissue damage.



**Figure (1): stem cell differentiation.** (M. Oertel and D. Shafritz, 2008)



**Figure (2): HSC niche in the endosteal region of the bone marrow.** (Ellis, S.L. and Nilsson, S.K., 2012)

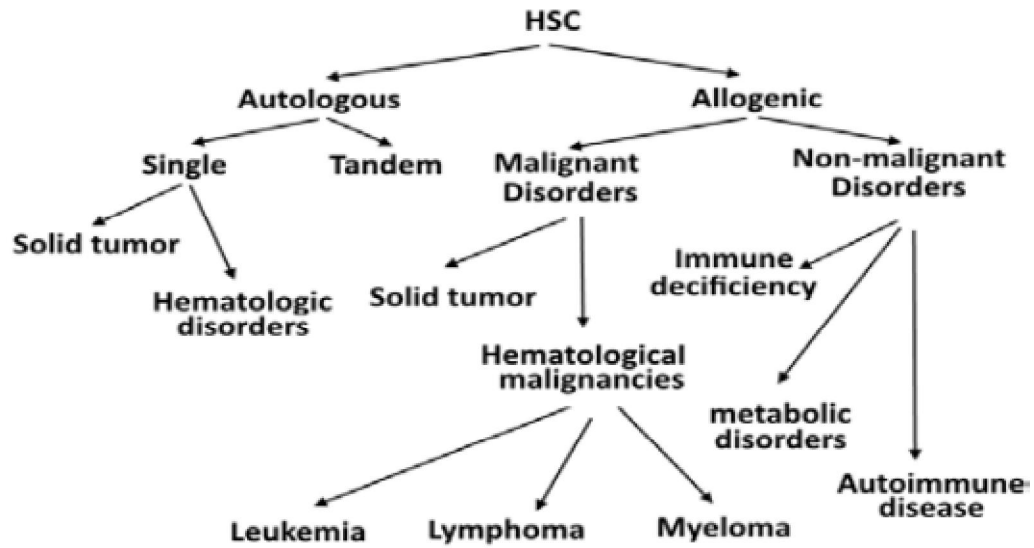


Figure (3): Indications for HSCT. (Hematopoietic stem cell transplantation)

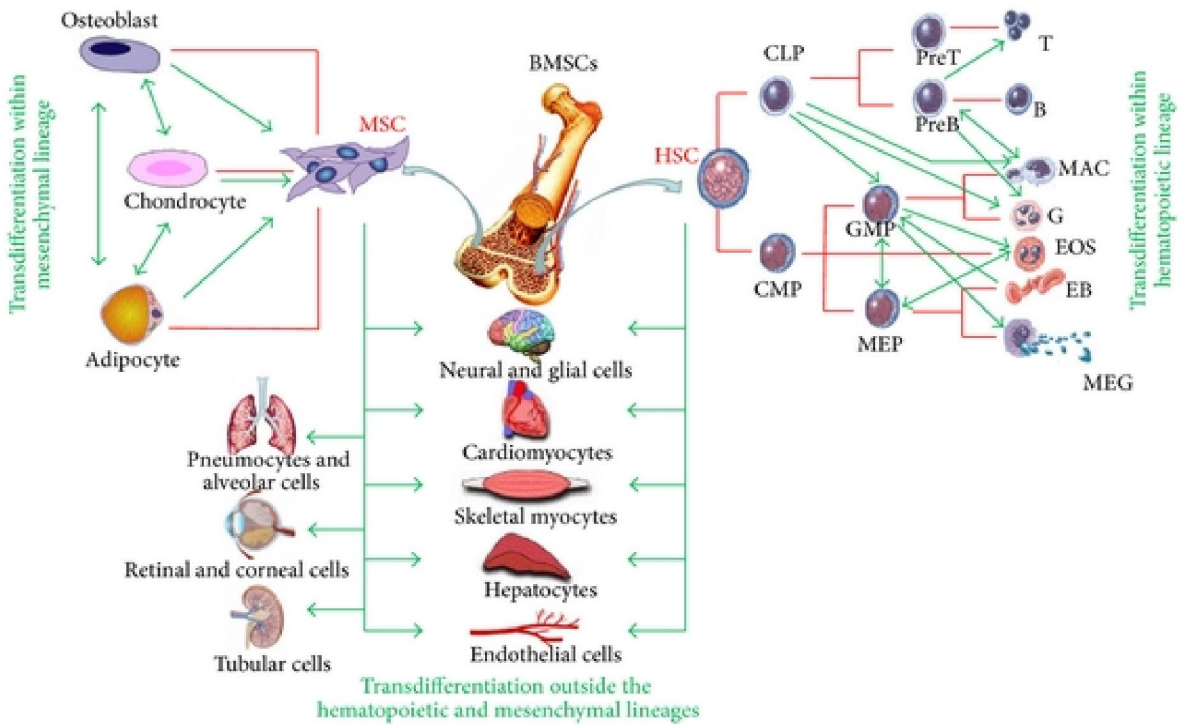
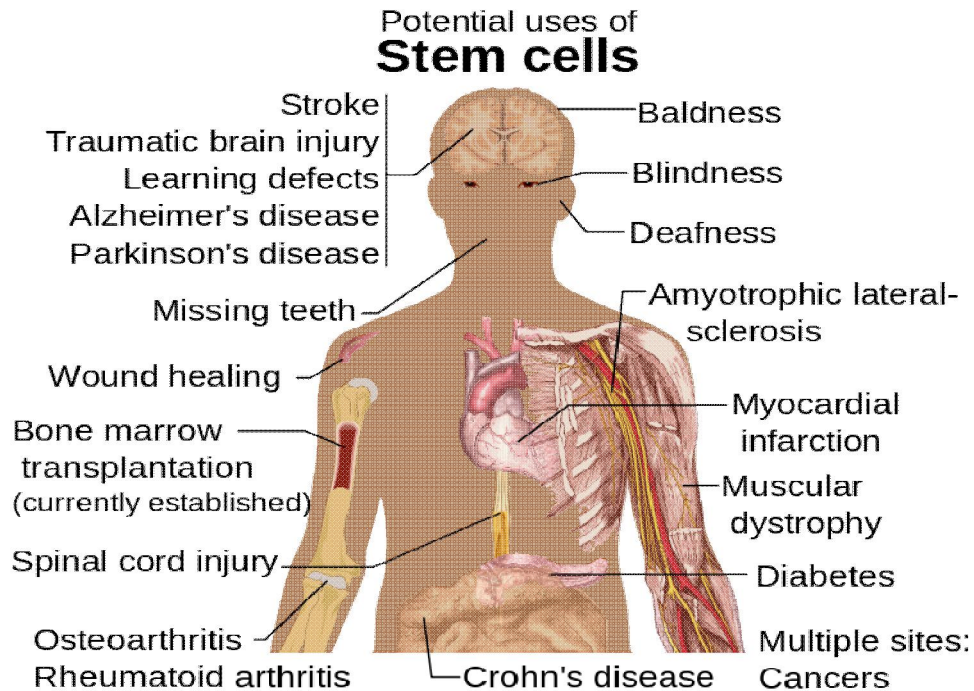


Figure (4): Plasticity of BM HSC and MSC. (Ivana Catacchio, et al.,2013)



**Figure (5): Potential uses of stem cells. (Häggröm, Mikael, 2014)**

### Conclusion

Stem cells are found in most adult mammalian tissues where they maintain normal tissue homeostasis and help in tissue repair and regeneration when exposed to damage. Stem cells can play important role in regenerative medicine because of their great ability to self-renew and to produce differentiated progeny. Large effort is exerted to produce stem cells differentiated along the pancreatic line as a possible cure for diabetes, but still under trial. Stem cells plasticity refers to the mutual substitutability of the organ specific stem cells. In a certain tissue, organ specific stem cell produces differentiated elements characteristic for a particular tissue. Under certain circumstances, stem cells may be forced to create elements not occurring in the original tissue. Studies have supported that stem/progenitor compartments play important role in the hemostasis of liver. Plasticity, from the point of view of normal development, is a property that should in principle be restricted to stem cells and progenitors.

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