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**Research Article**

# STEM CELLS APPLICATION IN MEDICINE AND DISEASE THERAPEUTICS

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**A B S T R A C T**

Stem cells can remain alive in human corpses for at least 17 days after death, researchers say. Dead bodies can provide organs for transplants, now they might become a source of stem cells too. Huge numbers of stem cells can still be mined from bone marrow five days after death to be potentially used in a variety of life-saving treatments. Corneal stem cells taken from the eyes of fresh cadavers have already been used to treat blindness in people with eye conditions that result from injury and scarring.Stem cells are useful for organ and tissue regeneration. In the treatment of cardiovascular disease, brain disease, cell deficiency therapy, blood diseases etc. Today stem cell research is a leading research. Basically, there are two 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. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues.

Stem cells can also be taken from umbilical cord blood just after birth. Of all stem cell types, autologous harvesting involves the least risk. By definition, autologous cells are obtained from one's own body, just as one may bank his or her own blood for elective surgical procedures.Dead bodies can provide organs for transplants, now they might become a source of stem cells too. Huge numbers of stem cells can still be mined from bone marrow five days after death to be potentially used in a variety of life-saving treatments.Corneal stem cells taken from the eyes of fresh cadavers have already been used to treat blindness in people with eye conditions that result from injury and scarring.



## INTRODUCTION

In many tissues they serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive (1). When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell (2). Stem cells differ from other kinds of cells in the body. (3). There are several sources of stem cell used in the clinical application including as therapeutics. The bone marrow is a key source of stem cell and gives raise various kinds of other cells for different physiological functions (3). Additionally, embryonic stem cells believed as a prime source of stem cell, and during embryonic development, all types of human tissues and cells are derived from three layers of the embryo; endoderm, mesoderm, and ectoderm.

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However, the use of embryo as the source of stem cell is highly regulated and faces various ethical issues as well (4).

The molecular biology plays an important role in the harvesting these multipotent cells for various therapeutic applications. The stem cells despite from their varying source are embryonic stem cells are believed most efficient and robust stem cells. The umbilical cord blood, bone marrow, and adipose tissues are a potential source of stem cells (5). The stem cell preservation especially cords blood is a quite common technique to store stem cell for future applications. These cells are present in a very limited amount, and their regeneration is dependent on several factors; stimulatory signals and nutrients. Stem cells have a long history and initially derived from other animals like mice and rodents (6). However, their clinical applications in context to human are highly limited, and hence human stem cells were investigated for their potential sources and harvesting methods. The uses of stem cell in modern medicine are increasing and have shown a promising result as well. There are several stem cell therapies under clinical trials studies (7). In case of several diseases

where conventional medicine faces difficulty to find cure stem cell technology have a great scope not only in diseases management but also tissue regeneration (8). The vital tissues including brain, liver, heart, kidney, and lungs entirely depend on stem cell biology. Additionally the use of stem cell in the production of blood and its components; cellular component in transfusion medicine have a great scope. The chimeric research (human-animal chimeras and animal chimeras) is possible due to recent advancement in stem cell biology and associated cutting edge medical molecular biology.

Cell potency is a cell's ability to differentiate into other cell types. Not all the human cells have cellular potency, and a few have selected potency as well. The cell potency is a unique feature of a cell to divide and differentiate into other types of cells. The classical example is zygote undergoes a rapid differentiation and develops a pool of cell to grow a complete organism (9).

Totipotency is the cell characteristic in which the potential for forming all the cell types in the adult organism retained (10). The embryonic stem cells can become a cell for any part of the body (nerve, muscle, blood, etc.). This ability to become any cell in the body is called pluripotent.. A stem cell can give rise to other types of cells.(11). These other types of cells are also limited in numbers.

Brain cells that give rise to neural cells and glial or hematopoietic cells. (12 There are numerous benefits and uses of multipotent stem cells.

Since multipotent stem cells derived from pluripotent stem cells, these stem cells have already partially differentiated.(13). Unipotent stem cells have a very limited ability to differentiate relative to other stem cells such as pluripotent, totipotent or multipotent cells (14). A multipotent stem cell is one can develop into a limited number of tissue types, which can give rise to almost any specialized cell in the body (15).

By taking a portion of a patient's own undamaged skin stem cells, sheets of skin can be developed for transplanting over burned areas of the patient's body (16). This technique is an important one for burn victims, particularly considering the pain and disfigurement that many burn victims are forced to experience during and after healing (17The stem cell harvesting is collection cells and purification of stem cells. The purified stem cells were grown in HEK media and other nutrient media based on nature of stem cell. There are no separate methods for stem cell harvesting, and the only difference is screening and growth of selected stem cells (18). The bone marrow and blood cells, adipose tissues are ideal somatic sources of stem cells. In case harvesting stem cells from blood need a density gradient centrifugation where all the blood cells differentiate based on their size and shape in density column. Similarly, stem cells from bone marrow and other somatic tissues are harvested based on cellular morphology. Stem cells can be reliably identified and accurately measured because they have a specific marker or label on the stem cell surface (19).

The human ES cells promises an essentially supply specific cell types for basic research and transplantation therapies for diseases ranging from heart disease to Parkinson's disease to leukemia (20. Fertilization normally occurs in the oviduct, and during the next few days, a series of cleavage divisions occur as the embryo travels down the oviduct and into the uterus (21

Stem cells are pluripotent cells widely distributed in human tissues and organs having a significant role in human physiology. These cells are capable of renewing damaged and lost cells in various tissues/organs. The life starts from one hybridized cell; zygote an ultimate source for stem cell and most of the stem cells in zygote are multipotent. The first and most significant role of stem cell in human physiology is growth and development. The embryonic layers endoderm, mesoderm, and ectoderm are key sources for multipotent stem cells differentiate into various tissues and organs (22).The most important tissue in the human body in context with stem cell is bone marrow-rich in various kinds of stem cells acting as progenitor cells for growth of red blood cells and white blood cells (23). The stem cells present in bone marrow are also pluripotent cells. Further, other somatic stem cells present in human tissues are having several functions- Growth ,Development ,Regeneration ,Maintenance of homeostasis and Disease management

Several viral human organs including brain, heart, lungs, kidney, and liver require a continuous supply of stem cells either natively and or from other tissues to maintain their structural and functional integrity. In case loos of such somatic stem cells due to infection and or any pathological condition growth and repair mechanism alter in greater extent affecting tissue/organ physiology (24). The cancer chemotherapy/ radiotherapy are one classical example where there is massive loss of normal cells along with tissue-specific stem cell primarily in bone marrow. The liver is having a large scale of tissue regeneration. Similarly, cells in the hair follicle and cells in adipose tissue have higher cell potency to help tissue regeneration. The stem cells also regulate organogenesis and aging and hence the external supply of stem cell may reduce aging symptoms (25). There is increasing scientific reports and finding towards the physiological significance of Stem cells, and hence stem cells may be used for cell replacement, for therapeutic interventions, and potentially to modify aging.

The ethical issue associated with embryonic stem cells and several other challenges forced the researcher to find an alternate for stem cell. The induced pluripotent cells (IPSCs) derived from stem cell engineering is growing concept to produced desired stem cell for clinical application (26). Induced pluripotent stem cells, commonly abbreviated as iPS cells or iPSCs are a type of pluripotent stem cell artificially derived from a non-pluripotent cell, expression of certain genes and transcription factors (27). These play a key role in determining the genetic information as early embryonic cells. (28).

Here, molecular biology plays an integral role in inserting selected four genes changes phenotype of a somatic cell (29). The location and orientation of selected genes in somatic cells to convert into a stem cell are also important

The gene editing is one of most recent technology in molecular biology capable of doing changes at gene level without affecting other genes (30). The gene editing allows us to change gene functioning by making changes at coding region and or regulatory region for a gene.. Here, CRISPR/Cas is one of the latest technology in gene editing available and quite efficient. Gene editing also associated in negative regulation of gene and inhibiting its function, RNAi, small pieces of double-stranded RNA (siRNA; small interfering RNA) are either chemically synthesized and introduced directly into cells, (31).

RNAi can work efficiently in somatic cells, and there has been some progress in applying this technology to human ES cells (32).

***History***

Scientists discovered ways to obtain or derive stem cells from early *mouse* embryos more than 20 years ago. Many years of detailed study of the biology of mouse stem cells led to the discovery, in 1998, of how to isolate stem cells from *human* embryosand grow the cells in the laboratory. These are called human embryonic stem cells. The embryos used in these studies were created for infertility purposes through in vitro fertilization procedures and when they were no longer needed for that purpose, they were donated for research with the informed consent of the donor. Stem cells are important for living organisms for many reasons. In the 3 to 5 day old embryo, called a blastocyst, a small group of about 30 cells called the inner cell mass gives rise to the hundreds of highly specialized cells needed to make up an adult organism. In the developing fetus, stem c ells in developing tissues give rise to the multiple specialized cell types that make up the heart, lung, skin, and other tissues. In some adult tissues, such as bone marrow, muscle, and brain, discrete populations of adult stem cells generate replacements for cells that are lost through normal wear and tear, injury, or disease.

Scientists want to study stem cells in the laboratory so they can learn about their essentialproperties and what makes them different from specialized cell types. As scientistslearn more about stem cells, it may become possible to use the cells not just in cell-basedtherapies, but also for screening new drugs and toxins and understanding birth defects.However, as mentioned above, human embryonic stem cells have only been studied since1998. Stem cells have been applied in the treatment of serious diseases for more than 30 years. The FDA has approved five hematopoietic stem-cell products derived from umbilical cord blood for the treatment of blood and immunological diseases. The therapeutic use of stem cell is vast and increasing rapidly due to their preliminary outcomes..

***Significance of stem cell biology***

The diseases where stem cell therapy has shown promising results are neurological disorders, cardiac disorders, inflammatory disorders, infectious diseases and wound healing (33). The infertility management with stem cell therapy is emerged as a new arena in modern medicine and had shown promising results. The cancer management and stem cell therapy become complementary to each other. Several clinical tails studies have been carried out and reported stem cell therapy quite successful. Here, stem cell therapy is applied especially to treat cancers, which require high-dose chemotherapy within the scope of medical care. The patient's stem cells are extracted blood before high-dose chemotherapy, stored and transplanted after the treatment to support the regeneration of destroyed cells (34). Several trails have been made on animals to benefit the development of stem cell treatments in veterinary medicine and can target a wide range of injuries and diseases such as myocardial infarction, stroke, tendon and ligament damage, osteoarthritis, osteochondrosis animals, as well as humans (35).

The use of stem cells therapies in orthopedics is quite successful and required as these physical abnormalities result in physical deformities. The cartilage damage in case autoimmune disorders including rheumatoid arthritis are prevailing (36), and till date, there is no cure. The stem cells from the patients either bone marrow and or adipose tissue also blood can provide symptomatic relief as selected stem cell allow a growth of cartilage and retain physical movements. The stem cells have a significant impact on the management of eye disorders as well as damaged cornea can be repaired by selected stem cell therapy. Most important neurological disorders where neurons are permanently damaged and lost have only way to treat by stem cell therapies. Here both IPSCs and stem cells from other source are being used, and a few are under clinical tails studies (37). Beta cells play a crucial role in insulin production and several other hormones in carbohydrate metabolism can be cured by stem cell therapies. (38). The tissue and organ transplantation have a great scope in clinical practice with the advancement of stem cells (39).

There are several diseases where stem cells have already been applied for clinical applications in finding disease management. Hematopoietic disorders ,Acute and chronic leukemia (AML/ALL or CML/CLL) ,Myelodysplastic syndrome, Lymphomas (Hodgkin lymphoma, non-Hodgkin lymphoma), Aplastic anemia, Sickle cell anemia ,Beta thalassemia Immunodeficiency, SCID, Whisk out Aldrich syndrome, Metabolic disorders Mucopolysaccharidosis Cancer, Multiple myeloma, Neuroblastoma Autoimmune diseases, Diabetes mellitus type 1, Rheumatoid arthritis, Lupus, Crohn's disease, Graft-versus-host disease (GvHD), Impairments of the brain, Dementia, in particular, Alzheimer's disease, Stroke, Brain injuries due to accidents or cancer, Infantile brain damage (cerebral paresis), Cardiovascular diseases, Cardiac infarction Multiple sclerosis, Amyotrophic lateral sclerosis, Autism, Hearing loss, HIV, Cirrhosis of the liver, Epidermolysis bullosa ("butterfly children")

HIV infection is complex and difficult to cure target immune cells. Loss of immune cell not only fails to have surveillance against invading infections but also associated with various immunological disorders.

***Ideas where the research go next?***

The major challenge in stem cell biology is their collection itself. The cutting-edge molecular biology techniques are competent in harvesting stem cells, but their efficiency is quite low and requires a repeated cell harvesting. The stem cell purification and processing is an expensive research exercise as well. The stem cell culture and maintenance are quite expensive and need a large laboratory setup and storage facility (41). The stem cells are much prone to contamination and are short-lived. The handling of stem cell is quite difficult; require specialized culture media and consumables enhanced research cost. Based on cell morphology and molecular marker we can only identify stem cell which requires further cutting-edge medical molecular biology skills and research setup. Though the stem cells have great potential in several clinical applications their handling start from harvesting, culture, storage and dispensing is complex (42). The genetic manipulations in stem cells are time-consuming as their grown time is quite slow. For example; E. coli doubles in 20 min while a human cell needs almost 24 hours to divide. The complex eukaryotic cellular and subcellular environment of stem cell is comparative complex to study for desired changes. The stem cell research needs ethical approval for its use in research and clinical applications. All these facts demonstrate

stem cells are quite challenging over other types of cells at research and application level.

Apart from these challenges at the research level, there are several ethical concerns as well with stem cell. The human embryo is a most competent source of all kinds of stem cells including totipotent, pluripotent and multipotent. There are other sources as well for stem cell harvesting, but the yield of stem cell is quite low. As a result, a human embryo is an ideal choice as a source of stem cell. The key ethical issues concern the destruction of human embryos for stem cell derivation. Because the human embryo is a human life with moral value justifying its protection, the extraction of embryonic stem cells is unethical (43). In the course of stem cell harvesting, there are medical risks of oocyte retrieval include ovarian hyperstimulation syndrome, bleeding, infection, and complications of anesthesia. The genetic manipulations to wild types of cells including stem cells called as unethical as we are intensely creating a change that is irreversible. The stem cells are being used extensively in the creation of human-animal and animal-animal chimeras (interspecies) gain a new debate in ethical committee. Though these interspecies are quite useful in research and development therapeutic products including tissues, organ, and diagnostics bioethics does not allow completely doing so. There are strict policies and regulation for the use of stem cells for research and clinical applications (44).

***Current Debate***

Stem cell biology is one of the most advanced fields in medical molecular biology and has shown a great scope in research and modern therapeutic development. The use of stem cell is rapidly increasing, and several stem cell therapies are under clinical trials studies as well. As a result of intensive research work for a period in the area now we are capable of producing stem cells from various sources and also can be preserved for future application. For example preservation of cord blood as a potential source of stem cell for future application. Similarly, bone marrow replacement and infusion with new potent stem cell is possible due to advanced medical molecular biology and cutting-edge bioengineering technologies. The current prospects of stem cell are highly promising and in the different part of the word these cells are being used for neurological disorders, cardiac disorder, cancer management, neonatal abnormalities and various progressive degenerative disorders as well. The present medical molecular biology technologies are competent in the harvesting and preservation of stem cells. Now, we have multiple choices as well including somatic stem cells, induced pluripotent stem cell and many more. The stem cell engineering and genome editing technologies are growing and having a positive impact on stem cell biology for clinical outcomes. There are increasing numbers of human diseases and disorders failed to find a cure for conventional medicine need integration with stem cell biology for complete cure. The neurological and progressive degenerative disorders are a prime target for stem cell biology. Though there are several challenges and issues associated with the harvesting, preservation, and use of stem cells due to their enormous potential in modern medicine, the use of stem cell is rapidly growing across the world.

## References


1. Carlen M, Cassidy RM, Brismar H, Smith GA, Enquist LW, Frisen J. Functional integration of adult-born neurons. *Curr Biol*. 2002;12:606-608.
2. Carleton A, Petreanu LT, Lansford R, Alvarez-Buylla A, Lledo PM. Becoming a new neuron in the adult olfactory bulb. *Nat Neurosci*. 2003;6:507-518.
3. Doetsch F, Garcia-Verdugo JM, Alvarez-Buylla A. Cellular Composition and Three-Dimensional Organization of the Subventricular Germinal Zone in the Adult Mammalian Brain. *J Neurosci.* 1997;17:5046-5061.
4. Doetsch F, Caille I, Lim DA, Garcia-Verdugo JM, Alvarez-Buylla A. Subventricular zone astrocytes are neural stem cells in the adult mammalian brain. *Cell*. 1999;97:703-716.
5. Eriksson PS, Perfilieva E, Bjork-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH. Neurogenesis in the adult human hippocampus. *Nat Med*. 1998a;4:1313-1317.
6. Eriksson PS, Perfilieva E, Bjork-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH. Neurogenesis in the adult human hippocampus. *Nat Med.* 1998b;4:1313-1317.
7. Evans MJ, Kaufman MH. Establishment in culture of pluripotential cells from mouse embryos. *Nature*. 1981;292:154-156.
8. Fusaki N, Ban H, Nishiyama A, Saeki K, Hasegawa M. Efficient induction of transgene-free human pluripotent stem cells using a vector based on Sendai virus an RNA virus, that does not integrate into the host genome. *Proc Jpn Acad Ser B Phys Biol Sci*. 2009;85:348-362.
9. Gould E, Reeves A, Graziano M, Gross C. Neurogenesis in the neocortex of adult primates. *Science*. 1999;286:548-552.
10. Gurdon JB. The developmental capacity of nuclei taken from intestinal epithelium cells of feeding tadpoles. *J Embryol Exp Morphol.* 1962;10:622-640
11. 22. Kempermann G, Gage FH. Neurogenesis in the adult hippocampus. Novartis Found Symp. 2000;231:220-235. *discussion* 235-241, 302-306.
12. Kornack DR, Rakic P. Continuation of neurogenesis in the hippocampus of the adult macaque monkey. Proc Natl Acad Sci U S A. 1999;96:5768-5773.]
13. Kuhn HG, Dickinson-Anson H, Gage FH. Neurogenesis in the dentate gyrus of the adult rat: age-related decrease of neuronal progenitor proliferation. *J Neurosci*. 1996;16:2027-2033.
14. Lois C, Alvarez-Buylla A. Long-distance neuronal migration in the adult mammalian brain. *Science*. 1996;264:1145-1148.
15. Markakis EA, Gage FH. Adult-generated neurons in the dentate gyrus send axonal projections to field CA3 and are surrounded by synaptic vesicles. *J Comp Neurol*. 1999;406:449-460.
16. McGrath J, Solter D. Nuclear transplantation in the mouse embryo by microsurgery and cell fusion. *Science*. 1983;220:1300-1302.
17. Ming GL, Song H. Adult neurogenesis in the mammalian central nervous system. *Annu Rev Neurosci*. 2005;28:223-250.

18. Rakic P. Mode of cell migration to the superficial layers of fetal monkey neocortex. *J Comp Neurol.* 1972;145:61-83.
19. Reynolds BA, Weiss S. Generation of neurons and astrocytes from isolated cells of the adult mammalian central nervous system. *Science*. 1992;255:1707-1710.
20. Richards LJ, Kilpatrick TJ, Bartlett PF. De novo generation of neuronal cells from the adult mouse brain. Proc Natl Acad Sci U S A. 1992;89:8591-8595.
21. Robinton DA, Daley GQ. The promise of induced pluripotent stem cells in research and therapy. *Nature*. 2012;481:295-305.
22. Sanes JR, Rubenstein JL, Nicolas JF. Use of a recombinant retrovirus to study post-implantation cell lineage in mouse embryos. *EMBO J.* 1986;5:3133-3142.
23. Seki T, Yuasa S, Oda M, Egashira T, Yae K, Kusumoto D, Nakata H, Tohyama S, Hashimoto H, Kodaira M, Okada Y, Seimiya H, Fusaki N, Hasegawa M, Fukuda K. Generation of induced pluripotent stem cells from human terminally differentiated circulating T. cells. *Cell Stem Cell.* 2010;7:11-14.
24. Shapiro LA, Ribak CE. Integration of newly born dentate granule cells into adult brains: hypotheses based on normal and epileptic rodents. *Brain Res Brain Res Rev*. 2005;48:43-56.
25. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell*. 2006;126:663-676.
26. Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K, Yamanaka S. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell*. 2007;131:861-872.
27. Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, Jones JM. Embryonic stem cell lines derived from human blastocysts. *Science*. 1998;282:1145-1147.
28. van Praag H, Schinder AF, Christie BR, Toni N, Palmer TD, Gage FH. Functional neurogenesis in the adult hippocampus. *Nature*. 2002;415:1030-1034.
29. Miyamoto T, Iwasaki H, Reizis B, *et al*. Myeloid or lymphoid promiscuity as a critical step in hematopoietic lineage commitment. *Dev Cell*. 2002;3:137-47.
30. Manz MG, Miyamoto T, Akashi K, *et al*. Prospective isolation of human clonogenic common myeloid progenitors. Proc Natl Acad Sci U S A. 2002;99:11872-7.
31. Arber C, BitMansour A, Sparer TE, *et al*. Common lymphoid progenitors rapidly engraft and protect against lethal murine cytomegalovirus infection after hematopoietic stem cell transplantation. *Blood*. 2003;102:421-8.
32. Rossi DJ, Bryder D, Zahn JM, *et al*. Cell intrinsic alterations underlie hematopoietic stem cell aging. Proc Natl Acad Sci U S A. 2005;102:9194-9.
33. Quesenberry PJ, Dooner GJ, Tatto MD, *et al*. Expression of cell cycle-related genes with cytokine-induced cell cycle progression of primitive hematopoietic stem cells. *Stem Cells Dev*. 2010;19:453-60.
34. Reddy GP, McAuliffe CI, Pang L, *et al*. Cytokine receptor repertoire and cytokine responsiveness of Ho(dull)/Rh(dull) stem cells with differing potentials for G1/S phase progression. *Exp Hematol*. 2002;30:792-800.
35. Berrios VM, Dooner GJ, Nowakowski G, *et al*. The molecular basis for the cytokine-induced defect in homing and engraftment of hematopoietic stem cells. *Exp Hematol*. 2001;29:1326-35.
36. Becker PS, Nilsson SK, Li Z, *et al*. Adhesion receptor expression by hematopoietic cell lines and murine progenitors: modulation by cytokines and cell cycle status. *Exp Hematol*. 1999;27:533-41.
37. Reddy GP, Tiarks CY, Pang L, *et al*. Cell cycle analysis and synchronization of pluripotent hematopoietic progenitor stem cells. *Blood*. 1997;90:2293-9.
38. Colvin GA, Lambert JF, Moore BE, *et al*. Intrinsic hematopoietic stem cell/progenitor plasticity:inversions. *J Cell Physiol*. 2004;199:20-31.
39. Colvin GA, Lambert JF, Carlson JE, *et al*. Rhythmicity of engraftment and altered cell cycle kinetics of cytokine-cultured murine marrow in simulated microgravity compared with static cultures. *In Vitro Cell Dev Biol Anim*. 2002;38:343-51.
40. Colvin GA, Dooner MS, Dooner GJ, *et al*. Stem cell continuum: directed differentiation hotspots. *Exp Hematol*. 2007;35:96-107.
41. Cerny J, Dooner M, McAuliffe C, *et al*. Homing of purified murine lymphohematopoietic stem cells: a cytokine-induced defect. *J Hematother Stem Cell Res*. 2002;11:913-22.
42. Habibian HK, Peters SO, Hsieh CC, *et al*. The fluctuating phenotype of the lymphohematopoietic stem cell with cell cycle transit. *J Exp Med*. 1998;188:393-8.
43. Peters SO, Kittler EL, Ramshaw HS, *et al*. Ex vivo expansion of murine marrow cells with interleukin-3 (IL-3), IL-6, IL-11, and stem cell factor leads to impaired engraftment in irradiated hosts. *Blood*. 1996;87:30-7.
44. Peters SO, Kittler EL, Ramshaw HS, *et al*. Murine marrow cells expanded in culture with IL-3, IL-6, IL-11, and SCF acquire an engraftment defect in normal hosts. *Exp Hematol*. 1995;23:461-9.
45. Nilsson SK, Dooner MS, Tiarks CY, *et al*. Potential and distribution of transplanted hematopoietic stem cells in a nonablated mouse model. *Blood*. 1997;89:4013-20.



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